

Supplementary Figure 1. Patient flow-chart

For cross-sectional analysis

1877

1337 patients excluded for fewer than 2 follow-up PWV measurements

For longitudinal analysis

540

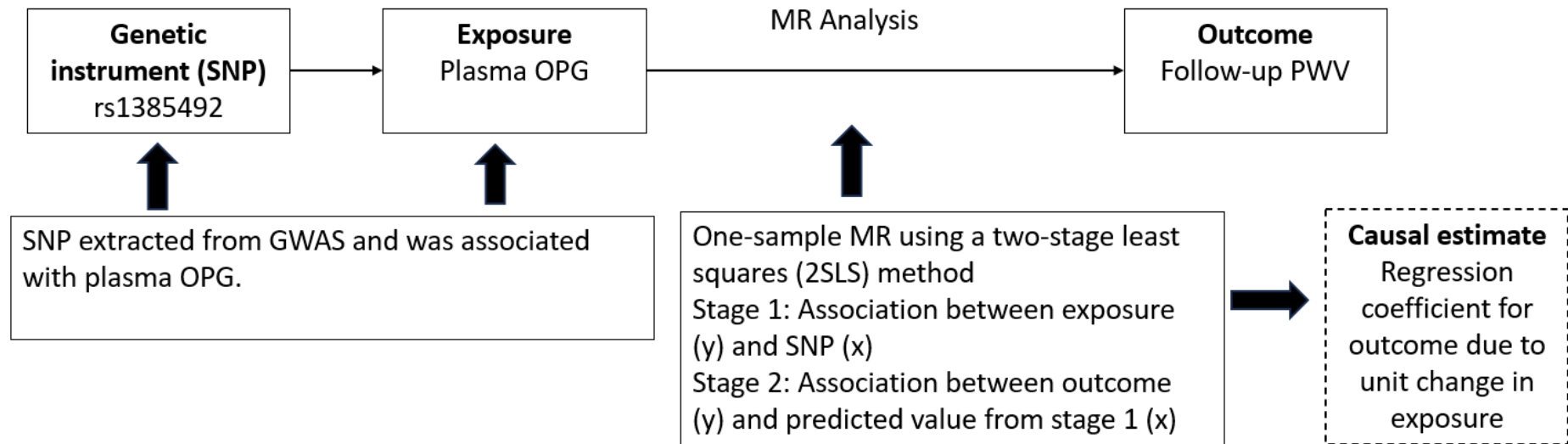
12 patients excluded for no SNP data for analysis

For Mendelian Randomization analysis

528

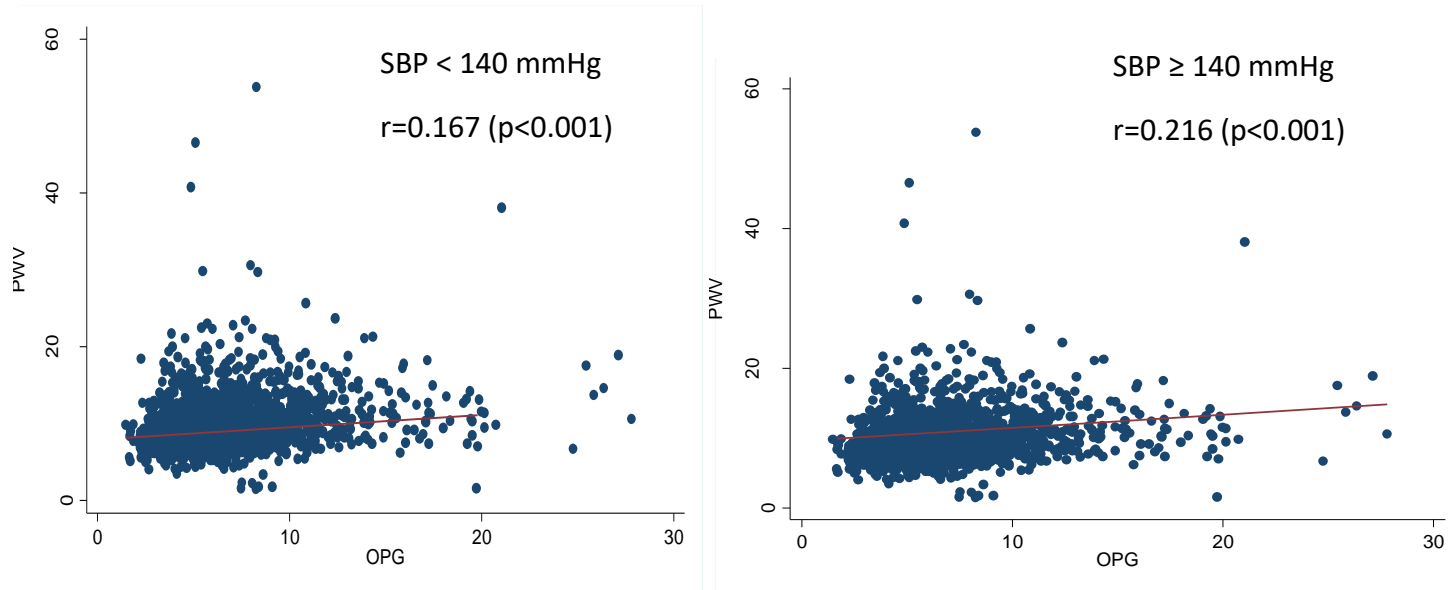
PWV, pulse wave velocity; SNP, single nucleotide polymorphism

Supplementary Figure 2. Mendelian Randomization

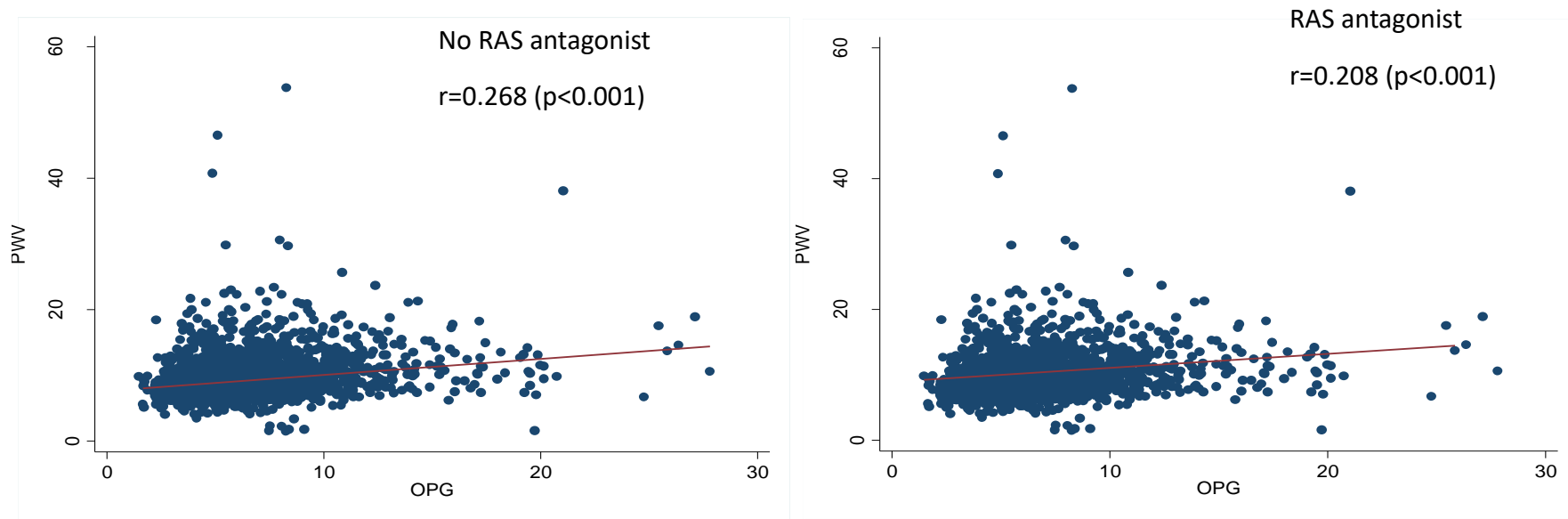


SNP, single-nucleotide polymorphism; OPG, osteoprotegerin; MR, Mendelian Randomization; PWV, pulse wave velocity; GWAS, genome-wide association study

Supplementary Figure 3. Spearman correlation between OPG and PWV at baseline stratified by systolic blood pressure

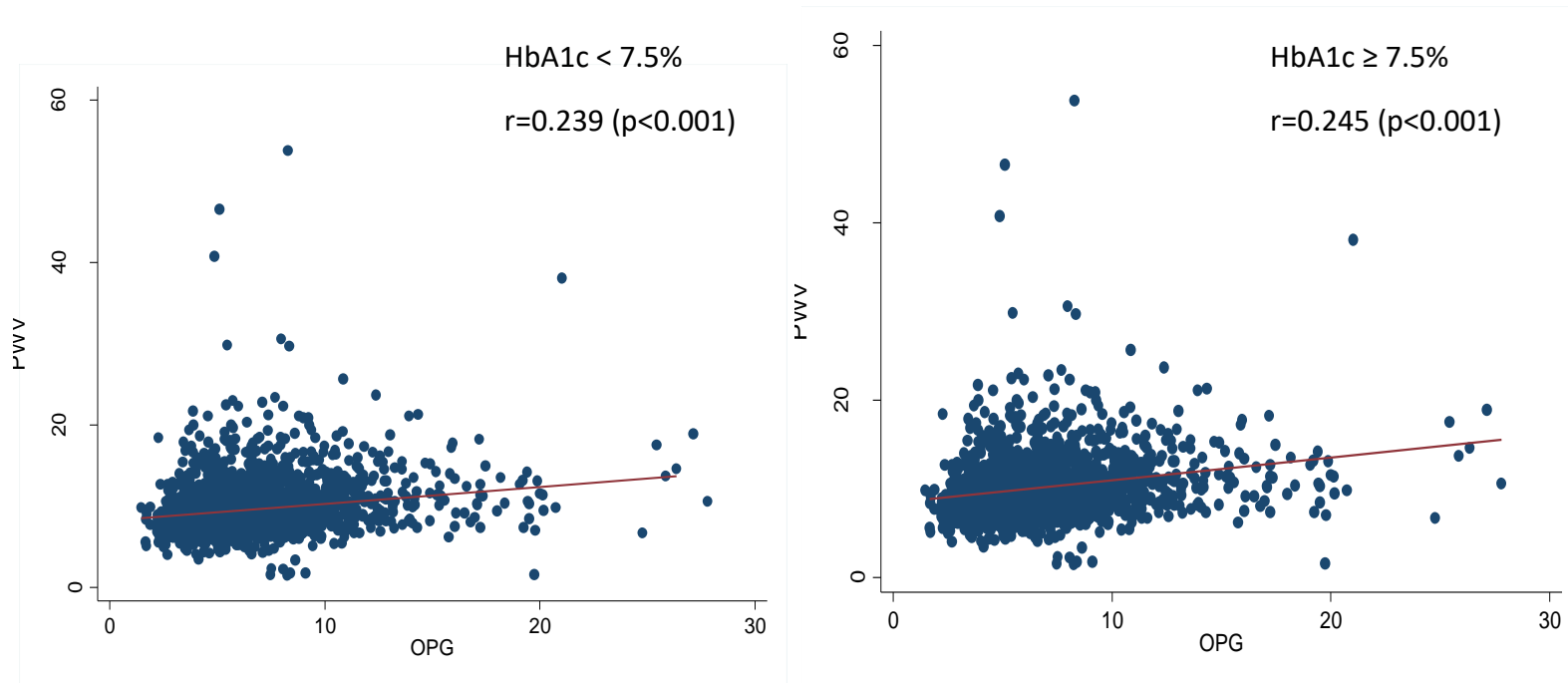


Supplementary Figure 4. Spearman correlation between OPG and PWV at baseline stratified by use of RAS antagonist

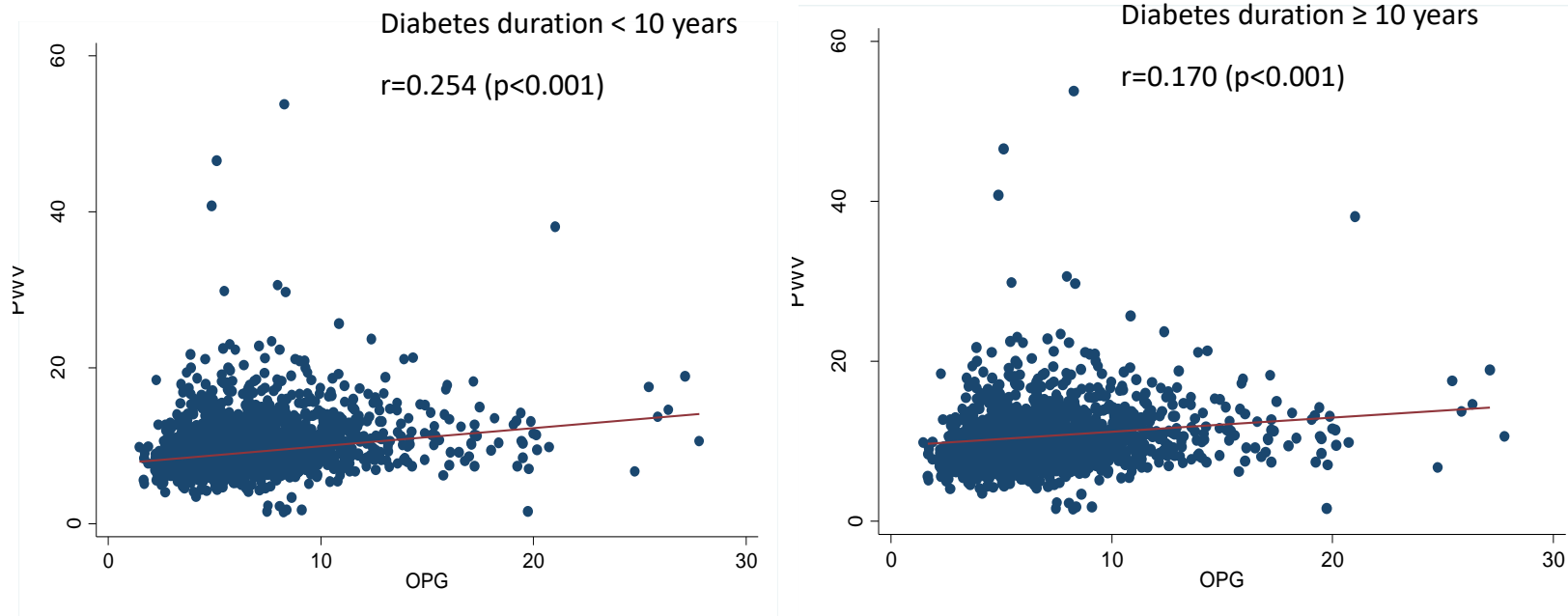


RAS, renin-angiotensin system

Supplementary Figure 5. Spearman correlation between OPG and PWV at baseline stratified by glycemic control



Supplementary Figure 6. Spearman correlation between OPG and PWV at baseline stratified by diabetes duration



Supplementary Table 1. Correlation between OPG and baseline characteristics

Clinical variable	Correlation Coefficient	P-value
Age	0.317	<0.001
BMI	0.024	0.306
SBP	0.220	<0.001
DBP	0.022	0.346
FPG	0.066	0.004
LDL-C	0.012	0.591

-0.261 <0.001

TG	0.074	0.001	
eGFR			
PWV		0.249	<0.001
VCAM-1		0.233	<0.001

SBP, systolic blood pressure; FPG, fasting plasma glucose; LDL, low-density lipoprotein; TG, triglycerides; eGFR, estimated glomerular filtration rate; PWV, pulse wave velocity; VCAM-1, vascular cell adhesion molecule

Supplementary Table 2. Proportion of OPG associated SNP (rs1385492) allele frequency stratified by OPG in tertiles

	All (N=528)	Tertile 1	Tertile 2	Tertile 3	p-value
AA	179 (33.9)	72 (40.7)	58 (33.0)	49 (28.0)	0.040
GA/GG	349 (66.1)	105 (59.3)	118 (67.1)	126 (72.0)	

OPG, osteoprotegerin

Supplementary Table 3. Association of OPG associated SNP with clinical variables

Clinical variable	Coefficient	Standard Error	P-value
SBP	-0.985	1.477	0.505
DBP	-0.145	0.801	0.857
FPG	0.215	0.232	0.355
LDL-C	-0.043	0.073	0.557
TG ^a	0.023	0.050	0.636
eGFR	-3.261	2.473	0.188

SBP, systolic blood pressure; FPG, fasting plasma glucose; LDL, low-density lipoprotein; TG, triglycerides; eGFR, estimated glomerular filtration rate

Adjusted for age, sex and population structure

a. Natural log-transformed