Baxter

Acute RRT Modalities: Comparisons and Considerations

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OVERVIEW

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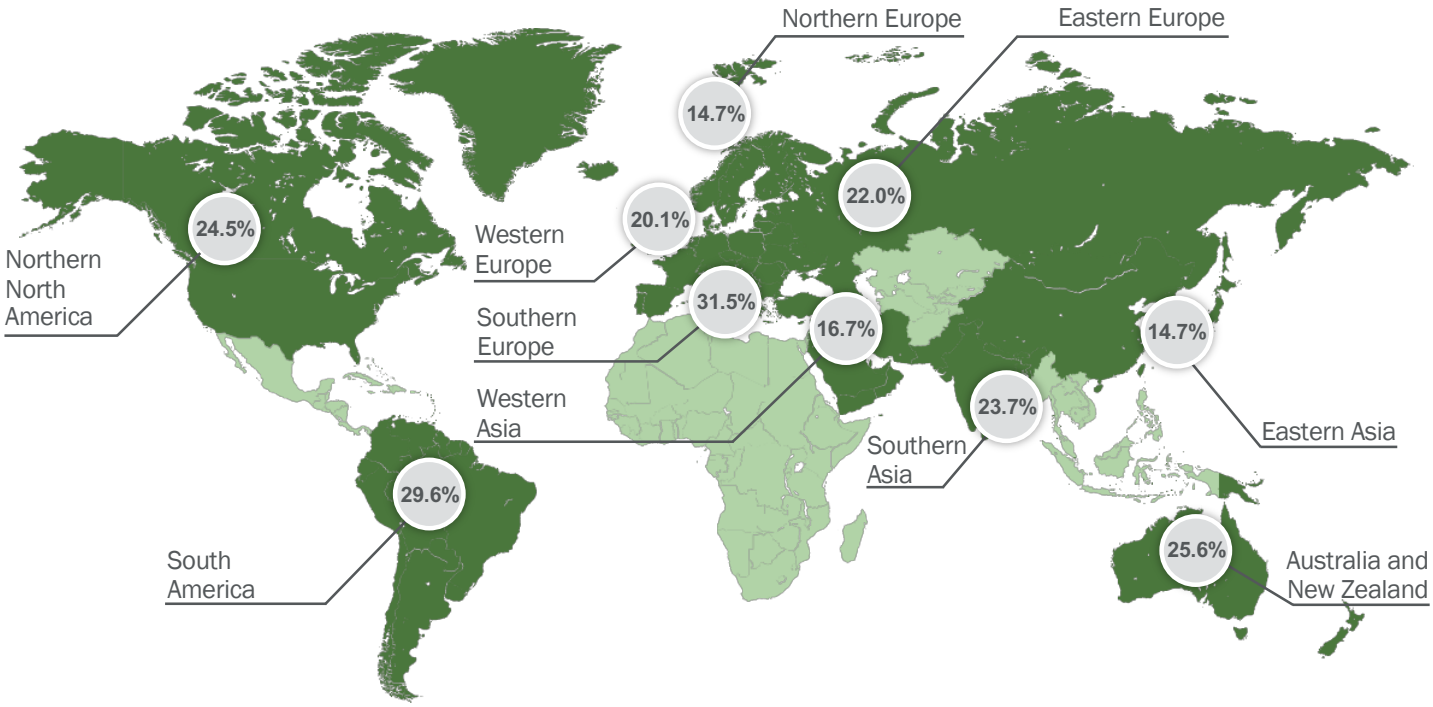
ACUTE KIDNEY INJURY OVERVIEW

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



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

AKI is a **serious** condition

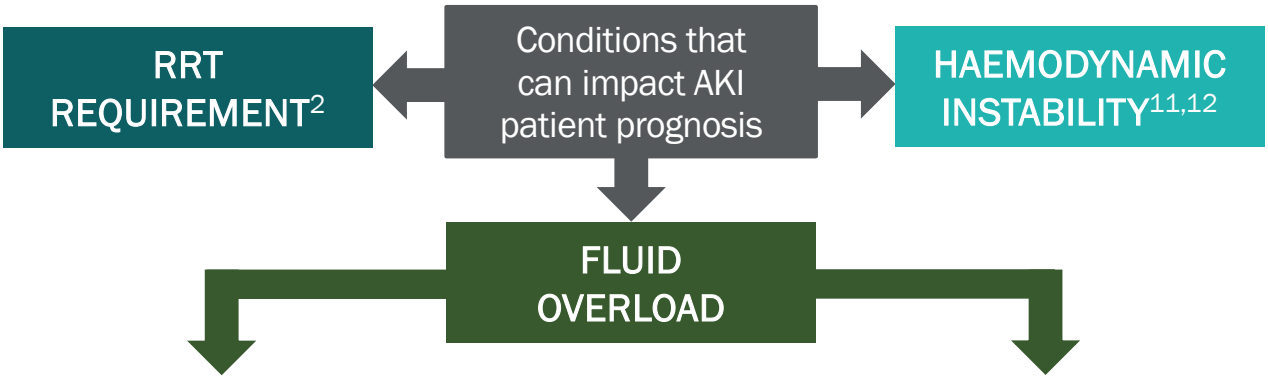
AKI IS ASSOCIATED WITH **AN INCREASED RISK** OF **MORBIDITY and MORTALITY**[2–6]

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

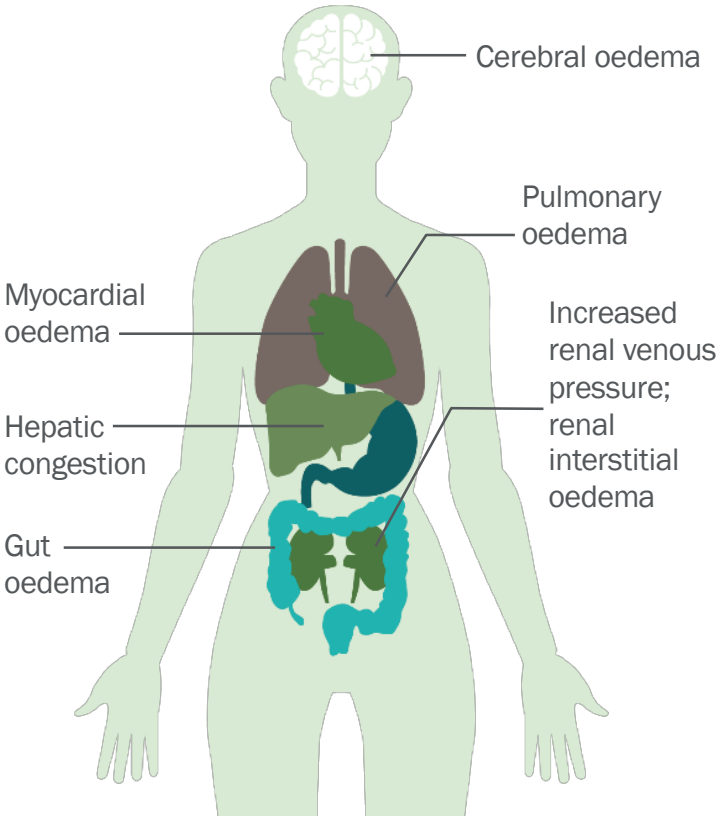
*Multicentre meta-analysis of 154 studies (n=3,585,911), primarily in hospital settings, that adopted a KDIGO-equivalent AKI definition between 2004 and 2012. Pooled rates.[1]

ACUTE KIDNEY INJURY OVERVIEW

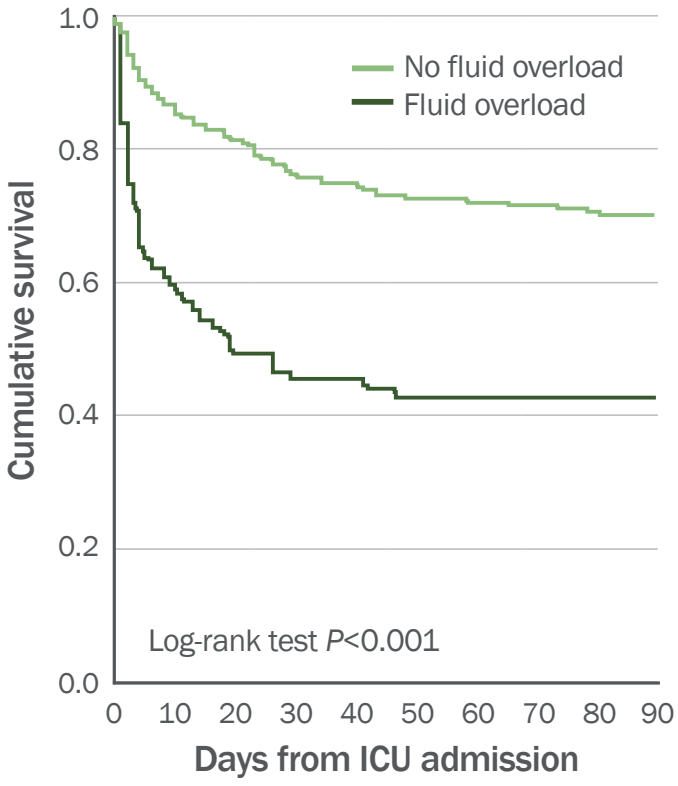
Fluid overload is one condition that may adversely impact AKI patient prognosis[10,11]



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]

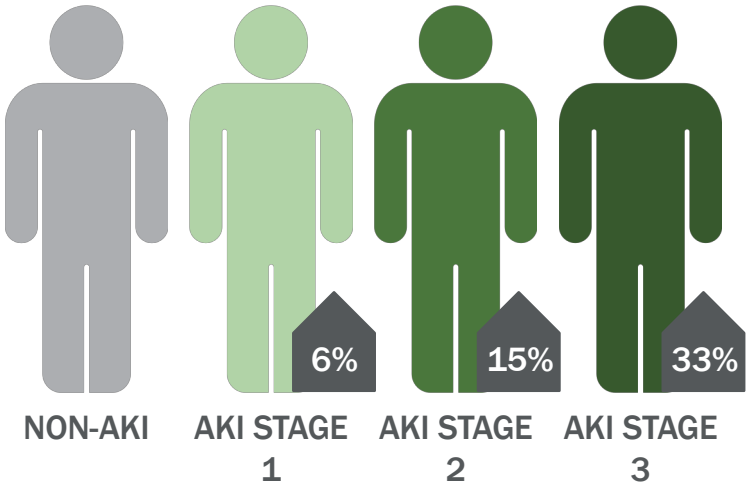
*Prospective, observational cohort study of 296 adults treated with RRT in 17 Finnish ICUs from Sep 2011–Feb 2012.[11]

ACUTE KIDNEY INJURY OVERVIEW

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)

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

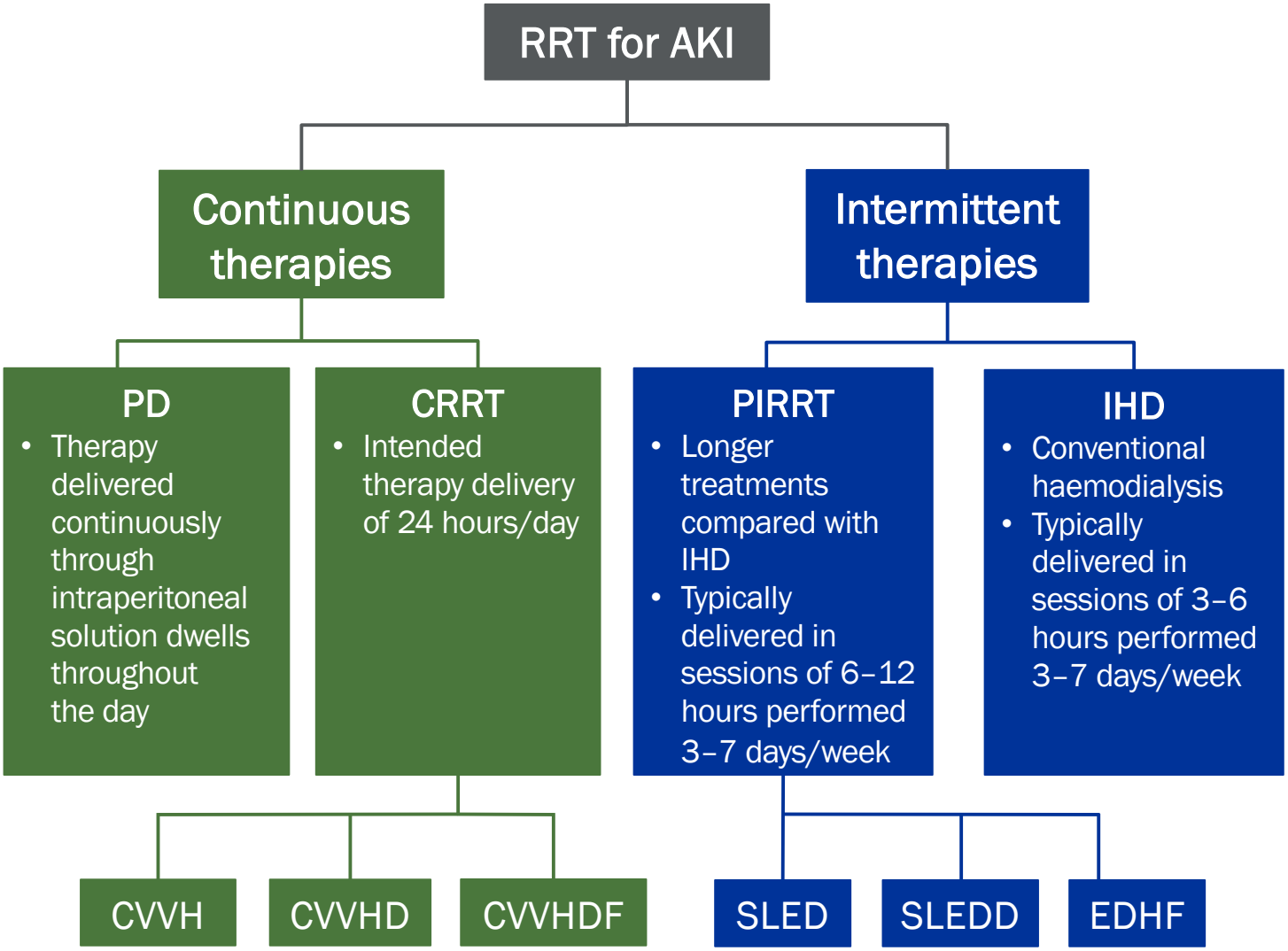
[a]Compared with reference group without the condition of interest.
[b]Compared with patients without AKI. [c]Includes patients with dialysis-requiring AKI (AKI-D).

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]

RRT MODALITIES FOR AKI

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

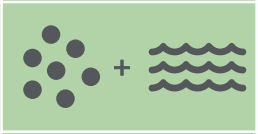


ACUTE RRT IS DELIVERED AS **EITHER A CONTINUOUS OR INTERMITTENT** THERAPY[20]

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					
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

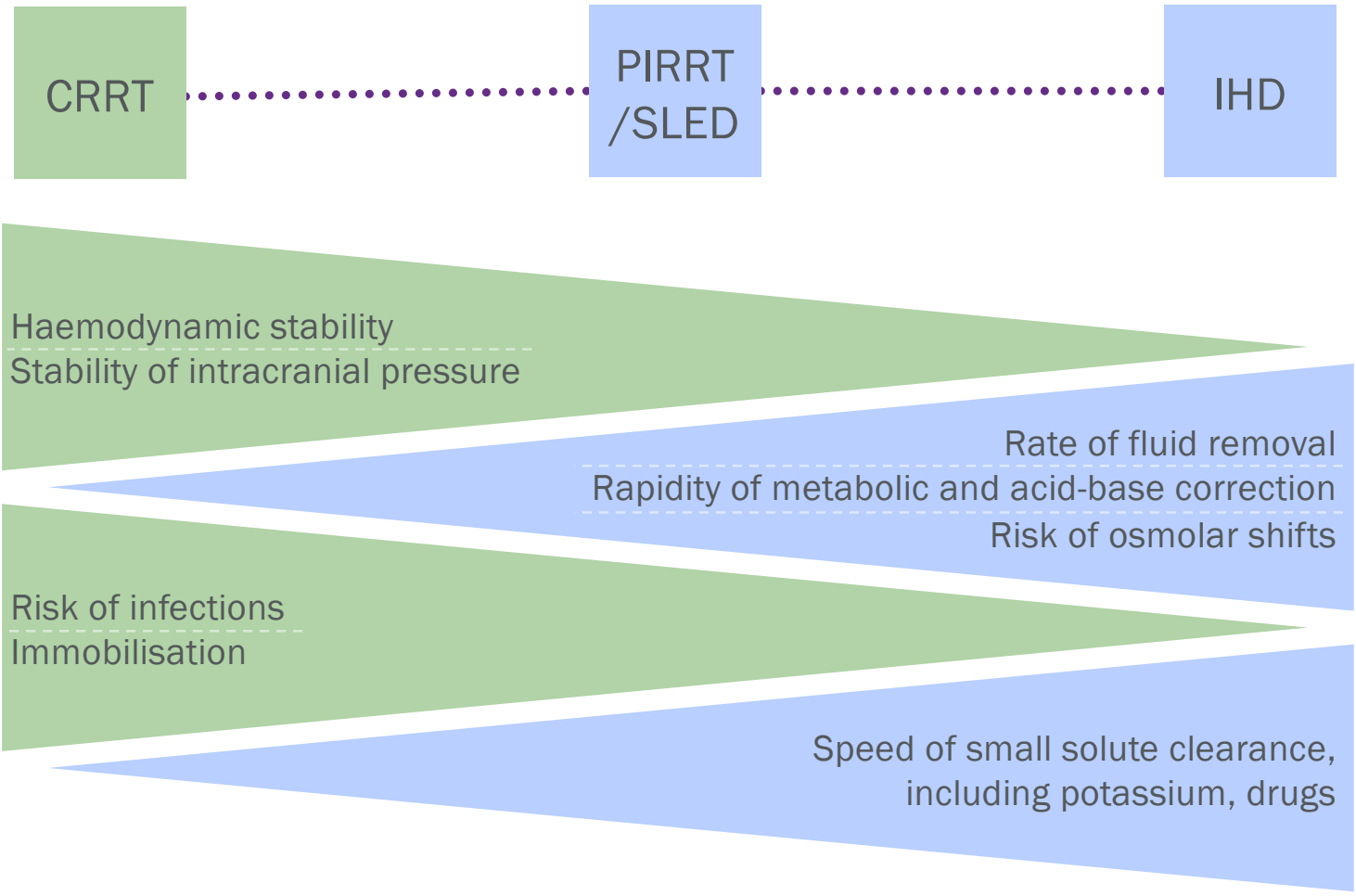
 Diffusion

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]

RRT MODALITY CONSIDERATIONS

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 HAEMODYNAMIC INSTABILITY
- CLINICAL CONSIDERATIONS: LONG-TERM OUTCOMES
- MACHINE AND PRESCRIPTION CONSIDERATIONS
- SOLUTION CONSIDERATIONS
- LONG-TERM COST CONSIDERATIONS
- EQUIPMENT FOOTPRINT AND MOBILITY CONSIDERATIONS

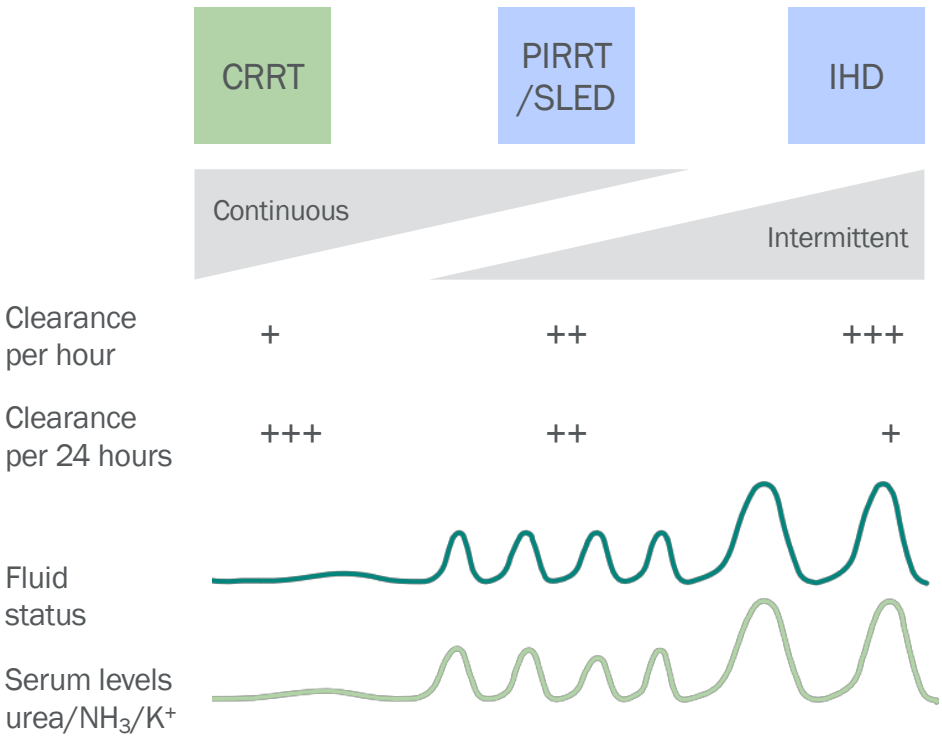
RRT MODALITY CONSIDERATIONS

Clinical considerations: fluid overload and haemodynamic 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 **haemodynamic instability**[25,29]

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

Modality comparisons[30]



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

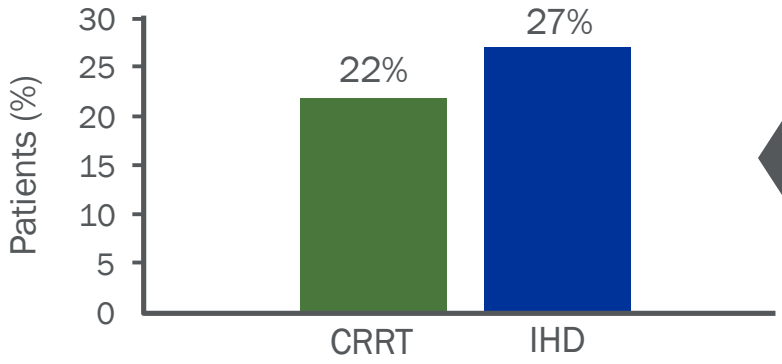
CRRT IS A **PREFERRED RRT** BY MANY CLINICIANS FOR AKI PATIENTS WHO ARE **HAEMODYNAMICALLY UNSTABLE**[25,29]

RRT MODALITY CONSIDERATIONS

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]

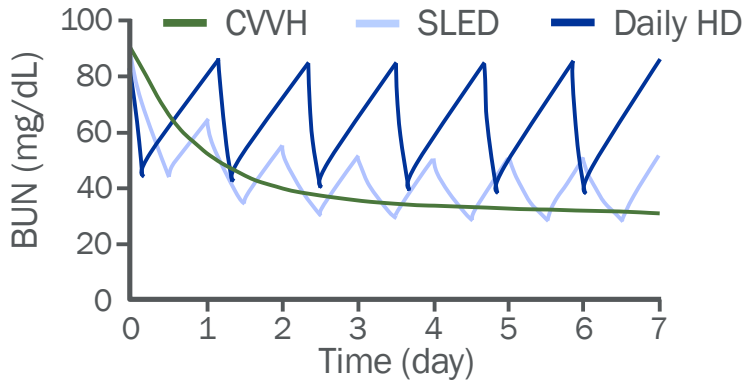
*Retrospective multicentre cohort study of critically ill adults with AKI between 1996 and 2009. 2004 patients originally treated with CRRT and 2004 patients originally treated with IHD were propensity matched and rates of dialysis dependence were compared.[31]

RRT MODALITY CONSIDERATIONS

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 • Monitoring water quality is not applicable	If a centralized water treatment system is unavailable in the ICU, individual water quality **monitoring is necessary** • If a centralized water treatment system is not used, **staff need to monitor dialysate quality** for individual patients • **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** • If a centralized water treatment system is not used, **staff need to monitor dialysate quality** for individual patients

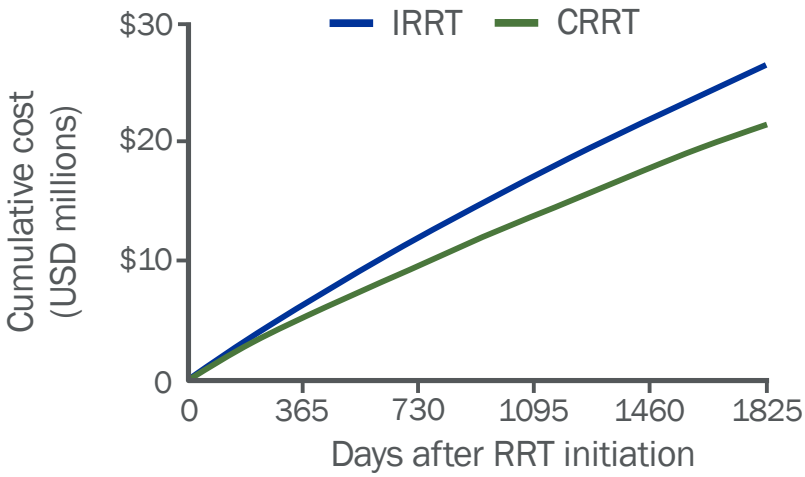
WATER TREATMENT AND QUALITY TESTING MAY CONTRIBUTE TO **INCREASED MONITORING** WHEN USING SOLUTIONS PREPARED ON-LINE FOR **IHD and PIRRT**[39,42]

RRT MODALITY CONSIDERATIONS

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]

RRT MODALITY CONSIDERATIONS

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

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

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 HAEMODYNAMIC 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 HAEMODYNAMICALLY 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 haemofiltration; CVVHD, continuous veno-venous haemodialysis; CVVHDF, continuous veno-venous haemodiafiltration; dL, decilitre; EDHF, extended daily haemofiltration; ESRD, end-stage renal disease; Feb, February; GI, gastrointestinal; h, hour; HD, haemodialysis; ICU, intensive care unit; IHD, intermittent haemodialysis; 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

1. Susantitaphong P, et al. *Clin J Am Soc Nephrol*. 2013;8:1482-1493.
2. Coca SG, et al. *Am J Kidney Dis*. 2009;53:961-973.
3. Ricci Z, et al. *Kidney Int*. 2008;73:538-546.
4. Chawla LS, et al. *Clin J Am Soc Nephrol*. 2014;9:448-456.
5. Brown JR, et al. *Ann Thorac Surg*. 2016;102:1482-1489.
6. Wu VC, et al. *J Am Soc Nephrol*. 2014;25:595-605.
7. Ishani A, et al. *J Am Soc Nephrol*. 2009;20:223-228.
8. Coca SG, et al. *Kidney Int*. 2012;81:442-448.
9. Wald R, et al. *JAMA*. 2009;302:1179-1185.
10. Bellomo R, et al. *Crit Care Med*. 2012;40:1753-1760.
11. Vaara ST, et al. *Crit Care*. 2012;16:R197.
12. Kaddourah A, et al. *N Engl J Med*. 2017;376:11-20.
13. Prowle JR, et al. *Nat Rev Nephrol*. 2010:6;107-115.
14. Zhang L, et al. *J Crit Care*. 2015;30:860.e7-13.
15. Bouchard J, et al. *Kidney Int*. 2009;76:422-427.
16. Heung M, et al. *Nephrol Dial Transplant*. 2012;27:956-961.
17. National Clinical Guideline Centre (UK). Acute Kidney Injury: Prevention, Detection and Management Up to the Point of Renal Replacement Therapy. 2013; NICE Clinical Guidelines, No. 169. Introduction.
18. Xu X, et al. *Clin J Am Soc Nephrol*. 2015;10:1510-1518.
19. Silver SA, et al. *J Hosp Med*. 2017;12:70-76.
20. Fleming GM. *Organogenesis*. 2011;7:2-12.
21. O'Reilly P, Tolwani A. *Crit Care Clin*. 2005;367-378.
22. Pannu N, Gibney RTN. *Ther Clin Risk Manag*. 2005;1:141-150.
23. Sun Z, et al. *Crit Care*. 2014;18:R70.
24. Kitchlu A, et al. *BMC Nephrol*. 2015;16:127.
25. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney Int Suppl*. 2012;2:1-138.
26. Baxter Corporation. REVACLEAR Dialyzer Technology. 2017. Available from: http://www.baxter.ca/en_CA/assets/downloads/2017/Revaclear%20Spec%20Sheet%20Brochure%20English.pdf (accessed December 2018).
27. Fresenius Medical Care. Optiflux Dialyzers. 2016. Available from: http://www.fmcna-dialyzers.com/images/pdf/101046-Optiflux-Dialyzer_SpecSheet.pdf (accessed December 2018).
28. Ostermann M, et al. *Blood Purif*. 2016;42:224-237.
29. Murugan R, et al. *Blood Purif*. 2016;42:266-278.
30. Ostermann M. In: Bellomo R, et al (eds). 40 Years of Continuous Renal Replacement Therapy. *Contrib Nephrol*. 2018;194:51-59.
31. Wald R, et al. *Crit Care Med*. 2014;42:868-877.
32. Bell M, et al. *Intensive Care Med*. 2007;33:773-780.
33. Cartin-Ceba R, et al. *Intensive Care Med*. 2009;35:2087-2095.
34. Lin YF, et al. *Am J Surg*. 2009;198:325-332.
35. Liao Z, et al. *Artif Organs*. 2003;27:802-807.
36. Coulliette AD, Arduino MJ. *Semin Dial*. 2013;26:427-438.
37. Glorieux G, et al. *Nephrol Dial Transplant*. 2012;27:4010-4021.
38. Azar AT, Ahmad S. Hemodialysis Water Treatment System. In: Azar A (eds). Modelling and Control of Dialysis Systems. Studies in Computational Intelligence. 2013;404:347-378.
39. BC Renal Agency. Clinical Practice Standards and Procedures for Dialysis Water Quality: 2b: Endotoxin Testing of Dialysis Water. 2011. Available from:. http://www.bcrenalagency.ca/resource-gallery/Documents/2bEndotoxin-Testing-of-Dialysis-Water-Final_2012.pdf (accessed December 2018).
40. Bellomo R, et al. *Crit Care Resusc*. 2002;4:281-290.
41. Fresenius Medical Care. 2008K^2 Hemodialysis Machine Operator's Manual. 2016. Available from: https://fmcna.com/wp-content/uploads/documents/490136_Rev_J.pdf (accessed December 2018).
42. Food and Drug Administration. Quality Assurance Guidelines for Hemodialysis Devices. 1991. Available from: https://www.fda.gov/downloads/medicaldevices.deviceregulationandguidance/guidancedocuments/ucm073435.pdf (accessed December 2018).
43. Ethgen O, et al. *Nephrol Dial Transplant*. 2015;90:54-61.
44. Mar Cor Purification. 700 Series Portable. 2014. Available from: http://www.mcpur.com/main/library/12_brochures/1238642_(700).pdf (accessed December 2018).
45. Mar Cor Purification. Millenium HX. 2015. Available from: http://www.mcpur.com/main/library/12_brochures/3027573_(MHX).pdf (accessed December 2018).
46. Baxter Healthcare Corporation. The PRISMAFLEX System. 2016. Available from: https://www.baxter.com/sites/g/files/ebysai746/files/2017-11/Prismaflex-07.11-Brochure-New_Accts.pdf (accessed December 2018).
47. Ledebo I, Blankestijn PJ. *NDT Plus*. 2010;3:8-16.
48. Kasparek T, Rodriguez OE. *Clin J Am Soc Nephrol*. 2015;10:1061-1071.
49. Poeppel K, et al. *Vet Clin Small Anim*. 2011;177-191.