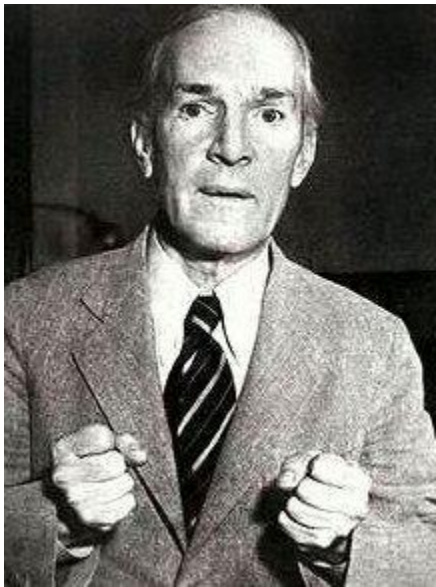
Interpréter un bilan de dyslipidémie et du bon usage des statines

il n'y a pas ou plus de définition quantitative des dyslipidémies…

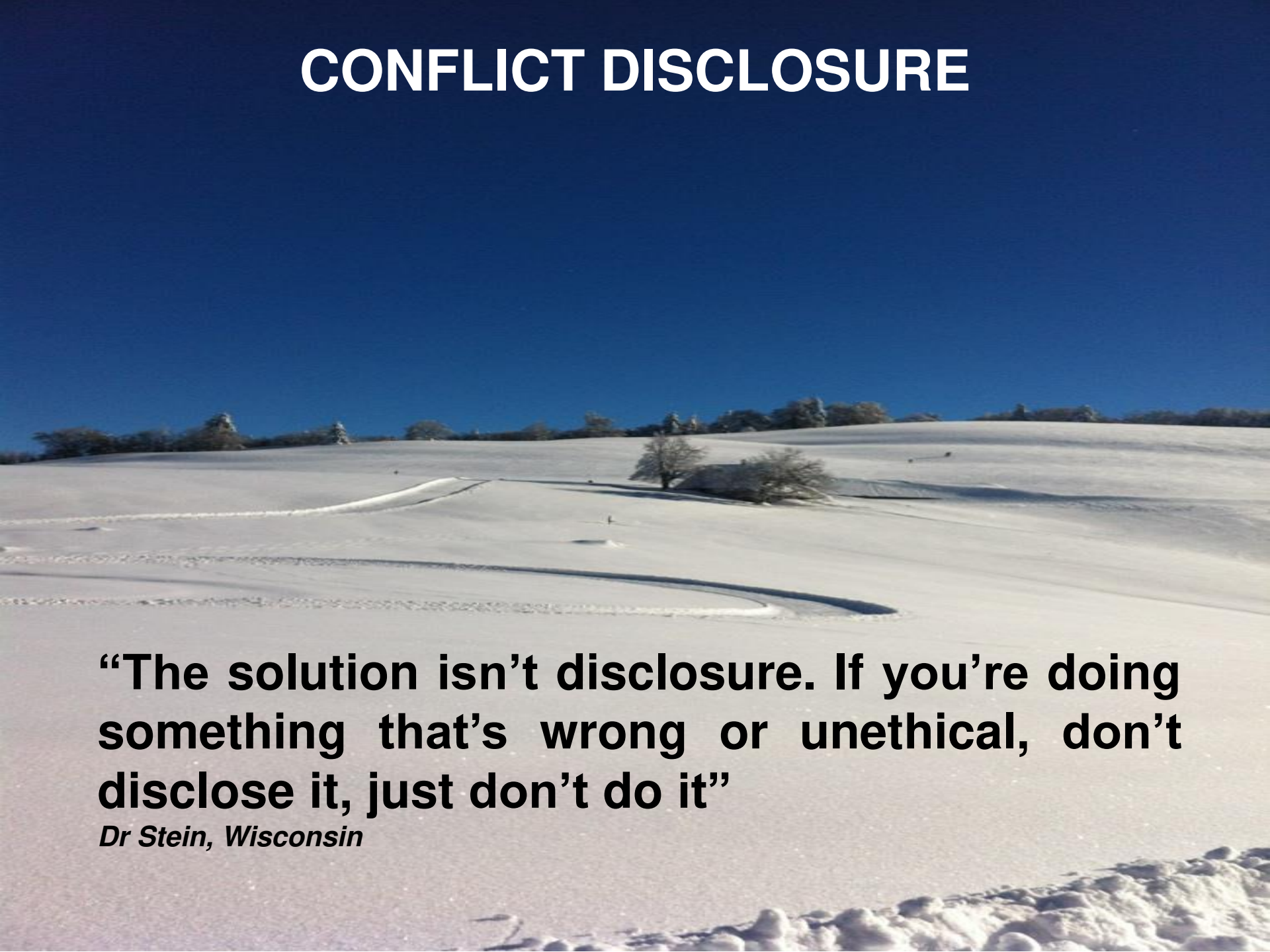
Docteur Pierre-Vladimir ENNEZAT

CHU Henri Mondor



“**It is difficult to get a man to understand something, when his salary depends on his not understanding it**.”
Upton Sinclair

CONFLICT DISCLOSURE



“The solution isn’t disclosure. If you’re doing something that’s wrong or unethical, don’t disclose it, just don’t do it”

Dr Stein, Wisconsin

4S

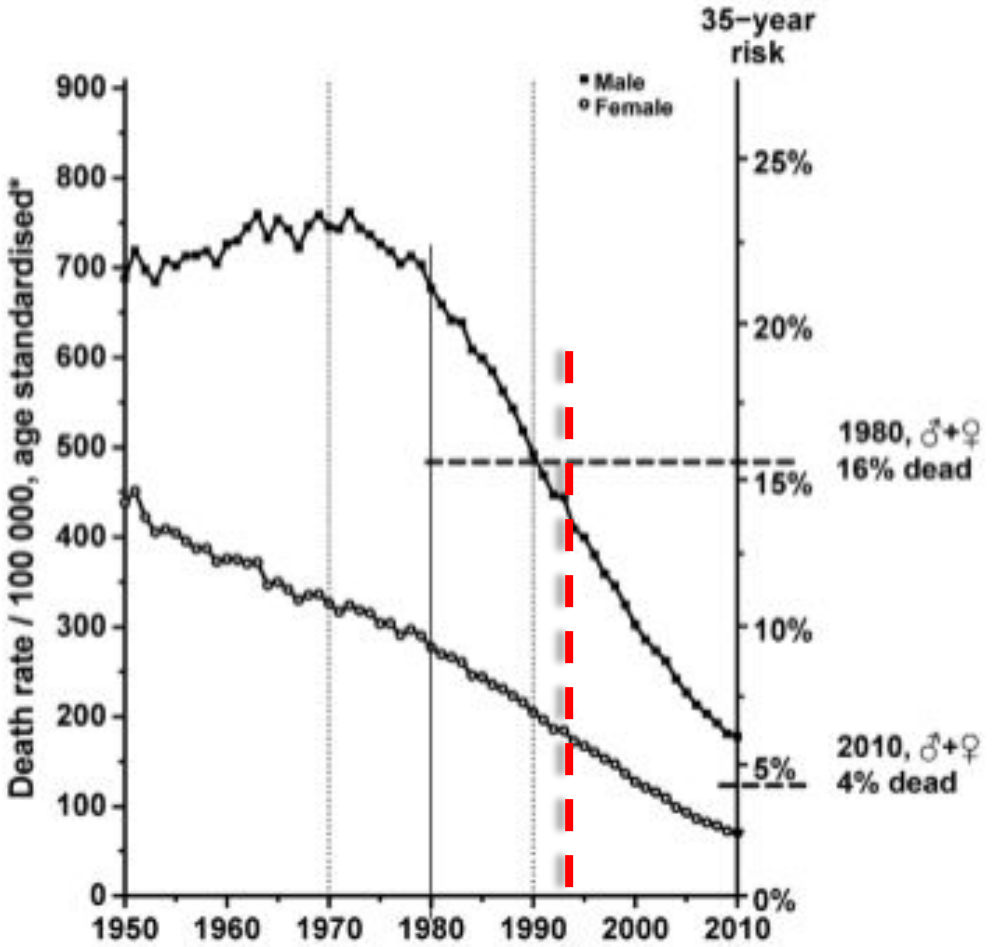
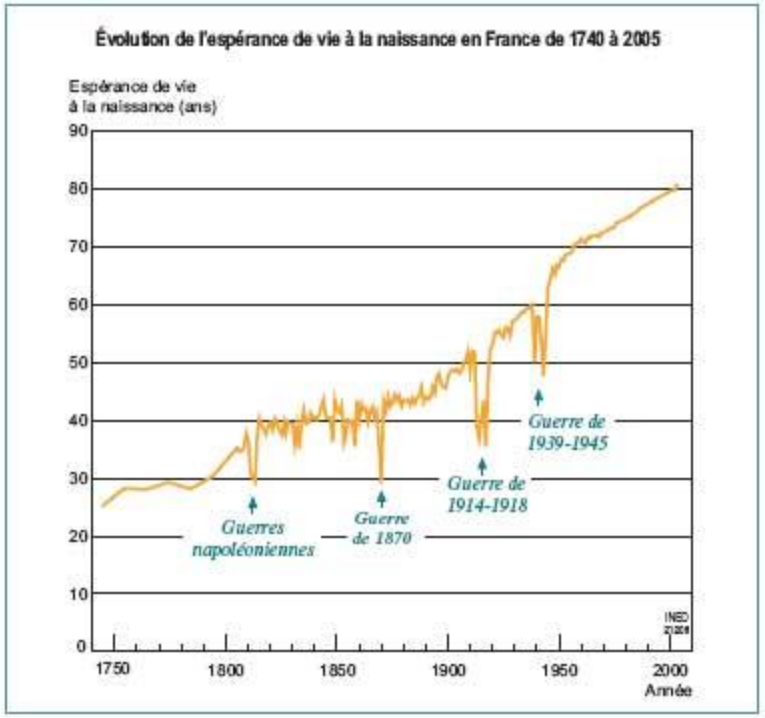
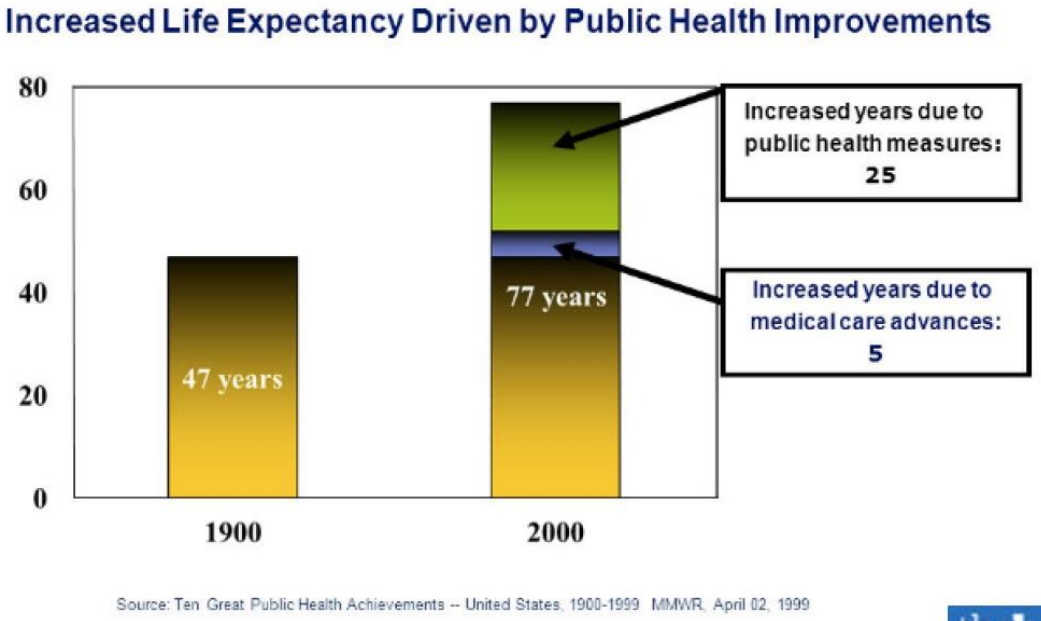


Figure 1. United Kingdom 1950 to 2010 vascular mortality rates at ages 35 to 69, by sex. Source: WHO mortality and UN population estimates. *Mean of annual rates in the 7 component 5-year age groups.

- Increased life expectancy we're all enjoying is considered to be much more due to public health than to modern medicine.
- Clean water, sanitation, nutrition, smoking cessation, seat belts, safer working conditions, all of those things have contributed to this rapid increase in life expectancy really over the last hundred years.



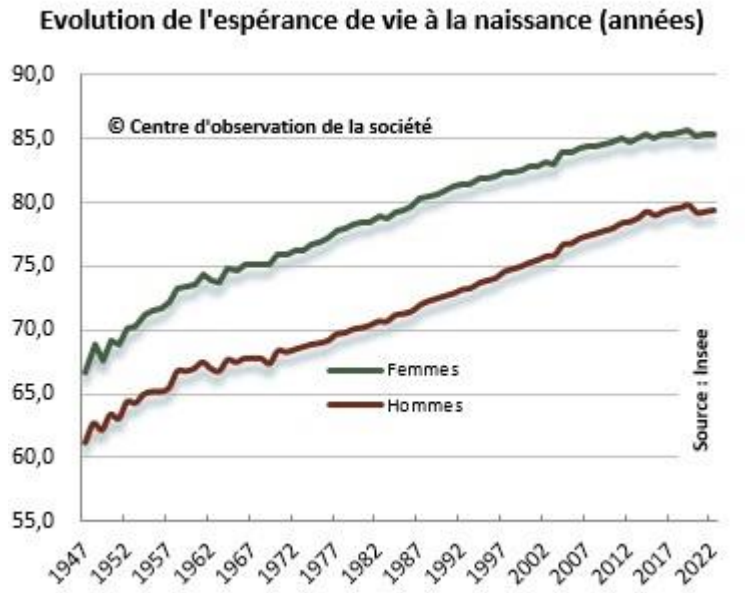


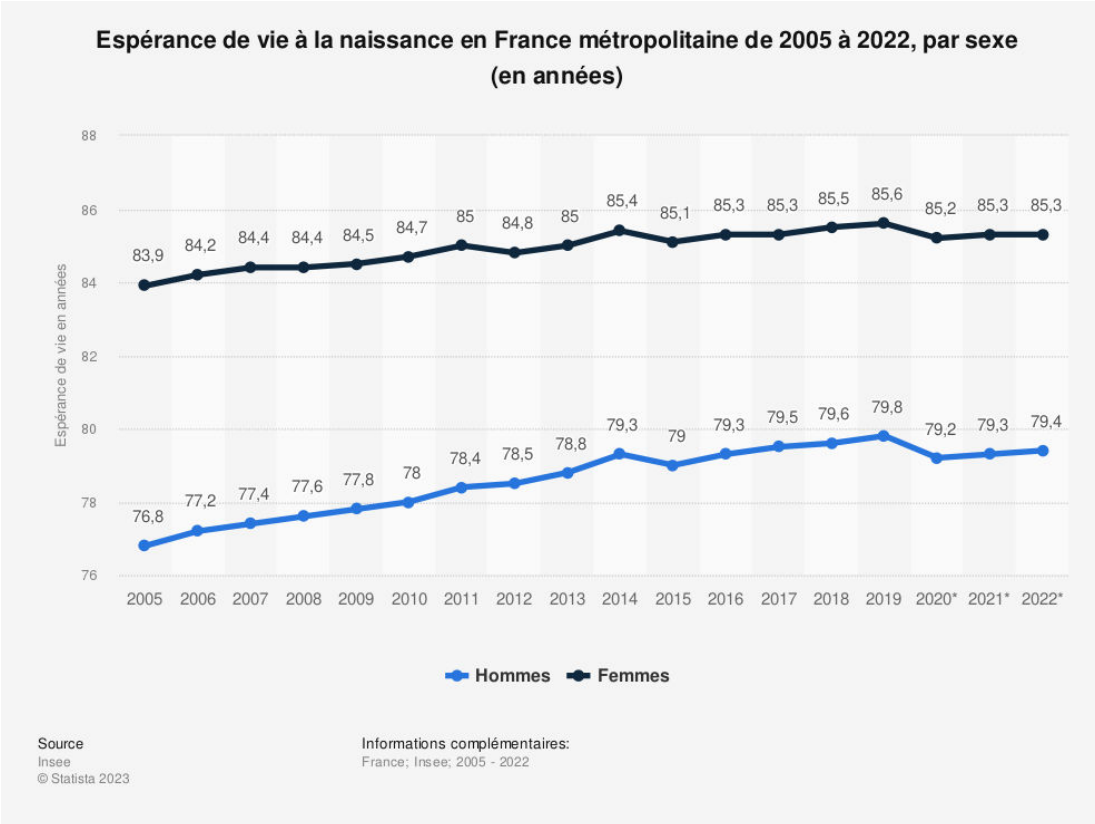
En France, les dépenses courantes de santé (DCS) représentaient:

- en 2000, 151 milliards € incluant 24 milliards pour le poste des médicaments
- en 2022, 313,6 milliards € soit 4 600 € par habitant (12% du PIB) dont 33 milliards pour les médicaments consommés en ville

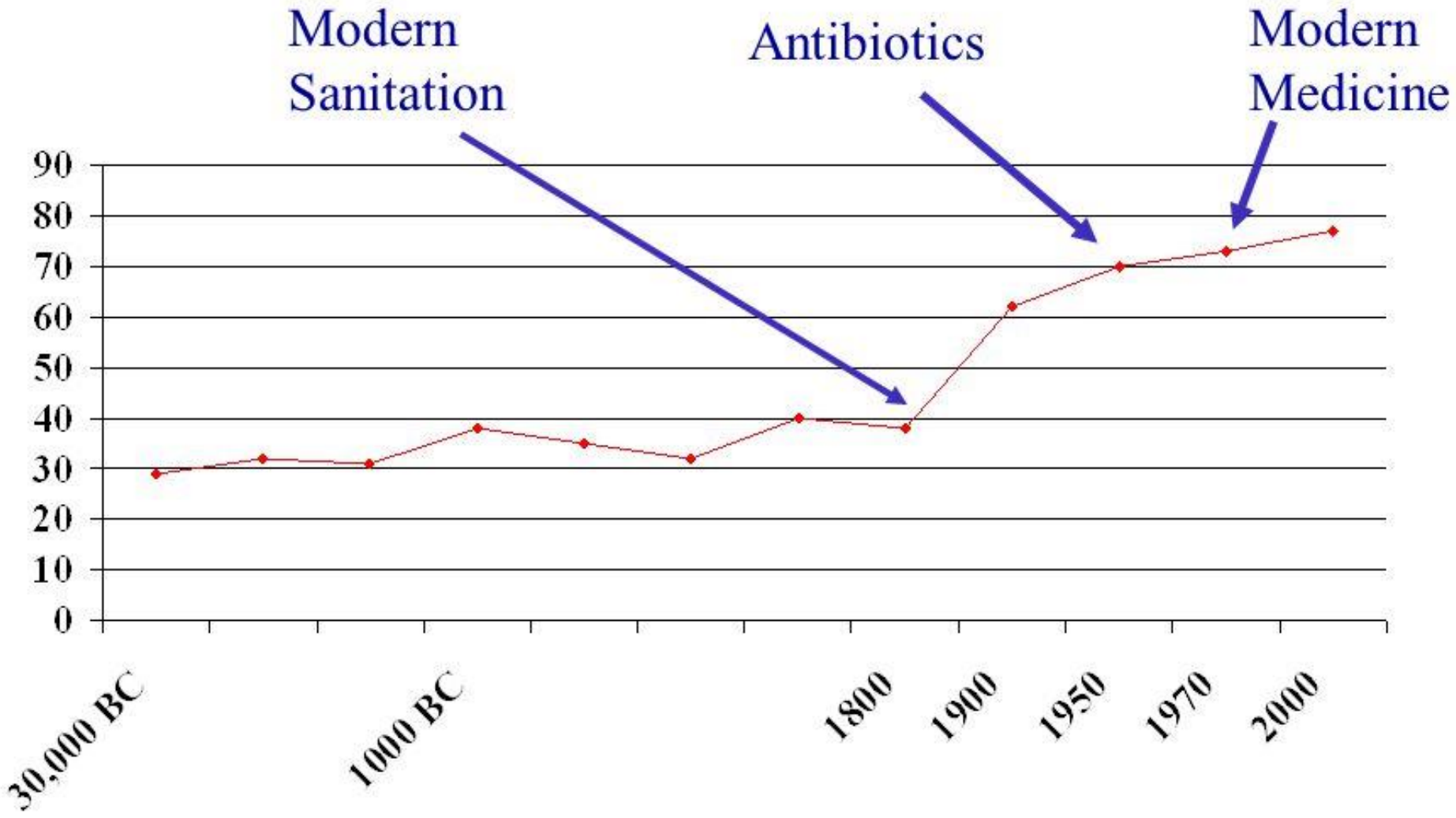
En proportion, l'espérance de vie n'a augmenté que de façon modeste (environ 1,04 milliards € dépensés par semaine de vie gagnée)

***USA**: $4.5 trillion (les dépenses de santé par personne aux États-Unis sont estimées à environ 13 493 dollars en 2022); 18% PIB*

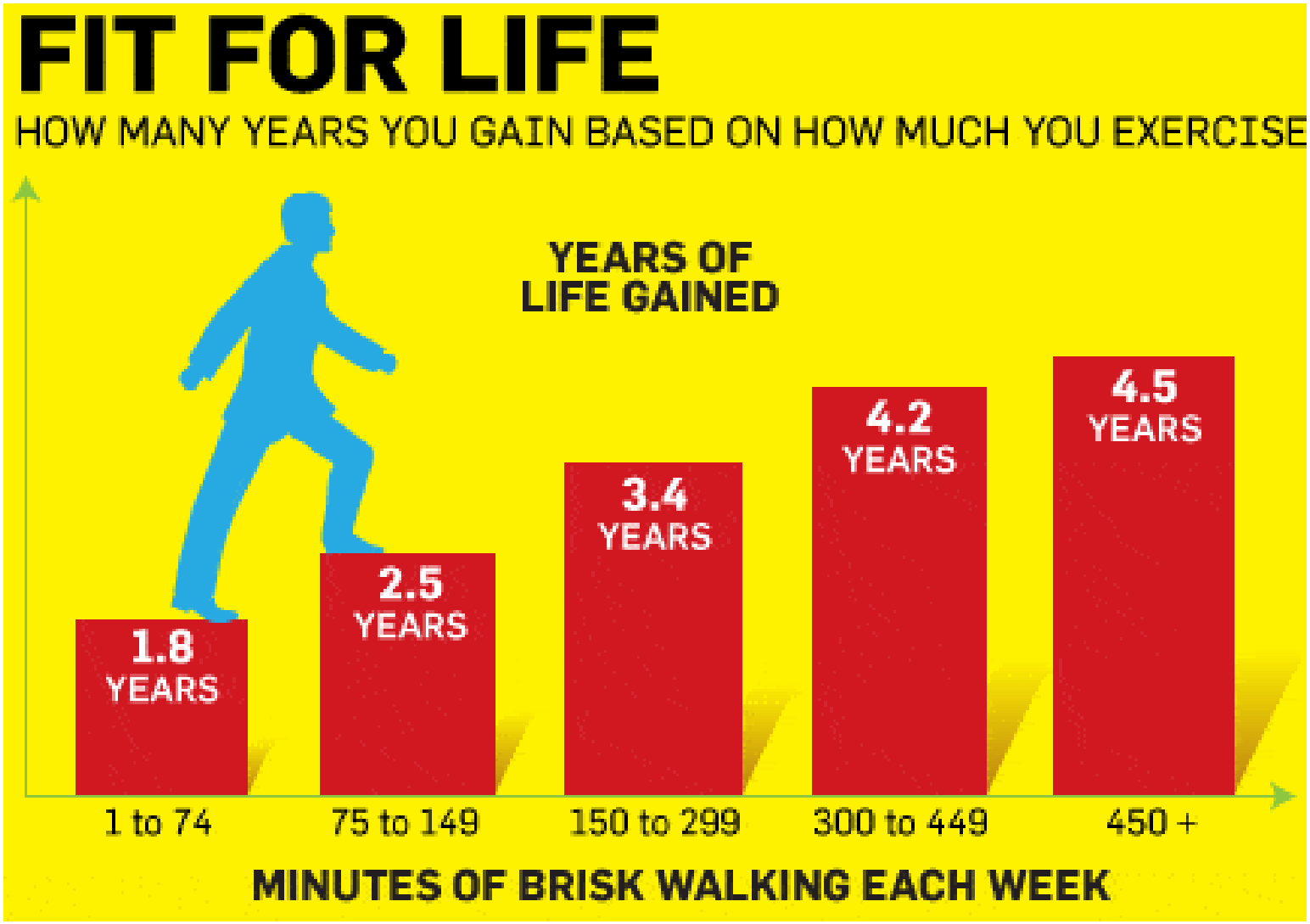




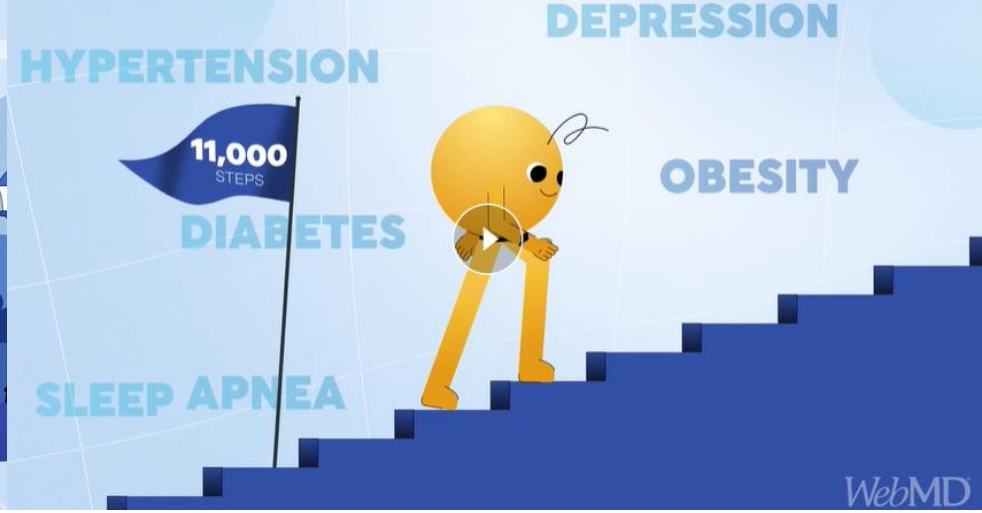
Median Life Expectancy in Years



Lifespan gain examples



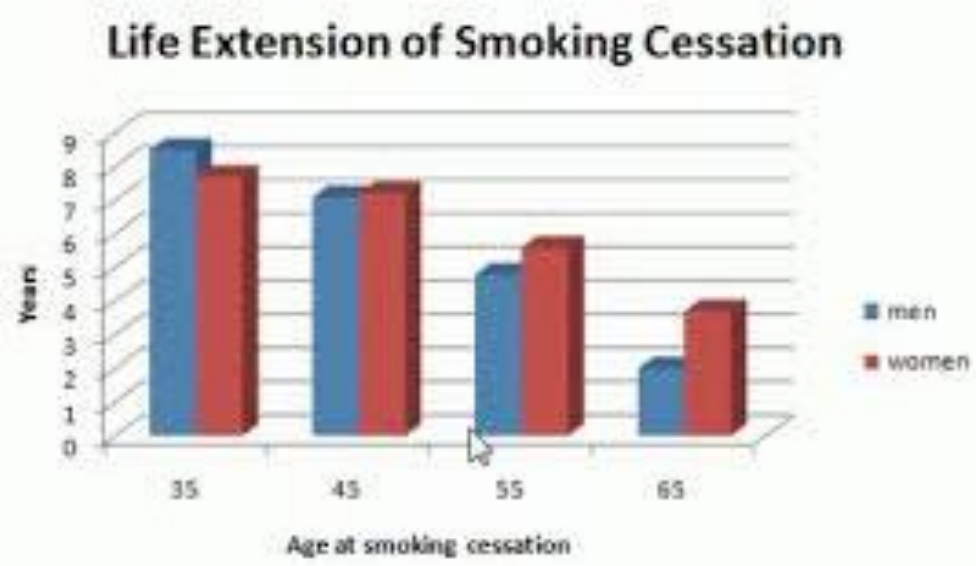
Plos medicine 2012

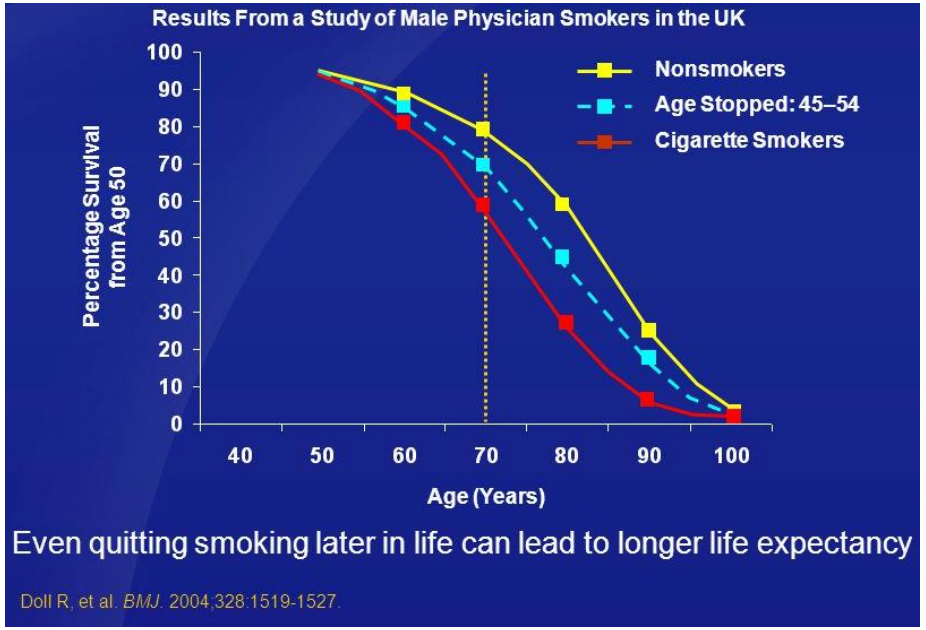


- At 10,500 steps, your risk of dying of cardiovascular disease may be 77% lower than it was at 2500 steps.
- At 11,000 steps, you've lowered your risk for hypertension, diabetes, depression, obesity, and sleep apnea by 25%-50% more than at 6000 steps.
- And at 11,500 steps, the risk for early death may be 67% lower than it was at 4000 steps.

Need Your Patients to Move More? Show Them This - Medscape - Jan 24, 2024.

Lifespan gain examples





If you want an official and simple Key messages regarding LDL-c….

« lower is better for every body, for every types of coronary syndromes… »

Roberts W “the statin drugs are to atherosclerosis what penicillin was to infectious disease.”

« Mass treatment of population with these wonder drugs which should be added to the water supply or put in table salt like iodine… »

Pr Fausto Pinto (ESC past-president):
« after antibiotics, statins have contributed more to prolonging life expectancy than any other type of medication »

Les personnes ayant des taux "normaux" de cholestérol peuvent tirer bénéfice de taux encore plus bas?

Le tiers de ce que nous mangeons suffirait à nous faire vivre

Les deux autres tiers servent à faire vivre les médecins.

Dr Paul

Le **cholestérol** est un constituant ubiquitaire des membranes cellulaires, des stéroïdes, des acides biliaires et des molécules de signalisation.
Les **triglycérides** stockent principalement de l'énergie dans les adipocytes et les cellules musculaires.
Les **lipoprotéines** sont des structures sphériques hydrophiles qui possèdent des protéines de surface (apoprotéines ou apolipoprotéines) qui sont des cofacteurs et des ligands des enzymes impliquées dans le métabolisme des lipides

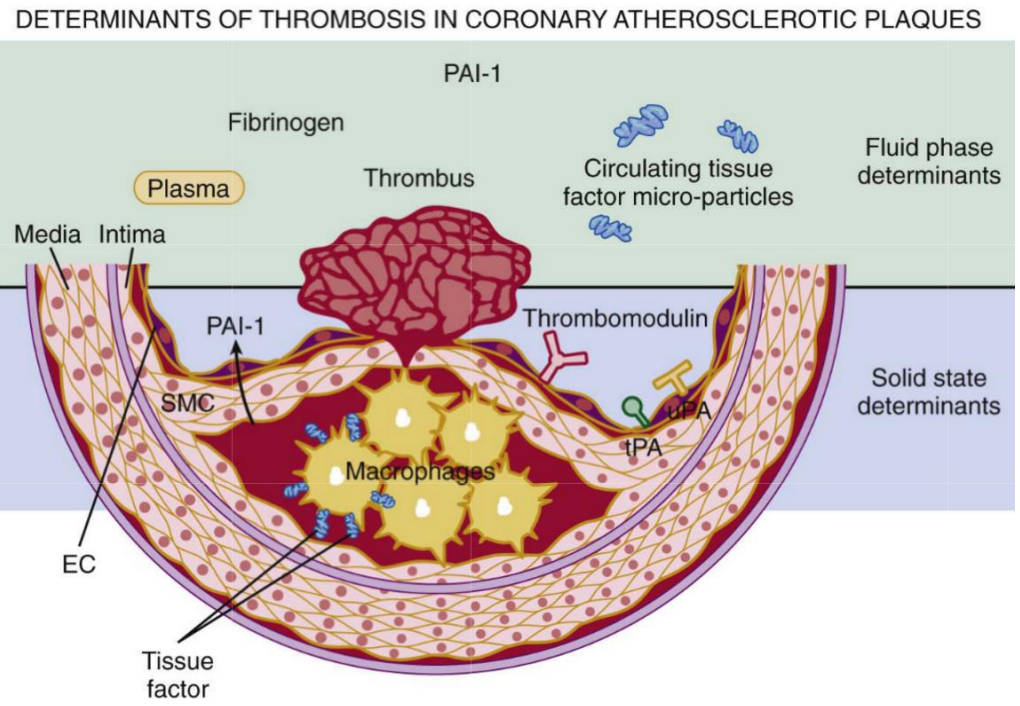
Plus de 95% des lipides alimentaires sont:

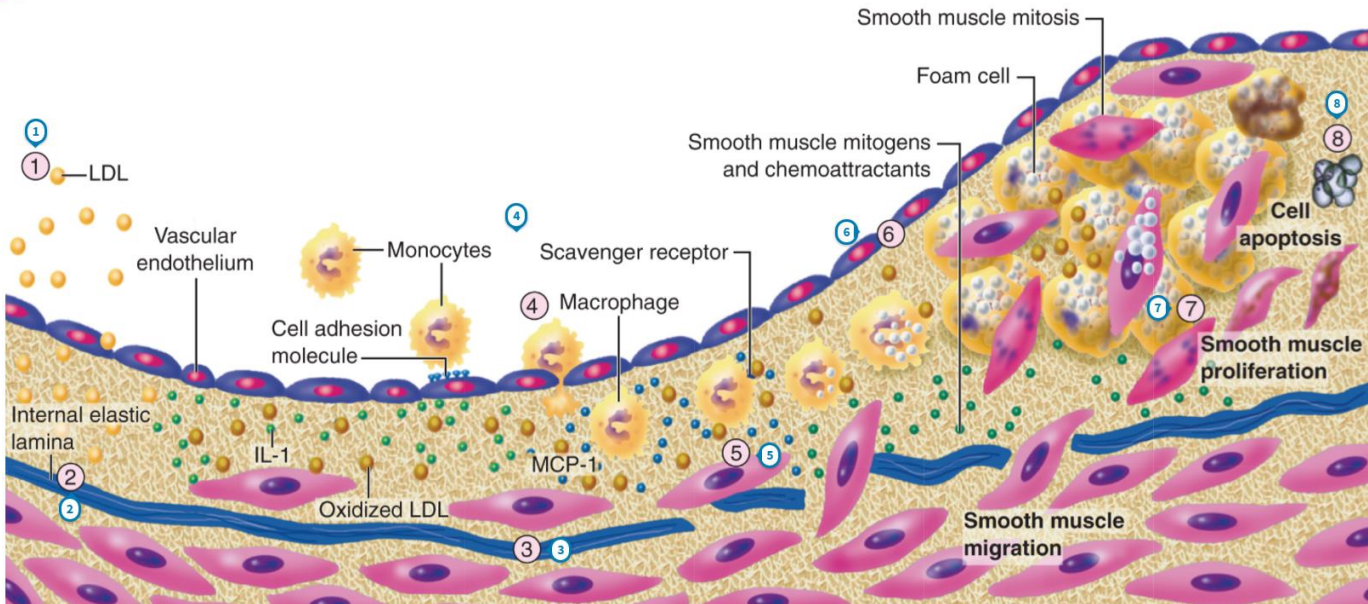
- Triglycérides (TG)

Le reste, environ 5% des lipides alimentaires, sont:

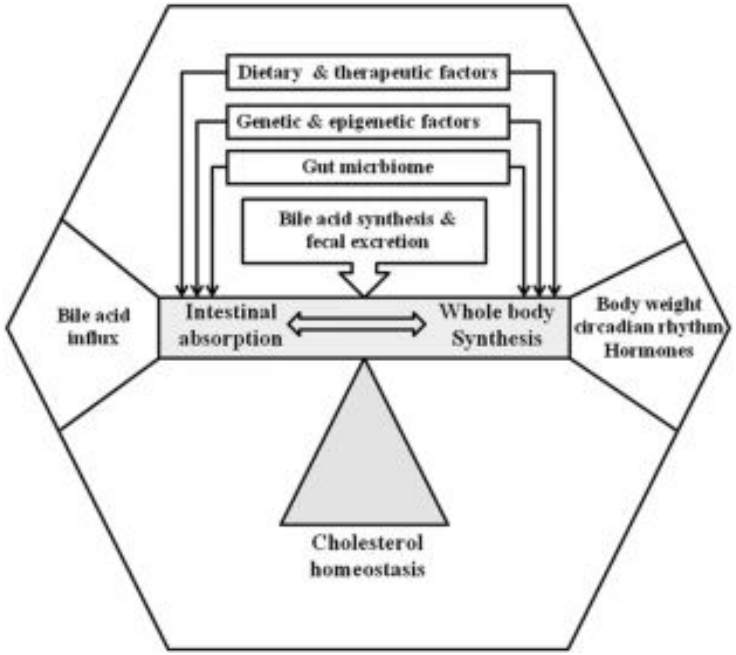
- Cholestérol (présent dans les aliments sous forme de cholestérol estérifié)
- Vitamines liposolubles
- Acides gras libres
- Phospholipides

Plaques de cholestérol docteur?





Cholestérol et Acides Gras

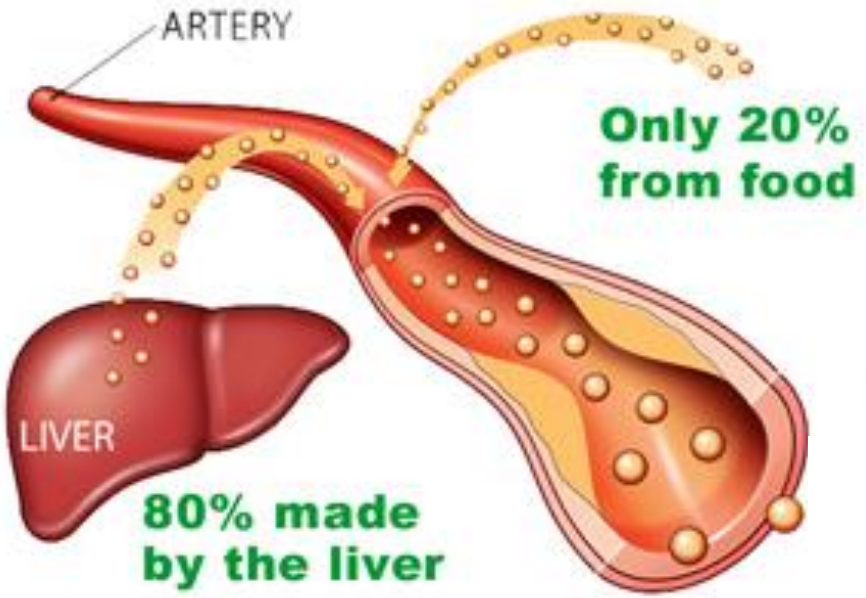


Le tiers de ce que nous mangeons suffirait à nous faire vivre

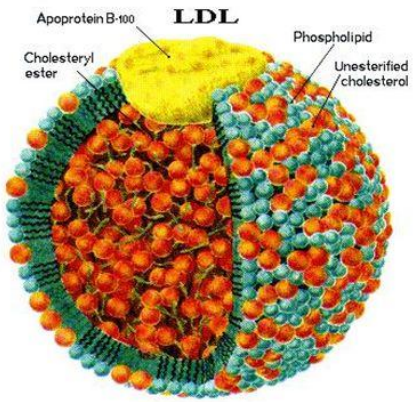
Les deux autres tiers servent à faire vivre les médecins.

Dr Paul

Cholesterol sources

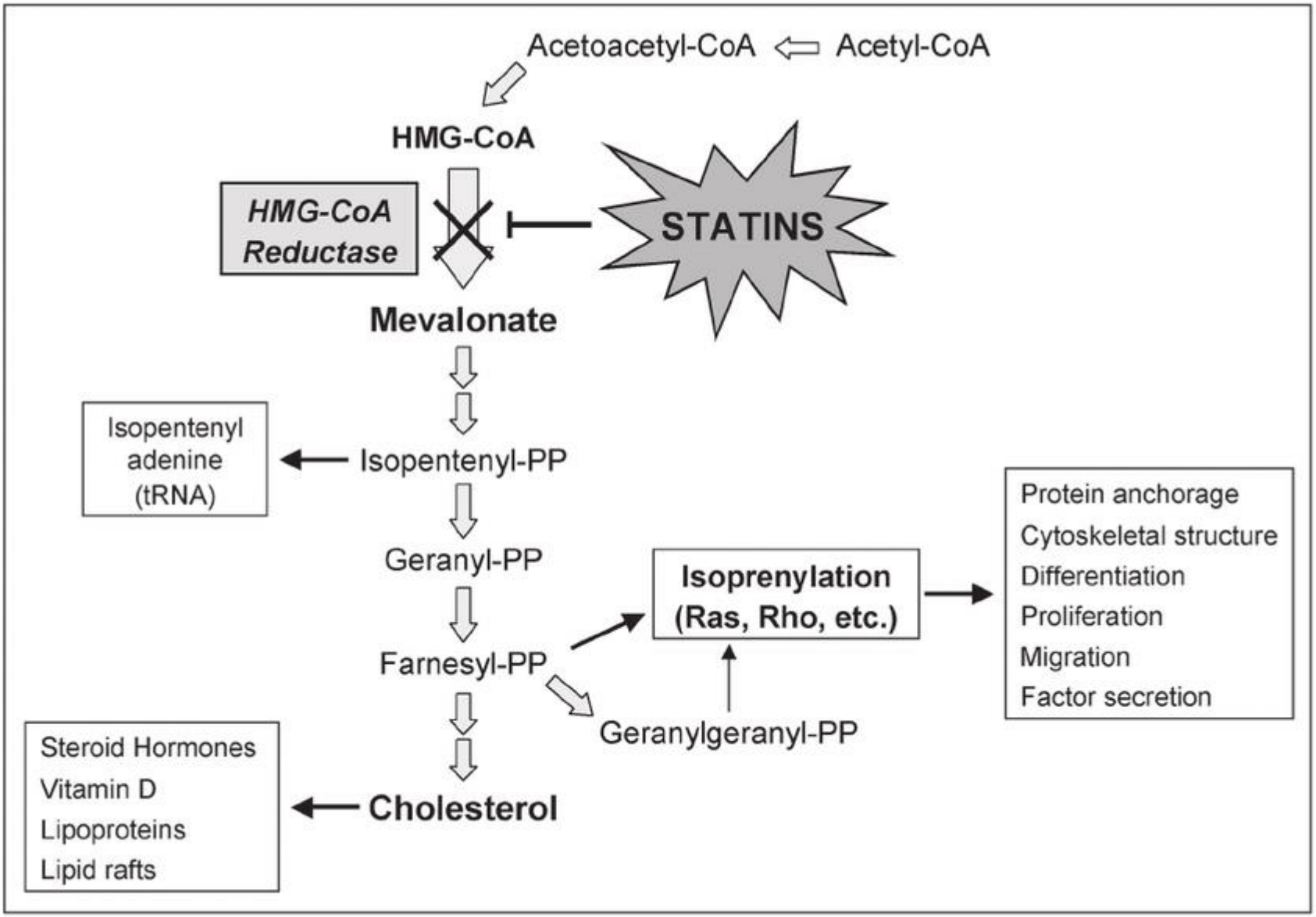


- from the diet
- can be synthesized de novo (about 800 mg of cholesterol per day)
  - in the liver (major site)
  - in the intestine



- Liver-derived and dietary cholesterol are both delivered to body cells by lipoproteins

Cholesterol produced by liver



Les acides gras omega-3 ou n-3 sont des acides gras polyinsaturés (AGPI). La dénomination n-3 vient du fait que la première double liaison est située sur le troisième atome de carbone à partir du CH3 de l'acide gras. Le chef de file est l'acide α-linolénique (ALA) provenant des végétaux (lin, colza, pourpier, noix...).

Les autres représentants des acides gras polyinsaturés sont les omega-6 dont le chef de file est l'acide Linoléique (LA), provenant des huiles de tournesol, du maïs et du soja.

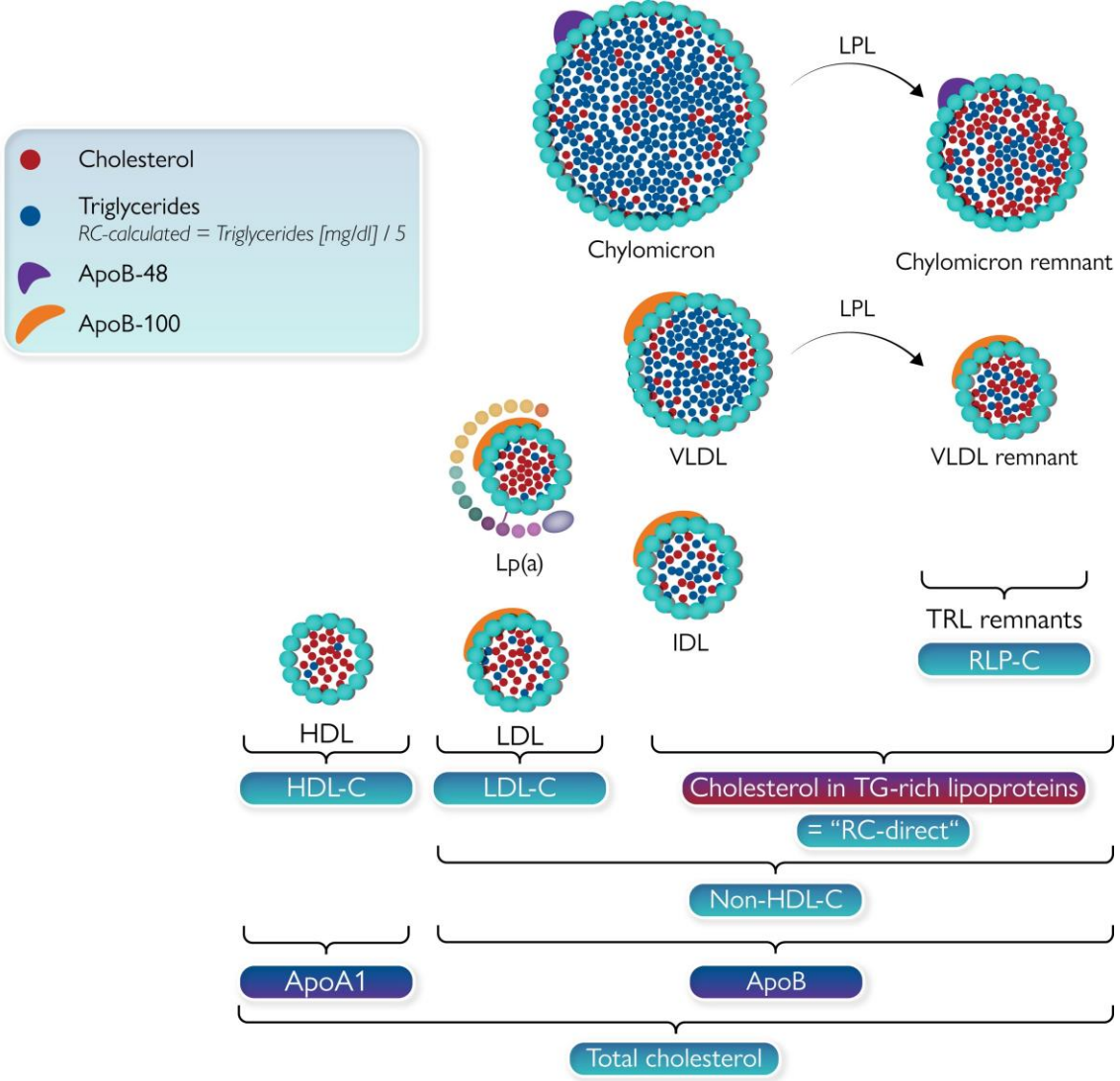
Ce sont des acides gras dits " essentiels ", en effet, leur taux dépend uniquement des apports alimentaires mais une fois dans l'organisme, ils sont métabolisés par désaturation et élongation et deviennent des dérivés à plus longue chaîne et plus désaturés. Ainsi, à partir de l'ALA, peuvent être synthétisés l'acide eicosapentaénoïque (20 : 5 n-3 = EPA) et l'acide docosahexaénoïque (22 : n-3 = DHA). Par ailleurs on trouve ces 2 acides gras à l'état naturel dans les algues, les poissons gras (maquereaux, harengs, anchois, sardines...), dans les œufs en fonction de l'alimentation donnée aux poules.

Serum cholesterol and triglycerides are transported in lipoproteins of different size and composition. Triglycerides of exogenous origin are carried in apoB-48-containing chylomicrons, while the triglycerides synthesized in the liver are mainly released in VLDL particles.

Chylomicrons and VLDL undergo hydrolysis by lipoprotein lipase, and thus reducing the triglyceride content, and forming chylomicron and VLDL remnants also referred to as ‘triglyceride-rich lipoprotein (TRL) remnants’, and their cholesterol content is denoted ‘remnant lipoprotein particle cholesterol’.

‘Remnant cholesterol’, additionally encompasses the cholesterol content of VLDL, chylomicrons, and IDL, and therefore the cholesterol carried by all TRL.

This ‘remnant cholesterol’ can either be measured (‘RC-direct’) or approximated by dividing total serum triglycerides in mg/dL by 5 or in mmol/L by 2.2 (‘RC-calculated’).

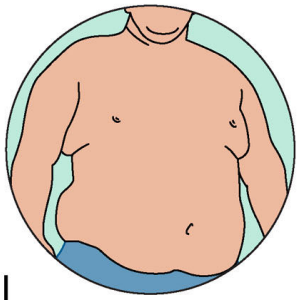


Eur Heart J, Volume 44, Issue 16, 21 April 2023, Pages 1446–1448

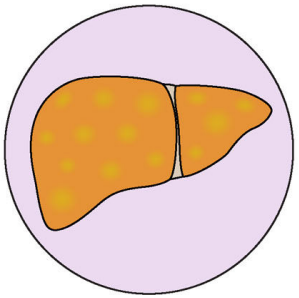
↑blood triglyceride
(LDL-C not necessarily high and could be at target)

1. Exclude secondary causes (e.g. excess alcohol, nephrotic syndrome, hypothyroidism)

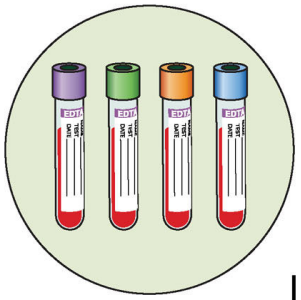
2. Check for signs of excess adiposity? (overweight or obese)



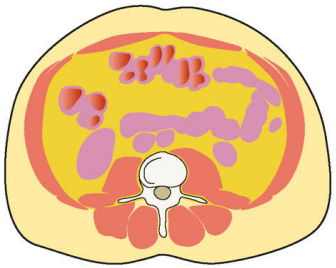
3. Check for excess liver fat intermediates (e.g. *high-normal* ALT (±GGT) levels OR liver ultrasound /MRI)



4. Check for dysglycemia? ↑HbA1c or fasting glucose? Ask about family history of type 2 diabetes



If Yes (to **2**, **3**, ±**4**), consider high triglyceride to be ectopic fat



Suggest weight loss ± ↑activity

If diagnosis correct, triglyceride, ALT, GGT, HbA1c levels will often improve in parallel with weight loss providing motivation to sustain weight improvements and lower cardiovascular and diabetes risks

Que dit la SFC ?

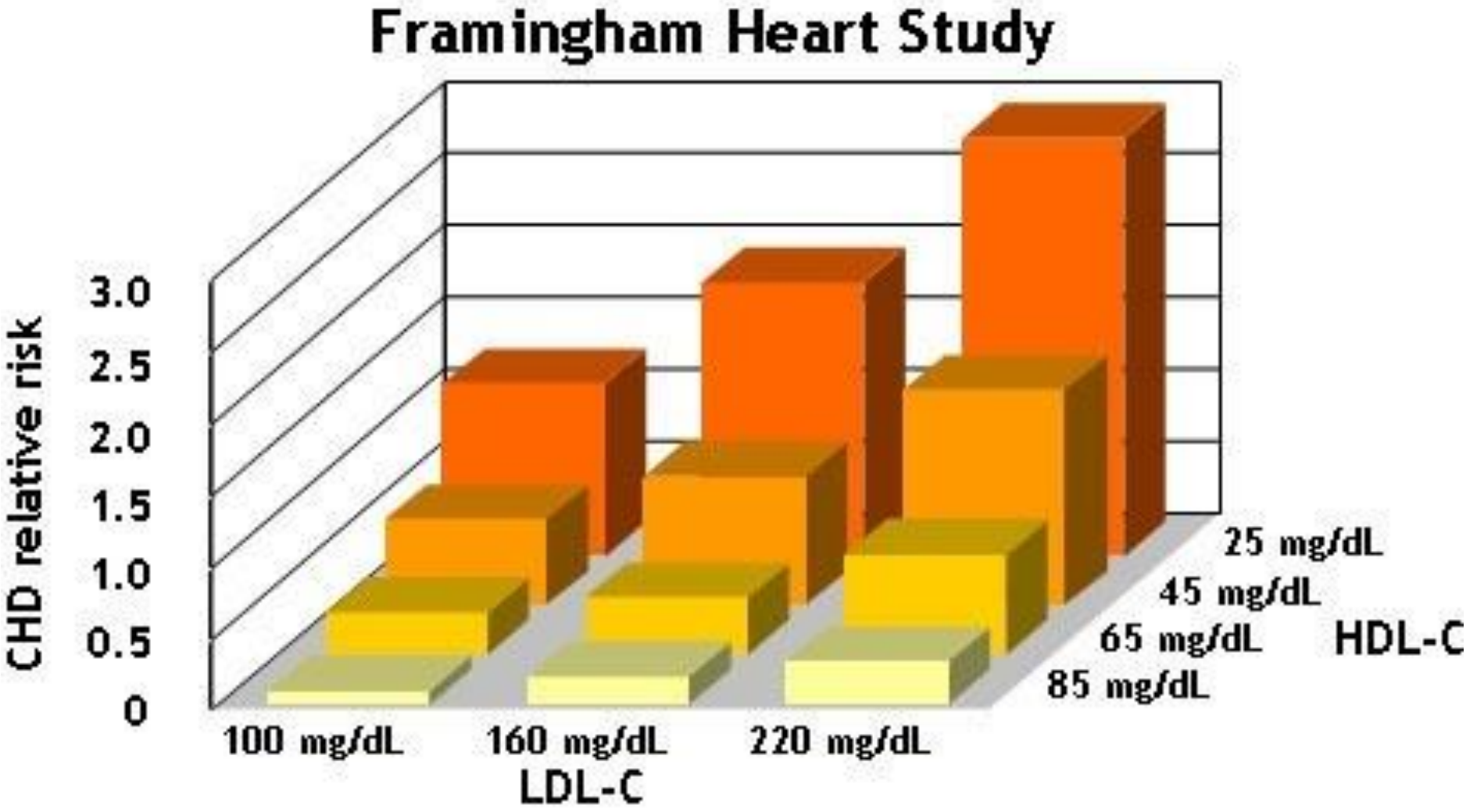
Les risques médicaux associés aux dyslipidémies sont essentiellement le risque de maladie cardiovasculaire athéromateuse quelle que soit la localisation. Le risque est associé :

- positivement, et de façon graduelle, à la concentration de LDL-cholestérol
- négativement, et de façon graduelle, à la concentration de HDL-cholestérol
- à l'hypertriglycéridémie (HTG) de façon en grande partie « dépendante »

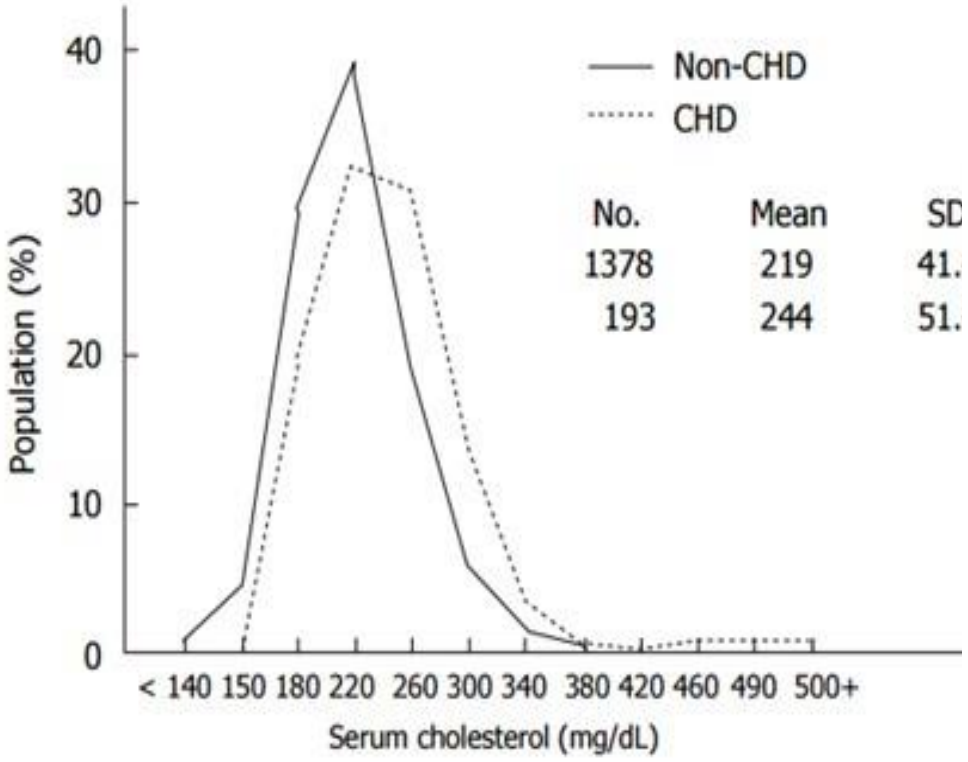
des autres marqueurs ou facteurs de risque, généralement associés à l'hypertriglycéridémie. Ces facteurs sont habituellement le surpoids, le diabète et l'HDL-cholestérol bas.

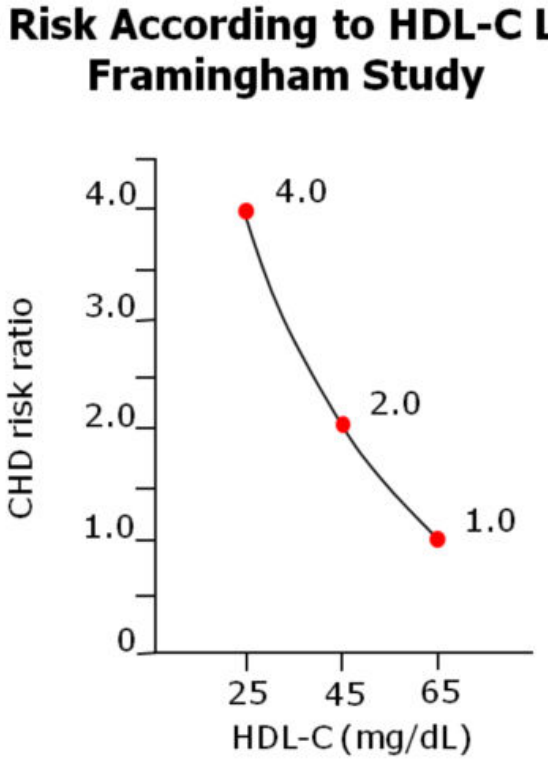
Les autres risques sont beaucoup plus rares à envisager : surtout le risque de pancréatite aiguë en cas d'hypertriglycéridémie supérieure à 10 g/L.

What told Framingham?

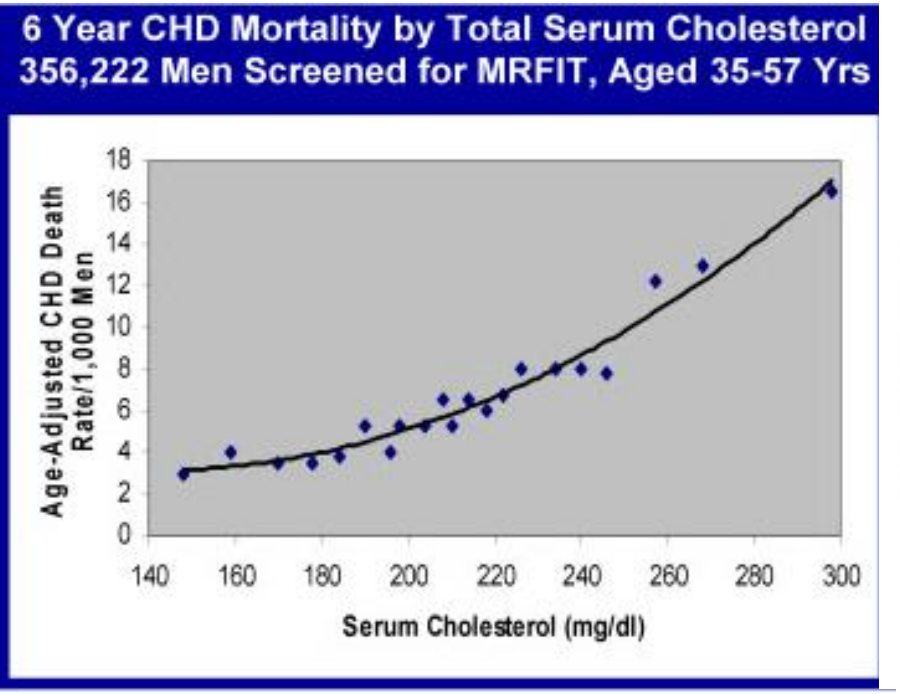


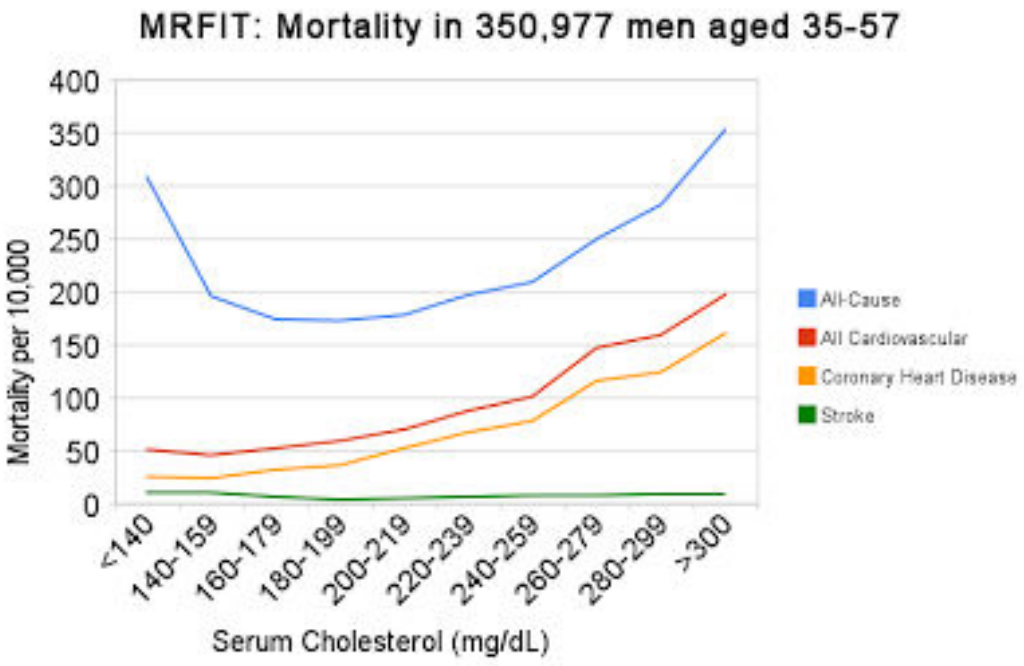
What told Framingham?





A simple relationship?





Association between elevated remnant cholesterol and cause-specific mortality was investigated in the Copenhagen General Population Study. Results are adjusted for age, sex, LDL-c, systolic blood pressure, smoking status, cumulative smoking, time since last meal, and birth year.

RC = TC – HDL-c – LDL-c

Key Question

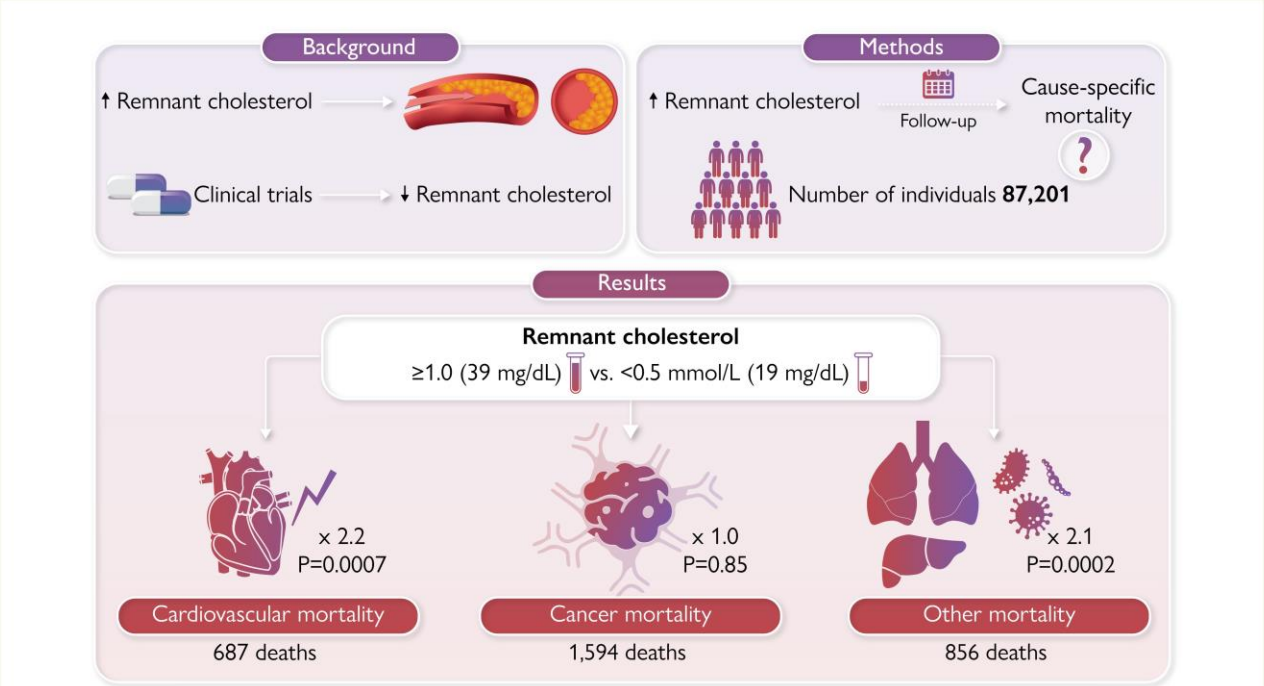
Is cholesterol carried in triglyceride-rich lipoproteins, also called remnant cholesterol, associated with increased mortality from cardiovascular disease, cancer, and other causes?

Key Finding

Remnant cholesterol above 1 mmol/L (39 mg/dL), observed in 22% of the population, was associated with 2-fold mortality from cardiovascular and other causes, but not from cancer.

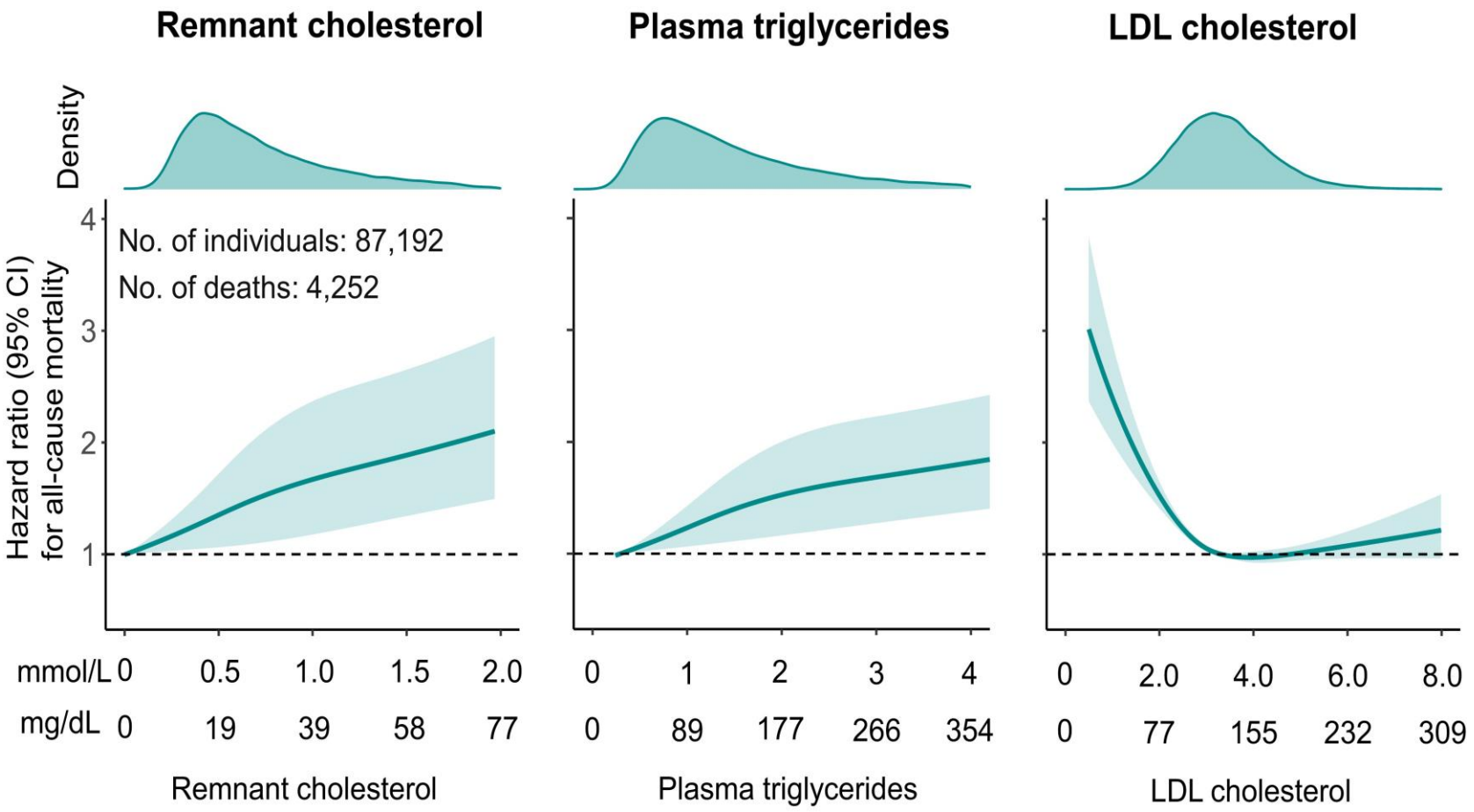
Take Home Message

Large randomized trials should investigate if remnant cholesterol-lowering therapy without increases in LDL cholesterol or apolipoprotein B reduces all-cause and cause-specific mortality in addition to atherosclerotic cardiovascular disease.



Eur Heart J, Volume 44, Issue 16, 21 April 2023, Pages 1432–1445, https://doi.org/10.1093/eurheartj/ehac822.

Figure 1 All-cause mortality as functions of remnant cholesterol, plasma triglycerides, and LDL cholesterol on continuous scales in the Copenhagen General Population Study



Remnant cholesterol was calculated as total cholesterol minus LDL cholesterol minus HDL cholesterol

Eur Heart J, Volume 44, Issue 16, 21 April 2023, Pages 1432–1445, https://doi.org/10.1093/eurheartj/ehac822

A simple relationship?

Is the use of cholesterol in mortality risk algorithms in clinical guidelines valid? Ten years prospective data from the Norwegian HUNT 2 study

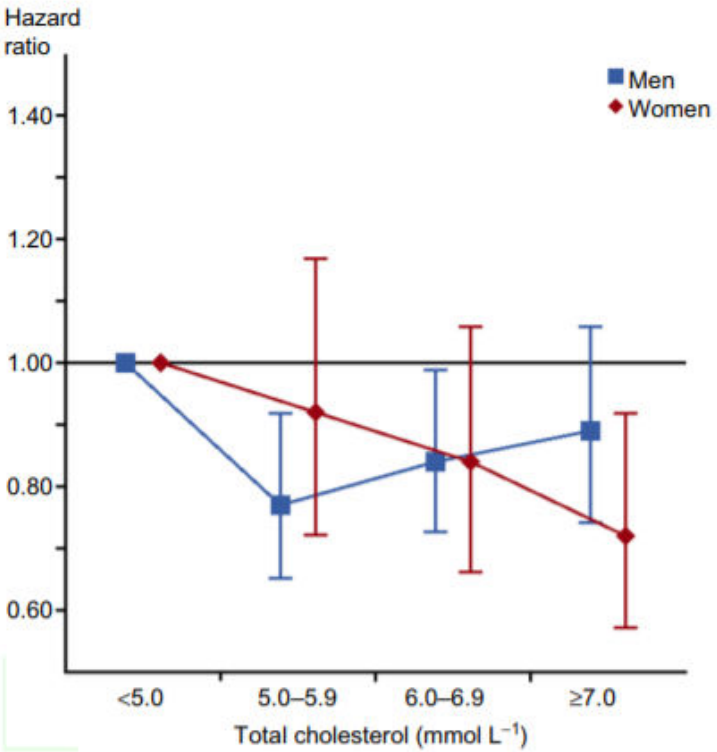


Figure 2 Risk of death (all causes) associated with different levels of total cholesterol. Hazard ratios and 95% confidence intervals for men (blue box) and women (red diamond) separately. Adjusted for age, smoking and systolic blood pressure.

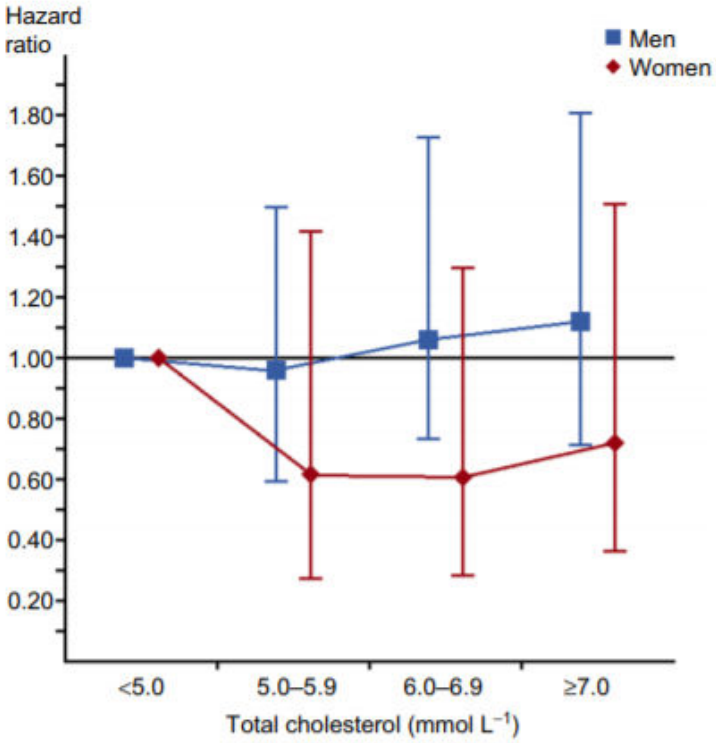


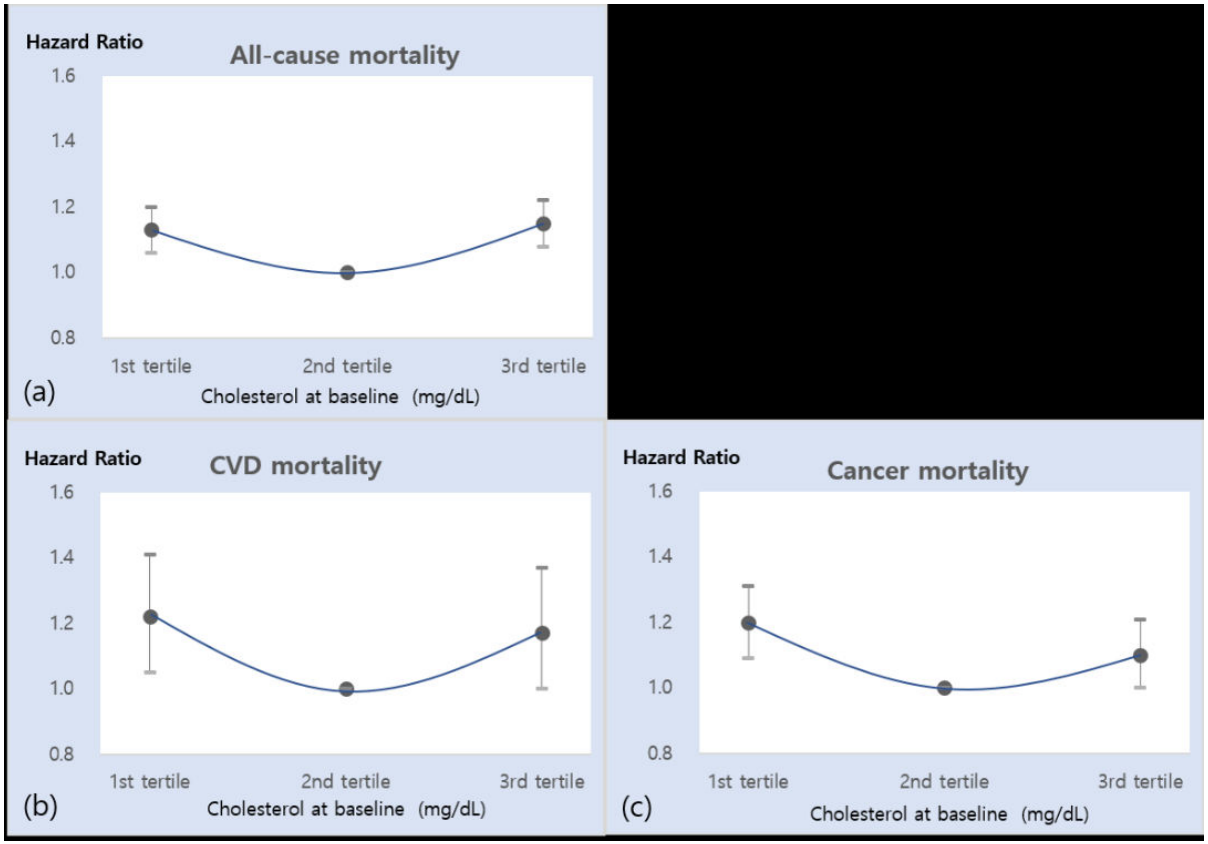
Figure 4 Risk of death from ischaemic heart disease associated with different levels of total cholesterol. Hazard ratios and 95% confidence intervals for men (blue box) and women (red diamond). Adjusted for age, smoking and systolic blood pressure.

"Clinical and public health recommendations regarding the 'dangers' of cholesterol should be revised"

Journal of Evaluation in Clinical Practice ***18*** *(2012) 159–168*

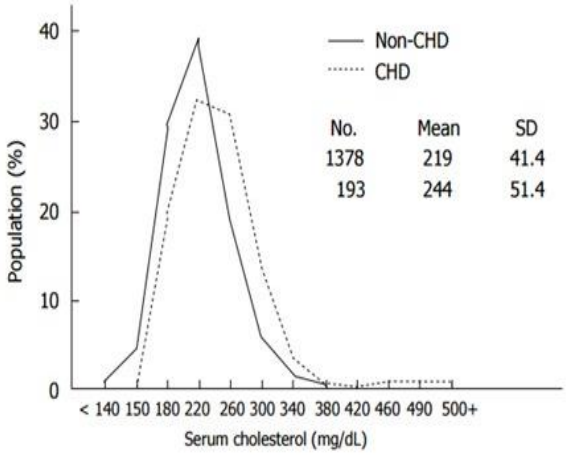
A simple relationship?

Association of change in total cholesterol level with mortality: A population-based study

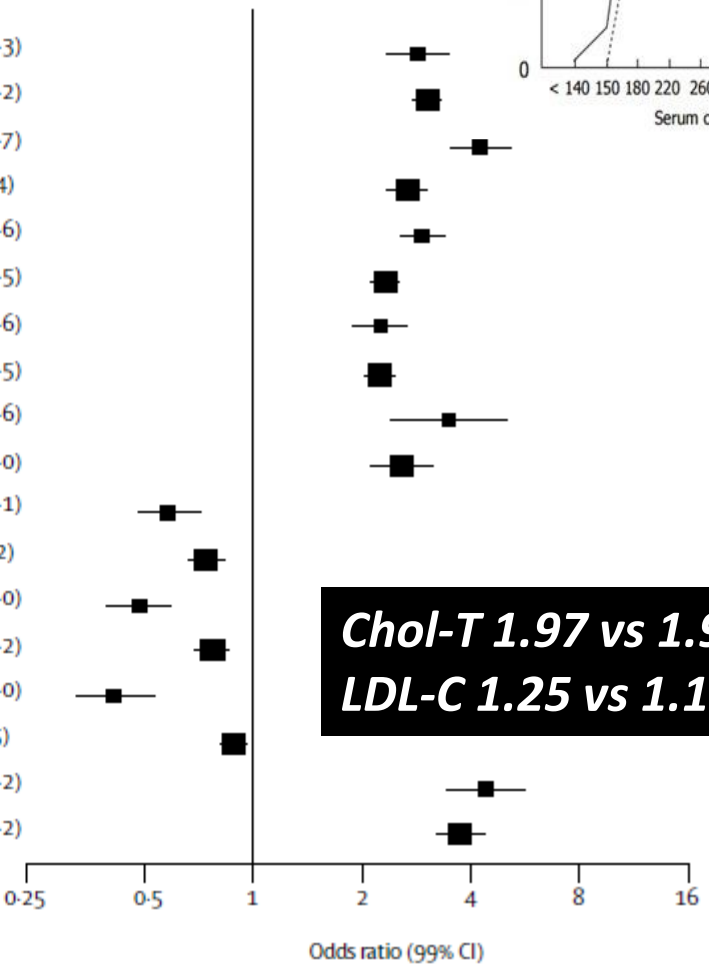


PLoS ONE 2018 13(4): e0196030

Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study



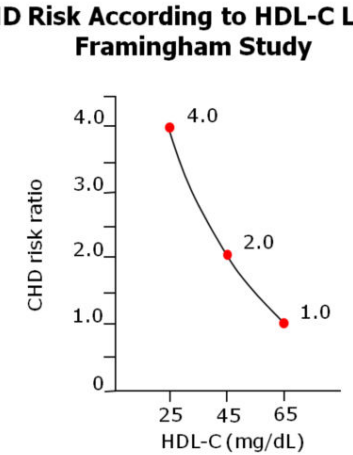
Risk factor	Sex	Control (%)	Case (%)	Odds ratio (99% CI)	PAR (99% CI)
Current smoking	F	9·3	20·1	2·86 (2·36–3·48)	15·8% (12·9–19·3)
	M	33·0	53·1	3·05 (2·78–3·33)	44·0% (40·9–47·2)
Diabetes	F	7·9	25·5	4·26 (3·51–5·18)	19·1% (16·8–21·7)
	M	7·4	16·2	2·67 (2·36–3·02)	10·1% (8·9–11·4)
Hypertension	F	28·3	53·0	2·95 (2·57–3·39)	35·8% (32·1–39·6)
	M	19·7	34·6	2·32 (2·12–2·53)	19·5% (17·7–21·5)
Abdominal obesity	F	33·3	45·6	2·26 (1·90–2·68)	35·9% (28·9–43·6)
	M	33·3	46·5	2·24 (2·03–2·47)	32·1% (28·0–36·5)
Psychosocial index	F	–	–	3·49 (2·41–5·04)	40·0% (28·6–52·6)
	M	–	–	2·58 (2·11–3·14)	25·3% (18·2–34·0)
Fruits/veg	F	50·3	39·4	0·58 (0·48–0·71)	17·8% (12·9–24·1)
	M	39·6	34·7	0·74 (0·66–0·83)	10·3% (6·9–15·2)
Exercise	F	16·5	9·3	0·48 (0·39–0·59)	37·3% (26·1–50·0)
	M	20·3	15·8	0·77 (0·69–0·85)	22·9% (16·9–30·2)
Alcohol	F	11·2	6·3	0·41 (0·32–0·53)	46·9% (34·3–60·0)
	M	29·1	29·6	0·88 (0·81–0·96)	10·5% (6·1–17·5)
ApoB/ApoA1 ratio	F	14·1	27·0	4·42 (3·43–5·70)	52·1% (44·0–60·2)
	M	21·9	35·5	3·76 (3·23–4·38)	53·8% (48·3–59·2)



Chol-T 1.97 vs 1.93 g/L
LDL-C 1.25 vs 1.16 g/L

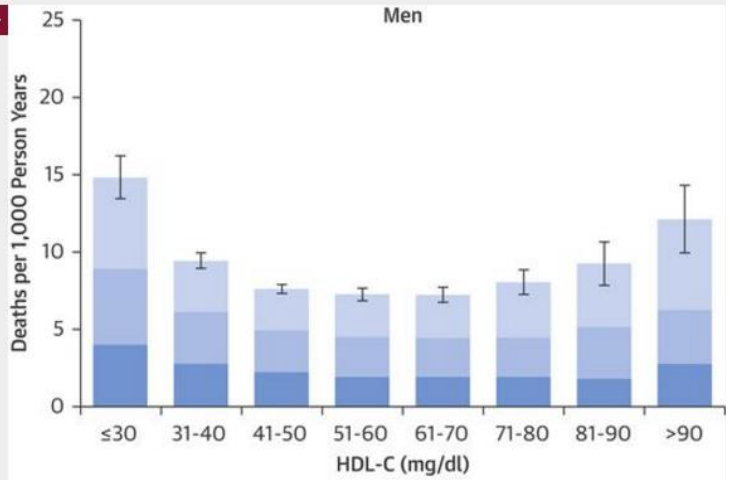
Figure 4: **Association of risk factors with acute myocardial infarction in men and women after adjustment for age, sex, and geographic region**
For this and subsequent figures, the odds ratios are plotted on a doubling scale. Prevalence cannot be calculated for psychosocial factors because it is derived from a model.

HDL good guy?



Age-Standardized Cause-Specific Mortality

Both men and women demonstrated a similar pattern in which lower levels of high-density lipoprotein cholesterol (HDL-C) levels were associated with significantly higher age-standardized all-cause mortality and cause-specific mortality. Mortality also rose with higher HDL-C levels, particularly in men. Error bars = 95% confidence intervals of the total mortality rates. CV = cardiovascular.



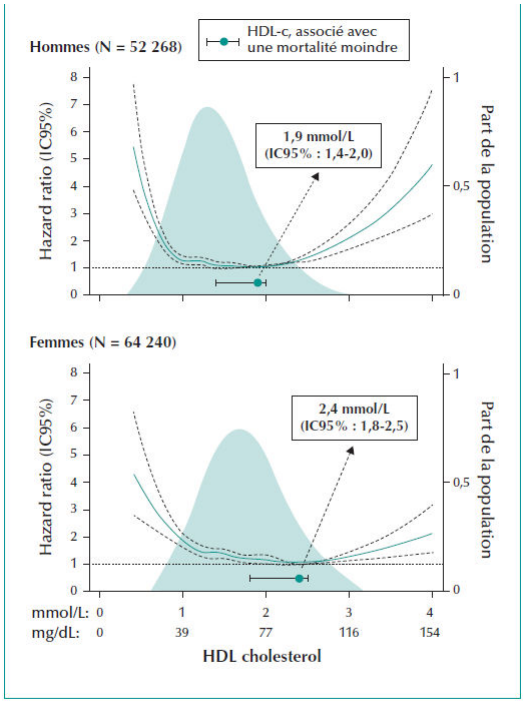
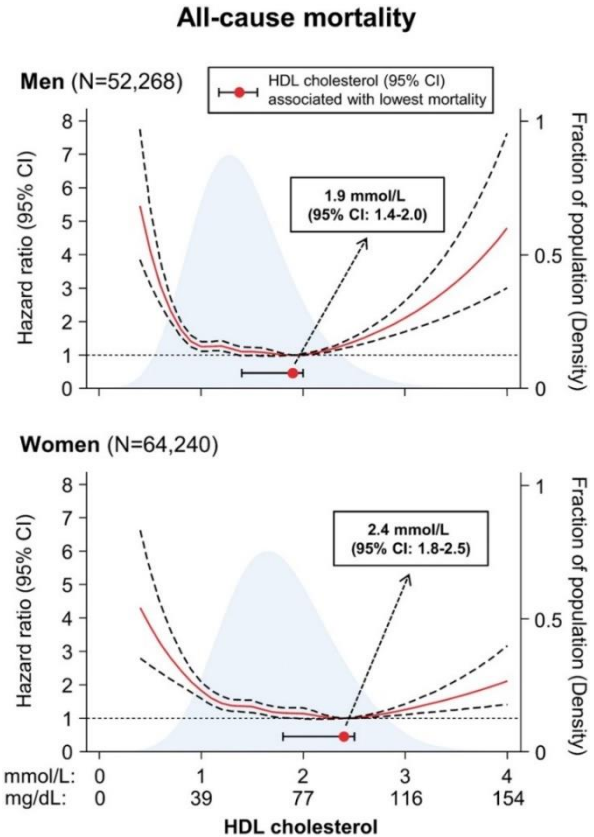
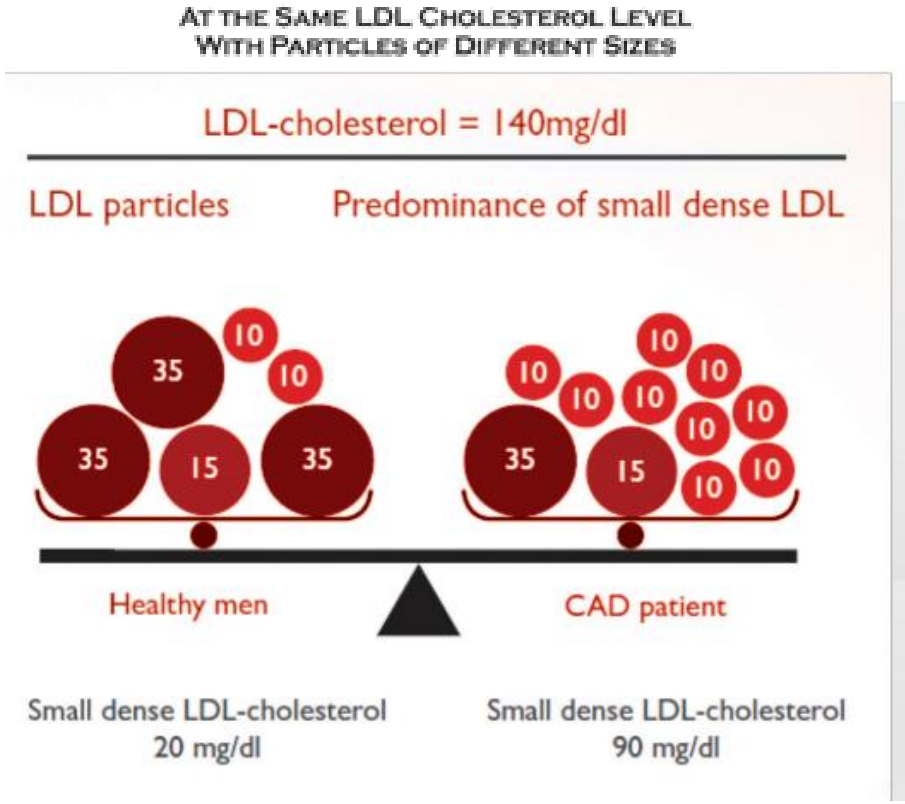
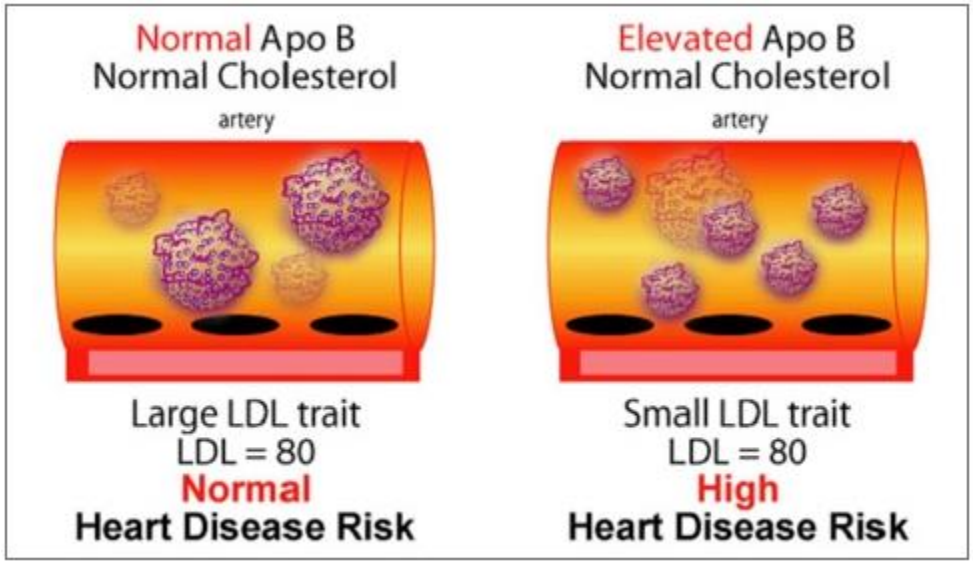


Figure 10. Données issues de 52 268 hommes et 64 240 femmes suivis dans deux registres prospectifs danois : Copenhagen City Heart Study et Copenhagen General Population Study [21].

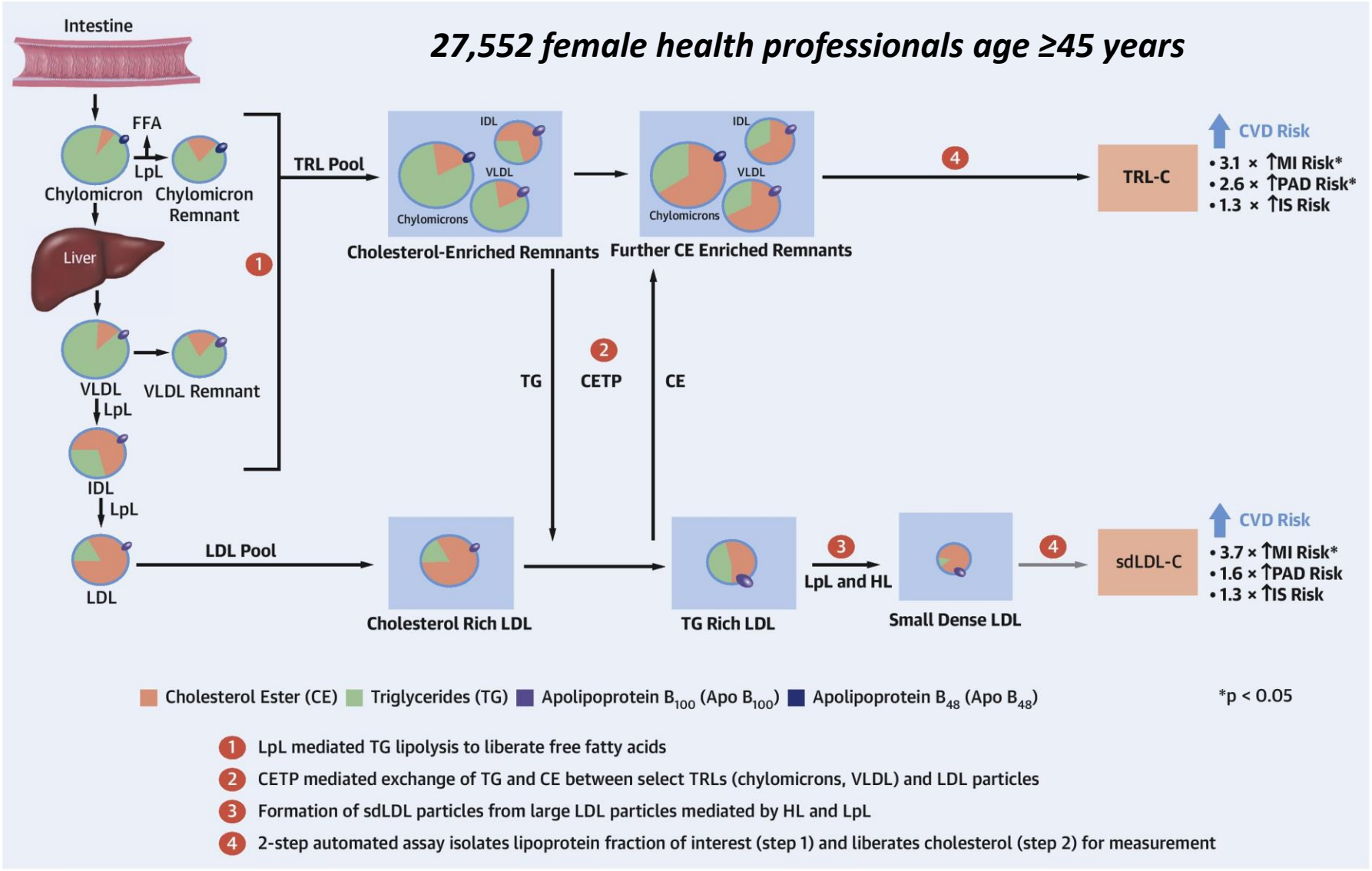


LDL-c inaccurate biomarker



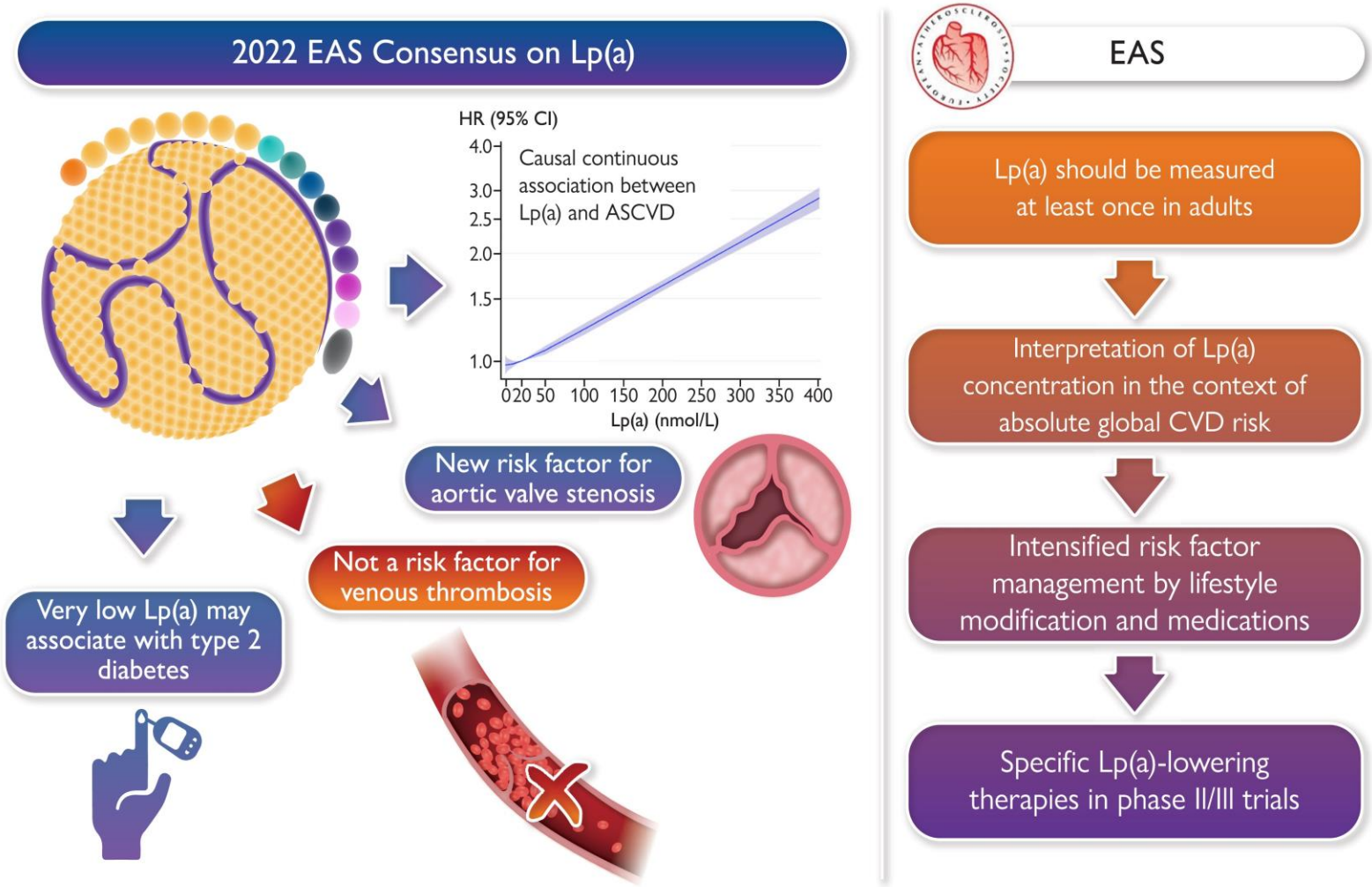


CENTRAL ILLUSTRATION: Cholesterol Content of Triglyceride-Rich Lipoproteins and Small-Dense Low-Density Lipoprotein



Duran, E.K. et al. J Am Coll Cardiol. 2020;75(17):2122-35.

La **lipoprotéine (a) [Lp(a)]** est une particule LDL-like qui contient l'apolipoprotéine (a), caractérisée par 5 régions riches en cystéïne appelées kringles.

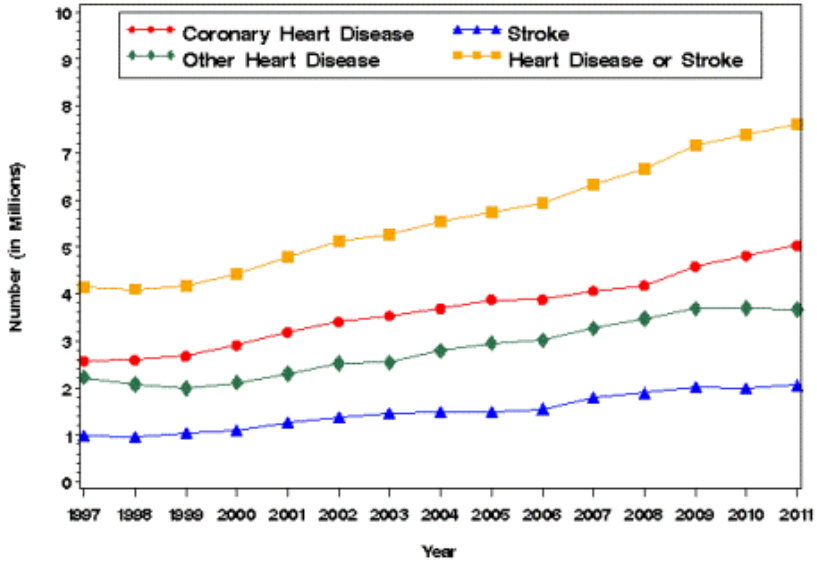


Eur Heart J, Volume 43, Issue 39, 14 October 2022, Pages 3925–3946, https://doi.org/10.1093/eurheartj/ehac361

Recommendations from Ancel Keys and most doctors… the war against saturated fat and cholesterol!

Incidence of CHD in the USA is rising steadily

Cholestérol	* 0,80	g/l	1,32 -3,20	
	2,06	mmol/l		
	Résultat Contrôlé			
Triglycérides	0,93	g/l		
	1,05	mmol/l		
Cholestérol HDL	0,52	g/l		
(Méthode directe sans précipitation)	1,34			mmol/l
Cholestérol LDL	* 0,09	g/l		
(Friedewald)				
Cholestérol / chol. HDL	1,54			



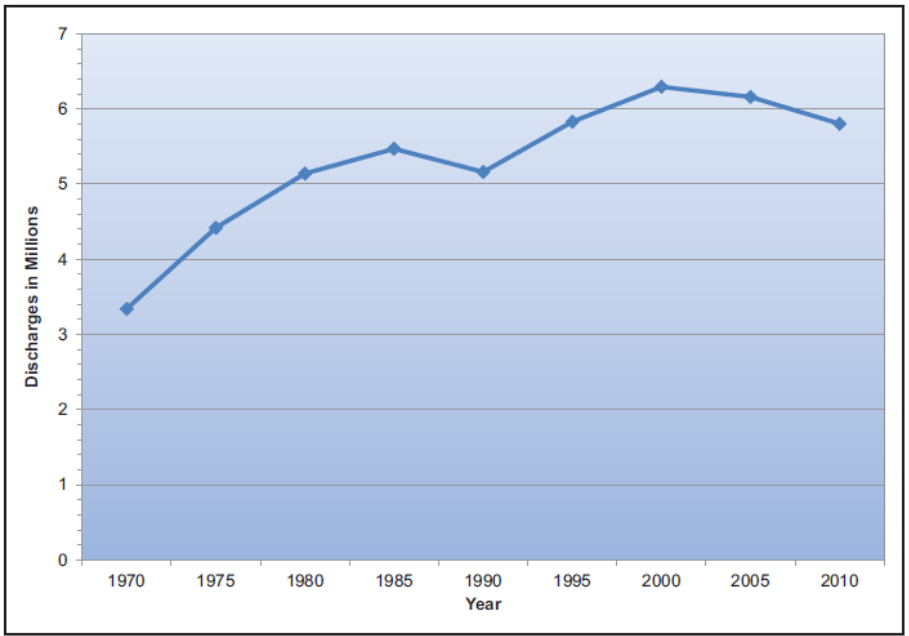
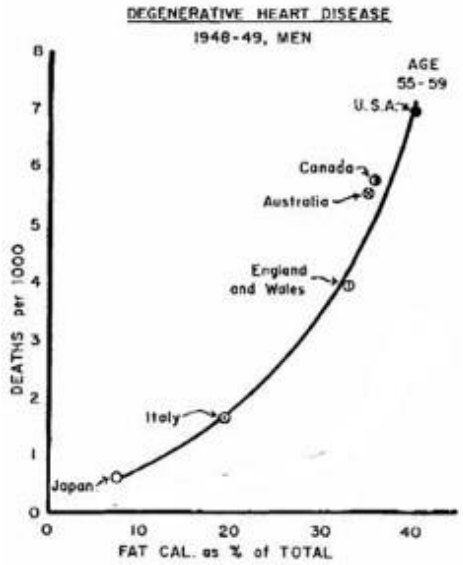


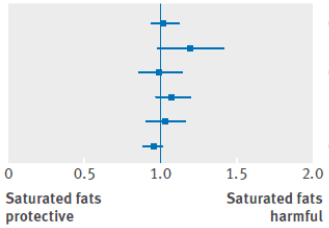
Chart 13-21. Hospital discharges for cardiovascular disease (United States: 1970–2010).
Hospital discharges include people discharged alive, dead, and "status unknown."
Source: National Center for Health Statistics and National Heart, Lung, and Blood Institute.

The Seven Countries Study have been misleading?

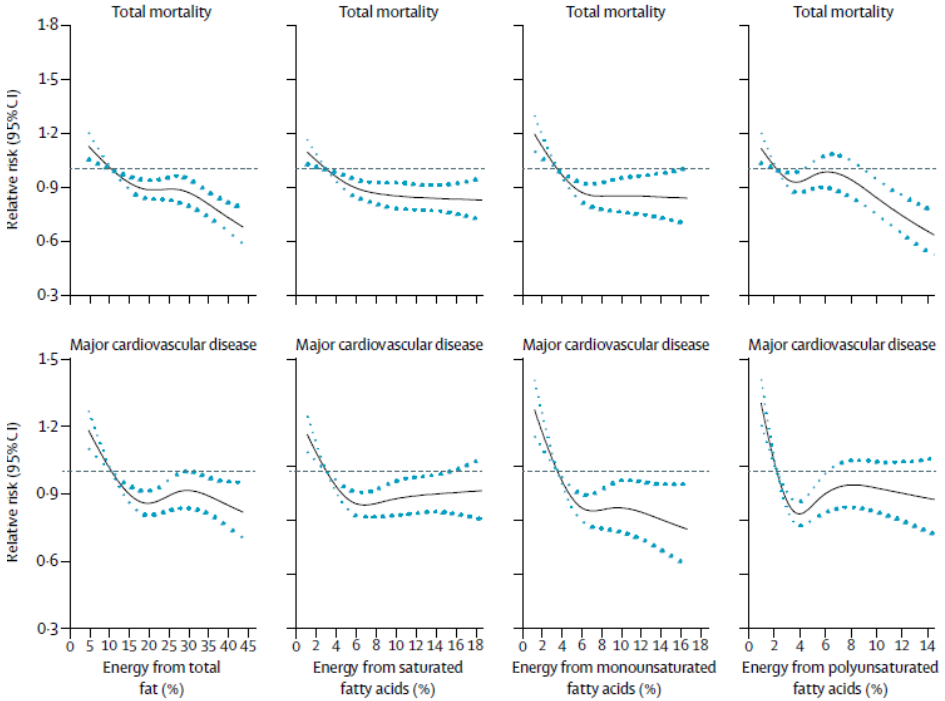


Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies

Outcome	No of studies /comparisons	No of events /participants	Relative risk (95% CI)	P	P_{het}	I^2 (%)
All cause mortality	5/7	14 090/99 906	0.99 (0.91 to 1.09)	0.91	0.17	33
CHD mortality	11/15	2970/101 712	1.15 (0.97 to 1.36)	0.10	<0.001	70
CVD mortality	3/5	3792/90 501	0.97 (0.84 to 1.12)	0.69	0.29	19
CHD total	12/17	6383/267 416	1.06 (0.95 to 1.17)	0.29	0.02	47
Ischemic stroke	12/15	6226/339 090	1.02 (0.90 to 1.15)	0.79	0.002	59
Type 2 diabetes	8/8	8739/237 454	0.95 (0.88 to 1.03)	0.20	0.61	0



Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study



‘In the adult man the serum cholesterol level is essentially independent of the cholesterol intake over the whole range of human diets. Ancel Keys 1956

“There’s no connection whatsoever between cholesterol in food and cholesterol in blood. And we’ve known that all along. Cholesterol in the diet doesn’t matter at all unless you happen to be a chicken or a rabbit.” Ancel Keys, Ph.D., professor emeritus at the University of Minnesota 1997.

Toujours éliminer une dyslipidémie secondaire

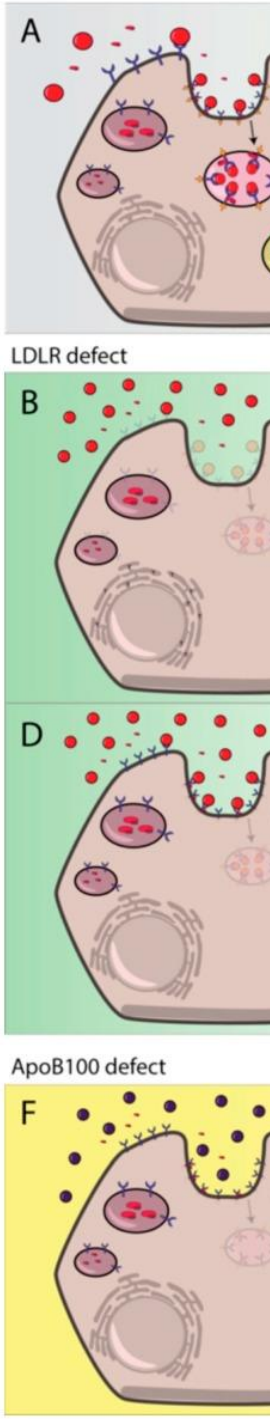
Étiologies	Moyen diagnostique	Type d'hyperlipidémie
Hypothyroïdie	TSH	HCH/HLM
Cholestase	Bilirubine, phosphatase alcaline	HCH
Syndrome néphrotique	Protéinurie, œdèmes	HLM
Insuffisance rénale chronique	Créatinine	HTG/HLM
Alcoolisme	Interrogatoire	HTG
Diabète	Glycémie, HbA1c	HTG
Hyperlipidémie iatrogène	Interrogatoire	
Œstrogènes	"	HTG
Corticoïdes	"	HLM/HTG
Rétinoïdes	"	HTG
Antirétroviraux	"	HTG
Ciclosporine	"	HCH/HLM
Diurétiques, bêtabloquants "	"	HTG modérée

Caractéristiques des hypercholestérolémies familiales monogéniques par mutation du gène du LDL-récepteur

Forme hétérozygote	Forme homozygote
50 % des récepteurs aux LDL touchés, 50 % fonctionnels	≈ 100 % des récepteurs LDL atteints
Fréquente (1/500 dans la population), 80 % de mutations retrouvées	Exceptionnelle (1/1 000 000 dans la population)
Élévation importante du LDL-C : entre 2 et 4 g/L	Élévation majeure du LDL-C : > 5 g/L
Dépôts lipidiques caractéristiques (inconstants) : xanthomes tendineux, arc cornéen prématuré	Dépôts lipidiques xanthomateux présents dès l'enfance
Risque cardiovasculaire élevé	Complications athéromateuses (y compris rétrécissement aortique) pouvant survenir dès la 1re décennie

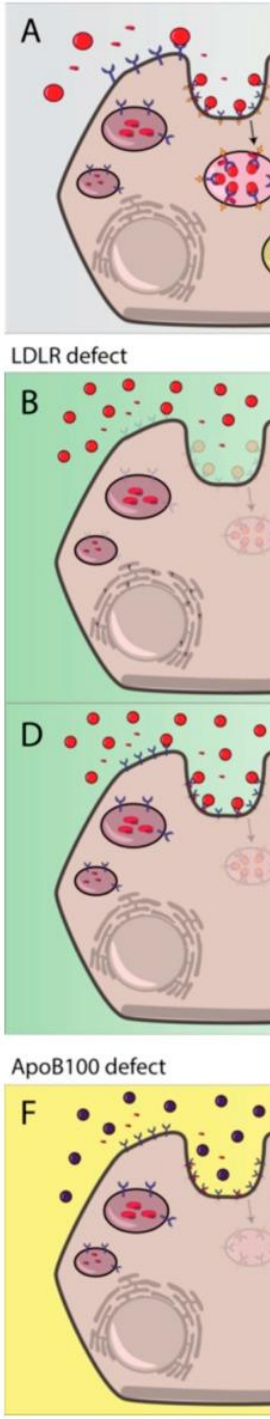
Hypercholestérolémies familiales monogéniques par mutation du gène de l'apolipoprotéine B

- RARE: il s'agit d'une mutation de l'apoB entraînant une moindre affinité des LDL pour le LDL-R.
- L'expression de l'hypercholestérolémie est plus modérée avec LDL-C classiquement entre 2 et 3 g/L.
- Les xanthomes sont rares



Hypercholestérolémies familiales monogéniques par mutation du gène de la protéine PCSK9

- Très rare
- Il s'agit d'une mutation « gain de fonction » entraînant une augmentation de l'affinité de PCSK9 pour le LDL-R.
- De ce fait, le LDL-R est dégradé après internalisation des LDL, et ne peut plus être réutilisé.



Autres dyslipidémies

Hyperlipidémie familiale combinée

- Elle est fréquente et concerne 1 à 2 % de la population.
- Le caractère polygénique est probable.
- Elle peut s'exprimer avec des phénotypes lipidiques variables dans la famille, et parfois chez un même individu (en fonction du poids et de l'alimentation) : hyperlipidémie mixte, hypercholestérolémie ou hypertriglycéridémie pures.
- Dans l'expression la plus fréquente (hyperlipidémie mixte modérée), le cholestérol total varie typiquement entre 2,5 et 3,5 g/L (LDL-C entre 1,6 et 2,5 g/L) et les triglycérides entre 1,5 et 5 g/L.
- Le risque cardiovasculaire dépend du niveau de l'hyperlipidémie et des autres facteurs de risque associés.

Autres dyslipidémies

Dysbêtalipoprotéinémie (ex-type III)

- Elle est rare, avec une fréquence d'environ 1/10 000 à 1/5 000.
- Deux conditions sont nécessaires pour l'expression d'une dysbêtalipoprotéinémie :
- – prédisposition génétique nécessaire : isoforme E2 de l'apolipoprotéine E à l'état homozygote E2/E2 ;
- – + un autre facteur : surpoids, diabète, hypothyroïdie, certains traitements.
- Le taux de cholestérol est de 3–6 g/L et celui des triglycérides de 4–10 g/L ; le lipidogramme (accumulation des IDL – Intermediate Density Lipoproteins) et le typage de l'apoE sont pertinents.
- Des xanthomes plans palmaires et xanthomes tubéreux jaune orangé sont caractéristiques mais rares.
- Le risque cardiovasculaire est élevé.
- Le traitement repose sur la diététique ; les fibrates sont souvent aussi efficaces que les statines dans cette forme.

Hypertriglycéridémie familiale (ex-type IV)

- Elle est assez fréquente.
- Il s'agit d'une hypertriglycéridémie pure (type IV) chez le sujet et les apparentés atteints.
- Les diagnostics différentiels sont l'hypertriglycéridémie dépendante de l'alimentation et l'hyperlipidémie familiale combinée (s'exprimant parfois sous forme d'une HTG).
- Il existe une grande variabilité du niveau de TG, dépendant du surpoids, de l'alcool et des sucres.
- Une chylomicronémie peut être associée (type V) en cas de poussée majeure d'HTG.
- Le risque athérogène est incertain.

Hyperchylomicronémies primitives (ex-types I et V)

- Elles sont très rares.
- Elles sont caractérisées par une HTG majeure > 10 g/L, pouvant aller jusqu'à 100 g/L.
- Il s'agit d'un type I en cas d'hyperchylomicronémie pure (enfant), d'un type V en cas d'élévation associée des chylomicrons et des VLDL (Very Low Density Lipoproteins).
- Une mutation génétique sous-jacente en est à l'origine.
- Il existe un risque majeur de pancréatite aiguë.

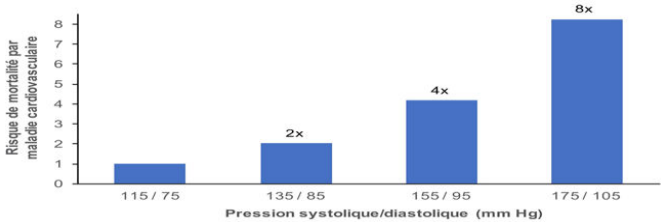
Évaluation du risque cardiovasculaire global

- **Identifier les FDR CV non modifiables**
- **Hérédité** : Sont pris en compte :
- Un IDM ou la mort subite du père ou d'un frère avant 55 ans ou de la mère ou d'une sœur avant 65 ans
- Un AVC d'un parent proche avant 45 ans
- Attention identifier les FDR CV chez les apparentés ! Le tabagisme était très important dans les années 70.
- **Age** : La probabilité d'avoir un accident CV ou cardiaque augmente nettement après 50 ans chez l'homme et après 60 ans chez la femme
- **Sexe** : Les femmes jusqu'à la ménopause sont plus protégées que les hommes face aux maladies cardio-vasculaires. En effet les hormones (oestrogène et progestérone) les protègent. Mais après 60 ans, une femme a une probabilité similaire à celle d'un homme de développer une maladie CV
- **Ménopause précoce** : Jusque 10% des femmes présentent une ménopause précoce définie comme sa survenue avant l'âge de 45 ans. La ménopause précoce est associée avec une augmentation du RCV par 1.5.
- **Origine ethnique** : Les migrants d'Asie du Sud (notamment RCV X 1.3 pour Inde et Bengladesh et RCV X 1.7 pour Pakistan) présentent un taux plus élevé de maladie CV, indépendamment des autres FDR CV

Évaluation du risque cardiovasculaire global

Identifier les FDR CV modifiables

- **La consommation d'aliments transformés, d'une alimentation riche en sucres non cachés et cachés** est clairement associée à un RCV accru et de cancers.
- **La sédentarité** est associée à une perte nette d'espérance de vie de plusieurs années. Toute personne qui pratique moins de 30 minutes d'exercice physique par jour est considérée comme sédentaire. Une demi-heure de marche active par jour peut suffire à réduire le RCV.
- **Les pollutions** de l'air (essentiellement issues de la combustion des énergies fossiles : pétrole, gaz, charbon), de l'eau et des sols (plomb, cadmium, arsenic…) sont associées à un RCV accru et responsables d'un excès de 8.8 millions de décès /an dans le monde.
- **Tabagisme** (quantifier le nombre de P.A.) : les maladies CV sont responsables de 25% des décès évitables chez les patients fumeurs, un fumeur perd en moyenne 10 ans de vie. Le RCV est accru quel que soit le type de tabagisme (cigarettes avec ou sans filtre, pipe, cigare, narguilé, tabac à mâcher, etc.). Le RCV du tabagisme est accru chez les femmes comparativement aux hommes.
- Le RCV (et particulièrement d'IDM) est aussi augmenté en cas de tabagisme passif.
- **Hypertension artérielle**
- En France, environ 12 millions de patients sont traités pour une HTA, mais 50% ne sont pas contrôlés, beaucoup ne sont pas pris en charge du tout ; inversement beaucoup trop de patients sont pris en charge inutilement pour une HTA non confirmée. L'observance est un problème majeur puisqu'après un an de prescription, la moitié des patients environ interrompent leurs traitements.
- L'élévation de la PA est reliée linéairement à partir de 115/75 mm Hg à une augmentation du RCV : le risque de mortalité totale et CV est multiplié par 2 lors d'une augmentation de la PAS de 20 mm Hg ou de la PAD de 10 mm Hg ; le risque d'AVC est multiplié par 7 à 9 et celui de l'IDM par 2,5



Évaluation du risque cardiovasculaire global

- **Diabète** :
- Un diabète est avéré lorsque la glycémie à jeun est ≥1.26 g/l à deux reprises ou ≥2 g/l à n'importe quel moment de la journée. En moyenne le diabète de type 2 double le RCV et réduit l'espérance de vie de 4 à 6 ans.
- Attention le diabète gestationnel est défini par une seule valeur de glycémie au-delà des seuils définis (0,92g/L à jeun; ou 1,80g/L 1h après la charge orale en glucose ; ou 1,53 g/L 2h après). Le risque de maladie CV lié à l'athérosclérose en milieu de vie chez les femmes ayant eu un diabète gestationnel n'est pas diminué même si elles reviennent à une glycémie normale
- **Obésité et tour de taille**
- On parle de surpoids si l'indice de masse corporelle (IMC) est supérieur à 25, et d'obésité s'il est supérieur à 30.
- La répartition des graisses corporelles est également un élément important. Si l'excès de graisse se situe au niveau de la taille et du ventre (obésité dite androïde en forme de pomme), le **RCV** est plus élevé que si les graisses se localisent plutôt en dessous de la ceinture (obésité dite gynoïde en forme de poire).
- Le tour de taille est jugé trop élevé s'il est ≥ 80 cm pour une femme ; ≥ 94 cm pour un homme.
- Syndrome métabolique
- Le syndrome associe une obésité abdominale (c'est-à-dire un tour de taille > 94 cm chez les hommes et > 80 cm chez les femmes) associée à au moins 2 des facteurs suivants :
- un taux élevé de triglycérides ≥150 g/L ;
- un faible taux de cholestérol HDL <0.40 mg/dL) chez l'homme et < 0.50 g/L) chez la femme ;
- une HTA
- une glycémie à jeun > 1 g/L **La stéatose hépatique (« NASH »)** est souvent associée au syndrome métabolique, à l'obésité, à la résistance à l'insuline au diabète et est un marqueur de RCV
- **Maladies rénales chroniques** : le risque de maladie coronaire augmente linéairement lorsque le DFG décline au-dessous de 60/min/1.73 m². Le risque de mortalité CV est multiplié par 3 lorsque le DFG ≤ 15 ml/min/1.73 m²
- **LDL-cholestérol, non HDL cholestérol (cholestérol total – HDL-cholestérol), concentration d'apolipoprotéines B** avec des seuils de risque variant avec le SCORE2 (Systemic Coronary Risk Estimation) et des cibles à atteindre (jusqu'à 0.55 voire 0.4 g/L pour LDL-cholestérol) variant avec le RCV. L'élévation du HDL-cholestérol (> 0.7-0.8 g/L) ou des triglycérides (> 1.5 g/L) sont aussi associés à un RCV accru.

Évaluation du risque cardiovasculaire global

- **La microalbuminurie (30 à 300 mg/24h)** est un marqueur de RCV, de diabète, d'altération de la fonction rénale et de mortalité totale.**Maladies inflammatoires** (polyarthrite rhumatoïde..), **BPCO, infection VIH**
- **ATCD d'HTA gravidique :** Les femmes avec antécédent de pré-éclampsie présentent un risque X 3-4 d'HTA et X2 de diabète, IDM et AVC comparées aux femmes sans antécédent de complications hypertensives pendant la grossesse.
- **ATCD d'irradiation thoracique importante** (maladie de Hodgkin, cancer du sein) : développement à long terme de maladies CV post-radiques
- **SAOS et troubles du sommeil**
- Le SAOS est facteur de risque de l'HTA et notamment d'absence de baisse de la PA durant le sommeil
- **Consommation de toxiques** : cannabis, cocaïne, amphétamines, anabolisants, ecstasy Quantifier la prise d'alcool par jour.
- **Médicaments** : AINS, corticoïdes, contraception œstro-progestative et traitements hormonaux prolongés de la ménopause, vasoconstricteurs, antipsychotiques, bronchodilatateurs, analgésiques opioïdes. Les sulfamides hypoglycémiants sont associés à un risque d'arythmies ventriculaires et de mort subite.

- **Stress Psycho-social (difficultés financières, professionnelles, familiales, anxio-dépression, solitude…)**
- Lorsque le stress s'installe dans la durée (stress chronique), il agit de différentes manières : au niveau physique (en favorisant notamment l'augmentation de la PA et de la glycémie) mais aussi au niveau mental et émotionnel.
- **Migraine avec aura**
- **Les maladies psychiatriques** sont associées à un RCV accru
- **Le syndrome des ovaires polykystiques** est associé à un risque de diabète multiplié par 2 à 4.

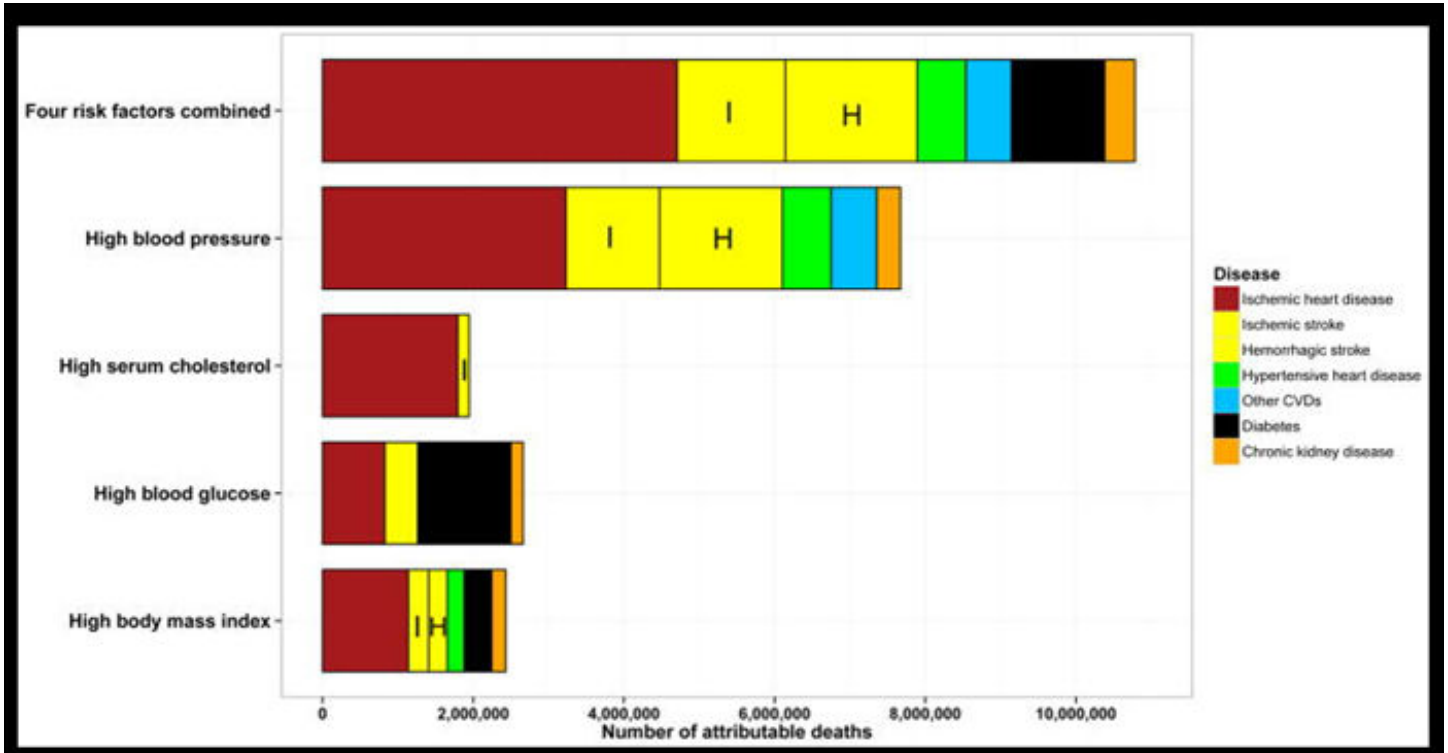
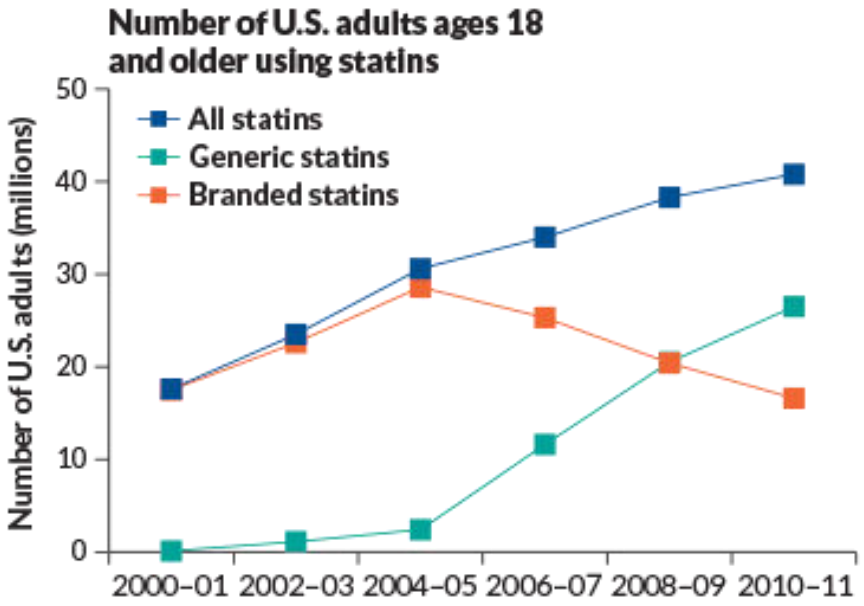
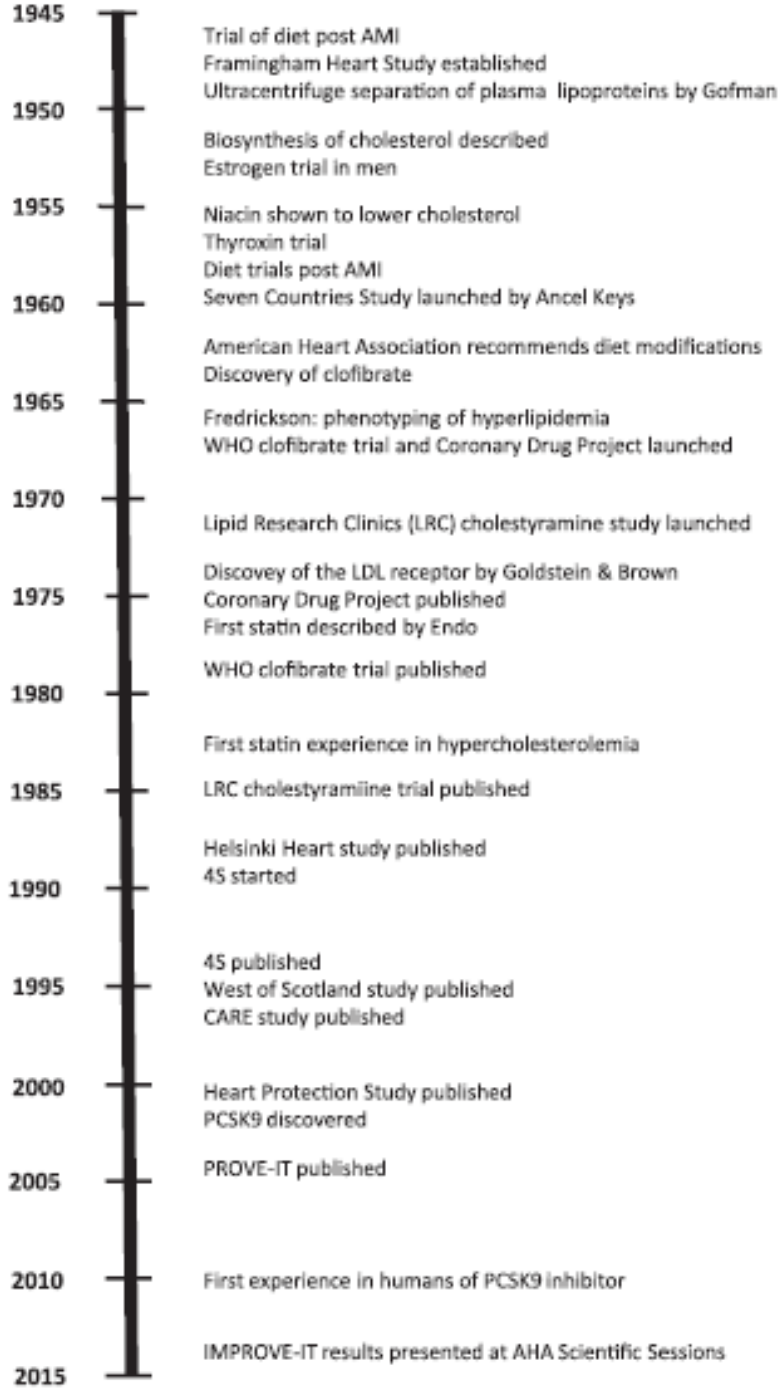
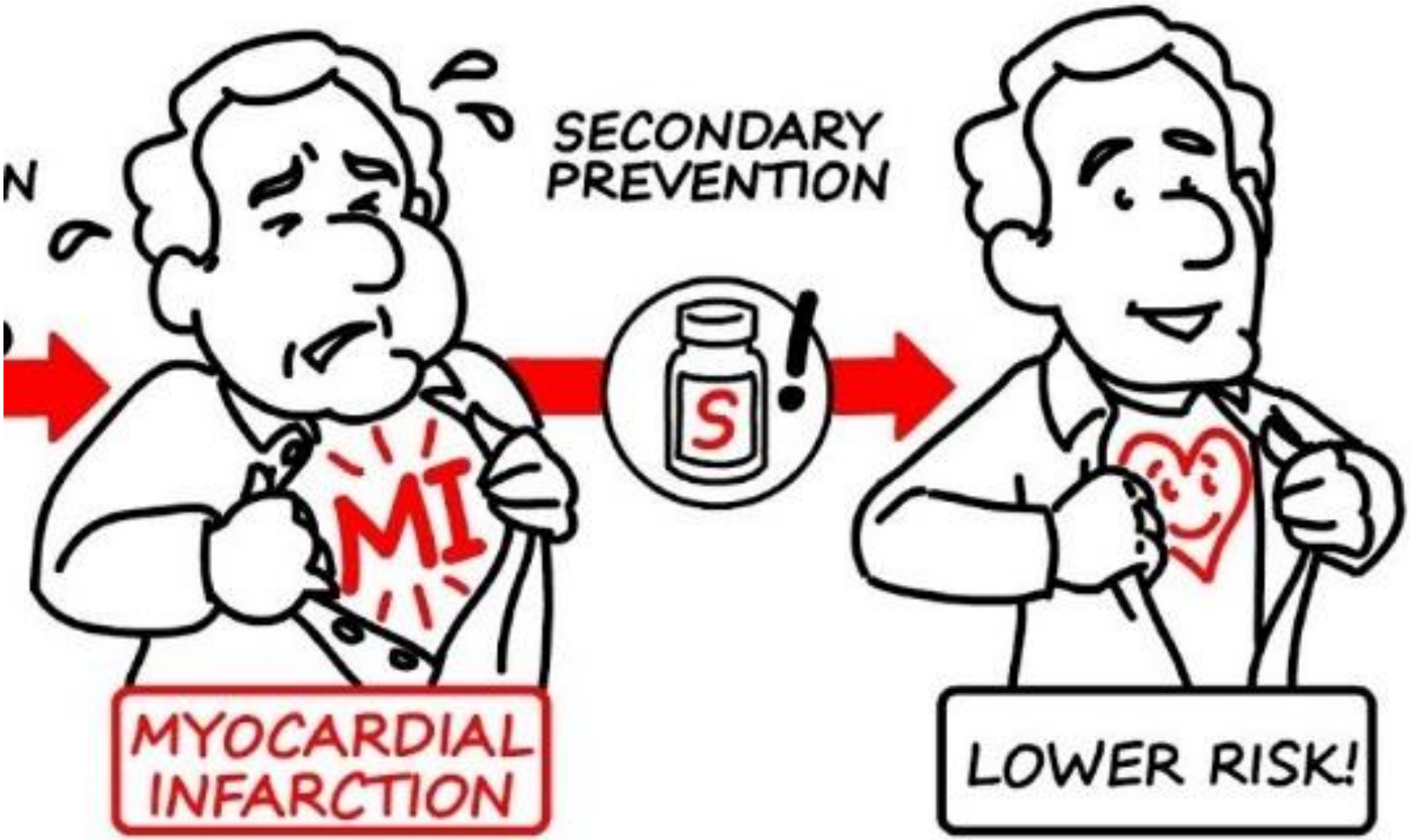


Figure 3 Deaths attributable to the individual and combined effects of high body mass index, blood pressure, cholesterol, and glucose in 2010, by disease.

Statin trials: a success story






SECONDARY
PREVENTION
MI
MYOCARDIAL
INFARCTION
LOWER RISK!

Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S)

Recruitment and randomisation

Patient records of men and women aged 35–70 years with a history of angina pectoris or acute myocardial infarction (MI) were systematically screened for study eligibility. The exclusion criteria were: premenopausal women of childbearing potential, secondary hypercholesterolaemia, unstable or Prinzmetal angina, tendon xanthomata, planned coronary artery surgery or angioplasty, MI during the preceding 6 months, antiarrhythmic therapy, congestive heart failure requiring treatment with digitalis, diuretics, or vasodilators, persistent atrial fibrillation, cardiomegaly, haemodynamically important valvular heart disease, history of completed stroke, impaired hepatic function, partial ileal bypass, history of drug or alcohol abuse, poor mental function, other serious disease, current treatment with another investigational drug, or hypersensitivity to HMG-CoA reductase inhibitors. Potentially eligible patients were invited to the clinic

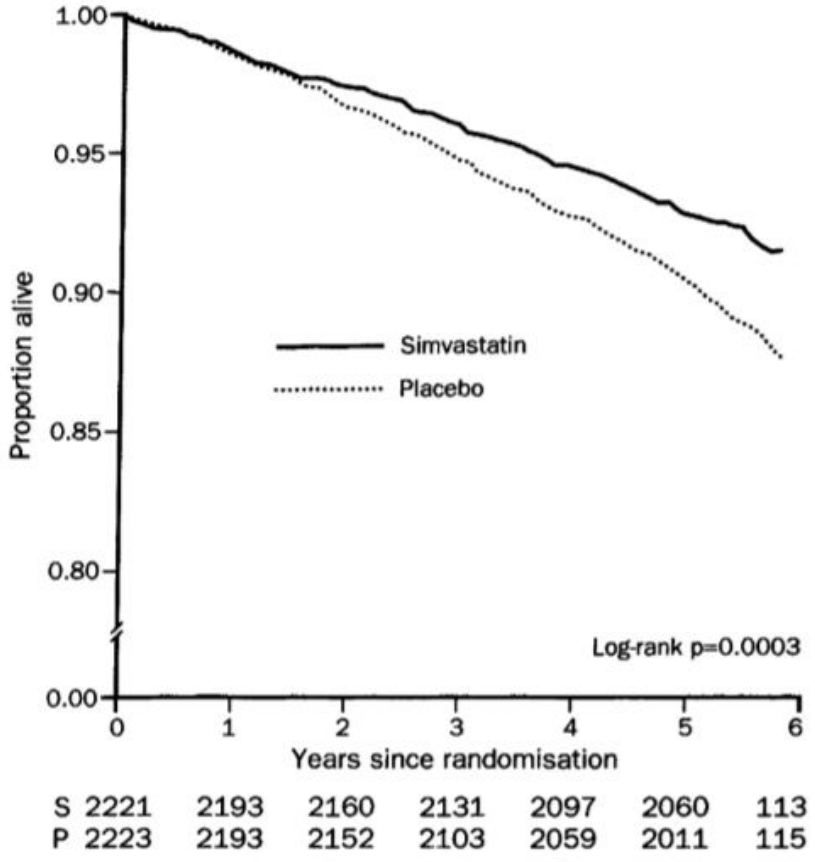


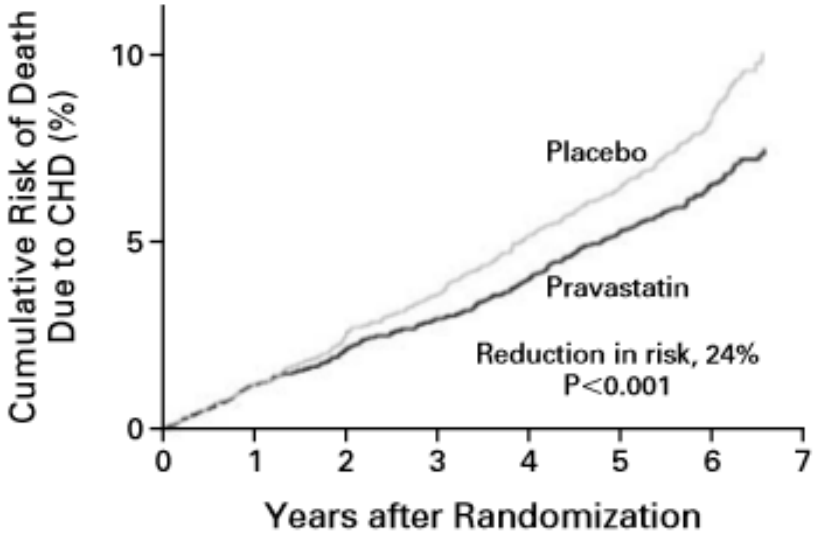
Figure 1: **Kaplan-Meier curves for all-cause mortality**

PREVENTION OF CARDIOVASCULAR EVENTS AND DEATH WITH PRAVASTATIN IN PATIENTS WITH CORONARY HEART DISEASE AND A BROAD RANGE OF INITIAL CHOLESTEROL LEVELS

THE LONG-TERM INTERVENTION WITH PRAVASTATIN IN ISCHAEMIC DISEASE (LIPID) STUDY GROUP*

TABLE 2. CARDIOVASCULAR EVENTS ACCORDING TO TREATMENT GROUP.

EVENT*	PLACEBO (N=4502)	PRAVASTATIN (N=4512)	REDUCTION IN RISK (95% CI)†	P VALUE‡
	no. (%)		%	
Death due to CHD	373 (8.3)	287 (6.4)	24 (12–35)	<0.001
Death due to CVD	433 (9.6)	331 (7.3)	25 (13–35)	<0.001
Death from any cause	633 (14.1)	498 (11.0)	22 (13–31)	<0.001
Death due to CHD or nonfatal MI	715 (15.9)	557 (12.3)	24 (15–32)	<0.001
Any MI	463 (10.3)	336 (7.4)	29 (18–38)	<0.001
CABG	520 (11.6)	415 (9.2)	22 (11–31)	<0.001
PTCA	253 (5.6)	210 (4.7)	19 (3–33)	0.024
CABG or PTCA	708 (15.7)	585 (13.0)	20 (10–28)	<0.001
Hospitalization for unstable angina	1106 (24.6)	1005 (22.3)	12 (4–19)	0.005
Any stroke	204 (4.5)	169 (3.7)	19 (0–34)	0.048



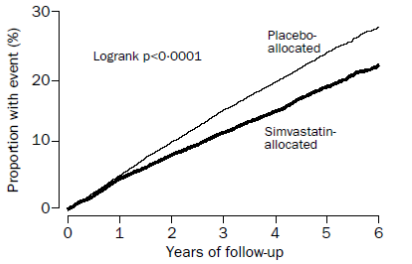
NO. AT RISK

Placebo	4502	4431	4338	4253	4134	3786	1766
Pravastatin	4512	4445	4373	4306	4215	3852	1869

Figure 1. Kaplan–Meier Estimates of Mortality Due to Coronary Heart Disease (CHD), the Primary Outcome, in the Pravastatin and Placebo Groups.

MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20 536 high-risk individuals: a randomised placebo-controlled trial

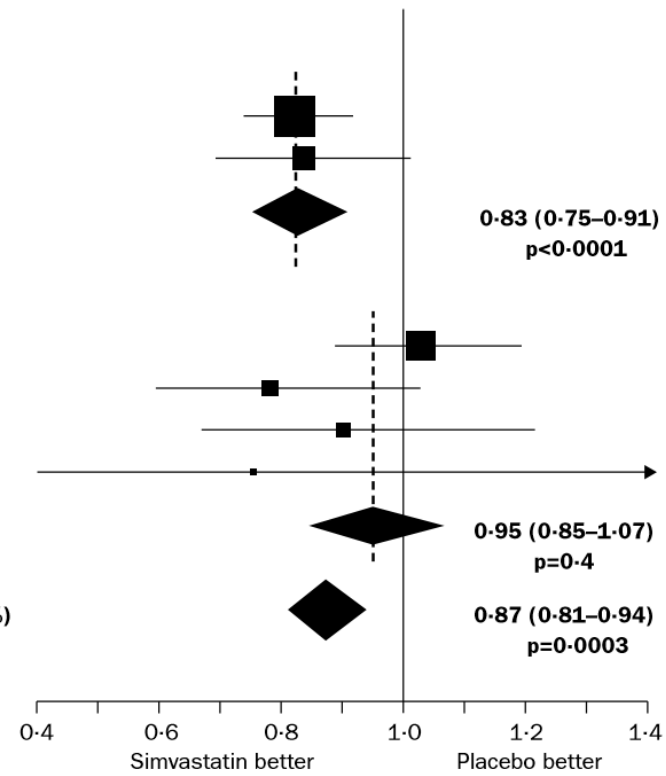
*Heart Protection Study Collaborative Group**



Benefit (SE)/1000 allocated simvastatin 5 (3) 20 (4) 35 (5) 46 (5) 54 (7) 60 (18)

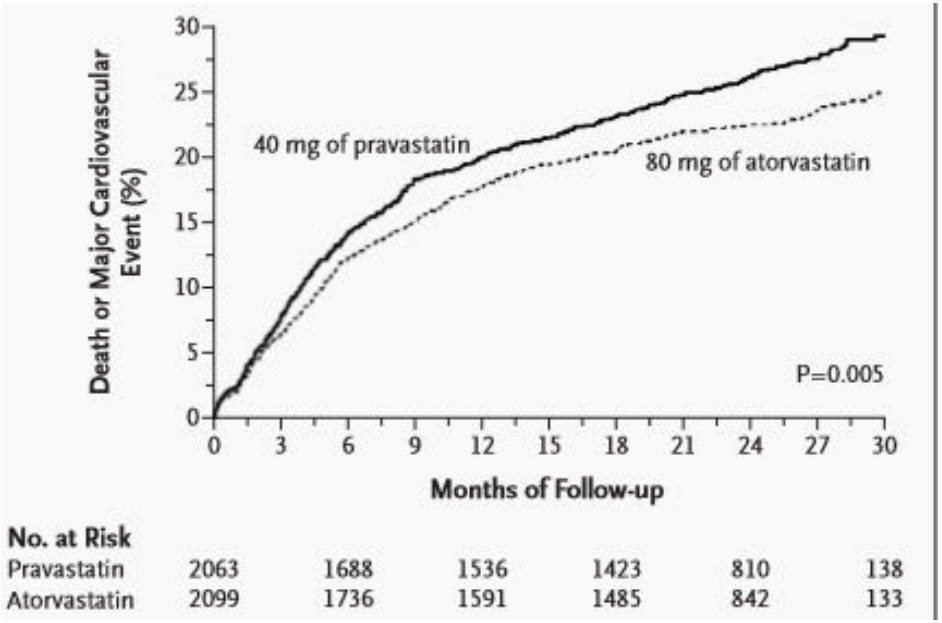
Figure 6: **Life-table plot of effects of simvastatin allocation on percentages having major vascular events**
See figure 5 for numbers of participants having a first event during each year of follow-up.

	Simvastatin-allocated (10 269)	Placebo-allocated (10 267)	Death rate ratio (95% CI)
Vascular causes			
Coronary	587 (5·7%)	707 (6·9%)	
Other vascular	194 (1·9%)	230 (2·2%)	
Subtotal: any vascular	**781 (7·6%)**	**937 (9·1%)**	**0·83 (0·75–0·91) p<0·0001**
Non-vascular causes			
Neoplastic	359 (3·5%)	345 (3·4%)	
Respiratory	90 (0·9%)	114 (1·1%)	
Other medical	82 (0·8%)	90 (0·9%)	
Non-medical	16 (0·2%)	21 (0·2%)	
Subtotal: any non-vascular	**547 (5·3%)**	**570 (5·6%)**	**0·95 (0·85–1·07) p=0·4**
ANY DEATH	**1328 (12·9%)**	**1507 (14·7%)**	**0·87 (0·81–0·94) p=0·0003**

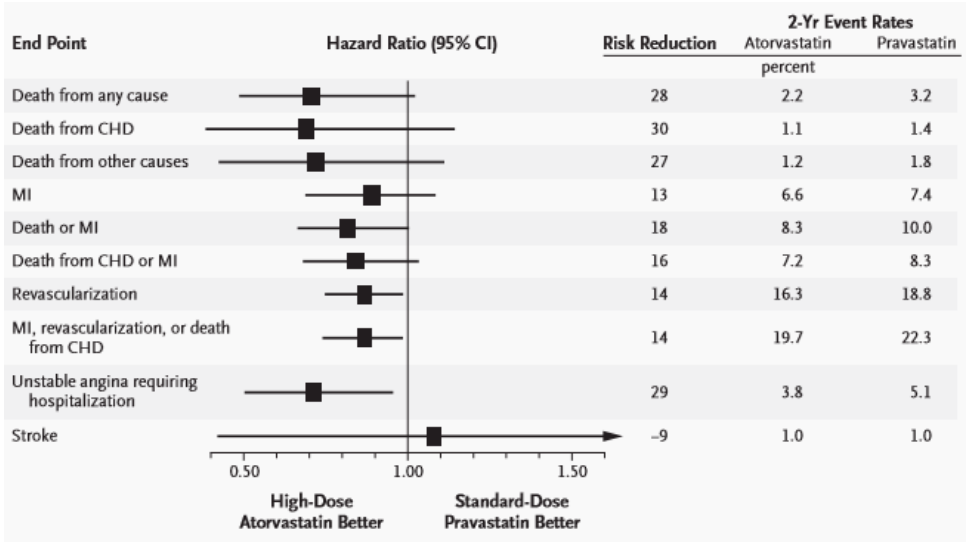


Prerandomisation LDL response			
Smaller (<38%)	700/3516 (19·9%)	911/3558(25·6%)	0·08
Average	649/3252 (20·0%)	822/3272(25·1%)	
Larger (≥48%)	684/3501 (19·5%)	852/3437(24·8%)	

Intensive versus Moderate Lipid Lowering with Statins after Acute Coronary Syndromes

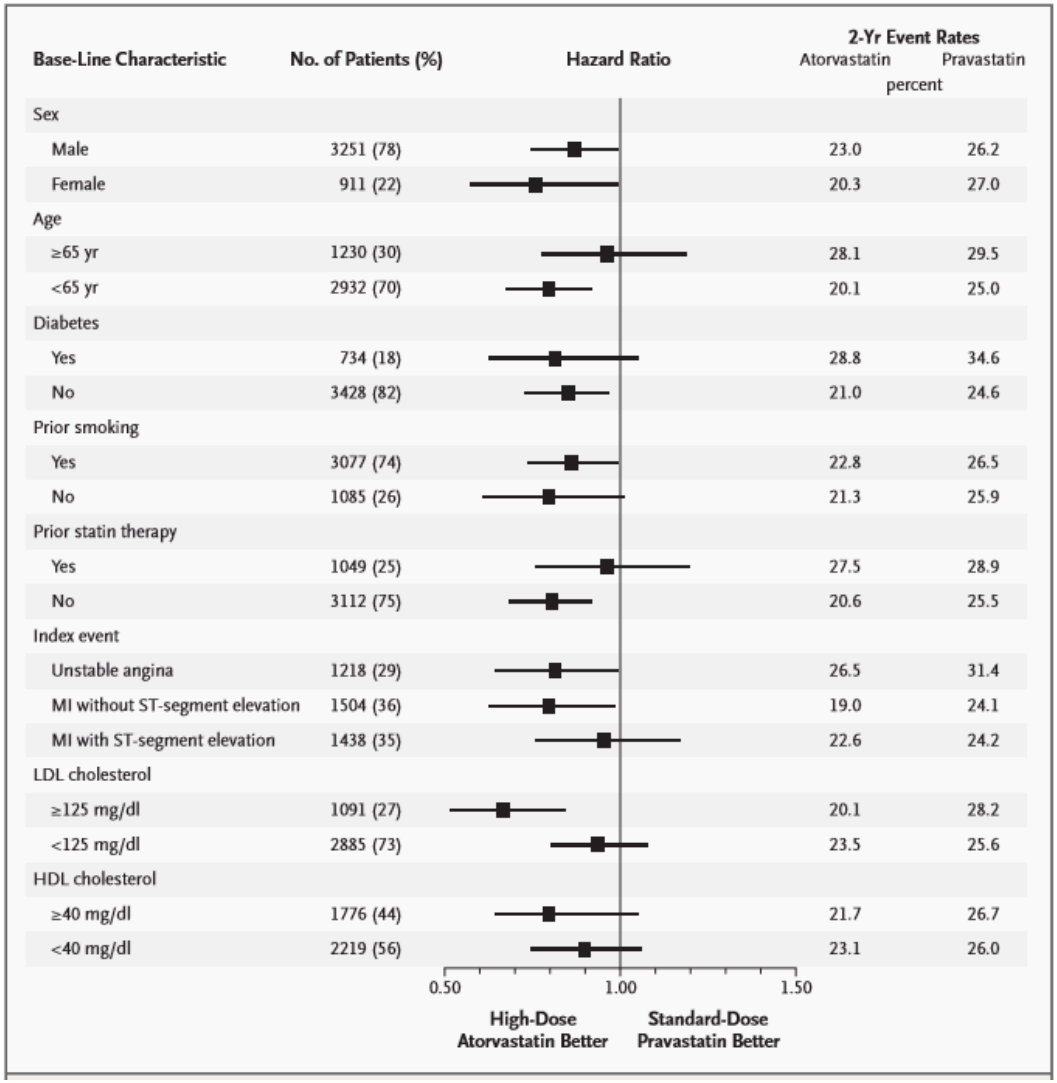


No. at Risk						
Pravastatin	2063	1688	1536	1423	810	138
Atorvastatin	2099	1736	1591	1485	842	133



End Point	Hazard Ratio (95% CI)	Risk Reduction	2-Yr Event Rates	
			Atorvastatin	Pravastatin
		percent		
Death from any cause		28	2.2	3.2
Death from CHD		30	1.1	1.4
Death from other causes		27	1.2	1.8
MI		13	6.6	7.4
Death or MI		18	8.3	10.0
Death from CHD or MI		16	7.2	8.3
Revascularization		14	16.3	18.8
MI, revascularization, or death from CHD		14	19.7	22.3
Unstable angina requiring hospitalization		29	3.8	5.1
Stroke		–9	1.0	1.0

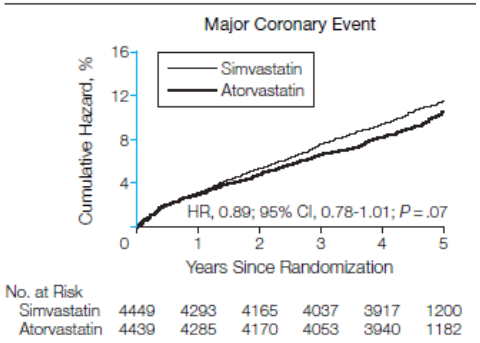
Intensive versus Moderate Lipid Lowering with Statins after Acute Coronary Syndromes



High intensity statin therapy

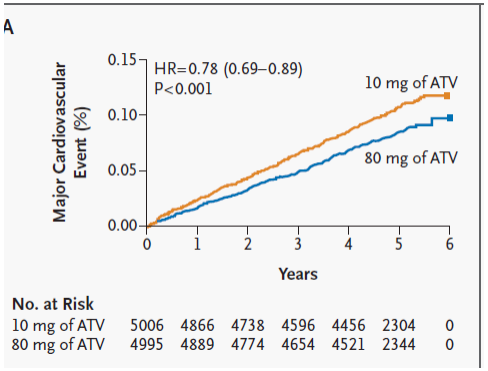
High-Dose Atorvastatin vs Usual-Dose Simvastatin for Secondary Prevention After Myocardial Infarction

The IDEAL Study: A Randomized Controlled Trial



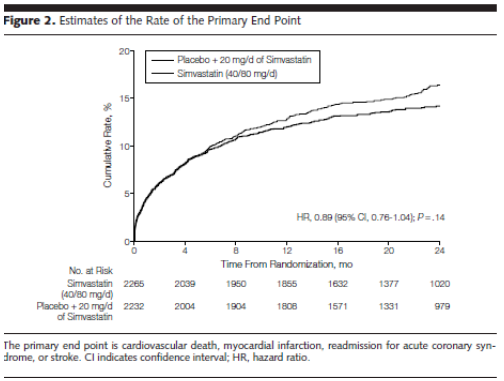
Intensive Lipid Lowering with Atorvastatin in Patients with Stable Coronary Disease

John C. LaRosa, M.D., Scott M. Grundy, M.D., Ph.D., David D. Waters, M.D., Charles Shear, Ph.D., Philip Barter, M.D., Ph.D., Jean-Charles Fruchart, Pharm.D., Ph.D., Antonio M. Gotto, M.D., D.Phil., Heiner Greten, M.D., John J.P. Kastelein, M.D., James Shepherd, M.D., and Nanette K. Wenger, M.D., for the Treating to New Targets (TNT) Investigators



Early Intensive vs a Delayed Conservative Simvastatin Strategy in Patients With Acute Coronary Syndromes

Phase Z of the A to Z Trial



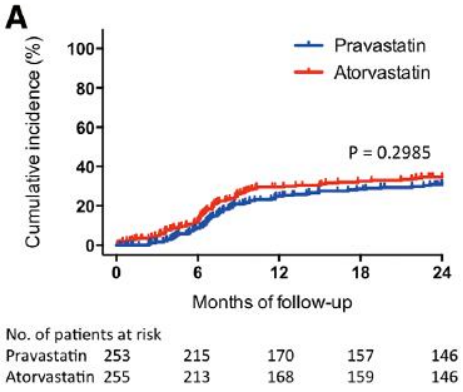
Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

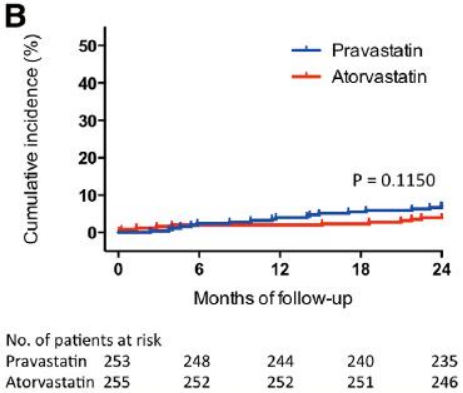
ORIGINAL ARTICLE
Ischemic Heart Disease

Assessment of Lipophilic vs. Hydrophilic Statin Therapy in Acute Myocardial Infarction

– ALPS-AMI Study –

Atsushi Izawa, MD; Yuichiro Kashima, MD; Takashi Miura, MD; Soichiro Ebisawa, MD; Hiroshi Kitabayashi, MD; Hiroaki Yamamoto, MD; Shunpei Sakurai, MD; Mitsuru Kagoshima, MD; Takeshi Tomita, MD; Yusuke Miyashita, MD; Jun Koyama, MD; Uichi Ikeda, MD
on behalf of the ALPS-AMI Investigators





On 2-year comparison of hydrophilic and lipophilic statins there was no significant difference in prevention of secondary cardiovascular outcome.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 18, 2015 VOL. 372 NO. 25

Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes

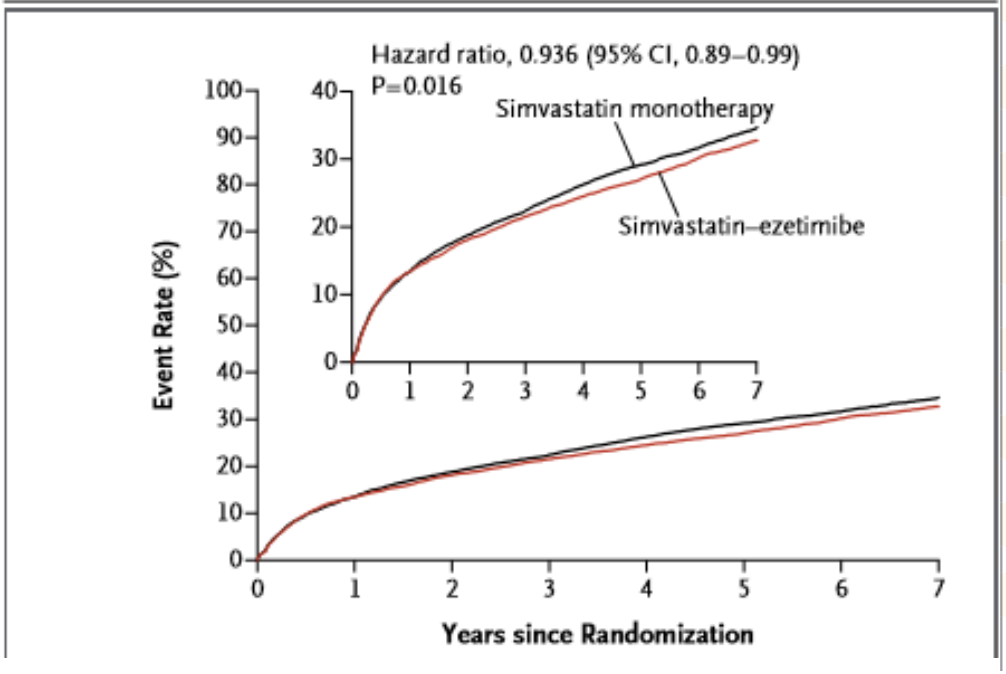
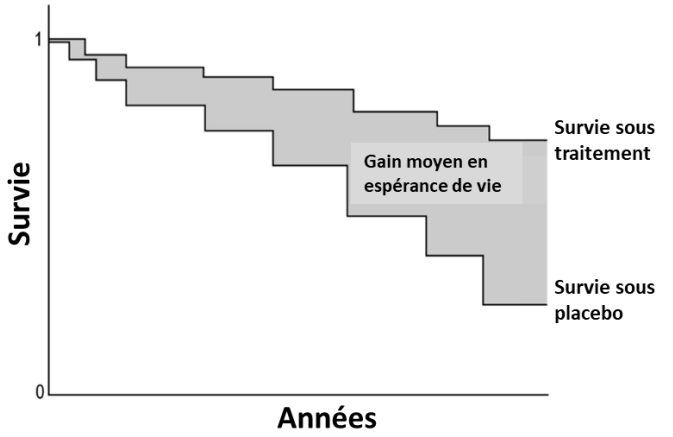


Table 2. Primary, Secondary, and Individual End Points.*

Outcome	Simvastatin Monotherapy (N=9077)	Simvastatin–Ezetimibe (N=9067)	Hazard Ratio (95% CI)	P Value
	no. of patients (%)			
Primary end point: death from cardiovascular causes, major coronary event, or nonfatal stroke	2742 (34.7)	2572 (32.7)	0.936 (0.89–0.99)	0.016
Secondary end points				
Death from any cause, major coronary event, or nonfatal stroke	3246 (40.3)	3089 (38.7)	0.95 (0.90–1.0)	0.03
Death from coronary heart disease, nonfatal MI, urgent coronary revascularization ≥30 days	1448 (18.9)	1322 (17.5)	0.91 (0.85–0.98)	0.02
Death from cardiovascular causes, nonfatal MI, hospitalization for unstable angina, all revascularization ≥30 days, nonfatal stroke	2869 (36.2)	2716 (34.5)	0.95 (0.90–1.0)	0.04
Tertiary end points†				
Death from any cause	1231 (15.3)	1215 (15.4)	0.99 (0.91–1.07)	0.78
Death from cardiovascular causes	538 (6.8)	537 (6.9)	1.00 (0.89–1.13)	1.00
Death from coronary heart disease	461 (5.8)	440 (5.7)	0.96 (0.84–1.09)	0.50
Any MI	1118 (14.8)	977 (13.1)	0.87 (0.80–0.95)	0.002
Nonfatal MI	1083 (14.4)	945 (12.8)	0.87 (0.80–0.95)	0.002
Fatal MI	49 (0.7)	41 (0.5)	0.84 (0.55–1.27)	0.41
Any stroke	345 (4.8)	296 (4.2)	0.86 (0.73–1.00)	0.05
Ischemic stroke	297 (4.1)	236 (3.4)	0.79 (0.67–0.94)	0.008
Hemorrhagic stroke	43 (0.6)	59 (0.8)	1.38 (0.93–2.04)	0.11
Coronary revascularization ≥30 days after randomization	1793 (23.4)	1690 (21.8)	0.95 (0.89–1.01)	0.11
Urgent coronary revascularization ≥30 days after randomization	626 (8.6)	510 (7.0)	0.81 (0.72–0.91)	0.001
Any revascularization ≥30 days after randomization	1962 (25.6)	1871 (24.2)	0.96 (0.90–1.02)	0.18
Hospitalization for unstable angina	148 (1.9)	156 (2.1)	1.06 (0.85–1.33)	0.62
Other prespecified end points				
Death from cardiovascular causes, MI, or stroke	1704 (22.2)	1544 (20.4)	0.90 (0.84–0.96)	0.003
Major vascular events: death from coronary heart disease, MI, stroke, or coronary revascularization ≥30 days after randomization‡	2685 (34.0)	2498 (31.9)	0.928 (0.88–0.98)	0.007

Impact des statines sur l'espérance de vie



- 17.4 days (PI, 6.0–28.8) for secondary prevention

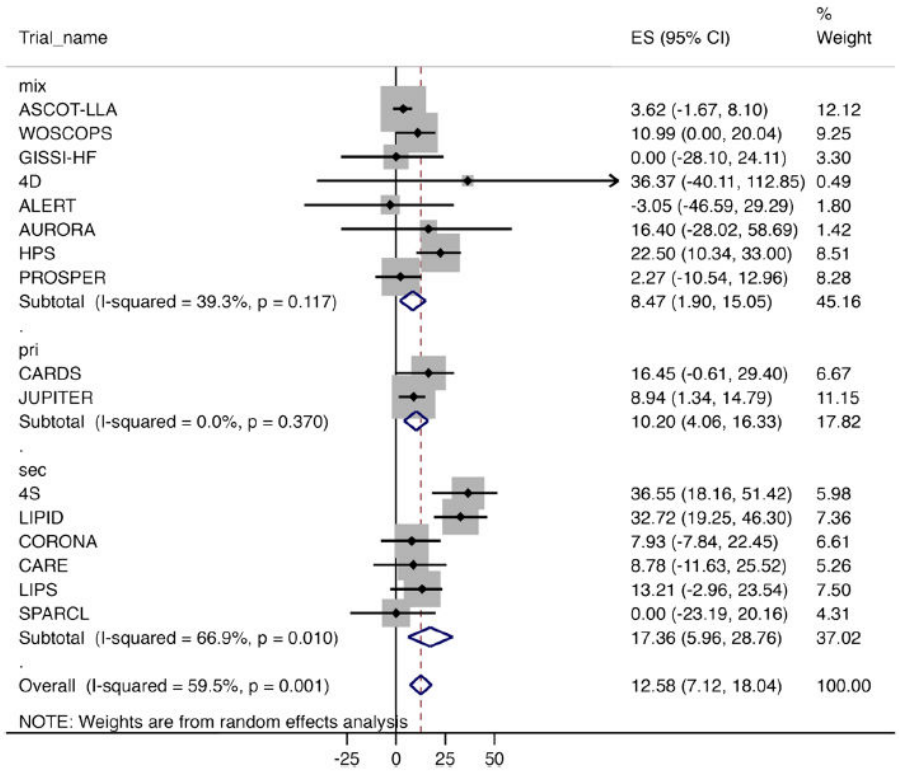


Figure 2 Forest plots of postponement of all-cause mortality.


PRIMARY
PREVENTION
S
HIGH RISK!
MI
MYOCARDIAL
INFARCTION

The New England
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Volume 333 NOVEMBER 16, 1995 Number 20

PREVENTION OF CORONARY HEART DISEASE WITH PRAVASTATIN IN MEN WITH HYPERCHOLESTEROLEMIA

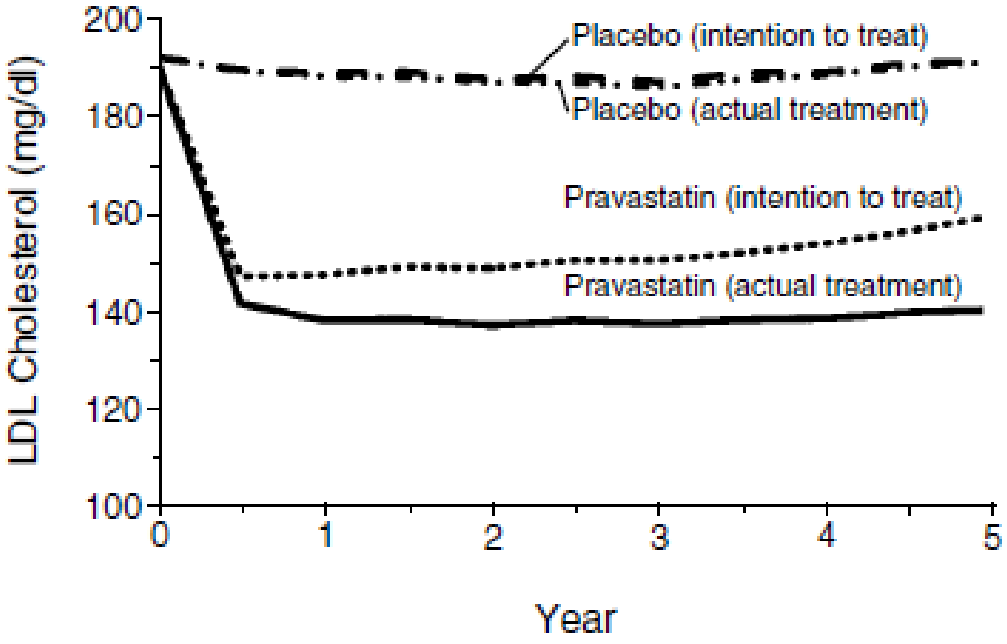
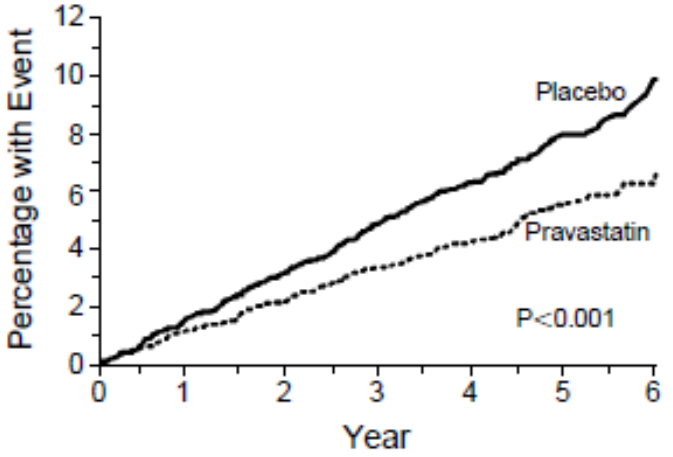


Figure 1. Effects of Pravastatin Therapy on Plasma LDL Cholesterol Levels.

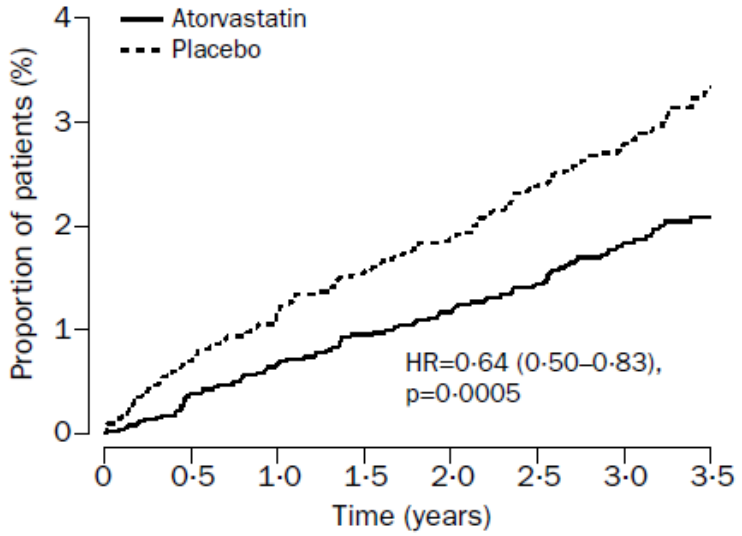


Placebo							
Cumulative events	0	55	105	159	205	240	248
No. at risk	3293	3230	3167	3099	2714	1241	83
Pravastatin							
Cumulative events	0	40	72	109	138	167	174
No. at risk	3302	3256	3215	3162	2807	1330	99

Figure 2. Kaplan–Meier Analysis of the Time to a Definite Nonfatal Myocardial Infarction or Death from Coronary Heart Disease, According to Treatment Group.

Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial

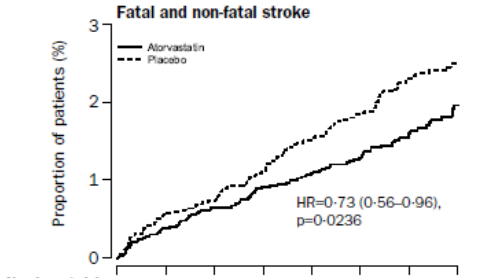
Early closure of the lipid-lowering arm



Number at risk

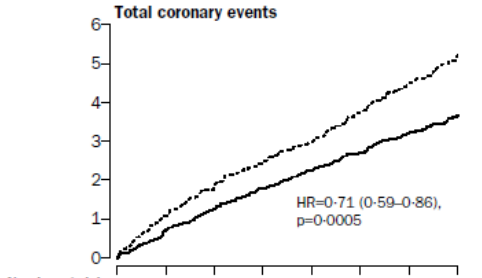
Placebo	5137	5085	5042	5007	4964	4603	3259	1801
Atorvastatin	5168	5134	5103	5063	5035	4679	3263	1801

Figure 2: **Cumulative incidence for primary endpoint of non-fatal myocardial infarction and fatal coronary heart disease**



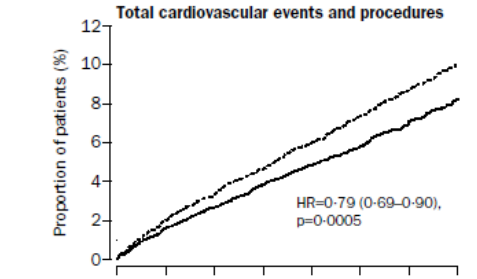
Number at risk

Placebo	5137	5085	5051	5014	4968	4609	3257	1808
Atorvastatin	5168	5128	5093	5054	5022	4669	3257	1797



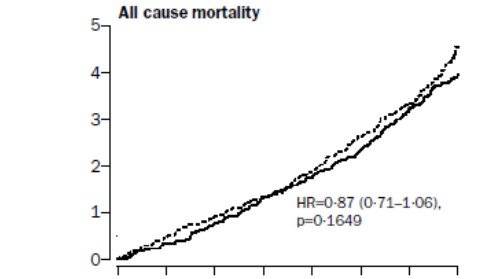
Number at risk

Placebo	5137	5064	5005	4961	4909	4540	3202	1764
Atorvastatin	5168	5115	5071	5020	4979	4618	3208	1772



Number at risk

Placebo	5137	5022	4939	4862	4775	4390	3066	1687
Atorvastatin	5168	5075	5007	4928	4861	4487	3090	1702

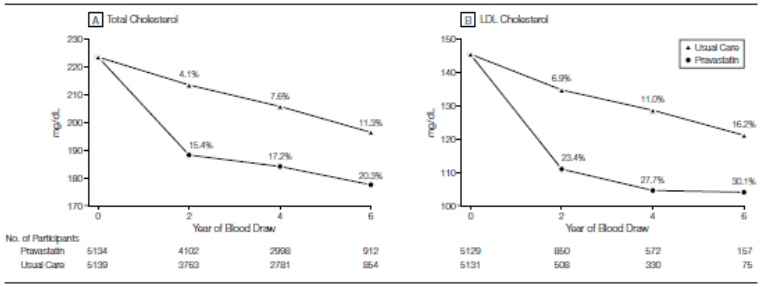


Number at risk

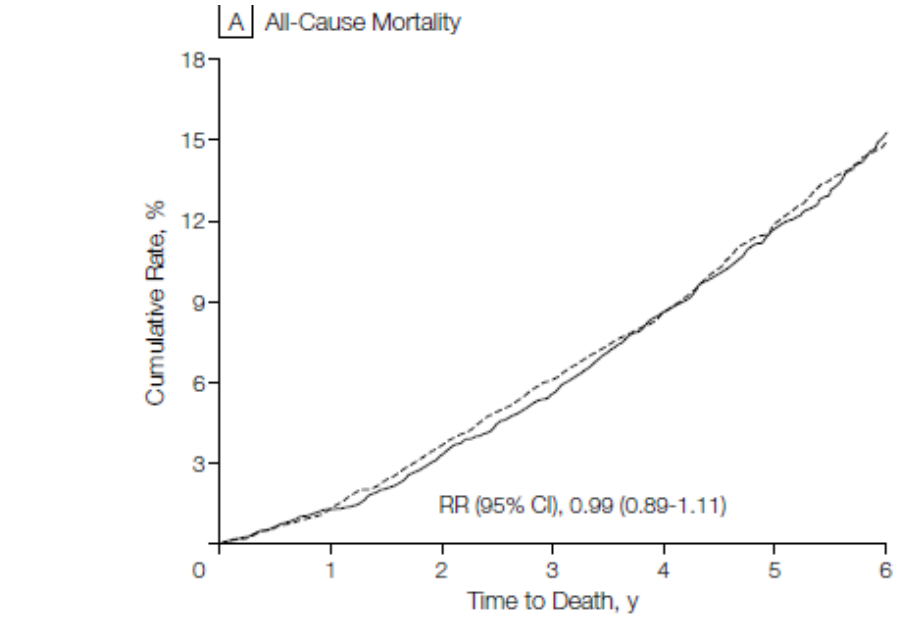
Placebo	5137	5110	5083	5061	5030	4680	3320	1846
Atorvastatin	5168	5147	5123	5094	5070	4719	3299	1821

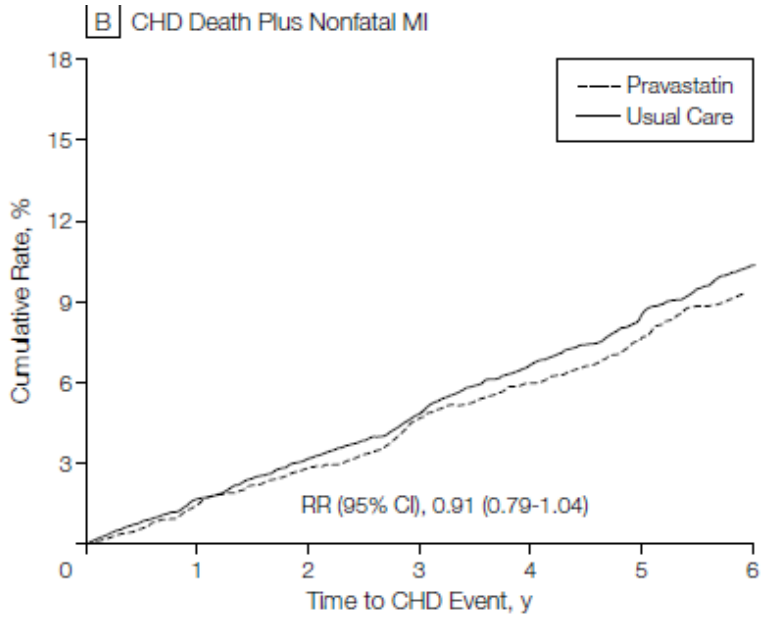
Major Outcomes in Moderately Hypercholesterolemic, Hypertensive Patients Randomized to Pravastatin vs Usual Care

The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT-LLT)

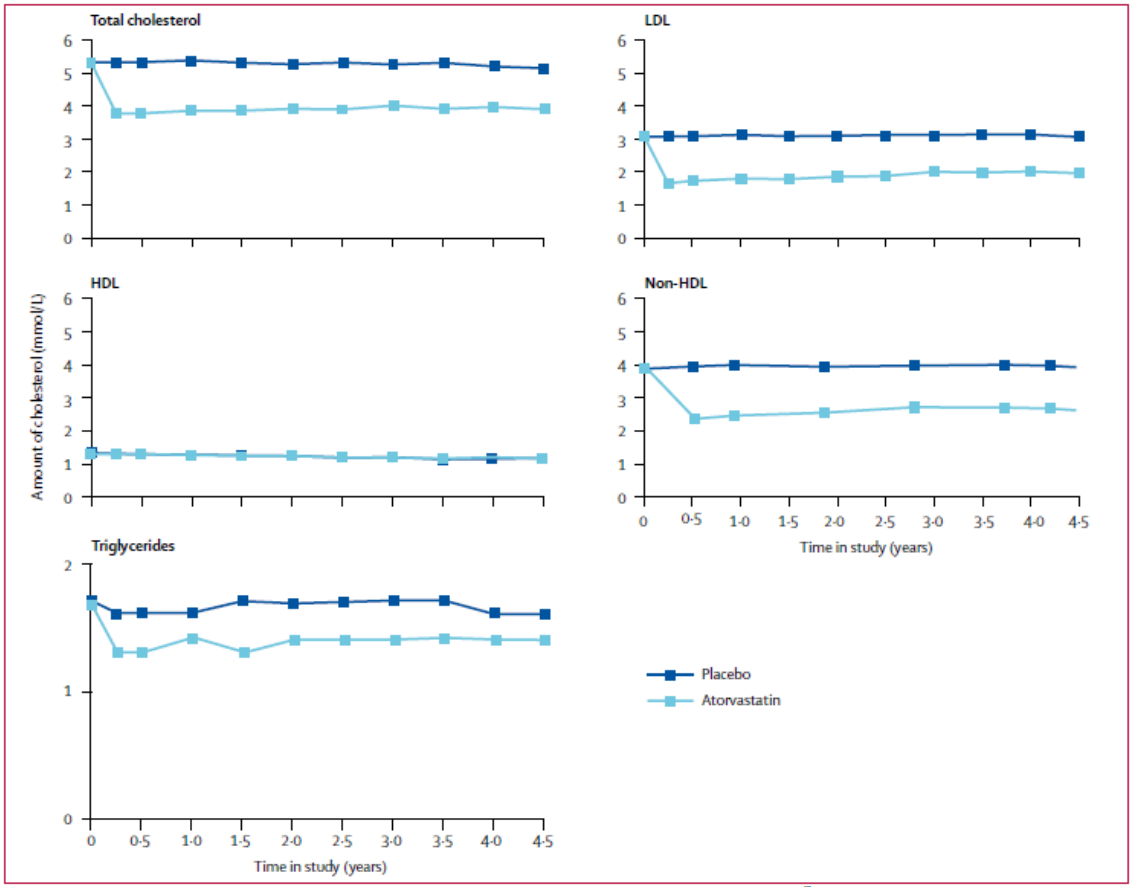


LDL indicates low-density lipoprotein. The percentage decrease from baseline is shown above each time point. To convert values to mmol/L, multiply by 0.0259.

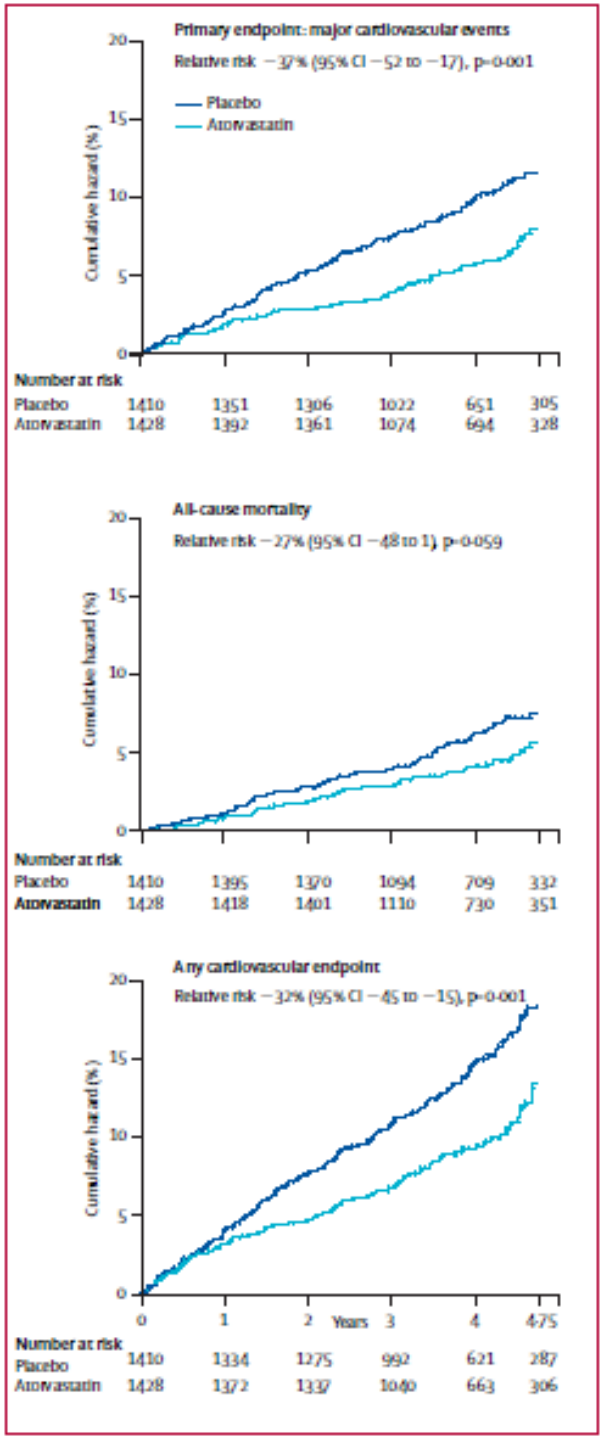




Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial



The trial was stopped 2 years earlier than planned because of significant benefit at the second interim analysis.

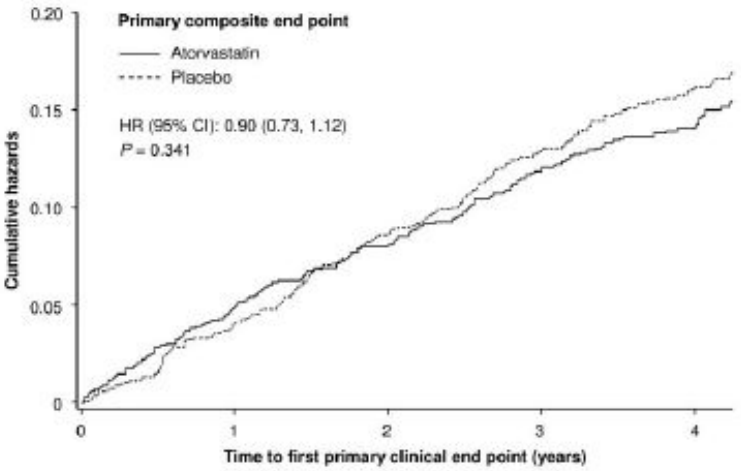


Efficacy and Safety of Atorvastatin in the Prevention of Cardiovascular End Points in Subjects With Type 2 Diabetes

The Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in Non-Insulin-Dependent Diabetes Mellitus (ASPEN)

	All subjects		Primary prevention		Secondary prevention	
	Atorvastatin	Placebo	Atorvastatin	Placebo	Atorvastatin	Placebo
n	1,211	1,199	959	946	252	253
Age (years)	61.1 ± 8.1	61.0 ± 8.2	60.5 ± 8.3	60.4 ± 8.3	63.1 ± 7.2	63.2 ± 7.4
≥65	448 (37)	422 (35)	332 (35)	305 (32)	116 (46)	117 (46)
Men	796 (66)	803 (67)	593 (62)	594 (63)	203 (81)	209 (83)
Race						
Caucasian	1,018 (84)	1,011 (84)	805 (84)	792 (84)	213 (85)	219 (87)
Black	81 (6.7)	74 (6.2)	73 (7.6)	68 (7.2)	8 (3.2)	6 (2.4)
BMI (kg/m^2)	28.9 ± 3.7	28.8 ± 3.8	28.9 ± 3.7	28.8 ± 3.7	28.9 ± 3.7	28.9 ± 3.8
Current smokers	147 (12)	153 (13)	119 (12)	132 (14)	28 (11)	21 (8)
Median duration of diabetes (years)	8.0	8.0	8.0	8.0	8.0	10.0
Blood pressure (mmHg)						
Systolic	133.1 ± 16.8	133.4 ± 16.4	133.0 ± 17.0	133.0 ± 16.7	133.6 ± 16.0	134.9 ± 15.3
Diastolic	76.9 ± 9.1	76.3 ± 9.0	77.1 ± 8.8	76.7 ± 8.8	76.0 ± 10.0	74.9 ± 9.6
History of hypertension	671 (55)	657 (55)	498 (52)	499 (53)	173 (69)	158 (63)
History of hyperlipidemia	343 (28)	369 (31)	265 (28)	275 (29)	78 (31)	94 (37)
Glomerular filtration rate (ml/min per 1.73 m^2)	65.7 ± 11.5	65.8 ± 11.9	66.1 ± 11.4	66.7 ± 11.8	64.0 ± 11.6	62.6 ± 11.9
CVD history						
Myocardial infarction	208 (17)	187 (16)	0	0	208 (83)	187 (74)
Interventional procedure	145 (12)	170 (14)	0	0	145 (58)	170 (67)
Angina	200 (17)	195 (16)	55 (6)	47 (5)	145 (58)	148 (58)
Peripheral arterial disease	101 (8)	107 (9)	64 (7)	53 (6)	37 (15)	54 (21)
Cerebrovascular disease	61 (5)	62 (5)	38 (4)	32 (3)	23 (9)	30 (12)
Arrhythmia	108 (9)	119 (10)	67 (7)	77 (8)	41 (16)	42 (17)
LDL cholesterol (mg/dl)						
Baseline	113 ± 25	114 ± 26	114 ± 26	114 ± 26	112 ± 24	113 ± 25
End of treatment (% change)	−30.29	−1.09	−30.48	−0.48	−29.65	−3.31
P value (% change)	<0.0001		<0.0001		<0.0001	
Total cholesterol (mg/dl)						
Baseline	194 ± 31	194 ± 31	195 ± 31	195 ± 31	188 ± 26	191 ± 29
End of treatment (% change)	−19.70	−1.41	−19.78	−1.38	−19.47	−1.45
P value (% change)	<0.0001		<0.0001		<0.0001	
HDL cholesterol (mg/dl)						
Baseline	47 ± 14	47 ± 13	48 ± 14	47 ± 13	42 ± 11	44 ± 12
End of treatment (% change)	2.17	−0.18	1.93	−0.33	2.98	0.52
P value (% change)	0.0005		0.002		0.143	
Triglycerides (mg/dl)						
Baseline	147 (101–208)	145 (102–213)	145 (99–205)	144.5 (103–211)	151.5 (104–219)	147 (99–219)
End of treatment (% change)	−3.90	10.01	−4.72	7.24	−0.79	20.44
P value (% change)	<0.0001		<0.0001		0.0005	
A1C (%)	7.6 ± 1.2	7.5 ± 1.3	7.6 ± 1.2	7.6 ± 1.3	7.6 ± 1.3	7.4 ± 1.2
Baseline	7.8 ± 1.4	7.7 ± 1.4	7.8 ± 1.4	7.7 ± 1.4	7.9 ± 1.5	7.8 ± 1.4
End of treatment						

A



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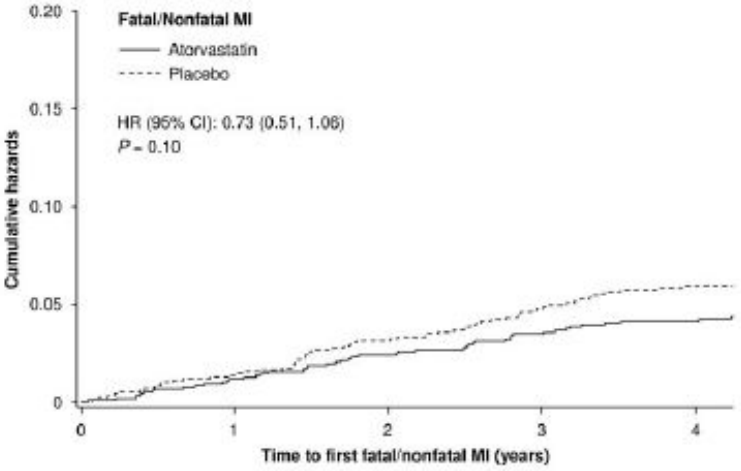


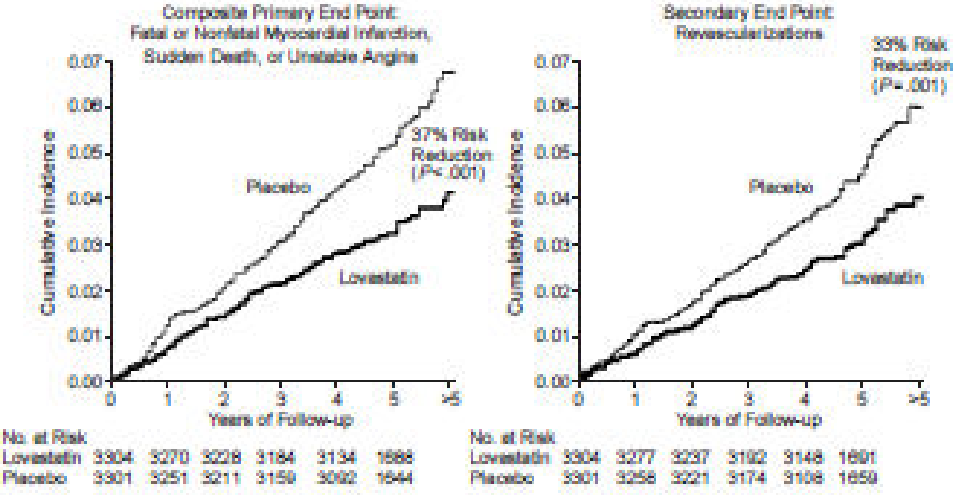
Primary Prevention of Acute Coronary Events With Lovastatin in Men and Women With Average Cholesterol Levels

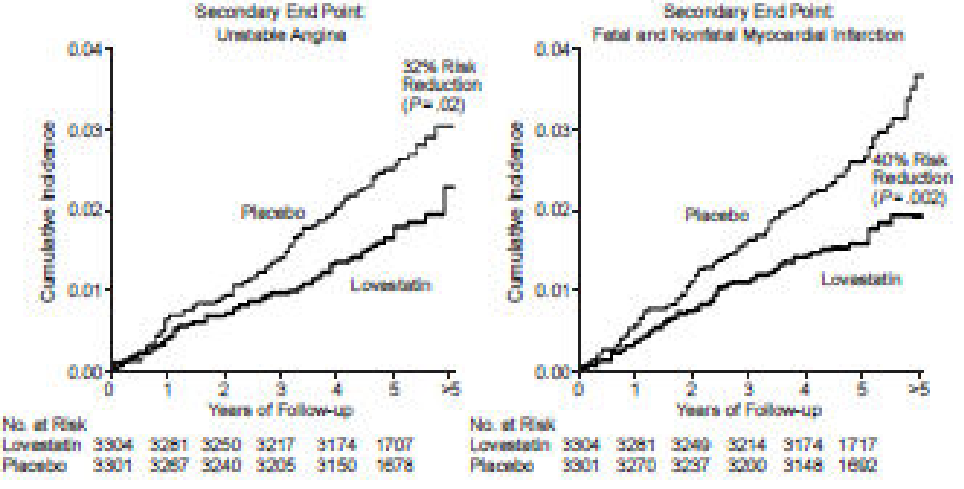
Results of AFCAPS/TexCAPS

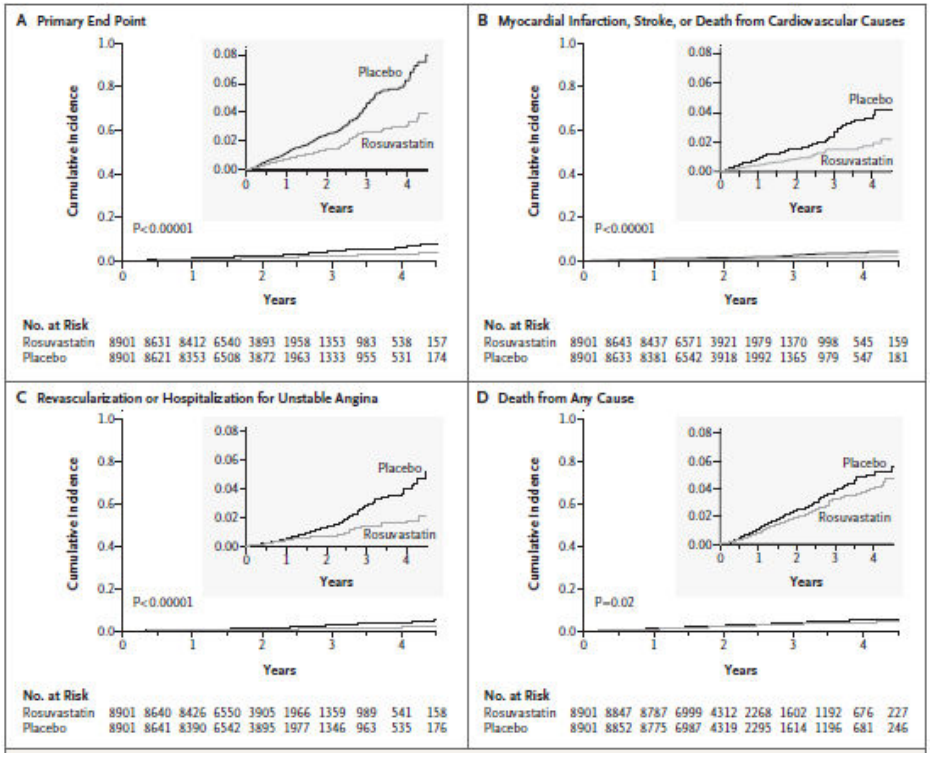
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 20, 2008 VOL. 359 NO. 21

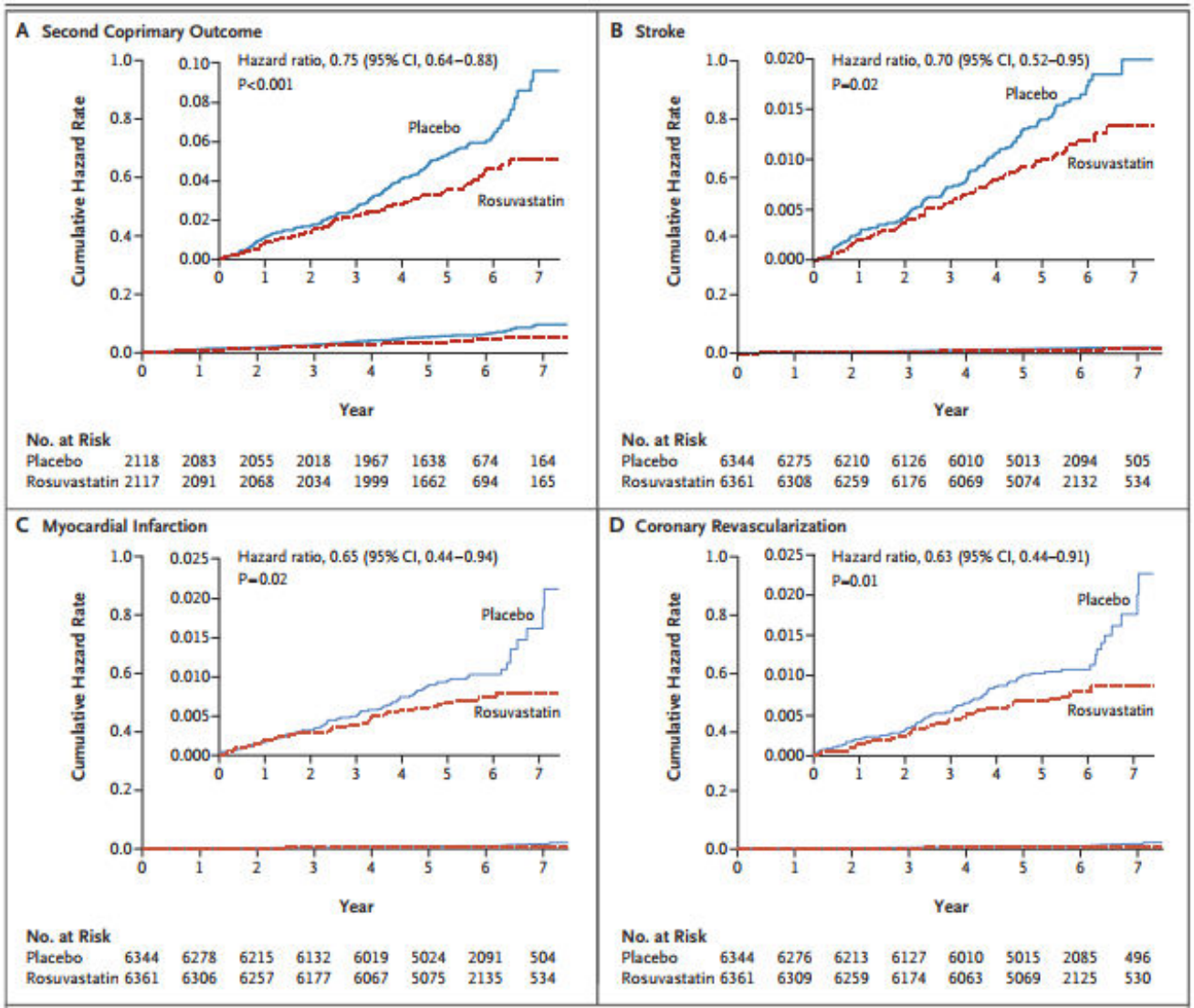
Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein







Cholesterol Lowering in Intermediate-Risk Persons without Cardiovascular Disease



Impact des statines sur l'espérance de vie

- 8.5 days (PI, 1.90–15.05) for primary prevention

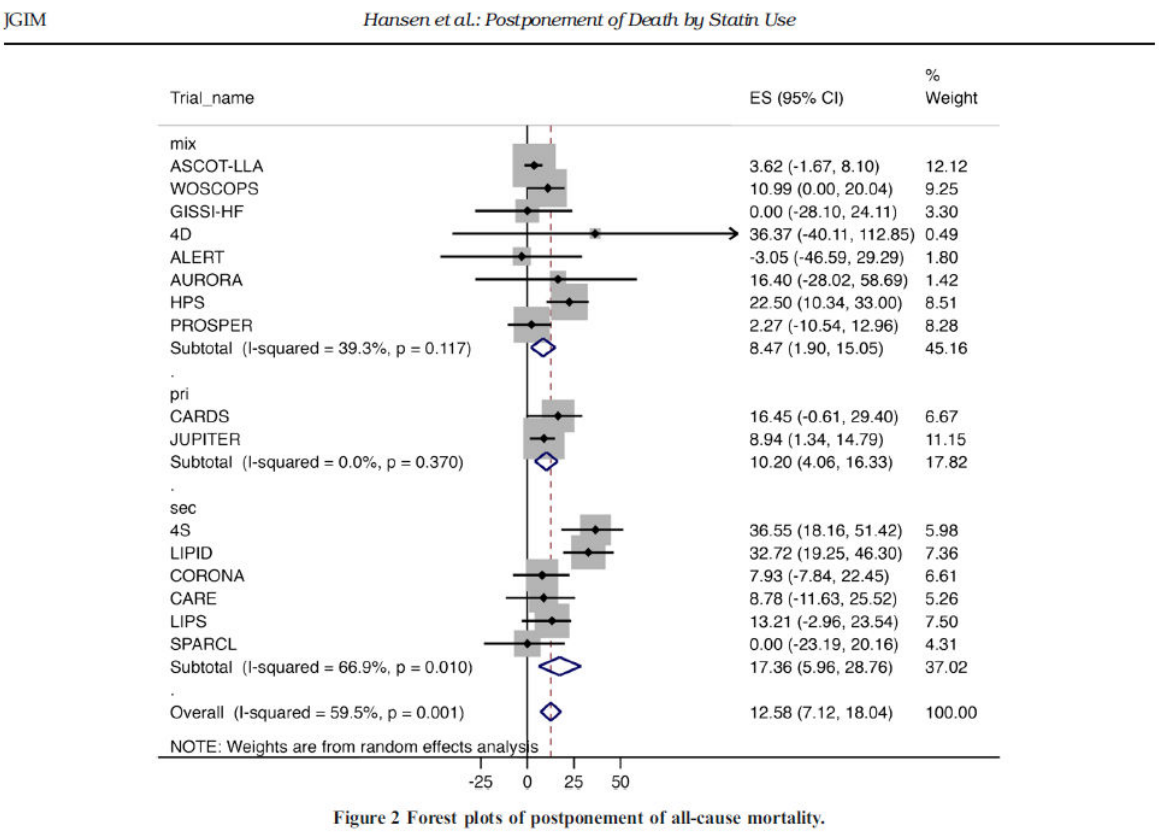
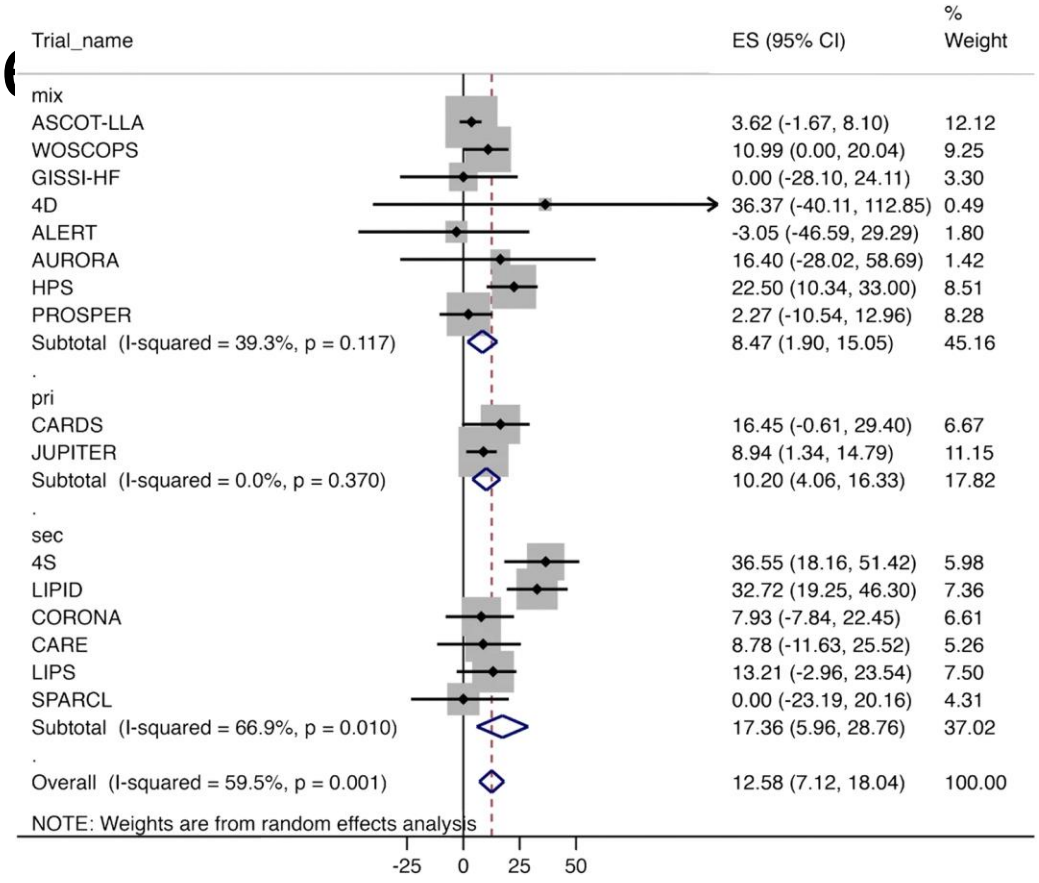


Figure 2 Forest plots of postponement of all-cause mortality.

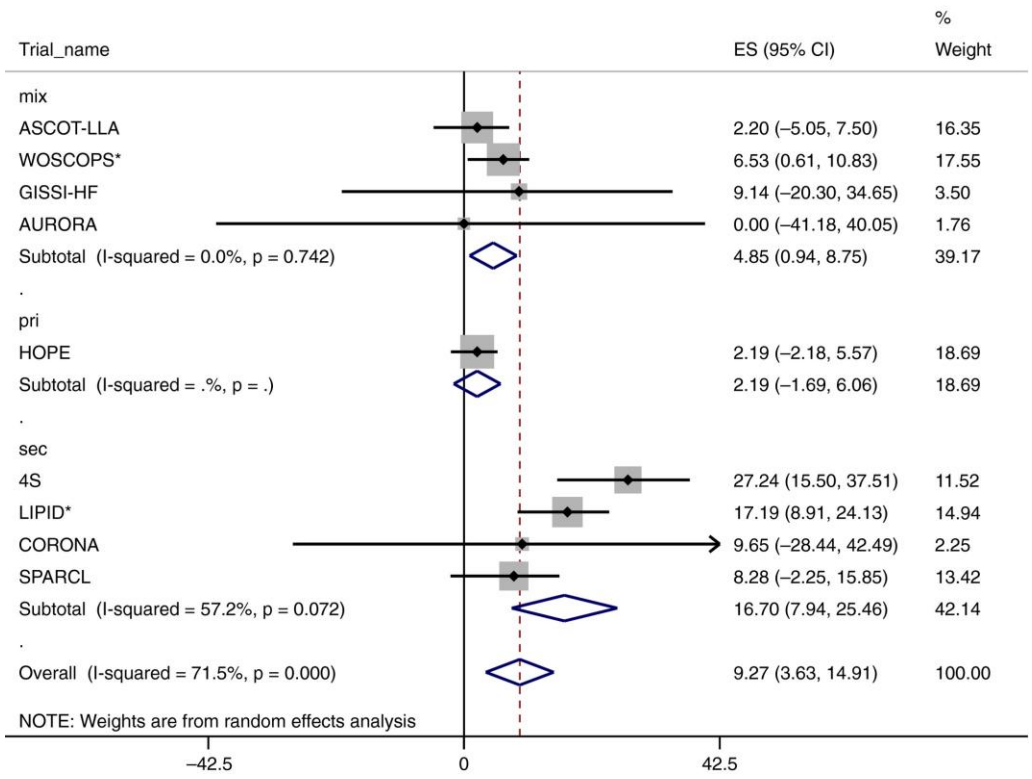
Postponement of Death by Statin Use: a Systematic Review and Meta-analysis of Randomize

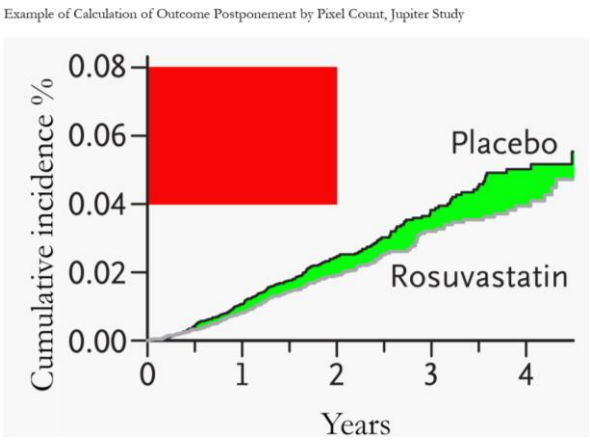
Meta-analysis of 16 trials provided a summary estimate of outcome postponement for all-cause mortality of 12.6 days, with a 95% postponement interval (PI) of 7.1–18.0. For primary, secondary, and mixed prevention trials, respectively, outcome postponements were 10.2 days (PI, 4.0–16.3), 17.4 days (PI, 6.0–28.8), and 8.5 days (PI, 1.9–15.0).

Journal of General Internal Medicine **volume 34**, pages1607–1614 (2019)



Postponement of cardiovascular outcomes by statin use: A systematic review and meta-analysis of randomized clinical trials





Summary outcome postponement in days as follows: CV mortality, 9.27 days (95% CI: 3.6 to 14.91; I^2 = 72%; 9 trials) non-vascular and non-CV mortality, 1.5 days (95% CI: −2.2 to 5.3; I^2 = 0%; 6 trials) any myocardial infarction 18.0 days (95% CI; 12.1 to 24.1; I^2 = 92%; 15 trials); and any stroke, 6.1 days (95% CI; 2.86 to 9.39; I^2 = 66%; 14 trials)

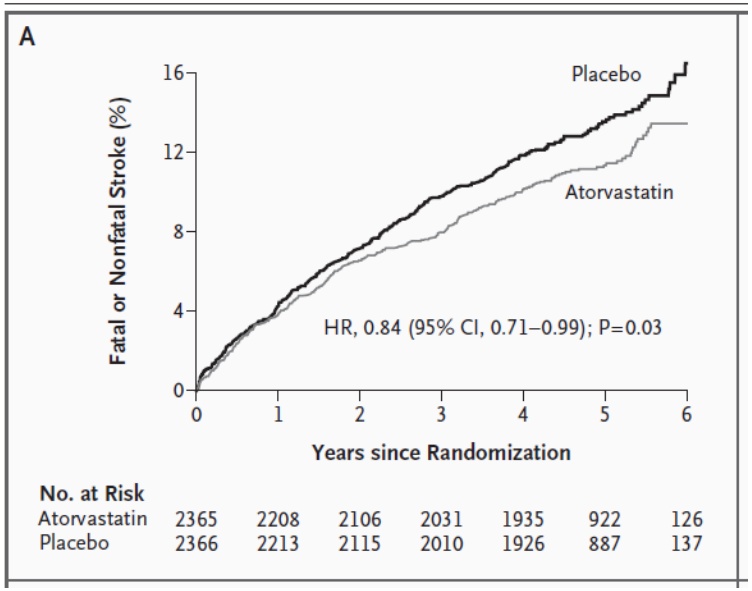
Basic Clin Pharma Tox, Volume: 128, Issue: 2, Pages: 286-296, First published: 07 September 2020, DOI: (10.1111/bcpt.13485)

NNT ? FI ? Postponement Gain ? LFU….

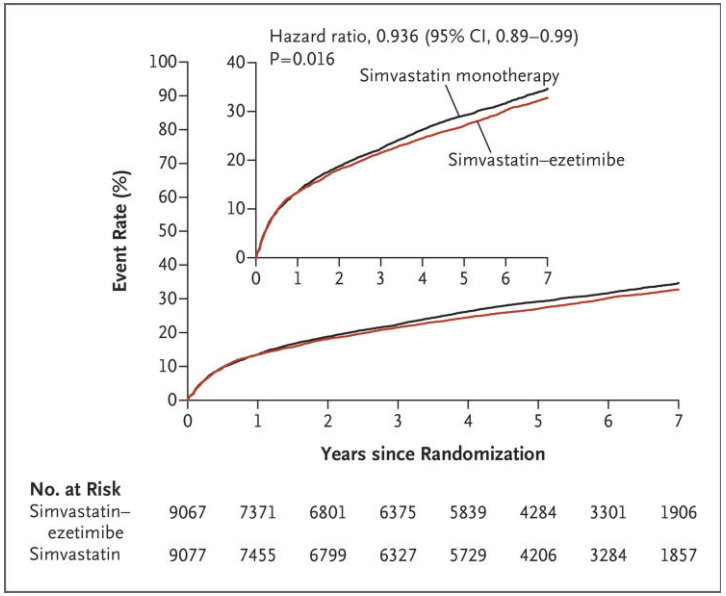
ESTABLISHED IN 1812 JUNE 18, 2015 VOL. 372 NO. 25

Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes

Statin Therapy after Stroke or Transient Ischemic Attack
FI 1; LFU 25; NNT 45; Gain 27 days



Ezetimibe Added to Statin Therapy after ACS
FI 47; LFU 168; NNT 50; Gain 35 days



The effect of statins on average survival in randomised trials, an analysis of end point postponement

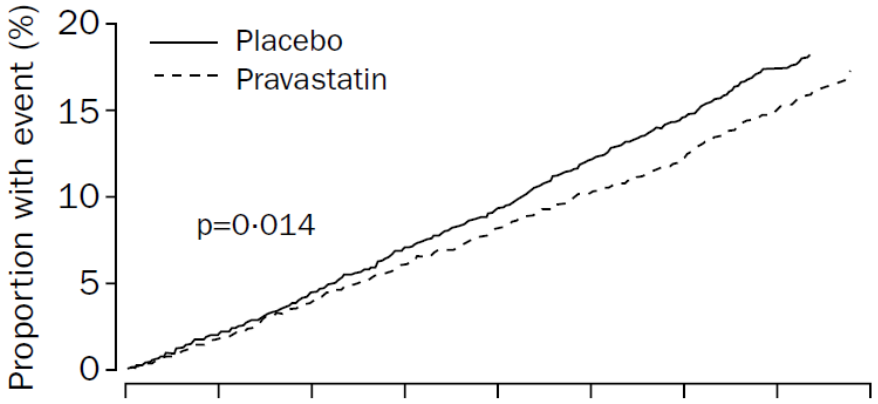
Study ID, reference, publication year	Number included	Intervention/ comparator	Prevention	Cut point, years	Dead: statin/ control, %	RR (95% CI)	NNT	Postponement, days (SD)
ALLHAT-LLT[22] 2002	10 355	Pravastatin (40 mg) vs usual care	Primary	6	14.9/15.3	0.99 (0.89 to 1.11)	250	–4.96 (0.06)
ASCOT-LLA[23] 2003	19 342	Atorvastatin (10 mg) vs placebo	Primary	3.5	3.6/4.1	0.87 (0.71 to 1.06)	200	1.99 (0.04)
CARDS[24] 2004	2838	Atorvastatin (10 mg) vs placebo	Primary	4.8	4.3/5.8	0.73 (0.52 to 1.01)	66.7	18.66 (0.04)
JUPITER[25] 2008	17 802	Rosuvastatin (20 mg) vs placebo	Primary	4	2.22/2.77	0.80 (0.67 to 0.97)	31	7.26 (0.01)
MEGA[26] 2006	7832	Pravastatin (5–20 mg) vs no treatment	Primary	5	1.11/1.66	0.68 (0.46 to 1.00)	182	4.42 (0.01)
WOSCOPS[27] 1995	6595	Pravastatin (40 mg) vs placebo	Primary	5	3.2/4.1	0.78 (0.60 to 1.00)	111	9.33 (0.10)
4S[28] 1994	4444	Simvastatin (10–40 mg) vs placebo	Secondary	5.8	8.7/12.3	0.7 (0.58 to 0.85)	27.8	27.18 (0.26)
GISSI-HF[29] 2008	4631	Rosuvastatin (10 mg) vs placebo	Secondary	4.4	28.8/28.1	1.00 (0.90 to 1.12)	–143	–9.51 (0.01)
GISSI-P[14] 2000	4271	Pravastatin (20 mg) vs no treatment	Secondary	2.0	3.37/4.13	0.84 (0.61 to 1.14)	132	1.76 (0.07)
LIPID[30] 1998	9014	Pravastatin (40 mg) vs placebo	Secondary	6.1	11.0/14.1	0.78 (0.69 to 0.87)	32.3	22.05 (0.21)
CORONA[13] 2007	5011	Rosuvastatin (10 mg) vs placebo	Secondary	2.7	29.0/30.4	0.95 (0.86 to 1.05)	71	4.09 (0.04)

Conclusions: Statin treatment results in a surprisingly small average gain in overall survival within the trials' running time. For patients whose life expectancy is limited or who have adverse effects of treatment, withholding statin therapy should be considered.

Statins and elderly

@ Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial

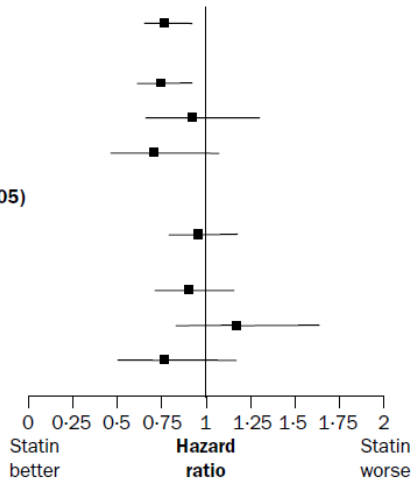
A



Number at risk

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

	Pravastatin	Placebo
Men	**(n=1396)**	**(n=1408)**
CHD death, non-fatal MI, and fatal or non-fatal stroke	222	279
CHD death, non-fatal MI	167	219
Fatal and non-fatal stroke	65	70
TIA	38	53
Women	**(n=1495)**	**(n=1505)**
CHD death, non-fatal MI, and fatal or non-fatal stroke	186	194
CHD death, non-fatal MI	125	137
Fatal and non-fatal stroke	70	61
TIA	39	49



5804 men (n=2804) and women (n=3000) aged 70–82 years with a history of, or risk factors for, vascular disease to pravastatin (40 mg per day; n=2891) or placebo (n=2913)

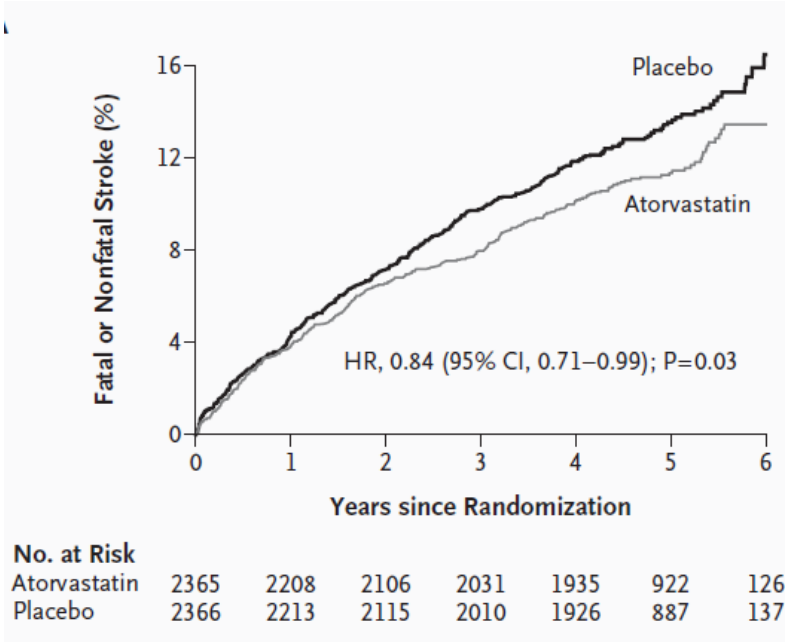
Statins and Stroke

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 10, 2006 VOL. 355 NO. 6

High-Dose Atorvastatin after Stroke or Transient Ischemic Attack

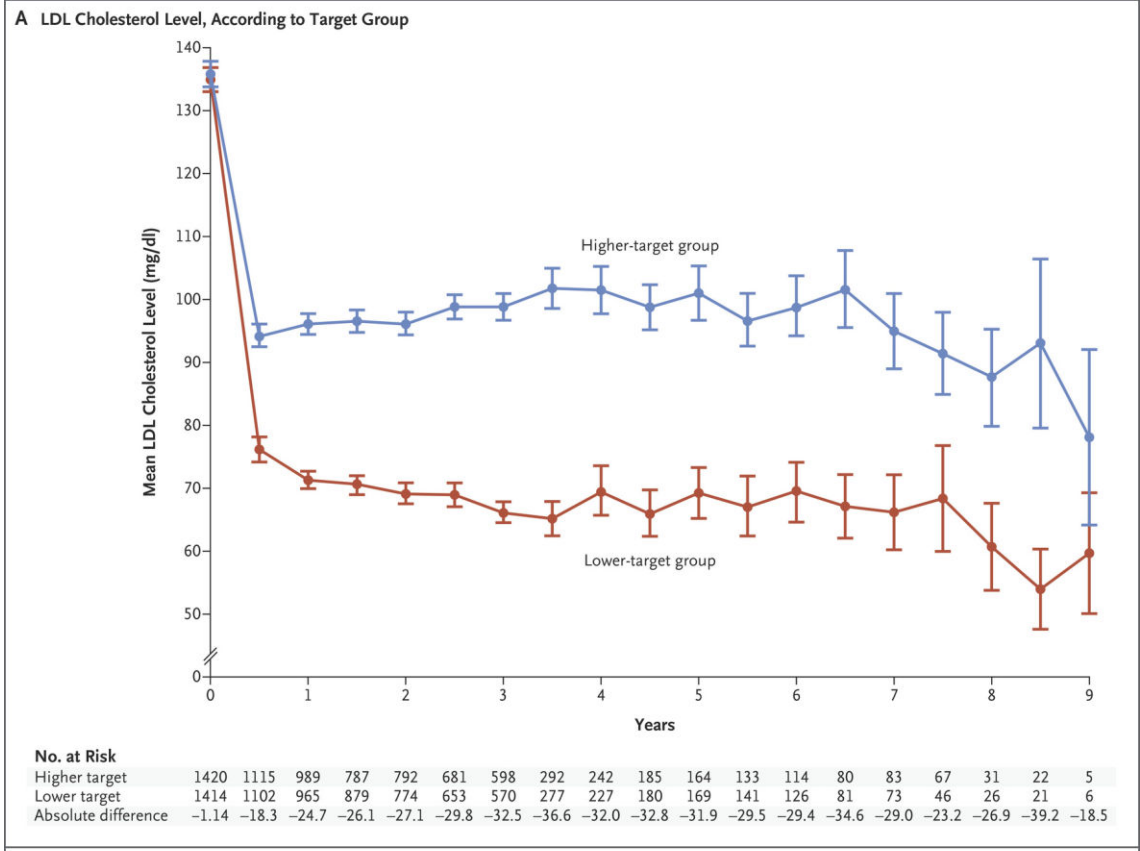
The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators*

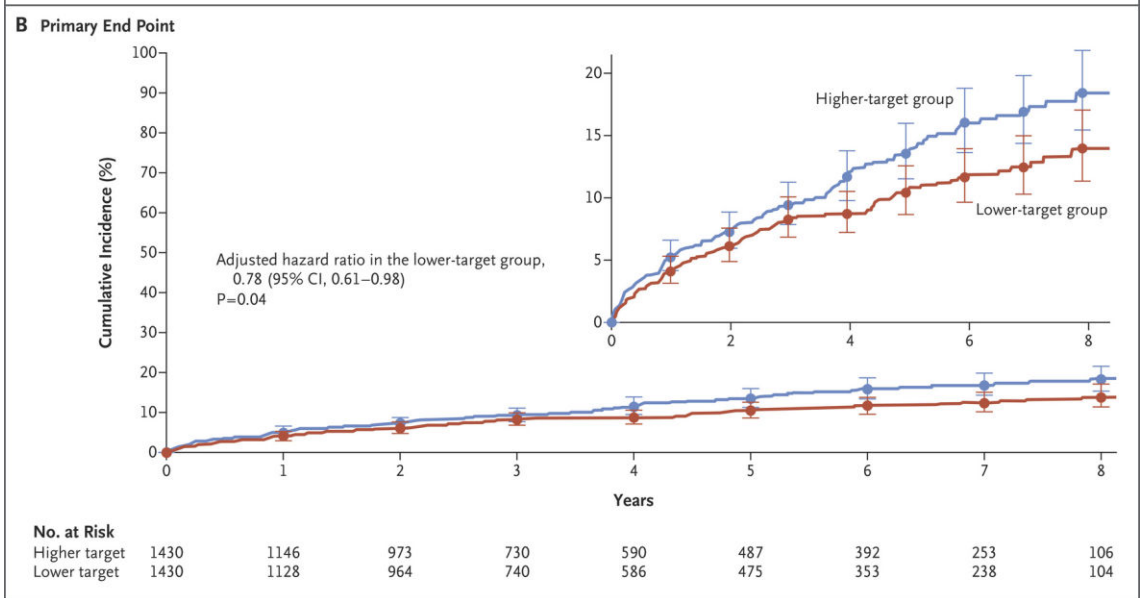


NNT 52 patients for 4,9 years
Fragility index: 1

TST trial

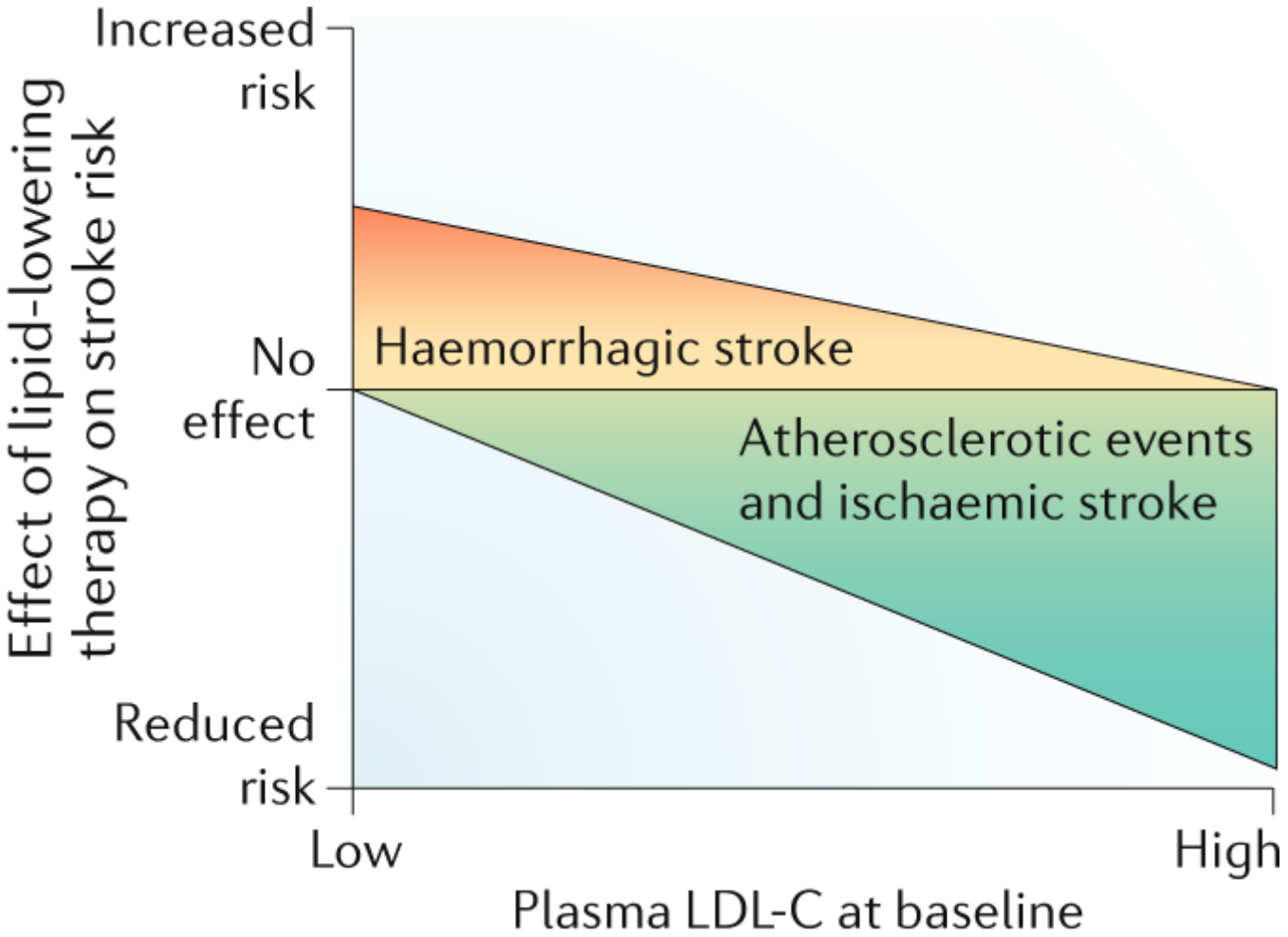
- a target LDL-c level of less than 70 mg per deciliter (lower-target group) or to a target range of 90 mg to 110 mg per deciliter (higher-target group)
- composite primary end point of ischemic stroke, myocardial infarction, new symptoms leading to urgent coronary or carotid revascularization, or death from CV causes.
- 85.4 days over 8.2 years of trial duration
- NNT 41
- FI 3 versus LFU 141





Recommendations	Class[a]	Level[b]
Patients with a history of ischaemic stroke or TIA are at very high-risk of ASCVD, particularly recurrent ischaemic stroke, so it is recommended that they receive intensive LDL-C-lowering therapy.[459,460]	I	A

Still a matter of debate…



Statins and Heart failure

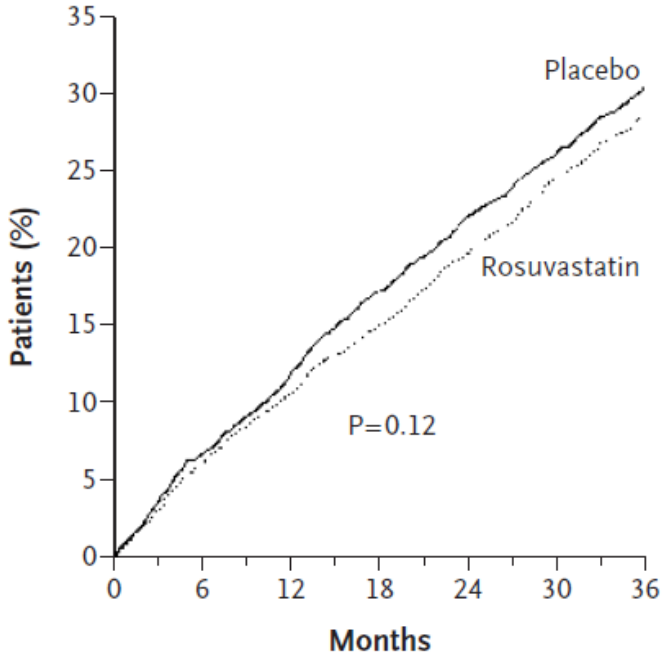
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of rosuvastatin in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial

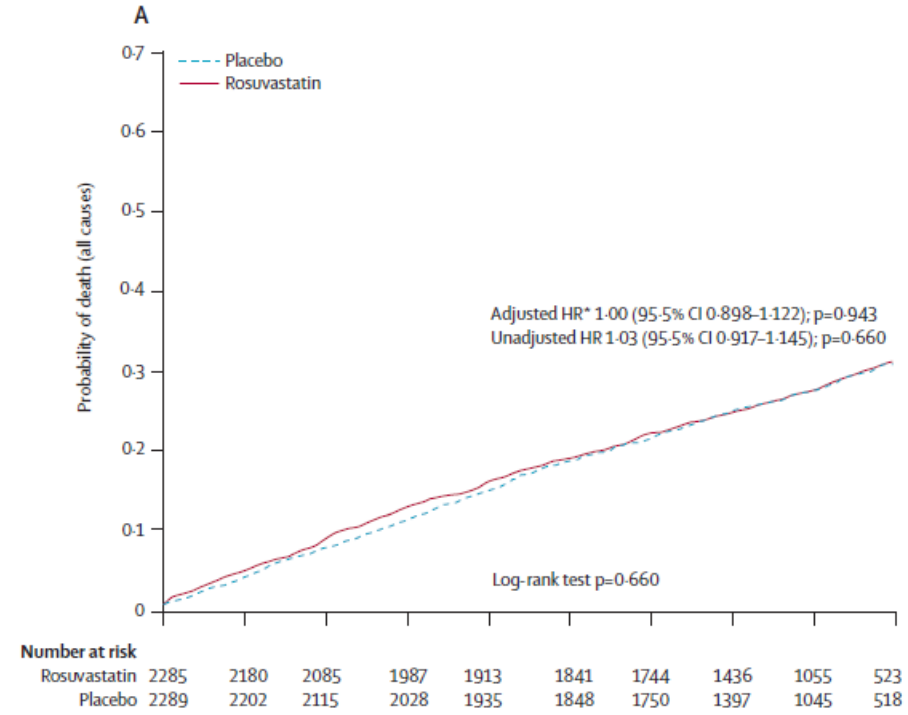
Rosuvastatin in Older Patients with Systolic Heart Failure

A Primary Outcome



No. at Risk

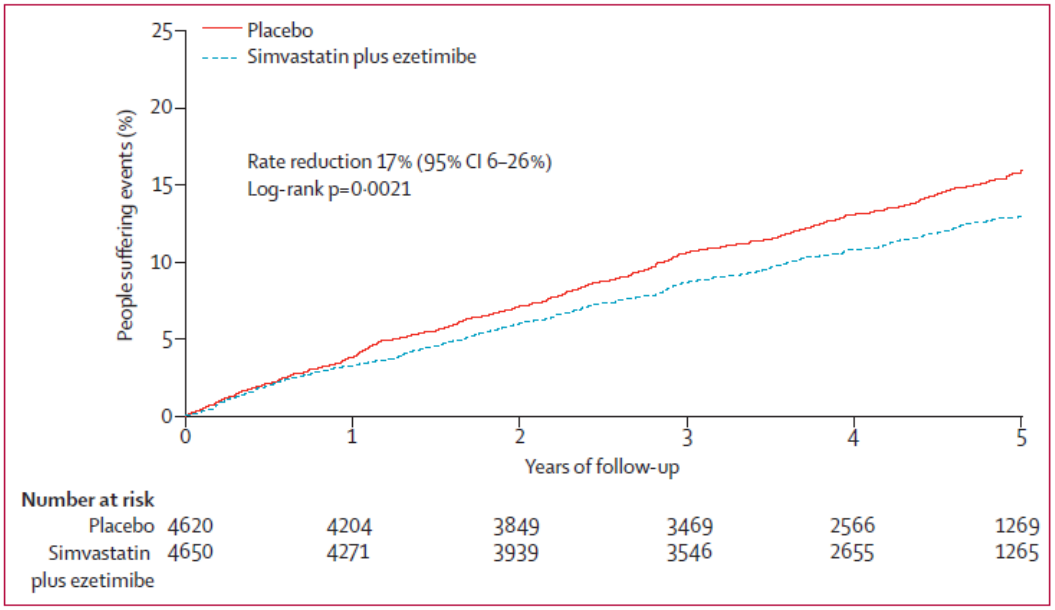
Placebo	2497	2315	2156	2003	1851	1431	811
Rosuvastatin	2514	2345	2207	2068	1932	1484	855



Statins and kidney failure

The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial

*Colin Baigent, Martin J Landray, Christina Reith, Jonathan Emberson, David C Wheeler, Charles Tomson, Christoph Wanner, Vera Krane, Alan Cass, Jonathan Craig, Bruce Neal, Lixin Jiang, Lai Seong Hooi, Adeera Levin, Lawrence Agodoa, Mike Gaziano, Bertram Kasiske, Robert Walker, Ziad A Massy Bo Feldt-Rasmussen, Udom Krairittichai, Vuddidhej Ophascharoensuk, Bengt Fellström, Hallvard Holdaas, Vladimir Tesar, Andrzej Wiecek, Diederick Grobbee, Dick de Zeeuw, Carola Grönhagen-Riska, Tanaji Dasgupta, David Lewis, William Herrington, Marion Mafham, William Majoni, Karl Wallendszus, Richard Grimm, Terje Pedersen, Jonathan Tobert, Jane Armitage, Alex Baxter, Christopher Bray, Yiping Chen, Zhengming Chen, Michael Hill, Carol Knott, Sarah Parish, David Simpson, Peter Sleight, Alan Young, Rory Collins, on behalf of the SHARP Investigators**



Number at risk

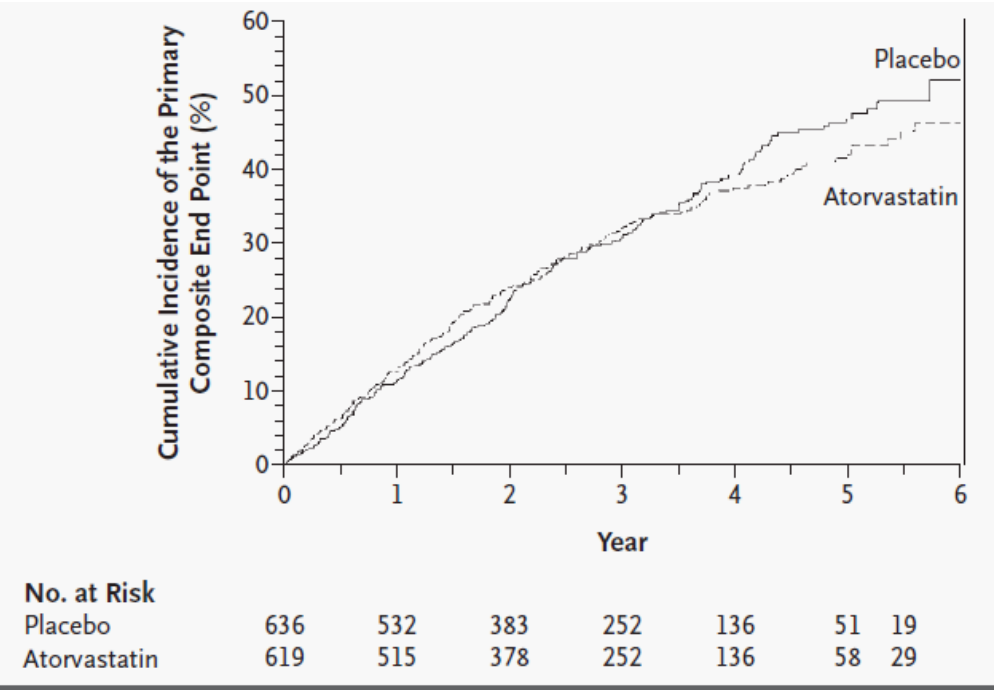
Placebo	4620	4204	3849	3469	2566	1269
Simvastatin plus ezetimibe	4650	4271	3939	3546	2655	1265

Statins and Dialysis

The NEW ENGLAND JOURNAL of MEDICINE

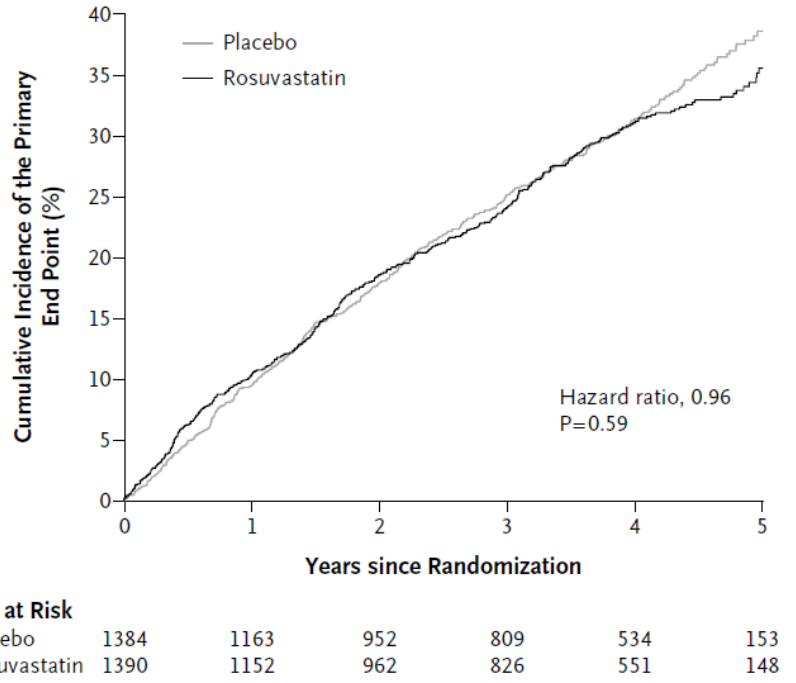
ORIGINAL ARTICLE

Atorvastatin in Patients with Type 2 Diabetes Mellitus Undergoing Hemodialysis



Rosuvastatin and Cardiovascular Events in Patients Undergoing Hemodialysis

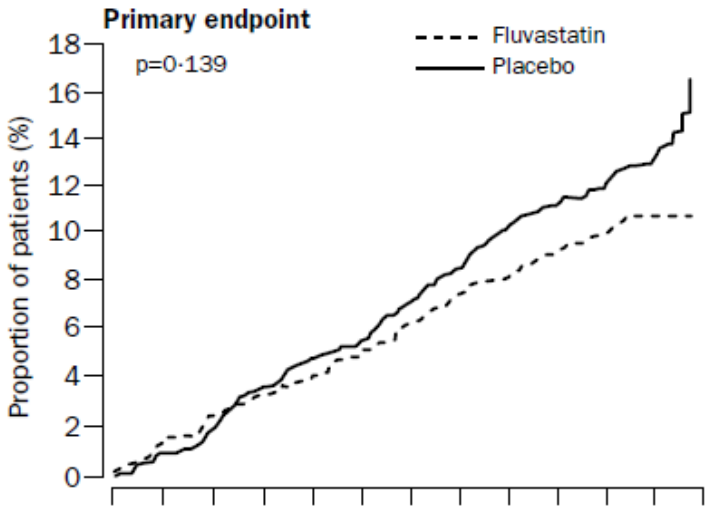
Bengt C. Fellström, M.D., Ph.D., Alan G. Jardine, M.D., Roland E. Schmieder, M.D., Hallvard Holdaas, M.D., Ph.D., Kym Bannister, M.D., Jaap Beutler, M.D., Ph.D., Dong-Wan Chae, M.D., Ph.D., Alejandro Chevaile, M.D., Stuart M. Cobbe, M.D., Carola Grönhagen-Riska, M.D., Ph.D., José J. De Lima, M.D., Ph.D., Robert Lins, M.D., Ph.D., Gert Mayer, M.D., Alan W. McMahon, M.D., Hans-Henrik Parving, M.D., D.M.Sc., Giuseppe Remuzzi, M.D., Ola Samuelsson, M.D., Ph.D., Sandor Sonkodi, M.D., Ph.D., D. Sci., Gultekin Süleymanlar, M.D., Dimitrios Tsakiris, M.D., Ph.D., Vladimir Tesar, M.D., Ph.D., Vasil Todorov, M.D., Ph.D., Andrzej Wiecek, M.D., Ph.D., Rudolf P. Wüthrich, M.D., Mattis Gottlow, M.Sc., Eva Johnsson, M.D., Ph.D., and Faiez Zannad, M.D., Ph.D., for the AURORA Study Group*



Statins and kidney transplant

Effect of fluvastatin on cardiac outcomes in renal transplant recipients: a multicentre, randomised, placebo-controlled trial

*Hallvard Holdaas, Bengt Fellström, Alan G Jardine, Ingar Holme, Gudrun Nyberg, Per Fauchald, Carola Grönhagen-Riska, Søren Madsen, Hans-Hellmut Neumayer, Edward Cole, Bart Maes, Patrice Ambühl, Anders G Olsson, Anders Hartmann, Dag O Solbu, Terje R Pedersen, on behalf of the Assessment of LEscol in Renal Transplantation (ALERT) Study Investigators**



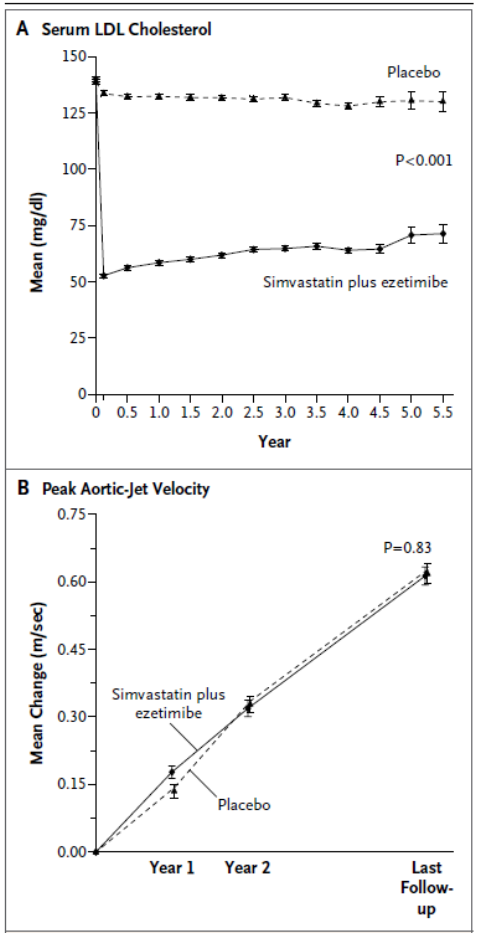
Number at risk							
Placebo	1052	1018	972	929	878	819	17
Fluvastatin	1050	1009	974	930	885	791	14

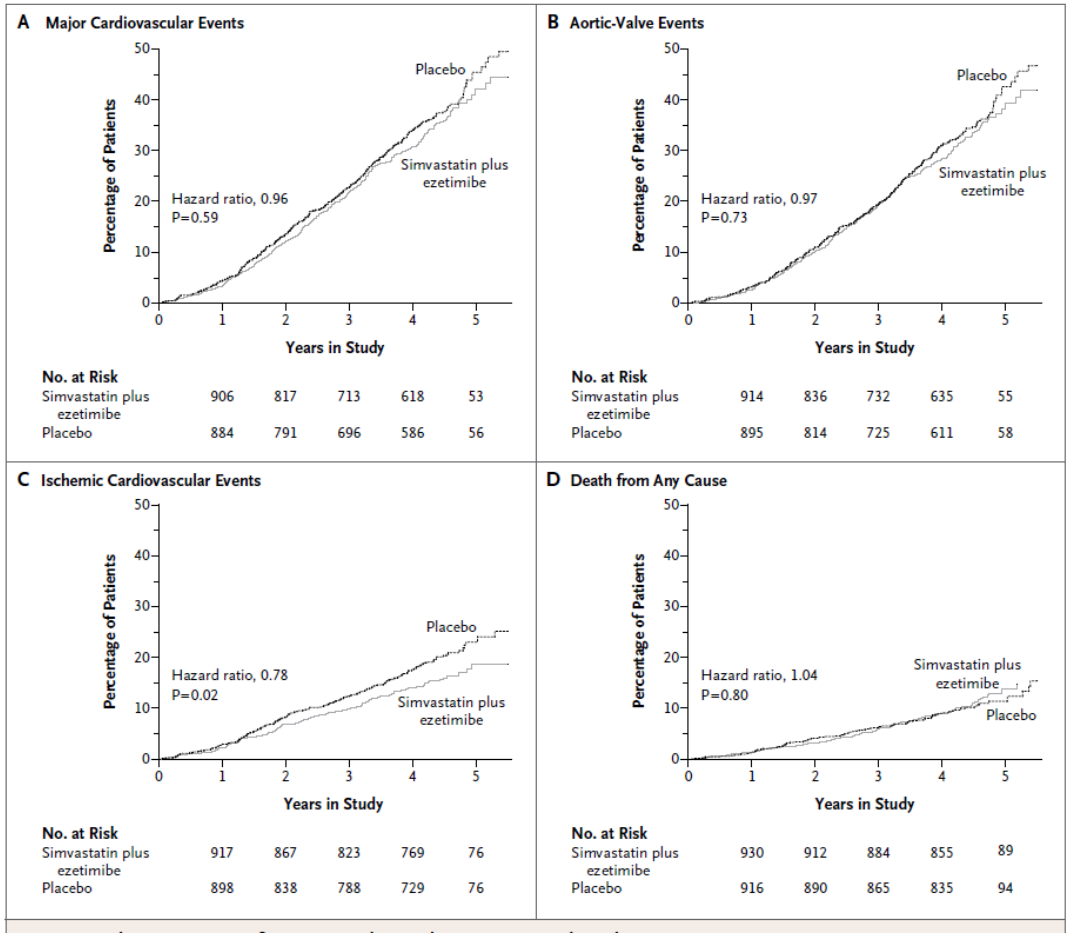
Recommendations	Class[a]	Level[b]
It is recommended that patients with Kidney Disease Outcomes Quality Initiative stage 3–5[c] CKD are considered to be at high or very-high risk of ASCVD.[489–493]	I	A
The use of statins or statin/ezetimibe combination is recommended in patients with non-dialysis-dependent stage 3–5 CKD.[214,222,495,496]	I	A
In patients already on statins, ezetimibe, or a statin/ezetimibe combination at the time of dialysis initiation, continuation of these drugs should be considered, particularly in patients with ASCVD.	IIa	C
In patients with dialysis-dependent CKD who are free of ASCVD, commencement of statin therapy is not recommended.[220,221]	III	A

Statins and aortic stenosis

Intensive Lipid Lowering with Simvastatin and Ezetimibe in Aortic Stenosis

Anne B. Rossebø, M.D., Terje R. Pedersen, M.D., Ph.D., Kurt Boman, M.D., Ph.D., Philippe Brudi, M.D., John B. Chambers, M.D., Kenneth Egstrup, M.D., Ph.D., Eva Gerdts, M.D., Ph.D., Christa Gohlke-Bärwolf, M.D., Ingar Holme, Ph.D., Y. Antero Kesäniemi, M.D., Ph.D., William Malbecq, Ph.D., Christoph A. Nienaber, M.D., Ph.D., Simon Ray, M.D., Terje Skjærpe, M.D., Ph.D., Kristian Wachtell, M.D., Ph.D., and Ronnie Willenheimer, M.D., Ph.D., for the SEAS Investigators*

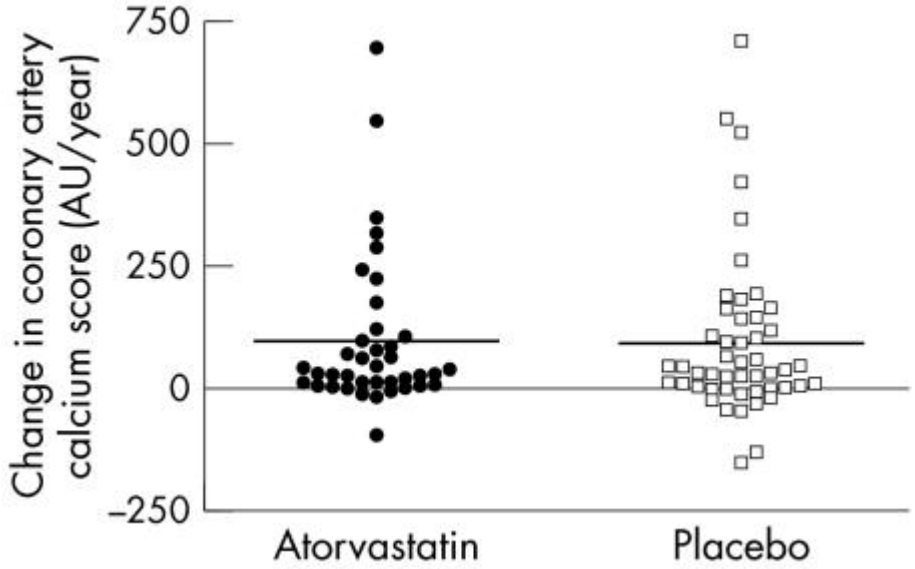




Recommendations	Class[a]	Level[b]
Initiation of lipid-lowering therapy is not recommended in patients with HF in the absence of other indications for their use.[466,470]	III	A
Initiation of lipid-lowering treatment in patients with aortic valvular stenosis without CAD to slow progression of aortic valve stenosis in the absence of other indications for their use is not recommended.[266,479–481]	III	A

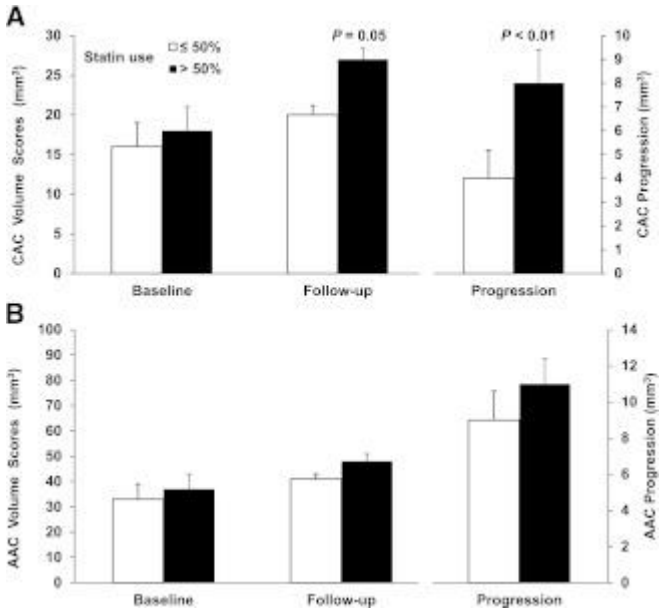
Statins and CAC

Intensive lipid-lowering treatment does not halt the progression, or induce regression, of coronary artery calcification



Scottish Aortic Stenosis and Lipid Lowering Therapy, Impact on Regression trial Investigators. Heart. 2006 Sep;92(9):1207-12.

Progression of Vascular Calcification Is Increased With Statin Use in the Veterans Affairs Diabetes Trial (VADT)



White bars represent less frequent statin use (in ≤50% of the visits during the study); black bars represent frequent statin use (in >50% of the visits during the study)

Diabetes Care. 2012; 35: 2390–2392

Association of Statin Therapy Initiation With Diabetes Progression

A Retrospective Matched-Cohort Study

This retrospective matched-cohort study (2003-2015) found that statin use was associated with diabetes progression, including greater likelihood of insulin treatment initiation, significant hyperglycemia, acute glycemic complications, and an increased number of prescriptions for glucose-lowering medication classes. The risk-benefit ratio of statin use in patients with diabetes should take into consideration its metabolic affects.

Table 2. Odds of Outcomes During Follow-up Period Between Statin Users and Active Comparators in Propensity Score–Matched Cohorts

	Overall cohort				Diabetes-prevalent cohort			
	No. (%)				No. (%)			
Outcomes	Statin users (n = 83 022)	Active comparators (n = 83 022)	OR (95% CI)	*P* value	Statin users (n = 51 467)	Active comparators (n = 51 467)	OR (95% CI)	*P* value
Primary								
Diabetes progression	46 434 (55.9)	39 868 (48.0)	1.37 (1.35 to 1.40)	<.001	30 494 (59.3)	27 189 (52.8)	1.30 (1.27 to 1.33)	<.001
Secondary								
Components of diabetes progression outcome								
New insulin starts during follow-up	11 947 (14.4)	10 540 (12.7)	1.16 (1.12 to 1.19)	<.001	9081 (17.6)	8215 (16.0)	1.13 (1.09 to 1.17)	<.001
Increased No. of glucose-lowering classes	42 579 (51.3)	35 533 (42.8)	1.41 (1.38 to 1.43)	<.001	27 299 (53.0)	23 443 (45.6)	1.35 (1.32 to 1.38)	<.001
Incident ≥5 measurements with blood glucose ≥200 mg/dL[a]	13 963 (16.8)	12 601 (15.2)	1.13 (1.10 to 1.16)	<.001	9858 (19.2)	9167 (17.8)	1.09 (1.06 to 1.13)	<.001
Incident diabetes with ketoacidosis/ uncontrolled diabetes	4468 (5.4)	3635 (4.4)	1.24 (1.19 to 1.30)	<.001	2837 (5.5)	2427 (4.7)	1.18 (1.12 to 1.25)	<.001
Difference in No. of glucose-lowering classes during follow-up vs baseline								
Mean (SD)	0.77 (0.99)	0.59 (0.89)	−0.19 to −0.17[b]	<.001	0.78 (1.0)	0.62 (0.94)	−0.18 to −0.15[b]	<.001
Median (IQR)	1 (0 to 1)	0 (0 to 1)	NA	<.001[c]	1 (0 to 1)	0 (0 to 1)	NA	<.001
Decreased No. of glucose-lowering medication classes	2132 (2.6)	2276 (2.7)	0.94 (0.88 to 0.99)	.03	2116 (4.1)	2272 (4.4)	0.93 (0.87 to 0.99)	.02
Change in mean blood glucose during follow-up vs baseline, mg/dL[a]								
Mean (SD)	6.3 (45.4)	5.5 (46.1)	−1.24 to −0.36[b]	<.001	0.32 (52.8)	−0.60 (52.8)	−1.6 to −0.28[b]	.005
Median (IQR)	6.1 (−8.5 to 24.2)	5.7 (−8.8 to 23.0)	NA	<.001[c]	2.8 (−17.7 to 23.8)	2.1 (−18.5 to 22.6)	NA	<.001

Abbreviations: NA, not applicable; OR, odds ratio.

[a] To convert to mmol/L, multiply by 0.0555.

[b] 95% CI of difference.

[c] Calculated using Wilcoxon rank-sum test.

The Role of Statins in Disease Modification and Cardiovascular Risk in Rheumatoid Arthritis

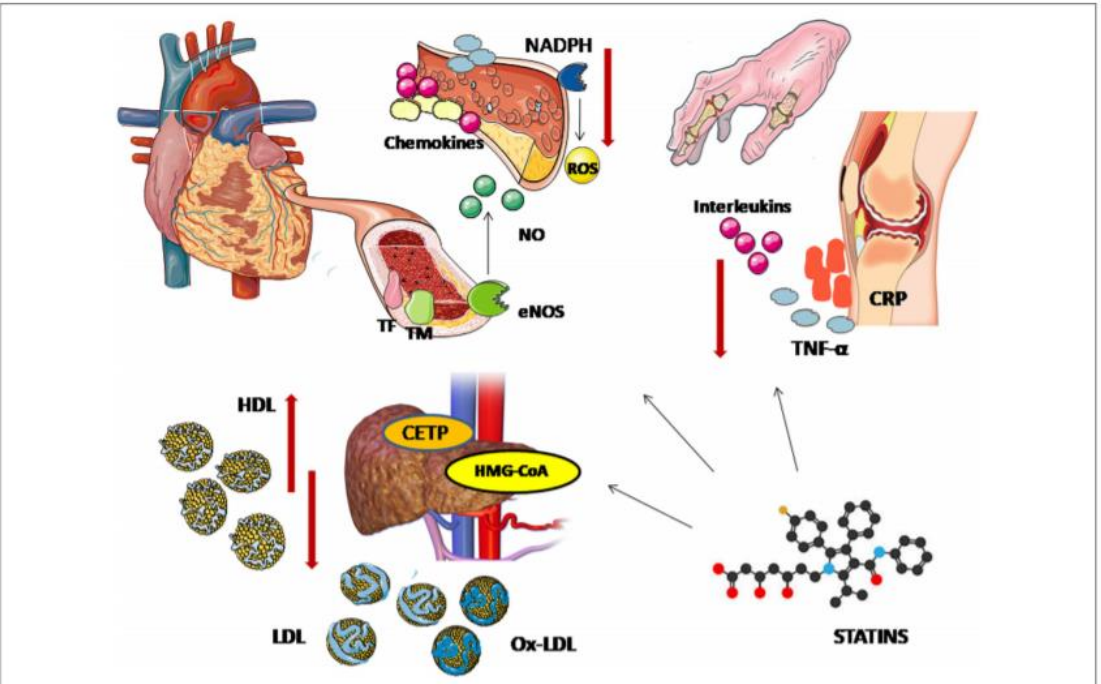


FIGURE 1 | Pleiotropic effects of statins. The lipid lowering effects of statins is attributed to their action on 3-hydroxy-methylglutaryl coenzyme A (HMG-CoA reductase). Statins block the pathway for synthesizing cholesterol in liver by competitively inhibiting HMG-CoA reductase, the rate-controlling enzyme of the mevalonate pathway, leading to lower circulating low-density lipoprotein (LDL) cholesterol levels. A decrease in cholesteryl ester transfer protein (CETP) results in a modest increase in apolipoprotein A-I and high-density lipoprotein (HDL) cholesterol levels. Through the upregulation of endothelial nitric oxide synthase (eNOS), statins promote nitric oxide production and enhance endothelium-dependent vasodilatation. Statins also modulate the endothelial expression of cytokines, chemokines and leukocyte adhesion molecules, decreasing vascular inflammation—an important contributor to the vascular atherogenetic process. Furthermore, affecting both the endothelial production of inflammatory factors and cholesterol uptake, statins stabilize the atheromatic plaques. Their benefit on vascular function is also associated with the downregulation of nicotinamide adenine dinucleotide phosphate (NADPH) which results in lower levels of reactive oxygen species (ROS). Their antioxidative effects are also reflected on a decrease in oxidized LDL (oxLDL) levels. Statins elicit downregulation of tissue factor (TF) and overexpression of thrombomodulin, showing antithrombotic properties. Finally, the potential systematic beneficial effect of statins on systemic inflammatory diseases can be attributed to their ability to reduce inflammatory cytokines, such as tumor necrosis factor-α (TNF-α), interleukins, and C-reactive protein (CRP).

Trial of Atorvastatin for the Primary Prevention of Cardiovascular Events in Patients with Rheumatoid Arthritis (TRACE RA)

2986 RA patients

In the atorvastatin 40 mg group 24 patients had a CVD event, compared to 36 in the placebo group (HR 0.66, 95% CI 0.40-1.11, p=0.12)

Alternatives analyses

4S

Mortalité vasculaire

PMC full text: Am J Public Health. 2013 July; 103(7): 1207–1218.
Published online 2013 July. doi: 10.2105/AJPH.2013.301226
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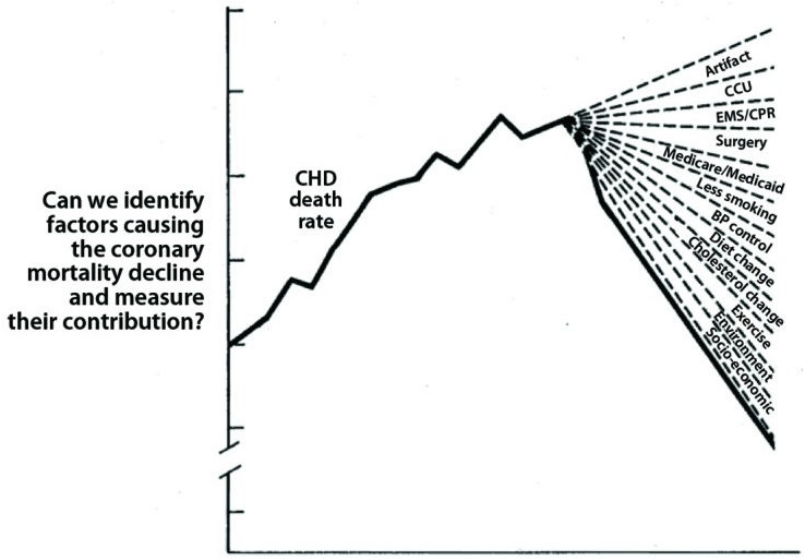
FIGURE 1—



Coronary heart disease decline and the problem of attribution of credit.

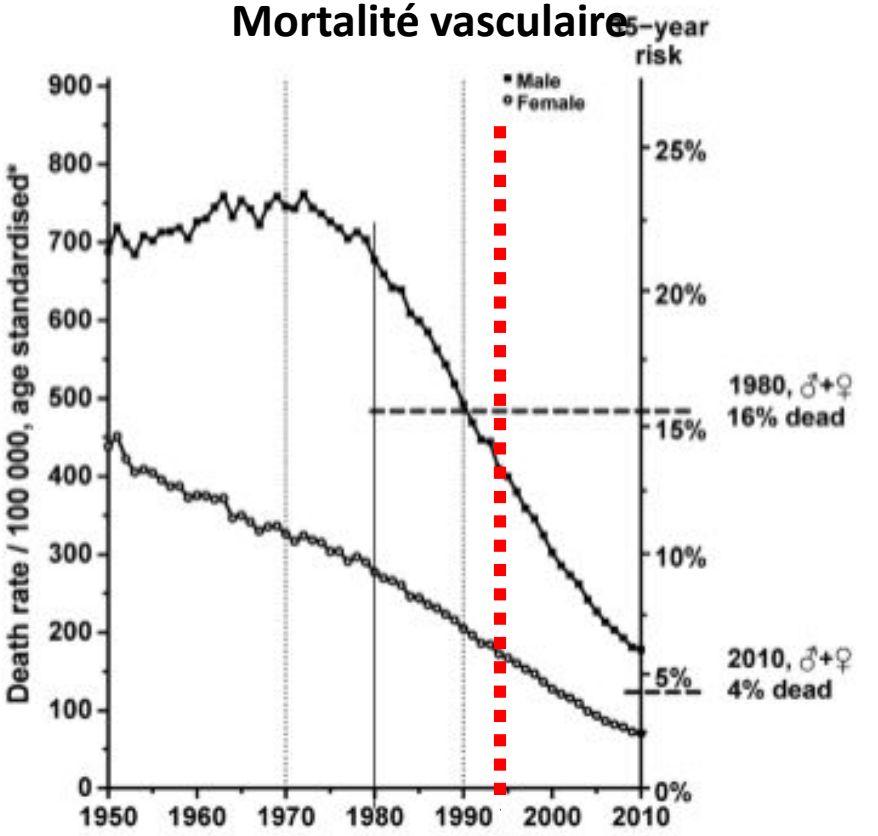
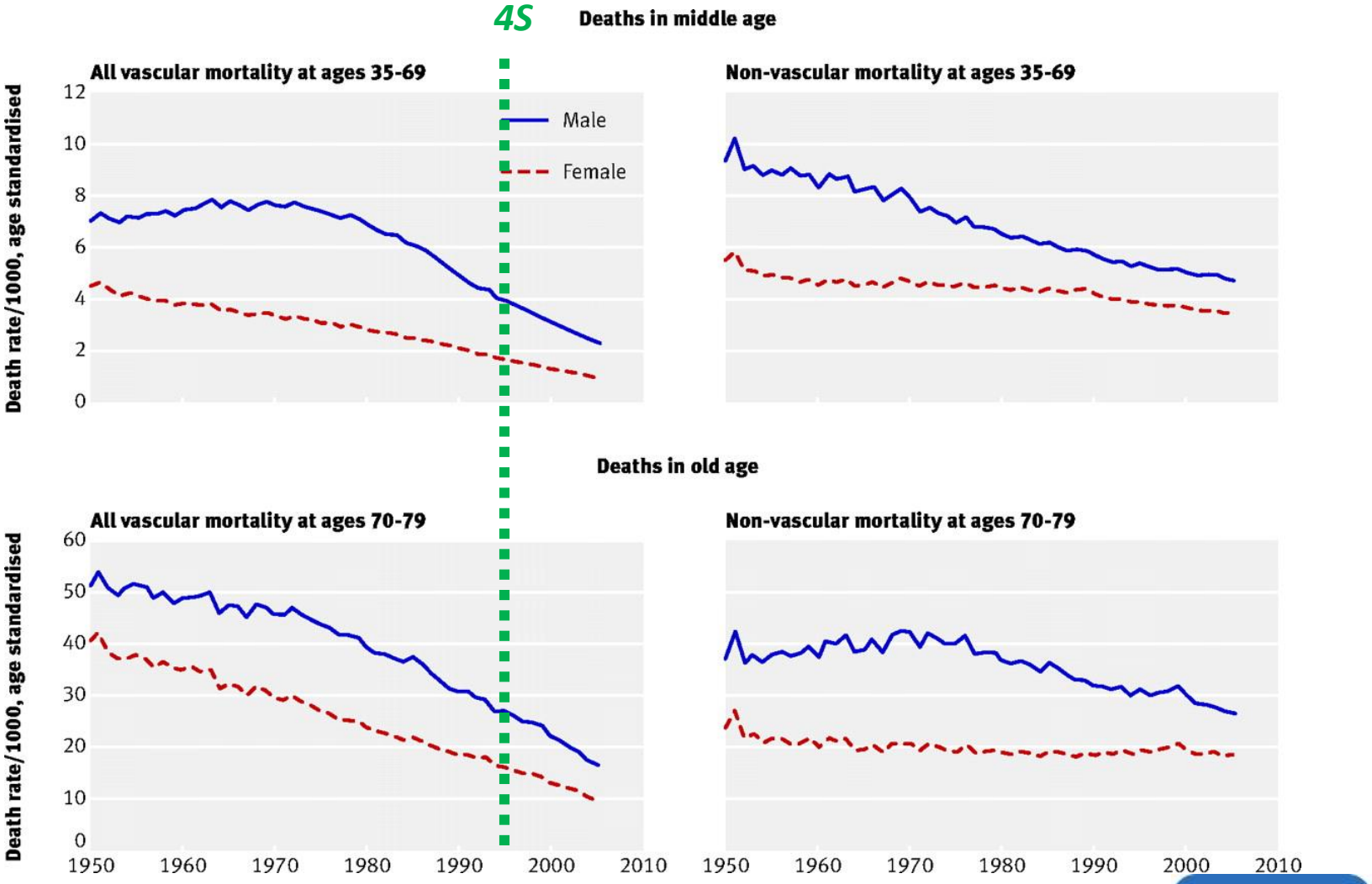


Figure 1. United Kingdom 1950 to 2010 vascular mortality rates at ages 35 to 69, by sex. Source: WHO mortality and UN population estimates. *Mean of annual rates in the 7 component 5-year age groups.

Trends in age standardised vascular and non-vascular mortality (mean of annual rates in component five year age groups) by age and sex for 1950-2005 for UK population (source: WHO and UN population estimates).



Robert Clarke et al. BMJ 2009;339:bmj.b3513

Statin trials: primary prevention
NNT = 1/(ARp-ARs)

Études de prévention primaire	Molécules testées *Durée moyenne de l'étude*	Population, *LDL-C moyen* (g/L) à l'enrôlement	Critère de jugement principal	Résultat du critère de jugement principal	Gain médian d'espérance de vie en jours	NNT/10 ans mortalité totale	NNT/10 ans IDM
WOSCOPS	Pravastatine 40 mg *vs* placebo *4,9 ans*	6 595 hommes, *1,92*	Décès d'origine coronaire ou IDM non fatal	5,5 % *vs* 7,9 %, RRA -2,4 %, RRR -30 %	9	55	22
CARDS	Atorvastatine 10 mg *vs* placebo *3,9 ans*	2 838 *1,17*	Événements coronariens, revascularisation coronaire et AVC	5,8 % *vs* 9 %, RRA -3,2 %, RRR -37 %	18	25	21
ASCOT-LLA	Atorvastatine 10 mg *vs* placebo *3,3 ans*	10 305 *1,31*	IDM non fatal et maladie coronaire fatale	1,9 % *vs* 3 %, RRA -1,1 %, RRR -37 %	2	60	23
AFCAPS/ TexCAPS	Lovastatine 20-40 mg *vs* placebo *5,2 ans*	6 605 *1,50*	IDM fatal et non fatal, angor instable, mort subite	6,8 % *vs* 10,9 %, RRA -4,1 %, RRR -38 %		-586	45
ALLHAT-LLT	Pravastatine 40 mg *vs* placebo *4,8 ans*	10 355	Mortalité toute cause	14,9 % *vs* 15,3 %, RRA -0,4 % (NS), RRR -3 %		305	62
JUPITER	Rosuvastatine 20 mg *vs* placebo *1,9 an*	17 802 *1.08*	IDM non fatal, AVC non fatal, angor instable, revascularisation artérielle, décès cardiovasculaire	2,8 % *vs* 1,6 %, RRA -1,2 %, RRR -43 %	7	35	45
HOPE-3	Rosuvastatine 10 mg *vs* placebo *5,6 ans*	12705 *1,28*	Décès cardiovasculaire, IDM non fatal, AVC non fatal	3,7 % *vs* 4,8 %, RRA -1,1 %, RRR -24 %		149	147

Statin trials: secondary prevention NNT = 1/(ARp-ARs)

Études de prévention secondaire	Molécules testées *Durée moyenne de l'étude*	Population *LDL-C moyen* (g/L) à l'enrôlement	Critère de jugement principal	Résultat principal	NNT/10 ans mortalité totale	NNT/10 ans IDM
4S	Simvastatine 20-40 mg *vs* placebo *5,4 ans*	4 444 *1,88*	Mortalité totale	8 % *vs* 12 %, RRA -4 %, RRR -33 %	16	8
LIPID	Pravastatine 40 mg *vs* placebo *6,1 ans*	9 014 *1,50*	Mortalité coronaire	6,4 % *vs* 8,3 %, RRA -1,9 %, RRR -24 %	20	21
CARE	Pravastatine 40 mg *vs* placebo *5 ans*	4 159 *1,39*	IDM non fatal ou décès coronaire	10,2 % *vs* 13,2 %, RRA -3 %, RRR -24 %	62	21
MRC/BHF HPS	Simvastatine 40 mg *vs* placebo *5 ans*	20 536 *1,31*	Mortalité totale	12,9 % *vs* 14,7 %, RRA -1,8 %, RRR -12 %	29	16
PROVE IT TIMI 22	Atorvastatine 80 mg *vs* pravastatine 40 mg *2 ans*	4 162 *1,06*	Décès, IDM, AVC, angor instable, revascularisation coronaire	22,4 % *vs* 26,3 %, RRA -3,9 %, RRR -15 %	20	25
TNT	Atorvastatine 80 mg *vs* 10 mg *4,9 ans*	10 001 *0,98*	Décès coronaire, IDM non fatal, arrêt cardiaque récupéré, AVC non fatal et fatal	3,7 % *vs* 4,8 %, RRA -1,1 %, RRR -24 %	-934	29
IDEAL	Atorvastatine 80 mg *vs* simvastatine 20 mg *4,8 ans*	8 888 *1,22*	Décès coronaire, IDM non fatal, arrêt cardiaque récupéré	9,3 % *vs* 10,4 %, RRA -1,1 %, RRR -11 %	298	418
A to Z	simvastatine 80 mg *Vs* 20 mg *2 ans*	4 497 *1,11*	Décès cardiovasculaire, IDM non fatal, syndrome coronaire aigu, AVC	14,4 % *vs* 16,7 %, RRA -2,3 %, RRR -14 % (NS)	161	67
IMPROVE-IT	Simvastatine 40 mg + ézétimibe 10 mg *vs* simvastatine 40 mg *6 ans*	18 144 *0,94*	Décès cardiovasculaire, IDM non fatal, angor instable, revascularisation coronaire, AVC non fatal	32,7 % *vs* 34,7 %, RRA -2 %, RRR -6 %	-314	39

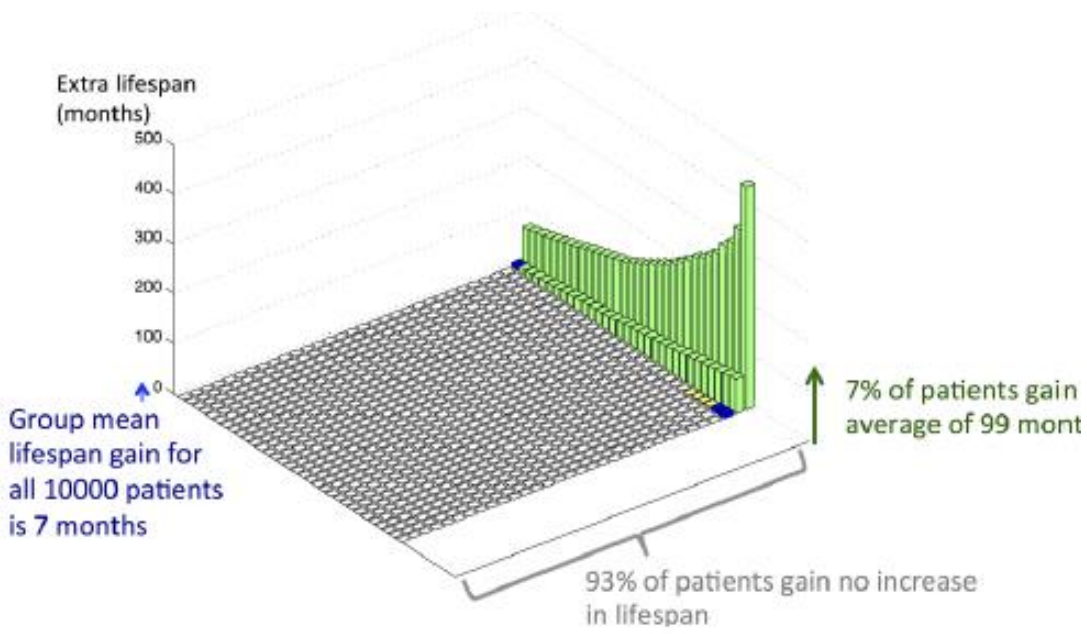
Fragility Index:

A measure of the robustness (or fragility) of the results of a clinical trial. The fragility index is a number indicating how many patients would be required to convert a trial from being statistically significant to not significant ($p \geq 0.05$). The larger the fragility index the better (more robust) a trial's data are.

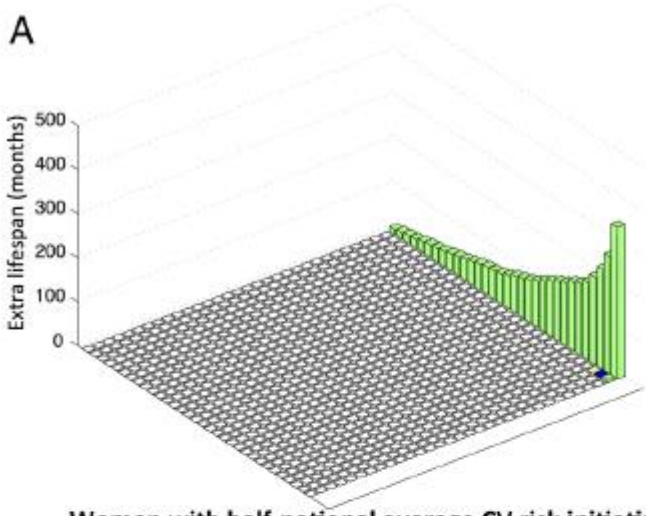
Clinical Trial (reference number)	Fragility index	Lost to follow up
WOSCOPS (2)	34	0
AFCAPS/TEXCAPS (3)	33	65
ALLHAT (4)	0	206
ASCOT-LLA (5)	22	119
CARDS (6)	17	24
MEGA (7)	7	102
ASPEN (8)	0	56
JUPITER (9)	67	81
HOPE 3 (10)	24	118
4S (11)	33	0
CARE (12)	21	1
POST CABG (13)		27
LIPID (14)	37	1
HPS (16)	81	7
PROSPER (17)	8	813
LIPS (18)	9	17
ALERT (19)	0	7
A TO Z (20)	0	44
ALLIANCE (21)	0	165
TNT (22)	53	73
IDEAL (23)	0	6
4D (24)	0	1
PROVE-IT TIMI (25)	27	8
SPARCL (26)	1	25
CORONA (27)	0	
GISSI-HF (28)	0	
AURORA (29)	0	
SHARP (30)	34	204
SEARCH (31)	0	119
IMPROVE-IT (32)	47	168
ODYSSEY O	65	86
FOURIER	118	211

Distribution of lifespan gain from primary prevention intervention

Judith A Finegold,[1] Matthew J Shun-Shin,[1] Graham D Cole,[1] Saman Zaman,[1] Annette Maznyczka,[2] Sameer Zaman,[1] Rasha Al-Lamee,[1] Siqin Ye,[3] Darrel P Francis[1]

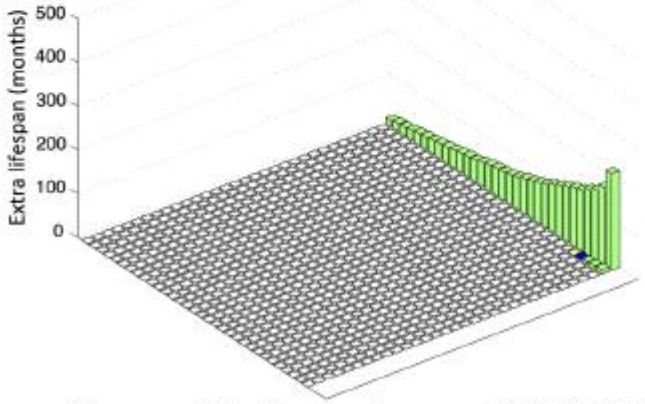


A



Women with half-national average CV risk initiating therapy at 50 years

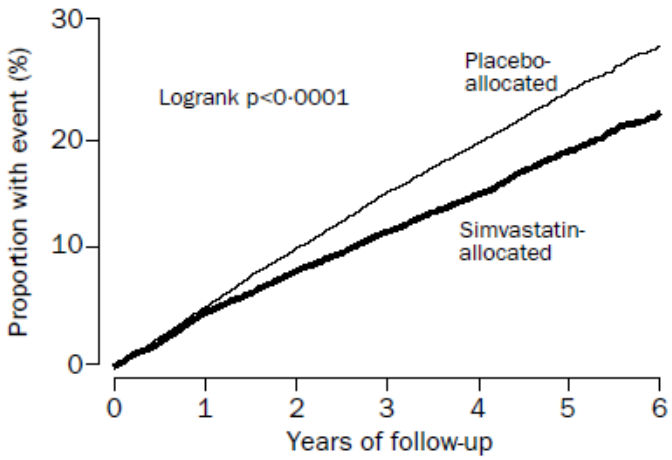
C



Women with half-national average CV risk initiating therapy at 80 years

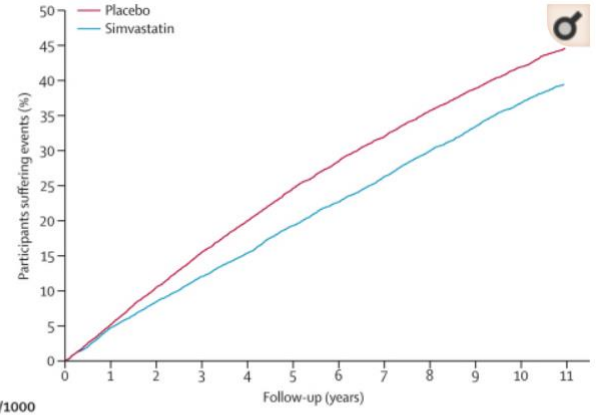
Long term randomized trials are badly lacking

MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20 536 high-risk individuals: a randomised placebo-controlled trial



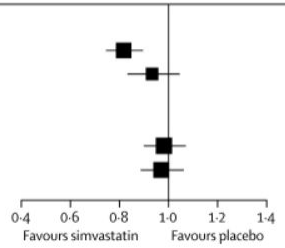
Benefit (SE)/1000 allocated simvastatin	5 (3)	20 (4)	35 (5)	46 (5)	54 (7)	60 (18)

Figure 6: **Life-table plot of effects of simvastatin allocation on percentages having major vascular events**
See figure 5 for numbers of participants having a first event during each year of follow-up.

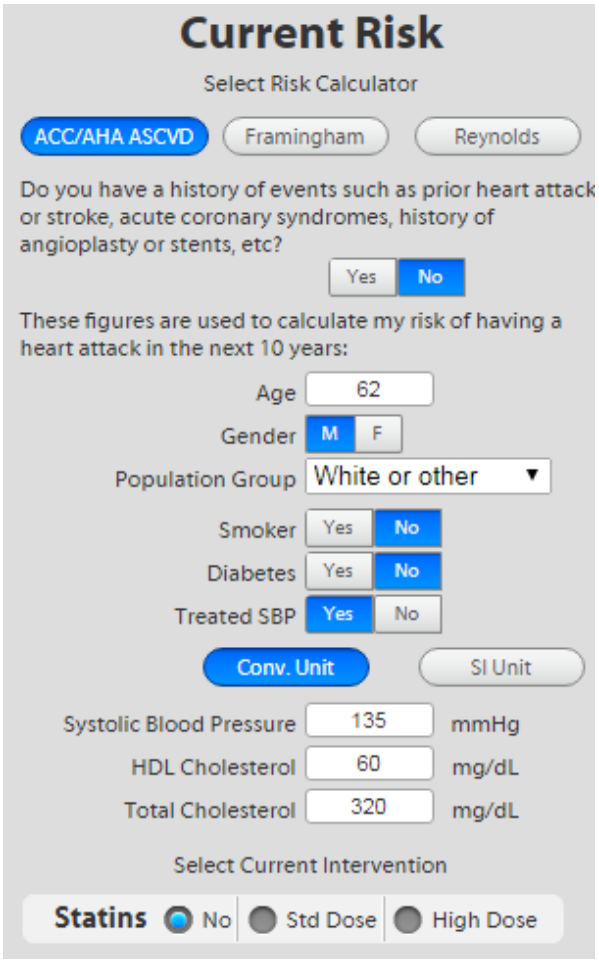


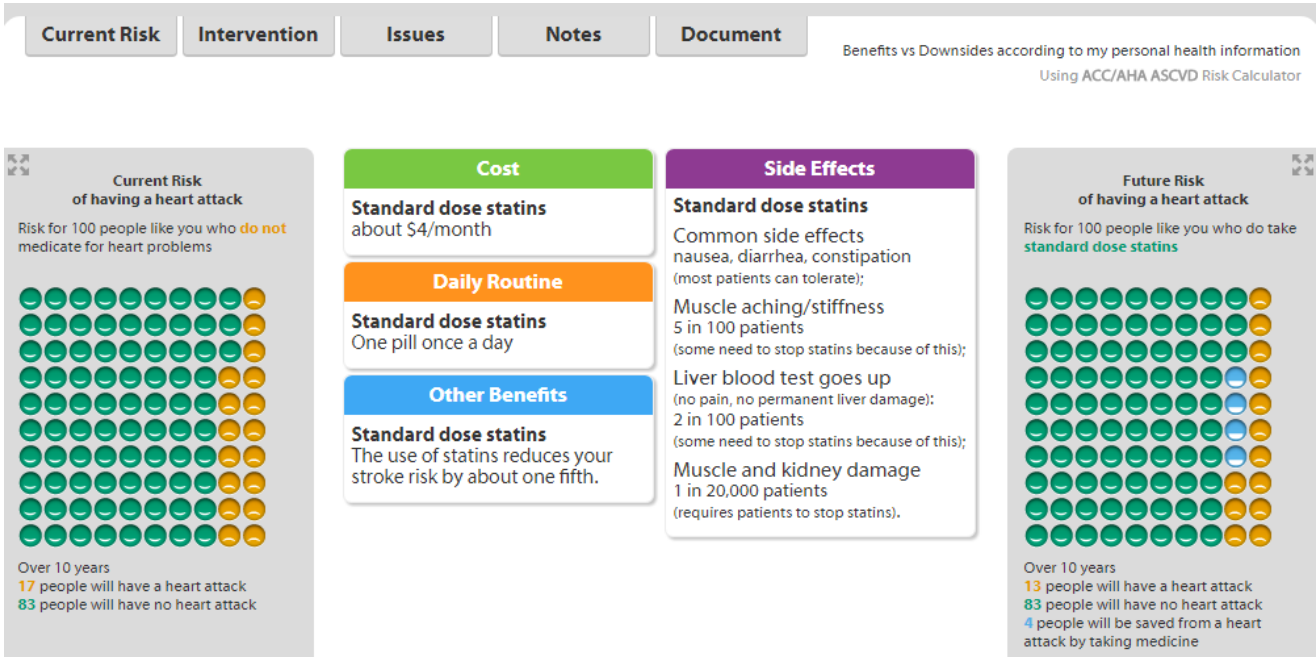
Benefit (SE)/1000 allocated simvastatin	5 (3)	20 (4)	35 (5)	46 (5)	53 (6)	58 (6)	58 (7)	57 (7)	55 (7)	52 (8)	51 (11)	
Number at risk												
Placebo	10267	9682	9055	8464	7894	7314	6785	6336	5848	5419	4822	2129
Simvastatin	10269	9744	9287	8814	8352	7845	7381	6931	6428	5965	5317	2403

	Simvastatin allocation		**Risk ratio (95% CI)**
	Simvastatin	Placebo	
In-trial			
Vascular death	826/10269 (8·0%)	998/10267 (9·7%)	0·82 (0·75–0·90)
Non-vascular death	580/10269 (5·6%)	613/10267 (6·0%)	0·94 (0·83–1·05)
Post-trial			
Vascular death	1019/8863 (11·5%)	1007/8656 (11·6%)	0·98 (0·90–1·07)
Non-vascular death	943/8863 (10·6%)	942/8656 (10·9%)	0·97 (0·89–1·06)



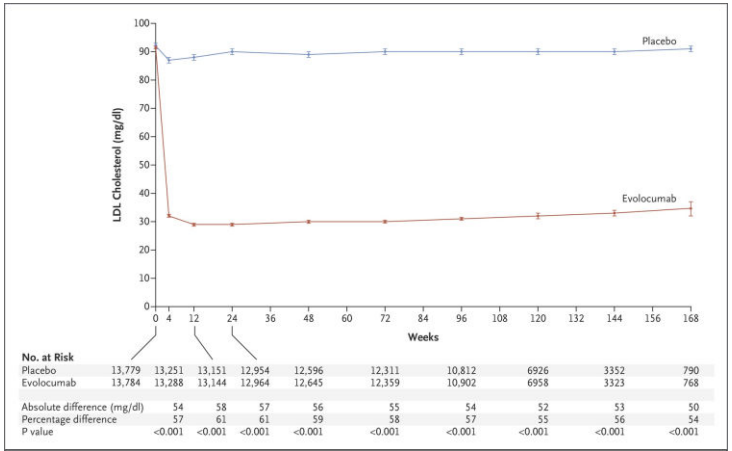
https://statindecisionaid.mayoclinic.org/

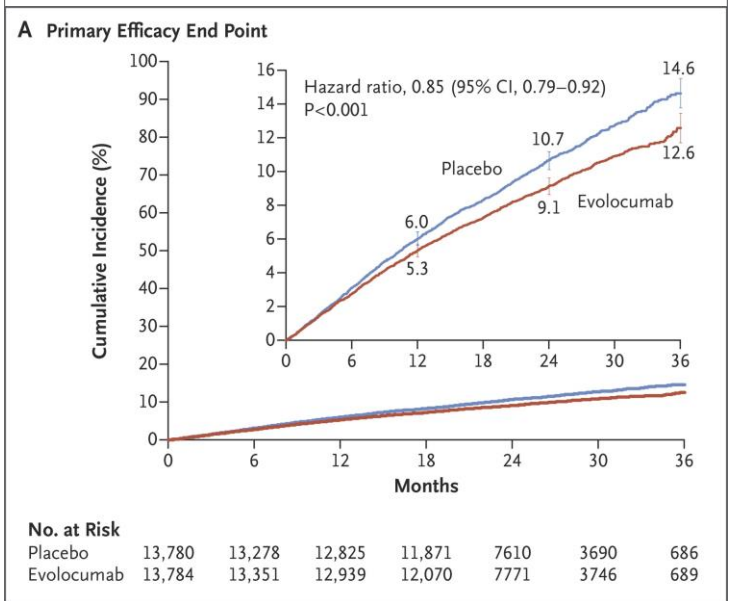




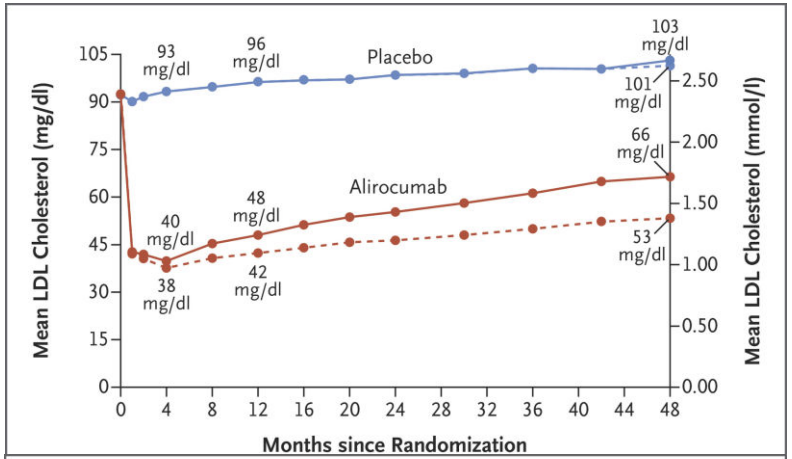
Anti PCSK9

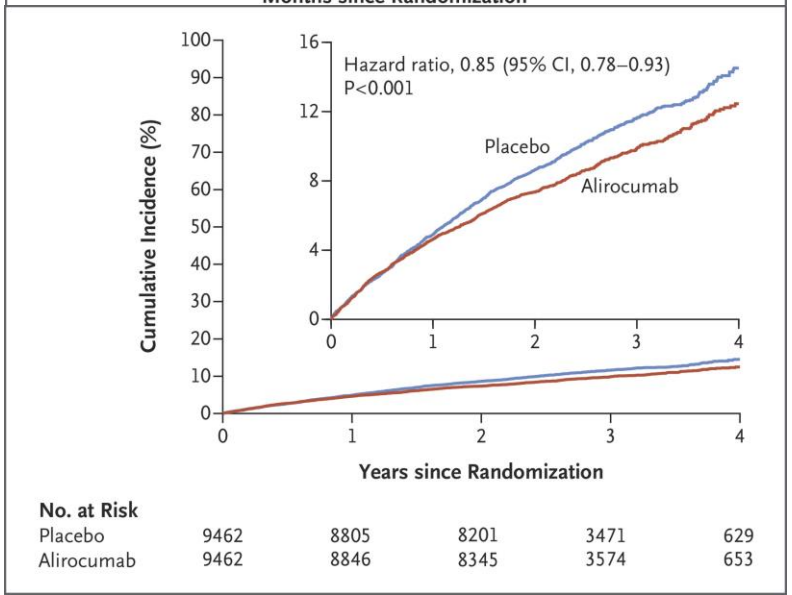
Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease





Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome





Anti PCSK9

Table 2. Primary and Secondary End Points.

Outcome	Evolocumab (N=13,784)	Placebo (N=13,780)	Hazard Ratio (95% CI)	P Value*
	no. of patients (%)			
Primary end point: cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization	1344 (9.8)	1563 (11.3)	0.85 (0.79–0.92)	<0.001
Key secondary end point: cardiovascular death, myocardial infarction, or stroke	816 (5.9)	1013 (7.4)	0.80 (0.73–0.88)	<0.001
Other end points				
Cardiovascular death	251 (1.8)	240 (1.7)	1.05 (0.88–1.25)	0.62
Due to acute myocardial infarction	25 (0.18)	30 (0.22)	0.84 (0.49–1.42)	
Due to stroke	31 (0.22)	33 (0.24)	0.94 (0.58–1.54)	
Other cardiovascular death	195 (1.4)	177 (1.3)	1.10 (0.90–1.35)	
Death from any cause	444 (3.2)	426 (3.1)	1.04 (0.91–1.19)	0.54
Myocardial infarction	468 (3.4)	639 (4.6)	0.73 (0.65–0.82)	<0.001
Hospitalization for unstable angina	236 (1.7)	239 (1.7)	0.99 (0.82–1.18)	0.89
Stroke	207 (1.5)	262 (1.9)	0.79 (0.66–0.95)	0.01
Ischemic	171 (1.2)	226 (1.6)	0.75 (0.62–0.92)	
Hemorrhagic	29 (0.21)	25 (0.18)	1.16 (0.68–1.98)	
Unknown	13 (0.09)	14 (0.10)	0.93 (0.44–1.97)	
Coronary revascularization	759 (5.5)	965 (7.0)	0.78 (0.71–0.86)	<0.001
Urgent	403 (2.9)	547 (4.0)	0.73 (0.64–0.83)	
Elective	420 (3.0)	504 (3.7)	0.83 (0.73–0.95)	
Cardiovascular death or hospitalization for worsening heart failure	402 (2.9)	408 (3.0)	0.98 (0.86–1.13)	0.82
Ischemic stroke or transient ischemic attack	229 (1.7)	295 (2.1)	0.77 (0.65–0.92)	0.003
CTTC composite end point†	1271 (9.2)	1512 (11.0)	0.83 (0.77–0.90)	<0.001

* Given the hierarchical nature of the statistical testing, the P values for the primary and key secondary end points should be considered significant, whereas all other P values should be considered exploratory.
† The Cholesterol Treatment Trialists Collaboration (CTTC) composite end point consists of coronary heart death, nonfatal myocardial infarction, stroke, or coronary revascularization.

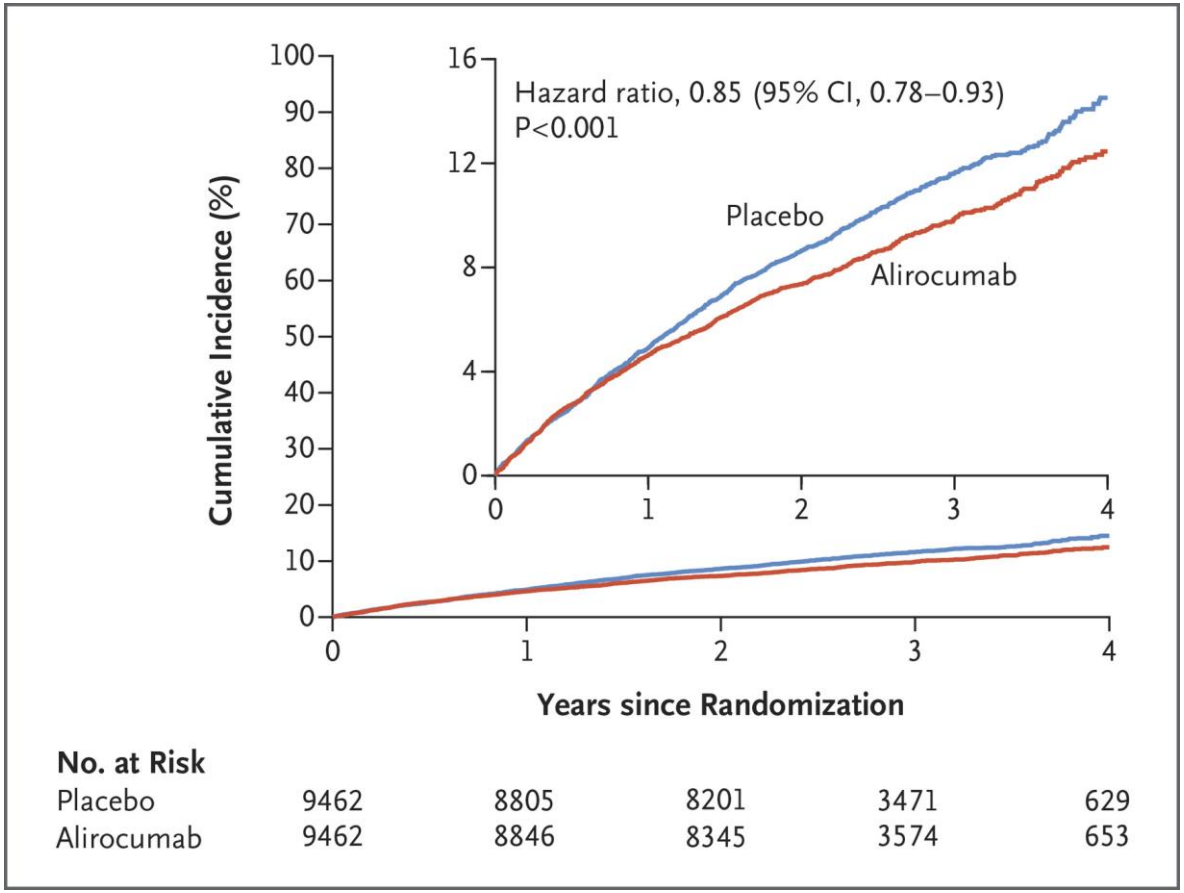
Table 2. Composite Primary End Point and Secondary End Points (Intention-to-Treat Population).

End Point	Alirocumab (N=9462)	Placebo (N=9462)	Hazard Ratio (95% CI)	P Value
	number of patients (percent)			
Primary end point: composite of death from coronary heart disease, nonfatal myocardial infarction, fatal or nonfatal ischemic stroke, or unstable angina requiring hospitalization	903 (9.5)	1052 (11.1)	0.85 (0.78–0.93)	<0.001
Major secondary end points, in order of hierarchical testing				
Any coronary heart disease event*	1199 (12.7)	1349 (14.3)	0.88 (0.81–0.95)	0.001
Major coronary heart disease event†	793 (8.4)	899 (9.5)	0.88 (0.80–0.96)	0.006
Any cardiovascular event‡	1301 (13.7)	1474 (15.6)	0.87 (0.81–0.94)	<0.001
Composite of death from any cause, nonfatal myocardial infarction, or nonfatal ischemic stroke§	973 (10.3)	1126 (11.9)	0.86 (0.79–0.93)	<0.001
Death from coronary heart disease	205 (2.2)	222 (2.3)	0.92 (0.76–1.11)	0.38¶
Death from cardiovascular causes	240 (2.5)	271 (2.9)	0.88 (0.74–1.05)	
Death from any cause	334 (3.5)	392 (4.1)	0.85 (0.73–0.98)	
Other end points‖				
Nonfatal myocardial infarction	626 (6.6)	722 (7.6)	0.86 (0.77–0.96)	
Fatal or nonfatal ischemic stroke	111 (1.2)	152 (1.6)	0.73 (0.57–0.93)	
Unstable angina requiring hospitalization	37 (0.4)	60 (0.6)	0.61 (0.41–0.92)	
Ischemia-driven coronary revascularization procedure	731 (7.7)	828 (8.8)	0.88 (0.79–0.97)	
Hospitalization for congestive heart failure	176 (1.9)	179 (1.9)	0.98 (0.79–1.20)	

* This end point includes death from coronary heart disease, nonfatal myocardial infarction, unstable angina requiring hospitalization, and an ischemia-driven coronary revascularization procedure (definitions can be found in the Supplementary Appendix).
† This end point includes death from coronary heart disease and nonfatal myocardial infarction.
‡ This end point includes any death from cardiovascular causes, nonfatal myocardial infarction, unstable angina requiring hospitalization, an ischemia-driven coronary revascularization procedure, or nonfatal ischemic stroke.
§ The widths of the confidence intervals for the secondary end points were not adjusted for multiplicity, so the intervals for the outcomes listed below this outcome should not be used to infer definitive treatment effects.
¶ The hierarchical analysis was stopped after the first nonsignificant P value was observed, in accordance with the hierarchical testing plan.
‖ The analysis for other end points was not adjusted for multiplicity; therefore, no P values are reported.

ODYSSEY OUTCOMES Committees and Investigators

- Gain 15.8 days over 4 years of trial duration
- NNT 63
- FI 65
- LFU 86



Thérapie génique !

GalNAc-siRNA conjugates facilitate rapid hepatic uptake

Background

Inclisiran:

siRNA conjugated to N-acetylgalactosamine

Subcutaneous administration

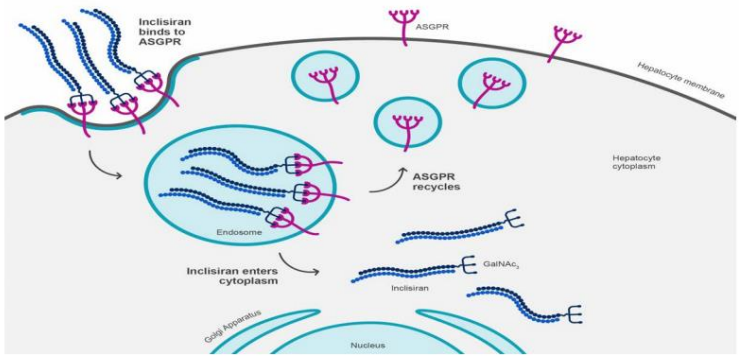
Targeted delivery to hepatocytes

Third generation with enhanced stablilisation chemistry

Asialoglycoprotein receptor (ASGPR):

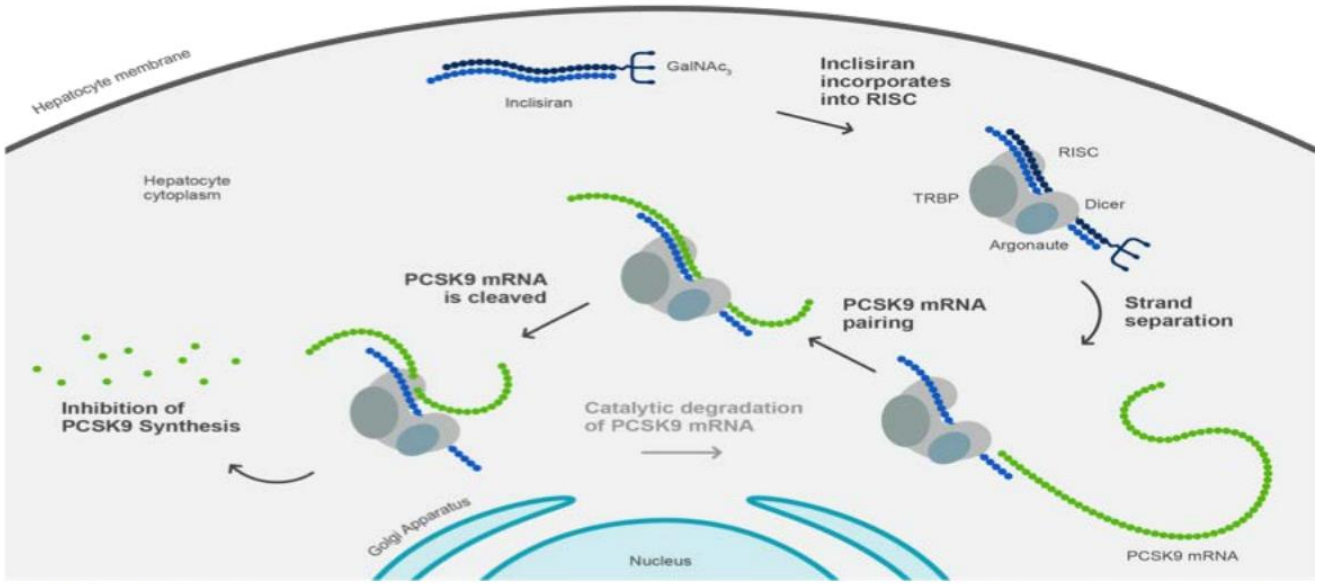
Highly expressed in hepatocytes only.

High rate of uptake



Small interfering RNA (siRNA) targeted to PCSK9

Mechanism of action



RISC = RNA induced silencing complex

Whitehead et al. *Nat Rev Drug Discov* 2009;8:129-38

The NEW ENGLAND JOURNAL of MEDICINE

Inclisiran in Patients with Elevated LDL Cholesterol

TWO PHASE 3, DOUBLE-BLIND, RANDOMIZED, CONTROLLED TRIALS

ORION-10
(U.S.)

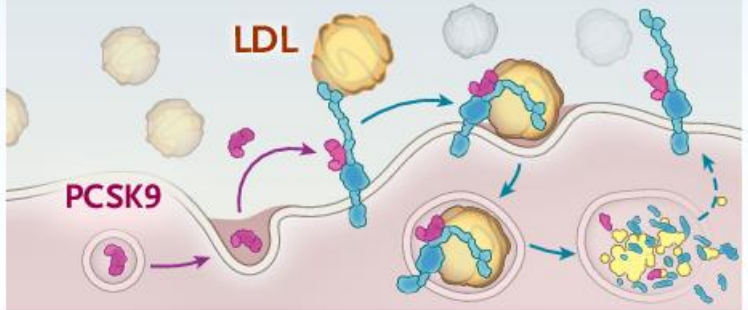
(N=1561)

–51.3% with Inclisiran

Difference, –52.3%
(95% CI, –55.7 to –48.8; P<0.001)

+1% with Placebo

Adults with CVD and elevated LDL



Percentage change in LDL cholesterol at 510 days

ORION-11
(Europe and South Africa)

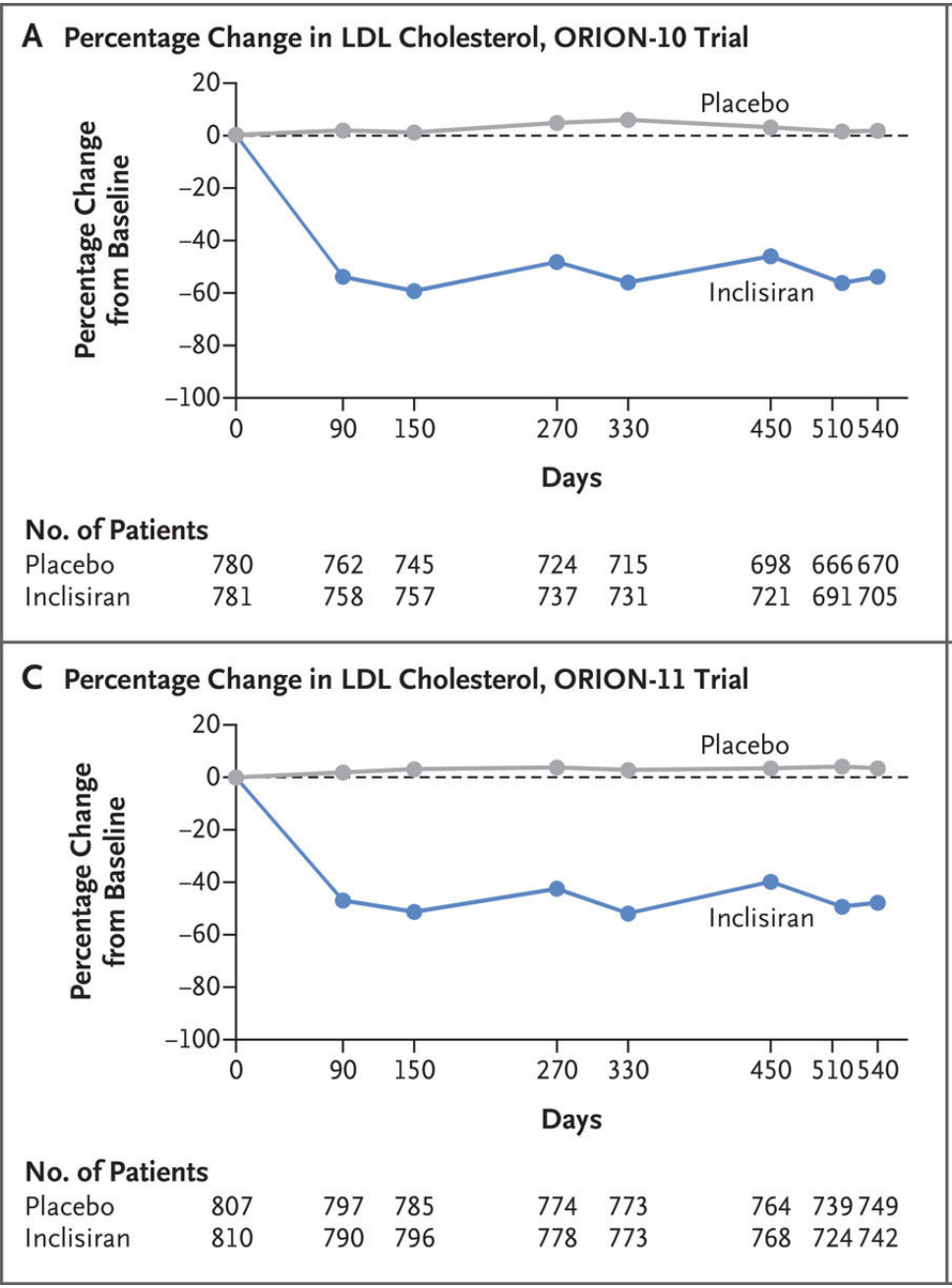
(N=1617)

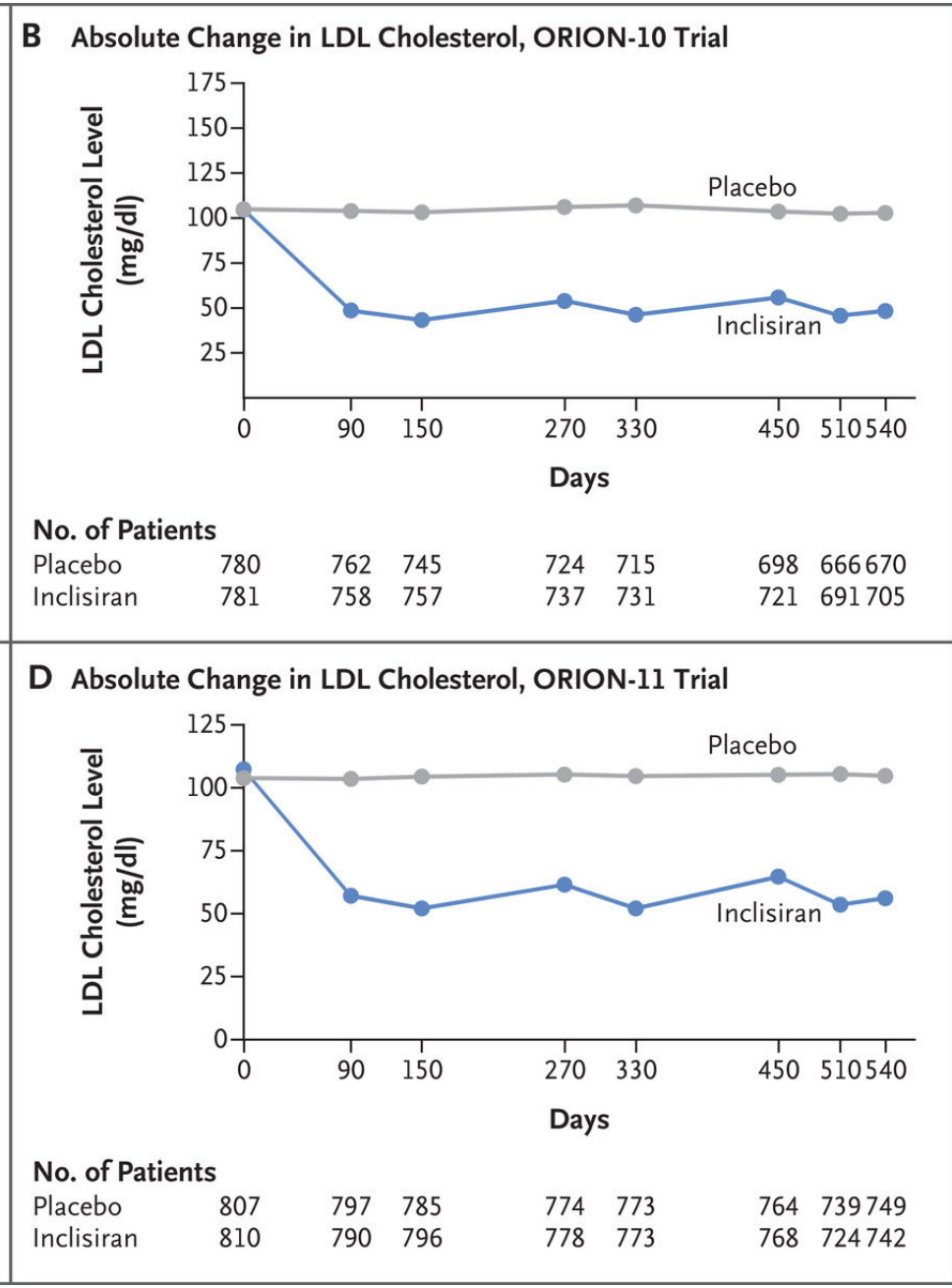
–45.8% with Inclisiran

Difference, –49.9%
(95% CI, –53.1 to –46.6; P<0.001)

+4% with Placebo

K.K. Ray et al. 10.1056/NEJMoa1912387


A Percentage Change in LDL Cholesterol, ORION-10 Trial
Percentage Change from Baseline
20
0
−20
−40
−60
−80
−100
Placebo
Inclisiran
0 90 150 270 330 450 510 540
Days
No. of Patients
Placebo 780 762 745 724 715 698 666 670
Inclisiran 781 758 757 737 731 721 691 705


B Absolute Change in LDL Cholesterol, ORION-10 Trial
LDL Cholesterol Level (mg/dl)
175
150
125
100
75
50
25
Placebo
Inclisiran
0 90 150 270 330 450 510 540
Days
No. of Patients
Placebo 780 762 745 724 715 698 666 670
Inclisiran 781 758 757 737 731 721 691 705

C Percentage Change in LDL Cholesterol, ORION-11 Trial
Percentage Change from Baseline
20
0
−20
−40
−60
−80
−100
Placebo
Inclisiran
0 90 150 270 330 450 510 540
Days
No. of Patients
Placebo 807 797 785 774 773 764 739 749
Inclisiran 810 790 796 778 773 768 724 742

D Absolute Change in LDL Cholesterol, ORION-11 Trial
LDL Cholesterol Level (mg/dl)
125
100
75
50
25
0
Placebo
Inclisiran
0 90 150 270 330 450 510 540
Days
No. of Patients
Placebo 807 797 785 774 773 764 739 749
Inclisiran 810 790 796 778 773 768 724 742

Table 2. Adverse Events and Key Safety Laboratory Findings.*

Variable	ORION-10 Trial			ORION-11 Trial		
	Inclisiran (N=781)	Placebo (N=778)	Risk Ratio (95% CI)	Inclisiran (N=811)	Placebo (N=804)	Risk Ratio (95% CI)
	no. of patients (%)			*no. of patients (%)*		
Adverse events						
≥1 Adverse event	574 (73.5)	582 (74.8)	1.0 (0.9–1.0)	671 (82.7)	655 (81.5)	1.0 (0.9–1.1)
≥1 Event leading to discontinuation of inclisiran or placebo	19 (2.4)	17 (2.2)	1.1 (0.6–2.1)	23 (2.8)	18 (2.2)	1.3 (0.7–2.3)
Serious adverse events						
≥1 Serious adverse event	175 (22.4)	205 (26.3)	0.9 (0.7–1.0)	181 (22.3)	181 (22.5)	1.0 (0.8–1.2)
Death	12 (1.5)	11 (1.4)	1.1 (0.5–2.4)	14 (1.7)	15 (1.9)	0.9 (0.4–1.9)
Death from cardiovascular causes	7 (0.9)	5 (0.6)	1.4 (0.4–4.4)	9 (1.1)	10 (1.2)	0.9 (0.4–2.2)
Cancer-related death	1 (0.1)	3 (0.4)	0.3 (0.0–3.2)	3 (0.4)	3 (0.4)	1.0 (0.2–4.9)
New, worsening, or recurrent cancer	26 (3.3)	26 (3.3)	1.0 (0.6–1.7)	16 (2.0)	20 (2.5)	0.8 (0.1–1.5)
Other cardiovascular adverse events						
Prespecified exploratory cardiovascular end point†	58 (7.4)	79 (10.2)	0.7 (0.5–1.0)	63 (7.8)	83 (10.3)	0.8 (0.6–1.0)
Fatal or nonfatal myocardial infarction	20 (2.6)	18 (2.3)	1.1 (0.6–2.1)	10 (1.2)	22 (2.7)	0.5 (0.2–0.9)
Fatal or nonfatal stroke	11 (1.4)	7 (0.9)	1.6 (0.6–4.0)	2 (0.2)	8 (1.0)	0.2 (0.1–1.2)
Injection-site adverse events‡						
Any reaction	20 (2.6)	7 (0.9)	2.9 (1.2–6.7)	38 (4.7)	4 (0.5)	9.4 (3.4–26.3)
Mild	13 (1.7)	7 (0.9)	1.9 (0.7–4.6)	23 (2.8)	3 (0.4)	7.6 (2.3–25.2)
Moderate	7 (0.9)	0	—	15 (1.8)	1 (0.1)	14.9 (2.0–112.3)
Severe	0	0	—	0	0	—
Persistent	0	0	—	0	0	—
Frequent adverse events§						
Diabetes mellitus	120 (15.4)	108 (13.9)	1.1 (0.9–1.4)	88 (10.9)	94 (11.7)	0.9 (0.7–1.2)
Nasopharyngitis	—	—	—	91 (11.2)	90 (11.2)	1.0 (0.8–1.3)
Bronchitis	46 (5.9)	30 (3.9)	1.5 (1.0–2.4)	—	—	—
Dyspnea	39 (5.0)	33 (4.2)	1.2 (0.7–1.9)	—	—	—
Hypertension	42 (5.4)	42 (5.4)	1.0 (0.7–1.5)	53 (6.5)	54 (6.7)	1.0 (0.7–1.4)
Upper respiratory tract infection	39 (5.0)	33 (4.2)	1.2 (0.7–1.9)	52 (6.4)	49 (6.1)	1.1 (0.7–1.5)
Arthralgia	—	—	—	47 (5.8)	32 (4.0)	1.5 (0.9–2.3)
Osteoarthritis	—	—	—	32 (3.9)	40 (5.0)	0.8 (0.5–1.2)
Back pain	39 (5.0)	39 (5.0)	1.0 (0.6–1.5)	—	—	—
Laboratory results						
Liver function						
Alanine aminotransferase >3× ULN	2 (0.3)	2 (0.3)	1.0 (0.1–7.1)	4 (0.5)	4 (0.5)	1.0 (0.2–4.0)
Aspartate aminotransferase >3× ULN	4 (0.5)	5 (0.6)	0.8 (0.2–3.0)	2 (0.2)	4 (0.5)	0.5 (0.1–2.7)
Alkaline phosphatase >3× ULN	5 (0.6)	3 (0.4)	1.7(0.4–6.9)	1 (0.1)	2 (0.2)	0.5 (0.0–5.5)
Bilirubin >2× ULN	4 (0.5)	3 (0.4)	1.3 (0.3–5.9)	6 (0.7)	8 (1.0)	0.7 (0.3–2.1)
Kidney function: creatinine >2 mg/dl	30 (3.8)	30 (3.9)	1.0 (0.6–1.6)	5 (0.6)	11 (1.4)	0.5 (0.2–1.3)
Muscle: creatine kinase >5× ULN	10 (1.3)	8 (1.0)	1.2 (0.5–3.1)	10 (1.2)	9 (1.1)	1.1 (0.5–2.7)
Hematology: platelet count <75×10^9/liter	1 (0.1)	0	—	0	1 (0.1)	—

JAMA Network™

QUESTION In statin-treated patients with high cardiovascular risk, high triglycerides, and low HDL cholesterol, does adding a carboxylic acid formulation of omega-3 fatty acids (EPA and DHA) to ongoing treatment improve cardiovascular outcomes?

CONCLUSION The findings from this randomized trial do not support use of this omega-3 fatty acid formulation to reduce major adverse cardiovascular events in patients at high cardiovascular risk.

POPULATION

8510 Men
4568 Women

Adults with high triglycerides and low HDL levels, treated with statins, and at high risk of adverse cardiovascular outcomes

Mean age: **62.5** years

LOCATIONS

675 Hospitals in **22** countries

INTERVENTION

13 078 Patients randomized

6539
Omega-3
4 g/d of omega-3 CA (carboxylic acid) capsules containing EPA and DHA for up to 5 years

6539
Corn oil
Comparator capsules for up to 5 years

PRIMARY OUTCOME

Composite of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or unstable angina requiring hospitalization

FINDINGS

Occurrence of composite outcome events

Omega-3
785 of 6539 patients

Corn oil
795 of 6539 patients

At early trial termination, there was no significant difference between groups in the primary outcome:

HR, **0.99** (95% CI, 0.90-1.09); *P* = .84

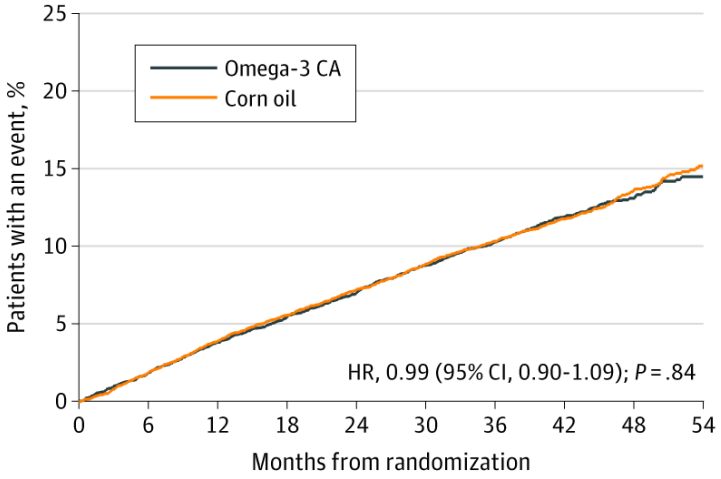
Nicholls SJ, Lincoff AM, Garcia M, et al. Effect of high-dose omega-3 fatty acids vs corn oil on major adverse cardiovascular events in patients at high cardiovascular risk: the STRENGTH randomized clinical trial. *JAMA*. Published online November 15, 2020. doi:10.1001/jama.2020.22258

JAMA | Original Investigation

Effect of High-Dose Omega-3 Fatty Acids vs Corn Oil on Major Adverse Cardiovascular Events in Patients at High Cardiovascular Risk

The STRENGTH Randomized Clinical Trial

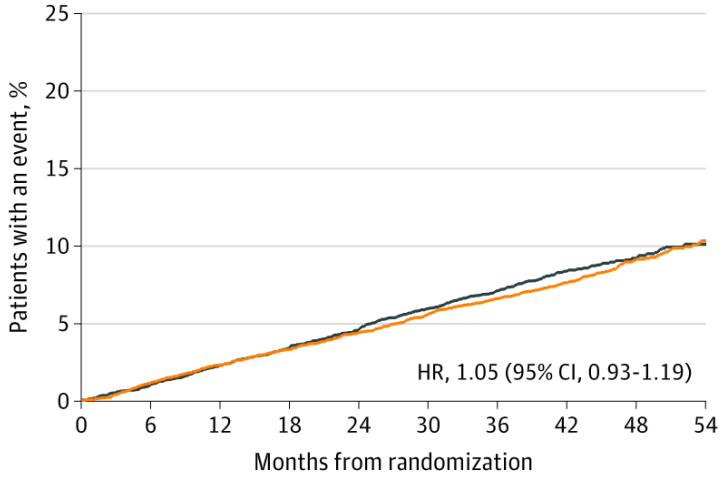
A Primary MACE, total population



No. at risk

Omega-3 CA	6539	6372	6200	6060	5917	5751	4900	2965	1535	567
Corn oil	6539	6373	6207	6083	5906	5754	4899	2995	1508	562

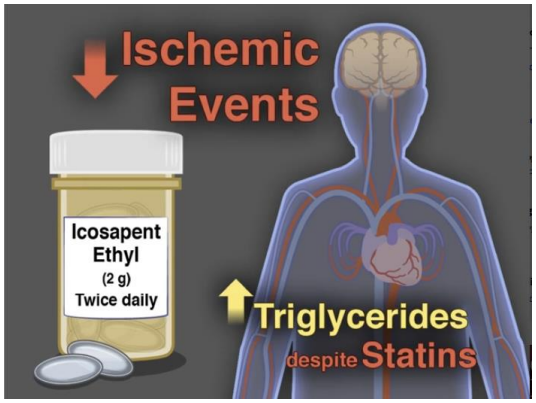
B Core MACE



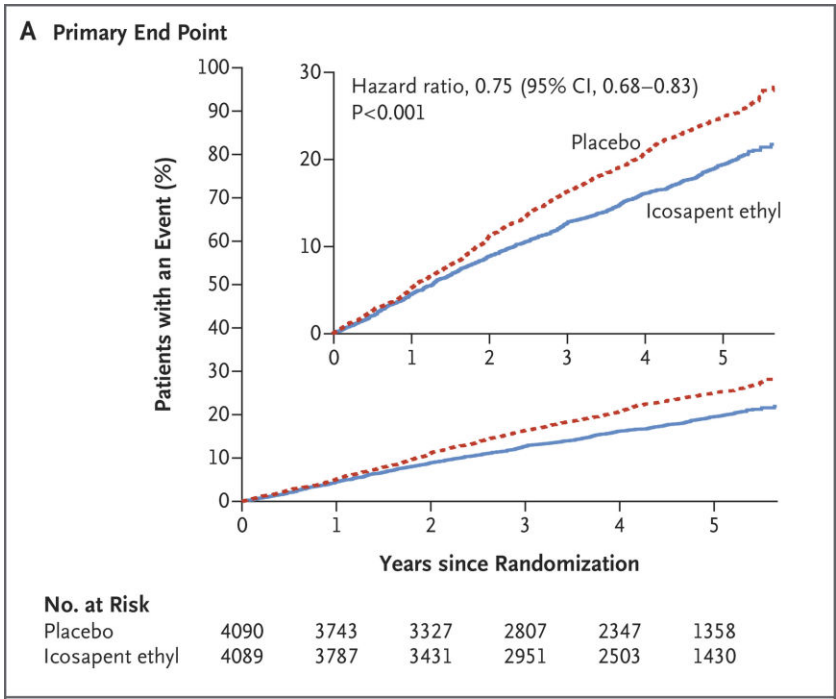
No. at risk

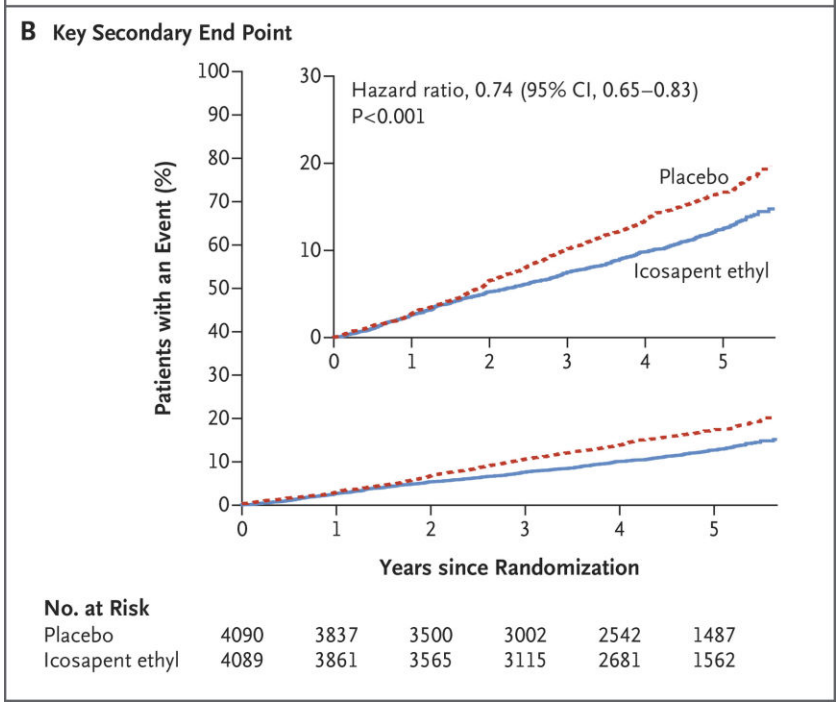
Omega-3 CA	6539	6426	6302	6190	6070	5933	5069	3091	1604	596
Corn oil	6539	6420	6312	6212	6091	5966	5093	3132	1588	595

Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia

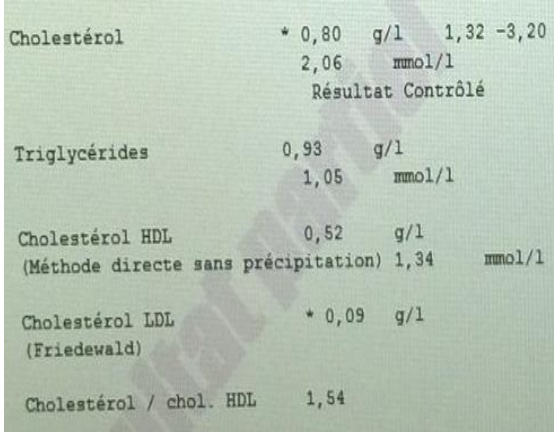


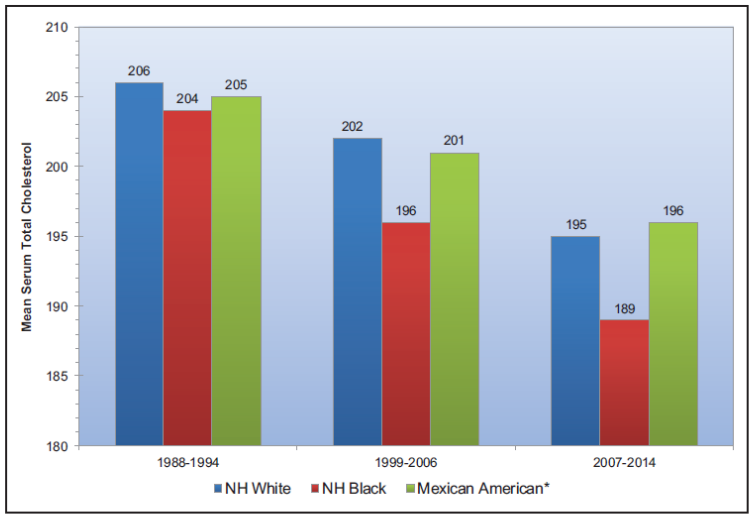
In-study AF hospitalization event rates were higher in patients with prior AF (12.5% versus 6.3%, IPE versus placebo; *P*=0.007) versus without prior AF (2.2% versus 1.6%, IPE versus placebo; *P*=0.09).





We have a problem: cholesterol levels fall while CHD rise…





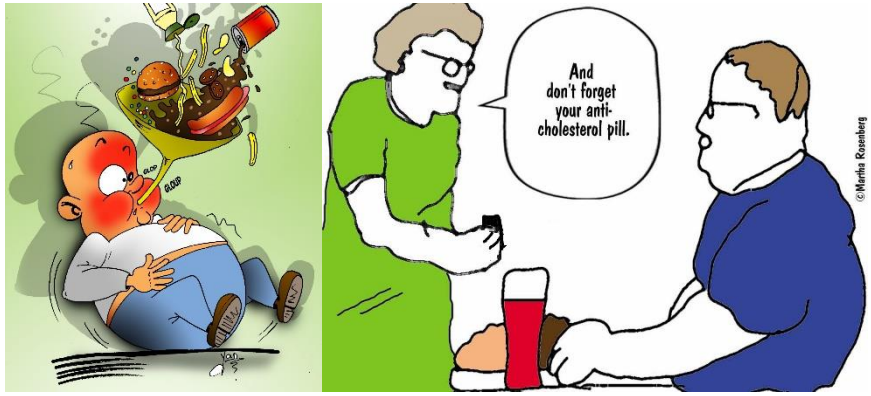
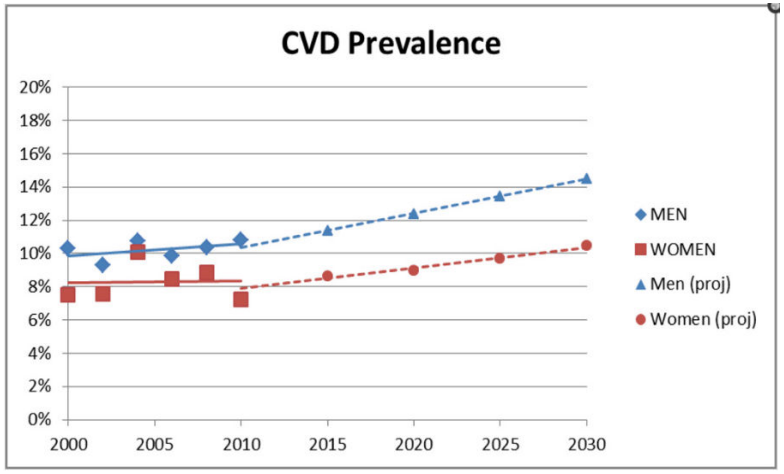
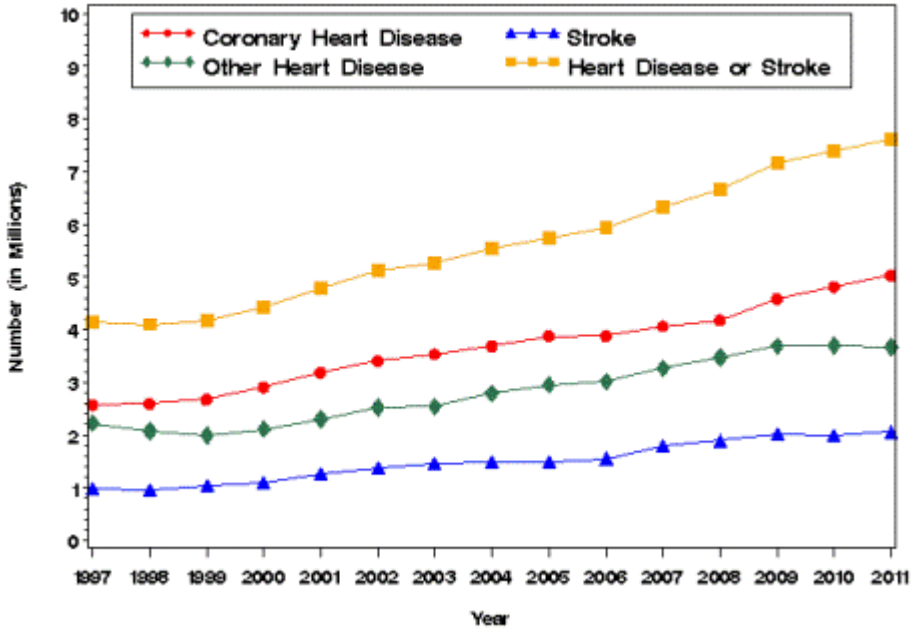


Chart 8-2. Age-adjusted trends in mean serum total cholesterol among adults ≥20 years old by race and survey year (NHANES 1988–1994, 1999–2006, and 2007–2014).

Incidence of CHD in the USA is rising steadily



Caption: Prevalence Of Cardiovascular Disease In The United States For Men And Women Ages 25–85, 2000–10 And 2015–30



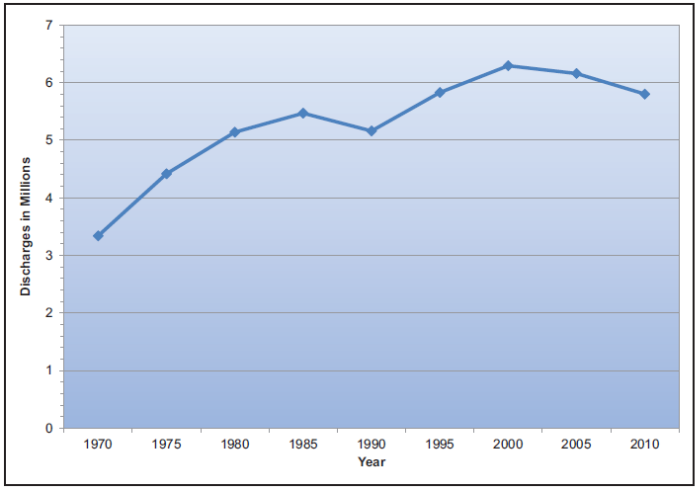
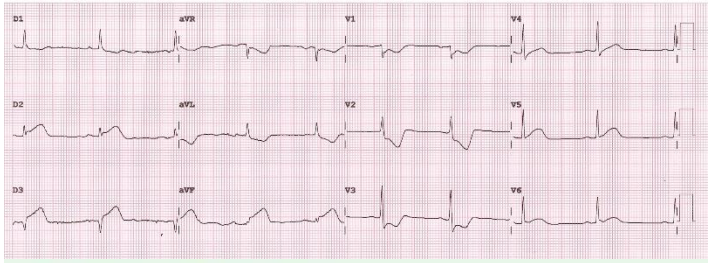


Chart 13-21. Hospital discharges for cardiovascular disease (United States: 1970–2010).
Hospital discharges include people discharged alive, dead, and "status unknown."
Source: National Center for Health Statistics and National Heart, Lung, and Blood Institute.

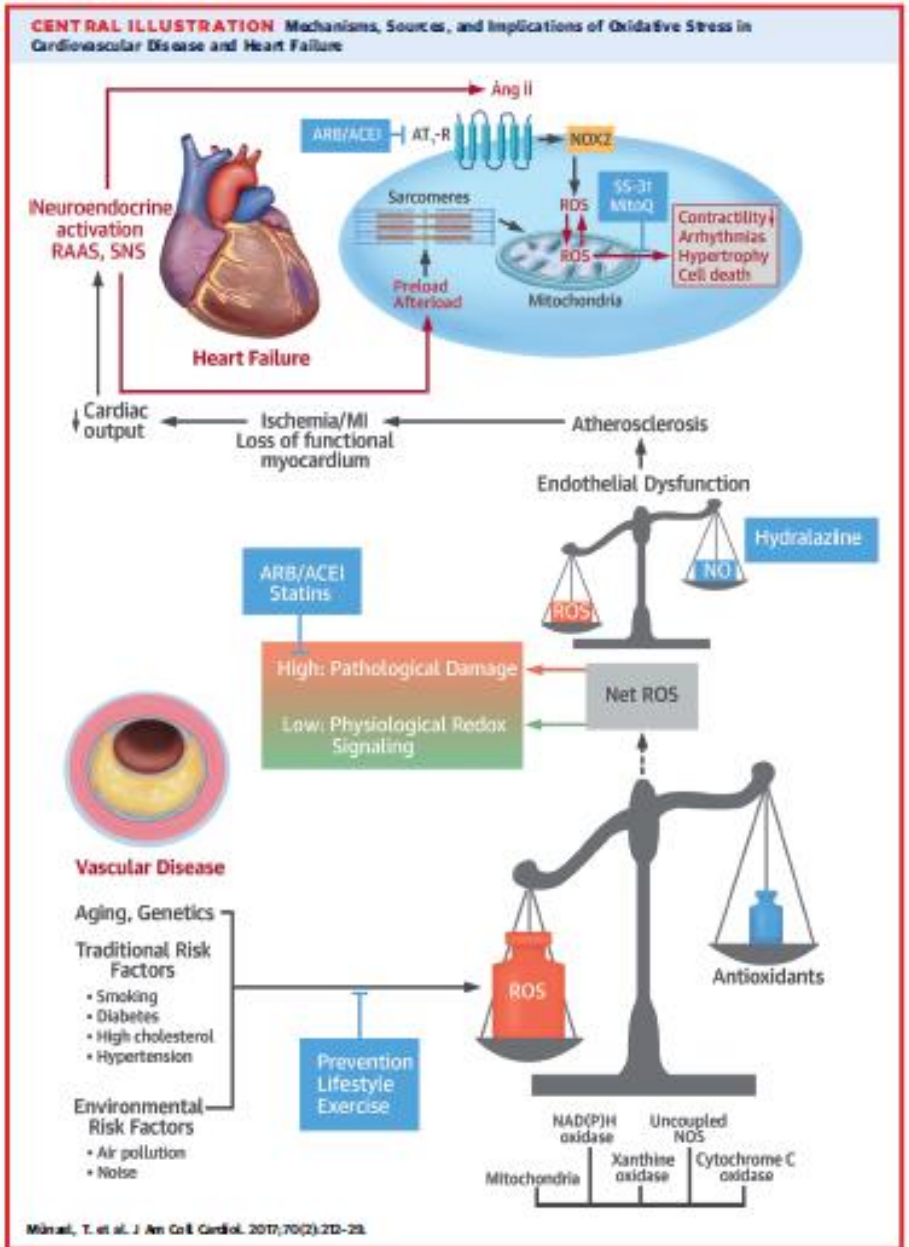


LIPIDES - LIPOPROTEINES
(Analyses effectuées sur automate Vista - Siemens)

Aspect du sérum	limpide		
Cholestérol	2,71	mmol/l	1
	1,05	g/l	
Triglycérides	0,32	mmol/l	1
	0,28	g/l	
Cholestérol HDL	1,55	mmol/l	
(Méthode directe sans précipitation)	0,60	g/l	
Cholestérol LDL	1,01	mmol/l	
(Friedewald)	0,39	g/l	
Cholestérol / chol. HDL	1,75		

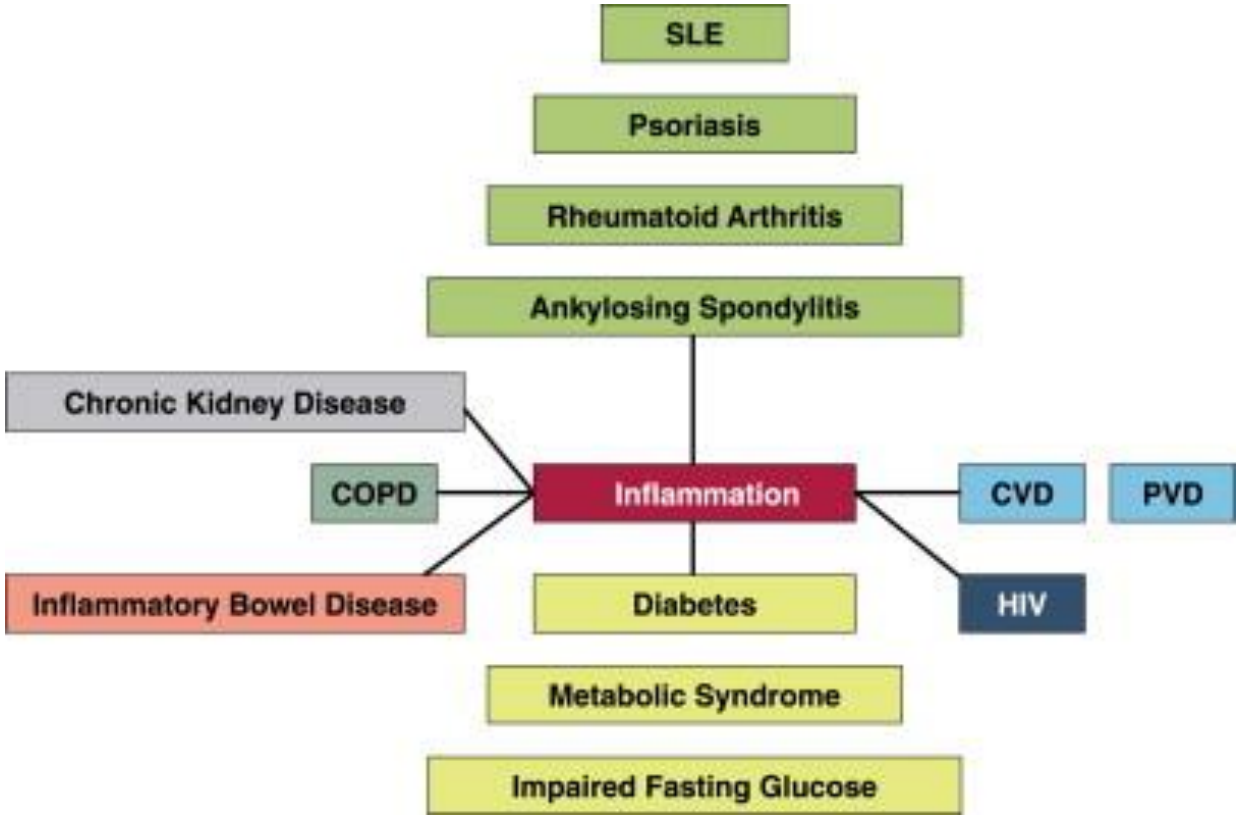
Atherosclerosis: a story of vascular inflammation

- Depression, stress
- Systemic diseases…

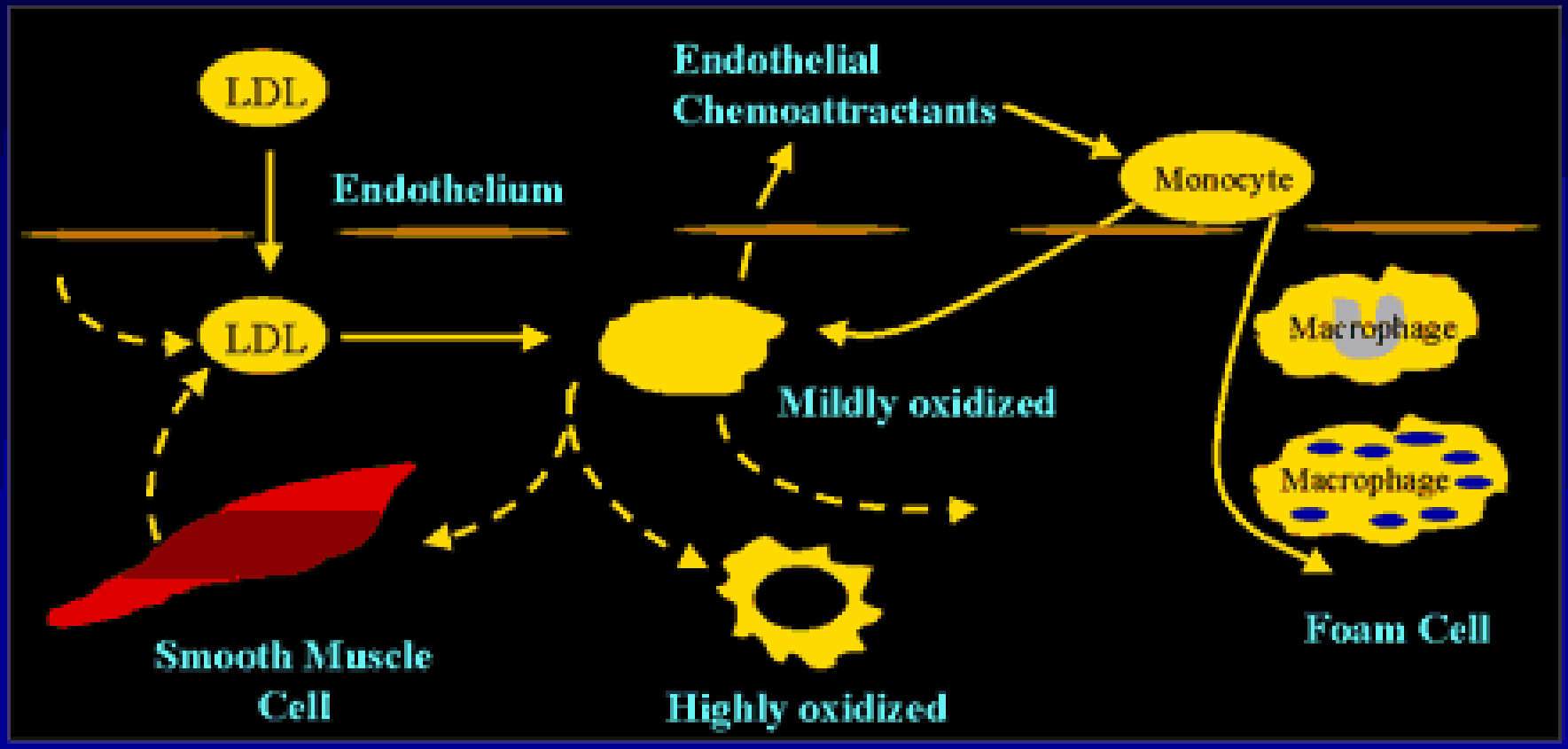


Individuals who particularly require attention

- Family history of premature CVD
- History of preeclampsia and pregnancy induced hypertension
- History of chest radiation
- Sedentarity, anxiety, depression



Atherogenicity of Small, Dense LDL



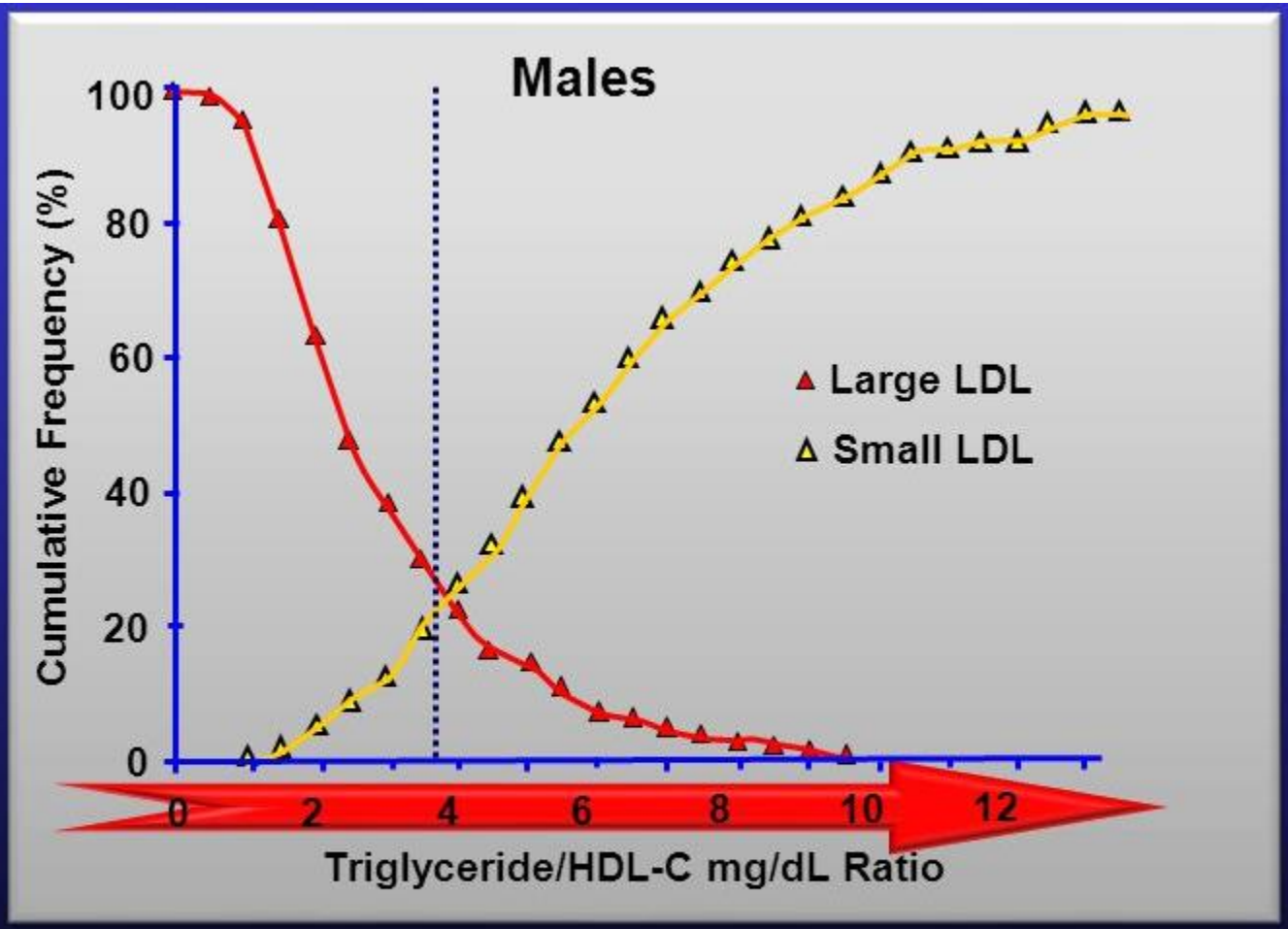
Evidence from in vitro studies suggests that large, buoyant LDL particles are more resistant to oxidative stress and small, dense LDL particles more susceptible to oxidation.

How to increase LDL size?

- Daily exercise
- Weight loss
- Reduce insulin resistance
- Reduce triglycerides
- Statins?

Volek et al. Lipids. 2009 Apr;44(4):297-309.

Relationship between Small LDL and Triglyceride/HDL-c ratio



In men, 76% of the LDL phenotype A was less than and 77% of phenotype B was greater than the cutoff of 3.8.

NMR Spectroscopy

Hanak, V. et al. Am J Cardiol 2004;94:219–222

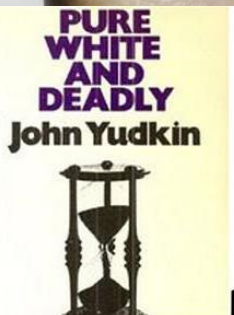
The true reason for CHD rise might not be only fat intake but sugar intake!

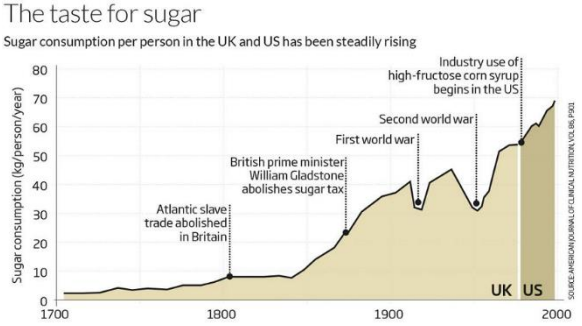
The 60 Names for Sugar

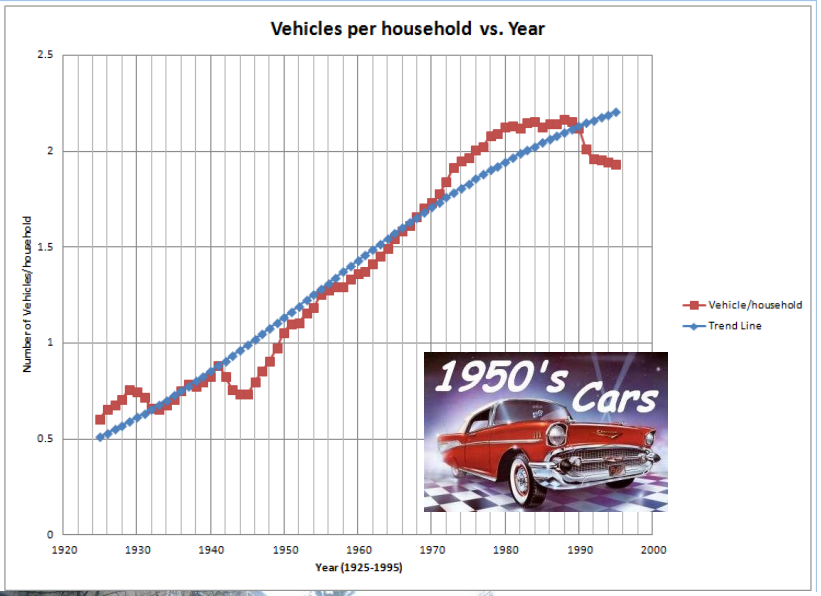
1. Agave nectar
2. Barbados sugar
3. Barley malt
4. Beet sugar
5. Blackstrap molasses
6. Brown rice syrup
7. Brown sugar
8. Buttered syrup
9. Cane juice crystals
10. Cane sugar
11. Caramel
12. Carob syrup
13. Castor sugar
14. Confectioner's sugar
15. Corn syrup
16. Corn syrup solids
17. Crystalline fructose
18. Date sugar
19. Demerara sugar
20. Dextran
21. Dextrose
22. Diastatic malt
23. Diatase
24. Ethyl maltol
25. Evaporated cane juice
26. Florida crystals
27. Fructose
28. Fruit juice
29. Fruit juice concentrate
30. Galactose
31. Glucose
32. Glucose solids
33. Golden sugar
34. Golden syrup
35. Grape sugar
36. High-fructose corn syrup
37. Honey
38. Icing sugar
39. Invert sugar
40. Lactose
41. Mannitol
42. Malt syrup
43. Maltodextrin
44. Maltose
45. Maple syrup
46. Molasses
47. Muscovado sugar
48. Organic raw sugar
49. Panocha
50. Powdered sugar
51. Raw sugar
52. Refiner's syrup
53. Rice syrup
54. Sorbitol
55. Sorghum syrup
56. Sucrose
57. Sugar
58. Treacle
59. Turbinado sugar
60. Yellow sugar

Fake Sugar:
Sucralose
Aspartame
Saccharine

Cultivated Wellbeing





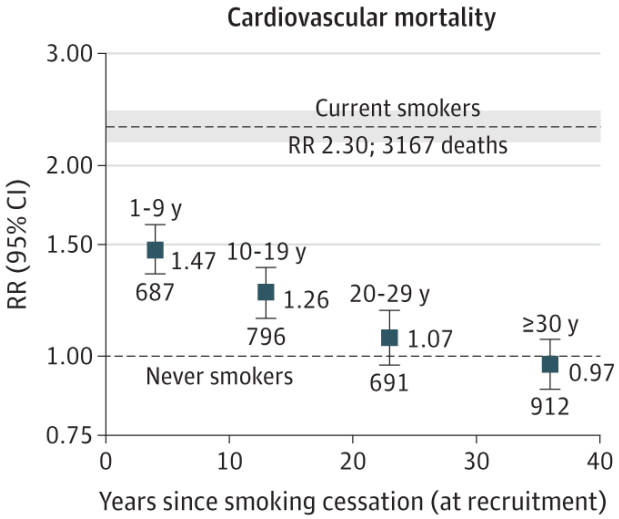

Vehicles per household vs. Year
Number of Vehicles/household
Year (1925-1995)
Vehicle/household
Trend Line
1950's Cars

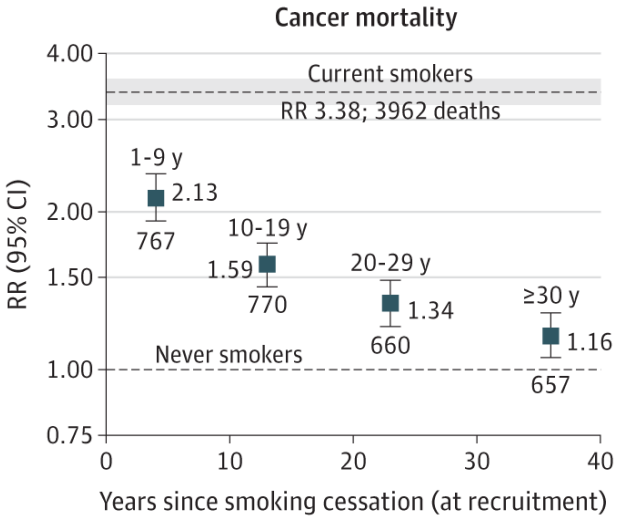

Tropicana
ORANGEADE
Singles
Motrin
Coca-Cola
CHEEZ-IT
HEINZ
TOMATO KETCHUP
Welch's
Grape Jelly
SWEET'N LOW
Twinkies

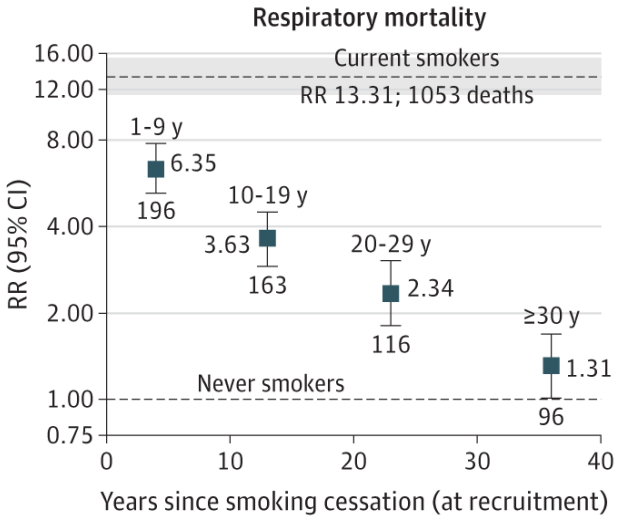

AHA, ACC, SFC, ADA.....

From: **Association of Smoking Cessation and Cardiovascular, Cancer, and Respiratory Mortality**

JAMA Intern Med. 2024;184(1):110-112. doi:10.1001/jamainternmed.2023.6419







Among 438 015 included adults (mean [SD] age, 47 [14] years; 56% female)

Cause-Specific Mortality Rate Ratios (RRs) by Years Since Quit Smoking Among Former Smokers Compared With Current and Never Smokers, Age at Risk, 25-89 . Data have been adjusted for age at risk, sex, education, race and ethnicity, and alcohol consumption.

10 WAYS TO DECREASE TRIGLYCERIDES

Decrease or Eliminate Sweets

Eat Healthy Oils

Decrease or Eliminate Alcohol

Avoid Trans-fat and Hidden Fats

Reduce Intake Of Refined Carbohydrate Containing Foods

Choose High Fibre Foods

Choose Foods Rich In Omega 3 Fatty Acids, The "Good" Fats!

Eat More Plant Foods!

Maintain a Healthy Weight

Exercise Regularly

Traiter Lp(a)

Table 1

Non-genetic influences on lipoprotein(a) concentration

Condition/intervention	Effect on Lp(a) levels
Lifestyle	
Replacement of dietary saturated fat with carbohydrate or unsaturated fat[32]	~10%–15% increase
Low carbohydrate diet high in saturated fat[33]	~15% decrease
Fasting[34]	None
Physical activity[35]	None/minimal
Hormones and related conditions	
Hyperthyroidism[36]	Decrease; 20%–25% increase with thyrostatic treatment or radioactive iodine therapy
Hypothyroidism[36]	Increase; 5%–20% decrease with replacement therapy
Growth hormones[37]	2x increase with therapy
Endogenous sex hormones[31]	None/minimal
Pregnancy[38,39]	2x increase
Menopause[31]	None/minimal
Postmenopausal hormonal replacement therapy[40]	~25% decrease
Surgical or biochemical castration in males[48]	Small increase
Ovariectomy, oestrogen receptor antagonist[49]	Small increase

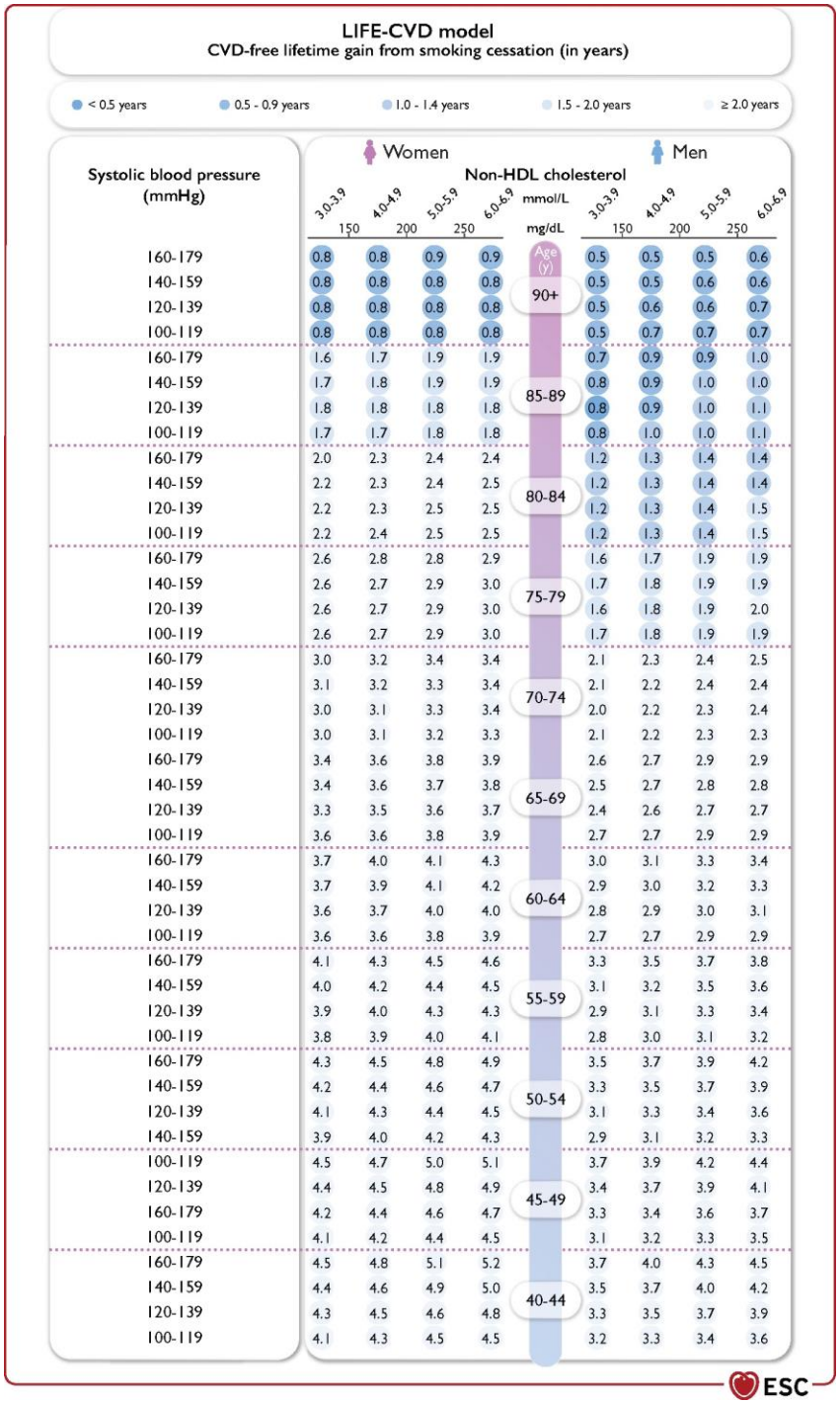
Traiter Lp(a)

Chronic kidney disease[41,42]	
Nephrotic syndrome[50,63]	3–5 x increase (vs. control)
Peritoneal dialysis patients[51]	2 x increase (vs. control)
Haemodialysis treatment and chronic kidney disease[51,52,64]	Increases in large apo(a) isoform carriers
Kidney transplantation[43]	~Normalization of levels
Hepatic impairment[44,59]	Decrease, depending on cause
Liver transplantation[53]	Changes of apo(a) isoform to that of the donor, with corresponding changes in Lp(a) levels
Inflammation and related conditions[55,60]	
Severe, life-threatening acute-phase conditions (sepsis, severe burns)[46]	Decrease
Several inflammatory conditions[45]	Increase
Tocilizumab (interleukin-6 inhibitor)[47,61]	~30%–40% decrease
Protease inhibitors or antiretroviral therapy[56,57]	Increase
Statins[65–68]	May slightly increase Lp(a) (but reports are heterogeneous)
Air pollution (fine particulate, PM2.5)[58]	Slight increase

CONCLUSION

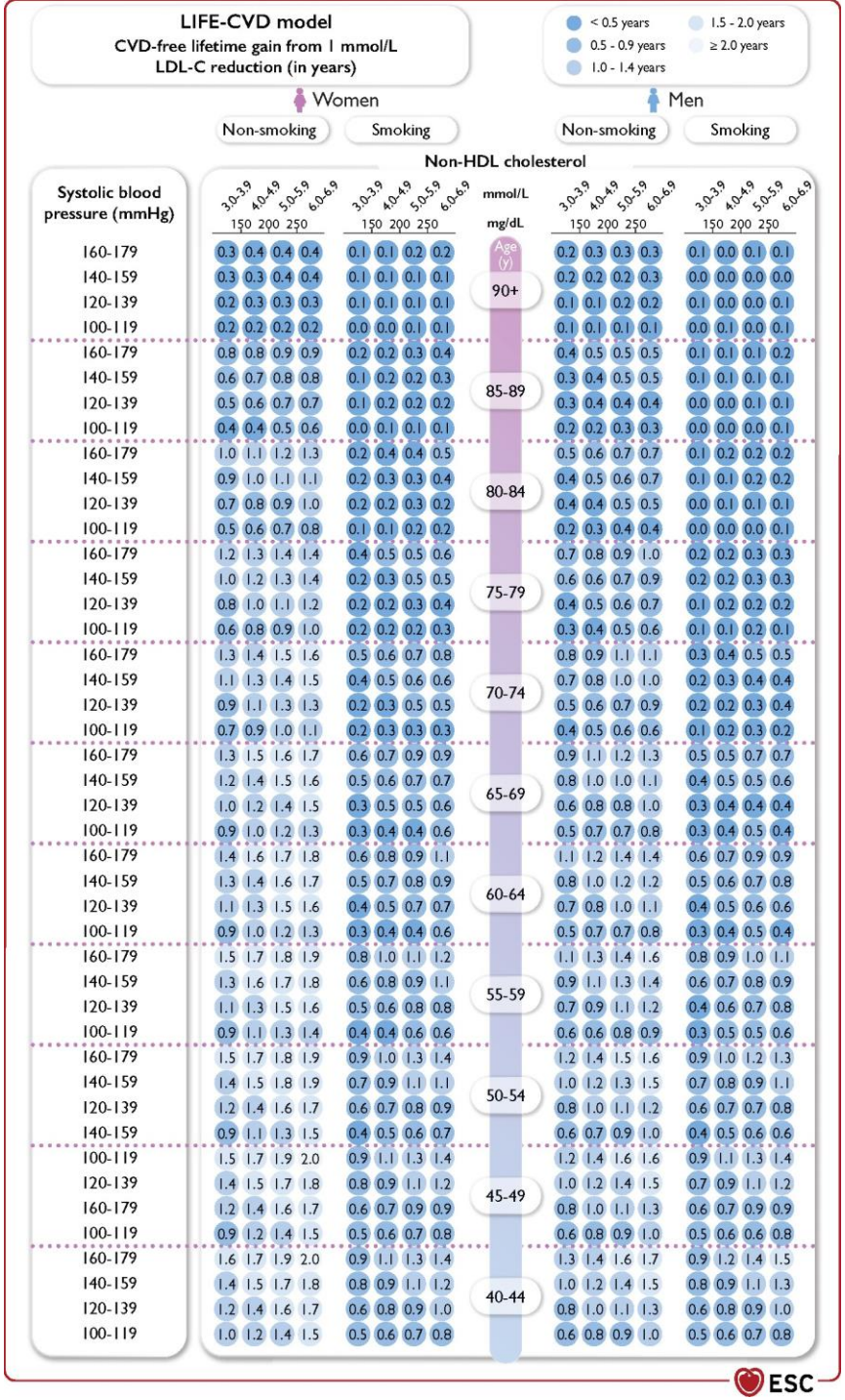
- Atherothrombosis is a complex disease
- To treat individual or population?
- We need better biomarker than LDL to identify patients who most derived benefits from statins
- No efficacy in aortic stenosis, heart failure, hemodialysis
- No robust data on older people, active smoker…
- Sharing data…..

Figure 11 Lifetime atherosclerotic cardiovascular disease benefit from smoking cessation for apparently healthy ...

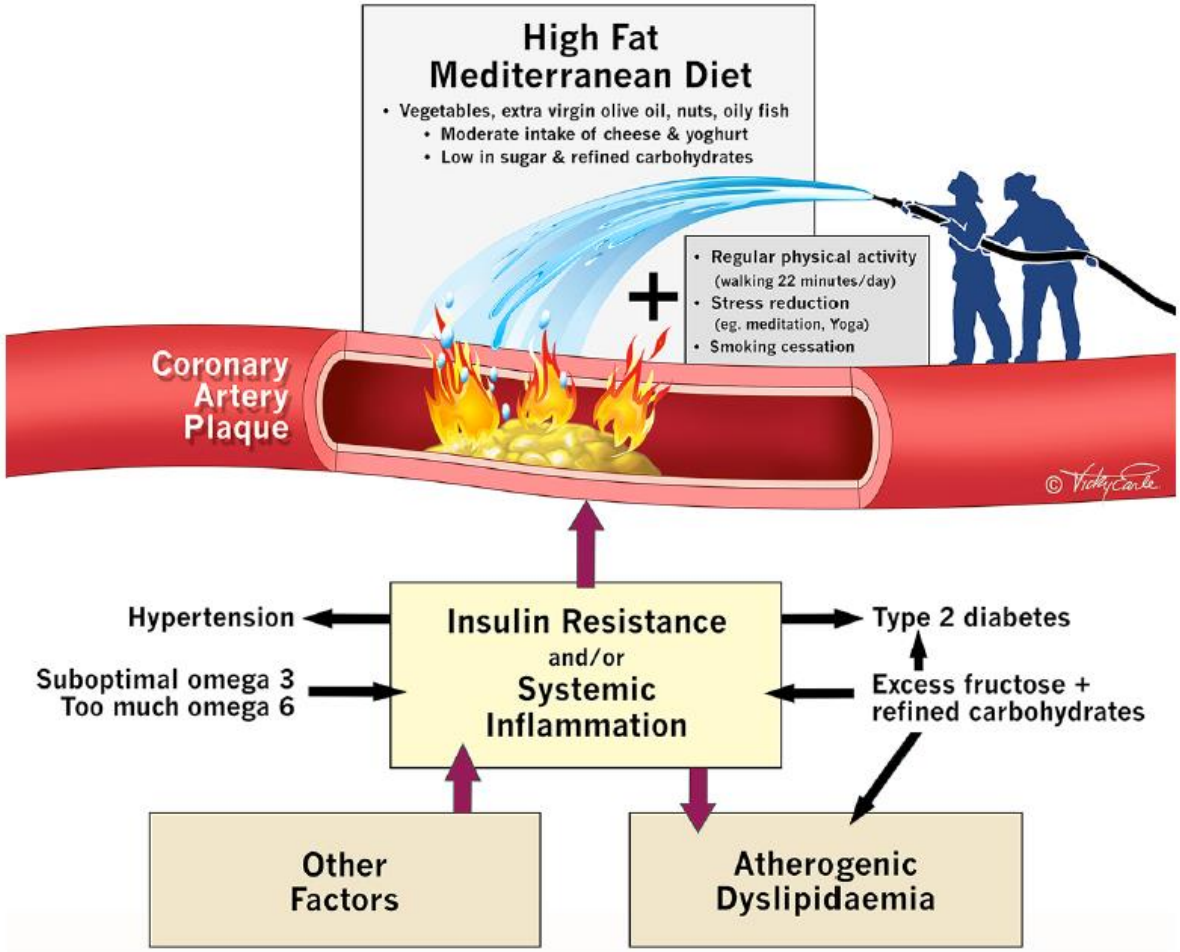


Eur Heart J, Volume 42, Issue 34, 7 September 2021, Pages 3227–3337, https://doi.org/10.1093/eurheartj/ehab484

Figure 12 Average years-free-of-cardiovascular disease gained per 1 mmol/L (40 mg/dL) low-density lipoprotein ...

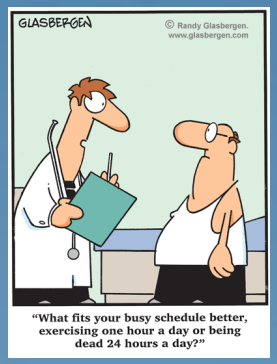


Eur Heart J, Volume 42, Issue 34, 7 September 2021, Pages 3227–3337, https://doi.org/10.1093/eurheartj/ehab484



Malhotra A, et al. Br J Sports Med August 2017

Thank you



"What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?"

Le tiers de ce que nous mangeons suffirait à nous faire vivre

Les deux autres tiers servent à faire vivre les médecins.

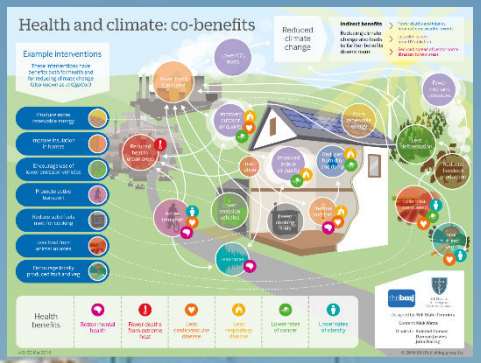
Dr Paul

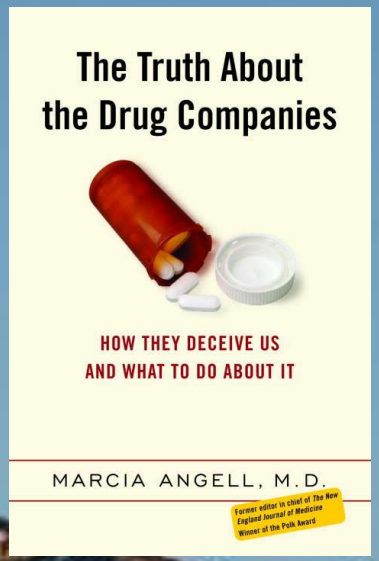
The case against science is straightforward: much of the scientific literature, perhaps half, may simply be untrue.

Ioannidis JPA (2005)
Why most published research findings are false.
PLoS Med 2(8): e124.

Too much medicine; too lit

BMJ 2013 ; 347 doi: https://doi.or



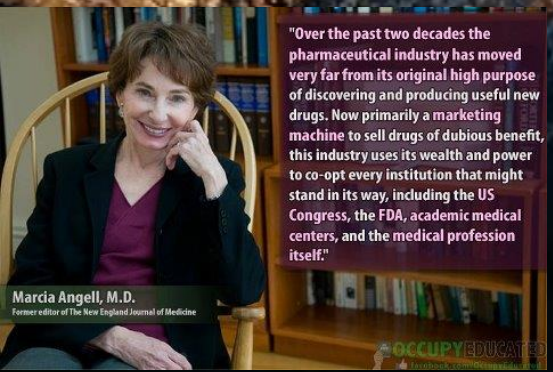


Statins: w

Fiona Godlee *edi*

The BMJ

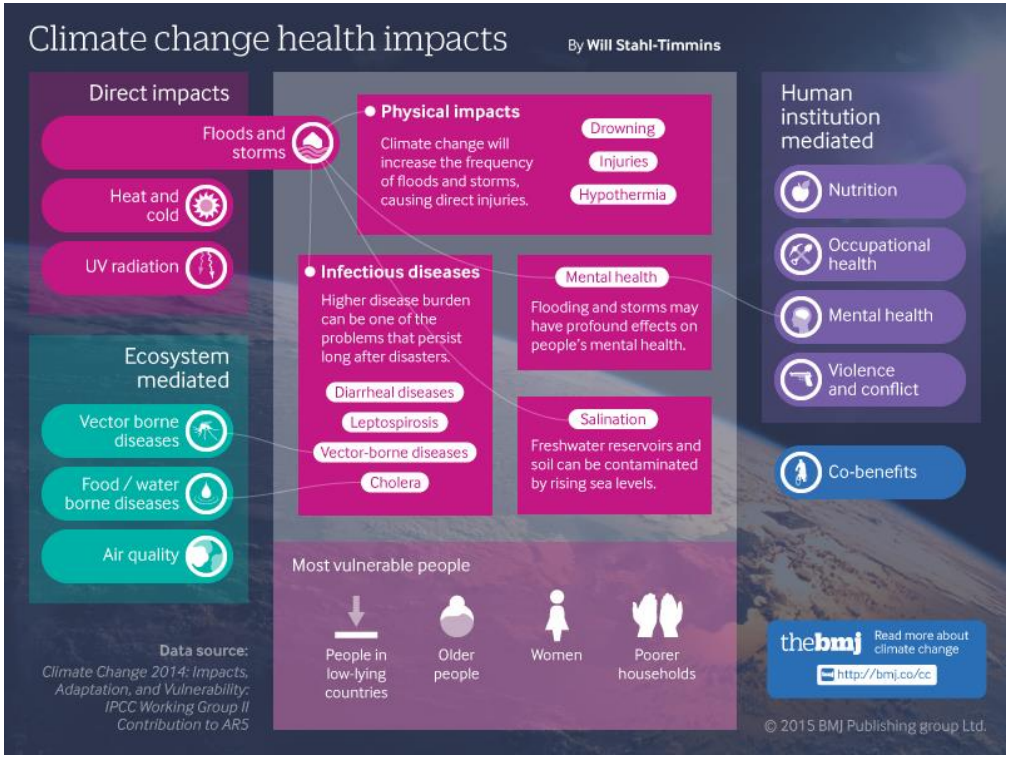
« L'idée de dire que le gras vous rend gras est aussi stupide que de dire que de manger des légumes verts vous rend vert. » Dr Uffe Ravnskov.



- « Doctors generate better knowledge of efficacy than of risk and this skews decision making. Patients are wildly enthusiastic about these treatments….» Pr David Jones Ackerman

CONCLUSION

"The problem is that you're overmedicated.
Luckily there are drugs that can help with that."


Climate change health impacts
By Will Stahl-Timmins
Direct impacts
Floods and storms
Heat and cold
UV radiation
Physical impacts
Climate change will increase the frequency of floods and storms, causing direct injuries.
Drowning
Injuries
Hypothermia
Infectious diseases
Higher disease burden can be one of the problems that persist long after disasters.
Diarrheal diseases
Leptospirosis
Vector-borne diseases
Cholera
Mental health
Flooding and storms may have profound effects on people's mental health.
Salination
Freshwater reservoirs and soil can be contaminated by rising sea levels.
Ecosystem mediated
Vector borne diseases
Food / water borne diseases
Air quality
Human institution mediated
Nutrition
Occupational health
Mental health
Violence and conflict
Co-benefits
Most vulnerable people
People in low-lying countries
Older people
Women
Poorer households
Data source:
Climate Change 2014: Impacts, Adaptation, and Vulnerability: IPCC Working Group II Contribution to AR5
thebmj
Read more about climate change
http://bmj.co/cc
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GoalSetting
PhysicalHealth
MentalHealth
AccessingValidInformation
GrowthDevelopment
PhysicalActivity
Prevention
Health
HealthyBehaviors
Tobacco
CoreConcepts
Advocacy
Nutrition
Education
PreventingDiseases
AnalyzingInfluences
DecisionMaking
AlcoholDrugs
SocialHealth
SelfManagement
Communication


COORDINATED SCHOOL HEALTH
Physical Education
Health Education
Health Services
Nutrition Services
Healthy School Environment
Family & Community Involvement
Counseling, Psychological & Social Services
Health Promotions for Staff