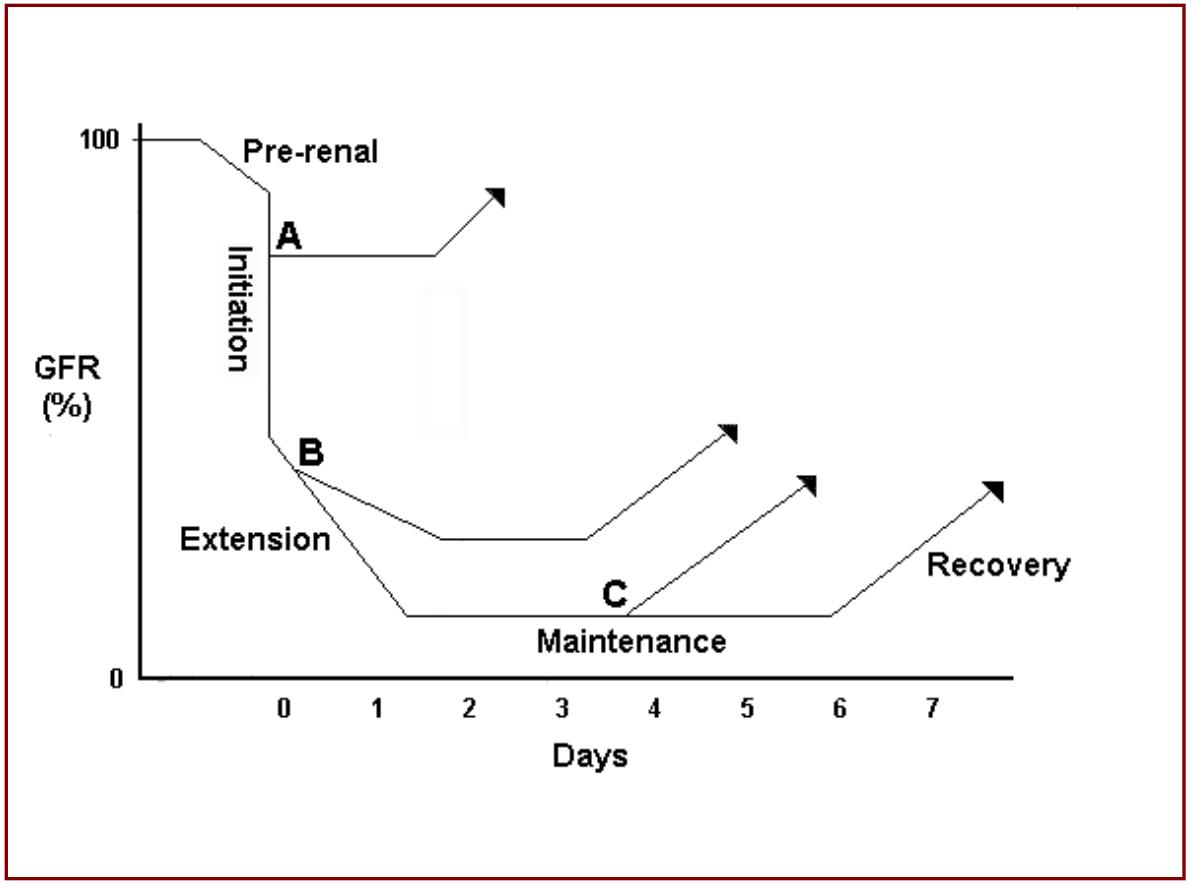
Supportive care of the AKI patient

N.S. Kanagasundaram
Consultant Nephrologist, **Newcastle Renal Services**
Honorary Clinical Senior Lecturer, **Institute of Cellular Medicine**

Newcastle University

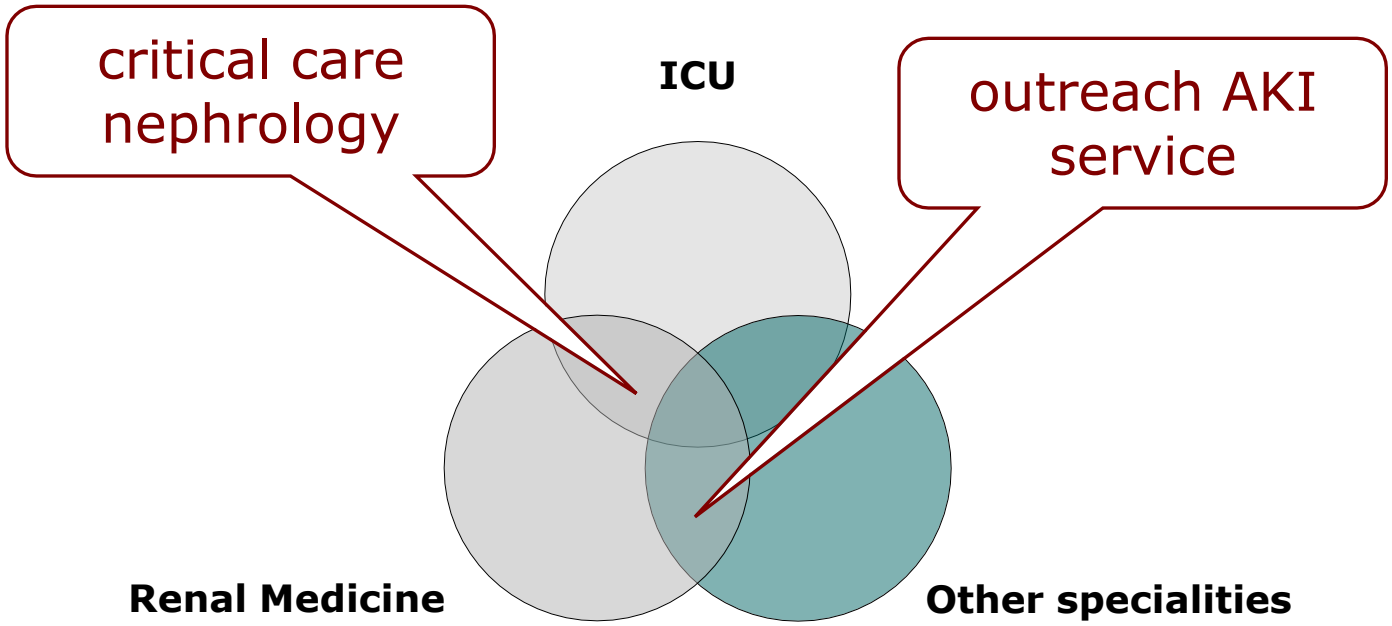
The Newcastle upon Tyne Hospitals NHS
NHS Foundation Trust

Phases of ischaemic AKI

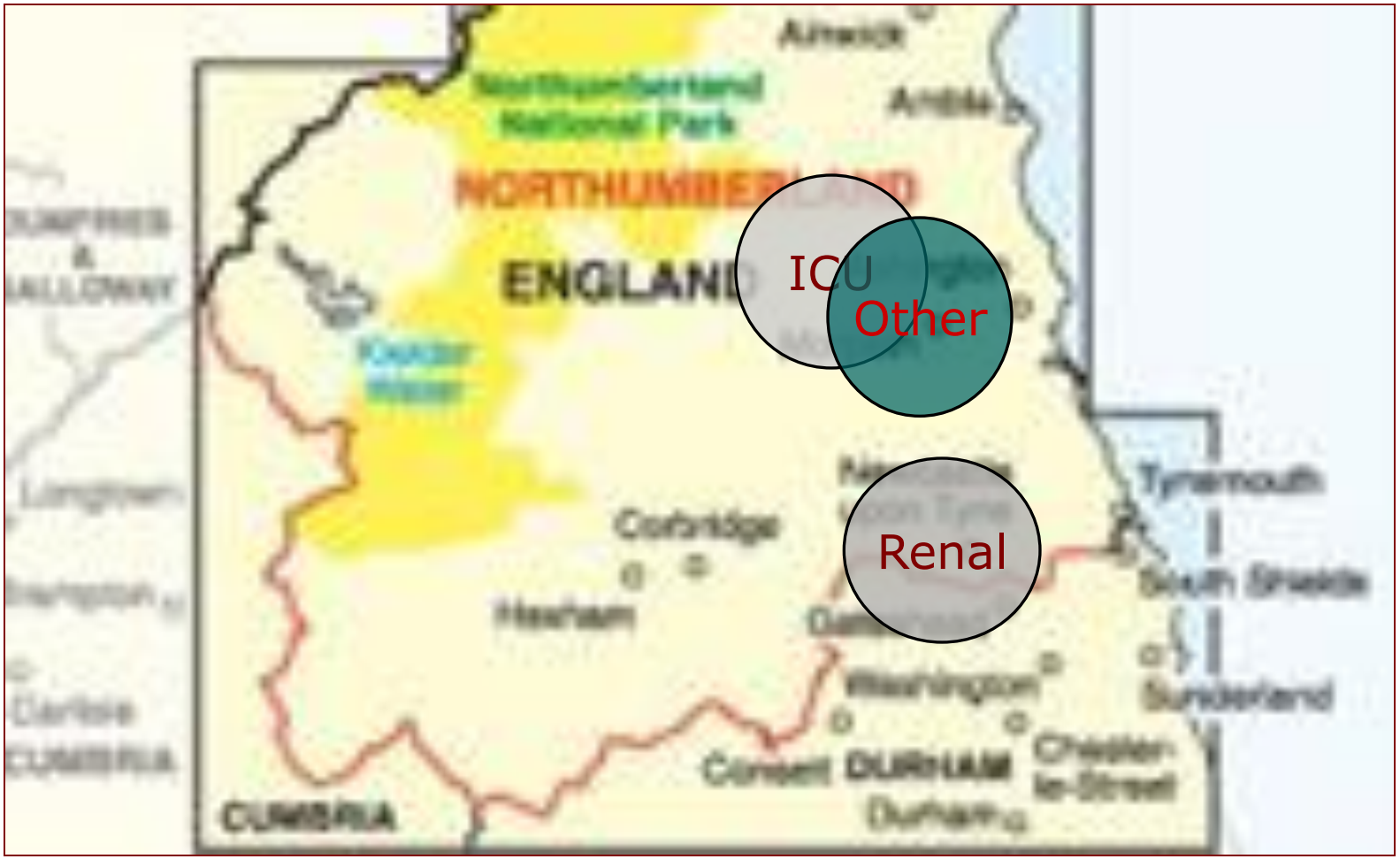


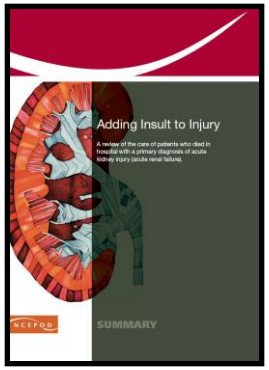
Molitoris, B. A. (2003) *J Am Soc Nephrol,* **14,** 265-7.

Venue


critical care nephrology
ICU
outreach AKI service
Renal Medicine
Other specialities

Venue


ICU
Other
Renal
ENGLAND
CUMBRIA
Hexham
Corbridge
Tynemouth
Sunderland
Washington
Consett
Durham



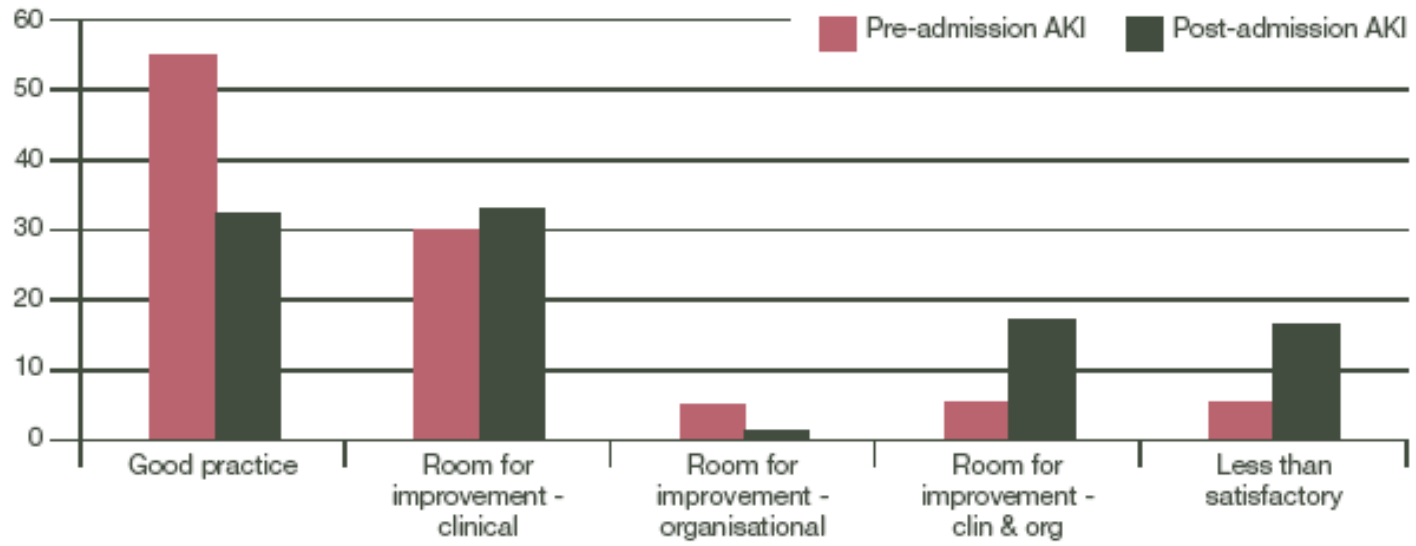


Figure 3.2 Overall assessment of care (pre-admission vs post-admission AKI)

n = 457 and 107 for pre- and post-admission AKI respectively

Sub-optimal delivery of renal aspects of care after step-down from critical care to non-specialist wards

TJ Hardy[1], AL Rhodes[1], N Kaudeer[1], SE Wright[2], SV Baudouin[2,3], NS Kanagasundaram[1]

Evaluation against markers of good renal practice:

- daily fluid balance, weights, regular bloods
- safe prescribing (avoidance of nephrotoxins; dose adjustments)
- long-term follow-up of persisting renal impairment

Results

N = 94 patients (including 6 chronic HD)

- 19% had daily fluid balance
- 2% had daily weights
- 19% had a clinical assessment of volume status

- at hospital discharge, 45% had stage 3 or 4 CKD - only 2 patients had documented plans for CKD management

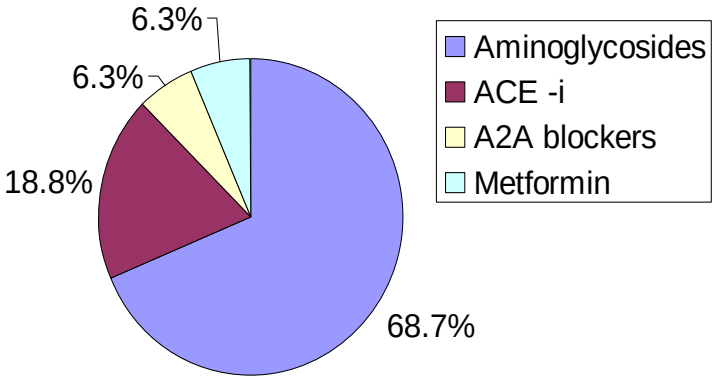
- of the 55% supported from **nephrology outreach service**, only 25% received daily fluid and weight monitoring

Renal Association, annual meeting, 2008

Sub-optimal delivery of renal aspects of care after step-down from critical care to non-specialist wards

TJ Hardy[1], AL Rhodes[1], N Kaudeer[1], SE Wright[2], SV Baudouin[2,3], NS Kanagasundaram[1]

- 15.5% were prescribed at least one class of potentially nephrotoxic drug



- 44.4% were on doses of drugs inappropriate to their level of kidney function
- The use of radiocontrast prophylaxis was documented in 13% to whom this applied

Renal Association, annual meeting, 2008

Diagnosis and management of Acute Kidney Injury (AKI): deficiencies in the knowledge base of non-specialist, junior medical staff

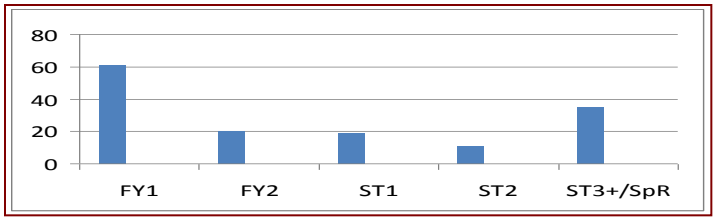
T.M. Muniraju[1], M.H. Lillicrap[1], J.L. Horrocks[2], J.M. Fisher, .R.M.W. Clark[4], N.S. Kanagasundaram[1,5]

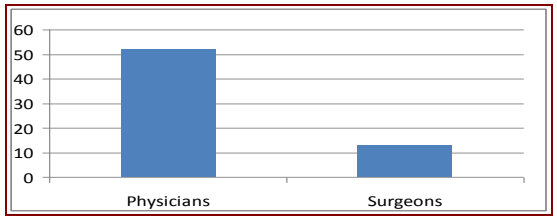
Clin Med. 2012 Jun;12(3):216-21

The Newcastle upon Tyne Hospitals NHS
NHS Foundation Trust

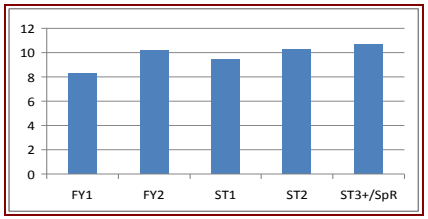
Findings

- Questionnaires were completed by 146 trainees

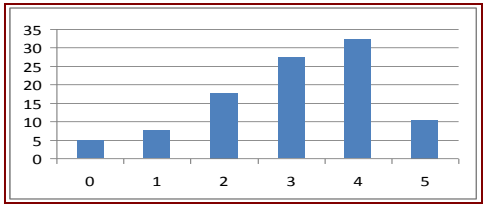




- The overall mean score was 9.4 / 20 (range 0-17); medics: 10.3 (2-17), surgeons: 10.2 (4-15)

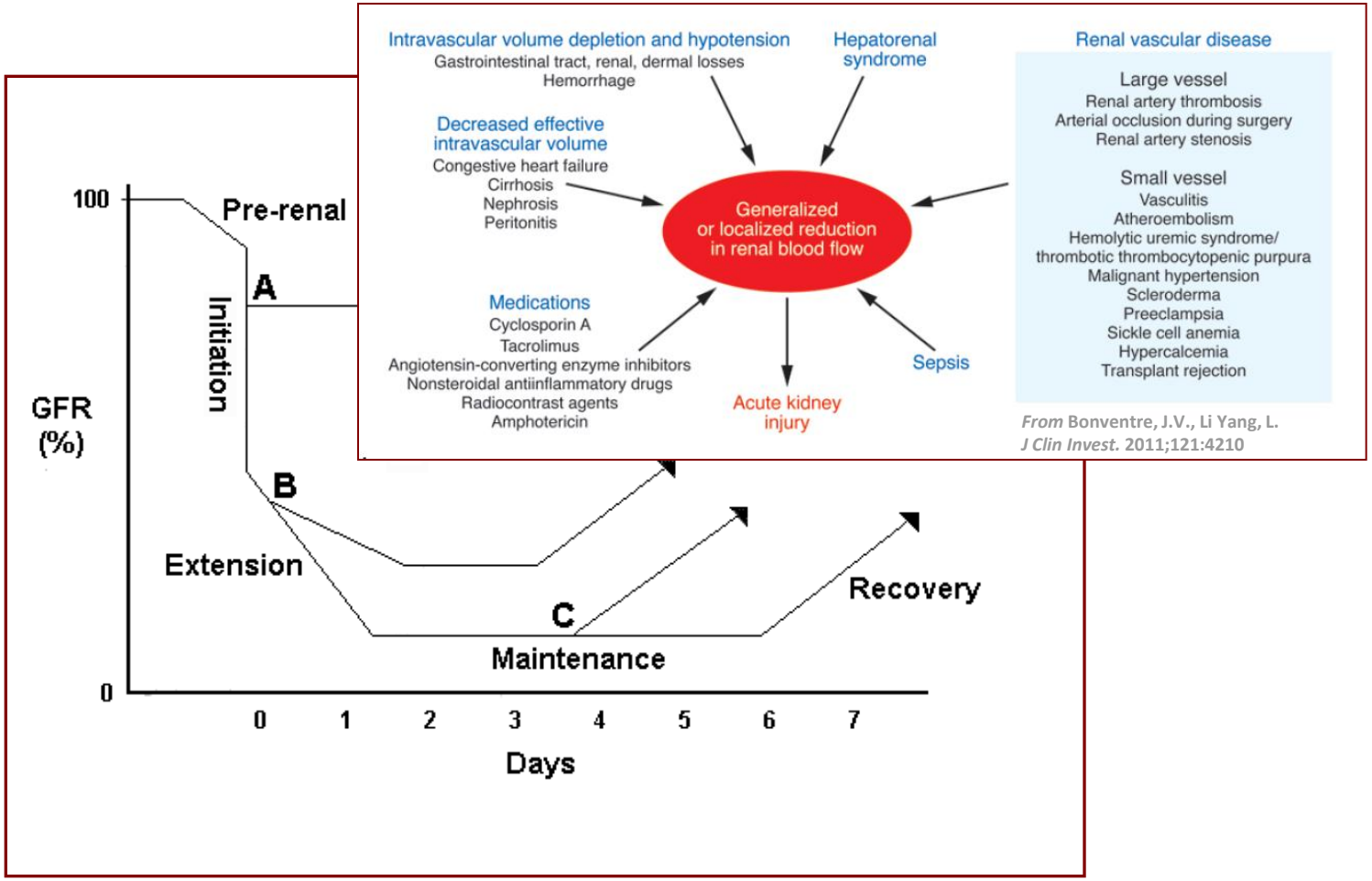


- 44% could not define AKI
- 37% could not categorise AKI
- Risk factor recognition was poor



- 40% could not name even 1 indication for renal referral
- 35% said they had never had teaching on AKI

Phases of ischaemic AKI



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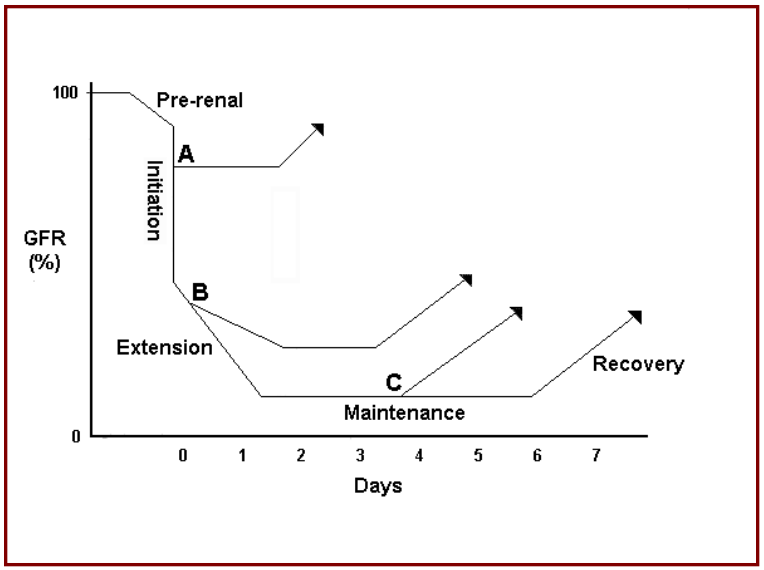
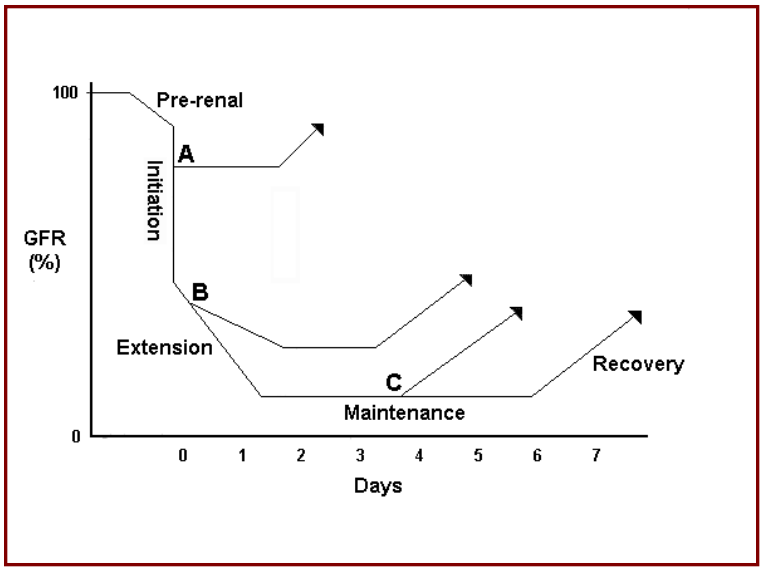
Supportive care of the AKI patient



- **Haemodynamic support**
  - Vulnerability of the acutely injured kidney
  - Volume assessment, fluid therapy, haemodynamic monitoring
- **Nutritional support**
- **Prescribing**
- **Esoteric causes**
- **Transfer of care**
- **Long term follow up**
- **Monitoring**
  - Biochemistry, haematology
  - Clinical variables: urine output, haemodynamic indices (non-invasive, invasive), fluid balance, daily weights, regular clinical assessment of volume status
  - Vigilance for sepsis

Supportive care of the AKI patient



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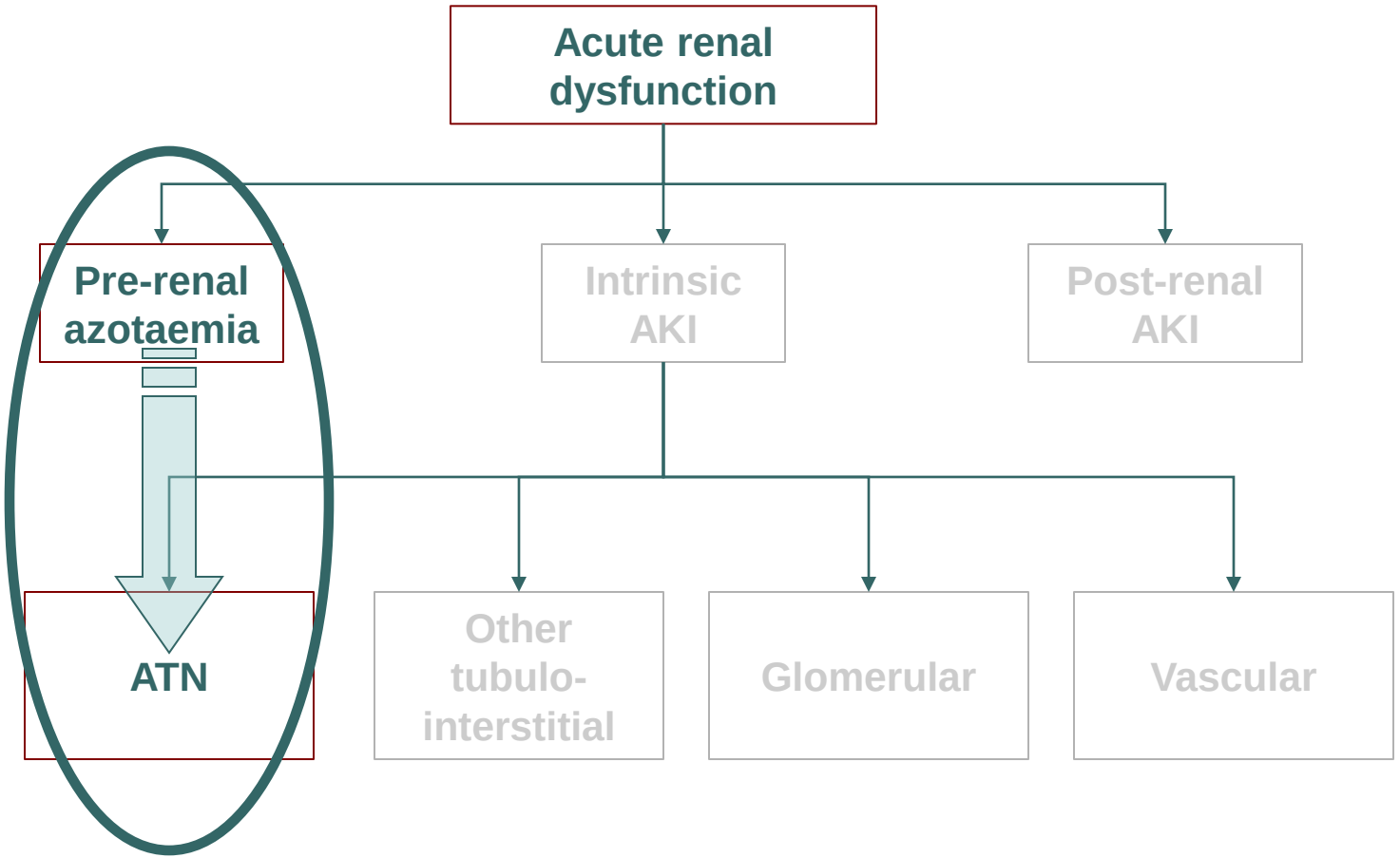
Haemodynamic support

aetiology



Haemodynamic support

pre-renal azotaemia vs. ischaemic AKI

Pre-renal azotaemia → **ischaemic AKI**

renal cell injury

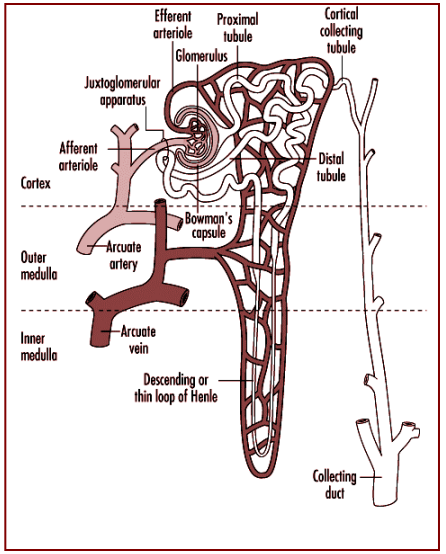
rapid restoration of excretory capacity

< 20	urine Na^+	> 40 mmol/L
< 1%	$FENa^+$	> 2%

Haemodynamic support
regional alterations in renal blood flow

- Decrease in total renal blood flow, alone, does not entirely account for reduction in GFR
- Regional alterations in RBF are probably more important
- Outer medullary blood flow is reduced disproportionately in experimental models
  - local oedema
  - structurally vulnerable capillary network

  compound…….
  - relative outer medullary hypoxia in health



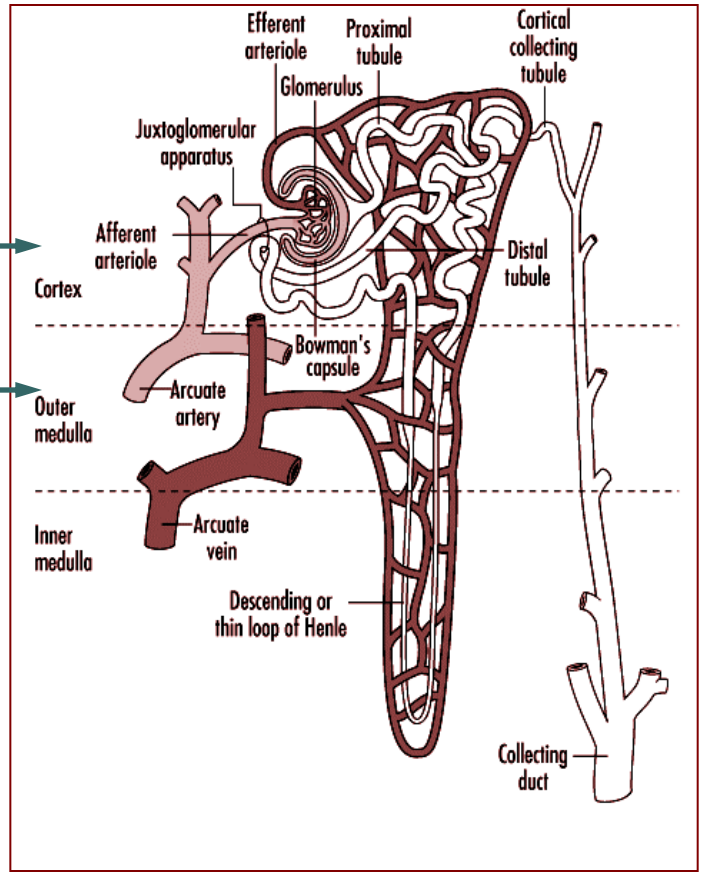
Haemodynamic support

relative outer medullary hypoxia

25% cardiac output

PO_2 6.65 – 13.3 kPa

PO_2 1.3 – 2.9 kPa



Haemodynamic support
renal auto-regulation

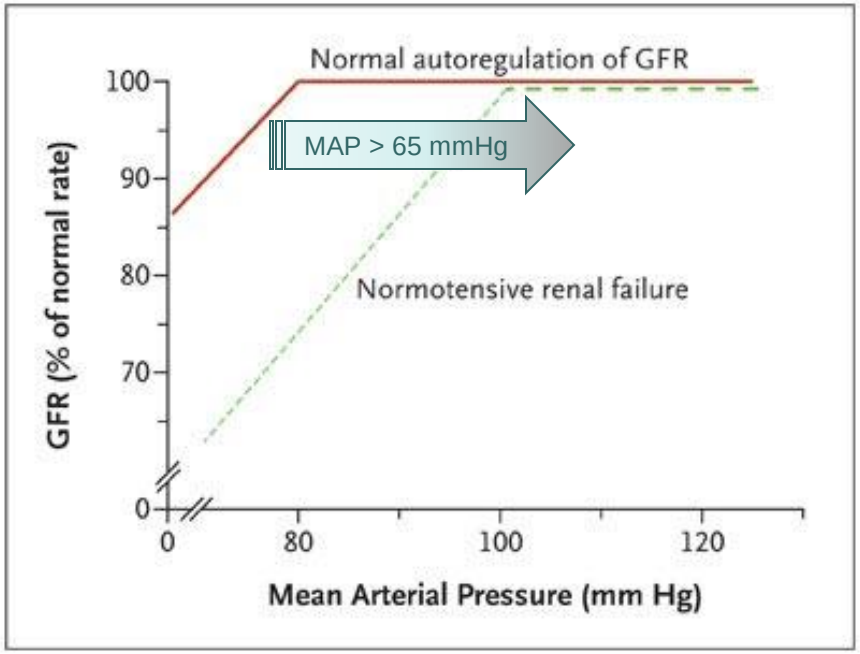


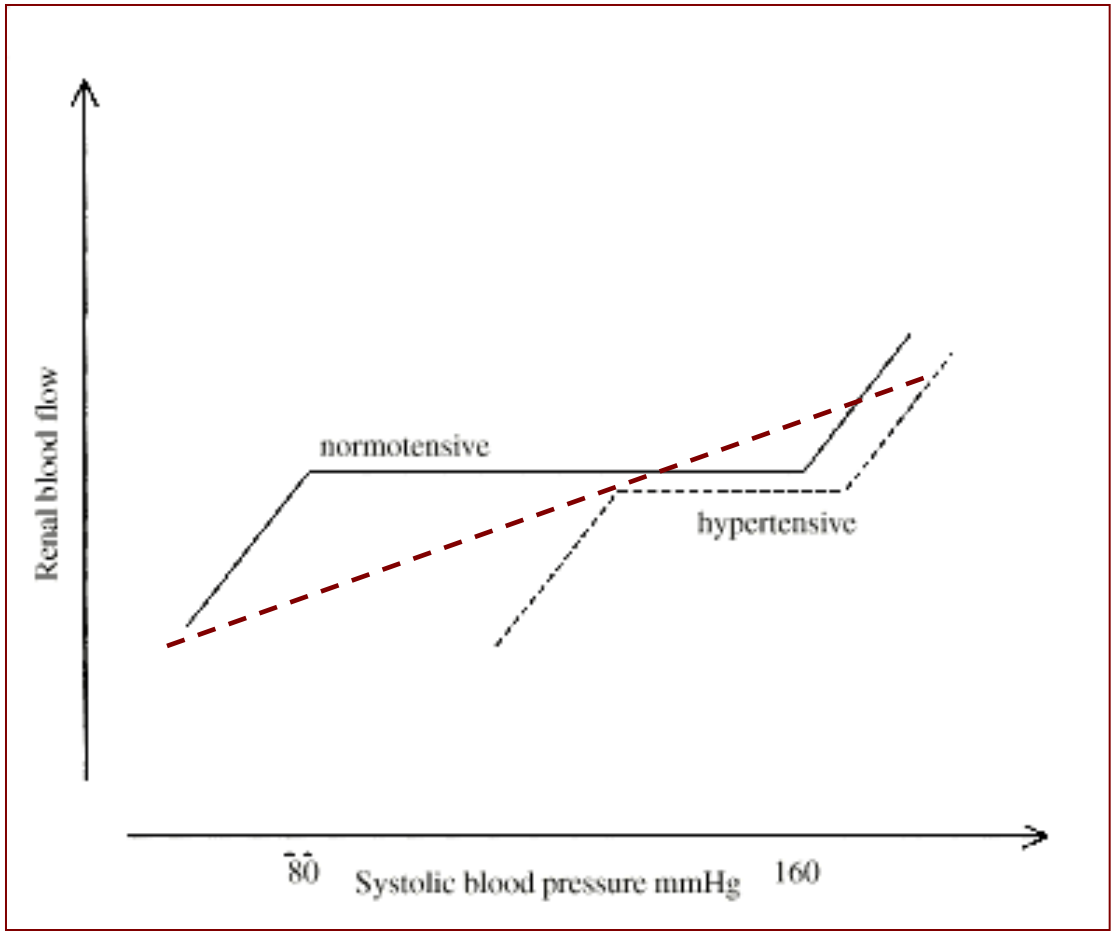
Table 1. Factors Increasing Susceptibility to Renal Hypoperfusion.

Failure to decrease arteriolar resistance
Structural changes in renal arterioles and small arteries
Old age
Atherosclerosis
Chronic hypertension
Chronic kidney disease
Malignant or accelerated hypertension
Reduction in vasodilatory prostaglandins
Nonsteroidal antiinflammatory drugs
Cyclooxygenase-2 inhibitors
Afferent glomerular arteriolar vasoconstriction
Sepsis
Hypercalcemia
Hepatorenal syndrome
Cyclosporine or tacrolimus
Radiocontrast agents
Failure to increase efferent arteriolar resistance
Angiotensin-converting–enzyme inhibitors
Angiotensin-receptor blockers
Renal-artery stenosis

From Abuelo, J.G. *NEJM* 2007: 357(8):797

Haemodynamic support

disrupted renal auto-regulation



Haemodynamic support

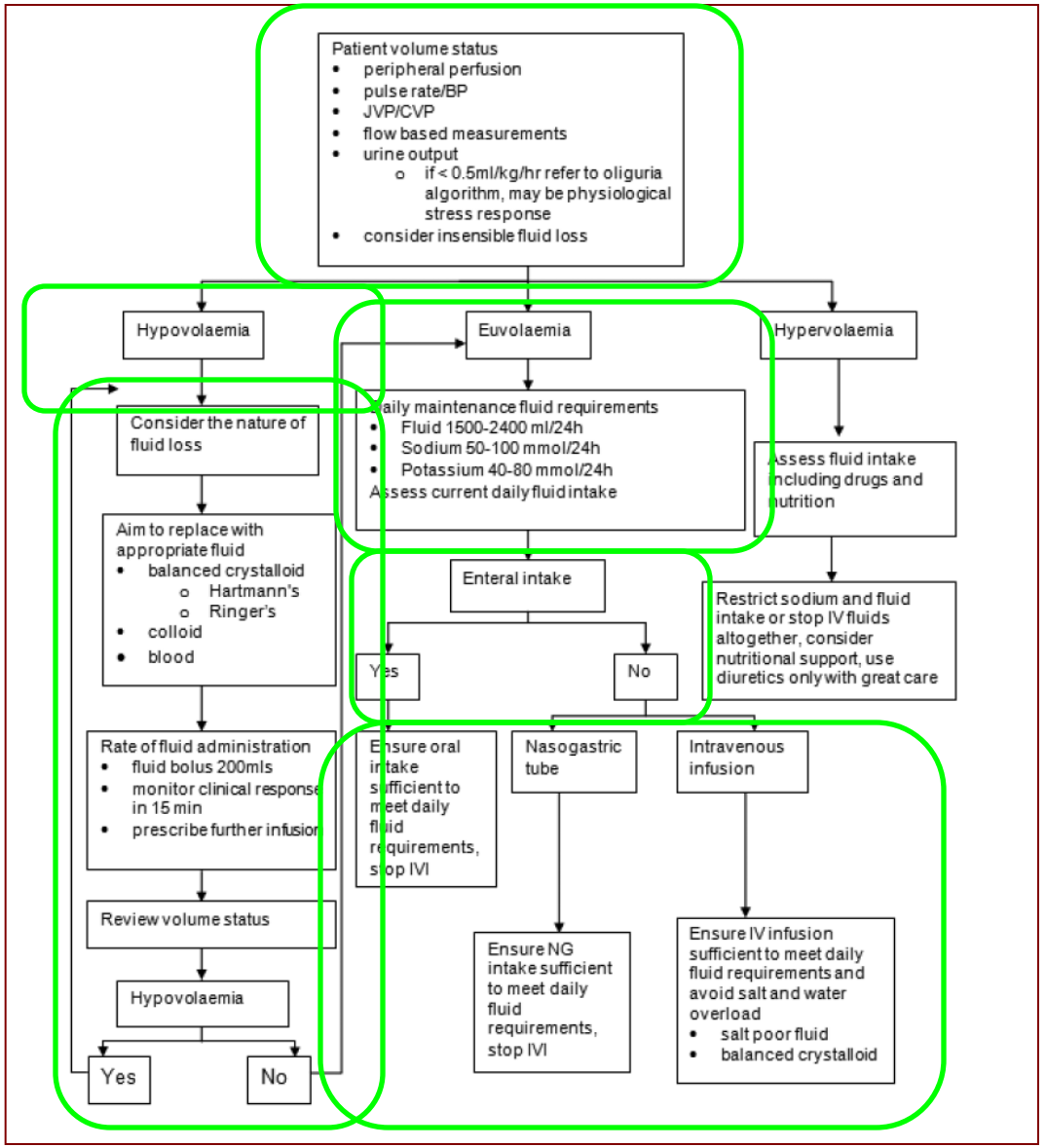
fluid therapy

British Consensus Guidelines on Intravenous Fluid Therapy for Adult Surgical Patients

GIFTASUP

Jeremy Powell-Tuck (chair)[1], Peter Gosling[2], Dileep N Lobo[1,3] Simon P Allison[1], Gordon L Carlson[3,4], Marcus Gore[3], Andrew J Lewington[5], Rupert M Pearse[6], Monty G Mythen[6]

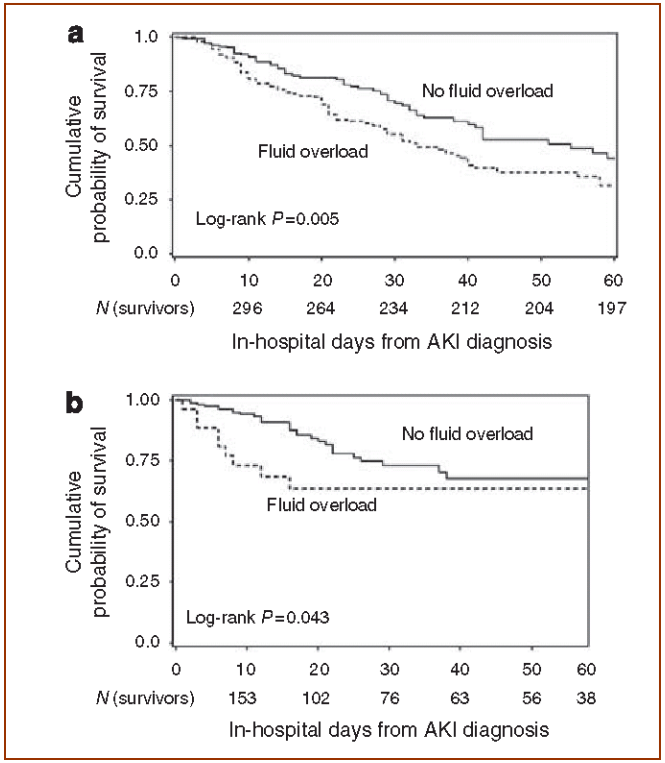
On behalf of [1]BAPEN Medical, [2]the Association for Clinical Biochemistry, [3]the Association of Surgeons of Great Britain and Ireland, [4]the Society of Academic and Research Surgery, [5]the Renal Association and [6]the Intensive Care Society.



Haemodynamic support
fluid therapy

A positive fluid balance is associated with increased mortality in AKI:

Bouchard J, Kidney Int 2009; 76: 422–427:

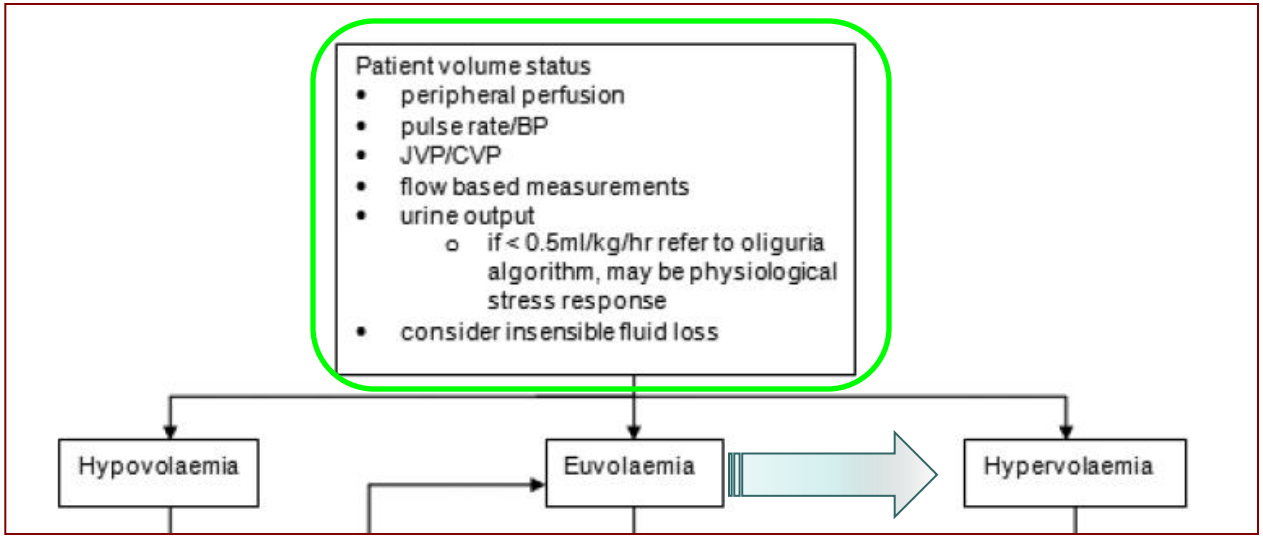


Fluid overload status at RRT initiation

Fluid overload status at AKI diagnosis (non-RRT patients

Also: Payen D, de Pont AC, Sakr Y, et al. A positive fluid balance is associated with a worse outcome in patients with acute renal failure. Crit Care 2008; 12: R74.

Haemodynamic support
fluid therapy



Assessment **(assessment, assessment)**

MAP 65 mmHg **(???)**

Stability **(avoid fluctuations)**

Judicious use of vasopressors

Haemodynamic support
diuretics

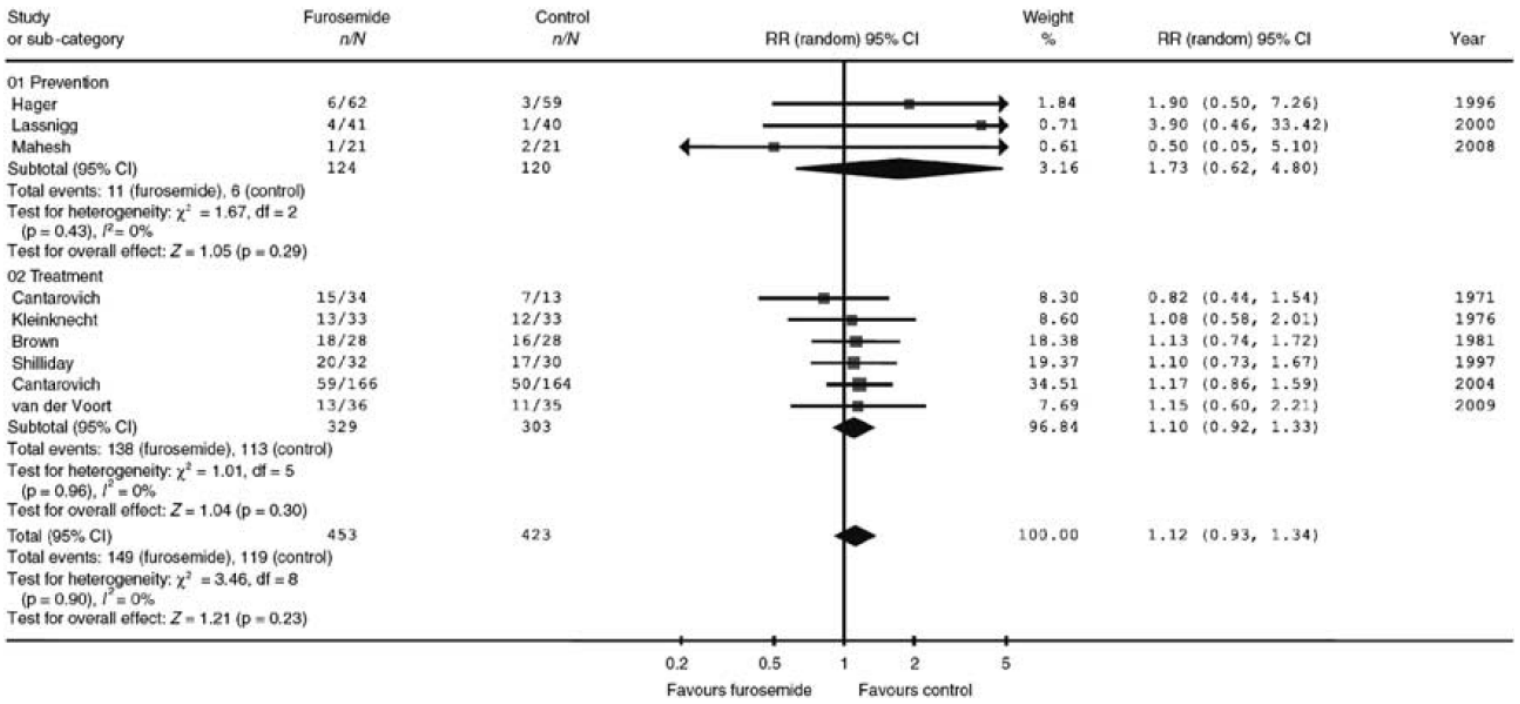


Figure 9 | Effect of furosemide vs. control on all-cause mortality. Reprinted from Ho KM, Power BM. Benefits and risks of furosemide in acute kidney injury. Anaesthesia 2010; 65: 283–293 with permission from John Wiley and Sons[193]; accessed http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2044.2009.06228.x/full

Haemodynamic support
diuretics

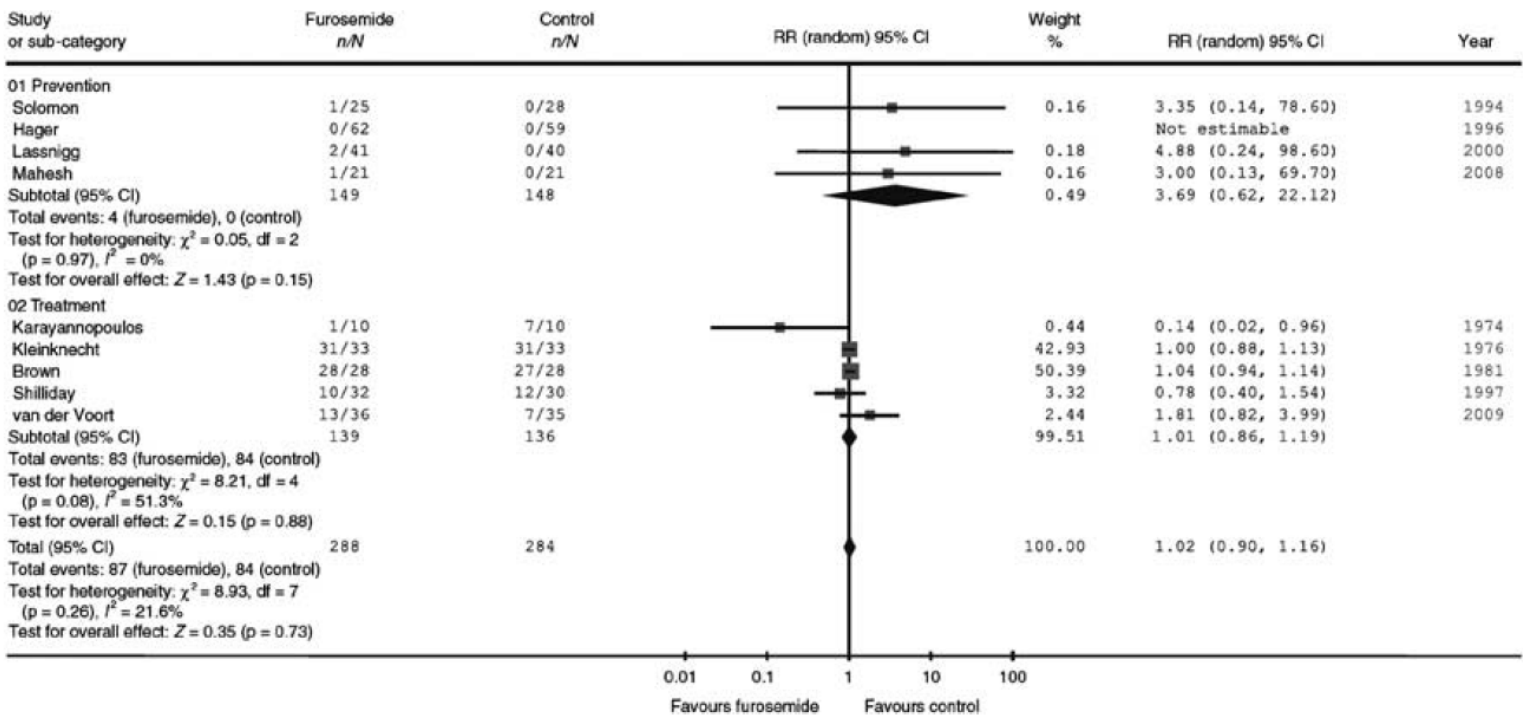


Figure 10 | Effect of furosemide vs. control on need for RRT. Reprinted from Ho KM, Power BM. Benefits and risks of furosemide in acute kidney injury. Anaesthesia 2010; 65: 283–293 with permission from John Wiley and Sons[193]; accessed http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2044.2009.06228.x/full

Haemodynamic support
fluid management

BP and volume control – salt and water management

Review dialysate sodium prescription	Reduce dialysate sodium towards usual pre-dialysis sodium Avoid sodium profiling
Review dietary salt intake	Reduce daily sodium intake to 80 – 100 mmol (a 'no added salt' diet)
Review fluid restriction	Aim for inter-dialytic weight gain ≤ 3% 'active' body weight • If non-obese, active and actual body weight are pragmatically equivalent • If obese, active body weight = 25*height^2 (weight in kg, height in meters; 'fat-free' BMI assumed as 25)

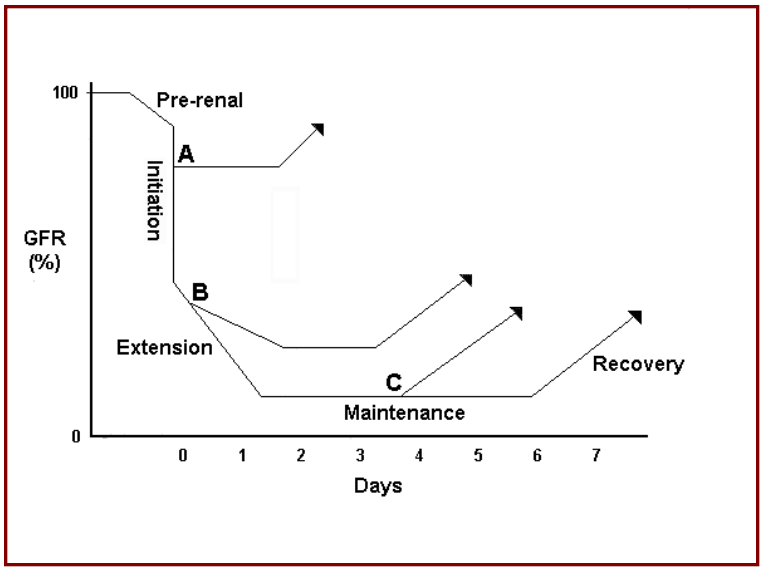
Haemodynamic support
fluid management

BP and volume control – salt and water restriction and patient education

Emphasise key role of sodium in hypertension, volume overload, thirst
Differentiate between sensations of thirst and dry mouth
Review drugs that may be contributing to dry mouth
Patient tips and tricks to manage restrictions:

- check sodium content of processed food
- take tablets with food where possible
- use small volume cups
- sip and savour, don't gulp
- use ice cubes, ice lollies, sweets or gum (n.b. sugar content), mouth washes, artificial saliva
- use pre-filled measuring jug to help guide daily fluid intake

Supportive care of the AKI patient



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  - Vigilance for sepsis

Nutritional support

tight glycaemic control

Supplementary table 3: Summary table of RCTs examining the effect of insulin for the prevention of AKI

Outcome	Author Year Country	Age	Baseline kidney function	Setting	Study duration	No. analyzed (No randomized)		Intervention/Control (target blood glucose)		Concomitant medication	Event rate Arm 1 (Arm 2)	RR* (95%CI)	P value	Quality
						Arm 1	Arm 2	Arm 1	Arm 2					
Critically Ill Patients														
Mortality														
Mortality by 90 d	NICE-SUGAR [56] 2008 Australia, New Zealand & Canada	60	nd	ICU	90 d	3010 (3054)	3012 (3050)	Intensive glucose (81-108 mg/dl)	Conventional glucose (≤180 mg/dl)	nd	28% (25%)	1.10[a] (1.01-1.20)	0.02	Good
Mortality by 28 d											22% (21%)	1.07[a] (0.97-1.18)	NS (0.17)	Good
RRT														
RRT	NICE-SUGAR [56] 2008 Australia, New Zealand & Canada	60	nd	ICU	90 d	3010 (3054)	3012 (3050)	Intensive glucose (81-108 mg/dl)	Conventional glucose (≤180 mg/dl)	nd	15% (15%)	1.06[a] (0.94-1.20)	NS (0.34)	Good
Days of RRT											0.8 (0.8)	--	NS (0.39)	Good
Sepsis Patients														
Mortality														
90 d	Brunkhorst [17] 2008 Germany	65	S_{Cr} 126.4 µmol/l	ICU	28 d	247 (247)	289 (290)	Intensive insulin (80-110 mg/dl)	Conventional insulin (180-200 mg/dl)	Per protocol	40% (35%)	1.14 (0.92-1.42)	NS (0.31)	Fair
28 d											25% (26%)	0.96 (0.72-1.29)	NS (0.74)	Fair
RRT														
RRT	Brunkhorst [17] 2008 Germany	65	S_{Cr} 126.4 µmol/l	ICU	nd	244 (247)	289 (290)	Intensive insulin (80-110 mg/dl)	Conventional insulin (180-200 mg/dl)	Per protocol	28% (23%)	1.22 (0.91-1.63)	NS (0.19)	Fair
AKI														
Doubling of baseline S_{Cr}	Brunkhorst [17] 2008 Germany	65	S_{Cr} 126.4 µmol/l	ICU	nd	244 (247)	289 (290)	Intensive insulin (80-110 mg/dl)	Conventional insulin (180-200 mg/dl)	Per protocol	31% (27%)	1.15 (0.88-1.50)	NS (0.25)	Fair

Annotations:

*Calculated by ERT with raw data from original studies when available. When study reported only event rates, calculations were done using percentages.

a. NICE-SUGAR: Mortality by 90 d, OR 1.14 (95% CI 1.02-1.28); Mortality by 28 d, OR 1.09 (95% CI 0.96-1.23); RRT, OR 0.9 (95% CI -0.9-2.7)

Nutritional support
maintenance and replacement

Protein-calorie malnutrition is common in patients with AKI, affecting 42% at admission to one renal unit

Fiaccadori, E. J Am Soc Nephrol 1999; 10: 581–593.

AKI:

- is pro-inflammatory
- is often associated with hypercatabolism:
  normalised protein catabolic rate (nPCR) ~ 1.8 g/kg/day
  (nPCR ~1.2 in steady state chronic HD – largely represents dietary intake)
- may require RRT which contributes through:
  nutrient losses (water-soluble essential nutrients e.g. 10 – 15 g amino acids / day on CRRT
  induction of hypercatabolic state (8 – 10 g protein lost per IHD session)

Compounded by:

- under-prescription of nutrient replacement

Sparse literature

Critical care literature**:** enteral > parenteral; early initiation if possible; re-feeding syndrome

Nutritional support
maintenance and replacement

Carbohydrate metabolism
AKI is associated with hyperglycaemia
insulin resistance
increased hepatic gluconeogenesis

Sufficient calories required to mitigate protein catabolism (for gluconeogenesis)

Resting energy expenditure is not raised by AKI *per se* and may be only 130% of normal even in critical illness

Near neutral nitrogen balance associated with energy intake of ~ 25 kcal/kg/day in one retrospective study:

Macias, W.L. JPEN J Parenter Enteral Nutr 1996; 20: 56

No difference in nitrogen balance with 30 vs. 40 kcal/kg/day but higher dose produced more hyperglycaemia and hypertriglyceridaemia:

Fiaccadori, E. Nephrol Dial Transplant 2005; 20: 1976

Nutritional support
maintenance and replacement

Carbohydrate metabolism

AKI is <u>associated</u> with hyperglycaemia

insulin resistance

increased hepatic gluconeogenesis

Suff sis)

Res %

of n

Nea

kcal

: 56

No

proc

Fiaccadori, E. Nephrol Dial Transplant 2005; 20: 1976

We suggest achieving a total energy intake of 20–30 kcal/kg/d in patients with any stage of AKI (2C)

Administer, predominantly, as carbohydrate due to inhibited lipolysis in critical illness

Nutritional support
maintenance and replacement

Protein intake
Protein hypercatabolism driven by stress, inflammation, acidosis

No clear evidence that increasing the prescription to supra-physiological levels can mitigate this (and extra protein load can contribute to uraemia and metabolic acidosis)

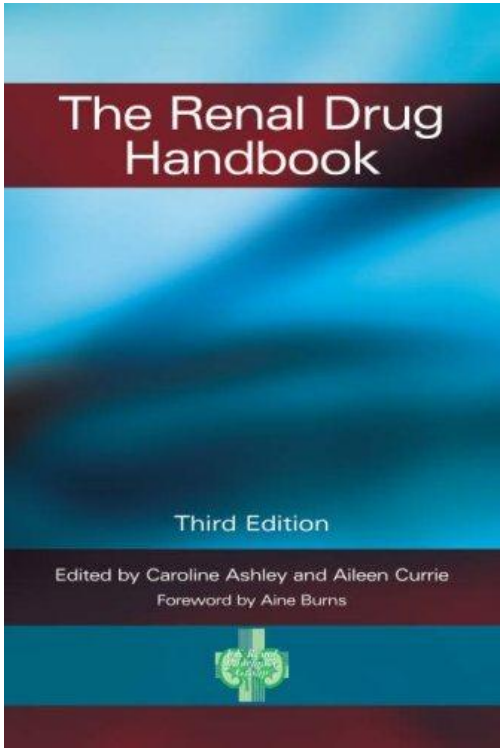
Burns patients – higher protein requirements

Nutritional support
maintenance and replacement

We suggest protein supplementation of:

- 0.8–1.0 g/kg/day in non-dialysis requiring, non-catabolic AKI patients
- 1.0–1.5 g/kg/day in patients with AKI on RRT
- up to a maximum of 1.7 g/kg/day in patients on CRRT / who are hypercatabolic

Supportive care of the AKI patient



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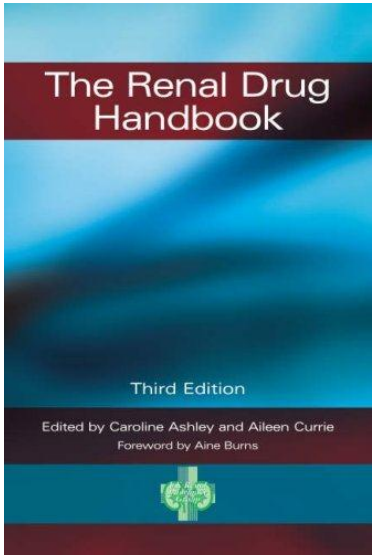
Prescribing

nephrotoxins and other drugs potentially deleterious to renal function

- Justify initiation or continuation, e.g.:
  - RAS modifying agents
  - Radio-contrast
  - Aminoglycoside antibiotics
- Seek alternatives if possible

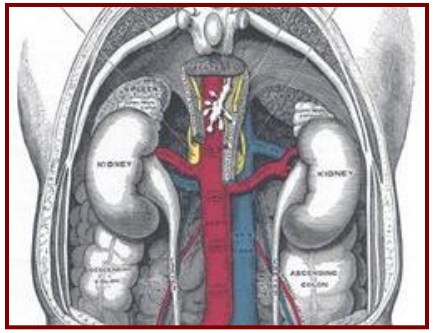
Prescribing
dose adjustment in renal support

- Drug dosing in renal support
- Advice broken down according to RRT technique, too

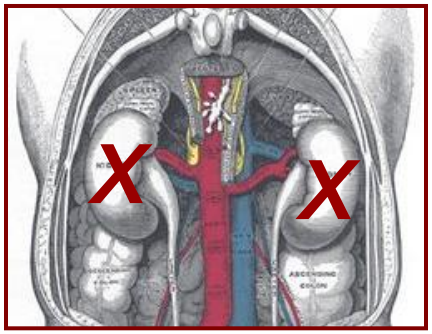


Prescribing

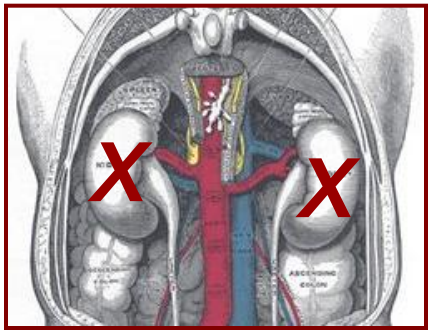
dose adjustment – AKI patients independent of RRT and assumptions about CrCl



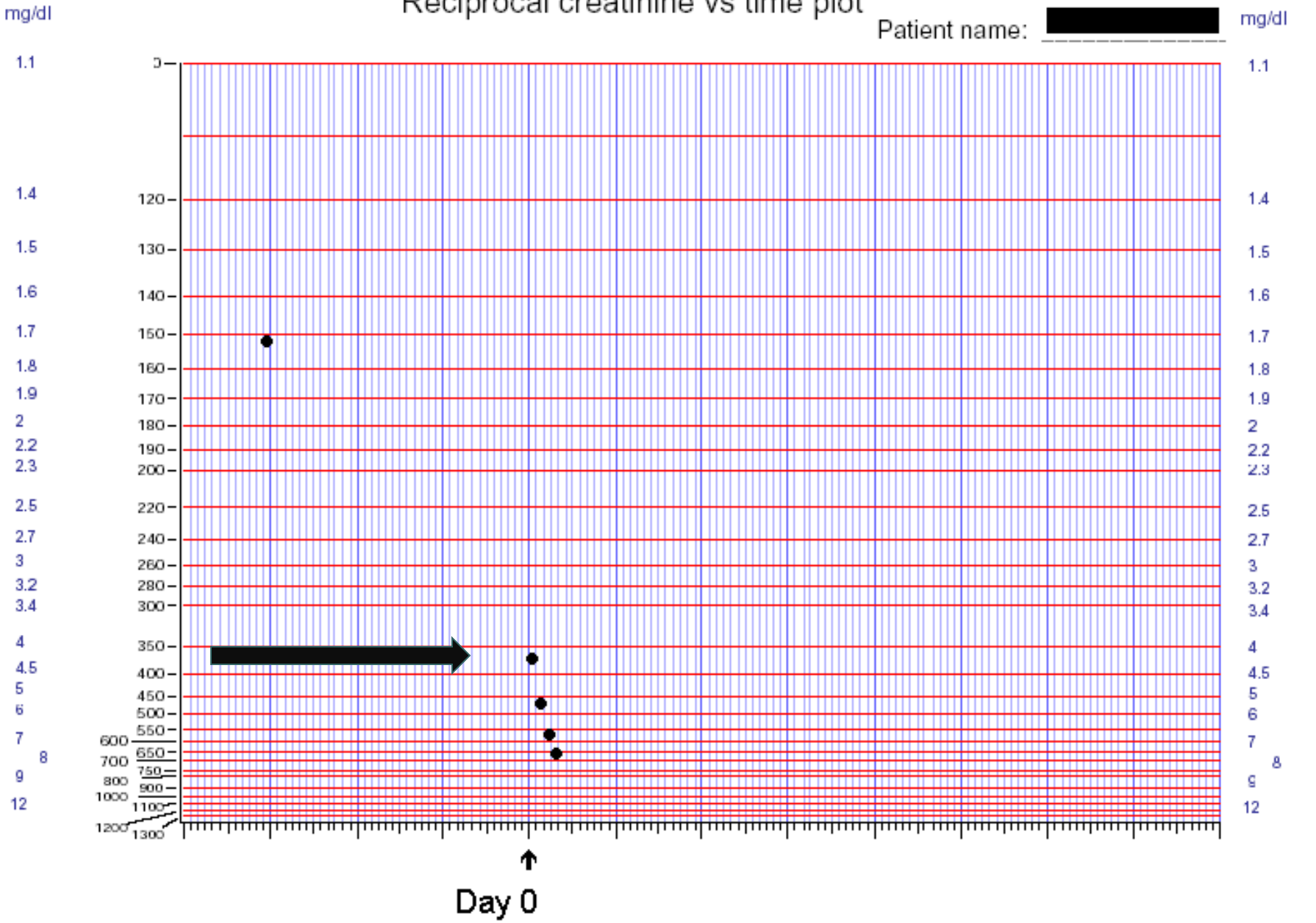
- time 0 hrs
- serum creatinine 90
- eGFR 99
- actual GFR normal



- time 24 hrs
- serum creatinine 200
- eGFR 39
- actual GFR 0



- time 72 hrs
- serum creatinine 800
- eGFR 8
- actual GFR 0



Downloadable from www.edren.org

Supportive care of the AKI patient

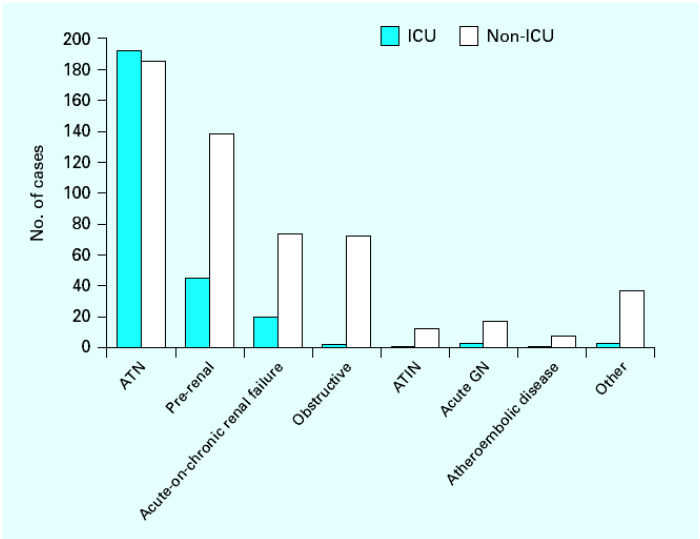
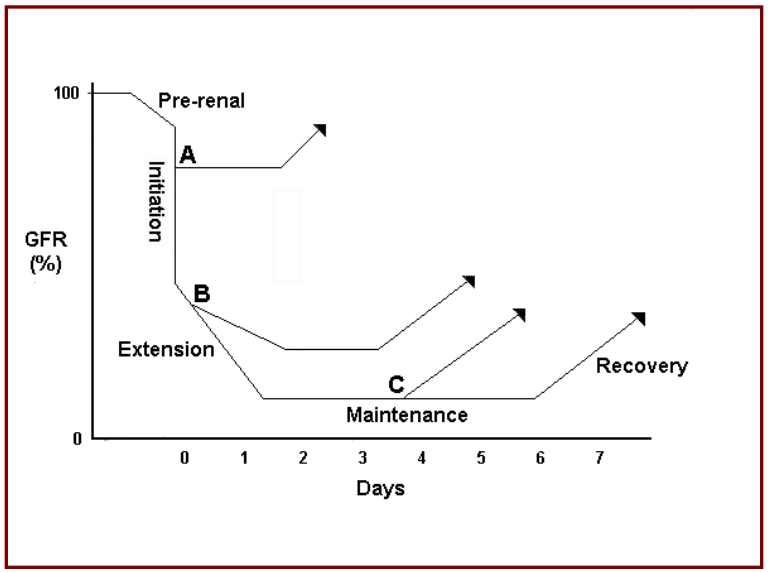


Fig 1. Spectrum of acute renal failure in intensive care unit (ICU) (253 patients) and non-ICU (495) settings. More than one type of ARF could be recorded for each ARF episode; the main ARF aetiologies are illustrated (ATN = acute tubular necrosis; ATIN = acute tubulo-interstitial nephritis; GN = glomerulonephritis (adapted from Ref 7).

Spectrum of ARF in ICU and non-ICU settings.
Kidney International 1998; 53:S16

- **Haemodynamic support**
  - Vulnerability of the acutely injured kidney
  - Volume assessment, fluid therapy, haemodynamic monitoring
- **Nutritional support**
- **Prescribing**
- **Esoteric causes**
- **Transfer of care**
- **Long term follow up**
- **Monitoring**
  - Biochemistry, haematology
  - Clinical variables: urine output, haemodynamic indices (non-invasive, invasive), fluid balance, daily weights, regular clinical assessment of volume status
  - Vigilance for sepsis

Esoteric causes
aetiology



Molitoris, B. A. (2003) *J Am Soc Nephrol,* **14,** 265-7.

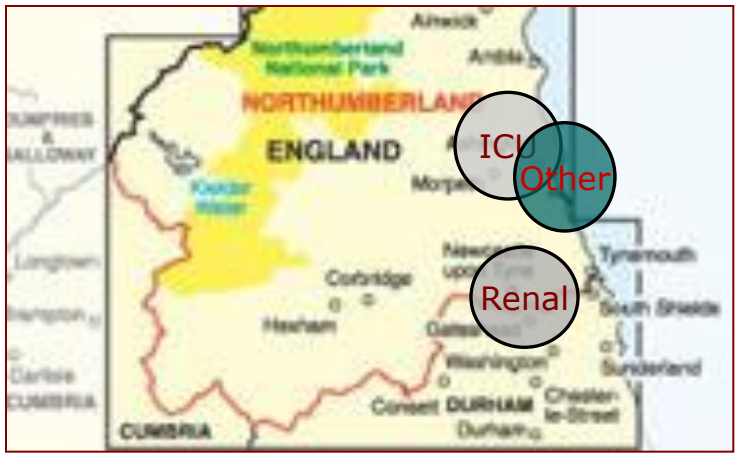
May be suggested by:

- Lack of clear, precipitating insult(s)
- Prolonged time-course
  - ATN usually recovers in 7–21 days
  - May be later, compounding insults

Maintain vigilance for obstruction

- May have been missed, at 1st, by initially non-compliant renal tract or superimposed ATN (urine is needed to dilate)

Supportive care of the AKI patient



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Transfer of care
Renal involvement

- If an esoteric diagnosis is possible
- If dialysis is indicated
- If AKI is prolonged, even if dialysis is not indicated

Q J Med 2008; **101**:643–648
doi:10.1093/qjmed/hcn071 Advance Access published on 24 June 2008

Patient flow from critical care to renal services: a year-long survey in a critical care network*

S.E. WRIGHT[1], S.V. BAUDOUIN[1,2], N. KAUDEER[3], S. SHRESTHA[3], J. MALONE[2], L. BURN[2] and N.S. KANAGASUNDARAM[3]

From the [1]Department of Anaesthesia, Royal Victoria Infirmary, Newcastle upon Tyne, [2]North East and Cumbria Critical Care Network, North Tyneside General Hospital, North Shields, Tyne and Wear, and [3]Department of Renal Medicine, Freeman Hospital, Newcastle upon Tyne, UK

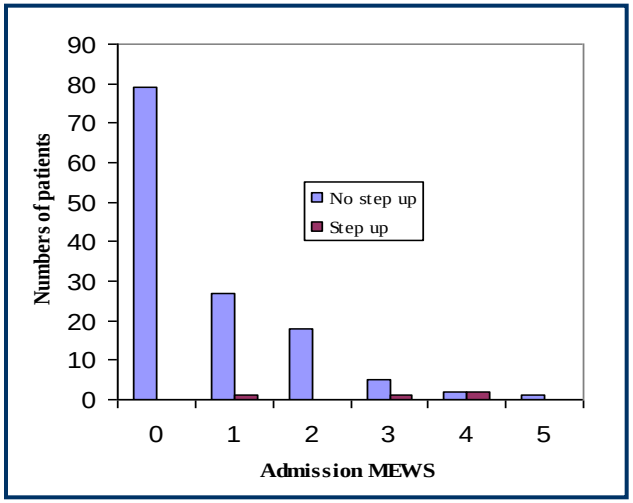
- Anecdotal evidence suggested inappropriately prolonged critical care stays due to delayed step-down to local renal units
- To determine the number of extra days patients spend in NE&CCCN critical care units receiving single-organ renal support before transfer to a renal unit
- 542 patients received RRT in critical care (12.5% already known ESRD)
- Median duration of RRT on critical care was 4 days (range 1–30)
- 127 (23%) discharged from critical care still requiring RRT
- Of these, 58% received a period of single-organ renal support (median 2 days, range 1–8) using 113 critical care bed days

Emergency transfer of in-patients to renal services – admission MEWS scoring may identify those at risk of needing early critical care

N.S. Kanagasundaram, S.A. Tee, M.Brady, L.Grant, J.F. Cosgrove

NUTH NHS Trust **M**odified **E**arly **W**arning **S**ystem (MEWS)[1]

Score	3	2	1	0	1	2	3	Home Team Variants Name & Date
CNS		Confused /agitated		Alert	Respond to Voice	Respond to Pain	U: No Response	
Respiratory rate	<8			8-20	21-30		>30	
Heart rate	<40		40-50	51-100	101-110	111-130	>130	
Systolic BP	<70	71-80	81-100	101-180	181-200	201-220	>220	
Temperature	<34	34.0-35.0		35.1-37.5	37.6-38.5	38.6-40.0	>40	
O2 Sats with appropriate oxygen therapy	<90%	91-93%		94-100%				
Urine Output (Over 2 hrs or more)	<30ml/hr							



Findings

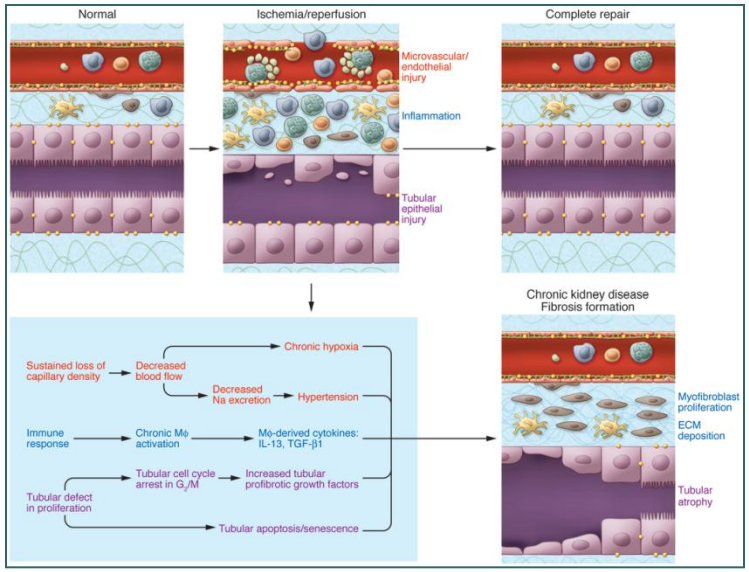
➢136 emergency transfers (127 patients inc. 36 chronic dialysis, 65 AKI):

➢4 patients required a step-up care on the day of admission (3 AKI, 1 ESRD, 2 from ward-level care, 2 from A+E)

MEWS	Stepped up on day of transfer (n = 4)
0 (n = 79)	0%
≥ 1	7%
≥ 2	10%
≥ 3	27%

➢ MEWS now used to facilitate discussions with ICU
➢ All transfers discussed with senior on-call nephrologist
➢ All critical care step-down transfers also discussed with senior intensivist

Supportive care of the AKI patient



From Bonventre, J.V. and Li Yang, L. *J Clin Invest.* 2011;121(11):4210.

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Long term follow up

Persisting CKD

Long-term prognosis after acute kidney injury requiring renal replacement therapy

Nephrol Dial Transplant (2009) 24: 2186–2189

Pierre-Alain Triverio[1], Pierre-Yves Martin[1], Jacques Romand[2], Jerome Pugin[2], Thomas Perneger[3] and Patrick Saudan[1]

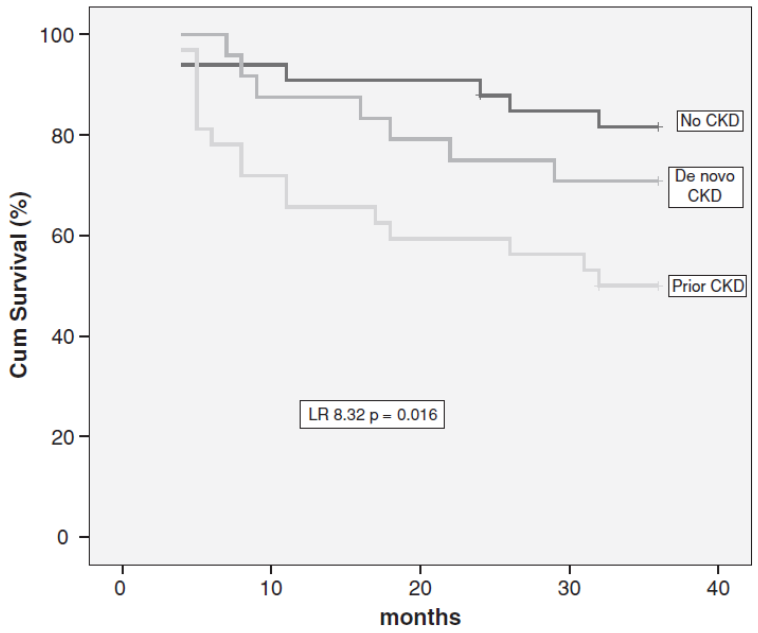

Fig. 1. Kaplan–Meyer analysis of 3-year survival rates in patients without (no CKD prior to AKI) and with prior (prior CKD to AKI) or *de novo* CKD after AKI.

- **N= 89 at 3 years**
- **ESRD developed in 9**
  - 8 had prior CKD

Long term follow up

Discharge advice

- Advice to patient and primary care:
  - Intercurrent illness
    - Early and regular monitoring of biochemistry
    - Drug holiday

Supportive care of the AKI patient

- **Haemodynamic support**
  - Vulnerability of the acutely injured kidney
  - Tightrope walk between dangerous hypo- and hyper-volaemia
- **Nutritional support**
  - Malnutrition is common in AKI
  - Maintenance and replacement needs to account for associated hypercatabolism and the effects of renal support
- **Prescribing**
  - Justify initiation / continuation of nephrotoxins
  - Consider need for drug dose adjustment if on renal support and according to renal support technique
  - Remember to play ‘catch-up’ with drug dosing when renal function is changing, quickly
- **Esoteric causes**
  - May be suggested by aberrance from expected natural history
- **Transfer of care**
  - Should be safe
- **Long term follow up**
  - CKD management where appropriate
  - Advice for intercurrent illness