West Yorkshire and Harrogate
HEALTHY HEARTS

West Yorkshire and Harrogate Lipid and Statin Background Document

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Summary

- High cholesterol is one of the most significant risk factors for CVD
- Raised cholesterol can also be caused by genetic conditions, where cholesterol is elevated from birth to very high levels, such as Familial Hypercholesterolaemia (FH). FH affects approximately 1 in 300
- The estimated adult population across West Yorkshire and Harrogate with a greater than 2 in 10 chance of a future heart attack or stroke is 175,000. Of those, just over half (89,250) aren't treated with a statin
- Statin therapy reduce cholesterol and reduces risk of CVD events by almost a quarter
- Data from UK general practice shows that **over half** of patients on statins do not reach their NICE cholesterol targets
- West Yorkshire and Harrogate Health Care Partnership (along with the nine CCGs) have developed a local treatment guidance and supporting information document for use in Primary Care; under the West Yorkshire and Harrogate Healthy Hearts project.
- The local guidance and supporting information is well aligned to NICE and only differs in two small areas:
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1. Local Lipid guidance advises usually starting people with 40mg Atorvastatin (NICE states 20mg initially and then to increase up to 80mg thereafter if not to cholesterol target) but provides suggested alternative of 20mg in two scenarios: 1) Dosage concerns; 2) Potential sensitivity of those of Asian or Chinese heritage.

2. NICE recommend a discussion with people who are stable on a low or middle intensity/strength statins the likely benefits and potential risks of changing to a high-intensity statin. This cohort is not included in this guidance document: the searches that support the work have excluded people with reasonably controlled cholesterol. This is due to the reduced absolute benefit from interventions in the "managed/controlled groups" and we are also mindful of the aim to maximise the impact of existing primary care resource, and maximising engagement of clinicians with a large-scale improvement programme.

1. Introduction

1.1. Poor cardiovascular (CVD) health can cause heart attacks, strokes, heart failure, chronic kidney disease, and the onset of vascular dementia. It disproportionately affects people from the poorest communities. CVD deaths still account for 1 in 4 of all deaths in England - the equivalent to 1 death every 4 minutes. Yearly healthcare costs in England relating to CVD are estimated at £7.4 billion, with an annual cost to the wider economy of £15.8 billion.

1.2. High cholesterol is one of the most significant risk factors for CVD. Too much bad cholesterol (non-HDL cholesterol) can be harmful because it sticks to the inside walls of the arteries. This can lead to fatty material (atheroma) building up - this process is known as atherosclerosis. It makes it harder for blood to flow through, which can lead to a heart attack or a stroke.

1.3. Raised cholesterol can also be caused by genetic conditions, where cholesterol is elevated from birth, such as Familial Hypercholesterolaemia (FH). FH affects approximately 1 in 300. If untreated, about 50% of men and 30% of women with FH will develop coronary heart disease by the time they are 55.

1.4. Encouraging healthy lifestyle changes such as improving diet, stopping smoking or reducing weight can help to lower cholesterol levels and reduce the risk of CVD. NICE guidelines advise offering lifestyle advice and statins to those people with high cholesterol and high CVD risk. NICE advise starting a high-dose statin in those who already have CVD.

1.5. Statin therapy reduce cholesterol and reduces risk of CVD events by around a quarter.

1.6. The estimated adult population across West Yorkshire and Harrogate with a greater than 2 in 10 chance of a future heart attack or stroke is 175,000. Of those, over half (89,250) aren't treated with a statin.

1.7. West Yorkshire and Harrogate Health Care Partnership (along with the nine CCGs) have developed a local treatment guidance and supporting information document for use in Primary Care; under the West Yorkshire and Harrogate Healthy Hearts project.

1.8. The project aims to identify and treat at least 10% of eligible adults (9000 people), aiming for an estimated 220 to 400 CVD events prevented over 5 years.

Sources:

- https://www.gov.uk/government/publications/health-matters-preventing-cardiovascular-disease/health-matters-preventing-cardiovascular-disease
- https://www.healthcheck.nhs.uk/commissioners-and-providers/data/size-of-the-prize-and-nhs-health-check-factsheet/

2. Rationale for the Local Clinical Guidance

2.1. Data from UK general practice shows that over half of patients on statins do not reach their NICE targets after 2 years of statin therapy.

2.2. Feedback from many GPs and nurses, in particular on phase one of Healthy Hearts (hypertension), has indicated that many liked the use of specific medicines and doses in a guidance since it streamlines the prescriber's approach.

2.3. Current NICE guidance was written in 2014 and is five years old. It is currently being reviewed and subject to changes.

2.4. In this Healthy Hearts programme across West Yorkshire, we want to improve care beyond current levels and we wish to maximise the impact of existing primary care resource, and maximising engagement of clinicians with a large-scale improvement programme.

Sources:

- https://www.nice.org.uk/guidance/cg181/resources/surveillance-report-2018-cardiovascular-disease-risk-assessment-and-reduction-including-lipid-modification-2014-nice-guideline-cg181-4724759773/chapter/Surveillance-decision?tab=evidence
- Akyea RK, et al. Heart 2019;105:975–981

3. What evidence base has been used in the local guidance

3.1. CTT evidence

Cholesterol Treatment Trialist's (CTT) collaborators 2009 - meta-analyses of mortality and morbidity from all relevant large-scale randomised trials of statin therapy. Findings were:

- Lipid lowering with statins confers similar CV risk reduction across all ranges of baseline dyslipidaemia
- Clinical benefit is related to the absolute reduction in LDL-C
- For secondary prevention, intensive therapy is safe and arrests atherosclerosis and provides further clinical benefit with CV risk reduction and hospitalisations for heart failure
- In acute coronary syndromes, high-dose statins provide a rapid early reduction in clinical events which may be related to non-LDL-C dependent anti-inflammatory effects

Further details of the CTT findings were:

- Data on 90,056 individuals from 14 trials were combined. Mean follow-up of 5 years
- Almost a half-million person years of observation
- Significant 12% reduction in all-cause mortality per 1mmol/l reduction in LDL- C
- 19% reduction in coronary mortality
- 24% reduction in the need for revascularisation
- 17% reduction in stroke
- 21% reduction in any major vascular event.

Importantly a similar proportional benefit was observed in different age groups, across genders, at different levels of baseline cholesterol/lipids (including triglycerides and high-density lipoprotein cholesterol) and equally among those with prior coronary artery disease (heart attacks, angina) and cardiovascular risk factors as in those without. This was important since it showed that relative risk reductions were equivalent in all patients studied.

Finally, the magnitude of clinical benefit in the CTT meta-analysis appeared related to the magnitude of LDL cholesterol reduction and is independent of the initial cholesterol/lipid readings or other baseline characteristics.

3.2. Safety

The safety data presented in CTT come from randomised control trials:

- Risk of rhabdomyolysis (serious muscle inflammation) was 3/100,000 person years
- Myopathy (muscle inflammation) was 11/100,000 person years
- Peripheral neuropathy (nerve damage) 12/100,000 person years
- Liver disease even rarer.

The authors conclude that side effects are rare and likely to be more common when drugs which block certain liver pathways (the CYP3A4 pathway) are given at the same time as statins.

3.3. NICE guidance

A review of NICE Clinical Guideline [CG181] Cardiovascular disease: risk assessment and reduction, including lipid modification has taken place (Appendix 1) The local guidance and supporting information that has been created makes only two small pragmatic changes to NICE guidance. These are as follows:

NICE: 1.3.18 Offer atorvastatin 20 mg for the primary prevention of CVD to people who have a 10% or greater 10year risk of developing CVD. Estimate the level of risk using the QRISK2 assessment tool. [new 2014]

Local Lipid guidance makes reference to usually starting people with 20mg and uptitrating to 40mg daily after two weeks since over half of patients will not achieve lipid targets and provides suggested alternative of 20mg in two scenarios 1) Dosage concerns 2) Potential sensitivity of those of Asian or Chinese heritage.

NICE 1.3.30 Discuss with people who are stable on a low or middle intensity statin the likely benefits and potential risks of changing to a high-intensity statin when they have a medication review and agree with the person whether a change is needed. [new 2014]

This cohort is not included in this guidance document: the searches that support the work have excluded people with reasonably controlled cholesterol. This is due to the reduced absolute benefit from interventions in the “managed/controlled groups” and we are also mindful of the aim to maximise the impact of existing primary care resource, and maximising engagement of clinicians with a large-scale improvement programme.

Statins are grouped in this guideline as seen in Table 36. This grouping was agreed by GDG consensus, informed by analyses in the literature. This grouping is discussed further in Section 11.8.

Table 36: Grouping of statins

	% reduction in low-density lipoprotein cholesterol				
Dose (mg/day)	**5**	**10**	**20**	**40**	**80**
Fluvastatin	10%[1]	15%[1]	21%[2]	27%[2]	33%[3]
Pravastatin	15%[1]	20%[2]	24%[2]	29%[2]	33%[1]
Simvastatin	23%[1]	27%[2]	32%[3]	37%[3]	42%[4*]
Atorvastatin	31%[1]	37%[3]	43%[4]	49%[4]	55%[4]
Rosuvastatin	38%[3]	43%[4]	48%[4]	53%[4]	58%[1]

It is noted that NICE classifies atorvastatin 20mg as high intensity whilst European Society of Cardiology lipid guidance classifies atorvastatin 20mg as weaker medium intensity and atorvastatin 40mg as high intensity. Both guidelines agree that treatment with statins should usually be "high intensity" not lower.

Regarding the choice of atorvastatin dose for primary prevention, NICE state that:

The base case analysis was based on an assumption of equivalent effectiveness between all high-intensity statins, due to a lack of evidence comparing the effectiveness of the different doses within the high-intensity class in terms of reducing clinical end points, although there is evidence of differing effectiveness of different doses in terms of reducing LDL-cholesterol levels. On this basis the cheapest high-intensity statin – atorvastatin 20 mg – was predicted to be the most cost effective. However, an additional threshold analysis showed that atorvastatin 40 mg would be cost effective compared to atorvastatin 20 mg if it was 1% relatively more effective in decreasing CV events than atorvastatin 20 mg and if there was no loss in utility due to increases in adverse events. It also showed that atorvastatin 80 mg would be cost effective compared to atorvastatin 20 mg if it was 2% relatively more effective than atorvastatin 20 mg in decreasing CV events and if there was no loss in utility due to increases in adverse events.

4. Conclusion

NICE recognises that primary care has limited capacity and lowering the QRISK2 threshold to include 10-20% has resulted in an extra 4.5 million people in the UK becoming eligible for statins and lifestyle advice. To fully implement NICE guidance for lipids across the WY&H population using traditional implementation methods would require hundreds of thousands of extra appointments. Current treatment with statins in primary care results in more than half of patients failing to reach NICE cholesterol targets. Local HCP guidance seeks to maximise the impact of existing primary care resource, to build on feedback from clinicians about previous HCP guidelines, and to maximise engagement of clinicians with a large-scale improvement programme.

5. Guidance Adoption / Shared Decision Making

It is noted that no guidance should be expected to be mandatory for all patients at all times: if clinically needed, flexibility can and should continue to be used by primary care clinicians at each treatment step, as would be expected as standard for all aspects of medical care. A local guidance is simply proposed as a facilitator to quality improvement within a healthcare system that has limited capacity for extra workload.

As is standard practice, informed decision making remains the norm and multiple sources of information can help this: localities will be supported and encouraged to use services such as:

- West Yorkshire and Harrogate Healthy Hearts website
- local community pharmacy services
- *me +my medicines* .

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Appendix 1 Key Points of alignment with NICE Clinical Guideline [CG181]

This document outlines the key points of alignment between West Yorkshire and Harrogate Healthy Hearts – Lipid Guidance and NICE Clinical Guideline [CG181].
Cardiovascular disease: risk assessment and reduction, including lipid modification. Clinical guideline [CG181] Published date: July 2014 Last updated: September 2016
https://www.nice.org.uk/guidance/cg181

1.1 Identifying and assessing cardiovascular disease (CVD) risk

Full formal risk assessment

1.1.8 Use the QRISK2 risk assessment tool to assess CVD risk for the primary prevention of CVD in people up to and including age 84 years. **[new 2014]**

Included in Lipid guidance document

1.2 Lifestyle modifications for the primary and secondary prevention of CVD

West Yorkshire and Harrogate Healthy Hearts website has links to cholesterol and lifestyle information

1.3 Lipid modification therapy for the primary and secondary prevention of CVD

1.3.18 Offer atorvastatin 20 mg for the primary prevention of CVD to people who have a 10% or greater 10year risk of developing CVD. Estimate the level of risk using the QRISK2 assessment tool. **[new 2014]**

Local Lipid guidance makes reference to usually starting people with 40mg but provides suggested alternative of 20mg in two scenarios: 1) Dosage concerns; 2) Potential sensitivity of those of Asian or Chinese heritage.

1.3.19 For people 85 years or older consider atorvastatin 20 mg as statins may be of benefit in reducing the risk of non-fatal myocardial infarction. Be aware of factors that may make treatment inappropriate (see recommendation 1.3.12). **[new 2014]**

Local lipid guidance aimed at <85 years – but supporting information has made reference to this recommendation.

1.3.2 When a decision is made to prescribe a statin, use a statin of high intensity[5] and low acquisition cost. **[new 2014]**

Lipid guidance makes reference to high intensity statins. Note – proposed switch of Simvastatin to Atorvastatin is consistent with NICE as only 80mg Simvastatin is considered as a high intensity statin by some guidelines but other data shows that 80mg of simvastatin is no more clinically effective in routine care than 40mg but has increased risk of side effects, hence resulting in the following MHRA warning:

Advice from the MHRA (The Medicines and Healthcare products Regulatory Agency) there is an increased risk of myopathy (muscle weakness) associated with high dose (80 mg) simvastatin. The 80 mg dose should be considered only in patients with severe

hypercholesterolaemia and high risk of cardiovascular complications who have not achieved their treatment goals on lower doses, when the benefits are expected to outweigh the potential risks.
https://www.nice.org.uk/guidance/cg181/chapter/appendix-a-grouping-of-statins

Lipid measurement and referral

1.3.4 Before starting lipid modification therapy for the primary prevention of CVD, take at least 1 lipid sample to measure a full lipid profile. This should include measurement of total cholesterol, HDL cholesterol, non-HDL cholesterol and triglyceride concentrations. A fasting sample is not needed. **[new 2014]**

Included in lipid guidance document

1.3.7 Consider the possibility of familial hypercholesterolaemia and investigate as described in familial hypercholesterolaemia (NICE guideline CG71) if they have:
- a total cholesterol concentration more than 7.5 mmol/litre **and**
- a family history of premature coronary heart disease. **[new 2014]**

1.3.8 Arrange for specialist assessment of people with a total cholesterol concentration of more than 9.0 mmol/litre or a non-HDL cholesterol concentration of more than 7.5 mmol/litre even in the absence of a first-degree family history of premature coronary heart disease. **[new 2014]**

1.3.9 Refer for urgent specialist review if a person has a triglyceride concentration of more than 20 mmol/litre that is not a result of excess alcohol or poor glycaemic control. **[new 2014]**

1.3.10 In people with a triglyceride concentration between 10 and 20 mmol/litre:
- repeat the triglyceride measurement with a fasting test (after an interval of 5 days, but within 2 weeks) **and**
- review for potential secondary causes of hyperlipidaemia **and**
- seek specialist advice if the triglyceride concentration remains above 10 mmol/litre. **[new 2014]**

1.3.11 In people with a triglyceride concentration between 4.5 and 9.9 mmol/litre:
- seek specialist advice if non-HDL cholesterol concentration is more than 7.5 mmol/litre. **[new 2014]**

FH / Specialist Lipid Pathway provides advice on referring to special lipid clinic in these scenarios

Primary prevention

1.3.14 Before offering statin treatment for primary prevention, discuss the benefits of lifestyle modification and optimise the management of all other modifiable CVD risk factors if possible. **[new 2014]**

1.3.15 Recognise that people may need support to change their lifestyle. To help them do this, refer them to programmes such as exercise referral schemes. (See the NICE guidelines on behaviour change: individual approaches and physical activity: exercise referral schemes.) **[new 2014]**

Included in Lipid Treatment Guidance and Behaviour change principles document

Follow up of people started on statin treatment

1.3.28 Measure total cholesterol, HDL cholesterol and non-HDL cholesterol in all people who have been started on high-intensity statin treatment (both primary and secondary prevention, including atorvastatin 20 mg for primary prevention) at 3 months of treatment and aim for a greater than 40% reduction in non-HDL cholesterol. If a greater than 40% reduction in non-HDL cholesterol is not achieved:

- discuss adherence and timing of dose
- optimise adherence to diet and lifestyle measures
- consider increasing the dose if started on less than atorvastatin 80 mg and the person is judged to be at higher risk because of comorbidities, risk score or using clinical judgement. **[new 2014]**

Included in Lipid Treatment Guidance and supporting information.

1.3.29 Provide annual medication reviews for people taking statins.

- Use these reviews to discuss medicines adherence and lifestyle modification and address CVD risk factors.
- Consider an annual non-fasting blood test for non-HDL cholesterol to inform the discussion. **[new 2014]**

Two points above not referenced in supporting information document.

1.3.30 Discuss with people who are stable on a low or middle intensity statin the likely benefits and potential risks of changing to a high-intensity statin when they have a medication review and agree with the person whether a change is needed. **[new 2014]**

Not include in guidance document. Searches have excluded people with managed/reasonably controlled cholesterol. This is to maximise the impact of existing primary care resource, and maximising engagement of clinicians with a large-scale improvement programme.

Advice and monitoring for adverse effects

1.3.31 Advise people who are being treated with a statin:

- that other drugs, some foods (for example, grapefruit juice) and some supplements may interfere with statins **and**
- to always consult the patient information leaflet, a pharmacist or prescriber for advice when starting other drugs or thinking about taking supplements. **[new 2014]**

Not included in guidance but support information on website will cover these areas.

Intolerance of statins

1.3.41 If a person is not able to tolerate a high-intensity statin aim to treat with the maximum tolerated dose. **[new 2014]**

1.3.42 Tell the person that any statin at any dose reduces CVD risk. If someone reports adverse effects when taking high-intensity statin discuss the following possible strategies with them:

- stopping the statin and trying again when the symptoms have resolved to check if the symptoms are related to the statin
- reducing the dose within the same intensity group
- changing the statin to a lower intensity group. **[new 2014]**

1.3.43 Seek specialist advice about options for treating people at high risk of CVD such as those with CKD, type 1 diabetes, type 2 diabetes or genetic dyslipidaemias, and those with CVD, who are intolerant to 3 different statins. Advice can be sought for example, by telephone, virtual clinic or referral. **[new 2014]**

Included in Lipid Guidance