

LDL-C Lowering and the Brain

Larry B. Goldstein, MD, FAAN, FANA, FAHA

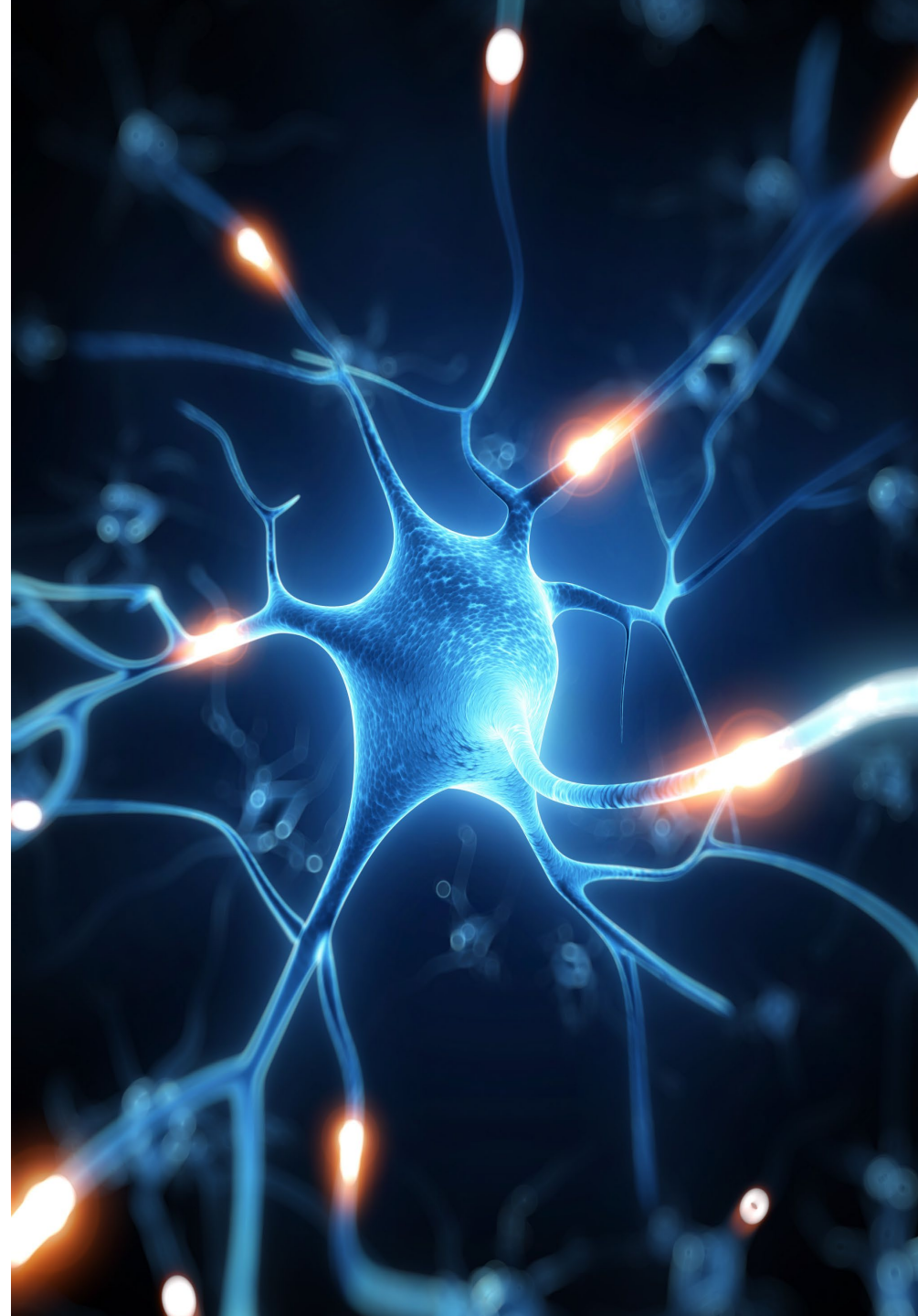
Ruth L. Works Professor and Chairman, Department of Neurology

Associate Dean for Clinical Research, College of Medicine

Co-Director, Kentucky Neuroscience Institute

Co-Director, UK Neuroscience Research Priority Area

Interim Director, UK-Norton Healthcare Stroke Care Network



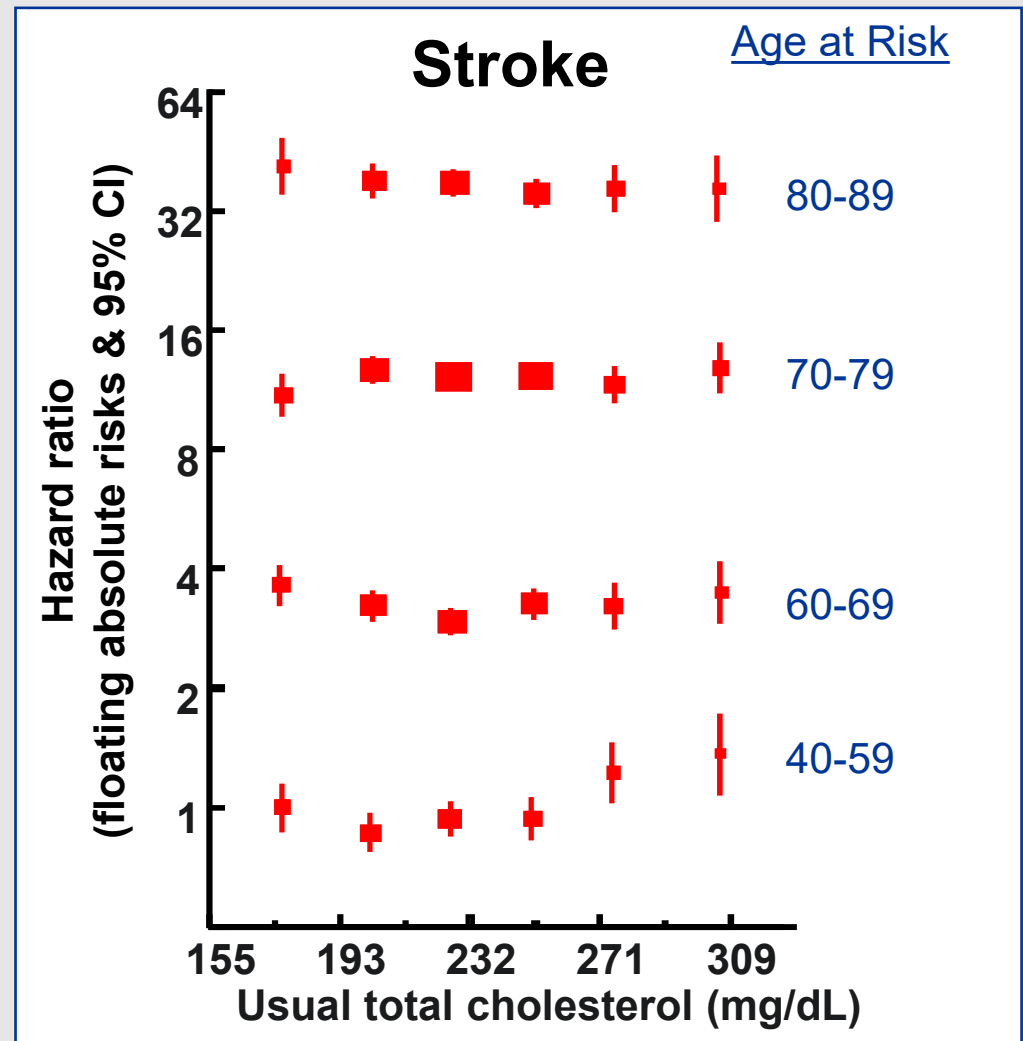
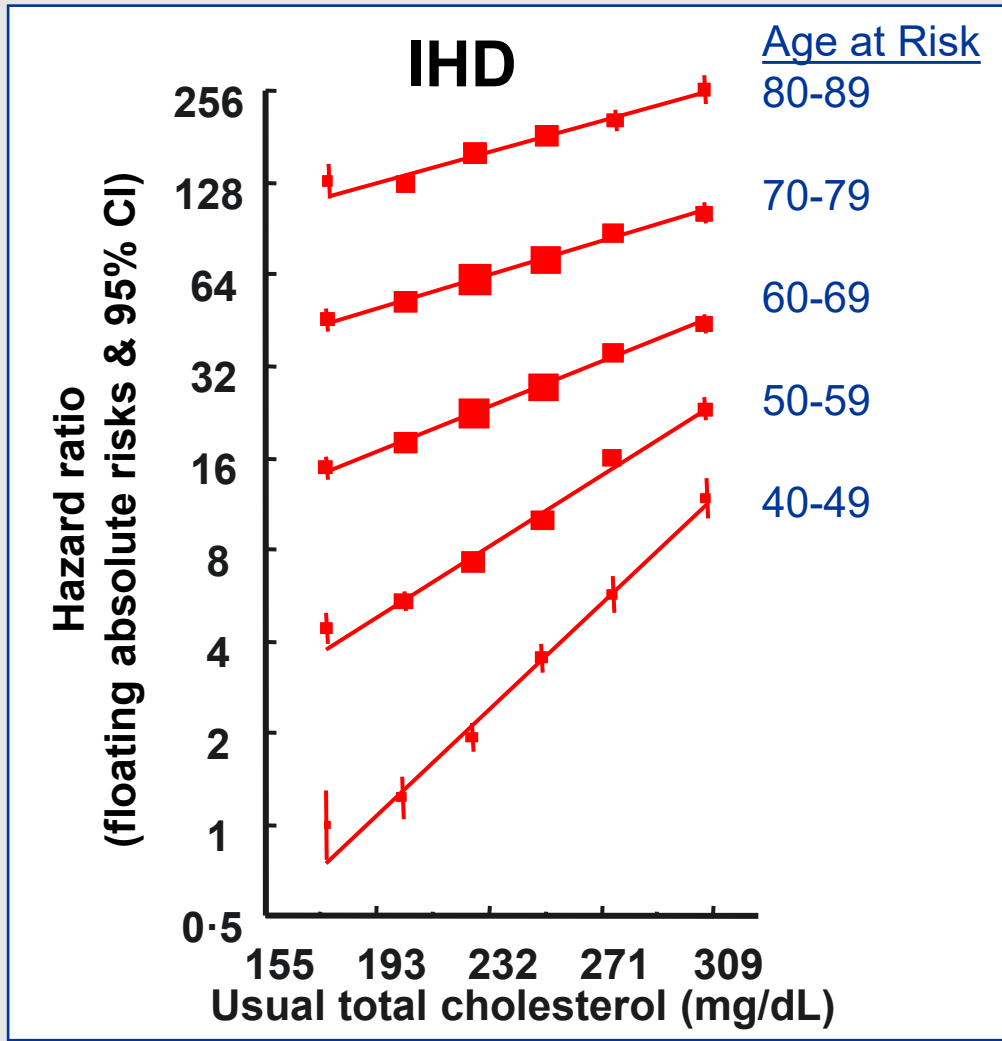
Arteriosclerosis, Thrombosis, and Vascular Biology

AHA SCIENTIFIC STATEMENT

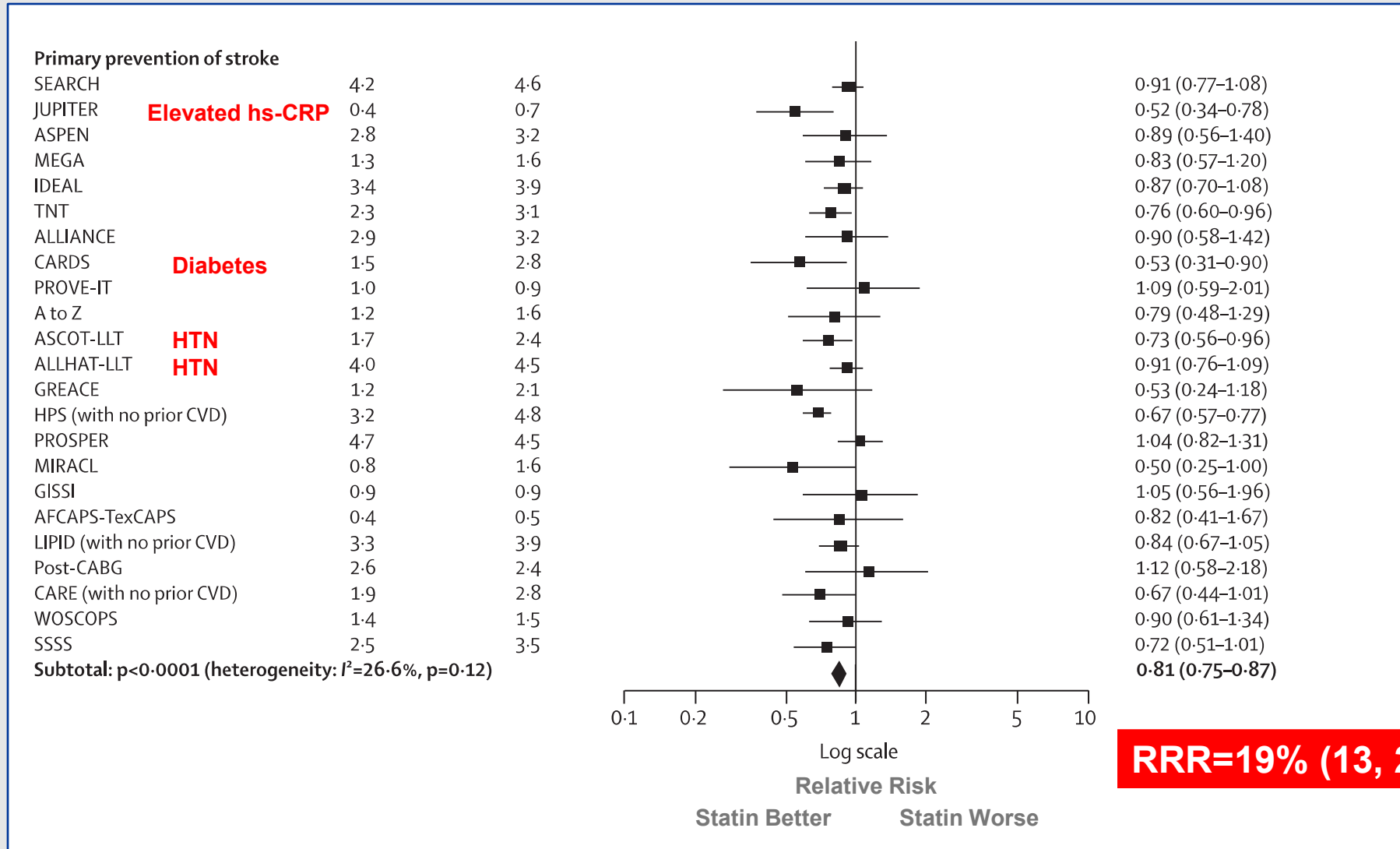
Aggressive LDL-C Lowering and the Brain: Impact on Risk for Dementia and Hemorrhagic Stroke: A Scientific Statement From the American Heart Association

Larry B. Goldstein, MD, FAHA, Chair; Peter P. Toth, MD, PhD, FAHA, Vice Chair; Jennifer L. Dearborn-Tomazos, MD, MPH; Robert P. Giugliano, MD, SM, FAHA; Benjamin J. Hirsh, MD, FAHA; Jessica M. Peña, MD, MPH; Magdy H. Selim, MD, PhD, FAHA; Daniel Woo, MD, MS; on behalf of the American Heart Association Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular and Stroke Nursing; Council on Peripheral Vascular Disease; and Stroke Council

Total Cholesterol and Vascular Death

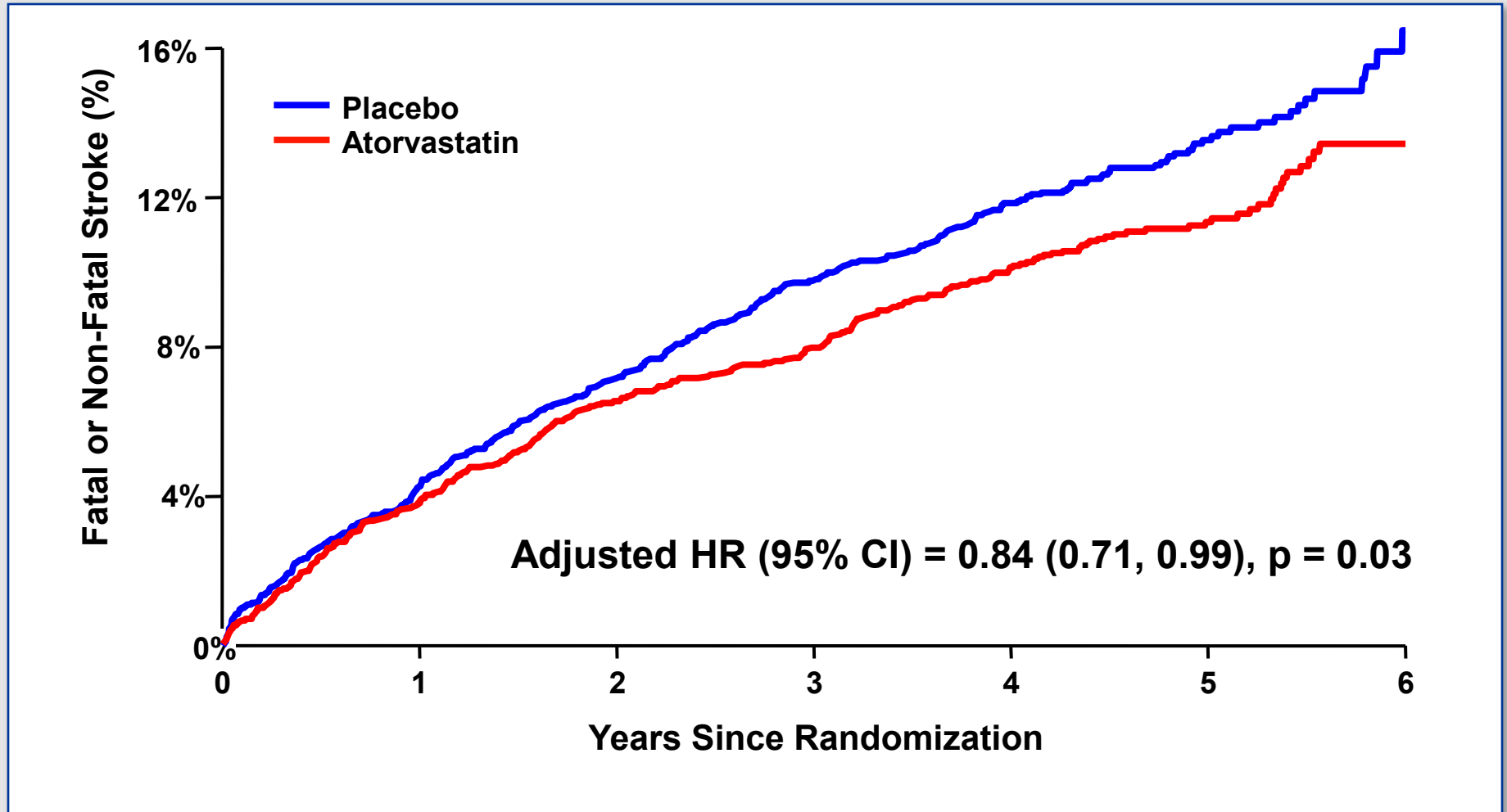


Statins For Primary Stroke Prevention



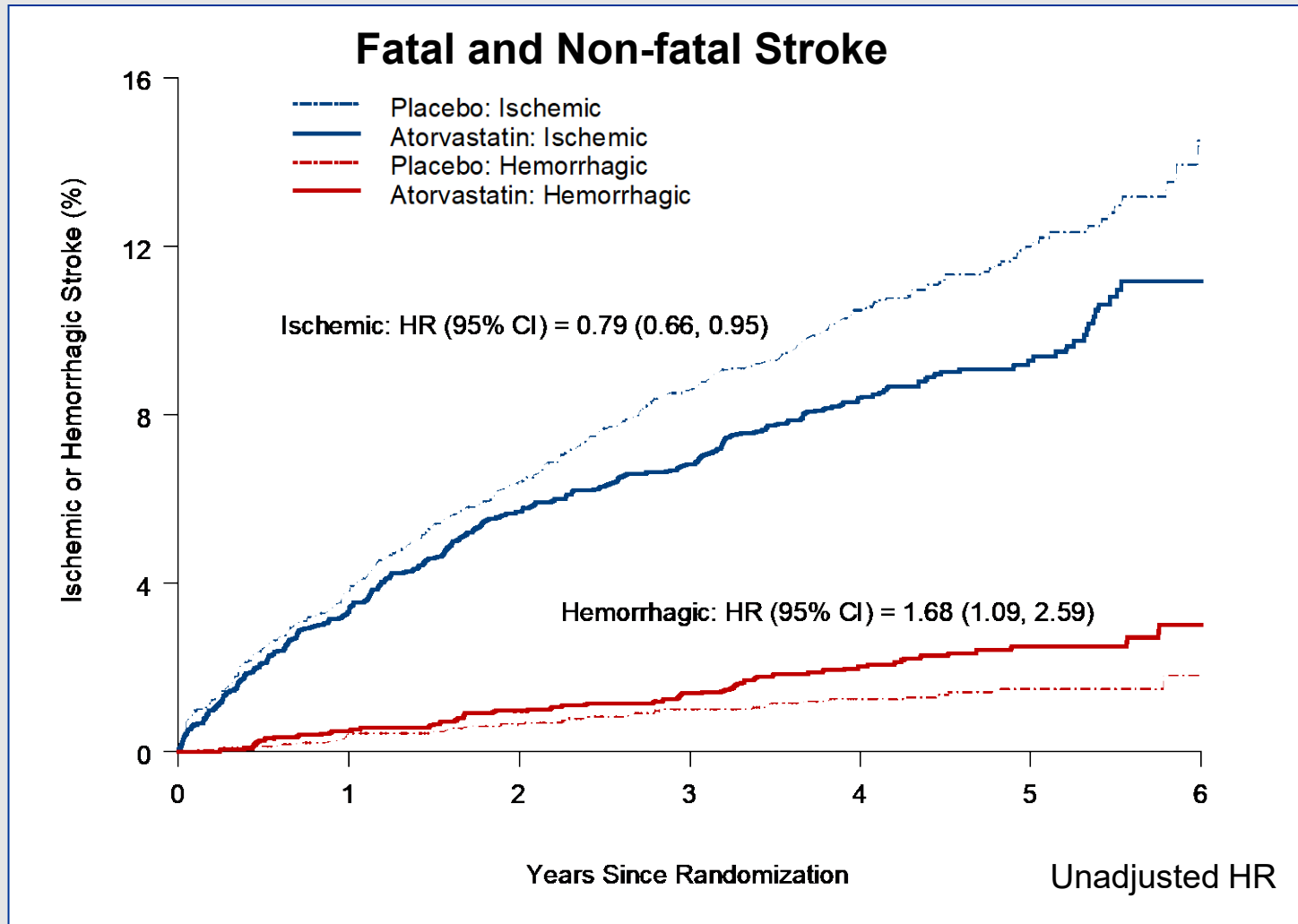
SPARCL Primary Endpoint

Time to Fatal or Non-Fatal Stroke



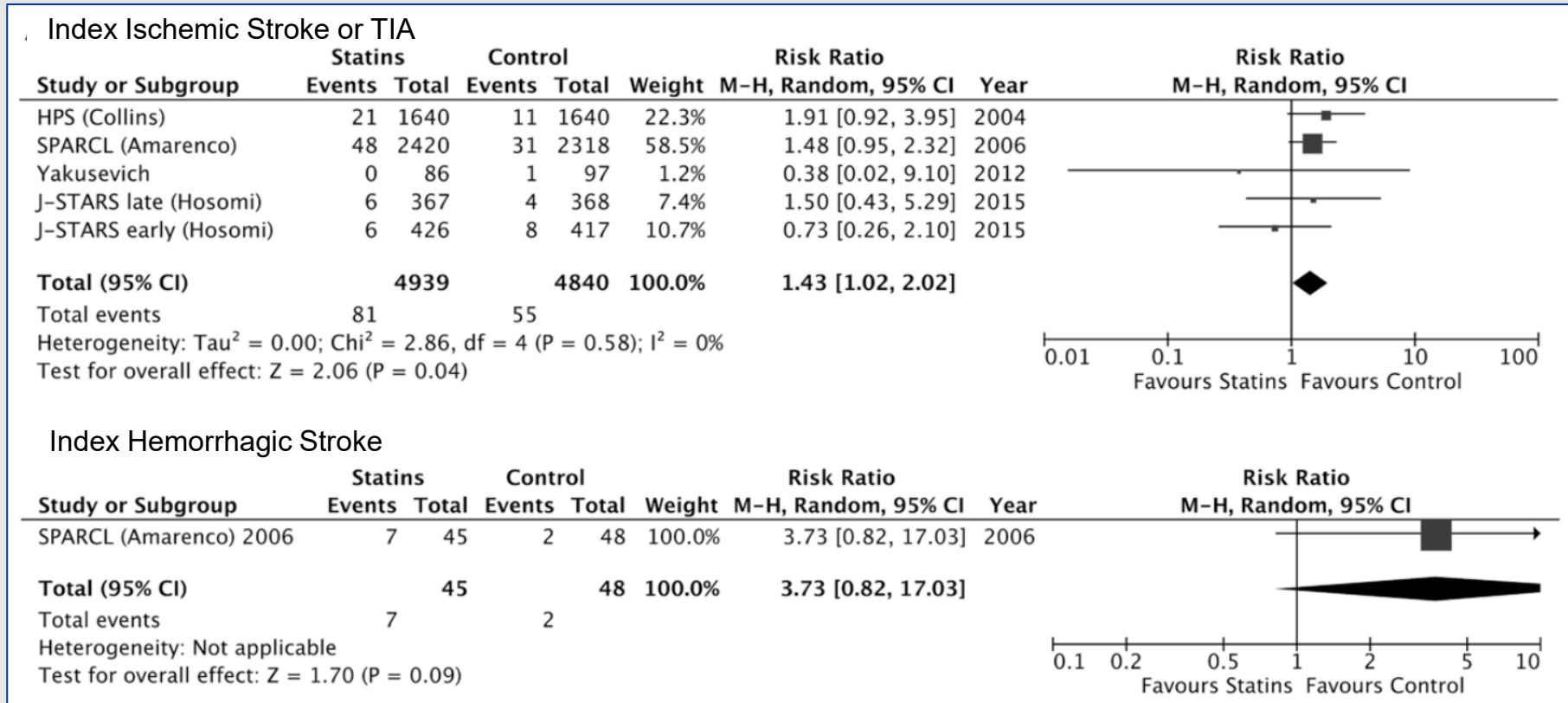
SPARCL Ischemic and Hemorrhagic Stroke

Post hoc analysis



Statins and Hemorrhagic Stroke

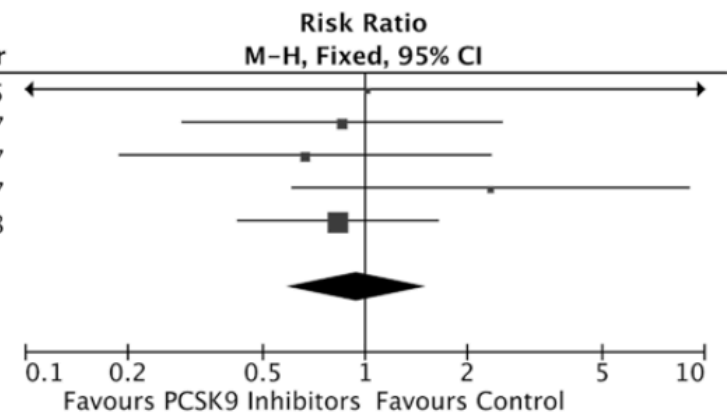
Meta-Analysis – Secondary Prevention



PCSK9 Inhibitors and Hemorrhagic Stroke Meta-Analysis

Index Ischemic Stroke or TIA

Study or Subgroup	PCSK9 Inhibitors		Control		Weight	Risk Ratio		Year
	Events	Total	Events	Total		M-H, Fixed, 95% CI		
ODYSSEY Long Term 2015	2	1550	1	788	3.8%	1.02	[0.09, 11.20]	2015
SPIRE-1 2017	6	8386	7	8374	19.8%	0.86	[0.29, 2.55]	2017
FOURIER 2017	4	13769	6	13756	17.0%	0.67	[0.19, 2.36]	2017
SPIRE-2 2017	7	5276	3	5297	8.5%	2.34	[0.61, 9.05]	2017
ODYSSEY Outcomes 2018	15	9482	18	9462	51.0%	0.83	[0.42, 1.65]	2018
Total (95% CI)		38463		37677	100.0%	0.94	[0.59, 1.51]	
Total events	34		35					
Heterogeneity: $\text{Chi}^2 = 2.19$, $\text{df} = 4$ ($P = 0.70$); $I^2 = 0\%$								
Test for overall effect: $Z = 0.24$ ($P = 0.81$)								



PCSK9 Inhibitors added to maximally-tolerated statins vs placebo added to maximally tolerated statins

Statin Intolerance

Meta-Analysis

	All studies	RCT studies	Cohort studies
No. of studies	176	112	64
Overall prevalence, % (95% CI)	9.1 (8.0–10)	4.9 (4.0–6.0)	17 (14–19)
NLA	7.0 (6.0–8.0)	4.8 (3.0–6.0)	11 (6.0–16)
ILEP	6.7 (5.0–8.0)	4.9 (3.5–6.2)	10 (7.2–15)
EAS	5.9 (4.0–7.0)	3.8 (2.4–5.4)	8.4 (5.7–11)
Sample size, n	4 143 517	195 575	3 947 942

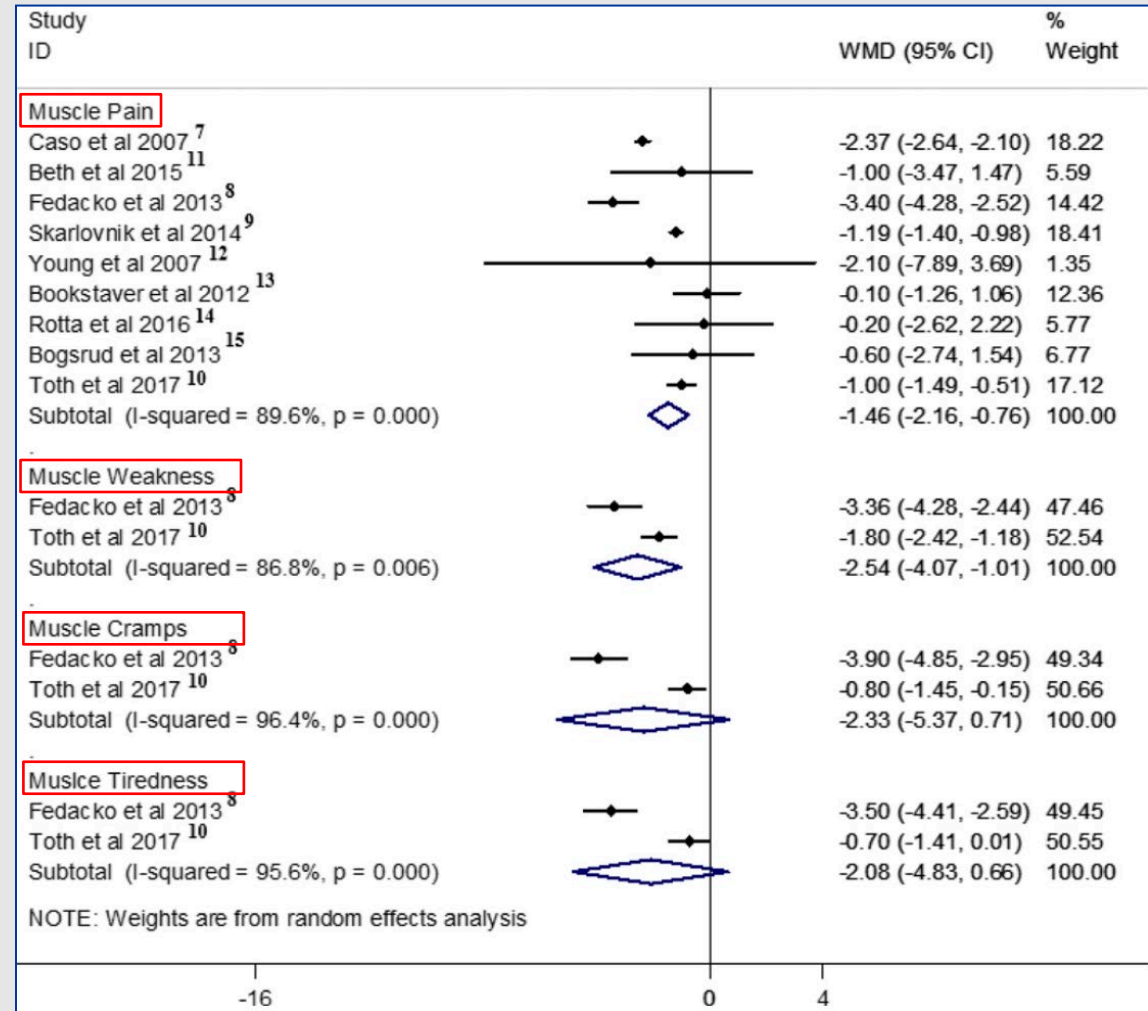
- **NLA – National Lipid Association**
 - Adverse effects relating to the quality of life, leading to decisions to decrease or stop the use of an otherwise beneficial drug
- **ILEP – International Lipid Expert Panel**
 - Inability to tolerate a dose of statin required to reduce a person’s CV risk sufficiently from their baseline risk
- **EAS – European Atherosclerosis Society**
 - The assessment of the probability of SAMS being due to a statin considering the nature of the muscle symptoms, the elevation in CK levels, and their temporal association with statin initiation, discontinuation, and re-challenge

Statin-Associated Muscle Symptoms

Meta-Analysis - Co-Q10 Supplementation

*50-100 cases with muscle pain or weakness per 10,000 treated over 5-years (5 cases of myopathy)

- 12 reports (2007-2017)
- Sample sizes 37-76 patients
- Treatment 30-days to 3-months
- CoQ10 100– 600 mg/d
- No reduction in the plasma CK level
 - Weighted Mean Difference
 - 0.09 (-0.06 to 0.24) p=0.23

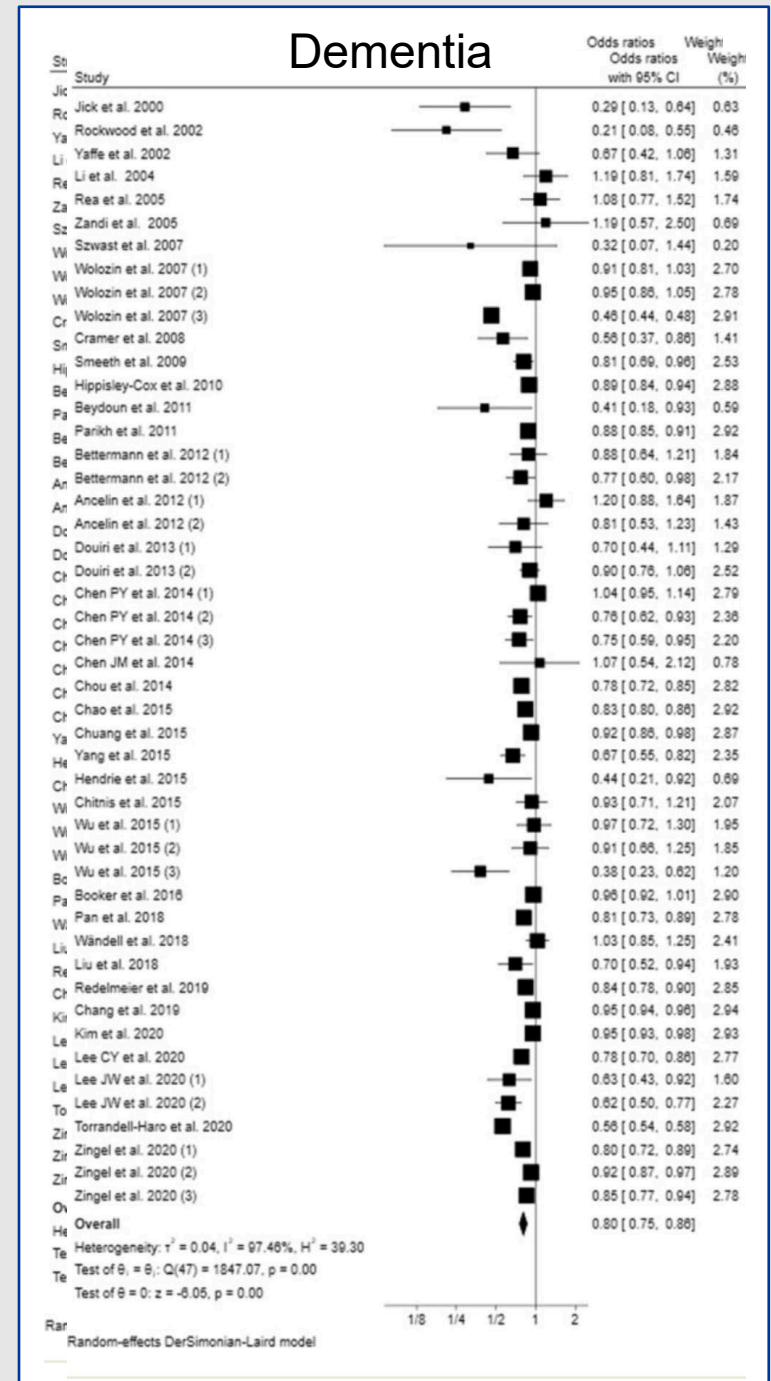
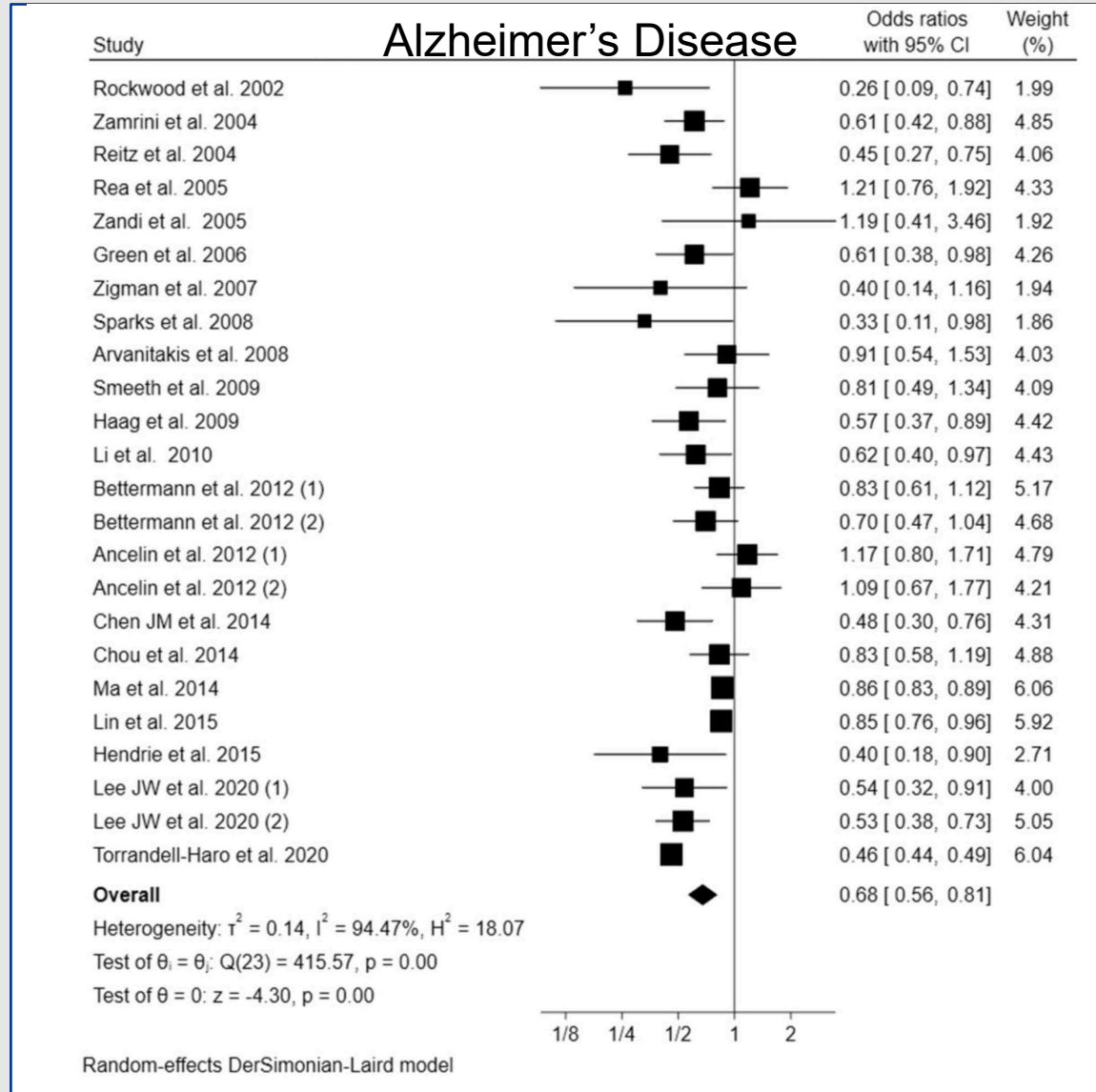


Qu et al. *JAHA* 2018;7:e009835

Collins et al. *Lancet* 2016;388:2532-2561*

Statins and Cognition

Meta-Analysis



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AHA SCIENTIFIC STATEMENT

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