Acute treatment effects on GFR in randomized clinical trials of kidney disease progression

Supplementary tables and figures

Table of Contents

Appendix 1: Study funding sources 2

Appendix 2: Abbreviations, units, and terms 4

Table S1. Search terms 5

Table S2. Study inclusion criteria 6

Table S3. Clinical characteristics of the population overall and stratified by disease 7

Table S4. Patient characteristics by study 8

Table S5. Estimated acute effects using different methods to compute the acute effect on GFR, overall and by intervention and disease 10

Table S6. Magnitude of acute effects on GFR, by intervention 11

Table S7. Multivariable meta-regression of acute effects on GFR, both for GFR and ACR 12

Figure S1. Evaluation of bias in studies included in meta-analysis 13

Figure S2. Mean baseline GFR and median baseline UACR across studies 15

Figure S3. Distribution and estimated mean acute effect on GFR by disease 16

Figure S4: Forest plot of acute effect on GFR by intervention, all studies, ANCOVA method 17

Figure S5: Forest plot of acute effects on GFR by intervention, all studies, sensitivity analysis using the linear mixed model 18

Figure S6: Variation in acute effect on GFR by year of study publication 19

Figure S7: Meta regression plot of variation in acute effect by (A) baseline natural log-transformed eGFR and (B) natural log acute effect by UACR 20

Figure S8: Meta regression plot of variation in acute effect by intervention by (A) baseline natural log-transformed eGFR and (B) natural log acute effect by UACR 21

Figure S9: Variation in acute effect on GFR by within-study GFR quartiles, by intervention 22

References 23

Appendix 1: Study funding sources

Study Name	Funding
AASK[1]	Supported by grants to each clinical center and the coordinating center from the National Institute of Diabetes and Digestive and Kidney Diseases. In addition, AASK was supported by the Office of Research in Minority Health (now the National Center on Minority Health and Health Disparities, NCMHD) and the following institutional grants from the National Institutes of Health: M01 RR-00080, M01 RR-00071, M0100032, P20-RR11145, M01 RR00827, M01 RR00052, 2P20 RR11104, RR029887, and DK 2818-02. King Pharmaceuticals provided monetary support and antihypertensive medications to each clinical center. Pfizer Inc., AstraZeneca Pharmaceuticals, Glaxo Smith Kline, Forest Laboratories, Pharmacia and Upjohn also donated antihypertensive medications.
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ADVANCE[3]	ADVANCE was funded by grants from Servier and the National Health and Medical Research Council of Australia
ALTITUDE[4]	Supported by Novartis
Brenner[5]	Supported by Merck & Co.
CanPREVENT[6]	Supported by the Memorial University of Newfoundland
Chan[7]	Supported by the Wai Hung Charitable Foundation and the Mr & Mrs Tam Wing Fan Edmund Renal Research Fund
Donadio 2001[8]	Supported by research grants from Pronova Biocare a.s. (Oslo, Norway) and Mayo Foundation (Rochester, MN)
EMPA-REG OUTCOME[9]	Supported by Boehringer Ingelheim (BI) and Eli Lilly
Goicoechea[10]	Supported by REDINREN RD016/0019 FEDER funds
HALT-PKD A[11] and B[12]	Supported by grants from the National Institute of Diabetes and Digestive and Kidney Diseases (DK62410 to Dr. Torres, DK62408 to Dr. Chapman, DK62402 to Dr. Schrier, DK082230 to Dr. Moore, DK62411 to Dr. Perrone, and DK62401 to Washington University at St. Louis) and the National Center for Research Resources General Clinical Research Centers (RR000039 to Emory University, RR000585 to the Mayo Clinic, RR000054 to Tufts Medical Center, RR000051 to the University of Colorado, RR023940 to the University of Kansas Medical Center, and RR001032 to Beth Israel Deaconess Medical Center), National Center for Advancing Translational Sciences Clinical and Translational Science Awards (RR025008 and TR000454 to Emory University, RR024150 and TR00135 to the Mayo Clinic, RR025752 and TR001064 to Tufts University, RR025780 and TR001082 to the University of Colorado, RR025758 and TR001102 to Beth Israel Deaconess Medical Center, RR033179 and TR000001 to the University of Kansas Medical Center, and RR024989 and TR000439 to Cleveland Clinic), by funding from the Zell Family Foundation (to the University of Colorado), and by a grant from the PKD Foundation.
Hannedouche[13]	Supported by Merck Sharp & Dohme
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IDNT[16]	Supported by the Bristol-Myers Squibb Institute for Medical Research and Sanofi–Synthelabo
Ihle/Kincaid[17]	Supported in part by Merck & Co, Inc., West Point, PA
Kamper[18]	Supported by Merck Sharp & Dohme
Lewis 1992[19]	Supported by grants (R01-AM-27769 and R01-AM-27770) from the Public Health Service
Lewis 1993[20]	Supported by grants from the Public Health Service (5 R01-DK 39908, 5 R01-DK 39826, MO1-RR00030, MO1-RR00034, MO1-RR00036, MO1-RR00051, MO1-RR00058, MO1-RR00059,

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Maes[21]	The study medication was kindly provided by Hoffmann-LaRoche, Basel, Switzerland
MASTERPLAN[22]	Supported by the Dutch Kidney Foundation, grant number PV-01, and the Netherlands Heart Foundation, grant number 2003B261. Unrestricted grants were providedby Amgen, Genzyme, Pfizer and Sanofi-Aventis
MDRD Study A[23] and B[23]	Supported by the National Institute of Diabetes, Digestive, and Kidney Diseases (NIDDK UO1 DK35073 and K23 DK67303, K23 DK02904). Funding for the MDRD Study included the formerly named Health Care and Financing Administration (HCFA); now the Center for Medicare and Medicaid Services.
ORIENT[24]	Supported by a research grant from Daiichi Sankyo
Ponticelli 1989[25]	Supported in part by a grant (82.01308.04) from the Consiglio Nazionale delle Ricerche.
Ponticelli 1998[26]	Supported in part by a grant from Ospedabc Maggiore di Milano
Ponticelli 2006[27]	This was a spontaneous clinical trial sponsored by the grant “Project Glomerulonephritis”
Pozzi 2004[28]	The authors did not receive any financial support
Pozzi 2010[29]	The authors did not receive any financial support
Pozzi 2012[30]	The authors did not receive any financial support
Praga 2007[31]	This study was partially supported by Astellas
REIN[32]	Supported in part by a grant from Aventis Pharma SA, Antony, France.
RENAAL[33]	Supported by Merck & Co.
ROAD[34]	Supported by a National Nature and Sciences Grant for Major Projects (30330300), a People's Liberation Army Grant for Major Clinical Research (2000), and National 11th Five-Years Plan Foundation (to F.F.H.)
Schena[35]	Supported in part by a grant of University of Bari
SHARP[36]	Funded by Merck & Co. and Schering Plough Corporation, which merged in 2009. Additional support was provided from the Australian National Health Medical Research Council, the British Heart Foundation and the Medical Research Council.
STOP- IgAN[37]	Supported by a grant (GFVT01044604) from the German Federal Ministry of Education and Research.
SUN- MACRO[38]	Sponsored by Keryx Biopharmaceuticals, Inc.
Toto[5]	By grant RO1 DK53869A from the U.S. National Institute of Diabetes and Digestive and Kidney Diseases (Dr. Levey); grant RO1 HS 10064 from the Agency for Healthcare Research and Quality (Dr. Schmid); a grant from Dialysis Clinic, Inc., Paul Teschan Research Fund 1097-5 (Dr. Jafar); New England Medical Center St. Elizabeth’s Hospital Clinical Research Fellowship, Boston, Massachusetts (Dr. Jafar); and an unrestricted grant from Merck Research Laboratories, West Point, Pennsylvania (Dr. Levey).
Van Essen[39]	Supported by Merck Sharp & Dohme, Haarlem, The Netherlands
Zucchelli[40]	None

Appendix 2: Abbreviations, units, and terms

AASK	African American Study of Kidney Disease and Hypertension
ABCD	Appropriate Blood Pressure Control in Diabetes trial
ADVANCE	Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation trial
ALTITUDE	Aliskiren Trial in Type 2 Diabetes Using Cardiorenal Endpoints
ANCOVA	ANalysis of COVariance
BP	blood pressure
CanPREVENT	Canadian Prevention of Renal and Cardiovascular Endpoints Trial
CCB	calcium channel blockers
CKD	chronic kidney disease
Diet	low protein diet
EMPA-REG OUTCOME	Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (referred to as EMPA-REG here on in)
ESKD	end-stage kidney disease
GFR	glomerular filtration rate (mL/min/1.73 m^2)
HALT-PKD	Halt Progression of Polycystic Kidney Disease study
HKVIN	Hong Kong study using Valsartan in IgA Nephropathy
IDNT	Irbesartan Diabetic Nephropathy Trial
IgA	immunoglobulin A nephropathy
Interv	intervention
IS	immunosuppresion
MASTERPLAN	Multifactorial Approach and Superior Treatment Efficacy in Renal Patients with the Aid of Nurse Practitioners study
MDRD Study	Modification of Diet in Renal Disease study
N	sample size
NKF	National Kidney Foundation
ORIENT	Olmesartan Reducing Incidence of Endstage Renal Disease in Diabetic Nephropathy Trial
RASB	renin-angiotensin system blockade
RCT	randomized controlled trial
REIN	Ramipril Efficacy In Nephropathy study
RENAAL	Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan study
ROAD	Renoprotection of Optimal Antiproteinuric Doses study
SCr	serum creatinine (mg/dL)
SD	standard deviation
SE	standard error
SGLT2	Sodium-glucose co-transporter-2
SHARP	Study of Heart and Renal Protection
STOP-IgAN	Supportive Versus Immunosuppressive Therapy for the Treatment of Progressive IgA Nephropathy trial
SUN-MACRO	Sulodexide Macroalbuminuria trial
UACR	Urine albumin to creatinine ratio

Table S1. Search terms

Database: Ovid MEDLINE(R)

Search Strategy:

1 kidney disease$.mp. (112999)
2 chronic renal insufficiency.mp. (4302)
3 chronic kidney disease.mp. (21120)
4 renal disease.mp. (41875)
5 IgA nephropathy.mp. (4903)
6 lupus nephritis.mp. (6931)
7 diabetic nephropathy.mp. (12605)
8 glomerular disease.mp. (2168)
9 polycystic kidney disease.mp. (5535)
10 focal sclerosis.mp. (118)
11 membranous nephropathy.mp. (2402)
12 CKD.mp. (12820)
13 Hypertension/ and (renal or kidney).mp. (36281)
14 albuminuria.mp. (15383)
15 proteinuria.mp. (38350)
16 or/1-15 (222355)
17 randomized controlled trial.pt. (403784)
18 controlled clinical trial.pt. (89947)
19 randomized controlled trials/ (100110)
20 Random Allocation/ (85054)
21 Double-blind Method/ (132413)
22 Single-Blind Method/ (21138)
23 clinical trial.pt. (495584)
24 Clinical Trials.mp. or exp Clinical Trial/ (939562)
25 (clinic$ adj25 trial$).tw. (271601)
26 ((singl$ or doubl$ or trebl$ or tripl$) adj (mask$ or blind$)).tw. (129554)
27 placebo$.tw. (159277)
28 Placebos/ (32953)
29 random$.tw. (710194)
30 trial$.tw. (636501)
31 (latin adj square).tw. (3512)
32 or/17-31 (1577197)
33 16 and 32 (23308)
34 limit 33 to (guideline or meta analysis or practice guideline or "review") (5907)
35 33 not 34 (17401)
36 limit 35 to comment and (letter or editorial).pt. (187)
37 limit 35 to (addresses or bibliography or biography or case reports or congresses or consensus development conference or consensus development conference, nih or dictionary or directory or editorial or festschrift or government publications or interview or lectures or legal cases or legislation or news or newspaper article or patient education handout or periodical index) (501)
38 35 not (36 or 37) (16778)
39 limit 38 to animals/ (2192)
40 38 not 39 (14586)
41 limit 40 to humans (14553)
42 limit 40 to english language (13398)
43 limit 42 to ("young adult (19 to 24 years)" or "adult (19 to 44 years)" or "young adult and adult (19-24 and 19-44)" or "middle age (45 to 64 years)" or "middle aged (45 plus years)" or "all aged (65 and over)" or "aged (80 and over)") (11047)
44 limit 43 to yr="2007 -Current" (5299)
45 remove duplicates from 44 (5257)

Table S2. Study inclusion criteria

1. Randomized controlled trial
2. Article published in English
3. Human subjects
4. Adults
5. Follow up > 12 months after first follow up measurement of UP or GFR
6. Quantifiable albuminuria/proteinuria (i.e. not dipstick)
7. Glomerular filtration rate > 15 mL/min/1.73 m^2
8. First follow up albuminuria/proteinuria or serum creatinine latest at 12 months
9. Number of events (differ by disease)*
   a. Glomerular disease : >10 events
   b. Kidney disease, diabetes, hypertension, polycystic kidney disease, non-specified or other: follow-up > 500 person years and > 30 events
   c. High risk population (diabetes, hypertension, cardiovascular disease, heart failure not selected for having kidney disease): follow-up > 1000 person years and > 30 events

*Events - (end-stage kidney disease, doubling of serum creatinine, 40% or 30% decline in glomerular filtration rate)

Table S3. Clinical characteristics of the population overall and stratified by disease

	N Studies	N participants	Age	Female	Black	Diabetes	GFR	ACR
Overall	53	56413	61.5 (11.2)	22514 (37.4)	4601 (7.6)	45342 (75.3)	61.8 (26.3)	59 (13, 539)
Disease								
CKD	25	13516	56.2 (13.9)	6055 (39.3)	3098 (20.1)	1854 (12.0)	38.3 (22.2)	140 (35, 700)
Diabetes	12	41752	64.0 (8.5)	15973 (36.7)	1484 (3.4)	43481 (100.0)	69.8 (22.2)	35 (9, 361)
Glomerular	16	1145	41.6 (12.7)	486 (36.2)	19 (1.4)	7 (0.5)	72.4 (29.2)	1497 (898, 2695)

Values for age and GFR are presented as mean (standard deviation) and for ACR as median (25^{th}, 75^{th} percentile). Values for other characteristics are presented as number (percentage). N, sample size; GFR, estimated glomerular filtration rate (mL/min/1.73m^2); ACR, albumin: creatinine ratio (mg/g); RASB, renin angiotensin system blockers; CB, calcium channel blockers; BP, low vs usual blood pressure control; Diet, low vs high protein diet; IS, immunosuppression; CKD, chronic kidney disease.
Note: The N participants presented here are for the primary analysis (ANCOVA).

Table S4. Patient characteristics by study

Intervention	Disease	Study	N participants	Age	Female	Black	Diabetes	eGFR	ACR
RASB v Control	CKD (CNS)	Kamper	55	49.8 (11.7)	28 (50.9)	0 (0.0)	0 (0.0)	14.8 (9.0)	654 (264, 1558)
	CKD (CNS)	Ihle/Kincaid	67	45.5 (12.8)	34 (50.7)	0 (0.0)	0 (0.0)	16.5 (6.7)	856 (449, 1766)
	CKD (CNS)	Hou	224	44.7 (15.4)	113 (50.4)	0 (0.0)	0 (0.0)	16.8 (4.4)	1012 (635, 1338)
	CKD (CNS)	Hannedouche	98	51.2 (14.1)	47 (48.0)	0 (0.0)	0 (0.0)	23.4 (7.8)	958 (359, 1916)
	CKD (CNS)	Brenner	106	46.7 (13.2)	38 (35.8)	37 (34.9)	0 (0.0)	35.4 (17.2)	747 (154, 1883)
	CKD (CNS)	Toto	122	52.4 (11.6)	44 (36.1)	74 (60.7)	0 (0.0)	37.0 (17.5)	136 (60, 585)
	CKD (CNS)	AIPRI	562	50.9 (12.5)	157 (27.9)	0 (0.0)	0 (0.0)	38.6 (11.6)	500 (78, 1473)
	CKD (CNS)	REIN	322	48.8 (13.6)	73 (22.7)	2 (0.6)	0 (0.0)	41.5 (18.8)	1646 (916, 2599)
	CKD (CNS)	Van Essen	103	50.6 (12.9)	35 (34.0)	1 (1.0)	0 (0.0)	48.1 (19.3)	299 (60, 1497)
	CKD (HTN)	AASK	876	54.6 (10.7)	339 (38.7)	876 (100.0)	0 (0.0)	48.9 (15.8)	74 (26, 364)
	CKD (PKD)	HALT-PKD B	462	48.8 (8.2)	238 (51.5)	12 (2.6)	0 (0.0)	48.2 (11.8)	30 (17, 76)
	CKD (PKD)	HALT-PKD A	542	36.6 (8.3)	270 (49.8)	13 (2.4)	0 (0.0)	91.9 (17.7)	18 (12, 33)
	Diabetes	ALTITUDE	8150	64.4 (9.7)	2572 (31.6)	267 (3.3)	8150 (100.0)	58.4 (21.2)	284 (57, 881)
	Diabetes	ADVANCE	10876	65.7 (6.4)	4611 (42.4)	37 (0.3)	10876 (100.0)	78.3 (17.3)	15 (7, 40)
	Diabetes (CKD)	RENAAL	1513	60.2 (7.4)	557 (36.8)	230 (15.2)	1513 (100.0)	41.3 (13.2)	1307 (616, 2732)
	Diabetes (CKD)	ORIENT	566	59.2 (8.1)	175 (30.9)	0 (0.0)	566 (100.0)	47.5 (12.1)	1270 (617, 2285)
	Diabetes (CKD)	IDNT	1135	58.8 (7.7)	363 (32.0)	139 (12.2)	1135 (100.0)	50.2 (19.5)	1816 (1051, 3234)
	Diabetes (CKD)	Lewis 1993	407	34.5 (7.6)	191 (46.9)	32 (7.9)	407 (100.0)	73.2 (25.3)	1111 (605, 2299)
	Glom (IgAN)	HKVIN	109	40.5 (9.5)	79 (72.5)	0 (0.0)	3 (2.8)	75.1 (29.0)	958 (629, 1560)
RASB v CCB	CKD (CNS)	Zucchelli	121	55.4 (10.9)	47 (38.8)	0 (0.0)	0 (0.0)	24.9 (10.1)	599 (251, 1557)
	CKD (HTN)	AASK	652	54.4 (10.8)	255 (39.1)	652 (100.0)	0 (0.0)	48.7 (15.8)	67 (25, 343)
	Diabetes	ABCD	392	59.0 (8.2)	130 (33.2)	63 (16.1)	392 (100.0)	72.1 (18.7)	127 (56, 661)
	Diabetes (CKD)	IDNT	1128	59.2 (7.5)	400 (35.5)	147 (13.0)	1128 (100.0)	50.1 (18.7)	1740 (1009, 3059)
Low v Usual BP	CKD (CNS)	MDRD Study B	255	50.8 (12.8)	104 (40.8)	13 (5.1)	13 (5.1)	20.3 (5.8)	425 (102, 1222)
	CKD (CNS)	MDRD Study A	584	52.2 (12.2)	228 (39.0)	53 (9.1)	30 (5.1)	40.7 (11.0)	120 (33, 668)
	CKD (HTN)	AASK	1093	54.6 (10.7)	425 (38.9)	1093 (100.0)	0 (0.0)	48.7 (15.7)	70 (25, 349)
	CKD (PKD)	HALT-PKD A	542	36.6 (8.3)	270 (49.8)	13 (2.4)	0 (0.0)	91.9 (17.7)	18 (12, 33)
	Diabetes	ABCD	392	59.0 (8.2)	130 (33.2)	63 (16.1)	392 (100.0)	72.1 (18.7)	127 (56, 661)
Low v Usual Diet	CKD (CNS)	MDRD Study B	255	50.8 (12.8)	104 (40.8)	13 (5.1)	13 (5.1)	20.3 (5.8)	425 (102, 1222)
	CKD (CNS)	MDRD Study A	584	52.2 (12.2)	228 (39.0)	53 (9.1)	30 (5.1)	40.7 (11.0)	120 (33, 668)
Immuno-suppression	Glom (IgAN)	Pozzi 2012	46	42.0 (11.5)	9 (19.6)	0 (0.0)	0 (0.0)	27.8 (7.0)	1497 (898, 2395)
	Glom (IgAN)	Donadio 2001	72	46.3 (13.1)	13 (18.1)	2 (2.8)	0 (0.0)	40.8 (14.4)	971 (441, 1886)
	Glom (IgAN)	STOP-IgAN	151	44.2 (12.4)	34 (22.5)	0 (0.0)	0 (0.0)	59.7 (27.6)	928 (641, 1229)
	Glom (IgAN)	Maes	34	44.8 (11.3)	10 (29.4)	0 (0.0)	0 (0.0)	62.2 (18.9)	596 (353, 1599)
	Glom (IgAN)	Donadio 1999	96	38.5 (13.4)	26 (27.1)	0 (0.0)	0 (0.0)	66.1 (22.5)	1257 (719, 2066)

Intervention	Disease	Study	N participants	Age	Female	Black	Diabetes	eGFR	ACR
	Glom (IgAN)	Pozzi 2010	197	39.2 (12.6)	55 (27.9)	0 (0.0)	0 (0.0)	74.7 (25.5)	1198 (898, 1617)
	Glom (IgAN)	Pozzi 2004	83	38.6 (11.7)	25 (30.1)	0 (0.0)	0 (0.0)	87.2 (21.6)	1138 (838, 1437)
	Glom (IgAN)	Schena	95	33.7 (11.1)	29 (30.5)	0 (0.0)	2 (2.1)	91.3 (23.7)	982 (790, 1497)
	Glom (Lupus)	Lewis 1992	79	32.6 (12.0)	66 (83.5)	17 (21.5)	0 (0.0)	56.4 (36.3)	2635 (1165, 4905)
	Glom (Lupus)	Chan	61	40.1 (9.9)	51 (83.6)	0 (0.0)	2 (3.3)	70.4 (26.3)	2359 (1557, 4216)
	Glom (Membran)	Ponticelli 1998	91	49.9 (10.7)	28 (30.8)	0 (0.0)	0 (0.0)	82.5 (19.9)	3293 (2395, 5210)
	Glom (Membran)	Ponticelli 1989	75	44.4 (10.9)	15 (20.0)	0 (0.0)	0 (0.0)	87.7 (23.0)	2874 (2275, 4731)
	Glom (Membran)	Ponticelli 1992	76	46.7 (13.3)	26 (34.2)	0 (0.0)	0 (0.0)	89.0 (25.1)	3234 (2455, 4641)
	Glom (Membran)	Praga 2007	48	46.6 (12.5)	8 (16.7)	0 (0.0)	0 (0.0)	89.3 (20.2)	4338 (2640, 5828)
	Glom (Membran)	Ponticelli 2006	31	49.3 (10.5)	12 (38.7)	0 (0.0)	0 (0.0)	92.6 (22.2)	3353 (2395, 4850)
SGLT2 inhibitors	Diabetes	EMPA-REG	6936	63.2 (8.6)	1977 (28.5)	354 (5.1)	6936 (100.0)	76.2 (19.9)	18 (7, 72)
Others	CKD (CNS)	Goicoechea	113	71.8 (8.7)	40 (35.4)	0 (0.0)	42 (37.2)	40.5 (12.4)	35 (15, 362)
	CKD (CNS)	ROAD	339	50.9 (13.7)	126 (37.2)	0 (0.0)	0 (0.0)	29.0 (13.4)	958 (641, 1599)
	CKD (CNS)	MASTERPLAN	640	60.5 (12.5)	199 (31.1)	49 (7.7)	156 (24.4)	36.7 (15.4)	147 (51, 449)
	CKD (CNS)	CanPREVENT	458	65.1 (7.5)	250 (54.6)	25 (5.5)	144 (31.4)	47.6 (9.9)	72 (48, 115)
	CKD (CNS)	SHARP	6245	62.9 (11.7)	2363 (37.8)	119 (1.9)	1426 (22.8)	26.2 (12.3)	206 (44, 762)
	Diabetes	ADVANCE	10876	65.7 (6.4)	4611 (42.4)	37 (0.3)	10876 (100.0)	78.3 (17.3)	15 (7, 40)
	Diabetes (CKD)	SUN-MACRO	1110	63.5 (9.3)	256 (23.1)	115 (10.4)	1110 (100.0)	33.7 (9.7)	1075 (569, 1798)

Note: Values for categorical variables are given as number (percentage); values for continuous variables, as mean (standard deviation) except ACR which is shown as median (25^{th}, 75^{th} percentile). Participants with missing data on age, race, sex, serum creatinine, urine albumin were excluded.

Table S5. Estimated acute effects using different methods to compute the acute effect on GFR, overall and by intervention and disease

Subgroup	N Studies	ANCOVA		Linear mixed model	
		Mean (95% CI)	Coverage interval	Mean (95% CI)	Coverage interval
Overall	53	-0.21 (-0.63, 0.22)	(-2.50, 2.08)	-0.15 (-0.54, 0.25)	(-2.31, 2.01)
Intervention					
RASB v CCB	4	-1.60 (-3.25, 0.05)	(-4.28, 1.07)	-1.39 (-3.10, 0.32)	(-4.30, 1.52)
RASB vs Control	19	-0.51 (-1.06, 0.04)	(-2.39, 1.38)	-0.30 (-0.83, 0.23)	(-2.16, 1.56)
Immunosuppression	15	1.97 (0.01, 3.93)	(-2.34, 6.29)	0.96 (-0.64, 2.56)	(-2.03, 3.95)
Low v Usual BP	5	-0.97 (-2.02, 0.09)	(-2.83, 0.89)	-0.91 (-2.02, 0.20)	(-2.97, 1.16)
SGLT2 inhibitors	1	-1.81 (-2.25, -1.36)	(-1.81, -1.81)	-1.43 (-1.92, -0.94)	(-1.43, -1.43)
Disease					
CKD	25	-0.02 (-0.56, 0.53)	(-2.30, 2.27)	0.10 (-0.42, 0.62)	(-2.14, 2.34)
Diabetes	12	-1.01 (-1.62, -0.40)	(-2.78, 0.76)	-0.88 (-1.43, -0.33)	(-2.46, 0.69)
Glomerular	16	1.55 (-0.08, 3.18)	(-1.72, 4.83)	0.55 (-0.73, 1.83)	(-1.10, 2.20)

ANCOVA, Analysis of covariance method; N, number of studies; CI, confidence interval; RASB, renin-angiotensin receptor blockers; CCB, calcium channel blockers; BP, blood pressure; SGLT2, sodium-glucose co-transporter-2; CKD, chronic kidney disease.

Table S6. Magnitude of acute effects on GFR, by intervention

Subgroup	Very Large Negative <=-2.5	Moderate-to-Large Negative >-2.5 & <=-1.25	Small Negative >-1.25 & <0	No Acute Effect 0	Small Positive >0 & <1.25	Moderate-to-Large Positive >=1.25 & <2.5	Very Large Positive >=2.5
Overall	5	8	10	0	17	5	8
RASB vs CCB	1	1	2	0	0	0	0
RASB vs Control	1	4	4	0	10	0	0
Immunosuppression	2	1	1	0	1	3	7
Low vs Usual BP	1	1	2	0	1	0	0
SGLT2 inhibitors	0	1	0	0	0	0	0

Values displayed are the number of studies in each magnitude category.
RASB, renin-angiotensin receptor blockers; CCB, calcium channel blockers; BP, blood pressure; SGLT2, sodium-glucose co-transporter-2.

Table S7. Multivariable meta-regression of acute effects on GFR, both for GFR and ACR

A. GFR

Model	Variable	Estimate (95% CI)	P-value
GFR	GFR	-0.21 (-0.39, -0.03)	0.019
GFR+Interv	GFR	-0.25 (-0.40, -0.10)	0.001
	RASB vs control	-0.74 (-1.22, -0.25)	0.003
GFR+Interv+Diab	GFR	-0.19 (-0.37, -0.02)	0.033
	RASB vs control	-0.48 (-1.10, 0.14)	0.132
	Diabetes	-0.26 (-0.66, 0.14)	0.199

B. ACR

Model	Variable	Estimate (95% CI)	P-value
ACR	ACR	0.18 (0.00, 0.37)	0.047
ACR+Interv	ACR	0.18 (0.02, 0.35)	0.029
	RASB vs control	-0.46 (-0.98, 0.07)	0.088
ACR+Interv+Diab	ACR	0.18 (0.03, 0.33)	0.019
	RASB vs control	-0.10 (-0.66, 0.45)	0.720
	Diabetes	-0.46 (-0.81, -0.10)	0.011
ACR+GFR	ACR	0.12 (-0.08, 0.32)	0.260
	GFR	-0.14 (-0.35, 0.08)	0.210

CI, confidence interval; GFR, glomerular filtration rate; interv, intervention; Diab, diabetes; ACR, albumin: creatinine ratio; RASB, renin-angiotensin receptor blocker

Note: Estimates for GFR are denoted in 10 unit increases in ml/min/1.73m^2

Figure S1. Evaluation of bias in studies included in meta-analysis

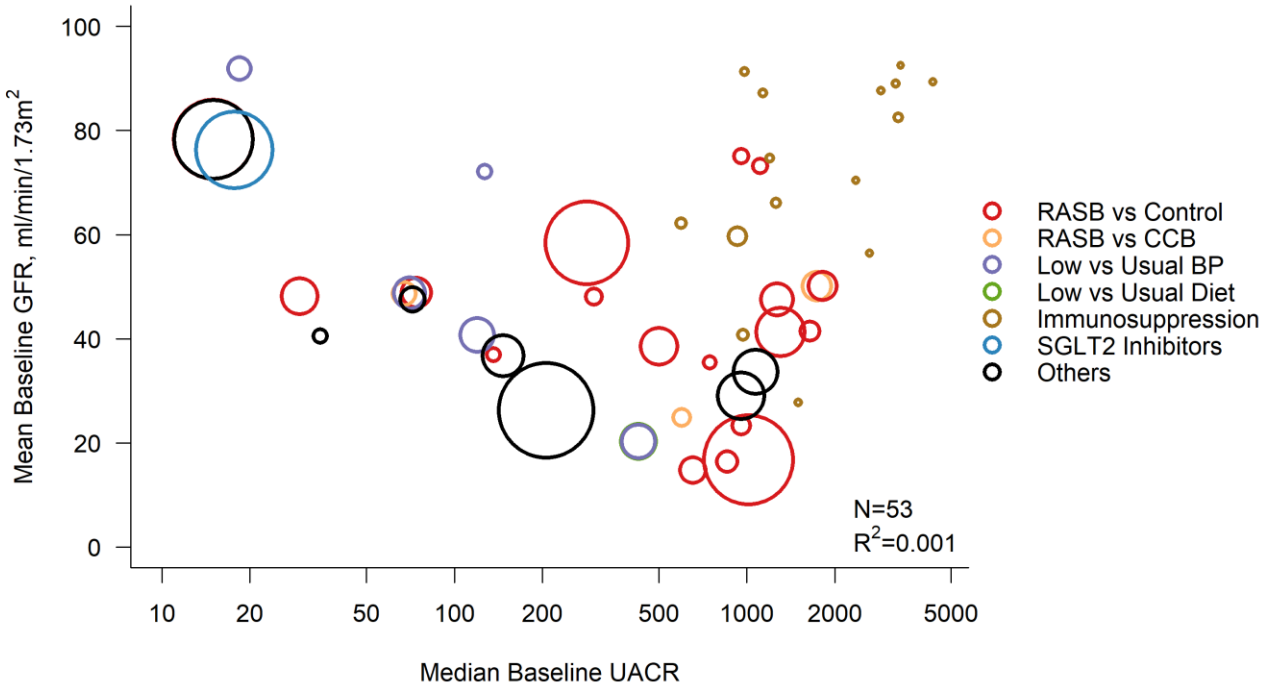
	Random sequence generation	Allocation concealment	Blinding of participants	Blinding of outcome assessment	Incomplete outcome data	Selective reporting
Kamper	+	+	-	+	?	+
Ihle/Kincaid	?	?	+	+	+	+
Hou	+	+	+	+	+	+
Hannedouche	+	?	-	+	?	+
Brenner	+	?	+	+	-	+
Toto	?	?	?	?	+	+
AIPRI	?	?	+	+	+	+
REIN	?	?	+	+	+	+
Van Essen	?	?	+	+	+	+
AASK	?	?	+	+	+	+
HALT-PKD B	+	?	+	+	+	+
HALT-PKD A	+	+	+	+	+	+
ALTITUDE	+	+	+	+	+	+
ADVANCE	+	+	+	+	+	+
RENAAL	+	+	+	+	+	+
ORIENT	?	?	+	+	?	+
IDNT	+	?	+	+	+	+
Lewis 1993	+	?	+	+	+	+
HKVIN	+	+	+	+	+	+
Zucchelli	?	?	?	+	+	+
ABCD	?	?	+	+	+	+
MDRD Study	+	+	-	+	?	+
Pozzi 2012	?	?	-	+	+	+
Donadio 2001	-	-	-	+	+	+
STOP-IgAN	+	?	-	+	+	+
Maes	?	?	?	+	+	+
Donadio 1999	?	?	-	+	?	+
Pozzi 2010	+	?	-	+	?	+
Pozzi 2004	+	?	-	+	+	+
Schena	+	+	-	+	+	+
Lewis 1992	+	+	?	?	+	+
Chan	+	?	-	+	+	+
Ponticelli 1998	+	?	-	+	+	+
Ponticelli 1989	+	+	-	+	+	+
Ponticelli 1992	?	?	?	+	+	+
Praga 2007	+	+	-	+	+	+
Ponticelli 2006	+	+	?	?	+	+
ROAD	+	+	-	+	+	+
SUN-MACRO	+	?	+	+	+	+
EMPA-REG OUTCOME	+	?	+	+	+	+
Goicoechea	+	?	?	+	+	+
MASTERPLAN	+	?	?	-	?	+
CanPREVENT	-	+	-	+	?	+
SHARP	+	+	+	+	+	+

(Legend on the following page)

Key: Green and + indicates low risk of bias; red and – indicates high risk of bias; yellow and ? indicates unclear risk of bias.

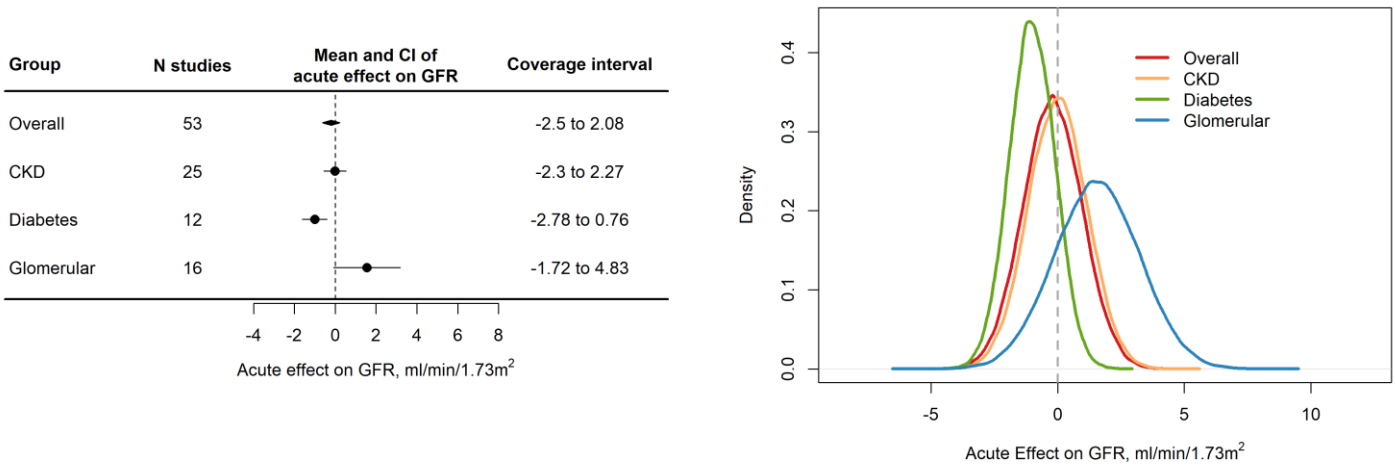
Risks of bias for each study were assessed using the risk-of-bias tool of the Cochrane collaboration. The tool includes these components: sequence generation (i.e. computer-generated random number, use of random number table or other truly random process); allocation concealment (i.e. web-based or telephone central randomization or consecutively numbered sealed opaque envelopes); blinding of participants, study personnel and outcome assessors; incomplete outcome data; selective outcome reporting. Each item of potential bias was scored as low, high or unclear based on criteria specified by the Cochrane Handbook1.

Figure S2. Mean baseline GFR and median baseline UACR across studies



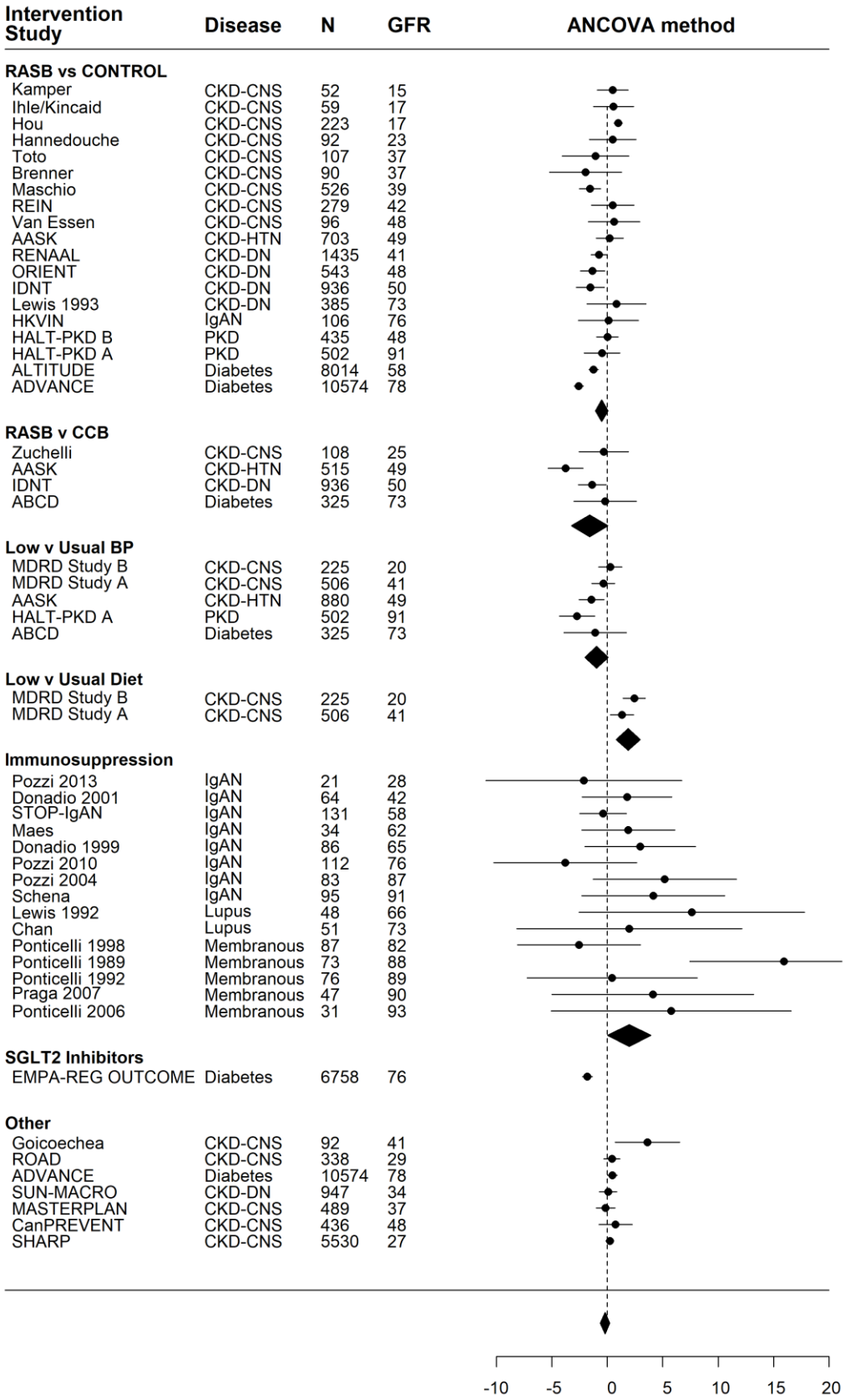
GFR, glomerular filtration rate; UACR, urine albumin creatinine ratio; RASB, renin-angiotensin receptor blockers; CCB, calcium channel blockers; BP, blood pressure; SGLT2, Sodium-glucose Cotransporter-2; N, number of studies.

Figure S3. Distribution and estimated mean acute effect on GFR by disease



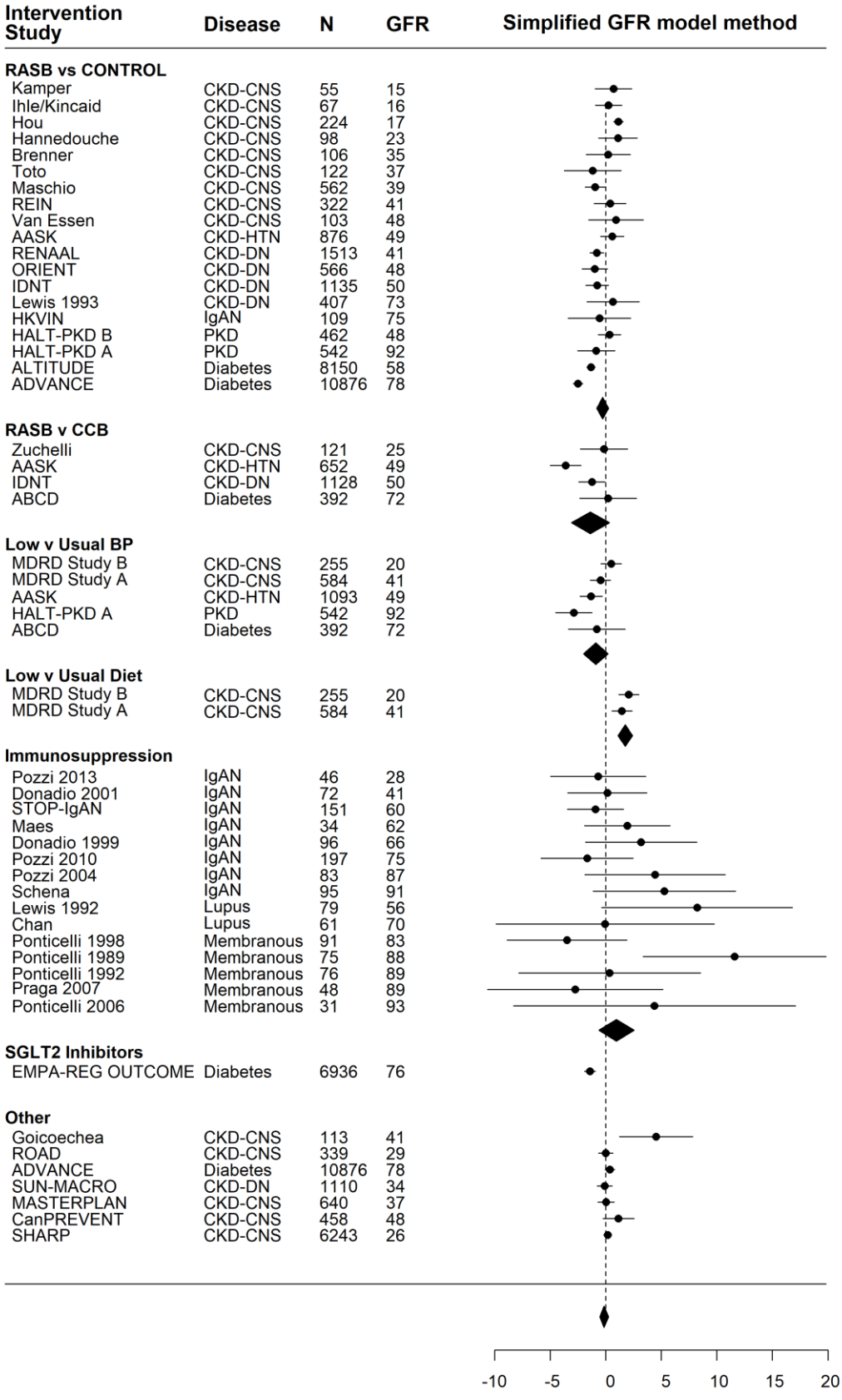
CI, confidence intervals; CKD, chronic kidney disease. Coverage interval refers to the interval under which 95% of the studies fall; N, sample size.

Figure S4: Forest plot of acute effect on GFR by intervention, all studies, ANCOVA method



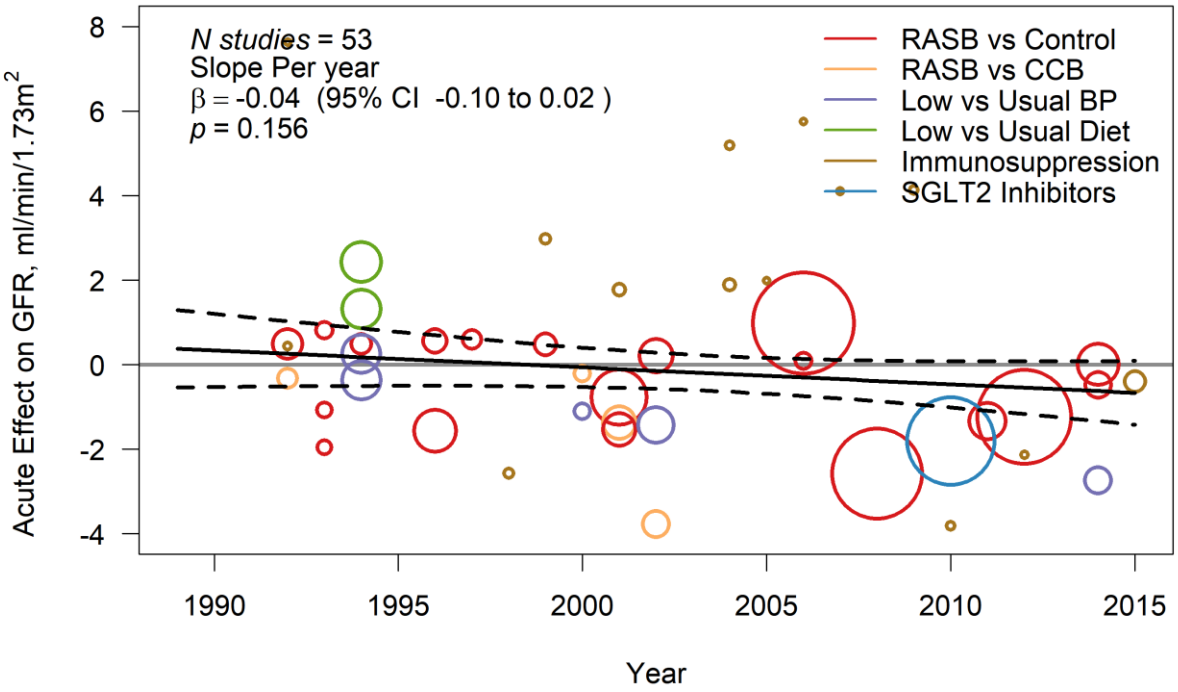
RASB, renin-angiotensin receptor blockers; CCB, calcium channel blockers; BP, blood pressure; SGLT2, sodium-glucose cotransporter-2; GFR, glomerular filtration rate; N, sample size (participants).

Figure S5: Forest plot of acute effects on GFR by intervention, all studies, sensitivity analysis using the linear mixed model



RASB, renin-angiotensin receptor blockers; CCB, calcium channel blockers; BP, blood pressure; SGLT2, sodium-glucose cotransporter-2; GFR, glomerular filtration rate; N, sample size (participants).

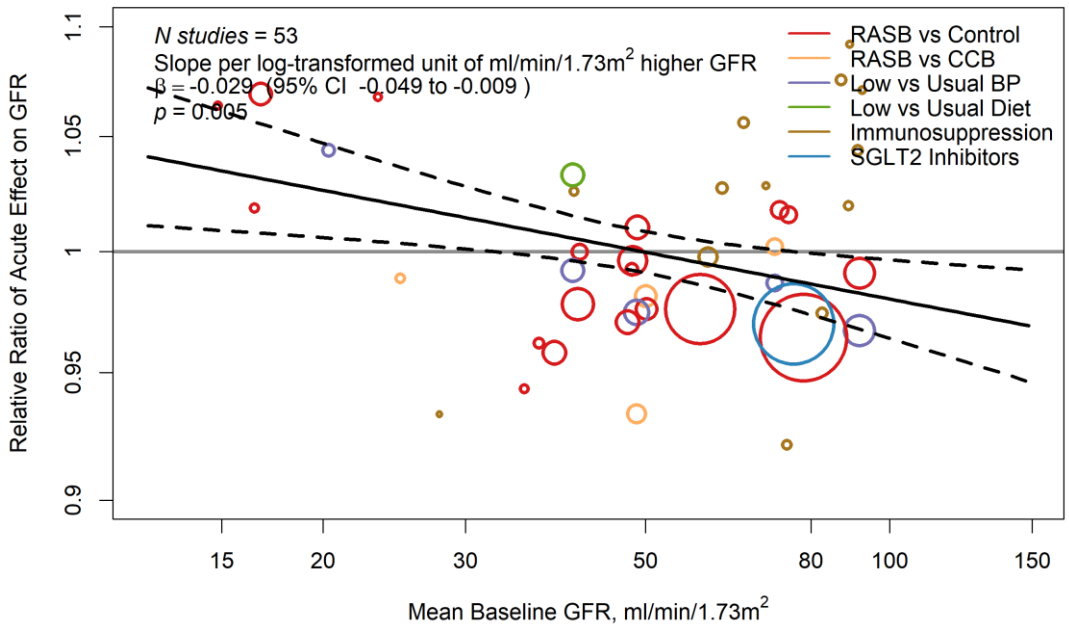
Figure S6: Variation in acute effect on GFR by year of study publication



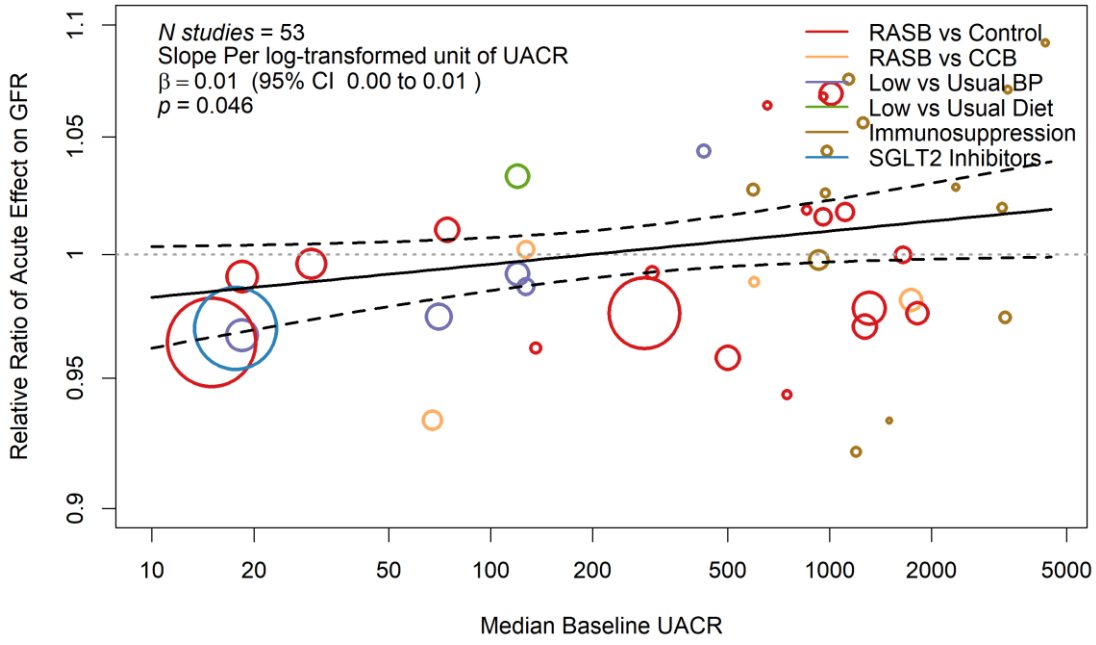
RASB, renin-angiotensin receptor blockers; CCB, calcium channel blockers; BP, blood pressure; SGLT2, sodium-glucose cotransporter-2; GFR, glomerular filtration rate; CI, confidence interval; β, slope; N, sample size.

Figure S7: Meta regression plot of variation in acute effect by (A) baseline natural log-transformed eGFR and (B) natural log acute effect by UACR

(A)



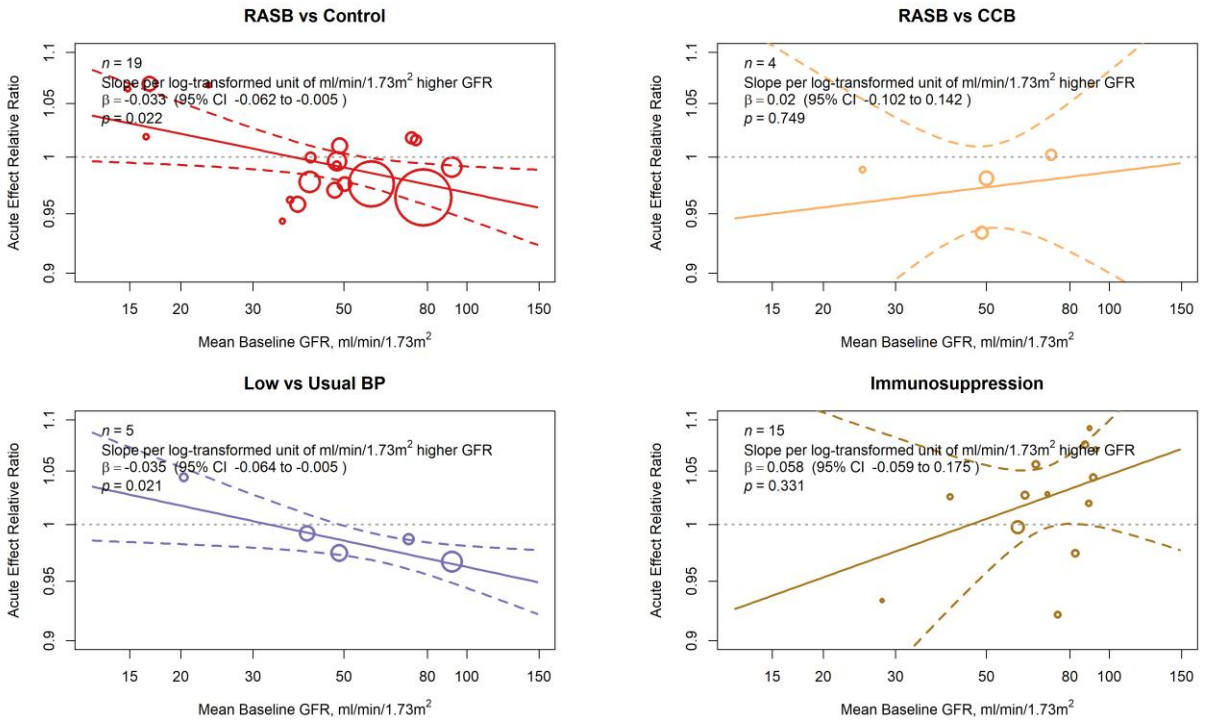
(B)



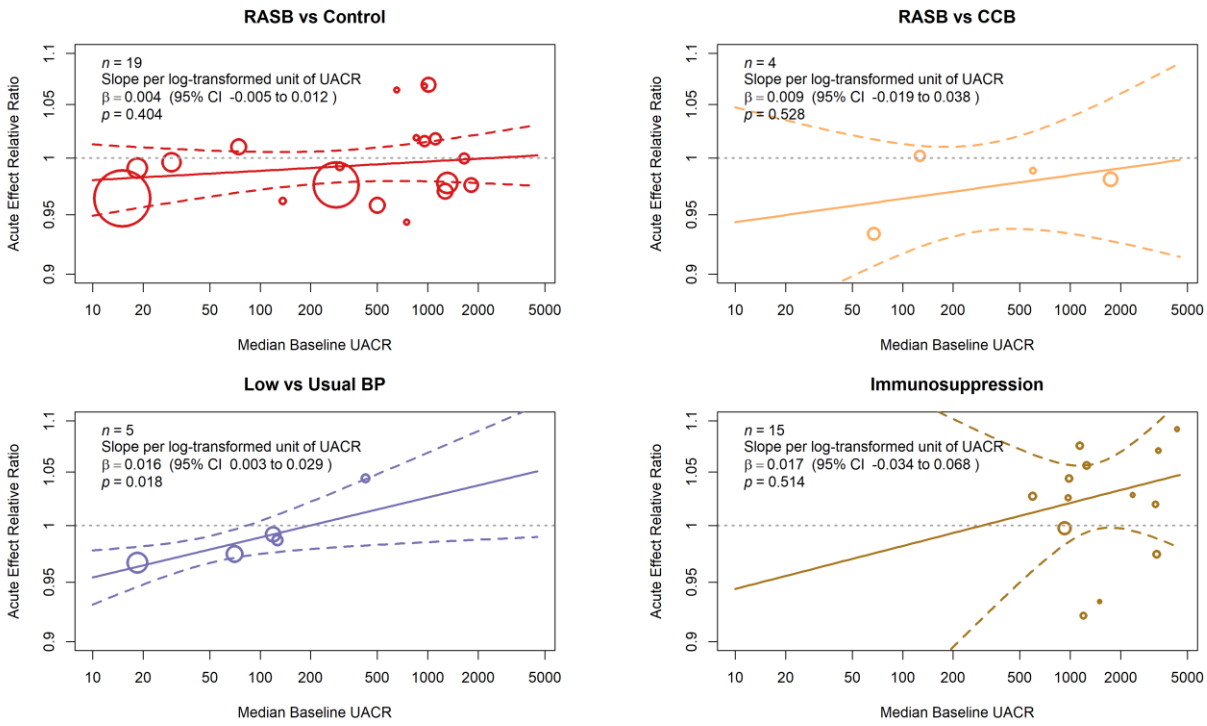
RASB, renin-angiotensin receptor blockers; CCB, calcium channel blockers; BP, blood pressure; SGLT2, Sodium-glucose Cotransporter-2; GFR, glomerular filtration rate.

Figure S8: Meta regression plot of variation in acute effect by intervention by (A) baseline natural log-transformed eGFR and (B) natural log acute effect by UACR

(A)

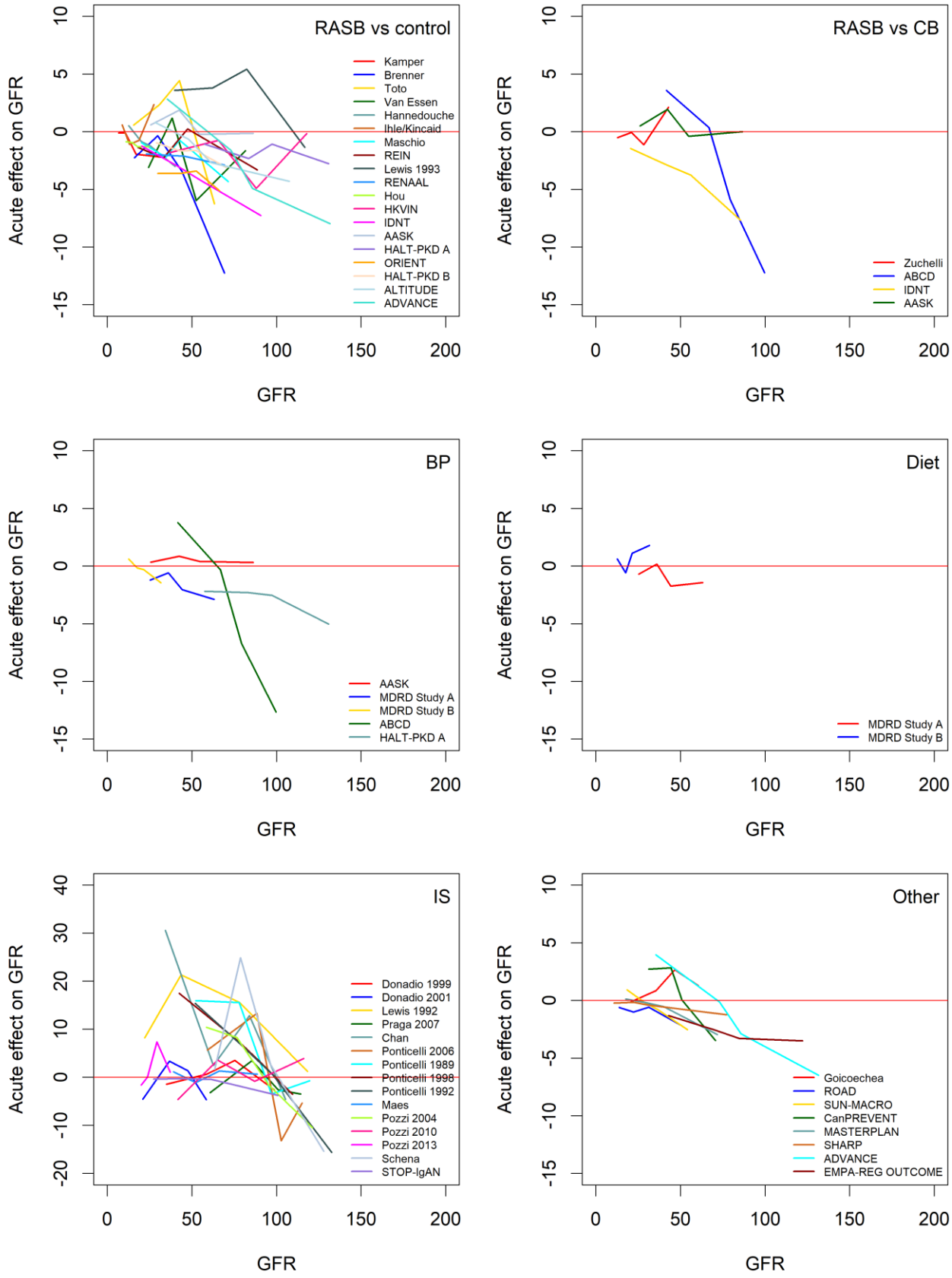


(B)



RASB, renin-angiotensin receptor blockers; CCB, calcium channel blockers; BP, blood pressure; UACR, urine albumin: creatinine ratio; GFR, glomerular filtration rate.

Figure S9: Variation in acute effect on GFR by within-study GFR quartiles, by intervention



RASB, renin-angiotensin receptor blockers; CCB, calcium channel blockers; BP, blood pressure; IS, immunosuppression; GFR, glomerular filtration rate

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