Baxter

# Acute RRT Modalities: Comparisons and Considerations

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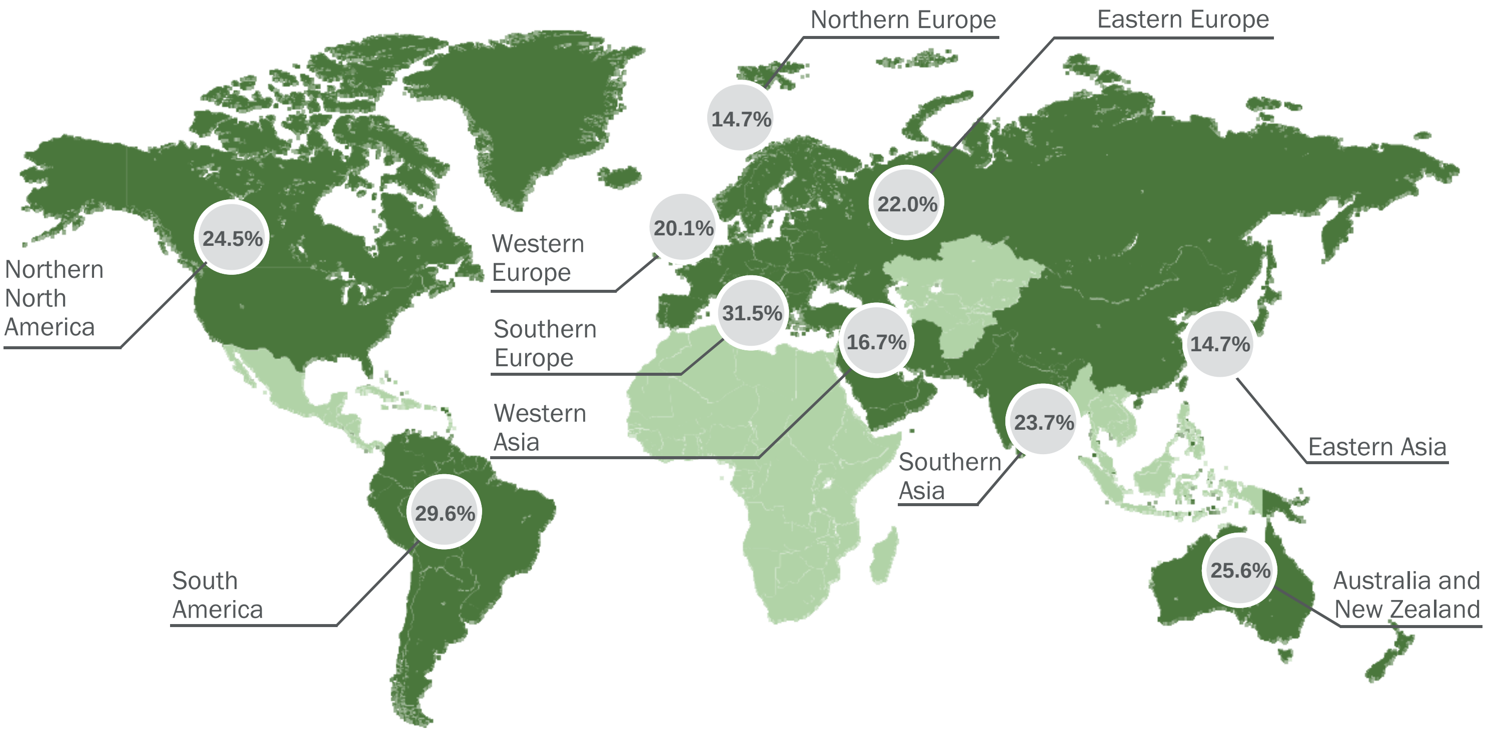
# ACUTE KIDNEY INJURY OVERVIEW

## Acute kidney injury is **common** among hospitalized patients globally[1]




**AKI** AFFECTS AN ESTIMATED **20%** OF HOSPITALIZED PATIENTS **WORLDWIDE**[1,*]

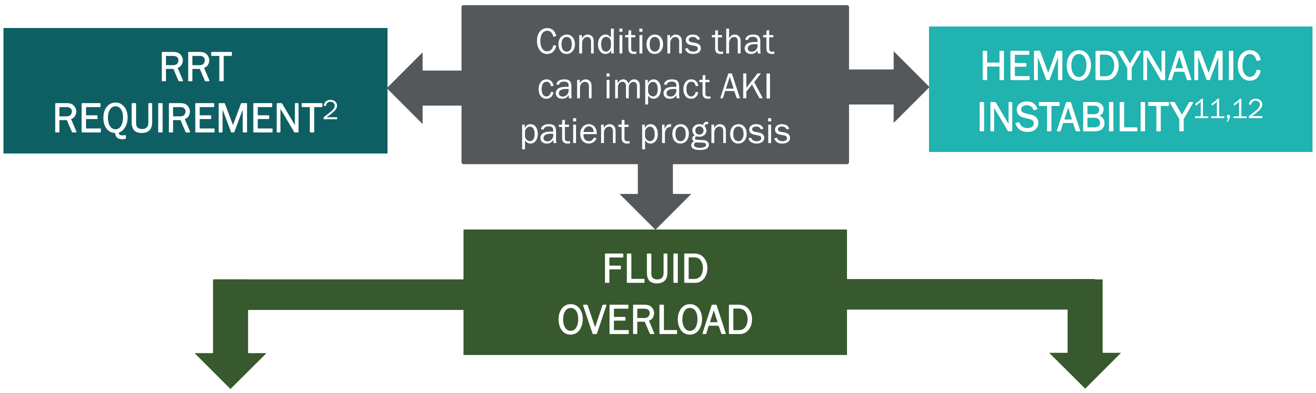
## AKI is a **serious** condition

AKI IS ASSOCIATED WITH **AN INCREASED RISK** OF **MORBIDITY and MORTALITY**[2–6]

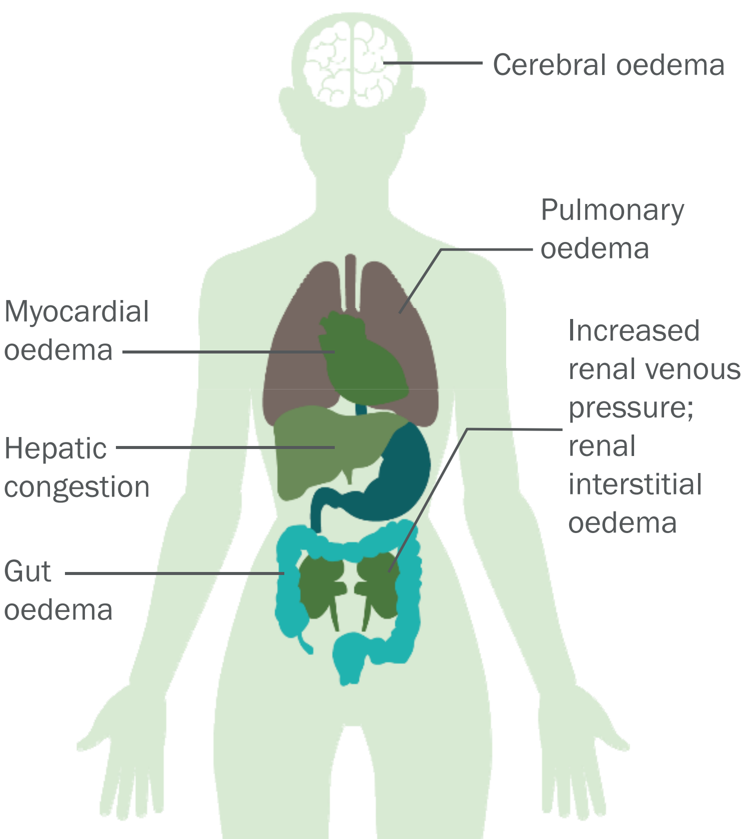
AKI IS ASSOCIATED WITH **AN INCREASED RISK** OF **CKD, including ESRD**[7–9]

*Multicentre meta-analysis of 154 studies (n=3,585,911), primarily in hospital settings, that adopted a KDIGO-equivalent AKI definition between 2004 and 2012. Pooled rates.[1]

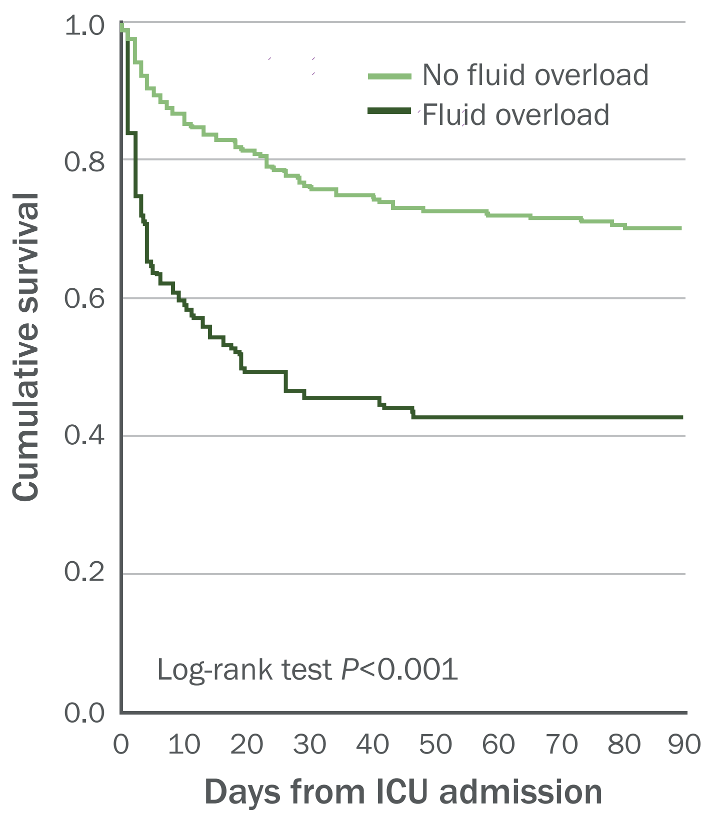
# **Fluid overload** is one condition that may **adversely** impact AKI patient prognosis[10,11]




## Consequences of fluid overload may lead to organ dysfunction[13]




## Fluid overload at RRT initiation for AKI has been associated with an increased risk of mortality[11,*]



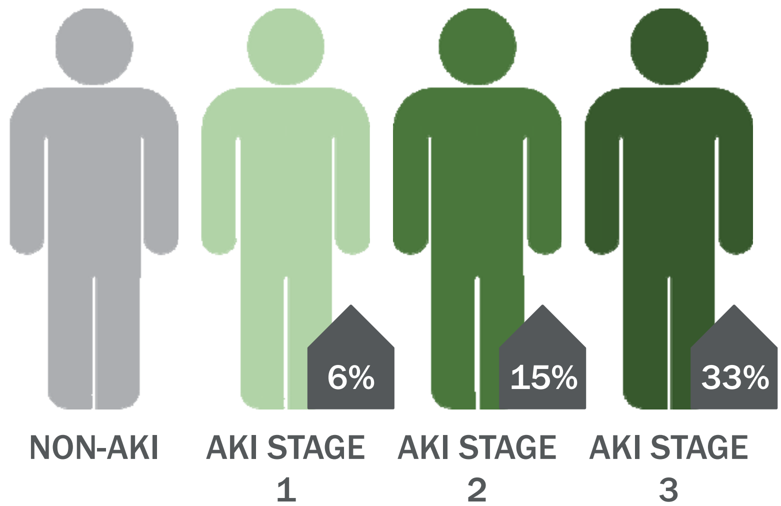

**FLUID OVERLOAD** IN PATIENTS WITH **AKI** IS A **SERIOUS CONDITION**[14–16]

*Prospective, observational cohort study of 296 adults treated with RRT in 17 Finnish ICUs from Sep 2011–Feb 2012.[11]

# AKI is associated with substantial financial burden[17–19,*]

## AKI status impacts daily costs[18]

PATIENTS **WITH AKI** HAVE SIGNIFICANTLY **HIGHER DAILY COSTS** COMPARED WITH PATIENTS **WITHOUT AKI**[18,†]




## AKI is expensive even relative to other acute medical conditions[19]

| Acute medical condition | Adjusted mean cost difference, in 2012 USD (95% CI)[a] |
|---|---|
| AKI-D[b] | 11,016 (10,468, 11,564) |
| Sepsis | 4822 (4696, 5068) |
| VTE | 3782 (3611, 3953) |
| Acute pancreatitis | 1802 (1676, 1929) |
| **AKI[c]** | **1795 (1692, 1899)** |
| Pneumonia | 1705 (1584, 1825) |
| Stroke | 1427 (1281, 1573) |
| MI | 14 (–91, 119) |
| GI bleed | –860 (–961, –759) |

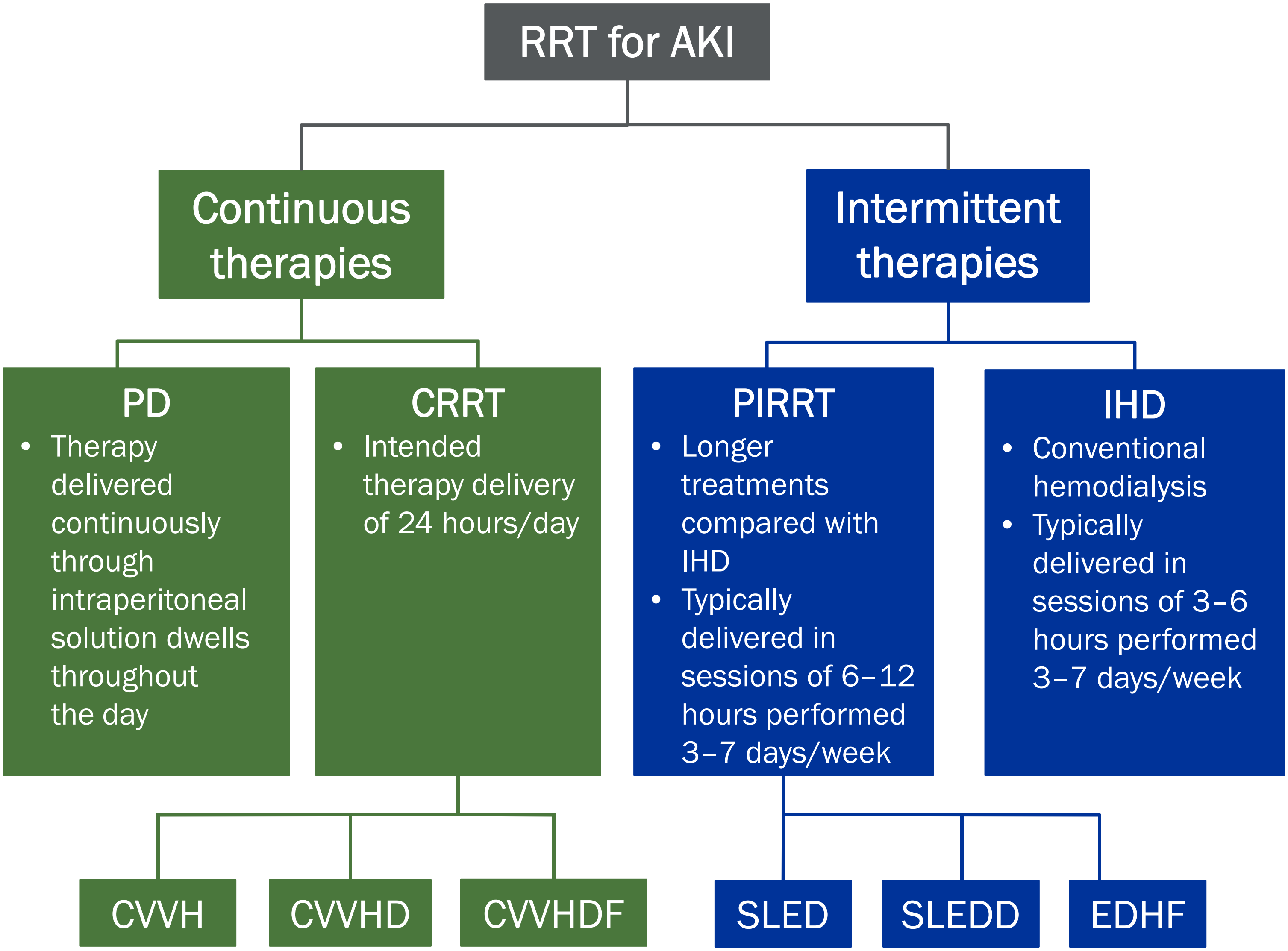
[a]Compared with reference group without the condition of interest.
[b]Compared with patients without AKI. [c]Includes patients with dialysis-requiring AKI (AKI-D).

THE INCREMENTAL **COST OF AKI-D OR AKI IS HIGHER** THAN FOR MANY OTHER CONDITIONS FOUND IN HOSPITALIZED PATIENTS[19,‡]

WHILE EXPENDITURES MAY VARY BY COUNTRY,
**AKI is a COSTLY CONDITION**[17–19]

*Costs for hospitalisation due to AKI may vary from country to country.
†Multicentre, retrospective cohort study of 659,945 adult hospital admissions across central China in 2013.[18]
‡2012 multicentre, retrospective study of 29,763,649 adult US hospitalisations without ESRD.[19]

## Various **renal replacement modalities** are available for the **management of AKI**[20–24]




**ACUTE RRT IS DELIVERED AS EITHER A CONTINUOUS OR INTERMITTENT THERAPY**[20]

# RRT MODALITIES FOR AKI

## Modalities **differ** in their typical characteristics[25]

### Typical RRT modality characteristics and settings for a 70-kg AKI patient[25–27]

| | CONTINUOUS THERAPIES | | | INTERMITTENT THERAPIES | |
|---|---|---|---|---|---|
| Parameter | CVVH | CVVHD | CVVHDF | SLED* | IHD |
| Blood flow ($Q_B$, mL/min) | 150–250 | 150–250 | 150–250 | 100–300 | 200–300 |
| Predominant solute transport principle | Convection | Diffusion | Diffusion + Convection | Diffusion | Diffusion |
| Ultrafiltrate (mL/h) | 1500–2000 | variable | 1000–1500 | variable | variable |
| Dialysate flow ($Q_D$, mL/h) | 0 | 1500–2000 | 1000–1500 | 6000–18,000 | 18,000–30,000 |
| Replacement fluid for zero balance (mL/h) | 1500–2000 | 0 | 1000–1500 | 0 | 0 |
| Urea clearance (mL/min) | 25–33 | 25–33 | 25–33 | 80–90 | 200–500 |

*SLED is a type of PIRRT.[21]

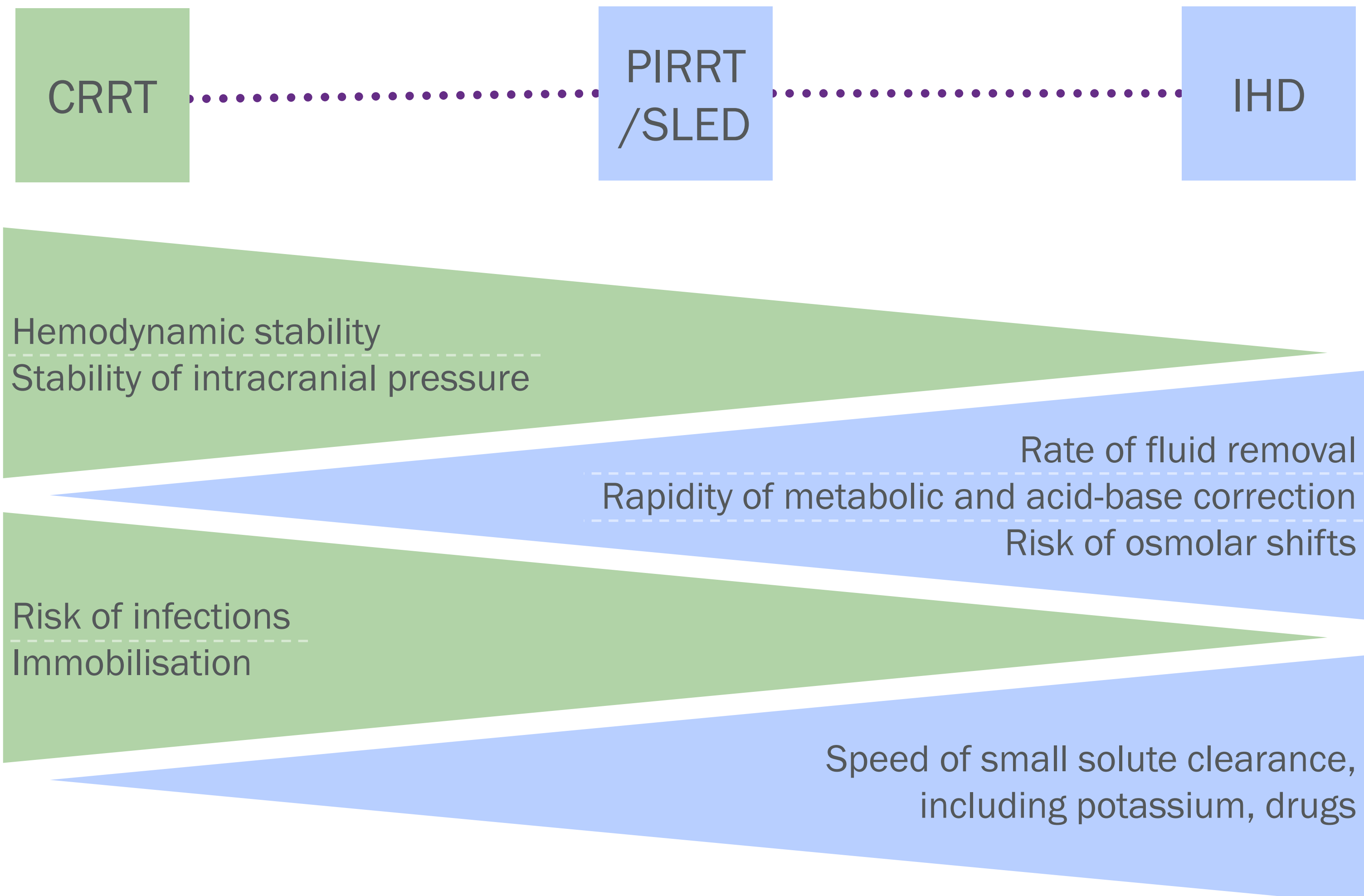
Convection    Diffusion

$Q_B$, $Q_D$, AND UREA CLEARANCE TEND TO BE **LOWER** IN **CONTINUOUS** THERAPIES THAN IN **INTERMITTENT** THERAPIES[25–27]

# RRT MODALITIES FOR AKI

## **Individual patient needs** can be addressed by considering the characteristics of the various **RRT modalities**[28]

### Relative **features**, **risks**, and **burdens** of different RRT modalities[28]




EACH RRT MODALITY HAS POTENTIAL **BENEFITS** AND **LIMITATIONS** FOR THE MANAGEMENT OF PATIENTS WITH AKI[28]

**Selection of RRT modality** requires careful consideration of many patient- and ICU-specific factors[25,28]

## Overview of modality considerations

CLINICAL CONSIDERATIONS:
FLUID OVERLOAD AND HEMODYNAMIC INSTABILITY

CLINICAL CONSIDERATIONS: LONG-TERM OUTCOMES

MACHINE AND PRESCRIPTION CONSIDERATIONS

SOLUTION CONSIDERATIONS

LONG-TERM COST CONSIDERATIONS

EQUIPMENT FOOTPRINT AND MOBILITY CONSIDERATIONS

# Clinical considerations: fluid overload and hemodynamic instability

Fluid overload in AKI patients can be treated by fluid removal during RRT, but rapid fluid removal that does not allow time for plasma refill may lead to **hemodynamic instability**[25,29]

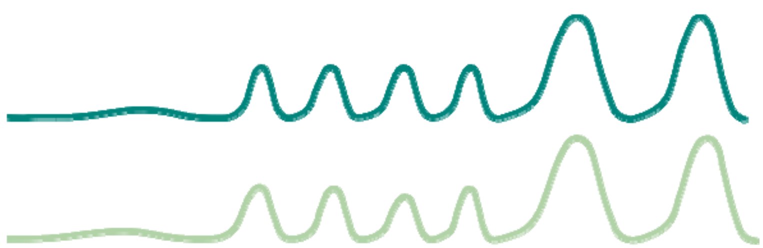
**Avoiding rapid fluid removal** to prevent hypovolaemia may **improve** AKI patient outcomes[25,29]

## Modality **comparisons**[30]

| | CRRT | PIRRT /SLED | IHD |
|---|---|---|---|
| | Continuous | | Intermittent |
| Clearance per hour | + | ++ | +++ |
| Clearance per 24 hours | +++ | ++ | + |

Fluid status

Serum levels urea/$NH_3$/$K^+$



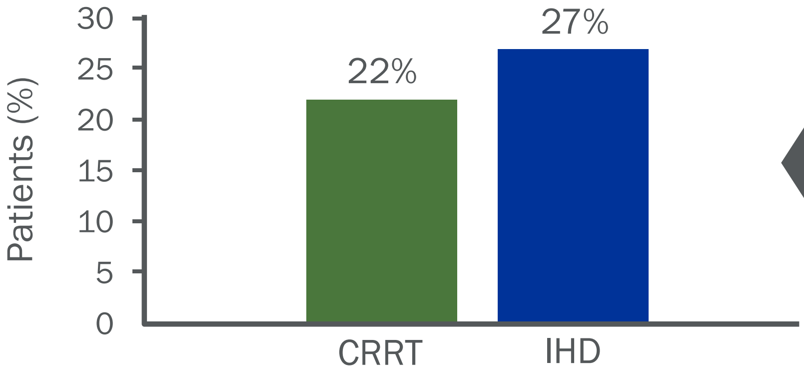
CRRT MAY OFFER MORE PRECISE FLUID MANAGEMENT VS IHD OR PIRRT/SLED[25,30]

**CRRT IS A PREFERRED RRT BY MANY CLINICIANS FOR AKI PATIENTS WHO ARE HEMODYNAMICALLY UNSTABLE**[25,29]

## Clinical considerations: long-term outcomes

**AKI is associated with an increased risk of long-term dialysis dependence;[8] acute RRT modality type may impact this risk[31–34]**

### Patients on chronic dialysis at day 90 by initial RRT modality[31,*]




CHRONIC DIALYSIS **HAZARD RATIO** (95% CI) FOR CRRT vs IHD WAS **0.75** (0.65–0.87), $P<0.0001$[31]

## Modality comparisons[31–34]

| CONTINUOUS | INTERMITTENT | |
|---|---|---|
| CRRT | PIRRT | IHD |
| Patients are **less likely to require chronic dialysis** following initial AKI episode compared with patients treated with IHD | ? Insufficient evidence | It has been reported that patients are **more likely to require chronic dialysis** following initial AKI episode compared with patients treated with CRRT |

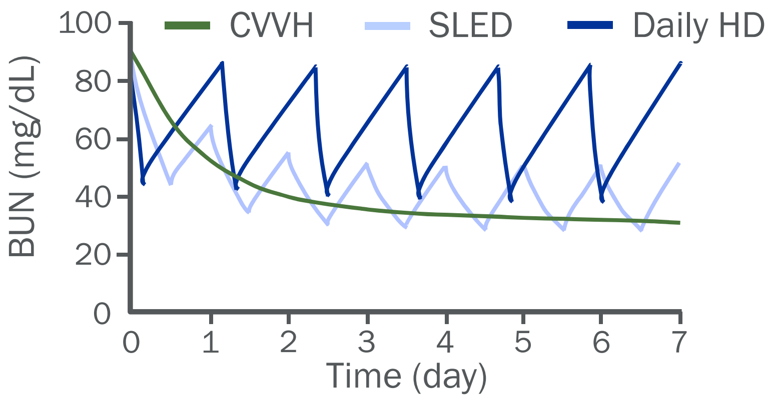
**USE OF CRRT FOR AKI MANAGEMENT HAS BEEN ASSOCIATED WITH A LOWER RISK of CHRONIC DIALYSIS COMPARED WITH IHD[31–34]**

*Retrospective multicentre cohort study of critically ill adults with AKI between 1996 and 2009. 2004 patients originally treated with CRRT and 2004 patients originally treated with IHD were propensity matched and rates of dialysis dependence were compared.[31]

## **Machine** and **prescription** considerations

RRT machines deliver **different** dose intensities over **different** durations of therapy[21,22,25]

### Kinetic modeling of urea clearance by different RRT modalities[35]




A **SAWTOOTH PATTERN** WAS OBSERVED WHEN USING **INTERMITTENT THERAPIES** TO REMOVE UREA, WHILE **CONTINUOUS THERAPY MAINTAINED A CONSISTENT** BUN LEVEL OVER TIME[35]

## Modality **comparisons**[21,22,35]

| CONTINUOUS | INTERMITTENT | |
|---|---|---|
| CVVH | SLED | IHD |
| Intended to run **24 h/day** • Slow but continuous urea **clearance helps avoid spikes in BUN levels** | Typically run in **6–12 h sessions** delivered 3–7 times/week • Intermittent nature does **not allow for continuous urea clearance**, which could result in variable BUN levels | Typically run in **3–6 h sessions** delivered 3–7 times/week • Intermittent nature does **not allow for continuous urea clearance**, which could result in variable BUN levels |

UNLIKE IHD OR PIRRT, **CRRT** IS RUN ON MACHINES THAT DELIVER **CONTINUOUS** SOLUTE REMOVAL[22,35]

# RRT MODALITY CONSIDERATIONS

## **Solution** considerations

Typically, CRRT solutions are **commercially** prepared, while IHD and PIRRT use **local water sources** to prepare dialysate[29,36,37]

Preparing solutions on-line from local water sources **necessitates** water **treatment** and routine water **quality monitoring** to assure clean water standards are met[36–38]

## Modality **comparisons**[29,36–40]

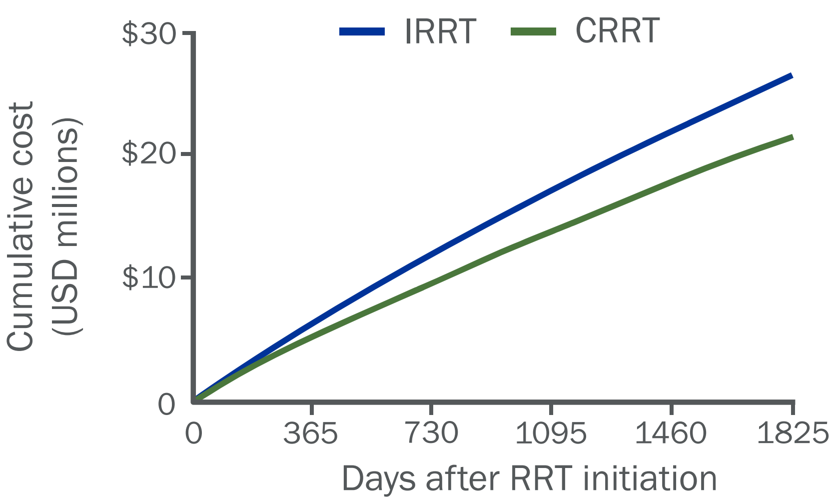
| CONTINUOUS | INTERMITTENT | |
|---|---|---|
| CRRT | PIRRT | IHD |
| Because no on-line solutions are typically used, **no water treatment systems** are required<br>•<br>Monitoring water quality is not applicable | If a centralized water treatment system is unavailable in the ICU, individual water quality **monitoring is necessary**<br>•<br>If a centralized water treatment system is not used, **staff need to monitor dialysate quality** for individual patients<br>•<br>**Disinfection requirements** may limit treatment duration to <12 hours[41] | If a centralized water treatment system is unavailable in the ICU, individual water quality **monitoring is necessary**<br>•<br>If a centralized water treatment system is not used, **staff need to monitor dialysate quality** for individual patients |

WATER TREATMENT AND QUALITY TESTING MAY CONTRIBUTE TO **INCREASED MONITORING** WHEN USING SOLUTIONS PREPARED ON-LINE FOR **IHD and PIRRT**[39,42]

## Long-term cost considerations

Because **initial RRT modality** may impact the risk of **chronic dialysis**,[31] **long-term costs** of AKI may also be influenced by **initial treatment modality**[43]

### Cumulative costs of dialysis dependence by initial AKI treatment modality[43,*]




MEAN 5-YEAR TOTAL COST/PATIENT OF AKI-D† WAS **$37,780 FOR CRRT** AS THE INITIAL MODALITY COMPARED WITH **$39,448 FOR IRRT**[43]

†Including cost of dialysis dependence. Cost in 2013 USD.

## Modality **comparisons**[43]

| CONTINUOUS | INTERMITTENT | |
|---|---|---|
| CRRT | PIRRT | IHD |
| Total costs may be lower due, in part, to a lower risk of chronic dialysis | Insufficient evidence to compare to CRRT or IHD | Total costs may be higher due, in part, to a higher risk of chronic dialysis |

**THE LONG-TERM COST OF AKI MAY BE LOWER FOR PATIENTS INITIALLY TREATED WITH CRRT COMPARED TO THOSE TREATED WITH IHD**[43]

*Health outcomes and healthcare costs were simulated and averaged for a cohort of 1000 patients initiated on CRRT and a cohort of 1000 patients initiated on IRRT. All costs were inflated to 2013 USD.[43]

## Equipment footprint and mobility considerations

Water treatment systems required for IHD and PIRRT add to physical **space** requirements and water lines may limit RRT mobility in ICUs without central water treatment systems[37,40]

In ICUs without central water treatment systems, portable **water treatment devices** may be necessary,[40] which can occupy as much as 0.13–0.16 $m^2$ of floor space[44,45]

### Modality comparisons[36,37,40,41,46–49]

| CONTINUOUS | INTERMITTENT | |
|---|---|---|
| CRRT | PIRRT | IHD |

**CRRT:**

Because the CRRT machine is the **only component** that contributes to the therapy's physical footprint, treatment mobility may be increased

•

**No space considerations** for water treatment systems are necessary

**PIRRT / IHD:**

Both the IHD machine and water treatment systems contribute to the therapy's physical footprint, which may **impact treatment mobility** in ICUs without central water treatment systems

•

In situations where a central water treatment system is not utilised, the **greater physical footprint** of the machine + water treatment system may impact ICU spacing

**WATER TREATMENT** EQUIPMENT MAY ADD TO THE FOOTPRINT OF **IHD** AND **PIRRT** SYSTEMS, POTENTIALLY DECREASING TREATMENT MOBILITY AND IMPACTING SPACING CONSIDERATIONS[40,47–49]

# SUMMARY

AKI is a **common** and **costly** condition among ICU patients,[1,17–19] and is associated with increased risks of **morbidity and mortality**[2–9]

Acute RRT is delivered as **either** a **continuous or** an **intermittent** therapy, each of which have unique characteristics, settings, and limitations[20,25–28]

**Selection of RRT modality** requires careful consideration of many patient- and ICU-specific factors[25,28]

- FLUID OVERLOAD AND HEMODYNAMIC INSTABILITY
- LONG-TERM CLINICAL OUTCOMES
- MACHINE AND PRESCRIPTION
- SOLUTIONS
- LONG-TERM COSTS
- EQUIPMENT FOOTPRINT AND MOBILITY

**CRRT** IS A PREFERRED RENAL REPLACEMENT THERAPY BY MANY CLINICIANS FOR PATIENTS WITH AKI WHO ARE HEMODYNAMICALLY UNSTABLE[25,28]

# ACRONYMS/ABBREVIATIONS/REFERENCES

AKI, acute kidney injury; AKI-D, dialysis-requiring AKI; BUN, blood urea nitrogen; CI, confidence interval; CKD, chronic kidney disease; CRRT, continuous renal replacement therapy; CVVH, continuous veno-venous hemofiltration; CVVHD, continuous veno-venous hemodialysis; CVVHDF, continuous veno-venous hemodiafiltration; dL, decilitre; EDHF, extended daily hemofiltration; ESRD, end-stage renal disease; Feb, February; GI, gastrointestinal; h, hour; HD, hemodialysis; ICU, intensive care unit; IHD, intermittent hemodialysis; IRRT, intermittent renal replacement therapy; $K^+$, potassium ion; KDIGO, Kidney Disease Improving Global Outcomes; kg, kilogram; $m^2$, square meters; mg, milligram; MI, myocardial infarction; min, minute; mL, millilitre; PD, peritoneal dialysis; PIRRT, prolonged intermittent renal replacement therapy; $NH_3$, ammonia; $Q_B$, blood flow rate; $Q_D$, dialysis flow rate; RRT, renal replacement therapy; Sep, September; SLED, sustained or slow low-efficiency dialysis; SLEDD, sustained or slow low-efficiency daily dialysis; US, United States; USD, United States dollar; vs, versus; VTE, venous thromboembolism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