Lipid Modification (update)
Minutes: Stakeholder Scoping Workshop
22nd May 2012, 14:00-17:00
The Derwent Room, NICE, 71 High Holborn, London, WC1V 6NA

No	Scope section	Stakeholders' feedback
4.1	**Population** Included ○ Adults (aged 18 years and older) without established CVD. ○ People with type 1 and type 2 diabetes (not covered in the original guideline). ○ People with CKD (not covered in the original guideline). Adults (aged 18 and older) with established CVD. ○ The following special groups will be considered for primary prevention: ○ black and minority ethnic groups, in particular South Asians ○ people with a family history of CHD ○ low socio-economic groups.	○ It was welcomed that diabetes is included in the scope. ○ It was generally agreed that the population was appropriate including people with diabetes and CKD as there is increased risk in these populations. It was felt that there was little evidence in Type 1 but more in Type 2. Evidence in haemodialysis patients/ end stage renal disease however was felt to be problematic ○ It was debated whether or not all stages of CKD are to be included. View was that end stage / renal dialysis should be excluded as the management is very different. It was confirmed this would be consistent with the CKD guideline update. ○ One stakeholder queried if people with severe mental illness could be included within the subgroups. They have a lower life expectancy and increased incidence / risk of CVD. Other members of the group supported this suggestion. Risk is due to obesity from drug related weight gain (due to antipsychotics) and reduced physical activity. Group were informed that the bipolar guideline is being updated and there could be some cross-referencing. ○ In addition, the following groups were suggested: – The elderly (>74yrs) – it was noted that they are at particular risk but are not covered by the current risk assessment tools, and so warrant specific consideration – Women – the tools do not work well for women, and there is some evidence that those with CVD have worse outcomes – People with chronic inflammatory disorders (e.g. rheumatoid arthritis / psoriasis) – Children – especially (but not solely) those with diabetes, who may need to start on preventative treatment before they are adults. It was clarified that lipid-lowering treatment of children with diabetes is being included in the childhood diabetes guideline, whereas treatment of adults with diabetes is proposed to be included in this guideline and not in the adult diabetes guideline ○ Whether or not high risk groups included primary and secondary prevention was queried – e.g. is it all adults, or adults with CVD considered to be high risk. It was confirmed this starts including all adults, then establishes if they are at risk, and flows on to the management of these people. Agreed this needs clarifying in the scope. ○ One stakeholder queried why children aren't included. It was confirmed that the DH remit was for adults, children weren't in the original guideline and we couldn't go beyond the remit. ○ There was a query whether "people with a family history of CHD" should say 'CVD' instead of 'CHD' ○ It was asked if it could be stated in 4.1.1e that these are groups at increased risk. A suggested re-ordering of these points was: a), then Adults considered to be at increased cardiovascular risk:

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		d,b,c,e. ○ Agreed it was a good idea to avoid the term 'high risk' ○ Why obesity wasn't included in the groups to be covered was queried. It was confirmed that obese people weren't excluded and would be included in the review population, but wouldn't be looked at as a subgroup. The management of obesity was not going to be included in the scope. ○ It was questioned why the special groups (black and minority ethnic groups etc.) had been selected and whether it was actually necessary to focus on special groups at all
4.1	4.1 **Population** <u>Excluded</u> ○ People with familial hypercholesterolaemia. ○ People with familial clotting disorders and/or other defined genetic disorders that increase cardiovascular risk. ○ People at high risk of CVD or abnormalities of lipid metabolism as a result of endocrine or other secondary disease processes or as a result of drug treatment.	○ There was concern that "other defined genetic disorders that increase cardiovascular risk" was vague. Some inherited disorders also increase cholesterol e.g. familial combined hypercholesterolemia. The Chair mentioned in his talk that others would be included, but it is not clear in the scope. ○ Familial clotting disorders. The question was asked whether these populations were covered by other guidance ○ Mental health was raised and the fact that their increased risk is partly due to medications, but also independent to this. The Whitehall study was noted and other studies which show that severe psychological stress and depression increases CVD risk. There was a lot of discussion on this point and some doubt about whether it should be in the scope or not. Main aim would be to raise the profile of the increased risk in mental health and one view was that including it in the guideline would help do that.
4.3.1 a)	4.3 **Clinical Management** 4.3.1 <u>Key clinical issues that will be covered</u> a) The assessment of cardiovascular risk and determination of an individual's absolute risk of developing CVD. This will include determining the most appropriate system for multiple risk-factor assessment to be used to estimate absolute cardiovascular risk and outcome i.e. 10 year or lifetime risk (1) People without diabetes, for example QRISK and Framingham risk assessment tools (2) People with diabetes, for example UKPDSrisk engine, Epic- Norfolk Cambridge diabetes tools, FInRISK	○ Two other tools were suggested: SCORE (used in European Guidelines) and the ASSIGN risk score (a Scottish risk score). ○ The JBS3 guidelines were also mentioned, but thought these would be covered within lifetime risk. Due out in July (possibly). ○ It was suggested that the words 'multiple risk factor assessment' should be replaced by' risk estimation' in the scope so that other strategies such as age only could be considered as well as formal assessment tools. ○ The question of the use of lifetime risk was also questioned as potentially unhelpful or even misleading. ○ It was suggested that the GDG did not have to recommend one (or more) tool(s), but could instead specify the criteria which any tool would need to satisfy to be judged suitable. Such criteria already exist in the literature ○ It was asked whether we should be looking at who is at risk, or instead just looking at who would not benefit from statin treatment.
4.3.1 b)	4.3 **Clinical Management** 4.3.1 <u>Key clinical issues that will be covered</u> b) Lipid modification strategy: fixed dose or	○ This was considered an important issue and the use of ratios was raised as being important. ○ It was queried whether this was absolute or relative target levels. It differs in existing guidelines. ○ Some stakeholders suggested a third alternative strategy: giving the highest tolerated dose. Others

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	treating to a target lipid level, in primary and secondary prevention.	commented that many, though not all, clinicians think that this is probably the best strategy, but without evidential proof. In practice it is commonly utilised ○ It was commented that the forthcoming revisions to the Quality and Outcomes Framework will specify a target lipid level for diabetics. The GDG would not be bound by this, and the QOF could change again in future in response to any recommendations the GDG makes
4.3.1 c)	4.3 **Clinical Management** 4.3.1 Key clinical issues that will be covered c) Assessment of clinical and cost effectiveness of pharmacological interventions (1) to reduce the risk of developing CVD and (2) for secondary prevention in people with established CVD: • First-line treatment: – Statins • Second-line treatment (alone and in combination with statins): – fibrates – anion-exchange resins – nicotinic acid group – omega-3 fatty acids	○ It was queried whether adherence to medications could be looked at. It was confirmed this will be part of the health economics sensitivity analysis. There can also be cross-reference to the Medications adherence guideline. Agreed this needs to be added to the related guidance list. ○ It was queried whether follow-up / review of patients will be included. It was agreed it would fall under risk assessment tools. Suggestion this should include how and when to review. Chair informed the group that with some medications they are bound by MHRA license. Otherwise, GDG can make a recommendation. ○ There was a lot of discussion about people who were put on statins who didn't have a risk assessment, and subsequently determined that they are not at risk. What should you do with these people? Is the statin modifying their risk? Should they stay on / come off? Should the guideline exclude people already on lipid lowering therapy? However, agreed this assumes that all of the population are naïve to statins which might not be the case. Could perhaps be considered when evidence reviewed. Group felt the scope should state one way or another if this group were included, just for clarity rather than a strong view either way. ○ The omission of ezetimibe from the list of second-line treatments was noted, especially since it is much more commonly used than the other options which are on the list. The stakeholders wanted the guidance on ezetimibe to be revised. No other additional drugs were suggested to be added to the list. ○ One stakeholder suggested that consideration should be given to whether people being assessed for the first time for primary prevention and being found to have a high (>30%) risk, could be immediately given a higher dose statin or a combination treatment, rather than all patients automatically being given the same treatment. ○ The stakeholders did not consider the hyper acute use (in the ambulance) of importance. Immediate Post MI statin administration was already an established part of secondary prevention ○ The issue of co-administration of Co-enzyme Q10 (an enabler) was raised here as an aid to adherence (see outcomes)
4.3.1 d)	4.3 **Clinical Management** 4.3.1 Key clinical issues that will be covered d) The assessment and monitoring of blood lipids and treatments: which fractions of blood lipids should be measured and in which situations (for example, fasting).	○ The importance of adherence was stressed, from both cost and effectiveness perspectives. There may be equality issues if there is differential adherence between groups. There is also evidence of a 'rebound' in state of health amongst those ceasing to take statins ○ Stakeholders asked about the measurement of HDL-cholesterol, which is not routine. It was clarified that lipid levels are only of interest for determining the best course of treatment, but not as surrogate outcomes. HDL-enhancing treatments would only be of interest insofar as they also improve hard outcomes

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		○ It was raised the issue of the (possible) difference between measuring HDL-cholesterol and non-LDL-cholesterol. The concept of the 'lipid triad' had never really been investigated properly (only covered in the 4S trial) and this could be helpful ○ Some concern was expressed that this was actually not that important an area and simplification in this area might be an advantage ○ Point of care testing issue was raised
4.3.1 e)	4.3 **Clinical Management** 4.3.1 Key clinical issues that will be covered e) Criteria for referral to specialist assessment and management for patients found to have lipid disorders	○ This was regarded as an important issue as some people are missed
4.3.2	4.3 **Clinical Management** 4.3.2 Key clinical issues that will **NOT** be covered a) The identification, assessment and management of people with pre-diabetes/metabolic syndrome. b) The clinical management of conditions considered to be risk factors for CVD, including people with raised blood pressure/hypertension, smoking, obesity, and blood clotting abnormalities. c) Self-medication of individuals with lipid-regulating drugs, specifically use of over-the-counter drugs including statins. d) The clinical management of people with lipid disorders considered to merit referral to secondary care for specialist assessment and follow-up. e) The clinical management of people with CHD, stroke and PAD except as it relates to lipid modification in the context of secondary prevention.	○ There was some discussion about point c). It was confirmed that this relates to the statin that is available in the UK over the counter, with pharmacy supervision. This falls outside of NHS care, and therefore NICE remit. ○ Prediabetes/metabolic syndrome was actually felt to be a big problem that should be covered
	Sections from the original guideline that will NOT be updated: Identification and assessment of CVD (Recs 1.1.1 to 1.1.6)	○ It was asked whether a change in guidance regarding the risk threshold at which statins should be given (i.e. lower than 20%) would necessitate at least some changes to this section, and in turn to the NHS Health Checks policy. The stakeholders agreed that it would. ○ It was felt that the mismatch between this section, the DH vascular health policy and the subsequent section that was being updated could be confusing. ○ The stakeholders commented that it would not be entirely clear which parts were 'evidence based'
	Sections from the original	○ The stakeholders did not have any comments on this point.

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	guideline that will NOT be updated: Communication about risk assessment and treatment (Recs 1.2.1 to 1.2.7)	
	Sections from the original guideline that will NOT be updated: Lifestyle modifications for the primary and secondary prevention of CVD (Recs 1.3.6 to 1.3.17) – Plant stanols and sterols – Physical activity – Combined interventions (diet and physical activity) – Weight management – Smoking cessation	○ It was queried why lifestyle modification was excluded. The stakeholders were not aware of new evidence based on outcomes that would change the recommendations. ○ It was discussed whether surrogate outcomes could be used. The stakeholders agreed that there is a lot of caution over extrapolating from surrogate outcomes. ○ It was considered that lifestyle modifications might be considered within the subgroup populations in the relevant guidelines (e.g. the diabetes update). ○ An inconsistency was noted between the evidence on cardioprotective diet (1.3.1-1.3.3) and that on stanols and sterols (1.3.6): 1.3.1 states general dietary advice of the kind given by governments and food regulators, such as replacing saturated fats with unsaturated fats. Whilst these are widely trusted, they are based only on evidence of changes in lipid levels, not on hard outcomes. In contrast, 1.3.6 states that plant stanols and sterols should not be routinely recommended, based on a lack of evidence of changes in hard outcomes (which has not changed since the original guideline), although there is evidence of changes to lipid levels. It was noted that different food regulators and standards agencies give different advice – for example the European Food Safety Authority does recommend plant stanols ○ It was suggested that the recommendations in the rest of the section (physical activity, weight, smoking etc) should be updated in line with current standard recommendations in these areas, without carrying out any new research.
4.4	4.4 **Main Outcomes** a) Morbidity and mortality b) Hospitalization c) 10 year risk of developing CVD d) Lifetime risk of developing CVD e) Adverse events f) Quality of life outcomes	○ It was queried whether patient reported outcomes would be included (POMS). Chair stated that if these could be captured in the QALY, they would be included. It was agreed that lay members of the GDG would help inform outcome selection for the protocols. ○ It was suggested that both total mortality and cardiovascular mortality should be looked at, with total mortality being the most important. ○ It was noted that hospitalization was rather broad- hospitalization for CVD events suggested ○ It was suggested amalgamate 10 year and lifetime risk of developing CVD ○ It was suggested the addition of 'adherence'
	Health economic issues	○ It was suggested to look at the cost-effectiveness of particular treatments for those at particular risk levels ○ One stakeholder asked for the part of the current guidance recommending use of the statin with the 'lowest acquisition cost' should be kept [the actual wording of the recommendation is a statin with 'a low acquisition cost']
	General comments	○ It was noted that there have now been some studies of the effects of long-term (20 years) use of statins, and it will be important to look at these ○ One stakeholder questioned how the relative contribution that lipid-lowering drugs can and

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		should make alongside other interventions (diet, exercise, anti-smoking etc) which are offered in primary care at the same time, can be assessed o It was felt that there was an equalities issue around people becoming 'patients' which might be detrimental. This was related to the focus on the risk equations- removing hurdles should be a priority o Statin withdrawal was considered to be an important area o End of life issues should be considered o It was noted that section 3.2 (current practice) should say 10 year risk, not 5 year. o It was raised that definition of CVD is confusing in section 3.1 (Epidemiology), it appears to contradict in next paragraph. Atherosclerotic TIA should be included within CVD as the disease process is the same and it is managed in the same way. o It was noted that in 3.2b blood lips aren't just a risk factor for CVD, also a possible sign / feature of metabolic disorders / underlying condition.
	GDG Constituency a) General practitioner x2 b) Patient member x2 c) Coronary heart disease nurse/ Practice nurse with a specialist interest in CVD prevention d) Pharmacist with an interest in CVD prevention e) Expert in risk assessment/public health physician f) Endocrinologist/diabetologist/ metabolic/general medicine physician x2 g) Cardiologist with interest in CVD prevention/risk assessment h) Chemical pathologist and lipidologist i) Renal physician with an interest in CVD prevention	o It was noted that there was no mental health / psychologist representation. o It was suggested that a dietician could be included (although agreed maybe not relevant if lifestyle not being considered) perhaps as a co-opted expert. o It was suggested to specify that 1 GP should have commissioning experience. o It was suggested 'with an interested in CVD prevention risk assessment, be included in point f. o The two patient /carers should reflect primary and secondary prevention therefore one person with CVD and one without was suggested o Inclusion of a stroke/ vascular physician was suggested o It was noted that the nurse in c) could also be a lipid nurse o It was felt that there should be a member representing elderly people o It was suggested that at least one of the members should be able to represent South Asian people, but that this should be a member on the group in another capacity as part of a generally diverse Group, not a additional member.