ESRD Mineral and Bone Disorder Measure Development Technical Expert Panel

May 24, 2024

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ESRD Mineral and Bone Disorder Measure Development

The Centers for Medicare & Medicaid Services (CMS) has contracted with the University of Michigan Kidney Epidemiology and Cost Center (UM-KECC) to develop facility-level measures in the area of mineral and bone disorder. The contract number is 75FCMC18D0041, task order number 75FCMC23F0001. As part of its measure development process, the University of Michigan Kidney Epidemiology and Cost Center convenes groups of stakeholders who contribute direction and thoughtful input to the measure developer during measure development and maintenance.

UM-KECC has been tasked by CMS to develop dialysis facility quality measures that evaluate the effectiveness of mineral and bone disorder (MBD) management as part of the treatment of end-stage renal disease (ESRD) among US dialysis facilities.

Technical Expert Panel Objectives

The TEP will use existing data and their expert opinion to formulate recommendations to UM-KECC regarding the development of a draft measure that addresses potentially important quality gaps in mineral and bone disorder management. Recommended measures should be evidence based, scientifically acceptable (reliable and valid), feasible, and usable by CMS, providers, and the public. Specifically, the TEP will engage in discussion to develop potential quality measures that could incentivize the best practice of MBD management given the lack of high quality evidence to guide specific therapies (e.g. nutritional, pharmacologic, surgical). TEP input will be sought regarding potential sources of data such as the EQRS system and Medicare claims that may provide useful information about MBD diagnoses, diagnostic testing, medication use, and procedures. The TEP should also consider whether risk adjustment strategies will be needed and if any exclusion criteria should be considered so that the measure is usable from both patients' and providers' perspectives.

Technical Expert Panel Composition

A public call for nominations opened on November 3rd, 2023 and closed on November 17th, 2023. Nominations were sought from individuals with the following areas of expertise or experiential perspectives:

- Nephrologist providers (physicians, advanced practice providers), nephrology trained social workers, dieticians, and dialysis facility nursing staff
- ESRD bone and mineral disorder experts
- Consumer/Patient/Family/Care Partner perspective
- Performance measurement experts
- Quality improvement experts
- Purchaser perspective
- Healthcare disparities experts

The following individuals were selected to serve on the TEP:

Name and Credentials	Organizational Affiliation, City, State	Conflicts of Interest Disclosed
Geoffrey Block, MD *(TEP Co-chair)* Nephrologist	US Renal Care Golden, CO	Former Director at Ardelyx, Inc with equity in company
Kamyar Kalantar-Zadeh, MD *(TEP Co-chair)* Nephrologist	LA County Department of Health Services Harbor- UCLA Torrance, CA	None Reported
Deborah Benner, MA, RDN, CSR Registered Dietician	DaVita Inc, Yorba Linda, CA	None Reported
Paul T. Conway, BA Chair, Policy and Global Affairs Patient Advocate	American Association of Kidney Patients Tampa, FL	None Reported
Dinesh K. Chatoth, MD Nephrologist Associate Chief Medical Officer	Fresenius Medical Care Suwanee, GA	Employee and Stakeholder of Fresenius Medical Care
Barbara Fox, MS, MPH Patient Advocate	Yuba City, CA	None Reported
Edward V. Hickey President, AAKP Chair	American Association of Kidney Patients(AAKP) Tampa, FL	None Reported
Klemens Meyer, MD Nephrologist	Tufts Medical Center and Dialysis Clinic, Inc Boston, MA	Develops MBD decision support tools for DCI, but no financial interest
Adrian Miller Patient Advocate	Vancouver, WA	None Reported
Lisa Modica, RD, BS Registered Dietician	Rogosin Institute Fort Lee, NJ	None Reported
Evan R. Norfolk, MD, MBA Nephrologist System Director for Nephrology	Geisinger Health System Danville, PA	Fresenius Pharmacy and Therapeutics Committee
Sherri Shivley Patient Advocate	Hamden, CT	None Reported
Francesca Tentori, MD, MS Nephrologist VP for Outcomes Research	DaVita, Inc Portland, TN	Employee of DaVita
Contractor Staff		
Jonathan Segal, MD, MS	*Professor of Internal Medicine*, Division of Nephrology, University of Michigan, Kidney Epidemiology and Cost Center	None Reported

Name and Credentials	Organizational Affiliation, City, State	Conflicts of Interest Disclosed
Joseph Messana, MD,	*Professor of Internal Medicine*, Division of Nephrology, University of Michigan, Kidney Epidemiology and Cost Center.	None Reported
Ananda Sen, PhD	*Professor of Biostatistics and Research Professor,* University of Michigan, School of Public Health	None Reported
Eric Young, MD, MS	*Senior Research Scientist* Arbor Research	None Reported
Shu Chen, BS, MS	*Senior Analyst,* University of Michigan, Kidney Epidemiology and Cost Center	None Reported
Quinton Hazen, MPH	*Intermediate Analyst,* University of Michigan, Kidney Epidemiology and Cost Center	None Reported
Lan Tong, MS	*Lead Analyst,* University of Michigan, Kidney Epidemiology and Cost Center	None Reported
Jennifer Sardone, BA, PMP	*Senior Lead Project Manager,* University of Michigan, Kidney Epidemiology and Cost Center	None Reported
Jaclyn George, BA	*Project Intermediate Manager,* University of Michigan, Kidney Epidemiology and Cost Center	None Reported
Mimi Dalaly, MPH	*Project Intermediate Manager,* University of Michigan, Kidney Epidemiology and Cost Center	None Reported

1. Introduction

This report summarizes the discussions and recommendations of the ESRD Mineral and Bone Disorder TEP meetings convened on January 29th, February 23rd, and February 26th of 2024. All meetings were public and held virtually via zoom video-conference. The TEP provided advice and expert input on the development of potential mineral and bone disorder quality measures. The discussions were informed by an annotated bibliography of relevant literature compiled by UM-KECC, and data provided by UM-KECC.

2. Preliminary Activities

2.1 Information Gathering

Prior to the in-person TEP meeting, UM-KECC provided TEP members with an Environmental Scan that include an annotated bibliography of published literature (Appendix B) related to ESRD Mineral and Bone Disorders. The time period for this review focused on new publications since the 2017 KDIGO Bone and Mineral Guideline Update. The Annotated Bibliography included primary studies as well as meta-analyses and was organized into three categories:

- Treatment of Parathyroid Hormone (PTH) abnormalities
- Phosphorus lowering strategies
- Outcomes associated with calcium and phosphorus abnormalities

UM_KECC also provided a summary of relevant clinical guideline updates since the last TEP was held in 2013, as well as a list of related measures that are currently developed/in use. This information was reviewed during the second TEP meeting (slides located in the appendix).

2.2 TEP Charter

The ESRD Mineral and Bone Disorder TEP Charter (Appendix A) was distributed to the TEP members for review prior to the first meeting. At the first TEP meeting, Dr. Segal reviewed key elements of the charter.

The role of the TEP was outlined and the following responsibilities were highlighted:

- Review evidence to determine the basis of support for the proposed measure
- Recommending draft measure specifications
- Assisting in completing the necessary documentation forms to support submission of the measures to CMS for review, and to the CBE for endorsement
- As needed, TEP members may be asked to provide input to UM-KECC as they prepare responses to CBE and public comments

There were no questions or concerns raised by TEP members about the TEP Charter.

3. Background for Mineral and Bone Disorder

A high level overview of mineral and bone disorder was provided by Dr. Eric Young. Dr. Young provided a breakdown on bone health, and how kidney failure is associated with changes in mineral metabolism as kidney disease progresses (including vitamin D, phosphorus, and PTH). Dr. Young reviewed the mineral metabolism regulatory pathways, and the importance of mineral and bone disease management including control of phosphorus, calcium, and PTH in promotion of bone health. Treatment strategies were reviewed as well including treatments for elevated phosphorus with diet and phosphorus binders. PTH management with Vitamin D, and calcimimetics was discussed as well. This information was intended to be a framework for the TEP as they began their discussions surrounding mineral and bone disorder quality measurement.

3.1 Overview of the 2017 KDIGO Guidelines

TEP Co-Chair Dr. Geoffrey Block provided the TEP with an overview of the guidelines developed by KDIGO for diagnosis, evaluation, prevention and treatment of CKD-MBD. Dr. Block reminded the TEP that the group is charged with designing a measure around the understanding that MBD is a systemic disorder and that the group should consider the measureable patient level outcomes that are the result of the these abnormalities.

Dr. Block focused on several points in the KDIGO guidelines for the TEP discussion. Recommendations made in the guidelines should be approached in the context of abnormalities, the severities of those abnormalities, and whether there are any interventions being done to treat those abnormalities. He referred to guideline 3.1.4- *therapeutic decisions should be based on trends and not on single lab values, and should take into account all MBD assessments*. In addition, KDIGO recommended the use of DEXA assessment of bone mineral density if low or declining results would impact treatment decisions since DEXA had the ability to predict fractures in all stages of CKD. He also noted the importance of assessing the patient for the presence or absence of vascular calcification as part of the diagnosis of CKD-MBD and cardiovascular risk stratification. Treatment of MBD should be based on serial assessment of the abnormalities and considered together and not separately. KDIGO recommended that phosphorus should be lowered to the normal range, and hypercalcemia should be avoided (compared to the prior recommendation that calcium be maintained in the normal range). Dr. Block drew the TEP's attention specifically to the KDIGO guideline 4.1.6 stating that for *patients receiving phosphate lowering therapy there should be a restriction on the dose of calcium-based phosphate binders*. Dr. Block challenged the TEP to consider the pending inclusion of phosphate lowering therapy in the ESRD payment bundle and the potential unintended consequences of measure development affecting care delivery. He also noted that for patients on dialysis, providing more dialysis is an appropriate therapy for the management of elevated phosphorus.

The KDIGO workgroup, in guideline 4.1.8, suggested *limiting dietary phosphate intake in the treatment of hyperphosphatemia and that it is reasonable to consider the phosphate source (e.g. animal, vegetable, additives).* This guideline was called out for the importance of how providers approach dietary phosphate restriction while maintaining adequate nutrition. Dr. Block pointed out one of the most controversial guidelines is 4.2, regarding the treatment of abnormal PTH levels. He noted that maintaining PTH within 2-9 times the upper limit of normal was not changed from 2017 to 2019, but that marked changes within that target range should prompt a change in therapy (vitamin D analogues, calcitriol, or calcimemetics). He noted that 4.2.5 is also important to think about, regarding patients who fail to respond to medical therapy since, in these cases, KDIGO recommends parathyroidectemy. Dr. Block also highlighted the importance of thinking about calcium, phosphorus, and PTH abnormalities in combination, rather than in silos, as it relates to cardiovascular risk.

One TEP member asked a question regarding the recommendation from KDIGO about asymptomatic hypocalcemia, since attributing a symptom to hypocalcemia can be difficult. It was suggested the TEP consider this as the discussions on upcoming calls continues given the increased use of calcimimetics. Dr. Block mentioned the EVOLVE study to the TEP members. The KDIGO workgroup was reluctant to exclude the potential benefits of calcimimetics that was observed in this study based on the lag-censored results, but was conflicted because calcimimetics at the time were not uniformly available around the world.

Dr. Block mentioned the pediatric recommendations in the KDIGO guidelines. Children need to be approached differently than adults. 4.1.3 states that serum calcium should be approached in an age appropriate range. He noted that if we want to consider children, then we need to consider separating pediatrics from adults for recommendations.

One TEP member asked Dr. Block to specify what additional evidence has come to light over the past 5-10 years that the group should consider. Dr. Block referenced the TEP charter, noting that the evidence we do have is not at a high level at this moment. As part of the TEP discussion, the group needs to decide the following:

- Is there any new evidence that have arose in the past five years that can influence how we think about quality care delivery?
- Is what exists today - the Hypercalcemia measure – something MBD TEP would endorse now in today's environment and is this the right measure for today and where we will be years from now?

Dr. Kalantar-Zadeh informed the TEP that there haven't been a lot of new discoveries over the past several years, but to remind the TEP that they are there to ensure the quality measures used are as current as possible, and to identify any unintended consequences. The TEP needs to review what has been done in the past, and to see how we can improve upon what already exists.

One TEP member asked about bundled payment, and a reference to the environment we are operating in, and implementation. This TEP members asked what the TEP should be looking at regarding new evidence, new science and what benefits patients, or CMS policy and what should be incorporated into the bundle payment. Dr. Block confirmed that the TEP is not charged with discussing payment policy, but is here to recommend to UM KECC what is the best quality measure to ensure patients are receiving quality care.

3.2 Previous MBD Technical Expert Panels

Dr. Joseph Messana presented the TEP with a summary of the prior Mineral and Bone Disorder Technical Expert Panels. Dr. Messana reminded the TEP that a lot has changed since the first TEP that took place in 2006. The context of developing measures back then did not include CROWNWeb/EQRS or the ESRD QIP. There was Dialysis Facility Compare, but there were much fewer measures during that time and they were more focused on mortality, adequacy and vascular access reporting.

- 2007-2008 ESRB MBD TEP measure recommendations for patients on dialysis:
  - Measurement of Serum Phosphorus Concentration: Phosphorus should be measured monthly.
  - Evaluation of Serum Phosphorus Concentration: Phosphorus should be maintained between 3.5 – 5.5 mg/dl.
  - Measurement of Serum Calcium Concentration: Calcium should be measured monthly.
  - Evaluation of Serum Calcium Concentration: Calcium should be maintained ≤ ULN.

  Note: of the four measures presented to the Consensus Body Endorsement group, only measurement of serum phosphorus and calcium were endorsed.

- 2010 ESRD MBD TEPs measure recommendations:
  - Upper Limit for Total Uncorrected Serum Calcium: 3 month rolling average of total serum calcium >10.2 mg/dl
  - Lower Limit for Serum Phosphorus: 3 month rolling average of serum phosphorus < 2.5 mg/dl
  - Process Measure for PTH: Monthly measurement of PTH

  Note: only the Calcium measure was endorsed.

- 2013 ESRD MBD TEP process measure recommendations:
  - Measurement of Uncorrected Serum Calcium monthly
  - Measurement of Serum Phosphorus monthly
  - Process Measurement of Plasma PTH measured at least once every 3 months.
  - Percentage of Patients with Dietary Counseling at least once in a 6 month period.
  - Additional recommendations
    - Hypercalcemia Measure - all TEP members unanimously recommended to leave the measure unchanged and to retain the current specification for uncorrected calcium. This is the current version of the measure as endorsed by NQF (#1454).
    - Serum versus Plasma Lab Samples - All TEP members voted and unanimously recommended to keep the measure unchanged (serum calcium and phosphorus values rather than plasma).
    - Bone Biopsy Measure Development The majority of the TEP members (eight out of nine) recommended that a quality measure for bone biopsies not be developed at this time due to insufficient evidence

3.3 MBD Quality Measures Endorsement Overview

Dr. Segal gave an overview of the existing Mineral and Bone Disorder measures, which include a measurement of phosphorus concentration and hypercalcemia.

NQF#	Title	Steward	Status Date	Status	QIP (Calendar Yr)
0570	CKD: Monitoring Phosphorus	IMS Health	5/8/2012	Endorsement Removed	
0574	CKD: Monitoring Calcium	IMS Health	5/8/2012	Endorsement Removed	
0255	Measurement of Phosphorus Concentration	CMS	10/2/15	Endorsed with Reserve Status	2012 2017 – Reporting 2019 – Removed

NQF#	Title	Steward	Status Date	Status	QIP (Calendar Yr)
1454	Proportion of Patients with Hypercalcemia	CMS	8/16/11 10/2/15	Initial Endorsement Endorsed with Reserve Status	2014 – Clinical 2023 – Reporting

Dr. Segal also explained that the Partnership for Quality Measurement (PQM) recently conducted a Measure Set Review of the ESRD QIP Program. The recommendation of the group was to retain the Hypercalcemia measure in the QIP, but encouraged developers to "thoughtfully consider" alternative measures.

4. Overview of Historical MBD Data and Literature Review

4.1 Historical MBD Data

To kick off the second TEP meeting, Dr. Kalantar-Zadeh provided the TEP with a background of the history of various treatments for CKD-MBD, from the 1970's to present day. Dr. Kalantar-Zadeh gave an overview of the literature supporting phosphorous and calcium levels from different measure guidelines, and reviewed the relationship between mortality and serum phosphorus, serum calcium in dialysis patients. More details regarding the information presented by Dr. Kalantar-Zadeh can be found in the slides in Appendix C.

Dr. Kalantar-Zadeh concluded the presentation by saying that MBD markers are related to survival in epidemiologic studies of dialysis patients. Causal Inference should be with the utmost caution given the observational nature of many of the studies presented.

4.2. Overview of MBD Literature Review

Dr. Block introduced the TEP to the literature review completed by UM-KECC and gave a detailed review of selected articles. Dr. Block described a DOPPS study that evaluated the phosphate Area Under the Curve (AUC) over a 6-month period. He noted that higher AUC levels (i.e., with worse phosphorus control) were strongly associated with increased mortality, in particular cardiovascular mortality, in both hemodialysis and peritoneal dialysis patients. He mentioned a meta-analysis that reported some phosphate lowering agents were associated with lower mortality and hospitalization. However, he noted that how the phosphorus is lowered may be important as some strategies may have unintended consequences (e.g. aluminum as a binder). Dr. Block explained that phosphate binders in particular have huge impact on quality of patient's life in terms of pill burden, side effects, and adversarial relationship with care team. The TEP was reminded that patient quality of life was an important consideration to keep in mind as the discussion progressed.

The EVOLVE study, and secondary analyses of that study, was discussed. Older patients randomized to cinacalcet had a significant reduction in the cardiovascular and mortality endpoints. Cinacalcet was also noted to reduce the incidence of Calcific Uremic Arteriopathy as well as bone fractures. It was noted that the comparison group in that study received active Vitamin D therapy. Dr. Block touched on parathyroidectomy and how it has increased in recent years, noting that the procedure is associated with improvement in mortality and cardiovascular outcomes. He described a study noting the inter-relationship between calcium, phosphorus and PTH and indicated that this highest risk is in patients with a high PTH and either a high calcium or high phosphorus. Dr. Block concluded with a facility-level analysis that found

facilities with a higher proportion of two or more of the three parameters out of range had higher rates of cardiovascular events and death.

6. MBD Quality Measure Concepts

6.1 PQM Evidence Criteria

Dr. Segal presented the PQM Evidence Criteria and noted that the criteria states that there should be a relationship between the healthcare process and the desired outcome.

a. For Process/ Intermediate Outcome Measures: Demonstrated association between the measure focus and a material health outcome
b. For Outcome measures: There is a demonstrated rational for considering the measure focus, which is a material health outcome

He encouraged the TEP to keep these requirements in mind as they discuss possible measure development.

6.2 TEP Measure Concept Discussion

Following the literature review, the TEP had an open discussion surrounding possible measure concepts. The following summarizes the topics that were discussed.

Area Under the Curve (AUC) phosphorus
This measure concept was raised since it offers a more defined approach than looking at multiple labs (see below) and encompasses a longer time frame. There was discussion about how easy or difficult it would be to explain AUC phosphorus to patients and there was discussion that most patients understand that there is variability in the result from month to month. The longer time frame may also reduce the tendency to repeat the lab test multiple times in a month to try and reach the target. The group considered whether there is there a conceptual alternative to AUC that is easier to interpret (e.g. quarterly average or 6 month average). One member nominated AUC Phos >2 (corresponding to a 6 month average phosphorus >6.5 mg/dl) as an intermediate outcome measure. Additional discussion about what the ULN value should be as part of the AUC threshold will be needed. One potential advantage of a longer term measure may help with patient engagement. However, concern was raised that a phosphorus measure could have the unintended consequence of impaired nutrition based on the way facilities counseled patients to lower phosphate intake.

Hyperphosphatemia (AUC phosphorus or other trend) and not on a phosphate binder
The broader notion of medication utilization or medication use based on a critical lab threshold was discussed. TEP members raised concern about use of lower cost alternatives (e.g. calcium-based binders) or no prescription altogether being potentially incentivized by upcoming PPS system changes. There are also difficulties with how to accurately measure medication use (ordered, dispensed, or taken).

PTH measurement (at some frequency)
There was at least minor interest in exploring whether a PTH process measure might be useful. The group noted that if a PTH metric is considered, timing of co-existent therapy (i.e. calcimimetics) and or blood draw schedules may need to be considered. Variation in assays was brought up as a limitation. Uncertainty of optimal frequency of measurement was brought up as an issue.

Hyperparathyroidism without evidence for either medical or surgical treatment
The TEP discussed issues related to physician vs. facility accountability, access to qualified surgeons that may be limited in some areas, and proportion of patients that would be impacted by the measure.

Overtreatment of hyperparathyroidism
This measure would capture patients who have low PTH levels but remain on medication to suppress PTH.

Facility Phenotype: 2 of the 3 (Ca/Phos/PTH) above threshold.
This measure would categorize patients into high-risk categories and/or facility-level data to identify those facilities with poorer outcomes associated with MBD results. A TEP member encouraged the group to keep unintended consequences of any measure definition in mind (e.g. ordering more frequent lab tests than what is clinically indicated). TEP members discussed some of the technical differences between a patient-level and facility-level analyses. A TEP member raised a concern about social determinants of health and that any facility level metric may be impacted by patient access to healthy food. Questions were also raised about realities of implementation of a metric that relies on multiple lab values in combination.

Patient-reported outcome related to MBD
There was interest in a potential patient reported outcome related to MBD, but it was acknowledged that the development timeline for such a measure means it's likely beyond the scope of this TEP.

Alkaline phosphatase
There was generally low interest in a measure in this area.

7. MBD Measure Concepts

Dr. Segal began the third TEP meeting by summarizing a set of four of potential measures that have been generated by the TEP discussion thus far.

1. Elevated Phosphorus
    a. AUC>2 Or other chronic measurement corresponding to a 6 month average phosphorus value > 6.5 or
    b. Elevated phosphorus and not on a binder with chronic phosphorus elevation paired with medication use
2. PTH Measures
    a. PTH above some threshold without evidence of treatment (either with medication or parathyroidectomy) or
    b. Overtreatment of PTH: Low PTH and concurrent medication use
3. Facility phenotype with 2 of 3 (Ca/PO4/PTH) above threshold
4. Patient-reported outcome

Dr. Segal proposed to the TEP to take a vote on which domains the TEP should continue to discuss in order to be more focused on details and sorting out the measure. Dr. Segal noted that the TEP will not be voting on a patient-reported outcome measure; the TEP will discuss that idea at the end of the measure discussion, since it requires long term development. A google poll was sent to all TEP members at the meeting via email, asking them to respond yes or no to the following questions:

1. Should the TEP continue discussion and development of a phosphorus-based measure?
2. Should the TEP continue discussion and development of a PTH-based measure?
3. Should the TEP continue discussion and development of a facility phenotype measure (2 of 3 out of range for Ca/PO4/PTH)?

Dr. Messana confirmed that the TEP can weigh in on all three measures, and Dr. Segal informed the TEP that we would need a 60% consensus in order to move forward with a measure concept. Dr. Kalantar-Zadeh asked if calcium has been removed consideration. Dr. Segal explained that we do have the current hypercalcemia measure, and that the TEP should hold off on a formal vote on the hypercalcemia measure

because it is currently in use. If the TEP cannot reach consensus on a potential measure then we can circle back and focus on hypercalcemia. TEP members should make no assumptions regarding the status of the hypercalcemia measure moving forward.

7.1 Voting Results

The TEP voting results were revealed, and approximately 75% of TEP members in attendance were in favor of a phosphorus-based measure, 37.5% were in favor of a PTH-based measure, and 60% were in favor of a facility phenotype measure.

7.2. Discussion

Dr. Segal began the discussion with the phosphorus- based measure. Dr. Segal asked the TEP what new evidence has come to light since the last in-depth phosphorus discussion (2013 TEP). Dr. Block started the conversation by explaining that he was on one of the previous TEPS and there are three differences now compared to the prior TEP: (1) at the time they did not consider a phosphorous based measure because it was considered in the light of a target, which they did not think was appropriate, (2); they had not considered a measure of *chronic* phosphorus elevation and (3) there was a lack of supporting literature that discussed the relationship of chronically elevated phosphorus levels and the specific outcomes that MBD is meant to address. In addition, TEP members noted that we have a better understanding of MBD physiology, and new innovations in technology and in patients being more informed.

Other TEP members commented that the change over the past decade has been more modest, but that the current measure is not satisfactory, we need to have some MBD measure, and setting a more lenient standard moving forward was reasonable. In relation to calcium and PTH, phosphorus is probably the easiest area to move the needle in terms of a quality measure.

The TEP then discussed how best to evaluate a chronically elevated phosphorus. There was clarification that if only one phosphorus value is obtained per month, then the phosphorus AUC will be the same at the time-averaged phosphorus. A question was raised regarding if patients will be able to meaningfully understand the 6 month average phosphorus concept and whether this was an actionable item. Other TEP members noted that they do think patients will understand, as long as it was explained well enough by their provider. A comment was made that the real indicator of quality should be the impact on the patient and that facilities, providers and advocacy groups will need to be able to educate their patients on the measure.

TEP members discussed the relationship between hyperphosphatemia and good nutrition and the concern that control of phosphorus should not come at the expense of impairing nutrition. Some TEP members voiced concern about using the AUC methodology and there was discussion about alternative approaches using a time-averaged mean phosphorus or months out of target for phosphorus. One TEP member shared his concerns with the TEP regarding patients becoming stigmatized and being blamed for their phosphorous levels. A very conservative phosphorous percentage above 7 mg/dl (similar to what is done in the VA healthcare system) to ensure this is a patient centered approach and the TEP needs to be careful that the measure does not cause unintended consequences and harm for the dialysis patients. Specifically, it was noted that phosphorus levels are heavily influenced by nutrition and diet, which could obscure its significance as a marker for MBD and a phosphorus measure could have the unintended consequence of leading to malnutrition depending on the approach of providers. The metric should be conservative enough for physicians and patients. A TEP member noted that there are numerous studies beyond the ones presented to the TEP using a threshold of 6.5 mg/dl and MBD outcomes and that the group should not be in the position to create their own threshold that is not supported by the literature. Other TEP members indicated that a more lenient standard could be used for a quality metric.

Discussion then turned to crafting a measure description for the proportion of patients with a 6 month average phosphorus above a threshold of 6.5 mg/dl. TEP members raised the question of whether 5.5 mg/dl should be used based on when risk begins to increase for MBD outcomes, but others indicated that the goal for this measure is to pick a threshold for which there is less harm for patients, keeping in mind the relationships between diet and phosphorous. There was interest in being more conservative with the 6.5 target. A TEP member requested we use the first phosphorous value of the month vs. the last value to prevent providers from continuing to draw the lab until they get the number they want.

Some TEP members were unsure if 6 months (average exposure) is the correct time to propose. One TEP member raised a concern around how many patients would be included in a measure with a longer time frame (e.g. due to death, transfer, etc.) Dr. Segal informed the TEP that most intermediate outcome measure require patients to be on dialysis for 90 days, and if the patient leaves the facility or passes away, they are excluded. A TEP member asked what the groups comfort level was regarding this smaller population and if we should decrease the length to 4 months. A 3 month time frame was also proposed and a TEP member agreed that 3 months would be easier to manage from an operational stand point. Several TEP members expressed their concern with shortening to 3 months.

Dr. Segal proposed allowing UM-KECC to conduct some initial analyses that might be able to guide the decision making with regards to 3 or 6 months. Dr. Segal proposed including 3-6 months in the draft specifications as a placeholder pending analyses to evaluate the number of patient months that would be included based on the time frame selected. He explained other commonly used criteria: patient has to be in facility for 90 days, and the patient is excluded from measure if patient leaves the facility or dies within the month. The measure is not restricted based on insurance type (includes both Medicare and non-Medicare patients).

Dr. Messana noted the hypercalcemia measure does exclude pediatric patients, and Dr. Segal asked TEP members to weigh in on whether pediatrics should also be excluded. Dr. Block is reluctant to include pediatric patients in the measure, and the TEP agreed. Dr. Segal noted patients in hospice are typically excluded, and the TEP agreed to exclude them for this measure as well.

Dr. Segal asked the TEP about possible risk adjustments and Dr. Block asked for examples of patients characteristics that could risk adjusted. Dr. Messana shared potential factors for risk adjustments such as area deprivation index, residing in skilled nursing facility, insurance status such as Medicare/commercial/duel eligible, and race. Dr. Messana asked the TEP if any of these factors, or any additional factors, should be added to minimize the bias in this measure. A TEP measure asked if there are populations that are not served well and that may be undertreated for MBD conditions. One TEP member mentioned that the community in which the patient lives in and what access the patient has to certain foods will impact their phosphorous levels. The TEP is willing to consider ADI as a risk adjustment; UM KECC can look into this particular risk adjustment further and report their findings back to the TEP.

Dr. Messana asked whether KECC should also create a parallel measure with AUC and have the TEP vote on how to proceed. TEP members did not think this would be necessary and agreed that just looking at the proportion of patients with an average phosphorus about 6.5 mg/dl would be sufficient. Measure specifications were discussed and draft specifications are listed below.

8. Measure Specifications

8.1 Phosphorus Measure

Measure Description: Proportion of patient with (3 or 6) month average phosphorus above > 6.5 mg/dl

Numerator: Number of patients with 3 or 6 month average phosphorus above 6.5

Denominator: Patients in the facility for 3 or 6 months

Risk Adjustment: explore ADI, possibly other factors

Exclusion Criteria: Patients with < 90 days ESRD; AKI patients, pediatric patients, hospice patients

8.2 Facility Phenotype

Measure Description: Facility Phenotype: proportion of patients in the facility with 2 of 3 above threshold (consider PTH 11x> ULN). 4 month average of 3 variables.

Additional specifications for this measure were not decided upon by the TEP at this time. Although there was support for the measure concept, particularly if it identified patients that might otherwise be overlooked, one TEP member noted that there is limited evidence linking simultaneous abnormalities in calcium, phosphorus and PTH with MBD outcomes. One of the challenges discussed for a composite measure is that for CBE consideration, each of the component measures typically needs to be able to stand on its own and there needs to be evidence for the composite measure itself. In addition, there was also a concern for a relatively small number of patient that would be in the numerator and thus limited opportunity to improve quality. Lastly, there was concern on reaching consensus on a PTH threshold. A TEP member asked if this could be made into a process measure. There was a recommendation that future TEPs consider a composite such as this one for development. It would also need to factor in 3-6 months of lab values. Dr. Segal informed the TEP that the UM-KECC team will look to see if there is something additional we can add to this particular measure specification.

8.3 Patient Choice/Patient Reported Outcomes

Dr. Segal asked the TEP if they have thoughts for future measure development with regards to a patient reported outcome and how to account for patient choice in their treatment options while accounting for shared decision-making. A TEP member mentioned it's more than just a voice of a patient, but it's their choice of treatment. The treatment should be defined as high quality, which hopefully include treatments that align with a patients aspirations to feel better, to work, to travel and to live their lives. There are quantitative factors that need to be explained to the patient so they understand the effects of treatment decisions and how it impacts their overall health. Qualitative factors include increased dietary discretion and how this impacts patients socially (e.g. going out to eat). Will the patient be freer in their diet so they are able to do more things in their lives, and do they have a voice and choice in their treatments? Are the treatments covered by CMS?

One TEP member noted that many providers believe that whatever provides maximum survival would be considered the best care, but that if we allowed patients to opt out of a phosphorus measure that many would even if it wasn't the best course of action for them in the long run.

A TEP member mentioned the idea of patient "pill burden" and considering getting to a lower phosphorus value with the least number of medications to do so. The TEP member also indicated "pill burden" related to phosphorous management had been a point discussed in a 2023 FDA Advisory Committee meeting that had approved a new phosphorous pill therapy for dialysis patients that reduced the need for phosphate binders. Another TEP member mentioned that patients need to be asked if they are being engaged in conversations as part of their treatment plans and that more dialog needs to take place between patients and providers. Patients shouldn't need to make a choice between long-term outcomes and pursuing their aspirations. A TEP member added that we should focus on ways to get patients access to low phosphorus nutrition options so it might be easier for them to control with less medication.

A TEP member asked if there should be a maximum number of binders that a patient should be prescribed to control phosphorus. An unintended consequence could be that the number of binders per meal will go up as providers strive to meet the measure goals. Another TEP member suggested that considering the number of phosphate binders that a patient takes in a day should be considered. There was discussion that phosphate lowering therapies are scheduled to enter the bundled payment system in 2025, and if not delayed by current bipartisan action in the House of Representatives, this could have a significant impact on patient choice given that providers would have to balance the cost of treatment provided with the level of reimbursement. Thus, a patient reported outcome in this scenario would be critical to have in place. Finally, another TEP member added that providers need to consider their role in managing phosphorus as it relates to the amount of dialysis prescribed, and concurrent medications that may make phosphorus control worse.

9. Next Steps

Dr. Segal presented the TEP with next steps. A fourth TEP meeting was scheduled for March 6th 2024. Dr. Segal mentioned that UM KECC will do some ground work from the discussions, and likely cancel the March 6th meeting and then schedule a follow up TEP meeting with all TEP members.

10. Public Comments

No public comments were received at any of the three TEP meetings.

11. Appendices

A. TEP Charter
B. TEP meeting slide presentations

Technical Expert Panel (TEP) Charter

Project Title: ESRD Mineral and Bone Disorder Measure Development

TEP Expected Time Commitment and Dates:

The call for nominations period opened on November 3rd and closes on November 17th 2023

Project Overview:

The Centers for Medicare & Medicaid Services (CMS) has contracted with the University of Michigan Kidney Epidemiology and Cost Center (UM-KECC) to develop facility-level measures in the area of mineral and bone disorder. The contract number is 75FCMC18D0041, task order number 75FCMC23F0001. As part of its measure development process, the University of Michigan Kidney Epidemiology and Cost Center convenes groups of stakeholders who contribute direction and thoughtful input to the measure developer during measure development and maintenance.

Project Objectives:

UM-KECC has been tasked by CMS to develop dialysis facility quality measures that evaluate the effectiveness of mineral and bone disorder (MBD) management as part of the treatment of end-stage renal disease (ESRD) among US dialysis facilities.

Technical Expert Panel (TEP) Objectives:

The TEP will use existing data and their expert opinion to formulate recommendations to UM-KECC regarding the development of a draft measure that addresses potentially important quality gaps in mineral and bone disorder management. Recommended measures should be evidence based, scientifically acceptable (reliable and valid), feasible, and usable by CMS, providers, and the public.

Specifically, the TEP will engage in discussion to develop potential quality measures that could incentivize the best practice of MBD management given the lack of high quality evidence to guide specific therapies (e.g. nutritional, pharmacologic, surgical). TEP input will be sought regarding potential sources of data such as the EQRS system and Medicare claims that may provide useful information about MBD diagnoses, diagnostic testing, medication use, and procedures. The TEP should also consider whether risk adjustment strategies will be needed and if any exclusion criteria should be considered so that the measure is usable from both patients' and providers' perspectives.

TEP Requirements:

A TEP of approximately 11-20 individuals will brainstorm to develop one or more measure concepts that can be further developed to determine other aspects such as reliability and validity. The TEP will need to consider the current state of evidence to support any measure concept that is developed for consensus based entity (CBE) endorsement.

The TEP will be composed of individuals with differing areas of expertise and perspectives, including:

- Nephrology providers (physicians, advanced practice providers), nephrology trained social workers, dieticians, and dialysis facility nursing staff
- ESRD bone and mineral disorder experts
- Consumer/Patient/Family/Care Partner perspective
- Performance measurement experts
- Quality improvement experts
- Purchaser perspective
- Healthcare disparities experts

Scope of Responsibilities:

UM-KECC is seeking balanced representation of dialysis stakeholders and clinical experts representing patients, patient advocates, and dialysis providers as well as clinical, statistical, and public health experts to identify and evaluate one or more potential quality measures intended to evaluate mineral and bone disorder in dialysis patients. It is UM-KECC's intent to facilitate TEP discussion through presentation of background information (peer reviewed publications, guidelines, and related existing quality measures) that will set the context for new measure development. The TEP will be led by one or two Chairpersons, whose responsibility is to guide the discussion and attempt to develop consensus opinions from TEP membership regarding the topics described in the TEP Objectives section above. The TEP is intended to be advisory to UM-KECC, as UM-KECC continues to develop and refine the draft measure described in this document.

Role of UM-KECC: As the CMS measure developer contractor, UM-KECC has a responsibility to support the development of quality measures for ESRD patients. The UM-KECC moderators will work with the TEP chair(s) to ensure the panel discussions focus on the review of draft measure specifications, as recommended by the contractor. During discussions, UM-KECC moderators may advise the TEP and chair(s) on the needs, requirements, and timeline of the CMS contract, and may provide specific guidance and criteria that must be met with respect to CMS and CBE review of revised candidate measures reflecting prevalent comorbidities.

Role of TEP chair(s): Prior to the TEP meetings, one or two TEP members are designated as the chair(s) by the measure contractor and CMS. The TEP chair(s) are responsible, in partnership with the moderator, for directing the TEP to meet the expectations for TEP members, including provision of advice to the contractor regarding measure specifications.

Duties and Role of TEP members: According to the CMS Measure Management System Blueprint, TEPs are advisory to the measure contractor. In this advisory role, the primary duty of the TEP is to review any existing measures, provide input as to data sources and feasibility, and to suggest measure specifications. TEP members are expected to attend conference calls in 2024 and be available for additional follow-up teleconferences and correspondence as needed to support the submission and review of the candidate measure(s) by the CBE. Some follow up activities may be needed after testing has occurred.

The TEP will review, edit (if necessary), and adopt a final charter at the first teleconference. A discussion of the overall tasks of the TEP and the goals/objectives of the ESRD Facility Level Measure Development

project will be described. TEP members will be provided with a summary of peer reviewed literature and other related quality measures. TEP members will have the opportunity to submit additional studies to be included in the literature review. A review of the CMS and CBE measure development criteria will also be covered during the teleconference.

During the TEP Meetings: The TEP will review evidence to determine the basis of support for proposed measure(s). The key deliverables of the TEP include:

- Recommending draft measure specifications
- Assisting in completing the necessary documentation forms to support submission of the measures to CMS for review, and to the CBE for endorsement
- As needed, TEP members may be asked to provide input to UM-KECC as they prepare responses to CBE and public comments

Following the TEP meetings, the TEP chair(s) and TEP members will prepare a summary of recommendations. As necessary, the TEP chair(s) will have additional contact with UM-KECC moderators to work through any other issues. This will include votes for draft and final measures. TEP members will review a summary report of the TEP meeting discussions, recommendations, draft measure specifications, and other necessary documentation forms required for submission to the CBE for endorsement

Guiding Principles:

Participation as a TEP member is voluntary and the measure developer records the participant's input in the meeting minutes, which the measure developer will summarize in a report that they may disclose to the public. If a participant has chosen to disclose private, personal data, then related material and communications are not covered by patient-provider confidentiality. Patient/caregiver participants may elect to keep their names confidential in public documents. TEP organizers will answer any questions about confidentiality.

The TEP will use both verbal consensus and formal voting by secret ballot for decision-making, depending on the context of the decision. For administrative and other decisions about agenda, direction of discussion, and other minor operational decisions, informal verbal consensus directed by the TEP chairs will be utilized. In order to objectively record TEP recommendations about the validity of the quality measures presented and recommended changes, formal votes utilizing secret ballot will be employed. These techniques have been used for nearly all clinical TEPs facilitated by the UM-KECC team over the last several years.

The measures evaluation standards included in the CMS Measures Blueprint and reflected in the CBE criteria are presented during an early TEP teleconference, typically during the first call. This is done so that TEP Charter approval and initial direction of the TEP discussion occur after TEP members are informed of the national consensus criteria that will ultimately be used to evaluate the quality measure(s) being considered by the TEP.

All potential TEP members must disclose any significant financial interest or other relationships that may influence their perceptions or judgment. It is unethical to conceal (or fail to disclose) conflicts of interest. However, there is no intent for the disclosure requirement to prevent individuals with particular perspectives or strong points of view from serving on the TEP. The intent of full disclosure is to

inform the measure developer, other TEP members, and CMS about the source of TEP members' perspectives and how that might affect discussions or recommendations.

Estimated Number and Frequency of Meetings:

4-6 virtual meetings each being between 1 to 4 hours long. Meetings are tentatively scheduled for January – March 2024.

Date Approved by TEP:

TBD

ESRD Mineral and Bone Disorder

2024 Technical Expert Panel

January 29th, 2024

1:00-4:00 pm

Agenda

1:00pm:	Introductions and Conflict of Interests
1:35pm:	Measure Development Process
1:45pm:	Roles of TEP and TEP Co-Chairs
1:50pm:	TEP Charter
2:00pm:	Background- Mineral and Bone Disorder
2:30pm:	Rationale for Measure
2:45pm:	Wrap Up
2:50pm:	Public Comment

Introductions and Conflict of Interests

- TEP members must disclose any current and past activities that may cause a conflict of interest. This includes financial interests or other relationships that may influence their perceptions or judgement.

- It is unethical to conceal (or fail to disclose) conflicts of interest. However, the disclosure requirement is not intended to prevent individuals with particular perspectives or strong points of view from serving on the TEP. The intent of full disclosure is to inform the measure developer, other TEP members, and CMS about the source of TEP members' perspectives and how that might affect discussions or recommendations.

- If a member's status changes and a potential conflict of interest arises at any time while a member is serving on the TEP, the TEP member is required to notify the measure developer and the TEP chair.

TEP Members

Name, Credentials, Professional Role*	Organizational Affiliation, City, State*	Conflict of Interest Disclosure*
Deborah Benner, MA, RDN, CSR Registered Dietician VP Clinical Support and Special Projects	DaVita Inc, Yorba Linda, CA	None Reported
Geoffrey Block, MD, FASN Nephrologist Medical Office, SVP Clinical Research	US Renal Care Golden, CO	Former Director at Ardelyx, Inc. with equity in company.
Paul T. Conway, BA Chair, Policy and Global Affairs Patient Advocate	American Association of Kidney Patients Tampa, FL	None Reported
Dinesh K. Chatoth, MD Nephrologist Associate Chief Medical Officer	Fresenius Medical Care Suwanee, GA	Employee and Stakeholder of Fresenius Medical Care
Barbara Fox, MS, MPH Patient Advocate	Yuba City, CA	None Reported
Edward V. Hickey President, AAKP Chair	American Association of Kidney Patients (AAKP) Tampa, FL	None Reported
Kamyar Kalantar-Zadah, MD, MPH, PhD Nephrologist LA County Dept. Health Services	LA County Department of Health Services Harbor- UCLA Torrance, CA	None Reported

TEP Members

Name, Credentials, Professional Role*	Organizational Affiliation, City, State*	Conflict of Interest Disclosure*
Klemens Meyer, MD Nephrologist	Tufts Medical Center and Dialysis Clinic, Inc Boston, MA	Develops MBD decision support tools for DCI, but no financial interest.
Adrian Miller Patient Advocate	Vancouver, WA	None Reported
Lisa Modica, RD, BS Registered Dietician	Rogosin Institute Fort Lee, NJ	None Reported
Evan R. Norfolk, MD, MBA Nephrologist System Director for Nephrology	Geisinger Health System Danville, PA	Fresenius Pharmacy and Therapeutics Committee
Sherri Shivley Patient Advocate	Hamden, CT	None Reported
Francesca Tentori, MD, MS Nephrologist VP for Outcomes Research	DaVita, Inc Portland, TN	Employee of DaVita

UM- KECC Team

Name and Credentials	Organizational Affiliation	Conflict of Interest
Jonathan Segal, MD	Professor of Internal Medicine, Division of Nephrology University of Michigan, Kidney Epidemiology and Cost Center	None
Joseph Messana, MD	Professor of Internal Medicine, Division of Nephrology Research Professor, Health Management and Policy, University of Michigan, Kidney Epidemiology and Cost Center	None
Ananda Sen, PhD	Professor of Biostatistics and Research Professor University of Michigan, School of Public Health	None
Eric Young, MD, MS	Senior Research Scientist Arbor Research	None
Shu Chen, BS, MS	Senior Analyst University of Michigan, Kidney Epidemiology and Cost Center	None
Quinton Hazen, MPH	Intermediate Analyst University of Michigan, Kidney Epidemiology and Cost Center	None

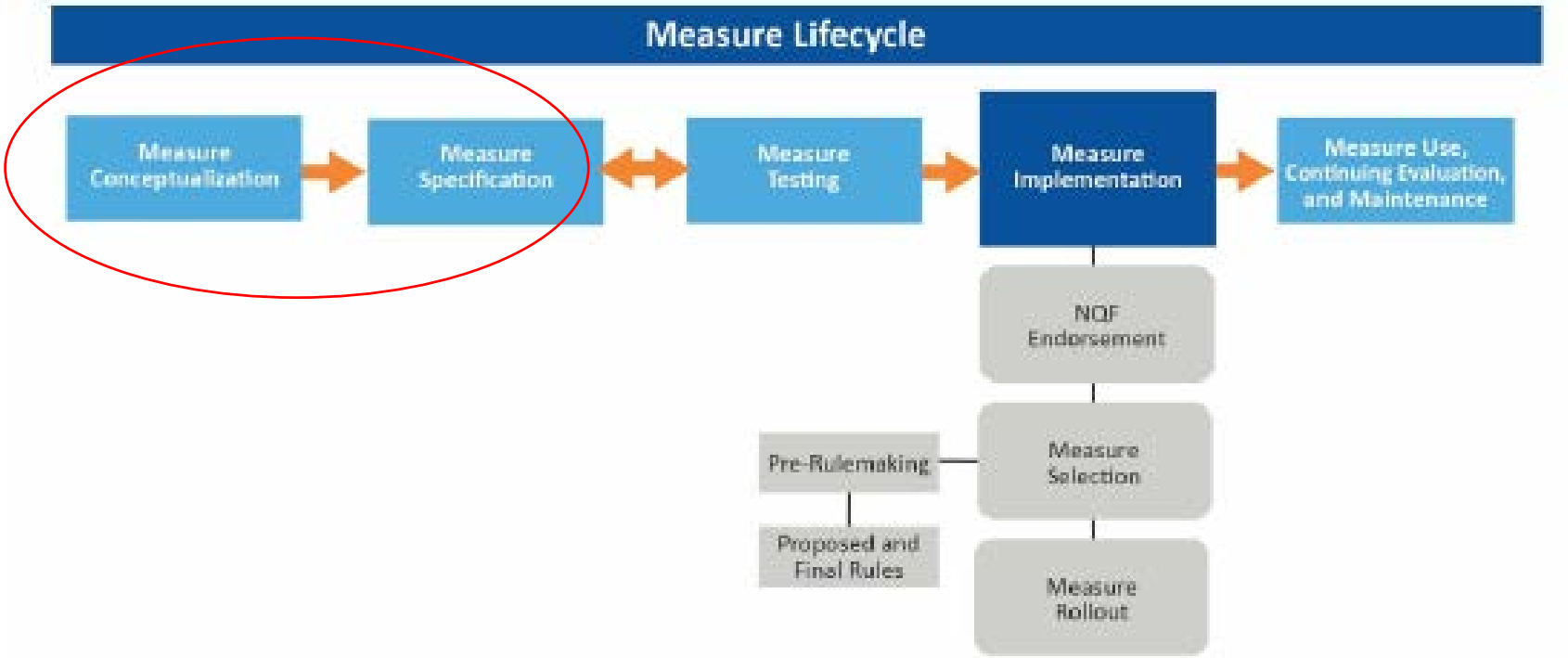
UM- KECC Team

Name and Credentials	Organizational Affiliation	Conflict of Interest
Lan Tong, MS	Lead Analyst University of Michigan, Kidney Epidemiology and Cost Center	None
Jennifer Sardone, BA, PMP	Senior Lead Project Manager University of Michigan, Kidney Epidemiology and Cost Center	None
Jaclyn George, BA	Project Intermediate Manager University of Michigan, Kidney Epidemiology and Cost Center	None
Mimi Dalaly, MPH	Project Intermediate Manager University of Michigan, School of Public Health	None

CMS
Stephanie Clark, MD
Golden Horton, MS
Wilfred Agbenyikey, PhD

Measure Development Process

Measure Development, Implementation, and Maintenance Process



Measure Evaluation Criteria

- Importance to Measure and Report
  - Evidence
  - Performance Gap
  - Priority to report measure outcome
- Scientific Acceptability
  - Reliability and Validity of measure
- Feasibility
  - Ability to obtain data to calculate measure
- Usability
  - Measure results are actionable to help improve performance
- Harmonization
  - Comparison to any related or competing measures

Role of the TEP

Duties and Role of TEP members:

- Review evidence to determine the basis of support for the proposed measure(s)
- Recommend draft measure specifications
- Review and approve summary report recommendations of the TEP Meeting, draft and final measure specifications, and provide input on other necessary documentation forms required for submission to the NQF for endorsement or for responses to public comments
- Be available for follow up conference calls, as needed

Role of the TEP

Role of UM-KECC (developer/contractor):

- Support the development of measures that are used in CMS quality programs, either for payment or public reporting.
- Work with the TEP chair(s) to ensure the panel discussions focus on the development of draft measure specifications, as recommended to the developer/contractor.
- Advise the TEP and the TEP chairs on the needs and requirements of the CMS contract and the timeline, and provide specific guidance and criteria that must be met with respect to CMS and NQF review of candidate measures.

Role of TEP chairs:

- The TEP chairs are responsible, in partnership with UM-KECC, for directing the TEP to meet the expectations for TEP members, including provision of advice to the developer/contractor regarding measure specifications.
  - Conduct the meeting according to the agenda.
  - Recognize speakers and call for votes when needed.

Role of the TEP

- TEPs are advisory to the measure developer/contractor (UM-KECC), and not CMS
- It is the responsibility of UM-KECC to consider input received by the TEP; however recommendations made to CMS are made by UM-KECC, and not by the TEP
- If UM-KECC makes recommendations to CMS that are not consistent with the recommendations from the TEP, it is the measure developer's responsibility to explain the rationale for any differences

ESRD Mineral and Bone Disorder TEP Charter

- The TEP will use existing data and their expert opinion to formulate recommendations to UM-KECC regarding the development of a draft measure that addresses potentially important quality gaps in mineral and bone disorder management. Recommended measures should be evidence based, scientifically acceptable (reliable and valid), feasible, and usable by CMS, providers, and the public.
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Background

Summery of Evidence

Annotated Bibliography organized studies into three categories:

1.

Summary Points

Measure Definition

Questions?

Wrap-up

- Next Meeting, Monday, February 19th 2:00pm – 5:00pm EDT (11:00am – 2:00pm PDT)
- Overview of Topics
- Public Comment Period

ESRD Mineral and Bone Disorder

2024 Technical Expert Panel

February 23rd, 2024

1:00-4:00 pm

Agenda

1:00 pm: Welcome and Attendance

1:10 pm: Literature Review Presentation

2:00- 3:50pm: Open Discussion

3:50- 4:00pm: Public Comment

TEP Members

Name, Credentials, Professional Role*	Organizational Affiliation, City, State*	Conflict of Interest Disclosure*
Deborah Benner, MA, RDN, CSR Registered Dietician VP Clinical Support and Special Projects	DaVita Inc, Yorba Linda, CA	None Reported
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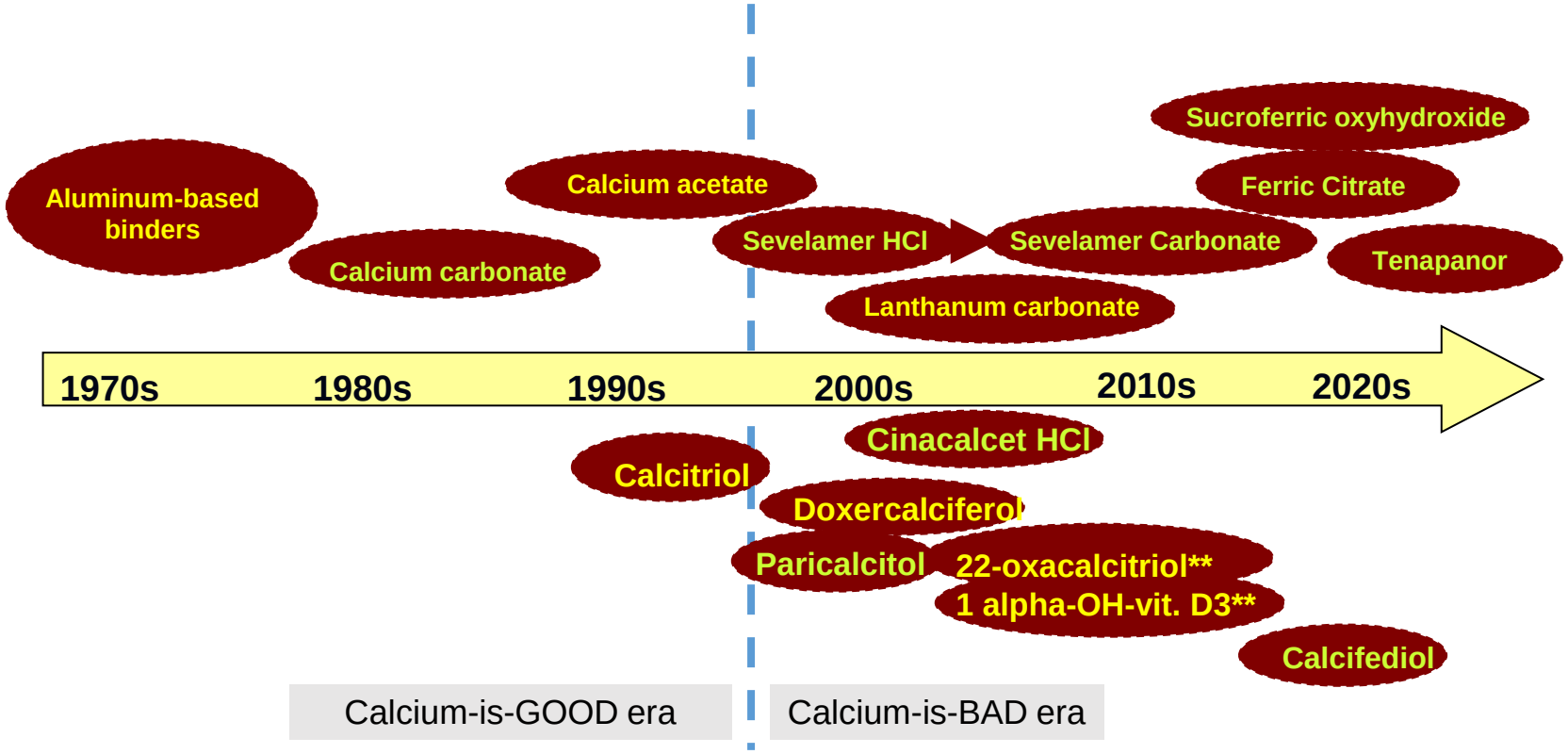
Mimi Dalaly, MPH	Project Intermediate Manager University of Michigan, School of Public Health	None

CMS
Stephanie Clark, MD
Golden Horton, MS
Wilfred Agbenyikey, PhD

Introduction and Historical MBD Data

Kam Kalantar-Zadeh, MD, MPH, PhD

Timeline of various treatments for CKD-MBD



*Not approved as phosphate binder

**Not approved in the US

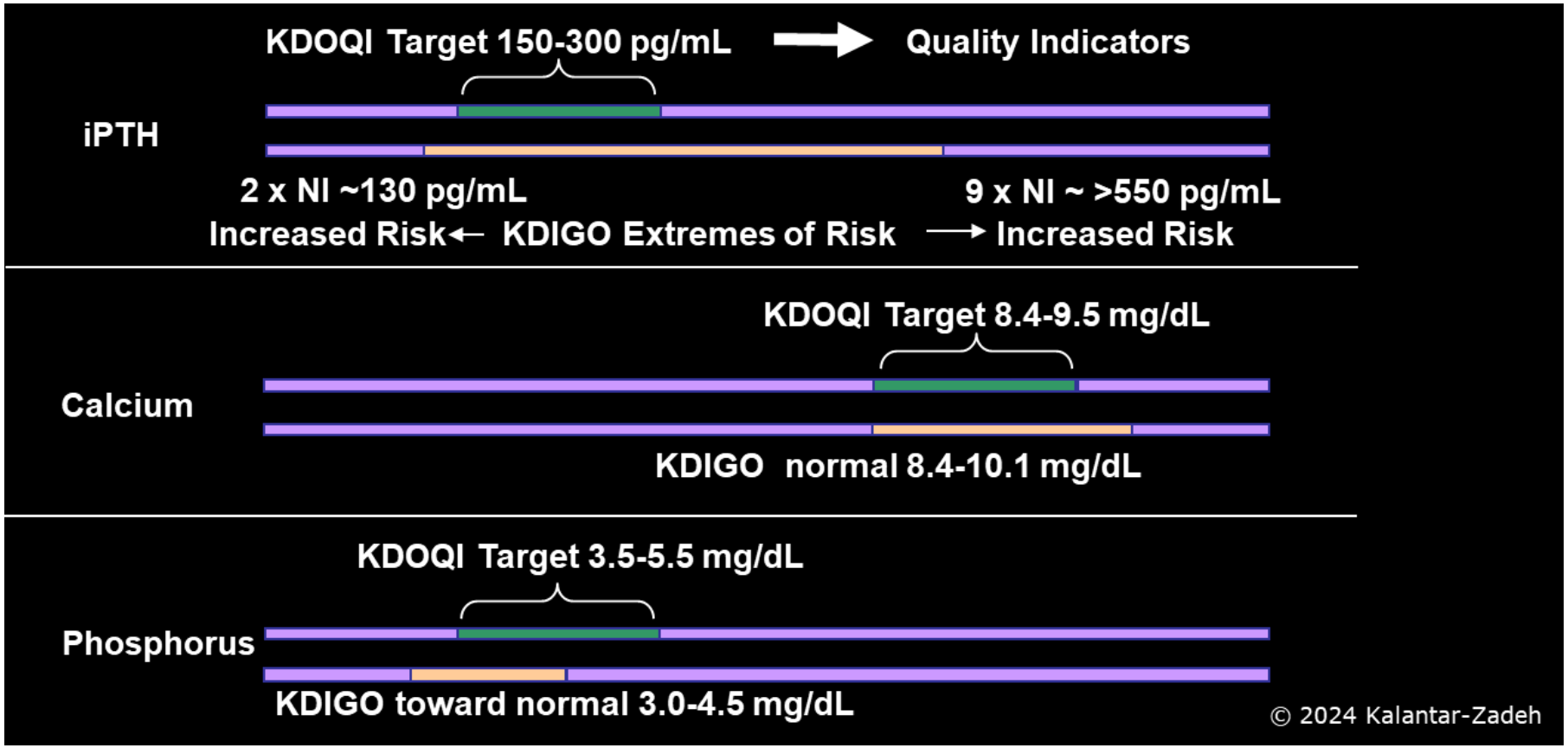
Adapted from Kovesdy, Mehrotra, & Kalantar-Zadeh. *Clin J Am Soc Nephrol* 2008:168-73

Earlier MBD Guidelines for Dialysis Patients

	UK-RA(2002) UK	CARI(2006) ANZ	EBPG(2002) ERA	KDOQI(2003) NKF (USA)	KDIGO (2009)	JSDT(2006) Japan
Calcium	8.8-10.4 mg/dL	8.4-9.5 mg/dL	8.8-10.8 mg/dL	8.4-9.5 mg/dL	8.4 -10.2 mg/dL	8.4-10.0 mg/dL
Phosphate	<5.5mg/dL	2.5-5.0 mg/dL	2.5-4.7 mg/dL	3.5-5.5 mg/dL	Normal range ?	3.5-6.0 mg/dL
Ca×P		<50mg^2/dL^2		<55mg^2/dL^2		
PTH	<4×ULN	2-3×ULN		150-300 pg/dL	130-~600 pg/dL	60-180 pg/mL
Alk Phos				recommended	More strongly recommended	

UK-RA: UK Renal Association; **CARI**: Caring for Australian w/ Renal Impairment; **EBPG**: European Best Practice Guideline; **JSDT**: Japanese Society for Dialysis Therapy; **ULN**: Upper Limit Number.

Historical CDK-MBD Guidelines: KDOQI vs KDIGO

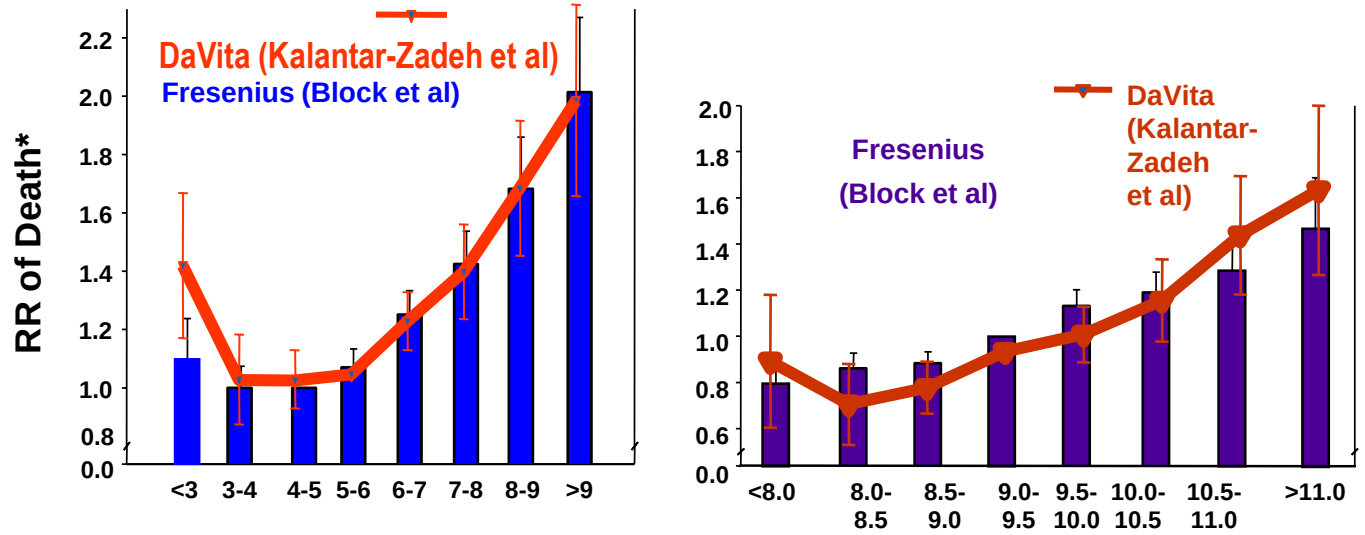


Are Minerals Associated with Death in ESRD?

Mortality Risk by Serum Phos and Ca Levels in Patients on Hemodialysis

N = 58,058 (DaVita 2001-2003, 2 years)

N = 40,538 (Fresenius 1997-1999, 12-18 moths)



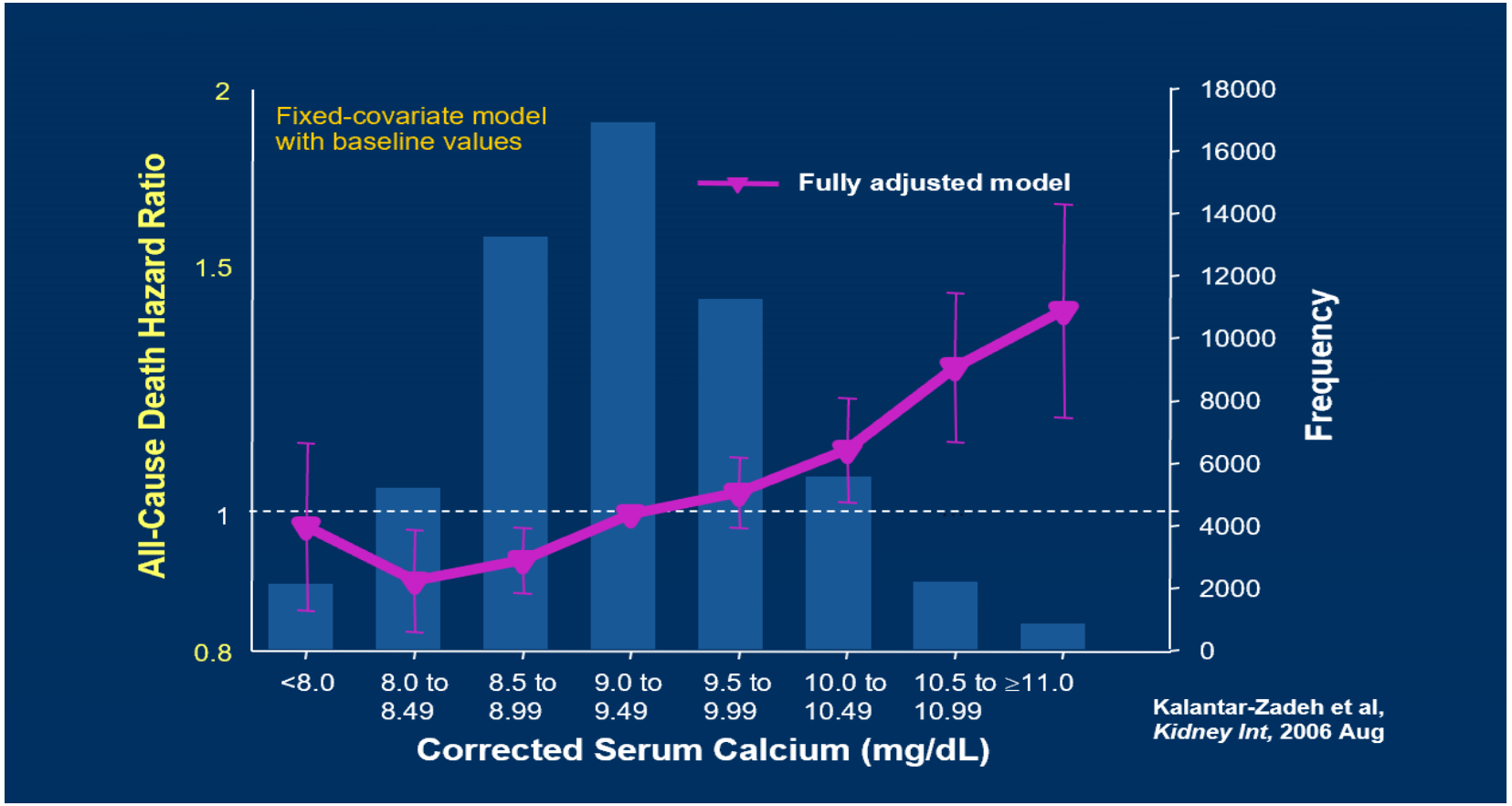
RR = relative risk.

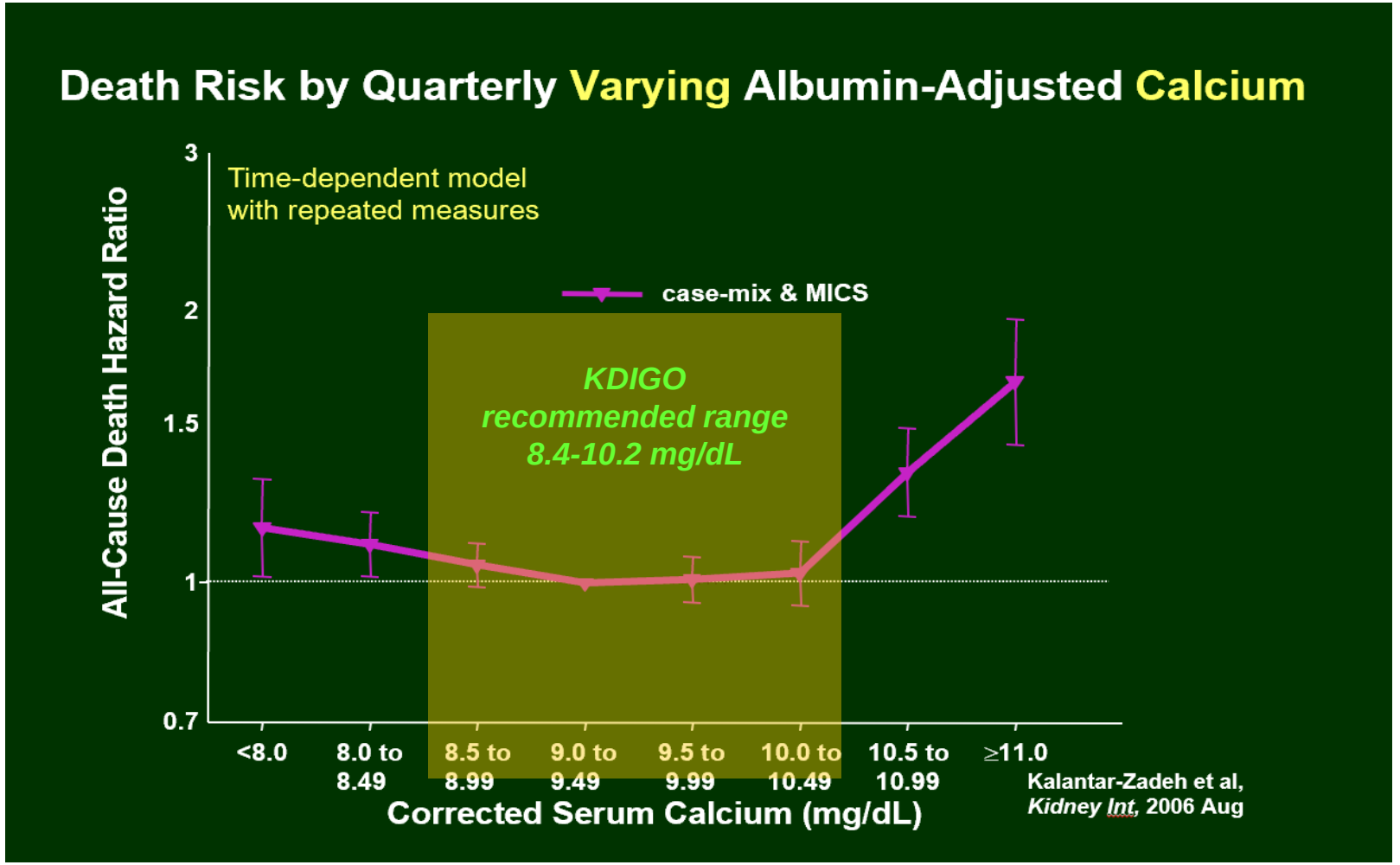
Block et al. *J Am Soc Nephrol.* 2004;15:2208-2218. Kalantar-Zadeh et al. *Kidney Inter.* 2006; 70:771-780

Serum Calcium and Survival

Albumin-Adjusted Calcium at Baseline and Prospective Mortality

58,058 hemodialysis patients: 2001-2003

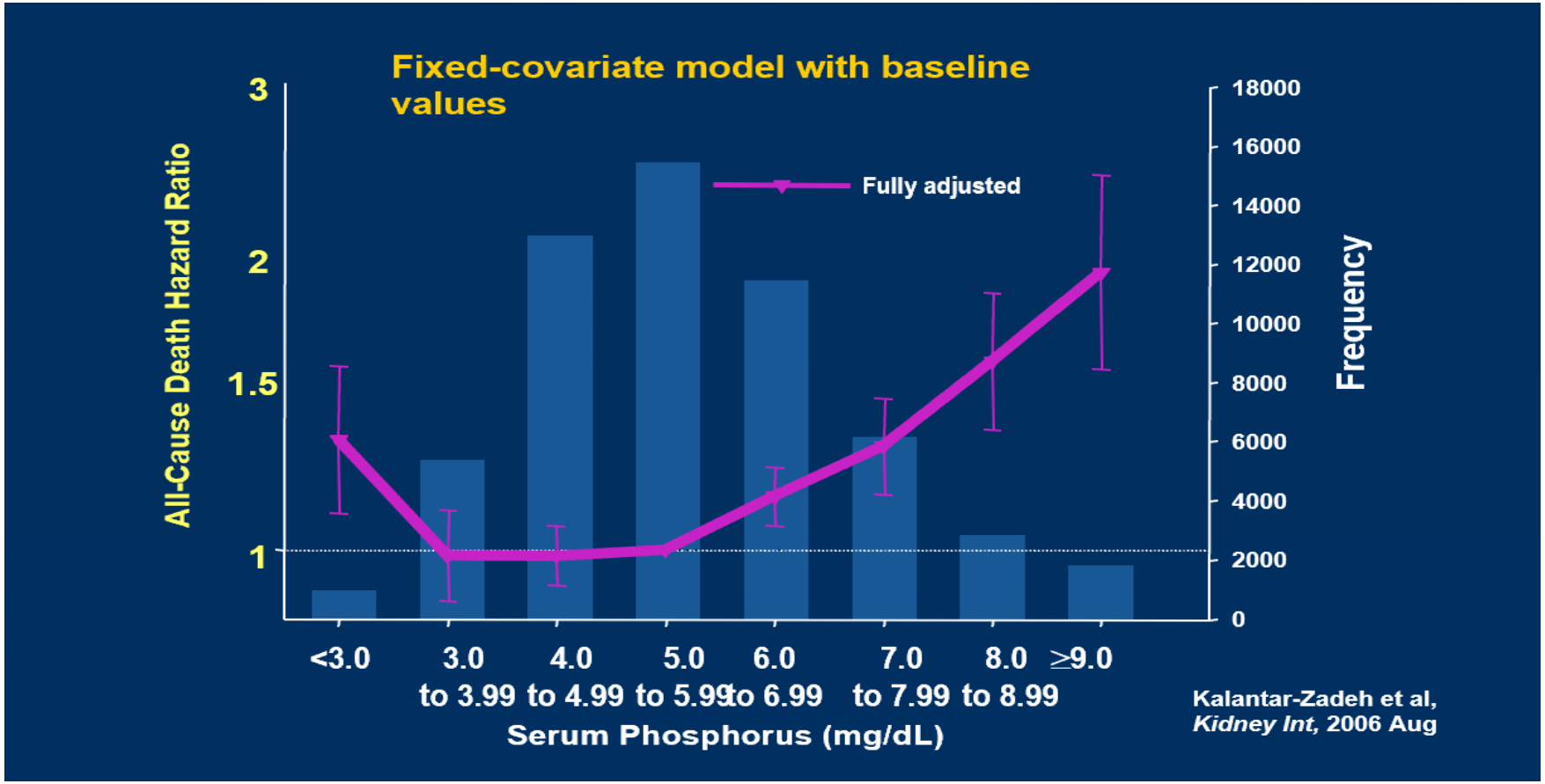



Death Risk by Quarterly Varying Albumin-Adjusted Calcium
Time-dependent model
with repeated measures
case-mix & MICS
KDIGO
recommended range
8.4-10.2 mg/dL
All-Cause Death Hazard Ratio
3
2
1.5
1
0.7
<8.0
8.0 to 8.49
8.5 to 8.99
9.0 to 9.49
9.5 to 9.99
10.0 to 10.49
10.5 to 10.99
≥11.0
Corrected Serum Calcium (mg/dL)
Kalantar-Zadeh et al,
Kidney Int, 2006 Aug

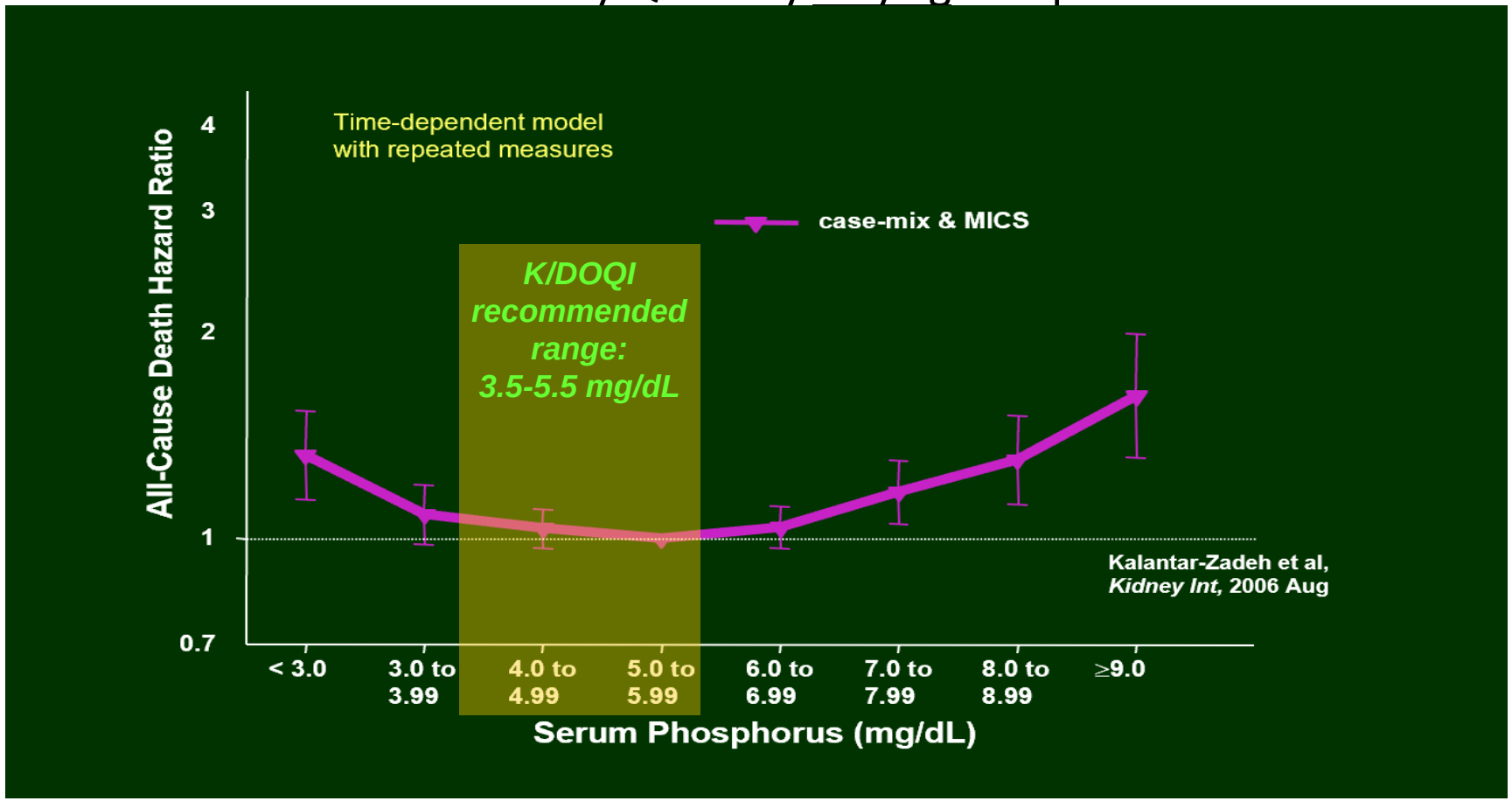
Serum Phosphorus and Survival

Serum Phosphorus at Baseline and Prospective Mortality

58,058 hemodialysis patients: 2001-2003

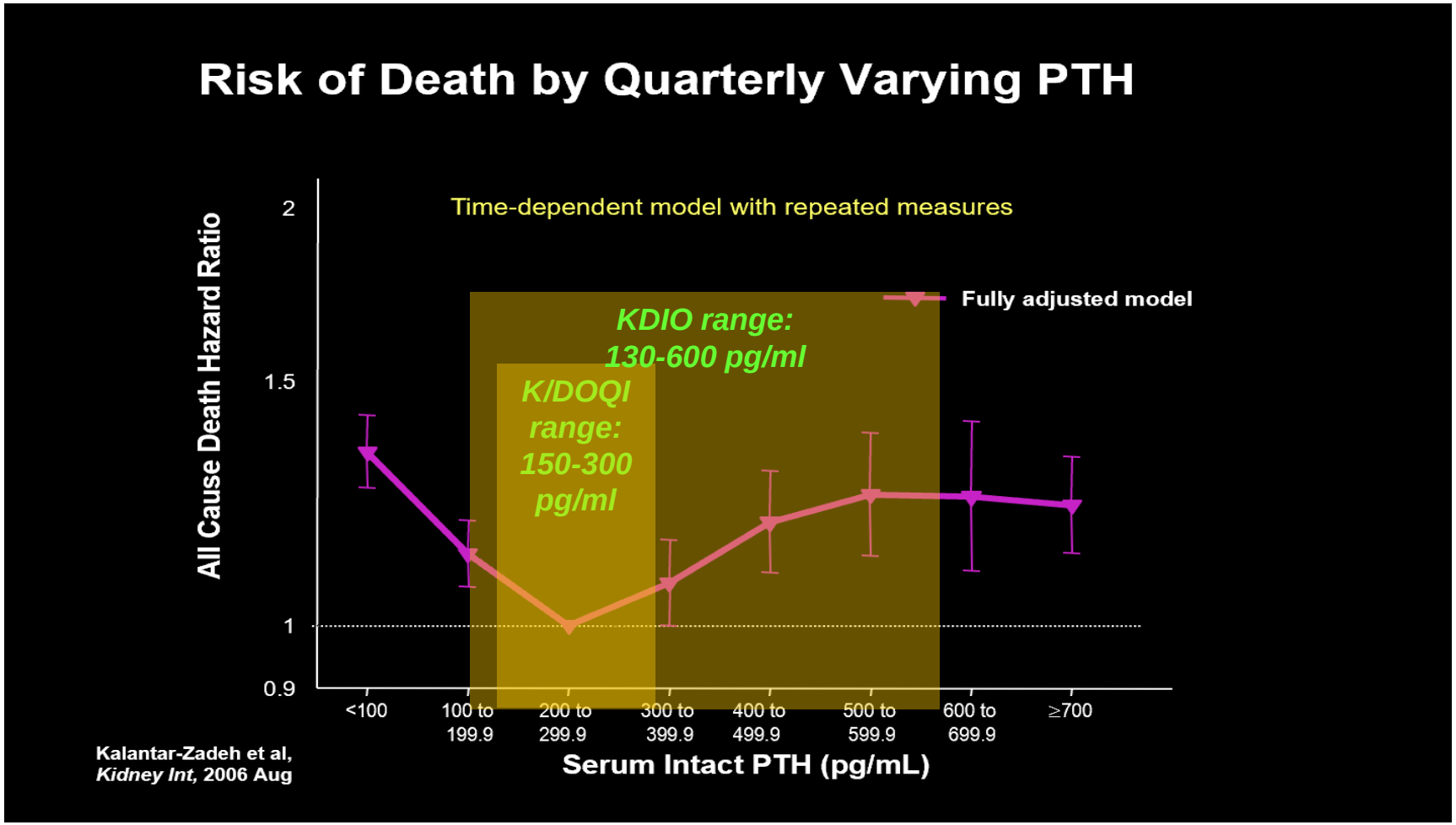


Risk of Death by Quarterly Varying Phosphorus



Do PTH levels impact mortality in dialysis patients?

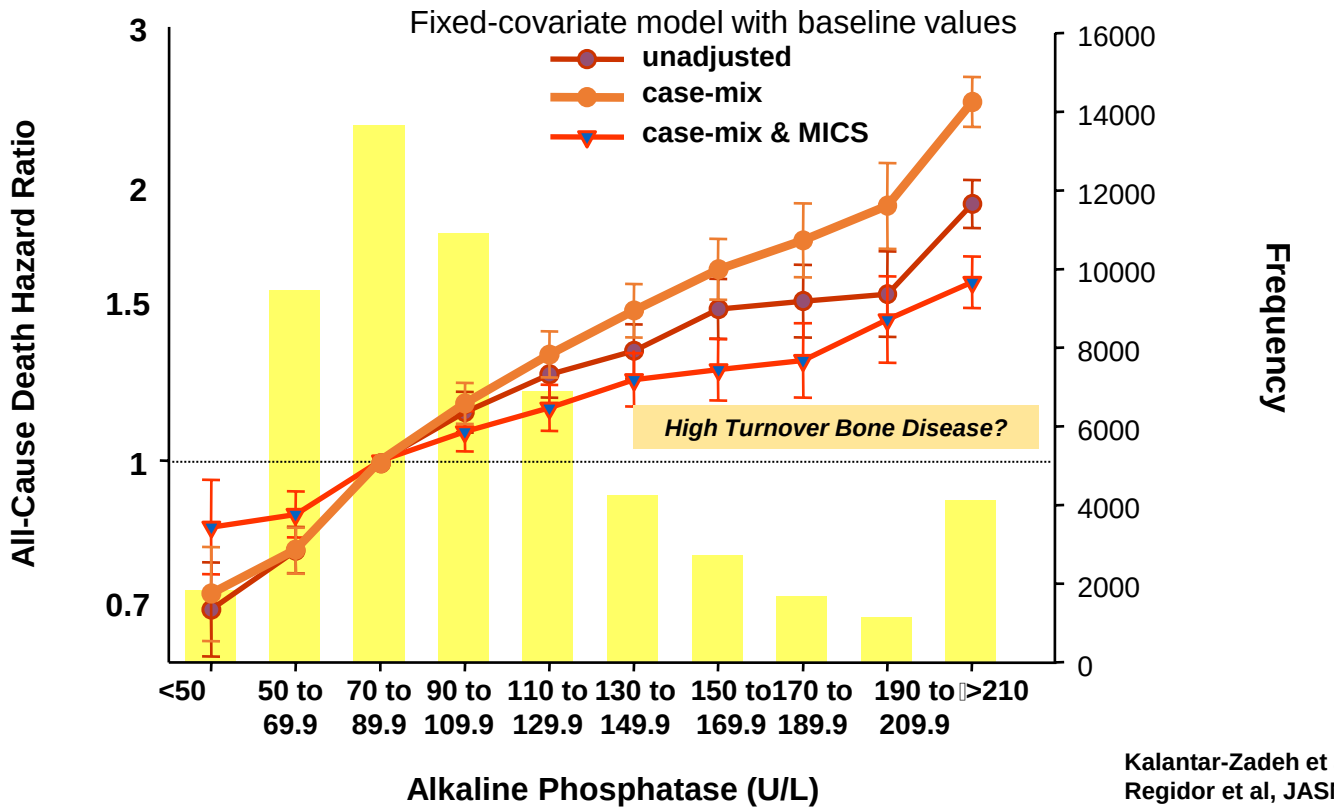
Risk of Death by Quarterly Varying PTH



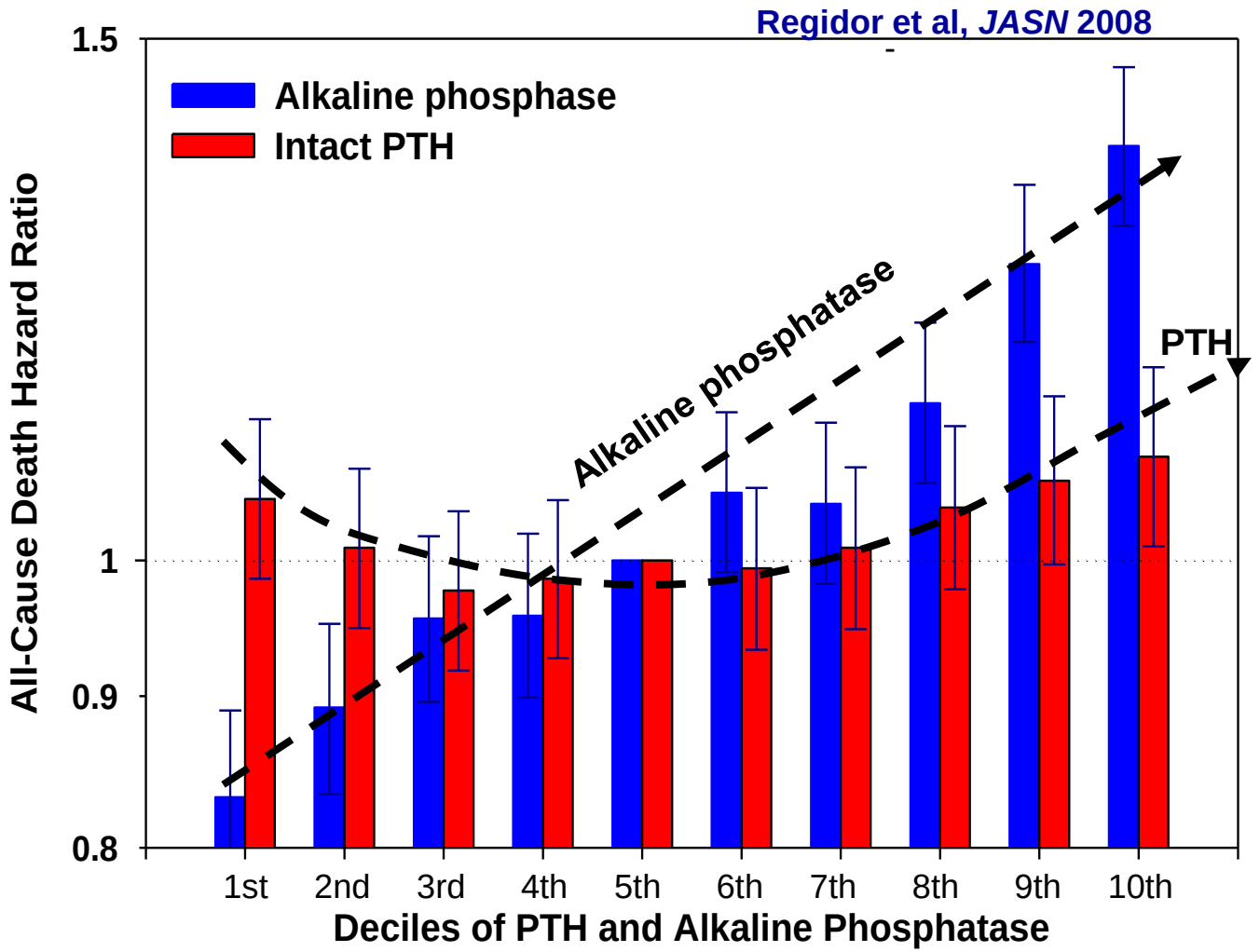
Alkaline Phosphatase and CKD Outcomes

Serum Alkaline Phosphatase and Mortality

58,058 hemodialysis patients: 2001-2003



Kalantar-Zadeh et al, *Kidney Int,* 2006,
Regidor et al, JASN 2008


Regidor et al, JASN 2008
Alkaline phosphase
Intact PTH
All-Cause Death Hazard Ratio
1.5
1
0.9
0.8
Alkaline phosphatase
PTH
1st
2nd
3rd
4th
5th
6th
7th
8th
9th
10th
Deciles of PTH and Alkaline Phosphatase

Conclusions

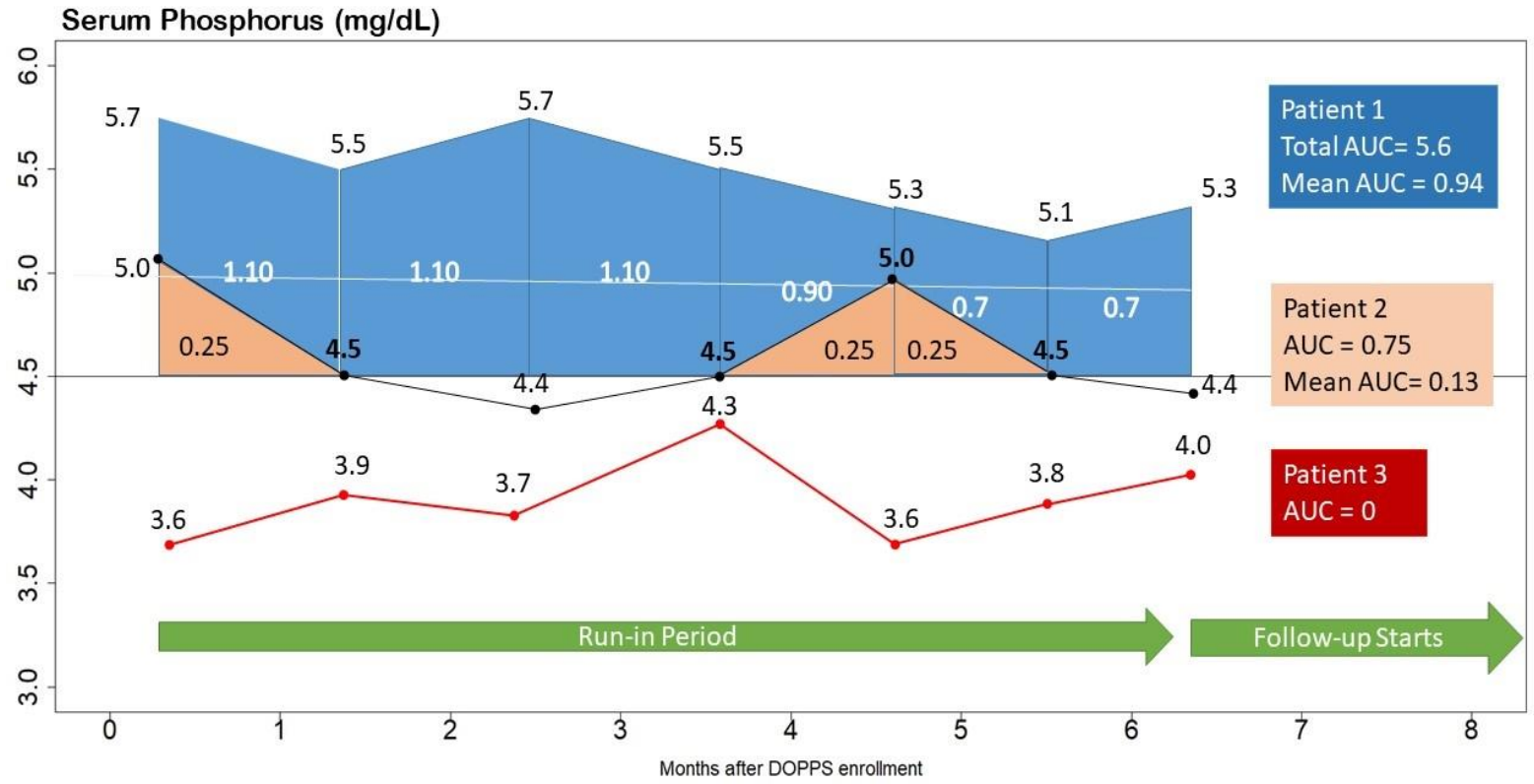
- MBD markers are related to survival in epidemiologic studies of dialysis patients.
- Causal Inference should be with outmost caution and conservative statements given the challenge of distinction between biologic plausibility vs. non-causal associations.

Literature Review

Geoff A Block, MD

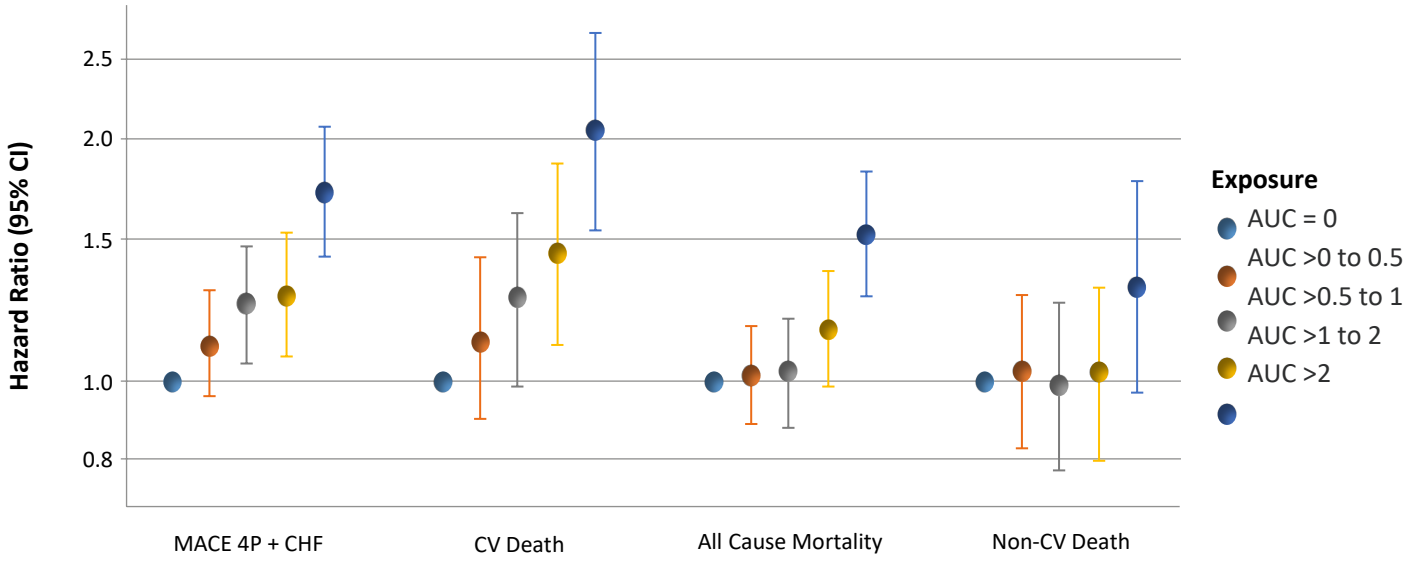
Phosphorus area under the curve [AUC] Approach

Phosphorus AUC = average of monthly levels >4.5 mg/dL over 6 months



Lopes et al. Nephrology Dialysis Transplantation 2020; 35(10): 1794 1801.

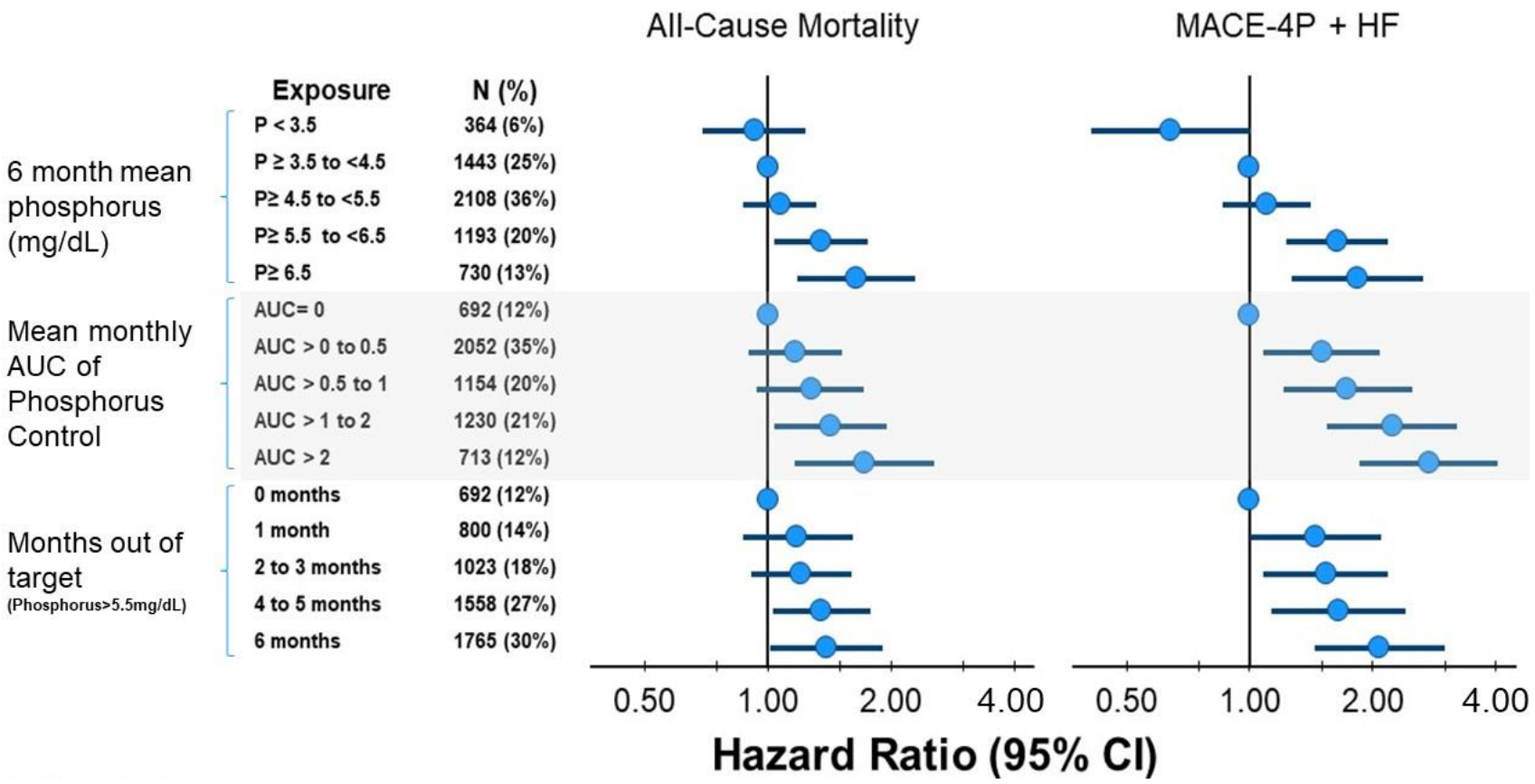
Duration and Extent of Phosphate Greater Than 4.5 mg/dL Association With CV Events and Mortality – Hemodialysis



AUC, area under the curve; CV, cardiovascular events; HD, hemodialysis; MACE 4P + CHF, major adverse CV events (CV death + non-fatal myocardial infarction + non-fatal angina + non-fatal stroke + congestive heart failure).
Lopes MB, et al. *Nephrol Dial Transplant*. 2020; doi: 10.1093/ndt/gfaa054.

Lopes et al. *Nephrol Dialysis Transplant*. 2020; doi: 10.1093/ndt/gfaa054.

Association of Single and Serial Measures of P Control with Outcomes in PD-DOPPS



Lopes et al. Nephrol Dial Transplant (2023) 38: 193 202

Impact of Phosphate Lowering agents on Clinical Outcomes in CKD: Systematic Review / Meta-analysis of RCTs

Search
- Source: MEDLINE, Scopus, CENTRAL
- until July 2020

Population:
Adults with CKD
(non-dialysis and dialysis)

Interventions
- Sevelamer
- Lanthanum
- Iron-based PBs
- Mg-based PBs
- Niacin-based agents
- Bixalomer
- Tenapanor

Controls
- Placebo
- Calcium based PBs
- Other non-calcium based PBs

127 RCTS (**187** study-arms)
20,215 patients (77% dialysis)

Results

Sevelamer and **lanthanum** significantly reduced all-cause mortality
(RR 0.610, 95%CI: 0.401 to 0.929 and 0.467, 95%CI: 0.337-0.647, respectively)

Sevelamer significantly decreased hospitalization rates
(RR 0.527; 95%CI 0.308 to 0.902).

Certain phosphate lowering agents improved biochemical parameters including serum phosphate, calcium, coronary artery calcium scores, fibroblast growth factor-23, bone biomarkers, and lipid profiles.

Conclusions

In addition to decreasing serum phosphate levels, various beneficial effects on clinical and laboratory parameters of phosphate lowering agents might play potential roles in diminishing morbidity and mortality in CKD patients.

Phannajit et al. Journal of Nephrology (2022) 35:473

Impact of Phosphate Management on Quality of Life

Patient Quotes About the Lack of Education for Phosphorus Control

- "Two hours with a renal dietician…doesn't make up for 50 years of 0 nutrition education. The nutrition information is a very slow trickle.
- "When they say, 'don't eat too much phosphorus,' well, how much is too much? Well, what does 1,000 mg of phosphorus look like? Four bell peppers? Nutrition labels don't list phosphorus, so it's all hidden … everything seems stacked against you."
- "No one told me how important phosphate control was and how it was tied to my chances to have a heart attack, stroke, and other cardiovascular events."
- "I felt that education for patients on dialysis was focused on fluid restriction, hemoglobin, and potassium. Very rarely was phosphate mentioned and certainly not emphasized in my dialysis center."

Patient Quotes About Dietary Restrictions

- "I am exhausted because I need to spend a lot of time cooking at home and trying to calculate phosphate intake."
- "I'm in a more rural or suburban area, and it's a healthy food desert … However, right around the corner, I had fast food and dollar stores with all the processed foods in a box or can. Many of us don't eat the right foods because we are just worn out from trying to find them."
- "I know what it is that I need to eat, but if I can't find it, what can I do? I'm just going to eat what I'm going to eat. I'm hoping the dialysis machine sucks out the majority of it and just deal with the backlash consequences."
- "When I go to someone's house for dinner, it's a huge stress. They are trying to be nice by offering lots of food. I want to be gracious and accept the food they are offering instead of being rude and saying that I can't eat it. It makes them feel bad. It makes me feel bad. More often than not, I secretly have to throw it away and pretend I loved it. I probably would have loved it too. Social and family gatherings are a difficult time."

Forfang et al. Kidney Med. 4(4):100437. 2022

Impact of Phosphate Management on Quality of Life

Patient Quotes About Phosphate Binders

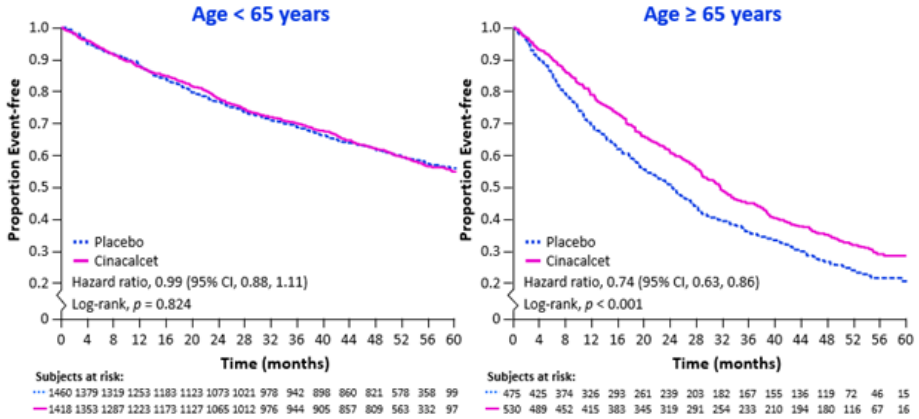
- "I take about 1,100 pills a month. Five hundred of those are phosphate binders. If I could get those 500 pills down to 50 or so, that would be enormous. I am chugging down 5 or 6 binders with every meal, which I'd rather not do."
- "It's stressful to constantly remind myself to take the binders every time I eat, it really makes spontaneous activities difficult, and I can't enjoy social activities as much. Sometimes I forget and feel really anxious and guilty."
- "The size and number of pills are hard to deal with every day. Sometimes I have trouble swallowing them, and I'm worried about taking them in public in case I can't swallow successfully on the first try."

Patient Quote About Negative Clinician–Patient Relationship

"I get harassed. I get a finger waved in my face by my doctor or dietician. They will say that I need to do better. I don't wanna get harassed, so I just need to do better. All of this makes me feel like it's my fault for not eating a near-perfect kidney-friendly diet. Once in a while, I get that smiley face next to my phosphorus lab. I look forward to that smiley face. The tradeoff for that smiley face is I'm not allowed to enjoy life if I want to have a little ice cream."

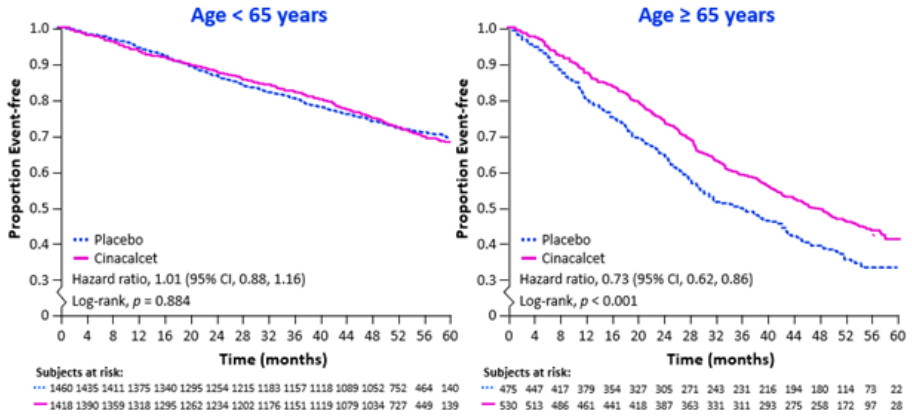
Forfang et al. Kidney Med. 4(4):100437. 2022

Effects of Cinacalcet in Older and Younger Patients on Hemodialysis- EVOLVE



Composite Cardiovascular Endpoint

Mortality



Parfrey et al. Clin J Am Soc Nephrol 10: 791 799, 2015

Effects of Cinacalcet in Older and Younger Patients on Hemodialysis - EVOLVE

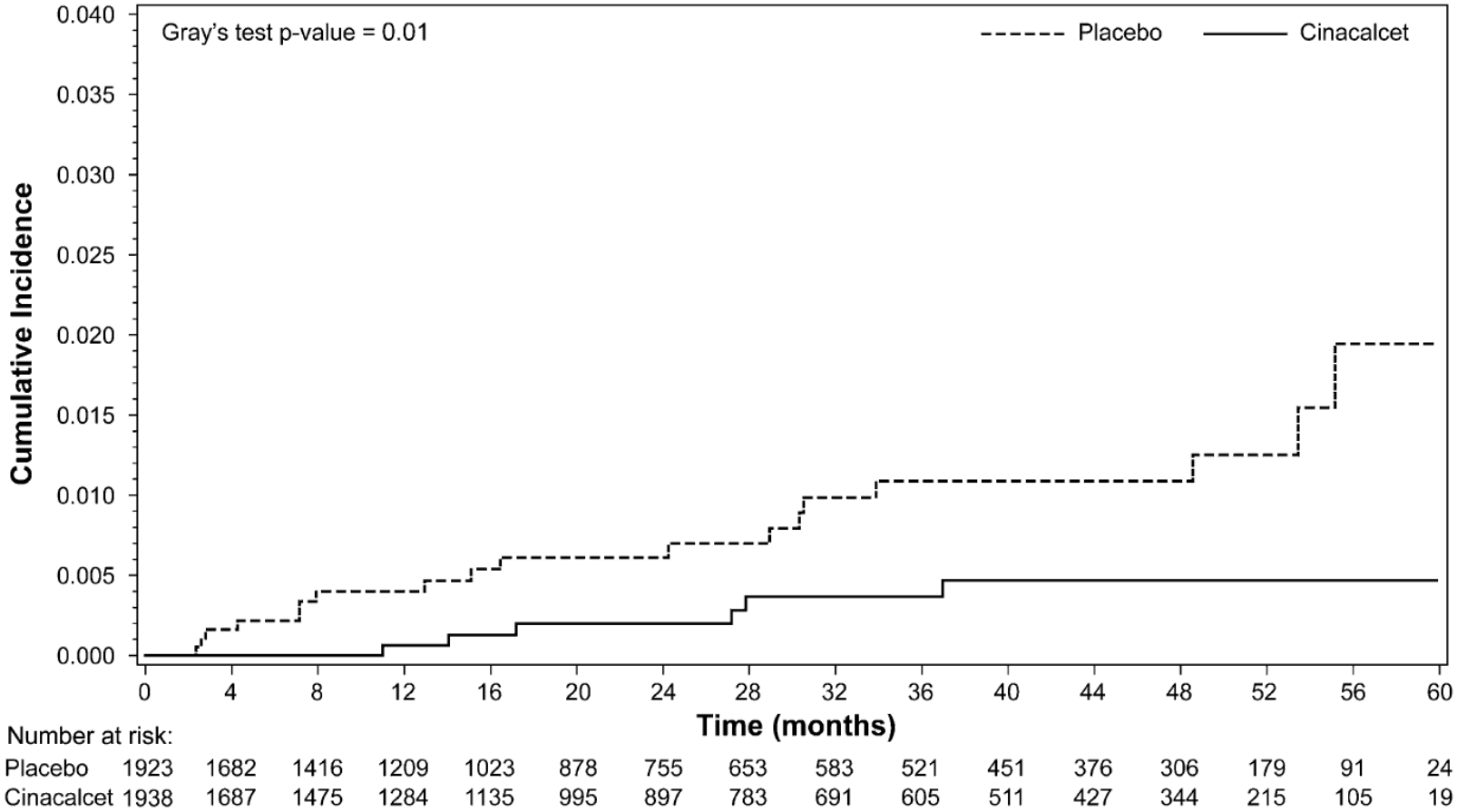
Table 2. Annualized event rates and hazard ratios for cardiovascular end points and mortality by age group

End Point	Age <65 yr (n=2878)			Age ≥65 yr (n=1005)		
	Annual Event Rate		Relative Hazard	Annual Event Rate		Relative Hazard
	Placebo (N_1=1460)	Cinacalcet (N_1=1418)		Placebo (N_1=475)	Cinacalcet (N_1=530)	
Primary composite CVD	11.4 (10.6 to 12.3)	11.3 (10.5 to 12.2)	0.99 (0.88 to 1.11)	28.3 (25.9 to 30.9)	22.6 (20.5 to 24.7)	0.74 (0.63 to 0.86)
All-cause mortality	7.0 (6.4 to 7.7)	7.1 (6.5 to 7.8)	1.01 (0.88 to 1.16)	20.4 (18.4 to 22.5)	15.9 (14.3 to 17.7)	0.73 (0.62 to 0.86)
Myocardial infarction	1.9 (1.6 to 2.3)	2.4 (2.0 to 2.8)	1.2 (0.92 to 1.57)	6.3 (5.0 to 7.8)	4.0 (3.1 to 5.0)	0.60 (0.43 to 0.85)
Unstable angina	0.9 (0.7 to 1.2)	0.6 (0.4 to 0.9)	0.66 (0.43 to 1.03)	1.2 (0.7 to 2.0)	1.4 (0.9 to 2.1)	1.19 (0.62 to 2.29)
Heart failure	2.9 (2.5 to 3.4)	2.5 (2.1 to 2.9)	0.82 (0.64 to 1.03)	6.6 (5.3 to 8.1)	4.8 (3.8 to 6.0)	0.76 (0.56 to 1.05)
Peripheral vascular disease	2.3 (1.9 to 2.7)	2.2 (1.8 to 2.7)	0.99 (0.76 to 1.28)	6.3 (5.0 to 7.8)	4.2 (4.2 to 5.3)	0.69 (0.49 to 0.96)

Data are presented with 95% confidence intervals. CVD, cardiovascular disease.

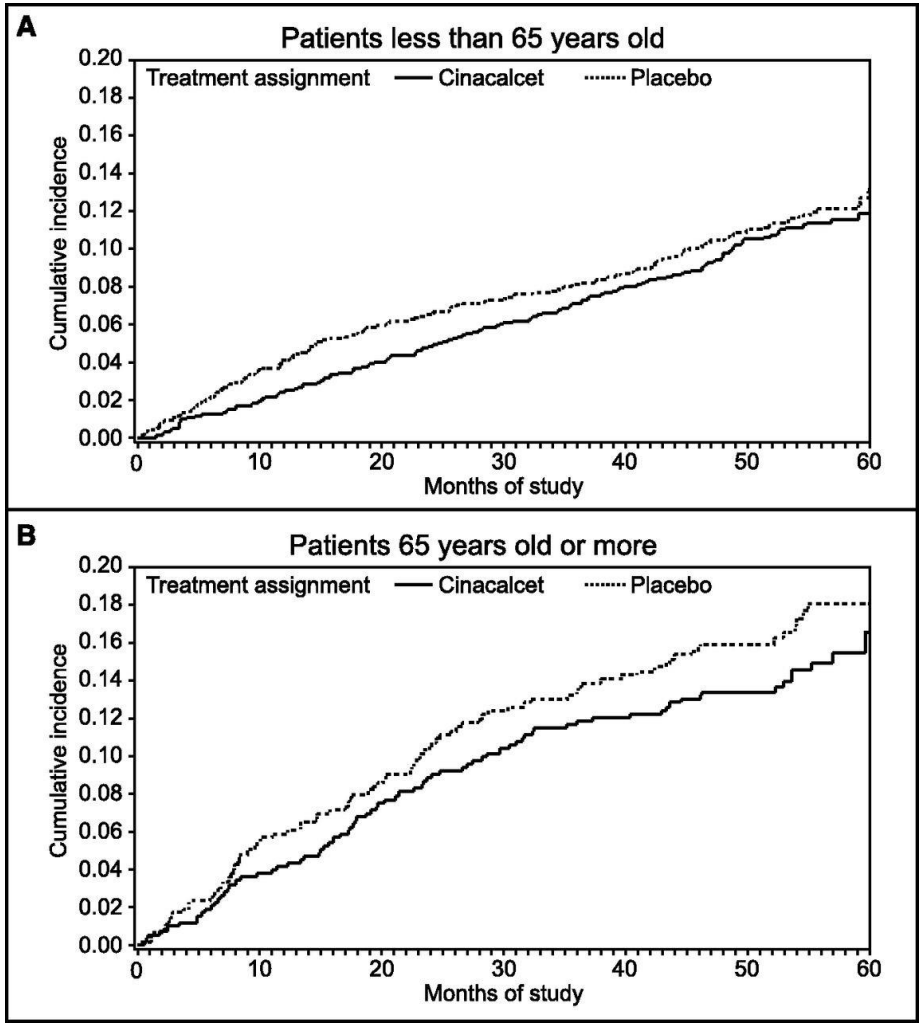
Parfrey et al. Clin J Am Soc Nephrol 10: 791 799, 2015

Effect of Cinacalcet on Calcific Uremic Arteriolopathy Events - EVOLVE



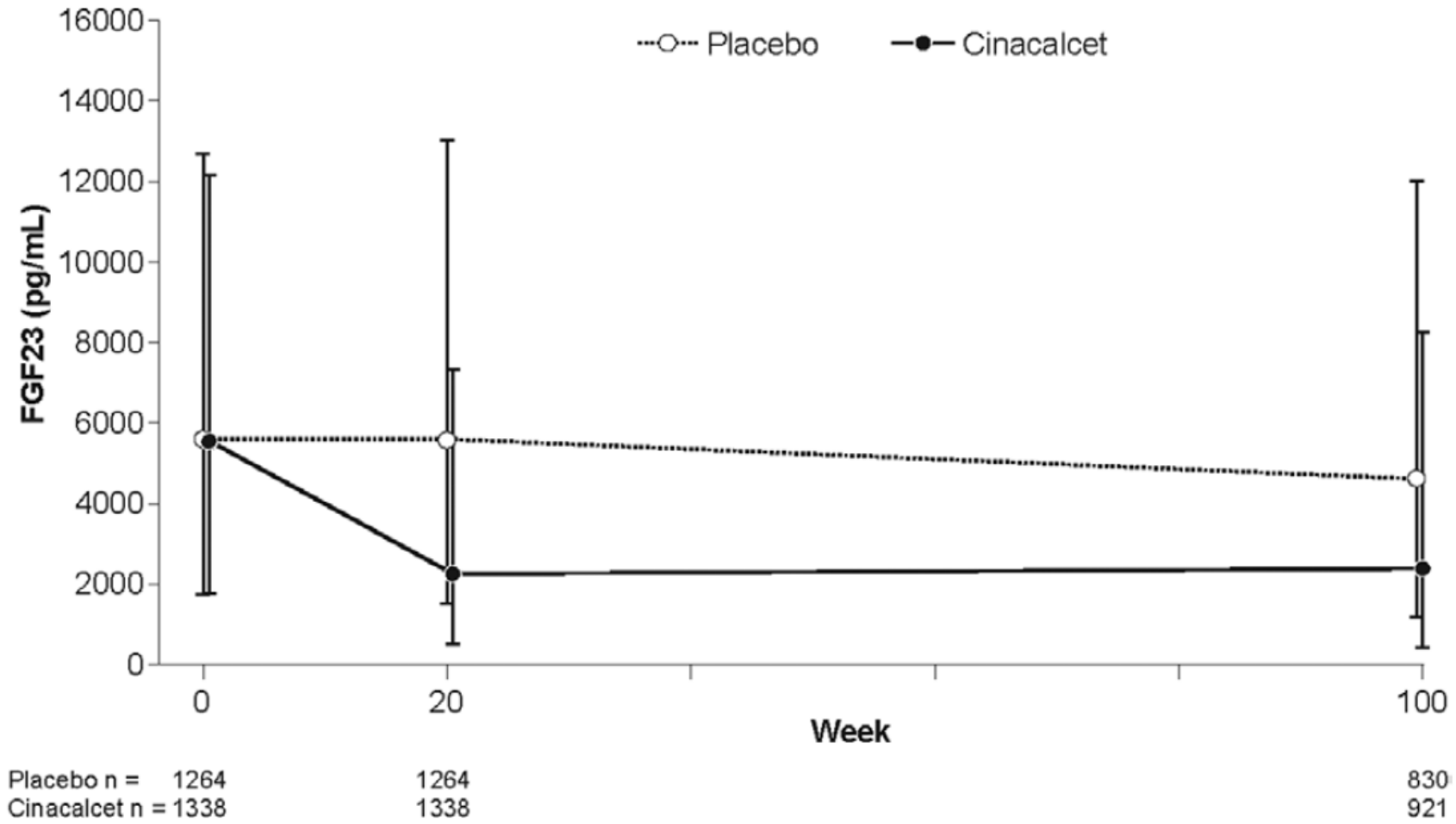
Floege et al. Clin J Am Soc Nephrol 10: 800 807, 2015

Cumulative Incidence of Fractures



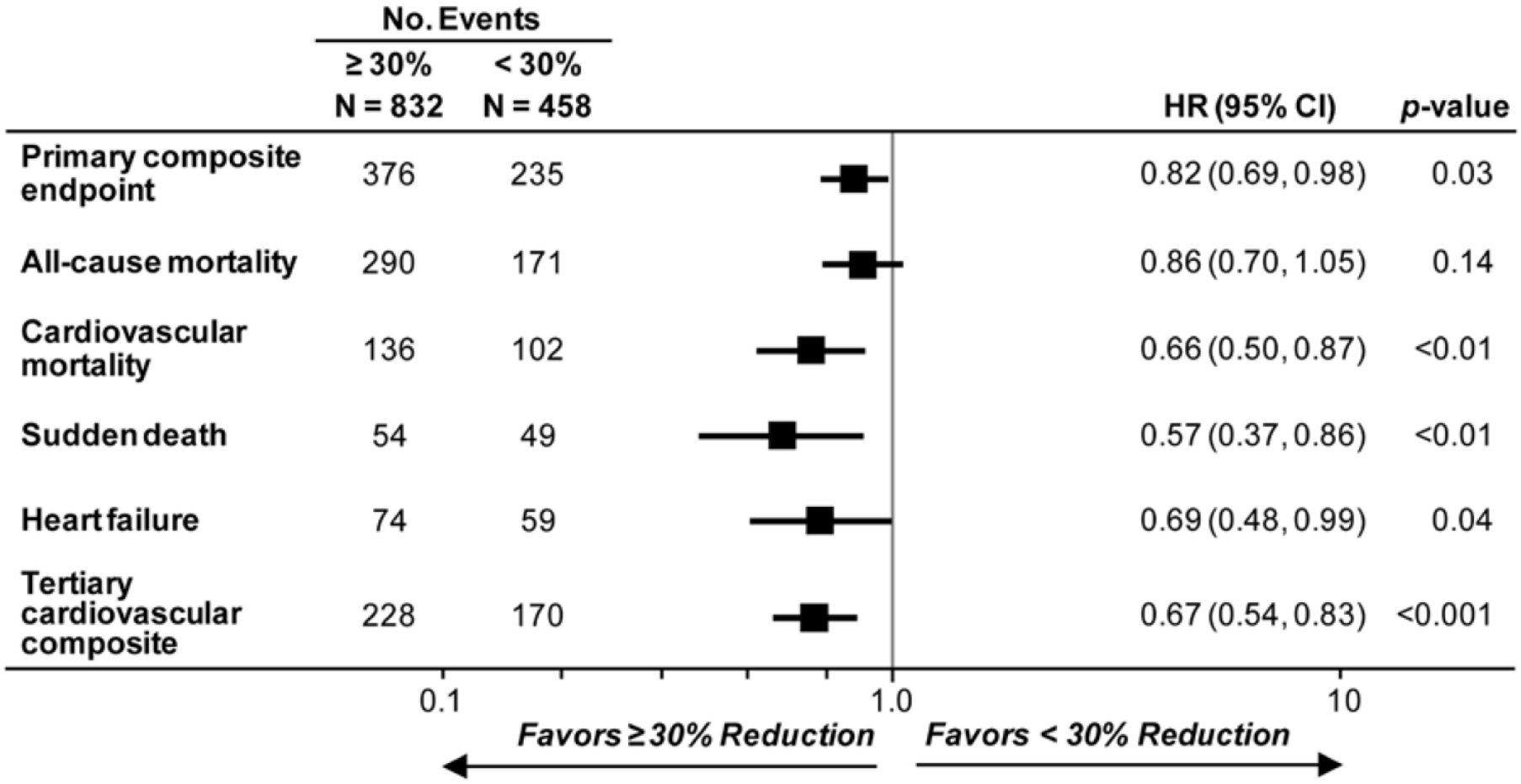
Sharon M. Moe et al. JASN 2015;26:1466 1475

Cinacalcet, Fibroblast Growth Factor-23, and Cardiovascular Disease in Hemodialysis - EVOLVE



Moe et al. Circulation. 2015;132:27 39.

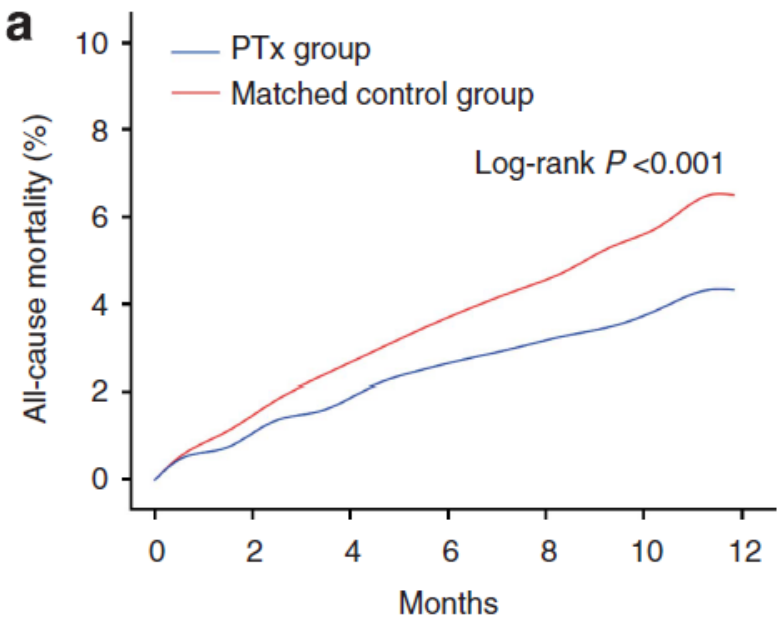
Cinacalcet, Fibroblast Growth Factor-23, and Cardiovascular Disease in Hemodialysis - EVOLVE



Moe et al. Circulation. 2015;132:27 39.

Parathyroidectomy and Survival among Japanese HD Patients

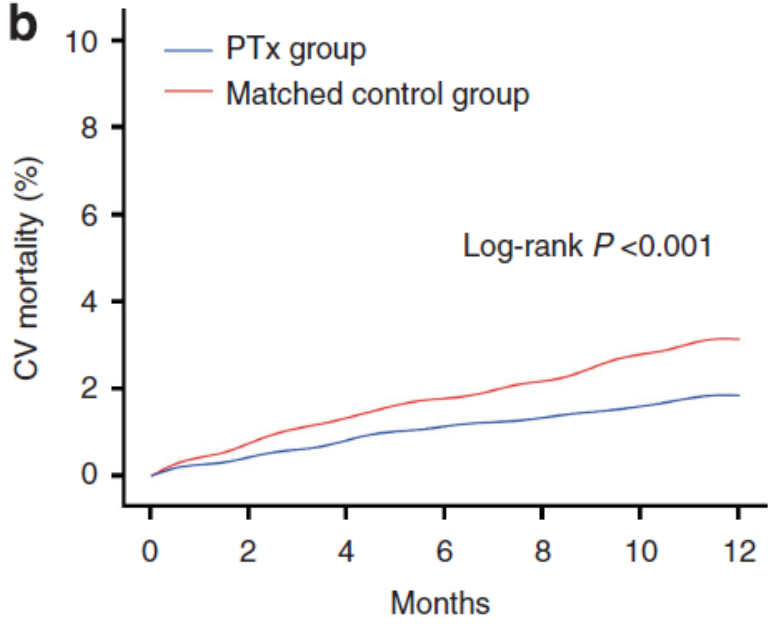
All-cause Mortality



Number at risk

PTx	4428	4395	4356	4317	4293	4270	4231
Control	4428	4378	4322	4274	4234	4189	4136

Cardiovascular Mortality



Number at risk

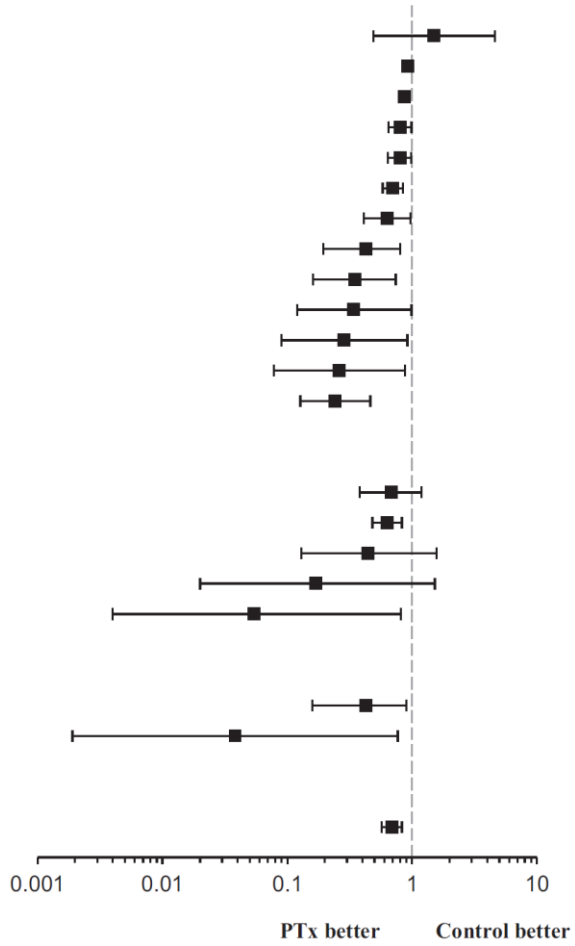
PTx	4428	4395	4356	4317	4293	4270	4231
Control	4428	4378	4322	4274	4234	4189	4136

PROPENSITY SCORE–MATCHED COHORT COMPARING PATIENTS WHO HAD UNDERGONE PTX WITH THOSE WHO HAD NOT UNDERGONE PTX

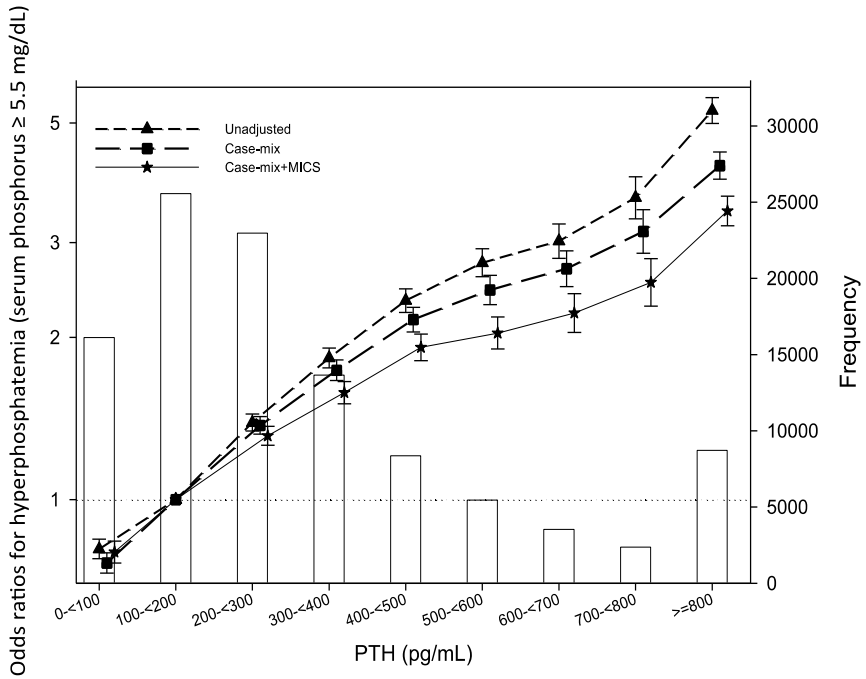
Komaba et al. Kidney International (2015) 88, 350 359

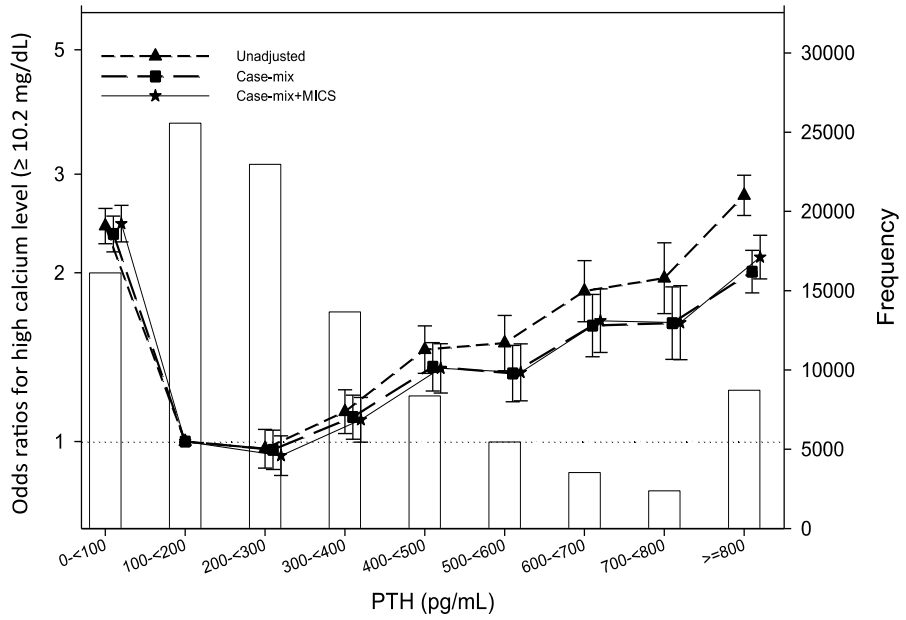
Associations among Parathyroidectomy (PTx) and all-cause Mortality, Cardiovascular Outcomes, and Fractures

	Region	PTx Total patients	Control Total patients	Relative Risk[a] (95% CI)
All-cause mortality				
Trombetti *et al.* [24]	Switzerland	40	80	
Li *et al.* [25]	China	53	92	
Kestenbaum *et al.* [26]	United States	4558	4558	
Ivarsson *et al.* [27▪▪]	Sweden	423	1234	
Ho *et al.* [28]	Taiwan	998	998	
Komaba *et al.* [29▪▪]	Japan	4428	4428	
Sharma *et al.* [30]	United States	150	1044	
Costa-Hong *et al.* [31]	Brazil	50	68	
Chen *et al.* [32]	Taiwan	161	354	
Ma *et al.* [33]	Taiwan	60	161	
Moldovan *et al.* (2015) [34]	Romania	26	26	
Iwamoto *et al.* [35]	Japan	88	88	
Goldstein *et al.* [36]	Brazil	123	128	
Cardiovascular mortality				
Sharma *et al.* [30]	United States	150	1044	
Komaba *et al.* [29▪▪]	Japan	4428	4428	
Ma *et al.* [33]	Taiwan	60	161	
Chen *et al.* [32]	Taiwan	161	354	
Iwamoto *et al.* [35]	Japan	88	88	
Cardiovascular events				
Costa-Hong *et al.* [31]	Brazil	50	68	
Lin *et al.* [37]	Taiwan	30	23	
Fracture				
Rudser *et al.* [38]	United States	5918	16328	



Tentori Clin J Am Soc Nephrol 10: 98 109, 2015

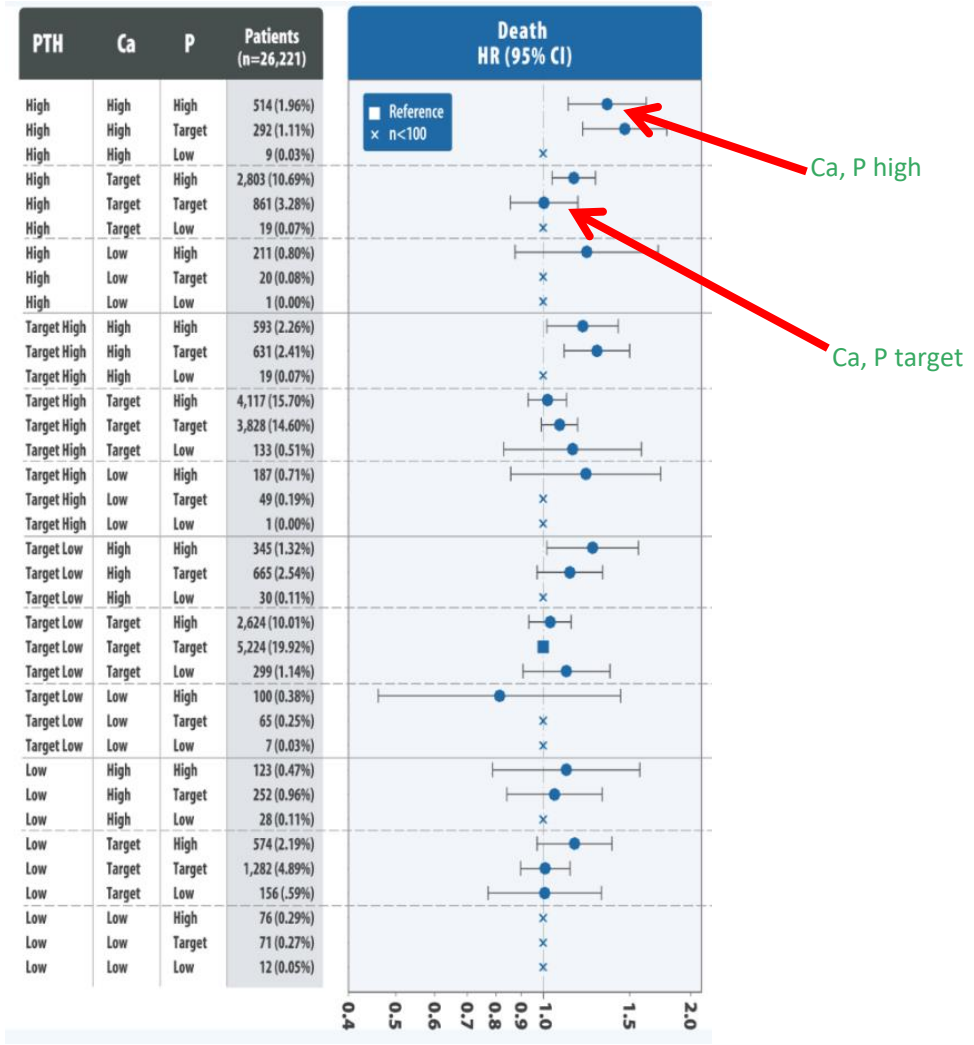




Li, et al. NDT 11 29 2012

Serial Assessment of PTH, Ca and P Considered Together

PTH high

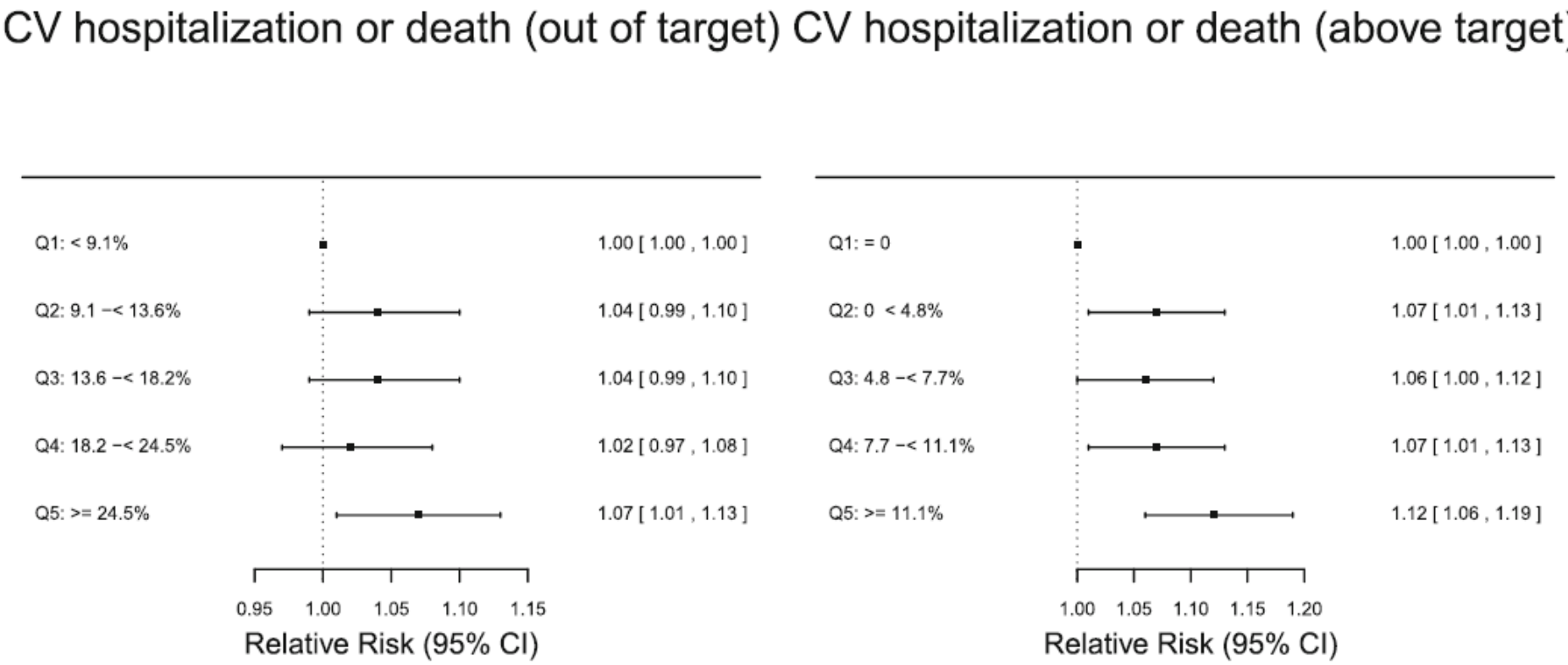


Ca, P high

Ca, P target

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

Facility-level CKD-MBD Composite Score and Risk of Adverse Clinical Outcomes



Block et al. BMC Nephrology (2016) 17:166

PQM Evidence Criteria

- There is a relationship between the healthcare process and the desired outcome
  - Process / Intermediate Outcome Measure: Demonstrated association between the measure focus and a material health outcome

CBE ID	Name
0256	Minimizing Long-term Catheters for Dialysis Access
0247	Kt/V Delivered Adequacy Above Minimum
1454	Proportion of Patients with Hypercalcemia

  - Outcome Measure: There is a demonstrated rationale for considering the measure focus, which is a material health outcome

CBE ID	Name
0369	Standardized Mortality Ratio for Dialysis Facilities
1463	Standardized Hospitalization Ratio for Dialysis Facilities
2979	Standardized Transfusion Ratio for Dialysis Facilities

Wrap-up

- Next Meeting, Monday, February 26th 1:00pm – 4:00pm EDT (10:00am – 1:00pm PDT)
- Overview of Topics
- Public Comment Period

Public Comment

ESRD Mineral and Bone Disorder

2024 Technical Expert Panel

February 26th, 2024

1:00-4:00 pm

Agenda

1:00 pm: Welcome and Attendance

1:10- 3:50pm: Discussion continued

3:50- 4:00pm: Public Comment

TEP Members

Name, Credentials, Professional Role*	Organizational Affiliation, City, State*	Conflict of Interest Disclosure*
Deborah Benner, MA, RDN, CSR Registered Dietician VP Clinical Support and Special Projects	DaVita Inc, Yorba Linda, CA	None Reported
Geoffrey Block, MD, FASN Nephrologist Medical Office, SVP Clinical Research	US Renal Care Golden, CO	Former Director at Ardelyx, Inc. with equity in company.
Paul T. Conway, BA Chair, Policy and Global Affairs Patient Advocate	American Association of Kidney Patients Tampa, FL	None Reported
Dinesh K. Chatoth, MD Nephrologist Associate Chief Medical Officer	Fresenius Medical Care Suwanee, GA	Employee and Stakeholder of Fresenius Medical Care
Barbara Fox, MS, MPH Patient Advocate	Yuba City, CA	None Reported
Edward V. Hickey President, AAKP Chair	American Association of Kidney Patients (AAKP) Tampa, FL	None Reported
Kamyar Kalantar-Zadeh, MD, MPH, PhD Nephrologist LA County Dept. Health Services	LA County Department of Health Services Harbor- UCLA Torrance, CA	None Reported

TEP Members

Name, Credentials, Professional Role*	Organizational Affiliation, City, State*	Conflict of Interest Disclosure*
Klemens Meyer, MD Nephrologist	Tufts Medical Center and Dialysis Clinic, Inc Boston, MA	Develops MBD decision support tools for DCI, but no financial interest.
Adrian Miller Patient Advocate	Vancouver, WA	None Reported
Lisa Modica, RD, BS Registered Dietician	Rogosin Institute Fort Lee, NJ	None Reported
Evan R. Norfolk, MD, MBA Nephrologist System Director for Nephrology	Geisinger Health System Danville, PA	Fresenius Pharmacy and Therapeutics Committee
Sherri Shivley Patient Advocate	Hamden, CT	None Reported
Francesca Tentori, MD, MS Nephrologist VP for Outcomes Research	DaVita, Inc Portland, TN	Employee of DaVita

UM- KECC Team

Name and Credentials	Organizational Affiliation	Conflict of Interest
Jonathan Segal, MD	Professor of Internal Medicine, Division of Nephrology University of Michigan, Kidney Epidemiology and Cost Center	None
Joseph Messana, MD	Professor of Internal Medicine, Division of Nephrology Research Professor, Health Management and Policy, University of Michigan, Kidney Epidemiology and Cost Center	None
Ananda Sen, PhD	Professor of Biostatistics and Research Professor University of Michigan, School of Public Health	None
Eric Young, MD, MS	Senior Research Scientist Arbor Research	None
Shu Chen, BS, MS	Senior Analyst University of Michigan, Kidney Epidemiology and Cost Center	None
Quinton Hazen, MPH	Intermediate Analyst University of Michigan, Kidney Epidemiology and Cost Center	None

UM- KECC Team

Name and Credentials	Organizational Affiliation	Conflict of Interest
Lan Tong, MS	Lead Analyst University of Michigan, Kidney Epidemiology and Cost Center	None
Jennifer Sardone, BA, PMP	Senior Lead Project Manager University of Michigan, Kidney Epidemiology and Cost Center	None
Jaclyn George, BA	Project Intermediate Manager University of Michigan, Kidney Epidemiology and Cost Center	None
Mimi Dalaly, MPH	Project Intermediate Manager University of Michigan, School of Public Health	None

CMS
Stephanie Clark, MD
Golden Horton, MS
Wilfred Agbenyikey, PhD

MBD Measure Concepts

Name	Description
Elevated Phosphorus AUC >2 vs. other chronic measurement Elevated phosphorus and not on binder	 Corresponds to a 6-mo average phosphorus value >6.5 Chronic phosphorus elevation paired with medication use
Elevated PTH Without evidence of treatment Evidence of overtreatment	Above some threshold Either medication use or parathyroidectomy Low PTH and concurrent medication use
Facility phenotype	2 of 3 (Ca/PO4/PTH) above threshold
Patient-reported outcome	

Voting

- Should the TEP continue discussion and development of a phosphorus-based measure?
  - Yes
  - No
- Should the TEP continue discussion and development of a PTH-based measure?
  - Yes
  - No
- Should the TEP continue discussion and development of a facility phenotype measure (2 of 3 out of range for Ca/PO4/PTH)?
  - Yes
  - No

Measure Specifications

- Measure Description:
- Numerator:
- Denominator:
- Risk Adjustment:
- Exclusion Criteria

Measure Specifications

- Measure Description:
- Numerator:
- Denominator:
- Risk Adjustment:
- Exclusion Criteria

Risk Adjustment

Potential factors for Risk Adjustment

- ADI
- Residing in Skilled Nursing Facility (SNF)
- Insurance status: Medicare Primary / Dual eligible / Commercial
- Race

Exclusion Criteria

Potential Exclusion Criteria

- Pediatric patients: Age < 18 ?
- Hospice?
- At facility fewer than 30 days
- ESRD treatment for < 90 days
- Minimum number of lab values:
- AKI
- Patients who have died or been discharged from facility prior to end of reporting month

Patient Choice / Patient Reported Outcome

Wrap-up

- Next Meeting, Wednesday, March 6th 1:00pm – 4:00pm EDT (10:00am – 1:00pm PDT)

Public Comment

Appendix