Can J Diabetes 43 (2019) 483–489

Contents lists available at ScienceDirect

Canadian Journal of Diabetes

journal homepage: www.canadianjournalofdiabetes.com

Original Research

Impact of Socioeconomic Status on Incidence of End-Stage Renal Disease and Mortality After Dialysis in Adults With Diabetes

Calvin Ke MD [a]; S. Joseph Kim MD [a]; Baiju R. Shah MD [a]; Arlene S. Bierman MD [b]; Lorraine L. Lipscombe MD [a]; Denice S. Feig MD [a]; Gillian L. Booth MD [a,*]

[a] Department of Medicine, University of Toronto, Toronto, Ontario, Canada
[b] Center for Evidence and Practice Improvement, Agency for Healthcare Research and Quality, Rockville, Maryland, United States

Key Messages

- Previous studies have shown that low socioeconomic status (SES) predicts increased end-stage renal disease (ESRD) among people with diabetes.
- We found that SES disparities in ESRD incidence were reduced in those ≥65 years of age who universally received prescription drug coverage.
- Low SES was associated with higher mortality post-ESRD, but this was eliminated after accounting for SES disparities in kidney transplantation.

ARTICLE INFO

Article history:
Received 13 November 2018
Received in revised form
13 March 2019
Accepted 12 April 2019

Keywords:
chronic
diabetes mellitus
epidemiology
kidney failure
socioeconomic status

ABSTRACT

Objectives: To determine whether low socioeconomic status (SES), with or without universal drug coverage, predicts end-stage renal disease (ESRD) and survival after dialysis in patients with diabetes.
Methods: We conducted a population-based retrospective cohort study in Ontario, Canada. We used ≥65 years of age as a surrogate for universal drug coverage. Adults with diabetes were followed from March 31, 1997 to March 31, 2011 for occurrence of the composite primary outcome (acute kidney injury, ESRD requiring dialysis or kidney transplantation). Patients on dialysis with diabetes were followed from April 1, 1994 to March 31, 2011 for occurrence of death or transplantation.
Results: SES quintile (Q) was inversely associated with the primary outcome in both age groups; however, the gradient was higher in those <65 years of age (Q1:Q5 hazard ratio [HR], 1.43; 95% confidence interval [CI], 1.37–1.49) compared with ≥65 years of age (HR, 1.19; 95% CI, 1.15–1.24). Low SES was associated with a lower likelihood of kidney transplantation among those <65 years of age (HR, 0.77; 95% CI, 0.65–0.92). In patients on dialysis, low SES was associated with higher mortality (HR, 1.09; 95% CI, 1.02–1.16) in both age groups. This association was eliminated after accounting for the decreased rates of kidney transplantation in lower SES groups.
Conclusions: SES is inversely associated with ESRD outcomes in individuals with diabetes, and this disparity is reduced in those ≥65 years of age who universally receive prescription drug coverage. Low SES is associated with a higher mortality after dialysis, largely explained by lower kidney transplantation rates in poorer populations.

Mots clés :
chronique
diabète sucré
épidémiologie
insuffisance rénale
statut socio-économique

RÉSUMÉ

Objectifs : Déterminer si le statut socioéconomique (SSE), avec ou sans couverture universelle des médicaments, peut prédire une insuffisance rénale terminale (IRSE) et la survie après dialyse chez les patients atteints de diabète.

* Address for correspondence: Gillian L. Booth MD, Li Ka Shing Knowledge Institute, 209 Victoria Street, Toronto, Ontario M5B 1T8, Canada.
E-mail address: boothg@smh.ca

1499-2671/
https://doi.org/10.1016/j.jcjd.2019.04.006

Méthodes : Nous avons mené une étude rétrospective d'une cohorte basée sur la population en Ontario, au Canada. Nous avons utilisé un âge ≥65 ans comme substitut à la couverture universelle des médicaments. Les adultes diabétiques ont été suivis du 31 mars 1997 au 31 mars 2011 pour l'occurrence du principal critère composite (lésion rénale aiguë, IRSE nécessitant une dialyse ou une transplantation rénale). Les patients dialysés diabétiques ont été suivis du 1er avril 1994 au 31 mars 2011 pour les cas de décès ou de transplantation.
Résultats : Le quintile du SSE (Q) était inversement associé au résultat principal dans les deux groupes d'âge; toutefois, le gradient était plus élevé chez les personnes <65 ans (rapport de risque [RR] Q1:Q5, 1.43; intervalle de confiance à 95% [IC], 1.37-1.49) comparativement à ceux ≥65 ans (RR, 1.19; IC, 1.15 à 1.24). Un faible SSE était associé à une probabilité plus faible de transplantation rénale chez les personnes <65 ans (RR, 0.77; IC à 95%, 0.65 à 0.92). Chez les patients sous dialyse, un faible SSE était associé à une mortalité plus élevée (RR, 1.09; IC à 95%, 1.02 à 1.16) dans les deux groupes d'âge. Cette association a été éliminée après avoir tenu compte de la diminution des taux de transplantation rénale dans les groupes de SSE inférieurs.
Conclusions : Le SSE est inversement associé aux conséquences d'une IRSE chez les personnes atteintes de diabète, et cette disparité est réduite chez les personnes ≥65 ans qui bénéficient d'une couverture universelle de médicaments sur ordonnance. Un faible SSE est associé à une mortalité plus élevée après dialyse, ce qui s'explique en grande partie par des taux de transplantation rénale plus faibles dans les populations plus pauvres.

Introduction

End-stage renal disease (ESRD) is a costly and potentially preventable complication of diabetes, which is associated with high morbidity and mortality (1,2). Dialysis alone costs the Canadian health-care system a staggering $2.5 billion annually (3).

The incidence of ESRD appears to be associated with low socioeconomic status (SES). In several studies from the United States, ESRD incidence and progression were increased in poorer vs wealthier neighborhoods (4–6). These disparities were partly driven by differences in insurance coverage; therefore, reducing access to therapy, such as angiotensin-converting enzyme (ACE) inhibitors (4–7). Even in countries with universal health care, low SES predicts increased ESRD incidence and severity (5). Canadian studies have demonstrated a growing gap in mortality between richer and poorer individuals with diabetes despite equitable access to health-care services (8). A study from Ontario, Canada, showed that SES differences in cardiovascular events and mortality were diminished substantially in those >65 years of age, a group that receives universal access to medications as an insurable benefit (9). In contrast, cardiovascular events were 50% higher among lower SES groups <65 years of age, who largely pay out of pocket for medications or use private insurance. These findings suggest that reduced access to drugs may have a particularly detrimental effect on diabetes outcomes.

In recent decades, widespread use of preventive therapies has remarkably reduced the incidence of diabetes complications (10). At the same time, 57% of Canadians with diabetes do not adhere to treatments because of their high cost burden (11). However, the potential effects of these financial barriers on renal complications have never been studied in the diabetes population.

To fill this knowledge gap, we examined whether low SES predicts ESRD incidence in individuals with diabetes, and whether this relationship varies based on the presence or absence of universal access to medications as an insurable benefit. Because the latter commences at 65 years of age in Ontario, we compared the influence of SES on ESRD and its outcomes between younger (<65 years of age) and older (≥65 years of age) adults with diabetes. We also assessed whether SES predicts all-cause mortality after dialysis, and, if so, whether this is modified by age. We hypothesized that lower SES would be associated with increased ESRD incidence and all-cause mortality after dialysis, but that these associations would be diminished at older ages potentially because of access to universal drug coverage. Because poorer access to kidney transplantation may compound existing disparities among those with ESRD (12), we also hypothesized that differences in kidney transplantation could partially offset the association between SES and mortality.

Methods

We conducted a population-based retrospective cohort study among adults with diabetes living in Ontario. This analysis was based on a prior cohort assembled for the Project for an Ontario Women's Health Evidence-based Report study.

Data sources

All residents of Ontario are covered under the Ontario Health Insurance Plan (OHIP). The Ontario Drug Benefit (ODB) program provides universal access to medications as an insurable benefit for those ≥65 years of age, and selective coverage for those <65 years of age (13). Individuals ≥65 years of age with a low personal income (<$16,018) or household income (<$24,175) are eligible for waiver of prescription copayments. Health encounters for virtually all Ontario residents are captured by OHIP billing codes and hospital discharge abstracts through the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD). Diabetes diagnosis was identified by the Ontario Diabetes Database, which has 86% sensitivity and 97% specificity (14). The provincial Registered Persons Database provided demographic data including postal code and vital status. Additional data were extracted from the Canadian Organ Replacement Register (CORR) and the Trillium Gift of Life Network database for dialysis and kidney transplantation records (15). These data were linked at ICES using unique, encoded identifiers. Laboratory measures were unavailable. The study protocol received ethics approval from the institutional review boards at St. Michael's Hospital and Sunnybrook Health Sciences Centre.

Study population

The study was restricted to residents of Ontario ≥30 years of age. Although the Ontario Diabetes Database does not specify diabetes type, the vast majority of these adults would be expected to have type 2 diabetes.

We defined 2 separate cohorts based on ESRD status. The pre-ESRD cohort consisted of individuals with preexisting diabetes, without ESRD, on March 31, 1997 (index date). This early index date was chosen to ensure sufficient numbers of outcome events across SES and age group strata. We defined ESRD as any physician billing claim for dialysis within 1 year prior to the index date (Supplementary Appendix 1). To ensure accurate baseline data, we also excluded individuals who became eligible for health coverage <5 years prior to the index date.

The post-ESRD cohort consisted of patients on dialysis with diabetes who were initiated on chronic dialysis between April 1, 1994 and March 31, 2010 (period selected to ensure sufficient numbers of outcome events). We defined the index date as the first dialysis event, and we excluded individuals who became eligible for health coverage <3 years prior to the index date.

Baseline covariates

The exposure variable was SES at baseline, defined as the median household income of each individual's neighborhood of residence according to the Canadian census, which was chronologically closest to their index date. Area income was divided into quintiles (1 to 5) and assigned to individuals using their postal code of residence. Household income was available for dissemination areas, which have a population of around 400 to 700 people. This method has been widely used to estimate SES and has been shown to correlate well with health outcomes (8,9).

For the pre-ESRD cohort, we identified baseline demographic covariates including age, sex and SES quintile. Additional covariates included the number of primary health-care provider visits and 2 binary variables representing whether the patient visited an endocrinologist or nephrologist within 3 years before the index date. We also included cardiovascular events and chronic kidney disease (CKD) diagnosed within 5 years before the index date. We defined cardiovascular events as hospitalizations for any acute myocardial infarction (*International Classification of Diseases*, *Ninth Revision* [ICD-9] code 410.*x*), cerebrovascular stroke (ICD-9 code 431, 434 and 436), percutaneous coronary intervention procedure (ICD-9 procedural codes 48.02, 48.03 and 48.09) or coronary artery bypass grafting procedure (ICD-9 procedural codes 48.11 to 48.19). We identified CKD using billing codes and hospital discharge abstracts (Supplementary Appendix 1) (16).

For the post-ESRD cohort, we characterized predialysis comorbidities, which have been shown to predict mortality in the dialysis population (congestive heart failure, high-risk malignancy, hypertension without complications, hypertension with complications, cerebrovascular disease, cardiomyopathy or chronic ulcer within 2 years of index date), in addition to the baseline covariates previously mentioned (17). Other variables included predialysis nephrology care (any nephrologist visit >4 months prior to index date), location of dialysis start (intensive care unit, hospital ward or outpatient), first dialysis modality as an outpatient (hemodialysis or peritoneal dialysis) and any hospitalization during the year prior to the index date. We identified baseline cardiovascular disease from hospital records and CORR (Supplementary Appendix 1).

In both the pre- and post-ESRD cohorts, we assessed the proportion of individuals <65 years of age who received any coverage under ODB as defined by ≥1 claims in the ODB database in the year prior to or after baseline. Although universal coverage under the ODB program is only available for those ≥65 years of age, the ODB database includes claims for drug reimbursement under several programs applicable to those <65 years of age, including Ontario Works (i.e. those on social assistance), Ontario Disability Support Program and Trillium Drug Program (those for whom prescription drug costs exceed 3% to 4% of after-tax income). Our data do not provide information on those covered through private insurers.

Outcomes

The primary outcome for the pre-ESRD cohort was a composite of adverse kidney outcomes, including acute kidney injury (AKI), ESRD (requiring dialysis) or kidney transplantation. Because most patients who develop AKI do not develop ESRD, we also examined AKI, ESRD (requiring dialysis) and kidney transplantation separately as secondary outcomes. We defined AKI as any *International Classification of Diseases* code for AKI during hospitalization (ICD-9 codes 584.5 to 584.9; *International Classification of Diseases 10th Revision* codes N17.*x*, N19.*x* and R34.*x*) or any billing code for acute dialysis or continuous renal replacement therapy (Supplementary Appendix 1). We defined ESRD requiring dialysis as chronic dialysis initiation as indicated by a record creation in CORR or a chronic dialysis billing code. Kidney transplantation was identified by the Trillium Gift of Life Network database, OHIP billing code or procedure code (Supplementary Appendix 1). We censored individuals at death.

The outcomes in the post-ESRD cohort were all-cause mortality and kidney transplantation. We followed individuals in both cohorts until March 31, 2011.

Statistical analysis

We compared baseline characteristics across SES quintiles using the chi-square test or analysis of variance as appropriate.

In the pre-ESRD cohort, we constructed Cox proportional hazard models to evaluate the impact of SES on time to the primary and secondary outcomes, adjusting for the covariates previously listed. We tested for interactions between SES and sex, and SES and age category (<65 vs ≥65 years of age). There was a significant interaction with age category; therefore, we stratified these models by age category. We conducted several sensitivity analyses. To ensure that median neighbourhood household income was a reasonable surrogate for an individual patient's household income, we repeated the analysis among seniors using an ODB flag to define low income based on an annual self-reported personal income <$16,018 or household income <$24,175 (13). To assess the potential role of death as a competing risk, we modelled the risk of mortality censoring for the primary outcome. We also conducted a competing risk analysis using Fine-Gray regression models to more formally account for death as a competing risk.

In the post-ESRD cohort, we constructed Cox proportional hazard models to examine the associations between SES and time to mortality, and SES and time to kidney transplantation (while censoring for death). We adjusted for baseline risk factors and tested for interactions as previously described. To assess whether disparities in kidney transplantation might explain the relationship between SES and mortality, we created separate models with and without adjusting for kidney transplantation as a time-varying covariate. We performed a competing risk analysis using the cause-specific approach by assessing the time to mortality while censoring for kidney transplantation.

We used SAS version 9.4 (SAS Institute, Cary, North Carolina, United States) for all analyses. Missing data were handled by censoring.

Results

ESRD incidence

The pre-ESRD cohort consisted of 396,593 individuals (Supplementary Figure 1). Baseline characteristics are summarized in Table 1 (Supplementary Tables 1 and 2). A disproportionate number of individuals were in the lowest 2 SES quintiles (45.2%). Individuals in the lowest SES quintile were more likely to be young

Table 1
Baseline characteristics of study population according to SES

Baseline characteristic	SES Quintile					
	Quintile 1 (lowest) (n=91,970)	Quintile 2 (n=86,508)	Quintile 3 (n=81,219)	Quintile 4 (n=71,088)	Quintile 5 (highest) (n=64,181)	Missing (n=1,627)
Age, mean ± SD, years	62.2±14.0	62.8±13.7	62.9±13.7	62.3±13.6	62.9±13.4	58.2±14.2
Age ≥65 years	43,991 (47.8)	42,448 (49.1)	39,827 (49.0)	33,306 (46.9)	31,183 (48.6)	540 (33.2)
Female	47,849 (52.0)	42,354 (49.0)	38,692 (47.6)	32,205 (45.3)	28,001 (43.6)	885 (54.4)
CVD event in previous 5 years	7,942 (8.6)	7,781 (9.0)	7,273 (9.0)	6,382 (9.0)	5,695 (8.9)	127 (7.8)
CKD in previous 5 years	15,469 (16.8)	14,003 (16.2)	13,148 (16.2)	11,085 (15.6)	10,113 (15.8)	234 (14.4)
Primary care visits in previous 1 year, median (IQR)	7 (3–12)	7 (3–12)	7 (3–11)	6 (3–11)	6 (3–10)	5 (2–9)
Any endocrinologist visit in previous 3 years	15,432 (16.8)	14,336 (16.6)	14,016 (17.3)	12,687 (17.8)	13,101 (20.4)	62 (3.8)
Any nephrologist visit in previous 3 years	4,761 (5.2)	4,265 (4.9)	3,979 (4.9)	3,484 (4.9)	3,323 (5.2)	55 (3.4)

CKD, chronic kidney disease; *CVD*, cardiovascular disease; *IQR*, interquartile range; *SES*, socioeconomic status.
Note: Values are n (%) or as otherwise indicated.

women. Baseline comorbidities were more common among those ≥65 years of age but varied little by SES. Primary care and nephrologist visits were higher in older groups, whereas endocrinologist visits were lower. Although all individuals ≥65 years of age receive prescription drug coverage under the ODB program, no individuals <65 years of age in the pre-ESRD cohort were receiving ODB coverage prior to index; 21.0% had ≥1 ODB claims in the year after index (including those turning 65 years of age during this window). In contrast, 40.5% of individuals <65 years of age in the post-ESRD cohort were receiving ODB coverage prior to initiating dialysis and 52.4% became eligible for ODB coverage in the year after initiation.

The total follow-up time was 4,091,931 person-years (mean, 10.3 years). There were 49,910 AKI events, 9,938 ESRD events requiring chronic dialysis, 1,447 kidney transplantation events and the primary outcome (any of the above) occurred in 56,227 individuals (14.2%).

SES was inversely associated with the risk of the primary outcome; however, the magnitude of this effect differed by age category (p<0.0001 for interaction). The relation between SES and the primary outcome was greater among those <65 years of age (quintiles 1:5 hazard ratio [HR], 1.43; 95% confidence interval [CI], 1.37–1.49) and was attenuated, although not eliminated, among those ≥65 years of age (quintiles 1:5 HR, 1.19; 95% CI, 1.15–1.24) (Table 2). These relationships were similar in both the age- and sex-adjusted model and the fully adjusted model. A sensitivity analysis among seniors using the ODB criteria for low income demonstrated a comparable HR (low vs high personal household income: HR, 1.12; 95% CI, 1.10–1.15).

A competing risk analysis demonstrated similar findings (Table 2). Mortality risks were similarly elevated in low SES groups <65 years of age with an attenuation among those ≥65 years of age (Supplementary Table 3).

Among individuals <65 years of age, we observed similar inverse gradients in the association between SES and both AKI and incident ESRD requiring chronic dialysis (Figure 1), but the opposite effect for SES and kidney transplantation. Being in the lowest SES was associated with a lower likelihood of receiving a kidney transplant. Among those ≥65 years of age, an inverse SES gradient was apparent for AKI, but there was no association between SES and ESRD (requiring chronic dialysis) or receipt of kidney transplantation.

Mortality after ESRD

For the post-ESRD cohort, low SES was associated with a modest increase in mortality in the lowest compared with the highest quintile (HR, 1.09; 95% CI, 1.02–1.16 among both age groups combined) (Table 3), with no interaction between SES and age category (p=0.24) or sex (p=0.08). Those in the lowest SES quintile were half as likely to receive a transplant compared with the highest quintile (HR, 0.55; 95% CI, 0.46–0.65), and the association between low SES and increased death was no longer present after adjusting for kidney transplantation as a time-varying covariate. A Fine-Gray competing risk analysis censoring for kidney transplantation showed similar results.

Table 2
Risk of AKI, ESRD requiring dialysis or kidney transplantation by SES quintile and age category

Age category, SES Q	Number of events	Event rate*	Age- and sex-adjusted model			Fully adjusted model†			Competing risk model†		
			HR	95% CI	p value	HR	95% CI	p value	HR	95% CI	p value
<65 years											
Q1 (lowest)	6,379	11.07	1.43	1.37–1.49	<0.0001	1.41	1.35–1.47	<0.0001	1.34	1.28–1.40	<0.0001
Q2	5,372	10.02	1.24	1.19–1.30	<0.0001	1.24	1.19–1.29	<0.0001	1.20	1.15–1.25	<0.0001
Q3	4,764	9.36	1.15	1.10–1.21	<0.0001	1.15	1.10–1.20	<0.0001	1.13	1.08–1.18	<0.0001
Q4	4,109	8.78	1.07	1.03–1.12	0.002	1.08	1.03–1.13	0.002	1.06	1.02–1.11	0.008
Q5 (highest)	3,432	8.34	1.00	-	-	1.00	-	-	1.00	-	-
≥65 years											
Q1 (lowest)	7,704	21.67	1.19	1.15–1.24	<0.0001	1.18	1.13–1.22	<0.0001	1.11	1.08–1.15	<0.0001
Q2	7,146	20.55	1.12	1.08–1.16	<0.0001	1.11	1.07–1.15	<0.0001	1.07	1.03–1.11	0.0005
Q3	6,629	20.16	1.08	1.05–1.13	<0.0001	1.08	1.05–1.13	<0.0001	1.05	1.01–1.09	0.009
Q4	5,475	19.67	1.05	1.01–1.09	0.01	1.05	1.01–1.09	0.01	1.03	0.99–1.07	0.19
Q5 (highest)	5,016	19.00	1.00	-	-	1.00	-	-	1.00	-	-

AKI, acute kidney injury; *CI*, confidence interval; *ESRD*, end-stage renal disease; *HR*, hazard ratio; *Q*, quintile; *SES*, socioeconomic status.
Note: Highest SES quintile is used as the reference group.
* Number of events per 1,000 person-years.
† Adjusted for age, sex, SES, baseline cardiovascular disease, baseline chronic kidney disease, primary care visits, any previous endocrinologist visit and any previous nephrologist visit.

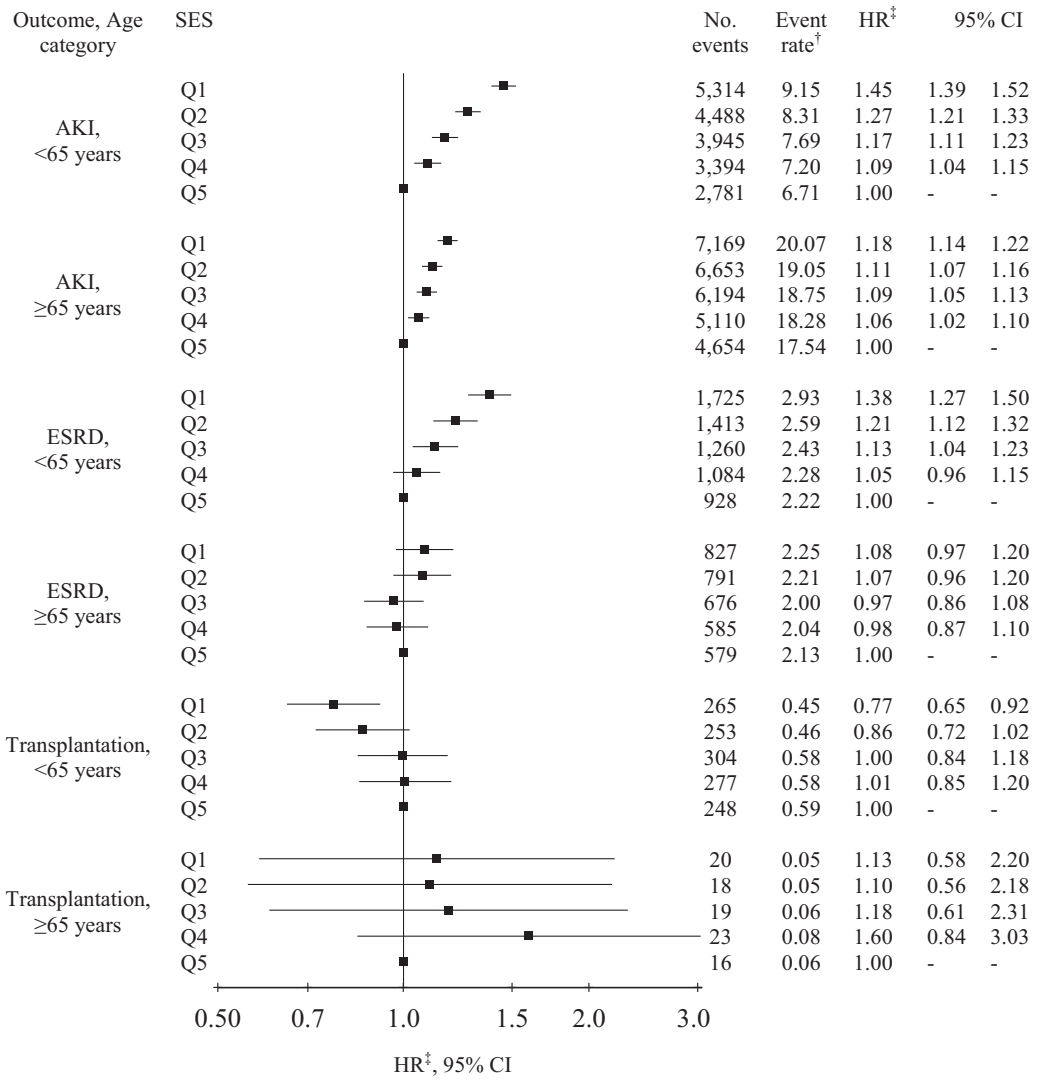

Figure 1. Risk of AKI, ESRD requiring dialysis or kidney transplantation by SES quintile (using highest quintile as the reference group) and age group. *AKI*, acute kidney injury; *CI*, confidence interval; *ESRD*, end-stage renal disease; *HR*, hazard ratio; *Q*, quintile; *SES*, socioeconomic status. †Number of events per 1,000 person-years. ‡Adjusted for age, sex, SES, baseline cardiovascular disease, baseline chronic kidney disease, primary care visits, any previous endocrinologist visit and any previous nephrologist visit.

Discussion

Our large population-based study demonstrated a significant inverse association between SES and adverse kidney outcomes in persons with diabetes. In a universal health-care setting with differential access to drug coverage, the SES gradient was attenuated in those ≥65 years of age—a group that universally receives prescription drug coverage as an insurable benefit. Furthermore, there was no association between SES and our secondary outcome of incident ESRD in this age group. Although there was a significant SES disparity in mortality within the post-ESRD cohort across ages, these effects were more modest and appeared to be explained by

Table 3
Risk of all-cause mortality and time to kidney transplantation after dialysis initiation by SES quintile

SES Q	Time to Death Models									Time to kidney transplantation model, censoring for death		
	Without adjusting for kidney transplantation			Adjusting for kidney transplantation			Censoring for kidney transplantation					
	HR	95% CI	p value	HR	95% CI	p value	HR	95% CI	p value	HR	95% CI	p value
Q1 (lowest)	1.09	1.02–1.16	0.01	1.06	0.99–1.13	0.10	1.05	0.98–1.13	0.14	0.55	0.46–0.65	<0.0001
Q2	1.07	0.99–1.14	0.07	1.04	0.97–1.12	0.22	1.04	0.97–1.12	0.23	0.63	0.53–0.75	<0.0001
Q3	1.00	0.93–1.07	0.93	0.98	0.92–1.06	0.64	0.97	0.91–1.05	0.47	0.80	0.67–0.95	0.01
Q4	1.03	0.96–1.11	0.38	1.03	0.96–1.11	0.43	1.04	0.97–1.12	0.28	0.85	0.71–1.01	0.06
Q5 (highest)	1.00	-	-	1.00	-	-	1.00	-	-	1.00	-	-

CI, confidence interval; *HR*, hazard ratio; *Q*, quintile; *SES*, socioeconomic status.
Notes: Highest SES quintile is used as the reference group. All models were adjusted for age, sex, predialysis care, location of care, dialysis modality, hospitalizations during previous year, baseline comorbidities and kidney transplantation.

differential access to kidney transplantation. Although the reasons for these disparities are multifactorial, our findings highlight the potential role of drug coverage in preventing ESRD, and the complex process of kidney transplantation appears to contribute to SES disparities in mortality after ESRD develops.

The SES differences in ESRD incidence that we observed are comparable with previous estimates (18). In one of the largest studies, the association between low SES and ESRD incidence varied according to ethnicity and sex, with relative risks ranging from 1.2 in black men to 2.8 in Native-American women in the US (7). However, the analysis could not control for health insurance status. Our results extend the literature by demonstrating an attenuation of SES disparities in the population ≥65 years of age with universal access to prescription drug coverage. These findings were robust even after accounting for death as a competing risk. Although these results are consistent with Canadian data showing similar phenomena with respect to cardiovascular outcomes (9), the degree to which policies pertaining to drug access contribute to these findings is unclear. Low SES may influence worse outcomes in diabetes in part because of poorer glycemic and blood pressure control (19). This complex relationship may be in turn mediated by factors including adherence and prescribing differences. In an American study, individuals with CKD without health insurance were 55% less likely to be receiving ACE inhibitor therapy (4). Small increases in Medicaid copay costs have been associated with decreased medication use (20). In contrast, among Canadian seniors with universal drug coverage, rates of ACE inhibitor use and statins did not differ across SES groups (21). Taken together, this evidence suggests that policies improving drug coverage could be expected to improve disparities in diabetes outcomes, but further research is required given the complexity of interrelated factors.

In the post-ESRD cohort, lower SES was associated with somewhat higher mortality and there was no significant interaction between SES and age. At the time of initiating dialysis, individuals <65 years of age were much more likely to be receiving drug reimbursement through ODB than their counterparts without ESRD. Furthermore, the association between SES and mortality among our post-ESRD cohort was not significant after accounting for differences in kidney transplantation. Other studies in the US have generally (22–25), but not consistently (26), found that lower SES is associated with reduced survival in patients on dialysis, particularly among blacks. However, only one study from 1990 (25) specifically examined people with diabetes. Our findings confirm this association in contemporary individuals with diabetes and extend the literature by highlighting the role of kidney transplantation as a potential cause for SES-related disparities in mortality in this population. Kidney transplantation is a cost-effective treatment that increases life expectancy and improves quality of life for most individuals with ESRD from diabetes (27). Compared with the highest quintile, we observed that those in the lowest SES quintile had a 23% lower HR of receiving a transplant. The HR was even lower for those in the post-ESRD cohort. Gaylin et al (28) reported that every $10,000 increase in income was associated with a 16% increase in the relative risk of receiving kidney transplantation. Higher SES has also been reported to be associated with reduced time on transplant waiting lists and an increased chance of receiving a live kidney donation (6,29).

The reasons for this association are thought to be multifactorial. Successful kidney transplantation is a complex process contingent on referral, assessment, medical clearance and survival while on the waiting list (12). Those with lower income seem to have fewer live kidney donors (30), and sociocultural issues such as lower educational attainment may be a barrier to accessing this complicated process (31). Insufficient medical insurance and lack of medication coverage for expensive immunosuppressive medications are also hypothesized to be barriers to transplantation (32); however, these factors were less relevant in our population because immunosuppressive medications are fully covered for kidney transplant recipients in Ontario. Finally, active substance abuse may be associated with lower SES, and this comorbidity reduces the likelihood of approval for transplantation because of concerns of graft loss (12). Addressing these multilevel barriers to kidney transplantation among individuals with low SES will require further targeted efforts in this population.

The strengths of our study include its population-based approach and data linkage using multiple, large health databases within a universal health-care setting. This resulted in standardized outcome measures, near-complete capture of baseline exposures and outcomes, virtually no loss to follow up and a sufficiently large sample size to allow multiple outcomes related to ESRD to be examined. However, there are some limitations to note. We did not directly measure household income, but our sensitivity analysis showed that area- and individual-level measures of SES provided comparable results. Unlike previous analyses that focused on the effect on race, we focused solely on SES because race was not captured in our administrative databases. We lacked information on access to private insurance plans, and our use of age as a surrogate for prescription medication coverage may have been subject to residual confounding from unaccounted factors. Our results may have been conservatively biased by access to ODB among some people <65 years of age (Supplementary Table 4). We also lacked information on laboratory parameters and self-funded prescriptions. However, evidence in our population suggests that medication adherence is similar across income levels when insurance coverage for medications is universal (21).

Conclusions

In our setting, universal access to medications as an insurable benefit and kidney transplantation were associated with reduced disparities in ESRD incidence and related mortality between higher and lower SES populations with diabetes. Considering that each ESRD event costs an estimated $100,000 per year per patient (33), addressing SES disparities may lead to substantial reductions in morbidity, mortality and overall health-care costs among low SES populations with diabetes.

Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Diabetes* at https://www.canadianjournalofdiabetes.com.

Acknowledgments

The Project for an Ontario Women's Health Evidence-based Report Study was funded by Echo: Improving Women's Health in Ontario, an agency of the Ministry of Health and Long-Term Care. GLB is funded by a Department of Medicine Mid-Career Research Award from the University of Toronto. CK is supported by the Canadian Institutes of Health Research Canada Graduate Scholarship and the University of Toronto Clinician Investigator Program. LLL is supported by a New Investigator Award from the Canadian Institutes for Health Research. ASB is funded by the Agency for Healthcare Research and Quality. This work was done as an outside activity. The views in this manuscript represent the authors and not necessarily the policy or views of the Agency for Health Care Research and Quality or the US Department of Health and Human Services. This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). Parts of this material are based on data and information compiled and provided by: MOHLTC, the Canadian

Institute for Health Information (CIHI), the Trillium Gift of Life Network (TGLN), and the Canadian Organ Replacement Register (CORR). The analyses, conclusions, opinions and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred.

Data from this study are held at ICES. Although data-sharing agreements prohibit ICES from making the data set publicly available, access may be granted to those who meet prespecified criteria for confidential access (www.ices.on.ca/DAS).

This study was previously presented in abstract form at the American Diabetes Association 77th Scientific Sessions, 9–13 June 2017, San Diego, California, United States.

Author Disclosures

Conflicts of interest: None.

Author Contributions

GLB conceptualized the study, designed the analyses and wrote the manuscript. CK researched data, interpreted the data and wrote the manuscript. SJK, BRS, ASB, LLL and DSF contributed to the design of the analyses, contributed to the discussion and edited the manuscript. GLB is the guarantor of this work, and as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Supplementary Appendix 1

Chronic Kidney Disease Codes

Description	CIHI-DAD diagnostic codes		OHIP fee codes
	ICD-9	ICD-10	
Acid/base/electrolyte/fluid imbalance	276.x	E86.0	
		E86.8	
		E87.0–E87.8	
Renal-related hypertension	403	I12.x	403
	403.1	I13.x	
	403.9	I15.00	
	404.0	I15.01	
	404.1	I15.10	
	404.9	I15.11	
	405.0		
	405.1		
	405.9		
Nephritis	582.0	N01.x	
	582.1	N03.x	
	582.2	N05.x	
	582.8	N07.x	
	582.9	N14.x	
	583.0	N15.0	
	583.1		
	583.2		
	583.4		
	583.8		
	583.9		
Acute renal disease	580.0	N00.x	580
	580.1	N04.x	581
	580.4	N08.x	584
	580.8	N17.x	
	580.9		
	581.0		
	581.1		
	581.2		
	581.3		
	581.8		
	581.9		
	584.6		
	584.7		
	584.8		
	584.9		
Renal failure	585	N18.x	585
	586.0	N19.x	
Renal sclerosis	587	N26.x	
Disorders resulting in impaired renal function	588.0	N25.x	
	588.1		
	588.8		
	588.9		
Other disorders of kidney, ureter	593.1	N13.4	593
	593.2	N13.5	
	593.3	N13.7	
	593.5	N28.0	
	593.6	N28.1	
	593.7	N28.80	
	593.8	N28.88	
	593.9		
Renal colic and urinary symptoms	788.0	N06.x	788
	788.1–788.9	N23	
		N39.2	
		R30.x	
		R33	
		R34	
		R35.x	
		R36	
		R39.x	
Transplant	V42.0	Z940	

Dialysis Definitions

Dialysis was defined as one the following:

a) CORR = first test date in Recipient_Haemodialysis and Recipient_peritoneal datasets.
b) Chronic dialysis based on Ontario Health Insurance Plan (OHIP) claims codes listed above with duration of ≥90 days. Duration was defined as the gap between any 2 consecutive claims, subtracted by any gaps in codes >21 days.

Definitions for locations of dialysis start are as follows:

a) ICU = first chronic dialysis OHIP claim during hospitalization from Canadian Institute of Health Information Discharge Abstract Database (CIHI-DAD) (admission date − 2 days to discharge date +2 days) and either:
   i. OHIP fee code for first chronic dialysis = ICU (see subsequently listed continuous renal replacement therapy [CRRT] codes) or
   ii. OHIP claim for admission to an ICU (G557, G558, G559, G400, G401, G402, G405, G406 or G407) with service date of first dialysis claim or earlier
b) Hospital ward = first chronic dialysis OHIP claim during hospitalization from CIHI-DAD (admission date − 2 days to discharge date +2 days) and not fulfilling criteria for ICU location in a) (first claim NOT an ICU [CRRT] fee code and no ICU admission fee codes of first dialysis claim or earlier)
c) Outpatient (all others)

Dialysis fee codes

1. Hemodialysis
   i. Acute hemodialysis: R849, R850, G323 or G325
   ii. Chronic hemodialysis: G326, G860, G862, G863, G865, G866 or G333
2. Peritoneal dialysis
   i. Acute peritoneal dialysis: G330 or G331
   ii. Chronic peritoneal dialysis: G332, G861 or G864
3. CRRT: G082, G083, G085, G090, G091, G092, G093, G095, G294, G295, G094 or G096

First outpatient dialysis modality definitions

a) Canadian Organ Replacement Register (CORR) variable: first test date in Recipient_Haemodialysis dataset = hemodialysis (HD) vs Recipient_peritoneal dataset = peritoneal dialysis (PD)
b) OHIP fee codes as first outpatient dialysis

Note for those starting in ICU (see previous variable) or hospital ward, first outpatient dialysis = first non-ICU claim after hospital discharge.

Coronary Artery Disease Definitions

CIHI-DAD

- Acute myocardial infarction: ICD-9 code 410.x (until March 31, 2002) or ICD-10 codes I21 and I22 (April 1, 2002 onwards) from CIHI-DAD (any diagnosis type, including suspected cases)
- History of percutaneous coronary intervention: Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (CCP) codes 48.02, 48.03 or 48.09 (until March 31, 2002) or Canadian Classification of Health Interventions (CCI) 1IJ50 or 1IJ57GQ (April 1, 2002 onwards) from CIHI-DAD or Canadian Institute of Health Information Same-day Surgery Database (CIHI-SDS)
- History of coronary artery bypass grafting: CCP codes 48.11 to 48.19, 48.2 (until March 31, 2002) or CCI 1IJ76 (April 1, 2002 onwards) from CIHI-DAD

CORR

- If myocardial_infarct_flag or coronary artery bypass graft flag = yes in RECIPIENT_TREATMENT dataset

Kidney Transplantation Definitions

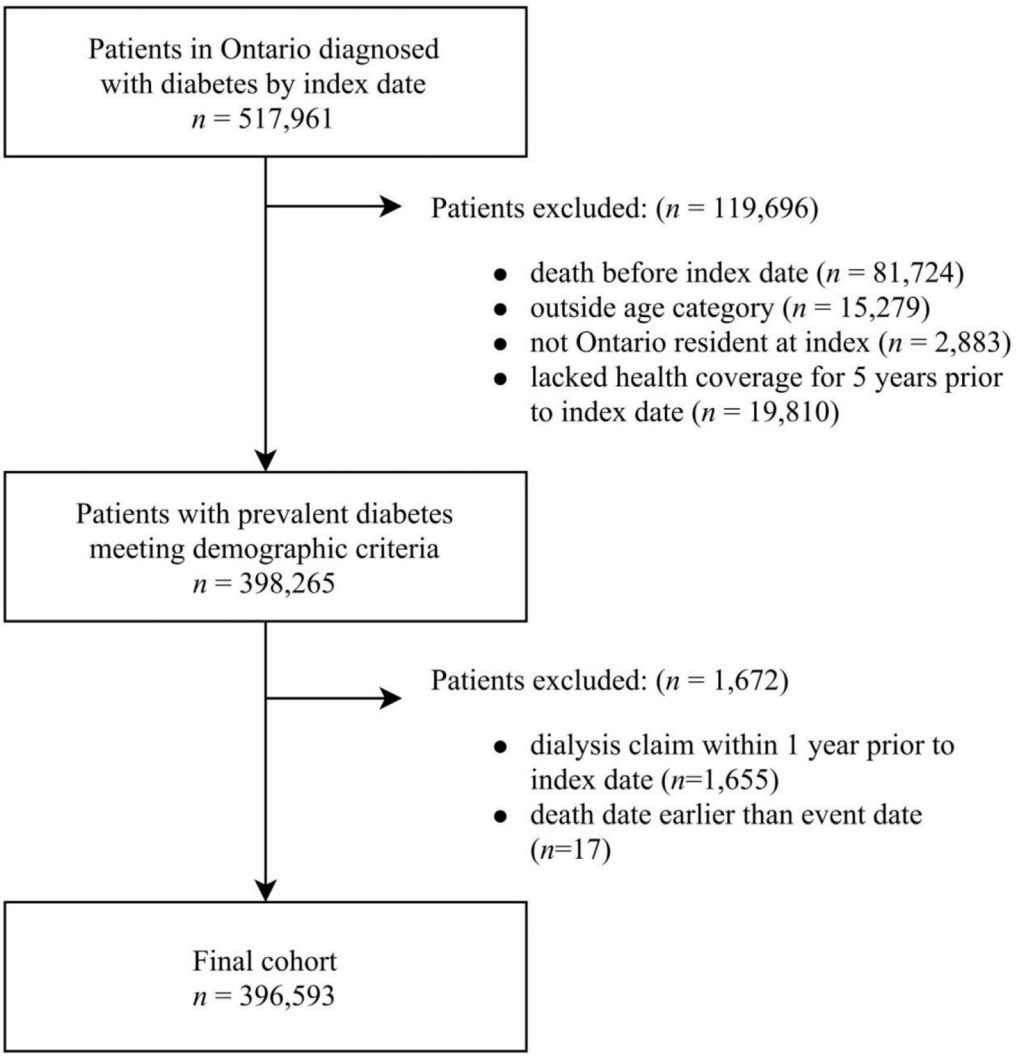
Kidney transplantation was defined based on any of the following:

- Record in Trillium Gift of Life Network database
- OHIP claim for kidney transplantation based on fee code: S434, S435, E769 or E771
- Procedure codes from CIHI-DAD: CCP V42.0 (April 1, 1997 to March 31, 2002) or incode Z940 (April 1, 2002 to March 31, 2011)

Kidney Transplantation Fee Codes

OHIP fee codes		CIHI-DAD procedure codes	
Description	Fee code	ICD-9	ICD-10
Retransplant	S434	6759	1PC85LAXXJ
Transplant	S435		1PC85LAXXK
Transplant team fee	E769	V42.0	Z940
Retransplant	E771		

CCI, Canadian Classification of Health Interventions; *CCP*, Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures; *CIHI-DAD*, Canadian Institute of Health Information Discharge Abstract Database; *CIHI-SDS*, Canadian Institute of Health Information Same-day Surgery Database; *CORR*, Canadian Organ Replacement Register; *CRRT*, continuous renal replacement therapy; *HD*, hemodialysis; *ICD-9*, *International Classification of Diseases, Ninth Revision*; *ICD-10*, *International Classification of Diseases 10th Revision*; *ICU*, intensive care unit; *OHIP*, Ontario Health Insurance Plan; *PD*, peritoneal dialysis.



Supplementary Figure 1. Flow diagram displaying patients meeting inclusion and exclusion criteria for the study cohort.

Supplementary Table 1
Baseline characteristics of the study population according to sex

Baseline characteristic	Female (n=189,986)	Male (n=206,607)	Total (N=396,593)
Age, mean ± SD, years	63.8±14.3	61.5±13.0	62.6±13.7
Age ≥65 years	99,527 (52.4)	91,768 (44.4)	191,295 (48.2)
SES quintile 1 (lowest)	47,849 (25.2)	44,121 (21.4)	91,970 (23.2)
SES quintile 2	42,354 (22.3)	44,154 (21.4)	86,508 (21.8)
SES quintile 3	38,692 (20.4)	42,527 (20.6)	81,219 (20.5)
SES quintile 4	32,205 (17.0)	38,883 (18.8)	71,088 (17.9)
SES quintile 5 (highest)	28,001 (14.7)	36,180 (17.5)	64,181 (17.9)
CVD event in previous 5 years	13,878 (7.3)	21,322 (10.3)	35,200 (8.9)
CKD in previous 5 years	29,641 (15.6)	34,411 (16.7)	64,052 (16.2)
Number of primary care visits in previous 1 year, median (IQR)	7 (4–12)	6 (3–11)	7 (3–11)
Any endocrinologist visit in previous 3 years	35,236 (18.5)	34,398 (16.6)	69,634 (17.6)
Any nephrologist visit in previous 3 years	9,294 (4.9)	10,573 (5.1)	19,867 (5.0)

CKD, chronic kidney disease; *CVD*, cardiovascular disease; *IQR*, interquartile range; *SES*, socioeconomic status.
Note: Values are n (%) or as otherwise indicated.

Supplementary Table 2
Baseline characteristics of the study population according to age category

Baseline characteristic	Age <65 years (n=205,298)	Age ≥65 years (n=191,295)	Total (N=396,593)
Age, years, mean ± SD	51.8±8.9	74.2±6.7	62.6±13.7
Female	90,459 (44.1)	99,527 (52.0)	189,986 (47.9)
SES quintile 1 (lowest)	47,979 (23.4)	43,991 (23.0)	91,970 (23.2)
SES quintile 2	44,060 (21.5)	42,448 (22.2)	86,508 (21.8)
SES quintile 3	41,392 (20.2)	39,827 (20.8)	81,219 (20.5)
SES quintile 4	37,782 (18.4)	33,306 (17.4)	71,088 (17.9)
SES quintile 5 (highest)	32,998 (16.1)	31,183 (16.3)	64,181 (16.2)
CVD event in previous 5 years	11,534 (5.6)	23,666 (12.4)	35,200 (8.9)
CKD in previous 5 years	26,971 (13.1)	37,081 (19.4)	64,052 (16.2)
Number of primary care visits in previous 1 year, median (IQR)	6 (3–10)	8 (4–12)	7 (3–11)
Any endocrinologist visit in previous 3 years	40,257 (19.6)	29,377 (15.4)	69,634 (17.6)
Any nephrologist visit in previous 3 years	9,084 (4.4)	10,783 (5.6)	19,867 (5.0)

CKD, chronic kidney disease; *CVD*, cardiovascular disease; *IQR*, interquartile range; *SES*, socioeconomic status.
Note: Values are n (%) or as otherwise indicated.

Supplementary Table 3
Risk of death by SES quintile and age category, censoring for primary outcome (AKI, chronic dialysis initiation or kidney transplantation)

Age category, SES Q	Number of events	Event rate*	Age- and sex-adjusted model			Fully adjusted model		
			HR	95% CI	p value	HR†	95% CI	p value
<65 years of age								
Q1 (lowest)	6,379	11.07	1.43	1.38–1.49	<0.0001	1.39	1.34–1.44	<0.0001
Q2	5,372	10.02	1.26	1.21–1.30	<0.0001	1.23	1.18–1.27	<0.0001
Q3	4,764	9.36	1.15	1.11–1.20	<0.0001	1.13	1.09–1.18	<0.0001
Q4	4,109	8.78	1.08	1.04–1.12	0.0002	1.07	1.03–1.11	0.0014
Q5 (highest)	3,432	8.34	1.00	-	-	1.00	-	-
≥65 years of age								
Q1 (lowest)	7,704	21.67	1.10	1.08–1.12	<0.0001	1.08	1.06–1.10	<0.0001
Q2	7,146	20.55	1.08	1.05–1.10	<0.0001	1.06	1.04–1.08	<0.0001
Q3	6,629	20.16	1.05	1.03–1.07	<0.0001	1.04	1.02–1.06	0.0002
Q4	5,475	19.67	1.04	1.02–1.06	0.0001	1.03	1.01–1.06	0.0026
Q5 (highest)	5,016	19.00	1.00	-	-	1.00	-	-

AKI, acute kidney injury; *CI*, confidence interval; *HR*, hazard ratio; *Q*, quintile; *SES*, socioeconomic status.
Note: Highest SES quintile is used as the reference group.
* Number of events per 1,000 person-years.
† Adjusted for age, sex, SES, baseline cardiovascular disease, baseline chronic kidney disease, primary care visits, any previous endocrinologist visit and any previous nephrologist visit.

Supplementary Table 4
Proportion of people <65 years of age who had at least 1 claim reimbursed through the ODB program

Cohort	At least 1 ODB claim (%)	
	1 year before index date	1 year after index date
Pre-ESRD	0.0	21.0
Post-ESRD	40.5	52.4

ESRD, end-stage renal disease; *ODB*, Ontario Drug Benefit.