4º CONGRESO AMAREVA

2025

27 y 28 de febrero

Auditorio Caja de Música
del Palacio de Cibeles

AMAREVA
ASOCIACIÓN MADRILEÑA DE RIESGO Y ENFERMEDAD VASCULAR

www.congreso2025.amareva.es

Objetivo LDL si hemorragia cerebral previa: ¿igual o no que para el resto?

Sebastián García Madrona
Unidad de Ictus. Servicio de Neurología
Hospital Universitario Ramón y Cajal.

Metabolismo de lípidos cerebral

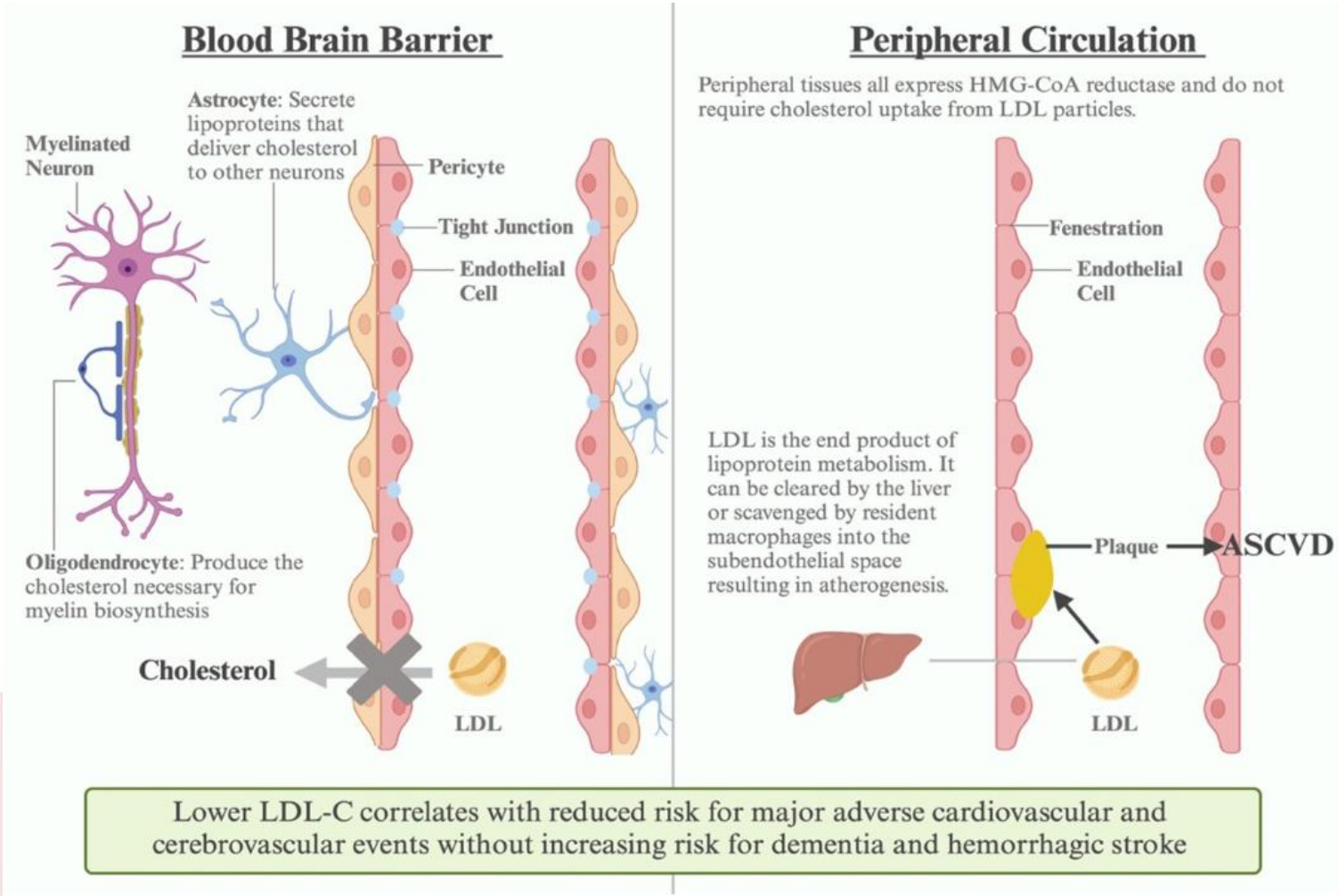
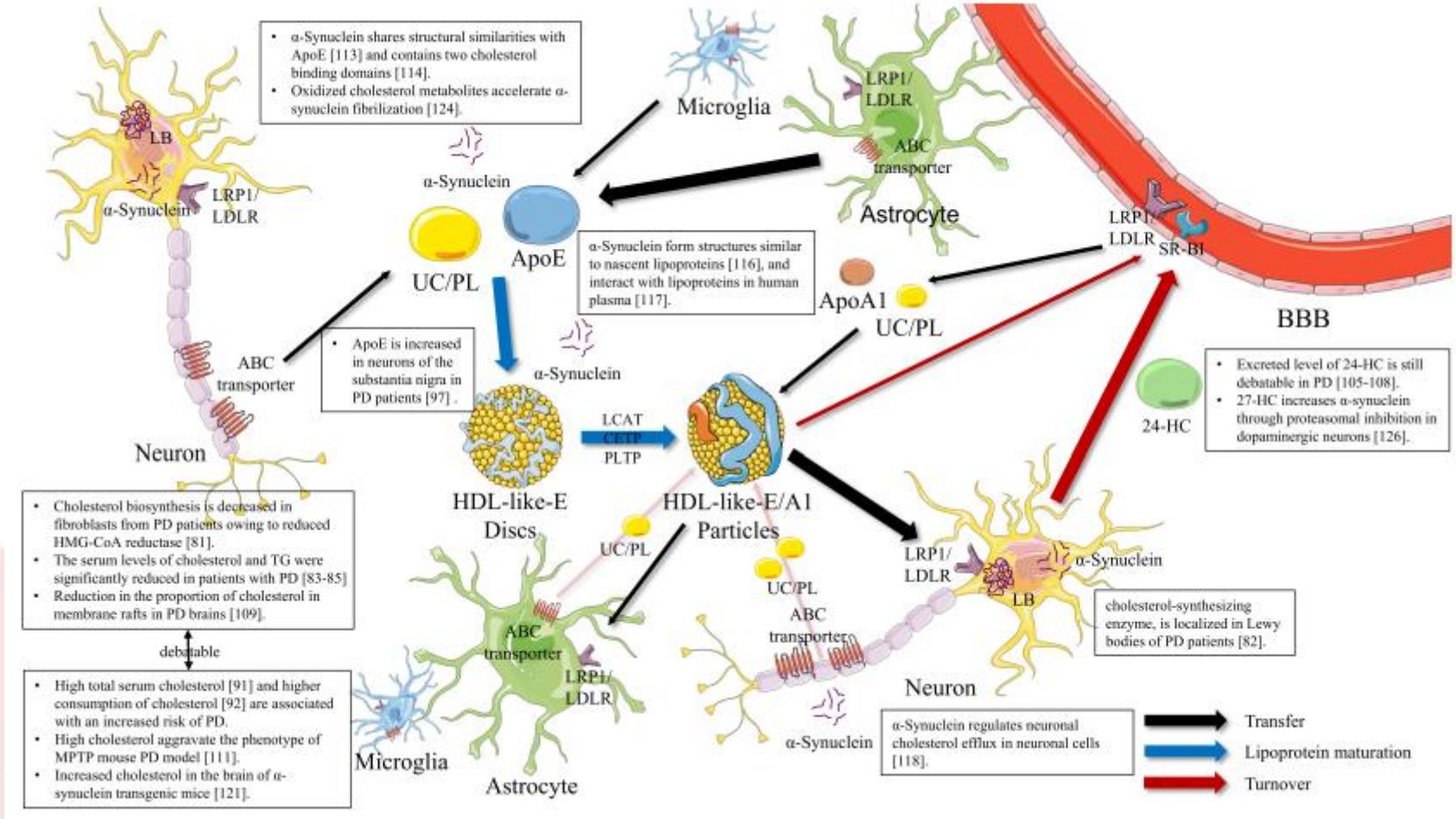


Figure 1: A Comparison of Transport of LDL-C in the Brain vs. the Peripheral Circulation. *Courtesy of Bimal T, Hirsh BJ, Saeed A, Toth*

Metabolismo de lípidos cerebral



Jin U, Park SJ, Park SM. Cholesterol Metabolism in the Brain and Its Association with Parkinson's Disease. Exp Neurobiol. 2019 Oct 31;28(5):554-567.

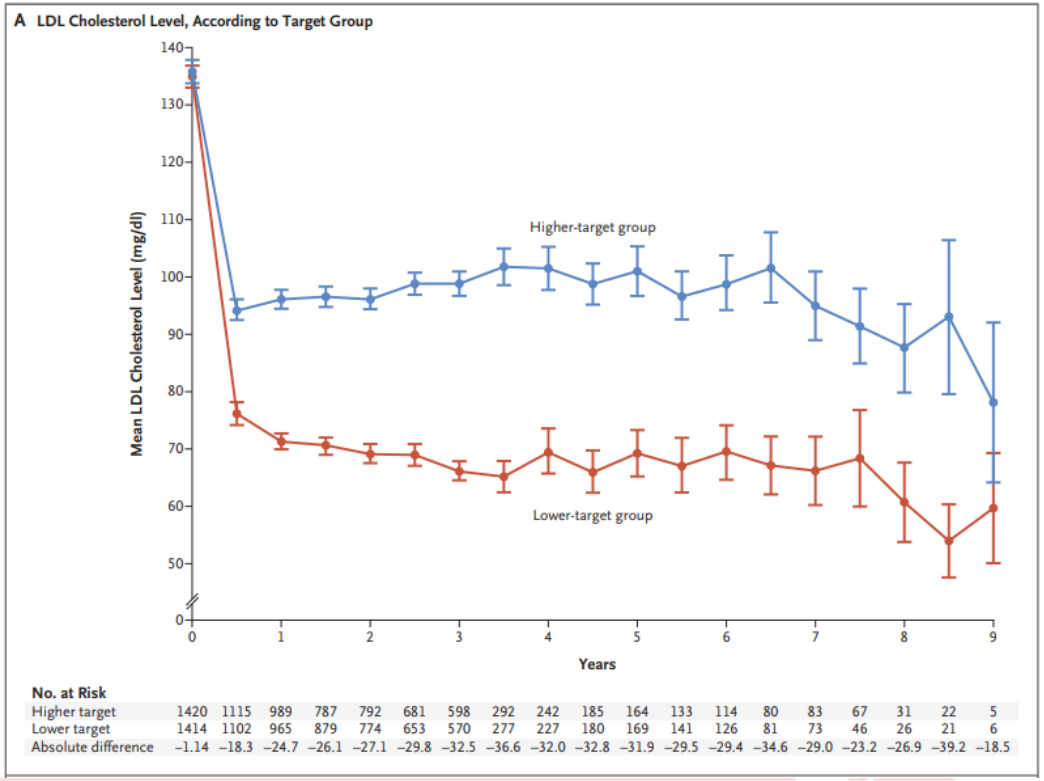
Objetivo c-LDL tras Ictus

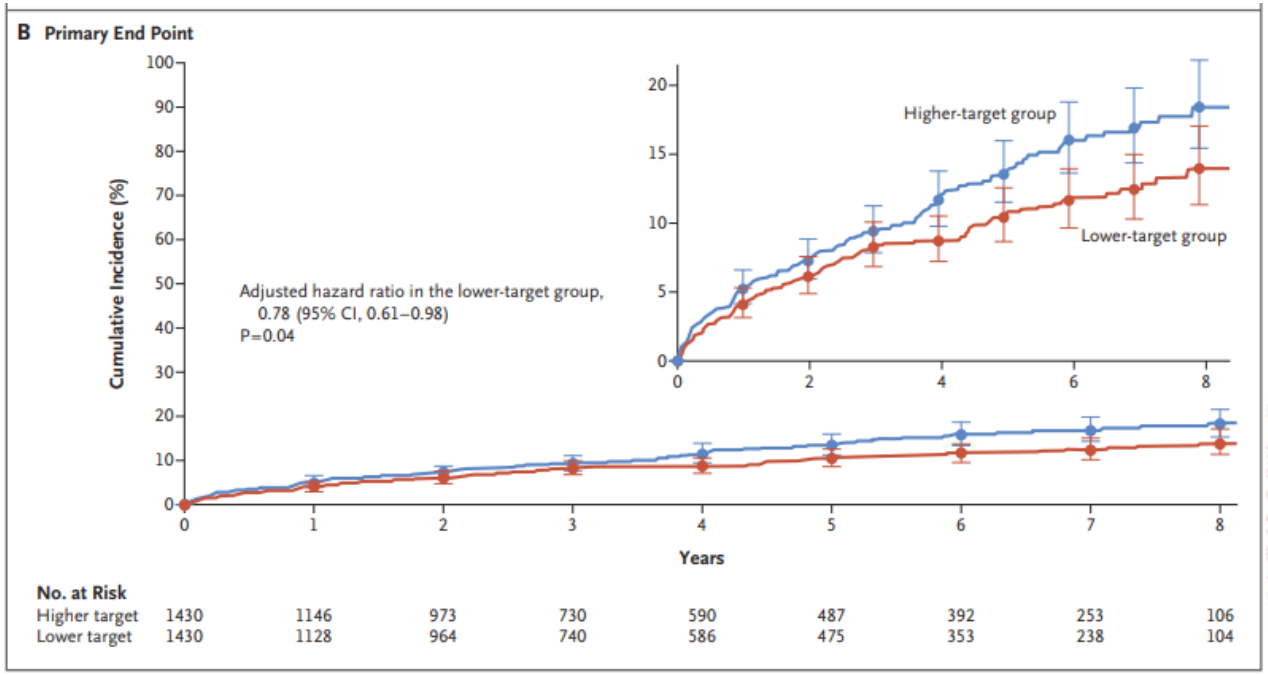
N= 2860. Seguimiento 3,5 años

Randomized Controlled Trial > N Engl J Med. 2020 Jan 2;382(1):9. doi: 10.1056/NEJMoa1910355. Epub 2019 Nov 18.

A Comparison of Two LDL Cholesterol Targets after Ischemic Stroke

Pierre Amarenco [1], Jong S Kim [1], Julien Labreuche [1], Hugo Charles [1], Jérémie Abtan [1],





Objetivo c-LDL tras Ictus

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Randomized Controlled Trial > N Engl J Med. 2020 Jan 2;382(1):9. doi: 10.1056/NEJMoa1910355. Epub 2019 Nov 18.

A Comparison of Two LDL Cholesterol Targets after Ischemic Stroke

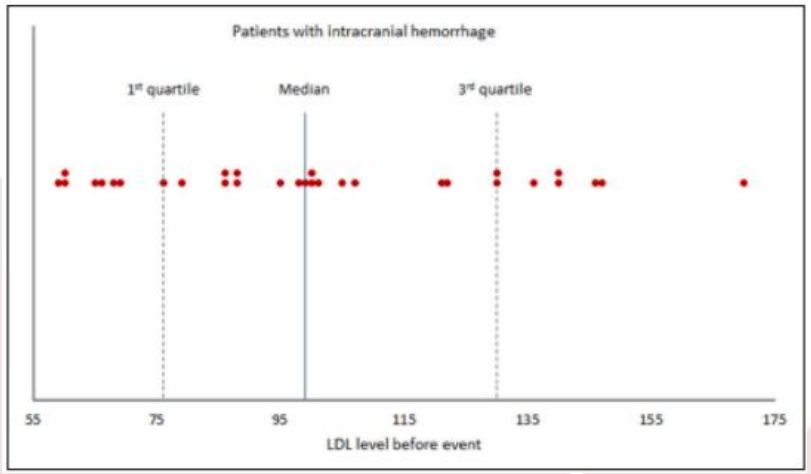
Pierre Amarenco [1], Jong S Kim [1], Julien Labreuche [1], Hugo Charles [1], Jérémie Abtan [1],

Intracranial hemorrhage — no. (%)	18 (1.3)	13 (0.9)	1.38 (0.68–2.82)
Newly diagnosed diabetes — no. (%)§	103 (7.2)	82 (5.7)	1.27 (0.95–1.70)

Randomized Controlled Trial > Stroke 2022 Feb;53(2):457-462. doi: 10.1161/STROKEAHA.121.035846. Epub 2021 Dec 29.

Intracranial Hemorrhage in the TST Trial

Pierre Amarenco [1], Jong S Kim [2], Julien Labreuche [3], Hugo Charles [1], Maurice Giroud [4],



Hemorragia intracraneal: 31

2,77/1000 pacientes/año (95% CI 1,68-3,86)

Characteristics	HR (95% CI)	*P* Value
Anticoagulant therapy	2.36 (1.00–5.62)	0.047
Dual antiplatelet therapy	1.12 (0.33–3.72)	0.86
Prehypertension	0.72 (0.33–1.58)	0.41
Stage 1 hypertension	1.45 (0.65–3.24)	0.36
Stage 2 hypertension	2.51 (1.01–6.31)	0.041
LDL-c		
≥90 mg/dL	1.00 (ref)	…
70–89 mg/dL	0.81 (0.28–2.30)	0.69
<70 mg/dL	0.84 (0.31–2.25)	0.73

Objetivo c-LDL

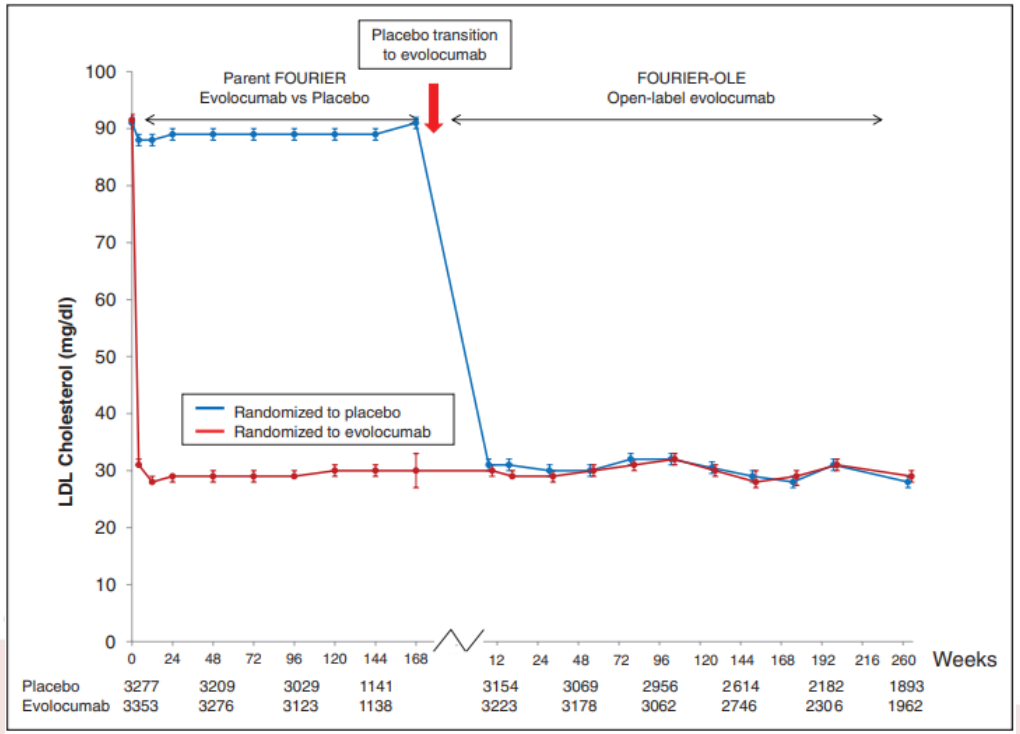
N= 6635. Seguimiento 4,8 años

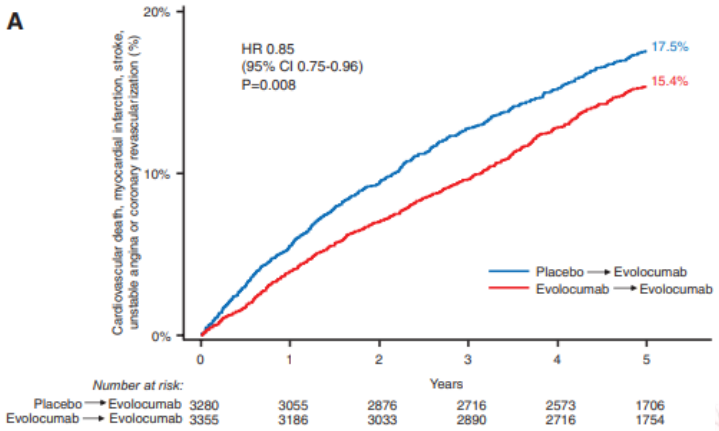
c-LDL medio 32 mg/dl (RIC 20-48 mg/dl)

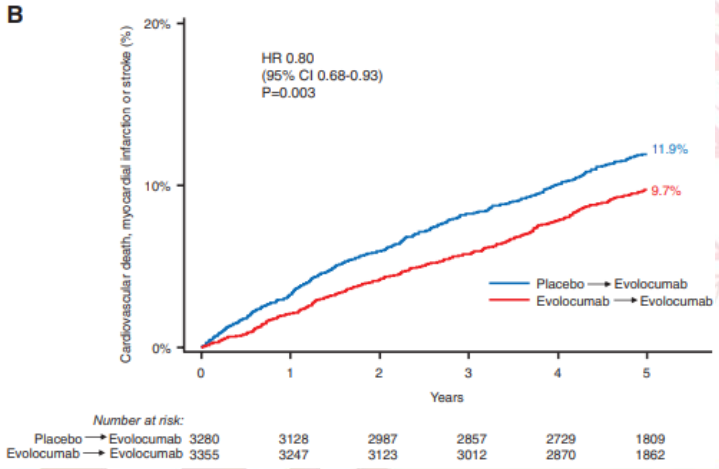
Randomized Controlled Trial > Circulation. 2022 Oct 11;146(15):1109-1119.
doi: 10.1161/CIRCULATIONAHA.122.061620. Epub 2022 Aug 29.

Long-Term Evolocumab in Patients With Established Atherosclerotic Cardiovascular Disease

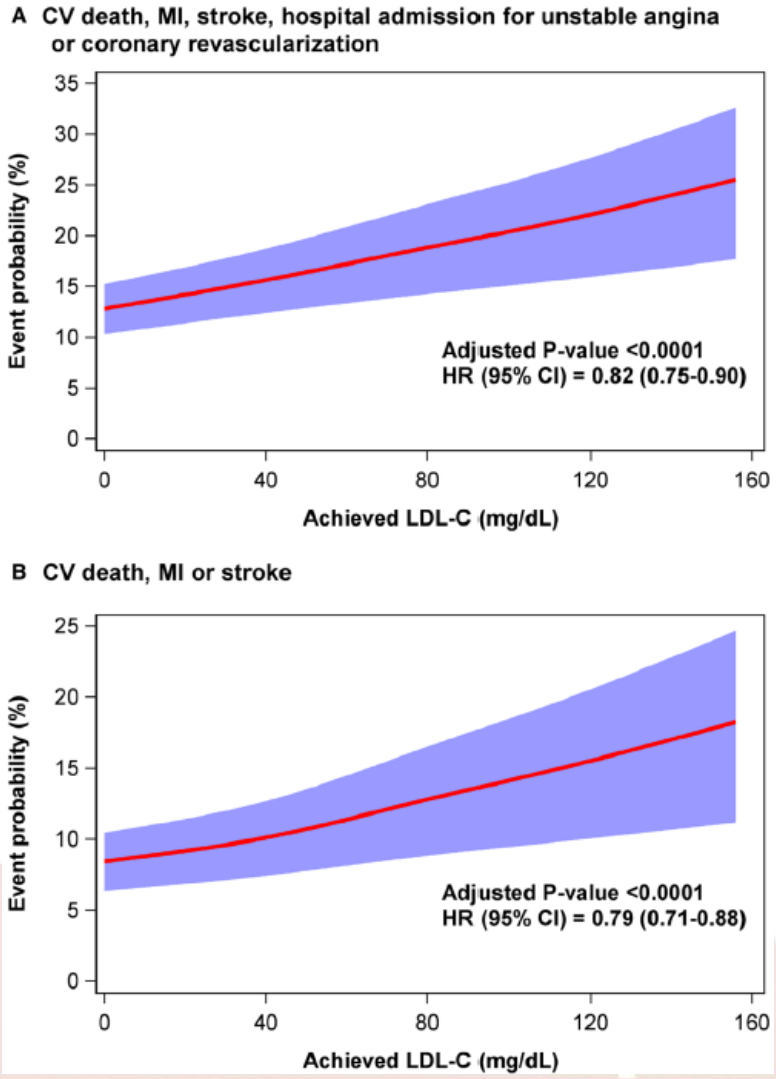
Michelle L O'Donoghue [1], Robert P Giugliano [1], Stephen D Wiviott [1], Dan Atar [2 3],







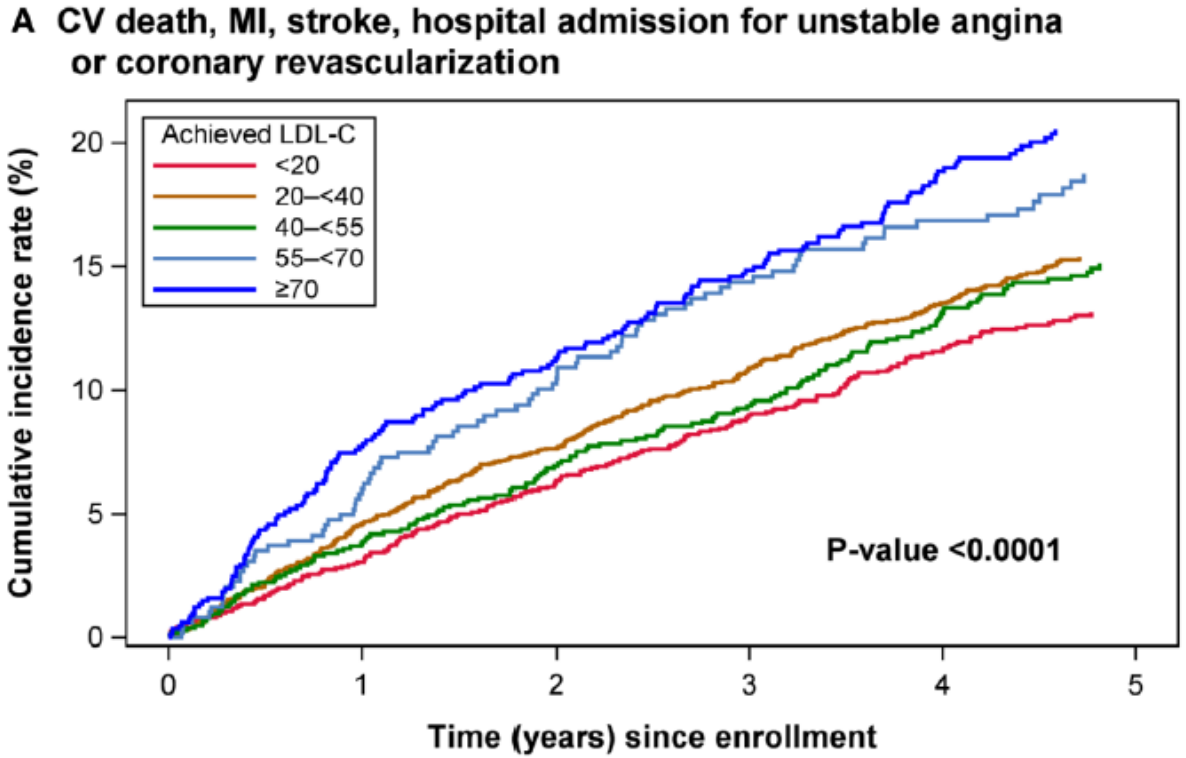
Objetivo c-LDL



Randomized Controlled Trial > Circulation. 2023 Apr 18;147(16):1192-1203.
doi: 10.1161/CIRCULATIONAHA.122.063399. Epub 2023 Feb 13.

Association Between Achieved Low-Density Lipoprotein Cholesterol Levels and Long-Term Cardiovascular and Safety Outcomes: An Analysis of FOURIER-OLE

Prakriti Gaba [1], Michelle L O'Donoghue [1], Jeong-Gun Park [1], Stephen D Wiviott [1], Dan Atar [2],



c-LDL < 55, ¿es seguro?

N= 6635. Seguimiento 4,8 años

C-LDL media: 32 mg/dl (RIC 20-48 mg/dl)

Randomized Controlled Trial > Circulation. 2023 Apr 18;147(16):1192-1203.
doi: 10.1161/CIRCULATIONAHA.122.063399. Epub 2023 Feb 13.

Association Between Achieved Low-Density Lipoprotein Cholesterol Levels and Long-Term Cardiovascular and Safety Outcomes: An Analysis of FOURIER-OLE

Prakriti Gaba [1], Michelle L O'Donoghue [1], Jeong-Gun Park [1], Stephen D Wiviott [1], Dan Atar [2],

Table 4. Safety Outcomes According to Achieved LDL-C Level in FOURIER-OLE

Safety outcomes	Achieved LDL-C level, mg/dL					Adjusted *P* trend
	<20 (n=1604)	20–<40 (n=2627)	40–<55 (n=1031)	55–<70 (n=486)	≥70 (n=811)	
Serious adverse events	12.15 (10.34, 14.27)	12.64 (10.89, 14.67)	12.65 (10.70, 14.97)	12.90 (10.63, 15.65)	12.18 (10.27, 14.43)	0.88
Neurocognitive events	0.50 (0.25, 0.98)	0.53 (0.28, 1.00)	0.53 (0.27, 1.07)	0.30 (0.12, 0.73)	0.43 (0.21, 0.89)	0.35
Cataract-related adverse events	0.82 (0.47, 1.44)	0.87 (0.51, 1.49)	0.91 (0.51, 1.62)	0.33 (0.14, 0.79)	0.64 (0.35, 1.20)	0.11
New or progressive malignancy	1.83 (1.26–2.66)	1.76 (1.23–2.50)	1.73 (1.17–2.57)	1.89 (1.21–2.96)	1.36 (0.89–2.10)	0.23
New-onset diabetes*	0.66 (0.32, 1.39)	0.52 (0.25, 1.05)	0.46 (0.20, 1.02)	0.45 (0.18, 1.12)	0.43 (0.20, 0.95)	0.13
Hemorrhagic stroke†	0.06 (0.02, 0.15)	0.09 (0.05, 0.17)	0.07 (0.02, 0.20)	–	0.06 (0.01, 0.23)	0.55
Muscle-related events	0.67 (0.38, 1.18)	0.62 (0.36, 1.07)	0.69 (0.38, 1.24)	0.76 (0.39, 1.46)	0.56 (0.30, 1.05)	0.84
Noncardiovascular death	1.33 (0.87, 2.04)	1.14 (0.76, 1.71)	1.65 (1.07, 2.56)	2.32 (1.46, 3.67)	1.49 (0.94, 2.36)	0.04
All-cause mortality	2.65 (1.98, 3.56)	2.87 (2.20, 3.76)	3.72 (2.77, 5.00)	4.30 (3.10, 5.98)	3.93 (2.92, 5.29)	0.0001

c-LDL < 55, ¿es seguro?

Meta-Analysis > J Stroke Cerebrovasc Dis. 2021 Apr;30(4):105655.
doi: 10.1016/j.jstrokecerebrovasdis.2021.105655. Epub 2021 Feb 9.

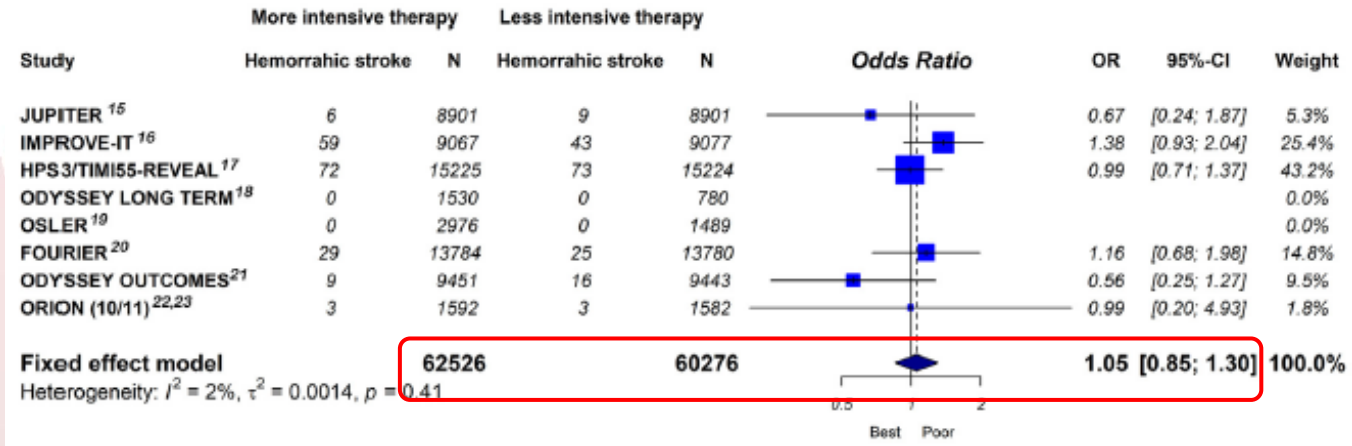
LDL-C Levels Below 55 mg/dl and Risk of Hemorrhagic Stroke: A Meta-Analysis

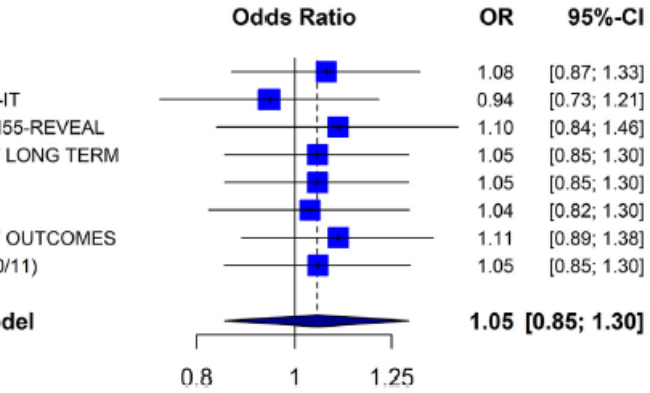
Walter Masson [1], Martín Lobo [2], Daniel Siniawski [3], Gerardo Masson [4], Augusto Lavalle-Cobo [5],

Table 1. *Characteristics of the studies included in the analysis.*

Study	More intensive arm	N	LDL-C achieved (mg/dL)*	Control arm	N	LDL-C achieved (mg/dL)*	Population	Median follow-Up (months)
JUPITER [5]	Rosuvastatin	8901	54	Placebo	8901	108	Primary prevention, LDL-C < 130 mg/dL and CRP ≥ 2 mg/dL	21
IMPROVE-IT [16]	Ezetimibe	9067	54	Placebo	9077	70	ACS	84
REVEAL [17]	Anacetrapib	15225	53	Placebo	15224	63	ASCVD	49
ODYSSEY LONG TERM [18]	Alirocumab	1530	48	Placebo	780	119	Patients with high CV risk	17.5
OSLER [19]	Evolocumab	2976	48	Placebo	1489	121	HeFH ASCVD High CV risk	12
FOURIER [20]	Evolocumab	13784	30	Placebo	13780	86	ASCVD	26
ODYSSEY OUTCOMES [21]	Alirocumab	9451	53	Placebo	9443	101	ACS	33.6
ORION (10/11) [22-23]	Inclisiran	1592	52	Placebo	1582	104	ASCVD or ASCVD equivalent	18

ACS: acute coronary syndrome; ASCVD: atherosclerosis cardiovascular disease; CRP: C-reactive protein; CV: cardiovascular risk; HeFH: heterocigotus familiar hypercholesterolemia.



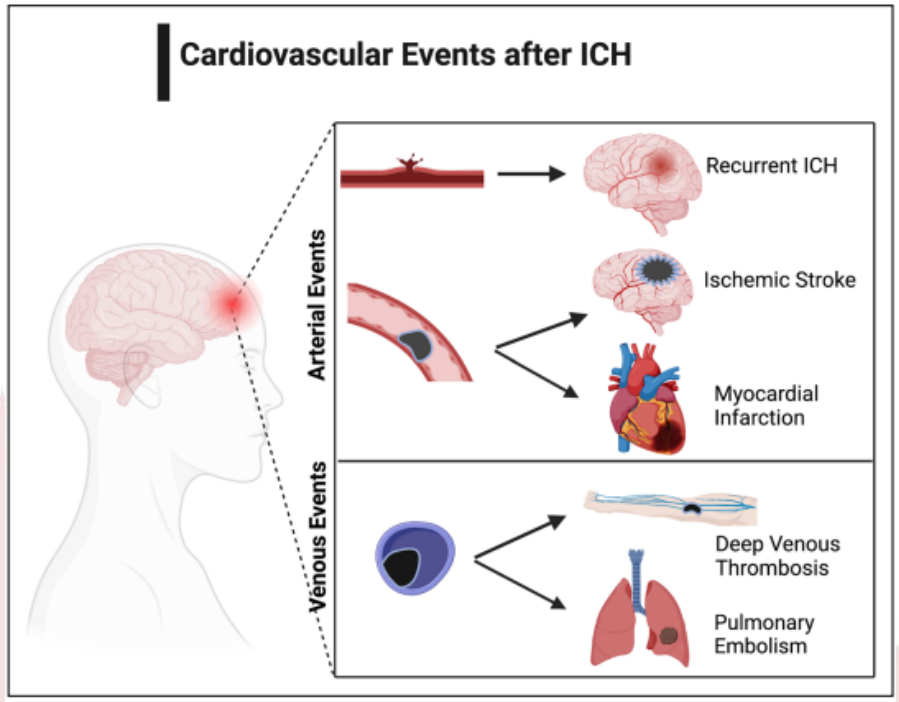


Si hemorragia intracraneal previa, ¿Objetivo LDL?

Review > Stroke. 2022 Jul;53(7):2131-2141. doi: 10.1161/STROKEAHA.122.036884. Epub 2022 Jun 8.

Cardiovascular Events After Intracerebral Hemorrhage

Linxin Li [1], Santosh B Murthy [2]



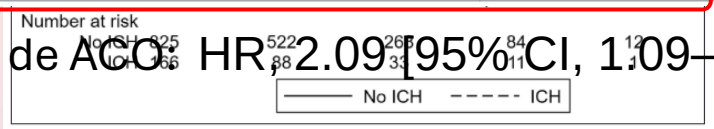
> Stroke. 2021 Dec;52(12):3883-3890. doi: 10.1161/STROKEAHA.120.032750. Epub 2021 Sep 9.

Long-Term Survival, Causes of Death, and Trends in 5-Year Mortality After Intracerebral Hemorrhage: The Tromsø Study

Maria Carlsson [1 2], Tom Wilsgaard [3], Stein Harald Johnsen [1 4], Liv-Hege Johnsen [1 5],

Supervivientes HIC vs controles (219 vs 1095)
Mortalidad vascular (22.9% vs 9.0%; *P*<0.001)

	HR (95% CI)
SBP, mm Hg	1.08 (0.94–1.24)
Diabetes (yes/no)	1.57 (0.93–2.64)
Daily smoking (yes/no)	1.59 (1.15–2.19)
Total cholesterol‡ (mmol/L) in subjects with	
No ICH	0.94 (0.81–1.10)
ICH	1.39 (1.04–1.86)
ICH‡ (yes/no) at total cholesterol level§, mmol/L	
4	0.69 (0.36–1.32)
6	1.22 (0.88–1.70)
8	2.17 (1.34–3.51)



Empleo de ACO: HR, 2.09 [95% CI, 1.09–4.00]

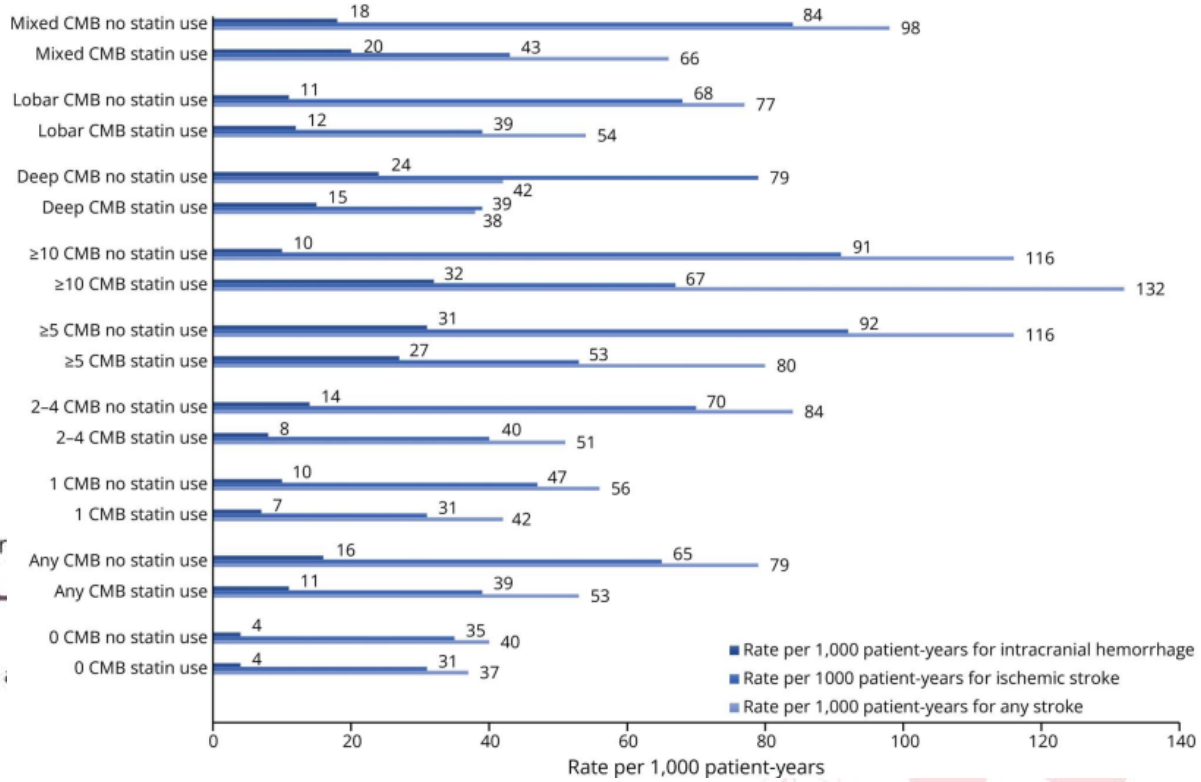
Microsangrados, ¿aumentan riesgo hemorragia?

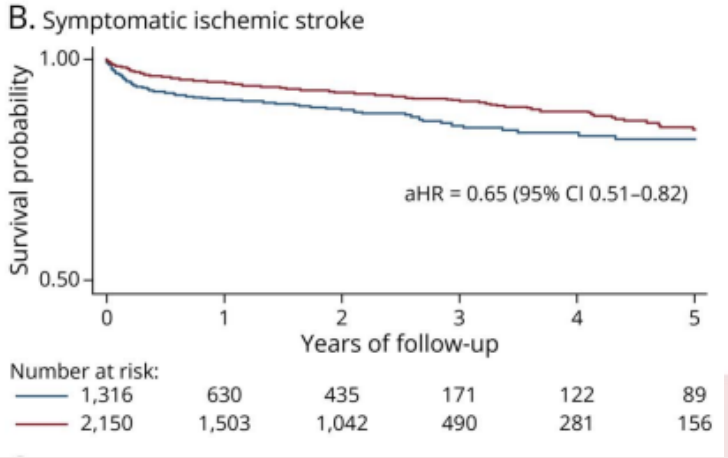
Neurology. 2024 Apr 9;102(7):e209173. doi: 10.1212/WNL.0000000000209173. Epub 2024 Mar 12.

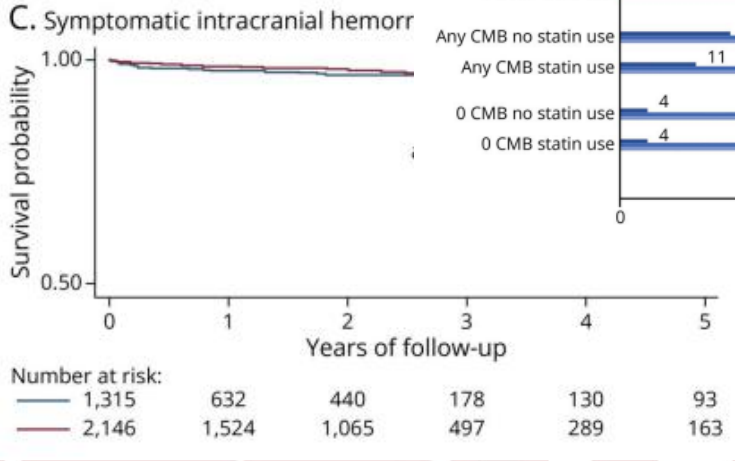
Statin Therapy for Secondary Prevention in Ischemic Stroke Patients With Cerebral Microbleeds

Luis Prats-Sanchez [1], Pol Camps-Renom [1], Philip S Nash [1], Duncan Wilson [1], Gareth Ambler [1],

Estudio multicéntrico, observacional y prospectivo
N= 16373. Seguimiento 1,34
Estatina vs no estatina tras Ictus isquémico







Resultados contradictorios

Review > Arterioscler Thromb Vasc Biol. 2023 Oct;43(10):e404-e442.
doi: 10.1161/ATV.0000000000000164. Epub 2023 Sep 14.

Aggressive LDL-C Lowering and the Brain: Impact on Risk for Dementia and Hemorrhagic Stroke: A Scientific Statement From the American Heart Association

Larry B Goldstein, Peter P Toth, Jennifer L Dearborn-Tomazos, Robert P Giugliano, Benjamin J Hirsh,

Prevención de eventos isquémicos >> riesgo hemorrágico

Resultados inconsistentes en asociación de c-LDL y riesgo hemorrágico

Hipolipemiantes con perfil de seguridad en hemorragia intracraneal

¿Es el riesgo de recurrencia hemorrágica dependiente de cohorte?, ¿dependiente del empleo de estatinas?

¿Estatina tras hemorragia intracraneal?

SATURN

Ensayo clínico multicéntrico. N = 1456

Pragmatic, prospective, randomized, open-label, and blinded end-point assessment (PROBE).

Suspensión vs continuación de estatina previa tras hemorragia intracraneal

Inclusion Criteria:

1. Age ≥ 50 years.
2. Spontaneous lobar ICH confirmed by CT or MRI scan
3. Patient was taking a statin drug at the onset of the qualifying/index ICH
4. Randomization can be carried out within 7 days of the onset of the qualifying ICH
5. Patient or legally authorized representative, after consultation with the statin prescriber, agrees to be randomized to statin continuation (restart) vs. discontinuation

Exclusion Criteria:

1. Suspected secondary cause for the qualifying ICH, such as an underlying vascular abnormality or tumor, trauma, venous infarction, or hemorrhagic transformation of an ischemic infarct.
2. History of recent myocardial infarction (attributed to coronary artery disease) or unstable angina within the previous 3 months
3. Diabetic patients with history of myocardial infarction or coronary revascularization
4. History of familial hypercholesterolemia
5. Patients receiving proprotein convertase subtilisin kexin 9 (PCSK9. inhibitors

Estatinas hidrofílicas:
-No atraviesan BHE
-No aumento riesgo hemorrágico OR 0,67 (0,24-1,67)
-EC Jupiter (Rosuvastatina)

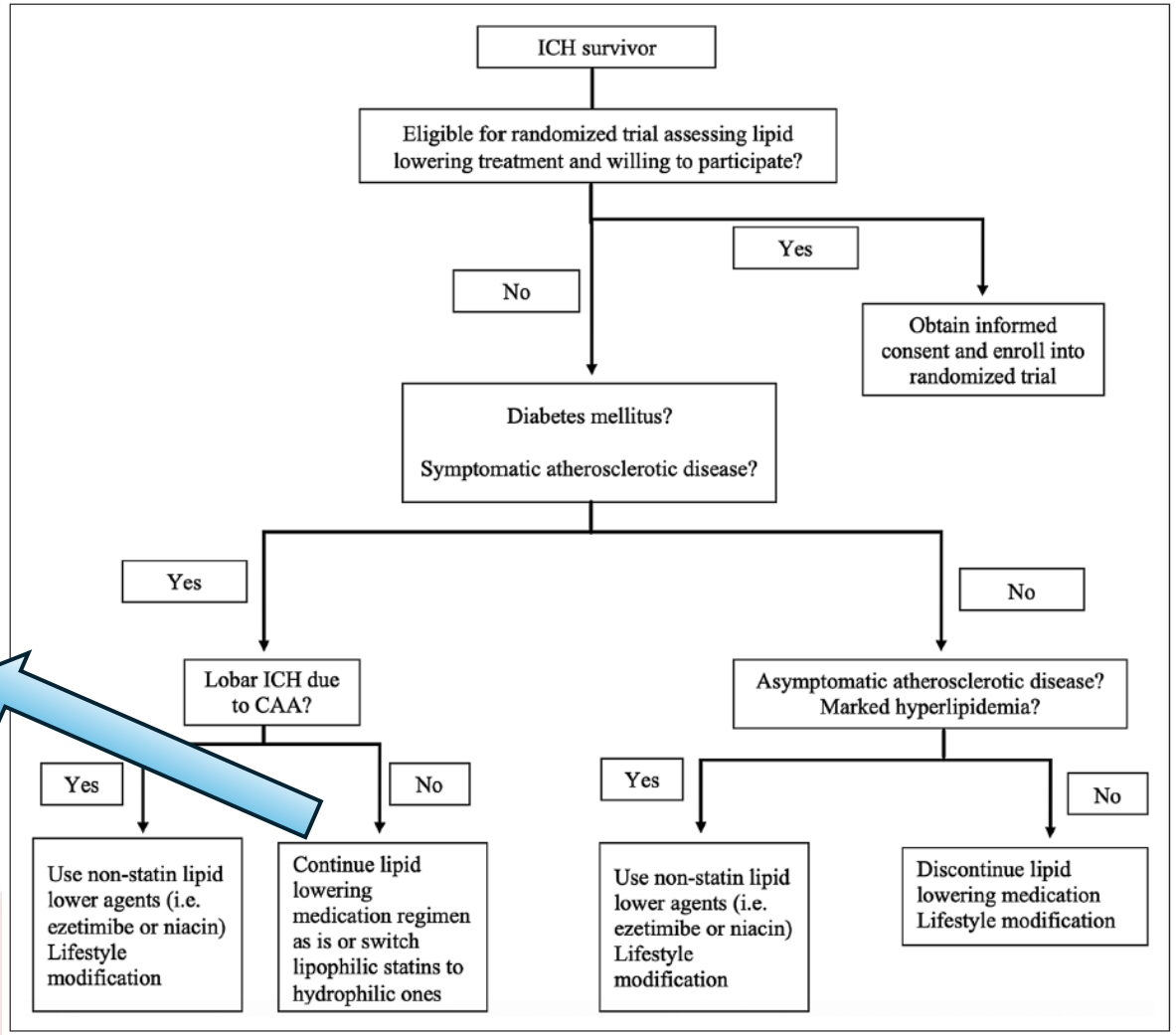


Figure. **Proposed treatment algorithm for hyperlipidemia after intracerebral hemorrhage (ICH) based on the totality of available evidence.**

Shoamanesh A, Selim M. Use of Lipid-Lowering Drugs After Intracerebral Hemorrhage. Stroke. 2022 Jul;53(7):2161-2170.

Randomized Controlled Trial > NEJM Evid. 2025 Jan;4(1):EVIDoa2400112.
doi: 10.1056/EVIDoa2400112. Epub 2024 Dec 24.

Long-Term Cognitive Safety of Achieving Very Low LDL Cholesterol with Evolocumab

André Zimerman [1 2], Michelle L O'Donoghue [1], Xinhui Ran [1], KyungAh Im [1], Brian R Ott [3],

- N=473
- Seguimiento 7.2 años (5,1 adicional)
- 62 años. LDL 35 mg/dl (RIC 21-55 mg/dl)

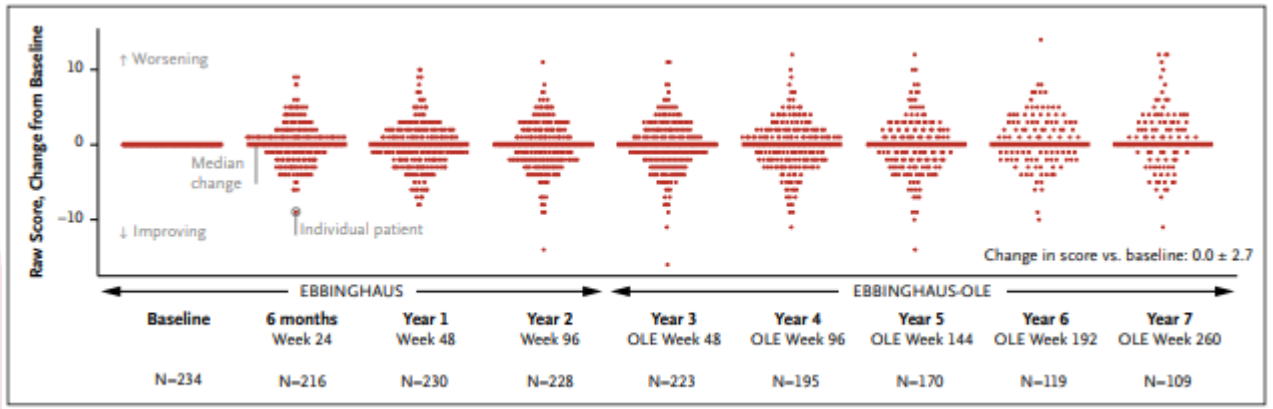
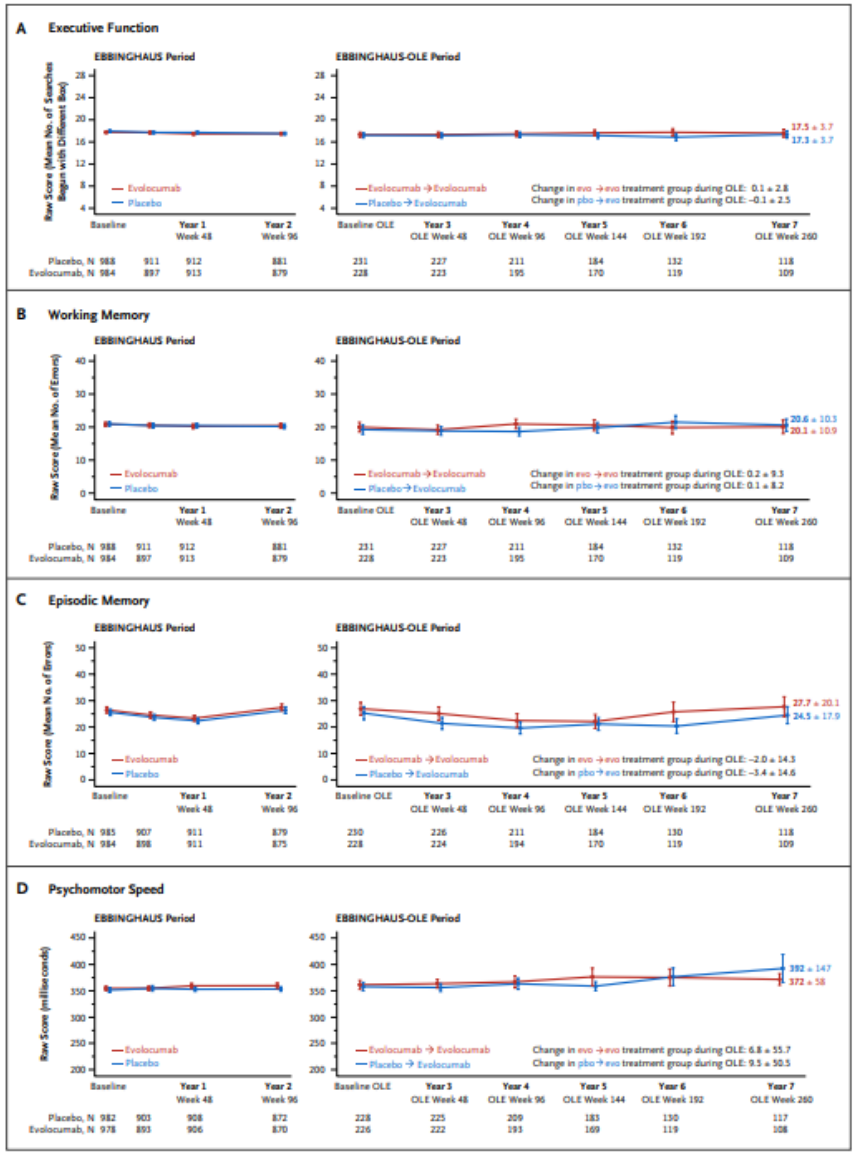


Figure 3. Long-term Change in Executive Function with Evolocumab.



Quick Takes

LDL Cholesterol Lowering: Is There a Risk for Dementia and Hemorrhagic Stroke?

May 22, 2024 | Tia Bimal, MD; Benjamin J. Hirsh, MD, FACC; Anum Saeed, MD; Peter P. Toth, MD, PhD, FACC

AMERICAN COLLEGE of CARDIOLOGY

Expert Analysis

hemorrhagic stroke associated with lowering LDL-C levels.

Stroke

EDITORIAL

Lowering Cholesterol and Intracerebral Hemorrhage: There Won't Be Blood!

Seemant Chaturvedi, MD

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