

# Temporal Trends in AKI: Insights from Big Data

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“Hiding within these mounds of data is knowledge that could change the life of a patient or change the world.” This quote by Atul Butte, a preeminent data scientist, perfectly encapsulates the alluring promise of big data for biomedical research. Using large, national administrative datasets is attractive to epidemiologic researchers for a variety of reasons. They allow for many more observations than would be feasible with primary data collection, they allow researchers to conduct sophisticated multilevel analyses because of a large sample size, and they require little to no institutional review board approval. In addition, because of their representative nature, trends and observations obtained from these datasets are likely to generalize nationally.

The Nationwide Inpatient Sample (NIS), maintained by the Agency for Healthcare Research and Quality, is such a database. It contains data on hospitalizations at about 1000 hospitals across the United States, comprising a 20% sample of hospitals (1,2). The sampling varies from year to year. Sampling is stratified across five criteria (geographic region, public versus private, urban versus rural, teaching versus nonteaching, and bed size). Data available through the NIS include patient demographics, The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnoses and procedures, hospital charges and length of stay, discharge disposition, anonymous physician and hospital identifiers, and hospital characteristics (*e.g.*, geographic region, teaching status, and bed size).

AKI is common in hospitalized patients and can affect >5% of hospitalizations, and it is associated with high morbidity and mortality (3). Moreover, there is growing evidence that sequelae of AKI include poor long-term survival, increased risk of readmissions, incident and worsening CKD, and progression to ESRD (4–6). These consequences also lead to increased disability, decreased quality of life, and disproportionate burden on health care resources. The incidence of nondialysis-requiring AKI has increased when assessed in either communities or hospitalized patients (7). Most studies on the temporal trends of AKI requiring dialysis (AKI-D) were restricted to certain geographic regions and/or critical care settings (8–10).

The use of national databases for AKI epidemiology research has been restricted by the poor validity of administrative codes (11). By using an innovative approach in the NIS, combining diagnosis and procedure codes capturing AKI-D incidence with high fidelity and using the US Census data, Hsu *et al.* (12) showed in 2013 that the population-level incidence rates of AKI-D

increased by >10% per year, with a near tripling in the absolute number of annual patients. However, adjustment for AKI risk factors, including acute heart failure, sepsis, and critical illness, and cardiac catheterizations only explained a fraction of this rise.

In this issue of the *Clinical Journal of the American Society of Nephrology*, Hsu *et al.* (13) build on their prior work by attempting to explain the reasons responsible for the temporal rise in AKI-D. Hsu *et al.* (13) again show that, from 2007 to 2009, the population incidence of AKI-D increased by 11% per year. Hsu *et al.* (13) also used the clinical classifications software to group a large variety of ICD-9-CM codes into clinically relevant categories, showing that temporal trends in acute and chronic disease categories (sepsis, hypertension, respiratory failure, coagulation/hemorrhagic disease, shock, and liver disease) accounted fully for this rise in AKI-D. Changes in procedures did not contribute to the rise in AKI-D. In addition, even if they excluded admissions with a concurrent diagnosis of ESRD, thus minimizing misclassification of hospitalizations, this temporal increase persisted.

Hsu *et al.* (13) need to be commended for conducting a rigorous and statistically complex study to identify predictors of increasing trends in AKI-D. This is especially important in a time when the public health burden of AKI and attendant CKD has attained critical importance. With the failure of several therapies aimed at preventing worsening of AKI (14), acute intermittent and continuous RRTs remain the cornerstone of severe AKI management. However, we may have approached a therapeutic threshold for both intermittent and continuous RRTs, beyond which there is no benefit to intensifying dialysis (15,16). Thus, early identification of those patients with AKI who are likely to worsen and need RRT as well as those who are likely to recover is of paramount importance from a public health perspective. This paper represents a strong effort to outline in broad strokes the comorbidities responsible for the increase in AKI-D (13).

The analysis, however, has limitations, most of which are representative of any analysis using large datasets (13). Although the NIS is a large dataset, it is not granular, lacking laboratory measurements, readmission information, and long-term outcomes. Thus, determination of whether this increasing trend is indicative of true rise in disease versus earlier initiation of dialysis by physicians is yet to be determined, although ascertainment of dialysis need by creatinine-based criteria is inadequate at best. In addition, the comorbidities explaining the rise were determined by administrative codes, which have varying

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validity, especially with chronic comorbidities (17). Also, the NIS data lack longitudinal information, and being deidentified, they lack linkage to other registries (including the US Renal Data System); thus, long-term ESRD outcomes cannot be defined with AKI-D.

In addition, this study presents an enigma (13). Although the prevalence rate of ESRD has been increasing (likely because of improved life expectancy), the incidence rate has been stable since 2010 (18). Thus, if AKI-D raises ESRD risk (as evidenced by several other epidemiologic studies) (19,20) and if incident AKI-D is on the rise, which this study indicates, why is the annual incidence rate of ESRD not rising in parallel? This might be possible if AKI-D conferred such an excess risk of mortality that patients died before getting to ESRD. However, the excess mortality attributed with AKI and AKI-D has been stable or declining (9). The second possibility is that, because AKI begets AKI (21,22), AKI-D increases the risk of additional admissions with AKI-D (even with recovery of renal function), and thus, the number of AKI-D hospitalizations could be inflated without an actual increase in the number of individual patients with AKI-D per year. This process may be at play; the NIS fails to capture this distinction, because all hospitalizations are deidentified and readmissions cannot be tracked.

Another point that this study engenders is far more pessimistic. If the rise in AKI-D is truly explained by rising comorbidities, the sheer variety of comorbidities that are responsible for the rising trend is daunting. Because of this heterogeneity in risk factors and etiologies, searching for a long-awaited therapy to prevent or ameliorate AKI is going to be extremely unlikely. Because of the complex and overlapping nature of AKI, it is conceivable that each patient with AKI will need a different therapeutic strategy, or subphenotyping of AKI using molecular, imaging, and other tools may be necessary to use the correct intervention. Although some generic pleuripotent prevention strategies to reduce the risk of AKI seemed to be promising (low chloride fluids, steroids, statins, and remote ischemic preconditioning), recent studies have not been able to confirm their efficacy, putting the scientific community back at square one for finding preventive or treatment strategies for AKI (23–29).

In summary, this big data study (13) provides a valuable foundation for future larger studies using longitudinal granular data from health care systems as well as currently ongoing cohort studies to delineate the epidemiology and precipitants of AKI-D (30). This, in turn, would provide early risk stratification for those hospitalized patients who are at highest risk of developing AKI-D. Understanding this epidemiology will play a vital role in diminishing the public health burden of this devastating condition.

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#### Disclosures

None.

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