Finding a Common Language for Patient Safety in CKD

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Summary
Improving patient safety has become a primary objective of health systems; however, the frequency of adverse safety events continues to be unacceptable despite the attention and dedicated efforts of many stakeholders. CKD that does not require dialysis increases the risk for adverse safety events, and adverse safety events can account for a substantial portion of the poor outcomes typical of CKD. Because much of CKD care occurs outside the typical health care setting, systems designed to detect and reduce adverse safety events are not necessarily effective in this population. Underrecognition (or underappreciation) of CKD and the associated impairment of renal function contribute to the high risk for adverse safety events. Medication errors are common in CKD and account for many lapses in patient safety, but a wide range of other potentially modifiable care processes in CKD also contribute to the high rate of observed adverse safety events. This review describes the spectrum of safety concerns specific to CKD and the need for a common set of standards to improve on current general constructs and to reduce adverse safety events in this chronic disease. An accepted set of disease-specific indicators is necessary to gauge the extent of the disease-specific patient safety problem and to design means to reduce adverse safety events and improve outcomes in CKD.

Given the broad national interest in this problem, it is worth considering the complex relationship between CKD and patient safety and the extent to which unintended harm from medical care might contribute to the adverse outcomes of this condition. Our objective is to bring attention to the need for a common set of safety measures designed specifically for CKD, such that adverse safety events can be monitored and prevented and thus lead to improved disease outcomes.

Introduction
The Institute of Medicine’s 1999 report “To Err Is Human: Building a Safer Health System” revealed the extent to which medical errors, and harm from medical care, contribute to the excess morbidity and mortality experienced by hospitalized patients in the United States health system (1). Up to 1 million injuries and 98,000 deaths were projected to be related to medical errors annually, more deaths than car accidents, breast cancer, or AIDS causes per year (1). The report launched an era in which patient safety became a principal quality metric by which to evaluate hospitals’ performance and outcomes.

Improvements since the report, however, have been somewhat disappointing. A Centers for Medicare and Medicaid Services Office of the Inspector General report showed that as many as 13% of hospitalized Medicare beneficiaries in 2008 experienced a medical care–related adverse safety event that led to some degree of harm, and 44% of these events were considered potentially or definitely preventable (2). The extrapolated death rate attributable to such adverse safety events was double that reported in the Institute of Medicine report (2). An independent survey of hospitalizations sampled from 14 North Carolina hospitals quarterly from 2002 until 2010 showed little change over time in the incidence of adverse safety events causing demonstrable harm (3). Most recently, the Obama administration has commissioned additional initiatives to improve patient safety because medical errors and harm related to care account for a substantial portion of growing medical costs (4).

CKD and Patient Safety: Significance of the Problem
Kidney disease stands out as a unique condition with factors that substantially raise the risk for adverse safety events. These factors have been outlined elsewhere and most prominently include impaired kidney function as a cause of excess adverse safety events (5). Adverse safety events, in turn, may increase the risk for poor outcomes in patients with CKD, including accelerated kidney function loss, increased frequency or length of hospitalization, and death (6–9). CKD expands the universe of risk for adverse safety events because patients with CKD carry their illness, and safety risk, to and from the hospital. These patients take multiple medications (10,11), encounter health care providers in numerous health venues, and face lifestyle hazards throughout their home environment. Surveillance mechanisms are not designed to track patient safety events in the broader health ecosystem of patients with CKD (5).

Although CKD complicates the challenges of patient safety, developing a common set of standards to
define and track adverse safety events offers the potential to improve outcomes, especially in individuals at risk for continued kidney function loss and where more definitive therapies remain elusive. In this article, we identify important considerations that need to be taken into account when thinking about the "common language" of CKD-specific patient safety. We call on the nephrology community to weigh the importance of these concepts, consider the broader role for patient safety in CKD disease management, and formulate a broadly recognized terminology of disease-specific adverse safety events for CKD.

The Role of Underrecognition of CKD in Patient Safety

An important contributor to the unique risks for adverse safety events in CKD is the persistent underrecognition (or underappreciation) of the condition. Individuals with stage 1–4 and nondialysis stage 5 CKD may not be identified because of a failure to use laboratory measurements of renal function in high-risk patients (12–14). Some health systems have implemented electronic medical records with automated GFR reporting when a serum creatinine level is obtained. However, patients with CKD migrate across health care venues, and medical information and laboratory values usually are not transportable. Even when GFR reporting is available to practitioners, they may not take appropriate action or tailor their care in patients with CKD (15–17). Although a causal relationship between disease recognition and patient safety has not been firmly established, it is plausible that increased recognition (and appreciation) of CKD in affected individuals can reduce adverse safety events. Effective alert strategies will need to transcend traditional health system boundaries and promote collaborative care between primary care agents and specialists (18,19).

Accounting for Standardized Kidney Function Measurement and Newer GFR Estimates in Drug Dosing

Substantial progress in nephrology has been made in developing reliable and unbiased estimates of GFR (eGFR) and standardizing kidney function measurements across laboratories. Recommendations about drug dosing in CKD and the related pharmacokinetic studies have, in many cases, preceded use of newer eGFR equations. Several studies have demonstrated a substantial discordance between drug dosing recommendations established via state-of-the-art estimates of kidney function and those based on older estimating equations, such as Cockcroft-Gault (20–22). The full implications of this discordance on safety of patients with CKD have yet to be determined. Newer eGFR reporting methods have not been universally adopted by physicians caring for patients or by pharmacists monitoring medication therapies. Many of these health agents rely on creatinine clearance as calculated with the Cockcroft-Gault equation—the dosing standard used by the pharmaceutical industry since the 1980s. Moreover, the effect of creatinine standardization on results from any estimating equation has not been fully disseminated among practitioners.

One example of how newer methods for measurement of kidney function have clinical implications is with the dosing of carboplatin (22,23). The U.S. Food and Drug Administration (FDA) has alerted clinicians that when new isotope dilution mass spectroscopy traceable serum creatinine assays are used, eGFR estimates are higher and, as a result, dosing of carboplatin, especially in children, can be excessive and lead to unanticipated toxicities (23,24). The FDA has also discussed the possibility of incorporating both Cockcroft-Gault and Modification of Diet in Renal Disease equation results in the labeling of new drugs (25). The American College of Clinical Pharmacy Nephrology Practice and Research Network recently reviewed this topic (26). The implications of standardized creatinine and use of contemporary estimating equations for determination of kidney function on dosing of other low-therapeutic-index drugs, such as carboplatin, will need to be explored further so that common drug-dosing standards can be set to avoid adverse safety events.

Therapy with Drugs That Have Nephrotoxic Risks

Numerous medications, including antivirals, antibiotics, and nonsteroidal anti-inflammatory drugs (NSAIDs), can cause nephrotoxicity. The broad range of potentially harmful medications in CKD and their mechanisms of toxicity have been reviewed extensively (27–30). Various nutritional supplements, herals, and over-the-counter supplements also have been shown to exhibit nephrotoxicity (31–33), and their use by patients is often underreported to practitioners (34). Moreover, the risk for medication toxicity is only amplified in patients with CKD, whose substantial polypharmacy leads to increased opportunities for medication mishaps (11,35). NSAIDs are a commonly used class of medication that has the potential to accelerate renal function loss and increase the risk for ESRD (36,37). However a broad range of drugs cause an increased incidence of adverse drug events in hospitalized patients with impaired renal function, and a majority of such events are thought to be preventable if such medications are avoided or appropriately adjusted in this population (6).

Beyond Medications when Considering Patient Safety in Kidney Disease

Although medications are a major concern in CKD, the array of potential CKD-pertinent adverse safety events goes beyond those resulting directly from inappropriate drug dosing and related toxicities. Other threats to patient safety in CKD stem from diagnostic testing with radiologic procedures. The nephrotoxicity of iodinated contrast agents is well known (38), and, recently, risks have been identified with use of gadolinium in magnetic resonance imaging of patients with impaired renal function (39). Moreover, the utility versus potential harm of stent-based interventions needs to be fully considered in the CKD population (40). The preponderance of comorbid conditions in CKD and the complexity of care for the disease can lead to countervailing management plans from independently acting health care providers who fail to communicate (11). Efforts to minimize the problems associated with such disjointed care have led to the concept of the medical home
to enhance care coordination (41). The nephrology community is likely to play a prominent role in the design of the medical home and its monitoring systems in the high-risk CKD population (42).

Another important class of adverse safety events in CKD includes electrolyte and metabolic disturbances. Although disruptions in laboratory measures often result from drugs, as is the case with hyperkalemia and renin-angiotensin-aldosterone system blockers or hypoglycemia with long-acting insulin therapy, these may also be the byproduct of unmodified dietary habits of patients with CKD (7,8,43). Adverse outcomes associated with these metabolic disturbances have been reported (7–9). Nonspecific recommendations that encourage abundant fluid drinking as a healthy lifestyle practice also might have dubious benefits and even harmful consequences in individuals with CKD (44,45). Additionally, providers need to ask whether continued recommendations for protein restriction as a tactic to slow CKD progression have the unintended consequences that encourage abundant fluid drinking as a healthy lifestyle practice. Recognizing the costs and benefits of accelerating protein wasting and sarcopenia (46,47).

Establishing a Common Language for Patient Safety in CKD

If we are to better understand the relationship between patient safety and CKD, we need to create universal standards by which to evaluate adverse safety events in this disease. Efforts in the broader medical community to develop a shared nomenclature for assessing patient safety have been primarily focused on in-hospital events as opposed to ambulatory care. The former are not entirely suited for a chronic disease such as CKD, for which much of the attendant care occurs out of the hospital. The emphasis of existing classifications on in-hospital events is illustrated by the National Quality Forum list of serious reportable events, which are used to evaluate safety (Table 1) (58). Review of these indicators reveals their relative unsuitability for processes of care pertinent to CKD. Nevertheless, proceedings from the National Quality Forum and other organizations, such as the Institute for Safe Medication Practices, introduce a wide range of best practices intended to safeguard patients from adverse safety events and are universally applicable to many disease populations and can be a starting point for formulating disease-specific safety indicators for CKD (59,60).

Defining adverse safety events specific to CKD is an important first step to more effectively monitor CKD care quality, determine the role of adverse safety events in CKD disease progression, and identify new opportunities to prevent ESRD. Table 2 offers a potential framework with which to start the consensus activities needed to classify CKD-specific safety indicators. Such a classification demonstrates many of the key challenges of establishing a recognized set of CKD-specific patient safety indicators. First, designating events as CKD-pertinent adverse safety events should meet the criteria of any general adverse safety event: Is the event the consequence of medical care or treatment versus poor health behaviors, and does it lead to harm? In the case of some candidate CKD-pertinent adverse safety measures, determining whether they are related to medical care versus the consequence of the disease process may not always be clear and should be determined. Second, it is important to determine whether acts of omission—failure to institute a recommended therapy or intervention—might be considered as an adverse safety event, such as failures to institute a renin-angiotensin-aldosterone system blocker or failures to preserve the nondominant arm for access. Third, it is important to determine to what extent high-risk practices only have the potential of an adverse safety events (and should be designated as safety hazards rather than events). For instance, use of intravenous saline may be indicated in some patients, but in others such an infusion might raise hazard of volume overload and would be considered an in-hospital safety event.

Any set of CKD-pertinent safety indicators should apply across many platforms. The Agency for Healthcare Research

Differing “Safety Phenotypes” across the Spectrum of Kidney Disease

Patient safety is also major concern in ESRD populations including those treated with dialysis and those receiving functioning renal transplants. The number of potential medication errors experienced in CKD is often augmented in the setting of both ESRD and transplantation (53–55). Moreover, the dialysis machine, a dominant component of medical care in the ESRD population, can threaten patient safety in several unique ways. Renal transplantation represents a special case of CKD with impaired renal function typical in most transplant recipients. Therefore, these patients experience many of the same problems as the CKD patient, but their risk is compounded by the use of more drugs and exposure to extracorporeal systems (53,54). Although ESRD and transplants are beyond the scope of this review, it is important to note that kidney disease is a continuum and the safety concerns for early predialysis CKD might differ from those for advanced disease. For instance, administration of an NSAID for a gout attack is likely to have different implications for a patient with stage 3 CKD (36,37) than for one with ESRD (56,57).
and Quality–derived general patient safety indicators are derived from International Classification of Diseases, Ninth Revision, codes found in administrative data and are designed to survey the rate of adverse safety events across hospitals and health systems (61). The Institute for Healthcare Improvement Global Trigger Tool is used to survey large numbers of hospital admissions and detect a set of high-risk conditions to localize a subset of charts that can be intensively reviewed for the occurrence of pertinent adverse safety events (62,63). Such an approach requires trained abstractors and physician adjudication and is not efficient for examination of large populations, such as those that might be monitored by the U.S. Renal Data System. Methods to identify medication issues in the setting of CKD would require review of complex pharmacy records preconditioned on measures

Table 1. National Quality Forum Serious Reportable Events in Healthcare—2011 Update

<table>
<thead>
<tr>
<th>Surgical or invasive procedure events</th>
<th>Care management events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery or other invasive procedure performed on the wrong site</td>
<td>Patient death or serious injury associated with a medication error (e.g., errors involving the wrong drug, wrong dose, wrong patient, wrong time, wrong rate, wrong preparation, or wrong route of administration)</td>
</tr>
<tr>
<td>Surgery or other invasive procedure performed on the wrong patient</td>
<td>Patient death or serious injury associated with unsafe administration of blood products</td>
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<tr>
<td>Wrong surgical or other invasive procedure performed on a patient</td>
<td>Maternal death or serious injury associated with labor or delivery in a low-risk pregnancy while being cared for in a health care setting</td>
</tr>
<tr>
<td>Unintended retention of a foreign object in a patient after surgery or other invasive procedure</td>
<td>(NEW) Death or serious injury of a neonate associated with labor or delivery in a low-risk pregnancy</td>
</tr>
<tr>
<td>Intraoperative or immediately postoperative/postprocedure death in an ASA class 1 patient</td>
<td>Patient death or serious injury associated with a fall while being cared for in a health care setting</td>
</tr>
<tr>
<td>Product or device events</td>
<td>Any stage 3, stage 4, and unstageable pressure ulcers acquired after admission/presentation to a health care setting</td>
</tr>
<tr>
<td>Patient death or serious injury associated with the use of contaminated drugs, devices, or biologics provided by the health care setting</td>
<td>Artificial insemination with the wrong donor sperm or wrong egg</td>
</tr>
<tr>
<td>Patient death or serious injury associated with the use or function of a device in patient care, in which the device is used or functions other than as intended</td>
<td>(NEW) Patient death or serious injury resulting from the irretrievable loss of an irreplaceable biologic specimen</td>
</tr>
<tr>
<td>Patient death or serious injury associated with intravascular air embolism that occurs while being cared for in a health care setting</td>
<td>(NEW) Patient death or serious injury resulting from failure to follow up or communicate laboratory, pathology, or radiology test results</td>
</tr>
<tr>
<td>Patient protection events</td>
<td>Environmental events</td>
</tr>
<tr>
<td>Discharge or release of a patient/resident of any age, who is unable to make decisions, to other than an authorized person</td>
<td>Patient death or serious injury associated with an electric shock in the course of a patient care process in a health care setting</td>
</tr>
<tr>
<td>Patient death or serious injury associated with patient elopement (disappearance)</td>
<td>Any incident in which systems designated for oxygen or other gas to be delivered to a patient contains no gas or the wrong gas or is contaminated by toxic substances</td>
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<tr>
<td>Patient suicide, attempted suicide, or self-harm that results in serious injury, while being cared for in a health care setting</td>
<td>Patient or staff death or serious injury associated with a burn incurred from any source in the course of a patient care process in a health care setting</td>
</tr>
<tr>
<td>Care management events</td>
<td>Patient death or serious injury associated with the use of physical restraints or bedrails while being cared for in a health care setting</td>
</tr>
<tr>
<td>Patient death or serious injury associated with a medication error (e.g., errors involving the wrong drug, wrong dose, wrong patient, wrong time, wrong rate, wrong preparation, or wrong route of administration)</td>
<td>Radiologic events</td>
</tr>
<tr>
<td>Patient death or serious injury associated with unsafe administration of blood products</td>
<td>(NEW) Death or serious injury of a patient or staff associated with the introduction of a metallic object into the MRI area</td>
</tr>
<tr>
<td>Maternal death or serious injury associated with labor or delivery in a low-risk pregnancy</td>
<td>Potential criminal events</td>
</tr>
<tr>
<td>(NEW) Death or serious injury of a neonate associated with labor or delivery in a low-risk pregnancy</td>
<td>Any instance of care ordered by or provided by someone impersonating a physician, nurse, pharmacist, or other licensed health care provider</td>
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<tr>
<td>Patient death or serious injury associated with a fall while being cared for in a health care setting</td>
<td>Abduction of a patient/resident of any age</td>
</tr>
<tr>
<td>Any stage 3, stage 4, and unstageable pressure ulcers acquired after admission/presentation to a health care setting</td>
<td>Sexual abuse/assault on a patient or staff member within or on the grounds of a health care setting</td>
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<tr>
<td>Artificial insemination with the wrong donor sperm or wrong egg</td>
<td>Death or serious injury of a patient or staff member resulting from a physical assault (i.e., battery) that occurs within or on the grounds of a health care setting</td>
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of kidney function and fairly intensive informatics data management.

Roadmap to Improving Patient Safety in CKD
Certainly finding consensus in a broad area such as patient safety is no simple undertaking; however, some feasible actions can be considered in an effort to reach the goal of establishing an accepted set of adverse safety events and improving patient safety in CKD. It will be important to develop empirical evidence demonstratting the frequency of occurrence of candidate adverse safety events and the strength of their associations with poor outcomes. Although the gold standard in evidence-based medicine calls for randomized trials, identifying diseases-pertinent safety indicators can be based on observational data, especially if processes of care are measured. A firm association between poor disease awareness and adverse safety events has not been established, but ongoing studies are examining the link between CKD recognition and patient safety (see ClinicalTrials.gov NCT # 01407367). Partnering with stakeholders in the pharmacy community (26) will be essential to guide industry and the FDA on the proper role of estimated measures of renal function in drug development and dosing recommendations. Developing consensus-based practice guidelines have strong precedents in the National Kidney Foundation Kidney Disease Outcomes Quality Initiatives and the Kidney Disease Improving Global Outcomes effort, with a set of established procedures and a typical timeline of development expected to be 18–24 months (64).

The first step in addressing the problems of patient safety in CKD will be developing universally accepted indicators that are proxies for CKD-specific adverse safety events and can be applied across various settings, including administrative datasets, medical records, and the clinic. Such an endorsed set of safety measures would broaden the scope of assessing quality of care, provide new tools for outcomes research, and offer new opportunities for disease management. Understanding the contribution of adverse safety events to the natural history of CKD will be instrumental in formulating more effective treatment strategies to treat this unique patient population.

Disclosures
None.

Table 2. Framework for development of CKD-specific safety indicators

<table>
<thead>
<tr>
<th>Adverse safety events</th>
<th>Adverse safety hazards</th>
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<tbody>
<tr>
<td>Events generally acknowledged to be the result of medical care and with realized or a high likelihood of harm</td>
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</tr>
<tr>
<td>CKD-specific examples: hyperkalemia, hypoglycemia, NSAID use</td>
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<tr>
<td>Conditional adverse safety events</td>
<td></td>
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<tr>
<td>Events requiring evidence of medical care as a precipitant, and with realized or high likelihood of harm</td>
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<tr>
<td>CKD-specific examples: acute kidney injury, congestive heart failure</td>
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<tr>
<td>Events generally acknowledged to be the result of medical care, and with potential for harm</td>
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<tr>
<td>CKD-specific examples: improperly dosed medications, blood transfusions</td>
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<tr>
<td>Adverse safety omissions</td>
<td></td>
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<tr>
<td>Failure to institute medical care, and with a high likelihood of harm</td>
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<tr>
<td>CKD-specific examples: failure to prescribe diuretic, inadequate laboratory monitoring</td>
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NSAID, nonsteroidal anti-inflammatory drug.

References


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