

2023 ESC guidelines on cardiovascular disease in patients with type 2 diabetes

The 2023 update of the European Society for Cardiology guidelines for the management of cardiovascular disease (CVD) in patients with diabetes incorporates significant new evidence that has emerged from cardiovascular outcome trials and cardiorenal studies since the previous version was published in 2019. Since there is lack of clear evidence on managing CVD in those with prediabetes, this section has been removed. The guideline is comprehensive and covers lifestyle, glycaemic targets, and blood pressure and lipid management, including recommending a multifactorial approach with a focus on person-centred care. Shared decision-making, personalised treatment plans and a multidisciplinary approach are recommended to optimise prognosis and health-related quality of life. There are sections on CVD screening; cardiovascular risk stratification; diagnosis and management of those with atherosclerotic CVD; target end-organ damage; heart failure; chronic kidney disease; arrhythmias including atrial fibrillation, ventricular arrhythmias and sudden cardiac death; aortic and peripheral arterial disease; and type 1 diabetes. For individuals without atherosclerotic CVD or severe target-organ damage, a novel 10-year cardiovascular risk score specific to type 2 diabetes, SCORE2-Diabetes, is introduced. The guideline recommends choosing drugs with cardiovascular benefits proven in cardiovascular and cardiorenal outcome trials, using drugs with proven cardiovascular safety, and switching away from glucose-lowering drugs which do not have proven cardiovascular efficacy or safety. The guideline has been developed by a multidisciplinary expert team to ensure all aspects of care are included.

The updated European Society for Cardiology (ESC) guidelines for the management of cardiovascular disease (CVD) in patients with diabetes 2023 incorporate significant new evidence that has emerged from cardiovascular outcome trials (CVOTs) and cardiorenal studies since the previous version was published in 2019. The guideline committee has made new recommendations, revised some existing recommendations and introduced some reviewed concepts. Some of these are outlined here. New recommendations for lipid lowering and antithrombotic therapy are not discussed. The full guideline, along with presentations from the ESC conference and downloadable resources, are open-access and [can be obtained here](#).

The recommendations fall into three categories:

- Class I, generally accepted as beneficial (“is recommended” or “is indicated”).

- Class II, where there is some disagreement (IIa = “should be considered” and IIb [where usefulness or efficacy is less] = “may be considered”).

- Class III, where there is agreement that treatment is not effective/useful or may be harmful (“is not recommended”).

Levels of evidence vary from A, based on multiple randomised controlled trials or meta-analyses; through B, single randomised or several non-randomised trials; to C, expert consensus opinion, small or retrospective studies, or registries. These are similar to other guidelines.

Diagnosis of CVD

Undetected type 2 diabetes is common in people presenting with CVD, so the guideline recommends screening everyone with CVD, including those presenting with an acute event, for type 2 diabetes. Likewise, regular review for



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CVD, heart failure and chronic kidney disease is recommended for people with type 2 diabetes.

People without symptomatic atherosclerotic CVD (ASCVD) or severe target end-organ damage (see below) should have their 10-year CVD risk evaluated using the new SCORE2-Diabetes risk calculator (Figure 1). This was developed from the SCORE2 calculator by adding age at diabetes diagnosis, HbA_{1c} and eGFR, and recalibrates risk according to CVD incidence in four European risk regions (the UK is considered a low-risk region). It was adapted using data from seven countries, including the SCI-Diabetes, CPRD and UK Biobank databases (SCORE2-Diabetes Working Group and ESC Cardiovascular Risk Collaboration, 2023).

As with the QRISK calculator used in NICE NG28, a 10-year risk of ≥10% is designated significant. Target end-organ damage (TOD) is defined as any one of the following:

- eGFR <45 mL/min/1.73 m² irrespective of albuminuria.
- eGFR 45–59 mL/min/1.73 m² and microalbuminuria (uACR 3–30 mg/mmol; stage A2).
- Proteinuria (uACR >30 mg/mmol; stage A3).
- Presence of microvascular disease in at least three different sites (e.g. microalbuminuria [stage A2] plus retinopathy plus neuropathy).

These conditions are classified as an ASCVD equivalent and, therefore, are recommended to

be managed in the same way as ASCVD, whereas other risk factor profiles behaved differently in CVOTs and, thus, warrant different management.

Lifestyle interventions

Adopting a Mediterranean diet or plant-based diet with high unsaturated fat content is recommended to lower cardiovascular risk. Weight reduction is recommended for those with overweight and obesity, and glucose-lowering drugs which assist with this are recommended, along with bariatric surgery for those at high and very high CVD risk with BMI ≥35 kg/m² when lifestyle and drug therapy do not result in maintained weight loss.

Increased physical activity, adapted to type 2 diabetes-associated comorbidities such as retinopathy, neuropathy and frailty, is recommended, along with structured exercise training for those with CVD, heart failure or atrial fibrillation to improve metabolic control, exercise capacity and quality of life, and to reduce overall CVD risk. Behavioural theory interventions such as goal-setting, self-monitoring and use of wearable activity trackers should be considered to assist with physical activity. Counselling and pharmacological support are recommended to increase smoking cessation.

ASCVD and/or target end-organ damage

In those with symptomatic ASCVD and/or TOD, treatment with **both** a GLP-1 RA and

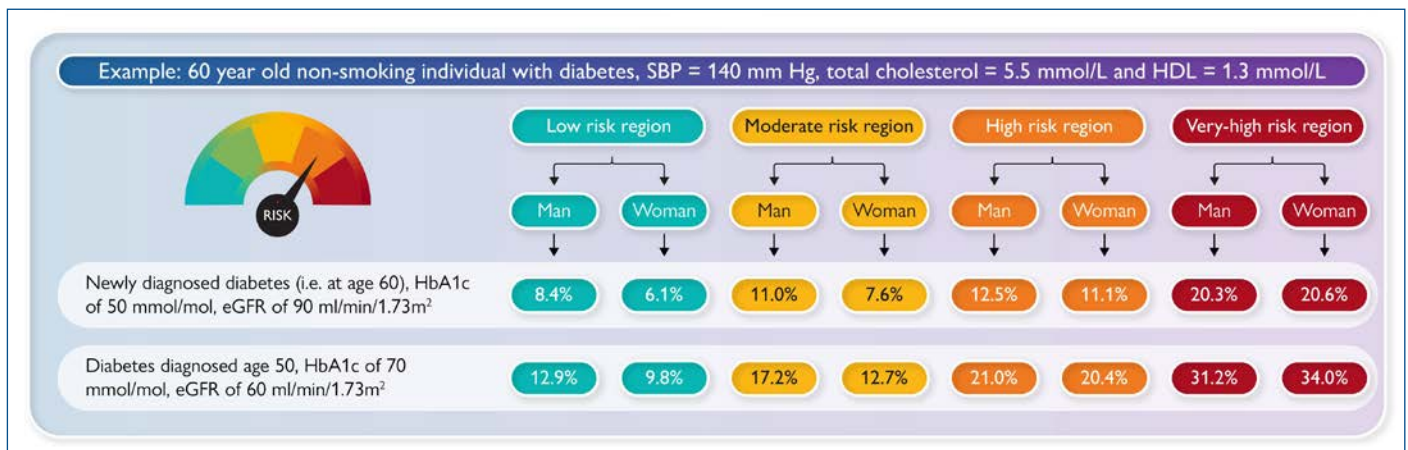


Figure 1. Illustrative example of the SCORE2-Diabetes 10-year CVD risk model.

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SGLT2 inhibitor with CVOT evidence of cardiovascular benefit is recommended, independent of HbA_{1c} and other current glucose-lowering medications. The guideline differs from some other guidelines such as NICE NG28 by making different recommendations for those with ASCVD (and those with TOD) and those at high risk of ASCVD, based on evidence from sub-group analyses of the CVOTs and cardiorenal studies such as CREDENCE, which demonstrated cardiovascular risk reduction in people with established ASCVD and renal disease but not in those with risk factors alone.

When additional glucose-lowering is required in those with ASCVD and/or TOD, metformin is recommended first-line, and pioglitazone may be offered in those who are suitable, as this drug has demonstrated statistically significant reductions in cardiovascular death, myocardial infarction and stroke in meta-analyses. Although there is a 32% increase in relative risk of heart failure in those treated with pioglitazone, this translates into a low absolute risk increase of 0.4%, with only one extra incidence of heart failure for every 250 people treated for 1 year. Heart failure with pioglitazone is due to plasma volume expansion rather than cardiac toxicity or structural changes, so the expert group felt this could be managed.

For additional glucose-lowering, the guideline recommends use of drugs with proven cardiovascular safety in CVOTs, and people should be switched away from drugs without this confirmed benefit or safety.

Based on expert consensus opinion, in people without ASCVD or TOD, but with $\geq 10\%$ CVD risk using the SCORE2-Diabetes calculator (high or very high risk), an SGLT2 inhibitor or GLP-1 RA may be considered to reduce cardiovascular risk. Metformin may also be considered to reduce cardiovascular risk both in those at low or moderate risk (calculated risk $< 10\%$) and in those at high and very high risk ($\geq 10\%$).

Based on evidence, the guideline recommends that aspirin 75–100 mg may be considered for primary prevention in those with type 2 diabetes without any contraindications (high risk of gastrointestinal bleeding or peptic ulcer within

the preceding 6 months, active hepatic disease or history of aspirin allergy). Proton pump inhibitors are recommended when combination anti-thrombotic drugs are used, and should be considered when single drugs are used, to reduce gastrointestinal bleeding. Full recommendations for anti-thrombotic therapies for different scenarios are included in the guideline.

Heart failure

Since heart failure risk is increased in those with diabetes, clinicians are recommended to assess for signs and symptoms of heart failure at each clinical encounter and, if found, check NT-proBNP or BNP levels; if these are elevated, arrange an echocardiogram to confirm and identify the type of heart failure. Those with confirmed heart failure (all types) should receive an SGLT2 inhibitor (dapagliflozin, empagliflozin or sotagliflozin, the latter of which is not available in the UK). Those with reduced ejection fraction (HFrEF) should receive an ACE inhibitor or sacubitril/valsartan, a beta-blocker and an MRA to reduce risk of hospitalisation for heart failure (HHF) and cardiovascular death. Additional drug therapies are recommended for some groups. Rapid initiation and uptitration to the target doses used in clinical trials is recommended for all four classes of drugs. Diuretics are also recommended both for those with HFrEF and for those with an ejection fraction of $> 40\%$ when there is evidence of excess fluid.

If additional glucose-lowering is needed in those with heart failure, GLP-1 RAs, DPP-4 inhibitors (sitagliptin or linagliptin), metformin, or insulin glargine or degludec should be considered, as these have a neutral effect on heart failure risk. Pioglitazone and saxagliptin are not recommended in those with or at risk of heart failure, as they increase the risk of HHF. As with other CVD, those with heart failure should be switched away from glucose-lowering drugs without proven cardiovascular benefit or safety.

Atrial fibrillation

As people with diabetes have an increased risk of atrial fibrillation at a younger age, the guidance has changed to include opportunistically



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screening people with diabetes, both under and over the age of 65, for AF by pulse check or ECG.

Chronic kidney disease

People with diabetes should be regularly screened for chronic kidney disease (CKD) using both eGFR, as a measure of function, and uACR, as a measure of kidney damage. Per KDIGO classification, an eGFR <60 mL/min/1.73 m² and/or a uACR ≥3 mg/mmol persisting for at least 3 months is diagnostic of CKD.

For those with type 2 diabetes and CKD, the dual aim is to reduce the risk of both cardiovascular events and to slow the progression of CKD. Significant changes to the recommendations are due to stronger evidence of the benefits of SGLT2 inhibitors even at a low eGFR, the effects of finerenone in people with albuminuria, the emphasis on glucose-lowering agents which reduce risks and a strong recommendation to treat CKD early.

The first line of treatment to prevent CVD is a statin or statin/ezetimibe combination to lower LDL cholesterol, and the first line for renal protection is an ACE inhibitor/ARB titrated to the trial-evidenced dose. Use of the combination of an ACE inhibitor and ARB is contraindicated due to risk of hyperkalaemia and acute kidney injury in studies.

Then, to achieve both goals, addition of a renoprotective SGLT2 inhibitor, blood pressure control to ≤130/80 mmHg, and finerenone if eGFR is >60 mL/min/1.73 m² and ACR ≥30 mg/mmol, or if eGFR is 25–60 and ACR ≥3 mg/mmol, are recommended. Individualised

HbA_{1c} targets of 48–64 mmol/mol are recommended, with a target of <53 mmol/mol to reduce microvascular complications when possible. A GLP-1 RA is recommended if eGFR is >15, to achieve glycaemic control and confer beneficial effects on weight, cardiovascular risk and albuminuria.

Concluding remarks

These guidelines differ from NICE NG28 and the ADA/EASD guidance on glycaemic management, and the current shortage of GLP-1 RAs makes it impossible to fully implement the management recommendations for those with ASCVD or TOD. However, the ESC guideline provides an updated evidence base for each of the recommendations, and this will be useful to us as we re-evaluate our practice. The new combined GLP-1/GIP receptor agonist tirzepatide is not included in the guidance, and evidence of benefits for CVD and CKD continues to evolve. ■

SCORE2-Diabetes Working Group and ESC Cardiovascular Risk Collaboration (2023) SCORE2-Diabetes: 10-year cardiovascular risk estimation in type 2 diabetes in Europe. *Eur Heart J* **44:** 2544–56

2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes

The full guidelines, along with resources such as slide sets and the ESC Pocket Guidelines App, is available online.

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