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# Personalised cardiovascular disease prevention in the new guidelines

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## PERSPECTIVES

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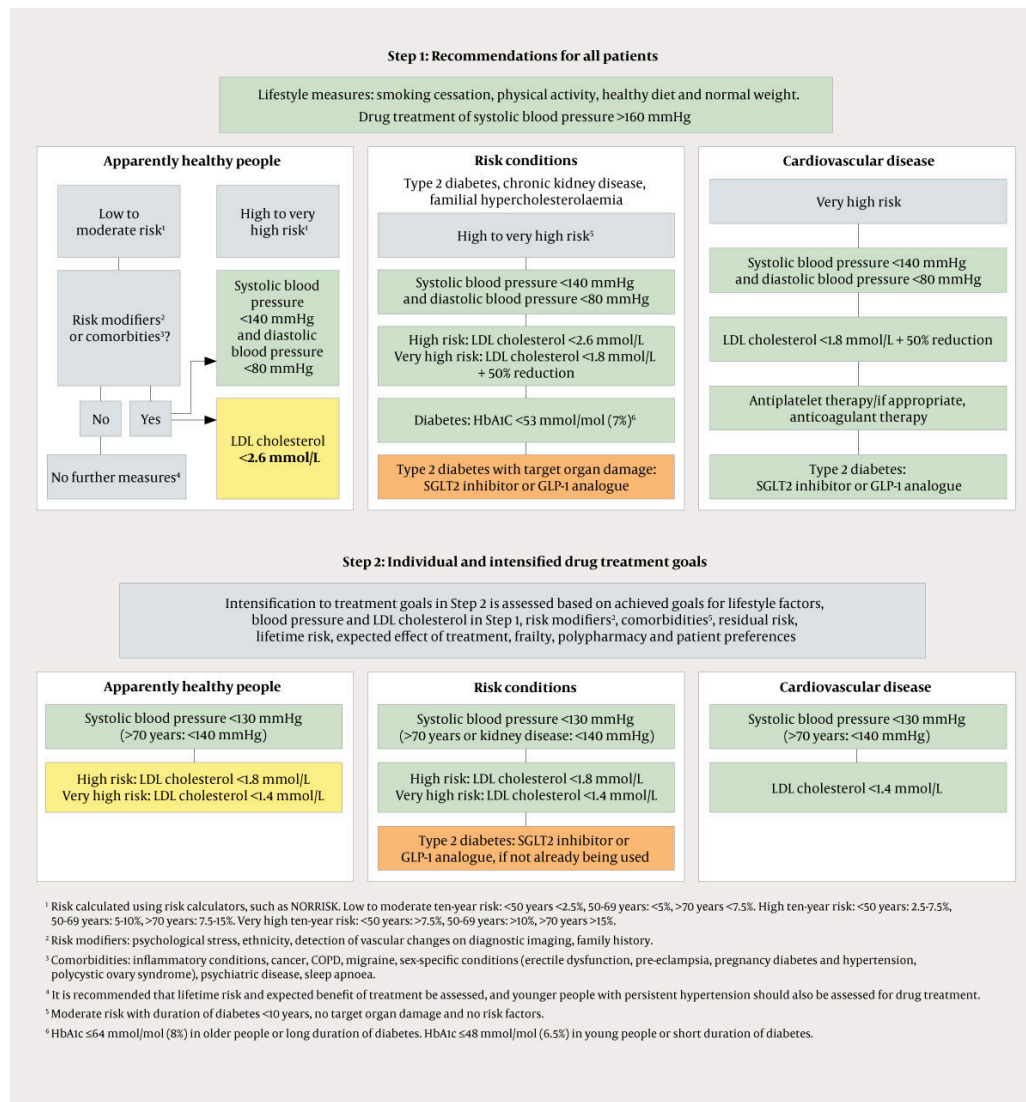
**The new European Guidelines for cardiovascular disease prevention have introduced a stepwise approach with lifestyle measures at the core. The use of drug treatment is recommended based on a risk assessment also taking into consideration the patient's frailty, comorbidities and own preferences.**



Illustration: Espen Friberg

New lipid-lowering, anticoagulant and antidiabetic drugs, as well as guidelines with constantly changing treatment goals, have made the prevention of cardiovascular disease more complex (1). Data from Norway and Europe have also revealed that many patients do not achieve the recommended treatment goals for cardiovascular risk factors (2–4). The large gap between recommended treatment goals and what is actually possible for most patients to achieve is unfortunate and may undermine confidence in the guidelines. This has been taken into consideration in the new European Guidelines for cardiovascular disease prevention published in 2021.

The guidelines have introduced a new two-step model (Figure 1). Step 1 applies to all patients, while the intensified treatment goals in Step 2 are recommended following an individual assessment of residual risk, estimated based on the extent to which the patient has managed to achieve the Step 1 goals. Frailty, comorbidities and risk factors, as well as the patient's own wishes and needs, will also be considered in the assessment.



**Figure 1** Risk classification and overview of treatment goals in the new guidelines (1). Green = class I recommendation, yellow = class IIa recommendation, orange = class IIb recommendation.

*«The two-step model is strongly recommended in the new European guidelines»*

The two-step model is strongly recommended in the new European Guidelines (1). The benefit of intensified treatment is greatest in those at highest risk and more marginal in those at lower risk. Thus, if the treatment goals for Step 1 can be achieved in the vast majority of patients, this will constitute an important improvement. There is a lack of data from randomised studies regarding a stepwise approach to blood pressure and cholesterol. There is, however, good evidence that stepwise treatment of diabetes can be just as effective as starting intensive treatment straightaway and also produces fewer adverse effects and

improved patient satisfaction (5). This 'Perspectives' article summarises key new concepts and recommendations in the new guidelines, along with practical advice adapted to the situation in Norway.

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## Individual assessment

An overview of risk classification and treatment goals in the new guidelines is illustrated in Figure 1. In both steps, the recommendations are based on the patient's risk of having a cardiovascular event in the next ten years. Patients can be divided into the following groups according to risk level: 1) apparently healthy, 2) patients with risk conditions such as type 2 diabetes, familial hypercholesterolaemia and chronic kidney disease and 3) patients with established cardiovascular disease. Patients with a risk condition or known cardiovascular disease are defined as having a high or very high risk. The exception is patients who have had diabetes for <10 years and have no other risk factors. These patients have a moderate risk. For the apparently healthy group, it is recommended that individual risk be calculated in all those who have at least one cardiovascular risk factor or cardiovascular disease in the family (1).

*«The guidelines now take account of this by differentiating risk level for treatment depending on age»*

The new guidelines recommend the use of European risk calculators developed for countries with low (Norway), moderate, high and very high risk of cardiovascular disease. In Norway, the risk calculator NORRISK 2 is validated and suitable for calculating individual risk in patients without cardiovascular disease. It is also similar to the European risk calculator. Risk increases with age. Younger people (men <40 years, women <50 years) will nearly always have a low ten-year risk, while patients > 70 years tend to have a high risk. At the same time, younger patients with multiple risk factors have a high *lifetime* risk. The guidelines now take this into account by differentiating risk level for treatment depending on age. This reduces the risk of overtreatment in the oldest patients and undertreatment in the youngest.

In the overall assessment, it is also recommended that risk modifiers such as ethnicity, family history and mental and somatic comorbidities should be taken into account (Figure 1). Furthermore, it is recommended that more caution be exercised in the treatment of patients with frailty and polypharmacy than the risk itself would suggest. Last, but not least, it is recommended that the patient's own preferences be taken into consideration. Ideally, a joint decision should be made about treatment level following an informed discussion between patient and doctor, also known as shared decision-making.

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## Step 1

Step 1 consists of recommendations that apply to everyone.

### **Lifestyle changes**

Lifestyle recommendations such as complete cessation of smoking, physical activity, normal weight and healthy diet apply to everyone, regardless of risk level and age (Figure 1). Smokers should be offered drug-assisted smoking cessation, in practice a combination of short-acting and long-acting nicotine replacement. Complete cessation of smoking is recommended regardless of the amount of weight gain.

Recommended levels of physical activity have increased from 150 minutes to 300 minutes of moderate intensity or from 75 minutes to 150 minutes of vigorous intensity per week, and there is a new recommendation that resistance training be performed at least twice a week. The importance of reducing sedentary behaviour is stressed.

The dietary advice is mainly in line with Norwegian guidelines. It is important to limit the intake of salt, saturated fat, sugar, processed food and meat, to consume fish regularly and increase the consumption of 'Mediterranean foods', fibre, pulses, nuts, fruit and vegetables. The maximum recommended consumption of alcohol should not exceed 100 g per week (equivalent to an average of no more than one unit of alcohol daily), which is a reduction compared to the previous guidelines. The recommendation to maintain a normal weight, or to lose weight if overweight, remains unchanged, but it is specified that the dietary advice applies even if other diets could result in weight loss.

### **Drug treatment depending on risk**

In Step 1, drug treatment is recommended in patients with systolic blood pressure  $\geq 160$  mmHg with a treatment goal of  $<140/80$  mmHg, irrespective of other risk. In principle, the Step 1 recommendations stop here for apparently healthy people with low and moderate risk without risk modifiers. Nonetheless, it is recommended that the lifetime risk and estimated benefit of treatment be assessed. Therefore, drug treatment should still be considered for younger people with persistent hypertension. For other groups, different treatment goals have been set for blood pressure, HbA1c and LDL cholesterol depending on risk level, as illustrated in the figure.

All those with high and very high risk should receive a high-intensity statin, in practice atorvastatin 40–80 mg or rosuvastatin 20–40 mg. Experience indicates that many patients need addition of ezetimibe to achieve the treatment goal. The use of a PCSK9 inhibitor (monoclonal antibodies that lower LDL) is also recommended for patients with cardiovascular disease not achieving the LDL cholesterol goal, but current reimbursement rules limit their use in Norway.

Combination treatment is recommended for all those with hypertension, with the exception of patients at increased risk of hypotension, who should be started on monotherapy. The guidelines stress that it is important to enquire about drug adherence before any intensification of treatment.

In patients with diabetes, a target HbA1c of <53 mmol/mol (7 %) is generally recommended, but the goal in young people with short duration of disease should be HbA1c <48 mmol/mol (6.5 %). A less stringent target of 64 mmol/mol (8 %) is accepted for older patients with long duration of disease or comorbidities, to avoid hypoglycaemia among other things. The first-line treatment for type 2 diabetes is metformin. The addition of a sodium-glucose cotransporter 2 (SGLT2) inhibitor or glucagon-like peptide-1 (GLP-1) analogue is recommended in Step 1 for patients with cardiovascular disease or target organ damage, and should also be considered for other patients with diabetes in Step 2. A SGLT2 inhibitor is preferable for patients with kidney disease or heart failure.

Single or dual antiplatelet therapy is indicated for all patients with established cardiovascular disease, but is not generally recommended for other patients at increased risk. Drug selection and duration of treatment with antiplatelet drugs is individual and depends on coronary anatomy, risk of bleeding and potential need for anticoagulation therapy. This should be considered in consultation with a specialist.

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## Step 2

If the Step 1 treatment goals for blood pressure and LDL cholesterol are achieved, an individual assessment must be performed as to whether the treatment should be intensified to Step 2 (Figure 1). Choice of drug treatment is the same as in Step 1. As with the initial risk assessment, consideration should be given to risk modifiers, age, frailty and patient preferences. A woman aged 45 years with familial hypercholesterolaemia, type 2 diabetes and a father who died from myocardial infarction at the age of 43 years, will have a very high lifetime risk, and the aim should be to achieve treatment goals in Step 2. Hopefully, she will also have motivation for intensive treatment. However, for a woman aged 75 years who is frail with sequelae following an ischaemic stroke and has difficulty swallowing tablets, consideration will probably be given to stopping at Step 1, even though she has established cardiovascular disease and is thus at very high risk according to the definition.

***«An individual assessment must be performed as to whether the treatment should be intensified to Step 2»***

It is recommended that systolic blood pressure be reduced to <130 mmHg for all groups, if tolerated. The exception is patients > 70 years and those with chronic kidney disease, in whom target blood pressure is <140 mmHg. The treatment goal for LDL cholesterol is <1.8 mmol/l for patients at high risk and <1.4 mmol/l for patients at very high risk. However, the guidelines state that

more knowledge is needed about the effect of lowering LDL cholesterol to  $<1.4$  mmol/l and that it is uncertain to what extent this is feasible in practice, particularly in the primary care service [\(1\)](#).

Long-term treatment ( $> 12$  months) with dual antiplatelet therapy and the addition of low-dose anticoagulation therapy, as well as anti-inflammatory treatment if appropriate, can be considered in selected patients with established cardiovascular disease and high residual risk. In our opinion, this treatment should only be initiated after discussion with a specialist.

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## Reviews of the two-step model

It is important that the new guidelines emphasise the significance of lifestyle changes as the first measure for all patients. We think that the stepwise approach is sound and a clear improvement on previous guidelines. The model allows for a greater degree of clinical judgement and more personalised treatment. This may contribute to the setting of more realistic and feasible treatment goals.

In addition, an increased focus on shared decision-making is ensured, which in turn contributes to patient involvement and awareness of responsibility for their own disease. Some patients may have strong preferences for or against a treatment, and we think that providing thorough information is particularly important for those with very high risk so that such patients can make the best possible choice for their own health. Nevertheless, with highly sceptical or poorly motivated patients, it may be better to achieve cooperation on a minimum treatment that will actually be carried out rather than to initiate more extensive treatment that the patient will not follow anyway.

The drawback of the two-step model is that a more individualised approach is more complex and thus time-consuming for doctors and other healthcare professionals to follow up in everyday clinical practice. In addition, there is a risk of being satisfied with achieving goals in Step 1 in patients who may indeed benefit from more intensive risk factor control.

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