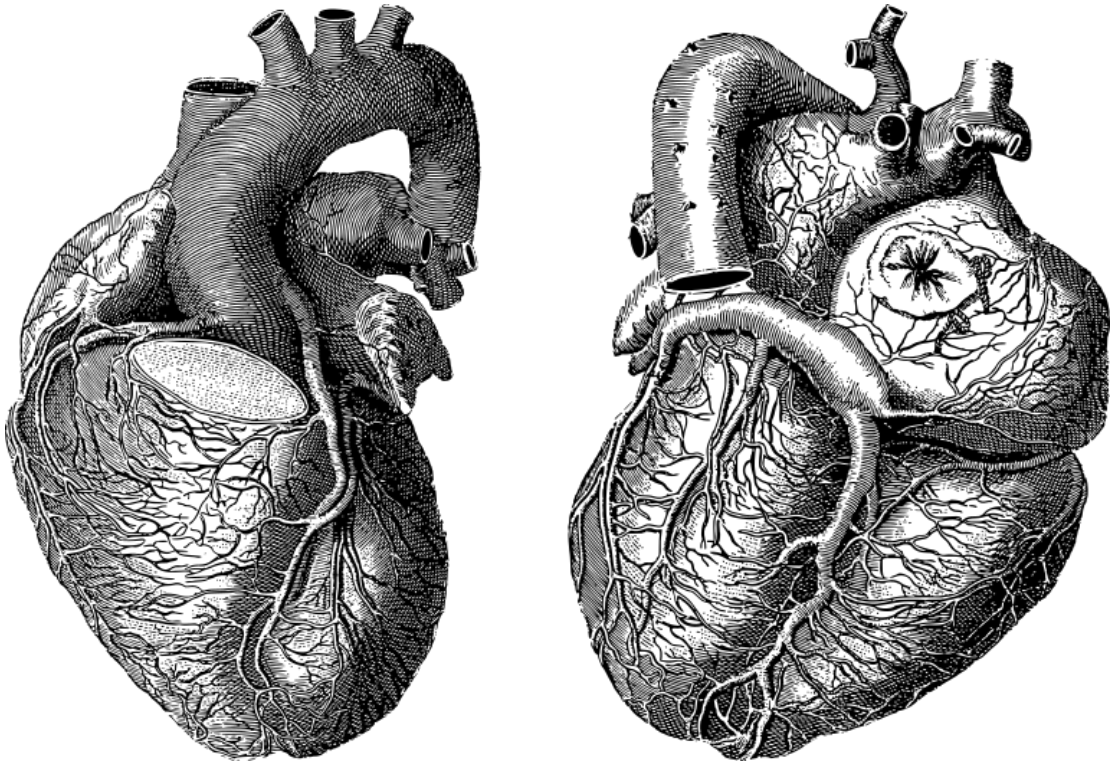
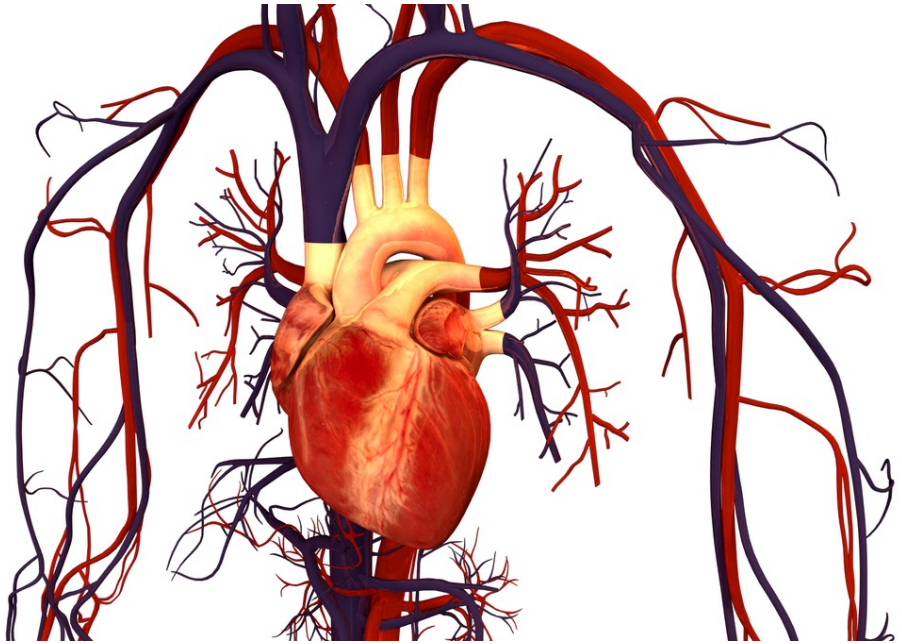
Heart disease: coronary heart disease.



Christopher Whitty
Gresham College 2023

The heart- an extraordinary organ.

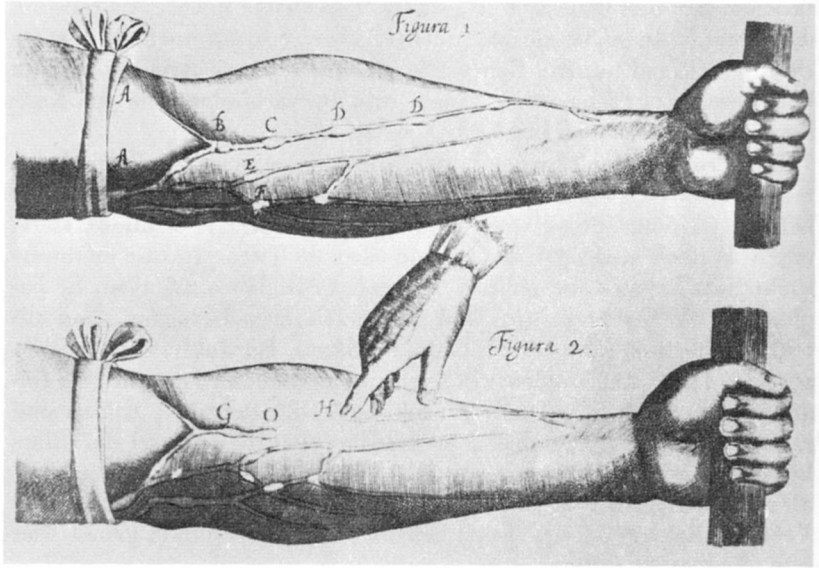
- Every day it pumps around 100,000 times- and will to the day you die.
- Provides oxygen to all other organs, removes waste.
- Very responsive to increased need.
- Keeps blood pressure and flow optimised.



Bryan Brandenburg / wiki

The function of the heart had not been realised when this College was founded (1597). Steady increase in understanding since.

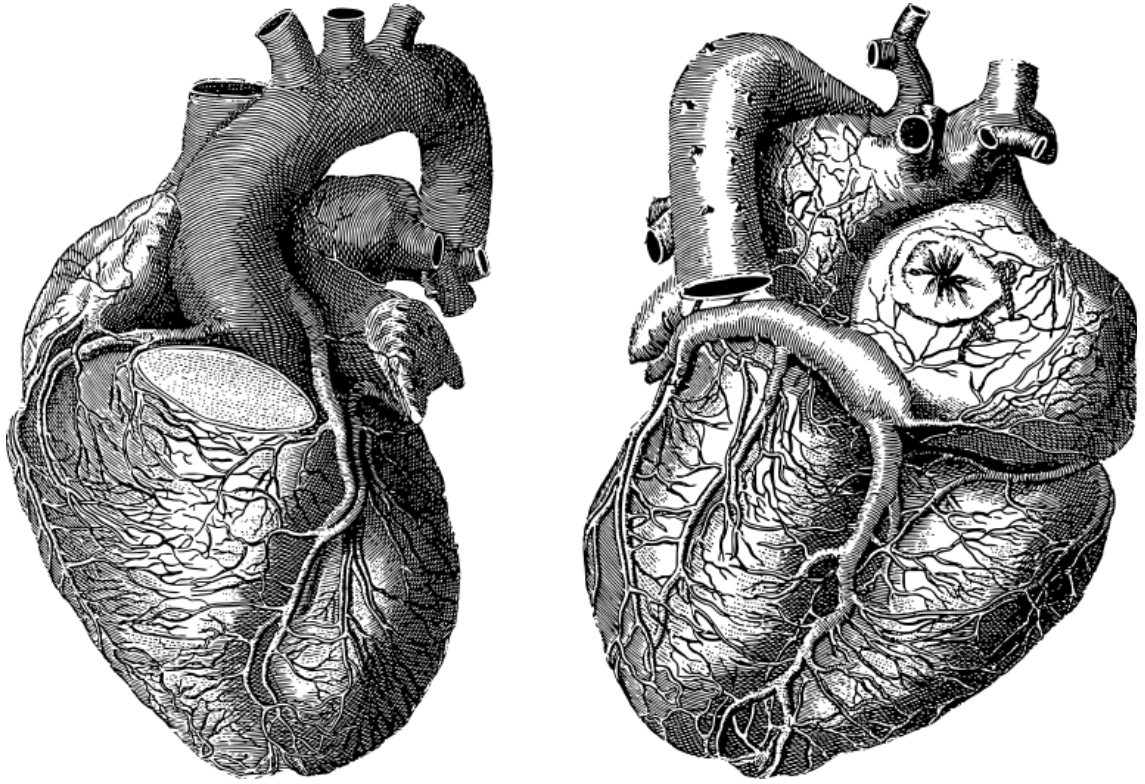
***De Motu Cordis* (1628)**



William Harvey 1578-1657

Three broad groups of things can lead to the heart failing or stopping.

- Myocardia ischaemia- lack of oxygen usually due to narrow or blocked coronary arteries. Also called coronary heart disease.
- The heart rhythm changes- either too fast, or too slow.
- The structures of the heart are damaged including muscle and valves.

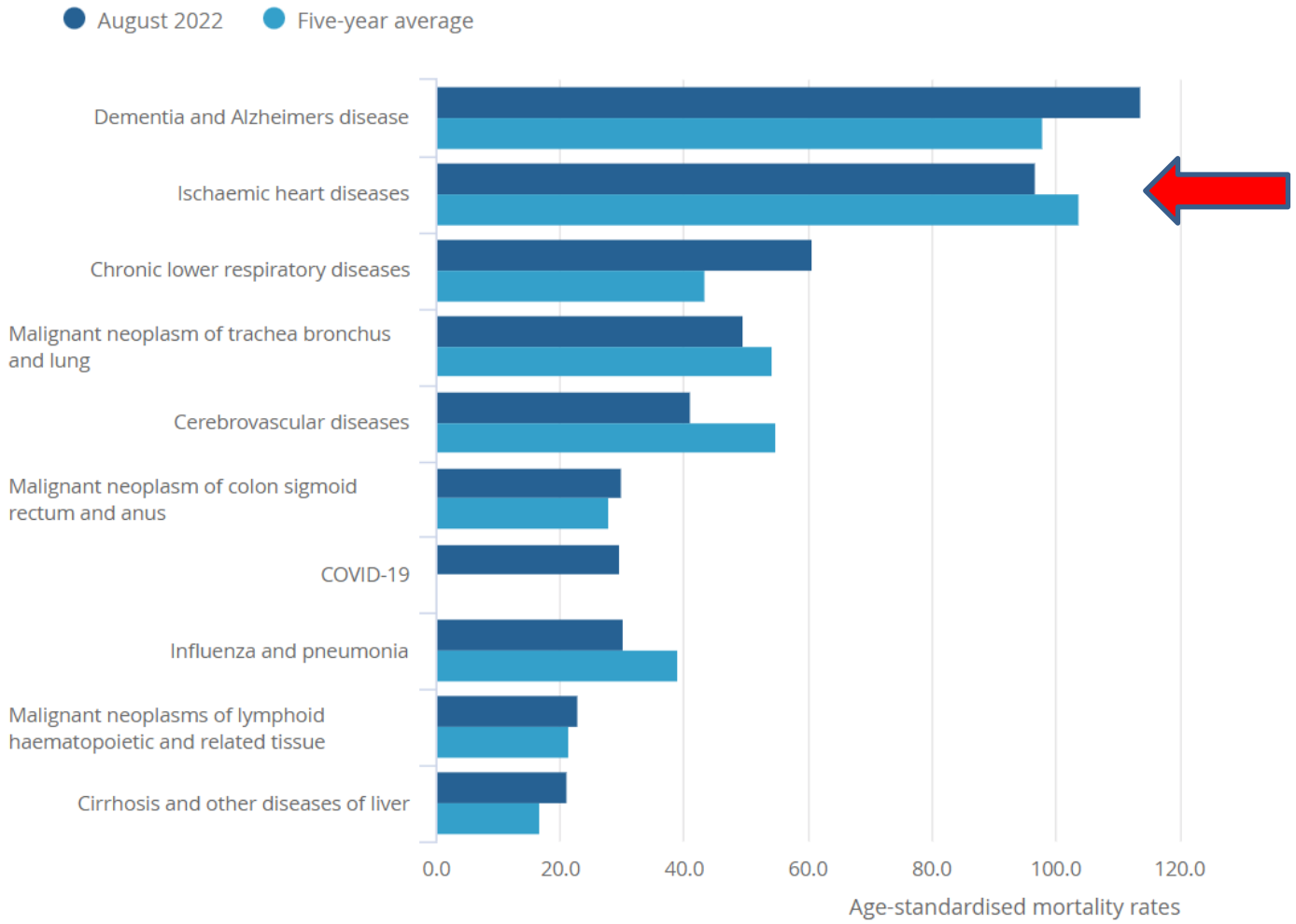


GDJ/wiki

Ischaemic heart disease (coronary heart disease) the second leading cause of recorded mortality in the UK, and the commonest worldwide.

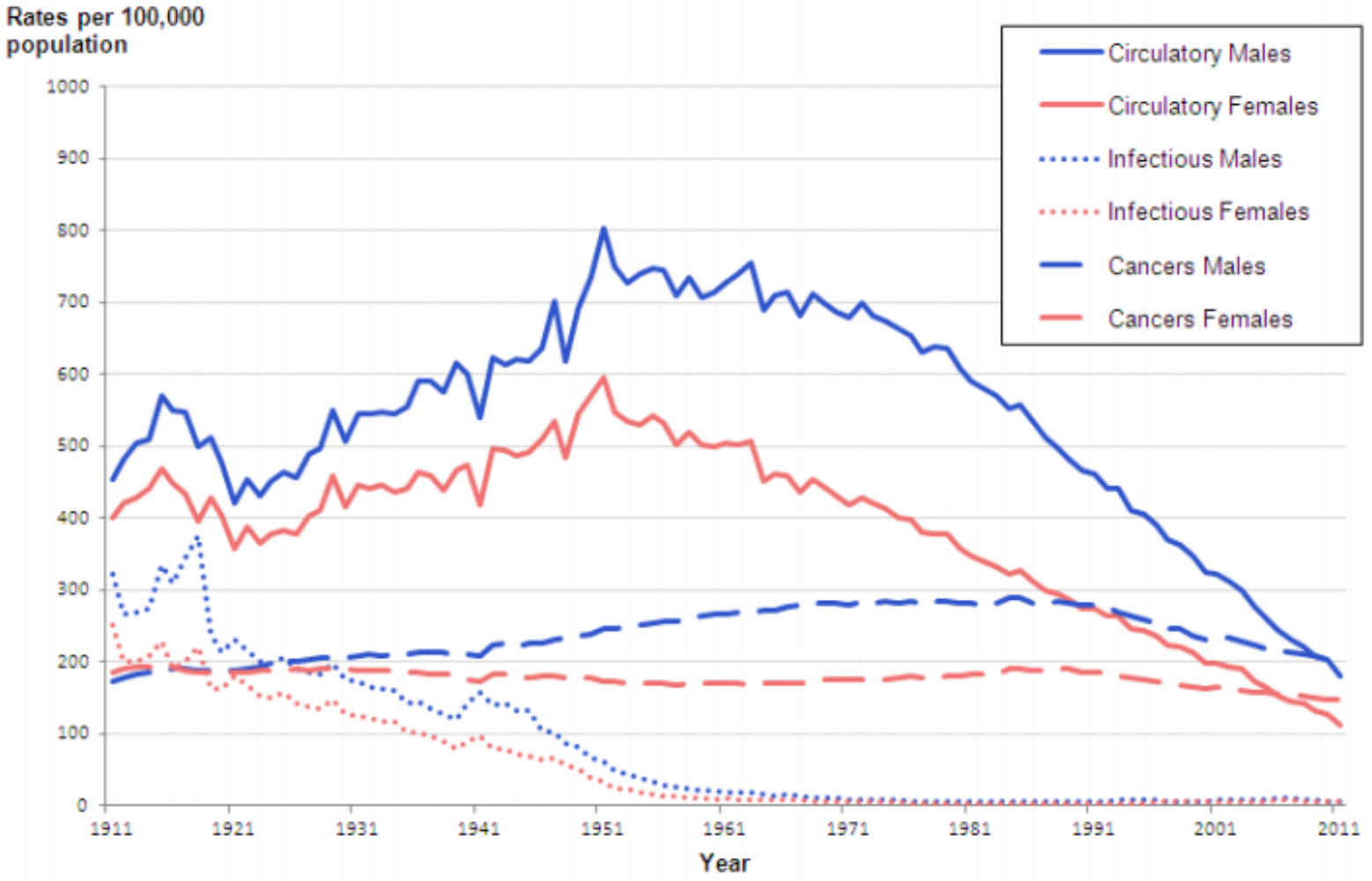
- Most frequently myocardial infarction (MI), commonly called a heart attack.

- ONS data (L) shows leading causes of mortality in Aug 2022 and 5 year average.



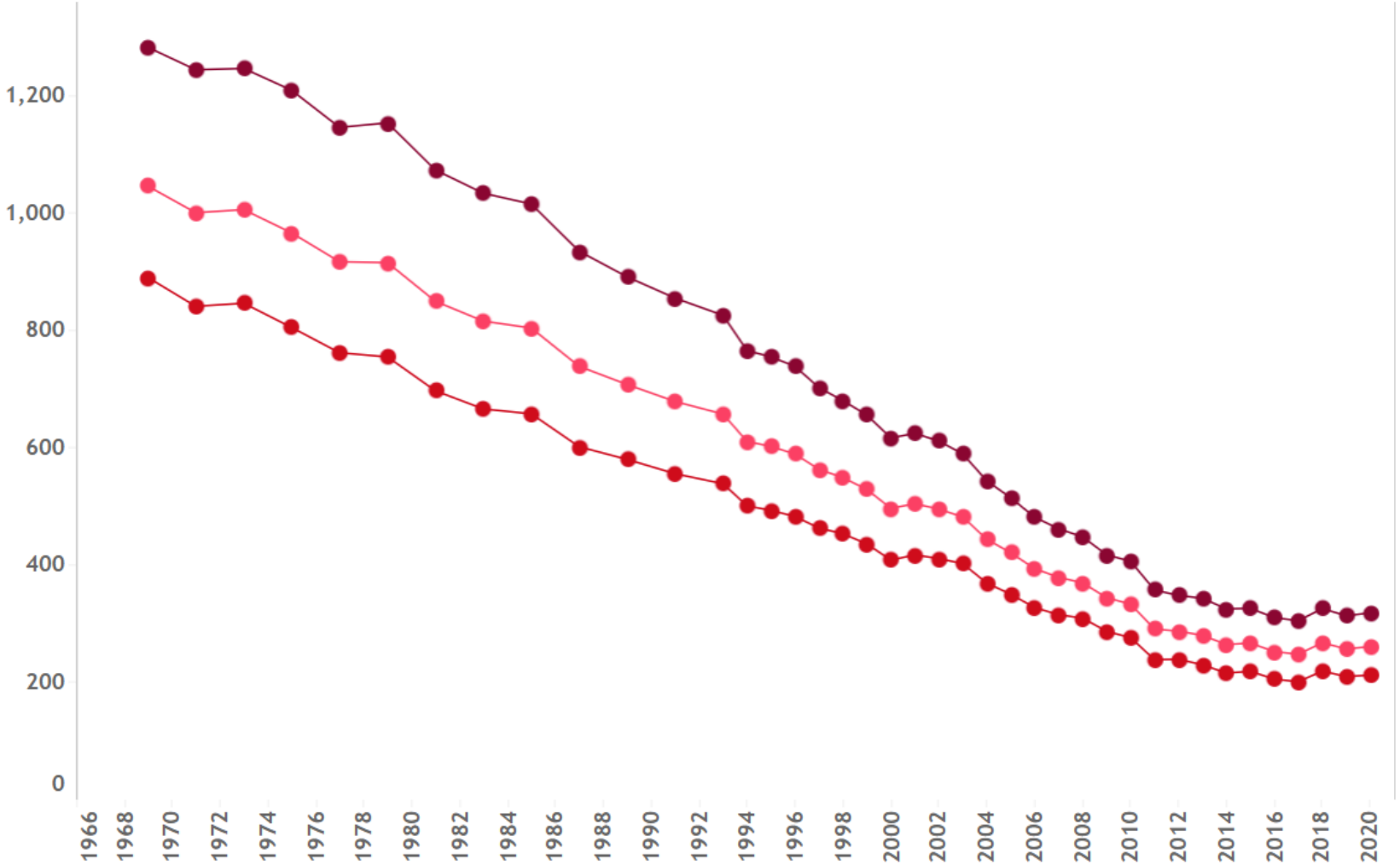
Heart and circulatory disease caused about half of deaths in the UK in early 1960s- now about a quarter of deaths.

Age-standardised mortality rates England and Wales- circulatory, cancer, infection 1911-2011. *(ONS)*



Age standardised mortality CHD per 100,000 people 1969-2020, UK.

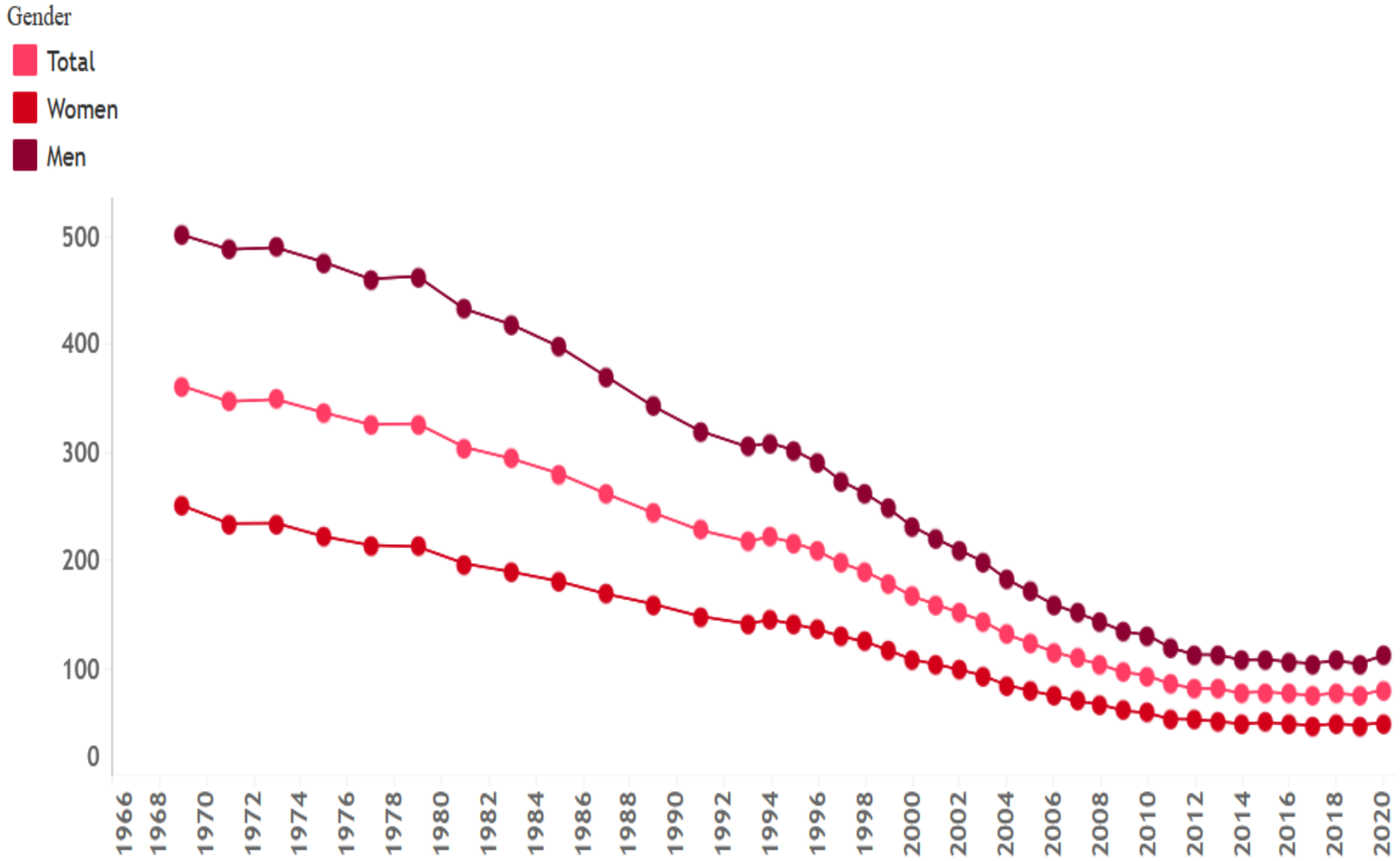
Men drop from 1281 to 317; women from 889 to 210 /100,000.



BHF 2022

Under 75 mortality coronary heart disease, UK 1969-2020.

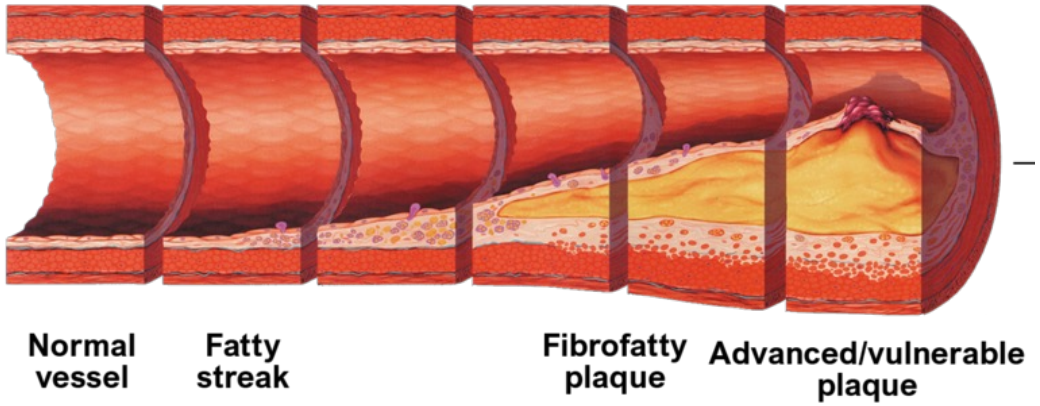
Women dropped from 250 to 48; men from 500 to 110/ 100,000.



BHF 2022

Atherosclerosis, leading to coronary heart disease.

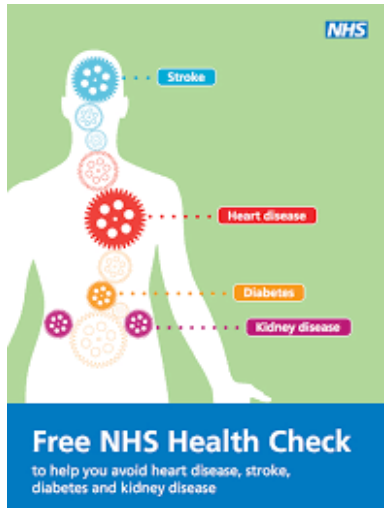
- The most important cause of narrowing of the coronary arteries supplying the heart.
- Fatty deposits cause a narrowing. Build up over a lifetime.
- Critical narrowing can cause angina.
- Rupture can cause a clot which blocks the blood vessel- heart attack (MI).
- Several modifiable risk factors.

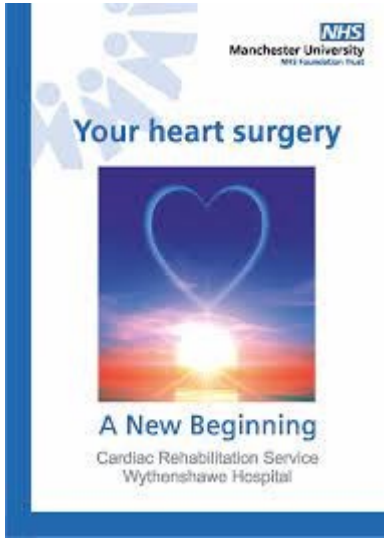


Npatchett / wiki

Primary prevention, secondary prevention and treatment.

- Primary prevention- generally things the State does to reduce risks to all in society.
- Secondary prevention- reducing the risk to an individual who has early disease or specific risk factors, usually with a healthcare worker.
- Treatment- which reduces mortality, symptoms and subsequent risk.





NHS

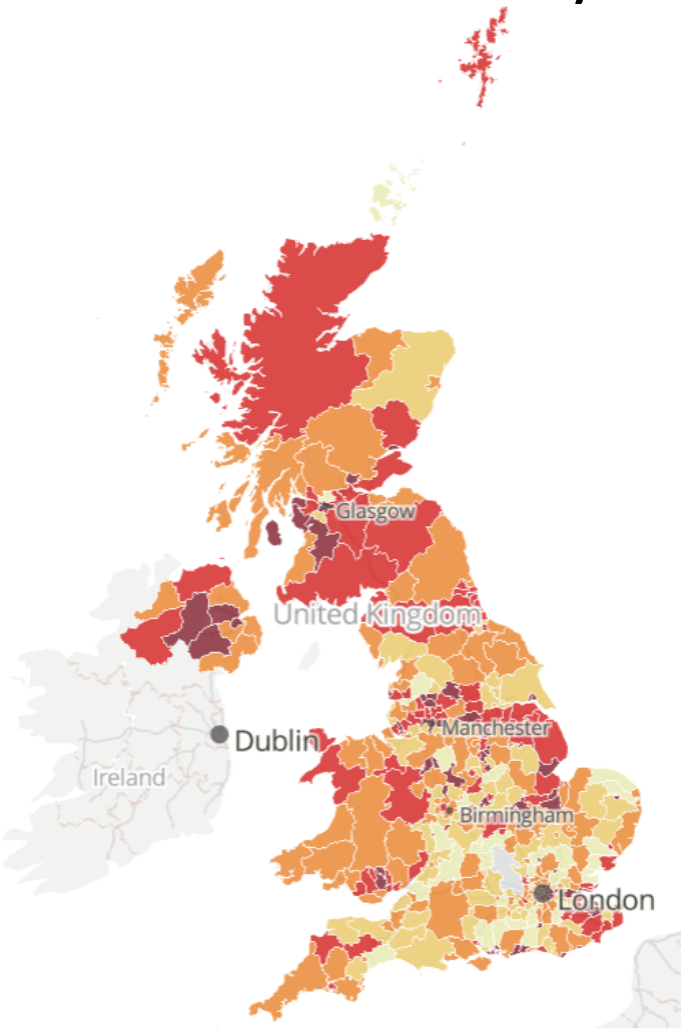
Primary prevention of IHD includes:

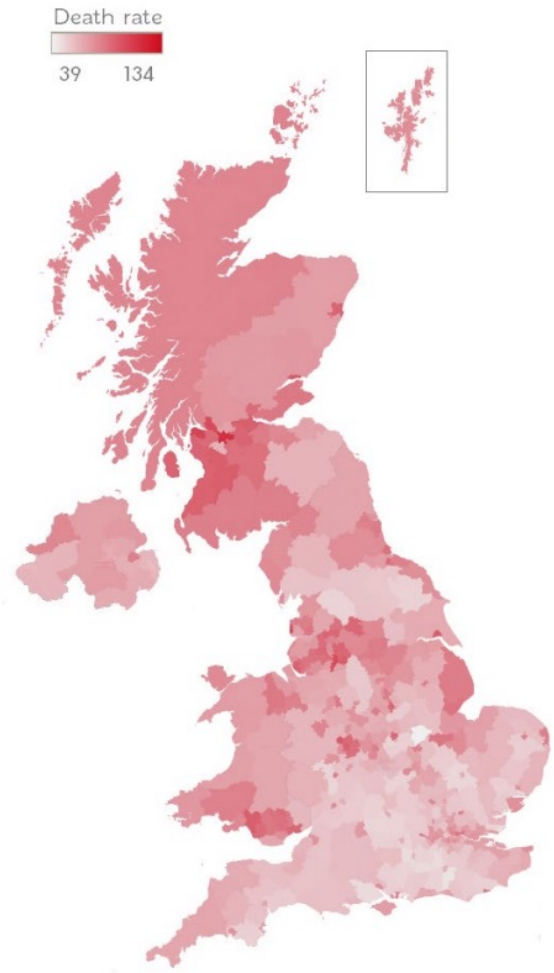
- Reducing smoking and second hand smoke (passive smoking).
- Reducing air pollution.
- Reducing salt and some fats in food.
- Making it easier to exercise.
- Reducing societal drivers of obesity.

NHS

Premature mortality from heart and circulatory disease (R), smoking prevalence (L).

Smokers 1.7x more likely to have CHD (higher in heavy smokers), passive smokers 1.25x.



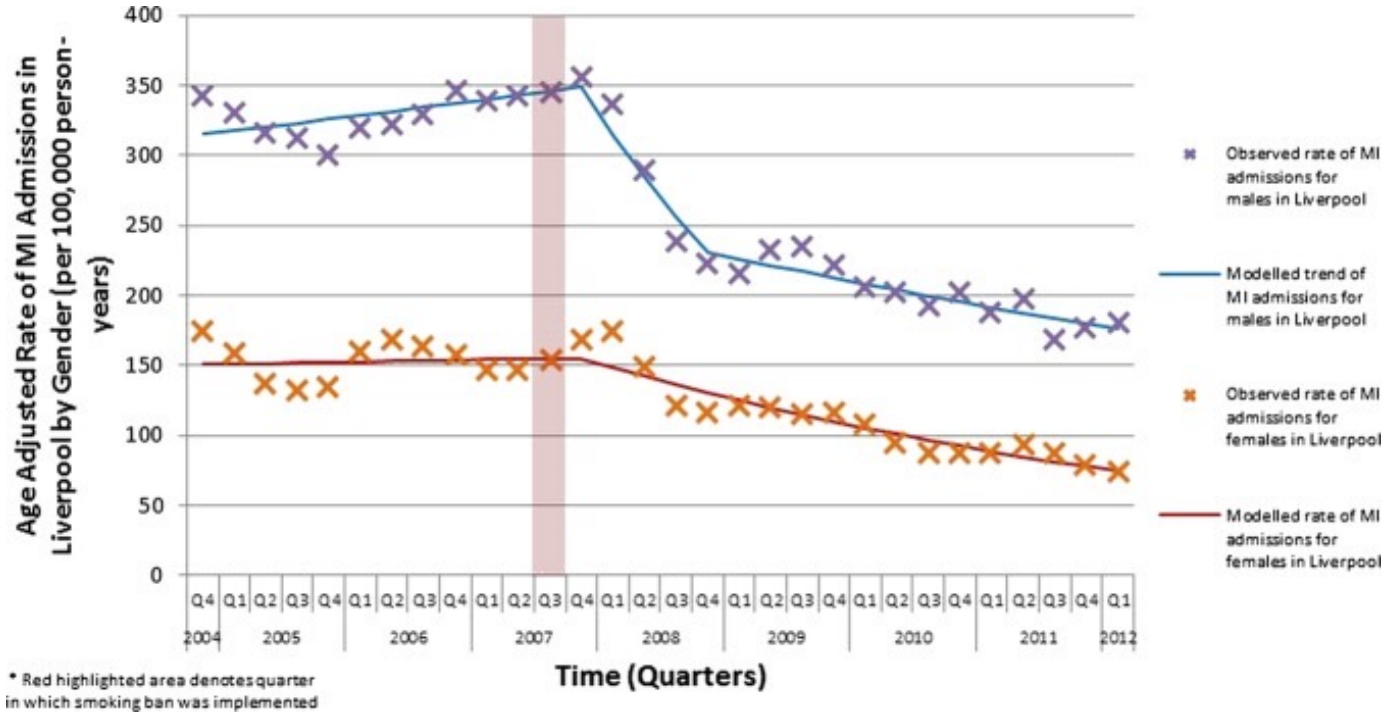


ONS 2022

BHF 2022

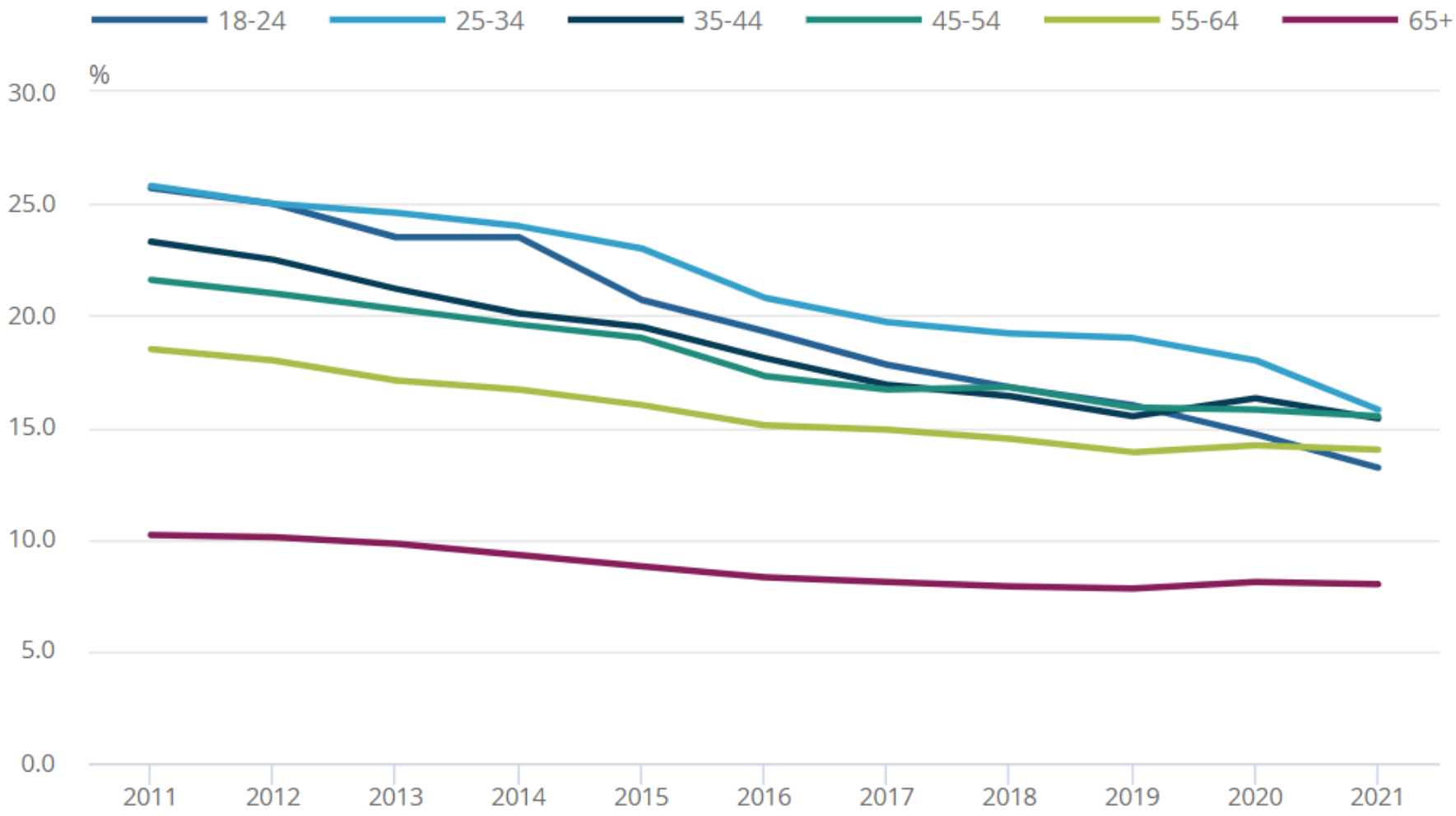
Improvements in heart disease can be very rapid when smoking reduces. Example: effect of smoke-free legislation.

- Meta-analysis of smoking bans in public places followed by a 12% reduction in coronary admissions.
- Data from Liverpool.
- Most smokers want to quit. Addiction prevents them.



Liu et al 2013

Smoking rates dropping in all age groups in the UK. Current smokers 2011 to 2021 by age.



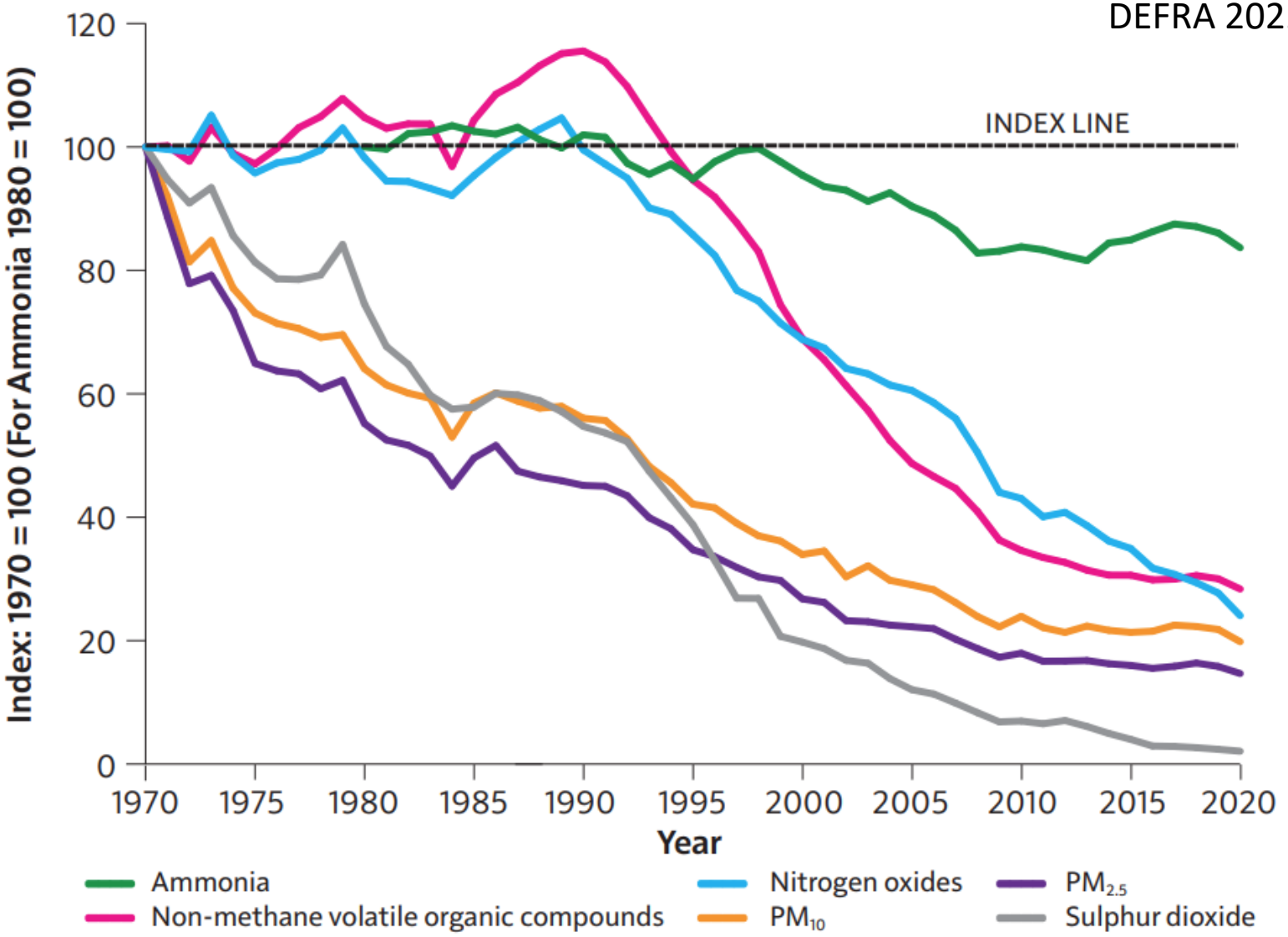
ONS 2022

UK air pollution emissions 1970-2020. $PM_{2.5}$ especially important.

Chief Medical Officer's
Annual Report 2022

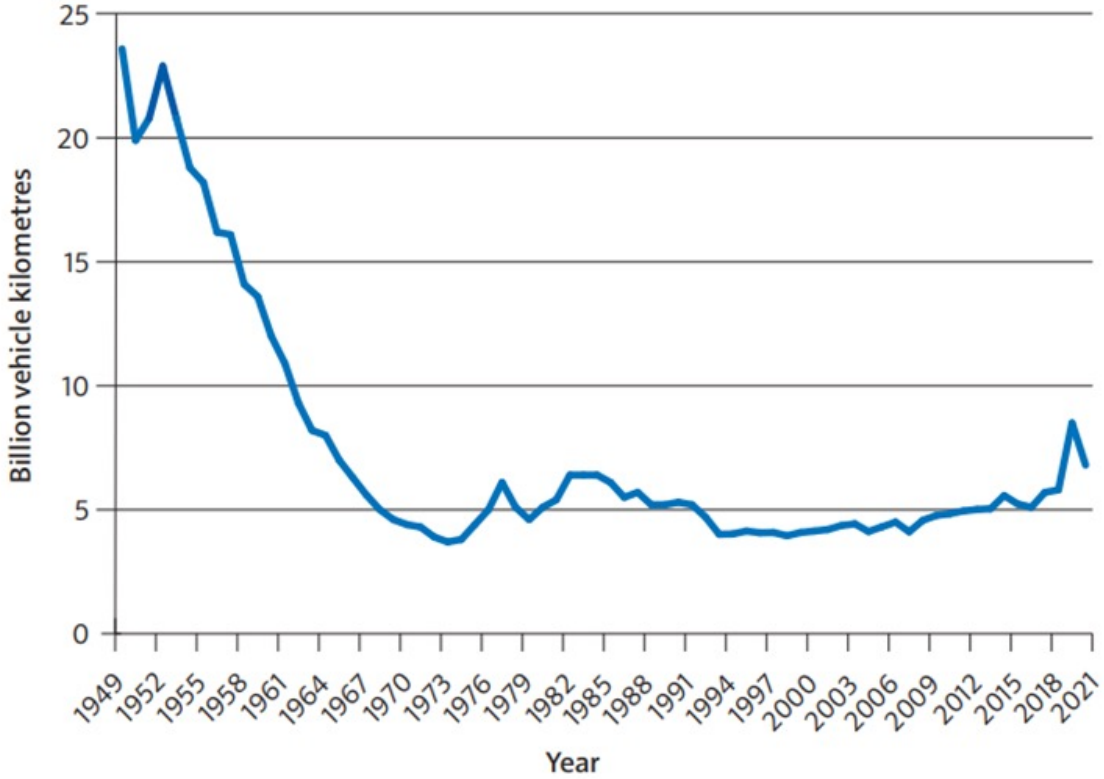
Air pollution

DEFRA 2022



Making exercise easier and fun throughout the life course.

The daily mile.co.uk
Richard Webb / Walking Football

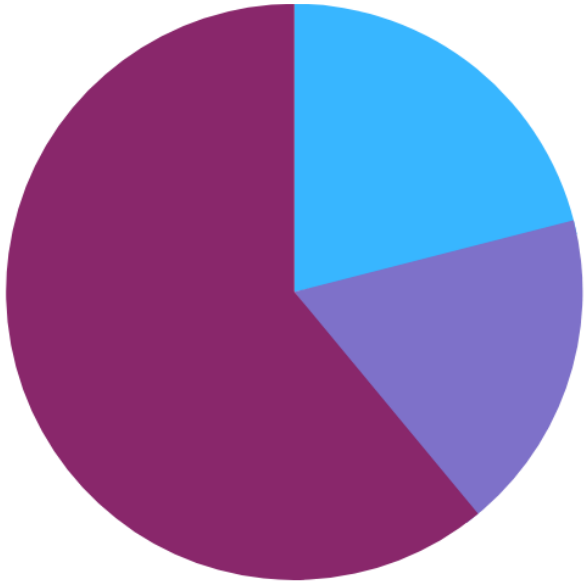


Distance travelled by bike, 1949-2022.

DfT

Reductions in salt to reduce population blood pressure.

- Salt increases blood pressure, and blood pressure of the elderly more salt-sensitive.
- UK 15% reduction in salt in the last decade, mainly processed food reformulation. Need to go further.
- Some products 20-40% less salt than 10 years ago.
- Most of the salt in the UK diet is involuntary- it was added during manufacture. Only 18% added by choice.

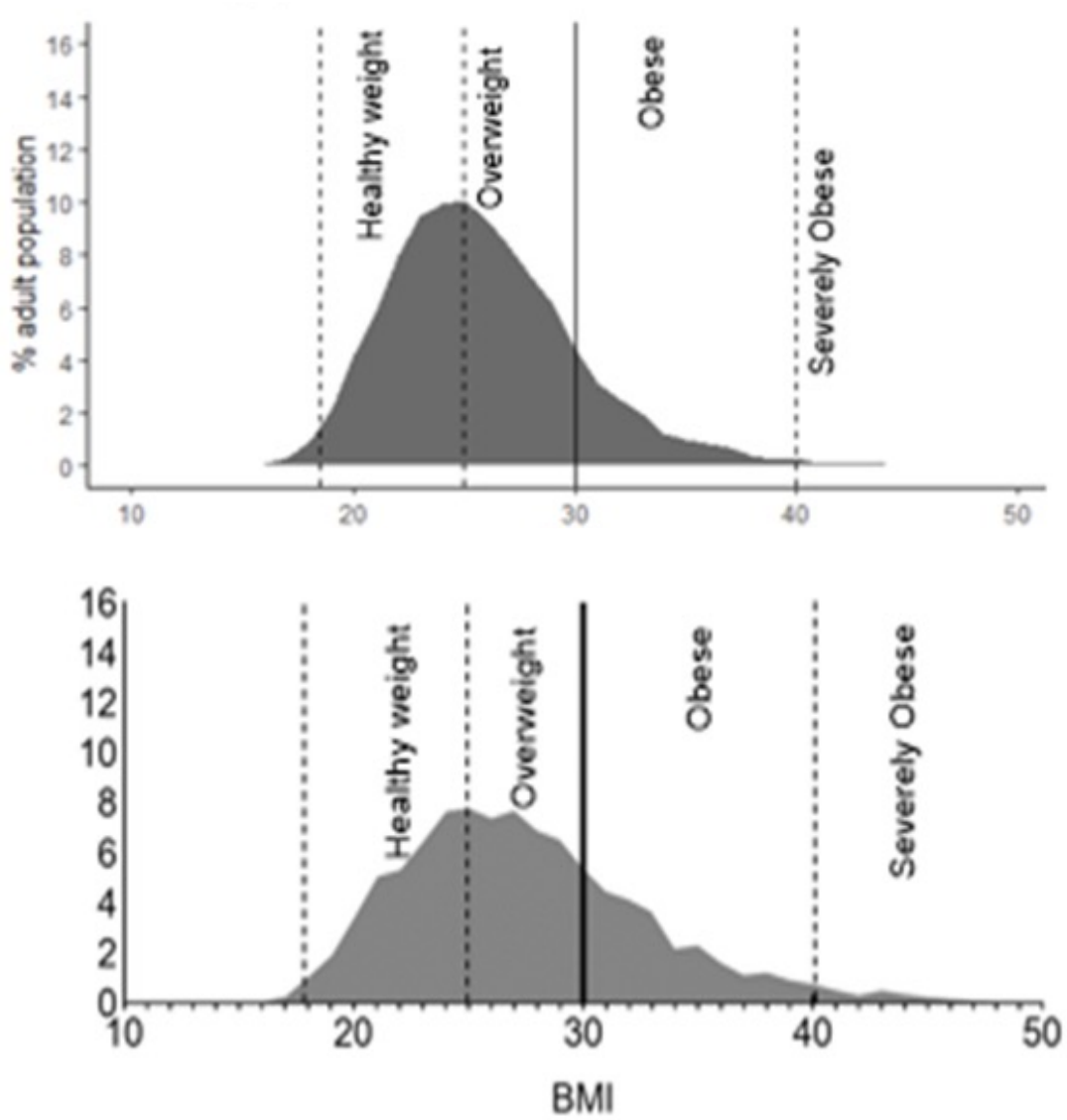


Sodium naturally present 21%;
salt in processed food 61%;
salt added by choice 18%. UK diet.

PHE/ Action on Salt

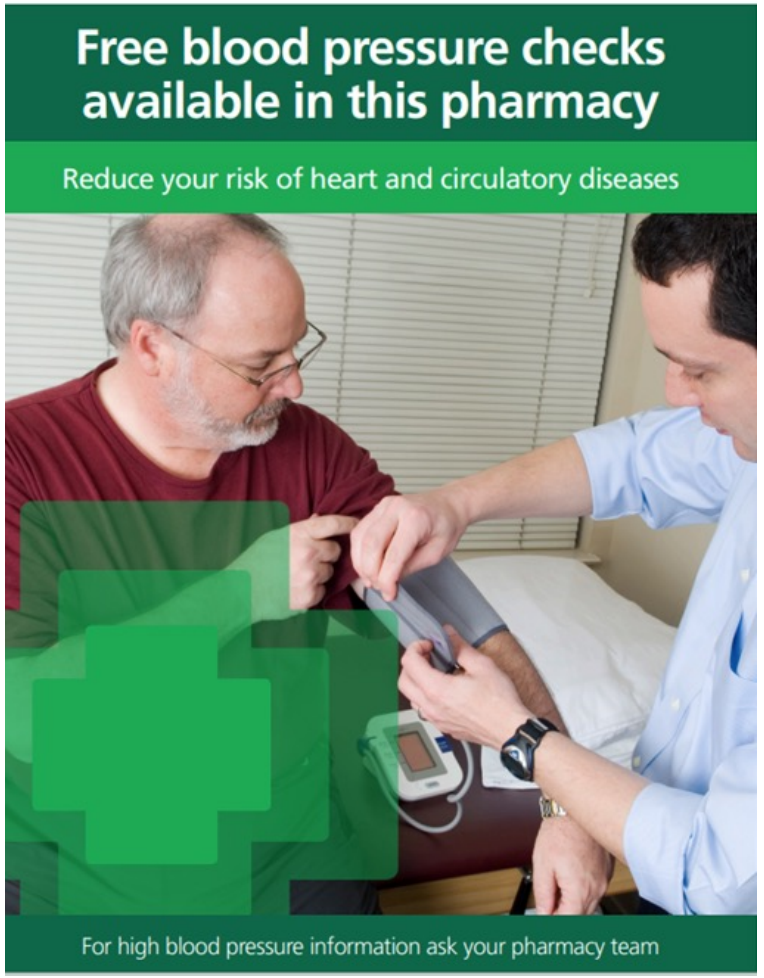
Reducing societal drivers of obesity.

- Obesity directly leads to increased cardiovascular mortality.
- Also accelerates risks of diabetes, hypertension and other risk factors.
- People living with overweight and obesity have risen from 15% to 28% of the adult population since 1993.
- At right: top 1993, bottom 2019.
- Rising obesity starts in childhood, especially in most deprived areas.



Secondary prevention- often well before the IHD is apparent.

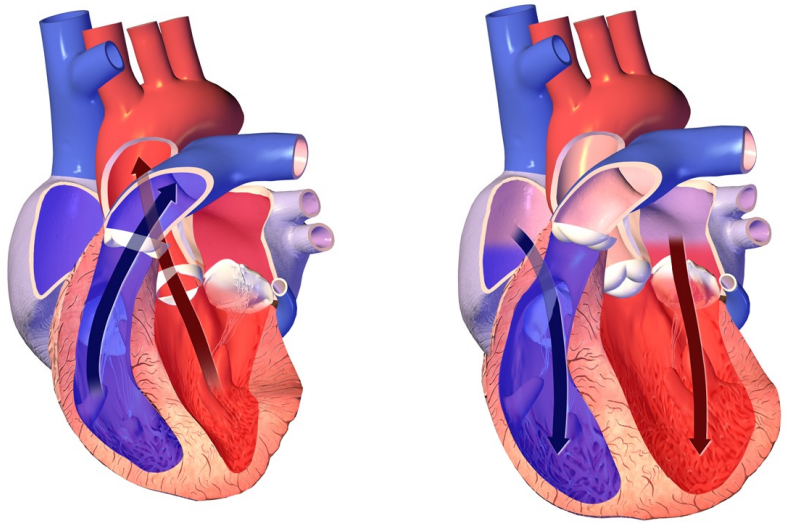
- Includes:
- Targeted help for an individual to stop smoking, lose weight, increase exercise.
- Treating hypertension.
- Treating high cholesterol (statins).
- Diagnosing and treating diabetes.



NHS

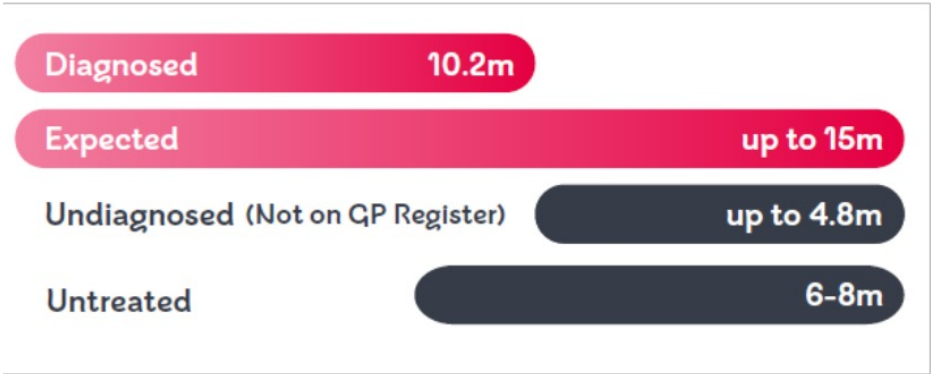
High blood pressure- hypertension.
A major, common, treatable risk factor for IHD.

- High systolic or diastolic blood pressure.
- Contributes to about half of heart and circulatory disease.
- Around 28% UK adult population.
- Multiple possible treatments- the key thing is to diagnose it early.



Systole *(pumping)*

Diastole *(filling)*



Bruce Blaus;
BHF 2022

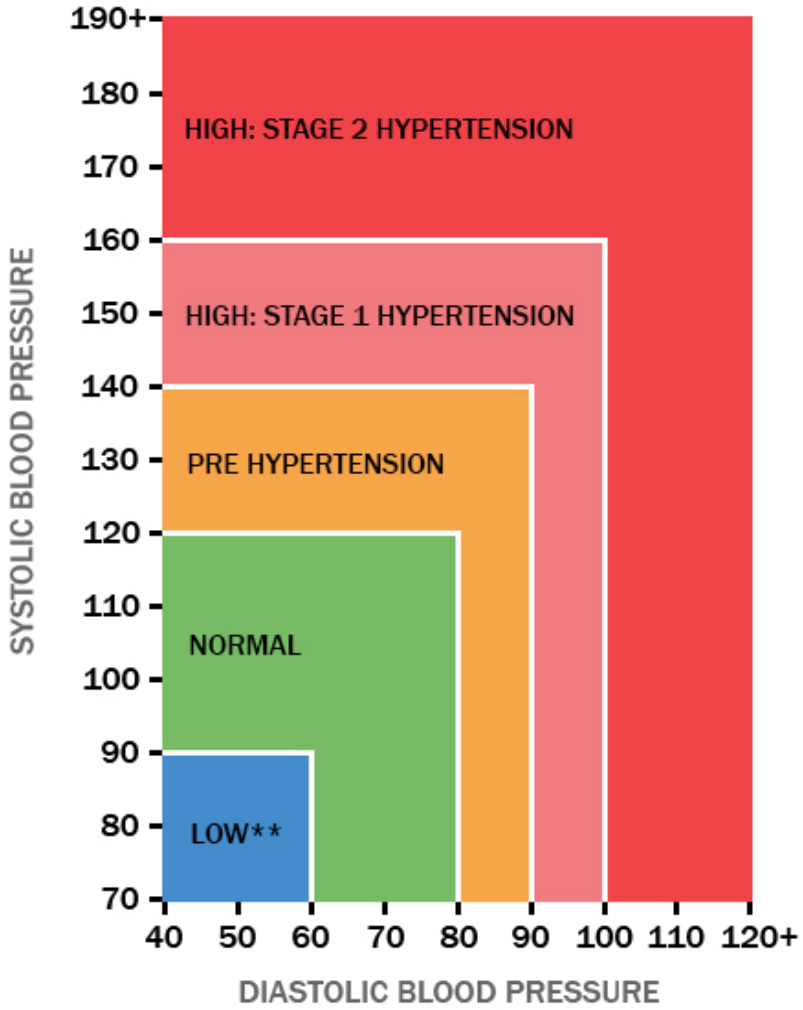
Blood pressure is easy to measure. Know your numbers.

- We can measure blood pressure at the doctor, at home, work, shops…
- High blood pressure is usually 140/90mmHg or higher (or an average of 135/85mmHg at home).
- May be possible to reduce with lifestyle changes including:

-Reduce salt intake, alcohol.

-Exercise.

-Lose weight- even a little helps.



Many drugs can reduce blood pressure by different mechanisms.

5 mm Hg reduction of systolic blood pressure reduces the risk of IHD by 8%.

- Best ones depend on age, existing heart disease, diabetes, ethnicity, side effects.
- Common ones include:

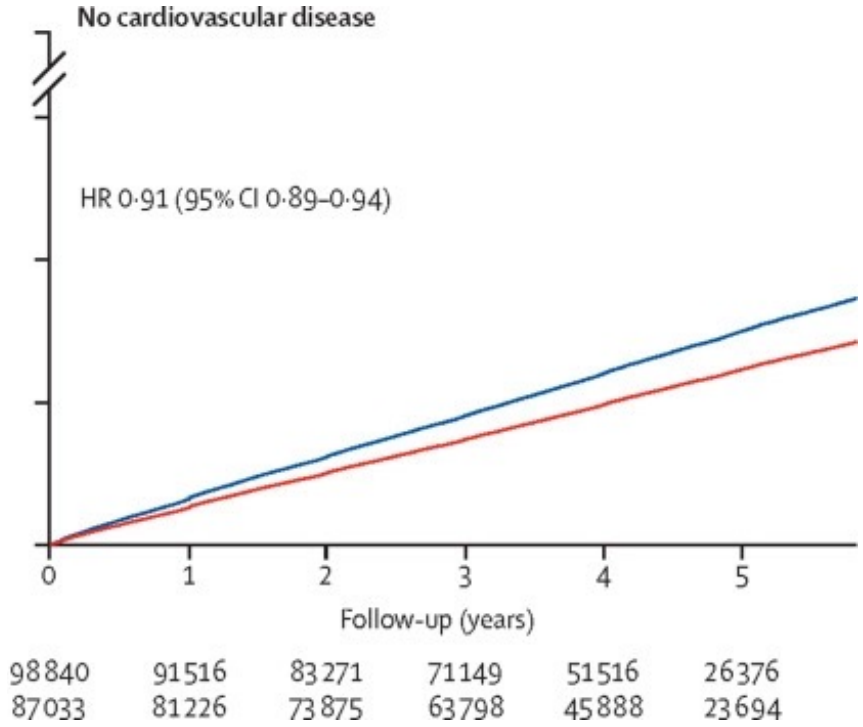
-ACE inhibitors, angiotensin II receptor blockers (ARB).

-Calcium channel blockers.

-Thiazide-like diuretics.

-Beta-blockers.

- May be used in combination.



Intervention.

Blood Pressure Lowering Treatment Trialists' Collaboration. Lancet 2021.

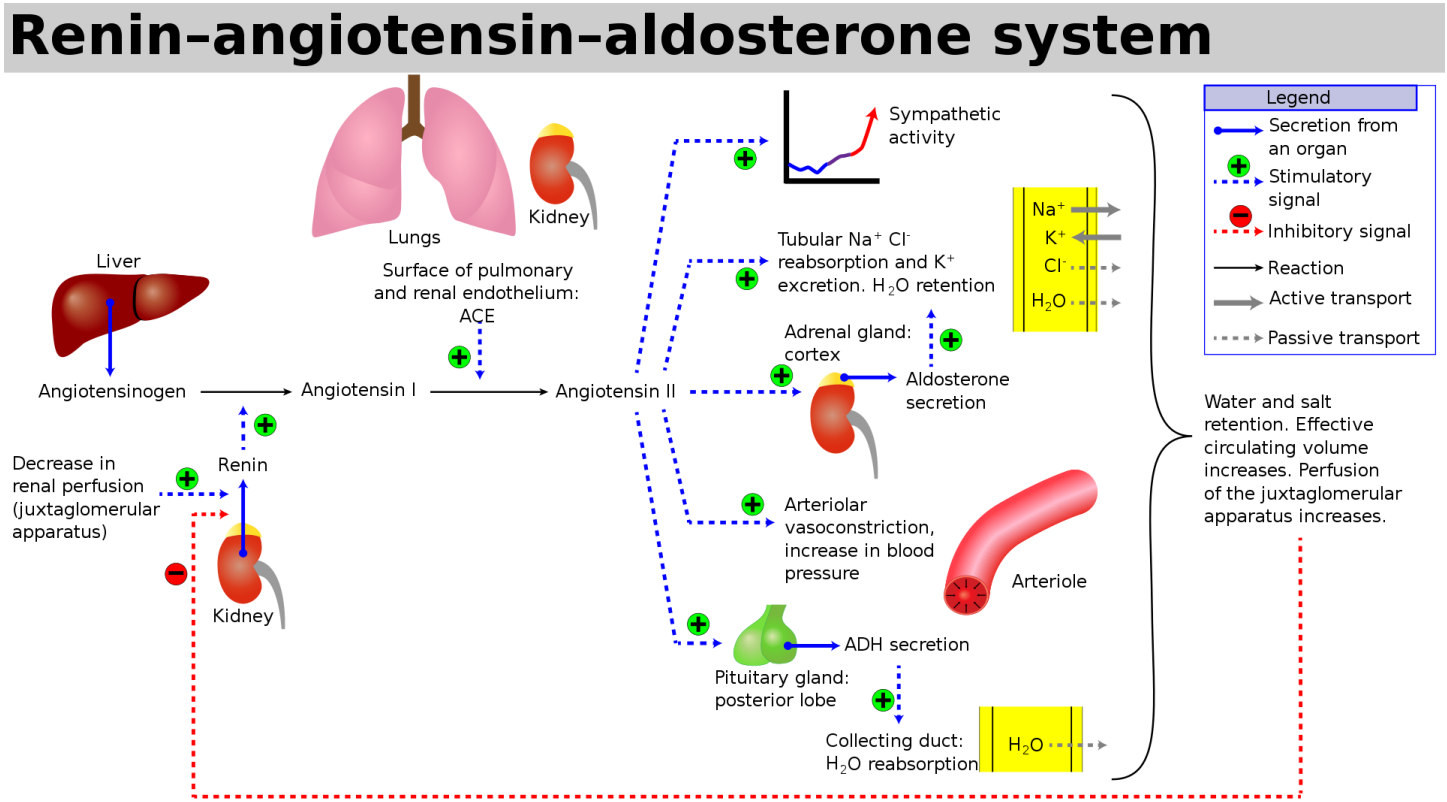
ACE-inhibitors.

- Renin-angiotensin system. Activated when the kidney senses a drop in blood pressure.
- Initial chemical shown to block this from *Bothrops jararaca,* Brazilian pit-viper.
- Led (by many steps) to captopril, the first of many ACE inhibitors. Other enalapril, lisinopril.
- ACE inhibitors prevent an enzyme producing angiotensin II, which narrows blood vessels and forces the heart to work harder.
- Leads to more relaxed and open veins and arteries.
- Side effects include cough (reverses when stop).

Leandro Avelar

Angiotensin receptor blockers (ARBs), also known as angiotensin II receptor antagonists.

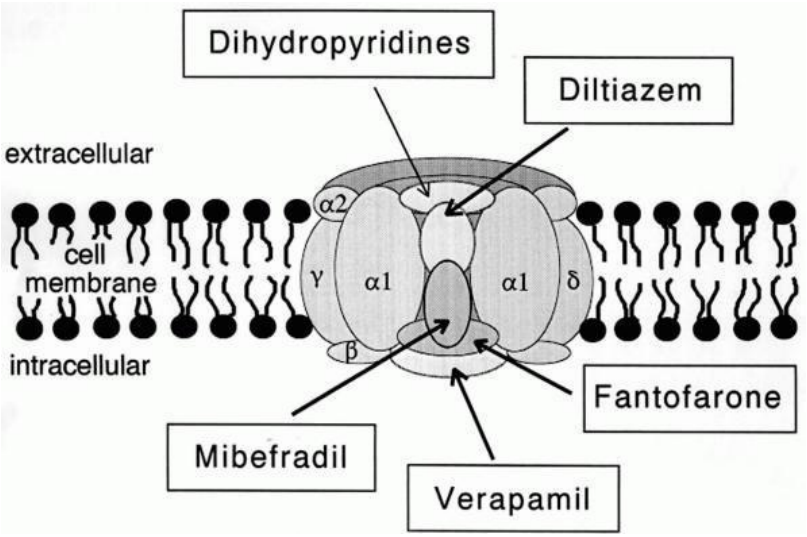
- Like ACE act on renin-angiotensin system.
- Examples irbesartan, valsartan, losartan, candesartan.
- Block AT1 receptors that angiotensin II acts on.



Soupvector/wiki

Calcium-channel blockers.

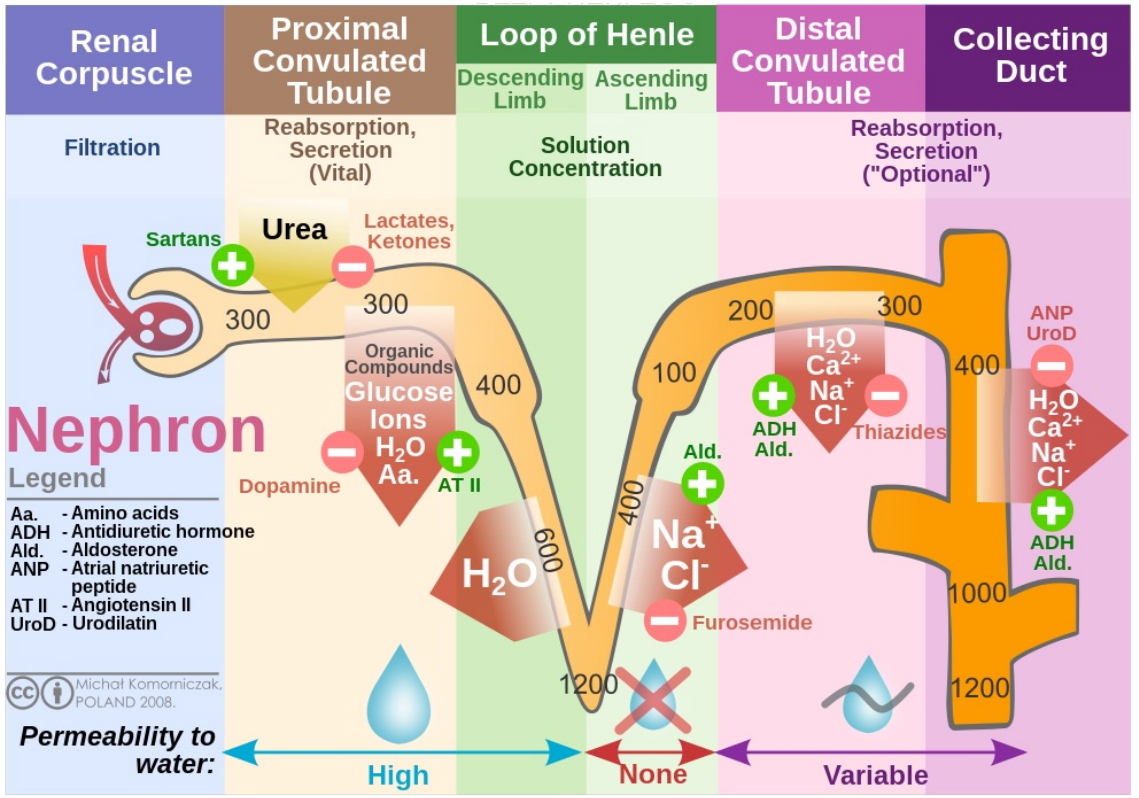
- The body uses calcium channels to signal and initiate action by cells.
- Some calcium channels opening signal to blood vessels they should constrict and initiate this.
- Dihydropyridine calcium channel blockers are relatively specific to these. They include amlodipine, nifedipine.
- Principle action to relax blood vessels and so reduce blood pressure.
- Can also reduce spasm of coronary arteries.
- SE include can lead to fluid retention.



Vet vijayraj / wiki

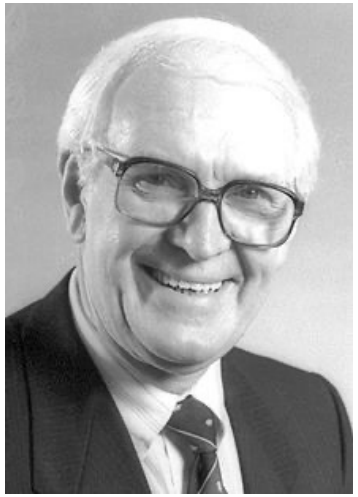
Thiazide diuretics.

- Thiazide diuretics work mainly by reducing reabsorption of sodium and chloride by the kidney and also water.
- This reduces blood pressure in part including by reducing total water.
- They may also dilate blood vessels.



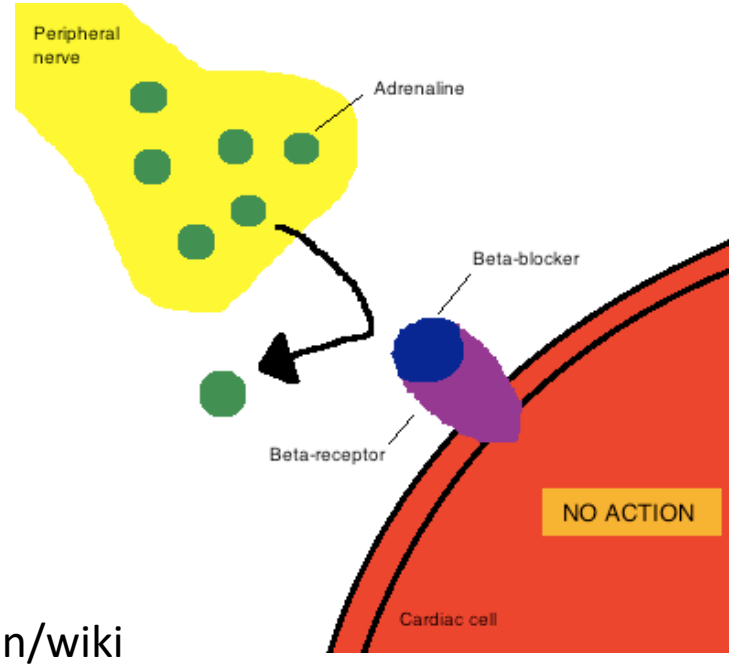
M.Komorniczak/ wiki.

Beta (ß) blockers.



- Adrenaline- key to flight-and-fight response- includes heart going faster, blood vessels constricted.
- Adrenaline stimulates beta receptors on several organs (among other things).
- Beta blockers block this selectively to cause the heart to beat more slowly and with less force, which lowers blood pressure. Beta blockers also help widen veins and arteries to improve blood flow.
- Examples include atenolol, bisoprolol, carvedilol.

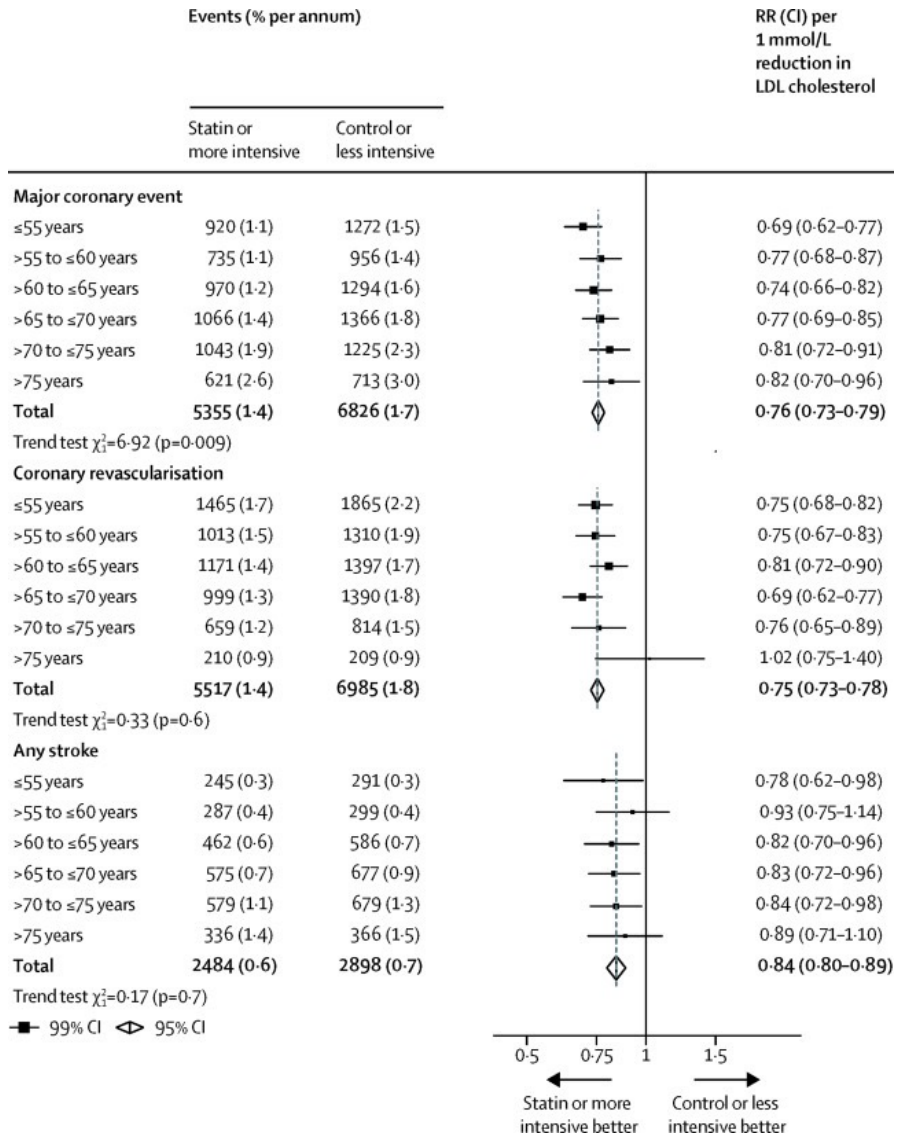
Sir James Black developed propranolol 1964.



Mogsan/wiki

Reducing cholesterol.

- High LDL cholesterol associated with coronary heart disease.
- Statins (HMG-CoA reductase inhibitors) reduce LDL cholesterol.
- LDL rises with age.
- Clear evidence of benefit in people with previous MI, cardiovascular disease, cardiac risk factors.
- Good evidence of advantage in delaying IHD before symptoms start.

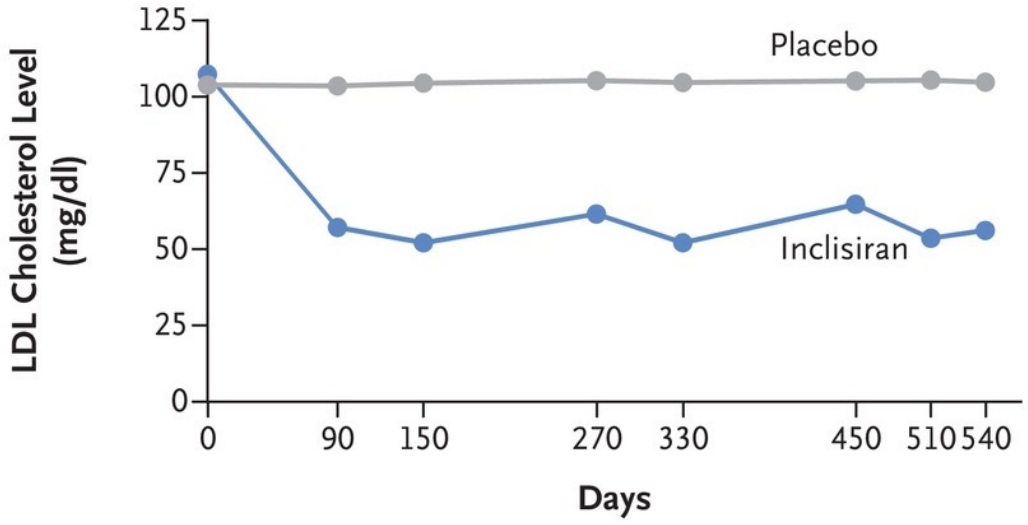


186 854 patients in 28 trials. Cholesterol Treatment Trialists' Collaboration. Lancet 2019.

Various drugs reduce LDL cholesterol, statins currently first line.

- Statins such as atorvastatin inhibit the enzyme HMG-CoA reductase which plays a central role in the production of cholesterol in the liver.
- PCSK9 inhibitors such as inclisiran given by injection. Increase liver's ability to reduce cholesterol. When statins not sufficient / tolerated. Not yet clear if reduce CHD.

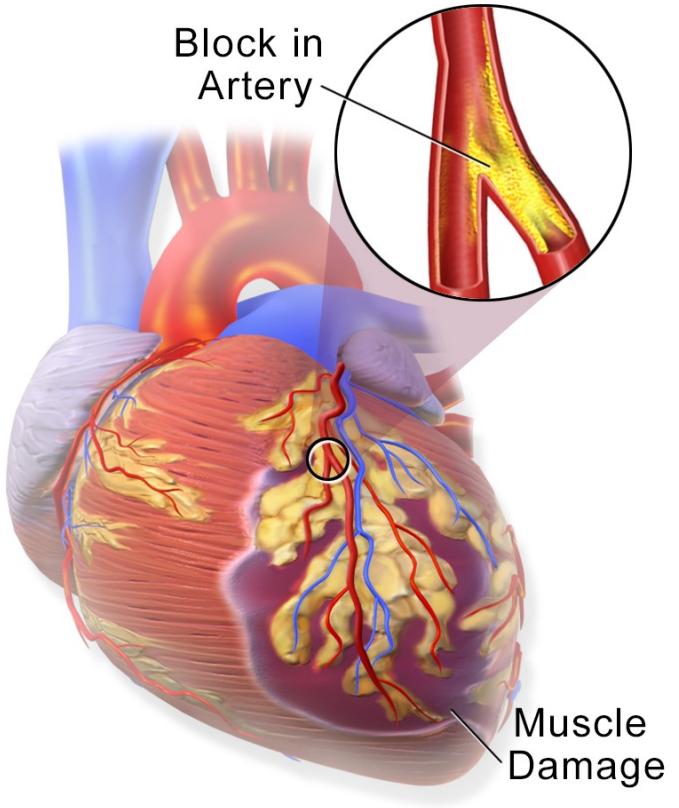
Absolute reduction LDL cholesterol.



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

K Ray et al, NEJM 2020 ORION 11 trial.

Even with optimal prevention many people will have cardiac events (but significantly fewer than without).



Heart Attack

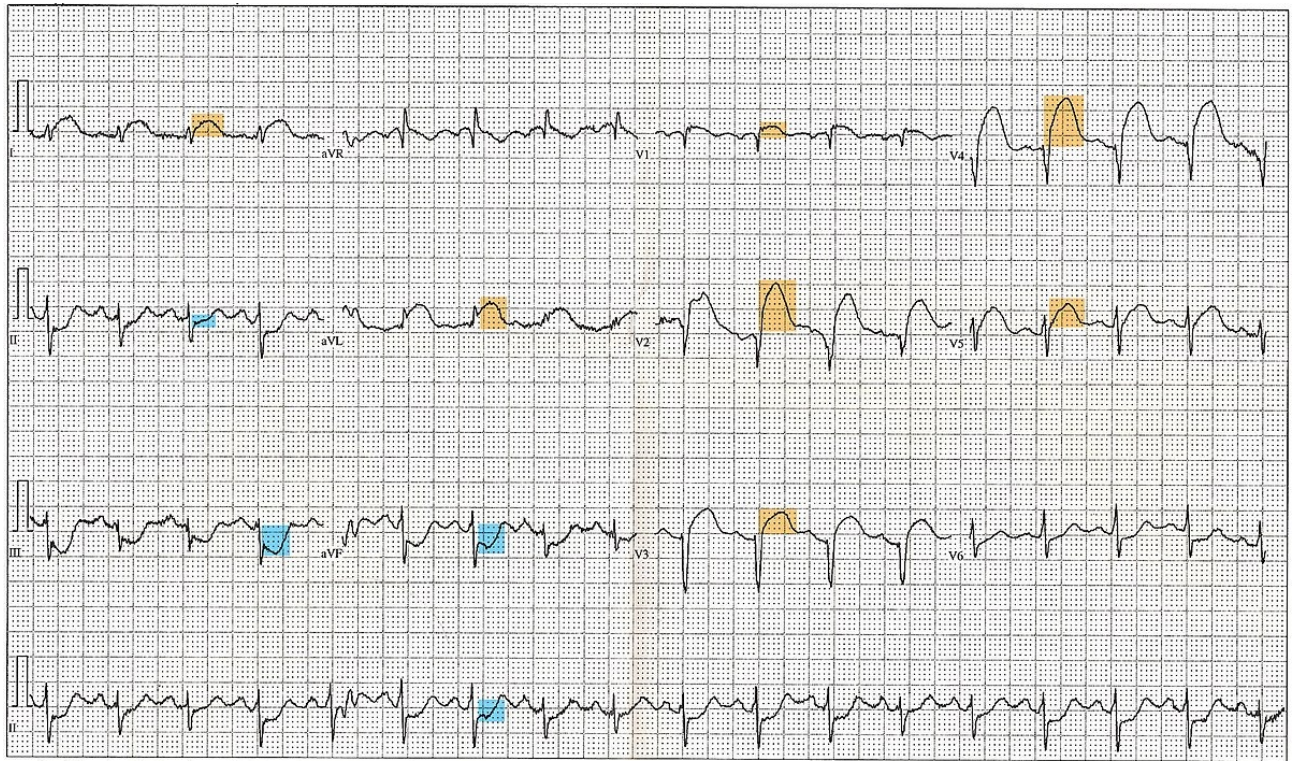
BHF/
Blausen Medical Communications

Angina, unstable angina, heart attack (MI).

- Angina occurs on exercise or other stress of the heart.
- Typically chest, jaw or arm pain.
- Predictable (e.g. ‘if I climb a flight of stairs’.), goes away on resting.
- Unstable angina and MI are chest pain or other symptoms that occur at rest. Medical emergency.
- Sudden shortness of breath, clammy, dizzy, nausea other possible symptoms. Not everyone has pain.

Three things help diagnose MI.

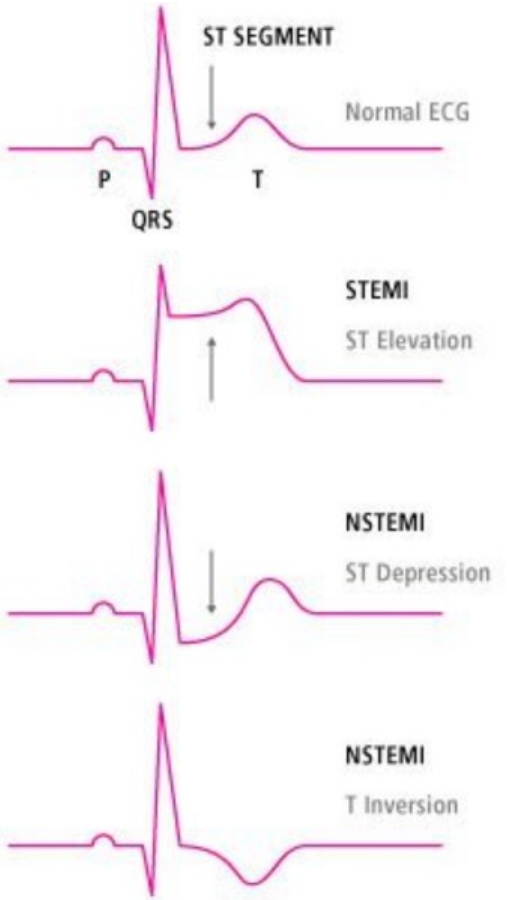
- Symptoms and history, including age.
- ECG- heart tracing.
- Blood tests (troponin).



Public domain.

Broadly 3 possible outcomes if heart attack symptoms.

- It is not from the heart.
- ECG shows raised ST segments, troponin raised. ‘STEMI’ heart attack- likely needs rapid cardiac intervention.
- Typical symptoms, but troponin and ECG does not show a heart attack. Unstable angina.
- Troponin raised, ECG may be normal. ‘NSTEMI’ heart attack. Needs urgent drugs.



Bayer AG 2008

In 1960s 7/10 died of MI. Now 7/10 people survive (BHF).

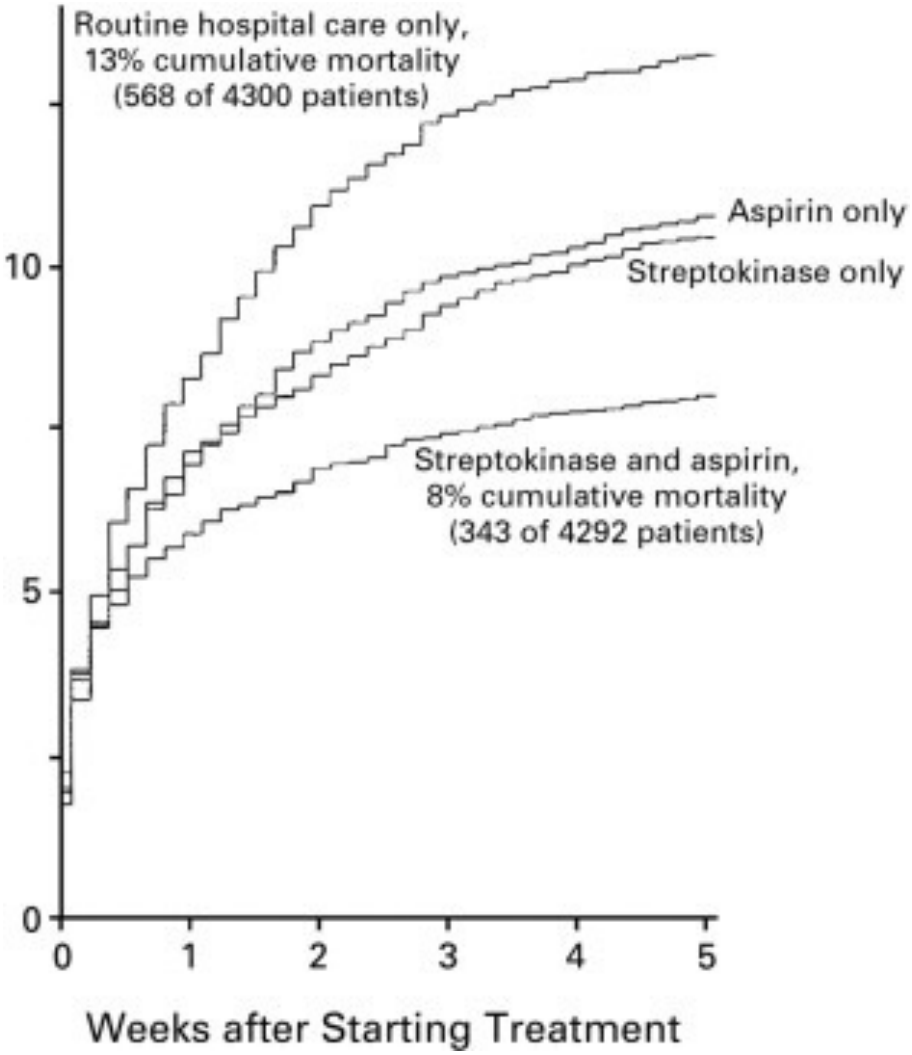
ISIS-2 (1988) trial, around 17k patients with heart attack (STEMI). Routine care 13% mortality.

Aspirin 20% better mortality.

Streptokinase ‘clot busting’ drug around 20% better mortality.

Mortality 40% better with combined treatment to 8%.

30 day mortality now less than 5% and can be down to 2%.



Aspirin- the first antiplatelet drug.

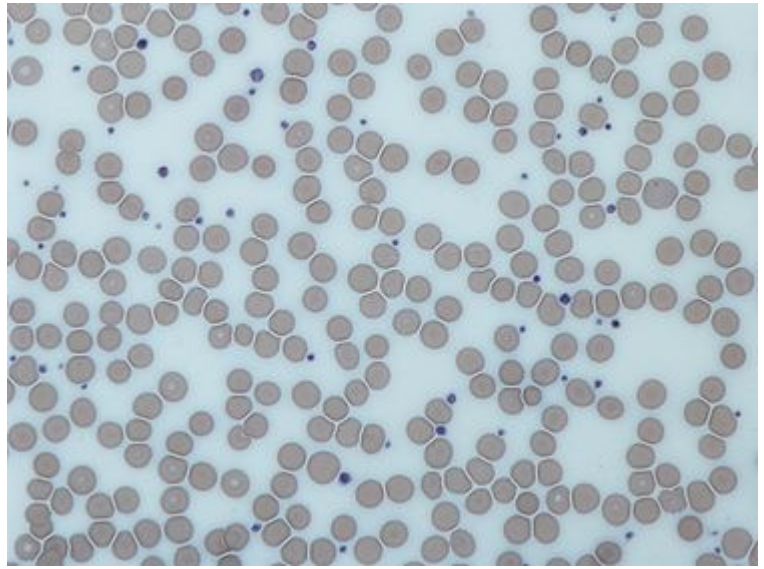
- Willow bark extracts used for fever from at least the time of Hippocrates (400BC).
- 1763 Rev Edward Stone promoted it for ague.
- Bayer company from around 1897- Aspirin.
- Not until 1971 recognised that its activity against prostaglandins reduce inflammation.
- First trial in heart disease 1971.
- Reduces platelet activity, clotting.

Otto Wilhelm Thomé 1885

Other antiplatelet drugs used in acute coronary events.

- Include:
- Clopidogrel
- Prasugrel
- Ticagrelor

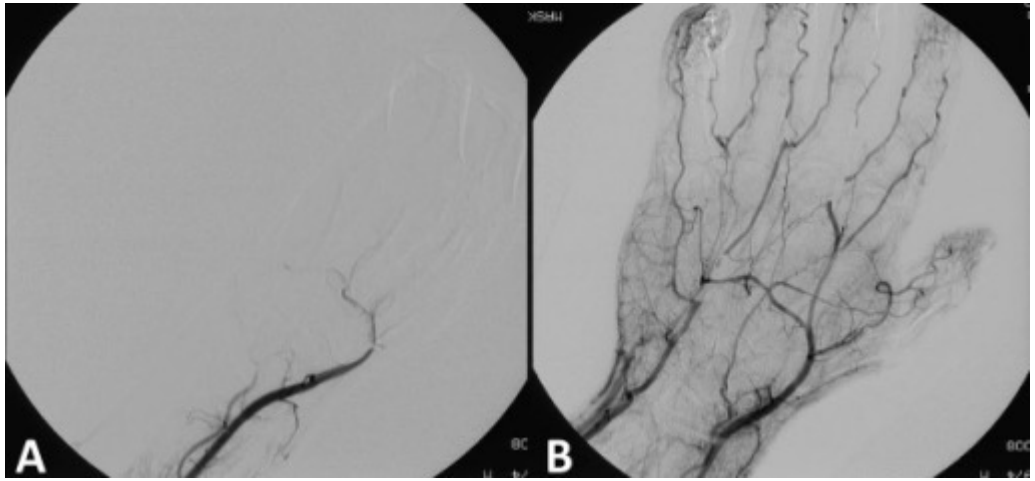
- Usually initially given with aspirin as dual antiplatelet therapy.



Thrombolytic (‘clot busting’) drugs.

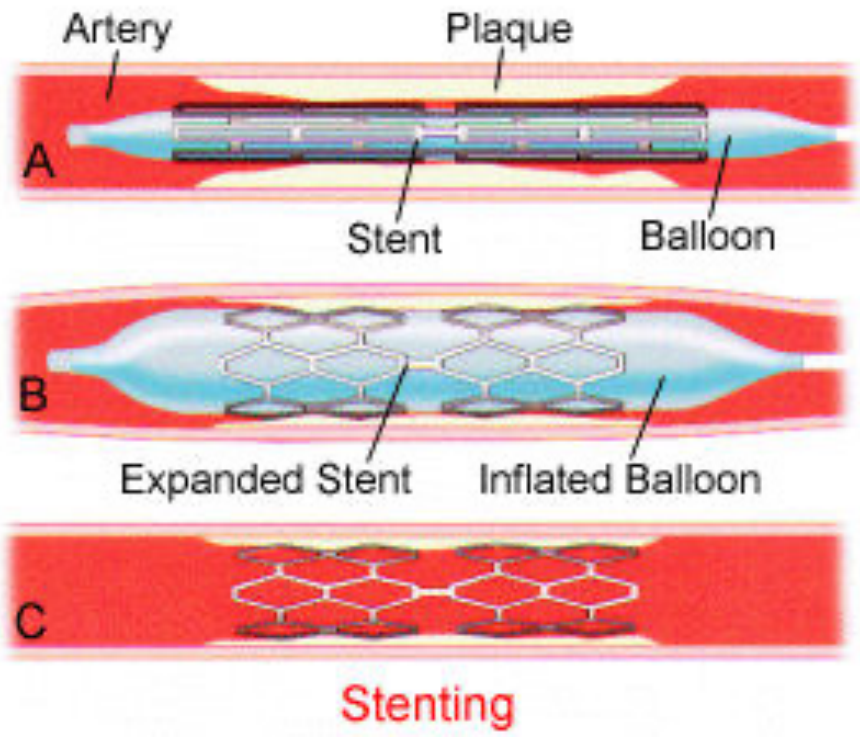
- The first was Streptokinase. Produced by beta-haemolytic streptococcus, isolated 1933.

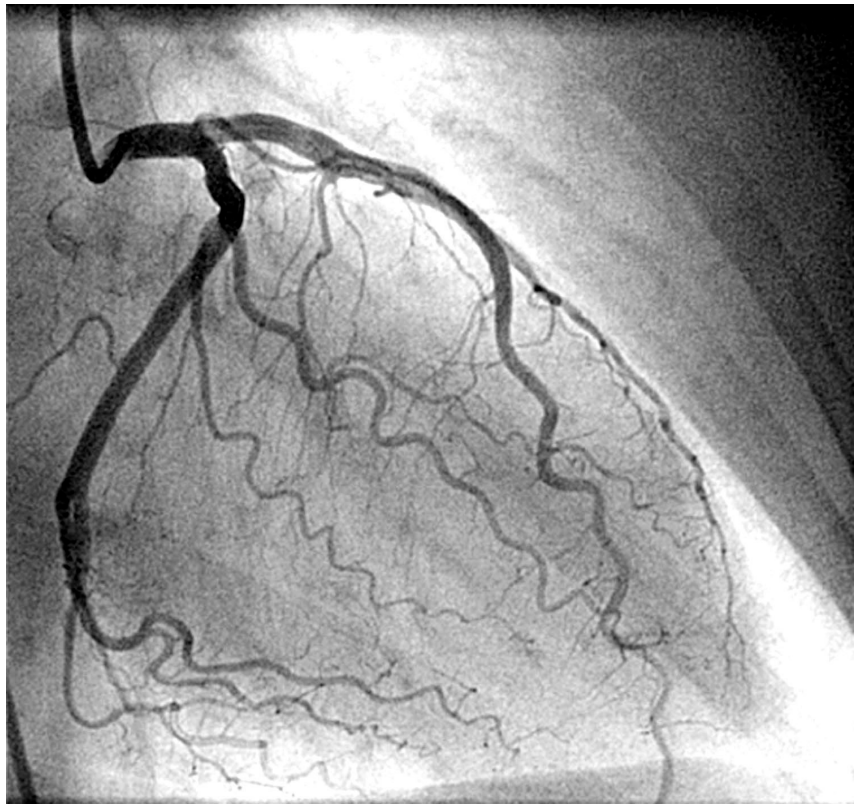
- Tissue plasminogen activator (abbreviated tPA) such as Alteplase, Reteplase.



Ipaktchi K

Coronary angiography and stenting (PCI).

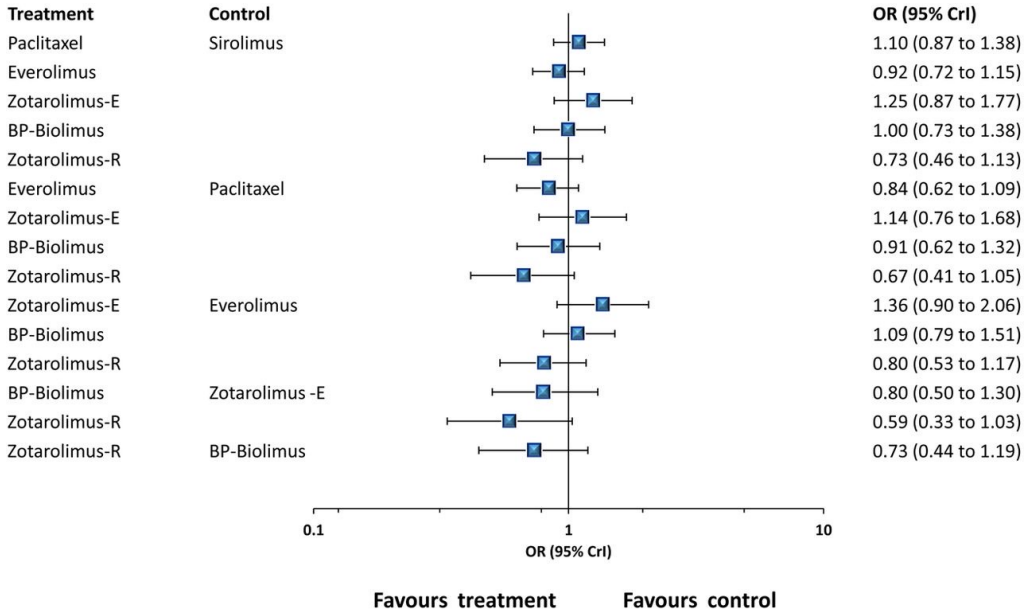




Credit Dr. David Lipkin / BHF

Coronary stenting- heart attack and angina

- Gradual improvements in stent design and technique.
- New drug-eluting-stents.
- Biodegradable stents.



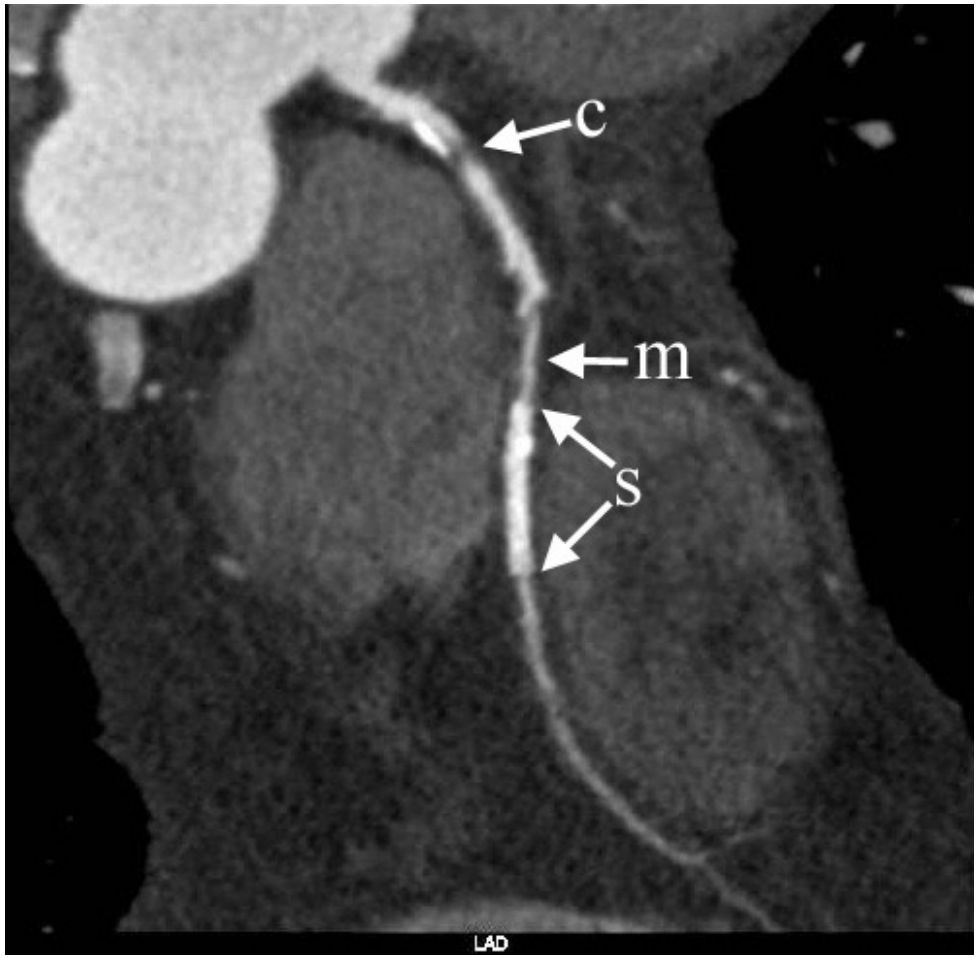
Navarese et al BMJ 2013

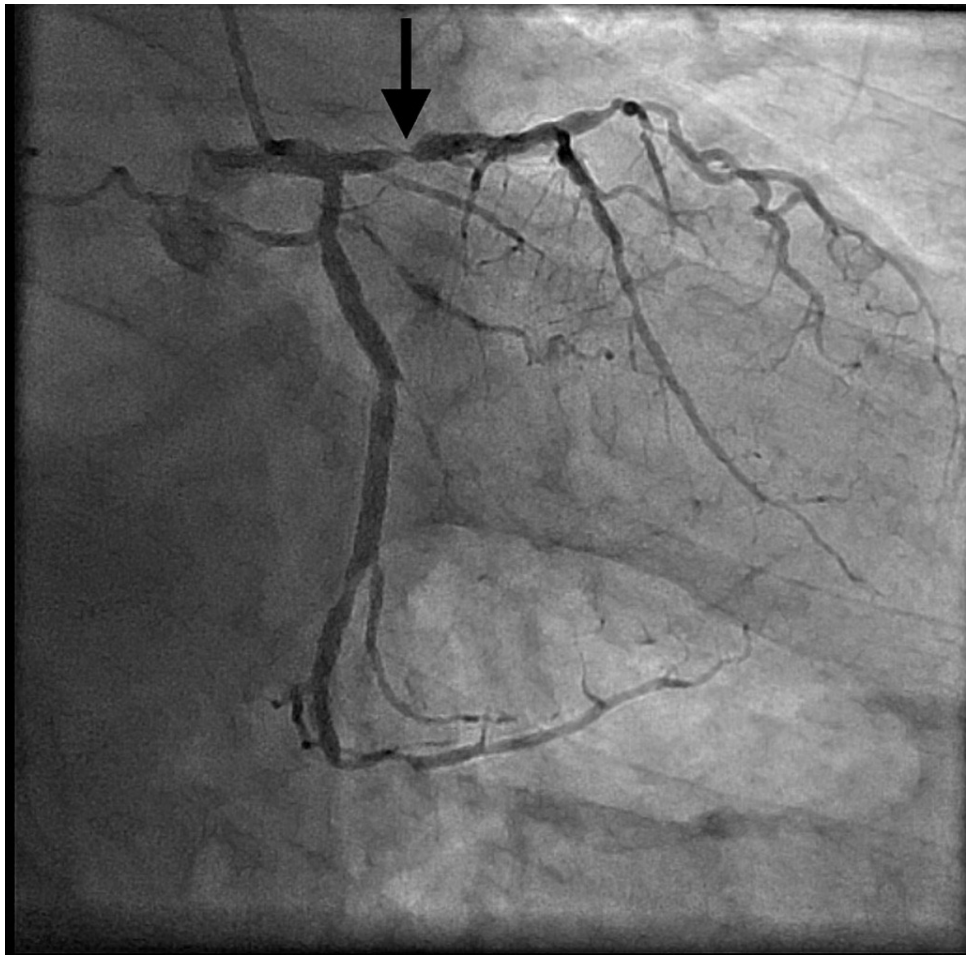
How rapidly go to angiography / stent depends on situation.

- Patient with ST elevation MI (STEMI) will go directly to PCI if within 12 hours of symptom onset and can be done rapidly.
- If cannot be done rapidly may need fibrinolytic (clot-busting) drug.
- NSTEMI / unstable angina may need urgent angiography within days but not immediate.
- Stable angina will be investigated as an elective procedure.

sv1ambo

CT angiogram, PCI angiography with a view to physical interventions.

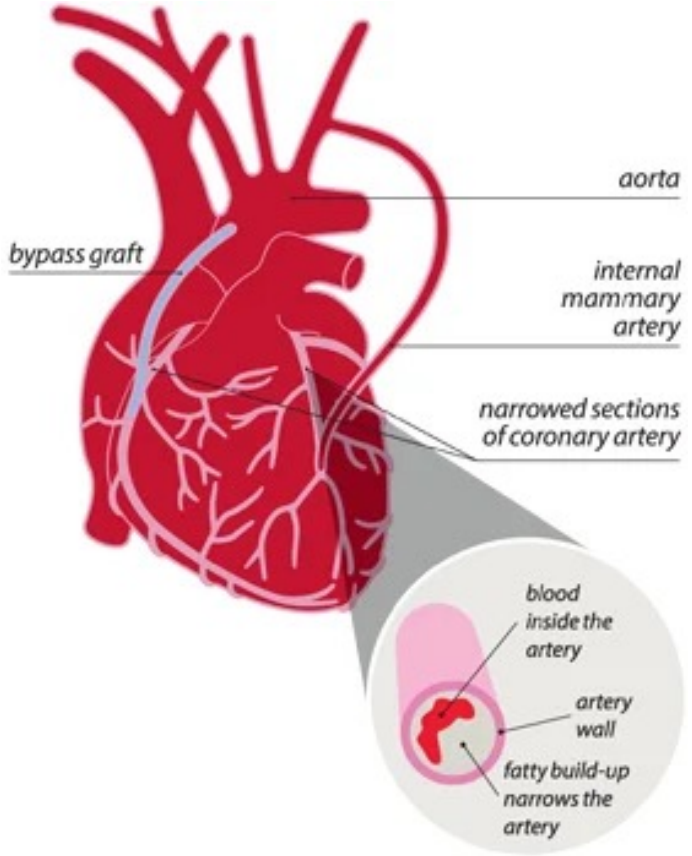




Case courtesy of Yune Kwong, Radiopaedia.org

Coronary stent (angioplasty) v bypass surgery (CABG).

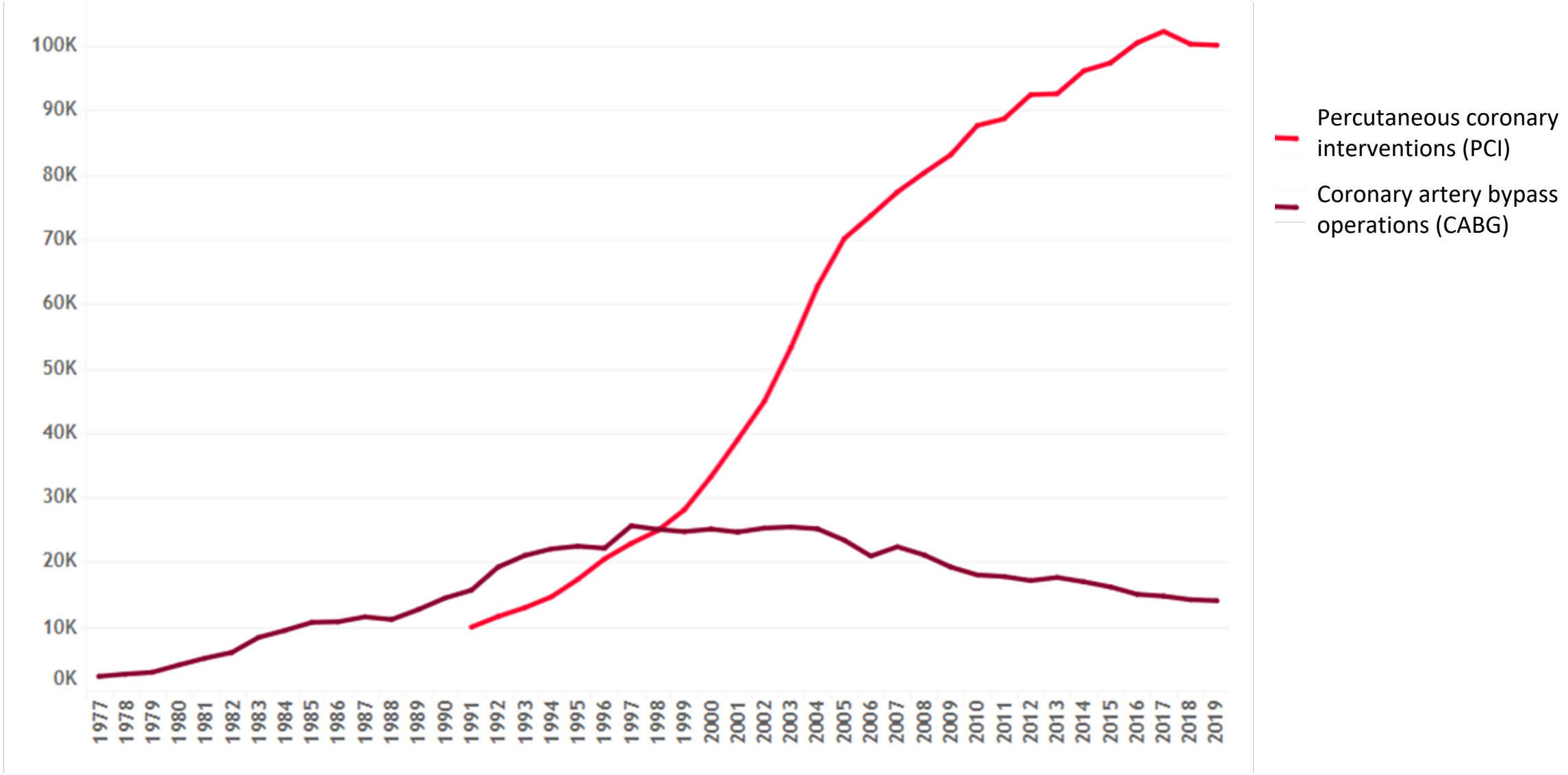
- Coronary artery bypass grafting (CABG) a major operation, but in the right patients highly effective.
- Angioplasty has continued to improve, but there remain situations CABG is the better option.
- Which is better will need discussion with cardiologists or surgeons.



BHF

Coronary artery bypass operations v angioplasty (PCI), UK since 1977.

(BHF 2022)



In those who have or had a cardiovascular event whether angina or a heart attack (MI):

- Antihypertensives if not on them.
- Reduce cholesterol (statins).
- Drugs acting on the neurohormonal system affecting the heart such as β-blockers, ACE inhibitors.
- Antiplatelet drugs- aspirin and others.

One more drug class for symptoms- nitrates.

- Initially noticed that people handing nitroglycerin exposives had symptoms from 1846.
- Recognised as a treatment for angina since 1879.
- Relaxes coronary and other arteries.
- Rapid, for relief of angina GTN spray or tablet under tongue.
- Isosorbide mononitrate and isosorbide dinitrate drugs, patches for prevention.

Whispyhistory

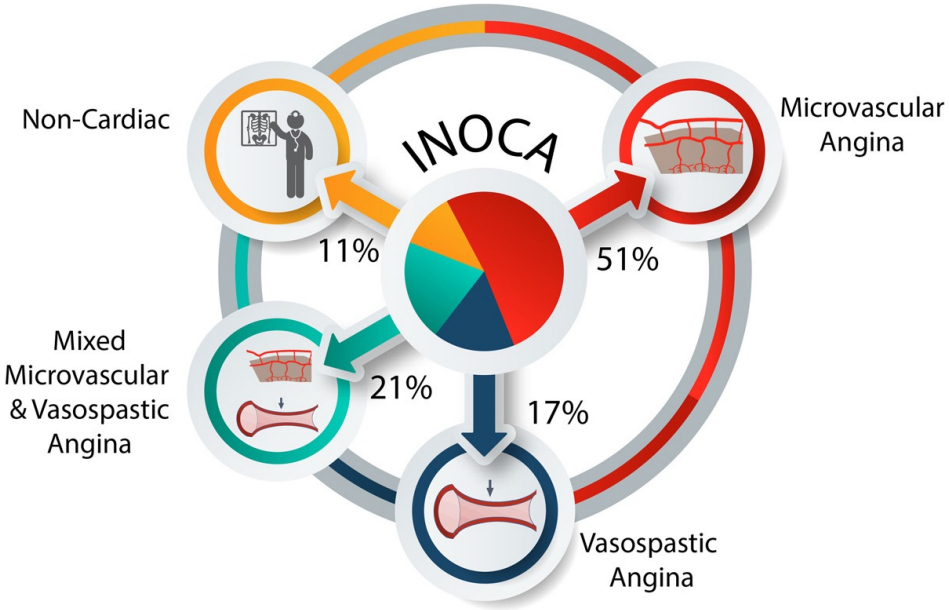
Not all angina is due to atherosclerosis or coronary arteries.

- Can have angina with normal coronary arteries.
- Ischeamia with Non-Obstructive Coronary Arteries (INOCA).
- Various causes including:

-coronary artery spasm

-microvascular angina (MVA)

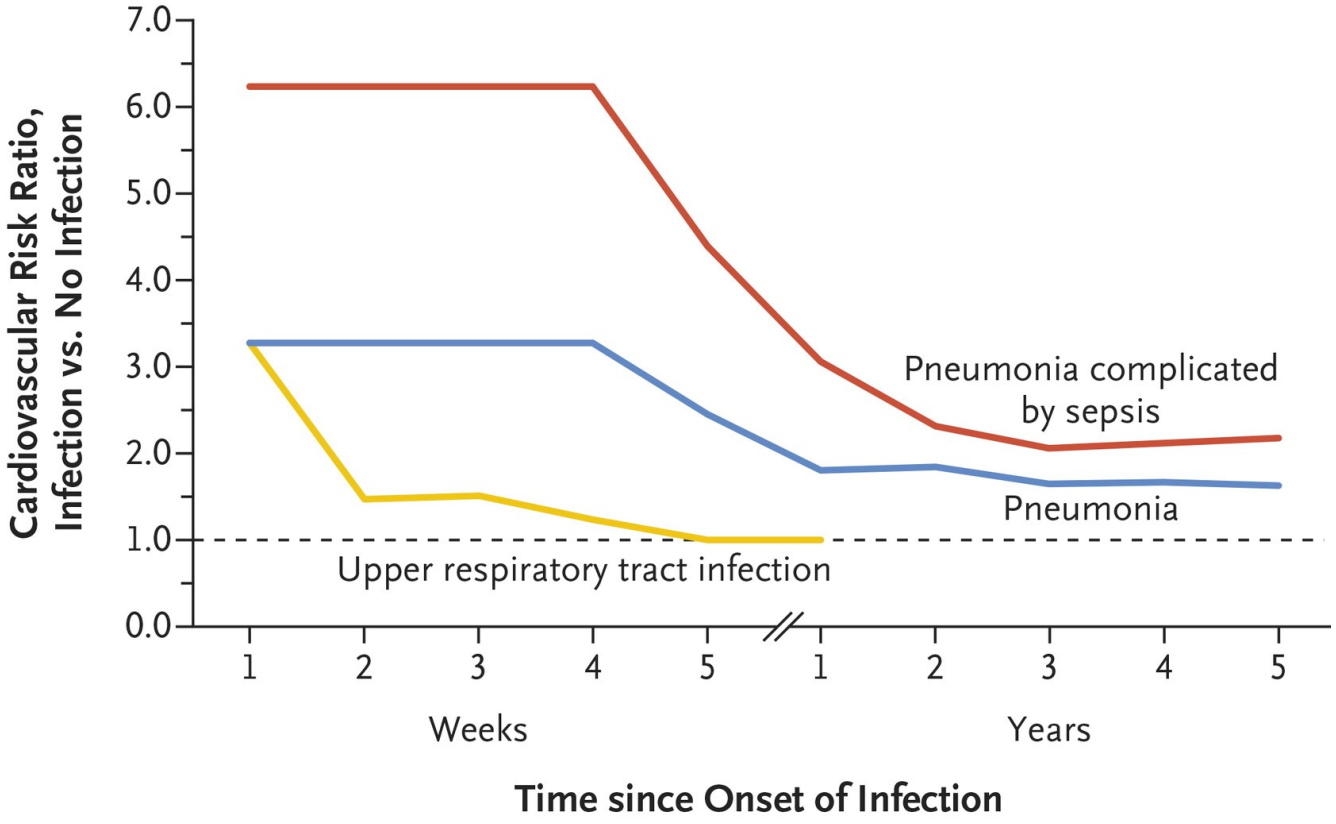
Treatment depends on the cause.
Evidence base less developed.



Study. T Ford et al, Circulation: Cardiovascular Interventions. 2019

Inflammatory conditions, including infections increase the risk of acute IHD. For example pneumococcal pneumonia increases the risk of heart attack (MI).

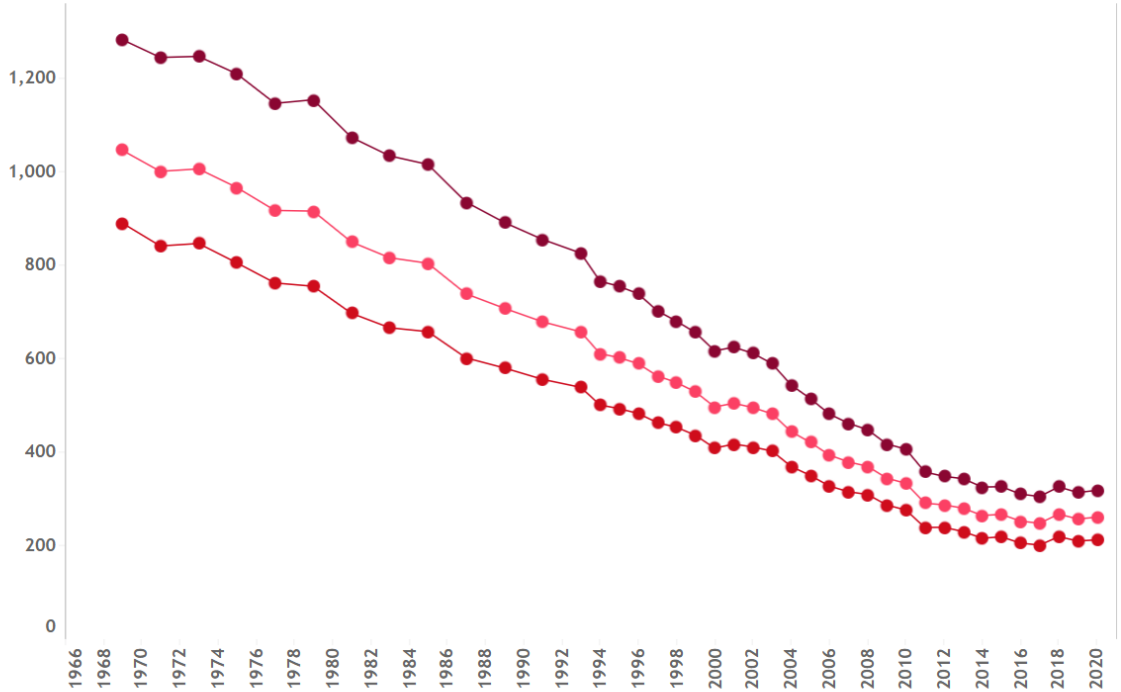
- There is also evidence of increased risks of myocardial infection after many other infections.
- Generally the more severe the higher the risk.
- Inflammation is part of the mechanism by which many risk factors increase heart disease- eg air pollution.



D. Musher et al NEJM 2019

The remarkable improvement in cardiovascular mortality and morbidity from IHD due to multiple incremental improvements.

- Primary prevention including on smoking, air pollution, exercise.
- Secondary prevention including antihypertensives, statins.
- Treatment of MI and angina including drugs, emergency stenting.
- Post-event prevention.
- Several headwinds including rising obesity, diabetes.



CHD mortality /100k people since 1969. BHF 2022