Supplementary Online Content

Medium and long-term health risks in living kidney donors:

a systematic review and meta-analysis

Appendix 1 MOOSE checklist

Item No	Recommendation	Reported on Page No
Reporting of background should include		
1	Problem definition	p4
2	Hypothesis statement	p4
3	Description of study outcome(s)	p5
4	Type of exposure or intervention used	P4
5	Type of study designs used	p5
6	Study population	p5
Reporting of search strategy should include		
7	Qualifications of searchers (eg, librarians and investigators)	p5
8	Search strategy, including time period included in the synthesis and key words	supp4,5
9	Effort to include all available studies, including contact with authors	
10	Databases and registries searched	p5
11	Search software used, name and version, including special features used (eg, explosion)	p5
12	Use of hand searching (eg, reference lists of obtained articles)	p5,24
13	List of citations located and those excluded, including justification	p24
14	Method of addressing articles published in languages other than English	
15	Method of handling abstracts and unpublished studies	
16	Description of any contact with authors	
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	p6,7
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	p6,7
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	p6,7
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	p7
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	p7
22	Assessment of heterogeneity	P7
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	p6,7
24	Provision of appropriate tables and graphics	p24-33
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	p25-27, supp13,15,18,20
26	Table giving descriptive information for each study included	p29-32
27	Results of sensitivity testing (eg, subgroup analysis)	p16
28	Indication of statistical uncertainty of findings	p8-11

Reporting of discussion should include		
29	Quantitative assessment of bias (eg, publication bias)	p9-11 supp17
30	Justification for exclusion (eg, exclusion of non-English language citations)	
31	Assessment of quality of included studies	supp10,11
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	p14
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	p14,15
34	Guidelines for future research	
35	Disclosure of funding source	p16

From: Stroup DF, Berlin JA, Morton SC, et al, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. *JAMA*. 2000;283(15):2008-2012. doi: 10.1001/jama.283.15.2008.

Transcribed from the original paper within the NEUROSURGERY® Editorial Office, Atlanta, GA, United Sates. August 2012.

Appendix 2 Details of search strategy

Health outcomes search strategy

Pubmed search strategy

Date: Up to July 20th 2017
Search: ((((((((("epidemiology"[Mesh]) OR "epidemiology"[Subheading]) OR "epidemiologic methods"[Mesh]) OR prospective) OR retrospective) OR longitudinal) OR cohort) OR follow-up) AND Humans[Mesh])) AND ((((((((((living donors) OR "living donors"[Mesh]) OR ("tissue donors"[Mesh] AND living)) OR (tissue donors AND living)) OR (organ donor AND living)) OR (kidney donor AND living)) OR (lung donor AND living)) OR (donor AND living)) OR (liver donor and living))) AND Humans[Mesh])

Embase search strategy

Date: 1974 to July 20th 2017
Search
1 living donor.mp. or exp living donor
2 donor.mp. or exp donor
3 living.mp.
4 2 and 3
5 ((Kidney or organ* or liver* or lung* or tissue*) adj3 (donor* or donat*)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
6 3 and 5
7 1 or 4 or 6
8 exp epidemiology/ or epidemiology.mp.
9 ep.fs.
10 exp cohort analysis/
11 cohort.mp.
12 follow-up.mp. or exp follow up/
13 (prospective or retrospective or longitudinal).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
14 8 or 9 or 10 or 11 or 12 or 13
15 7 and 14

Psychosocial health outcomes search strategy

Pubmed search strategy

Date: Up to July 20th 2017
Search: ((((((((((((living donor*) OR living donor[MeSH Terms]) OR (tissue donor* AND living)) OR ("tissue donor"[MeSH] AND living)))) AND ((((kidney) OR kidney[MeSH Terms]) OR "kidney donor") OR kidney donor[MeSH Terms])))) OR (nephrectomy AND donor)) OR (kidney AND donor))) AND ((((((((((((((((((health related quality of life) OR quality of life[MeSH Terms]) OR ((depression) OR depression[MeSH Terms])) OR ((anxiety) OR anxiety[MeSH Terms])) OR ((mental health) OR mental health[MeSH Terms])) OR ((psychology) AND psychology[MeSH Terms])) OR mental suffering[MeSH Terms]) OR HRQoL) OR ((psychosocial factor[MeSH Terms]) OR psychosocial factors[MeSH Terms])) OR mental fatigue[MeSH Terms]))))) OR SF-36) OR SF-12) OR "quality of life") OR "short-form questionnaire 36") OR "short-form questionnaire 12") OR "quality of health")

Embase search strategy

Date: Up to July 20th
1. exp donor/ or donor.mp.
2. living donor.mp. or exp living donor/

3. living.mp.

4. 1 and 3

5. (kidney adj3 (donor* or donat*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

6. 3 and 5

7. exp epidemiology/ or epidemiology.mp.

8. ep.fs.

9. exp cohort analysis/

10. cohort.mp.

11. follow-up.mp. or exp follow up/

12. (prospective of retrospective or longitudinal).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]

13. 7 or 8 or 9 or 10 or 11 or 12

14. human/

15. health related quality of life.mp. or exp "quality of life"/

16. depression.mp. or exp depression/

17. anxiety.mp. or exp anxiety/

18. mental health.mp. or exp mental health/

19. exp psychological aspect/

20. exp self esteem/

21. exp mental stress/

22. HRQoL.mp.

23. social function.mp.

24. psychosocial.mp.

25. empowerment.mp. or exp empowerment/

26. community awareness.mp.

27. SF-36.mp. or exp Short Form 36/

28. SF-12.mp. or exp Short Form 12/

29. quality of life.mp.

30. quality of health.mp.

31. exp nephrectomy/ or nephrectomy.mp.

32. 4 and 31

33. 1 and 31

34. kidney/ or kidney.mp.

35. 4 and 34

36. 6 or 33 or 35

37. 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30

38. 36 and 37

Appendix Table 1. Outcome definition and ascertainment for clinical endpoints

Outcome	Author	Definition	Ascertainment
All-cause mortality	Berger 2011		Record linkage
	Garg 2012		Record linkage
	Mjoen 2014		Record linkage
	Segev 2010		Record linkage
Cancer	Ibrahim 2009	Self-report of any cancer diagnosis	Self-reported
	Lentine 2012	ICD-9 codes: 105, 140-165, 170-208	Record linkage
	Mjoen 2012	Fatal cancer: ICD-8-10 codes	Record linkage
Cardiovascular disease	Garg 2012	First major cardiovascular event	Record linkage
	Ibrahim 2009	Any coronary heart disease, cerebrovascular event or transient ischemic attack	Self-reported
	Mjoen 2014	Fatal CVD ICD-10: I00-I99	Record linkage
	Rizvi 2016	Ischaemic Heart Disease	NR
End-stage Renal Disease	Lam 2012	Acute dialysis during any hospital stay	Record linkage
	Mjoen 2014	Chronic dialysis or kidney transplantation	Record linkage
	Muzaale 2014	Maintenance dialysis, transplant waiting list, or kidney transplantation	Record linkage
	Rogers 2009	eGFR < 10ml/min/1.73 m^2	Physical exam
Type 2 Diabetes	Doshi 2013	Fasting blood glucose ≥ 126mg/dl or use of an anti-hyperglycemic drug	Physical exam/medical history
	Garg 2008	Ontario Diabetes Database codes	Record linkage
	Ibrahim 2009	Self-reported	Self-reported
	Rizvi, 2016	Fasting blood glucose≥ 126mg/dl	Physical exam
	Reese 2014	Linkage to Medicare and outpatient records	Record linkage
Hypertension	D'Almedia 1996	BP >140/90mmHg at least twice or use of anti-hypertensive drugs	Physical exam/medical history
	Doshi 2013	BP >140/90mmHg or use of anti-hypertensive drugs	Physical exam/medical history
	Garg 2008	ICD-9-CM: 401x-405x; ICD-10: I10-I13, I15	Record linkage
	Hakim 1984	DBP ≥ 90 mm HG	Physical exam
	Ibrahim 2009	Average BP >140/90mmHg or use of anti-hypertensive drugs	Physical exam/medical history
	Massie 2014b	NR	Patient interview/medical records
	Miller 1985	BP >160/90mmHg or use of anti-hypertensive drugs	Physical exam/medical history
	Rizvi, 2016	BP >140/90mmHg on more than 1 occasion	Physical exam
	Rodriguez-Itubre 1985	BP >150/90mmHg	Physical exam
	Watnick 1988	BP >140/90mmHg or use of anti-hypertensive drugs	Physical exam/medical history
	Wiliams 1986	BP >140/90mmHg or use of anti-hypertensive drugs	Physical exam/medical history
Gestational Hypertension	Garg 2015	ICD-9: 6420,6423,6429 or ICD -10: O13, O16	Record linkage
	Reisaeter 2009	BP >140/90mmHg prior to pregnancy or 20 weeks gestation	Medical birth registry
Low birth weight	Garg 2015	<2500 g in birth weight	Record linkage
	Reisaeter 2009	≤2500 g in birth weight	Medical birth registry
Pre-eclampsia	Garg 2015	ICD-9: 6424,-6427 and ICD-10: O11, O14, O15	Record linkage
	Reisaeter 2009	BP >140/90mmHg prior to pregnancy or 20 weeks gestation and proteinuria*	Medical birth registry
Pre-term birth	Garg 2015	< 37 weeks of gestation	Record linkage
	Reisaeter 2009	< 22 weeks gestational age and <33 weeks gestational age	Medical birth registry

* Proteinuria was defined as excretion of ≥ 0.3 g per day, usually equivalent to ≥ 1+ on a standard urine test strip
BP: blood pressure, CVD: cardiovascular disease, DBP: diastolic blood pressure, eGFR: estimated glomerular filtration rate, ICD: international classification of diseases, NR: not reported

Appendix Table 2. Comparability of non-donor controls to living kidney donors

Author	Control selection	Matching criteria	Selection based on measure of renal function	Control selection criteria	Matching criteria
Doshi 2013	+++	+++	eGFR, urinalysis	No history of liver, heart or kidney disease, cancer, no hypertension or diabetic medication, BP<140/90mmHg, fasting blood sugar<126mg/dL, GFR≥80ml/min/1.73m^2, negative urinalysis	Age, gender, baseline SBP, duration of follow-up Method: nearest neighbour greedy algorithm matching without replacement
Rizvi 2016	+++	+++	NR	Potential donors (siblings) assessed and deemed medically suitable for kidney donation	Matched by age, sex, BMI
Moody 2016	+++	++*	Creatinine, GFR, urinary albumin, urinary protein	Fulfilled UK medical fitness criteria for nephrectomy, acceptable GFR by age, urinary albumin creatinine ratio ≤300 mg/g, protein- creatinine ratio ≤500 mg/g ,24hour total protein ≤300mg/day	Donors and controls not statistically different for age, sex, ethnicity, BMI, smoking, baseline hypertension, diabetes, medication use
Kasiske 2015	+++	++*	Yes (basic laboratory tests for kidney disease)	Fulfilled same criteria for nephrectomy as donors (medical history, vital signs, kidney function tests, no invasive testing or imaging of kidneys)	No significant difference in age, sex, ethnicity, height, weight, BMI, hip circumference, wait circumference or medication use (sf NSAIDs) between donors and controls
Seyahi 2007	+++	+	NR	Potential donors and healthy volunteers: fulfilled same exclusion criteria as for living kidney donors	Matched by age and sex
Berger 2011	++	+++	No	No known contraindications to kidney donation based on medical history, physical examination	Matched by age, BMI, SBP, education, ethnicity, smoking, using iterative expanding radius matching
Garg 2015	++	+++	No	No health condition contraindicating nephrectomy (record linkage) history of gestational hypertension or preeclampsia, diabetes, hypertension, CVD, cancer, pulmonary liver or genitourinary disease, systemic lupus erythematosus, rheumatoid arthritis, HIV	Matched by age, sex, index date, rural or urban residence, income, number of previous pregnancies
Mjoen 2014	++	+++	No	No self-reported diabetes, CVD or hypertension medication, BP≤140/90mmHg, BMI≤30kg/m^2	Matched by age, gender, SBP, BMI and smoking using coarsened exact matching
Muzaale 2014	++	+++	No	No health condition contraindicating nephrectomy (self-report, physical examination)	Matched for age, sex, ethnicity, educational background, BMI, smoking history, SBP using iterative expanding radius matching
Segev 2010	++	+++	No	NHANES participants: no health condition contraindicating nephrectomy (self-report, physical examination) including history of kidney disease, diabetes, heart disease and hypertension	Exact matching by sex Progressive radius matching by age, BMI, SBP, educational background.
Garg 2008	++	++	No	No health condition contraindicating nephrectomy (record linkage), hypertension, diabetes, CVD, renal disease or previous nephrectomy, overnight hospitalisation or >10 primary care visits	Matched on age, sex, neighbourhood income, frequency of non-physician healthcare visits
Garg 2012	++	++	No	No health condition contraindicating nephrectomy (record linkage): history of diabetes, hypertension, CVD, cancer,	Matched by age, sex, index date, rural or urban residence, income

				pulmonary, liver, genitourinary disease, rheumatological conditions, chronic infections, nephrology consultation, frequent physician visit (>4 in 2 years)	
Lam 2012	++	++	No	No health condition contraindicating nephrectomy (record linkage): history of diabetes, hypertension, CVD, cancer, pulmonary, liver, genitourinary disease, systemic lupus erythematosus, rheumatoid arthritis, HIV, gestational diabetes, pre-eclampsia	Matched by age, sex, index date, rural or urban residence, income
Reese 2014	++	++	No	No self-reported hypertension, diabetes, cancer, CVD, pulmonary disease, psychological or neurological illness, BMI<40, health status defined as good to excellent	Matched by sex, ethnicity, neighbourhood income, BMI
Bahous 2006	++		No	No biological or clinical history of liver, heart, kidney disease, cancer, smoking, no current medication	
Chavers 1985	++		Creatinine, creatinine clearance, intravenous pyelogram	Potential donors being screened, normal BP, normal urinalysis, normal creatinine, normal creatinine clearance	
Clemens 2011	++		No	Healthy individuals (no self-reported renal disease, hypertension, diabetes, CVD, pulmonary disease, cancer)	
Rodriguez-Iturbe 1985	++		Creatinine	Healthy volunteers with no self-reported history of systemic or kidney disease, normal urine analysis, serum creatinine, haematocrit and white cell count	
Talseth 1986	++		Creatinine	Presumed healthy, i.e. no self-reported history of kidney disease, no medication use, normal BP, sterile urine culture, dip-stick negative urine, creatinine clearance≥60ml/min/1.73m^2	
Ibrahim 2009	+	+++	No	NHANES participants	Matched by age, sex, ethnicity, BMI
Massie 2014	+	+++	No	Healthy individuals (ARIC/CARDIA participants)	Matched by age, sex, ethnicity, BMI
Miller 1985	+	++	No	General population	Matched by age, sex, ethnicity and duration of follow-up
Padrao 2009	+	++	No	Healthy volunteers (no acute chronic medical condition)	Matched by age, sex, ethnicity, education, socioeconomic level
Taskintuna 2009	+	++	No	Healthy volunteers	Matched
Undurraga 1998	+	++	No	Healthy individuals	Matched by age, sex, height
Watnick 1988	+	++	No	No known systemic disease, no current medication affecting blood pressure or GFR	Matched by age, sex, ethnicity
Williams 1986	+	++	No	Reportedly eligible for nephrectomy based on renal function and general health or no renal disease or nephrectomy	Matched by age, sex, ethnicity
Dunn 1986	+	+	NR	Prospective donors	Matched by age and sex
Hakim 1984	+	+	NR	Potential donors being screened	Matched by age and sex
Lentine 2012	+	+	No	General population (insurer database)	Matched by age and sex
Lima 2006	+	+	No	Healthy subjects (no chronic disease except controlled hypertension or previous surgery)	Matched by age and sex
Mjoen 2012	+	+	No	General population (Norwegian population census)	Matched by age, year of birth, sex

O'Donnell 1986	+	+	NR	Potential donors	Matched by age and sex
Yildirim 2017	+	+	No	Healthy individuals (no chronic disease)	Matched by age and sex
Albertsmeyer 2010	+		No	General population	
Dew 2016	+		No	No self-reported chronic disease	
D'Almeida 1996	+		No	Potential donors being screened	
Demir 2005	+		NR	Healthy subjects without history of disease, normal renal function	
Glotzer 2013	+		No	Potential donors	
Gross 2013	+		No	General population	
Guvence 2012	+		No	General population	
Hossain 2015	+		No	Healthy subjects (no diabetes, hypertension or renal disease)	
Ibrahim 2017	+		No	General population	
Liu 1992	+		No	Participants with normal blood pressure, no history of renal disease	
Mathillas 1985	+		No	Healthy non-hypertensive individuals	
Mjoen 2011	+		No	General population	
Najarian 1992	+		No	Siblings	
Reisaeter 2009	+		No	General population	
Rogers 2009	+		No	General population	
Shehab-Eldin 2009	+		No	Healthy individuals	
Shrestha 2008	+		No	Potential donors	
Sobh 1989	+		No	Healthy individuals	
Sommerer 2015	+		No	General population	
Young 2012	+		No	No self-reported kidney disease, diabetes, CVD or cancer	

*donors and non-donors not matched but comparability for age, sex and sociodemographic factors statistically tested
Selection criteria: +++: successfully completed living donor screening, or eligible for nephrectomy based on medical status and renal function tests; ++: eligible for nephrectomy based on medical status OR renal function test only, +: limited health screening selection or not selected based on eligibility for nephrectomy
Matching criteria: +++: age, sex, sociodemographic factors and/or health factors (medical history, smoking, BMI, blood pressure etc.); ++: age, sex and sociodemographic factors (ethnicity, income, education), or donors and controls not matched but comparability for age, sex and sociodemographic factors statistically tested ; +: age, sex; empty field= no matching
ARIC: Atherosclerosis Risk in Communities Study, BP: blood pressure, BMI: body mass index, CARDIA: Coronary Artery Risk Development in young Adults study, CKD: chronic kidney disease, CVD: cardiovascular disease, DBP: diastolic blood pressure, eGFR: estimated glomerular filtration rate, GFR: glomerular filtration rate, NHANES: National Health and Nutrition Examination Survey, NR: not reported, NSAID: non-steroidal anti-inflammatory drugs, SBP: systolic blood pressure

Appendix Table 3. Newcastle Ottawa Scale assessments of included studies

Author, year	Selection	Comparability	Ascertainment of Outcome	Total Score
Muzaale 2014/Segev 2010	3	2	3	8
Lentine 2012	2	1	3	6
Reese 2014	3	1	2	6
Gross 2013	3	0	3	6
Mjoen 2012	2	1	3	6
Garg 2012/Lam 2012	3	1	3	7
Ibrahim 2017	1	0	2	3
Mjoen 2014	3	2	3	8
Mjoen 2011	3	0	3	6
Garg 2008	3	2	3	8
Massie 2014	1	1	1	3
Dew 2016	3	0	2	5
Sommerer 2015	3	0	1	4
Ibrahim 2009	2	1	1	4
Clemens 2011	3	1	2	6
Berger 2011	3	1	3	7
Young 2012	1	0	3	4
Kasiske 2015	4	1	1	6
Chavers 1985	1	0	2	3
Demir 2005	2	0	1	3
D'Almeida 1996	1	0	3	4
Reisaeter 2009	2	0	3	5
Doshi 2013	3	1	3	7
Bahous 2006	2	1	2	5
Seyahi 2007	4	1	1	6
Lima 2006	2	1	2	5
Rizvi, 2016	3	1	3	7
Garg 2015	3	1	3	7
Glotzer 2013	3	0	1	4
Guvence 2012	1	0	2	3
Dunn 1986	2	0	0	2
Albertsmeyer 2010	3	0	2	5
Padrao 2009	3	2	1	6
Shrestha 2008	3	0	1	4
Najarian 1992	1	0	2	3
Moody 2016	3	2	2	7
Yildrim 2017	2	1	0	3
Hakim 1984	2	1	3	6
Sobh 1989	1	0	1	2
Williams 1986	2	1	2	5
Mathillas 1985	1	0	2	3
O'Donnell 1986	2	1	1	4
Talseth 1986	2	0	2	4
Undurraga 1998	1	1	2	4

Watnick 1988	1	1	3	5
Rodriguez-Iturbe 1985	2	0	2	4
Rogers 2009	2	0	1	3
Hossain 2015	2	0	1	3
Taskintuna 2009	1	1	1	3
Liu 1992	1	0	1	2
Miller 1985	1	1	1	3
Shehab-Eldin 2009	2	1	1	4

Study quality assessment was based on the nine star Newcastle-Ottawa Scale (NOS) using pre-defined criteria namely: selection (population representativeness), comparability (Adjustment for confounders), and ascertainment of outcome. The NOS assigns a maximum of four points for selection, two points for comparability and three points for outcome. Nine points on the NOS reflects the highest study quality.

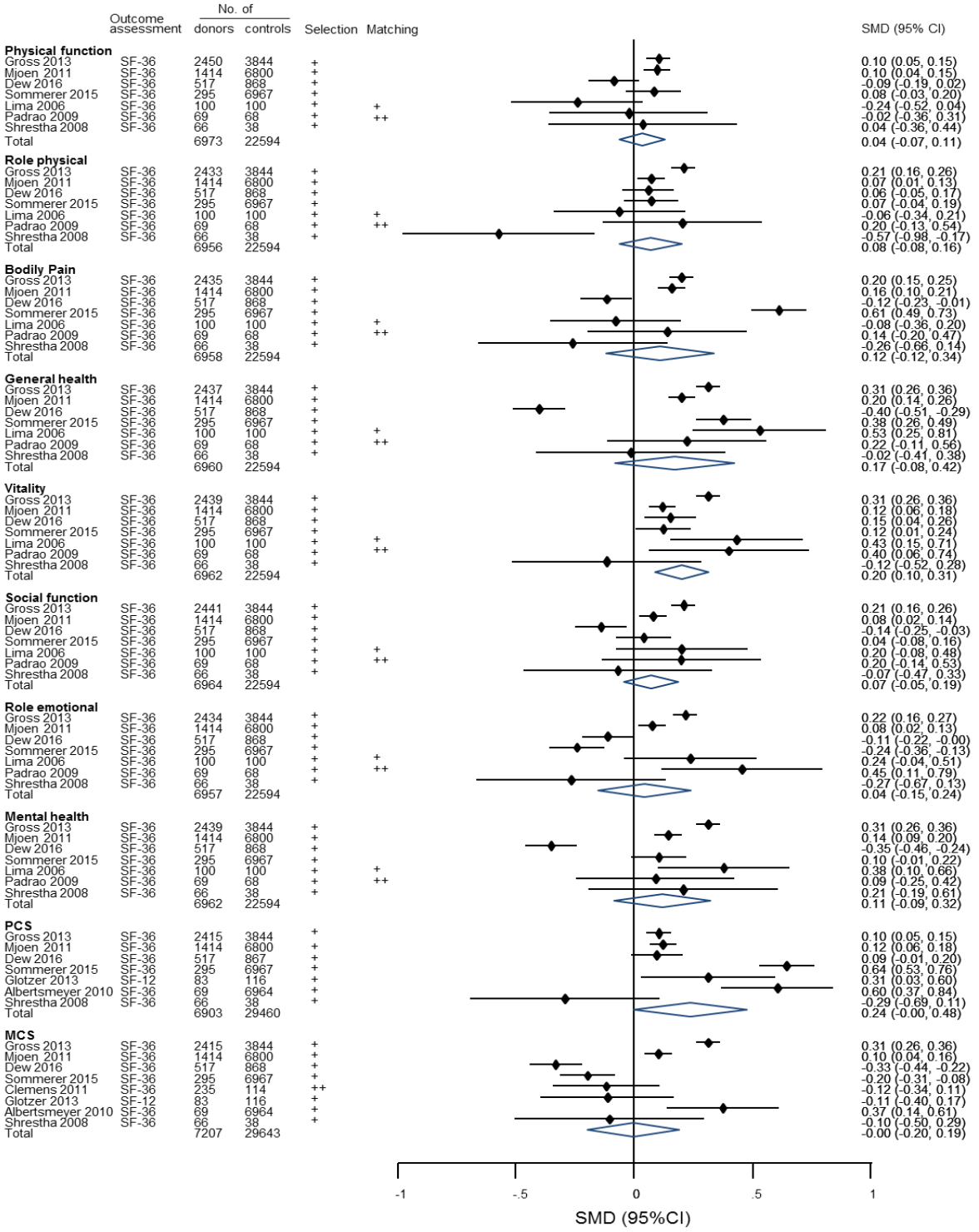
Appendix Table 4. Pooled SMD and mean difference in blood pressure and biomarkers between living kidney donors compared to controls *

Outcome	No. studies	No. donors	No. controls	SMD (95%CI)	Mean difference (95%CI)
DBP (mmHg)	6	712	830	0.17(0.03;0.34)	1.7 (0.3;3.2)
SBP (mmHg)	6	712	1123	0.14(-0.10;0.40)	1.7 (-0.6;5.2)
Triglycerides (mg/dL)	2	356	354	-0.03(-0.8;0.77)	-13.0 (-62.7;36.6)
Total cholesterol (mg/dL)	3	412	398	-0.22(-0.84;0.45)	-8.8 (-26.4;8.8)
HDL-cholesterol (mg/dL)	2	356	354	-0.29(-0.52;-0.11)	-4.5 (-7.3;-1.9)
LDL-cholesterol (mg/dL)	2	153	143	-0.06(-1.22;1.15)	-2.0 (-25.9;21.8)
Glucose (mg/dL)	4	425	422	-0.02(-0.43;0.5)	-1.2 (-9.7;8.0)
eGFR (mL/min/1.73m2)	6	894	901	-1.59(-1.86;-0.33)	-24.7 (-29.0;-20.7)
Serum creatinine (mg/dL)	3	391	423	1.02(0.44;1.60)	0.2 (0.1;0.3)

* Standardised mean difference from studies with baseline recruitment ending after 2000 and an NOS score≥4 were pooled using the random-effects profile likelihood meta-analysis method

DBP: diastolic blood pressure, eGFR: estimated glomerular filtration rate, HDL: high density lipoprotein, LDL: low density lipoprotein, SBP: systolic blood pressure, SMD: standardised mean difference

Appendix Figure 1. Association of living kidney donation with Health related quality of life scores in selected studies



MCS: mental component summary, PCS; physical component summary, SF-36: Short form 36SMD: standardised Mean Difference

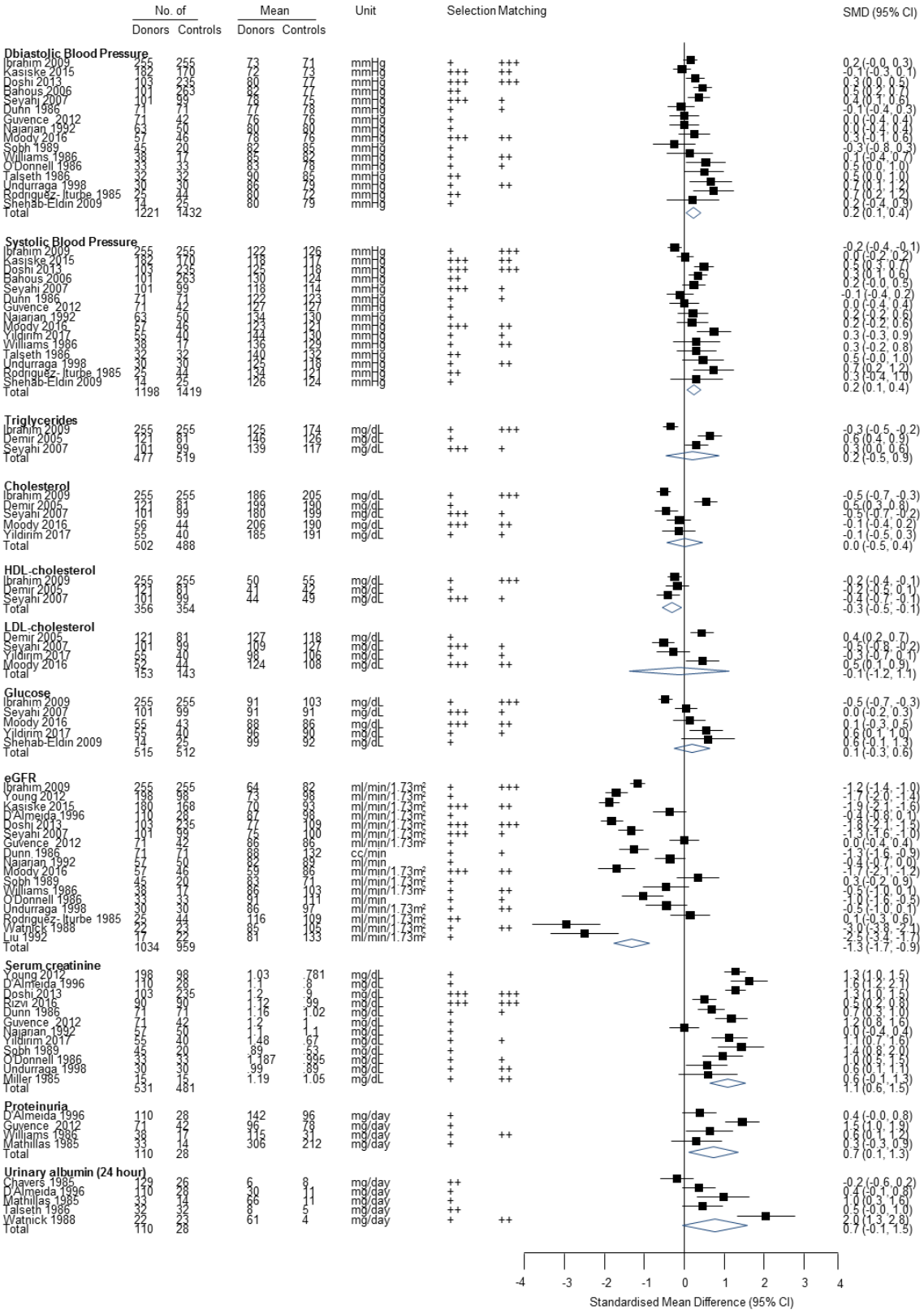
*The Standardised mean difference (Cohen's d statistic) was pooled across studies with baseline recruitment ending after 2000 and an NOS score≥4 using the profile likelihood meta-analysis method

Appendix Table 5 Pooled estimates of risk ratios for selected clinical endpoints in living kidney donors compared to controls *

Outcome	No. studies	Average follow-up time(y)*	No. events donors	No. events non donors	Pooled adjusted RR (95%CI) †	Pooled IR in donors (95%CI) ‡	Pooled IR non-donors (95%CI) ‡
All-cause mortality	4	6-15	1467	3121	0.60 (0.31,1.10)	4.3 (1.3, 14.1)	5.9 (1.6, 22.1)
Cancer	3	8-15	160	451	0.72 (0.58, 0.87)	2.9 (1.2, 6.9)	4.3 (1.3, 14.4)
Cardiovascular disease	4	6-15	107	991	1.11 (0.64, 1.70)	2.4 (1.6, 3.5)	1.9 (0.8, 5.1)
Diabetes	5	6-12	47	181	1.03 (0.77, 1.25)	3.8 (2.6, 5.4)	4.1 (3.4, 5.2)
Hypertension	4	6-12	297	862	1.08 (0.46, 2.34)	26.3 (12.8, 53.7)	25.9 (14.4, 48.0)
End stage renal disease	3	7-15	109	53	8.83 (1.02, 20.93)	0.5 (0.1, 4.9)	0.1 (0.02, 0.6)
Obstetric outcomes							
Gestational hypertension	2	5-11	10	331	2.27 (0.94, 5.36)	3.8 (1.4, 6.3)	1.6 (1.0, 2.2)
Pre-eclampsia	2	5-11	14	687	2.12 (1.06, 4.27)	5.9 (2.9, 8.9)	3.1 (2.9, 3.3)
Preterm birth	2	5-11	21	1449	1.47 (0.78, 2.64)	8.7 (5.1, 12.3)	6.5 (6.2, 6.8)
Low birthweight	2	5-11	17	1141	1.70 (0.91, 3.16)	7.0 (3.8, 10.2)	4.7 (3.6, 5.9)

*Mean or median follow-up time in donors
† Risk estimates from studies with baseline recruitment ending after 2000 and an NOS score≥4 were pooled using the random-effects profile likelihood meta-analysis method
‡Incidence rates per 1000 person-years for disease outcomes. For obstetric outcomes incidence of adverse outcomes per 100 pregnancies are reported
IR: incidence rate, RR: relative risk

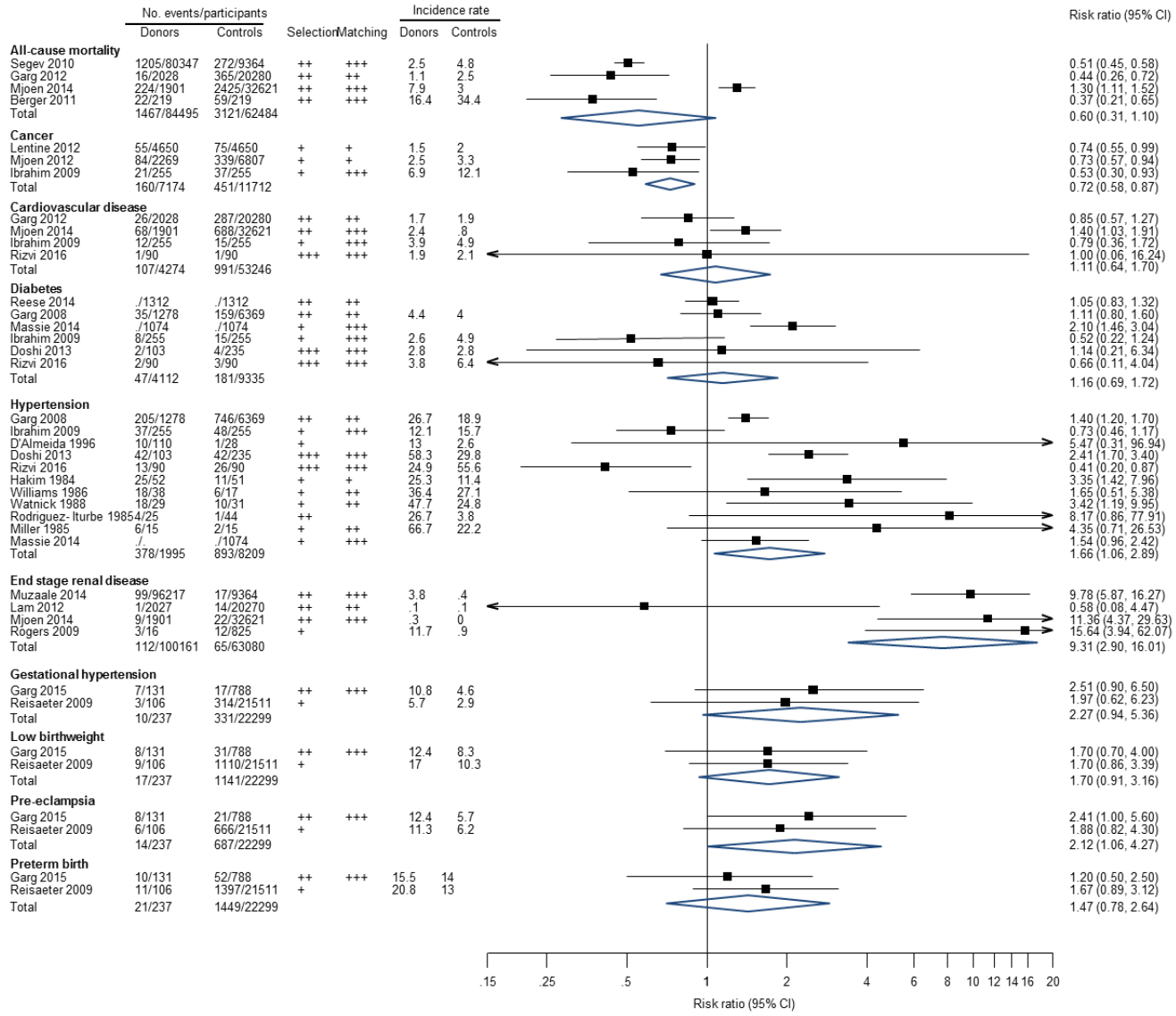
Appendix Figure 2. Association between living kidney donation and selected risk factors including all studies



Standardised Mean Differences (SMD) were pooled using the random-effects profile likelihood meta-analysis method

eGFR: estimated glomerular filtration rate, HDL: high density lipoprotein, LDL: low density lipoprotein

Appendix Figure 3. Association between living kidney donation and selected clinical endpoints including all studies



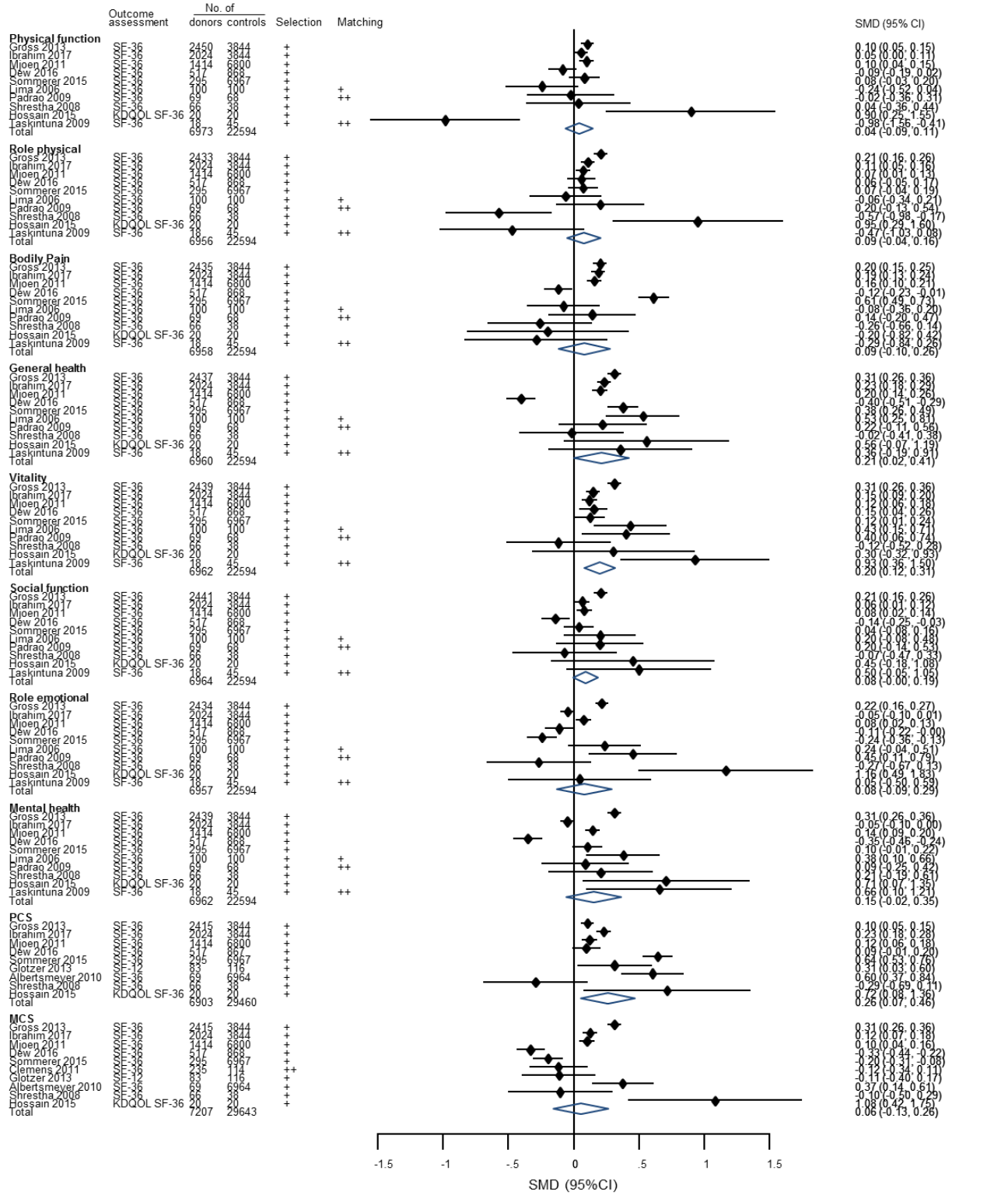
Pooled estimates are based on random effects meta-analysis. NR: not reported

Appendix Table 6. Pooled mean difference in Health related quality of life scores between living kidney donors and non-donor controls (all studies)

Outcome	No. studies	No. donors	No. controls	SMD (95%CI)*	I^2(95%CI)
Physical Component Summary	9	6903	29460	0.26 (0.07,0.46)	67% (33, 84)
Mental Component Summary	10	7207	29643	0.06 (-0.13,0.26)	64% (29, 82)
Physical function	10	6973	22594	0.04 (-0.09,0.11)	0% (0, 62)
Role physical	10	6956	22594	0.09 (-0.04,0.16)	0% (0, 62)
Bodily Pain	10	6958	22594	0.09 (-0.1,0.26)	55% (9, 78)
General health	10	6960	22594	0.21 (0.02,0.41)	62% (26, 81)
Vitality	10	6962	22594	0.2 (0.12,0.31)	0% (0, 62)
Social function	10	6964	22594	0.08 (0,0.19)	0% (0, 62)
Role emotional	10	6957	22594	0.08 (-0.09,0.29)	53% (4, 77)
Mental health	10	6962	22594	0.15 (-0.02,0.35)	56% (11, 78)

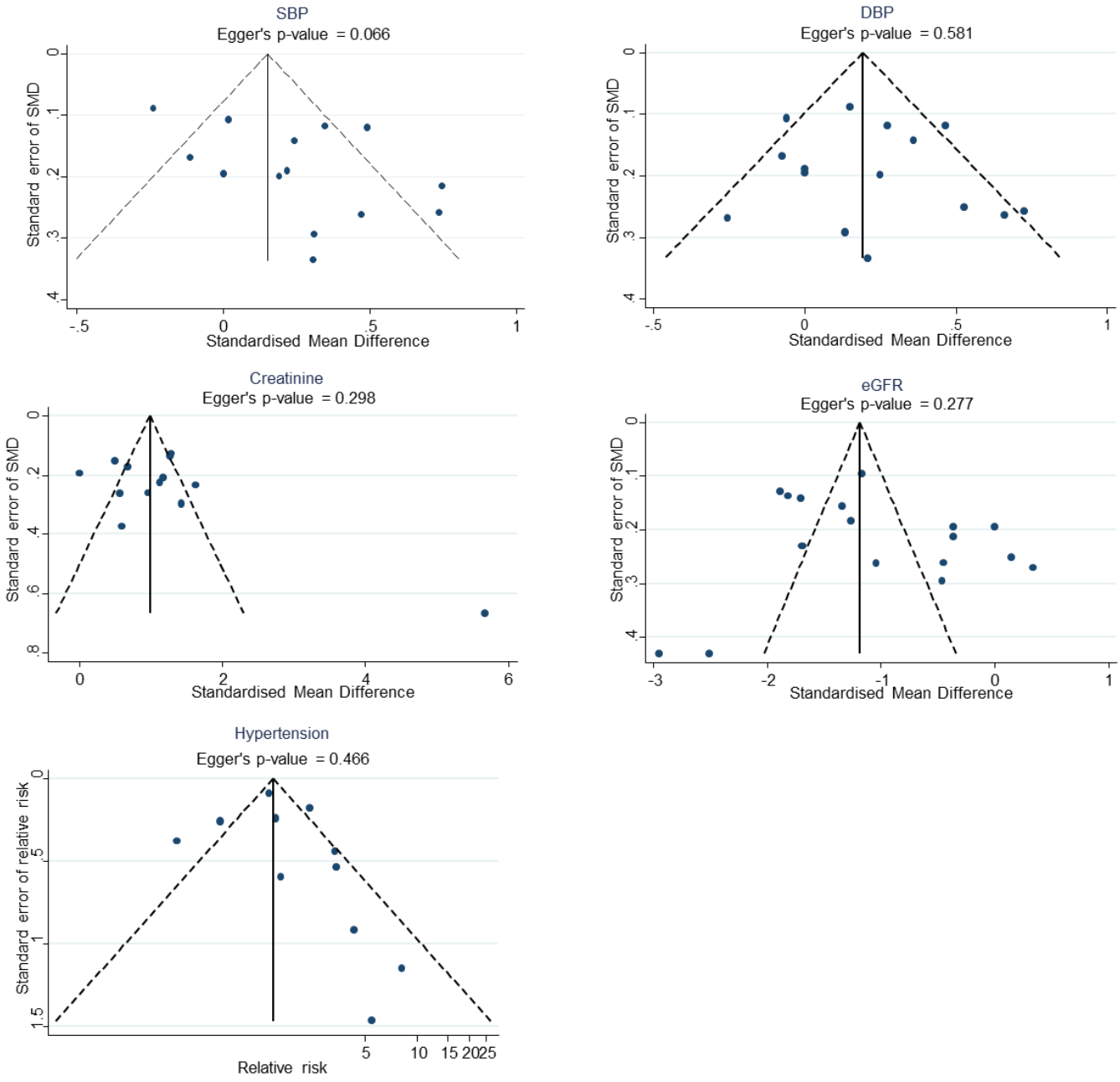
SMD: Standardised Mean Difference
*The standardised mean difference (Cohen's d statistic) was pooled across all studies using the profile likelihood meta-analysis method
Note: details of the studies included in this analysis are presented in **Appendix Figure 4**

Appendix Figure 4. Association of living kidney donation with Health related quality of life scores in all studies



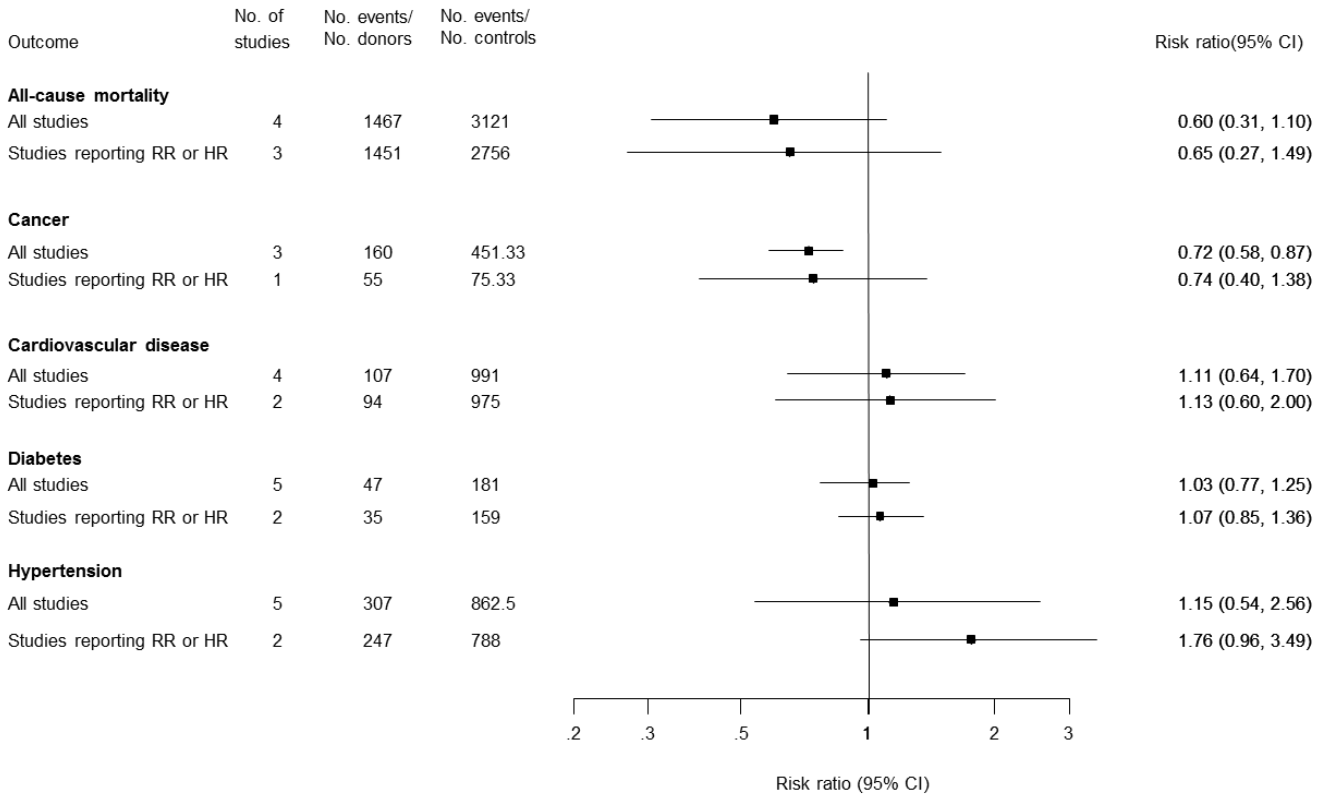
MCS: mental component summary, PCS; physical component summary, SMD: standardised Mean Difference
*The Standardised mean difference (Cohen's d statistic) was pooled across all studies using the profile likelihood meta-analysis method

Appendix Figure 5. Funnel plots for association of organ donation with selected risk factors and clinical outcomes



Funnel plots were used to assess publication bias for outcomes reported in at least 10 studies. Dotted lines show 95% confidence intervals around the overall summary estimate. Reported p-values are from Egger's asymmetry test of associations.
DBP: diastolic blood pressure, eGFR: estimated glomerular filtration rate, SBP: systolic blood pressure

Appendix Figure 6. Sensitivity analysis assessing the effect of Odds Ratios in assessment of clinical outcomes in donors vs. non-donors



Risk estimates were pooled across all studies with an NOS score>4 and last baseline year>1990 and compared with studies where the reported risk estimate was a relative risk or a hazard ratio. Estimates were pooled using the profile likelihood method.
HR: hazard ratio, RR: relative risk