Effective management of dyslipidaemia

*A summary of key guidance and ‘issues and answers’ from South African experts*

Lowering lipid-related cardiovascular (CV) risk in the developed world has again moved into the spotlight with the recent release of the latest American Heart Association/American College of Cardiology (AHA/ACC) guidelines and the United Kingdom’s National Institute of Clinical Excellence (NICE) lipid modification guidelines, which have also just been released for comment.¹ ²

The South African lipid guidelines published in November 2011 are based broadly on the European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) guidelines.³ These developments and clinical guidance are reviewed in this CPD-accredited report.

Also, a panel of South African clinicians provides answers to issues in the clinical management of dyslipidaemic patients.

### South African experts comment on common therapeutic issues and provide practical advice to primary care practitioners

#### Prof Derick Raal

**Issues**
1. How do you view the new AHA/ACC guidelines?
2. What do you recommend South African clinicians should do? ‘Fire and forget’ or ‘Treat to target’?
3. Why is it vital to lower LDL-cholesterol levels speedily?

#### Dr Dirk Blom

**Issues**
1. What practical advice can you give South African clinicians to improve success rates in lipid management?

#### Dr Naomi Rapeport

**Issues**
1. What is the best approach to lowering LDL-cholesterol and CV risk in women?
2. Should women be treated differently from men with regard to lowering overall CV risk and specifically LDL-cholesterol levels?
3. What are the facts about South African care of women when it comes to lowering their CV risk?
Summary of key guidance in the management of dyslipidaemia

Focus on South African guidelines

KEY MESSAGES

- LDL-cholesterol is the major causative risk factor in atherosclerotic CV disease (CVD).
- Reducing LDL-cholesterol unequivocally reduces CV events.
- Lipid levels should be measured (by means of a full lipogram) in the fasting state to facilitate LDL-cholesterol calculation.
- Point-of-care can be done first, followed by a full lipogram.
- Total cholesterol measurement is sufficient for screening in a young person.

The South African dyslipidaemia guidelines, which are based primarily on the European guidelines, underscore from the outset that lifestyle modification is the cornerstone of lowering CV risk. Thereafter, the guidelines advocate the use of the new Framingham Risk Score (only for those patients who do not have CVD, diabetes or genetic hyperlipidaemia), to determine overall risk and the use of statin therapy to lower LDL-cholesterol levels to specific targets (Table 1). Where these targets cannot be met, statin therapy should aim to reduce LDL-cholesterol levels by at least 50% with combined therapy advocated for very high-risk groups and for those patients intolerant of statins or for whom statins are contraindicated.

This approach of ‘treating-to-target’ is also advocated in the ESC/EAS guidelines for the management of dyslipidaemia.

Table 1: South African guidance on intervention strategies using the new Framingham total CVD risk score and LDL-cholesterol levels

<table>
<thead>
<tr>
<th>Total CVD risk score</th>
<th>LDL-cholesterol levels</th>
<th>&lt;1.8 mmol/l</th>
<th>1.8 - &lt;2.5 mmol/l</th>
<th>2.5 - 4.9 mmol/l</th>
<th>&gt;4.9 mmol/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3% Low risk</td>
<td>No lipid intervention</td>
<td>Lifestyle intervention</td>
<td>Lifestyle intervention, consider drug if uncontrolled</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 - 15% Moderate risk</td>
<td>Lifestyle intervention</td>
<td>Lifestyle intervention</td>
<td>Lifestyle intervention, consider drug if uncontrolled</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 - 30% High risk</td>
<td>Lifestyle intervention, consider drug†</td>
<td>Lifestyle intervention, consider drug‡</td>
<td>Lifestyle intervention and immediate drug intervention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;30% Very high risk</td>
<td>Lifestyle intervention, consider drug‡</td>
<td>Lifestyle intervention and immediate drug intervention</td>
<td>Lifestyle intervention and immediate drug intervention</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Based on Table 3 from Reiner Z, et al., Eur Heart J 2011;32:1769-1818.
†Based on the Framingham CVD risk tables.
‡In patients with myocardial infarction (MI), statin therapy should be considered regardless of LDL-cholesterol levels.
ACC and AHA new guidelines – advocating a new patient-centred intervention without LDL-cholesterol targets

The ACC/AHA guidelines released in November last year use a different approach, perhaps best summarised as ‘statin dose determined by risk and not by baseline or on treatment of LDL-cholesterol, with the highest-risk patients receiving the highest doses’. (Table 2)

Table 2: ACC and AHA guidelines

<table>
<thead>
<tr>
<th>4 identified groups for statin therapy</th>
<th>Recommended statin-based approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Individuals with clinical atherosclerotic CVD</td>
<td>Use high-intensity statin therapy (rosuvastatin 20-40mg or atorvastatin 40mg) to lower LDL-cholesterol by 50%. In cases of intolerance, replace with moderate-intensity statins.</td>
</tr>
<tr>
<td>2. Individuals with LDL-cholesterol levels ≥4.9mmol/l, such as those with familial hypercholesterolaemia</td>
<td>Use high-intensity statin to achieve a 50% reduction in LDL-cholesterol levels.</td>
</tr>
<tr>
<td>3. Individuals with type 1 or type 2 diabetes, 40-75 years and LDL-cholesterol between 1.8mmol/l/4.9mmol/l and without evidence of atherosclerotic CVD</td>
<td>Use a moderate-intensity statin (that lowers LDL-cholesterol 30-49%) or a high-intensity statin if patient has 10-year risk of atherosclerotic CVD greater than 7.5%.</td>
</tr>
<tr>
<td>4. Individuals without evidence of CVD or diabetes but who have LDL-levels between 1.8-4.9mmol/l and a 10-year risk of CVD above 7.5%. Also consider treatment in those with risk &gt;5%.</td>
<td>Use either moderate- or high-intensity statin therapy.</td>
</tr>
</tbody>
</table>

Table 3: Excerpt from South African practical guidance on initiating statin therapy

<table>
<thead>
<tr>
<th>Starting LDL-cholesterol (mmol)</th>
<th>Goal: &lt;1.8 mmol/l</th>
<th>Goal: &lt;2.5 mmol/l</th>
<th>Goal: &lt;3.0 mmol/l</th>
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<tbody>
<tr>
<td></td>
<td>% reduction required</td>
<td>Statin dose</td>
<td>% reduction required</td>
</tr>
<tr>
<td>&gt;6.2</td>
<td>&gt;70%</td>
<td>Rosuvastatin 40mg</td>
<td>&gt;60%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Atorvastatin 80mg</td>
<td></td>
</tr>
<tr>
<td>5.2 – 6.2</td>
<td>65 – 70%</td>
<td>Rosuvastatin 40mg</td>
<td>50 – 60%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Atorvastatin 80mg</td>
<td></td>
</tr>
<tr>
<td>4.4 – 5.2</td>
<td>60 – 65%</td>
<td>Rosuvastatin 40mg</td>
<td>40 – 50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Atorvastatin 80mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.9 – 4.4</td>
<td>55 – 60%</td>
<td>Rosuvastatin 40mg</td>
<td>35 – 40%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Atorvastatin 80mg</td>
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“ACC/AHA guidelines focus on effective statin use based on risk from the outset.”
The US guidelines focus primarily on statin use aimed at achieving at least a 50% reduction in LDL-cholesterol from the outset. Four major groups for statin therapy are identified in terms of using either a high-intensity statin or a moderate-intensity statin. Interestingly, there has been little criticism of this practical aspect of the American guidelines; rather the loss of targets is criticised, as is the use of a new pooled risk calculator.

The new ACC/AHA risk estimator is a pooled cohort of participants from the Framingham Heart Study (FHS), the Atherosclerosis Risk in Communities (ARIC) study and the Coronary Artery Risk Development in Young Adults (CARDIA) study and is available on the ACC website, Cardiosource (also available as an App).

Interestingly, the South African guidelines provide a practical guide to initiating statin use that shows some similarity to the new American guidelines (Table 3). They advocate high-intensity statin therapy when low- to high-risk patients present with high LDL-cholesterol in order to achieve maximum reductions quickly.

But because the South African guidelines recommend choosing statin dose based on target and baseline LDL-cholesterol, the practical effect is that patients with high LDL-cholesterol start on high doses but high-risk patients with low baseline LDL-cholesterol start on low doses, so there is a difference. The latter situation (high risk, low baseline LDL-cholesterol) is one of the reasons given for abandoning targets, as the American guideline authors feel this may result in undertreatment of high-risk patients.

**Impact of US guidance on South African clinical practice – Prof Derick Raal**

**How do you view the new AHA/ACC guidelines?**

The new ACC/AHA guidelines emphasise the importance of lifestyle, healthy diet and exercise in cardiovascular risk reduction. They have, however, abandoned LDL-cholesterol targets and instead focus on risk for atherosclerotic CVD (ACVD) and recommend high-intensity statin therapy for patients with overt ACVD, regardless of baseline lipid levels. This means that such patients will receive more aggressive lipid-lowering statin therapy, which should result in further reduction in CV morbidity and mortality. The new guidelines also recommend high-intensity statin therapy for subjects with marked hypercholesterolaemia (LDL-cholesterol > 4.9 mmol/l) and with an estimated 10-year risk of ACVD of > 7.5%. However, the chart used to estimate risk may not be appropriate for the South African population and may over- or underestimate risk.

**What do you recommend South African clinicians should do? ‘Fire and forget’ or ‘Treat to target’?**

I would still recommend that local clinicians ‘treat to target’ as has been recommended by the EAS and ESC, the Canadian Cardiovascular Society as well as the UK NICE guidelines. As with treating blood pressure and diabetes, physicians and patients need to have a goal to strive for.

**Why is it vital to lower LDL-cholesterol levels speedily?**

To date, all the lipid-lowering statin studies have consistently shown that the greater the LDL-cholesterol reduction, the greater the ACVD risk reduction; this holds true down to an LDL-cholesterol level of 1.8 mmol/l. There does not appear to be a lower threshold below which any further benefit is achieved. There is also trial evidence to show that rapid reduction of LDL-cholesterol post a coronary event can reduce CV event rates and reduce mortality. We need to be more aggressive in lowering LDL-cholesterol levels, particularly in high-risk patients, diabetics and those with established atherosclerosis.
Practical advice – Dr Dirk Blom

What practical advice can you give South African clinicians to improve success rates in lipid management?

Patient motivation is a very important aspect of successfully reaching and maintaining target cholesterol levels. It is important to discuss the risk profile of each patient, encouraging patients to reduce their overall risk. It is helpful to understand what patients have already been told about their risk and what their attitude to their future health is; also to explore their readiness to make changes and their attitude to long-term medication. The wisest course is to involve the patient in developing a shared management plan, with attainable goals in respect of smoking cessation, exercise, dietary changes and weight management. It is also important to assess the affordability of medication – if patients struggle to afford medication they are unlikely to take it - and to be open and supportive when patients report fears about side effects.

Patients need to understand that the higher their absolute risk, the greater the absolute benefit of lowering LDL-cholesterol. For this reason, prescribing an effective dose from the outset supports patients’ commitment to taking medication. The policy of ‘getting it right first time’ has been shown to enhance patient compliance. Many patients are left on their initial statin dose and the dose is not up-titrated even if they are not at target. This was shown in the Centralised Pan-South African Survey (CEPHEUS) study, which found that undertreatment of hypercholesterolaemia in everyday practice is common.6

Physicians should note that CVD is neither a rich man’s disease nor confined to the Caucasian population. In the INTERHEART study, African patients had their first myocardial infarction at a younger age than other population groups. CVD is increasing in the developing world while rates are decreasing in the developed world. Patients should be reassured that statins are remarkably well-tolerated and that these medications are now really affordable.

Spotlight on lowering CV and lipid-related risk in women – Dr Naomi Rapeport

What is the best approach to lowering LDL-cholesterol and CV risk in women?

CVD is the leading cause of death among women in every major developed country and most emerging economies. In South Africa, infectious disease (HIV and tuberculosis) is the major cause of mortality in young women; however, in older women, CVD is the major cause. There is still the misconception that the major cause of death in women is cancer, but the real big ‘C’ is CVD and not cancer. Much of the burden of CVD can be attenuated by addressing critical risk factors such as hyperlipidaemia, hypertension, type 2 diabetes mellitus, physical inactivity, tobacco use, overweight and obesity. Forty-six percent of South African women are physically inactive and 30% are obese. South African women have the distinction of being one of the most obese populations in the world. In women with hyperlipidaemia, lifestyle changes need to be implemented and if cholesterol levels are not reduced, then lipid-lowering therapy needs to initiated, together with continued lifestyle changes. The World Heart Federation, together with the AHA, has established an awareness campaign, ‘Go Red for Women’, to educate women about heart disease and risk factors. While most of the morbidity and mortality from CVD occurs at older ages, exposure to these risk factors starts earlier in life, and preventive interventions therefore need to target younger women.

Should women be treated differently from men with regard to lowering overall CV risk and specifically LDL-cholesterol levels?

The reality is that women are being treated differently from men! Many clinicians are unaware of the prevalence of CVD in women, resulting in an underestimation of women’s risk. In a retrospective review of clinical data from adults (age 55 years for men and less than 65 years for women)
hospitalised for acute myocardial infarction, none of the women had a calculated risk of greater than 20% prior to their infarction. Only 18% met criteria for lipid-lowering treatment. In Africa, data from the INTERHEART study showed that women of African ancestry presented with their first myocardial infarction at a younger age than those from Western Europe and North America (median age of 56 years versus 68 and 64 years, respectively). In patients who have suffered a myocardial infarction, younger women have higher rates of death during hospitalisation than men of the same age.

Effectiveness-Based Guidelines for the Prevention of Cardiovascular Disease in Women —2011 Update focuses on long-term risk for CVD. High-risk women have a 10% or greater risk of death from any CV event in the next 10 years (previously it was 20% or more) and need to be treated aggressively. New major risk categories include women with systemic autoimmune collagen-vascular disease (such as systemic lupus erythematosus and rheumatoid arthritis), as these disorders are known to be associated with a significantly increased relative risk for CVD as well as women with a history of preeclampsia, gestational diabetes mellitus or pregnancy-induced hypertension.

What are the facts about South African care of women when it comes to lowering their CV risk?

In the CEPHEUS survey on the under-treatment of hypercholesterolaemia in patients using lipid-lowering drugs, 1 424 (47%) of the cohort were female. Women were less likely to get to treatment targets than men.7 This was true across all race groups. This is of great concern, particularly in women of Asian and mixed descent who have the highest prevalence of coronary artery disease (CAD). Overall, in this study only 60% of patients reached the appropriate target levels — this is lower than experienced in the developed world. It’s important to note that although African men and women have a lower risk of CAD, the risk is increasing. In women of African descent on lipid-lowering medication, 14.3% had CAD. The Cardiovascular Risk in Black South Africans (CRIBSA) study (2008/9) of an urban adult black population in Cape Town showed that 38% of the cohort had raised LDL-cholesterol levels. Forty-seven percent of women in this study had elevated levels.8 These facts highlight the undertreatment of patients and indicate that the South African medical fraternity needs to be more aggressive in the management of women with hyperlipidaemia.

References