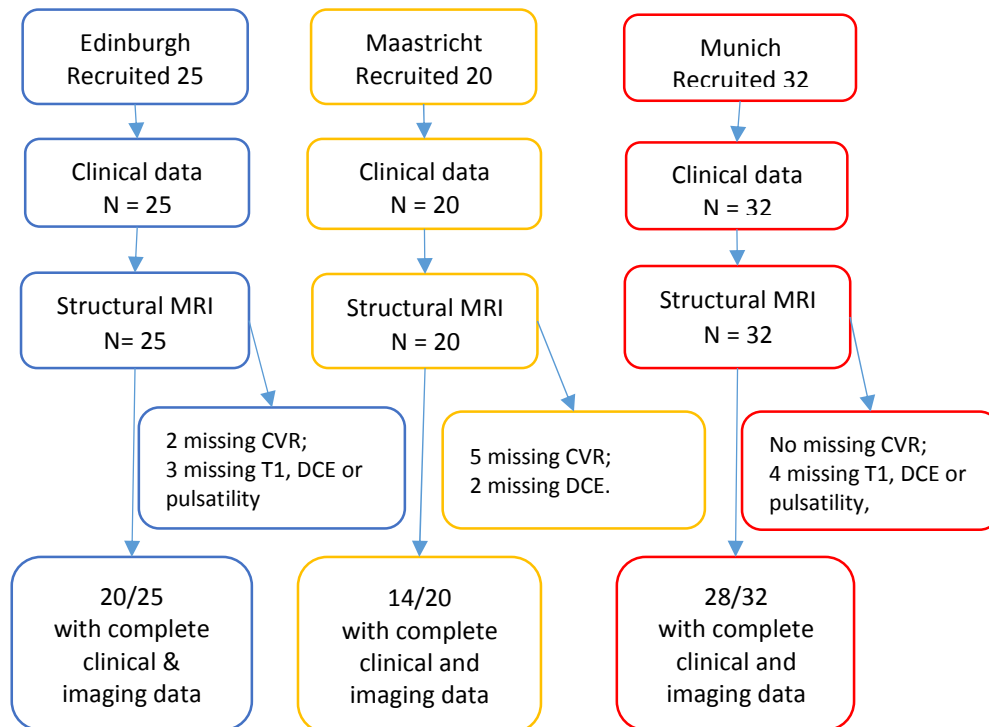


Participant Flow



Investigate@SVDs recruited 77 patients (flow diagram), 45 with sporadic SVD in Edinburgh and Maastricht and 32 with CADASIL in Munich. 62 provided complete imaging data for all functions (Flow chart).

Baseline Characteristics

Baseline clinical characteristics of all patients are given in Table 1, and of participants with CADASIL versus sporadic SVD in Table 2.

Table 1. Demographic and clinical characteristics of the patients by site

Institute	Edinburgh (sporadic)	Maastricht (sporadic)	Munich (CADASIL)	All sites
Total n	25 (100.0)	20 (100.0)	32 (100.0)	77 (100.0)
Male n (%)	13 (52.0)	13 (65.0)	16 (50.0)	42 (54.5)
Female n(%)	12 (48.0)	7 (35.0)	16 (50.0)	35 (45.5)
Age mean +/- std (range)	68.3 +/- 11.3 (44.8 to 87.0)	59.1 +/- 8.3 (43.0 to 70.7)	52.9 +/-11.1 (23.6 to 70.0)	59.5 +/- 12.3 (23.6 to 87.0)
Diabetes	6 (24.0)	3 (15.0)	1 (3.1)	10 (13.0)
Hypertension	20 (80.0)	15 (75.0)	11 (34.4)	46 (59.7)
Hyperlipidaemia	20 (80.0)	13 (65.0)	13 (40.6)	46 (59.7)
Current smoker	2 (8.0)	4 (20.0)	3 (9.4)	9 (11.7)
Ex-smoker	8 (32.0)	9 (45.0)	15 (46.9)	32 (41.6)
Never smoker	15 (60.0)	7 (35.0)	14 (43.8)	36 (46.8)
Does use alcohol	17 (68.0)	14 (70.0)	24 (75.0)	55 (71.4)
Alcohol units per week mean +/- std (range)	8.6 +/- 6.3 (1 to 24)	4.3 +/- 5.4 (1 to 21)	2.6 +/- 2.6 (1 to 10)	4.9 +/- 5.3 (1 to 24)
brainVol_ml Mean +/- std (range)	1071.19 +/-110.84 (881.47 to 1307.42)	1103.61 +/-105.8 (925.87 to 1305.02)	1132.08 +/-84.26 (963.88 to 1360.2)	1104.92 +/- 101.29 (881.47 to 1360.2)
NAWMVol_ml Mean +/- std (range)	530.75 +/-57.19 (432.54 to 649.13)	546.01 +/-54.23 (446.86 to 655.42)	526.05 +/-61.14 (421.07 to 701.99)	532.76 +/-57.96 (421.07 to 701.99)
WMHVol_ml Mean +/- std (range)	10.36 +/-8.56 (1.3 to 34.58)	13.95 +/-25.87 (0.64 to 119.92)	82.94 +/-57.22 (3.75 to 220.75)	41.46 +/-52.61 (0.64 to 220.75)
Microbleeds total N	26	108	204	338
Lacunae total N	93	60	191	344
Perivascular spaces score median score	1	1	4	1

Table 2. Patient characteristics by type of SVD.

Demographic	Sporadic	CADASIL	Difference	95% CI	P value
Male %	57.8	50.0	7.78	(-14.8 to 30.3)	0.50
Age yrs (mean)	64.2	52.9	11.3	(6.24 to 16.4)	<0.001
Diabetes %	20.0	3.13	16.9	(3.72 to 30.0)	0.030
Hypertension %	77.8	34.4	43.4	(22.9 to 63.9)	0.00013
Hyperlipidaemia %	73.3	40.6	32.7	(11.3 to 54.1)	0.0039
Current & ex-smoker %	51.1	56.3	-5.14	(-27.7 to 17.4)	0.66
Alcohol use %	68.9	75.0	-6.11	(-26.3 to 14.1)	0.56

Outcome Measures:

Table 3. BBB leakage values by site and whole group

Site	Edinburgh Mean +/- std (range)	Maastricht Mean +/- std (range)	Munich Mean +/- std (range)	All Mean +/- std (range)
BBB leak (PS) deep grey matter	1.05 +/- 1.62 (-3.38 to 4.70)	1.07 +/- 0.817 (-0.311 to 2.42)	0.361 +/- 1.01 (-2.27 to 2.34)	0.771 +/- 1.23 (-3.38 to 4.70)
BBB leak (PS) NA white matter	0.380 +/- 0.863 (-2.09 to 2.21)	0.634 +/- 1.08 (-1.07 to 2.19)	-0.583 +/- 0.906 (-2.14 to 0.971)	0.0507 +/- 1.08 (-2.14 to 2.21)
BBB leak (PS) WMH	0.966 +/- 1.35 (-2.14 to 3.31)	0.800 +/- 0.966 (-0.970 to 2.70)	0.307 +/- 0.827 (-2.08 to 1.83)	0.651 +/- 1.08 (-2.14 to 3.31)

Table 4 Cerebrovascular reactivity and vascular pulsatility by site and whole group

Site	Edinburgh Mean +/- std (range)	Maastricht Mean +/- std (range)	Munich Mean +/- std (range)	All Mean +/- std (range)
Deep Grey matter CVR	0.114 +/- 0.0862 (-0.182 to 0.237)	0.160 +/- 0.0394 (0.0846 to 0.212)	0.121 +/- 0.0709 (-0.101 to 0.220)	0.127 +/- 0.0724 (-0.182 to 0.237)
Normal appearing white matter CVR	0.0294 +/- 0.0450 (-0.128 to 0.0861)	0.0429 +/- 0.0126 (0.0299 to 0.0754)	0.0352 +/- 0.0356 (-0.0578 to 0.0934)	0.0349 +/- 0.0357 (-0.128 to 0.0934)
WMH CVR	0.0187 +/- 0.0926 (-0.284 to 0.109)	0.0267 +/- 0.0655 (-0.0763 to 0.167)	0.0212 +/- 0.0560 (-0.138 to 0.114)	0.0216 +/- 0.0707 (-0.284 to 0.167)
Arterial pulsatility	1.372 +/- 0.480 (0.687 to 2.898)	1.062 +/- 0.208 (0.556 to 1.408)	1.272 +/- 0.249 (0.893 to 2.038)	1.248 +/- 0.349 (0.556 to 2.898)
Superior sagittal sinus pulsatility	0.555 +/- 0.178 (0.207 to 0.949)	0.458 +/- 0.176 (0.218 to 0.705)	0.414 +/- 0.150 (0.097 to 0.761)	0.470 +/- 0.175 (0.097 to 0.949)
CSF stroke vol at foramen magnum	0.659 +/- 0.290 (0.236 to 1.644)	0.497 +/- 0.232 (0.096 to 0.964)	0.554 +/- 0.195 (0.110 to 0.850)	0.572 +/- 0.244 (0.096 to 1.644)

Table 5. Blood pressures during the MRI visit (Pre-CVR) and while at home (amb) assessed using pulse wave analysis.

Institute	Edinburgh mean +/-std (range)	Maastricht mean +/-std (range)	Munich mean +/-std (range)	All sites mean +/-std (range)
Pre-CVR diastolic	83.5 +/- 14.0 (50 to 107)	91.0 +/- 9.4 (76 to 110)	76.7 +/- 9.5 (60 to 90)	82.2 +/- 12.3 (50 to 110)
Pre-CVR systolic	159.0 +/- 27.0 (90 to 200)	153.6 +/- 17.4 (130 to 199)	127.7 +/- 13.9 (110 to 160)	143.6 +/- 24.3 (90 to 200)
Systolic BPV	0.0804 +/- 0.0242 (0.0340 to 0.1347)	0.0842 +/- 0.0244 (0.0432 to 0.1493)	0.0651 +/- 0.0169 (0.0321 to 0.1063)	0.0750 +/- 0.0229 (0.0321 to 0.1493)
Diastolic BPV	0.0806 +/- 0.0195 (0.0514 to 0.1215)	0.0801 +/- 0.0241 (0.0488 to 0.1444)	0.0796 +/- 0.0266 (0.0362 to 0.1400)	0.0801 +/- 0.0235 (0.0362 to 0.1444)
MAP BPV	0.0710 +/- 0.0217 (0.0386 to 0.1094)	0.0751 +/- 0.0221 (0.0449 to 0.1339)	0.0655 +/- 0.0191 (0.0321 to 0.1400)	0.0698 +/- 0.0209 (0.0321 to 0.1339)
Mean amb systolic BP	130.7 +/- 11.1 (106.1 to 149.2)	129.7 +/- 12.4 (105.7 to 157.1)	117.5 +/- 9.1 (100.7 to 139.9)	125 +/- 12.3 (100.7 to 157.1)
Mean amb diastolic BP	80.8 +/- 8.5 (62.4 to 93.8)	85.8 +/- 9.4 (73.6 to 105.4)	76.7 +/- 8.9 (60.6 to 90.2)	80.4 +/- 9.5 (60.6 to 105.4)
Mean amb MAP BP	97.5 +/- 8.4 (81.9 to 111.3)	100.4 +/- 9.6 (85.9 to 122.6)	90.3 +/- 8.2 (74.0 to 104.6)	95.2 +/- 9.6 (74.0 to 122.6)

BPV = blood pressure variability; MAP = mean arterial pressure;

Table 6. Differences in BP between sporadic and CADASIL

Blood pressure	Sporadic mean +/- std	CADASIL mean +/- std	Difference	95% CI*	P value*
Pre-CVR diastolic	86.7 +/- 12.7	76.7 +/- 9.5	10.0	4.78 to 15.3	0.0003
Pre-CVR systolic	156.7 +/- 23.2	127.7 +/- 13.9	29.0	20.1 to 37.9	<0.0001
Systolic BPV	0.0821 +/- 0.0241	0.0651 +/- 0.0169	0.0171	0.00776 to 0.0264	0.0005
Diastolic BPV	0.0804 +/- 0.0214	0.0796 +/- 0.0266	0.000773	-0.0106 to 0.0122	0.89
MAP BPV	0.0728 +/- 0.0217	0.0655 +/- 0.0191	0.00729	-0.00203 to 0.0166	0.12
Mean amb systolic BP	130.3 +/- 11.6	117.5 +/- 9.10	12.7	8.04 to 17.4	<0.0001
Mean amb diastolic BP	83.0 +/- 9.13	76.7 +/- 8.85	6.38	2.24 to 10.5	0.0030
Mean amb MAP BP	98.8 +/- 9.01	90.3 +/- 8.21	8.50	4.56 to 12.4	<0.0001

Adverse Events: There were no adverse events associated with this study.