Supplementary Appendix

Supplement to: Hildebrand AM, Liu K, Shariff SZ et al. Characteristics and outcomes of acute kidney injury treated with dialysis during pregnancy and the postpartum period.

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Figure S1. Selection of pregnancy cohort, 1997 to 2011 (1,918,789 deliveries)

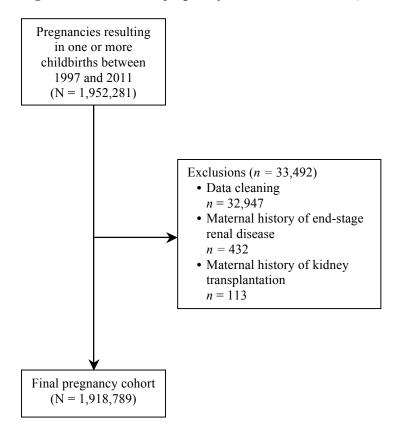


Table S1. Complications among pregnancies affected by acute kidney injury according to timing of dialysis initiation.

	Timi	ing of initiation	on of acute dia	lysis
	First	Second	Third	Post-
Complication, n (%)	Trimester	Trimester	Trimester	Partum
	N = 22	N = 23	N = 42	N = 101
Multifetal gestation	0	0	0	≤ 5
Caesarean delivery	≤ 5	6	16	≥ 54
Medical complications *				
Hyperemesis gravidarum	≤ 5	0	0	≥ 6
Diabetes mellitus †	≤ 5	≤ 5	≤ 5	8
Gestational hypertension	0	≤ 5	0	≤ 5
Preeclampsia	0	≤ 5	≤ 5	34
Thrombotic microangiopathy ‡	0	≤ 5	≤ 5	23
Pregnancy-related liver disease §	0	0	0	≤ 5
Heart failure	0	0	≤ 5	≥ 25
Pyelonephritis	0	0	≤ 5	≤ 5
Sepsis	0	≤ 5	≤ 5	30
Amniotic fluid embolism	0	0	0	≤ 5
Placenta previa	≤ 5	0	≤ 5	≤ 5
Placental abruption	≤ 5	≤ 5	≤ 5	≤ 5
Postpartum hemorrhage	≤ 5	≤ 5	≤ 5	28
Any of the above medical complications	10	8	24	88

To comply with privacy regulations for minimizing the chance of identification of a study participant, numbers of participants are suppressed in the case of 5 or fewer participants (reported as \le 5).

* Medical complications of pregnancy were ascertained from administrative database codes during pregnancy and the postpartum period.

† Diabetes mellitus includes preexisting type 1 diabetes mellitus, preexisting type 2 diabetes mellitus, and gestational diabetes.

† Thrombotic microangiopathy includes HELLP syndrome and thrombotic thrombocytopenic purpura.

Pregnancy-related liver diseases includes unspecified liver and biliary diseases in pregnancy.

Table S2. Checklist of Recommendations for Reporting of Observational Studies Using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Guidelines

	Item No.	Recommendation	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	Title, 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 prespecified hypotheses	Introduction
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	Methods
		(b) For matched studies, give matching criteria and number of exposed and unexposed	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders and effect modifiers. Give diagnostic criteria, if applicable	Methods
Data sources /	8	For each variable of interest, give sources of data and details of methods of assessment	Methods,
measurement		(measurement). Describe comparability of assessment methods if there is more than one group	Table S4
Bias	9	Describe any efforts to address potential sources of bias	Methods
Study size	10	Explain how the study size was arrived at	Methods
Quantitative	11	Explain how quantitative variables were handled in the analyses. If applicable,	Methods
variables		describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Methods
		(b) Describe any methods used to examine subgroups and interactions	Methods
		(c) Explain how missing data were addressed	Methods
		(d) If applicable, explain how loss to follow-up was addressed	Not applicable
		(e) Describe any sensitivity analyses	Not applicable
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 follow-up, and analyzed	Results
		(b) Give reasons for nonparticipation at each stage	Results
		(c) Consider use of a flow diagram	Methods, Figure S1
Descriptive data	14	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	Results, Tables 1-2
		(b) Indicate number of participants with missing data for each variable of interest	Table S3
		(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, Tables 3,4,S1
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g. 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Results, Tables 3-4
		(b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a	Results, Tables 1-2 Not applicable
Other analyses	17	meaningful time period Report other analyses done—e.g. analyses of subgroups and interactions, and	Not applicable
Discussion		sensitivity analyses	
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	Discussion
Interpretation	20	imprecision. Discuss both direction and magnitude of any potential bias Give a cautious overall interpretation of results considering objectives, limitations,	Discussion
Generalizability	21	multiplicity of analyses, results from similar studies, and other relevant evidence 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	Acknowledgements

Table S3. Missing data for cohort of 1,918,789 pregnancies resulting in childbirth, 1997 to 2011

Database	Dates Available	Dates Required	Pregnancies Affected	Data Affected
OHIP	July 1991 to March 2013	April 1991 to March 2012	Childbirths between January 1997 and April 1997	Selected pre-pregnancy maternal characteristics (chronic kidney disease, thrombotic microangiopathy treated with plasma exchange, nephrology consultation) in all affected pregnancies.
ORGD	January 1990 to December 2009	January 1997 to March 2012	Childbirths between January 2010 and December 2011	Cause of death in all affected pregnancies.
ORGD	January 1990 to March 2011	January 1997 to March 2012	Childbirths between April 2011 and December 2011	Timing of death in all affected pregnancies.
RPDB	April 1990 to March 2013	January 1997 to March 2012	Childbirths between January 1997 to March 2012	Income quintile in 9851 (0.51%) of affected pregnancies. Rural residence in 2488 (0.13%) of affected pregnancies.

Abbreviations: OHIP, Ontario Health Insurance Plan using fee and diagnostic codes; RPDB, Registered Persons Database; ORGD, Ontario Registrar General Death database.

Table S4. Healthcare database codes used for definition of exclusion criteria, baseline characteristics, and outcomes measurements.

Variable *	Source	Codes
Exclusion Criteria		
Chronic dialysis	CIHI-DAD OHIP	ICD-9: V451, V560, V568, 36104 ICD-10: T824, Y602, Y612, Y622, Y841, Z49, Z992, N180, E1022, E1023, E1122, E1123, E1322, E1323, E1422, E1423, V560, V568, 36104 CCP: 5127, 5142, 5143 CCI: 1OT53DATS, 1OT53HATS, 1OT53LATS, 1SY55LAFT, 7SC59QD, 1KY76 OHIP: R850, G324, G336, G327, G862, G865, G099, R825, R826, R827, R833, R840, R841, R843, R848, R851, Z450, Z451, Z452, G864, R852, R853, R854, R885, G333, H540, H740
Kidney transplantation	CIHI-DAD OHIP	ICD-9: V420, 99681 ICD-10: T861, N165, Z940 CCP: 6743, 675 CCI: 1PC85 OHIP: E762, S435, E769, S434, E771, Z631, G347, G348, G412, G408, G409
Maternal Outcomes		
Acute kidney injury treated with dialysis	CIHI-DAD OHIP	Hemodialysis CCI: 1PZ21HQBR CCP: 5195, 6698 OHIP: R849, G323, G325, G866 Continuous veno-venous hemodialysis CCI: 1PZ21HQBS OHIP: G082, G083, G085, G090, G091, G092, G093, G095, G294, G295 Peritoneal dialysis CCI: 1PZ21HPD4 OHIP: G330, G331
Mortality	RPDB ORGD	N/A
Chronic dialysis †	OHIP	OHIP: R849, G323, G325, G326, G860, G863, G866, G330, G331, G332, G861, G082, G083, G085, G090, G091, G092, G093, G094, G095, G096, G294, G295
Perinatal Outcomes		
Low birth weight	MOMBABY	MOMBABY: [WEIGHT] < 2500g in infant CIHI-DAD record
Small for gestational age (or intrauterine growth restriction)	CIHI-DAD	ICD-9: 65650, 65651, 65653, 76400, 76401, 76402, 76403, 76404, 76405, 76406, 76407, 76408, 76409, 76410, 76411, 76412, 76413, 76414, 76415, 76416, 76417, 76418, 76419, 76490, 76491, 76492, 76493, 76494, 76495, 76496, 76497, 76498, 76499 ICD-10: P0590, P0591, P0599
Preterm birth ‡	MOMBABY	MOMBABY: [B_GESTWKS_DEL] or [M_GESTWKS_DEL] < 37

weeks in infant/maternal CIHI-DAD record

ICD-9: 76500, 76501, 76502, 76503, 76504, 76505, 76506, 76507, 76508, 76509, 76510, 76511, 76512, 76513, 76514, 76515, 76516, 76517, 76518,

76519

ICD-10: P070, P071, P072, P073

OHIP: 765

Stillbirth **MOMBABY** MOMBABY: [B STILLBIRTH] or [M STILLBIRTH] in infant/maternal

CIHI-DAD record

Perinatal mortality **MOMBABY MOMBABY:** [DTHDATE] within 7 days of birth in infant RPDB record

or [B STILLBIRTH] or [M STILLBIRTH] in infant/maternal CIHI-DAD

record

Neonatal death MOMBABY: [DTHDATE] within 28 days of birth in infant RPDB record **MOMBABY**

Maternal Demographics

RPDB N/A Age

Neighborhood income N/A **RPDB**

Rural residence **RPDB** N/A

Previous pregnancy MOMBABY: [B BDATE] in the infant CIHI-DAD record **MOMBABY**

Maternal Preexisting Medical Conditions

Hypertension OHD § N/A

ODD | Diabetes mellitus N/A

ICD-9: 4030, 4031, 4039, 4040, 4041, 4049, 582, 583, 580, 581, 584, 585, Chronic kidney CIHI-DAD disease ¶ 586, 587, 5880, 5888, 5889, 5937 **OHIP**

ICD-10: E102, E112, E132, E142, I12, I13, N08, N18, N19

OHIP: 403, 585

Systemic lupus CIHI-DAD ICD-9: 7100 erythematosis

ICD-10: M320, M321, M328, M329

Thrombotic CIHI-DAD ICD-9: 4466 microangiopathy ** OHIP ICD-10: M311

OHIP: 287

Plasma exchange ** **OHIP** OHIP: G272, G277, G278, G290

Health Services Utilization

IPDB N/A General practitioner/family

physician consult

IPDB N/A

Internal medicine specialist

Nephrologist †† **OHIP OHIP:** C132, C101, C138, G860, G323, E083, C137, C135, A135

Prenatal visits	CIHI-DAD OHIP	ICD-9: V220, V221, V230, V231, V232, V233, V234, V235, V238, V239, V288, V289 ICD-10: Z34, Z35 CCP: 02.88 CCI: 5AB01, 5AB03 OHIP: P003, P004, P005
Ultrasonographic examinations	OHIP	OHIP: J128, J135, J138, J157, J158, J159, J160, J162, J428, J435, J438, J457, J458, J459, J460, J462
Assisted reproductive technologies	CIHI-DAD OHIP	ICD-9: V261, V260, V261, V262, V268, V269 ICD-10: N980, N981, N982, N983, N988, N989, Z37001, Z37101, Z37201, Z37301, Z37401, Z37501, Z37511, Z37521, Z37531, Z37581, Z37591, Z37601, Z37611, Z37621, Z37631, Z37681, Z37691, Z37701, Z37711, Z37721, Z37731, Z37781, Z37791, Z37901, Z37911, Z38001, Z38011, Z38101, Z38201, Z38301, Z38311, Z38401, Z38501, Z38601, Z38611, Z38621, Z38631, Z38641, Z38651, Z38661, Z38671, Z38681, Z38691, Z38701, Z38801, N982, N983, N988, N989, Z310, Z311, Z312, Z313, Z314, Z318, Z319 CCP: 81.92 OHIP: G367
Pregnancy Characteri	stics	
Multiple gestation	MOMBABY	MOMBABY: [B_MULTIPLE BIRTH] or [M_MULTIPLE BIRTH] in the infant/maternal CIHI-DAD record
Caesarean delivery **	CIHI-DAD	ICD-9: 66970, 66971 ICD-10: P034 CCP: 860, 861, 862 CCI: 5MD60AA, 5MD60CB, 5MD60CC, 5MD60CD, 5MD60CE, 5MD60CF, 5MD60CG, 5MD60JY, 5MD60JY, 5MD60JZ, 5MD60KA, 5MD60KB, 5MD60KC, 5MD60KD, 5MD60KE, 5MD60KF, 5MD60KG, 5MD60KT, 5MD60RA, 5MD60RB, 5MD60RC, 5MD60RD, 5MD60RE, 5MD60RF, 5MD60RG, 5MD60RH
Hyperemesis gravidarum	CIHI-DAD OHIP	ICD-9: 64300, 64301 ICD-10: O21001, O21003, O21009, O21101, O21103, O21109 OHIP: 643
Diabetes mellitus	CIHI-DAD	ICD-9: 6480 ICD-10: O24
Gestational hypertension §§	CIHI-DAD	ICD-9: 64290, 64291, 64292, 64293, 64294 ICD-10: O13
Preeclampsia ^{IIII}	CIHI-DAD OHIP	ICD-9: 64240, 64241, 64242, 64243, 64244, 64250, 64251, 64252, 64253, 64254, 64260, 64261, 64262, 64263, 64264, 64270, 64271, 64272, 64273, 64274 ICD-10: O14, O15 OHIP: 642

ICD-9: 4466 ICD-10: M311

CIHI-DAD

OHIP

Thrombotic

microangiopathy

OHIP: 287

Pregnancy-related liver disease	CIHI-DAD	ICD-9: 64670, 64671, 64673 ICD-10: O26601, O26602, O26603, O26604, O26609
Heart failure	CIHI-DAD OHIP	ICD-9: 425, 5184, 428, 514 ICD-10: 1500, I501, I509, I255, J81 CCP: 4961, 4962, 4963, 4964 CCI: 1HP53, 1HP55, 1HZ53GRFR, 1HZ53LAFR, 1HZ53SYFR OHIP: R701, R702, Z429, 428
Pyelonephritis	CIHI-DAD Ohip	ICD-9: 59000, 59001, 59010, 59011, 5902, 59080, 59081, 5909 ICD-10: N110, N111, N151, O23001, O23002, O23003, O23004, O23009 OHIP: 590
Sepsis	CIHI-DAD OHIP	ICD-9: 0031, 0380, 0381, 0382, 0383, 03840, 03841, 03842, 03843, 03844, 03849, 0388, 0389, 0545, 65930, 65931, 65933 ICD-10: A400, A401, A402, A403, A408, A409, A410, A411, A412, A413, A414, A4150, A4151, A4152, A4158, A4159, A4180, A4188, A419, R572, O85002, O85004, O85009 OHIP: 038
Amniotic fluid embolism	CIHI-DAD	ICD-9: 67310, 67311, 67312, 67313, 67314 ICD-10: O88101, O88102, O88103, O88104, O88109
Placenta previa	CIHI-DAD	ICD-9: 6410, 6411 ICD-10: O44
Placental abruption ¶	CIHI-DAD OHIP	ICD-9: 64120, 64121, 64123 ICD-10: O45 OHIP: 641
Postpartum hemorrhage ***	CIHI-DAD OHIP	ICD-9: 66600, 66602, 66604, 66610, 66612, 66614, 66620, 66622, 66624 ICD-10: O72 OHIP: 666
Admission to intensive care unit	OHIP	OHIP: C101, G400, G401, G402, G405, G406, G407, G557, G558, G559
Mechanical ventilation	OHIP	OHIP: G405, G406, G407, G557, G558, G559

Abbreviations: CIHI-DAD, Canadian Institute for Health Information Discharge Abstract Database using International Classification of Disease, Ninth Revision (ICD-9) and Tenth Revision (ICD-10), Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures (CCP), and Classification of Health Interventions (CCI) codes; OHIP, Ontario Health Insurance Plan using fee and diagnostic codes; RPDB, Registered Persons Database; OHD, Ontario Hypertension Database; ODD, Ontario Diabetes Database; N/A, not applicable.

^{*} Variables are defined by the presence of at least one of the listed codes unless otherwise specified.

[†] Chronic dialysis dependence was defined by receipt of at least two chronic dialysis codes on two separate days.

[‡] ICD-9 and ICD-10 codes were used to define preterm birth when infant data from MOMBABY dataset was missing.

Validity of preterm birth: ICD-10 codes P070, P071, P072, and P073 used together have a sensitivity of 91.2% and specificity of 98.8% for identification of preterm delivery as ascertained through chart review by trained personnel.¹

[§] The Ontario Hypertension Database is an ICES-derived database that contains all Ontario hypertension patients defined by a) one hospital admission with a hypertension diagnosis, or b) an OHIP claim with a hypertension diagnosis followed within two years by either an OHIP claim or a hospital admission with a hypertension diagnosis.²

The Ontario Diabetes Database is an ICES-derived database that contains all Ontario diabetes patients defined by the presence of at least one hospital admission with a diabetes diagnosis or an OHIP claim with a diabetes diagnosis.³

Validity of chronic kidney disease: Chronic kidney disease was defined using an algorithm of hospital diagnosis codes validated for older adults in the study region. This algorithm identified patients with a median estimated glomerular filtration rate of 38 mL/min/1.73 m2 (interquartile range, 27 to 52 mL/min per 1.73 m2), whereas its absence identified patients with a median estimated glomerular filtration rate of 69 mL/min/1.73 m2 (interquartile range, 56 to 82 mL/min per 1.73 m2).

- ** The variable 'thrombotic microangiopathy treated with plasma exchange' was defined by receipt of plasma exchange that falls within an admission for thrombotic microangiopathy (using CIHI-DAD codes) or within seven days of a diagnosis of thrombotic microangiopathy (using OHIP codes).
- †† Restricted to physicians who also billed at least 50 dialysis codes (one per day) within one year of consultation service date.
- ‡‡ **Validity of caesarean delivery:** ICD-10 code P034 has a sensitivity of 99.8% and a specificity of 98.7% for identification of caesarean delivery as ascertained through chart review by trained personnel.¹
- §§ Validity of gestational hypertension: ICD-10 code O13 has a sensitivity of 10.0-68.2% and specificity of 99.6-99.8% for identification of gestational hypertension as ascertained through chart review by experienced clinicians.^{5,6}
- Walidity of preeclampsia: Coding algorithms have a sensitivity of 66.7-100.0% and a specificity of 64.3-100.0% for identification of preeclampsia as ascertained through chart review by obstetricians or experienced coding specialists using well-described and accepted criteria 6-9
- **Nalidity of placental abruption:** ICD-9 codes 64120, 64121, and 64123 used together have a sensitivity of 89.0% and a positive predictive value of 89.0% for identification of placental abruption as ascertained through chart review by experienced accredited record technicians or certified coding specialists.⁹
- *** Validity of postpartum hemorrhage: ICD-10 code O72 has a sensitivity of 90.2% and a specificity of 98.2% for the identification of postpartum hemorrhage as ascertained through chart review by trained personnel.¹

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