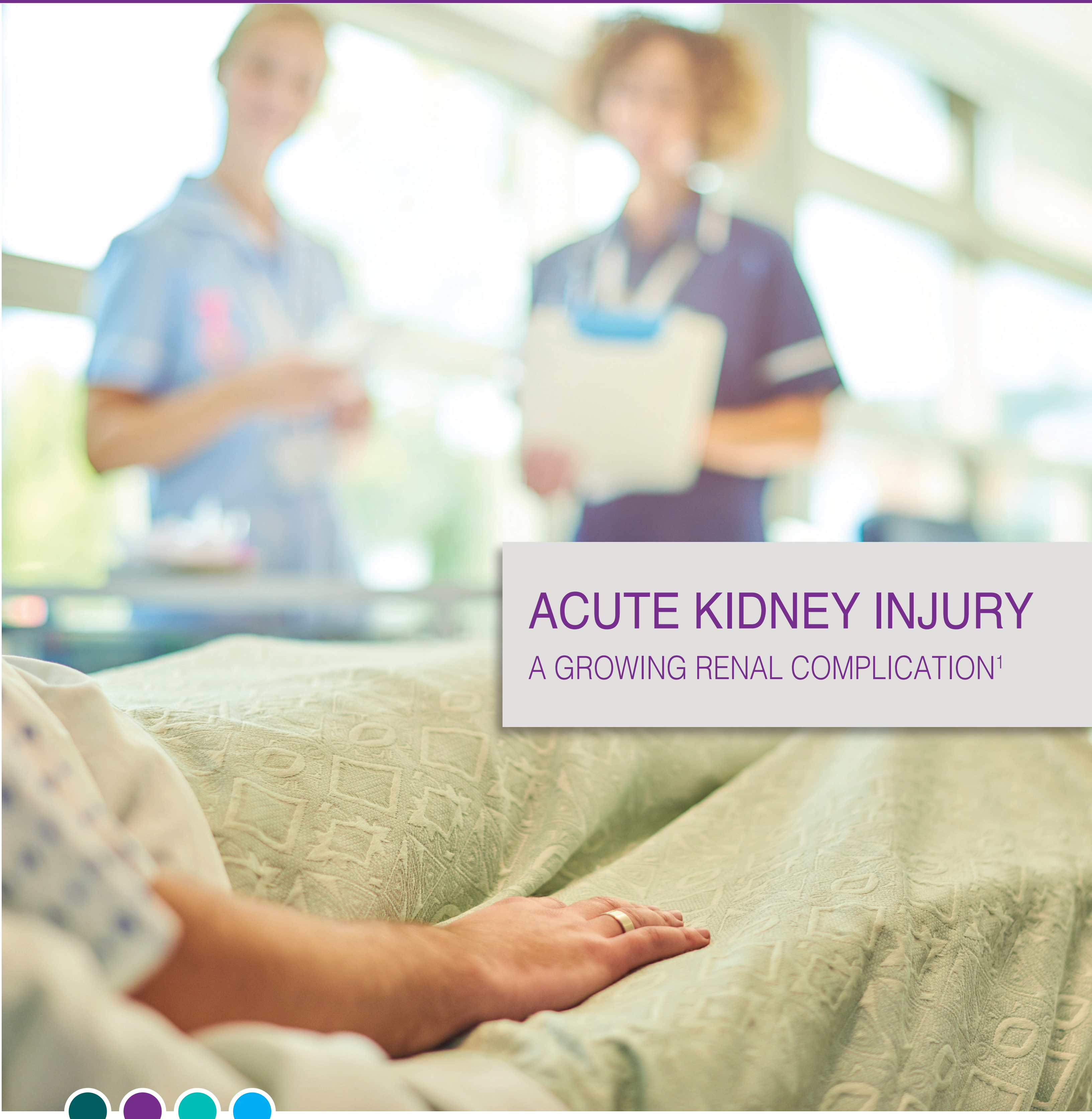


ACUTE KIDNEY INJURY

A GROWING RENAL COMPLICATION[1]

Baxter

AKI AWARENESS

THE DEFINITION OF AKI[2]

According to KDIGO, AKI is defined as any of the following (Not Graded):

- Increase in SCr by ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours; or
- Increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume <0.5 mL/kg/h for 6 hours

INCIDENCE OF AKI[1,3-5]

Worldwide, approximately **20–30%** of hospitalized patients have AKI.

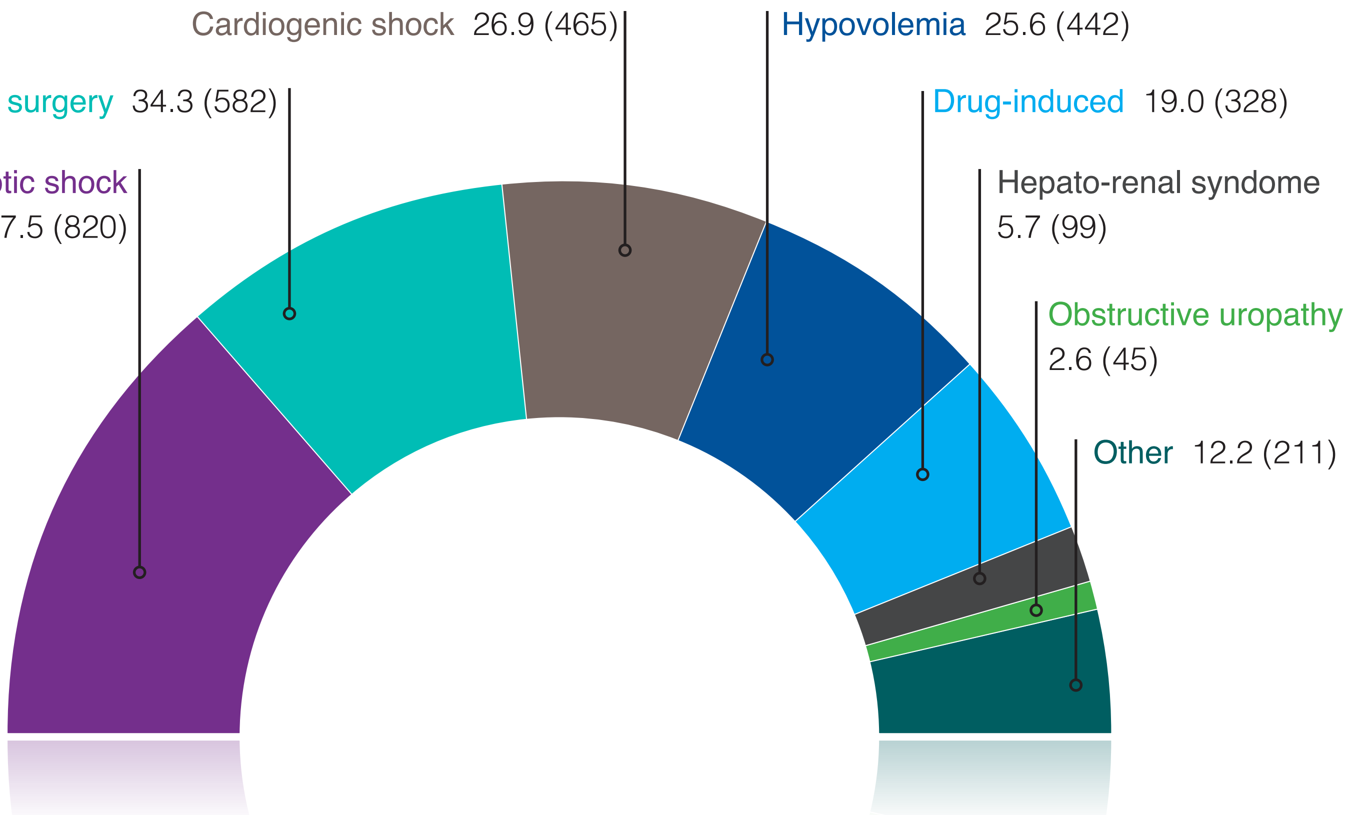
Approximately **60%** of adult ICU patients have AKI and about **20%** of them receive dialysis.

27% of children and young adults admitted to an ICU develop AKI.

The incidence of AKI treated with dialysis has **more than doubled** in the US in the last 10 years.

[1] Hoste EAJ, et al. *Intensive Care Med*. 2015
[2] Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. *Kidney Int Suppl*. 2012
[3] Susantitaphong P, et al. *Clin J Am Soc Nephrol*. 2013
[4] Kaddourah A, et al. *New Engl J Med*. 2017
[5] Hsu RK, et al. *J Am Soc Nephrol*. 2013

MAJOR CONTRIBUTING FACTORS FOR AKI IN ICU SETTINGS[6]



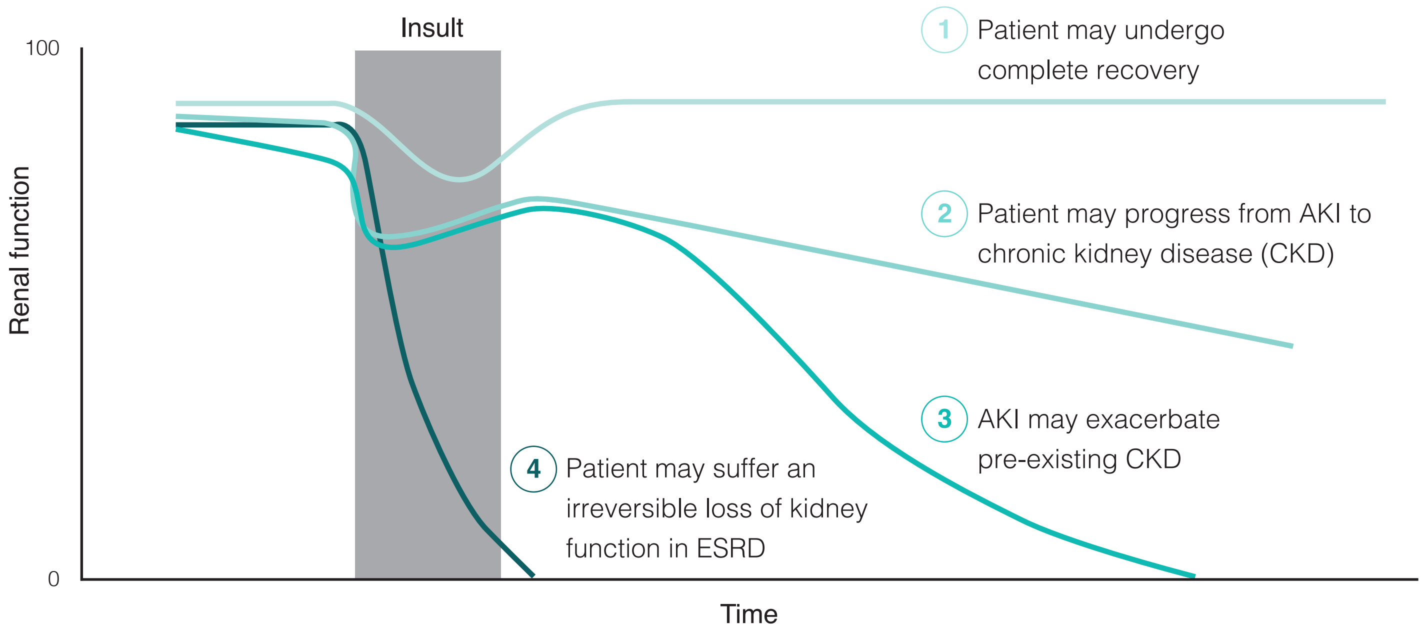
The above data are from a prospective epidemiological study of AKI in ICU patients in 54 hospitals in 23 countries. The study reviewed 29,269 patients admitted to ICUs. The goal of the study was to understand contributing factors of AKI in the ICU and determine patient outcomes.

[6] Uchino S, et al. *JAMA*. 2005

AKI is associated with an increased risk for morbidity and mortality.

AKI AWARENESS

NATURAL HISTORY OF AKI[7]

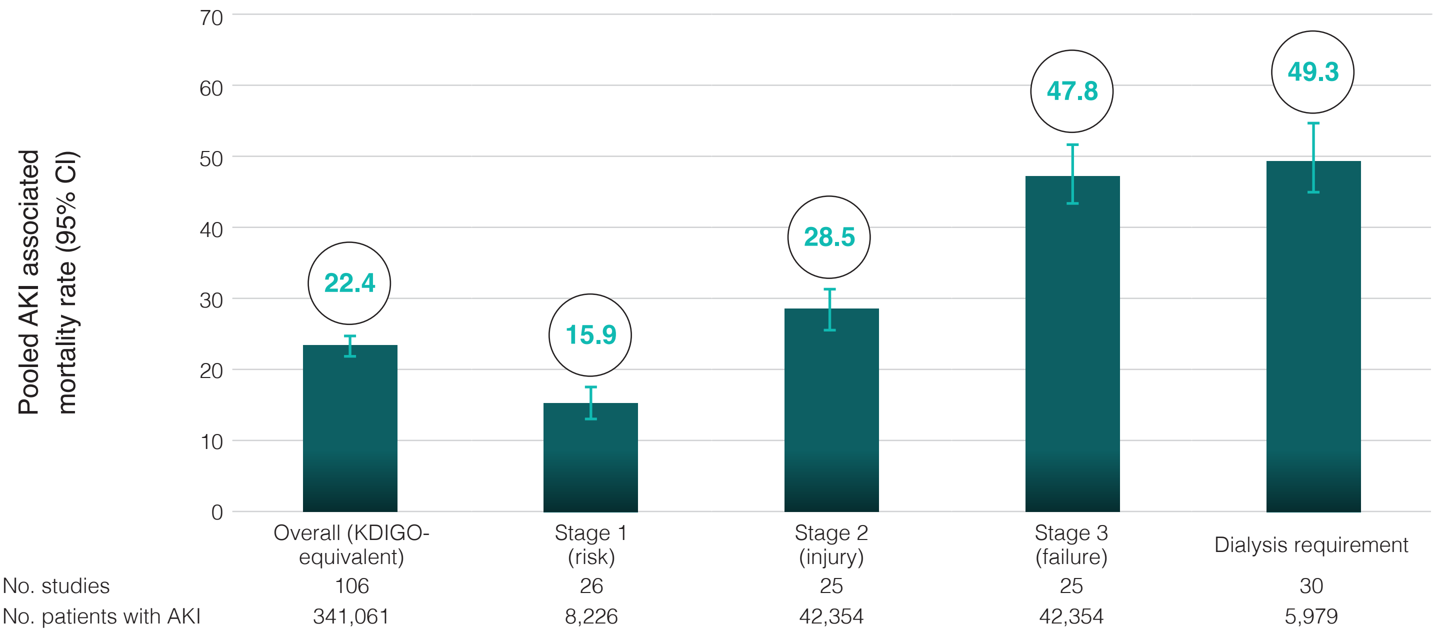


The graphic above depicts the potential course of a patient after AKI.

[7] Cerdá J, et al. *Clin J Am Soc Nephrol.* 2008

AKI is associated with an increased risk for chronic kidney disease, including end-stage renal disease.

AKI-ASSOCIATED MORTALITY[3]



As the KDIGO stage of AKI increases, the pooled AKI-associated mortality rate rises too. The above data are from a meta-analysis of 305 cohort studies assessing AKI incidence and outcomes (N=48,774,892). The analysis reviewed the KDIGO-equivalent AKI definition to evaluate AKI-associated mortality.

[3] Susantitaphong P, et al. *Clin J Am Soc Nephrol.* 2013

THERAPY

POTENTIAL APPLICATIONS FOR RENAL REPLACEMENT THERAPY[2]

Renal replacement

- Traditional approach based on utilization of RRT when little or no residual kidney function

Life-threatening indications

- Hyperkalemia
- Acidemia
- Pulmonary edema
- Uremic complications

Non-emergency indications

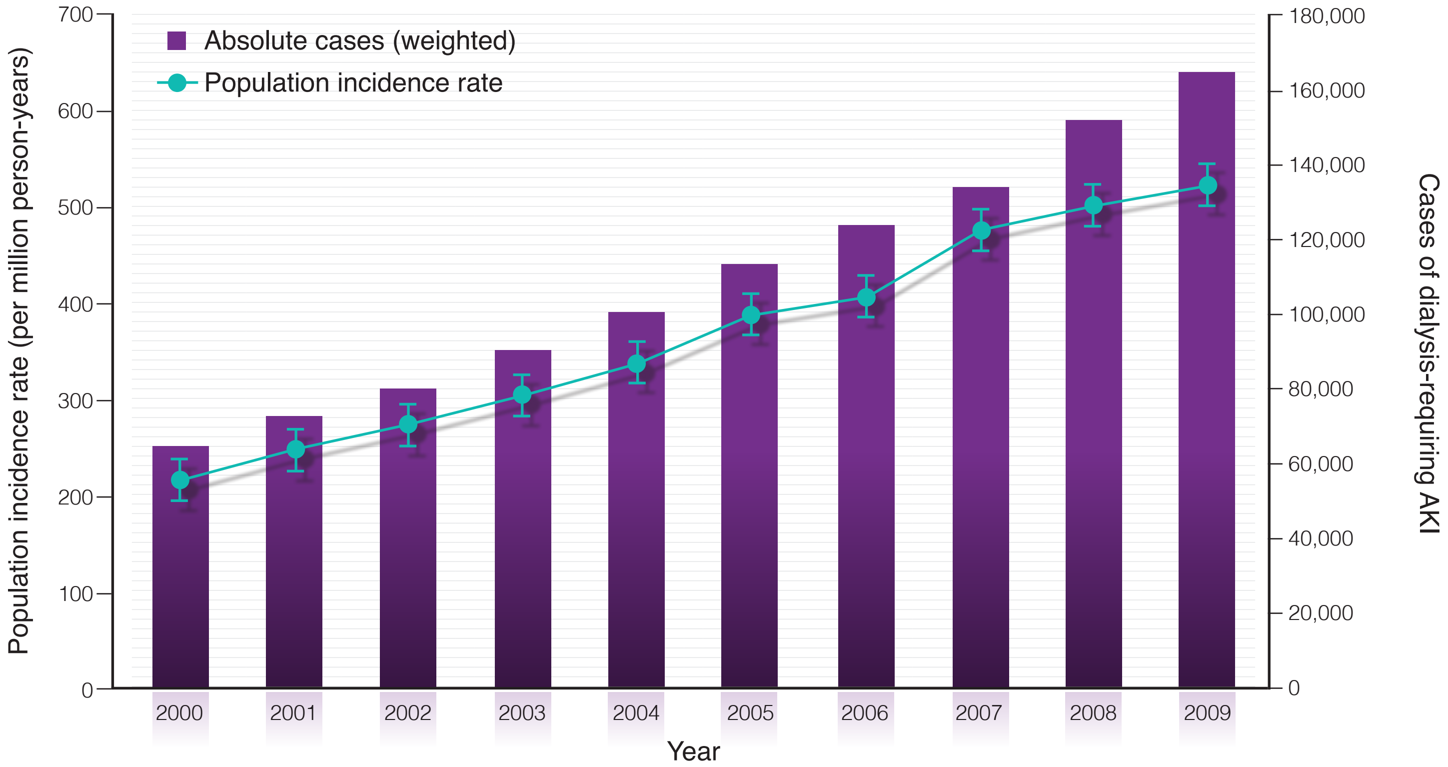
- Solute control
- Fluid removal
- Correction of acid-base abnormalities

Renal support

- Volume control
- Nutrition
- Drug delivery
- Solute modulation

[2] Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. *Kidney Int Suppl.* 2012

TEMPORAL CHANGES IN INCIDENCE OF DIALYSIS-REQUIRING AKI[5]



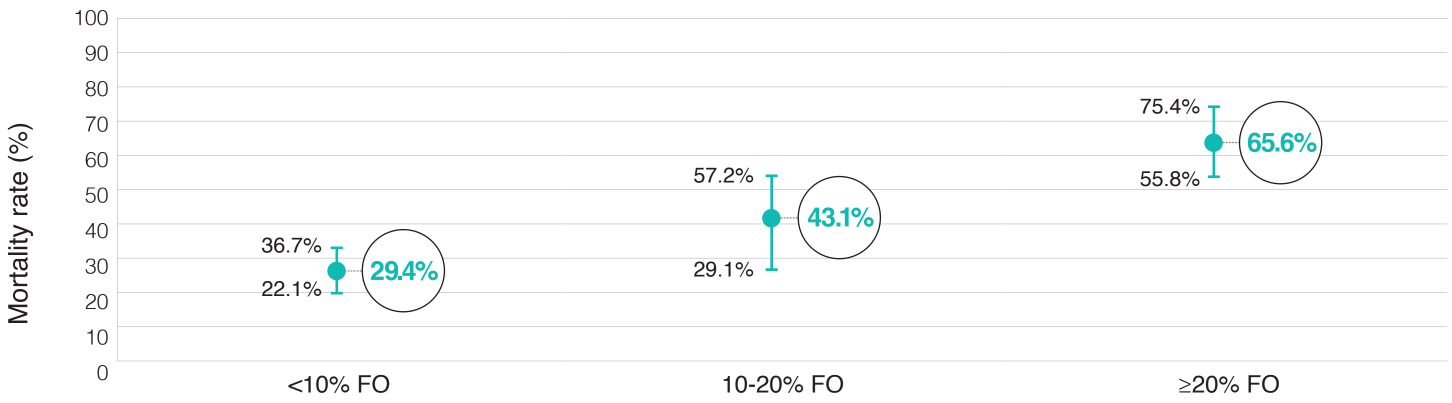
The above graph is from the Healthcare Cost and Utilization Project (HCUP): HCUP Nationwide Inpatient Sample (NIS) 2000–2009, designed to identify cases of dialysis-requiring AKI using validated International Classification of Diseases, Ninth Revision (ICD-9) codes. From 2000 to 2009, the incidence of AKI requiring dialysis increased on average by 10% per year.

KEY TAKEAWAY

Incidence of AKI requiring dialysis continues to increase

[5] Hsu RK, et al. *J Am Soc Nephrol.* 2013

FLUID OVERLOAD (FO) AND MORTALITY IN CHILDREN RECEIVING CRRT (CONTINUOUS RRT)[8]



The above chart shows data from a multicenter, prospective, observational study that examined the association of fluid overload severity with mortality risk in children receiving CRRT. The sample size was 297. The results demonstrated higher mortality observed in critically ill children who developed greater fluid overload before initiation of CRRT.

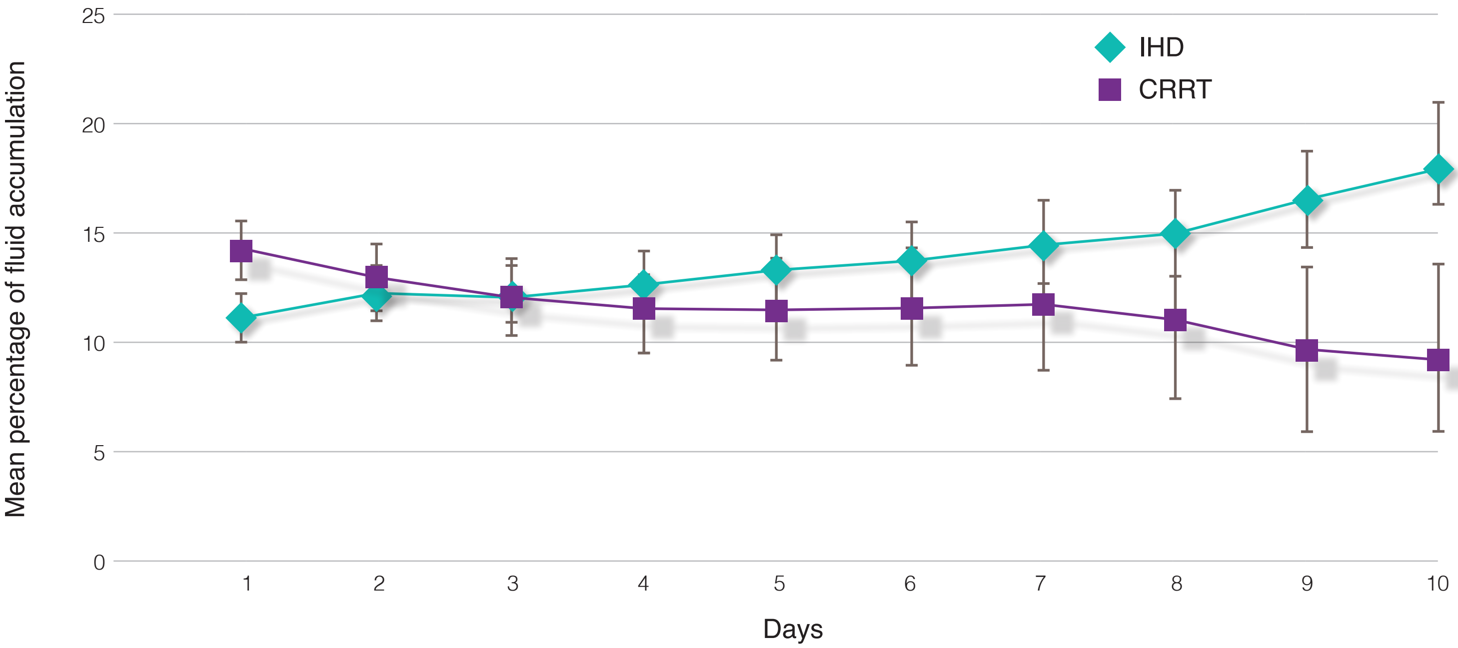
KEY TAKEAWAY

Fluid overload is independently associated with mortality

[8] Sutherland SM, et al. *Am J Kidney Dis.* 2010

CRRT is the preferred renal replacement therapy by many clinicians for patients with AKI who are hemodynamically unstable.

FLUID BALANCE HOMEOSTASIS[9]



In a multicenter, prospective observational study in North America consisting of 618 patients, mortality was higher in patients with fluid overload at 30 days, 60 days, and discharge. Patients with CRRT were more likely to have reduced fluid overload. Patient mortality was lower when fluid overload was corrected by dialysis. In addition, fluid overload was associated with non-recovery of kidney function.

KEY TAKEAWAY

Patients receiving CRRT had reduced fluid accumulation over time compared with those receiving IHD

[9] Bouchard J, et al. *Kidney Int.* 2009

LONG-TERM OUTCOMES

RECOVERY BY INITIAL MODALITY[10]

	CRRT		IHD		HR (95% CI) (CRRT vs IHD)
	Events (%)	Incidence	Events (%)	Incidence	
Chronic dialysis	435 (22)	6.5	533 (27)	8.2	0.75 (0.65–0.87)
Death	883 (44)	11.2	905 (45)	11.4	1.02 (0.91–1.14)

The above table shows the results of a retrospective cohort study in Ontario, Canada of critically ill adults with AKI from 1996 to 2009. Patients were propensity matched across RRT modalities at day 90. Results showed that more IHD patients remained on chronic dialysis. CRRT was associated with lower risk of progression to chronic dialysis.

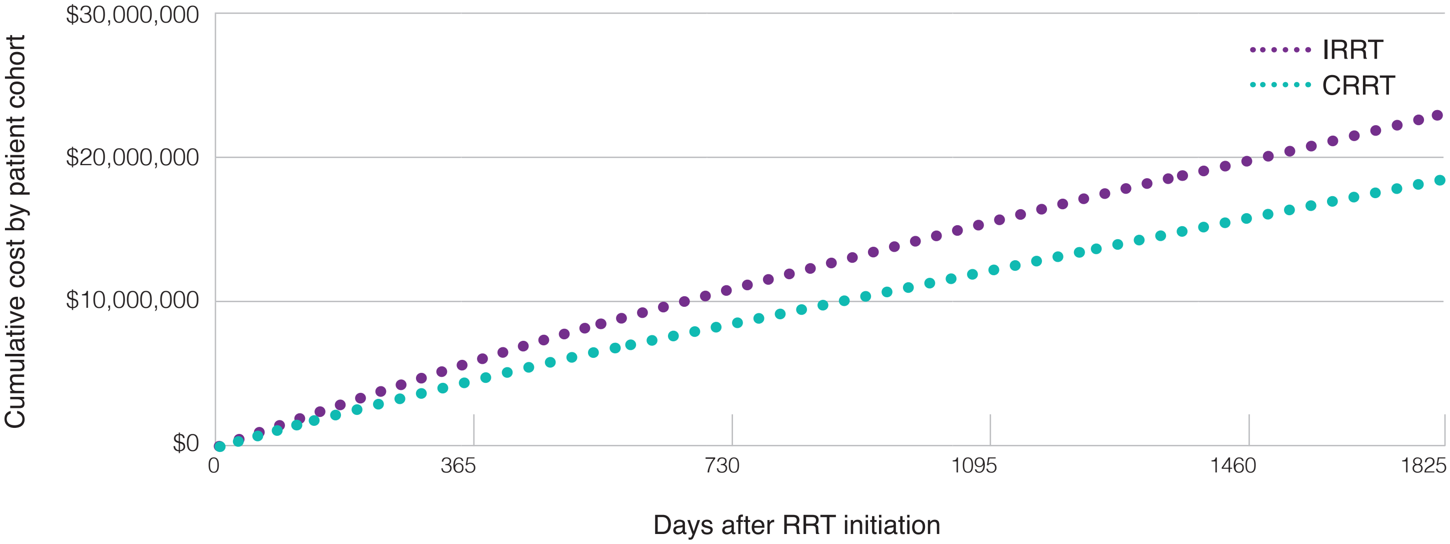
KEY TAKEAWAY

More IHD patients required chronic dialysis

[10] Wald R, et al. *Crit Care Med.* 2013

Use of CRRT for the management of AKI is associated with a lower risk for chronic dialysis compared with IHD.

5-YEAR CUMULATIVE COST OF DIALYSIS DEPENDENCE[11]



The objective of this study was to perform a cost-effectiveness analysis comparing IRRT with CRRT as initial therapy for AKI in the ICU. 1,000 IRRT patients and 1,000 CRRT patients were studied. The 5-year total cost, including the cost of dialysis dependence, was lower for CRRT ($37,780 for CRRT versus $39,448 for IRRT on average). The base-case incremental cost-effectiveness analysis showed that CRRT dominated IRRT. This dominance was confirmed by extensive sensitivity analysis. Initial CRRT is cost effective compared with initial IRRT by reducing the rate of long-term dialysis dependence among critically ill AKI survivors.

KEY TAKEAWAY

The 5-year total cost, including the cost of dialysis dependence, was lower for a CRRT patient

[11] Ethgen O, et al. *Nephrol Dial Transplant.* 2015

AKI AND ECONOMIC IMPLICATIONS

UNCOMPLICATED ACUTE RENAL FAILURE AND HOSPITAL RESOURCE UTILIZATION[12]

Diagnosis (ICD-9-CM)	Prevalence (%)	Direct costs (USD)	Hospital LOS (days)	Mortality (%)
AMI	2.9	3600	5 (3–6)	24
Stroke	3.0	2700	4 (3–7)	11
AKI	**0.6**	**2600**	**5 (3–8)**	**8**
HF	5.5	2200	4 (2–6)	4
Pneumonia	5.7	2100	4 (3–6)	4
GI bleed	2.7	2100	3 (2–5)	3

The above table shows data from 23 Massachusetts hospitals in a retrospective cohort study. Adults hospitalized with uncomplicated AKI (n=2,252) were analyzed by hospital costs and length of stay.

KEY TAKEAWAY

An episode of AKI costs nearly as much as the in-patients costs for stroke and more than for heart failure or pneumonia.

[12] Fischer MJ, et al. *Am J Kidney Dis.* 2005

COST ASSOCIATED WITH POSTOPERATIVE AKI[13]

	Risk-adjusted relative cost ratio (95% CI)	Risk-adjusted incremental cost per patient ($1000) mean (95% CI)	Risk-adjusted average cost per patient ($1000) mean (95% CI)
Patients with no AKI	1 (reference)	**0 (reference)**	**26.7 (26.5–27.0)**
Patients with any AKI	1.59 (1.57–2.61)	**15.8 (15.4–16.3)**	**42.6 (42.2–42.9)**
AKI, stage RIFLE-R	1.44 (1.42–1.46)	**10.7 (10.3–11.1)**	35.1 (34.7–35.5)
AKI, stage RIFLE-I	1.88 (1.84–1.910	**21.4 (20.7–22.2)**	45.8 (45.1–46.6)
AKI, stage RIFLE-F	2.57 (2.51–2.63)	**38.2 (37.0–39.5)**	62.6 (61.4–63.8)

Risk-adjusted average cost of postoperative care for surgical patients: $42,600 for AKI vs $26,700 for no AKI–159% higher for AKI versus no AKI

In a retrospective cohort study in the US on adult surgical patients with no history of CKD, AKI developed in 39% of patients, with 9% of them receiving RRT. The study design was to determine incremental hospital cost and mortality associated with postoperative AKI. Sample size was 50,314.

KEY TAKEAWAY

AKI adds significantly to postoperative cost of care, even among patients with the mildest degree of AKI

[13] Hobson C, et al. *Ann Surg.* 2015

[14] Baxter Internal Data on File. Facility Economics, 2016

IN 2016, A TYPICAL ICHD PATIENT COST **$42.0 K** ANNUALLY

BUT MEDICARE REIMBURSEMENT IS **$41.2 K** ANNUALLY

COSTING THE FACILITY OVER **$827** PER PATIENT/PER YEAR[14]

Notes

To learn more about Baxter and the company's CRRT offering, please call: **1-888-229-0001**

To learn more about AKI and Continuous Renal Replacement Therapy, please visit: **www.acutetherapiesinstitute.com**

[1] Hoste EAJ, et al. *Intensive Care Med.* 2015;41:1411-1423

[2] Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. *Kidney Int Suppl.* 2012;2:1-138

[3] Susantitaphong P, et al. [published correction appears in *Clin J Am Soc Nephrol.* 2014;9:1148]. *Clin J Am Soc Nephrol.* 2013;8:1482-1493

[4] Kaddourah A, et al. *New Engl J Med.* 2017;376:11-20

[5] Hsu RK, et al. *J Am Soc Nephrol.* 2013;24:37-42

[6] Uchino S, et al. *JAMA.* 2005;294:813-818

[7] Cerdá J, et al. *Clin J Am Soc Nephrol.* 2008;3:881-886

[8] Sutherland SM, et al. *Am J Kidney Dis.* 2010;55:316-325

[9] Bouchard J, et al. *Kidney Int.* 2009;76:422-427

[10] Wald R, et al. *Crit Care Med.* 2013;42:1-10

[11] Ethgen O, et al. *Nephrol Dial Transplant.* 2015;30:54-61

[12] Fischer MJ, et al. *Am J Kidney Dis.* 2005;46:1049-1057

[13] Hobson C, et al. *Ann Surg.* 2015;261:1207-1214

[14] Baxter Internal Data on File. Facility Economics, 2016

AKI, acute kidney injury; AMI, acute myocardial infarction; CI, confidence interval; CKD, chronic kidney disease; CRRT, continuous renal replacement therapy; ESRD, end-stage renal disease; FO, fluid overload; GI, gastrointestinal; HCUP, Healthcare Cost and Utilization Project; HF, heart failure; HR, hazard ratio; ICD-9, International Classification of Diseases, Ninth Revision; ICHD, in-center hemodialysis; ICU, intensive care unit; IHD, intermittent hemodialysis; IRRT, intermittent renal replacement therapy; KDIGO, Kidney Disease Improving Global Outcomes; LOS, length of stay; NIS, Nationwide Inpatient Sample; RIFLE, Risk, Injury, Failure, Loss, and End-stage renal disease; RRT, renal replacement therapy; SCr, serum creatinine; USD, United States dollar

USMP/MG230/18-0004 2/18

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