Published in final edited form as:

J Am Med Dir Assoc. 2014 October ; 15(10): 719–724. doi:10.1016/j.jamda.2014.03.014.

Determining the Incidence of Drug-Associated Acute Kidney Injury in Nursing Home Residents

Steven M. Handler, MD, PhD,

Department of Biomedical Informatics, School of Medicine, University of Pittsburgh, Pittsburgh, PA; Division of Geriatric Medicine, Department of Medicine, University of Pittsburgh, Pittsburgh, PA

Pui Wen Cheung, MD,

Department of Medicine, University of Pittsburgh, Pittsburgh, PA

Colleen M. Culley, PharmD,

Department of Pharmacy & Therapeutics, School of Pharmacy, University of Pittsburgh, Pittsburgh, PA

Subashan Perera, PhD,

Division of Geriatric Medicine, Department of Medicine, University of Pittsburgh, Pittsburgh, PA

Sandra L. Kane-Gill, PharmD, MS,

Department of Pharmacy & Therapeutics, Biomedical Informatics and Critical Care Medicine, School of Pharmacy and Medicine, University of Pittsburgh, Pittsburgh, PA

John A. Kellum, MD, and

Center for Critical Care Nephrology, Department of Critical Care Medicine, University of Pittsburgh, Pittsburgh, PA

Zachary A. Marcum, PharmD, MS

Division of Geriatric Medicine, Department of Medicine, University of Pittsburgh, Pittsburgh, PA

Abstract

Objective—Although acute kidney injury (AKI) is well-studied in the acute care setting, investigation of AKI in the nursing home (NH) setting is virtually nonexistent. The goal of this study was to determine the incidence of drug-associated AKI using the RIFLE (Risk, Injury, Failure, Loss of kidney function or End-Stage kidney disease) criteria in NH residents.

© 2014 American Medical Directors Association. Published by Elsevier Inc. All rights reserved.

Corresponding author information: Steven M. Handler, MD, PhD, University of Pittsburgh, Dept. of Biomedical Informatics, 5607 Baum Boulevard, Pittsburgh, PA 15206-3701, Phone Office: 412-648-9215, Mobile: 412-310-0033, Fax #: 412-648-9194, handler@pitt.edu.

Competing interests: The authors acknowledge no conflicts of interest.

Ethics approval: Ethics approval was provided by the University of Pittsburgh.

Provenance and peer review: Not commissioned; externally peer-reviewed.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Design/Setting/Participants/Measurements—We conducted a retrospective study between February 9, 2012 and February 8, 2013 for all residents at four UPMC NHs located in Southwest Pennsylvania. The TheraDoc™ Clinical Surveillance System, which monitors laboratory and medication data and fires alerts when patients have a sufficient increase in serum creatinine, was used for automated case detection. An increase in serum creatinine in the presence of an active medication order identified to potentially cause AKI triggered an alert, and drug-associated AKI was staged according to the RIFLE criteria. Data were analyzed by frequency and distribution of alert type by risk, injury, and failure.

Results—Of the 249 residents who had a drug-associated AKI alert fire, 170 (68.3%) were female, and the mean age was 74.2 years. Using the total number of alerts (n=668), the rate of drug-associated AKI was 0.35 events per 100 resident-months. Based on the RIFLE criteria, there were 191, 70, and 44 residents who were classified as AKI risk, injury, and failure, respectively. The most common medication classes included in the AKI alerts were diuretics, ACEIs/ARBs, and antibiotics.

Conclusion—Drug-associated AKI was a common cause of potential adverse drug events. The vast majority of the cases were related to the use of diuretics, ACEIs/ARBs and antibiotics. Future studies are needed to better understand patient, provider and facility risk factors as well as strategies to enhance the detection and management of drug-associated AKI in the NH.

Keywords

nursing homes; acute kidney injury; adverse drug events; clinical decision support systems

INTRODUCTION

Acute kidney injury (AKI) is defined as the rapid loss of kidney function, occurring over hours or days and resulting in the accumulation of metabolic waste products and the dysregulation of extracellular volume and electrolyte homeostasis.¹ AKI is diagnosed on the basis of clinical history and laboratory data, as measured by serum creatinine (SCr), or based on a rapid reduction in urine output.² Of note, the three main types of AKI are pre-renal, intrinsic, and post-renal AKI, and drugs can cause each type.¹ There had not been a standardized definition of AKI until the Risk, Injury, Failure, Loss of kidney function or End-stage kidney disease (RIFLE) criteria were proposed for its diagnosis by the Acute Dialysis Quality Initiative (ADQI) group.³

The RIFLE criteria for diagnosis and staging of AKI have been widely validated.⁴ Indeed, multiple studies have demonstrated a significant association between the RIFLE criteria and important clinical outcomes such as morbidity (e.g., hospitalization) and mortality across patient care settings.⁵⁻⁹ Furthermore, existing evidence supports the predictive validity of the RIFLE criteria to identify groups of hospitalized patients with increased risk of the need for renal replacement therapy and/or death.⁵⁻⁹ There is now emerging evidence of the long-term risks associated with AKI (even after apparent resolution) including the development of cardiovascular disease, chronic kidney disease and death.¹⁰⁻¹² Thus, early recognition and management of AKI is critical to prevent morbidity and mortality.

Although AKI is well-studied in the acute care setting, investigation of AKI in the nursing home (NH) setting is virtually nonexistent despite the fact that NH residents are at high risk of developing AKI. First, NH residents (given their older demographics) have a number of cellular, structural, functional, and hemodynamic changes in the kidney. These changes contribute to a gradual decrease in renal function, and estimates suggest that 50% of NH residents have chronic kidney disease, placing them at high risk for AKI.^{13,14} Second, older NH residents have a higher incidence of hypertension, diabetes mellitus, atherosclerosis and heart failure, which increase the risk of developing AKI. Third, older NH residents have high rates of polypharmacy, as a direct result of treating multiple comorbidities. Polypharmacy may expose NH residents to potentially nephrotoxic medications and drug-drug interactions, which can increase the risk of developing AKI.¹⁵

To the best of our knowledge, no prior studies have examined drug-associated AKI in the NH setting. In this paper we present a retrospective analysis of drug-associated AKI alerts detected by the TheraDoc™ Clinical Surveillance System which monitors laboratory and medication data and fires alerts when patients have a sufficient increase in serum creatinine as determined by the RIFLE criteria. The data presented here were collected in advance of a cluster randomized controlled trial funded by the Agency for Healthcare Research and Quality (AHRQ). The primary goal of the AHRQ-funded study is to determine the impact of a multicomponent intervention carried out by consultant pharmacists on the detection and management of ADEs in the NH setting.¹⁶ As an initial set of steps to improve early recognition and management of AKI, determine the consultant pharmacist resources needed and enhance the understanding of its epidemiology, we sought to determine the incidence of drug-associated AKI using the RIFLE criteria in NH residents.

METHODS

Study Design

We conducted our study within UPMC Senior Communities, which is the largest long-term care organization in Southwestern Pennsylvania, as well as the largest nationally that is part of an integrated healthcare delivery system. UPMC Senior Communities has approximately 2,500 beds, of which 752 are located in the NH setting. There are six UPMC NHs, all of which are non-profit, academically-affiliated, and not part of a national chain. Four of the six NHs (two urban and two suburban) have the same health information technology infrastructure and were included in the study. The number of beds in these NHs ranged from 50-179. We assessed all residents in the four NHs between February 9, 2012 and February 8, 2013. This study was approved by the University of Pittsburgh Institutional Review Board.

Detection of Drug-Associated Acute Kidney Injury

We used the serum creatinine part of the RIFLE criteria to operationally define AKI into risk, injury or failure. *Risk* was defined as an increase in serum creatinine (SCr) of 1.5 times from baseline, *injury* as a doubling of SCr from baseline, and *failure* as a tripling of SCr from baseline, or a SCr > 4mg/dl. Similar to other studies that have assessed AKI, we defined the baseline SCr as the lowest value (nadir SCr) that was recorded for the patient in the preceding year (including the current NH admission).¹⁷⁻¹⁹ No additional indices (e.g.,

urine sodium or fractional excretion of sodium) were drawn to determine the underlying type of AKI.

In addition to the RIFLE criteria, the patient had to be concurrently prescribed at least one medication that has been reported in the literature to be associated with AKI. The development of the knowledge base of medications associated with AKI and used for this determination has been previously described.^{20,21} Briefly, using a validated approach, a list of potentially causative medications was reviewed, edited, and agreed upon by an expert panel consisting of two clinical pharmacist/pharmacoepidemiology researchers, two geriatric clinical pharmacists, and a geriatrician (see Appendix for medications associated with AKI).

We used the TheraDoc™ Clinical Surveillance System (Hospira, Inc. Lake Forest, Illinois), which is licensed for use in the UPMC System, including the four participating NHs, to automate the detection of drug-associated AKI. The TheraDoc™ system integrates data from several disparate information source systems used by the select NHs including: admission/discharge/transfer, pharmacy, and laboratory. These data are integrated in real-time, so that they appear in TheraDoc™ within seconds of being entered into the source system. After consensus was reached on rule parameters, the AKI detection rule was developed by TheraDoc™ programmers with oversight by our investigative team. A sample drug-associated AKI alert can be seen in Figure 1.

Data Cleaning & Analysis

In order to analyze the included AKI alerts, a series of exclusionary steps were taken (Figure 2). The final dataset included 668 drug-associated AKI alerts involving 249 unique individuals. Descriptive statistics (means, standard deviations, frequencies) were used to summarize all variables for the sample, including the frequency and distribution of alert type by risk, injury, and failure. We characterized the number of unique residents, their gender, age, and baseline SCr. We also calculated the frequency of medication classes associated with the drug-associated AKI alerts, and further categorized the medication classes by AKI alert type. All analyses were conducted using SAS version 9.2 (SAS® Institute, Inc., Cary, North Carolina).

RESULTS

Of the 249 residents who had a drug-associated AKI alert fire, 170 (68.3%) were female, and the mean±standard deviation age was 74.2±14.0 years. The baseline SCr was 0.90±0.64 mg/dL. During the study period, there were a total of 1,475 admissions, providing 188,426 resident-days with an average length of stay of 75 days. The average length of stay for each of the four individual NHs was 69, 90, 92, and 120 days.

Using the total number alerts (n=668), the rate of drug-associated AKI among these residents was 0.35 cases per 100 resident days. Assuming a Poisson distribution (typical for multiple event counts), a person with a length of stay of 100 days had a 30% probability of having at least one drug-associated AKI event.

Based on the RIFLE criteria, there were 191, 70, and 44 residents who were classified as AKI risk, injury, and failure, respectively (total number sums to more than 249 since some residents triggered alerts in more than one category). Furthermore, the medication classes associated with the drug-associated AKI alerts are listed in Table 1. AKI risk was the most common category (n=674 total alerts), followed by injury (n=284) and failure (n=127). The most common medication classes included in the AKI alerts were diuretics, angiotensin converting enzyme inhibitors (ACEI)/angiotensin II receptor blockers (ARB), and antibiotics.

DISCUSSION

To the best of our knowledge, this is the first study to determine the incidence of drug-associated AKI using a validated set of diagnostic and staging criteria in the NH. We found a total of 668 drug-associated AKI alerts associated with 249 unique residents for an incidence rate of 0.35 cases per 100 resident days. In other words, among those residents with a length of stay of 100 days, 30% would be expected to have had at least one drug-associated AKI event during their stay. Comparing this incidence rate to prior research in other clinical settings is made difficult by the fact that previously there was an absence of a well-accepted definition of AKI, and the list of medications associated with AKI varied across studies.^{15;22-24} Nonetheless, we found the incidence rate of drug-associated AKI to be similar to a previously published rate in the NH setting of *all-causes* of adverse drug events (ADE) combined (10.8 per 100 patient-months, or 0.36 per 100 patient-days).²⁵ This is a particularly important finding and suggests that drug-associated AKI may be amongst the most common forms of ADEs, and that our Clinical Surveillance System, which used standardized criteria and an evidence-based list of medications, was an effective tool in detecting these cases. It is also important to note that multiple non-drug causes of AKI are possible in the NH setting, including volume depletion, bleeding, blocked PEG tubes, and sepsis, to name a few.

We found that the most common AKI RIFLE category detected was risk, followed by injury and failure. This is consistent with prior research showing that AKI risk is the most common stage.^{4,26} It is well-established that older NH residents are at high risk for AKI due to age-related changes in kidney structure and function. These changes contribute to a gradual decrease in renal function, leading to an estimated prevalence rate of CKD of 50% in NH residents.¹ Such high rates of CKD place NH residents at risk for AKI. While there are a limited number of pharmacological strategies to treat AKI, one can modify the dose or withdraw the offending agent(s) and address the underlying etiology.²⁷ In addition, emphasis should be on prevention and early detection/management of complications to prevent progression from risk to either injury or failure.²⁸ The development of our Clinical Surveillance System to detect potential AKI events using computerized alerts supports this goal in NH residents. This is a key finding because research is emerging that suggests that predicting AKI from underlying risk factors is challenging in older adults.²⁹

Our alert system identified the drugs most commonly associated with potential AKI, including diuretics, ACEI/ARBs, and antibiotics; some variation was seen in medications involved across the RIFLE categories (Table 1). In all groups, diuretics were the most

common medication class implicated in the AKI alerts. Diuretic use exacerbates the underlying predisposition to volume depletion and may contribute in up to 25–40% of cases of prerenal AKI in elderly patients.¹ For each of the risk and injury groups, diuretics and ACEI/ARBs accounted for more than 70% of the alerts. These two classes of medications are frequently used by older adults and also carry a significant risk of prerenal AKI.³⁰ Moreover, for AKI failure, antibiotics accounted for 30% of the alerts, which was a higher proportion than either the risk or injury groups. Of note, antibiotics have been shown to commonly be associated with AKI in ICU settings.³¹ Overall, these medication classes are consistent with a previous study assessing hospitalizations due to adverse drug reactions, which found that admission for AKI in older Veterans involved ACEIs, loop diuretics, antibiotics, and NSAIDs.³²

While this initial study did not assess outcomes, such as hospitalization due to AKI, it is important to note that there are relevant policy implications on the horizon. A recent report by the Office of Inspector General (OIG) found that one-quarter of Medicare NH residents experienced hospitalizations in FY 2011, costing Medicare \$14.3 billion.³³ AKI as a primary diagnosis on hospitalization was detected in 3.9% of all admissions, costing an estimated \$425 million.³³ As a result, CMS is developing a hospitalization outcome quality metric to measure the percent of long-stay residents who are hospitalized during a specific reporting period.³⁴ This measure has important policy implications since it will be associated with the Medicare Star Ratings and will also be used by state surveyors to detect potential quality problems in NHs. Furthermore, AKI is included among a list of 20 diagnoses that are associated with potentially avoidable hospitalizations from the NH, similar to ambulatory sensitive conditions.³⁴ There are significant reimbursement implications for NHs in the near future, as CMS is considering a reduction in payment to NHs that send residents to the hospital to treat these conditions which they believe could be effectively managed in the NH setting. If AKI is included in a new CMS policy, it becomes even more important to develop strategies for the prevention, as well as early detection and management of drug-associated AKI.

While this initial study advances the literature on drug-associated AKI in the NH, important work remains. Additional studies are needed to determine the patient, provider and facility risk factors associated with drug-associated AKI. Research is also needed to determine and describe AKI recovery trajectories,³⁵ as well as the impact of AKI on morbidity and mortality in older NH residents. In addition, future research is needed to determine if improving the prescribing of key medications can have a significant impact on the incidence and progression of AKI in this population. Future studies are also needed to determine if increasing the frequency of SCr monitoring can help to detect earlier changes in SCr, allowing for more timely interventions to reduce the progression of SCr from risk to injury or failure.^{36,37} Finally, more research is needed to determine if well-designed clinical decisions support systems that automate the early detection and management of drug-associated AKI by targeting prescribing and monitoring in the NH, can improve resident-specific outcomes, including potentially avoidable hospitalizations. The use of these systems are recommended by the Institute of Medicine and other patient safety organizations to improve medication safety³⁸⁻⁴¹ and could also be used to support the federal guidance for

state surveyors, that we continually monitor the safe use of medications in the NH setting.⁴²⁻⁴⁴

Our study has several limitations that deserve mention. First, the TheraDoc™ Clinical Surveillance system is currently limited to assessing medications prescribed. There is no current interface with medication administration records. It is possible that some of the medications associated with an AKI alert were prescribed, but not actually administered. This could falsely elevate the incidence of drug-associated AKI. Second, it is possible that we overestimated the attribution of medications to the development of AKI, as no formal causality assessment tool (e.g., Naranjo algorithm) was used to exclude competing factors such as co-morbid disease, polypharmacy, and volume depletion. Similarly, since no causality assessment tool was used, it was impossible to determine when multiple medications were prescribed, which were the most likely medications implicated. In addition, we were unable to attribute the underlying type (i.e., pre-renal, intrinsic, post-renal) of AKI to a specific cause given the retrospective nature of the study and the limited data available in NH medical records. Third, ideally for staging purposes, subjects should be staged according to both RIFLE and Acute Kidney Injury Network (AKIN) criteria that give them the highest stage.⁴⁵ However, the AKIN stage states that the increase in SCr must occur in less than 48 hours, and such frequent monitoring most likely exceeds NH clinical capabilities, thus using RIFLE criteria is more applicable for our data analysis. A similar problem exists for urine output, which is not routinely measured in NH residents and therefore unavailable for our analysis. Fourth, we were unable to measure the rationale for the laboratory test being completed since the precise reason for ordering serum creatinine values (e.g., due to routine monitoring, a potential ADE, or an acute change in condition) is not commonly documented in the medical record. Finally, this study included a limited number of NHs in Southwest Pennsylvania affiliated with an academic medical center, and thus it may decrease its generalizability.

CONCLUSION

This is the first study that assesses the incidence of drug-associated AKI in NHs. Based on our analysis, drug-associated AKI was a common cause of potential ADEs. The vast majority of the cases were related to the use of diuretics, ACEI/ARBs and antibiotics. Future studies are needed to better understand patient, provider and facility risk factors, as well as strategies to enhance the detection and management of drug-associated AKI in the NH.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding: This study was supported by the Agency for Healthcare Research and Quality (R01HS018721), the National Institute of Aging (R01AG027017; P30AG024827; K07AG033174), the National Institute of Diabetes, Digestive and Kidney Diseases (R01DK083961) and a CMS Cooperative Agreement/Health Care Innovation Award (1E1CMS331081-01-00). The content is solely the responsibility of the authors and does not represent the official views of the Agency for Healthcare Research and Quality or any of the other funding sources.

References

1. Abdel-Kader K, Palevsky PM. Acute kidney injury in the elderly. *Clin Geriatr Med.* 2009; 25:331–358. [PubMed: 19765485]
2. Lameire N, Van Biesen W, Vanholder R. Acute renal failure. *Lancet.* 2005; 365:417–430. [PubMed: 15680458]
3. 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:R204–12. [PubMed: 15312219]
4. Ricci Z, Cruz D, Ronco C. The RIFLE criteria and mortality in acute kidney injury: a systematic review. *Kidney Int.* 2008; 73:538–546. [PubMed: 18160961]
5. Uchino S, Bellomo R, Goldsmith D, et al. An assessment of the RIFLE criteria for acute renal failure in hospitalized patients. *Crit Care Med.* 2006; 34:1913–1917. [PubMed: 16715038]
6. Hoste EA, Clermont G, Kersten A, et al. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. *Crit Care.* 2006; 10:R73. [PubMed: 16696865]
7. Abosaif NJ, Tolba YA, Heap M, et al. The outcome of acute renal failure in the intensive care unit according to RIFLE: model application, sensitivity and predictability. *Am J Kidney Diseases.* 2005; 46:1038–1048.
8. Cruz DN, Bolgan I, Perazella MA, et al. North East Italian prospective hospital renal outcome survey on acute kidney injury (NEiPHROS-AKI). Targeting the problem with the RIFLE criteria. *Clin J Am Soc Nephrol.* 2007; 2:481–425.
9. 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. [PubMed: 17314324]
10. Dasta JF, Kane-Gill SL, Durtschi AJ, et al. Costs and outcomes of acute kidney injury (AKI) following cardiac surgery. *Nephrol Dial Transplant.* 2008; 23:1970–1974. [PubMed: 18178605]
11. Schiff H, Fischer R. Five-year outcomes of severe acute kidney injury requiring renal replacement therapy. *Nephrol Dial Transplant.* 2008; 23:2235–2241. [PubMed: 18408072]
12. Hobson CE, Yavas S, Segal MS, et al. Acute kidney injury is associated with increased long-term mortality after cardiothoracic surgery. *Circulation.* 2009; 119:2444–2453. [PubMed: 19398670]
13. Hsu CY, Ordonez JD, Chertow GM, et al. The risk of acute renal failure in patients with chronic kidney disease. *Kidney Int.* 2008; 74:101–107. [PubMed: 18385668]
14. McClellan WM, Resnick B, Lei L, et al. Prevalence and severity of chronic kidney disease and anemia in the nursing home population. *J Am Med Dir Assoc.* 2010; 11:33–41. [PubMed: 20129213]
15. Rosner MH. Acute kidney injury in the elderly. *Clin Geriatr Med.* 2013; 29:565–78. [PubMed: 23849008]
16. [March 18, 2014] Enhancing the Detection and Management of Adverse Drug Events in Nursing Homes. <http://clinicaltrials.gov/ct2/show/NCT01531088>
17. Gaiao S, Cruz DN. Baseline creatinine to define acute kidney injury: is there any consensus? *Nephrol Dial Transplant.* 2010; 25:3812–3814. [PubMed: 20663790]
18. Lafrance JP, Miller DR. Defining acute kidney injury in database studies: the effects of varying the baseline kidney function assessment period and considering CKD status. *Am J Kidney Dis.* 2010; 56:651–660. [PubMed: 20673605]
19. Ostermann M, Chang RW. Challenges of defining acute kidney injury. *QJM.* 2011; 104:237–243. [PubMed: 20934982]
20. Hanlon JT, Aspinall SL, Semla TP, et al. Consensus guidelines for oral dosing of primarily renally cleared medications in older adults. *J Am Geriatr Soc.* 2009; 57:335–40. [PubMed: 19170784]
21. Marcum ZA, Arbogast KL, Behrens MC, et al. Utility of an adverse drug event trigger tool in Veterans Affairs nursing facilities. *Consult Pharm.* 2013; 28:99–109. [PubMed: 23395810]
22. Rind DM, Safran C, Phillips RS, et al. Effect of computer-based alerts on the treatment and outcomes of hospitalized patients. *Arch Intern Med.* 1994; 154:1511–1517. [PubMed: 8018007]

23. Jensen JU, Hein L, Lundgren B, et al. Kidney failure related to broad-spectrum antibiotics in critically ill patients: secondary end point results from a 12000 patient randomized trial. *BMJ Open*. 2012; 2:e000635.
24. Goldstein SL, Kirkendall E, Nguyen H, et al. Electronic health record identification of nephrotoxin exposure and associated acute kidney injury. *Pediatrics*. 2013; 132:e756–e767. [PubMed: 23940245]
25. Gurwitz JH, Field TS, Rochon P, et al. Effect of computerized provider order entry with clinical decision support on adverse drug events in the long-term care setting. *J Am Geriatr Soc*. 2008; 56:2225–33. [PubMed: 19093922]
26. Selby NM, Crowley L, Fluck RJ, et al. Use of electronic results reporting to diagnose and monitor AKI in hospitalized patients. *Clin J Am Soc Nephrol*. 2012; 7:533–540. [PubMed: 22362062]
27. Dishart MK, Kellum JA. An evaluation of pharmacological strategies for the prevention and treatment of acute renal failure. *Drugs*. 2000; 59:79–91. [PubMed: 10718100]
28. [January 21, 2014] KDIGO Clinical Practice Guideline for Acute Kidney Injury. Available at: http://www.kdigo.org/clinical_practice_guidelines/pdf/KDIGO%20AKI%20Guideline.pdf
29. Kane-Gill SL, Kirisci L, Verrico MM, Rothschild JM. Analysis of risk factors for adverse drug events in critically ill patients. *Crit Care Med*. 2012; 40:823–828. [PubMed: 22036859]
30. van Kraaij DJ, Jansen RW, Gribnau FW, Hoefnagels WH. Diuretic therapy in elderly heart failure patients with and without left ventricular systolic dysfunction. *Drugs Aging*. 2000; 16:289–300. [PubMed: 10874524]
31. Anthes AM, Harinstein LM, Smithburger PL, et al. Improving adverse drug event detection in critically ill patients through screening intensive care unit transfer summaries. *Pharmacoepidemiol Drug Saf*. 2013; 22:510–516. [PubMed: 23440931]
32. Marcum ZA, Amuan ME, Hanlon JT, et al. Prevalence of unplanned hospitalizations caused by adverse drug reactions among older Veterans. *J Am Geriatric Soc*. 2012; 60:34–41.
33. Medicare Nursing Home Resident Hospitalization Rates Merit Additional Monitoring. Office of Inspector General; Available at: <https://oig.hhs.gov/oei/reports/oei-06-11-00040.pdf> [January 21, 2014]
34. [January 21, 2014] Cost Drivers for Dually Eligible Beneficiaries: Potentially Avoidable Hospitalizations from Nursing Facility, Skilled Nursing Facility, and Home and Community-Based Services Waiver Programs. Final Task 2 Report. Available at: <http://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Reports/downloads/costdriverstask2.pdf>
35. Murugan R, Kellum JA. Acute kidney injury: what's the prognosis? *Nat Rev Nephrol*. 2011; 7:209–217. [PubMed: 21343898]
36. Handler SM, Shirts BH, Perera S, et al. Frequency of laboratory monitoring of chronic medications administered to nursing facility residents: results of a national internet-based study. *Consult Pharm*. 2008; 23:387–95. [PubMed: 18540792]
37. Steinman MA, Handler SM, Gurwitz JH, et al. Beyond the prescription: medication monitoring and adverse drug events in older adults. *J Am Geriatr Soc*. 2011; 59:1513–20. [PubMed: 21797831]
38. Aspden, P.; Corrigan, J.; Wolcott, J.; Erickson, S. Institute of Medicine Patient Safety: Achieving a New Standard for Care. Washington, DC: The National Academies Press; 2004.
39. Aspden, P.; Wolcott, J.; Bootman, JL.; Cronenwett, LR. Institute of Medicine Preventing Medication Errors. Washington, DC: National Academies Press; 2007.
40. National Quality Forum. [January 21, 2014] Safe Practices for Better Healthcare: A Consensus Report. Available at: <http://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/resources/nqfpract.pdf>
41. Shojania KG, Duncan BW, McDonald KM, et al. Making health care safer: a critical analysis of patient safety practices. *Evid Rep Technol Assess (Summ)*. 2001; i-x:1–668.
42. Bain KT. Adverse drug reactions and current state of drug regimen review in nursing facilities: need for a change? *Consult Pharm*. 2007; 22:586–92. [PubMed: 17714003]
43. Martin CM, McSpadden CS. Changes in the state operations manual: implications for consultant pharmacy practice. *Consult Pharm*. 2006; 21:948–61. [PubMed: 17243847]

44. U.S. Department of Health and Human Services and Centers for Medicare & Medicaid Services. [January 21, 2014] Guidance to surveyors for long term care facilities. Available at: <http://www.cms.hhs.gov/transmittals/downloads/R22SOMA.pdf>
45. Mehta RL, Kellum JA, Shah SV, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care. 2007; 11:R31. [PubMed: 17331245]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

ADE: Drug-Associated Acute Kidney Injury		Admit Diagnosis: CARE INVOLVING OTHER SPECIFIED REHABILITATION PROCEDURE, OTHER			
Demographics & renal function					
Age: 79 years		Sex: F			
SCr: 4.18 ()		Height: 61 in (155 cm)			
CrCl: 9 mL/min(Cockcroft-Gault; weight used=55 kg)		Weight: 145.2 lb (66 kg)			
Possible drug associated ACUTE KIDNEY FAILURE.					
This patient's CREATININE has increased greater than or equal to 3 fold relative to the nadir value (1.2 mg/dL) found in the past 365 days and has at least 1 active order(s) for a drug associated with acute kidney injury.					
Most Recent Serum Creatinine: CREATININE= 4.18 MG/DL (COMPREHENSIVE METABOLIC PANEL W/EGFR Collected: 09/06/2012)					
Nadir Serum Creatinine: Creatinine= 1.2 mg/dL (Basic Metabolic Profile Collected: 07/10/2012 06:35:00)					
Drug	Dose	Start	End	Status	Pat Class
FUROSEMIDE TAB 40MG	40 MG PO QD	08/31/2012		ACTIVE	I

Figure 1.
Example of a Theradoc™ Drug-Associated Acute Kidney Injury (Failure) Alert

Figure 2.

Flow Diagram of Inclusion Criteria for Drug-Associated Acute Kidney Injury Alerts

*Identical/duplicate alerts were defined as those that had the identical SCr and medication information contained within the alert – a known limitation associated with the laboratory service provider’s information system that has since been resolved.

Table 1

Distribution of Drug-Associated Acute Kidney Injury (AKI) Alerts by Medication Classes

Medications	Medication Class-level Frequency of AKI Alerts (n=1,085)*	Medication Class-level Frequency of AKI Risk (n=674)	Medication Class-level Frequency of AKI Injury (n=284)	Medication Class-level Frequency of AKI Failure (n=127)
Diuretics	557 (51.4%)	357 (53.0%)	151 (53.2%)	49 (39.2%)
ACEI/ARBs	264 (24.4%)	176 (26.2%)	59 (20.1%)	29 (24.2%)
Antibiotics	199 (18.3%)	103 (15.2%)	58 (20.4%)	38 (30%)
NSAIDs	53 (4.9%)	29 (4.3%)	16 (5.6%)	8 (4.2%)
Miscellaneous	12 (1.1%)	9 (1.3%)	0 (0%)	3 (2.5%)

Abbreviations: ACEI: angiotensin converting enzyme inhibitor; ARB: angiotensin II receptor blocker; NSAID: non-steroidal anti-inflammatory drug

* Number is more than 668 since an alert could have more than one medication included