Clinical Chemistry
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PEARLS OF
LABORATORY MEDICINE

Management of Dyslipidemia: The European Approach

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Michel R. Langlois
AZ St-Jan Bruges & Ghent University, Belgium

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Introduction

- Catapano AL, Reiner Z, De Backer G, Graham I, Taskinen MR, Wiklund O, et al. ESC/EAS guidelines for the management of dyslipidaemias; the Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). Atherosclerosis 2011;217:3–46

Stepwise risk assessment and management approach

1. Initial investigations
2. Cardiovascular Disease (CVD) risk classification
3. Risk score adjustment
4. Preventive intervention strategies
5. Follow-up of lipid-lowering therapy

1. Initial lipid profiling

- Total cholesterol (TC)
- Triglycerides (TG)
- HDL-cholesterol
- LDL-cholesterol (measured or calculated)
- Glucose

- Take average of ≥ 2 fasting measurements with an interval of 1-2 weeks (12 weeks after acute major illness, surgery or trauma)

- Indications: diabetes type 2, CVD, hypertension, smoking, BMI >30 kg/m^2, waist circumference ≥94 (men) ≥80 (women), family history of CVD or dyslipidemia, chronic inflammatory disease, chronic kidney disease (CKD), men >40 y and women >50 y.

2. CVD risk classification

- SCORE (Systematic COronary Risk Evaluation)
  - Age
  - Gender
  - Systolic blood pressure (mmHg)
  - TC (mmol/l or mg/dl)
  - Smoking
- SCORE = 10-y risk (%) of CVD death
- SCORE calculation: *www.heartscore.org*

Perk J, De Backer G, Gohlke H, et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). Eur Heart J. 2012;33:1635-701

CVD Risk Classification

- **Very high risk**
  - Documented CVD, type 2 diabetes, type 1 diabetes with target organ damage/microalbuminuria, CKD (GFR <30 ml/min/1.73 m^2)
  - SCORE ≥10%
- **High risk**
  - Familial dyslipidemia, severe hypertension
  - SCORE ≥5% and<10%
- **Moderate risk**
  - SCORE ≥1% and<5%.
  - This risk can be further modified by HDL-C
- **Low risk**
  - SCORE <1%.

Catapano AL, Reiner Z, De Backer G, et al. ESC/EAS guidelines for the management of dyslipidaemias. Atherosclerosis 2011;217:3–46

3. Risk adjustment & reclassification

- **Consider high risk in *moderate-risk* patients with:**
  - family history of premature CVD (men <50 y, women <60 y); increases SCORE x2.0 in men and x1.7 in women
  - central obesity, sedentary lifestyle, low socio-economic status, impaired renal function, familial hypercholesterolemia (FH) ,
    elevated apoB, Lp(a), hs-CRP, hyperhomocysteinemia
- **HDL-multipliers of SCORE**

SCORE-modifying effect of HDL-C

Men

HDL range (mg/dl)	Factor X
< 23	1,6
≥ 23 < 27	1,4
≥ 27 < 31	1,3
≥ 31 < 36	1,2
≥ 36 < 41	1,1
≥ 41 < 47	1
≥ 47 < 55	0,9
≥ 55 < 63	0,8
≥ 63 < 72	0,7
≥ 72 < 83	0,6
≥ 83	0,5

Women

< 23	2,4
≥ 23 < 26	2,2
≥ 26 < 28	2
≥ 28 < 30	1,9
≥ 30 < 33	1,8
≥ 33 < 37	1,7
≥ 37 < 40	1,5
≥ 40 < 43	1,4
≥ 43 < 46	1,3
≥ 46 < 49	1,2
≥ 49 < 53	1,1
≥ 53 < 56	1
≥ 56 < 60	0,9
≥ 60 < 65	0,8
≥ 65 < 69	0,7
≥ 69 < 74	0,6
≥ 74 < 80	0,5
≥ 80	0,4

Descamps OS, et al. A simple multiplier to calculate the impact of HDL cholesterol on cardiovascular risk estimation using SCORE. Atherosclerosis 2012;222:564-6

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4. Intervention strategies

- Lifestyle modifications at all levels of risk
- SCORE ≥10 or very high-risk:
  - Immediate drug intervention if **LDL-C ≥ 70 mg/dl**
- SCORE ≥5 to <10 or high-risk:
  - Immediate drug intervention if **LDL-C ≥ 100 mg/dl**
- SCORE ≥1 to <5 or moderate-risk:
  - Consider drug intervention if **LDL-C ≥ 115 mg/dl**

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Primary treatment targets

- Very high-risk:
  - LDL-C <70 mg/dl (< 1.8 mmol/l)
  - or ≥50% reduction in LDL-C
- High-risk:
  - LDL-C <100 mg/dl (< 2.5 mmol/l)
- Moderate-risk:
  - LDL-C <115 mg/dl (< 3.0 mmol/l)

Secondary treatment targets

- **Non-HDL-cholesterol**
  - TC – HDL-C
  - Represents cholesterol in LDL, IDL, VLDL, and Lp(a)
- **ApoB**
  - Atherogenic particle number

Misleading LDL-cholesterol

- **Analytical**
  - Direct LDL-C: method bias ~hyperTG
  - Calculated LDL-C: inaccurate when TG>200 mg/dl and HDL-C method bias
- **Biological**
  - Residual (on-treatment) dyslipidemia
  - Small dense LDL subclass phenotype

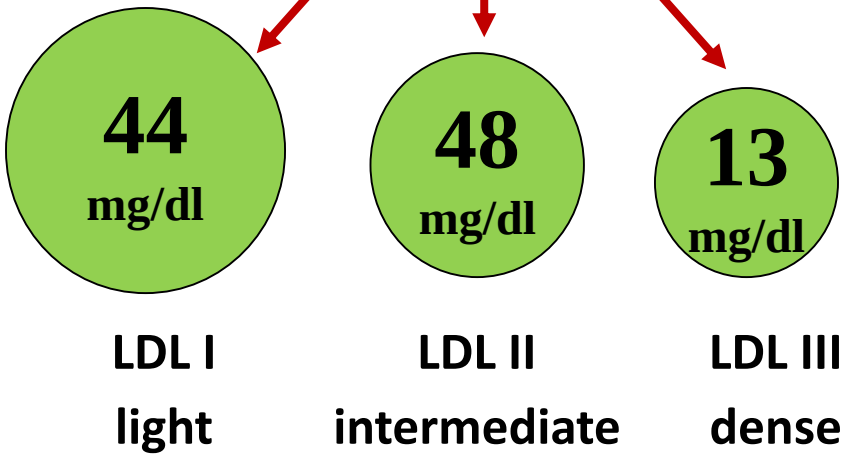
Langlois MR. Lab approaches for predicting and managing the risk of CVD. Clin Chem Lab Med. 2012;50:1169-81.

Misleading LDL-cholesterol

LDL cholesterol 105 mg/dl

Triglycerides 140 mg/dl

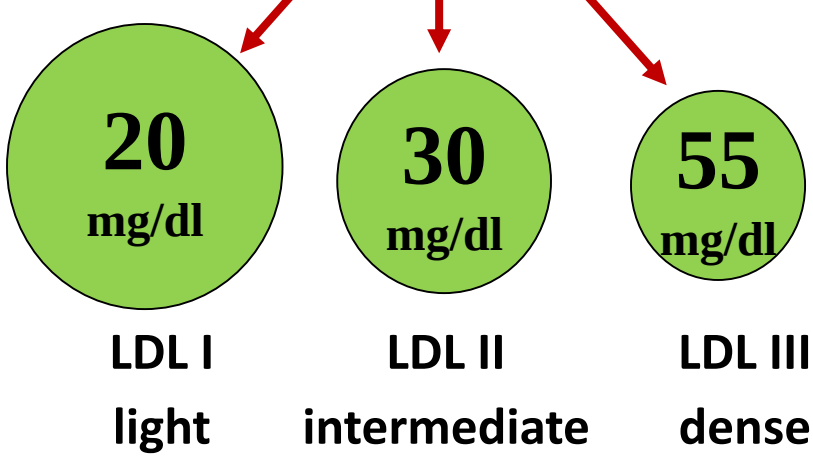
LDL cholesterol distribution



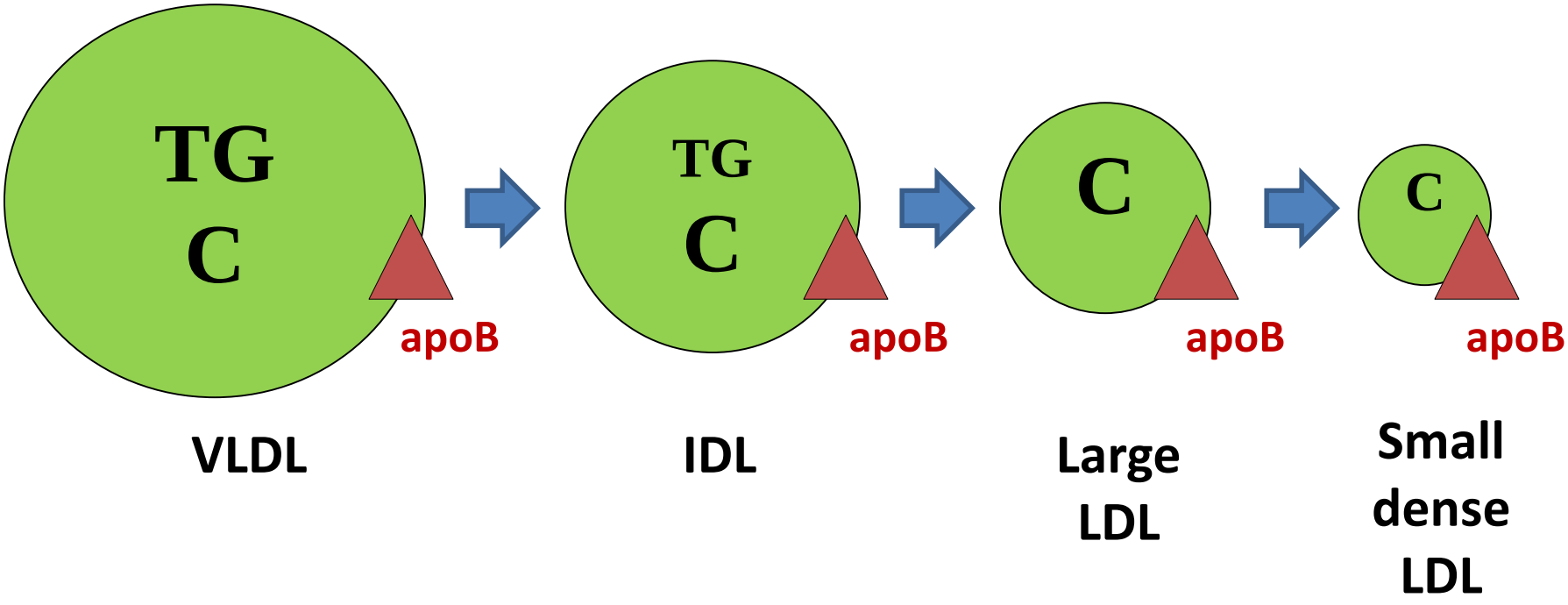
LDL cholesterol 105 mg/dl

Triglycerides 201 mg/dl

LDL cholesterol distribution



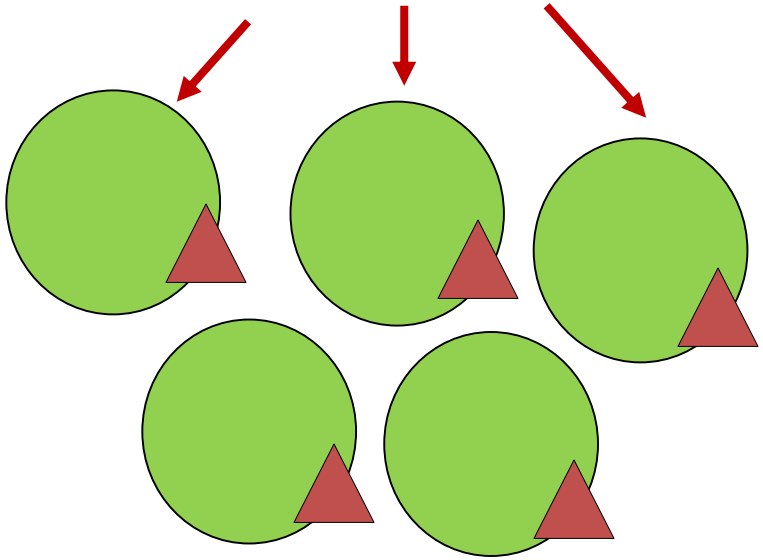
ApoB : atherogenic particle number

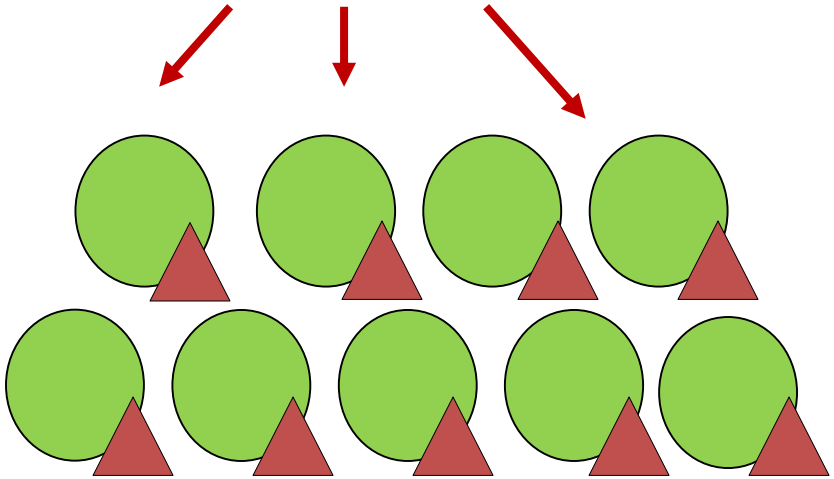


TG: triglycerides C: cholesterol

Misleading LDL-cholesterol

LDL cholesterol 115 mg/dl Triglycerides 120 mg/dl	LDL cholesterol 115 mg/dl Triglycerides 290 mg/dl
Apo B 0.8 g/l	Apo B 1.4 g/l





Treatment targets

Risk SCORE	LDL-C mg/dl (mmol/l)	Non-HDL-C * mg/dl (mmol/l)	ApoB * mg/dl (g/l)
Very high	< 70 (1.8)	< 100 (2.6)	< 80 (0.8)
High	< 100 (2.5)	< 130 (3.3)	< 100 (1.0)

* Primary target in cases of hypertriglyceridemia >400 mg/dl (invalid LDL calculation); secondary target in patients with combined dyslipidemia, metabolic syndrome, type 2 diabetes, or chronic kidney disease.

5. Follow-up of lipid-lowering drugs

- Lipid tests
  - Every 8±4 wks after starting drug treatment
  - Annually after reaching target
- Liver enzymes (ALT)
  - Before and after 8 wks treatment; annually thereafter
  - Stop statin or reduce dose if ALT ≥3xURL
- Myopathy (CK)
  - Before treatment and in case of on-treatment myalgia
  - Stop statin and check renal function if CK ≥5xURL

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Conclusions

- **Testing and treating LDL-C is not enough**
  - Non-HDL-C or apoB testing in case of hypertriglyceridemia (unreliable LDL-C)
  - Non-HDL-C or apoB therapeutic targeting to reduce residual (on-treatment) CVD risk
- **CVD risk management requires "clinical added value" of laboratory medicine**
  - Pre-analytical: test selection
  - Post-analytical: test reporting (risk cutpoints, targets)
  - Guiding clinicians in risk scoring & targeting strategies

References

- Catapano AL, Reiner Z, De Backer G, Graham I, Taskinen MR, Wiklund O, et al. ESC/EAS guidelines for the management of dyslipidaemias; the Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). Atherosclerosis 2011;217:3–46

- Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Eur Heart J. 2012;33:1635-701

- Descamps OS, Cooney MT, De Backer G, Graham I. A simple multiplier to calculate the impact of HDL cholesterol on cardiovascular risk estimation using SCORE. Atherosclerosis 2012;222:564-6

- Langlois MR. Laboratory approaches for predicting and managing the risk of cardiovascular disease: postanalytical opportunities of lipid and lipoprotein testing. Clin Chem Lab Med. 2012;50:1169-8

Disclosures/Potential Conflicts of Interest

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