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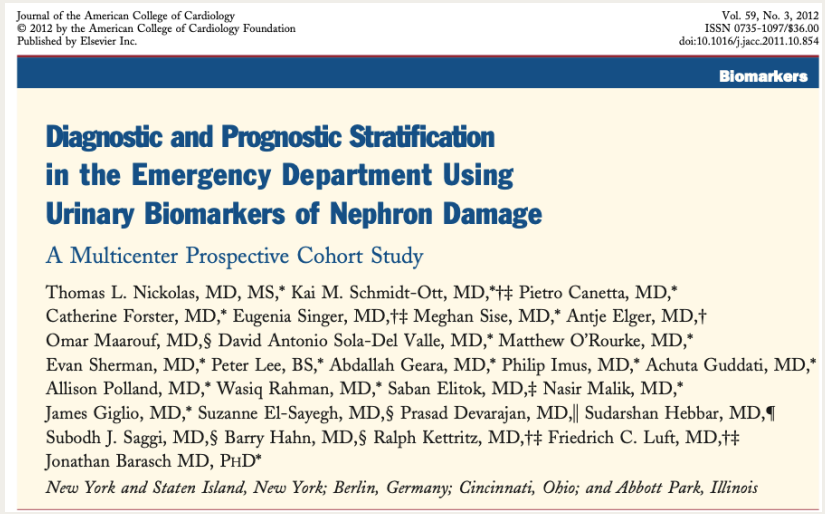
Experiences with AKI Clinical Trial Design

Sudarshan Hebbar MD
06 May 2025

Experience with AKI Clinical Trial Design



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Biomarkers

Diagnostic and Prognostic Stratification in the Emergency Department Using Urinary Biomarkers of Nephron Damage

A Multicenter Prospective Cohort Study

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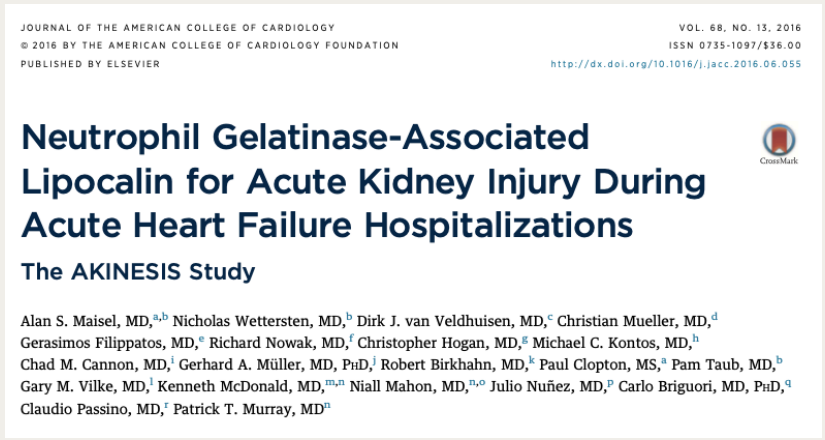
New York and Staten Island, New York; Berlin, Germany; Cincinnati, Ohio; and Abbott Park, Illinois



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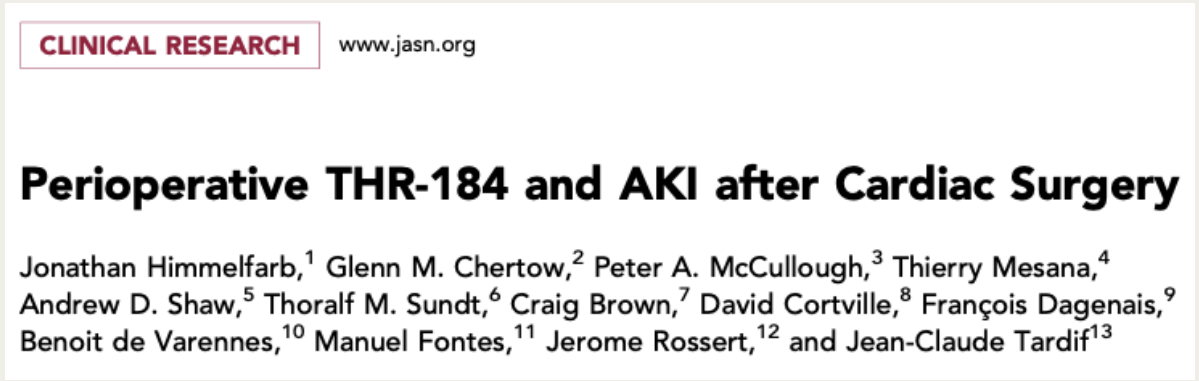
Neutrophil Gelatinase-Associated Lipocalin for Acute Kidney Injury During Acute Heart Failure Hospitalizations

The AKINESIS Study

Alan S. Maisel, MD,[a,b] Nicholas Wettersten, MD,[b] Dirk J. van Veldhuisen, MD,[c] Christian Mueller, MD,[d] Gerasimos Filippatos, MD,[e] Richard Nowak, MD,[f] Christopher Hogan, MD,[g] Michael C. Kontos, MD,[h] Chad M. Cannon, MD,[i] Gerhard A. Müller, MD, PHD,[j] Robert Birkhahn, MD,[k] Paul Clopton, MS,[a] Pam Taub, MD,[b] Gary M. Vilke, MD,[j] Kenneth McDonald, MD,[m,n] Niall Mahon, MD,[n,o] Julio Nuñez, MD,[p] Carlo Briguori, MD, PHD,[q] Claudio Passino, MD,[r] Patrick T. Murray, MD[n]



CLINICAL RESEARCH www.jasn.org

Perioperative THR-184 and AKI after Cardiac Surgery

Jonathan Himmelfarb,[1] Glenn M. Chertow,[2] Peter A. McCullough,[3] Thierry Mesana,[4] Andrew D. Shaw,[5] Thoralf M. Sundt,[6] Craig Brown,[7] David Cortville,[8] François Dagenais,[9] Benoit de Varennes,[10] Manuel Fontes,[11] Jerome Rossert,[12] and Jean-Claude Tardif[13]

Inhibition of Calcium Release-Activated Calcium (CRAC) channels to Treat Acute Kidney Injury: Design and Rationale of the KOURAGE study

Lakhmir S. Chawla[a], Patrick T. Murray[b], Stuart L. Goldstein[c], Andrew Cunningham[d], Sudarshan Hebbar[d], Richard G. Wunderink[e] , and Glenn M. Chertow[f]

Design of AKI Trials

SPECIAL ARTICLE www.jasn.org

Optimizing the Design and Analysis of Future AKI Trials

Matthieu Legrand,[1,2] Sean M. Bagshaw,[3] Jay L. Koyner,[4] Ivonne H. Schulman,[5] Michael R. Mathis,[6] Juliane Bernholz,[7] Steven Coca,[8] Martin Gallagher,[9] Stéphane Gaudry,[2,10,11] Kathleen D. Liu,[12] Ravindra L. Mehta,[13] Romain Pirracchio,[14] Abigail Ryan,[15] Dominik Steubl,[16,17] Norman Stockbridge,[18] Fredrik Erlandsson,[19] Alparslan Turan,[20,21] F. Perry Wilson,[22] Alexander Zarbock,[23] Michael P. Bokoch,[1] Jonathan D. Casey,[24] Patrick Rossignol,[2,25,26] and Michael O. Harhay[27]

Nephrol Dialysis Transplant (2023) 38: 834–844
https://doi.org/10.1093/ndt/gfac003
Advance Access publication date 12 January 2022

Overcoming barriers in the design and implementation of clinical trials for acute kidney injury: a report from the 2020 Kidney Disease Clinical Trialists meeting

Daniel Lazzareschi[1], Ravindra L. Mehta[2], Laura M. Dember[3], Juliane Bernholz[4], Alparslan Turan[5,6], Amit Sharma[7], Sachin Kheterpal[8], Chirag R. Parikh[9], Omar Ali[10,17], Ivonne H. Schulman[11], Abigail Ryan[12], Jean Feng[13], Noah Simon[14], Romain Pirracchio[1], Patrick Rossignol[15,16] and Matthieu Legrand[1,15]

Intensive Care Med
https://doi.org/10.1007/s00134-024-07560-y

CONFERENCE REPORTS AND EXPERT PANEL

Recommendations for clinical trial design in acute kidney injury from the 31st acute disease quality initiative consensus conference. A consensus statement

Alexander Zarbock[1,2*], Lui G. Forni[3,4], Jay L. Koyner[5], Samira Bell[6], Thiago Reis[7,8,9], Melanie Meersch[1], Sean M. Bagshaw[10], Dana Y. Fuhmann[11,12,13], Kathleen D. Liu[14], Neesh Pannu[15], Ayse Akcan Arikan[16], Derek C. Angus[13], D'Arcy Duquette[17], Stuart L. Goldstein[18], Eric Hoste[19], Michael Joannidis[20], Niels Jongs[21], Matthieu Legrand[22], Ravindra L. Mehta[23], Patrick T. Murray[24], Mitra K. Nadim[25], Marlies Ostermann[26], John Prowle[27], Emily J. See[28,29,30], Nicholas M. Selby[31], Andrew D. Shaw[32], Nattachai Srisawat[33], Claudio Ronco[34,35,36] and John A. Kellum[12,13]

Design of AKI Trials

Review Article | Published: 31 August 2023

Designing acute kidney injury clinical trials

Alexander Zarbock, Lui G. Forni, Marlies Ostermann, Claudio Ronco, Sean M. Bagshaw, Ravindra L. Mehta, Rinaldo Bellomo & John A. Kellum

Nature Reviews Nephrology **20**, 137–146 (2024) | Cite this article

Home > Intensive Care Medicine > Article

Randomised clinical trials in critical care: past, present and future

Review | Published: 02 December 2021

Volume 48, pages 164–178, (2022) Cite this article

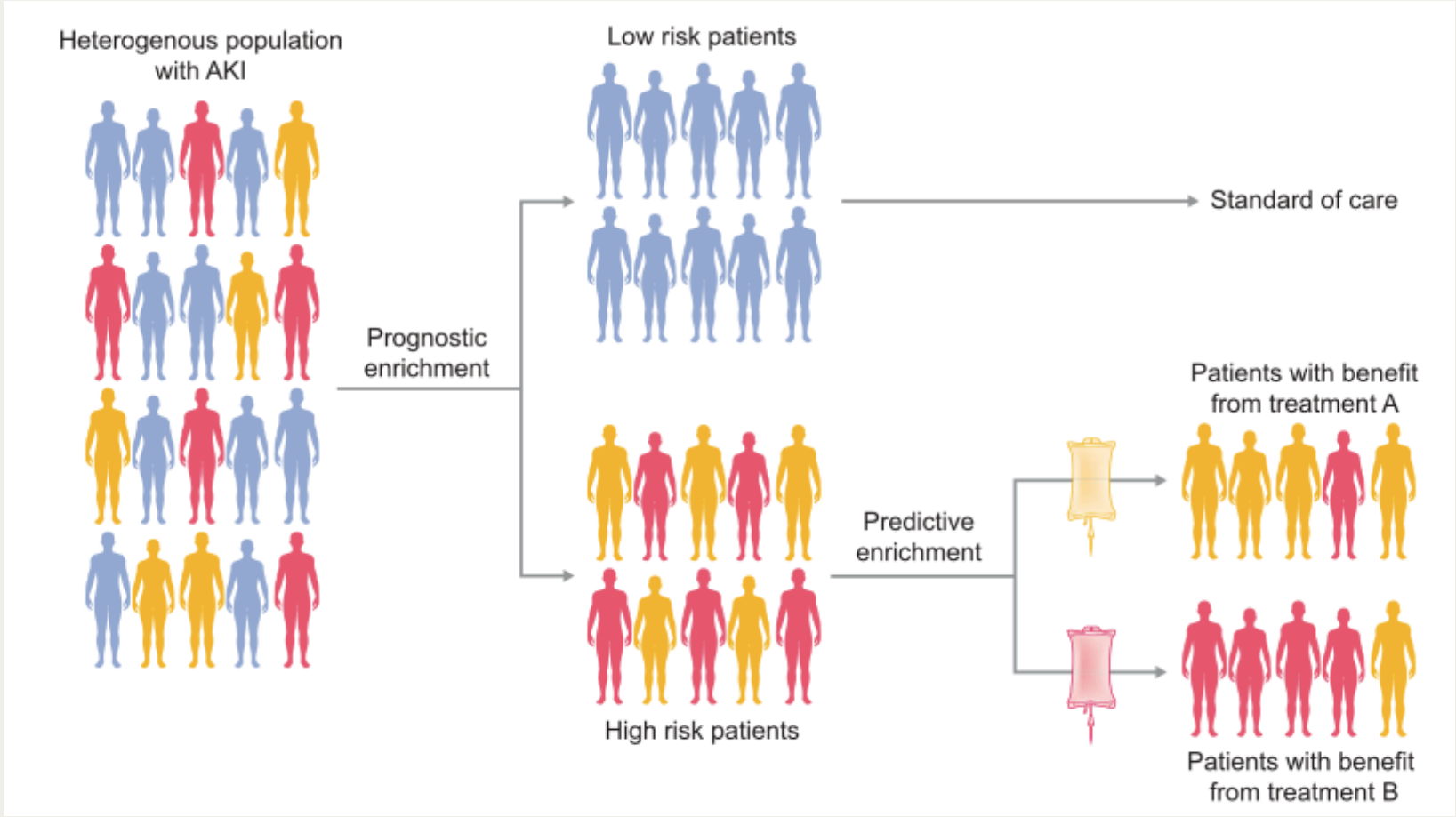
Patient Preferences and Priorities for the Design of an Acute Kidney Injury Prevention Trial

Findings from a Consensus Workshop

Meghan J. Elliott[1,2] Kirsten M. Fiest[2,3] Shannan Love,[1] Dale Birdsell,[4] Maureena Loth,[4] Heather Dumka,[4] Benny Rana,[3] Nusrat Shommu[1] Eleanor Benterud[1] Sarah Gil[1] Dilaram Acharya[1] Tyrone G. Harrison[1,2] Neesh Pannu[5] and Matthew T. James[1,2]

Elliott, Meghan J., et al. "Patient Preferences and Priorities for the Design of an AKI Prevention Trial: Findings from a Consensus Workshop." *Kidney360* (2024): 10-34067.

Prognostic and Predictive Enrichment



Lazzareschi, Daniel, et al. "Overcoming barriers in the design and implementation of clinical trials for acute kidney injury: a report from the 2020 Kidney Disease Clinical Trialists meeting." Nephrology Dialysis Transplantation 38.4 (2023): 834-844.

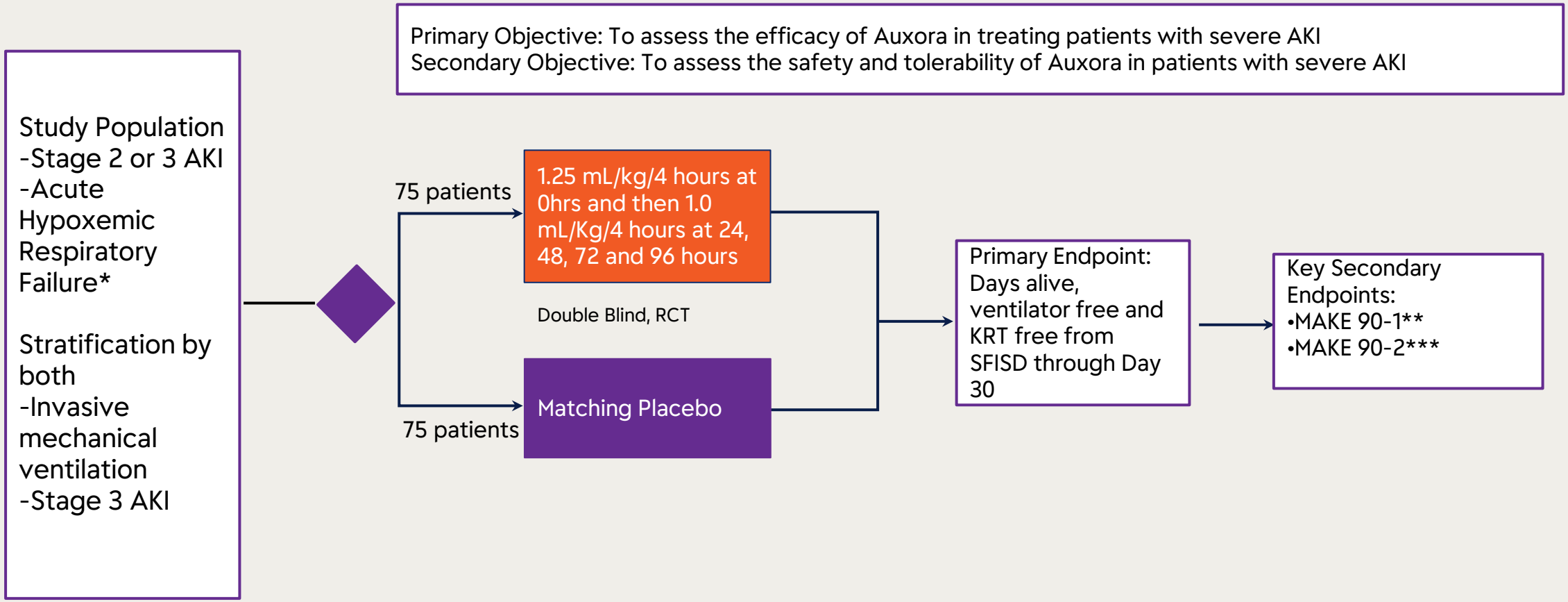
Outcomes

Prevention Trials[#]		Treatment Trials	
Endpoints	Clinical Trial Phase	Endpoints	Clinical Trial Phase
• Molecular biomarkers of kidney injury	1 or 2	• Rate of change in GFR	2
• Physiological biomarkers such as urinary oxygen tension	1 or 2	• Sustained change in GFR	2
• Molecular biomarkers of kidney injury or kidney function	2	• Change in biomarker values specific for kidney damage	2
• Renal functional reserve (physiological biomarker)	2	• Change in genomic or metabolomic variables	2
		• Change in levels of inflammatory mediators	2
		• Presence or progression of protenuria	2
• Stage of AKI	3	• Major Adverse Kidney Events	3 or 4
• AKI duration	3	• Days free of organ support therapies:	3 or 4
• Transition from AKI to acute kidney disease	3	-Renal replacement therapy free days -Invasive mechanical ventilation free days -Intensive care/hospital fre and alive days	
• Development or worsening of chronic kidney disease based on molecular biomarkers such as albuminuria	4	• Death	3 or 4
• Development or worsening of chronic kidney disease based on clinical endpoints such as eGFR (or eGFR slope) or reduction of eGFR by 50%	4	• AKI trajectories	3 or 4
		• Dialysis	3 or 4
		• Hospital readmission	3 or 4
• Development or worsening of chronic kidney disease based on clinical endpoints such as need for diasysis or kidney death	4	• eGFR reduction or CKD progression	3 or 4

Fig. 1 Different endpoints should be used in AKI trials on the bases of the type of intervention (prevention or treatment study) and the clinical trial phase (phase 1, 2, 3, or 4). [#] Endpoints that are used for phase 3 trials may also be used as endpoint in phase 4 trials

Zarbock, Alexander, et al. "Recommendations for clinical trial design in acute kidney injury from the 31st acute disease quality initiative consensus conference. A consensus statement." Intensive Care Medicine 50.9 (2024): 1426-1437.

Auxora for the Treatment of AKI and Modulation of Injurious "Crosstalk" with the Lung: A Randomized Control Trial (KOURAGE) NCT06374797



*AHRF will be defined as a P/F ≤ 300 that has been determined by either an arterial blood gas or imputed from the oxygen saturation (SpO2) recorded using pulse oximetry and is being treated with high flow nasal cannula with minimum flow rate ≥ 30 liters/min, or non-invasive mechanical ventilation, or invasive mechanical ventilation
**MAKE 90-1: ≥ 25% decline in eGFR from baseline, incident KRT, and all-cause mortality at 90 days
***MAKE 90-2: ≥ 35% decline in eGFR from baseline, incident KRT, and all-cause mortality at 90 days

Outcomes in AKI Trials

Intensive Care Med (2024) 50:1049–1063
https://doi.org/10.1007/s00134-024-07480-x

NARRATIVE REVIEW

Heterogeneity in the definition of major adverse kidney events: a scoping review

Akinori Maeda[1,2], Ryota Inokuchi[2,3], Rinaldo Bellomo[1,4,5,6,7] and Kent Doi[2*]

- Is incident dialysis equivalent to death?
- 36.4% different dialysis definitions!
- Is a 25% decrease in eGFR in a stage 1 patient the same as in a stage 3 patient?
- Muscle mass and critical illness!!!!

Intensive Care Med
https://doi.org/10.1007/s00134-024-07602-5

CORRESPONDENCE

Major adverse kidney events as an endpoint in acute kidney injury trials: is it time for a RE-MAKE?

Dana Y. Fuhrman[1*], Sean M. Bagshaw[2], Stuart L. Goldstein[3], Matthieu Legrand[4] and Andrew D. Shaw[5]

- Hierarchical composite using endpoints important to PWLE
- Statistically evaluated by win ratio:
- Mortality
- AKI
- Nonrecovery from AKI and dialysis dependency
- GFR slope

Maeda, Akinori, et al. "Heterogeneity in the definition of major adverse kidney events: a scoping review." Intensive Care Medicine 50.7 (2024): 1049-1063.
Fuhrman, Dana Y., et al. "Major adverse kidney events as an endpoint in acute kidney injury trials: is it time for a RE-MAKE?." Intensive Care Medicine 50.10 (2024): 1723-1724.

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Experiences With Conduct of an AKI Clinical Trial:

Diagnosis of AKI Patient Population

KDIGO Definition of AKI

KDIGO Classification of AKI

Stage	Serum Creatinine	Urine Output
1	≥ 0.3 mg/dL within 48 hours or 1.5 to 1.9 times baseline creatinine within prior 7 days	< 0.5 mL/kg/hour for ≥ 6 hours to < 12 hours
2	2.0 to 2.9 times baseline creatinine within prior 7 days	< 0.5 mL/kg/hour for ≥ 12 hours
3	≥ 3.0 times baseline creatinine within prior 7 days or ≥ 4.0 mg/dL or initiation of kidney replacement therapy	< 0.3 mL/kg/hour for ≥ 24 hours or anuria ≥ 12 hours

Community Acquired AKI: Baseline Creatinine >7 Days

- "In general, it is reasonable in patients without CKD to assume that SCr will be stable over several months or even years, so that a SCr obtained 6 months or even 1 year previously would reasonably reflect the patient's premorbid baseline."
- Protection Trial
  - Eligible patients had to have a baseline serum creatinine measurement before surgery — the most recently available measurement before randomization, obtained either during the current hospitalization or within 365 days before the current hospitalization.

- Should the prohibition on using an outpatient baseline creatinine in patients with CKD apply to patients with CKD Stages 1 and 2?

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-Chapter 2.4 Clinical Applications KDIGO Group. "KDIGO clinical practice guideline for acute kidney injury." Kidney Int. Suppl. 2 (2012): 1.
-Landoni, Giovanni, et al. "A randomized trial of intravenous amino acids for kidney protection." The New England journal of medicine 391.8 (2024): 687-698.

Overdiagnosis of CKD in Elderly Adults

Research

JAMA Internal Medicine | Original Investigation | LESS IS MORE

Accounting for Age in the Definition of Chronic Kidney Disease

Ping Liu, PhD; Rob R. Quinn, MD, PhD; Ngan N. Lam, MD, MSc; Meghan J. Elliott, MD, MSc; Yuan Xu, MD, PhD; Matthew T. James, MD, PhD; Braden Manns, MD, MSc; Pietro Ravani, MD, PhD

Invited Commentary

LESS IS MORE

Overdiagnosis of Chronic Kidney Disease in Older Adults—An Inconvenient Truth

Ann M. O'Hare, MA, MD; Rudolph A. Rodriguez, MD; Andrew D. Rule, MD, MS

Revival median age: 70
Protection median age: 66
Thrasos median age: 71-74

- Modeled the pragmatic implications of an alternative definition of CKD based on age-specific eGFR cut points for cohort members without significant albuminuria (<45 mL/min/1.73 m2 for those aged ≥65 years, <60 mL/min/1.73 m2 for those aged 40-64 years, and <75 mL/ min/1.73 m2 for those aged <40 years).
- The size of the affected population shrank by more than one-third (from 127 132 to 81 209 cohort members)
- This reduction in the size of the affected population was largely driven by a reclassification of older adults with isolated mild to moderate reductions in eGFR (75% of reclassified cohort members were age ≥65 years and had an eGFR of 45-59 mL/ min/1.73 m2).
- Those who are reclassified as having normal kidney function do not have a meaningfully higher risk of death or kidney failure

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Liu, Ping, et al. "Accounting for age in the definition of chronic kidney disease." JAMA internal medicine 181.10 (2021): 1359-1366.
O'Hare, Ann M., Rudolph A. Rodriguez, and Andrew D. Rule. "Overdiagnosis of chronic kidney disease in older adults—an inconvenient truth." JAMA internal medicine 181.10 (2021): 1366-1368.

Community Acquired AKI: No Baseline Creatinine

- Many patients will present with AKI without a reliable baseline SCr on record. Baseline SCr can be estimated using the Modification of Diet in Renal Disease (MDRD) Study equation assuming that baseline eGFR is 75 ml/min per 1.73 m^2.

Table 9 | Estimated baseline SCr

Age (years)	Black males mg/dl (μmol/l)	Other males mg/dl (μmol/l)	Black females mg/dl (μmol/l)	Other females mg/dl (μmol/l)
20–24	1.5 (133)	1.3 (115)	1.2 (106)	1.0 (88)
25–29	1.5 (133)	1.2 (106)	1.1 (97)	1.0 (88)
30–39	1.4 (124)	1.2 (106)	1.1 (97)	0.9 (80)
40–54	1.3 (115)	1.1 (97)	1.0 (88)	0.9 (80)
55–65	1.3 (115)	1.1 (97)	1.0 (88)	0.8 (71)
>65	1.2 (106)	1.0 (88)	0.9 (80)	0.8 (71)

Estimated glomerular filtration rate=75 (ml/min per 1.73 m^2)=186 × (serum creatinine [S_{Cr}]) − 1.154 × (age) − 0.203 × (0.742 if female) × (1.210 if black)=exp(5.228 − 1.154 × ln [S_{Cr}]) − 0.203 × ln(age) − (0.299 if female) + (0.192 if black).

Reprinted from Bellomo R, Ronco C, Kellum JA *et al.* Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004; 8: R204-212 with permission from Bellomo R *et al.*[22]; accessed http://ccforum.com/content/8/4/R204

- This approach is likely the most sensitive for detecting AKI among patients with no premorbid serum creatinine value and is anticipated to work well in populations with largely preserved kidney function.
- Will this "estimation" meet the rigorous standard needed for prospective trials needed for drug approval?

Chapter 2.4 Clinical Applications KDIGO Group. "KDIGO clinical practice guideline for acute kidney injury." Kidney Int. Suppl. 2 (2012): 1.

KDIGO Definition of AKI

KDIGO Classification of AKI

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Urine Output

- “Is it the mean urine output over the number of hours in the KDIGO or does it mean for every hour”?
- "Association of oliguria with acute kidney injury diagnosis, severity assessment, and mortality among patients with critical illness." JAMA network open 4.11 (2021): e2133094-e2133094., the authors state that they assessed urine output in the following manner:
  - "For every single hour of each ICU stay, we computed a 6-hour mean corresponding to the mean UO measured within the previous 6 hours. Similarly, we calculated a 12-hour mean (mean UO measured within the previous 12 hours) and a 24-hour mean (mean UO within the previous 24 hours)."

Importance of Urine Output in Assessing Risk

By Serum Creatinine ↓				
Stage 3	371 (11.6)	321 (38.6)	1019 (28.0)	2200 (51.1)
Stage 2	618 (11.3)	476 (23.9)	1553 (21.5)	831 (44.2)
Stage 1	1889 (8.0)	1262 (11.3)	3485 (13.0)	842 (32.1)
No AKI	8179 (4.3)	3158 (5.3)	5421 (7.9)	440 (17.7)
By Urine Output →	No AKI	Stage 1	Stage 2	Stage 3

32,045 patients treated between 2000 and 2008, of which 23,866 (74.5%) developed AKI.
Number of patients with Stage 1 AKI: 6,309
3158 urine output alone (50%)
Number of patients with Stage 2 AKI: 11,553
8906 reach stage 2 by urine output alone (77%)
Number of patients with Stage 3 AKI: 6,024
2113 reach stage 3 by urine output alone (35%)

Kellum, John A., et al. "Classifying AKI by urine output versus serum creatinine level." Journal of the American Society of Nephrology 26.9 (2015): 2231-2238.

Importance of Urine Output in Assessing Risk

AKI sCr stage, No. (90-d mortality, %)	No AKI	Stage 1	Stage 2	Stage 3
Stage 3	141 (13.67)	106 (33.02)	422 (29.52)	1184 (49.96)
Stage 2	185 (19.57)	176 (24.00)	622 (26.61)	255 (35.83)
Stage 1	663 (18.06)	571 (19.65)	1802 (21.75)	386 (32.81)
No AKI	**3477 (8.32)**	1793 (12.39)	**3544 (12.49)**	293 (21.23)

15,620 ICU patients between 2010 and 2020
12,143 developed AKI
Number of patients with Stage 1 AKI: 3,027
1793 urine output alone (59%)
Number of patients with Stage 2 AKI: 6329
5346 urine output alone (84%)
Number of patients with Stage 3 AKI: 2787
934 urine output alone (34%)

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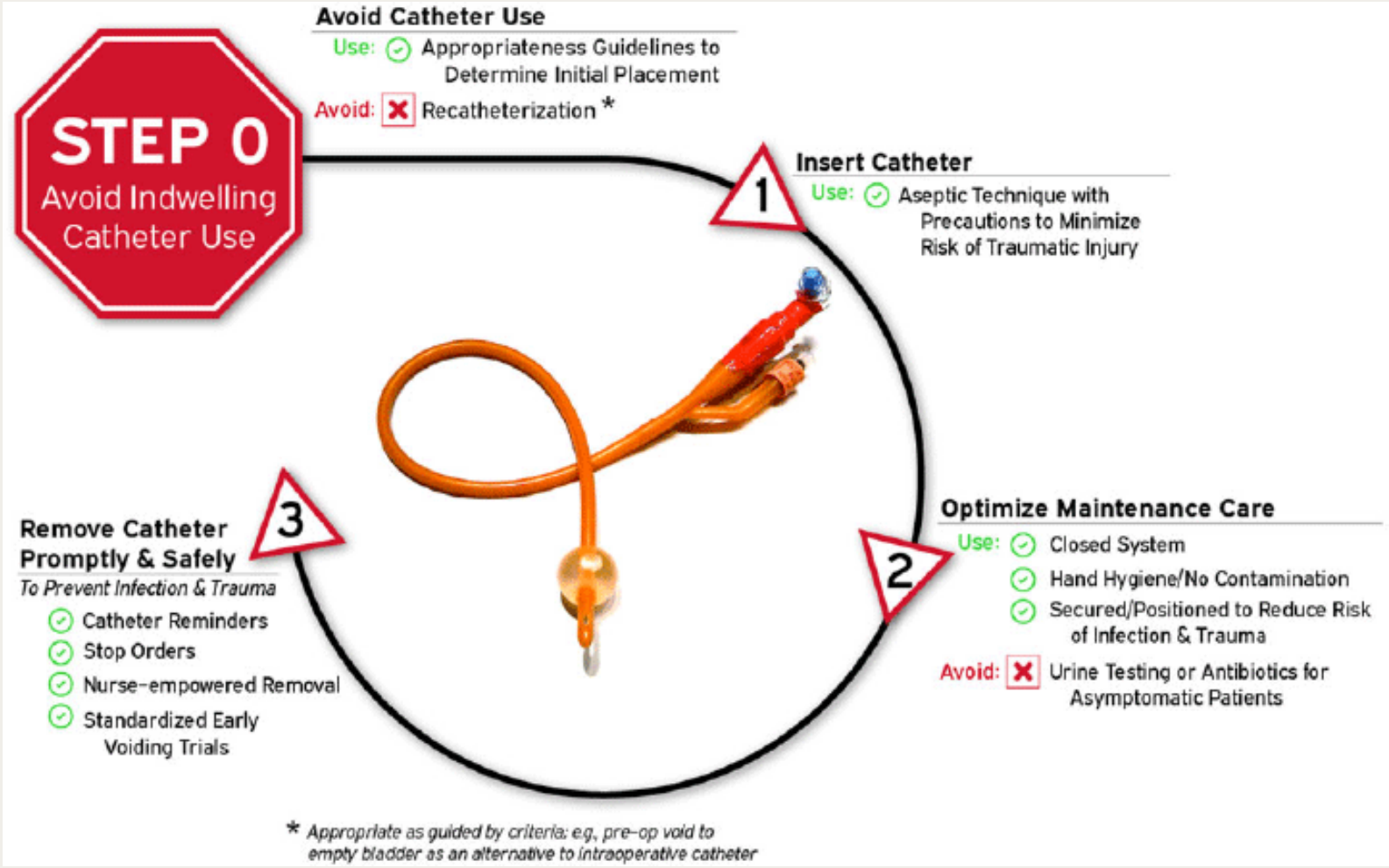
Bianchi, Nathan Axel, et al. "Association of oliguria with acute kidney injury diagnosis, severity assessment, and mortality among patients with critical illness." JAMA network open 4.11 (2021): e2133094-e2133094.

AHQR CAUTI Recommendations



Patel, Payal K., et al. "Strategies to prevent catheter-associated urinary tract infections in acute-care hospitals: 2022 Update." Infection Control & Hospital Epidemiology 44.8 (2023): 1209-1231.

No AKI by Urine Output in Many Studies

- Protection Trial: LIMITATIONS AND REMAINING QUESTIONS
  - Serum creatinine level alone was used to diagnose AKI because urinary catheters are typically removed within 48 to 72 hours after surgery.
- Development of a multicenter ward–based AKI prediction model
  - We were not able to apply the urine output portion of the AKI criteria to our cohort; however, this is a common limitation of many large–scale investigations of inpatient AKI, because the ability to amass and analyze hourly urine outputs is difficult.
- A Clinically Applicable Approach to Continuous Prediction of Future Acute Kidney Injury
  - The first two definitions were used to provide ground truth labels for the onset of an AKI; the third definition could not be used as urine output was not recorded digitally in the majority of sites that formed part of this work.
- Electronic health record alerts for acute kidney injury: multicenter, randomized clinical trial
  - Owing to missing and inaccurate urine output data, urine output was not used to classify acute kidney injury.
- Automated Electronic Alert for the Care and Outcomes of Adults With Acute Kidney Injury
  - Fourth, since most patients do not record urine output during hospitalization, the KDIGO creatinine standard was used to design AKI alerts, which may underestimate the actual incidence of AKI.

-Koyner, Jay L., et al. "Development of a multicenter ward–based AKI prediction model." Clinical Journal of the American Society of Nephrology 11.11 (2016): 1935-1943.
-Tomašev, Nenad, et al. "A clinically applicable approach to continuous prediction of future acute kidney injury." Nature 572.7767 (2019): 116-119.
-Wilson, F. Perry, et al. "Electronic health record alerts for acute kidney injury: multicenter, randomized clinical trial." bmj 372 (2021).
-Li, Ting, et al. "Automated electronic alert for the care and outcomes of adults with acute kidney injury: a randomized clinical trial." JAMA network open 7.1 (2024): e2351710-e2351710.

CKD Patient with AKI

- How to diagnose AKI in a patient with CKD using changes in serum creatinine?
  - Different criteria needed?
    - Stage 1: a 0.3-mg/dl increase over 24 h or a 0.5-mg/dl increase over 48 h
    - Stage 2: a 0.5-mg/dl increase over 24 h or a 1.0-mg/dl increase over 48 h
    - Stage 3: a 1.0-mg/dl increase over 24 h or a 1.5-mg/dl increase over 48 h
  - Emphasize urine output!!!!
- Patients with CKD are often excluded in trials of AKI therapeutics
  - REVIVAL: severe CKD (eGFR <25 mL/min/1.73 m^2) were excluded at some sites and moderate to severe CKD at other sites (eGFR <45 mL/min/1.73 m^2)
  - TIN816: History of CKD with a documented estimated GFR <45 mL/min prior to admission to hospital
  - Protection: Patients with chronic kidney disease (CKD) of equal or more than CKD stage IV* (glomerular filtration rate (GFR) <30 ml/min/1.73 m2)
  - Thrasos: exclusion of eGFR <20
  - KOURAGE: no exclusion

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Waikar, Sushrut S., and Joseph V. Bonventre. "Creatinine kinetics and the definition of acute kidney injury." Journal of the American Society of Nephrology 20.3 (2009): 672-679.
https://clinicaltrials.gov/study/NCT04411472?cond=AKI&term=am%20pharma&rank=2&tab=table
https://clinicaltrials.gov/study/NCT05996835?cond=AKI&term=novartis&rank=1&tab=table

Thrasos AKI Trial

- THR-184:
  - eGFR ≥ 20 and < 30 ml/min/1.73m2 OR
  - eGFR ≥ 30 and < 60 ml/min/1.73m2 and ONE of the following additional risk factors (other than age ≥ 75 years) OR
  - eGFR ≥ 60 ml/min/1.73m2 and TWO of the following additional risk factors
- Risk Factors
  - Age ≥ 75 years;
  - Combined valve & coronary surgery;
  - Previous cardiac surgery with sternotomy;
  - Documented NYHA Class III or IV within 1 year prior to surgery;
  - Left ventricular ejection fraction (LVEF) ≤ 35% by invasive or noninvasive diagnostic cardiac imaging - echocardiography, nuclear imaging, computed tomography, magnetic resonance imaging or angiography performed within 90 days prior to surgery. (If LVEF ≤ 35% by any invasive or noninvasive imaging procedure, patient meets the risk factor.)
  - Insulin-requiring diabetes;
  - Non-insulin-requiring diabetes and the presence of ≥+2 proteinuria on urinalysis (medical history or dipstick);
  - Preoperative anemia (hemoglobin <11g/dl for men and women).

https://clinicaltrials.gov/study/NCT01830920?cond=AKI&term=thrasos&rank=1&tab=table

CKD and Prognostic Enrichment

- Thrasos trial, AKI occurred in 78% of placebo patients.
  - 113 patients randomized to placebo
    - Median eGFR 59.5 IQR (44-79)
  - 57 patients randomized to placebo with eGFR <60
    - AKI KDIGO definition 86%
    - AKI KDIGO definition Scr only: 68.4%
- Protection trial, 31.7% of placebo group developed AKI
  - 1752 patients randomized to placebo
    - 597 stage 1 (21% developed AKI)
    - 747 stage 2 (30% developed AKI)
    - 408 Stages 3-5 (50% developed AKI)

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Landoni, Giovanni, et al. "A randomized trial of intravenous amino acids for kidney protection." The New England journal of medicine 391.8 (2024): 687-698.
Himmelfarb, Jonathan, et al. "Perioperative THR-184 and AKI after cardiac surgery." Journal of the American Society of Nephrology 29.2 (2018): 670-679.

Revival MAKE90 Predicted Probability

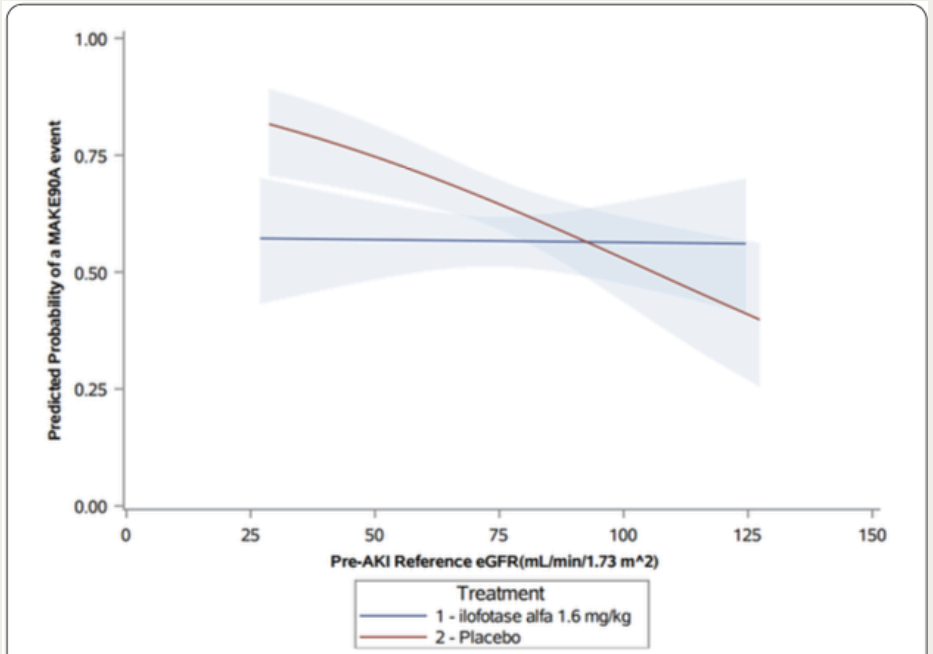

Fig. 2 Predicted probability of an MAKE90A event with 95% confidence limits. Predicted probabilities are taken from the results of the logistic regression model which included "MAKE through day 90" as the outcome of interest, and treatment, pre-AKI reference eGFR, and pre-AKI reference eGFR by treatment interaction (*p* for interaction = 0.0235). Patients who did not meet the criteria for having a confirmed "MAKE through day 90" event are assumed to not have a "MAKE through day 90" event in the logistic regression model

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Pickkers, Peter, et al. "Phase-3 trial of recombinant human alkaline phosphatase for patients with sepsis-associated acute kidney injury (REVIVAL)." Intensive care medicine 50.1 (2024): 68-78.

AKI Algorithm KOURAGE