Supplementary Online Content

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

a systematic review and meta-analysis

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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)	р5
4	Type of exposure or intervention used	P4
5	Type of study designs used	р5
6	Study population	р5
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	р5
11	Search software used, name and version, including special features used (eg, explosion)	р5
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15	Method of handling abstracts and unpublished studies	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)	р7
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	р7
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.

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Appendix 2 Details of search strategy

Health outcomes search strategy

Pubmed search strategy

Date: Up to July 20th 2017

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

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

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Pre-term birth Garg 2015 < 37 weeks of gestation Record linkage	
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Appendix Table 1. Outcome definition and ascertainment for clinical endpoints

* Proteinuria was defined as excretion of \geq 0.3 g per day, usually equivalent to \geq 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

Author	or Control Matching Selection based on selection criteria measure of renal function		measure of renal	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 \leq 300 mg/g, protein- creatinine ratio \leq 500 mg/g ,24hour total protein \leq 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 \leq 140/90mmHg, BMI \leq 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

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

				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

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	-	2	5
Seyahi 2007	4	-	1	6
Lima 2006	2	- 1	2	5
Rizvi, 2016	- 3	-	- 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	1	1	1	3 4
Talseth 1986	2	0	2	4
Undurraga 1998	1	1	2	4

Appendix Table 3. Newcastle Ottawa Scale assessments of included studies

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.NinepointsontheNOSreflectsthehigheststudyquality.

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 metaanalysis 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

	Outcome assessment	No. donors		Selection	Matching		SMD (95% CI)
Physical function Gross 2013 Mjoen 2011 Dew 2016 Sommerer 2015 Lima 2006 Padrao 2009 Shrestha 2008 Total	n SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36	2450 1414 517 295 100 69 66 6973	3844 6800 868 6967 100 68 38 22594	+ + + + + + +	+ ++		$\begin{array}{c} 0.10 & (0.05, \ 0.15) \\ 0.10 & (0.04, \ 0.15) \\ -0.09 & (-0.19, \ 0.02) \\ 0.08 & (-0.03, \ 0.20) \\ -0.24 & (-0.52, \ 0.04) \\ -0.02 & (-0.36, \ 0.31) \\ 0.04 & (-0.36, \ 0.44) \\ 0.04 & (-0.07, \ 0.11) \end{array}$
Role physical Gross 2013 Mjoen 2011 Dew 2016 Sommerer 2015 Lima 2006 Padrao 2009 Shrestha 2008 Total	SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36	2433 1414 517 295 100 69 66 6956	3844 6800 868 6967 100 68 38 22594	+ + + + + + +	+ ++		$\begin{array}{c} 0.21 & (0.16, 0.26) \\ 0.07 & (0.01, 0.13) \\ 0.06 & (-0.05, 0.17) \\ 0.07 & (-0.04, 0.19) \\ -0.06 & (-0.34, 0.21) \\ 0.20 & (-0.13, 0.54) \\ -0.57 & (-0.98, -0.17) \\ 0.08 & (-0.08, 0.16) \end{array}$
Bodily Pain Gross 2013 Mjoen 2011 Dew 2016 Sommerer 2015 Lima 2006 Padrao 2009 Shrestha 2008 Total	SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36	2435 1414 517 295 100 69 66 6958	3844 6800 868 6967 100 68 38 22594	+ + + + + + +	+ ++		$\begin{array}{c} 0.20 & (0.15, 0.25) \\ 0.16 & (0.10, 0.21) \\ -0.12 & (-0.23, -0.01) \\ 0.61 & (0.49, 0.73) \\ -0.08 & (-0.36, 0.20) \\ 0.14 & (-0.20, 0.47) \\ -0.26 & (-0.66, 0.14) \\ 0.12 & (-0.12, 0.34) \end{array}$
General health Gross 2013 Mjoen 2011 Dew 2016 Sommerer 2015 Lima 2006 Padrao 2009 Shrestha 2008 Total	SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36	2437 1414 517 295 100 69 66 6960	3844 6800 868 6967 100 68 38 22594	+ + + + + + +	+ ++		$\begin{array}{c} 0.31 & (0.26 , 0.36) \\ 0.20 & (0.14 , 0.26) \\ -0.40 & (-0.51 , -0.29) \\ 0.38 & (0.26 , 0.49) \\ 0.53 & (0.25 , 0.81) \\ 0.22 & (-0.11 , 0.56) \\ -0.02 & (-0.41 , 0.38) \\ 0.17 & (-0.08 , 0.42) \end{array}$
Vitality Gross 2013 Mjoen 2011 Dew 2016 Sommerer 2015 Lima 2006 Padrao 2009 Shrestha 2008 Total	SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36	2439 1414 517 295 100 69 66 6962	3844 6800 868 6967 100 68 38 22594	+ + + + + + +	+ ++		$\begin{array}{c} 0.31 & (0.26 & 0.36) \\ 0.12 & (0.06 & 0.18) \\ 0.15 & (0.04 & 0.26) \\ 0.12 & (0.01 & 0.24) \\ 0.43 & (0.15 & 0.71) \\ 0.40 & (0.66 & 0.74) \\ -0.12 & (-0.52 & 0.28) \\ 0.20 & (0.10 & 0.31) \end{array}$
Social function Gross 2013 Mjoen 2011 Dew 2016 Sommerer 2015 Lima 2006 Padrao 2009 Shrestha 2008 Total	SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36	2441 1414 517 295 100 69 66 6964	3844 6800 868 6967 100 68 38 22594	+ + + + + +	+ ++		$\begin{array}{c} 0.21 & (0.16, \ 0.26) \\ 0.08 & (0.02, \ 0.14) \\ -0.14 & (-0.25, \ -0.03) \\ 0.04 & (-0.08, \ 0.16) \\ 0.20 & (-0.08, \ 0.48) \\ 0.20 & (-0.14, \ 0.53) \\ -0.07 & (-0.47, \ 0.33) \\ 0.07 & (-0.05, \ 0.19) \end{array}$
Role emotional Gross 2013 Mjoen 2011 Dew 2016 Sommerer 2015 Lima 2006 Padrao 2009 Shrestha 2008 Total	SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36	2434 1414 517 295 100 69 66 6957	3844 6800 868 6967 100 68 38 22594	+ + + + + + +	+ ++		$\begin{array}{c} 0.22 & (0.16 & 0.27) \\ 0.08 & (0.02' & 0.13) \\ -0.11 & (-0.25 & -0.00) \\ -0.24 & (-0.36 & -0.13) \\ 0.24 & (-0.04' & 0.51) \\ 0.45 & (0.11 & 0.79) \\ -0.27 & (-0.67' & 0.13) \\ 0.04 & (-0.15' & 0.24) \end{array}$
Mental health Gross 2013 Mjoen 2011 Dew 2016 Sommerer 2015 Lima 2006 Padrao 2009 Shrestha 2008 Total	SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36 SF-36	2439 1414 517 295 100 69 66 6962	3844 6800 868 6967 100 68 38 22594	+ + + + + + + +	+ ++		$\begin{array}{c} 0.31 & (0.26, 0.36) \\ 0.14 & (0.09, 0.20) \\ -0.35 & (-0.46, -0.24) \\ 0.10 & (-0.01, 0.22) \\ 0.38 & (0.10, 0.66) \\ 0.09 & (-0.25, 0.42) \\ 0.21 & (-0.19, 0.61) \\ 0.11 & (-0.09, 0.32) \end{array}$
PCS Gross 2013 Mjoen 2011 Dew 2016 Sommerer 2015 Glotzer 2013 Albertsmeyer 201 Shrestha 2008 Total	SF-36 SF-36 SF-36 SF-36 SF-12 0 SF-36 SF-36 SF-36	2415 1414 517 295 83 69 66 6903	3844 6800 867 6967 116 6964 38 29460	+ + + + + + +			$\begin{array}{c} 0.10 & (0.05, \ 0.15) \\ 0.12 & (0.06, \ 0.18) \\ 0.09 & (-0.01, \ 0.20) \\ 0.64 & (0.53, \ 0.76) \\ 0.31 & (0.03, \ 0.60) \\ 0.60 & (0.37, \ 0.84) \\ -0.29 & (-0.69, \ 0.11) \\ 0.24 & (-0.00, \ 0.48) \end{array}$
MCS Gross 2013 Mjoen 2011 Dew 2016 Sommerer 2015 Clemens 2011 Glotzer 2013 Albertsmeyer 201 Shrestha 2008 Total	SF-36 SF-36 SF-36 SF-36 SF-36 SF-12 0 SF-36 SF-36 SF-36	2415 1414 517 295 235 83 69 66 7207	3844 6800 868 6967 114 116 6964 38 29643	+ + + + ++ + + + +			$\begin{array}{c} 0.31 & (0.26, 0.36) \\ 0.10 & (0.04', 0.6) \\ -0.33 & (-0.44, -0.22) \\ -0.20 & (-0.31, -0.08) \\ -0.12 & (-0.34, 0.11) \\ -0.11 & (-0.40, 0.17) \\ 0.37 & (0.14, 0.61) \\ -0.10 & (-0.50, 0.29) \\ -0.00 & (-0.20, 0.19) \end{array}$
					-1	5 0 .5 SMD (95%CI)	1

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 metaanalysis 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

es		Donors	o. of Controls	Mean Donors Co	ontrols	Unit	Selectio	on Matching							SMD (95% CI)
		9218233 1001 1771 17733 1001 1771 1001 10000 1000000	21225 50053 71226 712 712 712 712 712 712 712 712 712 712	73209287760002253306000	7777758606552855329		+ + + + + + + + + + + + + + + + + + +	**** *** * * * * * * *				╶ _{╇┷} ┿┿ _{╋┷┷┷}			$\begin{array}{c} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 $
	Systolic Blood Pressui Drahim 2009 Kasiske 2015 Doshi 2013 Bahous 2006 Seyahi 2007 Guvence 2012 Nogdy 2007 Widghy 2007 Widghy 2007 Widghy 2007 Vidghy	e25523 11011 1101 7713 76575 8823 71011 771 76575 8823 755 755 755 755 755 755 755 755 755 75	257259 57259 57259 7450 80 720 720 720 720 720 720 720 720 720 72	2025082774374604546	27-121-121-01-09280-4 121-121-121-01-09280-4		+ +++ +++ +++ ++ +++ +++ +++ +++ +++ ++	**** *** * * * * *				┺ ┿┿ ┿╴┺┿╋ ╄┿╋			$\begin{array}{c} 0 & 2 & (-0.4 & -0.1) \\ 0 & 1 & (-0.4 & -0.4) \\ 0 & 3 & (-0.4 & -0.4) \\ 0 & 3 & (-0.4 & -0.4) \\ 0 & 2 & (-0.4 & -0.4) \\ 0 & 2 & (-0.4 & -0.4) \\ 0 & 2 & (-0.4 & -0.4) \\ 0 & 2 & (-0.4 & -0.4) \\ 0 & 2 & (-0.4 & -0.4) \\ 0 & 2 & (-0.4 & -0.4) \\ 0 & 2 & (-0.4 & -0.4) \\ 0 & 2 & (-0.4 & -0.4) \\ 0 & 3 & (-0.4 & -0.4) \\$
	T riglycerides Ibrahim 2009 Demir 2005 Seyahi 2007 Total	255 121 101 477	255 81 519	125 146 139	174 126 117	mg/dL mg/dL mg/dL	+ + ++++	+++ +			+	*			-0,3(-0,5,-0,2) 0.6(0,4,0,9) 0.3(0,0,0,6) 0.2(-0.5,0.9)
	Cholesterol Ibrahim 2009 Demir 2005 Seyahi 2007 Moody 2016 Yildirim 2017 Total	255 101 56 55 502	255 89 44 40 488	186 189 180 206 185	205 199 199 190 191	mg/dL mg/dL mg/dL mg/dL mg/dL	+ + +++ +++ +	++++ + ++ +			+ 1 /	- -			$\begin{array}{c} -0.5 & (-0.7, -0.3) \\ 0.5 & (-0.7, -0.3) \\ -0.5 & (-0.7, -0.2) \\ -0.1 & (-0.4, 0.2) \\ -0.1 & (-0.5, 0.3) \\ 0.0 & (-0.5, 0.4) \end{array}$
	HDL-cholesterol Ibrahim 2009 Demir 2005 Seyahi 2007 Total	255 121 101 356	255 89 354	50 44	55 49	mg/dL mg/dL mg/dL	+ + +++	+++ +				-			-0.2 (-0.4, -0.1) -0.2 (-0.5, 0.1) -0.4 (-0.7, -0.1) -0.3 (-0.5, -0.1)
	LDL-cholesterol Demir 2005 Seyahi 2007 Yildirim 2017 Moody 2016 Total	121 55 153	81 40 44 143	127 124 124	118 127 108	mg/d_ mg/d_ mg/dL mg/dL	+ ++++ + ++++	+ + ++		_	*	-			0.4.(0.2.0.7) -0.5.(-0.80.2) -0.3.(-0.7.0.1) 0.5.(0.1.0.9) -0.1(-1.2, 1.1)
	Glucose Ibrahim 2009 Seyahi 2007 Moody 2016 Yildirim 2017 Shehab-Eldin 2009 Total	255 101 55 14 515	255 99 43 40 512	91 91 866 99	103 91 86 92	mg/dL mg/dL mg/dL mg/dL mg/dL	+ +++ +++ + +	++++ + ++ +			•				-0.5 (-0.7, -0.3) 0.0 (-0.2, 0.3) 0.1 (-0.3, 0.5) 0.6 (0-1, 1.0) 0.6 (-0.1, 1.3) 0.1 (-0.3, 0.6)
	eGFR 2009 (Varahim 2019 Katsike 2015 (Satsike 2013) Sevahi 2017 Sevahi 2017 Guvence 2012 Dunn 1986 (Wanna 1016 Soph 1989 Wanna 1016 Soph 1989 Wanna 1986 O'Donnell 1986 O'D	25800 11031 1107 1177 1575 43830 5277 1034	29122947594759 5868951 29122947594759 2912294759 2912294759 291229 2912929 2912 29129 2912 29129 2912 29129 2912 2	470777568555767666 6776777888555767676161	82038990 9909110632 818061331 818061331 91113 818061331 91113 91113	m/min/1 73m m/min/1 73m	+ + +++ +++ +++ + + + + + + + + + + +	++++ ++ ++ ++ ++ ++ ++ ++ ++ ++ ++	-	** * * * * * * * * * * * * * *	-₩ . 4 . 4 . 4 . 4 . 4 . 4 . 4 . 4 . 4 . 4	• • • • • •			$\begin{array}{c} \begin{array}{c}$
	Serum Creatinne D'Almeida 1996 Doshi 2018 Rizvi 2018 Guvence 2012 Villarim 2017 Villarim 2017 Sobh 1986 O'Donnell 1986 O'Donnell 1986 Miller 1985 Total	19100 1100 1100 1000 1000 1000 1000 1000 1000 1000 1000 1000 1000 1000 1000 1000 1000 1000000	900000 9000 90000 90000 90000 9000000	1.03 1.2 1.2 1.2 1.2 1.4 8 1.8 1.8 1.9 1.19 1.19	.781 .9999 1.02 1.1 .67355 1.05	mg/d mgydo mgydo mgydo mgydo mgydo mgydo mgydo mgydo mgydo mgydo mgydo mgydo mgydo mgydo mgydo	+ + +++ + + + + + + + + + + + + + + +	++++ + + + ++ ++			-4		∎ - 		$\begin{array}{c} 5,1\\ 1,1\\ 1,1\\ 1,1\\ 1,1\\ 1,1\\ 1,1\\ 1,1\\$
	Proteinuria D'Almeida 1996 Guvence 2012 Williams 1986 Mathillas 1985 Total	110 71 38 33 110	28 42 17 14 28	142 96 306	96 78 212	mg/day mg/day mg/day mg/day	+ + + +	++					F		0.4 (-0.0, 0.8) 1.5 (1.9, 1.9) 0.3 (-0.3, 0.9) 0.3 (-0.3, 0.9) 0.7 (0.1, 1.3)
	Urinary albumin (24 ho Chavers 1985 D'Almeida 1996 Mathillas 1985 Talseth 1986 Watnick 1988 Total	120 110 322 110	26 224 32 28 24 22 28 28	6706 61	811 54	mg/day mg/day mg/day mg/day mg/day	++ + + ++ +	++					- -		$\begin{array}{c} -0.2 & (-0.6, 0.2) \\ 0.4 & (-0.1, 0.8) \\ 1.0 & (0.3, 1.6) \\ 0.5 & (-0.0, 1.0) \\ 2.0 & (1.3, 2.8) \\ 0.7 & (-0.1, 1.5) \end{array}$
			(0)					-4		-		0 1 In Difference		3	4

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

	No. events/ Donors	participants Controls	Selectio	nMatching	Incide Donors	nce rate Controls		Risk ratio (95% CI)
All-cause mortality Segev 2010 Garg 2012 Mjoen 2014 Berger 2011 Total	1205/80347 16/2028 224/1901 22/219 1467/84495	272/9364 365/20280 2425/32621 59/219 3121/62484	++ ++ ++ ++	+++ ++ +++ +++	2.5 1.1 7.9 16.4	4.8 2.5 3 34.4		0.51 (0.45, 0.58) 0.44 (0.26, 0.72) 1.30 (1.11, 1.52) 0.37 (0.21, 0.65) 0.60 (0.31, 1.10)
Cancer Lentine 2012 Mjoen 2012 Ibrahim 2009 Total	55/4650 84/2269 21/255 160/7174	75/4650 339/6807 37/255 451/11712	+ + +	+ + +++	1.5 2.5 6.9	2 3.3 12.1		0.74 (0.55, 0.99) 0.73 (0.57, 0.94) 0.53 (0.30, 0.93) 0.72 (0.58, 0.87)
Cardiovascular dise Garg 2012 Mjoen 2014 Ibrahim 2009 Rizvi 2016 Total	ase 26/2028 68/1901 12/255 1/90 107/4274	287/20280 688/32621 15/255 1/90 991/53246	+++ +++ + ++++	++ +++ +++ +++	1.7 2.4 3.9 1.9	1.9 .8 4.9 2.1 <		0.85 (0.57, 1.27) 1.40 (1.03, 1.91) 0.79 (0.36, 1.72) 1.00 (0.06, 16.24) 1.11 (0.64, 1.70)
Diabetes Reese 2014 Garg 2008 Massie 2014 Ibrahim 2009 Doshi 2013 Rizvi 2016 Total	./1312 35/1278 ./1074 8/255 2/103 2/90 47/4112	./1312 159/6369 ./1074 15/255 4/235 3/90 181/9335	*** ** * **** ****	++ ++ +++ +++ +++ +++	4.4 2.6 2.8 3.8	4 4.9 2.8 6.4 <		1.05 (0.83, 1.32) 1.11 (0.80, 1.60) 2.10 (1.46, 3.04) 0.52 (0.22, 1.24) 1.14 (0.21, 6.34) 0.66 (0.11, 4.04) 1.16 (0.69, 1.72)
Hypertension Garg 2008 Ibrahim 2009 D'Almeida 1996 Doshi 2013 Rizvi 2016 Hakim 1984 Williams 1986 Wathick 1988 Rodriguez-Iturbe 198 Miller 1985 Massie 2014 Total	205/1278 37/255 10/110 42/103 13/90 25/52 18/29 18/29 18/29 154/25 6/15	746/6369 48/255 1/28 42/235 26/90 11/51 6/17 10/31 10/31 10/31 1/44 2/15 ./1074 893/8209	++ + +++ +++ + + + + + + + + + + + +	++ +++ +++ + ++ ++ ++ ++ ++	26.7 12.1 13 24.9 25.3 36.4 47.7 26.7 66.7	18.9 15.7 2.6 29.8 55.6 11.4 27.1 24.8 3.8 22.2		$\begin{array}{c} 1.40 \left(1.20 , 1.70 \right) \\ 0.73 \left(0.46 , 1.17 \right) \\ 5.47 \left(0.31 , 96 , 94 \right) \\ 2.41 \left(1.70 , 3.40 \right) \\ 0.41 \left(0.20 , 0.87 \right) \\ 3.35 \left(1.42 , 7.96 \right) \\ 3.45 \left(1.53 \right) \\ 3.42 \left(1.19 , 92 \right) \\ 3.45 \left(0.51 , 5.38 \right) \\ 3.42 \left(1.19 , 92 \right) \\ 4.35 \left(0.71 , 26 , 53 \right) \\ 1.54 \left(0.96 , 2.42 \right) \\ 1.66 \left(1.06 , 2.89 \right) \end{array}$
End stage renal dise Muzaale 2014 Lam 2012 Mjoen 2014 Rogers 2009 Total	ease 99/96217 1/2027 9/1901 3/16 112/100161	17/9364 14/20270 22/32621 12/825 65/63080	++ ++ ++ +	+++ ++ +++	3.8 .1 .3 11.7	.4 .1 < .9		9.78 (5.87, 16.27) 0.58 (0.08, 4.47) 11.36 (4.37, 29.63) 15.64 (3.94, 62.07) 9.31 (2.90, 16.01)
Gestational hyperte Garg 2015 Reisaeter 2009 Total	nsion 7/131 3/106 10/237	17/788 314/21511 331/22299	++ +	+++	10.8 5.7	4.6 2.9		2.51 (0.90, 6.50) 1.97 (0.62, 6.23) 2.27 (0.94, 5.36)
Low birthweight Garg 2015 Reisaeter 2009 Total	8/131 9/106 17/237	31/788 1110/21511 1141/22299	++ +	+++	12.4 17	8.3 10.3		1.70 (0.70, 4.00) 1.70 (0.86, 3.39) 1.70 (0.91, 3.16)
Pre-eclampsia Garg 2015 Reisaeter 2009 Total	8/131 6/106 14/237	21/788 666/21511 687/22299	++ +	+++	12.4 11.3	5.7 6.2		2.41 (1.00, 5.60) 1.88 (0.82, 4.30) 2.12 (1.06, 4.27)
Preterm birth Garg 2015 Reisaeter 2009 Total	10/131 11/106 21/237	52/788 1397/21511 1449/22299	++ +	+++		14 13		1.20 (0.50, 2.50) 1.67 (0.89, 3.12) 1.47 (0.78, 2.64)
						.15	.25 .5 1 2 4 6 8 10 12 14 16 20 Risk ratio (95% Cl)	D

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

Outcome	No. studies	No. donors	No. controls	SMD (95%CI)*	I²(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)

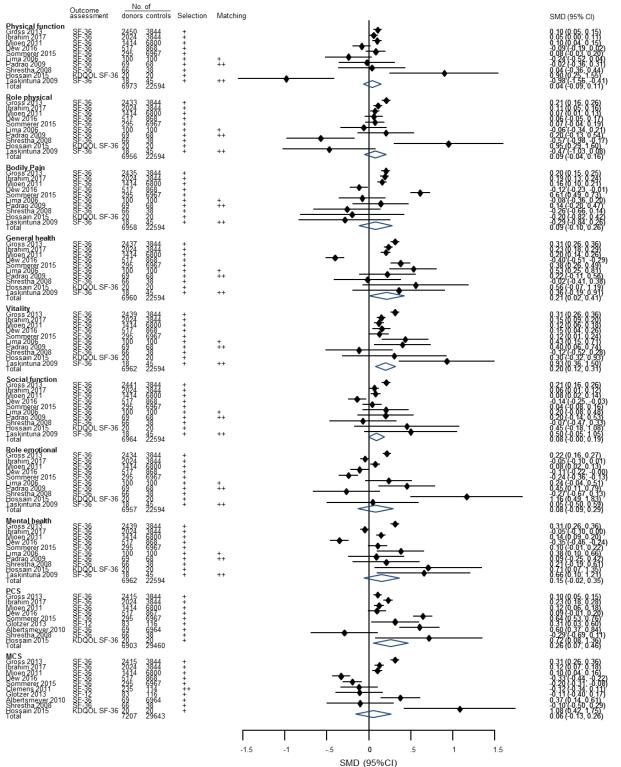
Appendix Table 6. Pooled mean difference in Health related quality of life scores between living kidney donors and non-donor controls (all studies)

SMD: Standardised Mean Difference

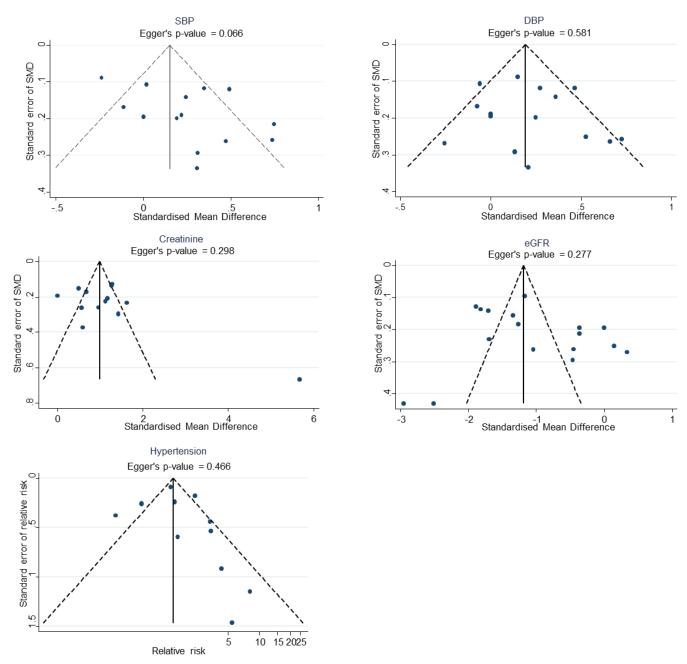
*The standardised mean difference (Cohen's d statistic) was pooled across all studies using the profile likelihood metaanalysis method

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 metaanalysis 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

Outcome	No. of studies	No. events/ No. donors	No. events/ No. controls	Risk ratio(95% CI)
All-cause mortality				
All studies	4	1467	3121	• 0.60 (0.31, 1.10)
Studies reporting RR or HR	3	1451	2756	• 0.65 (0.27, 1.49)
Cancer				
All studies	3	160	451.33	0.72 (0.58, 0.87)
Studies reporting RR or HR	t 1	55	75.33	0.74 (0.40, 1.38)
Cardiovascular disease				
All studies	4	107	991	——— 1.11 (0.64, 1.70)
Studies reporting RR or HR	2	94	975	1.13 (0.60, 2.00)
Diabetes				
All studies	5	47	181	1.03 (0.77, 1.25)
Studies reporting RR or HR	2	35	159	• 1.07 (0.85, 1.36)
Hypertension				
All studies	5	307	862.5	1.15 (0.54, 2.56)
Studies reporting RR or HR	2	247	788	1.76 (0.96, 3.49)
				.2 .3 .5 1 2 3
				Risk ratio (95% CI)

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