VALIDATION OF ACUTE KIDNEY INJURY CASES IN THE MINI-SENTINEL DISTRIBUTED DATABASE

Prepared by: Uptal D. Patel, MD,[1,2] N. Chantelle Hardy, MPH,[2] David H. Smith, RPh, PhD,[3] Jerry H. Gurwitz, MD,[4] Chi-yuan Hsu, MD, MSc,[5] Chirag R. Parikh, MD, PhD,[6] Steven M. Brunelli, MD, MSCE,[7] Meghan Baker, MD,ScD[8] Susan Forrow, BA,[8] Carly Comins, BS,[8] Denise M. Boudreau, PhD, RPh,[9] Chunfu Liu, ScD,[10] Pamala A. Pawloski, PharmD,[11] Nandini Selvam, PhD, MPH,[10] Mano S. Selvan, PhD,[12] Shannon Stratton, BS,[13] Jeffrey J. VanWormer, PhD,[14] George Aggrey, MD, MPH,[15] Melanie Blank, MD,[15] Patrick Archdeacon, MD[15]

Author Affiliations: 1. Divisions of Nephrology and Pediatric Nephrology, Departments of Medicine and Pediatrics, Duke University School of Medicine, Durham, NC. 2. Duke Clinical Research Institute, Durham, NC. 3. Kaiser Permanente Center for Health Research, Portland, OR. 4. Meyers Primary Care Institute, a joint endeavor of Fallon Community Health Plan, Reliant Medical Group, and University of Massachusetts Medical School, Worcester, MA. 5. University of California, San Francisco, San Francisco, CA. 6. Yale University, New Haven, CT. 7. Harvard Medical School, Boston, MA. 8. Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA 9. Group Health Cooperative, Seattle, WA. 10. Government & Academic Research, HealthCore, Alexandria, VA. 11. HealthPartners Institute for Education and Research, Minneapolis, MN. 12. Comprehensive Health Insights, Humana Inc., Louisville, KY. 13. Department of Preventive Medicine, Vanderbilt University School of Medicine, Nashville, TN. 14. Marshfield Clinic Research Foundation, Marshfield, WI. 15. U.S. Food and Drug Administration, Silver Spring, MD.

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Mini-Sentinel is a pilot project sponsored by the U.S. Food and Drug Administration (FDA) to inform and facilitate development of a fully operational active surveillance system, the Sentinel System, for monitoring the safety of FDA-regulated medical products. Mini-Sentinel is one piece of the Sentinel Initiative, a multi-faceted effort by the FDA to develop a national electronic system that will complement existing methods of safety surveillance. Mini-Sentinel Collaborators include Data and Academic Partners that provide access to health care data and ongoing scientific, technical, methodological, and organizational expertise. The Mini-Sentinel Coordinating Center is funded by the FDA through the Department of Health and Human Services (HHS) Contract number HHSF223200910006I.

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I. EXECUTIVE SUMMARY

A. OVERVIEW OF PROJECT AND SUMMARY OF FINDINGS

Acute kidney injury (AKI) associated with medical products is an important public health concern. The validity of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes to identify cases of AKI is not well known, especially for non-dialysis-requiring AKI. Among participating health plan members in the Mini-Sentinel Distributed Database (MSDD), this project examined the positive predictive values (PPVs) of hospital ICD-9-CM diagnoses in identifying AKI events and AKI events requiring dialysis.

We selected random samples of members from five Mini-Sentinel Data Partners within the MSDD who had any hospital diagnosis indicative of AKI (ICD-9-CM codes 584.5 [Acute kidney failure with lesion of tubular necrosis], 584.6 [Acute kidney failure with lesion of renal cortical necrosis], 584.7 [Acute kidney failure with lesion of renal medullary [papillary] necrosis], 584.8 [Acute kidney failure with other specified pathological lesion in kidney], 584.9 [Acute kidney failure, unspecified]), including cases requiring dialysis (any AKI ICD-9-CM code with a dialysis procedure code: V45.1 [Renal dialysis status], V56.0 [Encounter for dialysis and dialysis catheter care], V56.1 [Fitting and adjustment of extracorporeal dialysis catheter], 39.95 [Hemodialysis]) recorded in 2011. Medical records were obtained and reviewed by two nephrologists to confirm whether potential AKI cases were definite, probable, unlikely, unable to determine, or not AKI. In many cases, the baseline serum creatinine was either unavailable or the duration of time since its measurement was unknown. In these circumstances, AKI was considered to be probable if the clinical context and documentation was otherwise consistent with a new episode of AKI.

Records were requested for 225 members with hospital ICD-9-CM diagnoses for at least mild AKI (n=150) or dialysis-requiring AKI (n=75). Among 129 members with available medical records (86.0% yield), at least mild AKI was confirmed to be definite in 62 charts (PPV 48.1%; 95% CI, 39.4% – 56.7%). In sensitivity analyses, at least mild AKI was confirmed to be either definite or probable in 109 of 129 available charts, increasing the PPV to 84.5% (95% CI, 78.3% – 90.7%). Among 67 members with available medical records (89.3% yield), dialysis-requiring AKI was confirmed to be definite in 43 charts (PPV 64.4%; 95% CI, 52.7% – 75.7%). In sensitivity analyses, those with prior end-stage kidney disease were excluded, increasing the PPV for dialysis-requiring AKI to 81.1% (95% CI, 70.6% – 91.7%).

The individual pre-specified ICD-9-CM codes for identifying hospitalized AKI yielded a PPV of 48.1% for at least mild AKI and 64.4% for dialysis-requiring AKI. For at least mild AKI, the PPV increased to 84.5% when limitations in available data were acknowledged but allowed inclusion of probable AKI cases with the definite cases. An evaluation of probable AKI cases provides confidence that such cases can be considered along side definite cases of AKI, particularly for those cases defined by the presence of recovery from AKI. For dialysis-requiring AKI, the PPV increased to 81.1% when additional restrictions were applied to eligible cases. Each of these algorithms could be used to detect AKI events in surveillance activities and in claims-based databases, but further refinement and validation may be prudent to minimize false positive cases and allow application to community settings.

II. BACKGROUND

Acute kidney injury (AKI) can be defined as a reduction in kidney function of abrupt onset that is characterized by a fall in glomerular filtration rate (GFR) and is usually detected by a corresponding rise in serum creatinine. Although AKI may also be accompanied by oliguria, urine output is often poorly measured, limiting its use in defining cases of AKI. AKI is among the most common causes of morbidity and mortality observed in acutely ill, hospitalized patients, and is an important risk factor for progression to end-stage renal disease.[1] The community-based incidence and prevalence of AKI remain uncertain, however, the incidence of both non-dialysis-requiring AKI and dialysis-requiring AKI appear to be increasing.[2]

Because of its anatomy and function, the kidney is particularly vulnerable to drug toxicity. Drug-induced nephrotoxicity may occur in both inpatient and outpatient settings with variable presentations that range from mild and reversible AKI to dialysis-requiring AKI. In addition, some manifestations may not involve a fall in GFR, but involve more subtle changes including electrolyte abnormalities, acid-base abnormalities, proteinuria, hematuria, or pyuria.[3] Signals that exposure to a drug may result in nephrotoxicity may manifest early during drug development, during clinical trials, or only much later once the drug has been used widely in routine clinical practice.[4] Drug-induced nephrotoxicity has been estimated to contribute up to 25% of all AKI cases in critically ill patients.[5] Given the clinical impact and societal cost of drug-induced nephrotoxicity and the insensitivity of current methods to consistently detect it early during preclinical studies, active surveillance of medical products for associations with AKI is an important component of a post-market safety system. For that reason, it is imperative to develop algorithms that reliably identify AKI i using electronic healthcare and administrative claims-based databases.

To identify AKI in healthcare databases, validated definitions are needed. Although recent consensus definitions include those developed by the Acute Dialysis Quality Initiative (ADQI),[6] Acute Kidney Injury Network (AKIN),[7] and Kidney Disease: Improving Global Outcomes (KDIGO),[1] specific definitions of AKI have changed over time and definitions used in published reports vary widely.[8-11] Applying the results of these studies is limited by variation in AKI definitions precluding comparisons across AKI studies, and by a lack of validated methods. Among dozens of studies evaluating the predictive value of claims-based identification of AKI, only 1 was validated by chart review for dialysis-requiring AKI[12] and none have been validated for non-dialysis-requiring AKI.

In 2008, the U.S. Food and Drug Administration (FDA) launched the Sentinel Initiative, a program designed to create a national electronic monitoring system for postmarketing risk identification and analysis of medical product safety that will use automated healthcare data to complement its existing surveillance systems.[13,14] The Mini-Sentinel pilot, a component of the Sentinel Initiative, is a collaborative effort between the FDA and more than 30 organizations.[15] Since accurate and timely identification of health outcomes is an essential component of active safety surveillance, Mini-Sentinel convened a workgroup comprised of clinicians, pharmacoepidemiologists, Mini-Sentinel Data Partners, Mini-Sentinel Operations Center (MSOC) representatives, and members of the FDA (Appendix A) to establish a process for identification and validation of AKI. We evaluated the ability of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes to identify cases of AKI within the Mini-Sentinel Distributed Database (MSDD). The MSDD is a multi-site distributed

data network designed to implement the Mini-Sentinel Common Data Model (MSCDM) that is being piloted to assess postmarketing safety issues with FDA-regulated products. It contains data on health plan member demographics, enrollment, location of encounter, outpatient pharmacy dispensing (recorded using National Drug Codes [NDC]), as well as outpatient and hospital-associated medical diagnoses (recorded using ICD-9-CM diagnostic codes) and procedures (recorded using Current Procedural Terminology [CPT] codes).[16]

Since the accuracy of these codes might be different based on the severity of AKI, we first examined the positive predictive value (PPV) of these codes in identifying medical record-confirmed cases of at least mild AKI events among health plan members. We then evaluated the PPV among those who had dialysis-requiring AKI events.

III. METHODS

A. OVERVIEW OF DESIGN FOR THE AKI VALIDATION PROCESS

We conducted a cross-sectional analysis among participating health plan members in the MSDD who had a principal hospital diagnosis suggestive of AKI recorded between January 1, 2011 and December 31, 2011. We utilized administrative and claims data from five MSDD Data Partners, representing a total of eleven health plans (HealthCore, Inc.; HMO Research Network [HealthPartners Research Foundation, Marshfield Clinic Research Foundation, Group Health Research Institute, Henry Ford Health System]; Humana; Kaiser Permanente Center for Effectiveness and Safety Research [Kaiser Permanente Colorado, Kaiser Permanente Northwest, Kaiser Permanente Northern California, Kaiser Permanente Hawaii]; Vanderbilt University School of Medicine/TennCare Bureau).

In 2010, the Office for Human Research Protections (OHRP) at the Department of Health and Human Services determined that public health surveillance activities conducted through the Mini-Sentinel pilot do not require Institutional Review Board (IRB) approval.[17] The Mini-Sentinel Privacy Panel assembled a privacy packet and the AKI workgroup distributed this packet to the Data Partner health plans participating in this validation effort.[18] The privacy packet contained letters from the OHRP, FDA, and Mini-Sentinel Principal Investigator Richard Platt explaining the reasoning and implications of Mini-Sentinel being considered public health surveillance, rather than research.

For the chart retrieval process, the Data Partners were given a letter template to send to their provider sites explaining: the Mini-Sentinel Pilot program, its association with the FDA, and the determination that the project is public health surveillance (Appendix B). In addition to sending this letter, Data Partners were encouraged to submit the privacy packet to relevant medical records departments and IRBs of provider sites.

B. CASE IDENTIFICATION

In an effort to obtain sufficient sample sizes for analyses, we queried data from the MSDD from January 1, 2011 through December 31, 2011, inclusively. Patients must be 18 or older, but there were no restrictions for any other member characteristics, including continuous eligibility of prescription drug coverage. However, continuous health plan enrollment for 12 months (excluding gaps of ≤ 30 days) was required prior to the first appearance of an AKI code. Members were identified as having an AKI event by the presence of any ICD-9-CM hospital diagnosis code suggestive of possible AKI, with or without dialysis (Table 1). Selection of these diagnosis codes was based on discussions with collaborating nephrologists within the workgroup and results of prior observational studies that suggested that these codes were frequently recorded among cases with AKI.[8-11] Cases of AKI could be better identified by using laboratory results and data elements derived from electronic medical records, however, these data were not uniformly available in the MSDD for calendar year 2011. As such, hospital discharge codes consisting of administrative data and claims were used alone. A random sample of members with these codes was selected for this workgroup activity. The earliest date on which an AKI code was recorded for a member during the two-year period was considered the index date of hospitalization.

Table 1. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes evaluated during index hospitalizations for their ability to identify potential cases of at least mild acute kidney injury, and dialysis-requiring acute kidney injury.

CODE	DESCRIPTION
At Least Mild Acute Kidney Injury	
584.5	Acute kidney failure with lesion of tubular necrosis
584.6	Acute kidney failure with lesion of renal cortical necrosis
584.7	Acute kidney failure with lesion of renal medullary (papillary) necrosis
584.8	Acute kidney failure with other specified pathological lesion in kidney
584.9	Acute kidney failure, unspecified
Additional Codes for Dialysis-Requiring Acute Kidney Injury	
V45.1	Renal dialysis status
V56.0	Encounter for dialysis and dialysis catheter care
V56.1	Fitting and adjustment of extracorporeal dialysis catheter
39.95	Hemodialysis

1. Members with at least mild AKI

To evaluate the validity of AKI diagnoses, we randomly sampled 150 members within the five selected Data Partners, with a principal or secondary hospital AKI diagnosis code (Table 1; ICD-9-CM codes 584.5, 584.6, 584.7, 584.8, or 584.9). The number of charts requested was initially divided among the Data Partners regardless of membership size, with each Data Partner selecting a similar number of cases with possible AKI diagnoses. For the two Data Partners that had multiple health plans participating in this project, the number of charts within each of these two Partners was further divided equally.

2. Members with dialysis-requiring AKI (AKI-D)

To ensure sufficient sample sizes to evaluate the validity of inpatient AKI requiring dialysis, we randomly sampled 75 members, within the five participating Data Partners, who had a principal hospital diagnosis that suggested possible AKI (ICD-9-CM codes 584.5, 584.6, 584.7, 584.8, or 584.9) and an inpatient diagnosis procedure code suggestive of possible dialysis requirement (ICD-9-CM codes V45.1, V56.0, V56.1, or 39.95). The number of charts requested was again divided among the Data Partners using the same method as described for members with at least mild AKI.

3. Main outcomes

a) Outcome 1: At least mild AKI

The primary outcome was clinically significant AKI, defined as events meeting or exceeding the criteria for "at least mild AKI". Although hospital diagnosis codes were used to identify possible AKI cases, the definitive presence or absence of AKI during medical chart review was determined using standard definitions that are based upon changes in serum creatinine levels using consensus definitions, including those developed by ADQI, AKIN, and KDIGO.[1,6,7] At least Mild AKI was defined as an increase in serum

creatinine x 1.5 (or greater) from baseline, OR ≥ 0.3 mg/dL increase within 48 hours. This definition is consistent with the modified RIFLE severity 'Risk' and AKIN stage I (or greater). At least Moderate AKI was defined as an increase in serum creatinine x 2 (or greater), consistent with modified RIFLE severity 'Injury' and AKIN stage II (or greater). Severe AKI was defined in two ways: using serum creatinine change or AKI with the need for dialysis. Consistent with modified RIFLE severity 'Failure' and AKIN stage III, severe AKI was defined as an increase in serum creatinine x 3 (or greater), OR increase in serum creatinine to ≥ 4.0 mg/dL with at least 0.5 mg/dL absolute rise in serum creatinine. The dialysis-requiring AKI was defined as need for renal replacement therapy in the setting of AKI, and was classified separately (see below). If not otherwise specified in this report, AKI refers to any event meeting or exceeding the definition of mild AKI.

Each of these definitions is dependent upon some information regarding the baseline creatinine. Classification of AKI is highly sensitive to the specification of baseline creatinine.[19-21] Increases in serum creatinine could be assessed from pre-hospitalization baseline using values within the preceding 3 months,[20] or the mean within the preceding 1 year (days 7-365 prior to hospitalization).[21] However, we focused on AKI associated with hospitalizations because not all Data Partners had access to outpatient records. Although AKI events were associated with hospitalizations, the acute injury could have either occurred prior to the hospital admission (community-acquired) or during the index hospitalization (hospital-acquired). Thus, AKI cases in this validation study represent hospital identified (or hospital encounter-based identification of) AKI rather than community identified AKI.

In many cases, limiting the data collection to medical records associated with a hospitalization precluded accurate characterization of the baseline creatinine using prior values. For those cases with pre-hospitalization creatinine values available within the requested chart components, the baseline creatinine was established using the most recent outpatient serum creatinine to the index hospitalization from a non-acute episode of care (routine outpatient health maintenance exam; no urgent care, emergency room, inpatient encounters). However, the first admission creatinine was used in many cases to establish an individual's baseline creatinine if no preceding creatinine values were available. Using either outpatient serum creatinine values or the first admission creatinine, cases that clearly met any of the specific severity criteria above (At least Mild AKI, At least Moderate AKI, or Severe AKI) were considered to be ***Definite AKI*** cases.

The certainty of adjudicating AKI was diminished in two particular circumstances in which limited available data precluded definitive classification of AKI. Consequently, these participants were considered as potential cases of ***Probable AKI***. First, for some cases there was uncertainty of whether serum creatinine changes occurred within the 48 hour window specified by the AKI definition because of unknown time periods between the baseline creatinine measurement and creatinine elevations during index hospitalizations. Second, in other cases for which no baseline creatinine was available, AKI was considered to have probably occurred if the following 2 conditions were met: 1) the clinical context and documentation was consistent with an episode of new AKI, or acute on chronic renal failure; and 2) serum creatinine values during the index hospitalizations dropped at least as much as the minimum criteria for a corresponding rise according to the definition of at least mild AKI (reflecting recovery from at least mild AKI, with decrease in serum creatinine of > 33% OR ≥ 0.3 mg/dL). These probable cases could be inferred with considerable confidence based on the clinical evidence indicative of Recovering AKI, even though the strict AKI criteria were not met because baseline creatinine values were unknown.

Additional circumstances required additional classifications. In rare circumstances, cases of AKI were unlikely because the captured events appeared to reflect elevated creatinine values that were chronic rather than acute. These cases of probable progression of underlying chronic kidney disease were considered to be ***Unlikely AKI*** cases. When sufficient information was not available to determine whether AKI occurred, cases were considered to be ***Unable to determine***. Such cases could be related to unavailable baseline serum creatinine, insufficient frequency of serum creatinine values obtained during the index hospitalization, or other reasons. Finally, several cases were found to not reflect episodes of AKI and were considered to be ***No AKI***. Although not anticipated, many of these no AKI cases were related to the presence of end-stage renal disease requiring chronic dialysis therapy prior to the index hospitalization. In such circumstances, additional acute kidney injury is inconsistent with the patients underlying diagnosis of chronic kidney failure.

b) Outcome 2: Dialysis-requiring AKI

The second outcome of interest was dialysis-requiring AKI. As a subset among cases with AKI, we evaluated dialysis-requiring AKI cases which represent the most serious clinical severity of AKI. A diagnosis of Dialysis-requiring AKI was confirmed if, at any time during the index hospitalization, a member had: 1) at least mild AKI, defined in (a) above, and 2) a procedure code for dialysis (Table 1). Members with pre-existing kidney failure requiring dialysis prior to the index hospitalization did not meet the first of these two criteria and were therefore categorized as not having experienced dialysis-requiring AKI (i.e., they were considered to be false positives for purposes of calculating the performance metrics of the proposed algorithm).

c) Sensitivity Analyses

A number of sensitivity analyses were conducted to better understand the potential implications of alternative criteria and results among subgroups of interest. We examined variation according to Data Partner, age, gender, and race. In addition, sensitivity analyses were conducted for both at least mild AKI and dialysis-requiring AKI cases using alternative numerator and denominator criteria that may improve individual case classifications if alternate outcome definitions were used (e.g., classifying patients who have a clear recovery of kidney function as having experienced AKI) or if additional data were available (e.g., excluding patients with a history of chronic dialysis from case selection).

4. Program code to identify cases

In collaboration with the AKI workgroup, the MSOC used the criteria described above to develop a SAS program for the Data Partners to identify a total of 225 potential AKI cases for medical record review, including 150 cases of at least mild AKI and 75 cases of dialysis-requiring AKI. Program code was tested, and a test run was conducted at two Data Partner locations to ensure accuracy prior to distribution to all Data Partners. Each Data Partner then executed the SAS program locally and provided the MSOC with the output via the Mini-Sentinel Secure Portal.

C. CHART RETRIEVAL

The workgroup used the case retrieval process established by the Acute Myocardial Infarction (AMI) Health Outcome of Interest Validation workgroup in Year 1 of the Mini-Sentinel Pilot Program.[22]

1. Determination of chart components

The workgroup collaboratively identified a listing of the minimal data elements and chart components needed for the validation of AKI. The requested chart components included the following: emergency department notes, admission history and physical, nephrology consultation notes, discharge summary, all laboratory reports, and the chart face sheet.

All chart components were redacted of any data elements that directly identified individuals, but included dates of service.

The MSOC reviewed the list of requested chart components in relation to the HIPAA Privacy Rule's minimum necessary standard, and confirmed that the information requested constituted the minimum amount of information necessary for this project.

2. Obtaining chart information

Data Partners were provided with a privacy packet prepared by the Mini-Sentinel Privacy Panel which included: 1) the Mini-Sentinel Privacy Panel white paper discussing data privacy issues in Mini-Sentinel, 2) letters from OHRP to the FDA and from the FDA to the Mini-Sentinel Principal Investigator stating that the Sentinel and Mini-Sentinel activities, respectively, are not within OHRP's purview, and 3) letters from the FDA to the Mini-Sentinel Principal Investigator stating that the Mini-Sentinel is a public health activity under HIPAA.[18] Data Partners disseminated the provider request letter (Appendix B) and elements of the privacy packet identified as the most useful to all providers from which they were requesting charts.

In addition, Data Partners were provided with a structured extraction form and checklist (Appendix E) with a corresponding manual (Appendix F). It was requested that Data Partners complete this form for each potential case whose medical record was requested, even if the record was not obtained. If the chart could not be obtained, Data Partners were asked to indicate any of the following reasons: 1) Dates don't match, 2) Available information incomplete, 3) No record of date of service, 4) Cannot locate provider, 5) Chart archived/lost/destroyed, 6) No record of patient, 7) No record of patient in time span, 8) Refuses to participate/consent, or 9) No response from facility after max attempts.

Selected cases were identified at each Data Partner using the previously described SAS program. Data Partners gathered potential cases' identifying information and determined the providers housing each of the requested charts. The Data Partner requested charts from the provider directly or through a subcontract with a vendor. Various methods were used to retrieve and redact the chart components, including: 1) charts were retrieved by providers and sent to the Data Partner who performed redaction, 2) charts were retrieved at the provider site by the Data Partner's abstractor, who performed redaction, and 3) charts were retrieved at the hospital by a subcontracted vendor's abstractor, who performed redaction and forwarded an electronic copy to the Data Partner. These methods are discussed in detail in Appendix G. The MSOC confirmed the thoroughness of the redactions and, once confirmed, uploaded the charts to the Mini-Sentinel Secure portal, where they were available to the workgroup for abstraction and adjudication.

D. CHART ABSTRACTION

Two trained abstractors reviewed the redacted medical records of all potential cases. Data were abstracted onto an electronic version of a structured form (Appendix H) using Microsoft Word. The abstraction form collected information from emergency department notes, admission history and physical, nephrology consultation notes, discharge summary, all laboratory reports, and the chart face sheet. Details of specific data variables collected are shown in Table 2.

Table 2. Most common sources of data elements included in chart abstraction form for determination of acute kidney injury cases, by hospital medical record chart component.

Data Element	Emergency Department Note	Admission History and Physical	Nephrology Consultation Notes	Discharge Summary	All Laboratory Reports	Chart Face Sheet
Dates and times						
Admission	X	X		X		X
Discharge				X		X
Serum creatinines	X	X	X	X	X	
Demographic data						
Race		X				X
Ethnicity		X				X
Age		X				X
Gender		X				X
Medical history						
Weight	X	X	X	X		
Transfer status	X	X	X	X		
ICU stay	X	X	X	X		
Operation	X	X	X	X		
Dialysis initiation	X	X	X	X		
Serum creatinine						
Outpatient baseline	X	X	X	X	X	
First admission	X	X	X	X	X	
Peak value	X	X	X	X	X	
All values	X	X	X	X	X	
Events						
Dialysis initiation	X	X	X	X	X	
Death			X	X		
Chart components available						
	X	X	X	X	X	X

E. CASE ADJUDICATION

After medical record review, data abstraction forms and redacted records were independently reviewed by two nephrologists, who served as endpoint adjudicators. Using an electronic version of a structured form (Appendix I), they classified each AKI case as: 1) definite, 2) probable, 3) unlikely, 4) no AKI, or 5) unable to determine (for members with missing or insufficient serum creatinine values). If the two

reviewers could not reconcile disagreements on any of these classifications, the disagreements were resolved after review by a third nephrologist to adjudicate the event.

F. STATISTICAL ANALYSES

We sought to identify and determine the positive predictive value (PPV) of code-based algorithms for AKI separately in members with any AKI and those with dialysis-requiring AKI. The focus was on PPV because a sufficiently high PPV provides confidence that identified outcomes are true events while avoiding the much larger samples necessary and scope of work involved in estimating sensitivity and specificity.

For the algorithm intended to capture at least mild AKI events, we estimated that a sample of 150 cases would allow determination of the PPV of the diagnostic codes with a maximum 95% CI of ±0.07, assuming a PPV of 76% from the literature. For the algorithm intended to capture dialysis-requiring AKI events, we assumed a PPV of 94% from the literature and estimated that 75 cases would allow determination of the PPV of the diagnostic codes with a maximum 95% CI of 87-98%. Data were analyzed using Stata 12.0 (Stata Corp, College Station, TX) and Microsoft Excel.

Although we sought to identify algorithms with PPVs exceeding 80% in the MSDD, results from prior studies[8-11] suggested that there is considerable misclassification, and additional refinements to the algorithm informed by the results of this study might be necessary. A number of sensitivity analyses were conducted to better understand the potential implications of alternative inclusion and outcome criteria, as well as results among subgroups of interest. To understand variation across the sites included in this study, we examined variation according to Data Partners. To explore the influence of various patient characteristics that strongly influence serum creatinine (and by extension, changes in serum creatinine reflecting AKI), we examined variation in the PPV according to age, gender, and race. Finally, to minimize the impact of misclassification or uninformative cases, we restricted the sample according to the following criteria in order to determine whether higher PPV's could be achieved using various sample restrictions: 1) Definite AKI with indeterminate and baseline chronic dialysis cases excluded from the denominator; 2) Definite AKI and probable AKI cases included in the numerator; and 3) Definite AKI and probable AKI cases included in the numerator *with* indeterminate and baseline chronic dialysis cases excluded from the denominator.

IV. RESULTS

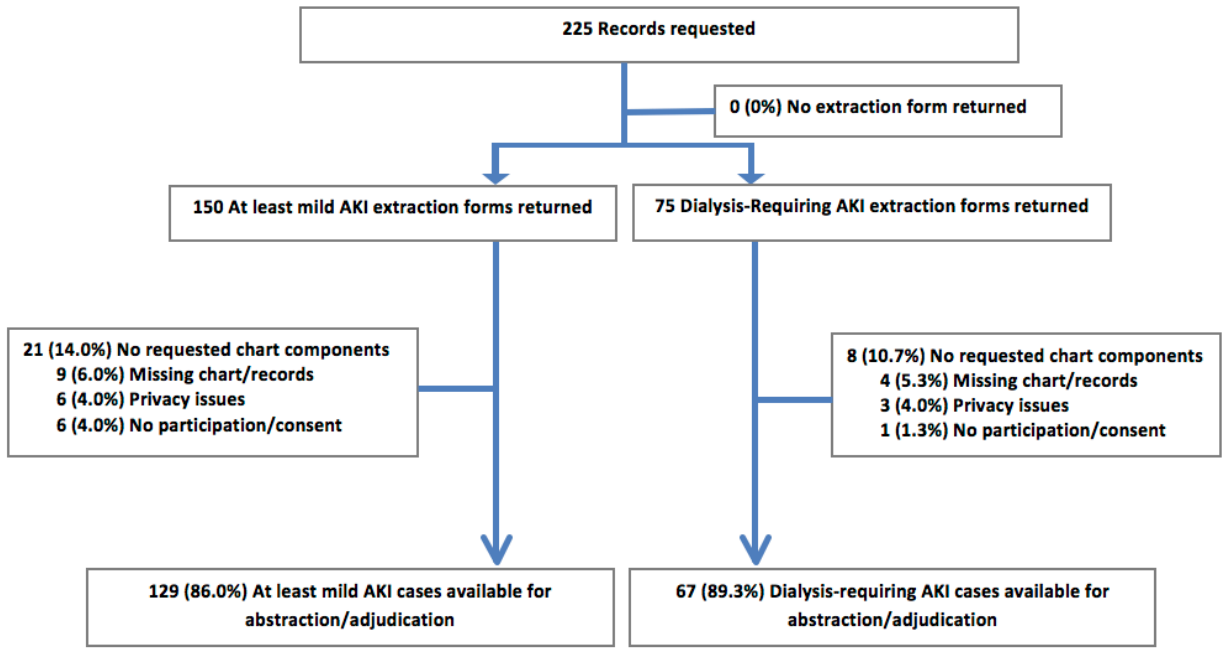
A. ANALYSIS OF AKI DIAGNOSES IN THE MSDD

Across the eleven participating Data Partner health plans within the MSDD, there were 55,570,935 covered members, of whom 24,559,025 had at least 12 months of continuous enrollment between 2010 and 2011. Among these members, 118,013 (0.48%) were identified with a hospital-associated AKI ICD-9-CM diagnosis code recorded in either a principal or secondary position. These potential cases of any AKI varied across Data Partner health plans, ranging from 0.25% to 1.39%. Among the 24,559,025 members, 4,588 (0.02%) were identified with a hospital-associated AKI ICD-9-CM diagnosis code and procedure code for dialysis recorded in either a principal or non-principal position. These potential cases of dialysis-requiring AKI also varied across Data Partner health plans, ranging from 0.01% to 0.06%.

B. CASE RETRIEVAL RESULTS

A summary of the case retrieval results can be found in Figure 1 and is described in the sections below.

Figure 1 Flow chart of overall case retrieval results. All percentages are based on the number of records requested.



1. Responses to chart requests

Among the 225 charts requested, 150 were for at least mild AKI and 75 were for dialysis-requiring AKI. Of the 225 charts requested overall, Data Partners were able to identify and return a completed extraction form for all cases (100%). In total, charts were received for 196 (87.1%) of the records requested, with 129 (86.0%) for at least mild AKI and 67 (89.3%) for dialysis-requiring AKI cases.

2. Proportion of requested charts provided

Of the 225 potential cases identified, the requested charts were not provided for twenty-nine (12.9%) of the potential cases. Of those, charts for 13 (5.8%) cases were missing or not found; 9 charts (4.0%) were not obtained because of authorization or privacy issues (i.e., HIPAA authorization was required, IRB restricted chart retrieval, or the site required that the individuals provide consent); and 7 charts (3.1%) were not obtained because the provider refused to participate or the site did not participate in research. Therefore, a total of 196 (87.1%) cases were available for chart abstraction.

The number of charts not provided and the reasons they could not be obtained varied widely by Data Partner (Table 3). Although two of the Data Partners accounted for most of the unattained charts, the overall yield was generally favorable (87.7% overall chart retrieval).

Table 3. Reasons requested charts were not provided, by Data Partner.

Data Partner	No. Charts Requested	Missing chart/ records	Privacy issues	No participation/ consent	Total (% of requested charts)
DP1	45	8	6	3	17 (7.6%)
DP2	45	2	1	0	3 (1.3%)
DP3	45	3	2	4	9 (4.0%)
DP4	45	0	0	0	0 (0%)
DP5	45	0	0	0	0 (0%)
Total	225	13 (5.8%)	9 (4.0%)	7 (3.1%)	29 (12.9%)

3. Proportion of requested chart components provided

Of the 196 charts provided by the Data Partners, 129 charts for potential cases of at least mild AKI were available (Table 4) and 67 charts for potential cases of dialysis-requiring AKI (Table 5) were available. The proportion of requested chart components provided for each of these groups varied substantially across Data Partners as well as individual chart. The average proportion of all six requested charts components provided ranged from 54.4% to 70.8% across Data Partners. Among individual components, nearly all charts included admission history and physical, as well as laboratory report data. However, nephrology consult notes were only included with approximately 1 in 4 charts. The lengths of returned charts also varied across Data Partners with means ranging from approximately 30 to 115 pages (overall average 58 pages).

Table 4. Chart components provided for at least mild AKI cases, by Data Partner.

		Chart Components Received						
Data Partner	**No. Charts Received**	**ED Notes**	**Admission history and physical**	**Nephrology consult notes**	**Discharge summary**	**All lab reports**	**Face sheet**	**Mean number of Pages**
DP1	19	16	19	7	1	19	15	94.3
DP2	28	28	28	7	28	28	9	37.7
DP3	22	14	21	6	20	20	16	114.6
DP4	30	23	30	3	30	30	21	40.8
DP5	30	24	27	13	29	30	26	29.9
Total	129	105 (81.4%)	125 (96.9%)	36 (27.9%)	108 (83.7%)	127 (98.4%)	87 (67.4%)	58.0

For the 67 cases of dialysis-requiring AKI (Table 5), the average proportion of all six requested charts components was slightly higher than for at least mild AKI cases, and ranged from 63.0% to 76.7% across Data Partners. Among individual components, nearly all charts included admission history and physical, discharge summaries, and laboratory report data. Nephrology consult notes were more common and included with approximately 3 in 4 charts. The lengths of returned charts were longer than for at least mild AKI cases and also varied across Data Partners with means ranging from approximately 34 to 258 pages (overall average 120 pages).

Table 5. Chart components provided for dialysis-requiring AKI cases, by Data Partner.

		Chart Components Received						
Data Partner	**No. Charts Received**	**ED Notes**	**Admission history and physical**	**Nephrology consult notes**	**Discharge summary**	**All lab reports**	**Face sheet**	**Mean number of Pages**
DP1	9	6	7	5	7	9	7	178.3
DP2	14	8	14	11	14	14	5	117.3
DP3	14	11	13	11	13	12	12	258.1
DP4	15	13	14	13	15	14	11	45.1
DP5	15	10	14	11	14	15	13	34.2
Total	67	48 (71.6%)	62 (92.5%)	51 (76.1%)	63 (94.0%)	67 (100%)	48 (71.6%)	120.2

C. VALIDITY OF AKI DIAGNOSES IN MEMBERS WITH AT LEAST MILD AKI

1. Characteristics of sample

Race was identified in half of the at least mild AKI cases, with considerable variation in the proportion unknown across Data Partners (Table 6). The sample of at least mild AKI cases was generally elderly with mean age 75.1 years. Nearly half of the sample (44%) was male.

Table 6. Case characteristics for at least mild AKI cases, by Data Partner.

	Any AKI				
	Race (n [%])			Age	Male
Data Partner	White	Black	Unknown	Mean y	n (%)
DP1	13(68.4%)	2 (10.5%)	4 (21.1%)	77.8	9 (47.4%)
DP2	8 (28.6%)	0 (0%)	20 (71.4%)	79.8	14 (50.0%)
DP3	7 (31.8%)	5 (22.7%)	10 (45.5%)*	72.1	12 (54.5%)
DP4	1 (3.3%)	0 (0%)	29 (96.7%)	72.0	14 (46.7%)
DP5	16 (53.3%)	13 (43.3%)	1 (3.3%)	74.3	8 (26.7%)
Total	45 (34.9%)	20 (15.5%)	64 (49.6%)	75.1	57 (44.2%)

* - 2 of these 10 cases were identified as Other race

2. Confirmation of at least mild AKI events

Of the 129 cases abstracted, nephrologist adjudicators determined that 62 cases were ***definite AKI*** cases with 67 cases that were judged not to be consistent with a definite case of AKI ("AKI+"; Table 7). In the primary analysis, the PPV for definite AKI cases was 48.1% (95% confidence interval [95% CI], 39.4% to 56.7%). Not surprisingly, this overall value is somewhat lower than the experience reported in prior studies and reflects the results of adjudication when using stringent criteria for AKI in the setting of variable documentation and availability of data in routine clinical care. If all cases requested were to be used in the denominator (n=150), the PPV would have been even lower at 41.3% (95% CI, 33.5% to 49.2%).

Table 7. Positive predictive values (with 95% confidence intervals) of at least mild AKI, including definite AKI cases only, by Data Partner.

Data Partner	AKI +	AKI -	Total # of charts	PPV (%)	95% Confidence Interval
DP1	10	9	19	52.6	30.2, 75.1
DP2	12	16	28	42.9	24.5, 61.2
DP3	10	12	22	45.5	24.6, 66.3
DP4	15	15	30	50.0	32.1, 67.9
DP5	15	15	30	50.0	32.1, 67.9
Overall	62	67	129	48.1	39.4, 56.7

Accordingly, the secondary analysis included cases that were either ***definite*** or ***probable AKI***. Of the 129 cases abstracted, nephrologist adjudicators determined that 109 cases were either definite or probable AKI (Table 8). In addition to the 62 definite cases, the nephrologist reviewers found 47 probable cases of AKI. They believed 17 of these cases were not definite because the interval for baseline creatinine was unknown, 29 of these cases were not definite because a baseline creatinine value was not available but decreases in serum creatinine during the index hospitalization reflected recovery from at least mild AKI, and 1 additional case was not definite because the baseline creatinine was 2 years old. When the clinical context was consistent with AKI, and the temporal criteria for the baseline creatinine were not required because the interval for baseline creatinine was unknown, 17 cases were probable: 12 of these cases were mild AKI, 2 cases were moderate AKI, and 3 cases were severe AKI. When baseline creatinine was

unknown but the clinical context and creatinine changes were consistent with recovering AKI, 29 cases were probable: the mean difference between peak and nadir creatinine during the index hospitalization was 0.79 mg/dL (SD 0.39 mg/dL), and 21 of 29 cases included absolute creatinine drops of at least 0.5 mg/dL. There were 20 cases that were judged not to be consistent with a definite or probable AKI ("AKI-"), either because no AKI was found to be present (6 cases), the patient already had pre-existing end-stage renal disease (1 case), the baseline creatinine value was needed but unavailable (9 cases), additional creatinine values were necessary but not obtained (2 cases), or for other reason (2 cases). The PPV varied across Data Partners, ranging from 78.6% to 89.5%, but were similar across subgroups of age, gender, and race (Table 9).

Table 8. Positive predictive values (with 95% confidence intervals) of at least mild AKI, including both definite and probable AKI cases, by Data Partner.

Data Partner	AKI +	AKI -	Total # of charts	PPV (%)	95% Confidence Interval
DP1	17	2	19	89.5	75.7, 100.0
DP2	22	6	28	78.6	63.4, 93.8
DP3	19	3	22	86.4	72.0, 100.0
DP4	25	5	30	83.3	70.0, 96.7
DP5	26	4	30	86.7	74.5, 98.8
Overall	109	20	129	84.5	78.3, 90.7

Table 9. Positive predictive values (with 95% confidence intervals) of at least mild AKI, by subgroup.

Characteristic	AKI +	AKI -	Total # of charts	PPV (%)	95% Confidence Interval
Age <75 y	43	8	51	84.3	76.3, 92.5
Age ≥75 y	65	12	77	84.4	76.3, 92.5
Female	61	11	72	84.7	76.4, 93.0
Male	48	9	57	84.2	74.7, 93.7
Black	18	3	21	85.7	70.7, 100.0

D. VALIDITY OF AKI DIAGNOSES IN MEMBERS WITH DIALYSIS-REQUIRING AKI

1. Characteristics of sample

Race was identified in almost half of the dialysis-requiring AKI cases, with considerable variation in the proportion unknown across Data Partners (Table 10). The sample of dialysis-requiring AKI cases was generally elderly with mean age 65.9 years. Over half of the sample (58%) was male.

Table 10. Case characteristics for dialysis-requiring AKI cases, by Data Partner.

	Dialysis-requiring AKI				
	Race (n [%])			Age	Male
Data Partner	White	Black	Unknown	Mean y	n (%)
DP1	4 (44.4%)	2 (22.2%)	3(33.3%)	71.4	3 (33.3%)
DP2	1 (7.1%)	2 (14.3%)	11(78.6%)	66.2	8 (57.1%)
DP3	4 (28.6%)	2 (14.3%)	8 (57.1%)	72.2	9 (64.3%)
DP4	0 (0%)	1 (6.7%)	14 (93.3%)	66.7	10 (66.7%)
DP5	8 (53.3%)	6 (40.0%)	1 (6.7%)	55.4	9 (60.0%)
Total	17 (25.4%)	13 (19.4%)	36 (55.2%)	65.9	39 (58.2%)

* - 1 of these 14 cases were identified as Asian race

2. Confirmation of dialysis-requiring AKI events

Of the 67 cases abstracted, nephrologist adjudicators determined that 43 cases were ***dialysis-requiring AKI*** cases, with 24 cases that were judged not to be consistent with a case of dialysis-requiring AKI (Table 11). Of these 24 cases, 14 patients had pre-existing end-stage renal disease requiring dialysis, 3 had definite AKI but no initiation of renal replacement therapy, 3 had probable AKI but no initiation of renal replacement therapy, 3 had insufficient creatinine data to adjudicate AKI and 1 was unlikely to have AKI based on gradual progression of outpatient CKD. Overall, the PPV for definite AKI cases was 64.2% (95% CI, 52.7% to 75.7%). Not surprisingly, this overall value is somewhat lower than the experience reported in prior studies and reflects the misclassification that results from including patients with end-stage renal disease already on chronic dialysis.

Table 11. Positive predictive values (with 95% confidence intervals) of dialysis-requiring AKI cases, by Data Partner.

Data Partner	AKI +	AKI -	Total # of charts	PPV (%)	95% Confidence Interval
DP1	5	4	9	55.6	23.1, 88.0
DP2	9	5	14	64.3	39.2, 89.4
DP3	11	3	14	78.6	57.1, 100.0
DP4	10	5	15	66.7	42.8, 90.5
DP5	8	7	15	53.3	28.1, 78.6
Overall	43	24	67	64.2	52.7, 75.7

The PPVs varied across subgroups of age, gender, and black race (Table 12). Although the number of cases was low and the confidence estimates wide, the PPV was slightly lower for younger patients (<75 years of age) and males. During adjudication of cases, one particular circumstance led to inclusion of potential cases that could have been avoided with additional longitudinal data for individuals within the MSDD. Specifically, patients with prior known history of end-stage renal disease requiring dialysis could be excluded using prior claims. Under a sensitivity analysis in which such cases were removed from the

denominator and the numerator included dialysis-requiring AKI cases, the PPV was 81.1% (95% CI, 70.6 to 91.7).

Table 12. Positive predictive values (with 95% confidence intervals) of dialysis-requiring AKI, by subgroups and alternative scenario.

Characteristic	AKI +	AKI -	Total # of charts	PPV (%)	95% Confidence Interval
Age <75 y	25	17	42	59.5	44.7, 74.4
Age ≥75 y	18	7	25	72.0	54.4, 89.6
Female	21	7	28	75.0	59.0, 91.0
Male	22	17	39	56.4	40.8, 72.0
Black	8	5	13	61.5	35.1, 88.0
Sensitivity analysis*	43	10	53	81.1	70.6, 91.7

V. SUMMARY AND CONCLUSIONS

In conclusion, the individual pre-specified ICD-9-CM codes for identifying hospitalized AKI yielded a PPV of 48.1% for at least mild AKI and 64.4% for dialysis-requiring AKI. For at least mild AKI, the PPV increased to 84.5% when limitations in available data were acknowledged by including probable cases of AKI with the definite cases. Despite using less rigid definitions for AKI, the overall clinical evidence was believed to be strongly consistent with AKI among these probable cases. For dialysis-requiring AKI, the PPV increased to 81.1% when additional restrictions were applied to eligible cases that excluded members with a prior history of chronic dialysis. We recommend that the algorithm for at least mild AKI may be used to detect AKI events in surveillance activities and in claims-based databases. We also recommend that the algorithm for dialysis-requiring AKI could be used, but that is should be modified to exclude the selection of cases with a history of prior claims for dialysis. While both algorithms appear reasonable to use for active surveillance purposes, further refinement and validation may be prudent. Surveillance activities seeking to identify AKI events using ICD-9-CM codes with greater precision should consider additional criteria available in longitudinal records that would minimize false positive cases.

Limitations of this validation study include the inability to fully characterize baseline serum creatinine without longitudinal laboratory data. Missing baseline creatinine data limited the ability to classify potential cases and characterize the severity of AKI among probable cases. AKI cases in this study represented hospital identified (or hospital encounter-based identification of) AKI rather than community identified AKI. Although most cases of probable AKI with demonstration of recovery likely occurred prior to the index hospitalization, the results from this study may not apply directly for outpatient surveillance of drug-induced AKI. Because only adults were included in this validation study, the results may not apply to children and adolescents. Finally, a number of other test characteristics of hospital ICD-9-CM diagnoses in identifying AKI events and AKI events requiring dialysis were not obtained (i.e. negative predictive value, sensitivity, specificity).

Strengths of this study include an evaluation of the validity of at least mild AKI diagnoses using contemporary, standardized definitions in administrative data from 5 large Data Partners located throughout the US. For cases that could not meet the formal criteria because of limitations in available data, this evaluation of probable AKI cases may provide sufficient confidence that such cases can be considered along side definite cases of AKI, particularly for those cases defined by the presence of recovery from AKI. In addition to at least mild AKI, this study evaluated the validity of dialysis-requiring AKI diagnoses and identified a readily feasible strategy to optimize this algorithm for identifying dialysis-requiring AKI. For both outcomes, two independent nephrology adjudicators confirmed all cases. Finally, the positive predictive value estimates in this study appear to be generally stable across diverse Data Partners and patient characteristics.

VI. ACKNOWLEDGMENTS

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Data Partner	
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HealthCore, Inc. Government & Academic Research, Alexandria, VA	Amanda Rodriguez, BA Fang Tian, PhD
HMO Research Network	
• Group Health Cooperative	Kristina L. Hansen, BA
• HealthPartners Institute for Education and Research, Saint Paul, Minnesota	Teri DeFor, MS Dianne Eggen, MPH Brian Owens, BA
• Henry Ford Health System, Department of Public Health Sciences, Detroit, MI	Lois Lamerato, PhD
• Marshfield Clinic Research Foundation, Marshfield, WI	Deborah L. Johnson, BA Valerie D. McManus, MPH
Humana, Inc., Comprehensive Health Insights, Miramar, FL	Vinit P. Nair, BPharm, MS, RPh
• Total Therapeutic Management, Inc., Kennesaw, GA**	Thomas A. Stacy, PharmD
Kaiser Permanente Center for Effectiveness and Safety Research	
• Kaiser Permanente Colorado Institute for Health Research, Denver, CO	Daniel A. Jaynes, MSHA, MBA Carsie A Nyirenda, MPH Marilyn Pearson, RHIA
• Kaiser Permanente Center for Health Research Hawai'i, Honolulu, HI	Yihe Daida, MS John Parker, BS
• Kaiser Permanente Northern California, Division of Research, Oakland, CA	Lisa J. Herrinton, PhD Rick Riordan, RHIA
• Kaiser Permanente Northwest Center for Health Research, Portland, OR	Jill Mesa, BA Kim Olson Amanda Petrik, MS
Vanderbilt University School of Medicine, Department of Preventive Medicine	Tony Morrow, AS

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VIII. APPENDICES

A. APPENDIX A. MEMBERS OF THE MINI-SENTINEL ACUTE KIDNEY INJURY (AKI) VALIDATION WORKGROUP

Collaborator	Role
U.S. Food and Drug Administration	Provided input in protocol development, development of AKI definitions, abstraction/adjudication forms development, validation of AKI, and interpretation of results.
Harvard Pilgrim Health Care Institute	**Mini-Sentinel Operations Center**. Provided administrative support and assistance; coordinated communication with Data Partners; coordinated chart retrieval process; provided Lead Site with de-identified data from Data Partners.
Duke Clinical Research Institute	**Lead Site**. Designed project specifications; created all forms and manuals for the project; completed abstraction and adjudication.
HMORN: Meyers Primary Care Institute	Provided input in development of AKI definitions, abstraction/adjudication forms development, , and interpretation of results.
Clinical Advisors	**Steven M. Brunelli, MD, MSCE** Brigham and Women's Hospital, Harvard Medical School **Chi-yuan Hsu, MD, MSc** University of California, San Francisco **Chirag Parikh, MD, PhD** Yale University
Vanderbilt University School of Medicine	**Data Partners**. Implemented SAS program code for case selection; retrieved, copied, and de-identified specified chart components for selected cases; submitted data outputs and redacted charts to the Mini-Sentinel Operations Center. Conducted data analyses (KPNW).
HealthCore	
HMO Research Network: Marshfield Henry Ford Group Health Health Partners	
Humana	
Kaiser Permanente KPNW KPCO KPHI KPNC	

B. APPENDIX B: LETTER FROM FDA TO CHART HOLDERS IDENTIFYING THE AKI VALIDATION PROJECT AS A PART OF MINI-SENTINEL

We are writing to ask your help with an important public health activity. The Food and Drug Administration (FDA) has initiated a chart validation activity of suspected acute kidney injury (AKI) events in its Mini-Sentinel pilot. The goal of the project is to validate an algorithm for identifying AKI in electronic databases. While no specific medical product will be studied as part of this project, FDA expects to use this algorithm in future projects that assess potential medical product safety concerns related to this health event.

Mini-Sentinel is a pilot project sponsored by the U.S. Food and Drug Administration (FDA) to inform and facilitate development of a fully operational active surveillance system, the Sentinel System, for monitoring the safety of FDA-regulated medical products. For additional information on the FDA's Sentinel Initiative, please visit: http://www.fda.gov/Safety/FDAsSentinelInitiative/default.htm. For more information on Mini-Sentinel, please visit: http://mini-sentinel.org/.

FDA is requesting your help to obtain medical records for this project. Medical records are important because they will allow investigators to verify that your patient truly had AKI. To ensure privacy and confidentiality, all personal identifying information will be redacted (deleted) from the chart by the requesting Mini-Sentinel Data Partner and only the minimum necessary information will be shared with investigators to enable the completion of the project. Further, project investigators will share only de-identified, summary data and final analyses with the FDA.

All Mini-Sentinel activities are considered public health practice and not research. As such, this effort does not require Institutional Review Board review, since it is considered to be in support of FDA's public health mission. For more information, please see Mini-Sentinel's *Principles and Policies* document at: http://mini-sentinel.org/about_us/principles_and_policies.aspx. The relevant section is also copied below for ease of reference:

> **4.1 Mini-Sentinel Activities Are Public Health Practice, Not Research**
> *The HHS Office of Human Research Protections (OHRP) determined that the regulations administered by OHRP (45 CFR Part 46, "Common Rule") do not apply to the activities that are included in the FDA's Sentinel Initiative. FDA stated that this assessment also applies to Mini-Sentinel, as it is part of the Sentinel Initiative.*
>
> *Additionally, FDA determined that Mini-Sentinel activities are public health activities in support of FDA's public health mission. It is therefore*

not necessary for the Collaborating Institutions to obtain approval from their respective Institutional Review Boards (IRBs) or Privacy Boards, or to obtain waivers of authorization under HIPAA, to participate in Mini-Sentinel activities (45 CFR §164.512(b)).

The HIPAA Privacy Rule permits covered entities the use and disclosure of protected health information (PHI) to public health authorities without patient authorization. Public health authorities include the FDA. The Operations Center and Collaborating Institutions are also public health authorities for purposes of the Mini-Sentinel pilot, because they are acting under contract with and under the authority of the FDA.

We very much appreciate your assistance with this important public health activity. FDA believes that the results will help better inform the Agency and healthcare providers worldwide. Please contact Patrick Archdeacon, FDA's Project Lead, (patrick.archdeacon@fda.hhs.gov), if you have questions or concerns about this letter, or Susan Forrow, Project Manager at Harvard Pilgrim Healthcare Institute (susan_forrow@harvardpilgrim.org), if you have further questions about the AKI validation project.

Sincerely,

Rachel E. Sherman

Rachel E. Sherman, M.D., M.P.H.,
Associate Director of Medical Policy and
Director, Office of Medical Policy
Center for Drug Evaluation and Research
Food and Drug Administration

C. APPENDIX C. LETTER TEMPLATE USED BY DATA PARTNERS FOR MEDICAL RECORD REQUESTS FROM PROVIDERS

<DATE>

<PROVIDER NAME>
<PROVIDER ADDRESS>

Re: Medical Records Request for FDA Medical Product Safety Monitoring System

We are contacting you regarding a project to facilitate development of a fully operational system for monitoring the safety of FDA-regulated medical products. <DATA PARTNER> is collaborating on this endeavor, Mini-Sentinel, with the FDA and the Department of Population Medicine, Harvard Medical School/Harvard Pilgrim Health Care Institute.

This pilot has been designed in response to a Congressional mandate for the FDA to monitor the safety of regulated medical products after they have been approved for use. Your cooperation is critical to successfully addressing this important FDA public health initiative. In order to conduct this project, we require review of medical records for some of your patients diagnosed with hospital-acquired acute kidney injury (AKI).

We request that you: 1) allow us access to the relevant records for the attached list of patients; 2) obtain the relevant records for the attached list of patients, redact the individually identifiable health information, and then send copies of the redacted records to us; or 3) send copies of the records to <VENDOR>, a redaction service provider with which the Mini-Sentinel Coordinating Center has contracted, which will send the information to us after it has been redacted.

Enclosed are letters from the FDA and Office of Human Research Protections identifying this as a priority public health surveillance activity that does not require authorization from your Institutional Review Board (IRB) or Privacy Board.

If you have any questions, please contact <NAME> at (###) ###-####. She/He is our leading project manager on this record review process and will be your key contact.

Please send charts to the address below:
Address

We greatly appreciate your time and assistance with this important public health initiative.

Sincerely,
NAME
TITLE

D. APPENDIX D. LIST OF INTERNATIONAL CLASSIFICATION OF DISESASES, NINTH REVISION, CLINICAL MODIFICATION (ICD-9-CM) CODES TO IDENTIFY ACUTE KIDNEY INJURY (AKI).

CODE	DESCRIPTION
584.5	Acute kidney failure with lesion of tubular necrosis
584.6	Acute kidney failure with lesion of renal cortical necrosis
584.7	Acute kidney failure with lesion of renal medullary [papillary] necrosis
584.8	Acute kidney failure with other specified pathological lesion in kidney
584.9	Acute kidney failure, unspecified

E. APPENDIX E. INTERNATIONAL CLASSIFICATION OF DISEASES, NINTH REVISION, CLINICAL MODIFICATION (ICD-9-CM) CODES TO IDENTIFY DIALYSIS PROCEDURES.

CODE	DESCRIPTION
V45.1	Renal dialysis status
V56.0	Encounter for dialysis and dialysis catheter care
V56.1	Fitting and adjustment of extracorporeal dialysis catheter
39.95	Hemodialysis

F. APPENDIX F. DATA PARTNER EXTRACTION FORM AND CHECKLIST

MINI-SENTINEL: AKI VALIDATION
DATA PARTNER EXTRACTION FORM AND CHECKLIST

This form needs to be filled out for **EACH and EVERY** case for which you seek to obtain the chart. If you are unable to obtain the chart for any reason, the question "Able to obtain chart for specified case?" should be answered "no" and the form should be forwarded along.

Case ID: _____

Medical Record Extraction Date (mm/dd/yyyy) ___ / ___ / _____

Able to obtain chart for specified case? (0 no, 1 yes) _____
If NO, please specify reason: _____

Same Name (0 no, 1 yes) _____

Same Date (0 no, 1 yes) _____

Actual day of admission
(+/- one day of specified date) (0 no, 1 yes) _____

Same Date of Birth (DOB) (0 no, 1 yes) _____

Sex is correct (0 no, 1 yes) _____

Do you have the correct chart? (0 no, 1 yes) _____
If NO, STOP!

ICD9 code listed (from eligible list below)?: ___ ___

Eligible ICD9 codes: 584.5, 584.6, 584.7, 584.8, 584.9, V45.1, V56.0, V56.1, 39.95

Were any of these codes (check one):
Principal/primary discharge code ____
Secondary ____
Cannot determine ____

Chart Components

1. Emergency Department notes (0 no, 1 yes) _____
2. Admission history and physical (0 no, 1 yes) _____
3. Nephrology consult notes (all) (0 no, 1 yes) _____
4. Discharge summary (0 no, 1 yes) _____
5. All laboratory reports (0 no, 1 yes) _____
6. Face sheet (0 no, 1 yes) _____

G. APPENDIX G. INSTRUCTION MANUAL FOR COMPLETING THEE DATA PARTNER EXTRACTION FORM

Mini-Sentinel: AKI Validation
Instructions for Completing
Data Partner Extraction Form

The purpose of this extraction form is to collect data from the medical record to use in validation of discharge diagnosis codes for acute kidney injury (AKI).

The AKI may be the reason for the hospitalization or it may be that the AKI occurs while the patient is hospitalized for an unrelated diagnosis. The hospital chart will be the only source used to extract data. There should be only one hospitalization per extraction.

PLEASE NOTE: The Data Partner Extraction form needs to be filled out for **EACH and EVERY** case for which you seek to obtain the chart. If you are unable to obtain the chart for any reason, the question "Able to obtain chart for specified case?" should be answered "no" and the form should be forwarded along, without additional materials. Likewise, if you determine that you do not have the correct chart for any reason, the question "Do you have the correct chart?" should be answered "no" and the form should be forwarded along, without additional materials.

Administrative Information

1. Case ID:
   An internally generated ID code that will allow the Data Partner to link back to original records but will not be identifiable beyond the Data Partner.

2. Medical Record Extraction Date:
   Date extraction was completed.

3. Able to obtain chart for specified case? If NO, please specify reason:
   If chart for specified case was obtained indicate "yes" and move to next item. If chart was not able to be obtained, the specific reason should be noted.

4. Same Name:
   Indicate "yes" if patient name is the same in the chart as derived from the administrative data. Indicate "no" if patient name is different than specified based on the administrative data.

5. Same Date:
   This item relates to the date the patient was admitted to the hospital. If the patient was transferred from another hospital or an emergency room, the date of admission will still be that date on which the patient was admitted to the hospital. Indicate "yes" if the admission date is the same in the chart as specified in the administrative data. Indicate "no" if the admission date is different in the chart than specified in the administrative data.

6. Actual day of admission (+/- one day of specified date):
   Date specified in the administrative data must be +/- one day of date of admission in the hospital record.

7. Same Date of Birth (DOB):
   Indicate "yes" if patient DOB is the same in the chart as it is in the administrative data. Indicate "no" if patient DOB is different in the chart than it is in the administrative data.

8. Sex:
   Indicate whether patient is male or female.

9. Do you have the correct chart? If NO, STOP!:
   If chart information does not correspond with administrative data and it seems that you do not have the correct chart, indicate "no" and do not proceed to next section. PLEASE NOTE: Even if you answer "NO" to this question, the Data Partner Extraction form must be forwarded to the Coordinating Center.

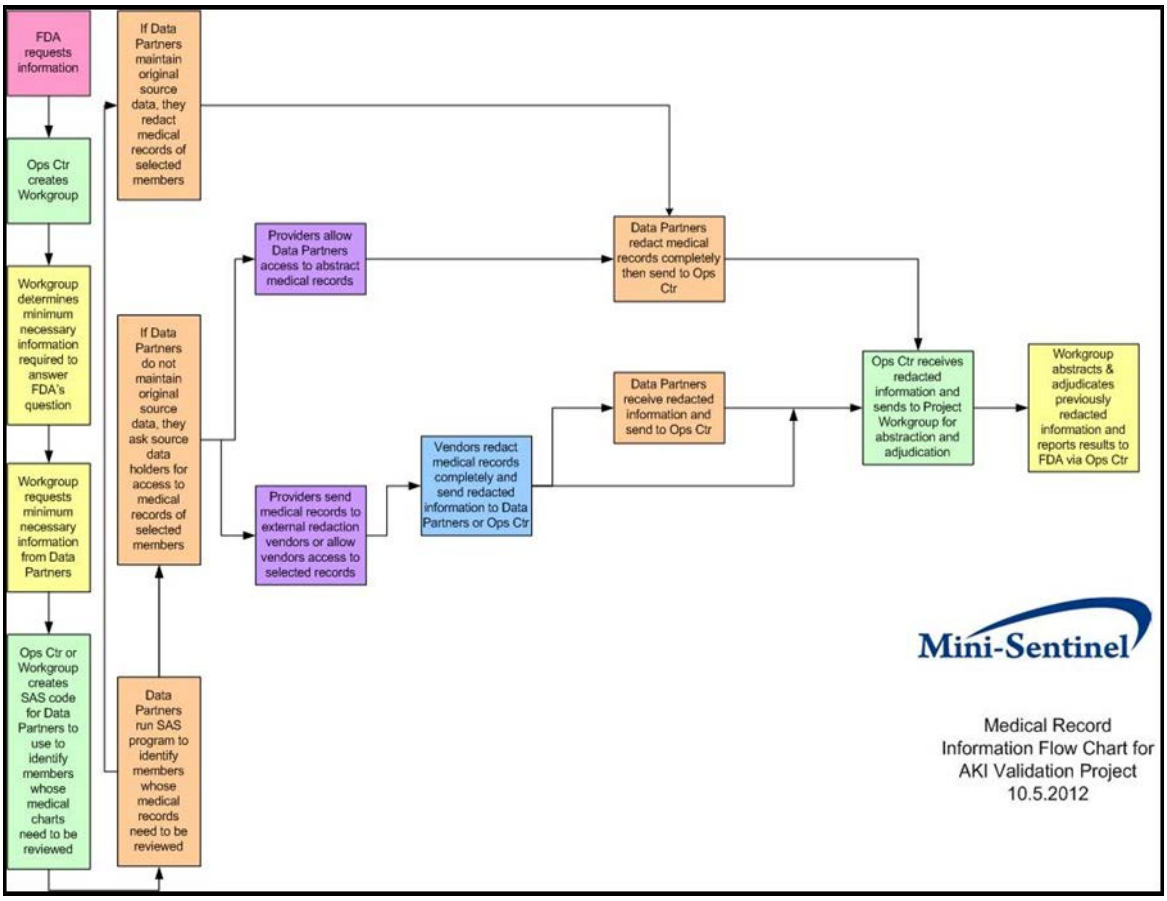
10. ICD9 code:
    Fill in specified code and mark whether this code was the principal/primary discharge code OR a secondary discharge code. Check "cannot determine" if you are unable to assess whether the discharge code for AKI is principal/primary or secondary.

Chart Components

Indicate for each chart component: "0" means missing or unavailable, "1" means present and included. Please be sure to write case ID number in the upper right hand corner of all copies. All of these materials should be de-identified.

1. Emergency Department notes
2. Admission history and physical
3. Nephrology consult notes (all)
4. Discharge summary
5. All laboratory reports
6. Face sheet

H. APPENDIX H. INFORMATION FLOW CHART FOR THE MINI-SENTINEL ACUTE KIDNEY INJURY (AKI) VALIDATION PROJECT



I. APPENDIX I. DATA ABSTRACTION FORM

Mini-Sentinel: AKI Validation
Acute Kidney Injury
Abstraction Form

Instructions: This form is for use in validation of acute kidney injury cases identified using discharge diagnosis codes. See Abstraction Manual for detailed guidelines for each form item.

Abstractor's Initials: __ __ __
Abstraction Date: __ __ /__ __ /__ __ __ __
Data Partner ID: _____

Section 1: General information

1. Date of admission: __ __ / __ __ / __ __ __ __

2. Date of discharge: __ __ / __ __ / __ __ __ __

3. Race (check all that apply):
   - WHITE ___
   - BLACK ___
   - NATIVE AMERICAN ___
   - ASIAN ___
   - OTHER ___
   - UNAVAILABLE/UNKNOWN ___

4. Ethnicity:
   - HISPANIC ___
   - NON-HISPANIC ___
   - UNAVAILABLE/UNKNOWN ___

5. Age: ___
   - UNAVAILABLE ___

6. Gender:
   - MALE ___ FEMALE ___ UNAVAILABLE ___

7. Weight:
   - _____ (lbs.) UNAVAILABLE ___

Section 2: Related Medical history

1. Was the patient transferred from another hospital?
   - YES ____ Date: __ __ / __ __ / __ __ __ __
   - NO _____

2. ICU Stay?
   - YES _____ Date: __ __ / __ __ / __ __ __ __ to Date: __ __ / __ __ / __ __ __ __
     Date: __ __ / __ __ / __ __ __ __ to Date: __ __ / __ __ / __ __ __ __

Date: __ __ / __ __ / __ __ __ __ to Date: __ __ / __ __ / __ __ __ __

NO _____

3. Is there evidence of an operation in the patient records?

YES ____ Date: __ __ / __ __ / __ __ __ __ Type of Operation _____

Date: __ __ / __ __ / __ __ __ __ Type of Operation _____

Date: __ __ / __ __ / __ __ __ __ Type of Operation _____

NO _____

4. Was the patient primarily admitted to initiate chronic dialysis (rather than initiate chronic dialysis as an outpatient)?

YES ____ Date: __ __ / __ __ / __ __ __ __

NO _____

4A. Please indicate the source that substantiates the chronic dialysis initiation below:

_____

5. Outpatient serum creatinine baseline value* _____ Date: __ __ / __ __ / __ __ __ __

*Historical value considered to be the patient's baseline or most recent stable pre-hospitalization value (documented in notes such as ED note, nephrology consult note, etc.)

5A. Please indicate the source of the outpatient creatinine values below:

_____

Section 3: Creatinine (SCr) Values Related to Hospitalization

1. First SCr value during index hospitalization: SCr_____ Date: _ _/_ _/_ _ _ _ Time_ _:_ _
2. Peak SCr value during index hospitalization: SCr _____ Date: _ _/_ _/_ _ _ _ Time_ _:_ _
3. Please list, in chronological order, all available creatinine values for the patient. Once listed, please **circle** the peak creatinine value.

Serum Creatinine Values			
1. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	2. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
3. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	4. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
5. SCr_____	Date: _ _/_ _/_ _ Time_ _:_ _	6. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
7. SCr_____	Date: _ _/_ _/_ _ Time_ _:_ _	8. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _

Serum Creatinine Values			
9. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	10. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
11. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	12. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
13. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	14. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
15. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	16. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
17. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	18. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
19. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	20. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
21. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	22. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
23. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	24. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
25. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	26. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
27. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	28. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
29. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	30. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
31. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	32. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
33. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	34. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _

Serum Creatinine Values			
35. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	36. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
37. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	38. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
39. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	40. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
41. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	42. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
43. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	44. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
45. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	46. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
47. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	48. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
49. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	50. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
51. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	52. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
53. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	54. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
55. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	56. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
57. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	58. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
59. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	60. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
61. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	62. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _

Serum Creatinine Values			
63. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	64. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
65. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	66. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
67. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	68. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
69. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	70. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
71. SCr_____	Date: _ _/_ _/_ _ Time_ _:_ _	72. SCr_____	Date: _ _/_ _/_ _ Time_ _:_ _
73. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	74. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
75. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	76. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
77. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	78. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
79. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	80. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
81. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	82. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
83. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	84. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
85. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	86. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
87. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	88. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
89. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	90. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _

Serum Creatinine Values			
91. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	92. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
93. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	94. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
95. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	96. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
97. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	98. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
99. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	100. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
101. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	102. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
103. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	104. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
105. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	106. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
107. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	108. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
109. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	110. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
111. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	112. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
113. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	114. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
115. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	116. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
117. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	118. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _

Serum Creatinine Values			
119. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	120. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
121. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	122. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
123. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	124. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
125. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	126. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
127. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	128. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
129. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	130. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
131. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	132. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
133. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	134. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
135. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	136. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
137. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	138. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
139. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	140. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
141. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	142. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
143. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	144. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
145. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	146. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _

Serum Creatinine Values			
147. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	148. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
149. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	150. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
151. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	152. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
153. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	154. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
155. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	156. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
157. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	158. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
159. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	160. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
161. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	162. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
163. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	164. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
165. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	166. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
167. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	168. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
169. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	170. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
171. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	172. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
173. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	174. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _

Serum Creatinine Values			
175. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	176. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
177. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	178. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
179. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	180. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
181. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	182. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
183. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	184. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
185. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	186. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
187. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	188. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
189. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	190. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
191. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	192. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
193. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	194. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
195. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	196. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
197. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	198. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _
199. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _	200. SCr_____	Date: _ _/_ _/_ _ _ _ Time_ _:_ _

4. Did the patient receive dialysis?

YES _____ Date of first dialysis treatment: __ __ / __ __ / __ __ __ __

NO _____

Unknown _____

5. Was patient discharged alive?
   YES _____ Date of discharge: __ __ / __ __ / __ __ __ __
   NO _____
   Unknown _____

Section 4: Materials available for review

Was a copy of the following types of documentation available:

1.	emergency department notes?	Yes_____	No _____
2.	admission history and physical?	Yes_____	No _____
3.	nephrology consultation?	Yes_____	No _____
4.	discharge summary?	Yes_____	No _____
5.	laboratory reports?	Yes_____	No _____
6.	face sheet?	Yes_____	No _____

J. APPENDIX J. ADJUDICATION FORM

MINI-SENTINEL: AKI VALIDATION
ADJUDICATION FORM
DATA COLLECTION PERIOD: 2011

CASE ID: _____ DATE OF REVIEW: ___
ADJUDICATOR INTIALS _____ Phase 1 ___ Phase 2 ___ Phase 3 ___

1. Type of Event (Choose one)

□$_1$ Definite AKI
□ Probable AKI
□$_{2A}$ Unknown interval for baseline creatinine
□$_{2B}$ Baseline creatinine value not available, but significant decreases during index hospitalization
□$_{2C}$ Other reason not 'definite' _____
□$_3$ Unlikely AKI
□$_{4A}$ No AKI (STOP if no AKI present)
□$_{4B}$ Patient with ESRD already on chronic dialysis
□ Unable to determine (STOP if unable to determine AKI)
What data were needed but not available?
□$_{5A}$ Baseline creatinine value
□$_{5B}$ Additional serum creatinine values (labs from routine care were too infrequent)
□$_{5C}$ Other: Specify _____

2. Was there more than one episode of AKI?

□ Yes Date of the most severe episode of AKI: _____
□ No
□ Unknown

3. What was the magnitude of increase in serum creatinine from baseline? (Choose one)

□$_1$ Increase in serum creatinine > 1.5x OR ≥ 0.3 mg/dL (mild)
□$_2$ Increase in serum creatinine > 2x (moderate)
□$_3$ > 3x OR increase in serum creatinine to ≥ 4.0 mg/dL with at least 0.5 mg/dL absolute rise in serum creatinine (severe)

4. Did the changes in serum creatinine for the episode of AKI above occur within a 48 hour period (rolling window)? (Choose one)

□ Yes

□ No
□ Unknown

5. Which creatinine value was used to establish the patient's **baseline creatinine** (for adjudicating where the episode of AKI likely occurred in question #6 below)? (Choose one)

□ Pre-hospitalization outpatient value documented in notes
□ First value during index hospitalization
□ Other: Specify _____

6. Where did the episode of AKI probably occur? (Choose one)

□ In the hospital (hospital-acquired)

□ Before hospitalization (community-acquired)

□ Unknown

7. Initiation of renal replacement therapy (no prior ESRD)? (Choose one)

$\square_1$ Yes
$\square_0$ No

8. What was the likely primary etiology for this AKI event? (Choose one)

□ Post-Renal Causes (e.g. obstruction)

□ Intrinsic Renal Causes (e.g. drug-induced nephrotoxicity, glomerulonephritis, etc.)

Specify _____

□ Pre-renal

Pre-renal Causes (Choose one)

□ Intravascular volume depletion (Check all that apply)

□ Diuresis

□ Decreased oral intake

□ GI loss (e.g. diarrhea, vomiting)

□ Third spacing (e.g. pancreatitis)

□ Hemorrhage

□ Skin/mucous membrane loss (burns, fever)

□ Other: Specify _____

□ Non-intravascular volume depletion (e.g. hypotension)

Specify _____

9. Was acute tubular necrosis (ATN) present?

□ Yes
□ No

If Yes, specify:

□ Septic ATN
□ Ischemic ATN
□ Nephrotoxic ATN
□ Multifactorial ATN
□ Insufficient information to determine
□ Other: Specify _____

□ Unknown

K. APPENDIX K. TIMELINE FOR THE COMPLETION OF THE MINI-SENTINEL ACUTE KIDNEY INJURY (AKI) VALIDATION

Task	Description of Task	Date
Task 1	Develop definitions and algorithms	Mon 7/23/12
Task 2	Determine number of charts to obtain	Mon 7/23/12
Task 3	Obtain Data Partners	Mon 8/10/12
Task 4	Develop programming specifications	Mon 8/20/12
Task 5	Develop, test, and finalize SAS program	Mon 11/5/12
Task 5A	MSOC/Kaiser develop, test, and distribute	Mon 10/22/12
Task 5B	DPs run program and return results	Mon 11/5/12
Task 6	DPs request, obtain, redact, and upload charts	Mon 3/25/13
Task 7	Develop list of data elements needed from charts	Mon 10/22/12
Task 8	Develop abstractor training manual	Mon 10/29/12
Task 9	Abstractor training completed	Mon 11/26/12
Task 10	Abstractors complete first 10 abstractions; assess inter-rater reliability	Fri 12/14/12
Task 11	Meeting with abstractors to review findings of inter-rater reliability assessment	Fri 12/21/12
Task 12	Orientation meeting with adjudicators	Fri 1/4/13
Task 13	Adjudicators begin work	Mon 1/7/13
Task 14	Complete abstraction	Fri 4/19/13
Task 15	Complete adjudication	Fri 8/2/2013
Task 16	**Complete draft report and submit to Coordinating Center and FDA**	Fri 8/16/2013
Task 17	Receive feedback from Coordinating Center and FDA	Fri 8/31/2013
Task 18	**Final Report**	**Fri 9/20/2013**
Task 19	**Present findings at FDA meeting**	**Thurs 9/19/2013**