



Diabetes: Lipids



1. Background information

- People with type 2 diabetes (T2D) are nearly 2.5 times more likely to have a heart attack, more than 2.5 times as likely to experience heart failure and 2 times as likely to have a stroke.¹
- Cardiovascular disease (CVD) remains the leading cause of death and disability in people with T2D.²



Guidelines

NICE NG28: *Type 2 diabetes in adults: Management* was published in 2015 and last updated in August 2019.³ It signposts to the recommendations in NICE CG181 *Cardiovascular disease: risk assessment and reduction*, including lipid modification for the diagnosis and management of dyslipidaemia in people with T2D.⁴

In 2019, the European Society of Cardiology (ESC) published new guidelines covering diabetes, people at high risk of T2D and CVD in collaboration with the European Association for the Study of Diabetes (EASD).⁵

2. Definitions

- Primary prevention of CVD: interventions that aim to prevent or delay the onset of CVD in people with no clinical evidence of CVD.
- Secondary prevention of CVD: interventions that aim to reduce the impact and prevent the progression of the disease in people with established CVD (e.g. angina, peripheral vascular disease, previous myocardial infarction or stroke).

3. Process



Determining CV risk⁴

- Obtain an initial non-fasting full lipid profile (total cholesterol [TC], high-density lipoprotein [HDL] cholesterol [C], non-HDL-C and triglycerides [TG]).
- Check smoking status, alcohol consumption, blood pressure, BMI, HbA_{1c}, renal function and estimated glomerular filtration rate (eGFR), transaminase levels, thyroid-stimulating hormone.

1. Review non-HDL-C (TC minus HDL-C)

- >7.5 mmol/l: **Consider performing CV risk assessment***
- >7.5 mmol/l: **Refer for specialist advice**

2. Review TC

- <7.5 mmol/l: Review non-HDL-C
- >7.5 mmol/l: Consider familial hypercholesterolaemia (refer to lipids clinic)
- >9 mmol/l: **Refer for specialist advice**



3. Review TG⁴

- <10 mmol/l: Review non-HDL-C and if >7.5 mmol/l refer for specialist opinion otherwise perform CV risk assessment
- 10–20 mmol/l: Repeat with fasted full lipid profile (TG, HDL-C and TG) 5–14 days later.
 - TG <10 mmol/l: Perform CV risk assessment
 - TG >10 mmol/l: **Refer for specialist advice**

Remember to identify and manage remedial causes of elevated lipids (e.g. poor glycaemic control or excess alcohol intake if elevated TGs).

*CV risk assessment tools

- Use the QRISK risk assessment tool to assess CV risk for primary prevention of CVD (up to age 84 years). NICE CG181 recommends QRisk to calculate CV risk⁴
- The JBS3 risk assessment tool offers some additional features, such as explaining life years gained by modifying risk factors⁶

4. Lipid targets



NICE CG181 recommended targets:

- **Aim for a >40% reduction in non-HDL-C⁴**

The 2019–20 QOF total cholesterol target ≤5 mmol/l was removed and replaced with the following indicators:⁷

- The percentage of patients with diabetes aged 40 years and over, with no history of CVD and without moderate or severe frailty, who are currently treated with a statin (excluding patients with T2D and CVD risk score of <10% recorded in the preceding 3 years) and,
- The percentage of patients with diabetes and a history of cardiovascular disease (excluding haemorrhagic stroke) who are currently treated with a statin.

The total cholesterol treatment target of <5 mmol/l is adopted within the National Diabetes Audit.⁸

The ESC (2019) recommended targets in T2D with:⁵

- Moderate CV risk: **LDL-C target of <2.6 mmol/l**
- High CV risk: **LDL-C target of <1.8 mmol/l** and LDL-C reduction of at least 50% with secondary goal of a **non-HDL-C target of <2.6 mmol/l**
- Very high CV risk: **LDL-C target of <1.4 mmol/l** and LDL-C reduction of at least 50% with secondary goal of a **non-HDL-C target of <2.2 mmol/l**

The typical lipid profile accompanying diabetes is a moderate elevation of fasting and non-fasting triglycerides, and low HDL-C. Another feature is normal-to-mildly elevated levels of low density lipoprotein cholesterol (LDL-C), with small dense LDL particles.⁵

5. Treatment/management



Offer advice on:⁴

- Alcohol consumption (moderate alcohol intake should not be promoted).
- Healthy eating (Mediterranean diet); the ideal amount of dietary fats remain controversial.⁵
- Weight management (reduced calorie intake).
- Smoking cessation.
- Physical activity (moderate to vigorous activity >150 min/week).
- Moderate-to-vigorous physical activity of ≥150 min/week is recommended for the prevention and control of diabetes.

In those with pre-existing CVD:⁴

- Do not delay offering high intensity statin therapy (atorvastatin 80 mg).
- Use a lower dose of atorvastatin or switch to a different statin if:
 - Potential drug interactions.
 - High risk of adverse effects.
 - Patient preference.

The key message from the ESC (2019) guideline is that statins effectively prevent CV events and reduce CV mortality.⁵



Given the high CV risk profile The Joint British Societies for the prevention of cardiovascular disease recommend statin therapy for all people with T2D above the age of 40 years irrespective of cholesterol level and also considered in those under 40 with evidence of persistent albuminuria, eGFR <60 ml/min, proliferative retinopathy, treated hypertension, or autonomic neuropathy.⁶

- Currently NICE recommend offering atorvastatin 20 mg for those whose CV risk score is ≥10%.⁴
- Check liver transaminase levels prior to starting statin therapy.⁴
- Do NOT routinely exclude from statin therapy people who have liver transaminase levels that are raised but are <3 times the upper limit of normal.⁴



Statin are contraindicated in pregnancy and MUST be avoided in women of childbearing potential. Advise women of childbearing potential of the teratogenic risk of statins. Stop statins 3 months prior to conception and do not restart until breastfeeding is complete.⁴

At 3-month review:⁴

- Discuss adherence and review tolerability.

Evidence indicates that most patients (70–90%) who report statin intolerance are able to take a statin when challenged.^{9,10}

Evidence supports a lower rate of side effects with low dose rosuvastatin or pravastatin.⁵

If person reports adverse effects when taking statins consider:

- Stopping the statin and then restarting it to assess if it is the true cause of symptoms.
- Reduce the dose or switch to a different statin.

- Optimise adherence to diet and lifestyle measures.

- Measure TC, HDL-C, non-HDL-C aiming for a greater than 40% reduction in non-HDL-C.

- Consider increasing dose of statin where target is not met.
- Measure liver transaminase enzymes (alanine aminotransferase or aspartate aminotransferase) within 3 months of starting treatment and at 12 months, but not again unless clinically indicated. No need to stop statin providing <3 times the upper limit of normal.
- Do NOT measure creatinine kinase levels in asymptomatic people who are being treated with a statin.

6. Ongoing monitoring



NICE CG181 recommends an annual review for all people on statins.⁴ An approach in which statins are simply prescribed and the cholesterol lowering effect is NOT checked (sometimes referred to as “fire and forget”) has previously been adopted.

A cholesterol measurement is one of the nine annual care processes recommended by NICE and measured within the National Diabetes Audit.⁸

Fibrates: can be considered in certain circumstances^{4,5}
 Ezetimibe: can be considered in certain circumstances^{4,5}



References

1. Diabetes UK (2019) *Us, diabetes and a lot of facts and stats*. Available at: https://www.diabetes.org.uk/resources-s3/2019-02/1362B_Facts%20and%20stats%20Update%20Jan%202019_LOW%20RES_EXTERNAL.pdf [Accessed March 2020].
2. International Diabetes Federation (2014) *Diabetes and cardiovascular disease*. Available at: www.idf.org/cvd [Accessed March 2020].
3. National Institute for Health and Care Excellence (2015) *Type 2 Diabetes in Adults: Management*. Available at: <https://www.nice.org.uk/guidance/ng28> [Accessed March 2020].
4. National Institute for Health and Care Excellence (2014) *Cardiovascular disease: risk assessment and reduction, including lipid modification*. Available at: www.nice.org.uk/guidance/cg181 [Accessed March 2020].
5. Cosentino F et al (2020) *Eur Heart J* 41:255-323.
6. JBS3 (2014) *Heart* 100:ii1-ii67.
7. NHS England (2019) *2019/20 General Medical Services (GMS) contract Quality and Outcomes Framework (QOF)*. Available at: <https://www.england.nhs.uk/wp-content/uploads/2019/05/gms-contract-qof-guidance-april-2019.pdf> [Accessed March 2020].
8. NHS Digital (2019) *National Diabetes Audit, 2017-18 Report 1: Care processes and treatment targets*. Available at: <https://digital.nhs.uk/data-and-information/publications/statistical/national-diabetes-audit/report-1-care-processes-and-treatment-targets-2017-18-full-report> [Accessed March 2020].
9. Mampuya WM et al (2013) *Am Heart J* 166:597-603.
10. Zhang H et al (2013) *Ann Intern Med* 158:526-34.