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Complete List of Authors:	Hwang, Y. Joseph; University of Western Ontario, Medicine/Nephrology; University of Western Ontario, Epidemiology and Biostatistics Shariff, Salimah; Institute for Clinical Evaluative Sciences, Gandhi, Sonja; University of Western Ontario, Medicine/Nephrology; University of Western Ontario, Epidemiology and Biostatistics Wald, Ron; Keenan Research Centre in the Li Ka Shing Knowledge Institute of St Michael's Hospital, ; University of Toronto, Medicine/Nephrology Clark, Edward; University of Ottawa, Kidney Research Centre, Ottawa Hospital Research Institute Fleet, Jamie; University of Western Ontario, Medicine/Nephrology Garg, Amit; University of Western Ontario, Medicine/Nephrology; University of Western Ontario, Epidemiology and Biostatistics
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Validity of the *International Classification of Diseases, Tenth Revision* code for acute kidney injury in elderly patients at presentation to emergency department and at hospital admission

Y. Joseph Hwang BMSc[1,2], Salimah Z. Shariff PhD[3], Sonja Gandhi BSc[1,2], Ron Wald MD, MPH[4,5], Edward Clark MD[6], Jamie L. Fleet BHSc[1], Amit X. Garg MD, PhD[1,2,3]

1. Division of Nephrology, Department of Medicine, Western University, London, Ontario, Canada
2. Department of Epidemiology & Biostatistics, Western University, London, Ontario, Canada
3. Institute for Clinical Evaluative Sciences, Ontario, Canada
4. Keenan Research Centre in the Li Ka Shing Knowledge Institute of St Michael's Hospital, Toronto, Ontario, Canada
5. Division of Nephrology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada
6. Kidney Research Centre, Ottawa Hospital Research Institute, University of Ottawa, Ottawa, Ontario, Canada

Correspondence: Dr. Amit Garg, London Kidney Clinical Research Unit, Room ELL-101, Westminster, London Health Sciences Centre, 800 Commissioners Road East, London, Ontario, Canada N6A 4G5, Tel: 519-685-8502, Fax: 519-685-8072, email: amit.garg@lhsc.on.ca

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ABSTRACT

Objective: To evaluate the validity of the *International Classification of Diseases, Tenth Revision* (ICD-10) code N17x for acute kidney injury (AKI) in elderly patients in two settings: at presentation to the emergency department and at hospital admission.

Design: Population-based retrospective validation study.

Setting: Southwestern Ontario, Canada, from 2003 to 2010.

Participants: Elderly patients with serum creatinine measurements at presentation to the emergency department (n=36,049) or hospital admission (n=38,566). The baseline serum creatinine measurement was a median of 102 days and 39 days prior to presentation to the emergency department and hospital admission, respectively.

Main outcome measures: Sensitivity, specificity, and positive and negative predictive values of ICD-10 diagnostic coding algorithms for AKI using a reference standard based on changes in serum creatinine from the baseline value. Median changes in serum creatinine of patients who were code positive and code negative for AKI.

Results: The sensitivity of the best-performing coding algorithm for AKI (defined as a ≥ 2-fold increase in serum creatinine concentration) was 37.4% (95% confidence interval (CI): 32.1% to 43.1%) at presentation to the emergency department and 61.6% (95% CI: 57.5% to 65.5%) at hospital admission. The specificity was greater than 95% in both settings. In patients who were code positive for AKI, the median (interquartile range) increase in serum creatinine from baseline was 133 (62 to 288) µmol/L at presentation to emergency department and 98 (43 to 200) µmol/L at hospital admission. In those who were code negative, the increase in serum creatinine was 2 (-8 to 14) and 6 (-4 to 20) µmol/L, respectively.

Conclusions: The presence or absence of ICD-10 code N17x differentiates two groups of patients with distinct changes in serum creatinine at the time of a hospital encounter. However, the code underestimates the true incidence of AKI due to limited sensitivity.

Keywords: acute kidney injury, acute renal failure, serum creatinine, validation, validity, sensitivity, specificity, International Classification of Diseases

Article Summary:

Article Focus

- Validation of administrative database codes is a prerequisite to their optimal use in research
- The aim of this study was to describe the validity of the ICD-10 code N17x for AKI compared to a reference standard based on changes in serum creatinine

Key Messages

- The ICD-10 N17x code for AKI has moderate sensitivity and high specificity
- The sensitivity of theN17x code improves for more severe forms of AKI
- The code was successful in identifying a group of patients admitted to hospital with a median increase in serum creatinine of 98 µmol/L

Strengths and Limitations

- This is the first study to provide information on the diagnostic performance of ICD-10 code N17x for AKI using laboratory values as the reference standard
- It was a large population-based validation study that included serum creatinine measurements from twelve hospitals
- Future validation studies in younger patients are required

BACKGROUND

Healthcare administrative databases can provide researchers and policy makers with information on a large number of patients in an efficient manner. When using these data sources for clinical or health services research, the validity of the research depends upon the accuracy of the diagnostic and procedural codes that have been recorded.[1] However, the accuracy of coding is not guaranteed because administrative databases are not primarily intended for research.[2]Consequently, understanding the validity of administrative codes is a prerequisite to their optimal use in the assessment of patient outcomes.

Clinically, acute kidney injury (AKI) is characterized by an abrupt decline in renal function that may result in disordered fluid, acid-base and electrolyte homeostasis and retention of nitrogenous waste products.[3, 4] Two systems for defining and quantifying the severity of AKI are widely used: the Acute Kidney Injury Network (AKIN) classification [5] and the Risk-Injury-Failure-Loss-ESRD (RIFLE) criteria.[6] These staging systems define AKI severity according to absolute and relative (percentage) increases in serum creatinine, a blood test universally used to indicate kidney function. While the incidence of AKI is dependent on the definition used, it is recognized that this condition is common, affecting 2 to 9% of patients at hospital admission.[7-10] Moreover, patients who develop AKI have both poor short and long-term outcomes and their care is costly.[7, 8, 11-19]

The purpose of the present study was to evaluate the accuracy of the *International Classification of Diseases, Tenth Revision* (ICD-10) code N17x for AKI for applications in clinical and health services research, particularly in pharmacoepidemiologic studies. We compared this code against changes in serum creatinine concentration in two settings: 1) at presentation to the emergency department and 2) at hospital admission. In addition, we investigated the effect of baseline chronic kidney disease (CKD) status on the diagnostic performance of the code in the two settings. Based on the findings of a previous validation study on ICD-9 codes, we anticipated the sensitivity for ICD-10 code N17x would be low, improving with more severe definitions of AKI.[7, 9, 20, 21] Moreover, we expected higher sensitivity in patients with CKD than those without, as the former typically have larger absolute increases in serum creatinine for a given amount of AKI.

METHODS

Study Design and Setting

We conducted a population-based retrospective validation study using Ontario's linked healthcare administrative databases and laboratory data from Southwestern Ontario. All residents receive universal access to hospital and physician services under a single provincial payer system, providing a comprehensive set of health administrative data.

Using a diagnostic test assessment framework, we obtained diagnostic performance characteristics (sensitivity, specificity, positive predictive value, and negative predictive value) of various diagnostic coding algorithms for ICD-10 code N17x, which is defined as "acute renal failure". We used changes in serum creatinine from the baseline value as the reference standard (see Supplementary Table 1 for a sample two-by-two table). Moreover, we compared the change in serum creatinine between patients who were N17x code positive with those who were N17x code negative.

Our protocol was approved by the institutional review board at Sunnybrook Health Sciences Centre (Toronto, Ontario). The relevant datasets are held at the Institute for Clinical Evaluative Sciences. The reporting of this study follows guidelines set out for studies assessing diagnostic accuracy (Supplementary Table 2).[22]

Data Sources

Patient records from the seven databases were linked using encrypted unique identifiers. We identified laboratory measurements, including serum creatinine, using a system that keeps patient electronic medical records (Cerner®, Kansas City, Missouri, USA).[23] This system contains inpatient, outpatient and the emergency department laboratory measurements for twelve Southwestern Ontario hospitals. For a subpopulation, we also obtained previous laboratory measurements from Gamma-Dynacare, a provider of outpatient laboratory services to residents in Southwestern Ontario. We obtained inpatient and emergency department patient diagnostic information from the Canadian Institute of Health Information (CIHI) Discharge Abstract Database (DAD) and National Ambulatory Care Reporting System database (NACRS), respectively. We obtained information on inpatient and outpatient physician services from the Ontario Health Insurance Plan database (OHIP). We ascertained patient demographic information from the Ontario's Registered Persons Database (RPDB) and prescribed drug use for patients 65 years

of age and older from the Ontario Drug Benefit database (ODB). These databases have been used extensively to research health outcomes and health services.[24-27]

Participants

We developed two separate cohorts. The first cohort consisted of patients with a serum creatinine measurement at presentation to the emergency department (Emergency Department Cohort). The second cohort consisted of patients with a serum creatinine measurement at hospital admission (Hospitalized Cohort). All patients had a baseline serum creatinine measurement (described below). The period of accrual was from June 1st, 2003 to September 30th, 2010.

We restricted cohort entry to patients 66 years of age and older to ensure at least one year of baseline prescription records for all patients. We excluded the following patients from both cohorts: i) those who had end-stage renal disease (defined by the receipt of dialysis in the 120 days prior to the hospital encounter), ii) those who received a kidney or liver transplant in the five years prior to the hospital encounter, iii) those whose date of serum creatinine measurement (from Cerner®) and the hospital encounter (from CIHI-DAD) did not align (less than 1.4% patients excluded for this reason; see Supplementary Figure 1 for explanation) and iv) those without at least one serum creatinine measurement in the 7 to 365 days prior to the hospital encounter to serve as the baseline value. In cases where a patient had multiple baseline measurements we selected the most recent one. Additional selection criteria for each cohort are described below and illustrated in Supplementary Figure 1.

We excluded patients who did not have a serum creatinine measurement in the emergency department from entry to the Emergency Department Cohort. We excluded the following patients from entry to the Hospitalized Cohort: i) those with a hospital admission that resulted in a stay greater than 90 days (to ensure we had data for the full hospital admission to the time of discharge i.e. particularly for patients accrued in the second half of year 2010) and ii) those without a serum creatinine measurement either in the emergency department prior to hospital admission or during the first two days of hospital admission. When multiple eligible hospital presentations were identified for a given patient over the study period, we randomly selected one hospital encounter for each cohort.

Within the two cohorts, we identified patients diagnosed with CKD (assessed by the presence of ICD-10 code N18x defined as "chronic kidney disease") in the 5 years prior to their hospital encounter to evaluate potential differential classification of AKI in patients with baseline CKD compared to those without.

The Reference Standard: Serum Creatinine-Based Definitions of AKI

Measuring changes in serum creatinine is the most common method of identifying AKI in clinical practice. We adapted the reference standard used in this study from four widely used serum creatinine-based definitions of AKI: i) AKIN Stage 1 or greater: ≥ 27 µmol/L (0.3 mg/dL) or 50% increase in serum creatinine concentration from baseline, ii) RIFLE Risk: ≥ 1.5-fold increase in serum creatinine concentration from baseline, iii) RIFLE Injury: ≥ 2-fold increase in serum creatinine concentration from baseline, and iv) RIFLE Failure**:** ≥ 3-fold increase in serum creatinine concentration from baseline or a baseline serum creatinine concentration ≥ 354 µmol/L (4.0 mg/dL) with ≥ 44 µmol/L (0.5 mg/dL) increase from baseline.[5, 6] A Roche Modular Ion Selective Electrode® system (Basel, Switzerland) was used to measure serum creatinine.

For the Emergency Department Cohort, we categorized the difference between patients' peak (highest) serum creatinine concentration at presentation to the emergency department and baseline serum creatinine concentration into the serum creatinine-based definitions. To be classified as having AKI in the Hospitalized Cohort, patients had to have a ≥ 27 µmol/L (0.3 mg/dL) or 50% increase in serum creatinine concentration from their baseline value at the emergency department or during the first two days of hospital admission. This was done to ensure all patients classified as having AKI by the serum creatinine-based definitions manifested AKI at hospital admission rather than developing the condition *de novo* during the hospital stay. However, there may be a delay from time of injury to when the peak serum creatinine concentration is realized. Thus, in those with AKI, we categorized the severity as defined by the serum creatinine-based definitions, using the peak serum creatinine concentration in either the emergency department or in the first five days of hospital admission.

ICD-10 Coding Algorithms for AKI

Following discharge from hospital, trained coders review all charts to record appropriate diagnosis codes and their associated attributes. The coders follow the Canadian Coding Standards developed by CIHI.[28] According to CIHI's guidelines, the coders are not permitted to interpret laboratory measurements, but can record a condition based on laboratory findings if the physician documents the condition as diagnosed in the patient's chart. For ambulatory care records (included in CIHI-NACRS), coders are allowed to include up to 10 diagnoses per visit. The

first diagnosis listed is the main problem for the patient's visit that required evaluation and/or treatment or management as determined by the physician at the end of the visit. For hospitalization records (included in CIHI-DAD), coders may record up to 25 conditions using ICD-10 diagnostic codes. Additionally, they must indicate diagnosis type 'M' for the condition that was most responsible for the greatest portion of the length of stay or used the greatest amount of resources. They may also indicate diagnosis type '1' for any condition that existed prior to the admission and was treated during the hospital stay.[28]

In this study, we tested two unique algorithms to identify patients with AKI at presentation to the emergency department and three unique algorithms to identify patients at hospital admission. Each of these algorithms used the ICD-10 code N17x but varied the possible diagnosis types. In the Emergency Department Cohort, we examined the code: i) as the main problem (referred to as "main diagnosis") or ii) in any of the 10 potential diagnostic fields with any diagnosis type (referred to as "all diagnosis"). In the Hospitalized Cohort, we examined the code: i) as the diagnosis type of 'M' (most responsible; referred to as the "most responsible diagnosis"), ii) as the diagnosis type of '1' (pre-admit comorbidity; referred to as "admission diagnosis") or iii) in any one of 25 potential diagnosis fields with any diagnosis type (referred to as "all diagnosis").

Statistical Analysis

We used descriptive statistics to summarize demographic characteristics, co-morbidities, prescription drug claim information, and baseline laboratory measurements for patients in both settings. We calculated sensitivity, specificity, positive predictive value, and negative predictive value for each diagnostic coding algorithm (formulas presented in Supplementary Table 1). We calculated 95% confidence intervals for single proportions using the Wilson Score method.[29] We performed these calculations against the four reference standard definitions. We expressed the changes in patient serum creatinine concentration from baseline as medians with interquartile ranges (IQR) and we compared the means using the Mann-Whitney test. We conducted all analysis using SAS (Statistical Analysis Software) version 9.2 (SAS Institute Incorporated, Cary, North Carolina, USA, 2008).

RESULTS

We identified a total of 36,049 patients for the Emergency Department Cohort and 38,566 patients for the Hospitalized Cohort. Baseline characteristics of the two cohorts are presented in Table 1, including the proportion of patients who satisfied different definitions of AKI. For example, 294 (0.8%) and 567 (1.5%) patients satisfied the RIFLE Injury definition of AKI (defined by ≥ 2-fold increase in serum creatinine concentration), in each cohort, respectively.

Table 1. Baseline characteristics for patients in the Emergency Department and Hospitalized Cohorts

	Emergency Department Cohort (n = 36,049)	**Hospitalized Cohort** (n = 38,566)
Demographics		
Median age (IQR), years	77 (72-83)	76 (71-82)
Women, *n (%)*	19,262 (53.4)	19,070 (49.4)
Income Quintile, *n (%)*		
one (lowest)	7,678 (21.3)	8,027 (20.8)
two	7,306 (20.3)	7,765 (20.1)
three (middle)	7,062 (19.6)	7,654 (19.8)
four	6,110 (16.9)	6,797 (17.6)
five (highest)	7,301 (20.3)	7,816 (20.3)
Year of Cohort Entry, *n (%)*		
2003-2004	3,648 (10.1)	6,733 (17.5)
2005-2006	8,348 (23.2)	9,256 (24.0)
2007-2008	11,954 (33.2)	11,380 (29.5)

2009-2010	12,099 (33.6)	11,197 (29.0)
Rural Location, *n (%)*	5,397 (15.0)	7,165 (18.6)
Resident in a Long-term Care Facility, *n (%)*	1,454 (4.0)	1,298 (3.4)
Co-morbidities[*], *n (%)*		
Chronic kidney disease[†]	1,526 (4.2)	1,632 (4.2)
Diabetes mellitus[‡]	8,497 (23.6)	8,650 (22.4)
Peripheral vascular disease	1,137 (3.2)	2,077 (5.4)
Coronary artery disease[§]	16,847 (46.7)	18,844 (48.9)
Congestive heart failure	8,860 (24.6)	9,224 (23.9)
Stroke/Transient ischemic attack	1,434 (4.0)	1,467 (3.8)
Chronic liver disease	837 (2.3)	1,074 (2.8)
Medication Use[*], *n (%)*		
Angiotensin-converting enzyme inhibitor	13,781 (38.2)	14,859 (38.5)
Angiotensin-receptor blocker	6,540 (18.1)	6,514 (16.9)
Potassium sparing diuretic	3,643 (10.1)	3,949 (10.2)
Non-potassium sparing diuretic	16,308 (45.2)	17,145 (44.5)
Calcium channel blocker	11,785 (32.7)	12,553 (32.5)
β-Adrenergic antagonist	13,646 (37.9)	14,662 (38.0)
Statins	15,706 (43.6)	16,602 (43.0)
NSAIDs (excluding aspirin)	6,520 (18.1)	7,761 (20.1)
Anticonvulsants	2,297 (6.4)	2,244 (5.8)
Antidepressants	9,187 (25.5)	8,938 (23.2)
Antipsychotics	1,883 (5.2)	1,692 (4.4)
Benzodiazepines	9,035 (25.1)	9,414 (24.4)
Antineoplastics	2,217 (6.1)	2,377 (6.2)
Thyroid hormone	6,172 (17.1)	6,150 (15.9)
Baseline Laboratory Measurements‖		
Serum creatinine concentration, µmol/L, *median (IQR)*	91 (75-113)	90 (75-114)
eGFR mL/min/1.73 m^2[¶], *median (IQR)*	61 (46-75)	62 (47-77)
eGFR category, *n (%)*		
≥ 60 mL/min/1.73m^2	18,382 (51.0)	20,716 (53.7)
45-59 mL/min/1.73m^2	9,043 (25.1)	9,011 (23.4)
30-44 mL/min/1.73m^2	5,622 (15.6)	5,633 (14.6)
15-29 mL/min/1.73m^2	2,415 (6.7)	2,537 (6.6)
< 15 mL/min/1.73m^2	587 (1.6)	669 (1.7)
Urine dipstick protein, *n (%)*		
negative	4,186 (84.0)	3,252 (81.4)
0.3g/L	415 (8.3)	409 (10.2)
1.0g/L	296 (5.9)	257 (6.4)
≥ 3.0g/L	87 (1.7)	79 (2.0)
Serum sodium concentration, mmol/L, *median (IQR)*	139 (137-142)	139 (137-141)
Serum potassium concentration, mmol/L, *median (IQR)*	4.0 (4.0-5.0)	4.0 (4.0-5.0)
AKI Definitions for All Patients, *n (%)*		
AKIN Stage 1 or greater	5,312 (14.7)	6,879 (17.8)

RIFLE Risk	473 (1.3)	884 (2.3)
RIFLE Injury	294 (0.8)	567 (1.5)
RIFLE Failure	527 (1.5)	920 (2.4)
AKI Definitions for Patients with CKD,[†] *n (%)*		
AKIN Stage 1 or greater	524 (34.3)	644 (39.5)
RIFLE Risk	25 (1.6)	65 (4.0)
RIFLE Injury	12 (0.8)	41 (2.5)
RIFLE Failure	154 (10.1)	246 (15.1)

Abbreviations: IQR, interquartile range; eGFR, estimated glomerular filtration rate

[*]Co-morbidities and medication usage in the 5 years and 6 months preceding the hospital encounter were considered, respectively

[†]CKD was assessed by the ICD-10 code N18x, defined as "chronic kidney disease"

[‡] Diabetes mellitus was assessed by diabetic medication use in previous 6 months

[§]Coronary artery disease includes receipt of coronary artery bypass graft surgery, percutaneous coronary intervention and diagnoses of angina

[‖]The baseline measurements for serum creatinine were taken at a median (IQR) of 102 (41-204) and 39 (16-128) days prior to the hospital encounter for the Emergency Department Cohort and the Hospitalized Cohort, respectively. Baseline urine protein and serum sodium and potassium were available for a subset of patients. Emergency Department cohort: A total of 4,984, 29,746 and 30,040 patients had a baseline urine protein and serum sodium and potassium measurement available in the 7 to 365 days prior to the index date, respectively. Hospitalized cohort: A total of 3,997, 34,407 and 34,538 patients had a baseline urine protein and serum sodium and potassium measurements available in the 7 to 365 days prior to the index date, respectively

[¶]eGFR was calculated using the CKD-Epi equation.

CKD-Epi equation:141 x min([serum creatinine in umol/L /88·4]/κ, 1)$^{\alpha}$ x max([serum creatinine in umol/L / 88·4]/κ, 1)$^{-1·209}$ x 0·993^{Age} x 1·018 [if female] x 1·159 [if African American] *κ=0·7 for females and 0·9 for males, α= -0·329 for females and -0·411 for males, min=the minimum of Scr/κ or 1, max=the maximum of Scr/κ or 1.Racial information was not available in our data sources and all patients were assumed not to be of non African-Canadian race. This was a reasonable assumption; as of 2006, African-Canadians represented less than 7% of the Ontario population. Source:*http://www12.statcan.ca/census-recensement/2006/dp-pd/hlt/97-562/index.cfm?Lang=E

The diagnostic performance of the various coding algorithms is presented in Table 2. For both types of hospital encounters, 'all diagnosis' was the best performing ICD-10 N17x coding algorithm. At presentation to the emergency department, the sensitivity of the ICD-10 code for the RIFLE Injury definition of AKI (≥ 2-fold increase in serum creatinine concentration from baseline) was 37.4% (95% confidence interval (CI): 32.1% to 43.1%). Sensitivities were higher at hospital admission than at presentation to the emergency department for all four serum creatinine-based definitions of AKI. For example, at hospital admission, the sensitivity of the code for the RIFLE Injury definition was 61.6% (95% CI: 57.5% to 65.5%). The sensitivity of the code improved for more severe definitions of AKI, peaking at the RIFLE Injury definition. There was no substantial difference in specificity for both types of hospital encounters, with values greater than 95% in both settings. The positive predictive value of the code decreased for more severe definitions of AKI, with a nadir at the RIFLE Injury definition in both settings.

Table 2. Diagnostic performance characteristics of three different algorithms for ICD-10 code N17x using four different serum creatinine-based definitions of AKI as the reference standard

Diagnostic Coding Algorithm	Definition	Diagnostic Performance Characteristics (95% CI)	
		Emergency Department Cohort	Hospitalized Cohort
All diagnosis	AKIN Stage 1	Sn=7.2 (6.6-8.0) Sp=99.9 (99.8-99.9) PPV=90.4 (87.2-92.8) NPV=86.2 (85.8-86.5)	Sn=21.8 (20.9-22.8) Sp=98.4 (98.2-98.5) PPV=74.2 (72.3-76.1) NPV=85.3 (84.9-85.6)
	RIFLE Risk	Sn=30.4 (26.5-34.7) Sp=99.2 (99.1-99.3) PPV=33.8 (29.5-38.4) NPV=99.1 (99.0-99.2)	Sn=56.4 (53.2-59.7) Sp=96.0 (95.8-96.2) PPV=24.7 (22.8-26.6) NPV=98.9 (98.8-99.1)
	RIFLE Injury	Sn=37.4 (32.1-43.1)	Sn=61.6 (57.5-65.5)

		Sp=99.1 (99.0-99.2) PPV=25.8 (21.9-30.2) NPV=99.5 (99.4-99.6)	Sp=95.6 (95.4-95.8) PPV=17.3 (15.7-19.0) NPV=99.4 (99.3-99.5)
	RIFLE Failure	Sn=30.2 (26.4-34.2) Sp=99.2 (99.2-99.3) PPV=37.3 (32.9-42.0) NPV=99.0 (98.9-99.1)	Sn=59.1 (55.9-62.3) Sp=96.1 (95.9-96.3) PPV=26.9 (25.0-28.9) NPV=99.0 (98.9-99.1)
Main Diagnosis/ Most Responsible Diagnosis	AKIN Stage 1	Sn=4.1 (3.6-4.6) Sp=100.0 (99.9-100.0) PPV=94.7 (91.0-97.0) NPV=85.8 (85.4-86.1)	Sn=5.1 (4.6-5.7) Sp=99.9 (99.8-99.9) PPV=90.7 (87.4-93.2) NPV=82.9 (82.5-83.3)
	RIFLE Risk	Sn=21.4 (17.9-25.3) Sp=99.6 (99.6-99.7) PPV=44.5 (38.2-51.0) NPV=99.0 (98.9-99.1)	Sn=18.7 (16.2-21.4) Sp=99.4 (99.3-99.5) PPV=42.5 (33.7-47.5) NPV=98.1 (98.0-98.3)
	RIFLE Injury	Sn=27.9 (23.1-33.3) Sp=99.6 (99.6-99.7) PPV=36.1 (30.2-42.6) NPV=99.4 (99.3-99.5)	Sn=22.8 (19.5-26.4) Sp=99.3 (99.2-99.4) PPV=33.3 (28.7-38.1) NPV=98.9 (98.7-99.0)
	RIFLE Failure	Sn=22.0 (18.7-25.7) Sp=99.6 (99.5-99.7) PPV=51.1 (44.6-57.5) NPV=98.9 (98.7-99.0)	Sn=22.9 (20.3-25.8) Sp=99.5 (99.5-99.6) PPV=54.4 (49.4-59.3) NPV=98.1 (98.0-98.3)
Admission Diagnosis	AKIN Stage 1	n/a	Sn=15.8 (15.0-16.7) Sp=99.2 (99.1-99.3) PPV=81.6 (79.4-83.6) NPV=84.5 (84.1-84.8)
	RIFLE Risk		Sn=43.1 (39.9-46.4) Sp=97.5 (97.3-97.6) PPV=28.5 (26.2-31.0) NPV=98.6 (98.5-98.8)
	RIFLE Injury		Sn=48.3 (44.2-52.4) Sp=97.2 (97.0-97.4) PPV=20.5 (18.4-22.8) NPV=99.2 (99.1-99.3)
	RIFLE Failure		Sn=47.4 (44.2-50.6) Sp=97.6 (97.5-97.8) PPV=32.6 (30.2-35.2) NPV=98.7 (98.6-98.8)

Abbreviations: ICD-10, International Classification of Diseases, tenth revision; CI, confidence interval; Sn, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value; n/a, not applicable
All values are presented as percentages (%)
To convert serum creatinine from µmol/L to mg/dL divide by 88.4

The absolute change in serum creatinine (peak value – baseline value) and relative change in serum creatinine [(peak value – baseline value) / baseline value)] for patients with hospital encounters who were positive and negative for the ICD-10 N17x code are presented in Table 3.When considering the 'all diagnosis' algorithm, 1.2% of patients at presentation to the emergency department and 5.2% of patients at hospital admission were code positive for AKI. The median (IQR) absolute change in serum creatinine concentration for code positive patients was 133 (62 to 288) µmol/L and 98 (43 to 200) µmol/L in each setting, respectively. The change for code negative

patients was 2 (-8 to 14) µmol/L and 6 (-4 to 20) µmol/L in each setting, respectively. When expressed in relative terms, the median (IQR) change for code positive patients was 87 (43 to 204) % and 69 (28 to 153) % in each setting, respectively. The relative change for code negative patients was 2 (-9 to 15) % and 7 (-5 to 22) % in each setting, respectively. In both settings, the difference in the mean absolute and relative change in serum creatinine between code positive and code negative patients was highly statistically significant (p<0.001).

Table 3. Change in serum creatinine concentration from baseline in all patients with and without the ICD-10 N17x code for AKI (referred to as code positive and code negative)

Diagnostic Coding Algorithm	Code	Emergency Department Cohort			Hospitalized Cohort		
		N	Absolute Change (µmol/L)	Relative Change (%)*	N	Absolute Change (µmol/L)	Relative Change (%)*
			Median(IQR)			Median(IQR)	
All diagnosis	+	426	133 (62 to 288)	87 (43 to 204)	2,023	98 (43 to 200)	69 (28 to 153)
	-	35,623	2 (-8 to 14)	2 (-9 to 15)	36,543	6 (-4 to 20)	7 (-5 to 22)
Main Diagnosis/ Most Responsible Diagnosis	+	227	187 (89 to 383)	128 (62 to 295)	388	196 (93 to 396)	121 (49 to 275)
	-	35,822	2 (-8 to 14)	2 (-9 to 16)	38,178	7 (-4 to 22)	7 (-4 to 24)
Admission Diagnosis	+	n/a			1,366	114 (39 to 187)	75 (30 to 169)
	-				37,230	6 (-4 to 21)	7 (-4 to 23)

Abbreviations: ICD-10, International Classification of Diseases, tenth revision; CKD, Chronic kidney disease; N, number; IQR, interquartile range; +, code positive; -, code negative; n/a, not applicable
Both absolute and relative changes in serum creatinine were significantly different between code positive and code negative patients in both types of hospital encounter (all p-values <0.001) (means presented in box plot; Supplementary Figure 2 and 3)
*[(peak serum creatinine – baseline serum creatinine) / baseline serum creatinine)]
To convert serum creatinine from µmol/L to mg/dL divide by 88.4

The diagnostic performance of the 'all diagnosis' algorithm at hospital admission in patients with and without CKD is presented in Table 4. The sensitivity of the ICD-10 code for AKIN Stage 1 or greater, RIFLE Risk and RIFLE Injury definitions was higher in patients with CKD than those without CKD. For example, the sensitivity of the code for the RIFLE Injury definition was 75.6% (95% CI: 60.7% to 86.2%) in patients with CKD and 60.5% (95% CI: 56.2% to 64.5%) in patients without CKD. The code demonstrated the highest sensitivity for the RIFLE Risk definition in patients with CKD and the RIFLE Failure definition in patients without CKD. The specificities of the code were lower in patients with CKD than those without CKD for all four definitions. For example, the specificity of the code for the RIFLE Injury definition was 82.6% (95% CI: 80.7% to 84.4%) in patients with CKD and 96.2% (95% CI: 96.0% to 96.4%) in patients without CKD.

Table 4. Diagnostic performance characteristics of the ICD-10 N17x code in hospitalized patients with and without CKD using serum creatinine-based definitions of AKI as the reference standard*

Definition	Diagnostic Performance Characteristics (95% CI)	
	Patients with CKD	Patients without CKD

AKIN Stage 1	Sn=35.6 (32.0-39.3) Sp=92.0 (90.2-93.5) PPV=74.4 (69.2-78.9) NPV=68.7 (66.1-71.1)	Sn=20.4 (19.4-21.4) Sp=98.6 (98.4-98.7) PPV=74.2 (72.1-76.2) NPV=85.9 (85.5-86.3)
RIFLE Risk	Sn=76.9 (65.4-85.5) Sp=83.5 (81.6-85.3) PPV=16.2 (12.5-20.8) NPV=98.9 (98.1-99.3)	Sn=54.8 (51.4-58.2) Sp=96.5 (96.3-96.7) PPV=26.2 (24.2-28.3) NPV=98.9 (98.8-99.1)
RIFLE Injury	Sn=75.6 (60.7-86.2) Sp=82.6 (80.7-84.4) PPV=10.1 (7.2-13.9) NPV=99.2 (98.6-99.6)	Sn=60.5 (56.2-64.5) Sp=96.2 (96.0-96.4) PPV=18.5 (16.8-20.5) NPV=99.4 (99.3-99.5)
RIFLE Failure	Sn=48.4 (42.2-54.6) Sp=86.4 (84.5-88.1) PPV=38.6 (33.4-44.2) NPV=90.4 (88.7-91.9)	Sn=63.1 (59.4-66.6) Sp=96.4 (96.3-96.6) PPV=24.8 (22.8-26.9) NPV=99.3 (99.2-99.4)

Abbreviations: ICD-10, International Classification of Diseases, tenth revision; CKD, Chronic kidney disease; CI, confidence interval; Sn, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value
All values are presented as percentages (%)
*The ICD-10 N17x coding algorithm considered is all diagnosis

The absolute and relative changes in serum creatinine at hospital admission in patients with and without CKD who were code positive and code negative are presented in Table 5. When considering the 'all diagnosis' algorithm, a total of 18.9% of patients with CKD and 4.6% of patients without CKD were code positive for AKI. The median (IQR) absolute change in serum creatinine concentration in patients with CKD who were code positive was 108 (48 to 215) µmol/L and in patients without CKD who were code positive was 95 (43 to 197) µmol/L. The difference in the absolute change in serum creatinine between patients with and without CKD who were AKI code positive was not significantly different (p=0.910). The median (IQR) absolute change in patients with CKD who were code negative was 16 (-8 to 51) µmol/L and in patients without CKD who were code negative was 6 (-4 to 19) µmol/L. When expressed in relative terms, the median (IQR) change in serum creatinine in patients with CKD who were code positive was significantly lower than in patients without CKD who were code positive (53 (20 to 104) % vs. 72 (29 to 161) %; p<0.0001). The median (IQR) relative change in patients with CKD who were code negative was 9 (-4 to 26) % and in patients without CKD who were code negative was 6 (-5 to 22) %. For both patients with and without CKD, the difference in the mean absolute and relative changes in serum creatinine between code positive and negative patients was highly statistically significant (p<0.001).

Table 5. Change in serum creatinine concentration from baseline in hospitalized patients with and without CKD where ICD-10 code N17x did and did not indicate AKI (referred as code positive and code negative)*

Code	Patients with CKD			Patients without CKD		
	N	Absolute Change (µmol/L)	Relative Change (%)†	N	Absolute Change (µmol/L)	Relative Change (%)†
		Median(IQR)			Median(IQR)	
+	308	108 (48 to 215)	53 (20 to 104)	1,715	95 (43 to 197)	72 (29 to 161)
-	1,324	16 (-8 to 51)	9 (-4 to 26)	35,219	6 (-4 to 19)	6 (-5 to 22)

Abbreviations: ICD-10, International Classification of Diseases, tenth revision; CKD, Chronic kidney disease; N, number; IQR, interquartile range; +, code positive; -, code negative; n/a, not applicable.
Code positive and code negative patients were significantly different (all p-values <0.001)
Relative changes in patients with and without CKD were statistically different (p<0.0001)
*The ICD-10 N17x coding algorithm considered is all diagnosis
† [(peak serum creatinine – baseline serum creatinine) / baseline serum creatinine)]
To convert serum creatinine from μmol/L to mg/dL divide by 88.4

DISCUSSION

In this population-based retrospective validation study, we evaluated the diagnostic performance of ICD-10 code N17x for AKI. We discovered that the best performing coding algorithm both at presentation to the emergency department and at hospital admission was when the code was expressed as 'all diagnosis' (i.e. when the code was indicated by any diagnosis type).

At hospital admission, the poorest performing coding algorithm was the 'most responsible diagnosis'. A likely explanation for this is that AKI frequently presents as a complication of other conditions requiring hospital admission, such as acute myocardial infarction or sepsis.[30] AKI is rarely the primary reason for hospital admission so would less likely be coded as the "most responsible diagnosis".

The ICD-10 code demonstrated modest sensitivity for the serum creatinine-based definitions of AKI, indicating its inability to identify a portion of patients who experienced a clinically significant increase in serum creatinine. However, the code demonstrated high specificity for all four serum creatinine-based definitions. These characteristics of the ICD-10 AKI code are similar to those described in ICD-9 code validation studies that used serum creatinine-based definitions as the reference standard.[7, 9, 20, 21] The use of a serum creatinine-based definition of AKI as the reference standard is preferred over chart review, recognizing the latter have appearing in a number of previous validation studies.[31-35]

The ICD-10 code showed improved sensitivity for more severe definitions of AKI and was highest for the RIFLE Injury definition. This characteristic of the ICD-10 code is similar to that of ICD-9 codes for AKI.[20] A greater increase in serum creatinine reflects a more severe AKI, is more likely to be documented in the medical chart and thus detected by coders.

The positive predictive value of the ICD-10 code decreased for more severe definitions of AKI and was the lowest for the RIFLE Injury definition. This fluctuation in the positive predictive values can in part be attributed to the varying prevalence of the four serum creatinine-based definitions.

At both types of hospital encounters, patients who were code positive had a significantly higher increase in serum creatinine than those who were code negative (p<0.001). In other words, the code does successfully differentiate between two groups of patients with and without distinct changes in serum creatinine.

We also assessed the diagnostic performance of the ICD-10 code in subgroups of patients with and without CKD prior to the hospital encounter. For all definitions, with the exception of RIFLE Failure, the code demonstrated higher sensitivity in patients with CKD than those without CKD. However, the specificity of the code was lower in patients with CKD than those without CKD (for all definitions of AKI). The latter finding suggests a portion of patients with stable CKD are misclassified as having AKI at their hospital encounter. For example, clinicians may not have access to patients' baseline serum creatinine measurements or make the diagnosis without investigating the baseline measurements. Consequently, an elevated serum creatinine concentration at hospital presentation that is no different than the baseline value may still be misdiagnosed as AKI.

Amongst patients with CKD, presence or absence of the ICD-10 AKI code was also able to differentiate between two groups of patients with distinct changes in their serum creatinine from the baseline value. Although the difference in mean absolute change in serum creatinine was no different in patients with and without CKD who had a positive AKI code, the relative change was lower in patients with CKD than those without CKD. This is consistent with physicians defining AKI more commonly in absolute rather than relative terms. With a given absolute increase in serum creatinine, the relative increase in serum creatinine is lower in patients with CKD than those without CKD.

Our study has several strengths. To our knowledge, it is the first study to provide information on the diagnostic performance of the ICD-10 code for AKI using serum creatinine-based definitions of AKI as the reference standard.[7, 9, 20, 21] We assessed different diagnostic coding algorithms of the ICD-10 code at both presentation to the emergency department and at hospital admission. Moreover, we evaluated the diagnostic performance of the code in subgroups of patients with and without CKD prior to the hospital encounter. We studied patients from twelve hospitals across Southwestern Ontario with representation from both academic and community care centres.

This helped to minimize selection bias. The large number of patients resulted in good precision for the estimates provided in the study.

Our study does have some limitations. We evaluated the validity of the ICD-10 code for AKI in patients 66 years of age and older. These findings should generalize well to elderly patients, a segment of the population at high risk of AKI.[10, 36] The findings are also useful for pharmacoepidemiologic studies using Ontario's healthcare administrative databases, where prescription information on Ontario residents age 65 and older is available from the universal drug benefit plan. However, future validation studies in younger patients are needed.

We did not know the degree to which patients with AKI were symptomatic from diminished kidney function or the indication that prompted presentation to the emergency department or hospital admission. Moreover, the median (IQR) period between the baseline serum creatinine measurements and the hospital encounter was 102 (41-204) days for patients who presented to the emergency department and 39 (16-128) days for patients admitted to hospital. While these are reasonable baseline measurements, the AKIN Stage 1 definition requires the change in serum creatinine to occur within 48 hours.[5] Although it is likely that serum creatinine changes occurred just prior to the hospital encounter, we cannot say this with complete certainty given the absence of available measurements during this period.

Finally, we could not examine the validity of outpatient claims for AKI in this study. However, the diagnostic performance of outpatient claims in our jurisdiction is notoriously poor. Nonetheless, emergency department and hospital inpatient records hold information on more severe forms of AKI, which are of particular interest to clinicians, researchers, and policymakers. Moreover, we recognize that we did not capture those patients who may have had severe forms of AKI, but did not present to the emergency department or hospital, or those who presented, but did not have their serum creatinine measured. However, the latter situation is unlikely given that serum creatinine measurements are a standard laboratory test for most patients who present to a hospital encounter for acute medical care.

CONCLUSION

Although the use of healthcare administrative databases for clinical or healthcare services research has several merits, there are inherent limitations, including the accuracy with which certain conditions (i.e. AKI) can be identified. The sensitivity of ICD-10 code N17x for AKI was limited, particularly for less severe definitions. This results in underestimation of the true incidence of the condition. Nonetheless, the presence or absence of the ICD-10 code successfully differentiates two groups of elderly patients with and without distinct increases in serum creatinine from baseline values at the time of a hospital encounter. The results from this study guide judicious use of ICD-10 code N17x in future research using large healthcare administrative databases.

Contributors

YJH participated in the study coordination and study design and analysis, provided interpretation of study results, and drafted the manuscript. SZS participated in the study design, acquisition of data, and performed the analysis. SG contributed to the study design and interpretation of study results. RW, EC, and JLF contributed to the study design and provided feedback on the manuscript. AXG conceived of the study, participated in its design and interpretation and provided feedback on the manuscript. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

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Supplementary Table 1. Sample 2 by 2 table for assessing diagnostic performance characteristics (sensitivity, specificity, positive predictive value, and negative predictive value) for ICD-10 code N17x

	Reference Standard: RIFLE Injury definition of AKI	
	≥ 2-fold increase in serum creatinine concentration from baseline	< 2-fold increase in serum creatinine concentration from baseline
Code N17x positive	True Positive (TP)	False Positive (FP)
Code N17x negative	False Negative (FN)	True Negative (TN)

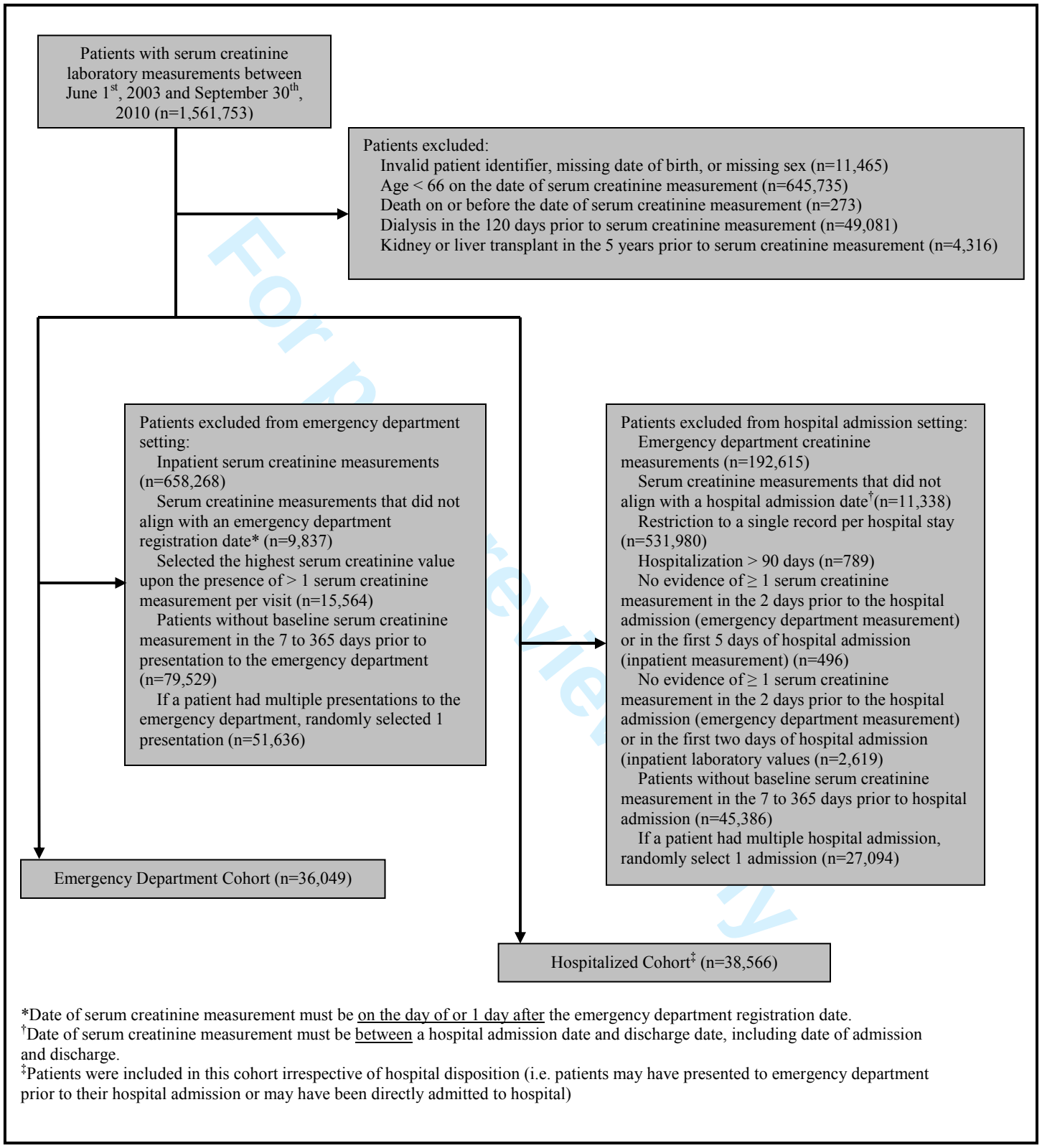
Sensitivity (Sn) = TP ÷ (TP + FN); the proportion of patients with ≥ 2-fold increase in serum creatinine concentration from baseline who are code N17x positive
Specificity (Sp) = TN ÷ (FP + TN); the proportion of patients with < 2-fold increase in serum creatinine concentration from baseline who are code N17x negative
Positive Predictive Value (PPV) = TP ÷ (TP + FP); the proportion of patients who are code N17x positive with ≥ 2-fold increase in serum creatinine concentration from baseline
Negative Predictive Value (NPV) = TN ÷ (FN + TN); the proportion of patients who are code N17x negative with < 2-fold increase in serum creatinine concentration from baseline

Supplementary Table 2. STARD (STAndards for the Reporting of Diagnostic accuracy studies) checklist

Section and Topic	Item #		Page
TITLE/ABSTRACT/ KEYWORDS	1	Identify the article as a study of diagnostic accuracy (recommend MeSH heading 'sensitivity and specificity').	1-2
INTRODUCTION	2	State the research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups.	3
METHODS			
Participants	3	The study population: The inclusion and exclusion criteria, setting and locations where data were collected.	3-4
	4	Participant recruitment: Was recruitment based on presenting symptoms, results from previous tests, or the fact that the participants had received the index tests or the reference standard?	3-4
	5	Participant sampling: Was the study population a consecutive series of participants defined by the selection criteria in item 3 and 4? If not, specify how participants were further selected.	N/A
	6	Data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?	3
Test methods	7	The reference standard and its rationale.	4
	8	Technical specifications of material and methods involved including how and when measurements were taken, and/or cite references for index tests and reference standard.	4-5
	9	Definition of and rationale for the units, cut-offs and/or categories of the results of the index tests and the reference standard.	4-5
	10	The number, training and expertise of the persons executing and reading the index tests and the reference standard.	4-5
	11	Whether or not the readers of the index tests and reference standard were blind (masked) to the results of the other test and describe any other clinical information available to the readers.	N/A
Statistical methods	12	Methods for calculating or comparing measures of diagnostic accuracy, and the statistical methods used to quantify uncertainty (e.g. 95% confidence intervals).	5, Supplementary Table 1
	13	Methods for calculating test reproducibility, if done.	N/A
RESULTS			
Participants	14	Report when study was done, including beginning and ending dates of recruitment.	4,5
	15	Report clinical and demographic characteristics of the study population (e.g. age, sex, spectrum of presenting symptoms, comorbidity, current treatments, recruitment centers).	5-7
	16	Report the number of participants satisfying the criteria for inclusion that did or did not undergo the index tests and/or the reference standard; describe why participants failed to receive either test (a flow diagram is strongly recommended).	4, Supplementary Figure 1
Test results	17	Report time interval from the index tests to the reference standard, and any treatment administered between.	Supplementary Figure 1

	18	Report distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition.	5-7
	19	Report a cross tabulation of the results of the index tests (including indeterminate and missing results) by the results of the reference standard; for continuous results, the distribution of the test results by the results of the reference standard.	7-11
	20	Report any adverse events from performing the index tests or the reference standard.	N/A
Estimates	21		
	22	Report estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals).	7-10
	23	Report how indeterminate results, missing responses and outliers of the index tests were handled.	N/A
	24	Report estimates of variability of diagnostic accuracy between subgroups of participants, readers or centers, if done.	N/A
DISCUSSION	25	Report estimates of test reproducibility, if done.	N/A

Supplementary Figure 1. Cohort Selection



*Date of serum creatinine measurement must be on the day of or 1 day after the emergency department registration date.
†Date of serum creatinine measurement must be between a hospital admission date and discharge date, including date of admission and discharge.
‡Patients were included in this cohort irrespective of hospital disposition (i.e. patients may have presented to emergency department prior to their hospital admission or may have been directly admitted to hospital)

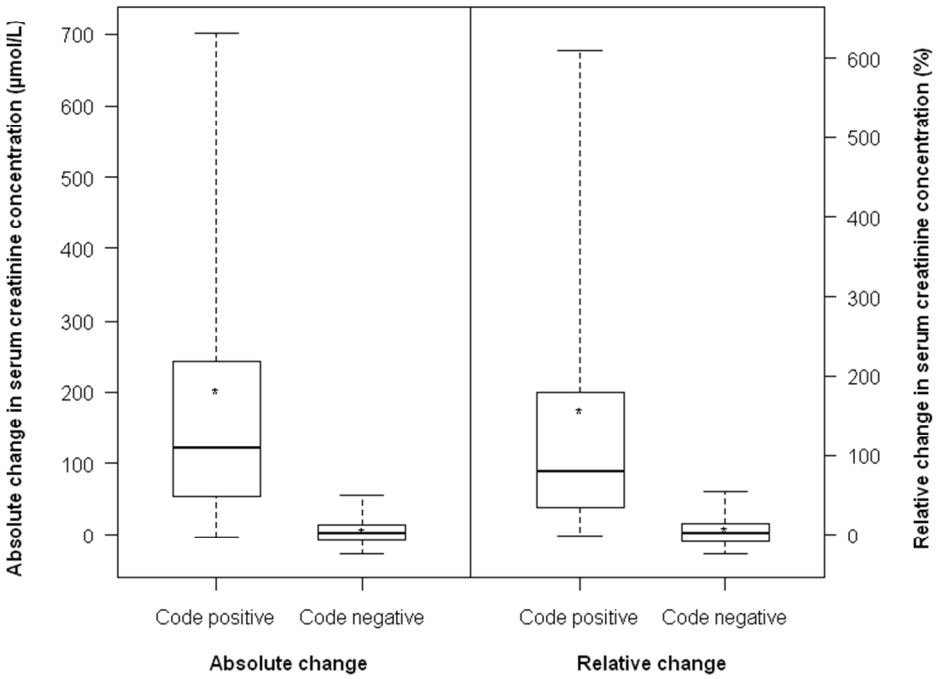
Supplementary Figure 2. Absolute and relative changes in serum creatinine concentration among patients who presented to the emergency department who were code positive and code negative for AKI.* Patients who were code positive for AKI had a significantly greater change in serum creatinine concentration from their baseline value than those patients who were code negative. The boxes represent the interquartile range (50% of the values). The line across the box indicates the median. The asterisk indicates the mean. The whiskers extend to the 95th and 5th percentile.

*The ICD-10 N17x coding algorithm considered is all diagnosis
†The baseline measurements for serum creatinine were taken at a median (IQR) of 102 (41-204) days prior to presentation to the emergency department

Supplementary Figure 3. Absolute and relative changes in serum creatinine concentration among hospitalized patients who were code positive and code negative for AKI. Patients who were code positive for AKI had significantly greater change in serum creatinine concentration from their baseline value than those patients who were code negative. The boxes represent the interquartile range (50% of the values). The line across the box indicates the median. The asterisk indicates the mean. The whiskers extend to the 95th and 5th percentile.

*The ICD-10 N17x coding algorithm considered is all diagnosis

† The baseline measurements for serum creatinine were taken at a median (IQR) 39 (16-128) days prior to the hospital admission



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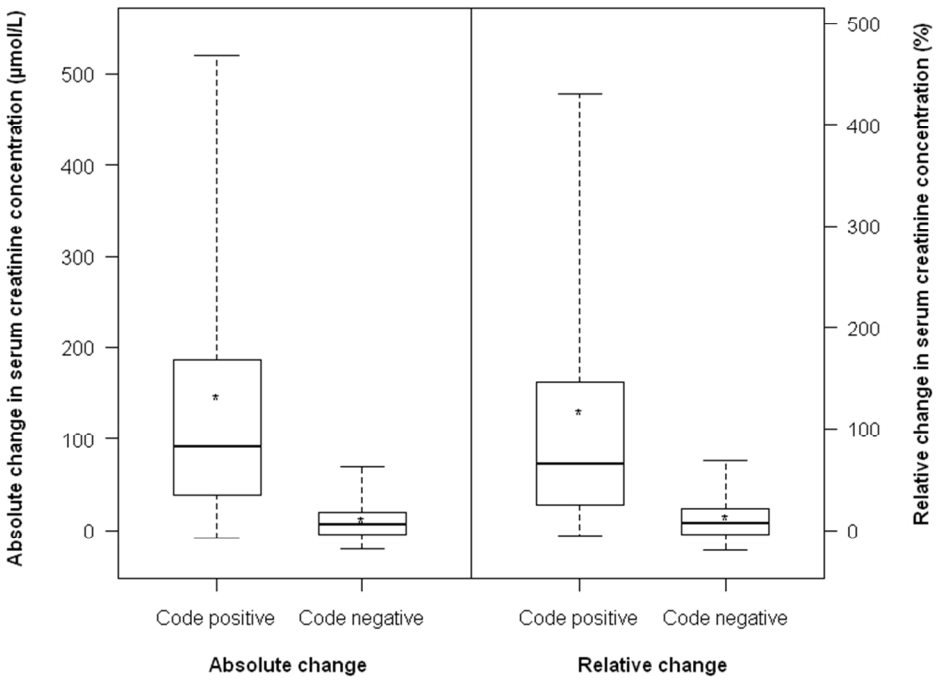
215x177mm (96 x 96 DPI)



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215x177mm (96 x 96 DPI)

Validity of the International Classification of Diseases, Tenth Revision code for acute kidney injury in elderly patients at presentation to emergency department and at hospital admission

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Validity of the *International Classification of Diseases, Tenth Revision* code for acute kidney injury in elderly patients at presentation to emergency department and at hospital admission

Y. Joseph Hwang BMSc[1,2], Salimah Z. Shariff PhD[3], Sonja Gandhi BSc[1,2], Ron Wald MD, MPH[4,5], Edward Clark MD[6], Jamie L. Fleet BHSc[1], Amit X. Garg MD, PhD[1,2,3]

1. Division of Nephrology, Department of Medicine, Western University, London, Ontario, Canada
2. Department of Epidemiology & Biostatistics, Western University, London, Ontario, Canada
3. Institute for Clinical Evaluative Sciences, Ontario, Canada
4. Keenan Research Centre in the Li Ka Shing Knowledge Institute of St Michael's Hospital, Toronto, Ontario, Canada
5. Division of Nephrology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada
6. Kidney Research Centre, Ottawa Hospital Research Institute, University of Ottawa, Ottawa, Ontario, Canada

Correspondence: Dr. Amit Garg, London Kidney Clinical Research Unit, Room ELL-101, Westminster, London Health Sciences Centre, 800 Commissioners Road East, London, Ontario, Canada N6A 4G5, Tel: 519-685-8502, Fax: 519-685-8072, email: amit.garg@lhsc.on.ca

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ABSTRACT

Objective: To evaluate the validity of the *International Classification of Diseases, Tenth Revision* (ICD-10) code N17x for acute kidney injury (AKI) in elderly patients in two settings: at presentation to the emergency department and at hospital admission.

Design: Population-based retrospective validation study.

Setting: Southwestern Ontario, Canada, from 2003 to 2010.

Participants: Elderly patients with serum creatinine measurements at presentation to the emergency department (n=36,049) or hospital admission (n=38,566). The baseline serum creatinine measurement was a median of 102 days and 39 days prior to presentation to the emergency department and hospital admission, respectively.

Main outcome measures: Sensitivity, specificity, and positive and negative predictive values of ICD-10 diagnostic coding algorithms for AKI using a reference standard based on changes in serum creatinine from the baseline value. Median changes in serum creatinine of patients who were code positive and code negative for AKI.

Results: The sensitivity of the best-performing coding algorithm for AKI (defined as a ≥ 2-fold increase in serum creatinine concentration) was 37.4% (95% confidence interval (CI): 32.1% to 43.1%) at presentation to the emergency department and 61.6% (95% CI: 57.5% to 65.5%) at hospital admission. The specificity was greater than 95% in both settings. In patients who were code positive for AKI, the median (interquartile range) increase in serum creatinine from baseline was 133 (62 to 288) µmol/L at presentation to emergency department and 98 (43 to 200) µmol/L at hospital admission. In those who were code negative, the increase in serum creatinine was 2 (-8 to 14) and 6 (-4 to 20) µmol/L, respectively.

Conclusions: The presence or absence of ICD-10 code N17x differentiates two groups of patients with distinct changes in serum creatinine at the time of a hospital encounter. However, the code underestimates the true incidence of AKI due to limited sensitivity.

Keywords: acute kidney injury, acute renal failure, serum creatinine, validation, validity, sensitivity, specificity, International Classification of Diseases

Article Summary:

Article Focus

- Validation of administrative database codes is a prerequisite to their optimal use in research
- The aim of this study was to describe the validity of the ICD-10 code N17x for AKI compared to a reference standard based on changes in serum creatinine

Key Messages

- The ICD-10 code N17x for AKI has moderate sensitivity and high specificity
- The sensitivity of the N17x code improves for more severe forms of AKI
- The code was successful in identifying a group of patients admitted to hospital with a median increase in serum creatinine of 98 µmol/L

Strengths and Limitations

- This is the first study to provide information on the diagnostic performance of ICD-10 code N17x for AKI using laboratory values as the reference standard
- It was a large population-based validation study that included serum creatinine measurements from twelve hospitals
- Future validation studies in younger patients are required

BACKGROUND

Healthcare administrative databases can provide researchers and policy makers with information on a large number of patients in an efficient manner. When using these data sources for clinical or health services research, the validity of the research depends upon the accuracy of the diagnostic and procedural codes that have been recorded.[1] However, the accuracy of coding is not guaranteed because administrative databases are not primarily intended for research.[2] Consequently, understanding the validity of administrative codes is a prerequisite to their optimal use in the assessment of patient outcomes.

Clinically, acute kidney injury (AKI) is characterized by an abrupt decline in renal function that may result in disordered fluid, acid-base and electrolyte homeostasis, and retention of waste products from nitrogen metabolism, such as creatinine and urea, and/or decreased urine output.[3-5] Two systems for defining and quantifying the severity of AKI are widely used: the Acute Kidney Injury Network (AKIN) classification [6] and the Risk-Injury-Failure-Loss-ESRD (RIFLE) criteria.[7] These staging systems define AKI severity according to absolute and relative (percentage) increases in serum creatinine, a blood test universally used to indicate kidney function. While the incidence of AKI is dependent on the definition used, it is recognized that this condition is common, affecting 2 to 9% of patients at hospital admission.[8-11] Moreover, patients who develop AKI have both poor short and long-term outcomes and their care is costly.[8, 9, 12-20]

The purpose of the present study was to evaluate the accuracy of the *International Classification of Diseases, Tenth Revision* (ICD-10) code N17x for AKI for applications in clinical and health services research, particularly in pharmacoepidemiologic studies. We compared this code against changes in serum creatinine concentration in two settings: 1) at presentation to the emergency department and 2) at hospital admission. In addition, we investigated the effect of baseline chronic kidney disease (CKD) status on the diagnostic performance of the code in the two settings. Based on the findings of a previous validation study on ICD-9 codes, we anticipated the sensitivity for ICD-10 code N17x would be low, improving with more severe definitions of AKI.[8, 10, 21, 22] Moreover, we expected higher sensitivity in patients with CKD than those without, as the former typically have larger absolute increases in serum creatinine for a given amount of AKI.

METHODS

Study Design and Setting

We conducted a population-based retrospective validation study using Ontario's linked healthcare administrative databases and laboratory data from Southwestern Ontario. All residents receive universal access to hospital and physician services under a single provincial payer system, providing a comprehensive set of health administrative data.

Using a diagnostic test assessment framework, we obtained diagnostic performance characteristics (sensitivity, specificity, positive predictive value, and negative predictive value) of various diagnostic coding algorithms for ICD-10 code N17x, which is defined as "acute renal failure". We used changes in serum creatinine from the baseline value as the reference standard (see Supplementary Table 1 for a sample two-by-two table). Moreover, we compared the change in serum creatinine between patients who were N17x code positive with those who were N17x code negative.

Our protocol was approved by the institutional review board at Sunnybrook Health Sciences Centre (Toronto, Ontario). The relevant datasets are held at the Institute for Clinical Evaluative Sciences. The reporting of this study follows guidelines set out for studies assessing diagnostic accuracy (Supplementary Table 2).[23]

Data Sources

Patient records from the seven databases were linked using encrypted unique identifiers. We identified laboratory measurements, including serum creatinine, using a system that keeps patient electronic medical records (Cerner®, Kansas City, Missouri, USA).[24] This system contains inpatient, outpatient and the emergency department laboratory measurements for twelve Southwestern Ontario hospitals. For a subpopulation, we also obtained previous laboratory measurements from Gamma-Dynacare, a provider of outpatient laboratory services to residents in Southwestern Ontario. We obtained inpatient and emergency department patient diagnostic information from the Canadian Institute of Health Information (CIHI) Discharge Abstract Database (DAD) and National Ambulatory Care Reporting System database (NACRS), respectively. We obtained information on inpatient and outpatient

physician services from the Ontario Health Insurance Plan database (OHIP). We ascertained patient demographic information from the Ontario's Registered Persons Database (RPDB) and prescribed drug use for patients 65 years of age and older from the Ontario Drug Benefit database (ODB). These databases have been used extensively to research health outcomes and health services.[25-28]

Accrual of Elderly Patients in Two Settings: at Presentation to Emergency Department and at Hospital Admission

We developed two separate cohorts. The first cohort consisted of patients with a serum creatinine measurement at presentation to the emergency department (Emergency Department Cohort). The second cohort consisted of patients with a serum creatinine measurement at hospital admission (Hospitalized Cohort). All patients had a baseline serum creatinine measurement (described below). The period of accrual was from June 1st, 2003 to September 30th, 2010.

We restricted cohort entry to patients 66 years of age and older to ensure at least one year of baseline prescription records for all patients. We excluded the following patients from both cohorts: i) those who had end-stage renal disease (defined by the receipt of dialysis in the 120 days prior to the hospital encounter), ii) those who received a kidney or liver transplant in the five years prior to the hospital encounter, iii) those whose date of serum creatinine measurement (from Cerner®) and the hospital encounter (from CIHI-DAD) did not align (less than 1.4% patients excluded for this reason; see Supplementary Figure 1 for explanation) and iv) those without at least one serum creatinine measurement in the 7 to 365 days prior to the hospital encounter to serve as the baseline value. In cases where a patient had multiple baseline measurements we selected the most recent one. Additional selection criteria for each cohort are described below and illustrated in Supplementary Figure 1.

We excluded patients who did not have a serum creatinine measurement in the emergency department from entry to the Emergency Department Cohort. We excluded the following patients from entry to the Hospitalized Cohort: i) those with a hospital admission that resulted in a stay greater than 90 days (to ensure we had data for the full hospital admission to the time of discharge i.e. particularly for patients accrued in the second half of year 2010) and ii) those without a serum creatinine measurement either in the emergency department prior to hospital admission or during the first two days of hospital admission. When multiple eligible hospital presentations were identified for a given patient over the study period, we randomly selected one hospital encounter for each cohort.

Within the two cohorts, we identified patients diagnosed with CKD (assessed by the presence of ICD-10 code N18x defined as "chronic kidney disease") in the 5 years prior to their hospital encounter to evaluate potential differential classification of AKI in patients with baseline CKD compared to those without.

The Reference Standard: Serum Creatinine-Based Definitions of AKI

Measuring changes in serum creatinine is the most common method of identifying AKI in clinical practice. We adapted the reference standard used in this study from four widely used serum creatinine-based definitions of AKI: i) AKIN Stage 1 or greater: ≥ 27 μmol/L (0.3 mg/dL) or 50% increase in serum creatinine concentration from baseline, ii) RIFLE Risk: ≥ 1.5-fold increase in serum creatinine concentration from baseline, iii) RIFLE Injury: ≥ 2-fold increase in serum creatinine concentration from baseline, and iv) RIFLE Failure**:** ≥ 3-fold increase in serum creatinine concentration from baseline or a baseline serum creatinine concentration ≥ 354 μmol/L (4.0 mg/dL) with ≥ 44 μmol/L (0.5 mg/dL) increase from baseline.[6, 7] A Roche Modular Ion Selective Electrode® system (Basel, Switzerland) was used to measure serum creatinine.

For the Emergency Department Cohort, we categorized the difference between patients' peak (highest) serum creatinine concentration at presentation to the emergency department and baseline serum creatinine concentration into the serum creatinine-based definitions. To be classified as having AKI in the Hospitalized Cohort, patients had to have a ≥ 27 μmol/L (0.3 mg/dL) or 50% increase in serum creatinine concentration from their baseline value at the emergency department or during the first two days of hospital admission. This was done to ensure all patients classified as having AKI by the serum creatinine-based definitions manifested AKI at hospital admission rather than developing the condition *de novo* during the hospital stay. However, there may be a delay from time of injury to when the peak serum creatinine concentration is realized. Thus, in those with AKI, we categorized the severity as defined by the serum creatinine-based definitions, using the peak serum creatinine concentration in either the emergency department or in the first five days of hospital admission.

ICD-10 Coding Administrative Database Algorithms for AKI

Following discharge from hospital, trained coders review all charts to record appropriate diagnosis codes and their associated attributes. The coders follow the Canadian Coding Standards developed by CIHI.[29] According to

CIHI's guidelines, the coders are not permitted to interpret laboratory measurements, but can record a condition based on laboratory findings if the physician documents the condition as diagnosed in the patient's chart. For ambulatory care records (included in CIHI-NACRS), coders are allowed to include up to 10 diagnoses per visit. The first diagnosis listed is the main problem for the patient's visit that required evaluation and/or treatment or management as determined by the physician at the end of the visit. For hospitalization records (included in CIHI-DAD), coders may record up to 25 conditions using ICD-10 diagnostic codes. Additionally, they must indicate diagnosis type 'M' for the condition that was most responsible for the greatest portion of the length of stay or used the greatest amount of resources. They may also indicate diagnosis type '1' for any condition that existed prior to the admission and was treated during the hospital stay.[29]

In this study, we tested two unique algorithms to identify patients with AKI at presentation to the emergency department and three unique algorithms to identify patients at hospital admission. Each of these algorithms used the ICD-10 code N17x but varied the possible diagnosis types. In the Emergency Department Cohort, we examined the code: i) as the main problem (referred to as "main diagnosis") or ii) in any of the 10 potential diagnostic fields with any diagnosis type (referred to as "all diagnosis"). In the Hospitalized Cohort, we examined the code: i) as the diagnosis type of 'M' (most responsible; referred to as the "most responsible diagnosis"), ii) as the diagnosis type of '1' (pre-admit comorbidity; referred to as "admission diagnosis") or iii) in any one of 25 potential diagnosis fields with any diagnosis type (referred to as "all diagnosis").

Statistical Analysis

We used descriptive statistics to summarize demographic characteristics, co-morbidities, prescription drug claim information, and baseline laboratory measurements for patients in both settings. We calculated sensitivity, specificity, positive predictive value, and negative predictive value for each diagnostic coding algorithm (formulas presented in Supplementary Table 1). We calculated 95% confidence intervals for single proportions using the Wilson Score method.[30] We performed these calculations against the four reference standard definitions. We expressed the changes in patient serum creatinine concentration from baseline as medians with interquartile ranges (IQR) and we compared the means using the Mann-Whitney test. We conducted all analysis using SAS (Statistical Analysis Software) version 9.2 (SAS Institute Incorporated, Cary, North Carolina, USA, 2008).

RESULTS

We identified a total of 36,049 patients for the Emergency Department Cohort and 38,566 patients for the Hospitalized Cohort. Baseline characteristics of the two cohorts are presented in Table 1, including the proportion of patients who satisfied different definitions of AKI. For example, 294 (0.8%) and 567 (1.5%) patients satisfied the RIFLE Injury definition of AKI (defined by ≥ 2-fold increase in serum creatinine concentration), in each cohort, respectively.

Table 1. Baseline characteristics for patients in the Emergency Department and Hospitalized Cohorts

	Emergency Department Cohort (n = 36,049)	**Hospitalized Cohort** (n = 38,566)
Demographics		
Median age (IQR), years	77 (72-83)	76 (71-82)
Women, *n (%)*	19,262 (53.4)	19,070 (49.4)
Income Quintile, *n (%)*		
one (lowest)	7,678 (21.3)	8,027 (20.8)
two	7,306 (20.3)	7,765 (20.1)
three (middle)	7,062 (19.6)	7,654 (19.8)
four	6,110 (16.9)	6,797 (17.6)
five (highest)	7,301 (20.3)	7,816 (20.3)
Year of Cohort Entry, *n (%)*		
2003-2004	3,648 (10.1)	6,733 (17.5)

2005-2006	8,348 (23.2)	9,256 (24.0)
2007-2008	11,954 (33.2)	11,380 (29.5)
2009-2010	12,099 (33.6)	11,197 (29.0)
Rural Location, *n (%)*	5,397 (15.0)	7,165 (18.6)
Resident in a Long-term Care Facility, *n (%)*	1,454 (4.0)	1,298 (3.4)
Co-morbidities[*], *n (%)*		
Chronic kidney disease[†]	1,526 (4.2)	1,632 (4.2)
Diabetes mellitus[‡]	8,497 (23.6)	8,650 (22.4)
Peripheral vascular disease	1,137 (3.2)	2,077 (5.4)
Coronary artery disease[§]	16,847 (46.7)	18,844 (48.9)
Congestive heart failure	8,860 (24.6)	9,224 (23.9)
Stroke/Transient ischemic attack	1,434 (4.0)	1,467 (3.8)
Chronic liver disease	837 (2.3)	1,074 (2.8)
Medication Use[*], *n (%)*		
Angiotensin-converting enzyme inhibitor	13,781 (38.2)	14,859 (38.5)
Angiotensin-receptor blocker	6,540 (18.1)	6,514 (16.9)
Potassium sparing diuretic	3,643 (10.1)	3,949 (10.2)
Non-potassium sparing diuretic	16,308 (45.2)	17,145 (44.5)
Calcium channel blocker	11,785 (32.7)	12,553 (32.5)
β-Adrenergic antagonist	13,646 (37.9)	14,662 (38.0)
Statins	15,706 (43.6)	16,602 (43.0)
NSAIDs (excluding aspirin)	6,520 (18.1)	7,761 (20.1)
Anticonvulsants	2,297 (6.4)	2,244 (5.8)
Antidepressants	9,187 (25.5)	8,938 (23.2)
Antipsychotics	1,883 (5.2)	1,692 (4.4)
Benzodiazepines	9,035 (25.1)	9,414 (24.4)
Antineoplastics	2,217 (6.1)	2,377 (6.2)
Thyroid hormone	6,172 (17.1)	6,150 (15.9)
Baseline Laboratory Measurements[‖]		
Serum creatinine concentration, μmol/L, *median (IQR)*	91 (75-113)	90 (75-114)
eGFR mL/min/1.73 m^2[¶], *median (IQR)*	61 (46-75)	62 (47-77)
eGFR category, *n (%)*		
≥ 60 mL/min/1.73m^2	18,382 (51.0)	20,716 (53.7)
45-59 mL/min/1.73m^2	9,043 (25.1)	9,011 (23.4)
30-44 mL/min/1.73m^2	5,622 (15.6)	5,633 (14.6)
15-29 mL/min/1.73m^2	2,415 (6.7)	2,537 (6.6)
< 15 mL/min/1.73m^2	587 (1.6)	669 (1.7)
Urine dipstick protein, *n (%)*		
negative	4,186 (84.0)	3,252 (81.4)
0.3g/L	415 (8.3)	409 (10.2)
1.0g/L	296 (5.9)	257 (6.4)
≥ 3.0g/L	87 (1.7)	79 (2.0)
Serum sodium concentration, mmol/L, *median (IQR)*	139 (137-142)	139 (137-141)
Serum potassium concentration, mmol/L, *median (IQR)*	4.0 (4.0-5.0)	4.0 (4.0-5.0)

AKI Definitions for All Patients, *n (%)*		
AKIN Stage 1 or greater	5,312 (14.7)	6,879 (17.8)
RIFLE Risk	473 (1.3)	884 (2.3)
RIFLE Injury	294 (0.8)	567 (1.5)
RIFLE Failure	527 (1.5)	920 (2.4)
AKI Definitions for Patients with CKD,[†] *n (%)*		
AKIN Stage 1 or greater	524 (34.3)	644 (39.5)
RIFLE Risk	25 (1.6)	65 (4.0)
RIFLE Injury	12 (0.8)	41 (2.5)
RIFLE Failure	154 (10.1)	246 (15.1)

Abbreviations: IQR, interquartile range; eGFR, estimated glomerular filtration rate

[*]Co-morbidities and medication usage in the 5 years and 6 months preceding the hospital encounter were considered, respectively

[†]CKD was assessed by the ICD-10 code N18x, defined as "chronic kidney disease"

[‡] Diabetes mellitus was assessed by diabetic medication use in previous 6 months

[§]Coronary artery disease includes receipt of coronary artery bypass graft surgery, percutaneous coronary intervention and diagnoses of angina

[‖]The baseline measurements for serum creatinine were taken at a median (IQR) of 102 (41-204) and 39 (16-128) days prior to the hospital encounter for the Emergency Department Cohort and the Hospitalized Cohort, respectively. Baseline urine protein and serum sodium and potassium were available for a subset of patients. Emergency Department cohort: A total of 4,984, 29,746 and 30,040 patients had a baseline urine protein and serum sodium and potassium measurement available in the 7 to 365 days prior to the index date, respectively. Hospitalized cohort: A total of 3,997, 34,407 and 34,538 patients had a baseline urine protein and serum sodium and potassium measurements available in the 7 to 365 days prior to the index date, respectively

[¶]eGFR was calculated using the CKD-Epi equation.

CKD-Epi equation:141 x min([serum creatinine in umol/L /88·4]/κ, 1)$^{\alpha}$ x max([serum creatinine in umol/L / 88·4]/κ, 1)$^{-1·209}$ x 0·993^{Age} x 1·018 [if female] x 1·159 [if African American] *κ=0·7 for females and 0·9 for males, α= -0·329 for females and -0·411 for males, min=the minimum of Scr/κ or 1, max=the maximum of Scr/κ or 1.Racial information was not available in our data sources and all patients were assumed not to be of non African-Canadian race. This was a reasonable assumption; as of 2006, African-Canadians represented less than 7% of the Ontario population. Source:* http://www12.statcan.ca/census-recensement/2006/dp-pd/hlt/97-562/index.cfm?Lang=E

The diagnostic performance of the various coding algorithms is presented in Table 2. For both types of hospital encounters, 'all diagnosis' was the best performing ICD-10 N17x coding algorithm. At presentation to the emergency department, the sensitivity of the ICD-10 code for the RIFLE Injury definition of AKI (≥ 2-fold increase in serum creatinine concentration from baseline) was 37.4% (95% confidence interval (CI): 32.1% to 43.1%).

Sensitivities were higher at hospital admission than at presentation to the emergency department for all four serum creatinine-based definitions of AKI. For example, at hospital admission, the sensitivity of the code for the RIFLE Injury definition was 61.6% (95% CI: 57.5% to 65.5%). The sensitivity of the code improved for more severe definitions of AKI, peaking at the RIFLE Injury definition. There was no substantial difference in specificity for both types of hospital encounters, with values greater than 95% in both settings. The positive predictive value of the code decreased for more severe definitions of AKI, with a nadir at the RIFLE Injury definition in both settings.

Table 2. Diagnostic performance characteristics of three different algorithms for ICD-10 code N17x using four different serum creatinine-based definitions of AKI as the reference standard

Diagnostic Coding Algorithm	Definition	Diagnostic Performance Characteristics (95% CI)	
		Emergency Department Cohort	Hospitalized Cohort
All diagnosis	AKIN Stage 1	Sn=7.2 (6.6-8.0) Sp=99.9 (99.8-99.9) PPV=90.4 (87.2-92.8) NPV=86.2 (85.8-86.5)	Sn=21.8 (20.9-22.8) Sp=98.4 (98.2-98.5) PPV=74.2 (72.3-76.1) NPV=85.3 (84.9-85.6)
	RIFLE Risk	Sn=30.4 (26.5-34.7) Sp=99.2 (99.1-99.3) PPV=33.8 (29.5-38.4) NPV=99.1 (99.0-99.2)	Sn=56.4 (53.2-59.7) Sp=96.0 (95.8-96.2) PPV=24.7 (22.8-26.6) NPV=98.9 (98.8-99.1)

	RIFLE Injury	Sn=37.4 (32.1-43.1) Sp=99.1 (99.0-99.2) PPV=25.8 (21.9-30.2) NPV=99.5 (99.4-99.6)	Sn=61.6 (57.5-65.5) Sp=95.6 (95.4-95.8) PPV=17.3 (15.7-19.0) NPV=99.4 (99.3-99.5)
	RIFLE Failure	Sn=30.2 (26.4-34.2) Sp=99.2 (99.2-99.3) PPV=37.3 (32.9-42.0) NPV=99.0 (98.9-99.1)	Sn=59.1 (55.9-62.3) Sp=96.1 (95.9-96.3) PPV=26.9 (25.0-28.9) NPV=99.0 (98.9-99.1)
Main Diagnosis/ Most Responsible Diagnosis	AKIN Stage 1	Sn=4.1 (3.6-4.6) Sp=100.0 (99.9-100.0) PPV=94.7 (91.0-97.0) NPV=85.8 (85.4-86.1)	Sn=5.1 (4.6-5.7) Sp=99.9 (99.8-99.9) PPV=90.7 (87.4-93.2) NPV=82.9 (82.5-83.3)
	RIFLE Risk	Sn=21.4 (17.9-25.3) Sp=99.6 (99.6-99.7) PPV=44.5 (38.2-51.0) NPV=99.0 (98.9-99.1)	Sn=18.7 (16.2-21.4) Sp=99.4 (99.3-99.5) PPV=42.5 (33.7-47.5) NPV=98.1 (98.0-98.3)
	RIFLE Injury	Sn=27.9 (23.1-33.3) Sp=99.6 (99.6-99.7) PPV=36.1 (30.2-42.6) NPV=99.4 (99.3-99.5)	Sn=22.8 (19.5-26.4) Sp=99.3 (99.2-99.4) PPV=33.3 (28.7-38.1) NPV=98.9 (98.7-99.0)
	RIFLE Failure	Sn=22.0 (18.7-25.7) Sp=99.6 (99.5-99.7) PPV=51.1 (44.6-57.5) NPV=98.9 (98.7-99.0)	Sn=22.9 (20.3-25.8) Sp=99.5 (99.5-99.6) PPV=54.4 (49.4-59.3) NPV=98.1 (98.0-98.3)
Admission Diagnosis	AKIN Stage 1	n/a	Sn=15.8 (15.0-16.7) Sp=99.2 (99.1-99.3) PPV=81.6 (79.4-83.6) NPV=84.5 (84.1-84.8)
	RIFLE Risk		Sn=43.1 (39.9-46.4) Sp=97.5 (97.3-97.6) PPV=28.5 (26.2-31.0) NPV=98.6 (98.5-98.8)
	RIFLE Injury		Sn=48.3 (44.2-52.4) Sp=97.2 (97.0-97.4) PPV=20.5 (18.4-22.8) NPV=99.2 (99.1-99.3)
	RIFLE Failure		Sn=47.4 (44.2-50.6) Sp=97.6 (97.5-97.8) PPV=32.6 (30.2-35.2) NPV=98.7 (98.6-98.8)

Abbreviations: ICD-10, International Classification of Diseases, tenth revision; CI, confidence interval; Sn, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value; n/a, not applicable
All values are presented as percentages (%)
To convert serum creatinine from μmol/L to mg/dL divide by 88.4

The absolute change in serum creatinine (peak value – baseline value) and relative change in serum creatinine [(peak value – baseline value) / baseline value)] for patients with hospital encounters who were positive and negative for the ICD-10 N17x code are presented in Table 3.When considering the 'all diagnosis' algorithm, 1.2%

of patients at presentation to the emergency department and 5.2% of patients at hospital admission were code positive for AKI.

The median (IQR) absolute change in serum creatinine concentration for code positive patients was 133 (62 to 288) µmol/L and 98 (43 to 200) µmol/L in each setting, respectively. The change for code negative patients was 2 (-8 to 14) µmol/L and 6 (-4 to 20) µmol/L in each setting, respectively.

When expressed in relative terms, the median (IQR) change for code positive patients was 87 (43 to 204) % and 69 (28 to 153) % in each setting, respectively. The relative change for code negative patients was 2 (-9 to 15) % and 7 (-5 to 22) % in each setting, respectively. In both settings, the difference in the mean absolute and relative change in serum creatinine between code positive and code negative patients was highly statistically significant ($p<0.001$).

Table 3. Change in serum creatinine concentration from baseline in all patients with and without the ICD-10 N17x code for AKI (referred to as code positive and code negative)

Diagnostic Coding Algorithm	Code	Emergency Department Cohort			Hospitalized Cohort		
		N	Absolute Change (µmol/L)	Relative Change (%)*	N	Absolute Change (µmol/L)	Relative Change (%)*
			Median(IQR)			Median(IQR)	
All diagnosis	+	426	133 (62 to 288)	87 (43 to 204)	2,023	98 (43 to 200)	69 (28 to 153)
	-	35,623	2 (-8 to 14)	2 (-9 to 15)	36,543	6 (-4 to 20)	7 (-5 to 22)
Main Diagnosis/ Most Responsible Diagnosis	+	227	187 (89 to 383)	128 (62 to 295)	388	196 (93 to 396)	121 (49 to 275)
	-	35,822	2 (-8 to 14)	2 (-9 to 16)	38,178	7 (-4 to 22)	7 (-4 to 24)
Admission Diagnosis	+	n/a			1,366	114 (39 to 187)	75 (30 to 169)
	-				37,230	6 (-4 to 21)	7 (-4 to 23)

Abbreviations: ICD-10, International Classification of Diseases, tenth revision; CKD, Chronic kidney disease; N, number; IQR, interquartile range; +, code positive; -, code negative; n/a, not applicable

Both absolute and relative changes in serum creatinine were significantly different between code positive and code negative patients in both types of hospital encounter (all p-values <0.001) (means presented in box plot; Supplementary Figure 2 and 3)

*[(peak serum creatinine – baseline serum creatinine) / baseline serum creatinine)]

To convert serum creatinine from µmol/L to mg/dL divide by 88.4

The diagnostic performance of the 'all diagnosis' algorithm at hospital admission in patients with and without CKD is presented in Table 4. The sensitivity of the ICD-10 code for AKIN Stage 1 or greater, RIFLE Risk and RIFLE Injury definitions was higher in patients with CKD than those without CKD. For example, the sensitivity of the code for the RIFLE Injury definition was 75.6% (95% CI: 60.7% to 86.2%) in patients with CKD and 60.5% (95% CI: 56.2% to 64.5%) in patients without CKD.

The code demonstrated the highest sensitivity for the RIFLE Risk definition in patients with CKD and the RIFLE Failure definition in patients without CKD. The specificities of the code were lower in patients with CKD than those without CKD for all four definitions. For example, the specificity of the code for the RIFLE Injury definition was 82.6% (95% CI: 80.7% to 84.4%) in patients with CKD and 96.2% (95% CI: 96.0% to 96.4%) in patients without CKD.

Table 4. Diagnostic performance characteristics of the ICD-10 N17x code in hospitalized patients with and without CKD using serum creatinine-based definitions of AKI as the reference standard*

Definition	Diagnostic Performance Characteristics (95% CI)	
	Patients with CKD	Patients without CKD
AKIN Stage 1	Sn=35.6 (32.0-39.3) Sp=92.0 (90.2-93.5) PPV=74.4 (69.2-78.9) NPV=68.7 (66.1-71.1)	Sn=20.4 (19.4-21.4) Sp=98.6 (98.4-98.7) PPV=74.2 (72.1-76.2) NPV=85.9 (85.5-86.3)
RIFLE Risk	Sn=76.9 (65.4-85.5) Sp=83.5 (81.6-85.3) PPV=16.2 (12.5-20.8) NPV=98.9 (98.1-99.3)	Sn=54.8 (51.4-58.2) Sp=96.5 (96.3-96.7) PPV=26.2 (24.2-28.3) NPV=98.9 (98.8-99.1)
RIFLE Injury	Sn=75.6 (60.7-86.2) Sp=82.6 (80.7-84.4) PPV=10.1 (7.2-13.9) NPV=99.2 (98.6-99.6)	Sn=60.5 (56.2-64.5) Sp=96.2 (96.0-96.4) PPV=18.5 (16.8-20.5) NPV=99.4 (99.3-99.5)
RIFLE Failure	Sn=48.4 (42.2-54.6) Sp=86.4 (84.5-88.1) PPV=38.6 (33.4-44.2) NPV=90.4 (88.7-91.9)	Sn=63.1 (59.4-66.6) Sp=96.4 (96.3-96.6) PPV=24.8 (22.8-26.9) NPV=99.3 (99.2-99.4)

Abbreviations: ICD-10, International Classification of Diseases, tenth revision; CKD, Chronic kidney disease; CI, confidence interval; Sn, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value
All values are presented as percentages (%)
*The ICD-10 N17x coding algorithm considered is all diagnosis

The absolute and relative changes in serum creatinine at hospital admission in patients with and without CKD who were code positive and code negative are presented in Table 5. When considering the 'all diagnosis' algorithm, a total of 18.9% of patients with CKD and 4.6% of patients without CKD were code positive for AKI.

The median (IQR) absolute change in serum creatinine concentration in patients with CKD who were code positive was 108 (48 to 215) µmol/L and in patients without CKD who were code positive was 95 (43 to 197) µmol/L. The difference in the absolute change in serum creatinine between patients with and without CKD who were AKI code positive was not significantly different (p=0.910). The median (IQR) absolute change in patients with CKD who were code negative was 16 (-8 to 51) µmol/L and in patients without CKD who were code negative was 6 (-4 to 19) µmol/L.

When expressed in relative terms, the median (IQR) change in serum creatinine in patients with CKD who were code positive was significantly lower than in patients without CKD who were code positive (53 (20 to 104) % vs. 72 (29 to 161) %; p<0.0001). The median (IQR) relative change in patients with CKD who were code negative was 9 (-4 to 26) % and in patients without CKD who were code negative was 6 (-5 to 22) %. For both patients with and without CKD, the difference in the mean absolute and relative changes in serum creatinine between code positive and negative patients was highly statistically significant (p<0.001).

Table 5. Change in serum creatinine concentration from baseline in hospitalized patients with and without CKD where ICD-10 code N17x did and did not indicate AKI (referred as code positive and code negative)*

Code	Patients with CKD			Patients without CKD		
	N	Absolute Change (µmol/L)	Relative Change (%)†	N	Absolute Change (µmol/L)	Relative Change (%)†
		Median(IQR)			Median(IQR)	

+	308	108 (48 to 215)	53 (20 to 104)	1,715	95 (43 to 197)	72 (29 to 161)
-	1,324	16 (-8 to 51)	9 (-4 to 26)	35,219	6 (-4 to 19)	6 (-5 to 22)

Abbreviations: ICD-10, International Classification of Diseases, tenth revision; CKD, Chronic kidney disease; N, number; IQR, interquartile range; +, code positive; -, code negative; n/a, not applicable.
Code positive and code negative patients were significantly different (all p-values <0.001)
Relative changes in patients with and without CKD were statistically different (p<0.0001)
*The ICD-10 N17x coding algorithm considered is all diagnosis
† [(peak serum creatinine – baseline serum creatinine) / baseline serum creatinine)]
To convert serum creatinine from μmol/L to mg/dL divide by 88.4

DISCUSSION

In this population-based retrospective validation study, we evaluated the diagnostic performance of ICD-10 code N17x for AKI. We discovered that the best performing coding algorithm both at presentation to the emergency department and at hospital admission was when the code was expressed as 'all diagnosis' (i.e. when the code was indicated by any diagnosis type).

At hospital admission, the poorest performing coding algorithm was the 'most responsible diagnosis'. A likely explanation for this is that AKI frequently presents as a complication of other conditions requiring hospital admission, such as acute myocardial infarction or sepsis.[5] AKI is rarely the primary reason for hospital admission so would less likely be coded as the "most responsible diagnosis".

The ICD-10 code demonstrated modest sensitivity for the serum creatinine-based definitions of AKI, indicating its inability to identify a portion of patients who experienced a clinically significant increase in serum creatinine. Of the patients who satisfied the RIFLE Injury definition of AKI from their increase in serum creatinine, 61.6 (95% CI: 57.5-65.5) % of them were code positive AKI when the ICD-10 code was expressed as 'all diagnosis'. However, the code demonstrated high specificity for all four serum creatinine-based definitions. Of the patients who did not satisfy the RIFLE Injury definition of AKI, 95.6 (95% CI: 95.4-95.8) % of them were code negative for AKI. These characteristics of the ICD-10 AKI code are similar to those described in ICD-9 code validation studies that used serum creatinine-based definitions as the reference standard.[8, 10, 21, 22] The use of a serum creatinine-based definition of AKI as the reference standard is preferred over chart review, recognizing the latter have appeared in a number of previous validation studies.[31-35]

The ICD-10 code showed improved sensitivity for more severe definitions of AKI and was highest for the RIFLE Injury definition. This characteristic of the ICD-10 code is similar to that of ICD-9 codes for AKI.[21] A greater increase in serum creatinine reflects more severe AKI, is more likely to be documented in the medical chart and thus detected by coders.

The positive predictive value of the ICD-10 code decreased for more severe definitions of AKI and was the lowest for the RIFLE Injury definition. This fluctuation in the positive predictive values can in part be attributed to the varying prevalence of the four serum creatinine-based definitions.

At both types of hospital encounters, patients who were code positive had a significantly higher increase in serum creatinine than those who were code negative (p<0.001). In other words, the code does successfully differentiate between two groups of patients with and without distinct changes in serum creatinine.

We also assessed the diagnostic performance of the ICD-10 code in subgroups of patients with and without CKD prior to the hospital encounter. For all definitions, with the exception of RIFLE Failure, the code demonstrated higher sensitivity in patients with CKD than those without CKD. However, the specificity of the code was lower in patients with CKD than those without CKD (for all definitions of AKI). The latter finding suggests a portion of patients with stable CKD are misclassified as having AKI at their hospital encounter. For example, clinicians may not have access to patients' baseline serum creatinine measurements, or may make an AKI diagnosis without investigating the baseline measurements. In such cases, an elevated serum creatinine concentration at hospital presentation that is no different than the baseline value may still be misdiagnosed as AKI.

Amongst patients with CKD, presence or absence of the ICD-10 AKI code was also able to differentiate between two groups of patients with distinct changes in their serum creatinine from the baseline value. Although the difference in mean absolute change in serum creatinine was no different in patients with and without CKD who had a positive AKI code, the relative change was lower in patients with CKD than those without CKD. This is consistent

with physicians defining AKI more commonly in absolute rather than in relative terms. With a given absolute increase in serum creatinine, the relative increase in serum creatinine is lower in patients with CKD than those without CKD.

Our study has several strengths. To our knowledge, it is the first study to provide information on the diagnostic performance of the ICD-10 code for AKI using serum creatinine-based definitions of AKI as the reference standard.[8, 10, 21, 22] We assessed different diagnostic coding algorithms of the ICD-10 code at both presentation to the emergency department and at hospital admission. Moreover, we evaluated the diagnostic performance of the code in subgroups of patients with and without CKD prior to the hospital encounter. We studied patients from twelve hospitals across Southwestern Ontario with representation from both academic and community care centres. This helped to minimize selection bias. The large number of patients resulted in good precision for the estimates provided in the study.

Our study does have some limitations. We evaluated the validity of the ICD-10 code for AKI in patients 66 years of age and older. These findings should generalize well to elderly patients, a segment of the population at high risk of AKI.[11, 36] The findings are also useful for pharmacoepidemiologic studies using Ontario's healthcare administrative databases, where prescription information on Ontario residents age 65 and older is available from the universal drug benefit plan. However, future validation studies in younger patients are needed. Moreover, we did not know the degree to which patients with AKI were symptomatic from diminished kidney function or the indication that prompted presentation to the emergency department or hospital admission.

It is important to acknowledge that for the definitions of AKI used in this study, we adapted the serum creatinine-based component of the AKIN and RIFLE classification systems. The AKIN and RIFLE classification systems recommend using both serum creatinine and urine output measurements in determining the presence and severity of AKI.[6, 7] In addition, it is recommended that the AKIN classification is applied only after an optimal state of hydration is achieved.[6] However, urine output measurement and hydration status were not available in the data sources used in the study. In truth, the accuracy of bedside urine output measurement is notoriously poor outside of intensive care settings with an indwelling catheter. Nonetheless, the change in serum creatinine is a widely used measure of kidney function in clinical settings. Moreover, the serum creatinine-based component has been solely used to identify patients with AKI using the AKIN and RIFLE classification systems in previous studies.[37, 38]

The median (IQR) period between the baseline serum creatinine measurements and the hospital encounter was 102 (41-204) days for patients who presented to the emergency department and 39 (16-128) days for patients admitted to hospital. While these are reasonable baseline measurements, the AKIN and RIFLE classification systems require the change in serum creatinine to occur within 48 hours and within 7 days, respectively.[6, 7] Although it is likely that serum creatinine changes occurred just prior to the hospital encounter, we cannot say this with complete certainty given the absence of available measurements during this period.

Finally, we could not examine the validity of outpatient claims for AKI in this study. However, the diagnostic performance of outpatient claims in our jurisdiction is notoriously poor. Nonetheless, emergency department and hospital inpatient records hold information on more severe forms of AKI, which are of particular interest to clinicians, researchers, and policymakers. Moreover, we recognize that we did not capture those patients who may have had severe forms of AKI, but did not present to the emergency department or hospital, or those who presented, but did not have their serum creatinine measured. However, the latter situation is unlikely given that serum creatinine measurements are a standard laboratory test for most patients who present to a hospital encounter for acute medical care.

CONCLUSION

Although the use of healthcare administrative databases for clinical or healthcare services research has several merits, there are inherent limitations, including the accuracy with which certain conditions (i.e. AKI) can be identified. The sensitivity of ICD-10 code N17x for AKI was limited, particularly for less severe definitions. This results in an underestimation of the true incidence of the condition. Nonetheless, the presence or absence of the ICD-10 code successfully differentiates two groups of elderly patients with and without distinct increases in serum creatinine from baseline values at the time of a hospital encounter. The results from this study guide judicious use of ICD-10 code N17x in future research using large healthcare administrative databases.

Contributors

YJH participated in the study coordination and study design and analysis, provided interpretation of study results, and drafted the manuscript. SZS participated in the study design, acquisition of data, and performed the analysis. SG contributed to the study design and interpretation of study results. RW, EC, and JLF contributed to the study design and provided feedback on the manuscript. AXG conceived of the study, participated in its design and interpretation and provided feedback on the manuscript. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Data Sharing

We cannot share due to the protection of patient privacy.

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Validity of the *International Classification of Diseases, Tenth Revision* code for acute kidney injury in elderly patients at presentation to emergency department and at hospital admission

Y. Joseph Hwang BMSc[1,2], Salimah Z. Shariff PhD[3], Sonja Gandhi BSc[1,2], Ron Wald MD, MPH[4,5], Edward Clark MD[6], Jamie L. Fleet BHSc[1], Amit X. Garg MD, PhD[1,2,3]

1. Division of Nephrology, Department of Medicine, Western University, London, Ontario, Canada
2. Department of Epidemiology & Biostatistics, Western University, London, Ontario, Canada
3. Institute for Clinical Evaluative Sciences, Ontario, Canada
4. Keenan Research Centre in the Li Ka Shing Knowledge Institute of St Michael's Hospital, Toronto, Ontario, Canada
5. Division of Nephrology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada
6. Kidney Research Centre, Ottawa Hospital Research Institute, University of Ottawa, Ottawa, Ontario, Canada

Correspondence: Dr. Amit Garg, London Kidney Clinical Research Unit, Room ELL-101, Westminster, London Health Sciences Centre, 800 Commissioners Road East, London, Ontario, Canada N6A 4G5, Tel: 519-685-8502, Fax: 519-685-8072, email: amit.garg@lhsc.on.ca

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ABSTRACT

Objective: To evaluate the validity of the *International Classification of Diseases, Tenth Revision* (ICD-10) code N17x for acute kidney injury (AKI) in elderly patients in two settings: at presentation to the emergency department and at hospital admission.

Design: Population-based retrospective validation study.

Setting: Southwestern Ontario, Canada, from 2003 to 2010.

Participants: Elderly patients with serum creatinine measurements at presentation to the emergency department (n=36,049) or hospital admission (n=38,566). The baseline serum creatinine measurement was a median of 102 days and 39 days prior to presentation to the emergency department and hospital admission, respectively.

Main outcome measures: Sensitivity, specificity, and positive and negative predictive values of ICD-10 diagnostic coding algorithms for AKI using a reference standard based on changes in serum creatinine from the baseline value. Median changes in serum creatinine of patients who were code positive and code negative for AKI.

Results: The sensitivity of the best-performing coding algorithm for AKI (defined as a ≥ 2-fold increase in serum creatinine concentration) was 37.4% (95% confidence interval (CI): 32.1% to 43.1%) at presentation to the emergency department and 61.6% (95% CI: 57.5% to 65.5%) at hospital admission. The specificity was greater than 95% in both settings. In patients who were code positive for AKI, the median (interquartile range) increase in serum creatinine from baseline was 133 (62 to 288) µmol/L at presentation to emergency department and 98 (43 to 200) µmol/L at hospital admission. In those who were code negative, the increase in serum creatinine was 2 (-8 to 14) and 6 (-4 to 20) µmol/L, respectively.

Conclusions: The presence or absence of ICD-10 code N17x differentiates two groups of patients with distinct changes in serum creatinine at the time of a hospital encounter. However, the code underestimates the true incidence of AKI due to limited sensitivity.

Keywords: acute kidney injury, acute renal failure, serum creatinine, validation, validity, sensitivity, specificity, International Classification of Diseases

Article Summary:

Article Focus

- Validation of administrative database codes is a prerequisite to their optimal use in research
- The aim of this study was to describe the validity of the ICD-10 code N17x for AKI compared to a reference standard based on changes in serum creatinine

Key Messages

- The ICD-10 code N17x for AKI has moderate sensitivity and high specificity
- The sensitivity of the N17x code improves for more severe forms of AKI
- The code was successful in identifying a group of patients admitted to hospital with a median increase in serum creatinine of 98 µmol/L

Strengths and Limitations

- This is the first study to provide information on the diagnostic performance of ICD-10 code N17x for AKI using laboratory values as the reference standard
- It was a large population-based validation study that included serum creatinine measurements from twelve hospitals
- Future validation studies in younger patients are required

BACKGROUND

Healthcare administrative databases can provide researchers and policy makers with information on a large number of patients in an efficient manner. When using these data sources for clinical or health services research, the validity of the research depends upon the accuracy of the diagnostic and procedural codes that have been recorded.[1] However, the accuracy of coding is not guaranteed because administrative databases are not primarily intended for research.[2] Consequently, understanding the validity of administrative codes is a prerequisite to their optimal use in the assessment of patient outcomes.

Clinically, acute kidney injury (AKI) is characterized by an abrupt decline in renal function that may result in disordered fluid, acid-base and electrolyte homeostasis, and retention of waste products from nitrogen metabolism, such as creatinine and urea, and/or decreased urine output.[3-5] Two systems for defining and quantifying the severity of AKI are widely used: the Acute Kidney Injury Network (AKIN) classification [6] and the Risk-Injury-Failure-Loss-ESRD (RIFLE) criteria.[7] These staging systems define AKI severity according to absolute and relative (percentage) increases in serum creatinine, a blood test universally used to indicate kidney function. While the incidence of AKI is dependent on the definition used, it is recognized that this condition is common, affecting 2 to 9% of patients at hospital admission.[8-11] Moreover, patients who develop AKI have both poor short and long-term outcomes and their care is costly.[8, 9, 12-20]

The purpose of the present study was to evaluate the accuracy of the *International Classification of Diseases, Tenth Revision* (ICD-10) code N17x for AKI for applications in clinical and health services research, particularly in pharmacoepidemiologic studies. We compared this code against changes in serum creatinine concentration in two settings: 1) at presentation to the emergency department and 2) at hospital admission. In addition, we investigated the effect of baseline chronic kidney disease (CKD) status on the diagnostic performance of the code in the two settings. Based on the findings of a previous validation study on ICD-9 codes, we anticipated the sensitivity for ICD-10 code N17x would be low, improving with more severe definitions of AKI.[8, 10, 21, 22] Moreover, we expected higher sensitivity in patients with CKD than those without, as the former typically have larger absolute increases in serum creatinine for a given amount of AKI.

METHODS

Study Design and Setting

We conducted a population-based retrospective validation study using Ontario's linked healthcare administrative databases and laboratory data from Southwestern Ontario. All residents receive universal access to hospital and physician services under a single provincial payer system, providing a comprehensive set of health administrative data.

Using a diagnostic test assessment framework, we obtained diagnostic performance characteristics (sensitivity, specificity, positive predictive value, and negative predictive value) of various diagnostic coding algorithms for ICD-10 code N17x, which is defined as "acute renal failure". We used changes in serum creatinine from the baseline value as the reference standard (see Supplementary Table 1 for a sample two-by-two table). Moreover, we compared the change in serum creatinine between patients who were N17x code positive with those who were N17x code negative.

Our protocol was approved by the institutional review board at Sunnybrook Health Sciences Centre (Toronto, Ontario). The relevant datasets are held at the Institute for Clinical Evaluative Sciences. The reporting of this study follows guidelines set out for studies assessing diagnostic accuracy (Supplementary Table 2).[23]

Data Sources

Patient records from the seven databases were linked using encrypted unique identifiers. We identified laboratory measurements, including serum creatinine, using a system that keeps patient electronic medical records (Cerner®, Kansas City, Missouri, USA).[24] This system contains inpatient, outpatient and the emergency department laboratory measurements for twelve Southwestern Ontario hospitals. For a subpopulation, we also obtained previous laboratory measurements from Gamma-Dynacare, a provider of outpatient laboratory services to residents in Southwestern Ontario. We obtained inpatient and emergency department patient diagnostic information from the Canadian Institute of Health Information (CIHI) Discharge Abstract Database (DAD) and National Ambulatory Care Reporting System database (NACRS), respectively. We obtained information on inpatient and outpatient

physician services from the Ontario Health Insurance Plan database (OHIP). We ascertained patient demographic information from the Ontario's Registered Persons Database (RPDB) and prescribed drug use for patients 65 years of age and older from the Ontario Drug Benefit database (ODB). These databases have been used extensively to research health outcomes and health services.[25-28]

Accrual of Elderly Patients in Two Settings: at Presentation to Emergency Department and at Hospital Admission

We developed two separate cohorts. The first cohort consisted of patients with a serum creatinine measurement at presentation to the emergency department (Emergency Department Cohort). The second cohort consisted of patients with a serum creatinine measurement at hospital admission (Hospitalized Cohort). All patients had a baseline serum creatinine measurement (described below). The period of accrual was from June 1st, 2003 to September 30th, 2010.

We restricted cohort entry to patients 66 years of age and older to ensure at least one year of baseline prescription records for all patients. We excluded the following patients from both cohorts: i) those who had end-stage renal disease (defined by the receipt of dialysis in the 120 days prior to the hospital encounter), ii) those who received a kidney or liver transplant in the five years prior to the hospital encounter, iii) those whose date of serum creatinine measurement (from Cerner®) and the hospital encounter (from CIHI-DAD) did not align (less than 1.4% patients excluded for this reason; see Supplementary Figure 1 for explanation) and iv) those without at least one serum creatinine measurement in the 7 to 365 days prior to the hospital encounter to serve as the baseline value. In cases where a patient had multiple baseline measurements we selected the most recent one. Additional selection criteria for each cohort are described below and illustrated in Supplementary Figure 1.

We excluded patients who did not have a serum creatinine measurement in the emergency department from entry to the Emergency Department Cohort. We excluded the following patients from entry to the Hospitalized Cohort: i) those with a hospital admission that resulted in a stay greater than 90 days (to ensure we had data for the full hospital admission to the time of discharge i.e. particularly for patients accrued in the second half of year 2010) and ii) those without a serum creatinine measurement either in the emergency department prior to hospital admission or during the first two days of hospital admission. When multiple eligible hospital presentations were identified for a given patient over the study period, we randomly selected one hospital encounter for each cohort.

Within the two cohorts, we identified patients diagnosed with CKD (assessed by the presence of ICD-10 code N18x defined as "chronic kidney disease") in the 5 years prior to their hospital encounter to evaluate potential differential classification of AKI in patients with baseline CKD compared to those without.

The Reference Standard: Serum Creatinine-Based Definitions of AKI

Measuring changes in serum creatinine is the most common method of identifying AKI in clinical practice. We adapted the reference standard used in this study from four widely used serum creatinine-based definitions of AKI: i) AKIN Stage 1 or greater: ≥ 27 µmol/L (0.3 mg/dL) or 50% increase in serum creatinine concentration from baseline, ii) RIFLE Risk: ≥ 1.5-fold increase in serum creatinine concentration from baseline, iii) RIFLE Injury: ≥ 2-fold increase in serum creatinine concentration from baseline, and iv) RIFLE Failure**:** ≥ 3-fold increase in serum creatinine concentration from baseline or a baseline serum creatinine concentration ≥ 354 µmol/L (4.0 mg/dL) with ≥ 44 µmol/L (0.5 mg/dL) increase from baseline.[6, 7] A Roche Modular Ion Selective Electrode® system (Basel, Switzerland) was used to measure serum creatinine.

For the Emergency Department Cohort, we categorized the difference between patients' peak (highest) serum creatinine concentration at presentation to the emergency department and baseline serum creatinine concentration into the serum creatinine-based definitions. To be classified as having AKI in the Hospitalized Cohort, patients had to have a ≥ 27 µmol/L (0.3 mg/dL) or 50% increase in serum creatinine concentration from their baseline value at the emergency department or during the first two days of hospital admission. This was done to ensure all patients classified as having AKI by the serum creatinine-based definitions manifested AKI at hospital admission rather than developing the condition *de novo* during the hospital stay. However, there may be a delay from time of injury to when the peak serum creatinine concentration is realized. Thus, in those with AKI, we categorized the severity as defined by the serum creatinine-based definitions, using the peak serum creatinine concentration in either the emergency department or in the first five days of hospital admission.

ICD-10 Coding Administrative Database Algorithms for AKI

Following discharge from hospital, trained coders review all charts to record appropriate diagnosis codes and their associated attributes. The coders follow the Canadian Coding Standards developed by CIHI.[29] According to

CIHI's guidelines, the coders are not permitted to interpret laboratory measurements, but can record a condition based on laboratory findings if the physician documents the condition as diagnosed in the patient's chart. For ambulatory care records (included in CIHI-NACRS), coders are allowed to include up to 10 diagnoses per visit. The first diagnosis listed is the main problem for the patient's visit that required evaluation and/or treatment or management as determined by the physician at the end of the visit. For hospitalization records (included in CIHI-DAD), coders may record up to 25 conditions using ICD-10 diagnostic codes. Additionally, they must indicate diagnosis type 'M' for the condition that was most responsible for the greatest portion of the length of stay or used the greatest amount of resources. They may also indicate diagnosis type '1' for any condition that existed prior to the admission and was treated during the hospital stay.[29]

In this study, we tested two unique algorithms to identify patients with AKI at presentation to the emergency department and three unique algorithms to identify patients at hospital admission. Each of these algorithms used the ICD-10 code N17x but varied the possible diagnosis types. In the Emergency Department Cohort, we examined the code: i) as the main problem (referred to as "main diagnosis") or ii) in any of the 10 potential diagnostic fields with any diagnosis type (referred to as "all diagnosis"). In the Hospitalized Cohort, we examined the code: i) as the diagnosis type of 'M' (most responsible; referred to as the "most responsible diagnosis"), ii) as the diagnosis type of '1' (pre-admit comorbidity; referred to as "admission diagnosis") or iii) in any one of 25 potential diagnosis fields with any diagnosis type (referred to as "all diagnosis").

Statistical Analysis

We used descriptive statistics to summarize demographic characteristics, co-morbidities, prescription drug claim information, and baseline laboratory measurements for patients in both settings. We calculated sensitivity, specificity, positive predictive value, and negative predictive value for each diagnostic coding algorithm (formulas presented in Supplementary Table 1). We calculated 95% confidence intervals for single proportions using the Wilson Score method.[30] We performed these calculations against the four reference standard definitions. We expressed the changes in patient serum creatinine concentration from baseline as medians with interquartile ranges (IQR) and we compared the means using the Mann-Whitney test. We conducted all analysis using SAS (Statistical Analysis Software) version 9.2 (SAS Institute Incorporated, Cary, North Carolina, USA, 2008).

RESULTS

We identified a total of 36,049 patients for the Emergency Department Cohort and 38,566 patients for the Hospitalized Cohort. Baseline characteristics of the two cohorts are presented in Table 1, including the proportion of patients who satisfied different definitions of AKI. For example, 294 (0.8%) and 567 (1.5%) patients satisfied the RIFLE Injury definition of AKI (defined by ≥ 2-fold increase in serum creatinine concentration), in each cohort, respectively.

Table 1. Baseline characteristics for patients in the Emergency Department and Hospitalized Cohorts

	Emergency Department Cohort (n = 36,049)	**Hospitalized Cohort** (n = 38,566)
Demographics		
Median age (IQR), years	77 (72-83)	76 (71-82)
Women, *n (%)*	19,262 (53.4)	19,070 (49.4)
Income Quintile, *n (%)*		
one (lowest)	7,678 (21.3)	8,027 (20.8)
two	7,306 (20.3)	7,765 (20.1)
three (middle)	7,062 (19.6)	7,654 (19.8)
four	6,110 (16.9)	6,797 (17.6)
five (highest)	7,301 (20.3)	7,816 (20.3)
Year of Cohort Entry, *n (%)*		
2003-2004	3,648 (10.1)	6,733 (17.5)

2005-2006	8,348 (23.2)	9,256 (24.0)
2007-2008	11,954 (33.2)	11,380 (29.5)
2009-2010	12,099 (33.6)	11,197 (29.0)
Rural Location, *n (%)*	5,397 (15.0)	7,165 (18.6)
Resident in a Long-term Care Facility, *n (%)*	1,454 (4.0)	1,298 (3.4)
Co-morbidities[*], *n (%)*		
Chronic kidney disease[†]	1,526 (4.2)	1,632 (4.2)
Diabetes mellitus[‡]	8,497 (23.6)	8,650 (22.4)
Peripheral vascular disease	1,137 (3.2)	2,077 (5.4)
Coronary artery disease[§]	16,847 (46.7)	18,844 (48.9)
Congestive heart failure	8,860 (24.6)	9,224 (23.9)
Stroke/Transient ischemic attack	1,434 (4.0)	1,467 (3.8)
Chronic liver disease	837 (2.3)	1,074 (2.8)
Medication Use[*], *n (%)*		
Angiotensin-converting enzyme inhibitor	13,781 (38.2)	14,859 (38.5)
Angiotensin-receptor blocker	6,540 (18.1)	6,514 (16.9)
Potassium sparing diuretic	3,643 (10.1)	3,949 (10.2)
Non-potassium sparing diuretic	16,308 (45.2)	17,145 (44.5)
Calcium channel blocker	11,785 (32.7)	12,553 (32.5)
β-Adrenergic antagonist	13,646 (37.9)	14,662 (38.0)
Statins	15,706 (43.6)	16,602 (43.0)
NSAIDs (excluding aspirin)	6,520 (18.1)	7,761 (20.1)
Anticonvulsants	2,297 (6.4)	2,244 (5.8)
Antidepressants	9,187 (25.5)	8,938 (23.2)
Antipsychotics	1,883 (5.2)	1,692 (4.4)
Benzodiazepines	9,035 (25.1)	9,414 (24.4)
Antineoplastics	2,217 (6.1)	2,377 (6.2)
Thyroid hormone	6,172 (17.1)	6,150 (15.9)
Baseline Laboratory Measurements[‖]		
Serum creatinine concentration, μmol/L, *median (IQR)*	91 (75-113)	90 (75-114)
eGFR mL/min/1.73 m^2[¶], *median (IQR)*	61 (46-75)	62 (47-77)
eGFR category, *n (%)*		
≥ 60 mL/min/1.73m^2	18,382 (51.0)	20,716 (53.7)
45-59 mL/min/1.73m^2	9,043 (25.1)	9,011 (23.4)
30-44 mL/min/1.73m^2	5,622 (15.6)	5,633 (14.6)
15-29 mL/min/1.73m^2	2,415 (6.7)	2,537 (6.6)
< 15 mL/min/1.73m^2	587 (1.6)	669 (1.7)
Urine dipstick protein, *n (%)*		
negative	4,186 (84.0)	3,252 (81.4)
0.3g/L	415 (8.3)	409 (10.2)
1.0g/L	296 (5.9)	257 (6.4)
≥ 3.0g/L	87 (1.7)	79 (2.0)
Serum sodium concentration, mmol/L, *median (IQR)*	139 (137-142)	139 (137-141)
Serum potassium concentration, mmol/L, *median (IQR)*	4.0 (4.0-5.0)	4.0 (4.0-5.0)

AKI Definitions for All Patients, *n (%)*		
AKIN Stage 1 or greater	5,312 (14.7)	6,879 (17.8)
RIFLE Risk	473 (1.3)	884 (2.3)
RIFLE Injury	294 (0.8)	567 (1.5)
RIFLE Failure	527 (1.5)	920 (2.4)
AKI Definitions for Patients with CKD,[†] *n (%)*		
AKIN Stage 1 or greater	524 (34.3)	644 (39.5)
RIFLE Risk	25 (1.6)	65 (4.0)
RIFLE Injury	12 (0.8)	41 (2.5)
RIFLE Failure	154 (10.1)	246 (15.1)

Abbreviations: IQR, interquartile range; eGFR, estimated glomerular filtration rate

[*]Co-morbidities and medication usage in the 5 years and 6 months preceding the hospital encounter were considered, respectively

[†]CKD was assessed by the ICD-10 code N18x, defined as "chronic kidney disease"

[‡] Diabetes mellitus was assessed by diabetic medication use in previous 6 months

[§]Coronary artery disease includes receipt of coronary artery bypass graft surgery, percutaneous coronary intervention and diagnoses of angina

[‖]The baseline measurements for serum creatinine were taken at a median (IQR) of 102 (41-204) and 39 (16-128) days prior to the hospital encounter for the Emergency Department Cohort and the Hospitalized Cohort, respectively. Baseline urine protein and serum sodium and potassium were available for a subset of patients. Emergency Department cohort: A total of 4,984, 29,746 and 30,040 patients had a baseline urine protein and serum sodium and potassium measurement available in the 7 to 365 days prior to the index date, respectively. Hospitalized cohort: A total of 3,997, 34,407 and 34,538 patients had a baseline urine protein and serum sodium and potassium measurements available in the 7 to 365 days prior to the index date, respectively

[¶]eGFR was calculated using the CKD-Epi equation.

CKD-Epi equation:141 x min([serum creatinine in umol/L /88·4]/κ, 1)$^{\alpha}$ x max([serum creatinine in umol/L / 88·4]/κ, 1)$^{-1·209}$ x 0·993^{Age} x 1·018 [if female] x 1·159 [if African American] *κ=0·7 for females and 0·9 for males, α= -0·329 for females and -0·411 for males, min=the minimum of Scr/κ or 1, max=the maximum of Scr/κ or 1.Racial information was not available in our data sources and all patients were assumed not to be of non African-Canadian race. This was a reasonable assumption; as of 2006, African-Canadians represented less than 7% of the Ontario population. Source:* http://www12.statcan.ca/census-recensement/2006/dp-pd/hlt/97-562/index.cfm?Lang=E

The diagnostic performance of the various coding algorithms is presented in Table 2. For both types of hospital encounters, 'all diagnosis' was the best performing ICD-10 N17x coding algorithm. At presentation to the emergency department, the sensitivity of the ICD-10 code for the RIFLE Injury definition of AKI (≥ 2-fold increase in serum creatinine concentration from baseline) was 37.4% (95% confidence interval (CI): 32.1% to 43.1%).

Sensitivities were higher at hospital admission than at presentation to the emergency department for all four serum creatinine-based definitions of AKI. For example, at hospital admission, the sensitivity of the code for the RIFLE Injury definition was 61.6% (95% CI: 57.5% to 65.5%). The sensitivity of the code improved for more severe definitions of AKI, peaking at the RIFLE Injury definition. There was no substantial difference in specificity for both types of hospital encounters, with values greater than 95% in both settings. The positive predictive value of the code decreased for more severe definitions of AKI, with a nadir at the RIFLE Injury definition in both settings.

Table 2. Diagnostic performance characteristics of three different algorithms for ICD-10 code N17x using four different serum creatinine-based definitions of AKI as the reference standard

Diagnostic Coding Algorithm	Definition	Diagnostic Performance Characteristics (95% CI)	
		Emergency Department Cohort	Hospitalized Cohort
All diagnosis	AKIN Stage 1	Sn=7.2 (6.6-8.0) Sp=99.9 (99.8-99.9) PPV=90.4 (87.2-92.8) NPV=86.2 (85.8-86.5)	Sn=21.8 (20.9-22.8) Sp=98.4 (98.2-98.5) PPV=74.2 (72.3-76.1) NPV=85.3 (84.9-85.6)
	RIFLE Risk	Sn=30.4 (26.5-34.7) Sp=99.2 (99.1-99.3) PPV=33.8 (29.5-38.4) NPV=99.1 (99.0-99.2)	Sn=56.4 (53.2-59.7) Sp=96.0 (95.8-96.2) PPV=24.7 (22.8-26.6) NPV=98.9 (98.8-99.1)

	RIFLE Injury	Sn=37.4 (32.1-43.1) Sp=99.1 (99.0-99.2) PPV=25.8 (21.9-30.2) NPV=99.5 (99.4-99.6)	Sn=61.6 (57.5-65.5) Sp=95.6 (95.4-95.8) PPV=17.3 (15.7-19.0) NPV=99.4 (99.3-99.5)
	RIFLE Failure	Sn=30.2 (26.4-34.2) Sp=99.2 (99.2-99.3) PPV=37.3 (32.9-42.0) NPV=99.0 (98.9-99.1)	Sn=59.1 (55.9-62.3) Sp=96.1 (95.9-96.3) PPV=26.9 (25.0-28.9) NPV=99.0 (98.9-99.1)
Main Diagnosis/ Most Responsible Diagnosis	AKIN Stage 1	Sn=4.1 (3.6-4.6) Sp=100.0 (99.9-100.0) PPV=94.7 (91.0-97.0) NPV=85.8 (85.4-86.1)	Sn=5.1 (4.6-5.7) Sp=99.9 (99.8-99.9) PPV=90.7 (87.4-93.2) NPV=82.9 (82.5-83.3)
	RIFLE Risk	Sn=21.4 (17.9-25.3) Sp=99.6 (99.6-99.7) PPV=44.5 (38.2-51.0) NPV=99.0 (98.9-99.1)	Sn=18.7 (16.2-21.4) Sp=99.4 (99.3-99.5) PPV=42.5 (33.7-47.5) NPV=98.1 (98.0-98.3)
	RIFLE Injury	Sn=27.9 (23.1-33.3) Sp=99.6 (99.6-99.7) PPV=36.1 (30.2-42.6) NPV=99.4 (99.3-99.5)	Sn=22.8 (19.5-26.4) Sp=99.3 (99.2-99.4) PPV=33.3 (28.7-38.1) NPV=98.9 (98.7-99.0)
	RIFLE Failure	Sn=22.0 (18.7-25.7) Sp=99.6 (99.5-99.7) PPV=51.1 (44.6-57.5) NPV=98.9 (98.7-99.0)	Sn=22.9 (20.3-25.8) Sp=99.5 (99.5-99.6) PPV=54.4 (49.4-59.3) NPV=98.1 (98.0-98.3)
Admission Diagnosis	AKIN Stage 1	n/a	Sn=15.8 (15.0-16.7) Sp=99.2 (99.1-99.3) PPV=81.6 (79.4-83.6) NPV=84.5 (84.1-84.8)
	RIFLE Risk		Sn=43.1 (39.9-46.4) Sp=97.5 (97.3-97.6) PPV=28.5 (26.2-31.0) NPV=98.6 (98.5-98.8)
	RIFLE Injury		Sn=48.3 (44.2-52.4) Sp=97.2 (97.0-97.4) PPV=20.5 (18.4-22.8) NPV=99.2 (99.1-99.3)
	RIFLE Failure		Sn=47.4 (44.2-50.6) Sp=97.6 (97.5-97.8) PPV=32.6 (30.2-35.2) NPV=98.7 (98.6-98.8)

Abbreviations: ICD-10, International Classification of Diseases, tenth revision; CI, confidence interval; Sn, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value; n/a, not applicable
All values are presented as percentages (%)
To convert serum creatinine from μmol/L to mg/dL divide by 88.4

The absolute change in serum creatinine (peak value – baseline value) and relative change in serum creatinine [(peak value – baseline value) / baseline value)] for patients with hospital encounters who were positive and negative for the ICD-10 N17x code are presented in Table 3.When considering the 'all diagnosis' algorithm, 1.2%

of patients at presentation to the emergency department and 5.2% of patients at hospital admission were code positive for AKI.

The median (IQR) absolute change in serum creatinine concentration for code positive patients was 133 (62 to 288) µmol/L and 98 (43 to 200) µmol/L in each setting, respectively. The change for code negative patients was 2 (-8 to 14) µmol/L and 6 (-4 to 20) µmol/L in each setting, respectively.

When expressed in relative terms, the median (IQR) change for code positive patients was 87 (43 to 204) % and 69 (28 to 153) % in each setting, respectively. The relative change for code negative patients was 2 (-9 to 15) % and 7 (-5 to 22) % in each setting, respectively. In both settings, the difference in the mean absolute and relative change in serum creatinine between code positive and code negative patients was highly statistically significant ($p<0.001$).

Table 3. Change in serum creatinine concentration from baseline in all patients with and without the ICD-10 N17x code for AKI (referred to as code positive and code negative)

Diagnostic Coding Algorithm	Code	Emergency Department Cohort			Hospitalized Cohort		
		N	Absolute Change (µmol/L)	Relative Change (%)*	N	Absolute Change (µmol/L)	Relative Change (%)*
			Median(IQR)			Median(IQR)	
All diagnosis	+	426	133 (62 to 288)	87 (43 to 204)	2,023	98 (43 to 200)	69 (28 to 153)
	-	35,623	2 (-8 to 14)	2 (-9 to 15)	36,543	6 (-4 to 20)	7 (-5 to 22)
Main Diagnosis/ Most Responsible Diagnosis	+	227	187 (89 to 383)	128 (62 to 295)	388	196 (93 to 396)	121 (49 to 275)
	-	35,822	2 (-8 to 14)	2 (-9 to 16)	38,178	7 (-4 to 22)	7 (-4 to 24)
Admission Diagnosis	+	n/a			1,366	114 (39 to 187)	75 (30 to 169)
	-				37,230	6 (-4 to 21)	7 (-4 to 23)

Abbreviations: ICD-10, International Classification of Diseases, tenth revision; CKD, Chronic kidney disease; N, number; IQR, interquartile range; +, code positive; -, code negative; n/a, not applicable
Both absolute and relative changes in serum creatinine were significantly different between code positive and code negative patients in both types of hospital encounter (all p-values <0.001) (means presented in box plot; Supplementary Figure 2 and 3)
*[(peak serum creatinine – baseline serum creatinine) / baseline serum creatinine)]
To convert serum creatinine from µmol/L to mg/dL divide by 88.4

The diagnostic performance of the 'all diagnosis' algorithm at hospital admission in patients with and without CKD is presented in Table 4. The sensitivity of the ICD-10 code for AKIN Stage 1 or greater, RIFLE Risk and RIFLE Injury definitions was higher in patients with CKD than those without CKD. For example, the sensitivity of the code for the RIFLE Injury definition was 75.6% (95% CI: 60.7% to 86.2%) in patients with CKD and 60.5% (95% CI: 56.2% to 64.5%) in patients without CKD.

The code demonstrated the highest sensitivity for the RIFLE Risk definition in patients with CKD and the RIFLE Failure definition in patients without CKD. The specificities of the code were lower in patients with CKD than those without CKD for all four definitions. For example, the specificity of the code for the RIFLE Injury definition was 82.6% (95% CI: 80.7% to 84.4%) in patients with CKD and 96.2% (95% CI: 96.0% to 96.4%) in patients without CKD.

Table 4. Diagnostic performance characteristics of the ICD-10 N17x code in hospitalized patients with and without CKD using serum creatinine-based definitions of AKI as the reference standard*

Definition	Diagnostic Performance Characteristics (95% CI)	
	Patients with CKD	Patients without CKD
AKIN Stage 1	Sn=35.6 (32.0-39.3) Sp=92.0 (90.2-93.5) PPV=74.4 (69.2-78.9) NPV=68.7 (66.1-71.1)	Sn=20.4 (19.4-21.4) Sp=98.6 (98.4-98.7) PPV=74.2 (72.1-76.2) NPV=85.9 (85.5-86.3)
RIFLE Risk	Sn=76.9 (65.4-85.5) Sp=83.5 (81.6-85.3) PPV=16.2 (12.5-20.8) NPV=98.9 (98.1-99.3)	Sn=54.8 (51.4-58.2) Sp=96.5 (96.3-96.7) PPV=26.2 (24.2-28.3) NPV=98.9 (98.8-99.1)
RIFLE Injury	Sn=75.6 (60.7-86.2) Sp=82.6 (80.7-84.4) PPV=10.1 (7.2-13.9) NPV=99.2 (98.6-99.6)	Sn=60.5 (56.2-64.5) Sp=96.2 (96.0-96.4) PPV=18.5 (16.8-20.5) NPV=99.4 (99.3-99.5)
RIFLE Failure	Sn=48.4 (42.2-54.6) Sp=86.4 (84.5-88.1) PPV=38.6 (33.4-44.2) NPV=90.4 (88.7-91.9)	Sn=63.1 (59.4-66.6) Sp=96.4 (96.3-96.6) PPV=24.8 (22.8-26.9) NPV=99.3 (99.2-99.4)

Abbreviations: ICD-10, International Classification of Diseases, tenth revision; CKD, Chronic kidney disease; CI, confidence interval; Sn, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value
All values are presented as percentages (%)
*The ICD-10 N17x coding algorithm considered is all diagnosis

The absolute and relative changes in serum creatinine at hospital admission in patients with and without CKD who were code positive and code negative are presented in Table 5. When considering the 'all diagnosis' algorithm, a total of 18.9% of patients with CKD and 4.6% of patients without CKD were code positive for AKI.

The median (IQR) absolute change in serum creatinine concentration in patients with CKD who were code positive was 108 (48 to 215) µmol/L and in patients without CKD who were code positive was 95 (43 to 197) µmol/L. The difference in the absolute change in serum creatinine between patients with and without CKD who were AKI code positive was not significantly different (p=0.910). The median (IQR) absolute change in patients with CKD who were code negative was 16 (-8 to 51) µmol/L and in patients without CKD who were code negative was 6 (-4 to 19) µmol/L.

When expressed in relative terms, the median (IQR) change in serum creatinine in patients with CKD who were code positive was significantly lower than in patients without CKD who were code positive (53 (20 to 104) % vs. 72 (29 to 161) %; p<0.0001). The median (IQR) relative change in patients with CKD who were code negative was 9 (-4 to 26) % and in patients without CKD who were code negative was 6 (-5 to 22) %. For both patients with and without CKD, the difference in the mean absolute and relative changes in serum creatinine between code positive and negative patients was highly statistically significant (p<0.001).

Table 5. Change in serum creatinine concentration from baseline in hospitalized patients with and without CKD where ICD-10 code N17x did and did not indicate AKI (referred as code positive and code negative)*

Code	Patients with CKD			Patients without CKD		
	N	Absolute Change (µmol/L)	Relative Change (%)†	N	Absolute Change (µmol/L)	Relative Change (%)†
		Median(IQR)			Median(IQR)	

+	308	108 (48 to 215)	53 (20 to 104)	1,715	95 (43 to 197)	72 (29 to 161)
-	1,324	16 (-8 to 51)	9 (-4 to 26)	35,219	6 (-4 to 19)	6 (-5 to 22)

Abbreviations: ICD-10, International Classification of Diseases, tenth revision; CKD, Chronic kidney disease; N, number; IQR, interquartile range; +, code positive; -, code negative; n/a, not applicable.
Code positive and code negative patients were significantly different (all p-values <0.001)
Relative changes in patients with and without CKD were statistically different (p<0.0001)
*The ICD-10 N17x coding algorithm considered is all diagnosis
† [(peak serum creatinine – baseline serum creatinine) / baseline serum creatinine)]
To convert serum creatinine from μmol/L to mg/dL divide by 88.4

DISCUSSION

In this population-based retrospective validation study, we evaluated the diagnostic performance of ICD-10 code N17x for AKI. We discovered that the best performing coding algorithm both at presentation to the emergency department and at hospital admission was when the code was expressed as 'all diagnosis' (i.e. when the code was indicated by any diagnosis type).

At hospital admission, the poorest performing coding algorithm was the 'most responsible diagnosis'. A likely explanation for this is that AKI frequently presents as a complication of other conditions requiring hospital admission, such as acute myocardial infarction or sepsis.[5] AKI is rarely the primary reason for hospital admission so would less likely be coded as the "most responsible diagnosis".

The ICD-10 code demonstrated modest sensitivity for the serum creatinine-based definitions of AKI, indicating its inability to identify a portion of patients who experienced a clinically significant increase in serum creatinine. Of the patients who satisfied the RIFLE Injury definition of AKI from their increase in serum creatinine, 61.6 (95% CI: 57.5-65.5) % of them were code positive AKI when the ICD-10 code was expressed as 'all diagnosis'. However, the code demonstrated high specificity for all four serum creatinine-based definitions. Of the patients who did not satisfy the RIFLE Injury definition of AKI, 95.6 (95% CI: 95.4-95.8) % of them were code negative for AKI. These characteristics of the ICD-10 AKI code are similar to those described in ICD-9 code validation studies that used serum creatinine-based definitions as the reference standard.[8, 10, 21, 22] The use of a serum creatinine-based definition of AKI as the reference standard is preferred over chart review, recognizing the latter have appeared in a number of previous validation studies.[31-35]

The ICD-10 code showed improved sensitivity for more severe definitions of AKI and was highest for the RIFLE Injury definition. This characteristic of the ICD-10 code is similar to that of ICD-9 codes for AKI.[21] A greater increase in serum creatinine reflects more severe AKI, is more likely to be documented in the medical chart and thus detected by coders.

The positive predictive value of the ICD-10 code decreased for more severe definitions of AKI and was the lowest for the RIFLE Injury definition. This fluctuation in the positive predictive values can in part be attributed to the varying prevalence of the four serum creatinine-based definitions.

At both types of hospital encounters, patients who were code positive had a significantly higher increase in serum creatinine than those who were code negative (p<0.001). In other words, the code does successfully differentiate between two groups of patients with and without distinct changes in serum creatinine.

We also assessed the diagnostic performance of the ICD-10 code in subgroups of patients with and without CKD prior to the hospital encounter. For all definitions, with the exception of RIFLE Failure, the code demonstrated higher sensitivity in patients with CKD than those without CKD. However, the specificity of the code was lower in patients with CKD than those without CKD (for all definitions of AKI). The latter finding suggests a portion of patients with stable CKD are misclassified as having AKI at their hospital encounter. For example, clinicians may not have access to patients' baseline serum creatinine measurements, or may make an AKI diagnosis without investigating the baseline measurements. In such cases, an elevated serum creatinine concentration at hospital presentation that is no different than the baseline value may still be misdiagnosed as AKI.

Amongst patients with CKD, presence or absence of the ICD-10 AKI code was also able to differentiate between two groups of patients with distinct changes in their serum creatinine from the baseline value. Although the difference in mean absolute change in serum creatinine was no different in patients with and without CKD who had a positive AKI code, the relative change was lower in patients with CKD than those without CKD. This is consistent

with physicians defining AKI more commonly in absolute rather than in relative terms. With a given absolute increase in serum creatinine, the relative increase in serum creatinine is lower in patients with CKD than those without CKD.

Our study has several strengths. To our knowledge, it is the first study to provide information on the diagnostic performance of the ICD-10 code for AKI using serum creatinine-based definitions of AKI as the reference standard.[8, 10, 21, 22] We assessed different diagnostic coding algorithms of the ICD-10 code at both presentation to the emergency department and at hospital admission. Moreover, we evaluated the diagnostic performance of the code in subgroups of patients with and without CKD prior to the hospital encounter. We studied patients from twelve hospitals across Southwestern Ontario with representation from both academic and community care centres. This helped to minimize selection bias. The large number of patients resulted in good precision for the estimates provided in the study.

Our study does have some limitations. We evaluated the validity of the ICD-10 code for AKI in patients 66 years of age and older. These findings should generalize well to elderly patients, a segment of the population at high risk of AKI.[11, 36] The findings are also useful for pharmacoepidemiologic studies using Ontario's healthcare administrative databases, where prescription information on Ontario residents age 65 and older is available from the universal drug benefit plan. However, future validation studies in younger patients are needed. Moreover, we did not know the degree to which patients with AKI were symptomatic from diminished kidney function or the indication that prompted presentation to the emergency department or hospital admission.

It is important to acknowledge that for the definitions of AKI used in this study, we adapted the serum creatinine-based component of the AKIN and RIFLE classification systems. The AKIN and RIFLE classification systems recommend using both serum creatinine and urine output measurements in determining the presence and severity of AKI.[6, 7] In addition, it is recommended that the AKIN classification is applied only after an optimal state of hydration is achieved.[6] However, urine output measurement and hydration status were not available in the data sources used in the study. In truth, the accuracy of bedside urine output measurement is notoriously poor outside of intensive care settings with an indwelling catheter. Nonetheless, the change in serum creatinine is a widely used measure of kidney function in clinical settings. Moreover, the serum creatinine-based component has been solely used to identify patients with AKI using the AKIN and RIFLE classification systems in previous studies.[37, 38]

The median (IQR) period between the baseline serum creatinine measurements and the hospital encounter was 102 (41-204) days for patients who presented to the emergency department and 39 (16-128) days for patients admitted to hospital. While these are reasonable baseline measurements, the AKIN and RIFLE classification systems require the change in serum creatinine to occur within 48 hours and within 7 days, respectively.[6, 7] Although it is likely that serum creatinine changes occurred just prior to the hospital encounter, we cannot say this with complete certainty given the absence of available measurements during this period.

Finally, we could not examine the validity of outpatient claims for AKI in this study. However, the diagnostic performance of outpatient claims in our jurisdiction is notoriously poor. Nonetheless, emergency department and hospital inpatient records hold information on more severe forms of AKI, which are of particular interest to clinicians, researchers, and policymakers. Moreover, we recognize that we did not capture those patients who may have had severe forms of AKI, but did not present to the emergency department or hospital, or those who presented, but did not have their serum creatinine measured. However, the latter situation is unlikely given that serum creatinine measurements are a standard laboratory test for most patients who present to a hospital encounter for acute medical care.

CONCLUSION

Although the use of healthcare administrative databases for clinical or healthcare services research has several merits, there are inherent limitations, including the accuracy with which certain conditions (i.e. AKI) can be identified. The sensitivity of ICD-10 code N17x for AKI was limited, particularly for less severe definitions. This results in an underestimation of the true incidence of the condition. Nonetheless, the presence or absence of the ICD-10 code successfully differentiates two groups of elderly patients with and without distinct increases in serum creatinine from baseline values at the time of a hospital encounter. The results from this study guide judicious use of ICD-10 code N17x in future research using large healthcare administrative databases.

Contributors

YJH participated in the study coordination and study design and analysis, provided interpretation of study results, and drafted the manuscript. SZS participated in the study design, acquisition of data, and performed the analysis. SG contributed to the study design and interpretation of study results. RW, EC, and JLF contributed to the study design and provided feedback on the manuscript. AXG conceived of the study, participated in its design and interpretation and provided feedback on the manuscript. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

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Supplementary Table 1. Sample 2 by 2 table for assessing diagnostic performance characteristics (sensitivity, specificity, positive predictive value, and negative predictive value) for ICD-10 code N17x

	Reference Standard: RIFLE Injury definition of AKI	
	≥ 2-fold increase in serum creatinine concentration from baseline	< 2-fold increase in serum creatinine concentration from baseline
Code N17x positive	True Positive (TP)	False Positive (FP)
Code N17x negative	False Negative (FN)	True Negative (TN)

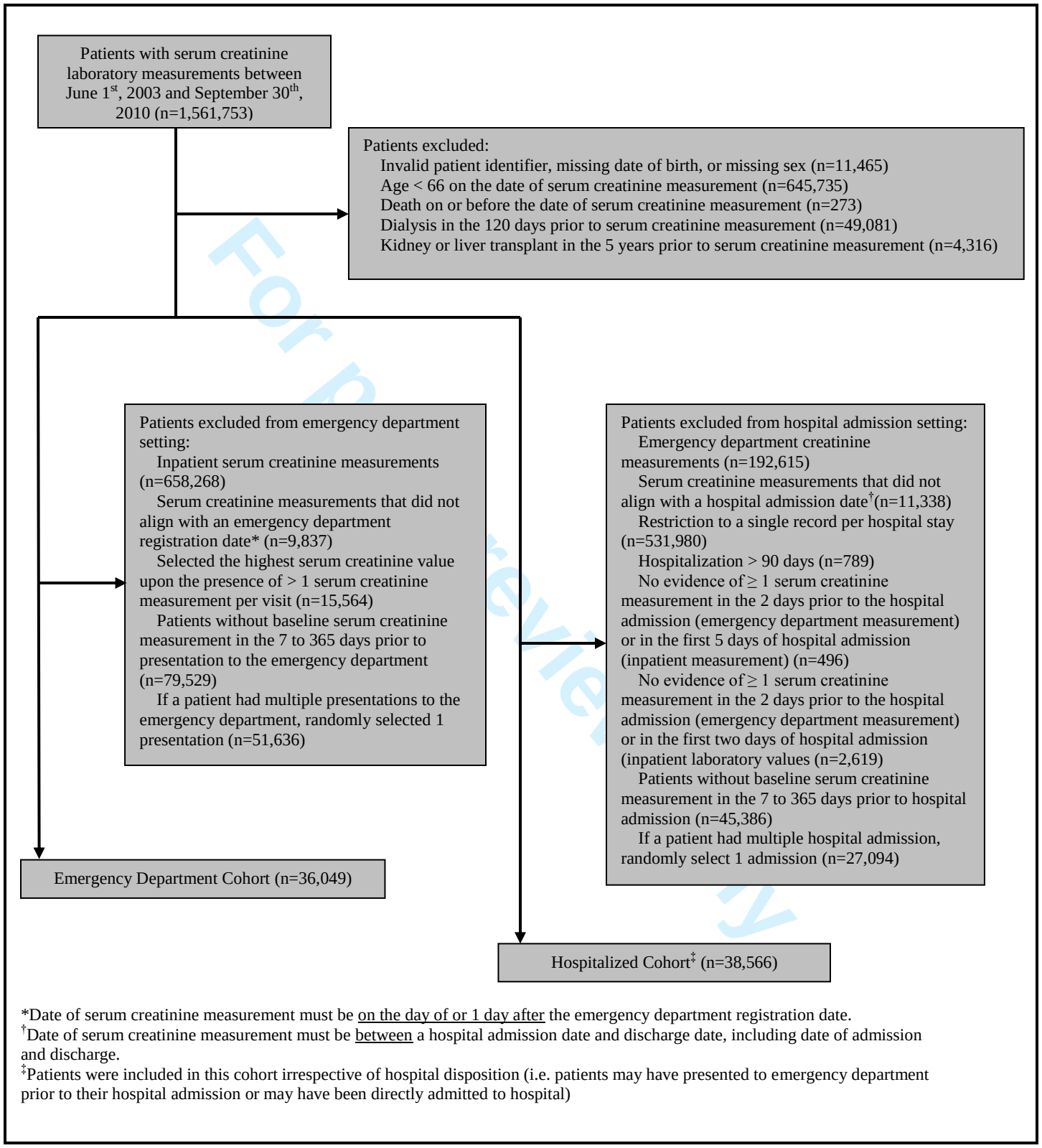
Sensitivity (Sn) = TP ÷ (TP + FN); the proportion of patients with ≥ 2-fold increase in serum creatinine concentration from baseline who are code N17x positive
Specificity (Sp) = TN ÷ (FP + TN); the proportion of patients with < 2-fold increase in serum creatinine concentration from baseline who are code N17x negative
Positive Predictive Value (PPV) = TP ÷ (TP + FP); the proportion of patients who are code N17x positive with ≥ 2-fold increase in serum creatinine concentration from baseline
Negative Predictive Value (NPV) = TN ÷ (FN + TN); the proportion of patients who are code N17x negative with < 2-fold increase in serum creatinine concentration from baseline

Supplementary Table 2. STARD (STAndards for the Reporting of Diagnostic accuracy studies) checklist

Section and Topic	Item #		Page
TITLE/ABSTRACT/ KEYWORDS	1	Identify the article as a study of diagnostic accuracy (recommend MeSH heading 'sensitivity and specificity').	1-2
INTRODUCTION	2	State the research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups.	3
METHODS			
Participants	3	The study population: The inclusion and exclusion criteria, setting and locations where data were collected.	3-4
	4	Participant recruitment: Was recruitment based on presenting symptoms, results from previous tests, or the fact that the participants had received the index tests or the reference standard?	3-4
	5	Participant sampling: Was the study population a consecutive series of participants defined by the selection criteria in item 3 and 4? If not, specify how participants were further selected.	N/A
	6	Data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?	3
Test methods	7	The reference standard and its rationale.	4
	8	Technical specifications of material and methods involved including how and when measurements were taken, and/or cite references for index tests and reference standard.	4-5
	9	Definition of and rationale for the units, cut-offs and/or categories of the results of the index tests and the reference standard.	4-5
	10	The number, training and expertise of the persons executing and reading the index tests and the reference standard.	4-5
	11	Whether or not the readers of the index tests and reference standard were blind (masked) to the results of the other test and describe any other clinical information available to the readers.	N/A
Statistical methods	12	Methods for calculating or comparing measures of diagnostic accuracy, and the statistical methods used to quantify uncertainty (e.g. 95% confidence intervals).	5, Supplementary Table 1
	13	Methods for calculating test reproducibility, if done.	N/A
RESULTS			
Participants	14	Report when study was done, including beginning and ending dates of recruitment.	4,5
	15	Report clinical and demographic characteristics of the study population (e.g. age, sex, spectrum of presenting symptoms, comorbidity, current treatments, recruitment centers).	5-7
	16	Report the number of participants satisfying the criteria for inclusion that did or did not undergo the index tests and/or the reference standard; describe why participants failed to receive either test (a flow diagram is strongly recommended).	4, Supplementary Figure 1
Test results	17	Report time interval from the index tests to the reference standard, and any treatment administered between.	Supplementary Figure 1

	18	Report distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition.	5-7
	19	Report a cross tabulation of the results of the index tests (including indeterminate and missing results) by the results of the reference standard; for continuous results, the distribution of the test results by the results of the reference standard.	7-11
	20	Report any adverse events from performing the index tests or the reference standard.	N/A
Estimates	21		
	22	Report estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals).	7-10
	23	Report how indeterminate results, missing responses and outliers of the index tests were handled.	N/A
	24	Report estimates of variability of diagnostic accuracy between subgroups of participants, readers or centers, if done.	N/A
DISCUSSION	25	Report estimates of test reproducibility, if done.	N/A

Supplementary Figure 1. Cohort Selection



*Date of serum creatinine measurement must be on the day of or 1 day after the emergency department registration date.
†Date of serum creatinine measurement must be between a hospital admission date and discharge date, including date of admission and discharge.
‡Patients were included in this cohort irrespective of hospital disposition (i.e. patients may have presented to emergency department prior to their hospital admission or may have been directly admitted to hospital)

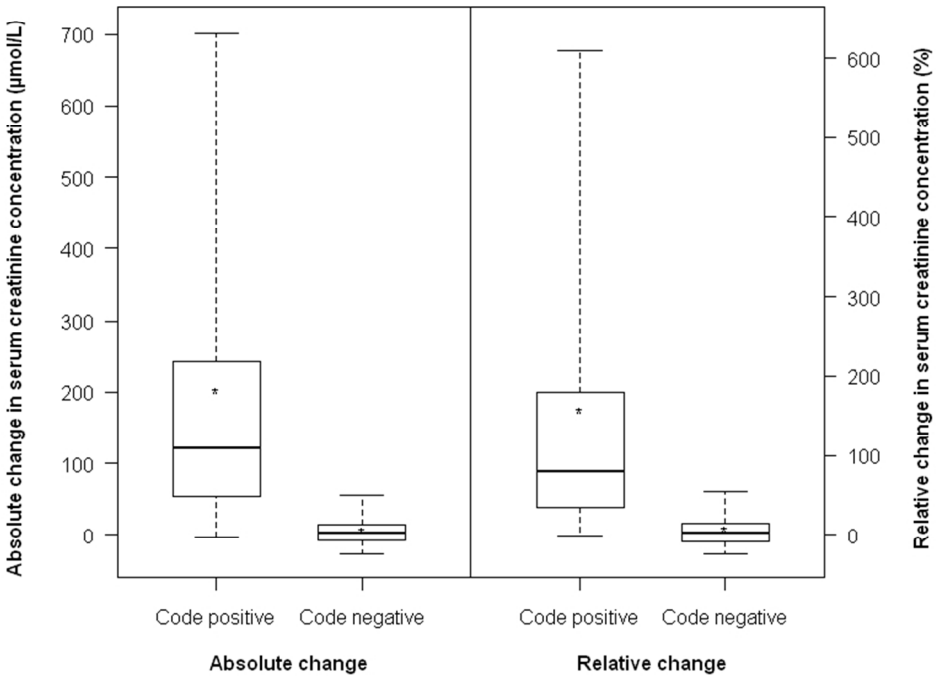
Supplementary Figure 2. Absolute and relative changes in serum creatinine concentration among patients who presented to the emergency department who were code positive and code negative for AKI.* Patients who were code positive for AKI had a significantly greater change in serum creatinine concentration from their baseline value than those patients who were code negative. The boxes represent the interquartile range (50% of the values). The line across the box indicates the median. The asterisk indicates the mean. The whiskers extend to the 95th and 5th percentile.

*The ICD-10 N17x coding algorithm considered is all diagnosis
†The baseline measurements for serum creatinine were taken at a median (IQR) of 102 (41-204) days prior to presentation to the emergency department

Supplementary Figure 3. Absolute and relative changes in serum creatinine concentration among hospitalized patients who were code positive and code negative for AKI. Patients who were code positive for AKI had significantly greater change in serum creatinine concentration from their baseline value than those patients who were code negative. The boxes represent the interquartile range (50% of the values). The line across the box indicates the median. The asterisk indicates the mean. The whiskers extend to the 95th and 5th percentile.

*The ICD-10 N17x coding algorithm considered is all diagnosis

† The baseline measurements for serum creatinine were taken at a median (IQR) 39 (16-128) days prior to the hospital admission



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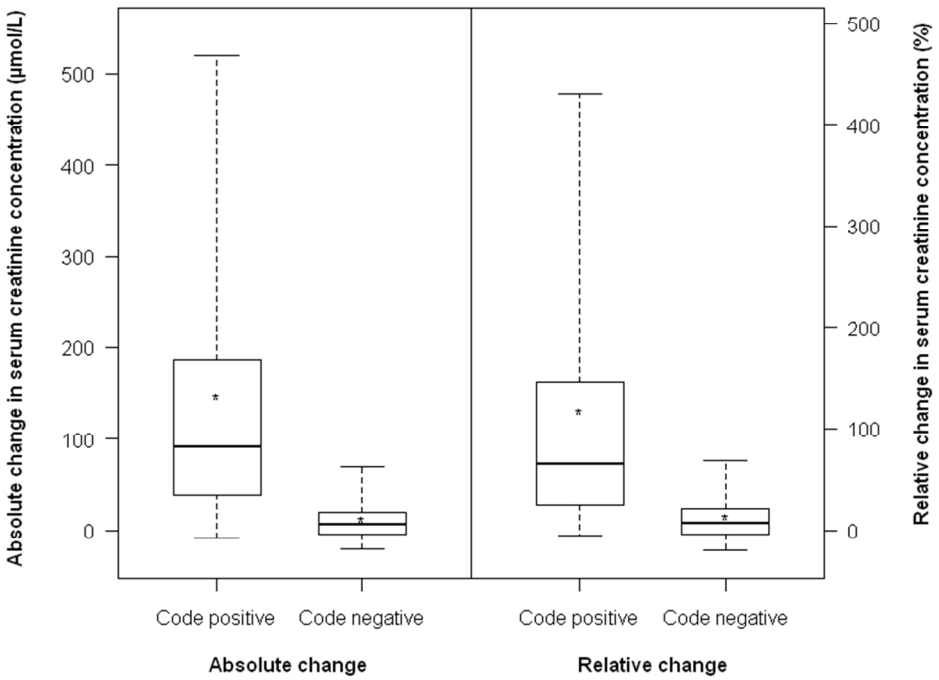
215x177mm (96 x 96 DPI)



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