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Clinical Perspective: Current LDL-cholesterol Goals- Are They Appropriate?

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The lipid targets and goals recommended in both the 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias and the 2016 Joint European Guidelines on Cardiovascular Disease prevention in clinical practice are:

Lipids	
LDL is the primary target	**Very high risk: < 1.8 mmol/L (< 70 mg/dL)**, or a reduction of at least 50% if the baseline is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL).[d] **High risk: < 2.6 mmol/L (< 100 mg/dL),** or a reduction of at least 50% if the baseline is between 2.6 and 5.1 mmol/L (100 and 200 mg/dL). **Low to moderate risk: < 3.0 mmol/L (< 115 mg/dL).**
HDL-C	No target but > 1.0 mmol/L (> 40 mg/dL) in men and > 1.2 mmol/L (> 45 mg/dL) in women indicate lower risk.
Triglycerides	No target but < 1.7 mmol/L (< 150 mg/dL) indicates lower risk and higher levels indicate a need to look for other risk factors.

Since then, several trials, particularly the FOURIER trial of evolocumab and the ODYSSEY trial of alirocumab have indicated that the addition of a PCSK9 inhibitor to a statin, or to those who are statin intolerant, can achieve a further reduction in LDL cholesterol with attendant further reductions in CVD events.

FOURRIER may be summarised:

- 25,982 pts with stable ACVD on background statin randomised to placebo or PCSK9 inhibitor evolocumab. Median follow-up 2.2 years
- LDL lowered to a median of 0.8mmol/L (31 mg/dL)
- Linear reduction in risk with lower LDL cholesterol
- Lowest risk was in the 2,669 subjects in the lowest LDLC category- <0.5mmol/L (20 mg/dL)
- No increase in side effects
- No effect on cognitive function

And ODYSSEY:

- 18,924 patients who were 1-12 months out from an ACS event were randomized, after a run-in phase of 2-16 weeks on high-intensity statin therapy, to PCSK-9 inhibitor alirocumab q2 weeks (n = 9,462) subcutaneously or placebo (n = 9,462). Drug was titrated between 75 and 150 mg to keep the low-density lipoprotein cholesterol (LDL-C) between 25 and 50 mg/dl, but above 15 mg/dl.
- All on high intensity statins, or statin intolerant
- The primary outcome, major adverse cardiac events (MACE), for alirocumab vs. placebo, was 9.5% vs. 11.1%, hazard ratio (HR) 0.85, 95% confidence interval 0.78-0.93, p = 0.0003.

Arising, we will discuss if the LDL cholesterol goal should be revised to-

- 1.8 mmol/l (70 mg/dl)
- 1.5 (60)
- 1.0 (40)
- 0.5 (20)

Meta-analyses indicate a linear reduction in CVD risk associated with LDL lowering, with no suggestion of a J-shaped association or of increased side-effects at very low levels. Nevertheless, while the relative risk reduction remains constant, the absolute reduction in risk is of necessity much less in lower risk subjects, and the price of PCSK9 inhibitors remains very high.