


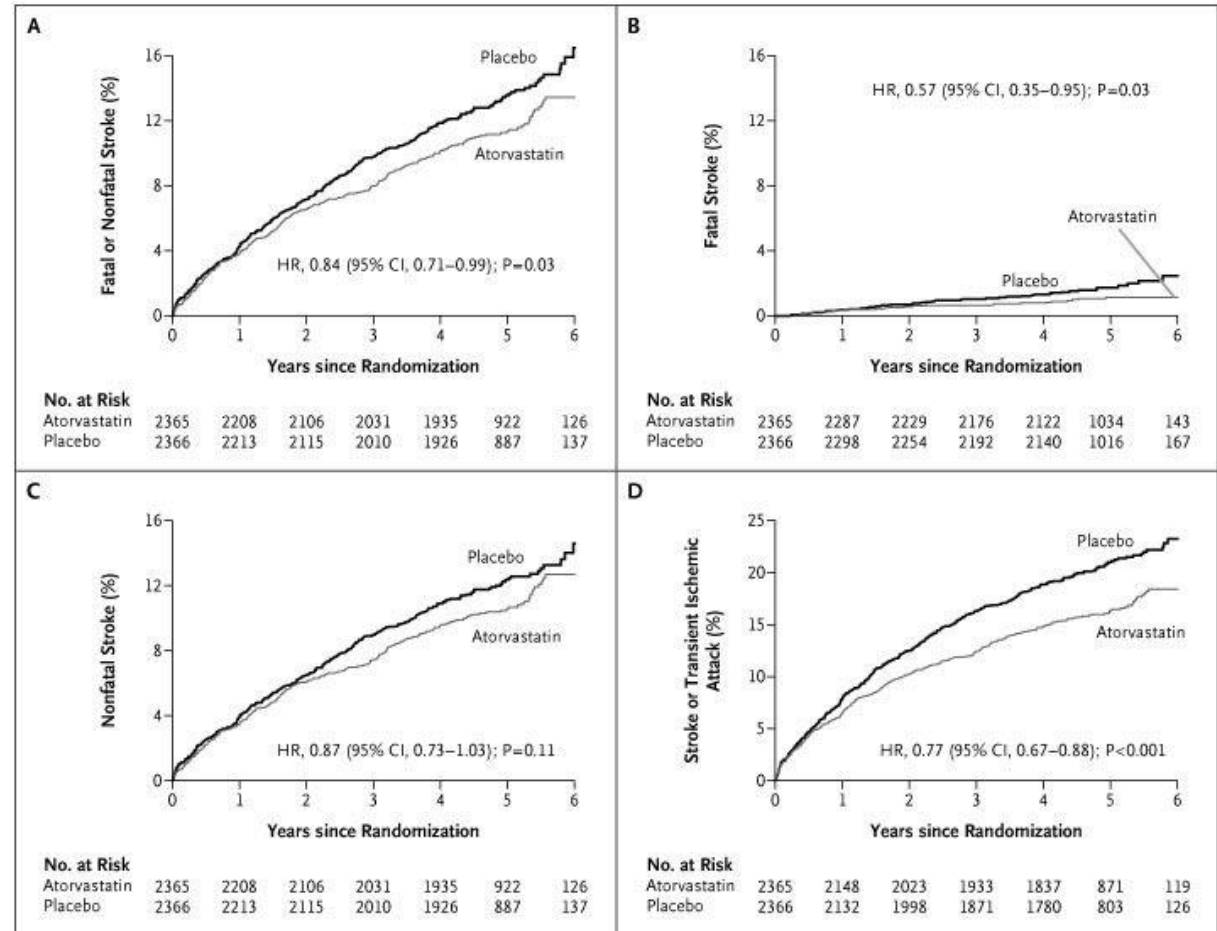
Il trattamento con
statine nei pazienti
con ictus embolico di
origine indeterminata

Background

- The term ESUS (embolic stroke of undetermined source) is used to describe patients with ischemic stroke for whom the source of embolism remains undetected despite recommended investigation.
 - ESUS is also a very heterogeneous population in terms of the underlying stroke mechanism as it may be caused by atherosclerotic plaques of low degree of stenosis, covert atrial fibrillation, patent foramen ovale, left ventricular disease, and others, which frequently overlap.
 - ESUS comprises about 17% of all ischemic stroke patients and have a considerable risk for stroke recurrence and cardiovascular events.
- 

SPARCL trial

High-dose atorvastatin reduced the risk for stroke recurrence in stroke patients without atrial fibrillation or other cardiac sources of embolism.

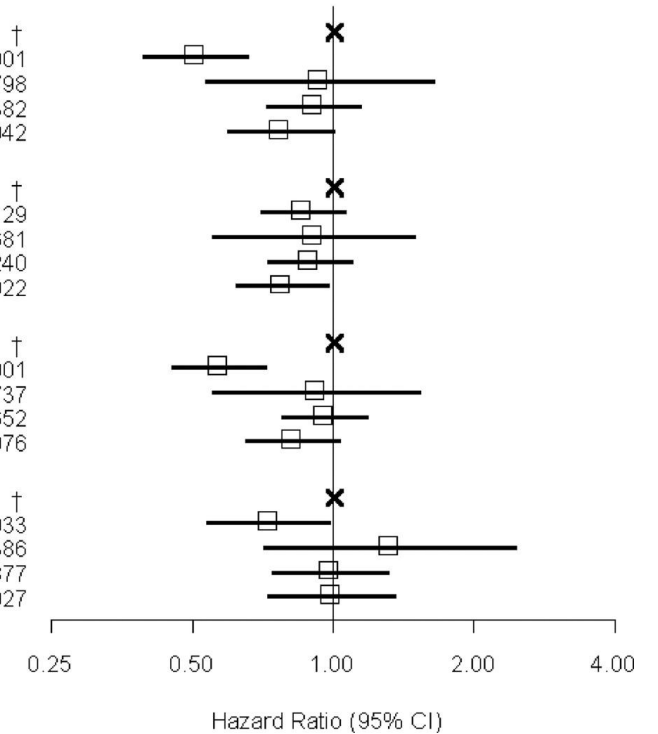


SPARCL trial subanalysis

High-dose atorvastatin was similarly efficacious in preventing strokes and other cardiovascular events, irrespective of baseline ischemic stroke subtype

Stroke 40(4):1405–1409

	Events (%)	HR (95% CI)	n	P Value
Stroke				
Large Vessel	119 (15.9)		†	†
TIA	120 (8.2)	0.50 (0.39, 0.65)		<.001
Hemorrhagic	14 (15.1)	0.93 (0.53, 1.62)		0.798
Small Vessel	202 (14.3)	0.90 (0.72, 1.13)		0.382
Unknown	121 (11.9)	0.77 (0.60, 0.99)		0.042
Stroke or TIA				
Large Vessel	154 (20.6)		†	†
TIA	257 (17.6)	0.86 (0.70, 1.05)		0.129
Hemorrhagic	18 (19.4)	0.90 (0.55, 1.47)		0.681
Small Vessel	262 (18.6)	0.89 (0.73, 1.08)		0.240
Unknown	160 (15.7)	0.77 (0.62, 0.96)		0.022
Major Cardiovascular Event				
Large Vessel	144 (19.2)		†	†
TIA	164 (11.2)	0.57 (0.45, 0.71)		<.001
Hemorrhagic	17 (18.3)	0.92 (0.55, 1.52)		0.737
Small Vessel	261 (18.5)	0.95 (0.78, 1.17)		0.652
Unknown	155 (15.2)	0.81 (0.65, 1.02)		0.076
Death				
Large Vessel	75 (10.0)		†	†
TIA	106 (7.3)	0.72 (0.54, 0.97)		0.033
Hemorrhagic	12 (12.9)	1.31 (0.71, 2.43)		0.386
Small Vessel	141 (10.0)	0.98 (0.74, 1.30)		0.877
Unknown	92 (9.0)	0.99 (0.72, 1.34)		0.927



Statin treatment and outcomes after embolic stroke of undetermined source

Dimitrios Sagris¹  · Kalliopi Perlepe¹ · Ioannis Leventis¹ · Stamatia Samara² · Efstathios Manios³ · Eleni Korompoki³ · Konstantinos Makaritsis¹ · Haralampos Milionis⁴ · Konstantinos Vemmos³ · George Ntaios¹

Aim of the study

To assess whether the rates of stroke recurrence, major cardiovascular events, and death in patients with ESUS differ between those receiving statin therapy and those not.

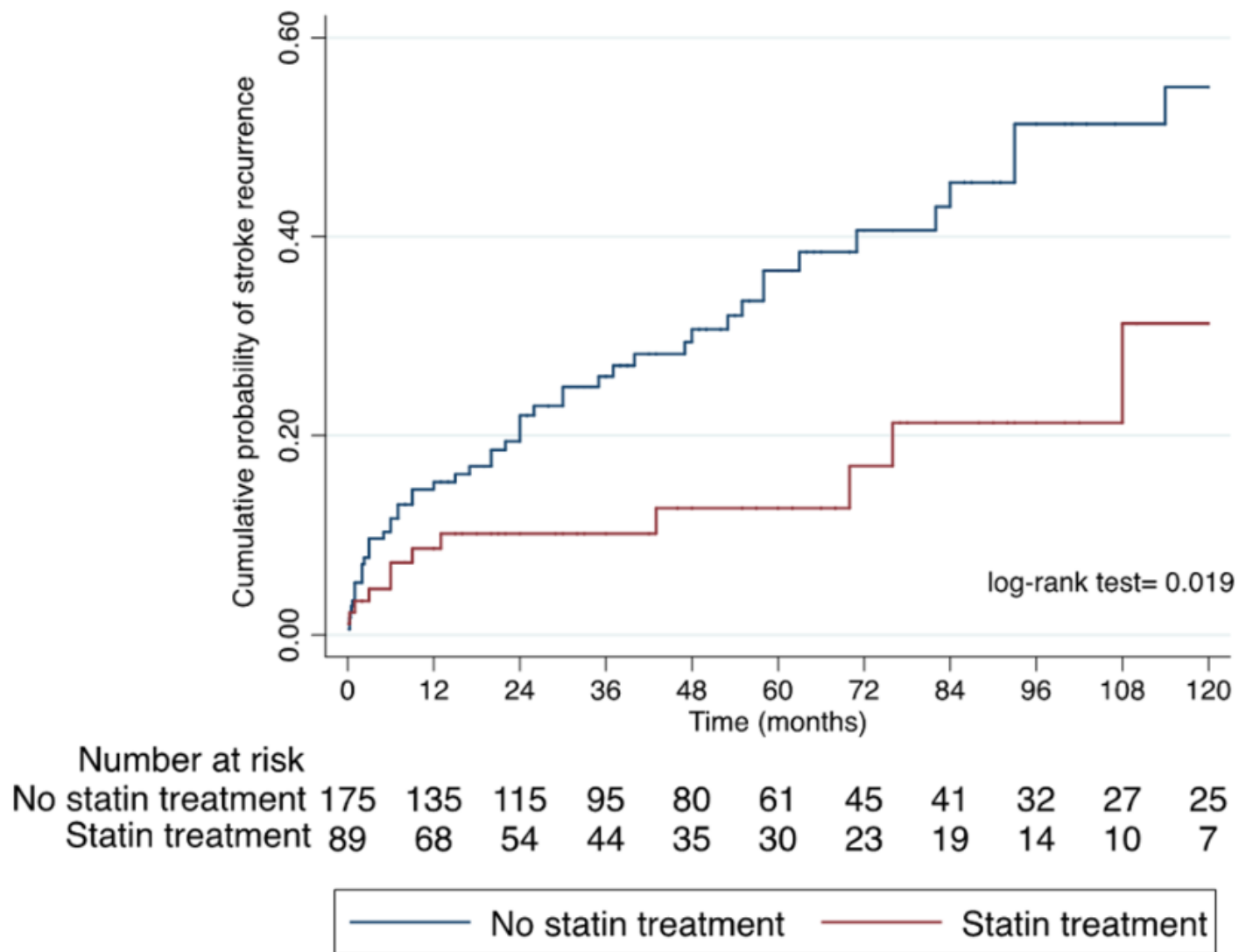
Methods

- Consecutive ESUS patients in the Athens Stroke Registry were prospectively followed-up to 10 years for stroke recurrence, MACE, and death.
- The Nelson–Aalen estimator was used to estimate the cumulative probability by statin allocation at discharge and cox-regression analyses to investigate whether statin at discharge was a predictor of outcomes.

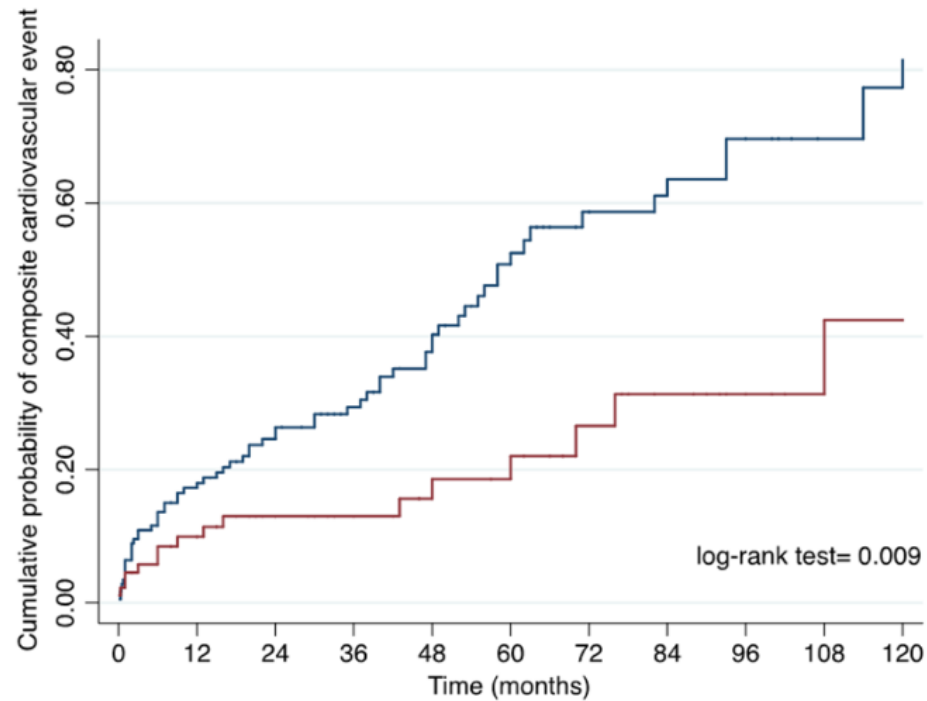
Baseline characteristics of patients with Embolic Stroke of Undetermined Source (ESUS)

Patient characteristics	All ESUS patients discharged (<i>n</i> = 264)	Statin at discharge (<i>n</i> = 89)	No statin at discharge (<i>n</i> = 175)	<i>p</i> value
Age (median ± IQR)	68 (58–76)	67 (58–74)	68 (58–76)	0.765
Female, <i>n</i> (%)	94 (35.6)	29 (32.6)	65 (37.1)	0.465
NIHSS on admission (median ± IQR)	4 (2–12)	6 (3–10)	4 (2–14)	0.346
Smoking, <i>n</i> (%)	79 (29.9)	22 (24.7)	57 (32.6)	0.188
Hypertension, <i>n</i> (%)	167 (63.3)	62 (69.7)	105 (60)	0.124
Diabetes, <i>n</i> (%)	63 (23.9)	23 (25.8)	40 (22.9)	0.591
Previous diagnosis of dyslipidemia, <i>n</i> (%)	136 (51.5)	65 (73)	71 (40.6)	<0.001
Coronary artery disease, <i>n</i> (%)	61 (23.1)	24 (27)	37 (21.1)	0.289
Heart failure, <i>n</i> (%)	20 (7.6)	7 (7.9)	13 (7.43)	0.899
Prior TIA, <i>n</i> (%)	25 (9.47)	10 (11.24)	15 (8.57)	0.485
Obesity, <i>n</i> (%)	65 (24.6)	27 (30.3)	38 (21.7)	0.124
Statin pre-stroke treatment, <i>n</i> (%)	16 (6.1)	15 (16.9)	1 (0.57)	<0.001
Antiplatelet at discharge, <i>n</i> (%)	233 (88.3)	78 (87.6)	155 (88.6)	0.824
Anticoagulant at discharge, <i>n</i> (%)	33 (12.5)	14 (15.7)	19 (10.9)	0.258
ACE inhibitors/ARBs at discharge, <i>n</i> (%)	81 (30.7)	46 (51.7)	35 (20)	<0.001
Ca blockers at discharge, <i>n</i> (%)	37 (14)	14 (15.7)	23 (13.1)	0.567
Diuretics at discharge, <i>n</i> (%)	50 (18.9)	24 (27)	26 (14.9)	0.018
CHA ₂ DS ₂ -VASc (median ± IQR)	3 (1–4)	2 (1–4)	3 (1–4)	0.831
LDL-cholesterol, mg/dl (median ± IQR)	130 (105–160)	149 (107–175)	122 (104–151)	0.004

Cumulative probability of stroke recurrence by statin treatment in patients with ESUS

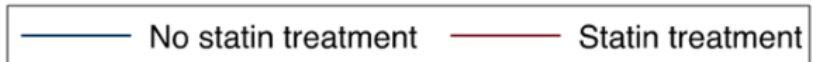


Cumulative probability of MACE by statin treatment in patients with ESUS

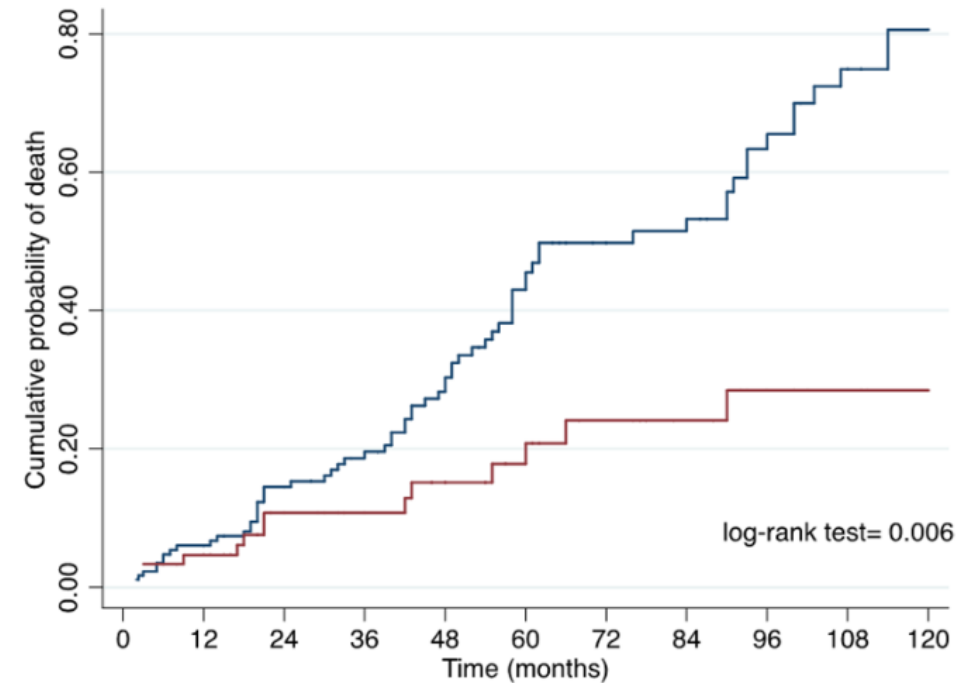


Number at risk

No statin treatment	175	133	112	94	78	59	43	40	31	26	24
Statin treatment	89	67	53	43	34	29	21	17	12	9	7

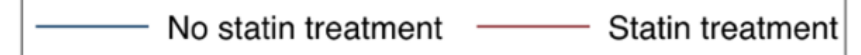


Cumulative probability of death by statin treatment in patients with ESUS



Number at risk

No statin treatment	175	153	133	116	98	79	61	57	46	39	33
Statin treatment	89	74	60	50	40	35	28	24	18	12	9



Multivariate Cox proportional hazard analyses showing the independent predictors of 10-years for stroke recurrence, MACE, and mortality

	10-year stroke recurrence	10-year MACE	10-year mortality
Statin treatment at discharge	0.48 (0.26–0.91)	0.48 (0.28–0.82)	0.50 (0.27–0.93)
Age	1.03 (1.01–1.05)	1.03 (1.01–1.05)	1.07 (1.04–1.09)
Male gender	–	–	0.50 (0.31–0.80)
Smoking	–	–	0.86 (0.47–1.54)
Hypertension	–	1.04 (0.62–1.73)	1.03 (0.59–1.80)
Diabetes	–	1.58 (0.98–2.55)	1.61 (1.00–2.59)
Previous diagnosis of dyslipidemia	–	–	0.65 (0.41–1.03)
Coronary artery disease	–	–	1.15 (0.66–2.01)
Heart failure	–	–	2.04 (0.99–4.19)
NIHSS on admission	–	–	1.04 (1.01–1.06)
Diuretics at discharge	–	–	1.67 (0.97–2.88)

Limitations

- Single-centre, retrospective nature.
- Potential unmeasured confounders.
- No assessment of socio-economic status, crossover treatment allocations and adherence to treatment.
- Unknown prescribed dose of statin or the achieved LDL-cholesterol levels.

Conclusions

- In conclusion, this study indicates that patients with ESUS discharged on a statin have lower rates of stroke recurrence, MACE and death compared to those not receiving statin therapy.
- Further research is needed to assess whether intensive LDL cholesterol-lowering further improve outcomes in the setting of ESUS.