

Table S1. Additional characteristic of studies included in the systematic review and meta-analysis

Study	GFR (ml/min /1.73 m ²)	Serum creatinine (mg/dl)	Disease status	Target BP control (mm Hg)	MACE definitions	Smoker (%)	DM (%)
Toto 1995 [22]	37.8	2.3	Hypertensive nephrosclerosis	DBP: 65-80 vs 85-95	-	NA	NA
HOT 1998 [23]	NA	1.0	Hypertension	DBP: ≤ 80; ≤ 85; ≤ 90	Non-fatal MI, non-fatal stroke, and cardiovascular death	15.9	8.0
UKPDS 38 1998 [24]	NA	NA	Type 2 DM	< 150/85 vs < 180/105	MI, stroke, and all-cause mortality	22.3	100.0
Estacio 2000 [25,26]	NA	NA	Type 2 DM	DBP: ≤ 75 vs 80-89	MI, stroke, congestive heart failure, cardiovascular death	NA	100.0
Schrier 2002 [27]	NA	1.3	PKD	120/80 vs 135–140/85–90	-	NA	NA

MDRD 2005 [28]	NA	NA	Nondiabetic	MAP: < 92 vs 107	-	NA	5.2
			CKD				
REIN-2 2005 [29]	35.0	2.7	Nondiabetic	DBP: ≤ 80 ; ≤ 90	NA	NA	NA
			CKD				
Estacio 2006 [30]	NA	0.9	Type 2 DM	DBP: ≤ 75 vs 80-90	MI and stroke	10.1	100.0
JATOS 2008 [31]	NA	NA	Hypertensive	SBP: <140 vs 140-160	Cardiac and vascular disease, and stroke	13.5	11.8
Cardio-Sis 2009 [32,33]	NA	0.9	Hypertensive	SBP: <130 vs 130-140	All-cause mortality, MI, stroke, admission for heart failure, angina, or coronary revascularization	21.5	0.0
ESCAPE 2009 [34]	45.9	NA	CKD	Below the 50th percentile vs	-	NA	NA

50th to 90th percentile							
ACCORD 2010 [35]	91.6	0.9	Type 2 DM	SBP: <120 vs 120-140	Nonfatal MI, nonfatal stroke, or cardiovascular death	13.2	100.0
VALISH 2010 [36]	NA	NA	Hypertensive	SBP: <140 vs 140-150	Sudden death, fatal and nonfatal stroke, fatal and nonfatal MI, heart failure death, other cardiovascular death, unplanned hospitalization because of cardiovascular diseases	19.2	13.0
AASK 2010 [37]	47.4	2.0	CKD	MAC: <92 vs 102-107	NA	29.3	NA
HOMED-BP 2012 [38]	NA	NA	Hypertensive	<125/<80 vs 125–134/80–84	Cardiovascular death plus stroke and MI	22.0	15.0
Wei 2013 [39]	NA	1.0	Hypertensive	<140/<90 vs 140-150/90	Fatal/nonfatal stroke, acute MI, and	24.9	23.3

					other cardiovascular deaths		
SPS3 2013 [40]	NA	NA	Lacunar stroke	SBP: <130 vs 130-149	MI, stroke, and all-cause mortality	20.5	36.5
PAST-BP 2015 [12]	NA	NA	Hypertensive	SBP: <130 vs 130-140	NA	NA	10.6
COPE 2017 [41]	NA	NA	Hypertensive	Achieved a target BP $\geq$ 66.7%	Cardiovascular death, non-fatal MI	39.1	14.2
				vs achieved target BP<66.6%	and non-fatal stroke		
SPRINT 2017 [42]	72.0	1.1	Hypertensive	SBP: <120 vs 120-140	NA	13.2	NA

*CKD: Chronic kidney disease; DBP: diastolic blood pressure; DM: diabetes mellitus; GFR: glomerular filtration rate; MACE: major cardiovascular events; MAP: mean arterial pressure; MI: myocardial infarction; NA: not available; PKD: polycystic kidney disease; SBP: systolic blood pressure.

Table S2. Sensitivity analysis for major cardiovascular events

Excluding study	RR and 95% CI	P value	Heterogeneity (%)	P value for heterogeneity
HOT 1998	0.84 (0.75-0.94)	0.002	29.1	0.138
UKPDS 38 1998	0.88 (0.80-0.97)	0.007	15.2	0.283
Estacio 2000 (a)	0.85 (0.77-0.94)	0.002	32.7	0.107
Estacio 2000 (b)	0.85 (0.76-0.94)	0.002	31.9	0.113
REIN-22005	0.85 (0.77-0.94)	0.002	32.9	0.105
Estacio 2006	0.85 (0.77-0.94)	0.002	31.9	0.114
JATOS 2008	0.84 (0.76-0.93)	0.001	29.2	0.138
Cardio-Sis 2009	0.87 (0.79-0.95)	0.002	22.3	0.206
ACCORD 2010	0.85 (0.76-0.95)	0.004	32.8	0.106
VALISH 2010	0.85 (0.77-0.94)	0.002	32.9	0.105
AASK 2010	0.83 (0.76-0.92)	<0.001	16.5	0.269
HOMED-BP 2012	0.85 (0.77-0.94)	0.001	31.4	0.117
Wei 2013	0.87 (0.80-0.96)	0.003	15.1	0.285
SPS3 2013	0.85 (0.76-0.95)	0.004	32.9	0.105
PAST-BP 2015	0.86 (0.78-0.94)	0.002	27.0	0.158

COPE 2017	0.86 (0.78-0.96)	0.004	27.7	0.151
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Table S3. Sensitivity analysis for myocardial infarction

Excluding study	RR and 95% CI	P value	Heterogeneity (%)	P value for heterogeneity
HOT 1998	0.89 (0.76-1.03)	0.109	0.0	0.990
UKPDS 38 1998	0.89 (0.77-1.04)	0.149	0.0	0.993
Estacio 2000 (a)	0.86 (0.76-0.99)	0.035	0.0	0.993
Estacio 2000 (b)	0.86 (0.75-0.98)	0.026	0.0	0.999
REIN-22005	0.87 (0.76-1.00)	0.044	0.0	0.987
JATOS 2008	0.87 (0.76-1.00)	0.043	0.0	0.987
Cardio-Sis 2009	0.88 (0.77-1.00)	0.051	0.0	0.989
ACCORD 2010	0.87 (0.74-1.03)	0.105	0.0	0.986
VALISH 2010	0.87 (0.76-0.99)	0.040	0.0	0.991
HOMED-BP 2012	0.88 (0.77-1.00)	0.050	0.0	0.988
Wei 2013	0.87 (0.76-1.00)	0.042	0.0	0.988
SPS3 2013	0.87 (0.76-1.00)	0.048	0.0	0.987
PAST-BP 2015	0.87 (0.76-1.00)	0.044	0.0	0.987

Table S4. Sensitivity analysis for stroke

Excluding study	RR and 95% CI	P value	Heterogeneity (%)	P value for heterogeneity
HOT 1998	0.74 (0.63-0.88)	<0.001	22.5	0.216
UKPDS 38 1998	0.79 (0.68-0.91)	0.001	17.2	0.271
Estacio 2000 (a)	0.76 (0.65-0.88)	<0.001	25.7	0.185
Estacio 2000 (b)	0.78 (0.68-0.89)	<0.001	13.8	0.306
REIN-22005	0.77 (0.66-0.89)	<0.001	23.9	0.202
JATOS 2008	0.75 (0.65-0.86)	<0.001	17.1	0.272
Cardio-Sis 2009	0.77 (0.67-0.89)	0.001	22.2	0.219
ACCORD 2010	0.79 (0.69-0.92)	0.002	14.8	0.295
VALISH 2010	0.77 (0.66-0.89)	0.001	26.2	0.180
AASK 2010	0.75 (0.64-0.87)	<0.001	21.7	0.224
HOMED-BP 2012	0.76 (0.66-0.87)	<0.001	16.4	0.279
Wei 2013	0.78 (0.68-0.91)	0.001	19.8	0.243
SPS3 2013	0.75 (0.63-0.89)	0.001	25.2	0.189
COPE 2017	0.78 (0.67-0.90)	0.001	20.7	0.234

Table S5. Sensitivity analysis for heart failure

Excluding study	RR and 95% CI	P value	Heterogeneity (%)	P value for heterogeneity
HOT 1998	0.76 (0.58-1.00)	0.049	41.1	0.084
UKPDS 38 1998	0.85 (0.67-1.08)	0.194	30.7	0.163
Estacio 2000 (a)	0.79 (0.60-1.03)	0.082	46.0	0.054
Estacio 2000 (b)	0.78 (0.60-1.01)	0.064	44.3	0.064
REIN-22005	0.79 (0.61-1.02)	0.072	44.6	0.062
JATOS 2008	0.78 (0.60-1.02)	0.069	45.1	0.059
Cardio-Sis 2009	0.81 (0.63-1.05)	0.118	43.9	0.066
ACCORD 2010	0.77 (0.57-1.04)	0.089	40.7	0.086
AASK 2010	0.76 (0.58-0.98)	0.034	37.5	0.109
Wei 2013	0.83 (0.65-1.06)	0.144	37.7	0.108
SPRINT 2017	0.86 (0.66-1.12)	0.250	29.3	0.175

Table S6. Sensitivity analysis for all-cause mortality

Excluding study	RR and 95% CI	P value	Heterogeneity (%)	P value for heterogeneity
Toto 1995	0.91 (0.81-1.02)	0.107	20.3	0.207
HOT 1998	0.88 (0.78-0.99)	0.028	5.2	0.392

UKPDS 38 1998	0.92 (0.81-1.05)	0.207	17.5	0.239
Estacio 2000 (a)	0.94 (0.85-1.04)	0.224	4.5	0.401
Estacio 2000 (b)	0.91 (0.80-1.02)	0.117	21.6	0.192
Schrier 2002	0.91 (0.81-1.02)	0.114	21.6	0.192
MDRD 2005	0.90 (0.81-1.01)	0.085	16.7	0.250
REIN-22005	0.91 (0.81-1.02)	0.118	21.1	0.197
Estacio 2006	0.91 (0.81-1.02)	0.107	20.0	0.211
JATOS 2008	0.91 (0.80-1.02)	0.104	21.2	0.197
Cardio-Sis 2009	0.91 (0.81-1.02)	0.118	21.4	0.195
ESCAPE 2009	0.91 (0.81-1.02)	0.117	20.5	0.205
ACCORD 2010	0.89 (0.78-1.01)	0.064	17.2	0.244
VALISH 2010	0.91 (0.81-1.03)	0.144	20.4	0.206
AASK 2010	0.91 (0.81-1.03)	0.141	20.9	0.200
HOMED-BP 2012	0.91 (0.80-1.03)	0.129	21.3	0.195
Wei 2013	0.98 (0.89-1.08)	0.672	0.0	0.797
SPS3 2013	0.89 (0.78-1.01)	0.068	18.2	0.232
PAST-BP 2015	0.91 (0.81-1.02)	0.105	20.0	0.211

COPE 2017	0.91 (0.81-1.03)	0.132	21.2	0.197
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Table S7. Sensitivity analysis for cardiac death

Excluding study	RR and 95% CI	P value	Heterogeneity (%)	P value for heterogeneity
HOT 1998	0.88 (0.70-1.11)	0.285	37.9	0.097
UKPDS 38 1998	0.96 (0.77-1.19)	0.710	33.7	0.129
Estacio 2000 (a)	0.93 (0.76-1.15)	0.513	42.4	0.067
Estacio 2000 (b)	0.89 (0.72-1.10)	0.285	42.1	0.069
REIN-22005	0.92 (0.74-1.13)	0.427	45.2	0.051
JATOS 2008	0.90 (0.73-1.12)	0.343	44.7	0.053
ACCORD 2010	0.89 (0.71-1.13)	0.357	44.6	0.054
VALISH 2010	0.91 (0.73-1.13)	0.395	45.9	0.047
AASK 2010	0.87 (0.71-1.06)	0.165	32.4	0.140
HOMED-BP 2012	0.92 (0.75-1.14)	0.450	45.0	0.052
Wei 2013	0.98 (0.83-1.15)	0.808	11.0	0.339
SPS3 2013	0.92 (0.73-1.16)	0.463	45.9	0.047

Table S8. Sensitivity analysis for non-cardiac death

Excluding study	RR and 95% CI	P value	Heterogeneity (%)	P value for heterogeneity
HOT 1998	0.93 (0.79-1.10)	0.403	0.0	0.536
UKPDS 38 1998	0.97 (0.84-1.12)	0.662	0.0	0.467
Estacio 2000 (a)	1.00 (0.87-1.14)	0.943	0.0	0.740
Estacio 2000 (b)	0.99 (0.87-1.14)	0.912	0.0	0.617
REIN-22005	0.98 (0.86-1.12)	0.771	0.1	0.439
JATOS 2008	0.98 (0.86-1.12)	0.793	0.0	0.476
ACCORD 2010	0.96 (0.83-1.12)	0.613	0.0	0.465
VALISH 2010	0.99 (0.86-1.13)	0.875	0.0	0.513
AASK 2010	0.99 (0.86-1.14)	0.867	0.0	0.457
HOMED-BP 2012	0.98 (0.86-1.13)	0.823	0.0	0.444
Wei 2013	1.01 (0.88-1.16)	0.905	0.0	0.630
SPS3 2013	0.96 (0.84-1.11)	0.611	0.0	0.493

Table S9. Sensitivity analysis for end stage renal disease

Excluding study	RR and 95% CI	P value	Heterogeneity (%)	P value for heterogeneity
Toto 1995	0.89 (0.75-1.04)	0.152	0.0	0.722

UKPDS 38 1998	0.91 (0.77-1.07)	0.260	0.0	0.517
Schrier 2002	0.89 (0.76-1.05)	0.180	0.0	0.485
MDRD 2005	0.91 (0.76-1.10)	0.326	0.0	0.448
REIN-22005	0.87 (0.73-1.03)	0.107	0.0	0.587
JATOS 2008	0.90 (0.76-1.06)	0.211	0.0	0.442
ESCAPE 2009	0.93 (0.79-1.11)	0.425	0.0	0.620
ACCORD 2010	0.87 (0.73-1.05)	0.139	0.0	0.506
AASK 2010	0.93 (0.78-1.12)	0.443	0.0	0.514

Table S10. Sensitivity analysis for retinopathy

Excluding study	RR and 95% CI	P value	Heterogeneity (%)	P value for heterogeneity
UKPDS 38 1998	0.88 (0.70-1.11)	0.272	59.9	0.083
Estacio 2000 (a)	0.81 (0.60-1.09)	0.168	74.9	0.019
Estacio 2000 (b)	0.85 (0.63-1.14)	0.283	75.3	0.018
ACCORD 2010	0.75 (0.65-0.87)	<0.001	22.9	0.273

Table S11. Sensitivity analysis for albuminuria

Excluding study	RR and 95% CI	P value	Heterogeneity (%)	P value for heterogeneity
UKPDS 38 1998	0.91 (0.84-0.98)	0.011	0.0	0.393
Estacio 2000 (a)	0.90 (0.83-0.97)	0.005	0.0	0.818
ACCORD 2010	0.93 (0.74-1.17)	0.547	0.0	0.396

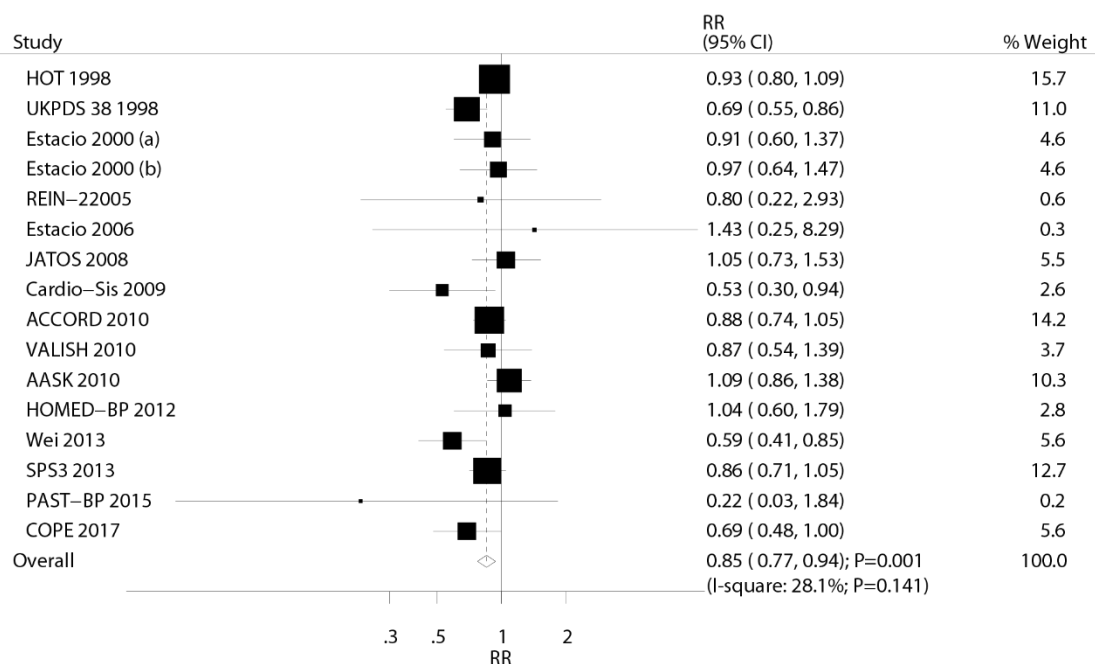


Fig. S1. Effect of IBP control on the risk of major cardiovascular events

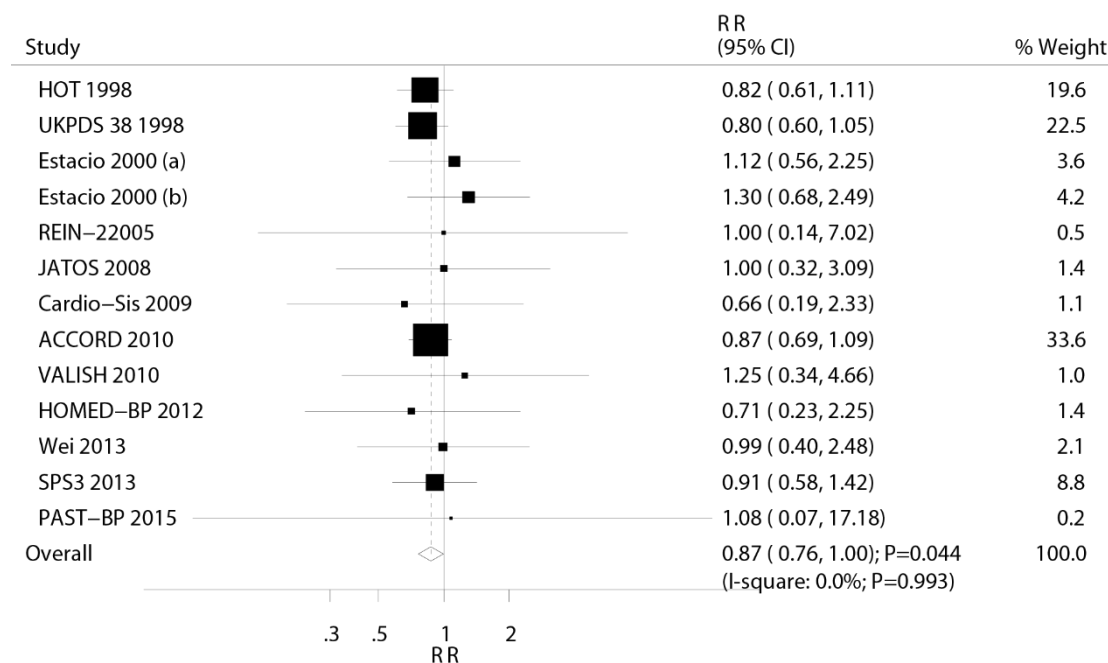


Fig. S2. Effect of IBP control on the risk of myocardial infarction

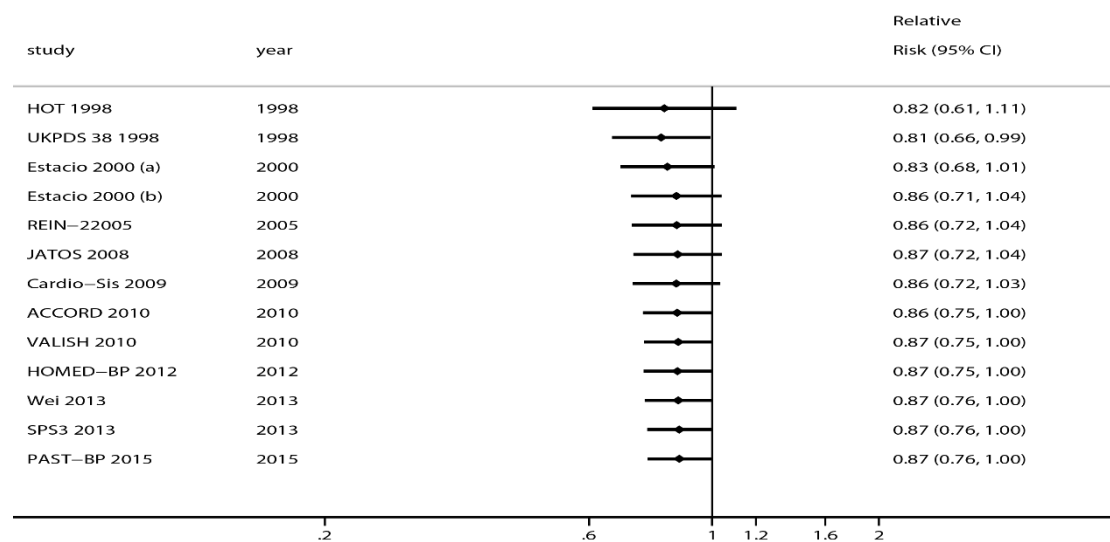


Fig. S3. Cumulative meta-analysis of the IBP control for myocardial infarction

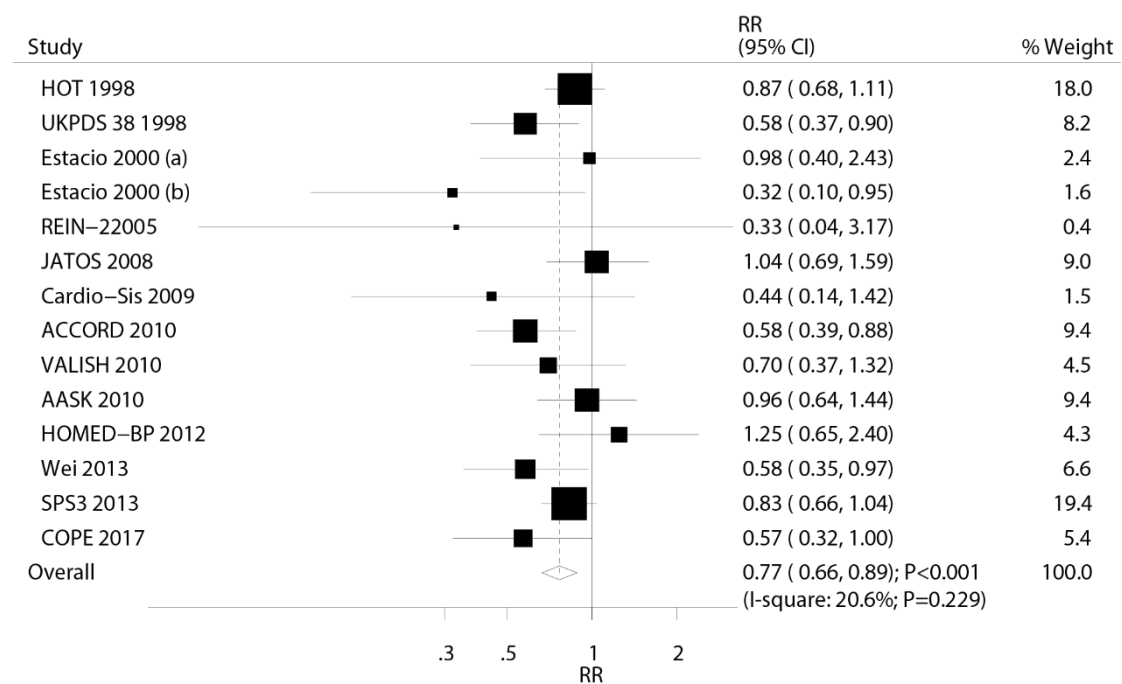


Fig. S4. Effect of IBP control on the risk of stroke

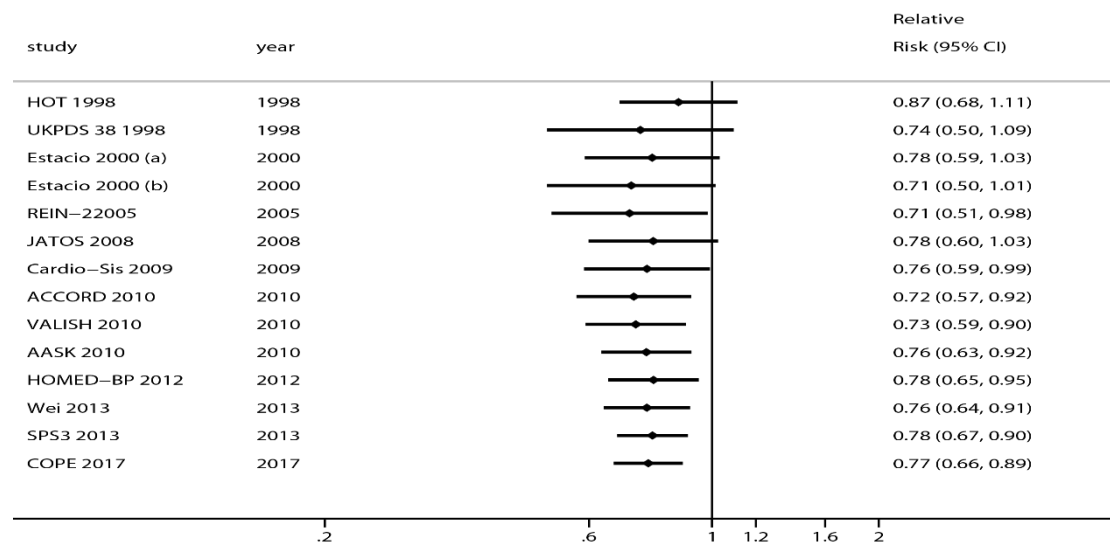


Fig. S5. Cumulative meta-analysis of the IBP control for stroke

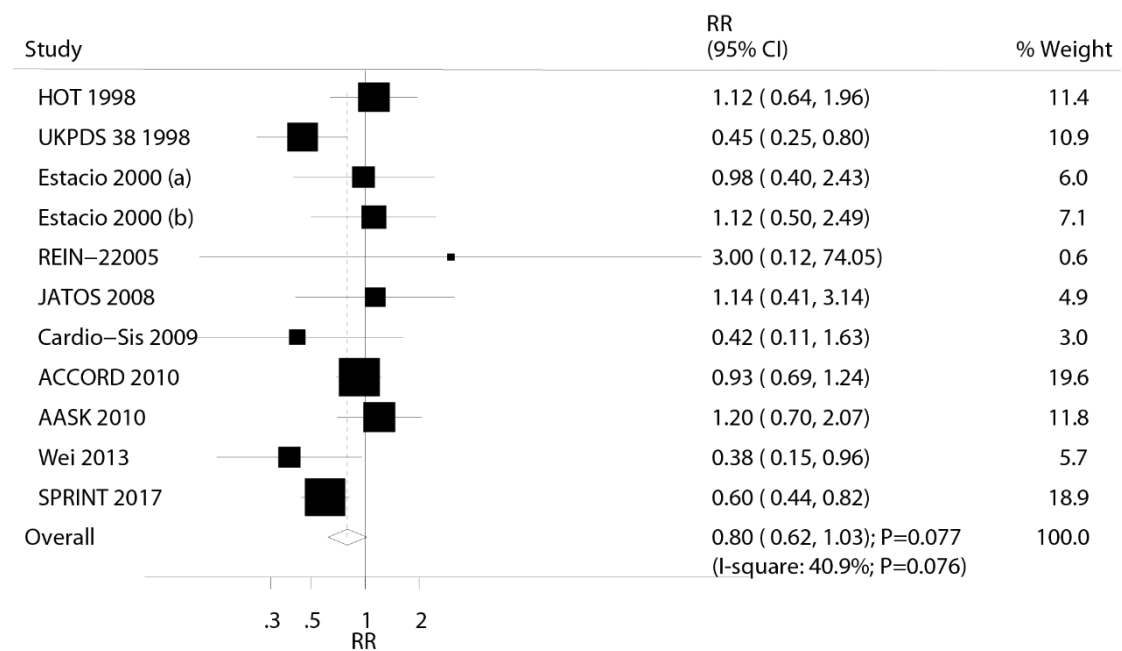


Fig. S6. Effect of IBP control on the risk of heart failure

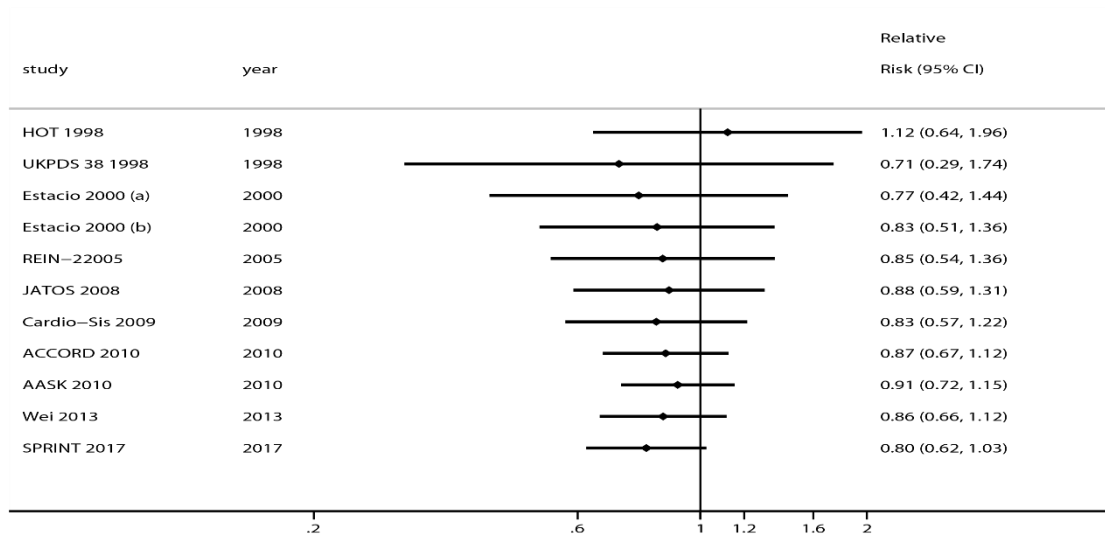


Fig. S7. Cumulative meta-analysis of the IBP control for heart failure

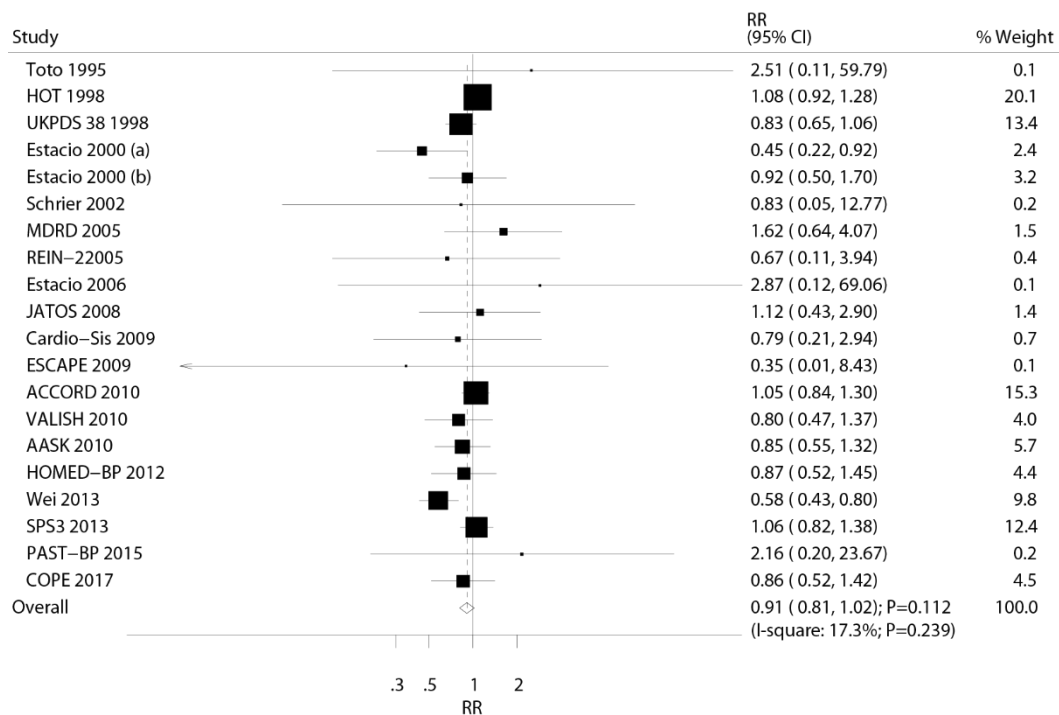


Fig. S8. Effect of IBP control on the risk of all-cause mortality

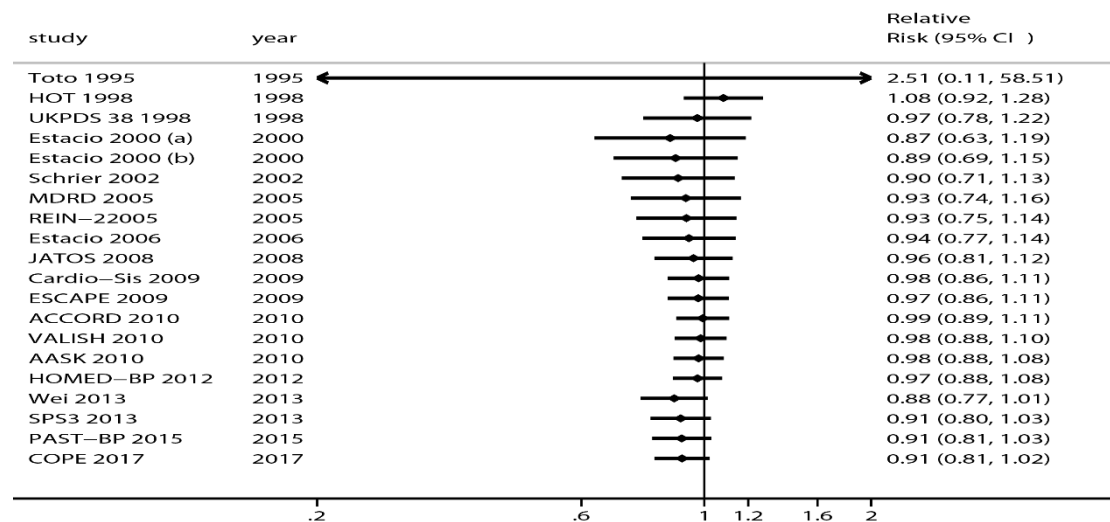


Fig. S9. Cumulative meta-analysis of the IBP control for all-cause mortality

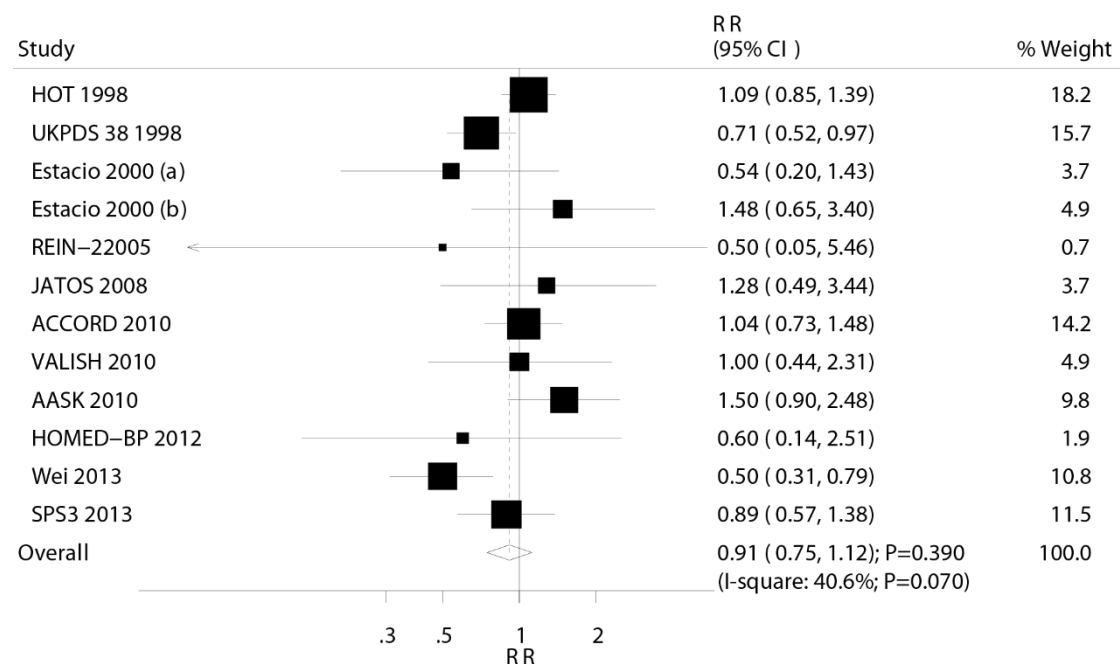


Fig. S10. Effect of IBP control on the risk of cardiac death

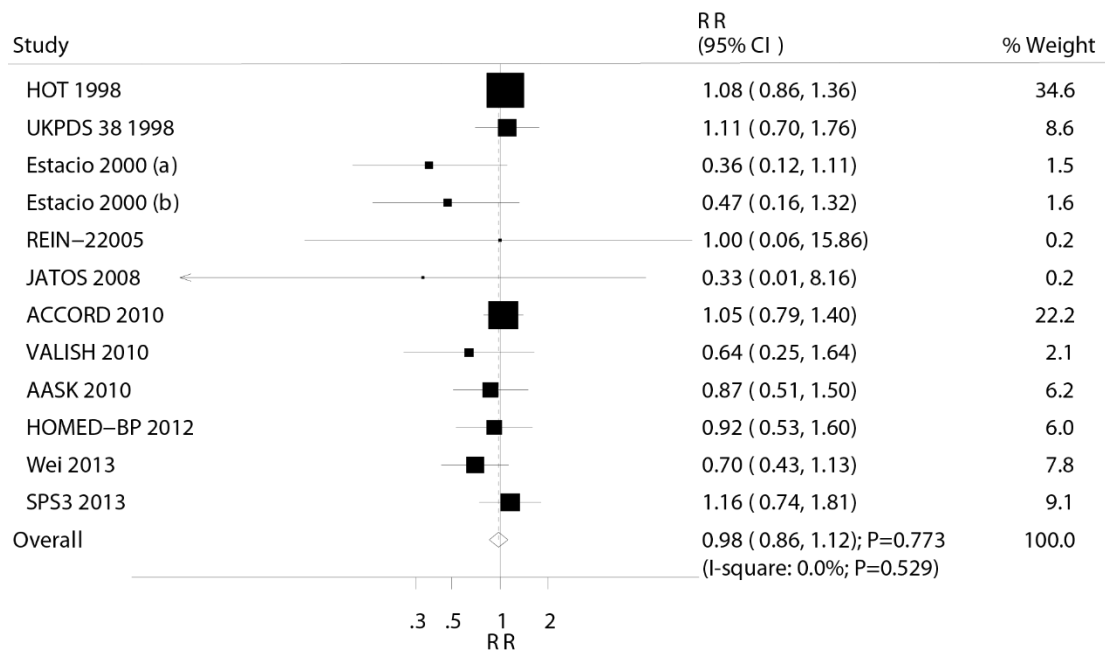


Fig. S11. Effect of IBP control on the risk of non-cardiac death

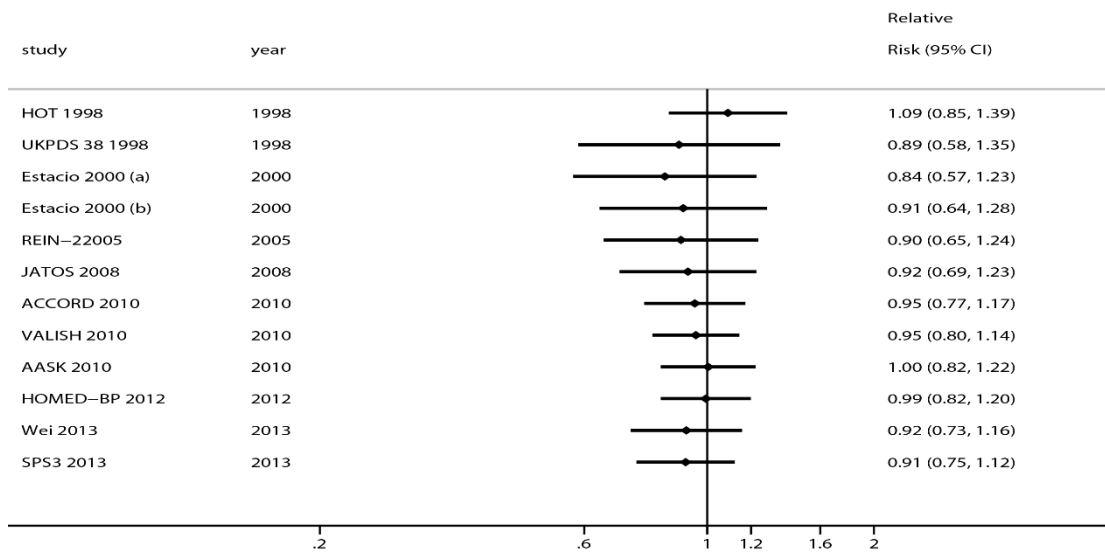


Fig. S12. Cumulative meta-analysis of the IBP control for cardiac death

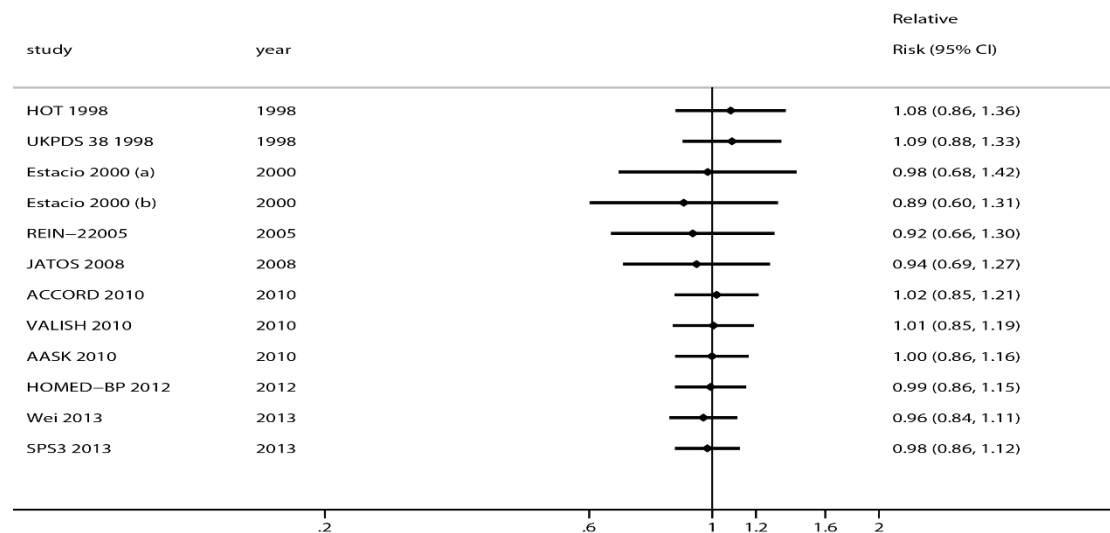


Fig. S13. Cumulative meta-analysis of the IBP control for non-cardiac death

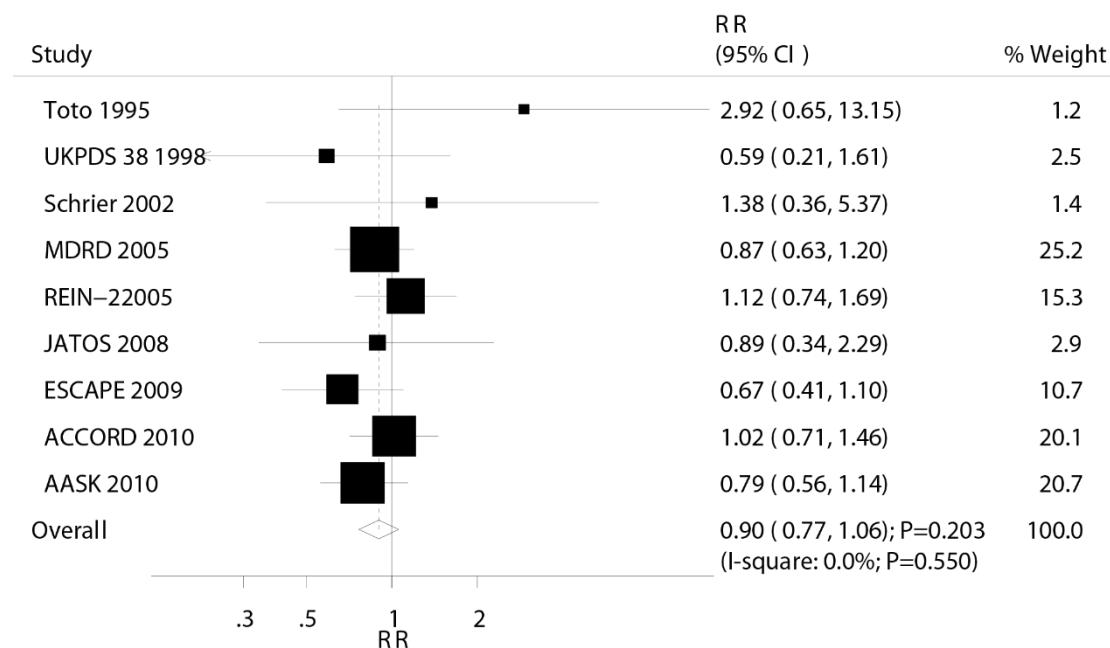


Fig. S14. Effect of IBP control on the risk of end-stage renal disease

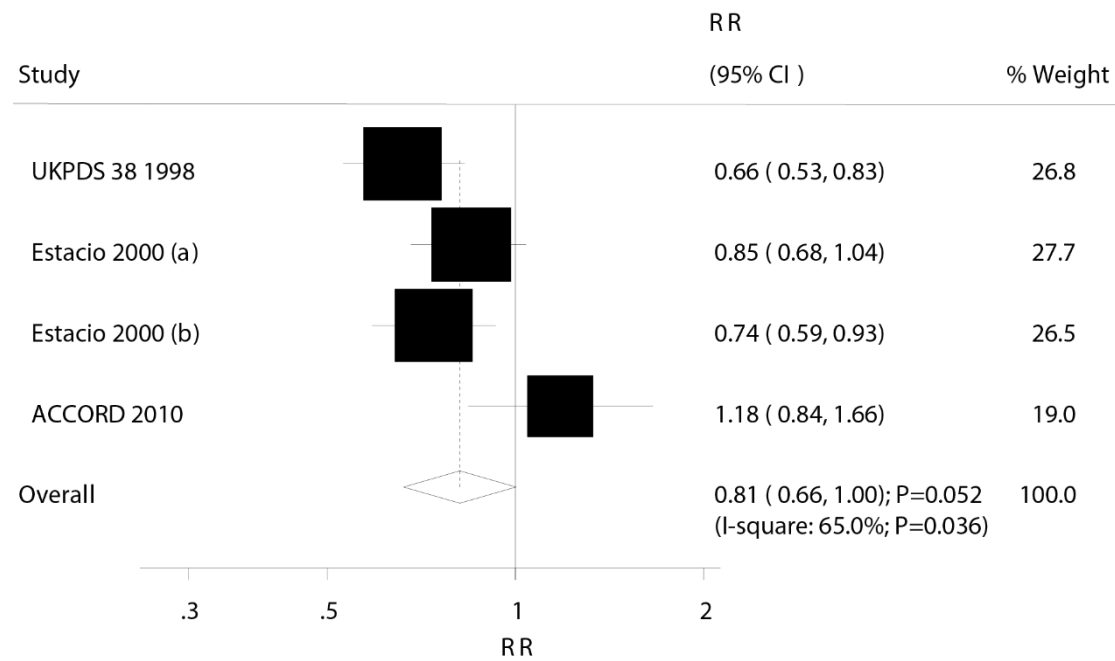


Fig. S15. Effect of IBP control on the risk of retinopathy

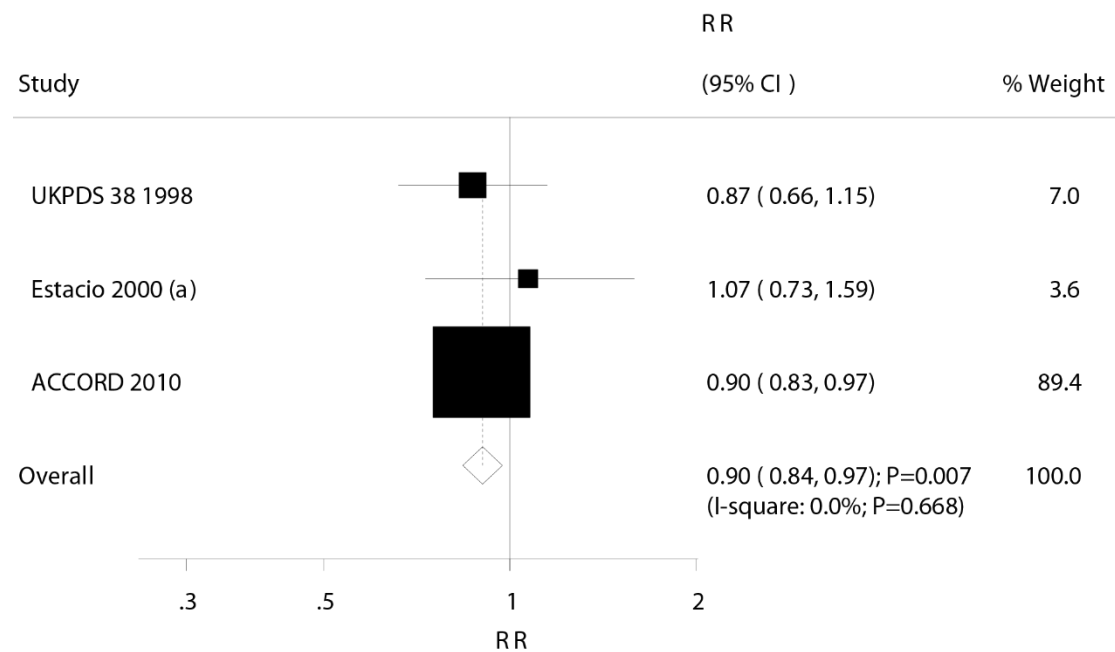


Fig. S16. Effect of IBP control on the risk of albuminuria

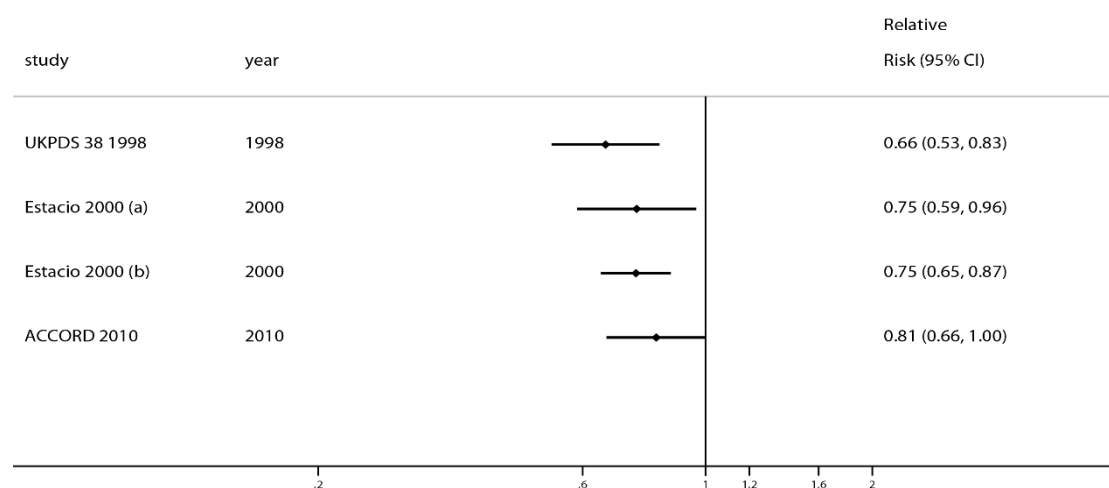


Fig. S17. Cumulative meta-analysis of the IBP control for retinopathy

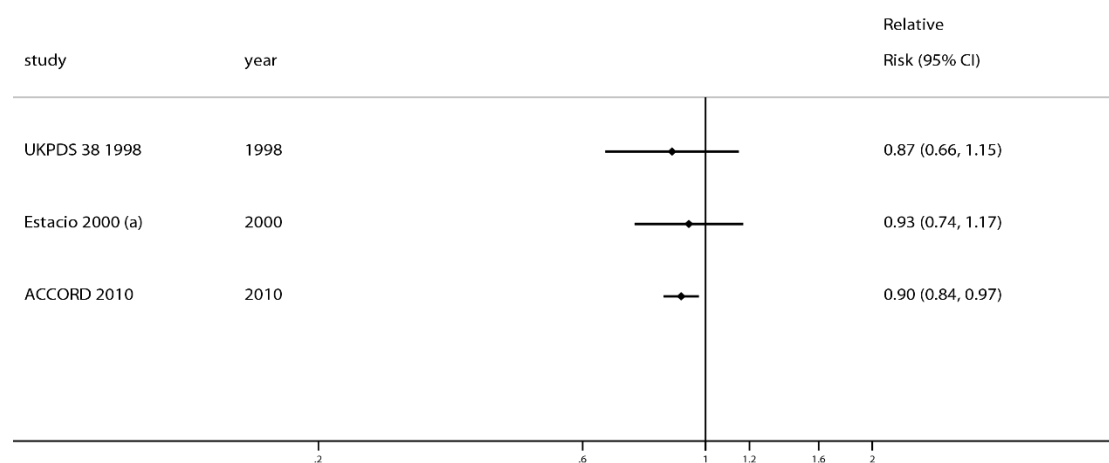
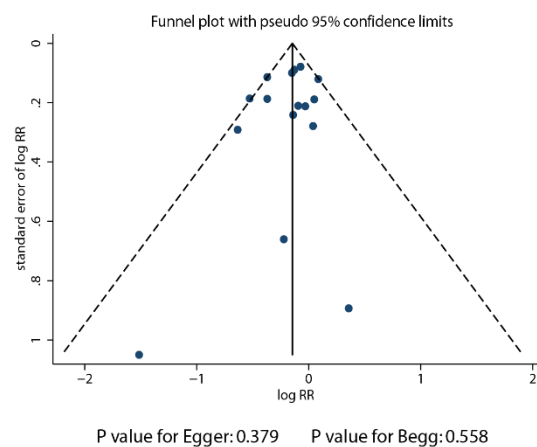
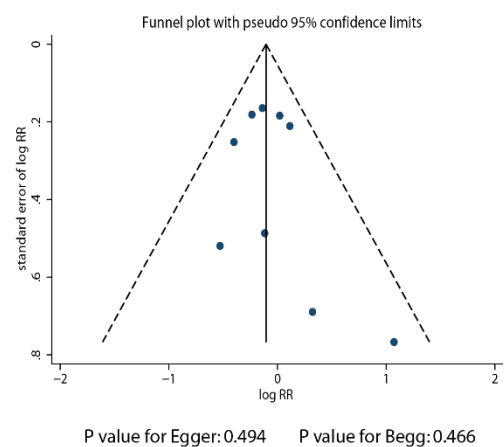


Fig. S18. Cumulative meta-analysis of the IBP control for albuminuria



A. major cardiovascular events



B. end-stage renal disease

Fig. S19. Funnel plots for major cardiovascular events and end-stage renal disease