Validity of the International Classification of Diseases Tenth Revision code for hyperkalemia in elderly patients at presentation to an emergency department and at hospital admission

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-002011
Article Type:	Research
Date Submitted by the Author:	23-Aug-2012
Complete List of Authors:	Fleet, Jamie; London Health Sciences Centre, Medicine/Nephrology Shariff, Salimah; Institute for Clinical Evaluative Sciences, Gandhi, Sonja; University of Western Ontario, Epidemiology and Biostatistics; London Health Sciences Centre, Medicine/Nephrology Weir, Matthew; London Health Sciences Centre, Medicine/Nephrology; University of Western Ontario, Epidemiology and Biostatistics Jain, Arsh; London Health Sciences Centre, Medicine/Nephrology; Institute for Clinical Evaluative Sciences, Garg, Amit; University of Western Ontario
Primary Subject Heading:	Diagnostics
Secondary Subject Heading:	Epidemiology, Renal medicine, Health services research
Keywords:	EPIDEMIOLOGY, Adult nephrology < NEPHROLOGY, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

Validity of the International Classification of Diseases Tenth Revision code for hyperkalemia in elderly patients at presentation to an emergency department and at hospital admission

Jamie L. Fleet[1], Salimah Z. Shariff[2], Sonja Gandhi[1,3], Matthew A. Weir[1,3], Arsh K. Jain[1,2], Amit X. Garg[1,2,3].

1. Division of Nephrology, Department of Medicine, Western University, London, Canada
2. Institute for Clinical Evaluative Sciences, Toronto, Canada
3. Department of Epidemiology & Biostatistics, Western University, London, Canada

Corresponding Author: 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

Publication Type: Research Article

Word Count: 3247 words

Abstract: 277 words

Short title: Validity of the ICD-10 code for hyperkalemia

This study was conducted at the Institute for Clinical Evaluative Sciences (ICES), which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). The opinions, results, and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by ICES or the Ontario MOHLTC is intended or should be inferred.

We thank Barbara Jones, Jeff Lamond, and the late Milton Haines for their help in providing access to Gamma-Dynacare laboratory data.

We thank the team at London Health Sciences Centre, St. Joseph's Health Care, and the Thames Valley Hospitals for providing access to the Cerner laboratory data.

ABSTRACT

Objectives: Evaluate the validity of the *International Classification of Diseases, Tenth Revision* (ICD-10) code for hyperkalemia (E87.5) in two settings: at presentation to an emergency department and at hospital admission.

Design: Population-based validation study

Setting: 12 hospitals in Southwestern Ontario, Canada, from 2003 to 2010

Participants: Elderly patients with serum potassium values at presentation to an emergency department (n=64,579) and at hospital admission (n=64,497).

Primary Outcome: Sensitivity, specificity, positive predictive value, and negative predictive value. Serum potassium values in patients with and without a hyperkalemia code (code positive and code negative, respectively)

Results: The sensitivity of the best performing ICD-10 coding algorithm for hyperkalemia (defined by serum potassium >5.5 mmol/L) was 14.1% (95% confidence interval (CI): 12.5 to15.9%) at presentation to an emergency department and 14.6% (95% CI: 13.3 to16.1%) at hospital admission. Both specificities were greater than 99%. In the two settings, the positive predictive values were 83.2% (95% CI: 78.4 to 87.1%) and 62.04% (95% CI: 57.9 to 66.0%), while the negative predictive values were 97.8% (95% CI: 97.6 to 97.9%) and 96.9% (95% CI: 96.8 to 97.1%). In patients who were code positive for hyperkalemia, median (interquartile range; IQR) serum potassium values were 6.1 (5.7 to 6.8) mmol/L at presentation to an emergency department and 6.0 (5.1to 6.7) mmol/L at hospital admission. For code negative patients median (IQR) serum potassium values were 4.0 (3.7 to 4.4) mmol/L and 4.1 (3.8 to 4.5) mmol/L in each of the two settings, respectively.

Conclusions: Patients with hospital encounters who were ICD-10 E87.5 hyperkalemia code positive and negative had distinct higher and lower serum potassium values, respectively. However, due to low sensitivity, the incidence of hyperkalemia is underestimated.

Keywords: Hyperkalemia, serum potassium, validation, sensitivity, specificity, validity, International Classification of Diseases

ARTICLE SUMMARY

Article Focus

- This study described the validity of the ICD-10 code for hyperkalemia (E87.5) compared to serum potassium laboratory values, where the latter served as the reference standard.
- Knowledge of the accuracy of the code at hospital encounters guides its judicious use in health services research.

Key Messages

- The ICD-10 hyperkalemia code has very high specificity, but low sensitivity, which underestimates the true incidence of hyperkalemia at presentation to an emergency department and at hospital admission.
- Being positive or negative for the code does distinguish between two groups of patients with distinct serum potassium measurements.

Strengths and Limitations

- This is the first study to provide diagnostic information on the validity of the ICD-10 code for hyperkalemia.
- It was a large population-based study and included serum potassium values from twelve hospitals across Ontario.
- Code validity in younger populations should be examined in future studies.

INTRODUCTION

Use of information in healthcare administrative databases is a relatively easy and efficient way to identify patients with prior or current disease. However, administrative codes are not always accurate.[1] This can lead to the underreporting or over reporting of some diseases (i.e. individuals who have the disease but where there is no evidence of the respective database code; or individuals who have evidence of the database code but where there is no evidence of the disease). Knowledge of the validity of various database codes guides their optimal use for research, quality assurance and health system planning.

Hyperkalemia, or high serum potassium, is a fairly common adverse event. Normal levels of serum potassium range from 3.3 to 5.1 mmol/L, with hyperkalemia defined by a value of 5.5 mmol/L or higher.[2] High serum potassium levels can have serious deleterious effects including arrhythmia and death.[3] Some comorbidities that predispose to hyperkalemia include chronic kidney disease and cancer. Hyperkalemia can also occur due to use of a variety of prescription medications, including angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB),beta blockers, and certain types of diuretics.[4] Approximately 10% of patients prescribed an ACE inhibitor develop hyperkalemia in the year following their initial prescription.[5]

The 10th revision of the International Classification of Diseases (ICD-10) system has been used to code healthcare encounters in Canada since 2002, and has also been implemented in over 100 other countries since its inception.[6] Yet, after careful bibliographic database searching, we could find no published validation for the ICD-10 hyperkalemia code using serum potassium laboratory values as the reference standard. There was a single validation study that considered the ICD-9 hyperkalemia code from the Kaiser Permanente Health Management Organization in the United States, but this study only focused on how accurately it was used in automated health care data.[7]

We conducted the current study to determine the accuracy of the ICD-10 code for hyperkalemia (E87.5) in two acute care settings: at presentation to an emergency department and at hospital admission. We compared the ICD-10 code to actual serum potassium laboratory values.

METHODS

Study Design

We conducted a retrospective population-based validation study using linked administrative databases housed at the Institute for Clinical Evaluative Sciences (ICES). The province of Ontario, Canada has approximately 13 million residents, 14% of whom are 65 years of age or older.[8] Residents have universal access to hospital care and physician services and those 65 years of age or older have universal prescription drug coverage. Within Southwestern Ontario, we considered a catchment area that included approximately 80,000 adults 65 years of age and older, according to census information from 2006.[unpublished work] There were 12 hospitals that served this area from which we gathered laboratory information. We compared the ICD-10 hyperkalemia code E87.5 to serum potassium laboratory values as the reference standard in two settings: i) at presentation to an emergency department and ii) at hospital admission. We

calculated the sensitivity, specificity, positive predictive value, and negative predictive value of several ICD-10 coding algorithms. Also, because serum potassium is a continuous measure, we compared patients who were positive for the code to those with hospital encounters who were negative for the code. The reporting of this study follows guidelines set out for studies of diagnostic accuracy (Appendix A).[9] We conducted our study according to a pre-specified protocol that was approved by the institutional review board at Sunnybrook Health Sciences Centre (Toronto, Ontario).

Data Sources

We ascertained outcome data as well as the presence of relevant comorbidities for exclusions and baseline characteristics using records from seven linked databases. The Ontario Drug Benefit Plan (ODB) database contains records of prescriptions from outpatient pharmacies. The dispensing of medications for patients aged 65 and older is accurately recorded in this database with an error rate of less than 1%.[10] The Canadian Institute for Health Information (CIHI) National Ambulatory Care Reporting System (NACRS) contains ambulatory care information on emergency room visits, outpatient procedures, and day surgeries. The CIHI Discharge Abstract Database (CIHI-DAD) reports inpatient procedures, diagnoses, and discharge summaries for patients hospitalized in Ontario. The Ontario Health Insurance Plan (OHIP) database contains all physician and other specific health care provider claims for medical services covered under the provincial health insurance plan. Lastly, the Registered Persons Database (RPDB) contains demographic information, such as birth date and sex, for all Ontario residents who have ever been covered by OHIP.

In addition to the five administrative databases described above, we also used two laboratory datasets to determine serum potassium values. An electronic medical record Cerner® (Kansas City, Missouri, USA) contains inpatient, outpatient, and emergency department laboratory values for 12 hospitals in Southwestern Ontario.[11] Gamma-Dynacare performs outpatient laboratory tests in Southwestern Ontario and was used to obtain baseline laboratory values for a subpopulation. We have successfully used these datasets in previous studies.[12-15]

Participants

Individuals included in our study had at least one hospital-based serum potassium laboratory value between June 1st, 2003 and September 30th, 2010. We considered patients 66 years of age or older, to allow for a minimum of one year of baseline prescription information. We excluded laboratory tests with missing demographic information (approximately 0.75% of the tests). We also excluded hospital stays that were longer than 90 days to ensure we had data for the entire hospitalization, particularly when these occurred towards the end of our accrual period. For hyperkalemia at presentation to an emergency department, the relevant potassium laboratory test must have occurred on an emergency department registration date or the day after. We allowed values for the date after registration to account for patients who may have come to an emergency department but did not receive their test until after midnight (i.e. the day after). For hyperkalemia at hospital admission, the relevant potassium laboratory test must have been done either in an emergency department up to two days prior to hospital admission, or up to one day after the date of hospital admission. We assigned this timeframe to account for any delays between an emergency department presentation and hospital admission, and any treatment that resulted in

subsequent lower potassium values from the initial measurement. In both the emergency room and hospital settings, if multiple tests occurred, we took the highest available value. When multiple eligible hospital presentations were identified for a given patient over the study period, we randomly selected one.

Administrative Database Codes (Diagnostic Test)

In Canada, trained coders record appropriate diagnostic codes and their associated attributes based on information from a patient's chart. Coders in Canada follow specific rules and guidelines set out by CIHI when assigning diagnostic codes based on a patient's file. They are not allowed to interpret any diagnostic tests, such as x-rays or lab values, unless a diagnosis is specifically written by the physician in the medical chart.[16] Within the NACRS database, 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. The CIHI-DAD provides the ability to record up to 25 diagnoses during a hospital admission, each of which can have additional diagnosis types. For example, coders must assign one of the diagnoses the diagnosis type 'M', which represents 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 assign a diagnosis type '1' to any of the listed diagnoses that existed prior to the admission and were treated during the hospital stay.

In this study, based on possible diagnosis types we developed two unique algorithms to assess hyperkalemia at presentation to an emergency department and three unique algorithms to assess hyperkalemia at hospital admission. We used the ICD-10 code E87.5, which is defined as "hyperkalemia". There is a Canadian Modification of the ICD-10 code system which provides additional information on other comorbidities but does not alter the hyperkalemia coding. The two emergency department algorithms identified records with code E87.5 recorded: i) as the main problem (referred to as "main diagnosis"), or ii) in any of the 10 potential diagnostic fields (referred to as "all diagnosis"). The three hospital admission algorithms identified records with code E87.5 recorded: i) with the diagnosis type of 'M' (most responsible; referred to as "most responsible diagnosis"), ii) with the diagnosis type of '1' (pre-admit comorbidity; referred to as "pre-admit diagnosis"), or iii) in any one of 25 potential diagnosis fields and any diagnosis type (referred to as "all diagnosis").

Potassium Laboratory Values (Reference Standard)

Serum potassium laboratory tests were done either in an emergency department or in hospital and were used as the reference standard. The laboratory tests were performed with the Roche Modular Ion Selective Electrode® system (Basel, Switzerland). The primary threshold to define hyperkalemia was a serum potassium value >5.5 mmol/L. Other thresholds were also considered: >5.0, >6.0, and >6.5 mmol/L.

Data Analysis

We assessed severity of hyperkalemia based on several thresholds of serum potassium values indicated above. In the emergency department and hospital admission settings, we calculated the sensitivity, specificity, positive predictive value, and negative predictive value of each coding algorithm for each serum potassium level (see Appendix B for two-by-two contingency table

describing the relevant formulae). For the different algorithms we also contrasted the mean, median, and interquartile ranges of serum potassium values for those who were positive for the code compared to patients with hospital encounters who had no evidence of the code (i.e. code negative). We calculated 95% confidence intervals (CI) for single proportions using the Wilson Score method.[17] We expressed continuous variables as medians with interquartile ranges (IQR) and compared means using independent samples t-tests.We performed all analyses with SAS version 9.2 (SAS Institute Incorporated, Cary, North Carolina, USA, 2008).

RESULTS

The cohort creation and specific exclusions for both settings are shown in Appendix C. Patient baseline characteristics are shown in Table 1.

Table 1. Baseline characteristics for patients with serum potassium values obtained at presentation to emergency department and at hospital admission.

	At emergency department N = 64579	At hospital admission N = 64497
Demographics		
Age, years, *median (IQR)*	77 (71-83)	77 (71-83)
Women, *n (%)*	35,630 (55.17)	32,965 (51.1)
Income quintile, *n (%)*		
One (lowest)	14,231 (22.0)	13,900 (21.6)
Two	12,921 (20.0)	12,928 (20.0)
Three (middle)	12,542 (19.4)	12,792 (19.8)
Four	11,496 (17.8)	11,601 (18.0)
Five (highest)	12,407 (19.2)	12,446 (19.3)
Rural Location, *n (%)*	11,438 (17.7)	13,248 (20.5)
Year of cohort entry, *n (%)*		
2003 – 2004	6,581 (10.2)	11,601 (18.0)
2005 – 2006	15,188 (23.5)	15,640 (24.3)
2007 – 2008	20,569 (31.9)	18,474 (28.6)
2009 – 2010	22,236 (34.4)	18,782 (29.1)
Long-term Care Facility Utilization, *n (%)*	4,137 (6.4)	3,681 (5.7)
Comorbidities, *n (%)*		
Chronic kidney disease‡	5,335 (8.3)	6,427 (10.0)
Diabetes mellitus£	13,142 (20.4)	13,632 (21.1)
Peripheral vascular disease	1,690 (2.6)	2,937 (4.6)
Coronary artery disease¶	26,979 (41.8)	30,528 (47.3)
Heart failure	13,691 (21.2)	15,173 (23.5)
Stroke/Transient ischemic attack	2,455 (3.8)	2,655 (4.1)
Chronic liver disease	1,238 (1.9)	1,645 (2.6)
Medication use in prior 6 months, *n (%)*		
Angiotensin-converting enzyme inhibitors	22,690 (35.1)	23,770 (36.9)
Angiotensin-receptor blockers	10,442 (16.2)	10,012 (15.5)
Potassium sparing diuretics	5,657 (8.8)	6,147 (9.5)
Loop diuretics	13,553 (21.0)	14,618 (22.7)
Thiazide diuretics	12,334 (19.1)	12,458 (19.3)
Calcium channel blockers	19,126 (29.6)	19,951 (30.9)
Beta adrenergic antagonists	21,989 (34.1)	23,382 (36.3)
Statins	24,892 (38.6)	25,273 (39.2)
NSAIDS (excluding aspirin)	11,621 (18.0)	12,573 (19.5)
Anticonvulstants	3,847 (6.0)	3,740 (5.8)
Antidepressants	15,662 (24.3)	15,075 (23.4)
Antipsychotics	4,001 (6.2)	3,532 (5.5)
Benzodiazepine	15,295 (23.7)	15,515 (24.1)
Antineoplastic drugs	3,285 (5.1)	3,624 (5.6)
Baseline Laboratory Measurements*		
Serum Creatinine levels		
Most recent serum creatinine, µmol/L, *median (IQR)*	90 (74-114)	90 (74-114)

GFR[Ŧ] Levels		
Most recent eGFR mL/min/1.73m², *median (IQR)*	63 (47-79)	63(47-79)
eGFR category, *n (%)*		
≥60mL mL/min/1.73m²	20,807 (54.7)	23,842 (55.3)
45-59 mL/min/1.73m²	8,527 (22.4)	9,566 (22.2)
30-44 mL/min/1.73m²	5,466 (14.4)	5989 (13.9)
15-29 mL/min/1.73m²	2,362 (6.2)	2,694 (6.2)
<15 mL/min/1.73m²	850 (2.2)	1,021 (2.4)
Serum Sodium Levels		
Most recent serum sodium, mmol/L, *median, (IQR)*	139(137-141)	139(137-141)
Serum Potassium Levels		
Most recent serum potassium, mmol/L, *median (IQR)*	4.2 (3.8-4.5)	4.1(3.8-4.5)

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

[€] The year of cohort entry is also referred to as the index date

[‡] Assessed by administrative database codes: CIHI ICD-9 codes – 4030, 3031, 4039, 4040, 4041, 4049, 582, 583, 580, 581, 584, 585, 586, 587, 5880, 5888, 5889, 5937; CIHI ICD-10 codes – I12, I13, N01, N03, N05, N07, N14, N15, N00, N04, N08, N18, N19, N26, N25, N137, N280, N2888, N06, N391; OHIP diagnostic codes – 403, 580, 581, 585

[£] 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

*Available from emergency department, inpatient or outpatient settings for a subpopulation. A total of 33104 (51.3%), 32844 (50.9%), and 38012 (58.9%) patients at presentation to emergency department had a baseline serum potassium, sodium, and creatinine measurement available in the 7 to 365 days prior to the index date, respectively.. Among these patients, the baseline measurements were taken at a median (IQR) of 75 (25-174), 75(25-174), and 76 (26-173) days, respectively. A total of 39552 (61.3%), 39422 (61.1%), and 43112 (66.9%) patients at hospital admission had a baseline serum potassium, sodium, and creatinine measurement available in the 7 to 365 days prior to the index date, respectively. Among these patients, the baseline measurements were taken at a median (IQR) of 29 (14-97), 29 (14-97), and 32(14-101) days, respectively.

[Ŧ] 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

Of the 64,579 patients who presented to an emergency department, 1,679 (2.6%) had a potassium value of >5.5 mmol/L. Of 64,497 patients who were admitted to hospital, 2,289 (3.5%) patients had a serum potassium level > 5.5 mmol/L. The diagnostic performance characteristics of the coding algorithms for hyperkalemia (defined by serum potassium >5.5mmol/L) in the two settings are presented in Table 2. The algorithm that considered the E87.5 code as 'all diagnoses' demonstrated the best sensitivity, recognizing the value still remained low. For example, the sensitivity of the 'all diagnoses' algorithm to detect a serum potassium > 5.5 mmol/L in an emergency department was 14.1% and the specificity was 99.9%. Similar results were obtained for individuals with hyperkalemia at hospital admission.

Table 2. Diagnostic performance characteristics for ICD-10 E87.5 coding algorithms for hyperkalemia defined by a serum potassium value > 5.5 mmol/L at presentation to an emergency department and at hospital admission.

ICD-10 E87.5 Coding Algorithm		Emergency department +	Emergency department -		Emergency department % (95% CI)		Hospital admission +	Hospital admission -		Hospital admission % (95% CI)
All diagnoses	+	237	48	Sn.	14.12 (12.53-15.86)	+	335	205	Sn.	14.64 (13.25-16.14)
	-	1442	62852	Sp.	99.92 (99.90-99.94)	-	1954	62003	Sp.	99.67 (99.62-99.71)
				PPV	83.16 (78.38-87.06)				PPV	62.04 (57.87-66.03)
				NPV	97.76 (97.64-97.87)				NPV	96.94 (96.81-97.08)
		+	-				+	-		
Main/most responsible diagnosis	+	98	19	Sn.	5.84 (4.81-7.06)	+	59	8	Sn.	2.58 (2.00-3.31%)
	-	1581	62881	Sp.	99.97 (99.95-99.98)	-	2230	62200	Sp.	99.99 (99.97-99.99)
				PPV	83.76 (76.03-89.35)				PPV	88.06 (78.17-93.82)
				NPV	97.55 (97.43-97.66)				NPV	96.54 (96.39-96.68)
							+	-		
Pre-admit diagnosis						+	276	94	Sn.	12.06 (10.79-13.46)
						-	2013	62114	Sp.	99.85 (99.82-99.88)
									PPV	74.59 (69.92-78.76)
									NPV	96.86 (96.72-96.99)

Abbreviations: ICD-10, International Classification of Diseases, 10th revision; Sn, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value, +, hyperkalemia yes; - hyperkalemia no

The performance characteristics of the coding algorithms for the additional thresholds of serum potassium (> 5 mmol/L, >6 mmol/L, and >6.5 mmol/L) are presented in Table 3. Of all the coding algorithms, those that considered the E87.5 code as 'all diagnoses' continued to demonstrate the best sensitivity across all the serum potassium thresholds. As well the sensitivity of the coding algorithm increased as hyperkalemia became more severe (i.e. a higher serum potassium level). For example, in an emergency department, for the 'all diagnoses' algorithm, the sensitivity was 6.6% for a potassium >5 mmol/L, and 21.8% for a potassium >6.5 mmol/L. Similarly, at hospital admission, for the 'all diagnoses' algorithm the sensitivity was 7.5% for a potassium > 5 mmol/L and 29.5% for a potassium > 6.5 mmol/L. The specificities were > 99% and comparable across the different thresholds of serum potassium.

Table 3. Diagnostic performance characteristics for other thresholds of serum potassium values at presentation to an emergency department and at hospital admission.

ICD-10 E87.5 Coding Algorithm		Emergency Department >5mmol/L % (95% CI)	Emergency Department >6mmol/L % (95% CI)	Emergency Department >6.5mmol/L % (95% CI)	Hospital admission >5mmol/L % (95% CI)	Hospital admission >6mmol/L % (95% CI)	Hospital admission >6.5mmol/L % (95% CI)
All diagnoses	Sn.	6.55 (5.84-7.35)	19.32 (16.73-22.21)	21.81 (18.17-25.95)	7.50 (6.83-8.22)	23.34 (20.95-25.91)	29.49 (25.76-33.51)
	Sp.	99.98 (99.96-99.98)	99.79 (99.76-99.83)	99.70 (99.66-99.74)	99.79 (99.75-99.82)	99.56 (99.50-99.61)	99.40 (99.34-99.46)
	PPV	94.74 (91.50-96.78)	54.04 (48.23-59.73)	32.98 (27.78-38.64)	76.85 (73.11-80.21)	48.15 (43.96-52.36)	28.89 (25.23-32.85
	NPV	94.01 (93.83-94.19)	99.00 (98.92-99.07)	99.48 (99.42-99.53)	92.00 (91.78-92.20)	98.66 (98.57-98.75)	99.42 (99.35-99.47)
Main/most	Sn.	2.65 (2.20-3.18)	8.53 (6.79-10.68)	9.05 (6.69-12.13)	1.16 (0.91-1.47)	4.94 (3.81-6.37)	7.94 (5.93-10.56)

responsible diagnosis	Sp.	99.99 (99.97-99.99)	99.92(99.90-99.94)	99.88 (99.85-99.90)	99.99 (99.99-100)	99.98 (99.97-99.99)	99.96 (99.94-99.97)
	PPV	93.16 (87.09-96.49)	58.12 (49.06-66.66)	33.33 (25.44-42.28)	95.52 (87.64-98.47)	82.09 (71.25-89.45)	62.69 (50.72-73.28)
	NPV	93.78 (93.59-93.96)	98.87 (98.78-98.95)	99.39 (99.33-99.45)	91.51 (91.29-91.72)	98.36 (98.26-98.45)	99.24 (99.17-99.31)
Pre-admit diagnosis					5.84 (5.25-6.49)	19.93 (17.69-22.38)	25.71 (22.17-29.60)
					99.92 (99.89-99.94)	99.77 (99.73-99.80)	99.63 (99.58-99.68)
					87.30 (83.52-90.31)	60.00 (54.93-64.86)	36.76 (32.00-41.78)
					91.87 (91.66-92.08)	98.61 (98.52-98.70)	99.39(99.32-99.44)

Abbreviations: ICD-10, International Classification of Diseases, 10th revision; Sn, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value

Serum potassium values as a continuous measure in groups of patients with hospital encounters that were code positive or negative are presented in Table 4 and Figure 1. There were highly statistically significant differences in serum potassium levels between the individuals who were code positive and code negative (for all algorithms; independent samples t-test; all p-values <0.0001). For example, in an emergency department using the 'all diagnosis' coding algorithm, the median (IQR) serum potassium value for patients who were code positive was 6.1 mmol/L (5.7 to 6.8 mmol/L), and 4.0 mmol/L (3.7 to 4.4 mmol/L) for those who were code negative. Similar results were evident for patients at hospital admission and for all algorithms.

Table 4. Serum potassium values (mmol/L) in patients who were code positive and code negative for ICD-10 code E87.5 at presentation to the emergency department and at hospital admission according to different algorithms.

		Emergency Department				Hospital Admission		
		N	Median	IQR		N	Median	IQR
All diagnosis	No	64294	4.0	3.7- 4.4	No	63957	4.1	3.8- 4.5
	Yes	285	6.1	5.7- 6.8	Yes	540	6.0	5.1- 6.7
Main/most responsible diagnosis	No	64462	4.0	3.7- 4.4	No	64430	4.1	3.8- 4.5
	Yes	117	6.2	5.7- 6.9	Yes	67	6.9	6.1- 7.5
Pre-admit diagnosis					No	64127	4.1	3.8- 4.5
					Yes	370	6.3	5.5- 6.9

Abbreviations: N, number of patients; IQR, interquartile range

A total of 51.3% of patients that presented to an emergency department had a baseline pre-hospital encounter serum potassium value. These baseline tests occurred at a median (IQR) of 75 (25 to 174) days prior to the emergency department presentation. This allowed us to examine the median change in serum potassium values (i.e. emergency department value minus the baseline value). These results are presented in Appendix D. In an emergency department, for code positive patients (using the 'all diagnoses' algorithm), the median (IQR) change in serum potassium values was 1.5 mmol/L (0.8 to 2.3 mmol/L) and for those who were code negative the

change was -0.1 mmol/L (-0.5 to 0.3 mmol/L). The mean difference in the change in serum potassium values between code positive and code negative patients was 1.6 mmol/L (95% CI: 1.5 to 1.7 mmol/L). Similar results were evident for the 61.3% of patients at hospital admission who had a baseline serum potassium measurement (which was taken a median (IQR) of 29 (14 to 97) days prior to hospital admission). In these patients using the 'all diagnosis' algorithm, the median (IQR) change (hospital value minus baseline value) in serum potassium was 1.3 mmol/L (0.4 to 2.3 mmol/L) for those who were code positive and 0.0 mmol/L (-0.3 to 0.4 mmol/L) for those who were code negative. The mean difference in the change in serum potassium values between code positive and code negative patients was 1.4 mmol/L (95% CI: 1.2 to 1.5 mmol/L).

DISCUSSION

In this population-based validation study, we found that the best performing ICD-10 coding algorithm for hyperkalemia at presentation to an emergency department and at hospital admission was when the code was present in any diagnosis field ('all diagnosis'), regardless of the threshold of serum potassium used to define hyperkalemia. Overall, the specificity for the ICD-10 hyperkalemia code was very high while the sensitivity was low. There was a high false negative rate in both the emergency room and hospital admission settings: just over 90% of patients with a serum potassium value of 5.5mmol/L or more did not receive a code for hyperkalemia using the all diagnoses category. Even when considering severe hyperkalemia (serum potassium >6.5mmol/L), the sensitivity only reached a maximum of about 29%.

The most responsible diagnosis is defined as the illness responsible for the longest length of stay or the greatest use of hospital resources. This algorithm demonstrated the lowest sensitivity amongst all the algorithms in our study, likely because the most responsible illness was attributed to the underlying problem that caused the hyperkalemia rather than the hyperkalemia itself.

We found that sensitivity increased as the severity of hyperkalemia increased. Milder forms of hyperkalemia tend to be asymptomatic and can be managed without aggressive treatment. Consequently, the physician may be less inclined in such cases to record a diagnosis of hyperkalemia in the medical chart.

Of the patients who had hyperkalemia at presentation to an emergency department and at hospital admission (defined by a value >5.5mmol/L), only 14.1% and 14.6%, respectively were correctly coded as hyperkalemic. The low sensitivity at this threshold may be due to less enthusiasm to act on values that are only modestly elevated. Despite this, the code was successful in differentiating between two groups of patients with distinct serum potassium values. Code negative patients had serum potassium values in the normal range (3.5 to 5.1mmol/L) and when the code was present, values were much higher (≥6 mmol/L).

Our study has several strengths. It is the first study to validate the ICD-10 code for hyperkalemia and first to validate hyperkalemia using laboratory values as the reference standard. We validated the ICD-10 code in both an emergency department and at hospital admission examining different types of diagnoses. Previous electrolyte validation studies have not looked at these settings nor did they examine all the possible diagnosis types as we did in our

study. Although there have been no similar hyperkalemia validation studies, other electrolyte studies have demonstrated similarly low sensitivities of the ICD codes. [18,19]

All citizens in Ontario receive universal healthcare and patients over 65 have their medications paid for by the provincial government. These two factors made collecting health administrative data relatively easy and gave us the ability to have a large sample size. We based our validation on laboratory data from twelve hospitals in the most populous province in Canada. Another study validating the ability of a computerized program to correctly identify hyperkalemia using the ICD-9 code restricted the analysis to a single centre and to the specific population of diabetics.[7] Additionally, another study describing the frequency of hyperkalemic events also focused on a specific population of veterans.[20] Because we used a more varied and larger population, we were able to obtain good precision for estimates that are quite generalizable.

The validity measures that we used in this study have also been used in several other studies comparing ICD codes with clinical outcomes, including two validations of another electrolyte disorder, hyponatremia.[21-26] Many validation studies compare diagnostic codes to information written in medical charts. However, the most accurate way to determine whether hyperkalemia is truly present is to use laboratory values as we did in the current study.

Our study does have some limitations. We validated the ICD-10 hyperkalemia code in a population of patients over age 65. This patient population is particularly vulnerable to developing hyperkalemia.[27] Additionally, these results inform future analyses of the Ontario healthcare databases since most pharmacoepidemiologic research using these data sources are conducted in patients over age 65 (where receipt of prescription medications is a universal benefit). Nonetheless, code validity in younger populations should be examined in future studies.

We were unable to determine if the patients who presented to an emergency department or at hospital admission showed arrhythmias or other sequelae of the high serum potassium value. However, we do know the code did identify acute changes, as demonstrated by a mean increase in serum potassium of 1.5 mmol/L above the baseline pre-hospital value. Patients with acute changes in serum potassium are most likely to be symptomatic from the condition.

Finally, we recognize that we did not capture those patients who may have had severe hyperkalemia but did not go to an emergency department or hospital, or those who presented but failed to have serum potassium measured. However, the latter is less of a concern as serum potassium is a common test for most patients who present for acute medical care. We were unable to detect outpatient claims for hyperkalemia in this study as there is no administrative code set available for this in our jurisdiction. Nevertheless, emergency department and hospital records do detect more severe forms of hyperkalemia making this of particular interest to clinicians and policy decision makers.

CONCLUSION

Analyses of administrative codes are a cost-efficient way to assess patient comorbidity and disease in large population-based studies. However, as observed by the low sensitivity in the current study, many individuals with an ICD-10 database code for hyperkalemia are missed leading to an underestimate of the true incidence of the condition at hospital encounters. Nonetheless, the group of patients who were positive for this code were distinguishable from the group of patients who were negative for the code with distinct serum potassium values in both

settings. The findings of this validation study guide proper use of the ICD-10 hyperkalemia code in future research using health administrative data.

Contributors

JLF participated in the coordination of the study, study design, provided interpretation of study results, and drafted the manuscript. SZS participated in the study design, performed the analysis and provided interpretation of study results. SG contributed to the study design and interpretation of study results. MAW and AKJ contributed to the study design and provided feedback on the manuscript. AXG conceived of the study, participated in its design and interpretation, helped draft the manuscript and provided feedback on the manuscript. All authors read and approved the final manuscript.

Funding

The study was supported by the Canadian Institutes of Health Research. Dr. Garg was supported by a Clinician Scientist Award from the Canadian Institutes of Health Research.

Competing interests

The authors declare that they have no competing interests.

Figure 1 Legend

Serum potassium measurements among patients who are code positive and code negative for hyperkalemia (when the code was considered in the format 'all diagnoses'). For both presentation to an emergency department and at hospital admission, patients who for positive for the hyperkalemia code had a significantly higher serum potassium measurement than patients who were code negative. The boxes represent the interquartile range (50% of the values). The line across the box indicates the median. The star indicates the mean. The whiskers extend to the 95th and 5th percentile

REFERENCES

1 Elixhauser A, Steiner C, Harris RD, et al. Comorbidity measures for use with administrative data. Med Care 1998;36:8-27.

2 Schaefer TJ, Wolford RW. Disorders of potassium. Emerg Med Clin N Am 2005;23:723-747.

3 Elliott MJ, Ronksley PE, Clase CM, et al. Management of patients with acute hyperkalemia. CMAJ 2010;182:1631-1635.

4 Palmer BF. Managing hyperkalemia caused by inhibitors of the renin-angiotensin-aldosterone system. N Engl J Med 2004;351:585-592.

5 Reardon LC, Macpherson DS. Hyperkalemia in outpatients using angiotensin-converting enzyme inhibitors. Arch Intern Med 1998;158:26-32.

6 World Health Organization. Fact Sheet May 2012: International Classification of Diseases (ICD). www.who.int/entity/classifications/icd/revision/icdfactsheet.pdf (accessed 18 May 2012).

7 Raebel MA, Smith ML, Saylor G, et al. The positive predictive value of a hyperkalemia diagnosis in automated health care data. Pharmacoepidemiol Drug Saf 2010;19:1204-1208.

8 Statistics Canada. Age and Sex Highlights Table 2011 Census. http://www12.statcan.gc.ca/census-recensement/2011/dp-pd/hlt-fst/as-sa/?Lang=E (accessed 29 May 2012).

9 STAndards for the Reporting of Diagnostic accuracy studies. STARD Checklist. http://www.stard-statement.org/ (accessed 13 December 2011).

10 Levy AR, O'Brien BJ, Sellors C, et al. Coding accuracy of administrative drug claims in the Ontario Drug Benefit database. Can J Clin Pharmacol 2003;10:67-71.

11 Cerner. Laboratory. http://www.cerner.com/solutions/Hospitals_and_Health_Systems/Laboratory/ (accessed 18 May 2012)

12 Zhao YY, Weir MA, Manno M et al. New fibrate use and acute renal outcomes in elderly adults: a population-based study. *Ann Intern Med* 2012;156:560-569

13 Jain AK, Cuerden MS, McLeod I et al. Reporting of the estimated glomerular filtration rate was associated with increased use of angiotensin-converting enzyme inhibitors and angiotensin-II receptor blockers in CKD. *Kidney Int* 2012;81:1248-1253.

14 Weir MA, Gomes T, Mamdani M, et al. Impaired renal function modifies the risk of severe hypoglycaemia among users of insulin but not glyburide: a population-based nested case–control study. *Nephrol Dial Transplant* 2011;26:1888-1894.

15 Molnar AO, Coca SG, Devereaux PJ, et al. Statin use associates with lower incidence of acute injury after major elective surgery. *J Am Soc Nephrol* 2011;22:939-946.

16 Canadian Institute for Health Information. Canadian coding standards for Version 2012 ICD-10-CA and CCI. https://secure.cihi.ca/free_products/canadian_coding_standards_2012_e.pdf (accessed 02 May 2012).

17 Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of seven methods. *Stat Med* 1998;17:857-872.

18 Movig KL, Leufkens HG, Lenderink AW, et al. Validity of hospital discharge International Classification of Diseases (ICD) codes for identifying patients with hyponatremia. *J Clin Epidemiol* 2003;56:530-535.

19 Shea AM, Curtis LH, Szczech LA, et al. Sensitivity of International Classification of Diseases codes for hyponatremia among commercially insured outpatients in the United States. *BMC Nephrol* 2008; 9:5.

20 Einhorn LM, Zhan M, Hsu VD, et al. The frequency of hyperkalemia and its significance in chronic kidney disease. *Arch Intern Med* 2009;169:1156-1162.

21 Waiker SS, Wald R, Chertow GM, et al. Validity of *International Classification of Diseases, Ninth Revision, Clinical Modification* codes for acute renal failure. *J Am Soc Nephrol* 2006;17:1688-1694.

22 Romano PS, Roos LL, Luft HS, et al. A comparison of administrative versus clinical data: coronary artery bypass surgery as an example. Ischemic Heart Disease Patient Outcomes Research Team. *J Clin Epidemiol* 1994;47:249–60.

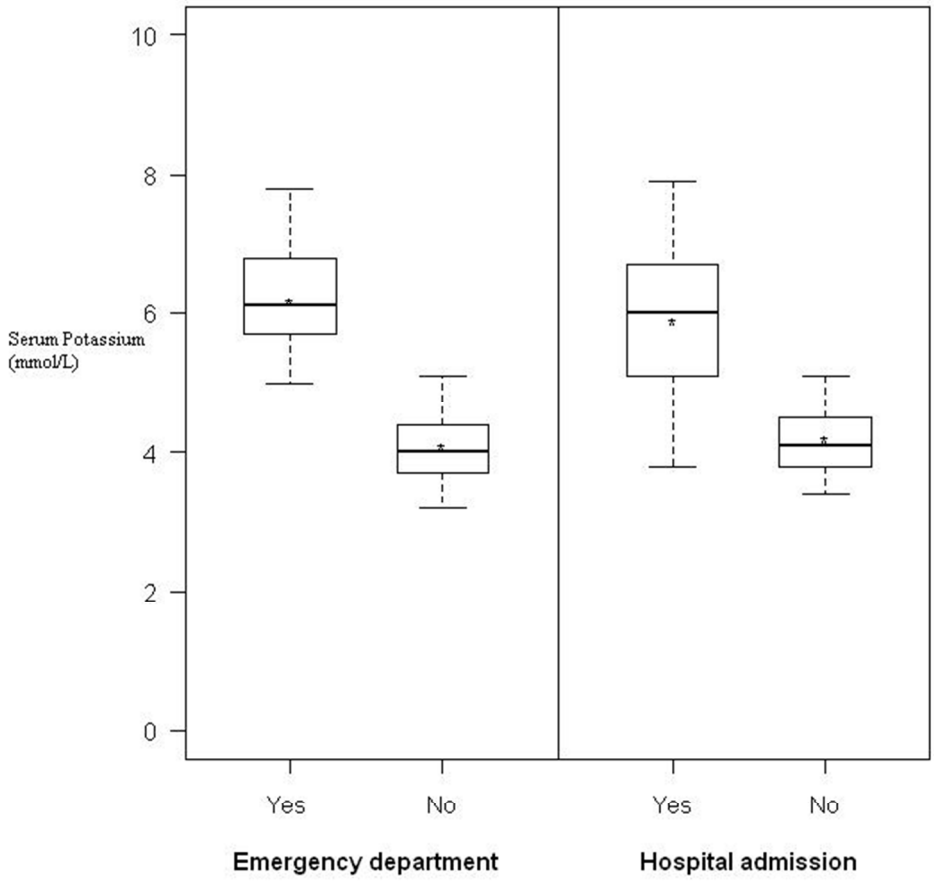
23 Quan H, Parsons GA, Ghali WA: Validity of procedure codes in International Classification of Diseases, 9th revision, clinical modification administrative data. *Med Care* 2004;42:801-809.

24 Raiford DS, Perez Gutthann S, Garcia Rodriguez LA. Positive predictive value of ICD-9 codes in the identification of cases of complicated peptic ulcer disease in the Saskatchewan hospital automated database. *Epidemiology* 1996;7:101–104.

25 Gankam KF, Andres C, Sattar L, et al. Mild hyponatremia and risk of fracture in the ambulatory elderly. *Q J Med* 2008;101:583-588.

26 Waikar SS, Mount DB, Curhan GC. Mortality after hospitalization with mild, moderate, and severe hyponatremia. *Am J Med* 2009;122: 857-865.

27 Obreli-Neto PR, Nobili A, de Oliveira Baldoni A, et al. Adverse drug reactions caused by drug-drug interactions in elderly outpatients: a prospective cohort study. *Eur J Clin Pharmacol* 2012 May 30. [Epub ahead of print]



177x177mm (96 x 96 DPI)

Appendix A

STARD checklist for reporting of studies of diagnostic accuracy

(version January 2003)

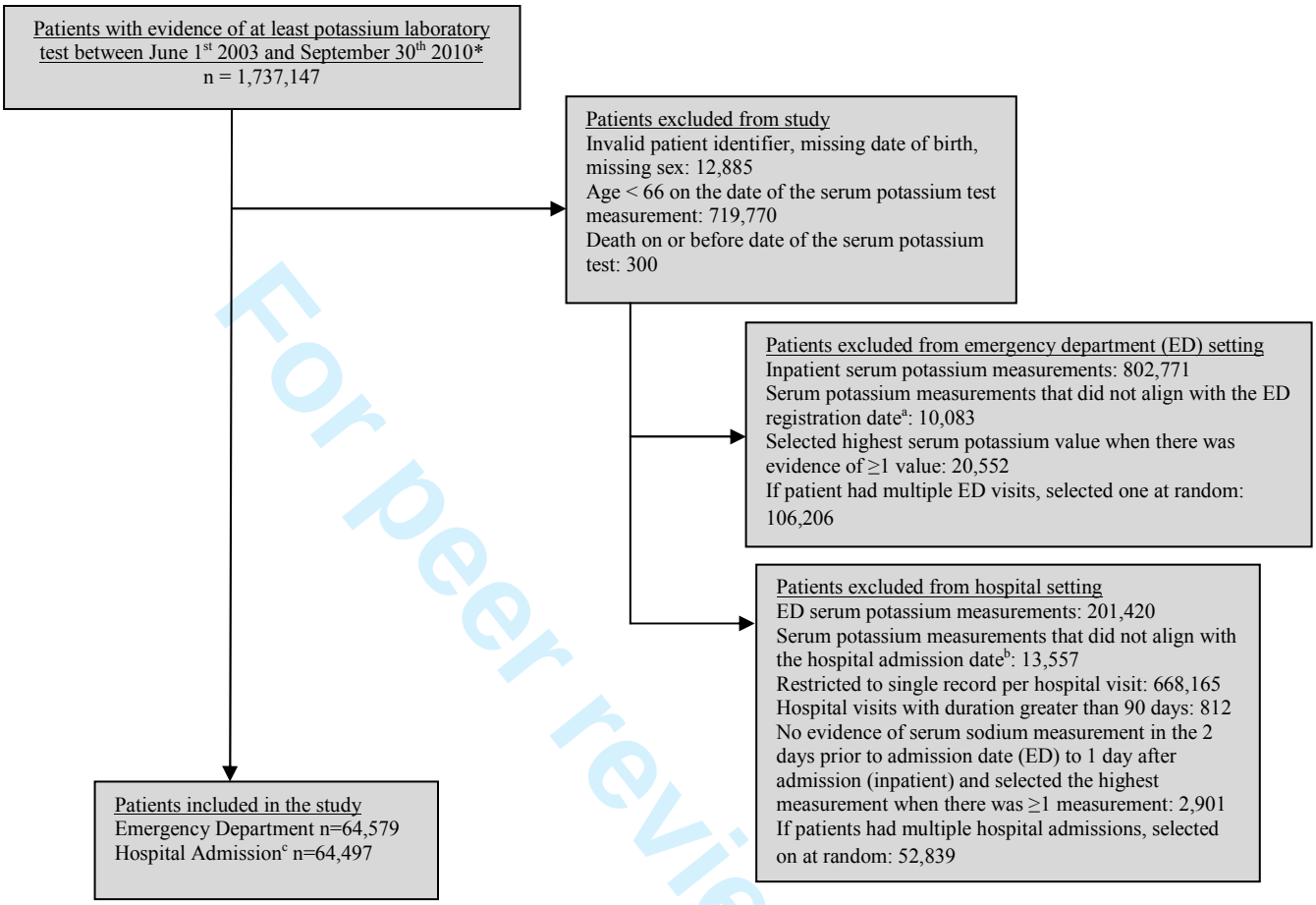
Section and Topic	Item #		On page #
TITLE/ABSTRACT/ KEYWORDS	1	Identify the article as a study of diagnostic accuracy (recommend MeSH heading 'sensitivity and specificity').	Abstract
INTRODUCTION	2	State the research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups.	Introduction
METHODS			
Participants	3	The study population: The inclusion and exclusion criteria, setting and locations where data were collected.	Methods – Participants; Appendix C
	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?	Methods – Participants
	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.	Methods – Participants; Appendix C
	6	Data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?	Methods – Study design
Test methods	7	The reference standard and its rationale.	Methods
	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.	Methods – Potassium laboratory value
	9	Definition of and rationale for the units, cut-offs and/or categories of the results of the index tests and the reference standard.	Methods – Potassium laboratory value
	10	The number, training and expertise of the persons executing and reading the index tests and the reference standard.	Methods – Administrative database codes
	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).	Methods – Data analysis; Appendix A
	13	Methods for calculating test reproducibility, if done.	n/a
RESULTS			
Participants	14	When study was performed, including beginning and end dates of recruitment.	Methods
	15	Clinical and demographic characteristics of the study population (at least information on age, gender, spectrum of presenting symptoms).	Results; Table 1
	16	The number of participants satisfying the criteria for inclusion who did or did not undergo the index tests and/or the reference standard; describe why participants failed to undergo either test (a flow diagram is strongly recommended).	Results; Table 1; Appendix C
Test results	17	Time-interval between the index tests and the reference standard, and any treatment administered in between.	Table 1 Footnote; Appendix C
	18	Distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition.	Results; Tables 2,3,4
	19	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.	Tables 2,3,4
	20	Any adverse events from performing the index tests or the reference standard.	n/a
Estimates	21	Estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals).	Results; Tables 2,3,4
	22	How indeterminate results, missing data and outliers of the index tests were handled.	n/a
	23	Estimates of variability of diagnostic accuracy between subgroups of participants, readers or centers, if done.	n/a
	24	Estimates of test reproducibility, if done.	n/a
DISCUSSION	25	Discuss the clinical applicability of the study findings.	Discussion

Appendix B

		Reference Standard: **Hyperkalemia** defined by a **potassium laboratory value >5.5mmol/L**	
		> 5.5 mmol/L	≤ 5.5 mmol/L
Hyperkalemia defined by **ICD-10 Code E87.5**	Code Positive	A	B
	Code Negative	C	D

Sensitivity=a/(a+c): the proportion of patients with serum potassium >5.5 mmol/L who are code E87.5 positive
Specificity=d/(b+d): the proportion of patients with serum potassium ≤5.5 mmol/L who are code E87.5 negative
Positive predictive value=a/(a+b): proportion of patients who are code E87.5 positive with serum potassium >5.5 mmol/L
Negative predictive value=d/(c+d): proportion of patients who are code E87.5 negative with serum potassium ≤5.5 mmol/L

Appendix C



*serum potassium measurements that were <0.5 mmol/L and >14 mmol/L were not considered as these were deemed data entry errors (occurred < 1.0% of the time).

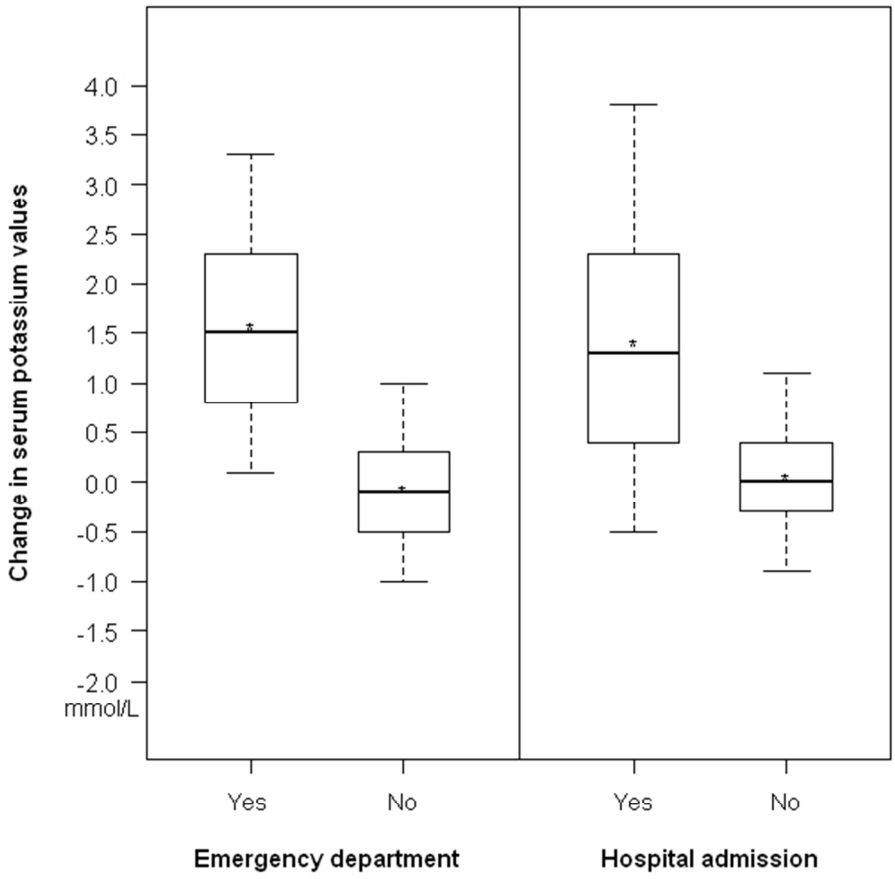
[a] date of serum potassium measurement must be on the day of or 1 day after an emergency department registration date.

[b] date of serum potassium measurement must be between a hospital admission date and discharge date, including date of admission and discharge.

[c] patients were included in this cohort irrespective of hospital disposition (i.e. patients may have presented to an emergency department prior to their hospital admission or may have been directly admitted to hospital)

Appendix D – Figure Caption

Change in serum potassium values among patients who had baseline pre-hospital encounter serum potassium result. Patients who were code positive had evidence of the code in the 'all diagnoses' format. Patients who were code negative had no such code. For both presentation to an emergency department, and at hospital admission, patients who were code positive for hyperkalemia had a significantly larger change in their serum potassium value (from baseline) than patients who were code negative. The boxes represent the interquartile range (50% of the values). The line across the box indicates the median. The star indicates the mean. The whiskers extend to the 95th and 5th percentile.



177x177mm (96 x 96 DPI)

Validity of the International Classification of Diseases Tenth Revision code for hyperkalemia in elderly patients at presentation to an emergency department and at hospital admission

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-002011.R1
Article Type:	Research
Date Submitted by the Author:	12-Nov-2012
Complete List of Authors:	Fleet, Jamie; London Health Sciences Centre, Medicine/Nephrology Shariff, Salimah; Institute for Clinical Evaluative Sciences, Gandhi, Sonja; University of Western Ontario, Epidemiology and Biostatistics; London Health Sciences Centre, Medicine/Nephrology Weir, Matthew; London Health Sciences Centre, Medicine/Nephrology; University of Western Ontario, Epidemiology and Biostatistics Jain, Arsh; London Health Sciences Centre, Medicine/Nephrology; Institute for Clinical Evaluative Sciences, Garg, Amit; University of Western Ontario
Primary Subject Heading:	Diagnostics
Secondary Subject Heading:	Epidemiology, Renal medicine, Health services research
Keywords:	EPIDEMIOLOGY, Adult nephrology < NEPHROLOGY, Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

Validity of the International Classification of Diseases Tenth Revision code for hyperkalemia in elderly patients at presentation to an emergency department and at hospital admission

Jamie L. Fleet[1], Salimah Z. Shariff[2], Sonja Gandhi[1,3], Matthew A. Weir[1,3], Arsh K. Jain[1,2], Amit X. Garg[1,2,3].

1. Division of Nephrology, Department of Medicine, Western University, London, Canada
2. Institute for Clinical Evaluative Sciences, Toronto, Canada
3. Department of Epidemiology & Biostatistics, Western University, London, Canada

Corresponding Author: 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

Publication Type: Research Article

Word Count: 3396 words

Abstract: 277 words

Short title: Validity of the ICD-10 code for hyperkalemia

This study was conducted at the Institute for Clinical Evaluative Sciences (ICES), which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). The opinions, results, and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by ICES or the Ontario MOHLTC is intended or should be inferred.

We thank Barbara Jones, Jeff Lamond, and the late Milton Haines for their help in providing access to Gamma-Dynacare laboratory data.

We thank the team at London Health Sciences Centre, St. Joseph's Health Care, and the Thames Valley Hospitals for providing access to the Cerner laboratory data.

ABSTRACT

Objectives: Evaluate the validity of the *International Classification of Diseases, Tenth Revision* (ICD-10) code for hyperkalemia (E87.5) in two settings: at presentation to an emergency department and at hospital admission.

Design: Population-based validation study

Setting: 12 hospitals in Southwestern Ontario, Canada, from 2003 to 2010

Participants: Elderly patients with serum potassium values at presentation to an emergency department (n=64,579) and at hospital admission (n=64,497).

Primary Outcome: Sensitivity, specificity, positive predictive value, and negative predictive value. Serum potassium values in patients with and without a hyperkalemia code (code positive and code negative, respectively)

Results: The sensitivity of the best performing ICD-10 coding algorithm for hyperkalemia (defined by serum potassium >5.5 mmol/L) was 14.1% (95% confidence interval (CI): 12.5 to15.9%) at presentation to an emergency department and 14.6% (95% CI: 13.3 to16.1%) at hospital admission. Both specificities were greater than 99%. In the two settings, the positive predictive values were 83.2% (95% CI: 78.4 to 87.1%) and 62.04% (95% CI: 57.9 to 66.0%), while the negative predictive values were 97.8% (95% CI: 97.6 to 97.9%) and 96.9% (95% CI: 96.8 to 97.1%). In patients who were code positive for hyperkalemia, median (interquartile range; IQR) serum potassium values were 6.1 (5.7 to 6.8) mmol/L at presentation to an emergency department and 6.0 (5.1to 6.7) mmol/L at hospital admission. For code negative patients median (IQR) serum potassium values were 4.0 (3.7 to 4.4) mmol/L and 4.1 (3.8 to 4.5) mmol/L in each of the two settings, respectively.

Conclusions: Patients with hospital encounters who were ICD-10 E87.5 hyperkalemia code positive and negative had distinct higher and lower serum potassium values, respectively. However, due to very low sensitivity, the incidence of hyperkalemia is underestimated.

Keywords: Hyperkalemia, serum potassium, validation, sensitivity, specificity, validity, International Classification of Diseases

ARTICLE SUMMARY

Article Focus

- This study described the validity of the ICD-10 code for hyperkalemia (E87.5) compared to serum potassium laboratory values, where the latter served as the reference standard.
- Knowledge of the accuracy of the code at hospital encounters guides its judicious use in health services research.

Key Messages

- The ICD-10 hyperkalemia code has very high specificity, but very low sensitivity, which underestimates the true incidence of hyperkalemia at presentation to an emergency department and at hospital admission.
- Being positive or negative for the code does distinguish between two groups of patients with distinct serum potassium measurements.

Strengths and Limitations

- This is the first study to provide diagnostic information on the validity of the ICD-10 code for hyperkalemia.
- It was a large population-based study and included serum potassium values from twelve hospitals across Ontario.
- Code validity in younger populations should be examined in future studies.

INTRODUCTION

Use of information in healthcare administrative databases is a relatively easy and efficient way to identify patients with prior or current disease. It is also a simple way for the medical community to assess resources and usage of healthcare services. However, administrative codes are not always accurate.[1] This can lead to the underreporting or over reporting of some diseases (i.e. individuals who have the disease but where there is no evidence of the respective database code; or individuals who have evidence of the database code but where there is no evidence of the disease). Knowledge of the validity of various database codes guides their optimal use for research, quality assurance, and health system planning.

Hyperkalemia, or high serum potassium, is a fairly common adverse event. Normal levels of serum potassium range from 3.3 to 5.1 mmol/L, with hyperkalemia often defined by a value of 5.5 mmol/L or higher.[2] High serum potassium levels can have serious deleterious effects including arrhythmia and death.[3] Some comorbidities that predispose to hyperkalemia include chronic kidney disease and cancer. Hyperkalemia can also occur due to use of a variety of prescription medications, including angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB),beta blockers, and certain types of diuretics.[4] Approximately 10% of patients prescribed an ACE inhibitor develop hyperkalemia in the year following their initial prescription.[5]

The 10th revision of the International Classification of Diseases (ICD-10) system has been used to code healthcare encounters in Canada since 2002, and has also been implemented in over 100 other countries since its inception.[6] Yet, after careful bibliographic database searching, we could find no published validation for the ICD-10 hyperkalemia code using serum potassium laboratory values as the reference standard. There was a single validation study that considered the ICD-9 hyperkalemia code from the Kaiser Permanente Health Management Organization in the United States, but this study only focused on how accurately it was used in automated health care data.[7]

We conducted the current study to determine the accuracy of the ICD-10 code for hyperkalemia (E87.5) in two acute care settings: at presentation to an emergency department and at hospital admission. We compared the ICD-10 code to actual serum potassium laboratory values.

METHODS

Study Design

We conducted a retrospective population-based validation study using linked administrative databases housed at the Institute for Clinical Evaluative Sciences (ICES). The province of Ontario, Canada has approximately 13 million residents, 14% of whom are 65 years of age or older.[8] Residents have universal access to hospital care and physician services and those 65 years of age or older have universal prescription drug coverage. Within Southwestern Ontario, we considered a catchment area that included approximately 80,000 adults 65 years of age and older, according to census information from 2006.[9] There were 12 hospitals that served this area from which we gathered laboratory information. We compared the ICD-10 hyperkalemia code E87.5 to serum potassium laboratory values as the reference standard in two settings: i) at

presentation to an emergency department and ii) at hospital admission. We calculated the sensitivity, specificity, positive predictive value, and negative predictive value of several ICD-10 coding algorithms. Also, because serum potassium is a continuous measure, we compared patients who were positive for the code to those with hospital encounters who were negative for the code. The reporting of this study follows guidelines set out for studies of diagnostic accuracy (Appendix A).[10] We conducted our study according to a pre-specified protocol that was approved by the institutional review board at Sunnybrook Health Sciences Centre (Toronto, Ontario).

Data Sources

We ascertained outcome data as well as the presence of relevant comorbidities for exclusions and baseline characteristics using records from seven linked databases. The Ontario Drug Benefit Plan (ODB) database contains records of prescriptions from outpatient pharmacies. The dispensing of medications for patients aged 65 and older is accurately recorded in this database with an error rate of less than 1%.[11] The Canadian Institute for Health Information (CIHI) National Ambulatory Care Reporting System (NACRS) contains ambulatory care information on emergency room visits, outpatient procedures, and day surgeries. The CIHI Discharge Abstract Database (CIHI-DAD) reports inpatient procedures, diagnoses, and discharge summaries for patients hospitalized in Ontario. The Ontario Health Insurance Plan (OHIP) database contains all physician and other specific health care provider claims for medical services covered under the provincial health insurance plan. Lastly, the Registered Persons Database (RPDB) contains demographic information, such as birth date and sex, for all Ontario residents who have ever been covered by OHIP.

In addition to the five administrative databases described above, we used two laboratory datasets to determine serum potassium values. An electronic medical record Cerner® (Kansas City, Missouri, USA) contains inpatient, outpatient, and emergency department laboratory values for 12 hospitals in Southwestern Ontario.[12] Gamma-Dynacare performs outpatient laboratory tests in Southwestern Ontario and was used to obtain baseline laboratory values for a subpopulation. We have successfully used these datasets in previous studies.[13-16]

Participants

Individuals included in our study had at least one hospital-based serum potassium laboratory value between June 1st, 2003 and September 30th, 2010. We considered patients 66 years of age or older, to allow for a minimum of one year of baseline prescription information. Older patients often have important risk factors for hyperkalemia and have full medication coverage through the provincial drug plan.[17] We excluded laboratory tests with missing demographic information (approximately 0.75% of the tests). We also excluded hospital stays that were longer than 90 days to ensure we had data for the entire hospitalization, particularly when these occurred towards the end of our accrual period. For hyperkalemia at presentation to an emergency department, the relevant potassium laboratory test must have occurred on an emergency department registration date or the day after. We allowed values for the date after registration to account for patients who may have come to an emergency department but did not receive their test until after midnight (i.e. the day after). For hyperkalemia at hospital admission, the relevant potassium laboratory test must have been done either in an emergency department

up to two days prior to hospital admission, or up to one day after the date of hospital admission. We assigned this timeframe to account for any delays between an emergency department presentation and hospital admission, and any treatment that resulted in subsequent lower potassium values from the initial measurement. In both the emergency room and hospital settings, if multiple tests occurred, we took the highest available value. When multiple eligible hospital presentations were identified for a given patient over the study period, we randomly selected one.

Administrative Database Codes (Diagnostic Test)

In Canada, trained coders record appropriate diagnostic codes and their associated attributes based on information from a patient's chart. Coders in Canada follow specific rules and guidelines set out by CIHI when assigning diagnostic codes based on a patient's file. They are not allowed to interpret any diagnostic tests, such as x-rays or lab values, unless a diagnosis is specifically written by the physician in the medical chart.[18] Within the NACRS database, 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. The CIHI-DAD provides the ability to record up to 25 diagnoses during a hospital admission, each of which can have additional diagnosis types. For example, coders must assign one of the diagnoses the diagnosis type 'M', which represents 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 assign a diagnosis type '1' to any of the listed diagnoses that existed prior to the admission and were treated during the hospital stay.

In this study, based on possible diagnosis types we developed two unique algorithms to assess hyperkalemia at presentation to an emergency department and three unique algorithms to assess hyperkalemia at hospital admission. We used the ICD-10 code E87.5, which is defined as "hyperkalemia". There is a Canadian Modification of the ICD-10 code system which provides additional information on other comorbidities but does not alter the hyperkalemia coding. The two emergency department algorithms identified records with code E87.5 recorded: i) as the main problem (referred to as "main diagnosis"), or ii) in any of the 10 potential diagnostic fields (referred to as "all diagnosis"). The three hospital admission algorithms identified records with code E87.5 recorded: i) with the diagnosis type of 'M' (most responsible; referred to as "most responsible diagnosis"), ii) with the diagnosis type of '1' (pre-admit comorbidity; referred to as "pre-admit diagnosis"), or iii) in any one of 25 potential diagnosis fields and any diagnosis type (referred to as "all diagnosis").

Potassium Laboratory Values (Reference Standard)

Serum potassium laboratory tests were done either in an emergency department or in hospital and were used as the reference standard. The laboratory tests were performed with the Roche Modular Ion Selective Electrode® system (Basel, Switzerland). The primary threshold to define hyperkalemia was a serum potassium value >5.5 mmol/L. Other thresholds were also considered: >5.0, >6.0, and >6.5 mmol/L.

Data Analysis

We assessed severity of hyperkalemia based on several thresholds of serum potassium values indicated above. In the emergency department and hospital admission settings, we calculated the sensitivity, specificity, positive predictive value, and negative predictive value of each coding algorithm for each serum potassium level (see Appendix B for two-by-two contingency table describing the relevant formulae). For the different algorithms we also contrasted the mean, median, and interquartile ranges of serum potassium values for those who were positive for the code compared to patients with hospital encounters who had no evidence of the code (i.e. code negative). We calculated 95% confidence intervals (CI) for single proportions using the Wilson Score method.[19] We expressed continuous variables as medians with interquartile ranges (IQR) and compared means using independent samples t-tests.We performed all analyses with SAS version 9.2 (SAS Institute Incorporated, Cary, North Carolina, USA, 2008).

RESULTS

The cohort creation and specific exclusions for both settings are shown in Appendix C. Patient baseline characteristics are shown in Table 1.

Table 1. Baseline characteristics for patients with serum potassium values obtained at presentation to emergency department and at hospital admission.

	At emergency department N = 64579	At hospital admission N = 64497
Demographics		
Age, years, *median (IQR)*	77 (71-83)	77 (71-83)
Women, *n (%)*	35,630 (55.2)	32,965 (51.1)
Income quintile, *n (%)*		
One (lowest)	14,231 (22.0)	13,900 (21.6)
Two	12,921 (20.0)	12,928 (20.0)
Three (middle)	12,542 (19.4)	12,792 (19.8)
Four	11,496 (17.8)	11,601 (18.0)
Five (highest)	12,407 (19.2)	12,446 (19.3)
Rural Location, *n (%)*	11,438 (17.7)	13,248 (20.5)
Year of cohort entry, *n (%)*		
2003 – 2004	6,581 (10.2)	11,601 (18.0)
2005 – 2006	15,188 (23.5)	15,640 (24.3)
2007 – 2008	20,569 (31.9)	18,474 (28.6)
2009 – 2010	22,236 (34.4)	18,782 (29.1)
Long-term Care Facility Utilization, *n (%)*	4,137 (6.4)	3,681 (5.7)
Comorbidities, *n (%)*		
Chronic kidney disease‡	5,335 (8.3)	6,427 (10.0)
Diabetes mellitus£	13,142 (20.4)	13,632 (21.1)
Peripheral vascular disease	1,690 (2.6)	2,937 (4.6)
Coronary artery disease¶	26,979 (41.8)	30,528 (47.3)
Heart failure	13,691 (21.2)	15,173 (23.5)
Stroke/Transient ischemic attack	2,455 (3.8)	2,655 (4.1)
Chronic liver disease	1,238 (1.9)	1,645 (2.6)
Medication use in prior 6 months, *n (%)*		
Angiotensin-converting enzyme inhibitors	22,690 (35.1)	23,770 (36.9)
Angiotensin-receptor blockers	10,442 (16.2)	10,012 (15.5)
Potassium sparing diuretics	5,657 (8.8)	6,147 (9.5)
Loop diuretics	13,553 (21.0)	14,618 (22.7)
Thiazide diuretics	12,334 (19.1)	12,458 (19.3)
Calcium channel blockers	19,126 (29.6)	19,951 (30.9)
Beta adrenergic antagonists	21,989 (34.1)	23,382 (36.3)
Statins	24,892 (38.6)	25,273 (39.2)
NSAIDS (excluding aspirin)	11,621 (18.0)	12,573 (19.5)
Anticonvulstants	3,847 (6.0)	3,740 (5.8)
Antidepressants	15,662 (24.3)	15,075 (23.4)

Antipsychotics	4,001 (6.2)	3,532 (5.5)
Benzodiazepine	15,295 (23.7)	15,515 (24.1)
Antineoplastic drugs	3,285 (5.1)	3,624 (5.6)
Baseline Laboratory Measurements*		
Serum Creatinine levels		
Most recent serum creatinine, µmol/L, *median (IQR)*	90 (74-114)	90 (74-114)
GFR[Ŧ] Levels		
Most recent eGFR mL/min/1.73m², *median (IQR)*	63 (47-79)	63(47-79)
eGFR category, *n (%)*		
≥60mL mL/min/1.73m²	20,807 (54.7)	23,842 (55.3)
45-59 mL/min/1.73m²	8,527 (22.4)	9,566 (22.2)
30-44 mL/min/1.73m²	5,466 (14.4)	5989 (13.9)
15-29 mL/min/1.73m²	2,362 (6.2)	2,694 (6.2)
<15 mL/min/1.73m²	850 (2.2)	1,021 (2.4)
Serum Sodium Levels		
Most recent serum sodium, mmol/L, *median, (IQR)*	139(137-141)	139(137-141)
Serum Potassium Levels		
Most recent serum potassium, mmol/L, *median (IQR)*	4.2 (3.8-4.5)	4.1(3.8-4.5)

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

[€] The year of cohort entry is also referred to as the index date

[‡] Assessed by administrative database codes: CIHI ICD-9 codes – 4030, 3031, 4039, 4040, 4041, 4049, 582, 583, 580, 581, 584, 585, 586, 587, 5880, 5888, 5889, 5937; CIHI ICD-10 codes – I12, I13, N01, N03, N05, N07, N14, N15, N00, N04, N08, N18, N19, N26, N25, N137, N280, N2888, N06, N391; OHIP diagnostic codes – 403, 580, 581, 585

[£] 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

*Available from emergency department, inpatient or outpatient settings for a subpopulation. A total of 33104 (51.3%), 32844 (50.9%), and 38012 (58.9%) patients at presentation to emergency department had a baseline serum potassium, sodium, and creatinine measurement available in the 7 to 365 days prior to the index date, respectively.. Among these patients, the baseline measurements were taken at a median (IQR) of 75 (25-174), 75(25-174), and 76 (26-173) days, respectively. A total of 39552 (61.3%), 39422 (61.1%), and 43112 (66.9%) patients at hospital admission had a baseline serum potassium, sodium, and creatinine measurement available in the 7 to 365 days prior to the index date, respectively. Among these patients, the baseline measurements were taken at a median (IQR) of 29 (14-97), 29 (14-97), and 32(14-101) days, respectively.

[Ŧ]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

Of the 64,579 patients who presented to an emergency department, 1,679 (2.6%) had a potassium value of >5.5 mmol/L. Of 64,497 patients who were admitted to hospital, 2,289 (3.5%) patients had a serum potassium level > 5.5 mmol/L. The diagnostic performance characteristics of the coding algorithms for hyperkalemia (defined by serum potassium >5.5mmol/L) in the two settings are presented in Table 2. The algorithm that considered the E87.5 code as 'all diagnoses' demonstrated the best sensitivity, recognizing the value still remained low. For example, the sensitivity of the 'all diagnoses' algorithm to detect a serum potassium > 5.5 mmol/L in an emergency department was 14.1% and the specificity was 99.9%. Similar results were obtained for individuals with hyperkalemia at hospital admission.

Table 2. Diagnostic performance characteristics for ICD-10 E87.5 coding algorithms for hyperkalemia defined by a serum potassium value > 5.5 mmol/L at presentation to an emergency department and at hospital admission.

		Emergency department					Hospital admission			
ICD-10 E87.5 Coding Algorithm		+	-		% (95% CI)		+	-		% (95% CI)
All diagnoses	+	237	48	Sn.	14.12 (12.53-15.86)	+	335	205	Sn.	14.64 (13.25-16.14)
	-	1442	62852	Sp.	99.92 (99.90-99.94)	-	1954	62003	Sp.	99.67 (99.62-99.71)
				PPV	83.16 (78.38-87.06)				PPV	62.04 (57.87-66.03)
				NPV	97.76 (97.64-97.87)				NPV	96.94 (96.81-97.08)
		+	-				+	-		
Main/most responsible diagnosis	+	98	19	Sn.	5.84 (4.81-7.06)	+	59	8	Sn.	2.58 (2.00-3.31%)
	-	1581	62881	Sp.	99.97 (99.95-99.98)	-	2230	62200	Sp.	99.99 (99.97-99.99)
				PPV	83.76 (76.03-89.35)				PPV	88.06 (78.17-93.82)
				NPV	97.55 (97.43-97.66)				NPV	96.54 (96.39-96.68)
							+	-		
Pre-admit diagnosis						+	276	94	Sn.	12.06 (10.79-13.46)
						-	2013	62114	Sp.	99.85 (99.82-99.88)
									PPV	74.59 (69.92-78.76)
									NPV	96.86 (96.72-96.99)

Abbreviations: ICD-10, International Classification of Diseases, 10th revision; Sn, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value, +, hyperkalemia yes; - hyperkalemia no

The performance characteristics of the coding algorithms for the additional thresholds of serum potassium (> 5 mmol/L, >6 mmol/L, and >6.5 mmol/L) are presented in Table 3. Of all the coding algorithms, those that considered the E87.5 code as 'all diagnoses' continued to demonstrate the best sensitivity across all the serum potassium thresholds. As well the sensitivity of the coding algorithm increased as hyperkalemia became more severe (i.e. a higher serum potassium level). For example, in an emergency department, for the 'all diagnoses' algorithm, the sensitivity was 6.6% for a potassium >5 mmol/L, and 21.8% for a potassium >6.5 mmol/L. Similarly, at hospital admission, for the 'all diagnoses' algorithm the sensitivity was 7.5% for a potassium > 5 mmol/L and 29.5% for a potassium > 6.5 mmol/L. The specificities were > 99% and comparable across the different thresholds of serum potassium.

Table 3. Diagnostic performance characteristics for other thresholds of serum potassium values at presentation to an emergency department and at hospital admission.

		Emergency Department			Hospital admission		
ICD-10 E87.5 Coding Algorithm		>5mmol/L % (95% CI)	>6mmol/L % (95% CI)	>6.5mmol/L % (95% CI)	>5mmol/L % (95% CI)	>6mmol/L % (95% CI)	>6.5mmol/L % (95% CI)
All diagnoses	Sn.	6.55 (5.84-7.35)	19.32 (16.73-22.21)	21.81 (18.17-25.95)	7.50 (6.83-8.22)	23.34 (20.95-25.91)	29.49 (25.76-33.51)
	Sp.	99.98 (99.96-99.98)	99.79 (99.76-99.83)	99.70 (99.66-99.74)	99.79 (99.75-99.82)	99.56 (99.50-99.61)	99.40 (99.34-99.46)

	PPV	94.74 (91.50-96.78)	54.04 (48.23-59.73)	32.98 (27.78-38.64)	76.85 (73.11-80.21)	48.15 (43.96-52.36)	28.89 (25.23-32.85
	NPV	94.01 (93.83-94.19)	99.00 (98.92-99.07)	99.48 (99.42-99.53)	92.00 (91.78-92.20)	98.66 (98.57-98.75)	99.42 (99.35-99.47)
Main/most responsible diagnosis	Sn.	2.65 (2.20-3.18)	8.53 (6.79-10.68)	9.05 (6.69-12.13)	1.16 (0.91-1.47)	4.94 (3.81-6.37)	7.94 (5.93-10.56)
	Sp.	99.99 (99.97-99.99)	99.92(99.90-99.94)	99.88 (99.85-99.90)	99.99 (99.99-100)	99.98 (99.97-99.99)	99.96 (99.94-99.97)
	PPV	93.16 (87.09-96.49)	58.12 (49.06-66.66)	33.33 (25.44-42.28)	95.52 (87.64-98.47)	82.09 (71.25-89.45)	62.69 (50.72-73.28)
	NPV	93.78 (93.59-93.96)	98.87 (98.78-98.95)	99.39 (99.33-99.45)	91.51 (91.29-91.72)	98.36 (98.26-98.45)	99.24 (99.17-99.31)
Pre-admit diagnosis					5.84 (5.25-6.49)	19.93 (17.69-22.38)	25.71 (22.17-29.60)
					99.92 (99.89-99.94)	99.77 (99.73-99.80)	99.63 (99.58-99.68)
					87.30 (83.52-90.31)	60.00 (54.93-64.86)	36.76 (32.00-41.78)
					91.87 (91.66-92.08)	98.61 (98.52-98.70)	99.39(99.32-99.44)

Abbreviations: ICD-10, International Classification of Diseases, 10th revision; Sn, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value

Serum potassium values as a continuous measure in groups of patients with hospital encounters that were code positive or negative are presented in Table 4 and Figure 1. There were highly statistically significant differences in serum potassium levels between the individuals who were code positive and code negative (for all algorithms; independent samples t-test; all p-values <0.0001). For example, in an emergency department using the 'all diagnosis' coding algorithm, the median (IQR) serum potassium value for patients who were code positive was 6.1 mmol/L (5.7 to 6.8 mmol/L), and 4.0 mmol/L (3.7 to 4.4 mmol/L) for those who were code negative. Similar results were evident for patients at hospital admission and for all algorithms.

Table 4. Serum potassium values (mmol/L) in patients who were code positive and code negative for ICD-10 code E87.5 at presentation to the emergency department and at hospital admission according to different algorithms.

		Emergency Department			Hospital Admission		
		N	Median	IQR	N	Median	IQR
All diagnosis	No	64294	4.0	3.7- 4.4	63957	4.1	3.8- 4.5
	Yes	285	6.1	5.7- 6.8	540	6.0	5.1- 6.7
Main/most responsible diagnosis	No	64462	4.0	3.7- 4.4	64430	4.1	3.8- 4.5
	Yes	117	6.2	5.7- 6.9	67	6.9	6.1- 7.5
Pre-admit diagnosis					No 64127	4.1	3.8- 4.5
					Yes 370	6.3	5.5- 6.9

Abbreviations: N, number of patients; IQR, interquartile range

A total of 51.3% of patients that presented to an emergency department had a baseline pre-hospital encounter serum potassium value. These baseline tests occurred at a median (IQR) of 75 (25 to 174) days prior to the emergency department presentation. This allowed us to examine the median change in serum potassium values (i.e. emergency department value minus the baseline

value). These results are presented in Appendix D. In an emergency department, for code positive patients (using the 'all diagnoses' algorithm), the median (IQR) change in serum potassium values was 1.5 mmol/L (0.8 to 2.3 mmol/L) and for those who were code negative the change was -0.1 mmol/L (-0.5 to 0.3 mmol/L). The mean difference in the change in serum potassium values between code positive and code negative patients was 1.6 mmol/L (95% CI: 1.5 to 1.7 mmol/L). Similar results were evident for the 61.3% of patients at hospital admission who had a baseline serum potassium measurement (which was taken a median (IQR) of 29 (14 to 97) days prior to hospital admission). In these patients using the 'all diagnosis' algorithm, the median (IQR) change (hospital value minus baseline value) in serum potassium was 1.3 mmol/L (0.4 to 2.3 mmol/L) for those who were code positive and 0.0 mmol/L (-0.3 to 0.4 mmol/L) for those who were code negative. The mean difference in the change in serum potassium values between code positive and code negative patients was 1.4 mmol/L (95% CI: 1.2 to 1.5 mmol/L).

DISCUSSION

In this population-based validation study, we found that the best performing ICD-10 coding algorithm for hyperkalemia at presentation to an emergency department and at hospital admission was when the code was present in any diagnosis field ('all diagnosis'), regardless of the threshold of serum potassium used to define hyperkalemia. Overall, the specificity for the ICD-10 hyperkalemia code was very high while the sensitivity was very low. There was a high false negative rate in both the emergency room and hospital admission settings: just over 90% of patients with a serum potassium value of 5.5mmol/L or more did not receive a code for hyperkalemia using the all diagnoses category. Even when considering severe hyperkalemia (serum potassium >6.5mmol/L), the sensitivity only reached a maximum of about 29%.

The most responsible diagnosis is defined as the illness responsible for the longest length of stay or the greatest use of hospital resources. This algorithm demonstrated the lowest sensitivity amongst all the algorithms in our study, likely because the most responsible illness was attributed to the underlying problem that caused the hyperkalemia rather than the hyperkalemia itself.

We found that sensitivity increased as the severity of hyperkalemia increased. Milder forms of hyperkalemia tend to be asymptomatic and can be managed without aggressive treatment. Consequently, the physician may be less inclined in such cases to record a diagnosis of hyperkalemia in the medical chart. In addition, hyperkalemia often co-occurs with other more serious disorders that the physician may find to be paramount to hyperkalemia when recording conditions in the medical chart. Furthermore, if the physician writes serum potassium 5.7 mmol/L for example, but does not write "hyperkalemia" or "high potassium" the coders are unable to assume any diagnosis and some events are not recorded for this reason.[18]

Of the patients who had hyperkalemia at presentation to an emergency department and at hospital admission (defined by a value >5.5mmol/L), only 14.1% and 14.6%, respectively were correctly coded as hyperkalemic. The low sensitivity at this threshold may be due to less enthusiasm to act on values that are only modestly elevated. Despite this, the code was successful in differentiating between two groups of patients with distinct serum potassium

values. Code negative patients had serum potassium values in the normal range (3.5 to 5.1mmol/L) and when the code was present, values were much higher (≥6 mmol/L).

Our study has several strengths. It is the first study to validate the ICD-10 code for hyperkalemia and first to validate hyperkalemia using laboratory values as the reference standard. We validated the ICD-10 code in both an emergency department and at hospital admission examining different types of diagnoses. Previous electrolyte validation studies have not looked at these settings nor did they examine all the possible diagnosis types as done in our study. Although there have been no similar hyperkalemia validation studies, other electrolyte studies have demonstrated similarly low sensitivities of the ICD codes. [20,21]

All citizens in Ontario receive universal healthcare and patients over 65 have their medications paid for by the provincial government. These two factors facilitated the collection of health administrative data and gave us the ability to have a large sample size. We based our validation on laboratory data from twelve hospitals in the most populous province in Canada. Another study validating the ability of a computerized program to correctly identify hyperkalemia using the ICD-9 code restricted the analysis to a single centre and to the specific population of diabetics.[7] Additionally, another study describing the frequency of hyperkalemic events also focused on a specific population of veterans.[22] Because we used a more varied and larger population, we were able to obtain good precision for estimates that are quite generalizable.

The validity measures that we used in this study have also been used in several other studies comparing ICD codes with clinical outcomes, including two validations of another electrolyte disorder, hyponatremia.[23-28] Many validation studies compare diagnostic codes to information written in medical charts. However, the most accurate way to determine whether hyperkalemia is truly present is to use laboratory values as we did in the current study.

Our study does have some limitations. We validated the ICD-10 hyperkalemia code in a population of patients over age 65. This patient population is particularly vulnerable to developing hyperkalemia.[29] Additionally, these results inform future analyses of the Ontario healthcare databases since most pharmacoepidemiologic research using these data sources are conducted in patients over age 65 (where receipt of prescription medications is a universal benefit). Moreover, a greater proportion of elderly patients receive a laboratory test compared to younger patients, reducing the potential for selection bias.[30] Nonetheless, code validity in younger populations should be examined in future studies.

We were unable to determine if the patients who presented to an emergency department or at hospital admission showed arrhythmias or other sequelae of the high serum potassium value. However, we do know the code did identify acute changes, as demonstrated by a mean increase in serum potassium of 1.5 mmol/L above the baseline pre-hospital value. Patients with acute changes in serum potassium are most likely to be symptomatic from the condition.

Finally, we recognize that we did not capture those patients who may have had severe hyperkalemia but did not go to an emergency department or hospital, or those who presented but failed to have serum potassium measured. However, the latter is less of a concern as serum potassium is a common test for most patients who present for acute medical care. We were unable to detect outpatient claims for hyperkalemia in this study as there is no administrative code set available for this in our jurisdiction. Nevertheless, emergency department and hospital records do detect more severe forms of hyperkalemia making this of particular interest to clinicians and policy decision makers.

CONCLUSION

Analyses of administrative codes are a cost-efficient way to assess patient comorbidity and disease in large population-based studies. However, as observed by the low sensitivity in the current study, many individuals with an ICD-10 database code for hyperkalemia are missed leading to an underestimate of the true incidence of the condition at hospital encounters. It is important that members of the health community responsible for making decisions about healthcare be aware of the conditions and limitations of these codes to make fully informed evaluations. Nonetheless, the group of patients who were positive for this code were distinguishable from the group of patients who were negative for the code with distinct serum potassium values in both settings. The findings of this validation study guide proper use of the ICD-10 hyperkalemia code in future research using health administrative data.

Contributors
JLF participated in the coordination of the study, study design, provided interpretation of study results, and drafted the manuscript. SZS participated in the study design, performed the analysis and provided interpretation of study results. SG contributed to the study design and interpretation of study results. MAW and AKJ contributed to the study design and provided feedback on the manuscript. AXG conceived of the study, participated in its design and interpretation, helped draft the manuscript and provided feedback on the manuscript. All authors read and approved the final manuscript.

Funding
The study was supported by the Canadian Institutes of Health Research. Dr. Garg was supported by a Clinician Scientist Award from the Canadian Institutes of Health Research.

Competing interests
The authors declare that they have no competing interests.

Figure 1 Legend
Serum potassium measurements among patients who are code positive and code negative for hyperkalemia (when the code was considered in the format 'all diagnoses'). For both presentation to an emergency department and at hospital admission, patients who for positive for the hyperkalemia code had a significantly higher serum potassium measurement than patients who were code negative. The boxes represent the interquartile range (50% of the values). The line across the box indicates the median. The star indicates the mean. The whiskers extend to the 95th and 5th percentile

REFERENCES

1 Elixhauser A, Steiner C, Harris RD, et al. Comorbidity measures for use with administrative data. Med Care 1998;36:8-27.

2 Schaefer TJ, Wolford RW. Disorders of potassium. Emerg Med Clin N Am 2005;23:723-747.

3 Elliott MJ, Ronksley PE, Clase CM, et al. Management of patients with acute hyperkalemia. CMAJ 2010;182:1631-1635.

4 Palmer BF. Managing hyperkalemia caused by inhibitors of the renin-angiotensin-aldosterone system. N Engl J Med 2004;351:585-592.

5 Reardon LC, Macpherson DS. Hyperkalemia in outpatients using angiotensin-converting enzyme inhibitors. Arch Intern Med 1998;158:26-32.

6 World Health Organization. Fact Sheet May 2012: International Classification of Diseases (ICD). www.who.int/entity/classifications/icd/revision/icdfactsheet.pdf (accessed 18 May 2012).

7 Raebel MA, Smith ML, Saylor G, et al. The positive predictive value of a hyperkalemia diagnosis in automated health care data. Pharmacoepidemiol Drug Saf 2010;19:1204-1208.

8 Statistics Canada. Age and Sex Highlights Table 2011 Census. http://www12.statcan.gc.ca/census-recensement/2011/dp-pd/hlt-fst/as-sa/?Lang=E (accessed 29 May 2012).

9 Gandhi S, Shariff S, Beyea M, et al. Identifying geographical regions serviced by hospitals to assess laboratory based outcomes. (under review at BMJ Open).

10 STAndards for the Reporting of Diagnostic accuracy studies. STARD Checklist. http://www.stard-statement.org/ (accessed 13 December 2011).

11 Levy AR, O'Brien BJ, Sellors C, et al. Coding accuracy of administrative drug claims in the Ontario Drug Benefit database. Can J Clin Pharmacol 2003;10:67-71.

12 Cerner. Laboratory. http://www.cerner.com/solutions/Hospitals_and_Health_Systems/Laboratory/ (accessed 18 May 2012)

13 Zhao YY, Weir MA, Manno M et al. New fibrate use and acute renal outcomes in elderly adults: a population-based study. *Ann Intern Med* 2012;156:560-569

14 Jain AK, Cuerden MS, McLeod I et al. Reporting of the estimated glomerular filtration rate was associated with increased use of angiotensin-converting enzyme inhibitors and angiotensin-II receptor blockers in CKD. *Kidney Int* 2012;81:1248-1253.

15 Weir MA, Gomes T, Mamdani M, et al. Impaired renal function modifies the risk of severe hypoglycaemia among users of insulin but not glyburide: a population-based nested case–control study. *Nephrol Dial Transplant* 2011;26:1888-1894.

16 Molnar AO, Coca SG, Devereaux PJ, et al. Statin use associates with lower incidence of acute injury after major elective surgery. *J Am Soc Nephrol* 2011;22:939-946.

17 Juurlink DN, Mamdani MM, Lee DS, et al. Rates of hyperkalemia after publication of the Randomized Aldactone Evaluation Study. *NEJM* 2004;351:543-551.

18 Canadian Institute for Health Information. Canadian coding standards for Version 2012 ICD-10-CA and CCI. https://secure.cihi.ca/free_products/canadian_coding_standards_2012_e.pdf (accessed 02 May 2012).

19 Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of

seven methods. *Stat Med* 1998;17:857-872.

20 Movig KL, Leufkens HG, Lenderink AW, et al. Validity of hospital discharge International Classification of Diseases (ICD) codes for identifying patients with hyponatremia. *J Clin Epidemiol* 2003;56:530-535.

21 Shea AM, Curtis LH, Szczech LA, et al. Sensitivity of International Classification of Diseases codes for hyponatremia among commercially insured outpatients in the United States. *BMC Nephrol* 2008; 9:5.

22 Einhorn LM, Zhan M, Hsu VD, et al. The frequency of hyperkalemia and its significance in chronic kidney disease. *Arch Intern Med* 2009;169:1156-1162.

23 Waiker SS, Wald R, Chertow GM, et al. Validity of *International Classification of Diseases, Ninth Revision, Clinical Modification* codes for acute renal failure. *J Am Soc Nephrol* 2006;17:1688-1694.

24 Romano PS, Roos LL, Luft HS, et al. A comparison of administrative versus clinical data: coronary artery bypass surgery as an example. Ischemic Heart Disease Patient Outcomes Research Team. *J Clin Epidemiol* 1994;47:249–60.

25 Quan H, Parsons GA, Ghali WA: Validity of procedure codes in International Classification of Diseases, 9th revision, clinical modification administrative data. *Med Care* 2004;42:801-809.

26 Raiford DS, Perez Gutthann S, Garcia Rodriguez LA. Positive predictive value of ICD-9 codes in the identification of cases of complicated peptic ulcer disease in the Saskatchewan hospital automated database. *Epidemiology* 1996;7:101–104.

27 Gankam KF, Andres C, Sattar L, et al. Mild hyponatremia and risk of fracture in the ambulatory elderly. *Q J Med* 2008;101:583-588.

28 Waikar SS, Mount DB, Curhan GC. Mortality after hospitalization with mild, moderate, and severe hyponatremia. *Am J Med* 2009;122:857-865.

29 Obreli-Neto PR, Nobili A, de Oliveira Baldoni A, et al. Adverse drug reactions caused by drug-drug interactions in elderly outpatients: a prospective cohort study. *Eur J Clin Pharmacol* 2012 May 30. [Epub ahead of print]

30 Singal BM, Hedges JR, Rousseau EW, et al. Geriatric patient emergency visits. Part 1: Comparison of visits by geriatric and younger patients. *Ann Emerg Med* 1992;21:802-807.

Validity of the International Classification of Diseases Tenth Revision code for hyperkalemia in elderly patients at presentation to an emergency department and at hospital admission

Jamie L. Fleet[1], Salimah Z. Shariff[2], Sonja Gandhi[1,3], Matthew A. Weir[1,3], Arsh K. Jain[1,2], Amit X. Garg[1,2,3].

1. Division of Nephrology, Department of Medicine, Western University, London, Canada
2. Institute for Clinical Evaluative Sciences, Toronto, Canada
3. Department of Epidemiology & Biostatistics, Western University, London, Canada

Corresponding Author: 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

Publication Type: Research Article

Word Count: 3396 words

Abstract: 277 words

Short title: Validity of the ICD-10 code for hyperkalemia

This study was conducted at the Institute for Clinical Evaluative Sciences (ICES), which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). The opinions, results, and conclusions reported in this paper are those of the authors and are independent from the funding sources. No endorsement by ICES or the Ontario MOHLTC is intended or should be inferred.

We thank Barbara Jones, Jeff Lamond, and the late Milton Haines for their help in providing access to Gamma-Dynacare laboratory data.

We thank the team at London Health Sciences Centre, St. Joseph's Health Care, and the Thames Valley Hospitals for providing access to the Cerner laboratory data.

ABSTRACT

Objectives: Evaluate the validity of the *International Classification of Diseases, Tenth Revision* (ICD-10) code for hyperkalemia (E87.5) in two settings: at presentation to an emergency department and at hospital admission.

Design: Population-based validation study

Setting: 12 hospitals in Southwestern Ontario, Canada, from 2003 to 2010

Participants: Elderly patients with serum potassium values at presentation to an emergency department (n=64,579) and at hospital admission (n=64,497).

Primary Outcome: Sensitivity, specificity, positive predictive value, and negative predictive value. Serum potassium values in patients with and without a hyperkalemia code (code positive and code negative, respectively)

Results: The sensitivity of the best performing ICD-10 coding algorithm for hyperkalemia (defined by serum potassium >5.5 mmol/L) was 14.1% (95% confidence interval (CI): 12.5 to15.9%) at presentation to an emergency department and 14.6% (95% CI: 13.3 to16.1%) at hospital admission. Both specificities were greater than 99%. In the two settings, the positive predictive values were 83.2% (95% CI: 78.4 to 87.1%) and 62.04% (95% CI: 57.9 to 66.0%), while the negative predictive values were 97.8% (95% CI: 97.6 to 97.9%) and 96.9% (95% CI: 96.8 to 97.1%). In patients who were code positive for hyperkalemia, median (interquartile range; IQR) serum potassium values were 6.1 (5.7 to 6.8) mmol/L at presentation to an emergency department and 6.0 (5.1to 6.7) mmol/L at hospital admission. For code negative patients median (IQR) serum potassium values were 4.0 (3.7 to 4.4) mmol/L and 4.1 (3.8 to 4.5) mmol/L in each of the two settings, respectively.

Conclusions: Patients with hospital encounters who were ICD-10 E87.5 hyperkalemia code positive and negative had distinct higher and lower serum potassium values, respectively. However, due to very low sensitivity, the incidence of hyperkalemia is underestimated.

Keywords: Hyperkalemia, serum potassium, validation, sensitivity, specificity, validity, International Classification of Diseases

ARTICLE SUMMARY

Article Focus

- This study described the validity of the ICD-10 code for hyperkalemia (E87.5) compared to serum potassium laboratory values, where the latter served as the reference standard.
- Knowledge of the accuracy of the code at hospital encounters guides its judicious use in health services research.

Key Messages

- The ICD-10 hyperkalemia code has very high specificity, but very low sensitivity, which underestimates the true incidence of hyperkalemia at presentation to an emergency department and at hospital admission.
- Being positive or negative for the code does distinguish between two groups of patients with distinct serum potassium measurements.

Strengths and Limitations

- This is the first study to provide diagnostic information on the validity of the ICD-10 code for hyperkalemia.
- It was a large population-based study and included serum potassium values from twelve hospitals across Ontario.
- Code validity in younger populations should be examined in future studies.

INTRODUCTION

Use of information in healthcare administrative databases is a relatively easy and efficient way to identify patients with prior or current disease. It is also a simple way for the medical community to assess resources and usage of healthcare services. However, administrative codes are not always accurate.[1] This can lead to the underreporting or over reporting of some diseases (i.e. individuals who have the disease but where there is no evidence of the respective database code; or individuals who have evidence of the database code but where there is no evidence of the disease). Knowledge of the validity of various database codes guides their optimal use for research, quality assurance, and health system planning.

Hyperkalemia, or high serum potassium, is a fairly common adverse event. Normal levels of serum potassium range from 3.3 to 5.1 mmol/L, with hyperkalemia often defined by a value of 5.5 mmol/L or higher.[2] High serum potassium levels can have serious deleterious effects including arrhythmia and death.[3] Some comorbidities that predispose to hyperkalemia include chronic kidney disease and cancer. Hyperkalemia can also occur due to use of a variety of prescription medications, including angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB),beta blockers, and certain types of diuretics.[4] Approximately 10% of patients prescribed an ACE inhibitor develop hyperkalemia in the year following their initial prescription.[5]

The 10th revision of the International Classification of Diseases (ICD-10) system has been used to code healthcare encounters in Canada since 2002, and has also been implemented in over 100 other countries since its inception.[6] Yet, after careful bibliographic database searching, we could find no published validation for the ICD-10 hyperkalemia code using serum potassium laboratory values as the reference standard. There was a single validation study that considered the ICD-9 hyperkalemia code from the Kaiser Permanente Health Management Organization in the United States, but this study only focused on how accurately it was used in automated health care data.[7]

We conducted the current study to determine the accuracy of the ICD-10 code for hyperkalemia (E87.5) in two acute care settings: at presentation to an emergency department and at hospital admission. We compared the ICD-10 code to actual serum potassium laboratory values.

METHODS

Study Design

We conducted a retrospective population-based validation study using linked administrative databases housed at the Institute for Clinical Evaluative Sciences (ICES). The province of Ontario, Canada has approximately 13 million residents, 14% of whom are 65 years of age or older.[8] Residents have universal access to hospital care and physician services and those 65 years of age or older have universal prescription drug coverage. Within Southwestern Ontario, we considered a catchment area that included approximately 80,000 adults 65 years of age and older, according to census information from 2006.[9] There were 12 hospitals that served this area from which we gathered laboratory information. We compared the ICD-10 hyperkalemia code E87.5 to serum potassium laboratory values as the reference standard in two settings: i) at

presentation to an emergency department and ii) at hospital admission. We calculated the sensitivity, specificity, positive predictive value, and negative predictive value of several ICD-10 coding algorithms. Also, because serum potassium is a continuous measure, we compared patients who were positive for the code to those with hospital encounters who were negative for the code. The reporting of this study follows guidelines set out for studies of diagnostic accuracy (Appendix A).[10] We conducted our study according to a pre-specified protocol that was approved by the institutional review board at Sunnybrook Health Sciences Centre (Toronto, Ontario).

Data Sources

We ascertained outcome data as well as the presence of relevant comorbidities for exclusions and baseline characteristics using records from seven linked databases. The Ontario Drug Benefit Plan (ODB) database contains records of prescriptions from outpatient pharmacies. The dispensing of medications for patients aged 65 and older is accurately recorded in this database with an error rate of less than 1%.[11] The Canadian Institute for Health Information (CIHI) National Ambulatory Care Reporting System (NACRS) contains ambulatory care information on emergency room visits, outpatient procedures, and day surgeries. The CIHI Discharge Abstract Database (CIHI-DAD) reports inpatient procedures, diagnoses, and discharge summaries for patients hospitalized in Ontario. The Ontario Health Insurance Plan (OHIP) database contains all physician and other specific health care provider claims for medical services covered under the provincial health insurance plan. Lastly, the Registered Persons Database (RPDB) contains demographic information, such as birth date and sex, for all Ontario residents who have ever been covered by OHIP.

In addition to the five administrative databases described above, we used two laboratory datasets to determine serum potassium values. An electronic medical record Cerner® (Kansas City, Missouri, USA) contains inpatient, outpatient, and emergency department laboratory values for 12 hospitals in Southwestern Ontario.[12] Gamma-Dynacare performs outpatient laboratory tests in Southwestern Ontario and was used to obtain baseline laboratory values for a subpopulation. We have successfully used these datasets in previous studies.[13-16]

Participants

Individuals included in our study had at least one hospital-based serum potassium laboratory value between June 1st, 2003 and September 30th, 2010. We considered patients 66 years of age or older, to allow for a minimum of one year of baseline prescription information. Older patients often have important risk factors for hyperkalemia and have full medication coverage through the provincial drug plan.[17] We excluded laboratory tests with missing demographic information (approximately 0.75% of the tests). We also excluded hospital stays that were longer than 90 days to ensure we had data for the entire hospitalization, particularly when these occurred towards the end of our accrual period. For hyperkalemia at presentation to an emergency department, the relevant potassium laboratory test must have occurred on an emergency department registration date or the day after. We allowed values for the date after registration to account for patients who may have come to an emergency department but did not receive their test until after midnight (i.e. the day after). For hyperkalemia at hospital admission, the relevant potassium laboratory test must have been done either in an emergency department

up to two days prior to hospital admission, or up to one day after the date of hospital admission. We assigned this timeframe to account for any delays between an emergency department presentation and hospital admission, and any treatment that resulted in subsequent lower potassium values from the initial measurement. In both the emergency room and hospital settings, if multiple tests occurred, we took the highest available value. When multiple eligible hospital presentations were identified for a given patient over the study period, we randomly selected one.

Administrative Database Codes (Diagnostic Test)

In Canada, trained coders record appropriate diagnostic codes and their associated attributes based on information from a patient's chart. Coders in Canada follow specific rules and guidelines set out by CIHI when assigning diagnostic codes based on a patient's file. They are not allowed to interpret any diagnostic tests, such as x-rays or lab values, unless a diagnosis is specifically written by the physician in the medical chart.[18] Within the NACRS database, 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. The CIHI-DAD provides the ability to record up to 25 diagnoses during a hospital admission, each of which can have additional diagnosis types. For example, coders must assign one of the diagnoses the diagnosis type 'M', which represents 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 assign a diagnosis type '1' to any of the listed diagnoses that existed prior to the admission and were treated during the hospital stay.

In this study, based on possible diagnosis types we developed two unique algorithms to assess hyperkalemia at presentation to an emergency department and three unique algorithms to assess hyperkalemia at hospital admission. We used the ICD-10 code E87.5, which is defined as "hyperkalemia". There is a Canadian Modification of the ICD-10 code system which provides additional information on other comorbidities but does not alter the hyperkalemia coding. The two emergency department algorithms identified records with code E87.5 recorded: i) as the main problem (referred to as "main diagnosis"), or ii) in any of the 10 potential diagnostic fields (referred to as "all diagnosis"). The three hospital admission algorithms identified records with code E87.5 recorded: i) with the diagnosis type of 'M' (most responsible; referred to as "most responsible diagnosis"), ii) with the diagnosis type of '1' (pre-admit comorbidity; referred to as "pre-admit diagnosis"), or iii) in any one of 25 potential diagnosis fields and any diagnosis type (referred to as "all diagnosis").

Potassium Laboratory Values (Reference Standard)

Serum potassium laboratory tests were done either in an emergency department or in hospital and were used as the reference standard. The laboratory tests were performed with the Roche Modular Ion Selective Electrode® system (Basel, Switzerland). The primary threshold to define hyperkalemia was a serum potassium value >5.5 mmol/L. Other thresholds were also considered: >5.0, >6.0, and >6.5 mmol/L.

Data Analysis

We assessed severity of hyperkalemia based on several thresholds of serum potassium values indicated above. In the emergency department and hospital admission settings, we calculated the sensitivity, specificity, positive predictive value, and negative predictive value of each coding algorithm for each serum potassium level (see Appendix B for two-by-two contingency table describing the relevant formulae). For the different algorithms we also contrasted the mean, median, and interquartile ranges of serum potassium values for those who were positive for the code compared to patients with hospital encounters who had no evidence of the code (i.e. code negative). We calculated 95% confidence intervals (CI) for single proportions using the Wilson Score method.[19] We expressed continuous variables as medians with interquartile ranges (IQR) and compared means using independent samples t-tests.We performed all analyses with SAS version 9.2 (SAS Institute Incorporated, Cary, North Carolina, USA, 2008).

RESULTS

The cohort creation and specific exclusions for both settings are shown in Appendix C. Patient baseline characteristics are shown in Table 1.

Table 1. Baseline characteristics for patients with serum potassium values obtained at presentation to emergency department and at hospital admission.

	At emergency department N = 64579	At hospital admission N = 64497
Demographics		
Age, years, *median (IQR)*	77 (71-83)	77 (71-83)
Women, *n (%)*	35,630 (55.2)	32,965 (51.1)
Income quintile, *n (%)*		
One (lowest)	14,231 (22.0)	13,900 (21.6)
Two	12,921 (20.0)	12,928 (20.0)
Three (middle)	12,542 (19.4)	12,792 (19.8)
Four	11,496 (17.8)	11,601 (18.0)
Five (highest)	12,407 (19.2)	12,446 (19.3)
Rural Location, *n (%)*	11,438 (17.7)	13,248 (20.5)
Year of cohort entry, *n (%)*		
2003 – 2004	6,581 (10.2)	11,601 (18.0)
2005 – 2006	15,188 (23.5)	15,640 (24.3)
2007 – 2008	20,569 (31.9)	18,474 (28.6)
2009 – 2010	22,236 (34.4)	18,782 (29.1)
Long-term Care Facility Utilization, *n (%)*	4,137 (6.4)	3,681 (5.7)
Comorbidities, *n (%)*		
Chronic kidney disease‡	5,335 (8.3)	6,427 (10.0)
Diabetes mellitus£	13,142 (20.4)	13,632 (21.1)
Peripheral vascular disease	1,690 (2.6)	2,937 (4.6)
Coronary artery disease¶	26,979 (41.8)	30,528 (47.3)
Heart failure	13,691 (21.2)	15,173 (23.5)
Stroke/Transient ischemic attack	2,455 (3.8)	2,655 (4.1)
Chronic liver disease	1,238 (1.9)	1,645 (2.6)
Medication use in prior 6 months, *n (%)*		
Angiotensin-converting enzyme inhibitors	22,690 (35.1)	23,770 (36.9)
Angiotensin-receptor blockers	10,442 (16.2)	10,012 (15.5)
Potassium sparing diuretics	5,657 (8.8)	6,147 (9.5)
Loop diuretics	13,553 (21.0)	14,618 (22.7)
Thiazide diuretics	12,334 (19.1)	12,458 (19.3)
Calcium channel blockers	19,126 (29.6)	19,951 (30.9)
Beta adrenergic antagonists	21,989 (34.1)	23,382 (36.3)
Statins	24,892 (38.6)	25,273 (39.2)
NSAIDS (excluding aspirin)	11,621 (18.0)	12,573 (19.5)
Anticonvulstants	3,847 (6.0)	3,740 (5.8)
Antidepressants	15,662 (24.3)	15,075 (23.4)

Antipsychotics	4,001 (6.2)	3,532 (5.5)
Benzodiazepine	15,295 (23.7)	15,515 (24.1)
Antineoplastic drugs	3,285 (5.1)	3,624 (5.6)
Baseline Laboratory Measurements*		
Serum Creatinine levels		
Most recent serum creatinine, µmol/L, *median (IQR)*	90 (74-114)	90 (74-114)
GFR[Ŧ] Levels		
Most recent eGFR mL/min/1.73m², *median (IQR)*	63 (47-79)	63(47-79)
eGFR category, *n (%)*		
≥60mL mL/min/1.73m²	20,807 (54.7)	23,842 (55.3)
45-59 mL/min/1.73m²	8,527 (22.4)	9,566 (22.2)
30-44 mL/min/1.73m²	5,466 (14.4)	5989 (13.9)
15-29 mL/min/1.73m²	2,362 (6.2)	2,694 (6.2)
<15 mL/min/1.73m²	850 (2.2)	1,021 (2.4)
Serum Sodium Levels		
Most recent serum sodium, mmol/L, *median, (IQR)*	139(137-141)	139(137-141)
Serum Potassium Levels		
Most recent serum potassium, mmol/L, *median (IQR)*	4.2 (3.8-4.5)	4.1(3.8-4.5)

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

[€] The year of cohort entry is also referred to as the index date

[‡] Assessed by administrative database codes: CIHI ICD-9 codes – 4030, 3031, 4039, 4040, 4041, 4049, 582, 583, 580, 581, 584, 585, 586, 587, 5880, 5888, 5889, 5937; CIHI ICD-10 codes – I12, I13, N01, N03, N05, N07, N14, N15, N00, N04, N08, N18, N19, N26, N25, N137, N280, N2888, N06, N391; OHIP diagnostic codes – 403, 580, 581, 585

[£] 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

*Available from emergency department, inpatient or outpatient settings for a subpopulation. A total of 33104 (51.3%), 32844 (50.9%), and 38012 (58.9%) patients at presentation to emergency department had a baseline serum potassium, sodium, and creatinine measurement available in the 7 to 365 days prior to the index date, respectively.. Among these patients, the baseline measurements were taken at a median (IQR) of 75 (25-174), 75(25-174), and 76 (26-173) days, respectively. A total of 39552 (61.3%), 39422 (61.1%), and 43112 (66.9%) patients at hospital admission had a baseline serum potassium, sodium, and creatinine measurement available in the 7 to 365 days prior to the index date, respectively. Among these patients, the baseline measurements were taken at a median (IQR) of 29 (14-97), 29 (14-97), and 32(14-101) days, respectively.

[Ŧ]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

Of the 64,579 patients who presented to an emergency department, 1,679 (2.6%) had a potassium value of >5.5 mmol/L. Of 64,497 patients who were admitted to hospital, 2,289 (3.5%) patients had a serum potassium level > 5.5 mmol/L. The diagnostic performance characteristics of the coding algorithms for hyperkalemia (defined by serum potassium >5.5mmol/L) in the two settings are presented in Table 2. The algorithm that considered the E87.5 code as 'all diagnoses' demonstrated the best sensitivity, recognizing the value still remained low. For example, the sensitivity of the 'all diagnoses' algorithm to detect a serum potassium > 5.5 mmol/L in an emergency department was 14.1% and the specificity was 99.9%. Similar results were obtained for individuals with hyperkalemia at hospital admission.

Table 2. Diagnostic performance characteristics for ICD-10 E87.5 coding algorithms for hyperkalemia defined by a serum potassium value > 5.5 mmol/L at presentation to an emergency department and at hospital admission.

		Emergency department					Hospital admission			
ICD-10 E87.5 Coding Algorithm		+	-		% (95% CI)		+	-		% (95% CI)
All diagnoses	+	237	48	Sn.	14.12 (12.53-15.86)	+	335	205	Sn.	14.64 (13.25-16.14)
	-	1442	62852	Sp.	99.92 (99.90-99.94)	-	1954	62003	Sp.	99.67 (99.62-99.71)
				PPV	83.16 (78.38-87.06)				PPV	62.04 (57.87-66.03)
				NPV	97.76 (97.64-97.87)				NPV	96.94 (96.81-97.08)
		+	-				+	-		
Main/most responsible diagnosis	+	98	19	Sn.	5.84 (4.81-7.06)	+	59	8	Sn.	2.58 (2.00-3.31%)
	-	1581	62881	Sp.	99.97 (99.95-99.98)	-	2230	62200	Sp.	99.99 (99.97-99.99)
				PPV	83.76 (76.03-89.35)				PPV	88.06 (78.17-93.82)
				NPV	97.55 (97.43-97.66)				NPV	96.54 (96.39-96.68)
							+	-		
Pre-admit diagnosis						+	276	94	Sn.	12.06 (10.79-13.46)
						-	2013	62114	Sp.	99.85 (99.82-99.88)
									PPV	74.59 (69.92-78.76)
									NPV	96.86 (96.72-96.99)

Abbreviations: ICD-10, International Classification of Diseases, 10th revision; Sn, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value, +, hyperkalemia yes; - hyperkalemia no

The performance characteristics of the coding algorithms for the additional thresholds of serum potassium (> 5 mmol/L, >6 mmol/L, and >6.5 mmol/L) are presented in Table 3. Of all the coding algorithms, those that considered the E87.5 code as 'all diagnoses' continued to demonstrate the best sensitivity across all the serum potassium thresholds. As well the sensitivity of the coding algorithm increased as hyperkalemia became more severe (i.e. a higher serum potassium level). For example, in an emergency department, for the 'all diagnoses' algorithm, the sensitivity was 6.6% for a potassium >5 mmol/L, and 21.8% for a potassium >6.5 mmol/L. Similarly, at hospital admission, for the 'all diagnoses' algorithm the sensitivity was 7.5% for a potassium > 5 mmol/L and 29.5% for a potassium > 6.5 mmol/L. The specificities were > 99% and comparable across the different thresholds of serum potassium.

Table 3. Diagnostic performance characteristics for other thresholds of serum potassium values at presentation to an emergency department and at hospital admission.

		Emergency Department			Hospital admission		
ICD-10 E87.5 Coding Algorithm		>5mmol/L % (95% CI)	>6mmol/L % (95% CI)	>6.5mmol/L % (95% CI)	>5mmol/L % (95% CI)	>6mmol/L % (95% CI)	>6.5mmol/L % (95% CI)
All diagnoses	Sn.	6.55 (5.84-7.35)	19.32 (16.73-22.21)	21.81 (18.17-25.95)	7.50 (6.83-8.22)	23.34 (20.95-25.91)	29.49 (25.76-33.51)
	Sp.	99.98 (99.96-99.98)	99.79 (99.76-99.83)	99.70 (99.66-99.74)	99.79 (99.75-99.82)	99.56 (99.50-99.61)	99.40 (99.34-99.46)

	PPV	94.74 (91.50-96.78)	54.04 (48.23-59.73)	32.98 (27.78-38.64)	76.85 (73.11-80.21)	48.15 (43.96-52.36)	28.89 (25.23-32.85
	NPV	94.01 (93.83-94.19)	99.00 (98.92-99.07)	99.48 (99.42-99.53)	92.00 (91.78-92.20)	98.66 (98.57-98.75)	99.42 (99.35-99.47)
Main/most responsible diagnosis	Sn.	2.65 (2.20-3.18)	8.53 (6.79-10.68)	9.05 (6.69-12.13)	1.16 (0.91-1.47)	4.94 (3.81-6.37)	7.94 (5.93-10.56)
	Sp.	99.99 (99.97-99.99)	99.92(99.90-99.94)	99.88 (99.85-99.90)	99.99 (99.99-100)	99.98 (99.97-99.99)	99.96 (99.94-99.97)
	PPV	93.16 (87.09-96.49)	58.12 (49.06-66.66)	33.33 (25.44-42.28)	95.52 (87.64-98.47)	82.09 (71.25-89.45)	62.69 (50.72-73.28)
	NPV	93.78 (93.59-93.96)	98.87 (98.78-98.95)	99.39 (99.33-99.45)	91.51 (91.29-91.72)	98.36 (98.26-98.45)	99.24 (99.17-99.31)
Pre-admit diagnosis					5.84 (5.25-6.49)	19.93 (17.69-22.38)	25.71 (22.17-29.60)
					99.92 (99.89-99.94)	99.77 (99.73-99.80)	99.63 (99.58-99.68)
					87.30 (83.52-90.31)	60.00 (54.93-64.86)	36.76 (32.00-41.78)
					91.87 (91.66-92.08)	98.61 (98.52-98.70)	99.39(99.32-99.44)

Abbreviations: ICD-10, International Classification of Diseases, 10th revision; Sn, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value

Serum potassium values as a continuous measure in groups of patients with hospital encounters that were code positive or negative are presented in Table 4 and Figure 1. There were highly statistically significant differences in serum potassium levels between the individuals who were code positive and code negative (for all algorithms; independent samples t-test; all p-values <0.0001). For example, in an emergency department using the 'all diagnosis' coding algorithm, the median (IQR) serum potassium value for patients who were code positive was 6.1 mmol/L (5.7 to 6.8 mmol/L), and 4.0 mmol/L (3.7 to 4.4 mmol/L) for those who were code negative. Similar results were evident for patients at hospital admission and for all algorithms.

Table 4. Serum potassium values (mmol/L) in patients who were code positive and code negative for ICD-10 code E87.5 at presentation to the emergency department and at hospital admission according to different algorithms.

		Emergency Department				Hospital Admission		
		N	Median	IQR		N	Median	IQR
All diagnosis	No	64294	4.0	3.7- 4.4	No	63957	4.1	3.8- 4.5
	Yes	285	6.1	5.7- 6.8	Yes	540	6.0	5.1- 6.7
Main/most responsible diagnosis	No	64462	4.0	3.7- 4.4	No	64430	4.1	3.8- 4.5
	Yes	117	6.2	5.7- 6.9	Yes	67	6.9	6.1- 7.5
Pre-admit diagnosis					No	64127	4.1	3.8- 4.5
					Yes	370	6.3	5.5- 6.9

Abbreviations: N, number of patients; IQR, interquartile range

A total of 51.3% of patients that presented to an emergency department had a baseline pre-hospital encounter serum potassium value. These baseline tests occurred at a median (IQR) of 75 (25 to 174) days prior to the emergency department presentation. This allowed us to examine the median change in serum potassium values (i.e. emergency department value minus the baseline

value). These results are presented in Appendix D. In an emergency department, for code positive patients (using the 'all diagnoses' algorithm), the median (IQR) change in serum potassium values was 1.5 mmol/L (0.8 to 2.3 mmol/L) and for those who were code negative the change was -0.1 mmol/L (-0.5 to 0.3 mmol/L). The mean difference in the change in serum potassium values between code positive and code negative patients was 1.6 mmol/L (95% CI: 1.5 to 1.7 mmol/L). Similar results were evident for the 61.3% of patients at hospital admission who had a baseline serum potassium measurement (which was taken a median (IQR) of 29 (14 to 97) days prior to hospital admission). In these patients using the 'all diagnosis' algorithm, the median (IQR) change (hospital value minus baseline value) in serum potassium was 1.3 mmol/L (0.4 to 2.3 mmol/L) for those who were code positive and 0.0 mmol/L (-0.3 to 0.4 mmol/L) for those who were code negative. The mean difference in the change in serum potassium values between code positive and code negative patients was 1.4 mmol/L (95% CI: 1.2 to 1.5 mmol/L).

DISCUSSION

In this population-based validation study, we found that the best performing ICD-10 coding algorithm for hyperkalemia at presentation to an emergency department and at hospital admission was when the code was present in any diagnosis field ('all diagnosis'), regardless of the threshold of serum potassium used to define hyperkalemia. Overall, the specificity for the ICD-10 hyperkalemia code was very high while the sensitivity was very low. There was a high false negative rate in both the emergency room and hospital admission settings: just over 90% of patients with a serum potassium value of 5.5mmol/L or more did not receive a code for hyperkalemia using the all diagnoses category. Even when considering severe hyperkalemia (serum potassium >6.5mmol/L), the sensitivity only reached a maximum of about 29%.

The most responsible diagnosis is defined as the illness responsible for the longest length of stay or the greatest use of hospital resources. This algorithm demonstrated the lowest sensitivity amongst all the algorithms in our study, likely because the most responsible illness was attributed to the underlying problem that caused the hyperkalemia rather than the hyperkalemia itself.

We found that sensitivity increased as the severity of hyperkalemia increased. Milder forms of hyperkalemia tend to be asymptomatic and can be managed without aggressive treatment. Consequently, the physician may be less inclined in such cases to record a diagnosis of hyperkalemia in the medical chart. In addition, hyperkalemia often co-occurs with other more serious disorders that the physician may find to be paramount to hyperkalemia when recording conditions in the medical chart. Furthermore, if the physician writes serum potassium 5.7 mmol/L for example, but does not write "hyperkalemia" or "high potassium" the coders are unable to assume any diagnosis and some events are not recorded for this reason.[18]

Of the patients who had hyperkalemia at presentation to an emergency department and at hospital admission (defined by a value >5.5mmol/L), only 14.1% and 14.6%, respectively were correctly coded as hyperkalemic. The low sensitivity at this threshold may be due to less enthusiasm to act on values that are only modestly elevated. Despite this, the code was successful in differentiating between two groups of patients with distinct serum potassium

values. Code negative patients had serum potassium values in the normal range (3.5 to 5.1mmol/L) and when the code was present, values were much higher (≥6 mmol/L).

Our study has several strengths. It is the first study to validate the ICD-10 code for hyperkalemia and first to validate hyperkalemia using laboratory values as the reference standard. We validated the ICD-10 code in both an emergency department and at hospital admission examining different types of diagnoses. Previous electrolyte validation studies have not looked at these settings nor did they examine all the possible diagnosis types as done in our study. Although there have been no similar hyperkalemia validation studies, other electrolyte studies have demonstrated similarly low sensitivities of the ICD codes. [20,21]

All citizens in Ontario receive universal healthcare and patients over 65 have their medications paid for by the provincial government. These two factors facilitated the collection of health administrative data and gave us the ability to have a large sample size. We based our validation on laboratory data from twelve hospitals in the most populous province in Canada. Another study validating the ability of a computerized program to correctly identify hyperkalemia using the ICD-9 code restricted the analysis to a single centre and to the specific population of diabetics.[7] Additionally, another study describing the frequency of hyperkalemic events also focused on a specific population of veterans.[22] Because we used a more varied and larger population, we were able to obtain good precision for estimates that are quite generalizable.

The validity measures that we used in this study have also been used in several other studies comparing ICD codes with clinical outcomes, including two validations of another electrolyte disorder, hyponatremia.[23-28] Many validation studies compare diagnostic codes to information written in medical charts. However, the most accurate way to determine whether hyperkalemia is truly present is to use laboratory values as we did in the current study.

Our study does have some limitations. We validated the ICD-10 hyperkalemia code in a population of patients over age 65. This patient population is particularly vulnerable to developing hyperkalemia.[29] Additionally, these results inform future analyses of the Ontario healthcare databases since most pharmacoepidemiologic research using these data sources are conducted in patients over age 65 (where receipt of prescription medications is a universal benefit). Moreover, a greater proportion of elderly patients receive a laboratory test compared to younger patients, reducing the potential for selection bias.[30] Nonetheless, code validity in younger populations should be examined in future studies.

We were unable to determine if the patients who presented to an emergency department or at hospital admission showed arrhythmias or other sequelae of the high serum potassium value. However, we do know the code did identify acute changes, as demonstrated by a mean increase in serum potassium of 1.5 mmol/L above the baseline pre-hospital value. Patients with acute changes in serum potassium are most likely to be symptomatic from the condition.

Finally, we recognize that we did not capture those patients who may have had severe hyperkalemia but did not go to an emergency department or hospital, or those who presented but failed to have serum potassium measured. However, the latter is less of a concern as serum potassium is a common test for most patients who present for acute medical care. We were unable to detect outpatient claims for hyperkalemia in this study as there is no administrative code set available for this in our jurisdiction. Nevertheless, emergency department and hospital records do detect more severe forms of hyperkalemia making this of particular interest to clinicians and policy decision makers.

CONCLUSION

Analyses of administrative codes are a cost-efficient way to assess patient comorbidity and disease in large population-based studies. However, as observed by the low sensitivity in the current study, many individuals with an ICD-10 database code for hyperkalemia are missed leading to an underestimate of the true incidence of the condition at hospital encounters. It is important that members of the health community responsible for making decisions about healthcare be aware of the conditions and limitations of these codes to make fully informed evaluations. Nonetheless, the group of patients who were positive for this code were distinguishable from the group of patients who were negative for the code with distinct serum potassium values in both settings. The findings of this validation study guide proper use of the ICD-10 hyperkalemia code in future research using health administrative data.

Contributors
JLF participated in the coordination of the study, study design, provided interpretation of study results, and drafted the manuscript. SZS participated in the study design, performed the analysis and provided interpretation of study results. SG contributed to the study design and interpretation of study results. MAW and AKJ contributed to the study design and provided feedback on the manuscript. AXG conceived of the study, participated in its design and interpretation, helped draft the manuscript and provided feedback on the manuscript. All authors read and approved the final manuscript.

Funding
The study was supported by the Canadian Institutes of Health Research. Dr. Garg was supported by a Clinician Scientist Award from the Canadian Institutes of Health Research.

Competing interests
The authors declare that they have no competing interests.

Figure 1 Legend
Serum potassium measurements among patients who are code positive and code negative for hyperkalemia (when the code was considered in the format 'all diagnoses'). For both presentation to an emergency department and at hospital admission, patients who for positive for the hyperkalemia code had a significantly higher serum potassium measurement than patients who were code negative. The boxes represent the interquartile range (50% of the values). The line across the box indicates the median. The star indicates the mean. The whiskers extend to the 95th and 5th percentile

REFERENCES

1 Elixhauser A, Steiner C, Harris RD, et al. Comorbidity measures for use with administrative data. Med Care 1998;36:8-27.

2 Schaefer TJ, Wolford RW. Disorders of potassium. Emerg Med Clin N Am 2005;23:723-747.

3 Elliott MJ, Ronksley PE, Clase CM, et al. Management of patients with acute hyperkalemia. CMAJ 2010;182:1631-1635.

4 Palmer BF. Managing hyperkalemia caused by inhibitors of the renin-angiotensin-aldosterone system. N Engl J Med 2004;351:585-592.

5 Reardon LC, Macpherson DS. Hyperkalemia in outpatients using angiotensin-converting enzyme inhibitors. Arch Intern Med 1998;158:26-32.

6 World Health Organization. Fact Sheet May 2012: International Classification of Diseases (ICD). www.who.int/entity/classifications/icd/revision/icdfactsheet.pdf (accessed 18 May 2012).

7 Raebel MA, Smith ML, Saylor G, et al. The positive predictive value of a hyperkalemia diagnosis in automated health care data. Pharmacoepidemiol Drug Saf 2010;19:1204-1208.

8 Statistics Canada. Age and Sex Highlights Table 2011 Census. http://www12.statcan.gc.ca/census-recensement/2011/dp-pd/hlt-fst/as-sa/?Lang=E (accessed 29 May 2012).

9 Gandhi S, Shariff S, Beyea M, et al. Identifying geographical regions serviced by hospitals to assess laboratory based outcomes. (under review at BMJ Open).

10 STAndards for the Reporting of Diagnostic accuracy studies. STARD Checklist. http://www.stard-statement.org/ (accessed 13 December 2011).

11 Levy AR, O'Brien BJ, Sellors C, et al. Coding accuracy of administrative drug claims in the Ontario Drug Benefit database. Can J Clin Pharmacol 2003;10:67-71.

12 Cerner. Laboratory. http://www.cerner.com/solutions/Hospitals_and_Health_Systems/Laboratory/ (accessed 18 May 2012)

13 Zhao YY, Weir MA, Manno M et al. New fibrate use and acute renal outcomes in elderly adults: a population-based study. *Ann Intern Med* 2012;156:560-569

14 Jain AK, Cuerden MS, McLeod I et al. Reporting of the estimated glomerular filtration rate was associated with increased use of angiotensin-converting enzyme inhibitors and angiotensin-II receptor blockers in CKD. *Kidney Int* 2012;81:1248-1253.

15 Weir MA, Gomes T, Mamdani M, et al. Impaired renal function modifies the risk of severe hypoglycaemia among users of insulin but not glyburide: a population-based nested case–control study. *Nephrol Dial Transplant* 2011;26:1888-1894.

16 Molnar AO, Coca SG, Devereaux PJ, et al. Statin use associates with lower incidence of acute injury after major elective surgery. *J Am Soc Nephrol* 2011;22:939-946.

17 Juurlink DN, Mamdani MM, Lee DS, et al. Rates of hyperkalemia after publication of the Randomized Aldactone Evaluation Study. *NEJM* 2004;351:543-551.

18 Canadian Institute for Health Information. Canadian coding standards for Version 2012 ICD-10-CA and CCI. https://secure.cihi.ca/free_products/canadian_coding_standards_2012_e.pdf (accessed 02 May 2012).

19 Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of

seven methods. *Stat Med* 1998;17:857-872.

20 Movig KL, Leufkens HG, Lenderink AW, et al. Validity of hospital discharge International Classification of Diseases (ICD) codes for identifying patients with hyponatremia. *J Clin Epidemiol* 2003;56:530-535.

21 Shea AM, Curtis LH, Szczech LA, et al. Sensitivity of International Classification of Diseases codes for hyponatremia among commercially insured outpatients in the United States. *BMC Nephrol* 2008; 9:5.

22 Einhorn LM, Zhan M, Hsu VD, et al. The frequency of hyperkalemia and its significance in chronic kidney disease. *Arch Intern Med* 2009;169:1156-1162.

23 Waiker SS, Wald R, Chertow GM, et al. Validity of *International Classification of Diseases, Ninth Revision, Clinical Modification* codes for acute renal failure. *J Am Soc Nephrol* 2006;17:1688-1694.

24 Romano PS, Roos LL, Luft HS, et al. A comparison of administrative versus clinical data: coronary artery bypass surgery as an example. Ischemic Heart Disease Patient Outcomes Research Team. *J Clin Epidemiol* 1994;47:249–60.

25 Quan H, Parsons GA, Ghali WA: Validity of procedure codes in International Classification of Diseases, 9th revision, clinical modification administrative data. *Med Care* 2004;42:801-809.

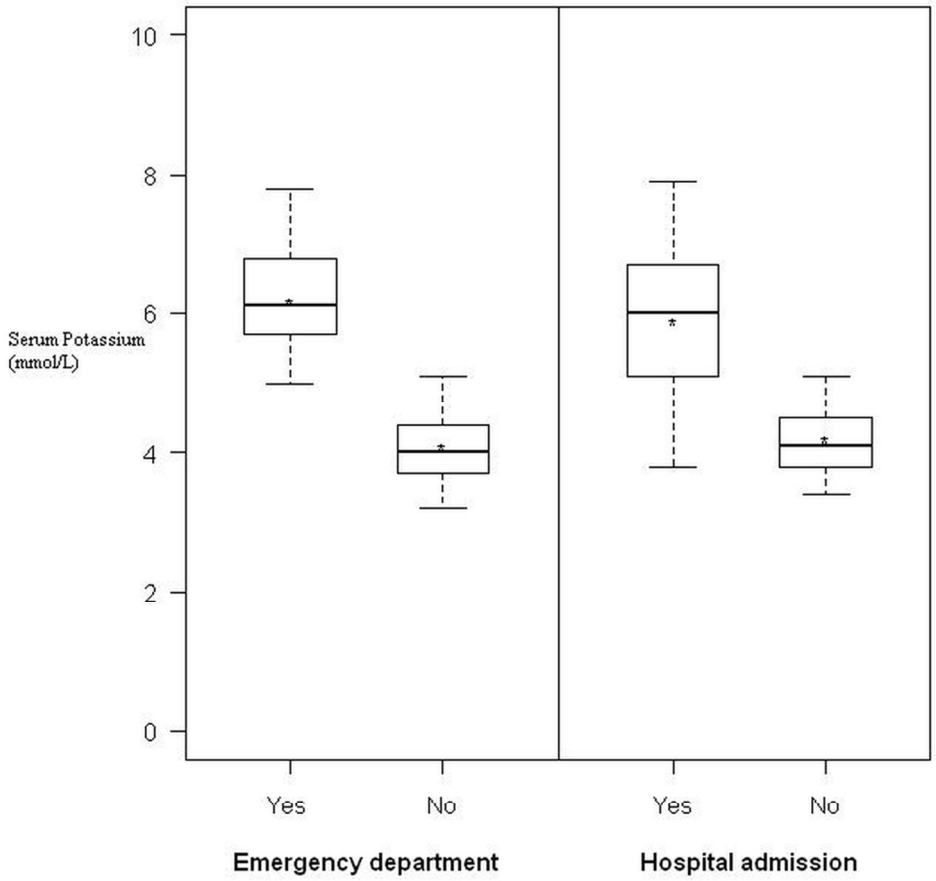
26 Raiford DS, Perez Gutthann S, Garcia Rodriguez LA. Positive predictive value of ICD-9 codes in the identification of cases of complicated peptic ulcer disease in the Saskatchewan hospital automated database. *Epidemiology* 1996;7:101–104.

27 Gankam KF, Andres C, Sattar L, et al. Mild hyponatremia and risk of fracture in the ambulatory elderly. *Q J Med* 2008;101:583-588.

28 Waikar SS, Mount DB, Curhan GC. Mortality after hospitalization with mild, moderate, and severe hyponatremia. *Am J Med* 2009;122:857-865.

29 Obreli-Neto PR, Nobili A, de Oliveira Baldoni A, et al. Adverse drug reactions caused by drug-drug interactions in elderly outpatients: a prospective cohort study. *Eur J Clin Pharmacol* 2012 May 30. [Epub ahead of print]

30 Singal BM, Hedges JR, Rousseau EW, et al. Geriatric patient emergency visits. Part 1: Comparison of visits by geriatric and younger patients. *Ann Emerg Med* 1992;21:802-807.



90x90mm (300 x 300 DPI)

Appendix A

STARD checklist for reporting of studies of diagnostic accuracy

(version January 2003)

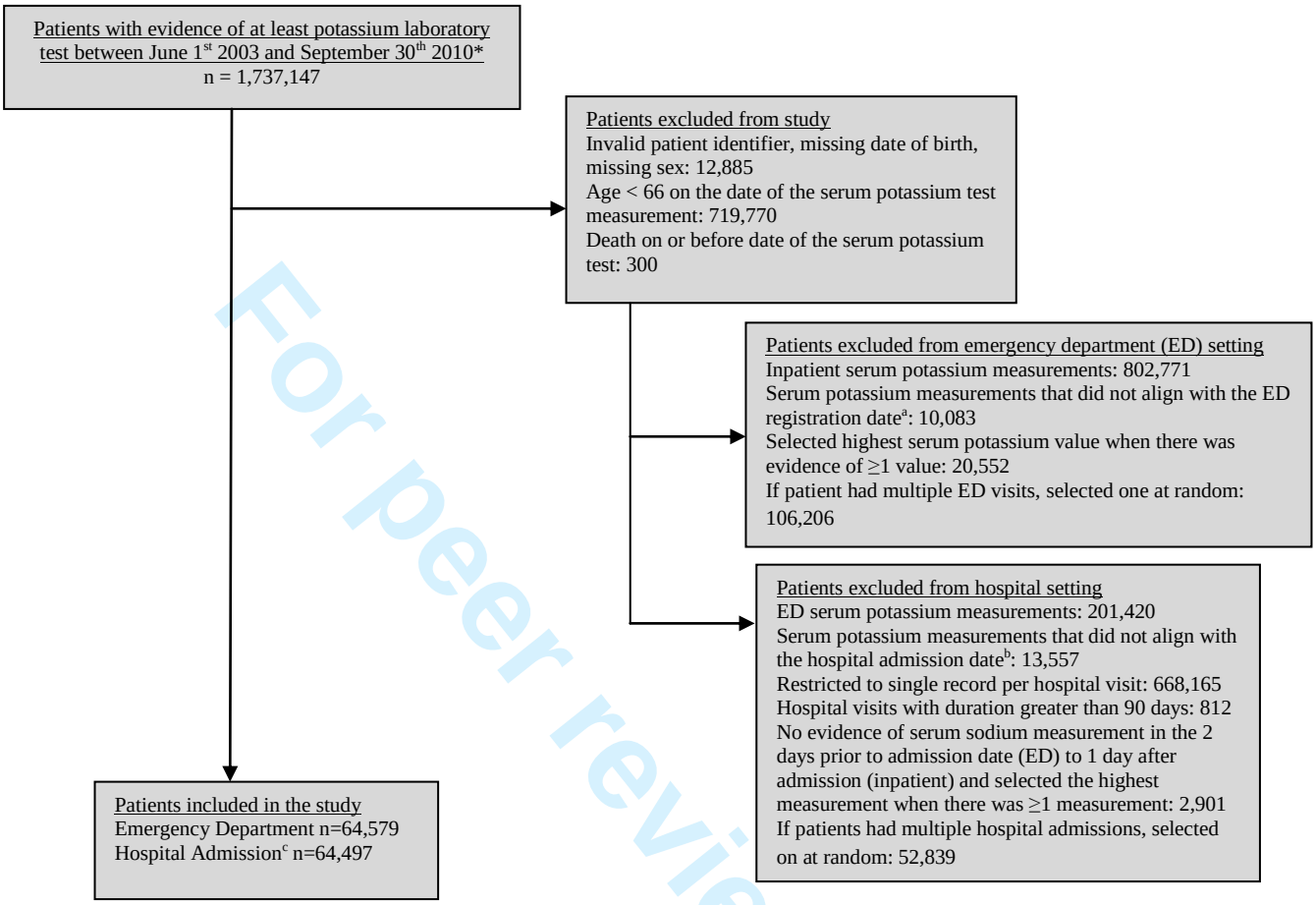
Section and Topic	Item #		On page #
TITLE/ABSTRACT/ KEYWORDS	1	Identify the article as a study of diagnostic accuracy (recommend MeSH heading 'sensitivity and specificity').	Abstract
INTRODUCTION	2	State the research questions or study aims, such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups.	Introduction
METHODS			
Participants	3	The study population: The inclusion and exclusion criteria, setting and locations where data were collected.	Methods – Participants; Appendix C
	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?	Methods – Participants
	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.	Methods – Participants; Appendix C
	6	Data collection: Was data collection planned before the index test and reference standard were performed (prospective study) or after (retrospective study)?	Methods – Study design
Test methods	7	The reference standard and its rationale.	Methods
	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.	Methods – Potassium laboratory value
	9	Definition of and rationale for the units, cut-offs and/or categories of the results of the index tests and the reference standard.	Methods – Potassium laboratory value
	10	The number, training and expertise of the persons executing and reading the index tests and the reference standard.	Methods – Administrative database codes
	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).	Methods – Data analysis; Appendix A
	13	Methods for calculating test reproducibility, if done.	n/a
RESULTS			
Participants	14	When study was performed, including beginning and end dates of recruitment.	Methods
	15	Clinical and demographic characteristics of the study population (at least information on age, gender, spectrum of presenting symptoms).	Results; Table 1
	16	The number of participants satisfying the criteria for inclusion who did or did not undergo the index tests and/or the reference standard; describe why participants failed to undergo either test (a flow diagram is strongly recommended).	Results; Table 1; Appendix C
Test results	17	Time-interval between the index tests and the reference standard, and any treatment administered in between.	Table 1 Footnote; Appendix C
	18	Distribution of severity of disease (define criteria) in those with the target condition; other diagnoses in participants without the target condition.	Results; Tables 2,3,4
	19	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.	Tables 2,3,4
	20	Any adverse events from performing the index tests or the reference standard.	n/a
Estimates	21	Estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals).	Results; Tables 2,3,4
	22	How indeterminate results, missing data and outliers of the index tests were handled.	n/a
	23	Estimates of variability of diagnostic accuracy between subgroups of participants, readers or centers, if done.	n/a
	24	Estimates of test reproducibility, if done.	n/a
DISCUSSION	25	Discuss the clinical applicability of the study findings.	Discussion

Appendix B

		Reference Standard: **Hyperkalemia** defined by a **potassium laboratory value >5.5mmol/L**	
		> 5.5 mmol/L	≤ 5.5 mmol/L
Hyperkalemia defined by **ICD-10 Code E87.5**	Code Positive	A	B
	Code Negative	C	D

Sensitivity=a/(a+c): the proportion of patients with serum potassium >5.5 mmol/L who are code E87.5 positive
Specificity=d/(b+d): the proportion of patients with serum potassium ≤5.5 mmol/L who are code E87.5 negative
Positive predictive value=a/(a+b): proportion of patients who are code E87.5 positive with serum potassium >5.5 mmol/L
Negative predictive value=d/(c+d): proportion of patients who are code E87.5 negative with serum potassium ≤5.5 mmol/L

Appendix C



*serum potassium measurements that were <0.5 mmol/L and >14 mmol/L were not considered as these were deemed data entry errors (occurred < 1.0% of the time).

[a] date of serum potassium measurement must be on the day of or 1 day after an emergency department registration date.

[b] date of serum potassium measurement must be between a hospital admission date and discharge date, including date of admission and discharge.

[c] patients were included in this cohort irrespective of hospital disposition (i.e. patients may have presented to an emergency department prior to their hospital admission or may have been directly admitted to hospital)

Appendix D – Figure Caption

Change in serum potassium values among patients who had baseline pre-hospital encounter serum potassium result. Patients who were code positive had evidence of the code in the 'all diagnoses' format. Patients who were code negative had no such code. For both presentation to an emergency department, and at hospital admission, patients who were code positive for hyperkalemia had a significantly larger change in their serum potassium value (from baseline) than patients who were code negative. The boxes represent the interquartile range (50% of the values). The line across the box indicates the median. The star indicates the mean. The whiskers extend to the 95th and 5th percentile.