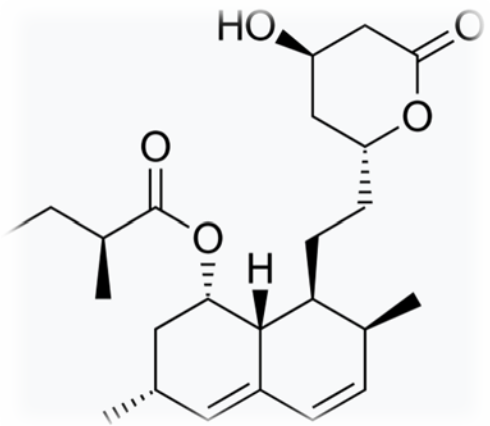
Azərbaycan Kardiologiya Cəmiyyəti

birincili və İkincili profilaktikada əsas statin tədqiqatları bizə nə deyir ?



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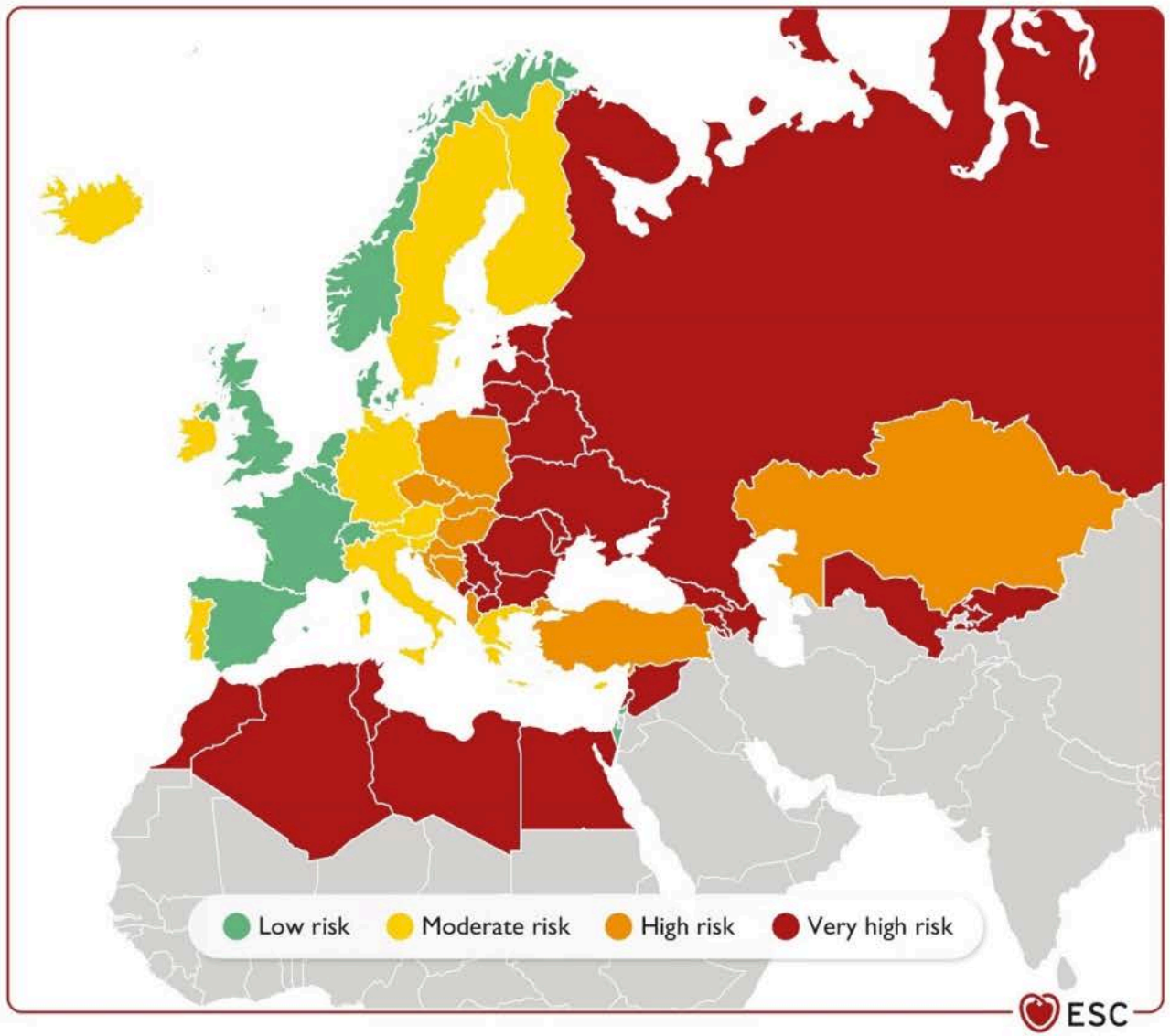
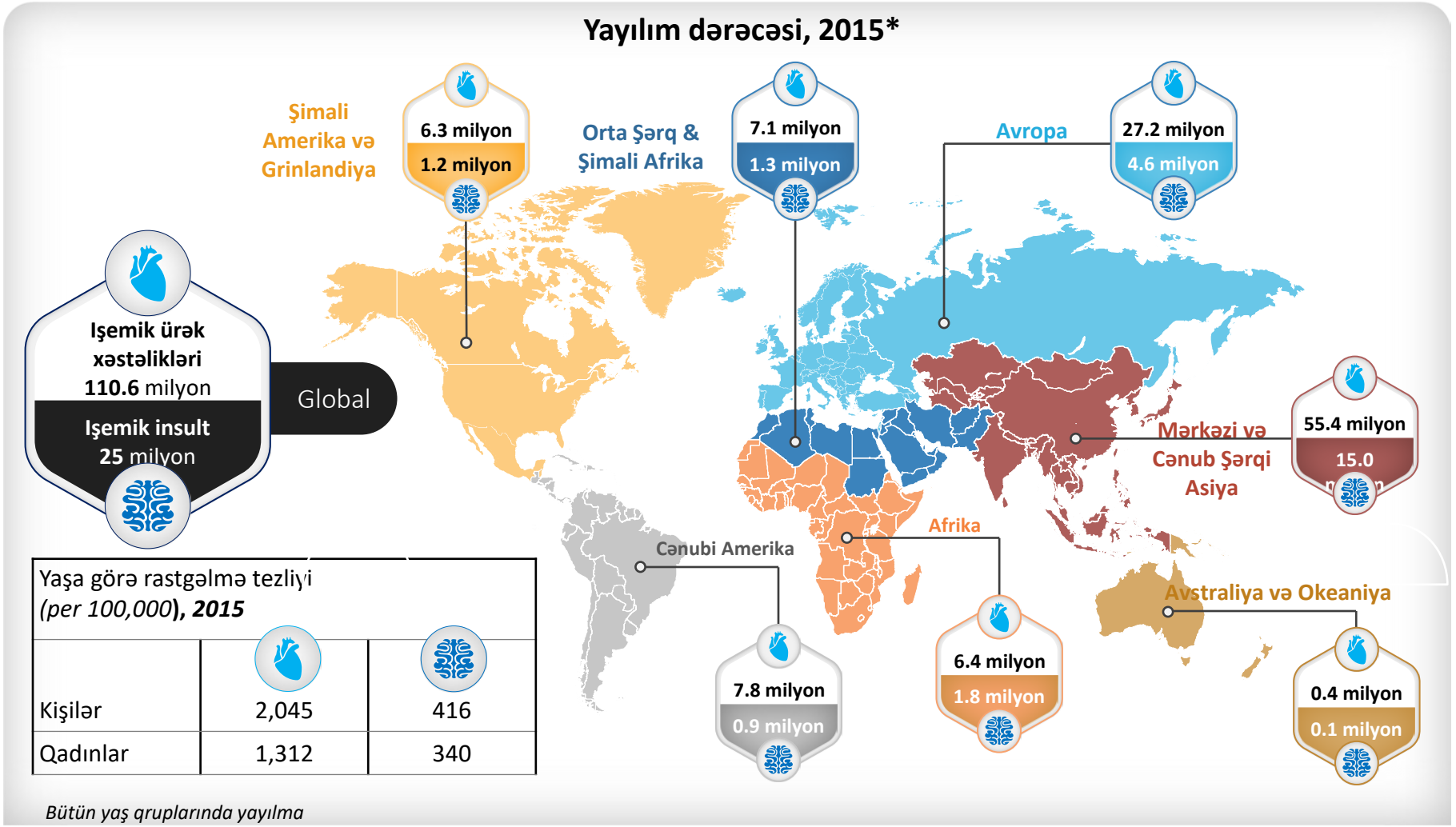


Risk regions based on World Health Organization cardiovascular mortality rates

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

ASVX global miqyasda 135 milyondan çox insana təsir edib

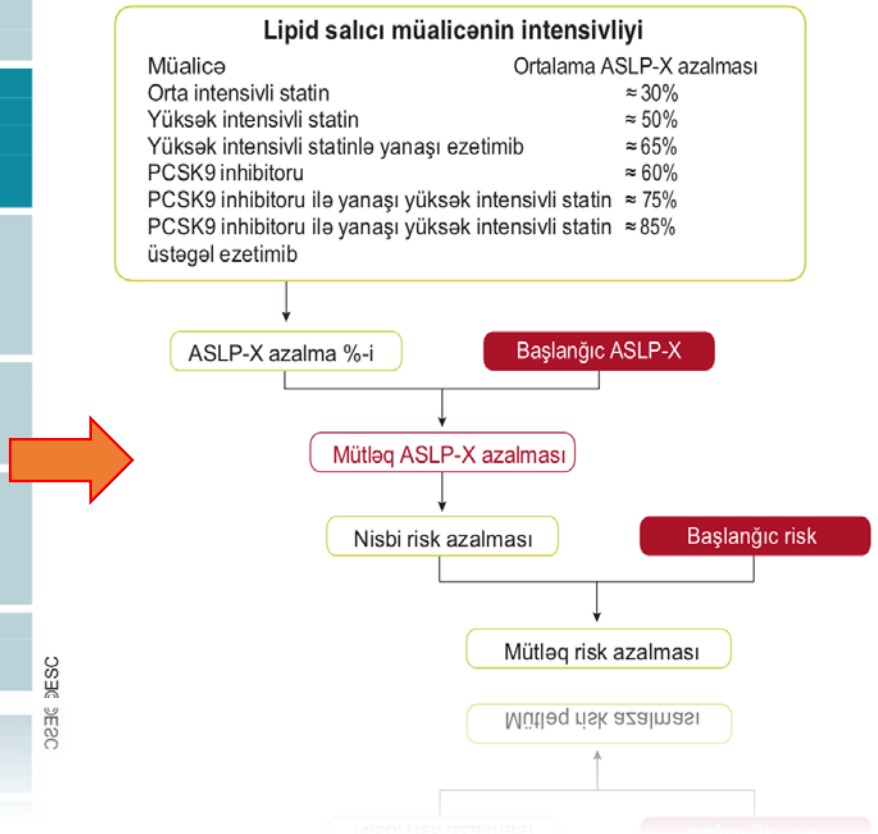


Roth GA et al. J Am Coll Cardiol. 2017;70(1):1-25 (and supplementary)

Aşağı sıxlıqlı lipoproteinli xolesterin salıcı farmakoloji müalicə üçün tövsiyyələr

Tövsiyyələr	Sinif[a]	Səviyyə[b]
Spesifik risk səviyyəsinə uyğun olaraq hədəf nəticə alana qədər qəbul oluna bilən ən yüksək doza statin ilə yüksək intensivlikli terapiya tövsiyə edilir.	I	A
Maksimal statinlə hədəf[c] əldə olunmazsa müalicəyə Ezetimib əlavə etmək tövsiyyə edilir.	I	B
Birincili profilaktika alan, AH olmayan, çox yüksək risk qrupunda maksimal statin və ezetimib ilə hədəf çatıla bilmədikdə PCSK9 inhibitorlarının kombinasiyası nəzərdə tutula bilər.	IIb	C
İkincili profilaktika alan, çox yüksək risk qrupuna aid olan pasientlərdə, maksimal statin və ezetimib ilə hədəf nəticə alınmırsa bir PCSK9 inhibitoru ilə kombinasiya tövsiyə olunur.	I	A
AH olan, çox yüksək risk qrupunda (ASÜDX və ya başqa böyük risk amili olan) maksimal statin+ ezetimib ilə hədəf nəticə alınmırsa PCSK9 inhibitorlarının kombinasiyası tövsiyə edilir.	I	C
Statin əsaslı müalicə rejimi qəbul oluna bilmədik (istənilən dozada, hətta təkrar başladıqdan sonra) ezetimib nəzərdə tutulmalıdır.	IIa	C
Statin əsaslı müalicə rejimi qəbul oluna bilmədik (istənilən dozada, hətta təkrar başladıqdan sonra) Ezetimibə PCSK9 inhibitorlarının əlavə olunması nəzərdə tutula bilər.	IIb	C
Maksimal statinlə hədəfə çatıla bilmədikdə öd turşusu sekvestrantları ilə kombinasiya nəzərdə tutula bilər	IIb	C

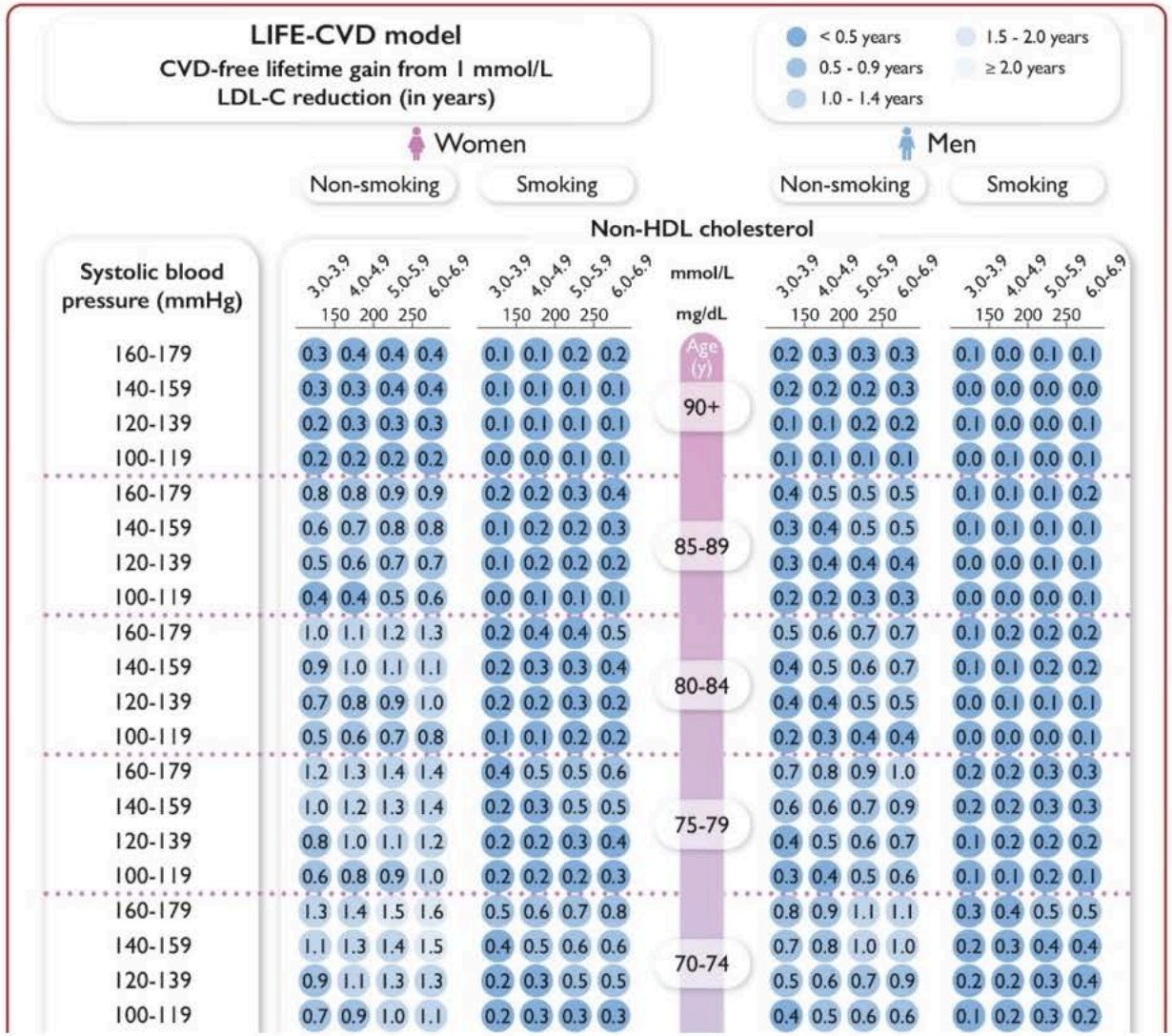
Hər hansı bir fərd üçün ASLP-X salıcı müalicənin gözlənilən klinik faydası təxmin edilə bilər; bu müalicənin intensivliyindən, başlanğıc ASLP-X səviyyəsindən, ASLP-X səviyyəsində gözlənilən mütləq azalmanın əldə olunması və ASÜDX-nin təxmin edilən başlanğıc riskindən asılıdır. Müalicənin intensivliyi fərdin təxmin edilən ASÜDX riskinə əsaslanmaqla ASLP-X-in tövsiyə olunan proporsional azalmasına nail olmaq üçün seçilməlidir. ASLP-X-də göstərilən proporsional azalma ilə başlanğıc ASLP-X səviyyəsinin hasili həmin müalicə ilə ASLP-X səviyyəsində gözlənilən mütləq azalmanı təxmin etməyə imkan verir. Çünki ASLP-X-də hər 1,0 mmol/l-lik azalma ÜD hadisəsi riskində 20%-lik azalma ilə əlaqədar olduğu üçün ASLP-X-də daha böyük proporsional azalmalarla nəticələnir. ASLP-X səviyyəsinin əldə ediləcək mütləq azalmasından gözlənilən mütənasib risk azalmasının fərdin ASÜDX-nin təxmin edilən başlanğıc riskinə vurulması həmin fərd üçün gözlənilən mütləq risk azalmasını müəyyən edir.



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	≥7.5%	≥10%	≥15%

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



Lifetime benefit:
Average # years free-of-CVD gained per 1 mmol/L LDL-C reduction

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
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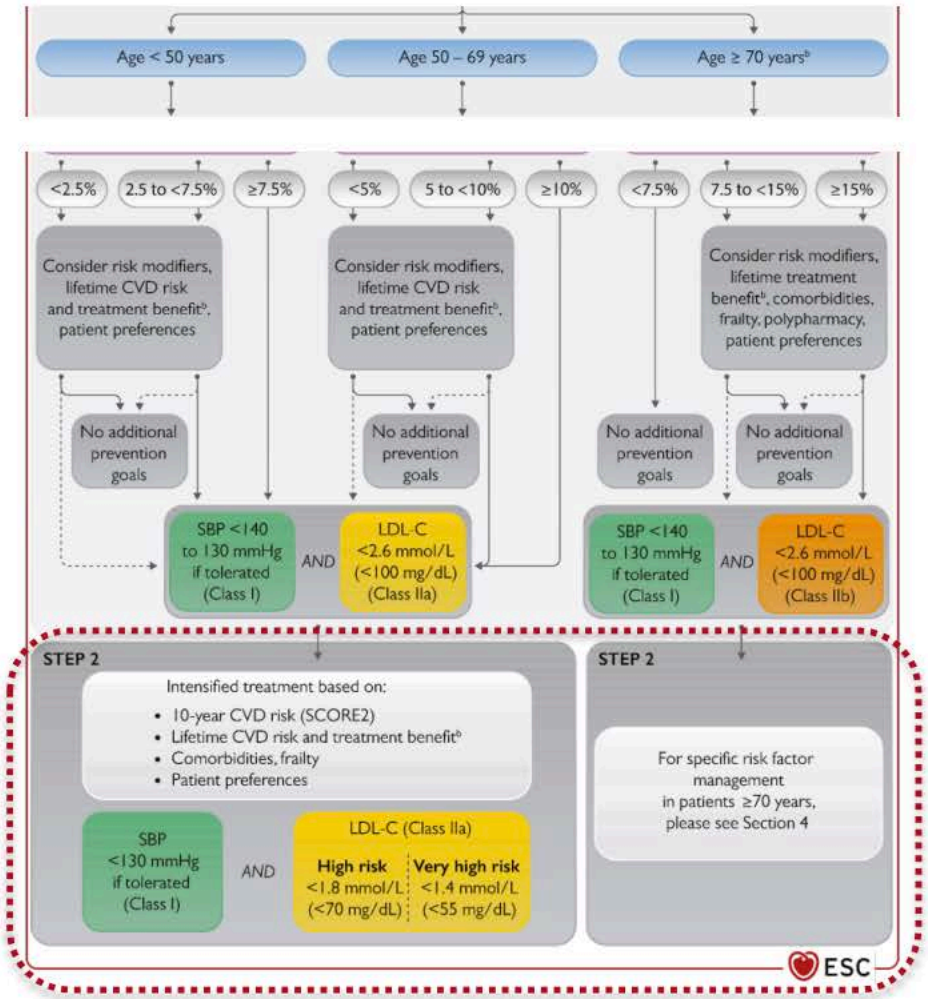
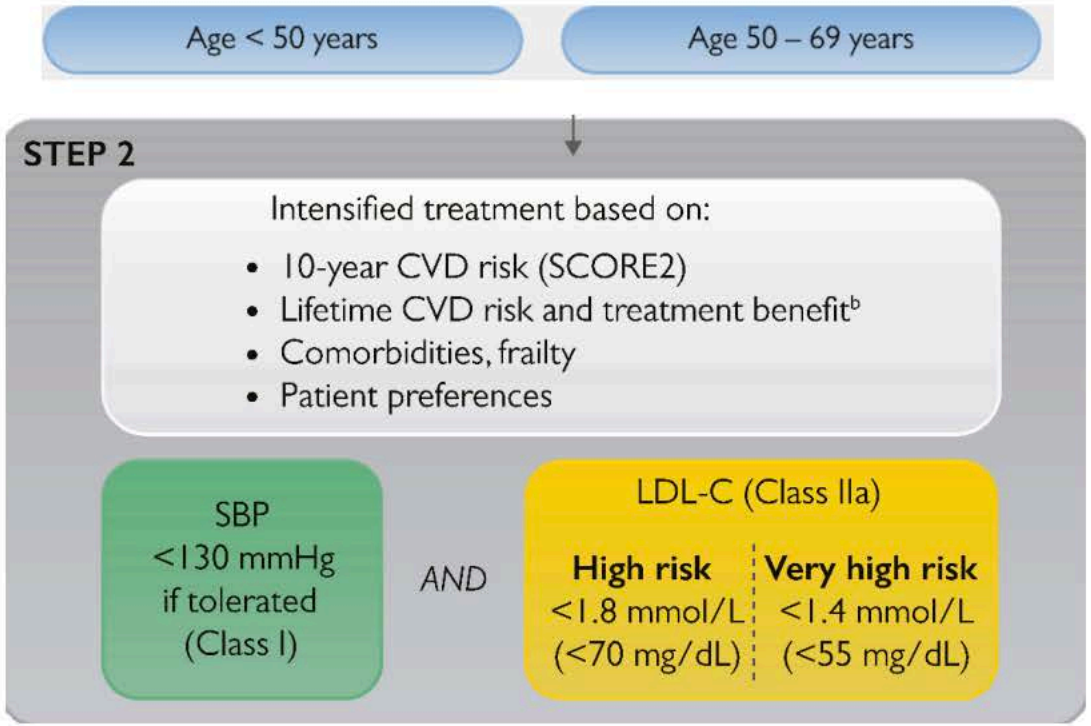


Always consider intensified treatment / step2



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

Among the lipid recommendations …

Recommendations	Class	Level
If the goals are not achieved with the maximum tolerated dose of a statin, combination with ezetimibe is recommended.	I	B
For primary prevention patients at very high risk, but without FH, if the LDL-C goal is not achieved on a maximum tolerated dose of a statin and ezetimibe, combination therapy including a PCSK9 inhibitor may be considered. …	IIb	C
Initiation of statin treatment for primary prevention in older people aged ≥70 may be considered, if at high risk or above.	IIb	B

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

WOSCOPS tədqiqatı

(West Of Scotland Coronary Primary Prevention Trial)

Birincili qoruma tədqiqatı - TXni 272 mg/dl, LDL-X'si 192 mg/dl, 45-64 yaş arası 6595 hiperkolesterolemik kişi pasientdə 40 mg pravastatinin, ÜİX mortallıq və morbiditə - iki ucu kor, plasebo kontrollu, randomize bir tədqiqatdır (4.9 il təqib)

The New England
Journal of Medicine

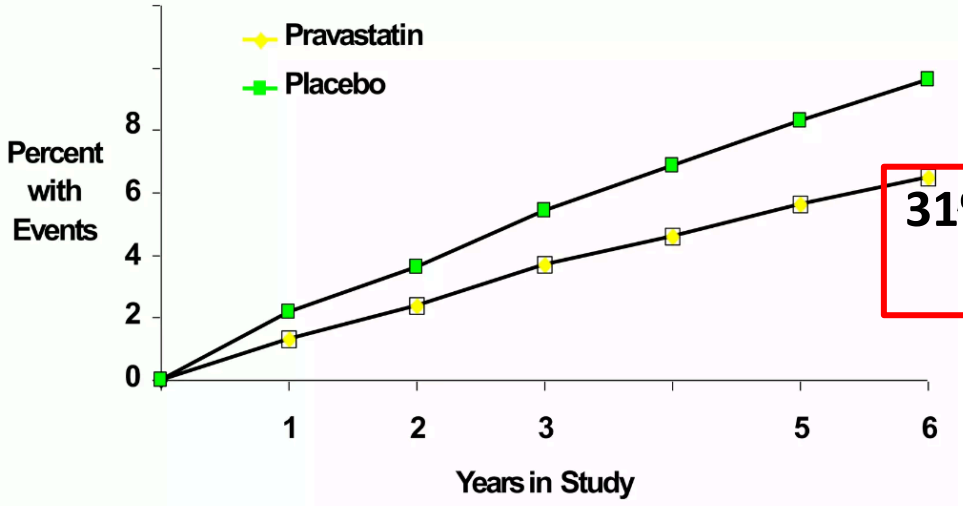
Volume 333 NOVEMBER 16, 1995 Number 20

PREVENTION OF CORONARY HEART DISEASE WITH PRAVASTATIN IN MEN WITH HYPERCHOLESTEROLEMIA

JAMES SHEPHERD, M.D., STUART M. COBBE, M.D., IAN FORD, PH.D., CHRISTOPHER G. ISLES, M.D., A. ROSS LORIMER, M.D., PETER W. MACFARLANE, PH.D., JAMES H. MCKILLOP, M.D., AND CHRISTOPHER J. PACKARD, D.SC., FOR THE WEST OF SCOTLAND CORONARY PREVENTION STUDY GROUP*

NONFATAL MI OR CHD DEATH

(PRIMARY ENDPOINT)



31% risk azalması
p = 0.0001

WOSCOPS RESULTS/CLINICAL EVENTS

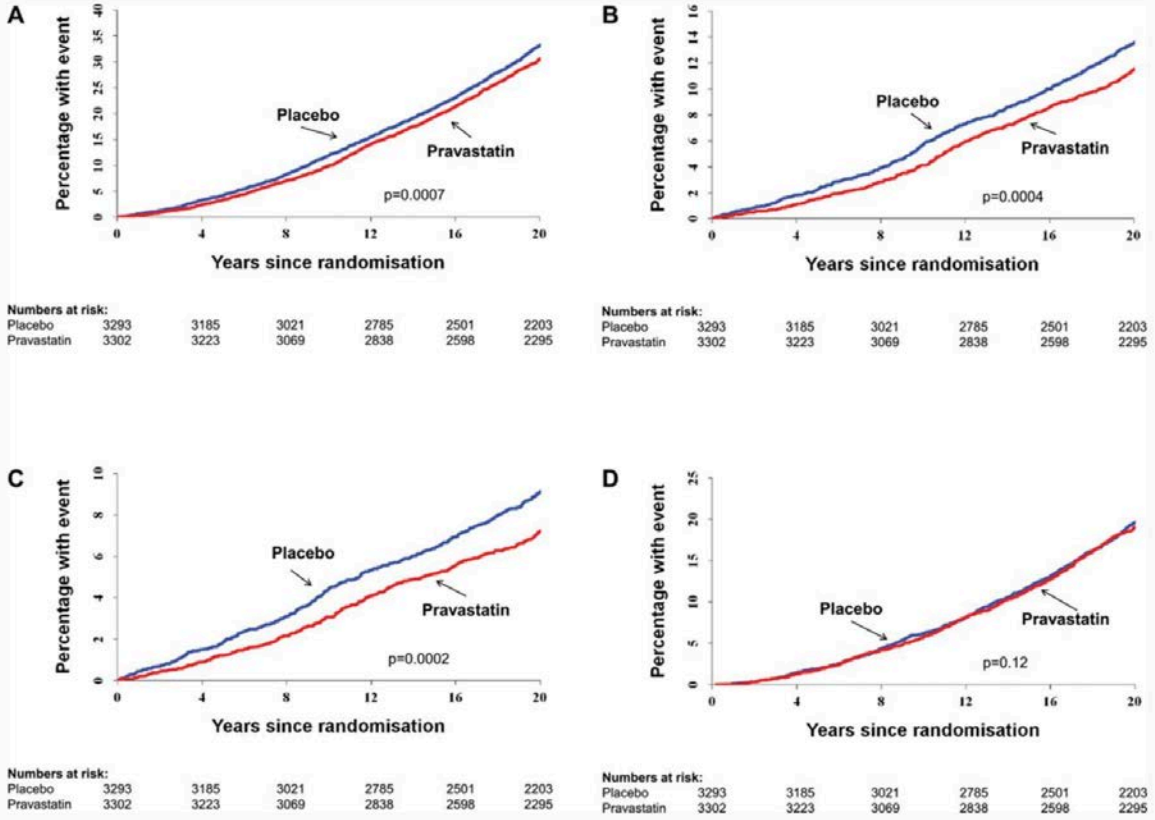
Event	% Reduction	p value
Nonfatal MI + CHD death	31%↓	< 0.001
Definite nonfatal MI	31%↓	< 0.001
Definite CHD death	28%↓	0.13 (NS)
Definite and suspected CHD death	33%↓	0.042
All cardiovascular deaths	32%↓	0.033
Total mortality	22%↓	0.051 (NS)
CABG/PTCA	37%↓	0.029

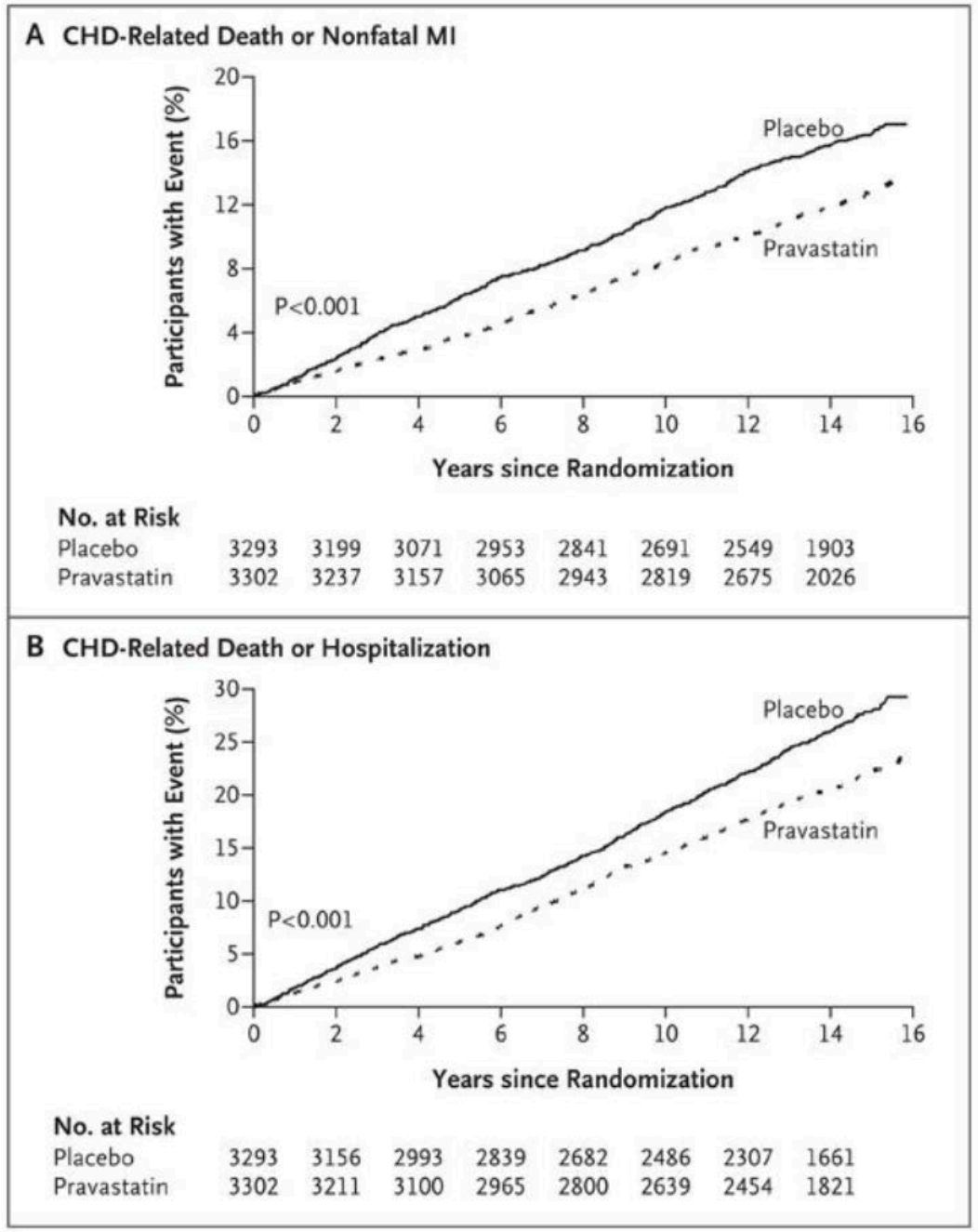
Long-Term Safety and Efficacy of Lowering Low-Density Lipoprotein Cholesterol With Statin Therapy

20-Year Follow-Up of West of Scotland Coronary Prevention Study

Ian Ford, **Heather Murray**, **Colin McCowan** ✉ and **Chris J. Packard**

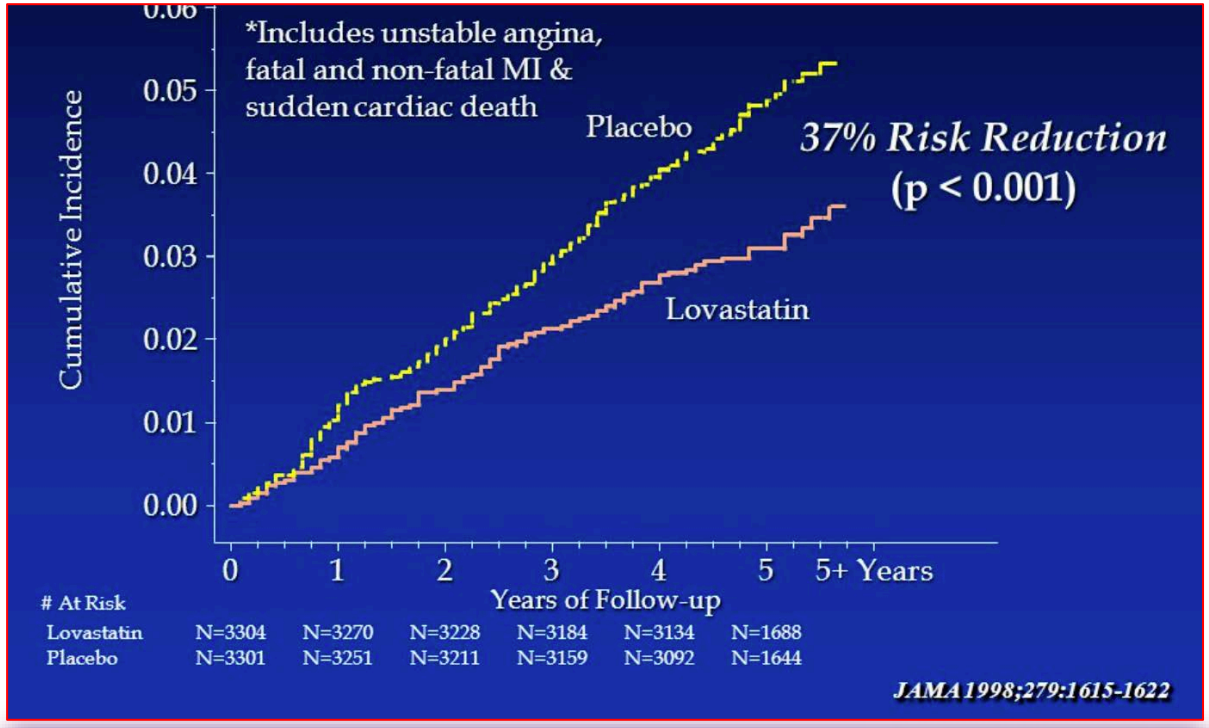
Originally published 10 Feb 2016 |
https://doi.org/10.1161/CIRCULATIONAHA.115.019014 |
Circulation. 2016;133:1073–1080

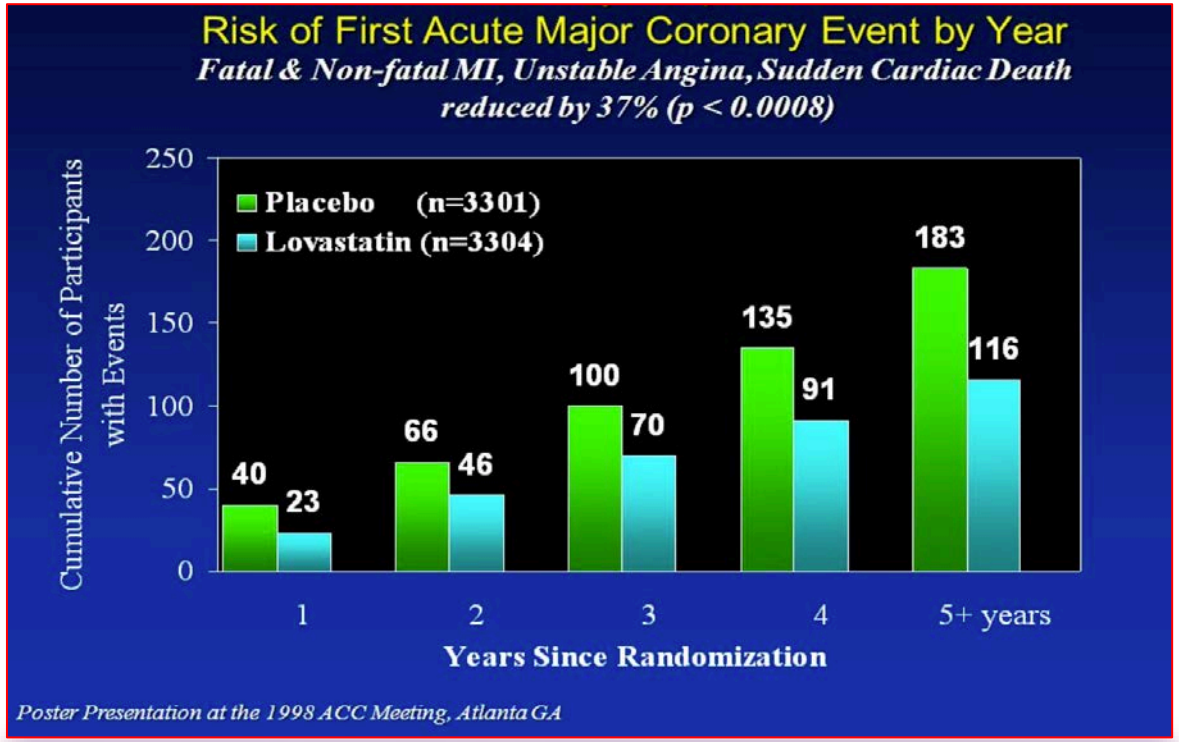




AFCAPS/TexCAPS tədqiqatı

(The Air Force/Texas Coronary Atherosclerosis Prevention Study)





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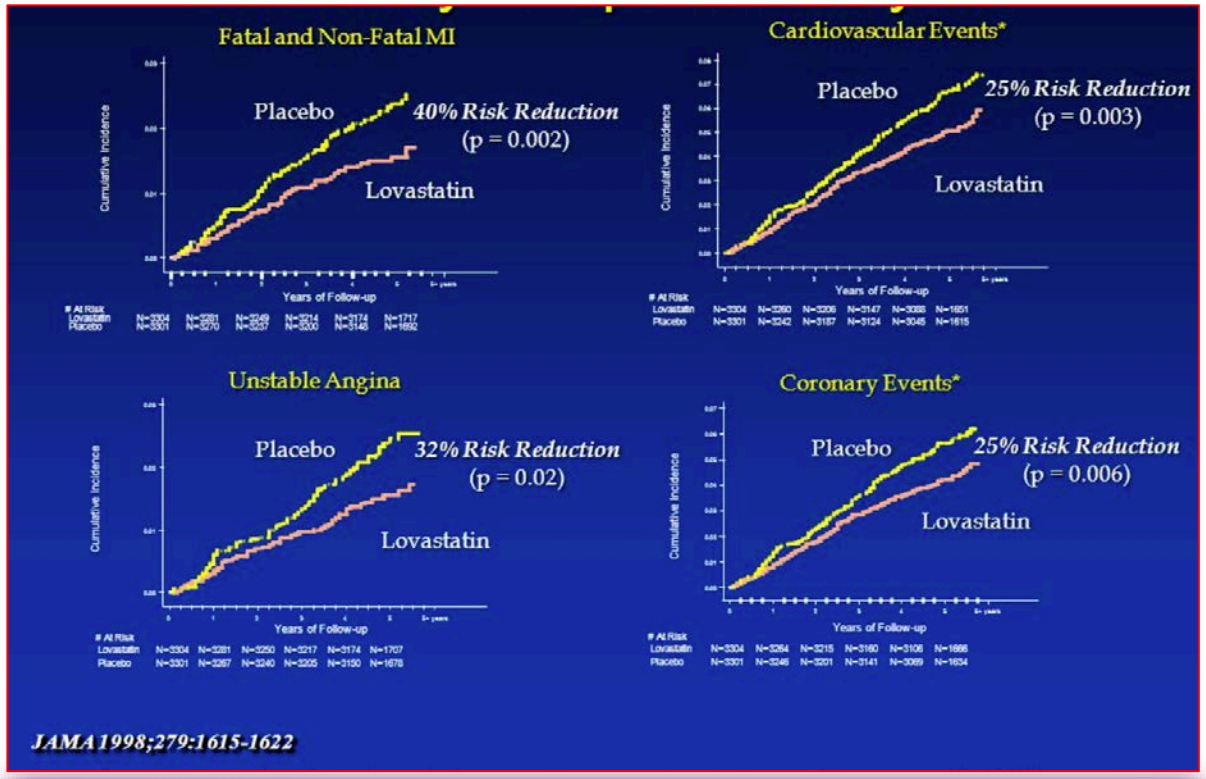


Men and women who are free of clinical evidence of atherosclerotic CVD, with average TC and LDL-C but below average HDL-C can obtain significant benefit from LDL-C reduction with lovastatin 20-40 mg/day.

Lovastatin 20-40 mg/day, (mean dose 30 mg/day) significantly reduced the risk of:

- ***The first acute major coronary event - by 37 % (p<0.001)***
- ***MI - by 40% (p=0.002)***
- ***Unstable angina - by 32% (p=0.02)***
- ***Coronary revascularization - by 33 % (p=0.001)***

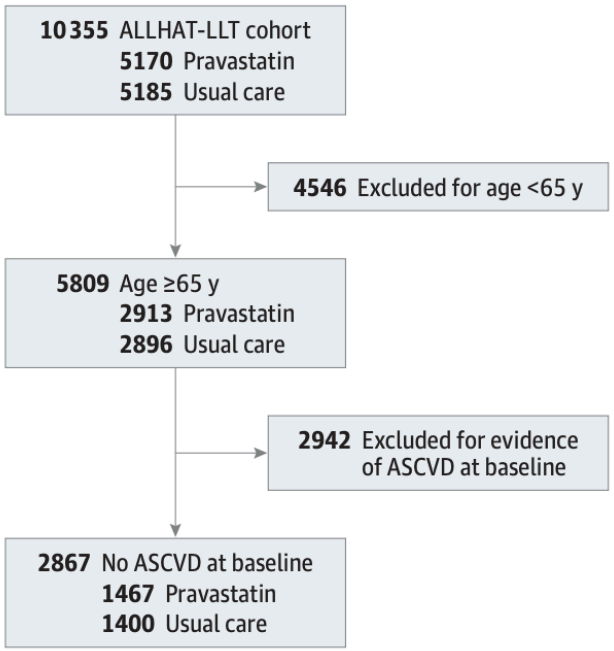
– ***Was generally well-tolerated (13.6% discontinuation rate compared with 13.8% for placebo)***

yaşlılarda primer qorumada statinlər (ALLHAT-LLT, JUPITER, HOPE-3)

JAMA Internal Medicine | Original Investigation

Effect of Statin Treatment vs Usual Care on Primary Cardiovascular Prevention Among Older Adults
The ALLHAT-LLT Randomized Clinical Trial

Benjamin H. Han, MD, MPH; David Sutin, MD; Jeff D. Williamson, MD; Barry R. Davis, MD, PhD; Linda B. Piller, MD, MPH; Hannah Pervin, PhD; Sara L. Pressel, MS; Caroline S. Blaum, MD; for the ALLHAT Collaborative Research Group



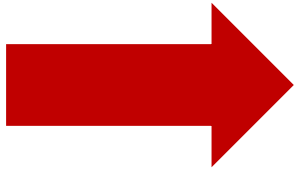
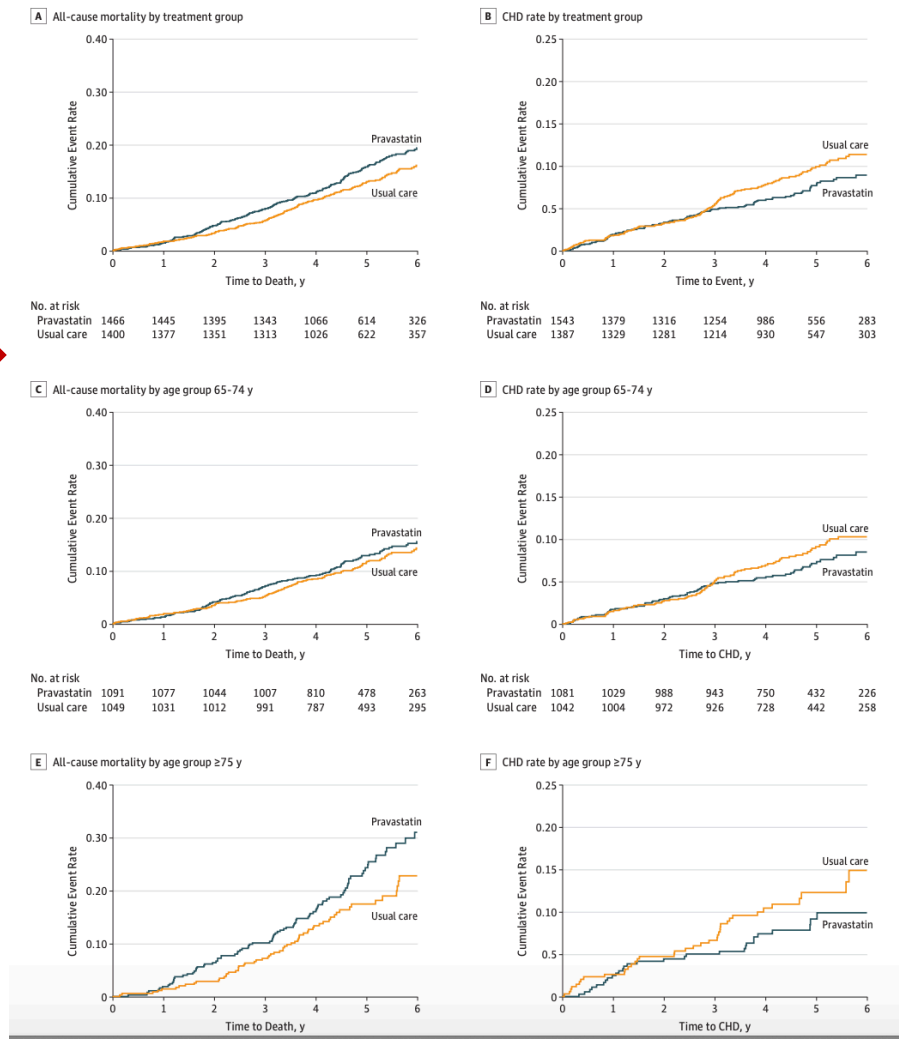


Figure 2. All-Cause Mortality and Coronary Heart Disease (CHD) Deaths Plus Nonfatal Myocardial Infarction by Treatment Group (Pravastatin vs Usual Care) and Age



yaşlılarda primer qorumada statinlər (ALLHAT-LLT, JUPITER, HOPE-3)

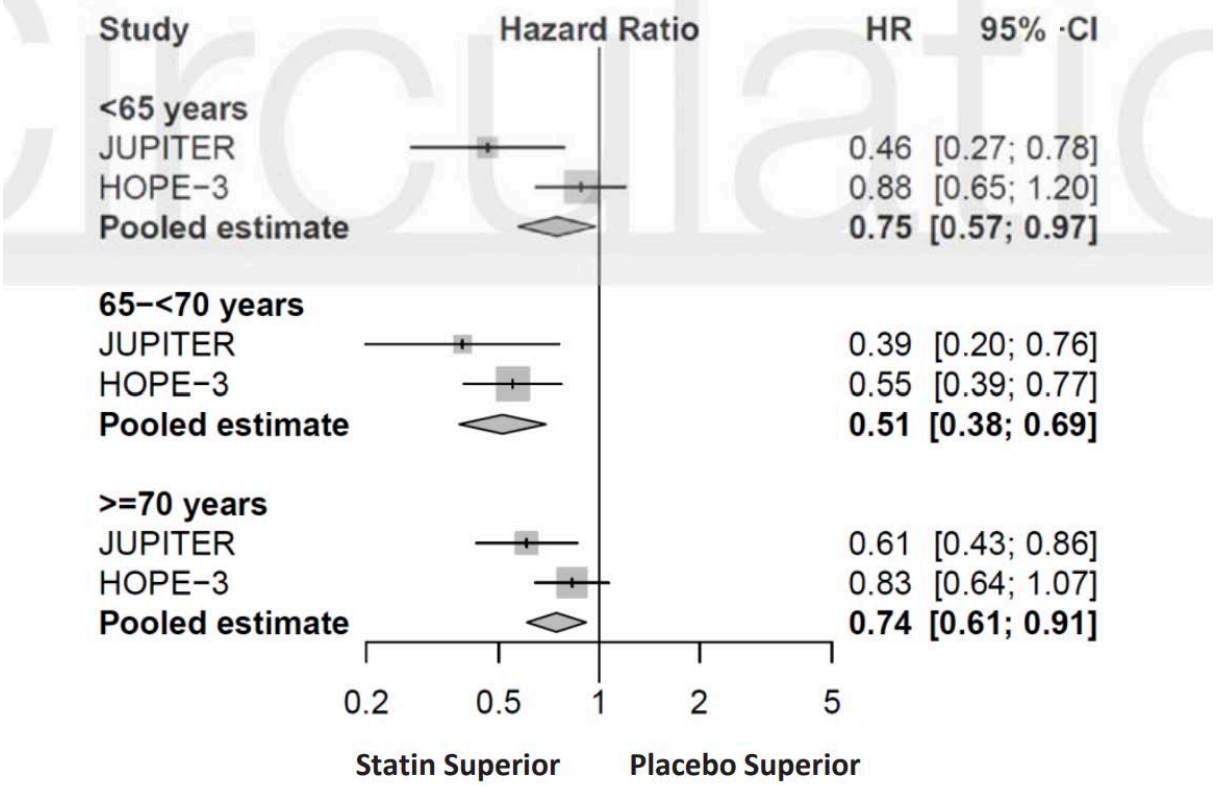
Effects of rosuvastatin on the composite endpoint of nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death in the JUPITER and HOPE-3 primary prevention trials, stratified by age.

Age Group	Trial	N	Rosuvastatin N (IR*)	Placebo N (IR*)
< 65 years	JUPITER	7,458	20 (0.27)	45 (0.59)
	HOPE-3	6,059	78 (0.46)	88 (0.53)
65-< 70 years	JUPITER	4,649	12 (0.24)	30 (0.61)
	HOPE-3	3,559	50 (0.50)	91 (0.91)
≥ 70 years	JUPITER	5,695	51 (0.82)	82 (1.36)
	HOPE-3	3,086	107 (1.25)	125 (1.50)

*rates are per 100 person-years. The test for heterogeneity by age for the effects of statin therapy on clinical outcomes was non-significant (P=0.10).

Primary Prevention With Statin Therapy in the Elderly:

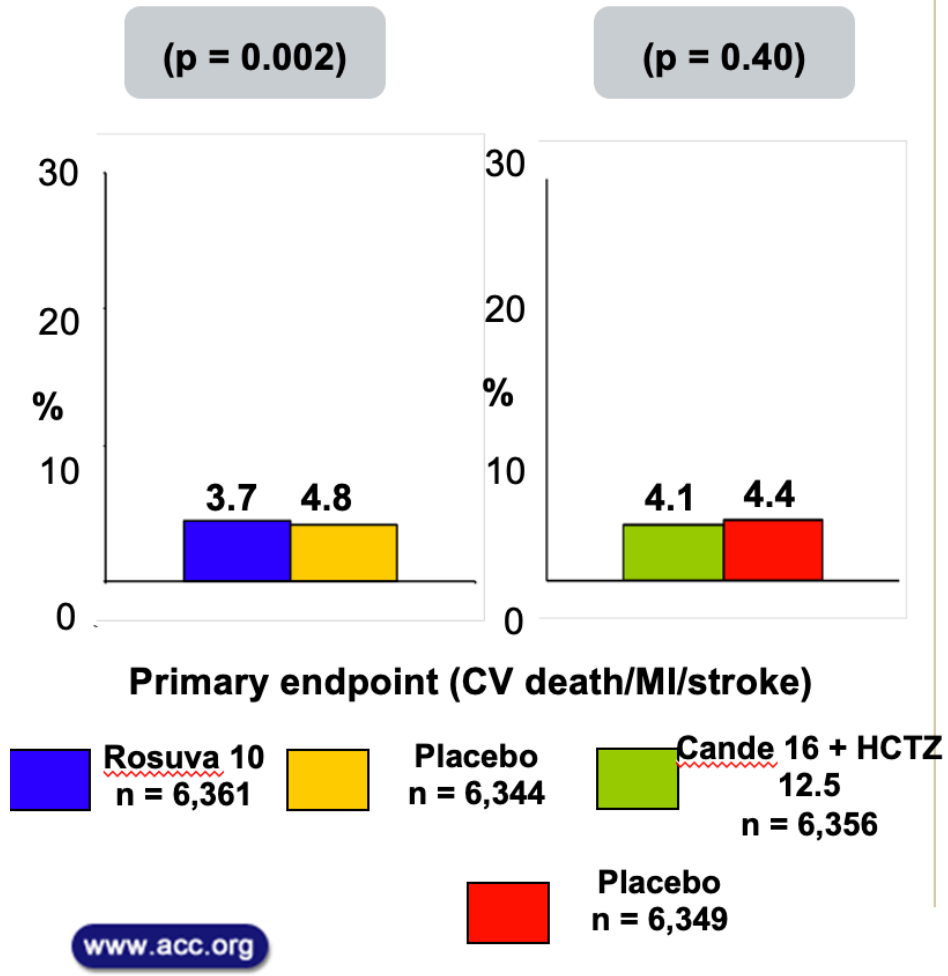
New Meta-Analyses from the Contemporary JUPITER and HOPE-3 Randomized Trials



doi:10.1161/circulationaha.117.028271

HOPE-3

Trial design: Patients without known cardiovascular disease, and with an intermediate risk of cardiovascular events, were randomized in a 2 x 2 factorial design to either cholesterol lowering or BP lowering or both. Patients were followed for a median of 5.6 years.



Results

- Primary endpoint: CV death/MI/stroke
- Rosuvastatin vs. placebo: 3.7% vs. 4.8%, HR 0.76, 95% CI 0.64-0.91, p = 0.002
- Candesartan + HCTZ vs. placebo: 4.1% vs. 4.4%, HR 0.93, 95% CI 0.79-1.1, p = 0.40
- Rosuvastatin + candesartan + HCTZ vs. placebo: 3.6% vs. 5.0%, HR 0.71, 95% CI 0.56-0.9, p = 0.005

Conclusions

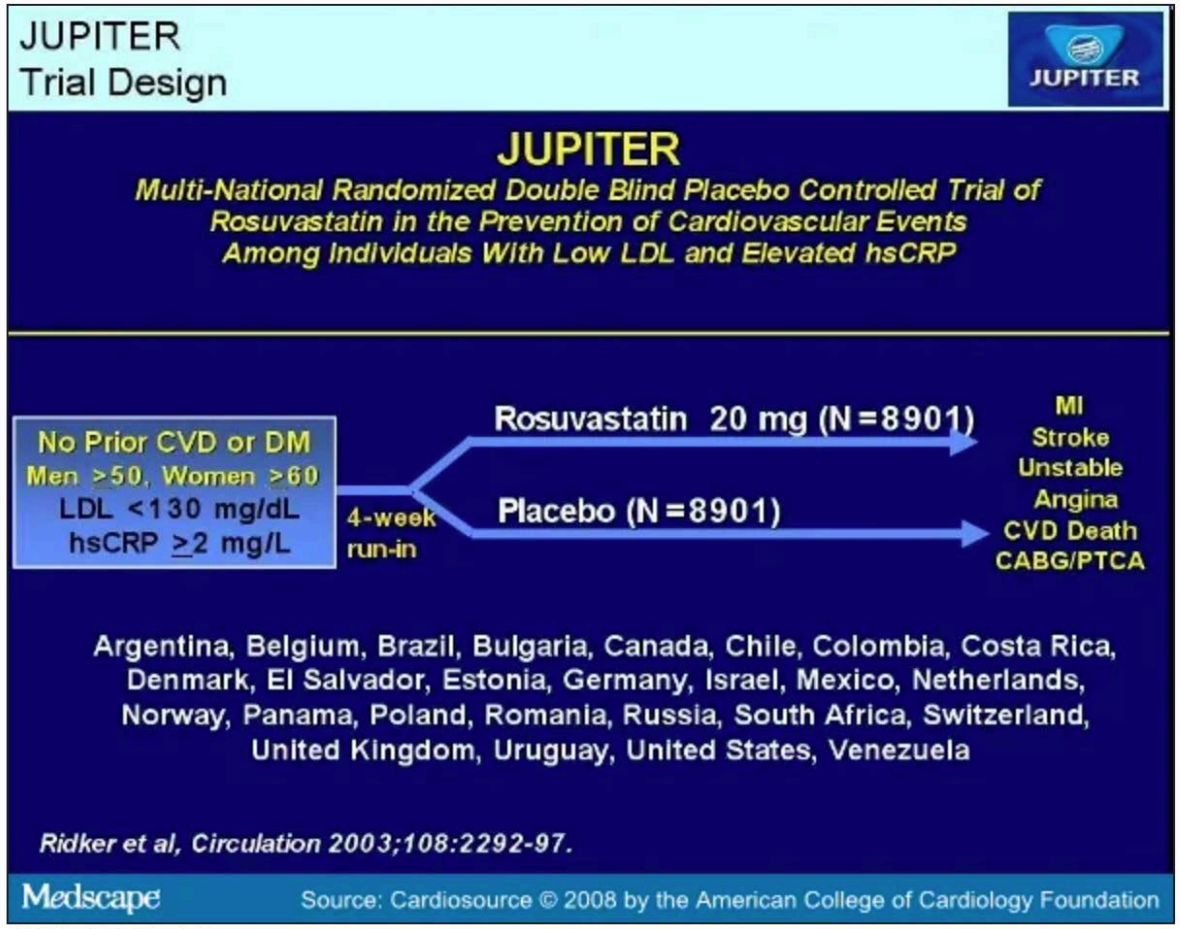
- Fixed-dose treatment with low-dose statin therapy, but not BP agents, was superior to placebo in reducing long-term cardiovascular events in an intermediate-risk population; combination group with benefits similar to statin arm
- Provides support for a risk-based approach to the management of patients with hyperlipidemia and hypertension

HOPE-3 Investigators. N Engl J Med 2016;Apr 2:[Epub]

ORIGINAL ARTICLE

Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein

Paul M Ridker, M.D., Eleanor Danielson, M.I.A., Francisco A.H. Fonseca, M.D., Jacques Genest, M.D., Antonio M. Gotto, Jr., M.D., John J.P. Kastelein, M.D., Wolfgang Koenig, M.D., Peter Libby, M.D., Alberto J. Lorenzatti, M.D., Jean G. MacFadyen, B.A., Børge G. Nordestgaard, M.D., James Shepherd, M.D., et al., for the JUPITER Study Group*



17802 xəstəni əhatə edən uzunmüddətli, randomizə edilmiş, ikiqat kor, plasebo kontrollu tədqiqatdır.
Rosuvastatinin 20 mq qəbulunun aşağı və ya normal LDL-xolesterin səviyyələri və KV riski yüksək olan xəstələrdə əsas ürək-damar hadisələrinə (miokard infarktı, insult, revaskulyarizasiya, qeyri-sabit angina ilə xəstəxanaya yerləşdirmə və ya CV ölümü) təsirini ortaya çıxarmaq üçün aparılmışıdır.
Tədqiqat SCORE risk balı ≥5 olan, gündəlik 20 mq rosuvastatin qəbul edən, aşağı və ya normal LDL-xolesterol səviyyələri olan kişilərdə və qadınlarda ilkin son nöqtənin plasebo ilə müqayisədə 44% azalması ilə nəticələndi
(miokard infarktı, insult və ya CV ölüm riski 53%, p 0.0001), ölümcül və ölümcül olmayan miokard infarktı riskinin demək olar ki, yarıba-yarı azalması (49%, p=0.03), insultda riskin yarıdan çox azalması (58%, p 0.0001) qeyd edildi.
Daha sonra orta LDL-xolesterol səviyyəsi 54 mg/dl olaraq ölçüldü.

JUPITER tədqiqatı

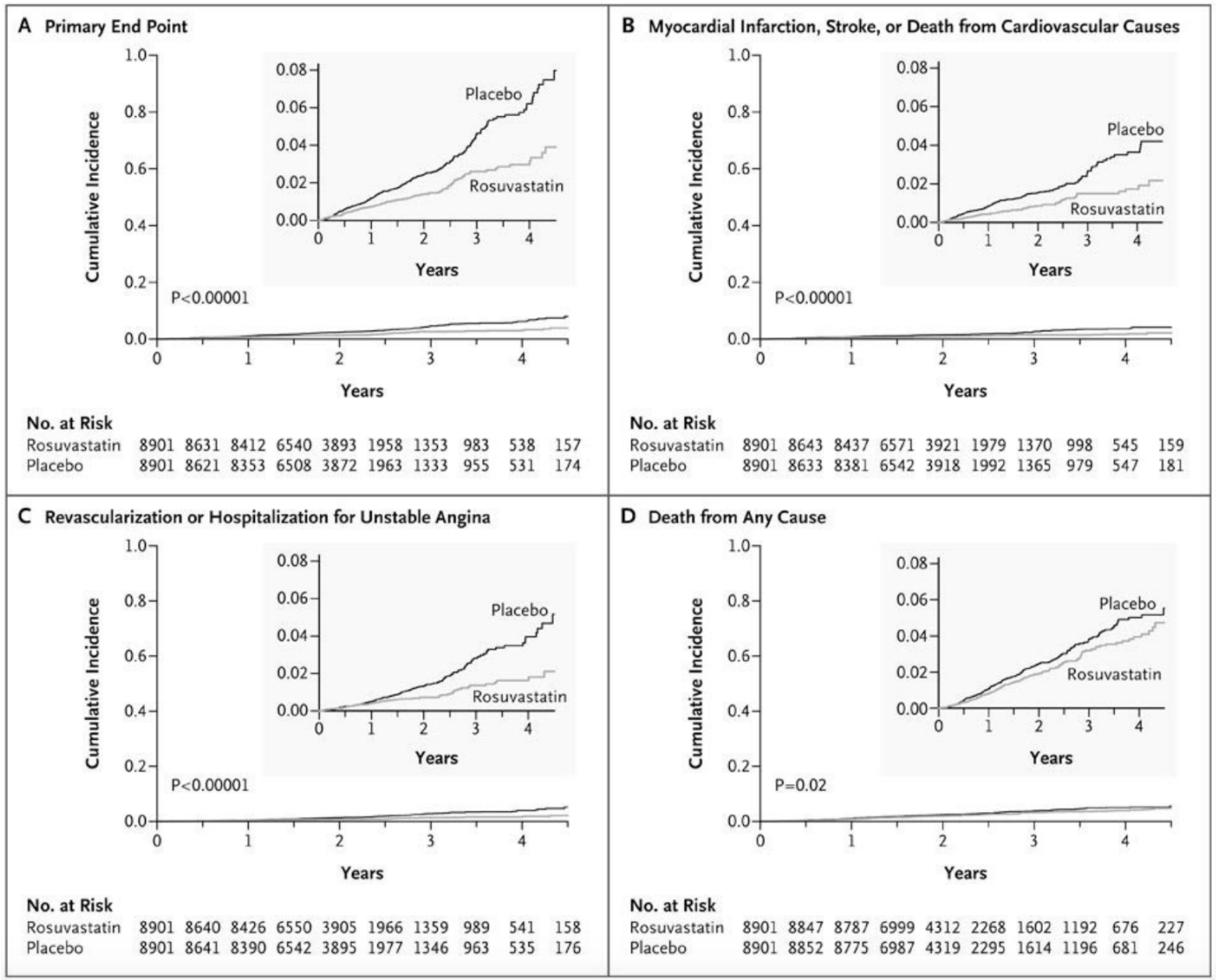


Table 4. Monitored Adverse Events, Measured Laboratory Values, and Other Reported Events of Interest during the Follow-up Period.*

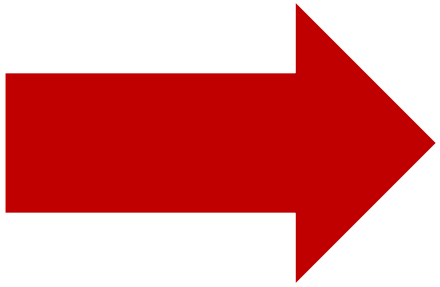
Event	Rosuvastatin (N=8901)	Placebo (N=8901)	P Value
Monitored adverse events			
Any serious adverse event — no. (%)	1352 (15.2)	1377 (15.5)	0.60
Muscular weakness, stiffness, or pain — no. (%)	1421 (16.0)	1375 (15.4)	0.34
Myopathy — no. (%)	10 (0.1)	9 (0.1)	0.82
Rhabdomyolysis — no. (%)†	1 (<0.1)	0	—
Newly diagnosed cancer — no. (%)	298 (3.4)	314 (3.5)	0.51
Death from cancer — no. (%)	35 (0.4)	58 (0.7)	0.02
Gastrointestinal disorder — no. (%)	1753 (19.7)	1711 (19.2)	0.43
Renal disorder — no. (%)	535 (6.0)	480 (5.4)	0.08
Bleeding — no. (%)	258 (2.9)	275 (3.1)	0.45
Hepatic disorder — no. (%)	216 (2.4)	186 (2.1)	0.13
Laboratory values‡			
Creatinine, >100% increase from baseline — no. (%)	16 (0.2)	10 (0.1)	0.24
Glomerular filtration rate at 12 mo — ml/min/1.73 m²			0.02
Median	66.8	66.6	
Interquartile range	59.1–76.5	58.8–76.2	
Alanine aminotransferase >3× ULN on consecutive visits — no. (%)	23 (0.3)	17 (0.2)	0.34
Glycated hemoglobin at 24 mo — %			0.001
Median	5.9	5.8	
Interquartile range	5.7–6.1	5.6–6.1	
Fasting glucose at 24 mo — mg/dl			0.12
Median	98	98	
Interquartile range	91–107	90–106	
>Trace of glucose in urine at 12 mo — no. (%)	36 (0.5)	32 (0.4)	0.64
Other events			
Newly diagnosed diabetes (physician-reported) — no. (%)	270 (3.0)	216 (2.4)	0.01
Hemorrhagic stroke — no. (%)	6 (0.1)	9 (0.1)	0.44

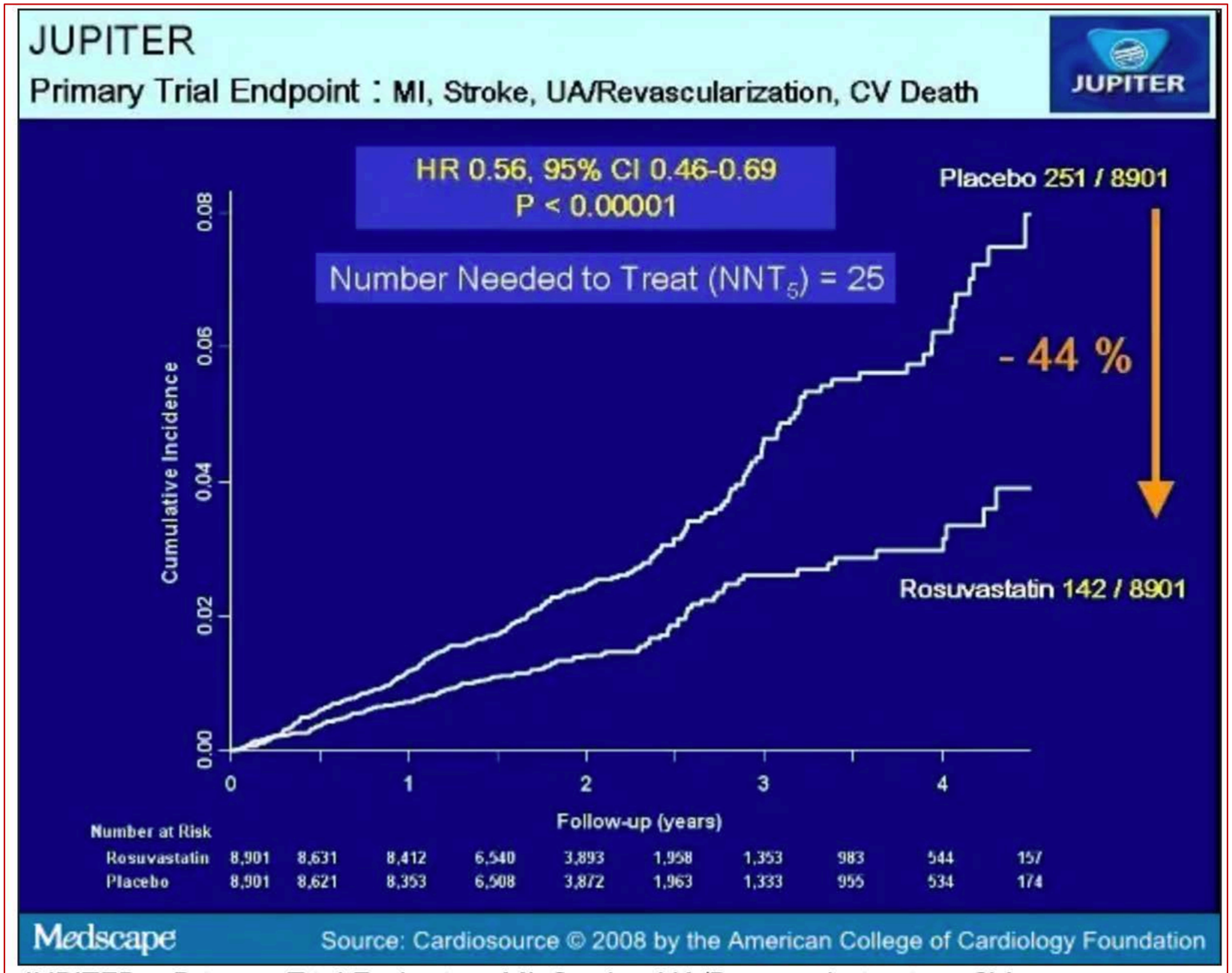
* Data were missing for some patients for some events.
† The single case of rhabdomyolysis occurred after closure of the trial.
‡ To convert values for creatinine to micromoles per liter, multiply by 88.4. To convert values for glucose to millimoles per liter, multiply by 0.05551. ULN denotes upper limit of the normal range.

JUPITER tədqiqatı

Table 3. Outcomes According to Study Group.

End Point	Rosuvastatin (N=8901)		Placebo (N=8901)		Hazard Ratio (95% CI)	P Value
	No. of Patients	Rate per 100 person-yr	No. of Patients	Rate per 100 person-yr		
Primary end point	142	0.77	251	1.36	0.56 (0.46–0.69)	<0.00001
Nonfatal myocardial infarction	22	0.12	62	0.33	0.35 (0.22–0.58)	<0.00001
Any myocardial infarction	31	0.17	68	0.37	0.46 (0.30–0.70)	0.0002
Nonfatal stroke	30	0.16	58	0.31	0.52 (0.33–0.80)	0.003
Any stroke	33	0.18	64	0.34	0.52 (0.34–0.79)	0.002
Arterial revascularization	71	0.38	131	0.71	0.54 (0.41–0.72)	<0.0001
Hospitalization for unstable angina	16	0.09	27	0.14	0.59 (0.32–1.10)	0.09
Arterial revascularization or hospitalization for unstable angina	76	0.41	143	0.77	0.53 (0.40–0.70)	<0.00001
Myocardial infarction, stroke, or confirmed death from cardiovascular causes	83	0.45	157	0.85	0.53 (0.40–0.69)	<0.00001
Death from any cause						
Death on known date	190	0.96	235	1.19	0.81 (0.67–0.98)	0.03
Any death	198	1.00	247	1.25	0.80 (0.67-0.97)	0.02





JUPITER – Primary Trial Endpoint : MI, Stroke, UA/Revascularization, CV

Randomized Controlled Trial > Arthritis Rheumatol. 2019 Sep;71(9):1437-1449.
doi: 10.1002/art.40892. Epub 2019 Jul 22.

A Multicenter, Randomized, Placebo-Controlled Trial of Atorvastatin for the Primary Prevention of Cardiovascular Events in Patients With Rheumatoid Arthritis

George D Kitas [1], Peter Nightingale [2], Jane Armitage [3], Naveed Sattar [4], Jill J F Belch [5], Deborah P M Symmons [6]; TRACE RA Consortium

Collaborators, Affiliations + expand

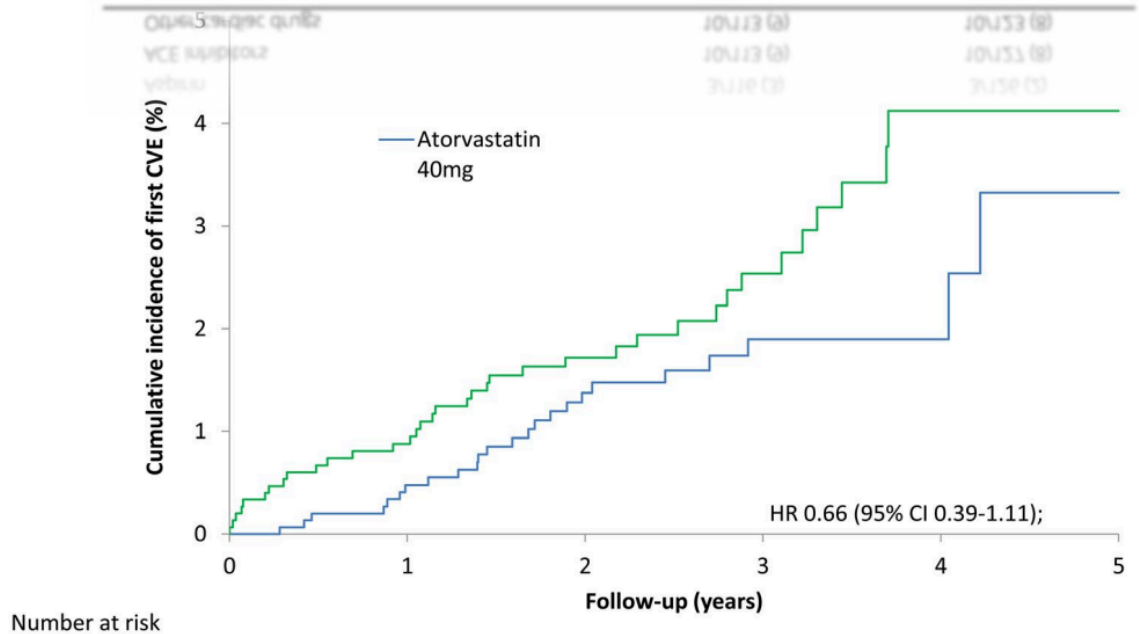
PMID: 30983166 PMCID: PMC6771601 DOI: 10.1002/art.40892

Methods: A randomized, double-blind, placebo-controlled trial was designed to detect a 32% CVE risk reduction based on an estimated 1.6% per annum event rate with 80% power at P < 0.05. RA patients age >50 years or with a disease duration of >10 years who did not have clinical atherosclerosis, diabetes, or myopathy received atorvastatin 40 mg daily or matching placebo. The primary end point was a composite of cardiovascular death, myocardial infarction, stroke, transient ischemic attack, or any arterial revascularization. Secondary and tertiary end points included plasma lipids and safety.

Results: A total of 3,002 patients (mean age 61 years; 74% female) were followed up for a median of 2.51 years (interquartile range [IQR] 1.90, 3.49 years) (7,827 patient-years). The study was terminated early due to a lower than expected event rate (0.70% per annum). Of the 1,504 patients receiving atorvastatin, 24 (1.6%) experienced a primary end point, compared with 36 (2.4%) of the 1,498 receiving placebo (hazard ratio [HR] 0.66 [95% confidence interval (95% CI) 0.39, 1.11]; P = 0.115 and adjusted HR 0.60 [95% CI 0.32, 1.15]; P = 0.127). At trial end, patients receiving atorvastatin had a mean ± SD low-density lipoprotein (LDL) cholesterol level 0.77 ± 0.04 mmoles/liter lower than those receiving placebo (P < 0.0001). C-reactive protein level was also significantly lower in the atorvastatin group than the placebo group (median 2.59 mg/liter [IQR 0.94, 6.08] versus 3.60 mg/liter [IQR 1.47, 7.49]; P < 0.0001). CVE risk reduction per mmole/liter reduction in LDL cholesterol was 42% (95% CI -14%, 70%). The rates of adverse events in the atorvastatin group (n = 298 [19.8%]) and placebo group (n = 292 [19.5%]) were similar.

Conclusion: Atorvastatin 40 mg daily is safe and results in a significantly greater reduction of LDL cholesterol level than placebo in patients with RA. The 34% CVE risk reduction is consistent with the Cholesterol Treatment Trialists' Collaboration meta-analysis of statin effects in other populations.

Cardiovascular characteristics		
Smoking status		
Current smoker	260/1,422 (18)	209/1,431 (15)
Ex-smoker	606/1,422 (43)	637/1,431 (45)
Never smoked	556/1,422 (39)	585/1,431 (41)
Hypertension	322/1,456 (22)	335/1,437 (23)
First degree relative with premature CVD	285/1,321 (22)	263/1,304 (20)
Total cholesterol, median (IQR) mmoles/liter (n)	5.4 (4.8, 6.1) (845)	5.3 (4.8, 6.0) (832)
Triglycerides, median (IQR) mmoles/liter (n)	1.26 (0.90, 1.80) (673)	1.30 (0.90, 1.80) (652)
HDL cholesterol, median (IQR) mmoles/liter (n)	1.56 (1.2, 1.90) (719)	1.52 (1.25, 1.85) (700)
LDL cholesterol, median (IQR) mmoles/liter (n)	3.2 (2.7, 3.8) (544)	3.2 (2.7, 3.8) (530)
CRP, median (IQR) mg/liter (n)	5 (3, 11) (780)	5 (3, 12) (776)
Estimated GFR, median (IQR) ml/minute/1.73 m^2 (n)	79 (59, 110) (1,124)	79 (58, 111) (1,109)
Treatment		
Aspirin	3/116 (3)	3/126 (2)
ACE inhibitors	10/113 (9)	10/127 (8)
Other cardiac drugs	10/113 (9)	10/123 (8)



Number at risk

Atorvastatin 40mg	1504	1398	1037	561	196

JAMA | US Preventive Services Task Force | EVIDENCE REPORT

Statin Use for the Primary Prevention of Cardiovascular Disease in Adults

Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

Roger Chou, MD; Amy Cantor, MD, MPH; Tracy Dana, MLS; Jesse Wagner, MA; Azrah Y. Ahmed, BA; Rongwei Fu, PhD; Maros Ferencik, MD, PhD, MCR

RESULTS Twenty-six studies were included: 22 trials (N = 90 624) with 6 months to 6 years of follow-up compared statins vs placebo or no statin, 1 trial (n = 5144) compared statin intensities, and 3 observational studies (n = 417 523) reported harms. Statins were significantly associated with decreased risk of all-cause mortality (risk ratio [RR], 0.92 [95% CI, 0.87 to 0.98]; absolute risk difference [ARD], −0.35% [95% CI, −0.57% to −0.14%]), stroke (RR, 0.78 [95% CI, 0.68 to 0.90]; ARD, −0.39% [95% CI, −0.54% to −0.25%]), myocardial infarction (RR, 0.67 [95% CI, 0.60 to 0.75]; ARD, −0.85% [95% CI, −1.22% to −0.47%]), and composite cardiovascular outcomes (RR, 0.72 [95% CI, 0.64 to 0.81]; ARD, −1.28% [95% CI, −1.61% to −0.95%]); the association with cardiovascular mortality was not statistically significant (RR, 0.91 [95% CI, 0.81 to 1.02]; ARD, −0.13%). Relative benefits were consistent in groups defined by demographic and clinical characteristics, although data for persons older than 75 years were sparse. Statin therapy was not significantly associated with increased risk of serious adverse events (RR, 0.97 [95% CI, 0.93 to 1.01]), myalgias (RR, 0.98 [95% CI, 0.86 to 1.11]), or elevated alanine aminotransferase level (RR, 0.94 [95% CI, 0.78 to 1.13]). Statin therapy was not significantly associated with increased diabetes risk overall (RR, 1.04 [95% CI, 0.92 to 1.19]), although 1 trial found high-intensity statin therapy was significantly associated with increased risk (RR, 1.25 [95% CI, 1.05 to 1.49]). Otherwise, there were no clear differences in outcomes based on statin intensity.

26 kliniki tədqiqat daxil edilib
22 tədqiqat – statin və plasebo/nonstatin qarşılaşdırdı
6 ay -6 il təqib müddətində,
1 tədqiqat – statin müalicəsinin intensivliyini qarşılaşdırdı
3 tədqiqat müşahidə xarakterli – zərərləri qeyd etdi

Əhəmiyyətli dərəcəcə bütün səbəblərə bağlı ölümü azaltdığı göstərildi

JAMA. 2022;328(8):754-771. doi:10.1001/jama.2022.12138

Clinician Summary of USPSTF Recommendation

Statin Use for the Primary Prevention of Cardiovascular Disease in Adults

August 2022

What does the USPSTF recommend?

B Grade **For adults aged 40 to 75 years who have 1 or more cardiovascular risk factors (ie, dyslipidemia, diabetes, hypertension, or smoking) and an estimated 10-year cardiovascular disease (CVD) risk of 10% or greater:** Initiate a statin.

C Grade **For adults aged 40 to 75 years who have 1 or more cardiovascular risk factors (ie, dyslipidemia, diabetes, hypertension, or smoking) and an estimated 10-year CVD risk of 7.5% to 10%:** Selectively offer a statin.

I Statement **For adults 76 years or older:** The evidence is insufficient to recommend for or against starting a statin.

To whom does this recommendation apply?

These recommendations apply to adults 40 years or older who do not already have CVD or signs or symptoms of CVD.

They do not apply to adults with a low-density lipoprotein cholesterol level greater than 190 mg/dL (4.92 mmol/L) or known familial hypercholesterolemia. These populations are at very high risk for CVD and considerations on the use of statins in these populations can be found in other organization's guidelines on management of hypercholesterolemia.

Population	Recommendation	Grade
Adults aged 40 to 75 years who have 1 or more cardiovascular risk factors and an estimated 10-year cardiovascular disease (CVD) risk of 10% or greater	The USPSTF recommends that clinicians prescribe a statin for the primary prevention of CVD for adults aged 40 to 75 years who have 1 or more CVD risk factors (i.e. dyslipidemia, diabetes, hypertension, or smoking) and an estimated 10-year risk of a cardiovascular event of 10% or greater.	B
Adults aged 40 to 75 years who have 1 or more cardiovascular risk factors and an estimated 10-year CVD risk of 7.5% to less than 10%	The USPSTF recommends that clinicians selectively offer a statin for the primary prevention of CVD for adults aged 40 to 75 years who have 1 or more CVD risk factors (i.e dyslipidemia, diabetes, hypertension, or smoking) and an estimated 10-year risk of a cardiovascular event of 7.5% to less than 10%. The likelihood of benefit is smaller in this group than in persons with a 10-year risk of 10% or greater.	C
Adults 76 years or older	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of initiating a statin for the primary prevention of CVD events and mortality in adults 76 years or older.	I

- ***2016-cı ildə ABŞ Preventiv Xidmətlər İşçi Qrupu (USPSTF) klinisyenlərə ən azı 1 KVX risk faktoru və hesablanmış 10 illik CVD hadisəsi riski 10% və ya daha çox olan 40-75 yaş arası yetkinlərdə ilkin profilaktika üçün statinlərə başlamağı tövsiyə etdi (B tövsiyəsi) və 10 illik riski 7,5%-dən 10%-ə qədər olanlara seçici olaraq statinlər təklif edin (C tövsiyəsi).***
- ***76 yaş və ya daha yuxarı yetkinlərdə statinlərin nəticələrini qiymətləndirmək üçün kifayət yetərli dəlil yox idi.***

JAMA. 2022;328(8):754-771. doi:10.1001/jama.2022.12138

- 22 randomize edilmiş tədqiqat (N = 95 768, 61 publikasiyada) statinlər plasebo (20 tədqiqat) və non-statinlərlə (2 tədqiqat) qarşılaşdırılmışdır.
- 1 yeni sınaq (TRACE-RA, n = 3002) və əvvəllər xaric edilmiş 2 (sekonder qoruma xəstələri 10%-lik həddi keçdiyi üçün) sınaqları (ALLHAT-LLT [n = 10 355; 8880) və PROSPER [n = 5804; 3239 birincili qoruma] hamısı 2016 USPSTF icmalına daxil edilmişdir.
- Əlavə olaraq, (n = 6595) WOSCOPS33 (n = 6595) tədqiqatı – hansı ki, miks olaraq birincili və ikincili qoruma qrupunu ehtiva edir (≤ 10% ikincili qoruma iştirakçıları) statinlərin yarar və zərərlərini qeyd edir.

Table 1. Characteristics of Randomized Clinical Trials

Source (quality)	Inclusion criteria	Follow-up, y	Statin intensity	Intervention and comparator (N)	Mean age, y	Sex (% female)	Race and ethnicity, %	Mean baseline lipids, mg/dL	Risk factors, %
ACAPS Furberg et al, 1994[19] (Fair)	Aged 40 to 79 y Early-onset carotid atherosclerosis LDL-C 160 to 189 mg/dL with ≤1 risk factor, 130 to 159 mg/dL with >1 risk factor at baseline, or triglycerides ≤400 mg/dL after intensive dietary treatment	3	Low (20 mg) and moderate (40 mg)	Lovastatin, 20 mg/d, titrated to 40 mg/d for target LDL-C of 90 to 110 mg/dL (n = 460) Placebo (n = 459)	62	50	White: 93 Other: NR	LDL-C: 156 HDL-C: 52 TC: 235 Triglycerides: 138	Diabetes: 2 Smoking: 12 Hypertension: 31 Mean BMI (men: 25.9)[a] Mean BMI (women): 25.7[a]
AFCAPS/TexCAPS Downs et al, 1998[17] (Fair)	Aged 45 to 73 y (men) or 55 to 73 y (women) TC 180 to 264 mg/dL LDL-C 130 to 190 mg/dL HDL-C ≤45 mg/dL (men) or ≤47 mg/dL (women) Triglycerides ≤400 mg/dL Also included patients with LDL-C 125 to 129 mg/dL if TC:HDL-C ratio >6.0	5	Low (20 mg) and moderate (40 mg)	Lovastatin, 20 mg/d, titrated to 20 to 40 mg/d for target LDL-C ≤110 mg/dL (n = 3304) Placebo (n = 3301)	58	15	White: 89 Other: NR	LDL-C: 150 HDL-C: 36 TC: 221 Triglycerides: 158	Diabetes: 3 Smoking: 12.5 Mean SBP: 138 mm Hg Mean DBP: 78 mm Hg Mean BMI (men): 27[a] Mean BMI (women): 26[a] Daily aspirin use: 17
ALLHAT-LLT Furberg et al, 2002[18] (Fair)	Aged ≥55 y with stage 1 or 2 hypertension and ≥1 additional CHD risk factor Excluded: use of lipid-lowering therapy, intolerant of statins, significant liver or kidney disease, secondary cause of dyslipidemia	6	Moderate	Pravastatin, 40 mg/d (total: n = 5170; primary prevention only: n = 4475) Usual care (total: n = 5185; primary prevention only: n = 4405)	71	49	Non-Hispanic Black: 33 White: 41 Hispanic Black: 4 White: 15 Other: 6	LDL-C: 129 HDL-C: 48 TC: 205 Triglycerides: 151	History of CHD: 14 Hypertension: 90 Diabetes: 35 Smoking: 23 Mean BMI: 29.9[a] Mean SBP: 145 mm Hg Mean DBP: 84 mm Hg
ASCOT-LLA Sever et al, 2003[29] (Fair)	Aged 40 to 79 y Untreated or treated hypertension TC ≤251 mg/dL No current fibrate or stain use ≥3 CVD risk factors Triglycerides <399 mg/dL	3	Moderate	Atorvastatin, 10 mg/d (n = 5168) Placebo (n = 5137)	63	19	White: 95 Other: NR	LDL-C: 131 HDL-C: 50 TC: 212 Triglycerides: 147	LVH: 14 Other ECG abnormalities: 14 PVD: 5 Other CVD: 4 Diabetes: 25 Smoking: 33 Mean BMI: 28.6[a] History of stroke or TIA: 10 Mean No. of risk factors: 4
ASPEN Knopp et al, 2006[23] (Fair)	Aged 40 to 75 y Diabetes LDL-C <160 mg/dL	4	Moderate	Atorvastatin, 10 mg/d (n = 959[b]) Placebo (n = 946[b])	60	38	Black: 6 White: 84 Other: NR	LDL-C: 114 HDL-C: 48 TC: 195 Triglycerides: 145	Diabetes: 100 (duration, 8 y) Smoking: 13 Mean SBP: 133 mm Hg Mean DBP: 77 mm Hg Mean BMI: 29[a]

JAMA. 2022;328(8):754-771. doi:10.1001/jama.2022.12138

Table 1. Characteristics of Randomized Clinical Trials (continued)

Source (quality)	Inclusion criteria	Follow-up, y	Statin intensity	Intervention and comparator (N)	Mean age, y	Sex (% female)	Race and ethnicity, %	Mean baseline lipids, mg/dL	Risk factors, %
ASTRONOMER Chan et al, 2010[14] (Good)	Aged 18 to 82 y Asymptomatic mild or moderate aortic stenosis (aortic valve velocity, 2.5 to 4.0 m/s) No clinical indications for statin use (CAD, cerebrovascular disease, PVD, diabetes) Lipids within target levels for respective risk categories according to Canadian guidelines	4	High	Rosuvastatin, 40 mg/d (n = 136) Placebo (n = 135)	58	38	White: 99 Other: NR	LDL-C: 122 HDL-C: 62 TC: 205 Triglycerides: 111	Smoking: 11 Mean BP: 129/71 mm Hg Mean BMI: 28[a]
Beishuizen et al, 2004[12] (Fair)	Aged 30 to 80 y Type 2 diabetes (duration ≥1 y) No history of CVD TC 155 to 267 mg/dL	2	Moderate	Cerivastatin, 0.4 mg/d; after mean of 15 mo, switched to simvastatin, 20 mg/d (n = 125) Placebo (n = 125)	59	53	Asian: 19 White: 68 Other: 13	LDL-C: 135 HDL-C: 48 TC: 215 Triglycerides: 164	Diabetes: 100 Current smoker: 24 Hypertension: 51 Mean BMI: 31.0[a]
Bone et al, 2007[13] (Fair)	Women aged 40 to 75 y LDL-C ≥130 to <190 mg/dL No history of diabetes or CHD Criteria modified during trial to women with LDL-C ≥160 mg/dL and ≥2 CVD risk factors	1	Moderate (10 to 20 mg) and high (40 to 80 mg)	Atorvastatin, 10 mg/d (n = 118) Atorvastatin, 20 mg/d (n = 121) Atorvastatin, 40 mg/d (n = 124) Atorvastatin, 80 mg/d (n = 122) Placebo (n = 119)	59	100 overall	White: 88 Other: NR	LDL-C: 157 HDL-C: 54 TC: 243 Triglycerides: 141	Current or former smoker: 47
CAIUS Mercuri et al, 1996[24] (Fair)	Aged 45 to 65 y with elevated LDL-C and no symptomatic coronary artery disease and ≥1 carotid artery lesion	3	Moderate	Pravastatin, 40 mg/d (n = 151) Placebo (n = 154)	55	47	NR	LDL-C: 181 HDL-C: 53 TC: 262 Triglycerides: 138	Smoking: 24 Mean SBP: 134 mm Hg Mean DBP: 82 mm Hg Mean BMI: 25[a] Family history of CVD: 45

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Table 1. Characteristics of Randomized Clinical Trials (continued)

Source (quality)	Inclusion criteria	Follow-up, y	Statin intensity	Intervention and comparator (N)	Mean age, y	Sex (% female)	Race and ethnicity, %	Mean baseline lipids, mg/dL	Risk factors, %
CARDS Colhoun et al, 2004[15] (Good)	Aged 40 to 75 y Diabetes and ≥1 additional risk factor for CHD No previous CVD events BMI <35[a] HbA_{1c} <12% SBP <200 mm Hg DBP <110 mm Hg Not receiving any other lipid-lowering medication LDL-C ≤160 mg/dL Triglycerides ≤600 mg/dL	4	Moderate	Atorvastatin, 10 mg/d (n = 1428) Placebo (n = 1410)	62	32	White: 95 Other: NR	LDL-C: 118 HDL-C: 55 TC: 207 Triglycerides: 150 (median)	Diabetes: 100 (mean duration, 8 y) Smoking: 23 Mean SBP: 144 mm Hg Mean DBP: 83 mm Hg Mean BMI: 29[a]
Heljić et al, 2009[20] (Fair)	Obese patients with diabetes No preexisting CHD Triglycerides ≤266 mg/dL States LDL-C used as entry criterion but values NR	1	Moderate	Simvastatin, 40 mg/d (n = 45) Placebo(n = 50)	61	58	NR	LDL-C: 170 HDL-C: 41 TC: 239 Triglycerides: 217	Mean BP: <140/90 mm Hg Mean BMI: 31.6[a]
HOPE-3 Yusuf et al, 2016[32] (Good)	Men aged ≥55 y and women aged ≥65 y with ≥1 cardiovascular risk factor (including elevated waist-hip ratio, low HDL-C, current or recent tobacco use, dysglycemia, family history of premature CHD, or mild kidney dysfunction) or women aged ≥60 y with ≥2 cardiovascular risk factors	6	Moderate	Rosuvastatin, 10 mg/d (n = 6361) Placebo (n = 6344)	66	46	Asian: 21 Black: 2 Chinese: 29 Hispanic: 28 White: 20 Other: 2	LDL-C: 128 HDL-C: 45 TC: 201 Triglycerides: 128	Diabetes: 6 IGF or IGT: 13 Smoking: 28 Mean SBP: 138 mm Hg Mean DBP: 82 mm Hg Hypertension: 38 Mean BMI: 27[a] Family history of early-onset CHD: 26 Early-onset kidney dysfunction: 3 Elevated waist-hip ratio: 87 Low HDL-C: 36
HYRIM Anderssen et al, 2005[10] (Fair)	Men aged 40 to 74 y Receiving drug treatment for hypertension TC 174 to 309 mg/dL Triglycerides <399 mg/dL BMI 25 to 35[a] <1 h/wk of regular exercise	4	Low	Fluvastatin, 40 mg/d (n = 142) Fluvastatin, 40 mg/d + lifestyle intervention (physical activity + dietary intervention) (n = 141) Placebo (n = 143) Placebo + lifestyle intervention (n = 142)	57	0	NR	LDL-C: 150 HDL-C: 49 TC: 230 Triglycerides: 158	Smoking: 16 Mean SBP: 141 mm Hg Mean DBP: 88 mm Hg Mean BMI: 29[a]

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Table 1. Characteristics of Randomized Clinical Trials (continued)

Source (quality)	Inclusion criteria	Follow-up, y	Statin intensity	Intervention and comparator (N)	Mean age, y	Sex (% female)	Race and ethnicity, %	Mean baseline lipids, mg/dL	Risk factors, %
JUPITER Ridker et al, 2008[27] (Good)	Men aged ≥50 y or women aged ≥60 y No history of CVD LDL-C <130 mg/dL CRP ≥2.0 mg/L triglycerides <500 mg/dL	2	High	Rosuvastatin, 20 mg/d (n = 8901) Placebo (n = 8901)	Median, 66 in each group	39	Black: 13 Hispanic: 13 White: 71 Other: 4	LDL-C: 108 (median, each group) HDL-C: 49 (median, each group) TC: 186 (median, intervention group), 185 (median, placebo group) Triglycerides: 118 (median, each group)	Median HbA_{1c}: 5.7% in each group Smoking: 16 Median BP: 134/80 mm Hg in each group Median BMI: 28 in each group[a] Median CRP: 4.2 mg/L in intervention group; 4.3 mg/L in placebo group Family history of CHD: 12 Metabolic syndrome: 42 Daily aspirin use: 17
KAPS Salonen et al, 1995[28] (Good)	Men aged 42, 48, 54, or 60 y LDL-C ≥164 mg/dL TC <308 mg/dL BMI <32[a] ALT <1.5 ULN	3	Moderate	Pravastatin, 40 mg/d (n = 224) Placebo (n = 223)	58	0	NR	LDL-C: 189 HDL-C: 46 TC: 259 Triglycerides: 151	Prior MI: 7.5 Diabetes: 2.5 Smoking: 27 Hypertension: 33
MEGA Nakamura et al, 2006[26] (Fair)	Aged 40 to 70 y TC 220 to 270 mg/dL No history of CHD or stroke	5	Low	Intensive lipid control with diet + pravastatin, 10 mg/d, titrated to 20 mg/d for target TC of <220 mg/dL (n = 3866) Standard lipid control with diet only (n = 3966)	58	69	NR	LDL-C: 157 HDL-C: 58 TC: 242 Triglycerides: 128	Diabetes: 21 Smoking: 21 Hypertension: 42 Mean BMI: 24[a]
METEOR Crouse et al, 2007[16] (Fair)	Men aged 45 to 70 y or women aged 55 to 70 y LDL-C 120 to <190 mg/dL if age only risk factor or LDL-C 120 to <160 mg/dL if ≥2 CHD risk factors and 10-y CHD risk <10% HDL-C ≤60 mg/dL Triglycerides <500 mg/dL Maximum CIMT 1.2 to <3.5 mm	2	High	Rosuvastatin, 40 mg/d (n = 702) Placebo (n = 282)	57	40	White: 60 Other race or ethnicity: NR	LDL-C: 155 HDL-C: 50 TC: 229 Triglycerides: 128	Smoking: 3.9 Hypertension: 20 BMI >30: 20[a] Family history of CHD: 9.6 Metabolic syndrome: 15 ≥2 risk factors: 34
Muldoon et al, 2004[25] (Fair)	Generally healthy men and women aged 35 to 70 y LDL-C 160 and 220 mg/dL	6 mo	Low (10 mg) and moderate (40 mg)	Simvastatin, 40 mg/d (n = 103) Simvastatin, 10 mg/d (n = 103) Placebo (n = 102)	54	52	White: 86 Other race or ethnicity: NR	LDL-C: 181 HDL-C: 51 TG 263 Triglycerides: 151	NR

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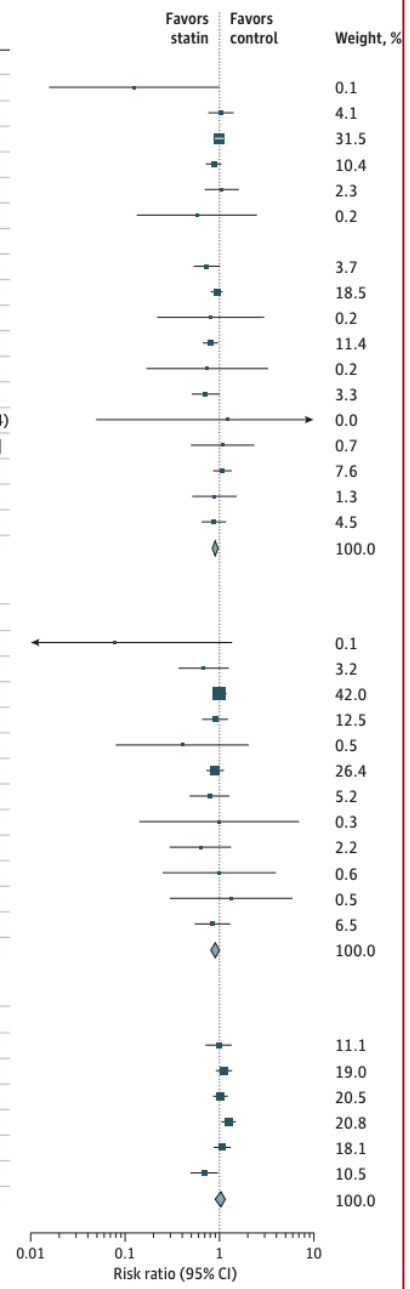
Table 1. Characteristics of Randomized Clinical Trials (continued)

Source (quality)	Inclusion criteria	Follow-up, y	Statin intensity	Intervention and comparator (N)	Mean age, y	Sex (% female)	Race and ethnicity, %	Mean baseline lipids, mg/dL	Risk factors, %
PREVEND-IT Asselbergs et al, 2004[11] (Fair)	Aged 28 to 75 y Persistent microalbuminuria (urine albumin >10 mg/L in 1 early-morning spot sample and 15 to 300 mg in two 24-hour samples) BP <160/100 mm Hg and no antihypertensive medication TC <309 mg/dL or <193 mg/dL if previous MI No lipid-lowering medications	4	Moderate	Pravastatin, 40 mg/d (n = 433) Placebo (n = 431)	52	35	White: 96 Other race or ethnicity: NR	LDL-C: 157 HDL-C: 39 TC: 224 Triglycerides: 120	Prior CVD event: 3 (MI, 0.4) Diabetes: 3 Smoking: 40 Mean SBP: 131 mm Hg Mean DBP: 77 mm Hg Mean BMI: 26[a] Use of aspirin and antiplatelet agents: 2.5
PROSPER Shepherd et al, 2002[30] (Good)	Aged 70 to 82 y with elevated risk of vascular disease due to smoking, hypertension, or diabetes	3	Moderate	Pravastatin, 40 mg/d (n = 1585) Placebo (n = 1654)	75	58	NR	LDL-C: 146 HDL-C: 51 TC: 220 Triglycerides: 135	Smoking (current): 33 Mean SBP: 157 mm Hg Mean DBP: 85 mm Hg Hypertension: 72 Diabetes: 12
TRACE-RA Kitas et al, 2019[22] (Fair)	Aged >50 y with RA diagnosis according to ACR 1987 criteria or RA disease duration >10 y Excluded: known CVD requiring statins, diabetes, myopathy	2	High	Atorvastatin, 40 mg/d (n = 1504) Placebo (n = 1498)	61	75	Asian/Asian British: 0.5 Black/Black British: 0.6 White: 98 Other or mixed race: 0.8	LDL-C: 124 HDL-C: 59 TC: 209 Triglycerides: 113	Smoking (current): 17[c] Mean SBP: 135 mm Hg Mean DBP: 79 mm Hg Hypertension: 23[c]
WOSCOPS Shepherd et al, 1995[33] (Good)	Men aged 45 to 64 y At risk for CAD TC >251 mg/dL LDL-C >155 mg/dL with ≥1 value within 173 to 232 mg/dL No significant CAD	5	Moderate	Pravastatin, 40 mg/d (n = 3302) Placebo (n = 3293)	55	0	NR	LDL-C: 192 HDL-C: 44 TC: 272 Triglycerides: 163	Smoking: 44 Mean SBP: 136 mm Hg Mean DBP: 84 mm Hg Mean BMI: 26[a]

Figure 3. Meta-analysis: Statins vs Placebo or No Statin and All-Cause Mortality, Cardiovascular Mortality, and Incident Diabetes

Study or subgroup	Statin No. of events	Statin Total	Control No. of events	Control Total	Risk ratio (95% CI)	Weight, %
All-cause mortality						
ACAPS,[19] 1994	1	460	8	459	0.12 (0.02-0.99)	0.1
AFCAPS/TexCAPS,[17] 1998	80	3304	77	3301	1.04 (0.76-1.41)	4.1
ALLHAT-LLT,[18] 2002[a]	549	4475	542	4405	1.00 (0.89-1.11)	31.5
ASCOT-LLA,[29] 2003	185	5168	212	5137	0.87 (0.71-1.05)	10.4
ASPEN,[23] 2006	44	959	41	946	1.06 (0.70-1.60)	2.3
Beishuaizen et al,[12] 2004	3	103	4	79	0.58 (0.13-2.50)	0.2
Bone et al,[13] 2007	0	485	0	119	Not estimable	
CARDS,[15] 2004	61	1428	82	1410	0.73 (0.53-1.01)	3.7
HOPE-3,[32] 2016	334	6361	357	6344	0.93 (0.81-1.08)	18.5
HYRIM,[10] 2005	4	283	5	285	0.81 (0.22-2.97)	0.2
JUPITER,[27] 2008	198	8901	247	8901	0.80 (0.67-0.96)	11.4
KAPS,[28] 1995	3	214	4	212	0.74 (0.17-3.28)	0.2
MEGA,[26] 2006	55	3866	79	3966	0.71 (0.51-1.00)	3.3
METEOR,[16] 2007	1	700	0	281	1.21 (0.05-29.54)	0.0
PREVEND-IT,[11] 2004	13	433	12	431	1.08 (0.50, 2.34]	0.7
PROSPER,[30] 2018[a]	139	1585	135	1654	1.07 [0.86-1.35)	7.6
TRACE RA,[22] 2019	24	1504	27	1498	0.89 (0.51-1.53)	1.3
WOSCOPS,[34] 1995[a]	80	2762	92	2767	0.87 (0.65-1.17)	4.5
Total (95% CI)	1774	42 991	1924	42 195	0.92 (0.87-0.98)	100.0
Heterogeneity: $\tau^2 = 0.00$; $\chi^2_{16} = 15.77$ ($P = .47$); $I^2 = 0\%$						
Test for overall effect: $z = 2.49$ ($P = .01$)						
Cardiovascular mortality						
ACAPS,[19] 1994	0	460	6	459	0.08 (0.00-1.36)	0.1
AFCAPS/TexCAPS,[17] 1998	17	3304	25	3301	0.68 (0.37-1.26)	3.2
ALLHAT-LLT,[18] 2002[a]	252	4475	248	4405	1.00 (0.84-1.19)	42.0
ASCOT-LLA,[29] 2003	74	5168	82	5137	0.90 (0.66-1.23)	12.5
ASRONOMER,[14] 2010	2	134	5	135	0.40 (0.08-2.04)	0.5
HOPE-3,[32] 2016	154	6361	171	6344	0.90 (0.72-1.11)	26.4
JUPITER,[27] 2008	29	8901	37	8901	0.78 (0.48-1.27)	5.2
KAPS,[28] 1995	2	214	2	212	0.99 (0.14-6.97)	0.3
MEGA,[26] 2006	11	3866	18	3966	0.63 (0.30-1.33)	2.2
PREVEND-IT,[11] 2004	4	433	4	431	1.00 (0.25-3.95)	0.6
TRACE RA,[22] 2019	4	1504	3	1498	1.33 (0.30-5.92)	0.5
WOSCOPS,[34] 1995[a]	37	2762	44	2767	0.84 (0.55-1.30)	6.5
Total (95% CI)	586	37 582	645	37 556	0.91 (0.81-1.02)	100.0
Heterogeneity: $\tau^2 = 0.00$; $\chi^2_{11} = 7.62$ ($P = .75$); $I^2 = 0\%$						
Test for overall effect: $z = 1.68$ ($P = .09$)						
Incident diabetes						
AFCAPS/TexCAPS,[17] 1998	72	3094	74	3117	0.98 (0.71-1.35)	11.1
ASCOT-LLA,[29] 2003	201	5168	179	5137	1.12 (0.92-1.36)	19.0
HOPE-3,[32] 2016	232	6361	226	6344	1.02 (0.86-1.23)	20.5
JUPITER,[27] 2008	270	8901	216	8901	1.25 (1.05-1.49)	20.8
MEGA,[26] 2006	172	3013	164	3073	1.07 (0.87-1.32)	18.1
WOSCOPS,[34] 1995[a]	57	2999	82	2975	0.69 (0.49-0.96)	10.5
Total (95% CI)	1004	29 536	941	29 547	1.04 (0.92-1.19)	100.0
Heterogeneity: $\tau^2 = 0.01$; $\chi^2_5 = 10.32$ ($P = .07$); $I^2 = 52\%$						
Test for overall effect: $z = 0.65$ ($P = .52$)						



Statin müalicəsinin faydaları demoqrafik, klinik və ya sosial-iqtisadi xüsusiyyətlərə görə müəyyən edilən qruplarda dəyişirmi?

- On tədqiqat (bu yeniləmə üçün 3 tədqiqat əlavə edildi) demoqrafik və ya klinik xüsusiyyətlərə görə stratifikasiya olunmuş nəticələr.
- Bütün nəticələrə baxdığımızda nisbi risk təxminləri yaş (9 tədqiqat), cinsiyyət (6 tədqiqat), irq və etnik mənsubiyyət (2 tədqiqat), lipid parametrləri (6 tədqiqat), hipertansiyonun olması (3 tədqiqat), ürək-damar risk skoru (3 tədqiqat) ilə müəyyən edilmiş qruplarda oxşar olmuşdur.
- Böyrək disfunksiyasının olması (3 tədqiqat), metabolik sindromun olması (2 tədqiqat) və ya diabetin olması (2 tədqiqat); yüksəlmiş C-reaktiv zülalın yüksək səviyyələri ilə bağlı nəticələr uyğunsuz idi (2 tədqiqat).
- 70 yaşdan yuxarı şəxslər üçün heç bir sınaq statin terapiyasının faydalarının sosial-iqtisadi xüsusiyyətlərə görə necə dəyişdiyini bildirməmişdir.

4S –dən sonra böyük statin tədqiqatları

1994	4S
1995	WOSCOPS
1996	CARE
1998	AFCAPS/TexCAPS LIPID

Erken dönem çalışmalar plaseboya göre morbidite ve mortalitede rölatif risk azalması

2001	MIRACL
2002	HPS PROSPER ALL-HAT LLT
2003	ASCOT-LLA
2004	PROVE IT ALLIANCE CARDS A to Z

İkinci dönem çalışmalar

- Diğer yüksek-riskli gruplar
  – AKS, yaşlı, DM, HT
- Plasebo dışı karşılaştırmalar
  – olağan tedaviye karşı (ALLIANCE, ALL-HAT)
  – aktif ilaca karşı (PROVE IT, A to Z)

2005	TNT IDEAL
2006	ASTEROİD

Güncel tedavi uygulanan stabil KKH hastalarında statin tedavisinin yoğunluğu

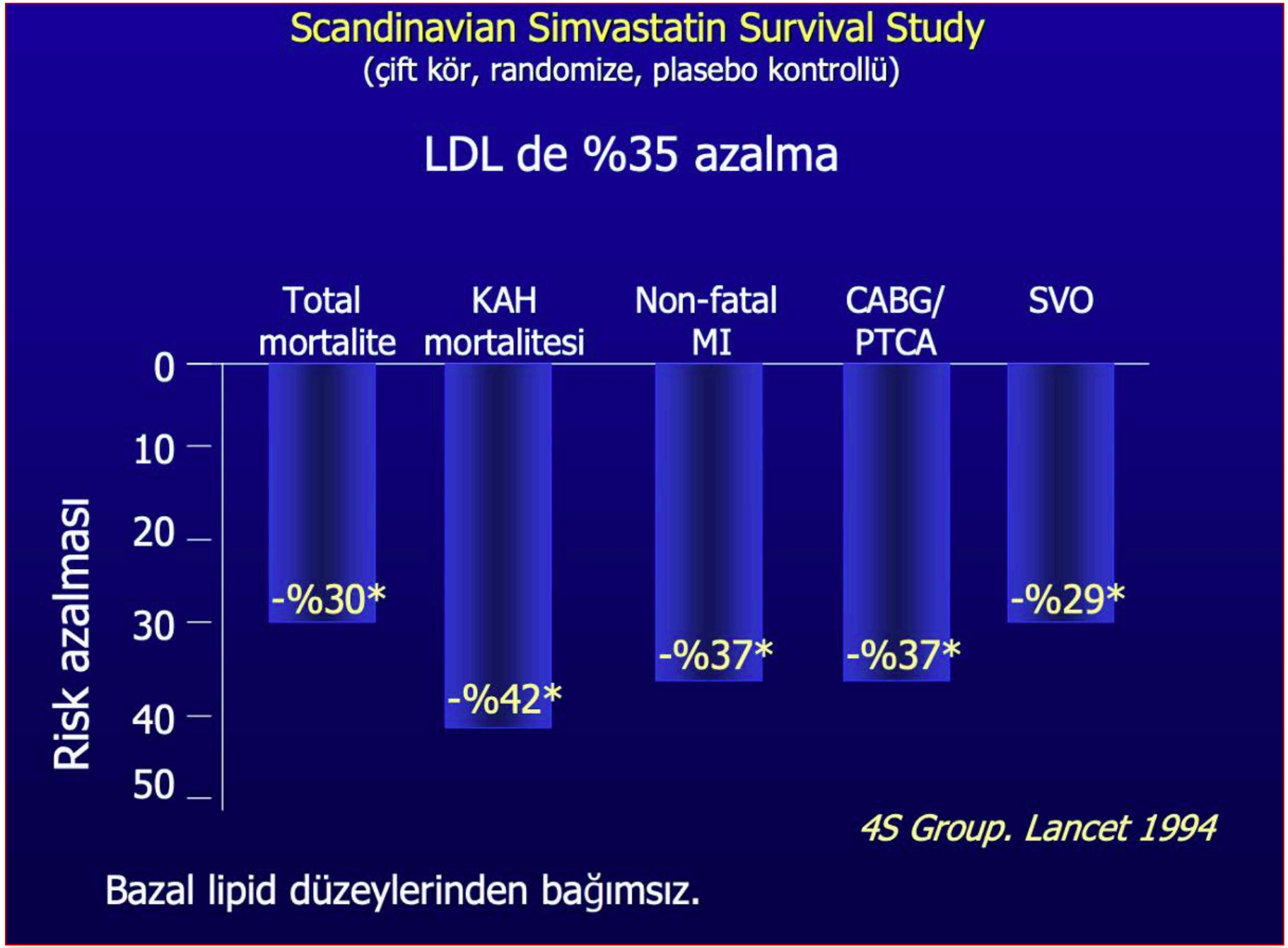
Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90 056 participants in 14 randomised trials of statins

Cholesterol Treatment Trialists' (CTT) Collaborators

Çalışma	Yayın yılı	İzlem	İlaç yılı	n:
4S	1994	5.2	S20-40/pl	4444
WOSCOPS	1995	4.8	P40/pl	6595
CARE	1996	4.8	P40/pl	4159
Post-CABG	1997	4.2	L40-80/L2.5-5	1351
AFCAPS/TexCAPS	1998	5.3	L20-40/pl	6605
LIPID	1998	5.6	P40/pl	9014
GISSI(Pr)	2000	1.9	P20/-	4271
LIPS	2002	3.1	F80/pl	1677
HPS	2002	5.0	S40/pl	20536
PROSPER	2002	3.2	P40/pl	5804
ALLHAT-LLT	2002	4.8	P40/	10355
ASCOT-LLA	2003	3.2	A10/pl	10305
ALERT	2003	5.1	F40/pl	2102
CARDS	2004	3.9	A10/pl	2838
Toplam:		4.7		90056

Lancet 2005; 366: 1267–78

4S

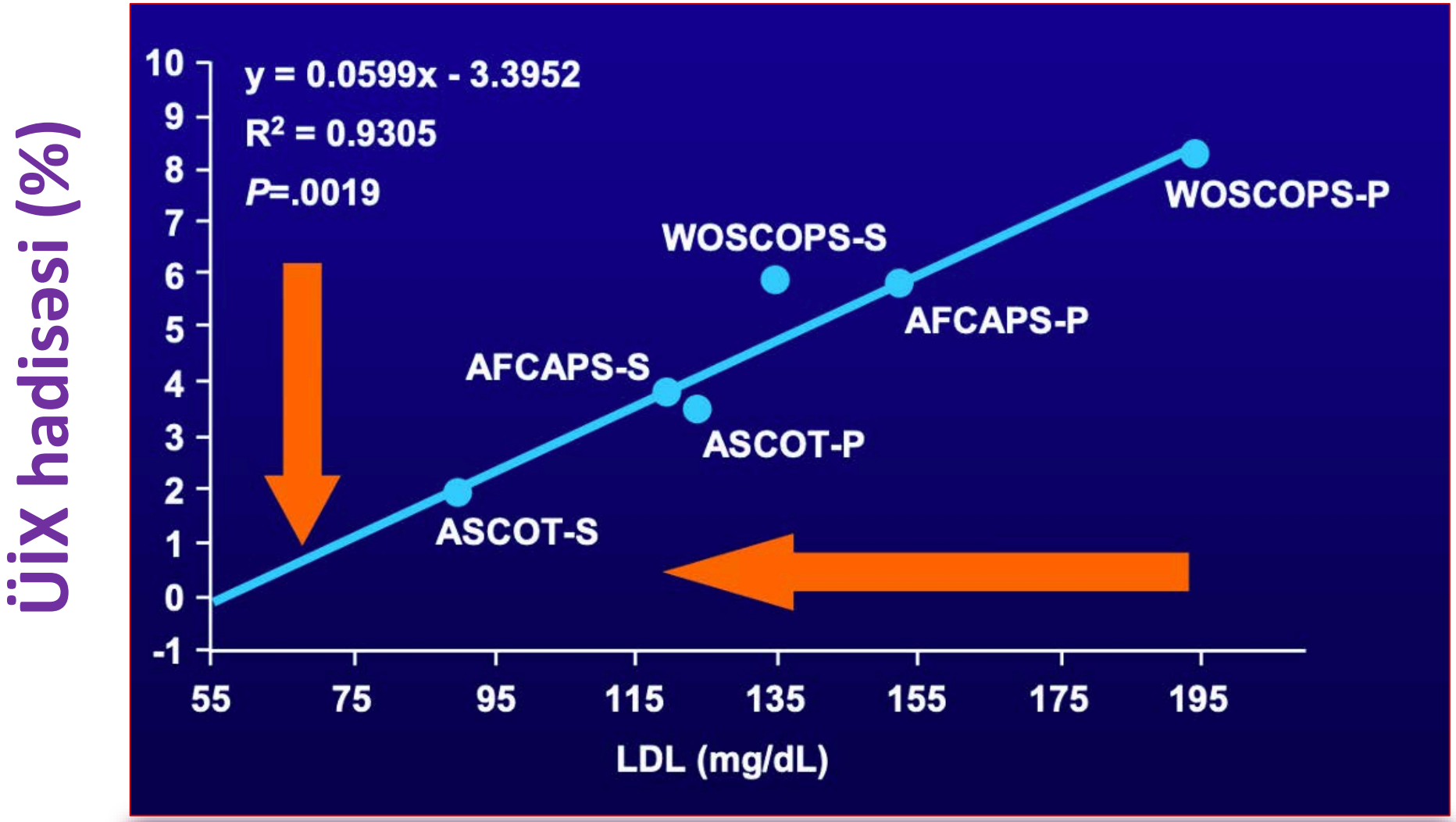

Scandinavian Simvastatin Survival Study
(çift kör, randomize, plasebo kontrollü)
LDL de %35 azalma
Total mortalite
KAH mortalitesi
Non-fatal MI
CABG/ PTCA
SVO
Risk azalması
0
10
20
30
40
50
-%30*
-%42*
-%37*
-%37*
-%29*
4S Group. Lancet 1994
Bazal lipid düzeylerinden bağımsız.

birincili və İkincili klinik statin tədqiqatları

Çalışma	bazal LDL (mg/dL)	LDL (% azalması)	Statin olay oranı (%)	olasebo olay oranı (%)	RRR (%)	ARR (%)	NNT
4S	188	122 (35)	19.4	28.0	34	8.6	12
LIPID	150	112 (25**)	12.3	15.9	24	3.6	28
CARE	139	98 (32)	10.2	13.2	24	3.0	34
HPS	~126	~89 (29**)	19.9	25.4	24	5.5	18
WOSCOPS	192	159 (26)	5.3	7.5	29	2.2	46
AFCAPS	150	115 (25)	3.5	5.5	37	2.0	50

*Nonfatal MI veya KAH a bağlı ölüm - WOSCOPS, CARE, LIPID;
nonfatal veya fatal MI, unstable angina, veya ani kardiyak ölüm- AFCAPS;
nonfatal MI, koroner ölüm, veya Kardiyak arrest- 4S;
major vaskuler olaylat (total KAD, total inme, revasküularizasyon) - HPS; **vs Plasebo.
ARR = absolute risk azalması; NNT = number needed to treat; RRR = relative risk azalması.

klinik hadisə LDL-X səviyyəsi ilə düz mütənasibdir



P- plasebo, S -statin

kəskin koronar sindromda statin tədqiqatları

tədqiqat	dərman və dozlaması	müddət	xəstə sayı
MIRACL (2001)	plasebo vs atorvastatin 80 mg	4 ay	3086
FLORIDA (2002)	plasebo vs fluvastatin 80 mg	1 yıl	540
PROVE-IT (2004)	Pravastatin 40 mg vs atorvastatin 80 mg	2 yıl	4162
A to Z (2004)	plasebo 4 ay ardından simvastatin 20 mg vs simvastatin 40 mg 1 ay ardından simvastatin 80 mg	2 yıl	4496
PACT (2004)	plasebo vs pravastatin 20-40 mg	1 ay	3408
PRINCESS (2004)	plasebo vs cerivastatin 0.4 mg	3 ay*	3605

Schwartz and Olsson. *Am J Cardiol*. 2005;96(suppl):45F

PROVE-İT (KMİ 3-14cü günündə başlanan statin müaliçəsi)

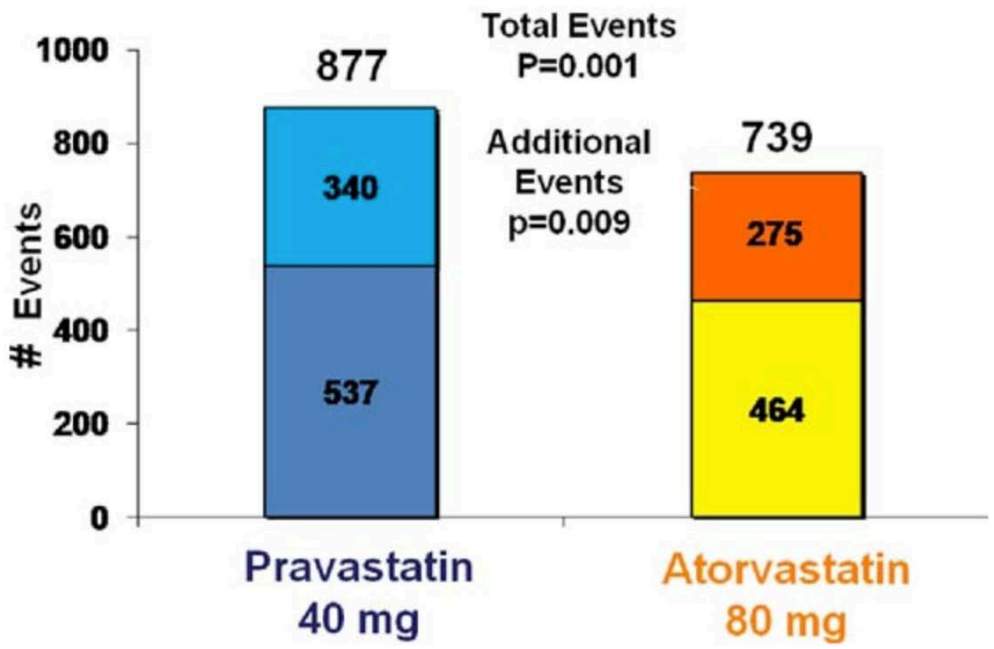
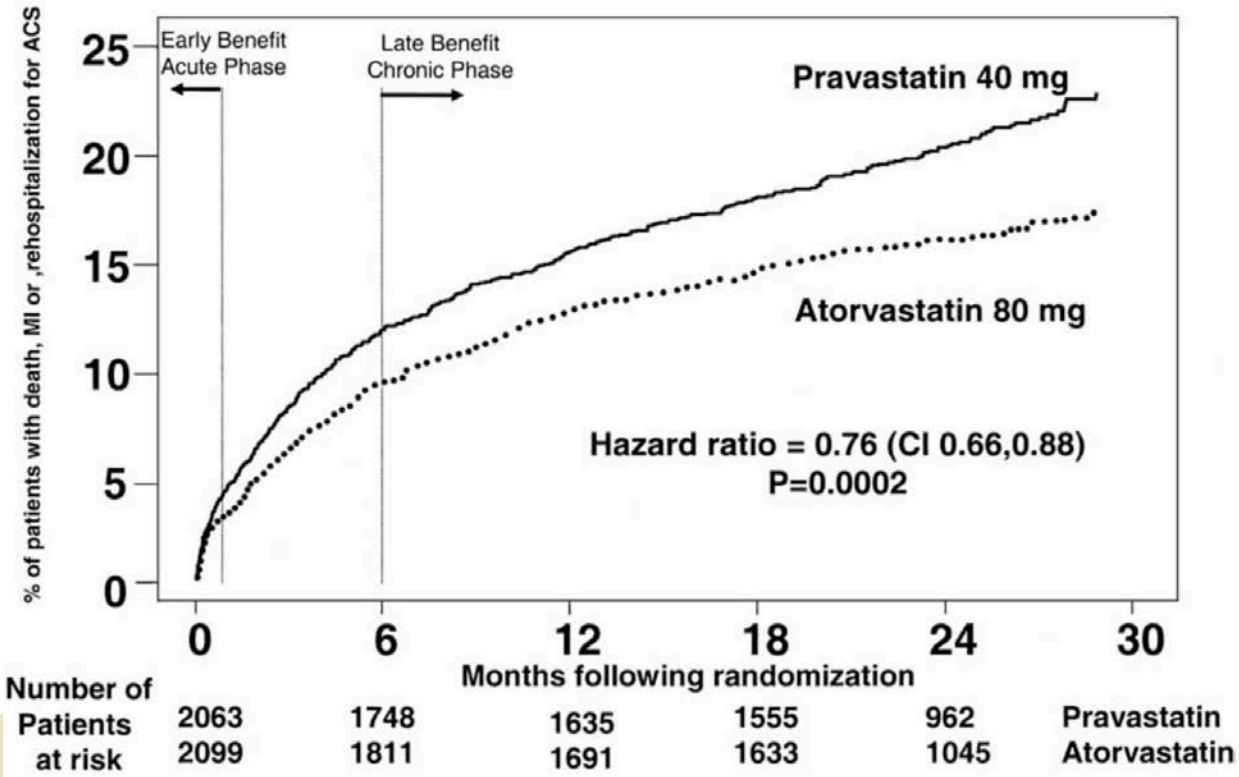


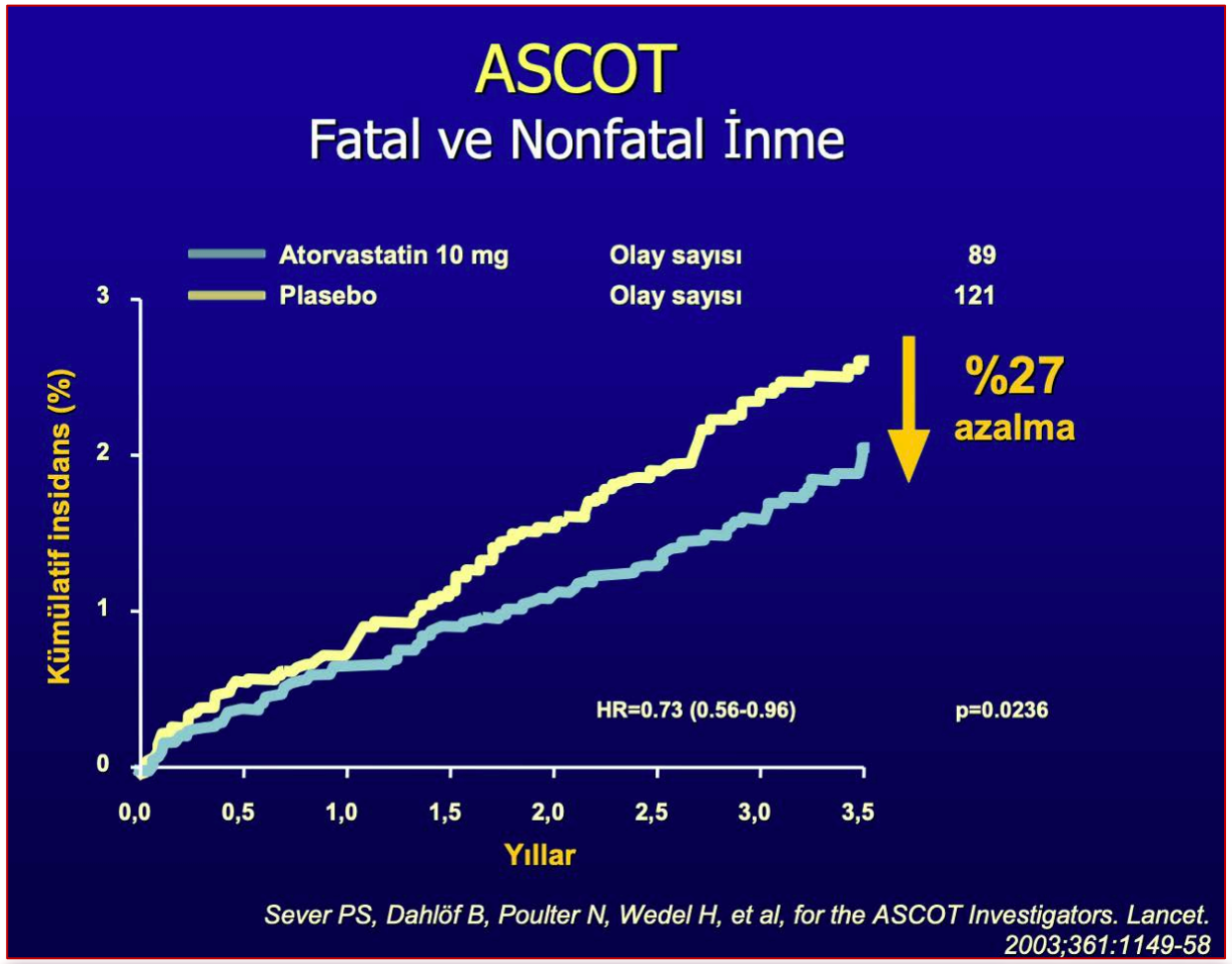
Figure 1 **Total Primary End Point Events by Randomized Therapy**

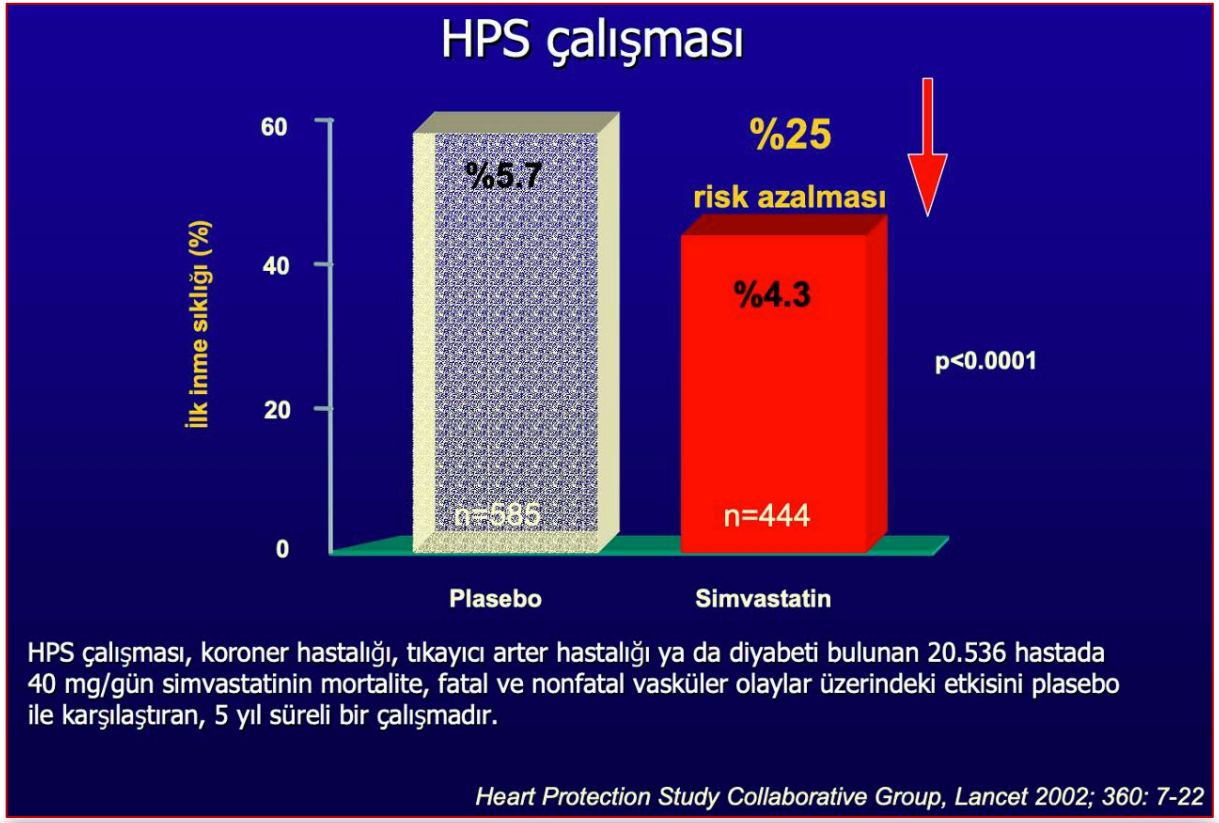
The atorvastatin 80 mg group had a lower number of first events, additional events, and total events as compared with the pravastatin 40 mg group. Bright blue **(top, left)** = additional events, pravastatin 40 mg; lighter blue **(bottom, left)** = first events, pravastatin 40 mg; orange **(top, right)** = additional events, atorvastatin 80 mg; and yellow **(bottom, right)** = first events, atorvastatin 80 mg.



https://doi.org/10.1016/j.jacc.2009.10.005

statinlər və SVH





Əvvəlki CVD hadisələri olmayan böyüklərdə statinlərin zərərləri nələrdir?

- Statin terapiyası, plaseboya qarşı və ya statinsiz, mənfi hadisələrə görə tədqiqatın dayandırılması riskinin artması ilə əhəmiyyətli dərəcədə əlaqəli deyildi (10 tədqiqat, n = 43 783;RR,0.97 [95%CI,0.78 to 1.19];I 2 = 84%; ARD, 0.03% [95% CI, −1.21% to 1.26%]),
- Ciddi advers hadisələr (10 trials, n = 55 419; RR, 0.97 [95% CI, 0.93 to 1.01]; I 2 = 0%; ARD, 0.09% [95% CI, −0.67% to 0.49%]),
- Xərçəng insidansı (13 trials, n = 71 733; RR, 0.98 [95% CI, 0.91 to 1.04]; I 2 = 0%; ARD, −0.10% [95% CI, −0.38% to 0.18%]),
- Ölümcül hallar (6 trials, n = 45 064; RR, 0.89 [95% CI, 0.66 to 1.19]; I 2 = 56%; ARD, −0.13% [95% CI −0.42% to 0.017%]),
- Mialgiya (9 trials, n = 46 388; RR, 0.98 [95% CI, 0.86 to 1.11]; I 2 = 30%; ARD, 0.02% [95% CI, −0.44% to 0.40%]),
- ALT yüksəlməsi (10 trials, n = 48 149; RR,0.94 [95% CI,0.78 to 1.13]; I 2 = 0%; ARD, −0.03% [95% CI, −0.20% to 0.14%]),
- AST yüksəlməsi (4 trials, n = 17 534; RR, 1.30 [95% CI, 0.78 to 2.17]; I 2 = 35%; ARD, 0.21% [95% CI, −0.05% to 0.46%])
- Miopati riski anlamlı artmamışdı. (3 trials, n = 33 345; RR, 1.09 [95% CI, 0.48 to 2.47]; I 2 = 0%; ARD, 0.00% [95% CI, −0.04% to 0.04%]), və ya rabdomioliz (4 trials, n = 59 672; RR, 1.54 [95% CI, 0.36 to 6.64]; I 2 = 0%; ARD, 0.01% [95% CI, −0.01% to 0.03%]),
- Diabet insidansı anlamlı artmamışdı (6 trials, n = 59 083 RR; 1.04 [95% CI, 0.92 to 1.19]; I 2 = 52%; ARD, 0.11% [95% CI, −0.32% to 0.55%]),
- JUPITER, yüksək intensivlikli statin terapiyasını qiymətləndirmək üçün yeganə sınaq, eyni zamanda artan riski aşkar edən yeganə sınaq idi.(n = 17 802; 3.0% vs 2.4; RR, 1.25 [95% CI, 1.05 to 1.49]).
- Üç müşahidə tədqiqatı (n = 417 523) statin istifadəsi və insident diabeti arasındakı əlaqə ilə bağlı qarışıq nəticələr bildirdi.

- Statinlər və böyrək və kognitiv funksiyanın pozulması arasında da pozitif korrelyasiya bildirilməmişdir,
- Sadəcə 1 tədqiqat 2016USPSTF icmalında statinlər və artan katarakt cərrahiyyəsi arasında pozitif korelyasiya olduğunu göstərdi (3.8% vs 3.1% 6 ildən sonra; RR, 1.24 [95% CI, 1.03 to 1.49])

Table 2. Summary of Evidence Table

Studies	Summary of findings	Consistency and precision	Other limitations	Strength of evidence	Applicability
KQ1a: Benefits of statins					
22 RCTs (19 in prior report, 3 new); n = 90 624 For individual outcomes, No. of studies ranged from 10 (for revascularization) to 18 (for all-cause mortality) and Ns ranged from 65 924 (revascularization) to 85 186 (all-cause mortality)	All-cause mortality: RR, 0.92 (95% CI, 0.87-0.98); I^2 = 0%; ARD, −0.35% Cardiovascular mortality: RR, 0.91 (95% CI, 0.81-1.02); I^2 = 0%; ARD, −0.13% Fatal or nonfatal stroke: RR, 0.78 (95% CI, 0.68-0.90); I^2 = 22%; ARD, −0.39% Fatal or nonfatal MI: RR, 0.67 (95% CI, 0.60-0.75); I^2 = 14%; ARD, −0.85% Revascularization: RR, 0.71 (95% CI, 0.63-0.80); I^2 = 15%; ARD, −0.59% Composite cardiovascular outcomes: RR, 0.72 (95% CI, 0.64-0.81); I^2 = 51%; ARD, −1.28%	Consistent Some imprecision for cardiovascular mortality; otherwise precise	Variability in inclusion criteria, statin therapy, duration of follow-up, and definition of composite cardiovascular outcomes Findings for cardiovascular mortality sensitive to inclusion of 1 trial with methodological limitations	Moderate (cardiovascular mortality) High (all other outcomes)	High applicability to US primary care settings All studies enrolled participants with CVD risk factors Trials primarily enrolled White participants; mean age was 52 to 66 y in all trials except for 1 (mean age, 75 y)
KQ1b: Benefits according to demographic, clinical or socioeconomic characteristics					
10 Studies (7 in prior report, 3 new); n = 81 093	Seven trials found no clear differences in risk estimates associated with statin therapy vs placebo or no statin defined by demographic and clinical factors Meta-analyses of 3 trials that reported results for participants aged >70 y were generally consistent with those for total populations No trial evaluated socioeconomic characteristics	Consistent Some imprecision in meta-analyses stratified according to age	Few studies reported outcomes according to clinical characteristics; no study reported on socioeconomic characteristics	Moderate for demographic characteristics (insufficient for age >75 y) Low to moderate for clinical characteristics	High applicability to US primary care settings Trials primarily enrolled White participants; no trial reported data for persons aged >80 y, and only 1 trial reported data for persons aged >75 y
KQc: Benefits according to fixed or titrated dose					
Titrated dose: 3 RCTs (all in prior report); n = 15 356 Fixed dose: 19 RCTs (16 in prior report, 3 new); n = 75 268	No trial directly compared a strategy of titrating statin doses to achieve target LDL-C levels vs fixed statin dose In indirect comparisons, there were no clear differences between trials that permitted limited dose titration compared with those that used fixed-dose therapy	Consistent Imprecise (dose titration)	No direct evidence	Low	High applicability to US primary care settings
KQ2a: Harms of statins					
19 RCTs (17 in prior review, 2 new); n = 75 005 3 Observational studies (2 in prior report, 1 new); n = 417 523	Study withdrawal due to AEs: RR, 0.97 (95% CI, 0.78-1.19); I^2 = 84%; ARD, 0.03% Serious AEs: RR, 0.97 (95% CI, 0.93-1.01); I^2 = 0%; ARD, 0.09% Cancer: RR, 0.98 (95% CI, 0.91-1.04); I^2 = 0%; ARD, −0.10% Diabetes: RR, 1.04 (95% CI, 0.92-1.19); I^2 = 52%; ARD, 0.11% Myalgia: RR, 0.98 (95% CI, 0.86-1.11); I^2 = 30%; ARD, 0.02% Rhabdomyolysis: RR, 1.54 (95% CI, 0.36-6.64); I^2 = 0%; ARD, 0.01% ALT elevation: RR, 0.94 (95% CI, 0.78-1.13); I^2 = 0%; ARD, −0.03% Kidney impairment (2 trials), cognition (1 trial): No increase in risk Cataract surgery (1 trial): 3.8% vs 3.3%; RR, 1.24 (95% CI, 1.03-1.49)	Some inconsistency (diabetes) Some imprecision (kidney impairment, rhabdomyolysis, cataract surgery, cognition) Otherwise consistent and precise	See KQ1a	Low (cognition and cataract surgery) Moderate (kidney impairment and diabetes) High (other harms)	See KQ1a

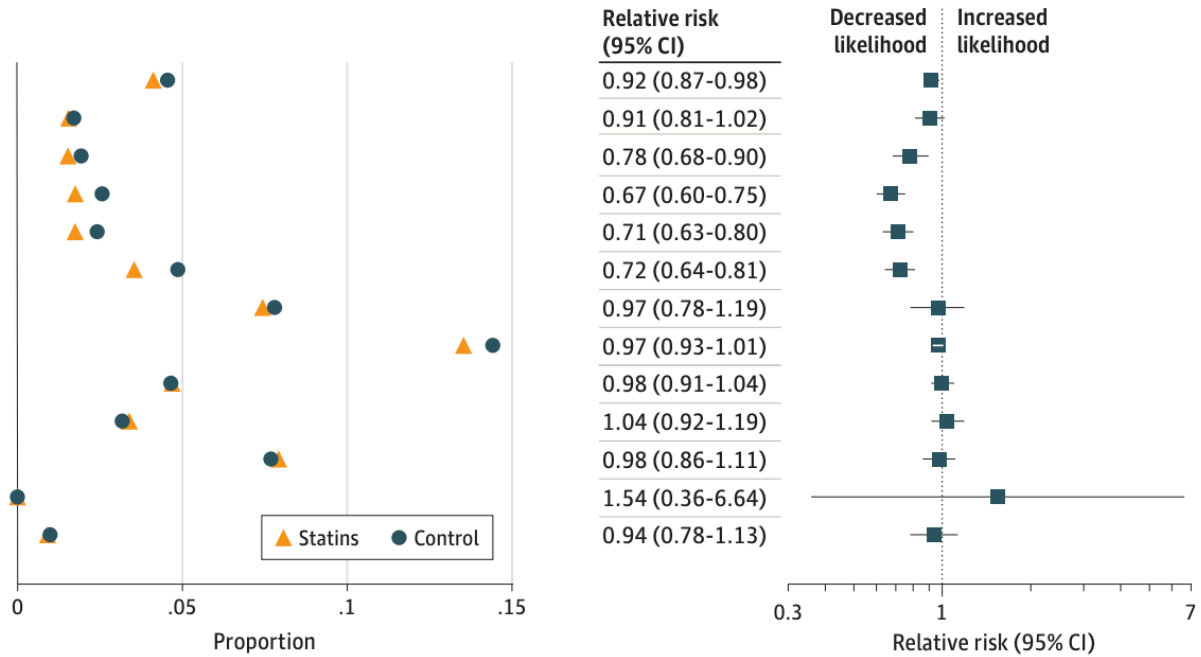
Table 2. Summary of Evidence Table (continued)

Studies	Summary of findings	Consistency and precision	Other limitations	Strength of evidence	Applicability
KQ2b: Harms according to demographic, clinical or socioeconomic characteristics					
4 RCTs (all included in prior report with new data identified); n = 38 806	No difference in harms of statin therapy based on within-study analyses stratified according to age (3 trials), sex (2 trials), or race and ethnicity (1 trial) One trial found high-intensity statin therapy associated with increased risk of incident diabetes in persons with 1 or more diabetes risk factors but not in those without diabetes risk factors	Unable to assess consistency (sex, race and ethnicity, and diabetes risk factors) Imprecise	Findings based on 1 or small number of studies	Low	High applicability to US primary care settings
KQ3: Benefits and harms according to statin intensity					
4 RCTs (3 in prior report, 1 new); n = 9360	One new trial found no difference in clinical outcomes with statin treatment of different intensities but achieved small between-group differences in LDL-C levels Three trials that evaluated different statin intensities were not adequately powered to detect differences in clinical outcomes Indirect comparisons of trials stratified according to intensity of therapy did not indicate a dose-dependent association	Consistent Some imprecision	The largest head-to-head trial of different statin intensities was conducted in Japan and used different statin intensity definitions than in the US; most findings based on indirect, across-study comparisons; most trials evaluated moderate-intensity statin therapy	Moderate	High applicability to US primary care settings Most trials evaluated moderate-intensity statin therapy

Abbreviations: AE, adverse event; ALT, alanine aminotransferase; ARD, absolute risk difference; CVD, cardiovascular disease; KQ, key question; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction; RCT, randomized clinical trial; RR, risk ratio.

Figure 4. Dot Plots for Primary Outcomes

	No. of events/total (proportion)		No. of trials	I^2, %	Strength of evidence	Relative risk (95% CI)
	Statins	Control				
All-cause mortality	1774/42991 (0.041)	1924/42195 (0.046)	18	0	High	0.92 (0.87-0.98)
CV mortality	586/37582 (0.016)	645/37556 (0.017)	12	0	Moderate	0.91 (0.81-1.02)
Stroke (fatal or nonfatal)	590/38295 (0.015)	743/38315 (0.019)	15	22	High	0.78 (0.68-0.90)
MI (fatal or nonfatal)	665/37723 (0.018)	971/37678 (0.026)	12	14	High	0.67 (0.60-0.75)
Revascularization	579/32966 (0.018)	799/32958 (0.024)	10	15	High	0.71 (0.63-0.80)
Composite CV outcomes	1318/37162 (0.035)	1813/37228 (0.049)	15	51	High	0.72 (0.64-0.81)
Withdrawal due to AEs	1648/22140 (0.074)	1689/21643 (0.078)	10	84	High	0.97 (0.78-1.19)
Serious AEs	3815/28191 (0.135)	3926/27228 (0.144)	10	0	High	0.97 (0.93-1.01)
Cancer	1637/35903 (0.046)	1669/35830 (0.047)	13	0	High	0.98 (0.91-1.04)
Diabetes	1004/29536 (0.034)	941/29547 (0.032)	6	52	Moderate	1.04 (0.92-1.19)
Myalgia	1871/23605 (0.079)	1743/22733 (0.077)	9	30	High	0.98 (0.86-1.11)
Rhabdomyolysis	4/30213 (0.000)	2/29459 (0.000)	8	0	High	1.54 (0.36-6.64)
ALT elevation	224/24276 (0.009)	238/23873 (0.010)	10	0	High	0.94 (0.78-1.13)



AE indicates adverse event; ALT, alanine aminotransferase; CV, cardiovascular; MA, meta-analysis; MI, myocardial infarction; RR, relative risk; SOE, strength of evidence.

Medical News in Brief

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April 26, 2023

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Emily Harris

Article Information

JAMA. Published online April 26, 2023. doi:10.1001/jama.2023.6619

People with HIV and a low to moderate traditional risk of cardiovascular disease who took a daily 4-mg dose of pitavastatin reduced their risk of major adverse cardiovascular events by 35% relative to a placebo group, according to interim results from a randomized clinical trial that enrolled nearly 7769 participants across 12 countries.

Adverse drug events among study participants, who were taking antiretroviral therapy, were no higher than among the general population receiving statins. The study's data and safety monitoring board recommended stopping the trial early for "adequate evidence of efficacy," according to a statement from the National Institutes of Health.

The ODYSSEY OUTCOMES trial: lipoprotein cholesterol levels and cardiovascular risk reduction, the role of **statin** and alirocumab after acute coronary syndrome. Read more in EHJ!
doi.org/10.1093/eurhea...
#LDL #ACS **#statin** #EHJ #cardiotwitter @ESC_Journals @escardio

Key Question

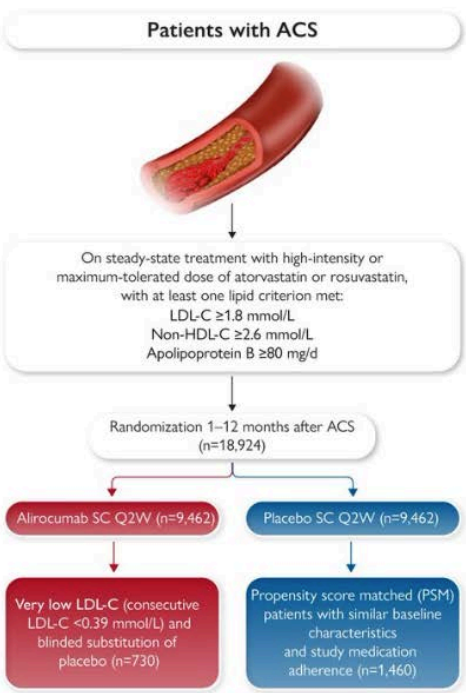
Does a short period of very low low-density lipoprotein cholesterol (LDL-C) achieved with statin and alirocumab result in prolonged cardiovascular risk reduction?

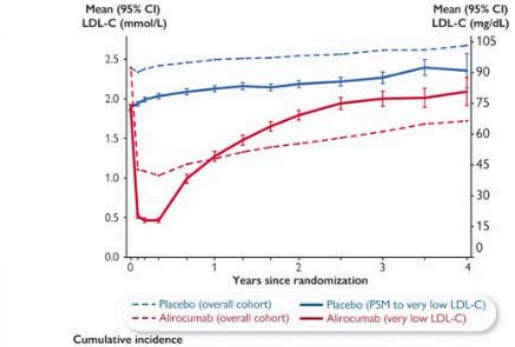
Key Finding

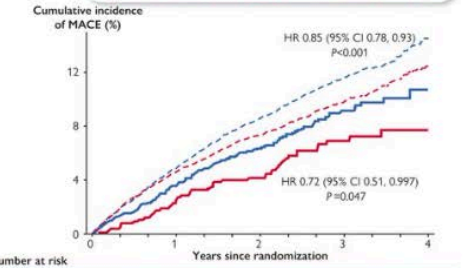
In a post hoc subgroup analysis of a randomized trial, 730 patients treated with statin and alirocumab achieved LDL-C levels <0.39 mmol/L (15 mg/dL) for a median of 6 months before protocol-specified, blinded substitution with placebo for alirocumab. Over 2.8 years' median follow-up, they had a lower risk of cardiovascular events than 1,460 matched patients treated with statin and placebo throughout the observation period.

Take Home Message

A short period of very low LDL-C levels (<0.39 mmol/L) may result in prolonged cardiovascular risk reduction.







Number at risk

Placebo (overall)	9,462	8,805	8,201	3,471	629
Alirocumab (overall)	9,462	8,846	8,345	3,574	653
Placebo (PSM)	1,460	1,359	1,244	494	89
Alirocumab (very low LDL-C)	730	702	669	309	78

Key Question

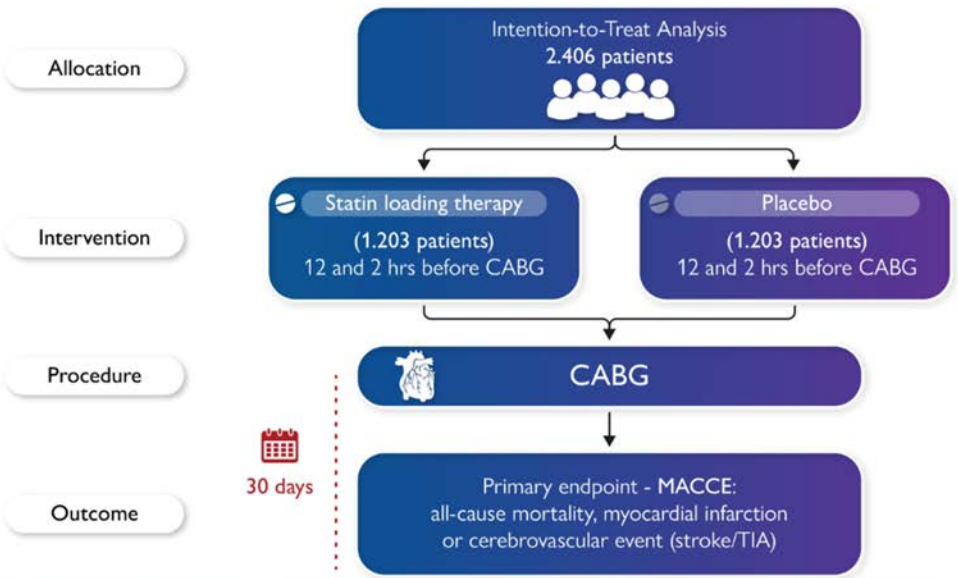
Does a statin loading therapy given at 12 and 2 hours before coronary artery bypass grafting (CABG) reduce 30-day major adverse cardiocerebral events (MACCE) in patients already on chronic statins (>30 days)?

Key Finding

In this randomized clinical trial, consisting of 2406 CABG patients in the modified intention-to-treat analysis, the 30-day MACCE rate was 13.9% among patients in the statin loading group and 14.9% among patients in the placebo group, a statistically non-significant difference (odds ratio 0.93; 95% CI 0.74–1.18; p=0.562).

Take Home Message

Statin loading therapy in patients prior to CABG does not reduce the rate of MACCE at 30 days.



	Statin	Placebo	Odds ratio (95% CI)	P value
Outcomes	n=1203	n=1203		
MACCE at 30 days	167 (13.9%)	179 (14.9%)	0.93 (0.74-1.18)	0.562
All-cause mortality	15 (1.2%)	14 (1.2%)	1.08 (0.52-2.24)	0.836
Myocardial infarction	141 (11.7%)	160 (13.3%)	0.86 (0.68-1.10)	0.239
Cerebrovascular event	23 (1.9%)	16 (1.3%)	1.71 (0.86-3.39)	0.127
Stroke	21 (1.7%)	11 (0.9%)	2.24 (1.02-4.91)	0.045
Transient ischaemic attack	2 (0.2%)	5 (0.4%)	0.52 (0.10-2.78)	0.442

https://doi.org/10.1093/eurheartj/ehad23

Statin use is associated with lower risk of stroke in patients with atrial fibrillation

16 Apr 2023

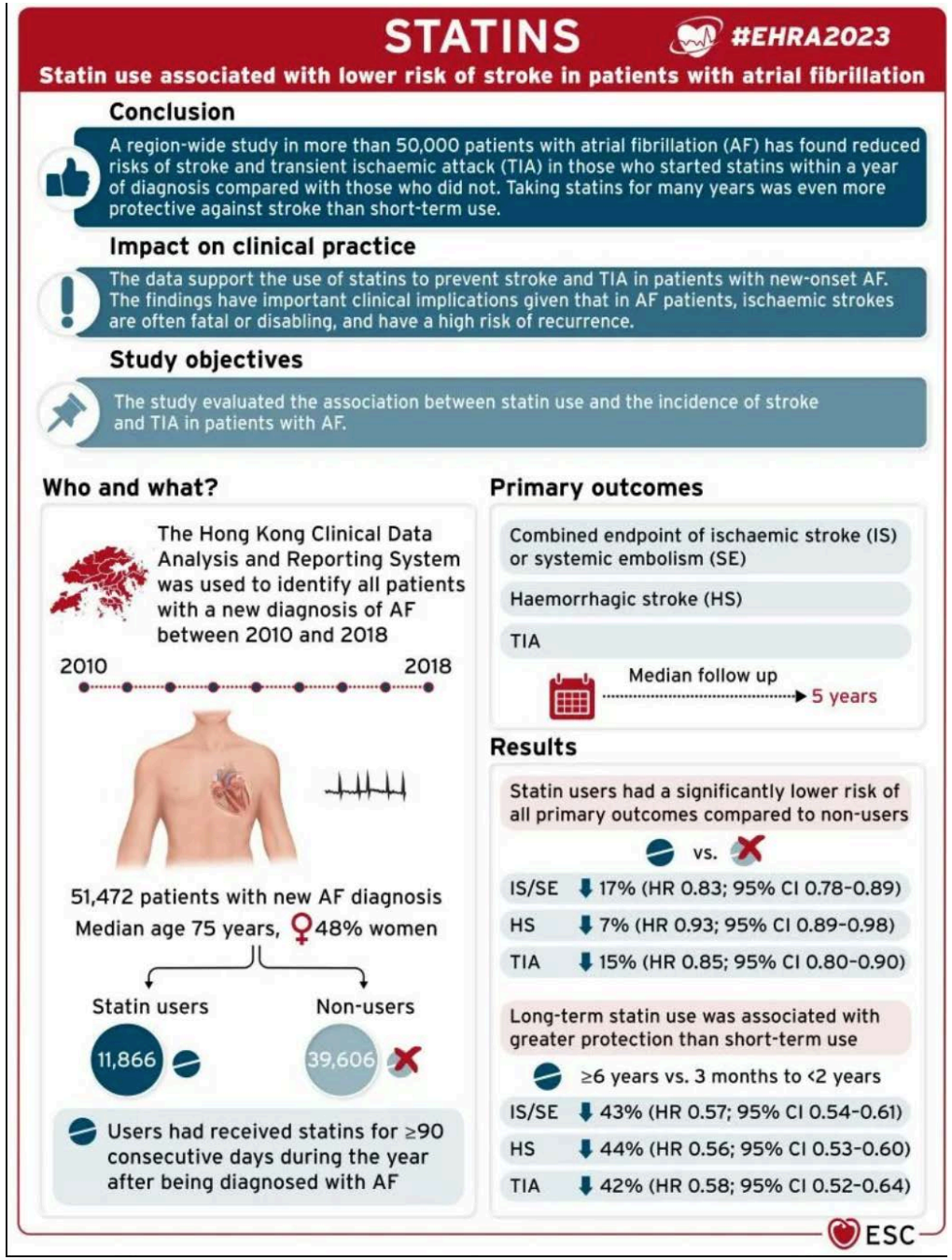
Topic(s): *Atrial Fibrillation; Stroke;*

Barcelona, Spain – 16 April 2023: A region-wide study in more than 50,000 patients with atrial fibrillation has found reduced risks of stroke and transient ischaemic attack in those who started statins within a year of diagnosis compared with those who did not. The findings are presented at EHRA 2023, a scientific congress of the European Society of Cardiology (ESC).[1]

"Our study indicates that taking statins for many years was even more protective against stroke than short-term use," said study author Ms. Jiayi Huang, a PhD student at the University of Hong Kong, China.

Atrial fibrillation is the most common heart rhythm disorder, affecting more than 40 million people worldwide.[2] Patients with the condition have a five times greater risk of stroke than their peers. Anticoagulant medication is recommended to prevent strokes in those with atrial fibrillation but does not completely eliminate risk. Statin therapy is widely prescribed to lower blood cholesterol and reduce the likelihood of heart attack and stroke. However, the benefit of statins for stroke prevention in patients with atrial fibrillation has been unclear.

This study evaluated the association between statin use and the incidence of stroke and transient ischaemic attack in patients with atrial fibrillation. The researchers used the Hong Kong Clinical Data Analysis and Reporting System to identify all patients with a new diagnosis of atrial fibrillation between 2010 and 2018. Participants were divided into two groups: statin users and non-users. Users had received statins for at least 90 consecutive days during the year after being diagnosed with atrial fibrillation.



Yüksək doz statin və aşağı doz statini qarşılaşdıran tədqiqatlar

The ASAP trial The Effect of Aggressive versus conventional lipid lowering in Atherosclerosis Progression in familial hypercholesterolemia trial randomized 325 patients with familial hypercholesterolemia to atorvastatin 80 mg daily or simvastatin 40 mg daily (Smilde et al 2001). The primary endpoint was change in atheroma volume as assessed by quantitative B-mode ultrasound of carotid intima media thickness (IMT). LDL cholesterol lowering was significantly greater ($p = 0.0001$) with atorvastatin (from 8.00 mmol/L to 3.88 mmol/L) than simvastatin (from 8.33 mmol/L to 4.81 mmol/L). After 2 years, IMT decreased in the patients randomized to atorvastatin therapy (−0.031 mm, 95% CI −0.007 to −0.055) but increased in the simvastatin-treated patients (+0.036 mm, 95% CI + 0.014 to + 0.058) – this between-group difference was highly statistically significant ($p = 0.0001$). Both treatment regimens were equally well tolerated.

The ARBITER trial The Arterial Biology for the Investigation of the Treatment Effects of Reducing cholesterol trial randomized 161 patients meeting National Cholesterol Education Program II criteria for lipid-lowering therapy (46% of whom had known cardiovascular disease) to atorvastatin 80 mg daily or pravastatin 40 mg daily (Taylor et al 2002). The primary endpoint was change in carotid IMT. LDL cholesterol lowering was significantly greater ($p < 0.001$) with atorvastatin (from 3.80 mmol/L to 1.95 mmol/L) than pravastatin (from 3.98 mmol/L to 2.82 mmol/L) at 12 months. After 12 months, IMT decreased in the patients randomized to atorvastatin therapy (−0.034 mm ± 0.021 mm) but did not appreciably change in the simvastatin-treated patients (+0.025 mm ± 0.017 mm) – this between-group difference was statistically significant ($p = 0.03$). No patient in either treatment arm suffered a drug-related side effect.

***Vasc Health Risk Manag.* 2007 Oct; 3(5): 615–627**.

Randomized trials comparing higher dose statin therapy with lower dose statin therapy in patients with coronary artery disease

Trial	Sample size	Comparators	Key eligibility criteria	Key demographics (mean age, % men, mean LDL at baseline)	LDL at follow-up (more intensive therapy arm)	LDL at follow-up (less intensive therapy arm)	Duration of follow-up
Post-CABG	1351	Lovastatin 80 mg vs lovastatin 5 mg	Post CABG 1–11 years before	62 years 92% 3.98 mmol/L	2.4 mmol/L	3.5 mmol/L	4.3 years
REVERSAL	654	Pravastatin 40 mg vs atorvastatin 80 mg	Stable CAD	56 years 72% 3.9 mmol/L	2.04 mmol/L	2.85 mmol/L	18 months
Vascular basis	300	Lovastatin 5 mg vs atorvastatin 80 mg vs atorvastatin 80 mg + antioxidant	Stable CAD	not reported 86% 3.9 mmol/L	2.2 mmol/L	3.2 mmol/L	12 months
PROVE IT-TIMI 22	4,162	Pravastatin 40 mg vs atorvastatin 80 mg	Post ACS	58 years 78% 2.74 mmol/L	1.60 mmol/L	2.46 mmol/L	24 months

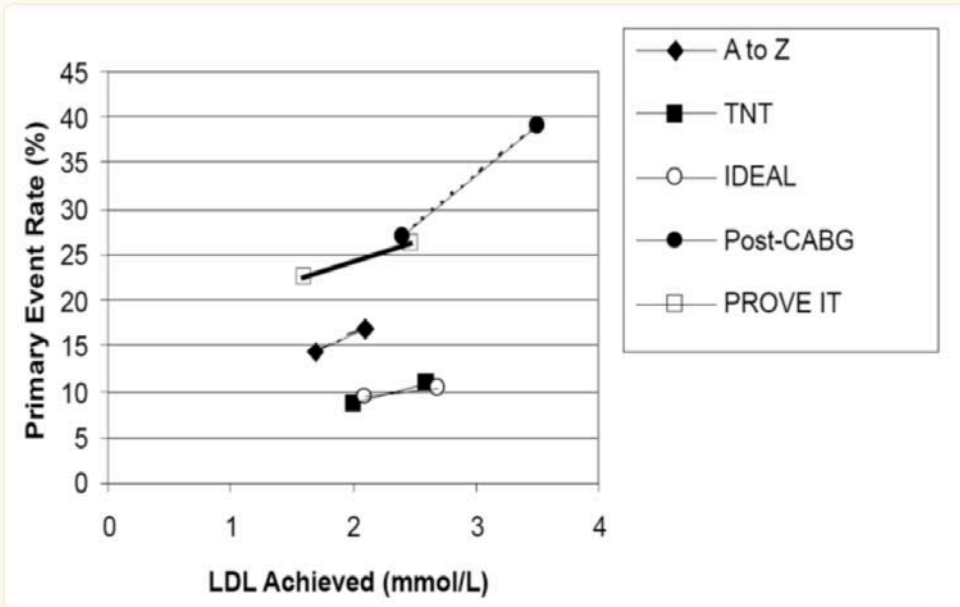
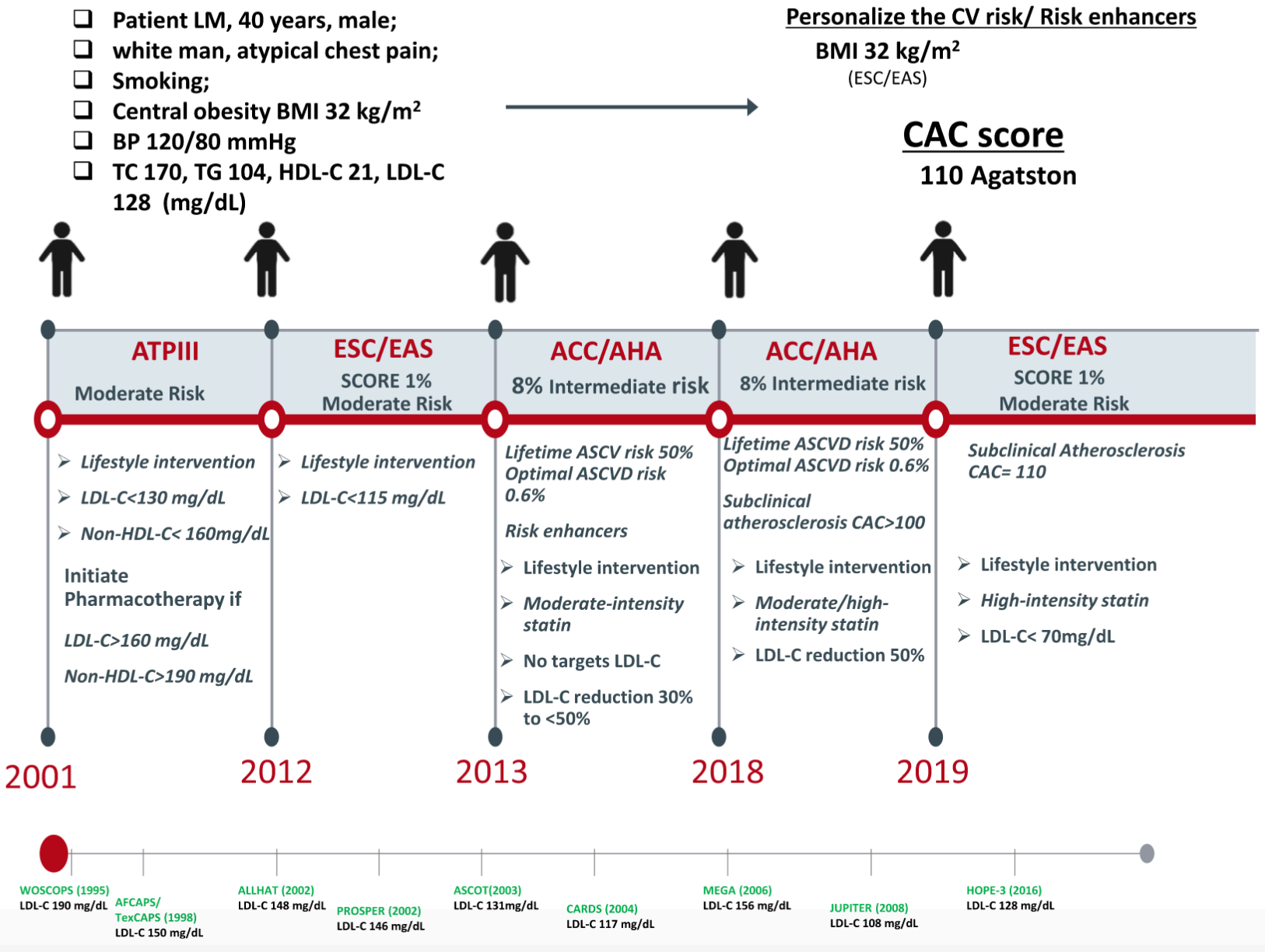


Figure 1

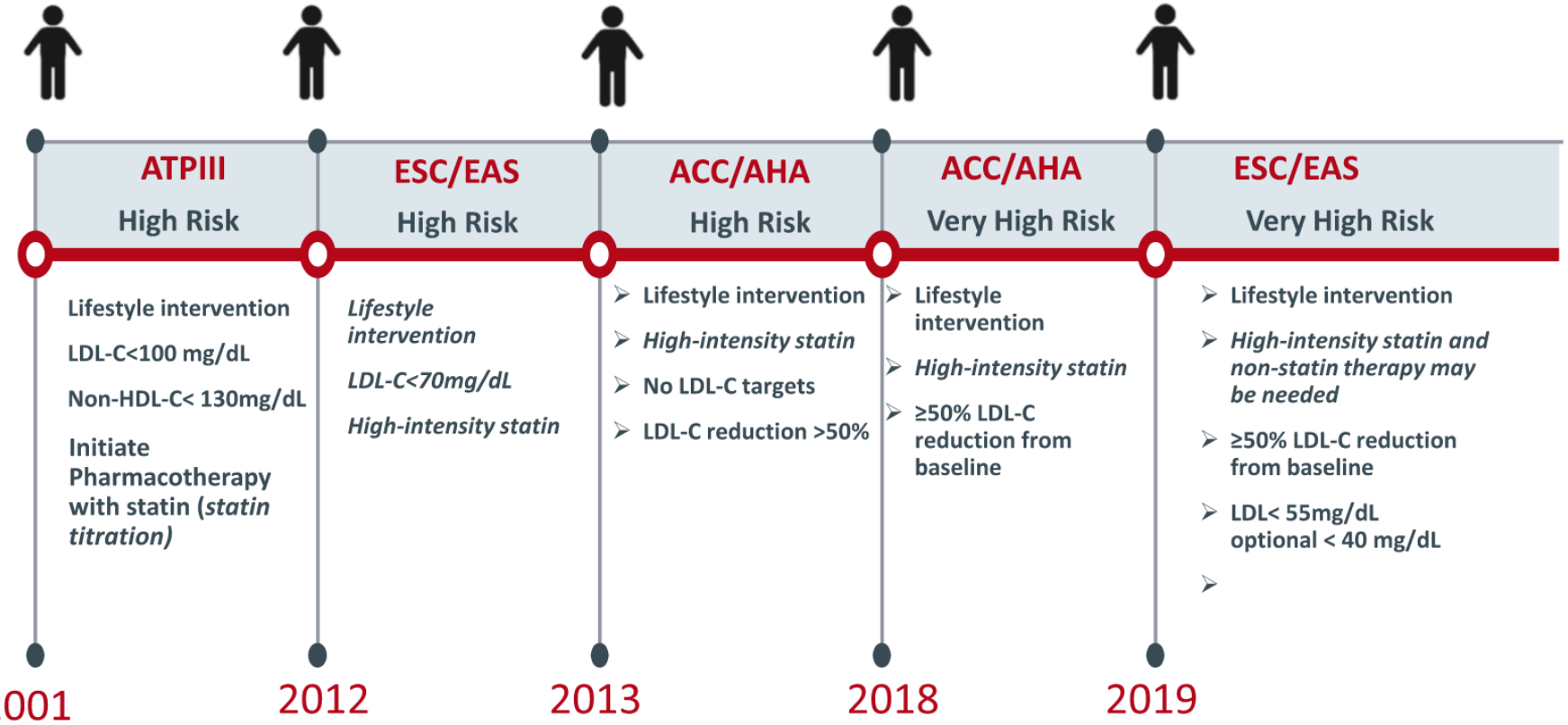
Association between achieved LDL cholesterol levels and primary outcome in both arms of the higher dose versus lower dose statin trials. The results for the less intensive arm of each trial are expressed on the right of each trial's line; the results for the more intensive arm of each trial are expressed on the left of each trial's line.

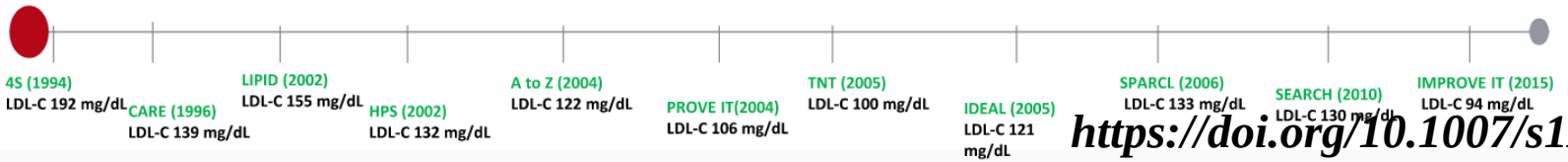


https://doi.org/10.1007/s11883-020-00861-9

- ❑ Patient OBG, 70 years, female;
- ❑ Recent acute myocardial infarction
- ❑ Obesity BMI 29 kg/m^2
- ❑ BP 145/95mmHg
- ❑ TC 225, TG 84, HDL-C 50, LDL-C 158 (mg/dL)

- ❖ Is this patient to goal?
- ❖ What would be our recommendations following the guidelines timeline?





https://doi.org/10.1007/s11883-020-00861-9

Koronar ateroskleratik plak həcminin böyüməsinin, LDL– C səviyyəsinin azaldılması ilə azaldıla bilər (1.8 mmol/L/70 mg/dL)[1,2]

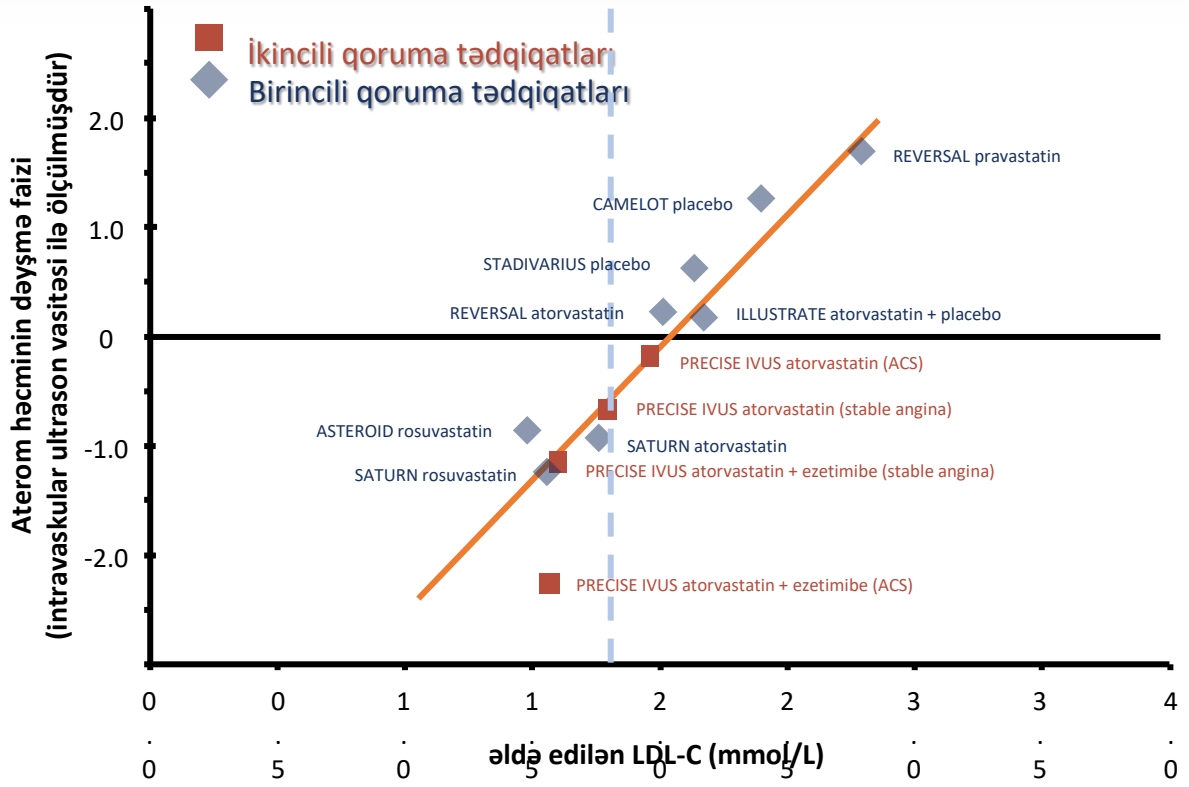


Figure from Ference et al Eur Heart J. 2017 [1]

AZ/SYB/04.2023/05/633408

1. Ference BA et al., Eur. Heart J. 2017; 38:2459–72; 2. Fernández-Friera L et al., J Am Coll Cardiol. 2017; 70(24):2979-91

Əldə edilmiş LDL-C səviyyəsi ilə mütləq CV hadisə tezliyi arasında güclü və xətti əlaqə var

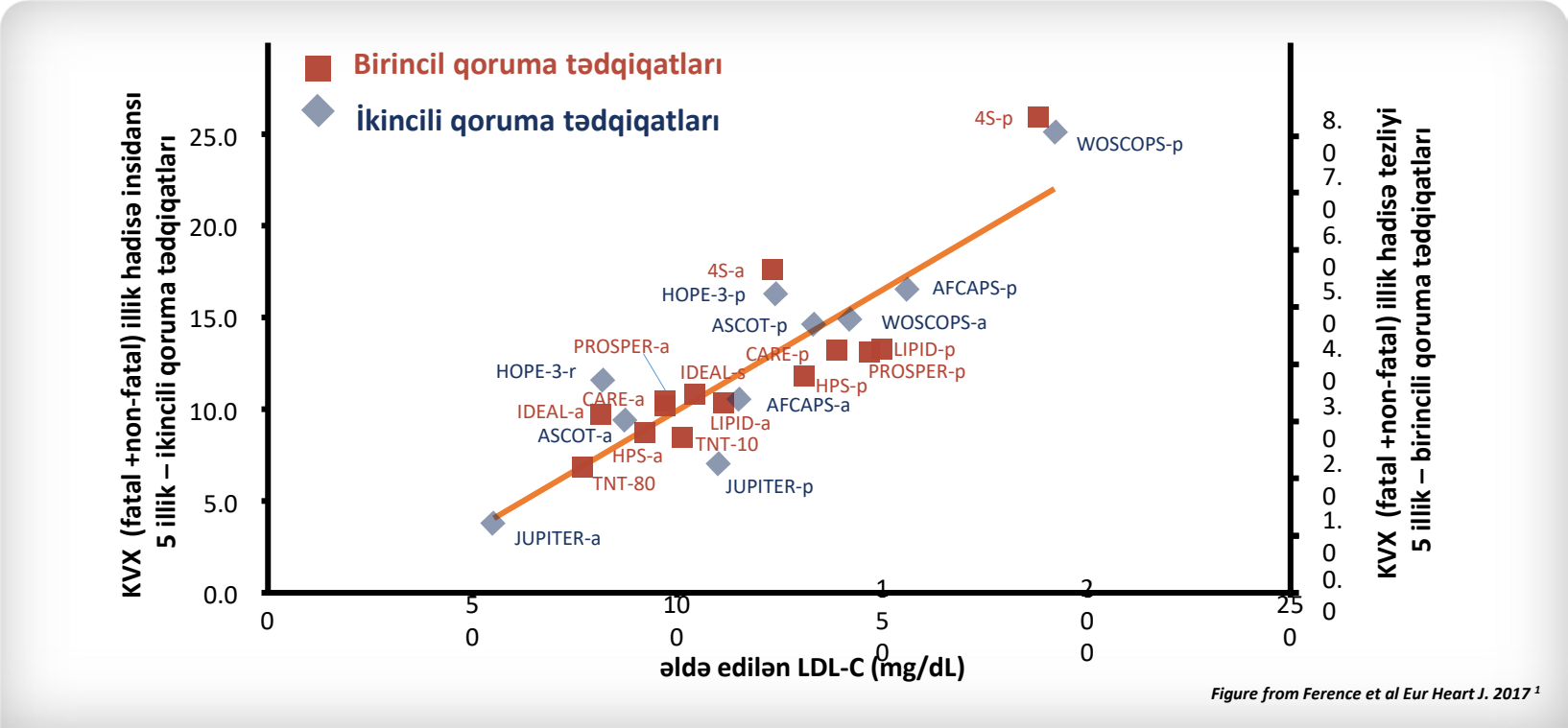


Figure from Ference et al Eur Heart J. 2017 [1]

- **ASKVX LDL-C səviyyələri ilə primer və sekonder qoruma güclü şəkildə əlaqəlidir**

Davamlı uzunmüddətli LDL-C azalması ASKVX riskinin ömür boyu mütənasib olaraq daha böyük azalmalarına səbəb olur.

- Hər LDL-C səviyyəsindəki 1 **mmol/L azalma ASKVX riskinin azalmasına səbəb olur**
  - **~10% - 1ci il**
  - **16% - ikinci ildən sonra**
  - **20% - 3 ildən sonra**
  - **1.5% - hər növbəti il**
- Beş illik lipid azaldıcı müalicə ASKVX-nin nisbi riskini LDL-C-nin hər mmol/l azalmasına görə ~20-25% azaltmalıdır
- 40 illik lipid düşürücü müalicənin **ASKVX hadisələrini LDL-C-də hər mmol/L azalmasına görə ~50-55%** azaltması gözlənilir.

LDL-Cnin hər vahid azalması və KV xəstəlik riskinin azalması arasında log-linear əlaqə

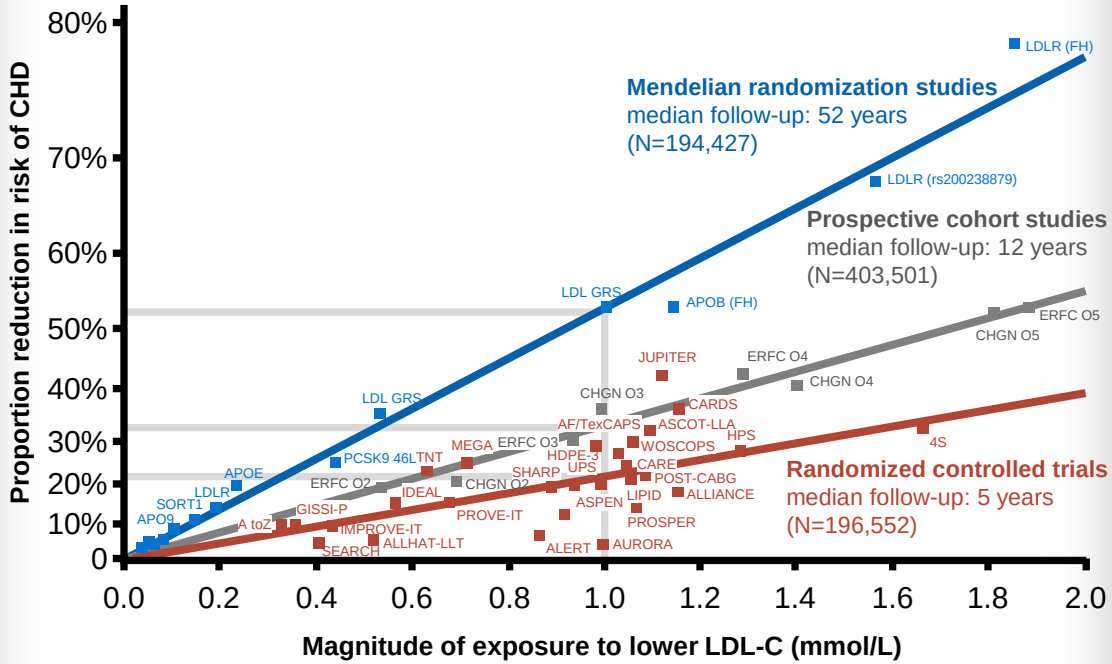
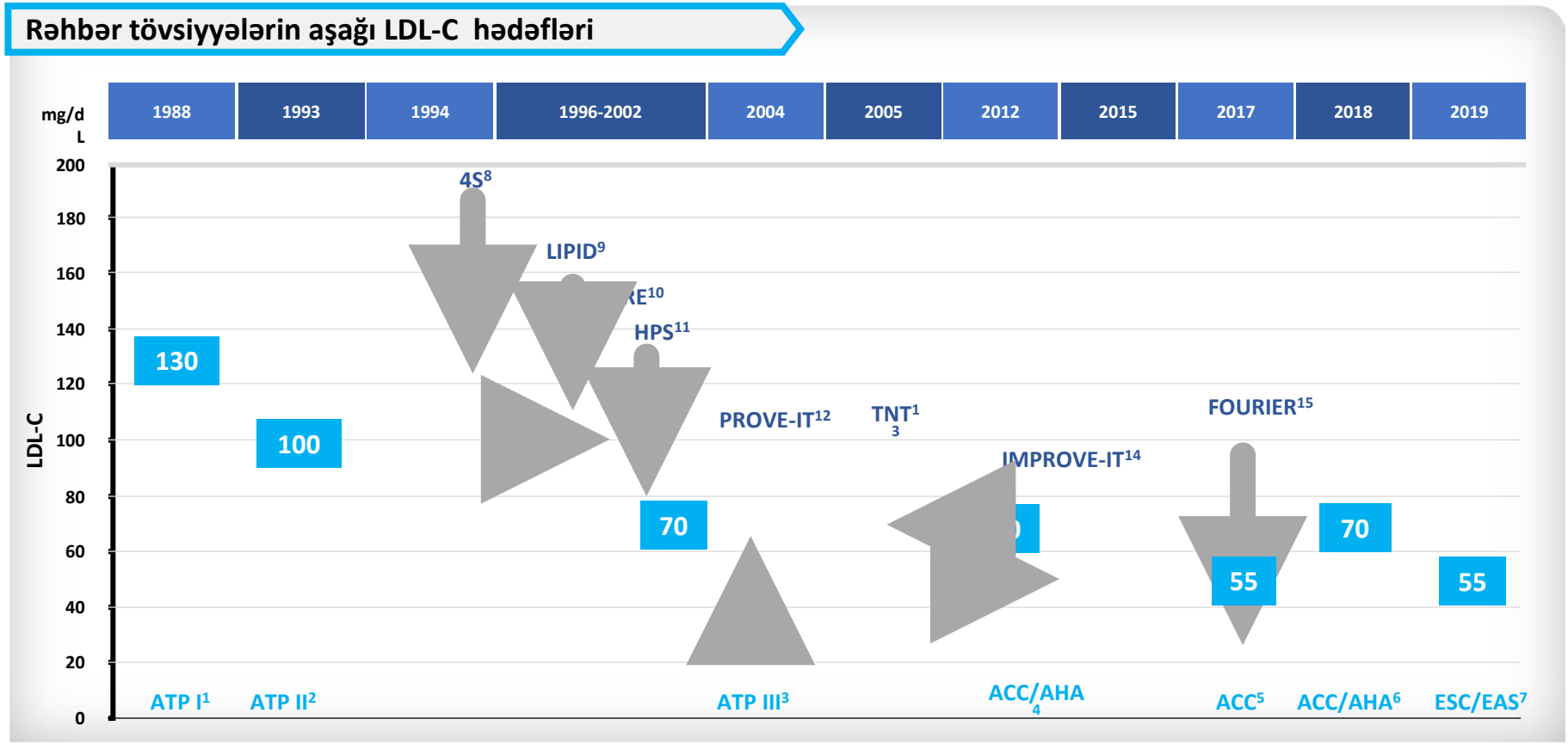


Figure from Ference et al Eur Heart J. 2017

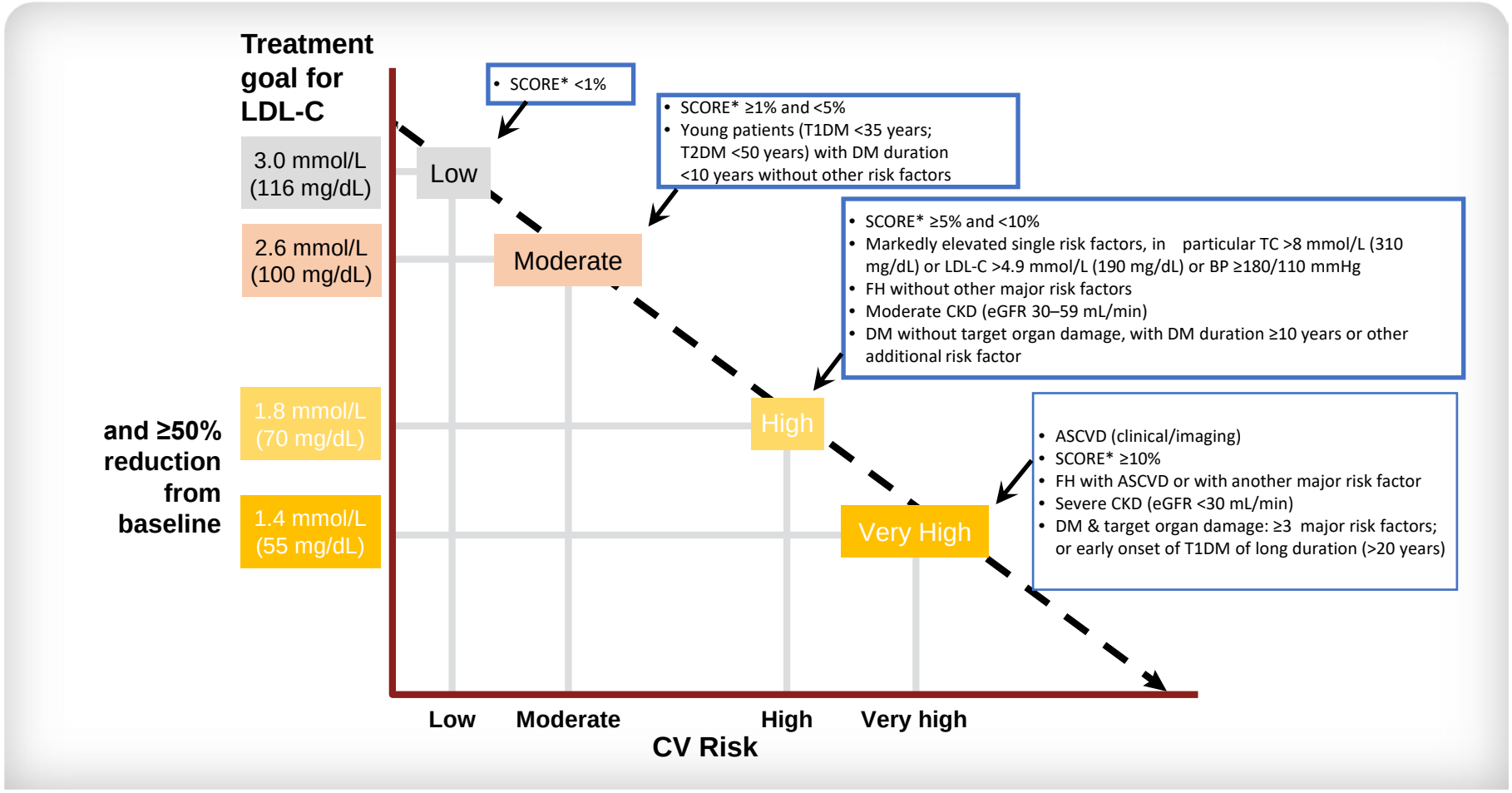
Ference BA et al., Eur. Heart J. 2017; 38:2459–72

25 illik tədqiqatlar aşağı LDL-C-nin fayda və təhlükəsizliyini sübut etdiyi ortadadır …



1.Goodman DS et al., Arch Intern Med. 1988;148:36-69; 2. Grundy SM et al. JAMA. 1993;269:3015-23; 3. Grundy SM et al. Circulation. 2004. 10;110:763; 4. Bangalore S et al. Am J Med.2016;129:384-91; 5.Lloyd-Jones DM et al. J Am Coll Cardiol. 2017;70:1785-1822; 6. Grundy SM, et al J Am Coll Cardiol. 2019;73(24):3168-3209; 7. Mach F et al. Eur Heart J. 2020; 41:111-88; 4S group. Lancet 1994;344:1383-9; LIPID Study group. N Engl J Med 1998; 339:1349-57; 10. Pfeffer MA et al. J Am Coll Cardiol. 1999;33:125-30; 11. HPS Collaborative Group.J Vasc Surg 2007;45:645-54; 12. Cannon CP et al. N Engl J Med. 2004;350:1495-504; 13. LaRosa JC et al. N Engl J Med 2005; 352:1425-35; 14. Cannon CP et al., N Engl J Med 2015; 372:2387-97;15. Sabatine MS et al., N Engl J Med 2017; 376:1713-22

Risk kateqoriyalarına görə LDL-C üçün 2019 ESC/EAS rəhbərinin müalicə məqsədləri



** Systematic Coronary Risk Estimation (SCORE) for 10-year risk of fatal CVD*

Mach F et al. Eur Heart J. 2020; 41:111-88

diqqətiniz üçün təşəkkür edirəm

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