



# Lipids and Statins

Hannah Beba – Senior Clinical Pharmacist

Diabetes and Endocrinology

County Durham and Darlington NHS Foundation Trust



Warm up



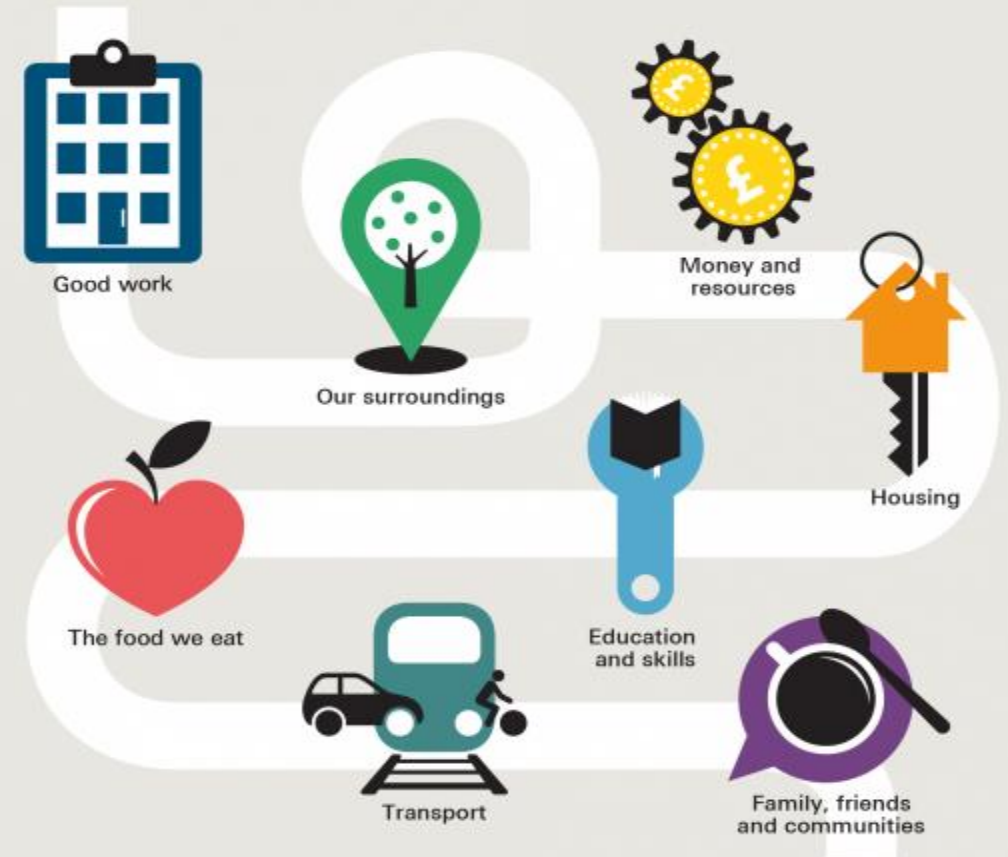
# Cardiovascular Health

- Cardiovascular Disease ( CVD) accounts for 25% of all deaths in the UK
- 7 million people in the UK have CVD
- Largely preventable
- Early detection and treatment will help people live longer and healthier lives
- CV disease is more prevalent in areas of high socio-economic deprivation
- CV disease is more prevalent in minority ethnic populations

## What makes us healthy?

Good health matters, to individuals and to society. But we don't all have the same opportunities to live healthy lives.

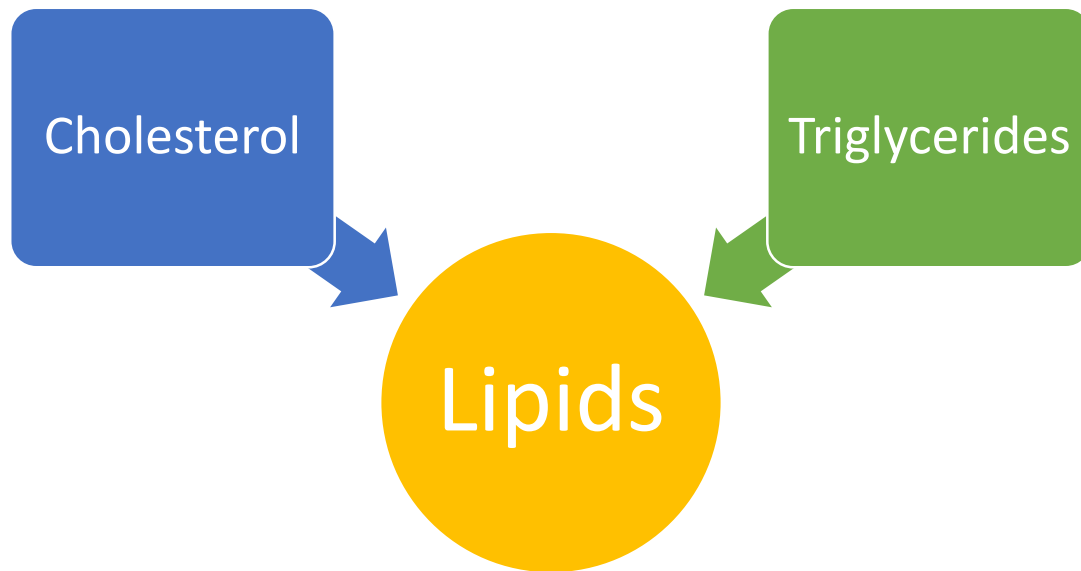
To understand why, we need to look at the bigger picture:



The healthy life expectancy gap between the most and least deprived areas in England is over **18** YEARS



# Lipids



- Fats that circulate in the blood
- **Cholesterol** – needed to build cell walls, hormones and vitamin D. Some comes from diet BUT most comes from the liver. When broken down cholesterol is used to make bile acids which help us digest our food.
- **Triglycerides** – found in our diet and made in the liver. This is an energy source for our muscles and organs



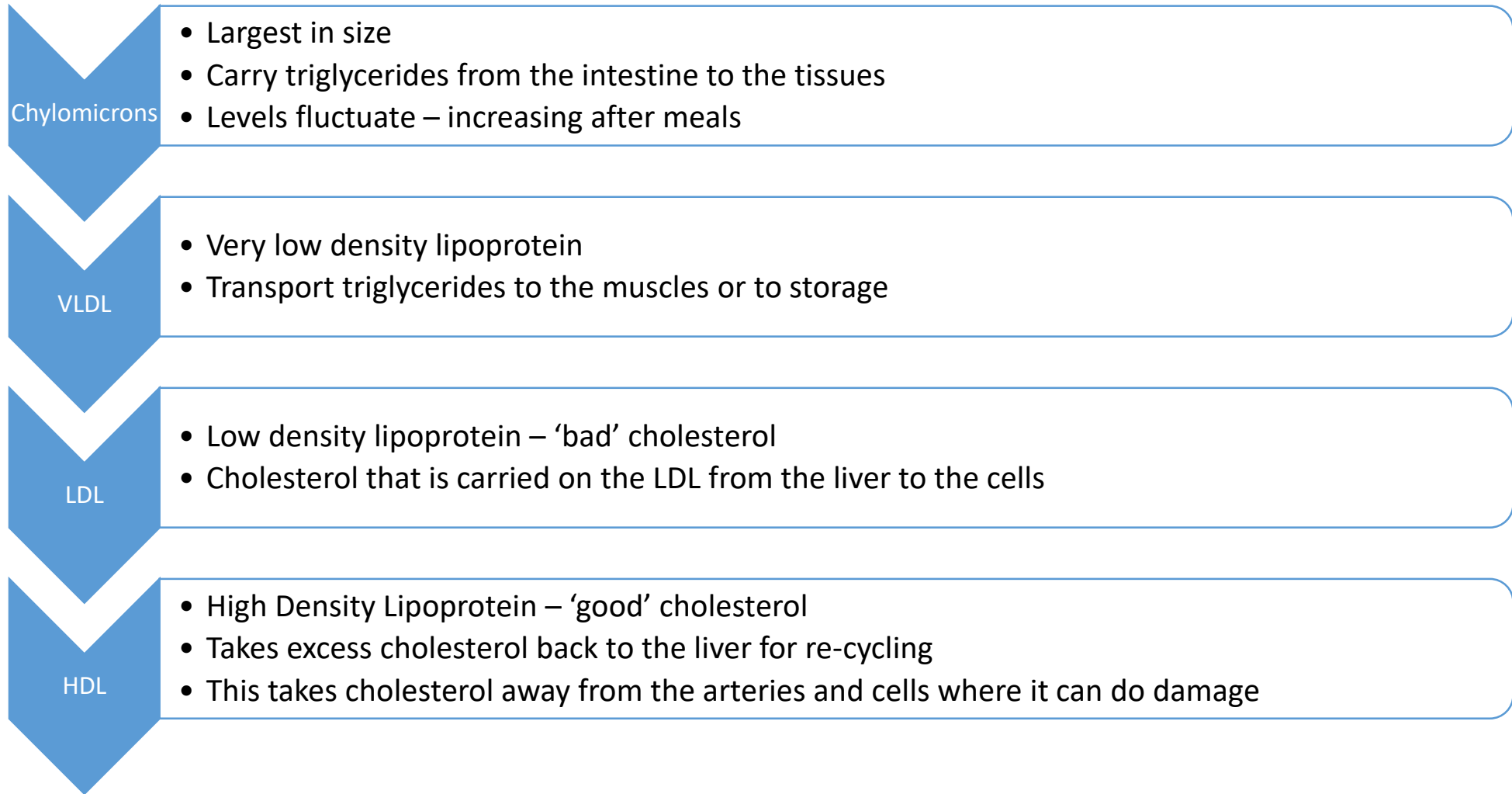


# Hitting it Hard – Deep Dive into Cholesterol



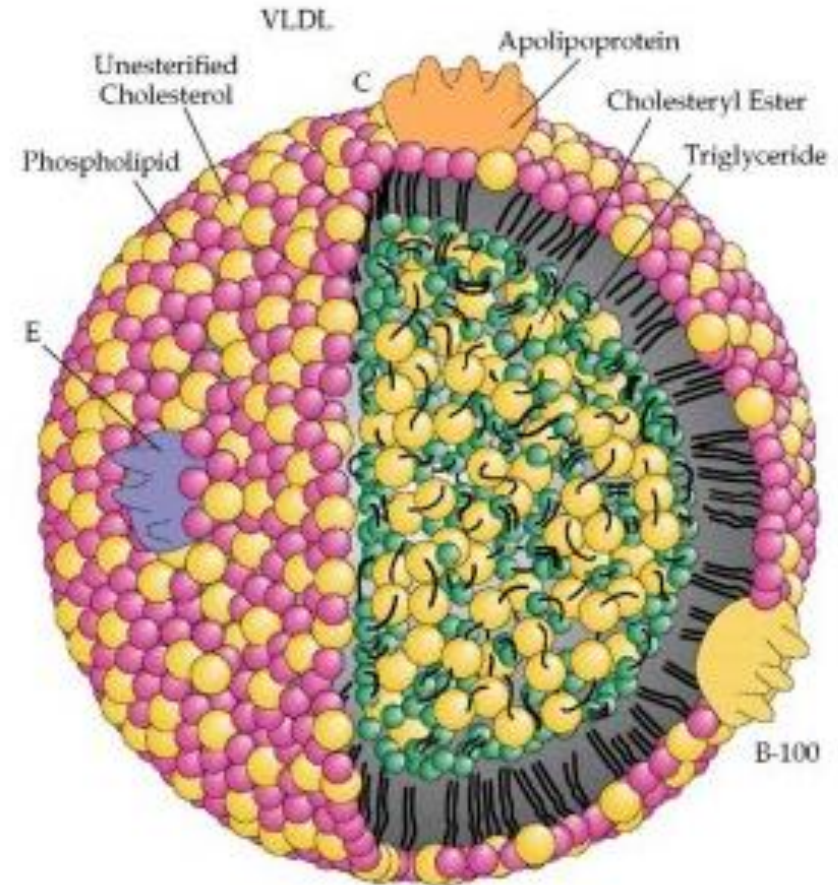
# Lipoproteins (Apolipoproteins)

Cholesterol and triglycerides will not circulate the body alone they travel in round parcels called lipoproteins



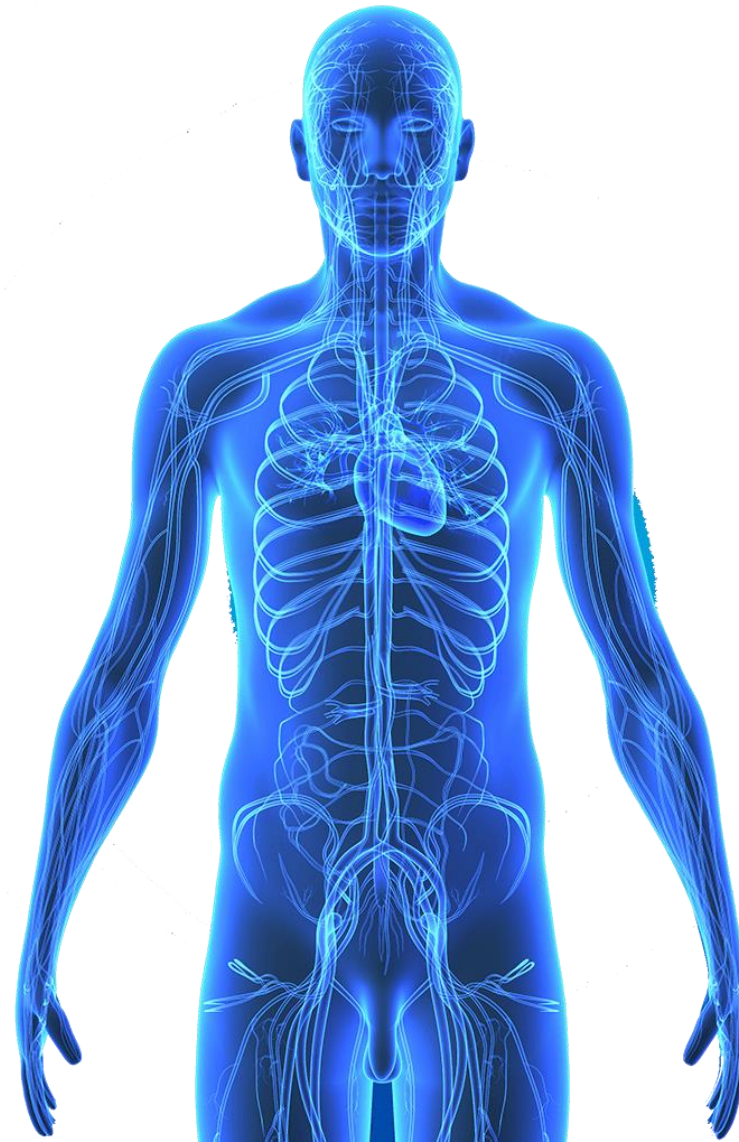
# Other Lipoproteins

- Apoprotein B – key protein for VLDL, LDL and chylomicrons
- Apoprotein A – key protein in HDL
- Lipoprotein (a)
  - largely decided in our genetic makeup
  - Sticky protein made in the liver
  - High levels increase the risk of circulatory disease and heart disease





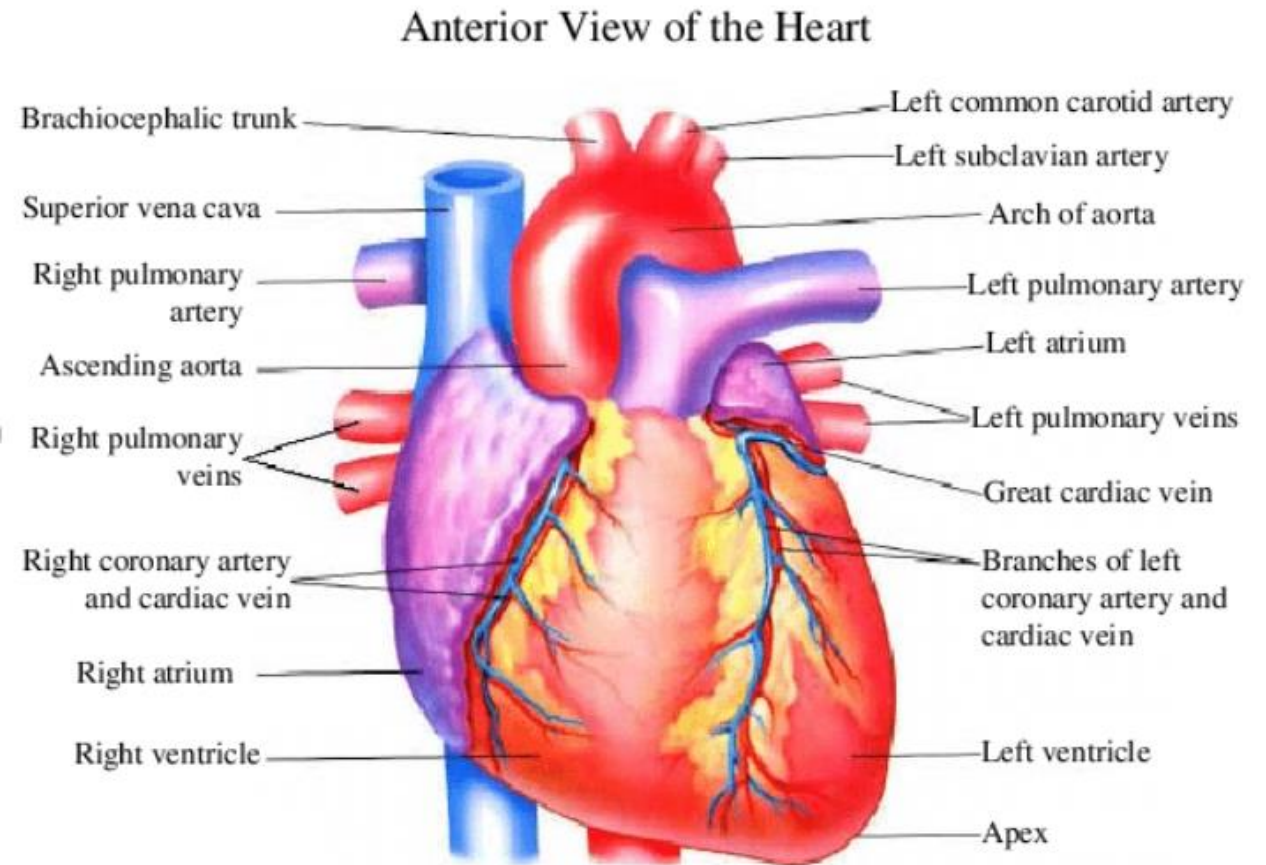
# Body Talk





# The Heart

- The heart, blood vessels and blood make up our circulatory system.
- The heart is a muscle which never stops beating, it pumps blood around the body.
- The left side pumps oxygen and nutrient rich blood to the brain, muscles, organs, and every cell in the body.
- The right side of the heart is slightly smaller and returns blood to the lungs to be topped up with oxygen.
- The heart has its own blood supply which comes from the coronary arteries. These divide many times to provide oxygen and nutrients to every part of the heart muscle to help keep it healthy and pumping normally



[https://www.researchgate.net/figure/Heart-anatomy-from-the-anterior-view-left-and-interior-view-right-Images-from\\_fig1\\_295706446](https://www.researchgate.net/figure/Heart-anatomy-from-the-anterior-view-left-and-interior-view-right-Images-from_fig1_295706446)



# Cardiovascular Disease ( CVD)

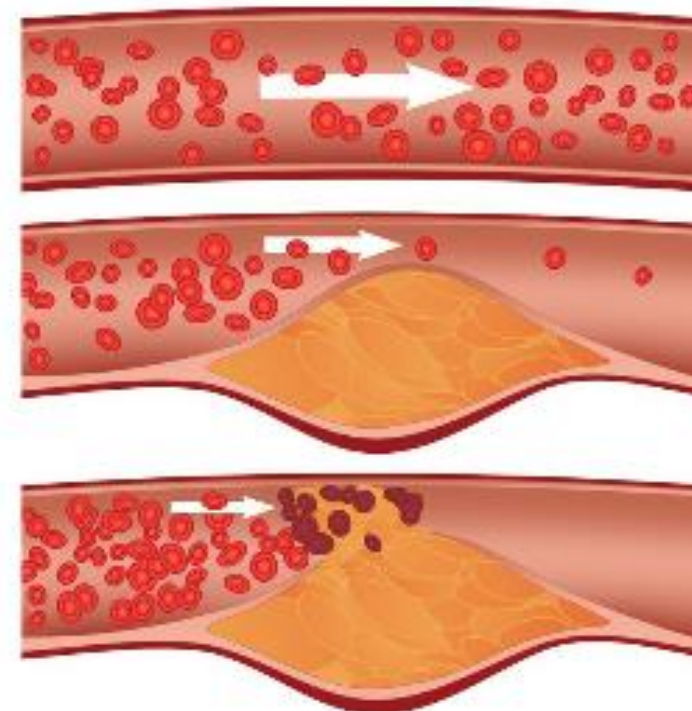


- Coronary Heart Disease ( CHD)
- Ischaemic Stroke
- TIA ( transient ischaemic attack) or ‘mini’ stroke
- Angina
- Peripheral Vascular Disease ( PVD)



# Heart Disease/Stroke/PVD

- Arteries become narrowed due to the slow build-up of fatty material (called **plaque or atheroma**).
- This process is called **atherosclerosis**
- This results in **warning symptoms** e.g. chest pain, claudication ( pain on walking in legs), TIA
- When these fatty deposits become very large or extended they may burst.
- This can cause blood clots and over time this may completely block an artery leading to more severe issues e.g. myocardial infarction (MI), stroke, unstable angina



<https://www.urmc.rochester.edu/highland/departments-centers/cardiology/conditions/coronary-artery-disease.aspx>



# Why is the liver important?



- Central role in controlling the amount of fat in your blood
- Liver cells have 'hooks' on them that can remove LDL cholesterol termed LDL receptors
- Any fat build up in the liver can damage it
- Most of our cholesterol is made in the liver.
- The liver is also the major site for changing excess sugars, proteins and alcohol into fatty acids and triglycerides, which are then either used for energy or stored for later



Risk

*Own it!*



# Very High Risk

## Descriptor

**Previous ACS (heart attack or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease.**

**Significant plaque on coronary angiography or CT scan (multi-vessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound.**

**Diabetes with target organ damage ( microalbuminuria, retinopathy, neuropathy)**

**Diabetes with at least three major risk factors**

**Early onset of T1DM of long duration (>20 years).**

**Severe Chronic Kidney Disease (eGFR <30 mL/min/1.73 m<sup>2</sup>).**

**Familial Hypercholesterolaemia with ASCVD (atherosclerotic cardiovascular disease) or with another major risk factor.**





# High and Moderate Risk

## Descriptor

**Markedly elevated single risk factors, in particular TC > 8 mmol/L (> 310 mg/dL), LDL-C > 4.9 mmol/L (> 190 mg/dL), or BP > 180/110 mmHg.**

**Patients with Familial Hypercholesterolaemia without other major risk factors.**

**Patients with Diabetes M without target organ damage with Diabetes duration > 10 years or another additional risk factor.**

**Moderate CKD (eGFR 30-59 mL/min/1.73 m<sup>2</sup>).**

**Young patients (T1DM < 35 years; T2DM < 50 years) with Diabetes duration < 10 years, without other risk factors.**



Prevention

**PREVENTION  
WORKS!**



# Primary Prevention vs. Secondary Prevention

No established CVD

Established CVD  
(Previous MI, stroke,  
TIA, PVD, angina)

## PRIMARY PREVENTION

Consider statin therapy for adults who do not have established CVD but fall into the categories below. Use QRISK risk assessment tool where appropriate (see page 2, 'Primary Prevention Risk Assessment')

Age  $\leq 84$   
& QRISK  
 $\geq 10\%$  over  
next 10  
years

Type 2  
diabetes  
& QRISK  
 $\geq 10\%$  over  
next 10  
years

Type 1 diabetes, if they have one  
or more of the following:

- Over 40 years
- Had diabetes for  $>10$  years
- Have established nephropathy
- Have other CVD risk factors

CKD eGFR  
 $< 60$   
mL/min/1.73m<sup>2</sup>  
and/or  
albuminuria

Age  $\geq 85$   
years  
if appropriate  
consider  
comorbidities,  
frailty & life  
expectancy

## SECONDARY PREVENTION

Offer statin therapy to adults with CVD, this includes angina, previous MI, revascularisation, stroke or TIA or symptomatic peripheral arterial disease. Do not delay statin treatment if a person has acute coronary syndrome. Take a lipid sample on admission (within 24 hours)



# Genetic Lipid Disorders

## Familial Hypercholesterolaemia (FH)

- Raises LDL cholesterol
- 1 in 250 people have it
- Often a strong family history of cardiovascular disease
- Total cholesterol is often >7.5mmol/L and LDL-C >4.9mmol/L and often normal triglycerides
- Physical signs – tendon xanthoma, corneal arcus ( if age <45yrs)

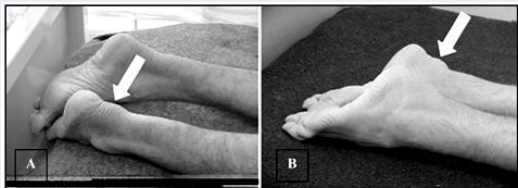


Fig 1. Achilles tendon xanthomas (arrows): case 1 (A) and case 2 (B).



## Familial Combined Hyperlipidaemia (FCH)

- 1 in 100 people have it
- Too much VLDL and apoprotein B
- Raised TC and triglycerides

## Others

Polygenic Hyperlipidaemia

Familial Chylomicronaemia Syndrome (FCS) or Lipoprotein Lipase Deficiency

Type 3 Hyperlipidaemia



# Targets



# What should my lipid levels be for most people ?

	UK Guidance
<p><u>Primary Prevention – for high risk and very high risk</u> Start on Atorvastatin 20mg</p> <p><u>Secondary Prevention</u> Start on Atorvastatin 80mg</p>	<p><u>LDL/non-HDL</u> Intensify lipid lowering therapy if: non-HDL-C reduction from baseline is less than 40% <u>OR</u> non-HDL-C &lt;2.5mmol/L (LDL-C &lt;1.8mmol/L)</p> <p><u>Triglycerides</u> – aim for &lt;1.7mmol/L (fasting)</p> <p><u>HDL</u> &gt;1mmol/L (men) or &gt;1.2mmol/L ( women)</p>

**Non-HDL-C = TC minus HDL-C**





Action



# Diet and Lifestyle

- **Be physically active** – 150 minutes of exercise /week that gets you slightly out of breath
- **Eat well**
  - A heart-healthy diet is rich in fruit and vegetables, whole grains, pulses, nuts, seeds, fish and vegetable proteins such as soya.
  - saturated for unsaturated swaps
  - Reduce amount of refined sugar being taken in
  - Increase foods that can lower cholesterol if eaten regularly
    - Foods rich in soluble fibre (oats, barley, beans, peas, lentils, vegetables, fruits)
    - Nuts (choose unsalted varieties)
    - Plant proteins such as soya and quorn
    - Dairy foods fortified with plant sterols and stanols
- **Reduce alcohol intake**



# Smoking

- Higher risks of stroke and CHD compared to those who do not smoke
- Toxins in cigarette smoke put a bigger strain on the heart - making it beat faster, increasing the risk of blood clots and damaging the inside of your blood vessels (arteries).
- Smoking also lowers your protective HDL-cholesterol.
- You can cut your risk of coronary heart disease in half, in just one year, by stopping smoking



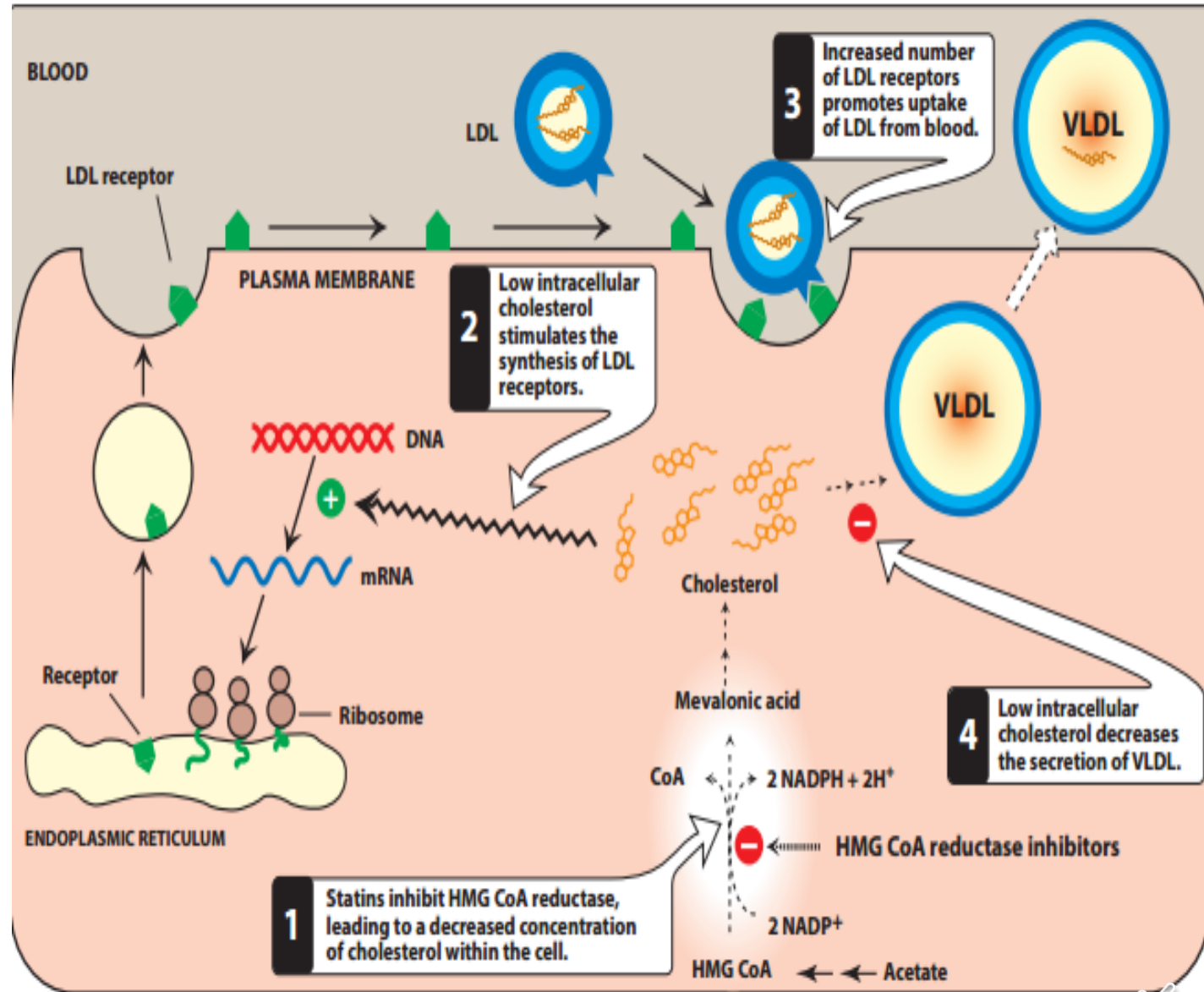
# A Helping Hand

Medications



# Statins

- Slow and reduce the amount of cholesterol our bodies make
- Safe and well tolerated
- Should not be used if planning pregnancy
- Should not be used if pregnant or breastfeeding



# Statins – efficacy and safety

Approximate reduction in LDL-C					
Dose mg/day	5	10	20	40	80
Fluvastatin			21%	27%	33%
Pravastatin		20%	24%	29%	
Simvastatin		27%	32%	37%	42%
Atorvastatin		37%	43%	49%	55%
Rosuvastatin	38%	43%	48%	53%	
Atorvastatin + Ezetimibe		52%	54%	57%	61%

Previous studies have shown that, in certain people, statins reduce the risk of heart attack, stroke, and even death from heart disease by about 25-35 %.

‘nocebo effect’ – may account for up to 90% of statin intolerance

**Statin Intolerance Pathway**

ACCELERATED  
ACCESS  
COLLABORATIVE

**NHS**  
England





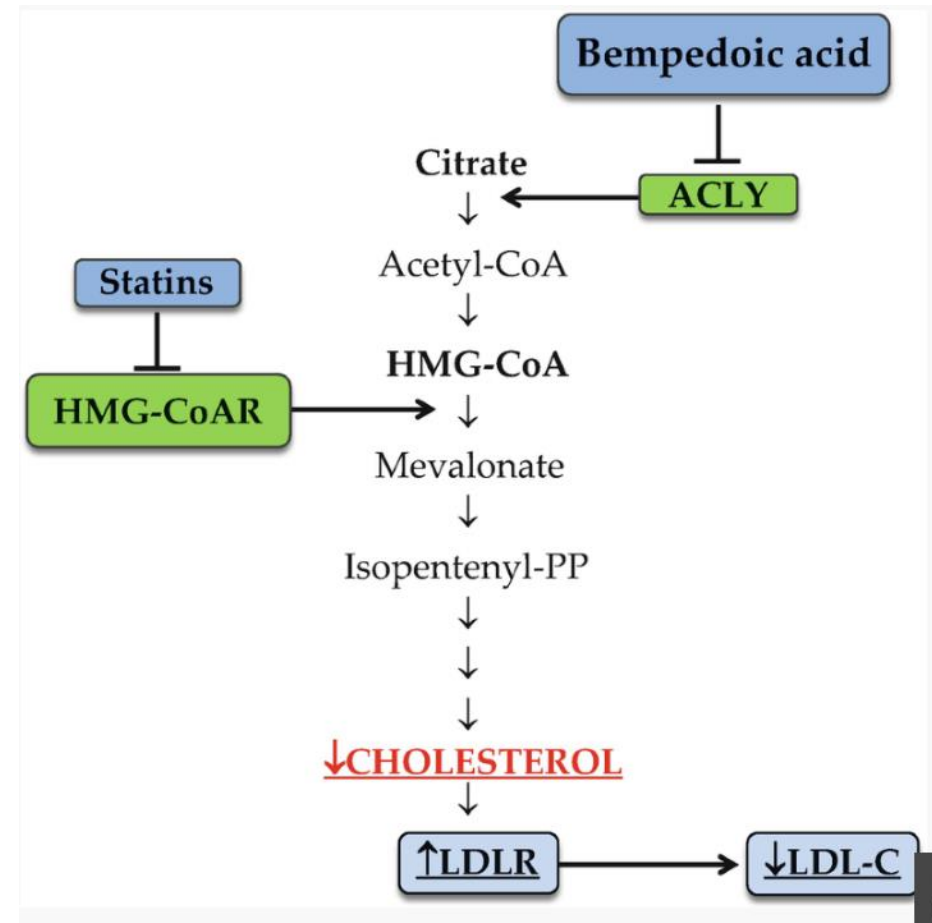
# Fibrates

- Reduce triglycerides
- To be used with statin ( if used alone can raise LDL-C)
- Questionable efficacy in people living with diabetes
- Should not be used during pregnancy
- Should not be used if liver or kidney health is an issue
- Usually only used if triglycerides  $>10\text{mmol/L}$



# Bempedoic Acid

- Bempedoic acid lowers LDL-C levels with similar efficacy to statins
- Non-HDL-C and apoB levels and LDL particle number were also significantly reduced
- May have a role in statin intolerance pathways
- Hypercholesterolemic patients with type 2 diabetes showed a greater LDL-C reduction
- The treatment with bempedoic acid did not result in a worsening of glycemic control, which is another relevant concern associated with statin therapy

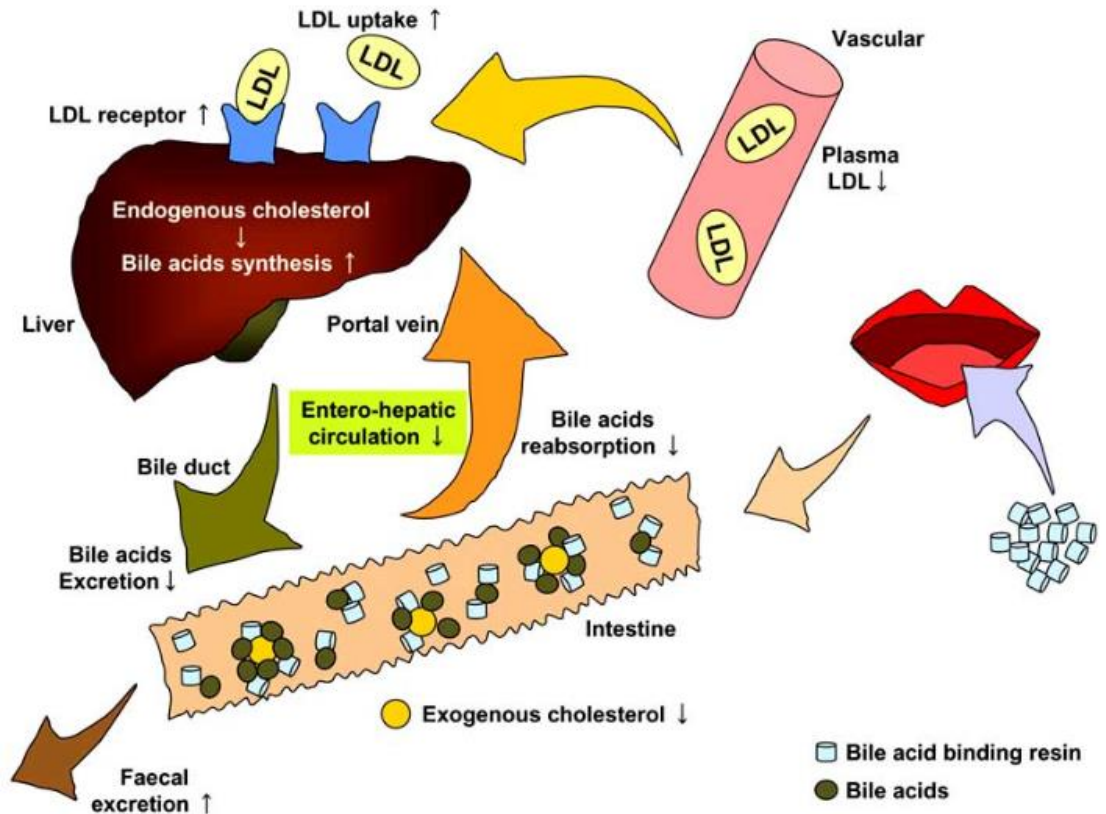


[https://link.springer.com/chapter/10.1007/164\\_2020\\_361](https://link.springer.com/chapter/10.1007/164_2020_361)



# Resins (Bile acid sequesterants)

- Powder, granules or tablets
- Can take powder or granules with water, fizzy drinks, yoghurt or fruit juice.
- Prevent reabsorption of bile acids in the gut which in turn decreases LDL
- Safe in children and pregnancy
- Can experience gastric discomfort which can lead to discontinuation

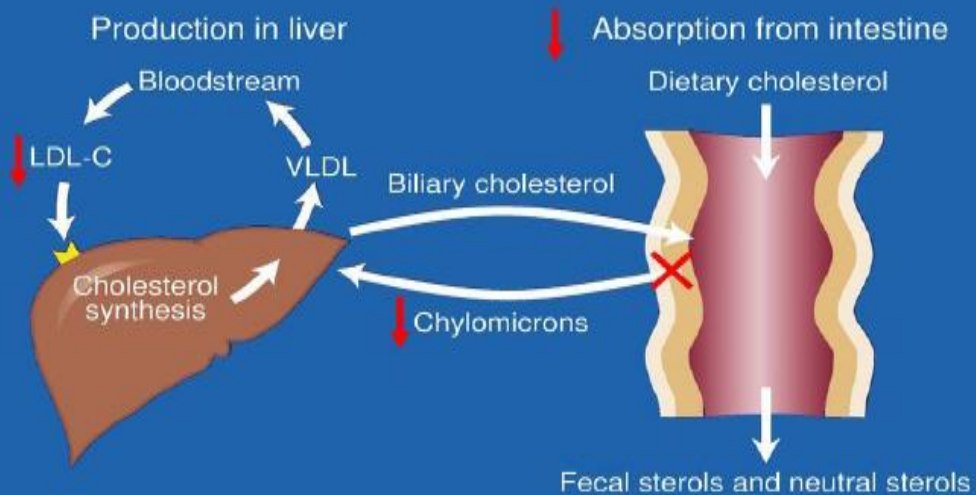


[https://www.researchgate.net/figure/fig1-The-mechanism-by-which-bile-acid-binding-resins-disrupt-the-enterohepatic\\_fig1\\_23317433](https://www.researchgate.net/figure/fig1-The-mechanism-by-which-bile-acid-binding-resins-disrupt-the-enterohepatic_fig1_23317433)



# Ezetimibe

## Ezetimibe: Mechanism of Action



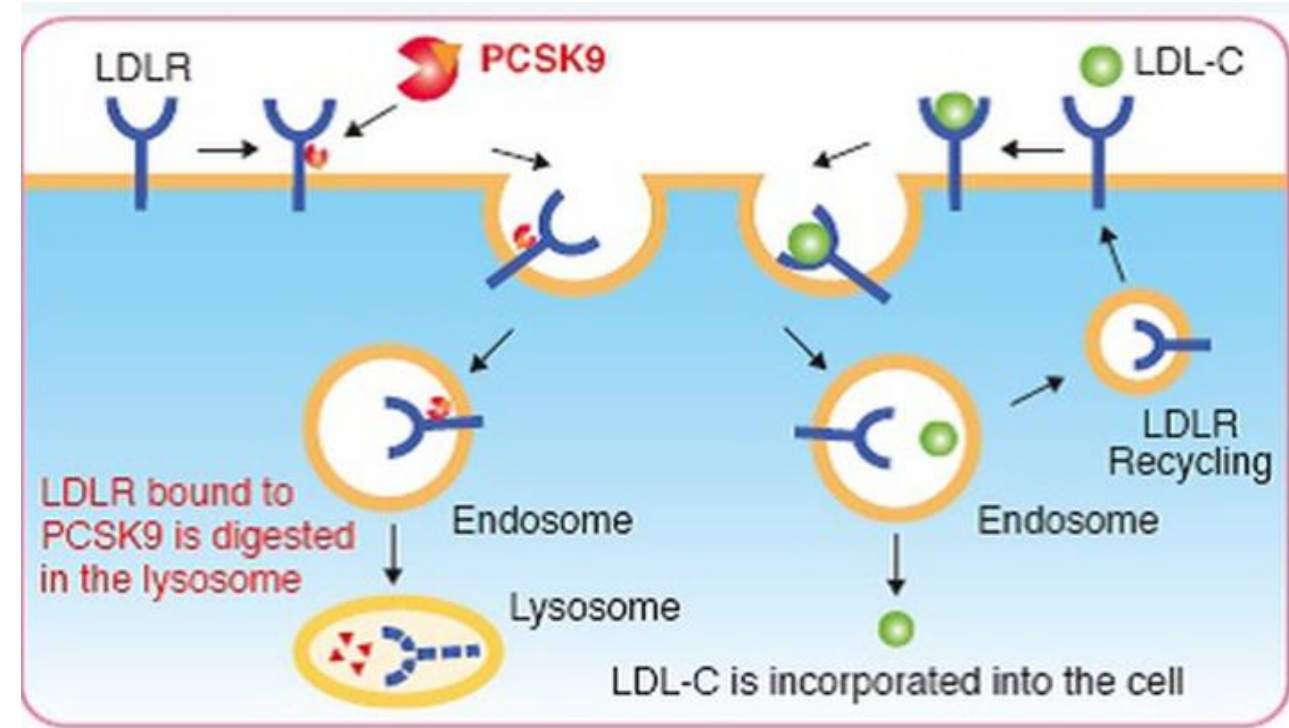
[http://ksumsc.com/download\\_center/Archive/1st/437/4.Cardiovascular%20Block/Teamwork/Pharmacology/9-10%20Antihyperlipidemia.pptx.pdf](http://ksumsc.com/download_center/Archive/1st/437/4.Cardiovascular%20Block/Teamwork/Pharmacology/9-10%20Antihyperlipidemia.pptx.pdf)

- Ezetimibe blocks the absorption of cholesterol and bile acids in the intestines.
- It is often given to help people who are already taking a statin but who need a little extra help to reach their cholesterol targets.
- Ezetimibe may also be prescribed for those unable to tolerate statin therapy



# PCSK9 Inhibitors

- Injectable therapy
- Currently only available as a 2 weekly injection (Repatha and Praluent)
- Inclisiran should be available in 2021 – 6 monthly injections after initial titration
- Reserved for very high risk people who are unable to reach target values



<https://vajiramias.com/current-affairs/pcsk9/5c63d3bf1d5def791df98669/>





Thank you

