CLINICAL RESEARCH ARTICLE

Evaluation of administrative case definitions for chronic kidney disease in children

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INTRODUCTION: Administrative data is increasingly used for chronic disease surveillance; however, its validity to define cases of chronic kidney disease (CKD) in children is unknown. We sought to evaluate the performance of case definitions for CKD in children.

METHODS: We utilized population-based administrative data from the Manitoba Center for Health Policy to evaluate the validity of algorithms based on a combination of hospital claims, outpatient physician visits, and pharmaceutical use over 1–3 years in children <18 years of age. Algorithms were compared with a laboratory-based definition (estimated glomerular filtration rate < 90 ml/min/1.73 m² and/or presence of proteinuria).

RESULTS: All algorithms evaluated had very low sensitivity (0.20–0.39) and moderate positive predictive value (0.52–0.68). Algorithms had excellent specificity (0.98–0.99) and negative predictive value (0.96–0.97). Receiver operating characteristic (ROC) curves indicate fair accuracy (0.60–0.68). Sensitivity improved with increasing years of data. One or more physician claims and one or more prescriptions over 3 years had the highest sensitivity and ROC.

CONCLUSIONS: The sensitivity of administrative data algorithms for CKD is unacceptably low for a screening test. Specificity is excellent; therefore, children without CKD are correctly identified. Alternate data sources are required for population-based surveillance of this important chronic disease.

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INTRODUCTION

Chronic kidney disease is a significant health problem in North America, affecting ~10–11% of the population.^{1,2} The disease is associated with significant morbidity^{3,4} and can ultimately progress to end-stage kidney disease (ESKD), requiring dialysis or kidney transplant to sustain life.⁵ The impacts of ESKD are significant with respect to quality of life⁶ as well as economic impacts.⁷

In Canada, children make up <2% of the entire ESKD population.⁸ However, when children develop CKD the consequences are dire, with significant impacts on quality of life, morbidity, and mortality.^{9–12} In addition, over the past few decades there is a growing burden of early-onset risk factors for CKD in Canadian children, including hypertension,¹³ obesity,¹⁴ and diabetes.¹⁵ Of concern is the lack of population-based data describing the prevalence of CKD, and therefore an incomplete understanding of the scope of this important health problem. Early identification is critical in order to implement therapy to slow the progression to ESKD.^{16–18} As children have a longer life expectancy than adults, their lifetime risk of ESKD may be significant. Unfortunately, there is a paucity of research describing the population burden of CKD in children; therefore, the prevalence of children at risk for progression to ESKD is unknown.

Administrative data are a valuable tool that can be used for chronic disease surveillance.¹⁹ They are reliably utilized for some chronic diseases such as diabetes and inflammatory bowel disease.^{20–22} Administrative case definitions for CKD have been evaluated in adult populations^{23,24} with discouraging results. To our knowledge, no published studies have examined the validity of using administrative data in defining cases of CKD in children.

In this study, we sought to evaluate the validity of administrative data definitions to identify children <18 years with CKD.

MATERIALS AND METHODS

In order to evaluate the performance of administrative case definitions for childhood CKD, we first identified a validation cohort utilizing laboratory data from Winnipeg, Manitoba, Canada. A gold standard cohort of children who reliably met the criteria for CKD (definitions described below) was identified, as was a cohort of children who had received testing for CKD and had normal results (no CKD cohort). Case definitions (described below) were then applied to the pediatric Winnipeg population and compared against this validation cohort of children with and without CKD. Approvals were obtained from the University of Manitoba Ethics Committee and the Manitoba Health Information Privacy Committee.

DATA SOURCES

The Manitoba Health Services Insurance Plan contains registration files, physician reimbursement claims (medical services data), hospital discharge abstracts, and records of outpatient prescriptions dispensed. These data are stored for research purposes in de-identified form in the Population Health Research Data Repository (herein referred to as the Repository) housed at the Manitoba Center for Health Policy.

Canada's health care system provides universal medical coverage to all Canadian citizens. Funding is public and administered on a provincial basis, within guidelines set by the federal

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government. In Manitoba, outpatient drugs are covered under a drug benefit program called Pharmacare, after a family income-based deductible is applied. Some citizens also have drug coverage linked to employment (private insurance).

Using de-identified personal health identification number (PHIN) codes and through the creation of a cross-walk file to the Repository, individuals can be linked between data sources at the person level. Physician reimbursement claims include International Classification of Diseases, 9th Revision, and Clinical Modification (ICD-9 CM) diagnostic codes at the 3-digit code level, and hospital abstract data include ICD-10 Canadian version (ICD-10CA) codes. Pharmaceutical data are from the Drug Program Information Network (DPIN). The following ICD codes, chosen based on the previous literature,²⁵ were utilized to identify children with CKD:

- Physician claims (ICD-9-CM: 403, 404, 580, 581, 582, 583, 585, 586, 587, 588, 593).
- Hospitalization codes (ICD-10-CA: E10.2, E11.2, I12, I13, N18, N19, N00-16, N25, N26, N28.82, N39.1, Q60, 61, 64).
- Prescriptions for the following CKD-specific medications were included: erythropoietin-like drugs, potassium binders, certain vitamins, including replavite and vitamin D analogs, and non-calcium-based phosphate binders. (See Supplemental Table S1 for detailed list.)

The Diagnostic Services Manitoba (DSM) is Manitoba's public sector diagnostic health care service provider and provides laboratory services for the major hospitals in the province of Manitoba. Many smaller rural and remote sites also send some or all of their tests to DSM for processing. Chemistry data were available for April 2006 to December 2011 for the six largest hospitals and health centers in the city of Winnipeg and for two additional sites (one urban and one rural) between November 2009 and December 2011. Isotope dilution mass spectrometry traceable serum creatinine (Cr) was used to calculate estimated glomerular filtration rate (eGFR),²⁶ and urine protein measures (urinalyses, albumin, and protein to calculate albumin and protein:Cr ratios) to assess for proteinuria.

Development of the validation cohorts

Laboratory data were utilized to identify children meeting criteria for CKD and those who had CKD reliably excluded. We included all children (<18 years) living in Winnipeg as of 1 April 2012 with a valid PHIN and with lab data required to identify CKD. This lab data included *at least two tests* of serum Cr and/or proteinuria between 31 March 2009 and 1 April 2012 *at least 90 days apart*. For children with normal tests, one test was considered acceptable as repeat testing would not be clinically indicated. We considered a child as having CKD if they had an eGFR <90 ml/min/1.73 m² and/or an albumin:Cr ratio ≥3 mg/mmol or protein:Cr ratio ≥15 mg/mmol based on the 2012 K-DIGO heatmap criteria.²⁷ We excluded from the analyses children on dialysis or with a kidney transplant as this was not the population of interest.

eGFR determination

As heights were not available for the majority of the cohort, the CKiD equation could not be applied.²⁸ We therefore used the height-independent Pottel formula (otherwise known as the Full Age Spectrum age equation, which has been validated as a population-based screening tool for children;²⁹ $eGFR = 107.3 / (Cr/Q)$, where Q is the median Cr for each given age class. Prior to applying the formula, we adapted the Q's to the Manitoba population based on the process established by De Sousa et al.²⁶ as it was unknown how the Q's from European children would compare to Q's in Canadian children. The first Cr available in the DSM database for each child 1–18 years of age during a 2-year

period was selected (1 April 2010–31 March 2012). All data below the detection limits and outliers as determined by the Grubbs test for outliers were excluded. The results of the median Cr values with lower and upper limits using nonparametric statistics (percentile (Pct) 2.5 and Pct 97.5) by age and sex are presented in Table 1 and compared to median's from the Lyon²⁹ and Belgium³⁰ cohorts.

Validation methods and analysis

Eighteen algorithms for pediatric CKD were evaluated using a combination of physician, hospital, and pharmaceutical use data over 1, 2, and 3 years (presented in Table 2). The same algorithms have been applied in previous validation studies of a similar nature.²⁰ We evaluated these algorithms in Winnipeg children by comparing them to the validation (CKD and no CKD) cohorts developed from laboratory data. The algorithms were evaluated for validity and level of agreement with the following measures: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), kappa (κ) statistic, and area under the receiver operating characteristic (ROC) curve.

Finally, demographic and health characteristics were compared between groups. Differences in characteristics of children identified with only laboratory (gold standard) vs. only administrative data were evaluated utilizing *t* tests and χ^2 tests where applicable. Characteristics evaluated included age, sex, income quintile (area level, based on postal code of residence), and urban vs. rural location of residence, as well as proportion seen by a pediatric nephrologist (captured by administrative data). The proportion of children within each stage of CKD based on eGFR threshold was also evaluated.

RESULTS

Characteristics of gold standard validation cohort and administrative data cohort

Table 3 describes the demographic characteristics of children from the gold standard cohort and the administrative data cohort. These two groups were quite similar, including the proportion seen by a Pediatric Nephrologist during the time period of study. The median eGFR for the whole gold standard cohort (*n* = 483) was 83.5 ml/min/1.73 m² (interquartile range = 68.34–98.6). A total of 23.4% of this cohort had proteinuria only, with an eGFR >90 ml/min/1.73 m², 57.8% had an eGFR of 60–<90 ml/min/1.73 m², 10.1% had an eGFR of 30–<60 ml/min/1.73 m², and 3.1% had an eGFR of <30 ml/min/1.73 m². Only 5.6% did not have a Cr available during the study period (proteinuria data only was available).

Creation of validation cohorts

The selection process for the development of the validation cohort is outlined in Fig. 1. A total of 150,218 children were residents of Winnipeg during the study period. Of these, 137,677 had no relevant laboratory data available, 2799 had only one abnormal test during the study period and 211 had two tests available only within 90 days. These children were excluded because CKD could not be reliably ruled in or out. Children already on renal replacement therapy (RRT) were also excluded (*n* = 8). This left us with 9523 children in Winnipeg who had either two laboratory tests to allow the determination of CKD or one normal test, thereby excluding the diagnosis of CKD. In our final validation cohort, 483 children with confirmed CKD were identified from laboratory data and became the gold standard cohort. The remaining 9040 children were confirmed not to have CKD and thereby classified as the No CKD cohort. The majority of children had stage 1–2 CKD (80.8%).

Case identification by administrative data

Table 2 shows the number of children identified with each algorithm, as well as those identified only with laboratory data and

Table 1. Mean, Median, and lower and upper limit of creatinine in the Manitoba population and the median creatinine as compared to the Belgium and Lyon populations

Age	Boys									
	Mean Cr (μmol/l)	StdDev	2.5%ile	Manitoba median	97.5%ile	Lyon median	Belgium median	Mean Cr (μmol/l)	StdDev	2.5%ile
1	20.6	4.3	13	20	30	22	24	21.1	4.8	13
2	23.3	5.0	14	22	35	25	27	23.8	4.8	16
3	26.7	5.4	16	26	38	27	29	26.0	5.6	16
4	28.8	5.6	18	28	43	30	32	28.9	6.1	18
5	30.9	5.9	20	30	44	31	34	31.2	6.8	18
6	33.5	6.3	23	33	47	34	37	34.2	6.6	22
7	36.3	6.9	24	36	53	36	39	37.1	6.5	27
8	37.5	7.0	26	37	52.5	39	40	38.1	6.1	26
9	39.8	7.3	22	40	54	40	43	39.7	7.5	27
10	41.2	7.1	30	40	58	41	46	42.3	8.7	28
11	43.4	8.1	30	43	61	43.5	47	44.6	8.0	30
12	46.3	8.9	29	46	68	46	50	47.7	9.2	31
13	50.3	9.6	33	50	71	48	54	52.4	11.2	34
14	53.8	9.7	36	53	74	52.5	55	59.5	12.6	36
15	55.1	10.1	35	55	76	55	59	65.3	12.6	42
16	56.2	10.2	37	56	77	56	62	70.0	11.8	48
17	57.2	10.9	37	57	80	57	62	72.7	12.7	51

Cr creatinine, StdDev standard deviation

those identified by both data sources. More children were identified with the algorithms that used more years of data. For all algorithms there was a significant number of children (>300) that were missed by administrative data (45–72%). Only a small percent of children were identified only by administrative data and not captured in the DSM data (8.7–26% depending on the algorithm).

Validation results administrative data algorithms

Table 4 outlines the validation results for all 18 algorithms. All algorithms had very low sensitivity (0.201–0.387) and PPV was similarly low (0.524–0.678). In contrast, they all had excellent specificity (0.982–0.995) and NPV was high (0.981–995). The ROC curves indicate poor to fair accuracy (0.598–0.684). Algorithm #15 which included one or more hospital records, one or more physician claims, and one or more prescriptions over 3 years had the highest sensitivity (0.387). It also had the highest ROC (0.684). The same ROC was seen for #17 with a slightly lower sensitivity. The PPV for #15 was 0.524. We present ROC curves for #15 and #17, as well as #13 in Fig. 2 as these algorithms had the highest area under the ROC.

Finally, the κ -coefficients were in the moderate range between 0.598 and 0.684. For most algorithms, the κ was between 0.60 and 0.68, demonstrating the moderate level of agreement.

DISCUSSION

Administrative data can be a powerful tool for disease surveillance. To our knowledge, this is the first study published to evaluate the validity of administrative case definitions for CKD in children. Our findings demonstrate an unacceptably low sensitivity for all tested algorithms and suggest that reliance on diagnostic codes and pharmaceutical data will significantly underestimate the prevalence of CKD in children. However, despite this limitation the specificity and NPVs are excellent, suggesting that administrative data does reliably identify children without CKD. These findings are important as they support the use of administrative data to rule out CKD in children, but that additional data sources are required for population-based CKD surveillance.

The validity of administrative data definitions for CKD in adults have been evaluated in a number of studies. The systematic review of available studies was published in 2011 by Vlasschaert et al.²⁴ This review summarized results from 19 CKD definition validation studies. The sensitivity across studies was a median of 41% (range 3–88%). The PPVs were quite variable; median 78% (range 29–100%). The results largely depended on the baseline prevalence of the disease in the population evaluated. Following this review, Ronksley et al.²³ published an additional validation study, which evaluated the validity of definitions over 3 years of administrative data. They similarly identified a low sensitivity for all algorithms; however, they were able to demonstrate that sensitivity increased when stage 4 CKD (GFR <30 ml/min/1.73 m²) was utilized as the reference standard. They suggested that there may be a place for administrative data in highly specific circumstances such as for advanced CKD.

Although previous studies have revealed a low sensitivity for CKD utilizing administrative data, these findings should not be generalized to children without specific evaluation as pediatric and adult disease can differ significantly with respect to health care utilization.³¹ Our validation results suggest that the sensitivity and PPV of administrative data for pediatric CKD is slightly lower than for adult CKD. In order for CKD to be captured by administrative data, it must be recognized by the physician seeing the patient. It is highly probable that primary care physicians are not recognizing CKD in children and therefore not coding for it in their billing claims. This is reflected by the overall low percentage of children in both groups having been

Table 2. Algorithms evaluated for chronic kidney disease in children <18 years of age and number of children identified with each algorithm, laboratory data only, and both data sources

Years of data collection	Algorithm	Hospital separations	Physician claims	DPIN records	Admin only	DSM only	Admin and DSM
1 (2011/12)	1	1 or more	1 or more	–	86	344	139
	2	1 or more	2 or more	–	46	386	97
	3	1 or more	1 or more	1 or more	98	340	143
	4	1 or more	2 or more	1 or more	58	379	104
	5	1 or more	1 or more	2 or more	91	340	143
	6	1 or more	2 or more	2 or more	51	381	102
2 (2010/11–11/12)	7	1 or more	1 or more	–	115	314	169
	8	1 or more	2 or more	–	77	338	145
	9	1 or more	1 or more	1 or more	135	309	174
	10	1 or more	2 or more	1 or more	98	332	151
	11	1 or more	1 or more	2 or more	120	310	173
	12	1 or more	2 or more	2 or more	83	334	149
3 (2009/10–11/12)	13	1 or more	1 or more	–	147	300	183
	14	1 or more	2 or more	–	96	321	162
	15	1 or more	1 or more	1 or more	170	296	187
	16	1 or more	2 or more	1 or more	120	317	166
	17	1 or more	1 or more	2 or more	154	297	186
	18	1 or more	2 or more	2 or more	104	318	165

Table 3. Characteristics of children identified with chronic kidney disease by administrative and laboratory definitions

	Administrative-only CKD cohort (N = 120)	Gold standard CKD cohort (N = 483)	p Value
Age (years) (mean, SD)	11.0 (5.6)	11.0 (5.2)	0.871
Male (%)	51.7%	47.8%	0.452
SES quintile (1 vs. 2–5)	22.5%	23.6%	0.798
Seen by pediatric nephrologist (%)	51.7%	45.8%	0.246
CKD stage by eGFR threshold (ml/min/1.73 m ²) (%)	NA	≥90–23.4% 60–<90–57.8% 30–<60–10.1% <30–3.1% Unknown–5.6%	NA

NA not available

referred to a pediatric kidney specialist. The similarity of demographic characteristics between children identified by administrative data and laboratory data is reassuring; suggesting, those children captured by administrative codes are reflective of the true CKD population.

The strengths of this study are its novel focus on pediatric CKD, an increasingly important health condition with long-term consequences³² and the availability of a population-based data Repository strengthened by the linkage to laboratory data, which provided access to validation cohorts. A potential strategy for future studies to increase the sensitivity of population-based surveillance is the utilization of capture–recapture methodology, which combines administrative and laboratory data, a strategy previously utilized by our group in adults with CKD.²⁵

In addition, we ensured that laboratory changes were chronic (abnormal at least 90 days apart). We included a height-independent eGFR, which has been shown to be a reliable screening tool when heights are not available with excellent performance characteristics.²⁹ The need for a measured height with most commonly utilized clinical eGFR equations²⁸ has been a

significant barrier for population-based surveillance studies in children as clinical parameters are not available in administrative data. Finally, we standardized the Q's in the height-independent equation. It was reassuring to see that median Cr's were essentially identical across populations for children over age 10 years. There was a small negative bias in Manitoba Cr's for younger children, but supporting the exercise to standardize Q's to the local population for younger children.

LIMITATIONS

There was a lack of universal provincial laboratory coverage of the DSM data. To address this limitation, we limited our analysis to Winnipeg residents only and excluded children that did not have any laboratory data available at all. Second, pediatric CKD is a heterogeneous disease and includes a spectrum of stages of CKD ranging from mild to severe.²⁷ Previous studies have attempted to stratify individuals by severity of CKD to evaluate differences in validity characteristics of case definitions. Unfortunately, we did not have sufficient sample size to subdivide our

Fig. 1 Validation cohort creation diagram. eGFR = estimated glomerular filtration rate

Table 4. Validation results for each administrative data algorithm for CKD in children <18 years of age

Years of data collection	Algorithm	Hospital separations	Physician claims	DPIN records	Sensitivity	Specificity	PPV	NPV	Kappa	Area under ROC
1 (2011/12)	1	1 or more	1 or more	–	0.288	0.991	0.618	0.963	0.373	0.639
	2	1 or more	2 or more	–	0.201	0.995	0.678	0.959	0.294	0.598
	3	1 or more	1 or more	1 or more	0.296	0.989	0.593	0.964	0.374	0.643
	4	1 or more	2 or more	1 or more	0.215	0.994	0.642	0.960	0.305	0.605
	5	1 or more	1 or more	2 or more	0.296	0.990	0.611	0.964	0.378	0.643
	6	1 or more	2 or more	2 or more	0.211	0.994	0.667	0.960	0.304	0.603
2 (2010/11–11/12)	7	1 or more	1 or more	–	0.350	0.987	0.595	0.966	0.419	0.669
	8	1 or more	2 or more	–	0.300	0.992	0.653	0.964	0.392	0.646
	9	1 or more	1 or more	1 or more	0.360	0.985	0.563	0.967	0.416	0.673
	10	1 or more	2 or more	1 or more	0.313	0.989	0.606	0.964	0.392	0.651
	11	1 or more	1 or more	2 or more	0.358	0.987	0.590	0.967	0.424	0.673
	12	1 or more	2 or more	2 or more	0.308	0.991	0.642	0.964	0.397	0.650
3 (2009/10–11/12)	13	1 or more	1 or more	–	0.379	0.984	0.555	0.968	0.427	0.681
	14	1 or more	2 or more	–	0.335	0.989	0.628	0.966	0.417	0.662
	15	1 or more	1 or more	1 or more	0.387	0.981	0.524	0.968	0.420	0.684
	16	1 or more	2 or more	1 or more	0.344	0.987	0.580	0.966	0.410	0.665
	17	1 or more	1 or more	2 or more	0.385	0.983	0.547	0.968	0.428	0.684
	18	1 or more	2 or more	2 or more	0.342	0.989	0.613	0.966	0.418	0.665

cohort. This could be a next step with an interprovincial data analysis with a larger sample size utilizing meta-analytic techniques.³³

Finally, it needs to be acknowledged that eGFR is an *estimate* of kidney function, and the accuracy of every equation has its

limitations. For children, there are a number of different eGFR equations that have been developed and validated in different populations and stages of CKD.^{26–30} The performance of the height-independent eGFR has been evaluated in a population of 359 children. The accuracy within 30% of the measured GFR was

Fig. 2 Receiver operating curves for algorithms highest area under ROCs. **a** 13 = 1 + Hospital Separations and/or 1 + Physician Claims in 3 years. **b** 15 = 1 + Hospital Separations and/or 1 + Physician Claims and/or 1 + DPIN Record in 3 years. **c** 17 = 1 + Hospital Separations and/or 1 + Physician Claims and/or 2 + DPIN Record in 3 years

found to be 79.6% overall, and 88.3% for children with eGFR >90 ml/min/1.73 m².²⁹ The concordance correlation coefficient was 0.75. These results compared favorably with the Schwartz 2009 equation, which includes a patient height, and therefore justify its use as a screening tool at the population level.

CONCLUSIONS

Administrative case definitions for chronic kidney disease in children have insufficient sensitivity to be used for disease surveillance. However, specificity was excellent, suggesting that there may be a role for administrative data to identify children without CKD in some circumstances. Additional data sources such as laboratory data need to be considered for active prevalence determination.

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AUTHOR CONTRIBUTIONS

A.D. drafted the article. R.W. performed all analyses. All authors provided substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data. All authors revised it critically for important intellectual content. Final approval of the version to be published was provided by all authors.

ADDITIONAL INFORMATION

The online version of this article (<https://doi.org/10.1038/s41390-019-0595-1>) contains supplementary material, which is available to authorized users.

Competing interests: Dr. Tangri receives honoraria from Takeda Inc. and serves on the Advisory Board for Takeda Inc. and Otsuka. Dr. Komenda is on the Advisory Board for NxStage Medical and is medical director of Quanta Dialysis Technologies Ltd.

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