Consistency of associations of systolic and diastolic blood pressure with white matter hyperintensities: a meta-analysis

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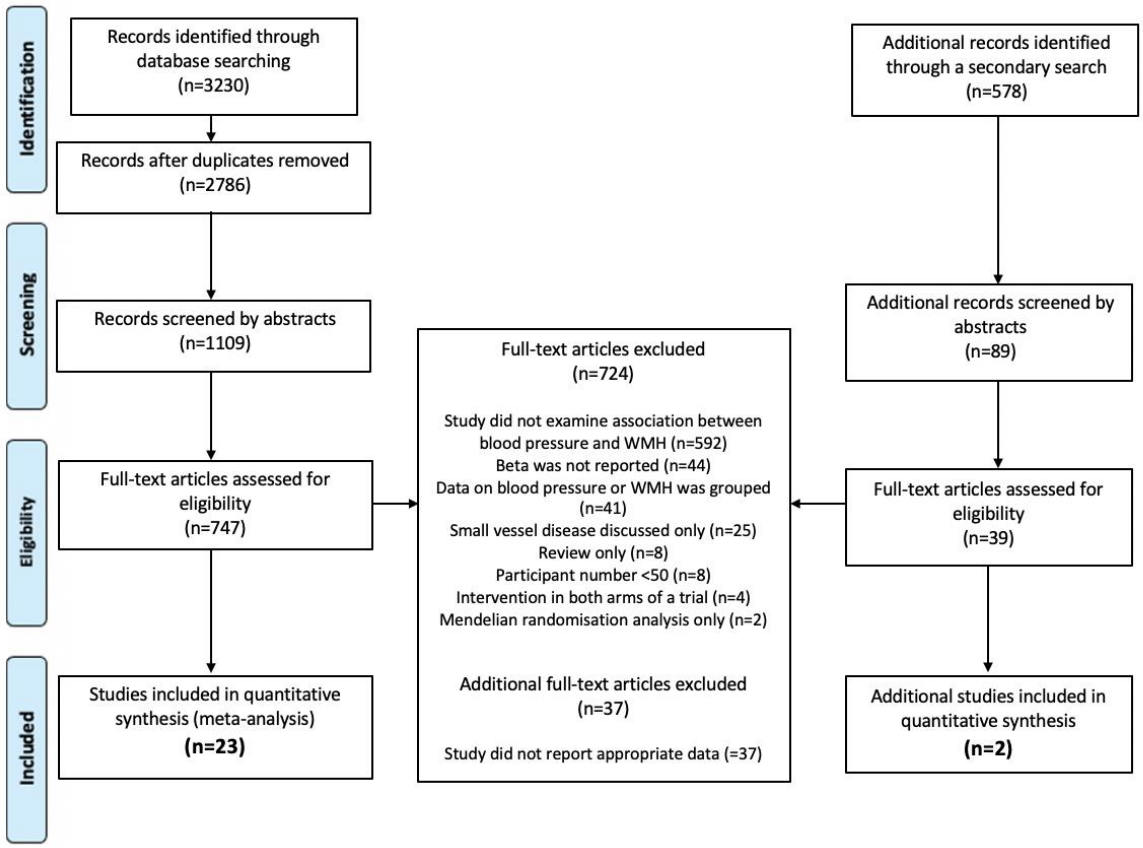
Supplementary Figure 1. Prisma Flow Chart



Supplementary Table 1. Characteristics of included studies

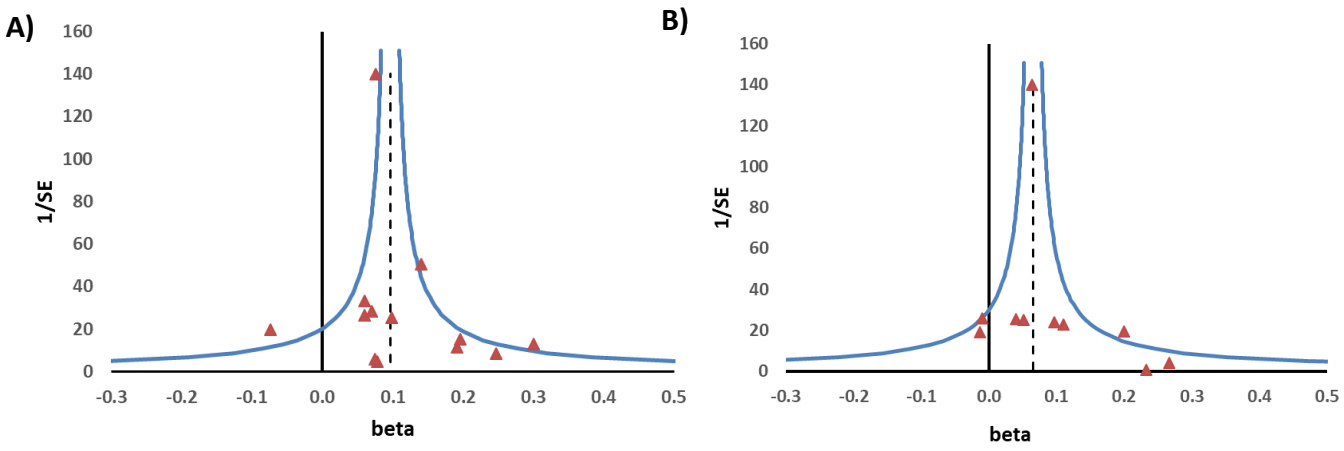
Study	N	Mean Age	SD of age	% Male	Mean WMHV (cm^3)	Median WMHV (cm3)
Shi	56	67.8	8.3	40.0	-	10.74
Cheng	60	31.7	6.3	32.0	0.174	-
Wolfson	67	85.8	3.8	39.0	n/a	n/a
White	71	82.1	3.9	40.0	13.9	-
Vesperman	107	64.2	5.9	34.6	2.9	-
Shimizu	133	69.7	3.2	48.0	6.5	-
Alkan	164	60.1	7.9	40.9	0.98	-
White, Jalil	199	81.2	4.1	45.7	n/a	n/a
Sander	227	n/a	n/a	n/a	9.3	-
Heye	264	66.9	11.8	35.0	n/a	n/a
Shokouhi	265	64.0	n/a	35.0	n/a	n/a
Lane	468	70.7	0.7	51.1	3.1	-
Maillard	579	39.2	8.4	40.4	1.7	-
Schwartz	610	62.9	n/a	35.4	-	6.8
Cui	663	68.6	5.7	43.4	-	2.75
Fuhrmann	667	54.6	18.5	n/a	2.15	-
Aribisala	694	69.6	0.8	53.0	0.012	-
Cloonan	809	65.6	14.7	53.0	-	6.25
Gutierrez	1009	64.0	8.0	41.0	n/a	n/a
Tsao	1118	61.0	9.0	44.0	n/a	n/a
King	1270	51.4	9.4	44.3	1.6	-
Godin	1391	72.0	n/a	39.3	5.4	-
Jeerakathil	1814	61.7	9.4	47.0	0.96	-
Lampe	1825	52.5	13.2	43.6	2.835	-
Wartolowska	37026	55.3	7.5	47.0	-	2.796

Supplementary Table 2. Quality assessment of factors that differed between included studies. 0 = no; 1 = yes.

Study	Question 3	Question 5	Question 6	Question 10	Question 12	Question 13	Total
Alkan	0	0	1	0	0	1	2
Aribisala	0	0	1	1	0	0	2
Cheng	1	0	0	0	0	1	2
Cloonan	0	0	1	0	0	1	2
Cui	1	0	1	0	1	1	4
Fuhrmann	1	0	1	0	0	0	2
Godin	1	0	1	1	0	0	3
Gutierrez	0	0	1	1	0	0	2
Habes	0	0	0	1	0	0	1
Jeerakathil	0	0	1	0	1	1	3
King	0	0	1	0	0	1	2
Lampe	0	0	1	0	0	0	1
Lane	0	0	1	1	0	1	3
Maillard	0	0	1	0	0	1	2
Sander	1	0	0	0	1	1	3
Schwartz	0	0	1	1	0	1	3
Shi	0	1	0	0	1	1	3
Shimizu	0	0	0	0	0	1	1
Shokouhi	0	0	1	1	0	0	2
Tsao	0	0	1	0	1	1	3
Vesperman	0	0	0	0	0	1	1
Wartolowska	0	0	1	1	0	1	3
White	1	0	1	1	1	0	4
White, Jalil	0	0	1	0	0	0	1
Wolfson	1	0	1	1	1	0	4

Question 3: Was the participation rate of eligible persons at least 50%?
Question 5: Was a sample size justification, power description or variance and effect estimates provided?
Question 6: For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s)?
Question 10: Was the exposure(s) assessed more than once over time?
Question 12: Were the outcome assessors blinded to the exposure status of the participants?
Question 13: Was loss to follow-up after baseline 20% or less?

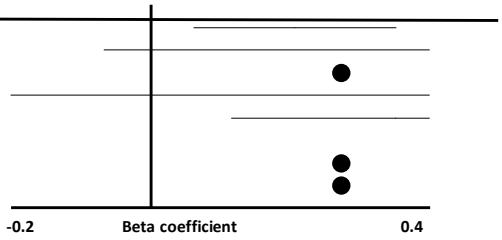
Supplementary figure 2. Funnel Plots for standardised beta-coefficients for systolic (A) and diastolic (B) blood pressure with white matter hyperintensity volume. SE = standard error, blue lines represent upper and lower confidence limits.



Supplementary figure 3. Unadjusted, standardised associations between SBP and DBP with WMHV. Results are combined by fixed and random effects meta-analysis, weighted by the inverse variance, with heterogeneity presented as I^2 statistics(I-sq), and the p-value for heterogeneity (p-het) determined by chi-squared testStdBeta = standardised beta; N= number;

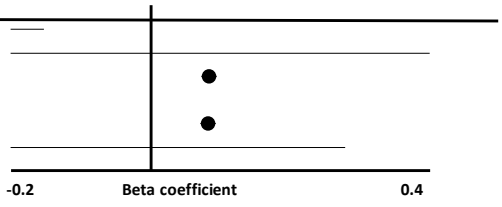
A) SBP

Study	N	StdBeta	Cilow	Cihigh	p-value	p-Het
Alkan	164	0.206	0.061	0.351	0.005	
Cloonan	809	0.207	-0.068	0.482	0.140	
Wartolowska - concurrer	37026	0.273	0.262	0.284	<0.001	
Shimizu	133	0.273	-0.404	0.950	0.430	
Fuhrmann	667	0.350	0.115	0.585	0.004	I-sq
						0%
Fixed Effects	38799	0.273	0.262	0.284	<0.001	p-het
Random Effects	38799	0.273	0.262	0.284	<0.001	0.84



B) DBP

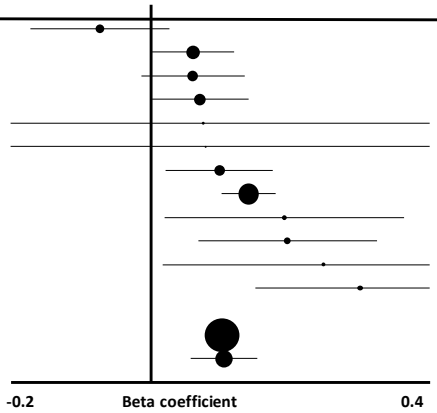
Study	N	StdBeta	Cilow	Cihigh	p-value	p-Het
Fuhrmann	667	-0.350	-0.546	-0.154	<0.001	
Cloonan	809	0.054	-0.864	0.972	0.910	
Wartolowska - concurrer	37026	0.083	0.071	0.095	<0.001	I-sq
						89%
Fixed Effects	38502	0.082	0.070	0.093	<0.001	p-het
Random Effects	38502	-0.099	-0.477	0.279	0.610	<0.001



Supplementary Figure 4. Standardised associations between SBP or DBP with WMH, excluding the largest study. Results are combined by fixed and random effects meta-analysis, weighted by the inverse variance, with heterogeneity presented as I^2 statistics(I-sq), and the p-value for heterogeneity (p-het) determined by chi-squared test StdBeta = standardised beta; N= number;

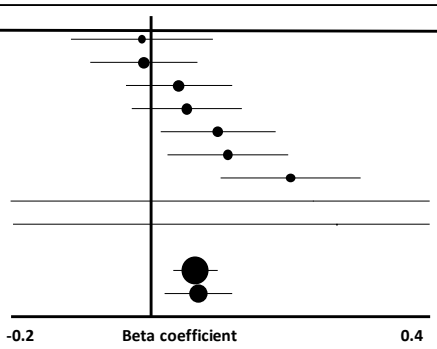
A) SBP

Study	N	StdBeta	Cilow	Cihigh	p-value	p-Het
Schwartz - white	343	-0.073	-0.173	0.026	0.150	
Godin	1391	0.060	0.001	0.119	0.050	
Aribisala - concurrent	694	0.060	-0.014	0.134	0.110	
Lane	468	0.070	0.001	0.140	0.050	
White	71	0.075	-0.261	0.411	0.660	
Sander	227	0.078	-0.348	0.504	0.720	
King	1270	0.098	0.021	0.175	0.010	
Lampe	1825	0.140	0.101	0.179	<0.001	
Cui	663	0.191	0.019	0.363	0.030	
Schwartz - black	267	0.195	0.068	0.323	0.003	
Cheng	60	0.247	0.017	0.477	0.040	
Shokouhi	265	0.300	0.150	0.450	<0.001	I-sq
						64%
Fixed Effects	7544	0.102	0.079	0.126	<0.001	p-het
Random Effects	7544	0.104	0.056	0.153	<0.001	0.0011



B) DBP

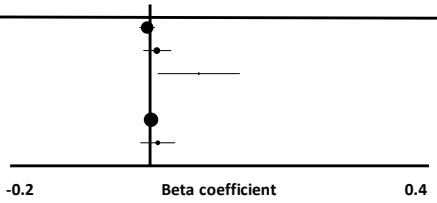
Study	N	StdBeta	Cilow	Cihigh	p-value	p-Het
King	1270	-0.013	-0.115	0.089	0.800	
Schwartz - white	343	-0.010	-0.087	0.066	0.790	
Aribisala - concurrent	694	0.040	-0.037	0.117	0.310	
Lane	468	0.051	-0.027	0.130	0.200	
Godin	1391	0.096	0.014	0.178	0.020	
Lampe	1825	0.110	0.024	0.196	0.010	
Shokouhi	265	0.200	0.100	0.300	<0.001	
Schwartz - black	267	0.233	-1.502	1.967	0.790	
Sander	227	0.266	-0.197	0.729	0.260	I-sq
						50%
Fixed Effects	6750	0.063	0.031	0.095	<0.001	p-het
Random Effects	6750	0.068	0.019	0.116	0.006	0.044



Supplementary Figure 5. Association between mean blood pressure (MBP) or pulse pressure (PP) with white matter hyperintensity volume. Results are combined by fixed and random effects meta-analysis, weighted by the inverse variance, with heterogeneity presented as I^2 statistics(I-sq), and the p-value for heterogeneity (p-het) determined by chi-squared test StdBeta = standardised beta; N= number;

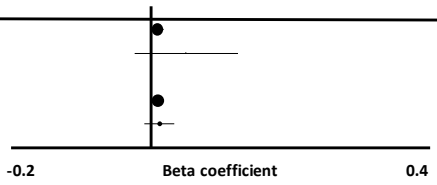
A) MBP

Study	N	StdBeta	Cilow	Cihigh	p-value	p-Het
Heye	264	-0.004	-0.015	0.007	0.520	
Shi	56	0.010	-0.010	0.030	0.330	
Tsao	1118	0.070	0.011	0.129	0.020	I-sq
						70%
Fixed Effects	1438	0.001	-0.008	0.011	0.770	p-het
Random Effects	1438	0.011	-0.013	0.036	0.370	0.034



B) PP

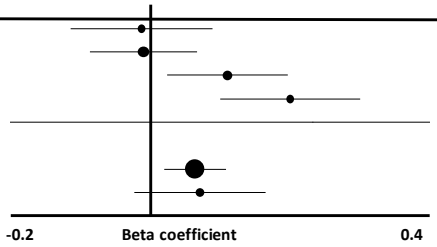
Study	N	StdBeta	Cilow	Cihigh	p-value	p-Het
Heye	264	0.009	0.001	0.018	0.040	
Aribisala - concurrent	694	0.050	-0.024	0.124	0.190	I-sq
						13%
Fixed Effects	958	0.010	0.001	0.018	0.026	p-het
Random Effects	958	0.012	-0.009	0.034	0.260	0.28



Supplementary Figure 6. Associations between DBP and WMH in studies with a mean age of less than 65 compared to greater than 65. Results are combined by fixed and random effects meta-analysis, weighted by the inverse variance, with heterogeneity presented as I^2 statistics(I-sq), and the p-value for heterogeneity (p-het) determined by chi-squared test StdBeta = standardised beta; N= number;

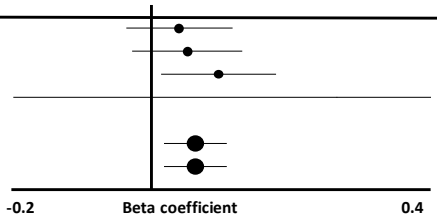
A) Studies in patients with a mean age <65

Study	N	StdBeta	Cilow	Cihigh	p-value	p-Het
King	1270	-0.013	-0.115	0.089	0.800	
Schwartz - white	343	-0.010	-0.087	0.066	0.790	
Lampe	1825	0.110	0.024	0.196	0.010	
Shokouhi	265	0.200	0.100	0.300	<0.001	
Schwartz - black	267	0.233	-1.331	1.796	0.770	I-sq
						72%
Fixed Effects	3970	0.064	0.019	0.108	0.005	p-het
Random Effects	3970	0.071	-0.023	0.165	0.140	0.007



B) Studies in patients with a mean age >65

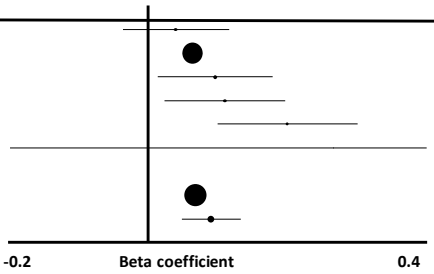
Study	N	StdBeta	Cilow	Cihigh	p-value	p-Het
Aribisala - concurrent	694	0.040	-0.037	0.117	0.310	
Lane	468	0.051	-0.027	0.130	0.200	
Godin	1391	0.096	0.014	0.178	0.020	
Sander	227	0.266	-0.197	0.729	0.260	I-sq
						0%
Fixed Effects	2780	0.063	0.018	0.108	0.007	p-het
Random Effects	2780	0.063	0.018	0.108	0.007	0.62



Supplementary Figure 7. Associations between DBP and WMH, stratified by time of exposure. Results are combined by fixed and random effects meta-analysis, weighted by the inverse variance, with heterogeneity presented as I^2 statistics(I-sq), and the p-value for heterogeneity (p-het) determined by chi-squared test StdBeta = standardised beta; N= number;

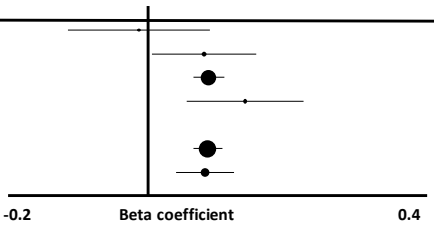
A) Concurrent DBP

Study	N	StdBeta	Cilow	Cihigh	p-value	p-Het
Aribisala - concurrent	694	0.040	-0.037	0.117	0.310	
Wartolowska - concurrer	37026	0.064	0.050	0.078	<0.001	
Godin	1391	0.096	0.014	0.178	0.020	
Lampe	1825	0.110	0.024	0.196	0.010	
Shokouhi	265	0.200	0.100	0.300	<0.001	
Sander	227	0.266	-0.197	0.729	0.260	I-sq
						48%
Fixed Effects	41428	0.068	0.054	0.081	<0.001	p-het
Random Effects	41428	0.090	0.048	0.132	<0.001	0.09



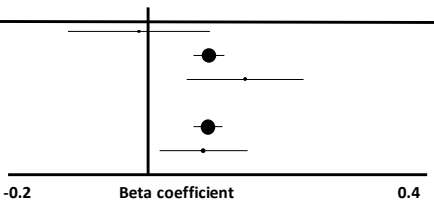
B) DBP measured > 2 years previously

Study	N	StdBeta	Cilow	Cihigh	p-value	p-Het
King	1270	-0.013	-0.115	0.089	0.800	
Aribisala - 2 years	694	0.080	0.005	0.155	0.040	
Wartolowska - past	37026	0.087	0.064	0.110	<0.001	
Lane - historic	468	0.140	0.056	0.224	0.001	I-sq
						43%
Fixed Effects	39458	0.086	0.065	0.106	<0.001	p-het
Random Effects	39458	0.082	0.040	0.123	<0.001	0.16



C) DBP measured >5 years previously

Study	N	StdBeta	Cilow	Cihigh	p-value	p-Het
King	1270	-0.013	-0.115	0.089	0.800	
Wartolowska - past	37026	0.087	0.064	0.110	<0.001	
Lane - historic	468	0.140	0.056	0.224	0.001	I-sq
						62%
Fixed Effects	38764	0.086	0.065	0.107	<0.001	p-het
Random Effects	38764	0.079	0.016	0.142	0.013	0.07



Search strategy

1. Primary Search

((“white matter hyperintensities" OR "leukoaraiosis" OR “leukoencephalopath*" OR “arteriosclerotic encephalopathy” OR "white matter hyperintensity" OR "white matter lesion*" OR "white matter disease" OR “white matter changes” OR “white matter damage” OR “ischaemic white matter disease” OR “binswanger disease” OR “hypertensive arteriopathy” OR “small vessel disease” OR “cerebral microangiopathy”) AND ("blood pressure" OR "systolic" OR "diastolic" OR "arterial pressure" OR "pulse pressure" OR "pulse wave velocity" OR "pulse transit time" OR "pulse wave transit time" OR "BP" OR "ABP" OR "pulsatile pressure” OR “cerebral blood flow” OR “cerebral blood velocity”))

2. Secondary Search Strategy

(“*Study Name”)* AND (“MRI” OR “Magnetic Resonance”)

Eg: (“Rotterdam Study” OR “Rotterdam Scan Study”) AND (“MRI” OR “Magnetic Resonance”)

References of included studies

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