South African Dyslipidaemia Guideline Consensus Statement

A joint statement from the South African Heart Association (SA Heart) and the Lipid and Atherosclerosis Society of Southern Africa (LASSA)

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The European Society of Cardiology together with the European Atherosclerosis Society published updated dyslipidaemia guidelines in 2011. SA Heart and the Lipid and Atherosclerosis Society of Southern Africa officially adopt these guidelines. This statement adapts aspects of the guidelines to the South African situation. Using the updated Framingham risk charts, interventional strategies are based according to the cardiovascular risk score and low-density lipoprotein cholesterol (LDL-C) levels. The Framingham risk score refers to the 10-year risk of any cardiovascular event, and includes four categories of risk. Treatment targets are those of the European guidelines. The LDL-C goal is 1.8 mmol/l for the very high-risk group (>30%), 2.5 mmol/l for the high-risk group (15 - 30%), and 3 mmol/l for those below 15% risk. Intensive management of dyslipidaemia in South Africa will significantly reduce the cardiovascular disease health burden.

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1. Introduction

In 2003, the South African Heart Association (SA Heart) and the Lipid and Atherosclerosis Society of Southern Africa (LASSA) officially adopted the European Guidelines for the Prevention of Cardiovascular Disease[1] to replace the South African Lipid Guidelines published in 2000.[2] The European document has recently been updated with the publication of the European Society of Cardiology (ESC)/European Society of Atherosclerosis (EAS) Guideline for the Management of Dyslipidaemias in 2011.[3] This Consensus Statement promotes current best management of dyslipidaemia and should be adopted by all health care professionals in South Africa.

South Africa is a multi-ethnic society, with a large range of cultures and lifestyles at different stages of epidemiological transition. In all sub-populations, cardiovascular disease is a major cause of morbidity and mortality. Every day, approximately 80 people die of myocardial infarction or heart failure, while another 60 die due to stroke.[4] The INTERHEART Africa study indicated that more premature acute myocardial infarctions occur in sub-Saharan Africa than in any other of the 52 countries participating in the INTERHEART study.[5,6] This statistic reflects a lack of prevention, early detection and effective management of cardiovascular risk factors in the countries of this region.[5] In particular, in the black population, with increasing urbanisation and adoption of an unhealthy lifestyle, the prevalence of CVD and the incidence of premature death are likely to continue to increase.[4] Consequently, the timely institution of lifestyle modification, early diagnosis and effective management of CVD risk factors are essential to curb the epidemic of CVD that has been seen in other countries.[5]

2. When to use the cardiovascular risk score

2.1 Very high-risk individuals do not require risk scoring

Individuals who are considered to be at very high risk of cardiovascular events are listed in Table 1. Patients in this group DO NOT require cardiovascular risk scoring, because the risk score will be an underestimate in these settings.

2.2 Individuals who do not fall into the very high-risk category

Risk scoring using well-documented key risk factors is appropriate to estimate the total cardiovascular risk in asymptomatic adults. Furthermore, risk scoring is especially important in individuals with the following:

- Hypertension and/or on antihypertensive medication
- Smoking: cigarette smoking is defined as any cigarette smoking in the past month or a history of 20 cigarettes per day for 10 years (10 pack years)

Table 1. Subjects considered to be at very high risk of cardiovascular events

Established atherosclerotic disease, i.e.
• Coronary artery disease
• Cerebrovascular disease
• Peripheral arterial disease
Type 2 diabetes
Type 1 diabetes with micro-albuminuria or proteinuria
Genetic dyslipidaemia, e.g. familial hypercholesterolaemia
Chronic kidney disease (GFR <60 ml/min/1.73 m^2)

- BMI ≥30 kg/m^2 or waist circumference >94 cm for men, >80 cm for women
- Family history of premature CVD (male before 55 years of age, female before 60 years)
- Auto-immune chronic inflammatory disease, e.g. rheumatoid arthritis, systemic lupus erythematosus, psoriasis.

3. When to start screening

In South Africa, because the prevalence of familial hypercholesterolaemia is as high as 1 in 100 in some communities, each individual should be tested, preferably with a full lipogram or at least TC/LDL-C, at least once in young adulthood (from 20 years of age). Particular attention should be paid to individuals with other risk factors for CVD.

4. How to screen using the Framingham Risk Score

The European guidelines use the Systematic Coronary Risk Estimation (SCORE) system to estimate cardiovascular risk. Because this scoring system is based on an exclusively European population, it may not accurately reflect coronary risk in South Africa. While it is recognised that it would be impossible to accurately estimate risk in all South African subpopulations with a single data set, the Adult Treatment Panel (ATP) III Framingham risk tables,[7] which provide an estimate of the 10-year risk of CHD, have been validated in white and black populations in the USA and are transportable to other culturally diverse populations. Consequently, we considered this approach to be more appropriate for South Africa. Nevertheless, these risk tables are likely to underestimate risk in South African black and Indian patients. The Framingham CHD tables may also underestimate total CVD risk in middle-aged and older women, whose risk of stroke and heart failure is typically higher than that of CHD. Even when multiple elevated risk factors are present, it is difficult for a woman younger than 75 years to exceed a 10% predicted risk for CHD, precluding her from qualification for more aggressive CVD prevention.[8] Consequently, more recent Framingham equations predict 10-year total CVD risk (including CHD, stroke, transient ischaemic attack and heart failure).[8,9] The updated Framingham CVD risk tables for men and women and an algorithm for management and cholesterol goals have been incorporated into these recommendations (Appendix 1).

5. Measuring lipids

5.1 Low-density lipoprotein cholesterol

LDL-C is preferred when deciding on treatment and assessing its effect. LDL-C is used in preference to other tests as it is modifiable by treatment and the beneficial effects of lowering LDL-C are known. LDL-C may be measured directly or calculated from the Friedewald equation (in mmol/l) (LDL-C = TC - HDL-C - TG/2.2), provided the triglycerides do not exceed 4.5 mmol/l.

5.2 Total cholesterol

Once the relationship between on-treatment TC and LDL-C is known, it may be appropriate to monitor TC only. TC may be used as an alternative for screening, risk assessment and monitoring of treatment efficacy if there are cost constraints or if there is difficulty in obtaining either direct or indirect LDL-C values. Equivalent target values for TC are:

- TC = 4.5 mmol/l is approximately equivalent to LDL-C = 2.5 mmol/l
- TC = 4.0 mmol/l is approximately equivalent to LDL-C = 1.8 mmol/l.

If TC values remain uncontrolled and LDL-C measurement is unavailable, the patient should be referred to a specialist physician.

5.3 Cost-effective testing

A full lipogram (TC, HDL-C, LDL-C and triglycerides) is recommended for initial diagnosis of dyslipidaemia. In patients with pure hypercholesterolaemia, LDL-C alone is adequate for follow-up, but a full lipogram is recommended where increased LDL-C is not the only abnormality in the lipid profile. After initiating TLC alone, follow-up testing should be performed every 6 months. After initiating pharmacoth erapy, changing the dose or changing the specific drug prescribed, testing should be repeated at 8 (± 4) weeks and thereafter, once the patient is at goal, every 6 months.

5.4 Point-of-care finger prick testing

Various point-of-care tests are available. They provide various results, ranging from TC alone to a full lipogram. Where finger prick testing is performed, the facility should ensure that adequate quality controls are in place, that the test strips and devices are stored under appropriate conditions of temperature, humidity and light, and that precautions are taken to perform the test properly, with an adequate blood sample volume and without contamination.[10] The finger should not be squeezed or"milked", as this will give inaccurate results.

Finger prick testing is appropriate for screening and follow-up to determine where advice on lifestyle intervention is required (e.g. TC >5 mmol/l), but is not appropriate to commit a patient to a lifetime of therapy. Where a screening finger prick TC measurement is high(>5 mmol/l), the patient should be encouraged to discuss their finger prick screening result with their doctor, who should have a full laboratory-performed fasting lipogram done and then perform a full cardiovascular risk assessment. Because inappropriately low results are a concern, TC <2.5 mmol/l on a finger prick test should be confirmed. Finger prick testing that measures TC

alone will not detect raised triglycerides.

5.5 Additional testing

The use of novel biomarkers of CVD (e.g. hsCRP) and imaging technologies (e.g. coronary calcium scoring, carotid intima-media thickness) is not recommended routinely and should be reserved to refine risk assessment in patients considered to be at moderate risk where there is uncertainty about whether to initiate drug therapy.8 It should be noted that hsCRP is a nonspecific inflammatory marker that may be elevated from many causes (e.g. acute infections or non-infectious inflammatory disorders). Measuring Lp(a) is only appropriate in HIGH CVD risk subjects and/or when there is a family history of premature CVD. When Lp(a) is used as a risk marker, the cut-off value is >50 mg/dl.

5.6 Secondary dyslipidaemias

Dyslipidaemia may occur in response to another condition or treatment. Table 2 lists those encountered most commonly. The appropriate diagnostic tests should be performed when secondary dyslipidaemia is suspected and the underlying abnormality treated.

6. Strategy for intervention

The risk levels determined for the SCORE system refer to the 10-year risk of a fatal CVD event, whereas the Framingham scoring system refers to the 10-year risk of any CVD event. Risk thresholds for the Framingham score are therefore approximately 3 times those for SCORE.

Table 3 sets out the recommended appropriate intervention strategies according to the percentage risk calculated from the Framingham risk score and the LDL-C value obtained.

7. Treatment targets

Although we recommend the use of the Framingham risk charts to estimate cardiovascular risk, the management of patients, once risk has been determined, and the goals of therapy, are those of the European guidelines.

LDL-C goals for patients at different levels of Framingham risk are listed in Table 4.

8. Management of dyslipidaemia

Because the total cardiovascular risk is the product of a number of risk factors, the treatment of dyslipidaemia must always be seen within the broader framework of cardiovascular disease prevention.

8.1 Lifestyle modification

It should be emphasised that the cornerstone of any programme to reduce cardiovascular risk is TLC (healthy diet, regular exercise). In order for the changes to be sustainable, dietary and exercise advice must be practical and tailored specifically to the individual's personal and cultural preferences.[11] Diets may need to be modified for people with unusual or specific

Table 2. Secondary causes of dyslipidaemia

Diabetes mellitus
Hypothyroidism
Liver disease
Renal disease, e.g. nephrotic syndrome
Alcohol excess
Medications:
- Progestins
- Steroids
- Antiretroviral agents
- Retinoids

Table 4. LDL-C treatment targets

Total Framingham CVD risk	ESC/EAS risk classification	ESC/EAS LDL-C target
<3%	Low risk	< 3.0 mmol/l
3-15%	Moderate risk	< 3.0 mmol/l
15-30%	High risk	< 2.5 mmol/l
>30%	Very high risk	< 1.8 mmol/l

Table 3. Intervention strategies as a function of Framingham total CVD risk score and LDL-C levels[a]

Total CVD risk score[b]	LDL-C levels			
	< 1.8 mmol/l	1.8 - < 2.5 mmol/l	2.5 – 4.9 mmol/l	> 4.9 mmol/l
<3% Low risk	No lipid intervention	No lipid intervention	Lifestyle intervention	Lifestyle intervention, consider drug if uncontrolled
3-15% Moderate risk	Lifestyle intervention	Lifestyle intervention	Lifestyle intervention, consider drug if uncontrolled	Lifestyle intervention, consider drug if uncontrolled
15-30% High risk	Lifestyle intervention, consider drug[c]	Lifestyle intervention, consider drug[c]	Lifestyle intervention, and immediate drug intervention	Lifestyle intervention, and immediate drug intervention
>30% Very high risk	Lifestyle intervention, consider drug[c]	Lifestyle intervention, and immediate drug intervention	Lifestyle intervention, and immediate drug intervention	Lifestyle intervention, and immediate drug intervention

[a]Based on Table 3 from Reiner Z, et al, Eur Heart J 2011;32:1769-1818.[3]
[b]Based on the Framingham CVD risk tables.[9]
[c]In patients with MI, statin therapy should be considered regardless of LDL-C levels.

disorders (e.g. hypertriglyceridaemia) and referral to a dietician and fitness professional is encouraged.

8.2 Dietary supplements

Epidemiological and interventional studies support the role of healthy dietary choices as a whole to help reduce the risk of cardiovascular events. However, insufficient evidence exists to recommend the use of dietary supplements in patients with dyslipidaemia. While some dietary supplements have been shown to influence plasma lipids, there are no outcomes data that show benefits with regard to CVD prevention. Conversely, there is evidence that some supplements may be harmful to health and may interact with prescription medicines.[12,13] Consumers should be advised to beware of unsubstantiated advertising claims relating to long-term health benefits. Although there are no known risks associated with its use, the routine use of coenzyme Q10 to reduce statin-related myalgia or myopathy is not supported by systematic reviews of the medical literature.[14,15]

8.3 Statin therapy

Statins have demonstrated effectiveness in both primary and secondary prevention. The effect is dependent on the extent to which LDL-C is lowered and not on the type of statin used. At their maximum doses, the various statins differ in their capacity to lower LDL-C.

For every mmol/l reduction in LDL-C there is a:

- 10% reduction in mortality
- 20% reduction in all-cause morbidity
- 23% reduction in major cardiac events
- 17% reduction in stroke.

The effect of statin therapy is similar in all patient subgroups and becomes significant after 1 year, increasing progressively thereafter.

8.4 High-dose simvastatin treatment

Although the incidence of myopathy is very low for all the statins, it is approximately 3 times as high with 80 mg simvastatin compared with maximum doses of atorvastatin and rosuvastatin. Accordingly, the American Food and Drug Administration (FDA) has mandated safety-labelling changes for medicines containing simvastatin, which include the following recommendations:[16]

- The use of 80 mg simvastatin should be restricted to those who have been using the dose chronically (longer than 12 months), without signs or symptoms of myopathy.
- Patients who are using simvastatin 80 mg and who need to start taking another drug that may interact with simvastatin should be switched to an alternative statin with a lower risk of drug interactions, such as rosuvastatin or atorvastatin.
- Patients who do not reach their LDL-C goal with 40 mg simvastatin should be switched to an appropriate alternative more potent statin with a lower potential for myopathy.
- To reduce the incidence of myopathy:
  - Do not exceed 10 mg simvastatin with amiodarone, verapamil, or diltiazem
  - Do not exceed 20 mg simvastatin with amlodipine
  - Simvastatin is contraindicated with azole antifungals, macrolide antibiotics, HIV protease inhibitors, gemfibrozil, cyclosporine and danazol.

8.5 Statin toxicity

When used in appropriate patients, statins are remarkably safe drugs and the benefits of cardiovascular protection far outweigh the potential for toxicity. However, patients should be encouraged to make and sustain healthy lifestyle choices and the lowest dose of statin to achieve LDL-C target should be used.

8.5.1 Statin-related myalgia and rhabdomyolysis

The presence of any musculoskeletal pain should be documented before starting statin therapy to facilitate the recognition of statin induced myalgia during treatment.

A CK measurement prior to commencing statin treatment is recommended. Statins should not be started if the CK is >5 times the ULN. Routine CK monitoring is not necessary during treatment, unless the patient develops myalgia. Increased vigilance regarding CK and myopathy is necessary in the elderly, in those on concomitant interfering treatment or on multiple medications, and in the presence of liver or renal disease.

If myalgia develops and the CK is >5 times the ULN:

- Stop treatment
- Check renal function
- Monitor CK every 2 weeks
- Consider causes of transient CK elevation, e.g. exercise
- Consider alternative causes of myopathy.

If myalgia develops and the CK is <5 times the ULN:

- Monitor symptoms
- Monitor CK regularly.

If the CK is <5 times the ULN and there are no muscle symptoms:

- Continue statin
- Alert patient to report symptoms
- Consider monitoring ck.

The incidence of rhabdomyolysis is very low.

In patients who are intolerant to statin therapy, potent statins, such as atorvastatin or rosuvastatin, may be used on alternate days (e.g. Monday, Wednesday, Friday) or even less frequently to reduce side effects.[17] Alternatively, a combination therapy of a low-dose statin with a lipid-lowering drug of another class (e.g. ezetimibe) can be considered.

8.5.2 Statin-induced rises in alanine aminotransferase

Baseline ALT measurement should be performed before initiating treatment with a statin. If the ALT is normal, it does not need to be repeated. Raised ALT does not exclude statin therapy, where treatment should be individualised. Alternative reasons for raised ALT (e.g. haemochromatosis, fatty liver) should be investigated where necessary.

If the ALT is raised <3 times the ULN while on treatment, continue the statin and recheck ALT in 4 - 6 weeks. If the ALT is raised >3 times the ULN on treatment, stop the statin and repeat ALT in 4 – 6 weeks. Cautious reintroduction of the statin can be considered once the ALT has returned to normal.

8.5.3 New-onset diabetes

Recent meta-analyses have demonstrated a very small increase in the risk of new-onset diabetes associated with statin use, notably in patients treated with intensive-dose statin therapy and in older patients.[18,19] However, this small potential adverse risk is outweighed by the absolute reduction in CV events and should not discourage initiation of statin therapy.[3,19,20]

8.6 Scheme for introducing statin treatment

- First evaluate the risk.
- Involve the patient in CV risk management decisions.
- Identify the appropriate LDL-C target.
- Calculate % reduction in LDL-C required to reach target.

Table 5. Practical guide to initiating statins depending on baseline LDL-C and target LDL-C values[a]

Starting LDL-C (mmol)	Goal: <1.8 mmol/l		Goal: <2,5 mmol/l		Goal: <3.0 mmol/l	
	% reduction required	Statin dose	% reduction required	Statin dose	% reduction required	Statin dose
>6.2	>70	Rosuvastatin 40 mg Atorvastatin 80 mg	>60[b]	Rosuvastatin 40 mg Atorvastatin 80 mg	>55	Rosuvastatin 40 mg Atorvastatin 80 mg
5.2 – 6.2	65 – 70[b]	Rosuvastatin 40 mg Atorvastatin 80 mg	50 - 60	Rosuvastatin 40 mg Atorvastatin 80 mg	40 - 55	Rosuvastatin 40 mg Atorvastatin 80 mg
4.4 – 5.2	60 -65[b]	Rosuvastatin 40 mg Atorvastatin 80 mg	40 - 50	Rosuvastatin 10 mg Atorvastatin 20 mg Simvastatin 40 mg	30 - 45	Rosuvastatin 5 mg Atorvastatin 10 mg Simvastatin 20 mg Lovastatin 40 mg Fluvastatin 80 mg
3.9 – 4.4	55 - 60	Rosuvastatin 40 mg Atorvastatin 80 mg	35 - 40	Rosuvastatin 5 mg Atorvastatin 10 mg Simvastatin 20 mg Lovastatin 40 mg Fluvastatin 80 mg	25 - 30	Rosuvastatin 5 mg Atorvastatin 10 mg Simvastatin 10 mg Lovastatin 20 mg Pravastatin 40 mg Fluvastatin 80 mg
3.4 – 3.9	45 - 55	Rosuvastatin 10 mg Atorvastatin 40 mg	25 - 35	Rosuvastatin 5 mg Atorvastatin 10 mg Simvastatin 10 mg Lovastatin 20 mg Pravastatin 40 mg Fluvastatin 80 mg	10 - 25	Any statin at lowest dose
2.9 – 3.4	35 - 45	Rosuvastatin 5 mg Atorvastatin 10 mg Simvastatin 20 mg Lovastatin 40 mg Fluvastatin 80 mg	10 – 25	Any statin at lowest dose	<10	Any statin at lowest dose
2.3 – 2.9	22 - 35	Rosuvastatin 5 mg Atorvastatin 10 mg Simvastatin 10 mg Lovastatin 10 mg Pravastatin 20 mg Fluvastatin 40 mg	<10	Any statin at lowest dose	-	
1.8 – 2.3	<22	Rosuvastatin 5 mg Atorvastatin 10 mg Simvastatin 10 mg Lovastatin 10 mg Pravastatin 20 mg Fluvastatin 40 mg	-		-	

[a] Based on weighted average of pooled analysis at starting dose. Dose should be titrated according to response.
[b] Maximum LDL-C reduction achievable with high-dostatin monotherapy is 50 – 60 %. To achive a reduction in LDL-C of >60%, another cholesterol-lowering agent in addition to statin therapy may be required
Adapted from Reiner Z, et al, Eur Heart J 2011; 32:1769-18183 and Weng T-C, et al, JCln Pharm Ther 2010;35:139-151.[21]

- Choose the statin (and dose) able to achieve the desired reduction (Table 5).
- It is mandatory to up-titrate the dose to achieve the LDL-C target.
- If target is not reached at maximal dose, consider a more potent statin or add a lipid-lowering drug from another class.
- The final statin choice will be influenced by concomitant conditions, concomitant drug therapy and tolerability.

8.7 Other cholesterol-lowering agents

The cholesterol absorption inhibitor ezetimibe in combination with simvastatin was shown to reduce major atherosclerotic events in patients with advanced chronic kidney disease.[22] Although no other outcome studies have been completed, ezetimibe is recommended:

- As second-line treatment in combination with a statin when the LDL-C target is not reached at the highest tolerated statin dose
- When there is intolerance to statins
- When there is a contraindication to a statin.

Bile acid sequestrants and nicotinic acid have cholesterol lowering properties. They may occasionally be useful alone or in combination with statin therapy. However, their side-effects limit wider application.

8.8 Treatment directed at other components of the lipid profile

Whereas low levels of HDL-C and high levels of TG are undoubtedly associated with a higher cardiovascular disease risk, no currently available treatment directed at reversing these changes has been shown to significantly benefit cardiovascular outcome.

A high triglyceride level, particularly if >10 mmol/l, can result in acute pancreatitis and should be treated without delay.

9. Special circumstances

9.1 Metabolic syndrome

The European Guidelines recognise the importance of identifying patients with the metabolic syndrome, who are at increased risk of cardiovascular disease. The presence of the syndrome approximately doubles the risk of cardiovascular disease. Lifestyle changes, particularly reducing body weight and increasing physical activity, are the cornerstone of management of the metabolic syndrome.[23]

9.2 Acute coronary syndromes

A lipid profile should be obtained at the time of admission in patients presenting with ACS. They should be treated with high-dose statin therapy during their acute care and the statin dose should be adjusted at the time of discharge according to the admission lipid profile.

9.3 HIV infection

Dyslipidaemia frequently accompanies HIV and may be aggravated by ARVs. While there is limited information, particularly in South Africa, it is important to measure lipids in patients with HIV and estimate their CVD risk, and a full lipogram should be performed before initiating ARV treatment. The Framingham tables will generally underestimate CVD risk in this population. In patients with high lipid levels already on ARV treatment, switching to an alternative ARV and cautious use of a statin or fibrate as necessary should be considered. Simvastatin is contraindicated in patients using protease inhibitors.

9.4 Unusual conditions

Unexplained cutaneous or tendinous deposits (xanthomata), very premature vascular disease, some endocrine, metabolic and neurological disorders constitute reasons for referral. Unusually low TC (<2.5 mmol/l), LDL-C (<1.5 mmol/l), HDL-C (<0.7 mmol/l) or unusually high TG (>10mmol/l), TC (>15 mmol/l), LDL-C (>12 mmol/l), HDL-C (>2.5 mmol/l) also deserve special consideration.

10. Conclusions: implementation of the 2011 guidelines

In order to implement the guidelines, we propose a simple chart that has been updated to accommodate the new Framingham CVD risk tables (Appendix 1). The chart is a guide to management only and should not replace an individualised assessment and treatment plan based on the clinical judgement of the doctor. We encourage the reader to read the 2011 European guidelines in full, which may be accessed on the ESC website www.escardio.org/guidelines. We hope that dissemination of these guidelines will go some way towards helping to reduce the burden of CVD in South Africa.

11. Mechanism of guideline preparation

In October 2011 a broad-based group of participants from the medical and allied health community, medical funders, pharmaceutical companies, the Department of Health, the Board of Health Funders and the Heart and Stroke Foundation met together with Professor Marja-Riitta Taskinen in Sandton, Johannesburg, to examine and discuss the joint ESC/EAS dyslipidaemia guidelines. Professor Taskinen is a co-author and Task Force Member of these guidelines and attended on behalf of the European Atherosclerosis Society.

The following day a writing committee met to construct the South African Consensus Document.

Additional delegates attending the Dyslipidaemia Guidelines Meeting Discussion Group were Dr A Amod (SEMDSA), Ms G Bartlett (Universal Health), Ms U Behrtel, Dr S Bhana (Netactive), Ms M Campbell (Discovery), Mr D Craythorne (Cipla), Mr A Dansay (PharmaDynamics), Ms L Doms (Medscheme), Ms A du Plessis (Vital Health), Ms U du Preez (Astra Zeneca), Dr R Espaillat (Abbott Laboratories), Dr C Golding (Solal Laboratories), Ms K Jamaloodien (National Department of Health), Dr D Katzman (MSD), Dr S Kahn, Mr M Lambert (Aspen), Dr M Makotoko, Mr M Mashego (Adcock Ingram), Ms Y Misra (MediKredit), Dr M Mpe, Dr V Munga-Singh (Heart and Stroke Foundation), Ms L Naidoo (Sanlam Healthcare), Ms N Nel, Dr R Patel (Board of Healthcare Funders), Ms D Pithey (MSD), Mr J Rall (Ranbaxy), Dr J Snyman (Agility Global Health Solutions), Dr M Sussman (SA Heart), Dr M Swanepoel (Medihelp), Professor JP van Niekerk *(South African Medical Journal)*, Ms L Xiphu (QUALSA/Metropolitan).

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Abbreviations

ACS	acute coronary syndromes
ALT	alanine aminotransferase
ARVs	antiretroviral drugs
BP	blood pressure
CHD	coronary heart disease
CK	creatine kinase
CVD	cardiovascular disease
GFR	glomerular filtration rate
HDL-C	high-density lipoprotein cholesterol
LDL-C	low-density lipoprotein cholesterol
hsCRP	high-sensitivity C-reactive protein
Lp(a)	lipoprotein (a)
MI	myocardial infarction
TC	total cholesterol
TG	triglyceride
TLC	therapeutic lifestyle change
ULN	upper limit of normal

Appendix 1. Cardiovascular risk stratification

Framingham 10-year risk assessment chart for patients without diabetes
Risk of CVD: coronary heart disease, stroke, peripheral artery disease, or heart failure

Estimate of 10-year risk of CVD for men

Age (yrs)	Points
30 - 34	0
35 - 39	2
40 - 44	5
45 - 49	6
50 - 54	8
55 - 59	10
60 - 64	11
65 - 69	12
70 - 74	14
75 years or older	15

Total cholesterol (mmol/l)	Points
<4.10	0
4.10 - 5.19	1
5.2 - 6.19	2
6.20 - 7.20	3
>7.20	4

HDL-cholesterol (mmol/l)	Points
≥1.50	-2
1.30 - 1.49	-1
1.20 - 1.29	0
0.90 - 1.19	1
<0.90	2

Systolic BP – untreated (mmHg)	Points
<120	-2
120 - 129	0
130 - 139	1
140 - 159	2
≥160	3

Systolic BP – on antihypertensive treatment (mmHg)	Points
<120	0
120 - 129	2
130 - 139	3
140 - 159	4
≥160	5

Smoker	Points
No	0
Yes	4

Estimate of 10-year risk of CVD for women

Age (yrs)	Points
30 - 34	0
35 - 39	2
40 - 44	4
45 - 49	5
50 - 54	7
55 - 59	8
60 - 64	9
65 - 69	10
70 - 74	11
75 years or older	12

Total cholesterol (mmol/l)	Points
<4.10	0
4.10 - 5.19	1
5.2 - 6.19	3
6.20 - 7.20	4
>7.20	5

HDL-cholesterol (mmol/l)	Points
≥1.50	-2
1.30 - 1.49	-1
1.20 - 1.29	0
0.90 - 1.19	1
<0.90	2

Systolic BP – untreated (mmHg)	Points
<120	-3
120 - 129	0
130 - 139	1
140 - 149	2
150 - 159	4
≥160	5

Systolic BP – on antihypertensive treatment (mmHg)	Points
<120	-1
120 - 129	2
130 - 139	3
140 - 149	5
150 - 159	6
≥160	7

Smoker	Points
No	0
Yes	3

Points total for men

Points total	10-year risk (%)
-3 or less	<1
-2	1.1
-1	1.4
0	1.6
1	1.9
2	2.3
3	2.8
4	3.3
5	3.9
6	4.7
7	5.6
8	6.7
9	7.9
10	9.4
11	11.2
12	13.2
13	15.6
14	18.4
15	21.6
16	25.3
17	29.4
18 or more	>30

Points total for women

Points total	10-year risk (%)
-2 or less	<1
-1	1.0
0	1.1
1	1.5
2	1.8
3	2.1
4	2.5
5	2.9
6	3.4
7	3.9
8	4.6
9	5.4
10	6.3
11	7.4
12	8.6
13	10.0
14	11.6
15	13.5
16	15.6
17	18.1
18	20.9
19	24.0
20	27.5
20 or more	>30

Point totals indicate the 10-year risk of cardiovascular disease (coronary, cerebrovascular and peripheral arterial disease, and heart failure).

Low risk Moderate risk High risk Very high risk

Adapted from D'Agostino RB, et al, General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation 2008;117:743-753[9] and Mosca L, et al, Effectiveness-based guidelines for the prevention of cardiovascular disease in women 2011 update: A guideline from the American Heart Association. Circulation 2011;123:1243-1262.[8]

Management and cholesterol goals according to Framingham risk score

Category 1: Individuals considered to be at very high risk who do not need scoring

1. Established atherosclerosis
   - Coronary heart disease
   - Cerebrovascular disease
   - Peripheral vascular disease
2. Type 2 diabetes*
3. Type 1 diabetes with target organ damage
4. Chronic kidney disease (GFR <60 ml/min/1.73 m^2)
5. Genetic dyslipidaemias (e.g. familial hypercholesterolaemia)

*In patients with type 2 diabetes younger than age 40 years or with duration of diabetes <10 years and no other CVD risk factors, the LDL-C target is <2.5 mmol/l.

Goal:†
LDL cholesterol <1.8 mmol/l**
**and/or a >50% LDL-C reduction when the LDL-C target cannot be achieved

Category 2:‡ Risk scoring required – use the Framingham risk tables§

Use correct gender table:	Score:
1. Age	1. _____
2. Total cholesterol¶	2. _____
3. Non-smoker/smoker	3. _____
4. HDL-C	4. _____
5. Systolic BP	5. _____

10-year CVD event risk:___%

Initial CVD risk <3%	Initial CVD risk 3-<15%	Initial CVD risk 15-<30%	Initial CVD risk >30%
• Institute lifestyle changes • Consider statin if LDL-C persistently >4.9 mmol/l	• Institute lifestyle changes • Consider statin if LDL-C persistently >3.0 mmol/l	• Institute lifestyle changes • Consider statin if LDL-C <2.5 mmol/l	• Institute lifestyle changes • Start statin immediately
Goal:† LDL-C <3.0 mmol/l		**Goal:†** LDL-C <2.5 mmol/l	**Goal:†** LDL-C <1.8 mmol/l

†Pharmacological treatment is required if LDL cholesterol remains above these levels despite lifestyle modification. At present statins are first-line drugs for lowering LDL cholesterol.
‡Secondary causes of dyslipidaemia should be excluded before progressing to risk assessment.
§See limitations of Framingham Risk Assessment Score on this page.
¶Total cholesterol level is used to assign risk score and may be used for follow-up cholesterol measurement in patients on drug therapy, but LDL cholesterol is the target of treatment.

Limitations of the Framingham Risk Assessment Score charts

1. Patients who are classified in the very high-risk category do not require further risk scoring for management decisions. Risk will also be underestimated in patients who have a markedly elevated single risk factor (e.g. severe hypertension: systolic BP >180 mmHg and/or diastolic BP >110 mmHg), or associated target organ damage.
2. Severe hypercholesterolaemia and hypertriglyceridaemia: The Framingham risk assessment chart is only accurate up to total cholesterol values of 7.25 mmol/l and cannot be used for patients with TC levels above this value. It also does not apply to hypertriglyceridaemia (triglyceride >5 mmol/l).
3. Family history of early atherosclerotic disease is not taken into account. Clinicians should use their judgement in deciding whether to place a patient with an impressive family history in the high-risk category regardless of their Framingham score.
4. Despite these factors being important risk factors for CVD, impaired glucose tolerance and abdominal obesity are not taken into account in the risk score.

LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; TG = triglyceride; CHD = coronary heart disease; CVD = cardiovascular disease; BP = blood pressure.

Conversion from mg/dl

Cholesterol:	***Triglyceride:***
mmol/l = mg/dl × 0.0259	mmol/l = mg/dl × 0.0113
mg/dl = mmol/l × 38.6	mg/dl = mmol/l × 88.5

Appendix 2. South African Heart Association/LASSA guidelines for lifestyle modification for patients with dyslipidaemia

1. Stop smoking and avoid exposure to environmental tobacco smoke.
2. Increase your physical activity. Try to do exercise of moderate intensity, such as brisk walking, for at least 30 minutes on all or most days of the week.
3. Achieve and maintain ideal body weight.
4. Reduce your intake of saturated fats, trans-fats and cholesterol. Avoid eating fatty meats, processed meats, chicken skin, processed meats, confectionery such as pies, pastries and cookies, fast foods, deep-fried potato chips ('slap chips'), butter, ghee, cream, hard cheeses and salty crackers.
5. Replace saturated fats with unsaturated fats. Avoid the use of hard margarines, butter and ghee for cooking or adding to food. Use unsaturated fats such as canola oil, olive oil and sunflower oil for cooking. Use oils sparingly and avoid all deep-frying of food. Remove all visible fat before cooking. Increase your intake of all types of fish, especially oily fish such as sardines and salmon, to a minimum of twice a week.
6. Increase your intake of fibre, especially soluble fibre. Include foods such as oats, fresh fruit and legumes (dry beans, soya beans, chickpeas, all types of lentils). Include a minimum of five portions of fresh fruit and vegetables in your daily diet.
7. Replace all refined carbohydrate types of foods with foods high in fibre, such as whole grains. Avoid eating products made from white flour, such as white bread and rolls, pizzas, vetkoek, samoosas, pies, prego rolls and bakery items such as cakes and biscuits. Incorporate whole- grain foods such as oats, barley, stampkoring (pearl wheat), crushed wheat, samp and beans, brown rice, brown/wild rice, whole-grain breakfast cereals, health and seed breads.
8. Avoid foods high in free sugars (sucrose, high-fructose corn syrup, fructose) such as sweets, chocolates, all fizzy soft drinks, fruit juices, all flavoured and sweetened waters, low-fat sweetened milky drinks.
9. If you consume alcohol, do so in moderation – no more than 2 drinks for men and 1 drink for women per day.
10. Avoid adding salt to food after cooking. Choose and prepare foods with little or no salt by using more herbs and spices.