Cardiovascular disease risk assessment and reduction: summary of updated NICE guidance

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How patients were involved in the creation of this article
Committee members involved in this guideline update included lay members,

Satwinder Kaur and Colin Wilkinson, who contributed to the formulation of the recommendations summarised here.

Competing Interests

We declared the following interests based on NICE's policy on conflicts of interests (https://www.nice.org.uk/Media/Default/About/Who-we-are/Policies-and-procedures/declaration-of-interests-policy.pdf):

EJS is an employee of NICE, which is funded to develop clinical guidelines. CEC, SK, RSP and JM provide full statements in the NICE guideline.

Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide, with dyslipidaemia being a highly modifiable risk factor for CVD[1]. In England, high cholesterol affects 43% of adults[2] and is estimated to account for 7.1% of all deaths and 3.7% of disability-adjusted life years [3,4]. Importantly, for every 1mmol/L of lowered low density lipoprotein cholesterol (LDL-C), CVD event risk is reduced by 21%[5], and thus lipid-lowering therapy forms a cornerstone of CVD risk management, regardless of baseline cholesterol levels. However, many people at significant risk of CVD do not receive any lipid-lowering therapies, or they receive inadequate treatment, and there has been a decline in UK statin prescribing as a result of the COVID-19 pandemic[6]. For example, 2022 national audit data reports only 46% of people with a QRISK score of 10% or more are on lipid-lowering therapy for primary prevention[7]. In secondary prevention, this figure is around 80%[7], with less than 50% on the recommended high-intensity dose[8], despite the overwhelming evidence for lipid lowering in this population.

In May, the National Institute for Health and Care Excellence (NICE) published its updated guideline on CVD risk assessment and reduction, including lipid modification. The scope of the guidance was limited to reviewing evidence that has emerged since it was last updated in 2014 focussing on CVD risk assessment tools, dietary cholesterol, and statins for primary and secondary prevention of CVD. Although multiple areas of CVD prevention have advanced in recent years, several other topics such as new biomarkers including lipoprotein(a), coronary calcium scoring, and genetic risk scores, were considered out of scope, and will instead be considered for a future update of this guideline. In parallel, recommendations for cholesterol targets are currently being developed by NICE.

This article summarises the most recent recommendations from NICE {https://www.nice.org.uk/guidance/indevelopment/gid-ng10178} and includes information considered to be most relevant to primary care teams. Key changes to current practice

include allowing consideration of statin treatment for primary prevention in people with a 10-year risk of CVD below 10%, and removal of previous reference to restricting dietary cholesterol intake.

Recommendations

NICE recommendations are based on systematic reviews of the best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the guideline committee's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are given in italic in square brackets.

CVD risk estimation and communication

Tools assessing a combination of modifiable and non-modifiable risk factors can estimate a person's risk of experiencing a first cardiovascular event, either over the next 10 years or over their lifetime. The guideline committee (GC) agreed that such tools can be useful for stratifying people into low and high risk groups to guide management, including use of pharmacotherapy. However, using an appropriate risk assessment tool should not replace clinical judgement. Risk score interpretation should be individualised, including considering other risk factors that may not be captured by the tools leading to underestimation of risk (see Box 1). In this regard, the previous update of this guideline recommended the QRISK2 tool for estimation of 10-year risk, but the additional fields included in QRISK3 (such as severe mental illness, regular corticosteroid use and atypical antipsychotic use) have refined risk prediction for people with these risk factors who could benefit from risk reduction, including statin treatment. Moving to QRISK3 is also important since this is now the version that will be kept up to date by annual remodelling to the latest data. Therefore:

- Use the QRISK3 tool to calculate the estimated CVD risk within the next 10 years for people aged between 25 and 84 without CVD. (Updated recommendation) *[Based on high to low quality data from observational studies]*

The GC recognised that, until primary care clinical systems are updated with QRISK3, it will be necessary to continue using QRISK2. However, when assessing risk for people taking corticosteroids or atypical antipsychotics or people with systemic lupus erythematosus, migraine, severe mental illness or erectile dysfunction, QRISK3 should be used as QRISK2 may underestimate the 10-year CVD risk in these populations. Underestimation of risk was considered by the GC to lead to greater harm, by excluding people from primary prevention strategies, than overestimation.

The GC considered whether it was appropriate to recommend the use of a risk tool for people with either chronic kidney disease (CKD) or type 1 diabetes. Although type 1

diabetes was included within QRISK3, this does not capture factors considered clinically important, such as length of time the person has had diabetes or urinary albumin. As evidence in this population is still limited the GC agreed that a recommendation not to use a risk tool in this group, already at high CVD risk, should be retained.

QRISK3 has expanded the definition of CKD to include stage 3. However, the GC agreed that people with CKD are often at high CVD risk, including those with stage 1 or 2 CKD which is not captured in QRISK3 and in whom risk can actually be higher than in many people with stage 3 without albuminuria. Therefore, they considered that QRISK3 is likely to significantly underestimate CVD risk, especially those with CKD stage 1 or 2. The GC agreed that a recommendation not to use a risk tool in people with CKD should be retained (see Box 1).

Box 1: Risk assessment in special populations

- Do not use a risk assessment tool for people who are at high risk of CVD, including people with:
    - type 1 diabetes
    - an estimated glomerular filtration rate less than 60 ml/min/1.73 m^2 and/or albuminuria
    - familial hypercholesterolaemia or other inherited disorders of lipid metabolism. (Updated recommendation) *[Based on the experience and opinion of the GC]*
- Recognise that CVD risk tools may underestimate risk in certain groups of people, including but not limited to:
    - people treated for HIV
    - people already taking medicines to treat CVD risk factors
    - people who have recently stopped smoking
    - people taking medicines that can cause dyslipidaemia such as immunosuppressant drugs
    - people with severe mental illness
    - people with autoimmune disorders, and other systemic inflammatory disorders. (Updated recommendation) *[Based on the experience and opinion of the GC]*
- Consider people aged 85 or older to be at increased risk of CVD because of age alone, particularly people who smoke or have raised blood pressure. (Reviewed recommendation) *[Based on the experience and opinion of the GC]*

There was enthusiasm to explore use of lifetime risk models, but evidence supporting lifetime risk tools was not considered sufficiently robust to recommend their use instead of 10-year risk tools to guide interventions. However, the GC recognised their value in communication of risk, especially to motivate behaviour change in younger people with risk factors who score low on 10-year risk tools due to age or gender.

- Consider using a lifetime risk tool such as QRISK-lifetime to inform discussions on CVD risk and to motivate lifestyle changes, particularly for people with a 10-year QRISK3 score less than 10%, and people under 40 who have CVD risk factors. (New recommendation) *[Based on moderate quality data from observational studies and the experience and opinion of the GC]*

Person-centred care and lifestyle modification

An individualised approach, that takes a holistic view of individual risk factors and reinforces the importance of lifestyle changes to reduce CVD risk, remains crucial. The GC agreed that saturated fat intake has greater impact on a person's plasma cholesterol levels and corresponding risk of CVD events than dietary cholesterol and removed the reference to restricting dietary cholesterol intake because there was no evidence to support this (Box 2).

Box 2: Risk communication and lifestyle modification advice

- Set aside adequate time during the consultation to provide information on risk assessment and to answer any questions. Arrange for further consultation if needed. (Updated recommendation) *[Based on the experience and opinion of the GC]*
- Advise and support people at high risk of or with CVD to achieve a healthy lifestyle in line with NICE's guideline on behaviour change: general approaches.[9] (Updated recommendation) *[Based on the experience and opinion of the GC]*
- Advise people at high risk of or with CVD to eat a diet in which total fat intake is 30% or less of total energy intake, saturated fats are 7% or less of total energy intake, and where possible saturated fats are replaced by mono unsaturated and polyunsaturated fats. (Updated recommendation) *[Based on the experience and opinion of the GC]*
- Decide whether to start statin therapy after an informed discussion between the clinician and the person about the risks and benefits of statin treatment, taking into account additional factors such as potential benefits from lifestyle changes, informed patient preference, comorbidities, polypharmacy, general frailty and life expectancy.

(See also NICE's guideline on multimorbidity.[10]) (Updated recommendation) *[Based on the experience and opinion of the GC]*

- Offer people the opportunity to have their risk of CVD assessed again after they have tried to change their lifestyle. (Reviewed recommendation) *[Based on the experience and opinion of the GC]*

Statins for preventing CVD

Evidence on both the effectiveness and adverse effects of statins showed high-intensity statins to be clinically effective and cost-effective compared to no statins, low-intensity statins, or medium-intensity statins for preventing CVD in people with or without CVD. Crucially, for people without CVD, high-intensity statins were found to be cost-effective across all plausible combinations of age and 10-year CVD risk scores in a recent economic model[11]. However, the GC agreed that increasing uptake among people with the most potential to benefit (the highest risk scores) would have greater impact on reducing overall CVD events at a population level than lowering the statin treatment threshold. Therefore, the 10-year QRISK threshold of 10% was retained. Consideration was given to allowing the statin dose to be either 20 mg or 40 mg of atorvastatin according to clinical judgement and patient preference. However, stakeholder feedback highlighted that this lack of clarity was unhelpful. Therefore, in the absence of evidence for dose stratification, atorvastatin 20 mg was retained with dose escalation as appropriate.

- Offer atorvastatin 20 mg for the primary prevention of CVD to people who have a 10-year QRISK3 score of 10% or more. (Updated recommendation) *[Based on high to very low quality randomised trial data and economic modelling]*

The GC agreed that statins should also not be restricted to people with 10-year CV risk scores over 10%. A more person-centred approach should be adopted and the eligibility criteria for consideration of statin treatment broadened, acknowledging that models of risk prediction are inherently imperfect. Healthcare professionals are, therefore, encouraged to discuss risks and benefits of statin treatment with people achieving a lower cardiovascular risk score whom they consider may benefit. For example, younger people close to the 10-year risk treatment threshold or with multiple risk factors will have significantly higher lifetime risk and potential to benefit from lipid lowering and should not be excluded from earlier treatment.

Therefore:

- Do not rule out treatment with atorvastatin 20 mg for the primary prevention of CVD just because the person's 10-year QRISK3 score is less than 10% if they have an

informed preference for taking a statin or there is concern that risk may be underestimated. (New recommendation) *[Based on economic modelling and the experience and opinion of the GC]*

Evidence showed that high-intensity statins are cost effective for secondary prevention of CVD, and the likely additional benefit of a higher dose (80 mg) of atorvastatin for reducing CVD events made this this best option.

- Start statin treatment in people with CVD with atorvastatin 80 mg. Use a lower dose of atorvastatin if any of the following apply:
    - potential drug interactions
    - high risk of adverse effects
    - patient preference. (Reviewed recommendation) *[Based on high to very low quality randomised trial data, economic modelling and the experience and opinion of the GC]*

Additional evidence for muscle pain and rhabdomyolysis has become available since the 2014 update[12]. This adds certainty to conclusion that the risk of muscle-related adverse effects being caused by statins is low. For example, when using high-intensity statins approximately 16% of people reported experiencing muscle pain, but of these cases only around 1 in 12 were likely to be due to the statin.

- Advise people who are being offered a statin that the risk of muscle pain, tenderness or weakness associated with statin use is small and the rate of severe muscle adverse effects (rhabdomyolysis) because of statins is extremely low. (New recommendation) *[Based on high to moderate quality randomised trial data]*
- Advise people who are being treated with a statin to seek medical advice if they develop unexplained muscle symptoms (pain, tenderness or weakness). If this occurs, measure creatine kinase. (Updated recommendation) *[Based on the experience and opinion of the GC]*
- If people report muscle pain, tenderness or weakness while taking a statin and have a creatine kinase level less than 5 times the upper limit of normal, reassure them that their symptoms are unlikely to be due to the statin and explore other possible causes. (Updated recommendation) *[Based on high to moderate quality randomised trial data and the experience and opinion of the GC]*

Implementation

Using QRISK3 instead of QRISK2 will require clinical systems to be updated by software developers for the impact on practice to be minimised. Although, QRISK3 requires some

additional clinical information than QRISK2, when integrated into electronic clinical systems QRISK3 is not likely to require additional resources. Guidance on using QRISK3 in NHS health checks and how to deal with the transition period is available[13]. Whilst these recommendations do not require any additional risk estimation than the previous version, considering statin treatment for people with a 10-year CVD event risk below 10% may mean that more people require treatment and monitoring. This may result in additional primary care follow up appointments but will reduce future cardiovascular events, thus reducing future workload and avoiding the associated costs to the NHS. NICE acknowledges that the greatest individual risk reductions will be attained by offering statins to individuals with the highest baseline risk. However, the evidence also supports considering individual statin prescribing, as part of a holistic approach to risk factors, for people below the 10% risk threshold. There is a patient decision aid to help healthcare professionals to assist patients and carers in making decisions about taking a statin for people who do not already have heart disease and have not had a stroke. This has been updated based on the latest evidence identified for this update of the guideline {PDA citation TBC}.

Future research

The committee agreed to retain the following recommendations for research from the previous version of the guideline because there is still a lack of evidence in these areas:

- What is the effectiveness of statin therapy in older people?
- What is the effectiveness of statins and/or other LDL-C lowering treatment in people with type 1 diabetes?

What you need to know

- Reinforcement of the importance of a healthy lifestyle with appropriate modification of risk factors related to lifestyle should remain the cornerstone of all CVD prevention activities.
- In the absence of established CVD and where there is perceived increased CVD risk, an individualised, formal risk assessment using QRISK3 should be performed. The communication and appreciation of CVD risk may be improved with the use of a lifetime risk calculator, especially in younger people and women where 10-year risk may be low despite the presence of risk factors.
- Statin therapy is a highly cost-effective intervention at all levels of CVD risk and is associated with infrequent side-effects. Patient preference, medication adherence,

co-morbidity, frailty and life-expectancy are all important considerations when discussing the initiation or continuation of statin therapy.

Guidelines into practice

- Do you use a QRISK tool to assess 10-year risk of CVD in those without prior CV events?
- Do you offer atorvastatin 20 mg to people with a 10-year risk of CVD over 10%, and consider it for those with a lower or borderline calculated risk in line with patient preference and clinical judgement?
- Do you offer atorvastatin 80 mg to people with CVD?

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Further information on the guidance

This guidance was developed in accordance with NICE guideline methodology (www.nice.org.uk/media/default/about/what-we-do/our-programmes/developing-nice-guidelines-the-manual.pdf). A guideline committee (GC), including co-opted members, was established by the National Guideline Centre, which incorporated healthcare and allied healthcare professionals (two consultant cardiologists, one honorary consultant cardiologist, one consultant stroke physician, one honorary consultant in metabolic medicine, one consultant physician in ageing and health, one consultant nephrologist, one honorary consultant physician in hypertension, one nurse educator and associate lecturer, one advanced clinical pharmacist for cardiovascular services, one consultant physician in diabetes, endocrinology and lipid metabolism, one chair of geriatric and stroke medicine, professor of genetic epidemiology and honorary consultant, clinical pharmacology and general (internal) medicine, one senior lecturer nutrition and health) and two lay members.

The guideline is available at https://www.nice.org.uk/guidance/indevelopment/gid-ng10178/documents

The GC identified relevant review questions and collected and appraised clinical and cost effectiveness evidence. Quality ratings of the evidence were based on GRADE methodology (www.gradeworkinggroup.org). These relate to the quality of the available evidence for assessed outcomes rather than the quality of the study. The GC agreed recommendations for clinical practice based on the available evidence or,

when evidence was not found, based on their experience and opinion using informal consensus methods.

The scope and the draft of the guideline went through a rigorous reviewing process, in which stakeholder organisations were invited to comment; the GC took all comments into consideration when producing the final version of the guideline.

NICE will conduct regular reviews after publication of the guidance, to determine whether the evidence base has progressed significantly enough to alter the current guideline recommendations and require an update.

Contributorship and the guarantor

EJS is responsible for the overall content as guarantor.

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