Acute Kidney Injury as a risk factor for Chronic Kidney Disease

Alan Cass, MBBS FRACP PhD
Menzies School of Health Research
Darwin, Australia
Global burden of kidney disease

Jha et al – *Lancet* 2013
Globalization and kidney disease

Kidney disease – winning the war?

Is incidence falling in high-income countries?
Ageing population
Kidney Disease: Improving Global Outcomes

Ageing population

2050
## Ageing across Asia-Pacific region

<table>
<thead>
<tr>
<th>Country</th>
<th>15-59:60+</th>
<th>Rank</th>
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<tr>
<td>Vietnam</td>
<td>7.63</td>
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</table>
## Ageing across Asia-Pacific region

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<td>USA</td>
<td>3.45</td>
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<td>S. Korea</td>
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<td>Taiwan</td>
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<td>7</td>
<td>Australia</td>
<td>1.82</td>
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<tr>
<td>China</td>
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<td>2.03</td>
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<td>Vietnam</td>
<td>7.63</td>
<td>9</td>
<td>Vietnam</td>
<td>2.13</td>
<td>9</td>
</tr>
</tbody>
</table>
Increasing burden of diabetes
Coming wave of obesity in children

- Low-income
- Upper-middle-income
- Lower-middle-income
- High-income

WHO 2010
Who is at risk of CKD?

1 in 3 adult Australians is at an increased risk of developing CKD.

Adult Australians are at increased risk of developing CKD if they:
- are 60 years or older
- have diabetes
- have a family history of kidney disease
- have established cardiovascular disease
- have high blood pressure
- are obese (body mass index ≥ 30)
- are a smoker
- are of Aboriginal or Torres Strait Islander origin*

Typically previous episode of AKI not featured amongst risk factors

Kidney Health Australia 2012
2.1.1: AKI is defined as any of the following:

- Increase in SCr by $\geq 0.3$ mg/dl ($\geq 26.5$ µmol/l) within 48 hours; or

- Increase in SCr to $\geq 1.5$ 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
### KDIGO – AKI staging/ severity

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum creatinine</th>
<th>Urine output</th>
</tr>
</thead>
</table>
| 1     | 1.5–1.9 times baseline  
       OR  
       ≥0.3 mg/dl (≥26.5 µmol/l) increase | <0.5 ml/kg/h for  
 6–12 hours |
| 2     | 2.0–2.9 times baseline | <0.5 ml/kg/h for  
 ≥12 hours |
| 3     | 3.0 times baseline  
       OR  
       Increase in serum creatinine to  
       ≥4.0 mg/dl (≥353.6 µmol/l)  
       OR  
       Initiation of renal replacement therapy  
       OR, In patients <18 years, decrease in  
       eGFR to <35 ml/min per 1.73 m² | <0.3 ml/kg/h for  
 ≥24 hours  
 OR  
 Anuria for ≥12 hours |
## KDIGO – AKI causes

<table>
<thead>
<tr>
<th>Causes of AKI: exposures and susceptibilities for non-specific AKI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exposures</strong></td>
</tr>
<tr>
<td>Sepsis</td>
</tr>
<tr>
<td>Critical illness</td>
</tr>
<tr>
<td>Circulatory shock</td>
</tr>
<tr>
<td>Burns</td>
</tr>
<tr>
<td>Trauma</td>
</tr>
<tr>
<td>Cardiac surgery (especially with CPB)</td>
</tr>
<tr>
<td>Major noncardiac surgery</td>
</tr>
<tr>
<td>Nephrotoxic drugs</td>
</tr>
<tr>
<td>Radiocontrast agents</td>
</tr>
<tr>
<td>Poisonous plants and animals</td>
</tr>
</tbody>
</table>
Traditional concept of AKI recovery

- Pre-renal phase
- Acute kidney injury that is reversible
- Predictable and complete recovery
- No long-term sequelae
Acute Kidney Injury

- Increasing incidence, especially in hospitalized elderly patients
- Prolongs hospital stay
- Often requires ICU transfer/dialysis support
- In hospital mortality remains high
Patients with at least one recognized AKI event

Medicare patients age 66 & older. USRDS 2013
Rate of first AKI - 2011

Medicare (age: 66+)

- 85+
- 80-84
- 75-79
- 70-74
- 66-69

Truven Health MS (0-64)

- 55-64
- 45-54
- 20-44
- 0-19

Clinformatics DataMart (0-64)

USRDS 2013
Probability of a recurrent AKI hospitalization in next 12 months

- Probability of recurrent AKI:
  - Recurrent AKI: 1
  - Recurrent AKI: 2
  - Recurrent AKI: 3
  - Recurrent AKI: 4

Probabilities:
- 34% after 12 months following AKI discharge
- 11% after 12 months following AKI discharge

USRDS 2013

Kidney Disease: Improving Global Outcomes
AKI and CKD - Interplay

• Accept that CKD is a risk factor for AKI
• Concentrate on AKI as a risk factor for CKD
• Long-term follow-up of survivors RCT of intense vs standard CRRT for severe AKI
• Is there any evidence to suggest that modality of treatment for severe AKI affects dialysis dependence in survivors?
CKD as a risk factor for AKI

Alberta Kidney Disease Network study

- 920,985 adults living in Alberta
- Followed median 35 months
- 6520 (0.7%) admitted with AKI
- Stratified by eGFR and proteinuria
- Examined risk for hospitalization with AKI

James et al – *Lancet* 2010
Risk factors for AKI admission

Reference group eGFR ≥60mLs/min/1.73m² and no proteinuria

• eGFR ≥60mLs/min/1.73m² and heavy proteinuria
  ➢ AKI admission ARR 4.4, needing dialysis ARR 7.7

• eGFR 45.0 – 59.9 mLs/min/1.73m² and no proteinuria
  ➢ AKI admission ARR 2.3, needing dialysis ARR 1.9

• eGFR 30.0 – 44.9 mLs/min/1.73m² and no proteinuria
  ➢ AKI admission ARR 5.6, needing dialysis ARR 4.6

• eGFR 15.0 – 29.9 mLs/min/1.73m² and no proteinuria
  ➢ AKI admission ARR 13, needing dialysis ARR 15

James et al – Lancet 2010
CKD after AKI – meta-analysis and SR

- SR comparing risk for death, CKD and ESRD in patients with and without AKI
- 13 studies with long-term renal and non-renal outcomes selected
  - 11 followed more than 3,000 patients
  - 1 in HIV, 2 included stem cell Tx recipients
- 8 cardiac surgery, ICU, coronary angiography, post MI, hospitalized cohort

Coca et al – KI 2012
Mortality after AKI

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Weight (%)</th>
<th>Hazard ratio IV, random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newson et al. (14)</td>
<td>11.2</td>
<td>1.39 (1.35–1.43)</td>
</tr>
<tr>
<td>Ishani et al. (20)</td>
<td>11.2</td>
<td>2.38 (2.31–2.46)</td>
</tr>
<tr>
<td>Hsu et al. (10)</td>
<td>10.9</td>
<td>1.30 (1.03–1.64)</td>
</tr>
<tr>
<td>Lo et al. (11)</td>
<td>10.8</td>
<td>2.30 (1.76–2.99)</td>
</tr>
<tr>
<td>Wald et al. (17)</td>
<td>11.2</td>
<td>0.95 (0.89–1.02)</td>
</tr>
<tr>
<td>Choi et al. (12)</td>
<td>11.2</td>
<td>1.20 (1.13–1.28)</td>
</tr>
<tr>
<td>Lafrance et al. (18)</td>
<td>11.1</td>
<td>2.32 (2.04–2.63)</td>
</tr>
<tr>
<td>James et al. (16)</td>
<td>11.2</td>
<td>12.99 (12.08–13.96)</td>
</tr>
<tr>
<td>Ishani et al. (21)</td>
<td>11.1</td>
<td>1.38 (1.28–1.59)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>100.0</td>
<td>1.98 (1.26–3.11)</td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 4001.87$, d.f. = 8 ($P < 0.00001$); $I^2 = 100\%$. Test for overall effect: $Z = 2.96$ ($P < 0.003$)
CKD after AKI

<table>
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<tr>
<th>Study or subgroup</th>
<th>Weight (%)</th>
<th>Hazard ratio IV, random, 95% CI</th>
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</thead>
<tbody>
<tr>
<td>Weiss et al. (13)</td>
<td>10.0</td>
<td>32.79 (4.30–249.77)</td>
</tr>
<tr>
<td>Amdur et al. (22)</td>
<td>15.5</td>
<td>6.64 (5.05–8.74)</td>
</tr>
<tr>
<td>Lo et al. (11)</td>
<td>15.5</td>
<td>28.08 (21.01–37.53)</td>
</tr>
<tr>
<td>James et al. (16)</td>
<td>15.6</td>
<td>29.99 (24.32–36.99)</td>
</tr>
<tr>
<td>James et al. (15,23)</td>
<td>15.5</td>
<td>1.60 (1.20–2.14)</td>
</tr>
<tr>
<td>Ando et al. (19)</td>
<td>12.4</td>
<td>9.91 (2.48–39.63)</td>
</tr>
<tr>
<td>Ishani et al. (21)</td>
<td>15.6</td>
<td>2.33 (1.83–2.96)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>100.0</td>
<td>8.82 (3.05–25.48)</td>
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</table>

Heterogeneity: $\tau^2 = 1.87; \chi^2 = 446.89$, d.f. = 6 ($P < 0.00001$); $I^2 = 99\%$. Test for overall effect: $Z = 4.02$ ($P < 0.0001$)
## ESKD after AKI

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Weight (%)</th>
<th>Hazard ratio IV, random, 95% CI</th>
</tr>
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<tbody>
<tr>
<td>Newsome et al. (14)</td>
<td>15.0</td>
<td>3.26 (2.87–3.70)</td>
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<tr>
<td>Ishani et al. (20)</td>
<td>14.8</td>
<td>12.99 (10.57–15.96)</td>
</tr>
<tr>
<td>Wald et al. (17)</td>
<td>14.9</td>
<td>3.22 (2.70–3.85)</td>
</tr>
<tr>
<td>Hsu et al. (10)</td>
<td>13.5</td>
<td>1.47 (0.95–2.28)</td>
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<tr>
<td>James et al. (15,23)</td>
<td>12.5</td>
<td>4.15 (2.32–7.41)</td>
</tr>
<tr>
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<td>15.0</td>
<td>2.33 (2.08–2.61)</td>
</tr>
<tr>
<td>Choi et al. (12)</td>
<td>14.4</td>
<td>1.37 (1.02–1.84)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>100.0</td>
<td>3.10 (1.91–5.03)</td>
</tr>
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</table>

Heterogeneity: $\tau^2 = 0.40; \chi^2 = 252.85$, d.f. = 6 ($P < 0.00001$); $I^2 = 98\%$. Test for overall effect: $Z = 4.58$ ($P < 0.00001$)
Outcomes in CA vs HA-AKI

- Electronic record review of 15,976 patients admitted to two district general hospitals in UK.
- Baseline SCr established from blood tests taken 12 months prior to admission.
- No baseline available in 49 and used upper limit of normal range SCr.
- CA = AKI apparent on admission blood test.
- HA = AKI occurred during hospitalization.

Wonnacott et al – cJASN 2012
Outcomes in CA vs HA-AKI

- No dedicated onsite renal service or cardiothoracic surgery
- 1020 (6.4%) admission with AKI
- 686 or approx 2/3 AKI cases were CA
- 334 or approx 1/3 were HA
- CA mean age 74.4 vs 76.8, admitted to ICU 4.7% vs 9.9%, median LOS 7 vs 15 days

Wonnacott et al – cJASN 2012
Mortality after AKI

14 month mortality outcomes according to AKI severity, CA AKI (n=686), HA AKI (n=334)

Adjusted HR mortality HA-AKI 1.75 (1.44 to 2.13)
AKI - renal and CV outcomes

• Patients in VA database with discharge Dx of AKI or MI
• 36,980 patients admitted (and discharged) 1999 to 2005 analysed
• Known CKD and baseline eGFR <45mLs/min excluded
• Outcomes for people with MI, AKI, MI + AKI compared
• Median follow-up 1.4 years
• Outcomes death, kidney (dialysis, loss >25% eGFR or died), cardiac (CVA, MI or CHF admission) and combined kidney and cardiac

Chawla et al – cJASN 2014
Mortality after AKI
Poor outcomes with reversible AKI?

- Propensity matched cohort study of patients admitted to a US medical center
- Excluded patients with eGFR < 60 in preceding 12 months, known CKD or receiving RRT
- “Recovery” of renal function defined as eGFR of at least 90% of baseline within 90 days of AKI
- Cohort 1610 with reversible AKI
- Median follow-up 3.3 years
- De novo CKD = occurrence of two eGFR measures <60mLs/min/1.73m² separated 90 days

Bucaloiu et al – KI 2012
De novo CKD after “reversible” AKI

Adjusted HR for de novo CKD 1.95 (1.75 to 2.09)
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

OCTOBER 22, 2009

VOL. 361 NO. 17

Intensity of Continuous Renal-Replacement Therapy in Critically Ill Patients

The RENAL Replacement Therapy Study Investigators*
Kidney Disease:
Improving Global Outcomes

Renal Study

1508 Underwent randomization

747 Were assigned to receive higher-intensity therapy
- 1 Was lost to follow-up
- 2 Withdrew consent
- 23 Refused delayed consent
721 Were analyzed

761 Were assigned to receive lower-intensity therapy
- 2 Withdrew consent
- 16 Refused delayed consent
743 Were analyzed

Figure 1. Numbers of Patients Enrolled in the Study, Randomly Assigned to a Treatment Group, and Included in the Analysis.

Kidney Disease: Improving Global Outcomes
Figure 2. Kaplan–Meier Estimates of the Probability of Death.
Mortality at 28 days was similar in the higher-intensity and lower-intensity treatment groups (38.5% and 36.9%, respectively), and mortality at 90 days was the same (44.7%) in both groups.
### Table 3. Primary and Secondary Outcomes.*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Higher-Intensity CRRT</th>
<th>Lower-Intensity CRRT</th>
<th>Odds Ratio</th>
<th>P Value†</th>
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</thead>
<tbody>
<tr>
<td>Death — no./total no. (%)</td>
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<tr>
<td>By day 90</td>
<td>322/721 (44.7)</td>
<td>332/743 (44.7)</td>
<td>1.00 (0.81–1.23)</td>
<td>0.99</td>
</tr>
<tr>
<td>By day 28</td>
<td>278/722 (38.5)</td>
<td>274/743 (36.9)</td>
<td>1.07 (0.87–1.32)</td>
<td>0.52</td>
</tr>
<tr>
<td>Place of death — no./total no. (%)</td>
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<td></td>
</tr>
<tr>
<td>ICU</td>
<td>251/722 (34.8)</td>
<td>254/743 (34.2)</td>
<td>1.026 (0.827–1.273)</td>
<td>0.81</td>
</tr>
<tr>
<td>Hospital ward</td>
<td>68/722 (9.4)</td>
<td>76/743 (10.2)</td>
<td>0.913 (0.647–1.288)</td>
<td>0.60</td>
</tr>
<tr>
<td>Outside hospital, after discharge</td>
<td>3/722 (0.4)</td>
<td>2/743 (0.3)</td>
<td>1.546 (0.258–9.279)</td>
<td>0.63</td>
</tr>
<tr>
<td><strong>RRT dependence among survivors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At day 28</td>
<td>64/443 (14.4)</td>
<td>57/469 (12.2)</td>
<td>1.22 (0.83–1.79)</td>
<td>0.31</td>
</tr>
<tr>
<td>At day 90</td>
<td>27/399 (6.8)</td>
<td>18/411 (4.4)</td>
<td>1.59 (0.86–2.92)</td>
<td>0.14</td>
</tr>
<tr>
<td>No. of days of RRT, from randomization to day 90</td>
<td>13.0±20.8</td>
<td>11.5±18.0</td>
<td>—</td>
<td>0.14</td>
</tr>
</tbody>
</table>
Post-RENAL Study

- Extended follow-up of survivors from 90 days to 4 years
- Primary and secondary outcomes – death and commencement RRT – ascertained for 1464 (97%) of original participants at median of 43.9 months
- Tertiary outcomes assessed in 350 participants included eGFR and spot ACR

More than 40% of participants seen at follow-up had micro or macroalbuminuria

Mortality

No of Patients

Death

Censored

Median Survival

95% CI

Log Rank P-Value

Survival Time (Months)

Higher

Lower

720

742

457 (63.47%)

453 (61.05%)

203 (36.53%)

289 (38.95%)

8.08 mths

8.88 mths

[3.29, 15.56]

[3.91, 15.43]

0.4869
Death and dialysis after Day 90

- Low rates progression to ESKD
- Ongoing high death rate
Modality and renal recovery


SYSTEMATIC REVIEW

Choice of renal replacement therapy modality and dialysis dependence after acute kidney injury: a systematic review and meta-analysis

Antoine G. Schneider
Rinaldo Bellomo
Sean M. Bagshaw
Neil J. Glassford
Serigne Lo
Min Jun
Alan Cass
Martin Gallagher
**OBJECTIVES:** To compare recovery to RRT independence in AKI survivors according to initial RRT modality.

**DATA SOURCES:** We searched MEDLINE and EMBASE for the keywords “renal replacement therapy” and “acute kidney injury” and their equivalents.

**STUDY SELECTION:** We retrieved all English language studies (2000 to 2010) reporting renal recovery to RRT independence after adult AKI.

**DATA EXTRACTION:** Two authors independently assessed study quality and extracted data. We used pooled analyses and the chi-square test for comparison. We performed sensitivity analyses with stratification by study type, size, pre-morbid chronic kidney disease, and illness severity. Secondarily, studies were pooled into Low (<50% exposed) or High-exposure (>50% exposed) according to the percentage of patients exposed to intermittent RRT (IRRT) (essentially intermittent HD).
Dialysis dependence in AKI survivors

Kidney Disease: Improving Global Outcomes
Dialysis dependence in AKI survivors

- Low Exposure to IRRT
- High exposure to IRRT

- Hospital discharge
- 28d
- 60d
- 90d
- Longest

KDIGO
Dialysis dependence in AKI survivors

### 1.1.1 Observational

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>IRRT Events</th>
<th>Total</th>
<th>CRRT Events</th>
<th>Total</th>
<th>Weight</th>
<th>M–H, Random, 95% CI</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andrikos</td>
<td>1</td>
<td>4</td>
<td>5</td>
<td>33</td>
<td>1.5%</td>
<td>1.65 [0.25, 10.81]</td>
<td></td>
</tr>
<tr>
<td>Bagshaw 2006</td>
<td>15</td>
<td>42</td>
<td>12</td>
<td>54</td>
<td>7.0%</td>
<td>1.61 [0.84, 3.06]</td>
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</tr>
<tr>
<td>Bell 2007</td>
<td>26</td>
<td>158</td>
<td>78</td>
<td>944</td>
<td>9.8%</td>
<td>1.99 [1.32, 3.00]</td>
<td></td>
</tr>
<tr>
<td>CaritnCeba 2009</td>
<td>256</td>
<td>555</td>
<td>26</td>
<td>229</td>
<td>10.3%</td>
<td>4.06 [2.80, 5.90]</td>
<td></td>
</tr>
<tr>
<td>Chang 2004</td>
<td>4</td>
<td>44</td>
<td>1</td>
<td>11</td>
<td>1.3%</td>
<td>1.00 [0.12, 8.08]</td>
<td></td>
</tr>
<tr>
<td>Elsevier 2010</td>
<td>37</td>
<td>175</td>
<td>13</td>
<td>98</td>
<td>7.7%</td>
<td>1.59 [0.89, 2.85]</td>
<td></td>
</tr>
<tr>
<td>Garcia-Fernandes 2011</td>
<td>0</td>
<td>16</td>
<td>0</td>
<td>55</td>
<td>Not estimable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gonwa 2001</td>
<td>1</td>
<td>6</td>
<td>4</td>
<td>25</td>
<td>1.4%</td>
<td>1.04 [0.14, 7.71]</td>
<td></td>
</tr>
<tr>
<td>Jacka 2005</td>
<td>9</td>
<td>14</td>
<td>3</td>
<td>24</td>
<td>3.5%</td>
<td>5.14 [1.66, 15.89]</td>
<td></td>
</tr>
<tr>
<td>Lin 2009</td>
<td>11</td>
<td>54</td>
<td>10</td>
<td>83</td>
<td>5.7%</td>
<td>1.69 [0.77, 3.71]</td>
<td></td>
</tr>
<tr>
<td>Lins 2006</td>
<td>9</td>
<td>37</td>
<td>1</td>
<td>4</td>
<td>1.6%</td>
<td>0.97 [0.16, 5.83]</td>
<td></td>
</tr>
<tr>
<td>Marshall 2012</td>
<td>5</td>
<td>56</td>
<td>2</td>
<td>16</td>
<td>2.1%</td>
<td>0.71 [0.15, 3.34]</td>
<td></td>
</tr>
<tr>
<td>Park 2005</td>
<td>37</td>
<td>83</td>
<td>1</td>
<td>9</td>
<td>1.5%</td>
<td>4.01 [0.62, 25.86]</td>
<td></td>
</tr>
<tr>
<td>Swartz 2005</td>
<td>24</td>
<td>110</td>
<td>10</td>
<td>64</td>
<td>6.7%</td>
<td>1.40 [0.71, 2.73]</td>
<td></td>
</tr>
<tr>
<td>Uchino 2007</td>
<td>37</td>
<td>110</td>
<td>52</td>
<td>360</td>
<td>10.5%</td>
<td>2.33 [1.62, 3.35]</td>
<td></td>
</tr>
<tr>
<td>Waldrop 2005</td>
<td>7</td>
<td>12</td>
<td>6</td>
<td>14</td>
<td>5.8%</td>
<td>1.36 [0.63, 2.94]</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>1476</strong></td>
<td><strong>232</strong></td>
<td><strong>2023</strong></td>
<td><strong>76.4%</strong></td>
<td><strong>1.99 [1.53, 2.59]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 479
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 RCT

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>IRRT Events</th>
<th>Total</th>
<th>CRRT Events</th>
<th>Total</th>
<th>Weight</th>
<th>M–H, Random, 95% CI</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abe</td>
<td>2</td>
<td>25</td>
<td>3</td>
<td>19</td>
<td>1.8%</td>
<td>0.51 [0.09, 2.74]</td>
<td></td>
</tr>
<tr>
<td>Augustine</td>
<td>8</td>
<td>12</td>
<td>8</td>
<td>13</td>
<td>7.6%</td>
<td>1.08 [0.60, 1.95]</td>
<td></td>
</tr>
<tr>
<td>Kumar 2004</td>
<td>3</td>
<td>12</td>
<td>1</td>
<td>8</td>
<td>1.3%</td>
<td>2.00 [0.25, 15.99]</td>
<td></td>
</tr>
<tr>
<td>Lins 2009</td>
<td>15</td>
<td>60</td>
<td>11</td>
<td>65</td>
<td>6.5%</td>
<td>1.48 [0.74, 2.96]</td>
<td></td>
</tr>
<tr>
<td>Mehta</td>
<td>3</td>
<td>43</td>
<td>4</td>
<td>29</td>
<td>2.4%</td>
<td>0.51 [0.12, 2.09]</td>
<td></td>
</tr>
<tr>
<td>Uehlinger</td>
<td>1</td>
<td>27</td>
<td>1</td>
<td>37</td>
<td>0.8%</td>
<td>1.37 [0.09, 20.95]</td>
<td></td>
</tr>
<tr>
<td>Vinsonneau</td>
<td>6</td>
<td>61</td>
<td>4</td>
<td>61</td>
<td>3.1%</td>
<td>1.50 [0.45, 5.05]</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>240</strong></td>
<td><strong>32</strong></td>
<td><strong>232</strong></td>
<td><strong>23.6%</strong></td>
<td><strong>1.15 [0.78, 1.68]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 38
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 3.20$, df = 6 ($P = 0.78$); $I^2 = 0$

Test for overall effect: $Z = 0.71$ ($P = 0.48$)

### Subtotal (95% CI)

**Total (95% CI)**

**Total events**

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 ($P = 0.02$), $I^2 = 81.7$
Summary

- AKI is common
- CKD is a risk factor for AKI
- AKI is a risk factor for development of CKD, progression to ESKD and death
- Need to identify high-risk patients - elderly, diabetes, people with CKD, undergoing major surgery
- Need to improve clinical follow-up after hospital discharge
- Further research necessary to examine whether modality of dialysis for severe AKI affects long-term dialysis dependence