data, and the assessment of renal recovery was dependent on clinical collection of blood samples, which risks ascertainment bias (i.e., patients more at nonrecovery risk are also those more likely to have a Cr follow-up check). Patients without preceding baseline values who may have had AKI were excluded, potentially reducing the reported AKI incidence and favoring the exclusion of community-acquired AKI more than that of hospital-acquired AKI; the 2 may not have the same outcomes.

In conclusion, the study by Holmes *et al.* adds to published data showing that AKI is common in pediatric and neonatal patients. AKI is associated with adverse outcomes, and we can speculate that earlier diagnosis and treatment may reduce the number of patients who subsequently develop CKD, although we currently lack data on interventions proven to influence outcome. However, there is an essential need to develop strategies and resources that will allow better AKI stratification as currently defined by Cr-based criteria, which will lead to risk ascertainment on an individual patient basis and ultimately to personalized approaches for AKI management and follow-up.

DISCLOSURE
All the authors declared no competing interests.

REFERENCES

1. Sutherland SM, Ji J, Sheikhi FH, et al. AKI in hospitalized children: epidemiology and clinical associations in a national cohort. *Clin J Am Soc Nephrol*. 2013;8:1661–1669.
2. Sutherland SM, Byrnes JJ, Kothari M, et al. AKI in hospitalized children: comparing the pRIFLE, AKIN, and KDIGO definitions. *Clin J Am Soc Nephrol*. 2015;10:554–561.
3. Nada A, Bonachea EM, Askenazi DJ. Acute kidney injury in the fetus and neonate. *Semin Fetal Neonatal Med*. 2017;22:90–97.
4. McGregor TL, Jones DP, Wang L, et al. Acute kidney injury incidence in noncritically Ill hospitalized children, adolescents, and young adults: a retrospective observational study. *Am J Kidney Dis*. 2016;67:384–390.
5. Holmes J, Roberts G, May K, et al. The incidence of pediatric acute kidney injury is increased when identified by a change in a creatinine-based electronic alert. *Kidney Int*. 2017;92:432–439.
6. Selby NM, Hill R, Fluck RJ. Standardizing the early identification of AKI: the NHS England national patient safety alert. *Nephron*. 2015;131:113–117.
7. Sawhney S, Fluck N, Marks A, et al. Acute kidney injury-how does automated detection perform? *Nephrol Dial Transplant*. 2015;30:1853–1861.
8. Ali T, Khan I, Simpson W, et al. Incidence and outcomes in acute kidney injury: a comprehensive population-based study. *J Am Soc Nephrol*. 2007;18:1292–1298.
9. Basu RK, Wang Y, Wong HR, et al. Incorporation of biomarkers with the renal angina index for prediction of severe AKI in critically ill children. *Clin J Am Soc Nephrol*. 2014;9:654–662.

Outcomes and renal function trajectory after acute kidney injury: the narrow road to perdition

Steven G. Coca[1]

Analyses of the Grampian Laboratory Outcomes Morbidity and Mortality Study-II cohort support the notion that acute kidney injury (AKI) increases the risk of progression of glomerular filtration rate after recovery from AKI to a new baseline. However, the findings have to be considered in the bigger context of the absolute event rates for *de novo* progression versus nonrecovery and the competing risk of death after AKI. Examination of the data raises important implications for the design and implementation of clinical trials with interventions that target the AKI-to–chronic kidney disease transition.

Kidney International (2017) **92,** 288–291; http://dx.doi.org/10.1016/j.kint.2017.03.044

see clinical investigation on page 440

The epidemiology of acute kidney injury (AKI) and subsequent long-term outcomes has been extensively studied, particularly over the last 15 years. It is now well known that AKI is independently associated with risk of death, cardiovascular events, incident chronic kidney disease (CKD), and progressive CKD. Epidemiology can serve as a tool to determine resources for investment, in both basic science research and clinical trials. Indeed, tantalizing and intriguing pathophysiology has emerged that has elucidated the mechanisms of CKD progression after AKI.[1] Elegant work in experimental animals has highlighted the role of maladaptive repair and endothelial injury leading to vascular dropout and kidney hypoxia, resulting in a vicious cycle of interstitial fibrosis and glomerular filtration rate (GFR) decline.[1,2] It is the hope of all scientists and clinicians that a better understanding of the AKI–to-CKD transition would eventually lead to the discovery and implementation of a therapy to prevent its progression. In fact, several opinion leaders have deemed the AKI-to-CKD transition as the most appealing window of opportunity to identify efficacious peri-AKI interventions,[3–5] as opposed to preventive strategies (plagued by low incidence rates necessitating huge sample sizes) or interventions during the AKI episode (complicated by acute illness and the need for adjusting treatment timing based on the injury, depending on the mechanism of action of the drug).

[1]*Division of Nephrology, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York, USA*

Correspondence: *Steven G. Coca, One Gustave Levy Place, Box 1243, New York, New York 10029, USA. E-mail: steven.coca@mssm.edu*

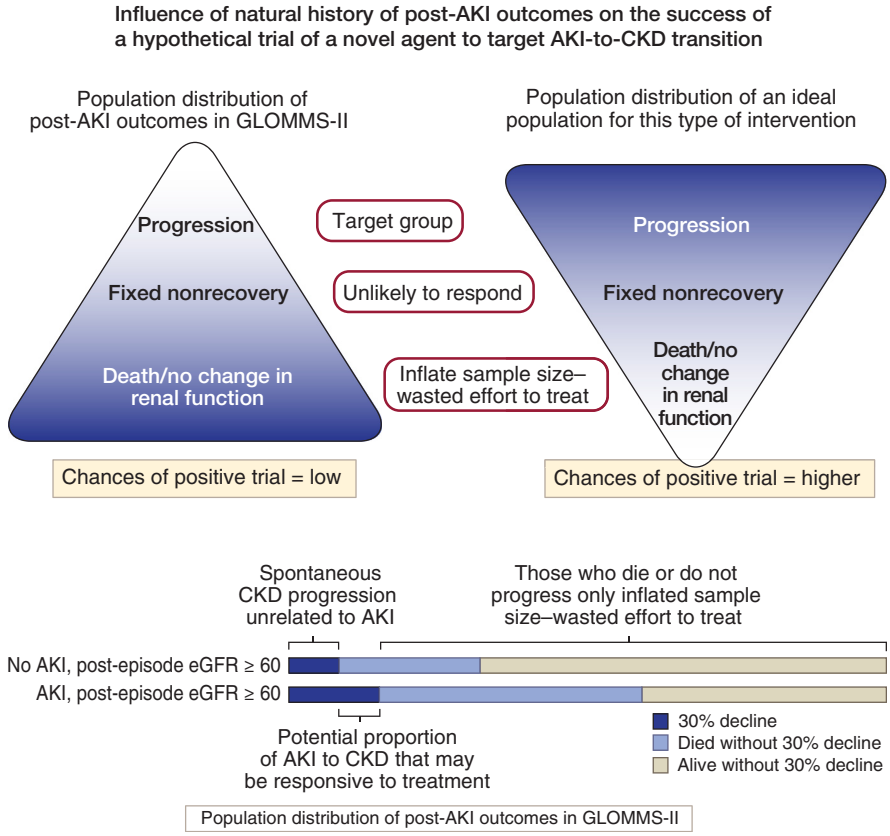

Figure 1 | Influence of natural history of post–acute kidney injury (AKI) outcomes on the success of a hypothetical trial of a novel agent targeting AKI-to-chronic kidney disease (CKD) transition. GLOMMS-II, Grampian Laboratory Outcomes Morbidity and Mortality Study-II.

However, much of the previous clinical literature has not been sufficiently stringent in meticulously identifying the extent by which CKD after AKI results from an irreversible fixed defect due to nonrecovery from tubular injury manifesting as a steep drop and plateau of renal function at a new baseline versus *de novo* progression after recovery from AKI.[4] Understanding the relative contributions of these very different pathways to CKD is important for caring of patients after AKI and potentially designing new trials.

Sawhney *et al.*(2017) aimed to determine this distinction among after AKI trajectories by using the Grampian Laboratory Outcomes Morbidity and Mortality Study-II (GLOMMS-II), a population-based virtual cohort of the Grampian population of 438,332 individuals.[6] Patients admitted in 2003 (n = 17,630) and who survived up to 1 year post-hospitalization without estimated GFR (eGFR) of <30 ml/min per 1.73 m^2 or end-stage renal disease were included in the final analysis cohort (n = 14,106). The investigators demonstrated that AKI increased the risk of progression of CKD after AKI after achieving a new post-AKI baseline level of kidney function, supporting the basic notion that fibrosis is the end result of maladaptive repair after AKI. The adjusted hazard ratios for renal function decline among patients with and without AKI was 2.3 in those with post-AKI eGFR of >60 and 1.5 in those with baseline eGFR of 45 to 59. One of the most novel aspects of this project was the assessment of the renal function trajectory after achieving post-AKI new baseline, which for analysis purposes, was determined at 1-year post-hospital discharge to enable full recovery after the episode.[7] Other notable strengths of their analyses exist. The GLOMMS-II cohort has granular and comprehensive cohort data (inpatient, outpatient, and community), and all laboratory tests are provided by a single service; these limit concerns for missing data or variations among different laboratories. Since the cohort inception was in 2003, there was an approximate median follow-up of 8 years. The investigators used 2 separate definitions for renal progression: one employing a relative change that sustained a 30% decline (in line with relatively recent recommendations from National Kidney Foundation and US Food and Drug Administration as an acceptable endpoint) and the other achieving a CKD stage 4 status. Multiple sensitivity analyses were also performed to validate the findings in various subgroups and between subjects with and without missing data.

While the investigators should be applauded for trying to assess post-AKI GFR trajectories from a different aspect, data reported are also enlightening from a clinical and public