


# Healthcare Utilization after Acute Kidney Injury in the Pediatric Intensive Care Unit

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## Abstract

**Background and objectives** Little is known about the long-term burden of AKI in the pediatric intensive care unit. We aim to evaluate if pediatric AKI is associated with higher health service use post-hospital discharge.

**Design, setting, participants, & measurements** This is a retrospective cohort study of children ( $\leq 18$  years old) admitted to two tertiary centers in Montreal, Canada. Only the first admission per patient was included. AKI was defined in two ways: serum creatinine alone or serum creatinine and/or urine output. The outcomes were 30-day, 1-year, and 5-year hospitalizations, emergency room visits, and physician visits per person-time using provincial administrative data. Univariable and multivariable Poisson regression were used to evaluate AKI associations with outcomes.

**Results** A total of 2041 children were included (56% male, mean admission age  $6.5 \pm 5.8$  years); 299 of 1575 (19%) developed AKI defined using serum creatinine alone, and when urine output was included in the AKI definition 355 of 1622 (22%) children developed AKI. AKI defined using serum creatinine alone and AKI defined using serum creatinine and urine output were both associated with higher 1- and 5-year hospitalization risk (AKI by serum creatinine alone adjusted relative risk, 1.42; 95% confidence interval, 1.12 to 1.82; and 1.80; 1.54 to 2.11, respectively [similar when urine output was included]) and higher 5-year physician visits (adjusted relative risk, 1.26; 95% confidence interval, 1.14 to 1.39). AKI was not associated with emergency room use after adjustments.

**Conclusions** AKI is independently associated with higher hospitalizations and physician visits postdischarge.

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## Introduction

AKI is common in children admitted to the pediatric intensive care unit and is associated with higher hospital mortality and morbidity (1–5). In adults, AKI during a hospitalization is associated with higher risk for long-term kidney disease, cardiovascular morbidity, and hospital readmission (6–11). Although some data suggest that AKI in children may be a risk factor for future kidney disease (12,13), little is known about the long-term burden of illness of survivors of pediatric AKI and the extent to which AKI is associated with long-term morbidity. One way to evaluate this is to determine whether AKI is associated with higher post-hospital discharge use of health services.

We conducted a retrospective cohort study, utilizing provincial administrative data, to evaluate if AKI in critically ill children is associated with higher hospitalizations, emergency room visits, and physician visits 5 years after hospital discharge. We hypothesized that AKI is associated with higher health care utilization, independent of other factors.

## Materials and Methods

### Design, Setting, and Patient Selection

We conducted a retrospective cohort study of children ( $\leq 18$  years old) admitted to the pediatric intensive

care unit at one of two tertiary centers in Montreal, Canada (Montreal Children's Hospital; Centre Hospitalier Universitaire Sainte-Justine) between January 1, 2003 and March 31, 2005. Patients with preexisting ESKD, or no health care number, were excluded *a priori*. We included only the first hospitalization during the study period. We excluded patients who could not be linked to provincial data, did not survive the hospitalization, or underwent cardiac surgery during the index admission (Figure 1). Patients transferred to long-term care facilities were included in all analyses ( $n=9$ ). Approvals from institutional research ethics boards and the Commission d'accès à l'information du Québec (provincial data monitoring board) were obtained. Requirement for patient consent was waived.

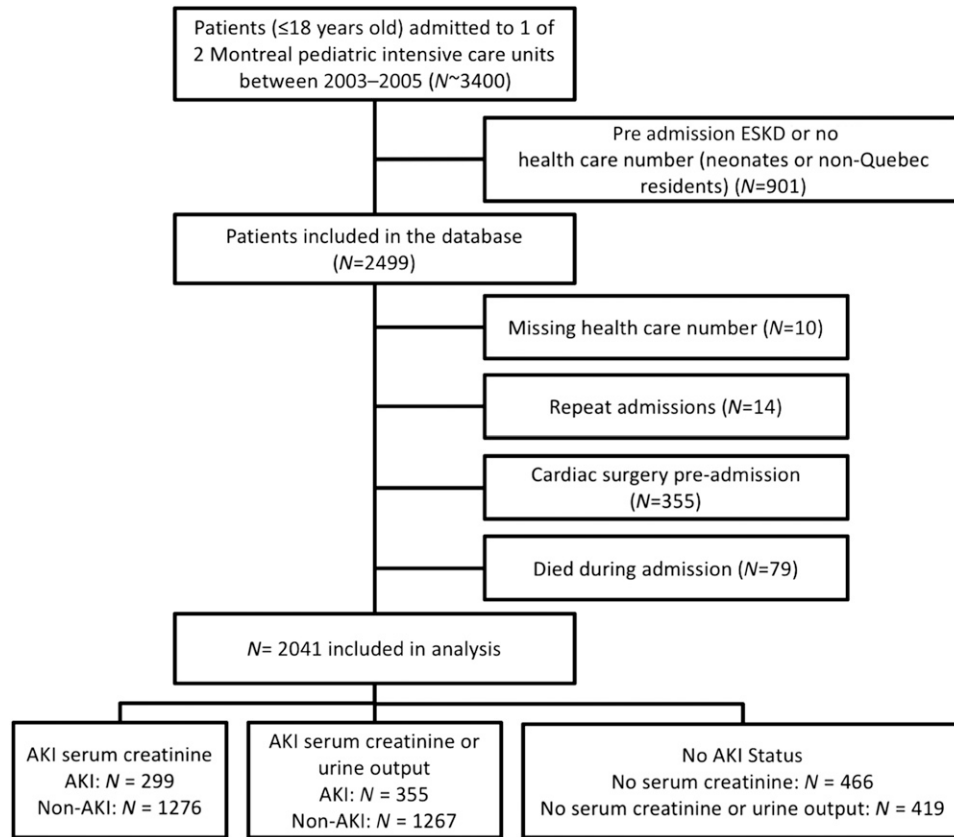
### Data Collection and Sources

Index hospitalization data were collected by retrospective chart review (described previously) (14). Before final analysis, independent reviewers from each center reassessed 50 randomly selected charts to evaluate and correct for sources of reduced reliability (92% of continuous variables had inter-rater correlation  $\geq 0.90$  and 96% of categorical variables had  $\geq 90\%$  agreement). Variables collected included primary diagnosis (categorized on the basis of the chart

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**Figure 1.** | Study flow and selection criteria leading to the analysis population.

admission note), treatments, and illness severity measures (Supplemental Table 1).

The chart data were merged with the Quebec Vital Statistics Registry and administrative health databases (Régie de l'assurance maladie du Québec and Med-Echo) from which data from January 1, 2003 to March 31, 2010 (5 years after the last hospital admission in our cohort) were available. The provincial administrative database contains three datasets: (1) demographic information (including patient postal code and community health center region, used to calculate the deprivation index) (15); (2) medical services data (including outpatient services date, service type, physician type, billing codes, and International Classification of Disease [ICD-9 and ICD-10] diagnostic codes); and (3) outpatient prescription data for patients whose medications are insured by the provincial health plan. The Med-Echo database (maintained by the Quebec Ministry of Health and Social Affairs) contains acute care hospitalization data including admission and discharge dates and primary diagnoses, physician information, procedures, and up to 15 secondary diagnoses (ICD-9/10 codes). We used this data to define complex chronic illnesses in our population using the Pediatric Medical Complexity Algorithm (16), as well as if the patient had a primary care physician (Supplemental Table 1).

#### Primary Exposure: AKI

AKI was defined using serum creatinine alone or combining serum creatinine and/or urine output criteria,

on the basis of the Kidney Disease: Improving Global Outcomes definition (17). AKI staging by serum creatinine was as follows: stage 1 (serum creatinine rise  $\geq 1.5$ – $1.9 \times$  baseline in 7 days or  $\geq 0.3$  mg/dl rise within 48 hours), stage 2 ( $\geq 2.0$ – $2.9 \times$  baseline), or stage 3 ( $\geq 3.0 \times$  baseline,  $\geq 4.0$  mg/dl, dialysis treatment for AKI, or eGFR  $< 35$  ml/min per  $1.73$  m<sup>2</sup> [if  $> 3$  months old]). Baseline serum creatinine was the lowest measurement 3 months before admission. If unavailable we back-calculated baseline using a previously validated method (14).

Urine output AKI was classified as stage 1 ( $< 0.5$  ml/kg per hour for 8 hours), stage 2 ( $< 0.5$  ml/kg per hour for 16 hours), or stage 3 ( $< 0.3$  ml/kg per hour for 24 hours, anuric for 12 hours, or dialysis treatment for AKI) (18).

For the combined AKI definition, if a patient fulfilled criteria for either serum creatinine or urine output, they were classified as having AKI. The maximum AKI stage defined by serum creatinine or urine output criteria was used to classify AKI severity.

#### Outcome: Health Care Utilization

We evaluated the number of 30-day, 1-year, and 5-year hospitalizations, emergency room visits, or physician visits per person-time (events per person-month for 30-day outcomes, person-year for 1- and 5-year outcomes), where day zero was date of hospital discharge. Physician visits included outpatient clinics with specialists or general practitioners, local community services centers, and family medicine group clinics (claim codes in Supplemental Table 1). We excluded billing codes from physical rehabilitation

centers, laboratory testing claims, long-term care facilities, and dental claims.

### Analysis

The associations between patient characteristics and AKI were evaluated using appropriate univariable tests. In the whole study population (including patients with no serum creatinine or urine output measured), associations between patient and hospitalization characteristics with 30-day, 1-year, and 5-year outcomes were evaluated using univariable Poisson regression, and reported as relative risk (RR) (95% confidence interval [95% CI]). Analyses evaluating the associations between AKI and outcomes only included patients with an ascertainable AKI status. Selection of variables for inclusion in multivariable analyses was on the basis of (1) *a priori* selected known AKI risk factors and (2) univariable associations with outcomes ( $P < 0.05$ ). We evaluated two sets of multivariable Poisson regression models. Model 1 included baseline patient characteristics and index admission variables (age, sex, center, Pediatric Risk of Mortality death rate score [fourth quartile versus others] [19], nephrotoxic antibiotics, vasopressors, steroids) and primary admission diagnoses significant in univariable analyses (oncologic, diabetes, trauma, infection, cardiac [nonsurgical], kidney, and neurologic/gastrointestinal/respiratory). Model 2 additionally included social and material deprivation indices (fourth/fifth quintiles [most deprived] versus others) (15), Pediatric Medical Complexity Algorithm classification (17), rural versus urban, and number of hospitalizations 12 months before admission. For 5-year hospitalization and emergency room visit outcomes we also controlled for evidence of a primary care physician (this variable requires at least 2 years of observation to ascertain). To determine if any associations between AKI and physician visits were being driven by nephrology visits we repeated the final multivariable analysis excluding nephrology visits from the outcome.

We evaluated effect modification of the 5-year AKI-outcome associations. A preplanned evaluation of variables selected for inclusion in the multivariable analysis was performed by developing interaction terms with AKI (*e.g.*, AKI  $\times$  age). Statistical significance of interaction terms was evaluated one-by-one in a Poisson regression including AKI, the variable of interest, and the interaction term for 5-year hospitalizations, emergency room visits, and physician visits. Interaction terms with a  $P < 0.05$  were added one-by-one to model 2. If the interaction term remained significant in the full model it was included in the final multivariable analysis. *A priori*, it was decided that stratified (subgroup) analyses would be performed on variables showing significant effect modification on AKI–health care utilization associations.

Because mortality has a large effect on health care utilization we also performed a sensitivity analysis by excluding patients who died during follow-up and re-running the multivariable analysis for 5-year outcomes. Statistical assumptions of multivariable analyses were evaluated.

All analyses were planned *a priori* and conducted using SAS statistical software, release 9.2 (SAS Institute Inc., Cary, NC). Reporting was prepared in accordance with guidelines (20).

## Results

### Patient Characteristics

A total of 2041 children were eligible for this analysis (56% male, mean age at admission  $6.5 \pm 5.8$  years, mean follow-up  $4.8 \pm 0.8$  years). Of these, 1575 (77%) patients had serum creatinine measured and, of these, 299 (19%) developed AKI. Of the eligible children, 1622 (80%) patients had either serum creatinine or urine output data and, of these, 355 (22%) patients had AKI (Figure 1). Those excluded due to missing health care number did not differ significantly in patient or hospitalization characteristics from the remaining population (data not shown). Table 1 shows patient and admission characteristics stratified by AKI. Patients with AKI had higher illness severity measures and a longer duration of admission (Table 1).

Many patient and treatment characteristics were associated with 5-year outcomes in univariable analyses. Younger age; higher illness severity and complexity scores; and use of nephrotoxic antibiotics, steroids, and invasive mechanical ventilation were all significantly associated with outcomes (Supplemental Table 2). Similar results were found for 30-day and 1-year outcomes (Supplemental Tables 3 and 4).

### Hospitalizations after AKI

The 30-day, 1-year, and 5-year postdischarge cumulative number of rehospitalizations was 354, 2290, and 5315, respectively, for 2041 patients. Of the total 5-year postdischarge hospitalizations, 14% (740 of 5315) required intensive care admissions. AKI was associated with higher hospitalizations per person-time over the 5-year follow-up (Table 2) and for 30-day and 1-year follow-up periods (Supplemental Table 5).

Figure 2 shows the unadjusted and adjusted analyses for the association between AKI and rehospitalization. In model 1 (includes baseline, index admission characteristics), AKI was associated with 30% higher risk of hospitalization within 30 days, 1 year, and 5 years. In model 2 (including socioeconomic variables and effect modifiers), AKI remained associated with risk for 1- and 5-year hospitalizations (too few events for 30-day hospitalizations for full adjustments) (Figure 2). The results for stage 2/3 AKI versus no AKI/stage 1 were very similar (Supplemental Table 6).

### Emergency Room Visits after AKI

The cumulative number of emergency room visits for 30 days, 1 year, and 5 years postdischarge was 444, 3292, and 9606, respectively. AKI was associated with more emergency room visits per person-time at all three follow-up periods (Table 2 shows 5-year results; 30-day and 1-year results in Supplemental Table 5). In multivariable analyses, AKI was no longer associated with emergency room use (Supplemental Figure 1). This was also true for severe AKI (Supplemental Table 6).

### Outpatient Physician Visits after AKI

The 30-day, 1-year, and 5-year postdischarge cumulative numbers of physician visits were 2800, 20763, and 60083, respectively. AKI was associated with higher physician visits per person-time over 5 years (Table 2) and over 30-day

**Table 1. Comparison of patient characteristics by AKI (yes/no)**

Variables	Serum Creatinine Only		Serum Creatinine and Urine Output	
	No AKI (n=1276)	AKI (n=299)	No AKI (n=1267)	AKI (n=355)
<b>Baseline characteristics</b>				
Age, yr	5 (11)	5 (10)	5 (11)	6 (11)
Female sex	583 (46%)	143 (48%)	574 (45%)	168 (47%)
Sainte-Justine Hospital	822 (64%)	212 (71%)	803 (63%)	255 (72%)
Admission diagnosis				
Cardiac (nonsurgical)	69 (5%)	26 (9%)	71 (6%)	28 (8%)
Trauma	158 (12%)	26 (9%)	151 (12%)	37 (10%)
Kidney	4 (0.3%)	15 (5%)	4 (0.3%)	15 (4%)
Infection (excluding bronchiolitis)	253 (20%)	67 (22%)	244 (19%)	86 (24%)
Neurologic/neurosurgical	217 (17%)	32 (11%)	216 (17%)	41 (12%)
Gastrointestinal <sup>a</sup>	44 (4%)	26 (9%)	45 (4%)	27 (8%)
Oncologic	43 (3%)	12 (4%)	43 (3%)	12 (3%)
Respiratory	121 (10%)	31 (10%)	125 (10%)	34 (10%)
Diabetes	14 (1%)	18 (6%)	17 (1%)	18 (5%)
Other <sup>b</sup>	353 (28%)	46 (15%)	351 (28%)	57 (16%)
Baseline kidney abnormality	22 (2%)	26 (9%)	22 (2%)	27 (8%)
Postoperative (noncardiac)	485 (38%)	87 (29%)	481 (38%)	101 (29%)
PRISM score	6 (6)	9 (10)	6 (6)	9 (9)
PRISM death rate (%)	1.9 (3.3)	3.2 (9.2)	1.9 (3.4)	2.8 (7.3)
<b>Treatment characteristics</b>				
Nephrotoxic antibiotics	289 (23%)	111 (37%)	278 (22%)	126 (36%)
Vasopressors	87 (7%)	72 (24%)	77 (6%)	82 (23%)
Steroids	339 (27%)	116 (39%)	336 (27%)	130 (37%)
Mechanically ventilated (yes/no)	526 (41%)	146 (49%)	510 (40%)	185 (52%)
Length of mechanical ventilation, d	0 (2)	0 (4)	0 (2)	1 (4)
<b>Kidney related</b>				
Nephrology consultation during admission	49 (4%)	76 (25%)	47 (4%)	80 (23%)
Kidney Replacement Therapy	0	12 (4%)	0	12 (3%)
<b>Outcomes</b>				
Intensive care length of stay, d	1.4 (2.3)	2.5 (5.8)	1.3 (2.1)	2.7 (6.0)
Hospital length of stay, d	9 (12)	13 (19)	9 (11)	13 (19)

Continuous variables presented as median (interquartile range) and categorical variables presented as number (percentage). PRISM, Pediatric Risk of Mortality.

<sup>a</sup>Gastrointestinal includes liver, stomach, pancreas, and intestine.

<sup>b</sup>Includes hematologic (nononcologic), inborn error of metabolism and metabolic (noninborn error of metabolism), immunologic, intoxication, burn, orthopedic, otolaryngologic, endocrinologic (nondiabetes), and bronchiolitis.

and 1-year periods (Supplemental Table 5). The proportion of outpatient visits to a nephrologist was higher in patients with AKI versus patients without AKI 5 years postdischarge (11% versus 0.8% of total physician visits,  $P < 0.001$ ). Of 299 patients with AKI (serum creatinine only), 72 (24%) saw a nephrologist at least once in the 5 years after discharge; 54 (18%) saw a nephrologist within 1 year of discharge.

Figure 3 shows that in multivariable models 1 and 2, AKI was associated with higher risk for 30-day, 1-year, and 5-year postdischarge physician visits. In the models controlling for effect modification, AKI only remained significantly associated with higher physician visits 5 years postdischarge (Figure 3). Overall, outcome associations for AKI by serum creatinine alone and AKI by serum creatinine and urine output were similar, with slightly larger magnitudes of association when AKI was defined using only serum creatinine. Furthermore, the results for stage 2/3 AKI versus no AKI/stage 1 were very similar (Supplemental Table 6). When nephrology visits were excluded from the outpatient physician visits ascertainment, there was no difference in the associations of AKI with 5-year postdischarge physician

visits (adjusted RR, 1.14; 95% confidence interval, 1.08 to 1.20).

### Sensitivity Analysis

When we excluded patients who died during the 5-year follow-up period, AKI remained significantly associated with 5-year hospitalizations and physician visits (Supplemental Table 7). AKI was not associated with 5-year emergency room visits.

### Subgroup Analyses

Subgroup (stratified) analyses on effect modifiers of the AKI associations with 5-year outcomes are shown in Supplemental Tables 8–10. In patients with higher socioeconomic status (first to third quintiles), AKI was more strongly associated (greater RR) with 5-year outcomes than in patients with lower socioeconomic status. AKI was more strongly associated with 5-year hospitalizations and emergency room visits in patients with no prior hospitalizations versus those with  $\geq 1$  hospitalization 12 months before index admission. AKI was more strongly associated with outcomes in the patients with lower illness severity scores compared with those with the highest scores (fourth quartile).

**Table 2. Comparison of 5-yr hospitalizations, emergency room visits, and physician visits between patients with versus without AKI**

AKI Definition	Hospitalizations			Emergency Room Visits		Outpatient Physician Visits		
	# Visits	# Intensive Care Admissions	Events/Person Year (95% CI)	# Visits	Events/Person Year (95% CI)	# Visits	# Nephrology Visits	Events/Person Year (95% CI)
<b>Serum creatinine only</b>								
No AKI	3183	415 (13%)	0.52 (0.50 to 0.53)	5650	0.91 (0.89 to 0.94)	34937	295 (0.8%)	5.65 (5.60 to 5.71)
AKI	1033	134 (13%)	0.73 (0.68 to 0.77) <sup>a</sup>	1422	1.00 (0.95 to 1.06) <sup>a</sup>	11683	1300 (11%)	8.25 (8.10 to 8.40) <sup>a</sup>
<b>Serum creatinine or urine output</b>								
No AKI	3165	414 (13%)	0.52 (0.50 to 0.53)	5693	0.93 (0.90 to 0.95)	35111	297 (0.8%)	5.72 (5.66 to 5.78)
AKI	1186	158 (13%)	0.71 (0.67 to 0.75) <sup>a</sup>	1640	0.98 (0.93 to 1.02) <sup>a</sup>	13023	1308 (10%)	7.75 (7.61 to 7.88) <sup>a</sup>

95% CI, 95% confidence interval.

<sup>a</sup> $P < 0.001$  for comparison between AKI and non-AKI by univariable Poisson regression.

## Discussion

We found that AKI in the pediatric intensive care unit is associated with higher risk for postdischarge hospitalizations and physician visits, independent of baseline, admission, and chronic illness variables. This suggests that AKI either contributes to long-term morbidity or is at least an important marker of long-term morbidity after intensive care unit admission.

AKI was associated with approximately 40% higher adjusted risk of rehospitalization 1 year postdischarge and 60%–80% higher risk (depending on the AKI definition) for 5-year rehospitalizations. A recent American study reported that 1-year rehospitalization rate after pediatric intensive care unit admission was 62 readmissions per 100 person-years (21). In our cohort, the overall 1-year rehospitalization rate was almost double (113 hospitalizations per 100 person-years). This discrepancy may be due to the larger sample size in the United States study or differences between health care systems. Contrary to our findings, this United States study found that AKI was only associated with 1-year rehospitalization in patients with cancer and not the remaining population (21). These conflicting findings may be because AKI was defined by diagnostic codes in the American study, leading to an underestimation of AKI in their population (22). We defined AKI using internationally accepted guidelines (serum creatinine and urine output data), likely enhancing sensitivity and specificity of our main exposure variable. In the fully adjusted model, children with complex chronic illness were at approximately 300% higher risk of readmission at all three time points. These results reflect what has been found previously (23).

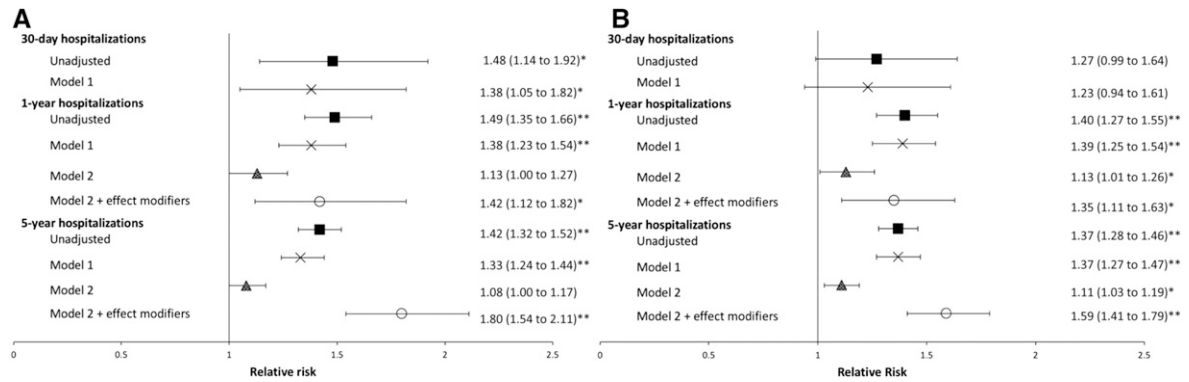
After adjustments, AKI was associated with more frequent 5-year outpatient physician visits. This was true even when nephrology visits were removed, indicating that children with AKI have higher health care use to other providers as well. It is important to note that <25% of these children with AKI saw a nephrologist 5 years postdischarge. There are currently no follow-up guidelines for

children with AKI, a population with significant morbidity. Future research should evaluate what factors, including AKI, are associated with poor long-term outcomes.

Given the paucity of data on this topic, our study adds to the global understanding of factors associated with long-term morbidity and health care use in critically ill children. We evaluated variables that are easily ascertainable at the time of discharge, providing a starting point for risk stratifying which patients should be targeted for follow-up intervention strategies, with the ultimate goal of decreasing the number of hospitalizations and emergency room visits.

It is challenging to understand if AKI is simply a marker for illness severity or if it directly affects health care utilization. One hypothesis is that children with AKI may progress to develop CKD, requiring more care; however, future research would have to evaluate the hospitalization causes in this population to elucidate this (24–27). AKI may have underappreciated acute and/or chronic nonkidney organ complications that contribute to prolonged recovery (example: cardiac, respiratory), contributing to higher health care utilization (28–30). What remains unknown is the effect of provider biases on health care utilization postdischarge. The perceptions of health care providers on what follow-up patients with versus without AKI need, and whether this affects health care utilization independent of patient health events, is unknown. Future research should aim to evaluate current health care provider perceptions on post-AKI follow-up, devise rational guidelines for AKI follow-up targeted to primary care physicians as well as nephrologists, and determine the extent to which instituting such guidelines affects patient outcomes.

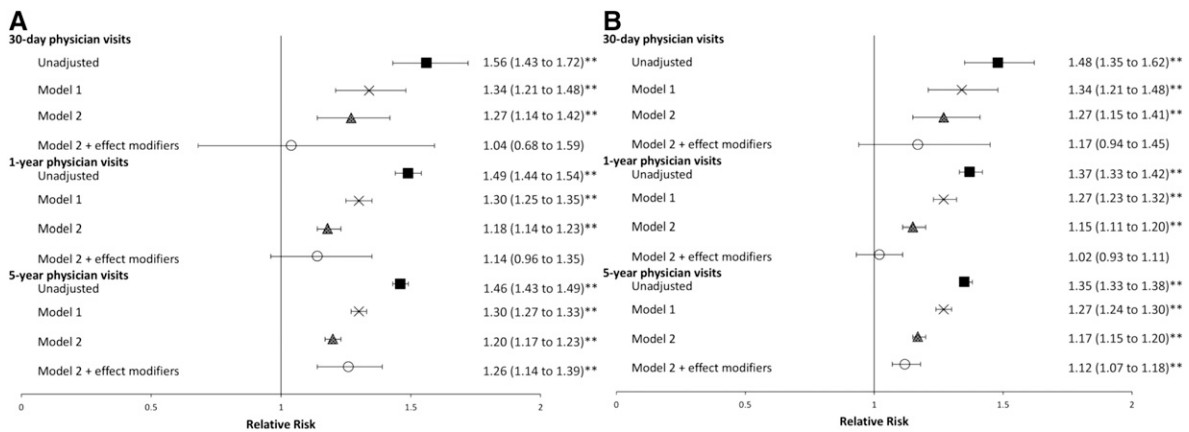
This study had some limitations. Although we controlled for effects of multiple variables, there are postdischarge variables (new treatments, diagnoses) that we could not account for. For example, we did not evaluate postdischarge CKD or recurrence of AKI during future hospitalizations. There are no validated definitions for



**Figure 2. | Unadjusted and adjusted associations of AKI with 30-day, 1-year, and 5-year postdischarge hospitalizations.** Relative risk (95% confidence interval) for 30-day, 1-year, and 5-year hospitalizations for patients with (A) AKI defined using serum creatinine alone ( $n=1575$ ) and (B) AKI defined using serum creatinine and urine output ( $n=1622$ ). The unadjusted (squares), model 1 adjustments (crosses), model 2 adjustments (triangles), and model 2 adjustments with effect modifiers (circles) relative risks and 95% confidence intervals for (A) AKI by serum creatinine criteria and (B) AKI by serum creatinine and urine output criteria, for 30-day, 1-year, and 5-year hospitalizations for patients. Multivariable Poisson regression was used in all multivariable analyses to calculate adjusted relative risks. Model 2 adjustments were not made for the 30-day outcomes due to low numbers of hospitalizations. Model 1 adjusted for age (continuous), sex, center, significant diagnoses from univariable analysis (oncologic, diabetes, trauma, infection, cardiac [nonsurgical], kidney, neurology/gastrointestinal/respiratory), death rate fourth quartile versus others, nephrotoxic antibiotics, vasopressors, and steroids. Model 2 adjusted for all variables in model 1 plus deprivation index (fourth/fifth quintile versus others), Pediatric Medical Complexity Algorithm score, rural versus urban, baseline number of hospitalizations, and family doctor/pediatrician (5 years only). Effect modifiers added to model 2 include: AKI×death rate, AKI×material deprivation index, AKI×social deprivation index, AKI×number of hospitalizations 12 months prior, and AKI×primary care doctor (yes/no). For model 2 the total  $N$  decreases because the deprivation index could not be calculated on all patients.  $n$  values for model 2: (A) AKI serum creatinine alone ( $n=1497$ ), (B) AKI serum creatinine and urine output ( $n=1539$ ). \* $P<0.05$ ; \*\* $P<0.001$ .

administrative data-defined pediatric CKD or AKI. Future research should evaluate how to best define CKD and AKI in children using diagnostic and procedure codes to garner knowledge on these postdischarge outcomes and their effects on other patient outcomes. We did not control for

hospital discharge kidney function, because few patients had serum creatinine measured near hospital discharge. Given recent evidence on the potential effect of hospital discharge kidney function on long-term outcomes, future research in children should evaluate this exposure in a



**Figure 3. | Unadjusted and adjusted associations of AKI with 30-day, 1-year, and 5-year postdischarge physician visits.** Relative risk (95% confidence interval) for 30-day, 1-year, and 5-year physician visits for patients with (A) AKI defined using serum creatinine alone ( $n=1575$ ) and (B) AKI defined using serum creatinine and urine output ( $n=1622$ ). The unadjusted (squares), model 1 adjustments (crosses), model 2 adjustments (triangles), and model 2 adjustments with effect modifiers (circles) relative risks and 95% confidence intervals for (A) AKI by serum creatinine criteria and (B) AKI by serum creatinine and urine output criteria, for 30-day, 1-year, and 5-year physician visits for patients. Multivariable Poisson regression was used in all multivariable analyses to calculate adjusted relative risks. Model 1 and model 2 are the same as described in Figure 2 except we did not control for family physician/pediatrician for the 5-year outcome in model 2. Effect modifiers added to model 2 include: AKI×sex, AKI×center, AKI×oncologic, AKI×infection, AKI×cardiac (nonsurgical), AKI×kidney, AKI×neurology/gastrointestinal/respiratory, AKI×death rate, AKI×material deprivation index, AKI×Pediatric Medical Complexity Algorithm, and AKI×number of hospitalizations 12 months prior. For model 2 the total  $N$  decreases because the deprivation index could not be calculated on all patients.  $n$  values for model 2: (A) AKI serum creatinine alone ( $n=1497$ ), (B) AKI serum creatinine and urine output ( $n=1539$ ). \*\* $P<0.001$ .

larger sample size, considering other discharge characteristics (13). We excluded patients undergoing cardiac surgery, because this population undergoes very specific treatments with a unique AKI pathophysiology; very specific factors will drive long-term health care utilization in this population, who should be studied separately in future research. This study was conducted in Quebec and therefore may not be generalizable to patient populations in other provinces or countries without universal health care. We were unable to determine if patients moved out of province and whether this was different across AKI groups, leading to bias. However, during the study period, on average <0.5% of the Quebec population emigrated per year and there is little reason to suspect that this should differ between patients with AKI versus patients without AKI (31). Inherent to all studies on pediatric AKI was the lack of serum creatinine measurements in a substantial proportion of patients, required for AKI ascertainment. We believe that with increasing awareness of the importance of AKI on short- and long-term outcomes, guidelines on which patients should have kidney function systematically monitored, and knowledge translation interventions to apply such guidelines, should be developed. Our evaluation of AKI defined using only serum creatinine criteria (as used in the majority of pediatric AKI studies) as well as the AKI definition including urine output criteria was useful to enhance sensitivity of identifying patients with AKI. However, our results show that adding urine output to AKI ascertainment did not lead to substantial differences in AKI-outcome associations, suggesting that for determining AKI status for such studies, utilizing only serum creatinine criteria may be adequate.

AKI in critically ill children was associated with higher hospitalizations and physician visits in the long-term. Future research should elucidate the mechanism of this association and begin to identify and target at-risk groups for long-term studies and health interventions. Research should aim to develop evidence-based recommendations on postdischarge follow-up of children with AKI and evaluate the effectiveness and cost of such monitoring interventions.

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#### Disclosures

None.

#### References

- Alkandari O, Eddington KA, Hyder A, Gauvin F, Ducruet T, Gottesman R, Phan V, Zappitelli M: Acute kidney injury is an independent risk factor for pediatric intensive care unit mortality, longer length of stay and prolonged mechanical ventilation in critically ill children: A two-center retrospective cohort study. *Crit Care* 15: R146, 2011
- Kaddourah A, Basu RK, Bagshaw SM, Goldstein SL; AWARE Investigators: Epidemiology of acute kidney injury in critically ill children and young adults. *N Engl J Med* 376: 11–20, 2017
- Schneider J, Khemani R, Grushkin C, Bart R: Serum creatinine as stratified in the RIFLE score for acute kidney injury is associated with mortality and length of stay for children in the pediatric intensive care unit. *Crit Care Med* 38: 933–939, 2010
- Sutherland SM, Byrnes JJ, Kothari M, Longhurst CA, Dutta S, Garcia P, Goldstein SL: AKI in hospitalized children: Comparing the pRIFLE, AKIN, and KDIGO definitions. *Clin J Am Soc Nephrol* 10: 554–561, 2015
- Volpon LC, Sugo EK, Consulín JC, Tavares TL, Aragon DC, Carlotti AP: Epidemiology and outcome of acute kidney injury according to pediatric risk, injury, failure, loss, end-stage renal disease and kidney disease: Improving global outcomes criteria in critically ill children—A prospective study. *Pediatr Crit Care Med* 17: e229–e238, 2016
- Brown JR, Hisey WM, Marshall EJ, Likosky DS, Nichols EL, Everett AD, Pasquali SK, Jacobs ML, Jacobs JP, Parikh CR: Acute kidney injury severity and long-term readmission and mortality after cardiac surgery. *Ann Thorac Surg* 102: 1482–1489, 2016
- Coca SG, Singanamala S, Parikh CR: Chronic kidney disease after acute kidney injury: A systematic review and meta-analysis. *Kidney Int* 81: 442–448, 2012
- Horkan CM, Purtle SW, Mendu ML, Moromizato T, Gibbons FK, Christopher KB: The association of acute kidney injury in the critically ill and postdischarge outcomes: A cohort study\*. *Crit Care Med* 43: 354–364, 2015
- Koulouridis I, Price LL, Madias NE, Jaber BL: Hospital-acquired acute kidney injury and hospital readmission: A cohort study. *Am J Kidney Dis* 65: 275–282, 2015
- Sawhney S, Marks A, Fluck N, McLernon DJ, Prescott GJ, Black C: Acute kidney injury as an independent risk factor for unplanned 90-day hospital readmissions. *BMC Nephrol* 18: 9, 2017
- Silver SA, Harel Z, McArthur E, Nash DM, Acedillo R, Kitchlu A, Garg AX, Chertow GM, Bell CM, Wald R: 30-Day readmissions after an acute kidney injury hospitalization. *Am J Med* 130: 163–172.e4, 2017
- Greenberg JH, Coca S, Parikh CR: Long-term risk of chronic kidney disease and mortality in children after acute kidney injury: A systematic review. *BMC Nephrol* 15: 184, 2014
- Hollander SA, Montez-Rath ME, Axelrod DM, Krawczeski CD, May LJ, Maeda K, Rosenthal DN, Sutherland SM: Recovery from acute kidney injury and CKD following heart transplantation in children, adolescents, and young adults: A retrospective cohort study. *Am J Kidney Dis* 68: 212–218, 2016
- Hessey E, Ali R, Dorais M, Morissette G, Pizzi M, Rink N, Jovet P, Lacroix J, Phan V, Zappitelli M: Evaluation of height-dependent and height-independent methods of estimating baseline serum creatinine in critically ill children. *Pediatr Nephrol*, 32: 1953–1962, 2017
- Pampalon R, Gamache P, Hamel D: The Québec Index of Material and Social Deprivation. In: *Institut national de santé publique du Québec*, Québec city, QC, Government of Québec, 2011
- Simon TD, Cawthon ML, Stanford S, Popalisky J, Lyons D, Woodcox P, Hood M, Chen AY; Center of Excellence on Quality of Care Measures for Children with Complex Needs (COE4CCN) Medical Complexity Working Group: Pediatric medical complexity algorithm: A new method to stratify children by medical complexity. *Pediatrics* 133: e1647–e1654, 2014
- Kidney Disease: Improving global outcomes (KDIGO) acute kidney injury work group: KDIGO clinical practice guideline for acute kidney injury. *Kidney Int* 2[Suppl]: 1–138, 2012
- Akcan-Arkan A, Zappitelli M, Loftis LL, Washburn KK, Jefferson LS, Goldstein SL: Modified RIFLE criteria in critically ill children with acute kidney injury. *Kidney Int* 71: 1028–1035, 2007
- Pollack MM, Ruttimann UE, Getson PR: Pediatric risk of mortality (PRISM) score. *Crit Care Med* 16: 1110–1116, 1988
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative: The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. *J Clin Epidemiol* 61: 344–349, 2008

21. Hartman ME, Saeed MJ, Bennett T, Typpo K, Matos R, Olsen MA: Readmission and late mortality after critical illness in childhood. *Pediatr Crit Care Med* 18: e112–e121, 2017
22. Waikar SS, Wald R, Chertow GM, Curhan GC, Winkelmayr WC, Liangos O, Sosa MA, Jaber BL: Validity of international classification of diseases, ninth revision, clinical modification codes for acute renal failure. *J Am Soc Nephrol* 17: 1688–1694, 2006
23. O'Mahony L, O'Mahony DS, Simon TD, Neff J, Klein EJ, Quan L: Medical complexity and pediatric emergency department and inpatient utilization. *Pediatrics* 131: e559–e565, 2013
24. Arora P, Kausz AT, Obrador GT, Ruthazer R, Khan S, Jenuleson CS, Meyer KB, Pereira BJ: Hospital utilization among chronic dialysis patients. *J Am Soc Nephrol* 11: 740–746, 2000 [PubMed]
25. Gerson AC, Riley A, Fivush BA, Pham N, Fiorenza J, Robertson J, Chandra M, Trachtman H, Weiss R, Furth SL: Council on Pediatric Nephrology and Urology of New York/New Jersey; Kidney and Urology Foundation of America: Assessing health status and health care utilization in adolescents with chronic kidney disease. *J Am Soc Nephrol* 16: 1427–1432, 2005 [PubMed]
26. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY: Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 351: 1296–1305, 2004
27. Khan SS, Kazmi WH, Abichandani R, Tighiouart H, Pereira BJ, Kausz AT: Health care utilization among patients with chronic kidney disease. *Kidney Int* 62: 229–236, 2002
28. Basu RK, Wheeler DS: Kidney-lung cross-talk and acute kidney injury. *Pediatr Nephrol* 28: 2239–2248, 2013
29. Doi K, Rabb H: Impact of acute kidney injury on distant organ function: Recent findings and potential therapeutic targets. *Kidney Int* 89: 555–564, 2016
30. Doyle JF, Forni LG: Acute kidney injury: Short-term and long-term effects. *Crit Care* 20: 188, 2016
31. *Ministère de l'Immigration, de la Diversité et de l'Inclusion. Recueil de statistiques sur l'immigration et la diversité au Québec*, Montreal, QC, Gouvernement du Québec, 2014

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