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Developing an AKI Consensus Definition for Database Research: Findings From a Scoping Review and Expert Opinion Using a Delphi Process

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Abstract

Rationale & Objective

The Kidney Disease Improving Global Outcomes (KDIGO) definition of Acute Kidney Injury (AKI) is frequently used in studies to examine the epidemiology of AKI. This definition is variably interpreted and applied to routinely collected healthcare data. The aim of this study was to examine this variation and to achieve consensus in how AKI should be defined for research using routinely collected healthcare data.

Sources of Evidence and Study Design

A scoping review was performed by searching MEDLINE and EMBASE for studies using healthcare data to examine AKI by utilizing the KDIGO creatinine-based definition. An international panel of experts was formed to participate in a modified Delphi process to attempt to generate consensus about how AKI should be defined when using routinely collected laboratory data.

Charting Methods and Analytical Approach

The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) extension for scoping reviews was followed. Two rounds of questions were distributed via internet-based questionnaires to all participants with a pre-specified cut-off of 75% agreement used to define consensus.

Results

The scoping review found 174 studies which met the inclusion criteria. The KDIGO definition was inconsistently applied and the methods for application were poorly described. 58 (33%) of papers did not provide a definition of how the baseline creatinine value was determined

and only 34 (20%) defined recovery of kidney function. Of 55 invitees, 35 respondents participated in round 1 and 25 participated in round 2 of the Delphi process. Some consensus was achieved in areas relating to defining baseline creatinine, which patients should be excluded from analysis of routinely collected laboratory data, and how persistent chronic kidney disease or non-recovery of AKI should be defined.

Limitations

The Delphi panel members predominantly came from the UK, USA and Canada with low response rates for some questions in round one.

Conclusion

Current methods for defining AKI using routinely collected data are inconsistent and poorly described in the available literature. Experts could not achieve consensus for many aspects of defining AKI and describing its sequelae. The KDIGO guidelines should be extended to include a standardized definition for how AKI should be defined when using routinely collected data.

Index Words

Acute Kidney Injury; AKI; KDIGO definition; data

Plain Language Summary

Challenges of adapting the KDIGO definition of AKI for database research

The KDIGO definition of AKI is used in both clinical practice and in research. Our scoping review demonstrated that there is a wide variation of practice in how this definition is applied and also a lack of transparency about how researchers applied it. An international panel of experts in AKI was formed in an attempt to achieve consensus on how this definition should be applied. They participated in a Delphi process and while they were able to agree on some aspects of how the definition should be implemented, there were many areas in which no agreement could be reached. We recommend that researchers clearly state how they applied the KDIGO definition for AKI when basing it absence or presence on healthcare data.

Background

The epidemiology of acute kidney injury (AKI) and its consequences have historically been poorly understood due to the lack of a universally accepted definition. In 2012, the Kidney Disease Improving Global Outcome (KDIGO) group proposed a definition which is now widely accepted for both clinical and research purposes (Table 1) allowing a greater understanding of its incidence and outcomes. AKI is estimated to affect 1 in 5 adults who are admitted to hospital (1) and is associated with adverse outcomes including increased mortality^{1,2}, and the development of chronic kidney disease (CKD), heart failure and hypertension³⁻⁷.

The KDIGO definition has underpinned research, allowing a greater understanding of the incidence, prevalence and long-term outcomes following AKI. However, there is variation in how the KDIGO definition is applied to routine healthcare datasets for research purposes, usually because data to allow exact application of the criteria are absent. This is important as small variations in interpretation of the KDIGO definition can significantly affect the number of AKI events identified⁸.

The aim of this study was to systematically examine variation in how the KDIGO definition is used to define AKI in routinely collected healthcare data, and to identify where there is (and is not) consensus in how AKI should be defined for research using routine data.

Methods

We performed a scoping review to examine how KDIGO AKI measurement has been operationalised in research. We then assembled a panel of people with expertise in the areas of data science, epidemiology and AKI. We provided them with the results of the scoping review and used a modified Delphi process to explore consensus about how AKI should be assessed using routinely collected data. National Health Service Research Ethics Committee approval was not required for this study as it falls out with the requirements for ethical approval.

Scoping Review

MEDLINE and EMBASE were searched for all studies reporting AKI using the KDIGO creatinine-based definition in healthcare data from their inception until 22nd June 2017. We used the search terms “Kidney Disease Improving Global Outcomes” or “KDIGO”. There were no restrictions on the types of study design and studies in both community and hospital setting in any country were included. Titles and abstracts of studies identified in the literature search were screened for full text examination by two reviewers independently. Full text was examined by two reviewers independently with disagreements resolved by mutual discussion and involvement of a third reviewer if required.

Data extraction was performed independently by two reviewers. Data on year, country of origin and clinical context of the AKI episode were recorded. Other information collected included: definition of baseline, timeframe for AKI, whether the absolute change in creatinine included within the KDIGO definition was used (i.e. a rise in creatinine of $\geq 0.3\text{mg/dL}$ within 48 hours), definition of recovery of AKI, definition of prior CKD and patient

groups excluded from the study. Absence of a definition for any variable above was also recorded.

Delphi study

Participants were approached with an introductory email including a letter of invitation outlining the method and reason their participation in the whole process was important. All participants were active researchers in the field of AKI. A subpanel of five researchers, including two with expertise in Delphi methodology, was created to provide input to refine each round of questioning. Two rounds of questions were distributed via internet-based questionnaires to all participants with the respondents from round 1 invited to take part in round 2. Reminder emails were sent to non-respondents after distribution of each round. A pre-specified cut-off of 75% agreement was used to define consensus.

Round 1. Panellists were emailed a link to a Microsoft Forms online survey. The first round was focused on AKI development asking respondents to give their opinions using scenario-based questions, with a number of areas open to interpretation, as identified from the scoping review. This included KDIGO definition methods for selecting a value for baseline creatinine, methods for differentiating separate AKI episodes and methods for evaluating the presence of pre-existing CKD.

Round 2. The second survey asked more focused questions that further explored areas where consensus was not achieved in round 1. Based on feedback from round 1 pertaining to large survey burden, we did not explore recovery of kidney function further as there was

a distinct lack of consensus, opting to clarify areas where consensus was more achievable without excessive participant burden.

Results

Scoping review

The search strategy yielded 972 unique records after removal of duplicates. There were 174 studies that met the screening criteria and were included in the review. A flow diagram of the screening process is shown in Figure 1. These were carried out in a wide range of clinical settings (Table 2, Table S1). The clinical context of the study was most frequently post-operative AKI (66 studies; 37.9%), followed by intensive care unit admissions (52 studies, 29.9%), and exposure to nephrotoxic agents (10 studies, 5.7%). 19 studies (10.9%) were in the context of hospital admissions, community-acquired AKI or both. 34 (19.5%) studies did not describe exclusion criteria for patients receiving kidney replacement therapy (KRT). 139 (79.9%) studies stated that they excluded patients receiving chronic dialysis, and 62 (35.6%) that they excluded patients with kidney transplants.

All included studies stated that the KDIGO definition of AKI was used, but 27 (15.5%) did not provide an explicit definition of how they measured AKI beyond that statement. Only 49 (28.2%) used change in urine output to measure AKI, and 135 (77.4%) used a creatinine rise of 0.3 mg/dL in 48 hours to measure AKI. 12 (6.9%) studies implemented part elements of the creatinine-based definition, including 6 where only stage 3 or stage 2-3 AKI were reported, and one including only AKI with requirement for KRT.

There was also considerable heterogeneity in how key elements of the remaining KDIGO definition of AKI were operationalised in terms of definition of baseline creatinine and AKI

measurement when there were no baseline creatinine values available. 44 studies (25.3%) lacked a definition for an acceptable time between the index creatinine value and the value used as a baseline, 50 (28.7%) did not state how a value would be chosen if there were two or more eligible values and 36 (20.7%) lacked definitions for both. There was considerable heterogeneity in how the remaining 130 studies measured baseline creatinine, varying in terms of both the timeframe used and the value chosen. The most common timeframe was a creatinine measured at admission or prior to either surgery or a dose of nephrotoxic medication. For studies without an easily defined a priori event potentially causing AKI, the most common timeframes for defining baseline used creatinine values measured within 3 months (28 studies, 16.1%) or within a year (32, 18.4%). The creatinine value used as a baseline was most commonly the most recent (76, 43.7%) or lowest within the timeframe (33, 19.0%). 27 studies (15.5%) defined a minimum timeframe before AKI onset to exclude creatinine values from baseline value.

Overall 36 (20.7%) studies did not define baseline creatinine measurement in any way, 22 (12.6%) provided a partial definition, and 116 studies (67%) provided a measurement definition that included both the timeframe for eligible baseline creatinine values and a method for selecting from multiple eligible values. These 116 studies used 21 unique definitions of baseline creatinine (Table 3).

Most studies excluded patients without a baseline creatinine (123 studies, 71%), and the remainder estimated baseline creatinine, mostly commonly by back calculation of the CKD-EPI equation⁹ or the MDRD equation¹⁰ assuming an eGFR of 75 ml/min (26 studies, 14.9%) (Table 2). 16 studies (9.2%) used a post-AKI nadir value as a surrogate baseline value. 6 papers (3.5%) used an estimate for the baseline for all patients included in the study with 5

of these using a post-recovery nadir. Four of the papers estimating creatinine using a nadir were validating the technique for estimation.

Recovery of kidney function was only defined in 34 studies (19.5%), with 21 studies defining a threshold creatinine for recovery from AKI, although there was significant variation as to what threshold was chosen. 6 studies used freedom from kidney replacement therapy (KRT) as a definition for recovery.

Delphi study

Fifty-five individuals were invited to participate in the Delphi process with 35 respondents to the round 1 survey and 25 respondents to the round 2 survey. The participants were primarily nephrologists and epidemiologists and the majority came from the UK, USA and Canada (full demographics in Table S3). The key areas of consensus are summarised in table 4, and the Delphi study findings by topic and whether consensus was achieved are shown in Tables S4-9. Although the panel was able to agree on some aspects of the practical application of the KDIGO AKI definitions there were significant differences in opinion where the creatinine rose above 4mg/dL in patients with raised baseline creatinine values (Table S4).

The Delphi panel came to some consensus about defining which baseline creatinine should be used. There was consensus that the use of inpatient creatinine values was acceptable for defining a baseline (88%), that estimation of creatinine based on an ideal eGFR was not acceptable (80%) and that at least one prior creatinine value was needed (77.1%). However, there were significant areas where consensus was lacking in defining baseline creatinine, including the suitability of using post-AKI nadir values, using values more than a year before a potential AKI event, and the method for selecting a creatinine value where more than one

eligible measurement was available (these are shown in Table S5). The Delphi panel generated 14 unique methods of defining baseline creatinine, compared to the 21 unique methods identified in the literature review. The most common definition of baseline creatinine was to use the median value within the previous year. The unique definitions of baseline creatinine are summarised in Table 5.

There was consensus that analyses should exclude patients currently receiving haemodialysis or peritoneal dialysis. In contrast, there was consensus that patients with a kidney transplant should *not* be excluded. There was consensus that people with stages of CKD not resulting in need for KRT should not be excluded from analysis based on routinely collected data. (Table S6).

There was consensus that AKI present on the day of admission should be defined as a community-acquired AKI, but no consensus regarding other potential definitions of community-acquired AKI relating to AKI reaching threshold after a time period in hospital or the minimum interval following discharge from hospital before an AKI can be considered to be community-acquired (Table S7).

Need for ongoing KRT or persistence of peak AKI stage (i.e. creatinine not dropping below 50/100/200% of baseline) were both agreed to be acceptable definitions of absence of biochemical recovery by 85% of the panel. No consensus was reached regarding the definition of either complete or partial resolution of AKI (Table S8). The most favoured definition of complete biochemical recovery used the return of serum creatinine to level less than 50% above baseline but this was favoured by only 25% of respondents. The most favoured definition of partial biochemical recovery were an improvement from peak creatinine with persistent decrease of serum creatinine to level more than 50% above

baseline (favoured by 30% of respondents) and fall in AKI stage but with creatinine still fulfilling AKI definition (favoured by 20% of respondents). A further 35% of respondents felt that either definition was acceptable although this still resulted in falling short of consensus.

There was consensus that progression of CKD could not be defined on a single post-AKI creatinine value, but no consensus was reached as to what criteria should be used to define this (Table S9).

Figure 2 is a hypothetical scenario depicting the change in creatinine values during an AKI episode. The panel were asked to define the point when AKI started based on which of the values in figure 1 were available. The panel came to consensus that the date of the first result that reached a value high enough over the baseline to be defined as an AKI should be the date of AKI onset (Table S10).

Discussion

We found a lack of consistency in application of the KDIGO definition for AKI to analyse routinely collected healthcare datasets, and a lack of transparency in reporting the definition utilised. Using a modified Delphi method with a mix of panellists from across Europe and North America with expertise in AKI research using healthcare data, we demonstrate that considerable variability persists in opinion on how the KDIGO definition for AKI should be applied. We have summarized areas where the panel was able to reach consensus discussed, and these have been used to make recommendations for reporting of future research.

The development of the KDIGO criteria for AKI (and the RIFLE and AKIN criteria which preceded the KDIGO criteria) allow for like-for-like comparisons of AKI in patients with both

normal and abnormal chronic kidney function. It does have the limitation that it requires a creatinine within the last 7 days to generate a diagnosis of AKI. This presents a challenge to research investigating AKI using routinely-collected data where the spirit of the KDIGO criteria (rise in creatinine from a lower preceding value) is followed but the guidelines are not followed to the letter (change in creatinine over 48 hours or 7 days) due to the lack of a creatinine within the lead-in period. As described in our scoping review, this has led to a situation where the KDIGO criteria have been modified in many different ways.

Use of algorithms to identify important medical conditions in other disease areas has been demonstrated to lack validity in identifying the presence of a condition and in assessing the severity and response to therapy^{11, 12}. With respect to AKI, use of creatinine measurements has been demonstrated to be more sensitive as compared to clinical coding in identifying AKI¹³. The parameters whereby AKI is defined using routine biochemical data should be standardised to allow for direct comparisons. This is illustrated by a change in the duration of follow-up that resulted in a six-fold increase in the number of AKI episodes identified in a large cohort study¹⁴. Estimation of creatinine values has been demonstrated to lack accuracy, with even the most commonly used methods having a significant degree of inaccuracy of identifying and staging AKI¹⁵.

The scoping review demonstrated marked heterogeneity in the methods used to identify AKI. This creates challenges in comparing the results of studies in a like-for-like manner. As noted above, changes to the criteria used may result in large differences in the number of AKI events identified and result in challenges when meta-analysis is used. When altering the parameters of a validated diagnostic criteria (KDIGO) the lack of transparency in methodology presents a further challenge.

The Delphi panel was able to reach consensus on several aspects of the definition of baseline creatinine (minimum number of creatinine measurements required to be present to allow calculation of a baseline creatinine is at least 1, preferred measurements used for baseline are within 7-30 days prior to AKI but acceptable to use measurements up to 1 year prior), the definition of community-acquired AKI (AKI present on the day of admission) and how to define progression of CKD following an episode of AKI (new onset CKD or progression of CKD should not be diagnosed based on a single creatinine measurement). Significant differences remained between panellists in terms of what constituted AKI (including disagreements with the KDIGO definition), use of a post-AKI nadir to estimate a baseline and defining recovery from AKI. These aspects need further refinement towards a unified definition of the diagnosis of AKI using routinely collected data.

Strengths of the study include a comprehensive literature scoping review and the modified Delphi process involving a diverse range of clinicians and epidemiologists and covered the areas of inconsistency identified from the scoping review. There were some limitations to what this study was able to ascertain. The Delphi panel predominantly came from the UK, USA and Canada with only two respondents from outside those three countries. Some of the questions in round one had a low response rate which limited their usefulness. There was some attrition between round 1 and round 2 with 71.4% of panel members being retained from the first round to the second. The study was purely designed to investigate the applications of AKI in relation to the use of routinely collected laboratory data to define AKI. This is distinct from the use of the definition in clinical care, where clinical judgement based on other information about an individual patient should be used to make a diagnosis of AKI. Clearer definitions and applications are required in routinely collected healthcare

data research as there is the loss of elements of clinical context and diagnosis is based solely on the data.

This review clearly demonstrates that although the KDIGO definition is commonly cited by studies investigating AKI, the application and interpretation of the definition varies widely between researchers. This potentially results in limitations when it comes to comparing apparent “like-for-like” studies (for example in post-operative AKI) if the diagnosis of AKI has been made using different parameters⁸. There is also a lack of transparency in the methodology of studies investigating AKI in terms of the description of how they generated their AKI definition. Recovery of AKI/development of CKD was sparsely reported and the definition for a threshold creatinine defining recovery varied widely.

This review highlights the importance of methodological transparency in studies involving the identification of AKI from routinely collected biochemical data. It also clearly demonstrates that there are considerable areas of disagreement between researchers in how to measure AKI in observational studies using large databases. At a minimum, researchers should explicitly report in detail how they have measured AKI. Box 1 shows our suggested reporting recommendations when defining AKI in healthcare datasets. More broadly, methods for defining AKI in routinely collected data need to be refined, including the range within which variation is acceptable. The Delphi panel in this study were unable to reach consensus on many important aspects of definition. Future consensus studies would be usefully informed by research to explore the implications of different definitions on the estimation of AKI incidence, and associations with AKI outcomes of AKI identified by different definitions.

Supplementary Material

Table S1: Summary of characteristics in the scoping review of studies examining AKI utilising the KDIGO creatinine-based definition

Table S2: Characteristics of studies from the scoping review examining AKI utilising the KDIGO creatinine-based definition

Table S3: Demographics of Delphi study respondents

Table S4: Delphi study survey results summary for topic area - KDIGO definition

Table S5: Delphi study survey results summary for topic area – defining baseline

Table S6: Delphi study survey results summary for topic area – Exclusions

Table S7: Delphi study survey results summary for topic area – Community-acquired AKI

Table S8: Delphi study survey results summary for topic area – Recovery of kidney function

Table S9: Delphi study survey results summary for topic area – Progression of CKD

Table S10: Delphi study survey results summary for topic area – AKI onset

Article Information

Authors' Contributions: research idea and study design: BG, MJ, MT, NS; data acquisition: GG, HW, SB; data analysis/interpretation: BG, GG, SB; supervision or mentorship: BG, SB.

Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual's own contributions and

to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated and resolved, including with documentation in the literature if appropriate.

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References

1. Chawla LS, Eggers PW, Star RA, Kimmel PL. Acute kidney injury and chronic kidney disease as interconnected syndromes. *N Engl J Med*. 2014;371(1): 58-66.
2. Walker H, De Souza N, Hapca S, Witham MD, Bell S. Effect of multiple episodes of acute kidney injury on mortality: an observational study. *Clin Kidney J*. 2021;14(2): 696-703.
3. Rodriguez E, Arias-Cabrales C, Bermejo S, et al. Impact of Recurrent Acute Kidney Injury on Patient Outcomes. *Kidney Blood Press Res*. 2018;43(1): 34-44.
4. Horne KL, Packington R, Monaghan J, Reilly T, Selby NM. Three-year outcomes after acute kidney injury: results of a prospective parallel group cohort study. *BMJ Open*. 2017;7(3): e015316.
5. Arias-Cabrales C, Rodriguez E, Bermejo S, et al. Short- and long-term outcomes after non-severe acute kidney injury. *Clin Exp Nephrol*. 2018;22(1): 61-67.
6. Hsu C-y, Hsu RK, Yang J, Ordonez JD, Zheng S, Go AS. Elevated BP after AKI. *Journal of the American Society of Nephrology*. 2016;27(3): 914.
7. Go AS, Hsu C-y, Yang J, et al. Acute Kidney Injury and Risk of Heart Failure and Atherosclerotic Events. *Clinical Journal of the American Society of Nephrology*. 2018;13(6): 833.
8. Wiersema R, Jukarainen S, Eck RJ, et al. Different applications of the KDIGO criteria for AKI lead to different incidences in critically ill patients: a post hoc analysis from the prospective observational SICS-II study. *Critical Care*. 2020;24(1): 164.
9. Levey AS, Stevens LA, Schmid CH, et al. A New Equation to Estimate Glomerular Filtration Rate. *Annals of Internal Medicine*. 2009;150(9): 604-612.
10. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med*. 2006;145(4): 247-254.
11. Al Sallakh MA, Vasileiou E, Rodgers SE, Lyons RA, Sheikh A, Davies GA. Defining asthma and assessing asthma outcomes using electronic health record data: a systematic scoping review. *European Respiratory Journal*. 2017;49(6): 1700204.
12. Captieux M, Prigge R, Wild S, Guthrie B. Defining remission of type 2 diabetes in research studies: A systematic scoping review. *PLOS Medicine*. 2020;17(10): e1003396.
13. Logan R, Davey P, De Souza N, Baird D, Guthrie B, Bell S. Assessing the accuracy of ICD-10 coding for measuring rates of and mortality from acute kidney injury and the impact of electronic alerts: an observational cohort study. *Clin Kidney J*. 2020;13(6): 1083-1090.
14. Holmes J, Roberts G, Meran S, Williams JD, Phillips AO. Understanding Electronic AKI Alerts: Characterization by Definitional Rules. *Kidney International Reports*. 2017;2(3): 342-349.
15. Cooper DJ, Plewes K, Grigg MJ, et al. An Evaluation of Commonly Used Surrogate Baseline Creatinine Values to Classify AKI During Acute Infection. *Kidney International Reports*. 2021;6(3): 645-656.

Table 1: KDIGO AKI staging definitions

AKI Stage	Serum creatinine	Urine output
1	Increase in serum creatinine of 0.3 mg/dL within 48 hours or an increase of 1.5-1.9 times the baseline, which is known or presumed to have occurred within the prior 7 days	<0.5ml/kg/h for 6-12 hours
2	Increase in serum creatinine of 2.0–2.9 times the baseline value	<0.5ml/kg/h for ≥12 hours
3	Increase in serum creatinine of ≥ 3 times the baseline or a serum creatinine of ≥ 4 mg/dL or initiation of RRT	<0.3ml/kg/h for ≥24 hours or anuria for ≥12 hours

Table 2: Definition of AKI in studies citing KDIGO as the source of AKI definition

	N (%) N=174
Timeframe for defining baseline creatinine	
At point of presentation/admission/pre-operative/pre-dose	46 (26.4%)
Within last 10 days	5 (2.9%)
Within last 3 months	29 (16.7%)
Within last 6 months	7 (4.0%)
Within last 6 months (minimum timeframe) ¹	4 (2.3%)
Within last year	10 (5.7%)
Within last year (minimum timeframe) ¹	22 (12.6%)
Post-AKI nadir value used	5 (2.9%)
Baseline creatinine estimated for all patients ²	1 (0.6%)
Not explicitly defined	44 (25.3%)
Creatinine used to define baseline	
Most recent	75 (43.1%)
Not explicitly defined	47 (27.0%)
Lowest	33 (19.0%)
Mean	12 (6.9%)
Other	7 (4.0%)
Creatinine estimation used if no baseline creatinine available	
None (patient excluded)	123 (70.7%)
Estimated based on “ideal” eGFR using MDRD equation ²	24 (13.8%)
Post-AKI nadir used	16 (9.2%)
All values estimated – validation for estimate	4 (2.3%)
Other	5 (2.9%)
Estimated based on “ideal” eGFR using CKD-EPI equation ²	2 (1.1%)
¹ There was a minimum time between the baseline creatinine value and the index creatinine value ² The creatinine was estimated based on an “ideal” eGFR (based on age/sex/race) which was defined in the paper.	

Table 3: Unique definitions of baseline creatinine used

Unique definitions of baseline creatinine used		Method for choosing between multiple eligible creatinine values						
		Lowest (n=33)	Mean (n=12)	Median (n=1)	Most recent (n=76)	Estimate (n=1)	Other ¹ (n=1)	Not defined (n=50)
Time period for selecting a baseline creatinine	Prior to surgery/drug (n=31)	1	1		23			6
	</=1 week (n=5)	2			3			
	</=1 month but >1 week (n=5)				5			
	</=3 months but >1 month (n=24)	12	1	1	7			3
	6 months (n=11)	5	1		4		1	
	1 year (n=32)	6	7		14			5
	Admission to hospital or unit (e.g. ICU) (n=15)				15			
	All values estimated using ideal eGFR (n=1)					1		
	Nadir (n=5)	5						
	During hospital admission (n=1)				1			
	Not defined (n=44)	2	2		4			36

¹- This paper compared two different methods for determining a baseline creatinine value.

Table 4: Areas of consensus derived from Delphi study

Topic area	Consensus reached	No. (%) of respondents
KDIGO definition	Round 1 – KDIGO definition for AKI Stage 1 should include a rise in serum creatinine of >50% increase from baseline serum creatinine	30 (85.7%) yes
	Round 1 – In patients with a baseline serum creatinine of <3.7mg/dL, a rise of 0.3mg/dl over 48 hours should be Stage 1 AKI rather than Stage 3	28 (80.0%) stage 1
Defining baseline creatinine	Round 1 – What is the minimum number of creatinine measurements that need to be present in the baseline period in order to calculate a baseline (1 = at least one test, 2 = at least 2 tests etc.)?	27 (77.1%) at least 1
	Round 1 – If creatinine measurements in the previous year are NOT present. Can you assume a prior eGFR of 75 ml/min and back calculate a creatinine based on the laboratory's values/calibration	12 (80.0%) no
	Round 2 – If you are a researcher only using creatinine measurements to define AKI, please say which creatinines it is ACCEPTABLE to use when defining the baseline:	19 (76.0%) Use all creatinines in the previous 7-30 days but if 7-30 not available, otherwise use all creatinines in the previous 31-90 days but if 7-90 not available, then use all creatinines in the previous 91-180 days but if 91-180 days not available, then use all creatinines in the previous 181-365 days, ignore all >365 days
	Round 2 – Should only out-patient creatinine values be used to define baseline?	20 (88.0%) would use inpatient

	Round 2 – How would you exclude AKI in the baseline period when calculating baseline creatinine (for this response, please assume that baseline is being defined from values over the previous year)? Please indicate which is PREFERRED?	24 (96.0%) “If an episode of AKI is present in the baseline, then remove the peak serum creatinine and values from +/- 7days of peak creatinine?”
Exclusions	Round 1 – Groups of patients who should be excluded from routine analysis of AKI. For epidemiological studies examining AKI using routinely collected data, should the following groups of patients be excluded from analysis? Please select all that you think should be excluded.	20 (100%) would not include patients currently on haemodialysis or peritoneal dialysis 4 (20.0%) would not include patients with a kidney transplant
Community-acquired AKI	Round 2 – How should community acquired AKI be defined?	20 (80.0%) AKI present on day of admission to hospital should be defined as community-acquired AKI
Recovery of kidney function/Progression of CKD	Round 1 – How should absence of biochemical recovery of AKI be defined?	0 only ongoing need for RRT 1 (5.0%) only persistence of peak AKI stage 17 (85.0%) both acceptable
	Round 1 – If a patient has pre-existing CKD, is it appropriate to assess for CKD progression on a single measure of kidney function after an episode of AKI?	4 (20.0%) yes 16 (80.0%) no 15 did not answer
	Round 2 – If a patient has pre-existing CKD, is it appropriate to assess for CKD progression on a single measure of kidney function after an episode of AKI?	20 (80.0%) no

Table 5: Unique definitions of baseline creatinine given by the Delphi questionnaire respondents in round 1

		Method for choosing between multiple eligible creatinine values					
		Lowest (n=2)	Mean (n=4)	Median (n=8)	Most recent (n=3)	Estimate (n=0)	Not defined (n=18)
Time period for selecting a baseline creatinine	Prior to surgery/ drug (n=0)						
	</=1 week (n=1)						1
	</=1 month but >1 week (n=3)			2			1
	</=3 months but >1 month (n=2)						2
	6 months (n=2)						2
	1 year (n=22)	2	3	6	2		9
	2 years (n=1)						1
	Estimate (n=0)						
	Post-AKI nadir (n=0)						
	During hospital admission (n=0)						
	Not defined (n=4)		1		1		2

Box 1: Reporting Recommendations when defining AKI using KDIGO definition in healthcare data

Reporting Recommendations when defining AKI using KDIGO definition in healthcare data

1. "Studies should report whether 0.3 mg/dL rise over 48 hours is included (required for full alignment with the KDIGO definition) and whether staging criteria for stages 1,2 and 3 is used.
2. Studies should state the timeframe for development of AKI examined.
3. Studies should state definition of baseline kidney function including timeframe of measurement, whether both in and out-patient creatinine were used and what was used in the absence of a baseline creatinine.
4. Studies should state which patient groups were excluded from the analyses
5. The KDIGO guidelines should be extended to include a standardised definition for how AKI should be defined when using routinely collected data.