
# Acute kidney injury – a problem for today and tomorrow

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# Disclosures

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- Alere – Research support
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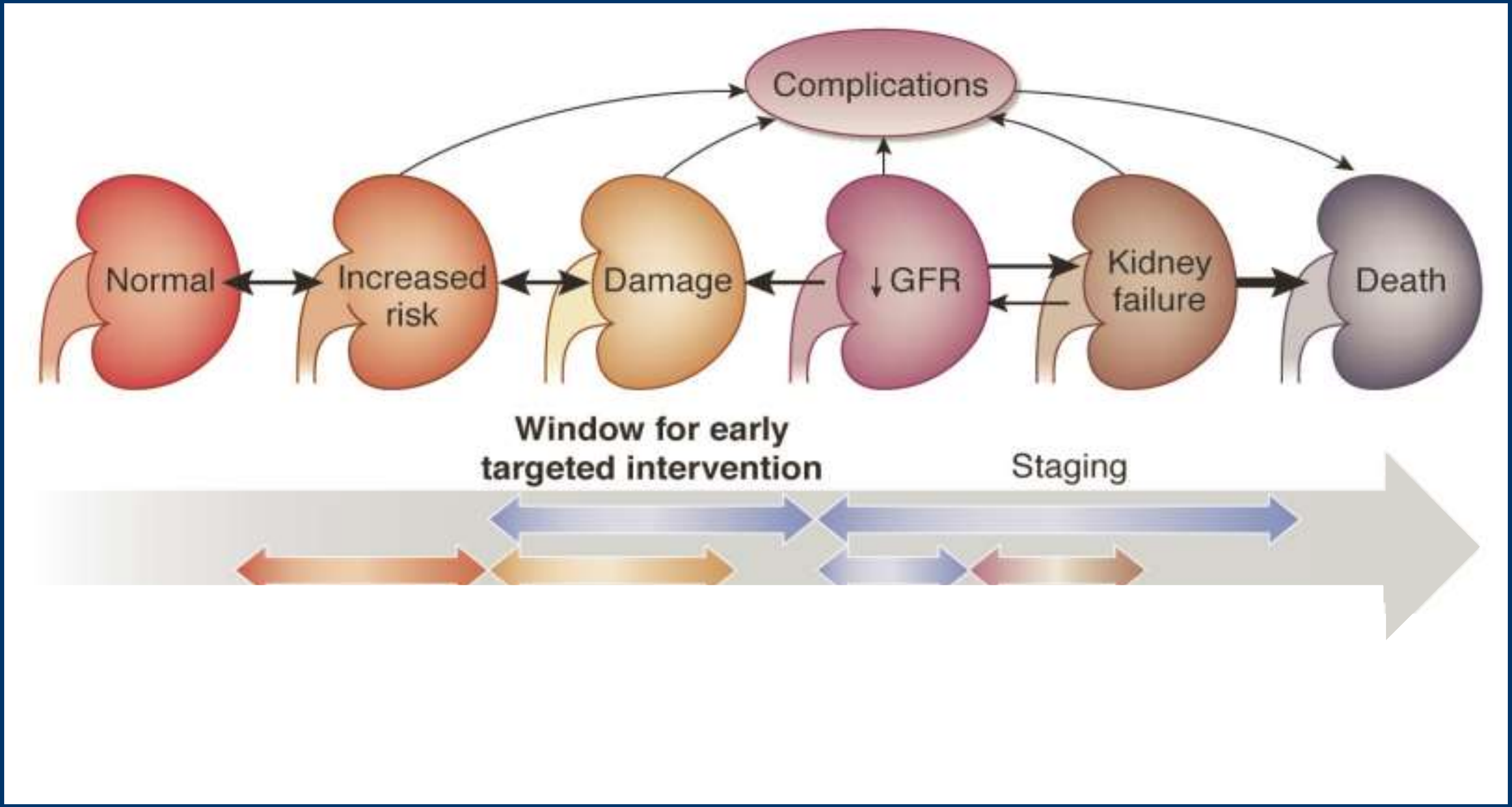
# AKI: key points

- AKI requiring renal replacement therapy (AKI-D) is associated with
  – High short-term mortality and morbidity
  – Long-term consequences including CKD and ESRD
- Methodological constraints limit our understanding of the recovery process, and hamper intervention
- AKI management may impact recovery

AKI, acute kidney injury; RRT, renal replacement therapy; CKD, chronic kidney disease; ESRD, end-stage renal disease

Cerdá J, et al. Clin J Am Soc Nephrol 2015;

# The natural history of AKI




Lewington, Cerda, Mehta, Kidney Int 2013;84:457–67

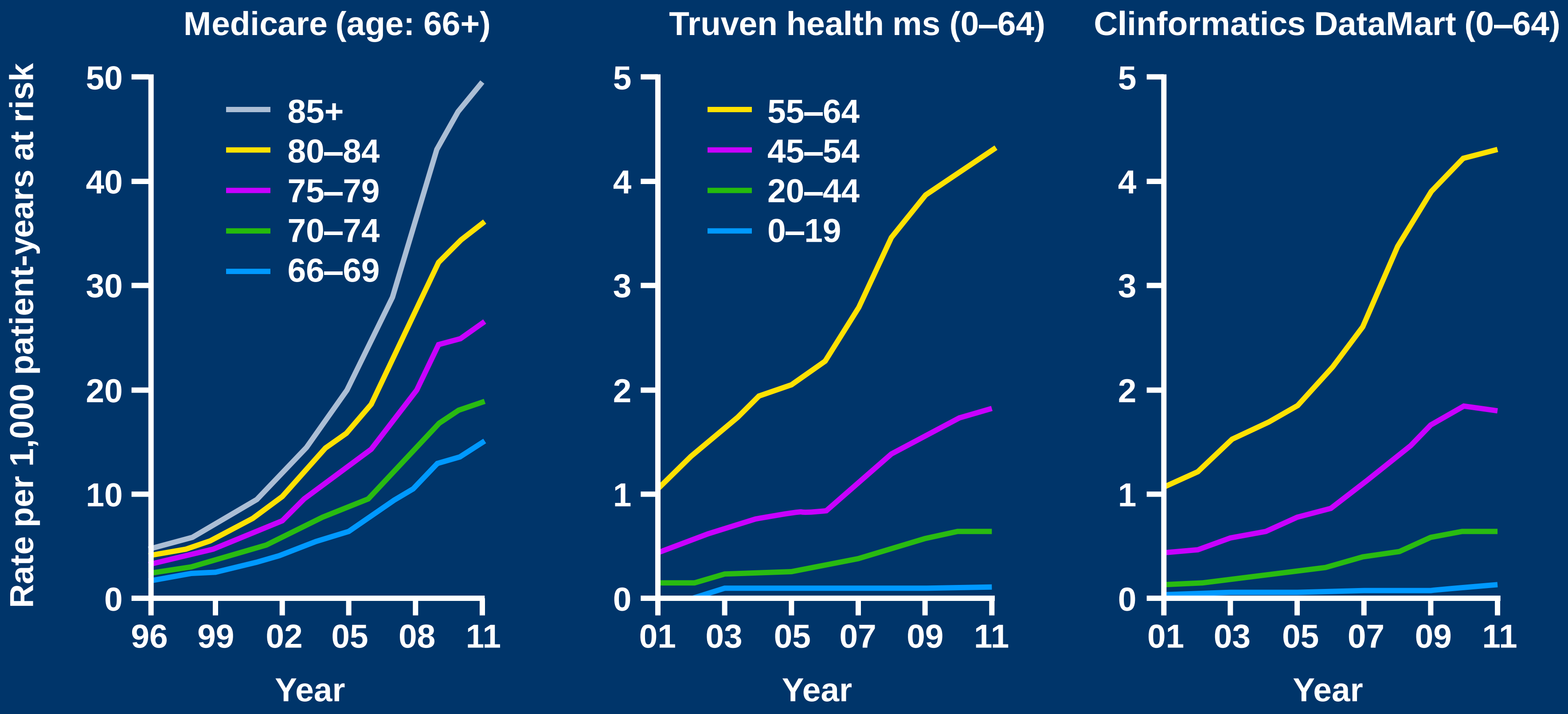
# The consequences of AKI

- The incidence of AKI seems to be increasing

**Worldwide, approximately**
**2,000,000 people**
**will die of AKI**
**this year**

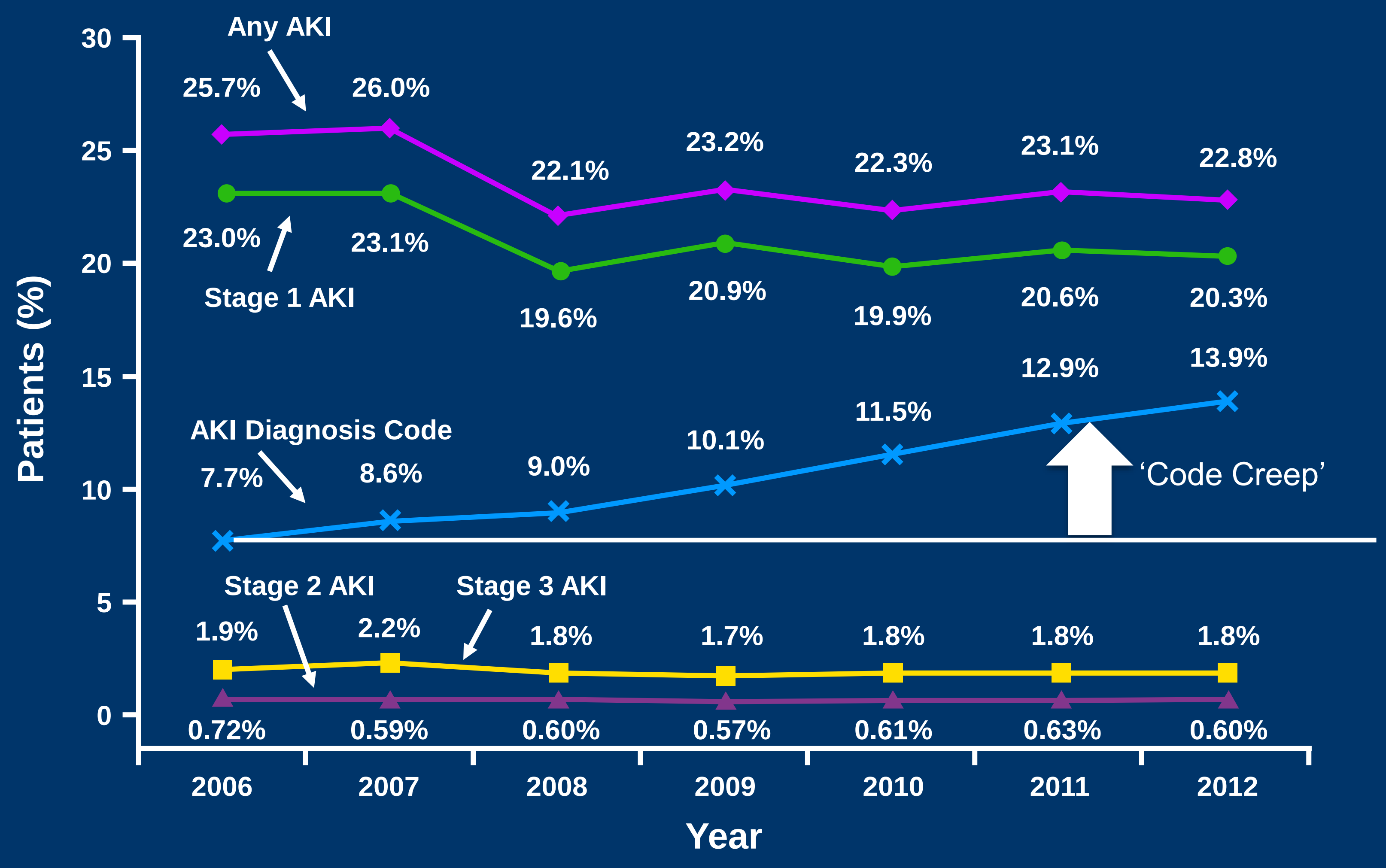
Hsu RK, et al. J Am Soc Nephrol 2013;24:37–42; Prescott GJ, et al. Nephrol Dial Transplant 2007;22:2513–9;
Cerdá J, et al. Clin J Am Soc Nephrol 2015; Mehta,Cerdá et al. Lancet 2015;
Uchino S, et al. JAMA 2005;294:813–8; Hoste EA, et al. Crit Care 2006;10:R73;
Ali T, J Am Soc Nephrol 2007;18:1292–8; Cerdá J, et al. Nat Clin Pract Nephrol 2008;4:138–53

# Increasing incidence of AKI: rates of AKI by age and dataset (US)




United States Renal Data System Annual Data Report 2013; Volume 1, Chapter 6
http://www.usrds.org/atlas.aspx

# Hospitalised patients experiencing AKI (US veterans, 2006–2012)

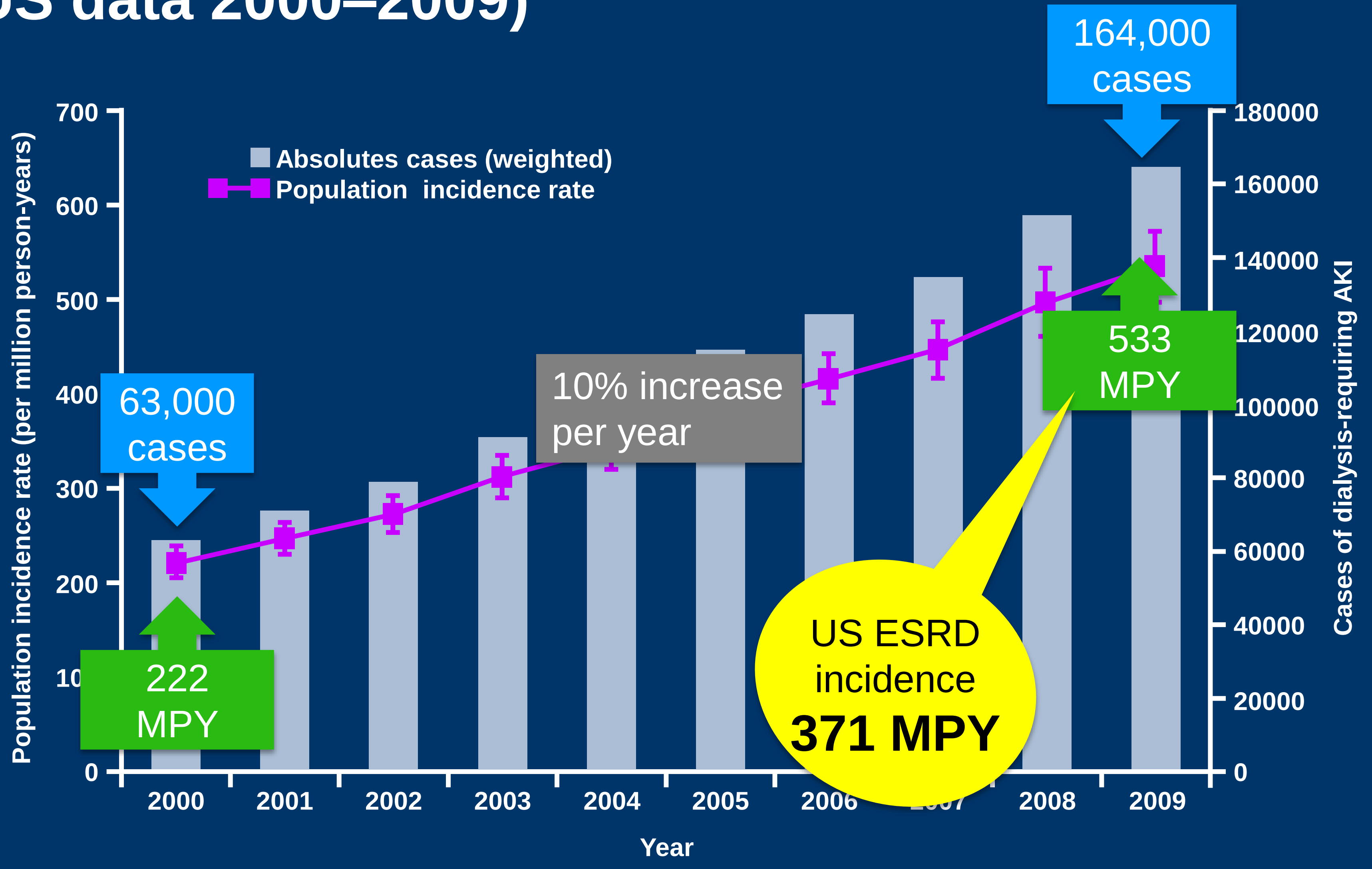



Heung M, et al. ASN Renal Week 2014

# Rising incidence of AKI


Hsu RK, et al. Kidney Int 2007

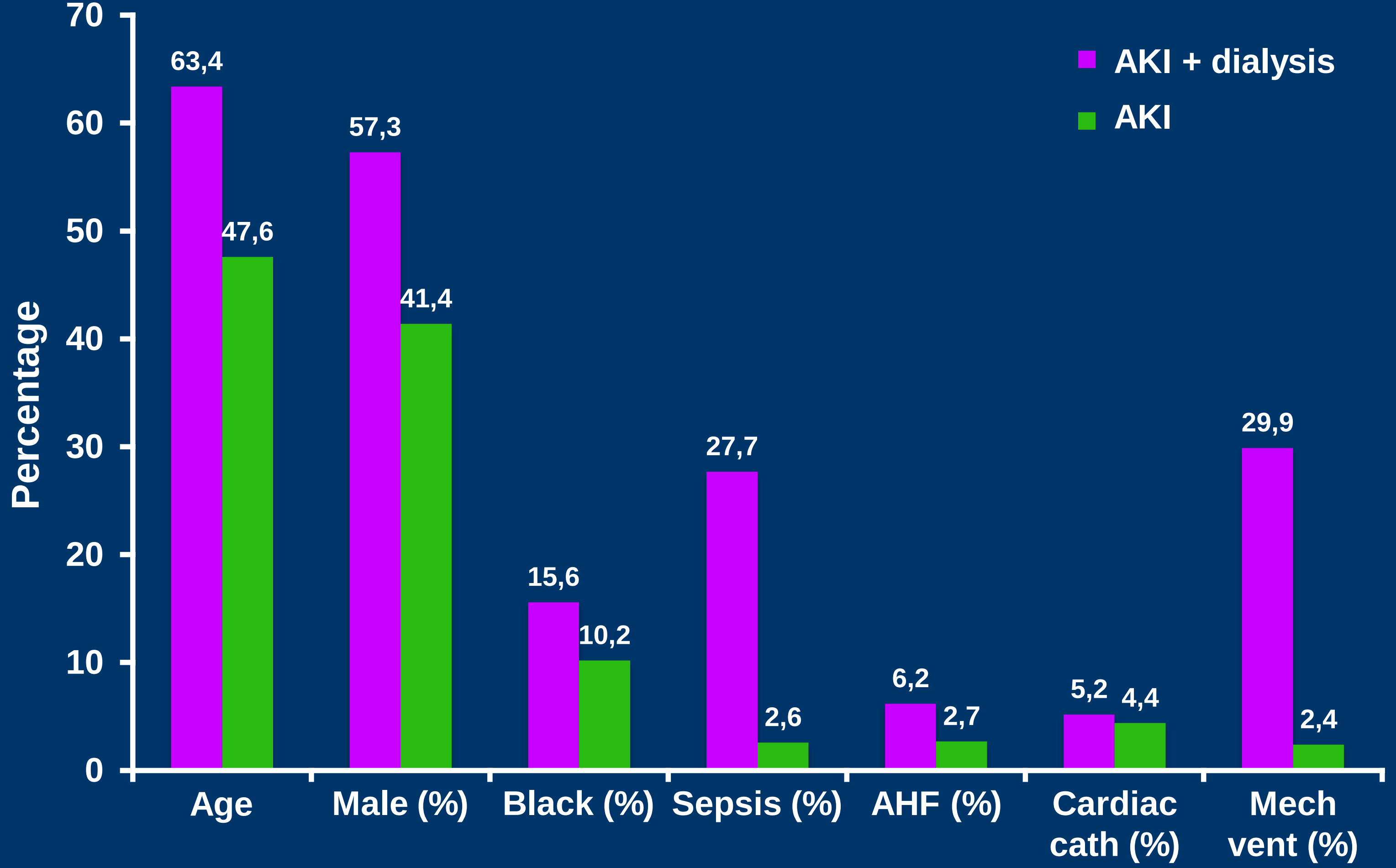
# Incidence of dialysis-requiring AKI (US data 2000–2009)




MPY, million person-years

Hsu RK, et al. J Am Soc Nephrol 2013;24:37–42

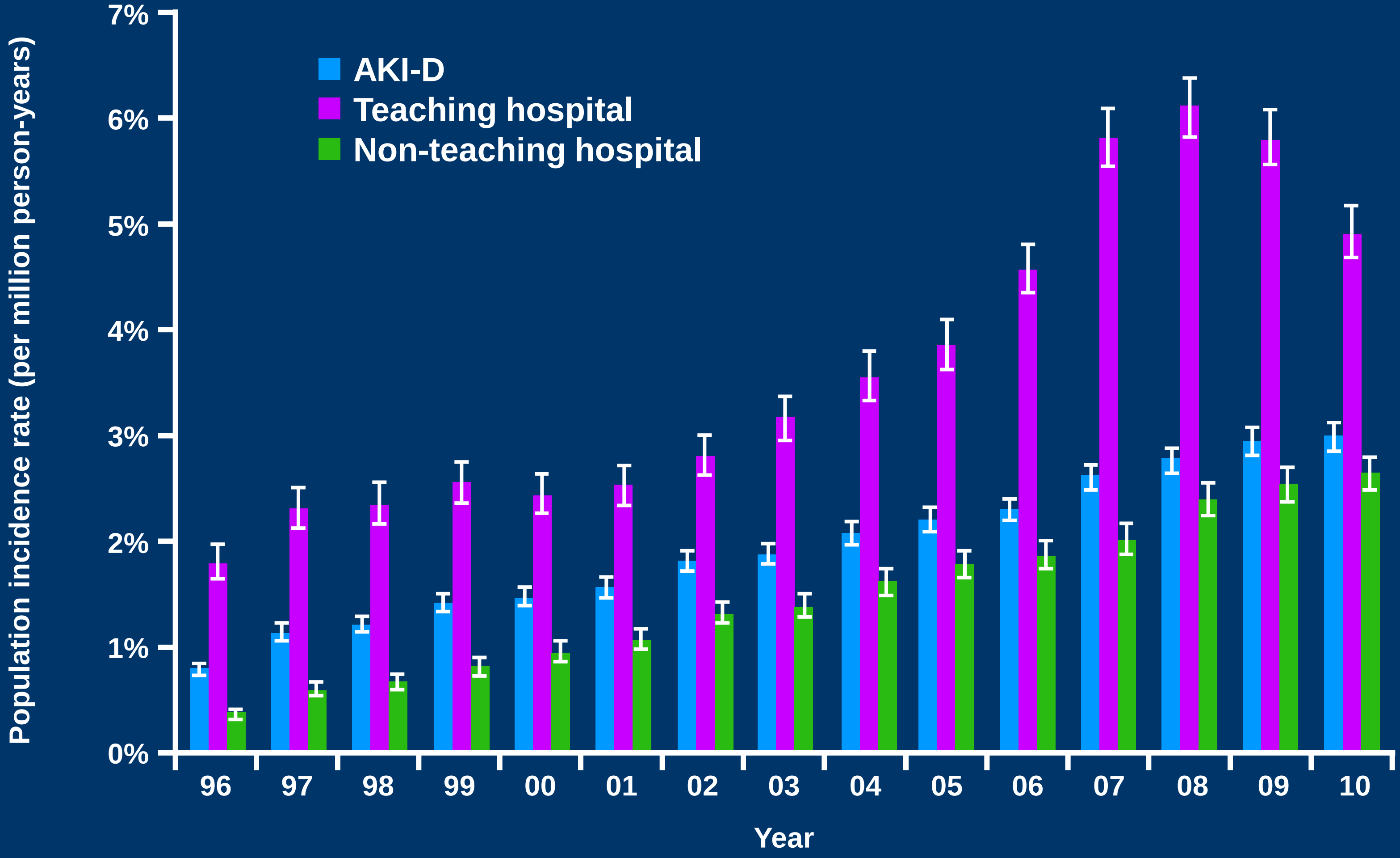
# Demographic and baseline disease characteristics of patients with dialysis-requiring AKI




AHF, acute heart failure; Cardiac cath, cardiac catheterisation;
Mech ventilation, mechanical ventilation

Hsu RK, et al. J Am Soc Nephrol 2013;24:37–42

# Annual incidence of severe AKI has increased




Annual incidence of dialysis-requiring AKI (AKI-D) as a proportion of intensive care unit admissions, stratified by hospital teaching status

Wald R, et al. Am J Kidney Dis 2014; Dec 17 [Epub ahead of print]

# Over time, AKI-D mortality seems to be diminishing

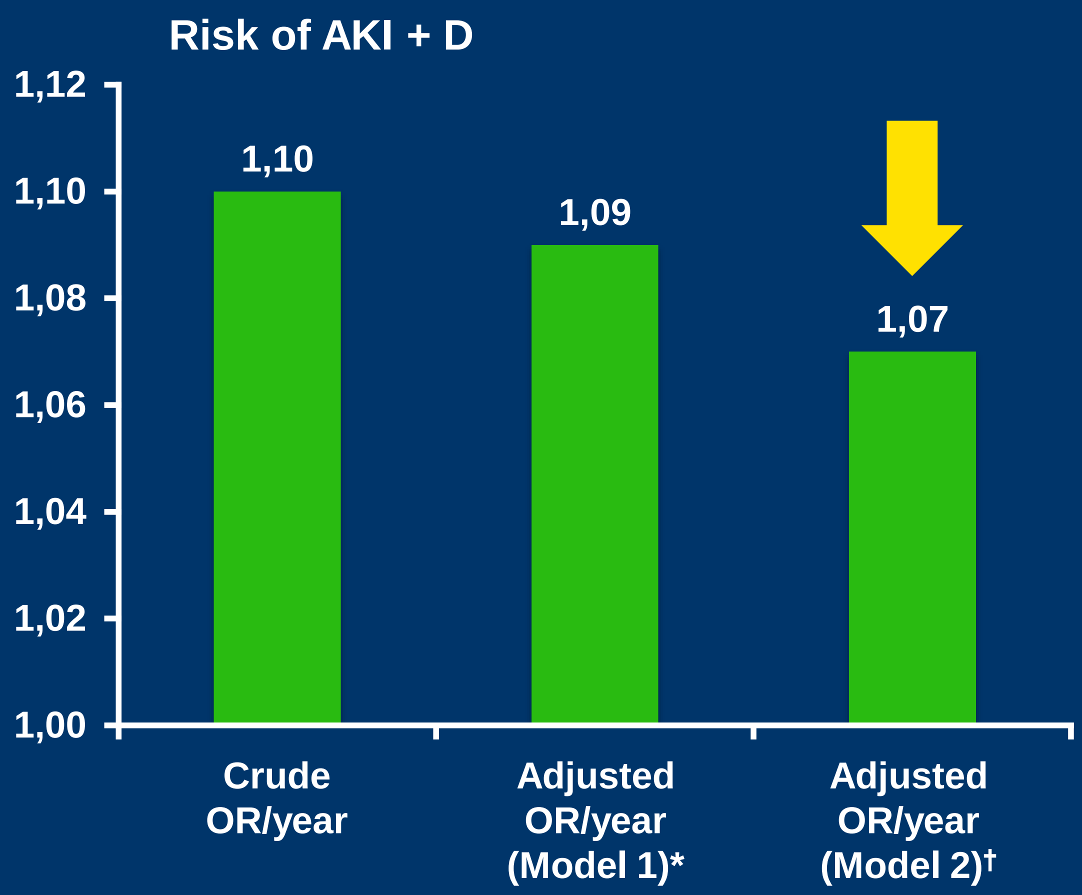
## The 90-day and 1-year all-cause mortality following dialysis-requiring AKI, by era

| Outcome | 1996–2000 (n=4771) | 2001–2005 (n=6820) | 2006–2010 (n=9643) |
|---|---|---|---|
| **Death up to day 90** | | | |
| N (%) | 2381 (49.9) | 3115 (45.7) | 4345 (45.0) |
| Adjusted HR (95% CI) | 1.00 (reference) | 0.8 (0.84–0.93) | 0.83 (0.79–0.87) |
| **Death up to day 365** | | | |
| N (%) | 2728 (57.2) | 3663 (53.7) | 5096 (52.8) |
| Adjusted HR (95% CI) | 1.00 (reference) | 0.90 (0.85–0.94) | 0.84 (0.80–0.88) |

HR, hazard ratio; CI, confidence interval

Wald R, et al. Am J Kidney Dis 2014;

# Risk of AKI-D among hospitalised US patients (2000–2009)



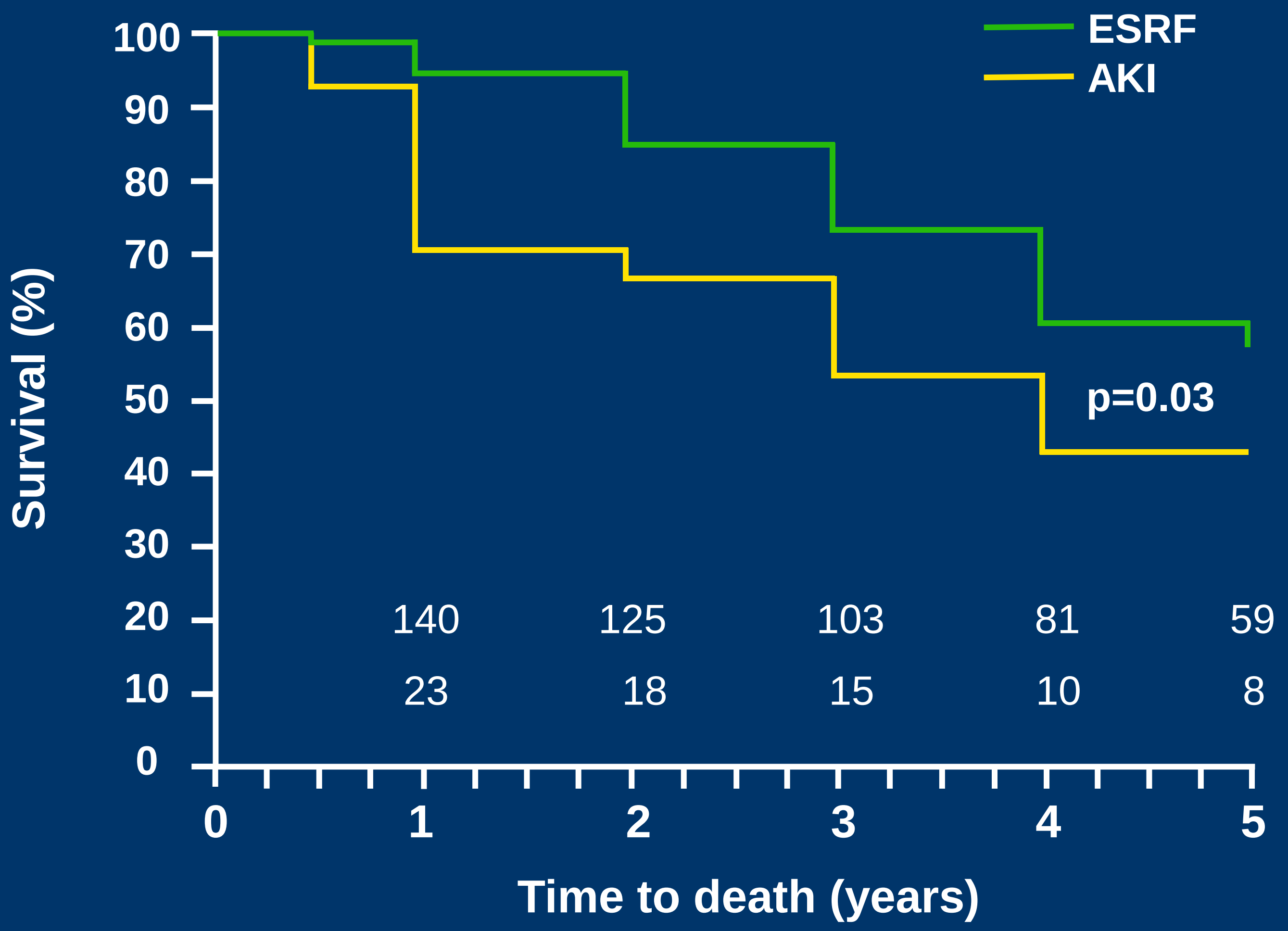

**1/3**
of increased risk

Adjusted for:
- Demographics
- Sepsis
- Acute heart failure
- Cardiac catheterisation
- Mechanical ventilation

**OR, odds ratio**
***Adjusted for age, sex and race; †adjusted for age, sex, race, sepsis, acute heart failure, cardiac catheterisation and mechanical ventilation**

**Hsu RK, et al. J Am Soc Nephrol 2013;24:37–42**

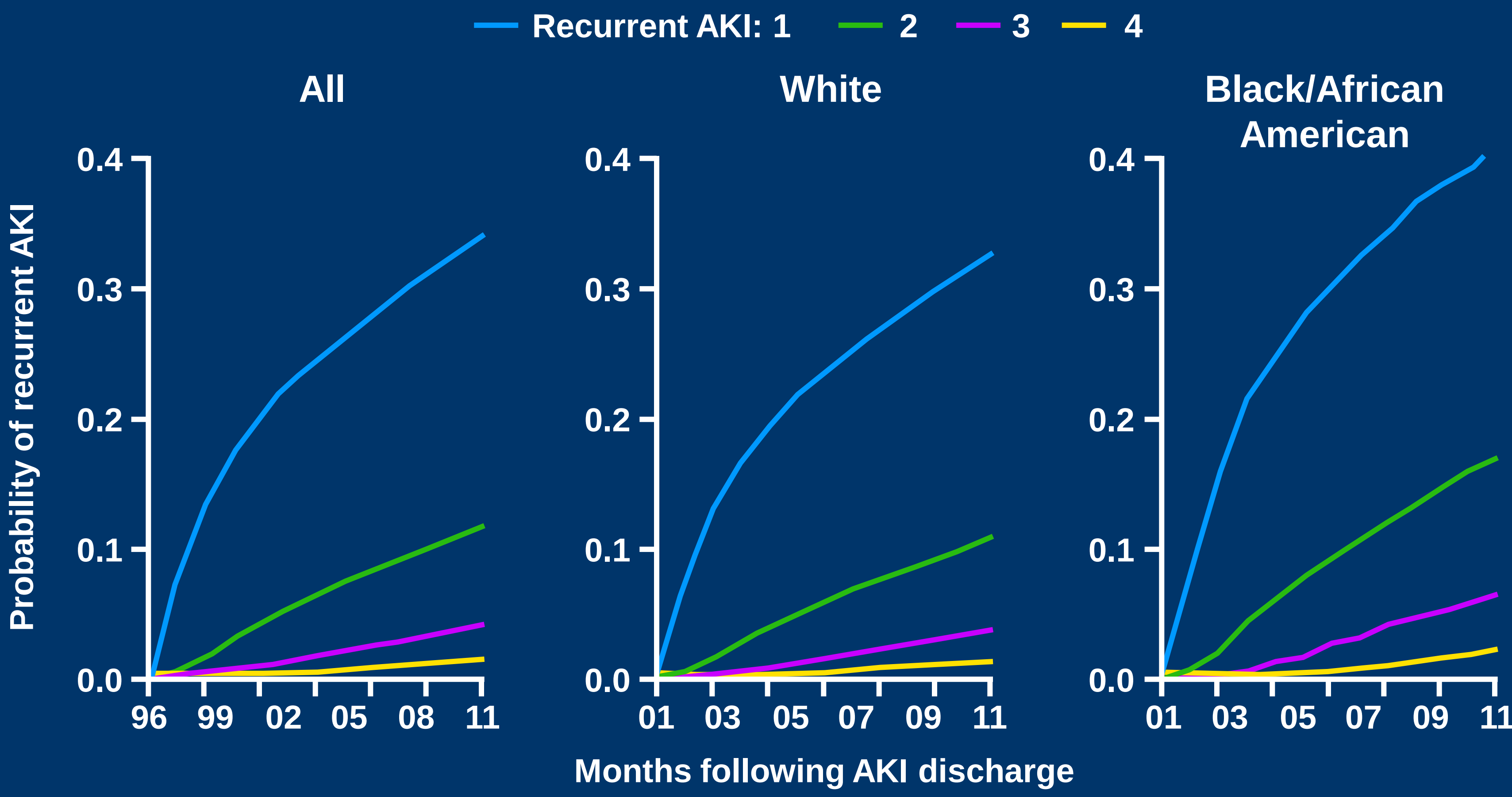
# ESRF after acute renal failure: effect on survival




Age 50–64 years
ESRF, end-stage renal failure

Bhandari S, Turney JH. QJM 1996;89:415–21

# Probability of a recurrent AKI re-hospitalisation in Medicare patients, by number of recurrent events and race (2010–2011)




Medicare AKI patients aged 66 and older

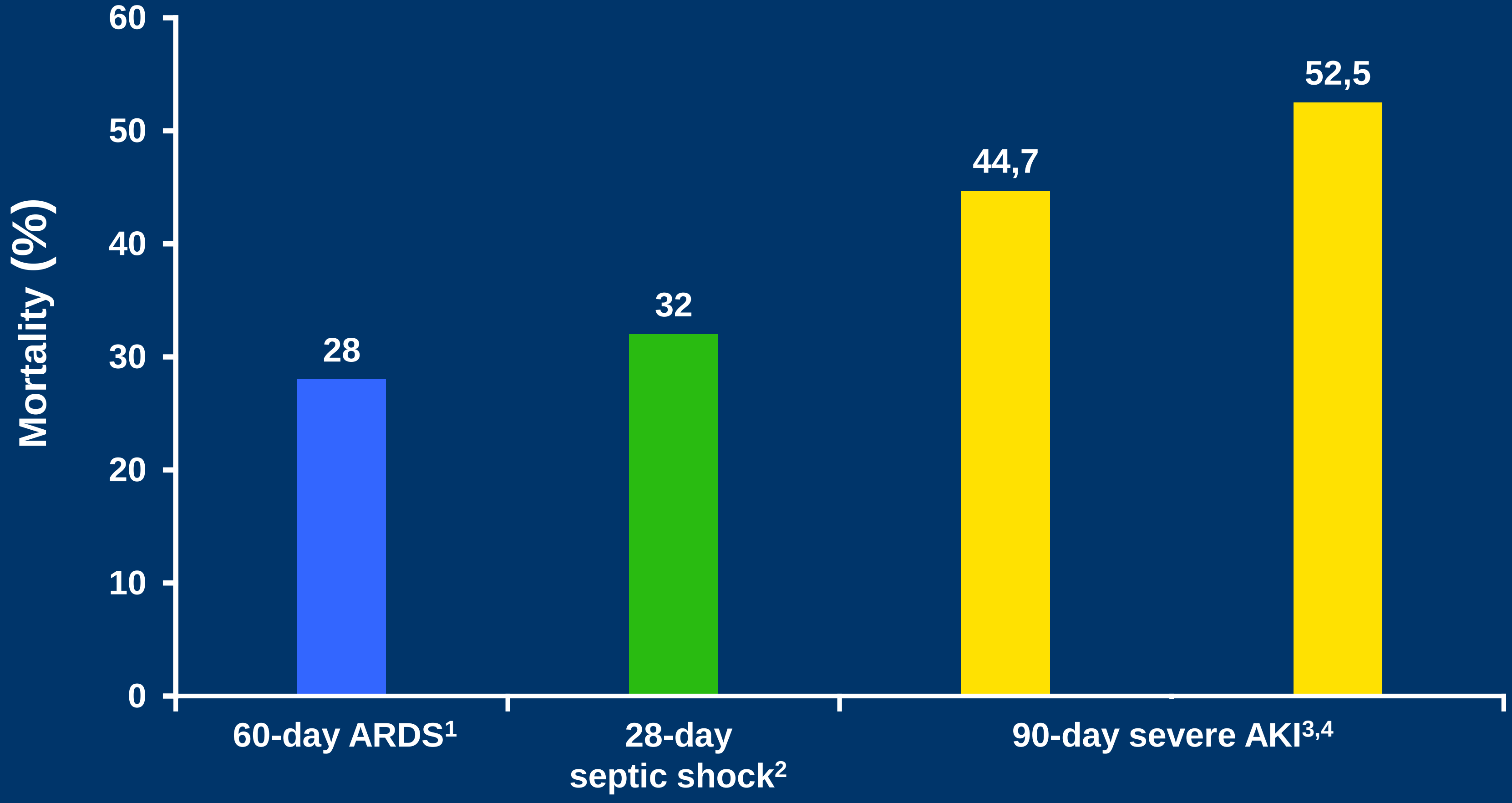
United States Renal Data System Annual Data Report 2013; Volume 1, Chapter 6
http://www.usrds.org/atlas.aspx

# The consequences of AKI

- AKI-associated mortality is high, and greater than other acute serious conditions
  - Adverse outcomes are mitigated when severity is less and duration of AKI is shorter
  - But we currently don't have measures to further decrease severity or shorten duration

Xue JL, et al. J Am Soc Nephrol 2006;17:1135–42;
Uchino S, et al. Intensive Care Med 2007;33:1563–70;
Palevsky PM, et al. N Engl J Med 2008;359:7–20

# AKI-associated mortality is more severe than other common ICU conditions





1. Wiedemann HP, et al. N Engl J Med 2006;354:2564–75;
2. Sprung CL, et al. N Engl J Med 2008;358:111–24;
3. Bellomo R, et al. N Engl J Med 2009;361:1627–38;
4. Palevsky PM, et al. N Engl J Med 2008;359:7–20

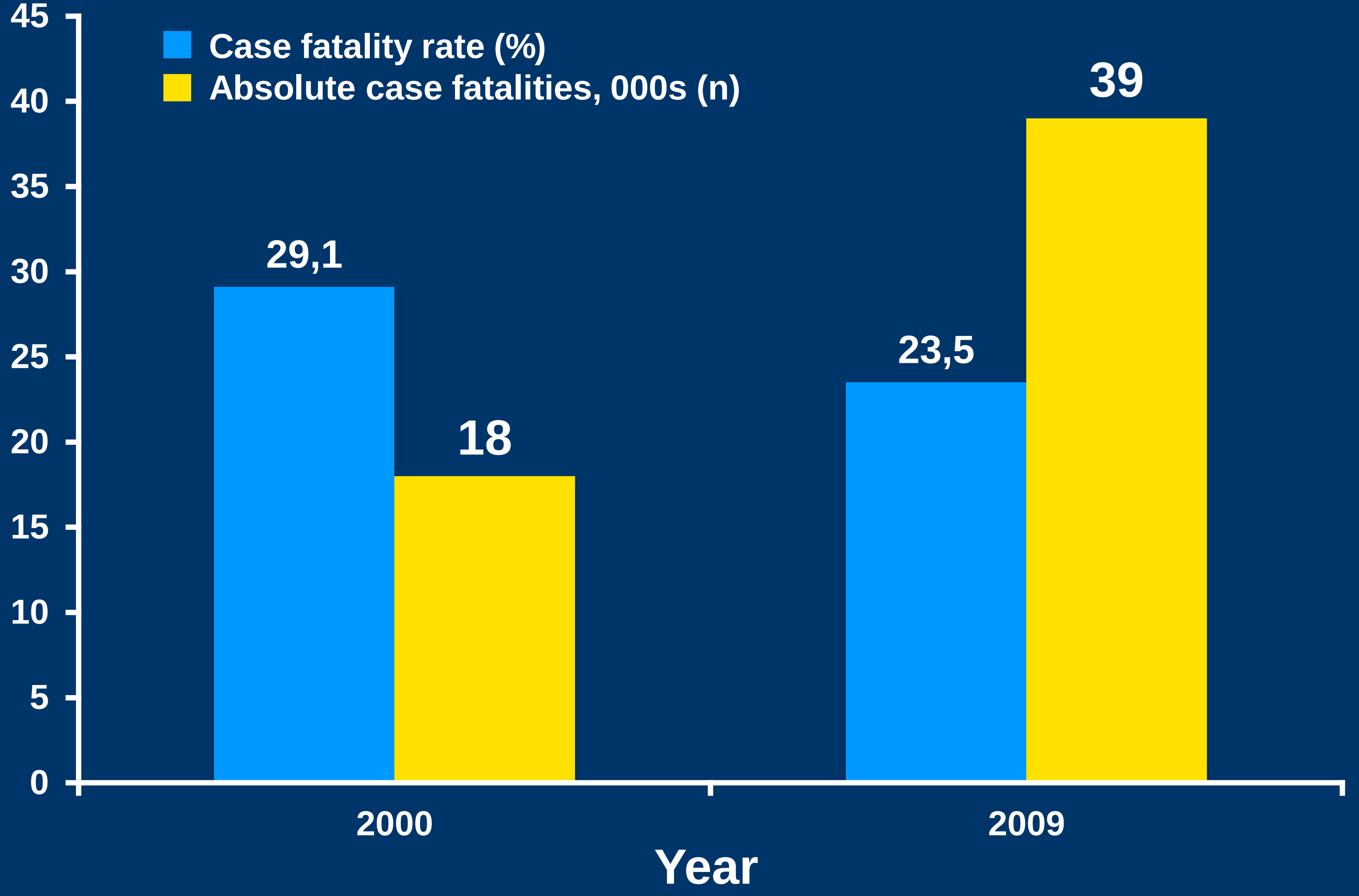

ARDS, acute respiratory distress syndrome;
ICU, intensive care unit

# The consequences of AKI

- AKI-associated mortality is high, and greater than other acute serious conditions[1–3]
- We need new research to:
  - Identify effective AKI management strategies
  - Identify strategies to improve kidney recovery

1. Xue JL, et al. J Am Soc Nephrol 2006;17:1135–42;
2. Uchino S, et al. Intensive Care Med 2007;33:1563–70;
3. Palevsky PM, et al. N Engl J Med 2008;359:7–20

# Although case fatality rate is lower, absolute number of deaths increased



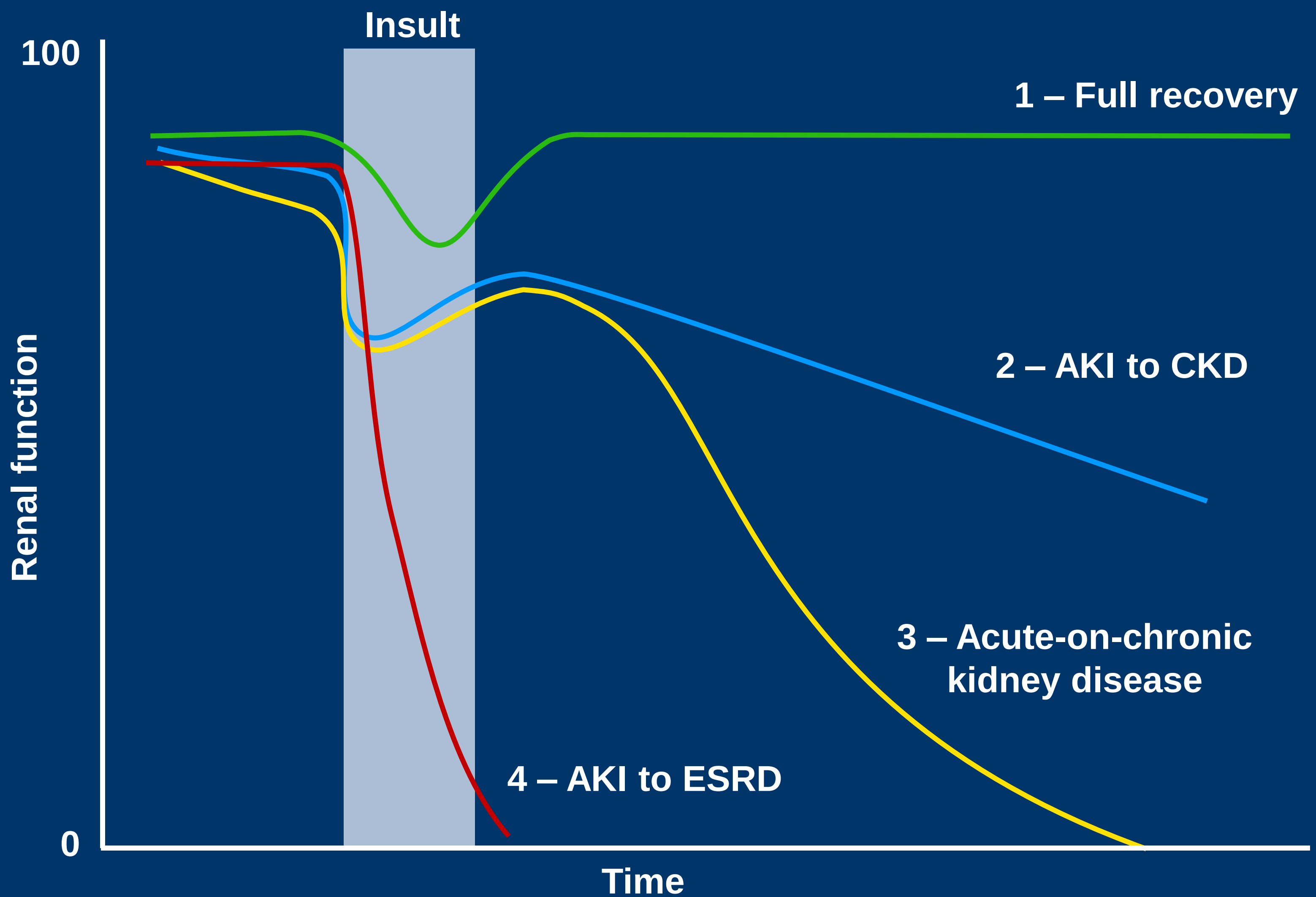

Hsu RK, et al. J Am Soc Nephrol 2013;24:37–42

# The consequences of AKI

- Kidney function recovery in AKI-D is best studied in the context of ICU stay
  - 10–30% of AKI-D survivors remain dialysis-dependent at discharge
  - Majority of evidence: B.E.S.T. study (n=1,006, 54 ICUs, 23 countries): 15% survivors were RRT-dependent at hospital discharge

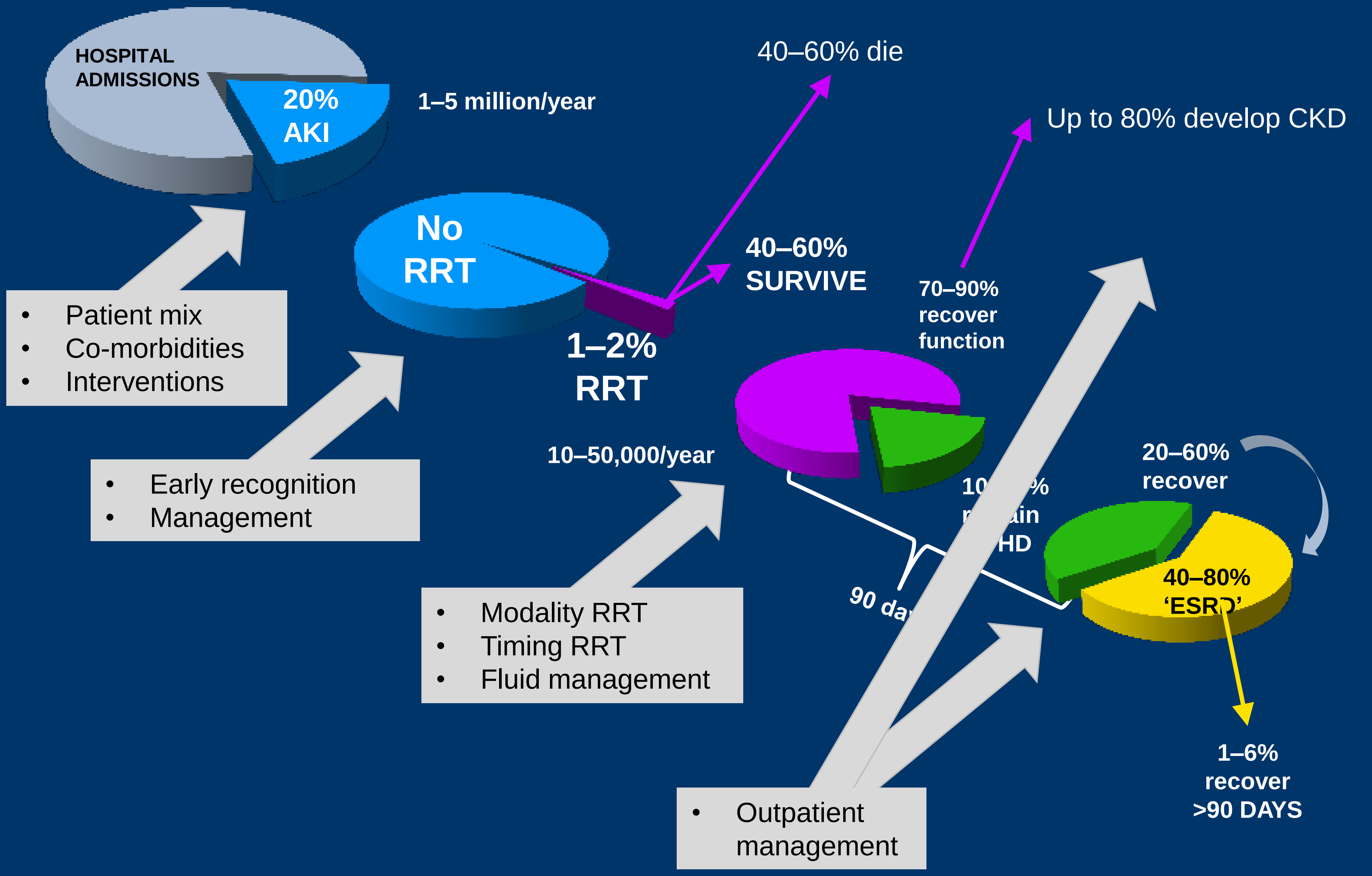
Uchino S, et al. Intensive Care Med 2007;33:1563–70

# Natural history of AKI




Cerdá J, et al. Clin J Am Soc Nephrol 2008;3:881–6

# Natural history of AKI-D




HD, haemodialysis

Cerdá J, et al. Clin J Am Soc Nephrol 2015

# The consequences of AKI-D

- Kidney function recovery in AKI-D post discharge is poorly understood
  - By convention, 90 days is an important time point because it (usually) defines when ESRD has been reached
  - Continued RRT dependence up to 90 days ranges between 16–29%

Bagshaw SM, Crit Care 2005;9:R700–9;
Bhandari S, Turney JH. QJM 1996;89:415–21

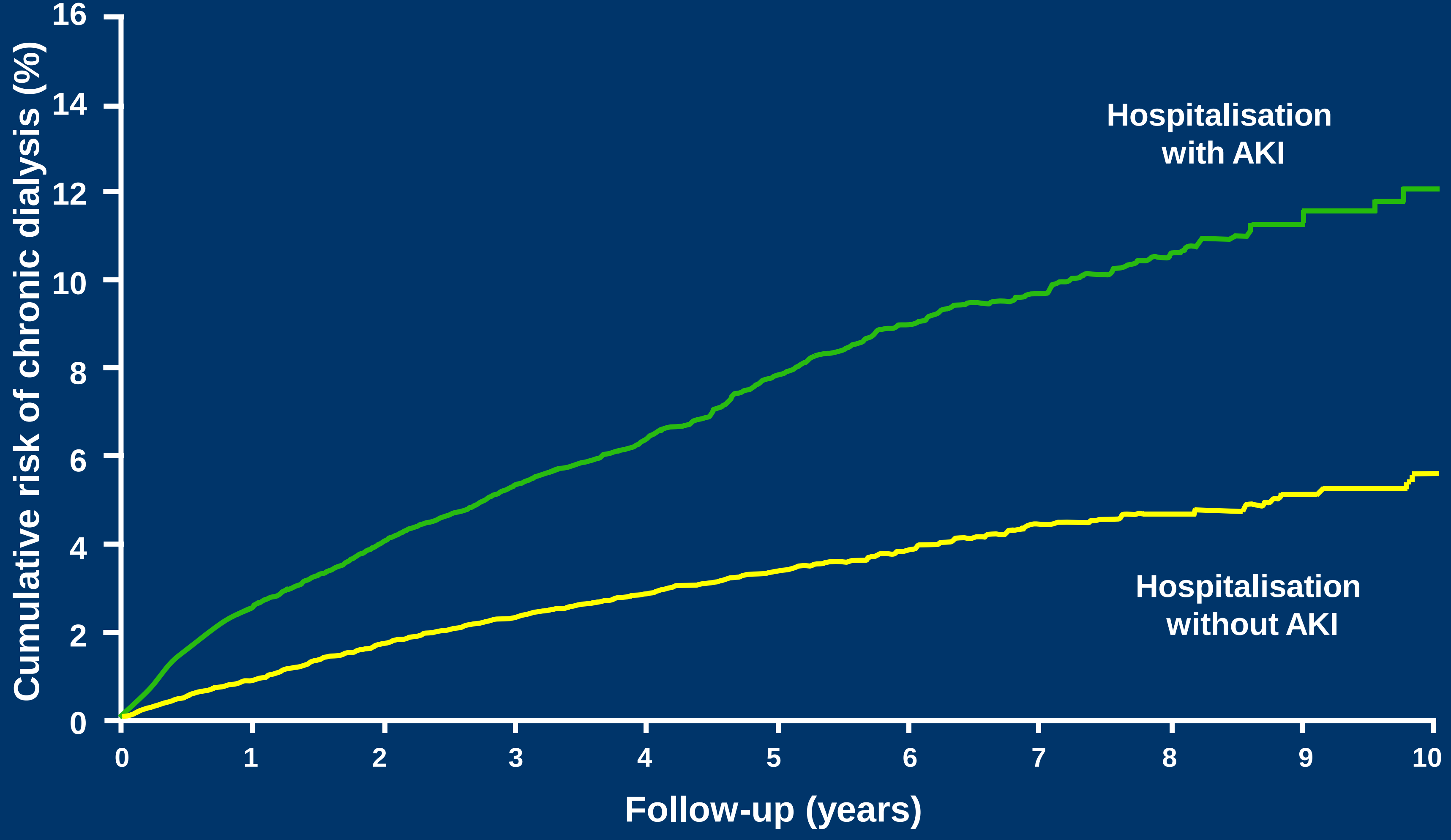
# Long-term, patients with AKI-D, who become independent within 90 days, experience multiple complications:

- CKD and ESRD
- Bone fractures
- Upper GI bleed
- Stroke
- Cardiovascular events
- Death

GI, gastrointestinal

Cerdá J, et al. Clin J Am Soc Nephrol 201; submitted

# Severe AKI is associated with CKD




Wald R, et al. Am J Med 2012;125:585–93

# AKI increases risk of CKD and death post-discharge

**Risk of chronic dialysis, all-cause mortality and rehospitalisation among hospitalised patients with acute kidney injury versus hospitalised patients with no acute kidney injury**

| | Acute kidney injury in the index hospitalisation (n=41,327) | | No acute injury in the index hospitalisation (n=41,327) | | Hazard ratio (95% CI) | |
|---|---|---|---|---|---|---|
| Outcome | Number of events (%) | Incidence rate per 100 person-years | Number of events (%) | Incidence rate per 100 person-years | Unadjusted* | Adjusted† |
| Chronic dialysis | 1876 (4.5) | 1.78 | 839 (2.0) | 0.74 | 2.66 (2.39–2.95) | 2.70 (2.42–3.00) |
| All-cause mortality | 16,897 (40.9) | 15.34 | 16,742 (40.5) | 14.51 | 1.09 (1.06–1.13) | 1.10 (1.07–1.13) |
| Rehospitalisation | 26,387 (63.8) | 44.93 | 24,372 (59.0) | 37.18 | 1.20 (1.17–1.22) | 1.21 (1.18–1.24) |

*Reflects the effect of acute kidney injury versus matched individuals without kidney injury
†Further adjusted for age (continuous in years) and the propensity score for acute kidney injury

Wald R, et al. Am J Med 2012;125:585–93

# Long-term outcomes of patients with AKI-D who become independent within 90 days

- Large cohort data suggest that 1 in every 12 AKI-D survivors who become RRT-independent will eventually need long term dialysis within 3–5 years[1,2]
- Therefore, 90-day post-discharge nephrology care is essential
  - Avoid progression
  - Prepare for ESKD

1. Harel Z, et al. BMC Nephrol 2014;15:114;
2. Wald R, et al. JAMA 2009;302:1179–85

# What management factors affect recovery?

- No single management strategy has been proven beneficial to promote recovery
- The lack of evidence-based clinical guidelines is concerning

# What management factors affect recovery?

- Do modifications in RRT hasten recovery?
  - Modality
  - Fluid overload
  - Timing of RRT
  - Dialysis dose
  - Anticoagulation strategies
  - Dialysis membranes

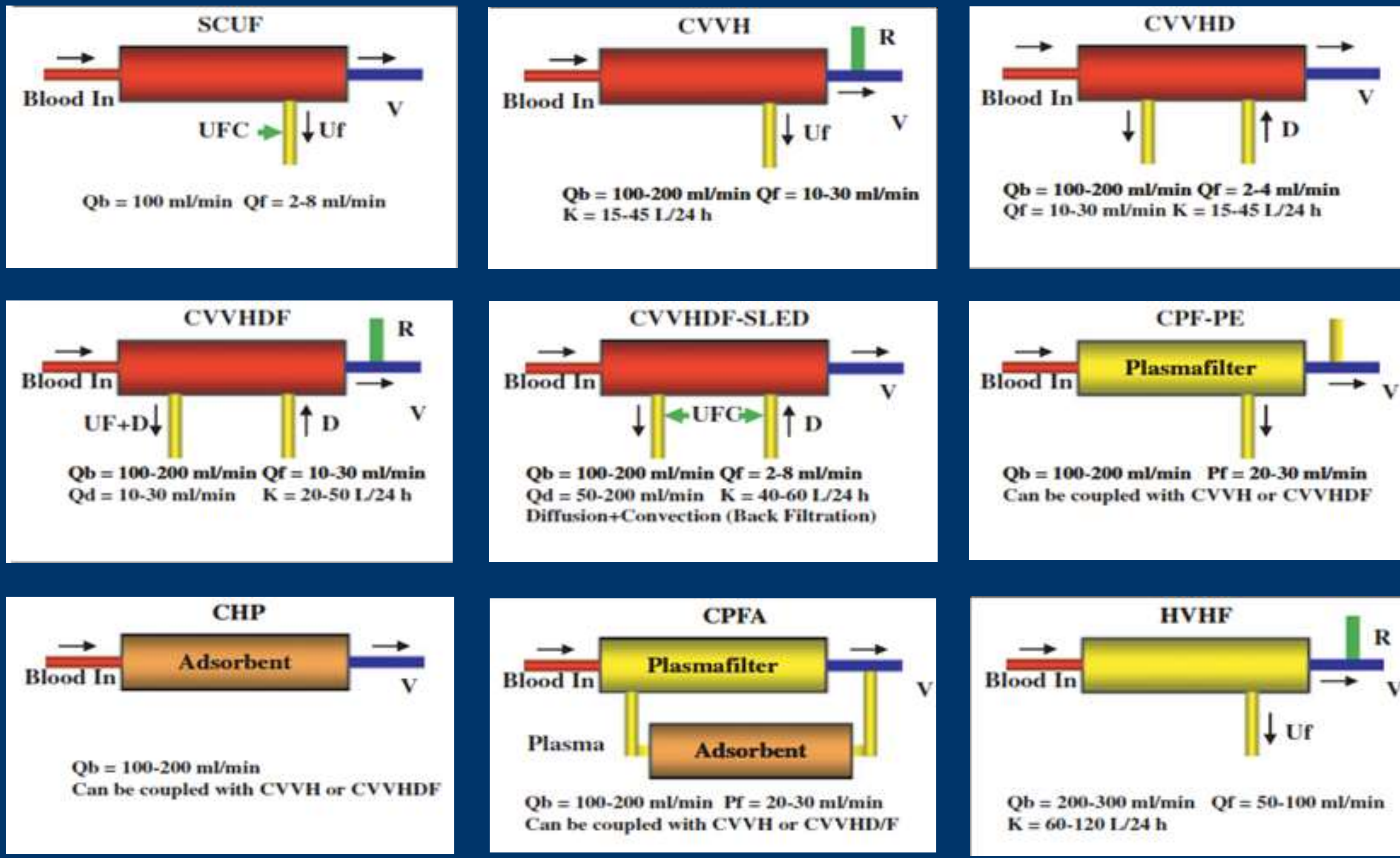
# Considerations in renal replacement therapy for AKI

| Consideration | Components | Varieties |
|---|---|---|
| Dialysis modality | Intermittent haemodialysis<br>Continuous renal replacement therapies<br>Peritoneal dialysis | Daily, every other day, SLED<br>AV, VV |
| Dialysis biocompatibility | Membrane characteristics | |
| Dialysis performance | Efficiency<br>Flux | |
| Dialysis delivery | Timing of initiation<br>Intensity of dialysis<br>Adequacy of dialysis | Early, late<br>Prescription vs delivery<br>Dialysis dose |

SLED, sustained low-efficiency dialysis;
AV, arterio-venous; VV, veno-venous

Cerdá J, Ronco C. Semin Dial 2009;22:114–22

# Modalities of CRRT




CAVH, continuous arterio–venous haemofiltration; CHP, continuous haemoperfusion; CPFA, plasma filtration coupled with adsorption; CPF-PE, continuous plasmafiltration–plasma exchange; CVVH, continuous veno–venous haemofiltration; CVVHD, continuous veno–venous haemodialysis; CVVHDF, continuous veno–venous haemodiafiltration; CVVHDF, continuous high-flux dialysis; D, dialysate; HVVF, high-volume haemofiltration; K, clearance, Pf, plasmafiltrate flow; Qb, blood flow; Qd, dialysate flow; Qf, ultrafiltration rate; R, replacement; SCUF, slow continuous ultrafiltration; UFC, ultrafiltration control system

Cerdá J, Ronco C. Semin Dial 2009;22:114–22

# Indications for specific RRT modalities

| Therapeutic Goal | Haemodynamics | Preferred therapy |
|---|---|---|
| Fluid removal | Stable | Intermittent isolated UF |
| | Unstable | Slow continuous UF |
| Urea clearance | Stable | Intermittent haemodialysis |
| | Unstable | CRRT |
| | | Convection: CAVH, CVVH |
| | | Diffusion: CAVHD, CVVHD |
| | | Both: CAVHDF, CVVHDF |
| Severe hyperkalaemia | Stable/unstable | Intermittent haemodialysis |
| Severe metabolic acidosis | Stable | Intermittent haemodialysis |
| | Unstable | CRRT |
| Severe hyperphosphoraemia | Stable/unstable | CRRT |
| Brain oedema | Unstable | CRRT |

Cerdá J, Ronco C. Semin Dial 2009;22:114–22

# VA/NIH Acute Renal Failure Trial Network (ATN) study

**1124 patients**
**27 sites**
**3 years**

***Randomisation***

**Intensive management strategy (n=561)**

**Less intensive management strategy (n=563)**

| | Intensive management strategy | Less intensive management strategy |
|---|---|---|
| **Stable** haemodynamics *(SOFA 0–2)* | • IHD 6x/week @ Kt/V of ~1.2/session | • IHD 3x/week @ Kt/V of ~1.2/session |
| **Unstable** haemodynamics *(SOFA 3–4)* | • CVVHDF @ 35 mL/kg/hr, or<br>• SLED/EDD 6x/week | • CVVHDF @ 20 mL/kg/hr, or<br>• SLED/EDD 3x/week |

**SOFA, sequential organ failure assessment;**
**EDD, extended daily dialysis**

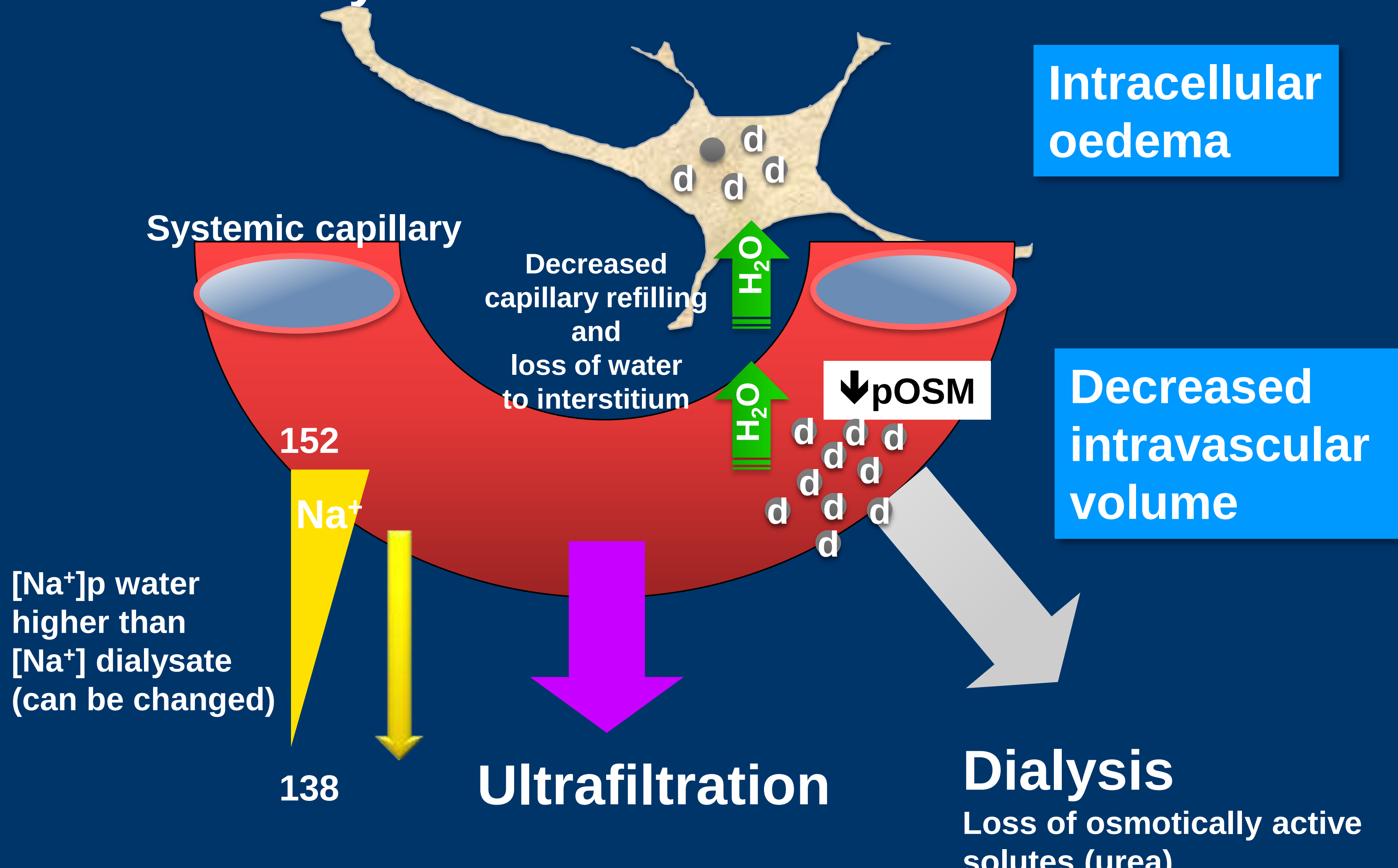
**Palevsky PM, et al. N Engl J Med 2008;359:7–20**

# Haemodynamic stability during haemofiltration

- Intermittent haemodialysis
  - Fluid removal rate 12.5 mL/min = 3 L fluid removal over 4 hours
- Continuous haemofiltration
  - Fluid removal rate 2 mL/min = 3 L fluid removal over 24 hours
- If more fluid must be removed
  - To increase from 3 to 4 L/day:
    - IHD increases UFR 12.5 to 16.7 mL/min = 750 to 1002 mL/hr
    - CRRT increases UFR 2 to 2.7 mL/min = 120 to 162 mL/hr

UFR, ultrafiltration rate

# Haemodialysis

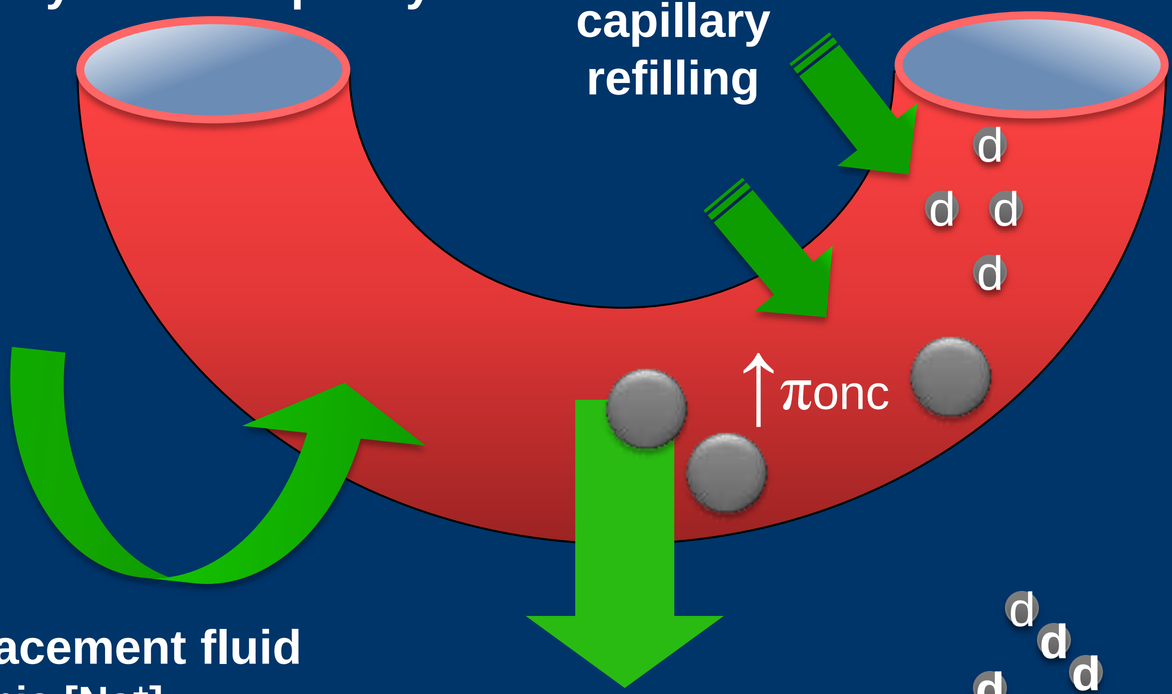



pOSM, plasma osmolarity

# Haemofiltration

Systemic capillary

**Higher plasma oncotic pressure facilitates capillary refilling**



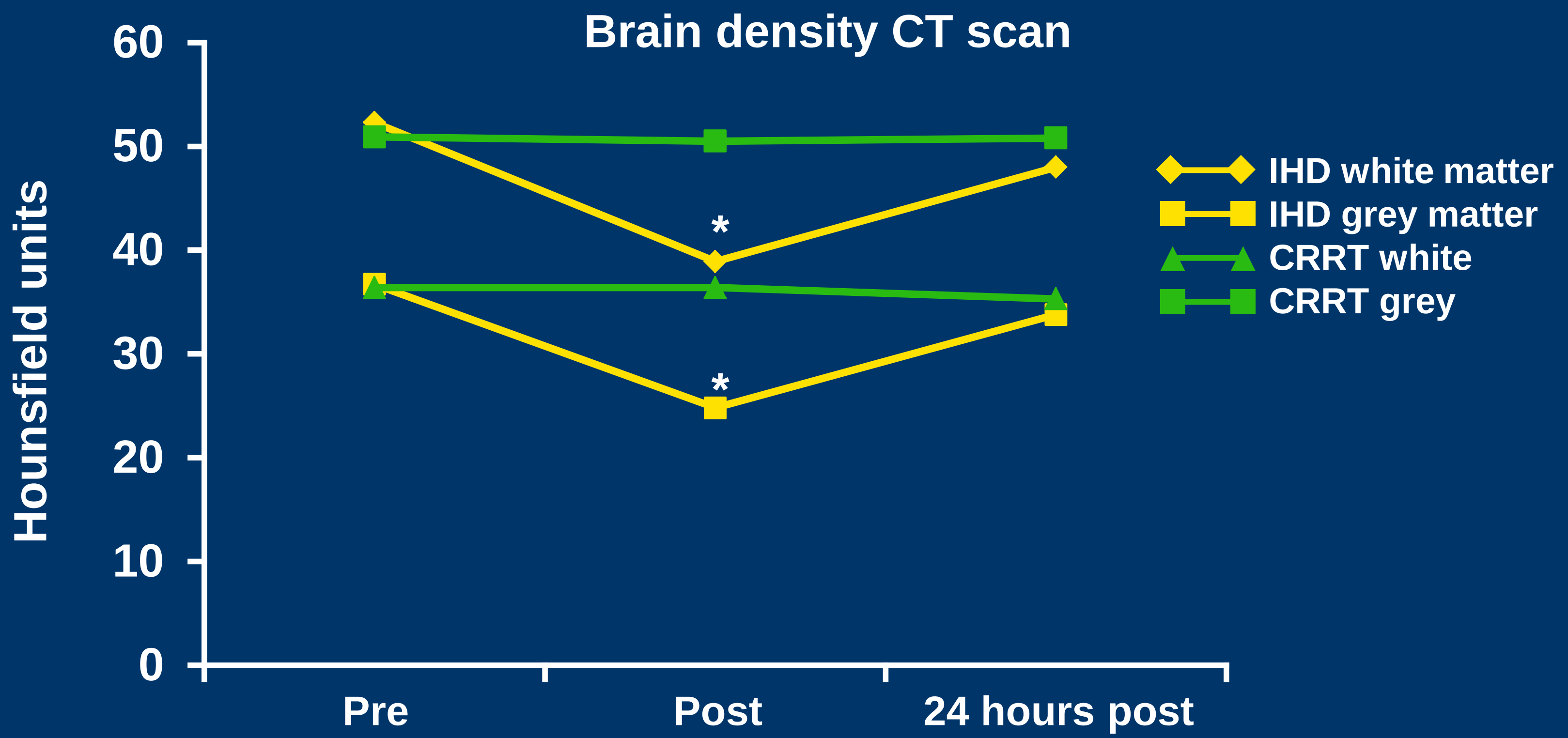

Little change in intravascular volume

**Replacement fluid**
**isotonic [$Na^+$]**
**150 mEq/L**

**Haemofiltration**
**Small solute concentrations equal to plasma (no transcapillary osmotic pressure gradient)**

$\pi$ onc, plasma oncotic pressure

# Brain density changes during renal replacement in critically ill patients with acute renal failure: continuous HF vs. IHD




*p <0.01
Crossover, prospective, randomised study (n=12)
CT, computed tomography

Ronco C, et al. J Nephrol 1999;12:173–8

# What management factors affect recovery?

- Do modifications in RRT hasten recovery?
  - Modality
    - CRRT generally considered superior to IHD to promote recovery
    - Better haemodynamic stability
      - Data are inconclusive

CRRT, continuous renal replacement therapy;
IHD, intermittent haemodialysis

Manns B, et al. Crit Care Med 2003;31:449–55;
Mehta RL, et al. Kidney Int 2001;60:1154–63;
Jacka MJ, et al. Can J Anaesth 2005;52:327–32;
Palevsky PM, et al. Curr Opin Crit Care 2005;11:548–54;
Uchino S, et al. Int J Artif Organs 2007;30:281–92;
Bell M, et al. Intensive Care Med 2007;33:773–80;
Augustine JJ, et al. Am J Kidney Dis 2004;44:1000–7;
Lins RL, et al. Nephrol Dial Transplant 2009;24:512–8

# What management factors affect recovery?

- Do modifications in RRT hasten recovery?
  - Modality

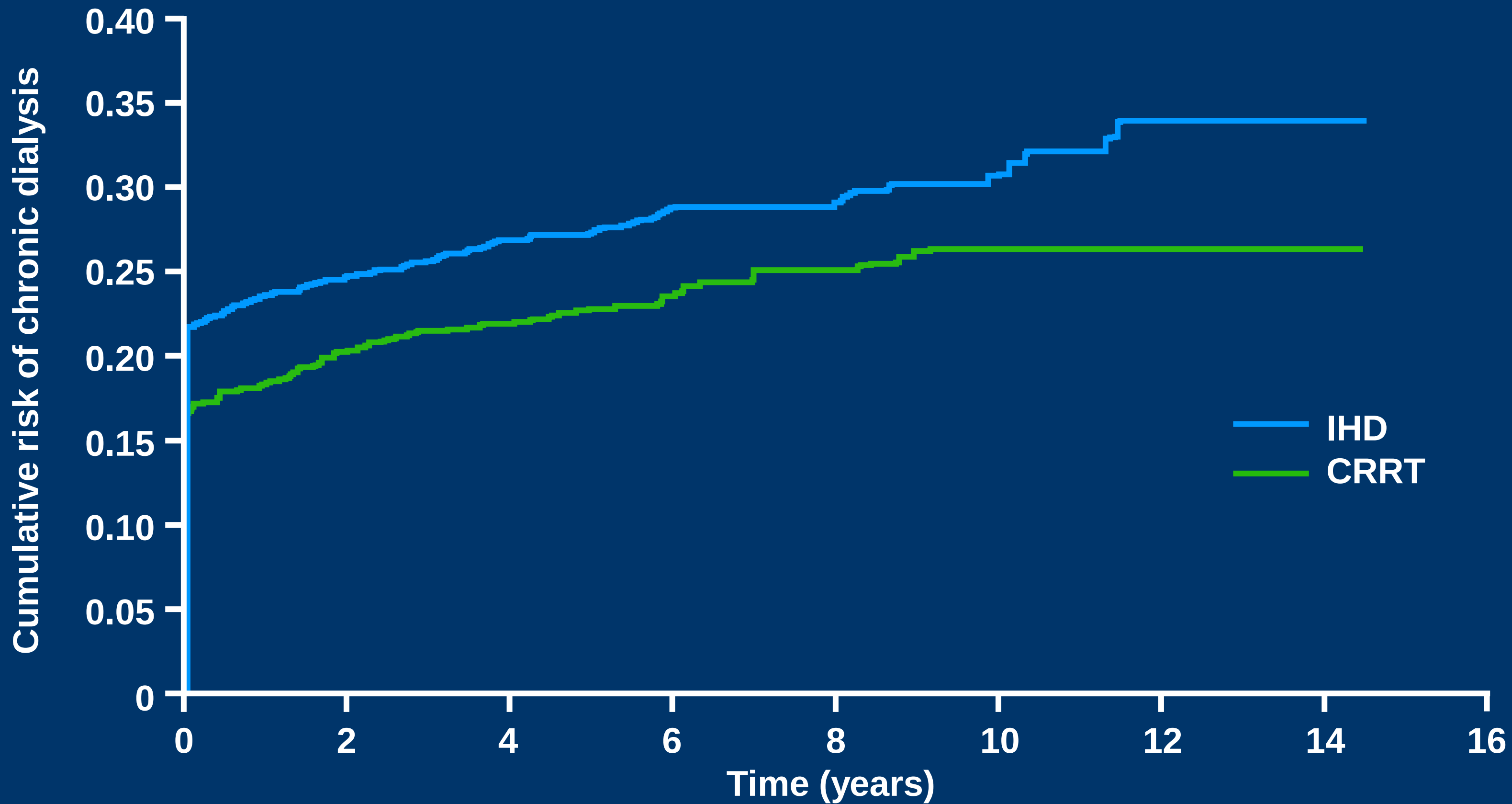
**Outcomes for patients with AKI surviving to 90 days, initiated on CRRT versus IHD**

| | CRRT (n=2004) | | IHD (n=2004) | | | |
|---|---|---|---|---|---|---|
| Outcome | n (%) | Incidence rate per 100 person-years | n (%) | Incidence rate per 100 patient-years | Hazard ratio (95% CI) for CRRT vs IHD | p |
| Chronic dialysis | 435 (22) | 6.5 | 533 (27) | 8.2 | 0.75 (0.65–0.87) | <0.0001 |
| Death | 883 (44) | 11.2 | 905 (45) | 11.4 | 1.02 (0.91–1.14) | 0.73 |

Wald R, et al. Crit Care Med 2014;42:868–77

# What management factors affect recovery?

## Modality appears associated with recovery




Critically ill patients with AKI surviving to day 90 after initiation of RRT, initially treated with CRRT or IHD

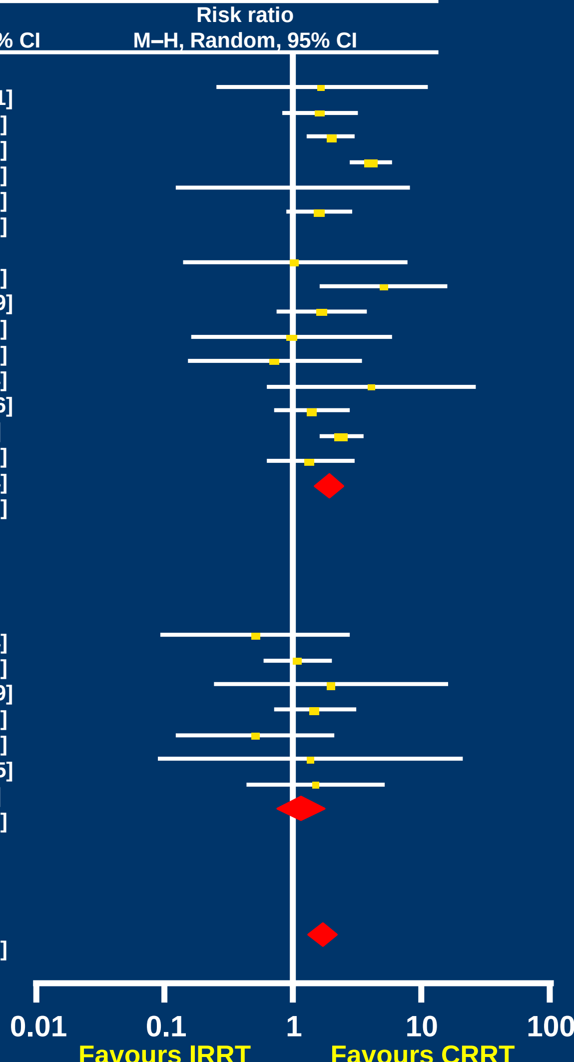
Wald R, et al. Crit Care Med 2014;42:868–77

# What management factors affect recovery?

## MODALITY – Meta-analysis

### Dialysis dependence among survivors

| Study or subgroup | IRRT Events | IRRT Total | CRRT Events | CRRT Total | Weight (%) | Risk ratio M–H, Random, 95% CI |
|---|---|---|---|---|---|---|
| **1.1.1 Observational** | | | | | | |
| Andrikos 2009 | 1 | 4 | 5 | 33 | 1.5 | 1.65 [0.25, 10.81] |
| Bagshaw 2006 | 15 | 42 | 12 | 54 | 7.0 | 1.61 [0.84, 3.06] |
| Bell 2007 | 26 | 158 | 78 | 944 | 9.8 | 1.99 [1.32, 3.00] |
| CartinCeba 2009 | 256 | 555 | 26 | 229 | 10.3 | 4.06 [2.80, 5.90] |
| Chang 2004 | 4 | 44 | 1 | 11 | 1.3 | 1.00 [0.12, 8.08] |
| Elsevier 2010 | 37 | 175 | 13 | 98 | 7.7 | 1.59 [0.89, 2.85] |
| Garcia-Fernandes 2011 | 0 | 16 | 0 | 55 | | Not estimable |
| Gonwa 2001 | 1 | 6 | 4 | 25 | 1.4 | 1.04 [0.14, 7.71] |
| Jacka 2005 | 9 | 14 | 3 | 24 | 3.5 | 5.14 [1.66, 15.89] |
| Lin 2009 | 11 | 54 | 10 | 83 | 5.7 | 1.69 [0.77, 3.71] |
| Lins 2006 | 9 | 37 | 1 | 4 | 1.6 | 0.97 [0.16, 5.83] |
| Marshall 2012 | 5 | 56 | 2 | 16 | 2.1 | 0.71 [0.15, 3.34] |
| Park 2005 | 37 | 83 | 1 | 9 | 1.5 | 4.01 [0.62, 25.86] |
| Swartz 2005 | 24 | 110 | 10 | 64 | 6.7 | 1.4 [0.71, 2.73] |
| Uchino 2007 | 37 | 110 | 52 | 360 | 10.5 | 2.33 [1.62, 3.35] |
| Waldrop 2005 | 7 | 12 | 6 | 14 | 5.8 | 1.36 [0.63, 2.94] |
| Subtotal (95% CI) | | 1476 | | 2023 | 76.4 | 1.99 [1.53, 2.59] |
| Total events | 479 | | 224 | | | |
| Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 24.14$, df = 14 (p = 0.04); $I^2 = 42\%$ | | | | | | |
| Test for overall effect: Z = 5.14 (p <0.00001) | | | | | | |
| **1.1.2 Randomised controlled trials** | | | | | | |
| Abe 2010 | 2 | 25 | 3 | 19 | 1.8 | 0.51 [0.09, 2.74] |
| Augustine 2004 | 8 | 12 | 8 | 13 | 7.6 | 1.08 [0.60, 1.95] |
| Kumar 2004 | 3 | 12 | 1 | 8 | 1.3 | 2.00 [0.25, 15.99] |
| Lins 2009 | 15 | 60 | 11 | 65 | 6.5 | 1.48 [0.74, 2.96] |
| Mehta 2001 | 3 | 43 | 4 | 29 | 2.4 | 0.51 [0.12, 2.09] |
| UehlingeR 2005 | 1 | 27 | 1 | 37 | 0.8 | 1.37 [0.09, 20.95] |
| Visonneau 2006 | 6 | 61 | 4 | 61 | 3.1 | 1.5 [0.45, 5.05] |
| Subtotal (95% CI) | | 24 | | 232 | 23.6 | 1.15 [0.78, 1.68] |
| Total events | 38 | | 32 | | | |
| Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.20$, df = 6 (p = 0.78); $I^2 = 0\%$ | | | | | | |
| Test for overall effect: Z = 0.71 (p = 0.48) | | | | | | |
| **Total (95% CI)** | | 1716 | | 2555 | 100.0 | 1.73 [1.35, 2.20] |
| Total events | 517 | | 256 | | | |
| Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 37.19$, df = 21 (p = 0.02); $I^2 = 44\%$ | | | | | | |
| Test for overall effect: Z = 4.36 (p <0.00001) | | | | | | |
| Test for subgroup differences: $Chi^2 = 5.45$, df = 1 (p = 0.02, $I^2 = 81.7\%$ | | | | | | |




IRRT, intermittent renal replacement therapy

Schneider AG, et al. Intensive Care Med 2013;39:987–97

# What management factors affect recovery?

- Do modifications in RRT hasten recovery?
  - Modality
    - Association is physiologically plausible:
      - Animal models show lost autoregulation of blood flow during AKI
      - Hypotension likely induces repeated damage
      - Renal biopsies in patients with IHD show areas of new ischemia and tubular necrosis, absent in patients treated with CRRT

Schneider AG, et al. Intensive Care Med 2013;39:987–97

# Why is CRRT associated with better haemodynamic stability?

- Maintenance of intravascular compartment volume
  - Prolonged treatments permit lower fluid removal rates
    - IHD: 3 L in 3 hours = 1 L/h UF rate
    - CRRT: 3 L in 24 hours = 0.125 mL/h UF rate
  - Urea diffusion is faster with IHD than CRRT
    - IHD: Urea clearance ~160 mL/min
    - CRRT: Urea clearance ~15–30 mL/min
  - Convective sodium removal rate [haemofiltration/heamodiafiltration] is less than diffusive removal rate [haemodialysis]
- Decreased core temperature
- Avoidance of ‘myocardial stunning’ described in IHD
- Convective removal of inflammatory mediators may contribute to hemodynamic stability

# Initiating a new CRRT program: “What is the evidence?”

- Timing of initiation
  - ? benefit of early vs. late initiation: next most important study
  - No RCT available
- Modality
  - No RCT demonstrates differences
    - Design problems: sample size, randomisation
    - Study will never be done again
- Dose
  - Ronco: Yes
  - ATN: No
  - RENAL: No
  - Are studies really comparable: convection vs diffusion
  - Can you realistically deliver the minimum dose in your critically ill patient?
- Haemodynamic stability
  - Brain oedema
  - Other non-renal apps
  - Renal functional recovery
- Renal functional recovery
- Cost

RCT, randomised controlled trial

# What management factors affect recovery?

- Do modifications in RRT hasten recovery?
  - Modality
    - CRRT generally considered superior to IHD to promote recovery in observational studies
    - Clinical trials need to address this question

Schneider AG, Bagshaw SM. Nephron Clin Pract 2014;127:35–41;
Goldstein SL, et al. Crit Care 2014;18:301

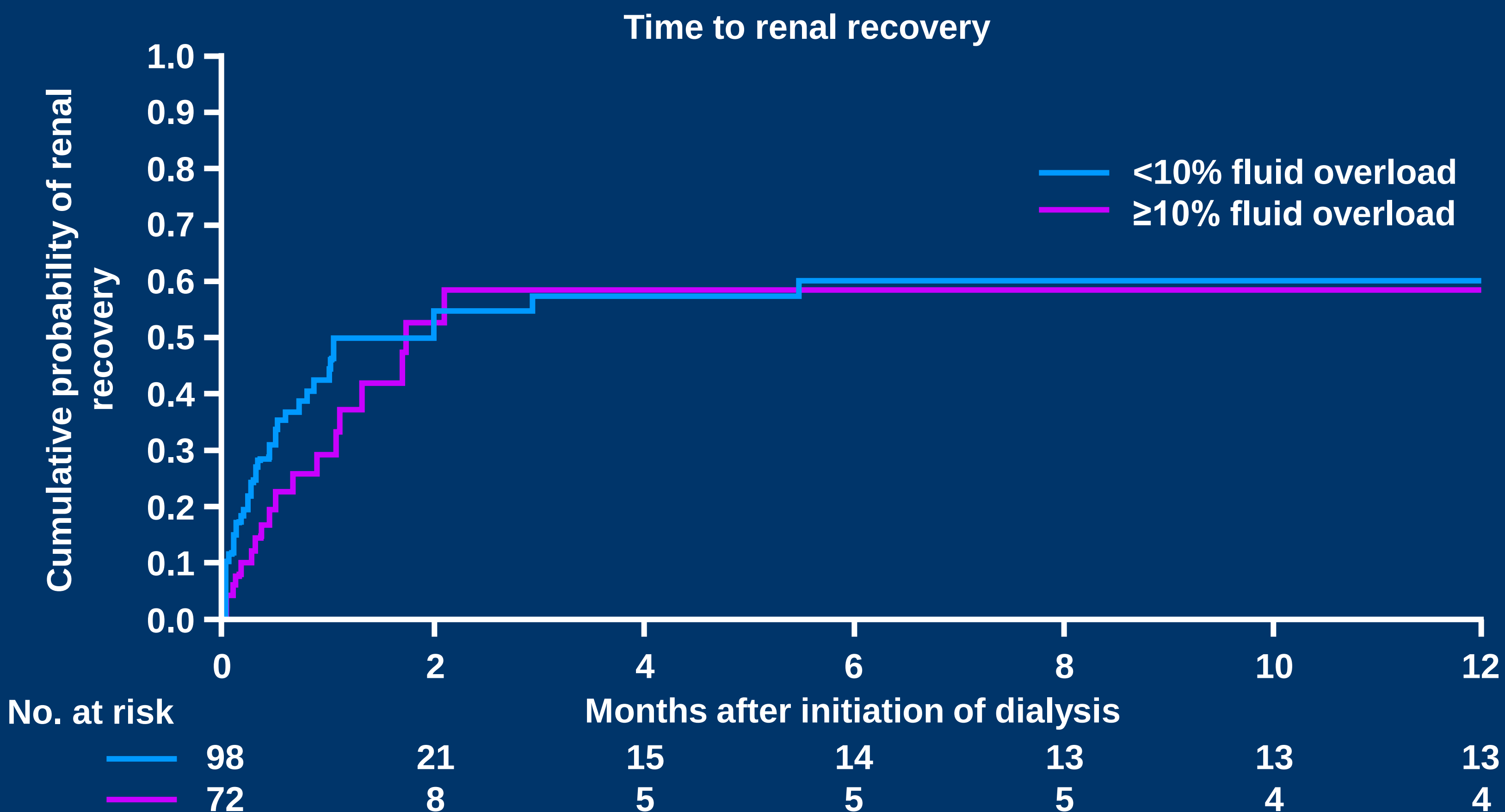
# What management factors affect recovery?

- Do modifications in RRT hasten recovery?
  - Fluid overload
  - Initiation of dialysis to avoid fluid overload may have a beneficial effect on recovery
    - Initiation of RRT at >20% fluid overload may *delay* recovery

Heung M, et al. Nephrol Dial Transplant 2012;27:956–61;
Hayes LW, et al. J Crit Care 2009;24:394–400

# What management factors affect recovery?

- Do modifications in RRT hasten recovery?
  - Fluid overload




Heung M, et al. Nephrol Dial Transplant 2012;27:956–61;
Hayes LW, et al. J Crit Care 2009;24:394–400

# What management factors affect recovery?

- Do modifications in RRT hasten recovery?
  - Timing of RRT
    - Optimal timing is unknown
    - Two systematic reviews found no benefit in ‘early’ initiation[1,2]
    - What is timing?

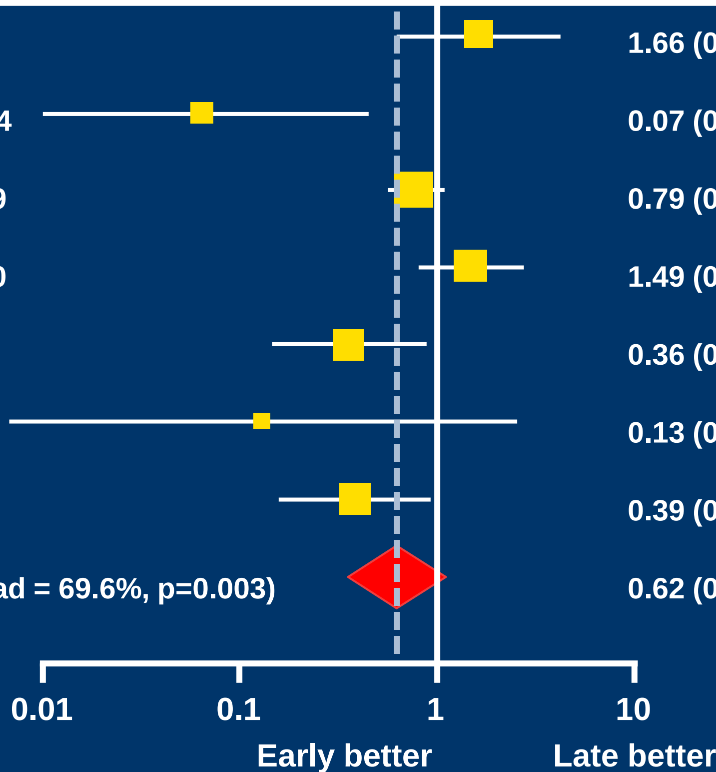
1. Karvellas CJ, et al. Crit Care 2011;15:R72;
2. Seabra VF, et al. Am J Kidney Dis 2008;52:272–84

# What management factors affect recovery?

## Timing of initiation of RRT

### Reported RRT independence

| Study | OR (95% CI) | Events, Early | Events, Late | % Weight |
|---|---|---|---|---|
| Bouman 2002 | 1.66 (0.65, 4.27) | 22/36 | 17/35 | 15.28 |
| Sugahara 2004 | 0.07 (0.01, 0.44) | 2/14 | 10/14 | 7.04 |
| Bagshaw 2009 | 0.79 (0.57, 1.09) | 74/619 | 91/618 | 23.10 |
| Bagshaw 2010 | 1.49 (0.80, 2.77) | 30/117 | 22/117 | 19.53 |
| Gettings 1999 | 0.36 (0.14, 0.89) | 11/59 | 16/41 | 15.73 |
| Iyem 2009 | 0.13 (0.01, 2.57) | 87/90 | 95/95 | 3.42 |
| Shiac 2009 | 0.39 (0.16, 0.94) | 10/47 | 21/51 | 15.90 |
| Overall (I-squad = 69.6%, p=0.003) | 0.62 (0.34, 1.13) | 236/962 | 271/971 | 100.00 |




Karvellas CJ, et al. Crit Care 2011;15:R72;
Seabra VF, et al. Am J Kidney Dis 2008;52:272–84

# What management factors affect recovery?

- **Do modifications in RRT hasten recovery?**
  - **Dialysis dose**
    - **A higher dose does *not* improve recovery**
    - **Meta-analysis of the effects of intensity show no effect on recovery**

Ronco C, et al. Lancet. 2000;356:26–30;
Palevsky PM, et al. Crit Care 2009;13:310

# What management factors affect recovery?

- Do modifications in RRT hasten recovery?
  - Dialysis membrane
    - Systematic Cochrane review demonstrates no benefit

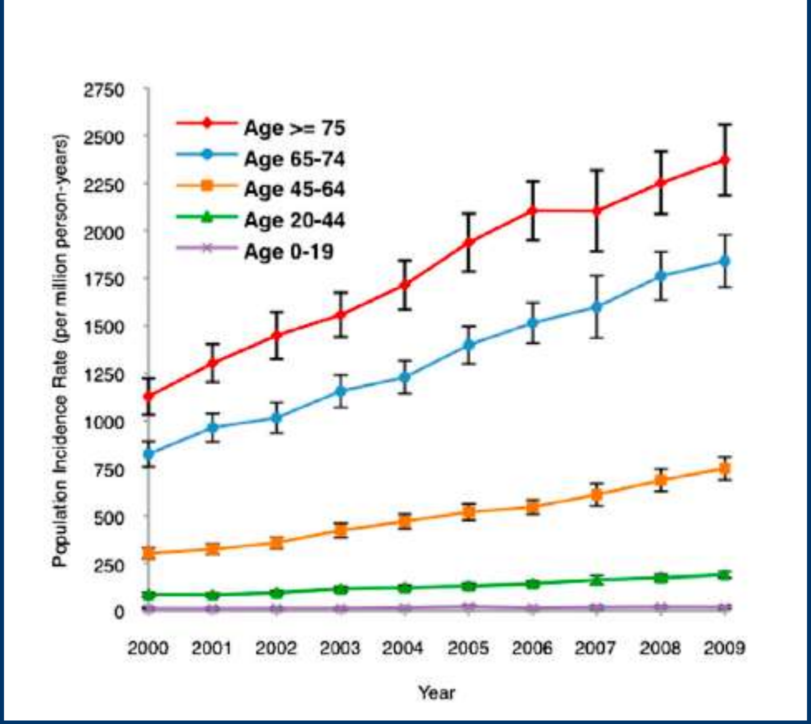
Alonso A, et al. Cochrane Database Syst Rev 2008(1):Cd005283

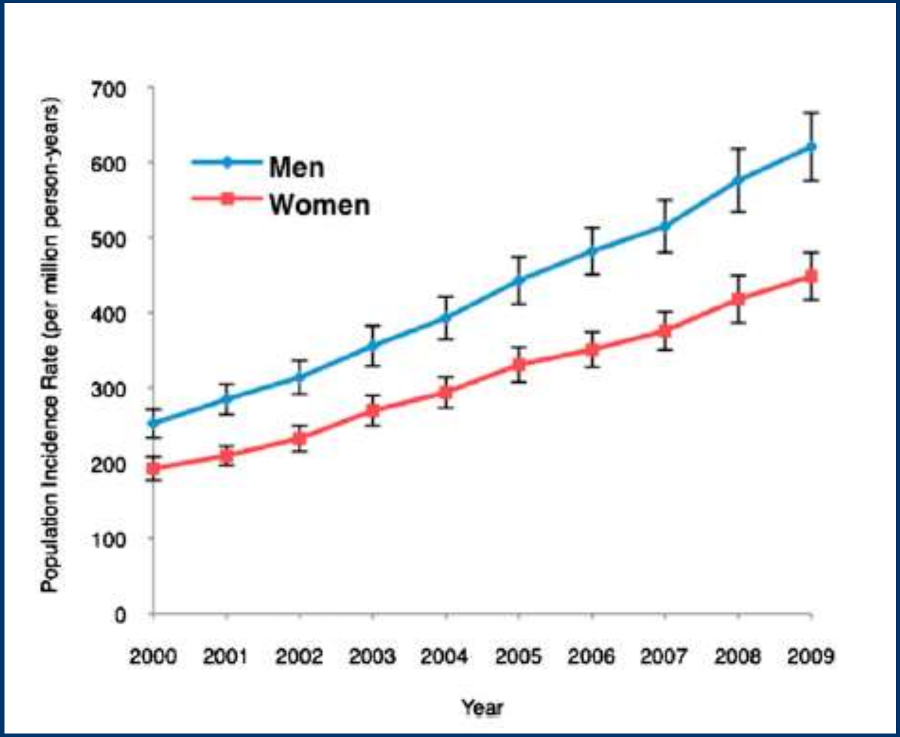
# Conclusions

- AKI-D is associated with severe morbidity and short- and long-term consequences
- AKI of lesser severity or duration is associated with better outcomes
- Significant methodological constraints limit understanding
- Haemodynamically unstable AKI patients may benefit from continuous RRT modalities
- RRT modality, timing and fluid management may promote better kidney recovery

Note to Dr Cerdá – suggest removing this slide

# requiring AKI

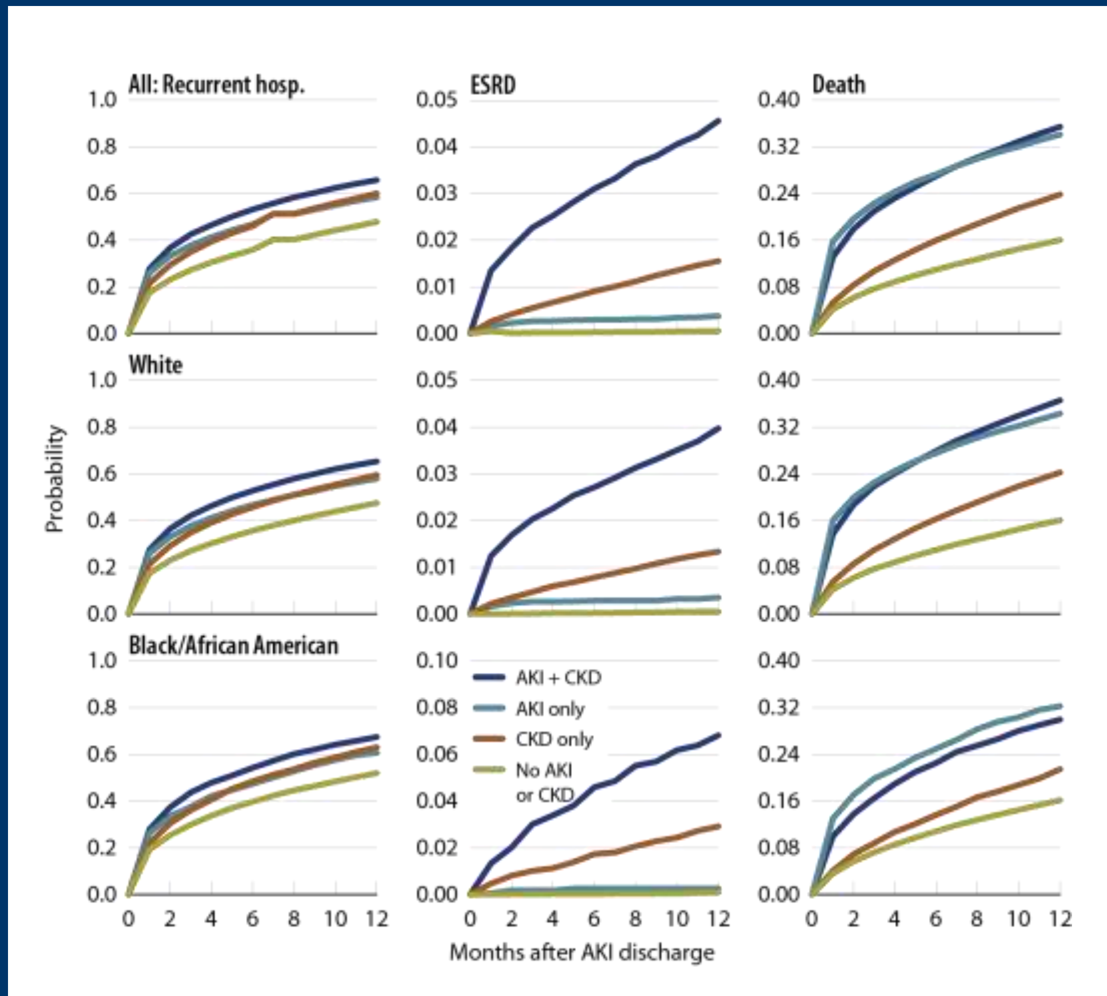



Hsu RK, et al. J AmSoc Nephrol 2013;24:37–42

**Note to Dr Cerdá – suggest removing this slide**

# death following AKI hospitalisation by race (2010)



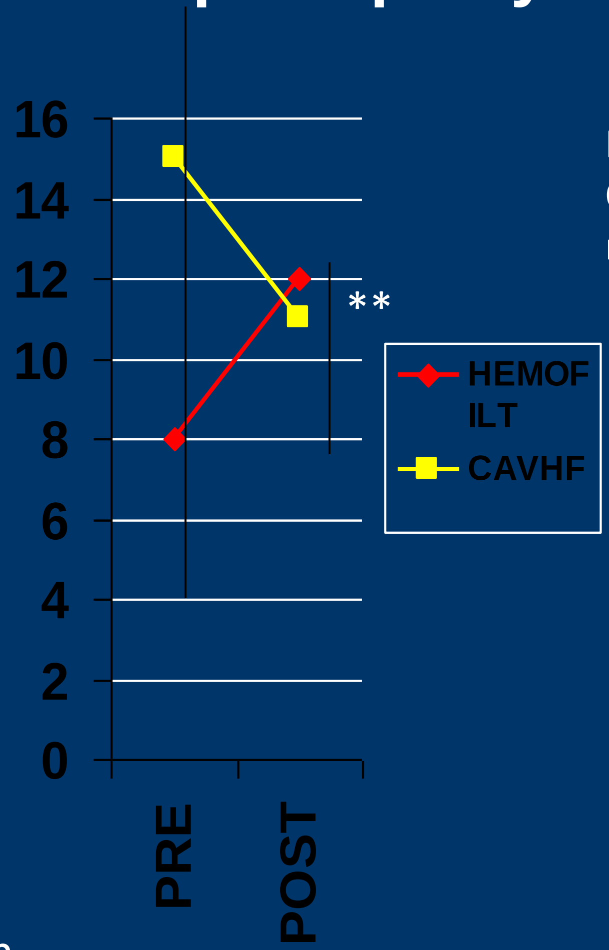

Medicare AKI patients aged 66 and older

USRDS 2012

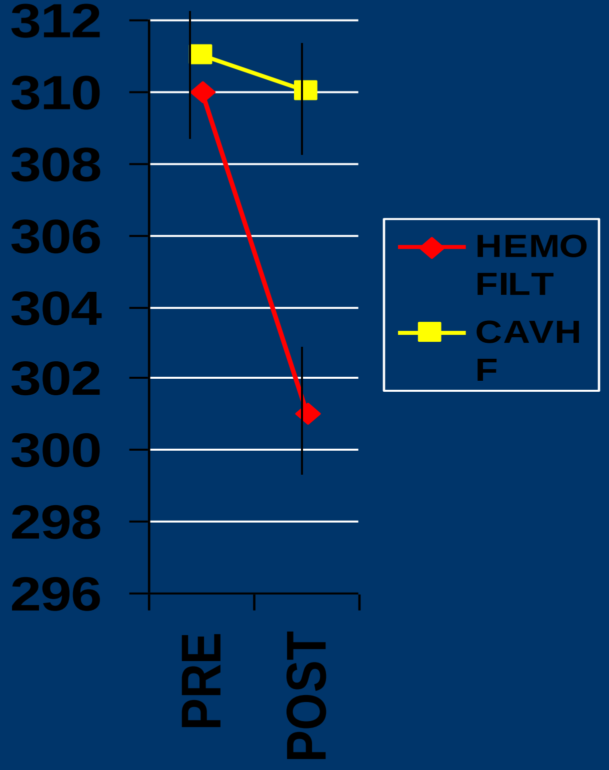
**Note to Dr Cerdá – suggest removing this slide**

# haemofiltration in oliguric patients with grade IV hepatic encephalopathy

INTRA-
CRANIAL
PRESSURE
mmHg




PLASMA
OSMOLAL
mOsm/Kg




HF: Gambro
Qb 200-250
Isovolemic 17 L exchanges
3.5-4 hrs.

CAVHF:
400-1000 ml/h
24-160 hrs.

**Davenport A et al Nephron 1989;53:142–6**