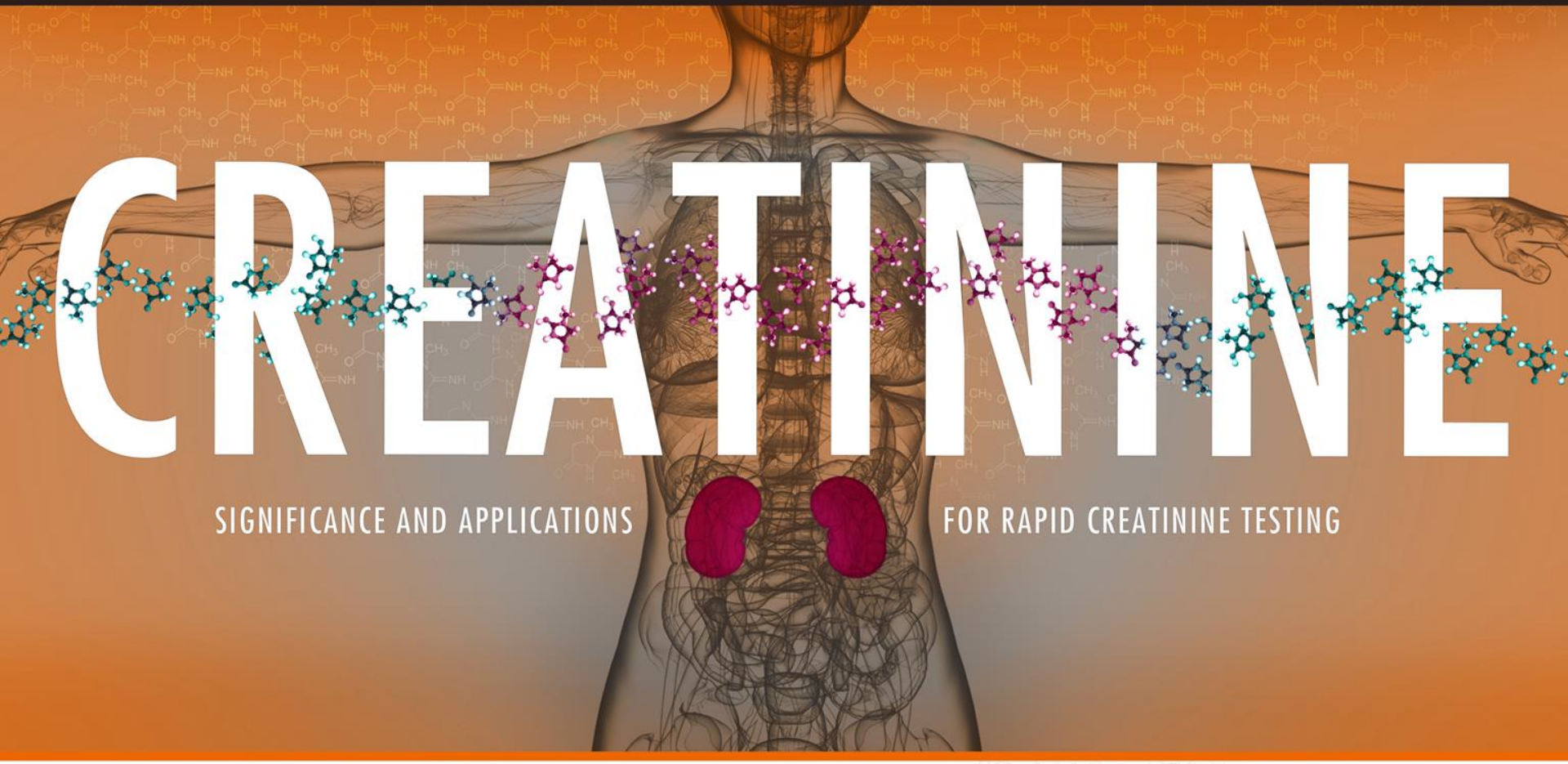

CREATININE

SIGNIFICANCE AND APPLICATIONS FOR RAPID CREATININE TESTING

A SELF STUDY
COURSE FOR CREDIT

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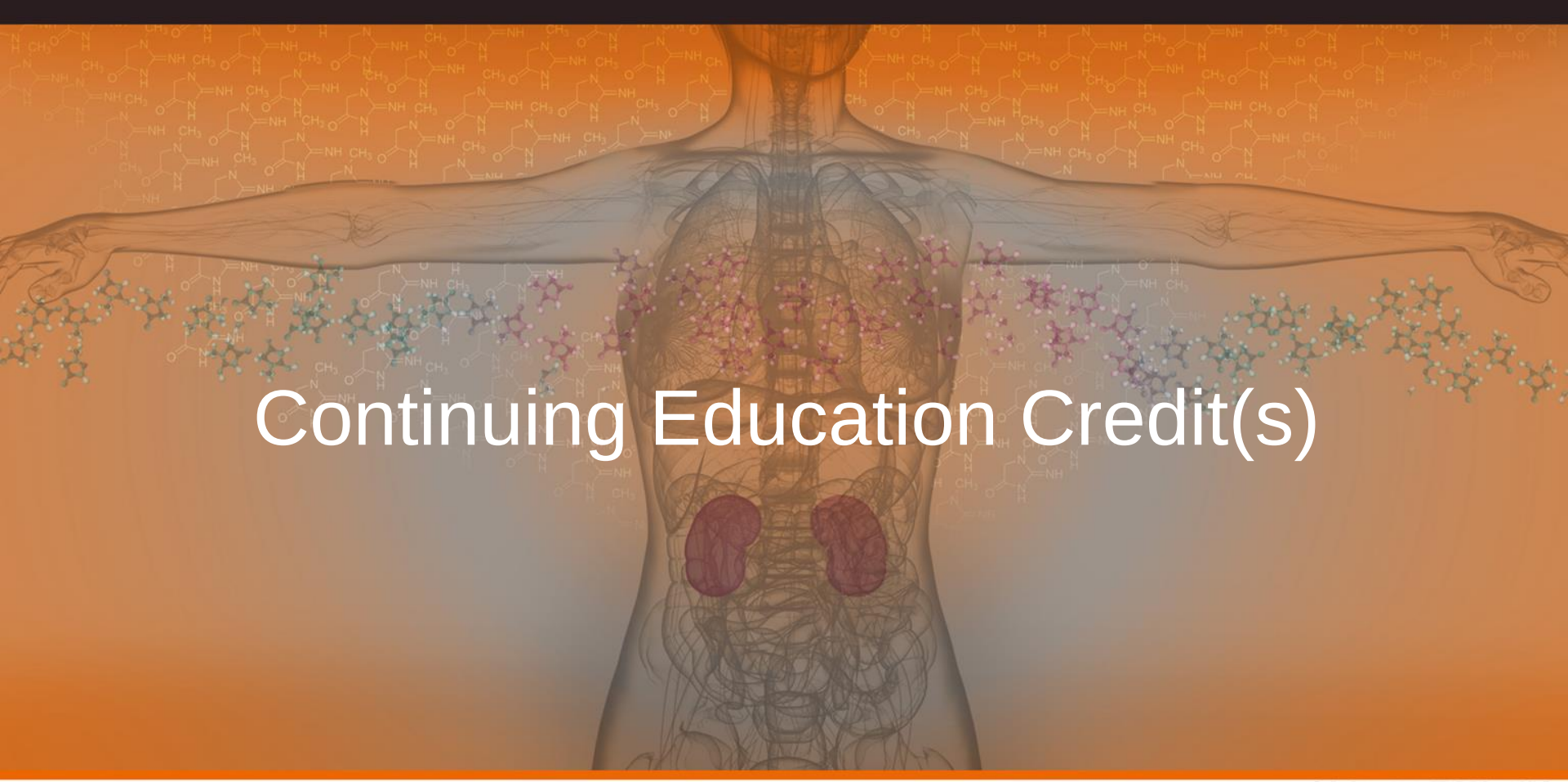

Continuing Education Credit(s)

Date of Release: 7/1/2023

Date of Expiration: 7/1/2025

Estimated time to complete this educational activity: 1.5 hours

Continuing Education Credit(s)

- **Physicians** – This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through Synativ. Synativ is accredited by the ACCME to provide continuing medical education for physicians. Synativ designates this educational activity for a maximum of 1 AMA PRA Category 1 Credit(s)™ toward the AMA Physician's Recognition Award. Physicians should only claim credit commensurate with the extent of their participation in the activity.
- **Nursing** - Educational Review Systems is an approved provider of continuing education in nursing by ASNA, an accredited provider by the ANCC/Commission on Accreditation. Provider #5-115. This program is approved for one and a half (1.5) hours. Educational Review Systems is also approved for nursing continuing education by the State of California and the District of Columbia.
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Disclosures

There are no disclosures for this learning activity.

Statement of Need

Acute kidney injury (AKI) may lead to morbidity and mortality in many types of patients. One of the difficulties in treating AKI is making the diagnosis early enough to alter the course of the disease.

This learning activity will describe how rapid creatinine testing may assist with therapeutic decision making and improve the prognosis for patients with AKI.

Intended Audience

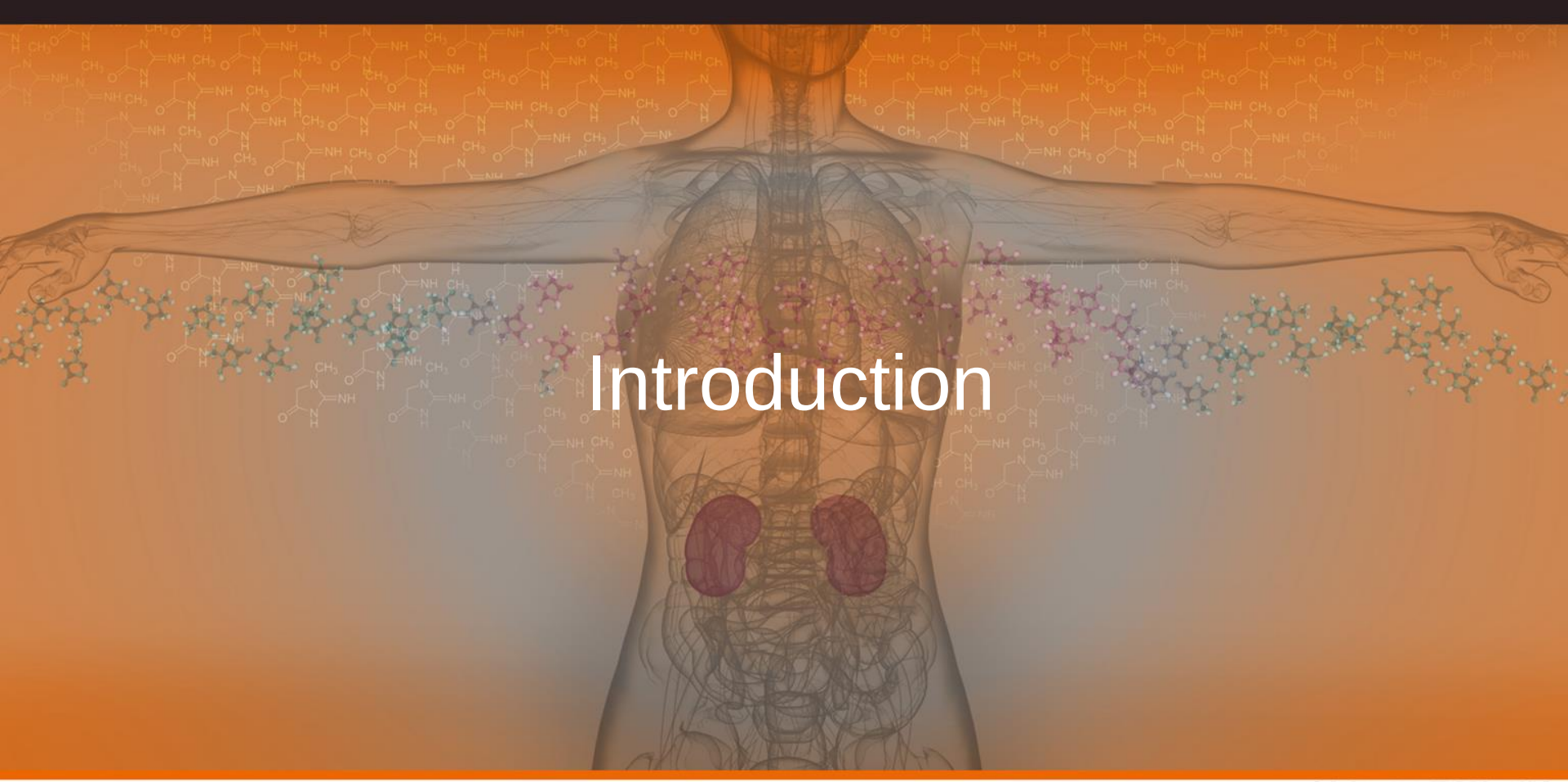
The primary audience for this learning activity are healthcare professionals (physicians, nurses, respiratory therapists and laboratory staff) involved in the testing, diagnosis, treatment, and management of acute kidney injury and who are interested in the role of rapid testing to improve care for these patients.

Learning Objectives

After completing this activity, the participant should be able to:

1. Discuss the risk factor for development of AKI.
2. Explain the importance of early identification of changes in renal function.
3. Discuss how rapid creatinine testing can assist in mitigating kidney injury.
4. List future applications for a rapid creatinine test.

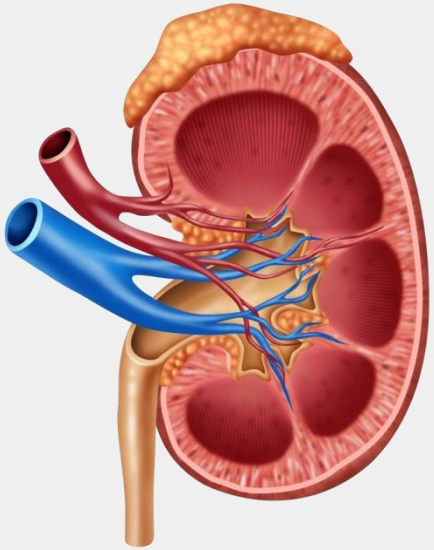
Table of Contents



Introduction

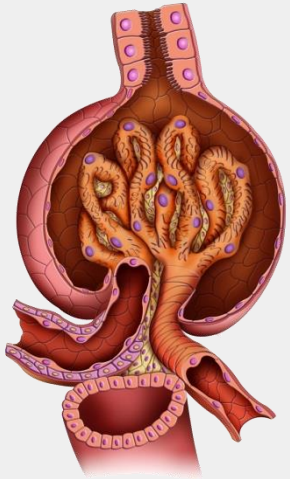
Kidney Anatomy

The kidney is supplied with blood by the renal artery.



The renal artery branches and eventually the blood feeds into the cortex, or outer part of the kidney and the nephrons, or functional units that filter the blood and produce urine.

The nephron filters blood to form urine, and is comprised of several parts.



- Glomerulus: group of capillaries where filtration takes place
- Bowman's capsule: absorbs filtrate from the glomerulus
- Tubules: sites of secretion and absorption of solutes and waste

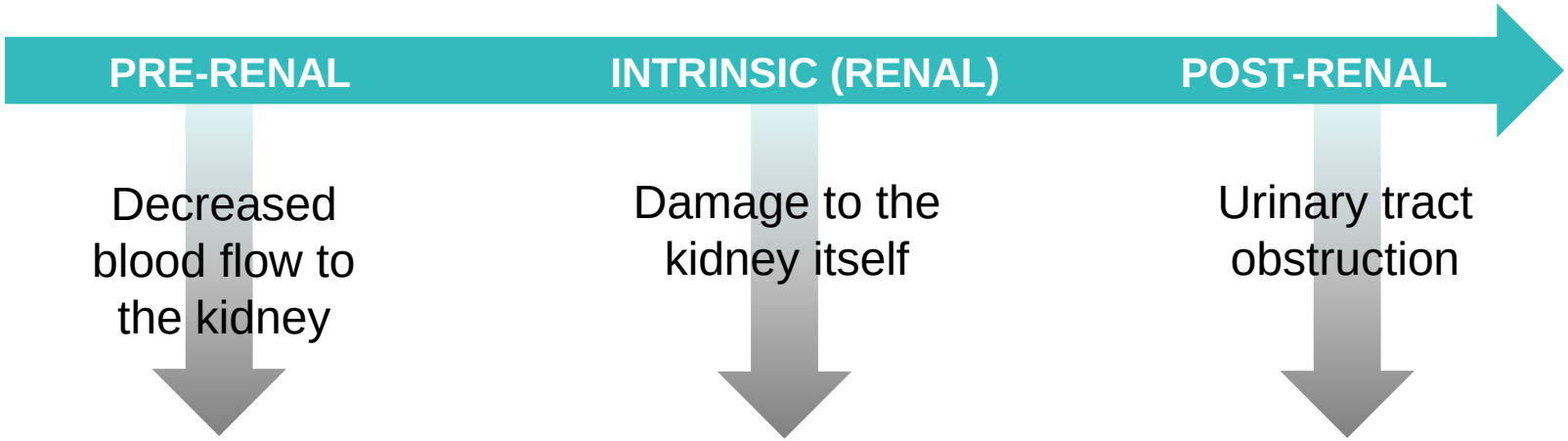
Acute Kidney Injury

- AKI is a rapid loss of kidney function including:
  - Rapid time course
  - Rise in serum creatinine
  - Change in urine output

AKI can lead to an increased risk for chronic kidney disease (CKD).

Ostermann M, et al. *JAMA Network Open*. 2020;3(10):e2019209. doi:10.1001/jamanetworkopen.2020.19209

AKI Causes: Physiological



PRE-RENAL	INTRINSIC (RENAL)	POST-RENAL
Decreased blood flow to the kidney	Damage to the kidney itself	Urinary tract obstruction
• Low blood pressure • Low blood volume • Heart failure • Arterial changes leading to kidney	• Glomerulonephritis • Acute tubular necrosis • Acute interstitial nephritis	• Benign prostatic hyperplasia • Kidney stones • Obstructed urinary catheter • Bladder, ureteral or renal malignancy

https://www.amboss.com/us/knowledge/Acute_kidney_injury. Updated November 30, 2020. Accessed May 31, 2021.

Four Phases of AKI

Phase	Characteristic Features	Duration
Kidney injury	• Symptoms of the underlying illness causing AKI may be present.	Hours to days
Oliguria or anuria	• Progressive deterioration of kidney function • Reduced urine production (oliguria), < 50 ml/24 hrs = anuria • Increased retention of urea and creatinine (azotemia) • Complications: fluid retention (pulmonary edema), hyperkalemia, metabolic acidosis, uremia, lethargy, asterixis	1-3 weeks
Polyuric or diuretic	• Glomerular filtration returns to normal, which increases urine production (polyuria), while tubular reabsorption remains disturbed. • Complications: loss of electrolytes and water (dehydration, hyponatremia, and hypokalemia)	~2 weeks
Recovery	• Kidney function and urine production normalize.	Months to years

https://www.amboss.com/us/knowledge/Acute_kidney_injury. Updated November 30, 2020. Accessed May 31, 2021.

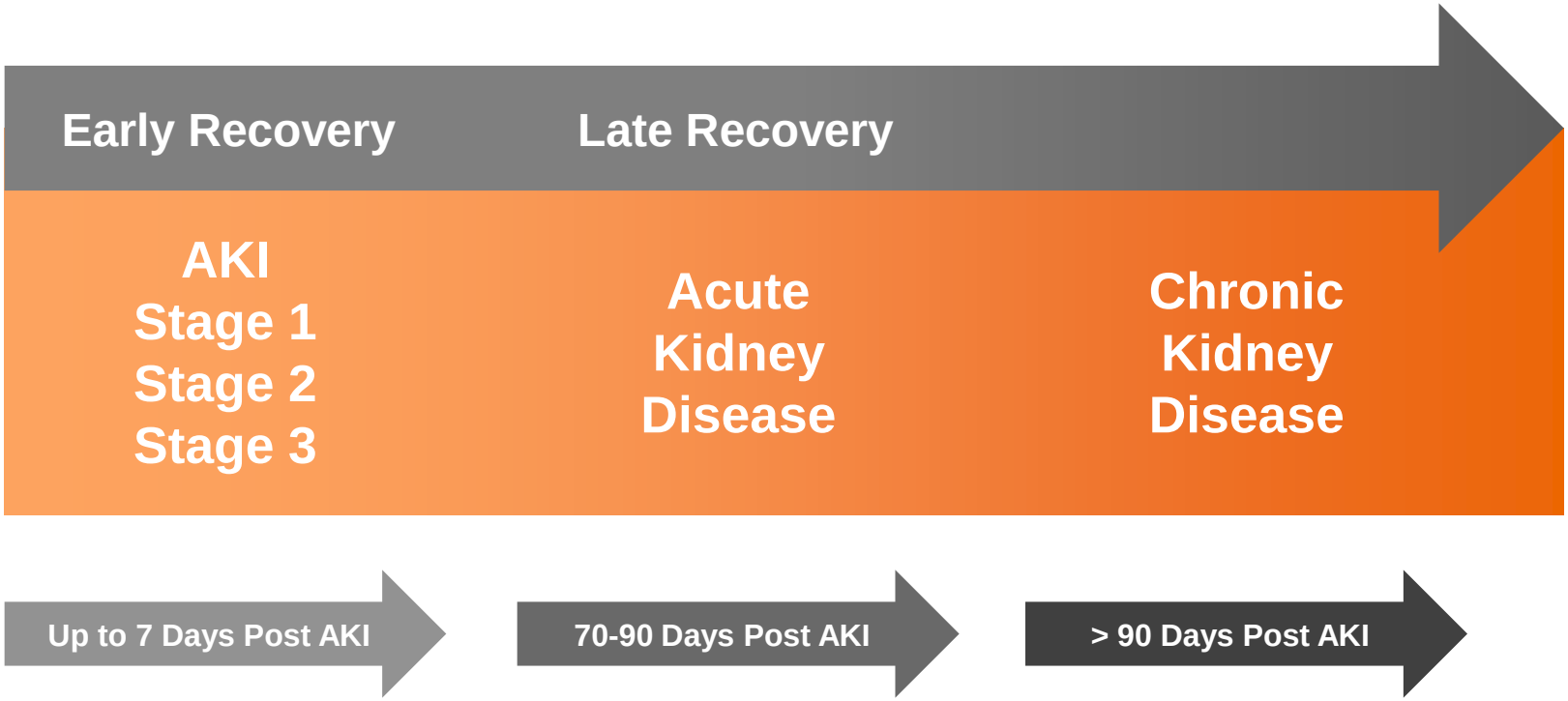
Long-Term Risk of ESKD After AKI

	Risk of ESKD (%)
AKI	
1 year	2%
5 years	3.9%
Non-AKI	
1 year	0.08%
5 years	0.3%
AKI + RRT	
90 days	30%
1 year	20%
5 years	11.7%
7 years	3.4%

ESKD: end-stage kidney disease; RRT: renal replacement therapy

Forni LG, et al. *Intensive Care Med*. 2017;43:855–66.

Recovery Can Occur Early or Late



Forni LG, et al. *Intensive Care Med*. 2017;43:855–66.
https://www.amboss.com/us/knowledge/Acute_kidney_injury. Updated November 30, 2020. Accessed May 31, 2021.
Ostermann M, et al. *JAMA Network Open*. 2020;3(10):e2019209. doi:10.1001/jamanetworkopen.2020.19209

Risk Factors for Short-Term Non-Recovery

Patient Related Factors

Age
Race/Ethnicity
Genetic Factors
CKD
Comorbidity

Acute Disease Severity

High Illness Severity
Hemodynamic Instability
Medical Admission

AKI Severity

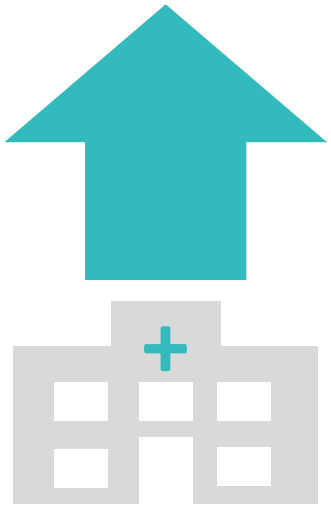
Higher KDIGO Stage

KDIGO: kidney disease improving global outcomes

Forni LG, et al. *Intensive Care Med*. 2017;43:855–66.
Chen JJ, et al. *J For Med Assoc*. 2021; https://doi.org/10.1016/j.jfma.2021.02.013

AKI Increases Costs

$24 Billion



U.S. Hospital Costs Due to AKI

$42,000

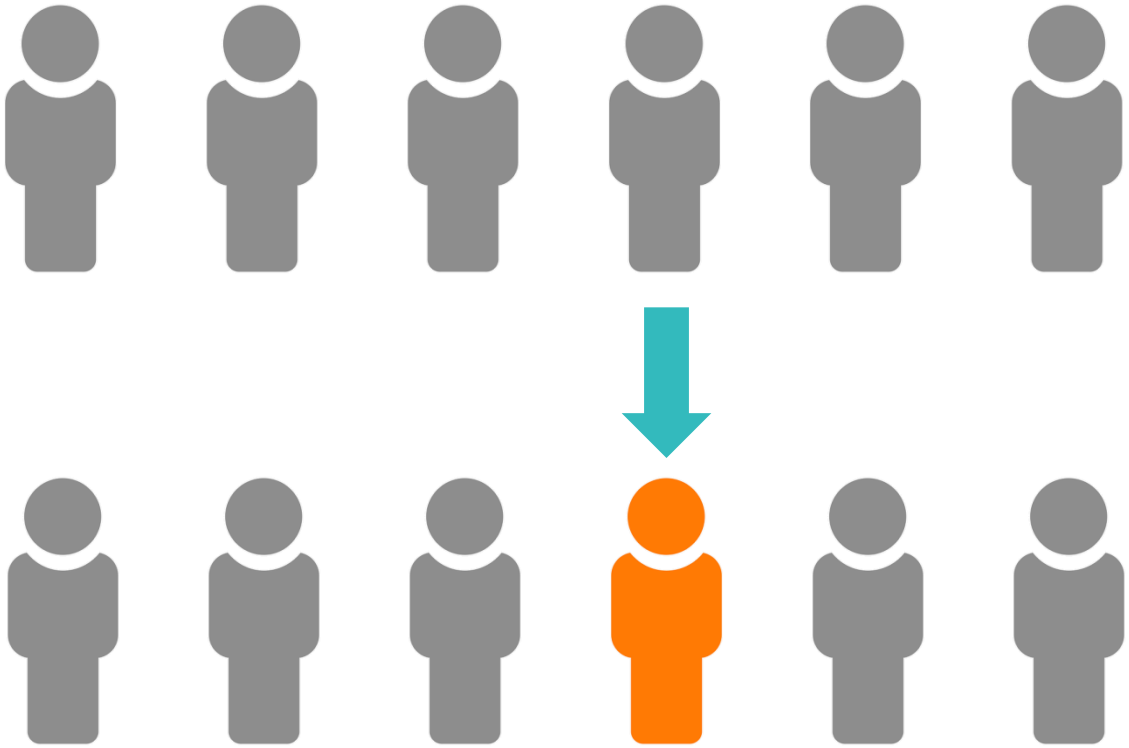
Per Hospitalization

U.S. Patient Cost With Dialysis

Silver SA, Chertow GM. *Nephron*. 2017;137:297–301.
Selby NM, et al. *Kidney Int Rep*. 2021;6(3):636–44.

AKI Incidence

10-15% of patients admitted to the hospital have AKI

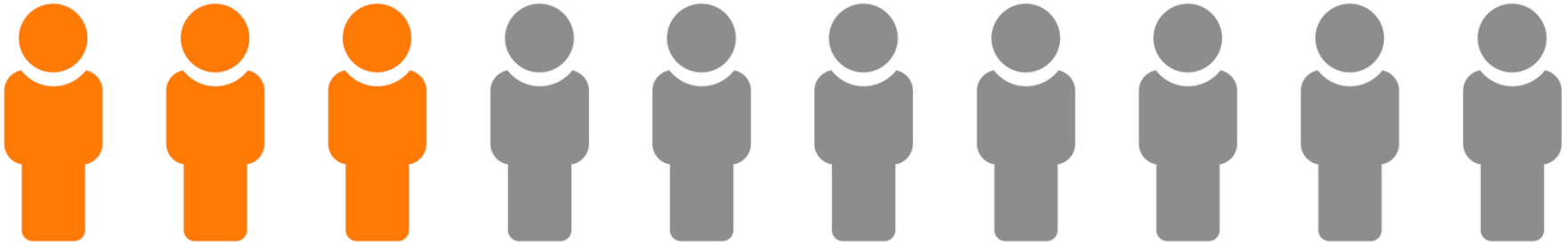


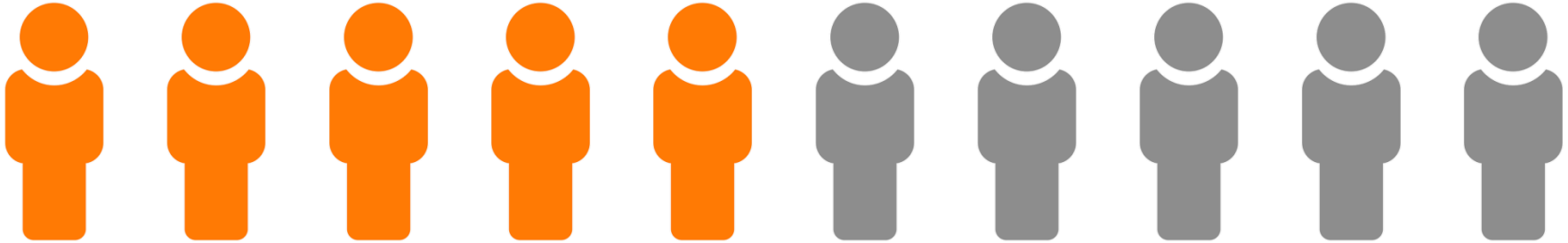
10% to 20% of these patients progress to late-stage CKD

Ronco C, et al. *Lancet*. 2019;394(10212):1949-64.
Meersch M, et al. *Anesth Analg*. 2017;125:1223–32.

AKI Incidence Among COVID-19 Patients

28% of patients with COVID-19 develop AKI

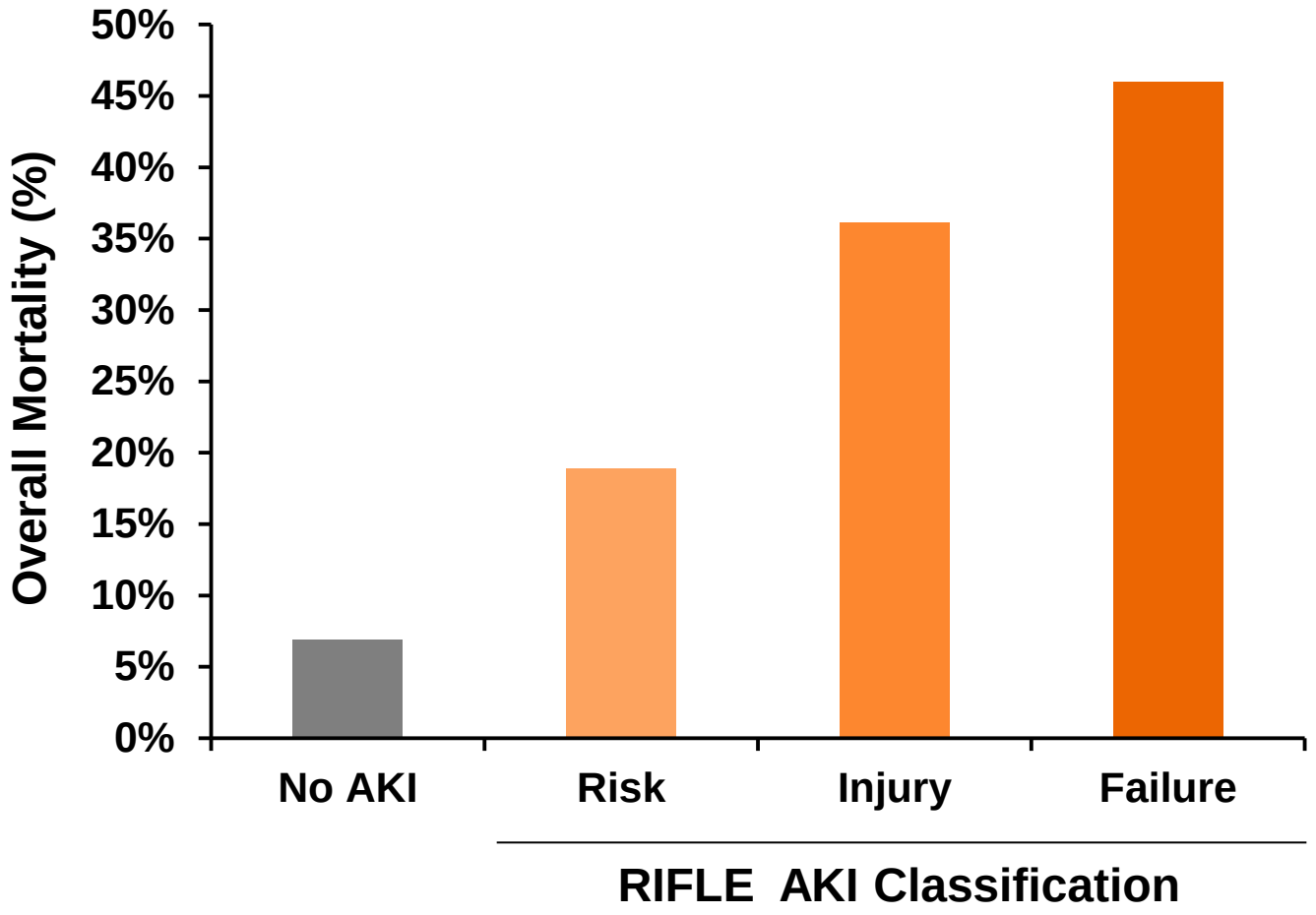




AKI rates raise to 46-50% among critically ill patients

Palevsky PM. *J Am Soc Nephrol*. 2021;32(5):1029-32.

AKI Mortality

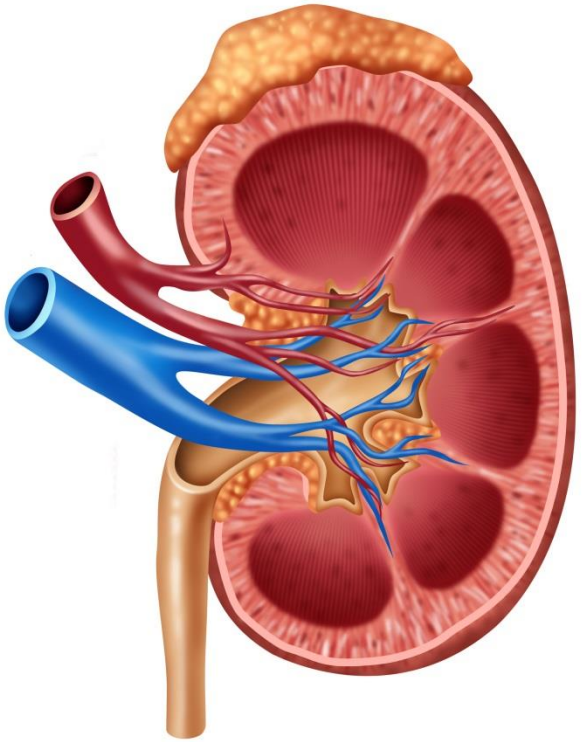


Meersch M, et al. *Anesth Analg*. 2017;125:1223–32.

Patients at Risk for AKI

AKI Risk Factors

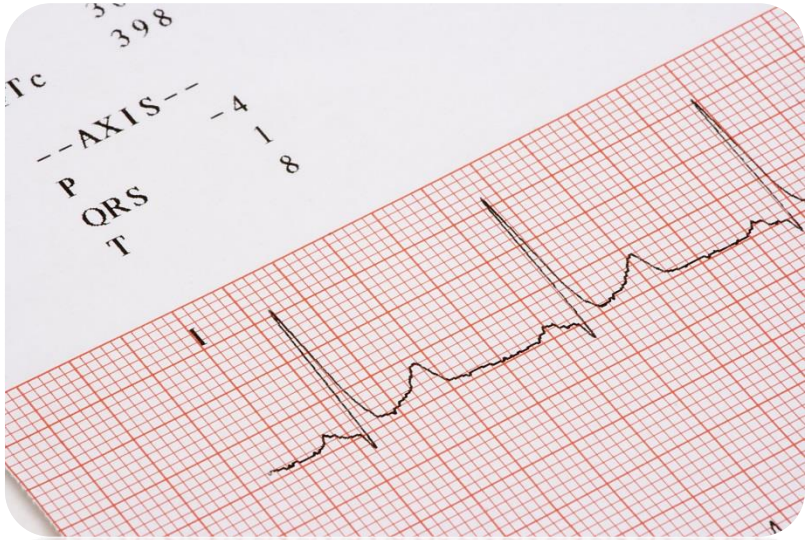
- Sepsis
- Age > 65 years
- Low cardiac output
- Major surgery
- Trauma
- Hypervolemia
- Cirrhosis
- Nephrotoxic medications



https://www.kidneyfund.org/kidney-disease/kidney-problems/acute-kidney-injury.html. Accessed June 1, 2021.
Chen JJ, et al. *J For Med Assoc*. 2021; https://doi.org/10.1016/j.jfma.2021.02.013

Surgery-Associated AKI

- AKI is associated with cardiac surgical procedures in up to 40% of patients.
- Associated medical costs of more than $1 billion
- Most epidemiological studies are in cardiac surgical procedures
  - Hazard ratio of 3.8 for developing ESKD
- Increased mortality
  - Postoperative mortality rates increase to 70% if dialysis is required.



Thongprayoon C, et al. *J Clin Med.* 2020;9(6):1767.

Risk Factors for Postoperative AKI

Preoperative Risk Factors

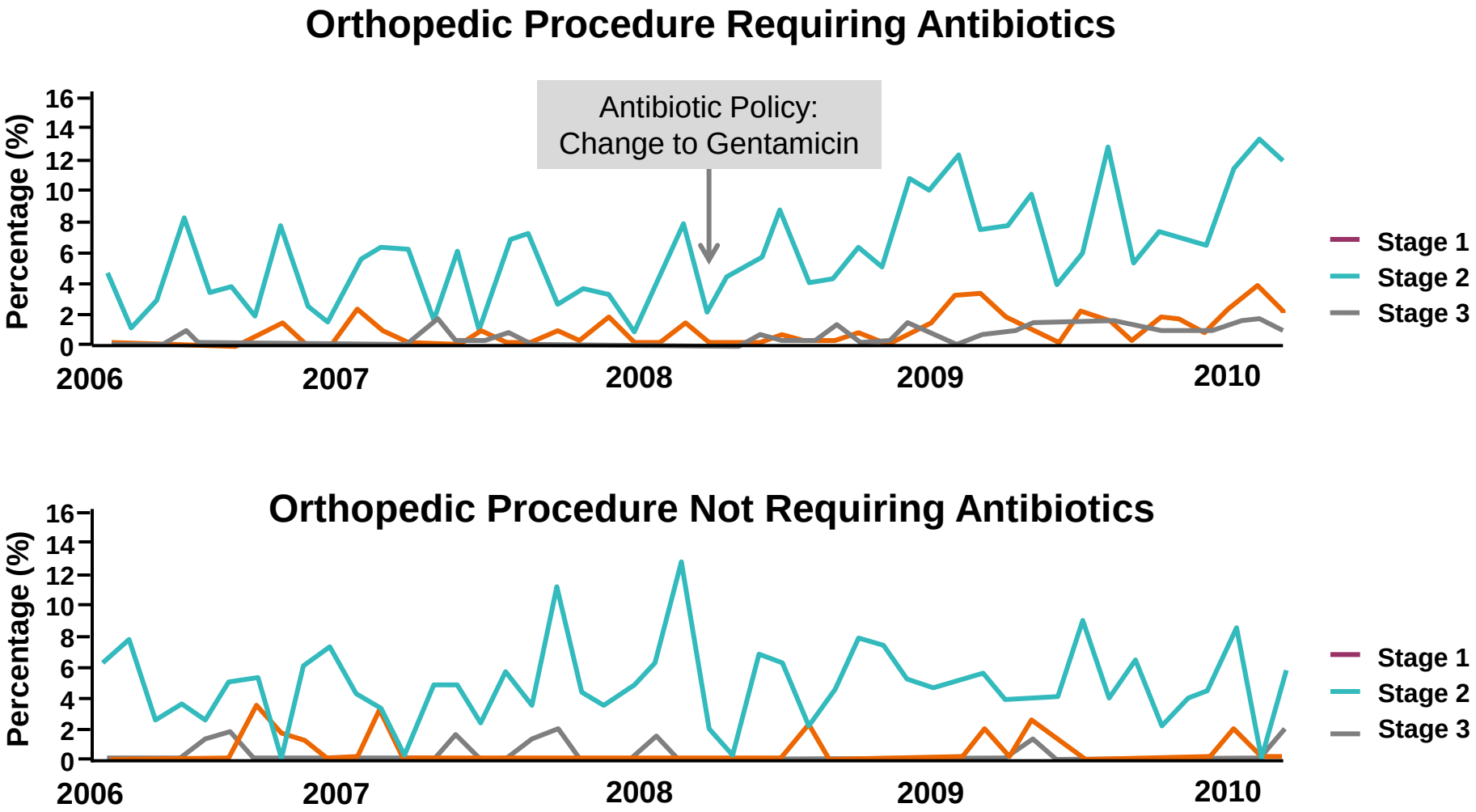
Age
Female sex
Body mass index
Hypertension
Chronic kidney disease
Diabetes
COPD
Peripheral vascular disease
Cerebrovascular disease
Congestive heart failure
Sepsis
Ascites

Intraoperative Risk Factors

Duration of surgery
Intraperitoneal surgery
Repair of abdominal aortic aneurysm
Intraoperative hypotension
Transplantation of solid non-renal organs
Transfusion of packed red blood cells
Intraabdominal hypertension
Length of cardiopulmonary bypass
Cross-clamp time
Hemodilution
Use of intraaortic balloon pump
Type of cardiac surgical procedure
Nephrotoxic agents

Meersch M, et al. *Anesth Analg*. 2017;125:1223–32.

Antibiotics May Be Nephrotoxic and Lead to AKI



Sawhney S, et al. *Adv Chronic Kidney Dis*. 2017;24(4):194–204.

Pharmacologic Prevention of Perioperative AKI

Vasoactive Agents and Diuretics

Dopamine
Fenoldopam
Theophyline
Recombinate atrial natriuretic peptide
Angiotensin-converting enzyme inhibitor
Angiotensin-II receptor antagonists
Furosemide

Cytoprotective Therapy

Dexmedetomidine
Proinflammatory cytokines
Steroids
N-acetylcysteine
Intensive glucose control
HMG-CoA reductase inhibitors (statins)
Sodium bicarbonate

Meersch M, et al. *Anesth Analg*. 2017;125:1223–32.

Critically Ill Patients

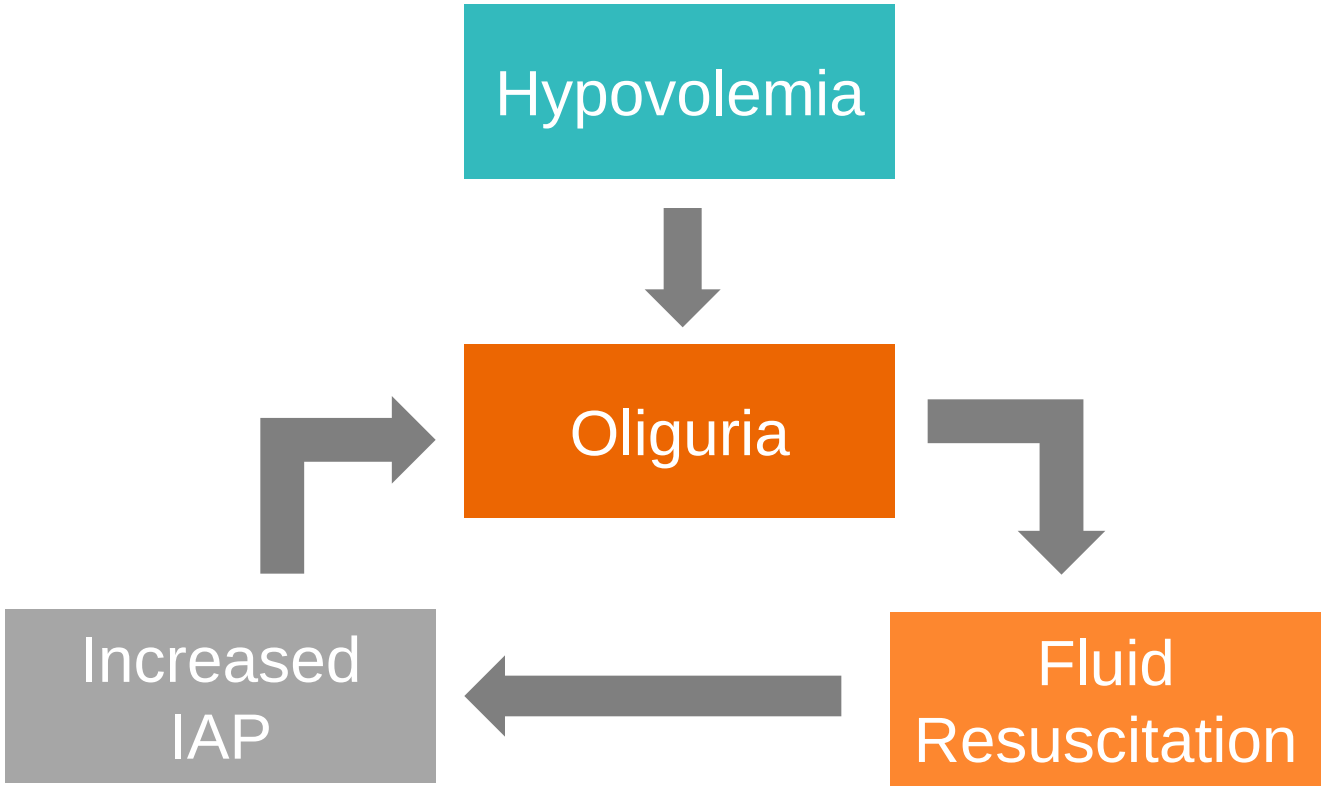
- AKI is seen in approximately 50% of patients in the intensive care unit (ICU).[1]
- The incidence is rising due to more aggressive diagnostic and therapeutic interventions.
- Five to 15% percent of ICU patients with AKI require RRT.[1]
  - Associated with up to 70% mortality[1-2]

Mortality in Critically Ill Patients with AKI

	In ICU	5 Years
No RRT	7.4%	32.4%
RRT	35.4%	69.9%

1. Vásquez JE, et al. *Nephron*. 2021;145(2):91-8.
2. Oliveros H, et al.. *J Intens Care.* 2020;8:63.

Vicious Cycle of Critical Illness and AKI



IAP: intra-abdominal pressure

Bellomo R, et al. *Ann Intensive Care*. 2017;7:49.

Cancer and AKI

- Chemotherapy toxicity affects many organ systems including kidneys.
- The most common cytotoxic chemotherapeutic agents related to the development of AKI are cisplatin, mitomycin-C, gemcitabine, methotrexate, ifosfamide and pemetrexed.
- Creatinine clearance is a direct indicator of chemotherapy toxicity.

Cosmai L, et al. *Clin Kidney J.* 2021;14:70–83.

Causes of AKI in Patients With Malignancies

Prerenal
- Nausea, vomiting and diarrhea
- Stomatitis and cachexia
- 'Third spacing' (including hepatorenal syndrome)
- Neutropenia and resulting sepsis
- Capillary leak syndrome (from interleukin-2 treatment)

Renal
- Antineoplastic agents (either cytotoxics, targeted agents or immune checkpoint inhibitors)
- Contrast medium
- Bisphosphonates
- Nonsteroidal anti-inflammatory drugs
- Thrombotic microangiopathies
- Paraneoplastic glomerulonephitis
- Immunomediated nephritis
- Hypercalcaemia

Veno-occlusive disease (less common in solid tumors)

Tumor lysis syndrome (less common in solid tumors)

Light-chain-associated glomerular disease

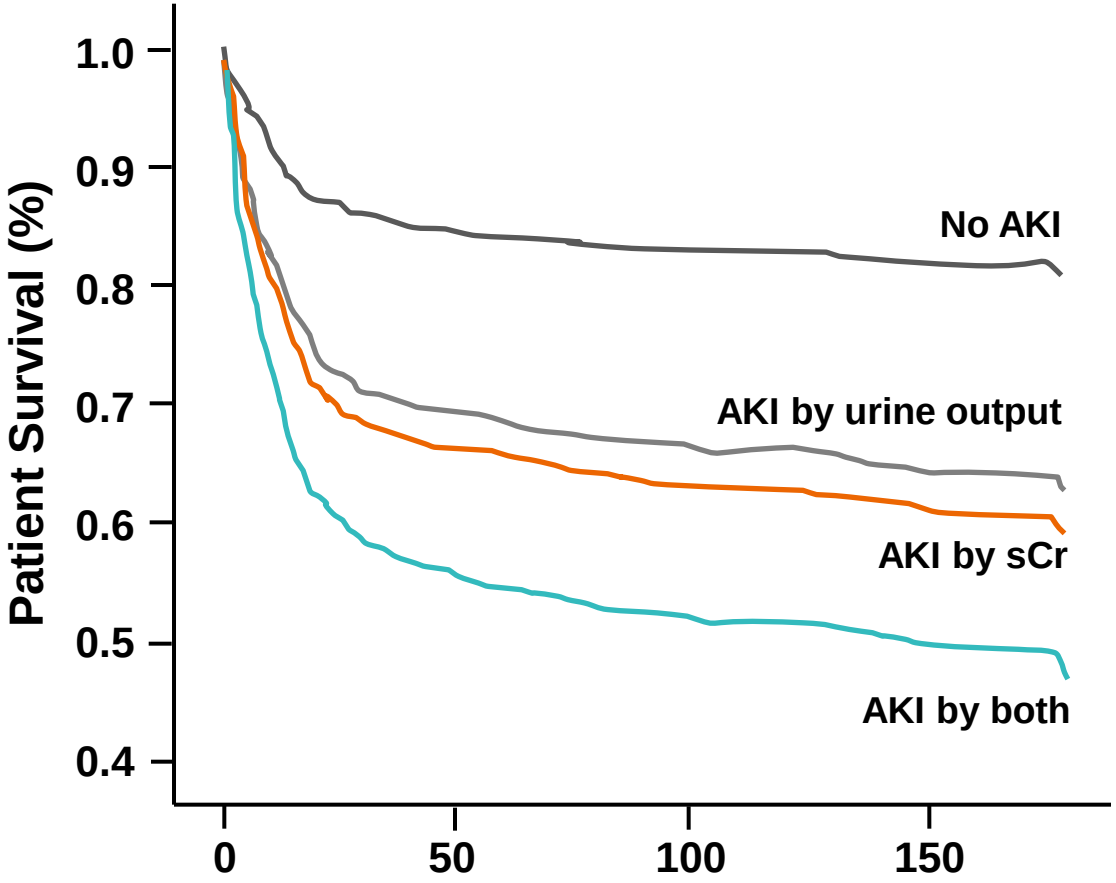
Cancer infiltration

Hematopoietic stem cell transplants

Postrenal
- Compression/obstruction

Cosmai L, et al. *Clin Kidney J.* 2021;14:70–83.

Cancer Patient Mortality by AKI Diagnosis



Córdova-Sánchez BM, et al. *BioMed Res Intern*. 2016:6805169.

AKI in the Emergency Department

- Many cases of AKI come through the emergency department (ED).
- Outpatients and patients from resource-limited clinics with a KDIGO stage 2 or 3 should be sent to the ED for evaluation of AKI.
- Recommendations include measuring creatinine and urine output for all patients at risk.
  - Isotonic fluid administration causing a downtrend in creatinine is a gold standard diagnostic measure for AKI in the ED

Manzoor H. StatPearls. 2020. https://www.statpearls.com/ArticleLibrary/viewarticle/91960. Accessed May 30, 2021.

Contrast-Associated AKI

- Iodinated contrast-associated AKI (CA-AKI) is the third most common hospital-acquired AKI
- CA-AKI can be caused by hypoxia damage to renal parenchyma or a toxic effect of contrast medium on renal tubules and capillaries
- More likely to develop CA-AKI if other risk factors are present in prior 48 hours
  - Nephrotoxic drugs
  - Hemodynamic failure
  - Diabetes

Li Y, et al. *Contrast Media Mol Imaging*. 2020; 2020: 3295176.

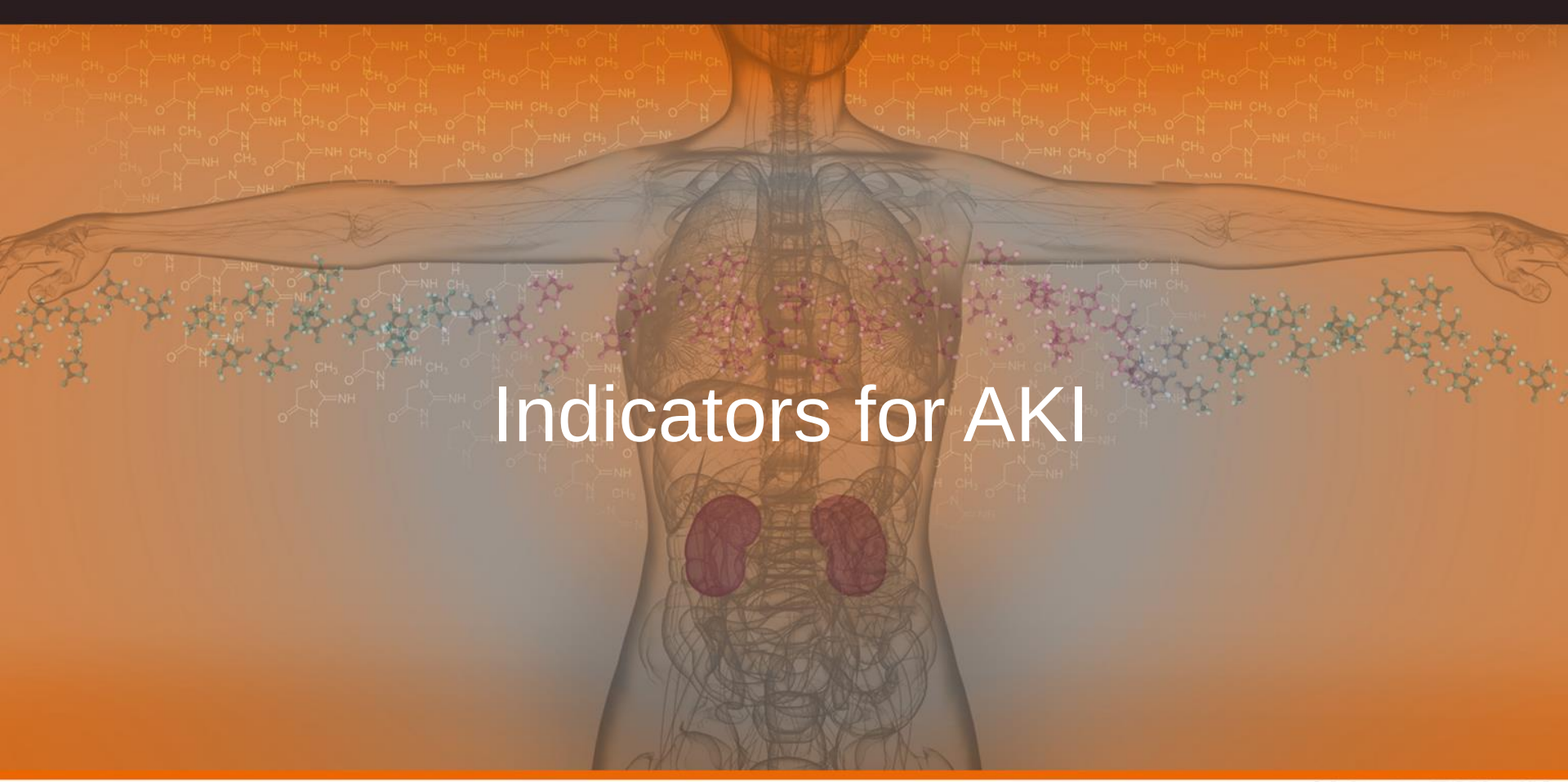
Predictors of Contrast-Induced Acute Kidney Injury

Emergency Versus Elective Percutaneous Coronary Intervention

	Univariate OR (95% CI)	*P*-Value	Multivariate OR (95% CI)	*P*-Value
Age >75 years	1.19 (0.86–1.64)	0.290		
Male	1.01 (0.69–1.47)	0.960		
CV/eGFR	1.14 (1.05–1.25)	0.002	1.08 (0.98–1.19)	0.100
Diabetes mellitus	0.96 (0.70–1.33)	0.830		
Emergency procedure	3.83 (2.74–5.36)	< 0.001	3.70 (2.55–5.37)	< 0.001
Prior CHF	1.89 (1.08–3.28)	0.020	1.74 (0.87–3.50)	0.120
IABP use	3.67 (1.71–7.90)	< 0.001	1.67 (0.74–3.80)	0.220
LVEF < 40%	3.30 (2.16–5.05)	< 0.001	2.04 (1.24–3.36)	0.005
Diuretic use	2.04 (1.43–2.92)	< 0.001	1.46 (0.95–2.25)	0.080
Hb < 10 g/dl	2.80 (1.53–5.13)	< 0.001	2.31 (1.17–4.55)	0.020
SAP	1.00	(ref.)	1.00	(ref.)
UAP/NSTEMI	2.71 (1.73–4.25)	< 0.001	2.82 (1.74–4.57)	< 0.001
STEMI	4.34 (3.03–6.24)	< 0.001	3.75 (2.52–5.59)	< 0.001

CV, contrast volume; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; IABP, intra-aortic balloon pumping; LVEF; left ventricular ejection fraction; NSTEMI, non-ST-segment elevation myocardial infarction; SAP, stable angina pectoris; STEMI, ST-segment elevation myocardial infarction; UAP, unstable angina pectoris.

Abe D, et al. *Circ J.* 2014;78:85–91.



Indicators for AKI

Definitions of AKI, CKD, and AKD

	Functional Criteria	Structural Criteria
AKI	Increase in SCr by 50% within 7 days, OR Increase in SCr by 0.3 mg/dL (26.5 µmol/L) within 2 days OR oliguria	No criteria
CKD	GFR < 60 mL/min for > 3 months	Kidney damage > 3 months
AKD	AKI, OR GFR < 60 mL/min for < 3 months, OR Decrease in GFR by ≥ 35 % or increase in SCr by > 50 % for < 3 months	Kidney damage for < 3 months
NDK	GFR ≥ 60 mL/min Stable SCr	No damage

GFR assessed from measured or estimated GFR. Estimated GFR does not reflect measured GFR in AKI as accurately as in CKD. Kidney damage assessed by pathology, urine, or blood markers, imaging, and – for CKD – presence of a kidney transplant. AKD, acute kidney diseases and disorders; AKI, acute kidney injury; CKD, chronic kidney disease; GFR, glomerular filtration rate; NKD, no known kidney disease; SCr, serum creatinine.

Kidney Disease: Improving Global Outcomes (KDIGO)
Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney Int Suppl* 2012; Volume 2, Issue 1:1–126.

Urine Output

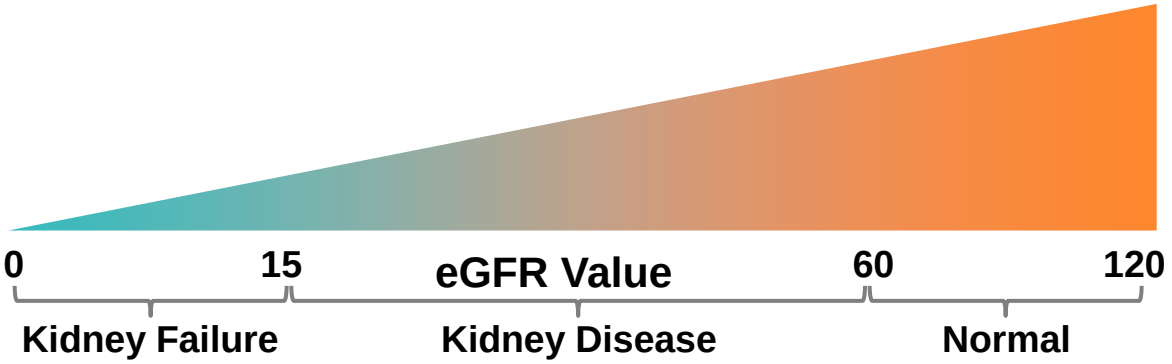
- May be misleading.
  - Lack of clarity on measuring urine output
  - Consecutive hourly readings or mean hourly output?

- KDIGO staging may have different outcomes depending on whether urine output, serum creatinine, or both are considered.

Allen JC, et al. *BMC Nephrol.* 2020;21:19. https://doi.org/10.1186/s12882-019-1678-2

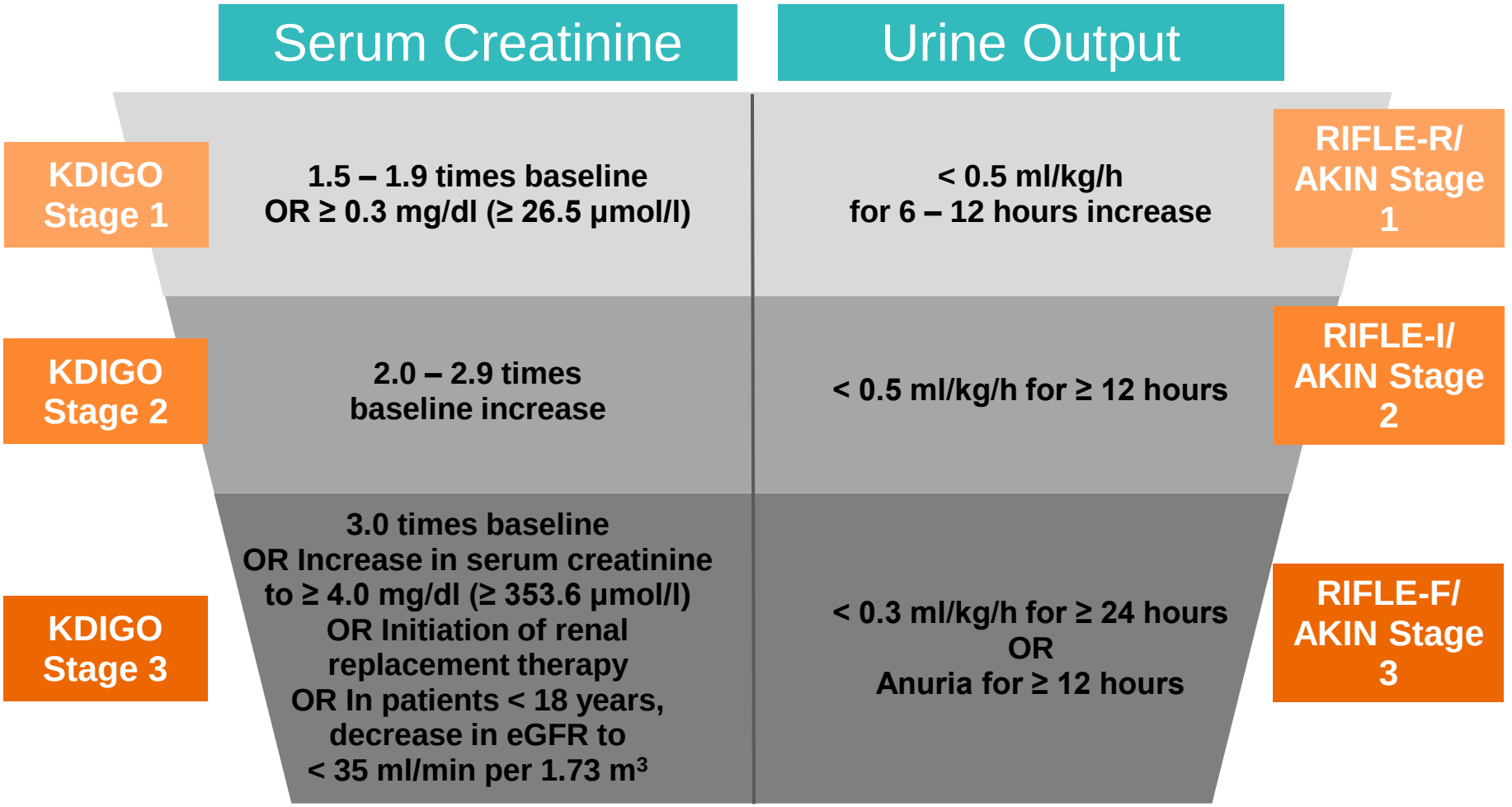
Creatinine and GFR

- Creatinine
  - Breakdown product of creatinine
  - Exclusively filtered out by the kidneys (no resorption)
  - Estimates renal function
- GFR
  - Glomerular filtration rate
  - Volume of creatinine cleared per unit time
  - Some equations also take age and sex into account.



https://www.mayoclinic.org/tests-procedures/creatinine-test/about/pac-20384646. Accessed May 28, 2021.

KDIGO, RIFLE, and AKIN Staging



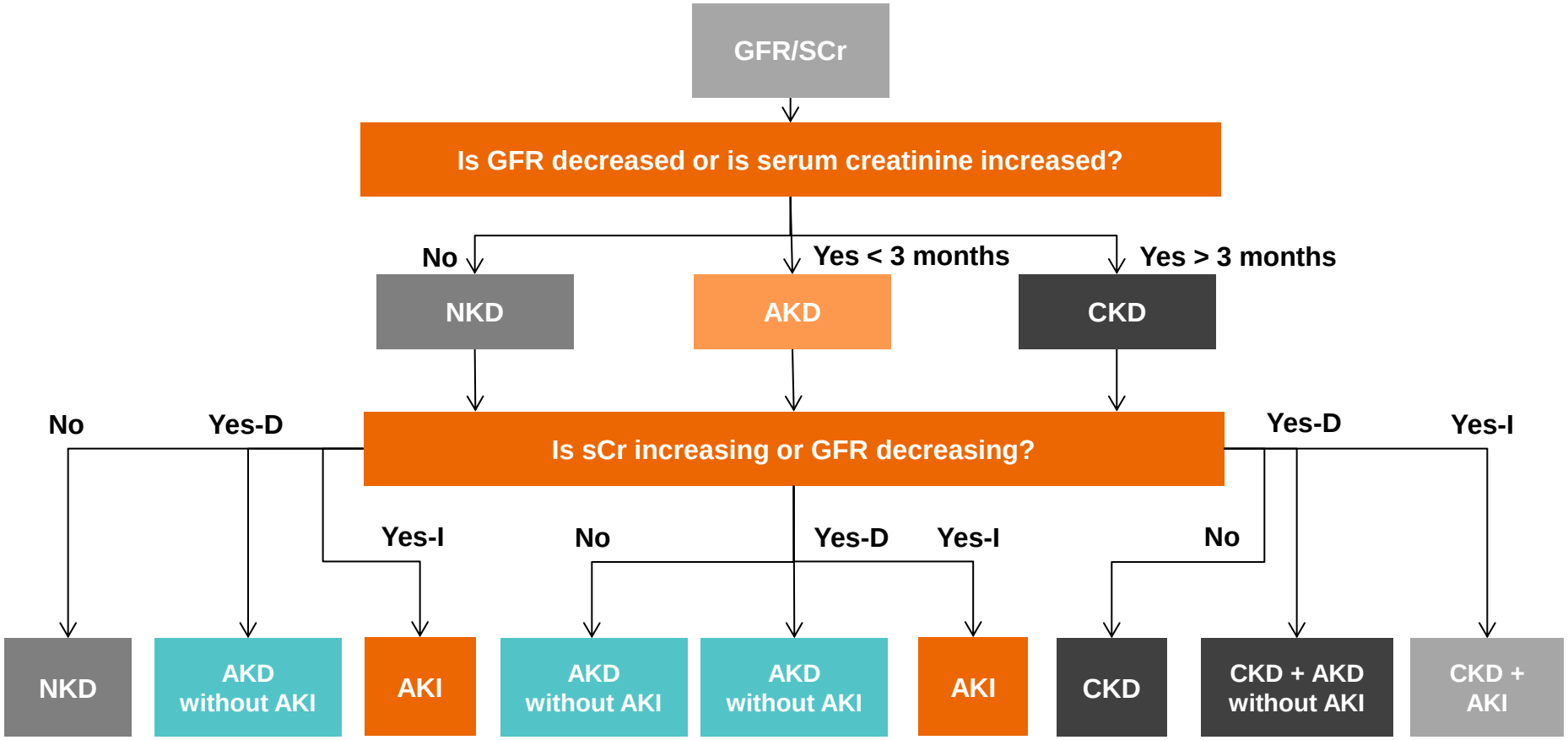
Kidney Disease: Improving Global Outcomes (KDIGO)
Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney Int Suppl* 2012; Volume 2, Issue 1:1–126.

AKI Diagnosis

Serum Creatinine (mg/dL)						Diagnosis AKI	
Case	Baseline	Day 1	Day 2	Day 3	Day 7	Criterion 1: 50% from Baseline	Criterion 2: ≥ 0.3 mg/dL Rise in ≤ 48 Hours
A	1.0	1.3	1.5	2.0	1.0	Yes	Yes
B	1.0	1.1	1.2	1.4	1.0	No	Yes
C	0.4	0.5	0.6	0.7	0.4	Yes	No
D	1.0	1.1	1.2	1.3	1.5	Yes	No
E	1.0	1.3	1.5	1.8	2.2	Yes	Yes
F	?	3.0	2.6	2.2	1.0	?	No
G	?	1.8	2.0	2.2	1.6	?	Yes
H	?	3.0	3.1	3.0	2.9	?	No

Kidney Disease: Improving Global Outcomes (KDIGO)
Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney Int Suppl* 2012; Volume 2, Issue 1:1–126.

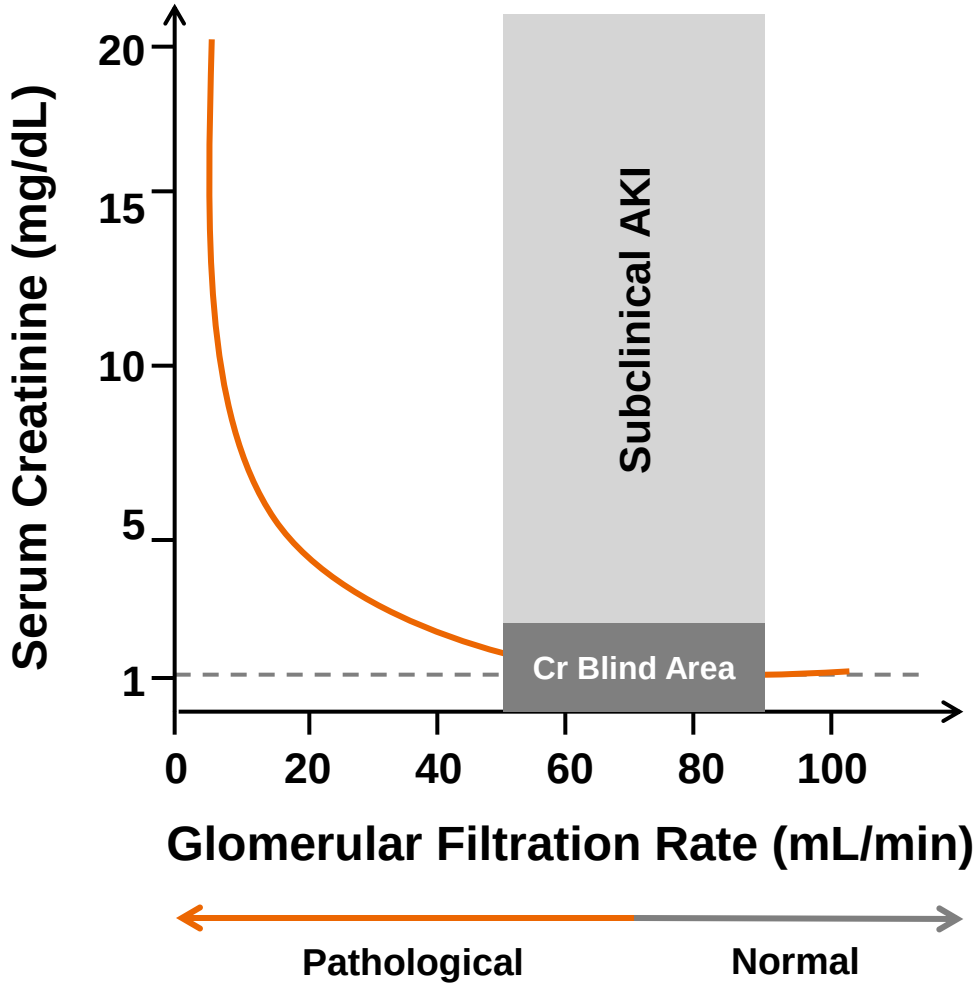
GFR/SCr Algorithm



AKD, acute kidney disease/disorder; AKI, acute kidney injury; CKD, chronic kidney disease; GFR, glomerular filtration rate; NKD, no known kidney disease; sCr, serum creatinine

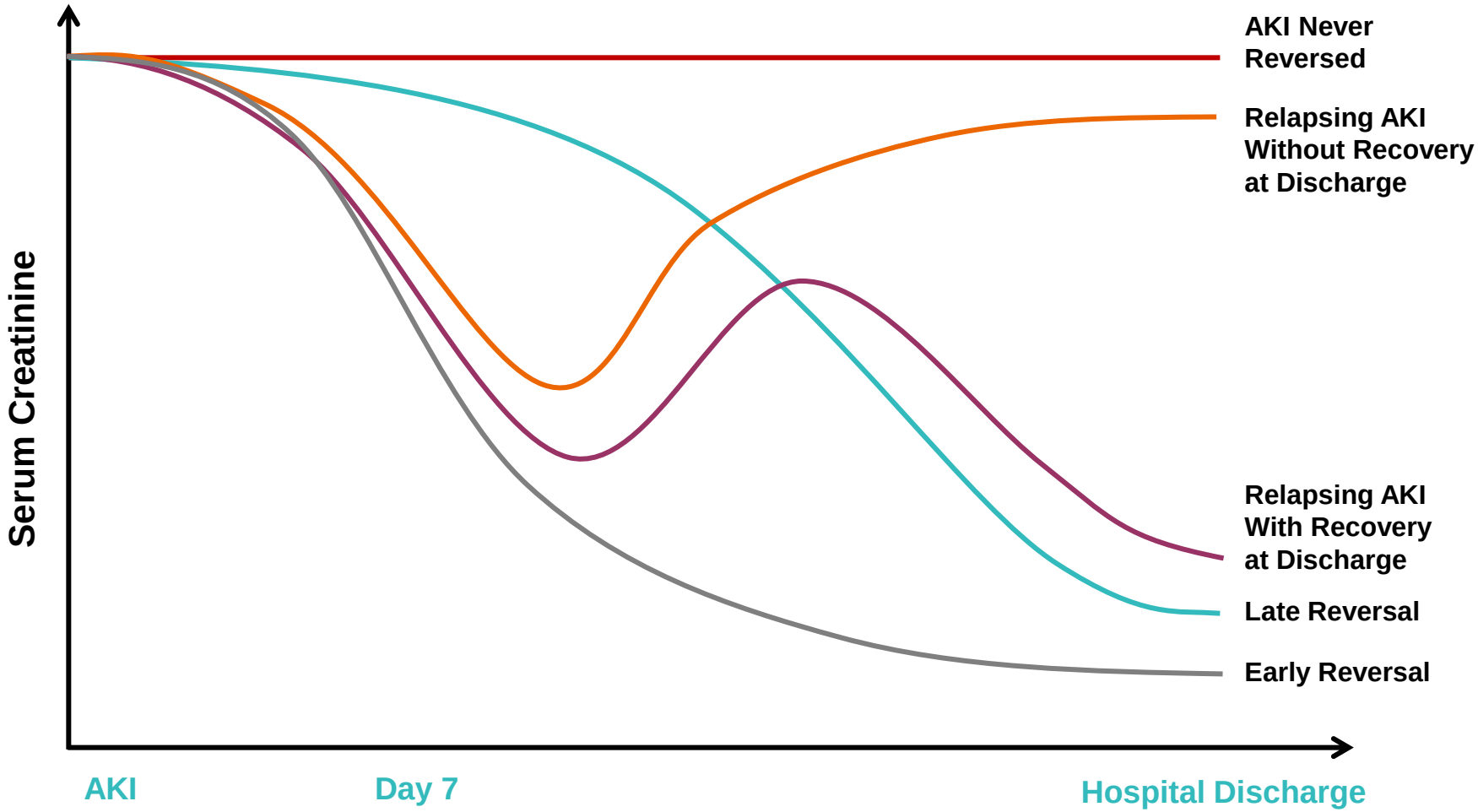
Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney Int Suppl* 2012; Volume 2, Issue 1:1–126.

Creatinine in Subclinical AKI



Meersch M, et al. *Anesth Analg*. 2017;125:1223–32.

Time Course of AKI by Serum Creatinine



Gamerio J, et al. *Clin Kidney J.* 2021;14(3):789–804.

Urine Creatinine Clearance

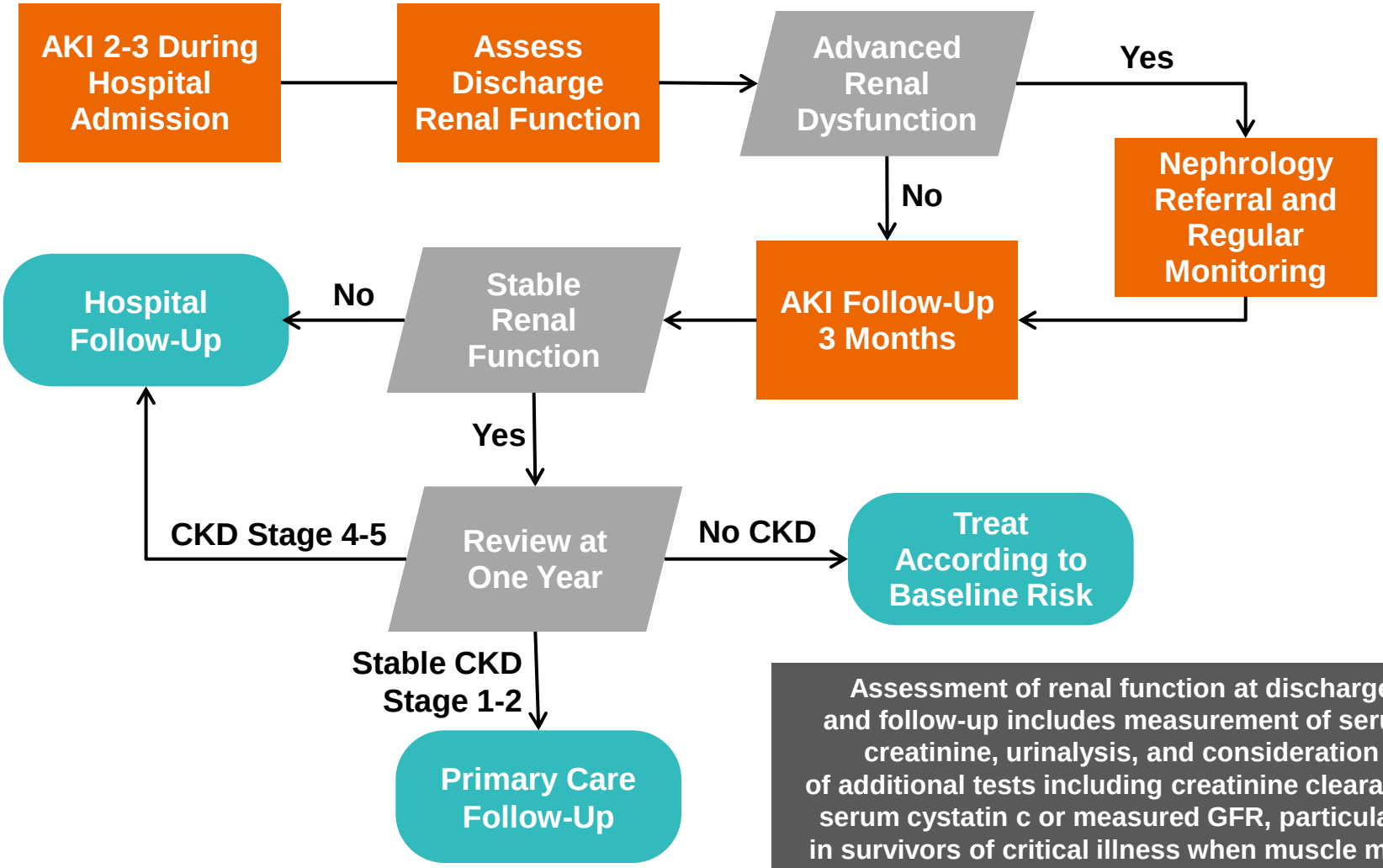
- Computed from a timed 24-hour urine collection
- Often used to estimate GFR
- May not be reliable in critically ill patients or patients with comorbidities
  - Requires a steady hemodynamic state over 24 hours
- May overestimate GFR due to tubal secretion of creatinine

Shahbaz H, et al. Creatinine Clearance. Updated Sept 2, 2020. https://www.ncbi.nlm.nih.gov/books/NBK544228/

Other Methods of Diagnosis

- Serum markers
  - Urea nitrogen, interleukins, NGAL
- Urine
  - Fractional excretion (sodium, urea), protein/creatinine ratio, sediment (casts, WBCs, eosinophils), enzyme activity
- Imaging
  - Ultrasound, CT, MRI, nuclear renal scan

Assessment of AKI Progression

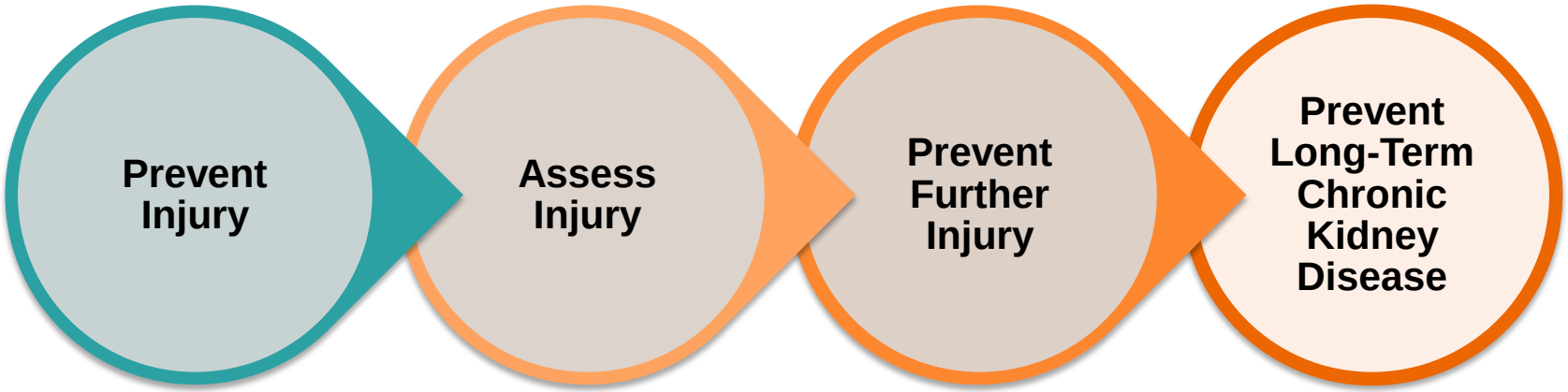


Assessment of renal function at discharge and follow-up includes measurement of serum creatinine, urinalysis, and consideration of additional tests including creatinine clearance, serum cystatin c or measured GFR, particularly in survivors of critical illness when muscle mass and creatinine generation are likely to be abnormal.

Forni LG, et al. *Intensive Care Med*. 2017;43:855–66.

Biomarkers and Rapid Assessment

Why is Rapid Assessment Important in AKI?



Potential Biomarkers of AKI

AKI Biomarker	Risk Assessment	Prediction of AKI	Diagnosis of AKI	Severity of AKI	Kidney Recovery
Alanine aminopeptidase; alkaline phosphatase; γ-glutamyl transpeptidase			X	X	
Calprotectin			X		
C-C motif chemokine ligand 14					X
Chitinase 3-like protein 1			X		
Cystatin C			X	X	
Dickkopf-3	X				
α glutathione S-transferase			X		
π glutathione S-transferase			X		
Hepatocyte growth factor				X	X
Hepcidin			X	X	
Tissue metalloproteinase-2; insulin-like growth factor binding protein-7		X	X	X	
Interleukin-18		X	X		

Ostermann M, et al. *JAMA Network Open.* 2020;3(10):e2019209. doi:10.1001/jamanetworkopen.2020.19209

Potential Biomarkers of AKI

AKI Biomarker	Risk Assessment	Prediction of AKI	Diagnosis of AKI	Severity of AKI	Kidney Recovery
Kidney injury molecule–1		X	X	X	
Liver-type fatty acid-binding protein			X		
MicroRNA			X		
Monocyte chemoattractant peptide-1				X	
N-acetyl-β-D-glucosaminidase			X		
Neutrophil gelatinase-associated lipocalin			X	X	
Netrin-1			X		
Osteopontin			X	X	
Proenkephalin A			X	X	X
Tumor necrosis factor			X		

Ostermann M, et al. *JAMA Network Open.* 2020;3(10):e2019209. doi:10.1001/jamanetworkopen.2020.19209

Refined Staging System for the Diagnosis of AKI

Current Diagnostic AKI Criteria

AKI Stage 1

- Increase in sCr level
- Decrease in UO

Expanded Diagnostic AKI Criteria

AKI Stage 1S	**Biomarker +**	**AND**	No increase in sCr level No decrease in UO	**AND**
AKI Stage 1A	**Biomarker -**	**AND**	Increase in sCr level Decrease in UO	**OR**
AKI Stage 1B	**Biomarker +**	**AND**	Increase in sCr level Decrease in UO	**OR**

Ostermann M, et al. *JAMA Network Open.* 2020;3(10):e2019209. doi:10.1001/jamanetworkopen.2020.19209

Proposed New Definition of AKI With Biomarkers

Functional Criteria	Stage	Damage Criteria
No change or sCr level increase < 0.3 mg/dL and no UO criteria	1S	Biomarker +
Increase of sCr level by ≥ 0.3 mg/dL for ≤ 48 h or ≥ 150% for ≤ 7 days and/or UO < 0.5 mL/kg/h for > 6 h	1A	Biomarker -
	1B	Biomarker +
Increase of sCr level by > 200% and/or UO < 0.5 mL/kg/h for > 12 h	2A	Biomarker -
	2B	Biomarker +
Increase of sCr level by > 300% (≥ 4.0 mg/dL with an acute increase of ≥ 0.5 mg/dL) and/or UO < 0.3 mL/kg/h for > 24 h or anuria for > 12 h and/or acute KRT	3A	Biomarker -
	3B	Biomarker +

Ostermann M, et al. *JAMA Network Open.* 2020;3(10):e2019209. doi:10.1001/jamanetworkopen.2020.19209

Physiological Biomarkers of AKI

Physiological Biomarker	Parameter	Unit	Bedside	Invasive	Continuous	Clinical Performance	Cost
Urine indices	Urine Na, Fe_{Na}, Fe_{urea} osmolality	mEq/l, AU, mosm/kg H_2O	+	−	−	+	+
Serial serum creatinine	Estimated GFR	mg/dl	+	−	−	?	+
Real-time measured GFR	Measured GFR	ml/min	+	+	−	?	+++
Continuous urine flow	Urine output	ml/kg/h	+	−	+	?	+
Doppler ultrasound	Macrocirculation	resistive index	+	−	−	?	++
Contrast-enhanced ultrasound	Macro/ microcirculation	AU	+	+	−	?	+++
Urine pO_2	Renal medullary O_2 tension	mm Hg	+	−	+	?	++
Bladder pO_2	Tissue O_2 tension	mm Hg	+	+	+	?	++
BOLD MRI	Renal O_2 availability	Hb O_2/Hb	−	−	−	?	++++
Positron emission tomography	O_2 uptake/ renal metabolism	mCi/μg	−	+	−	?	++++
Near infrared spectroscopy	Renal O_2 availability	Hb O_2/Hb	+	−	+	?	++++
Bioelectrical impedance analysis	Renal tissue perfusion	AU	+	−	+	?	+

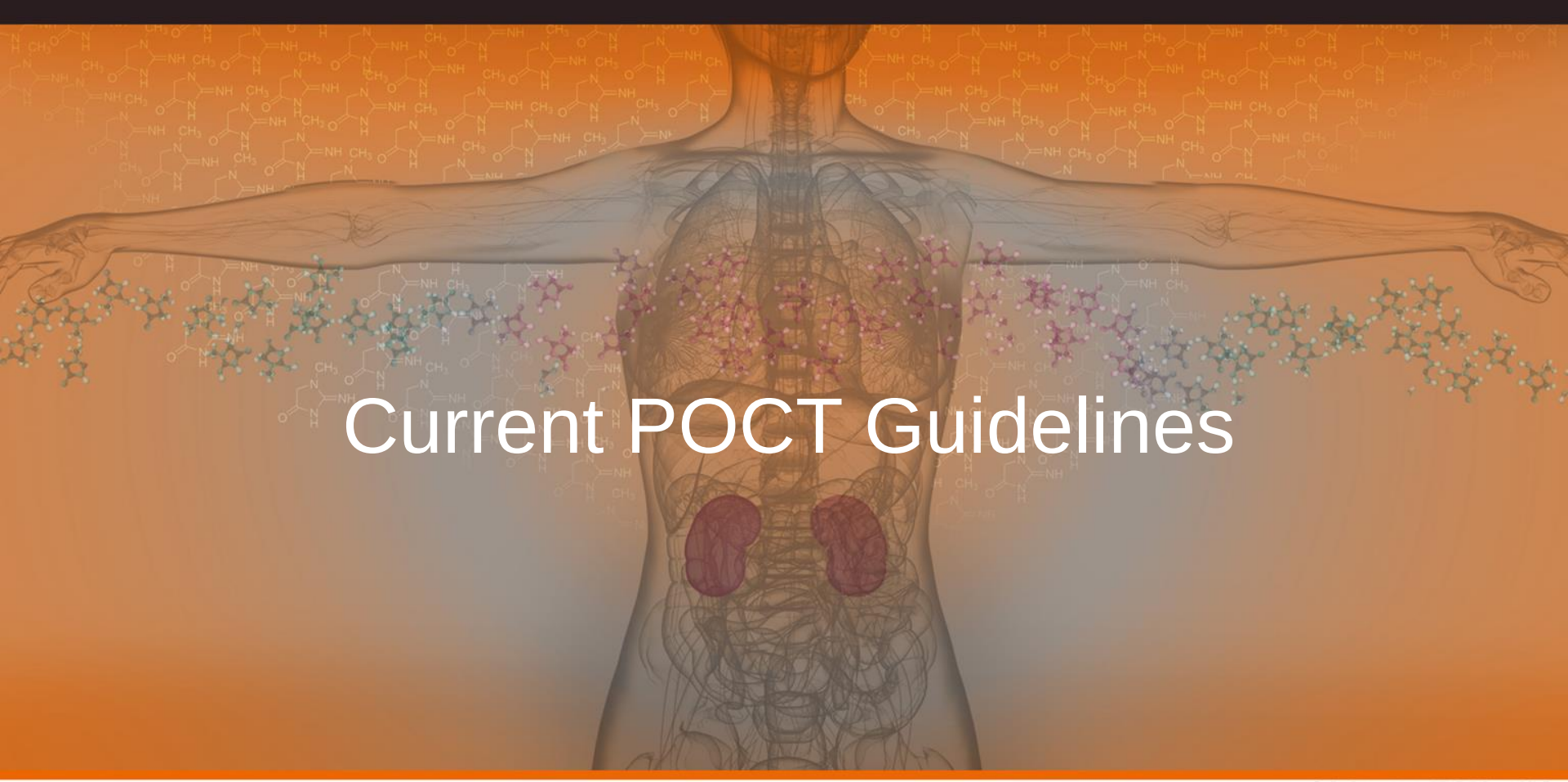
Okusa MD, Jaber BL, Doran P, et al. *Contrib Nephrol.* 2013;182.

Biomarkers of Short-Term AKI Recovery Versus AKD

AKI Biomarker		
Angiotensinogen	Acute CRS, cardiac surgery, ICU	AKI progression
Cystatin C	ICU	RRT
Hepatocyte growth factor	ICU	RRT
IGFBP7/TIMP-2	ICU, cardiac surgery	RRT
IL-18	ICU, acute CRS, cardiac surgery, renal transplantation	AKI progression, RRT, DGF
KIM-2	ICU, hospitalized patients, renal transplantation	AKI progression, need for RRT, DGF
L-FABP	ICU, cardiac surgery	AKI progression, RRT
MicroRNA	ICU, cardiac surgery	AKI progression, RRT
NAG	Hospitalized patients	RRT
NGAL	ICU, cardiac surgery, acute CRS, renal transplantation	AKI progression, RRT, DGF

CRS: cardiorenal syndrome; DGF: delayed graft function; IGFBP-7 insulin-like growth factor binding protein 7; IL-18: interleukin 18; L-FABP liver-type fatty acid-binding protein; KIM-1 kidney injury molecule-1; NAG N-acetyl-β-d-glucosaminidase; NGAL neutrophil gelatinase-associated lipocalin; TIMP-2 tissue metalloproteinase 2; RRT renal replacement therapy

Forni LG, et al. *Intensive Care Med*. 2017;43:855–66.



Current POCT Guidelines

National Academy of Clinical Biochemistry Point-of-Care Guideline

Guideline 156.

Recommend that clinicians routinely provide point-of-care testing (POCT) in the cardiovascular diagnostics laboratory (CVDL) for creatinine and BUN; we found fair evidence that POCT in this environment improves important patient outcomes and that the benefits outweigh any potential harm.

Strength/consensus of recommendation: B

Level of evidence: II

Nichols JH. *Evidence-Based Practice for Point-of-Care Testing.* National Academy of Clinical Biochemistry. 2007.

Guideline Level of Evidence

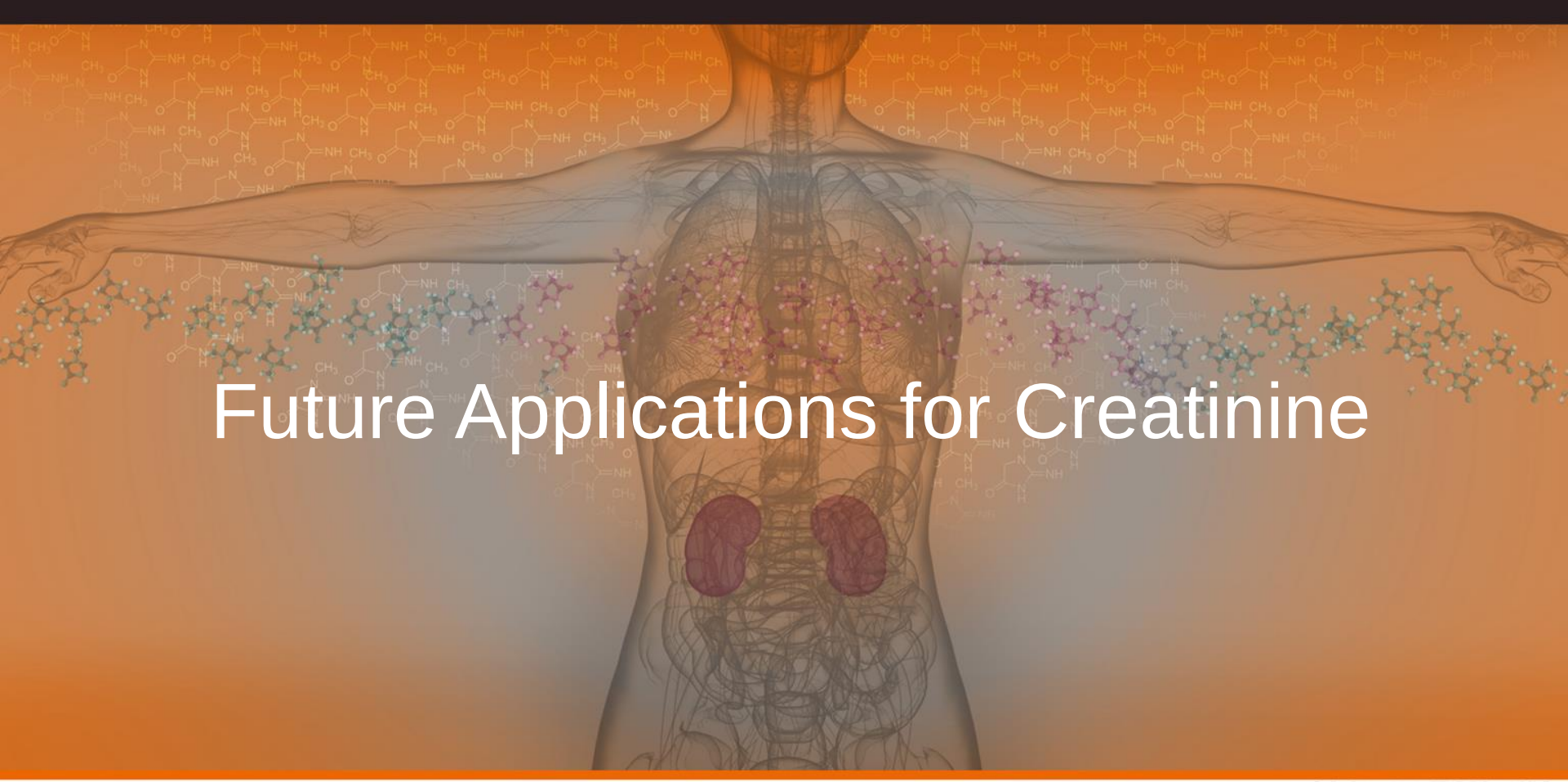
- Without POCT 44% of renal function test results are not available before scheduled procedures
  - Central lab testing
- Wait times drastically reduced with POCT
  - 188 versus 141 minutes ($P = 0.02$)

Nichols JH. *Evidence-Based Practice for Point-of-Care Testing.* National Academy of Clinical Biochemistry. 2007.

AACC Guidance Document on Management of Point-of-Care Testing

Creatinine testing prior to contrast radiology studies speaks for itself with respect to how it improves patient process. Glomerular filtration rate (GFR) based on blood creatinine levels is used to assess for underlying chronic kidney disease; a risk factor for contrast induced nephropathy (CIN), and an individual's subsequent risk for CIN. Provision of creatinine near/prior to such radiology studies allows for a rapid assessment of renal function without waiting for a central lab assayed result. POCT in this process should theoretically improve radiology throughput.

Nichols JH, et al. *J Appl Lab Med*. 2020;doi:10.1093/jalm/jfaa059.

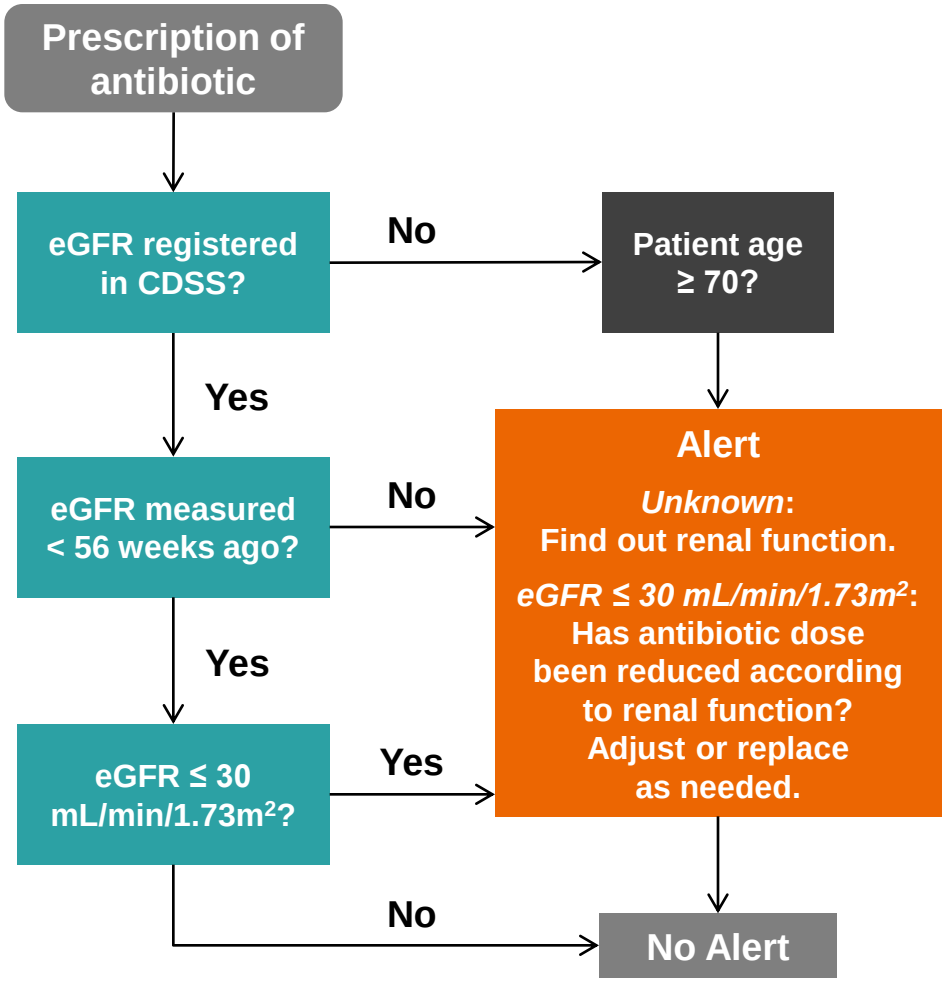


Future Applications for Creatinine

Other Creatinine Applications

- Assessment of kidney function in other conditions
  - Hypertension
  - Cardiac conditions
  - Cancers
  - Diabetes
  - Polycystic kidney disease
  - Trauma
  - Perioperative levels for risk stratification
  - OTC medications
  - Infection
  - Emergency department
    - Prior to CT or MRI
  - Infusion centers
    - Chemotherapy
    - Antibiotics
    - Nephrotoxic agents

POCT Creatinine in the Pharmacy



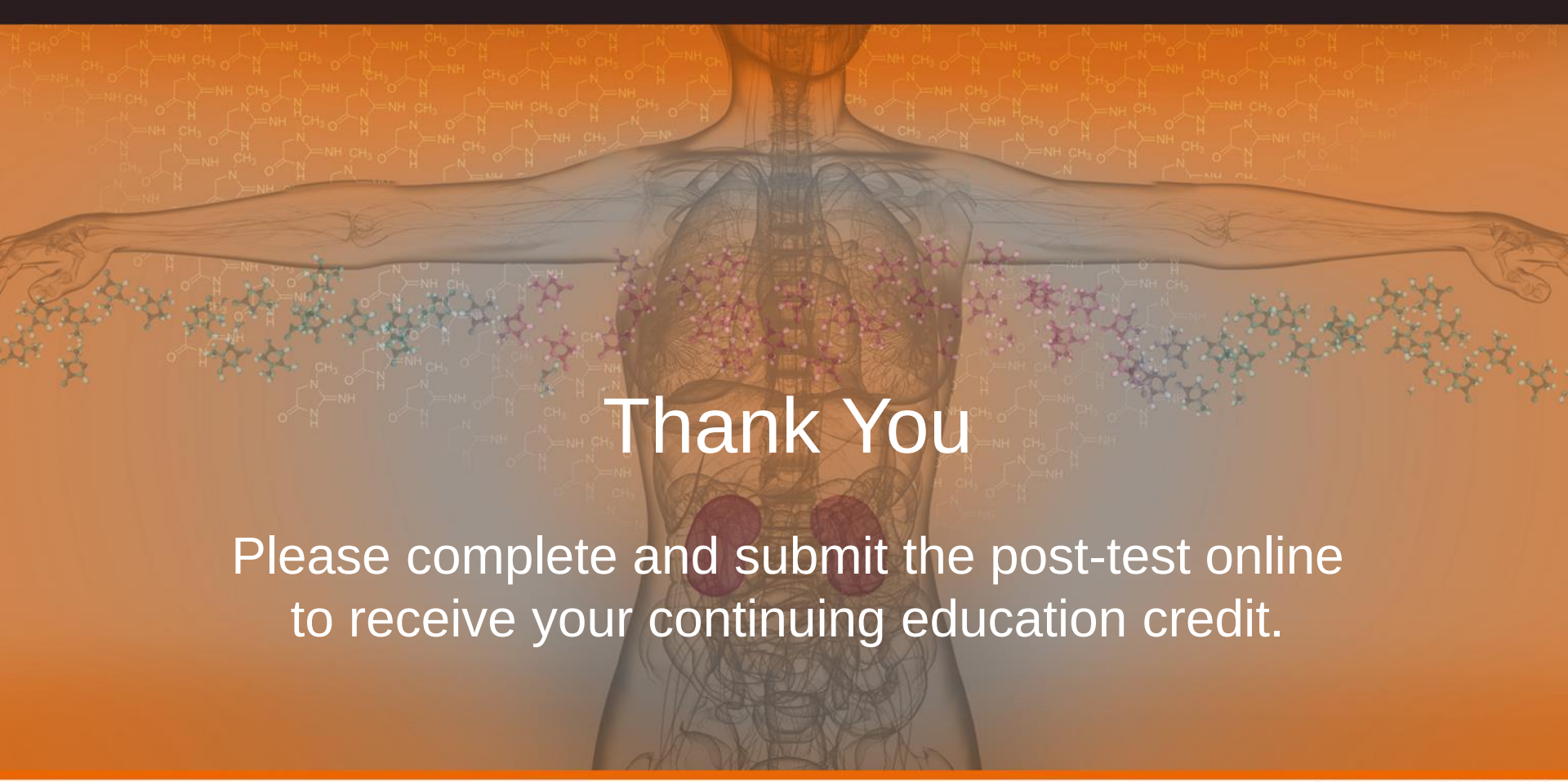
- eGFR calculated by POCT creatinine
- Allowed pharmacists to identify potential renal impairment prior to filling antibiotic prescriptions and as part of chronic condition management

CDSS: clinical decision making support system

Heringa M, et al. *Drugs Aging*. 2017;34:851–58.
https://www.pharmacytoday.org/article/S1042-0991(21)00168-7/fulltext. Accessed June 1, 2021.

When to Use POCT for Creatinine

- Patient is currently undergoing chemotherapy or being treated with nephrotoxic medications.
  - Or these treatments are planned
- Patient is going to receive a scan with contrast.
- Patient is hypertensive or has other cardiac conditions.
- AKI is suspected.



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