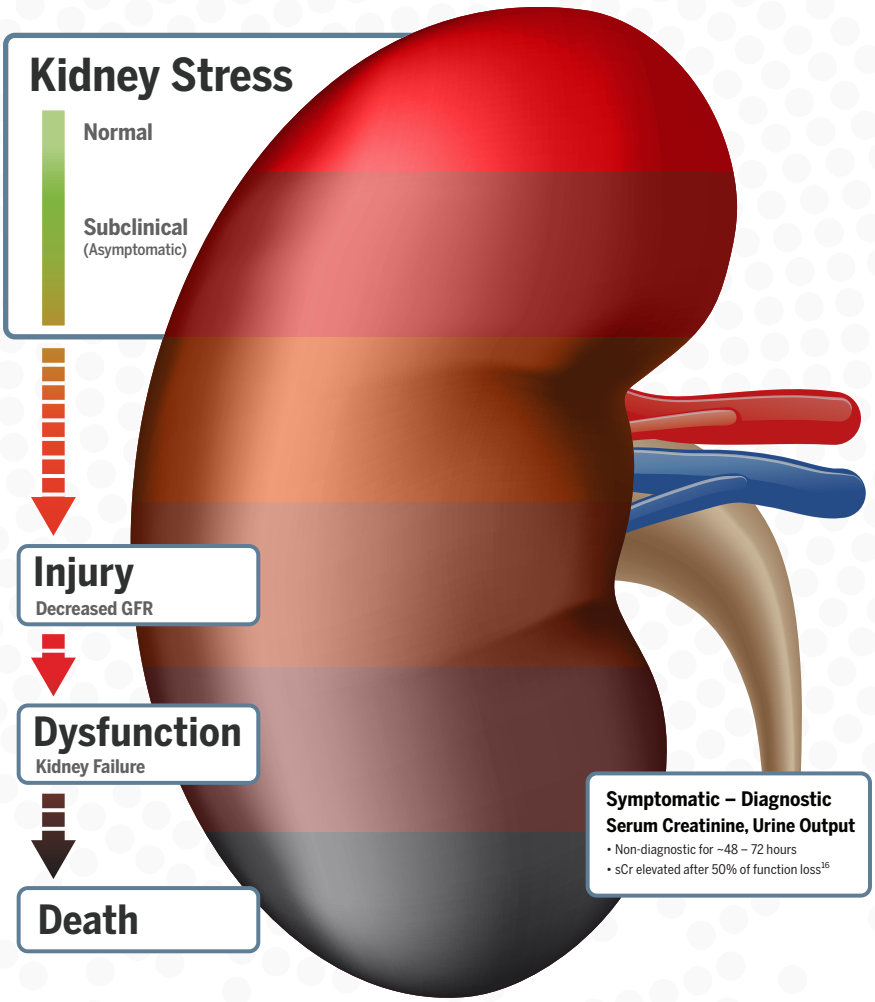
BIOMÉRIEUX

VIDAS® NEPHROCHECK®
[TIMP-2 • IGFBP-7]

Know Earlier. Intervene Sooner. Avoid AKI.

42% OF CRITICALLY ILL PATIENTS WITH SEPSIS DEVELOP AKI[1]

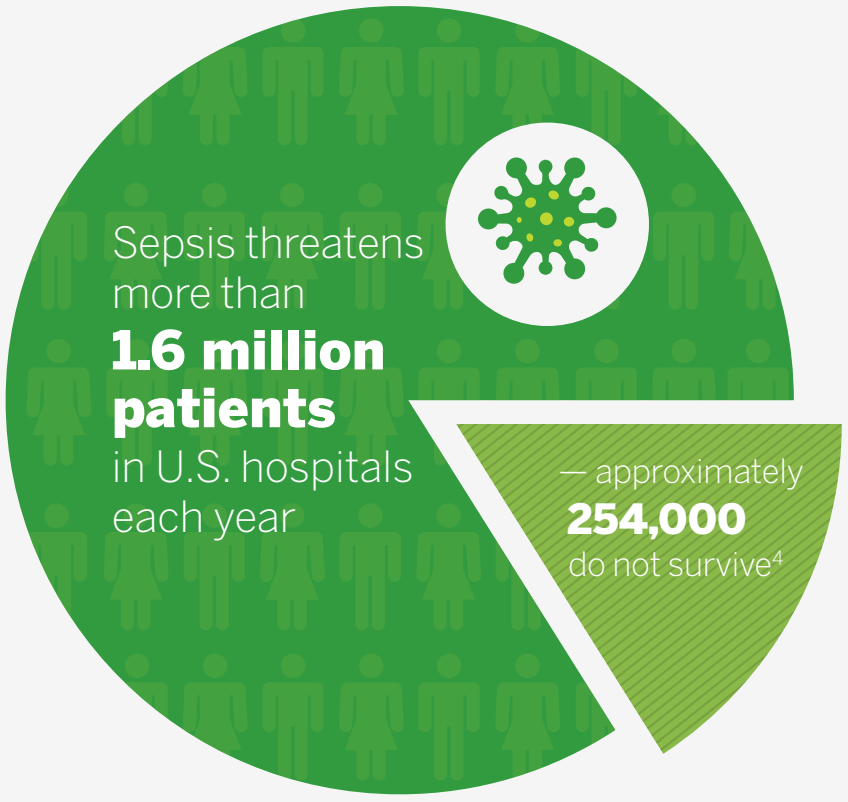


AKI (Acute Kidney Injury)

SEPSIS AND ACUTE KIDNEY INJURY (AKI) ARE OFTEN CO-MORBIDITIES.

SEPSIS

Sepsis — a life-threatening organ dysfunction caused by a dysregulated host response to infection[3] — is a serious medical threat.[4]



Sepsis is Common

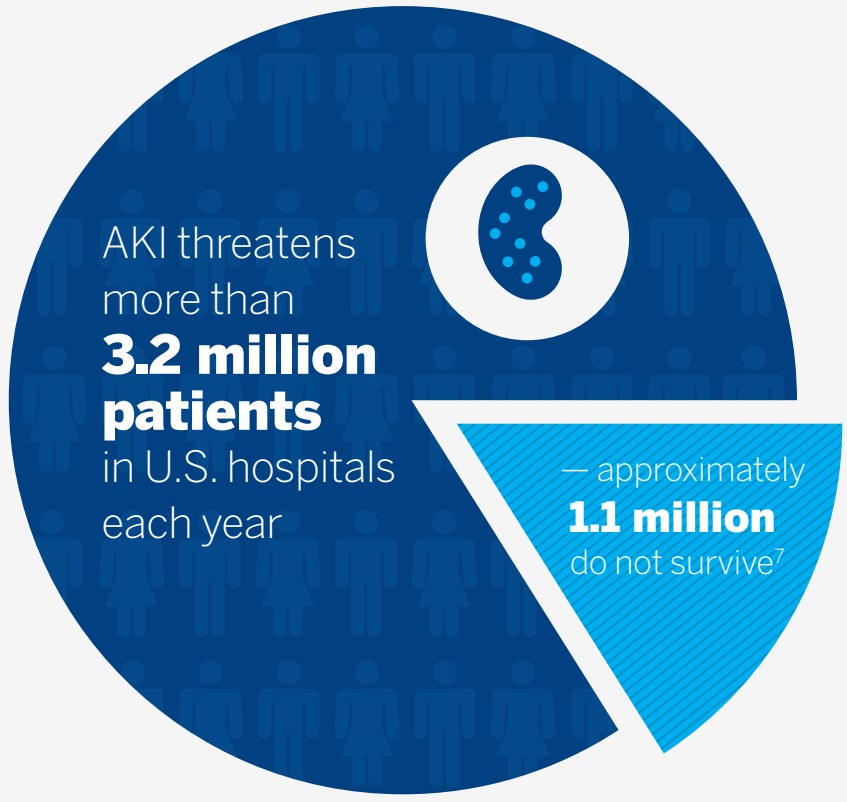
- Number four in clinically addressable potential inpatient complications (PIC)[5]
- Length of stay for sepsis more than doubled between 2000-2008[4]

Sepsis is Dangerous

- Sepsis is complex and deadly
- Delays in proper antibiotic treatment decrease survival rates
- This leads to early use of broad-spectrum antibiotics

AKI

AKI — a rapid loss of kidney function that includes, but is not limited to, acute renal failure — is a serious medical threat.[6,7]



AKI is Common

- Number one in clinically addressable potential inpatient complications (PIC)[5]
- Length of stay for AKI more than doubled between 1998-2002[8]

AKI is Dangerous

- Patient outcomes are significantly compromised with AKI[8-10]
- AKI is a common complication of sepsis[6]
- Antibiotic exposure can be nephrotoxic[6]

SEPSIS & AKI CAN HAVE SIGNIFICANT ECONOMIC AND CLINICAL IMPLICATIONS.

SEPSIS IS COSTLY

$15B

Estimated spending per year on sepsis in the U.S.[4]

AKI IS COSTLY

>$10B

Estimated spending per year on AKI in the U.S.[11]

SEPSIS IS DEADLY

16%

In-hospital mortality rate (2009)[4]

14.7%

Overall mortality rate (2009)[4]

8x

Higher mortality than overall inpatient rate[4]

AKI IS DEADLY

>20%

In-hospital mortality rate (2013)[12,13]

25%

Overall mortality rate (2015)[14,26]

10x

Higher mortality than overall inpatient rate[8]

FOR AKI ALONE, THE RAMIFICATIONS ARE SERIOUS.

LENGTH OF STAY
2 – 3 Times Worse[8]

HOSPITAL COSTS
2 – 3 Times Worse[8]

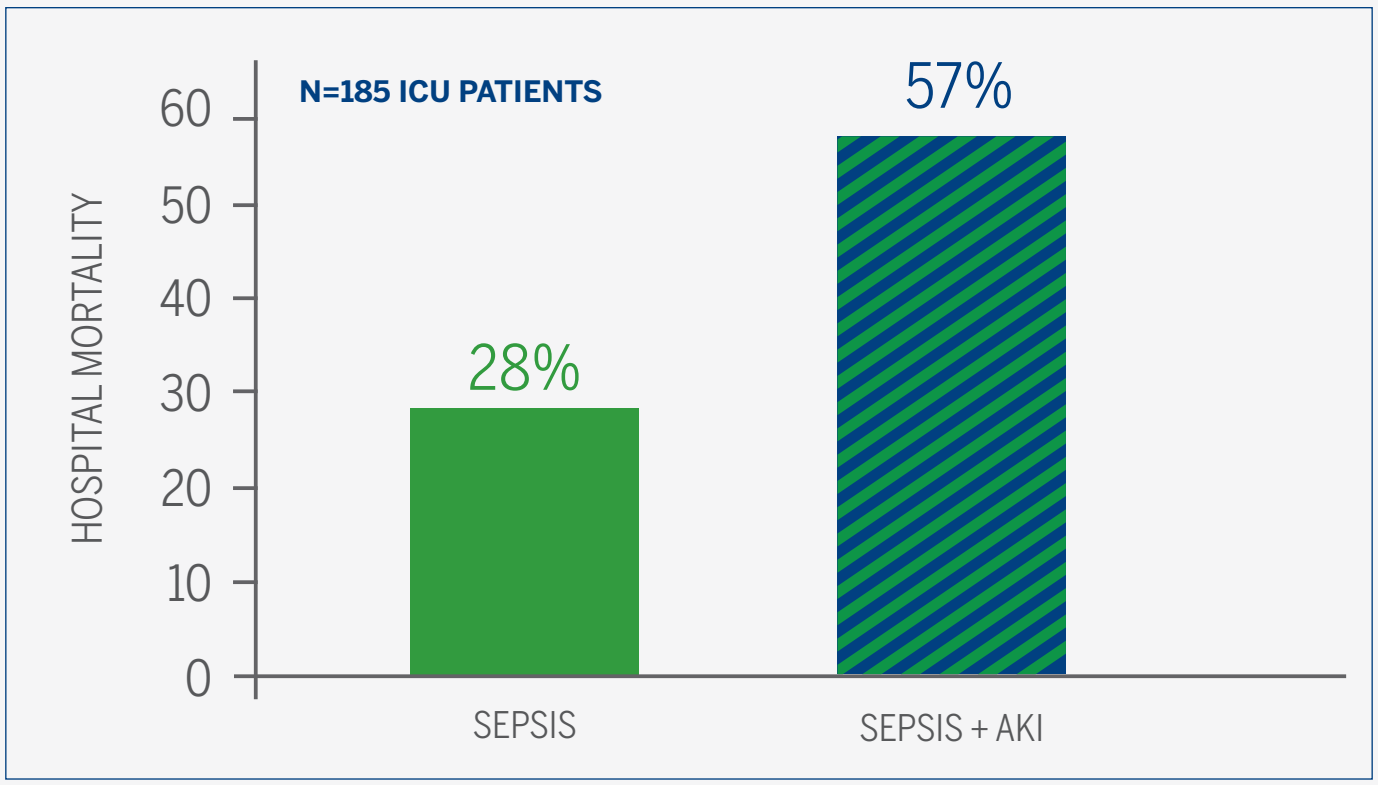
READMISSIONS
2 – 3 Times Worse[9]

CHRONIC KIDNEY DISEASE INCIDENCE
2 – 3 Times Worse[10]

HOSPITAL MORTALITY
6 – 13 Times Worse[8]

Mortality doubles in patients with sepsis *and* acute kidney injury (AKI).[15]

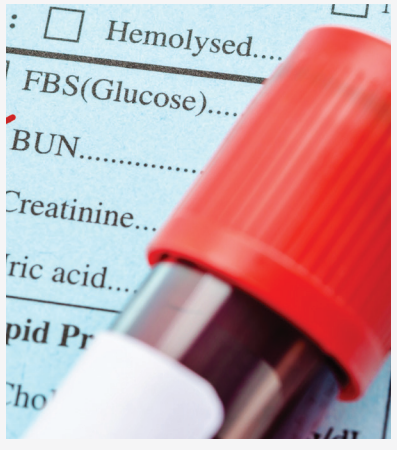
- Results from a large multinational cross-sectional study on the epidemiology of AKI in ICU patients using the complete Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group criteria.[6]
  - Adjusted risks for AKI and mortality were similar across different continents and regions.



CURRENT DIAGNOSTIC TOOLS ARE INADEQUATE FOR ASSESSING THE RISK OF AKI.

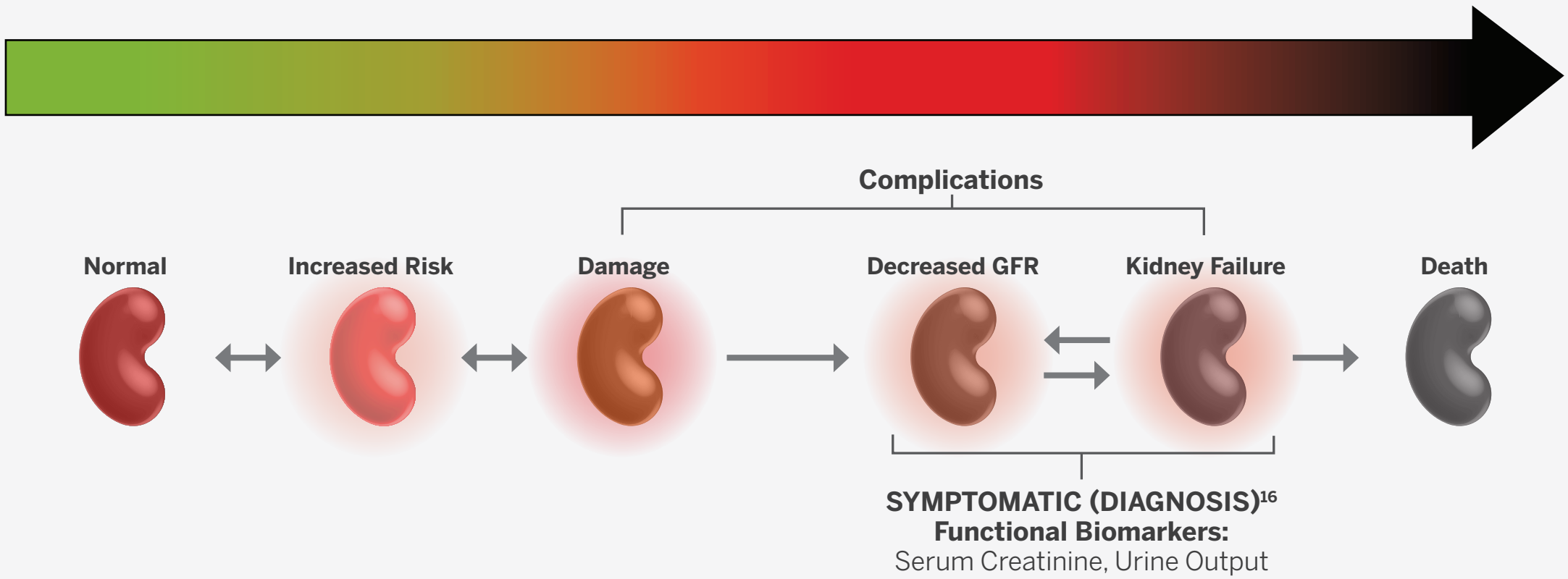
Serum Creatinine

- Lagging indicator – only elevates after 50% of function loss[16]
- Nondiagnostic for 48% of moderate/severe AKI[17]
- Inconsistencies due to muscle mass, hydration, etc[18]
- 24-48 hours for serum creatinine to rise[19]



Urine Output

- Lagging indicator[17]
- Not consistently measured[17]
- Compromised by HAI initiatives (e.g., early foley removal)[20]
- 6 hours required for changes in urine output[17]

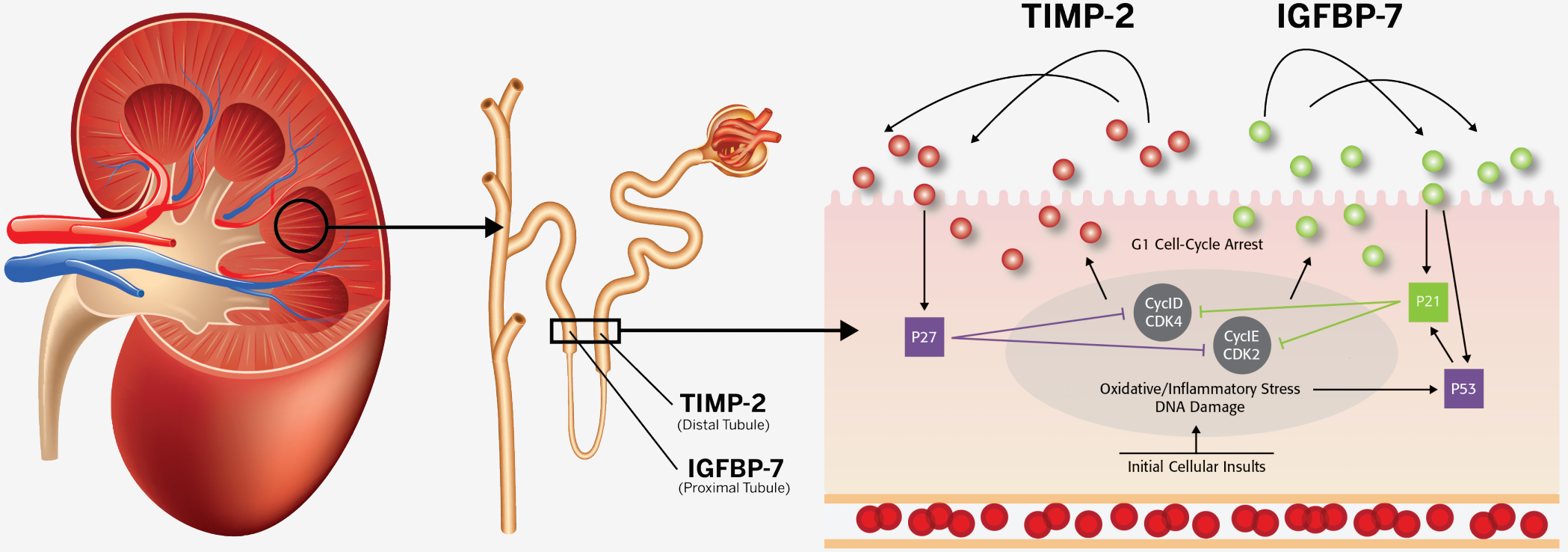


BIOMARKERS ARE PRODUCED DURING KIDNEY STRESS BEFORE SIGNIFICANT DAMAGE OCCURS.[21,22]

TIMP-2 and IGFBP-7

- Expressed by tubular cells in response to stress
- Results in G1 cell cycle arrest, presumably to prevent cells with possible damage from dividing
- Injured cells spread the alarm to nearby cells via TIMP-2 and IGFBP-7

A cellular alarm prior to actual damage — when intervention can still make a difference.[22]



TIMP-2: Tissue Inhibitor of Metalloproteinase-2
IGFBP-7: Insulin-like Growth Factor Binding Protein-7

Adapted from proposed model Kashani K. *Crit Care.* 2013;17:R25.

Know earlier. Intervene sooner. Avoid AKI.

VIDAS® NEPHROCHECK®
[TIMP-2 • IGFBP-7]

FDA-CLEARED TO AID CLINICIANS IN THE RISK ASSESSMENT OF AKI

In a multicenter study, clinical trials demonstrated that patients* with an AKIRISK™ Score > 0.30 are at greater risk for developing moderate to severe AKI.[21]

The combination of urinary biomarkers TIMP-2 and IGFBP-7 demonstrated:

- A single cutoff of AKIRISK Score > 0.30 achieves high sensitivity up to 89.9% with a specificity of 45.2%.

VIDAS NEPHROCHECK
captures the majority of AKI positive cases:
UP TO
89.9%

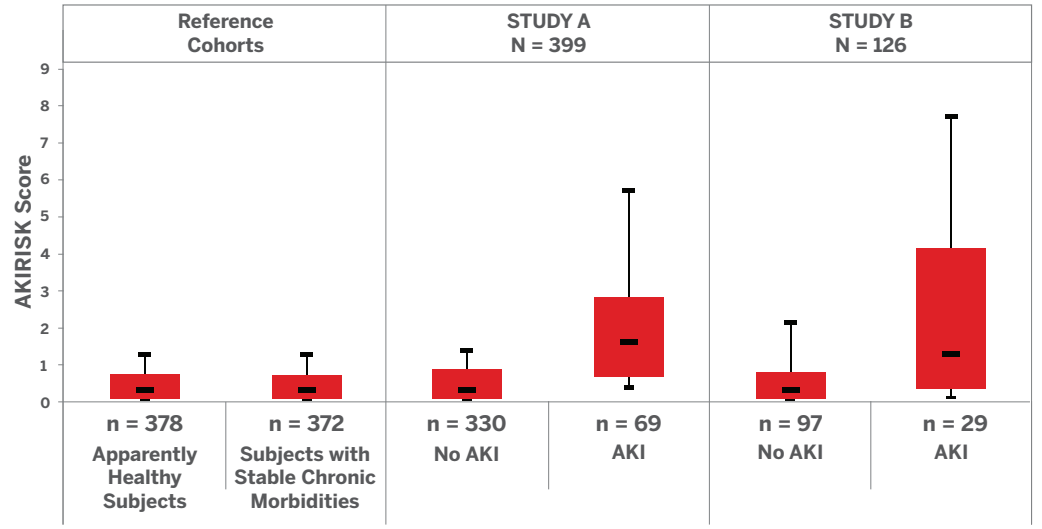
*The VIDAS NEPHROCHECK assay is intended to be used in conjunction with clinical evaluation in patients who currently have or have had within the past 24 hours acute cardiovascular and or respiratory compromise and are ICU patients as an aid in the risk assessment for moderate or severe acute kidney injury (AKI) within 12 hours of patient assessment. The VIDAS NEPHROCHECK test is intended to be used in patients 21 years of age or older.

VIDAS NEPHROCHECK is an automated test for use on the VIDAS 3 instrument.

$$\text{VIDAS NEPHROCHECK Result (AKIRISK Score)} = \frac{[\text{TIMP-2} \bullet \text{IGFBP-7}]}{1000}$$

(units=(ng/mL)²/1000)

VIDAS NEPHROCHECK SIGNIFICANTLY DISCRIMINATES AKI FROM NO-AKI (P < 0.05)[21]



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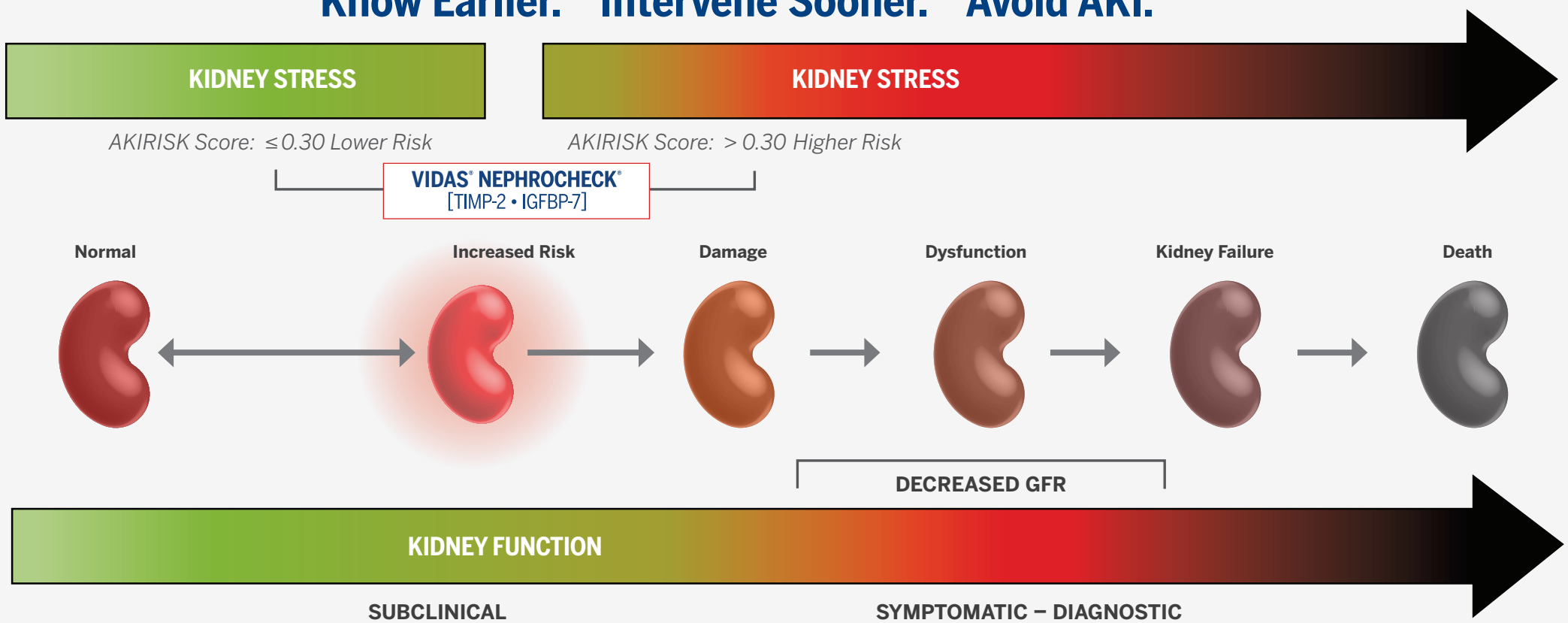

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[TIMP-2 • IGFBP-7]

ALTHOUGH OFTEN UNDER-REPORTED,[24] AKI HITS HOME AT A TYPICAL 350-BED HOSPITAL.

Estimated National CMS Average AKI Impact: 350-Bed Hospital

Annual AKI Diagnoses

1,687 CMS PUBLIC REPORTED HOSPITAL DIAGNOSES[25]

516 ESTIMATED MODERATE/SEVERE ICU DIAGNOSES[26]

$38,000	10 DAYS	16.1%
AVG COST INCREASE PER PATIENT[27]	AVG LENGTH OF STAY INCREASE PER PATIENT[27]	READMISSION RATE INCREASE PER PATIENT[9]

AKI is one of the more prevalent and serious morbidities in hospitalized patients[21, 27]

Associated with a **10-fold increase in hospital mortality**

Decreased survival for up to **15 years post-surgery**

Increased risk for **chronic kidney disease (CKD)**

AKI COMPLICATES PATIENT MANAGEMENT

AT ICU ADMISSION

Stabilize patient

Identify specific disease states

Input orders for care

Communicate, set expectations with patient and family

Essential communication and handoff at shift change

RENAL FUNCTION CHANGES

Urine output has decreased

Serum creatinine has not elevated significantly

Kidneys may be going down

SHIFT IN CARE STRATEGY

Rethink fluids, drugs, perfusion… reactive to damage

Call for renal consult?

Communicate with family: new complication could affect condition, prognosis, and length of ICU stay

Each step could increase length of stay.

KNOW EARLIER. INTERVENE SOONER WITH VIDAS NEPHROCHECK.

FDA-cleared for the risk assessment of AKI.

- Specific to AKI[21]
- Easy, fast, and simple, ~45 - minute urine test
- Up to 12 tests at a time including VIDAS B·R·A·H·M·S PCT™
- Controls can be run day of use with patient tests
- Bidirectonal LIS connection with VIDAS® 3

Reducing complications associated with AKI can save lives and reduce hospital costs.[21]

Intended Use: The VIDAS NEPHROCHECK assay is intended to be used in conjunction with clinical evaluation in patients who currently have or have had within the past 24 hours acute cardiovascular and or respiratory compromise and are ICU patients as an aid in the risk assessment for moderate or severe acute kidney injury (AKI) within 12 hours of patient assessment. The VIDAS NEPHROCHECK test is intended to be used in patients 21 years of age or older.

VIDAS NEPHROCHECK is an automated test for use on the VIDAS 3 instrument.

IDENTIFICATION OF HIGH-RISK PATIENTS ALLOWS FOR PROTECTIVE MEASURES:[28]

CLINICAL EVALUATION OF ICU PATIENTS

With acute cardiovascular and/or respiratory compromise

Within 24 hours

VIDAS® NEPHROCHECK®
[TIMP-2 • IGFBP-7]

VIDAS NEPHROCHECK Test Results	What It Means*
Negative AKIRISK™ Score ≤ 0.30	Patient is at lower risk of developing moderate to severe AKI within 12 hours of evaluation
Positive AKIRISK™ Score > 0.30	Patient is at increased risk of developing moderate to severe AKI within 12 hours of assessment

*Refer to the VIDAS NEPHROCHECK Instructions for Use for full interpretation information.

Early knowledge that a patient is likely to develop AKI may prompt closer patient monitoring and help prevent permanent kidney damage or death.

Optimize patient outcomes.

Know earlier. Intervene sooner. Avoid AKI.

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[TIMP-2 • IGFBP-7]

References

1. Bagshaw SM, George C, Bellomo R; ANZICS Database Management Committee. **Early acute kidney injury and sepsis: a multicentre evaluation.** *Crit Care.* 2008;12(2):R47.
2. Gómez H, Kellum JA. **Sepsis-induced acute kidney injury.** *Curr Opin Crit Care.* 2016;22(6):546-553.
3. Singer M, Deutschman CS, Seymour CW, et al. **The third international consensus definitions for sepsis and septic shock (Sepsis-3).** *JAMA.* 2016;315(8):801–810.
4. Elixhauser A, Friedman B, Stranges E. **Septicemia in U.S. hospitals, 2009: statistical brief #122.** *Healthcare cost and utilization project (HCUP) statistical briefs.* Rockville (MD): Agency for Healthcare Research and Quality (US); 2011.
5. Premier, Inc. Identifying hospital-wide harm associated with increased cost, length of stay and mortality in U.S. hospitals. Complications Research. Available at: http://ftpcontent4.worldnow.com/wtoc/web/Complications-Whitepaper-6-11-14.pdf. Accessed June 8, 2020.
6. Kidney Disease: Improving Global Outcomes (KDIGO). **Clinical practice guideline for acute kidney injury.** *Kidney Inter, Suppl.* 2012; 2:1-138.
7. Brown JR, Rezaee ME, Marshall EJ, et al. **Hospital mortality in the United States following acute kidney injury.** *Biomed Res Int.* 2016;2016:4278579.
8. Dasta JF, Kane-Gill SL, Durtschi AJ, et al. **Costs and outcomes of acute kidney injury (AKI) following cardiac surgery.** *Nephrol Dial Transplant.* 2008;23(6):1970-1974.
9. Brown JR, Parikh CR, Ross CS, et al, for the Northern New England Cardiovascular Disease Study Group. **Impact of perioperative acute kidney injury as a severity index for thirty-day readmission after cardiac surgery.** *Ann Thorac Surg.* 2014;97(1):111-117.
10. Heung M, Steffick DE, Zivin K, et al. **Acute kidney injury recovery pattern and subsequent risk of CKD: an analysis of Veterans Health Administration data.** *Am J Kidney Dis.* 2016;67(5):742-752.
11. Chertow GM, Burdick E, Honour M, et al. **Acute kidney injury, mortality, length of stay, and costs in hospitalized patients.** *J Am Soc Nephrol.* 2005;16:3365-3370.
12. Susantitaphong P, Cruz DN, Cerda J, et al. **World incidence of AKI: a meta-analysis.** *Clin J Am Soc Nephrol.* 2013;8:1482-1493
13. Selby NM, Kolhe NV, McIntyre CW, et al. **Defining the cause of death in hospitalised patients with acute kidney injury.** *PLoS One.* 2012;7:e48580.
14. Doyle JF, Forni LG, **Acute kidney injury: short-term and long-term effects.** *Crit Care.* 2016;20:188
15. Hoste EAJ, Lameire NH, Vanholder RC, et al. **Acute renal failure in patients with sepsis in a surgical ICU: predictive factors, incidence, comorbidity, and outcome.** *J Am Soc Nephrol.* 2003;14(4):1022-1030.
16. Mårtensson J, Martling C-R, Bell M. **Novel biomarkers of acute kidney injury and failure: clinical applicability.** *Brit J Anaesth.* 2012;109(6):843-850.
17. Wlodzimirow KA, Abu-Hanna A, Slabbekoorn M, et al. **A comparison of RIFLE with and without urine output criteria for acute kidney injury in critically ill patients.** *Crit Care.* 2012;16:R200.
18. Baxmann AC, Ahmed MS, Marques NC, et al. **Influence of muscle mass and physical activity on serum and urinary creatinine and serum cystatin C.** *Clin J Am Soc Nephrol.* 2008;3(2):348–354.
19. Ostermann M, Jannidis M. **Acute kidney injury 2016: diagnosis and diagnostic workup.** *Crit Care.* 2016;20(1):299.
20. Gould CV, Umscheid CA, Agarwal RK, et al, Healthcare Infection Control Practices Advisory Committee. **Guideline for Prevention of Catheter-Associated Urinary Tract Infections 2009.** *Infect control Hosp Epidemiol.* 2010;31(4):319-326.
21. VIDAS NEPHROCHECK Package Insert US - 057209 - 01 - 2022-07.
22. Kashani K, Al-Khafaji A, Ardiles T, et al. **Discovery and validation of cell cycle arrest biomarkers in human acute kidney injury.** *Crit Care.* 2013;17:R25.
23. Legrand M, Payen D. **Understanding urine output in critically ill patients.** *Ann Intensive Care.* 2011;1:13.
24. Massicotte-Azarniouch D, Magder S, Goldberg P, et al. **Acute Kidney Injury in the Intensive Care Unit: Risk Factors and Outcomes of Physician Recognition Compared with KDIGO.** *Crit Care Med.* 2015;43(12):245.
25. **Critical Care Statistics.** Society of Critical Care Medicine website. http://www.sccm.org/Communications/Critical-Care-Statistics. Accessed June 9, 2020.
26. Hoste EAJ, Bagshaw SM, Bellomo R, et al. **Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study.** *Intensive Care Med.* 2015;41(8):1411–1423.
27. Hobson C, Ozrazgat-Baslanti T, Kuxhausen A, et. al. **Cost and mortality associated with postoperative acute kidney injury.** *Ann Surg.* 2015;261(6):1207-1214.
28. Meersch M, Schmidt C, Hoffmeier A, et al. **Prevention of cardiac surgery-associated AKI by implementing the KDIGO guidelines in high risk patients identified by biomarkers: the PrevAKI randomized controlled trial.** *Intensive Care Med.* 2017;43:1551-1561.

VIDAS® NEPHROCHECK®

The bioMérieux Solution for Acute Kidney Injury

(Product #421172-01)

DESCRIPTION	QUANTITY
Test Strip	60 each
Solid Phase Receptacle	60 each
S1 Calibrator (1.6 mL)	1 each
C1 Calibrator (1.2 mL)	1 each

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[TIMP-2 • IGFBP-7]

Enhance your Antimicrobial Stewardship with bioMérieux Sepsis Care Management Solutions

- VIDAS® B·R·A·H·M·S PCT™
- VIDAS® 3
- VIRTUO®
- BACT/ALERT® 3D
- BIOFIRE® BCID2 PANEL
- VITEK® MS PRIME
- VITEK® 2
- CLARION®

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