The Changing Lipids Landscape for Primary Care

.

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Professor of Primary Care Cardiovascular Medicine

Immediate Past President, British and Irish Hypertension Society

Northern Lipids Forum, Hilton Gateshead Hotel, 19 October 2023

Declarations of Interest

- Guideline Committees: NICE CG127, NG136, NG158, NG180, Covid NG186 and Update NG9. AAGBI/BHS Pre-operative Hypertension 2016. Cardio-Oncology Guidance[1,2]
- Research grants: Amgen, Bayer, Daichi-Sankyo, Esperion, Novartis, National Institute of Health Research and Yorkshire Cancer Research
- Industry sponsorship for personal financial gain: Amarin, Amgen, AstraZeneca, Bayer, Daichi-Sankyo, Medtronic, Omron, Novartis and Sanofi-Aventis

1. Plummer C, Michael A, Shaikh G, Stewart M, Buckley L, Miles T, Ograbek A, McCormack T. Expert recommendations on the management of hypertension in patients with ovarian and cervical cancer receiving bevacizumab in the UK. *British Journal of Cancer (June 2019)* *https://doi.org/10.1038/s41416-019-0481-y*
2. Tang CPS, Lip GY, McCormack T, Lyon AR, Hillmen P, Iyengar S, Martinez-Calle N, Parry-Jones N, Patten PE, Schuh A, Walewska R, on behalf of the BSH guidelines committee, UK CLL Forum (2021). Management of cardiovascular complications of bruton tyrosine kinase inhibitors. *Br J Haematol*. *https://doi.org/10.1111/bjh.17788*

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Agenda

- Cholesterol myths
- QOF, CVD Prevent, NICE
- Ezetimibe
- Bempedoic Acid
- PCSK9 inhibitors
- Inclisiran
- Icosapent Ethyl
- Summary/Discussion

Cholesterol Myths

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Cholesterol Myths

- Take statins at night

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Cholesterol Myths

- Take statins at night
- LDL-C “bad cholesterol”
- HDL-C “good cholesterol”
- Total cholesterol <5mmol/l “normal”

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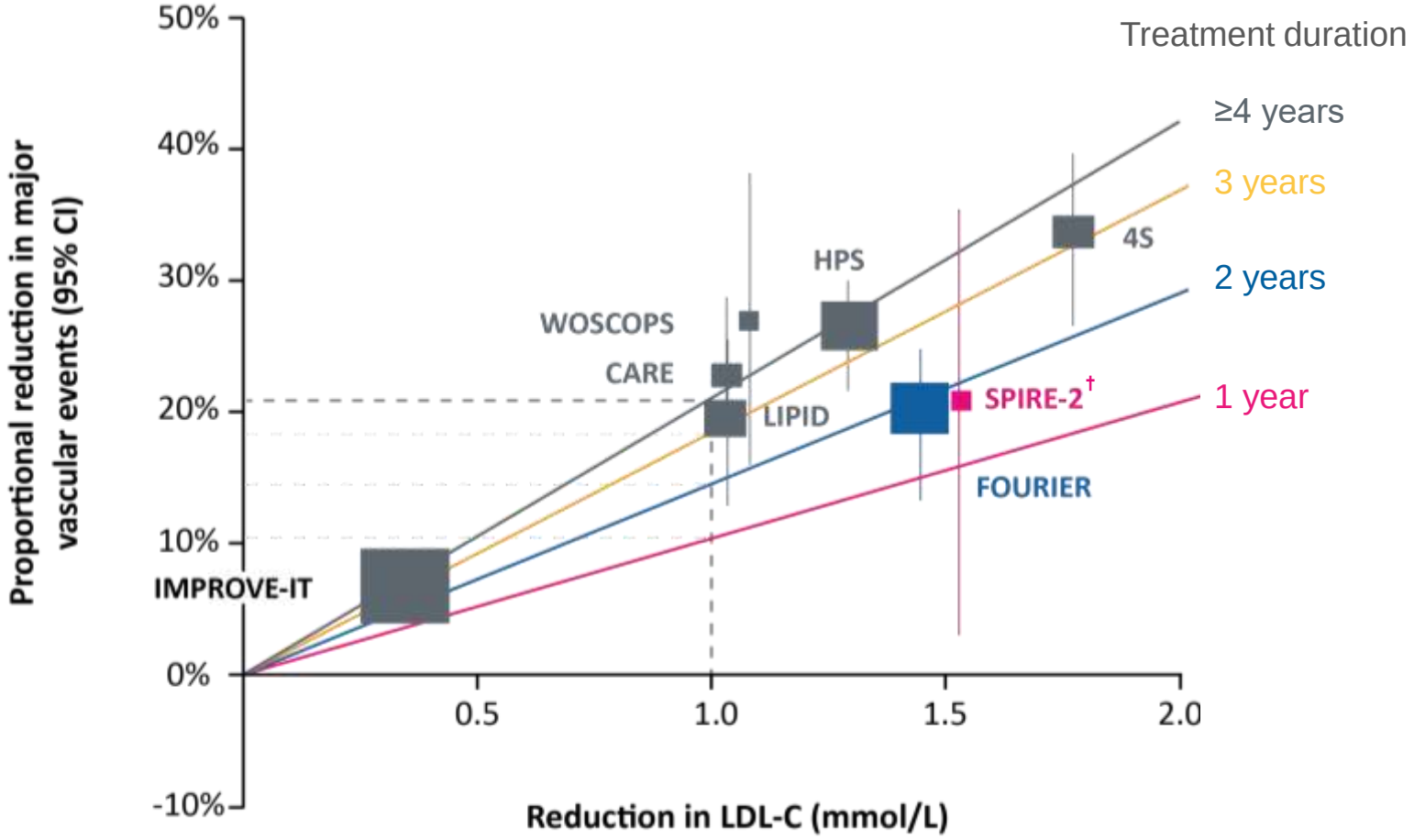
CVD Risk Reduction & Duration of Treatment[1]



1. Ference BA, et al. Eur Heart J 2018;39:2540–2545. † Bococizumab

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Cholesterol Myths

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- Nocebo effect

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Cholesterol Myths

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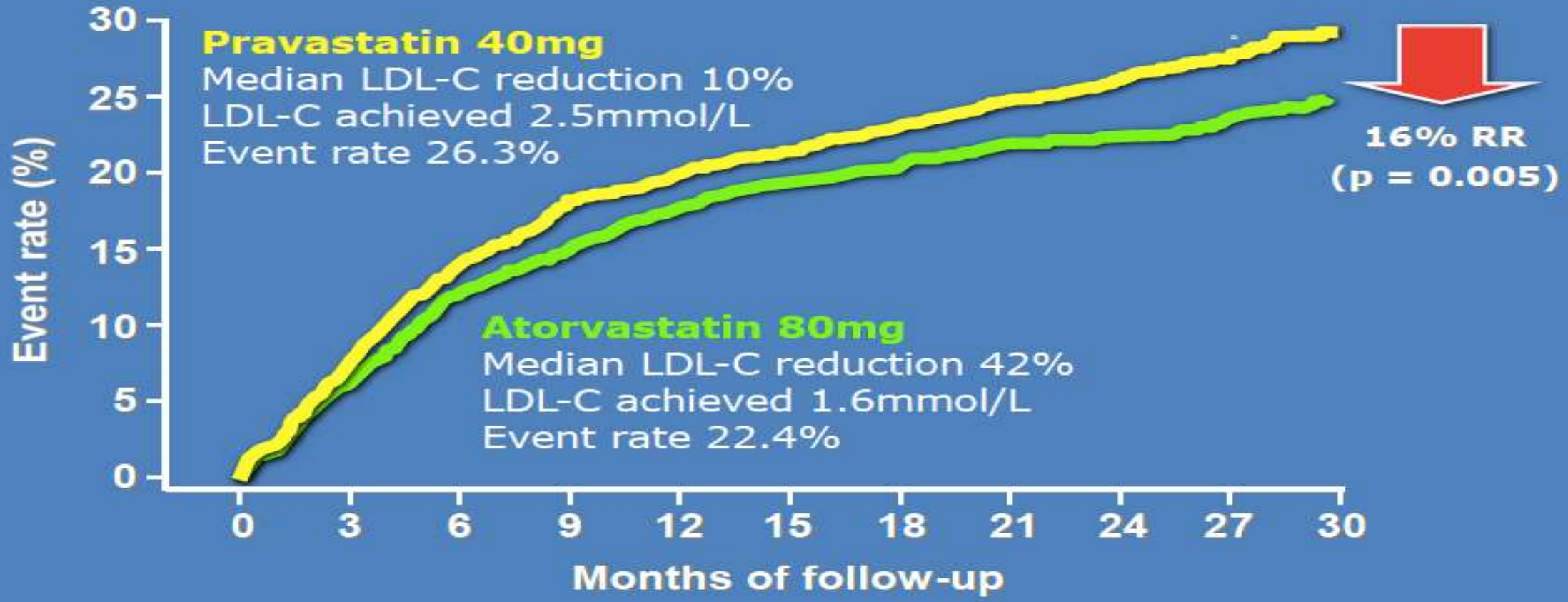
- HDL-C “good cholesterol”
- Total cholesterol <5mmol/l “normal”
- Nocebo effect
- The pleomorphic effect

PROVE-IT

All-cause death or major cardiovascular events
in all randomised subjects



Adapted from Cannon CP, *et al.*. *N Engl J Med* 2004;350:1495-504

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Cholesterol Myths

- Take statins at night
- LDL-C “bad cholesterol”
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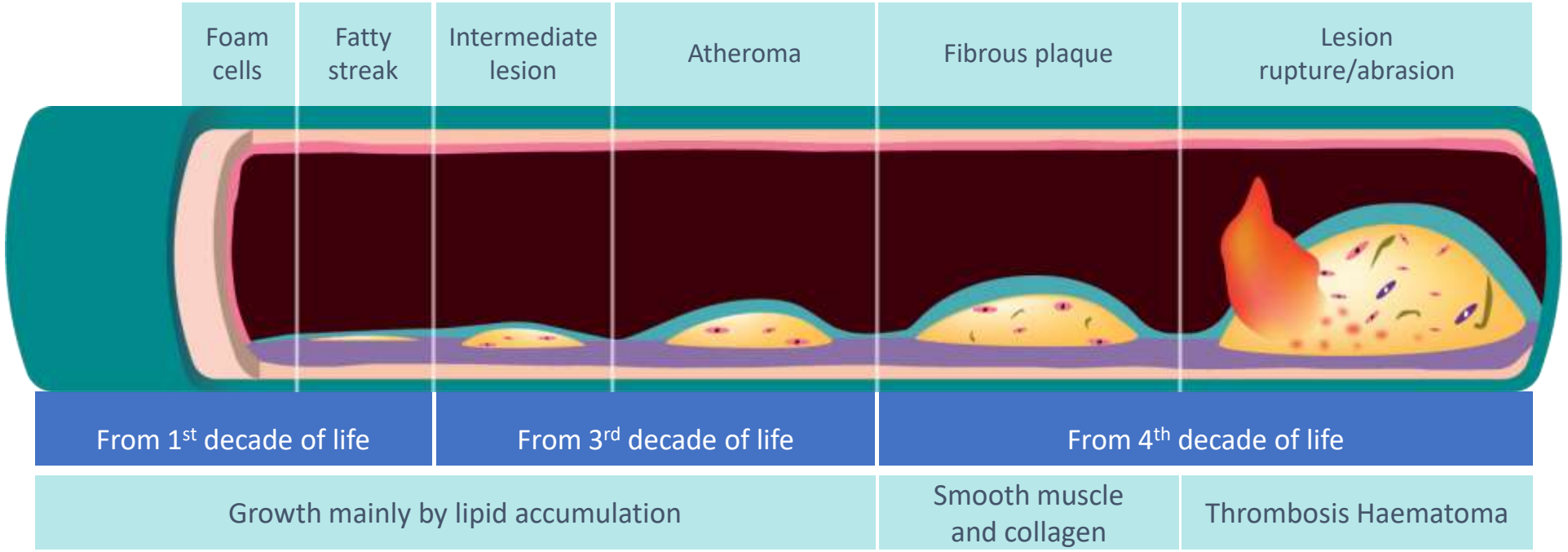
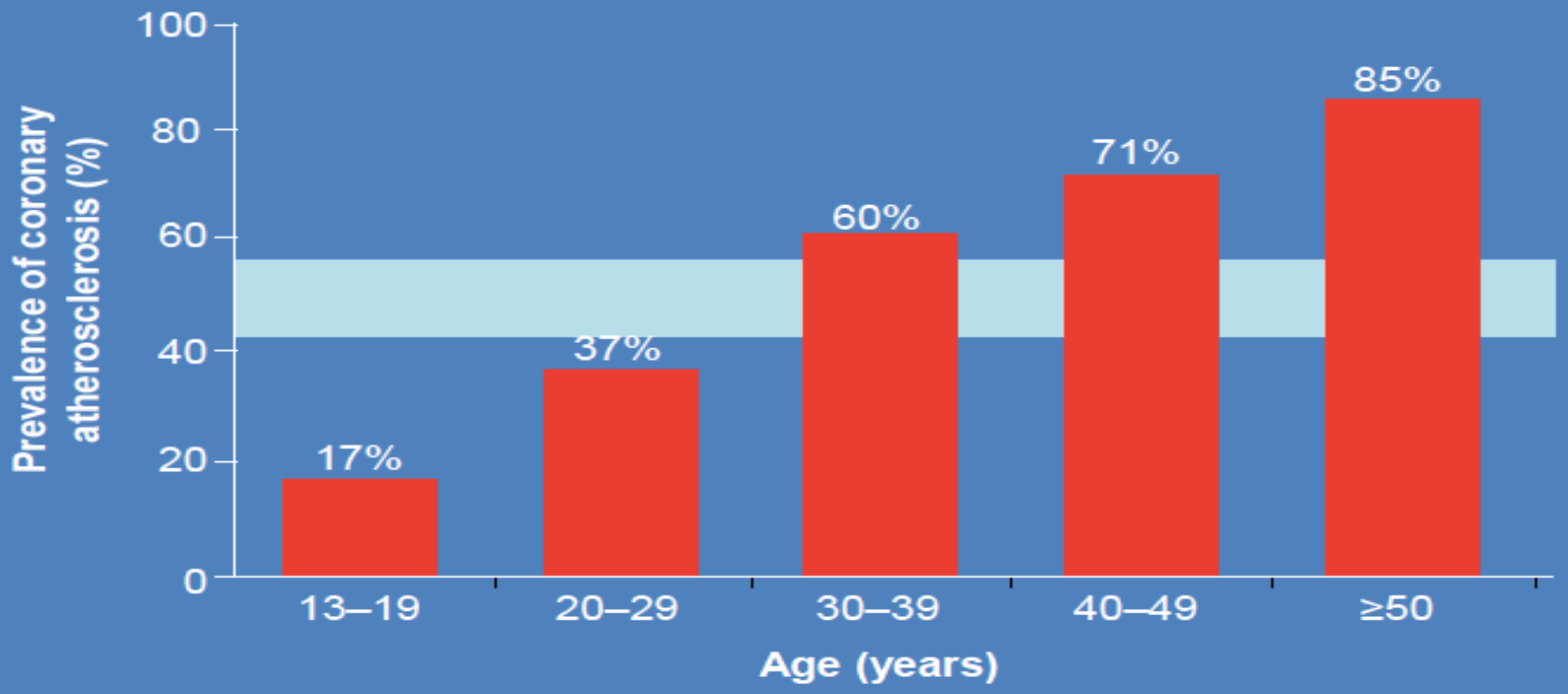
- Atherosclerosis is a disease of the elderly

Atherosclerosis is a disease of the elderly



1. Pepine CJ. Am J Cardiol. 1998;82:23S-27S.

Atherosclerosis: When does it begin?[1]



Data from 262 heart transplant donors.
Sites with intimal thickness ≥0.5 mm were defined as atherosclerotic.

1. Adapted from Tuzcu EM, *et al*,. *Circulation*. 2001;**103**:2705-2710

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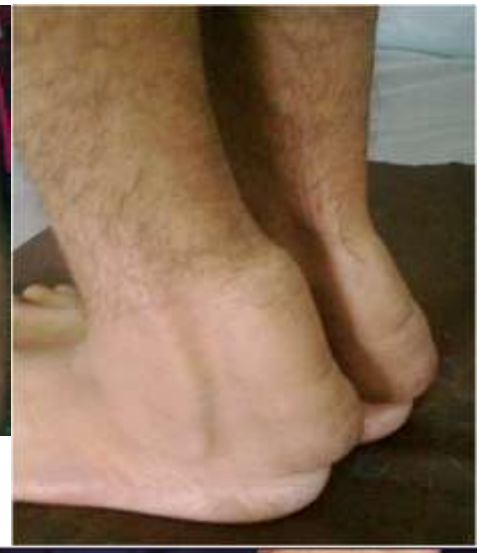
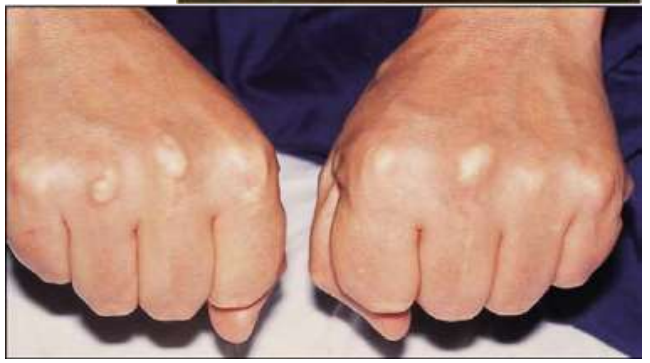
Cholesterol Myths

- Take statins at night
- LDL-C “bad cholesterol”
- HDL-C “good cholesterol”
- Total cholesterol <5mmol/l “normal”
- Nocebo effect
- The pleomorphic effect
- Atherosclerosis is a disease of the elderly
- Familial Hypercholesterolaemia is untreatable

Familial Hypercholesterolaemia





- Homozygotes
  - *One in a million people*
  - *Apheresis*
- *Heterozygotes*
  - *One in 250 people*
  - *One in six myocardial infarctions*[1,2,3]
- Simon Broome criteria[4]
  - Family history
  - Tendon xanthoma, xanthelsma
- *Dutch Lipid Network Score >6*
- *Index case finding and family gene sequencing*

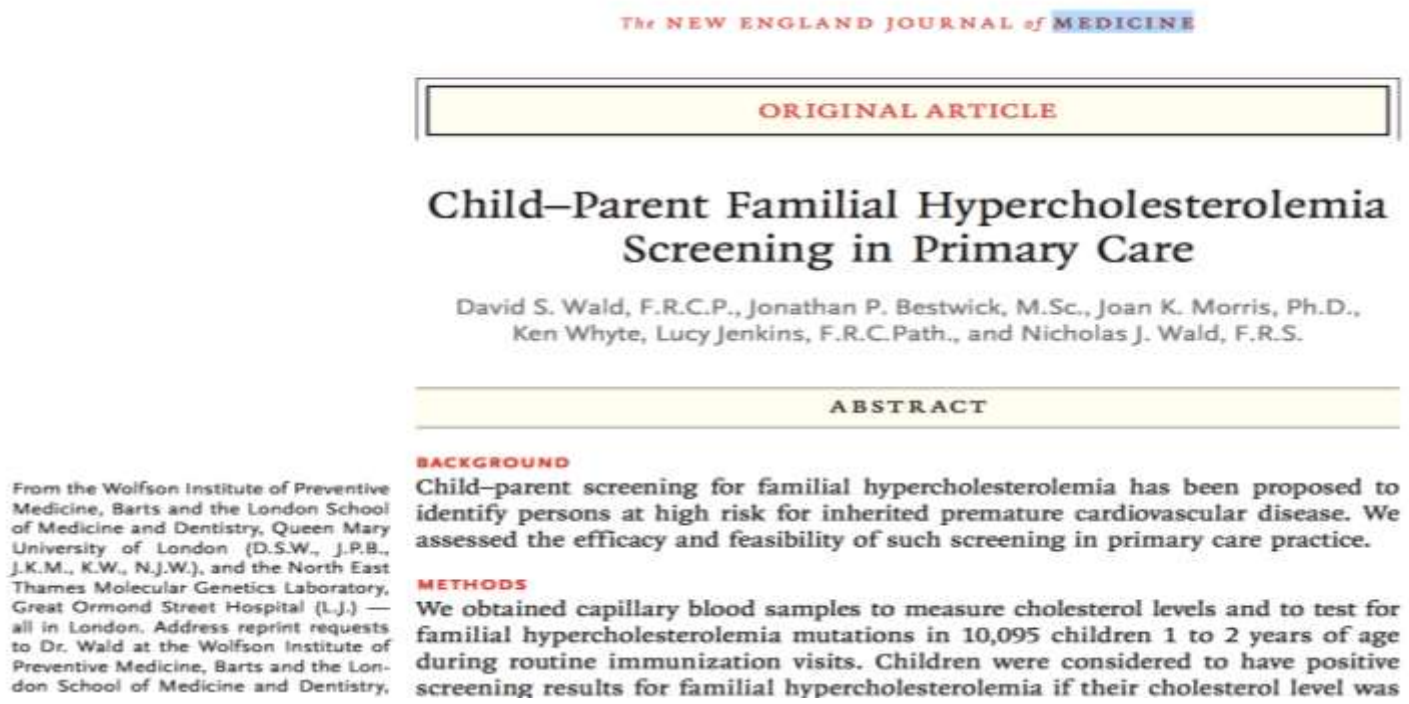
1. Nanchen D. European Heart Journal (2015) 36, 2438–2445 doi:10.1093/eurheartj/ehv289

2. Genest JJ Jr. Circulation 1992;85: 2025 – 2033.

3. Dorsch MF. BMJ 2001;322:111 4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3976735/

Child-parent screening in UK General Practice?

- 10,095 one – two year olds
- *Heel prick with routine immunisation*
- 40 children and 40 parents found
- *FH incidence is 1 in 250*



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Child–Parent Familial Hypercholesterolemia Screening in Primary Care

David S. Wald, F.R.C.P., Jonathan P. Bestwick, M.Sc., Joan K. Morris, Ph.D., Ken Whyte, Lucy Jenkins, F.R.C.Path., and Nicholas J. Wald, F.R.S.

ABSTRACT

BACKGROUND

Child–parent screening for familial hypercholesterolemia has been proposed to identify persons at high risk for inherited premature cardiovascular disease. We assessed the efficacy and feasibility of such screening in primary care practice.

METHODS

We obtained capillary blood samples to measure cholesterol levels and to test for familial hypercholesterolemia mutations in 10,095 children 1 to 2 years of age during routine immunization visits. Children were considered to have positive screening results for familial hypercholesterolemia if their cholesterol level was

From the Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine and Dentistry, Queen Mary University of London (D.S.W., J.P.B., J.K.M., K.W., N.J.W.), and the North East Thames Molecular Genetics Laboratory, Great Ormond Street Hospital (L.J.) — all in London. Address reprint requests to Dr. Wald at the Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine and Dentistry,

1. Wald DS. NEJM 2016; 375:17.

QOF, CVD Prevent, NICE

Quality and Outcomes Framework (QOF) 2023/24

- **CHOL001**
- % of patients on the QOF Coronary Heart Disease, Peripheral Arterial Disease, Stroke/TIA or Chronic Kidney Disease Register who are currently prescribed a statin, or where a statin is declined or clinically unsuitable, another lipid-lowering therapy
- **Points 14 – Threshold 70-95%**

- **CHOL002**
- % of patients on the QOF Coronary Heart Disease, Peripheral Arterial Disease, or Stroke/TIA Register, who have a recording of non-HDL cholesterol in 40-80% the preceding 12 months that is lower than 2.5 mmol/L, or where non-HDL cholesterol is not recorded a recording of LDL cholesterol in the preceding 12 months that is lower than 1.8 mmol/L
- **Points 16 – Threshold 20-35%**

CVD Prevent Audit of practices across Primary Care Networks

- **Individual practice data highlighting treatment gaps, identify inequalities and opportunities for improvement**

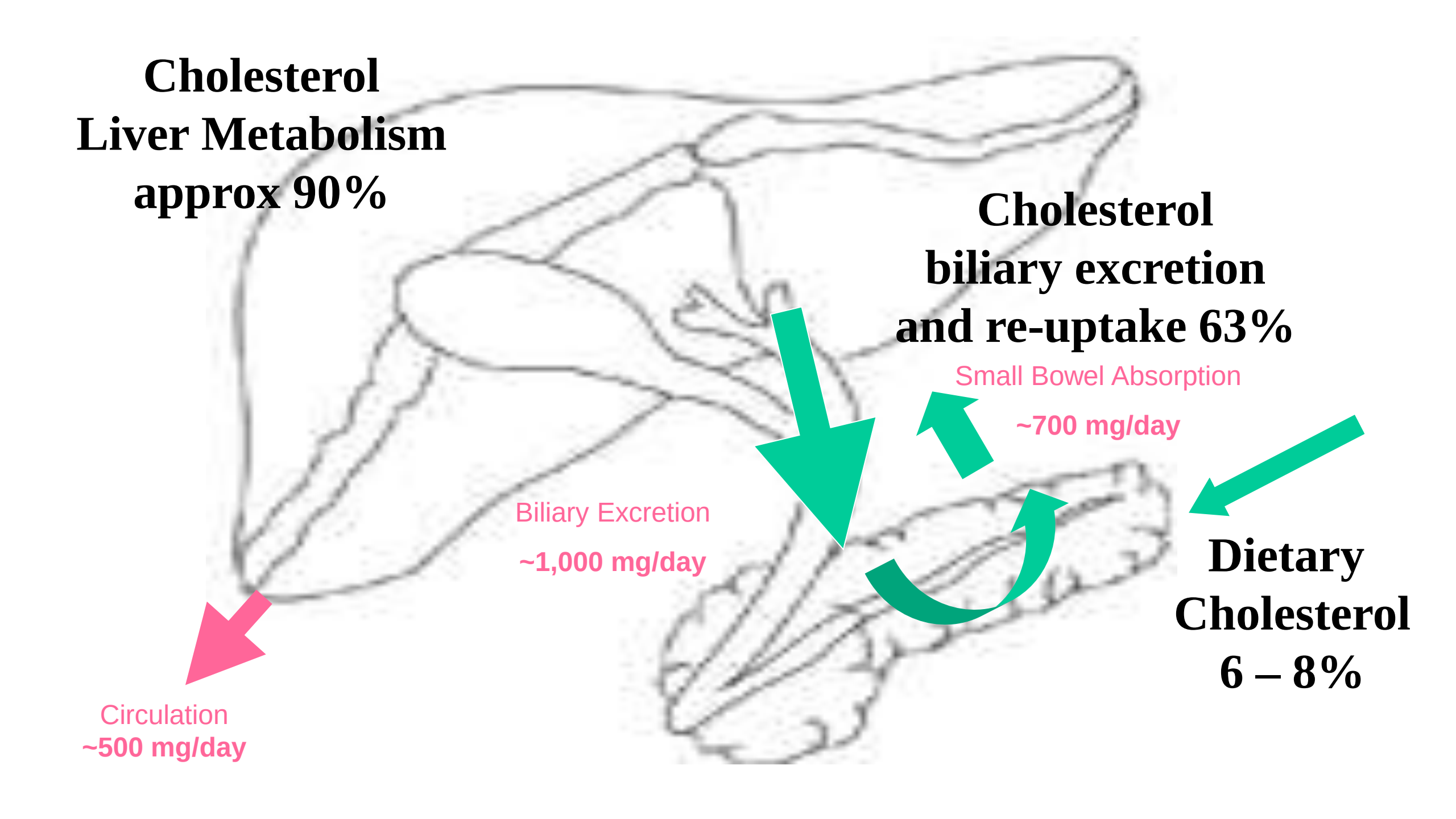
- **CVD009CHOL**
- % patients with cardiovascular disease who are currently treated with lipid lowering therapy
- **CVD010CHOL**
- % patients with chronic kidney disease who are currently treated with lipid lowering therapy

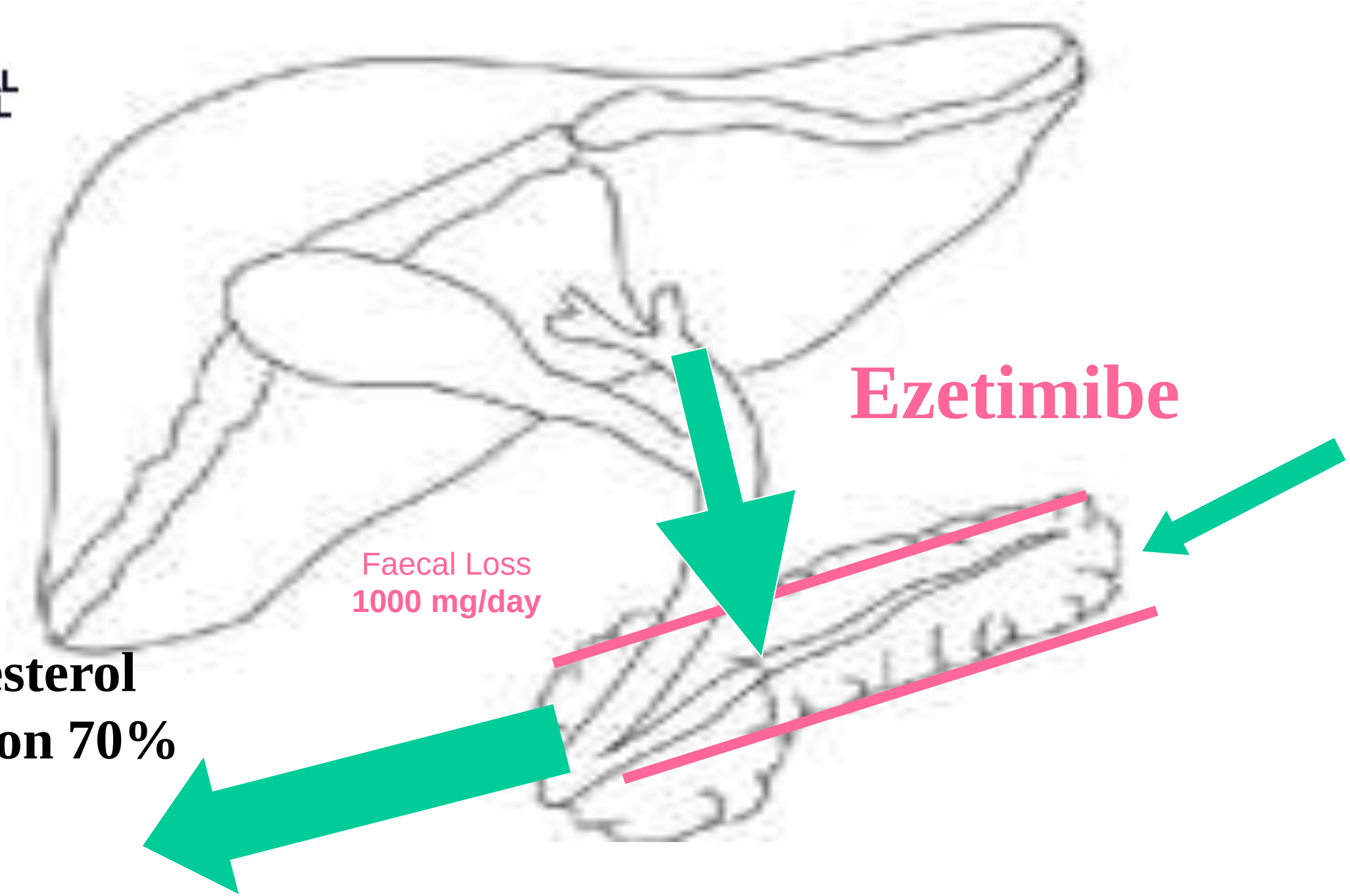
NICE Hypertension/Lipids Guideline 2023

- **Mostly British and Irish Hypertension Society Members**
- Age 25 – 84 including DM2 without CVD
- QRisk3 >10% Offer atorvastatin 20mg
- “Do not rule out” if <10%

- **Consultation**
- Secondary Prevention Targets non-HDL-C <2.6mmol/L or LDL-C <2.0mmol/L

Ezetimibe

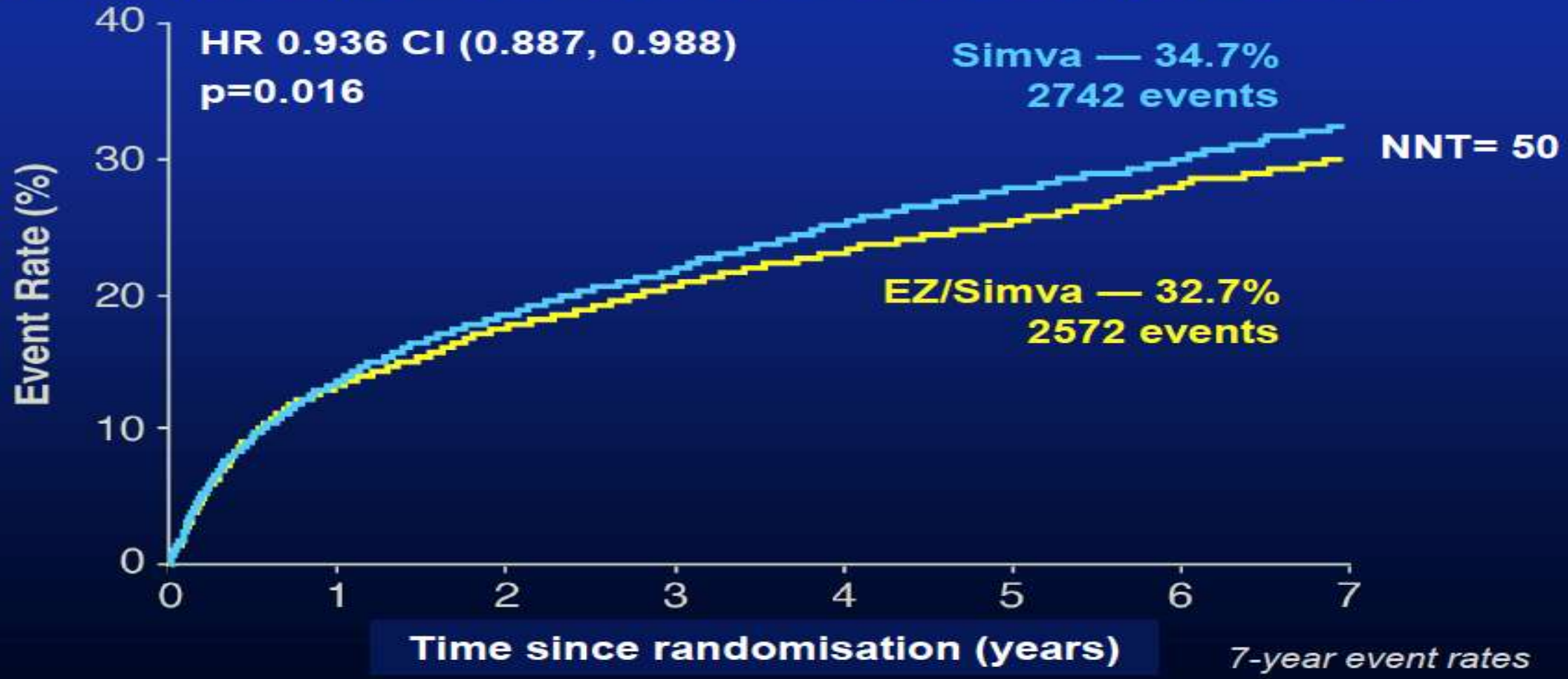

Cholesterol
Liver Metabolism
approx 90%
Cholesterol
biliary excretion
and re-uptake 63%
Small Bowel Absorption
~700 mg/day
Biliary Excretion
~1,000 mg/day
Dietary
Cholesterol
6 – 8%
Circulation
~500 mg/day


Ezetimibe
Faecal Loss
1000 mg/day
Cholesterol
excretion 70%

Primary Endpoint — ITT

IMPROVE-IT

Cardiovascular death, MI, documented unstable angina requiring rehospitalisation, coronary revascularisation (≥30 days), or stroke



7-year event rates

IN-PRACTICE: INcremental cholesterol reduction with ezetimibe/simvastatin, atorvastatin and rosuvastatin in UK General PRACTICE[1]

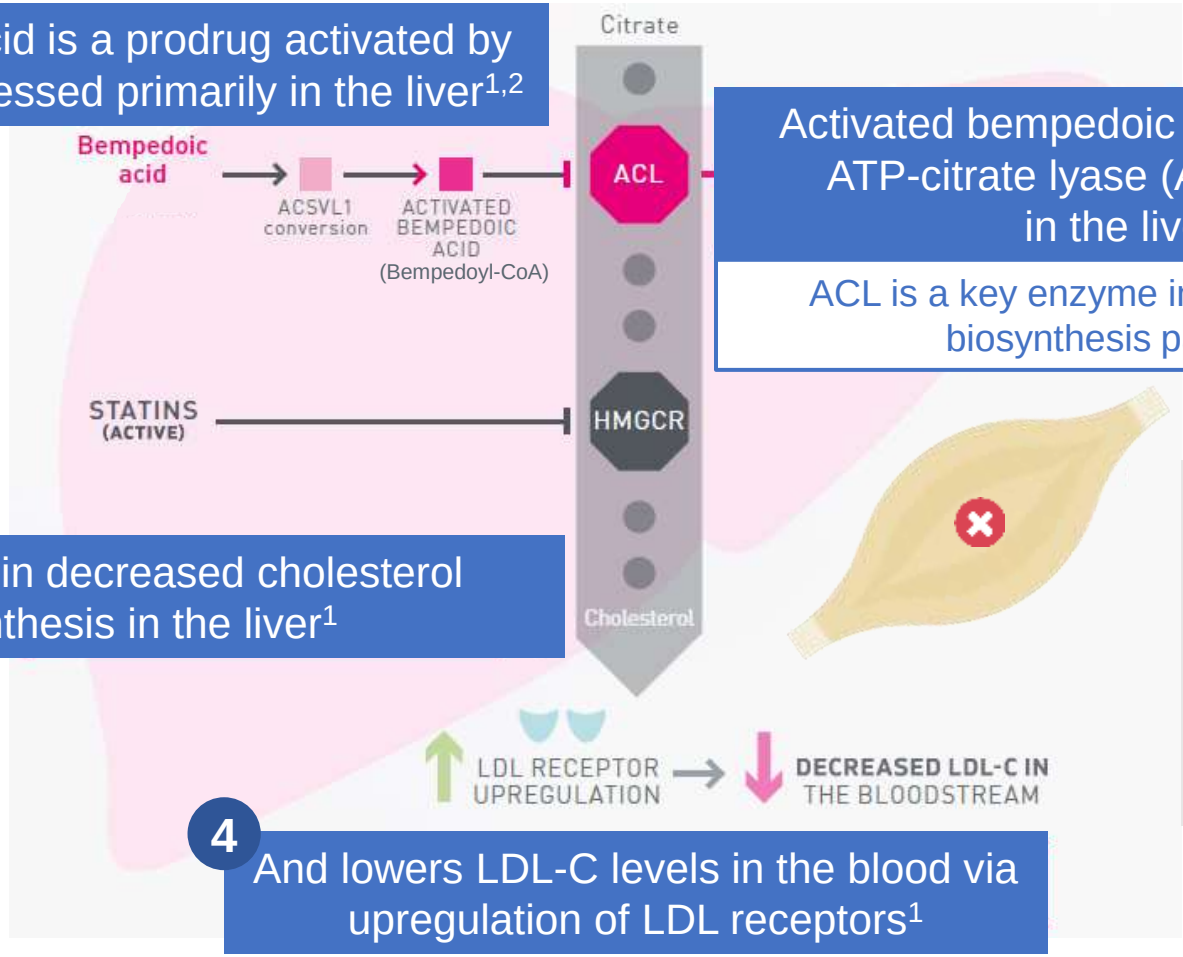
- Aim: To identify the most appropriate treatment algorithm (ezetimibe/simvastatin combination therapy vs intensified statin monotherapy) for high-risk patients already treated with simvastatin 40 mg who are not at the appropriate national target*
- Prospective, double-blind, randomised trial:
  - 786 patients with established CVD, diabetes or high risk of CVD who had been taking simvastatin 40 mg for ≥6 weeks and with fasting LDL-C ≥2.0 mmol/L (and <4.2 mmol/L) at screening and after a further 6-week run-in period on simvastatin 40 mg
  - Patients were randomised to ezetimibe/simvastatin 10/40 mg (n=261), atorvastatin 40 mg (n=263), or rosuvastatin† 5 mg (n=73) or 10 mg (n=189) once daily for 6 weeks
  - Primary efficacy endpoint: % of patients achieving LDL-C <2.0 mmol/L at the end of the study
- Results:
  - 69.4% of patients treated with ezetimibe/simvastatin 10/40 mg achieved LDL-C <2 mmol/L compared with 33.5% for atorvastatin 40 mg [OR 4.5 (95% CI: 3.0–6.8); p<0.001] and 14.3% for rosuvastatin 5 or 10 mg [OR 13.6 (95% CI: 8.6–21.6); p<0.001]
  - All study treatments were well tolerated
- Conclusion:
  - ~45% of patients screened had not achieved LDL-C <2.0 mmol/L after ≥12 weeks of treatment with simvastatin 40 mg
    - In this group, treatment with ezetimibe/simvastatin 10/40 mg achieved target LDL-C levels in a significantly higher proportion of patients during a 6-week period than switching to either atorvastatin 40 mg or rosuvastatin 5–10 mg

- *JBS2 Guideline Target:[2] Total cholesterol (TC) target = 4.0 mmol/L; LDL cholesterol (LDL-C) target = 2.0 mmol/L. †Rosuvastatin dose based on UK prescribing instructions.
- CVD, cardiovascular disease; LDL-C: low-density lipoprotein cholesterol; OR, odds ratio.
- 1. McCormack T, Harvey P, Gaunt R et al. Incremental cholesterol reduction with ezetimibe/simvastatin, atorvastatin and rosuvastatin in UK General Practice (IN-PRACTICE). Int J Clin Pract 2010; 64: 1052-61; 2. Joint British Societies guidelines on prevention of cardiovascular disease in clinical practice. Heart 2005; 91;1-52.

Bempedoic Acid

The mechanism of action of bempedoic acid is complementary yet distinct from statins[1]

1 Bempedoic acid is a prodrug activated by ACSVL1, expressed primarily in the liver[1,2]



2 Activated bempedoic acid inhibits the ATP-citrate lyase (ACL) enzyme in the liver[1]

ACL is a key enzyme in the cholesterol biosynthesis pathway[2]

3 Resulting in decreased cholesterol synthesis in the liver[1]

4 And lowers LDL-C levels in the blood via upregulation of LDL receptors[1]

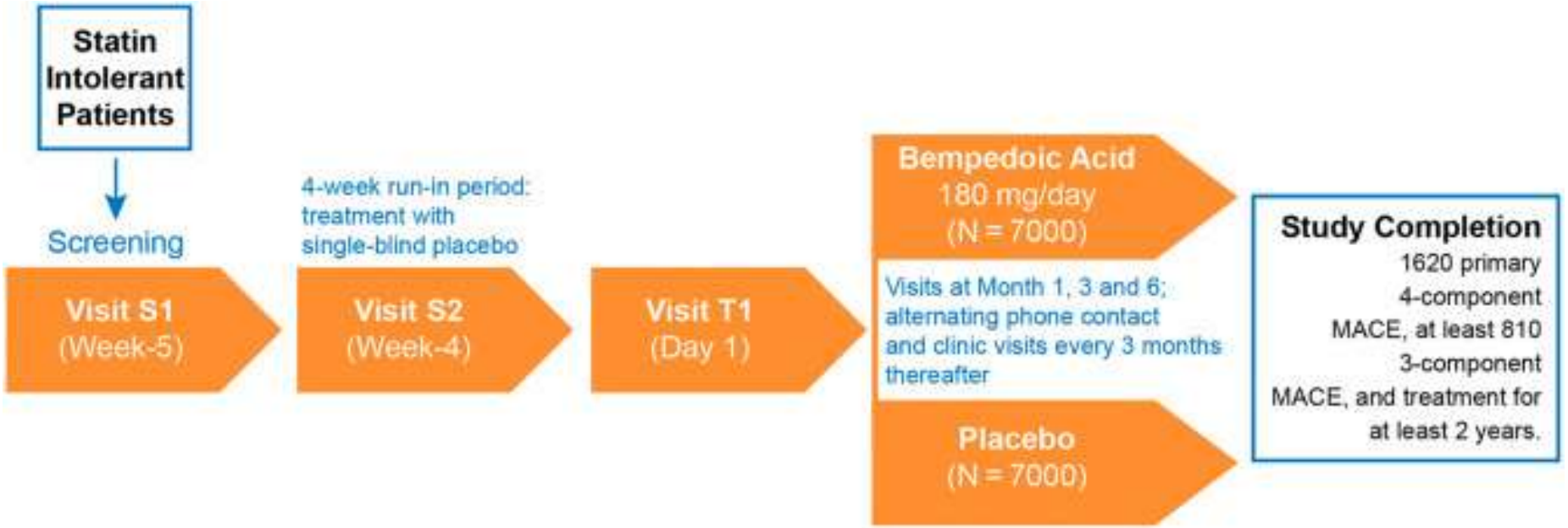
ACSVL1, the activating enzyme of bempedoic acid, is expressed primarily in the liver and not in skeletal muscle[2]

- Adapted from Pinkosky SL, et al. Nat Commun 2016.
- ACL: ATP-citrate lyase; ACSVL1: very long-chain acyl-CoA synthetase-1; HMGR: 3-hydroxy-3-methylglutarate-CoA reductase; LDL: low-density lipoprotein; LDL-C: low-density lipoprotein cholesterol.
- 1. Pinkosky SL, et al. Nat Commun 2016;7:13457; 2. NUSTENDI®. Summary of Product Characteristics.

Bempedoic acid

- Oral inhibitor of ATP – citrate lyase
- No skeletal muscle activity
- Raises uric acid so caution in gout
- 19-23% reduction in LDL-C, 36% in combination with ezetimibe

CLEAROutcomes
a CLEARProgram study



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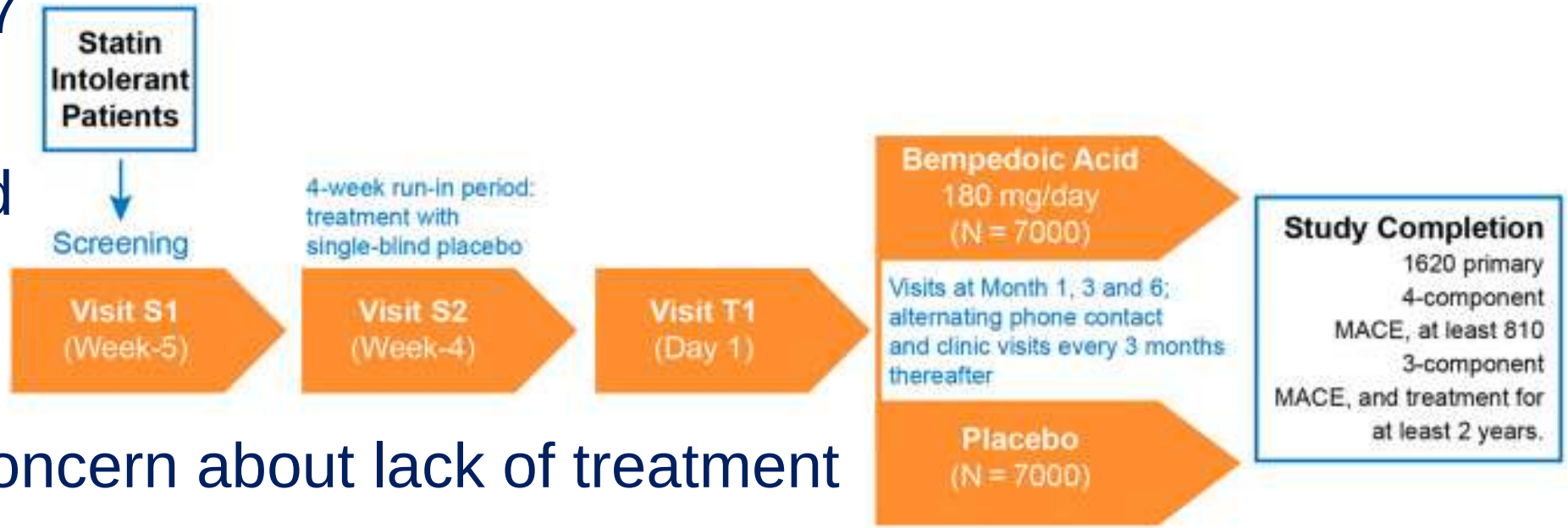
CLEAROutcomes
a CLEARProgram study

Patient SR - Male - Age 58 – Clinical Drug Trial - 2019

- Bempedoic acid 180mg/day vs placebo - Visit S2
- Rash below both knees 2/7, nausea & vomit 3/7, stopped medication 4/7
- Resolved 5/7
- Very surprized



- 25 patients, concern about lack of treatment

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ACC.23 TOGETHER WITH WCC

MARCH 4 - 6, 2023
NEW ORLEANS

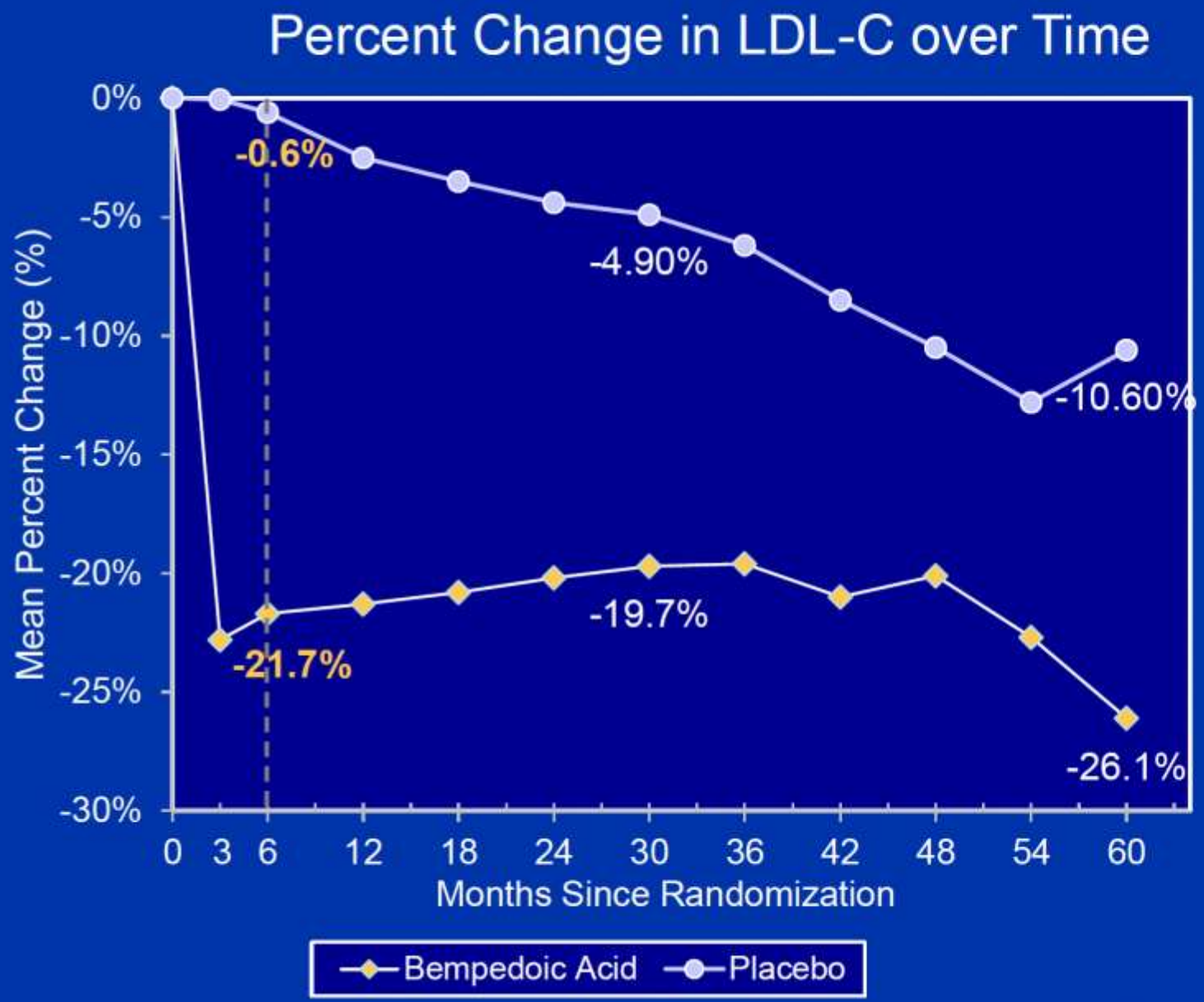
AMERICAN COLLEGE of CARDIOLOGY.

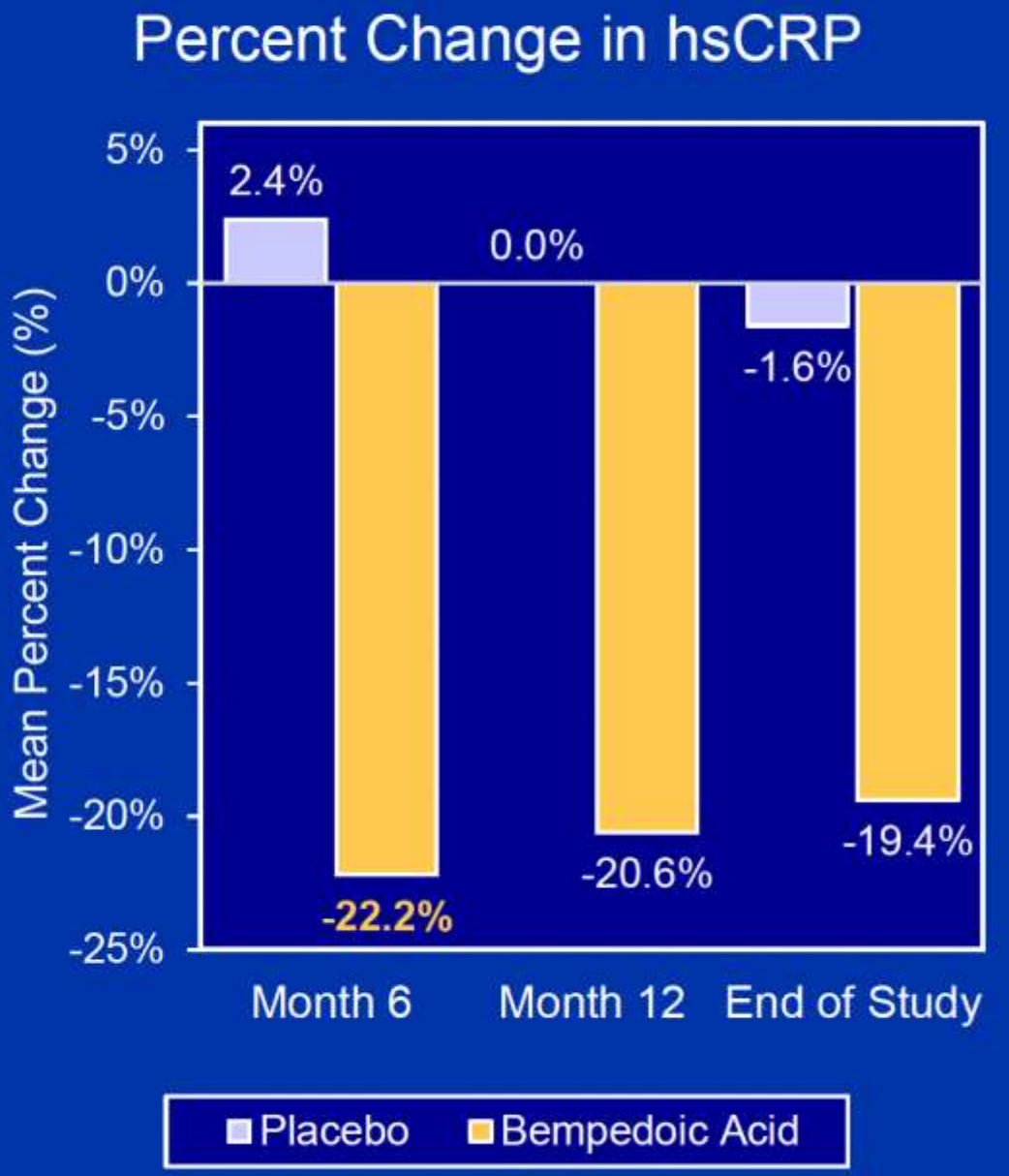
WORLD HEART FEDERATION

Welcome Terry McCormack
My ACC

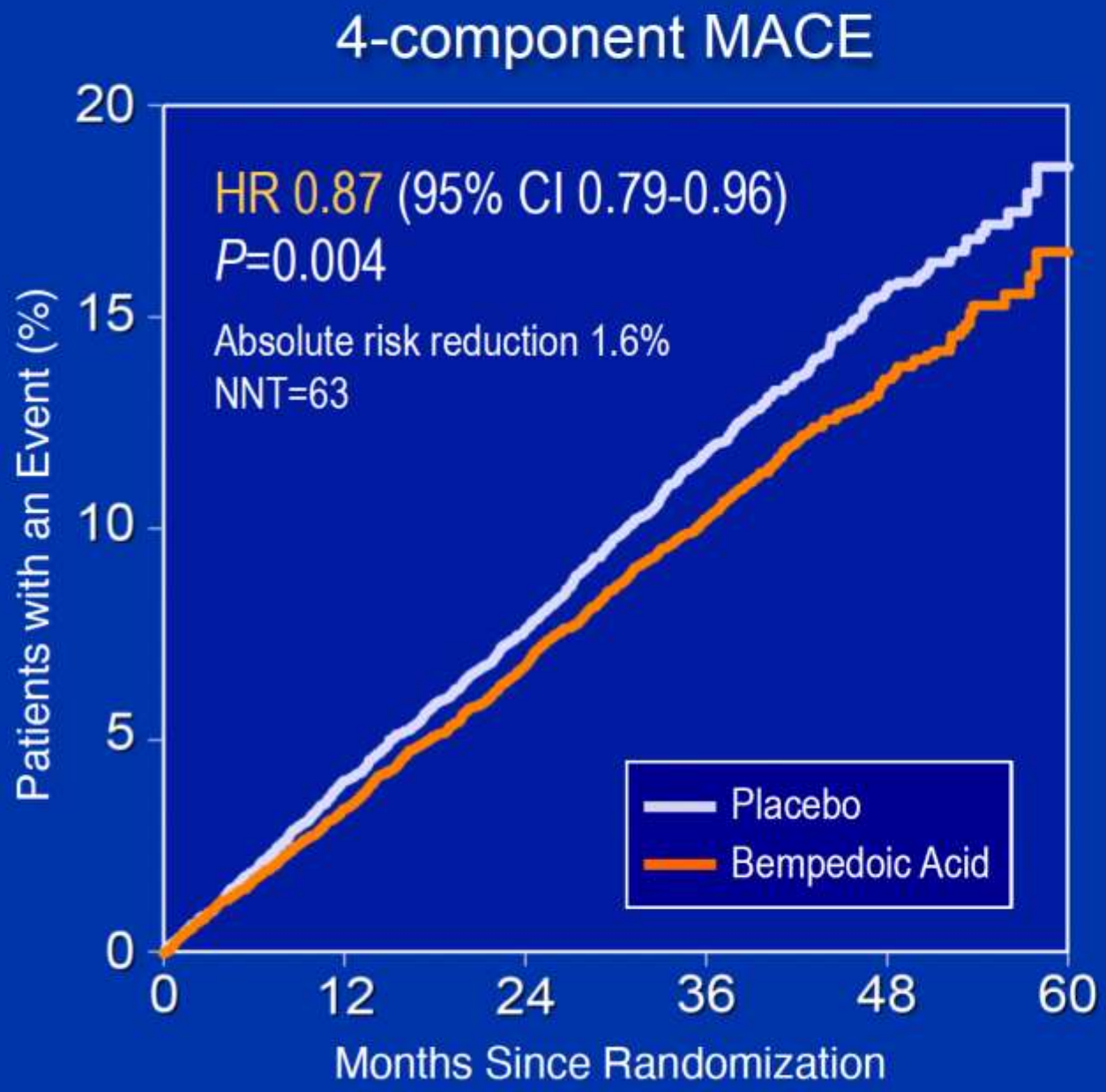
Logout

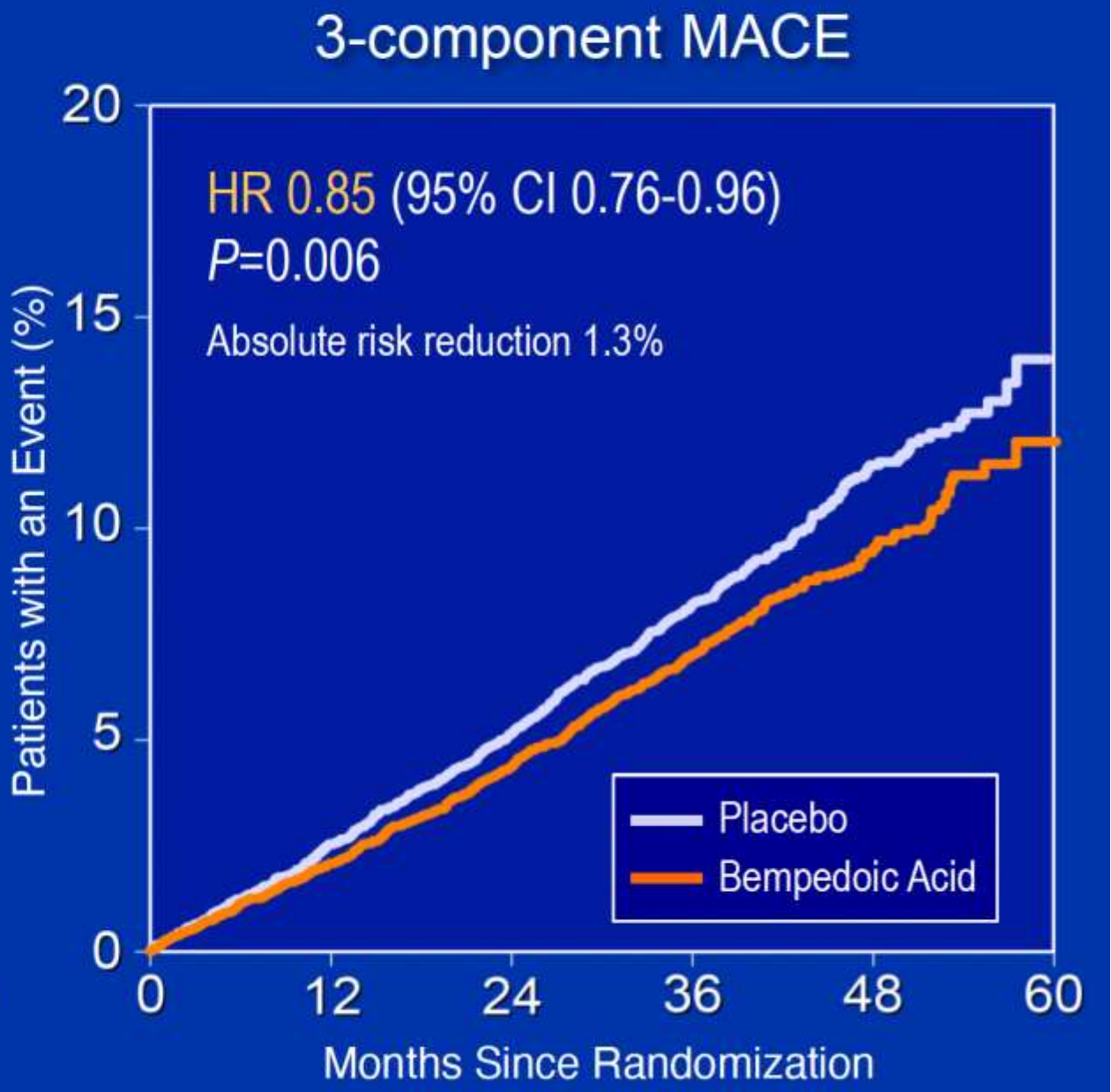
Effect of Trial Regimens on LDL-C and hsCRP



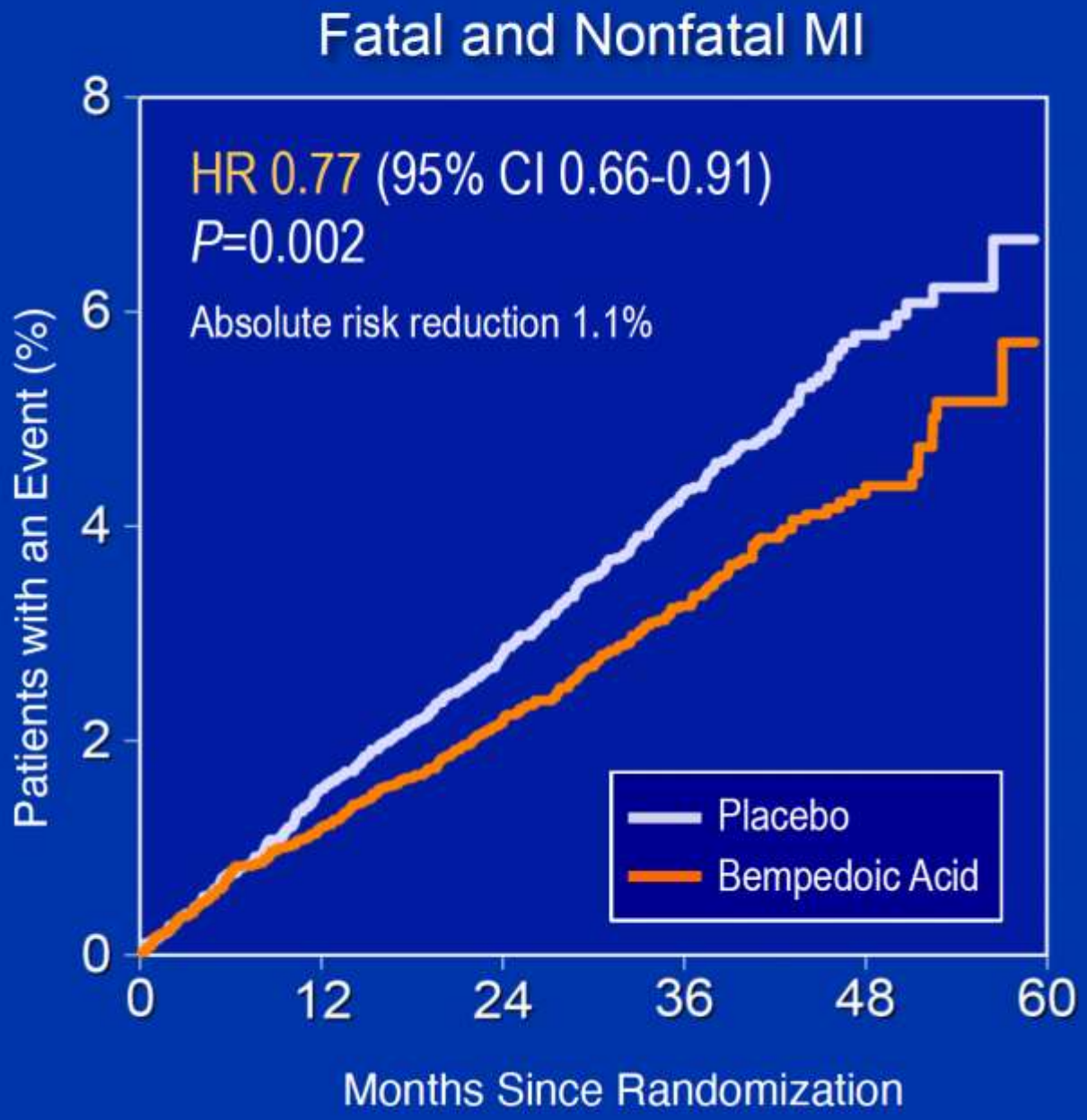


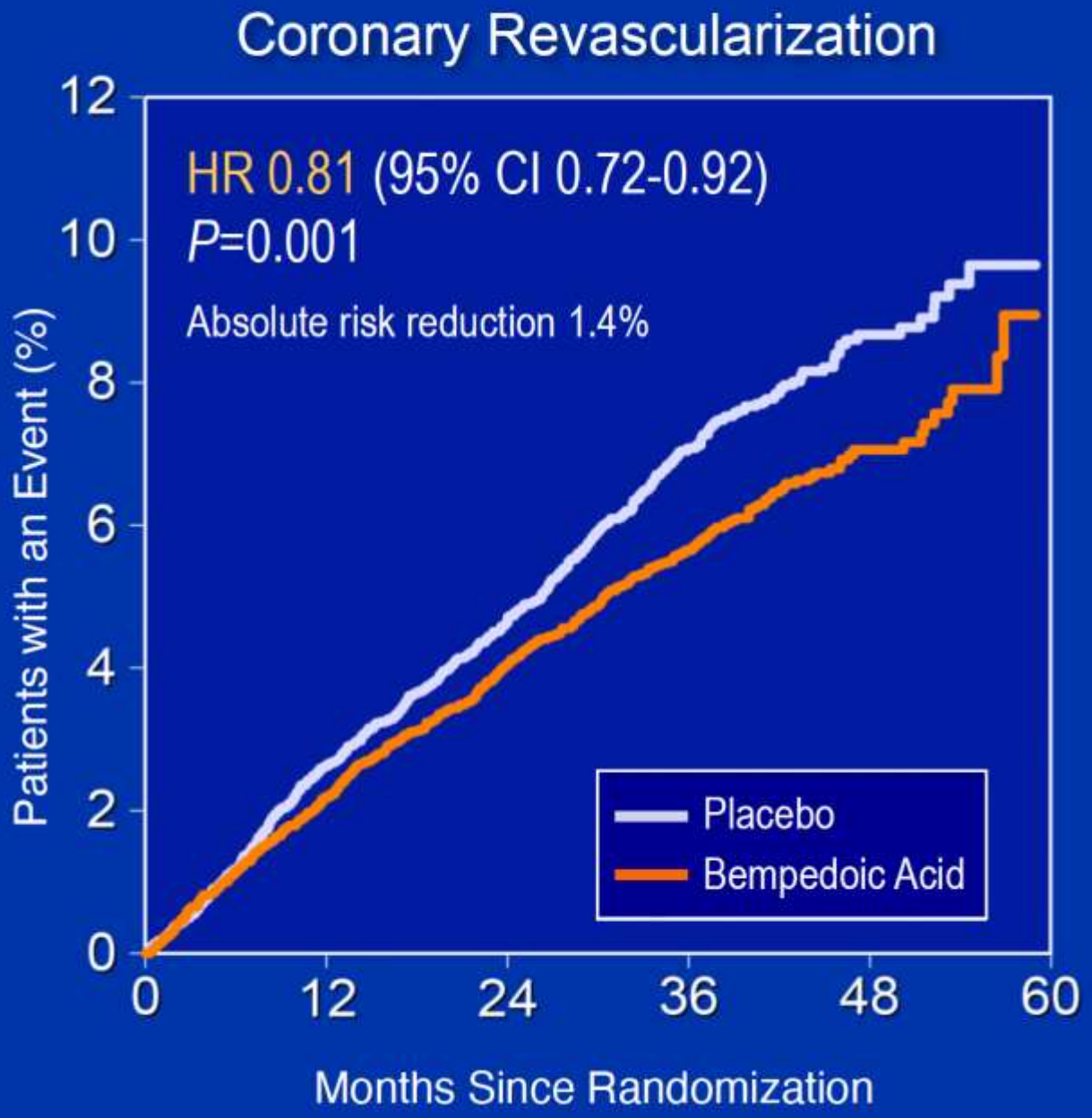
Primary and First Key Secondary Cardiovascular End Points



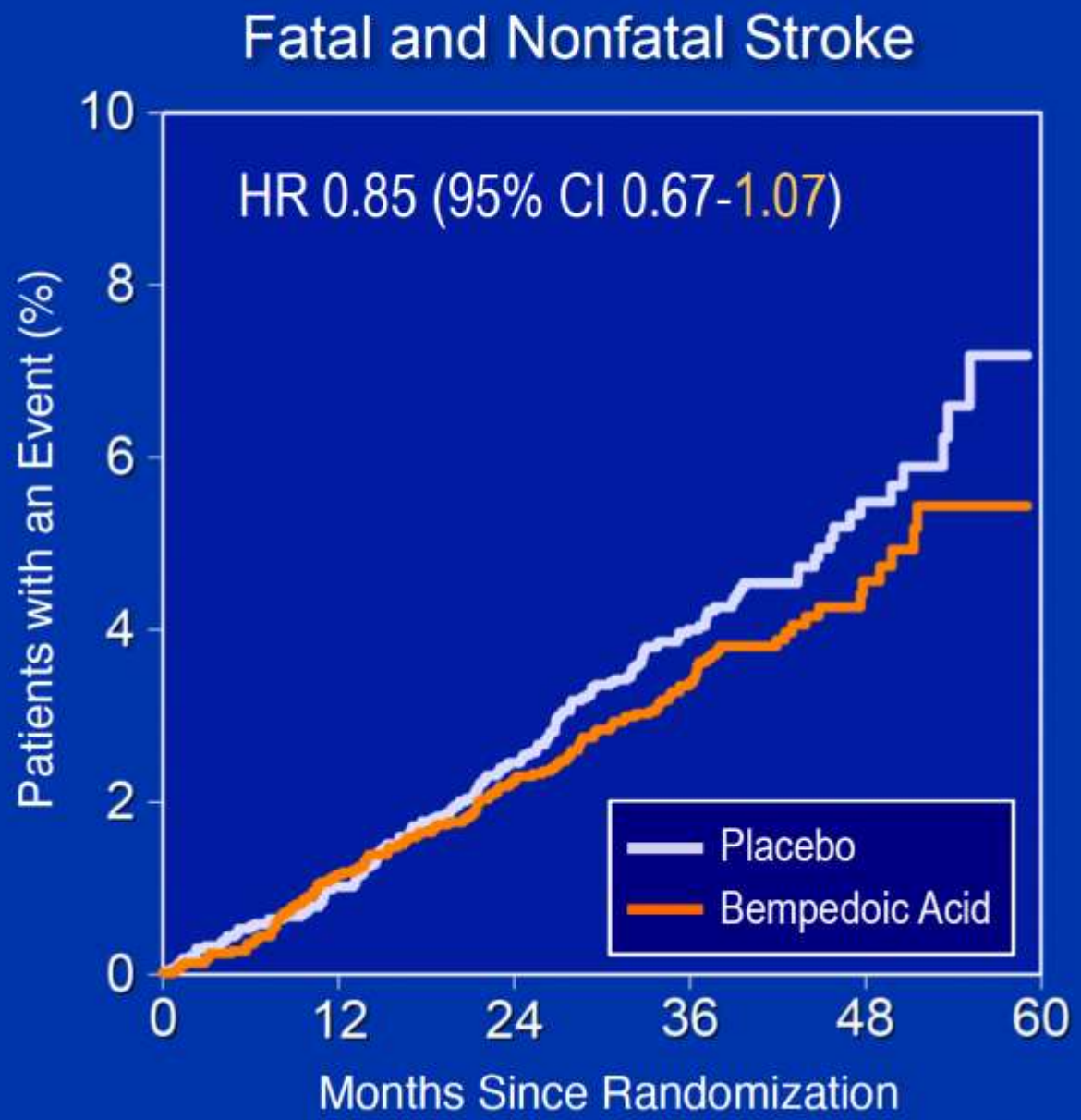


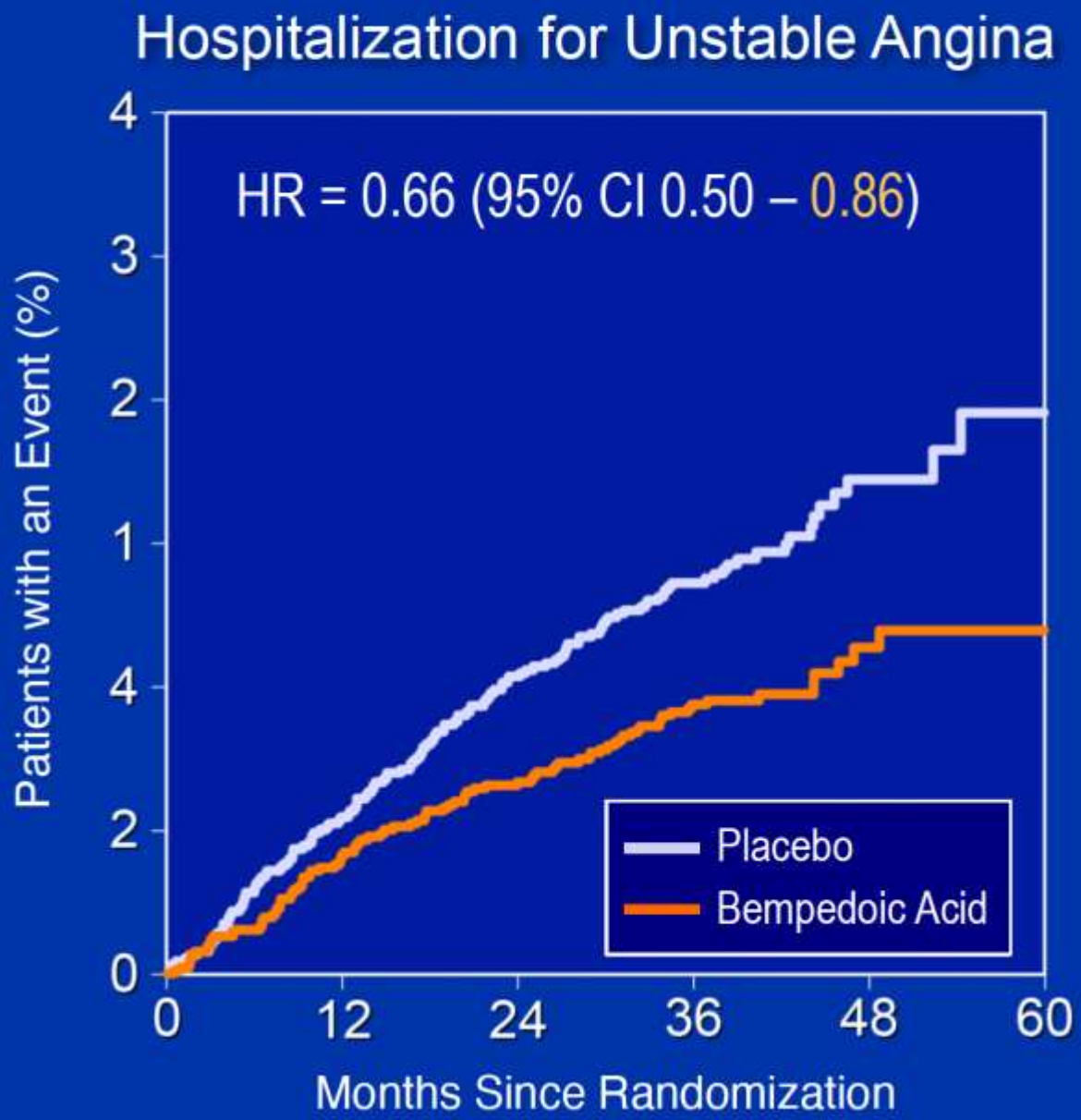
Key Secondary End Point: MI and Coronary Revascularization



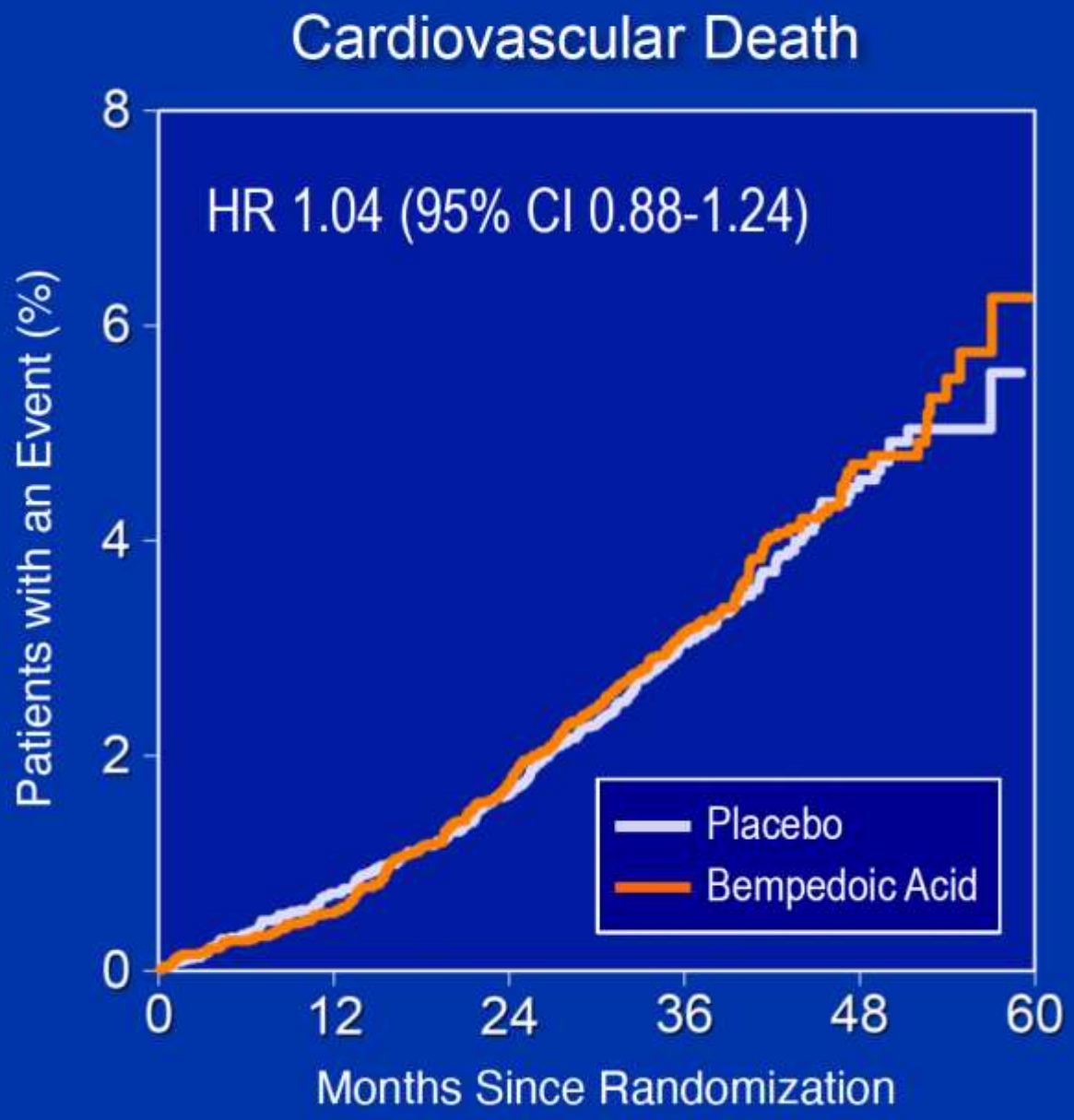


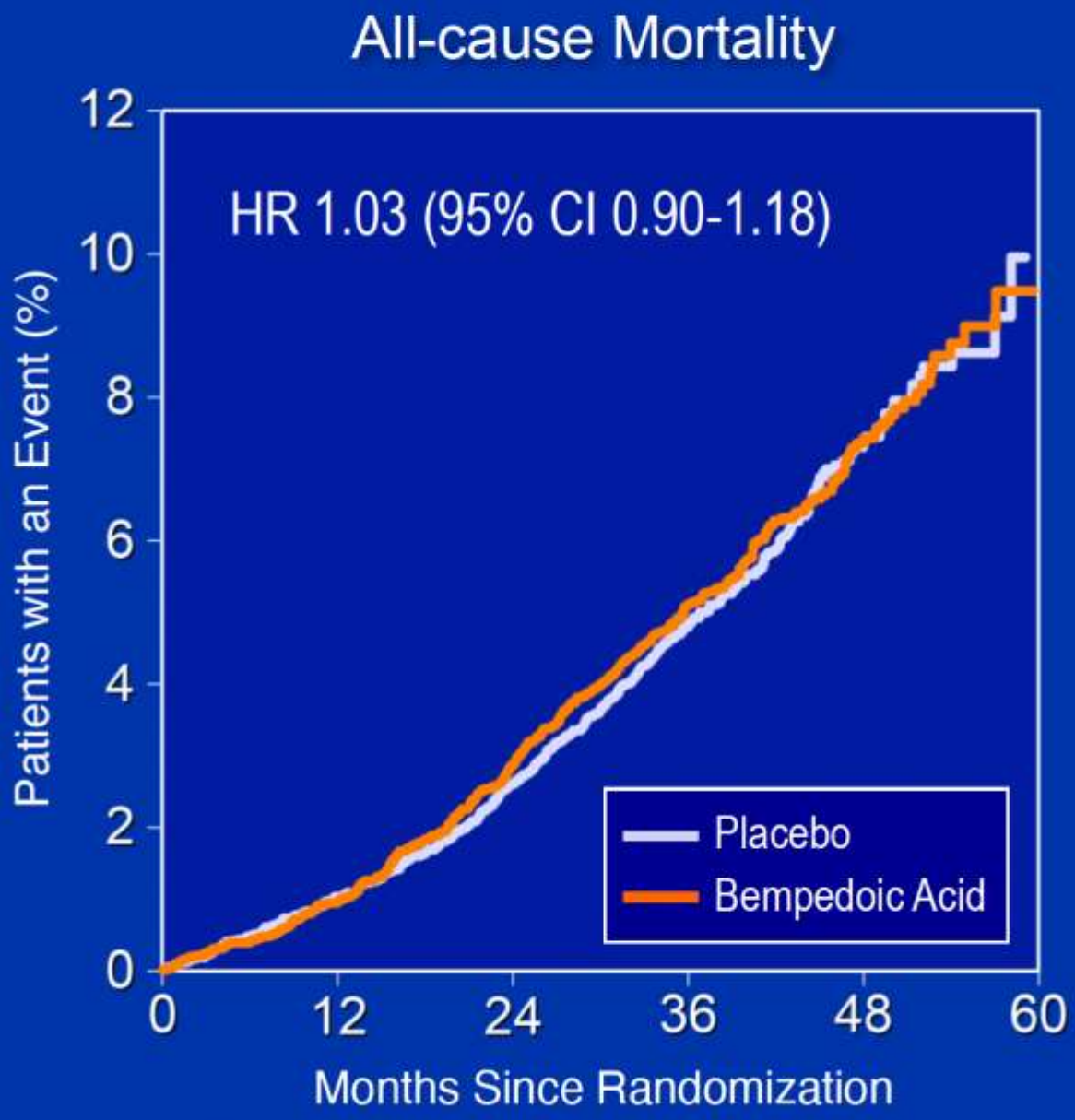
Effect on Stroke and Hospitalization for Unstable Angina





Effects of Trial Regimens on Mortality End Points





Investigator-Reported Adverse Effects

Characteristic	Bempedoic Acid N=7001	Placebo N=6964
Serious Treatment Emergent Adverse event	25.2%	24.9%
Adverse event leading to drug discontinuation	10.8%	10.4%
Any muscle disorder	15.0%	15.4%
New onset diabetes	16.1%	17.1%
Elevated hepatic enzymes	4.5%	3.0%
Prespecified renal events	11.5%	8.6%
Gout	3.1%	2.1%
Cholelithiasis	2.2%	1.2%
Adjudicated tendon rupture	1.2%	0.9%

Bempedoic Acid +/- Ezetimibe

- New license application
- 180mg once daily
- Bempedoic acid raises uric acid
- Ezetimibe can cause constipation
- Nustendi is bembedoic acid 180mg plus ezetimibe 10 mg

Many lipid disorders can be managed in primary care[1]

Treat in primary care

There are a number of resources available to support primary care physicians:

- NHS advice & guidance[2]
- AHSN Involvement[3]
- PCN CVD DES[4]

Referral to secondary care

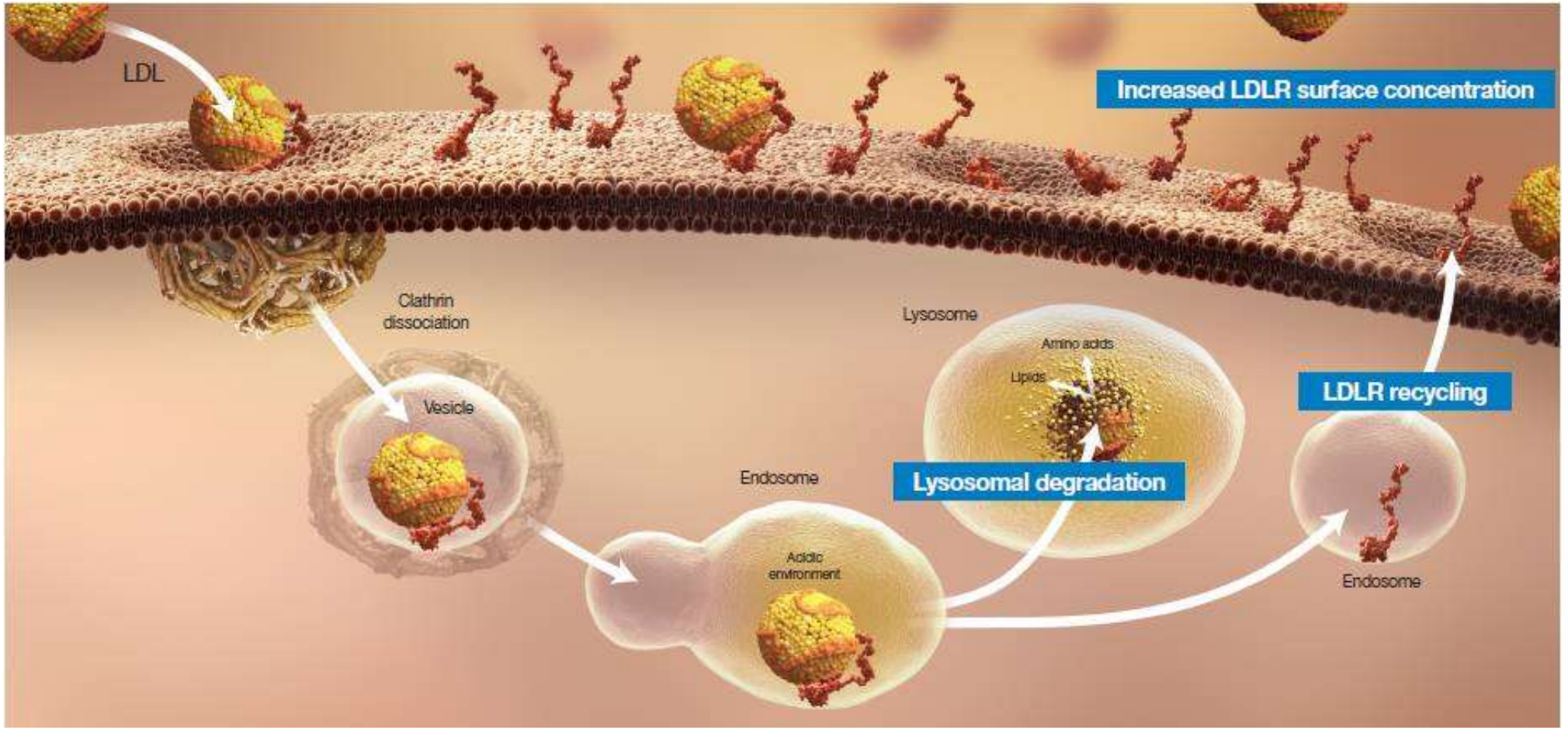
Need to take into account the current backlog of patients in secondary care[5]

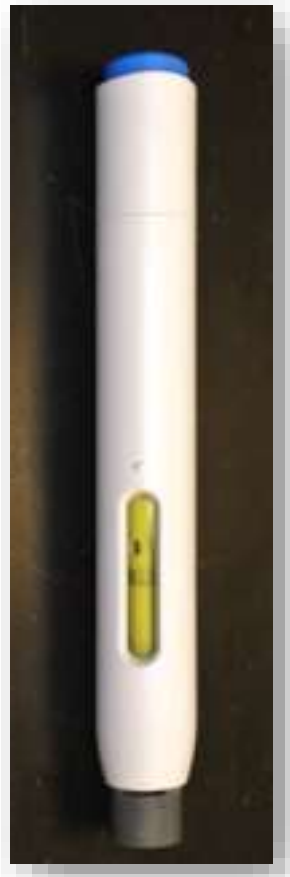
- Referrals into secondary care may be rejected due to a **lack of capacity[5]**
- Patients experience long waiting times after referral which can **delay treatment initiation[5]**

- AAC: Accelerated Access Collaborative; AHSN: Academic Health Science Networks; CVD: cardiovascular disease; DES: Directed Enhanced Service; NHS: National Health Service; NICE: National Institute for Health and Care Excellence; PCN: primary care network.
- 1. Khatib R & Neely D on behalf of the AAC Clinical Subgroup. National Guidance for Lipid Management. November 2022. Pathway approved by NICE November 2022. Available at: https://www.england.nhs.uk/aac/publication/summary-of-national-guidance-for-lipid-management/ (accessed August 2023); 2. Khatib R & Neely D on behalf of the AAC Clinical Subgroup. Statin intolerance pathway. January 2022. Available at: NHS Accelerated Access Collaborative » Summary of national guidance for lipid management (england.nhs.uk)); 3. AHSN. Lipid management and familial hypercholesterolaemia. Available at: https://www.ahsnnetwork.com/about-academic-health-science-networks/national-programmes-priorities/lipid-management-and-fh (accessed August 2023); 4. NHS England. Network Contract Directed Enhanced Service: Cardiovascular disease prevention and diagnosis. Available at: https://www.england.nhs.uk/wp-content/uploads/2021/09/B0951-v-network-contract-des-20-21-cvd-supplementary-guidance.pdf (accessed August 2023); 5. British Medical Association: NHS backlog data analysis. November 2022. Available at: https://www.bma.org.uk/advice-and-support/nhs-delivery-and-workforce/pressures/nhs-backlog-data-analysis (accessed August 2023).

PCSK9 Inhibitors

Recycling of LDLR Enables Efficient Clearance of LDL Particles





1. *Brown MS, Goldstein JL. Proc Natl Acad Sci U S A. 1979;76:3330-3337.*
2. *Steinberg D, Witztum JL. Proc Natl Acad Sci U S A. 2009;106:9546-9547.*
3. *Goldstein JL, Brown MS. Arterioscler Thromb Vasc Biol. 2009;29:431-438.*

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WHITBY GP

PCSK9 Studies In Whitby

- LaPlace 2 2012 - 14
- Osler 2 2013 - 18
- Fourier 2014 - 17
- Ebbinghaus 2015 - 17
- Spire 1 2015 - 17
- Spire 2 2015 - 17
- Vesalius 2019 - 25
- Fourier Legacy 2020

Mutations in *PCSK9* cause autosomal dominant hypercholesterolemia

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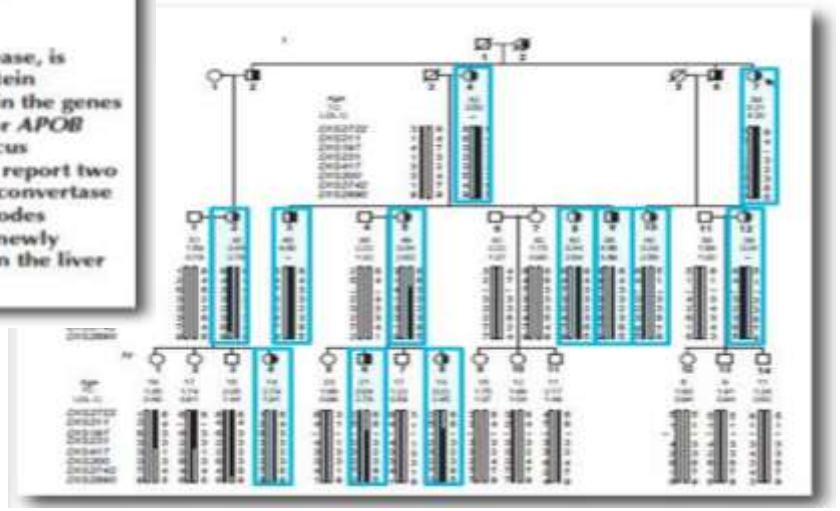
Autosomal dominant hypercholesterolemia (ADH; OMIM144400), a risk factor for coronary heart disease, is characterized by an increase in low-density lipoprotein cholesterol levels that is associated with mutations in the genes *LDLR* (encoding low-density lipoprotein receptor) or *APOB* (encoding apolipoprotein B). We mapped a third locus associated with ADH, *HCHOLA3* at 1p32, and now report two mutations in the gene *PCSK9* (encoding proprotein convertase subtilisin/kexin type 9) that cause ADH. *PCSK9* encodes NARC-1 (neural apoptosis regulated convertase), a newly identified human subtilase that is highly expressed in the liver and contributes to cholesterol homeostasis.



Case History 1 – WMW – now 54 ♂

- **Intermittent Claudication aged 39**
  - **Stops smoking**
  - **Total cholesterol 11.4 mmol/l = mixed hyperlipidaemia**
  - **Left and right saphenous-femoral angioplasty**

Both patients have given consent for their case histories to be used. TM has received research grants and advisory fees from Amgen, Daiichi-Sankyo, Esperion, Novartis and Sanofi-Aventis.

Case History 1 – WMW – now 54 ♂

- Intermittent Claudication aged 39
  - Stops smoking
  - Total cholesterol 11.4 mmol/l = mixed hyperlipidaemia
  - Left and right saphenous-femoral angioplasty
- **Family History**
  - **Father suffered MI age 49, died aged 58 MI**
  - **Aunt died age 47**
  - **Grandfather died age 47**
  - **Brother lost leg to peripheral arterial disease**

MI = Myocardial Infarction

Case History 1 – WMW – now 54 ♂

- Intermittent Claudication aged 39
  - Stops smoking
  - Total cholesterol 11.4 mmol/l = mixed hyperlipidaemia
  - Left and right saphenous-femoral angioplasty
- **Transient Ischaemic Attack age 44**
- **Coronary artery stenting age 48**
- **Long term depression**

Medication 2013

- Atorvastatin 80mg od
- Bisoprolol 5mg od
- Clopidogrel 75mg od
- Ezetimibe 10mg od
- Glyceryl trinitrate sublingual spray 1 prn
- Lansoprazole 30mg od
- Ramipril 10mg od

od = once daily, prn = as required

Case History 1 – WMW – at 39

	1997		
Lipid Treatment	None		
Total Cholesterol mmol/l	11.4		
Triglycerides mmol/l	4.7		
HDL mmol/l	0.88		
LDL mmol/l	8.35		

Case History 1 – WMW – at 54

	1997	2013 La Place II	
Lipid Treatment	None	Atorvastatin 80 mg and ezetimibe 10 mg	
Total Cholesterol mmol/l	11.4	4.92	
Triglycerides mmol/l	4.7	2.89	
HDL mmol/l	0.88	0.98	
LDL mmol/l	8.35	2.62	

Case History 1 – WMW – at 54

	1997	2013 La Place II	
Lipid Treatment	None	Atorvastatin 80 mg and ezetimibe 10 mg	?PCSK9 Inhibitor
Total Cholesterol mmol/l	11.4	4.92	BLINDED
Triglycerides mmol/l	4.7	2.89	BLINDED
HDL mmol/l	0.88	0.98	BLINDED
LDL mmol/l	8.35	2.62	BLINDED

Case History 1 – WMW – at 55

	1997	2013 La Place II	2014 Osler II
Lipid Treatment	None	Atorvastatin 80 mg and ezetimibe 10 mg	A80 + E10 +evolocumab 420 mg (AMG 145)
Total Cholesterol mmol/l	11.4	4.92	1.90
Triglycerides mmol/l	4.7	2.89	2.73
HDL mmol/l	0.88	0.98	0.62
LDL mmol/l	8.35	2.62	0.13 (0.54)

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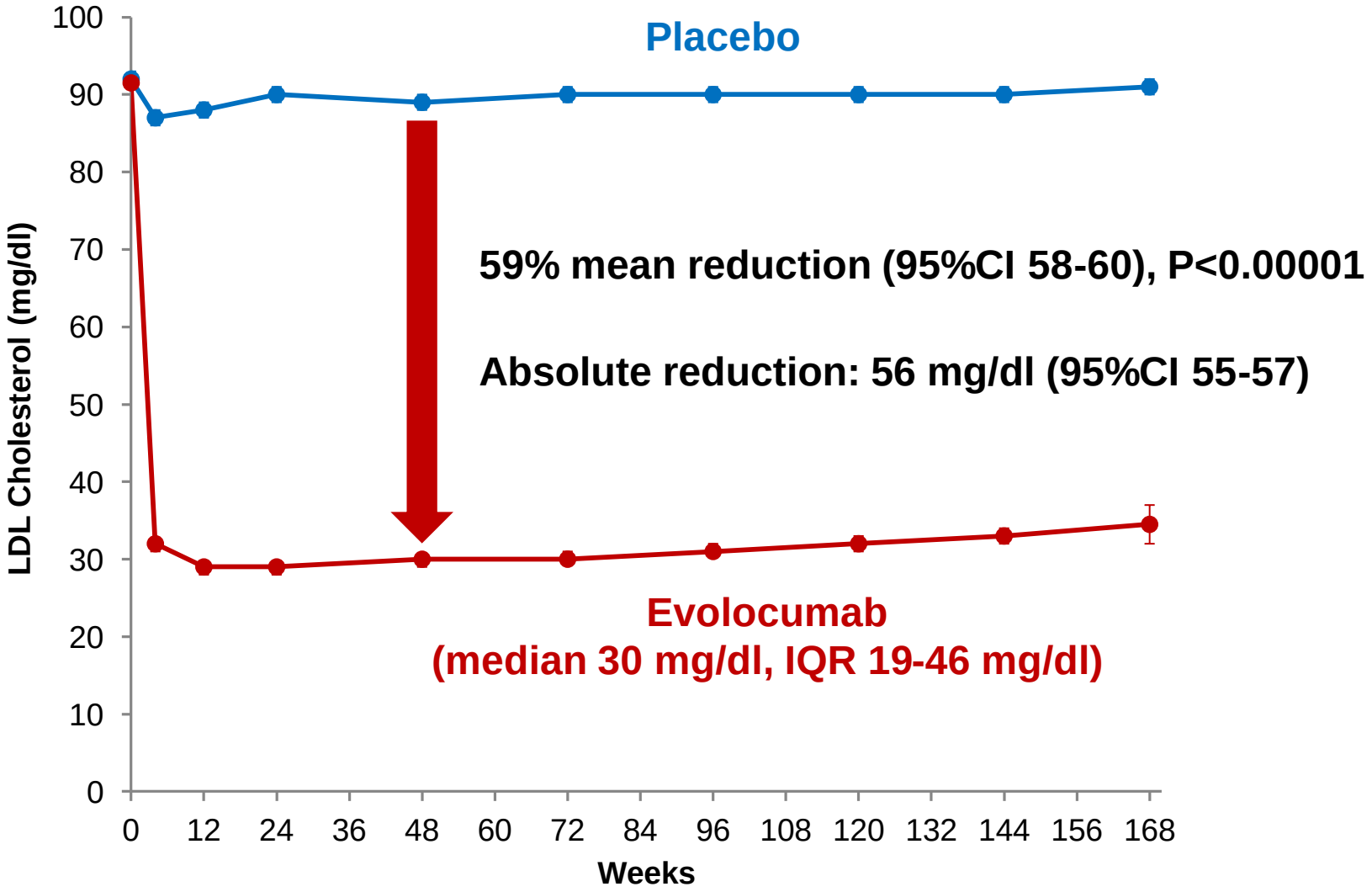
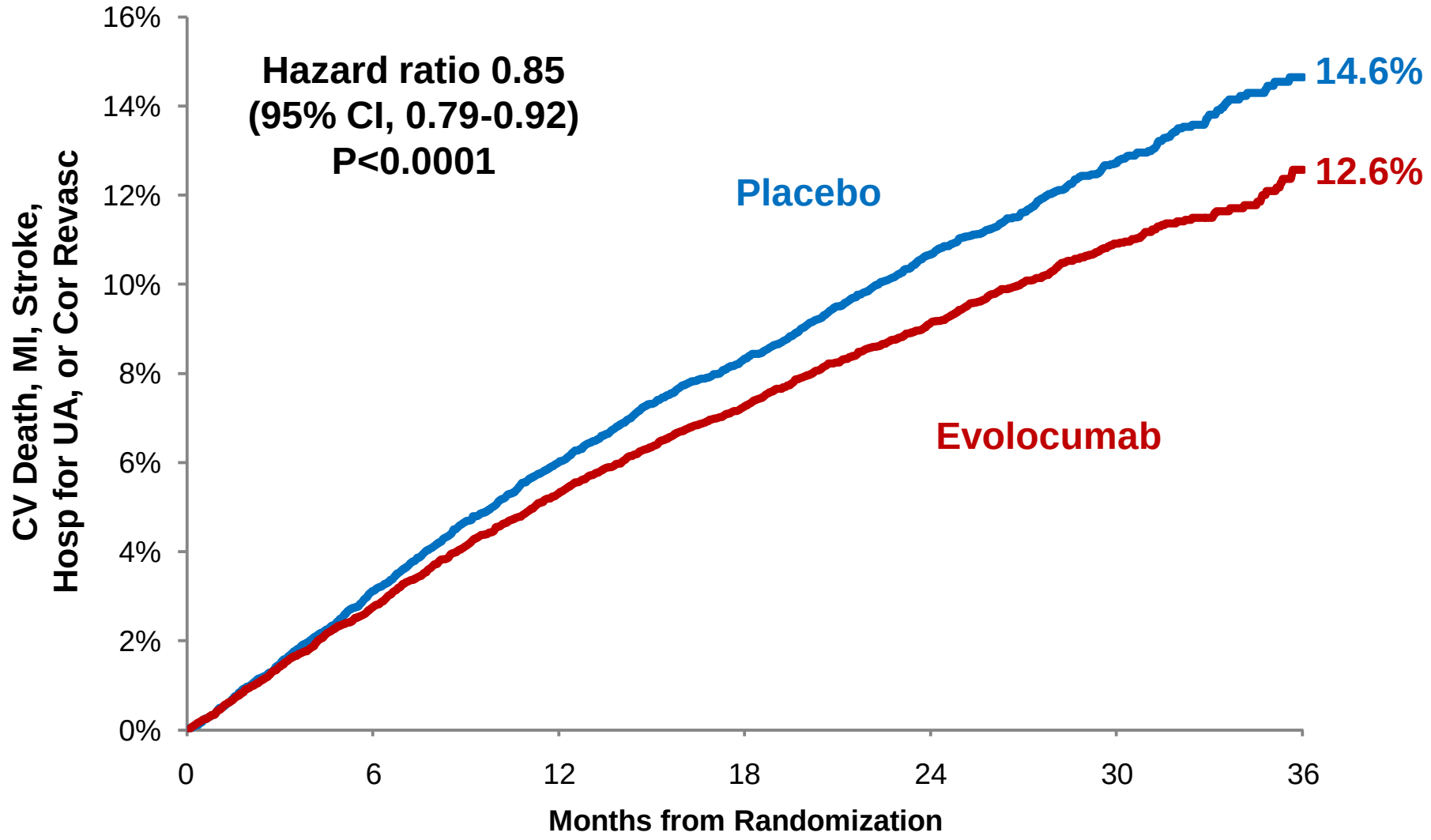
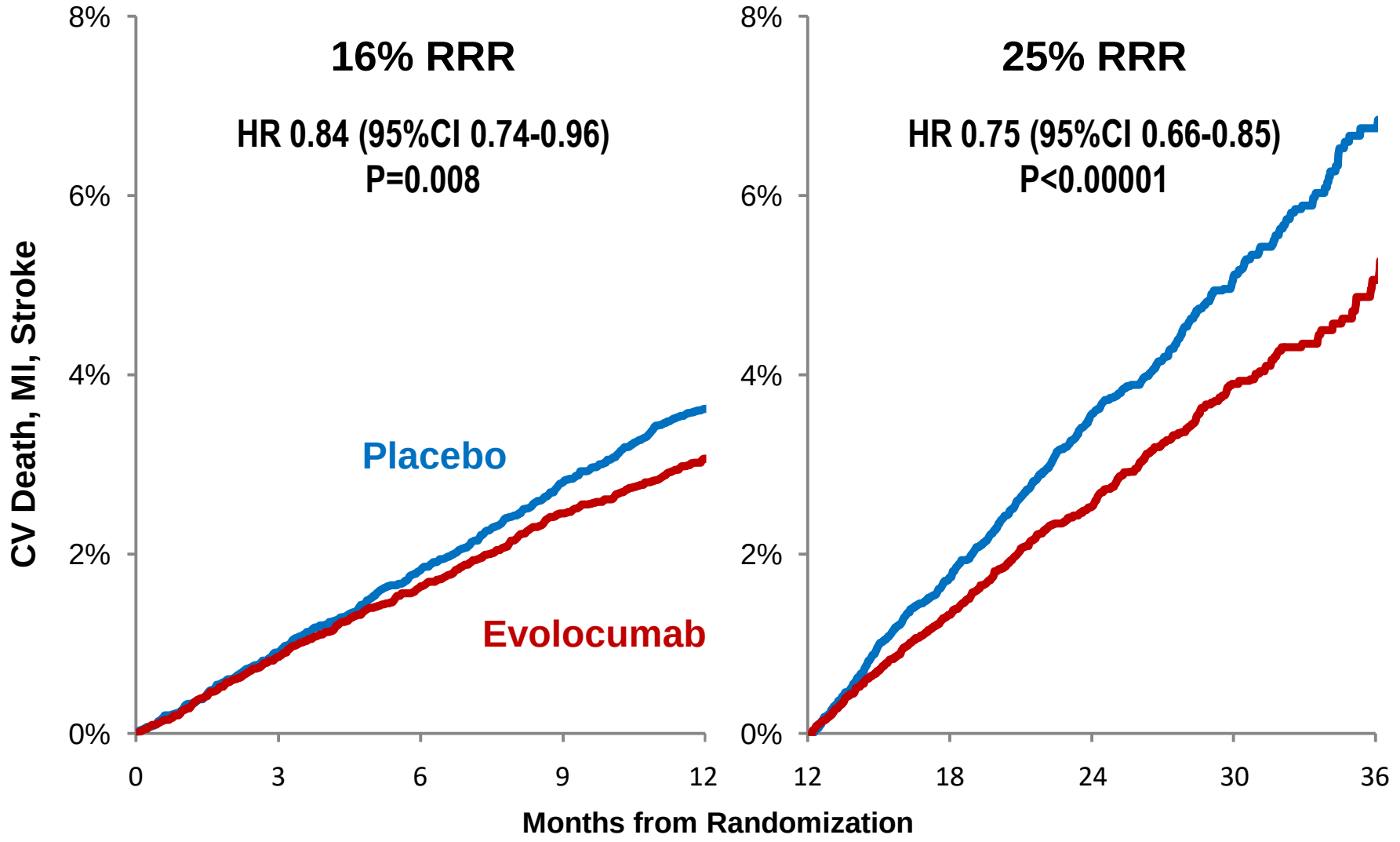
LDL Cholesterol



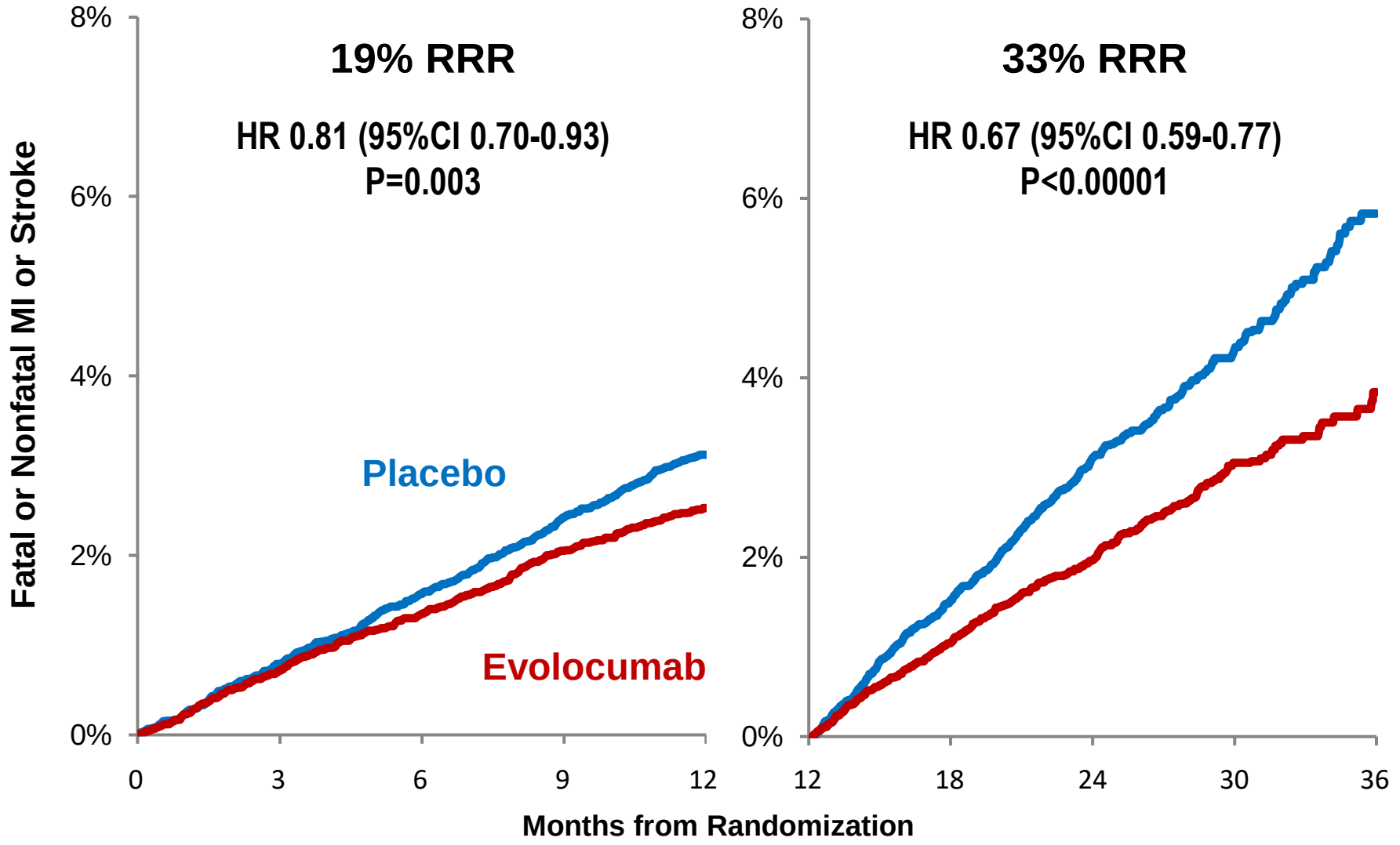
Primary Endpoint



Landmark Analysis



Fatal or Nonfatal MI or Stroke



NICE TA393 Alirocumab[1] and TA394 Evolocumab[2]

FH = Familial hypercholesterolaemia
CVD = cardiovascular disease

- The dosage is every 2 weeks
- LDL-C persistently above thresholds despite maximal tolerated lipid-lowering therapy

	Without CVD	With high risk CVD	With very high risk CVD
Non FH	Not recommended	LDL-C > 4.0 mmol/l	LDL-C > 3.5 mmol/l
FH	LDL-C > 5.0 mmol/l	LDL-C > 3.5 mmol/l	LDL-C > 3.5 mmol/l

- High risk = history acute coronary syndrome, arterial revascularisation, stroke or peripheral arterial disease
- Very high risk = history of recurrent events or disease in more than one vascular bed or recurrent events

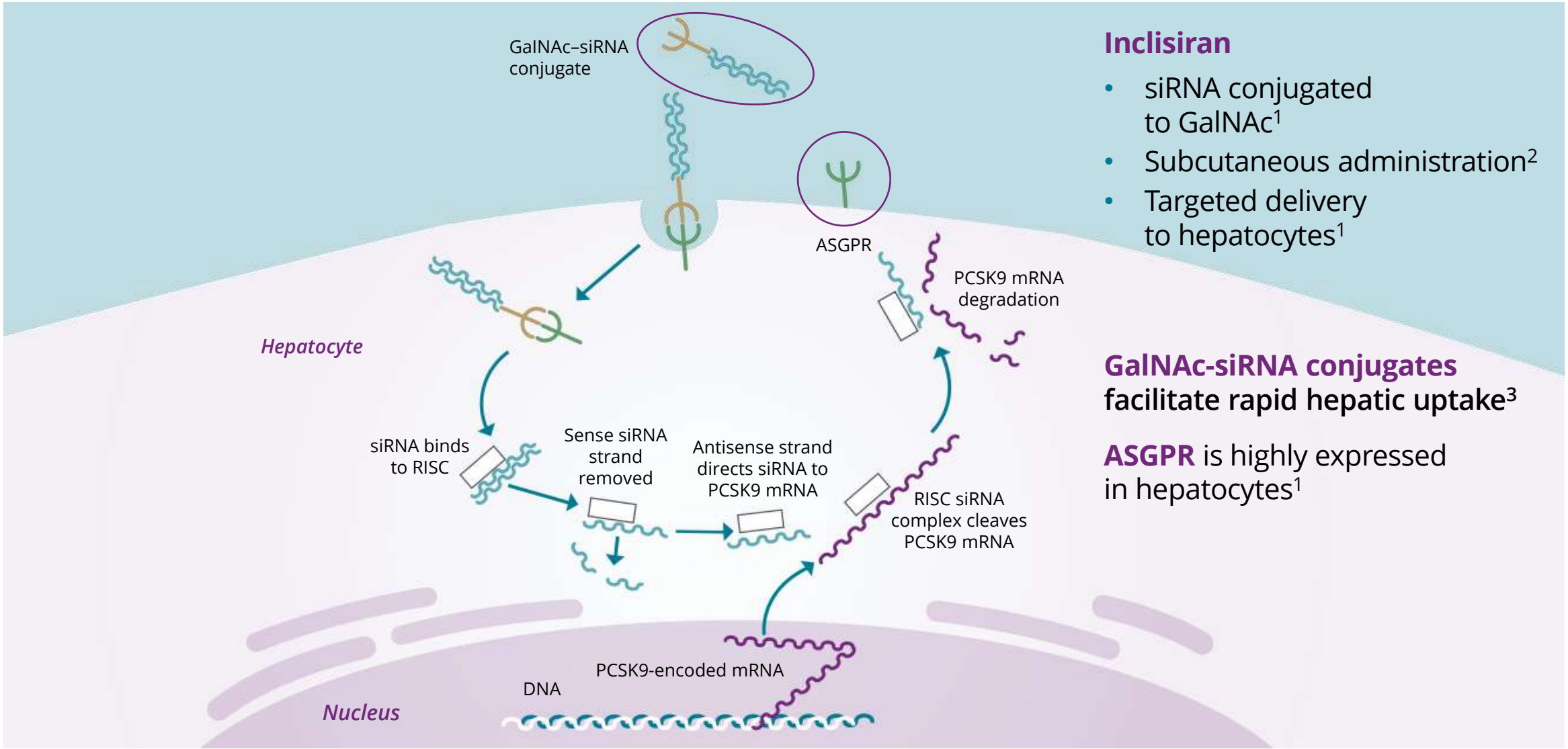
Case History 1 – WMW – now 64 ♂

- Finished OSLER 2 Oct 2016
- Referred to lipid clinic Nov 2016
- MI and primary PCI Feb 2017
- Appointment for lipid clinic Apr 2017

- Feb 2023 - alive and well

Inclisiran

MECHANISM OF ACTION



Inclisiran

- siRNA conjugated to GalNAc[1]
- Subcutaneous administration[2]
- Targeted delivery to hepatocytes[1]

GalNAc-siRNA conjugates facilitate rapid hepatic uptake[3]

ASGPR is highly expressed in hepatocytes[1]

Adapted from Khvorova A. N Engl J Med 2017.[1]

ASGPR – asialoglycoprotein receptor; DNA – deoxyribonucleic acid; GalNAc – triantennary N-acetylgalactosamine; mRNA – messenger ribonucleic acid; PCSK9 – proprotein convertase subtilisin/kexin type 9; RISC – RNA-induced silencing complex; siRNA – small interfering ribonucleic acid

References: 1. Khvorova A. N Engl J Med 2017;376(1):4-7. **2.** Leqvio® Summary of Product Characteristics.
3. Klinovski M et al. CADTH Issues in Emerging Health Technologies, 2019. Canadian Agency for Drugs and Technologies in Health.

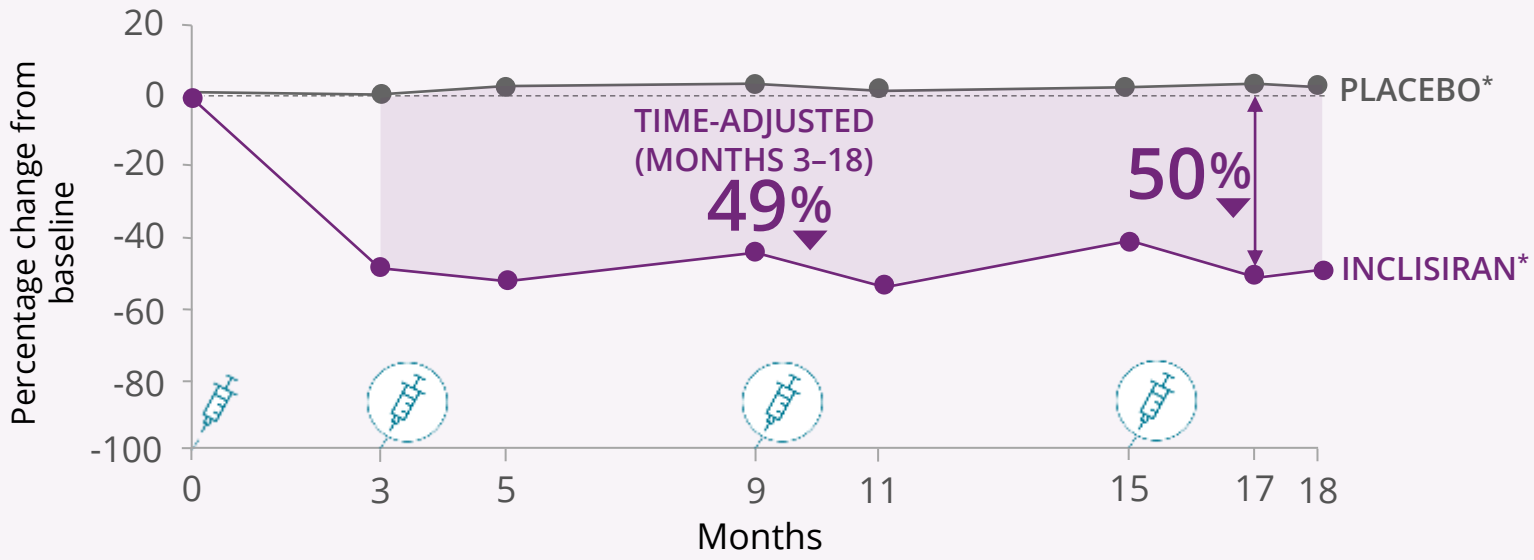
ORION-11: EFFICACY IN ASCVD (OR RISK EQUIVALENTS)

Primary endpoints:

In patients with ASCVD (or risk equivalents) on a maximally tolerated statin, inclisiran:

Reduced LDL-C by 50% relative to placebo at Month 17, as compared with baseline (95% CI: −53.1 to −46.6; P<0.0001)[1,2]

Delivered a time-adjusted LDL-C reduction of 49% from baseline between Months 3 and 18 relative to placebo (95% CI: −51.6 to −46.8; P<0.0001)[1,2]



No. of Patients								
Placebo	807	797	785	774	773	764	739	749
Inclisiran	810	790	796	778	773	768	724	742

Adapted from Ray KK et al. N Engl J Med 2020.[1]

* Reductions were achieved on top of a maximally tolerated statin and/or other lipid-lowering therapies.[1]
ASCVD – atherosclerotic cardiovascular disease; CI – confidence interval; LDL-C – low-density lipoprotein cholesterol

References: 1. Ray KK et al. N Engl J Med 2020;382(16):1507-1519. **2.** Leqvio® Summary of Product Characteristics.

NICE TA733 Inclisiran

FH = Familial hypercholesterolaemia
CVD = cardiovascular disease

- The dosage is every 6 months after initial 3 month injection
- LDL-C persistently above thresholds despite maximal tolerated lipid-lowering therapy

	Without CVD	With high risk CVD
Non FH	Not recommended	LDL-C > 2.5 mmol/l
FH	Research Only	LDL-C > 2.5 mmol/l

- Or statins not tolerated/contra-indicated

Case History 2 – JF – aged 48 ♂

- △ hypertension aged 32
- Early 2017 QRisk2 = 15.76 (age 43)
- Later in 2017 △ IHD, impaired left ventricular function
- ℞ carotid endarterectomy
- Could not tolerate two statins, ℞ ezetimibe alone
- 2018 ℞ CABG, 2019 △ CKD3
- 2022 DLNS>6, ℞ inclisiran

Adeyalo B, McCormack T. New options for treating people with hypertension and intolerance to statins; a primary and a secondary prevention case history. P-16, *J Hum Hypertens* 36 (Suppl 1), 1–22 (2022).

IHD = Ischaemic Heart Disease, CABG – Coronary Artery Bypass Graph, CKD = Chronic Kidney Disease, DLNS = Dutch Lipid Network Score

Case History 2 – JF – aged 48 ♂

- TC 7.2 mmol/l on no ℞
- TC 6.9 mmol/l on ezetimibe alone
- TC 4.3 mmol/l on inclisiran

Adeyalo B, McCormack T. New options for treating people with hypertension and intolerance to statins; a primary and a secondary prevention case history. P-16, *J Hum Hypertens* 36 (Suppl 1), 1–22 (2022).

TC = Total Cholesterol

Inclisiran

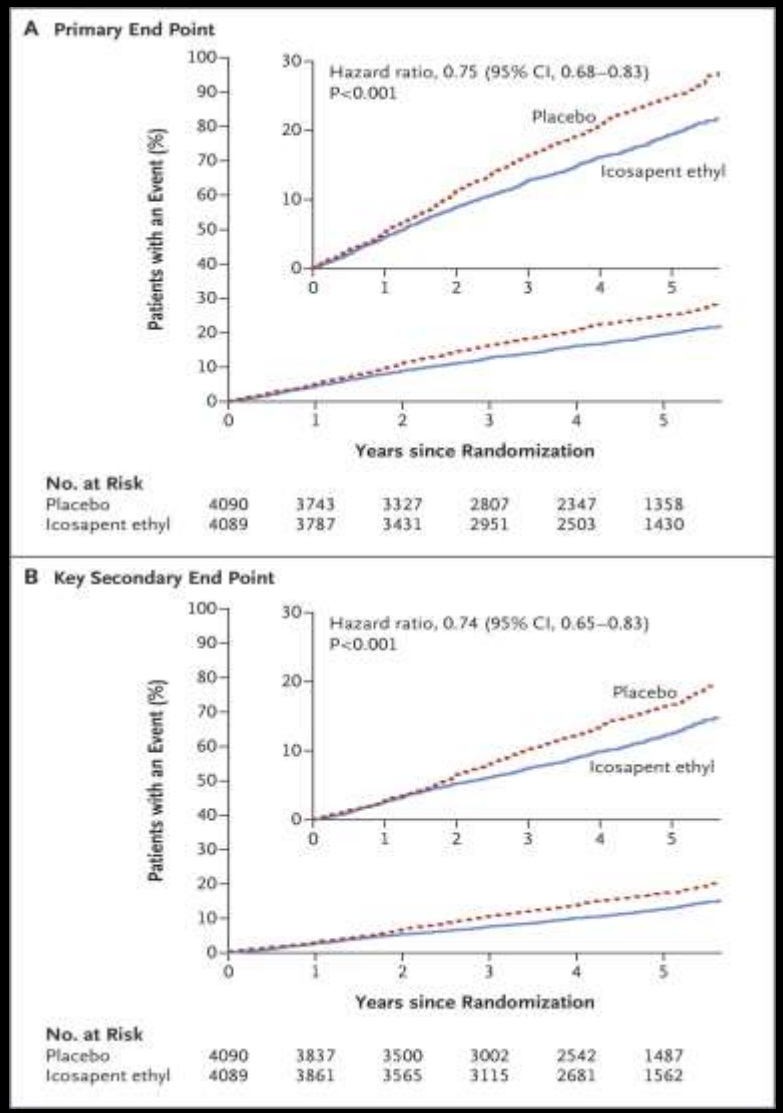
- Small interfering RNA inhibits synthesis of PCSK9
- Two subcutaneous injections a year, active for 48 hours
- ORION Trial programme
- No drug interactions and few side effects
- Complex deal with UK government

- 40-50% reduction in LDL-C
- No Outcome Evidence

Icosapent Ethyl

Cumulative Incidence of Cardiovascular Events.

ICOSAPENT ETHYL
Vaskepa
REDUCE-IT



Statin treated, high risk
and TG>1.6 mmol/L
NICE TA807

DL Bhatt et al. N Engl J Med 2019;380:11-22.

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Summary/Discussion

Summary

- QRisk will underestimate the true risk in the young
- We have patients with CVD sub-optimally controlled on maximally tolerated statin therapy
- We have patients with CVD sub-optimally controlled on no statin therapy
- The lipid clinics are over-run and will not cope alone
- In primary prevention think **bempedoic acid + ezetimibe**
- In secondary prevention think **inclisiran**

https://northyorkshireccg.nhs.uk/clinical-portal/cardiovascular-disease/

Discussion

https://northyorkshireccg.nhs.uk/clinical-portal/cardiovascular-disease/