Lowering Cholesterol.

Saving Lives.

TheAHSNNetwork

ACCELERATED ACCESS COLLABORATIVE

HEART UK THE CHOLESTEROL CHARITY

NHS

Tackling Cholesterol Together

Diabetes, Obesity and Lipids

Welcome to the ninth in a series of webinars as part of the national education programme Tackling Cholesterol Together.

Delivered in partnership by The NHS Accelerated Access Collaborative (AAC), The AHSN Network and the cholesterol charity, HEART UK

The webinar will start at 1pm

Feb 2022

All programme content, recordings and next webinar bookings will be housed in the HEART UK pages. Visit the site for the **new** series of 5 short videos on key themes for lipid management https://www.heartuk.org.uk/tackling-cholesterol-together/home

Housekeeping

- **This meeting will be recorded** and will be made available in the HEART UK Tackling Cholesterol Together pages
- **There will be time** to stop and ask questions at the end of the webinar
- **Feel free to ask questions** or upvote questions in the chat function when it becomes available
- **Any questions that we are not able to cover in the Q&A** sections today will be addressed following the event
- **Any questions you provided** during registration will be covered during the session

Agenda

	Topic	Presenter
01	**Welcome**	Sue Critchley
02	**The Metabolic Syndrome**	Dr Derek Connolly
03	**Obesity and Diabetic Dislipidaemia**	Professor Handrean Soran
04	**Weight Management**	Dr Matthew Capehorn
05	**Q&A. Close and next steps**	Panel led by Dr Derek Connolly

Objectives of today's webinar

01

Understand the metabolic syndrome, its history, risk factors and how to diagnose and manage it.

02

Review the impact of higher consumption of dietary cholesterol on higher risk of CVD incident

03

Understand the numbers needed to treat NNT using current recommended therapies is lower in diabetics compared with non-diabetics

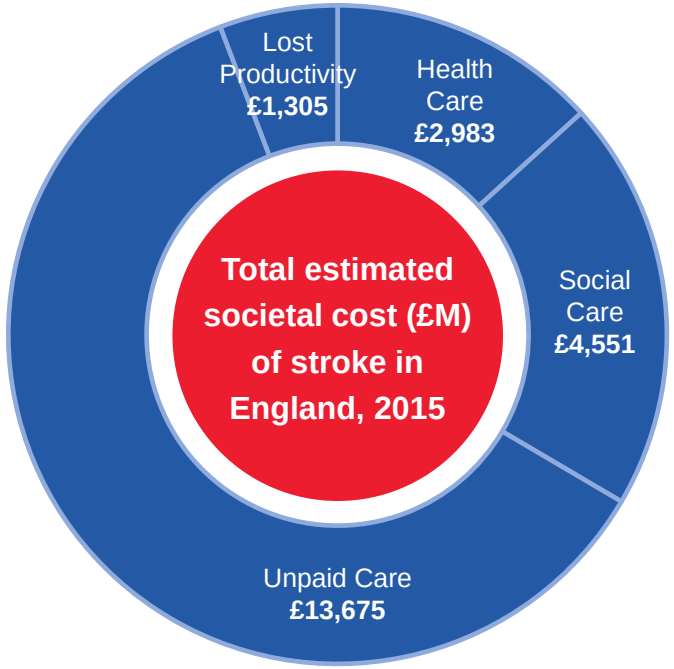
04

Consider the multiple factors leading to obesity and take an evidence-based approach to weight loss and weight management. **See** how weight loss reduces CVD risk

Why is CVD a priority?

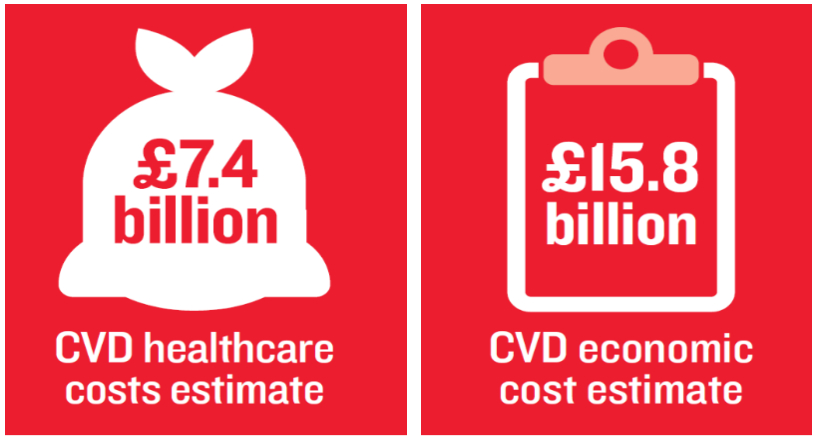
- **CVD kills 136,000 people a year**
- CVD differentially targets **ethnic minority communities**
- CVD differentially targets **deprived communities**
- As well as death, CVD can cause **significant disability**
- **CVD can be prevented**

STROKE IS THE LARGEST CAUSE OF ADULT DISABILITY



Source: Stroke Association. Current, future and avoidable costs of stroke

CVD IS EXPENSIVE



Source: BHF analysis of European Heart Network (2017)
European Cardiovascular Disease Statistics 2017

CVD Burden Remains a Significant Unmet Need across all risk factors

CVD in the UK[1]

- >7 million people have CVD
- CVD has an annual total healthcare cost of £9 billion
- CVD is one of the biggest causes of death despite the availability of medical interventions and strategies

The NHS Long-Term Plan:[2]

Up to 10 year outlook for a variety of healthcare topics

- Cholesterol was highlighted for the first time in a decade
- CV risk management is a combined approach: ABC (AF, Blood pressure, Cholesterol)

167,000 deaths/year from CVD; **44,000** are premature[1]

Improve early detection and treatment of CVD
NHS Long-Term Plan[2]

>100,000 hospital admissions/year for an MI[1]
>100,000 strokes/year[1]

Prevent 150,000 heart attacks, strokes and dementia cases
NHS Long-Term Plan[2]

Up to **260,000** people in the UK have HeFH[3]

Expand access to genetic testing for identification of FH cases to at least 25% in 5 years
NHS Long-Term Plan[2]

- AF, atrial fibrillation; CV, cardiovascular; CVD, cardiovascular disease; FH, familial hypercholesterolaemia; HeFH, heterozygous familial hypercholesterolaemia; MI, myocardial infarction.

- 1. BHF. UK Factsheet, August 2019. Available at: https://www.bhf.org.uk/what-we-do/our-research/heart-statistics. Accessed November 2019;
  2. NHS Long-Term Plan. Available at: https://www.longtermplan.nhs.uk/wp-content/uploads/2019/08/nhs-long-term-plan-version-1.2.pdf;
  3. NICE Clinical Guidance [CG71]. Available at: https://www.nice.org.uk/guidance/cg71/. Accessed December 2019.

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NHS

02

The Metabolic Syndrome

Dr Derek Connolly BSc[Hons] MB ChB [Edin] PhD[Cantab] FRCP

Consultant Interventional Cardiologist

Birmingham City Hospital

Director of Research & Development SWB

Honorary Senior Lecturer

Institute of Cardiovascular Sciences at the University of Birmingham

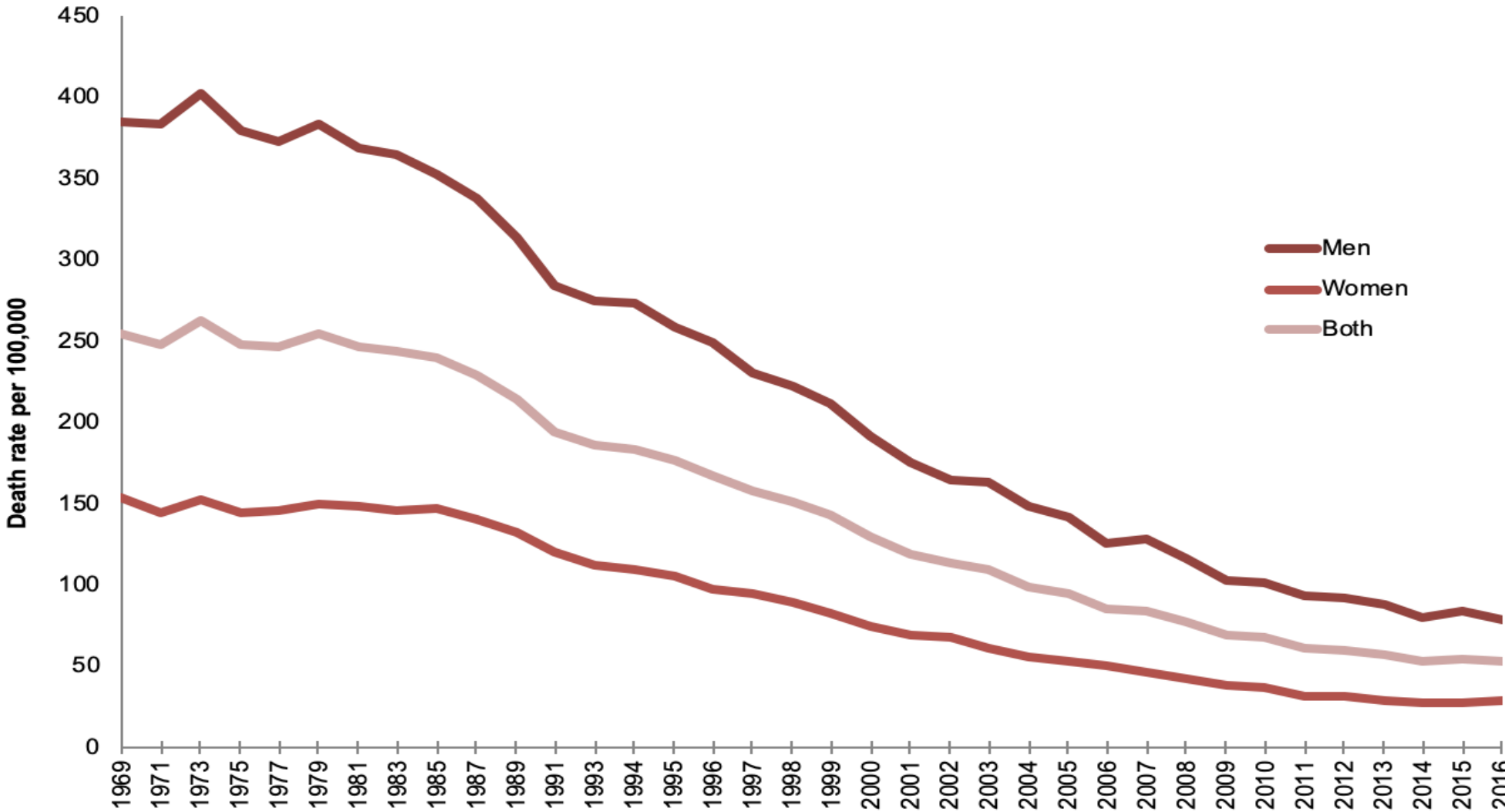
MIDLAND METROPOLITAN UNIVERSITY HOSPITAL

Primary Care Cardiovascular Society

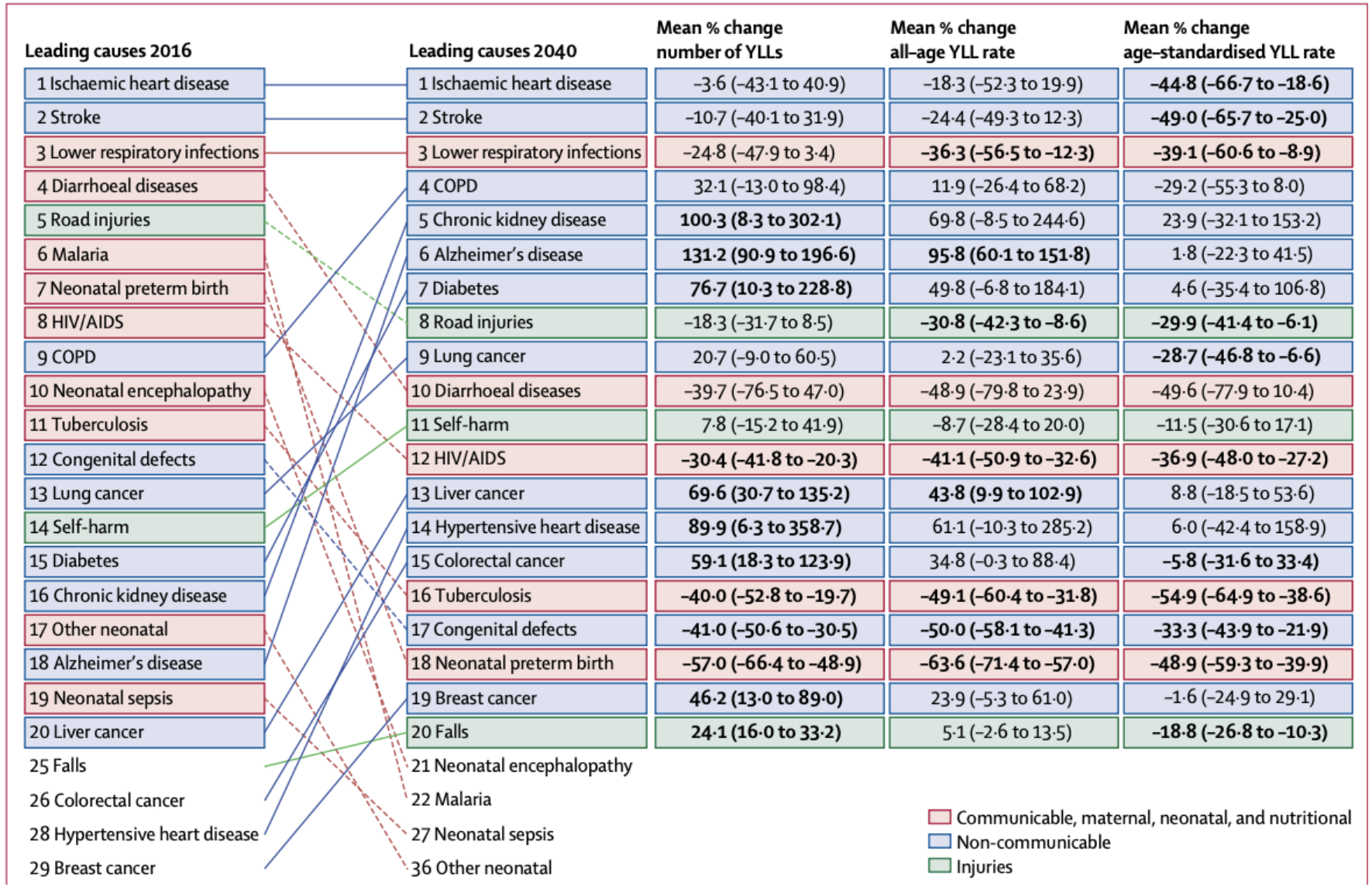
Driving primary care to deliver the best in cardiovascular health

UNIVERSITY OF BIRMINGHAM

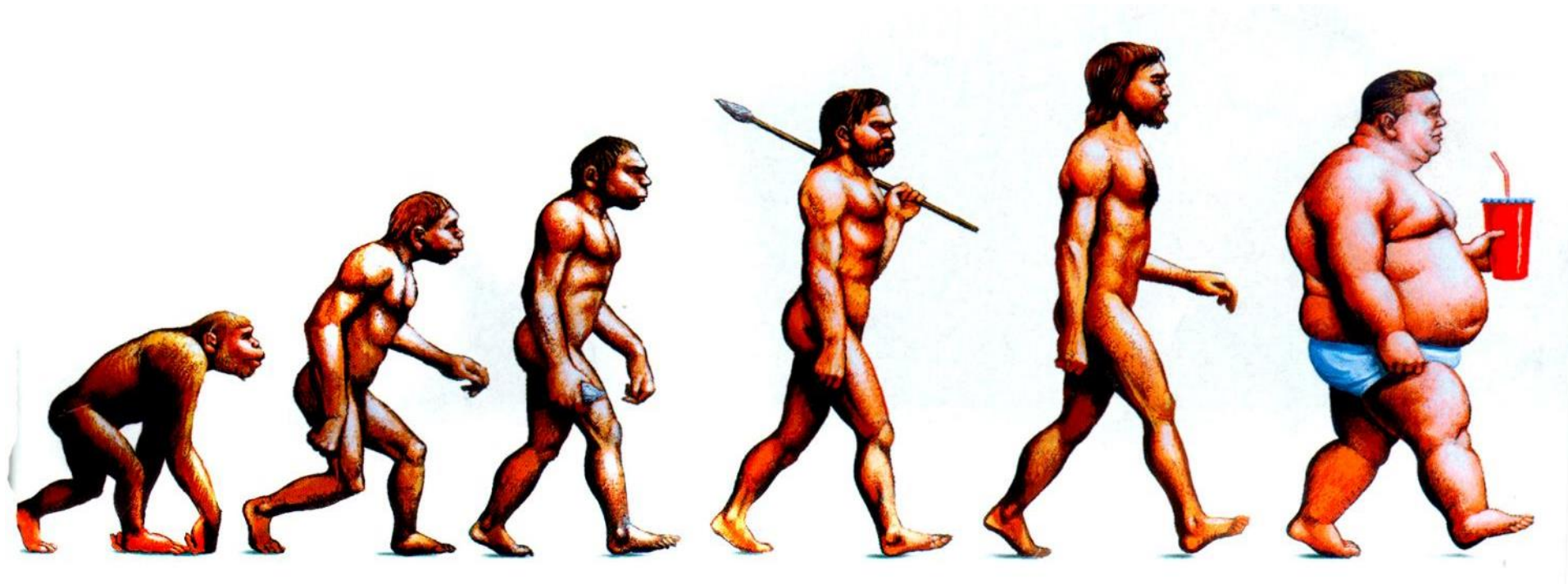
Age-standardised death rate per 100,000 from coronary heart disease (CHD), under 75, by gender, 1969 to 2016



Leading 20 causes of Years of Life Lost globally in 2016 and 2040 by rank order



Lancet October 2018



Journal of the American Heart Association

ORIGINAL RESEARCH

Adverse Trends in Premature Cardiometabolic Mortality in the United States, 1999 to 2018

Nilay S. Shah, MD, MPH; Donald M. Lloyd-Jones, MD, ScM; Namratha R. Kandula, MD, MPH; Mark D. Huffman, MD, MPH; Simon Capewell, DSc, MD, MBBS; Martin O'Flaherty, MD, MSc, PhD; Kiarri N. Kershaw, PhD; Mercedes R. Carnethon, PhD; Sadiya S. Khan, MD, MSc

BACKGROUND: Life expectancy in the United States has recently declined, in part attributable to premature cardiometabolic mortality. We characterized national trends in premature cardiometabolic mortality, overall, and by race-sex groups.

J Am Heart Assoc. 2020;9:e018213. DOI: 10.1161/JAHA.120.018213

A history of metabolic syndrome

- 1923 Kylin ; a syndrome involving HBP, hyperglycaemia and hyperuricaemia.
- 1965 Avogaro and Crepaldi a syndrome which comprised hypertension, hyperglycaemia, and obesity.
- 1988 Reaven. ‘a cluster of risk factors for diabetes and cardiovascular disease’ and named it ‘Syndrome X’. His main contribution was the introduction of the concept of insulin resistance.

George Alberti
European Heart Journal Supplements, Volume 7, Issue suppl_D, June 2005, Pages D3–D5, https://doi.org/10.1093/eurheartj/sui021

Metabolic Syndrome

- A combination of diabetes, high blood pressure, abnormal lipids and obesity.
- Greater risk of getting coronary heart disease, stroke and other conditions that affect the blood vessels.
- On their own, diabetes, high blood pressure and obesity can damage your blood vessels, but having all 3 together is particularly dangerous.
- 1 in 3 older adults aged 50 or over in the UK.

Metabolic syndrome may be diagnosed if you have 3 or more of the following:

- **Obesity ;** being very overweight or having too much fat around your waist
- **Abnormal Lipids ;** High blood triglyceride levels and low levels of HDL
- **High blood pressure ;**
- **Diabetes ;** An inability to control blood sugar levels

Clinical Diagnosis of the Metabolic Syndrome

Table 1. Clinical Diagnosis of the Metabolic Syndrome.

Risk Factors	Defining Level
Abdominal obesity, given as waist circumference[a,b]	
Men	>102 cm (>40 in)
Women	>88 cm (>35 in)
Triglycerides	≥150 mg/dL
HDL cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	≥130/≥85 mm Hg
Fasting glucose	≥110 mg/dL

Abbreviations: BMI, body mass index; HDL, high-density lipoprotein.
[a]Overweight and obesity are associated with insulin resistance and the metabolic syndrome. However, the presence of abdominal obesity is more highly correlated with the metabolic risk factors than is an elevated BMI. Therefore, the simple measure of waist circumference is recommended to identify the body weight component of the metabolic syndrome.
[b]Some male patients can develop multiple metabolic risk factors when the waist circumference is only marginally increased, for example, 94 to 102 cm (37 to 39 in). Such patients may have a strong genetic contribution to insulin resistance. They should benefit from changes in life habits, similarly to men with categorical increases in waist circumference.

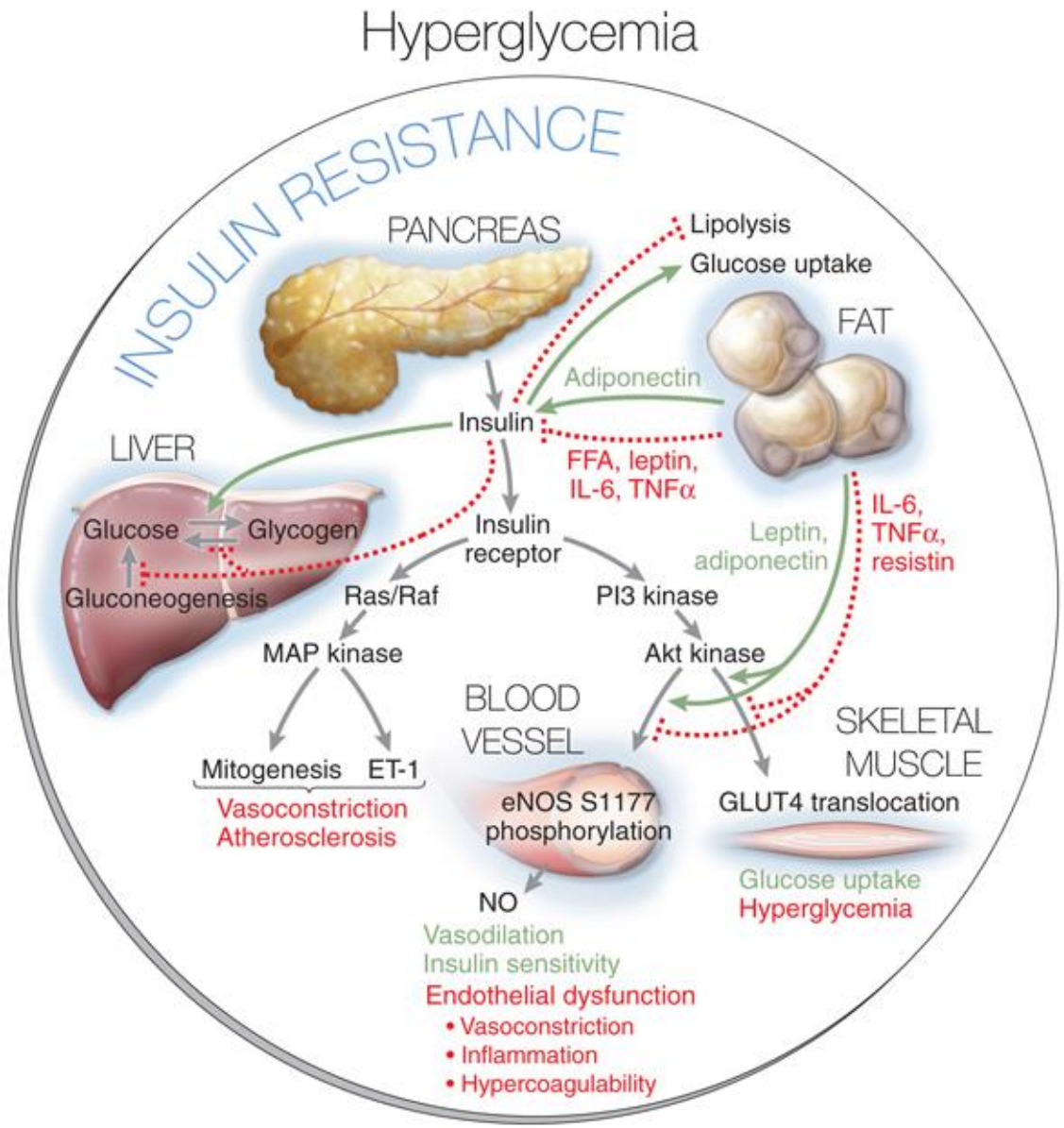
Source DOI: 10.1177/1074248416686187.

What Does Metabolic Syndrome do to you?

- Increases the risk of strokes and heart attacks
  - Increases your triglyceride levels
  - Raises your blood pressure
  - Making your blood more likely to clot
- Increases your insulin resistance thus making it more likely you will develop diabetes
- Gives you a fatty liver [with or without exposure to alcohol] making liver cirrhosis a possibility

Higher Risk Groups for Metabolic Syndrome

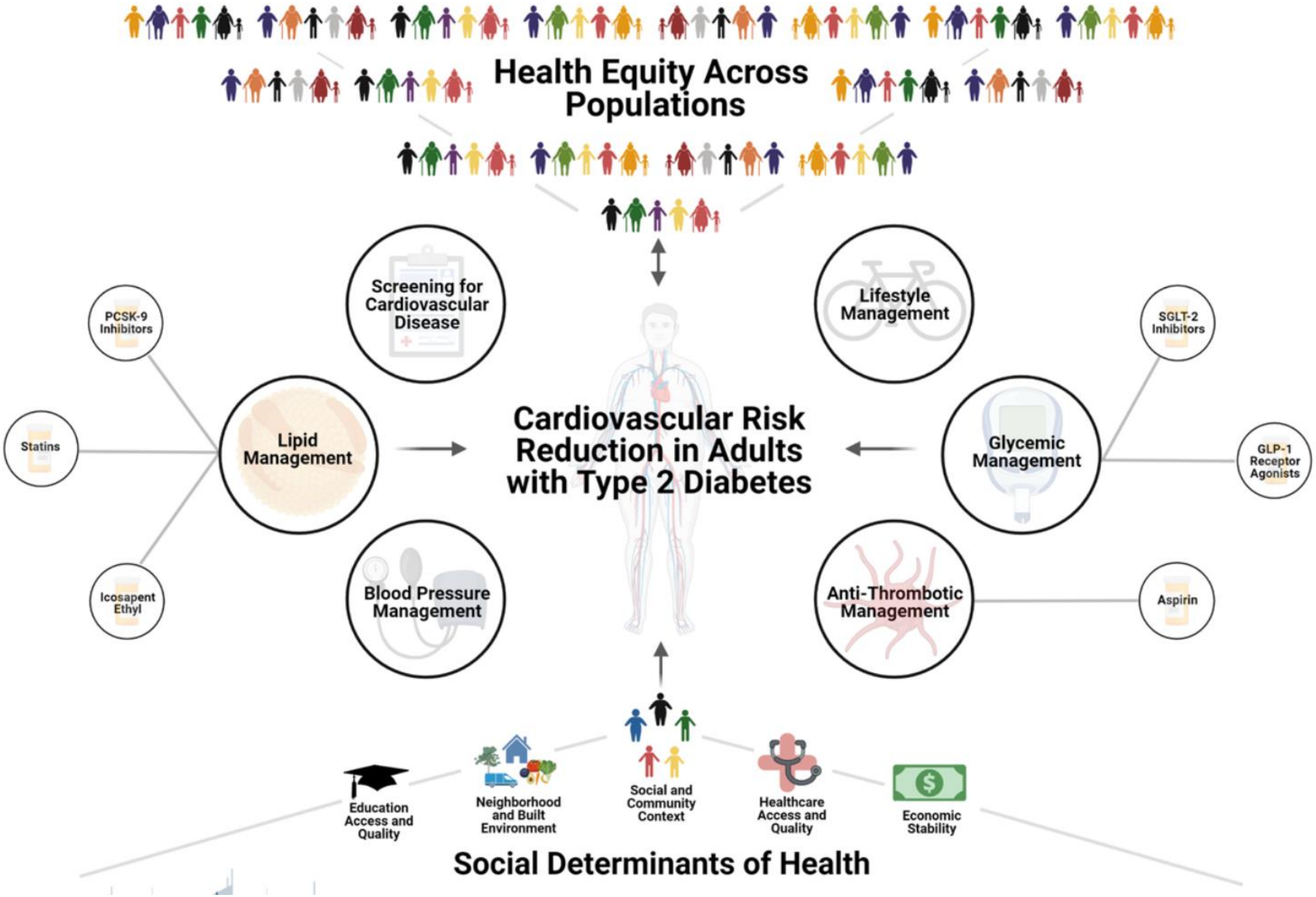
- Polycystic Ovarian Syndrome
- Sleep apnoea
- Fatty liver disease
- High Alcohol intake
- Certain ethnic groups

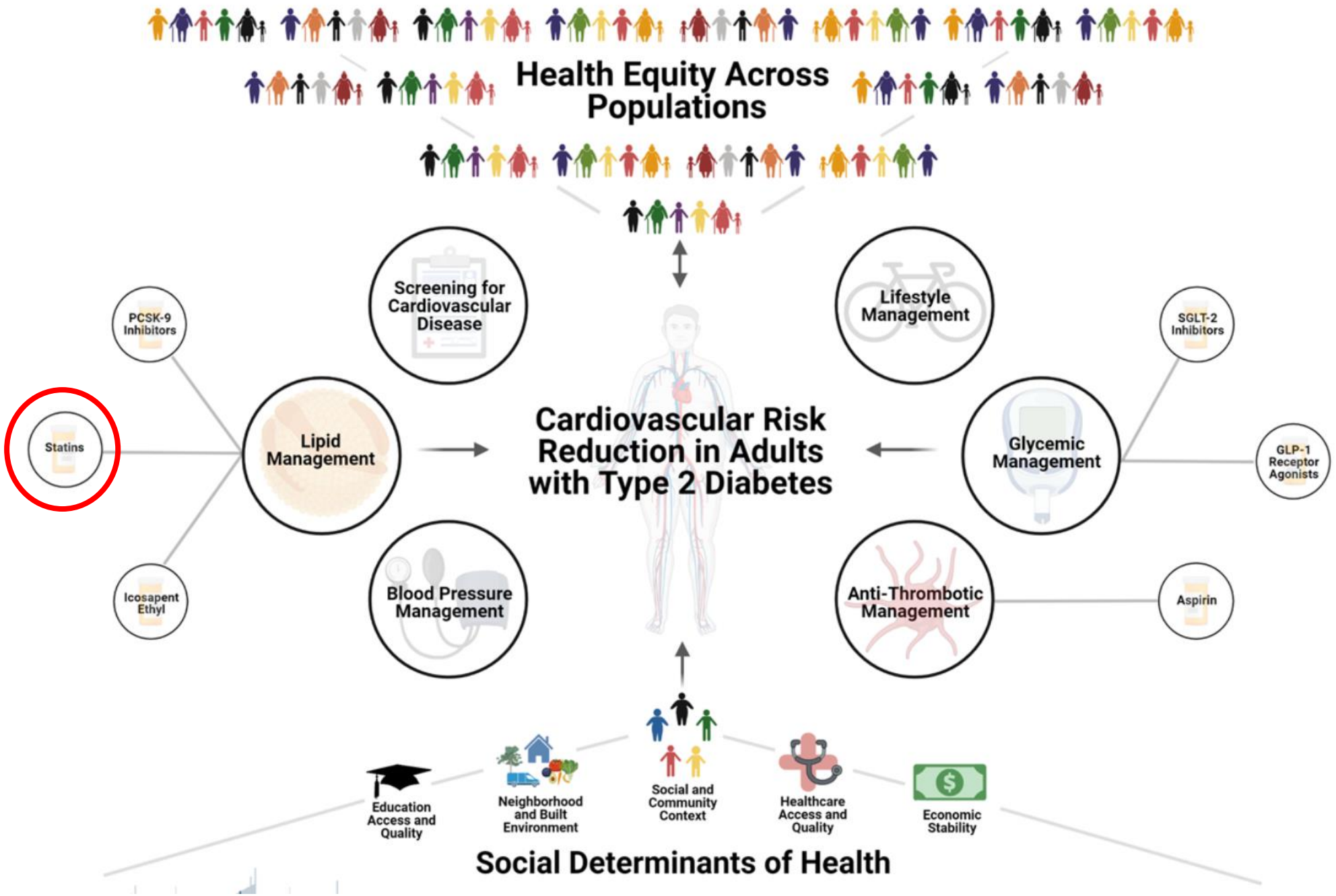


Huang, P. L. (2009). Dis. Model. Mech. 2, 231-237

Treatments for metabolic syndrome

- Eat a healthy diet
- Avoid refined carbohydrates
- Exercise daily
- Keep your weight to a healthy body mass index
- Stop smoking
- Cut down or stop drinking alcohol


Health Equity Across Populations
Screening for Cardiovascular Disease
PCSK-9 Inhibitors
Statins
Lipid Management
Icosapent Ethyl
Blood Pressure Management
Lifestyle Management
SGLT-2 Inhibitors
Glycemic Management
GLP-1 Receptor Agonists
Anti-Thrombotic Management
Aspirin
Cardiovascular Risk Reduction in Adults with Type 2 Diabetes
Education Access and Quality
Neighborhood and Built Environment
Social and Community Context
Healthcare Access and Quality
Economic Stability
Social Determinants of Health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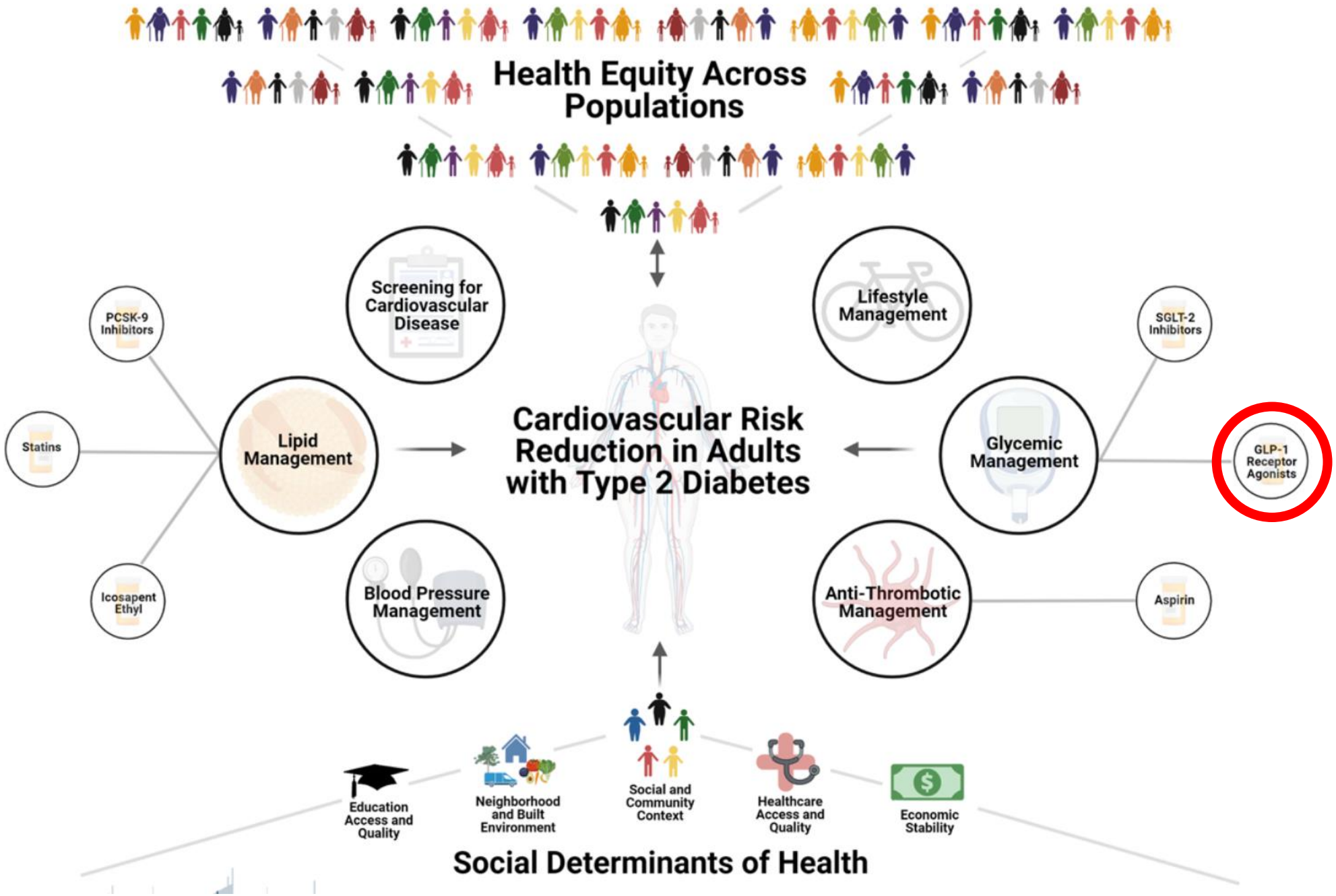
Do statins cause diabetes?

- Meta analysis of 13 statin trials with 91 140 participants,
- Statin therapy was associated with a slightly increased risk [9%] of development of diabetes, but the risk is low both in absolute terms and when compared with the reduction in coronary events.

Naveed Sattar et al LANCET 2010 Feb 27;375(9716):735-42.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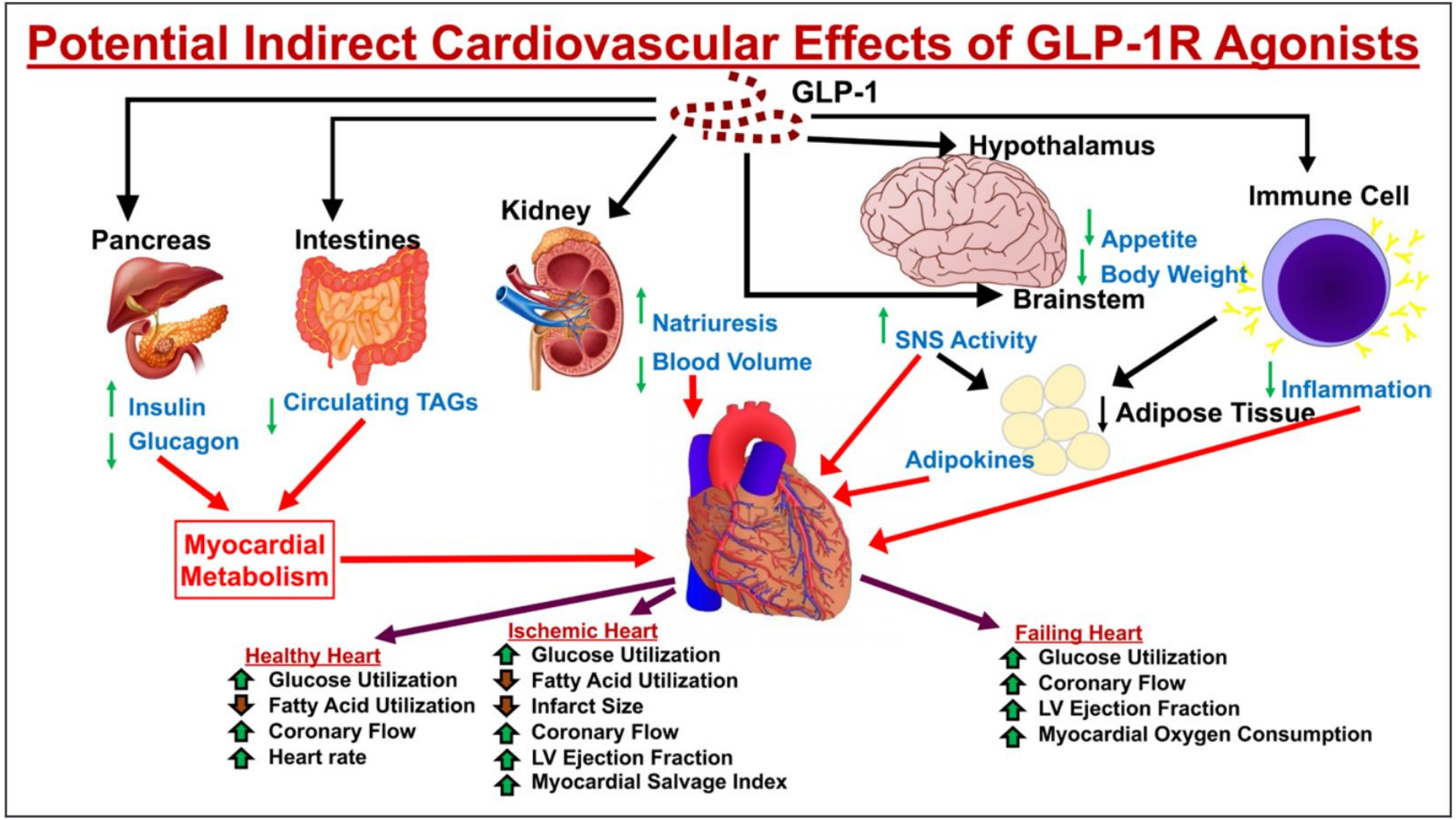
Potential Indirect Cardiovascular Effects of GLP-1R Agonists



Once-Weekly Semaglutide in Adults with Overweight or Obesity

Wilding JPH. et al. DOI: 10.1056/NEJMoa2032183

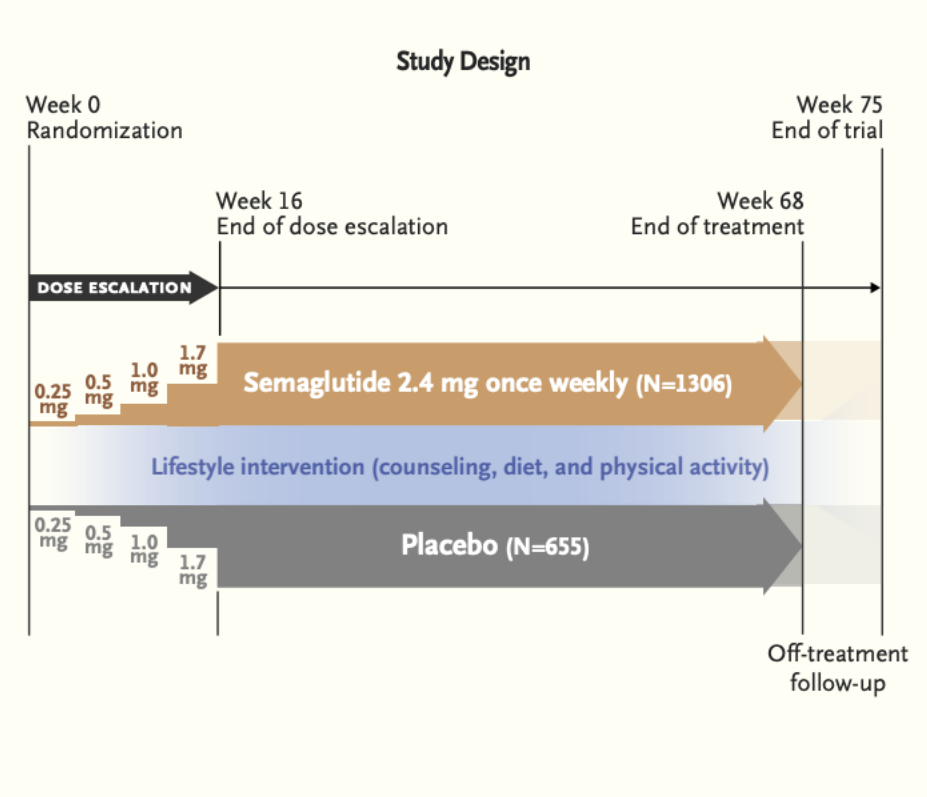
CLINICAL PROBLEM

Clinical guidelines suggest pharmacologic intervention in addition to diet and exercise to promote weight loss among adults with BMI ≥30 (or ≥27 in those with coexisting conditions). Barriers to medication use include limited efficacy, adverse effects, and cost. Subcutaneous semaglutide, a glucagon-like peptide-1 analogue FDA-approved to treat type 2 diabetes in adults, has been accompanied by weight loss in previous clinical trials.

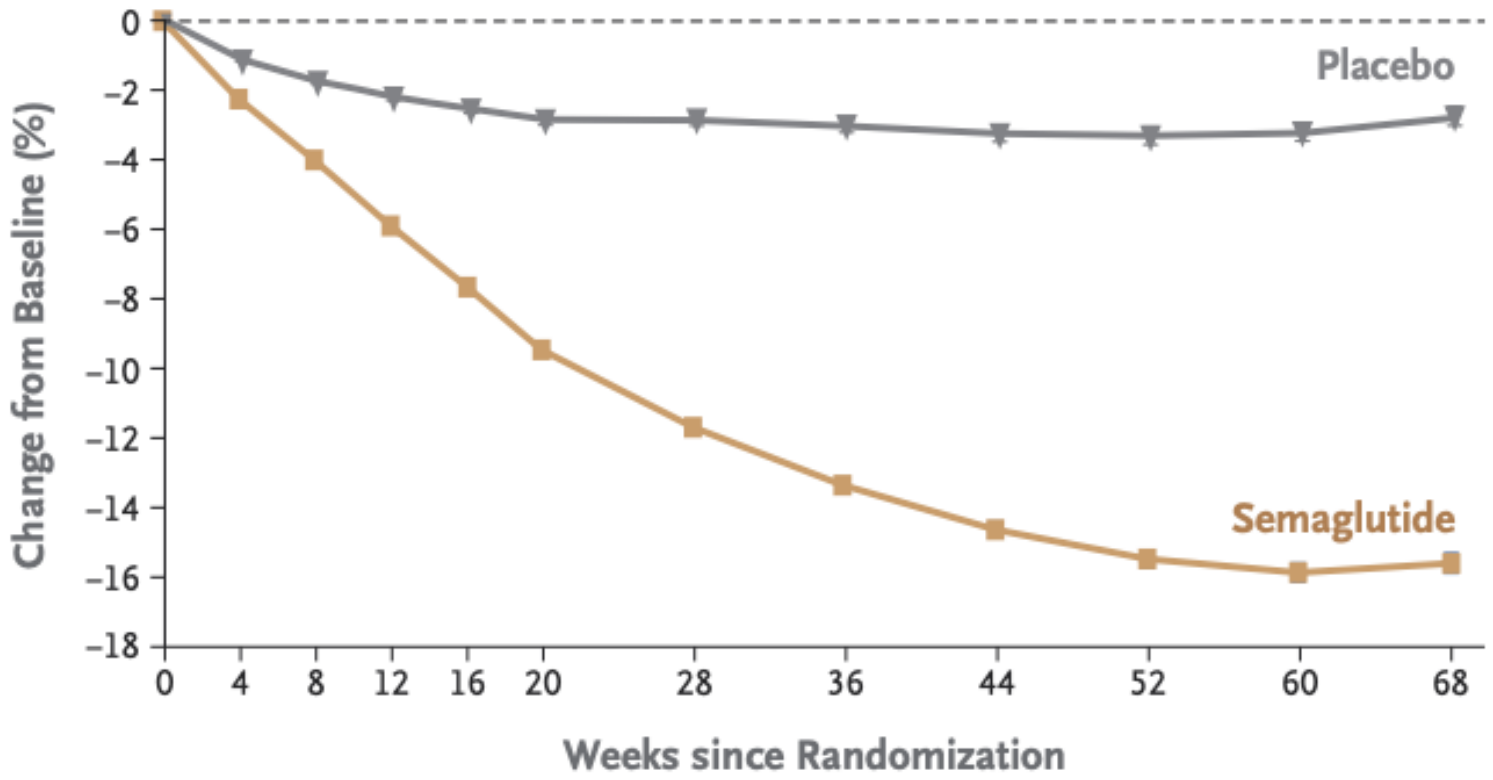
CLINICAL TRIAL

A phase 3, double-blind, randomized, controlled trial comparing semaglutide with placebo, plus lifestyle changes, in overweight or obese adults without diabetes.

1961 participants were assigned to receive 2.4 mg of subcutaneous semaglutide (with gradual increase to the 2.4 mg dose) or placebo weekly for 68 weeks; both groups received a counseling intervention involving diet and exercise. Coprimary end points were percentage change in body weight and weight reduction ≥5%.



Body Weight Change from Baseline by Week, Observed In-Trial Data



No. at Risk

Placebo	655	649	641	619	615	603	592	571	554	549	540	577
Semaglutide	1306	1290	1281	1262	1252	1248	1232	1228	1207	1203	1190	1212

1 Recommendations

1.1 Semaglutide is recommended as an option for weight management, including weight loss and weight maintenance, alongside a reduced-calorie diet and increased physical activity in adults, only if:

- they have at least 1 weight-related comorbidity and:
  - a body mass index (BMI) at least 35.0 kg/m^2, or
  - exceptionally, a BMI of 30.0 kg/m^2 to 34.9 kg/m^2 if they are referred to tier 3 services based on the criteria in NICE's clinical guideline on obesity: identification, assessment and management.

    Use lower BMI thresholds (usually reduced by 2.5 kg/m^2) for people from south Asian, Chinese, and Black African or Caribbean family backgrounds.

1.2 Prescribe semaglutide as part of a specialist weight management service with multidisciplinary input (such as a tier 3 or tier 4 service).

1.3 Only use semaglutide for a maximum of 2 years.

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03

Obesity and Diabetic Dislipidaemia

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Consultant Physician and Endocrinologist, Central Manchester University Hospitals NHS Foundation Trust

Chair Medical, Scientific and Research Committee HEART UK

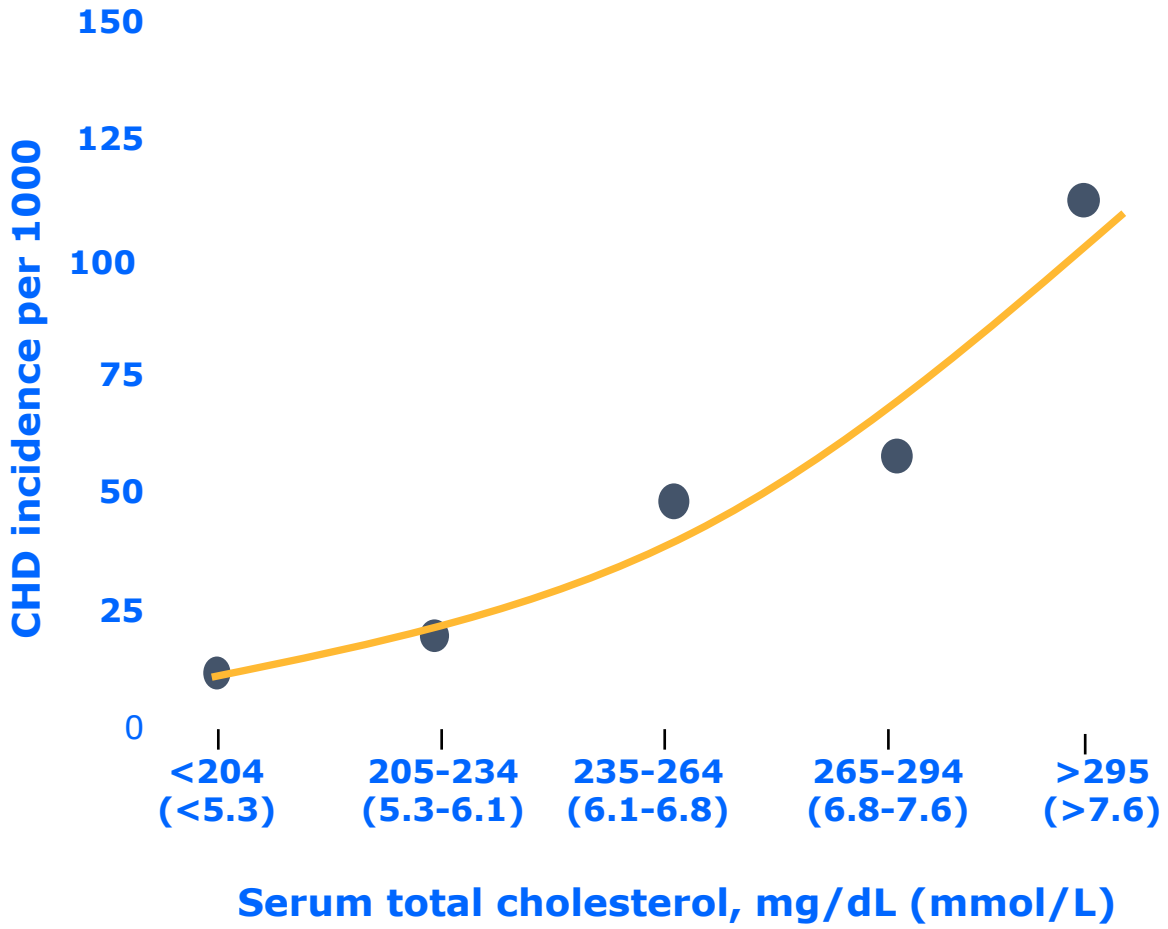
NHS Manchester University NHS Foundation Trust

Disclosures

H.S. has received personal fees from Amgen, Akcea, Synageva, NAPP, Takeda, Sanofi, Pfizer and Kowa.

H.S. received research grants and donations from Akcea, Pfizer, MSD, AMGEN, Genzyme-Sanofi, Synageva, Amryt, Synageva and Alexion.

The Framingham Study: Relationship Between Cholesterol and CHD Risk

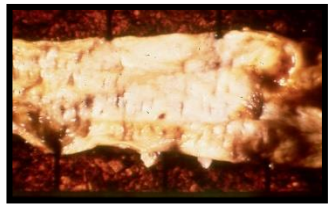


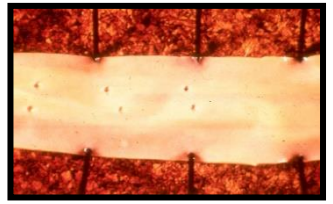
Castelli WP. *Am J Med.* 1984;**76**:4-12

Nikolaj Nikolajewitsch Anitschkow (1885 – 1964)

Lots of Egg Yolk

Vegitables





"Without cholesterol there can be no atherosclerosis"

Stehbens WE. Anitschkow and the cholesterol over-fed rabbit. Cardiovasc Pathol 1999;8:177-8.
Finking G, Hanke H. Nikolaj Nikolajewitsch Anitschkow (1885-1964) established the cholesterol-fed rabbit as a model.
Igor E. Konstantinov, Nicolai Mejevoi, and Nikolai M. Anichkov. Nikolai N. Anichkov and His Theory of Atherosclerosis. Tex Heart Inst J. 2006; 33(4): 417–423.

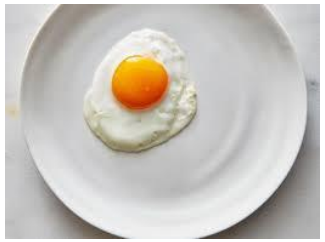
Dietary cholesterol and Egg consumption Again!

Individual participant data were pooled from **six** prospective US cohorts using data collected between March 25, 1985, and August 31, 2016. Self-reported diet data were harmonized using a standardized protocol.

29 615 adults pooled. HR and ARD over the entire follow-up for incident CVD and all-cause mortality, adjusting for demographic, socioeconomic, and behavioral factors.

Each additional 300 mg of dietary cholesterol consumed per day was significantly associated with higher risk of incident CVD (adjusted HR, 1.17 [95% CI, 1.09-1.26]; adjusted ARD, 3.24% [95% CI, 1.39%-5.08%]) and all-cause mortality (adjusted HR, 1.18 [95% CI, 1.10-1.26]; adjusted ARD, 4.43% [95% CI, 2.51%-6.36%]).

Each additional half an egg consumed per day was significantly associated with higher risk of incident CVD (adjusted HR, 1.06 [95% CI, 1.03-1.10]; adjusted ARD, 1.11% [95% CI, 0.32%-1.89%]) and all-cause mortality (adjusted HR, 1.08 [95% CI, 1.04-1.11]; adjusted ARD, 1.93% [95% CI, 1.10%-2.76%]).



The **associations between egg consumption and incident CVD** (adjusted HR, 0.99 [95% CI, 0.93-1.05]; adjusted ARD, −0.47% [95% CI, −1.83% to 0.88%]) and all-cause mortality (adjusted HR, 1.03 [95% CI, 0.97-1.09]; adjusted ARD, 0.71% [95% CI, −0.85% to 2.28%]) were no longer significant after adjusting for dietary cholesterol consumption.

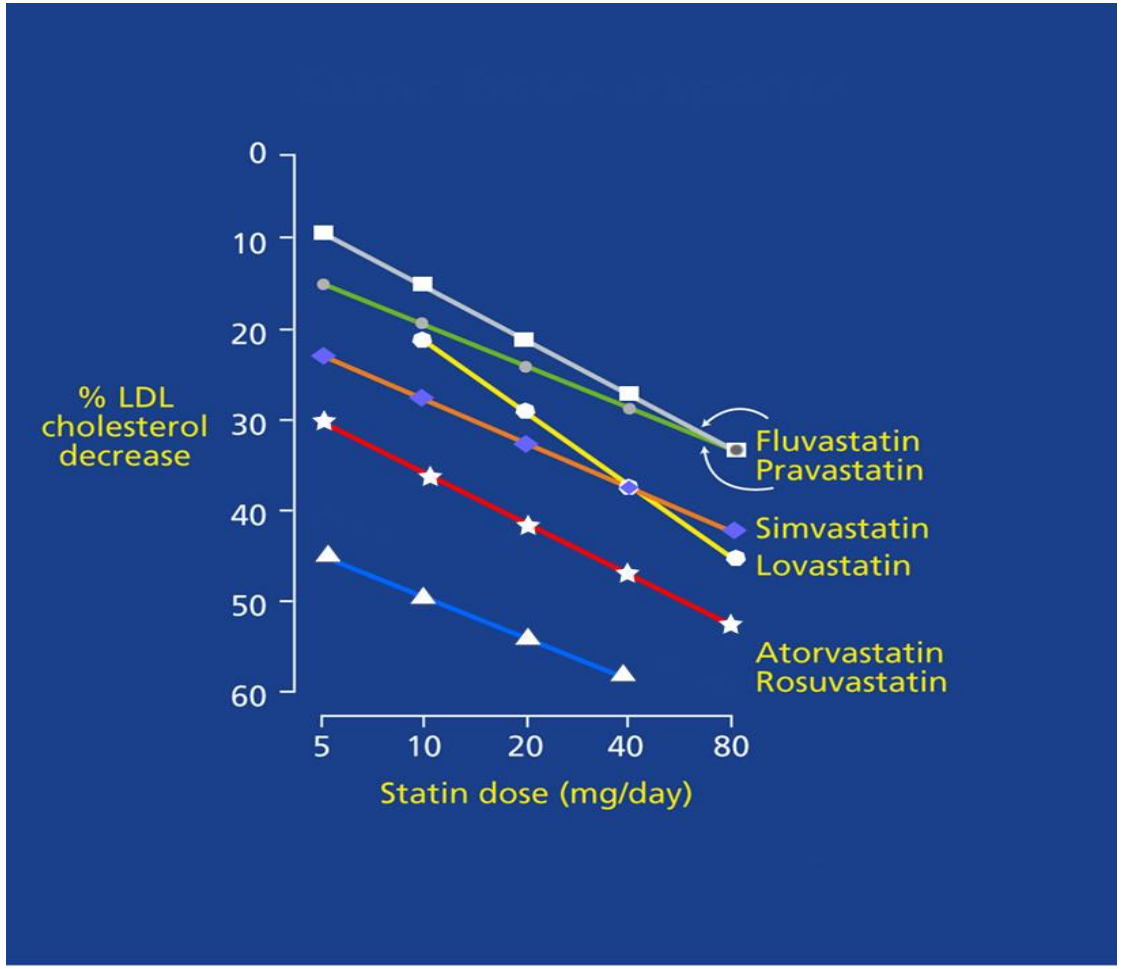
Conclusion:
Among US adults, higher consumption of dietary cholesterol or eggs was significantly associated with higher risk of incident CVD and all-cause mortality in a dose-response manner.

Victor W. Zhong et al. JAMA 2020.

Statins potency

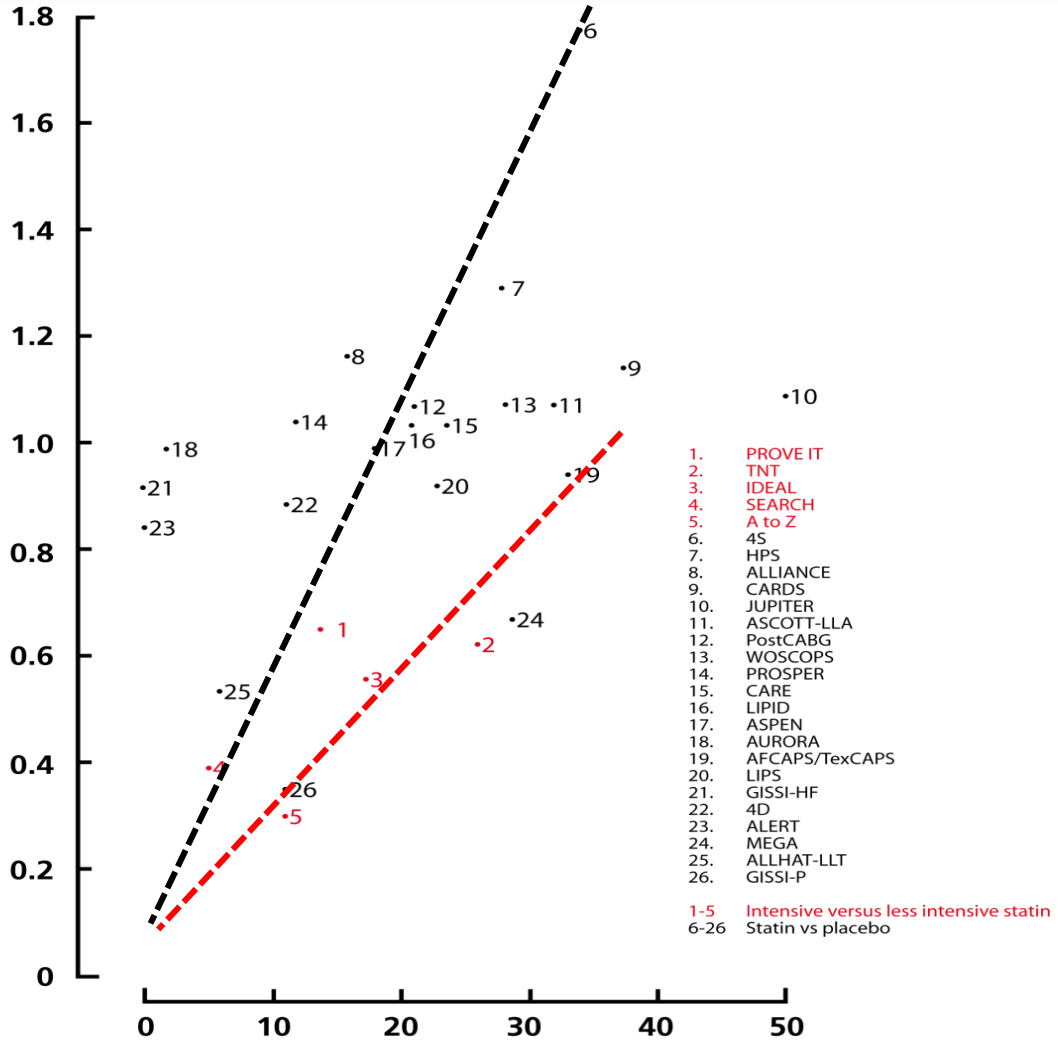
Statin trials support LDL-C as a risk factor for CV events

Different statins potency to lower LDL-C



Soran H, Durrington N. Curr Opin Pharmacol 2008

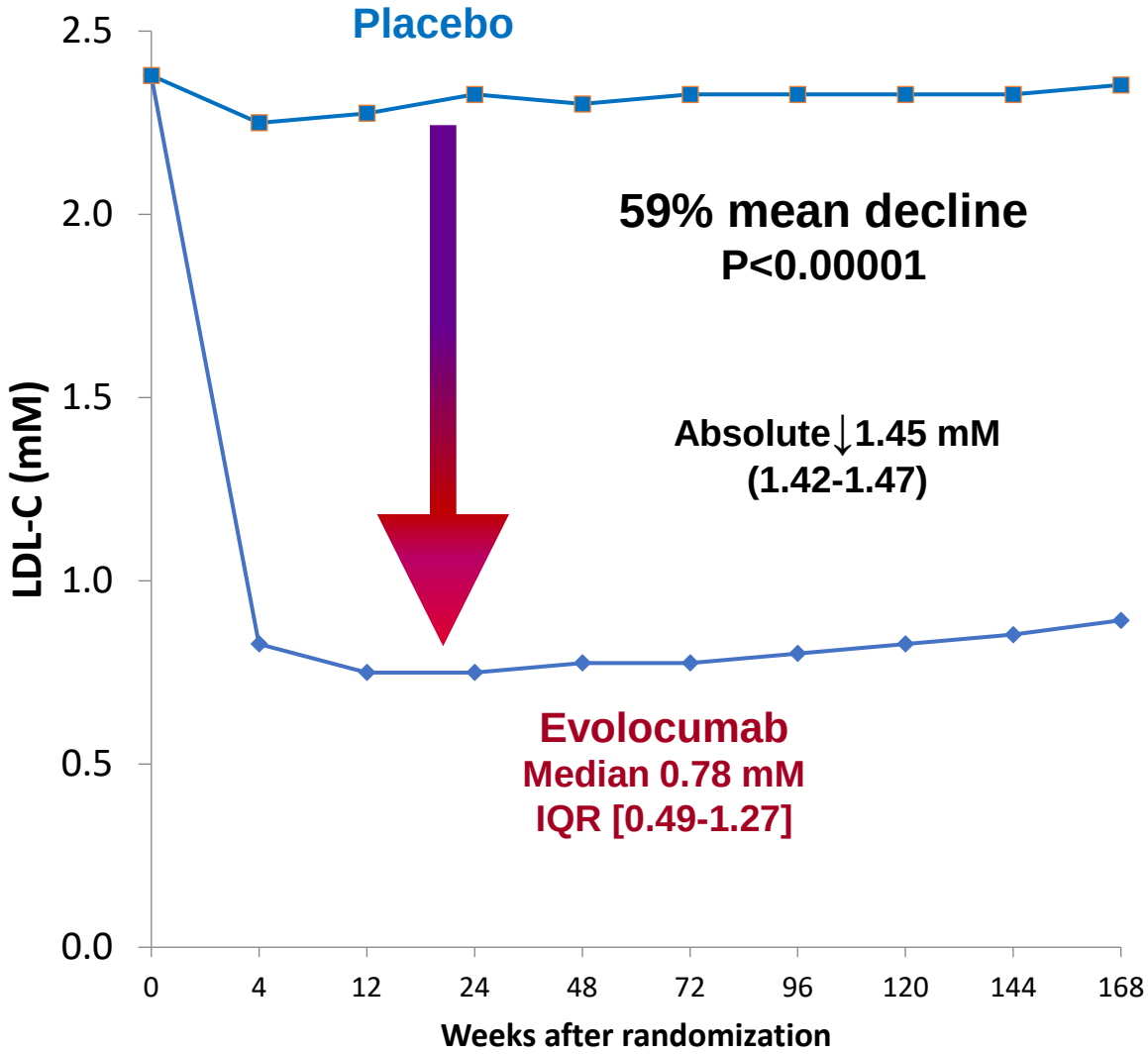
22% reduction in CHD risk per 1mmol/L lower LDL-C

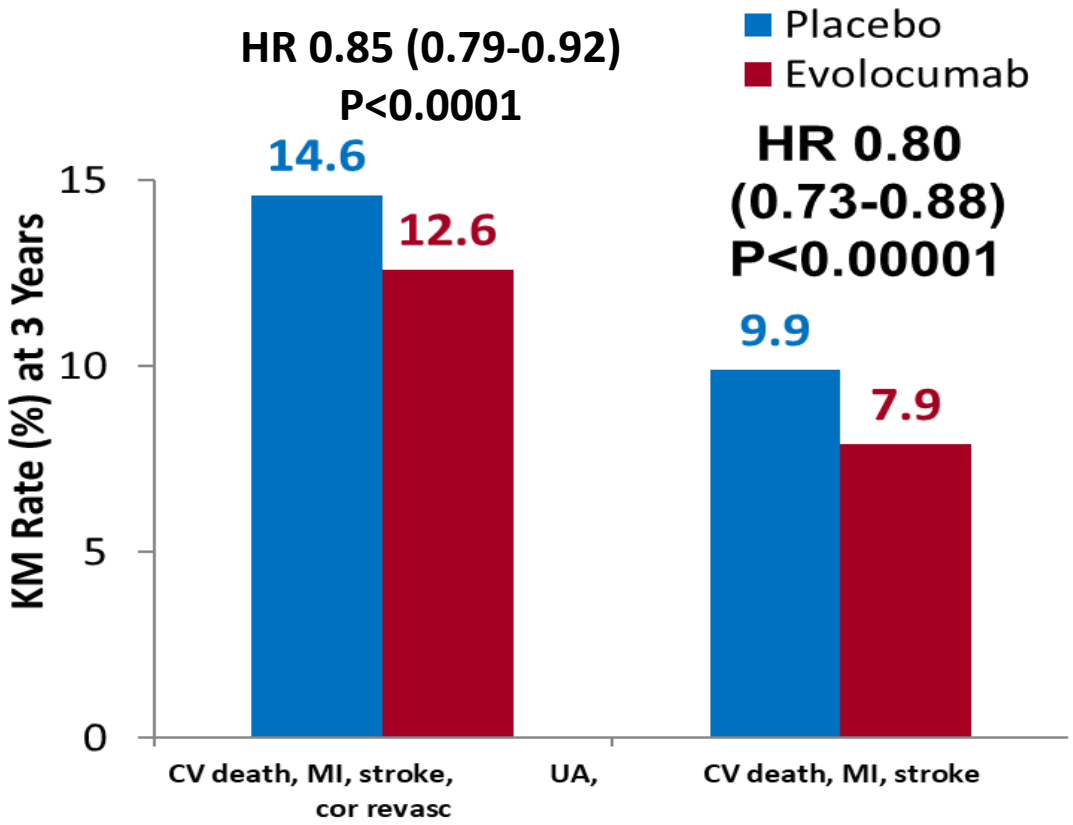


Soran H et al. European Heart J 2016

Summary of FOURIER

- ↓ LDL-C by 59% (from 2.4 -> 0.8 [0.5, 1.2] mM)
- ↓ CV outcomes in patients already on statin therapy
- Evolocumab was well-tolerated

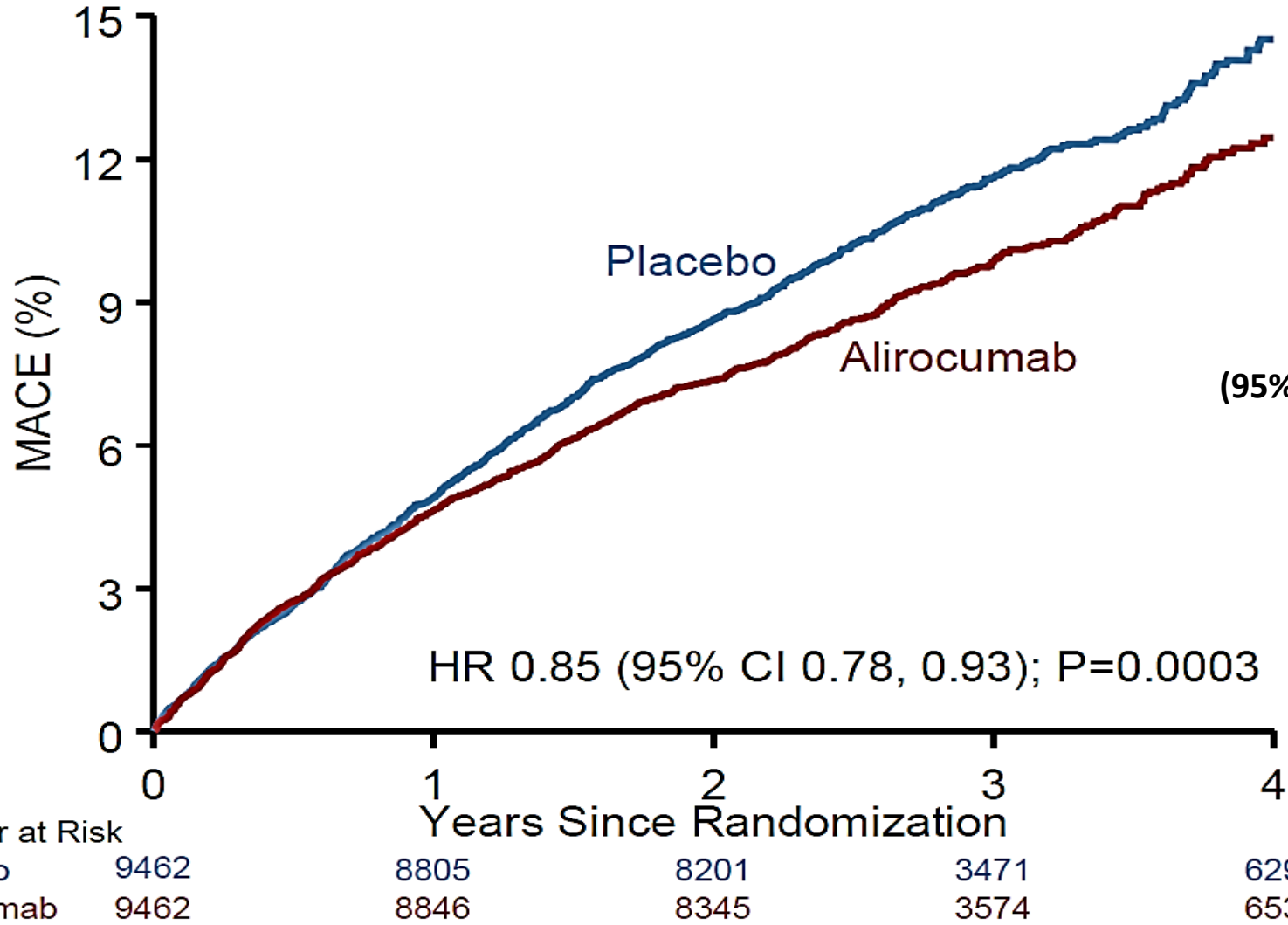




Sabatine MS et al. *New Engl J Med* 2017;376:1713-22

MACE: CHD death, non-fatal MI, ischemic stroke, or unstable angina requiring hospitalization

*Based on cumulative incidence



ARR* 1.6%

HR 0.85
(95% CI 0.78, 0.93)
P=0.0003

NEJM 2018

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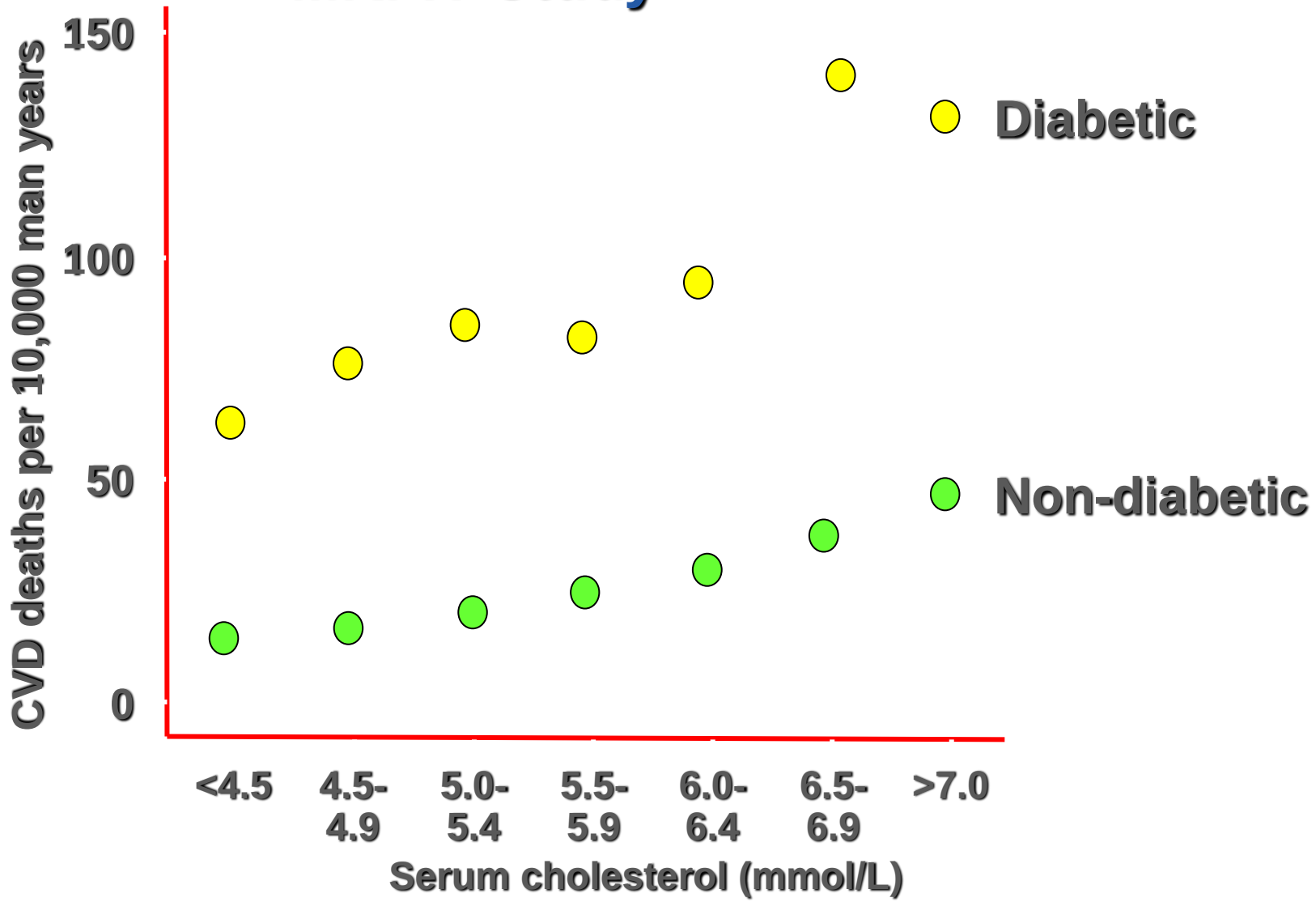
Lipid Lowering and Diabetes

21st century Mona Lisa

Cardiovascular risk in diabetes in relation to serum cholesterol

MRFIT Study



Stamler et al, Diabetes Care 1993;16:434-44

Cardiovascular risk in diabetes in relation to serum cholesterol

MRFIT Study

Why same level of LDL-C is associated with higher risk in patients with DM?

- Other risk factors
- Compromised HDL functionality
- LDL quality
  - Small-dense LDL particles
  - Glycation
  - Oxidation

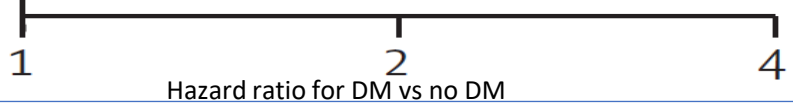
Younis *et al*. Diab Vasc Dis Res. 2013
Soran *et al*. Current Opinion Lipidology. 2012
Soran *et al*. Current Opinion Lipidology. 2015
Soran *et al*. Current Opinion Lipidology. 2016
Soran *et al*. Frontier Pharmacology. 2015

Serum cholesterol (mmol/L)

Stamler et al, Diabetes Care 1993;16:434-44

Diabetes doubles the risk of having vascular events

	Number of cases	HR (95% CI)
Coronary heart disease*	26 505	2·00 (1·83–2·19)
Coronary death	11 556	2·31 (2·05–2·60)
Non-fatal myocardial infarction	14 741	1·82 (1·64–2·03)
Stroke subtypes*		
Ischaemic stroke	3799	2·27 (1·95–2·65)
Haemorrhagic stroke	1183	1·56 (1·19–2·05)
Unclassified stroke	4973	1·84 (1·59–2·13)
Other vascular deaths	3826	1·73 (1·51–1·98)

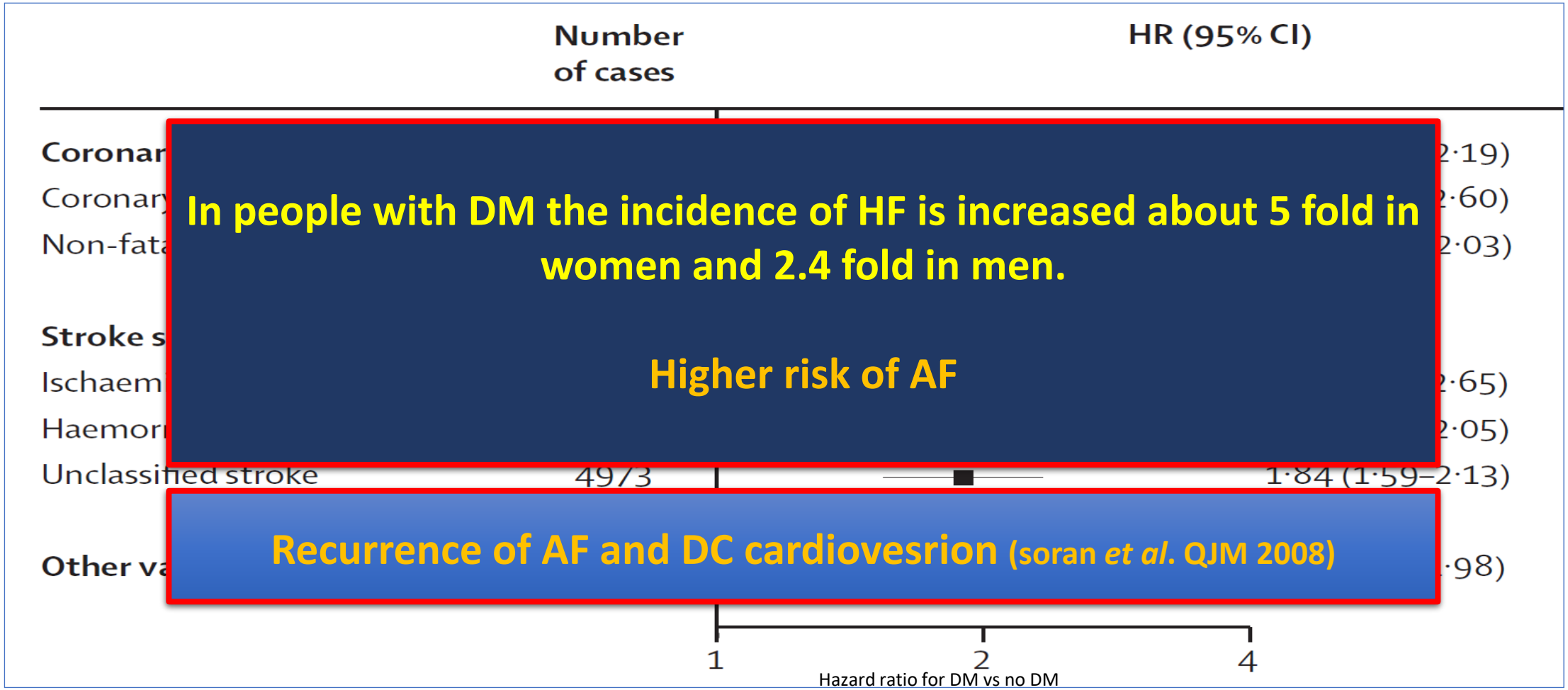


*Includes both fatal and non-fatal events

Emerging Risk Factors Collaboration, et al. Lancet 2010;375:2215–2222.

CI, confidence interval; DM, diabetes mellitus; HR, hazard ratio

Diabetes doubles the risk of having vascular events



In people with DM the incidence of HF is increased about 5 fold in women and 2.4 fold in men.

Higher risk of AF

Recurrence of AF and DC cardiovesrion (soran *et al*. QJM 2008)

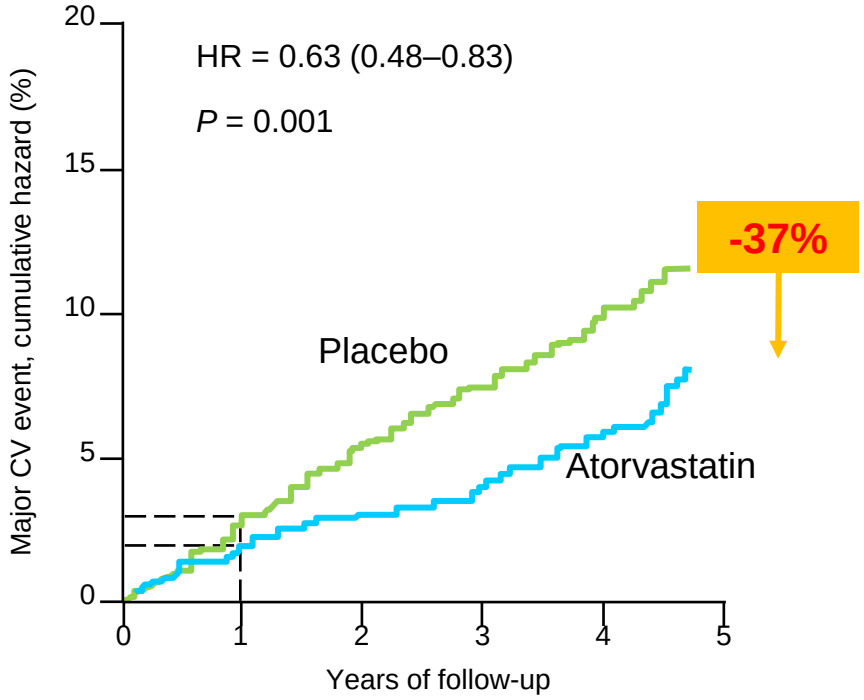
*Includes both fatal and non-fatal events

Emerging Risk Factors Collaboration, et al. Lancet 2010;375:2215–2222.

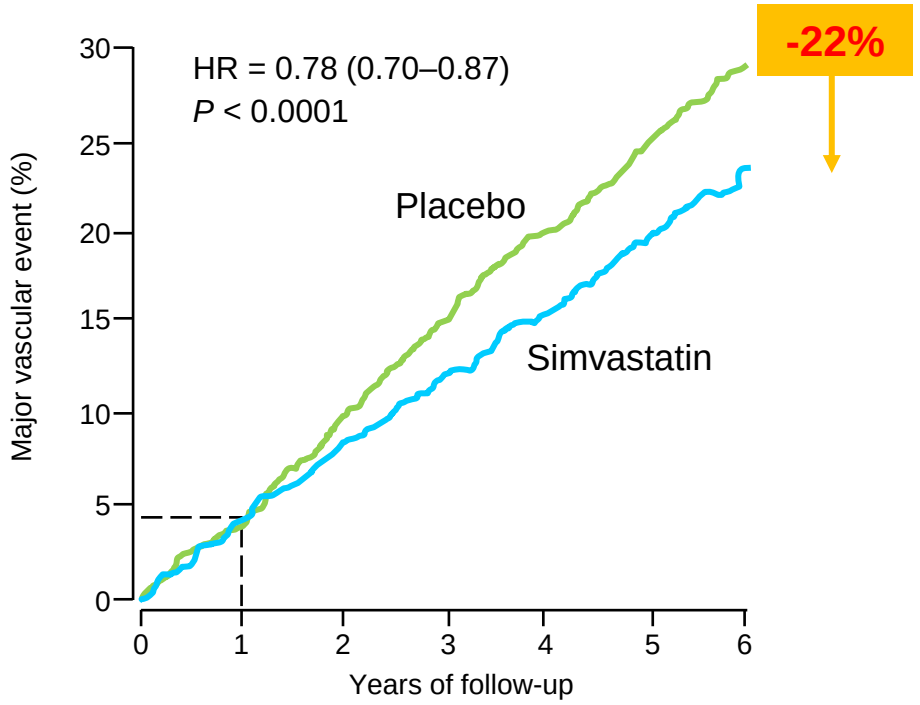
CI, confidence interval; DM, diabetes mellitus; HR, hazard ratio

Statin therapy reduces CV risk by 22–37% in diabetics when LDL-C is reduced by ~1 mmol/

CARDS[1]
LDL-C reduction from 3.04 = 0.9 mmol/L



HPS Diabetics[2]
LDL-C reduction from 3.2 mmol/L = 0.9 mmol/L

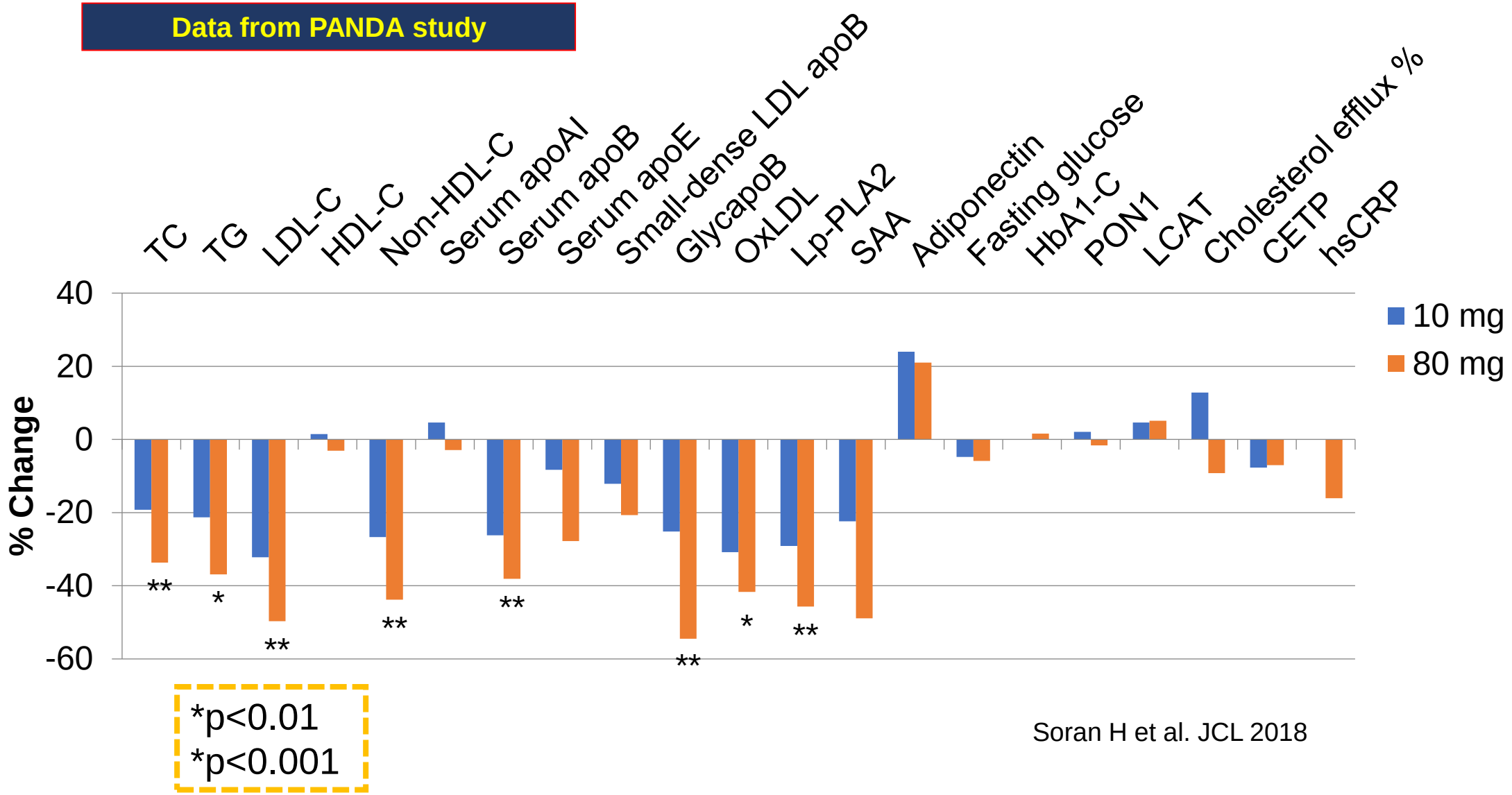


CV, cardiovascular; HR, hazard ratio; LDL-C, low-density lipoprotein cholesterol.

1. Colhoun HM et al. Lancet 2004;364:685–96.
2. HPS Collaborative Group. Lancet 2003;361:2005–16.

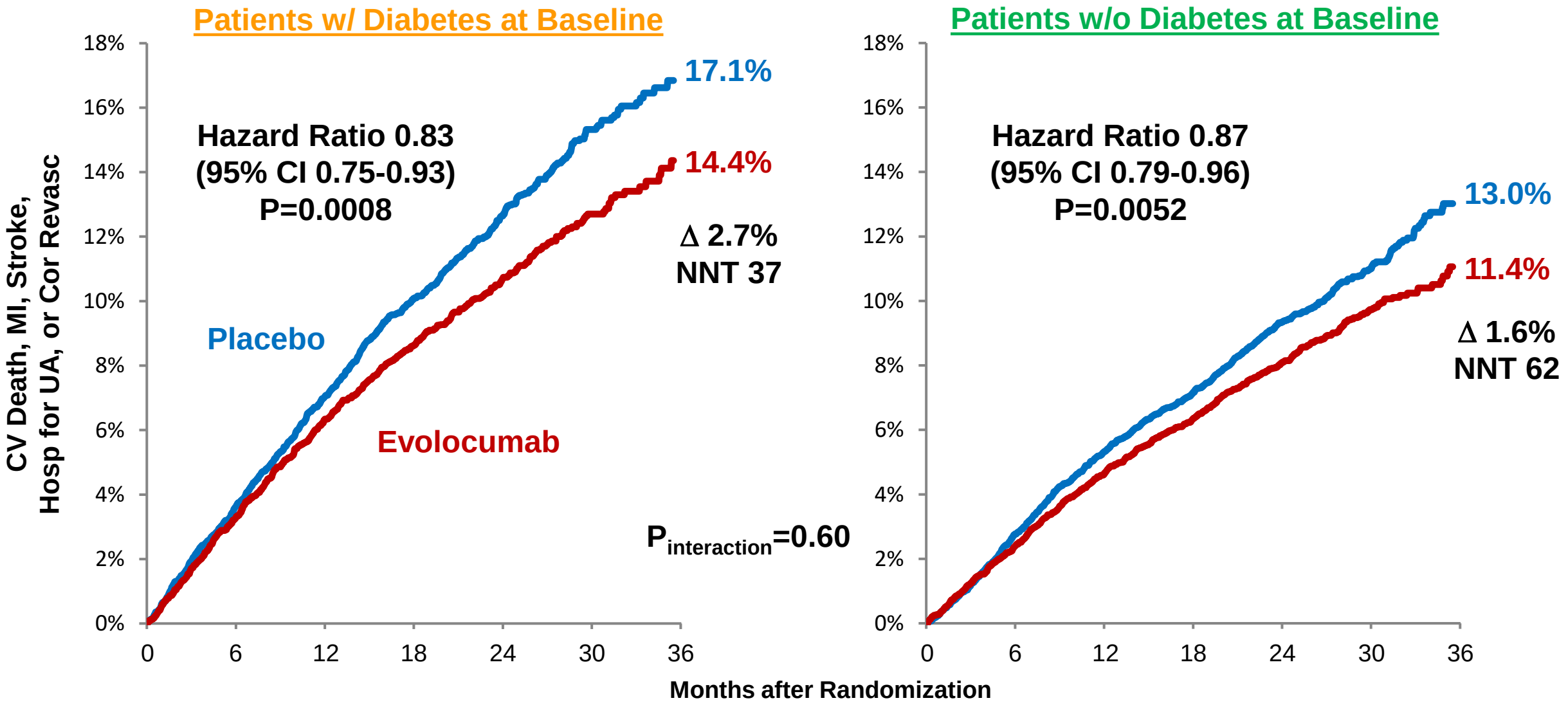
Atorvastatin 10mg daily compared to 80mg daily on glycated and oxidised LDL

Data from PANDA study



Soran H et al. JCL 2018

Effect of Evolocumab on Primary Endpoint



Development of diabetes
Statin trials

Meta-analysis of 13 RCT's

91,140 participants Mean duration 4years

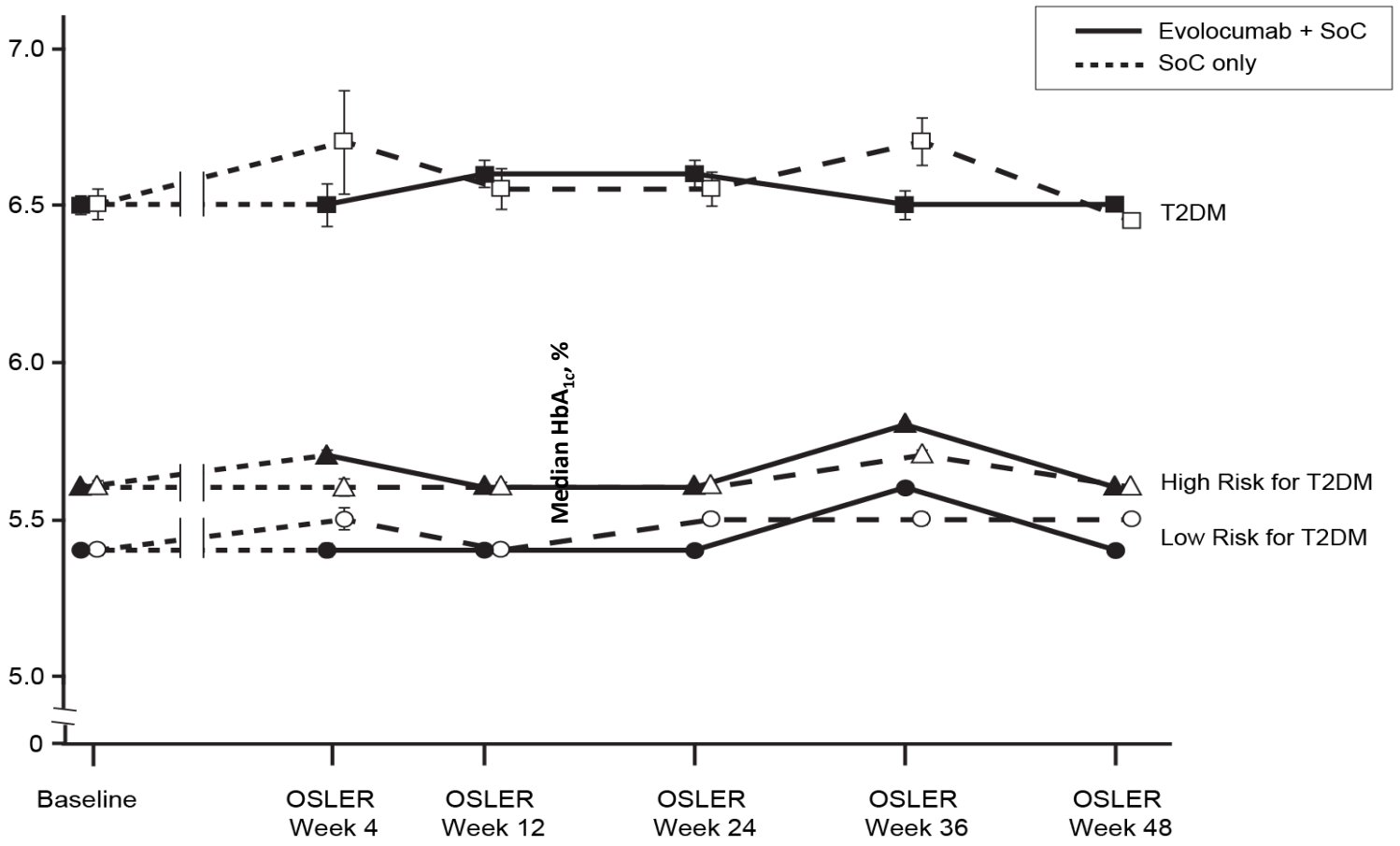
9%(CI 2-17%) increase in incident diabetes

Treating 255 non-diabetics for 4 years causes 1 extra case of diabetes

Dose-related

Sattar et al Lancet 2010; 375: 735-42

Preiss and Sattar Curr Opin Lipidol 2011



*48 weeks of open-label treatment
Error bars represent SE of the median
HbA_{1c}, glycated haemoglobin; SoC, standard of care; T2DM, type 2 diabetes mellitus

The American Journal of Cardiology

American Journal Cardiology 2017

Effect of the Proprotein Convertase Subtilisin/Kexin Type 9 Inhibitor Evolocumab on Glycemia, Body Weight, and New-Onset Diabetes Mellitus

Sattar N, Toth PP, Blom DJ, Koren MJ, Soran H, Uhart M, Elliott M, Cyrille M, Somaratne R, Preiss D.

REDUCE-IT
Vascepa (Icosapent ethyl, a highly purified eicosapentaenoic acid ethyl ester)

- REDUCE-IT Is First Outcomes Study to Assess Treatment of Patients with LDL-C Controlled by Statin Therapy, Persistent Elevated Triglycerides and Other Cardiovascular Risk Factors
- Results Specific to Pure EPA Vascepa at 4 Grams Daily
  - established cardiovascular disease (secondary prevention cohort) or

Efficacy:
Approximately **25%** relative risk reduction, demonstrated to a high degree of statistical significance ($p<0.001$), in the primary endpoint composite of the first occurrence of MACE, including cardiovascular death, nonfatal myocardial infarction (MI), nonfatal stroke, coronary revascularization, or unstable angina requiring hospitalization. This result was supported by robust demonstrations of efficacy across multiple secondary endpoints.
Median follow up 4.9 years

- Fibrates increase the concentration of HDL-c by 2% to 18%.
- They also can decrease plasma triglyceride by up to 50% but less effective in chylomicronaemia.

- The results of cardiovascular clinical outcome trials with fibrates have been mixed:
  - 2 achieved a significant reduction in their primary outcome
  - 3 did not.

ACCORD

Action to Control Cardiovascular Risk in Diabetes

ACCORD Lipid (Fenofibrate)

A non-significant 8% reduction in the primary endpoints

Subgroup with high TG and low HDL-C benefited but this was not related to increase in HDL-C

Microvascular disease

	Fenofibrate vs **Placebo**
	% difference
Triglycerides	-15
LDL cholesterol	-1
HDL cholesterol	+2
CVD events	-8 (NS)
CVD events in 941 in lowest HDL and highest triglyceride tertiles	**-29**

ACCORD Study Group. N Engl J Med 2010

Elam et al. JAMA 2017

Main Fibrate Randomised Controlled Trials

	HSS	VA-HIT	BIP	FIELD	ACCORD
Study duration (years)	5.0	5.1	6.2	5.0	4.7
No of cohort	4081	2531	3090	9795	5518
No of cohort high TG	1046	788	459	2517	1822
Baseline TG mmol/L All	1.99	1.82	1.64	1.74	1.83
High TG	≥2.31	>2.03	>2.26	≥2.31	>2.31
Baseline TG mg/dL All	176	161	145	154	162
High TG	≥204	>180	≥200	≥204	≥ 204
RRR in All cohort (%)	-34	-22	-9.4	-11	-8
RRR in High TG (%)	-56	-30	-43	-22	-13

Frick MH et al NEJM 1987; Manninen V et al Circulation 1992; Robins SJ, et al. JAMA 2001;285:1585–1591; BIP study, Circulation 2000; Tenenbaum A et al, Arch Int Med 2005; KeechA et al, Lancet 2005; Scott R et al, Diabetes Care 2009; Group AS et al, NEJM 2010; Ginsberg HN et al, Diabetes Care 2012.

Main Fibrate Randomised Controlled Trials

Pooled Relative Risk Reduction by Baseline		
	RRR (%)	95% CI
Triglycerides more than 2.26 mmol/L (200 mg/dL)	25	14-45
HDL cholesterol <1.04 mmol/L (40 mg/dL)	16	9-23
Triglycerides more than 2.26 mmol/L (200 mg/dL) & HDL cholesterol <1.04 mmol/L (40 mg/dL)	29	18-38

Frick MH et al NEJM 1987; Manninen V et al Circulation 1992; Robins SJ, et al. JAMA 2001;285:1585–1591; BIP study, Circulation 2000; Tenenbaum A et al, Arch Int Med 2005; KeechA et al, Lancet 2005; Scott R et al, Diabetes Care 2009; Group AS et al, NEJM 2010; Ginsberg HN et al, Diabetes Care 2012.

Conclusions

- LDL cholesterol is a strong risk factor for CVD
- Lowering LDL cholesterol by 1 mmol/l (37.8 mg/l) is associated with 22% reduction is CVD risk.
  - No limit below which further reducing LDL-C ceases to be beneficial
  - The lower the LDL-C is better
- Ezetimibe and Clesevelam
- PCSK9 monoclonal antibodies
  - NNT is lower in diabetics compared with non-diabetics
  - No increase in risk of T2DM or deterioration of glycaemia in diabetics
- Fibrates can be used in patients with features of metabolic syndrome
  - Never combine Gemfibrozil with statins
  - Other fibrates can be combined with statin therapy
  - Patients with high TG and low HDL-C benefit most
  - Fenofibrate and DR

Tackling Cholesterol Together

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HEART UK THE CHOLESTEROL CHARITY

NHS

04

Weight Management

Dr Matthew S Capehorn

GPwSI Obesity & Bariatric Physician

Clinical Manager – Rotherham Institute for Obesity

Medical Director – LighterLife

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Love it in RIO

ROTHERHAM RIO INSTITUTE for OBESITY

Disclosures:

Dr Matthew S Capehorn

- **Unpaid:**
  - Faculty member of the Primary care Academy of Diabetes Specialists (PCADS)
  - Expert Advisor to NICE
  - Professional Advisor to the Obesity Empowerment Network (OEN)

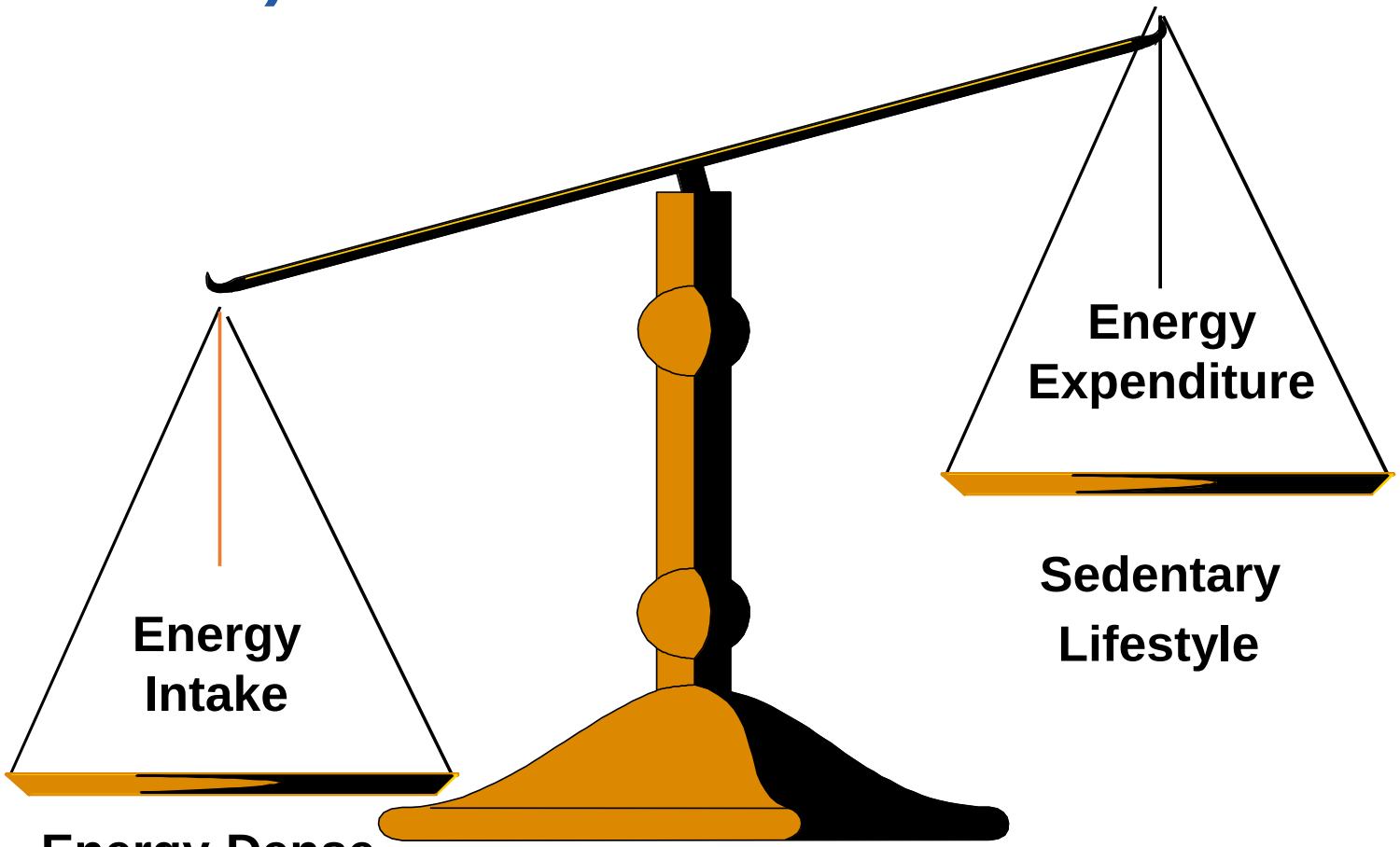
- **Paid:**
  - Director – RIO Weight management Limited
  - Medical Director – Lighterlife (commercial VLCD company)
  - Ad-hoc Medical Advisor – McDonalds UK

- **Advisory work:**
  - Novo Nordisk, BI/Lilly Alliance, Janssen, MSD, Abbott

- **Speaker fees/travel:**
  - BI/Lilly Alliance, Novo Nordisk, Janssen

- **Research income (RIO):**
  - BI/Lilly Alliance, Novo Nordisk, Novartis, GSK, Abbott, Leo, Syneous

Etiology of Obesity (traditional view)



Epigenetic factors

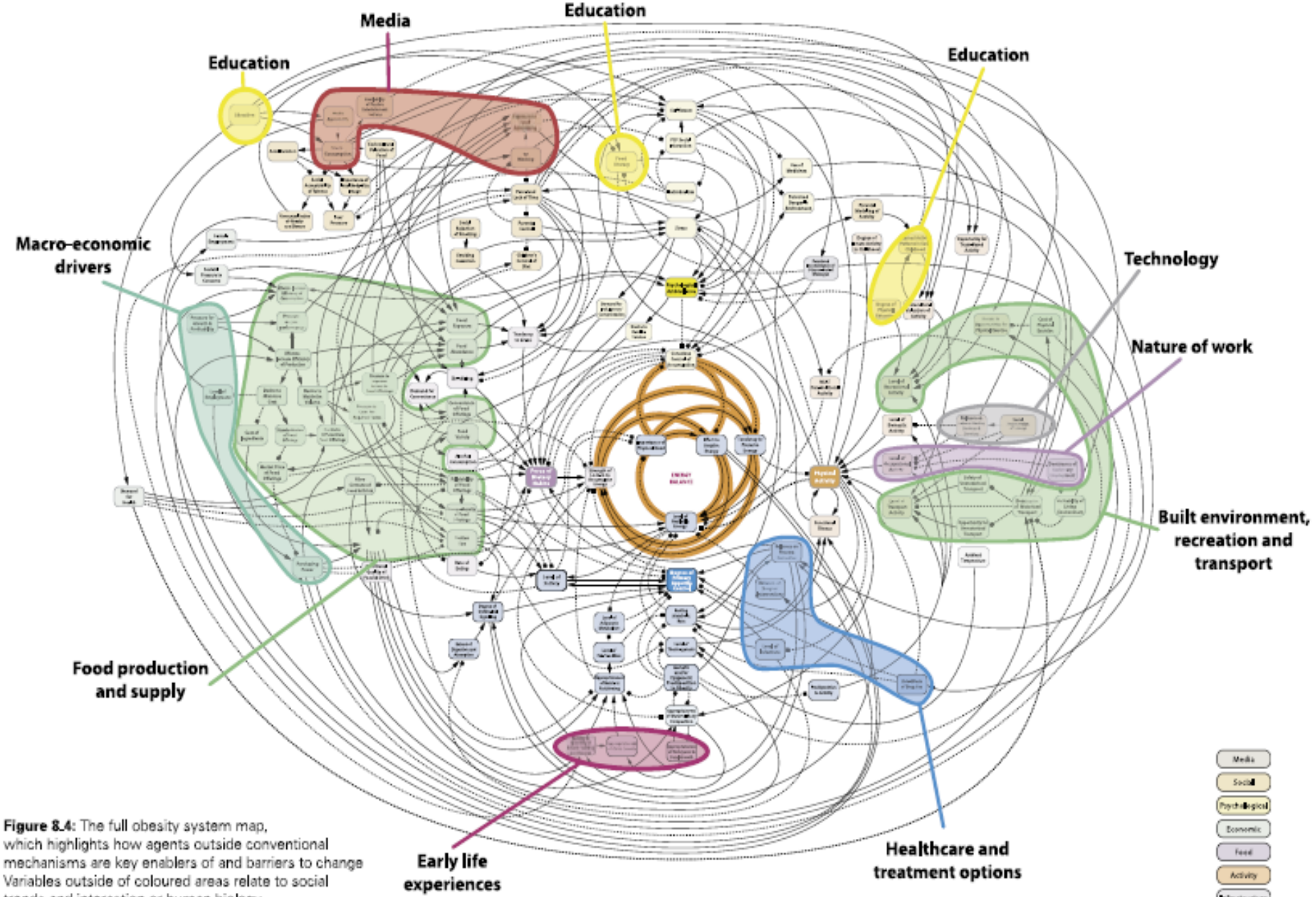


Figure 8.4: The full obesity system map, which highlights how agents outside conventional mechanisms are key enablers of and barriers to change Variables outside of coloured areas relate to social trends and interaction or human biology. Variables are represented by boxes, positive causal relationships are represented by solid arrows and negative relationships by dotted lines. The central engine is highlighted in orange at the centre of the map.

Foresight. Tackling Obesities: Future Choices. Gov.UK. 2007

How can we solve a problem like obesity?

1) Tackle all 100+ causes

Nanny state or “nudge”

Increase physical activity

Decrease food consumption

Food tax/subsidy

Etc

Where is the evidence that we can “prevent” obesity?

2) Treat the overweight/obese

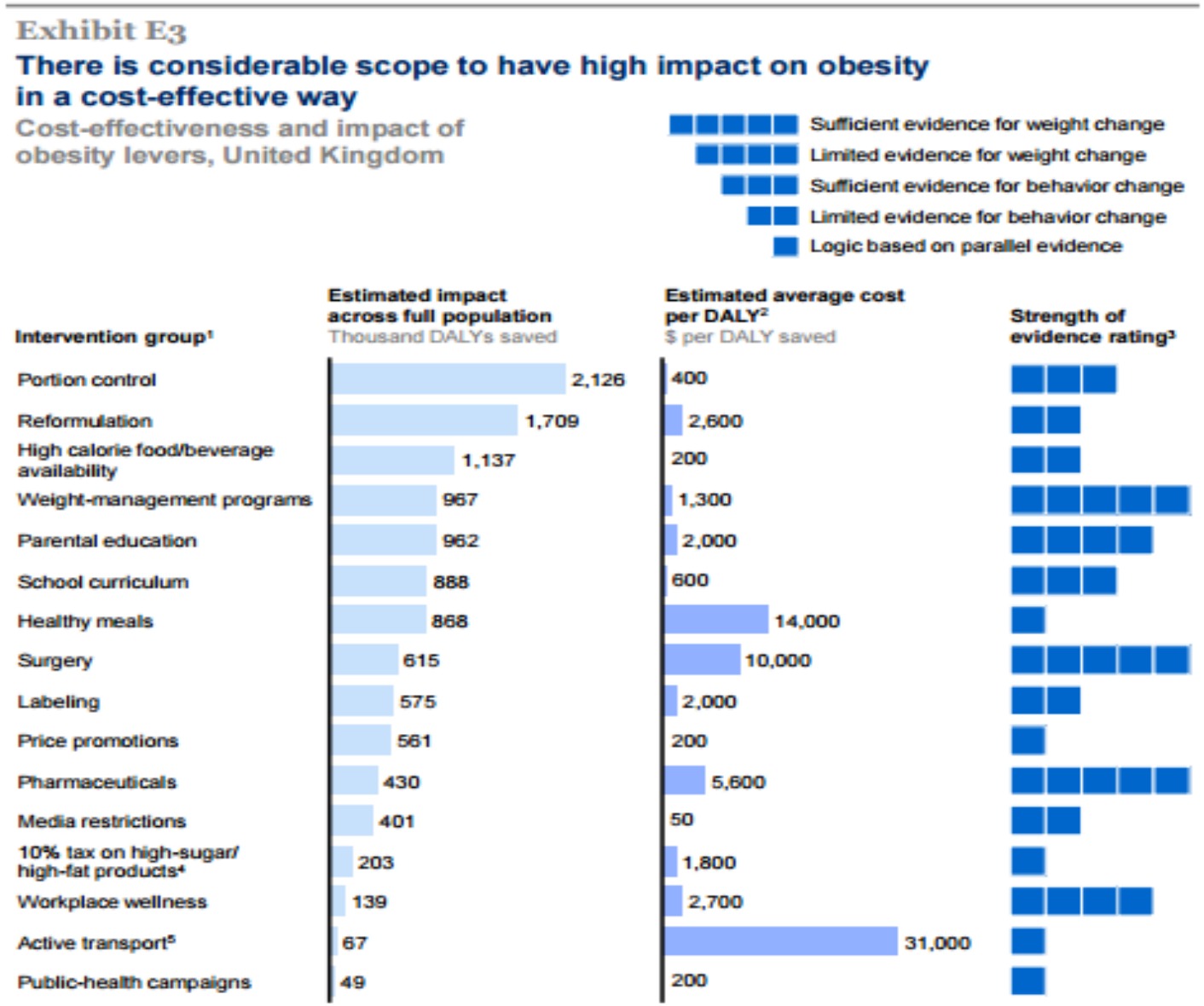
“Treating” the overweight “prevents” more obesity etc

NICE Recommends (for adults):

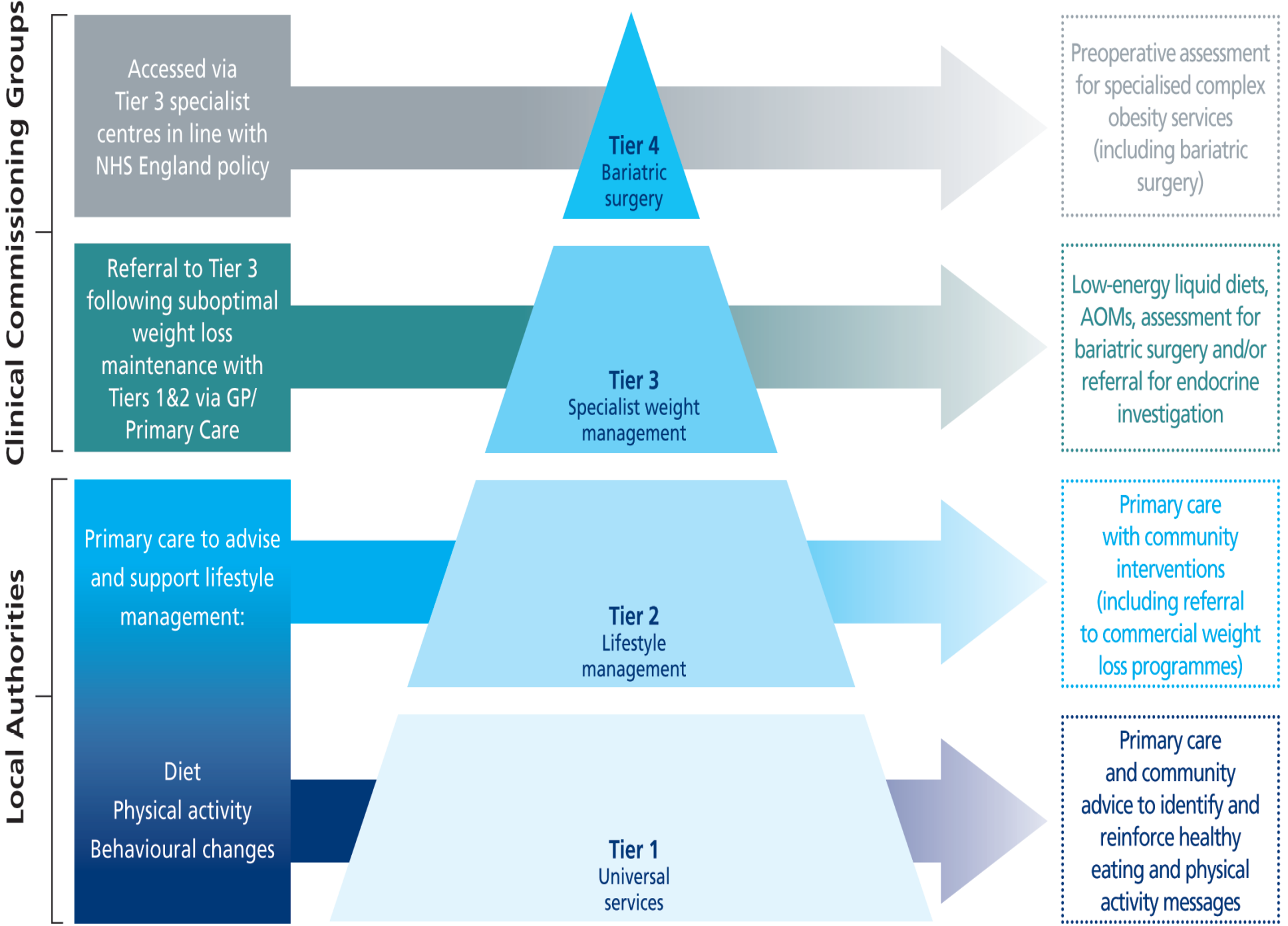
- Diet
- Exercise
- Behavioural therapy
- Drug treatment
- Surgery (if BMI >40, or >35 with co-morbidities)

NICE Clinical Guideline 43; Treating people who are overweight or obese. Dec 1996

Where should we focus our attentions?



Tackling Cholesterol Together



Taken from: Wilding J. Beyond lifestyle interventions. Clin Ob. May 2018

Facilities and staff at RIO:

Job Description	Role
Health Trainers	Brief Interventions and Motivational Interviewing. Goal setting and Life-coaching
Healthcare Assistant	Weighing & Measuring. Follow-up care. VLCD monitoring OSA screening
Obesity Specialist Nurse	Initial triage. Basic nutrition and advice. VLCD initiation OSA screening
Dietitian	Complex dietary needs including VLCD support. Pre-/post-op bariatric surgery
"Cook & Eat"	Basic nutrition and advice. Cooking skills (on-site kitchen facilities)
Exercise Therapists	Personal exercise programme (on-site gym). Education & motivation Liaison with other local physical activity events/sites
Talking Therapists	Life-coaching. Cognitive Behavioural Therapy (CBT) Neurolinguistic Programming (NLP) Emotional Freedom Techniques (EFT)
GPwSI	Pharmacotherapy. Pre-bariatric surgery and pre-residential Camp assessments. OSA referrals.
Admin Supervisor	Liaison with patients, referrers and other service providers. Allocation of appointments
Clinical Manager	Managing service and Clinical Governance.
Education Room/library	Resource room. Group work.
Bariatric surgery centre	Potential for Bariatric Intragastric Balloons (BIB) & endobarriers. Potential for overnight sleep studies
Other specialists	Eg, obstetric pre-conception care
RIO Market stall	Advice at the point of sale of fruit & veg Promotion of Healthy Weight Framework services.

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Lose it in RIO

- Cost-effective behaviour change

- Assessment by clinical nursing team is essential to provide the tailored individualised care needed for success with weight management
"one size does not fit all"
(ScHARR – April 2015)

- Targeted use of resources

- The wish of Simon Stevens, NHSE

- Does exercise have a role?
"You cannot outrun a bad diet"
(BJSM – April 2015)

- To address underlying psychological barriers to weight loss (and address findings in NCEPOD Report 2012)

- To take all the glory!

Weight loss reduces mortality

Weight loss of 10 kg produces a marked improvement in mortality

Mortality	Blood Pressure	Diabetes	Lipids
• > 20-25% fall in mortality • > 30-40% fall in diabetes-related deaths • > 40-50% fall in obesity-related cancer deaths	• Fall of approximately 10 mmHg SBP and DBP	• Fall of 50% in fasting glucose	• Fall of 10% in total cholesterol • Fall of 15% in LDL-C • Fall of 30% in triglycerides • Rise of 8% in HDL-C

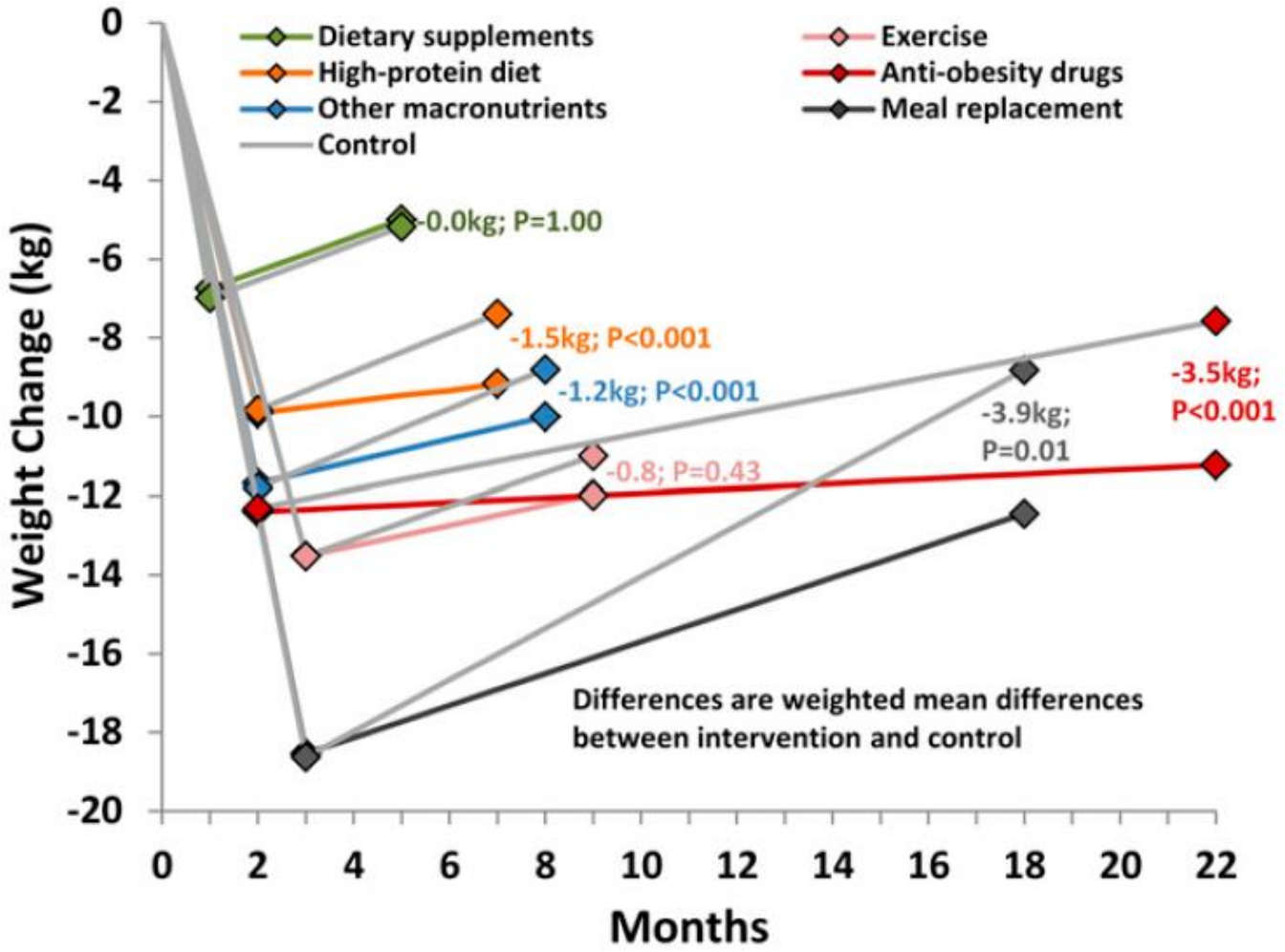
Betteridge DJ and Morrell JM. *Clinicians' Guide to Lipids and Coronary Heart Disease* Second edition Arnold, London 2003 p173 (based on Jung R. Obesity as a disease. *Br Med Bull* 1997; 53 (2): 307-321).

Treatment options:

- Tier 2 community weight loss interventions 5%
- Tier 3 specialist MDT 10%
  - Pharmacotherapy 5 - 15%
    - Orlistat
    - Mysimba (Naltrexone/Bupropion)
    - Saxenda (Liraglutide 3.0mg daily)
    - Wegovy (Semaglutide 2.4mg weekly)
  - VLCD/VLED 20%
- Tier 4 Bariatric Surgery 25% +

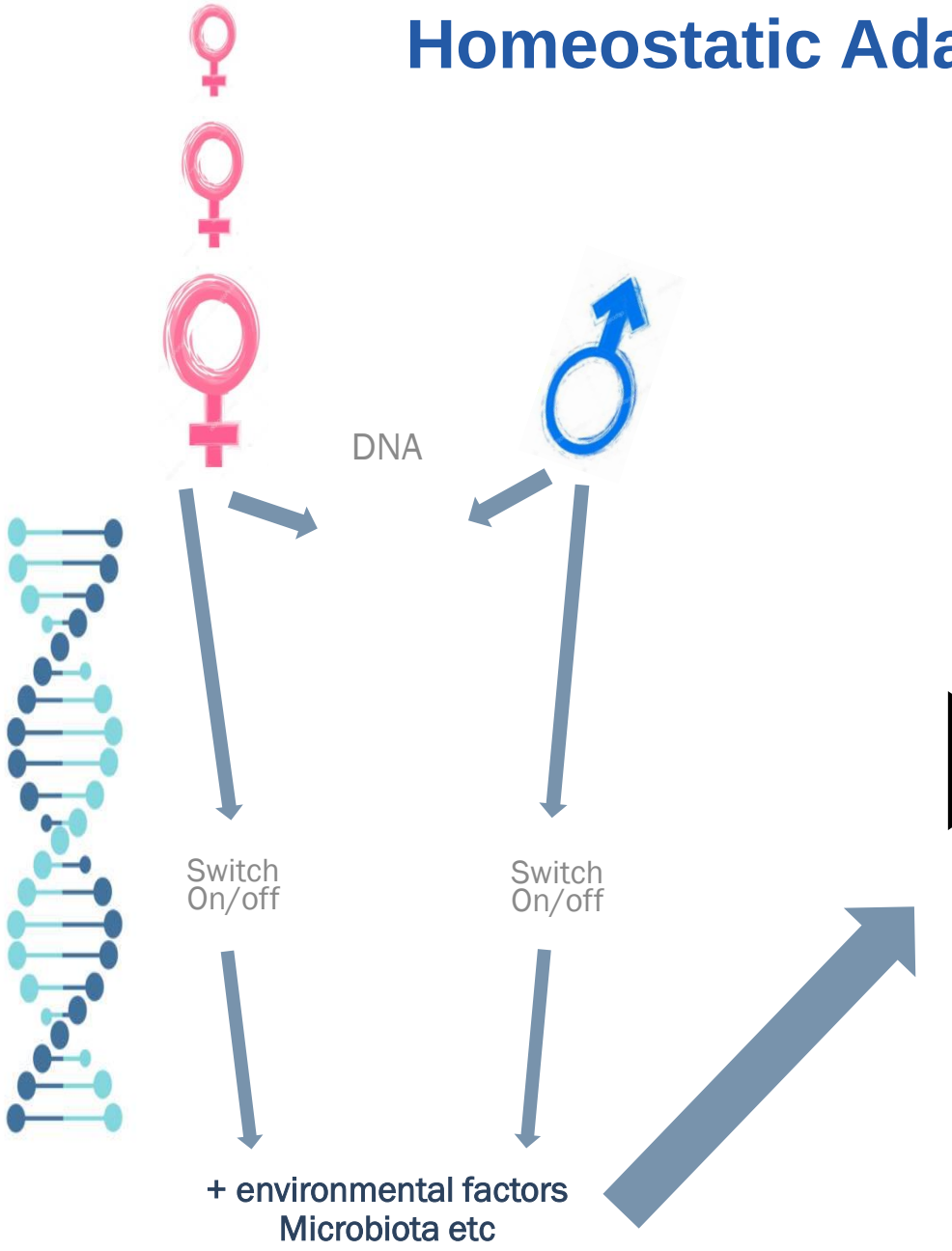
Weight Maintenance – Systematic Review

Johansson et al. (2014)



- Behavioural Therapy, medication, and longer reintroduction phase post intervention – helps maintenance (Mulholland et al. 2012)

Homeostatic Adaptation



Long-Term

ghrelin
PYY /
CCK
leptin
NEAT

Endocrine disrupters

- BPA
- Viruses
- Microbiota etc

Interventions

ghrelin
leptin
PYY /
CCK

- Pharmacotherapy
- VLCD's
- Bariatric surgery

Conclusion

- Metabolic syndrome is increasing. Treatments are both lifestyle and medical
- Lipids, Blood pressure, Diabetes and Obesity can be treated
- Lowering LDL cholesterol by 1 mmol/l (37.8 mg/l) is associated with 22% reduction is CVD risk.
- No limit below which further reducing LDL-C ceases to be beneficial . The lower the LDL-C is better
- New therapies are coming

05 Q&A

Next steps:

We are having a break from the webinar series whilst we form some exciting new partnerships. Keep an eye on the pages and your local AHSN comms. Meanwhile, visit the site for the new e-Learning modules on diet launching in Spring. Identifying FH in primary care, Statin Intolerance, and the Lipid Management Pathway modules AND a new series of 5 short videos on key themes for lipid management are also available. An interactive version of the Summary of National Guidance (national lipid pathway) will be available soon.

Keep an eye out on the TCT home pages on the HEART UK website for the informal case based interactive clinics, which will be re designed for real case based learning with attendees bringing the case for discussion.

All programme content, recordings and next webinar bookings will be housed in the HEART UK pages. Visit the site for the new e-Learning modules on Identifying FH in primary care, Statin Intolerance, and the Lipid Management Pathway

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Saving Lives.

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Thank you

This webinar has now finished.

Today's slides and recording will be available after the webinar on the HEART UK pages. Visit the site for the **new** e-Learning modules on diet launching in Spring. Identifying FH in primary care, Statin Intolerance, and the Lipid Management Pathway modules AND a new series of 5 short videos on key themes for lipid management are also available.

All programme content, recordings and next webinar bookings will be housed here: https://www.heartuk.org.uk/tackling-cholesterol-together/home