# Acute Kidney Injury: Definitions, Epidemiology & Scoring Systems

Paul Stevens

Kent Kidney Care Centre

# Talk Outline

- Early descriptions
- Yesterday's conceptual model and yesterday's definitions
- Today's conceptual model
- Essential components of a definition
- Which one?
- Scoring systems

BRITISH MEDICAL JOURNAL

LONDON SATURDAY MARCH 22 1941

# CRUSH INJURIES WITH IMPAIRMENT OF RENAL FUNCTION

BY

E. G. L. BYWATERS, M.B., B.S., M.R.C.P.

*Beit Memorial Fellow*

AND

D. BEALL, Ph.D.Toronto

(From the Departments of Medicine and Pathology, British Postgraduate Medical School)

[WITH SPECIAL PLATE]

Amongst air-raid casualties seen at this hospital have been four cases of crush injury of the limbs which, because of the general similarity of their clinical course, were thought to represent a specific and hitherto unreported syndrome, and one which has been and will be seen elsewhere during the war. Such a condition may have been observed in civil practice, but we have been unable to find any account of it in the literature. The cases are of interest on account of the problem propounded by both pathogenesis and treatment. The picture presented by these four cases, and substantiated by others, is briefly as follows:

The patient has been buried for several hours with pressure on a limb. On admission he looks in good condition except for swelling of the limb, some local anaesthesia, and wheals. The haemoglobin, however, and progress even though the crushed limb be amputated. The urinary output, initially small, owing perhaps to the severity of the shock, diminishes further. The urine contains albumin and many dark brown or black granular casts. These later decrease in number. The patient is alternately drowsy and anxiously aware of the severity of his illness. Slight generalized oedema, thirst, and incessant vomiting develop, and the blood pressure often remains slightly raised. The blood urea and potassium, raised at an early stage, become progressively higher, and death occurs comparatively suddenly, frequently within a week. Necropsy reveals necrosis of muscle and, in the renal tubules, degenerative changes and casts containing brown pigment.

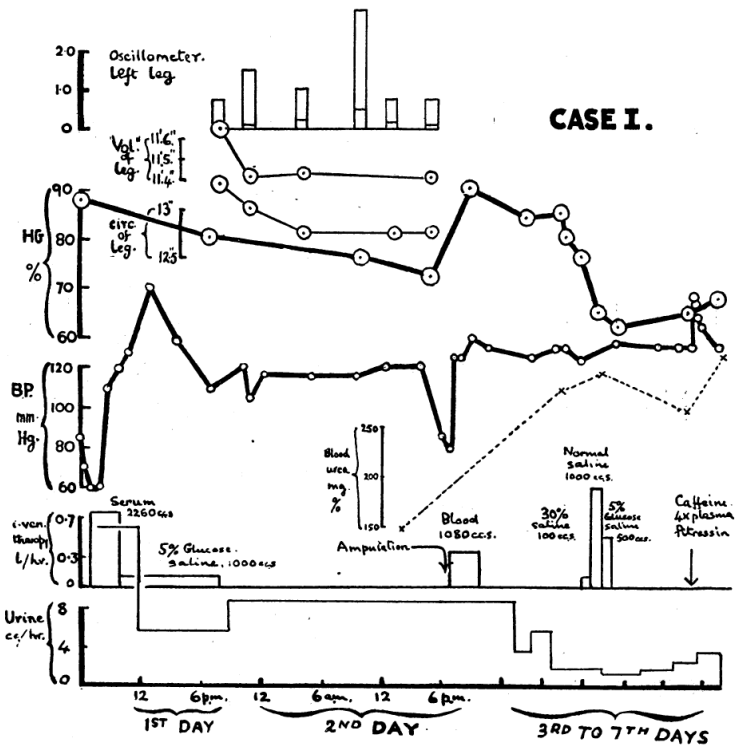



CHART I.—Case I.

## Case I

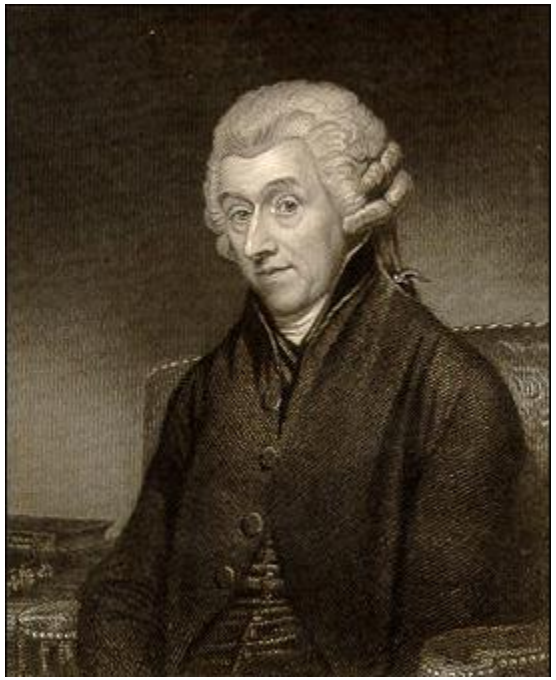
A female aged 17 had been buried

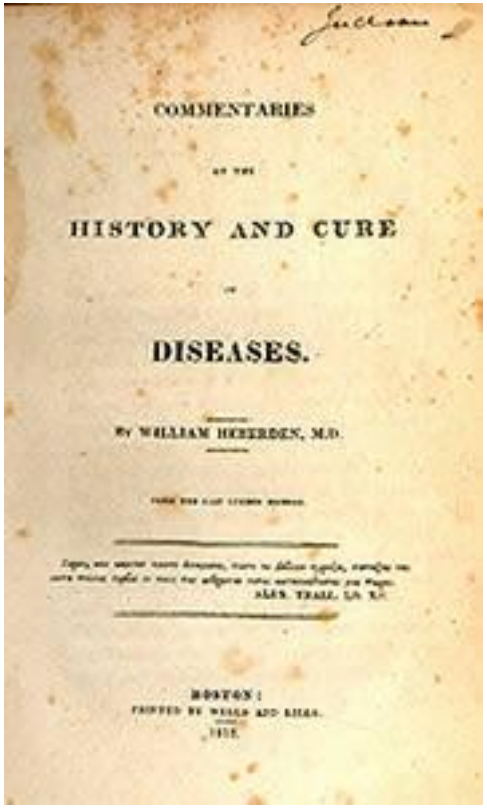
# Early Descriptions

Greeks……

and Israelites

# Father and Son





COMMENTARIES

ON THE

HISTORY AND CURE

OF

DISEASES.

BY WILLIAM HEBERDEN, M.D.

BOSTON:

# Chapter 55: Ischuria

Extreme restlessness, and sometimes a lethargic stupor, accompanies an ischuria, together with vomiting, hiccup, fever, and pains in the loins. One of these patients complained of a strangury; but I have not remarked that others have shown any desire of making water. One man also complained of an urinous taste in his mouth, in whom I had reason to suspect, that urine was secreted in the kidneys, but could not pass off.

A total suppression has lasted seven days, and yet the patient has recovered. It has been fatal so early as on the fourth day. But in general those patients, who could not be cured, have sunk under their malady on the sixth or seventh day.

A draught with spirit of turpentine from ten drops to thirty has been given every five hours; a clyster with half an ounce of spirit of turpentine has been injected twice a day; half a grain of cantharides has been taken every four hours; and clysters have been employed with half an ounce of diuretic salt; and warm bathing as often, and as long as the patients could bear it; and with all these the distemper has ended happily. But on the other hand all these remedies have in some cases been tried without success.

Printed for Payne & Foss, Pall Mall, London

# TREATMENT OF RENAL FAILURE IN A UNIT WITH FACILITIES FOR HAEMODIALYSIS (TWIN-COIL ARTIFICIAL KIDNEY)

## RESULTS WITH 80 PATIENTS

BY

**R. C. JACKSON, F.R.C.P.Ed.**
*Group-Captain, Officer-in-Charge Medical Division and Renal Unit*

**N. V. D. BUNKER, M.B., B.Chir.**
*Flight-Lieutenant*

**W. J. ELDER, M.B., B.S.**
*Flight-Lieutenant*

AND

**A. M. JOEKES, M.A., M.R.C.P.**
*Civil Principal Specialist in Renal Disorders to the Royal Air Force; Senior Lecturer, Institute of Urology, London, and Honorary Physician to Associated Hospitals*

*From the Renal Unit, Princess Mary's Royal Air Force Hospital, Halton, Bucks*

Jackson RC et al Br Med J. 1960 Dec 31;2(5217):1909-16

# Early ARF in the UK – 1957-59

80 patients, 45 recoverable ARF, 12 “irrecoverable ARF”, 17 ESRD, 4 poisonings, 2 miscellaneous

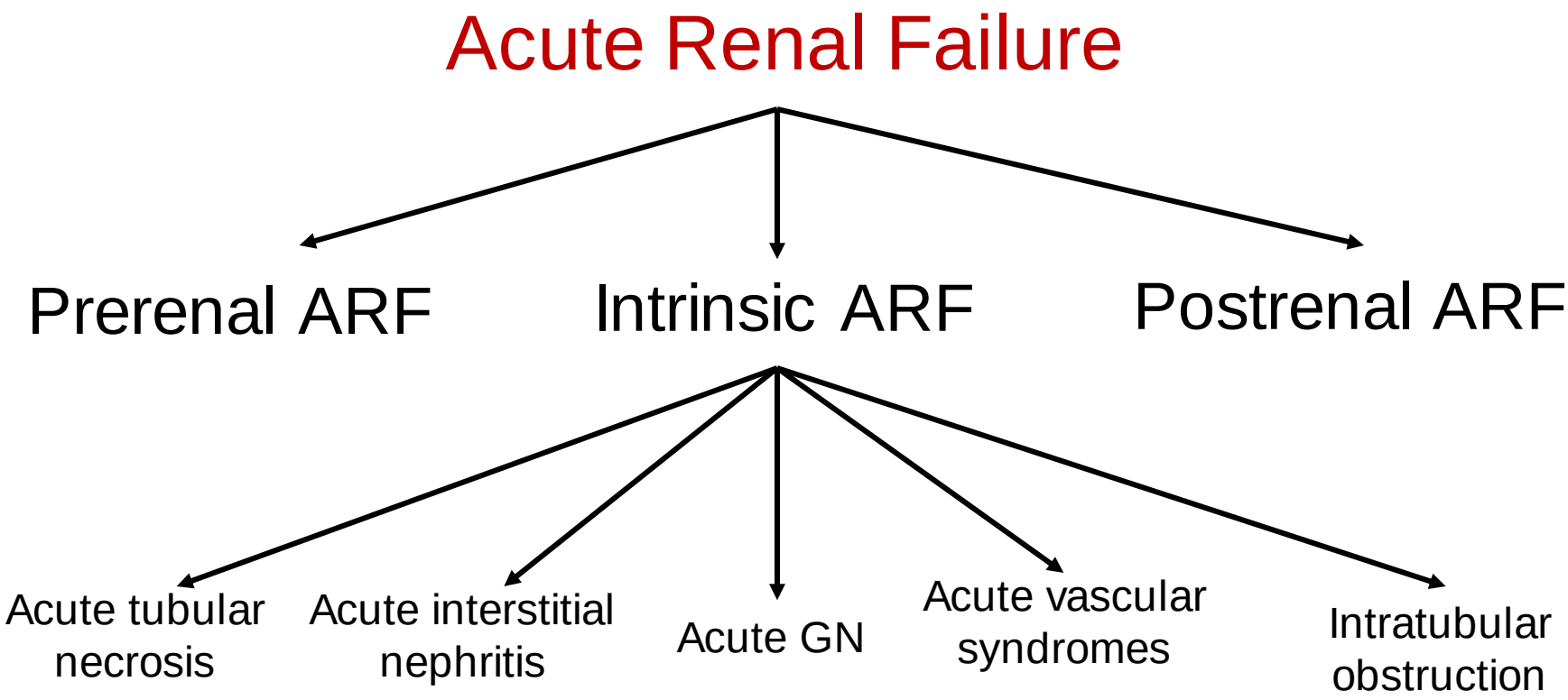
Of the 45 recoverable ARF 29 were male, 16 female

Mean age 36.2 ± 16.5 yr (range 7–73)

| Aetiology | N(%) | Survival N (%) |
|---|---|---|
| Medical | 13 (29) | 10 (77) |
| Surgical | 14 (31) | 7 (50) |
| Trauma | 11 (24) | 5 (45) |
| Obs/Gyn | 7 (16) | 5 (71) |
| Total | 45 | 27 (60) |

Jackson RC et al Br Med J. 1960 Dec 31;2(5217):1909-16

# Acute Renal Failure Conceptual Model



# Acute Renal Failure Definition(s)

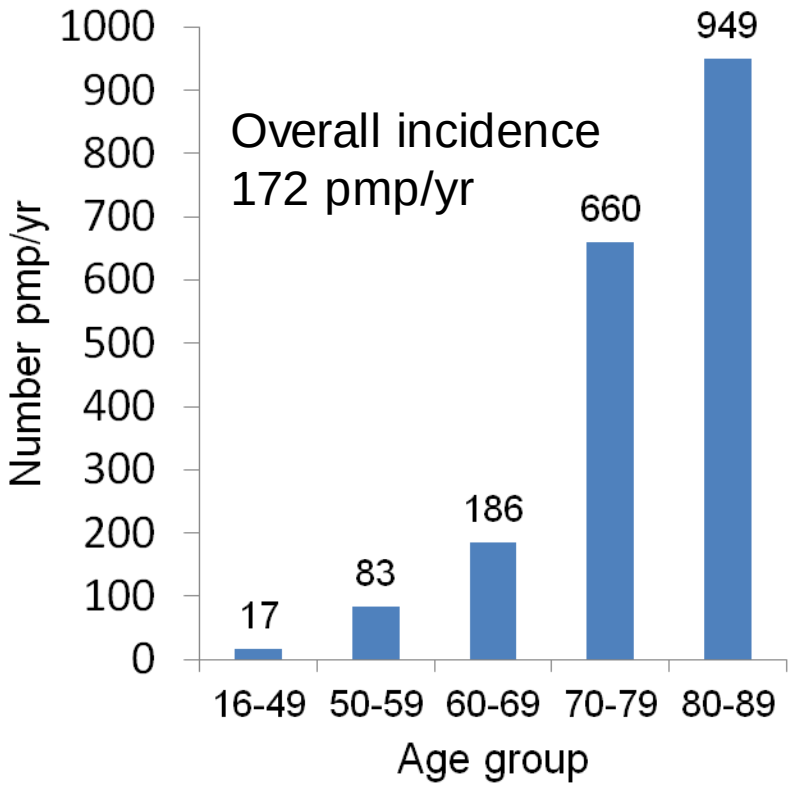
## Acute Renal Failure

'The abrupt transition from functioning kidneys to kidney function which is unable to accomplish biochemical homeostasis'

- Dialysis dependency
- Serum creatinine ≥500 μmol/L ± dialysis
- Serum creatinine ≥300 μmol/L (RA Standards Subcommittee, 1994)
- Oliguric and non-oliguric

# ARF Incidence

## ARF in Devon 1986-88



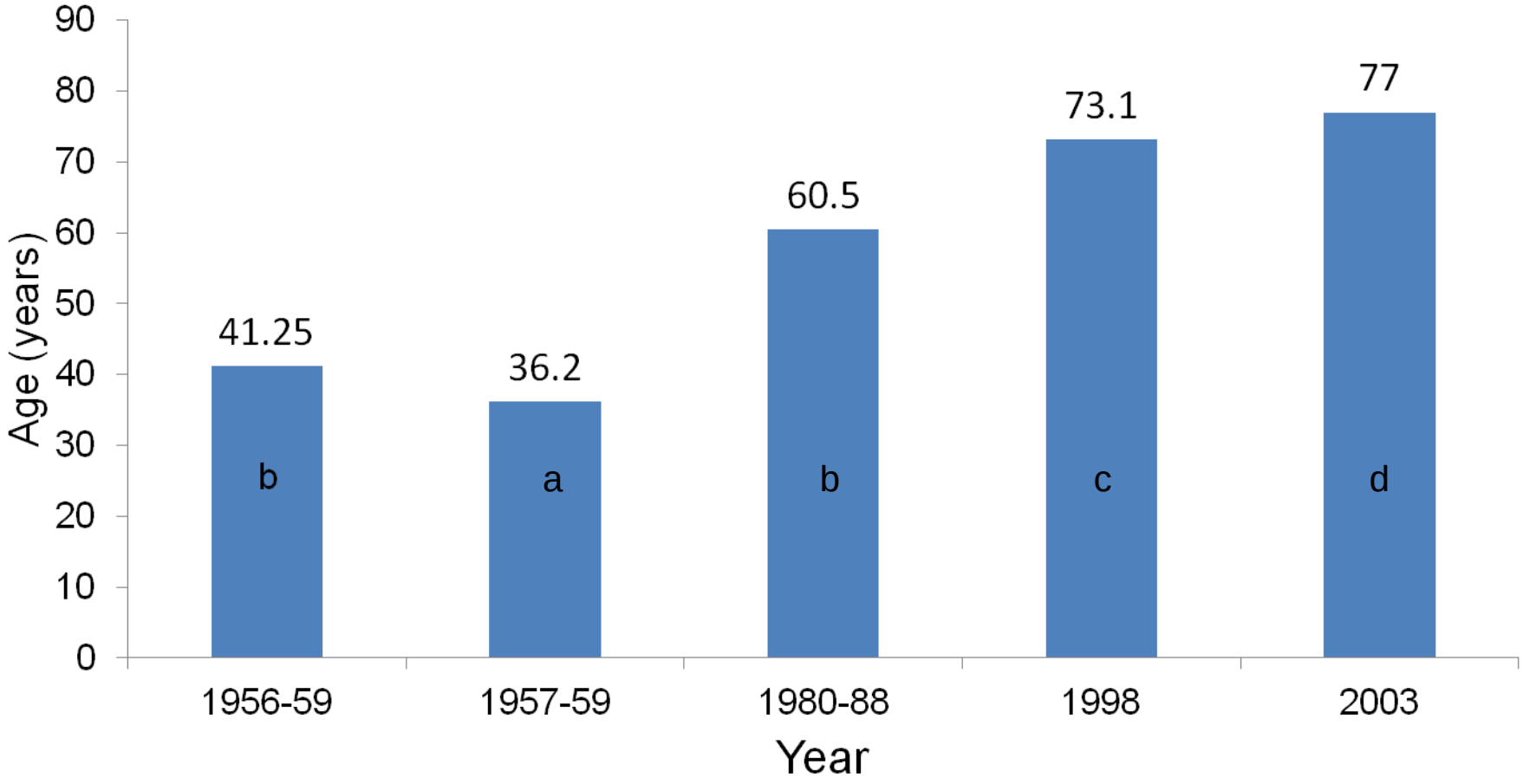

Feest et al. BMJ 1993;306:481-483

## ARF in Scotland 1989-90

- ARF defined as a temporary rise in serum creatinine to ≥ 300 μmol/L
- 311 cases identified over 12 months
- Incidence 620 pmp/year
- 25 patients dialysed, 50 pmp/year

Khan et al. QJM 1997;90:781–785

# Age at Presentation by Year




[a]Jackson RC et al Br Med J. 1960;2:1909-16

[b]Turney et al. Q J Med. 1990;74:83-104

[c]Stevens et al. QJ Med 2001;94:553-560

[d]Ali et al. JASN 2007;18: 1292–1298, 2007

# Aetiology of ARF: Leeds by Decade

| | 1956-59 | 1960-69 | 1970-79 | 1980-88 |
|---|---|---|---|---|
| Medical | 31% | 35% | 40% | 55% |
| Surgical | 39% | 36% | 47% | 41% |
| Trauma | 3% | 11% | 6% | 3% |
| Obstetric | 26% | 13% | 3% | 1% |
| Other | 1% | 5% | 4% | 1% |

Turney et al. Q J Med. 1990 Jan;74(273):83-104

# Aetiology of ARF – Moving Forward

KKRG
Kent Kidney Research Group

## East Kent 1997/98

| | |
|---|---|
| Medical | 70% |
| Surgical | 29% |
| Trauma | 0.7% |
| Obs/Gyn | 0.3% |

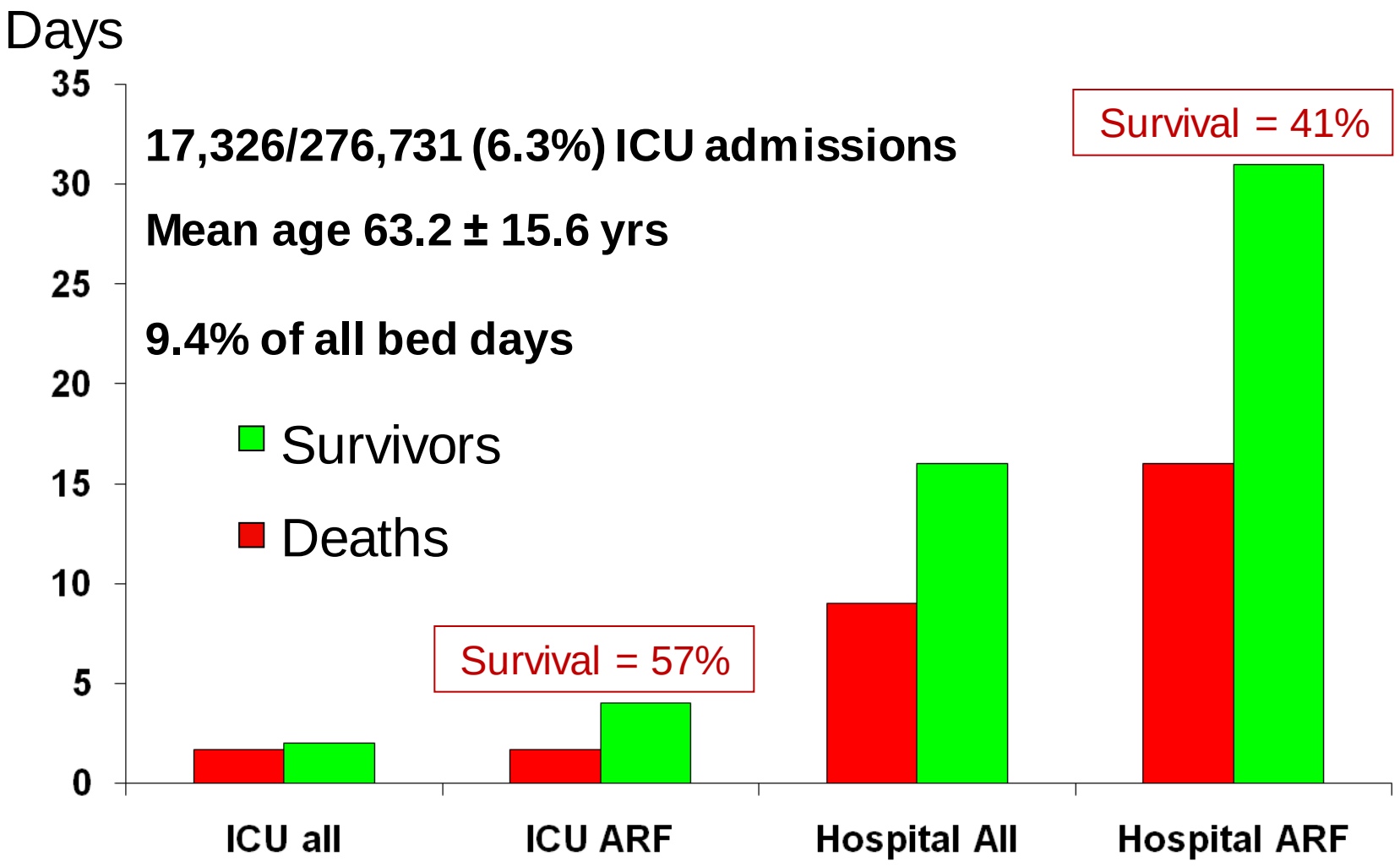
Stevens et al, QJ Med 2001;94:553-560

## ICNARC 1995-2001

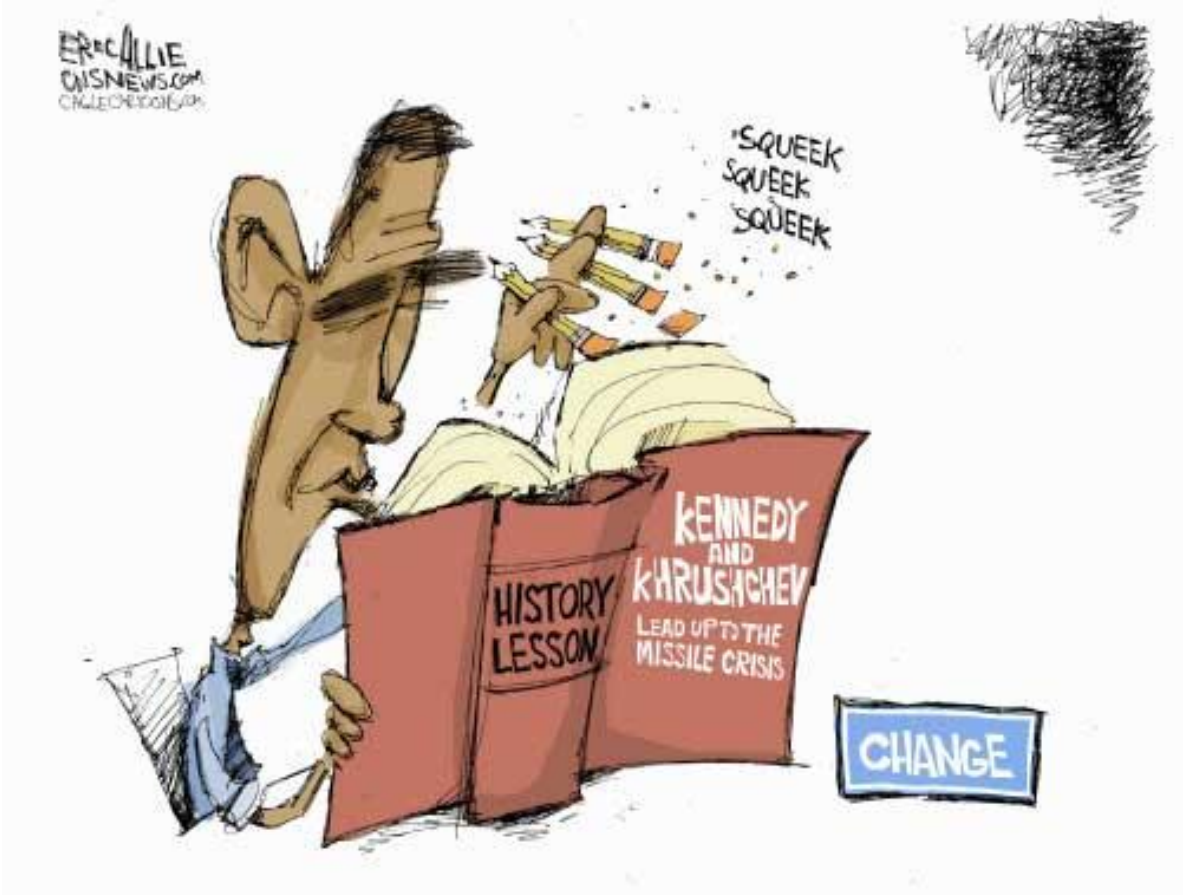
| | |
|---|---|
| Non-surgical | 82.3% |
| Elective surgery | 6.2% |
| Emergency surgery | 11.6% |

Kolhe et al Critical Care 2008;12:S2

# ARF Length of Stay



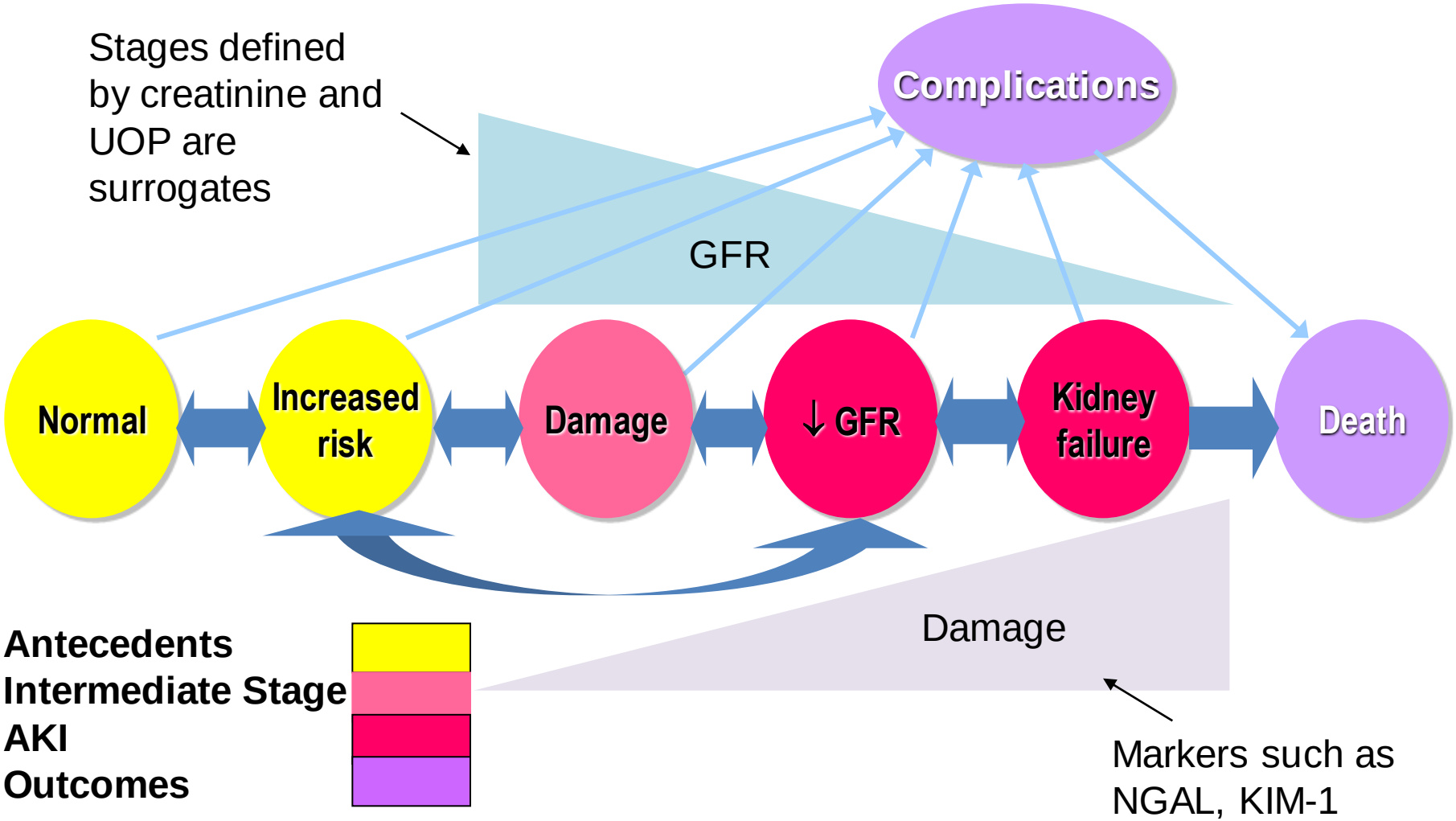

Kolhe et al *Critical Care* 2008;12(Suppl 1):S2 (13 October 2008)




"Political language is designed to make lies sound truthful and murder respectable, and to give an appearance of solidity to pure wind."

(George Orwell)

# Acute Kidney Injury Conceptual Model




Mehta et al . Critical Care 2007;11:R31

# Essential Components of a Workable Definition

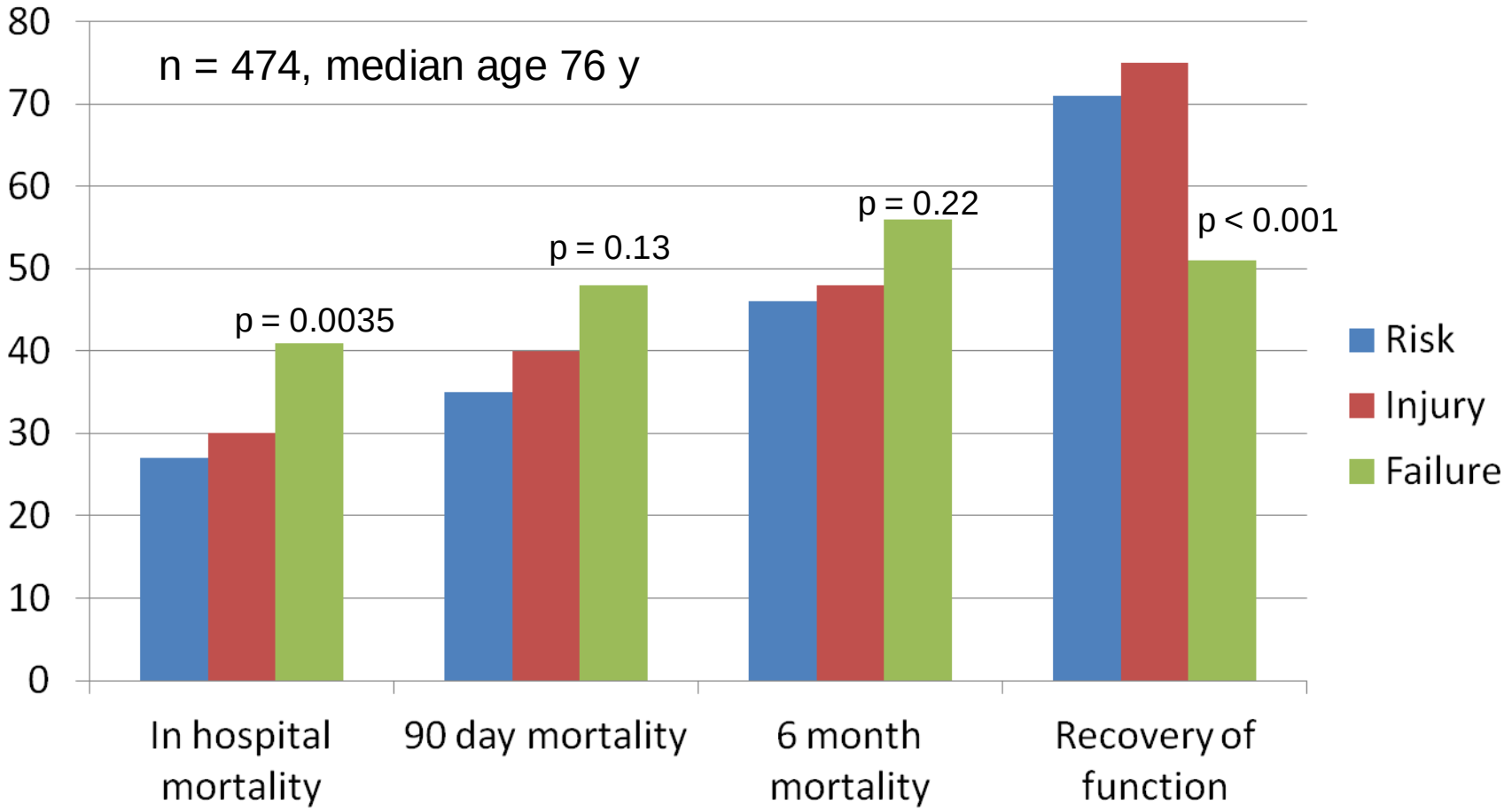
- Clearly establish the presence or absence of a disease
- Must give an idea of the severity of a disease
- Must correlate disease severity with outcome
- Should be easy to understand and apply in a variety of clinical and research settings

# RIFLE Criteria for AKI

| | GFR criteria | UOP criteria | |
|---|---|---|---|
| Risk | ↑SCr x1.5 or GFR↓ >25% | UOP < .5ml/kg/h for 6 hrs | High sensitivity |
| Injury | ↑SCr x2 or GFR↓ >50% | UOP < .5ml/kg/h for 12 hrs | |
| Failure | ↑SCr x3 or GFR↓ >75% | UOP < .5ml/kg/h for 24 hrs or anuria for 12 hrs | High specificity |
| Loss | Persistent ARF = complete loss of kidney function > 4 weeks | | |
| ESRF | ESRF > 3 months | | |

Bellomo et al. Crit Care 2004;8:R204-R212

# Outcomes From AKI by RIFLE Category




Ali T et al. JASN 2007;18:1292-1298

# RIFLE and Mortality: Systematic Review

- 24 studies, including over 71,000 patients
- ICU and non-ICU settings
- Stepwise increase in relative risk of death by RIFLE category versus non-AKI
  - Risk 2.40
  - Injury 4.15
  - Failure 6.37

Ricci et al. Kidney Int 2008;73:538-546

# New Developments Have Limitations


- AKI initiation pre-dates SCr & GFR changes
- Urine output confounders
- Baseline SCr
- Small changes in SCr below RIFLE predict outcomes

# Acute Kidney Injury Network Criteria

| Stage | Creatinine Criteria | UOP Criteria |
|---|---|---|
| 1 | ↑SCr ≥ 26.4 µmol/L **or** ↑SCr ≥ 150-200% | < 0.5 mL/kg/hr for > 6 hr |
| 2 | ↑SCr > 200-300% | < 0.5 mL/kg/hr for >12 hr |
| 3 | ↑ SCr >300% **or** SCr ≥354 µmol/L + acute ↑ ≥44 µmol/L in ≤24hr **or** RRT initiated | < 0.3 mL/kg/hr for 24 hr **or** anuria for 12 hr |

48 hour time constraint

Mehta et al. Crit Care 2007;11:R31

# Impact of AKI

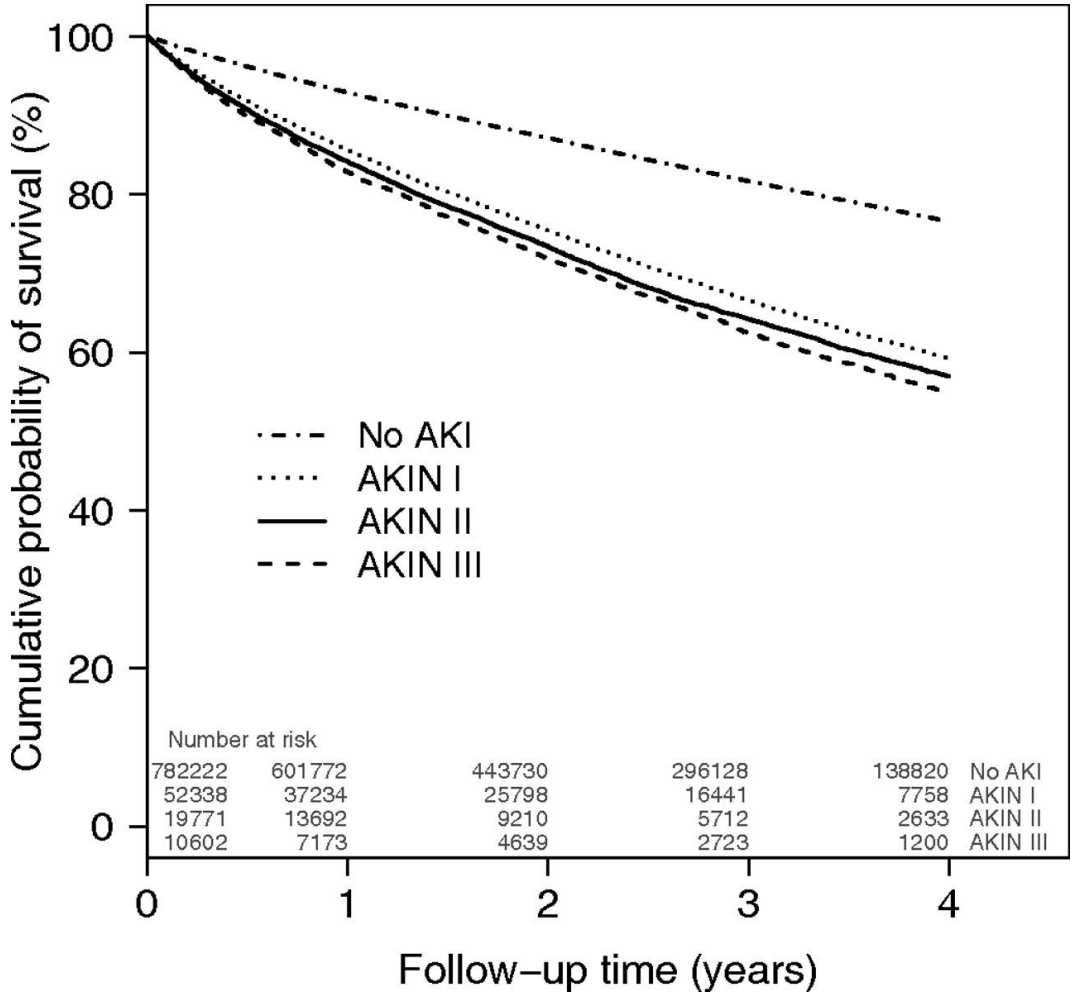
## Correlation between AKIN classification and outcome

22,303 adult patients admitted to 22 ICUs in UK and Germany between 1989–1999 with ICU stay ≥24 hours

| | No AKI | AKIN 1 | AKIN 2 | AKIN 3 |
|---|---|---|---|---|
| **Percentage** | 65.6% | 19.1% | 3.8% | 12.5% |
| **Mean age** | 60.5 | 62.1 | 60.4 | 61.1 |
| **ICU mortality** | 10.7% | 20.1% | 25.9% | 49.6% |
| **Hospital mortality** | 16.9% | 29.9% | 35.8% | 57.9% |
| **LOS in ICU (median)** | 2 d | 5 d | 8 d | 9 d |

Ostermann et al, Critical Care 2008;12:R144

# Non-RRT AKIN & Long Term Survival

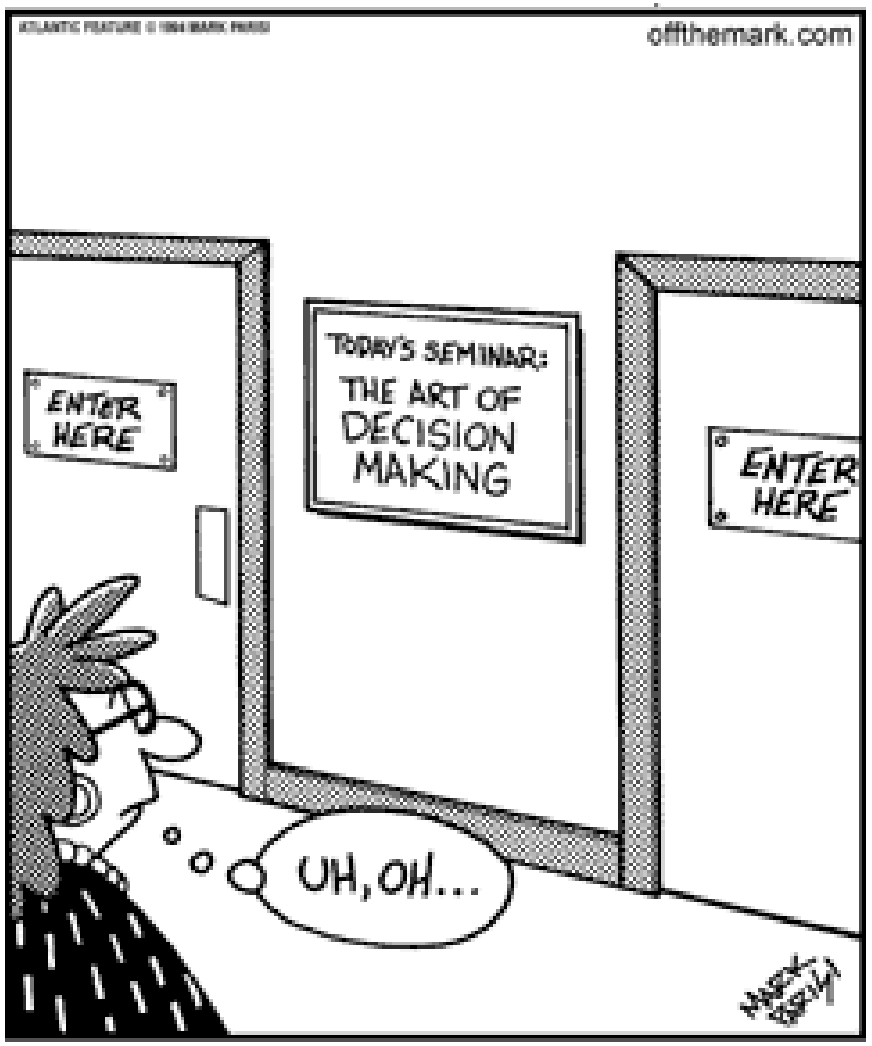



Adj mortality risk for AKI 1.41 (95%CI, 1.39-1.43)

JASN

Lafrance, J.-P. et al. J Am Soc Nephrol 2010;21:345-352

# RIFLE or AKIN?



# AKIN vs RIFLE, SAPS3 Database

- 16,784 pts from 303 ICUs, 14,356 pts in the analysis

| AKIN | | RIFLE | |
|---|---|---|---|
| Stage 1 | 1,077 | Risk | 1,092 |
| Stage 2 | 1,033 | Injury | 1,596 |
| Stage 3 | 1,983 | Failure | 2,405 |
| Total | 4,093 | Total | 5,093 |

- 1,504 (10.5%) classified as AKI by RIFLE missed by AKIN*
- 504 (3.5%) classified as AKI by AKIN missed by RIFLE

***RRT not included**

Joannidis et al. Intensive Care Med 2009;35:1692-1702

# Cross Tabulation of Patients Classified by RIFLE vs. AKIN

| AKIN | RIFLE | | | | Total (AKIN) |
|---|---|---|---|---|---|
| | Non-AKI | Risk | Injury | Failure | |
| Non-AKI | 8759 | 781 | 452 | 271 | 10263 |
| Stage 1 | 457 | 282 | 243 | 95 | 1077 |
| Stage 2 | 36 | 21 | 885 | 91 | 1033 |
| Stage 3 | 11 | 8 | 16 | 1948 | 1983 |
| Total (RIFLE) | 9263 | 1092 | 1596 | 2405 | 14356 |

Joannidis et al. Intensive Care Med 2009;35:1692-1702

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| AKIN | RIFLE<br>Non-AKI | Risk | Injury | Failure | Total (AKIN) |
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| Non-AKI | 8759 (12.9%) | 781 | 452 | 271 | 10263 (15.9%) |
| Stage 1 | 457 | 282 (33.0%) | 243 | 95 | 1077 (34.5%) |
| Stage 2 | 36 | 21 | 885 (25.9%) | 91 | 1033 (29.0%) |
| Stage 3 | 11 | 8 | 16 | 1948 (41.3%) | 1983 (41.2%) |
| Total (RIFLE) | 9263 (13.6%) | 1092 (29.2%) | 1596 (32.3%) | 2405 (42.6%) | 14356 |

Joannidis et al. Intensive Care Med 2009;35:1692-1702

# KDIGO AKI Definition

Acute kidney injury/impairment (AKI) is defined as any of the following:

- Increase in SCr by >0.3 mg/dl (>26.4 µmol/L) within 48 hours, *or*
- Increase in SCr by >1.5-fold above baseline which is known or presumed to have occurred within 7 days, *or*
- Urine volume <0.5 ml/kg/h for 6 hours.

KDIGO AKI GL. Kidney inter., Suppl. 2012; 2: 1–138

# KDIGO AKI Staging

| Stage | Serum creatinine | Urine output |
|---|---|---|
| 1 | ≥ 1.5-1.9 times baseline (7 days)<br>OR<br>0.3mg/dl increase (48 hrs) | < 0.5 ml/kg/hr for 6-12 hrs |
| 2 | ≥ 2.0-2.9 times baseline | < 0.5 ml/kg/hr for ≥12hrs |
| 3 | ≥ 3.0 times baseline<br>OR<br>increase in creatinine to ≥ 4.0 mg/dl*<br>OR<br>Renal replacement therapy | < 0.3 ml/kg/hr for ≥24hrs<br>OR<br>Anuria for ≥ 12hrs |

KDIGO AKI Guideline. Kidney inter., Suppl. 2012; 2: 1–138

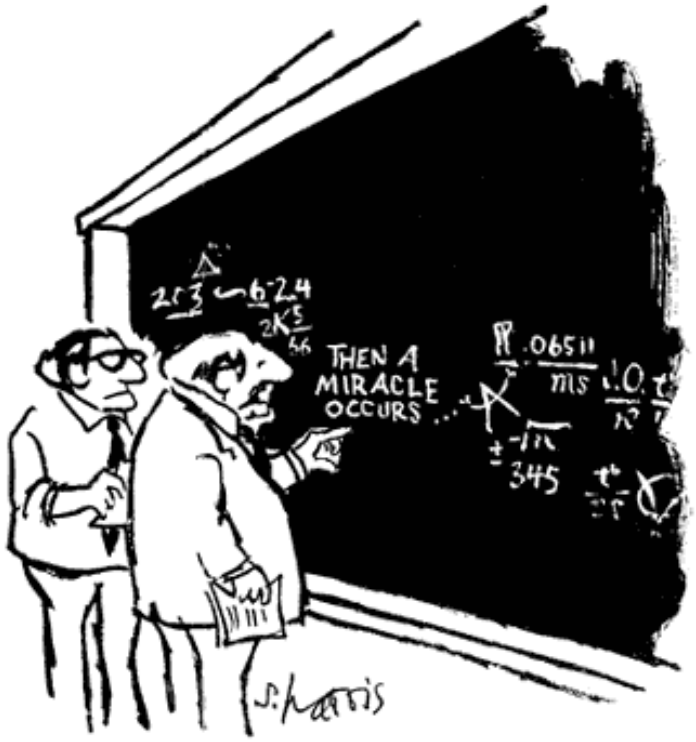
# The Purists: Baseline vs. Reference SCr

- Baseline creatinine
  - Value most reflective of pre-morbid function
  - Important for determining prior (and recovery) CKD
  - Should be based on SCr > 3/12 prior to event
- Reference creatinine
  - Value used as the point from which change in SCr is measured to determine AKI has occurred
  - Lowest SCr within 90 days of the event

# Pragmatism

## Baseline/reference choice

- Varying the baseline from admission to 365 days prior[1]
- Averaging prior 7-356 days prior data as baseline[2]
- MDRD back estimation from eGFR 75 for missing values[3]
- Multiple imputation for missing values[4]



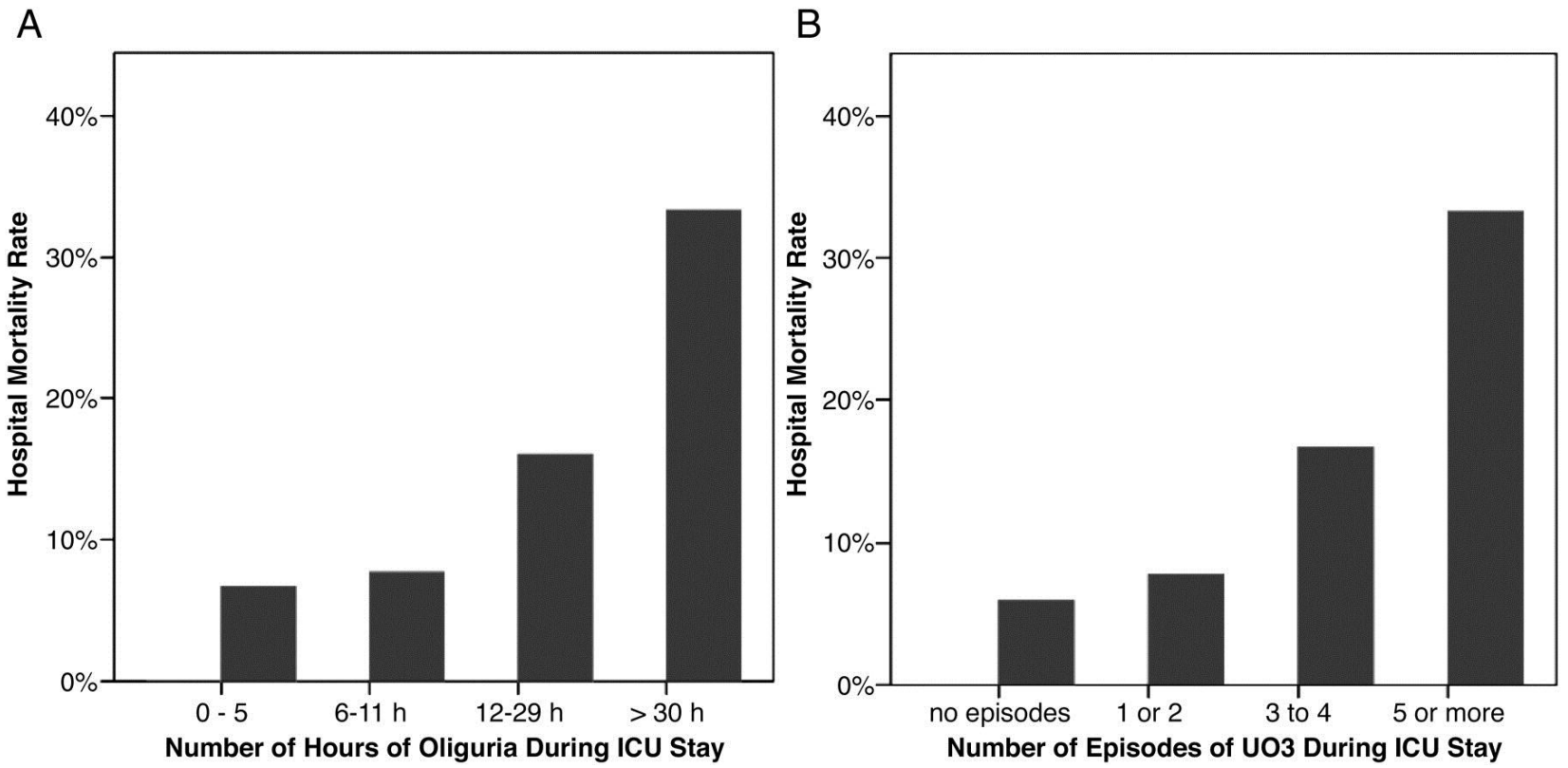

"I think you should be more explicit here in step two."

[1]Lafrance and Miller. Am J Kidney Dis 2010;56:651-660
[2]Siew et al. CJASN 2012; 7:712–9
[3]Siew et al. Kidney Int 2010;77:536–542
[4]Siew et al. CJASN advance on line November 2012

# Urine Output Criteria

- May over-estimate severity
- Issues with diuretics
- UOP may be reduced early in pre-renal azotaemia but late in the course of established AKI
- Issues with measurement

# Defining UOP for AKI




**Macedo E et al. Nephrol. Dial. Transplant. 2011;26:509-515**



NDT Nephrology Dialysis Transplantation

# East Kent Hospitals

KKRG
Kent Kidney Research Group



- Population 720,000

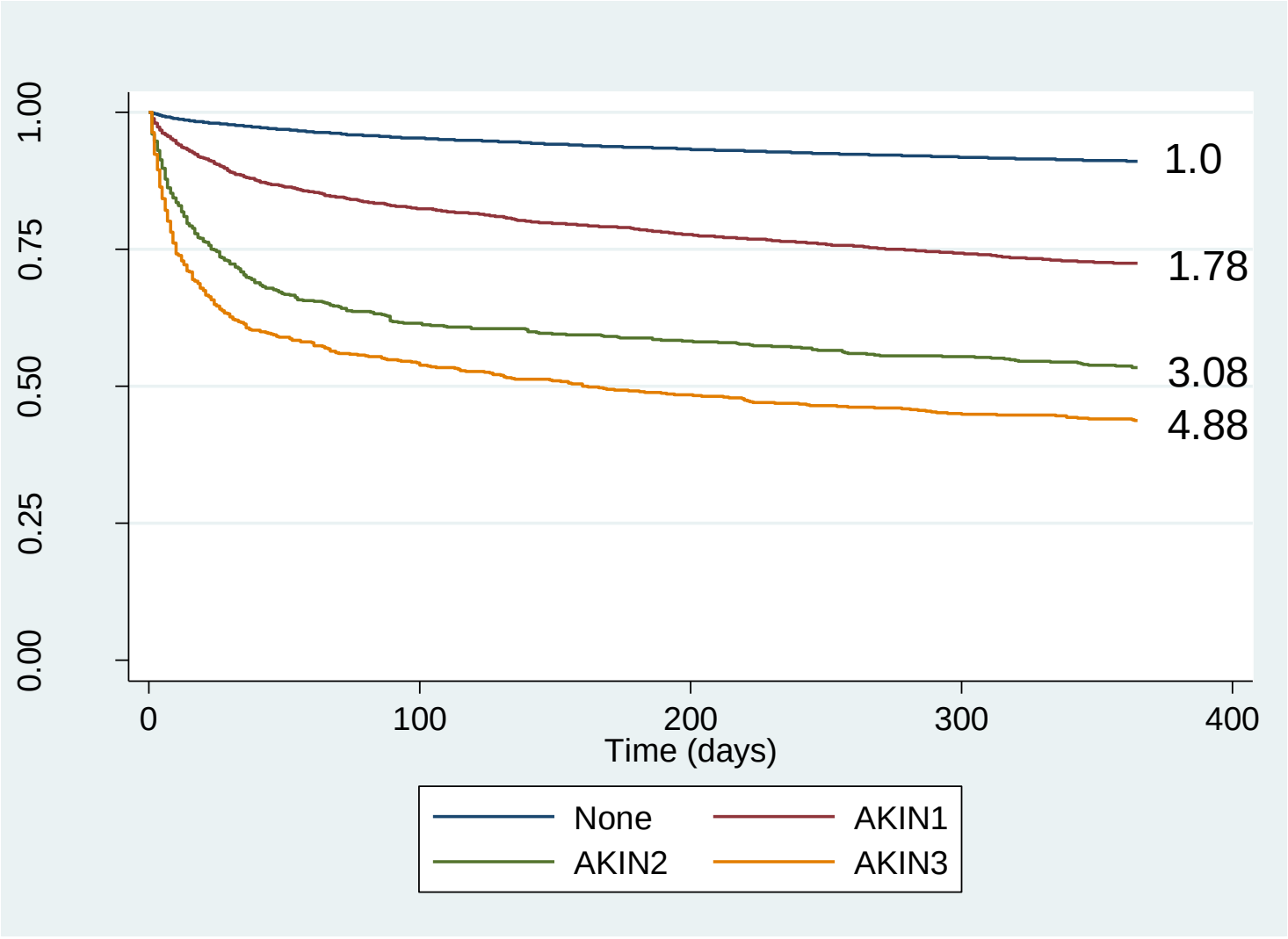
# AKI in East Kent Feb- Jul 2009

43,617 elective & non-elective admissions in 6 months
18,215 with insufficient SCr data to categorise AKI, LOS 0.79 days

| AKI Stage | Number | Age (y) | M:F |
|---|---|---|---|
| No AKI | 20323 | 63.2 (20.3) | 0.84 |
| 1 | 3636 | 75.0 (16.1) | 1.11 |
| 2 | 864 | 75.9 (14.8) | 0.84 |
| 3 | 579 | 72.3 (15.9) | 0.95 |

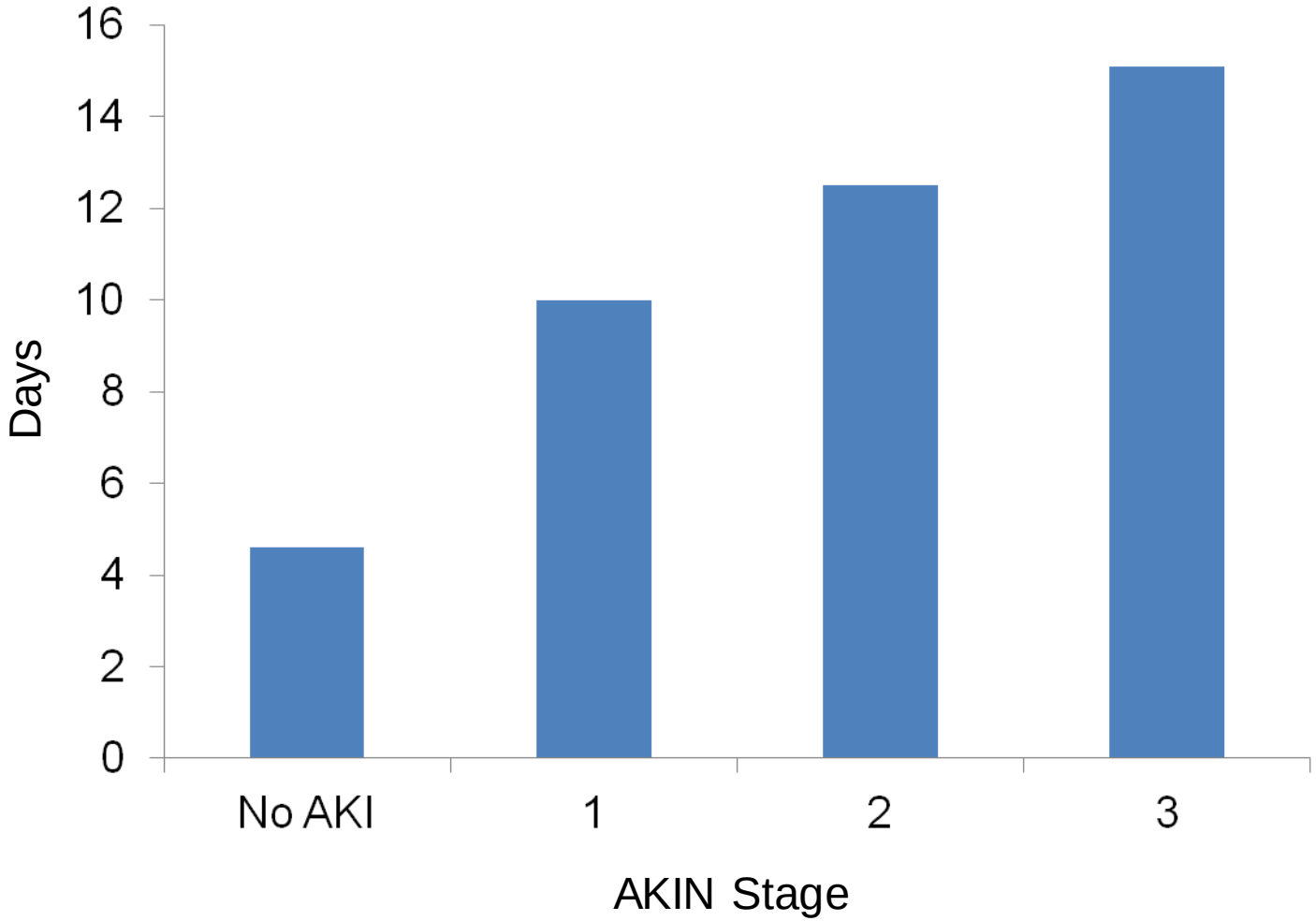
Bedford M et al, unpublished

# Survival 12 month follow-up




Adjusted hazard ratio for death

# Length of Stay in Survivors



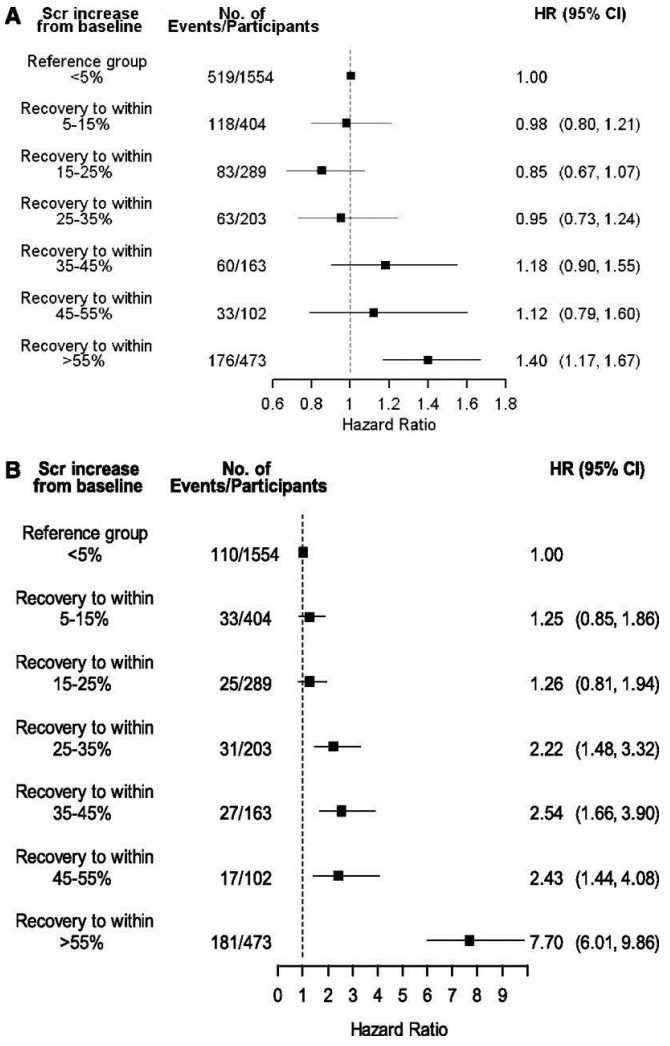
# AKI as a Risk Factor for CKD

| Study | Population | Main Findings |
|---|---|---|
| Ishani et al, 2009 | 233,803 age ≥67 y at hospital discharge | 72.1% with AKI and no prior CKD developed CKD within 2 y of the AKI episode |
| Triverio et al, 2009 | 89 patients requiring RRT on ITU | 50% of patients without prior CKD progressed to CKD within 3 y |
| Mehta et al, 2004 | 618 ITU patients with ARF; data from PICARD | In-hospital mortality rate, 37%; rate of mortality/non-recovery of kidney function, 50% |
| Mehta et al, 2002 | 552 ITU patients with ARF | Of 258 patients who survived 17 (7%) were dialysis dependent after discharge |

Bedford et al. AJKD 2012;59(4):485-491

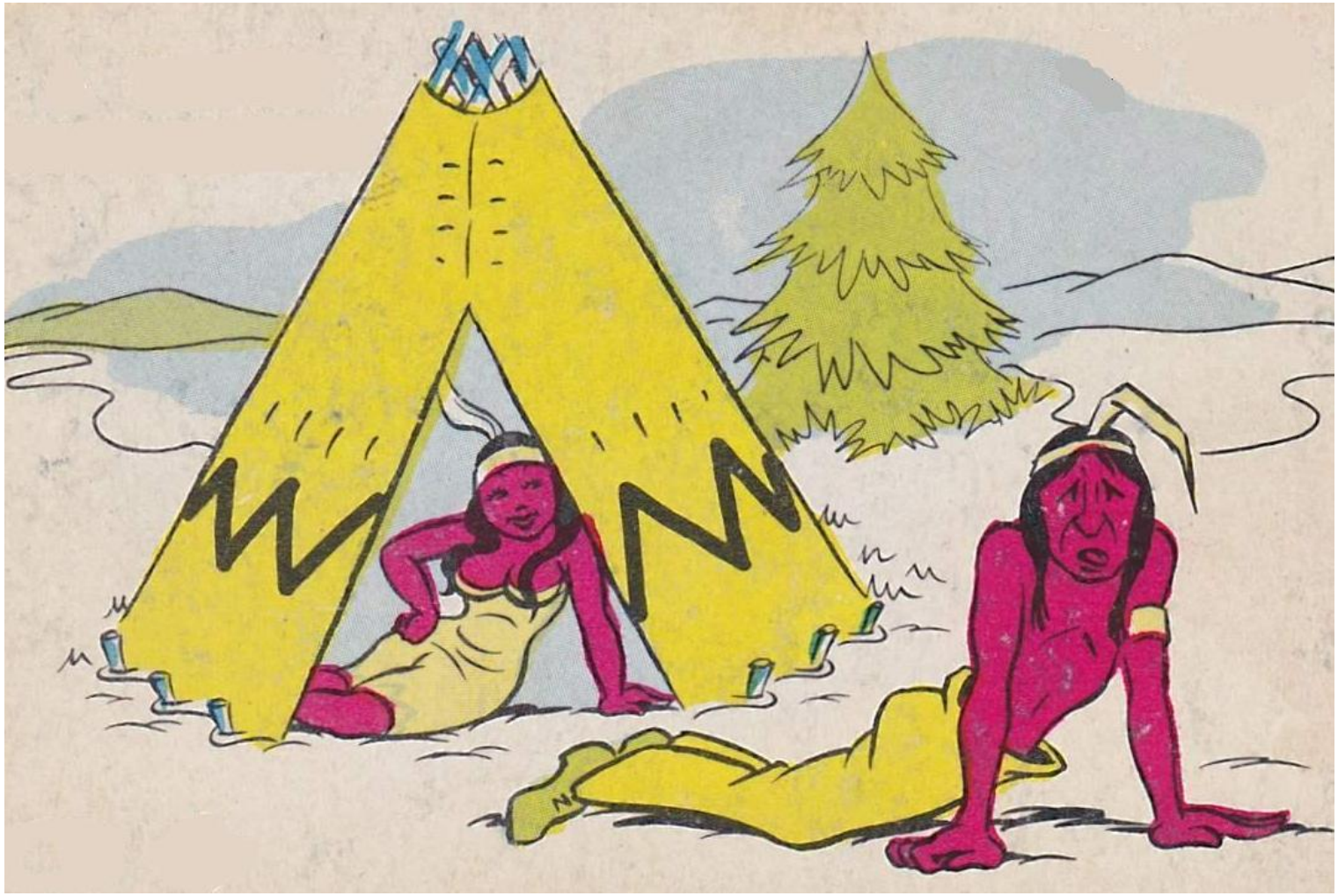
# AKI: Renal Recovery & Patient and Renal Survival

- Population based cohort
- 190,714 subjects over a 5 y period, AKI defined by 2-fold rise in SCr from baseline to peak admission value
- 7014 with AKI, 4400 surviving to 90 days
- 3231 with data enabling recovery assessment, median FU 34 months
- 1268 (30.8%) died, 85 (2.1%) progressed to renal failure




Pannu N et al. CJASN doi:10.2215/CJN.06480612

# Scoring Systems



"Now that's what I call an APACHE Score!"

# Potential Uses for Scoring Systems

- Recognition of risk
- Disease severity
- Management decisions
- Counselling patients/carers
- Futility of care
- Randomisation for clinical trials

# Refining Predictive Models for AKI

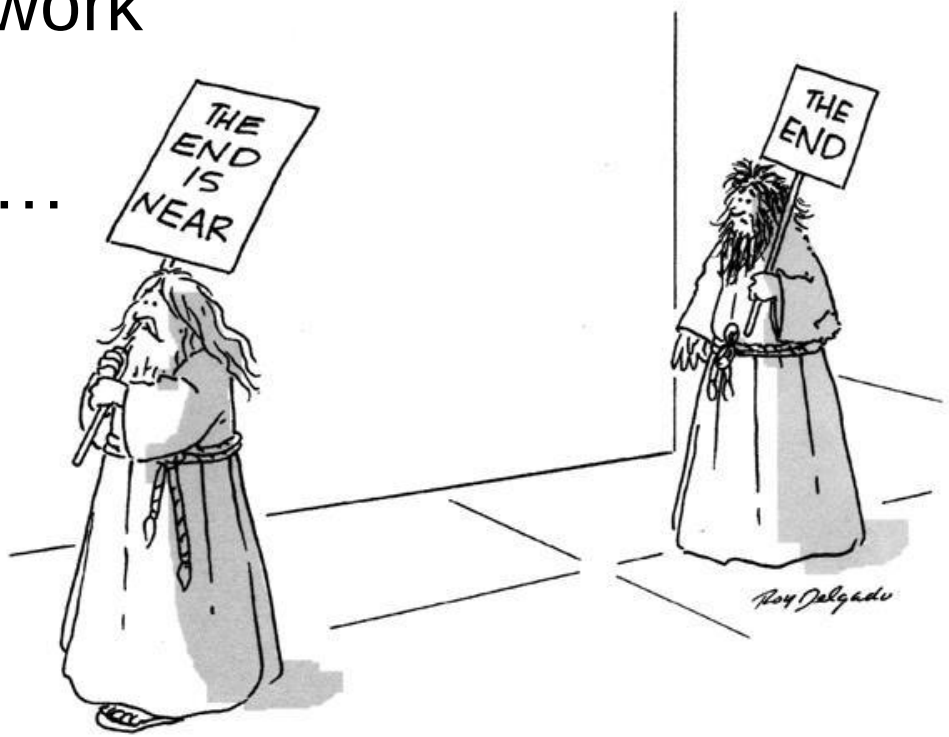
| Model | Area under ROC Curve | 95% CI | Hosmer-Lemeshow Goodness-of-Fit *P* |
|---|---|---|---|
| Mehta | 0.832 | (0.80, 0.86) | 0.86 |
| APACHE II | 0.634 | (0.59, 0.68) | 0.78 |
| APACHE III | 0.756 | (0.72, 0.80) | 0.19 |
| SAPS2 | 0.766 | (0.73, 0.80) | 0.03 |
| LOD | 0.734 | (0.69, 0.77) | 0.26 |
| MOD | 0.735 | (0.70, 0.77) | 0.10 |
| SOFA | 0.756 | (0.72, 0.79) | 0.35 |
| Brussels | 0.726 | 0.69, 0.77) | 0.94 |
| Liano | 0.630 | 0.59, 0.67) | 0.16 |
| Schaefer | 0.650 | 0.61, 0.69) | 0.06 |
| ANP Study | 0.726 | 0.69, 0.77) | 0.59 |
| SHARF | 0.645 | (0.60, 0.69) | 0.54 |
| SHARF II | 0.733 | (0.69, 0.77) | 0.03 |
| CCF | 0.718 | (0.67, 0.75) | 0.002 |

Mehta R L et al. JASN 2002;13:1350-1357

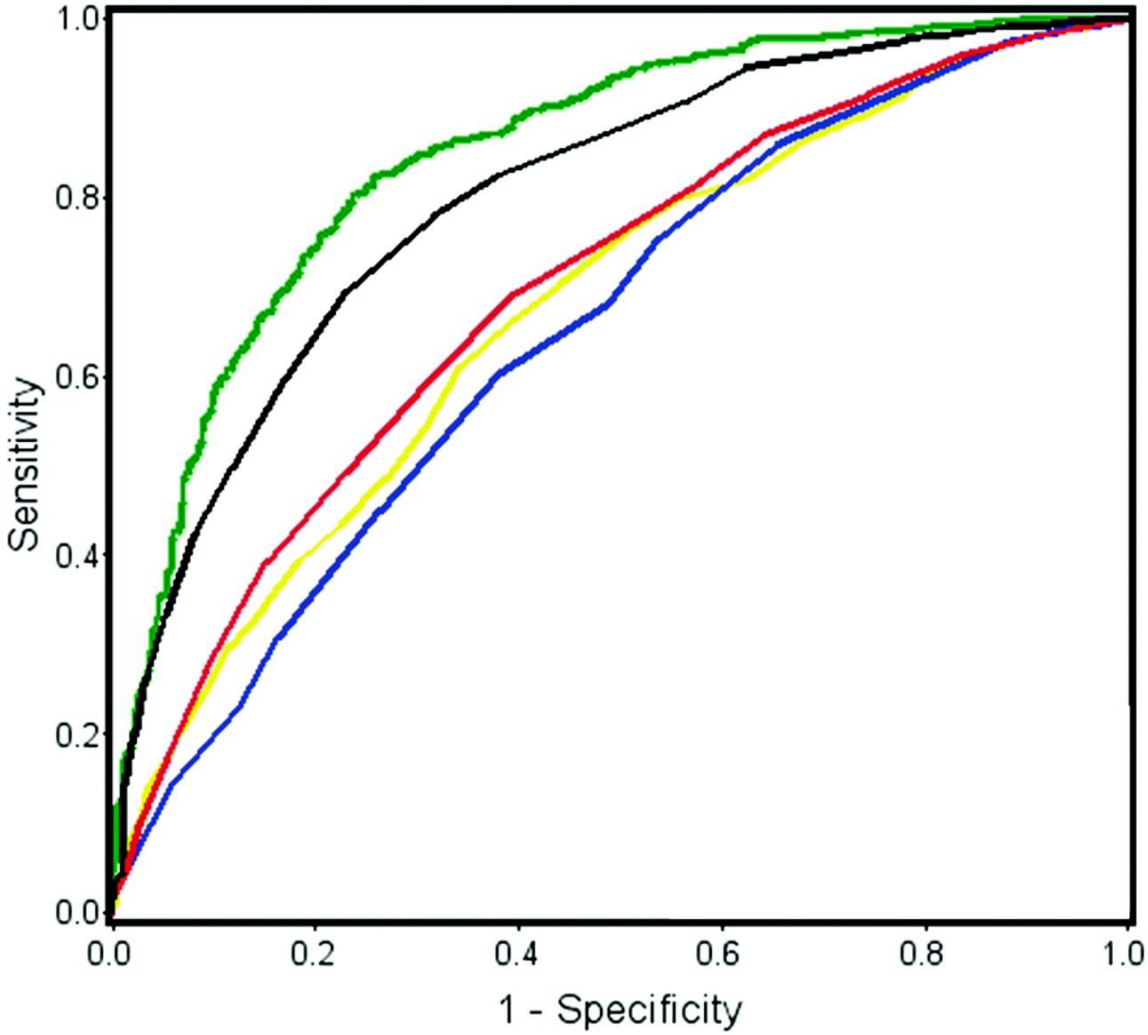
# Problems With Scoring Systems

- General severity of illness scores lack accuracy for AKI

- AKI specific risk scores work well in the populations they're developed in but…
- AKI specific risk scores don't work in other populations



**Area under receiver operating characteristic (ROC) curves for the new risk score (0.85), integer risk score (0.80), APACHE II (0.68), total SOFA (0.69), and Cleveland Clinic score (0.65).**




**Demirjian S et al. CJASN 2011;6:2114-2120**

# Development of Inpatient Risk Stratification Models of Acute Kidney Injury for Use in Electronic Health Records

*Michael E. Matheny, MD, MS, MPH, Randolph A. Miller, MD, T. Alp Ikizler, MD, Lemuel R. Waitman, PhD, Joshua C. Denny, MD, MS, Jonathan S. Schildcrout, PhD, Robert S. Dittus, MD, MPH, Josh F. Peterson, MD, MPH*

***Objective***. *Patients with hospital-acquired acute kidney injury (AKI) are at risk for increased mortality and further medical complications. Evaluating these patients with a prediction tool easily implemented within an electronic health record (EHR) would identify high-risk patients prior to the development of AKI and could prevent iatrogenically induced episodes of AKI and improve clinical management.* ***Methods***. *The authors used structured clinical data acquired from an EHR to identify patients with normal kidney function for admissions from 1 August 1999 to 31 July 2003. Using administrative, computerized provider order entry and laboratory test data, they developed a 3-level risk stratification model to predict each of 2 severity levels of in-hospital AKI as defined by RIFLE criteria. The severity levels were defined as 150% or 200% of baseline serum creatinine. Model discrimination and calibration were evaluated using 10-fold cross-validation.* ***Results***. *Cross-validation of the models resulted in area under the receiver operating characteristic (AUC) curves of 0.75 (150% elevation) and 0.78 (200% elevation). Both models were adequately calibrated as measured by the Hosmer-Lemeshow goodness-of-fit test chi-squared values of 9.7 (*$P = 0.29$*) and 12.7 (*$P = 0.12$*), respectively.* ***Conclusions***. *The authors generated risk prediction models for hospital-acquired AKI using only commonly available electronic data. The models identify patients at high risk for AKI who might benefit from early intervention or increased monitoring.* ***Key words:*** *clinical prediction rules; decision rules; pharmacoepidemiology; risk adjustment; risk stratification; artificial neural networks.* ***(Med Decis Making 2010;30:639–650)***


"Sometimes I think why am I here?
What's the point?"

# Conclusions

- AKI is very common
- With standardised definitions we recognise that even minor degrees of AKI confer adverse outcomes
  - ↑hospital LOS
  - ↑hospital & long-term mortality
  - subsequent new onset CKD and progression of prior CKD
- Scoring systems would be good if they really worked
- If we could predict could we prevent? Ask Lui


"Marlies, I would have concentrated on the facts, but they weren't in my favour!"

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