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Standardising lipid testing and reporting in the United Kingdom; a joint statement by HEART UK and The Association for Laboratory Medicine

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Article

Citation (please note it is advisable to refer to the publisher's version if you intend to cite from this work)

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(If triglycerides ≥1.5 mmol/L recommend Non-HDL-c or Apolipoprotein B for screening)

Table 1. Current lipid targets used in the UK and in selected international guidelines

*Figure 1. A. Composition of lipoprotein particles. B. Underlying composition of analytes measured or calculated in a lipid profile in a fasting and non-fasting state.*HDL subclasses include HDL-2a, HDL-2b, HDL-3a, HDL-3b, HDL-3c, pre-beta1-HDL, and pre-beta2-HDL. **ApoB48 can cross react with ApoB assay but since the levels of these particles are much lower in concentration than ApoB100 containing lipoproteins, the major contributors to an ApoB result are Lp(a), LDL, VLDL and IDL. *** IDL is not a significant contributor to a standard triglyceride measurement but can be an important particle measured in the hypertriglyceridaemia seen with dysbetalipoproteinaemia. HDL-c – High Density Lipoprotein cholesterol, Lp(a) lipoprotein (a), LDL -c – low density lipoprotein cholesterol, refers to a calculated LDL, IDL intermediate density lipoprotein, VLDL - very low density lipoprotein, CM chylomicron, CM remnants – Chylomicron remnants*

Table 2. Instances when a fasting sample should be considered[40]. For Sampson calculated LDL-c, fasting and non-fasting samples can be used. Fasting is preferred but values may be reported where TG <9.0 mmol/L.

Table 3. Pre-analytical factors to consider when performing a lipid profile. TGs = triglycerides, TC = total cholesterol

Table 4. Secondary causes of dyslipidaemias to be considered when performing a lipid profile

Table 5. Proposed testing intervals for lipid profiles

The wording used in the following and subsequent recommendations denotes the current level of evidence to support that recommendation as per the 2016 ACC/AHA Clinical Guideline Recommendation Classification System [66]

Table 6. Clinical decision thresholds for HDL

see Table 2 in

Section 3.[40]

Table 7. Clinical decision thresholds for triglycerides. Fasting target (F), Non-fasting target (NF). In those with diabetes and a typical picture of raised triglycerides and low HDL, there may be benefit to additional triglyceride lowering over and above simply statin therapy alone.[12]

$$LDL-c=$$

$$\frac{\text{Total cholesterol}}{0.948}-\frac{\text{HDL-c}}{0.971}-\left(\frac{\text{triglycerides}}{3.74}+\frac{\text{triglycerides}\times\text{non-HDL-c}}{24.16}-\frac{\text{triglycerides}^2}{79.36}\right)-0.244$$

Box 1 – Sampson-NIH equation (mmol/L)

~

Table 8. Adapted from HEART UK recommendation for Lp(a) measurement in those with the following characteristics

Table 9. The risk of cardiovascular disease based on classified Lp(a) concentration

Table 10. Recommended thresholds for laboratories to flag results and suggested comments.

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DP = decimal place

European heart journal

Circulation

JAMA : the journal of the American Medical Association

JAMA

The Lancet

Eur Heart J

Curr Opin Lipidol

Lancet

Circulation

European heart journal

Annals of Clinical Biochemistry

Diabetic Medicine

Current atherosclerosis reports

The Lancet Regional Health – Europe

Clinical chemistry

Heart

The Journal of Clinical Endocrinology & Metabolism

Curr Opin Lipidol

JAMA : the journal of the American Medical Association

JAMA Cardiol

Heart

European heart journal

Canadian Journal of Cardiology

European heart journal

Clinica chimica acta; international journal of clinical chemistry

Circulation

Circulation

JAMA internal medicine

Atherosclerosis

European heart journal

Bmj

Atherosclerosis

European journal of cardiovascular prevention and rehabilitation : official journal of the European Society of Cardiology, Working Groups on Epidemiology & Prevention and Cardiac Rehabilitation and Exercise Physiology

Atherosclerosis

Annals of clinical biochemistry

European journal of obstetrics, gynecology, and reproductive biology

American journal of obstetrics and gynecology

Journal of lipid research

Advances in laboratory medicine

EXCLI journal

Annals of clinical biochemistry

Kidney international

Lancet

Trends in endocrinology and metabolism: TEM

Arterioscler Thromb Vasc Biol

Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences

Gastroenterology

Annals of the New York Academy of Sciences

Cureus

Metabolites

American journal of kidney diseases : the official journal of the National Kidney Foundation

Journal of lipid research

JAMA : the journal of the American Medical Association

Ontario health technology assessment series

Ann Intern Med

Circulation

Jama

Uptodate

Am J Cardiol

Eur J Clin Chem Clin Biochem

ACB analyte

Atherosclerosis

Clinica Chimica Acta

Annals of clinical biochemistry

Clinical chemistry

The Lancet

European heart journal

Curr Opin Lipidol

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Circulation

Annals of internal medicine

Arterioscler Thromb Vasc Biol

Circulation

Glob Cardiol Sci Pract

New England Journal of Medicine

New England Journal of Medicine

JAMA : the journal of the American Medical Association

European heart journal

Journal of the American Heart Association

Journal of Clinical Lipidology

Current Opinion in Lipidology

Circulation

Circulation

The Journal of Clinical Endocrinology & Metabolism

Progress in cardiovascular diseases

Canadian Journal of Cardiology

Clinical chemistry

Clinical chemistry

Clinical chemistry

Annals of internal medicine

Frontiers in endocrinology

Lancet

Circulation

Circulation

Nature Reviews Genetics

Circulation

New England Journal of Medicine

Cardiovascular diabetology

Atherosclerosis

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JAMA : the journal of the American Medical Association

JAMA internal medicine

Clinical chemistry

Clinica Chimica Acta

Practical Laboratory Medicine

Atherosclerosis Plus

Clinical chemistry

New England Journal of Medicine

The Journal of clinical endocrinology and metabolism

BMC endocrine disorders

Lipids Health Dis

Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists

Arteriosclerosis, Thrombosis, and Vascular Biology

New England Journal of Medicine

PloS one

Atherosclerosis Supplements

Clinical chemistry

Clinical chemistry

Journal of clinical pathology

JAMA Network Open

Journal of clinical lipidology

Clinical Chemistry and Laboratory Medicine (CCLM)

Clinical chemistry

Atherosclerosis

Curr Opin Lipidol

Journal of Clinical Lipidology

European heart journal

European heart journal

J Am Coll Cardiol

Clinical chemistry

Jama

J Lipid Res

European heart journal

European Journal of Preventive Cardiology

International journal of rheumatology

Arterioscler Thromb Vasc Biol

European heart journal

Atherosclerosis

Annals of clinical biochemistry

JAMA cardiology

Journal of lipid research

Curr Opin Lipidol

J Am Heart Assoc

JAMA cardiology

J Am Coll Cardiol

Journal of Clinical Lipidology

Lipids in Health and Disease

J Clin Lipidol

Clinical chemistry

Frontiers in genetics

Clinical chemistry

Clinical Lipidology

Journal of the American Heart Association

The Journal of biological chemistry

Lancet

International journal of cardiology

Lancet

Clinical chemistry

Biochimica et biophysica acta Molecular and cell biology of lipids

Circulation

Atherosclerosis

Clinical chemistry and laboratory medicine

Ann Intern Med

The Journal of clinical endocrinology and metabolism

Paediatrics and Child Health

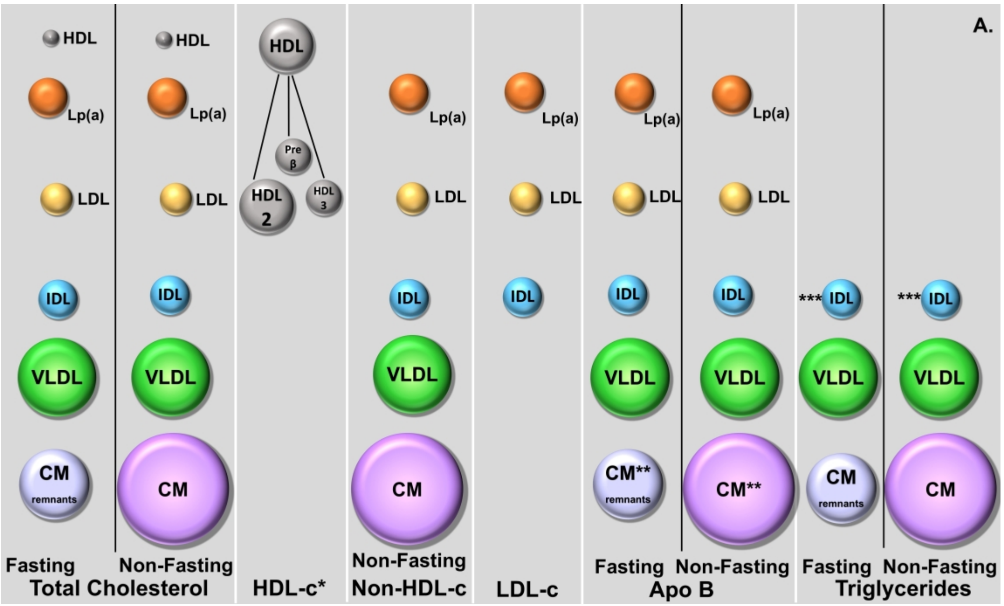
Journal of Clinical Lipidology

Critical reviews in clinical laboratory sciences

Clinical chemistry

Clinica chimica acta; international journal of clinical chemistry

Clinical chemistry and laboratory medicine



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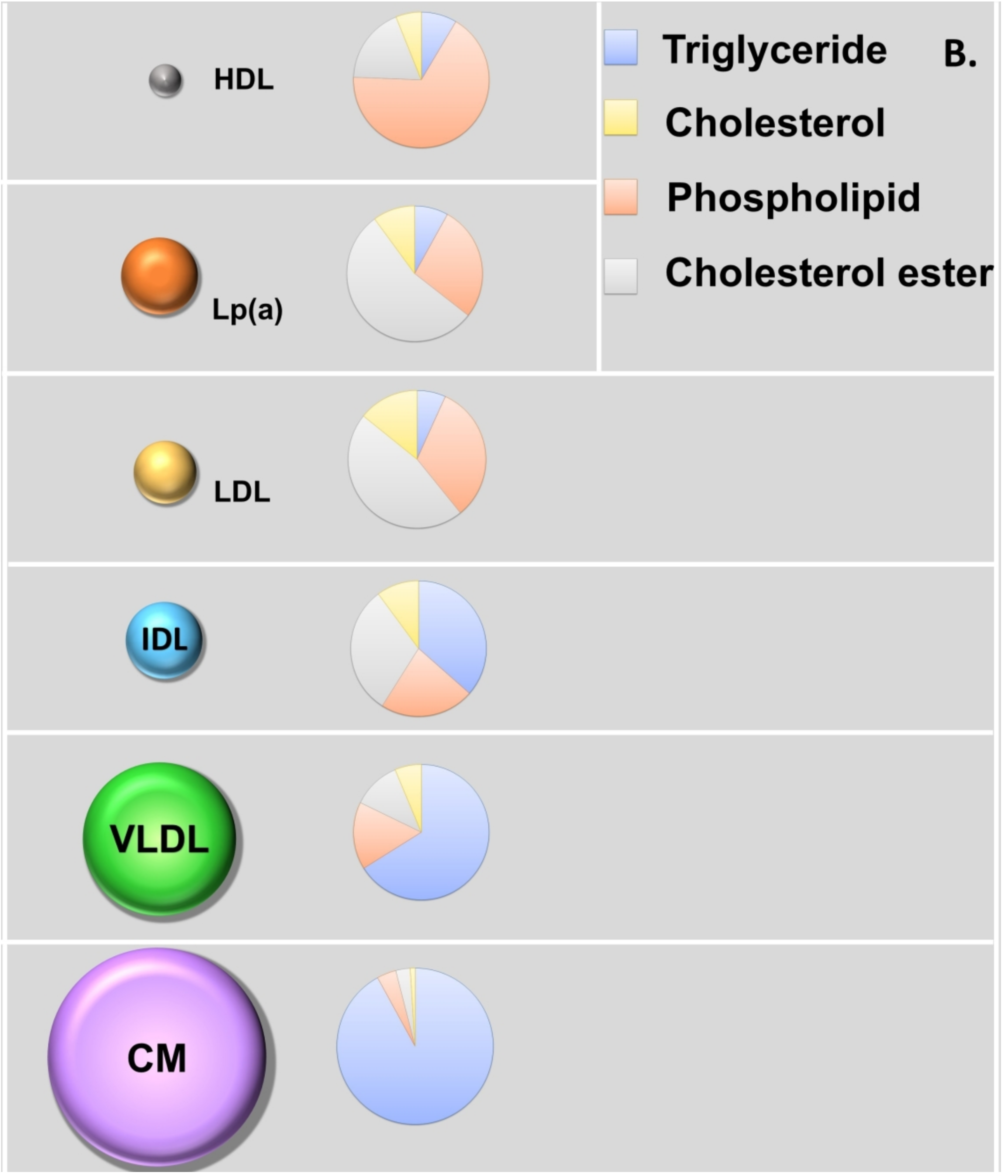

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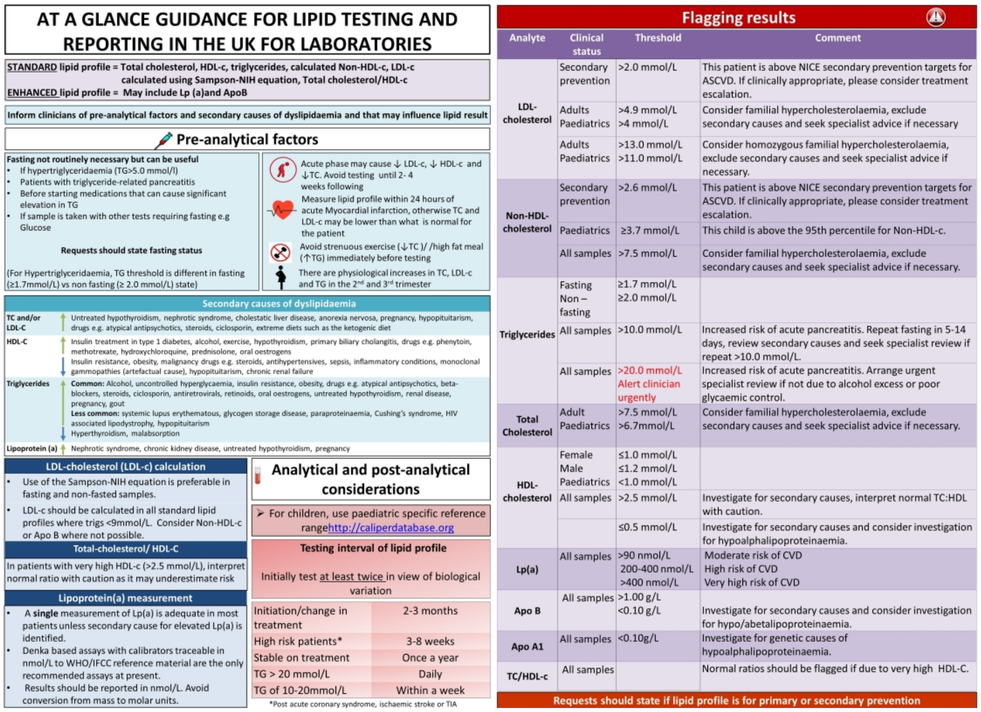

AT A GLANCE GUIDANCE FOR LIPID TESTING AND REPORTING IN THE UK FOR LABORATORIES

STANDARD lipid profile = Total cholesterol, HDL-c, triglycerides, calculated Non-HDL-c, LDL-c calculated using Sampson-NIH equation, Total cholesterol/HDL-c

ENHANCED lipid profile = May include Lp (a)and ApoB

Inform clinicians of pre-analytical factors and secondary causes of dyslipidaemia and that may influence lipid result

Pre-analytical factors

Fasting not routinely necessary but can be useful

- If hypertriglyceridaemia (TG>5.0 mmol/l)
- Patients with triglyceride-related pancreatitis
- Before starting medications that can cause significant elevation in TG
- If sample is taken with other tests requiring fasting e.g Glucose

Requests should state fasting status

(For Hypertriglyceridaemia, TG threshold is different in fasting (≥1.7mmol/L) vs non fasting (≥ 2.0 mmol/L) state)

Acute phase may cause ↓ LDL-c, ↓ HDL-c and ↓TC. Avoid testing until 2- 4 weeks following

Measure lipid profile within 24 hours of acute Myocardial infarction, otherwise TC and LDL-c may be lower than what is normal for the patient

Avoid strenuous exercise (↓TC)/ /high fat meal (↑TG) immediately before testing

There are physiological increases in TC, LDL-c and TG in the 2nd and 3rd trimester

Secondary causes of dyslipidaemia

TC and/or LDL-C	↑	Untreated hypothyroidism, nephrotic syndrome, cholestatic liver disease, anorexia nervosa, pregnancy, hypopituitarism, drugs e.g. atypical antipsychotics, steroids, ciclosporin, extreme diets such as the ketogenic diet
HDL-C	↑	Insulin treatment in type 1 diabetes, alcohol, exercise, hypothyroidism, primary biliary cholangitis, drugs e.g. phenytoin, methotrexate, hydroxychloroquine, prednisolone, oral oestrogens
	↓	Insulin resistance, obesity, malignancy drugs e.g. steroids, antihypertensives, sepsis, inflammatory conditions, monoclonal gammopathies (artefactual cause), hypopituitarism, chronic renal failure
Triglycerides	↑	**Common:** Alcohol, uncontrolled hyperglycaemia, insulin resistance, obesity, drugs e.g. atypical antipsychotics, beta-blockers, steroids, ciclosporin, antiretrovirals, retinoids, oral oestrogens, untreated hypothyroidism, renal disease, pregnancy, gout **Less common:** systemic lupus erythematous, glycogen storage disease, paraproteinaemia, Cushing's syndrome, HIV associated lipodystrophy, hypopituitarism
	↓	Hyperthyroidism, malabsorption
Lipoprotein (a)	↑	Nephrotic syndrome, chronic kidney disease, untreated hypothyroidism, pregnancy

LDL-cholesterol (LDL-c) calculation

- Use of the Sampson-NIH equation is preferable in fasting and non-fasted samples.
- LDL-c should be calculated in all standard lipid profiles where trigs <9mmol/L. Consider Non-HDL-c or Apo B where not possible.

Total-cholesterol/ HDL-C

In patients with very high HDL-c (>2.5 mmol/L), interpret normal ratio with caution as it may underestimate risk

Lipoprotein(a) measurement

- A **single** measurement of Lp(a) is adequate in most patients unless secondary cause for elevated Lp(a) is identified.
- Denka based assays with calibrators traceable in nmol/L to WHO/IFCC reference material are the only recommended assays at present.
- Results should be reported in nmol/L. Avoid conversion from mass to molar units.

Analytical and post-analytical considerations

- For children, use paediatric specific reference rangehttp://caliperdatabase.org

Testing interval of lipid profile

Initially test at least twice in view of biological variation

Initiation/change in treatment	2-3 months
High risk patients*	3-8 weeks
Stable on treatment	Once a year
TG > 20 mmol/L	Daily
TG of 10-20mmol/L	Within a week

*Post acute coronary syndrome, ischaemic stroke or TIA

Flagging results

Analyte	Clinical status	Threshold	Comment
LDL-cholesterol	Secondary prevention	>2.0 mmol/L	This patient is above NICE secondary prevention targets for ASCVD. If clinically appropriate, please consider treatment escalation.
	Adults Paediatrics	>4.9 mmol/L >4 mmol/L	Consider familial hypercholesterolaemia, exclude secondary causes and seek specialist advice if necessary
	Adults Paediatrics	>13.0 mmol/L >11.0 mmol/L	Consider homozygous familial hypercholesterolaemia, exclude secondary causes and seek specialist advice if necessary.
Non-HDL-cholesterol	Secondary prevention	>2.6 mmol/L	This patient is above NICE secondary prevention targets for ASCVD. If clinically appropriate, please consider treatment escalation.
	Paediatrics	≥3.7 mmol/L	This child is above the 95th percentile for Non-HDL-c.
	All samples	>7.5 mmol/L	Consider familial hypercholesterolaemia, exclude secondary causes and seek specialist advice if necessary.
Triglycerides	Fasting Non – fasting	≥1.7 mmol/L ≥2.0 mmol/L	
	All samples	>10.0 mmol/L	Increased risk of acute pancreatitis. Repeat fasting in 5-14 days, review secondary causes and seek specialist review if repeat >10.0 mmol/L.
	All samples	>20.0 mmol/L Alert clinician urgently	Increased risk of acute pancreatitis. Arrange urgent specialist review if not due to alcohol excess or poor glycaemic control.
Total Cholesterol	Adult Paediatrics	>7.5 mmol/L >6.7mmol/L	Consider familial hypercholesterolaemia, exclude secondary causes and seek specialist advice if necessary.
HDL-cholesterol	Female Male Paediatrics	≤1.0 mmol/L ≤1.2 mmol/L <1.0 mmol/L	
	All samples	>2.5 mmol/L	Investigate for secondary causes, interpret normal TC:HDL with caution.
		≤0.5 mmol/L	Investigate for secondary causes and consider investigation for hypoalphalipoproteinaemia.
Lp(a)	All samples	>90 nmol/L 200-400 nmol/L >400 nmol/L	Moderate risk of CVD High risk of CVD Very high risk of CVD
Apo B	All samples	>1.00 g/L <0.10 g/L	 Investigate for secondary causes and consider investigation for hypo/abetalipoproteinaemia.
Apo A1	All samples	<0.10g/L	Investigate for genetic causes of hypoalphalipoproteinaemia.
TC/HDL-c	All samples		Normal ratios should be flagged if due to very high HDL-C.

Requests should state if lipid profile is for primary or secondary prevention

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