

Table 1: Baseline characteristics of case and control subjects enrolled in the three studies.

	ACUTE CEREBRO-CARDIOVASCULAR OUTCOMES			ALL-CAUSE HOSPITALIZATIONS			ALL-CAUSE MORTALITY		
	Case patients	Controls	p-value *	Case patients	Controls	p-value *	Case patients	Controls	p-value *
Number	25,204	55,325		19,237	20,102		17,996	45,431	
Baseline characteristics									
Men	12,279 (48.72)	27,416 (49.55)	MV	10,008 (52.02)	10,545 (52.46)	MV	8,289 (46.06)	22,026 (48.48)	MV
Age (years)									
65-69	3,366 (13.36)	9,042 (16.34)	MV	3,128 (16.26)	3,269 (16.26)	MV	1,224 (6.80)	4,734 (10.42)	MV
70-74	5,283 (20.96)	12,657 (22.88)		4,450 (23.13)	4,695 (23.36)		2,305 (12.81)	8,633 (19.00)	
75-79	6,536 (25.93)	14,046 (25.39)		4,692 (24.39)	4,874 (24.25)		4,073 (22.63)	12,702 (27.96)	
80-84	5,669 (22.49)	11,453 (20.70)		3,987 (20.73)	4,177 (20.78)		5,181 (28.79)	11,579 (25.49)	
>84	4,350 (17.26)	8,127 (14.69)		2,980 (15.49)	3,087 (15.36)		5,213	7,783 (17.31)	
Geographical area									
Region of Lazio	6,300 (25.00)	14,066 (16,728)	MV	3,404 (17.70)	3,537 (17.60)	MV	2,348 (13.05)	5,265 (11.59)	MV
Region of Lombardy	3,799 (15.07)	8,951 (16.18)		10,002 (51.99)	10,315 (51.31)		10,110 (56.18)	26,137 (57.53)	
Region of Tuscany	13,955 (55.37)	30,109 (54.42)		5,057 (26.29)	5,352 (26.62)		4,729 (26.28)	12,124 (26.69)	
LHA of Caserta	778 (3.09)	1,601 (2.89)		609 (3.17)	725 (3.61)		595 (3.31)	1,468 (3.23)	
LHA of Treviso	598 (1.08)	372 (1.48)		165 (0.86)	173 (0.86)		214 (1.19)	437 (0.96)	
CV disease at entry									
Ischemic heart disease	10,117 (40.14)	23,200 (41.93)	0.000	7,598 (39.50)	7,703 (38.32)	0.017	6,729 (34.89)	18,916 (41.46)	0.000
Heart failure	8,177 (32.44)	10,447 (18.88)	0.000	4,940 (25.68)	3,322 (16.53)	0.000	6,144 (34.14)	9,742 (21.44)	0.000
Cardiac arrhythmia	8,852 (35.12)	13,982 (25.27)	0.000	5,689 (29.57)	5,412 (26.92)	0.000	5,359 (29.78)	13,033 (28.69)	0.006
Stroke	8,096 (32.12)	22,029 (39.82)	0.000	7,117 (37.00)	8,623 (42.90)	0.000	7,105 (39.48)	17,269 (38.01)	0.001
CV procedures									

Coronary Artery Bypass Surgery	2,626 (10.42)	4,522 (8.17)	0.000	1,573 (8.18)	1,519 (7.56)	0.022	1,410 (7.84)	4,053 (8.92)	0.000
Percutaneous Transluminal Coronary Angioplasty	4,512 (17.90)	10,547 (19.06)	0.000	3,472 (18.05)	3,451 (17.17)	0.022	2,149 (11.94)	8,646 (19.03)	0.000
Cerebral Revascularization	1,751 (6.95)	3,530 (6.38)	0.003	1,300 (6.76)	1,393 (6.93)	n.s.	1,019 (5.66)	3,132 (6.89)	0.000
Other heart surgery procedures	2,589 (10.27)	2,473 (4.47)	0.000	1,265 (6.58)	821 (4.08)	0.000	1,005 (5.58)	2,737 (6.02)	0.034
Charlson comorbidity index (CCI) score									
0	2,459 (9.76)	8,776 (15.86)	0.000	2,390 (12.42)	3,765 (18.73)	0.000	842 (4.68)	6,778 (14.92)	0.000
1-2	10,552 (41.87)	32,006 (57.85)		9,551 (49.65)	12,861 (63.98)		6,869 (38.17)	25,256 (55.59)	
≥3	12,193 (48.38)	14,543 (26.29)		7,296 (37.93)	3,476 (17.29)		10,285 (57.15)	13,397 (29.49)	
Treatment with CCBs before entry in the study									
Use of CCBs in the 6 months before entry	16,649 (66.06)	36,013 (65.09)	0.008	13,021 (67.69)	13,348 (66.40)	0.007	11,775 (65.43)	29,441 (64.80)	n.s.
Treatment with CCBs during follow-up									
Current use of CCBs	16,088 (63.83)	37,251 (67.33)	0.000	13,672 (71.07)	14,726 (73.26)	0.000	7,008 (38.94)	27,946 (61.51)	0.000
Long-acting DHPs	13,504 (53.58)	32,236 (58.27)	0.000	11,607 (60.34)	12,962 (64.48)	0.000	5,922 (32.91)	24,214 (53.30)	0.000
Short-acting DHPs	129 (0.51)	150 (0.27)	0.000	94 (0.49)	56 (0.28)	0.002	50 (0.28)	120 (0.26)	n.s.
Long-acting n-DHPs	1,739 (6.90)	3,549 (6.41)	0.010	1,423 (7.40)	1,251 (6.22)	0.000	664 (3.69)	2,589 (5.70)	0.000
Short-acting n-DHPs	1,080 (4.29)	1,779 (3.22)	0.000	784 (4.08)	616 (3.06)	0.000	493 (2.74)	1,372 (3.02)	n.s.
Other antihypertensive treatments at index date									
Anti-hypertensive drugs (ATC C02)	2,677 (10.62)	4,300 (7.77)	0.000	1,870 (9.72)	1,524 (7.58)	0.000	1,096 (6.09)	3,536 (7.78)	0.000
Diuretics (ATC C03)	10,288 (40.82)	13,567 (24.52)	0.000	6,089 (31.65)	4,245 (21.12)	0.000	7,619 (42.34)	12,598 (27.73)	0.000

Beta-blockers (ATC C07)	5,771 (22.90)	12,494 (22.58)	n.s.	4,375 (22.74)	4,672 (23.24)	n.s.	1,820 (10.11)	10,183 (22.41)	0.000
Agents acting on the Renin-Angiotensin System (ATC C09)	17,273 (68.53)	38,251 (69.14)	n.s.	13,566 (70.52)	14,500 (72.13)	0.000	8,011 (44.52)	31,153 (68.57)	0.000

*p-value from chi-square test

CCB=Calcium Channel Blockers; DHPs= Dihydropyridines; n-DHPs=non- Dihydropyridines; MV=matching variable; LHA=Local Health Authority