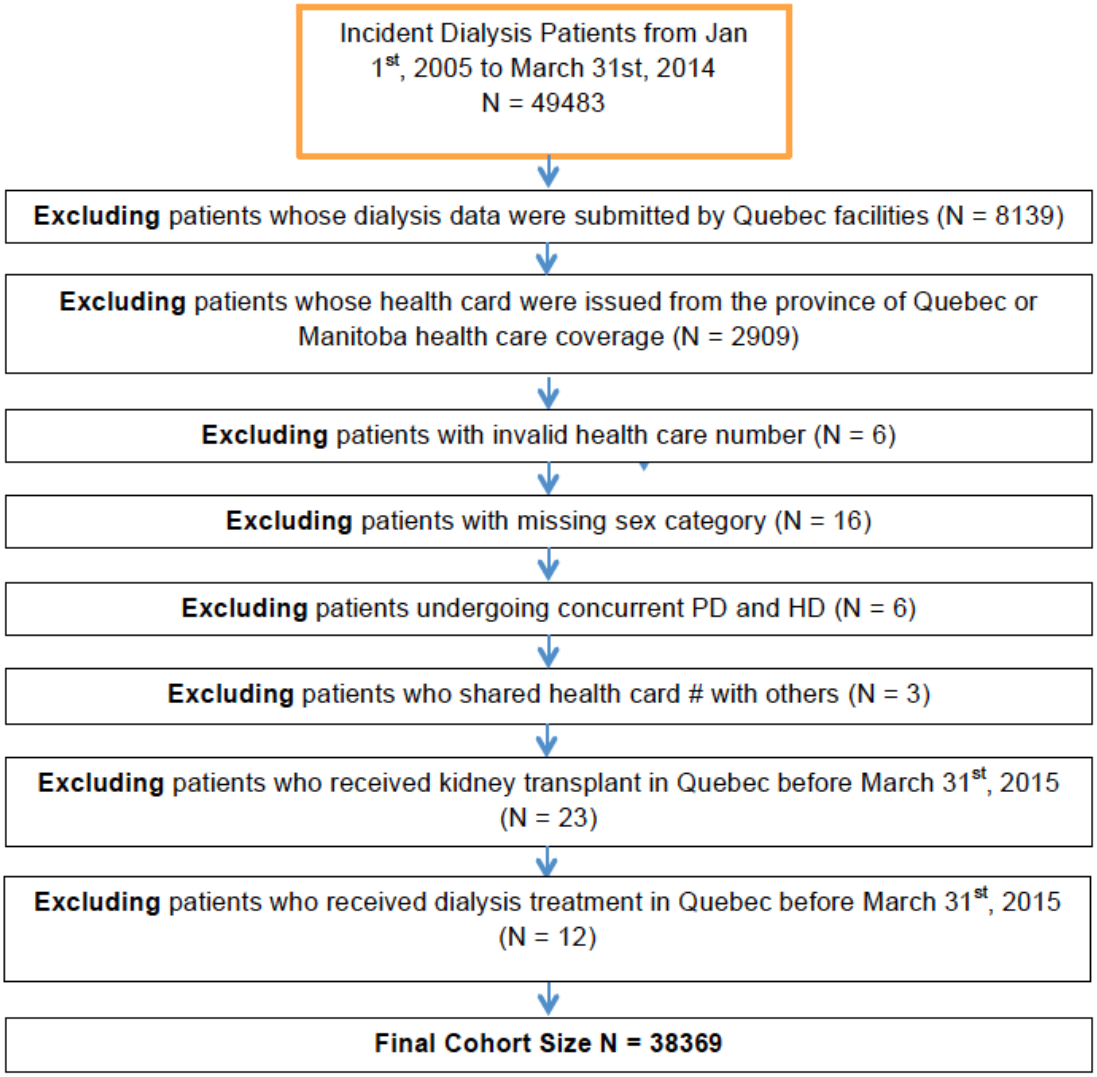
Supplementary Material



Supplementary Figure 1: Cohort creation

Supplementary Table 1: Crude all-cause hospitalization rate (admissions per patient year) over time by age group

Age group	7 days[a]	30 days	3 months	6 months	1 year
0-17	1.67	2.48	2.49	2.42	2.47
18-44	1.38	1.31	1.22	1.18	1.14
45-64	1.27	1.32	1.18	1.12	1.06
≥65	1.40	1.35	1.26	1.18	1.10

[a]All time points are relative to the start of dialysis

Supplementary Table 2: Crude infection-related hospitalization rate (admissions per patient year) over time by age group

Age group	7 days[a]	30 days	3 months	6 months	1 year
0-17	0.00	0.13	0.16	0.18	0.21
18-44	0.08	0.12	0.12	0.11	0.12
45-64	0.09	0.13	0.12	0.12	0.12
≥65	0.12	0.13	0.13	0.13	0.12

[a]All time points are relative to the start of dialysis

Supplementary Table 3: Crude all-cause in-hospital mortality rate (per patient year) over time by age group

Age group	7 days[a]	30 days	3 months	6 months	1 year
0-17	0.000	0.000	0.015	0.008	0.013
18-44	0.013	0.018	0.019	0.025	0.022
45-64	0.033	0.047	0.057	0.058	0.060
≥65	0.089	0.127	0.139	0.131	0.129

[a]All time points are relative to the start of dialysis

Supplementary Table 4: Comparative risk of hospitalization over time by dialysis modality

Modality effect by time on dialysis	All-cause hospitalizations HR (95% CI)	Infection-related hospitalizations HR (95% CI)
HD		
≤7 days (referent)	1.00	1.00
8-30 days	0.76 (0.68-0.86)	0.87 (0.56-1.36)
31-90 days	0.62 (0.53-0.72)	0.98 (0.55-1.74)
91 days-6 months	0.56 (0.47-0.63)	0.69 (0.37-1.29)
6 months-1 year	0.53 (0.45-0.63)	0.52 (0.22-1.24)
PD		
≤7 days (referent)	1.27 (1.07-1.50)	2.05 (1.19-3.55)
8-30 days	0.73 (0.62-0.85)	1.24 (0.70-2.19)
31-90 days	0.52 (0.44-0.62)	1.38 (0.77-2.49)
91 days-6 months	0.53 (0.45-0.63)	1.43 (0.76-2.71)
6 months-1 year	0.56 (0.47-0.67)	1.34 (0.56-3.22)

Appendix A

Checklist of recommendations for reporting of observational studies using the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement

	Item No	STROBE items	RECORD items	Reported
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract. (b) Provide in the abstract an informative and balanced summary of what was done and what was found.	(1.1) The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. (1.2) If applicable, the geographic region and time frame within which the study took place should be reported in the title or abstract. (1.3) If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Abstract
Introduction				
Background/ rationale	2	Explain the scientific background and rationale for the investigation being reported.		Introduction
Objectives	3	State specific objectives, including any		Introduction

		prespecified hypotheses.		
Methods				
Study design	4	Present key elements of study design early in the paper.		Methods
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection.		Methods
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. (b) For matched studies, give matching criteria and number of exposed and unexposed.	(6.1) The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. (6.2) Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published	Methods, Supplemental Figure 1

			elsewhere, detailed methods and results should be provided. (6.3) If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	(7.1) A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Methods
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of		Methods

		assessment methods if there is more than one group.		
Bias	9	Describe any efforts to address potential sources of bias.		Methods
Study size	10	Explain how the study size was arrived at.		Methods and Supplemental Figure 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why.		Methods
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding. (b) Describe any methods used to examine subgroups and interactions. (c) Explain how missing data were addressed. (d) If applicable, explain how loss to follow-up was addressed. (e) Describe any sensitivity analyses.		Methods
Data access and cleaning methods		N/A	(12.1) Authors should describe the extent to	

			which the investigators had access to the database population used to create the study population. (12.2) Authors should provide information on the data cleaning methods used in the study.	
Linkage		N/A	(12.3) State whether the study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	Methods
Results				
Participants	13	(a) Report numbers of individuals at each stage of study--e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing	(13.1) Describe in detail the selection of the persons included in the study (i.e., study population selection), including filtering based on data quality, data availability, and linkage. The selection of included persons	Supplemental Figure 1 & Results

		follow-up, and analyzed. (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram.	can be described in the text and/or by means of the study flow diagram.	
Descriptive data	14	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders. (b) Indicate number of participants with missing data for each variable of interest. (c) Summarize follow-up time (e.g. average and total amount).		Results
Outcome data	15	Report numbers of outcome events or summary measures over time.		Results
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g. 95% confidence		Results

		interval). Make clear which confounders were adjusted for and why they were included. (b) Report category boundaries when continuous variables were categorized. (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period.		
Other analyses	17	Report other analyses done (e.g. analyses of subgroups and interactions, and sensitivity analyses).		Results
Key results	18	Summarize key results with reference to study objectives.		Discussion
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	(19.1) Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured	Discussion

			confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.		Discussion
Generalizability	21	Discuss the generalizability (external validity) of the study results.		Discussion
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based.		Acknowledgments & Funding
Accessibility of protocol, raw data, and programming code		N/A	(22.1) Authors should provide information on how to access any supplemental information such	

		as the study protocol, raw data, or programming code.

Appendix B: Codes used to define infection related hospitalizations

Infection	ICD-10-CA diagnosis codes	Diagnosis type
1. Infection due to a vascular access device used for hemodialysis	T82.7 Infection and inflammatory reaction due to other cardiac and vascular devices, implants and grafts AND Y84.1 Kidney dialysis NOTE: T82.7 will include all types of infections associated with a VAD, such as cellulitis, abscess, sepsis, endocarditis, etc. • Endocarditis associated with a VAD will be identified with an additional code I33.- as a diagnosis type (3) on the abstract along with codes T82.7 and Y84.1. • Sepsis associated with a VAD will be identified with an additional code A40-A41 as a diagnosis type (3) on the abstract along with codes T82.7 and Y84.1.	T82.7 as diagnosis type (M, 1, 2, W, X or Y) AND Y84.1 as diagnosis type (9) To specifically identify endocarditis associated with a VAD: T82.7 as diagnosis type (M, 1, 2, W, X or Y) I33.- as diagnosis type (3) Y84.1 as diagnosis type (9) To specifically identify sepsis associated with a VAD: T82.7 as diagnosis type (M, 1, 2, W, X or Y) A40-A41 as diagnosis type (3) Y84.1 as diagnosis type (9)
Infection	**ICD-10-CA diagnosis codes**	**Diagnosis type**
2. Infection due to a peritoneal catheter used for peritoneal dialysis	T85.7 Infection and inflammatory reaction due to other internal prosthetic devices, implants and grafts AND Y84.1 Kidney dialysis NOTE: T85.7 will include all types of infections associated with a peritoneal catheter, such as cellulitis, abscess, sepsis, endocarditis, peritonitis, etc. • Endocarditis associated with a peritoneal catheter will be identified with an additional code I33.- as a diagnosis type (3) on the abstract along with codes T85.7 and Y84.1. • Sepsis associated with a peritoneal catheter will be identified with an additional code A40-A41 as a diagnosis type (3) on the abstract along with codes T85.7 and Y84.1. • Peritonitis associated with a peritoneal catheter will be identified with an additional code	T85.7 as diagnosis type (M, 1, 2, W, X or Y) AND Y84.1 as diagnosis type (9) To specifically identify endocarditis with a peritoneal catheter: T85.7 as diagnosis type (M, 1, 2, W, X or Y) I33.- as diagnosis type (3) Y84.1 as diagnosis type (9) To specifically identify sepsis associated with a peritoneal catheter T85.7 as diagnosis type (M, 1, 2, W, X or Y) A40-A41 as diagnosis type (3) Y84.1 as diagnosis type (9) To specifically identify peritonitis associated with a peritoneal catheter

	K65.- as a diagnosis type (3) on the abstract along with codes T85.7 and Y84.1.	T85.7 as diagnosis type (M, 1, 2, W, X or Y) K65.- as diagnosis type (3) Y84.1 as diagnosis type (9)
Infection	**ICD-10-CA diagnosis codes**	**Diagnosis type**
3. Infection due to cardiac and vascular devices, implants and grafts (for arteriovenous fistula)	T82.7 Infection and inflammatory reaction due to other cardiac and vascular devices, implants and grafts AND Y83.2 Surgical operation with anastomosis, bypass or graft NOTE: T82.7 will include all types of infections associated with a cardiac and vascular devices, implants and grafts, such as cellulitis, abscess, sepsis, endocarditis, etc. Endocarditis associated with cardiac and vascular devices, implants and grafts will be identified with an additional code I33.- as a diagnosis type (3) on the abstract along with codes T82.7 and Y83.2. Sepsis associated with cardiac and vascular devices, implants and grafts will be identified with an additional code A40-A41 as a diagnosis type (3) on the abstract along with codes T82.7 and Y83.2.	T82.7 as diagnosis type (M, 1, 2, W, X or Y) AND Y83.2 as diagnosis type (9) Data limitation: Cannot strictly identify that this is an infection of an 'arteriovenous fistula'. AV fistulas are lumped together with other types of bypasses and grafts. To know if this is a qualifying case of infection due to arteriovenous fistula there would have to be data linkage to find out if this patient's mode of dialysis is via an arteriovenous fistula. To specifically identify endocarditis associated with a with cardiac and vascular devices, implants and grafts T82.7 as diagnosis type (M, 1, 2, W, X or Y) I33.- as diagnosis type (3) Y83.2 as diagnosis type (9) To specifically identify sepsis associated with a with cardiac and vascular devices, implants and grafts T82.7 as diagnosis type (M, 1, 2, W, X or Y) A40-A41 as diagnosis type (3) Y83.2 as diagnosis type (9)
Infection	**ICD-10-CA diagnosis codes**	**Diagnosis type**
4. Peritonitis following peritoneal dialysis	T80.2 Infections following infusion, transfusion and therapeutic injection AND K65.- Peritonitis AND Y84.1 Kidney dialysis Sepsis following peritoneal dialysis will be identified with an additional code A40-A41 as a	T80.2 as diagnosis type (M, 1, 2, W, X or Y) AND K65.- as diagnosis type (3) AND Y84.1 as diagnosis type (9) T80.2 as diagnosis type (M, 1, 2, W, X or Y) AND

	diagnosis type (3) on the abstract along with codes T80.2 and Y84.1.	A40-A41 as diagnosis type (3) AND Y84.1 as diagnosis type (9)
5. Peritonitis in a dialysis patient	K65.- Peritonitis	K65.- as diagnosis type (M, 1, 2, W, X or Y)
6. Acute and subacute endocarditis in a dialysis patient	I33.- Acute and subacute endocarditis	I33.- as diagnosis type (M, 1, 2, W, X or Y)
7. Sepsis in a dialysis patient	A40.- Streptococcal sepsis OR A41.- Other sepsis	A40.- as diagnosis type (M, 1, 2, W, X or Y) OR A41.- as diagnosis type (M, 1, 2, W, X or Y)
8. Infection of intervertebral disc (pyogenic) in a dialysis patient	M46.3- Infection of intervertebral disc (pyogenic)	M46.3- as diagnosis type (M, 1, 2, W, X or Y)
9. Discitis, unspecified in a dialysis patient	M46.4- Discitis, unspecified	M46.4- as diagnosis type (M, 1, 2, W, X or Y)

Hospitalizations in Dialysis Patients in Canada: A National Cohort Study

Word count: 408

Abrégé

Contexte : Le taux d'hospitalisation des patients dialysés n'avait jamais fait l'objet d'une étude pancanadienne. Une connaissance approfondie de la portée et des variables associées aux hospitalisations orientera les mesures d'amélioration.

Objectif de l'étude : L'étude visait à mieux évaluer les risques d'hospitalisations des patients dialysés; toutes causes confondues ou liées spécifiquement à une infection.

Type d'étude : Il s'agit d'une étude de cohorte rétrospective fondée sur des bases de données administratives en santé.

Cadre de l'étude : L'étude couvrait les provinces et territoires du Canada à l'exception du Québec et du Manitoba.

Patients : L'étude a porté sur tous les patients dialysés à vie dont le traitement avait commencé entre le 1er janvier 2005 et le 31 mars 2014. Les patients ayant reçu une greffe rénale ont été exclus.

Mesures : Les caractéristiques initiales des patients ont été consignées, et la modalité de dialyse a été traitée comme une co-variable sujette à changement dans le temps. La principale issue d'intérêt était une hospitalisation due à une infection directement liée à la dialyse, ou une hospitalisation toutes causes confondues.

Méthodologie : Les taux bruts d'hospitalisations toutes causes confondues (global) et d'hospitalisations liées à une infection ont été calculés en années-patients (HAP) à différents moments suivant le début de la dialyse (7 jours, 30 jours, 3 mois, 6 mois et 12 mois). Un modèle stratifié de fragilité à distribution gamma a été employé pour i) répertorier les hospitalisations répétées; ii) déterminer l'interrécurrence et le lien de dépendance entre les hospitalisations pour chaque patient; et iii) établir le rapport de risque (RR) attribué à chaque covariable d'intérêt.

Résultats : En tout, 38 369 patients dialysés, soit 38 088 adultes et 281 patients mineurs (moins de 18 ans) ont été inclus dans l'étude. Au cours de la période étudiée, on a répertorié 112 374 hospitalisations, dont 11,5 % étaient dues à une infection en lien direct avec la dialyse. Le taux d'hospitalisations global était similaire pour tous les groupes d'âge chez les patients adultes. Par exemple, chez les patients âgés de 65 ans et plus, ce taux se situait respectivement à 1,40 HAP, à 1,35 HAP et à 1,18 HAP lorsque calculé 7 jours, 30 jours et 6 mois après l'initiation de la dialyse. Lorsque comparé au groupe des 45-64 ans, le taux d'hospitalisations global s'est avéré plus élevé chez les patients pédiatriques (1,67 HAP à 7 jours,

2,48 HAP à 30 jours et 2,47 HAP à 6 mois) post-initiation de la dialyse (RR : 2,73; IC 95 % : 2,37-3,15). Dans les 7 jours suivant l'initiation du traitement, les patients traités par dialyse péritonéale présentaient un risque plus élevé d'hospitalisation toutes causes confondues (RR : 1,27; IC 95 % : 1,07-1,50) ou d'hospitalisation liée à une infection (RR : 2,05; IC 95 % : 1,19-3,55) que les patients hémodialysés. Par contre, cet écart entre les modalités de dialyse n'était plus observable au-delà des sept premiers jours. Enfin, le fait d'être autochtone ou de sexe féminin s'avérait un facteur de risque d'hospitalisation significatif (toutes causes confondues).

Limites de l'étude : Plusieurs facteurs limitent la portée des résultats : i) la cohorte comptait trop peu de patients hémodialysés à domicile pour permettre une analyse de ce sous-groupe; ii) les hospitalisations relatives à une infection ont été établies à l'aide de codes diagnostiques; et iii) les patients dialysés résidant au Québec et au Manitoba étaient exclus de l'étude.

Conclusion : Au Canada, au-delà des sept jours suivant l'initiation de la dialyse, la modalité employée n'a plus d'influence sur les taux d'hospitalisations. Cependant, à tous les moments post-initiation mesurés, les taux d'hospitalisations se sont avérés plus élevés chez les patients pédiatriques que chez les adultes.