Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Table S1. STROBE checklist

STROBE checklist			
	Item No	**Recommendation**	**Where reported**
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Abstract
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	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	Methods
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Methods Appendix
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Methods Appendix
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 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	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	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 follow-up, and analysed	Results
		(b) Give reasons for non-participation at each stage	Results
		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	Results Table 1 Table 2
		(b) Indicate number of participants with missing data for each variable of interest	Methods

		(c) Summarise follow-up time (e.g. average and total amount)	Results
Outcome data	15	Report numbers of outcome events or summary measures over time	Results Table 3 Appendix
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 Table 3
		(b) Report category boundaries when continuous variables were categorized	Table 1 Table 2 Table 3
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Results
Other analyses	17	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses	Results Figure 1
Discussion			
Key results	18	Summarise 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	Discussion
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion Table 4
Generalisability	21	Discuss the generalisability (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	Disclosure

Table S2. Databases and coding definitions for restriction criteria, baseline characteristics, and outcome measurements.

Characteristic/Condition	Database	Codes
Exclusion Criteria for Donors		
Hypertensive Disorders of Pregnancy	CIHI-DAD OHIP	**ICD-9:** 6420, 6523, 6427, 6429, 6424, 6425, 6426 **ICD-10:** O11, O13, O14, O15, O16 **OHIP:** 642
Restrictions Applied to Healthy Non-Donors (excluded as eligible non-donors if there was evidence of any of the following conditions)		
Hypertensive Disorders of Pregnancy	CIHI-DAD OHIP	As above
Diabetes	ODD [a]	**ICD-9:** 250 **ICD-10:** E10, E11, E13, E14 **OHIP:** 250, Q040, K029, K030, K045, K046
Hypertension	CIHI-DAD OHIP	**ICD-9:** 401, 402, 403, 404, 405 **ICD-10:** I10, I11, I12, I13, I15 **OHIP:** 401, 402, 403
Cardiovascular Disease	CIHI-DAD	**ICD-9:** 39, 40, 41, 42, 43, 44, 45 **ICD-10:** I
Cardiovascular Procedure	CIHI-DAD OHIP	**CCI:** 1IJ50, 1IJ76, 1KA76, 1KG76 **CCP:** 4802, 4803, 4909, 481, 5024, 5034, 5125 **OHIP:** N220, R742, R743, R780, R783, R785, R787, R792, R797, R802, R804, R814, R816, R817, Z434
Cancer	CIHI-DAD OHIP	**ICD-9:** V10, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 170, 171, 172, 173, 174, 175, 176, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 1950, 1951, 1952, 1953, 1954, 1955, 1958, 196, 197, 198, 1990, 1991, 2000, 2001, 2002, 2008, 2010, 2011, 2012, 2014, 2015, 2016, 2017, 2019, 2020, 2026, 2028, 2029, 203, 204, 205, 206, 207, 208, 230, 231, 232, 233, 234 **ICD-10:** 80003, 80006, 80013, 80023, 80033, 80043, 80102, 80103, 80106, 80113, 80123, 80203, 80213, 83123, 87202, 87203, 959, 965, 966, 967, 968, 969, 970, 971, 980, 982, 984, 985, 986, 987, 988, 989, 990, 991, 993, C00, C01, C02, C03, C04, C05, C06, C07, C08, C09, C10, C11, C12, C13, C14, C15, C16, C17, C18, C19, C20, C21, C22, C23, C24, C25, C26, C30, C31, C32, C33, C34, C37, C38, C39, C40, C41, C43, C44, C45, C46, C47, C48, C49, C50, C51, C52, C53, C54, C55, C56, C57, C58, C60, C61, C62, C63, C64, C65, C66, C67, C68, C69, C70, C71, C72, C73, C74, C75, C76, C77, C78, C79, C80, C81, C82, C83, C84, C85, C90, C91, C92, C93, C94, C95, C96, C97, D00, D01, D02, D03, D04, D05, D06, D07, D09 **OHIP:** 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 170, 171, 172, 173, 174, 175, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208
Pulmonary Disease	CIHI-DAD	**ICD-9:** 46, 47, 48, 49, 50, 51 **ICD-10:** J
Liver Disease	CIHI-DAD	**ICD-9:** 57

		ICD-10: K7
Genitourinary Disease	CIHI-DAD	**ICD-9:** 58, 59, 60, 61, 62
		ICD-10: N
Systemic Lupus Erythematosis	CIHI-DAD	**ICD-9:** 7100
		ICD-10: M32
Rheumatoid Arthritis	CIHI-DAD	**ICD-9:** 714
		ICD-10: M05, M06
Human Immunodeficiency Virus Infection	CIHI-DAD OHIP	**ICD-9:** 042, 043, 044, V08, 176
		ICD-10: B24, C46, Z21
		OHIP: 042, 043, 044
Nephrectomy/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
Renal Biopsy	CIHI-DAD OHIP	**CCP:** 6781, 6782
		CCI: 1PC87
		OHIP: Z601
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
		CCP: 5127, 5195, 6698
		CCI: 7SC59QD, 1KY76, 1PZ21
		OHIP: R849, G323, G336, G325, G326, G860, G862, G863, G865, G866, R825, R826, R827, R833, R840, R851, G330, G331, G332, G861, G864, R852, G082, G083, G085, G090, G091, G092, G093, G094, G095, G096, G294, G295, G333, H540, H740
Nephrology Consultation [b]	OHIP	**OHIP:** C132, C101, C138, G860, G323, E083, C137, C135, A135
Family Physician Visit	IPDB	N/A
Baseline Characteristics		
Sex	RPDB	N/A
Age	RPDB	N/A
Year of Cohort Entry	TGLN	N/A
Rural Residence	RPDB	N/A
Income Quintile	RPDB	N/A
Pregnancy	MOMBABY	[B_BDATE] infant/maternal CIHI-DAD record
Family Physician Visit	IPDB	N/A
Prenatal Physician Visit	CIHI-DAD OHIP	**ICD-9:** V220, V221, V230, V231, V232, V233, V234, V235, V238, V239, V288, V289
		ICD-10: Z34, Z35
		CCP: 0288
		CCI: 5AB01, 5AB03
		OHIP: 970, P003, P004, P005
Pregnancy Ultrasound	OHIP	**OHIP:** J128, J135, J138, J157, J158, J159, J160, J162, J428, J435, J438, J457, J458, J459, J460, J462
Outcomes		
Gestational Hypertension	CIHI-DAD	**See Table S3 in the Supplement**
Preeclampsia (includes eclampsia)	CIHI-DAD OHIP	**See Table S3 in the Supplement**
Caesarean Section	CIHI-DAD OHIP	**ICD-9:** 6697
		ICD-10: O82

		CCP: 860, 861, 862, 868, 869 **CCI:** 5MD60 **OHIP:** P018, P041, P042
Post-partum hemorrhage	CIHI-DAD	**ICD-9:** 666 **ICD-10:** O72
Preterm Birth	MOMBABY	[B_GESTWKS_DEL] or [M_GESTWKS_DEL] < 37 weeks in infant/maternal CIHI-DAD record
Low Birth Weight	MOMBABY	[WEIGHT] < 2500g in infant CIHI-DAD record
Maternal Death	RPDB	N/A
Stillbirth	MOMBABY	[B_STILLBIRTH] or [M_STILLBIRTH] in infant/maternal CIHI-DAD record
Neonatal Death	MOMBABY	[DTHDATE] within 28 days of birth in infant RPDB record

Abbreviations: CCI, Canadian Classification of Health Interventions; CCP, Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures; CIHI-DAD, Canadian Institute for Health Information Discharge Abstract Database; ICD-9 International Classification of Disease, Ninth Revision; ICD-10, International Classification of Disease, Tenth Revision; ICES, Institute for Clinical Evaluative Sciences; IPDB, ICES Physician Database; ODB, Ontario Drug Benefit; ODD, Ontario Diabetes Database; OHIP, Ontario Health Insurance Plan; RPDB, Registered Persons Database; TGLN, Trillium Gift of Life Network; N/A, Not applicable

[a] The Ontario Diabetes Database is an ICES-derived database that contains all Ontario diabetes patients defined by the presence of any of the specified codes.

[b] Nephrology consultation was defined by the presence of any nephrology consultation code billed by a nephrologist, who was defined as a physician who, during the study period, billed at least 25 nephrology consultation codes (on separate days) and at least 50 dialysis codes (on separate days).

Table S3. Operating characteristics of hospital diagnosis codes used to define gestational hypertension and preeclampsia

Outcome	Dates	Codes used in study	Codes used in validation	Reference Standard	Operating Characteristics (%)			Reference
					Sn	Sp	PPV	
Gestational hypertension	1992 to 2002 (ICD-9)	6420, 6423, 6429	…	…	…	…	…	…
	2002 to 2013 (ICD-10)	013, 016	013	Identification of 'hypertension in pregnancy (onset >20 weeks gestation)' on chart review by experienced clinicians	68.2	99.6	99.4	Hadfield et al, 2008
			013	Identification of 'gestational hypertension' on chart review using a well-described and accepted definition	10.0	99.8	56.3	Klemmensen et al, 2007
Preeclampsia (including eclampsia)	1992 to 2002 (ICD-9)	6424, 6425, 6426, 6427	6424	Identification of 'mild or unspecified preeclampsia' on chart review by obstetricians using criteria established by the American College of Obstetrics and Gynecology	78.4	64.3	45.3	Geller et al, 2004
			6425	Identification of 'severe preeclampsia' on chart review by obstetricians using criteria established by the American College of Obstetrics and Gynecology	66.7	85.0	84.8	Geller et al, 2004
			6426	Identification of 'eclampsia' on chart review by obstetricians using criteria established by the American College of Obstetrics and Gynecology	83.3	94.6	41.7	Geller et al, 2004
			6425, 6426	Identification of 'severe preeclampsia and eclampsia' on chart review by obstetrician	100	100	100	Korst et al, 2004
			6425, 6427	Identification of 'preeclampsia' on chart review by experienced accredited record technicians or certified coding specialists	76.0	…	94.0	Yasmeen et al, 2006
	2002 to 2013 (ICD-10)	011, 014, 015	014, 015	Identification of 'preeclampsia' on chart review using a well-described and accepted definition	69.3	99.3	74.4	Klemmensen et al, 2007
	1992 to 2013 (OHIP)	642	…	…	…	…	…	…
Gestational hypertension or preeclampsia (including eclampsia)	1992 to 2002 (ICD-9)	6420, 6423, 6424, 6425, 6426, 6427, 6429	6423, 6424, 6425, 6427	Identification of 'gestational hypertension or preeclampsia' on chart review by experienced accredited record technicians or certified coding specialists	88.0	…	91.0	Yasmeen et al, 2006
	2002 to 2013 (ICD-10)	011, 013, 014, 015, 016	013, 014, 015	Identification of 'hypertensive disorders of pregnancy' on chart review using a well-described and accepted definition	48.9	99.6	88.8	Klemmensen et al, 2007
	1992 to 2013 (OHIP)	642	…	…	…	…	…	…

Abbreviations: Sn, Sensitivity (indicates the percentage of women with the condition who are correctly identified as having the condition); Sp, Specificity (indicates the percentage of healthy women who are correctly identified as not having the condition); PPV, Positive predictive value (indicates the percentage of women whose diagnosis is recorded correctly). Ellipses (…) indicate data not reported. ICD-9 International Classification of Disease, Ninth Revision; ICD-10, International Classification of Disease, Tenth Revision. OHIP, Ontario Health Insurance Plan

All ICD-9 and ICD-10 codes were hospital based diagnosis codes recorded in the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD). In this study all the observed OHIP diagnostic fee codes for preeclampsia (OHIP Dx 642 – Complications of pregnancy, childbirth and the peurperium – preeclampsia, eclampsia or toxemia) were claims with a date either during a hospital stay, or in very close proximity to the hospital stay.

Interpretation of Hospital Database Diagnosis Codes of Gestational Hypertension and Preeclampsia

- The operating characteristics for the hospital diagnosis ICD-9 and ICD-10 codes used to define the outcomes of gestational hypertension and preeclampsia are shown in the table above. This coding algorithm was prespecified in

the study protocol. In summary, most coding algorithms used to identify gestational hypertension or preeclampsia within a hospital admission have moderate to high specificity (64.3 in one study, 85-100.0% in all others) and a moderate to high positive predictive value (41.7-100.0%). While sensitivity is variable (10.0-100.0%), it appears to improve for coding algorithms used to identify more severe disease (66.7-100.0% for preeclampsia vs. 10.0-68.2% for gestational hypertension).

- These coding algorithms were validated against a gold standard from chart review, which in many cases, was performed by a clinician using a well-described and accepted definition of the condition. Therefore, we expect these codes to accurately reflect clinician diagnosis of gestational hypertension and preeclampsia (albeit subjective) despite not having access to laboratory data or clinical parameters at the time of this study.

- Whether the operating characteristics for these coding algorithms vary by donor status is unknown, However, our study population had universal healthcare benefits, where all healthcare encounters were recorded, and the pregnancies of donors and non-donors had a similar high level of health surveillance [in the current study both the donors and non-donors had the same number of healthcare visits during pregnancy: 10 prenatal visits and 3 pregnancy ultrasounds; also all the pregnancies in donors and non-donors were delivered in hospital]. It is our understanding that physicians in our province demonstrate a low threshold for admitting women to hospital for the management of complicated hypertension in pregnancy regardless of donor status, and that preeclampsia is almost exclusively managed as an inpatient. We would expect similar access to laboratory data and clinical parameters to confirm diagnoses of gestational hypertension and preeclampsia, should these conditions be present, among both donors and non-donors.

- Of note, neither the medical coders nor the physician / healthcare teams caring for the donors and non-donors were aware of the hypothesis of the current study, or even that a study was being undertaken. So we are not concerned that study awareness influenced the ascertainment of outcomes. Furthermore, a prominent 2004 Amsterdam international consensus conference on living kidney donation (a guideline that was available for a large portion of pregnancies during the study period) concluded that there was insufficient evidence to be concerned that living donation increases the risk of gestational hypertension or preeclampsia. We also undertook an analysis and confirm that the incidence of gestational hypertension and preeclampsia diagnoses in living donors was no higher after 2009 when two studies, one from the United States and the other from Norway, suggested that kidney donation could increase the risk of gestational hypertension and preeclampsia.

- As a limitation, the operating characteristics reported in the table above only apply to the coding algorithm specified and do not necessarily reflect the entire collection of codes used to define the primary outcomes in our study. Therefore, these statistics should be used as a reference source from which the actual operating characteristics of coding algorithms used in this study can be approximated. Our rationale for including some codes not previously validated was to improve sensitivity to capture the outcomes. In cases where individual and combinations of codes have been validated this strategy has resulted in modest gains in sensitivity with essentially no change to specificity.

References

Geller SE, Ahmed S, Brown ML, Cox SM, Rosenberg D, Kilpatrick SJ. International Classification of Diseases-9th revision coding for preeclampsia: how accurate is it? Am J Obstet Gynecol 2004;190(6):1629–33; discussion 1633–4.

Hadfield RM, Lain SJ, Cameron CA, Bell JC, Morris JM, Roberts CL. The prevalence of maternal medical conditions during pregnancy and a validation of their reporting in hospital discharge data. Aust N Z J Obstet Gynaecol 2008;48(1):78–82.

Klemmensen AK, Olsen SF, Osterdal ML, Tabor A. Validity of preeclampsia-related diagnoses recorded in a national hospital registry and in a postpartum interview of the women. Am J Epidemiol 2007;166(2):117–24.

Korst LM, Gregory KD, Gornbein JA. Elective primary caesarean delivery: accuracy of administrative data. Paediatr Perinat Epidemiol 2004;18(2):112–9.

Yasmeen S, Romano PS, Schembri ME, Keyzer JM, Gilbert WM. Accuracy of obstetric diagnoses and procedures in hospital discharge data. Am J Obstet Gynecol 2006;194(4):992–1001.

Table S4 Secondary study outcomes and their definitions

- Each component of the primary outcome (gestational hypertension or preeclampsia) examined separately. When diagnostic codes for both gestational hypertension and preeclampsia were present in a given pregnancy, we categorized the event as preeclampsia.

- Caesarean section, defined with healthcare database procedural codes (Table S2)

- Post-partum hemorrhage, defined with healthcare database codes (Table S2)

- Pre-term birth (<37 weeks gestation)

- Low birth weight (<2500 g)

- Maternal death (death during pregnancy or within 42 days of childbirth)

- Stillbirth (delivery with no signs of life)

- Neonatal death (death within 28 days of birth)

Table S5. Outcomes in pregnancies with and without a hospital diagnosis for gestational hypertension or preeclampsia examined separately in donors and non-donors.

	Donor Pregnancies (n = 131)		Non-donor pregnancies (n = 788)	
	Gestational hypertension or preeclampsia		Gestational hypertension or preeclampsia	
	Yes (n = 15)	No (n = 116)	Yes (n = 38)	No (n = 750)
Caesarean section	7 (46.7%)	34 (29.3%)	16 (42.1%)	208 (27.7%)
Low birth weight (< 2500 g)	(…)	(…)	7 (18.4%)	22 (2.9%)

Presented is the number of events (%).

(…) the cell count was ≤ 5 and results are not reported in order to comply with privacy regulations. The proportion of women with a low birth weight was higher when gestational hypertension or preeclampsia was present, compared to when it was absent (8-fold higher, similar to the 6-fold higher proportion observed in non-donor pregnancies).

Table S6. Non-donor restrictions, characteristics and outcomes for kidney donors matched to the general population (3 tables)**, followed by an interpretation of the results**

Non-donor restrictions: As reported in the manuscript, we had an original sample of 731,823 general population women. In the primary analysis this sample was restricted to eligible non-donors (52% of the original sample) who had an absence of health conditions prior to their cohort entry date. Eligible non-donors were then matched to donors. In the current analysis we simply restricted the general population to women without evidence of hypertension in pregnancy prior to their cohort entry date (an exclusion applied to donors), and women who saw a physician at least once in the two years prior to their cohort entry date (to ensure non-donors had the same opportunity to access physicians for healthcare). Applying these restrictions left 597,726 women (82% of the original sample) eligible to be selected as non-donors.

Matching procedures: As in the primary analysis, we matched six eligible non-donors to each donor on baseline characteristics that can be associated with gestational hypertension and preeclampsia risk: age at cohort entry (exact age in years), cohort entry date (within two years), urban or rural residence (population less than 10,000), income (categorized into fifths of average neighborhood income), number of pregnancies carried to at least 20 weeks gestation prior to cohort entry (0, 1 or ≥ 2), and the time to first birth after cohort entry (live or stillbirth; matched within two years). Each non-donor could only be selected once.

Characteristics of kidney donors and matched general population non-donors at cohort entry. [a]			
	Donors	**Matched General Population Non-donors**	**P value** [b]
Women, number	85	510	
Age, years	29 [26 to 32]	29 [26 to 32]	1.00
Year of cohort entry			0.12
1992 – 1995	16 (18.8%)	87 (17.1%)	
1996 – 1999	19 (22.4%)	101 (19.8%)	
2000 – 2004	22 (25.9%)	151 (29.6%)	
2005 – 2009	28 (32.9%)	171 (33.5%)	
Rural residence	≤ 5 (≤ 5.9%)	30 (5.9%)	1.00
Income quintile [c]			1.00
1st quintile (lowest)	12 (14.1%)	72 (14.1%)	
2nd quintile	15 (17.6%)	90 (17.6%)	
3rd quintile (middle)	13 (15.3%)	78 (15.3%)	
4th quintile	24 (28.2%)	144 (28.2%)	
5th quintile (highest)	16 (18.8%)	96 (18.8%)	
At least one pregnancy before cohort entry [d]	25 (29.4%)	150 (29.4%)	1.00
Time from last pregnancy, years [e]	3 [1 to 5]	2 [1 to 6]	0.36
Physician visits in prior year, number	4 [2 to 8]	4 [2 to 6]	0.30
Data presented as median [interquartile range] or as number (percent).			
[a] For living kidney donors the date of cohort entry was the date of nephrectomy, and for non-donors it was randomly assigned (simulated nephrectomy date) to establish the date follow-up began.			
[b] Derived from generalized estimating equations with default link function accounting for the correlation structure within matched sets. A normal distribution was specified when the variable was continuous, a Poisson distribution when the variable was count data, a multinomial distribution when the variable was categorical, and a binomial			

Characteristics at the time of follow-up pregnancies in kidney donors and matched general population non-donors.

	Donors	Matched General Population Non-donors	P value [a]
Pregnancies, number	131	792	
Women, number	85	510	
Age, years	32 [29 to 35]	32 [29 to 36]	0.89
Year of pregnancy			0.75
1994 – 1998	10 (7.6%)	63 (8.0%)	
1999 – 2003	24 (18.3%)	155 (19.6%)	
2004 – 2008	61 (46.6%)	327 (41.3%)	
2009 – 2012	36 (27.5%)	247 (31.2%)	
Prior pregnancies, number [b]			0.43
0 (none)	60 (45.8%)	360 (45.5%)	
1	51 (38.9%)	333 (42.0%)	
≥ 2	20 (15.3%)	99 (12.5%)	
First pregnancy after cohort entry	85 (64.9%)	510 (64.4%)	1.00
Second pregnancy after cohort entry	36 (27.5%)	230 (29.0%)	
Third or more pregnancy after cohort entry	10 (7.6%)	52 (6.6%)	
Time from last prior pregnancy, years [c]	3 [2 to 4]	3 [2 to 5]	0.19
Time since cohort entry, years [d]	4 [2 to 7]	4 [2 to 7]	0.67
Prenatal physician visits, number	10 [7 to 12]	10 [9 to 12]	0.06
Pregnancy ultrasounds, number	3 [2 to 4]	3 [2 to 4]	0.08

Data presented as median [interquartile range] or as number (percent).

[a] Derived from generalized linear mixed models with a random intercept with default link function accounting for the correlation structure within matched sets and pregnancies within a woman. A normal distribution was specified when the variable was continuous, a Poisson distribution when the variable was count data, a multinomial distribution when the variable was categorical, and a binomial distribution when the variable was binary.

[b] This includes the pregnancies both before and after the date of cohort entry.

[c] Analysis restricted to those with at least one prior pregnancy; a prior pregnancy could be either before or after the date of cohort entry.

[d] For living kidney donors the date of cohort entry was the date of nephrectomy, and for non-donors it was randomly assigned (simulated nephrectomy date) to establish the date follow-up began.

Maternal and fetal outcomes in pregnancies of living kidney donors and matched general population non-donors.				
	Number of events (%)			
	Donors (131 pregnancies)	Matched General Population Non-Donors (792 pregnancies)	Odds Ratio (95% CI)	P value [a]
Primary outcome				
Gestational hypertension or preeclampsia	15 (11.5%)	29 (3.7%)	3.2 (1.5 to 6.8)	<0.01
Secondary outcomes				
Gestational hypertension [b]	7 (5.3%)	11 (1.4%)	3.9 (1.4 to 10.6)	0.01
Preeclampsia	8 (6.1%)	18 (2.3%)	2.7 (1.1 to 7.0)	0.04
Caesarean section	41 (31.3%)	234 (29.5%)	1.1 (0.7 to 2.0)	0.64
Post-partum hemorrhage	≤ 5 (≤ 3.8%) [c]	32 (4.0%)	0.7 (0.2 to 2.2)	0.58
Pre-term birth (< 37 weeks gestation)	10 (7.6%)	46 (5.8%)	1.1 (0.6 to 2.0)	0.65
Low birth weight (< 2500 g)	8 (6.1%)	34 (4.3%)	1.7 (0.7 to 3.9)	0.20

Abbreviations: CI, confidence interval.

[a] Derived from random-effects logistic regression models for binary outcome data, accounting for the correlation structure within matched sets and in women with multiple pregnancies.

[b] When diagnostic codes for both gestational hypertension and preeclampsia were present in a given pregnancy, we categorized the event as preeclampsia.

[c] Small cell sizes (count numbers of 1 to 5) were reported as ≤ 5 to comply with privacy regulations.

Interpretation of the Results

- The risks of various pregnancy outcomes in donors versus non-donors in the primary analysis and this analysis are highly comparable. In other words, a higher risk of the primary outcome in kidney donors persisted when fewer restrictions were placed on the eligibility of non-donors.

- This may be attributed to the good health of most young women with childbearing potential, and a matching technique that in both analyses ensured balance between the two groups on key baseline biological and non-biological characteristics associated with gestational hypertension and preeclampsia risk (as listed in detail at the beginning of Table S6). The median [interquartile] age in donors and non-donors at cohort entry in both sets of analyses is 29 [interquartile range 26 to 32] years. At this age most women in the general population are quite healthy, even when they have certain diagnostic conditions recorded in healthcare databases.

Table S7. Table 4 in the manuscript with detailed footnotes.

Study characteristics and maternal and fetal outcomes in post-donation pregnancies from Norway, Minnesota (United States) and Ontario (Canada)			
	Norway[12]	**Minnesota, United States[13]**	**Ontario, Canada**
Study characteristics			
Number of transplant centres	one [a]	one	five
Healthcare system	public universal healthcare	private insurance	public universal healthcare
Retrospective study	yes	yes	yes
Data source	national birth registry	study data	provincial healthcare data
Outcomes recorded at time of pregnancy	yes, mandatory reporting to birth registry	no, self-reported patient surveys; completed an average of 4 years after post-donation pregnancies and 12 years after first pregnancies	yes, mandatory hospital reporting during pregnancy and fee for service physician claims
Eligible pregnancies	> 16 weeks gestation	all pregnancies	> 20 weeks gestation
Loss to follow-up after donation	< 4% [b]	24 - 39% [c]	< 4%
Primary groups being compared	pregnancies before and after donation	pregnancies before and after donation	follow-up pregnancies in matched donors and non-donors
Type of non-donor comparison	sample from same data source, but not selected for donor similarity and no statistical adjustment for baseline differences between the two groups [d]	general population estimates from published literature; other than race not selected for donor similarity	sample from the same data source selected for donor similarity on demographics and other prognostic factors [e]
Blood pressure or kidney function values during pregnancy	no	no	no
Donor characteristics			
Number of women	69	239	85
Years of donation	1967 to 2002	1963 to 2007	1992 to 2009
Family history of kidney failure (%)	(…)	96% [f]	65% [f]
Mean pre-donation GFR, mL/min per 1.73 m^2	(…)	91 [g]	114 [g]
White race (%)	98% [h]	97%	70% [h]
Number of post-donation pregnancies	106	490	131
Mean age at donation, years	27	26	29
Mean age at pregnancy, years	32	29 [i]	32
Number of women with at least one pre-donation pregnancy (%)	(…)	98 (41%)	25 (29%)
Mean or median time from donation	5	5 [i]	4

to post-donation pregnancies, years			
	Number of events (% of pregnancies)		
Post-donation maternal outcomes			
Gestational hypertension or preeclampsia	9 (8.5%)	55 (11.2%)	15 (11.5%)
Gestational hypertension	3 (2.8%) [j]	28 (5.7%) [k]	7 (5.3%)
Preeclampsia	6 (5.7%)	27 (5.5%) [l]	8 (6.1%)
Maternal death	(…)	(…)	0 (0.0%)
Post-donation fetal outcomes			
Pre-term birth (< 37 weeks gestation)	10 (9.4%)	35 (7.1%)	10 (7.6%)
Low birth weight (< 2500 g)	9 (8.5%)	(…)	8 (6.1%)
Stillbirth	3 (2.8%) [m]	2 (0.4%) [m]	0 (0.0%)
Neonatal death (< 28 days after birth)	0 (0.0%)	(…)	0 (0.0%)

Abbreviations: (…) not reported, GFR glomerular filtration rate.

a. All solid organ transplants in Norway are performed at Rikshospitalet University Hospital. Until 1983 some kidney transplants (<5% of the Norwegian cohort) were also performed at Ullevål University Hospital in Oslo.

b. Not reported in the manuscript. Given that Norway has a national birth registry and national healthcare, the only loss to follow-up would likely be caused by country emigration.

c. This is difficult to ascertain from the report. There were 2102 female donors (and incomplete information about the number who still had future child bearing potential) and maternal outcomes were assessed in the second of two patient surveys. Between 1280 to 1589 of the 2102 female donors responded to the surveys. 180 female donors did not respond to any survey, and 333 female donors were not contacted due to lack of contact information or if it was known that they had died.

d. A random sample of 21 511 pregnancies was obtained from the registry, not selected for baseline similarity to the donors (e.g. pregnancies after donation are more likely to occur in older women where a reasonable proportion have a prior delivery history; maternal age in post-donation pregnancies was on average 5 years more than the registry pregnancies). Statistical tests that compared donors and non-donor outcomes (Fisher Exact test) did not adjust for age or other important baseline differences between the two groups.

e. Non-donors and donors were matched on characteristics associated with gestational hypertension and preeclampsia risk: age (older age is associated with greater risk), cohort entry date (to account for any secular trends), history of at least one previous delivery and number of previous deliveries (previous uneventful pregnancies reduce the risk), urban versus rural place of residence (rural residence increases risk), socioeconomic status based on neighborhood income quintile (lower socioeconomic status increases the risk) and time to first birth after cohort entry (a greater interval from a previous pregnancy increases the risk). Non-donors were also selected to have good baseline health.

f. In the Minnesota study this was defined as 'related to the recipient'; in the Ontario study this was defined as 'a first degree relative of the recipient'.

g. In the Minnesota study this was estimated with the Modification of Diet in Renal Disease (MDRD) study equation; in the Ontario study this was estimated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-Epi) study equation.

h. Best estimates using Organ Procurement Organization records, Census data and other sources. The Ontario study database contains race information for 46% of donors in the study sample.

i. Defined at the time of first pregnancy after donation; this information was not reported for all post-donation pregnancies included in the analyses, only for women who had post-donation pregnancies without pre-donation pregnancies.

j. Information in the Medical Birth Record of Norway, where submitted forms were completed by the attending obstetrician or midwife. During the observational period in Norway, gestational hypertension was defined as a blood pressure ≥ 140/90 mmHg or increase in diastolic blood pressure of at least 15 mmHg or systolic blood pressure of at least 30 mmHg from the woman's average blood pressure before 20 weeks gestation, without proteinuria. Preeclampsia was defined as gestational hypertension with proteinuria. Proteinuria was defined as an excretion of ≥ 0.3 g per day, usually equivalent to ≥ 1+ on a standard urine test strip.

k. Defined as participant reporting of the need for hypertension treatment during pregnancy, but not before or after.

l. Typically defined as hypertension associated with new-onset proteinuria or edema, recorded by the woman's recall of the diagnosis by the primary care provider.

m. In the Norway study, a fetus was recorded as stillborn if it died before or during labor; in the Minnesota study, we defined stillbirths from reports of fetal death.