AMPATH LAB UPDATE

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Update of LDL-cholesterol targets

Low-density lipoprotein (LDL) cholesterol (LDL-C) is a well-known target for therapy in patients with hyperlipidaemia.[1,2] Retention of LDL-C and other cholesterol-rich apolipoprotein (Apo)B-containing lipoproteins within the arterial wall is considered an initiating event in atherogenesis.[2]

Several recent meta-analyses/clinical trials have established that **increased LDL-C values are related to atherosclerotic vascular disease (ASCVD)**, and that lowering LDL particles and other ApoB-containing lipoproteins reduces cardiovascular events directly and proportionally to the absolute LDL-C reduction.[2] These trials have also shown that there is no lower limit for LDL-C values, as previously believed, and that very low LDL-C levels are safe.[1,2] These are usually only achievable by the addition of **ezetimibe and sometimes proprotein convertase subtilisin/kexin type 9 (PCSK-9) inhibitors.** PCSK-9 inhibitors are members of a new class of lipid-lowering drugs that reduce LDL-C levels on average by 60% when administered alone or when added to maximally tolerated statin therapy with or without ezetimibe.[2]

During 2019, the Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) published new guidelines with lowered LDL-C targets for patients at high or very high ASCVD risk[1]. With the recent availability of PCSK-9 inhibitors in South Africa, **the Lipid and Atherosclerosis Society of Southern Africa (LASSA) and the South African Heart Association** have also announced an update of their previously published LDL-C target goals, as well as a revised cardiovascular risk stratification, in keeping with the 2019 ESC/EAS guidelines. These changes are especially relevant to high- and very high-risk patients. Indications for appropriate treatment with PCSK-9 inhibitors have also been included in the guidelines[2,3] – please refer to the table and flow diagrams below.

Table 1: Cardiovascular risk categories and LDL-C targets

Cardiovascular risk categories	Previous LDL-C target	Updated LDL-C target
Very high risk: According to ESC/EAS risk criteria or > 30% total Framingham cardiovascular disease risk	< 1.8 mmol/L	LDL-C reduction ≥50% from baseline AND LDL-C < 1.4 mmol/l (< 1 mmol/l for patients with ASCVD who experience a second vascular event within two years)
High risk: According to the ESC/EAS risk criteria or 15 ≤ 30% total Framingham cardiovascular risk	< 2.5 mmol/L	LDL-C reduction ≥50% from baseline AND LDL-C <1.8 mmol/l
Moderate risk: 3 ≤ 15% total Framingham cardiovascular risk	< 3.0 mmol/L	< 2.6 mmol/L
Low risk: < 3% total Framingham carciovascular risk	< 3.0 mmol/L	< 3.0 mmol/L

References:

1. South African Dyslipidaemia Guideline Consensus Statement. *South African Medical Journal. 2018. November;* 108(11):975–1000. http://www.samj.org.za/index.php/samj/article/view/12479/8686
2. ESC/EAS Lipid Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk 2019. *European Heart Journal.* 2020. 41: 111–188.
3. Klug EQ and Raal FJ. New cholesterol targets for patients at high or very high cardiovascular risk and the indications for PCSK9 inhibitors. Letter to the editor. *South African Medical Journal.* 2020. November; 110(11): 1059; https://doi.org/10.7196/SAMJ.2020.v110i11.15191

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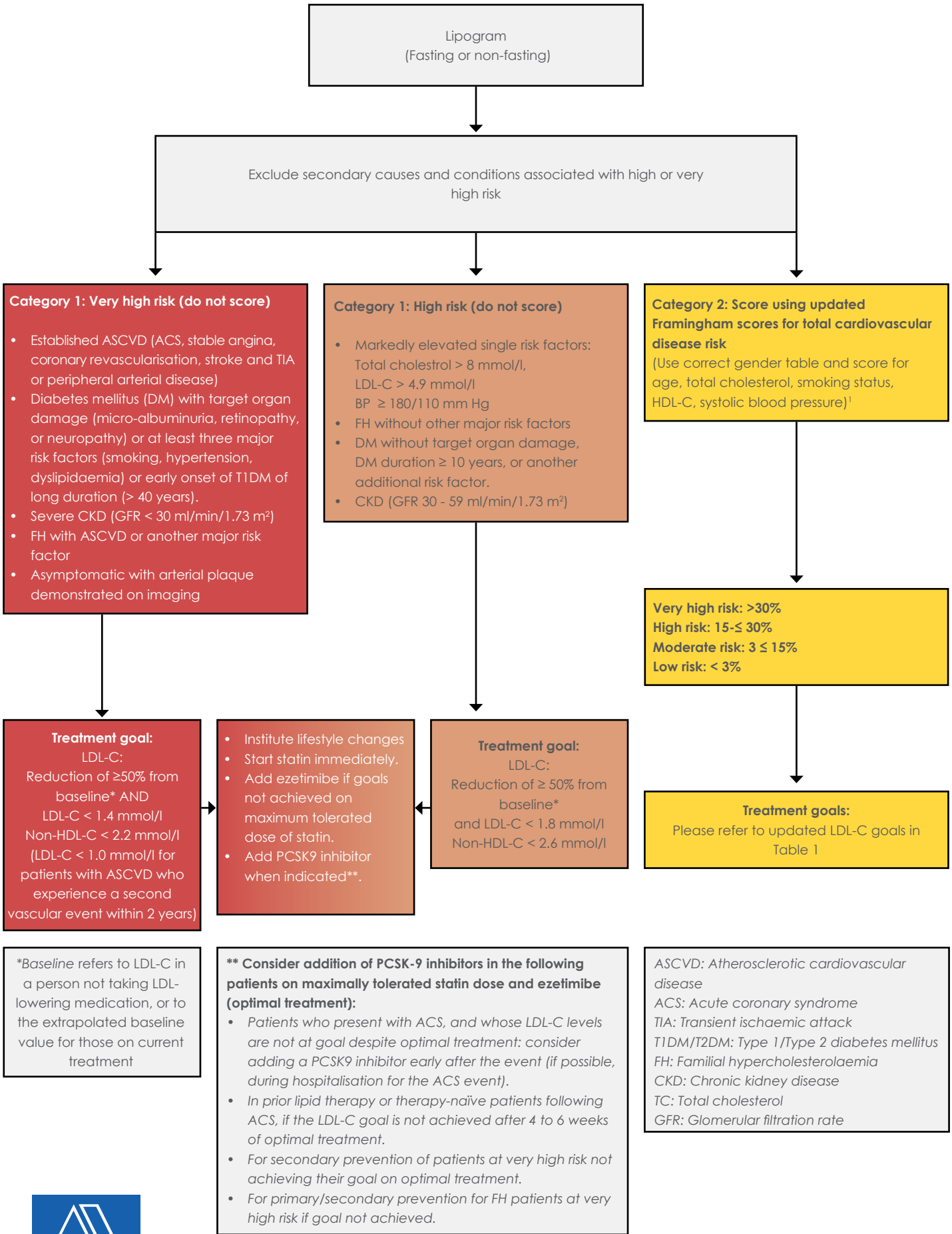
Figure 1: Cardiovascular disease risk stratification and cholesterol targets (Updated 2019 ESC/EAS Lipid Guidelines)



*Baseline refers to LDL-C in a person not taking LDL-lowering medication, or to the extrapolated baseline value for those on current treatment

**** Consider addition of PCSK-9 inhibitors in the following patients on maximally tolerated statin dose and ezetimibe (optimal treatment):**

- *Patients who present with ACS, and whose LDL-C levels are not at goal despite optimal treatment: consider adding a PCSK9 inhibitor early after the event (if possible, during hospitalisation for the ACS event).*
- *In prior lipid therapy or therapy-naïve patients following ACS, if the LDL-C goal is not achieved after 4 to 6 weeks of optimal treatment.*
- *For secondary prevention of patients at very high risk not achieving their goal on optimal treatment.*
- *For primary/secondary prevention for FH patients at very high risk if goal not achieved.*

ASCVD: Atherosclerotic cardiovascular disease
ACS: Acute coronary syndrome
TIA: Transient ischaemic attack
T1DM/T2DM: Type 1/Type 2 diabetes mellitus
FH: Familial hypercholesterolaemia
CKD: Chronic kidney disease
TC: Total cholesterol
GFR: Glomerular filtration rate

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