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 — is a serious medical threat.

Sepsis threatens more than **1.6 million patients** in U.S. hospitals each year — approximately **254,000** do not survive.

**Sepsis is Common**

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

**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.

AKI threatens more than **3.2 million patients** in U.S. hospitals each year — approximately **1.1 million** do not survive.

**AKI is Common**

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

**AKI is Dangerous**

- Patient outcomes are significantly compromised with AKI
- AKI is a common complication of sepsis
- Antibiotic exposure can be nephrotoxic
SEPSIS & AKI CAN HAVE SIGNIFICANT ECONOMIC AND CLINICAL IMPLICATIONS.

SEPSIS IS COSTLY

$15B
Estimated spending per year on sepsis in the U.S.\textsuperscript{4}

SEPSIS IS DEADLY

16%
In-hospital mortality rate (2009)\textsuperscript{4}

14.7%
Overall mortality rate (2009)\textsuperscript{4}

8x
Higher mortality than overall inpatient rate\textsuperscript{4}

AKI IS COSTLY

>$10B
Estimated spending per year on AKI in the U.S.\textsuperscript{11}

AKI IS DEADLY

>20%
In-hospital mortality rate (2013)\textsuperscript{12,13}

25%
Overall mortality rate (2015)\textsuperscript{14,26}

10x
Higher mortality than overall inpatient rate\textsuperscript{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\(^\text{16}\)
- Nondiagnostic for 48% of mod/severe AKI\(^\text{17}\)
- Inconsistencies due to muscle mass, hydration, etc\(^\text{18}\)
- 24-48 hours for serum creatinine to rise\(^\text{19}\)

Urine Output

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

Complications

- Symptomatic (Diagnosis)\(^\text{16}\)
- Functional Biomarkers: Serum Creatinine, Urine Output

Normal ↔ Increased Risk ↔ Damage ↔ Decreased GFR ↔ Kidney Failure → Death
BIOMARKERS ARE PRODUCED DURING KIDNEY STRESS BEFORE SIGNIFICANT DAMAGE OCCURS.\textsuperscript{21,22}

**TIMP-2 & 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.\textsuperscript{22}


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

TIMP-2: (Distal Tubule)
IGFBP-7: (Proximal Tubule)
**IDENTIFY KIDNEY STRESS BEFORE DAMAGE OCCURS.**

In a multicenter study, clinical trials demonstrated that patients* with an AKIRISK® Score > 0.3 are at greater risk for developing moderate to severe AKI. The combination of urinary biomarkers TIMP-2 and IGFBP-7 demonstrated:

- A single cutoff of AKIRISK Score > 0.3 achieves high sensitivity up to 92% with a specificity of 46%.

*The NEPHROCHECK Test 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 in the ICU. Intended use patients 21 years of age or older.

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

**Know earlier. Intervene sooner. Avoid AKI.**

**KIDNEY STRESS**

AKIRISK® Score: \( \leq 0.3 \) Lower Risk  
AKIRISK® Score: > 0.3 Higher Risk

**NEPHROCHECK® TEST**  
\([\text{TIMP-2} \times \text{IGFBP-7}]\)

**KIDNEY FUNCTION**

ASYMPTOMATIC  
SYMPTOMATIC (DIAGNOSIS)\(^{23}\)  
Serum Creatinine, Urine Output

**DECREASED GFR**

**The NEPHROCHECK TEST Significantly Discriminates AKI from No-AKI \((P=0.0001)\)\(^{21}\)**

Boxes and whiskers show interquartile ranges and 10th to 90th percentiles, respectively
Although often under-reported, AKI hits home at a typical 350-bed hospital.

### AKI is one of the more prevalent and serious morbidities in hospitalized patients

- 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)**

---

<table>
<thead>
<tr>
<th>Estimated National CMS Average AKI Impact: 350-Bed Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Annual AKI Diagnoses</strong></td>
</tr>
<tr>
<td><strong>1,687</strong> CMS PUBLIC REPORTED HOSPITAL DIAGNOSES</td>
</tr>
<tr>
<td><strong>516</strong> ESTIMATED MODERATE/SEVERE ICU DIAGNOSES</td>
</tr>
<tr>
<td><strong>$38,000</strong> AVG COST INCREASE PER PATIENT</td>
</tr>
<tr>
<td><strong>10 DAYS</strong> AVG LENGTH OF STAY INCREASE PER PATIENT</td>
</tr>
<tr>
<td><strong>16.1%</strong> READMISSION RATE INCREASE PER PATIENT</td>
</tr>
</tbody>
</table>

### AKI Complicates Your 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 NEPHROCHECK.

FDA cleared for the risk assessment of AKI.

• Specific to AKI
• Fast & Simple: 20-minute urine test
• Peer-reviewed evidence
• Easy, cost-effective to implement
• Low capital expense

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

Identification of high-risk patients allows for protective measures:

**CLINICAL EVALUATION OF ICU PATIENTS**
With acute cardiovascular and/or respiratory compromise
*Within 24 hours*

**NEPHROCHECK® TEST**
[TIMP-2 • IGFBP-7]

<table>
<thead>
<tr>
<th>NEPHROCHECK Test Result</th>
<th>What It Means</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative AKIRISK® Score ≤ 0.3</td>
<td>Patient is unlikely to develop moderate to severe AKI within 12 hours of evaluation</td>
</tr>
<tr>
<td>Positive AKIRISK® Score &gt; 0.3</td>
<td>Patient could develop moderate to severe AKI within 12 hours of evaluation</td>
</tr>
</tbody>
</table>

**Intended Use:** The Astute Medical NEPHROCHECK Test System 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 NEPHROCHECK Test System is intended to be used in patients 21 years of age or older.

Know earlier, intervene sooner, avoid AKI. 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.
References


IMPORTANT INFORMATION

The information in this brochure is gathered from third-party sources and is provided on a complimentary basis for your informational and educational purposes only. This information does not constitute medical advice and should not be considered a substitute for the individual professional judgment of any physician or other health care practitioner regarding the appropriate course of action for a particular patient. Any treatment or intervention should be adopted without an independent medical review performed by qualified practitioners acting to ensure the best quality care in the most cost-effective manner. bioMérieux makes no guarantee or representation regarding the accuracy, completeness, or usefulness of this information for any particular purpose, including but not limited to any cost savings. This information has no independent value, and there is no obligation to purchase, recommend, prescribe, or otherwise endorse bioMérieux or any products sold by bioMérieux as a result of accessing and/or using this information. bioMérieux makes no guarantee or representation that the information provided is an accurate representation of your hospital’s annual impact of AKI or potential savings with the implementation of the NEPHROCHECK® TEST.
# The bioMérieux Solution for Acute Kidney Injury

## PRODUCT #  DESCRIPTION

<table>
<thead>
<tr>
<th>PRODUCT #</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>100000</td>
<td>ASTUTE140° Printer Paper Rolls</td>
</tr>
<tr>
<td>400016</td>
<td>ASTUTE140° Electronic Quality Control Device</td>
</tr>
<tr>
<td>500009</td>
<td>NEPHROCHECK® Calibration Verification Kit</td>
</tr>
<tr>
<td>500011</td>
<td>NEPHROCHECK® Test Kit</td>
</tr>
<tr>
<td>500013</td>
<td>NEPHROCHECK® Liquid Controls Kit</td>
</tr>
<tr>
<td>500017</td>
<td>ASTUTE140° Meter Kit</td>
</tr>
</tbody>
</table>

NEPHROCHECK® LOINC code: 88993-1

# The bioMérieux Solution for Sepsis Care Management

- VIDAS® B.R.A.H.M.S. PCT™
- VIDAS® 3
- VIRTUO®
- BACT/ALERT® 3D
- FILMARRAY®
- VITEK® MS
- VITEK® 2
- MYLA®