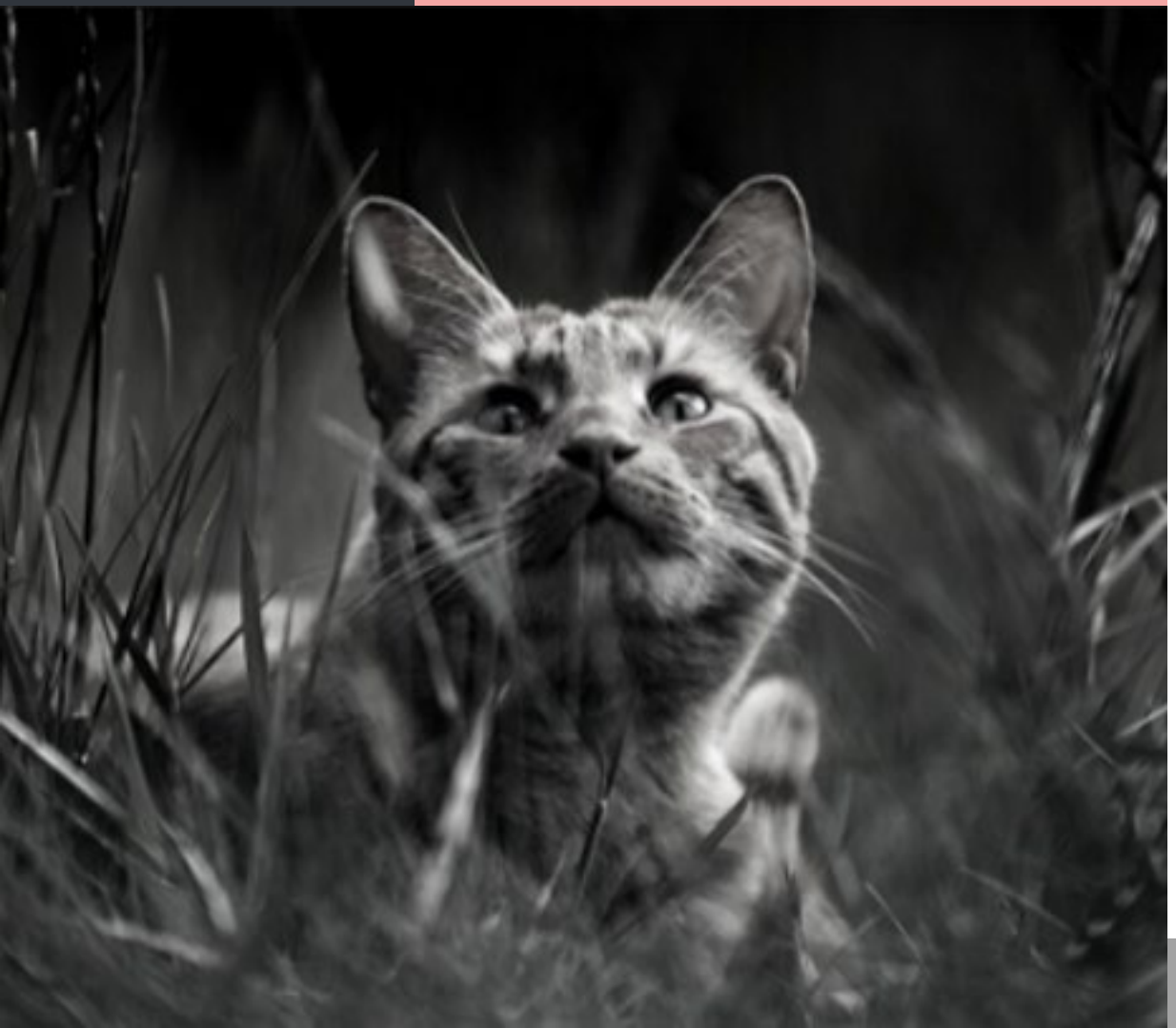


Rebekah Mack DVM, DACVIM-SAIM, M.S.Ed. (Candidate)

The CKD lifecycle: take it one “stage” at a time

+ Update on IDEXX FGF-23

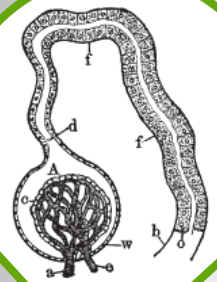
Learning Outcomes/Objectives

- Recall essential components of kidney function markers
- Describe the importance & limitations of GFR
- Describe current kidney diagnostics and practical application in health & disease
- Provide an overview on how CKD in cats can be seen as an independent lifecycle
- Review the standard methods for diagnosing, staging, treatment and monitoring of CKD patients
- Visit each stage of CKD as defined by the IRIS CKD guidelines: explore detailed assessment, treatment choices, prognosis, and client communications.
- Understand how early, and comprehensive care at each point in the Lifecyle of CKD can improve morbidity and mortality of cats with CKD
- Discern the right clinical case and timing to run an IDEXX FGF-23

Kidney biomarker evolution over time in medicine

Proteinuria

Described by Hippocrates 400 B.C.

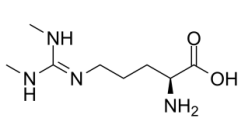


Creatinine

Jaffe reaction 1886

Glomerular Filtration Rate

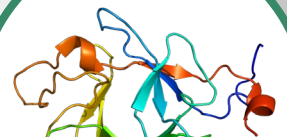
Cockcroft-Gault equation for estimating GFR in 1973



SDMA

SDMA first discovered in brain tissue 1971 (Nakama et al)

ADMA → SDMA noted to be associated with GFR clearance (Mcdermot et al 1976)



FGF-23

Identified in early 1980's (Brown et al)

Extensive research in cancer, Vit D dysregulation, CKD, and cardiac disease.

Acute Kidney Injury

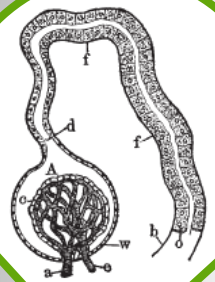
Extensive human literature from 1940's to now. Detects both active and acute kidney injury

NGAL,VGEF, Clusterin, Inosine, MRNA, RBP…

Veterinary adoption and application of kidney biomarkers

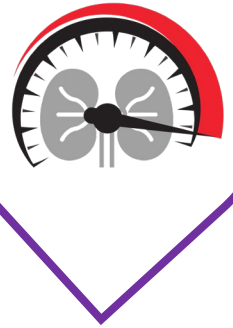
Proteinuria

- UA chemistry evaluation
- UPC ratio
- Reference Laboratory or Point-of Care



Creatinine

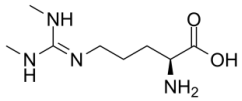
- Jaffe reaction + Enzymatic
  (Lab Dependent)
- Reference Laboratory or Point-of-Care



Glomerular Filtration Rate

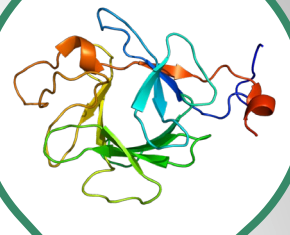
"GFR not a gold, but a gold-plated standard"

- Body size, GFR may be influenced by age, gender or breed. While some studies have demonstrated an influence of age on GFR (Quex et al, Hiac et al 2007, Bexfield, 2008)
- Surrogate markers can represent GFR at points in time with moderate accuracy (CREA, BUN) (Gleadhill 1994, Finco et al 1995)



IDEXX SDMA

- Validated & established in cats and dogs for use 2014 & 2015 (Hall et al 2014, Nabity et al 2015)
- Surrogate marker for GFR in normal and abnormal function
- Specific use case expansion



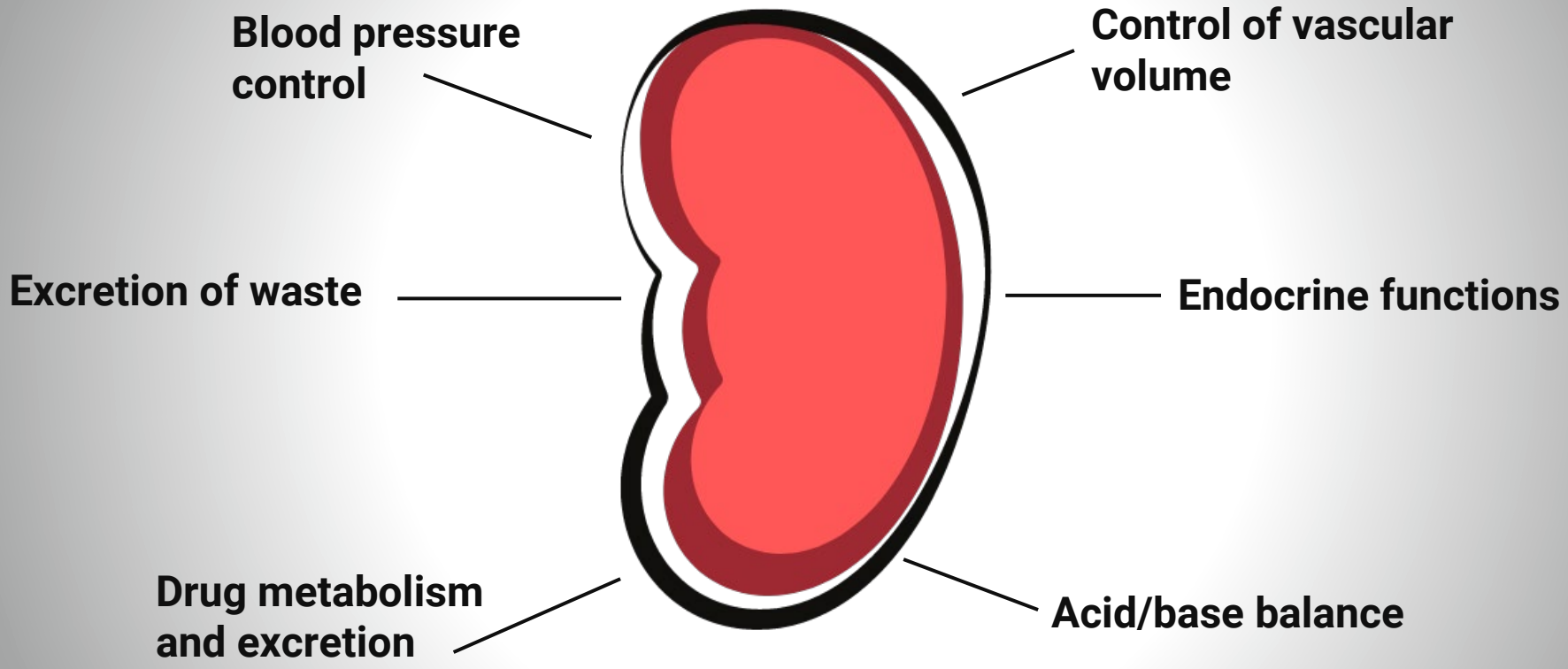
IDEXX FGF-23

- Validated at RVC in 2013 for felines focused on CKD and phosphate reduction treatment (Finch et al 2013, Geddes et al 2013 & 2015)
- Renal Management Marker - Launched in North America for felines with chronic kidney disease 2022

Acute Kidney Injury

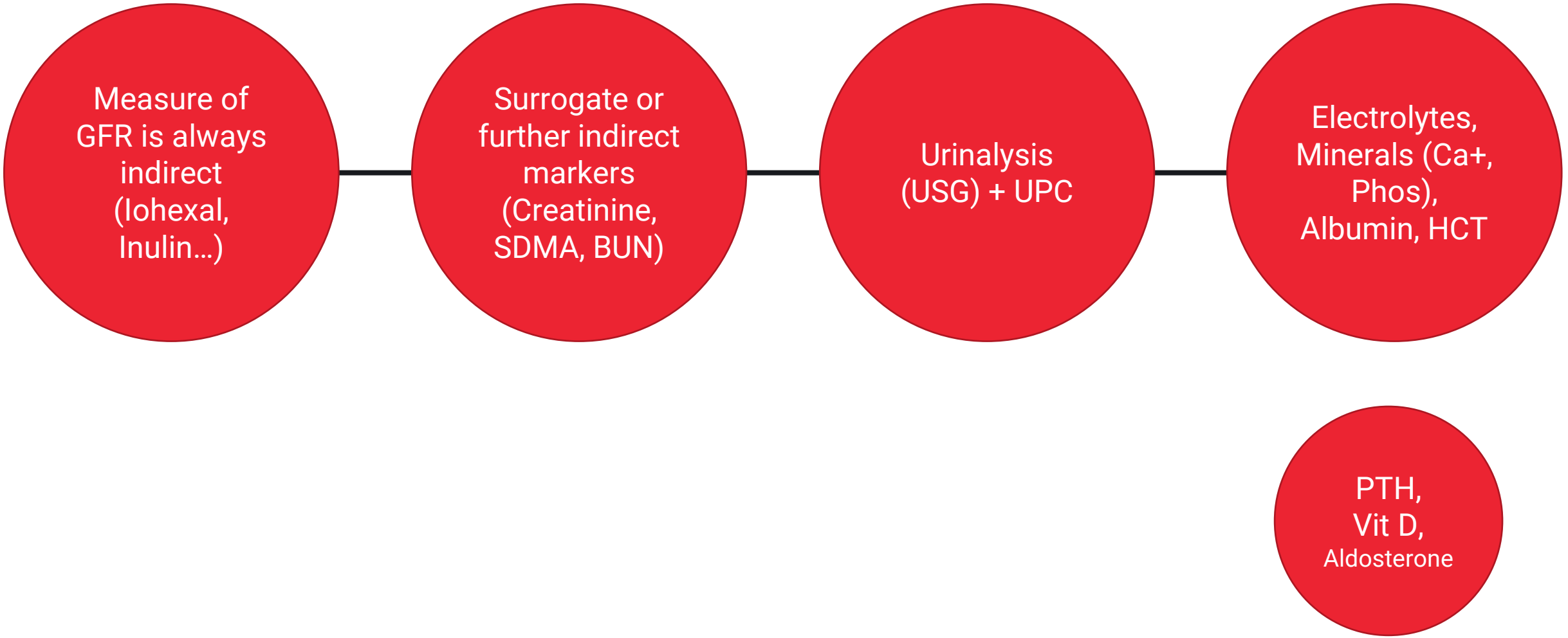
- Many, many, active kidney injury markers have been investigated – primarily tubular and some glomerular
- NGAL is a primary area of focused discovered in the 1940's and has continued to be used in research though with limited commercial application.
- In veterinary medicine the focus has been on NGAL, urine clusterin, Kim-1, and Cystatin B

Level set on the importance of the kidney for daily function



Robertson SA, Gogolski SM, Pascoe P, Shafford HL, Sager J, Griffenhagen GM. AAFP Feline anaesthetic Guidelines. *Journal of Feline Medicine and Surgery*. 2018;20(7):602-634. doi:10.1177/1098612X18781391

Kidney function is defined by GFR and the methods in which we measure it in clinical practice



“GFR not a gold, but a gold-plated standard”

60+ GFR measurement publications for cats and dogs

1991 - 2022

15+ methods of measurement

- Renal & Plasma Inulin clearance
- Creatinine Clearance
- Plasma iohexal
- Plasma inulin
- Estimated GFR iohexal
- Renal Scintigraphy

N Value from 5 -97 (control & CKD/AKI)
*majority < 30

- GFR specific (method)
- GFR & Disease State
- GFR & Disease State & Treatment

Renal Populations:
Controls
CKD/AKI (natural & induced)
Convenience Samples

- GFR in CKD (cats & dogs)
  - Diagnostic Capacity
  - Comparison of Surrogate markers
  - GFR + Disease + Therapy
- GFR in AKI

Von Hendy-Willson VE, Pressler BM. An overview of glomerular filtration rate testing in dogs and cats. Vet J. 2011 May;188(2):156-65. doi: 10.1016/j.tvjl.2010.05.006. Epub 2010 Jun 11. PMID: 20541957; PMCID: PMC2980797
Michael H, Szlosek D, Clements C, Mack R. Symmetrical Dimethylarginine: Evaluating Chronic Kidney Disease in the Era of Multiple Kidney Biomarkers. Vet Clin North Am Small Anim Pract. 2022 May;52(3):609-629. doi: 10.1016/j.cvsm.2022.01.003. Epub 2022 Apr 1. PMID: 35379500..

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- Plasma inulin
- Estimated GFR iohexal
- Renal Scintigraphy

There is no single protocol or methodology for measurement of GFR

Methodology can affect the results and can cause substantial differences in measured GFR

- 1.38 to 4.85 mL/min/kg for dogs
- 0.85 to 3.05 mL/min/kg for cats

Measuring GFR is often cumbersome in clinical practice

Von Hendy-Willson VE, Pressler BM. An overview of glomerular filtration rate testing in dogs and cats. Vet J. 2011 May;188(2):156-65. doi: 10.1016/j.tvjl.2010.05.006. Epub 2010 Jun 11. PMID: 20541957; PMCID: PMC2980797
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“GFR not a gold, but a gold-plated standard”

Definition for control can vary

- Clinical Healthy
- Convenience Sample
- Senior Patients (Cats)

Methodology of GFR varies

- Iohexal
- Inulin
- Scintigraphy

Methodology of surrogate marker measurement varies

- Creatinine (Jaffe versus Enzymatic)
- SDMA (LCMS, Immunoassay, ELISA)

N Value from 5 -97 (control & CKD/AKI)
*majority < 30

- GFR specific (method)
- GFR & Disease State
- GFR & Disease State & Treatment

Renal Populations:
Controls
CKD/AKI (natural & induced)
Convenience Samples

- GFR in CKD (cats & dogs)
  - Diagnostic Capacity
  - Comparison of Surrogate markers
  - GFR + Disease + Therapy
- GFR in AKI
- Retrospective more common

Von Hendy-Willson VE, Pressler BM. An overview of glomerular filtration rate testing in dogs and cats. Vet J. 2011 May;188(2):156-65. doi: 10.1016/j.tvjl.2010.05.006. Epub 2010 Jun 11. PMID: 20541957; PMCID: PMC2980797
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My lightbulb moment for understanding GFR

ml

Volume of blood in the animal IE dehydration or volume expansion with fluids

min

Rate at which blood is moving into the kidney and glomerulus IE hypertension

kg

The size of the cat or dog IE larger has lower and smaller has higher baseline GFR

Additive value of diagnostics for the kidney function dampen the limitations of individual components

Surrogate Biomarkers

Urinalysis + Protein (UPC)

Electrolytes Mineral HCT

Repeated Evaluation "Trending"

Ultrasound
CT
Fluoroscopy

Blood Pressure

FGF-23
PTH
Aldosterone

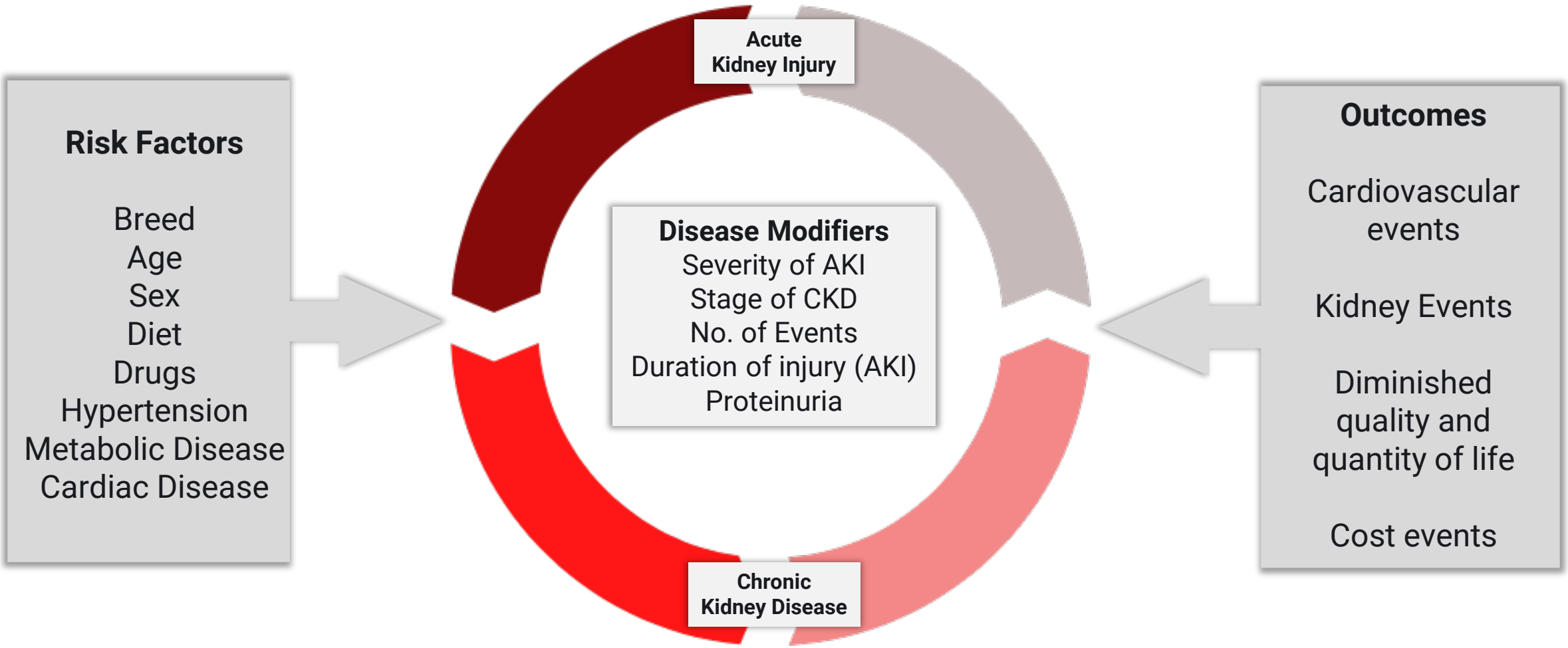
To get the most consistent repeated evaluation

Subject Specific – Individualized care

Early diagnosis & intervention

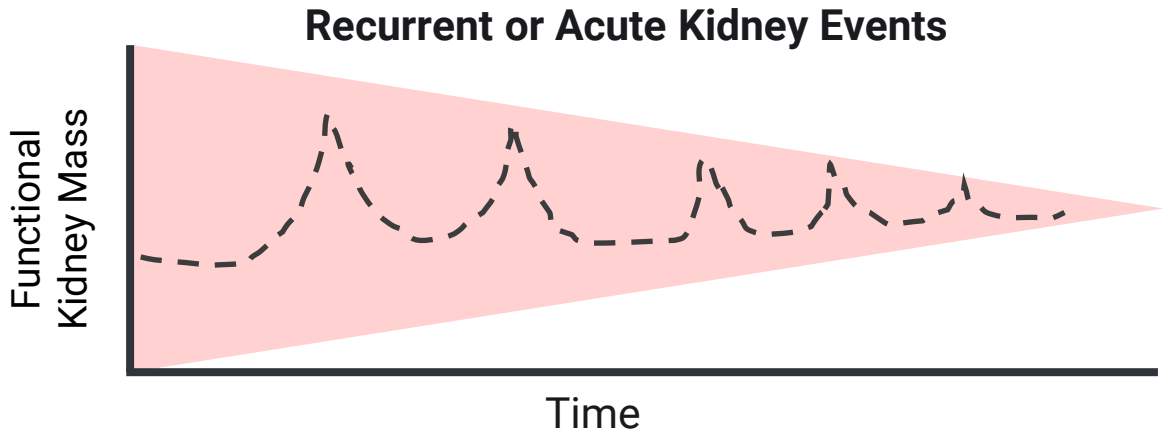
Continuum of Kidney Health

Kidney function and disease is defined by risk factors, injury, and outcomes

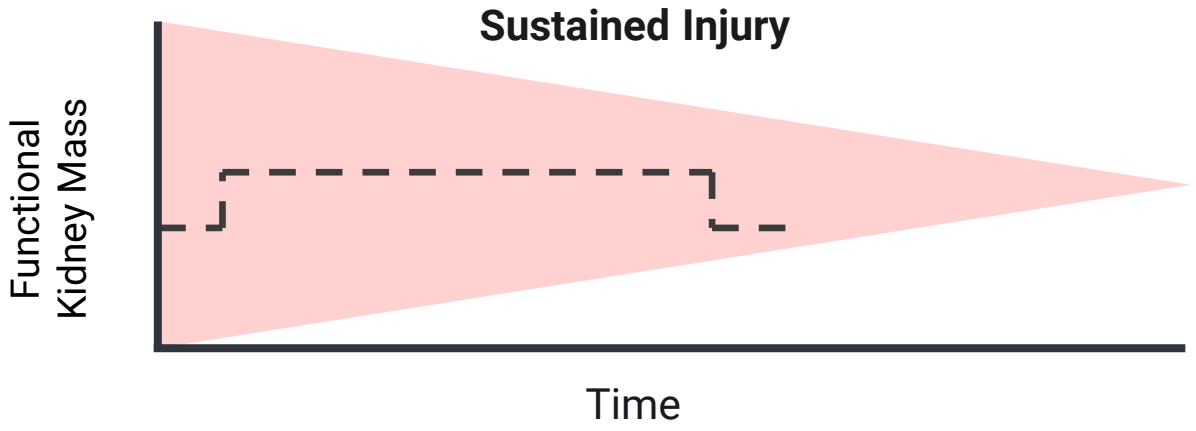


Chawla, Lakhmir S., Eggers, Paul W., Star, Robert A., Kimmel, Paul L. Acute Kidney Injury and Chronic Kidney Disease as Interconnected Syndromes. 2014 NEJM: 58-66; https://www.nejm.org/doi/full/10.1056/NEJMra1214243

Acute Kidney Event/Insult – Recurrent versus Sustained

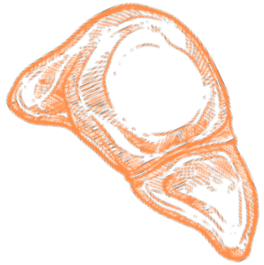


- Infection, Infectious Disease
- Toxicities
- Anesthesia
- Obstructive Disease (Urethral)
- Comorbidities – pancreatitis, chronic GI disease



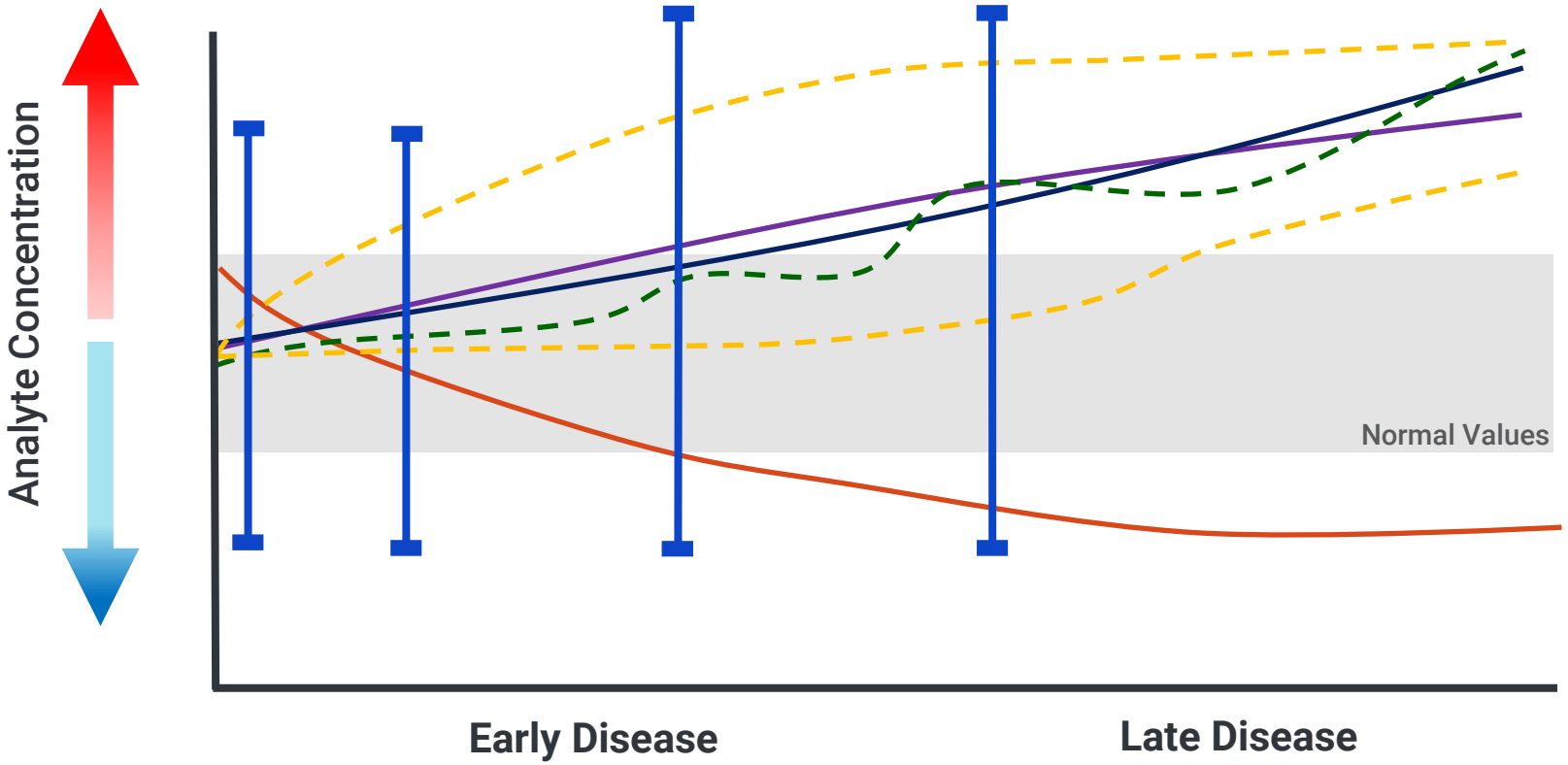
- Infection Recurrent/unresolved
- Infectious Disease
- Toxicities – medications (NSAIDs)
- Obstructive Disease (Ureteral)
- Comorbidities – Cardiac Disease

Comorbidities or disease states can heavily impact kidney health and management

Heart Disease	Liver disease	Gastrointestinal Disease	Endocrinopathy	Infectious
				
Cardiorenal or Renocardial Syndrome	**Hepatic Disease, Congestion**	**Inflammatory effect, hypoproteinemia**	**Hormone imbalance, catabolic state**	**Inflammatory/Immune Acute or Chronic**
NT-proBNP Troponin SDMA	CRP Iron	CRP Microbiome	Aldosterone PTH Vitamin D Iron	Regional infectious testing Leishmaniasis Ehrlichiosis Lyme Disease

*suppor citation listed in bibliography

Kidney injury markers could provide a more holistic understanding of kidney health in combination with current biomarkers



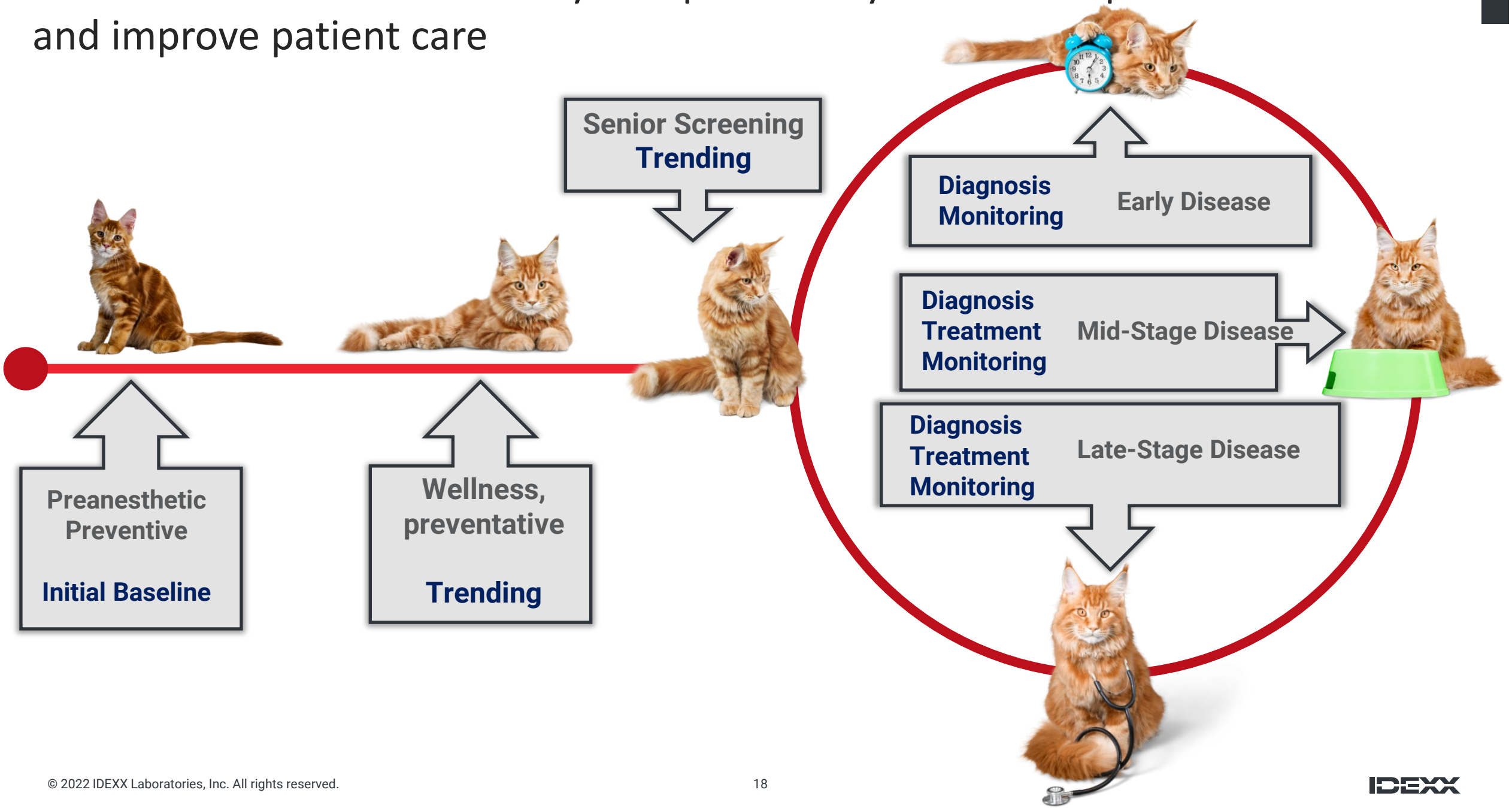
SDMA
Creatinine
BUN

Proteinuria (multiple trajectories in disease)
USG

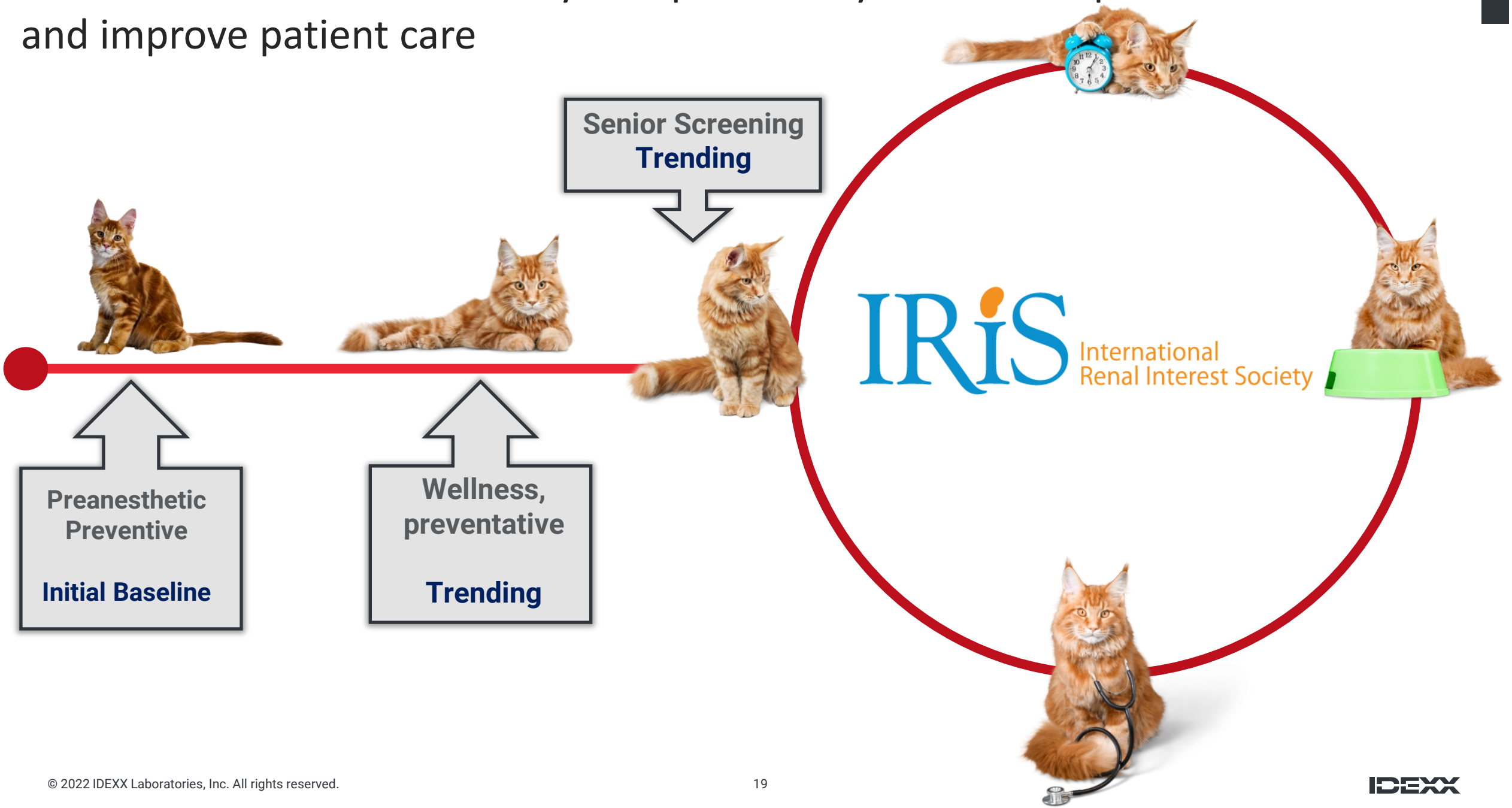
*support citation listed in bibliography

CKD -Lifecycle

Over the lifetime of animal key timepoint analysis could help individualize and improve patient care



Over the lifetime of animal key timepoint analysis could help individualize and improve patient care



The high points of CKD Diagnosis

Physical Exam

Kidney Palpation
Muscle Mass
Cardiac Auscultation

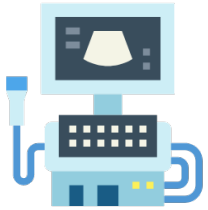
Medical History

Appetite- Weight loss
Energy
Water consumption

Diagnostics: Lab work

Chemistry
Urinalysis

Imaging



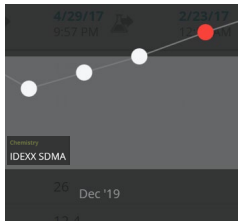
Radiographs
Ultrasound

Clinical Decision Points

diagnostics for diagnosing CKD

Biochemistry

- Trended Values



- Persistent SDMA

Chemistry Click to view Differentials	11/14/17 3:42 AM	2/3/17 2:21 AM	11/5/16 2:53 AM
Glucose	87	84	75
IDEXX SDMA Learn More	g 15	j 15	k 17
Creatinine	1.9	1.4	1.4

- Value above the reference interval

Chemistry Click to view Differentials	6/16/17 12:28 AM	5/26/17 3:04 PM
Glucose	94	97
IDEXX SDMA Learn More	t 20	x 17 ab
Creatinine	2.7	2.8

Urinalysis

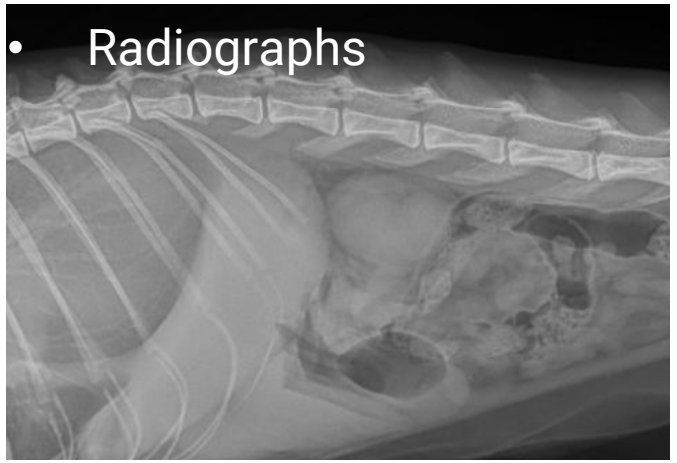
- Feline 1.035 – 1.008

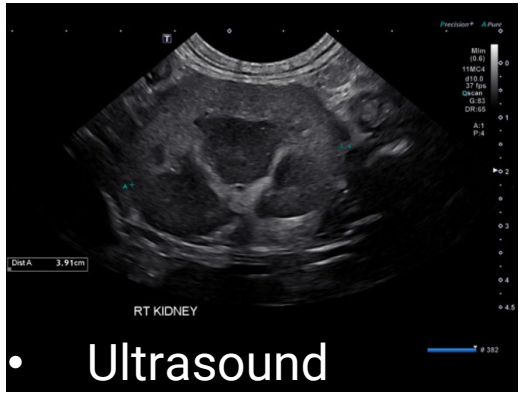
OTHER	CYSTOCENT...	CYSTOCENT...	CYSTOCENT...
YELLOW	YELLOW	YELLOW	STRAW
CLEAR	CLEAR	CLEAR	HAZY
1.030	1.030	1.049	1.039
5.5	5.5	6.0	6.0
1+	g TRACE	h NEGATIVE	i NEGATIVE

- Persistent Proteinuria

Imaging

- Radiographs

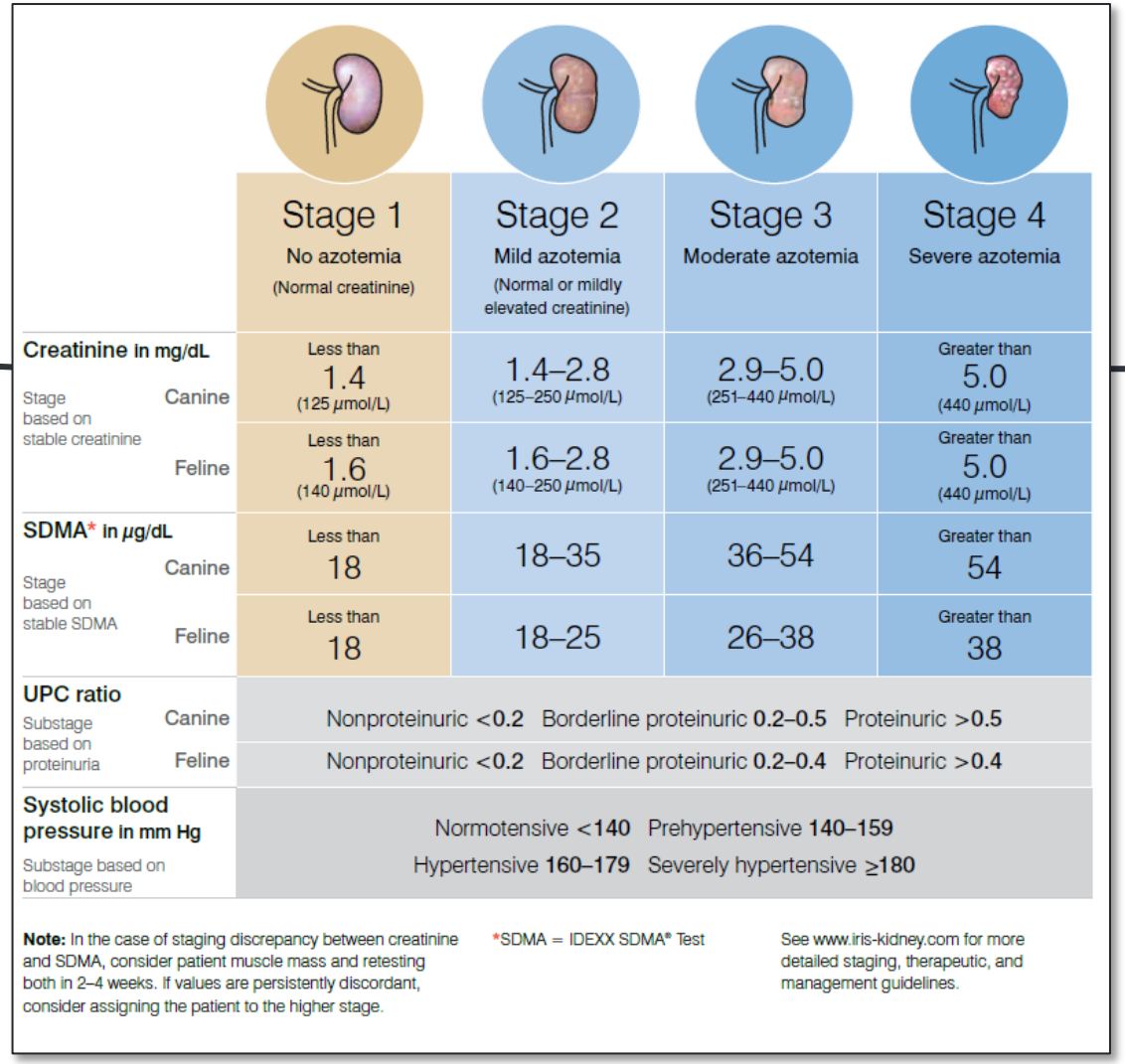




- Ultrasound

Staging CKD using the IRIS guidelines

Diagnosis



	Stage 1 No azotemia (Normal creatinine)	Stage 2 Mild azotemia (Normal or mildly elevated creatinine)	Stage 3 Moderate azotemia	Stage 4 Severe azotemia
Creatinine in mg/dL Stage based on stable creatinine — Canine	Less than 1.4 (125 µmol/L)	1.4–2.8 (125–250 µmol/L)	2.9–5.0 (251–440 µmol/L)	Greater than 5.0 (440 µmol/L)
Feline	Less than 1.6 (140 µmol/L)	1.6–2.8 (140–250 µmol/L)	2.9–5.0 (251–440 µmol/L)	Greater than 5.0 (440 µmol/L)
SDMA* in µg/dL Stage based on stable SDMA — Canine	Less than 18	18–35	36–54	Greater than 54
Feline	Less than 18	18–25	26–38	Greater than 38
UPC ratio Substage based on proteinuria — Canine	Nonproteinuric <0.2	Borderline proteinuric 0.2–0.5	Proteinuric >0.5	
Feline	Nonproteinuric <0.2	Borderline proteinuric 0.2–0.4	Proteinuric >0.4	
Systolic blood pressure in mm Hg Substage based on blood pressure	Normotensive <140	Prehypertensive 140–159	Hypertensive 160–179	Severely hypertensive ≥180

Note: In the case of staging discrepancy between creatinine and SDMA, consider patient muscle mass and retesting both in 2–4 weeks. If values are persistently discordant, consider assigning the patient to the higher stage.

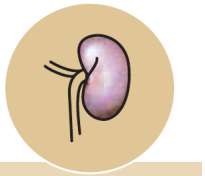
SDMA = IDEXX SDMA Test

See www.iris-kidney.com for more detailed staging, therapeutic, and management guidelines.

Therapy

http://www.iris-kidney.com/guidelines/index.html

Stage 1 considerations:



IRIS International Renal Interest Society

		Stage 1 No azotemia (Normal creatinine)
Creatinine in mg/dL		
Stage based on stable creatinine	Canine	Less than 1.4 (125 µmol/L)
	Feline	Less than 1.6 (140 µmol/L)
SDMA* in µg/dL		
Stage based on stable SDMA	Canine	Less than 18
	Feline	Less than 18

Can still use USG, imaging proteinuria, to diagnose just biomarkers to stage

***persistent and stable**

- ❑ Blood Pressure
- ❑ Proteinuria

Treatment:

- Pre/Post Renal
- Comorbidities
- UPC > 0.4 x 2
- BP > 160 mmhg
- Phos > 4.6
- Free water
- Review Anesthetic Choices
- Avoid Nephrotoxic Drugs

Monitor

- CREA/SDMA
- Phosphorus
- Urinalysis
- Serial Weights

Diet?

IDEXX

Let’s take a second to dig into the diet discussion

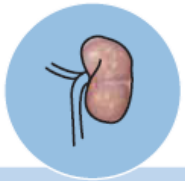
Early versus Moderate

Protein

Phosphorus

Stage 2 considerations:

IRIS International Renal Interest Society



Stage 2
Mild azotemia (Normal or mildly elevated creatinine)
Creatinine in mg/dL
Canine: 1.4–2.8 (125–250 µmol/L)
Feline: 1.6–2.8 (140–250 µmol/L)
SDMA* in µg/dL
Canine: 18–35
Feline: 18–25

Stage based on stable creatinine

Stage based on stable SDMA

Can still use USG, imaging proteinuria, to diagnose just biomarkers to stage

***persistent and stable**

- ❑ Blood Pressure
- ❑ Proteinuria

Treatment:

- Pre/Post Renal
- Comorbidities
- UPC > 0.4 x 2
- BP > 160 mmhg
- Phos > 4.6
- Hypokalemia
- Free water
- Review Anesthetic Choices
- Avoid Nephrotoxic Drugs

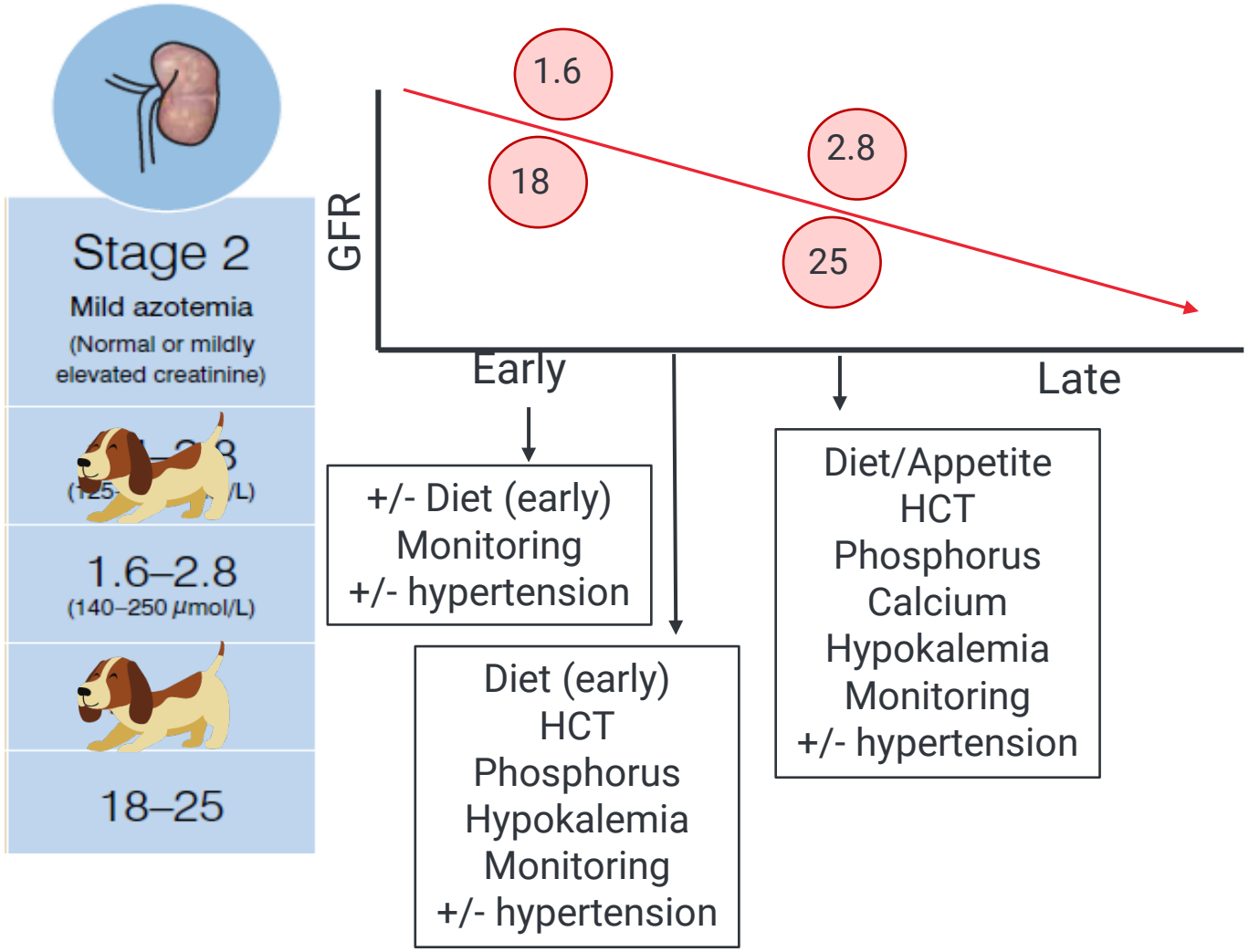
Monitor

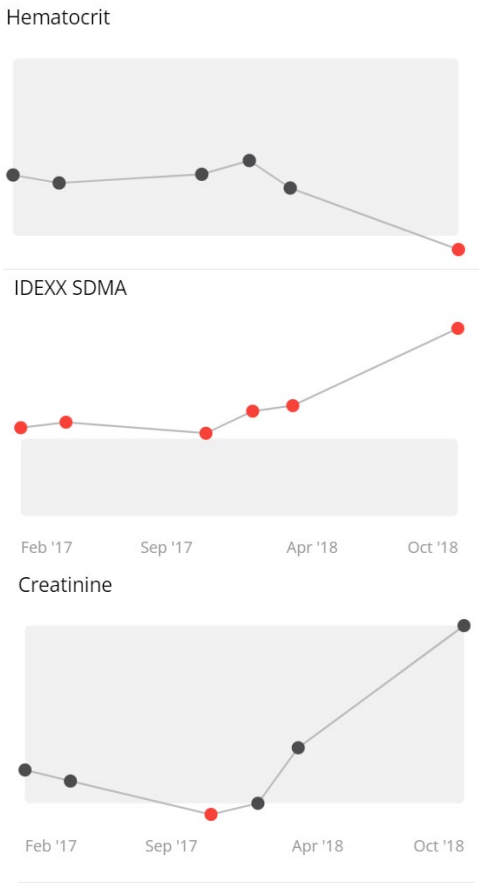
- CREA/SDMA
- Phosphorus
- Urinalysis
- PCV/TS
- Serial Weights

Diet?

IDEXX

Some additional Stage 2 notes





Trending:

- Phosphorus
- Potassium
- Calcium

Progressive, Irreversible

- Recheck every 6 months
- Renal Profile & PCV

Sidebar on managing hypertension

How to blood pressure:

- Quiet, with owner present
- No sedation allow 5-10 minutes to acclimatize
- Gently restrained, ventral or lateral recumbency
- Cuff width should be approximately 30%-40% of circumference of the cuff site, limb or the tail
- Train your technicians!
- First measurement should be discarded, 5-7 consecutive consistent values, BP trends downward as the process continues.
- Average all remaining values to obtain the BP measurement.
- Record (cuff and limb)!

When to treat:

- Systolic pressure >160mmhg (repeated)
- Evidence end organ damage
  - Retinal Changes
  - Increasing kidney biomarkers
  - Cardiac
  - Neurologic

How to treat:

Hypertension Alone (no proteinuria)

- Amlodipine (0.625mg PO Q24)
- Telmisartan (Semintra™) – off label for hypertension alone (1.5-2mg/kg/day)

Hypertension + proteinuria

- Telmisartan
- Amlodipine + ACEI (Benazepril, Enalapril)

★Amlodipine maybe more appropriate for cats >200mmhg (acute presentation)

★Telmisartan increases in effectiveness over 28 days

How to monitor:

Blood Pressure

Acute Hypertension Hospitalization:

- Amlodipine Q2-4hrs after initial administration
- Q12 once stabilized in hospital
- Recheck at 48 hours post discharge

Starting Parental Therapy

- Amlodipine +/- ACEi 48hr-7 days
- Telmisartan 14 and 28 days
- Every 3-4 months

Renal Profile

- 2-4 weeks after starting therapy
- Every 6 months on therapy

Acierno, MJ, Brown, S, Coleman, AE, et al. ACVIM consensus statement: Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats. *J Vet Intern Med*. 2018; 32: 1803– 1822. https://doi.org/10.1111/jvim.15331
Coleman, AE, Brown, SA, Traas, AM, Bryson, L, Zimmering, T, Zimmerman, A. Safety and efficacy of orally administered telmisartan for the treatment of systemic hypertension in cats: Results of a double-blind, placebo-controlled, randomized clinical trial. *J Vet Intern Med*. 2019; 33: 478– 488. https://doi.org/10.1111/jvim.15429
Glaus, TM, Elliott, J, Herberich, E, Zimmering, T, Albrecht, B. Efficacy of long-term oral telmisartan treatment in cats with hypertension: Results of a prospective European clinical trial. *J Vet Intern Med*. 2019; 33: 413– 422. https://doi.org/10.1111/jvim.15394

Sidebar on proteinuria in cats

How to measure UPC?

- Uncontaminated samples are appropriate – don't need to be pooled
- Free-catch, cystocentesis
- Microscopic blood contamination won't affect
- UPC > 0.4, serial sample within 2-4 weeks
- 2x samples >0.4 IRIS
- Rule out: neoplasia, infectious disease
- Significant UPC >1.0 should be followed up with more haste

When to treat:

- 2x samples > 0.4 IRIS

How to treat:

Hypertension Alone (no proteinuria)

- Benazapril
- Telmisartan (Semintra™)

Both are well supported by literature

Looking for 25-50% reduction in UPC if < 2.0

How to monitor:

Recheck UPC 10-14 days after starting or changing

UPC every 6 months

Renal Profile

- 2-4 weeks after starting therapy or changing therapy
- Every 6 months on therapy

Acierno, MJ, Brown, S, Coleman, AE, et al. ACVIM consensus statement: Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats. *J Vet Intern Med*. 2018; 32: 1803– 1822. https://doi.org/10.1111/jvim.15331
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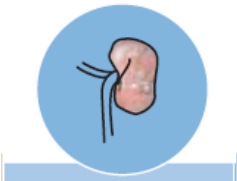
As you approach Stage 3 – several categories of medication to consider

Appetite Stimulant	Anti-emetic	Phosphate binder	Potassium supplementation	RBC stimulant
Mirtazapine 5HT2c receptor antagonist	Mirtazapine 5HT2c receptor antagonist	Aluminum Hydroxide	OTC formations	Darbepoetin
Capromorelin (Elura®) ghrelin receptor agonist	Maropitant (Cerenia®) NK-1 Emetic center, CRTZ, GI			
Cyproheptadine serotonin and histamine antagonist	Ondansetron 5HT3 CRTZ and GI afferent			

ISFM Consensus Guidelines on the Diagnosis and Management of Feline Chronic Kidney Disease. Journal of Feline Medicine and Surgery (2016) 18, 219–239

Stage 3 considerations:

IRIS International Renal Interest Society



Stage 3 Moderate azotemia	
Creatinine in mg/dL	
Stage based on stable creatinine — Canine	2.9–5.0 (251–440 µmol/L)
Feline	2.9–5.0 (251–440 µmol/L)
SDMA* in µg/dL	
Stage based on stable SDMA — Canine	36–54
Feline	26–38

***persistent and stable**

- ❑ Blood Pressure
- ❑ Proteinuria

Treatment:

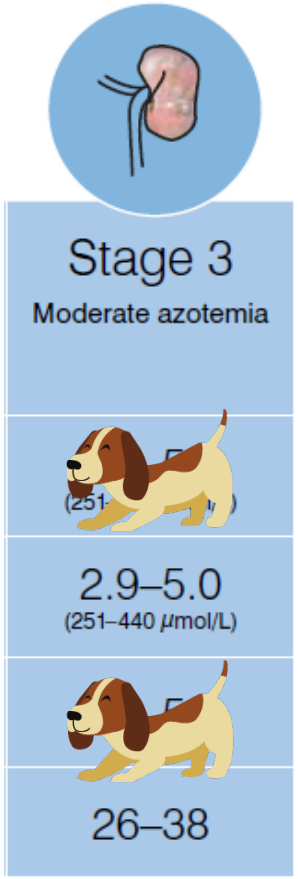
- Pre/Post Renal
- Comorbidities
- UPC > 0.4 x 2
- BP > 160 mmhg
- Phos > 5.0
- Hypokalemia
- Free water
- Review Anesthetic Choices
- Avoid Nephrotoxic Drugs

Monitor

- CREA/SDMA
- Phosphorus
- Urinalysis
- Potassium
- HCT/PCV
- Serial Weights

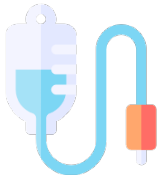
IDEXX

Stage 3, managing comfort and acute on chronic events



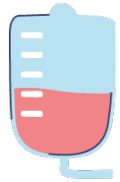
Maintenance

- Appetite Stimulant
- Phosphorus
  - Food & Binders
- Potassium
  - Supplements
- Acidosis
  - Supplements



SQ fluids

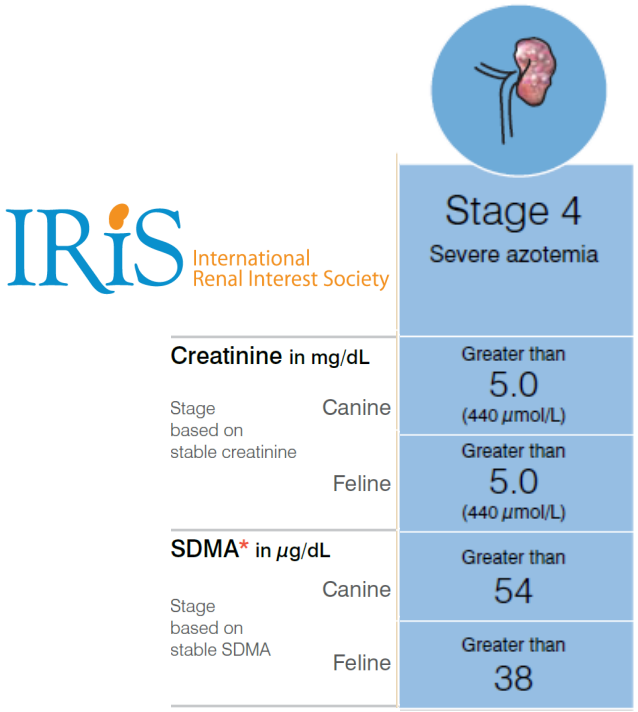
- Case dependent
- Risk Factors
  - Cardiac
- ¼ shock dose
  - IE 5kg cat (90ml x kg) 315mls so 80mls at least
- Fluid choice
  - LRS or 0.45% Nacl (+ K+)
- Exceed animal's patience
- Quality animal owner bond



RBC support

- Acute on Chronic
  - Transfusion is one the best things you can do – appetite, oxygen, energy level
- Blood Transfusion
  - Type
  - pRBC, WB (4 hours)
  - Xenotransfusions
- Darbepoetin
  - If you need to transfuse you likely need to treat
  - <20% but downward trend < 30 or <25 acute presentation

Stage 4 considerations:



IRIS International Renal Interest Society

		Stage 4 Severe azotemia
Creatinine in mg/dL		
Stage based on stable creatinine	Canine	Greater than 5.0 (440 µmol/L)
	Feline	Greater than 5.0 (440 µmol/L)
SDMA* in µg/dL		
Stage based on stable SDMA	Canine	Greater than 54
	Feline	Greater than 38

- ❑ Blood Pressure
- ❑ Proteinuria

Treatment:

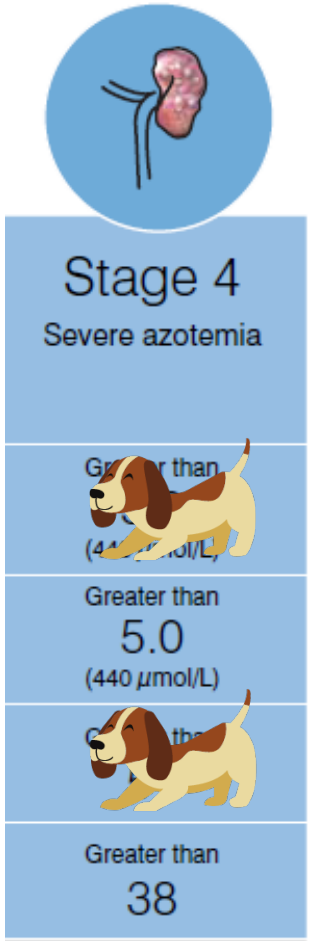
- Acute on Chronic
- Comorbidities
- UPC > 0.4 x 2
- BP > 160 mmhg
- Phos > 6.0
- Hypokalemia
- Free water
- Review Anesthetic Choices
- Avoid Nephrotoxic Drugs

Monitor

- CREA/SDMA
- Phosphorus
- Urinalysis
- Potassium
- HCT/PCV
- Serial Weights

IDEXX

Nutritional and fluids support

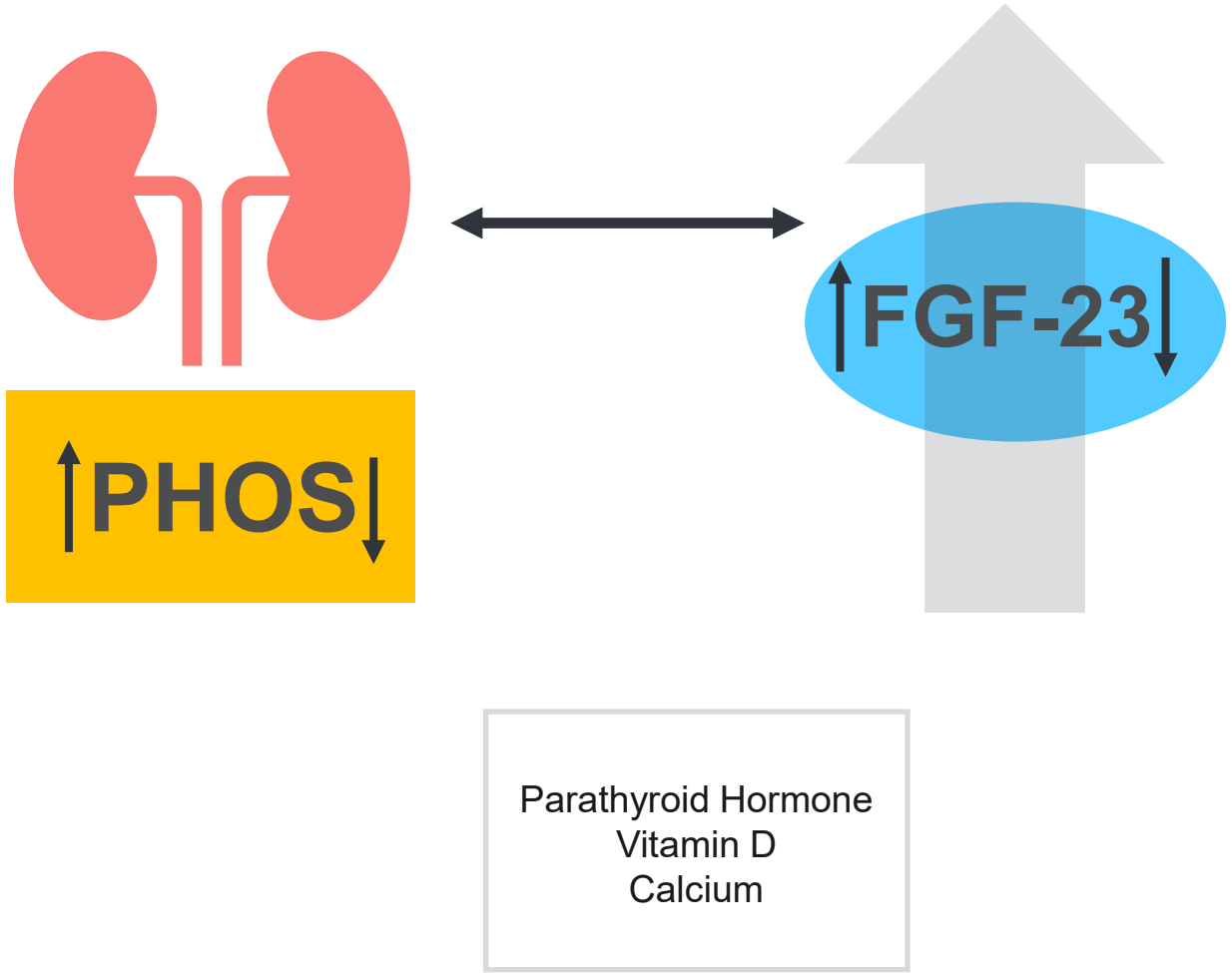


Feeding Tube:

- Esophageal
- Gastric

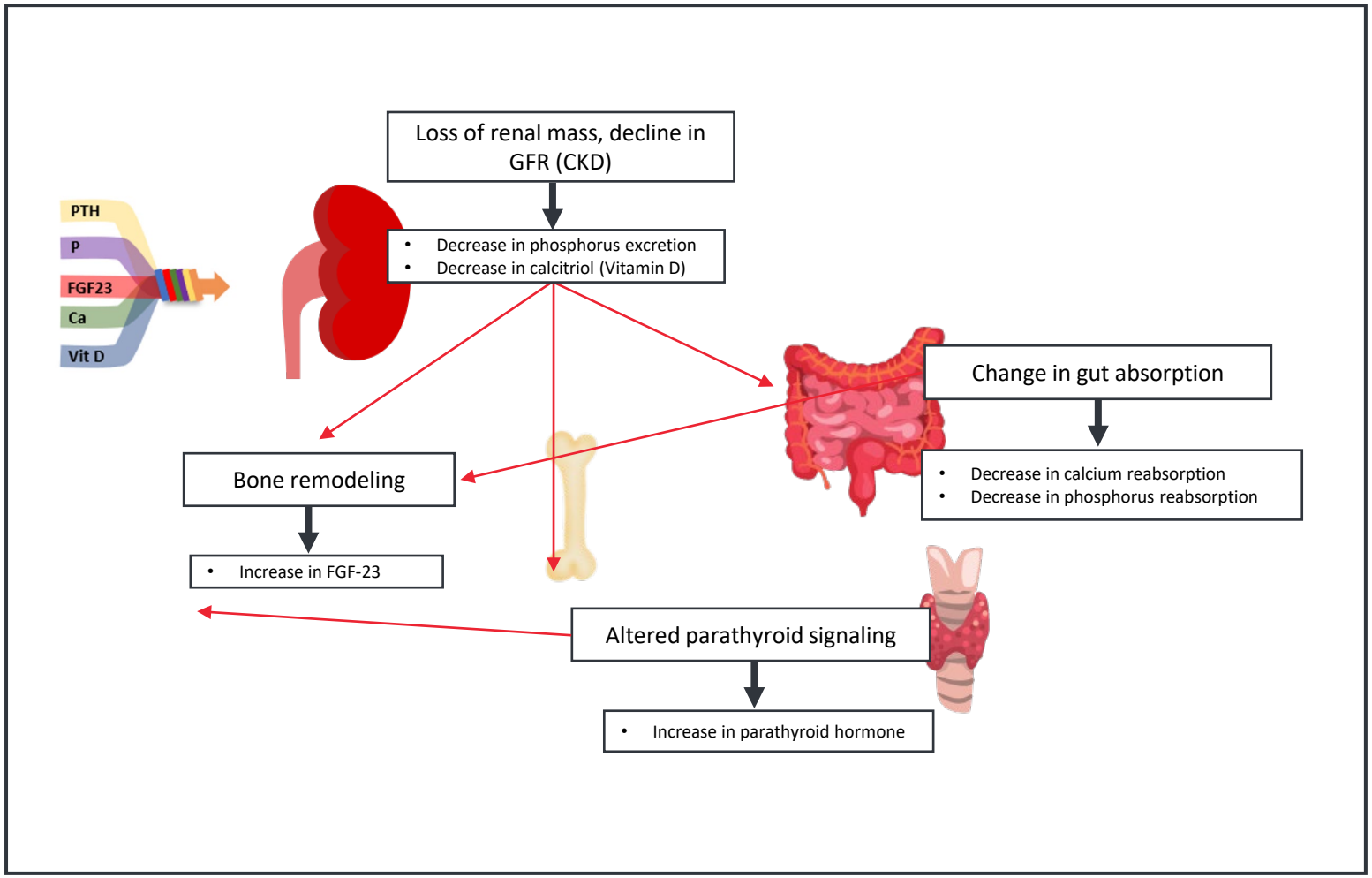
IDEXX FGF-23 Feline Kidney Management Marker

Phosphorus and FGF-23 feedback loop but not a linear relationship



- Main action at kidneys
- PHOS and FGF-23 have a feedback loop
- PHOS is easily and routinely measured but slower to show disease change and influenced by other comorbidities or medications
- FGF-23 can be an earlier indication for intervention in CKD in cats

Simplified metabolism of FGF-23 in CKD



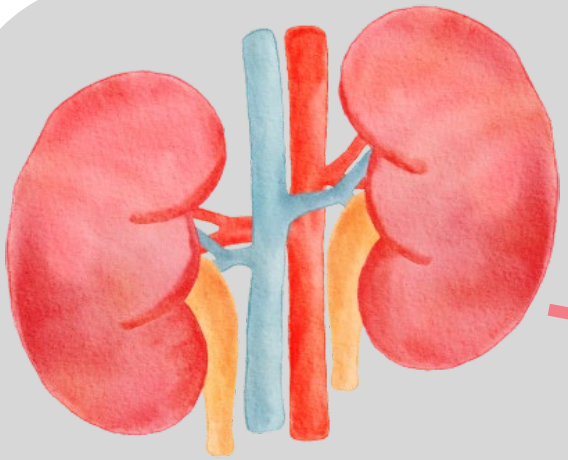
Loss of GFR leads to a **decrease in phosphorus excretion** and calcitriol production, leading to bone remodeling and **increases in circulating FGF-23.**

Mineral imbalances in calcium and phosphorus alter gut metabolism and mineral reabsorption, which further promote mineral bone disorder.

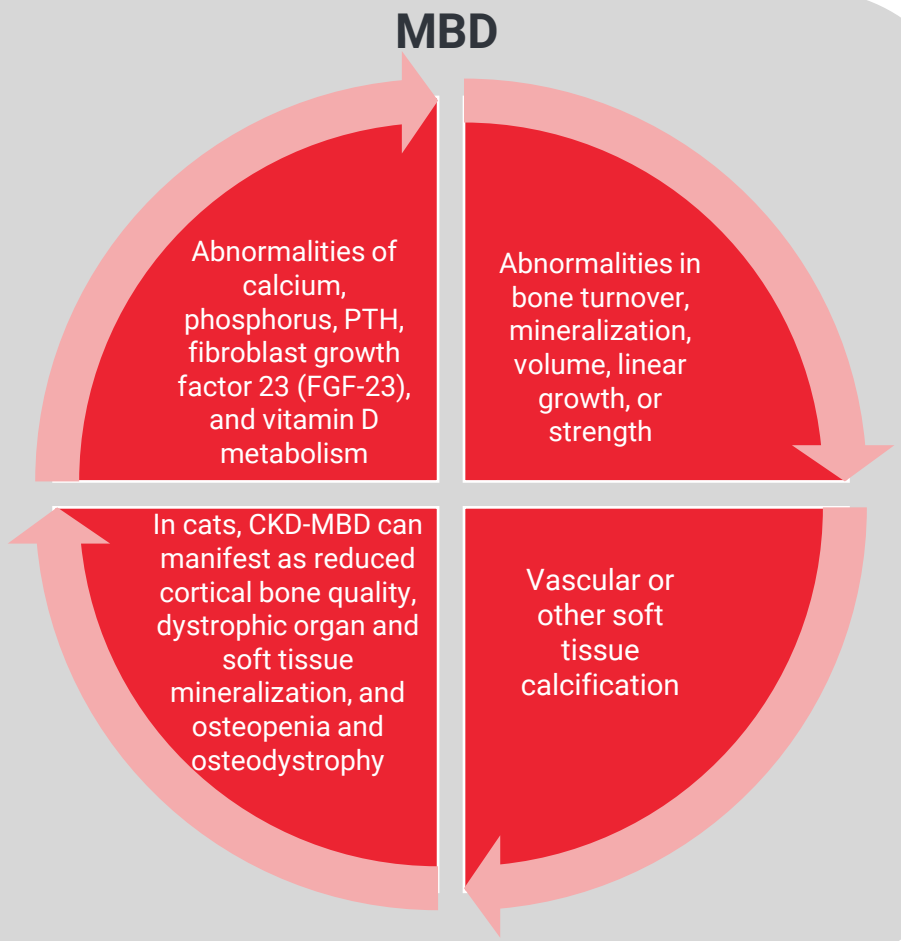
Decreased calcium absorption, a secondary increase in PTH is eventually seen, which leads to secondary renal hyperparathyroidism.

*αklotho – not mentioned here but important in signaling

> 60% of cats may have changes in kidney function in their lifetime



Decreased Functional Mass & GFR



Chronic kidney disease (CKD) is common in older cats and can be associated with mineral dysregulation and mineral bone disorder (MBD). Fibroblast growth factor 23 (FGF-23) is a phosphotonin peptide hormone that regulates renal phosphorus excretion and calcitriol formation. FGF-23 is a biomarker of interest in feline CKD

What we know about phosphorus alone

Total serum phosphorus

- Serum or plasma inorganic phosphate only represents a small fraction of phosphate in the body IE not a sensitive reflection of total body stores
- Only 1% of total body phosphate (the rest in soft tissues, such as skeletal muscle)
- Especially relevant in early kidney disease where understanding phosphate management influences treatment

Total body phosphorus

- Total body phosphate is found mostly in bone (80-85%)
- Inorganic and Organic phosphate in body
- Organic phoshate is not measured by current assays
- Metabolism involves: PTH, Vitamin D, Calcium, FGF-23, Klotho and many other hormonal components

What we know about phosphorus with FGF-23

IDEXX FGF-23 renal management marker

- FGF-23 rises to control circulating “free phosphorus”
- More effective for understanding of mineral metabolism and early phosphate overload than total serum phosphorus
- Chronic kidney disease induces metabolic bone disease – dysregulation of phosphorus
- Demonstrates in cats earlier indication for phosphate overload leading to more actionable care evidence-based care.

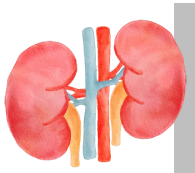
- PTH, Vitamin D, Calcium relationship to FGF-23 in CKD
- Klotho impact and changes due to alterations in renal mass
- RAAS impact

Medical Positioning: In cats with diagnosed early IRIS stage CKD an increased FGF-23 supports starting target therapy to reduce phosphorus intake

The prevalence of CKD in cats is substantial (>60% in senior and geriatric)

Total body phosphorus measurement is often delayed in relation to cats medical and clinical needs

Rising phosphorus is common in CKD, contributing to deleterious effects to the cat, causing clinical signs such as decreased appetite

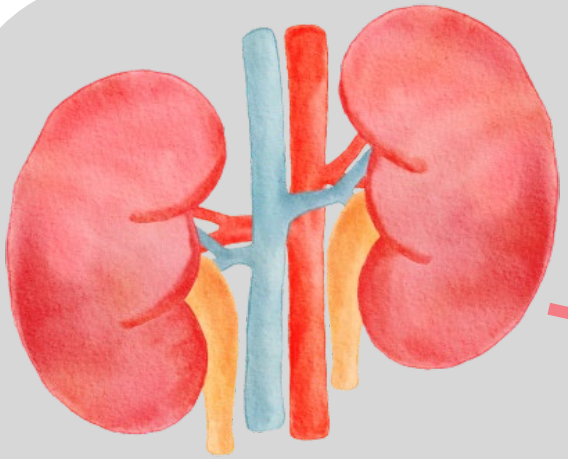


FGF-23 often identifies phosphorus overload (*CKD-MBD) in cats earlier than total phosphorus

FGF-23 provides evidence-based medicine for dietary change in early IRIS stage CKD cats

Diet & phosphate reduction is correlated to improved quality and quantity life for cats with CKD.

> 60% of cats may have changes in kidney function in their lifetime

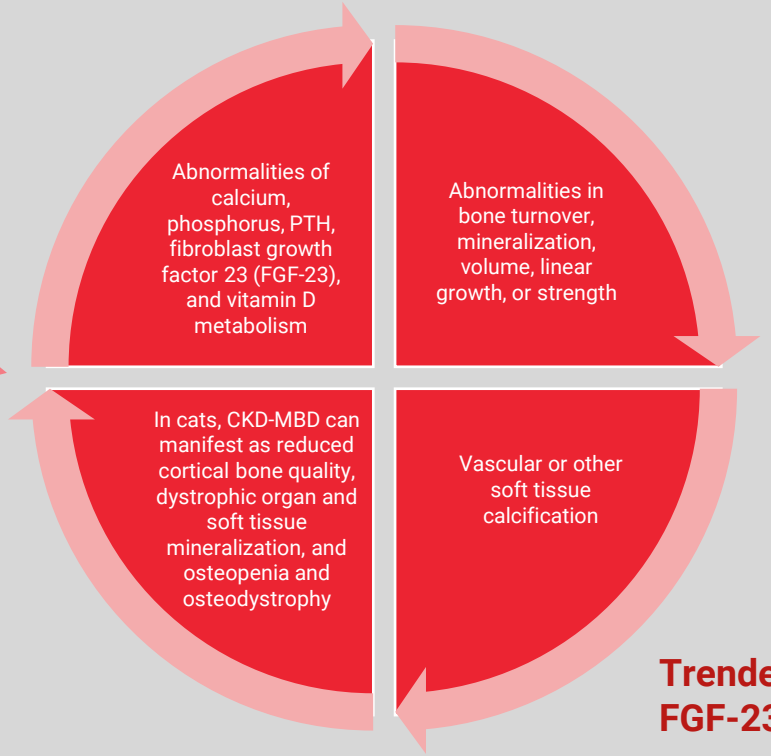


Decreased Functional Mass & GFR

Change in Kidney Biomarkers

Initial FGF-23

Early Stage (IRIS 1&2)
Ensure Stable Disease
Consider Comorbidities

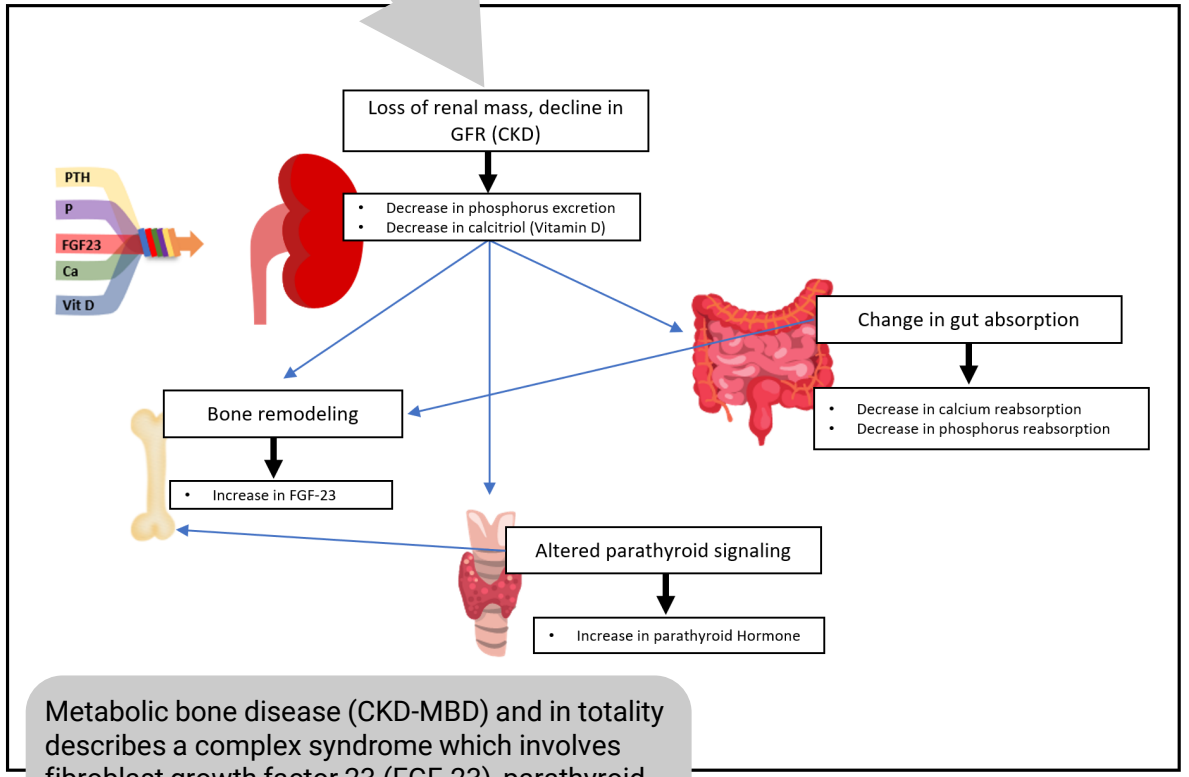


Trended FGF-23

Chronic kidney disease (CKD) is common in older cats and can be associated with mineral dysregulation and mineral bone disorder (MBD). Fibroblast growth factor 23 (FGF-23) is a phosphotonin peptide hormone that regulates renal phosphorus excretion and calcitriol formation. FGF-23 is a biomarker of interest in feline CKD

When should IDEXX FGF-23 renal management marker be run?

Persistent Findings of CKD – IRIS Stage 1 or 2 Diagnosis

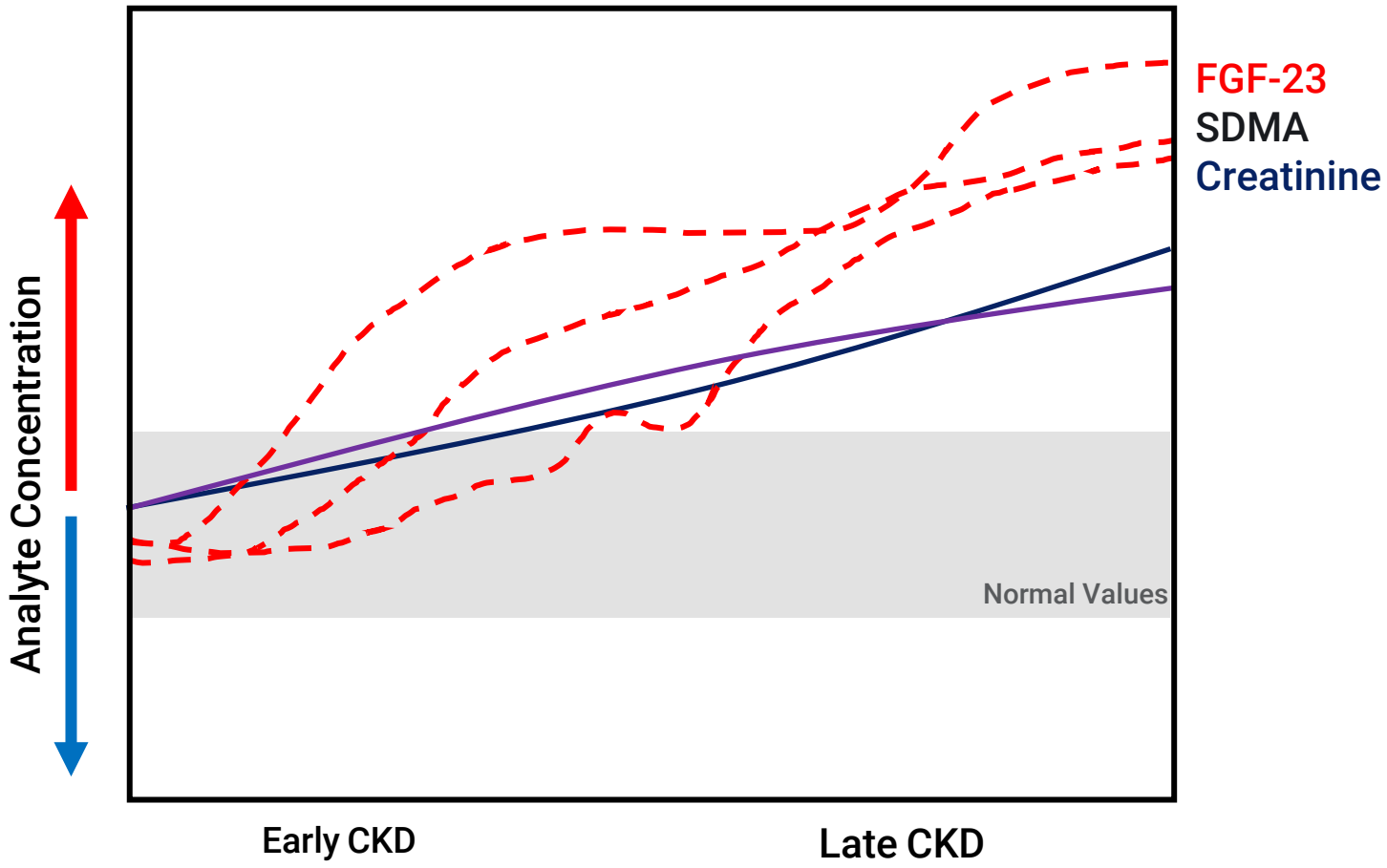


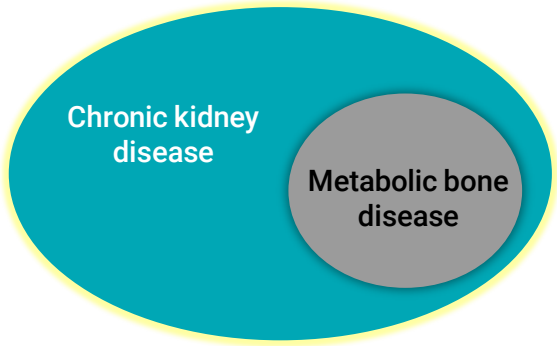
Metabolic bone disease (CKD-MBD) and in totality describes a complex syndrome which involves fibroblast growth factor 23 (FGF-23), parathyroid hormone (PTH), 1,25-dihydroxy D3 (1,25 vitamin D_3, calcitriol), calcium, and phosphorus

FGF-23 is protein excreted in the body in response to increases in phosphorus and calcitriol

FGF-23 can precede a rise in total serum phosphorus giving earlier insight to the need for phosphorus reduction

Elevated FGF-23 in early in feline CKD suggests mineral imbalance, phosphate overload

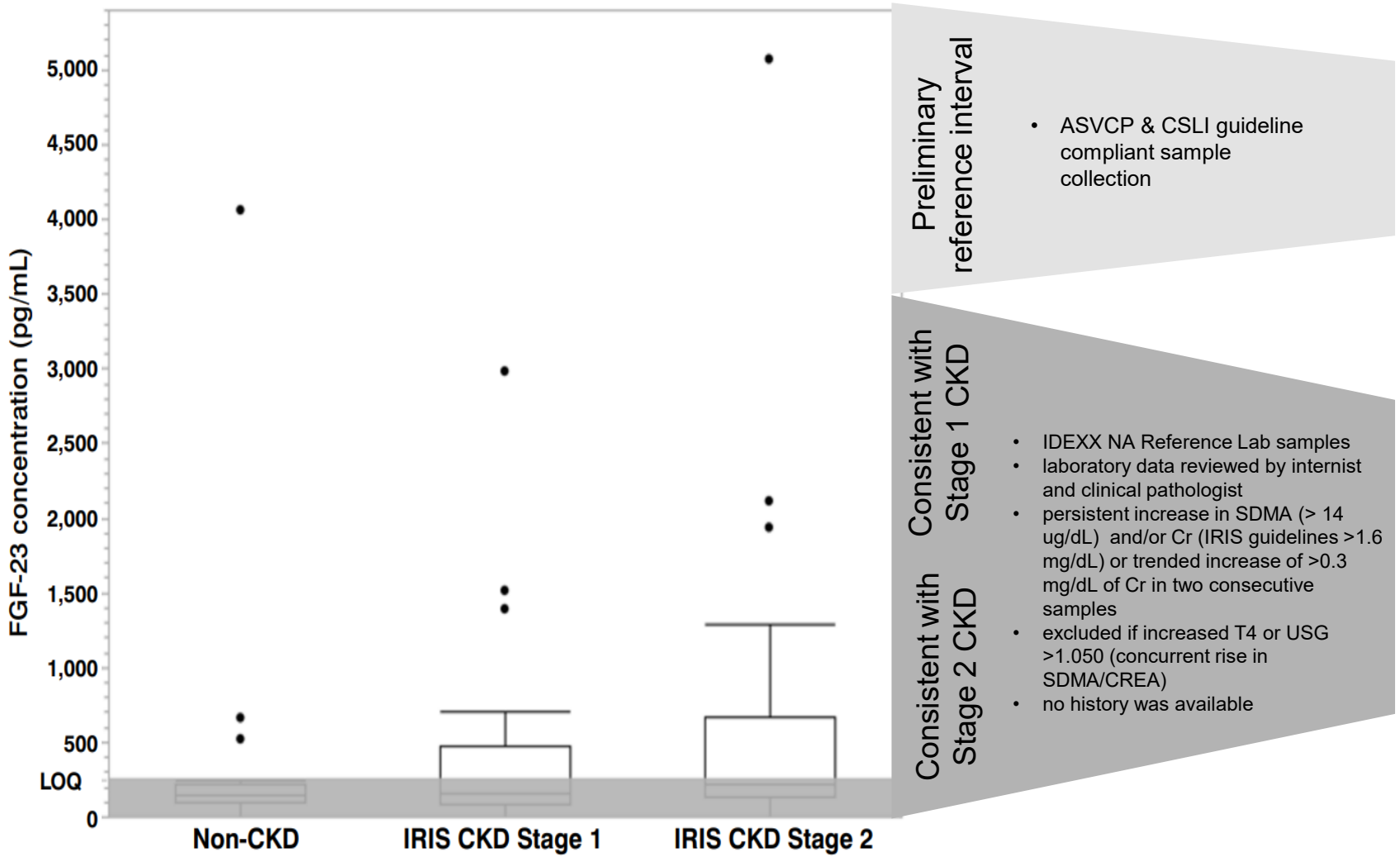


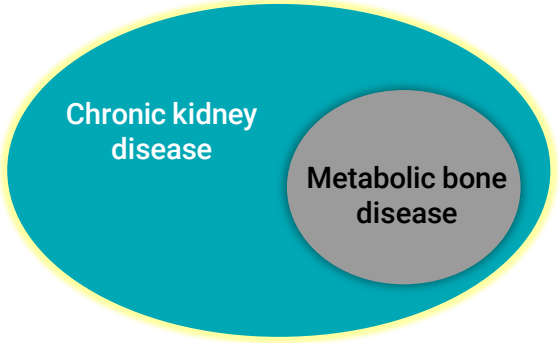


- CKD-MBD is not the same as CKD (chronic kidney disease – metabolic bone disease)
- MBD is likely dependent on multiple factors including CKD etiology, comorbidities, and current therapies
- **The relationship between SDMA or CREA and FGF-23 is not linear**

*support citation listed in bibliography

Subset of cats with early-stage CKD have elevated FGF-23





Key Takeaways

- Moderate overlap of FGF-23 in healthy cats and early-stage CKD cats
- Clear tail offers clinical insight for cats in need of therapy (phosphorus overload)

Claim: In cats with a clinical diagnosis of early CKD, elevated FGF-23 supports targeted therapies to reduce phosphorus overload.

IDEXX Feline FGF-23 ELISA at the Reference Laboratory

- Sandwich ELISA optimized for feline FGF-23
- Large biological range of FGF-23 values

- Assumption: all samples submitted are post CKD diagnosis, feline values in this state are higher and require dilution to evaluate to upper end, we achieve this by diluting all samples 1:5
  - If we failed to dilute, highest values would be artificially low
- Precise values at low end of range are not clinically important, similar medical message
- We will report <300pg/mL for low end (limit of quantification)

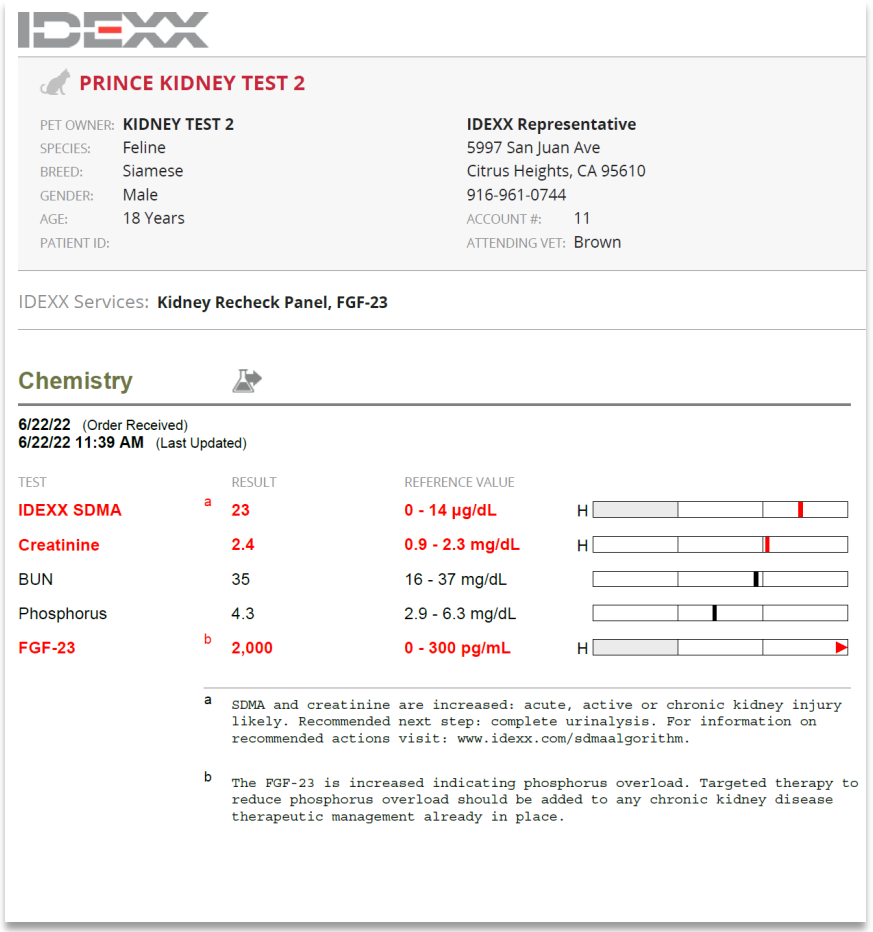
Contraindications for performing:

- Systemic Inflammation
- Uncontrolled Hyperthyroidism
- Severe Anemia

IDEXX FGF-23 reported ranges and clinical interpretations

Clinical Cutoffs:

<299 pg/mL	Within normal limits	FGF-23 is within expected range for normal cats. For cats with IRIS Stage 1 or 2 CKD, recommend rechecking IDEXX FGF-23 in 6 to 12 months alongside kidney biomarkers to identify progressive disease or onset of phosphorus overload.
≥300-399 pg/ml	Borderline	This result is higher than expected for normal cats and most cats with IRIS Stage 1 or 2 kidney disease. In cats with diagnosed CKD, recommend rechecking IDEXX FGF-23 in 3 to 6 months alongside kidney biomarkers to identify onset of phosphorus overload. If indicated by clinical context and/or other kidney diagnostics, targeted therapies (such as diet changes) should be initiated.
≥400 pg/ml	Abnormal, elevated	Elevated result indicating phosphorus overload. Targeted therapy to reduce phosphorus levels should be added to existing CKD therapies.



IDEXX

PRINCE KIDNEY TEST 2

PET OWNER: **KIDNEY TEST 2**
SPECIES: Feline
BREED: Siamese
GENDER: Male
AGE: 18 Years
PATIENT ID:

IDEXX Representative
5997 San Juan Ave
Citrus Heights, CA 95610
916-961-0744
ACCOUNT #: 11
ATTENDING VET: Brown

IDEXX Services: **Kidney Recheck Panel, FGF-23**

Chemistry

6/22/22 (Order Received)
6/22/22 11:39 AM (Last Updated)

TEST		RESULT	REFERENCE VALUE	
IDEXX SDMA	a	23	0 - 14 µg/dL	H
Creatinine		2.4	0.9 - 2.3 mg/dL	H
BUN		35	16 - 37 mg/dL	
Phosphorus		4.3	2.9 - 6.3 mg/dL	
FGF-23	b	2,000	0 - 300 pg/mL	H

a SDMA and creatinine are increased: acute, active or chronic kidney injury likely. Recommended next step: complete urinalysis. For information on recommended actions visit: www.idexx.com/sdmaalgorithm.

b The FGF-23 is increased indicating phosphorus overload. Targeted therapy to reduce phosphorus overload should be added to any chronic kidney disease therapeutic management already in place.

A snapshot of how FGF-23 adds to IDEXX renal portfolio

Signalment: Neutered Male 9-year-old DLH
Presentation/PE: Senior Wellness Check, maybe increased thirst– PE no major findings
Plan: CBC, Chemistry with SDMA, UA, T4

Chemistry

Click to view Differentials

	4/30/22		7/28/22
Glucose	110	72 - 175 mg/dL	112
IDEXX SDMA (Learn More)	ax 15	0 - 14 µg/dL	be 17
Creatinine	2.0	0.9 - 2.5 mg/dL	2.3
BUN	21	16 - 37 mg/dL	31
BUN: Creatinine Ratio	10.5		13.5
Phosphorus	3.4	2.9 - 6.3 mg/dL	3.2

Urinalysis

Click to view Differentials

	4/30/22
Collection	CYSTOCENTESIS
Color	YELLOW
Clarity	CLOUDY
Specific Gravity	1.029
pH	6.5
Urine Protein	d NEGATIVE
Glucose	NEGATIVE
Ketones	NEGATIVE
Blood / Hemoglobin	NEGATIVE
Bilirubin	NEGATIVE
Urobilinogen	NORMAL
White Blood Cells	0-2
Red Blood Cells	0-2
Bacteria	NONE SEEN

CBC and T4: Within Normal Limits

Clinical Evidence of CKD

PU/PD

↓

SDMA > 14 µg/dL x 2

↓

CREA > 1.6 mg/dL x 2

↓

USG < 1.035

BUT normal phosphorus, minimal history

SO WHAT do I suggest a diet change?

A snapshot of how FGF-23 adds to IDEXX renal portfolio

Signalment: Neutered Male 9 -ear-old DLH
Presentation/PE: Senior Wellness Check, maybe increased thirst– PE no major findings
Plan: CBC, Chemistry with SDMA, UA, T4

Chemistry — Click to view Differentials — 4/30/22

Glucose	110	72 - 175 mg/dL
IDEXX SDMA (Learn More)	ax 15	0 - 14 µg/dL
Creatinine	2.0	0.9 - 2.5 mg/dL
BUN	21	16 - 37 mg/dL
BUN: Creatinine Ratio	10.5	
Phosphorus	3.4	2.9 - 6.3 mg/dL

Urinalysis — Click to view Differentials — 4/30/22

Collection	CYSTOCENTESIS
Color	YELLOW
Clarity	CLOUDY
Specific Gravity	1.029
pH	6.5
Urine Protein	d NEGATIVE
Glucose	NEGATIVE
Ketones	NEGATIVE
Blood / Hemoglobin	NEGATIVE
Bilirubin	NEGATIVE
Urobilinogen	NORMAL
White Blood Cells	0-2
Red Blood Cells	0-2
Bacteria	NONE SEEN

CBC and T4: Within Normal Limits

7/28/22

112
be 17
2.3
31
13.5
3.2

Chemistry — Click to view Differentials — 7/28/22

FGF-23	988	>300 pg/dL

YES, diet is warrant in this cat

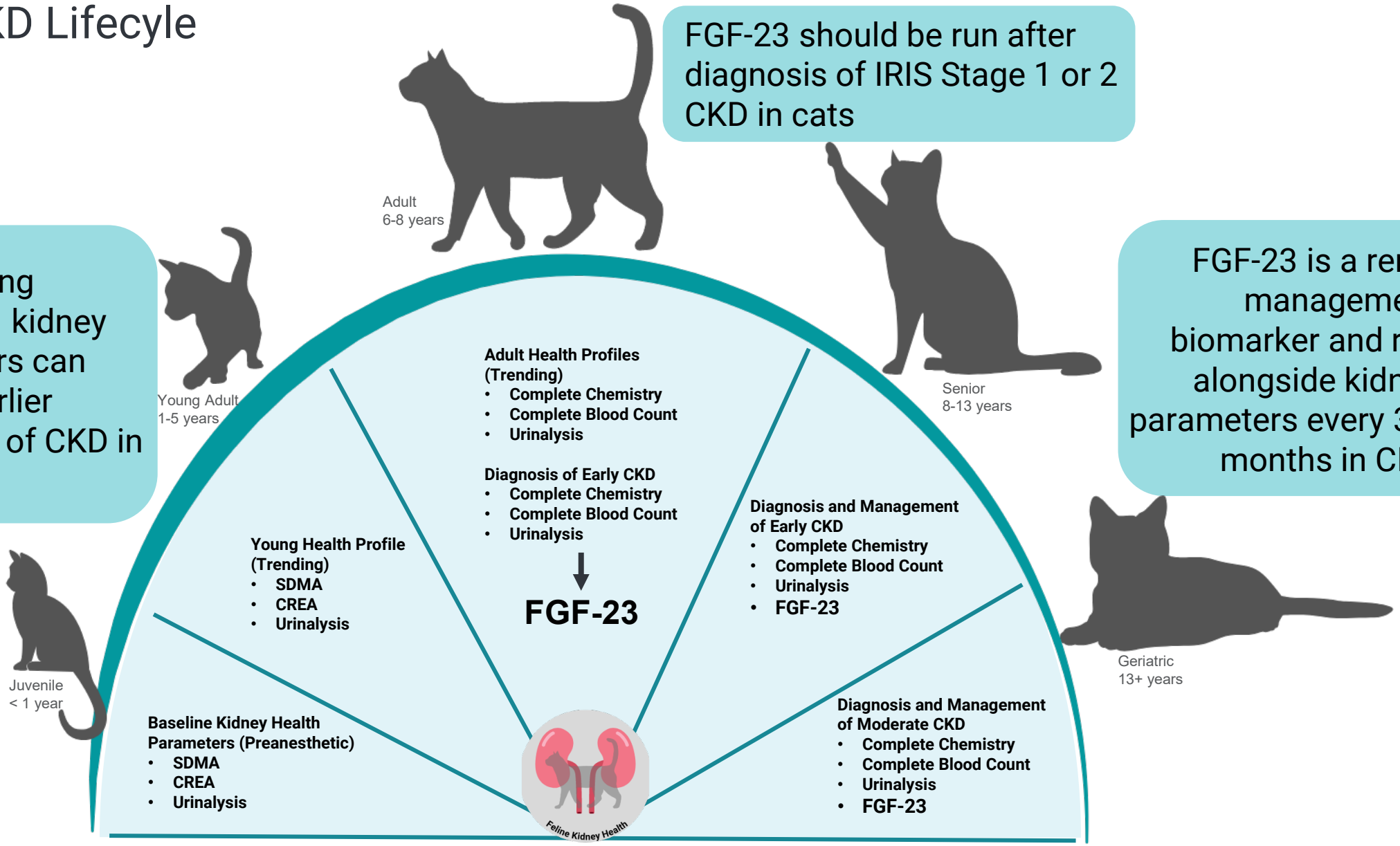
Recheck in 3-6 months is recommended

Where does FGF-23 fit in Feline CKD Lifecyle

FGF-23 should be run after diagnosis of IRIS Stage 1 or 2 CKD in cats

Establishing individual kidney parameters can enable earlier diagnosis of CKD in cats

FGF-23 is a renal management biomarker and run alongside kidney parameters every 3-6 months in CKD



Discussion is Welcome

Thank You!

rebekah-mack-Gertig@idexx.com