Online Supplement

Retinal Vascular Caliber and the Development of Hypertension:

A Meta-analysis of Individual Participant Data

Supplementary Table I. Retinal vascular caliber measurements of 6 studies contributing data

Study abbreviation	Year of publication	Retinal camera	Angle of field of view	Mydriasis (Yes/no)	Image type	Eye & field of image graded	Image processing software	Summary Formula
ARIC	2004	Canon CR6-45NM	45^{o}	no	Non-stereoscopic; Film	Right; OD	Retinal Analysis [computer program]. Version 1. Madison, WI: Optimate	Parr-Hubbard
MESA	2009	Canon CR6-45NM	45^{o}	no	Non-stereoscopic; Digital	Right; OD	Retinal Analysis (later version)	Knudtson
BMES	2004/2008	Zeis FF3	30^{o}	yes	Stereoscopic; Film	Right; OD	Retinal Analysis [computer program]. Version 1. Madison, WI: Optimate	Parr-Hubbard
AusDiab	*	Canon CR45UAF	45^{o}	no	Stereoscopic; Digital	Right; OD	Retinal Analysis (later version)	Parr–Hubbard
Funagata	2010	Canon CR5-NM45	45^{o}	no	Non-stereoscopic; Film	Right; OD	Retinal Analysis [computer program]. Version 1. Madison, WI: Optimate	Parr-Hubbard
BDES	2004	Zeis FF3	30^{o}	yes	Stereoscopic; Film	Right; OD	Retinal Analysis [computer program]. Version 1. Madison, WI: Optimate	Parr-Hubbard

*Studies that had not previously published their findings;

Abbreviations: ARIC, Atherosclerosis Risk in Communities; AusDiab, Australian Diabetes, Obesity and Lifestyle; BDES, Beaver Dam Eye study; BMES, Blue Mountains Eye Study; MESA, Multi-Ethnic Study of Atherosclerosis; OD: field centred on optic disc.

Supplementary Table II. Blood pressure assessment of 6 studies contributing data

Study abbreviation	Device	Body position	Location of measurement	Number of measurements	Readings used in analysis
ARIC	random zero sphygmomanometer	Sitting	arm	3	Mean of the 2nd and 3rd readings
MESA	automated oscillometric sphygmomanometer	Sitting	arm	3	Mean of the 2nd and 3rd readings
BMES	mercury sphygmomanometer	Sitting	arm	1	Single reading
AusDiab	mercury sphygmomanometer (baseline)/ automated blood pressure monitor(follow-up)	Supine(baseline) /sitting (follow-up)	arm	3	Mean of the first two readings or mean of the two closest readings if the difference between the first two readings greater than 10 mmHg
Funagata	mercury sphygmomanometer	Sitting	arm	1	Single reading
BDES	random zero sphygmomanometer	Sitting	arm	3	Mean of the 2nd and 3rd readings

Abbreviations: ARIC, Atherosclerosis Risk in Communities; AusDiab, Australian Diabetes, Obesity and Lifestyle; BDES, Beaver Dam Eye study; BMES, Blue Mountains Eye Study; MESA, Multi-Ethnic Study of Atherosclerosis.

Supplementary Table III. Overall odds ratios (OR) of incident hypertension by retinal vascular caliber, adjusted for risk factors

	No. of participants	No. of events	CRAE		CRVE	
			Overall OR (95%CI)	I-squared (p)*	Overall OR (95%CI)	I-squared (p)*
Progressive adjustment						
Model 1: age, sex, race	10229	2590	1.65(1.53,1.79)	11.4%(0.34)	1.28(1.21,1.36)	0.0%(0.72)
Model 2: plus smoking, BMI, total cholesterol	10092	2544	1.61(1.49,1.75)	15.7%(0.31)	1.23(1.16,1.31)	0.0%(0.60)
Model 3: plus SBP	10092	2544	1.29(1.20,1.39)	0.0%(0.58)	1.14(1.06,1.23)	21.7%(0.27)

***** p value of test for heterogeneity; BMI, body mass index; SBP, systolic blood pressure.

Supplementary Table IV. Overall odds ratio (OR) of incident hypertension, by retinal vascular caliber variables in subgroups

Variable	Persons at risk	Incident cases of hypertension	Odds Ratio (95%CI)*			
			CRAE†	P for interaction§	CRVE‡	P for interaction‖
Age group, years				0.03		0.07
<60	6430	1429	1.44(1.30,1.60)		1.13(1.04,1.23)	
60-69	2940	815	1.18(1.03,1.34)		1.14(1.02,1.27)	
≥70	850	355	0.99(0.80,1.21)		0.93(0.80, 1.09)	
Sex				0.54		0.68
Men	4482	1105	1.25(1.12,1.40)		1.13(1.03,1.24)	
Women	5747	1494	1.30(1.18,1.44)		1.07(1.00,1.17)	
Ethnicity				0.28		0.25
White	7502	1728	1.30(1.18,1.42)		1.09(1.01,1.17)	
Non-white	2727	871	1.26(1.11,1.44)		1.13(1.02,1.26)	
Prehypertension				0.09		0.04
Yes	3941	1775	1.22(1.11,1.34)		1.07(1.00,1.16)	
No	6,288	824	1.40(1.24,1.59)		1.16(1.05,1.28)	
Current smoker				0.15		0.25
Yes	1832	486	1.34(1.12,1.59)		1.09(0.96,1.25)	
No	8364	2102	1.28(1.17,1.39)		1.11(1.03,1.18)	
BMI, kg/m^2				0.99		0.16
<25.0	3897	827	1.23(1.08,1.40)		1.11(1.00,1.24)	
25.0-29.0	3533	923	1.32(1.16,1.50)		1.15(1.04,1.28)	
⩾29.0	2785	841	1.31(1.15,1.50)		1.03(0.93,1.14)	

* Odds ratios from a multilevel effects discrete time logistic model with retinal arteriolar and venular calibers as the main exposures, age, sex, race/ethnicity, current smoker, body mass index, total cholesterol level and systolic blood pressure at baseline as covariates (where appropriate) and study as the random effect; † Per 20 µm narrower CRAE; ‡ Per 20 µm larger CRVE.; § p-value for CRAE*covariate; ‖p-value for CRVE*covariate.

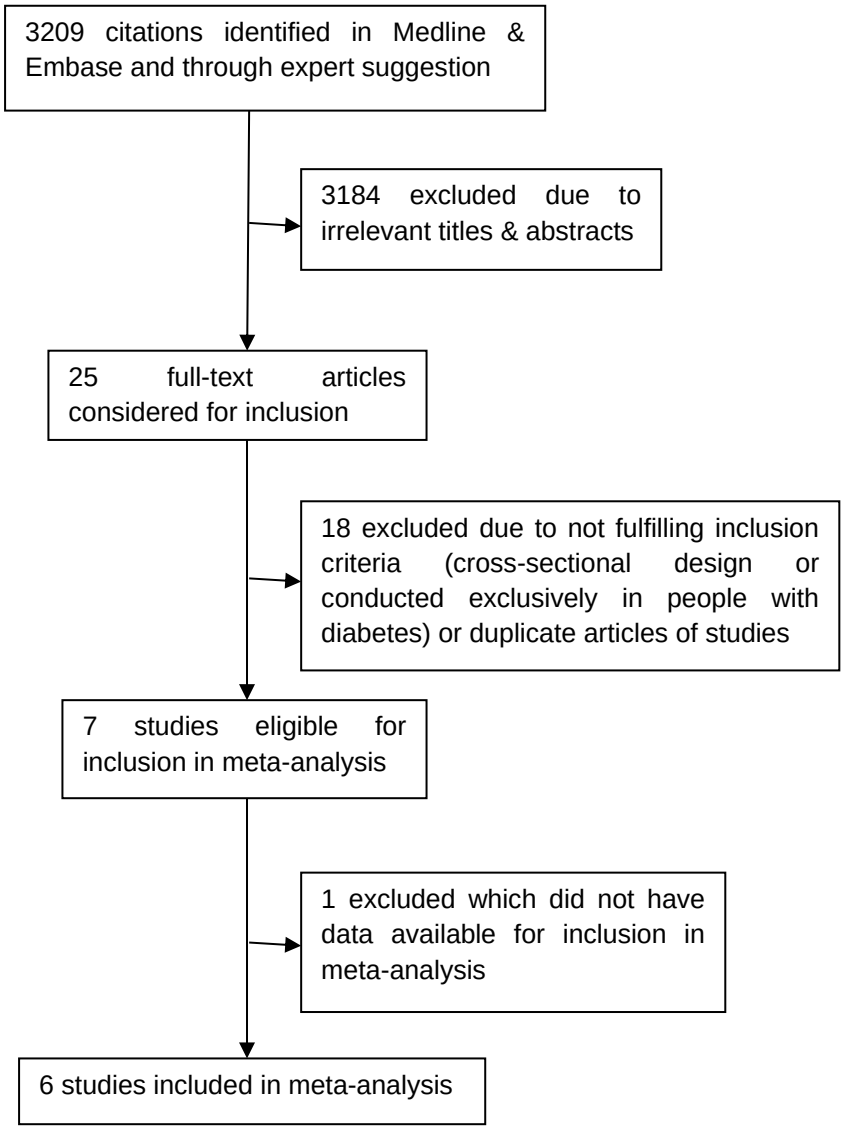
Supplementary Table V. Associations of retinal vascular caliber with baseline systolic blood pressure and the average rate of change in systolic blood pressure over 5 years (meta-analysis of regression coefficients in 6 studies)

	Baseline SBP (mmHg)			Rate of Change in SBP (mmHg)		
Retinal arteriolar narrowing	Pooled β Estimate§	95%CI	I-squared(p)‖	Pooled β Estimate§	95%CI	I-squared(p)‖
Per 20μm difference in CRAE	2.99	(1.56,4.42)‡	88.9%(<0.001)	1.12	(0.25, 1.99)*	40.3%(0.14)
Retinal venular widening						
Per 20μm difference in CRVE	1.38	(0.73,2.04)‡	61.3%(0.02)	0.44	(-0.34,1.21)	41.9%(0.13)

P values *<0.05; †<0.01; ‡<0.001;

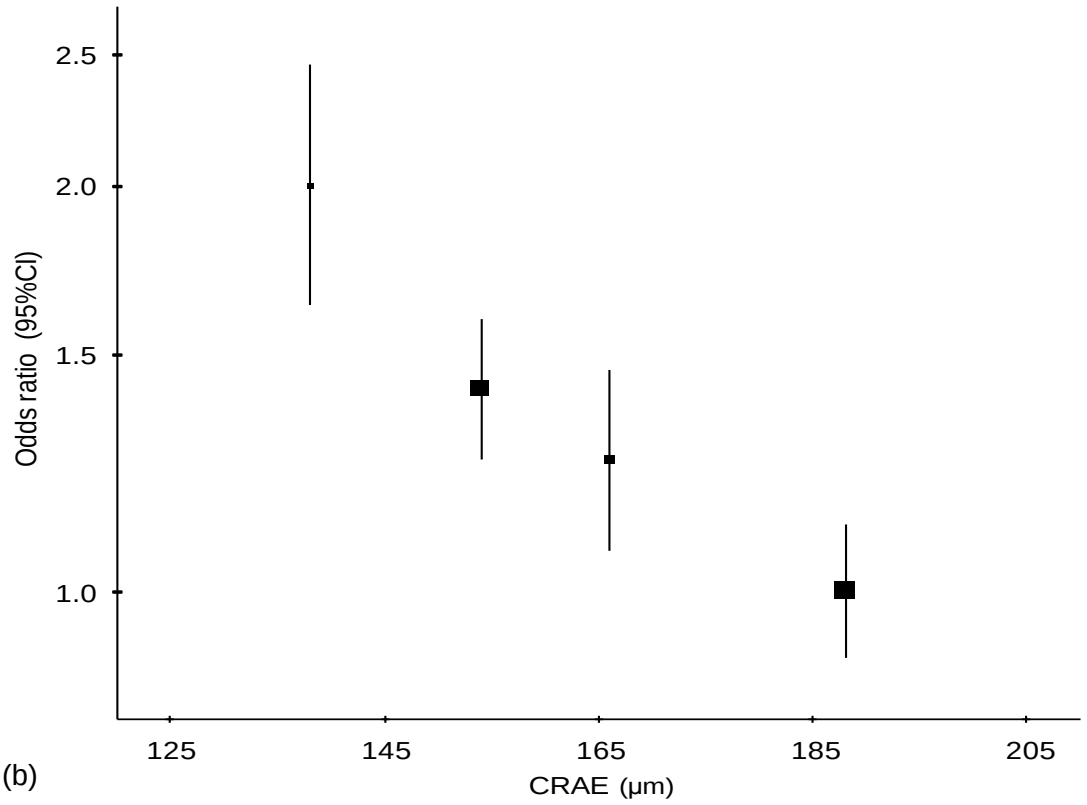
§ The regression coefficient was adjusted for age, sex, race, follow-up time or occasions, baseline smoking status, BMI, total cholesterol and the fellow retinal vascular caliber in a mixed linear model in each study. Results were pooled using random effect meta-analysis.

‖ p value of test for heterogeneity .

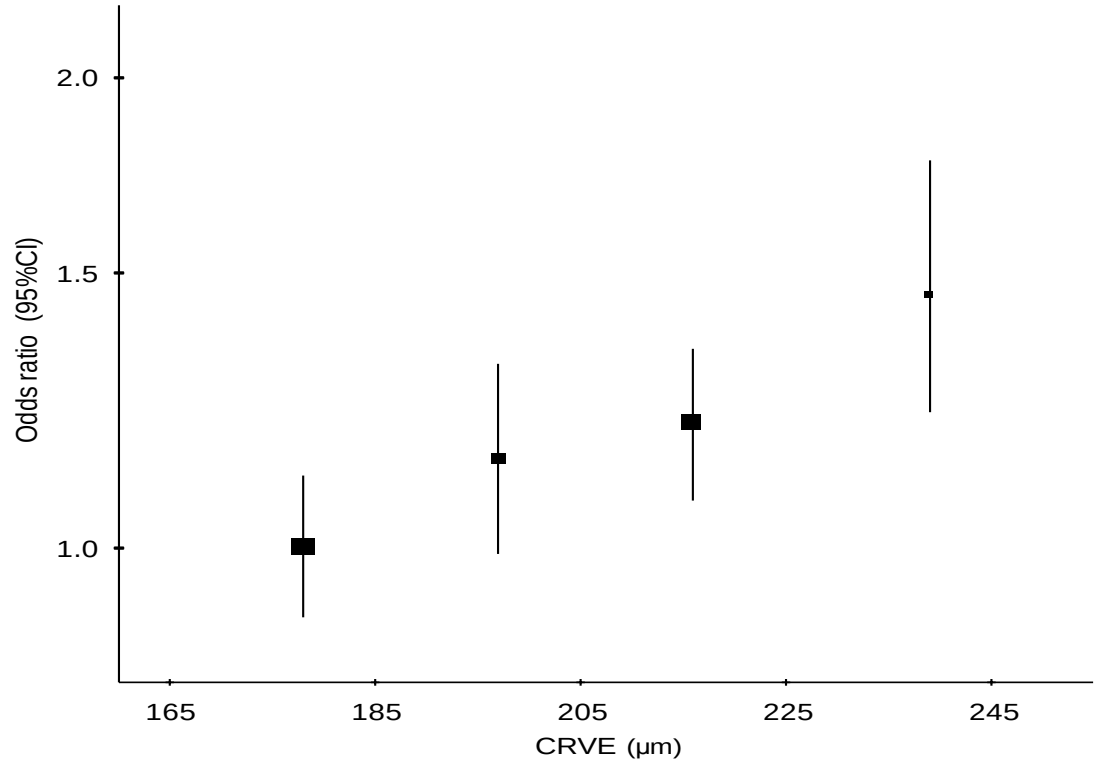


Supplementary Figure I. Flow diagram of selection of studies for inclusion in meta-analysis.

(a)


2.5
2.0
1.5
1.0
Odds ratio (95%CI)
125
145
165
185
205
CRAE (μm)

(b)


2.0
1.5
1.0
Odds ratio (95%CI)
165
185
205
225
245
CRVE (μm)

Supplementary Figure II. Overall adjusted odds ratios (OR) (model 3) of incident hypertension by quartiles of baseline retinal vascular caliber. Data shown for CRAE (A) and CRVE (B) relative to the highest or lowest quartile. Vertical error bars show 95% CIs estimated from variances reflecting the amount of information within each group including the reference group. Sizes of the data markers are proportional to the inverse of the variance of the $\log_e$ ORs.