Appendix A- Checklist of recommendations for reporting of observational studies using Strengthening the Reporting of Observation Studies in Epidemiology (STROBE) guidelines(1)

	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	Title
		(*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 pre-specified hypotheses	Introduction
Methods			
Study design	4	Present key elements of study design early in the paper	Methods- Design, setting and participants
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods- Design, setting and participants Figure S1
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Methods- Design, setting and participants; Methods – Costing methods and measures
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Methods – Costing methods and measures; Appendix A
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 – Costing methods and measures; Appendix A
Bias	9	Describe any efforts to address potential sources of bias	Methods – Statistical analysis
Study size	10	Explain how the study size was arrived at	Methods – Design, setting, and participants
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Methods – Statistical analysis
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Methods – Statistical analysis
		(*b*) Describe any methods used to examine subgroups and interactions	Methods – Statistical analysis
		(*c*) Explain how missing data were addressed	Methods – Statistical analysis
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	Methods – Statistical analysis

		(*e*) Describe any sensitivity analyses	Methods – Statistical analysis
Results			
Participants	13	(a) Report numbers of individuals at each stage of study—eg 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
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Results; Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Results
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Results
Outcome data	15	*Cohort study*—Report numbers of outcome events or summary measures over time	Results; Table 2
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Results; Table 2 & 3
		(*b*) Report category boundaries when continuous variables were categorized	Results; Table 2 & 3
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Results; Table 4
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
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	Title page

Appendix B- Supplementary methods

Micro-Costing Methods

Resource Identification

Resources were identified through the economic outcomes framework as either out-of-pocket or lost donor productivity costs, and the unit of each resource was defined. Out-of-pocket costs included money spent directly on travel, accommodation, and medications. Lost donor productivity costs were associated with time and productivity losses including: lost income, home productivity, and caring for dependents.

Resource Measurement

The three-month economic case report form captured out-of-pocket and lost productivity costs borne by donors in the form of both units of resources consumed and costs by category. Quantifying resource utilization in each cost category by collecting the number of units consumed (e.g. the number of nights spent in paid accommodation) allows for portability of the results, allowing for comparisons across jurisdictions.

Resource Valuation

To describe costs, resource units were assigned a value using conventional costing techniques and appropriate provincial or local rates and estimates (e.g. provincial age- and sex-specific average wage rates for unpaid days of work missed due to donation). For resources where no unit cost or rate was available (e.g. expenses associated with dependent care) donor reported costs were used instead.

Calculation of out-of-pocket costs

Ground Travel Costs

In the 3-month post-donation economic assessment, donors reported the number of round-trips to see health professionals for living donor evaluation and the transplant centre where these evaluations took place. The driving distance between donors' homes and transplant centres was calculated using Google Maps application programming interface (API). The postal codes of

donors and their respective centre were entered into the Google Maps API which produced the shortest driving distance between the locations. This driving distance was doubled to produce a round-trip distance-travelled, which was then multiplied by the reported number of round-trips to determine the donor's total driving distance during evaluation. The donor's total driving distance was then multiplied by the provincial kilometric rate for their province of residence to estimate the total costs of ground travel.(2)

Donors who flew to the transplant centre which they reported as the site of their evaluations were expected to have minimal ground travel costs; and for the purposes of this analysis had 0 kilometers inputted for their ground travel.

Donors were also asked to report the number of days and total expenses for paid parking due to ground travel for evaluation, testing, and surgery.

Air Travel Costs

In the 3-month post-donation economic assessment, donors were asked if they travelled by airplane during the donation process. Donors who flew were asked to report the city of departure, the city of arrival, and the number of round-trip and/or one-way flights between these cities. Air travel rates were estimated using Google Flights between the cities of departure and arrival for either round-trip or one-way flights. The cost of air travel was estimated for the day of April 11, 2016, returning on April 12, 2016 (if round-trip). Rates were chosen using Google Flights' price graph as follows: 1) lowest available economy-class flight regardless of time of departure or arrival, 2) direct flight, when available, and 3) use of Air Canada (Canada's most popular domestic airline), when available. Air travel rates between cities were obtained on February 27, 2016 and included taxes and fees.

Air travel rates were then multiplied by the appropriate number of round-trip or one-way flights for each donor. The total air travel cost for each donor was the sum of the cost of flights during the donation process.

Accommodation Costs

Donors reported the number of nights spent in paid accommodation during the evaluation and donation processs at the 3-month post-donation economic assessment. The three hotels nearest the hospital where each donor's surgery took place were identified using Google Maps "hotels nearby" function. Hotel rates were chosen using the following criteria: 1) single occupancy room, 2) lowest available rate, and 3) accommodation for the night of April 11, 2016. Rates were averaged across the three hotels per hospital, and appropriate federal taxes, provincial taxes, and municipal destination marketing fees were applied. The tax-inclusive nightly rate was multiplied by the number of nights in paid accommodation for each donor to determine the total cost of paid accommodation. Rates for three hotels per hospital were obtained on February 27, 2016.

Donors were also asked to report i) the number of nights and total out-of-pocket expenses related to staying with family and/or friends, and ii) the cost of staying in hospital (e.g. cable, telephone etc.) for testing and/or surgery throughout the donation process.

Total accommodation cost for each donor was the sum of the cost of paid accommodation, the total cost for staying with family and/or friends, and the total cost related to staying in hospital.

Medication Costs

In the 3-month economic assessment, donors were asked to estimate their total costs for medications prescribed due to kidney donation. Donors were not asked to report the type or duration of prescribed medications; therefore, self-reported costs were used to estimate medication costs.

Calculation of Lost Donor Productivity

Lost Workforce Productivity

In the 3-month economic assessment, donors were asked to report the number of days or part days they were unable to work following donation (if they were employed) and the number of these days that were unpaid. The number of unpaid days away from work was multiplied by an 8-hour work-day. We then multiplied the number of hours of lost pay by the 2016 (age-, sex-, and province-specific) average wage rates from the Labour Force Survey to estimate lost workforce productivity due to donation.(3) We did not collect donor reported wage rates due to

the invasiveness of the question and anticipated poor response rate. The human capital approach and use of average wage rates are suggested by the Canadian Agency for Drugs and Technologies in Health's guidelines for economic evaluations, have been used previously in the evaluation of the costs incurred by living kidney donors, and are frequently used in health economic evaluations to estimate workforce productivity.(4,5) In accordance with Drummond *et al.*'s recommendations based on equity concerns in estimating productivity losses, a sensitivity analysis using 2016 average provincial wage rates to value lost wages was performed: the results did not change.(6,7)

Lost Non-Workforce Productivity

Donors were asked to report the number of days they were unable to perform household activities (e.g. housework, shopping etc.) and their costs related to these productivity losses even if they were fully or partially reimbursed at the 3-month economic assessment.

Donors were asked to report the number of days they were unable to care for dependents (e.g. children, spouse etc.) and their total costs related to these productivity losses even if they were fully or partially reimbursed.

Additional Methods

Using multivariable models to analyze costs does not avoid the same distributional issues of heavily skewed cost data encountered in univariate analyses. Ordinary least squares (OLS) regressions of untransformed and transformed costs, though the most common approaches to cost analysis, face problems with violations of the assumptions of homoscedasticity and normally distributed error terms, and problems with retransformation.

Generalized linear models (GLM) have become increasingly used as an alternative to OLS models to analyze costs. GLMs have emerged because of the flexibility they offer in allowing mean and variance to be directly specified, and because they avoid distributional problems in cost analysis, as mean and variance can be modelled on the original scales. To employ GLMs in cost analysis we determine a link function and a family based on the data. The link function describes how the mean on the original scale is related to the linear combination of the coefficients and regressors in the model, and so does not face issues of retransformation. The log

link has been used widely in healthcare cost literature as it predicts the log of the mean, and thus, exponentiation of the predictions from the GLM to arrive at the arithmetic means does not require smearing factors. Specification of a distributional family reflecting the mean-variance relationship allows for heteroscedasticity to be modelled. For example, the gamma family specifies the variance as being proportional to the square of the mean.

Misspecification of the link function and family may affect model fit, and result in inefficient and biased parameter estimates. For our multivariable analysis, the choice of link function was guided by the Stata program *glmdiag* which performs the Pregibon linktest, Pearson's correlation test, and the modified Hosmer-Lemeshow test. Specification of the distributional family was informed by the modified Park test. Candidate families assessed included: Gaussian (constant variance), gamma (variance proportional to square of the mean), Poisson (variance proportional to the mean), and inverse Gaussian (variance proportional to cube of the mean).

Deviance residuals were assessed using normal plots to judge goodness of fit for our model. The Stata program *collin*, which provides variance inflation factors, tolerance, and condition index, was used to detect multicollinearity across covariates.

With GLMs, non-linear retransformations when estimating costs can introduce covariate imbalances. To overcome this problem, we estimated differences between groups as incremental costs using the technique of recycled predictions. Recycled predictions generate an identical covariate structure for each group by treating each observation as if they were in one group, predicting costs, and then treating each observation as if they were in the comparison group, and again predicting the cost for each.

Differences in the costs between individual observations reflect the marginal effect of being in the comparison group; the average of these individual effects results in an average marginal effect (AME) comparing costs between groups while holding all other covariates constant. Stata performs recycled predictions using the margins and *mimrgns* commands.

As costs were modeled at the aggregate level, issues of zero-inflated data were assumed to be insignificant. Beyond this, GLMs are flexible to the violations of assumptions introduced by zero-inflated data.

Appendix C – Supplementary tables and figures

Table S1. Pattern of missingness for costing variables

Out-of-pocket costs						Lost productivity costs			n (%)
Number of trips	Nights in hotels	Hospital stay costs	Friends/ family accomodation costs	Parking costs	Medication costs	Days off without pay	Unable to care for dependants	Unable to perform household activities	
+	+	+	+	+	+	+	+	+	757
-	-	-	-	-	-	-	-	-	91
+	+	+	+	+	+	+	-	-	13
+	+	+	+	+	+	-	+	+	8
+	+	+	+	-	+	+	+	+	5
+	+	+	+	+	-	+	+	+	5
+	+	-	+	+	+	+	+	+	4
+	+	+	+	+	+	+	-	+	4
-	+	+	+	+	+	+	+	+	3
+	+	+	+	+	+	-	-	-	2
-	-	-	-	+	+	+	+	-	1
-	-	-	-	+	+	+	+	+	1
-	+	-	+	-	+	-	-	-	1
-	+	+	-	+	+	-	+	-	1
-	+	+	+	-	+	+	-	-	1
-	+	+	+	+	-	+	+	+	1
+	-	-	-	-	-	+	-	-	1
+	-	+	+	+	-	-	-	-	1
+	+	-	-	-	-	-	-	-	1
+	+	-	-	+	+	+	+	+	1
+	+	-	+	-	+	+	+	+	1
+	+	-	+	+	+	-	+	+	1
+	+	+	-	-	+	+	+	+	1
+	+	+	-	+	+	+	+	-	1
+	+	+	+	-	-	+	+	+	1
+	+	+	+	-	+	+	-	-	1
+	+	+	+	+	-	-	-	-	1
+	+	+	+	+	-	+	-	-	1
+	+	+	+	+	-	+	-	+	1
+	+	+	+	+	+	+	+	-	1

Table S2. Comparing demographic characteristics between donors with all or partially complete economic data, and donors missing all economic data

	All donors	Donors with all or partially economic complete data	Donors missing all economic data
	n = 912	**n = 821**	**n = 91**
Age at donation, years, mean (SD)	46.8 (11.4)	47.4 (11.3)	40.7 (10.9%)
Women, n (%)	609 (67%)	555 (68%)	54 (59%)
White, n (%)	789 (87%)	720 (88%)	69 (76%)
Marital status, n (%)			
Married/living with partner	707 (78%)	651 (79%)	56 (62%)
Separated or divorced	83 (9%)	66 (8%)	17 (19%)
Never married	109 (12%)	93 (11%)	16 (18%)
Widowed	13 (1%)	11 (1%)	2 (2%)
Donor evaluation >100 km of home, n (%)	366 (40%)	329 (40%)	37 (41%)
Employment status, n (%)			
Employed (full or part-time)	701 (77%)	633 (77%)	68 (75%)
Retired	87 (10%)	86 (10%)	1 (1%)
Other	124 (14%)	102 (12%)	22 (24%)
Education level, n (%)			
Primary school	22 (2%)	15 (2%)	7 (8%)
High school	288 (32%)	241 (29%)	47 (52%)
Trade school	61 (7%)	53 (6%)	8 (9%)
College	233 (26%)	215 (26%)	18 (20%)
University	308 (34%)	297 (36%)	11 (12%)
Annual household income, median (IQR), (CAD 2016) [1]	$87,125 (57,365-114,730)	$81,184 (57,365-114,730)	$68,495 (42,798-113,135)
Donor-recipient relationship type, n (%)			
Genetic	443 (49%)	386 (47%)	57 (63%)
Emotionally related, non-spouse	177 (19%)	160 (19%)	17 (19%)
Emotionally related, spouse	139 (15%)	130 (16%)	9 (10%)
Paired	118 (13%)	111 (14%)	7 (8%)
Non-directed	35 (4%)	34 (4%)	1 (1%)

Abbreviations: IQR, inter-quartile range; SD (standard deviation).

[1] The median income for all donors was derived from the mid-point of imputed categorical values inflated to 2016 CAD (e.g. $15,000 was used for donors reporting incomes of $10,000 to $20,000); an income of $110,000 was used for donors reporting incomes >$100,000 and $5000 for donors reporting incomes <$10,000. Income was missing in 223/912 (24%) donors.

Table S3. Out-of-pocket costs (2016 CAD dollars) incurred by living donors, scenario analysis of multiple imputation for all donors, n = 912

Cost category	Description	Mean (SE)
Travel	Ground travel	$999 (53)
	Air travel	$637 (35)
	Parking[1]	$122 (10)
Accommodation	Family and friends[1]	$203 (30)
	Non-hospital paid	$474 (42)
	Hospital[1]	$133 (13)
Medication	Post-donation pain medication or antibiotics after hospital discharge[1,2]	$43 (6)
TOTAL		**$2,110 (84)+**

[1]Self-reported costs (not micro- costed).

[2]Medications provided in hospital are covered through universal health care. Some outpatient drugs are also covered through universal healthcare plans for segments of the population (e.g. in the province of Ontario, Canada those 65 years and older have universal drug benefits).

+Total mean out-of-pocket costs not significantly different from primary analysis ($p>0.05$)

Table S4. Lost productivity costs (2016 CAD dollars) incurred by living kidney donors, scenarnio analysis of multiple imputation for all donors, n = 912

Cost category	Description	Mean (SE)
Lost income	Unpaid time off work	$2215 (155)
Lost productivity	Unable to perform household activities[1]	112 (39)
	Unable to care for dependants[1]	97 (28)
TOTAL		**$2,424 (164)+**

[1] Self-reported costs (not micro-costed).).+no difference with total mean out-of-pocket costs of primary analysis (p>0.05)

Table S5. Adjusted[1] out-of-pocket, lost productivity, and total costs (2016 CAD dollars) for all donors, n=912

Sub-group	Out-of-pocket costs (CAD)		Lost productivity costs (CAD)		Total costs (CAD)	
	Average difference in cost (95% CI)	*p*	Average difference in cost (95% CI)	*p*	Average difference in cost (95% CI)	*p*
Donor relationship with receipient[2]						
Spousal	*ref*		*ref*		*ref*	
Genetically related	-$202 (-710 to 307)	0.44	-$143 (-1,446 to 1,159)	0.83	-$558 (-1,982 to 867)	0.44
Emotionally related, non-spousal	-$462 (-1,118 to 536)	0.17	-$860 (-2,145 to 425)	0.19	-$1,526 (-2,823 to -228)	0.021
Donor-recipient relationship[3]						
Directed	*ref*		*ref*		*ref*	
Non-directed	$153 (-586 to 891)	0.69	-$745 (-2,308 to 818)	0.35	-$759 (-2,028 to 509)	0.24
Kidney paired	$257 (-140 to 654)	0.20	-$306 (-934 to 323)	0.34	-$31 (-873 to 811)	0.94
Age (years)						
<35	*ref*		*ref*		*ref*	
35 to 54	$572 (137 to 1,008)	0.01	-$787 (-1,920 to 346)	0.17	-$77 (-1,358 to 1,204)	0.91
≥55	$753 (151 to 1,355)	0.014	-$1,597 (-2,600 to -594)	0.002	-$603 (-1,764 to 558)	0.31
Distance from centre						
<100 km	*ref*		*ref*		*ref*	
≥100 km	$2657 (2,226 to 3,088)	<0.001	-$222 (-862 to 418)	0.50	$2,626 (1,860 to $3,392)	<0.001
Employment status						
Employed	*ref*		*ref*		*ref*	
Unemployed	-$553 (-1,122 to 17)	0.06	-$1,868 (-26,00 to -1,137)	<0.001	-$2,420 (-3,367 to -1,473)	<0.001
Retired	-$219 (-542 to 105)	0.19	-$2,613 (-3,209 to -2,017)	<0.001	-$2,501 (-3,275 to -1,726)	<0.001
Other	$173 (-654 to 999)	0.68	-$72 (-2,173 to 2,028)	0.95	$24 (-2,292 to 2,350)	0.98

Note: A positive number reflects higher costs compared to the referent group; a negative number reflects lower costs compared to the referent group

[1]Adjusted using marginal effects for age, sex, income, and transplant centre (with the exception of the age subgroup, which was adjusted for sex, income, and transplant centre).

[2] Excludes 35 non-directed donors and 118 kidney paired donors.

[3]Directed is donation to a specified recipient, kidney paired is the swapping of kidneys in incompatible donor/recipient pairs, and non-direct donors are not known to the recipient and may have initiated a chain of paired donations.

References

1. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Prev Med (Baltim). 2007;45(4):247–51.

2. Statistics Canada. Meal and vehicle rates used to calculate travel expenses for 2016 and previous years [Internet]. 2017. Available from: http://www.cra-arc.gc.ca/travelcosts/

3. Statistics Canada. Labour force survey estimates (LFS), wages of employees by job permanence, union coverage, sex and age groupannual (current dollars). [Internet]. 2017. Available from: http://www5.statcan.gc.ca/cansim/a26?lang=eng&id=2820074#F7

4. Klarenbach S, Gill JS, Knoll G, Caulfield T, Boudville N, Prasad GVR, et al. Economic consequences incurred by living kidney donors: a Canadian multi-center prospective study. Alam A Boudville N, Bugeya A, Dipchand C, Doshi M, Feldman L, Garg A, Geddes C, Gibney E, Gill J, Karpinski M, Kim J, Klarenbach S, Knoll G, Lok C, McFarlane P, Monroy-Cuadros M, Muirhead N, Nevis I, Nguan CY, Parikh C, Poggio E, Prasad G, Storsley L, Ta AJ, editor. Am J Transplant. 2014;14(4):916–22.

5. Krol M, Brouwer W. How to estimate productivity costs in economic evaluations. Pharmacoeconomics. 2014/02/08. 2014;32(4):335–44.

6. Statistics Canada. Average hourly earnings (including overtime) for employees paid by the hour, by province and territory [Internet]. 2017. Available from: http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/labr80-eng.htm

7. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes. Oxford university press; 2015.