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Characteristics and Outcomes of Patients Discharged Home from an Emergency Department with Acute Kidney Injury: A Population-Based Cohort Study

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Abstract

We designed a population-based cohort study to describe the characteristics and outcomes of 6346 adults discharged home from an emergency department (ED) with acute kidney injury (AKI). Within 30 days of discharge, 149 (2.3%) patients died (stage 1: 2.1%, stage 2: 5.2%, and stage 3 AKI: 15.9%). We also compared 30-day mortality to patients hospitalized with AKI and patients discharged home with no AKI in two separate propensity score-matched analyses. An ED discharge versus hospitalization was associated with lower 30-day mortality (3.0% vs. 11.9%, relative risk (RR): 0.25, 95% confidence interval (CI): 0.21-0.30). An ED discharge home with AKI versus no AKI was associated with higher 30-day mortality (2.2% vs. 1.4%, RR: 1.56, 95% CI: 1.20-2.04). Although sicker patients are appropriately hospitalized, patients discharged home from the ED with AKI remain at risk of adverse outcomes. A better understanding of care appears warranted, as is testing strategies to improve care.

Keywords

Acute kidney injury, emergency department, discharge home, hospitalization, all-cause mortality

Dedications

This thesis is dedicated to Tanya, Simon, and Cesare for their love and support.

Co-Authorship Statement

The study presented here was conceived, designed, and executed by Rey Acedillo. Dr. Amit Garg was the primary supervisor and was involved in all aspects of this work. Dr. Neil Klar was a thesis committee supervisor and provided comprehensive feedback.
A version of the manuscript presented in this thesis was published in the Clinical Journal of the American Society of Nephrology on July 20, 2017. Each co-author critically appraised the manuscript and provided important feedback for manuscript revision. Danielle Nash and Eric McArthur also contributed to the study design, acquisition, and analysis of data.

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List of Abbreviations

ACR	albumin-to-creatinine ratio
ADG	Aggregated Diagnosis Group
ADP	Assistive Device Program
AKI	acute kidney injury
AKIN	Acute Kidney Injury Network
CA-AKI	community-acquired acute kidney injury
CAPE	Client Agency Program Enrolment
CCI	Canadian Classification of Health Interventions
CCP	Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures
CCRS	Continuing Care Reporting System
CI	confidence interval
CIHI	Canadian Institute for Health Information
CIHI-DAD	Canadian Institute for Health Information Discharge Abstract Database
CKD	chronic kidney disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CT	computed tomography
CTAS	Canadian Triage Acuity Scale
ED	emergency department
eGFR	estimated glomerular filtration rate
GFR	glomerular filtration rate
GP/FP	general practitioner/family physician
HCD	Home Care Database
ICD	International Classification of Diseases
ICES	Institute for Clinical Evaluative Sciences
IPDB	Institute for Clinical Evaluative Sciences Physician Database
IQR	interquartile range
KDIGO	Kidney Diseases: Improving Global Outcomes
LUTS	lower urinary tract symptoms

MOHLTC	Ministry of Health and Long-Term Care
NACRS	National Ambulatory Care Reporting System
NR	not reported
NRS	National Rehabilitation Reporting System
ODB	Ontario Drug Benefit
OHIP	Ontario Health Insurance Plan
OMHRS	Ontario Mental Health Reporting System
PCR	protein-to-creatinine ratio
RIFLE	Risk, Injury, Failure, Loss, End-stage renal disease
RPDB	Registered Persons Database of Ontario
RR	relative risk
SCr	serum creatinine
SD	standard deviation
SNRI	serotonin-norepinephrine reuptake inhibitor
SSRI	selective serotonin reuptake inhibitor
STROBE	Strengthening The Reporting of OBservational studies in Epidemiology

Glossary of Terms

Acute kidney injury	a sudden deterioration in kidney function over a period of hours to days, defined by relative changes in serum creatinine concentration from baseline.
Admission	the need for patient care under a medical service in the hospital setting.
Aggregated Diagnosis Group	a point score derived from the John Hopkins Adjusted Clinical Groups® system. It is a weighted measure of health care utilization as a proxy measure for co-morbidity and accounts for the duration of condition, severity of condition, diagnostic certainty, etiology of the condition, and specialty care involvement.
Albumin-to-creatinine ratio	a ratio between urine albumin and urine creatinine. It is used to diagnose and monitor kidney disease.
Angiotensin II receptor blocker	a class of medication that blocks (inhibits) the binding of angiotensin II to its receptor on smooth muscles surrounding blood vessels. As a result, blood vessels enlarge or dilate, and blood pressure is reduced. This medication also benefits patients with heart and chronic kidney disease.
Angiotensin-converting enzyme inhibitor	a class of medication that slows (inhibits) the activity of the enzyme angiotensin-converting enzyme, which decreases the production of angiotensin II. As a result, blood vessels enlarge or dilate, and blood pressure is reduced. This medication also benefits patients with heart and chronic kidney disease.
Anti-retroviral	one of several classes of medications used to control an HIV (a retrovirus) infection.
Anticoagulant	commonly referred to as blood thinners, a class of medication that prevents or reduces the coagulation of blood, prolonging the clotting time.

Antiplatelet	a class of medication that decreases the ability of a blood clot to form by interfering with platelet activation (clumping or aggregation).
Antipsychotic	also known as neuroleptics or major tranquilizers, a class of medication used to manage psychosis (delusions, hallucinations, paranoia or disordered thought), principally in schizophrenia and bipolar disorder.
Abdominal aortic aneurysm	an enlargement of the abdominal aorta (main artery of the human body).
Atrial fibrillation or flutter	atrial fibrillation is an abnormal heart rhythm characterized by rapid and irregular beating by the top chambers (atria) of the heart. Atrial flutter is characterized by a rapid, regular beating by the atria.
Beta-adrenergic antagonist	commonly referred to as a beta-blocker, a class of medication that blocks the beta receptors of the adrenergic sympathetic nervous system (flight or fight response), which are located on a number of organs (e.g. kidneys, heart, arteries). The net effect depends on the organ and type of beta receptor. Effects include (but not limited to) the reduction of heart rate and/or blood pressure.
Calcium channel blocker	also known as calcium channel antagonist, a class of medication that disrupts the movement of calcium. Depending on the type of calcium channel blocker, the net effect is a reduction of blood pressure by relaxing smooth muscle in blood vessels or the slowing of the heart rate by depressing the atrioventricular node in the heart.
Canadian Triage Acuity Scale	a system that categorizes patients by both injury and physiological findings, and ranks them by severity from 1–5 (1 being highest). The model is used by both paramedics and Emergency Department nurses, and also for pre-arrival notifications.

Cerebrovascular disease	Vascular disease of the cerebral circulation involving arteries supplying oxygen to the brain. A stroke is a manifestation of cerebrovascular disease.
Charlson co-morbidity index	also known as the Charlson score, an index that predicts the one-year mortality for a patient who may have a range of co-morbid conditions. The Charlson co-morbidity index is based on the International Classification of Diseases diagnosis codes found in administrative data.
Chronic kidney disease	the progressive loss in kidney function over a period of months or years.
Chronic liver disease	progressive disease of the liver over a period of at least six months.
Chronic obstructive pulmonary disease	a progressive obstructive lung disease characterized by long-term breathing problems and poor airflow. Symptoms include shortness of breath, cough, and sputum production.
Coronary angiogram	a minimally invasive procedure to access the coronary circulation and blood-filled chambers of the heart using a catheter.
Coronary artery disease	disease in which a blockage (such as a waxy substance called a plaque) develops inside the coronary arteries. Coronary arteries supply oxygen-rich blood to the heart muscle. An acute myocardial infarction (heart attack) is a manifestation of coronary artery disease.
Coronary events	a term researchers and clinicians use to encompass a number of important outcomes for patients with heart disease. These outcomes may include myocardial infarction, ischemic heart failure, unstable angina, sudden death, and procedures such as a coronary angiogram or coronary artery bypass surgery.
Corticosteroid	a class of synthetic steroid hormone medication that reduces inflammation and suppresses the immune system through a variety of mechanisms.

Creatinine	a byproduct of muscle breakdown that appears in the blood, is filtered by the kidneys, and excreted in the urine.
Dementia	a set of symptoms that are caused by disorders affecting the brain. Symptoms include memory loss, difficulties with thinking, problem-solving or language, which may be severe enough to reduce a person's ability to perform everyday activities.
Dialysis	the process of removing waste products and excess fluid from the body through a machine. Dialysis is necessary when the kidneys are not able to adequately filter toxins and waste products from the blood.
Discharge	the release of a patient from a course of care, typically referring to a patient who leaves hospital and goes home.
Disposition	the plan for continuing health care of a patient following discharge or transfer from a given health care facility.
Diuretic	a class of medication that increases production of urine (diuresis). Fluid (water and electrolytes) is excreted from the body by the kidney, which may result in blood pressure reduction. Certain diuretics promote the excretion of potassium (non-potassium sparing) while others do not (potassium-sparing).
Echocardiogram	an ultrasound of the heart.
Electronic health record	also known as an electronic medical record, a collection of patient electronically-stored health information in a digital format, which may supplement or replace a physical (paper) form of the medical chart.
End-stage kidney disease	the final stage of chronic kidney disease in which the kidneys do not function well enough to meet the needs of daily life. At this stage, renal replacement therapy is required to sustain life.

Glomerular filtration rate	the sum of all filtration rates of all functioning nephrons in the kidney. This metric is used to assess kidney function in routine care.
Heart failure	also known as congestive heart failure, heart failure occurs when the heart is unable to pump sufficiently to maintain blood flow to meet the body's needs.
Hypertension	elevated blood pressure.
Immunosuppressive medication	a class of medication that suppresses or reduces the strength of the body's immune system. Corticosteroids are also considered immunosuppressive medications. However, they have been separated into a class of their own in this study.
Kidney transplant rejection	the process of when a transplanted kidney is rejected by the person’s (recipient’s) immune system, destroying the transplanted tissue.
Lower urinary tract symptoms	a group of clinical symptoms involving the bladder, urinary sphincter, urethra, and, in men, the prostate.
Myocardial infarction	also known as a heart attack, the blockage of blood flow to a section of the heart. If blood flow is not restored quickly, that section of the heart begins to die and the level of damage depends on how long blood supply is cut off.
Nephrolithiasis	kidney stones.
Nephron	the basic structural and functional unit of the kidney. The chief function of the nephron is to regulate the concentration of water, soluble substances, and metabolic waste products substances by filtering the blood, reabsorbing what is needed, and excreting the rest as urine.
Non-steroidal anti-inflammatory drug	a class of medication used to reduce pain, decrease fever, and decrease inflammation. Non-steroidal anti-inflammatory drugs work by inhibiting the activity of cyclooxygenase-1 and cyclooxygenase-2 (COX-2) enzymes, thereby inhibiting the synthesis of prostaglandins and thromboxanes.

Oral hypoglycemic agents	also known as anti-hyperglycemic agents, a broad class of medications aimed to lower blood glucose levels. Mechanism of action depends on the type of oral hypoglycemic agent.
Osteoarthritis	a degenerative joint disease also known as “wear and tear” arthritis. The cartilage or cushion between joints breaks down leading to pain, stiffness and swelling.
Outpatient	a patient who receives medical treatment without being admitted to a hospital.
Palliative care	a multidisciplinary approach to specialized medical and nursing care for people with life-limiting illnesses, focusing on providing people with relief from the symptoms, pain, physical stress, and mental stress of the terminal diagnosis.
Parkinson’s disease	a progressive disorder of the nervous system that affects movement.
Peripheral vascular disease	also known as peripheral arterial disease, the narrowing of the blood vessels other than those that supply the heart or the brain.
Proton pump inhibitor	a class of medication that reduces gastric (stomach) acid production. Proton pump inhibitors block the hydrogen/potassium adenosine triphosphatase (ATP) pump found in gastric cells.
Renal replacement therapy	a therapy that replaces the normal blood-filtering function of the kidneys. Renal replacement therapy is a broad term that refers to all types of dialysis modalities as well as kidney transplantation.
Revascularization	the restoration of perfusion to a body part or organ that has suffered ischemia (reduction of blood supply resulting in the shortage of oxygen in tissues). It is typically accomplished by surgery. Vascular bypass and angioplasty are two primary methods of revascularization.

Rheumatoid arthritis	a long-term autoimmune disorder that primarily affects joints. It typically results in warm, swollen, and painful joints. In a person with an autoimmune disorder, their immune system attacks their own body's tissues.
Statin	a class of lipid-lowering (cholesterol) medications that inhibit the HMG-CoA (3-hydroxy-3-methyl-glutaryl-coenzyme A) reductase enzyme, which plays a central role in the production of cholesterol.
Ultrasound	an imaging method that uses high-frequency sound waves to produce images of structures within the body.
Uricosuric agents	a class of medication used to treat or prevent gout. Uricosuric medications promote excretion of uric acid in the urine.
Urine albumin	also known as albuminuria, the presence of albumin in the urine. The amount of urine albumin is not expected to exceed a threshold of 150 mg per day in patients with normal kidney function. Albumin is a protein made by the liver.
Urine dipstick	also known as a urine test strip, a basic diagnostic tool used to determine if there are abnormal changes in a patient's urine. A standard urine dipstick may comprise of several tests. Common tests include protein (albumin), glucose, white blood cells, and hemoglobin (a component of red blood cells).
Xanthine oxidase inhibitors	a class of medication used to treat or prevent gout. Xanthine oxidase inhibitors slow the enzyme xanthine oxidase, which is involved in the production of uric acid.

Chapter 1

1 Introduction

Acute kidney injury (AKI) is the sudden deterioration of kidney function which affects at least 10% of hospitalized patients.[1–3] AKI associates with increased morbidity, mortality, and health care costs exceeding $10 billion annually in the United States.[4–7]
Our understanding of AKI epidemiology is largely informed by studies conducted in hospitalized and critically ill patients.[1,3,4,8] Less is known about patients who present to the emergency department (ED), have evidence of AKI, and are discharged home. A discharge home may mean the ED health care staff felt the AKI was reversible and could be managed as an outpatient in the community or it may represent an unrecognized population at risk of adverse outcomes.

As of August 10, 2017, no study has described the characteristics and adverse outcomes of patients discharged home from the ED with AKI in comprehensive detail, nor has any study compared these outcomes to other relevant ED patient groups. To address this knowledge gap, we conducted a population-based cohort study to describe the characteristics and outcomes of this AKI subpopulation. To provide context to our results, we used propensity score methods to investigate whether an ED discharge home with AKI compared to an admission to hospital, or ED discharge home with no AKI, is associated with an altered risk of 30-day all-cause mortality.

This thesis is structured into the following chapters: 2 Literature Review, 3 Rationale and Research Questions, 4 Methods, 5 Results, and 6 Discussion. In Chapter 2, we provide an explanation of normal kidney function and define AKI. We then describe our current understanding of AKI epidemiology. Finally, we highlight a knowledge gap regarding patients discharged home from the ED with AKI. In Chapter 3, we state our research questions and rationale for each question. In Chapter 4, we provide a detailed summary of our methods. In Chapter 5, we present our results with accompanying figures and tables. In Chapter 6, we discuss our findings and their implications relative to our current

understanding of AKI in the community and in hospital. Finally, we discuss the strengths and weaknesses of this work and conclude with recommendations for future research.

Chapter 2

2 Literature Review

2.1 The Normal Kidney

2.1.1 Overview of Kidney Function

The kidney is a vital organ with several key functions. These functions include the excretion of metabolic waste products such as urea and creatinine, regulation of fluid and electrolytes such as sodium and potassium, and the production of hormones that regulate local and systemic processes involved in hemodynamics, bone mineral metabolism, and the production of red blood cells.[9]

2.1.2 Measurement of Kidney Function

The kidney is comprised of millions of nephrons, which are the main filtration units of the kidney.[9] The sum of all functioning nephron filtration rates is called the glomerular filtration rate (GFR).[10] Certain waste products of metabolism have specific properties that make them suitable candidates as biomarkers to estimate the GFR.[10] The most common biomarker used by clinicians is serum creatinine (SCr). SCr is a byproduct of muscle metabolism that is filtered and excreted unchanged by the kidneys.[10] Despite the availability of other biomarkers such as cystatin C, SCr remains the most convenient and cost-effective test for measuring kidney function in routine care.[11] SCr concentrations are incorporated into an equation to calculate the estimated GFR (eGFR).[10] The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation is a recent and accepted method of calculating the eGFR. Developed in 2009, the CKD-EPI equation has replaced the Modification of Diet in Renal Disease (MDRD) equation because of greater precision and accuracy.[12] All GFR-estimating equations assume relative stability in SCr concentrations over time and cannot be used to assess abrupt changes in kidney function.[10,13] Because of this major limitation, clinicians continue to rely on relative changes in SCr concentrations to assess AKI.[14]

2.2 Acute Kidney Injury

AKI is serious clinical condition defined by a sudden loss of kidney function, which results in the rapid accumulation of waste products, fluids, and electrolytes.[10] Acute kidney injury replaces the term acute renal failure following the recognition that smaller decrements in kidney function are clinically relevant.[14] The term AKI will be used throughout the entire thesis.

2.2.1 Definition of Acute Kidney Injury

The use of relative changes in SCr concentration is considered the standard of care for the detection of AKI. Standardized, consensus definitions for AKI have been developed for use in the general population (Table 2-1). The most recent consensus definition for AKI was developed by the Kidney Diseases: Improving Global Outcomes (KDIGO) AKI working group in 2012,[14] adapted from two criteria: RIFLE (Risk, Injury, Failure, Loss, End-stage renal disease) in 2004,[15] and AKIN (Acute Kidney Injury Network) in 2007.[16]

Table 2-1: Diagnostic Criteria for Acute Kidney Injury

Criteria	**SCr criteria**			**Urine output criteria**
	RIFLE[15]	**AKIN[16]**	**KDIGO[14]**	
Definition	Relative increase in SCr from baseline of ≥50% developing within 7 days	Relative increase in SCr of ≥26.5 μmol/L or ≥50% from baseline developing within 48 hours	Absolute increase in SCr of ≥26.5 μmol/L developing within 48 hours or relative increase ≥50% developing within 7 days	Urine output of <0.5 mL/kg/hour for >6 hours

Adapted from the 2012 KDIGO clinical practice guidelines for AKI.[14]

AKI can be diagnosed when one of the following criteria is met: (1) SCr increase of ≥26.5 μmol/L within 48 hours; (2) a 50% increase or more from baseline (compared to a known or suspected baseline value) within seven days; (3) a reduction in urine output to <0.5 mL/kg/day for at least six hours.[14] AKI can be stratified into three stages of severity. Stage 1 AKI is defined as a relative increase in SCr ≥50% to <100% within seven days, an absolute increase in SCr of ≥26.5 μmol/L within 48 hours, or a decrease in urine

output to <0.5 mL/kg/hour for 6 to <12 hours. Stage 2 AKI is defined as a relative increase in SCr value of ≥100% to <200% from baseline within seven days or a reduction in urine output to <0.5 mL/kg/hour for 12 to <24 hours. Stage 3 AKI is defined as a relative increase in SCr value of >200% from baseline or an increase in SCr value to ≥354 μmol/L within seven days, or the initiation of dialysis (renal replacement therapy).

2.3 Acute Kidney Injury Epidemiology

AKI is a serious clinical condition that affects at least 10% of all patients in hospital.[1–3,17] In the United States, the incremental health care costs attributed to AKI in hospitalized patients are in excess of $10 billion per year.[4] Morbidity and mortality associated with AKI escalates with severity.[4,8,18–20] Among patients who receive dialysis for the management of their AKI, short-term mortality exceeds 50%.[8,21] Large cohort studies have also shown that AKI as defined by modest increments in SCr concentration (e.g. increase by 50% or more) independently associates with a 3.5 day increase in hospital length of stay and a 4.4-fold increase in mortality.[4]

Individuals who survive an episode of AKI during hospitalization remain at risk of short and long-term adverse outcomes.[7,18,22] Within the first 3 to 6 months, survivors of AKI are at 10-fold greater risk of developing *de novo* chronic kidney disease (CKD), at 3-fold greater risk of progression to end-stage kidney disease, and have double the risk of death.[20,23,24] In the long-term AKI is associated with an increased risk of coronary events (non-fatal myocardial infarction, need for coronary angiogram, or coronary artery bypass surgery),[25,26] stroke,[27] and hypertension.[28] Despite accumulating evidence that AKI survivors are a high risk group, follow-up care remains poor and inadequate.[29–31]

2.4 Emergency Department Setting

The ED is a common place for patients to seek health care. From 2015 to 2016, the Canadian Institute for Health Information (CIHI) reported that 4,865,575 adults 20 years and older visited an ED in Ontario, 556,786 (11.4%) of whom required admission to hospital.[32] The reasons for the ED visits varied widely, ranging from acute abdominal and

pelvic pain (3.6%) to gastroenteritis (1.6%).[32] The ED was also a point of access to receive primary care for patients with non-urgent issues despite being registered with a family physician.[33,34]

The ED is an environment where visits are brief and transient.[35–37] Following their clinical assessment, ED physicians are challenged with the task of determining the disposition of the patient. The patient may be discharged home to the community with or without outpatient follow-up, transferred to another hospital, or referred to another medical service to be admitted to hospital. The final decision on disposition is influenced by several patient-, physician-, facility-, and regional-related factors.[38,39]

The ED is a common clinical setting for patients to present with AKI,[40,41] and studies have primarily focused on patients admitted to hospital from the ED.[42,43] However, in some circumstances patients with AKI who present to the ED will be discharged home rather than be admitted to hospital.

2.5 Patients Discharged from the Emergency Department with Acute Kidney Injury

2.5.1 Search Strategy and Quality Assessment of Prior Studies

A single reviewer conducted a literature search to identify prior studies that described patients discharged home from the ED with AKI. MEDLINE Ovid and Pubmed were searched for relevant articles in March 2016. The search was updated on August 10, 2017. The final search strategy combined two previously published search strategies for AKI- and ED-related studies (Appendix A).[44,45] Key words included “community-acquired”, “outpatient”, “ambulatory care”, and “primary care” because patients discharged home from the ED may be described in studies investigating community-acquired AKI. The reviewer also used the related articles option in Pubmed and searched relevant review articles and reference lists of included articles.

Our inclusion and exclusion criteria were developed a priori. Any study published in English was eligible for review. Studies were excluded using any one of the following criteria: (1) duplicate studies; (2) reviews, editorial articles, or consensus guidelines; (3) pediatric (age less than 18 years) or non-human studies; (3) studies that did not describe patients with AKI; (4) studies in which AKI did not occur in the ED setting; and (5) studies that did not describe patients discharged home.

A single reviewer screened all citations for potentially relevant articles, reviewed full-text articles for eligibility, and then abstracted the data from eligible studies. The same reviewer evaluated the quality of individual studies using the Downs and Black quality assessment method, a list of 27 criteria to evaluate both randomized and non-randomized studies.[46] This scale assesses the completeness and clarity of study reporting, external validity, internal validity (e.g. bias and confounding), and power. The tool was modified slightly for use in our review. Specifically, the scoring for question 27 dealing with statistical power was simplified to a choice of awarding either 1 or 0 points depending on whether there was sufficient power to detect a clinically important effect. On the modified scale, we gave all included studies a score from 0 to 28, grouped into the following four quality levels: excellent (26 to 28), good (20 to 25), fair (15 to 19) and poor (14 or less).

2.5.2 Summary of Previous Literature

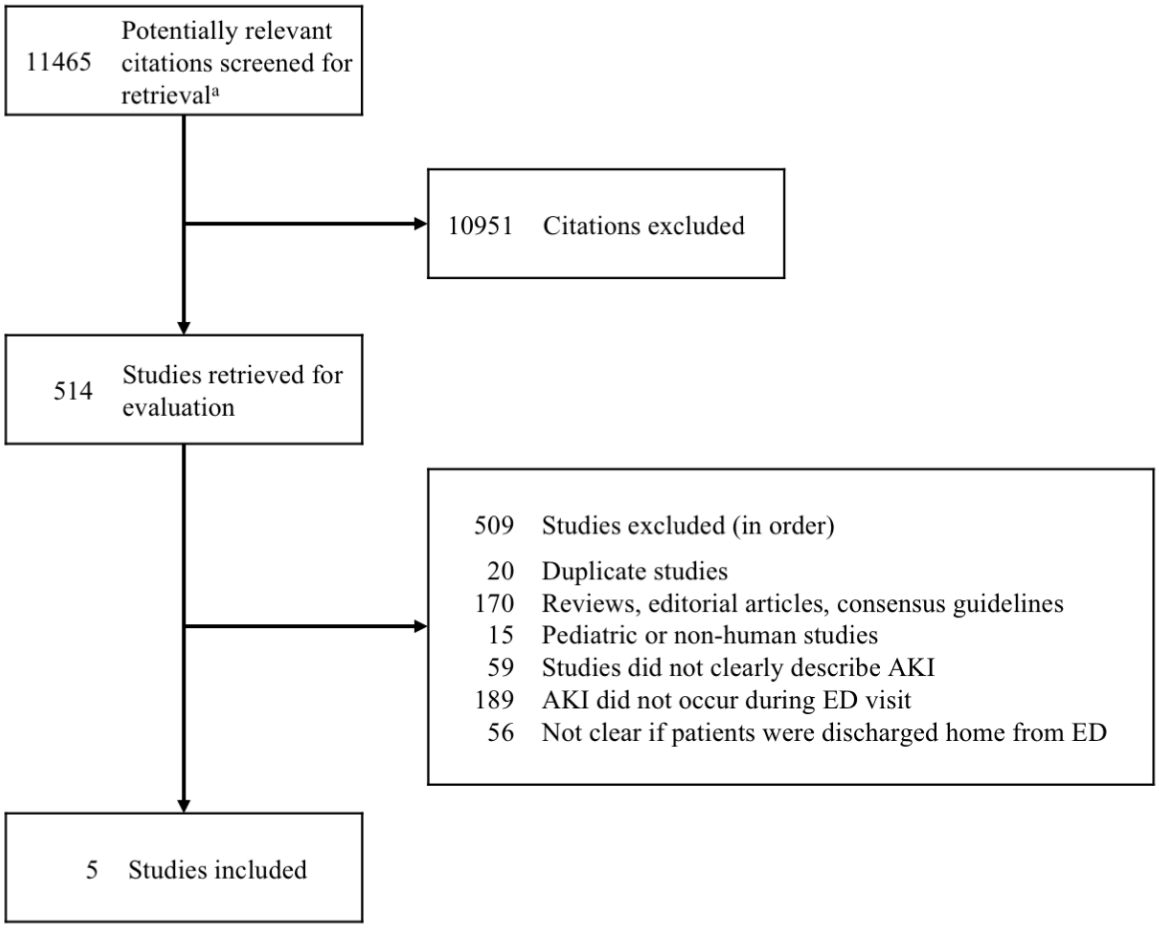
A study flow diagram of the literature search is shown in Figure 2-1 and from the beginning excludes the citation related to this thesis.[47] A single reviewer screened 11,465 articles for potentially relevant citations and selected 514 studies for evaluation. There were 509 articles excluded, leaving five studies which distinctly described patients who visited an ED, had evidence of AKI, and were discharged home (Table 2-2).[48–52]

Three studies were from the United Kingdom,[49–51] one was from the United States,[48] and one was from Canada.[52] A total of 3031 patients visited the ED, had evidence of AKI, and were discharged home. In all five studies, patients discharged from the ED with AKI were described as a subgroup of larger patient population. The 2013 study by Roghmann

et al. showed 71 (0.01%) of 1,066,135 patients presenting to the ED with lower urinary tract symptoms were discharged home with AKI.[48] In 2014, Talabani *et al.* identified 230 consecutive patients in the United Kingdom with community-acquired AKI who visited either a primary care physician or acute care centre (i.e. emergency department).[49] The mean age of the entire cohort was 70 years and the 90-day mortality was 17%. In a subset of 119 patients who visited an acute care centre, 49 (41%) were discharged home. The 2017 study by Hazara *et al*. used an electronic AKI alerting system to identify 1277 AKI episodes in 1185 patients who visited the ED.[51] The mean age was 72 years, 50% were male, and the 30-day mortality was 25%. The authors also found 13% (161) of all AKI alerts represented ED patients discharged home. However, for all three studies, baseline characteristics and outcomes specific to patients discharged home from the ED with AKI were lacking.

The 2016 study by Holmes *et al.* examined 9375 patients with AKI assessed in accident and emergency or acute assessment units. The mean age ranged between 68 and 71 years and 40 to 49% had pre-existing CKD. In a subgroup of 2719 patients (29%) discharged home, the 90-day mortality was 10 to 15%.[50] There was no additional information on baseline characteristics. In 2017, Scheuermeyer *et al.* studied 1651 consecutive ED patient visits over a one-week period, 90 (6%) of whom were diagnosed with AKI.[52] Among patients with AKI, 31 (34%) were discharged home. The age ranged between 29 and 93 years, co-morbidities were described in select cases, and there were no deaths within 30 days of an ED discharge home. Only four patients (13%) had renal-specific follow up.

Figure 2-1: Literature Review Flow Diagram



Abbreviations: AKI, acute kidney injury; ED, emergency department.

[a] Details of the literature review search strategy is shown in Appendix A. The numbers shown in the figure exclude the citation related to this thesis.[47]

Table 2-2: Summary of Studies Examining Patients Discharged Home from the Emergency Department with Acute Kidney Injury

Author	**Year**	**Location**	**Population**	**Description**	**Key findings**	**Limitations**	**Quality score (0-28)[a]**
Roghmann *et al*.	2013	United States, 2006-2009	1,178,423 patients presenting to the ED with LUTS	Patients stratified by ED disposition (admitted vs. discharged), various outcomes defined as adverse events, (e.g. ICD-9 code for AKI: 584)	Of the 1,066,135 patients with LUTS discharged home from the ED, 71 (0.01%) had AKI.	No baseline characteristics specific to AKI patients.	18
Talabani *et al.*	2014	United Kingdom (Cardiff), Apr 2009	230 patients identified with CA-AKI on health region	Patients stratified by type and location of CA-AKI diagnosis. AKI defined by SCr values using KDIGO criteria. Outcomes included mortality, CKD progression, and renal recovery.	119 patients diagnosed with AKI in an acute care setting (ED), with 49 (41%) discharged home.	Descriptive study only. No baseline characteristics or outcomes specific to this subgroup of patients with CA-AKI.	17
Holmes *et al.*	2016	United Kingdom (Wales), Mar - Aug 2015	17,689 AKI episodes generated using e-alert system in the health region	Patients stratified by either CA-AKI vs HA-AKI, and AKI severity. AKI defined using KDIGO criteria. Outcome was	Of the 9375 AKI episodes diagnosed in the ED, 2719 (29%) were discharged home (similar for all AKI stages),	Descriptive study. Except for age and CKD, no other baseline characteristic for our patient population of	16

				location of diagnosis and 90-day mortality.	respectively. The 90-day mortality was 10-15%.	interest was present.	
Hazara *et al*.	2016	United Kingdom (Kingston-upon-Hull), Nov 2013 – Apr 2014	1277 AKI episodes generated in 1185 ED patients using an e-alert system.	AKI defined using KDIGO criteria. Outcome was 30-day mortality.	Of the 1277 AKI episodes identified in the ED, 161 (13%) AKI episodes (98% stage 1 AKI) represented patients discharged home.	Descriptive study. No detailed baseline characteristics. 30-day mortality not described for subgroup.	15
Scheuermeyer *et al*.	2017	Canada (Vancouver), Jan 2014	1651 unique patient ED visits screened for AKI in two EDs over a 1-week period	AKI defined using KDIGO criteria. Outcomes included follow-up SCr testing, mortality, and need for renal replacement therapy at 30 days.	Of the 90 patients who had AKI, 31 (34%) were discharged home. Four patients (13%) were deemed to have appropriate follow-up and none died. ED diagnosis provided, detailed chart review for each patient.	Small study. Clinical vignette for each case. No detailed list of baseline characteristics for subgroup.	14

Abbreviations: AKI, acute kidney injury; CA-AKI, community-acquired acute kidney injury; CKD, chronic kidney disease; ED, emergency department; HA-AKI, hospital-acquired acute kidney injury; ICD, International Classification of Diseases; KDIGO, Kidney Disease: Improving Global Outcomes; LUTS, lower urinary tract symptoms; SCr, serum creatinine.

[a] We evaluated the quality of individual studies using the Downs and Black quality assessment method, which is a list of 27 criteria to evaluate both randomized and non-randomized trials.[46] This scale assesses the completeness and clarity of study reporting, external validity, internal validity (e.g. bias and confounding) and power. The tool was modified slightly for use in our review. Specifically, the scoring for question 27 dealing with statistical power was simplified to a choice of awarding either 1 or 0 points

depending on whether there was sufficient power to detect a clinically important effect. On the modified scale, we gave all included studies a score from 0 to 28, grouped into the following four quality levels: excellent (26 to 28), good (20 to 25), fair (15 to 19) and poor (14 or less).

Chapter 3

3 Rationale and Research Questions

3.1 The Need for Research

No study has investigated the characteristics and outcomes of patients discharged home from the ED with AKI in detail nor has any study provided context for these outcomes by comparing this group to other relevant ED subpopulations. A better understanding of this patient population is required.

The research questions and hypotheses for this study are separated into (1) a descriptive analysis of the characteristics and outcomes of patients discharged home from the ED with AKI (Chapter 3.2.1) and (2) a propensity score matching analysis (Chapter 3.2.2).

3.2 Research Questions and Hypotheses

3.2.1 Descriptive Analysis

3.2.1.1 Primary Questions

1) In the ED setting, what are the characteristics of patients discharged home with AKI?

   Hypothesis: Co-morbid conditions, such as diabetes, hypertension, and CKD and the use of certain medications such as angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and diuretics will be common in this patient population.

2) In the ED setting, what is the 30-day risk of all-cause mortality in patients discharged home with AKI?

   Hypothesis: Based on our literature review,[48–52] the 30-day risk of all-cause mortality is estimated to be between 0% and 15%. This risk will increase with AKI severity.

3.2.1.2 Secondary Questions

1) In the ED setting, what is the 30-day risk of receipt of hospital-based acute dialysis in patients discharged home with AKI?

   Hypothesis: Our literature search did not inform the expected rate for the receipt of hospital-based acute dialysis. Given these patients are discharged home rather than admitted to hospital, the receipt of hospital-based acute dialysis is expected is to be low, and increase with AKI severity.

2) In the ED setting, what is the 30-day risk of five additional outcomes: (1) need for subsequent hospitalization after an ED discharge home, (2) at least one outpatient physician visit (family physician, internist, nephrologist, or urologist), (3) at least one outpatient SCr test, (4) at least one outpatient urine test for protein, and (5) total health care costs?

   Hypothesis: Our literature search did not inform the expected rate for these additional outcomes. However, these outcomes are expected to increase with AKI severity.

3.2.2 Propensity Score Matching Analysis

3.2.2.1 Primary Questions

1) In the ED setting, does a group of patients discharged home with AKI compared to a group of patients admitted to hospital with AKI with similar baseline characteristics have an altered 30-day risk of all-cause mortality?

   Hypothesis: An ED discharge home with AKI will be associated with a lower risk of mortality compared to a hospital admission with AKI. It is expected that critically ill patients will be appropriately admitted to hospital for ongoing management. It is unlikely that an ED discharge home with AKI would confer a higher risk of mortality compared to a hospital admission with AKI.

2) In the ED setting, does a group of patients discharged home with AKI compared to a group of patients discharged home with no AKI with similar baseline characteristics have an altered 30-day risk of all-cause mortality?

   Hypothesis: An ED discharge home with AKI will be associated with a higher risk of mortality compared to an ED discharge home with no AKI. It is expected our findings to be similar in studies that compared hospitalized patients with AKI versus no AKI.

3.2.2.2 Secondary Questions

1) In the ED setting, does a group of patients discharged home with AKI compared to a group of patients admitted to hospital with AKI with similar baseline characteristics have an altered 30-day risk of receipt of hospital-based acute dialysis?

   Hypothesis: An ED discharge home with AKI will be associated with a lower risk of receipt of hospital-based acute dialysis compared to a hospital admission with AKI.

2) In a subgroup analysis, is the association between an ED discharge home with AKI (versus a hospital admission with AKI) and 30-day risk of all-cause mortality modified by AKI stage?

   Hypothesis: Compared with a hospital admission with AKI, the relative association between an ED discharge home with AKI and all-cause mortality may be attenuated with an increase in AKI stage. Based on previous literature, higher stages of AKI associate with increased mortality in a group patients with AKI who are managed as outpatients.[49,53]

3) In the ED setting, does a group of patients discharged home with AKI compared to a group of patients discharged home with no AKI with similar baseline characteristics have an altered 30-day risk of receipt of hospital-based acute dialysis?

Hypothesis: An ED discharge home with AKI will be associated with a higher risk of receipt of hospital-based acute dialysis compared to an ED discharge home with no AKI.

4) In a subgroup analysis, is the association between an ED discharge home with AKI (versus an ED discharge home with no AKI) and the risk of 30-day all-cause mortality modified by the presence of pre-ED visit CKD?

   Hypothesis: Compared with an ED discharge home with no AKI, an ED discharge home with AKI will be associated with a higher risk of all-cause mortality by the presence of CKD.[54,55]

Chapter 4

4 Methods

4.1 Study Design and Setting

We conducted a population-based, retrospective cohort study of adults 40 years and older from June 1, 2003 to March 31, 2012 in Southwestern Ontario, Canada at the Institute for Clinical Evaluative Sciences (ICES) Western facility. Southwestern Ontario has approximately 1.6 million residents with universal access to hospital care and physician services through the Ontario Health Insurance Plan (OHIP).[56] Universal prescription drug coverage is available for adults 65 years and older through the Ontario Drug Benefit (ODB) program. Ontario's linked health administrative databases provide research studies with rich information, large sample sizes, and complete short- and long-term follow-up. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational studies (Appendix B).[57]

4.2 Ethics

Our study was approved by the research ethics board at Sunnybrook Health Sciences Centre in Toronto, Ontario. Participant informed consent was not required for this study. However, to comply with privacy regulations for minimizing the chance of patient re-identification, results were suppressed in cells with five or fewer patients (reported at ≤5). The total number of patients was not reported (NR) if there were other calculations that could also result in the re-identification of five or fewer patients.

4.3 Data Sources

We ascertained patient, ED, and hospital characteristics, prescription drug information, and outcome data from 13 health administrative and laboratory databases. These datasets were linked using unique, encoded identifiers and analyzed at the ICES Western facility.

4.3.1 Administrative Databases

Ontario Registered Persons Database (RPDB): We obtained patient demographics (age, sex, and vital status), income (averaged quintiles of neighbourhood income), and residential location (urban vs. rural). Vital statistics are available for all Ontario residents who have ever been issued a health card. We used vital statistics information to ascertain the outcome of all-cause mortality.

Ontario Drug Benefit (ODB): The ODB database contains records of all outpatient drug prescriptions dispensed to residents 65 years and older. Drug prescription accuracy in the ODB database is high, with an error rate of less than 1%.[58] We used this database to obtain baseline medication use for ODB program eligible individuals in the 120 days prior to the ED visit date (referred to as the cohort entry or index date) and to determine residential status (community-dwelling vs. long-term care).

Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD) and National Ambulatory Care Reporting System (NACRS): We identified diagnostic and procedural information on ED visits from NACRS and hospitalizations from CIHI-DAD. Diagnostic codes were based on the International Classification of Diseases (ICD), 9th revision (ICD-9; pre-2002) and 10th revision (ICD-10; post-2002). Procedural codes were derived from the CIHI-DAD Canadian Classification of Health Interventions (CCI), Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures (CCP) (Appendix C). We also used the CIHI-DAD and NACRS to obtain information on health care utilization (Appendix D), application of patient exclusion criteria (Appendix E), and health care costs associated with ED visits and hospitalizations (Appendix F).

Ontario Health Insurance Plan (OHIP): The OHIP database contains information on physician claims for all health care services (inpatient and outpatient) using fees outlined in the OHIP Schedule of Benefits and ICD-9 diagnostic codes. The sensitivity of information recorded in the OHIP database is over 90% when procedural codes abstracted from the database are compared to the actual code recorded on the chart by the physician.[59] In addition to diagnostic (ICD-9 and ICD-10) and procedural information

(CCI and CCP) obtained from CIHI-DAD and NACRS, we also used the OHIP database to develop our patient exclusion criteria and obtain additional information on baseline co-morbidities, health care utilization, and outcome variables (Appendix C–F).

Institute for Clinical Evaluative Sciences Physician Database (IPDB): The IPDB records contains demographic, specialty, education, and practice information on all practicing physicians in Ontario. We used this database to measure the number of family physician/general practitioner, nephrologist, internal medicine, and urologist visits and to determine ED physician practicing specialty (emergency medicine, family medicine, and other) (Appendix D).

4.3.2 Laboratory Databases

We used two laboratory databases to obtain outpatient and inpatient test results for Ontario residents.

Cerner: Cerner is one of the largest electronic health record vendors in the world (Missouri, United States of America).[60] Thirteen hospitals in Southwestern Ontario share the same electronic health record. The Cerner database contains outpatient, ED, and inpatient laboratory results for five blood tests (SCr, sodium, potassium, creatine kinase, and glucose) for adults 40 years and older from June 1, 2002 and March 31, 2012. We used this database to ascertain SCr, sodium, and potassium measurements.

Dynacare Medical Laboratories: The Dynacare database contains outpatient laboratory test results from all Dynacare laboratory locations across Ontario since 2002. Dynacare is one of the three largest laboratory providers in Ontario, contains records on over 59 million tests each year, and represents approximately one-third of all Ontario residents.[61] Dynacare does not represent testing in the ED or hospital. We used Dynacare to ascertain outpatient SCr and urine protein measurements (albumin, total protein, and dipstick) to define baseline kidney function and outcome variables (Appendix F).

Due to the inherent limitations of these two databases, this cohort study was restricted to patients 40 years and older who visited a Southwestern Ontario hospital equipped with the Cerner electronic health record and used Dynacare Medical Laboratories for outpatient testing.

4.3.3 Databases for Health Care Cost Estimation

We used six data sources in addition to the CIHI-DAD, NACRS, OHIP, and ODB databases to estimate total health care costs incurred by Ontario residents.[62]

Assistive Device Program (ADP): The ADP database is operated by the Ministry of Health and Long-Term Care and records information on consumer-centered support to Ontario residents with long-term disabilities such as personalized assistive devices.

Client Agency Program Enrolment (CAPE): The CAPE database accounts for the services provided by multidisciplinary family health teams comprised of family physicians, nurses, and other allied health care professionals.

Continuing Care Reporting System (CCRS): The CCRS for chronic care database records clinical and demographic information on residents receiving facility-based continuing care services, including hospital-based continuing care (complex continuing care, extended/chronic care) and residential care providing 24-hour nursing services (nursing home, home for the aged).

Home Care Database (HCD): The HCD is derived from either the Ontario Association of Community Care Access Centres or the Ministry of Health and records information on individuals requiring any home care service provided by the province's Community Care Access Centres.

National Rehabilitation Reporting System (NRS): The NRS database collects, processes, and analyzes adult inpatient rehabilitation services at the hospital, regional, and provincial/territorial levels.

Ontario Mental Health Reporting System (OMHRS): The OMHRS database collects data on patients in adult designated inpatient mental health beds, which includes beds in General, Provincial Psychiatric, and Specialty Psychiatric facilities.

4.4 Patients

4.4.1 Inclusion Criteria

We established a cohort of Ontario adults 40 years and older who visited an ED for any reason and had at least one SCr measurement at the ED visit between June 1, 2003 and March 31, 2012. The date of the ED visit served as the cohort entry or index date.

4.4.2 Exclusion Criteria

Before matching (Chapter 4.7), we excluded the following patients from the cohort who: (1) died on arrival or during the ED visit, (2) did not have a SCr measurement 7 to 365 days prior to the ED visit (pre-ED visit baseline) as a baseline SCr measurement was needed to diagnose AKI in the ED, (3) received dialysis one year prior to the ED visit as AKI would not be relevant on dialysis and to ensure stable kidney function after the discontinuation of dialysis, (4) received a kidney transplant in the five years prior to the ED visit to ensure AKI was not related to transplant rejection, (5) spent more than 48 hours in the ED to exclude those without a disposition plan, (6) left against medical advice or without being seen by an ED physician, (7) were transferred to another facility, or (8) received palliative care 30 days prior to or 14 days after the ED visit to exclude those who did not receive active medical management.

4.4.3 Main Cohort and Referent Groups

Following the application of our inclusion and exclusion criteria, patients were assigned to one of three groups based on AKI and ED disposition. The main cohort was a group of patients discharged home from the ED with AKI (Figure 5-1). The two referent ED groups were patients (1) admitted to hospital from the ED with AKI (Figure 5-2) and (2) discharged home from the ED with no AKI (Figure 5-3).

For all ED visits with AKI, we excluded patients with an improvement in AKI severity during the ED visit. For an ED discharge home with AKI, we excluded those assigned a main ED diagnosis of AKI (ICD-10 code: N17) to concentrate on patients less likely to be treated and resolved prior to discharge home. For ED visits with no AKI, we selected the first ED visit in which the individual had both ED and pre-ED visit baseline SCr measurements.

If an individual had multiple ED SCr measurements, we selected the highest value. If multiple pre-ED visit baseline SCr values were available, we selected the most recent one prior to the ED visit. Pre-ED visit baseline SCr measurements were chosen no earlier than seven days prior to the ED visit to avoid potentially unstable baseline values that may occur prior to an acute illness. There was no crossover of patients between groups. Preference was given to the group discharged home from the ED with AKI if patients were also eligible for one of the other two groups.

4.5 Characteristics

4.5.1 Baseline Characteristics

We considered several patient demographics, co-morbid conditions, medication use in ODB eligible patients, prior health care utilization, pre-ED visit baseline kidney function, and ED visit patient and facility characteristics as baseline characteristics in this study (Appendix G). We assessed baseline co-morbid conditions in the five years prior to the index date.

For ODB program eligible patients, we assessed medication use in the 120 days prior to the index date. We evaluated prior health care use including ED or hospital visits, physician visits, and diagnostic or screening tests conducted in the previous 365 days.

We used the Charlson co-morbidity index and Aggregated Diagnosis Groups (ADG) point score to measure the burden of co-morbidity in our patient population. The

Charlson co-morbidity index is based on the International Classification of Diseases diagnosis codes found in administrative data.[63] Derived from the Charlson score, the metric measures the general co-morbidity based on the relative effects of a combination of diseases or risk factors on outcomes for a given individual to show the expected one-year mortality.[64] The ADG point score, derived from the John Hopkins Adjusted Clinical Groups® system,[65,66] is a weighted measure of health care utilization as a proxy measure for co-morbidity and accounts for the duration of condition, severity of condition, diagnostic certainty, etiology of the condition, and specialty care involvement.

4.6 Kidney Function

4.6.1 Acute Kidney Injury

Acute kidney injury was defined as a relative increase in SCr by 50% or more, or an absolute increase in a SCr value of 26.5 μmol/L or more, from the most recent pre-ED visit baseline SCr. We adapted the 2012 KDIGO guidelines to identify and stage patients according to AKI severity.[14] Stage 1 AKI was defined as evidence of a relative increase in SCr value of ≥50% to <100% or ≥26.5 μmol/L from baseline; stage 2 AKI: evidence of a relative increase in SCr value of ≥100% to <200% from baseline; and stage 3 AKI: evidence of a relative increase in SCr value of >200% from baseline or an increase in SCr value to ≥354 μmol/L or the initiation of renal replacement therapy. Urine output was not available in our data sources.

We defined AKI using SCr measurements because our group showed that the ICD-10 diagnostic code N17 demonstrated poor sensitivity in the identification of AKI in ED setting (7-30%).[41] Validation of the AKI code in a subset of patients discharged home from the ED with AKI is unknown and may demonstrate even lower sensitivities. Reliance of ICD-10 diagnostic codes would likely result in the exclusion of many patients who truly had AKI, as well as falsely identifying some patients as not having AKI when they in fact had AKI.

4.6.2 Baseline Kidney Function

We used pre-ED visit SCr measurements to assess baseline kidney function and used the CKD-EPI equation to calculate the eGFR.[12] All eGFR values were reported in mL/min/1.73m^2. CKD was defined as an eGFR<60.[67] We also stratified baseline kidney function into the following groups: normal renal function, stage 1 or 2: eGFR≥60 mL/min/1.72m^2, stage 3a: 45≤eGFR<60, stage 3b: 30≤eGFR<45, stage 4 or 5: eGFR<30 but not on dialysis. Patients with an eGFR 15 to <30 were combined with patients with an eGFR <15 to comply with ICES privacy regulations on reporting small numbers.

4.7 Propensity Score Matching

To provide context for our primary and secondary outcome (Chapter 4.8), we conducted two separate propensity score matching analyses. In the first matching study, we compared patients discharged home from the ED with AKI to patients admitted to hospital from the ED with AKI (referred to as the AKI subpopulation). In the second matching study, we compared patients discharged home from the ED with AKI to patients discharged home from the ED with no AKI (referred to as the discharged subpopulation).

We used propensity scores to achieve balance on measured baseline characteristics and eliminate systematic differences between comparison groups of each matching study (Appendix G).[68–71] Propensity score is defined as the probability ("propensity") of an exposure, treatment, or intervention for an individual given a set of measured, relevant characteristics.[70,71] Propensity scores are often estimated using a multivariable logistic regression model. Individuals are then matched based on the same or similar propensity scores,[72] which is described in Chapters 4.7.1 and 4.7.2.

4.7.1 AKI Subpopulation

We formed a matched set of ED patients with AKI in two groups with a similar ED disposition probability (discharged home vs. admission to hospital) for a given set of

baseline covariates.[68–71] We estimated propensity scores using a multivariable logistic regression model with 92 baseline characteristics selected because of potential influence on outcomes between comparison groups (Appendix G).[71,73,74] We matched one ED patient discharged home with AKI (comparison group) to one ED patient admitted to hospital with AKI (referent group) on the logit of the propensity score [with a specified caliper width of ± 0.2 times the standard deviation (SD)] and AKI stage (1, 2, or 3).[72] Several matching techniques are available, including individual versus frequency matching,[70] and greedy versus optimal matching.[71] The implementation of greedy matching is simple, straightforward, and efficient in studies involving large health care administrative databases and performs as well as optimal matching in forming balanced groups.[75] For these reasons, we selected the greedy matching technique. One ED patient discharged home with AKI was first selected at random to the nearest patient admitted to hospital with AKI within the specified caliper distance, even if there was a better match for a subsequent ED patient discharged home with AKI.[71] The process was repeated for ED patents with AKI until patients admitted to hospital had been matched to ED patients discharged home, or until the list of patients discharged home for whom a matched patient admitted to hospital could be found had been exhausted. Patients were matched without replacement and those who were not matched successfully were excluded from the analysis.

4.7.2 Discharged Subpopulation

We formed a matched set of ED patients discharged home in two groups with a similar probability of having AKI for a given set of baseline covariates.[68–71] We estimated propensity scores using a multivariable logistic regression model with 91 baseline characteristics (Appendix G).[71,73,74] We matched one ED patient discharged home with AKI (comparison group) to one ED patient discharged home with no AKI (referent group) on the logit of the propensity score (with a specified caliper width of ± 0.2 times the SD) and CKD stage using eGFR categories: ≥60 mL/min/1.72m^2, 45≤eGFR<60; 30≤eGFR<45, 15≤eGFR<30, and an eGFR<15, but not on dialysis. We used the same matching techniques and preferences described for the AKI subpopulation.

4.7.3 Incomplete or Missing Data

Information on medication use was not be available in patients under 65 years of age as they are not eligible for universal drug coverage through the ODB program. A large proportion of ED patients discharged home with AKI would be excluded from the analysis had we restricted our cohort to individuals 65 years and older. However, our propensity score includes ODB program eligibility and several co-morbid conditions for which these missing medications would be indicated. For these reasons, we included ED patients with AKI regardless of age and accepted the limitations associated with missing medication information in patients under 65 years of age.

We anticipated all baseline characteristics to be complete with a few exceptions. First, income quintile was expected to be missing in less than 2% of patients.[41,76,77] Second, location of residence was expected to be missing in up to 0.2%.[78] To account for incomplete or missing data before matching, we imputed 'no' for missing rural residency status and the middle quintile for missing income (income quintile 3). We also imputed the median value for missing serum sodium and potassium concentrations.[79] The proportion of missing serum sodium and potassium concentrations was expected to be low because physicians routinely request serum sodium, potassium, and creatinine collectively in a panel of tests.

4.8 Outcomes

4.8.1 Primary Outcome

The primary outcome for all analyses was all-cause mortality. We restricted our analysis to 30 days after the index date, which is an acceptable timeframe to attribute an outcome to the ED visit.[80] All-cause mortality was obtained from vital statistics in the RPDB. The mortality flag in the RPDB has a sensitivity of 94% and a positive predictive value of 100%.[81]

4.8.2 Secondary Outcome

The secondary outcome for all analyses was the receipt of hospital-based acute dialysis. We restricted our analysis to 30 days after the index date. Physicians report billing and procedural codes related to the initiation of hospital-based acute dialysis. Dialysis billing and procedural codes in the setting of AKI have a specificity of greater than 94% (median 99%).[82]

4.8.3 Additional Outcomes

As outlined in Chapter 3.2.1.2, we assessed five additional outcomes for the main cohort of patients discharged from the ED with AKI. We did not assess these outcomes for the two propensity score matching analyses. The five additional outcomes were (1) hospitalization after an ED discharge home, (2) at least one outpatient physician visit (family physician, internist, nephrologist, or urologist), (3) at least one outpatient SCr test, (5) at least one outpatient urine test for protein, and (5) total health care costs (Appendix F). We restricted our analysis to 30 days after the index date for all five additional outcomes. We used an ICES macro to estimate total health care cost associated with health care use (Appendix F).[62] Cost was reported in Canadian dollars and adjusted for inflation to the year 2013.

4.9 Statistical Analyses

4.9.1 All Analyses

We compared baseline characteristics using standardized differences. This metric compares two group means relative to a pooled standard deviation. A standardized difference of 10% or greater is considered meaningful,[83] and it is preferred over hypothesis testing (using *P* values) for large samples because it is not influenced by sample size.[84–86] In propensity score matching studies with large groups, one can compare balance in characteristics in both an unmatched and matched sample.[85,86]

4.9.2 AKI Subpopulation

We estimated propensity scores using 92 baseline characteristics (Appendix G). SCr at ED visit and AKI stage were variables in the propensity score specific to the AKI subpopulation. ED length of stay was not included because it is dependent on when the patient physically leaves the ED. The transfer of care from the ED physician to an admitting service may have occurred several hours before the patient was physically moved to a hospital bed. Therefore, ED length of stay will always differ between these two groups.

We estimated the relative risk (RR) and 95% confidence intervals (CI) for our primary and secondary outcome using a modified Poisson regression model that accounted for matched data.[87,88] Compared to the odds ratio, the RR is a more intuitive measure of effect and does not overestimate risk with increasing frequency of the outcome.[89] Patients admitted to hospital from the ED with AKI served as the referent group. We also evaluated the association between ED disposition (discharge home vs. admission to hospital) and our primary outcome in a pre-specified subgroup defined by AKI stage (Chapter 4.6.1).[14] We determined interaction *P* values by including interaction terms in the modified Poisson regression model.

4.9.3 Discharged Subpopulation

We estimated propensity scores with 91 baseline characteristics, 90 of which were identical to those used in the AKI subpopulation (Appendix G). ED length of stay was a variable in the propensity score specific to the discharged subpopulation. Because this analysis compared patients with AKI versus no AKI, SCr at ED visit and AKI stage were not included in the propensity score.

We estimated the RR and 95% CI for our outcomes using a modified Poisson regression model that accounted for matched data.[87,88] Patients discharged home from the ED with no AKI served as the referent group. We also evaluated the association between AKI and our primary outcome in a pre-specified subgroup defined by CKD stage (Chapter

4.6.2).[67] We determined interaction *P* values by including interaction terms in the modified Poisson regression model.

Chapter 5

5 Results

5.1 Descriptive Analysis

5.1.1 Characteristics of Patients Discharged Home from the Emergency Department with Acute Kidney Injury

There were 6346 patients discharged home from the ED with AKI included in the cohort over a 10-year period (Figure 5-1 and Table 5-1). Among these patients, 6012 (94.7%) had stage 1, 290 (5.2%) had stage 2, and 44 (0.7%) had stage 3 AKI. The mean (SD) age was 69 (14) years, 46.5% were female, and 15.3% lived in a rural residence. The most common pre-existing co-morbidities were hypertension (75.4%), CKD (38.2%), diabetes (37.9%), coronary artery disease (34.0%), heart failure (~21.7%), and major cancer (16.6%). There were 4605 (72.6%) patients with universal drug coverage through the ODB program and they were prescribed a median of five medications in the 120 days prior to the ED visit. The most commonly prescribed medications were angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (59.7%), non-potassium sparing diuretics (56.7%), statins (47.2%), antibiotics (44.3%), beta-adrenergic antagonists (38.7%), and proton pump inhibitors (35.9%). Non-steroidal anti-inflammatory drugs were prescribed in 19.4% of patients.

Before the index date, there were 1114 (17.6%) patients in the previous 30 days and 3624 (57.1%) patients in the previous 31 to 365 days who had at least one ED visit. There were 481 (7.6%) patients in the previous 30 days and 1933 (30.5%) patients in the previous 31 to 365 days who required at least one hospitalization. In the 365 days before the index date, 98.5% of patients had at least one family physician visit. Outpatient clinic visits with a general internist (23.2%), nephrologist (~4.6%), and urologist (17.8%) were less common. The most frequently ordered diagnostic test, procedure, or intervention in the previous 365 days was an abdominal ultrasound (24.1%). The median [interquartile range (IQR)] pre-ED visit baseline SCr concentration was 87 (71-112) μmol/L and was

measured a median (IQR) 106 (44-207) days prior to the index date. A urine albumin-to-creatinine ratio (ACR) was measured in 26.6% of patients with approximately 10% having micro- or macroalbuminuria.

During the index ED visit, the majority (80.6%) of patients were assigned to urgent or emergent triage acuity scores [Canadian Triage Acuity Scale (CTAS) 1 to 3]. The 90th percentile for ED length of stay was 8 to 9 hours. The median (IQR) ED SCr concentration was 129 (109-162) μmol/L. The three most frequent main diagnoses assigned by ED physicians were throat or chest pain (8.1%), abdominal or pelvic pain (7.0%), and renal colic (4.9%) (Appendix H).

Income quintile was not available for 99 (1.6%) patients. Serum potassium and sodium, both measured in a panel of electrolytes, were not available for 492 (7.8%) patients.

5.1.2 Characteristics by Acute Kidney Injury Severity

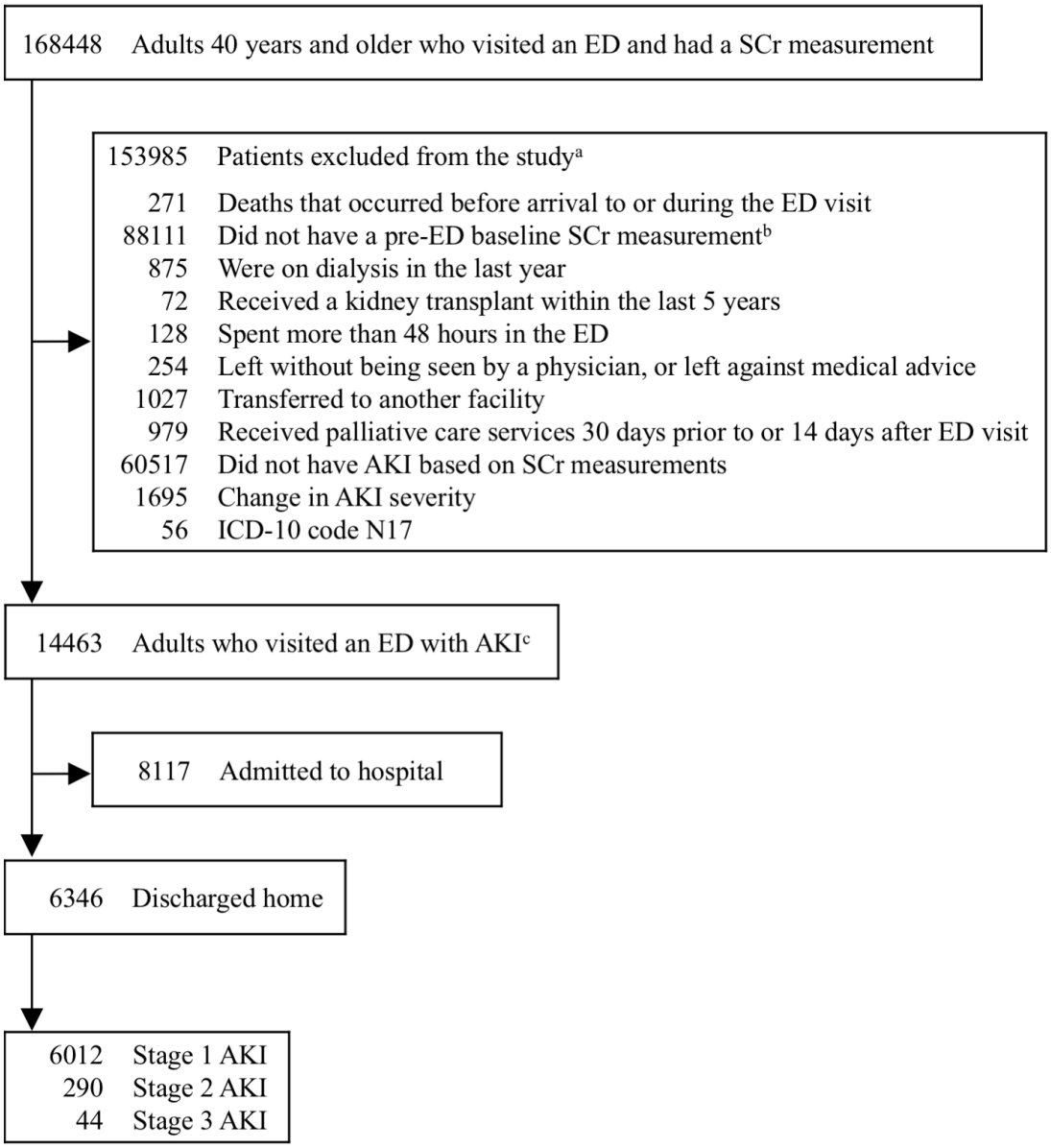
Cohort characteristics by AKI stage are shown in Table 5-1. Consistent with the diagnostic criteria for AKI, ED visit SCr concentrations increased with AKI stage. Compared to patients with stage 1 AKI, patients with stage 2 AKI were more likely to be female, have lower income, reside in long-term care, have dementia, be prescribed immunosuppressive medications and potassium-sparing diuretics, and have lower pre-ED visit baseline SCr concentrations. They were less likely to have coronary artery disease, CKD, and heart failure, be prescribed beta-adrenergic antagonists, oral hypoglycemic agents or insulin, and xanthine oxidase inhibitors or uricosuric agents, be seen by a urologist, have cardiac imaging, and be assigned an emergent triage acuity level (CTAS 1 or 2).

Compared to patients with stage 1 AKI, patients with stage 3 AKI were younger and more likely to be female, have higher income, hypertension, major cancer, and an Aggregated Diagnosis Group (ADG) point score of ≥6. Although these patients were prescribed fewer medications in the previous 120 days, they were more likely to be prescribed antibiotics, antidepressants, non-potassium sparing diuretics, non-steroidal

anti-inflammatory drugs, and proton pump inhibitors. There were also more likely to have a remote pre-ED visit baseline SCr measurement, lower serum sodium concentration, require hospitalization in the previous 30 days, have a previous abdominal ultrasound, and be assigned a less urgent triage acuity level (CTAS 4 or 5). They were less likely to have coronary artery disease, dementia, and diabetes, be prescribed calcium channel blockers, oral hypoglycemic agents or insulin, and statins, have an ED visit or hospitalization in the previous 31 to 365 days, be seen at least once by a family physician, and be assigned a CTAS of 1 or 2.

Compared to patients with stage 2 AKI, patients with stage 3 AKI were younger and more likely to have higher income, hypertension, a Charlson co-morbidity index of ≥3, and an ADG point score of ≥6. Although these patients were prescribed fewer medications in the previous 120 days, they were more likely to be prescribed antibiotics, antidepressants, beta-adrenergic antagonists, non-steroidal anti-inflammatory drugs, and proton pump inhibitors, have a higher pre-ED visit baseline SCr concentration, higher ED serum potassium concentration, lower ED serum sodium concentration, have a previous abdominal ultrasound, require hospitalization in the previous 30 days, be seen at least once by a urologist, and be assigned a CTAS of 4 or 5. They were less likely to live in a rural residence, have dementia and diabetes, be prescribed calcium channel blockers, corticosteroids, and statins, have an ED visit or hospitalization in the previous 31 to 365 days, be seen at least once by a family physician, and be assigned a CTAS of 3.

Figure 5-1: Selection of Cohort of Patients Discharged Home from the Emergency Department with Acute Kidney Injury from 2003 to 2012



Abbreviations: AKI, acute kidney injury; ED, emergency department; ICD, International Classification of Diseases; SCr serum creatinine.

[a] Patients were excluded in order as listed.

[b] We selected the most recent pre-ED visit baseline SCr measurement.

[c] If an individual had more than one ED visit with AKI, we selected the first ED visit.

Table 5-1: Baseline Characteristics of Patients Discharged Home from the Emergency Department with Acute Kidney Injury

	Number of patients, n (%)[a]			
	All patients	AKI stage[b]		
		1	2	3
Cohort size	6346	6012	290	44
Demographics				
Age, in years				
Mean (SD)	69 (14)	69 (13)	68 (14)	65 (13)‡§
Median (IQR)	70 (58-79)	70 (58-79)	70 (57-79)	62 (58-77)
40 to <65	2326 (36.7)	2189 (36.4)	112 (38.6)	25 (56.8)‡§
65 to <80	2475 (39.0)	2351 (39.1)	114 (39.3)	10 (22.7)‡§
≥80	1545 (24.3)	1472 (24.5)	64 (22.1)	9 (20.5)
Sex, female	2948 (46.5)	2745 (45.7)	177 (61.0)†	26 (59.1)‡
Year of cohort entry				
2003 to 2005	1593 (25.1)	1497 (24.9)	87 (30.0)†	9 (20.5)‡§
2006 to 2008	2903 (45.7)	2769 (46.1)	116 (40.0)†	18 (40.9)‡
2009 to 2011	1850 (29.2)	1746 (29.0)	87 (30.0)	17 (38.6)‡§
Rural residence	969 (15.3)	912 (15.2)	51 (17.6)	6 (13.6)§
Neighbourhood income quintile				
1	1401 (22.1)	1314 (21.9)	78 (26.9)†	9 (20.5)§
2	1353 (21.3)	1290 (21.5)	54 (18.6)	9 (20.5)
3	1307 (20.6)	1238 (20.6)	62 (21.4)	7 (15.9)‡§
4	1046 (16.5)	996 (16.6)	42 (14.5)	8 (18.2)§
5	1140 (18.0)	1079 (17.9)	50 (17.2)	11 (25.0)‡§
Pharmacy forward sortation area[c]	5214 (82.2)	4945 (82.3)	233 (80.3)	36 (81.8)
Co-morbid conditions[d]				
Abdominal aortic aneurysm repair	48 (0.8)	37 (0.8)	≤5 (≤1.7)	≤5 (≤11.4)‡
Atrial fibrillation or flutter	NR	627 (10.4)	23 (7.9)	≤5 (≤11.4)‡
Cerebrovascular disease	NR	243 (4.0)	14 (4.8)	≤5 (≤11.4)‡§

Chronic liver disease	NR	399 (6.6)	24 (8.3)	≤5 (≤11.4)[§]
Chronic obstructive pulmonary disease	NR	369 (6.1)	22 (7.6)	≤5 (≤11.4)[‡§]
Coronary artery disease[e]	2160 (34.0)	2069 (34.4)	78 (26.9)[†]	13 (29.5)[‡]
Dementia	NR	591 (9.8)	39 (13.4)[†]	≤5 (≤11.4)[‡§]
Diabetes	2405 (37.9)	2292 (38.1)	100 (34.5)	13 (29.5)[‡§]
Heart failure	NR	1325 (22.0)	48 (16.6)[†]	≤5 (≤11.4)[‡§]
Hypertension	4783 (75.4)	4525 (75.3)	222 (76.6)	36 (81.8)[‡§]
Major cancer[f]	1056 (16.6)	994 (16.5)	53 (18.3)	9 (20.5)[‡]
Nephrolithiasis	NR	162 (2.7)	11(3.8)	≤5 (≤11.4)[‡§]
Osteoarthritis	NR	431 (7.2)	26 (9.0)	≤5 (≤11.4)[‡§]
Parkinson's disease	NR	32 (0.5)	≤5 (≤1.7)	≤5 (≤11.4)[‡§]
Peripheral vascular disease	NR	178 (3.0)	≤5 (≤1.7)	≤5 (≤11.4)
Rheumatoid arthritis	NR	429 (7.1)	22 (7.6)	≤5 (≤11.4)
Charlson co-morbidity index[g]				
0	4181 (65.9)	3962 (65.9)	188 (64.8)	31 (70.5)[§]
1	NR	661 (11.0)	33 (11.4)	≤5 (≤11.4)
2	NR	606 (10.1)	35 (12.1)	≤5 (≤11.4)[‡§]
≥3	824 (13.0)	783 (13.0)	34 (11.7)	7 (15.9)[§]
Aggregated Diagnosis Groups score[h]				
0-5	1757 (27.7)	1669 (27.8)	79 (27.2)	9 (20.5)[‡§]
≥6	4589 (72.3)	4343 (72.2)	211 (72.8)	35 (79.5)[‡§]
Medication utilization[i]				
ODB program eligible patients	4605 (72.6)	4367 (72.6)	213 (73.4)	25 (56.8)[‡§]
Patients in long-term care[j]	NR	171/4367 (3.9)	13/213 (6.1)[†]	≤5/25 (≤20.0)[‡]
Medication class[k]				
Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker	2750/4605 (59.7)	2614/4367 (59.9)	122/213 (57.3)	14/25 (56.0)
Alpha-1-adrenoceptor antagonist or 5-alpha-reductase inhibitor	NR	279/4367 (6.4)	13/213 (6.1)	≤5/25 (≤20.0)

Anti-retroviral	NR	7/4367 (0.2)	≤5/213 (≤2.3)	≤5/25 (≤20.0)
Antibiotic	2041/4605 (44.3)	1931/4367 (44.2)	97/213 (45.5)	13/25 (52.0)‡§
Anticoagulant	NR	689/4367 (15.8)	32/213 (15.0)	≤5/25 (≤20.0)
Antidepressant (SSRI or SNRI)	774/4605 (16.8)	728/4367 (16.7)	40/213 (18.8)	6/25 (24.0)‡§
Antineoplastic (chemotherapy)	NR	108/4367 (2.5)	≤5/213 (≤2.3)	≤5/25 (≤20.0)‡§
Antiplatelet	NR	714/4367 (16.3)	31/213 (14.6)	≤5/25 (≤20.0)‡§
Antipsychotic	NR	284/4367 (6.5)	18/213 (8.5)	≤5/25 (≤20.0)
Beta-adrenergic antagonist	1781/4605 (38.7)	1705/4367 (39.0)	66/213 (31.0)†	10/25 (40.0)§
Calcium channel blocker	NR	1499/4367 (34.3)	64/213 (30.0)	≤5/25 (≤20.0)‡§
Corticosteroid	1188/4605 (25.8)	1119/4367 (25.6)	63/213 (29.3)	6/25 (24.0)§
Immunosuppressive medication	NR	166/4367 (3.8)	13/213 (6.1)†	≤5/25 ≤20.0)
Lithium	NR	30/4367 (0.7)	≤5/213 (≤2.3)†	≤5/25 ≤20.0)‡
Non-potassium sparing diuretic	2609/4605 (56.7)	2465/4367 (56.4)	128/213 (60.1)	16/25 (64.0)‡
Non-steroidal anti-inflammatory drug[l]	892/4605 (19.4)	849/4367 (19.4)	34/213 (16.0)	9/25 (36.0)‡§
Oral hypoglycemic agent or insulin	NR	1346/4367 (30.8)	52/213 (24.4)†	≤5/25 (≤20.0)‡§
Potassium-sparing diuretic	NR	511/4367 (11.7)	34/213 (16.0)†	≤5/25 (≤20.0)‡§
Proton pump inhibitor	1651/4605 (35.9)	1571/4367 (36.0)	68/213 (31.9)	12/25 (48.0)‡§
Statin	2174/4605 (47.2)	2072/4367 (47.4)	93/213 (43.7)	9/25 (36.0)‡§
Xanthine oxidase inhibitor or uricosuric agent	NR	302/4367 (6.9)	≤5/213 (≤2.3)†	≤5/25 (≤20.0)‡§
Unique drug names				
Mean (SD)	6 (6)	6 (6)	6 (6)	3 (5)‡§
Median (IQR)	5 (0-10)	5 (0-10)	5 (0-10)	0 (0-7)
Unique drug identification numbers				
Mean (SD)	6 (6)	6 (6)	6 (7)	4 (6)‡§
Median (IQR)	5 (0-10)	5 (0-10)	5 (0-10)	0 (0-7)
Pre-ED visit baseline kidney function[m]				
Baseline SCr, in μmol/L				
Mean (SD)	101 (55)	102 (56)	76 (30)†	96 (88)§
Median (IQR)	87 (71-112)	88 (72-112)	71 (56-87)	75 (57-88)
Days baseline SCr measured pre-ED visit				

Mean (SD)	133 (102)	132 (102)	140 (105)	152 (116)[‡§]
Median (IQR)	106 (44-207)	106 (44-206)	126 (45-215)	115 (46-256)
Baseline SCr ≤50 μmol/L	NR	215 (3.6)	44 (15.2)[†]	≤5 (≤11.4)[‡§]
Baseline eGFR				
≥60 ml/min/1.73m^2	3919 (61.8)	3654 (60.8)	230 (79.3)[†]	35 (79.5)[‡]
45 to <60 ml/min/1.73m^2	NR	1029 (17.1)	34 (11.7)[†]	≤5 (≤11.4)[‡§]
30 to <45 ml/min/1.73m^2	NR	833 (13.9)	19 (6.6)[†]	≤5 (≤11.4)[‡]
<30 ml/min/1.73m^2	NR	496 (8.3)	7 (2.4)[†]	≤5 (≤11.4)[§]
CKD risk category[n]				
Low risk	NR	678 (11.3)	41 (14.1)	≤5 (≤11.4)
Moderate risk	NR	293 (4.9)	15 (5.2)	≤5 (≤11.4)[‡§]
High risk	NR	366 (6.1)	16 (5.5)	≤5 (≤11.4)
Very high risk	NR	654 (10.9)	12 (4.1)[†]	≤5 (≤11.4)[§]
Urine ACR measured	1689 (26.6)	1602 (26.6)	77 (26.6)	10 (22.7)
<30 mg/mmol	NR	959 (16.0)	49 (16.9)	≤5 (≤11.4)[‡§]
30 to <300 mg/mmol	NR	262 (4.4)	13 (4.5)	≤5 (≤11.4)
≥300 mg/mmol	NR	381 (6.3)	15 (5.2)	≤5 (≤11.4)
ED visit laboratory values				
Serum potassium, in mmol/L				
Mean (SD)	4.2 (0.6)	4.2 (0.6)	4.1 (0.8)[†]	4.2 (0.8)[§]
Median (IQR)	4.1 (3.8-4.5)	4.1 (3.8-4.5)	4.1 (3.6-4.5)	4.2 (3.6-4.8)
Serum sodium, in mmol/L				
Mean (SD)	137 (5)	137 (5)	136 (5)[†]	134 (5)[‡§]
Median (IQR)	138 (135-140)	138 (135-140)	137 (134-139)	134 (131-139)
SCr, in μmol/L				
Mean (SD)	147 (70)	145 (66)	174 (75)[†]	335 (182)[‡§]
Median (IQR)	129 (109-162)	128 (108-159)	159 (128-205)	301 (200-427)
Absolute change in SCr, in μmol/L				
Mean (SD)	47 (31)	43 (19)	98 (46)[†]	239 (122)[‡§]
Median (IQR)	38 (31-51)	37 (31-48)	88 (68-119)	217 (139-328)

Percent change in SCr, in %				
Mean (SD)	52 (34)	48 (18)	129 (26)†	294 (128)‡§
Median (IQR)	45 (35-60)	44 (34-57)	121 (108-144)	265 (224-359)
Previous health care utilization[o]				
ED visit in the previous				
30 days	1114 (17.6)	1062 (17.7)	45 (15.5)	7 (15.9)
31 to 365 days	2510 (39.5)	2384 (39.7)	114 (39.3)	12 (27.3)‡§
Hospitalization in the previous				
30 days	481 (7.6)	451 (7.5)	24 (8.3)	6 (13.6)‡§
31 to 365 days	1452 (22.9)	1366 (22.7)	78 (26.9)	8 (18.2)‡§
Outpatient physician visits				
Family physician	6251 (98.5)	5924 (98.5)	283 (97.6)	44 (70.5)‡§
0 to 4 visits	1069 (16.8)	1017 (16.9)	46 (15.9)	6 (13.6)
5 to 10 visits	2287 (36.0)	2161 (35.9)	109 (37.6)	17 (38.6)
≥11 visits	2990 (47.1)	2834 (47.1)	135 (46.6)	21 (47.7)
General internist (≥1 visit)	1470 (23.2)	1385 (23.0)	76 (26.2)	9 (20.5)§
Nephrologist (≥1 visit)	NR	270 (4.5)	14 (4.8)	≤5 (≤11.4)
Urologist (≥1 visit)	1132 (17.8)	1084 (18.0)	40 (13.8)†	8 (18.2)§
Diagnostic imaging and procedures				
Abdominal ultrasound[p]	1530 (24.1)	1456 (24.2)	59 (20.3)	15 (34.1)‡§
Cardiac stress test	NR	931 (15.5)	34 (11.7)†	≤5 (≤11.4)‡§
Coronary angiogram or revascularization	NR	138 (2.3)	6 (2.1)	≤5 (≤11.4)‡§
CT scan with contrast	NR	175 (2.9)	7 (2.4)	≤5 (≤11.4)
Echocardiogram	NR	1097 (18.2)	34 (11.7)†	≤5 (≤11.4)‡§
Intervention for kidney stones[q]	NR	73 (1.2)	≤5 (≤1.7)	≤5 (≤11.4)
ED and hospital characteristics				
Institution[r]				
1	1754 (27.6)	1665 (27.7)	78 (26.9)	11 (25.0)

2	1482 (23.4)	1400 (23.3)	70 (24.1)	12 (27.3)
3	NR	608 (10.1)	36 (12.4)	≤5 (≤11.4)[‡§]
4	NR	435 (7.2)	26 (9.0)	≤5 (≤11.4)
5	NR	145 (2.4)	10 (3.4)	≤5 (≤11.4)[‡]
6	NR	42 (0.7)	≤5 (≤1.7)	≤5 (≤11.4)[‡§]
7	NR	569 (9.5)	35 (12.1)	≤5 (≤11.4)
8	NR	241 (4.0)	7 (2.4)	≤5 (≤11.4)
9	NR	338 (5.6)	10 (3.4)[†]	≤5 (≤11.4)[§]
10	NR	366 (6.1)	10 (3.4)[†]	≤5 (≤11.4)
11	NR	148 (2.5)	≤5 (≤1.7)	≤5 (≤11.4)[‡§]
12	NR	32 (0.5)	≤5 (≤1.7)	≤5 (≤11.4)[‡§]
13	NR	23 (0.4)	≤5 (≤1.7)	≤5 (≤11.4)
ED and hospital activity				
Standardized number of ED registrations in the last 12h[s]				
Mean (SD)	1.1 (0.3)	1.1 (0.3)	1.1 (0.3)	1.0 (0.3)[‡§]
Median (IQR)	1.1 (0.9-1.3)	1.1 (0.9-1.3)	1.1 (0.9-1.3)	1.0 (0.8-1.3)
Standardized number of hospital admissions in the last 24h[t]				
Mean (SD)	1.1 (0.3)	1.1 (0.3)	1.1 (0.3)	1.1 (0.3)[‡]
Median (IQR)	1.1 (0.8-1.3)	1.1 (0.8-1.3)	1.1 (0.8-1.3)	1.2 (0.9-1.3)
Standardized number of hospital discharges in the last 24h[u]				
Mean (SD)	1.1 (0.4)	1.1 (0.3)	1.1 (0.4)	1.1 (0.4)[‡§]
Median (IQR)	1.1 (0.8-1.2)	1.1 (0.8-1.2)	1.1 (0.8-1.2)	1.3 (0.9-1.4)
Standardized proportion of ED registrations resulting in hospitalization, in %[v]	47.0	47.0	49.0	48.0
ED seasonal and time characteristics				
Time of day				
0700 to <1700	3320 (52.3)	3128 (52.0)	162 (55.9)	30 (71.1)[‡§]

1700 to <2400	2226 (35.1)	2125 (35.3)	91 (31.4)	≥9 (≥20.5)‡§
0000 to <0700	NR	759 (12.6)	37 (12.8)	≤5 (≤11.4)‡§
Season[w]				
Fall	1502 (23.7)	1418 (23.6)	71 (24.5)	13 (29.5)‡§
Winter	1446 (22.8)	1358 (22.6)	77 (26.6)	11 (25.0)
Spring	1635 (25.8)	1563 (26.0)	63 (21.7)†	9 (20.5)‡
Summer	1763 (27.8)	1673 (27.8)	79 (27.2)	11 (25.0)
ED physician training				
Emergency medicine	4642 (73.1)	4403 (73.2)	210 (72.4)	29 (65.9)‡§
Family medicine	1338 (21.1)	1264 (21.0)	62 (21.4)	≥10 (≥22.7)‡§
Other	NR	345 (5.7)	18 (6.2)	≤5 (≤11.4)
ED patient acuity and wait times				
CTAS[x]				
1 or 2	1321 (20.8)	1271 (21.1)	43 (14.8)†	7 (15.9)‡
3	3797 (59.8)	3579 (59.5)	193 (66.6)†	25 (56.8)§
4 or 5	1228 (19.4)	1162 (19.3)	54 (18.6)	12 (27.3)‡§
Time (in hours) waiting for physician assessment, mean (SD)				
CTAS 1 or 2	0.6 (0.8)	0.6 (0.8)	0.5 (0.6)†	0.3 (0.5)‡§
CTAS 3	1.3 (1.3)	1.3 (1.3)	1.5 (1.3)	1.6 (1.1)‡§
CTAS 4 or 5	1.6 (1.4)	1.6 (1.4)	1.7 (1.4)	1.4 (1.2)‡§
90% percentile ED length of stay, in hours				
CTAS 1 or 2	9	9	10	7
CTAS 3	9	9	8	10
CTAS 4 or 5	8	8	9	8

Abbreviations: ACR, albumin-to-creatinine ratio; AKI, acute kidney injury; CKD, chronic kidney disease; CT, computed tomography; CTAS, Canadian Triage Acuity Scale; ED, emergency department; eGFR, estimated glomerular filtration rate; IQR, interquartile range; ODB: Ontario Drug Benefit; NR, not reported; SCr, serum creatinine; SD, standard deviation; SNRI, serotonin-norepinephrine reuptake inhibitors; SSRI, selective serotonin reuptake inhibitor.
A standardized difference of ≥10% was found between two AKI stage comparisons: † stage 1 vs. stage 2; ‡ stage 1 vs. stage 3; and § stage 2 vs. stage 3. To convert SCr from SI units (μmol) to traditional units (mg/dL), divide by 88.42.

[a] Numbers reported as n (%) unless otherwise noted. To comply with privacy regulations for minimizing the chance of patient re-identification, numbers of patients were suppressed in the case of five or fewer patients. The total number of patients was not reported if there were other calculations that could result in the re-identification of five or fewer patients.

[b] Stage 1, evidence of a relative increase in SCr value of ≥50% to <100% or ≥26.5 μmol/L from baseline; stage 2, evidence of a relative increase in SCr value of ≥100% to <200% from baseline; and stage 3, evidence of a relative increase in SCr value of >200% from baseline or an absolute increase in SCr value to ≥354 mg/dL or the initiation of dialysis.

[c] Pharmacy forward sortation area refers to a region in Ontario represented by the first three letters of the postal code. This variable describes the number and proportion of individuals who live in the same region as the pharmacy that provided them with prescription medications.

[d] Look-back window for co-morbidities was five years unless otherwise noted.

[e] Does not include angina.

[f] Major cancers include the following tissues/organs: lung/bronchi, colon/rectum, breast, pancreas, prostate, leukemia, non-Hodgkin lymphoma, liver, ovaries, and esophagus.

[g] Look-back window for the Charlson co-morbidity index was two years.[63,64]

[h] The Aggregated Diagnosis Groups (ADG) point score, derived from the John Hopkins Adjusted Clinical Groups® system, score is a weighted measure of health care utilization as a proxy measure for co-morbidity and accounts for the duration of condition, severity of condition, diagnostic certainty, etiology of the condition, and specialty care involvement.[65,66] The higher ADG score, the greater the co-morbidity. Individuals with an ADG score of 0 to 2 reflect low health care costs with no prior hospitalizations; ADG score 3 to 5, high health care costs but no prior hospitalizations; ADG score 6 or more, high health care costs and at least one prior hospitalization.

[i] Look-back window for medication utilization was 120 days.

[j] Patients in long-term care were identified from the ODB database.

[k] Percentages reported are based on the number of ODB program eligible patients (age 65 years and older).

[l] Does not include acetylsalicylic acid.

[m] Pre-ED visit look-back window was 7 to 365 days.

[n] CKD risk categories derived from 2012 Kidney Diseases: Improving Global Outcomes guidelines. In addition to using urine ACR measurements, urine dipstick and protein values were converted to an estimate urine ACR.[67]

[o] Look-back window for health care utilization was 365 days unless otherwise noted.

[p] An abdominal ultrasound is not specific for the assessment of the kidneys.

[q] Urological procedures included extracorporeal shockwave lithotripsy, percutaneous nephrolithotomy, or ureteroscopic lithotripsy with stone removal.

[r] For privacy considerations, individual hospital institutions were not identified.

[s] Standardized to the mean number of ED registrations that occurred in the last 12-hour period over the last 14 days.

[t] Standardized to the mean number of hospital admissions that occurred in the last 24-hour period over the last 14 days.

[u] Standardized to the mean number of hospital discharges that occurred in the last 24-hour period over the last 14 days.

[v] Proportion of registrations resulting in hospitalization standardized to each ED/hospital institution's number of ED registrations occurring in the last 24 hours.

[w] Fall: September 21 to December 20; Winter: December 21 to March 20; Spring: March 21 to June 20; Summer: June 21 to September 20.

[x] Patients with a Canadian Triage Acuity Scale (CTAS) of 1 or 2 need to be seen immediately 98% of the time or within 15 minutes 95% of the time, respectively. Patients with a CTAS of 3 or 4 need to be seen within 30 minutes 90% of the time or 60 minutes 85% of the time, respectively. Patients with a CTAS of 5 need to be seen within 120 minutes 80% of the time.

5.1.3 Outcomes

In the 30 days following an ED discharge home with AKI, 149 (2.3%) patients died, 22 (0.3%) received hospital-based acute dialysis, and 1032 (16.3%) required hospitalization. In the outpatient setting, 4287 (67.6%) were seen by a physician (family physician, general internist, nephrologist, or urologist), 1446 (22.8%) had a SCr test, and 12% had a urine test for protein (Table 5-2). The median (IQR) 30-day health care cost was $1172 ($661-$3020) dollars.

In the 30 days following an ED discharge home, 127 (2.1%) patients with stage 1, 15 (5.2%) with stage 2, and 7 (15.9%) with stage 3 AKI died. There were 956 (15.9%) patients with stage 1, 62 (21.4%) with stage 2, and 14 (31.8%) with stage 3 AKI who required hospitalization. In the outpatient setting, 4062 (67.6%) patients with stage 1, 197 (67.9%) with stage 2, and 28 (63.6%) with stage 3 AKI visited a physician and 1339 (22.8%) patients with stage 1, 89 (30.7%) with stage 2, and 18 (40.9%) with stage 3 AKI had a SCr measurement. Mean and median health care costs appeared to increase with AKI severity.

Table 5-2: Thirty-Day Outcomes of Patients Discharged Home from the Emergency Department with Acute Kidney Injury

Outcome	Number of patients, n (%)[a]			
	All patients (N=6346)	AKI stage[b]		
		1 (N=6012)	2 (N=290)	3 (N=44)
Primary Outcome				
All-cause mortality	149 (2.3)	127 (2.1)	15 (5.2)	7 (15.9)
Secondary Outcome				
Receipt of hospital-based acute dialysis	22 (0.3)	NR	≤5 (≤1.7)	≤5 (≤11.4)
Additional Outcomes				
At least one hospitalization	1032 (16.3)	956 (15.9)	62 (21.4)	14 (31.8)
At least one outpatient:				
Physician clinic visit[c]	4287 (67.6)	4062 (67.6)	197 (67.9)	28 (63.6)
SCr test	1446 (22.8)	1339 (22.3)	89 (30.7)	18 (40.9)
Urine test for protein[d]	NR	713 (11.9)	41 (14.1)	≤5 (≤11.4)
Total health care costs[e]				
Mean (SD)	$3522 ($7079)	$3499 ($7135)	$3856 ($6065)	$4429 ($5454)
Median (IQR)	$1172 ($661-3020)	$1164 ($657-2955)	$1342 ($749-4372)	$1748 ($699-6478)

Abbreviations: AKI, acute kidney injury; IQR, interquartile range; NR, not reported; SCr, serum creatinine; SD, standard deviation.

[a] Reported as n (%) unless otherwise noted. To comply with privacy regulations for minimizing the chance of patient re-identification, numbers of patients were suppressed in the case of five or fewer patients. The total number of patients was not reported if there were other calculations that could result in the re-identification of five or fewer patients.

[b] AKI stage 1, evidence of a relative increase in SCr value of ≥50% to <100% or ≥26.5 μmol/L from baseline; stage 2, evidence of a relative increase in SCr value of ≥100% to <200% from baseline; and stage 3, evidence of a relative increase in SCr value of >200% from baseline or an absolute increase in SCr value to ≥354 μmol/L or the initiation of dialysis.[14]

[c] Outpatient physician specialties included any one of: family medicine, internal medicine, nephrology, or urology.

[d] Tests for urine protein included any one of: dipstick, protein, or ACR.

[e] Reported in Canadian dollars, adjusted for inflation to 2013.

5.2 Propensity Score Matching Analysis

5.2.1 AKI Subpopulation

5.2.1.1 Unmatched Cohort

Cohort selection for the AKI subpopulation is presented in Figure 5-2. Baseline characteristics before and after matching are presented in Table 5-3.

Before matching, there were 14,463 patients who visited an ED and had evidence of AKI. Among these patients, 6346 were discharged home and 8117 were admitted to hospital. Patients discharged home from the ED with AKI as compared to those admitted to hospital from the ED with AKI were younger (mean age 69 vs. 73 years) and more likely to have a slightly more remote pre-ED visit baseline SCr measurement [mean (median) 133 (106) vs. 121 (90) days], a slightly lower pre-ED visit baseline SCr concentration [mean (median) 101 (87) vs. 115 (96) μmol/L], and a previous urine ACR measurement (26.6 vs. 22.1%). In the ED, they were more likely to have a slightly lower serum potassium [mean (median) 4.2 (4.1) vs. 4.4 (4.3) mmol/L], slightly higher serum sodium concentration [mean (median) 137 (138) vs. 136 (136) mmol/L], lower ED SCr concentration [mean (median) 147 (129) vs. 208 (162) μmol/L], stage 1 AKI (94.7 vs. 78.9%), be assigned a less urgent triage acuity level (CTAS 3: 59.8 vs 52.4%, CTAS 4 or 5: 19.4 vs. 8.8%), and in patients assigned an urgent or emergent triage acuity level, spend more time waiting for a physician assessment (CTAS 1 or 2: 0.8 vs. 0.6 hours, CTAS 3: 1.3 vs. 1.2 hours).

These patients had fewer co-morbidities (coronary artery disease: 34.0 vs. 38.5%, CKD: 38.2 vs. 51.9%, diabetes: 37.9 vs. 43.1%, hypertension: 75.4 vs. 79.5%, major cancer: 16.6 vs. 21.4%, Charlson co-morbidity index of ≥3: 13.0 vs. 20.4%, and ADG point score of ≥6: 72.3 vs. 76.7%), and were less likely to have universal drug coverage (72.6 vs. 83.1%), be prescribed non-potassium sparing diuretics (56.7 vs. 62.4%), have stage 2 or 3 AKI (5.3 vs. 21.1%), require hospitalization in the previous 365 days (30.5 vs. 43.3%), be seen by a family physician ≥11 times in the past year (47.1 vs. 53.1%), be seen at least once by a general internist (23.2 vs. 30.6%), be seen in the ED during daytime (52.3 vs.

71.5%) and overnight hours (12.6 vs. 17.1%), and be assigned an emergent triage acuity level (CTAS 1 or 2: 20.8 vs. 38.7%).

There was no difference in female sex, rural residence, income, abdominal aortic aneurysm repair, cerebrovascular disease, chronic liver disease, coronary artery disease, nephrolithiasis, osteoarthritis, Parkinson's disease, peripheral vascular disease, rheumatoid arthritis, use of all medications except non-potassium sparing diuretics, proportion of patients with a pre-ED visit baseline SCr ≤50 μmol/L, at least one ED visit in the previous 365 days, at least one family physician visit, at least one nephrologist visit, at least one urologist visit, abdominal ultrasound, cardiac stress test, coronary angiogram or revascularization, intervention for kidney stones, season of the year, and two ED physician specialties (Emergency Medicine and Family Medicine).

5.2.1.2 Matched Cohort

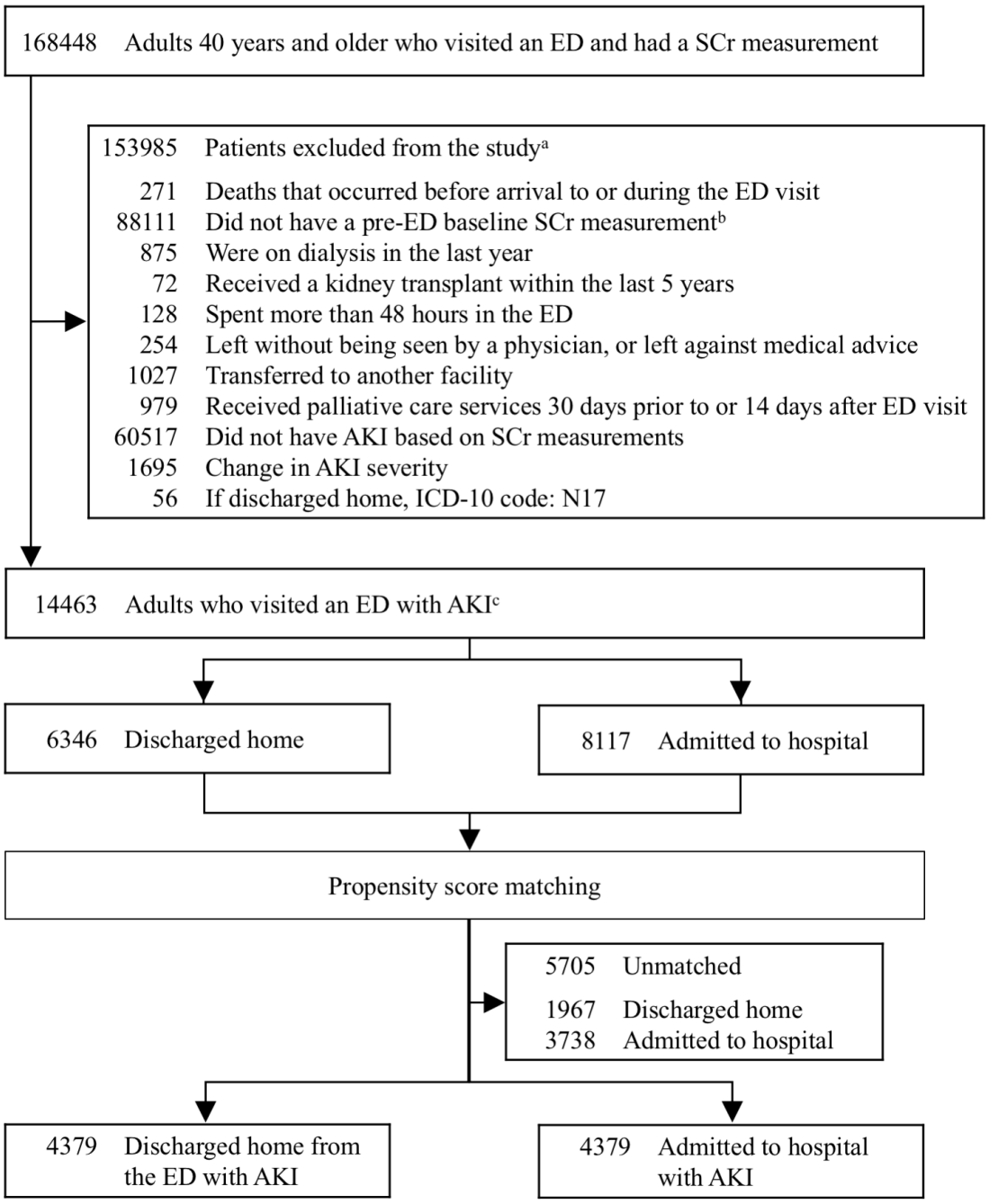
A total of 4379 patients discharged from the ED with AKI were successfully matched to 4379 patients admitted to hospital from the ED with AKI (Table 5-3). The matched cohort comprised of 4091 (93.4%) patients with stage 1, 244 (5.6%) with stage 2, and 44 (1.0%) with stage 3 AKI. The two groups were well-balanced and showed no meaningful differences in 91 of 92 measured baseline characteristics (Appendix G). The ED serum sodium was slightly higher in the group of ED discharges with AKI [mean (SD) 137 (5) vs. 136 (6) mmol/L, standardized difference 22%, reference range for serum sodium: 135 to 145 mmol/L].

The mean (SD) age of the entire matched cohort was 71 (13) years and 46.5% were women. The most common co-morbid conditions were hypertension (79.4%), diabetes (39.2%), CKD (45.0%), coronary artery disease (37.1%), and heart failure (26.7%). Among patients with universal drug coverage through the ODB program (79.2%), 5.2% resided in a long-term care facility and a median of five medications were prescribed in the 120 days prior to the index date. The most commonly prescribed medications were angiotensin-converting enzyme inhibitor or angiotensin receptor blockers (59.7%), non-

potassium sparing diuretics (59.2%), statins (45.4%), antibiotics (45.2%), beta-adrenergic antagonists (39.9%), proton pump inhibitors (36.8%), and calcium channel blockers (34.4%). A urine ACR was measured in 23.9% of patients in the previous 365 days. Most patients did not have a prior ED visit (previous 30 days: 81.1%, 31 to 365 days: 60.2%) or hospitalization (previous 30 days: 90.0%, 31 to 365 days: 73.2%). Nearly all patients (98.3%) were seen by their family physician at least once in the previous 365 days. Prior visits to the general internist (26.4%), nephrologist (4.9%), or urologist (17.4%) were less common.

The mean (median) pre-ED visit baseline SCr concentration among both groups was approximately 107 (91) μmol/L. The mean (median) ED serum potassium, sodium, and creatinine concentration was approximately 4.3 (4.1) mmol/L, 137 (138) mmol/L, and 158 (139) μmol/L, respectively. Most patients were triaged to emergent or urgent acuity levels (CTAS 1 or 2: 27.1%, CTAS 3: 59.9%).

Figure 5-2: Cohort Selection for the AKI Subpopulation



Abbreviations: AKI, acute kidney injury; ED, emergency department; ICD, International Classification of Diseases; SCr, serum creatinine.

[a] Patients were excluded in order as listed.

[b] We selected the most recent pre-ED visit baseline SCr measurement.

[c] If an individual had more than one ED visit with AKI, we selected the first ED visit.

Table 5-3: Baseline Characteristics of Patients in the AKI Subpopulation Pre- and Post-Match

Variable	Unmatched			Matched		
	Patient in the ED with AKI[a]			Patient in the ED with AKI[a]		
	Discharged home (N = 6346)	Admitted to hospital (N= 8117)	Standardized difference (%)	Discharged home (N= 4379)	Admitted to hospital (N= 4379)	Standardized difference (%)
Demographics						
Age, in years						
Mean (SD)	69 (13)	73 (13)	32	71 (13)	71 (13)	2
Median (IQR)	70 (58-79)	75 (64-83)		73 (62-81)	74 (62-81)	
40 to <65	2326 (36.7)	2055 (25.3)	25	1267 (28.9)	1298 (29.6)	2
65 to <80	2475 (39.0)	3178 (39.2)	0	1819 (41.5)	1681 (38.4)	6
≥80	1545 (24.3)	2884 (35.5)	25	1293 (29.5)	1400 (32.0)	5
Sex, female	2948 (46.5)	3737 (46.0)	1	2037 (46.5)	2037 (46.5)	0
Year of cohort entry						
2003 to 2005	1593 (25.1)	1999 (24.6)	1	1114 (25.4)	1117 (25.5)	0
2006 to 2008	2903 (45.7)	3189 (39.3)	13	1881 (43.0)	1911 (43.6)	1
2009 to 2011	1850 (29.2)	2929 (36.1)	15	1384 (31.6)	1351 (30.9)	2
Rural residence	969 (15.3)	1302 (16.0)	2	685 (15.6)	652 (14.9)	2
Neighbourhood income quintile						
1	1401 (22.1)	1892 (23.3)	3	971 (22.2)	989 (22.6)	1
2	1353 (21.3)	1748 (21.5)	1	942 (21.5)	932 (21.3)	1
3	1307 (20.6)	1608 (19.8)	2	978 (22.3)	957 (21.9)	1
4	1046 (16.5)	1342 (16.5)	0	731 (16.7)	732 (16.7)	0
5	1140 (18.0)	1391 (17.1)	2	757 (17.3)	769 (17.6)	1
Pharmacy forward sortation area[b]	5214 (82.2)	6513 (80.2)	5	3562 (81.3)	3573 (81.6)	1
Co-morbid conditions[c]						

Abdominal aortic aneurysm repair	NR	78 (1.0)	2	38 (0.9)	38 (0.9)	0
Atrial fibrillation or flutter	NR	1133 (14.0)	11	539 (12.3)	547 (12.5)	1
Cerebrovascular disease	NR	396 (4.9)	4	221 (5.0)	208 (4.7)	1
Chronic liver disease	NR	722 (8.9)	8	327 (7.5)	325 (7.4)	0
Chronic obstructive pulmonary disease	NR	907 (11.2)	18	352 (8.0)	364 (8.3)	1
Coronary artery disease[d]	2160 (34.0)	3124 (38.5)	9	1614 (36.9)	1636 (37.4)	1
Dementia	NR	1204 (14.8)	15	531 (12.1)	540 (12.3)	1
Diabetes	2405 (37.9)	3496 (43.1)	11	1728 (39.5)	1703 (38.9)	1
Heart failure	NR	2591 (31.9)	23	1168 (26.7)	1170 (26.7)	0
Hypertension	4783 (75.4)	6454 (79.5)	10	3475 (79.4)	3475 (79.4)	0
Major cancer[e]	1056 (16.6)	1735 (21.4)	12	829 (18.9)	843 (19.3)	1
Nephrolithiasis	NR	191 (2.4)	2	117 (2.7)	110 (2.5)	1
Osteoarthritis	NR	631 (7.8)	2	344 (7.9)	330 (7.5)	1
Parkinson's disease	NR	82 (1.0)	5	32 (0.7)	32 (0.7)	0
Peripheral vascular disease	NR	371 (4.6)	9	154 (3.5)	156 (3.6)	0
Rheumatoid arthritis	NR	604 (7.4)	1	317 (7.2)	309 (7.1)	1
Charlson co-morbidity index[f]						
0	4181 (65.9)	4338 (53.4)	26	2676 (61.1)	2574 (58.8)	5
1	NR	1017 (12.5)	5	515 (11.8)	541 (12.4)	2
2	NR	1110 (13.7)	11	489 (11.2)	575 (13.1)	6
≥3	824 (13.0)	1652 (20.4)	20	699 (16.0)	689 (15.7)	1
Aggregated Diagnosis Groups score[g]						
0-5	1757 (27.7)	1892 (23.3)	10	1124 (25.7)	1114 (25.4)	1
≥6	4589 (72.3)	6225 (76.7)	10	3255 (74.3)	3265 (74.6)	1

Medication utilization[h]

ODB program eligible	4605 (72.6)	6748 (83.1)	26	3459 (79.0)	3477 (79.4)	1
Patients in long-term care[i]	NR	458 (5.6)	12	172 (5.0)	188 (5.4)	2
Medication class[j]						
Alpha-1-adrenoceptor antagonist or 5-alpha-reductase inhibitor	NR	439 (6.5)	0	217 (6.3)	211 (6.1)	1
Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker	2750 (59.7)	4026 (59.7)	0	2065 (59.7)	2074 (59.6)	0
Anti-retroviral	NR	12 (0.2)	0	6 (0.2)	≤5 (≤0.1)	6
Antibiotic	2041 (44.3)	3214 (47.6)	7	1567 (45.3)	1569 (45.1)	0
Anticoagulant	NR	1253 (18.6)	7	594 (17.2)	609 (17.5)	1
Antidepressant (SSRI or SNRI)	774 (16.8)	1151 (17.1)	1	566 (16.4)	563 (16.2)	0
Antineoplastic (chemotherapy)	NR	150 (2.2)	2	83 (2.4)	82 (2.4)	0
Antiplatelet	NR	1028 (15.2)	3	557 (16.1)	558 (16.0)	0
Antipsychotic	NR	497 (7.4)	3	226 (6.5)	228 (6.6)	0
Beta-adrenergic antagonist	1781 (38.7)	2712 (40.2)	3	1385 (40.0)	1381 (39.7)	1
Calcium channel blocker	NR	2357 (34.9)	2	1193 (34.5)	1196 (34.4)	0
Corticosteroid	1188 (25.8)	1904 (28.2)	5	935 (27.0)	943 (27.1)	0
Immunosuppressive medication	NR	291 (4.3)	2	144 (4.2)	127 (3.7)	3
Lithium	NR	45 (0.7)	0	23 (0.7)	21 (0.6)	1
Non-potassium sparing diuretic	2609 (56.7)	4213 (62.4)	12	2034 (58.8)	2071 (59.6)	2
Non-steroidal anti-inflammatory drug[k]	892 (19.4)	1245 (18.4)	2	660 (19.1)	657 (18.9)	0
Oral hypoglycemic agent or insulin	NR	2069 (30.7)	0	1039 (30.0)	1016 (29.2)	2

Potassium-sparing diuretic	NR	1013 (15.0)	9	445 (12.9)	481 (13.8)	3
Proton pump inhibitor	1651 (35.9)	2563 (38.0)	4	1260 (36.4)	1289 (37.1)	1
Statin	2174 (47.2)	2932 (43.4)	8	1584 (45.8)	1563 (45.0)	2
Xanthine oxidase inhibitor or uricosuric agent	NR	576 (8.5)	7	245 (7.1)	262 (7.5)	2
Unique drug names						
Mean (SD)	6 (6)	7 (5)	27	6 (6)	6 (6)	1
Median (IQR)	5 (0-10)	6 (0-10)		6 (0-10)	6 (0-10)	
Unique drug identification numbers						
Mean (SD)	6 (6)	8 (7)	27	7 (6)	7 (6)	2
Median (IQR)	5 (0-10)	7 (0-11)		6 (0-11)	6 (0-11)	
Pre-ED visit baseline kidney function[l]						
Baseline SCr, in µmol/L						
Mean (SD)	101 (55)	115 (69)	23	106 (57)	107 (59)	2
Median (IQR)	87 (71-112)	96 (76-130)		90 (74-118)	91 (73-120)	
Days baseline SCr measured pre-ED visit						
Mean (SD)	133 (102)	121 (99)	12	127 (101)	128 (101)	1
Median (IQR)	106 (44-207)	90 (36-188)		98 (41-197)	100 (40-203)	
Baseline SCr ≤50 µmol/L	NR	277 (3.4)	4	164 (3.7)	165 (3.8)	1
Baseline eGFR						
≥60 ml/min/1.73m^2	3919 (61.8)	3907 (48.1)	28	2435 (55.6)	2386 (54.5)	2
45 to <60 ml/min/1.73m^2	NR	1610 (19.8)	8	815 (18.6)	834 (19.0)	1
30 to <45 ml/min/1.73m^2	NR	1470 (18.1)	13	695 (15.9)	685 (15.6)	1
<30 ml/min/1.73m^2	NR	1130 (13.9)	19	434 (9.9)	474 (10.8)	3
CKD risk category[m]						
Low risk	NR	558 (6.9)	16	422 (9.6)	352 (8.0)	6

Moderate risk	NR	382 (4.7)	1	201 (4.6)	208 (4.7)	1
High risk	NR	394 (4.9)	5	248 (5.7)	236 (5.4)	1
Very high risk	NR	1358 (16.7)	18	551 (12.6)	586 (13.4)	2
Urine ACR measured	1689 (26.6)	1794 (22.1)	11	1078 (24.6)	1019 (23.3)	3
<3 mg/mmol	NR	1014 (12.5)	10	633 (14.5)	567 (12.9)	4
3 to <30 mg/mmol	NR	363 (4.5)	1	186 (4.2)	208 (4.7)	2
≥30 mg/mmol	NR	417 (5.1)	5	259 (5.9)	244 (5.6)	1
ED visit laboratory characteristics						
Serum potassium, in mmol/L						
Mean (SD)	4.2 (0.6)	4.4 (0.9)	31	4.2 (0.6)	4.3 (0.8)	7
Median (IQR)	4.1 (3.8-4.5)	4.3 (3.8-4.9)		4.1 (3.8-4.5)	4.1 (3.7-4.7)	
Serum sodium, in mmol/L						
Mean (SD)	137 (5)	136 (7)	25	137 (5)	136 (6)	22
Median (IQR)	138 (135-140)	136 (133-139)		138 (135-140)	137 (134-139)	
SCr, in µmol/L						
Mean (SD)	147 (70)	208 (158)	50	156 (74)	158 (73)	3
Median (IQR)	129 (109-162)	162 (124-230)		136 (113-174)	139 (114-178)	
AKI severity						
Stage 1	6012 (94.7)	6407 (78.9)	48	4091 (93.4)	4091 (93.4)	0
Stage 2	290 (4.6)	1007 (12.4)	28	244 (5.6)	244 (5.6)	0
Stage 3	44 (0.7)	703 (8.7)	38	44 (1.0)	44 (1.0)	0
Previous health care utilization[n]						
ED visits in the previous						
30 days	1114 (17.6)	1638 (20.2)	7	818 (18.7)	840 (19.2)	1
31 to 365 days	2510 (39.5)	3252 (40.1)	1	1744 (39.8)	1743 (39.8)	0
Hospitalizations in the						

previous						
30 days	481 (7.6)	1130 (13.9)	21	419 (9.6)	454 (10.4)	3
31 to 365 days	1452 (22.9)	2387 (29.4)	15	1102 (25.2)	1245 (28.4)	7
Outpatient physician visits						
Family physician	6251 (98.5)	7965 (98.1)	3	4319 (98.6)	4294 (98.1)	4
0 to 4 visits	1069 (16.8)	1239 (15.3)	4	646 (14.8)	732 (16.7)	5
5 to 10 visits	2287 (36.0)	2571 (31.7)	9	1521 (34.7)	1429 (32.6)	4
≥11 visits	2990 (47.1)	4307 (53.1)	12	2212 (50.5)	2218 (50.7)	0
General internist (≥1 visit)	1470 (23.2)	2486 (30.6)	17	1143 (26.1)	1171 (26.7)	1
Nephrologist (≥1 visit)	NR	496 (6.1)	7	226 (5.2)	204 (4.7)	2
Urologist (≥1 visit)	1132 (17.8)	1390 (17.1)	2	791 (18.1)	729 (16.6)	4
Diagnostic imaging and procedures						
Abdominal ultrasound[o]	1530 (24.1)	2210 (27.2)	7	883 (20.2)	886 (20.2)	0
Cardiac stress test	NR	1056 (13.0)	6	619 (14.1)	627 (14.3)	0
Coronary angiogram or revascularization	NR	157 (1.9)	2	91 (2.1)	102 (2.3)	2
CT scan with contrast	NR	407 (5.0)	11	157 (3.6)	158 (3.6)	0
Echocardiogram	NR	1820 (22.4)	11	1080 (24.7)	1083 (24.7)	0
Intervention for kidney stones[p]	NR	96 (1.2)	0	50 (1.1)	50 (1.1)	1
ED and hospital characteristics						
Institution[q]						
1	1754 (27.6)	2565 (31.6)	9	1336 (30.5)	1317 (30.1)	1
2	1482 (23.4)	2051 (25.3)	4	1060 (24.2)	1089 (24.9)	2
3	NR	806 (9.9)	1	464 (10.6)	472 (10.8)	1
4	NR	74 (0.9)	33	61 (1.4)	62 (1.4)	0
5	NR	150 (1.8)	4	94 (2.1)	107 (2.4)	2

6	NR	70 (0.9)	2	36 (0.8)	31 (0.7)	1
7	NR	833 (10.3)	2	466 (10.6)	447 (10.2)	1
8	NR	332 (4.1)	1	180 (4.1)	186 (4.2)	1
9	NR	369 (4.5)	5	246 (5.6)	242 (5.5)	0
10	NR	657 (8.1)	8	308 (7.0)	295 (6.7)	1
11	NR	139 (1.7)	5	88 (2.0)	90 (2.1)	0
12	NR	39 (0.5)	1	22 (0.5)	23 (0.5)	0
13	NR	32 (0.4)	1	18 (0.4)	18 (0.4)	0
ED and hospital activity						
Standardized number of ED registrations in the last 12h[r]						
Mean (SD)	1.1 (0.3)	1.1 (0.3)	14	1.1 (0.3)	1.1 (0.3)	0
Median (IQR)	1.1 (0.9-1.3)	1.1 (0.9-1.3)		1.9 (0.9-1.3)	1.9 (0.9-1.3)	
Standardized number of hospital admissions in the last 24h[s]						
Mean (SD)	1.1 (0.3)	1.1 (0.3)	3	1.1 (0.3)	1.1 (0.3)	0
Median (IQR)	1.1 (0.8-1.3)	1.1 (0.8-1.3)		1.1 (0.8-1.3)	1.1 (0.8-1.3)	
Standardized number of hospital inpatient discharges in the last 24h[t]						
Mean (SD)	1.1 (0.4)	1.1 (0.4)	3	1.1 (0.3)	1.1 (0.4)	3
Median (IQR)	1.1 (0.8-1.2)	1.1 (0.8-1.3)		1.1 (0.8-1.3)	1.1 (0.8-1.3)	
Standardized number of ED registrations resulting in hospitalization, in %[u]	47.0	51.0	8	49.5	49.3	0
ED seasonal and time characteristics						
Time of day						

0700 to <1700	3320 (52.3)	4538 (71.5)	40	2298 (52.5)	2381 (54.4)	4
1700 to <2400	2226 (35.1)	2495 (39.3)	9	1497 (34.2)	1423 (32.5)	4
0000 to <0700	800 (12.6)	1084 (17.1)	13	584 (13.3)	575 (13.1)	1
Season[v]						
Fall	1502 (23.7)	2141 (26.4)	6	1067 (24.4)	1105 (25.2)	2
Winter	1446 (22.8)	1925 (23.7)	2	1033 (23.6)	1013 (23.1)	1
Spring	1635 (25.8)	1959 (24.1)	4	1108 (25.3)	1086 (24.8)	1
Summer	1763 (27.8)	2092 (25.8)	5	1171 (26.7)	1175 (26.8)	0
ED physician training						
Emergency medicine	4642 (73.1)	5781 (71.2)	4	3140 (71.7)	3152 (72.0)	1
Family medicine	1338 (21.1)	1602 (19.7)	3	945 (21.6)	936 (21.4)	1
Other	NR	734 (9.0)	13	294 (6.7)	291 (6.6)	0
ED patient acuity and wait times						
CTAS[w]						
1 or 2	1321 (20.8)	3142 (38.7)	40	1192 (27.2)	1185 (27.1)	0
3	3797 (59.8)	4257 (52.4)	15	2620 (59.8)	2626 (60.0)	0
4 or 5	1228 (19.4)	718 (8.8)	31	567 (12.9)	568 (13.0)	0
Time (hours) waiting for physician assessment, mean (SD)						
CTAS 1 or 2	0.6 (0.8)	0.5 (0.8)	16	0.6 (0.8)	0.5 (0.6)	7
CTAS 3	1.3 (1.3)	1.2 (1.2)	12	1.3 (1.1)	1.2 (1.2)	3
CTAS 4 or 5	1.6 (1.4)	1.7 (1.7)	2	1.4 (1.3)	1.6 (1.6)	9

Abbreviations: ACR, albumin-to-creatinine ratio; AKI, acute kidney injury; CKD, chronic kidney disease; CT, computed tomography; CTAS, Canadian Triage Acuity Scale; ED, emergency department; eGFR, estimated glomerular filtration rate; IQR, interquartile range; ODB, Ontario Drug Benefit; NR, not reported; SD, standard deviation; SCr, serum creatinine; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.
To convert SCr from SI units (μmol/L) to traditional units (mg/dL), divide by 88.42.

[a] Data reported as n (%) unless otherwise noted. To comply with privacy regulations for minimizing the chance of patient re-identification, numbers of patients were suppressed in the case of five or fewer patients. The total number of patients was not reported if there were other calculations that could result in the re-identification of five or fewer patients.

[b] Pharmacy forward sortation area refers to a region in Ontario represented by the first three letters of the postal code. This variable describes the number and proportion of individuals who live in the same region as the pharmacy that provided them with prescription medications.

[c] Look-back window for co-morbidities was five years unless otherwise noted.

[d] Does not include angina.

[e] Major cancers include the following tissues/organs: lung/bronchi, colon/rectum, breast, pancreas, prostate, leukemia, non-Hodgkin lymphoma, liver, ovaries, and esophagus.

[f] Look-back window for the Charlson co-morbidity index was two years.[63,64]

[g] The Aggregated Diagnosis Groups (ADG) point score, derived from the John Hopkins Adjusted Clinical Groups® system, score is a weighted measure of health care utilization as a proxy measure for co-morbidity and accounts for the duration of condition, severity of condition, diagnostic certainty, etiology of the condition, and specialty care involvement.[65,66] The higher ADG score, the greater the co-morbidity. Individuals with an ADG score of 0 to 2 reflect low health care costs with no prior hospitalizations; ADG score 3 to 5, high health care costs but no prior hospitalizations; ADG score 6 or more, high health care costs and at least one prior hospitalization.

[h] Look-back window for medication utilization was 120 days.

[i] Patients in long-term care were identified from the ODB database.

[j] Percentages reported are based on the number of ODB program eligible patients (age 65 years and older).

[k] Does not includes acetylsalicylic acid.

[l] Pre-ED look-back window was 7 to 365 days.

[m] CKD risk categories derived from the 2012 Kidney Diseases: Improving Global Outcomes consensus guidelines. In addition to using urine ACR measurements, urine dipstick and protein values were converted to an estimate urine ACR.[67]

[n] Look-back window for health care utilization was 365 days unless otherwise noted.

[o] Not specific for the assessment of the kidneys.

[p] Urological procedures included extracorporeal shockwave lithotripsy, percutaneous nephrolithotomy, or ureteroscopic lithotripsy with stone removal.

[q] For privacy considerations, individual hospital institutions were not identified.

[r] Standardized to the mean number of ED registrations that occurred in the last 12-hour period over the last 14 days.

[s] Standardized to the mean number of hospital admissions that occurred in the last 24-hour period over the last 14 days.

[t] Standardized to the mean number of hospital discharges that occurred in the last 24-hour period over the last 14 days.

[u] Proportion of registrations resulting in hospitalization standardized to each ED/hospital institution's number of ED registrations occurring in the last 24 hours.

[v] Fall: September 21 to December 20; Winter: December 21 to March 20; Spring: March 21 to June 20; Summer: June 21 to September 20.

[w] Patients with a CTAS of 1 or 2 need to be seen immediately 98% of the time or within 15 minutes 95% of the time, respectively. Patients with a CTAS of 3 or 4 need to be seen within 30 minutes 90% of the time or 60 minutes 85% of the time, respectively. Patients with a CTAS of 5 need to be seen within 120 minutes 80% of the time.

5.2.1.3 Outcomes

The primary and secondary outcome for the AKI subpopulation is shown in Table 5-4. In the 30-day follow-up period across the entire cohort, 652 (7.4%) patients died and 52 (0.6%) received hospital-based acute dialysis.

Compared to patients admitted to hospital from the ED with AKI, fewer patients discharged home from the ED with AKI died within 30 days of the index date [130 (3.0%) vs. 522 (11.9%), RR: 0.25, 95% CI: 0.21-0.30, $P<0.001$]. Fewer patients discharged home from the ED with AKI received hospital-based acute dialysis within 30 days of the index date, although the difference did not reach statistical significance [19 (0.43%) vs. 33 (0.75%), RR: 0.57, 95% CI: 0.33 to 1.01, $P=0.06$].

5.2.1.4 Subgroup Analysis

A subgroup analysis for all-cause mortality by AKI stage is shown in Table 5-5. The relative association between an ED discharge and the risk of all-cause mortality was attenuated with more severe forms of AKI [stage 1 RR (95% CI): 0.23 (0.18-0.29), stage 2: 0.40 (0.22-0.69), and stage 3: 1.00 (0.38-2.64); *P* value for interaction <0.001)].

Table 5-4: Thirty-Day Risk of All-Cause Mortality and Need for Hospital-Based Acute Dialysis in a Matched Cohort of Patients in the AKI Subpopulation

Outcome	ED patient events, *n* (%)		Relative risk[a] (95% CI)	*P* value
	Discharged home with AKI (N = 4379)	Admitted to hospital with AKI (N = 4379)		
All-cause mortality	130 (3.0)	522 (11.9)	0.25 (0.21-0.30)	<0.001
Receipt of hospital-based acute dialysis	19 (0.4)	33 (0.8)	0.57 (0.33-1.01)	0.06

Abbreviations: AKI, acute kidney injury; CI, confidence interval; ED, emergency department.

[a] Patients admitted to hospital from the ED with AKI served as the referent group.

Table 5-5: The Association Between Emergency Department Disposition and 30-Day All-Cause Mortality in the AKI Subpopulation Examined in a Subgroup Defined by Acute Kidney Injury Stage

AKI stage	ED patient events, *n/N* (%)[a]		Relative risk[b] (95% CI)	Interaction *P* value
	Discharged home with AKI	Admitted to hospital with AKI		
1	108/4091 (2.6)	477/4091 (11.7)	0.23 (0.18-0.28)	<0.001
2	15/244 (6.1)	38/244 (15.6)	0.40 (0.22-0.69)	
3	7/44 (15.9)	7/44 (15.9)	1.00 (0.38-2.64)	

Abbreviations: AKI, acute kidney injury; CI, confidence interval; ED, emergency department.

[a] *n* = number of events, *N* = number at risk.

[b] Patients admitted to hospital from the ED with AKI served as the referent group.

5.2.2 Discharged Subpopulation

5.2.2.1 Unmatched Cohort

Cohort selection for the AKI subpopulation is presented in Figure 5-3. Baseline characteristics before and after matching are presented in Table 5-6.

Before matching, there were 49,768 patients who visited an ED and were discharged home. Among these patients, 6346 had AKI and 43,422 did not have AKI. ED patients discharged home with AKI as compared to those with no AKI were older (mean age 69 vs. 63 years) and more likely to have coronary artery disease (34.0 vs. 20.0%), CKD (38.2 vs. 17.3%), diabetes (37.9 vs. 24.6%), hypertension (75.4 vs. 59.2%), a Charlson co-morbidity index of ≥3: 13.0 vs. 4.5%, an ADG score of ≥6: 72.3 vs. 59.5%, universal drug coverage (72.6 vs. 52.6%), be prescribed a greater number of medications (median 6 vs. 3) in the previous 120 days such as angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, antibiotics, beta-adrenergic antagonists, non-potassium sparing medications, oral hypoglycemic agents or insulin, proton pump inhibitors, and statins, have a higher pre-ED visit baseline SCr concentration [mean (median) 101 (87) vs. 81 (76) μmol/L], have a previous abdominal ultrasound (24.1 vs. 19.1%), a prior ED visit (previous 30 days: 17.6 vs. 8.6%; 31 to 365 days: 39.5 vs. 32.0%) or hospitalization (previous 31 to 365 days: 22.9 vs. 13.7%), be seen by a family physician ≥11 times in the past year (47.1 vs. 31.1%), and be seen at least once by a urologist (17.8 vs. 11.7%). These patients were more likely to visit the ED in the evening (35.1 vs. 27.8%), have a higher ED serum potassium concentration [mean (median) 4.2 (4.1) vs. 4.0 (3.9) mmol/L], and have a lower ED serum sodium concentration [mean (median) 137 (138) vs. 138 (139) mmol/L].

ED patients discharged home with AKI as compared to those with no AKI were less likely to be female (46.5 vs. 56.5%), have an eGFR ≥60 mL/min/1.73m^2 (61.8 vs. 82.7%), and visit an ED during daytime hours (52.3 vs. 57.6%).

There was no difference in rural residence, income, abdominal aortic aneurysm repair, chronic liver disease, major cancer, nephrolithiasis, osteoarthritis, Parkinson's disease, and rheumatoid arthritis, use of alpha-one-adrenoceptor antagonists or five-alpha-reductase inhibitors, anti-retrovirals, antidepressants, antineoplastics, antipsychotics, corticosteroids, immunosuppression, lithium, or non-steroidal anti-inflammatory drugs, number of days the pre-ED visit baseline SCr was measured prior to the index date, proportion of patients with pre-ED visit baseline SCr ≤50 μmol/L, proportion of patients with a pre-ED visit urine ACR measurement, hospitalization in the previous 30 days, at least one family physician visit, at least one general internist visit, cardiac stress test, coronary angiogram or revascularization, intervention for kidney stones, season of the year, CTAS, time waiting for a physician assessment, any ED physician specialty, and 90th percentile for ED length of stay.

5.2.2.2 Matched Cohort

A total of 6188 patients discharged home from the ED with AKI were successfully matched to 6188 patients discharged home from the ED with no AKI (Table 5-6). The matched cohort comprised of 3904 (63.1%) patients with an eGFR ≥60, 1054 (17.0%) with an eGFR 45 to <60, 803 (13.0%) with an eGFR 30 to <45, and 427 (6.9%) with an eGFR <30 mL/min/1.73m^2. The two groups were well-balanced and showed no meaningful differences in 89 of 91 measured baseline characteristics (Appendix G). The group discharged home from the ED with AKI had a higher mean (SD) ED serum potassium concentration [4.2 (0.6) vs. 4.0 (0.5) mmol/L, standardized difference 21%, reference range: 3.5 to 5.0 mmol/L] and was more likely to visit an ED in the previous 30 days (17.1 vs. 13.5%, standardized difference 10.1%).

The mean (SD) age of the entire matched cohort was 69 (14) years and 47.2% were women. The most common co-morbid conditions were hypertension (75.1%), diabetes (37.2%), CKD (36.9%), coronary artery disease (33.2%), and heart failure (20.2%). In patients with universal drug coverage through the ODB program (72.6%), 3.6% resided in a long-term care facility and a median of five medications were prescribed in the 120

days prior to the index date. The most commonly prescribed medications were angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (59.2%), non-potassium sparing diuretics (55.4%), statins (46.3%), antibiotics (43.7%), beta-adrenergic antagonists (38.0%), proton pump inhibitors (34.9%), and calcium channel blockers (32.9%). A urine ACR was measured in 26.2% of patients in the previous 365 days. Most patients did not have a prior ED visit (previous 30 days: 84.7%, 31 to 365 days: 61.4%) or hospitalization (previous 30 days: 92.8%, 31 to 365 days: 77.7%). Nearly all patients (98.5%) were seen by their family physician at least once in the previous 365 days. Prior visits to the general internist (22.8%), nephrologist (3.8%), and urologist (17.4%) were less common.

The mean (median) pre-ED visit baseline SCr concentration was approximately 98 (87) μmol/L. The mean (median) ED serum potassium and sodium concentration was approximately 4.2 (4.0) mmol/L and 138 (139) mmol/L, respectively. Most patients were triaged to emergent or urgent acuity levels (CTAS 1 or 2: 20.9%, CTAS 3: 58.1%). The 90th percentile for ED length of stay ranged between 8 and 9 hours.

5.2.2.3 Outcomes

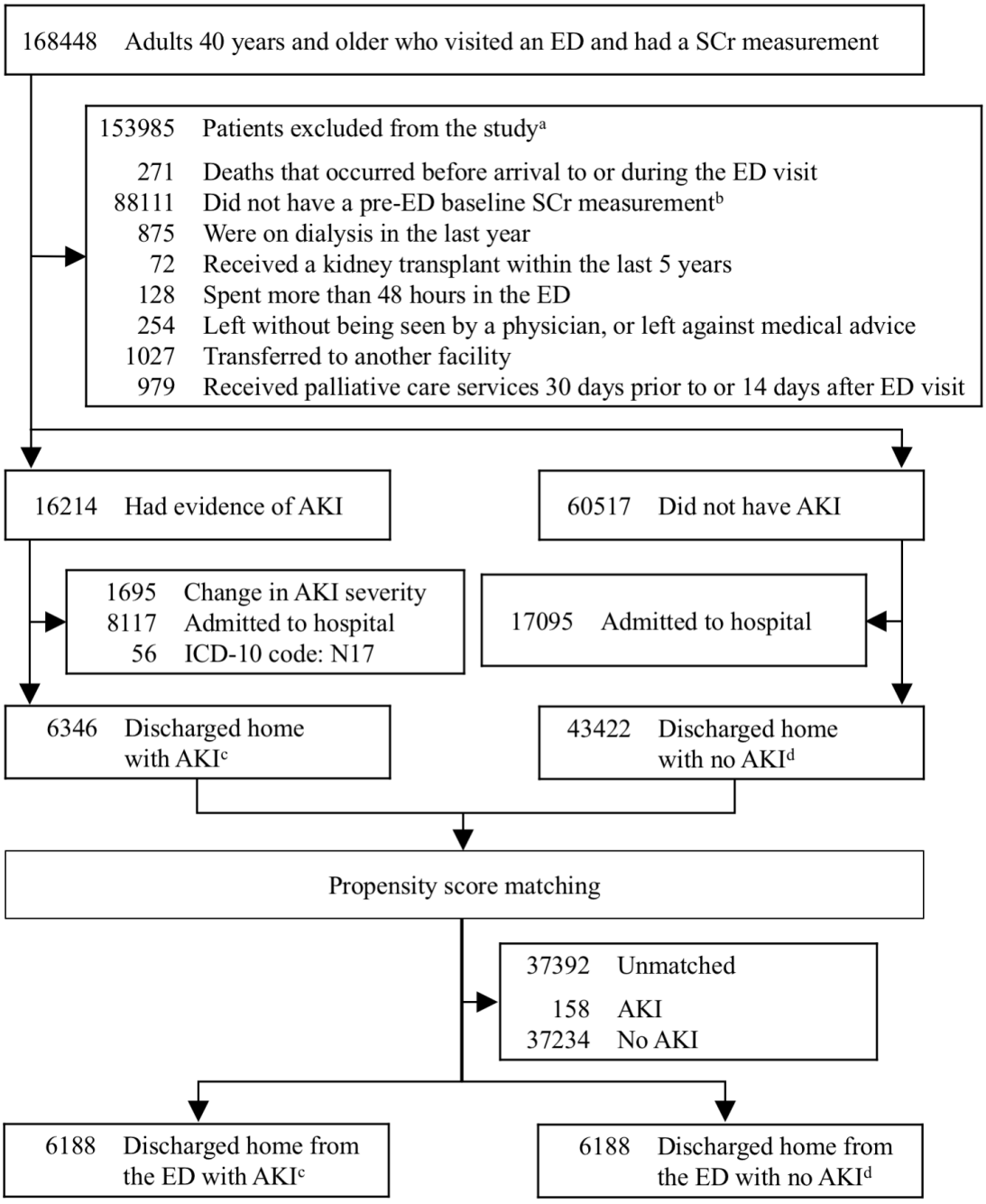
The primary and secondary outcome for the discharged subpopulation is shown in Table 5-7. In the 30-day follow-up period across the entire cohort, 223 (3.6%) patients died and 26 (0.4%) received hospital-based acute dialysis.

Compared to patients discharged from the ED with no AKI, more patients discharged home from the ED with AKI died [136 (2.2%) vs. 87 (1.4%), RR: 1.56, 95% CI: 1.20 to 2.04, *P*=0.001] and received hospital-based acute dialysis within 30 days of the index date [19 (0.43%) vs. 7 (0.11%), RR: 2.71, 95% CI: 1.22 to 6.02, *P*=0.01].

5.2.2.4 Subgroup Analysis

A subgroup analysis for all-cause mortality by CKD stage is shown in Table 5-8. The association between AKI and the risk of all-cause mortality was not modified by CKD stage (*P* value for interaction <0.57).

Figure 5-3: Cohort Selection for the Discharged Subpopulation



Abbreviations: AKI, acute kidney injury; ED, emergency department; ICD, International Classification of Diseases; SCr, serum creatinine.

[a] Patients were excluded in order as listed.

[b] We selected the most recent pre-ED visit baseline SCr measurement.

[c] If an individual had more than one ED visit with AKI, we selected the first ED visit.

[d] If an individual had more than one ED visit with no AKI, we selected the first ED visit. However, preference was given to the group discharged home from the ED with AKI if patients were also eligible for this referent group.

Table 5-6: Baseline Characteristics of Patients in the Discharged Subpopulation Pre- and Post-Match

Variable	Unmatched			Matched		
	Discharged home[a]		Standardized difference (%)	Discharged home[a]		Standardized difference (%)
	AKI (N = 6346)	No AKI (N = 43422)		AKI (N = 6188)	No AKI (N = 6188)	
Demographics						
Age, in years						
Mean (SD)	69 (13)	63 (14)	42	68 (13)	69 (14)	2
Median (IQR)	70 (58-79)	62 (51-74)		70 (58-79)	71 (58-80)	
40 to <65	2326 (36.7)	24036 (55.4)	38	2309 (37.3)	2190 (35.4)	4
65 to <80	2475 (39.0)	13061 (30.1)	19	2401 (38.8)	2429 (39.3)	1
≥80	1545 (24.3)	6325 (14.6)	25	1478 (23.9)	1569 (25.4)	3
Sex, female	2948 (46.5)	24532 (56.5)	20	2900 (46.9)	2940 (47.5)	1
Year of cohort entry						
2003 to 2005	1593 (25.1)	8611 (19.8)	13	1559 (25.2)	1558 (25.2)	0
2006 to 2008	2903 (45.7)	17056 (39.3)	13	2811 (45.4)	2839 (45.9)	1
2009 to 2011	1850 (29.2)	17755 (40.9)	25	1818 (29.4)	1791 (28.9)	1
Rural residence	969 (15.3)	6299 (14.5)	2	940 (15.2)	957 (15.5)	1
Neighbourhood income quintile						
1	1401 (22.1)	8814 (20.3)	4	1372 (22.2)	1416 (22.9)	2
2	1353 (21.3)	9012 (20.8)	1	1306 (21.1)	1323 (21.4)	1
3	1307 (20.6)	8757 (20.2)	1	1372 (22.2)	1330 (21.5)	2
4	1046 (16.5)	7896 (18.2)	4	1023 (16.5)	999 (16.1)	1
5	1140 (18.0)	8520 (19.6)	4	1115 (18.0)	1120 (18.1)	0
Pharmacy forward sortation area[b]	5214 (82.2)	34871 (80.3)	5	5089 (82.2)	5059 (81.8)	1
Co-morbid conditions[c]						
Abdominal aortic aneurysm	NR	162 (0.4)	5	47 (0.8)	55 (0.9)	1

repair						
Atrial fibrillation or flutter	NR	1759 (4.1)	24	606 (9.8)	581 (9.4)	1
Cerebrovascular disease	NR	706 (1.6)	15	234 (3.8)	230 (3.7)	0
Chronic liver disease	NR	2203 (5.1)	7	412 (6.7)	392 (6.3)	1
Chronic obstructive pulmonary disease	NR	1140 (2.6)	17	359 (5.8)	337 (5.4)	2
Coronary artery disease[d]	2160 (34.0)	8678 (20.0)	32	2062 (33.3)	2049 (33.1)	0
Dementia	NR	2428 (5.6)	16	607 (9.8)	614 (9.9)	0
Diabetes	2405 (37.9)	10678 (24.6)	29	2294 (37.1)	2308 (37.3)	0
Heart failure	NR	3460 (8.0)	39	1280 (20.7)	1226 (19.8)	2
Hypertension	4783 (75.4)	25725 (59.2)	35	4630 (74.8)	4668 (75.4)	1
Major cancer[e]	1056 (16.6)	5918 (13.6)	8	1026 (16.6)	1016 (16.4)	0
Nephrolithiasis	NR	666 (1.5)	8	169 (2.7)	170 (2.7)	0
Osteoarthritis	NR	2580 (5.9)	5	444 (7.2)	434 (7.0)	1
Parkinson's disease	NR	114 (0.3)	4	32 (0.5)	38 (0.6)	1
Peripheral vascular disease	NR	1759 (4.1)	13	174 (2.8)	163 (2.6)	1
Rheumatoid arthritis	NR	2595 (6.0)	5	445 (7.2)	437 (7.1)	1
Charlson co-morbidity index[f]						
0	4181 (65.9)	35911 (82.7)	39	4139 (66.9)	4246 (68.6)	4
1	NR	2900 (6.7)	15	683 (11.0)	640 (10.3)	2
2	NR	2657 (6.1)	15	618 (10.0)	639 (10.3)	1
≥3	824 (13.0)	1954 (4.5)	30	748 (12.1)	663 (10.7)	4
Aggregated Diagnosis Groups score[g]						
0-5	1757 (27.7)	17586 (40.5)	27	1738 (28.1)	1777 (28.7)	1
≥6	4589 (72.3)	25836 (59.5)	27	4450 (71.9)	4411 (71.3)	1
Medication utilization[h]						
ODB eligible	4605 (72.6)	22849 (52.6)	42	3459 (79.0)	3477 (79.4)	3
Patients in long-term	NR	441 (1.9)	12	172 (3.9)	188 (4.3)	2

care[i]						
Medication class[j]						
Alpha-1-adrenoceptor antagonist or 5-alpha-reductase inhibitor	NR	1078 (4.7)	7	277 (6.2)	255 (5.6)	3
Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker	2750 (59.7)	10530 (46.1)	28	2644 (59.4)	2680 (59.1)	1
Anti-retroviral	NR	40 (0.2)	0	7 (0.2)	8 (0.2)	0
Antibiotic	2041 (44.3)	8297 (36.3)	16	1954 (43.9)	1972 (43.5)	1
Anticoagulant	NR	2287 (10.0)	17	673 (15.1)	646 (14.2)	2
Antidepressant (SSRI or SNRI)	774 (16.8)	3534 (15.5)	4	738 (16.6)	767 (16.9)	1
Antineoplastic (chemotherapy)	NR	463 (2.0)	3	110 (2.5)	121 (2.7)	1
Antiplatelet	NR	2442 (10.7)	16	705 (15.8)	712 (15.7)	0
Antipsychotic	NR	1335 (5.8)	3	286 (6.4)	298 (6.6)	1
Beta-adrenergic antagonist	1781 (38.7)	6467 (28.3)	22	1697 (38.1)	1716 (37.8)	1
Calcium channel blocker	NR	5647 (24.7)	21	1488 (33.4)	1468 (32.4)	2
Corticosteroid	1188 (25.8)	5280 (23.1)	6	1155 (25.9)	1172 (25.8)	0
Immunosuppressive medication	NR	784 (3.4)	3	175 (3.9)	184 (4.1)	1
Lithium	NR	171 (0.7)	1	30 (0.7)	30 (0.7)	0
Non-potassium sparing diuretic	2609 (56.7)	8421 (36.9)	40	2476 (55.6)	2504 (55.2)	1
Non-steroidal anti-inflammatory drug[k]	892 (19.4)	4347 (19.0)	1	871 (19.6)	894 (19.7)	0
Oral hypoglycemic agent or insulin	NR	4221 (18.5)	28	1320 (29.6)	1328 (29.3)	1
Potassium-sparing	NR	1431 (6.3)	20	512 (11.5)	505 (11.1)	1

diuretic						
Proton pump inhibitor	1651 (35.9)	6878 (30.1)	12	1588 (35.7)	1548 (34.1)	3
Statin	2174 (47.2)	9087 (39.8)	15	2085 (46.8)	2075 (45.8)	2
Xanthine oxidase inhibitor or uricosuric agent	NR	703 (3.1)	17	273 (6.1)	269 (5.9)	1
Unique drug names						
Mean (SD)	6 (6)	3 (4)	54	5 (5)	5 (5)	0
Median (IQR)	5 (0-10)	3 (0-9)		5 (0-9)	5 (0-9)	
Unique drug identification numbers						
Mean (SD)	6 (6)	3 (5)	54	6 (6)	6 (6)	0
Median (IQR)	5 (0-10)	3 (0-10)		5 (0-10)	5 (0-10)	
Pre-ED visit baseline kidney function[l]						
Baseline SCr, in μmol/L						
Mean (SD)	101 (55)	81 (28)	45	98 (50)	98 (49)	1
Median (IQR)	87 (71-112)	76 (65-90)		86 (71-109)	87 (71-110)	
Days baseline SCr measured pre-ED visit						
Mean (SD)	133 (102)	137 (103)	4	133 (102)	134 (103)	0
Median (IQR)	106 (44-207)	114 (46-215)		107 (45-209)	106 (43-210)	
Baseline SCr ≤50 μmol/L	NR	1309 (3.0)	6	263 (4.3)	264 (4.3)	0
Baseline eGFR						
≥60 ml/min/1.73m^2	3919 (61.8)	35924 (82.7)	48	3904 (63.1)	3904 (63.1)	0
45 to <60 ml/min/1.73m^2	NR	4836 (11.1)	16	1054 (17.0)	1054 (17.0)	0
30 to <45 ml/min/1.73m^2	NR	2022 (4.7)	31	803 (13.0)	803 (13.0)	0
<30 ml/min/1.73m^2	NR	640 (1.5)	31	427 (6.9)	427 (6.9)	0
CKD risk category[m]						

Low risk	NR	6393 (14.7)	10	721 (11.7)	679 (11.0)	2
Moderate risk	NR	1436 (3.3)	8	304 (4.9)	296 (4.8)	1
High risk	NR	1910 (4.4)	7	377 (6.1)	391 (6.3)	1
Very high risk	NR	988 (2.3)	34	578 (9.3)	570 (9.2)	0
Urine ACR measured	1689 (26.6)	10210 (23.5)	7	1648 (26.6)	1591 (25.7)	2
<3mg/mmol	NR	7404 (17.1)	3	999 (16.1)	964 (15.6)	2
3 to <30 mg/mmol	NR	978 (2.3)	12	267 (4.3)	228 (3.7)	3
≥30 mg/mmol	NR	1828 (4.2)	9	382 (6.2)	399 (6.4)	1
ED visit laboratory characteristics						
Serum potassium, in mmol/L						
Mean (SD)	4.2 (0.6)	4.0 (0.5)	33	4.2 (0.6)	4.0 (0.5)	21
Median (IQR)	4.1 (3.8-4.5)	3.9 (3.7-4.2)		4.0 (3.8-4.5)	4.0 (3.7-4.3)	
Serum sodium, in mmol/L						
Mean (SD)	137 (5)	138 (4)	20	138 (5)	138 (4)	10[n]
Median (IQR)	138 (135-140)	139 (137-141)		138 (136-140)	139 (136-140)	
Previous health care utilization[o]						
ED visits in the previous						
30 days	1114 (17.6)	3745 (8.6)	27	1061 (17.1)	836 (13.5)	10[p]
31 to 365 days	2510 (39.5)	13880 (32.0)	16	2438 (39.4)	2335 (37.7)	3
Hospitalizations in the previous						
30 days	481 (7.6)	2421 (5.6)	8	460 (7.4)	429 (6.9)	2
31 to 365 days	1452 (22.9)	5928 (13.7)	24	1375 (22.2)	1390 (22.5)	1
Outpatient physician visits						
Family physician	6251 (98.5)	42483 (97.8)	5	6095 (98.5)	6098 (98.5)	0
0 to 4 visits	1069 (16.8)	11584 (26.7)	24	1058 (17.1)	1072 (17.3)	1

5 to 10 visits	2287 (36.1)	18323 (42.2)	13	2258 (36.5)	2314 (37.4)	2
≥11 visits	2990 (47.1)	13515 (31.1)	33	2872 (46.4)	2802 (45.3)	2
General internist (≥1 visit)	1470 (23.2)	6619 (15.2)	4	1407 (22.7)	1420 (22.9)	1
Nephrologist (≥1 visit)	NR	561 (1.3)	29	260 (4.2)	209 (3.4)	4
Urologist (≥1 visit)	1132 (17.8)	5085 (11.7)	40	1103 (17.8)	1046 (16.9)	2
Diagnostic imaging or procedures						
Abdominal ultrasound[q]	1530 (24.1)	8291 (19.1)	12	1480 (23.9)	1465 (23.7)	1
Cardiac stress test	NR	5584 (12.9)	7	948 (15.3)	929 (15.0)	1
Coronary angiogram or revascularization	NR	702 (1.6)	5	144 (2.3)	135 (2.2)	1
CT with contrast	NR	636 (1.5)	10	172 (2.8)	175 (2.8)	0
Echocardiogram	NR	5204 (12.0)	17	1077 (17.4)	1004 (16.2)	3
Intervention for kidney stones[r]	NR	270 (0.6)	6	77 (1.2)	79 (1.3)	0
ED and hospital characteristics						
Institution[s]						
1	1754 (27.6)	13190 (30.4)	6	1724 (27.9)	1679 (27.1)	2
2	1482 (23.4)	11867 (27.3)	9	1448 (23.4)	1445 (23.4)	0
3	NR	3128 (7.2)	11	626 (10.1)	629 (10.2)	0
4	NR	2967 (6.8)	2	456 (7.4)	469 (7.6)	1
5	NR	1108 (2.6)	0	156 (2.5)	154 (2.5)	0
6	NR	262 (0.6)	1	42 (0.7)	41 (0.7)	0
7	NR	3143 (7.2)	8	587 (9.5)	579 (9.4)	0
8	NR	1583 (3.6)	1	242 (3.9)	250 (4.0)	1
9	NR	1651 (3.8)	8	337 (5.4)	327 (5.3)	1
10	NR	2883 (6.6)	3	369 (6.0)	382 (6.2)	1
11	NR	1174 (2.7)	2	145 (2.3)	158 (2.6)	1

12	NR	271 (0.6)	1	34 (0.5)	48 (0.8)	4
13	NR	195 (0.4)	1	22 (0.4)	27 (0.4)	0
ED and hospital activity						
Standardized number of ED registrations in the last 12h[t]						
Mean (SD)	1.1 (0.3)	1.1 (0.3)	20	1.1 (0.3)	1.1 (0.3)	0
Median (IQR)	1.1 (0.9-1.3)	1.0 (0.8-1.3)		1.1 (0.9-1.3)	1.1 (0.9-1.3)	
Standardized number of hospital admissions in the last 24h[u]						
Mean (SD)	1.1 (0.3)	1.1 (0.3)	3	1.1 (0.3)	1.1 (0.3)	3
Median (IQR)	1.1 (0.8-1.3)	1.1 (0.8-1.2)		1.1 (0.8-1.3)	1.1 (0.8-1.3)	
Standardized number of hospital inpatient discharges in the last 24h[v]						
Mean (SD)	1.1 (0.4)	1.1 (0.3)	3	1.1 (0.3)	1.1 (0.4)	0
Median (IQR)	1.1 (0.8-1.2)	1.1 (0.8-1.3)		1.1 (0.8-1.2)	1.1 (0.8-1.2)	
Standardized number of ED registrations resulting in hospitalization, in %[w]	47.0	49.0	4	47.3	47.1	0
ED seasonal and time characteristics						
Time of day						
0700 to <1700	3320 (52.3)	24996 (57.6)	11	3241 (52.4)	3314 (53.6)	2
1700 to <2400	2226 (35.1)	12086 (27.8)	16	2166 (35.0)	2060 (33.3)	4
0000 to <0700	800 (12.6)	6340 (14.6)	4	781 (12.6)	814 (13.2)	2
Season[x]						
Fall	1502 (23.7)	11053 (25.5)	4	1475 (23.8)	1469 (23.7)	0
Winter	1446 (22.8)	9991 (23.0)	1	1412 (22.8)	1421 (23.0)	0
Spring	1635 (25.8)	11008 (25.4)	1	1585 (25.6)	1545 (25.0)	1

Summer	1763 (27.8)	11370 (26.2)	4	1716 (27.7)	1753 (28.3)	1
ED physician training						
Emergency Medicine	4642 (73.1)	33336 (76.8)	8	4542 (73.4)	4541 (73.4)	0
Family Medicine	1338 (21.1)	7563 (17.4)	9	1289 (20.8)	1304 (21.1)	1
Other	NR	2523 (5.7)	0	357 (5.8)	343 (5.5)	1
ED patient acuity and wait times						
CTAS[y]						
1 and 2	1321 (20.8)	9072 (20.9)	0	1294 (20.9)	1290 (20.8)	0
3	3797 (59.8)	25241 (58.1)	3	3693 (59.7)	3736 (60.4)	1
4 and 5	1228 (19.4)	9108 (21.0)	4	1201 (19.4)	1162 (18.8)	2
Time (hours) waiting for physician assessment, mean (SD)						
CTAS 1 and 2	0.6 (0.8)	0.6 (0.9)	6	0.6 (0.8)	0.6 (0.8)	1
CTAS 3	1.3 (1.3)	1.4 (1.3)	5	1.3 (1.3)	1.3 (1.2)	2
CTAS 4 and 5	1.6 (1.4)	1.8 (1.6)	14	1.6 (1.4)	1.6 (1.4)	4
90% percentile ED length of stay, in hours						
CTAS 1 and 2	9	8		9	8	
CTAS 3	8	8		9	8	
CTAS 4 and 5	8	8		8	8	

Abbreviations: ACR, albumin-to-creatinine ratio; AKI, acute kidney injury; CKD, chronic kidney disease; CT, computed tomography; CTAS, Canadian Triage Acuity Scale; ED, emergency department; eGFR, estimated glomerular filtration rate; IQR, interquartile range; NR, not reported; SCr, serum creatinine; SD, standard deviation; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.
To convert SCr from SI units (μmol/L) to traditional units (mg/dL), divide by 88.42.

[a] Data reported as n (%) unless otherwise noted. To comply with privacy regulations for minimizing the chance of patient re-identification, numbers of patients were suppressed in the case of five or fewer patients. The total number of patients was not reported if there were other calculations that could result in the re-identification of five or fewer patients.

[b] Pharmacy forward sortation area refers to a region in Ontario represented by the first three letters of the postal code. This variable describes the number and proportion of individuals who live in the same region as the pharmacy that provided them with prescription medications.

[c] Look-back window for co-morbidities was five years unless otherwise noted.

[d] Does not include angina.

[e] Major cancers include the following tissues/organs: lung/bronchi, colon/rectum, breast, pancreas, prostate, leukemia, non-Hodgkin lymphoma, liver, ovaries, and esophagus.

[f] Look-back window for the Charlson co-morbidity index was two years.[63,64]

[g] The Aggregated Diagnosis Groups (ADG) point score, derived from the John Hopkins Adjusted Clinical Groups® system, score is a weighted measure of health care utilization as a proxy measure for co-morbidity and accounts for the duration of condition, severity of condition, diagnostic certainty, etiology of the condition, and specialty care involvement.[65,66] The higher ADG score, the greater the co-morbidity. Individuals with an ADG score of 0 to 2 reflect low health care costs with no prior hospitalizations; ADG score 3 to 5, high health care costs but no prior hospitalizations; ADG score 6 or more, high health care costs and at least one prior hospitalization.

[h] Look-back window for medication utilization was 120 days.

[i] Patients in long-term care were identified from the Ontario Drug Benefit (ODB) database.

[j] Percentages reported are based on the number of ODB program eligible patients (age 65 years and older).

[k] Does not includes acetylsalicylic acid.

[l] Pre-ED look-back window was 7 to 365 days.

[m] CKD risk categories derived from the 2012 Kidney Diseases: Improving Global Outcomes consensus guidelines. In addition to using urine ACR measurements, urine dipstick and protein values were converted to an estimate urine ACR.[67]

[n] Standardized difference was 9.6%.

[o] Look-back window for health care utilization was 365 days unless otherwise noted.

[p] Standardized difference was 10.1%.

[q] Not specific for the assessment of the kidneys.

[r] Urological procedures included extracorporeal shockwave lithotripsy, percutaneous nephrolithotomy, or ureteroscopic lithotripsy with stone removal.

[s] For privacy considerations, individual hospital institutions were not identified.

[t] Standardized to the mean number of ED registrations that occurred in the last 12-hour period over the last 14 days.

[u] Standardized to the mean number of hospital admissions that occurred in the last 24-hour period over the last 14 days.

[v] Standardized to the mean number of hospital discharges that occurred in the last 24-hour period over the last 14 days.

[w] Proportion of registrations resulting in hospitalization standardized to each ED/hospital institution's number of ED registrations occurring in the last 24 hours.

[x] Fall: September 21 to December 20; Winter: December 21 to March 20; Spring: March 21 to June 20; Summer: June 21 to September 20.

[y] Patients with a CTAS of 1 or 2 need to be seen immediately 98% of the time or within 15 minutes 95% of the time, respectively. Patients with a CTAS of 3 or 4 need to be seen within 30 minutes 90% of the time or 60 minutes 85% of the time, respectively. Patients with a CTAS of 5 need to be seen within 120 minutes 80% of the time.

Table 5-7: Thirty-Day Risk of All-Cause Mortality and Need for Hospital-Based Acute Dialysis in a Matched Cohort of Patients in the Discharged Subpopulation

Outcome	ED patient events, *n* (%)		Relative risk[a] (95% CI)	*P* value
	Discharged home with AKI (N = 6188)	Discharged home with no AKI (N = 6188)		
All-cause mortality	136 (2.2)	87 (1.4)	1.56 (1.20-2.04)	0.001
Receipt of hospital-based acute dialysis	19 (0.3)	7 (0.1)	2.71 (1.22-6.02)	0.014

Abbreviations: AKI, acute kidney injury; CI, confidence interval; ED, emergency department.

[a] Patients discharged home from the ED with no AKI served as the referent group.

Table 5-8: The Association Between Acute Kidney Injury and 30-Day All-Cause Mortality in the Discharged Subpopulation Examined in a Subgroup Defined by Pre-Emergency Department Chronic Kidney Disease Stage

Pre-ED CKD stage[a]	ED patient events, *n/N* (%)[b]		Relative risk[c] (95% CI)	Interaction *P* value
	Discharged home with AKI	Discharged home with no AKI		
eGFR≥60	67/3904 (1.7)	47/3904 (1.2)	1.43 (0.99-2.06)	0.57
45≤eGFR<60	34/1054 (3.2)	16/1054 (1.5)	2.13 (1.19-3.80)	
30≤eGFR<45	16/803 (2.0)	13/803 (1.6)	1.23 (0.59-2.56)	
eGFR<30[d]	19/427 (4.4)	11/427 (2.6)	1.73 (0.83-3.59)	

Abbreviations: AKI, acute kidney injury; CI, confidence interval; CKD, chronic kidney disease; ED, emergency department; eGFR, estimated glomerular filtration rate.

[a] CKD stage was defined using eGFR categories, reported in mL/min/1.73m^2.

[b] *n* = number of events, *N* = number at risk.

[c] Patients discharged home from the ED with no AKI served as the referent group.

[d] Patients with an eGFR 15 to <30 were combined with patients with an eGFR <15 (but not on dialysis) to comply with ICES privacy regulations for reporting small numbers.

Chapter 6

6 Discussion

6.1 Summary of Findings

In this population-based cohort study of adults discharged home from the ED with AKI, 149 (2.3%) died within 30 days and this proportion increased with AKI severity. Compared to patients who were hospitalized with AKI, patients discharged home from the ED with AKI had a lower risk of death (3.0% vs. 11.9%) and a trend towards a lower risk of subsequent dialysis (0.4% vs 0.8%). Although the two groups in the AKI subpopulation had comparable characteristics, the divergence in outcomes highlights the accuracy of ED clinicians in discerning subtle clinical differences in patients with AKI. Sicker patients destined for worse outcomes were appropriately hospitalized. Nonetheless, the adverse outcomes of AKI following an ED discharge are clearly highlighted when the relative association between an ED discharge and mortality was attenuated with more severe forms of AKI. Furthermore, patients discharged home with AKI as compared to a similar cohort of ED patients discharged home with no AKI was associated with a 1.6-fold increase in mortality (2.2% vs. 1.4%) and an increased need for hospital-based acute dialysis (0.3% vs. 0.1%) within 30 days. Among the three groups studied, an ED discharge home with AKI represents an intermediate risk population.

6.2 Interpretation of Findings

6.2.1 Mortality

The 30-day mortality risk in patients discharged home from the ED with AKI is not insignificant when compared to studies of other ED patient populations. For example, fewer patients died within 30 and 90 days of an ED discharge with chest pain (0.2%) and a transient ischemic attack (2%), respectively.[90,91] Without conducting a formal analysis and accounting for differences in study methodology, the higher risk of mortality in our cohort is likely because of a greater burden of co-morbidity. Conversely, other studies showed that more patients died within 30 days of ED discharge with heart failure (4%) or

unstable angina (5%).[92,93] The lower risk of mortality is likely because a proportion of AKI in our cohort may be caused by mild, reversible hemodynamic changes and therefore may confer better short-term outcomes.

Two of the five studies we identified in our literature review examined mortality on patients discharged home from the ED with AKI. No deaths were observed within 30 days of an ED discharge home with AKI among 31 patients.[52] It is unclear whether the risk of 30-day mortality would be similar to our study had the authors examined a larger sample size. In the study by Holmes *et al*., the 90-day mortality for 2719 ED patients with AKI not hospitalized was 10-15%.[50] A similar risk of 90-day mortality was observed by Talabani *et al.*, although their study included patients diagnosed or managed either in the community or hospital setting.[49] Future studies in our region could examine outcomes with a similar follow-up period.

We found that most patients had mild AKI and that mortality was far more common than the need for hospital-based acute dialysis. In this setting, our study suggests that AKI may be a marker of illness severity.[94]

6.2.1.1 Subgroup Analysis of the AKI Subpopulation

We explored AKI stage as a subgroup in the analysis of the AKI subpopulation as prior studies demonstrated that severe forms of AKI confer worse outcomes.[4,8,18–20] Our results demonstrated comparable mortality in a matched subgroup of patients with stage 3 AKI, where regardless of ED disposition, one in six patients with similar baseline characteristics died within 30 days of the index date. The high risk of mortality may reflect the progression of an underlying illness as approximately one-third of patients inevitably required admission to hospital within the same follow-up period.

6.2.1.2 Subgroup Analysis of the Discharged Subpopulation

We explored CKD stage as a subgroup in the analysis of the discharged subpopulation. CKD did not modify the association between AKI and short-term mortality. Prior studies suggest there is an interaction between AKI and CKD on mortality. In one study by Han

et al. showed that the presence of CKD exaggerated the association between AKI and the one-year risk of mortality in patients who had coronary artery bypass graft surgery.[55] In our subgroup analysis, the effect of CKD on the association between AKI and mortality was not apparent within 30 days of an ED visit and could have been observed with longer follow-up periods. Another explanation is that we studied a group of patients whose characteristics and outcomes were unknown and who differ from patients with AKI in other clinical settings.[42,43] How CKD modifies the association between AKI and mortality in non-hospitalized patients requires further study.

6.2.2 Hospitalization and Follow-Up

The need for hospitalization within 30 days of an ED discharge with AKI occurred in 1032 (16.3%) patients. Our findings are similar to the 30-day readmission rates (15-20%) among AKI survivors discharged after hospitalization.[95–97] We also found a discrepancy between a proportion of patients who received outpatient physician follow-up (68%) and those who had repeat SCr measurements (23%), raising questions on whether AKI was the main reason for the outpatient visit, physicians recognized the presence of AKI, or appropriate measures were taken to avoid hospitalization. Our findings suggest outpatient follow-up is inadequate, consistent with the study by Scheuermeyer *et al.* where only 4 of 31 patients discharged home from the ED with AKI received renal-specific follow-up.[52]

6.3 Study Strengths

This is the first comprehensive study to examine the characteristics and outcomes of patients discharged home from the ED with AKI. We are not aware of any studies describing this group since the publication of this work.[47] None of the studies identified in our literature review examined the AKI subpopulation as the primary cohort of interest.[48–52]

Using a combination of administrative and laboratory databases at ICES, we were able to obtain a large sample size and examine clinically important outcomes. With a large number of baseline characteristics available, we were able to provide context for these

outcomes using propensity scores and two ED referent groups. Finally, we were able to use most current definition for the diagnosis and staging of AKI with SCr concentrations.[14] We ascertained patients who would have otherwise been missed had we exclusively relied on diagnostic codes.[41] As shown on Figure 5-1, only 56 patients discharged home from the ED were assigned an ICD-10 code for AKI.

6.4 Limitations

6.4.1 Generalizability

Our results are generalizable to residents in Southwestern Ontario captured by our data sources. We had access to SCr concentrations from two laboratory databases. The Cerner electronic health record is used in 13 hospital institutions and Dynacare Medical Laboratories represents approximately one-third of Ontario residents.[60,61] We could not obtain patients who had pre-ED visit baseline SCr measurements done in other outpatient laboratories or hospitals in Ontario.

In the analysis of the AKI and discharged subpopulations, our results are generalizable to patients included in the match. We could not match 1967 (31%) patients in the AKI subpopulation and 158 (3%) patients in the discharged subpopulation using our propensity score models. Furthermore, medication information was only available for a subset of patients eligible for universal drug coverage. We minimized the impact of missing medication information by balancing the co-morbidities for which these medications are indicated.

6.4.2 Interpretation of Findings

Factors such as hemodynamic stability and the ED physician's clinical assessment of patient safety and appropriateness for discharge home cannot be ascertained by administrative data. We also could not determine with certainty if ED physicians did not recognize the AKI. For many patients, we suspect that AKI was in fact recognized, appropriately managed, and deemed safe for discharge home.[52] Further details would require a detailed chart review best collected in a prospective fashion.

A significant proportion of individuals discharged home from the ED with AKI required hospitalization within 30 days. We are unable to establish if the need for hospitalization was preventable or inevitable. Patients may have been appropriately hospitalized after being strategically discharged from a rural ED and instructed to seek further care at a tertiary care centre. Such patients would be considered an ED discharge.

6.4.3 Selection Bias

We excluded patients discharged home from the ED with an improvement in AKI severity (1695 patients) and those assigned an ICD-10 code for AKI (56 patients). These individuals may differ systematically from those who did not have an improvement in AKI severity or were recognized by physicians with an ED main diagnosis of AKI.[98] We elected to restrict our analysis to a specific group of patients less likely to be recognized and treated by ED physicians because we felt these patients would most likely benefit from an intervention that combines active surveillance and increased awareness with timely renal-specific outpatient follow-up (Chapter 6.5). Interpretation of the characteristics and outcomes of our main cohort and two matched analyses should bear this limitation in mind.

6.4.4 Residual Confounding

Our results are subject to confounding as propensity score matching will only ensure balance on measured characteristics. We did not include the ED main diagnosis in our propensity score models as the diagnosis is often preliminary and there is significant disagreement with main diagnoses assigned at later stages of patient care.[99–101] There was also significant variability in the ED main diagnosis assigned to patients (Appendix H). Inclusion of the ED main diagnosis would have resulted in very few matched patients. Although the exclusion of the ED main diagnosis is a source residual confounding, we felt it was both valuable and worthwhile to provide health care providers context for our outcomes.

6.5 Study Implications

6.5.1 Recommendations for Future Research

We restricted our cohort to a very specific group of patients with AKI. Additional studies could be performed to include patients with AKI who were excluded from our main cohort. Future data sets linked at ICES may include larger laboratory databases more representative of all residents in Ontario. We would also be able to include new baseline characteristics and help confirm the association between an ED discharge home with AKI and mortality. However, there are several other knowledge gaps in this area that warrant further attention. A prospective chart review would be required to understand why some patients are at high risk of death or early hospitalization and to establish the reasons for a discrepancy between the proportion of outpatient physician visits and kidney function testing. Additional research is required to ascertain differences in patient characteristics between those destined for adverse outcomes and poor outpatient follow-up. Finally, future studies could examine long-term outcomes similar to those done for survivors of AKI patients after hospitalization.[22,26,28]

6.5.2 Health System Strategies

There is an opportunity to explore health system strategies to improve the identification and management of patients discharged home from the ED with AKI. Studies have demonstrated that rapid access clinics for patients discharged home from the ED with chest pain, heart failure, or a transient ischemic attack can improve patient outcomes.[102–104] Furthermore, AKI survivors discharged after hospitalization appear to benefit from follow-up clinics.[30] A similar model could be adapted for patients discharged home from the ED with AKI, supported by an automated surveillance system to facilitate AKI identification and increased awareness by all health care providers.[105] AKI surveillance systems have become increasingly popular in the United Kingdom and could serve as a model for design and implementation to improve the process of care for patients in our region.[50]

6.6 Conclusion

Patients with moderate-to-severe AKI at significant risk of 30-day adverse outcomes such as all-cause mortality and subsequent hospitalization. Compared to a hospital admission with AKI and an ED discharge with no AKI, patients discharged home from the ED with AKI are an intermediate risk population. Additional research into risk factors for adverse outcomes, further characterization of ED and outpatient care, and testing health system strategies to identify and mitigate gaps in care appears warranted.

References

1. Selby NM, Crowley L, Fluck RJ, et al. Use of electronic results reporting to diagnose and monitor AKI in hospitalized patients. *Clin J Am Soc Nephrol*. 2012;7(4):533-540.
2. Garg AX, Kurz A, Sessler DI, et al. Perioperative aspirin and clonidine and risk of acute kidney injury: A randomized clinical trial. *JAMA*. 2014;312(21):2254-2264.
3. Porter CJ, Juurlink I, Bisset LH, et al. A real-time electronic alert to improve detection of acute kidney injury in a large teaching hospital. *Nephrol Dial Transpl*. 2014;29(10):1888-1893.
4. Chertow GM, Burdick E, Honour M, et al. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol*. 2005;16(11):3365-3370.
5. Liangos O, Wald R, O'Bell JW, et al. Epidemiology and outcomes of acute renal failure in hospitalized patients: a national survey. *Clin J Am Soc Nephrol*. 2006;1(1):43-51.
6. Waikar SS, Curhan GC, Wald R, et al. Declining mortality in patients with acute renal failure, 1988 to 2002. *J Am Soc Nephrol*. 2006;17(4):1143-1150.
7. Coca SG, Yusuf B, Shlipak MG, et al. Long-term risk of mortality and other adverse outcomes after acute kidney injury: a systematic review and meta-analysis. *Am J Kidney Dis*. 2009;53(6):961-973.
8. Palevsky PM, Zhang JH, O'Connor TZ, et al. Intensity of renal support in critically ill patients with acute kidney injury. *N Engl J Med*. 2008;359(1):7-20.
9. Koeppen B, Stanton B. *Berne and Levy Physiology*. 6th ed. St. Louis: Mosby; 2008.
10. Gilbert SJ, Weiner DE, Gipson DS, et al. *National Kidney Foundation Primer on Kidney Diseases*. 6th ed. National Kidney Foundation; 2014.
11. Inker LA, Schmid CH, Tighiouart H, et al. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med*. 2012;367(1):20-29.
12. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604-612.
13. Nguyen MT, Maynard SE, Kimmel PL. Misapplications of commonly used kidney equations: renal physiology in practice. *Clin J Am Soc Nephrol*. 2009;4(3):528-534.
14. Kidney Disease: Improving Global Outcomes (KDIGO) acute kidney injury work group. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl*. 2012;2(1):1-138.
15. Bellomo R, Ronco C, Kellum JA, et al. Acute Dialysis Quality Initiative workgroup. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the second international

consensus conference of the Acute Dialysis Quality Initiative (ADQI) group. *Crit Care*. 2004;8(4):R204-212.

16. Mehta RL, Kellum JA, Shah SV, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care*. 2007;11(2):R31.
17. Wang HE, Muntner P, Chertow GM, Warnock DG. Acute kidney injury and mortality in hospitalized patients. *Am J Nephrol*. 2012;35(4):349-355.
18. Wald R, Quinn RR, Luo J, et al. Chronic dialysis and death among survivors of acute kidney injury requiring dialysis. *JAMA*. 2009;302(11):1179-1185.
19. Chawla LS, Kimmel PL. Acute kidney injury and chronic kidney disease: an integrated clinical syndrome. *Kidney Int*. 2012;82(5):516-524.
20. Coca SG, Singanamala S, Parikh CR. Chronic kidney disease after acute kidney injury: a systematic review and meta-analysis. *Kidney Int*. 2012;81(5):442-448.
21. Nisula S, Kaukonen K-M, Vaara ST, et al. Incidence, risk factors and 90-day mortality of patients with acute kidney injury in Finnish intensive care units: the FINNAKI study. *Intensive Care Med*. 2013;39(3):420-428.
22. Wald R, Quinn RR, Adhikari NK, et al. Risk of chronic dialysis and death following acute kidney injury. *Am J Med*. 2012;125(6):585-593.
23. Lo LJ, Go AS, Chertow GM, et al. Dialysis-requiring acute renal failure increases the risk of progressive chronic kidney disease. *Kidney Int*. 2009;76(8):893-899.
24. Bucaloiu ID, Kirchner HL, Norfolk ER, et al. Increased risk of death and de novo chronic kidney disease following reversible acute kidney injury. *Kidney Int*. 2012;81(5):477-485.
25. Chawla LS, Amdur RL, Shaw AD, et al. Association between AKI and long-term renal and cardiovascular outcomes in United States veterans. *Clin J Am Soc Nephrol*. 2014;9(3):448-456.
26. Wu VC, Wu CH, Huang TM, et al. Long-term risk of coronary events after AKI. *J Am Soc Nephrol*. 2014;25(3):595-605.
27. Wu VC, Wu PC, Wu CH, et al. The impact of acute kidney injury on the long-term risk of stroke. *J Am Heart Assoc*. 2014;3(4):e000933.
28. Hsu CY, Hsu RK, Yang J, et al. Elevated BP after AKI. *J Am Soc Nephrol*. 2016;27(3):914-923.
29. Siew ED, Peterson JF, Eden SK, et al. Outpatient nephrology referral rates after acute kidney injury. *J Am Soc Nephrol*. 2012;23(2):305-312.
30. Harel Z, Wald R, Bargman JM, et al. Nephrologist follow-up improves all-cause mortality of severe acute kidney injury survivors. *Kidney Int*. 2013;83(5):901-908.
31. Goldstein SL, Jaber BL, Faubel S, Chawla LS. AKI transition of care: a potential opportunity to detect and prevent CKD. *Clin J Am Soc Nephrol*. 2013;8(3):476-483.
32. Canadian Institute for Health Information: Quick stats.

https://www.cihi.ca/en/quick-stats. Published 2017. Accessed August 8, 2017.

33. Uscher-Pines L, Pines J, Kellermann A, et al. Emergency department visits for nonurgent conditions: systematic literature review. *Am J Manag Care*. 2013;19(1):47-59.

34. Palmer E, Leblanc-Duchin D, Murray J, Atkinson P. Emergency department use: is frequent use associated with a lack of primary care provider? *Can Fam Physician*. 2014;60(4):e223-229.

35. Canadian Institute for Health Information: Understanding emergency department wait times. https://secure.cihi.ca/free_products/Wait_times_e.pdf. Published 2005. Accessed October 14, 2014.

36. McCarthy DM, Engel KG, Buckley BA, et al. Talk-time in the emergency department: duration of patient-provider conversations during an emergency department visit. *J Emerg Med*. 2014;47(5):1-7.

37. Yoon J, Cordasco KM, Chow A, Rubenstein LV. The relationship between same-day access and continuity in primary care and emergency department visits. *PLoS One*. 2015;10(9):e0135274.

38. Kirk JD, Diercks DB. Challenges in the management of acutely decompensated congestive heart failure: disposition decisions in the emergency department. *Calif J Emerg Med*. 2003;4(2):39-42.

39. Calder LA, Forster AJ, Stiell IG, et al. Mapping out the emergency department disposition decision for high-acuity patients. *Ann Emerg Med*. 2012;60(5):567-576.e4.

40. Joslin J, Ostermann M. Care of the critically ill emergency department patient with acute kidney injury. *Emerg Med Int*. 2012;2012:760623.

41. Hwang YJ, Shariff SZ, Gandhi S, et al. Validity of the International Classification of Diseases, Tenth Revision code for acute kidney injury in elderly patients at presentation to the emergency department and at hospital admission. *BMJ Open*. 2012;2(6):e001821.

42. Wonnacott A, Meran S, Amphlett B, et al. Epidemiology and outcomes in community-acquired versus hospital-acquired AKI. *Clin J Am Soc Nephrol*. 2014;9(6):1007-1014.

43. Xu X, Nie S, Liu Z, et al. Epidemiology and clinical correlates of AKI in chinese hospitalized adults. *Clin J Am Soc Nephrol*. 2015;10(9):1-9.

44. Campbell S. A filter to retrieve studies related to emergency departments from the OVID MEDLINE database. John W. Scott Health Sciences Library, University of Alberta. Rev. November 24, 2015. http://guides.library.ualberta.ca/ld.php?content_id=14026195.

45. Hildebrand AM, Iansavichus AV, Haynes RB, et al. High-performance information search filters for acute kidney injury content in PubMed, Ovid Medline and Embase. *Nephrol Dial Transplant*. 2014;29(4):823-832.

46. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *J Epidemiol Community Health*. 1998;52(6):377-384.

47. Acedillo RR, Wald R, McArthur E, et al. Characteristics and outcomes of patients discharged home from an emergency department with AKI. *Clin J Am Soc Nephrol*. 2017;12(8):1215-1225.

48. Roghmann F, Ghani KR, Kowalczyk KJ, et al. Incidence and treatment patterns in males presenting with lower urinary tract symptoms to the emergency department in the United States. *J Urol*. 2013;190(5):1798-1804.

49. Talabani B, Zouwail S, Pyart RD, et al. Epidemiology and outcome of community-acquired acute kidney injury. *Nephrology*. 2014;19(5):282-287.

50. Holmes J, Rainer T, Geen J, et al. Acute kidney injury in the era of the AKI e-alert. *Clin J Am Soc Nephrol*. 2016;11(12):2123-2131.

51. Hazara AM, Elgaali M, Naudeer S, et al. The use of automated electronic alerts in studying short-term outcomes associated with community-acquired acute kidney injury. *Nephron*. 2017;135(3):181-188.

52. Scheuermeyer FX, Grafstein E, Rowe B, et al. The clinical epidemiology and 30-day outcomes of emergency department patients with acute kidney injury. *Can J Kidney Heal Dis*. 2017;4:205435811770398.

53. Hobbs H, Bassett P, Wheeler T, et al. Do acute elevations of serum creatinine in primary care engender an increased mortality risk? *BMC Nephrol*. 2014;15(1):206.

54. Wu VC, Huang TM, Lai CF, et al. Acute-on-chronic kidney injury at hospital discharge is associated with long-term dialysis and mortality. *Kidney Int*. 2011;80(11):1222-1230.

55. Han SS, Shin N, Baek SH, et al. Effects of acute kidney injury and chronic kidney disease on long-term mortality after coronary artery bypass grafting. *Am Heart J*. 2015;169(3):419-425.

56. Statistics Canada. Estimates of population, Canada, provinces and territories. https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000901. Published 2015. Accessed July 21, 2015.

57. von Elm E, Altman DG, Egger M, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61(4):344-349.

58. 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(2):67-71.

59. Goel V, Williams J, Anderson G, et al. *Patterns of Health Care in Ontario, 2nd Edition*. Toronto, ON Canada; 1996. http://www.ices.on.ca/Publications/Atlases-and-Reports/1996/Patterns-of-health-care-2nd-ed.

60. Cerner Laboratory.

http://www.cerner.com/solutions/Hospitals_and_Health_Systems/Laboatory/. Published 2015.

61. Dynacare Medical Laboratories. https://www.dynacare.ca. Published 2016.
62. Wodchis WP, Bushmeneva K, Nikitovic M, McKillop I. Guidelines on person level cost using administrative databases in Ontario. *Health System Performance Research Working Paper Series*. 2013;1:1-70.
63. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005;43(11):1130-1139.
64. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383.
65. Austin PC, Walraven CV. The mortality risk score and the ADG score. *Med Care*. 2011;49(10):940-947.
66. Johns Hopkins Bloomberg School of Public Health. The Johns Hopkins ACG Case-Mix System Reference Manual (Version 10). Baltimore: https://www.hopkinsacg.org. Published 2013.
67. Kidney Disease: Improving Global Outcomes (KDIGO) CKD work group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3(1):1-150.
68. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika*. 1983;70(1):41-55.
69. Paul R, Rosenbaum DB. Reducing bias in observational studies using subclassification on the propensity score. *J Am Stat Assoc*. 1984;79(387):516-524.
70. Szklo M, Nieto J. *Epidemiology: Beyond the Basics*. Third. Jones & Bartlett Learning; 2014.
71. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res*. 2011;46(3):399-424.
72. Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. *Pharm Stat*. 2011;10(2):150-161.
73. Austin PC, Grootendorst P, Anderson GM. A comparison of the ability of different propensity score models to balance measured variables between treated and untreated subjects: a Monte Carlo study. *Stat Med*. 2007;26(4):734-753.
74. Brookhart MA, Schneeweiss S, Rothman KJ, et al. Variable selection for propensity score models. *Am J Epidemiol*. 2006;163(12):1149-1156.
75. Gu XS, Rosenbaum PR. Comparison of multivariate matching methods : structures, distances, and algorithms. *J Comput Graph Stat*. 1993;2(4):405-420.
76. Patel AM, Shariff S, Bailey DG, et al. Statin toxicity from macrolide antibiotic

coprescription: a population-based cohort study. *Ann Intern Med*. 2013;158(12):869-876.

77. Gandhi S, Fleet JL, Bailey DG, et al. Calcium-channel blocker-clarithromycin drug interactions and acute kidney injury. *JAMA*. 2013;310(23):2544-2553.

78. Hwang YJ, Dixon SN, Reiss JP, et al. Atypical antipsychotic drugs and the risk for acute kidney injury and other adverse outcomes in older adults: a population-based cohort study. *Ann Intern Med*. 2014;161(4):242-248.

79. Yuan YC. Multiple imputation for missing data : concepts and new development (version 9.0). *SUGI Proc*. 2000:1-13.

80. Baker M, Clancy M. Can mortality rates for patients who die within the emergency department, within 30 days of discharge from the emergency department, or within 30 days of admission from the emergency department be easily measured? *Emerg Med J*. 2006;23(8):601-603.

81. Jha P, Deboer D, Sykora K, Naylor CD. Characteristics and mortality outcomes of thrombolysis trial participants and nonparticipants: a population-based comparison. *J Am Coll Cardiol*. 1996;27(6):1335-1342.

82. Vlasschaert MEO, Bejaimal SAD, Hackam DG, et al. Validity of administrative database coding for kidney disease: A systematic review. *Am J Kidney Dis*. 2011;57(1):29-43.

83. Austin PC. Using the standardized difference to compare the prevalence of a binary variable between two groups in observational research. *Commun Stat - Simul Comput*. 2009;38(6):1228-1234.

84. Imai K, King G, Stuart EA. Misunderstandings between experimantalists and observationalists about causal inference. *J R Stat Soc*. 2014;171(2):481-502.

85. Austin PC. Propensity-score matching in the cardiovascular surgery literature from 2004 to 2006: a systematic review and suggestions for improvement. *J Thorac Cardiovasc Surg*. 2007;134(5):1128-1135.

86. Austin PC. Primer on statistical interpretation or methods report card on propensity-score matching in the cardiology literature from 2004 to 2006: a systematic review. *Circ Cardiovasc Qual Outcomes*. 2008;1(1):62-67.

87. Zou G. A modified Poisson regression approach to prospective studies with binary data. *Am J Epidemiol*. 2004;159(7):702-706.

88. Zou GY, Donner A. Extension of the modified Poisson regression model to prospective studies with correlated binary data. *Stat Methods Med Res*. 2013;22(6):661-670.

89. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. *JAMA*. 1998;280(19):1690-1691.

90. Czarnecki A, Chong A, Lee DS, et al. Association between physician follow-up and outcomes of care after chest pain assessment in high-risk patients. *Circulation*. 2013;127(13):1386-1394.

91. Wasserman J, Perry J, Dowlatshahi D, et al. Stratified, urgent care for transient ischemic attack results in low stroke rates. *Stroke*. 2010;41(11):2601-2605.

92. Lee DS, Schull MJ, Alter DA, et al. Early deaths in patients with heart failure discharged from the emergency department a population-based analysis. *Circ Hear Fail*. 2010;3(2):228-235.

93. Pope JH, Aufderheide TP, Ruthazer R, et al. Missed diagnoses of acute cardiac ischemia in the emergency department. *N Engl J Med*. 2000;342(16):1163-1170.

94. Hoste EAJ, De Corte W. Clinical consequences of acute kidney injury. *Contrib Nephrol*. 2011;174:56-64.

95. Koulouridis I, Price LL, Madias NE, Jaber BL. Hospital-acquired acute kidney injury and hospital readmission: A cohort study. *Am J Kidney Dis*.

96. Siew ED, Parr SK, Abdel-Kader K, et al. Predictors of recurrent AKI. *J Am Soc Nephrol*. 2016;27(4):1190-1200.

97. Silver SA, Harel Z, McArthur E, et al. 30-day readmissions after an acute kidney injury hospitalization. *Am J Med*. 2017;130(2):163-172.e4.

98. Kleinbaum DG, Morgenstern H, Kupper LL. Selection bias in epidemiologic studies. *Am J Epidemiol*. 1981;113(4):452-463.

99. Campbell SG, Murray DD, Hawass A, et al. Agreement between emergency physician diagnosis and radiologist reports in patients discharged from an emergency department with community-acquired pneumonia. *Emerg Radiol*. 2005;11(4):242-246.

100. Farchi S, Camilloni L, Giorgi Rossi P, et al. Agreement between emergency room and discharge diagnoses in a population of injured inpatients: determinants and mortality. *J Trauma*. 2007;62(5):1207-1214.

101. Raven MC, Lowe RA, Maselli J, Hsia RY. Comparison of presenting complaint vs discharge diagnosis for identifying "nonemergency" emergency department visits. *JAMA*. 2013;309(11):1145-1153.

102. Sekhri N, Feder GS, Junghans C, et al. How effective are rapid access chest pain clinics? Prognosis of incident angina and non-cardiac chest pain in 8762 consecutive patients. *Heart*. 2007;93(4):458-463.

103. Lee DS, Stukel TA, Austin PC, et al. Improved outcomes with early collaborative care of ambulatory heart failure patients discharged from the emergency department. *Circulation*. 2010;122(18):1806-1814.

104. Dutta D, Bowen E, Foy C. Four-year follow-up of transient ischemic attacks, strokes, and mimics: a retrospective transient ischemic attack clinic cohort study. *Stroke*. 2015;46(5):1227-1232.

105. Colpaert K, Hoste EA, Steurbaut K, et al. Impact of real-time electronic alerting of acute kidney injury on therapeutic intervention and progression of RIFLE class. *Crit Care Med*. 2012;40(4):1164-1170.

Appendices

Appendix A: MEDLINE/Ovid Search Strategy to Identify Studies Describing Patients Discharged Home from the Emergency Department with Acute Kidney Injury.

#	MEDLINE/Ovid search	Results[a]
1[b]	((acute adj2 (kidney or renal or nephr$ or glomer$ or h?emodialy$ or dialysis)).mp OR exp Acute Kidney Injury/ OR ((kidney or renal) adj injur$).tw OR exp Kidney Diseases/ci OR (tubul$ adj (injury or necrosis or damage)).tw OR nephrotox$.tw OR Nephritis, Interstitial/ OR ((tubulointerstitial or interstitial) adj nephr$).tw OR ((kidney$ or renal) adj isch?emi$).tw OR (induced adj (kidney or renal)).tw OR (h?emolytic ur?emi$).tw OR *Hemolytic-Uremic Syndrome/ OR aki.tw OR oliguri$. mp or anuri$.mp OR anti-glomerular.mp OR antiglomerular.mp OR Kidney Cortex Necrosis/ OR pre-renal.tw or prerenal.tw OR anti-gbm.tw OR (obstruct$ adj2 (kidney$ or nephropath$ or renal or uropathy)).tw OR hepatorenal syndrome. mp OR *Hemorrhagic Fever with Renal Syndrome/ OR (thrombotic adj (thrombocytopeni$ or microangiopathy)).tw OR exp Acidosis/ci OR renal hypoperfusion.tw OR (worsening and renal).tw OR ((improved or recover$ or impair$) adj2 renal function).tw OR azot?emi$.mp OR (renal adj2 thrombosis).tw OR ((Reperfusion Injury/ OR (isch?emi$ adj (reperfusion or injury)).tw OR (critical$ adj (care or ill$ or patient$)).mp OR sepsis.mp OR septic.mp OR intensive care.mp OR icu.tw OR tubular cell$.tw OR rhabdomyolysis.mp OR thrombocytopeni$.tw OR life-threatening.mp OR vasculit$.mp OR polyarteritis.mp OR ((multi$ organ or multiorgan) adj (failure or dysfunction)).mp OR cardiogenic shock.tw OR Blood Urea Nitrogen/ OR polyangiitis.mp OR wegener$ granulomatosis.mp) AND (kidney.mp OR renal.mp OR dialysis.mp OR ur?emi$.tw OR dehydrat$.mp OR creatinin$.mp)) OR (nephropath$ AND ((contrast$ adj (medi$ OR induced OR agent$)) OR radiocontrast$ OR iodinated OR crystal$ OR cast)).mp. OR ((glomerulonephritis.mp OR nephrit$.tw) AND (acute.tw OR crescentic.mp OR anca$.tw OR rapidly progressive.tw)) OR ((Kidney Diseases/ OR (renal adj (insufficienc$ or failure or function or impairment)).mp OR ischemia-reperfusion injury.tw OR glomerular filtration rate.tw) AND (exp *Cardiovascular Surgical Procedures/ OR Cardiovascular Diseases/ OR exp *Cardiovascular System/ su OR cardiac surg$.mp OR cardiopulmonary.tw OR Ischemia/ OR exp *diagnostic imaging/ OR exp Neurologic Manifestations/ OR *Contrast Media/ OR preoperative$.tw OR pre-operative$.tw OR postoperative$.tw OR post-operative$. tw OR exp Substance-Related Disorders/ OR microangiopath$.tw OR cirrhosis.ti OR revers$.tw OR ci.fs)) OR ((injury.mp or isch?emi$.mp or reperfusion.mp or contrast medi$.mp) AND (renal tubul$.tw or tubular.tw)))	257042

2[c]	Emergency Treatment/ or Emergency Medicine/ or emergency medical services/ or emergency service, hospital/ or trauma centers/ or triage/ or exp Evidence-Based Emergency Medicine/ or exp Emergency Nursing/ or Emergencies/ or emergicent* or casualty department* or ((emergenc* or ED) adj1 (room* or accident or ward or wards or unit or units or department* or physician* or doctor* or nurs* or treatment*orvisit*)).mp. or (triage or critical care or (trauma adj1 (cent* or care))).mp	275615
3	(communit$ OR community OR community-acquired OR community acquired OR outpatien$ OR ambul$ OR ambul$ care OR primar$ care)	890577
4	1 and 2	7694
5	1 and 3	5924
6	4 or 5	13251
7	Limit 6 to English language	11465

[a] Results are up to date as of August 10, 2017 and excludes the citation related to this thesis.[47]

[b] Search filters for acute kidney injury are described by Hildebrand *et al*.[45]

[c] Search filters for emergency department studies are described by Campbell, S.[44]

Appendix B: Checklist of Recommendations for Reporting of Observational Studies Using the STrengthening the Reporting of OBservational Studies in Epidemiology (STROBE) Guidelines

Section	Item no.	Recommendation	Reported
Title and abstract	1a	Indicate the study's design with a commonly used term in the title or the abstract	i
	1b	Provide in the abstract an informative and balanced summary of what was done and what was found	ii
Introduction			
Background	2	Explain the scientific background and rationale for the investigation being reported	Chapters 1-2
Objectives	3	State specific objectives, including any prespecified hypotheses	Chapter 3
Methods			
Study design	4	Present key elements of study design early in the paper	Chapter 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Chapter 4
Participants	6	Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.	Chapter 4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Chapter 4
Data sources and measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Chapter 4
Bias	9	Describe any efforts to address potential sources of bias	Chapter 4
Study size	10	Explain how the study size was arrived at	Chapter 4
Quantitative Variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Chapter 4
Statistical methods	12a	Describe all statistical methods, including those used to control for confounding	Chapter 4
	12b	Describe any methods used to examine subgroups and interactions	Chapter 4
	12c	Explain how missing data were addressed	Chapter 4
	12d	If applicable, explain how loss to follow-up was addressed	Not applicable

	12e	Describe any sensitivity analyses	Not applicable
Results			
Participants	13a	Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Chapter 5
	13b	Give reasons for non-participation at each stage	Chapter 5
	13c	Consider use of a flow diagram	Chapter 5
Descriptive data	14a	Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	Chapter 5
	14b	Indicate number of participants with missing data for each variable of interest	Chapter 5
	14c	Summarise follow-up time (e.g., average and total amount)	Chapter 5
Outcome data	15	Report numbers of outcome events or summary measures over time	Chapter 5
Main results	16	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Chapter 5
		Report category boundaries when continuous variables were categorized	Chapter 5
		If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Chapter 5
Other analyses	17	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses	Chapter 5
Discussion			
Key results	18	Summarise key results with reference to study objectives	Chapter 6
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	Chapter 6
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Chapter 6
Generalizability	21	Discuss the generalizability (external validity) of the study results	Chapter 6
Other information			

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Acknowlege-ments

Appendix C: Coding Definitions for Co-Morbid Conditions

Variable	Database	Code set	Code
Abdominal aortic aneurysm repair	CIHI-DAD	CCP	5024, 5034
		CCI	1KA76
	OHIP	Fee code	R802, R816, R817, R783, R784, R785, R814
Atrial fibrillation or flutter	CIHI-DAD	ICD-9	4273
		ICD-10	I48
Major cancer[a]	CIHI-DAD	ICD-9	150, 154, 155, 157, 162, 174, 175, 185, 203, 204, 205, 206, 207, 208, 2303, 2304, 2307, 2330, 2312, 2334
		ICD-10	971, 980, 982, 984, 985, 986, 987, 988, 989, 990, 991, 993, C15, C18, C19, C20, C22, C25, C34, C50, C56, C61, C82, C83, C85, C91, C92, C93, C94, C95, D00, D010, D011, D012, D022, D075, D05
	OHIP	Diagnosis	203, 204, 205, 206, 207, 208, 150, 154, 155, 157, 162, 174, 175, 183, 185
Chronic liver disease	CIHI-DAD	ICD-9	4561, 4562, 070, 5722, 5723, 5724, 5728, 573, 7824, V026, 571, 2750, 2751, 7891, 7895
		ICD-10	B16, B17, B18, B19, I85, R17, R18, R160, R162, B942, Z225, E831, E830, K70, K713, K714, K715, K717, K721, K729, K73, K74, K753, K754, K758, K759, K76, K77
	OHIP	Diagnosis	571, 573, 070
		Fee code	Z551, Z554
Chronic obstructive pulmonary disease	CIHI-DAD	ICD-9	491, 492, 496
		ICD-10	J41, J43, J44
Coronary artery disease (excluding angina)	CIHI-DAD	CCP	4801, 4802, 4803, 4804, 4805, 481, 482, 483
		CCI	1IJ50, 1IJ76
		ICD-9	412, 410, 411
		ICD-10	I21, I22, Z955, T822
	OHIP	Diagnosis	410, 412
		Fee code	R741, R742, R743, G298, E646, E651, E652, E654, E655, Z434, Z448
Dementia	CIHI-DAD	ICD-9	2900, 2901, 2903, 2904, 2908, 2909, 2948, 2949, 3310, 3311, 3312, 2941, 797
		ICD-10	F065, F066, F068, F069, F09, F00, F01, F02, F03, F051, G30, G31, R54

	OHIP	Diagnosis	290, 331, 797
Diabetes[b]	CIHI-DAD	ICD-9	250
		ICD-10	E10, E11, E13, E14
	OHIP	Diagnosis	250
		Fee code	Q040, K029, K030, K045, K046
Heart failure	CIHI-DAD	ICD-9	425, 5184, 428, 514
		ICD-10	I500, I501, I509, I255, J81
		CCP	4961, 4962, 4963, 4964
		CCI	1HP53, 1HP55, 1HZ53GRFR, 1HZ53LAFR, 1HZ53SYFR
	OHIP	Diagnosis	428
		Fee code	R701, R702, Z429
Hypertension[b]	CIHI-DAD	ICD-9	401, 402, 403, 404, 405
		ICD-10	I10, I11, I12, I13, I15
	OHIP	Diagnosis	401, 402, 403
Nephrolithiasis	CIHI-DAD	ICD-9	5920, 5921, 5929, 5940, 5941, 5942, 5948, 5949, 27411
		ICD-10	N200, N201, N202, N209, N210, N211, N218, N219, N220, N228
Osteoarthritis	CIHI-DAD	ICD-9	715
		ICD-10	M15, M16, M17, M18, M19, M47
Parkinson's disease	CIHI-DAD	ICD-9	332
		ICD-10	G20, F023
Peripheral vascular disease	CIHI-DAD	ICD-9	4402, 4408, 4409, 5571, 4439, 444
		ICD-10	I700, I702, I708, I709, I731, I738, I739, K551
		CCP	5125, 5129, 5014, 5016, 5018, 5028, 5038, 5126, 5159
		CCI	1KA76, 1KA50, 1KE76, 1KG50, 1KG57, 1KG76MI, 1KG87, 1IA87LA, 1IB87LA, 1IC87LA, 1ID87LA, 1KA87LA, 1KE57
	OHIP	Fee code	R787, R780, R797, R804, R809, R875, R815, R936, R783, R784, R785, E626, R814, R786, R937, R860, R861, R855, R856, R933, R934, R791, E672, R794, R813, R867, E649
Rheumatoid arthritis	CIHI-DAD	ICD-9	714
		ICD-10	M05, M06
	OHIP	Diagnosis	714

Cerebrovascular disease[c]	CIHI-DAD	ICD-9 ICD-10	430, 431, 432, 4340, 4341, 4349, 435, 436, 3623 I62, I630, I631, I632, I633, I634, I635, I638, I639, I64, H341, I600, I601, I602, I603, I604, I605, I606, I607, I609, I61, G450, G451, G452, G453, G458, G459, H340

Abbreviations: CCI, Canadian Classification of Health Interventions; CCP, Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures; CIHI-DAD, Canadian Institute for Health Information Discharge Abstract Database; ICD-9, International Classification of Diseases, Ninth Revision; ICD-10, International Classification of Diseases, Tenth Revision; OHIP, Ontario Health Insurance Plan.

[a] List of major cancers include lung/bronchi, colon/rectum, breast, pancreas, prostate, leukemia, non-Hodgkin lymphoma, liver, ovarian, and esophageal cancers.

[b] Oral hypoglycemic medications and insulin were not considered as not all patients have medication information available.

[c] Cerebrovascular disease: stroke or transient ischemic attack.

Appendix D: Diagnostic Codes for Health Care Utilization Characteristics

Variable	Database	Code set	Code
Family physician visit	OHIP	Fee code	A001, A003, A004, A005, A006, A007, A008, A900, A901, A905, A911, A912, A967, K131, K132, K140, K141, K142, K143, K144, W003, W008, W121
	IPDB	Main specialty	GP/FP
Internal medicine physician visit	OHIP	Fee code	A135, C135
	IPDB	Main specialty	INTERNAL MEDICINE
Nephrologist visit	OHIP	Fee code	A135, A161, A163, A164, A165, A166, A168, C101, C138, G860, G323, G333, E083, C132, C135, C137, C139, H540, G325, G326, G860, G865, G866, G330, G331, G332, G861, G864
	IPDB	Main specialty	NEPHROLOGY
Urologist visit	OHIP	Fee code	A355, A356, A353, A354, C355, C356, C353, C354 Z606, Z628, Z632, Z633, Z634, S655, S654
	IPDB	Main specialty	UROLOGY
Coronary angiogram or revascularization	CIHI-DAD	CCP	4892, 4893, 4894, 4895, 4896, 4897, 4898, 481, 482, 483, 480
		CCI	3IP10, 3IS10, 1IJ50, 1IJ26, 1IJ27, 1IJ57, 1IJ76, 1IJ57GQ, 1IJ54GQAZ
	OHIP	Fee code	G297, G509, R741, R742, R743, E651, E652, E654, E646, G298, Z434, G262
CT scan with contrast	CIHI-DAD	CCI	3AF20WC, 3AN20WC, 3CA20WC, 3DR20WC, 3EA20WC, 3EL20WC, 3ER20WC, 3EY20WC, 3FX20WC, 3FY20WC, 3GE20WC, 3GT20WC, 3GY20WC, 3ID20WC, 3IP20WC, 3JE20WC, 3JX20WC, 3JY20WC, 3KE20WC, 3KG20WC, 3KT20WC, 3NM20WC, 3OT20WC, 3PC20WC, 3PZ20WC, 3QT20WC, 3SC20WC, 3SF20WC, 3TZ20WC, 3VZ20WC, 3WZ20WC, 3YM20WC, 3ZZ20WC, 3FY20VZ, 3FY20VC
Echocardiogram	CIHI-DAD	CCP	0282
		CCI	3IP30

	OHIP	Fee code[a]	G560, G561, G562, G566, G567, G568, G570, G571, G572, G574, G575, G576, G577, G578, G581
Cardiac stress test	CIHI-DAD	CCP	0341, 0342, 0343, 0344, 0605
		CCI	2HZ08, 3IP70
	OHIP	Fee code	G315, G174, G111, G112, G319, G582, G583, G584, J607, J608, J807, J808, J809, J866, J609, J666
Abdominal ultrasound[b]	OHIP	Fee code	J128, J135, J428, J435
Kidney stone interventions[c]	OHIP	Fee code	Z630, Z628, E760, E761, Z624, Z627

CCI, Canadian Classification of Health Interventions; CCP, Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures; CIHI-DAD, Canadian Institute for Health Information Discharge Abstract Database; CT, computed tomography; OHIP, Ontario Health Insurance Plan.

[a] G560, G561, G562, G566, G567, G568, G576 are no longer in fee schedule as of 2014/11.

[b] An abdominal ultrasound is not specific to the kidneys.

[c] Urological procedures included extracorporeal shockwave lithotripsy, percutaneous nephrolithotomy, or ureteroscopic lithotripsy with stone removal.

Appendix E: Diagnostic Codes for Exclusion Criteria

Variable	Database	Code set	Code
Dialysis	CIHI-DAD	ICD-9	V451, V560, V568, 99673
		ICD-10	T824, Y602, Y612, Y622, Y841, Z49, Z992
		CCP	5127, 5142, 5143, 5195, 6698
		CCI	1PZ21, 1OT53DATS, 1OT53HATS, 1OT53LATS, 1SY55LAFT, 7SC59QD, 1KY76, 1KG76MZXXA, 1KG76MZXXN, 1JM76NC, 1JM76NCXXN
	OHIP	Fee code	R850, G324, G336, G327, G862, G865, G099, R825, R826, R827, R833, R840, R841, R843, R848, R851, R946, R943, R944, R945, R941, R942, Z450, Z451, Z452, G864, R852, R853, R854, R885, G333, H540, H740, R849, G323, G325, G326, G860, G863, G866, G330, G331, G332, G861, G082, G083, G085, G090, G091, G092, G093, G094, G095, G096, G294, G295
Kidney transplant	CIHI-DAD	CCI	1PC85
	OHIP	Fee code	S435, S434
Palliative care	CIHI-DAD	PATSERV	58
	OHIP	Fee code	C945, C882, C982, W872, W972, B966, B998, B997, G511, W882, W982, K023 (inpatient or LTC use only)
AKI	CIHI-DAD/ NACRS	ICD-10	N17

Abbreviations: AKI; acute kidney injury; CCI, Canadian Classification of Health Interventions; CCP, Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures; CIHI-DAD, Canadian Institute for Health Information Discharge Abstract Database; ICD-9, International Classification of Diseases, Ninth Revision; ICD-10, International Classification of Diseases, Tenth Revision; NACRS, National Ambulatory Care Reporting System; OHIP, Ontario Health Insurance Plan; PATSERV, patient service.

Appendix F: Diagnostic Codes for Outcome Variables

Variable	Database	Code set	Code
Mortality	RPDB	Vital status	Vital status field
Receipt of hospital-based acute dialysis	OHIP	Fee code	R849, G323, G866, G330, G331, G093, G095, G294, G2955 associated with hospital admission
Health care cost	ADP, CAPE, CCRS, CIHI-DAD/NACRS, HCD, NRS, ODB, OHIP, OMHRS		ICES costing macro[62]
Outpatient physician visit by any one of:	OHIP	Fee code	GP/FP: A001, A003, A004, A005, A006, A007, A008, A900, A901, A905, A911, A912, A967, K131, K132, K140, K141, K142, K143, K144, W003, W008, W121
Family physician			
General internist			Internal Medicine: A135, C135
Nephrologist			Nephrology: A135, A161, A163, A164, A165, A166, A168, C101, C138, G860, G323, G333, E083, C132, C135, C137, C139, H540, G325, G326, G860, G865, G866, G330, G331, G332, G861, G864
Urologist			Urology: A355, A356, A353, A354, C355, C356, C353, C354 Z606, Z628, Z632, Z633, Z634, S655, S654
	IPDB	Main specialty	GP/FP, INTERNAL MEDICINE, NEPHROLOGY, UROLOGY
SCr measurement	Dynacare		067A
	Cerner		Test done=”A”
	OHIP	Fee code	L067
Urine protein measurement (dipstick, ACR, or PCR)	Dynacare		05DR, 05DU, P/CR, P/CM, 208Y, 208Z, 253
	OHIP	Fee code	L253, L254, L255, L633, L634, L641, G009, G010

Abbreviations: ACR, albumin-to-creatinine ratio; ADP, Assistive Devices Program; CAPE, Client Agency Program Enrolment; CCRS, Continuing Care Reporting System; CIHI-DAD, Canadian Institute for Health Information Discharge Abstract Database; GP/FP, general practitioner/family physician; HCD, Home Care Database; ICES, Institute for Clinical Evaluative Sciences; IPDB, ICES Physician Database; NACRS, National Ambulatory Care Reporting System; NRS, National Rehabilitation Reporting System; ODB,

Ontario Drug Benefit; OHIP, Ontario Health Insurance Plan; OMHRS, Ontario Mental Health Reporting System; PCR, protein-to-creatinine ratio; RPDB, Ontario's Registered Persons Database; SCr, serum creatinine.

Appendix G: Characteristics Used to Derive Propensity Scores for the AKI Subpopulation and Discharged Subpopulation

Category	Variable	Number of variables[a]
Demographics	Age, sex, income quintile, year of cohort entry, rural location, long-term care status, Pharmacy forward sortation area	7
Co-morbid conditions	Abdominal aortic aneurysm repair, atrial fibrillation/flutter, cerebrovascular disease, chronic liver disease, chronic obstructive pulmonary disease, coronary artery disease, dementia, diabetes, heart failure, hypertension, major cancer, nephrolithiasis, osteoarthritis, Parkinson's disease, peripheral vascular disease, rheumatoid arthritis,	16
Co-morbidity indices	Charlson co-morbidity index, Aggregated Diagnosis Group point score	2
Laboratory characteristics	Pre-ED visit baseline SCr[b], number of days pre-ED visit baseline SCr was measured[b], pre-ED visit baseline SCr ≤50 μmol/L, SCr value at ED visit[b], urine ACR, serum potassium[b], serum sodium[b], AKI stage, eGFR category	9
Health care utilization	Prior hospitalizations, prior ED visits, family physician visit, general internist visit, nephrologist visit, urologist visit, coronary angiogram or revascularization, CT scan with contrast, echocardiogram, cardiac stress test, abdominal ultrasound, intervention for kidney stones	12
Medication characteristics and classes[d]	ODB program eligibility, number of unique drug identification numbers, number of unique drug names Angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker, alpha-1-adrenoceptor antagonist or 5-alpha-reductase inhibitor, antibacterial, anticoagulant, antidepressant (SSRI or SNRI), antineoplastic, antiplatelet, antipsychotic medication, beta-adrenergic antagonist, calcium channel blocker, corticosteroid, xanthine oxidase inhibitor or uricosuric agent, anti-retroviral medication, immunosuppressive medication, lithium, non-potassium sparing diuretic, non-steroidal anti-inflammatory drug, oral hypoglycemic agent or insulin, potassium-sparing diuretic, , proton pump inhibitor, statin	24

ED and hospital characteristics	Institution (1-13)[c], ED registrations in last 12 hours[b], hospital admissions in last 24 hours[b], hospital discharges in last 24 hours[b], proportion of ED registrations admitted to hospital, ED length of stay[b], time waiting for physician assessment[b], Canadian Triage Acuity Scale, time of day, season of the year, ED physician specialty training.	23
	Total	**93**

Abbreviations: ACR, albumin-to-creatinine ratio; AKI, acute kidney injury; CT, computed tomography; ED, emergency department; eGFR, estimated glomerular filtration rate; ODB, Ontario Drug Benefit; SCr, serum creatinine; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitor.

[a] We considered 93 variables to derive propensity scores for the AKI and discharged subpopulations. In the AKI subpopulation (comparing patients discharged home from the ED with AKI versus patients admitted to hospital with AKI), 92 variables were used to derive the propensity score. The ED length of stay variable was not included because admitted patients may remain in the ED until an inpatient bed is available, inflating the ED length of stay (defined as time of registration to time patient physically left the ED). In the discharged subpopulation (comparing patients discharged home from the ED with AKI versus patients discharged home from the ED with no AKI), 91 variables were used to derive the propensity score. ED visit SCr and AKI stage were not included in the model.

[b] Continuous variables used to derive propensity scores for both the AKI and discharged subpopulation.

[c] Each hospital institution (13 total) was included to derive propensity scores for both the AKI and discharged subpopulation. For privacy considerations, individual hospital institutions were not identified.

Appendix H: Most Common Main Diagnoses Assigned by Physicians to a Cohort of 6346 Patients Discharged Home from the Emergency Department with Acute Kidney Injury

No.	ICD-10	Description	*n* (%)
1	R07	Pain in throat and chest	515 (8.1%)
2	R10	Abdominal and pelvic pain	447 (7.0%)
3	N23	Unspecified renal colic	309 (4.9%)
4	N39	Other disorders of urinary system	248 (3.9%)
5	R55	Syncope and collapse	219 (3.5%)
6	J18	Pneumonia, organism unspecified	175 (2.8%)
7	R53	Malaise and fatigue	159 (2.5%)
8	K52	Other noninfective gastroenteritis and colitis	150 (2.4%)
9	E86	Volume depletion	128 (2.0%)
10	I48	Atrial fibrillation and flutter	123 (1.9%)
11	R06	Abnormalities of breathing	116 (1.8%)
12	R42	Dizziness and giddiness	116 (1.8%)
13	N20	Calculus of kidney and ureter	111 (1.7%)
14	I50	Heart failure	110 (1.7%)
15	R11	Nausea and vomiting	98 (1.5%)
16	I20	Angina pectoris	89 (1.4%)
17	L03	Cellulitis	88 (1.4%)
18	A09	Diarrhoea and gastroenteritis of presumed infectious origin	77 (1.2%)
19	J44	Other chronic obstructive pulmonary disease	77 (1.2%)
20	R00	Abnormalities of heart beat	76 (1.2%)

Abbreviation: ICD, International Classification of Diseases.

Appendix I: Copyright Permission

From: **Shari Leventhal** [redacted]
Subject: re: Permission to include published manuscript in Master's Thesis
Date: October 5, 2017 at 1:21 PM
To: [redacted]

SL

Dear Dr. Acedillo,

This email confirms approval for you to re-print the CJASN material as you outlined below. Please include a notation indicating prior publication in CJASN with the relevant citations. No further permissions or fees are needed. Thank you!

Sincerely yours,

Shari Leventhal
Managing Editor, CJASN

From: Rey Acedillo [redacted]
Sent: Sunday, October 1, 2017 12:10 PM
To: Shari Leventhal [redacted]
Subject: Permission to include published manuscript in Master's Thesis

Hello there,

I recently had the following article published in CJASN:

Acedillo RR, Wald R, McArthur E, Nash DM, Silver SA, James MT, Schull MJ, Siew ED, Matheny ME, House AA, Garg AX.
Characteristics and Outcomes of Patients Discharged Home from an Emergency Department with AKI.
Clin J Am Soc Nephrol. 2017 Jul 20. pii: CJN.10431016. doi: 10.2215/CJN.10431016. [Epub ahead of print] PubMed PMID: 28729384; PubMed Central PMCID: PMC5544515.

This is the content of my Master's thesis and I would like permission to include a version of this manuscript as a chapter in my thesis. How do I go about obtaining a letter of permission from the publisher?

Thanks,

Rey

Rey Acedillo, MD FRCPC
Nephrologist, Research Fellow
MSc Candidate, Clinical Epidemiology & Biostatistics
Western University
London, Ontario, Canada

Curriculum Vitae

REY ACEDILLO

EDUCATION

Degrees

2013.09 – Present	Master of Science, Clinical Epidemiology and Biostatistics, Western University, London, ON, Canada. Supervisor: Dr. Amit Garg.
2005.08 – 2009.05	Doctor of Medicine, University of British Columbia, Vancouver, BC, Canada.
1999.09 – 2004.05	Bachelor of Science, Microbiology and Immunology (in conjunction with the Cooperative Education Program), University of British Columbia, Vancouver, BC, Canada.

Postgraduate, Research, and Specialty Training

2014.07 – 2017.06	Research Fellow, Acute Kidney Injury, Clinical Investigator Program (2014-2016), Western University, London, ON, Canada. Supervisor: Dr. Amit Garg.
2012.07 – 2014.06	Nephrologist Resident, London Health Sciences Centre and Western University, London, ON, Canada. Program Director: Dr. Nabil Sultan.
2009.07 – 2012.06	Internal Medicine Resident, London Health Sciences Centre and Western University, London, ON, Canada. Program Directors: Drs. Sheri-Lynn Kane and Claude Kortas.

Qualifications, Certifications, and Licenses

2014.09 – Present	Fellow of the Royal College of Physicians and Surgeons, Nephrology, Royal College of Physicians and Surgeons of Canada. RCPSC ID: 2023453.
2013.06 – Present	Fellow of the Royal College of Physicians and Surgeons, Internal Medicine, Royal College of Physicians and Surgeons of Canada. RCPSC ID: 2023453.
2013.06 – Present	Nephrologist, College of Physicians and Surgeons of Ontario. CPSO ID: 91232.

EMPLOYMENT

Current Appointment

2018.01 – Present	Nephrologist, Department of Medicine, Thunder Bay Regional Health Sciences Centre, Thunder Bay, ON, Canada.

Previous Appointments

Clinical

2017.02 – 2017.08	Nephrologist (Locum), Division of Nephrology, Department of Medicine, Kingston Health Sciences Centre, Kingston, ON, Canada.
2014.07 – 2017.01	Nephrologist (Locum), Division of Nephrology, Department of Medicine, London Health Sciences Centre, Victoria Campus, London, ON, Canada.
2013.06 – 2017.01	Internist, Clinical Teaching Unit, Department of Medicine, London Health Sciences Centre, University Campus, London, ON, Canada.

University

2013.06 – 2017.06	Adjunct Professor, Western University, London, ON, Canada.
2017.07 – 2018.06	Assistant Professor, Queen's University, Kingston, ON, Canada.

PROFESSIONAL AFFILIATIONS AND ACTIVITIES

Peer Review Activities

2017.08 – Present	Reviewer, Nephrology, Dialysis, and Transplantation, Oxford University Press, Oxford, UK.
2017.03 – Present	Reviewer, Clinical Journal of the American Society of Nephrology, American Society of Nephrology, Washington, DC, USA.
2016.07 – Present	Reviewer, Nephron, Karger Publishers, Basel, Switzerland.

FUNDING AND AWARDS

Peer-Reviewed Grants

2016.07 – 2018.06	Co-applicant. Clinical Health Informatics Program. Academic Medical Organization of Southwestern Ontario Grant, Principal Investigator: Dr. Blayne Welk, $133,000 CAD.

Trainee Salary Support

2014.07 – 2016.06	Clinical Investigator Program, Western University, London, ON, Canada. Amount: $150,000 CAD.

Awards

2013.09 – 2015.12 Schulich Graduate Scholarship, Department of Epidemiology and Biostatistics, Western University, London, ON. Canada. Amount: $1,500 CAD per semester.

PUBLICATIONS

Peer-Reviewed Publications

1. Silver SA, Harel Z, McArthur E, Nash DM, **Acedillo R**, Kitchlu A, Garg AX, Chertow GM, Bell CM, Wald R. Causes of Death after a Hospitalization with AKI. *J Am Soc Nephrol.* 2018 Mar;29(3):1001-1010. doi: 10.1681/ASN.2017080882.
2. McTavish RK, Richard L, McArthur E, Shariff SZ, **Acedillo R**, Parikh CR, Wald R, Wilk P, Garg AX. Association Between High Environmental Heat and Risk of Acute Kidney Injury Among Older Adults in a Northern Climate: A Matched Case-Control Study. *Am J Kidney Dis.* 2018 Feb;71(2):200-208. doi: 10.1053/j.ajkd.2017.07.011.
3. **Acedillo RR,** Wald R, McArthur E, Nash DM, Silver SA, James MT, Schull MJ, Siew ED, Matheny ME, House AA, Garg AX. Characteristics and outcomes of patients discharged home from an emergency department with acute kidney injury. *CJASN*. 2017 Jul 20. pii: CJN.10431016. doi: 10.2215/CJN.10431016.
4. Presseau J, Mutsaers B, Al-Jaishi AA, Squires J, McIntyre CW, Garg AX, Sood MM, Grimshaw JM; Major outcomes with personalized dialysate TEMPerature (MyTEMP) investigators (**Acedillo, RR a MyTEMP co-investigator)**. Barriers and facilitators to healthcare professional behaviour change in clinical trials using the Theoretical Domains Framework: a case study of a trial of individualized temperature-reduced haemodialysis. *Trials.* 2017 May 22;18(1):227. doi: 10.1186/s13063-017-1965-9.
5. Roshanov PS, Walsh M, Devereaux PJ, MacNeil SD, Lam NN, Hildebrand AM, **Acedillo RR**, Mrkobrada M, Chow CK, Lee VW, Thabane L, Garg AX. External validation of the Revised Cardiac Risk Index and update of its renal variable to predict 30-day risk of major cardiac complications after non-cardiac surgery: rationale and plan for analyses of the VISION study. *BMJ Open.* 2017 Jan 9;7(1):e013510. doi: 10.1136/bmjopen-2016-013510.
6. 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.* 2016 Oct 14. pii: S0002-9343(16)31023-3. doi: 10.1016/j.amjmed.2016.09.016.
7. Habbous S, Przech S, **Acedillo R**, Sarma S, Garg AX, Martin J. The efficacy and safety of sevelamer and lanthanum versus calcium-containing and iron-based binders in treating hyperphosphatemia in patients with chronic kidney disease: a systematic review and meta-analysis. *Nephrol Dial Transplant.* 2016 Sep 20. pii: gfw312.
8. **Acedillo RR**, Govind M, Kashgary A, Clark WF. Treatment of severe, refractory and rapidly evolving thrombotic thrombocytopenic purpura. *BMJ Case Rep*. 2016. pii: bcr2016215491. doi: 10.1136/bcr-2016-215491.
9. Silver SA, Harel Z, Harvey A, Adhikari NK, Slack A, **Acedillo R,** Jain AK, Richardson R, Chan CT, Chertow GM, Bell CM, Wald R. Improving Care after Acute Kidney Injury: A Prospective Time Series Study. *Nephron*. 2015;131(1):43-50

10. Silver SA, Goldstein SL, Harel Z, Harvey A, Rompies EJ, Adhikari NK, **Acedillo R,** Jain AK, Richardson R, Chan CT, Chertow GM, Bell CM, Wald R. Ambulatory care after acute kidney injury: an opportunity to improve patient outcomes. *Can J kidney Heal Dis*. 2015;2:36.
11. **Acedillo RR**, Garg AX, James MT. ACP Journal Club. In hospitalized patients, an electronic alert for acute kidney injury did not differ from usual care. *Ann Intern Med*. 2015;162(12):JC6.
12. Garg AX, Kurz A, Sessler DI, et al (**Acedilllo RR** a co-author). Perioperative aspirin and clonidine and risk of acute kidney injury. *JAMA*. 2014;312(21):2254.
13. Garg AX, Kurz A, Sessler DI, et al (**Acedilllo RR** a co-author). Aspirin and clonidine in non-cardiac surgery: acute kidney injury substudy protocol of the Perioperative Ischaemic Evaluation (POISE) 2 randomised controlled trial. *BMJ Open*. 2014;4(2):e004886.
14. Botto F, Alonso-Coello P, Chan MT V, et al (**Acedilllo RR** an investigator). Myocardial injury after noncardiac surgery: a large, international, prospective cohort study establishing diagnostic criteria, characteristics, predictors, and 30-day outcomes. *Anesthesiology*. 2014;120(3):564-578.
15. **Acedillo RR**, Tangri N, Garg AX. The kidney failure risk equation: on the road to being clinically useful? *Nephrol Dial Transplant.* 2013;28(7):1623-1624.
16. **Acedillo RR**, Shah M, Devereaux PJ, Li L, Iansavichus A, Walsh M, Garg A. The risk of perioperative bleeding in patients with chronic kidney disease: a systematic review and meta-analysis. *Ann Surg*. 2013;258(6):901-913.
17. Hasan K, Lazo-Langner A, **Acedillo R**, Zeller M, Hackam DG. Anticoagulant response after dalteparin overdose. *J Thromb Haemost*. 2010;8(10):2321-2323.
18. Taboada EN, van Belkum A, Yuki N, **Acedillo RR**, Godschalk PC, Koga M, Endtz HP, Gilbert M, Nash JHE. Comparative genomic analysis of Campylobacter jejuni associated with Guillain-Barré and Miller Fisher syndromes: neuropathogenic and enteritis-associated isolates can share high levels of genomic similarity. *BMC Genomics*. 2007;8:359.
19. Taboada EN, **Acedillo RR**, Luebbert CC, Findlay WA, Nash JHE. A new approach for the analysis of bacterial microarray-based Comparative Genomic Hybridization: insights from an empirical study. *BMC Genomics*. 2005;6:78.
20. Taboada EN, **Acedillo RR**, Carrillo CD, et al. Large-scale comparative genomics meta-analysis of Campylobacter jejuni isolates reveals low level of genome plasticity. *J Clin Microbiol*. 2004;42(10):4566-4576.

Books

1. Thomson B, Acedillo R. Critical References Nephrology: Expert Commentary of the Most Important Clinical Nephrology Studies. 2013.

ABSTRACTS AND PRESENTATIONS

1. Oral Presentation. Institute for Clinical Evaluative Sciences (ICES) 25th Anniversary Research Symposium (October 2017), Toronto, ON: Characteristics and Outcomes of Adults Discharged Home from the Emergency Department with Acute Kidney Injury

2. Poster Presentation. American Society of Nephrology Kidney Week, November 2016, Chicago, IL: Characteristics and Outcomes of Adults Discharged Home from the Emergency Department with Acute Kidney Injury.
3. Poster Presentation. Canadian Society of Nephrology Kidney Week, May 2016, Montreal, QC: Characteristics and Outcomes of Adults Discharged Home from the Emergency Department with Acute Kidney Injury.
4. Poster Presentation. London Health Research Day, March 2016, London, ON: Characteristics and Outcomes of Adults Discharged Home from the Emergency Department with Acute Kidney Injury.
5. Oral Presentation. London Kidney Clinical Research Unit Renal Research Day (August 2015), London, ON: Characteristics and Outcomes of Adults Discharged Home from the Emergency Department with Acute Kidney Injury.
6. Poster Presentation. Department of Medicine Resident's Research Day (May 2011), London, ON: The risk of perioperative bleeding in patients with chronic kidney disease: a systematic review and meta-analysis.
7. Oral Presentation. London Kidney Clinical Research Unit Renal Research Day (August 2010), London, ON: The risk of perioperative bleeding in patients with chronic kidney disease: a systematic review and meta-analysis.
8. Poster Presentation. Department of Medicine Resident's Research Day (May 2010), London, ON: Anticoagulant response after dalteparin overdose.

TEACHING AND EDUCATIONAL ACTIVITIES

Lectures

2017.02 – 2017.07	Lecturer, Academic Half-Day Teaching for Nephrology Residents, Queen's University, Kingston, ON.
2014.10	Lecturer, Academic Half-Day Teaching for First-Year Residents, Western University, London, ON.

Supervision

2017.02 – 2017.07	Examiner, Observed Standardized Clinical Examination (OSCE), Queen's University, Kingston, ON.
2016.09 – 2017.06	Mentor, Professional Identify Course, Quality Improvement Group Project for Second Year Medical Students, Western University, London, ON.
2015.05 – 2017.01	Facilitator, Procedure Courses for Internal Medicine Residents, Western University, London, ON.
2015.04 – 2016.05	Facilitator, Medical Student Small Group Teaching, Western University, London, ON
2015.01 – 2017.01	Examiner, Observed Standardized Clinical Examination, Western University, London, ON.
2014.05 – 2016.06	Teaching Assistant, First-Year Medicine: Nephology, Western University, London, ON.