CVD Secondary prevention

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Learning outcomes

- An overview of CVD secondary prevention and Lipids
- Defining roles and responsibilities in primary and secondary care
  – what can we achieve in primary care
  – secondary care and lipid services
- Prioritising patients for review with lipid management in primary care
- Referral pathways to secondary care clinics
- Case study

Definition of CVD secondary prevention

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- Patients with established atherosclerotic cardiovascular disease (ASCVD)
  - Definition by NICE:

  "Atherosclerosis is a condition where there is a build-up of fatty deposits (plaques or atheroma) inside an artery which cause the artery to harden and narrow, restricting blood flow.'' → Increase BP, risk of thrombosis and myocardial infarction

Atherosclerotic CVD diseases:

- Acute Coronary Syndromes (ACS): NSTEMI, STEMI, Unstable Angina
- Coronary heart disease or previous coronary revascularisation procedures (Stent implantation, CABG)
- Symptomatic Peripheral Artery Disease (PAD)
- Ischaemic stroke/Transient Ischaemic Attack (TIA)

UCLP Proactive Care Frameworks Overview: Cardiovascular Conditions

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Healthcare Assistants/Health & Wellbeing Coaches and other trained staff

Self management e.g.	Education (signposting online resources), self care (eg BP measurement, foot checks, red flags), signpost shared decision-making resources (eg statins, anticoagulants)
Behaviour change e.g.	Brief interventions and signposting e.g. smoking, weight, diet, exercise, alcohol
Support holistic care	Identify wider needs and signpost to eg social prescriber, care coordinator
Gather information e.g.	Up to date bloods, BP, weight, smoking status, run risk scores: QRISK, ChadsVasc, HASBLED

Risk Stratification & Prioritisation

Atrial Fibrillation

Blood Pressure

Cholesterol

Diabetes

Prescribing Clinician

Optimise therapy and mitigate risk

1. Review blood results, risk scores & symptoms
2. Initiate or optimise therapy
3. Check adherence and adverse effects
4. Review complications and co-morbidities
5. CVD risk – BP, cholesterol, pre-diabetes, smoking, obesity

Cholesterol – Secondary Prevention (pre-existing CVD)

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Diagnosed Atherosclerotic CVD diseases: Acute Coronary Syndromes -ACS (NSTEMI,STEMI, Unstable Angina); Coronary heart disease or previous revascularisation (Stent implantation, CABG); Peripheral Artery Disease; Ischaemic stroke/Transient Ischaemic Attack (TIA)

Healthcare assistants/other appropriately trained staff

Gather information e.g.	Up to date bloods, BP, weight, smoking status.
Self-management e.g.	Education (cholesterol, CVD risk), BP monitors (what to buy, how to use), signpost to shared decision making resources.
Behaviour change e.g.	Brief interventions and signposting e.g. smoking, weight, diet, exercise, alcohol.

Stratification

Priority One	Priority Two	Priority Three	Priority Four
Not on statin therapy	On suboptimal intensity statin*	On suboptimal statin dose**	Sub-optimal non-HDL (>2.5mmol/l) levels despite maximal statin therapy

Prescribing clinician

Optimise lipid modification therapy and CVD risk reduction

1. Review CVD risk factors, lipid results and liver function tests.
2. Initiate or optimise statin to high intensity – e.g. atorvastatin 80mg.
3. Titrate therapy against reduction in LDLc/non-HDLc (statin>ezetimibe>PCSK9i mAB/inclisiran).
4. Optimise BP and other comorbidities.
5. Use intolerance pathway and shared decision-making tools to support adherence.
6. Arrange follow-up bloods and review if needed.

* E.g simvastatin
** E.g atorvastatin 40mg

Prioritising patients in primary care

1. Focus on UCLP priority 1 patient group: CVD not on statin
   - Discuss reasons for not being prescribed a statin (e.g. non-adherence, stopped a few months, check records ? statin repeat prescription not collected for a while)
   - Statin hesitancy- refer to SWL guideline for shared decision making table
   - Document statin decision reason using SNOMED codes and/or restart HI as per patient
   - Reinforce behavioural interventions and lifestyle
2. Opportunistic UCLP priority 2 patient group: CVD on suboptimal statin dose
3. Group 3 CVD patients on maximum dose HIST but non-HDL>2.5mmol/L (NICE recommends at least 40% reduction)→ mostly will just need repeat bloods
4. Identifying patients at greatest risk and optimising their treatment through appropriate therapies, including HIST and ezetimibe; identify multimorbidity where you can make several interventions in one consultation

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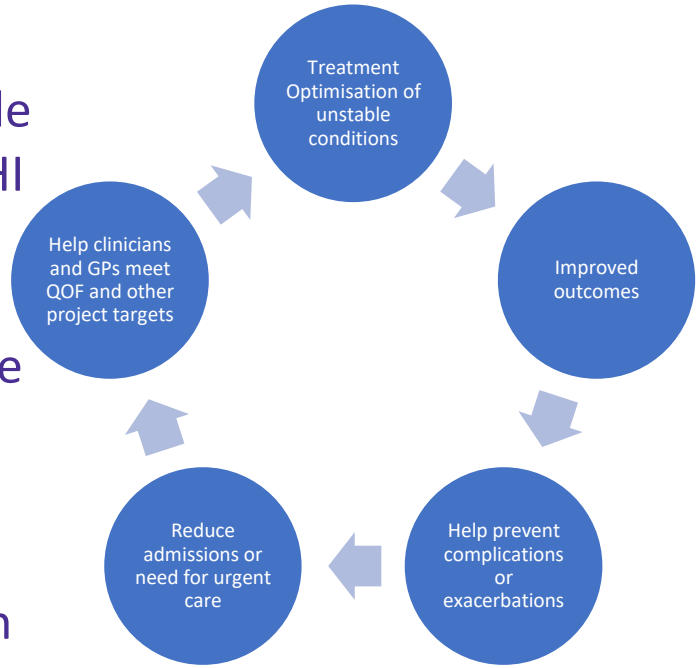

What can we achieve in primary care?

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1. Provide CV risk management and reduction with lifestyle and dietary modifications (smoking cessation, weight management, alcohol reduction)
2. Request/check recent blood tests within last 3-6 months (Full lipids,HbA1C, TFTs, LFTs)→ treat/manage secondary causes of hypercholesterolaemia (alcohol >40iu, ALT >40, TG >5, HbA1c >53, TSH >15, CKD 3, liver failure)
3. Offer second-line therapies with ezetimibe +/- alternative statin choice or dose adjustment if statin intolerance (follow statin intolerance pathway)
4. Optimise other CV conditions (''ABCD''); support adherence, remote and self-management
5. Utilise SWL Lipid management guidelines and UCLP proactive care frameworks
6. Implement primary care pathways for referral to secondary care, for possible treatment with bempedoic acid, PCSK9 inhibitors/Inclisiran or other therapies where appropriate
7. Identify patients with CVD and possible diagnosis of FH for specialist referral
   - TC >7.5 mmol/L (LDL>4.7mmol/L) or personal history of persistent high cholesterol
   - Family history of premature coronary heart disease (MI before age 60 in 1st degree or MI before 50 in 2nd degree relative)
   - Physical signs e.g. tendon xanthomata, corneal arcus

Optimisation Pathway for Secondary Prevention

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Is patient on high dose, high intensity statin*?
(atorvastatin 80mg or equivalent)

Yes

No

Initiate / increase to high dose high intensity statin **
and re-enforce lifestyle and diet measures

Is non-HDL cholesterol < 2.5mmol/L? ***

Yes

No

Check adherence to statin and lifestyle measures ****

Consider ezetimibe 10mg daily
Reassess after three months. If non-HDL-C remains > 2.5mmol/L; consider injectable therapies arrange a fasting blood test and assess eligibility

Consider injectable therapies
If non-HDL chol > 2.5mmol/L; Arrange fasting blood test to assess eligibility:

- Inclisiran - if fasting LDL-C ≥ 2.6mmol/L

OR

- **Refer for PCSK9i (mAB)⁺** if fasting LDL-C > 4mmol/L (or > 3.5mmol/L if recurrent events)

If eligibility criteria are not met, consider ezetimibe 10mg daily (if not previously considered)

Review annually for adherence to drugs and support for diet and lifestyle measures

Optimal High Intensity Statin for secondary prevention (High intensity statins are substantially more effective at preventing cardiovascular events than low/medium intensity statins)	
Atorvastatin	80mg
Rosuvastatin	20mg

* Dose may be limited if:

- eGFR<30ml/min
- Drug interactions
- Intolerance
- Older age / frailty

** See statin intensity table

*** Current NICE Guidance recommends at least a 40% reduction in non- HDL cholesterol

**** **If statin not tolerated**, follow statin intolerance pathway and consider ezetimibe 10mg daily +/- bempedoic acid 180mg daily. If non HDL-C remains > 2.5mmol/L despite other lipid lowering therapies consider injectable therapies.

⁺ NICE Guidance: Evolocumab, Alirocumab

Primary care reviews- Points to consider:

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- **Establish CVD Hx (procedures/events), PMHx history, FHx and LLT history**
- Take a thorough allergy and intolerance history (types of statins tried, which doses, side-effect profile, previous therapies and correlate this with previous cholesterol levels → update primary care codes (contraindication/exceptional reporting)
- Screen and address CV risk factors (smoking, BP/HR, HbA1C, BMI, alcohol)
- Consider CVD proforma when reviewing patients
- CVD register code cleansing or updates to reflect recent clinical history
- Ask patients for hospital only meds (not always recorded in primary care records)
- Provide individualised benefit vs risk discussion of LLTs based on co-morbidities and current meds (look for interactions) →Adherence? Re-challenge when appropriate with non-HIST doses or statin regimens **(any statin is better than no statin)**
- Reinforce patient education through patient leaflets (Heart UK, BHF, NHS resources)
- Ask for Lipid specialist advice via advice and guidance/refer when appropriate
- Treat vitamin D levels –deficiency increases risk of statin-related side-effects

Role of secondary care and Lipid services

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- Screen, detect and treat primary causes of hypercholesterolaemia (e.g. FH)
- Manage cardiovascular risks (HPTN, new AF, hyperlipidaemia, T2DM, smoking cessation, alcohol reduction)
- Identify secondary causes of hypercholesterolaemia and refer to relevant teams
- Provide treatment optimisation with specialist medicines: bempedoic acid (addition to ezetimibe), PCSK9mabs, Inclisiran, Icosapent ethyl
- Treat complex patients with multiple statin intolerance (3 or more) or patients with severe adverse reaction and not meeting LDL-C/Non-HDL targets on ezetimibe
- Optimise CVD secondary prevention patients on maximum tolerated statin and ezetimibe to national/personalised lipid target levels
- Treat severe hypertriglyceridaemia
- Family screening of identified patients with a genetic diagnosis of FH

Secondary Prevention: Medicines optimisation for Lipid Management

1) **Check baseline bloods** (non-fasting full lipid profile, LFTs, HbA1c, thyroid and renal function)- consider secondary causes of hyperlipidaemia and manage as needed, consider if lipid profile may indicate FH- (see pages 9-11)
2) **Offer high dose high intensity statin** therapy with **atorvastatin 80mg^** (**alternative is rosuvastatin 20-40mg**)* to adults with CVD: this includes acute coronary syndromes (ACS), angina, previous myocardial infarction (MI), revascularisation, stroke or transient ischaemic attack (TIA), symptomatic peripheral arterial disease (PAD) or abdominal aortic aneurysm (AAA)
3) **Support the self-management** (*see page 6*) of modifiable risk factors eg. smoking, diet, obesity, alcohol intake, physical activity, blood pressure and glycaemic control (HbA1c)

In primary care check: **Is patient on high dose, high intensity statin? atorvastatin 80mg^ (alternative is rosuvastatin 20mg-40mg)***

Yes ← **Has non-HDL-C reduced by 40% or more from baseline at 3 months?** NICE[6] (if no baseline value: consider a target of non-HDL-C < 2.5 mmol/L or LDL-C <1.8 mmol/L: JBS) → No

Discuss with patient statin choice: reinforce lifestyle, dietary measures, check adherence to medication (*for statin intolerance pathway see page 5),* consider dose increase if on < atorvastatin 80mg^ if judged at higher risk based on co-morbidities, risk score or clinical judgement. After 3 months check non-fasting full lipid profile (TC, TG, HDL, LDL-C); LFTs

Yes ← **Has non-HDL-C reduced by 40% or more from baseline at 3 months?** NICE[6] (if no baseline value: consider a target of non-HDL-C < 2.5mmol/L or LDL-C <1.8 mmol/L). Check adherence to statin and lifestyle measures (*for statin intolerance see page 5*) then consider the following options based on shared decision making with the patient → No

Consider adding ezetimibe 10mg daily SPC
After 3 months, check non-fasting full lipid profile (TC, TG, HDL, LDL-C); LFTs

Check LDL-C (fasting sample if possible) **and consider inclisiran ▼** if LDL-C ≥ 2.6 mmol/L (*see page 8*): refer to specialist for initiation- *Formulary status- Red*

Check LDL-C (fasting sample if possible) **and consider alirocumab or evolocumab (PCSK9i mAB: Refer to lipid** clinic if LDL-C >4 mmol/L (or LDL-C >3.5 mmol/L with recurrent CVD event or multivascular disease)

PCSK9i (*see page 7)-Formulary status- Red*

For Statin intolerance options- (*see page 5*):

- **ezetimibe**
- **specialist initiation of [bempedoic acid plus ezetimibe] ▼** (NICE[8])
  Formulary status- Amber 2
- **specialist initiation of inclisiran ▼** (*see page 8*)-
  Formulary status- Red

Yes ← **Has non-HDL-C reduced by 40% or more from baseline at 3 months?** (if no baseline value: consider a target non-HDL-C < 2.5 mmol/L or LDL-C <1.8 mmol/L) → No

Discuss lipid lowering options with your patient. In SWL it is recommended to prescribe **high intensity statin with ezetimibe** for at least 3 months before considering other options or referring to lipid clinic.

Review annually for adherence to medications, support for diet and lifestyle measures, and check required bloods eg lipid profile, LFTs if indicated

^Atorvastatin: use a lower dose- potential drug interaction; high risk of or experiencing adverse effects; intolerance; for CKD eGFR<60ml/min/1.73m^2- consider initial dose of **atorvastatin 20mg**, can up-titrate (note: if eGFR< 30ml/min/1.73m^2 seek specialist input to initiate and up-titrate)

***Rosuvastatin: CrCl 30-60ml/min- initiate a lower dose- see BNF, (note: if CrCl < 30ml/min- seek specialist input to initiate and up-titrate; use of 40mg dose- specialist supervision recommended)

For all drugs listed- check SPC or BNF for cautions, contraindications & interactions

Lipid-lowering targets

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Strategy/Guidance	NICE target	JBS3 target	ESC target
Primary prevention	40% non-HDL-C reduction from baseline	-	LDL-C <3 in moderate risk and <2.5mmol/L in high-risk patients
Secondary prevention	40% non-HDL-C reduction from baseline	Non-HDL-C<2.5mmol/L (LDL-C<1.8mmol/L)	LDL-C <1.8mmol/L
Familial Hypercholesterolaemia	At least 50% reduction in LDL-C from baseline (LDL-C <5mmol/L)	-	LDL-C <1.8mmol/L

Pharmacist-led Inclisiran clinic in SWL

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- Implementation in early stages, pending SOP and referral pathways
- Based at SGH and/or St. John's Therapy one day every fortnight
- For patients who meet NICE criteria and have tried first line therapies (statins AND ezetimibe +/- bempedoic acid in statin intolerance) *RAG rating in SWL: RED
- **NICE TA for Inclisiran: Secondary prevention lipid strategy ONLY**

  Patients with a history of cardiovascular disease e.g. ACS, coronary/arterial revascularisation, CHD, ischaemic stroke or peripheral arterial disease (PAD)
  with **persistent LDL-C levels ≥2.6 mmol/l** despite having the maximum tolerated lipid-lowering therapy (HI statins and/or ezetimibe)
  Alone or in combination with lipid lowering medication if **statin intolerant/contra-indicated**
- Primary care referrals:
  - Identify patients using UCLP searches or QOF searches
  - Follow SWL Lipid guidance CVD secondary prevention optimisation pathways
  - SWL Inclisiran initiation checklist → Going to be circulated once approved
  - Further details to be disseminate in future webinars/ SWL newsletter

SWL Inclisiran initiation checklist

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NHS South West London

South West London Inclisiran Initiation Checklist

Please check your patient is suitable for Inclisiran. It should be completed before seeking advice and guidance (A&G) from a lipid specialist and attached to the eRS A&G request. Please also attach the lipid profile result.

Patient name:		NHS number:	Date of Birth:
			Additional
1	Does the patient have a CVD history?	▫ YES ▫ NO	*Tick all that apply* ▫ Acute Coronary Syndrome (ACS) e.g. NSTEMI/STEMI or Coronary Heart Disease (CHD) e.g., angina ▫ Previous coronary/arterial revascularisation e.g. PCI/Coronary Artery Bypass Graft (CABG) ▫ Ischaemic stroke/transient ischaemic attack (TIA) ▫ Peripheral arterial disease (PAD)
2	Check lipid profile and LDL-C cholesterol. Is it ≥ 2.6mmol/L?	▫ YES ▫ NO	LDL-C level is …… Please attach a copy of baseline full lipid profile result (triglycerides, HDL, total cholesterol, LDL, and non-HDL), full liver profile (LFT), renal profile and dates of test results:
3	Has the patient taken a **maximum tolerated dose of a high-intensity statin such as atorvastatin or rosuvastatin, ezetimibe and, preferably, bempedoic acid for at least 3 months** prior to this referral?	▫ YES ▫ NO	**If yes:** add the medicines and doses **If no:** indicate why - intolerance/non-adherence/ hesitancy etc
4	If statin intolerance: Have you followed the SWL lipid management guidance CVD secondary prevention or statin intolerance pathways (page 4 and 5) or the NHS AAC statin intolerance pathway?	▫ YES ▫ NO	Which statins and doses have been prescribed previously? List here:
5	Is the patient adherent to their medication regime and lifestyle interventions?	▫ YES ▫ NO	Please detail here:
6	Have you discussed the **risks and benefits of Inclisiran therapy** with your patient? (Refer to SWL lipid management guidance and Inclisiran prescribing guidance for primary care	▫ YES ▫ NO	**Please ensure that your patient is aware that Inclisiran does not have long term safety data or cardiovascular outcome data yet**. Detail any discussions in the medical record and add key information here:
7	Is your patient aware of the **requirement to attend regular appointments for injections and follow-up?**	▫ YES ▫ NO	Initial dose is repeated at 3 months and then 6-monthly i.e., month 0, month 3, month 9 for 1st year, then every 6 months thereafter.
8	Does your patient have any **cautions/contra-indications** to inclisiran? (Tick any that apply)	▫ YES ▫ NO	▫ Severe renal impairment (e.g., CrCl <30ml/min) or requiring haemodialysis ▫ Severe liver impairment (e.g., Child-Pugh score >3) ▫ Pregnancy/breastfeeding ▫ Age <18 years **If yes to any of the above, patient does NOT qualify for Inclisiran. Please seek advice from the appropriate specialist**
9	Does your patient have any **special circumstances/needs** e.g., housebound, requires a carer, has oxygen therapy, needle phobia?	▫ YES ▫ NO	Detail here:
The Inclisiran eligibility checklist MUST be checked by two clinicians before initiation (a clinician and a lipid specialist).			
10	First clinician check Practice/clinic details: **Form completed by:** **Surname:** **First Name:**		Please send this request via eRS (e-referral service advice and guidance) to the relevant Trust lipid specialist to receive advice concerning your patient's suitability for inclisiran initiation in primary care.
	Outcome from lipid specialist advice: ***Is the patient suitable for Inclisiran initiation?*** Lipid Specialist clinic contact details:		**Form reviewed by:** **Surname:** **First Name:**

Case study- CV risk and lipid management Lipid clinic

Cardiovascular risk factors	Patient profile: 56 YO male referred by stroke team for CV risk& lipid optimisation
CVD history/PMHx	Hypertension, Hyperlipidaemia, ischaemic stroke March 2023 (started on rosuvastatin 5mg daily on discharge); ruled out embolic stroke secondary to AF
Allergies/intolerances	Pravastatin, simvastatin, atorvastatin (myalgia, lethargy, debilitating upper arm/lower limb joint pain, brain fog), ADR on pravastatin 10mg, atorvastatin 20mg, simvastatin 20mg
Family history	Father stroke at 50, maternal uncle had cardiac disease (unknown); Has estranged 1brother and 2 sisters; 2 estranged children; personal history of high chol for over 10 years (Tchol>8, LDL <6)
Social history, smoking, alcohol, exercise, BMI, diet	Non-smoker/alcohol, low exercise tolerance (SALT rehab done), BMI 35.8kg/m2; HGV driver (unable to work 12/12), dietary changes since stroke, oats, fish, vegetables
Medication history	Amlodipine 10mg OD, candesartan 8mg OD, clopidogrel 75mg OD, lansoprazole 30mg OD, rosuvastatin 5mg OD (mild/tolerable ADRs), colecalciferol 1000units OD, plant sterols
Relevant blood tests and lipid levels (12th May 23)	Tchol 7.8, LDL 5.3, TG 3.15, non-HDL 6.8; Lp(a)=55nmol/L; HbA1C 38, TFT normal, vitamin D 34, folate 2.6, ALT 18, CK 208, sensitive CRP 19.2 (high), no other 2nd causes of Tchol
Other clinical issues/results	Bilateral eye-lid xanthelasma for 7 years; no tendon xanthomata; BP 143/75, HR 62 Meets Simon Broome Criteria for FH; LDL-C 2.3/non-HDL 3.1mmol/L-rosuvastatin 5mg OD
Treatment plan	FH genetic test, PCSK9-I initiation, treat vitamin D/folate, weight loss plan in community, signpost Heart UK/diet changes, repeat BP and optimise, f/up + repeat bloods 3/12

Communication skills and behaviour changes

Communication skills to engage patients – See example here

Behaviour change strategies to motivate change – See example here

Further resources

- Healthcare Professionals:

- National-Guidance-for-Lipid-Management-Prevention-Dec-2022.pdf (england.nhs.uk) UCLP Proactive Care Frameworks Oct 2021 (pcdn.co)
- Proactive care frameworks – UCLPartners
- CVD resources – UCLPartners (AF, Blood pressure, Cholesterol, Diabetes)
- Lipid management and Familial Hypercholesterolaemia (FH) - UCLPartners
- UCLP Cholesterol Size of the Prize Modelling Sept 2022 (pcdn.co)
- Tackling Cholesterol Together - HEART UK
- Lipid Management: Medicines Optimisation Pathways (icb.nhs.uk)
- UCLP-Proactive-Care-Consultations-Guide-May-2023.pdf (pcdn.co)