ΣΤΑΤΙΝΕΣ ΣΤΗΝ ΤΡΙΤΗ ΗΛΙΚΙΑ

Ευάγγελος Λυμπερόπουλος

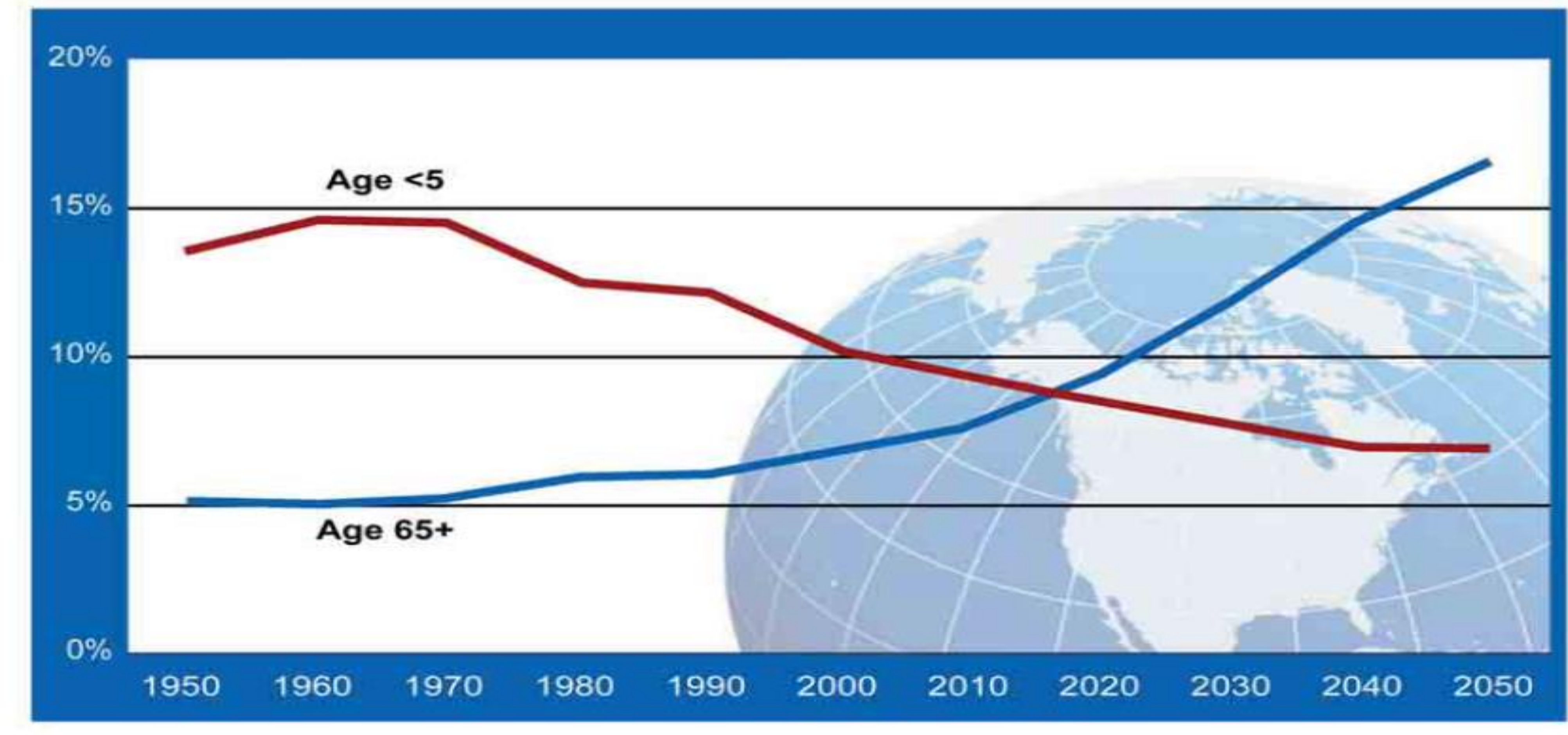
Καθηγητής Παθολογίας-Μεταβολικών Νοσημάτων Ιατρικής Σχολής Εθνικού και Καποδιστριακού Πανεπιστημίου Αθηνών, Α΄ Προπαιδευτική Παθολογική Κλινική, ΓΝΑ 'Λαϊκό'

Disclaimer-Δήλωση Σύγκρουσης Συμφερόντων

- Τα τελευταία 2 χρόνια έλαβα τιμητική αμοιβή από τις εταιρίες: ASTRA-ZENECA, VIANEX, MSD, LILLY, BAYER, AMGEN, ELPEN, VIATRIS, BOEHRINGER-INGELHEIM, INNOVIS, NOVARTIS, SERVIER, CHIESI, GENESIS, SANOFI, NOVO NORDISK

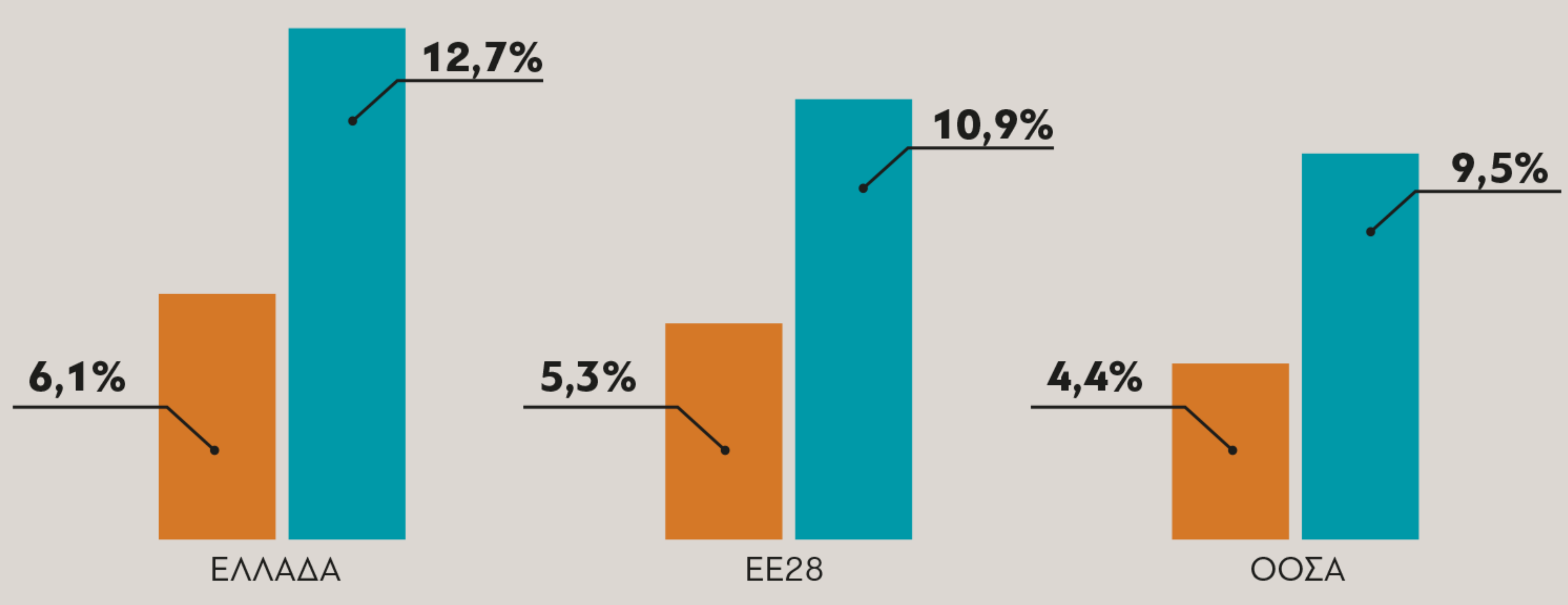
Δημογραφικό πρόβλημα.
Ένα παγκόσμιο φαινόμενο

Young Children and Older People as a Percentage of Global Population: 1950-2050



Source: United Nations. *World Population Prospects: The 2010 Revision.*
Available at: http://esa.un.org/unpd/wpp.

ΠΡΟΒΛΕΨΗ ΠΛΗΘΥΣΜΟΥ
ΑΝΩ ΤΩΝ 80 (2015 - 2050)



Πηγή: διαΝΕΟσις/Eurostat/ΟΟΣΑ/ΙΟΒΕ

ΠΕΡΙΣΤΑΤΙΚΟ

- Άνδρας 83 ετών με υπέρταση

✓ Δεν καπνίζει

✓ ΣΒ 85 Kg, BMI 28.5 Kg/m^2, eGFR 61 mL/min/1.73 m^2

✓ Σε καλή υγεία-Ελεύθερο λοιπό ατομικό αναμνηστικό

✓ ΑΠ 135/80 mmHg υπό αγωγή

✓ TCHOL 200 mg/dL, LDL-C 130 mg/dL, TGs 150 mg/dL, HDL-C 40 mg/dL, non-HDL-C 160 mg/dL

ΔΙΛΗΜΜΑ: Να δώσω στατίνη στον ασθενή;

1) ΟΧΙ

2) ΝΑΙ

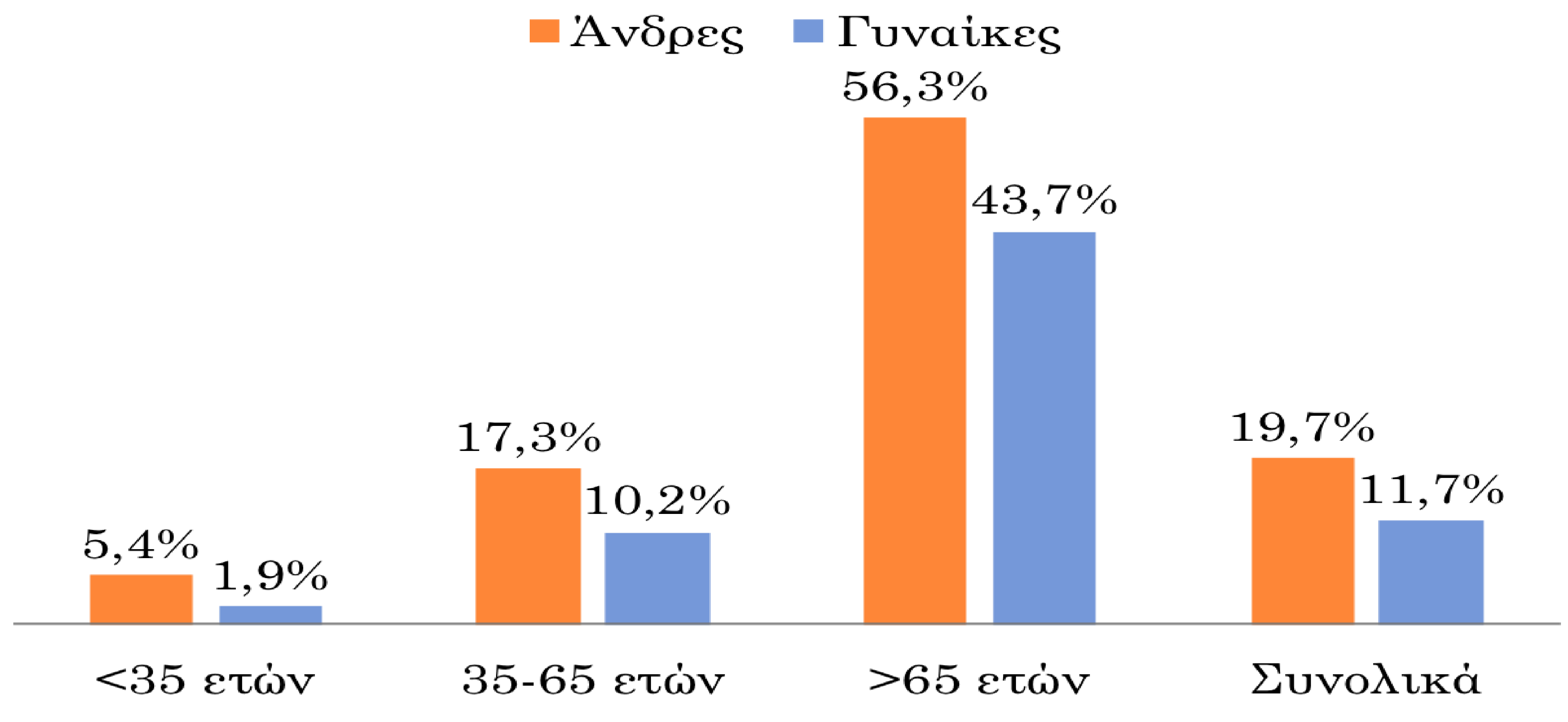
ΕΡΩΤΗΣΗ 1: ΤΙ ΠΡΟΣΔΟΚΙΜΟ ΕΠΙΒΙΩΣΗΣ ΕΧΕΙ Ο ΗΛΙΚΙΩΜΕΝΟΣ;

ΠΡΟΣΔΟΚΙΜΟ ΖΩΗΣ ΣΕ ΗΛΙΚΑ 80 ΕΤΩΝ

- ΑΝΔΡΕΣ ~ 8.7 ΕΤΗ
- ΓΥΝΑΙΚΕΣ ~ 10.0 ΕΤΗ

https://stats.oecd.org/Index.aspx/DataSetCode=HEALTH_STAT

10ΕΤΗΣ ΕΠΙΠΤΩΣΗ ΚΑΡΔΙΑΓΓΕΙΑΚΗΣ ΝΟΣΟΥ, ΑΝΑ ΦΥΛΟ & ΗΛΙΚΙΑ (n = 3042 συμμετέχοντες)

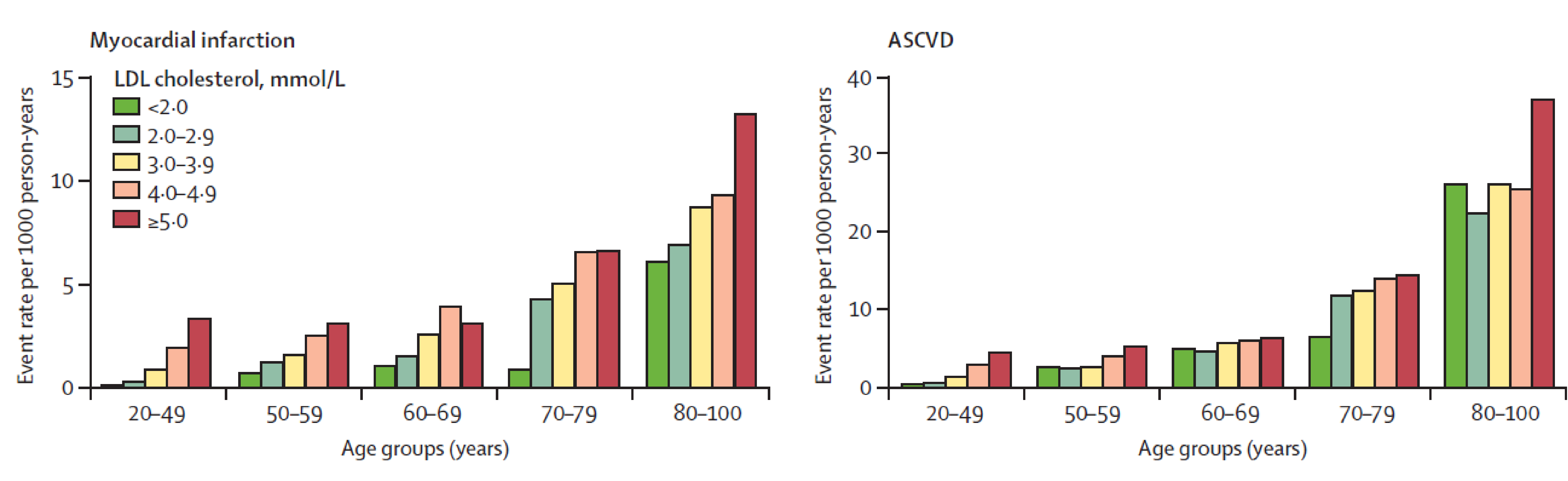


Μελέτη ΑΤΤΙΚΗ
2002-2012

Panagiotakos D, et al., Int J Cardiol 2014

ΕΡΩΤΗΣΗ 2: ΣΥΣΧΕΤΙΖΕΤΑΙ Η LDL-C ΜΕ ΤΑ ΚΑΡΔΙΑΓΓΕΙΑΚΑ ΕΠΕΙΣΟΔΙΑ ΣΕ ΑΥΤΕΣ ΤΙΣ ΗΛΙΚΙΕΣ;

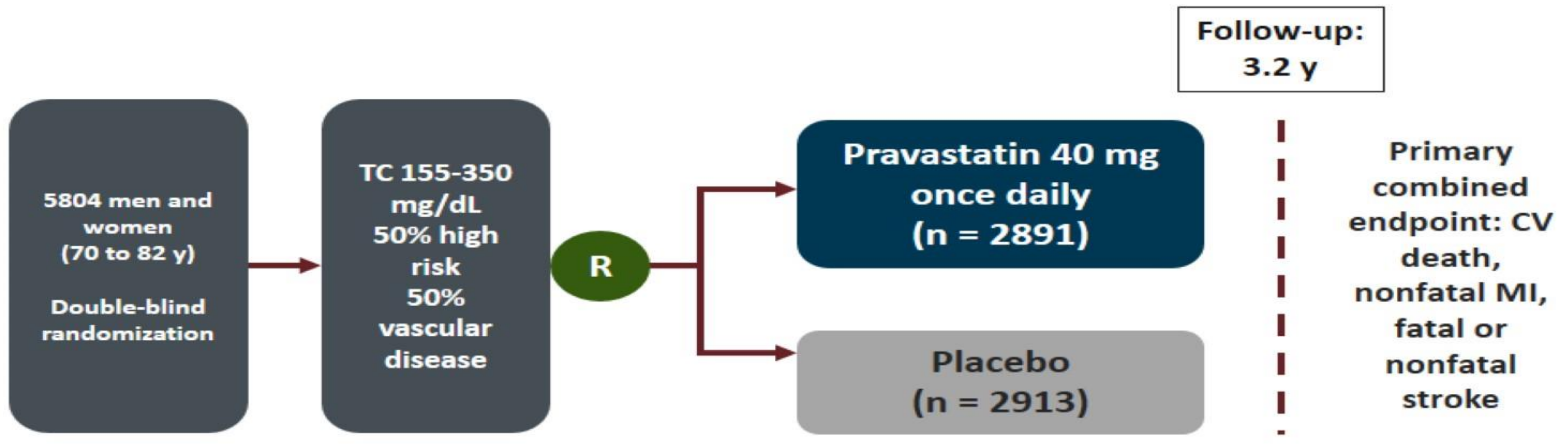
Elevated LDL cholesterol and increased risk of myocardial infarction and atherosclerotic cardiovascular disease in individuals aged 70–100 years: a contemporary primary prevention cohort



www.thelancet.com Published online November 10, 2020 https://doi.org/10.1016/S0140-6736(20)32233-9

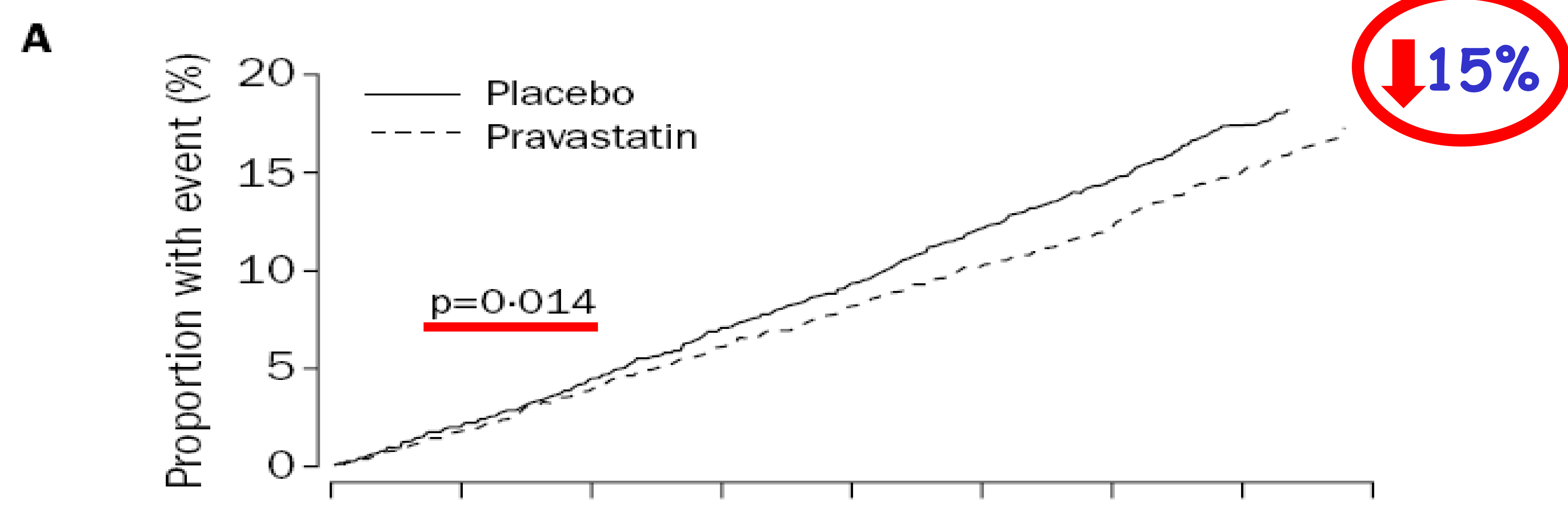
ΕΡΩΤΗΣΗ 3: ΤΙ ΔΕΔΟΜΕΝΑ ΥΠΑΡΧΟΥΝ ΟΤΙ Η ΥΠΟΛΙΠΙΔΑΙΜΙΚΗ ΑΓΩΓΗ ΜΕΙΩΝΕΙ ΤΑ ΚΑΡΔΙΑΓΓΕΙΑΚΑ ΕΠΕΙΣΟΔΙΑ ΣΤΟΥΣ ΥΠΕΡΗΛΙΚΕΣ;

PROSPER
Study Design



Shepherd J, et al. *Lancet*. 2002;360:1623-1630.

PROSPER

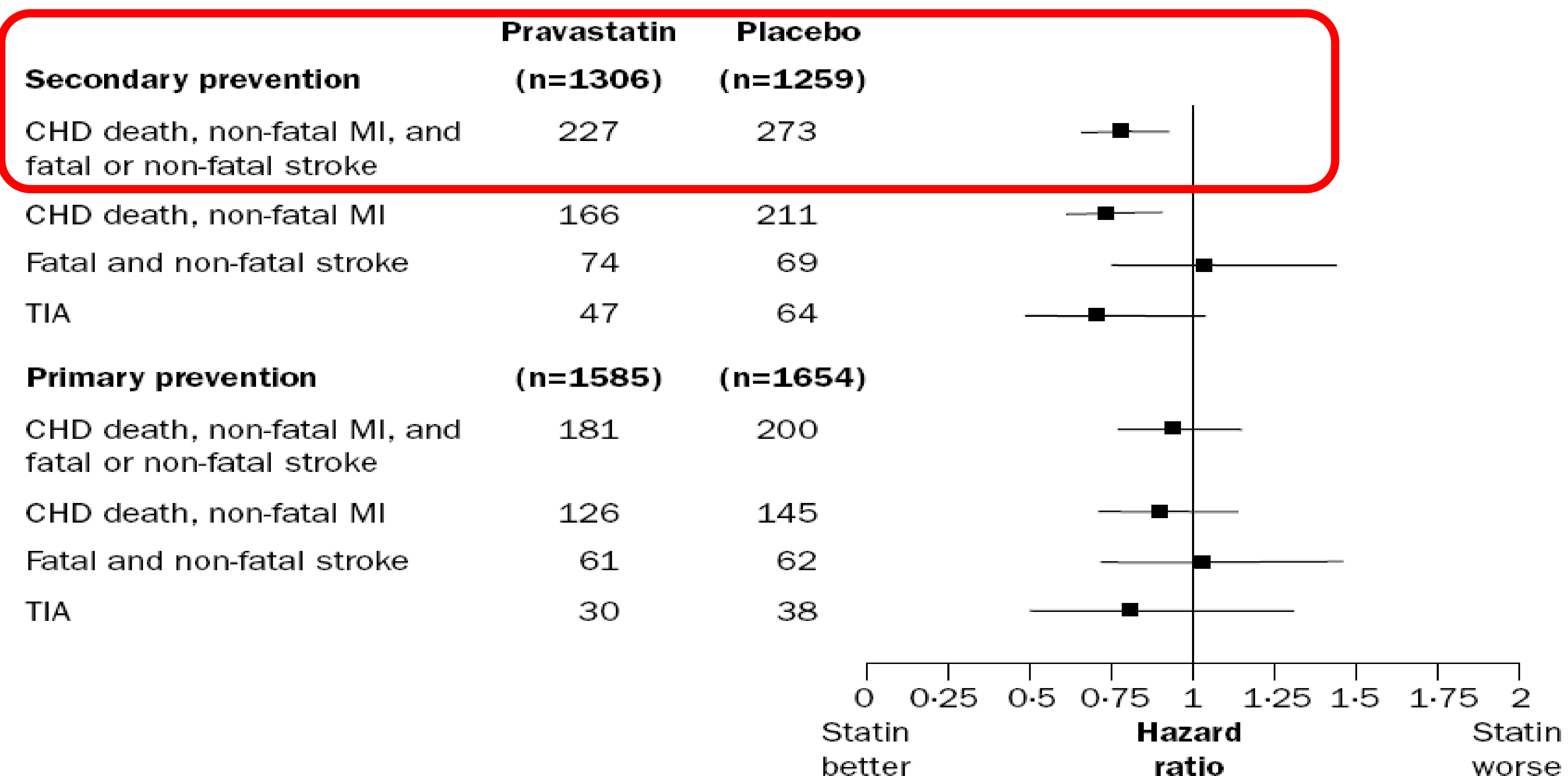


Number at risk

Placebo	2913	2832	2748	2651	2560	2458	2128	730	44
Pravastatin	2891	2812	2738	2655	2562	2483	2167	770	40

Lancet 2002;360:1623-30

PROSPER



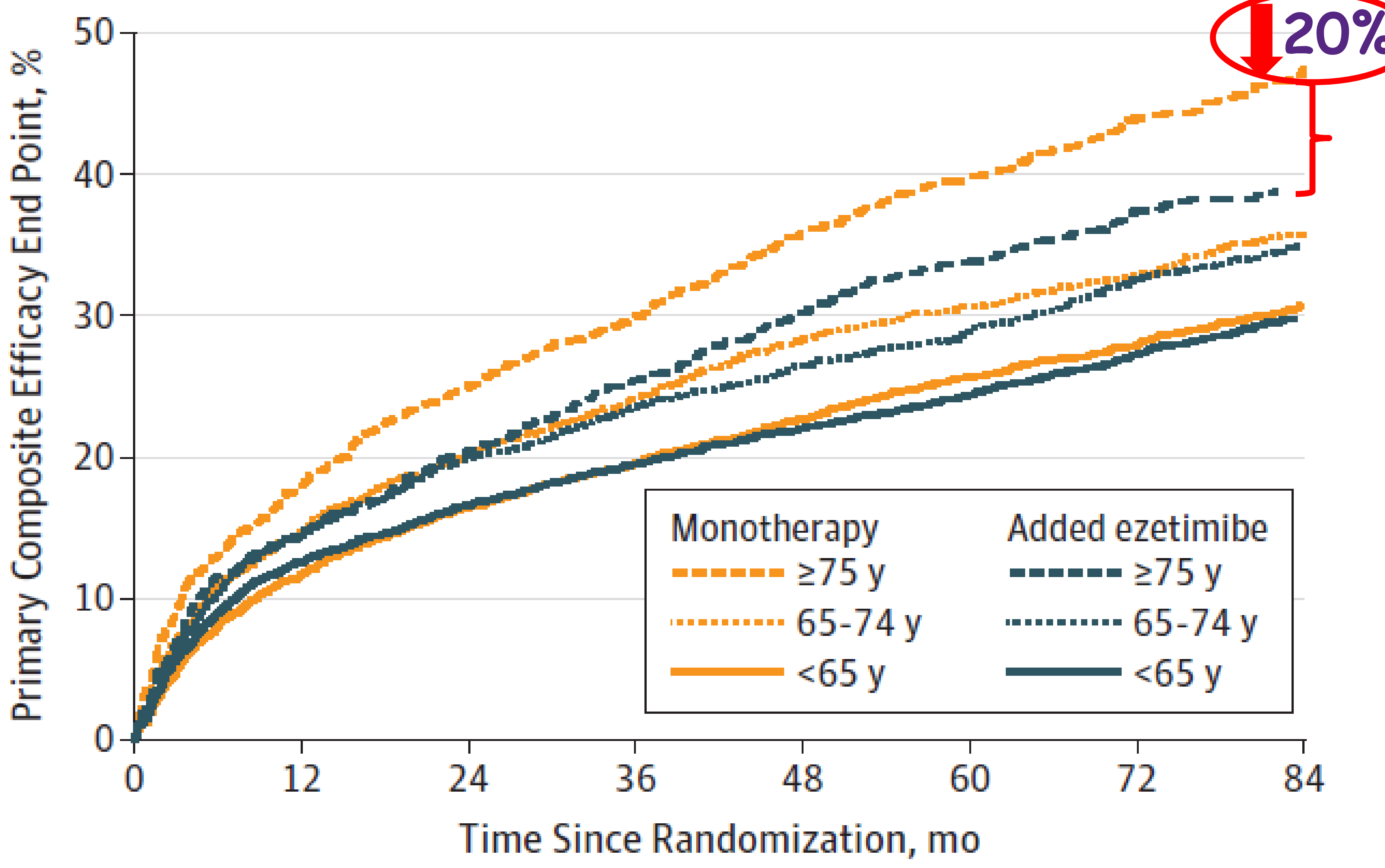
Lancet 2002;360:1623-30

JAMA Cardiology | Original Investigation

Effect of Simvastatin-Ezetimibe Compared With Simvastatin Monotherapy After Acute Coronary Syndrome Among Patients 75 Years or Older

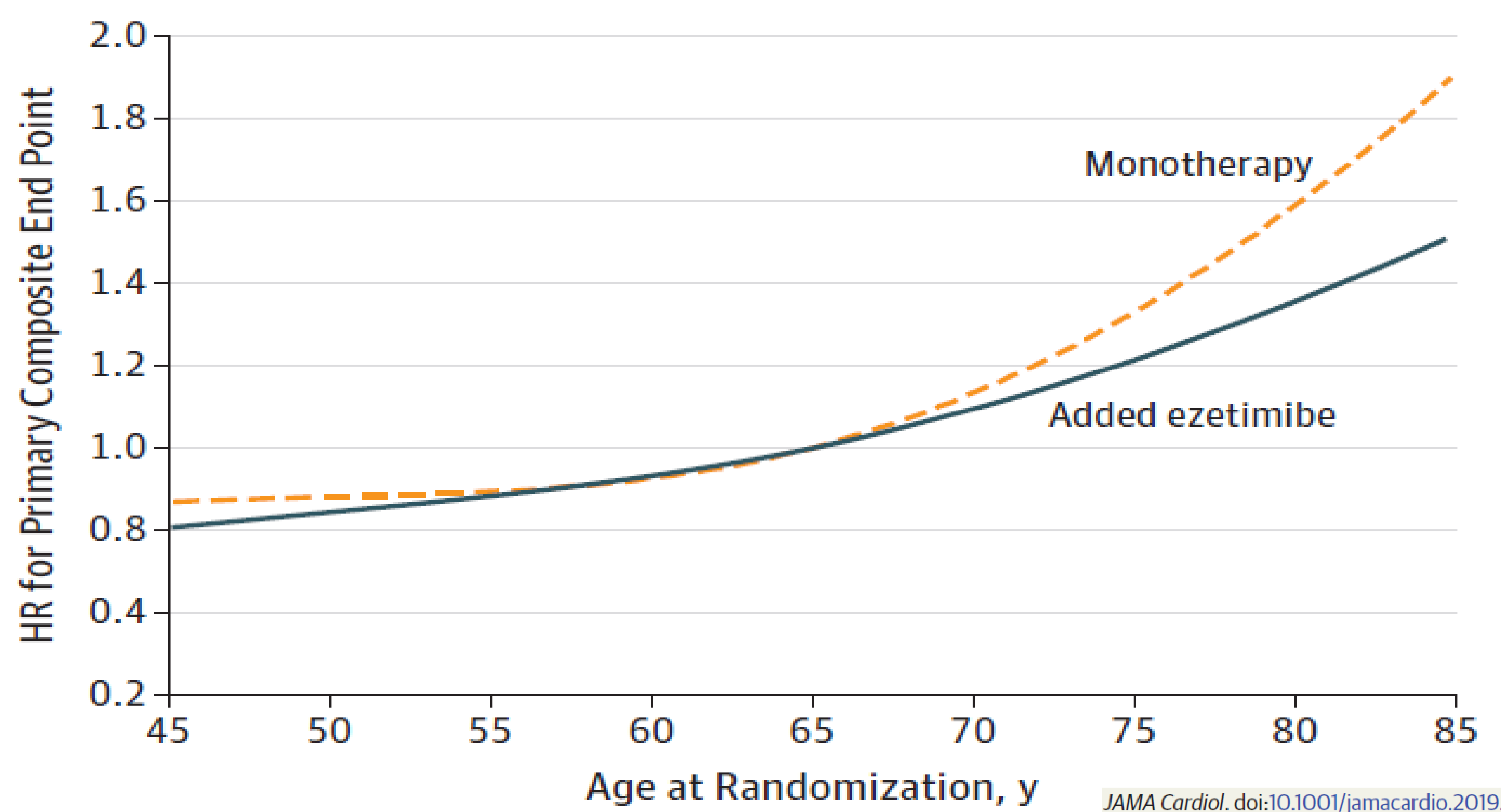
A Secondary Analysis of a Randomized Clinical Trial

A Primary composite efficacy end point

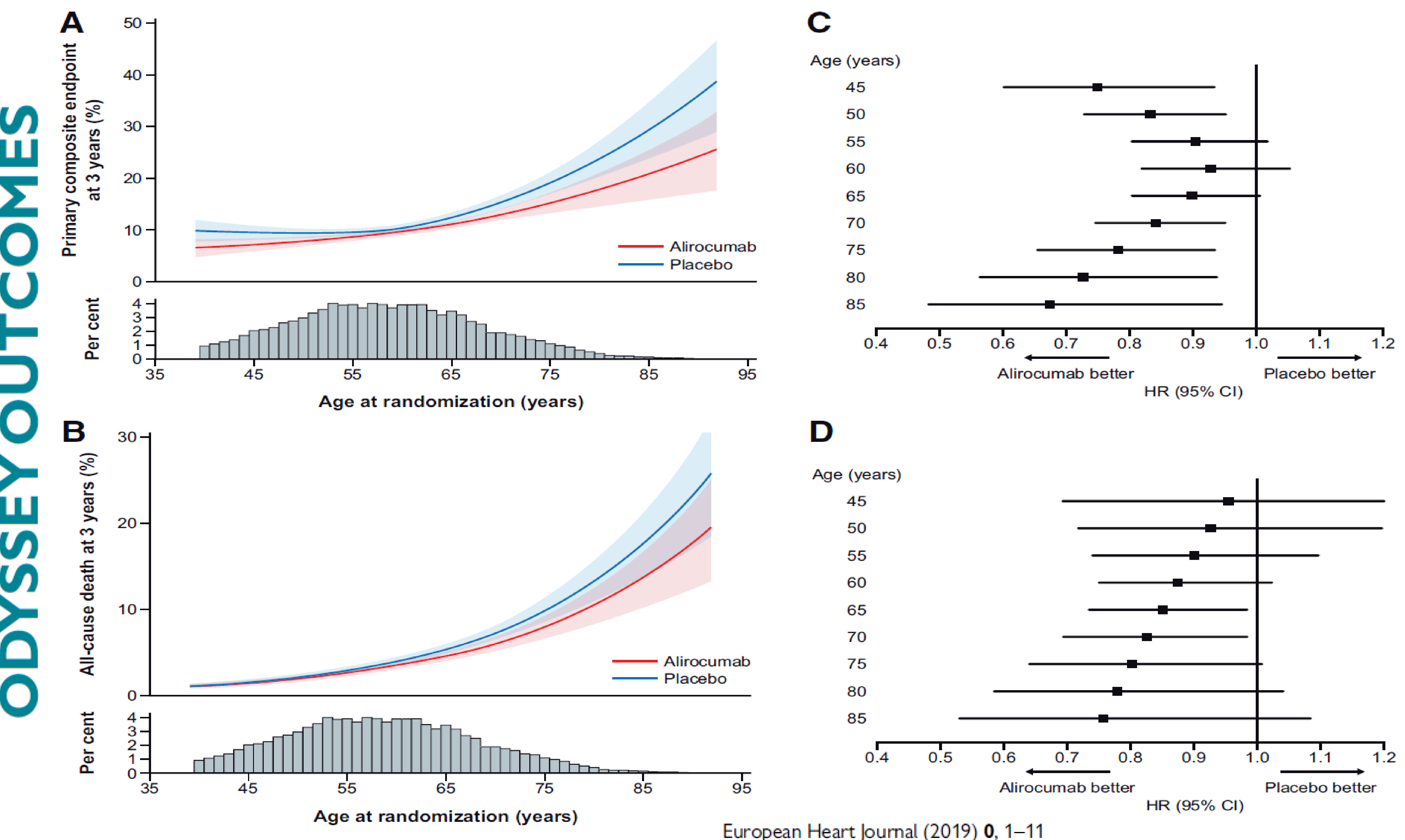


JAMA Cardiol. doi:10.1001/jamacardio.2019.2306
Published online July 17, 2019.

A Association between continuous age and outcome by assigned treatment



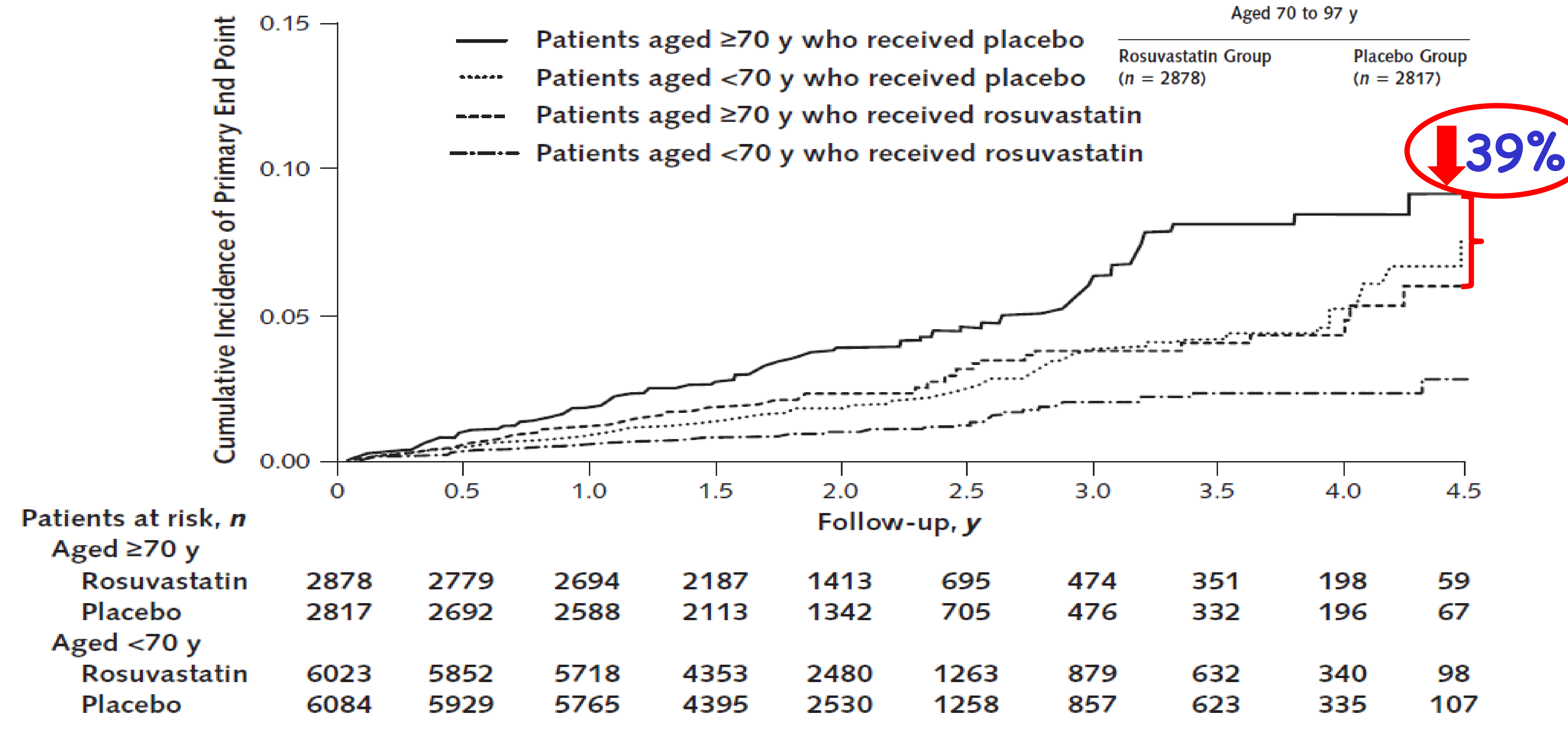
JAMA Cardiol. doi:10.1001/jamacardio.2019.2306
Published online July 17, 2019.



European Heart Journal (2019) **0**, 1–11

ARTICLE | *Ann Intern Med.* 2010;152:488-496. **Annals of Internal Medicine**

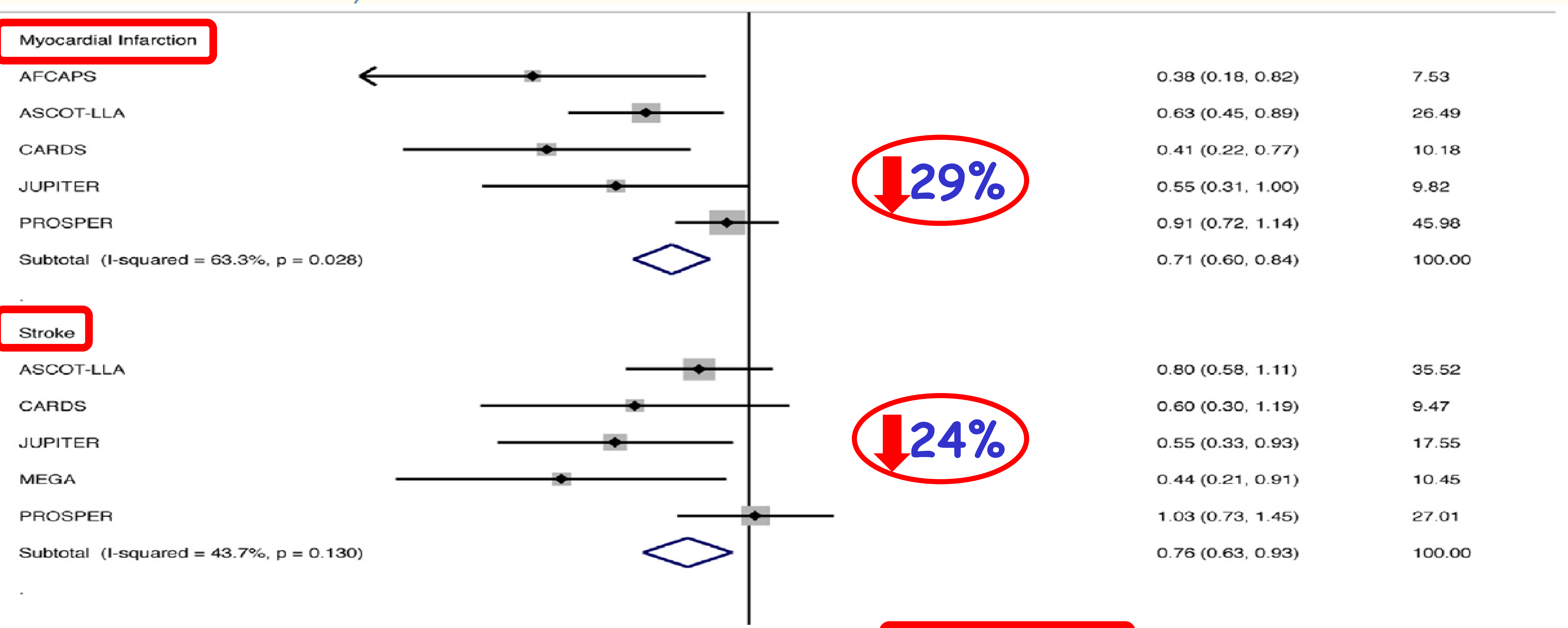
Rosuvastatin for Primary Prevention in Older Persons With Elevated C-Reactive Protein and Low to Average Low-Density Lipoprotein Cholesterol Levels: Exploratory Analysis of a Randomized Trial



Patients at risk, *n*										
Aged ≥70 y										
Rosuvastatin	2878	2779	2694	2187	1413	695	474	351	198	59
Placebo	2817	2692	2588	2113	1342	705	476	332	196	67
Aged <70 y										
Rosuvastatin	6023	5852	5718	4353	2480	1263	879	632	340	98
Placebo	6084	5929	5765	4395	2530	1258	857	623	335	107

Benefits of Statins in Elderly Subjects Without Established Cardiovascular Disease

A Meta-Analysis



Eight trials enrolling 24,674 subjects (42.7% females; mean age 73.0 ± 2.9 years; mean follow up 3.5 ± 1.5 years)

.179 | 1 | 5.59

Better Statins | Better Placebo

J Am Coll Cardiol 2013;62:2090–9

Ezetimibe in Prevention of Cerebro- and Cardiovascular Events in Middle- to High-Risk, Elderly (75 Years Old or Over) Patients With Elevated LDL-Cholesterol: A Multicenter, Randomized, Controlled, Open-Label Trial

EWTOPIA 75

*The present study is registered, number UMIN000001988.

Hidenori Arai, Jun Sasaki, Koutaro Yokote, Masanari Kuwabara, Kazumasa Harada, Takumi Imai, Shiro Tanaka, Yasuo Ohashi, Hideki Ito, Yasuyoshi Ouchi, on behalf of the EWTOPIA investigators

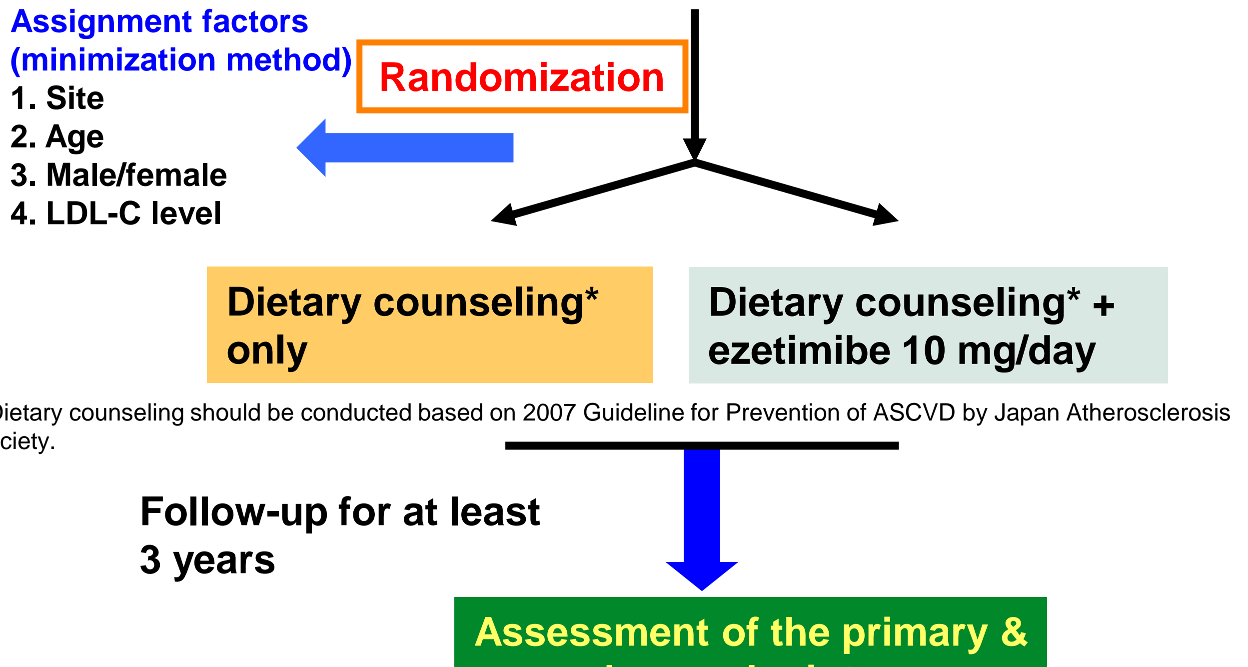
P.I.: **Yasuyoshi Ouchi**, M.D., Ph.D.
Federation of National Public Service Personnel
Mutual Aid Associations Toranomon Hospital, Tokyo, Japan
Professor Emeritus, University of Tokyo

Late-breaking clinical trials session
November 10, 2018 Chicago, IL, USA

Study Design of EWTOPIA 75

PROBE design

Prospective Randomized Open-label Blinded- Endpoint



【Inclusion criteria】

Patients with at least 1 of 7 conditions

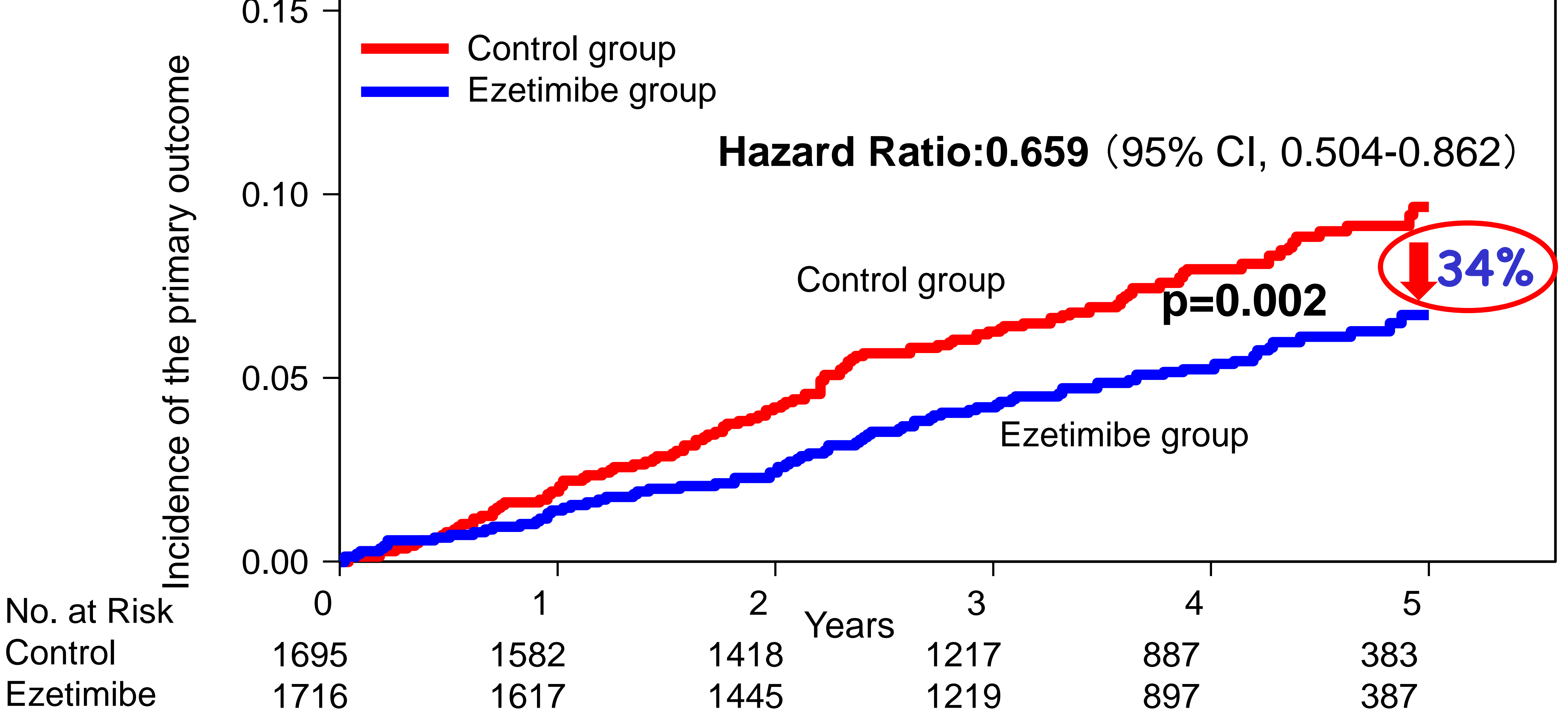
1. Diabetes mellitus
2. Hypertension
3. Low HDL-cholesterolemia
4. Hypertriglyceridemia
5. Smoking
6. Previous history of cerebral infarction documented by apparent clinical symptoms and CT/MRI scanning
7. Peripheral artery disease

◉ **Enrollment period: February 2009 to December 2014 (363 institutions participated.)**

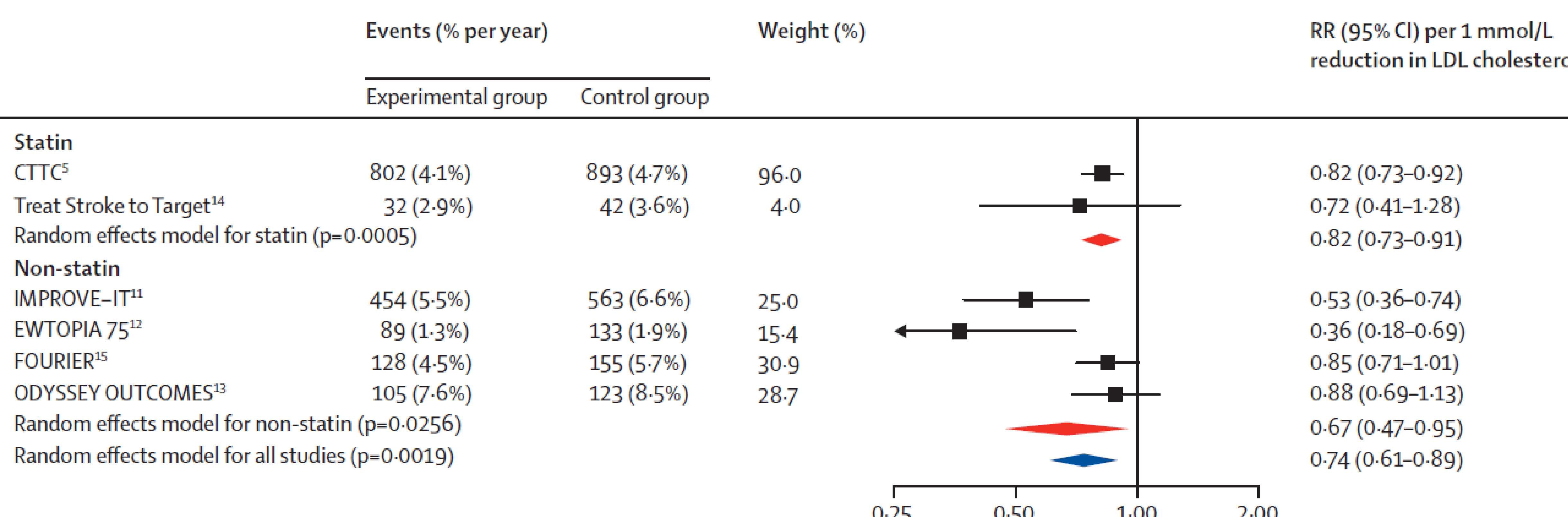
◉ **Follow-up period: February 2009 to March 2016**

Effect of ezetimibe treatment on the primary end-point

A composite of the atherosclerotic cardiovascular events (Sudden cardiac death, myocardial infarction, PCI or CABG, and/or stroke)

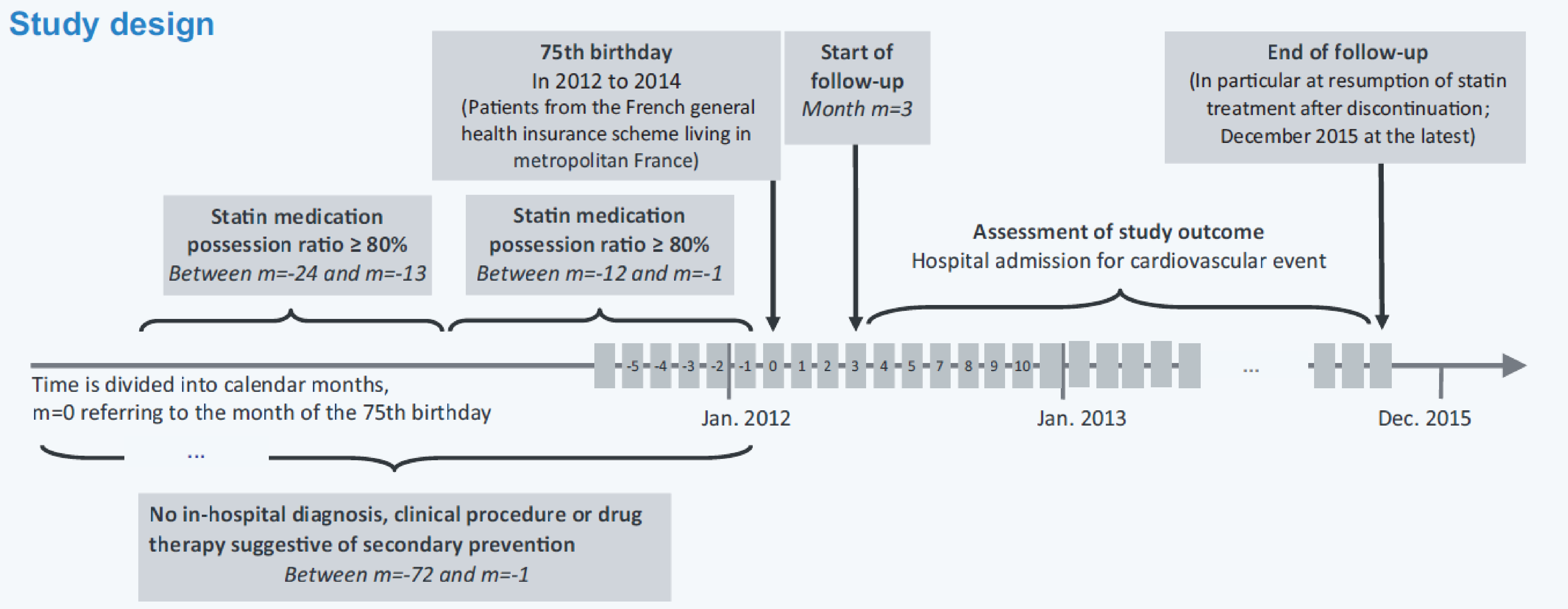


Efficacy and safety of lowering LDL cholesterol in older patients: a systematic review and meta-analysis of randomised controlled trials



www.thelancet.com **Published online November 10, 2020** **https://doi.org/10.1016/S0140-6736(20)32332-1**

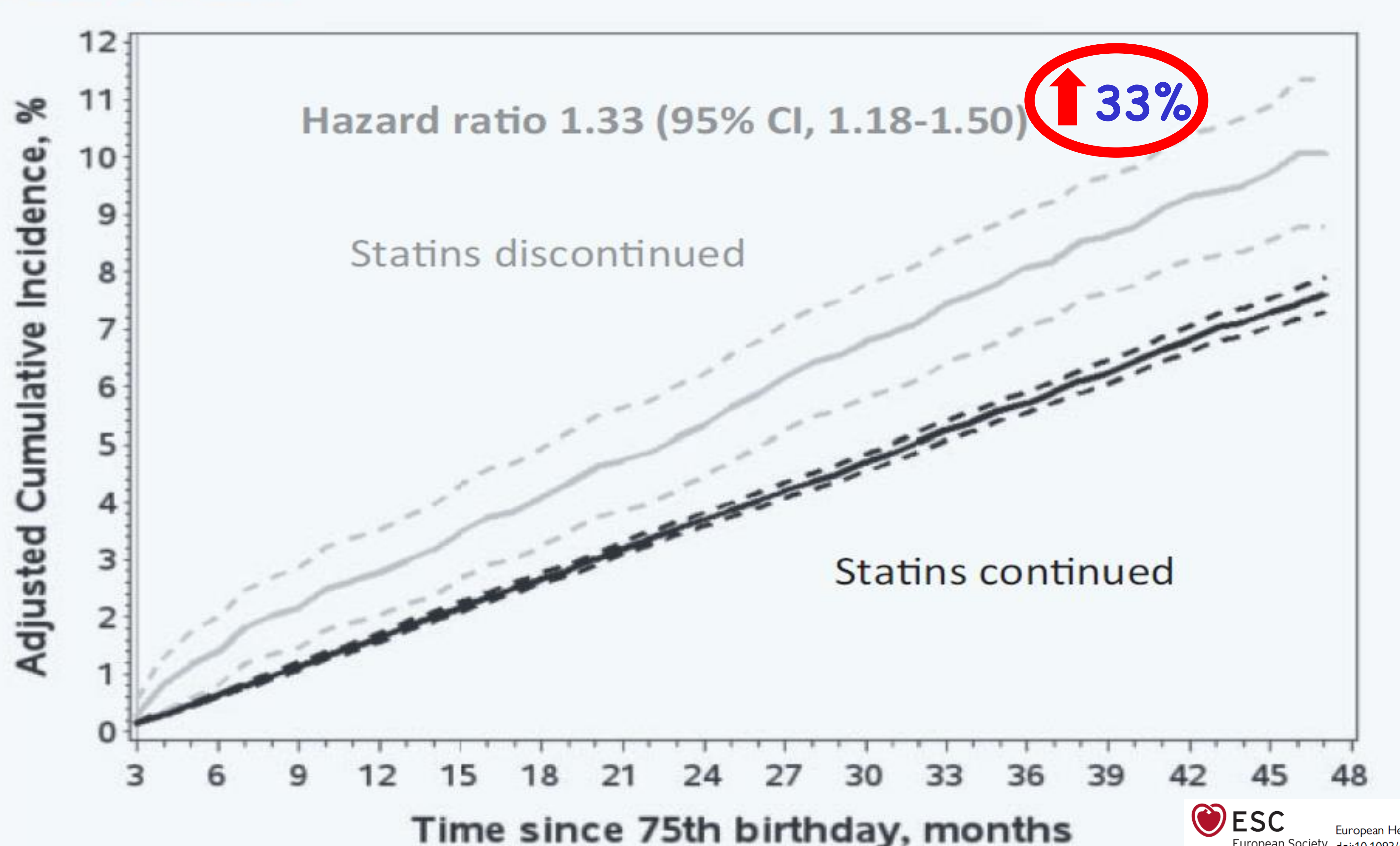
Cardiovascular effect of discontinuing statins for primary prevention at the age of 75 years: a nationwide population-based cohort study in



ESC European Society of Cardiology

European Heart Journal (2019) **0**, 1–10
doi:10.1093/eurheartj/ehz458

Principal result



ESC
European Society of Cardiology
European Heart Journal (2019) **0**, 1–10
doi:10.1093/eurheartj/ehz458

CV Outcome Trials on the Horizon

A clinical trial of STAtin therapy for Reducing Events in the Elderly (STAREE)

- Double-blind, randomized, placebo-controlled trial
- 18,000 primary prevention men and women age >70 years across Australia
  - Atorvastatin 40 mg daily vs placebo
- Primary Endpoint: death, development of dementia, development of disability, or major fatal or non-fatal cardiovascular event
- 5-year duration; estimated completion December 2023

https://www.monash.edu/medicine/staree/home
https://clinicaltrials.gov/ct2/show/NCT02099123

PRagmatic EValuation of evENTs And Benefits of Lipid-lowEring in older adults (PREVENTABLE)

- Double-blind, randomized, placebo-controlled trial
- 20,000 primary prevention men and women age ≥75 years in the US
  - Atorvastatin 40 mg daily vs placebo
- Primary Endpoint: development of dementia or persistent disability
- Secondary Endpoint: composite CV events
- 5-year duration; estimated completion July 2027

https://preventabletrial.org/home.cfm
https://clinicaltrials.gov/ct2/show/NCT04262206

ΕΡΩΤΗΣΗ 3: ΤΙ ΛΕΝΕ ΟΙ ΟΔΗΓΙΕΣ;

Secondary ASCVD Prevention

Recommendations for Statin Therapy Use in Patients With ASCVD		
COR	**LOE**	**Recommendations**
IIa	**B-R**	**In patients older than 75 years of age with clinical ASCVD, it is reasonable to initiate moderate- or high-intensity statin therapy after evaluation of the potential for ASCVD risk reduction, adverse effects, and drug–drug interactions, as well as patient frailty and patient preferences.**
IIa	**C-LD**	**In patients older than 75 years of age who are tolerating high-intensity statin therapy, it is reasonable to continue high-intensity statin therapy after evaluation of the potential for ASCVD risk reduction, adverse effects, and drug-drug interactions, as well as patient frailty and patient preferences.**

Primary Prevention in Older Adults

Recommendations for Older Adults		
COR	LOE	Recommendations
IIb	B-R	In adults 75 years of age or older with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), initiating a moderate-intensity statin may be reasonable.
IIb	B-R	In adults 75 years of age or older, it may be reasonable to stop statin therapy when functional decline (physical or cognitive), multimorbidity, frailty, or reduced life-expectancy limits the potential benefits of statin therapy.
IIb	B-R	In adults 76 to 80 years of age with an LDL-C level of 70 to 189 mg/dL_(1.7 to 4.8 mmol/L), it may be reasonable to measure CAC to reclassify those with a CAC score of zero to avoid statin therapy.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

Recommendations for the treatment of dyslipidaemias in older people (aged >65 years)

Recommendations	Class	Level
Treatment with statins is recommended for older people with ASCVD in the same way as for younger patients.	I	A
Treatment with statins is recommended for primary prevention, according to level of risk, in older people aged ≤75.	I	A
Initiation of statin treatment for primary prevention in older people aged >75 may be considered, if at high risk or above.	IIb	B
It is recommended that the statin is started at a low dose if there is significant renal impairment and/or the potential for drug interactions, and then titrated upwards to achieve LDL-C treatment goals.	I	C

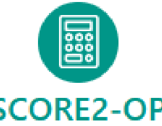
2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

New calculators based on European populations

Apparently healthy < 70 years
No previous cardiovascular disease or type 2 diabetes mellitus

SCORE2

Apparently healthy ≥ 70 years
Elderly without previous cardiovascular disease or type 2 diabetes mellitus



SCORE2-OP

Cardiovascular disease risk categories based on SCORE2 and SCORE2-OP in apparently healthy people according to age

	<50 years	50-69 years	≥70 years[a]
Low-to-moderate CVD risk: risk factor treatment generally not recommended	<2.5%	<5%	<7.5%
High CVD risk: risk factor treatment should be considered	2.5 to <7.5%	5 to <10%	7.5 to <15%
Very high CVD risk: risk factor treatment generally recommended[a]	≥7.5%	≥10%	≥15%

©ESC

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

SCORE2 and SCORE2-OP risk chart for fatal and non-fatal (MI, stroke) ASCVD

Moderate CVD Risk (1)

SCORE2 & SCORE2-OP

10-year risk of (fatal and non-fatal) CV events in populations at moderate CVD risk

	<50 years	50-69 years	≥70 years
Green	<2.5%	<5%	<7.5%
Orange	2.5 to <7.5%	5 to <10%	7.5 to <15%
Red	≥7.5%	≥10%	≥15%

Columns: Women (Non-smoking, Smoking), Men (Non-smoking, Smoking); Non-HDL cholesterol mmol/L: 3.0-3.9, 4.0-4.9, 5.0-5.9, 6.0-6.9 (mg/dL: 150, 200, 250)

Age (y)	Systolic blood pressure (mmHg) SCORE2-OP	Women Non-smoking 3.0-3.9	4.0-4.9	5.0-5.9	6.0-6.9	Women Smoking 3.0-3.9	4.0-4.9	5.0-5.9	6.0-6.9	Men Non-smoking 3.0-3.9	4.0-4.9	5.0-5.9	6.0-6.9	Men Smoking 3.0-3.9	4.0-4.9	5.0-5.9	6.0-6.9
85-89	160-179	37	39	40	42	41	43	44	46	37	45	53	62	37	45	53	61
	140-159	35	36	38	39	39	40	42	43	36	43	51	59	35	43	51	59
	120-139	32	34	35	37	36	38	39	41	34	41	49	57	34	41	48	57
	100-119	30	32	33	34	34	35	37	38	32	39	47	55	32	39	46	55
80-84	160-179	27	28	30	31	34	35	37	39	30	35	41	47	34	40	46	53
	140-159	24	25	27	28	30	32	33	35	27	32	37	43	31	36	42	48
	120-139	21	22	24	25	27	28	30	31	25	29	34	40	28	33	38	44
	100-119	19	20	21	22	24	25	27	28	22	26	31	36	25	30	35	40
75-79	160-179	19	20	21	23	27	29	30	32	24	27	31	35	31	35	39	44
	140-159	16	17	18	19	24	25	26	28	21	23	27	30	27	30	34	38
	120-139	14	15	15	16	20	21	22	24	17	20	23	26	23	26	29	33
	100-119	12	12	13	14	17	18	19	20	15	17	19	22	19	22	25	29
70-74	160-179	13	14	15	16	22	23	25	26	19	21	23	25	28	31	34	36
	140-159	11	11	12	13	18	19	20	22	15	17	18	20	23	25	28	30
	120-139	9	9	10	11	15	16	17	18	12	13	15	16	19	20	22	24
	100-119	7	7	8	8	12	13	13	14	10	11	12	13	15	16	18	20

©ESC

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

5-years risk
10-years risk
Current 10-year risk of myocardial infarction, stroke or cardiovascular death
0
5
29.5%
Current risk
Future treatment
LDL-cholesterol
Current 10-year risk of myocardial infarction, stroke, hospitalization for heart failure, or cardiovascular death
0
5
10
15
20
25
30
35
40
Percentage
Reset
Print
Copy

Hellenic Atherosclerosis Society
Guidelines
for the Diagnosis & Treatment
of Dyslipidemias 2023
HELLENIC ATHEROSCLEROSIS SOCIETY
25.05.2002

Recommendations for the management of dyslipidemia in the elderly.

TABLE 26. Recommendations for the management of dyslipidemia in the elderly.

Recommendation	Class of recommendation
Lipid-lowering treatment must aim at LDL-C levels <55, <70 and <100 mg/dL in very high, high, and moderate risk elderly patients (≤ 75 years old).	I
In very high- and high-risk elderly patients (≤ 75 years old), a reduction in baseline LDL-C levels by >50% is recommended	I
In very high- and high-risk elderly patients >75 years old, initiation of statin therapy should be considered	IIa
In the presence of renal impairment and/or drug interactions, statin therapy must be initiated at a low dose, and then titrated, if needed, to attain LDL-C target	I

LDL-C: low-density lipoprotein cholesterol

ΕΡΩΤΗΣΗ 4: ΤΙ ΠΡΕΠΕΙ ΝΑ ΠΡΟΣΕΧΩ ΟΤΑΝ ΣΥΝΤΑΓΟΓΡΑΦΩ ΥΠΟΛΙΠΙΔΑΙΜΙΚΗ ΘΕΡΑΠΕΙΑ ΣΤΟΥΣ ΥΠΕΡΗΛΙΚΕΣ;

ΣΤΑΤΙΝΕΣ ΣΕ ΗΛΙΚΙΩΜΕΝΟΥΣ

1) Νεφρική λειτουργία

2) Φαρμακευτικές αλληλεπιδράσεις-Πολυφαρμακία

3) Μυοπάθεια

4) Συννοσηρότητες

5) Μεταβολές στη φαρμακοκινητική και φαρμακοδυναμική

ΑΝΤΙΜΕΤΩΠΙΖΟΝΤΑΣ ΤΟΝ ΥΠΕΡΗΛΙΚΑ ΑΣΘΕΝΗ ΣΕ ΚΑΛΗ ΓΕΝΙΚΗ ΚΑΤΑΣΤΑΣΗ

- ROSUVASTATIN 10 mg Ή ΑΤΟΡΒΑΣΤΑΤΙΝΗ 20 mg Ή ΠΙΤΑΒΑΣΤΑΤΙΝΗ 4 mg

↓ LDL-C κατά ~40% → LDL-C 78 mg/dL

+ ΕΖΕΤΙΜΙΜΠΗ → LDL-C 62 mg/dL

ΣΥΜΠΕΡΑΣΜΑΤΑ

ΣΤΑΤΙΝΕΣ ΣΤΗΝ 3η ΗΛΙΚΙΑ

1. ΛΑΜΒΑΝΩ ΥΠΟΨΗ ΤΟ ΠΡΟΣΔΟΚΙΜΟ ΕΠΙΒΙΩΣΗΣ ΚΑΙ ΤΗ ΒΙΟΛΟΓΙΚΗ ΗΛΙΚΙΑ

2. ΣΤΗΝ ΕΓΚΑΤΕΣΤΗΜΕΝΗ ΑΓΓΕΙΑΚΗ ΝΟΣΟ Ή ΔΙΑΒΗΤΗ ΘΕΡΑΠΕΥΩ ΟΠΩΣ ΚΑΙ ΤΟΥΣ ΝΕΟΤΕΡΟΥΣ

3. ΔΕΝ ΣΤΑΜΑΤΑΩ ΤΗΝ ΑΓΩΓΗ ΛΟΓΩ ΤΗΣ ΗΛΙΚΙΑΣ per se ΕΚΤΟΣ End-of-life care

4. ΣΤΗΝ ΠΡΩΤΟΓΕΝΗ ΠΡΟΛΗΨΗ: ΜΕΤΡΙΕΣ ΔΟΣΕΙΣ ΣΤΑΤΙΝΩΝ

ΕΛΛΗΝΙΚΗ ΕΤΑΙΡΕΙΑ
ΑΘΗΡΟΣΚΛΗΡΩΣΗΣ
33η ΕΑΡΙΝΗ ΣΥΝΑΝΤΗΣΗ
ΔΙΗΜΕΡΙΔΑ
ΣΥΓΧΡΟΝΕΣ ΕΛΛΗΝΙΚΕΣ
ΚΑΤΕΥΘΥΝΤΗΡΙΕΣ ΟΔΗΓΙΕΣ
ΓΙΑ ΤΗ ΔΙΑΓΝΩΣΗ ΚΑΙ ΤΗΝ ΑΝΤΙΜΕΤΩΠΙΣΗ
ΤΩΝ ΔΥΣΛΙΠΙΔΑΙΜΙΩΝ
Web: atherosclerosis.gr
THE LAKE HOTEL
ΙΩΑΝΝΙΝΑ
31 ΜΑΡΤΙΟΥ
01 ΑΠΡΙΛΙΟΥ
2023

16ο Θερινό σχολείο
ΕΛΛΗΝΙΚΗΣ ΕΤΑΙΡΕΙΑΣ
ΑΘΗΡΟΣΚΛΗΡΩΣΗΣ
EAS
16 & 17
ΙΟΥΝΙΟΥ
2023
Αναργύρειος και
Κοργιαλένειος Σχολή
ΣΠΕΤΣΕΣ

10ο
Πανελλήνιο Συνέδριο
των Ομάδων
Εργασίας
1-2
Δεκεμβρίου
2023
Ξενοδοχείο Divani Caravel
ΑΘΗΝΑ
www.has2023.gr

94TH EAS CONGRESS
EUROPEAN ATHEROSCLEROSIS SOCIETY
ATHENS
May 24-27, 2026