



# Clinical Outcomes and Healthcare Utilization in Patients Receiving Maintenance Dialysis After the Onset of the COVID-19 Pandemic in Ontario, Canada

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## Abstract

**Background:** The impact of the COVID-19 pandemic on clinical outcomes and healthcare utilization in patients receiving maintenance dialysis is unclear.

**Objective:** To compare the rates of clinical outcomes and healthcare utilization in patients receiving maintenance dialysis (in-center and home modalities) before and during the COVID-19 pandemic.

**Design:** Population-based, repeated cross-sectional study.

**Setting:** Linked administrative healthcare databases from Ontario, Canada.

**Patients:** Adults receiving maintenance dialysis from March 15, 2017, to March 14, 2020 (pre-COVID-19 pandemic period) and from March 15, 2020, to March 14, 2023 (COVID-19 pandemic period).

**Measurements:** Our primary outcome was all-cause mortality. Our secondary outcomes included non-COVID-19-related mortality, all-cause hospitalizations (excluding elective surgeries), emergency room visits, intensive care unit admissions, and hospital admissions with mechanical ventilation. We also examined cardiovascular-related hospitalizations, kidney-related outcomes, and ambulatory visits.

**Methods:** We used Poisson generalized estimating equations to model pre-COVID outcome trends and used these to predict post-COVID outcomes and to estimate the relative change (i.e., the ratio of the observed to the expected rate).

**Results:** In 31 900 individuals receiving maintenance dialysis during the study period, the crude incidence rate (per 1000 person-years) of all-cause mortality was 165.0 in the pre-COVID-19 period, compared to 173.2 during the first year of the pandemic and 171.7 during the first 36 months of the pandemic. After adjustment, there was a statistically significant increase in all-cause mortality in 14 out of the 36 months of the COVID-19 period compared to the pre-COVID-19 period, with 494 recorded COVID-19-related deaths. However, when examining the overall all-cause mortality across the months, the adjusted relative rate (aRR) comparing the observed to expected all-cause mortality rate was not statistically significant in the first year of the pandemic (1.08, 95% CI: 1.00, 1.16) and the first 36 months of the pandemic (1.08, 95% CI: 0.99, 1.18) compared to the pre-pandemic period. The crude incidence rate of non-COVID-19-related mortality was 165.0 in the pre-COVID-19 period, compared to 163.3 during the first year of the pandemic and 157.7 during the first 36 months. After adjustment, there was no substantial change in the rate of non-COVID-19-related deaths in the first year of the pandemic (aRR 1.01, 95% CI: 0.94, 1.09), but there was a substantial decrease in all-cause hospitalization, with an aRR of 0.92 (95% CI: 0.88, 0.97), and a substantial decrease in emergency room visits and intensive care unit admissions; findings were consistent 36 months into the pandemic.

**Limitations:** External generalizability to other jurisdictions may be limited, with each region experiencing different COVID-19 rates and implementing different mitigation strategies.



**Conclusions:** In the maintenance dialysis population, all-cause mortality was significantly higher during several months of the pandemic; however, the overall rate of all-cause mortality was not substantially higher than expected in the first 36 months of the COVID-19 pandemic. There was no substantial increase in non-COVID-19-related mortality despite a substantial decrease in acute healthcare utilization. Ongoing monitoring of the dialysis population will offer further insights into the long-term effects of the pandemic.

## Abrégé

**Contexte:** On connaît mal les conséquences de la pandémie de COVID-19 sur les résultats cliniques des patients recevant une dialyse d'entretien et sur leur utilisation des soins de santé.

**Objectif:** Comparer les taux d'utilisation des soins de santé et les résultats cliniques des patients recevant une dialyse d'entretien (en centre et à domicile) avant et pendant la pandémie de COVID-19.

**Type d'étude:** Étude populationnelle transversale répétée.

**Cadre:** Les bases de données couplées du système de santé de l'Ontario (Canada).

**Sujets:** Les adultes recevant une dialyse d'entretien entre le 15 mars 2017 et le 14 mars 2020 (période pré-pandémie de COVID-19) ainsi que du 15 mars 2020 au 14 mars 2023 (période pandémique).

**Mesures:** Notre principal critère de jugement était la mortalité toutes causes confondues. Nos critères de jugement secondaires comprenaient les décès non liés à la COVID-19, les hospitalisations toutes causes confondues (à l'exclusion des chirurgies électives), les visites aux urgences, les admissions aux soins intensifs et les admissions à l'hôpital avec ventilation mécanique. Nous avons aussi examiné les hospitalisations liées aux maladies cardiovasculaires, les résultats liés à la fonction rénale et les visites ambulatoires.

**Méthodologie:** Nous avons utilisé des équations d'estimation généralisées de Poisson pour modéliser les tendances dans les résultats pré-COVID et nous avons utilisé celles-ci pour prédire les résultats post-COVID et estimer la variation relative (c.-à-d., le ratio entre le taux observé et le taux attendu).

**Résultats:** Chez les 31 900 personnes qui recevaient une dialyse d'entretien au cours de la période étudiée, le taux d'incidence brut (pour 1 000 personnes-années) de mortalité toutes causes confondues était de 165,0 au cours de la période pré-COVID-19, comparativement à 173,2 dans la première année de la pandémie et à 171,7 pendant les 36 premiers mois de la pandémie. Après correction, on a observé une augmentation statistiquement significative de la mortalité toutes causes confondues pour 14 des 36 mois de la pandémie par rapport à la période pré-COVID-19, avec 494 décès enregistrés en lien avec la COVID-19. Cependant, lors de l'examen de la mortalité globale toutes causes confondues au fil des mois, le risque relatif corrigé (RRc) comparant les taux observé et attendu de mortalité toutes causes confondues n'était pas statistiquement significatif au cours de la première année de la pandémie (RRc: 1,08; IC à 95 %: 1,00-1,16) et des 36 premiers mois de la pandémie (RRc: 1,08; IC à 95 %: 0,99-1,18) par rapport à la période pré-pandémie. Le taux d'incidence brut de mortalité non liée à la COVID-19 était de 165,0 dans la période pré-COVID-19, contre 163,3 au cours de la première année de la pandémie et 157,7 au cours des 36 premiers mois. Après correction, aucun changement important n'a été observé dans le taux de décès non liés à la COVID-19 dans la première année de la pandémie (RRc: 1,01; IC à 95 %: 0,94-1,09), mais une

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diminution substantielle a été observée dans les hospitalisations toutes causes confondues, avec un taux de 0,92 (IC à 95 %: 0,88-0,97), ainsi que dans les visites aux urgences et les admissions aux soins intensifs; ces résultats étaient constants 36 mois après le début de la pandémie.

**Limites:** La généralisabilité externe à d'autres provinces est limitée, chaque région ayant connu des taux de COVID-19 différents et ayant mis en œuvre des stratégies d'atténuation différentes.

**Conclusion:** Dans la population sous dialyse d'entretien, la mortalité toutes causes confondues était significativement plus élevée pendant plusieurs mois au cours de la pandémie. Cependant, le taux global de mortalité toutes causes confondues n'a pas été plus élevé que prévu au cours des 36 premiers mois de la pandémie de COVID-19. La mortalité non liée à la COVID-19 n'a pas augmenté de façon substantielle, malgré une importante diminution de l'utilisation des soins de santé aigus. La surveillance continue de cette population permettra de mieux comprendre les effets à long terme de la pandémie.

## Keywords

COVID-19, pandemic, maintenance dialysis, clinical outcomes, healthcare utilization

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## Introduction

Individuals receiving maintenance dialysis often have multiple comorbidities (e.g., diabetes, cardiovascular disease), and the majority are older than 65 years.<sup>1,2-4</sup> Mortality is high in this population, approximately 50% within 5 years.<sup>5</sup> During the early phase of the pandemic (i.e., between March and August 2020), approximately 60% of Canadians receiving maintenance dialysis who were infected with SARS-CoV-2 were admitted to the hospital and 28% of all infected patients died (approximately 4 times higher than the general population).<sup>1</sup>

The long-term direct and indirect effects of the pandemic on the general population have been well described, with excess mortality continuing to be reported 4 years since the outset of the pandemic.<sup>6</sup> Early on in the COVID-19 pandemic, the general population experienced substantial reductions in acute healthcare utilization (e.g., hospitalizations).<sup>6,7</sup> It is important to understand clinical outcomes (e.g., mortality) and changes in healthcare utilization during the pandemic to inform care gaps that may continue to persist and to improve preparedness for future pandemics.

Given the high healthcare needs of the maintenance dialysis population, they may have been particularly affected by the COVID-19 pandemic, both directly and indirectly. The United States Renal Data System reported that in 2021, all-cause mortality was higher in patients receiving maintenance dialysis compared to before the pandemic (203 vs. 173 deaths per 1000 person-years).<sup>8</sup> This was accompanied by a decrease in hospitalizations (1.49 vs. 1.63 hospitalizations per person-years).<sup>9</sup> A study in Thailand found that among patients with kidney failure during the first 30 months of the pandemic, there were 5.7% more deaths than expected had there been no pandemic.<sup>10</sup> There is a lack of literature providing a comprehensive evaluation of the long-term effect of the COVID-19 pandemic on clinical outcomes and healthcare utilization in the maintenance dialysis population. Therefore, we conducted this study to examine the rates of

all-cause mortality, non-COVID-19-related mortality, healthcare utilization, cardiovascular-related hospitalizations, kidney-related outcomes, and ambulatory visits in patients receiving maintenance dialysis in Ontario, Canada, before and during the COVID-19 pandemic. Compared to the pre-pandemic period, we hypothesized that the rate of all-cause mortality would significantly rise during the first few years of the pandemic due to reduced healthcare utilization and due to deaths directly attributable to SARS-CoV-2 infection. More information on our hypotheses for the anticipated effect of the COVID-19 pandemic on each of our outcomes is included in Table S1.

## Methods

### Design and Setting

Using administrative healthcare databases from Ontario, Canada held at ICES ([ices.on.ca/](https://ices.on.ca/)), we conducted a population-based, repeated cross-sectional study. These datasets were linked using unique encoded identifiers and analyzed at ICES. ICES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health system evaluation and improvement. The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board. To report this study, we followed the Reporting of studies Conducted using Observational Routinely collected health Data guidelines for observational studies (the RECORD statement) (Table S2).<sup>11</sup>

### Data Sources

We used several linked administrative databases in this study. In brief, we used the Ontario Renal Reporting System to identify individuals receiving maintenance dialysis. The

Ontario Renal Reporting System is a mandatory reporting system, with all kidney care service providers in Ontario submitting data on people receiving dialysis care.<sup>12</sup> The Ontario Health Insurance Plan provided information on physician claims for diagnosis and billing, while the Registered Persons Database (RPDB) provided information on vital status and demographic information. To identify hospital admissions and their associated procedural and diagnostic codes, we used the Canadian Institute for Health Information (CIHI) Discharge Abstract Database. To identify day surgeries, we used the CIHI Same Day Surgery Database; and to identify emergency room visits, we used the CIHI National Ambulatory Care Reporting System database. To capture deaths associated with a positive SARS-CoV-2 test result, we used the ICES-derived COVID-19 Integrated Testing Dataset, which is a combination of 3 data sources (Public Health Case and Contact Management Solution [CCM], Ontario Laboratories Information System, and distributed testing data from laboratories within the COVID-19 diagnostic network) and the CCM (i.e., Ontario's central repository for COVID-19 reporting). Additional details on coding definitions and administrative databases used can be found in Table S3.

## Cohort

**Time periods.** We created monthly cross-section populations of adults receiving maintenance dialysis as of the 15<sup>th</sup> of every month. This resulted in 36 monthly populations before the COVID-19 pandemic (March 15, 2017, to February 15, 2020) and 36 since the outset of the COVID-19 pandemic (March 15, 2020, to February 15, 2023). We analyzed monthly populations to capture the frequent changes during the pandemic (e.g., changes in care delivery and changes in SARS-CoV-2 infection rates). March 15, 2020, was the pandemic start date, and at that time, public health officials in Ontario requested hospitals to ramp down non-emergent clinical activity (i.e., this was the date many changes in clinical practice began).<sup>13</sup> In Ontario, waves of COVID-19 occurred from March 15, 2020, to August 31, 2020 (wave 1), September 1, 2020, to February 28, 2021 (wave 2), March 1, 2021, to July 31, 2021 (wave 3), August 1, 2021, to December 14, 2021 (wave 4), December 15, 2021, to February 28, 2022 (wave 5), March 1, 2022, to June 18, 2022 (wave 6), and June 19, 2022, to March 14, 2023 (wave 7).<sup>14</sup>

**Maintenance dialysis population.** We identified adults from Ontario, Canada who were receiving maintenance dialysis (including in-center hemodialysis and home dialysis modalities). To ensure we were not capturing patients receiving acute outpatient dialysis, we required patients to remain on dialysis for at least 30 days. Patients who had a kidney transplant were not eligible to be included until they had been on maintenance dialysis for at least 30 days. We excluded non-Ontario residents, individuals aged <18

years, and individuals who were no longer receiving maintenance dialysis in Ontario (i.e., withdrew from dialysis, died, recovered kidney function, transferred out of the region, received a kidney transplant, or lost to follow-up). Patients who did not meet the eligibility criteria for one month could be included in subsequent months. Patients could therefore be included for multiple months during the study period.

## Outcomes

**Overview.** We examined clinical outcomes and healthcare utilization outcomes that we hypothesized, based on literature and clinical expertise, could be affected by the COVID-19 pandemic. Each outcome was measured in patients within each monthly group.

**Primary outcome.** Our primary outcome was all-cause mortality. Mortality is accurately identified in our administrative databases.<sup>15</sup>

**Secondary outcomes.** Secondary outcomes included non-COVID-19-related deaths, all-cause hospitalizations (excluding elective surgeries), intensive care unit admissions, emergency room visits, and hospital admissions with mechanical ventilation. We defined non-COVID-19-related deaths by excluding any deaths during the pandemic period that were associated with a positive SARS-CoV-2 test in the 30 days prior to death or deaths captured in CCM.<sup>16</sup> For all outcomes associated with hospitalization, we attributed the outcome to the month when the patient was first admitted to the hospital.

**Other outcomes.** We also examined the following outcomes: hospitalizations for elective surgery, hospitalizations for myocardial infarction, hospitalizations for heart failure, hospitalizations for stroke (excluding transient ischemic attack), switching from in-center dialysis to home dialysis (patients were required to be on home dialysis for at least 28 days to be considered a switch), home care visits, long-term care admissions, non-nephrology specialist visits (i.e., any physician specialty that is not a nephrologist or a general practitioner/family physician), and receipt of a kidney transplant.

## Statistical Analysis

We reported baseline characteristics for 3 time periods (study start [March 15, 2017]; the beginning of the COVID-19 pandemic period [March 15, 2020]; and the last monthly study interval [February 15, 2023]). We did not include individuals who died or received a kidney transplant in the next month's population (kidney transplant recipients could re-enter in a subsequent month if they met the criteria for maintenance dialysis). We reported all outcomes as monthly rates per 1000 person-years, and we combined the monthly rates to present an overall rate both before and during the COVID-19



pandemic. For the primary and secondary outcomes, we reported results during the first year of the pandemic (March 15, 2020, to March 14, 2021) and the first 36 months of the pandemic (March 15, 2020, to March 14, 2023).

As described previously,<sup>17,18</sup> we used multivariable Poisson generalized estimating equations to analyze clustered count data to model trends for the primary and secondary outcomes, and kidney transplant, during the pre-COVID-19 period (March 15, 2017, to March 14, 2020). The analytical unit was the age group-sex-month strata. The dependent variable was the stratum-specific count of each outcome of the population within that stratum; the log (stratum-specific population) was the offset. The multivariable Poisson model included: age group-sex indicators, and a continuous linear term to be measured in months since March 15, 2017, to estimate the general trend in pre-COVID rates. An autoregressive working correlation was included to account for autocorrelated outcomes. The model used 3 years of pre-pandemic baseline data to compute the predicted monthly outcome rates, accounting for seasonality and changing patterns over time. Modeled trends from the pre-COVID-19 period were used to predict the expected trend that would have occurred during the COVID-19 period if there had been no pandemic. The expected rate was generated by applying a linear combination of the pre-COVID-19 regression coefficients to the post-COVID-19 age group-sex month strata after exponentiating. We estimated the relative change as the ratio of the observed and expected rates (i.e., adjusted relative rate), including 95% confidence intervals.

A two-sided *P*-value of  $<.05$  was considered statistically significant, and confidence interval widths were not adjusted for multiple testing. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

### Additional Analysis

To further ensure we were not capturing patients receiving acute dialysis, in a post-hoc analysis, we required patients to remain on dialysis for at least 90 days. We then examined the incidence rates per 1000 person-years for the outcomes of all-cause mortality, non-COVID-19-related deaths, and all-cause hospitalization during the first year of the pandemic and the first 36 months of the pandemic.

## Results

### Baseline Characteristics

During our study period, we included 31 900 unique patients receiving maintenance dialysis. Baseline characteristics are presented across 3 time periods in Table 1. In general, characteristics of patients receiving maintenance dialysis were comparable across the 3 time periods, with the median age of patients between 67 and 68 years, and approximately 74% were receiving in-center hemodialysis (versus home

dialysis). Slight changes in comorbidities and prescription medication use were observed across periods. For example, across the 3 time periods, there was a slight increase in major cancer from 15.2% to 16.4% and a decrease in prescriptions for angiotensin-converting enzyme inhibitors from 16.4% to 12.2%.

### Mortality

The crude incidence rate (per 1000 person-years) of all-cause mortality was 165.0 (95% CI: 160.7, 169.4) in the pre-COVID-19 period, compared to 173.2 (95% CI: 166.1, 180.6) during the first year of the pandemic (Table 2) and 171.7 (95% CI: 167.4, 176.0) during the first 36-months of the pandemic (Table 3). When examining monthly all-cause mortality rates, in the first few months of the pandemic (April, May, and June 2020) all-cause mortality was consistently higher (Figure 1) with the adjusted relative rate (aRR) of all-cause mortality in April 2020 being 1.22-fold (95% CI: 1.17, 1.27) higher than expected due to pre-COVID trends. The largest difference between the observed and expected monthly mortality rates occurred in November 2022 with an aRR of 1.50 (95% CI: 1.42, 1.58) (Table S4). The observed monthly all-cause mortality rate was significantly higher than expected in 14 of the months examined (Table S4). However, when examining the overall all-cause mortality across the months, the adjusted relative rate comparing the observed to expected all-cause mortality rate was not statistically significant in the first year of the pandemic (1.08, 95% CI: 1.00, 1.16) (Table 4) and the first 36 months of the pandemic (1.08, 95% CI: 0.99, 1.18) compared to the pre-pandemic period (Table 5).

### Secondary Outcomes

There were 494 recorded COVID-19-related deaths during the study period. After removing COVID-19-related deaths, the crude incidence rate of non-COVID-19-related mortality was 165.0 (95% CI: 160.7, 169.4) in the pre-COVID-19 period, compared to 163.3 (95% CI: 156.4, 170.5) during the first year of the pandemic (Table 2) and 157.7 (95% CI: 153.6, 161.9) during the first 36 months of the pandemic (Table 3). When examining monthly non-COVID-19-related deaths, the adjusted relative rate was substantially lower than expected during the pandemic compared to what was expected in 25 of the 36 months examined (Figure 2, Table S4). However, there was no overall difference in the observed versus expected rate of non-COVID-19 mortality, with an aRR of 0.99 (95% CI: 0.91, 1.08) in the first 36 months of the pandemic, and similar results were found when examining the first year of the pandemic (Tables 4 and 5).

For crude estimates, there was an overall decrease in events for all secondary outcomes related to acute health utilization during the pandemic period compared to the pre-pandemic period. For example, the pre-COVID-19 rate of

**Table 1.** Baseline Characteristics for Patients Receiving Maintenance Dialysis From March 2017 to February 2023.

Characteristic	March 15, 2017 (N= 11 272)	March 15, 2020 (N= 11 954)	February 15, 2023 (N = 12 205)
<b>Demographics</b>			
Age, years	67 (56.77)	68 (57.77)	68 (57.77)
Female	4493 (39.9)	4788 (40.1)	4850 (39.7)
Neighborhood income quintile <sup>†</sup>			
Quintile 1, low	3458 (30.7)	3643 (30.5)	3598 (29.5)
Quintile 2	2505 (22.2)	2679 (22.4)	2719 (22.3)
Quintile 3, middle	2136 (18.9)	2293 (19.2)	2318 (19.0)
Quintile 4	1736 (15.4)	1767 (14.8)	1971 (16.1)
Quintile 5, high	1437 (12.7)	1572 (13.2)	1599 (13.1)
Rural residence <sup>‡</sup>	1118 (9.9)	1197 (10.0)	1225 (10.0)
<b>Dialysis characteristics</b>			
Dialysis modality			
Home dialysis	2973 (26.4)	3060 (25.6)	3069 (25.1)
In-center hemodialysis	8299 (73.6)	8894 (74.4)	136 (74.9)
Dialysis vintage, years <sup>‡</sup>	4 (2.6)	4 (2.7)	5 (3.8)
Primary cause of end-stage kidney disease			
Glomerulonephritis	1706 (15.1)	1648 (13.8)	1576 (12.9)
Polycystic kidney disease	550 (4.9)	539 (4.5)	586 (4.8)
Diabetes	4146 (36.8)	4476 (37.4)	4388 (36.0)
Renal vascular disease	1631 (14.5)	1538 (12.9)	1441 (11.8)
Other	3056 (27.1)	3617 (30.3)	4065 (33.3)
Missing	183 (1.6)	136 (1.1)	149 (1.2)
<b>Comorbidities*</b>			
Charlson comorbidity index **, categories			
2	5306 (47.1)	5517 (46.2)	6005 (49.2)
3 to 4	2944 (26.1)	3159 (26.4)	3291 (27.0)
5+	3022 (26.8)	3278 (27.4)	909 (23.8)
Major cancers	1709 (15.2)	1927 (16.1)	1998 (16.4)
Chronic liver disease	1358 (12.0)	1535 (12.8)	1587 (13.0)
Chronic obstructive pulmonary disease	956 (8.5)	945 (7.9)	800 (6.6)
Diabetes	6720 (59.6)	7331 (61.3)	7344 (60.2)
Dementia	1063 (9.4)	1139 (9.5)	1227 (10.1)
Hypertension	9028 (80.1)	9506 (79.5)	10 075 (82.5)
Peripheral vascular disease	1425 (12.6)	1474 (12.3)	1288 (10.6)
<b>Medication use<sup>‡</sup></b>			
Angiotensin-converting enzyme inhibitor	1611 (16.4)	1551 (14.8)	1327 (12.2)
Angiotensin receptor blocker	2212 (22.5)	2611 (25.0)	2721 (24.9)
Beta blocker	4829 (49.0)	5247 (50.2)	4969 (45.6)
Calcium channel blockers	4537 (46.1)	5053 (48.3)	5287 (48.5)
Diabetic drugs (not including SGLT2 inhibitor)	3563 (36.2)	4061 (38.8)	4070 (37.3)

Data are presented as median (25th, 75th percentile) or N (%).

<sup>†</sup>Neighborhood income was categorized into quintiles based on the average neighborhood income, with missing income categorized as income quintile 3.

<sup>‡</sup>Rural was defined as residing in an area with a population <10 000. Missing was categorized as urban.

<sup>‡</sup>Dialysis vintage was defined as the period of interest (i.e., March 15, 2017, March 15, 2020, or February 15, 2023) minus the dialysis initiation date.

\*Comorbidities assessed in the 5 years before each period of interest unless otherwise indicated.

\*\*The Charlson comorbidity index is a method of predicting mortality using administrative database-identified patient comorbidities. Kidney disease is a variable in the index given a score of 2; therefore, individuals in our cohort with a score of 0 were given a score of 2 and individuals with a score of 1 were given a 3. This characteristic was assessed in the 2 years before the period of interest.

<sup>‡</sup>The denominator for medications is restricted to individuals who had at least one prescription medication recorded in the Ontario Drug Benefits (ODB) database in the 1-year before the period of interest, or who are at least ≥66 years of age on the period of interest (i.e., eligible for ODB coverage).

Therefore, the denominator for each of the 3 periods of interest is 9852, 10 462, and 10 908, respectively.

**Table 2.** Primary and Secondary Outcomes in the Pre-COVID-19 and COVID-19 Pandemic Periods, Restricting to the First Year of the COVID-19 Period (March 15, 2020, to March 14, 2021).

Outcomes	Pre-COVID-19 pandemic (March 15, 2017, to March 14, 2020)			First year of the COVID-19 pandemic (March 15, 2020, to March 14, 2021)		
	Number of events	% (average of the monthly proportions)	Incidence rate per 1000 person-years (95% confidence interval)	Number of events	% (average of the monthly proportions)	Incidence rate per 1000 person-years (95% confidence interval)
<b>Primary Outcome</b>						
All-cause mortality	5526	1.3%	165.0 (160.7, 169.4)	2183	1.4%	173.2 (166.1, 180.6)
<b>Secondary Outcomes</b>						
Non-COVID-19-related deaths	n/a	n/a	n/a	2058	1.3%	163.3 (156.4, 170.5)
All-cause hospitalization* (excluding elective surgeries)	30 308	7.3%	946.1 (935.5, 956.9)	10 429	6.7%	861.0 (844.6, 877.6)
Intensive care unit admission <sup>€</sup>	8720	2.1%	262.7 (257.2, 268.3)	2912	1.8%	232.7 (224.4, 241.4)
Hospitalization with mechanical ventilation <sup>¶</sup>	4052	1.0%	122.6 (118.9, 126.5)	1389	0.9%	111.4 (105.7, 117.4)
Emergency room visits for any cause*	58 752	14.2%	1908.8 (1893.4, 1924.3)	18 674	11.9%	1588.9 (1566.3, 1611.8)

\*For all outcomes associated with a hospitalization or an emergency room visit we excluded from the denominator patients who were already hospitalized before the start of the monthly interval and remained hospitalized throughout the entire monthly interval.

<sup>€</sup>For intensive care unit admissions, we excluded from the denominator patients who were already in the intensive care unit before the start of the monthly interval and remained in the intensive care unit throughout the entire monthly interval.

<sup>¶</sup>For hospitalization with mechanical ventilation we excluded from the denominator patients who were already in hospital before the start of the interval with evidence of mechanical ventilation and remained in hospital throughout the entire monthly.

**Table 3.** Primary, Secondary Outcomes, and Other Outcomes in the Pre-COVID-19 Period and During the First 36 Months of the COVID-19 Pandemic (March 15, 2020, to March 14, 2023).

Outcomes	Pre-COVID-19 pandemic (March 15, 2017, to March 14, 2020)			COVID-19 pandemic (March 15, 2020, to February 15, 2023)		
	Number of events	% (average of the monthly proportions)	Incidence rate per 1000 person-years (95% confidence interval)	Number of events	% (average of the monthly proportions)	Incidence rate per 1000 person-years (95% confidence interval)
<b>Primary outcome</b>						
All-cause mortality	5526	1.3%	165.0 (160.7, 169.4)	6058	1.4%	171.7 (167.4, 176.0)
<b>Secondary outcomes</b>						
Non-COVID-19-related deaths	n/a	n/a	n/a	5564	1.3%	157.7 (153.6, 161.9)
All-cause hospitalization* (excluding elective surgeries)	30 308	7.3%	946.1 (935.5, 956.9)	30 042	6.8%	886.3 (876.3, 896.3)
Intensive care unit admission <sup>€</sup>	8720	2.1%	262.7 (257.2, 268.3)	8056	1.8%	230.0 (225.0, 235.0)
Hospitalization with mechanical ventilation <sup>¶</sup>	4052	1.0%	122.6 (118.9, 126.5)	3832	0.9%	109.8 (106.4, 113.3)
ER visits for any cause*	58 752	14.2%	1908.8 (1893.4, 1924.3)	54 800	12.5%	1669.8 (1655.9, 1683.9)
<b>Other outcomes</b>						
Hospitalization for an elective surgery	5686	1.4%	172.3 (167.9, 176.9)	5183	1.2%	148.7 (144.7, 152.8)
Hospitalization with myocardial infarction*	1416	0.3%	42.8 (40.6, 45.0)	1178	0.3%	33.7 (31.8, 35.7)

(continued)

**Table 3.** (continued)

Outcomes	Pre-COVID-19 pandemic (March 15, 2017, to March 14, 2020)			COVID-19 pandemic (March 15, 2020, to February 15, 2023)		
	Number of events	% (average of the monthly proportions)	Incidence rate per 1000 person-years (95% confidence interval)	Number of events	% (average of the monthly proportions)	Incidence rate per 1000 person-years (95% confidence interval)
Hospitalization with heart failure*	1337	0.3%	40.4 (38.3, 42.6)	1301	0.3%	37.2 (35.2, 39.3)
Hospitalization with stroke*	599	0.1%	18.1 (16.7, 19.6)	600	0.1%	17.1 (15.8, 18.6)
Switch from in-center dialysis to home dialysis**	1520	0.5%	61.3 (58.3, 64.4)	1643	0.5%	63.0 (60.0, 66.1)
Home care visits	117 330	29.7%	4969.2 (4940.8, 4997.7)	118 735	28.1%	4609.6 (4583.4, 4635.9)
Long-term care admission <sup>‡</sup>	1099	0.3%	34.1 (32.2, 36.2)	923	0.2%	26.9 (25.3, 28.7)
Kidney transplant	1875	0.4%	56.0 (53.5, 58.6)	1693	0.4%	48.0 (45.7, 50.3)
Non-nephrology specialist visit	255 858	61.1%	12 389.8 (12 341.9, 12 437.9)	263 277	59.6%	11 928.0 (11 882.5, 11 973.6)

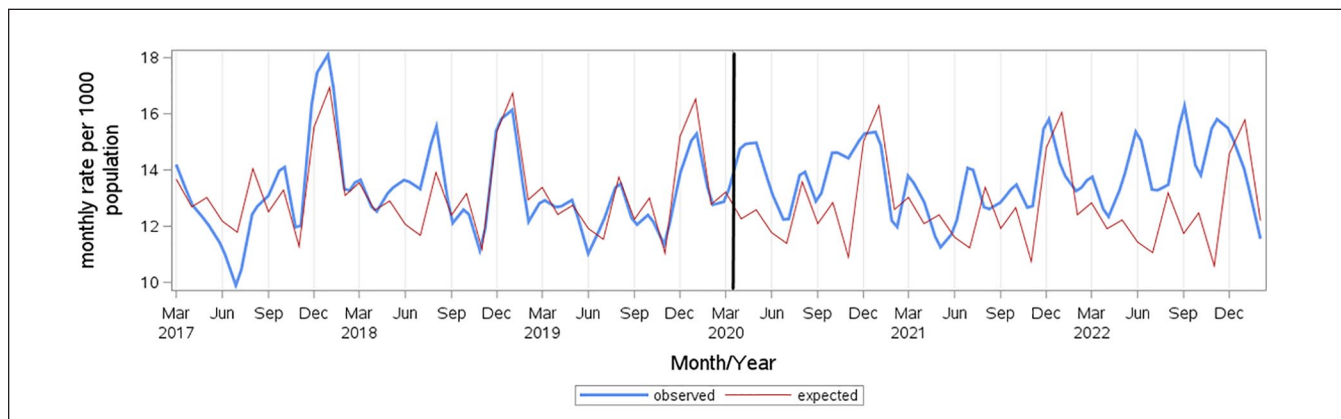
\*For all outcomes associated with a hospitalization or an emergency room visit we excluded from the denominator patients who were already hospitalized before the start of the monthly interval and remained hospitalized throughout the entire monthly interval.

‡For intensive care unit admissions, we excluded from the denominator patients who were already in the intensive care unit before the start of the monthly interval and remained in the intensive care unit throughout the entire monthly interval.

†For hospitalization with mechanical ventilation we excluded from the denominator patients who were already in hospital before the start of the interval with evidence of mechanical ventilation and remained in hospital throughout the entire monthly interval.

\*\*For home dialysis start we excluded from the denominator patients who were already hospitalized before the start of the interval and remained in this state throughout the entire monthly interval. Individuals who had evidence of home dialysis in the 30 days prior to the start of the interval were excluded from the interval.

‡For long-term care admission, we excluded individuals from the denominator who were already in long-term care before the start of the monthly interval.



**Figure 1.** Observed vs. expected monthly all-cause mortality rates for patients receiving maintenance dialysis prior to the COVID-19 pandemic (March 15, 2017, to March 14, 2020) and during the COVID-19 pandemic (March 15, 2020, to March 14, 2023). Vertical solid line indicates the onset of the COVID-19 pandemic.

all-cause hospitalization was 946.1 (95% CI: 935.5, 956.9) per 1000 person-years, compared to 861.0 (95% CI: 844.6, 877.6) during the first year of the pandemic (Table 2) and 886.3 (95% CI: 876.3, 896.3) during the 36-month pandemic period (Table 3). When examining monthly rates, there was a substantial decrease in all-cause hospitalizations (Figure 3)

and emergency room visits (Figure 4), during the pandemic period, with the most substantial reductions generally observed in the first 3 months of the pandemic (i.e., March, April, and May 2020). This decrease in hospitalizations and emergency room visits generally persisted throughout the pandemic months (Tables S5 and S6). When examining the



overall rate of all-cause hospitalizations across months, it was substantially lower than expected, with an overall adjusted rate ratio of 0.90 (95% CI: 0.87, 0.93) during the first year of the pandemic (Table 4); similar results were found when examining the first 36 months of the pandemic and when examining ICU admissions (Table 5). After adjustment, the overall rates of hospitalizations with mechanical ventilation were not substantially lower than expected (Tables 4, 5). Monthly ICU admission and mechanical ventilation rates are shown in Tables S7, S8 and Figures 5 and 6.

### Other Outcomes

For most of our other outcomes, we observed substantial decreases during the pandemic period (Table 3 and monthly rates demonstrated in Figures S1–S9). For example, we found the rate of kidney transplant during the COVID-19 period was substantially lower than expected (aRR 0.72, 95% CI: 0.59, 0.88) (Table 5), with the observed versus expected monthly rates of kidney transplant substantially lower for most of the 36 months of the pandemic period (Table S9, Figure S1).

There was a decline in hospitalizations with myocardial infarction, hospitalizations with heart failure, and elective surgeries, while hospitalizations with stroke changed minimally when comparing the pre-COVID-19 pandemic to the COVID-19 pandemic period (monthly rates: Figures S2–S5; overall rate: Table 3). There was a substantial decrease in long-term care admissions, home care visits, and non-nephrology specialist visits (monthly rates: Figures S6–S8; overall rates: Table 3). Home dialysis initiation increased slightly during the pandemic (monthly rate: Figure S9; overall rate: Table 3).

### Additional Analysis

The incidence rates were similar when requiring patients receiving maintenance dialysis to remain on dialysis for 90 days versus the originally defined 30 days. Specifically, the incidence rate (per 1000 person-years) for all-cause mortality during the pandemic period was ~172 vs ~172, ~158 vs ~158 for non-COVID-related deaths, and ~886 versus ~888 for all-cause hospitalization, using the 30-day versus 90-day definition, respectively.

## Discussion

We found that all-cause mortality was significantly higher in 14 out of the 36 months of the COVID-19 period compared to the pre-COVID-19 period in adults receiving maintenance dialysis from Ontario, Canada. However, the rate of all-cause mortality was not substantially higher than expected in the first year and the first 36 months of the COVID-19 pandemic. This finding was consistent after

**Table 4.** Overall Adjusted Relative Rates Using Poisson Generalized Estimated Equations, Comparing the Ratio for the Observed Rate With the Expected Rate Prior (March 15, 2017, to March 14, 2020) and During the First Year of the COVID-19 Pandemic (March 15, 2020, to March 14, 2021).

Outcome	Adjusted relative rate <sup>¶</sup> (95% confidence interval)
All-cause mortality	1.08 (1.00, 1.16)
Non-COVID-19-related mortality	1.01 (0.94, 1.09)
All-cause hospitalization	<b>0.90 (0.87, 0.93)</b>
Intensive care unit admission	<b>0.90 (0.84, 0.98)</b>
Hospital admission with mechanical ventilation	0.92 (0.82, 1.02)
Emergency room visits	<b>0.85 (0.83, 0.87)</b>

<sup>¶</sup>The multivariable Poisson model included the following covariates: age group-sex indicators, a linear term measured as months since March 15, 2017, and pre-COVID month indicators.

Bold font indicates 95% confidence intervals that do not include the null value (i.e., adjusted relative rate=1.00); confidence intervals have not been adjusted for multiplicity.

**Table 5.** Overall Adjusted Relative Rates Using Poisson Generalized Estimated Equations, Comparing the Ratio for the Observed Rate With the Expected Rate Prior (March 15, 2017, to March 14, 2020) and During the First 36-Months of the COVID-19 Pandemic (March 15, 2020, to March 14, 2023).

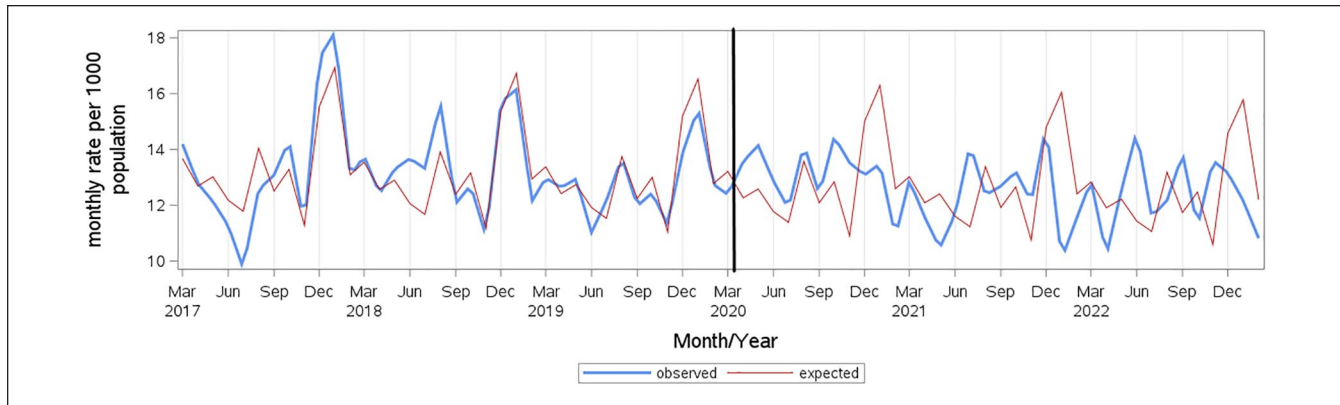
Outcome	Adjusted relative rate <sup>¶</sup> (95% confidence interval)
All-cause mortality	1.08 (0.99, 1.18)
Non-COVID-19-related mortality	0.99 (0.91, 1.08)
All-cause hospitalization	<b>0.92 (0.88, 0.97)</b>
Intensive care unit admission	<b>0.91 (0.82, 0.996)</b>
Hospital admission with mechanical ventilation	0.91 (0.80, 1.03)
Emergency room visits	<b>0.90 (0.88, 0.92)</b>
Kidney transplant	<b>0.72 (0.59, 0.88)</b>

<sup>¶</sup>The multivariable Poisson model included the following covariates: age group-sex indicators, a linear term measured as months since March 15, 2017, and pre-COVID month indicators.

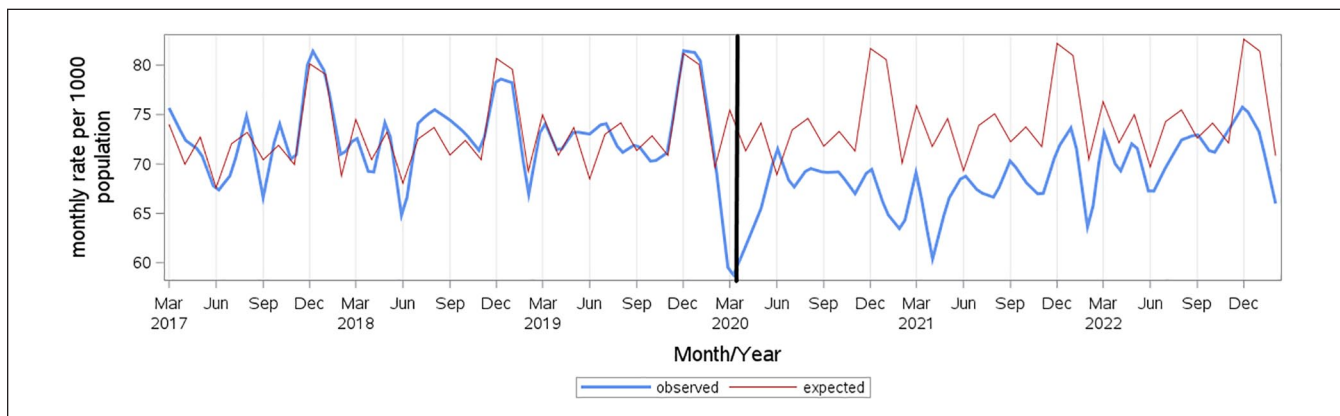
Bold font indicates 95% confidence intervals that do not include the null value (i.e., adjusted relative rate=1.00); confidence intervals have not been adjusted for multiplicity.

removing COVID-19-related deaths. Acute healthcare utilization decreased substantially during the pandemic, including hospitalizations and emergency room visits. Despite substantial reductions in acute healthcare utilization during the first 36 months of the pandemic, there was not a corresponding substantial increase in non-COVID-19-related mortality.

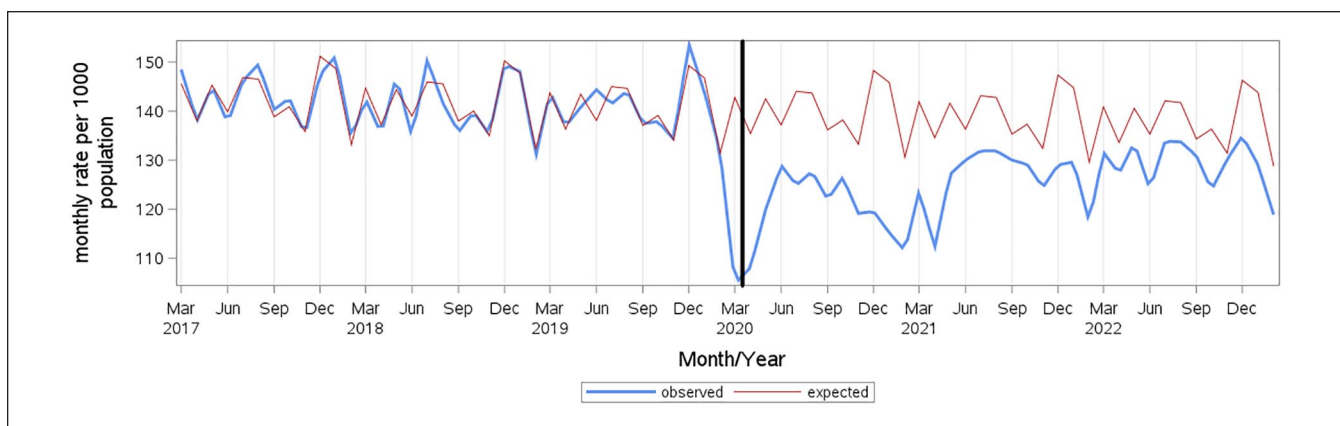
In the first 36 months of the COVID-19 pandemic, Ontario recorded 494 COVID-19-related deaths in the maintenance dialysis population. Compared to the pre-pandemic rate, the change in all-cause mortality during the pandemic was less



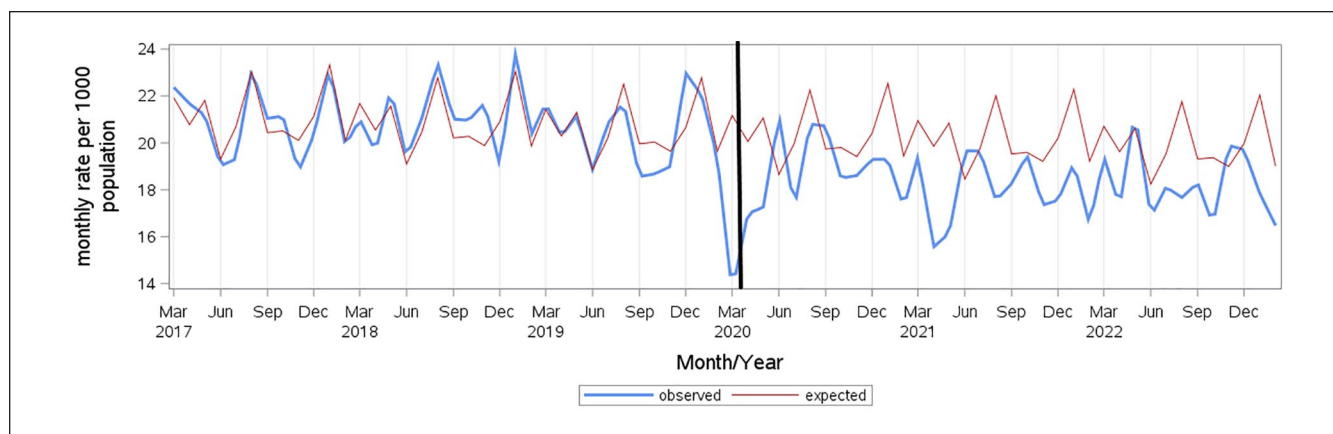
**Figure 2.** Observed vs. expected monthly non-COVID-related mortality rates for patients receiving maintenance dialysis prior to the COVID-19 pandemic (March 15, 2017, to March 14, 2020) and during the COVID-19 pandemic (March 15, 2020, to March 14, 2023). Vertical solid line indicates the onset of the COVID-19 pandemic.



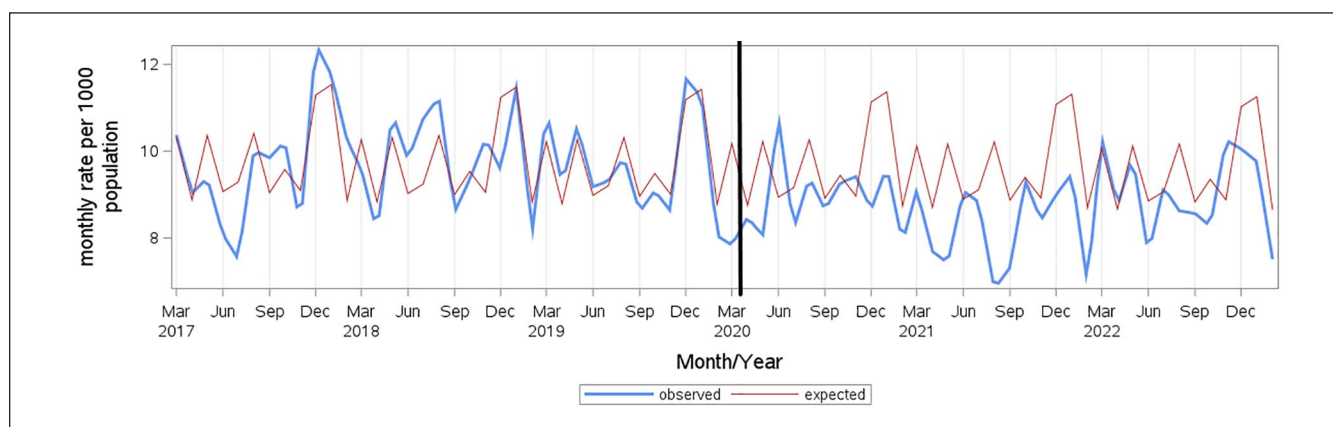
**Figure 3.** Observed vs. expected monthly all-cause hospitalization (excluding elective surgeries) rates for patients receiving maintenance dialysis prior to the COVID-19 pandemic (March 15, 2017, to March 14, 2020) and during the COVID-19 pandemic (March 15, 2020, to March 14, 2023). Vertical solid line indicates the onset of the COVID-19 pandemic.



**Figure 4.** Observed vs. expected monthly emergency room visit rates for patients receiving maintenance dialysis prior to the COVID-19 pandemic (March 15, 2017, to March 14, 2020) and during the COVID-19 pandemic (March 15, 2020, to March 14, 2023). Vertical solid line indicates the onset of the COVID-19 pandemic.



**Figure 5.** Observed vs. expected monthly intensive care unit admission rates for patients receiving maintenance dialysis prior to the COVID-19 pandemic (March 15, 2017, to March 14, 2020) and during the COVID-19 pandemic (March 15, 2020, to March 14, 2023). Vertical solid line indicates the onset of the COVID-19 pandemic.



**Figure 6.** Observed vs. expected monthly hospital admission with mechanical ventilation rates for patients receiving maintenance dialysis prior to the COVID-19 pandemic (March 15, 2017, to March 14, 2020) and during the COVID-19 pandemic (March 15, 2020, to March 14, 2023). Vertical solid line indicates the onset of the COVID-19 pandemic.

pronounced than what was observed in the United States. For example, in patients receiving maintenance dialysis in the United States, the all-cause mortality rate in 2019 was 172.7 per 1000 person-years, increasing to 203.4 in 2020 and to 203.0 in 2021. This occurred after maintenance dialysis patients from the US experienced decades of declining mortality rates.<sup>8</sup> In comparison, our study found the rate of all-cause mortality pre-pandemic was 165.0 per 1000 person-years and 173.2 during the first year of the pandemic. A study conducted on US veterans receiving maintenance dialysis found that compared to the pre-pandemic period (January 1, 2007, to January 31, 2020), there was an increase in mortality during the pandemic (February 1, 2020, to December 31, 2021) with an adjusted rate ratio of 1.023 (95% CI: 1.015, 1.031).<sup>19</sup> Similar to the general Canadian population, patients receiving maintenance dialysis in

Canada may have been less directly affected by the pandemic as COVID-19 deaths per capita were substantially higher in the United States compared to Canada.<sup>20</sup>

There are several potential reasons why the post-pandemic all-cause mortality rate was lower than we initially expected. First, Taji et al,<sup>1</sup> found that compared to many other jurisdictions, including the United States, the rate of SARS-CoV-2 infection was lower in patients receiving maintenance dialysis in Ontario, potentially decreasing the number of COVID-19-related deaths. Moreover, similar to the general Canadian population, COVID-19 vaccine uptake was likely higher in the Canadian dialysis population compared to the United States dialysis population.<sup>21,22</sup> Second, unlike in the general population, patients receiving maintenance dialysis continued to be regularly monitored by nephrologists and nurses throughout the pandemic, with

patients receiving in-center hemodialysis being seen at the dialysis center 3 times per week. Therefore, despite our study observing a substantial decrease in acute healthcare utilization during the pandemic, we may not have found a corresponding substantial increase in mortality due to a compensatory rise in issues being handled safely as outpatients. Nonetheless, it is probable that, in addition to deaths from COVID-19, the substantial decline in acute healthcare utilization during the pandemic contributed to the higher all-cause mortality during several months of the pandemic. In the general Canadian population, there continues to be a higher number of deaths compared to what would be expected if there was no pandemic, with individuals under age 45 years disproportionately affected; however, the reasons for this are unclear.<sup>23</sup> Third, there may have been a decrease in deaths from infections such as influenza and bacterial pneumonia due to strict social distancing rules in Ontario for many months of the pandemic and increased infection control practices at dialysis centers. Banshodani et al,<sup>24</sup> found hospitalizations for non-SARS-CoV-2-related respiratory infectious disease decreased during the pandemic, potentially due to COVID-19 infection control measures; however, mortality rates for non-COVID-19 respiratory infections were comparable prior to and during the pandemic. Fourth, in Ontario, during the pandemic, fewer patients started dialysis compared to the pre-pandemic period, which could contribute to lower overall mortality rates given mortality is often highest in the first several months of starting dialysis.<sup>25</sup> Last, there was a substantial decline in kidney transplants during the first 36 months of the pandemic; this could result in healthier transplant eligible patients (i.e., lower death rate compared to non-eligible patients) remaining on dialysis longer.

We found a substantial decline in kidney transplants which persisted for 3-years into the pandemic. This is concerning as kidney transplantation is the best treatment option for most patients with kidney failure, resulting in improved survival.<sup>26</sup> Potential reasons for this sustained decreased rate of kidney transplants include a continued backlog of transplant assessments and surgeries and a reduced emphasis on kidney transplant education as dialysis units needed to switch focus to infection control. Similar trends have been found in other jurisdictions.<sup>27,28</sup> For example, in the United States, the number of kidney transplants decreased sharply at the beginning of the pandemic but rebounded in 2021, with a rate of 3.9 per 100 person-years in 2019, 3.7 in 2020, and 4.0 in 2021.<sup>27</sup> In Ontario, the most recent data suggests kidney transplant numbers have rebounded as well with 797 transplants in 2023, compared to 609 in 2020 and 747 in 2019.<sup>29,30</sup>

There are several strengths of our study. To our knowledge, this is the first Canadian study to provide a comprehensive examination of the direct and indirect effects of the COVID-19 pandemic, with follow-up spanning several years. This information is important to improve preparedness

of future pandemics, including to update the Ontario pandemic clinical guidelines for patients with chronic kidney disease, which is distributed to Ontario's 27 regional renal programs.<sup>31</sup> Furthermore, our findings that substantial declines in kidney transplant persisted several years into the pandemic provides insights into the need to balance patients' continued access to healthcare while minimizing infection spread. Finally, our use of administrative healthcare databases provided us with a comprehensive capture of patients receiving maintenance dialysis in Ontario.

Several limitations of this work deserve mention. First, due to the relatively small number of events each month, we were not able to present results by dialysis modality (i.e., in-center hemodialysis versus home dialysis modalities). Given differences in patient characteristics (e.g., patients receiving hemodialysis are often older and have more comorbidities than those receiving home dialysis),<sup>32</sup> it is possible that results may differ between the 2 groups. Second, we did not present differences by other subgroups (e.g., sex and race) with previous work finding substantial differences in excess mortality across racial and ethnic groups in the early waves of the pandemic.<sup>33</sup> Third, external generalizability to other jurisdictions may be limited as other regions may have experienced different COVID-19 rates while implementing different mitigation strategies. Fourth, there could be outcome misclassification for non-COVID-19-related deaths, with it often being difficult to distinguish between deaths with COVID-19 versus deaths from COVID-19. Last, studies in the general population have found long-term adverse effects of SARS-CoV-2 infection (e.g., cardiovascular events), which need to be explored further in this population.

In conclusion, this study helped us understand the continued impact of the COVID-19 pandemic on the maintenance dialysis population. Further research is needed to understand the long-term effects of the COVID-19 pandemic on this population.

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### Declaration of Conflicting Interest

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Amit Garg received an investigator-initiated grant from Astellas, which featured as partnership funds in CIHR-funded research. Dr. Oliver is the owner of DMAR systems, received honoraria from Baxter Healthcare, and is Contracted Medical Lead at Ontario Renal Network, Ontario Health. Kevin Yau has received speaking honoraria from GlaxoSmithKline. The other authors declare no conflicts of interest.

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### Ethics Approval and Consent to Participate

ICES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze healthcare and demographic data, without consent, for health system evaluation and improvement. The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a Research Ethics Board.

### Consent for Publication

All authors consent to the publication of this study.

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### Availability of Data and Materials

The dataset from this study is held securely in coded form at ICES. While data-sharing agreements prohibit ICES from making the data

set publicly available, access can be granted to those who meet pre-specified criteria for confidential access, available at [www.ices.on.ca/DAS](http://www.ices.on.ca/DAS). The full data set creation plan and underlying analytic code are available from the authors upon request, understanding that the programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

### Supplemental Material

Supplemental material for this article is available online.

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