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CURRENT OPINION

Fasting is not routinely required for determination of a lipid profile: clinical and laboratory implications including flagging at desirable concentration cut-points—a joint consensus statement from the European Atherosclerosis Society and European Federation of Clinical Chemistry and Laboratory Medicine

Børge G. Nordestgaard[1]*, Anne Langsted[1], Samia Mora[2], Genovefa Kolovou[3], Hannsjörg Baum[4], Eric Bruckert[5], Gerald F. Watts[6], Grazyna Sypniewska[7], Olov Wiklund[8], Jan Borén[8], M. John Chapman[9], Christa Cobbaert[10], Olivier S. Descamps[11], Arnold von Eckardstein[12], Pia R. Kamstrup[1], Kari Pulkki[13], Florian Kronenberg[14], Alan T. Remaley[15], Nader Rifai[16], Emilio Ros[17,18], and Michel Langlois[19,20], for the European Atherosclerosis Society (EAS) and the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) joint consensus initiative

Table 1 Key recommendations

Fasting is not required routinely for assessing the plasma lipid profile
When non-fasting plasma triglyceride concentration >5 mmol/L (440 mg/dL), consideration should be given to repeating the lipid profile in the fasting state
Laboratory reports should flag abnormal values based on desirable concentration cut-points
Life-threatening or extremely high concentrations should trigger an immediate referral to a lipid clinic or to a physician with special interest in lipids

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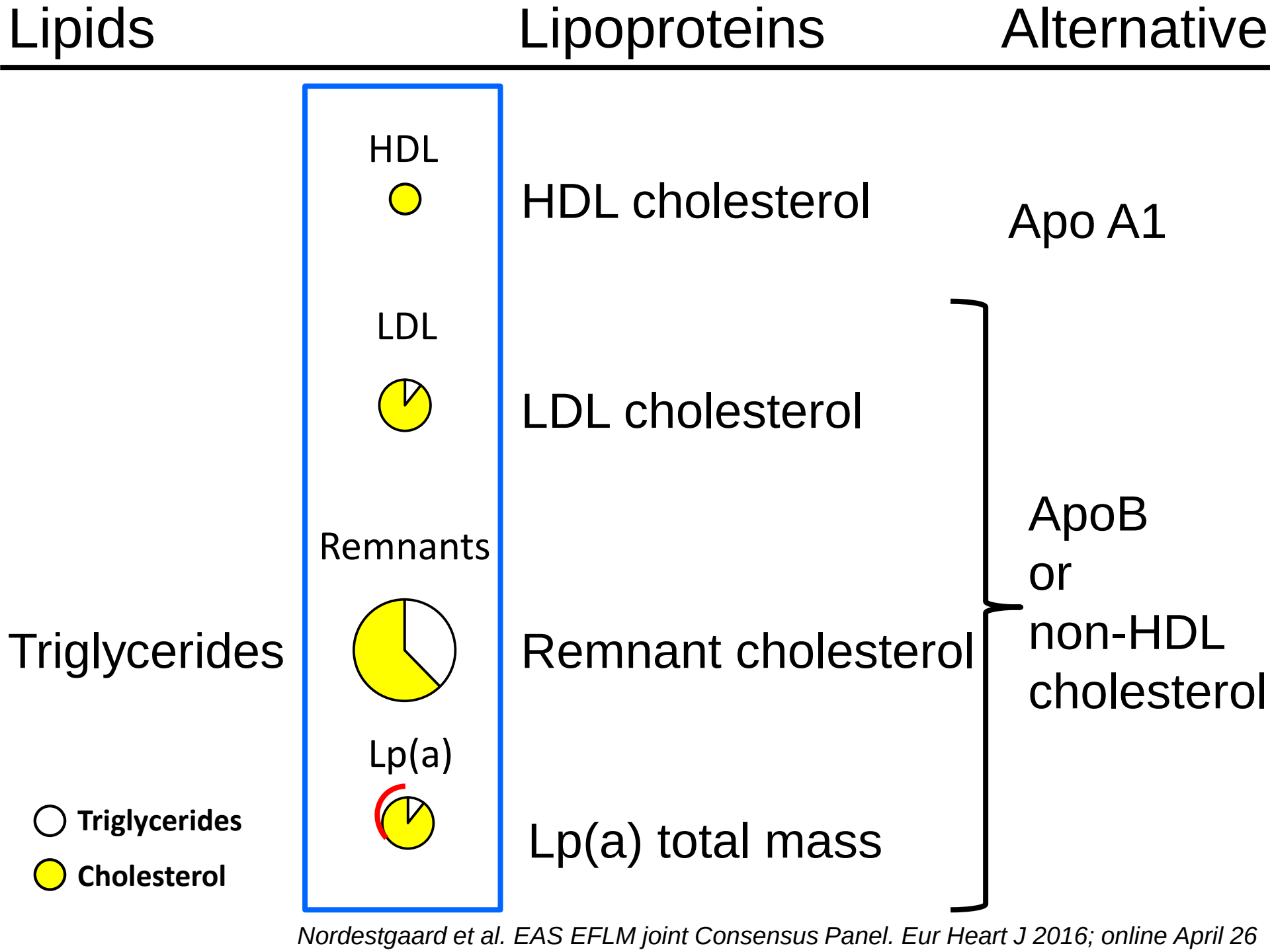

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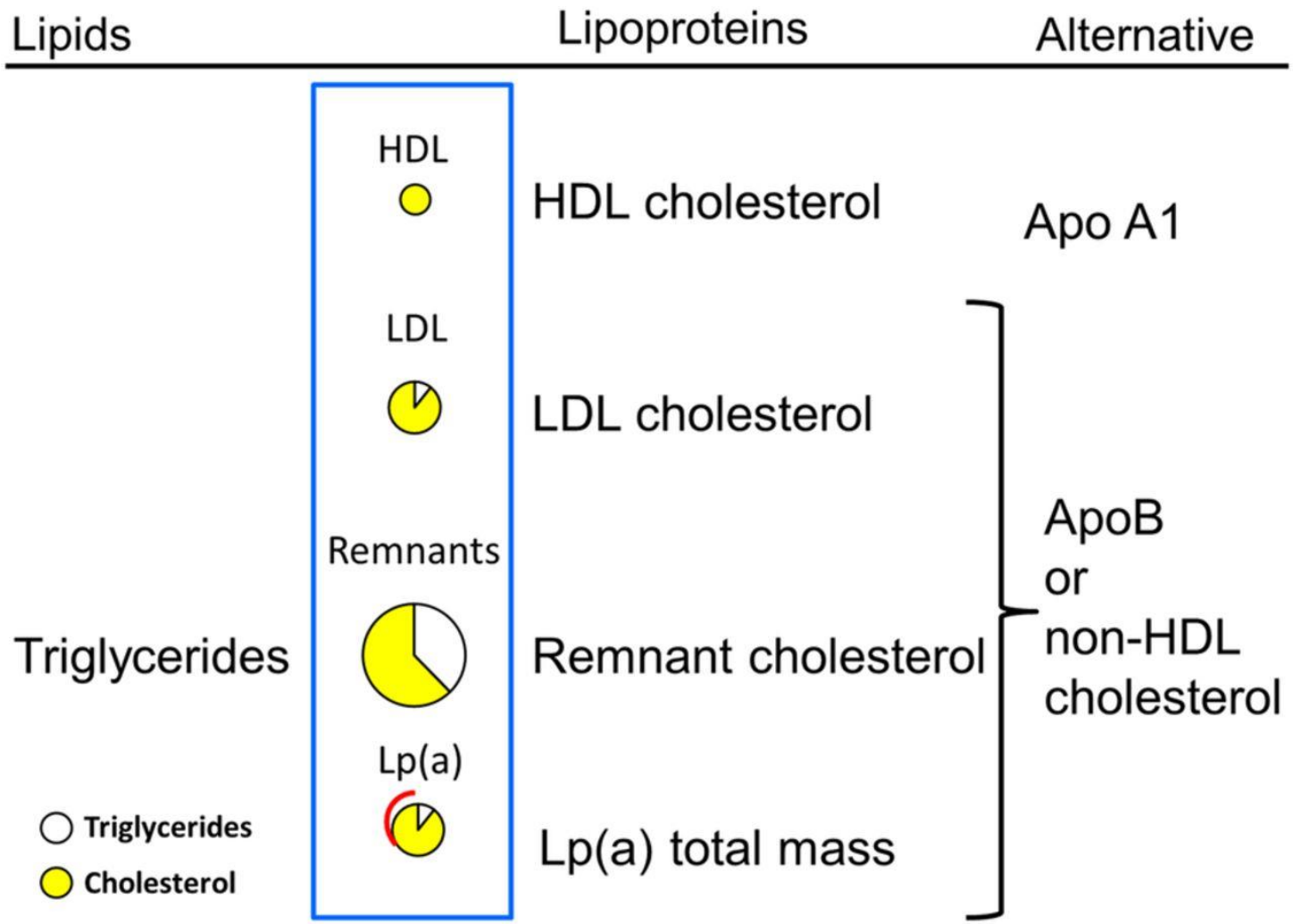
Lipids, lipoproteins, and apolipoproteins as part of standard and expanded lipid profiles.



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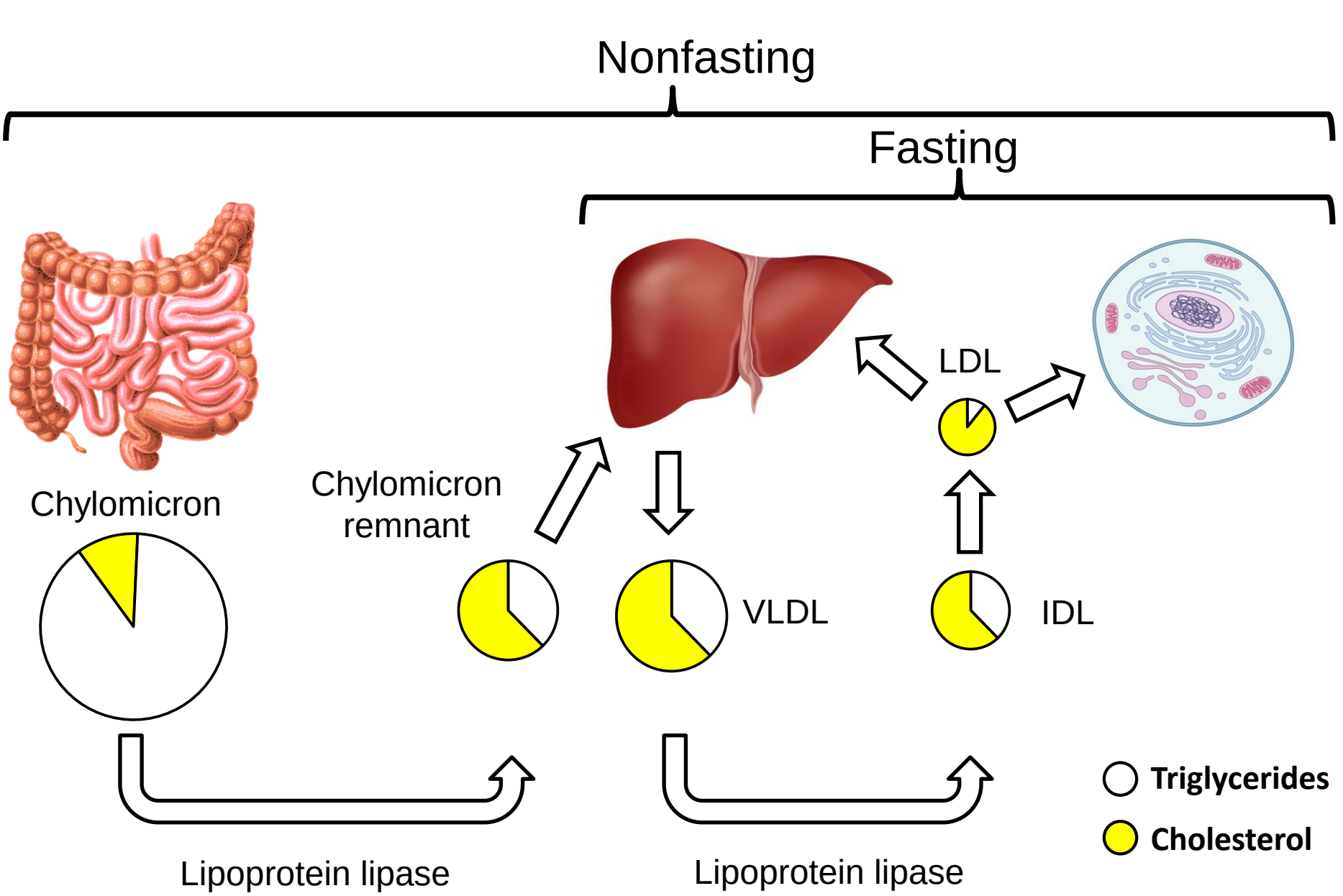

Nordestgaard 2016

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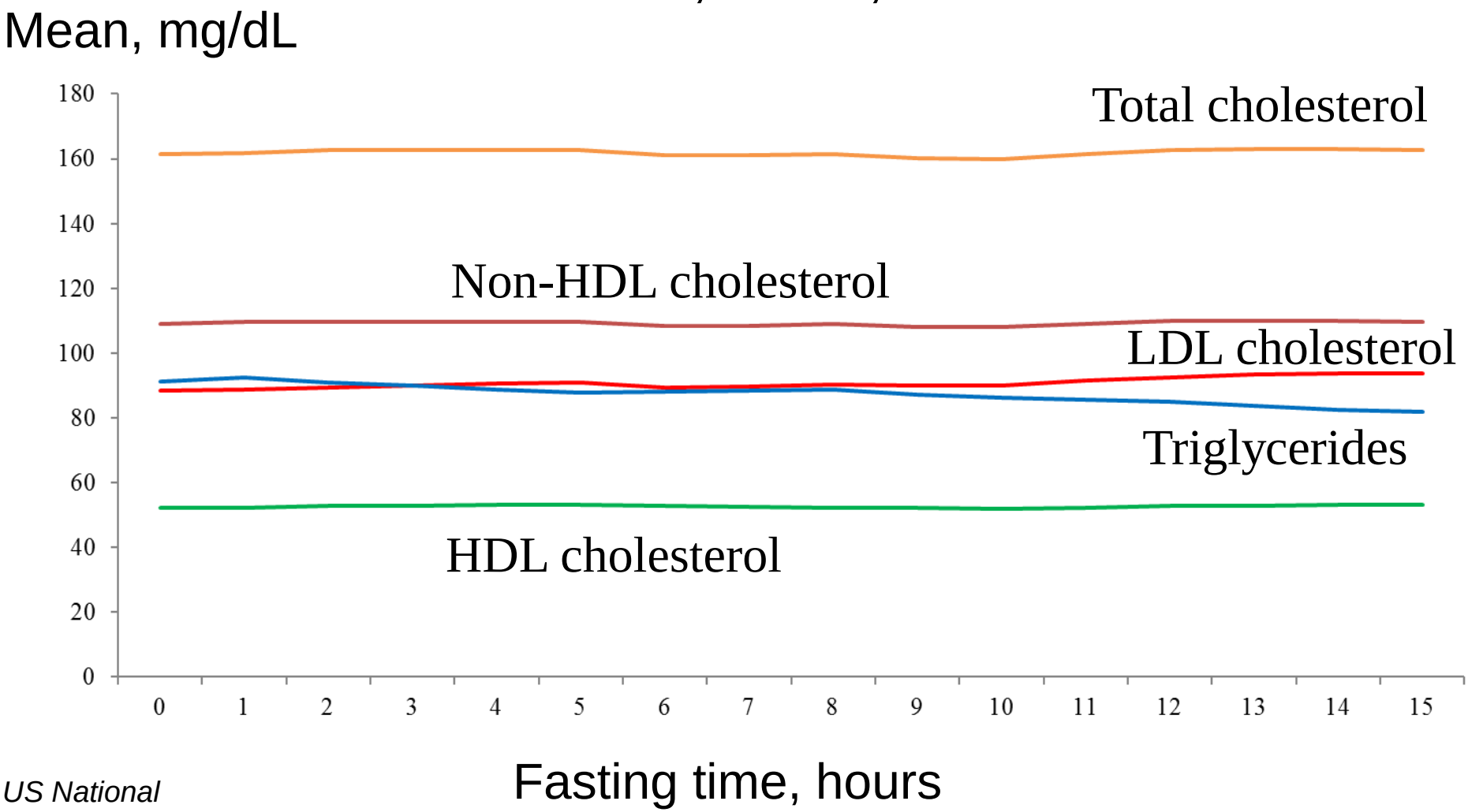
Children, N=12,744



US National Health and Nutrition Examination Survey

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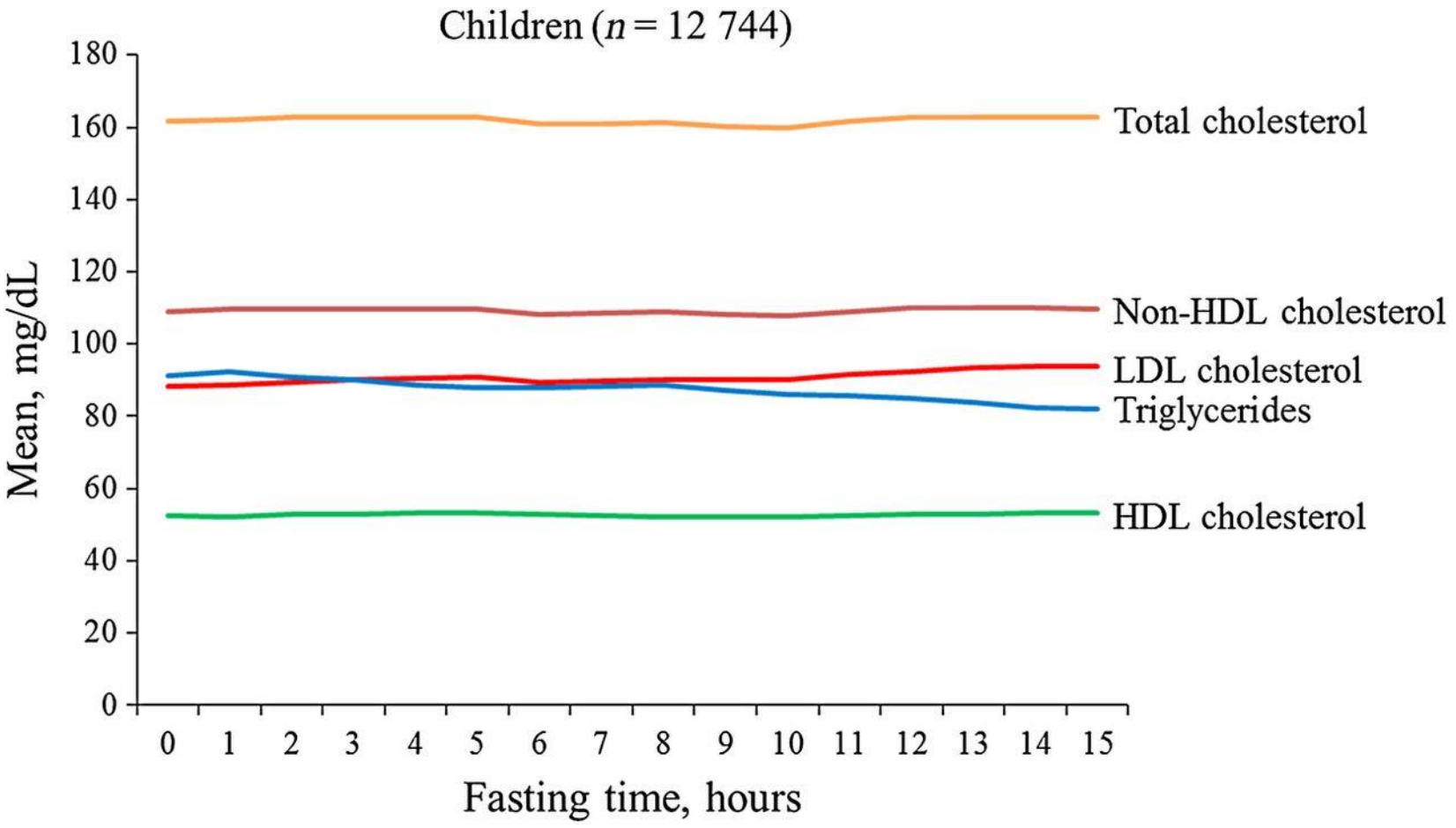
Mean concentrations of lipids and lipoproteins as a function of the fasting period following the last meal in children from the US general population.



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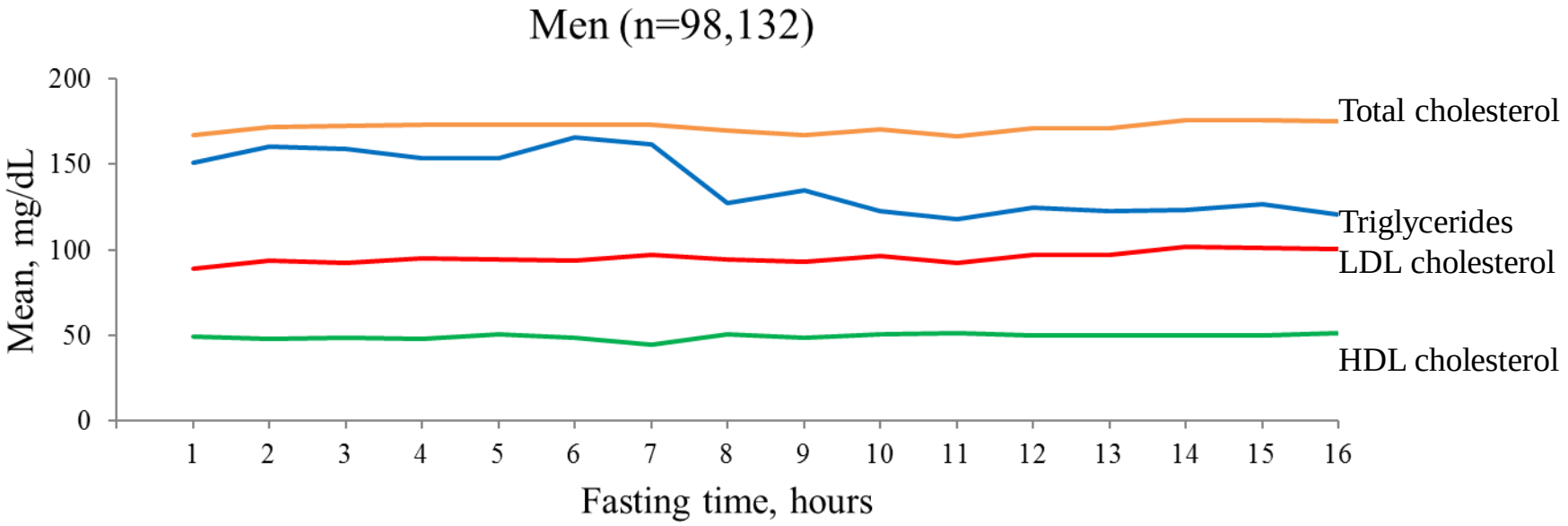

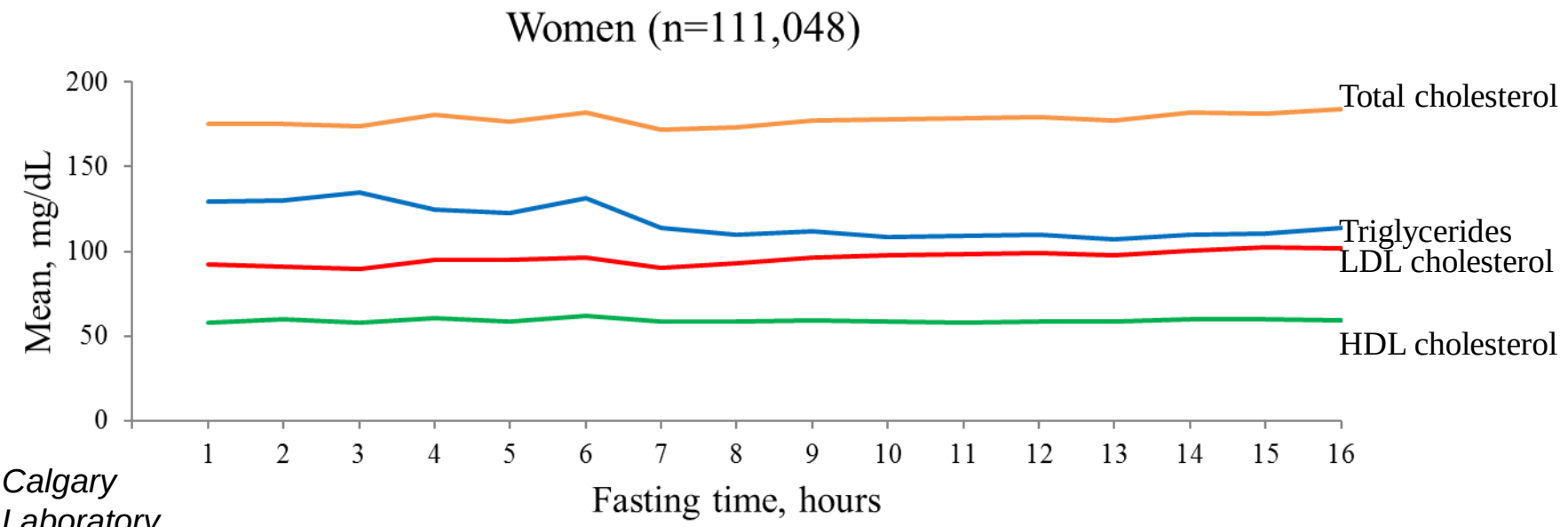

Calgary Laboratory Services in Canada

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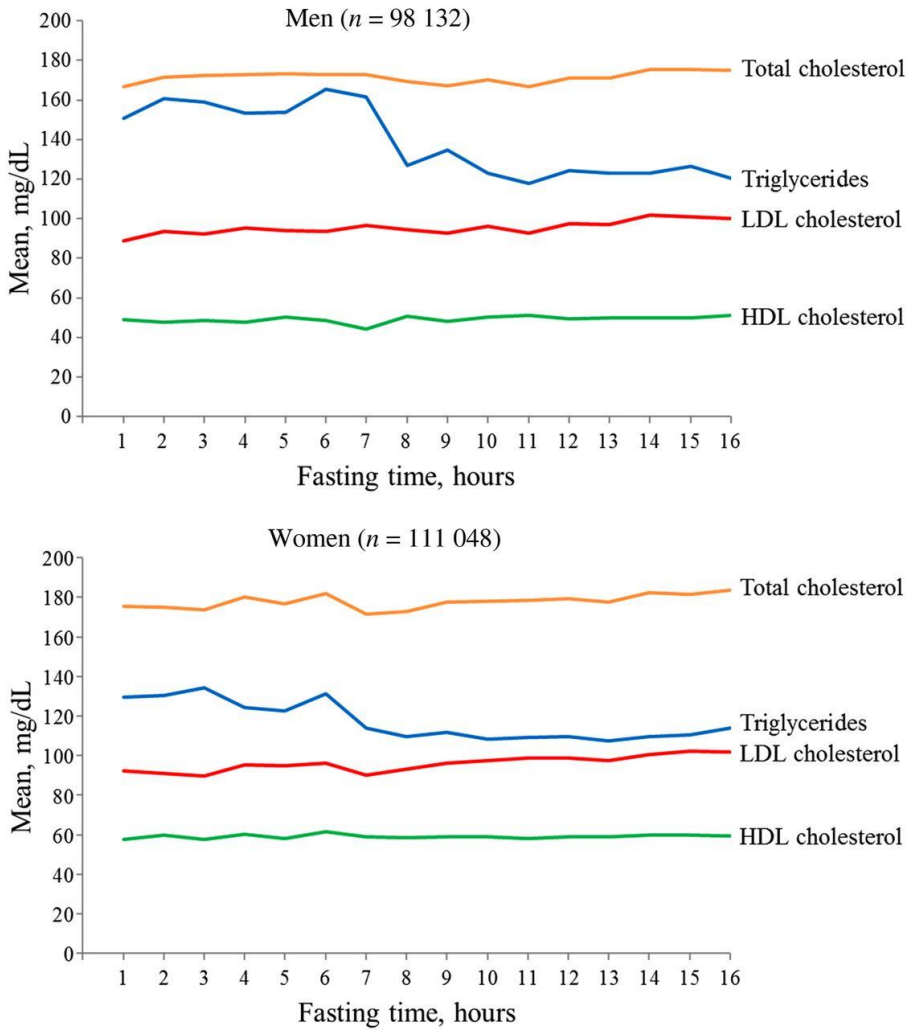
Mean concentrations of lipids and lipoproteins as a function of the period of fasting following the last meal in men and women from the Canadian general population.



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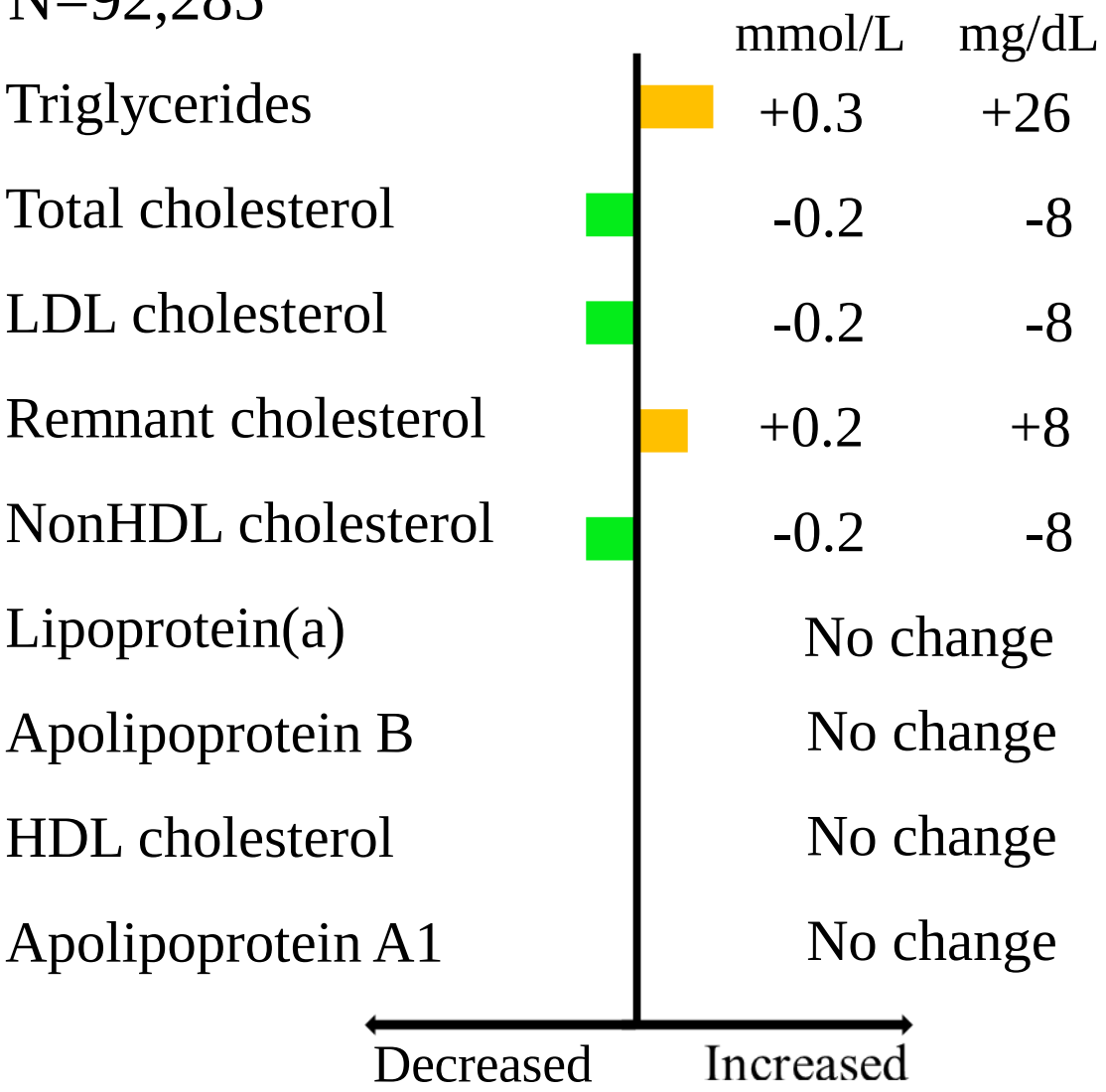
N=92,285



Maximal mean change after habitual food intake

Copenhagen General Population Study

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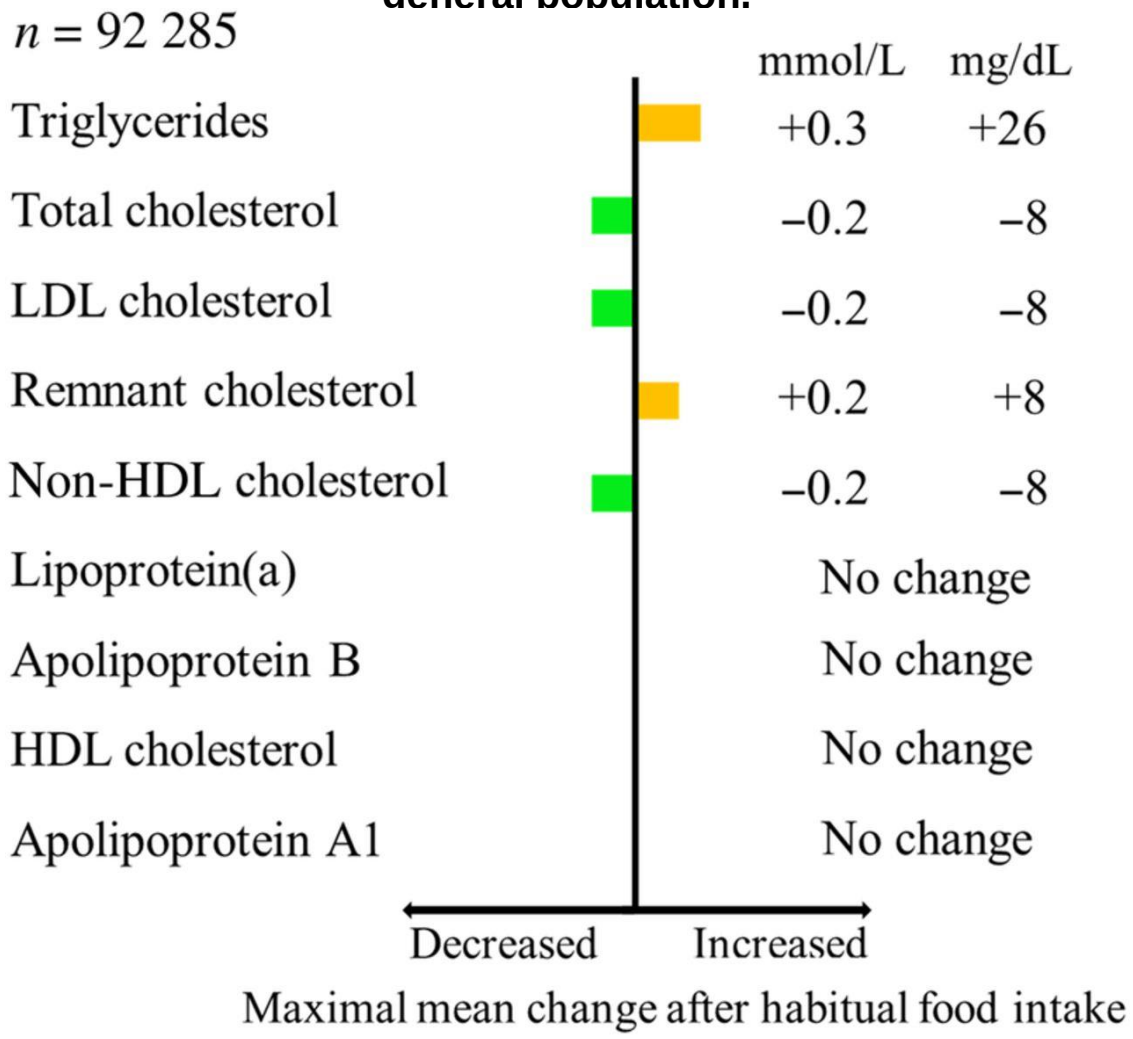
Maximal mean changes at 1–6 h after habitual food intake of lipids, lipoproteins, and apolipoproteins as part of standard and expanded lipid profiles in individuals in the Danish general population.



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Copenhagen General Population Study

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Table 3 Maximal mean changes in lipids and lipoproteins at 1–6 h after consumption of habitual meals as part of a standard lipid profile in individuals in large-scale population-based studies and registries

	Study population	Random non-fasting compared with fasting concentrations			
		Triglycerides	Total cholesterol	LDL cholesterol	HDL cholesterol
Mora *et al.* (2008)[4]	26 330 women from the Women's Health Study	↑ 0.2 mmol/L ↑ 18 mg/dL ↑ 16%	↓ 0.1 mmol/L ↓ 4 mg/dL ↓ 1%	↓ 0.2 mmol/L ↓ 8 mg/dL ↓ 5%	No change
Langsted *et al.* (2008)[3]	33 391 men and women from the Copenhagen General Population Study	↑ 0.3 mmol/L ↑ 26 mg/dL ↑ 21%	↓ 0.2 mmol/L[a] ↓ 8 mg/dL ↓ 4%	↓ 0.2 mmol/L[a] ↓ 8 mg/dL ↓ 6%	↓ 0.1 mmol/L ↓ 4 mg/dL ↓ 6%
Steiner *et al.* 2011[30]	12 744 children from the National Health and Nutrition Examination Survey	↑ 0.1 mmol/L ↑ 9 mg/dL ↑ 10%	↓ 0.1 mmol/L ↓ 4 mg/dL ↓ 2%	↓ 0.1 mmol/L ↓ 4 mg/dL ↓ 4%	No change
Langsted and Nordestgaard (2011)[9]	2270 men and women with diabetes from the Copenhagen General Population Study	↑ 0.2 mmol/L ↑ 18 mg/dL ↑ 11%	↓ 0.4 mmol/L[a] ↓ 15 mg/dL ↓ 8%	↓ 0.6 mmol/L[a] ↓ 23 mg/dL ↓ 25%[b]	No change
	56 164 men and women without diabetes from the Copenhagen General Population Study	↑ 0.2 mmol/L ↑ 18 mg/dL ↑ 14%	↓ 0.3 mmol/L[a] ↓ 12 mg/dL ↓ 5%	↓ 0.3 mmol/L[a] ↓ 12 mg/dL ↓ 9%	No change
Sidhu and Naugler (2012)[29]	209 180 men and women from Calgary Laboratory Services	↑ 0.3 mmol/L ↑ 26 mg/dL ↑ 21%	No change	↓ 0.1 mmol/L ↓ 4 mg/dL ↓ 4%	No change

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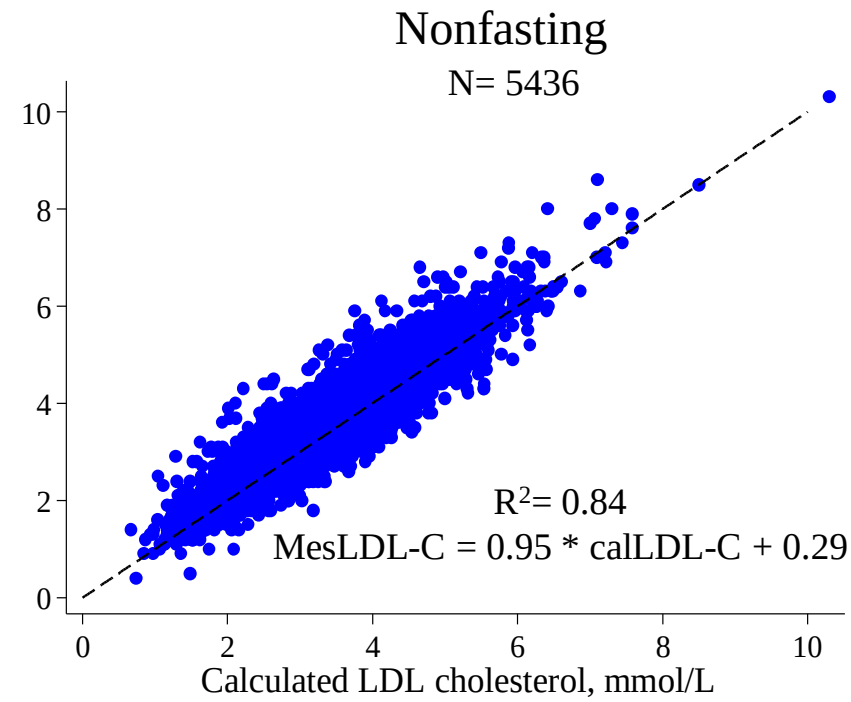

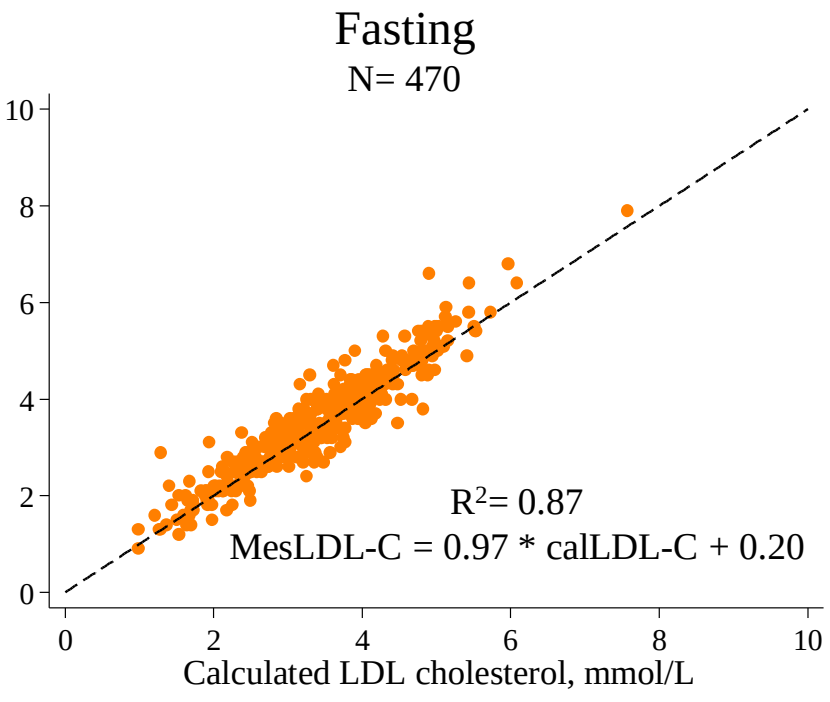

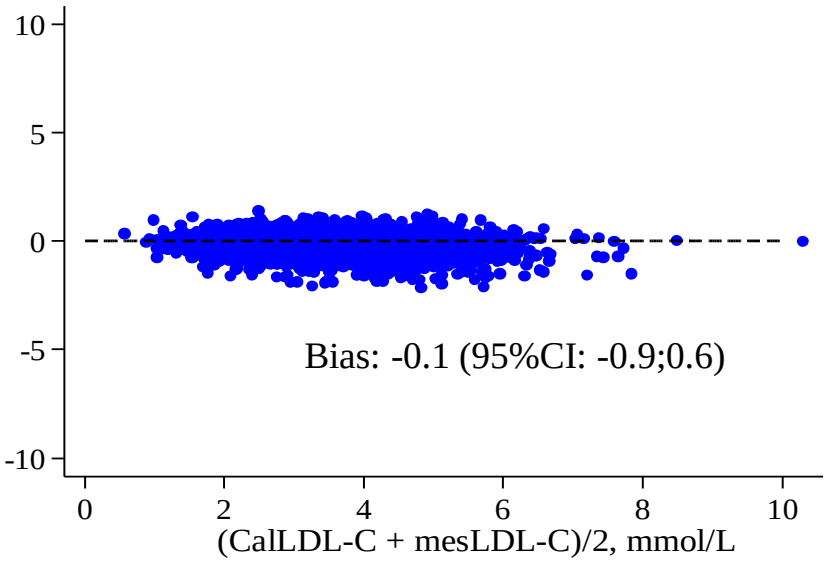

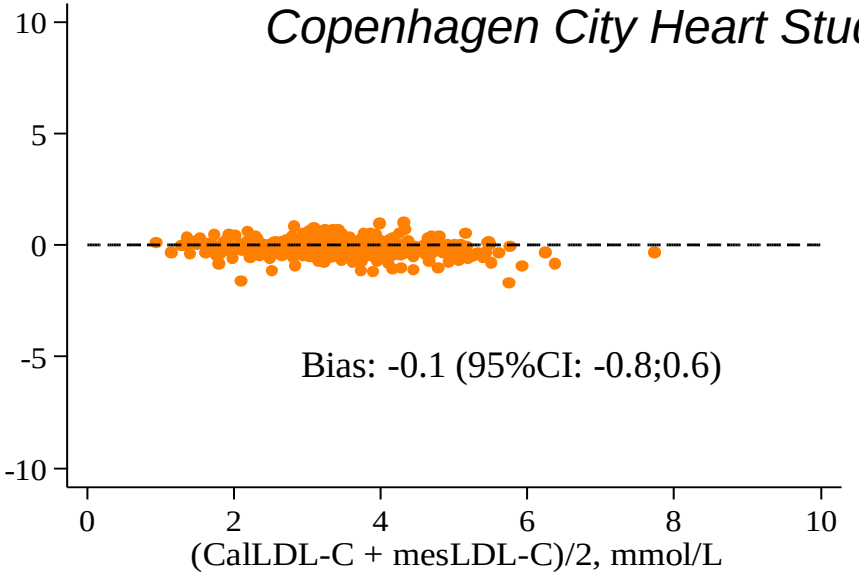

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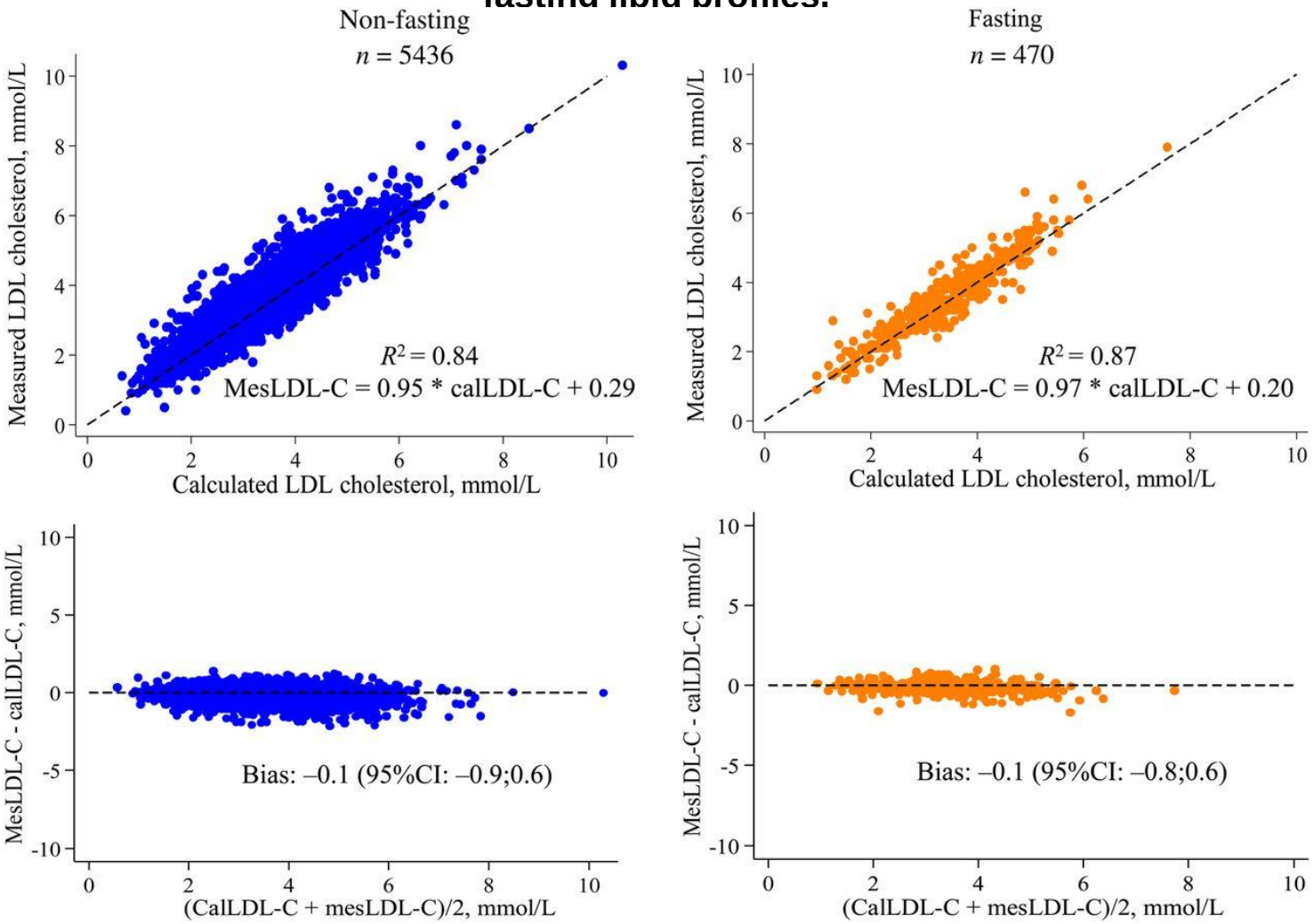
Comparison of calculated low-density lipoprotein cholesterol using the Friedewald equation with low-density lipoprotein cholesterol measured directly using random non-fasting and fasting lipid profiles.



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Copenhagen City Heart Study

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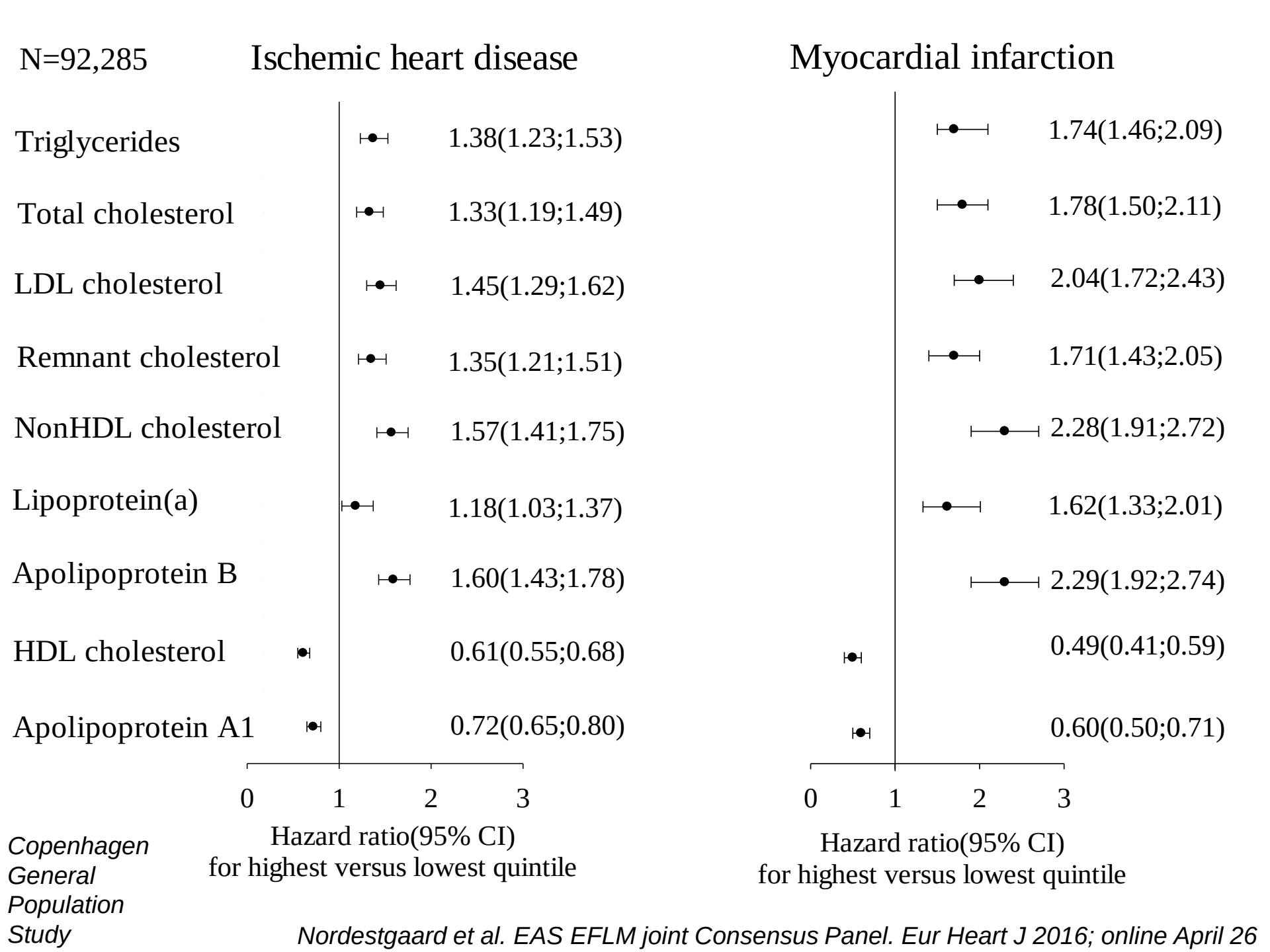

Copenhagen General Population Study

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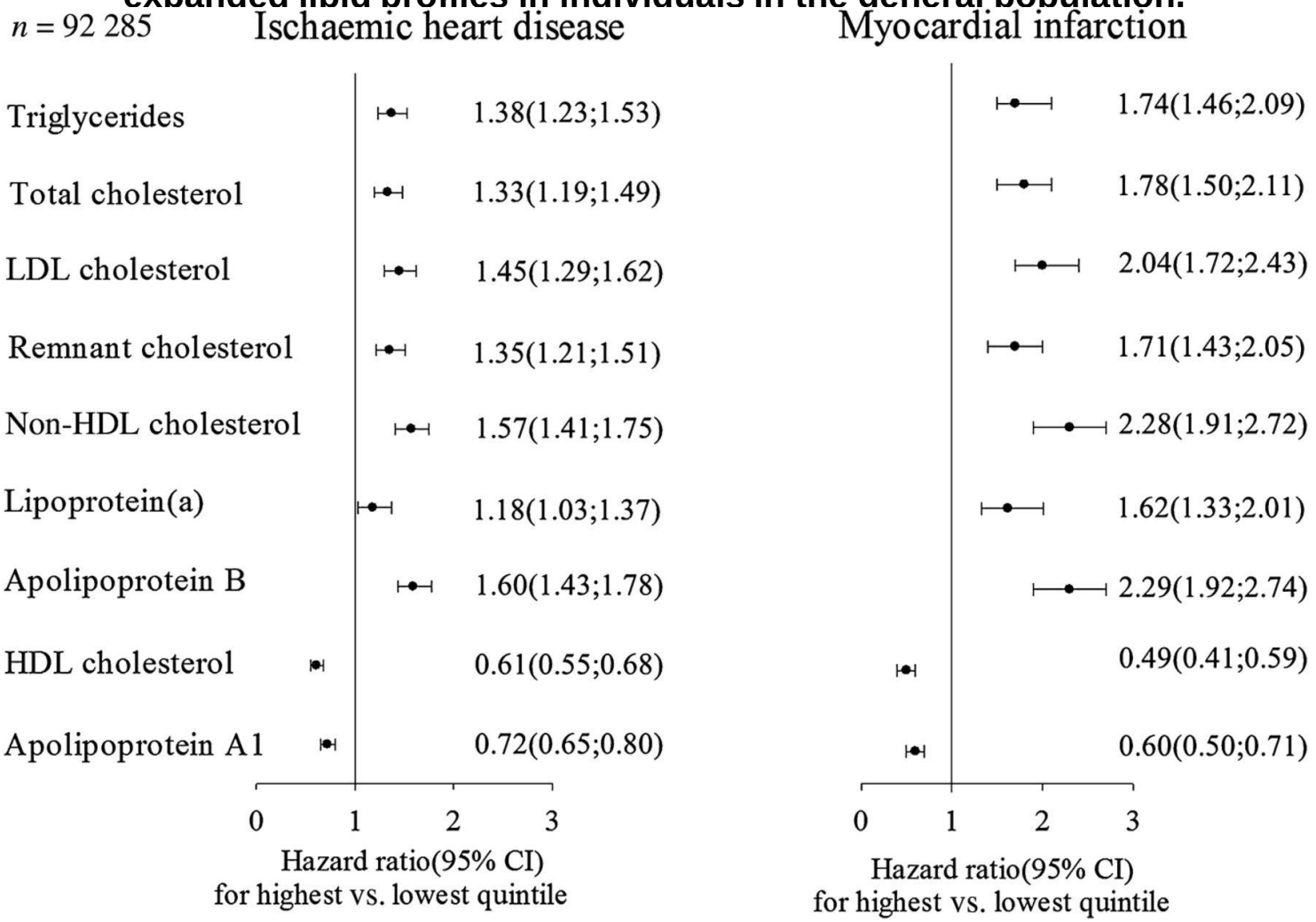
Risk of ischaemic heart disease and myocardial infarction for highest vs. lowest quintile of random non-fasting lipids, lipoproteins, and apolipoproteins as part of standard and expanded lipid profiles in individuals in the general population.



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Population-based studies totalling >300 000 non-fasting individuals	Statin trials totalling 43 000 non-fasting individuals
Tromsø Heart Study	Heart Protection Study
Norwegian National Health Service	Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm
British Population Studies	Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine
European Prospective Investigation of Cancer–Norfolk	
Northwick Park Heart Study	
Apolipoprotein-related Mortality Risk	
Copenhagen City Heart Study	
Women's Health Study	
Nurses' Health Study	
Physicians' Health Study	
National Health and Nutrition Examination Survey III	
Circulatory Risk in Communities Study	
Copenhagen General Population Study	
The global 52-country case-control INTERHEART study	

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Patients for lipid profile testing

Non-fasting	In most patients, including: • Initial lipid profile testing in any patient • For cardiovascular risk assessment • Patients admitted with acute coronary syndrome[a] • In children • If preferred by the patient • In diabetic patients[b] (due to hypoglycaemic risk) • In the elderly • Patients on stable drug therapy
Fasting	Can sometimes be required if: • Non-fasting triglycerides >5 mmol/L (440 mg/dL) • Known hypertriglyceridaemia followed in lipid clinic • Recovering from hypertriglyceridaemic pancreatitis • Starting medications that cause severe hypertriglyceridaemia • Additional laboratory tests are requested that require fasting[c] or morning samples (e.g. fasting glucose[c], therapeutic drug monitoring)

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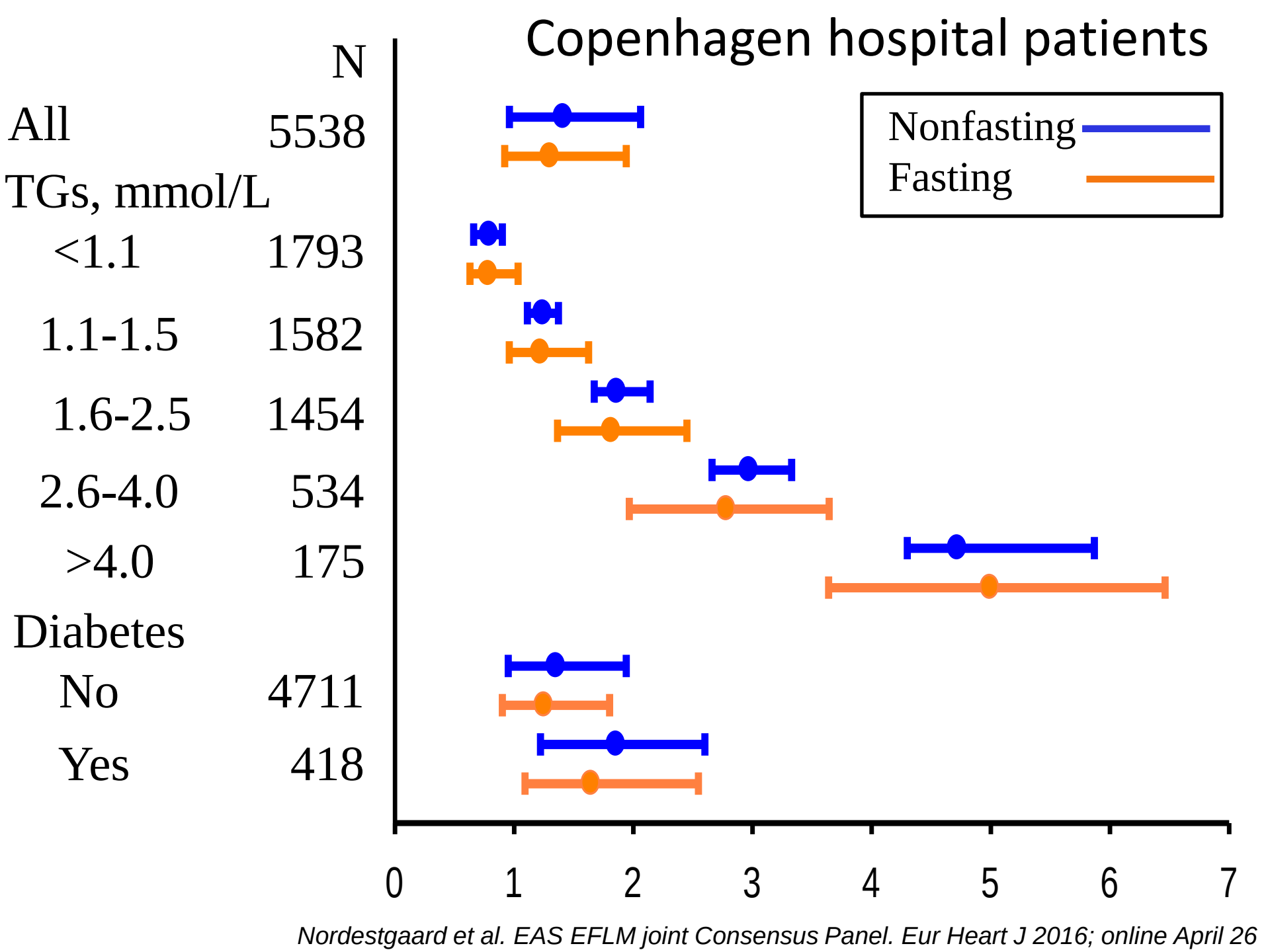

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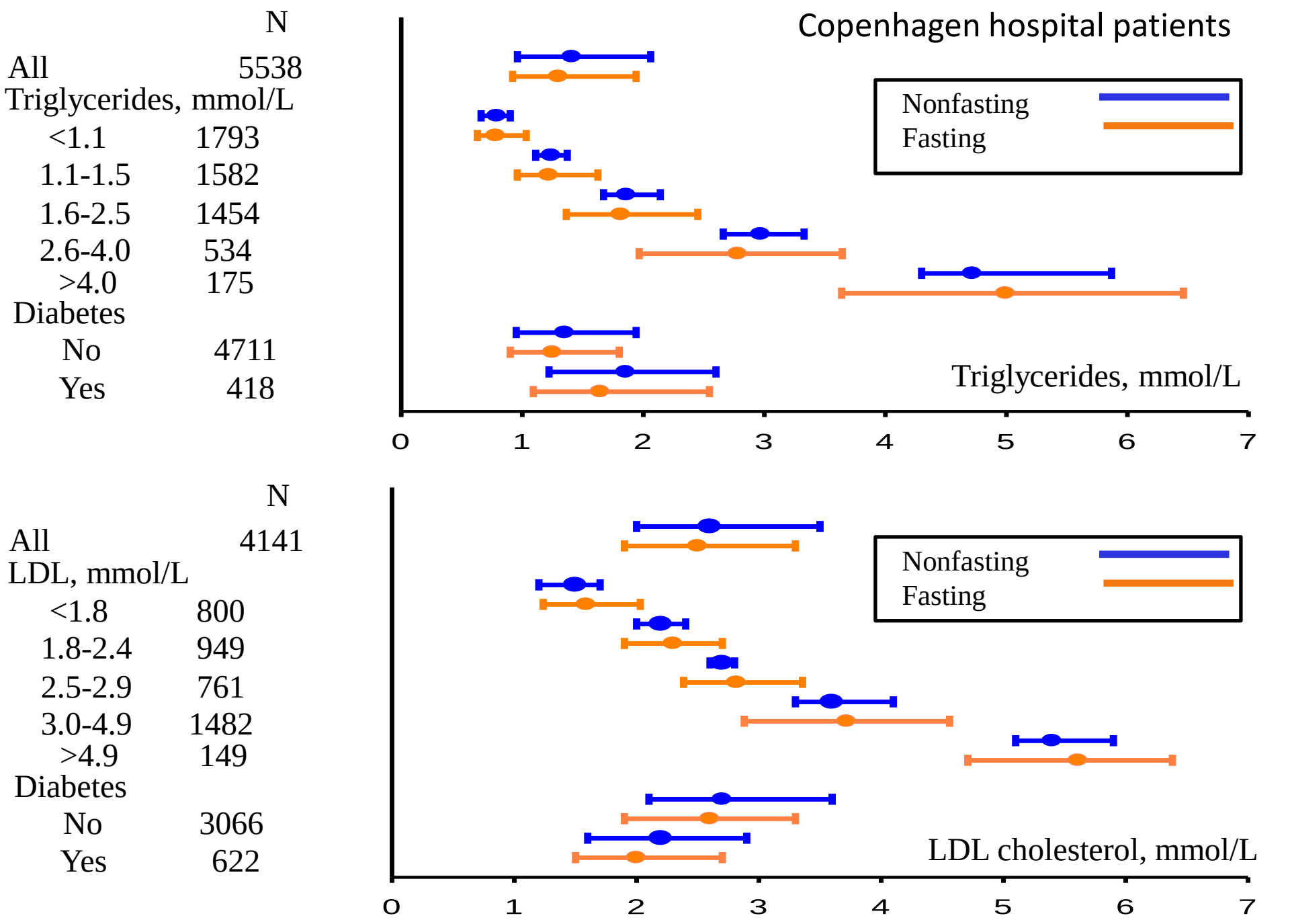

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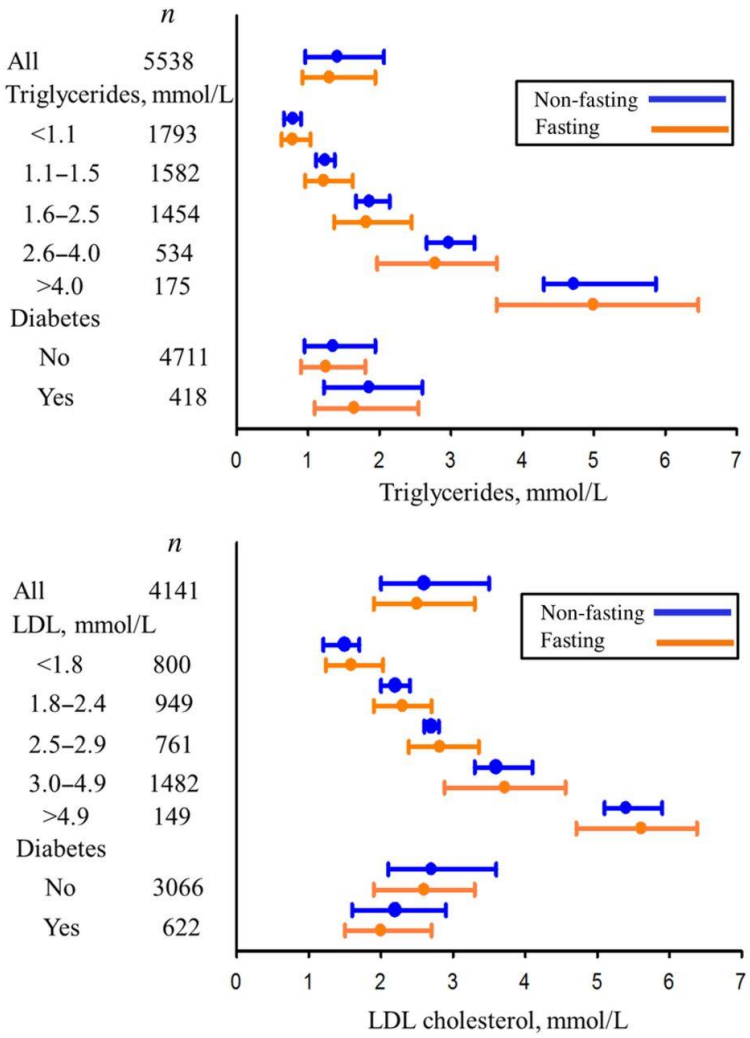
Comparison of concentrations of plasma triglycerides and low-density lipoprotein cholesterol measured in the non-fasting and fasting states in the same patients.



Copenhagen hospital patients

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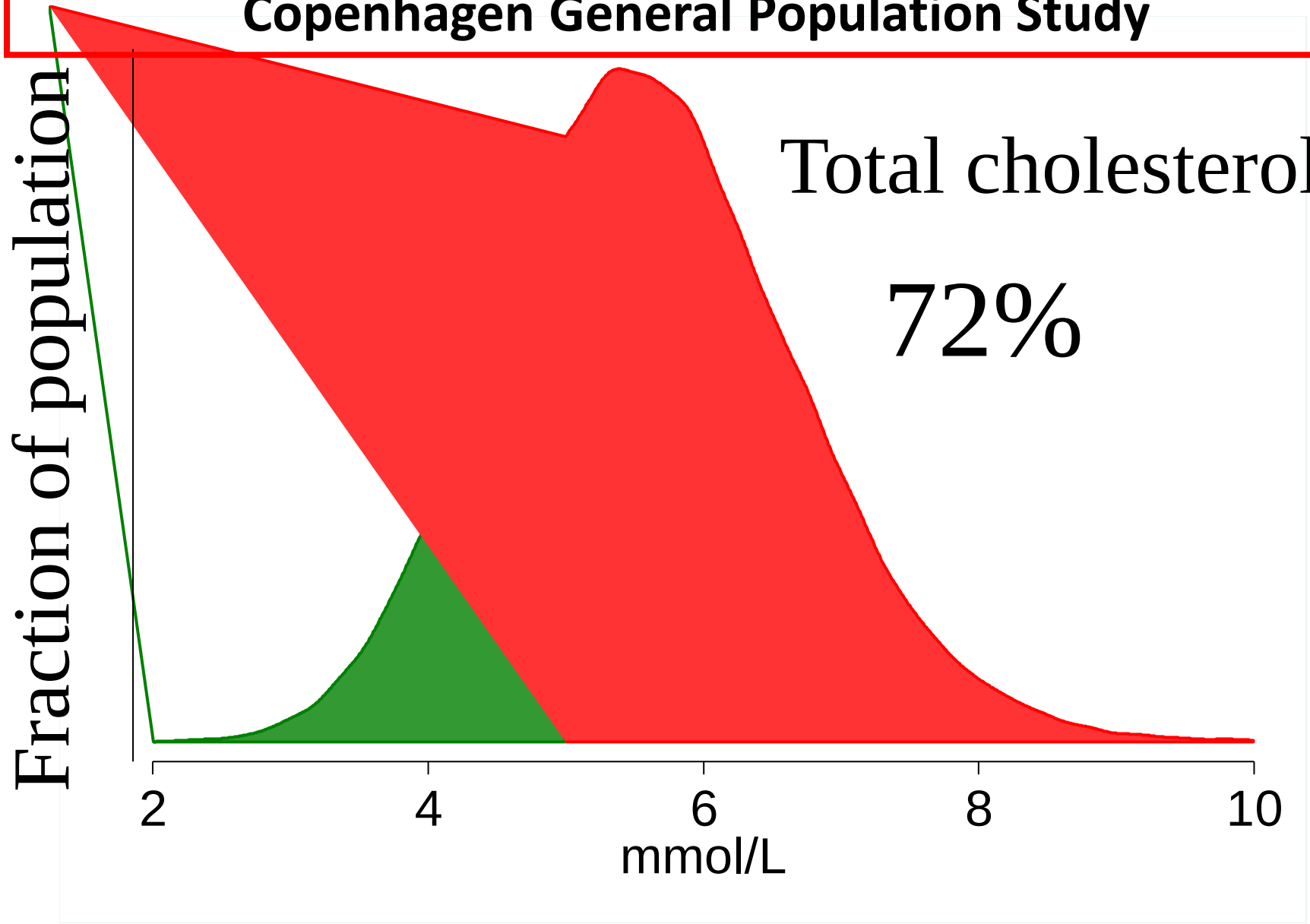
92,000 nonfasting samples from the Copenhagen General Population Study



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Abnormal concentrations	Non-fasting	
	mmol/L	mg/dL[a]
Triglycerides[b]	≥2	≥175
Total cholesterol	≥5	≥190
LDL cholesterol	≥3	≥115
Remnant cholesterol[c]	≥0.9	≥35
Non-HDL cholesterol[d]	≥3.9	≥150
Lipoprotein(a)	[e]	≥50[f]
Apolipoprotein B		≥100
HDL cholesterol[g]	≤1	≤40
Apolipoprotein A1		≤125

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Table 5 **Abnormal plasma lipid, lipoprotein, and apolipoprotein concentration values that should be flagged in laboratory reports based on desirable concentration cut-points**

Abnormal concentrations	Non-fasting			Fasting		
	mmol/L	mg/dL[a]	g/L	mmol/L	mg/dL[a]	g/L
Triglycerides[b]	≥2	≥175	≥1.75	≥1.7	≥150	≥1.50
Total cholesterol	≥5	≥190	≥1.90	≥5	≥190	≥1.90
LDL cholesterol	≥3	≥115	≥1.15	≥3	≥115	≥1.15
Remnant cholesterol[c]	≥0.9	≥35	≥0.35	≥0.8	≥30	≥0.30
Non-HDL cholesterol[d]	≥3.9	≥150	≥1.50	≥3.8	≥145	≥1.45
Lipoprotein(a)	[e]	≥50[f]	≥0.50	[e]	≥50[f]	≥0.50
Apolipoprotein B		≥100	≥1.00		≥100	≥1.00
HDL cholesterol[g]	≤1	≤40	≤0.40	≤1	≤40	≤0.40
Apolipoprotein A1		≤125	≤1.25		≤125	≤1.25

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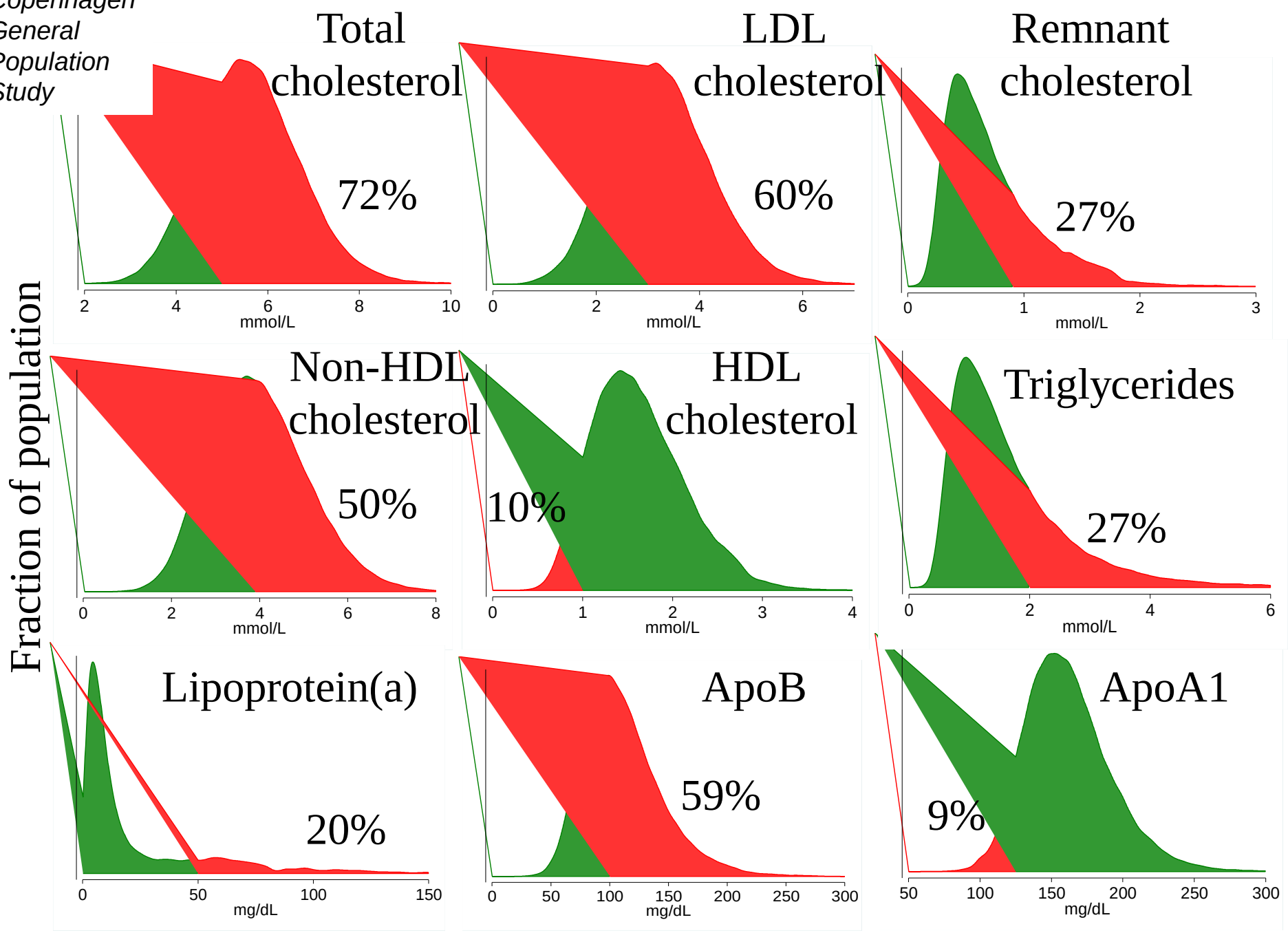
Copenhagen General Population Study



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Proportion of non-fasting individuals in the general population with flagged abnormal concentrations in laboratory reports using desirable concentration cut-points as shown in Table 5.

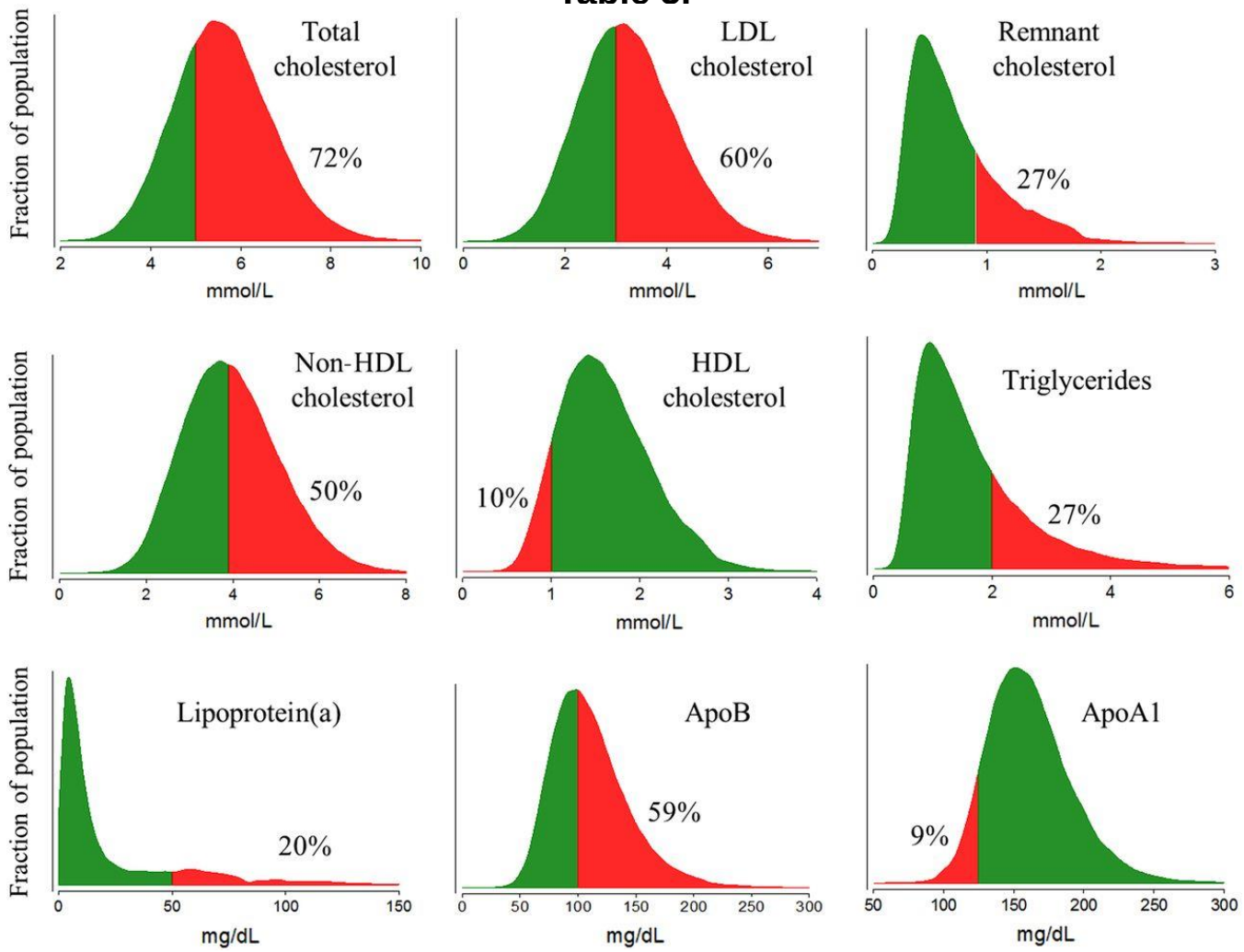

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Table 6 Treatment goals for prevention of cardiovascular disease according to current European Atherosclerosis Society/European Society of Cardiology guidelines[13]

Cardiovascular disease risk	LDL cholesterol		Non-HDL cholesterol		Apolipoprotein B	
	mmol/L	mg/dL	mmol/L	mg/dL	mg/dL	g/L
Very high	<1.8	<70	<2.6	<100	<80	<0.8
High	<2.5	<100	<3.3	<125	<100	<1.0
Moderate	<3.0	<115	<3.8	<145		

Table 7 Definition of hypertriglyceridaemia by European Atherosclerosis Society consensus statement[24]

Severe hypertriglyceridaemia	>10 mmol/L	>880 mg/dL
Mild-to-moderate hypertriglyceridaemia	2–10 mmol/L	180–880 mg/dL

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Separate referral to lipid specialist at

	Life-threatening concentrations	
Triglycerides	>10 mmol/L >880 mg/dL[a]	Pancreatitis risk?
LDL cholesterol	>13 mmol/L >500 mg/dL[a]	HoFH?
LDL cholesterol	>5 mmol/L >190 mg/dL[a]	HeFH?
LDL cholesterol in children	>4 mmol/L >155 mg/dL[a]	HeFH?

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Table 8 **Life-threatening and extremely abnormal concentrations with separate reporting and consequent direct referral to a lipid clinic or to a physician with special interest in lipids**

	Life-threatening concentrations	Refer patient to a lipid clinic or to a physician with special interest in lipids for further assessment of the following conditions
Triglycerides	>10 mmol/L >880 mg/dL[a]	Chylomicronaemia syndrome with high risk of acute pancreatitis[24]
LDL cholesterol	>13 mmol/L >500 mg/dL[a]	Homozygous familial hypercholesterolaemia with extremely high cardiovascular risk[44]
LDL cholesterol	>5 mmol/L >190 mg/dL[a]	Heterozygous familial hypercholesterolaemia with high cardiovascular risk[43]
LDL cholesterol in children	>4 mmol/L >155 mg/dL[a]	Heterozygous familial hypercholesterolaemia with high cardiovascular risk[45]
Lipoprotein(a)	>150 mg/dL >99th percentile	Very high cardiovascular risk, i.e for myocardial infarction and aortic valve stenosis[11,46,47]
LDL cholesterol Apolipoprotein B	<0.3 mmol/L <10 mg/dL	Genetic abetalipoproteinaemia
HDL cholesterol Apolipoprotein A1	<0.2 mmol/L <10 mg/dL	Genetic hypoalphalipoproteinaemia (e.g. lecithin cholesterol acyltransferase deficiency)

[a]Values in mmol/L were converted to mg/dL by multiplication with 38.6 for cholesterol and by 88 for triglycerides, followed by rounding to nearest 5 mg/dL.

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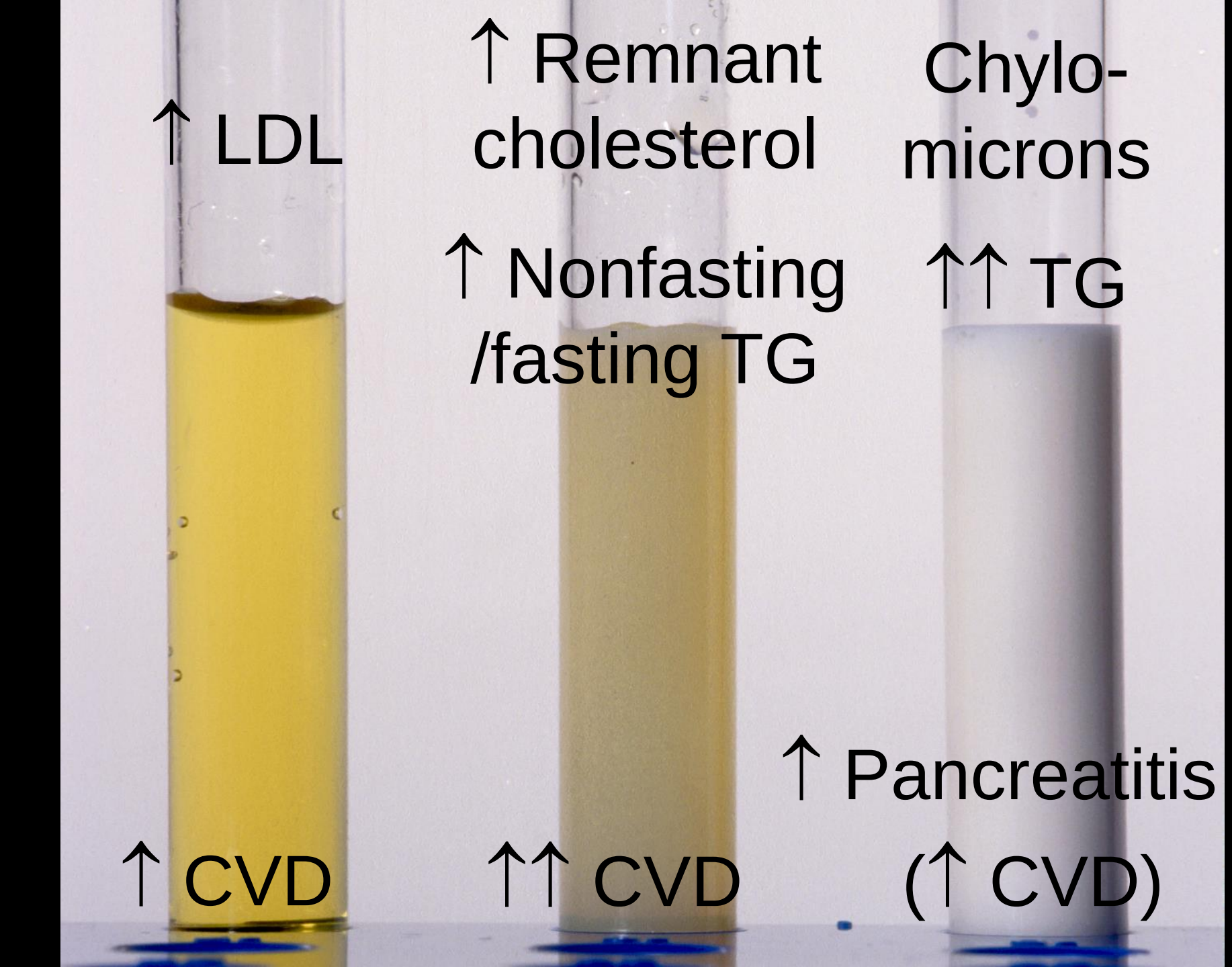
↑ LDL
↑ Remnant cholesterol
Chylo-microns
↑ Nonfasting /fasting TG
↑↑ TG
↑ Pancreatitis
↑ CVD
↑↑ CVD
(↑ CVD)
Nordestgaard 2015

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Lipoprotein(a)	>150 mg/dL >99th percentile	Very high cardiovascular risk, i.e for myocardial infarction and aortic valve stenosis[11,46,47]
LDL cholesterol Apolipoprotein B	<0.3 mmol/L <10 mg/dL	Genetic abetalipoproteinaemia
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[a]Values in mmol/L were converted to mg/dL by multiplication with 38.6 for cholesterol and by 88 for triglycerides, followed by rounding to nearest 5 mg/dL.

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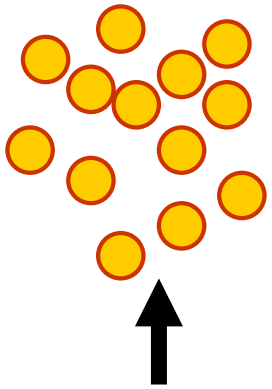
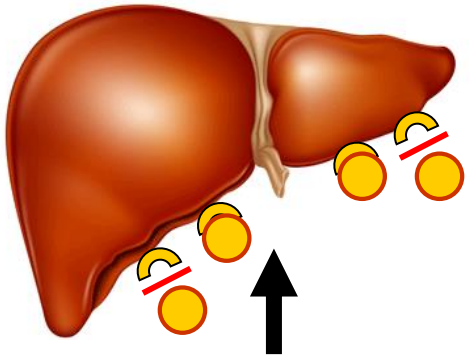
Elevated LDL cholesterol

LDLR >95%
APOB 2-5%
PCSK9 <1%

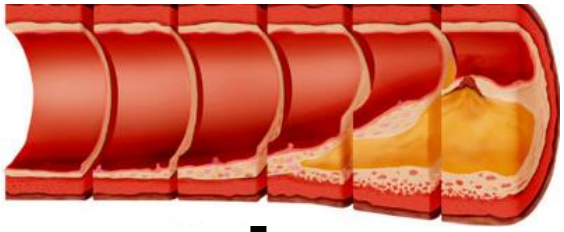


Liver with only 50% functional LDL receptors

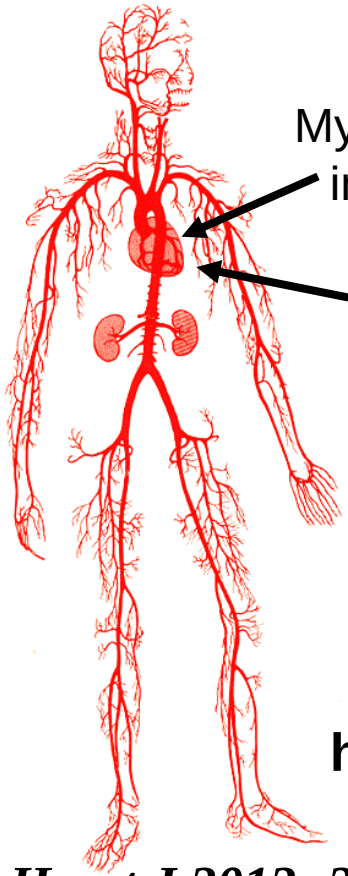


Mutations in LDL receptor, apolipoproteinB or PCSK9

Atherosclerosis



Coronary heart disease

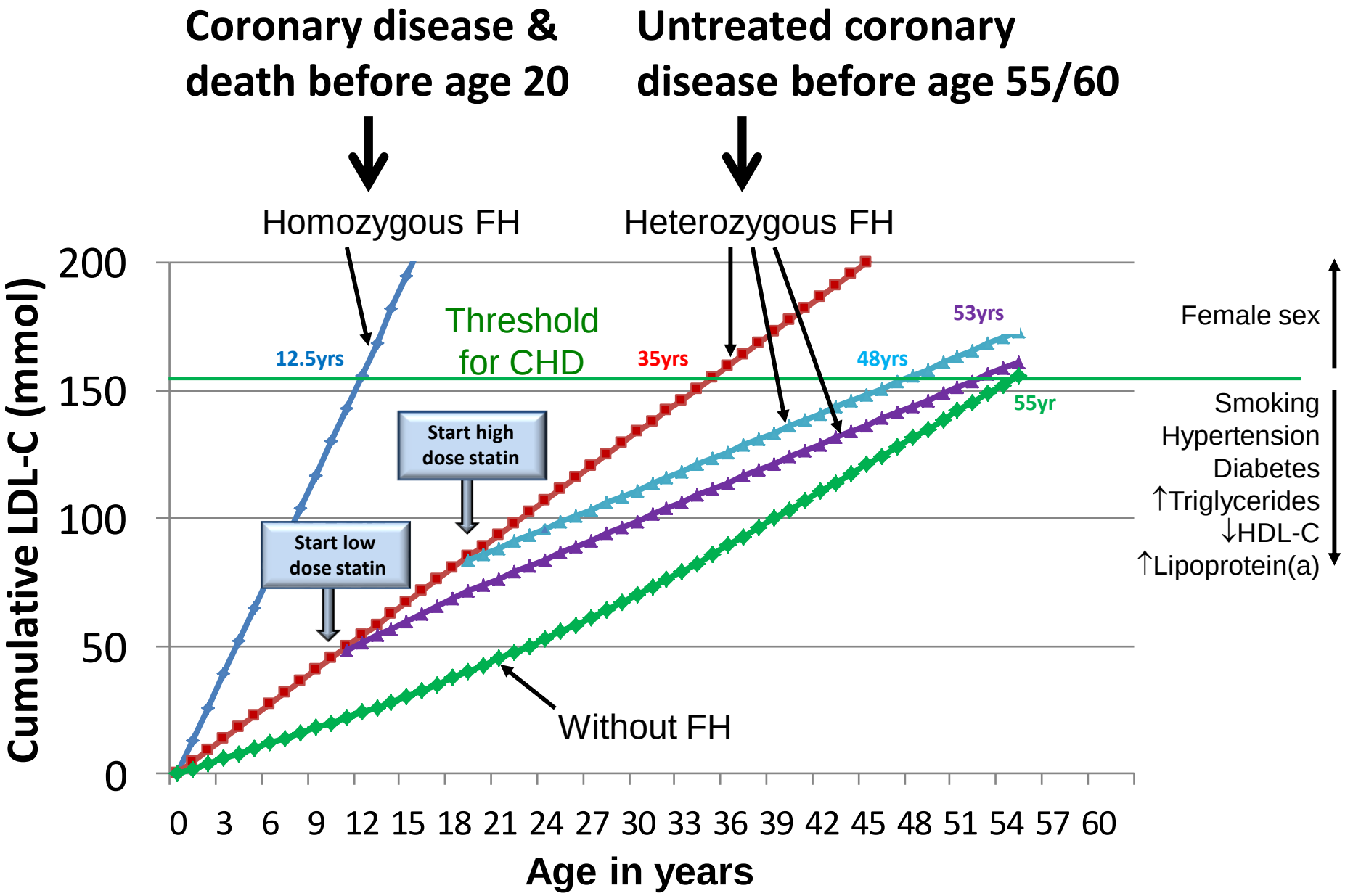


Myocardial infarction

Angina pectoris

Heterozygous familial hypercholesterolaemia

Nordestgaard et al. EAS Consensus. Eur Heart J 2013; 34: 3478-90 (open access)



Nordestgaard et al. EAS Consensus. Eur Heart J 2013; 34: 3478-90 (open access)

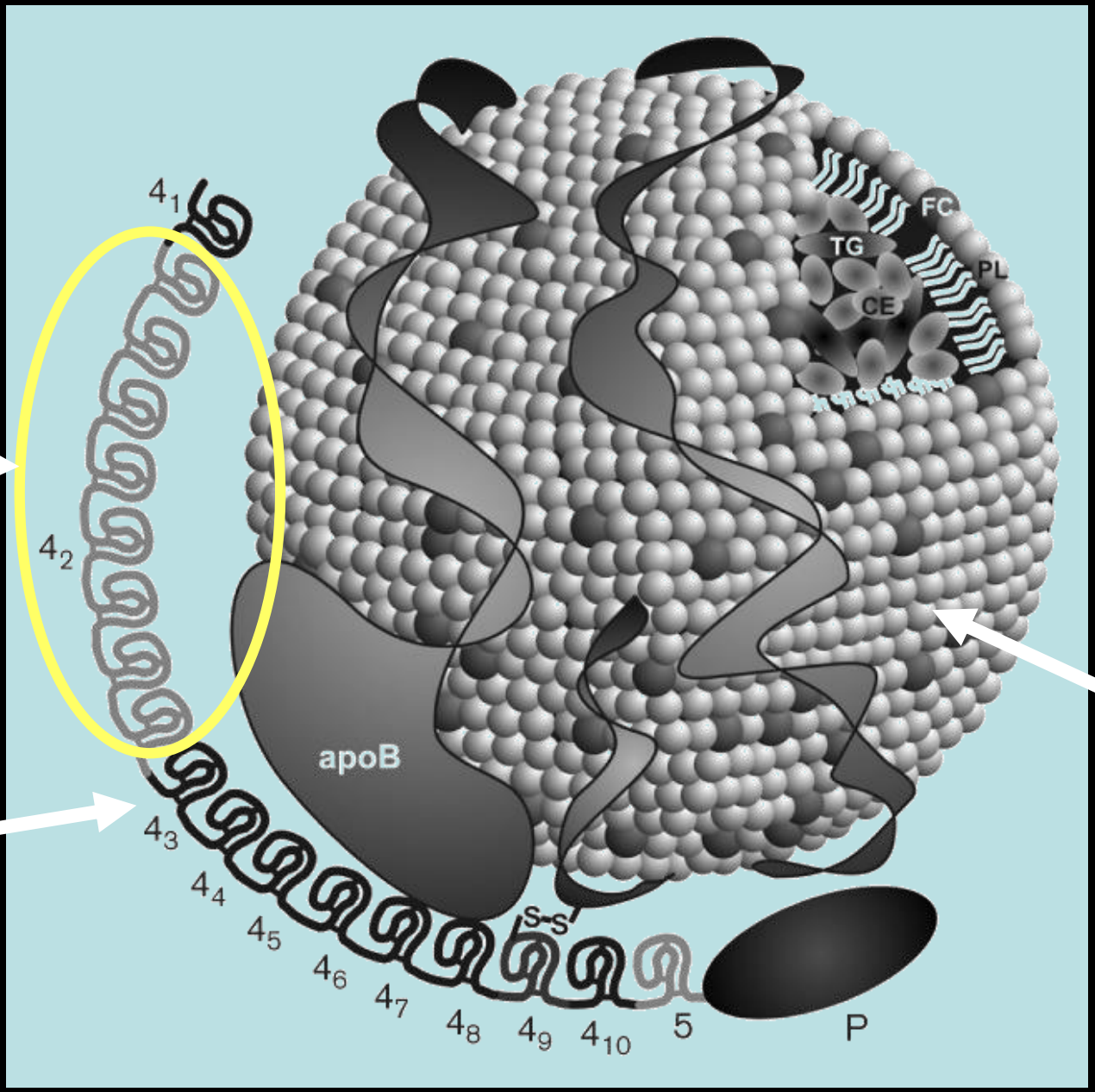
Table 8 **Life-threatening and extremely abnormal concentrations with separate reporting and consequent direct referral to a lipid clinic or to a physician with special interest in lipids**

	Life-threatening concentrations	Refer patient to a lipid clinic or to a physician with special interest in lipids for further assessment of the following conditions
Triglycerides	>10 mmol/L >880 mg/dL[a]	Chylomicronaemia syndrome with high risk of acute pancreatitis[24]
LDL cholesterol	>13 mmol/L >500 mg/dL[a]	Homozygous familial hypercholesterolaemia with extremely high cardiovascular risk[44]
LDL cholesterol	>5 mmol/L >190 mg/dL[a]	Heterozygous familial hypercholesterolaemia with high cardiovascular risk[43]
LDL cholesterol in children	>4 mmol/L >155 mg/dL[a]	Heterozygous familial hypercholesterolaemia with high cardiovascular risk[45]
Lipoprotein(a)	>150 mg/dL >99th percentile	Very high cardiovascular risk, i.e for myocardial infarction and aortic valve stenosis[11,46,47]
LDL cholesterol Apolipoprotein B	<0.3 mmol/L <10 mg/dL	Genetic abetalipoproteinaemia
HDL cholesterol Apolipoprotein A1	<0.2 mmol/L <10 mg/dL	Genetic hypoalphalipoproteinaemia (e.g. lecithin cholesterol acyltransferase deficiency)

[a]Values in mmol/L were converted to mg/dL by multiplication with 38.6 for cholesterol and by 88 for triglycerides, followed by rounding to nearest 5 mg/dL.

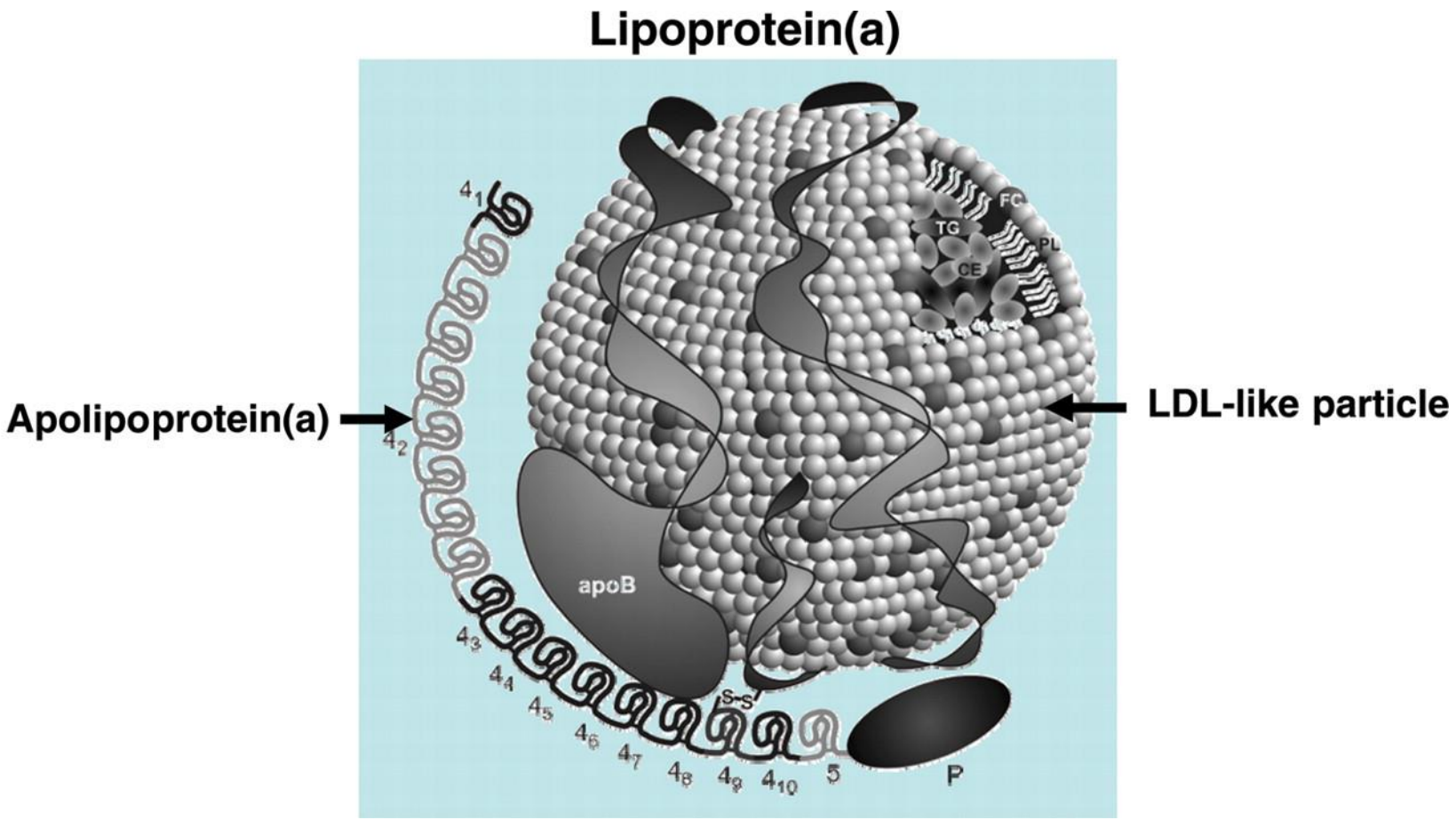
Nordestgaard et al. EAS EFLM joint Consensus Panel. Eur Heart J 2016; online April 26

Lipoprotein(a)



Koschinsky et al. Cur Opin Lipidol 2004;15:167-174

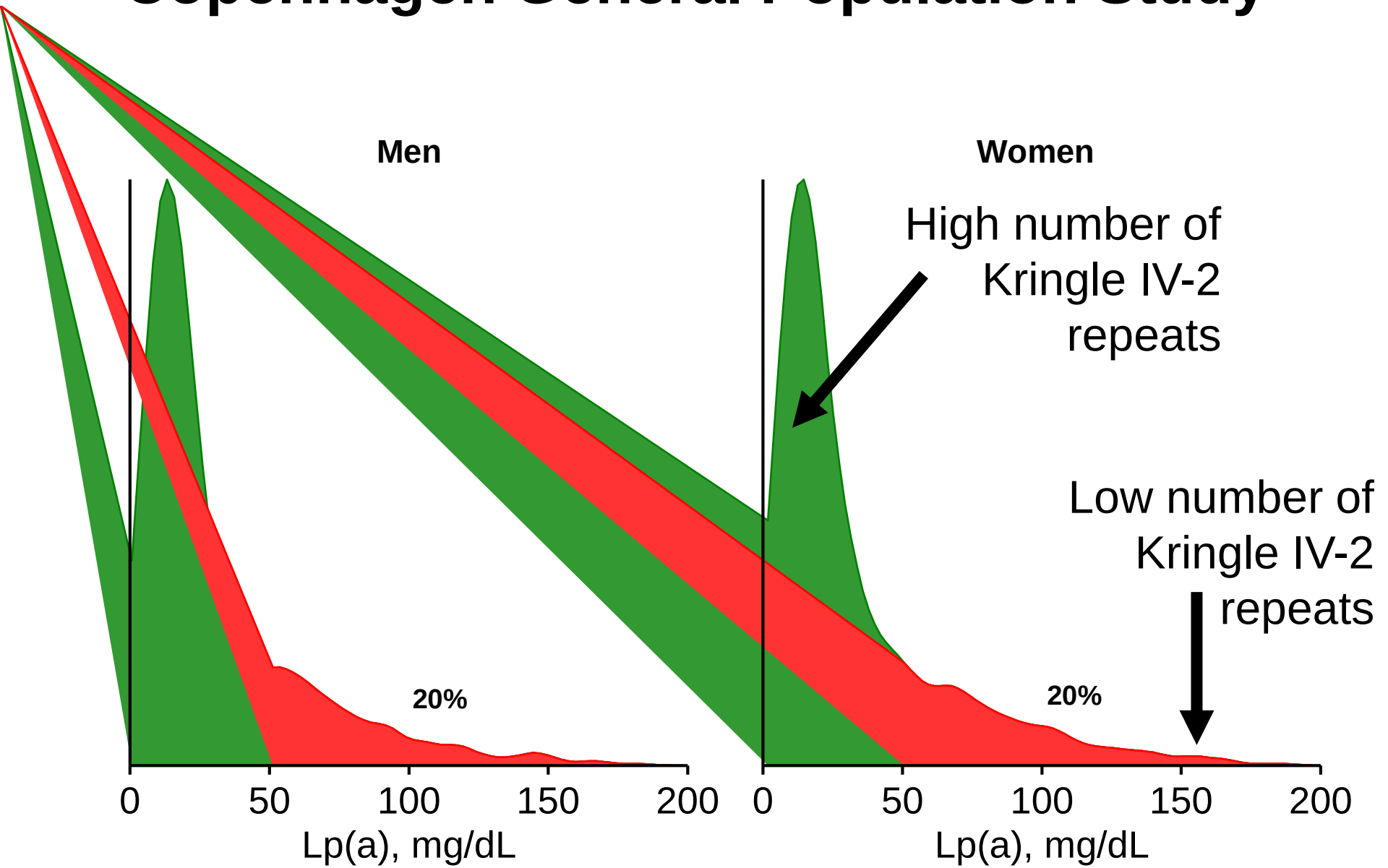
Lipoprotein(a) consists of an LDL-like particle to which apolipoprotein(a) is covalently linked.



Nordestgaard B G et al. Eur Heart J 2010;31:2844-2853

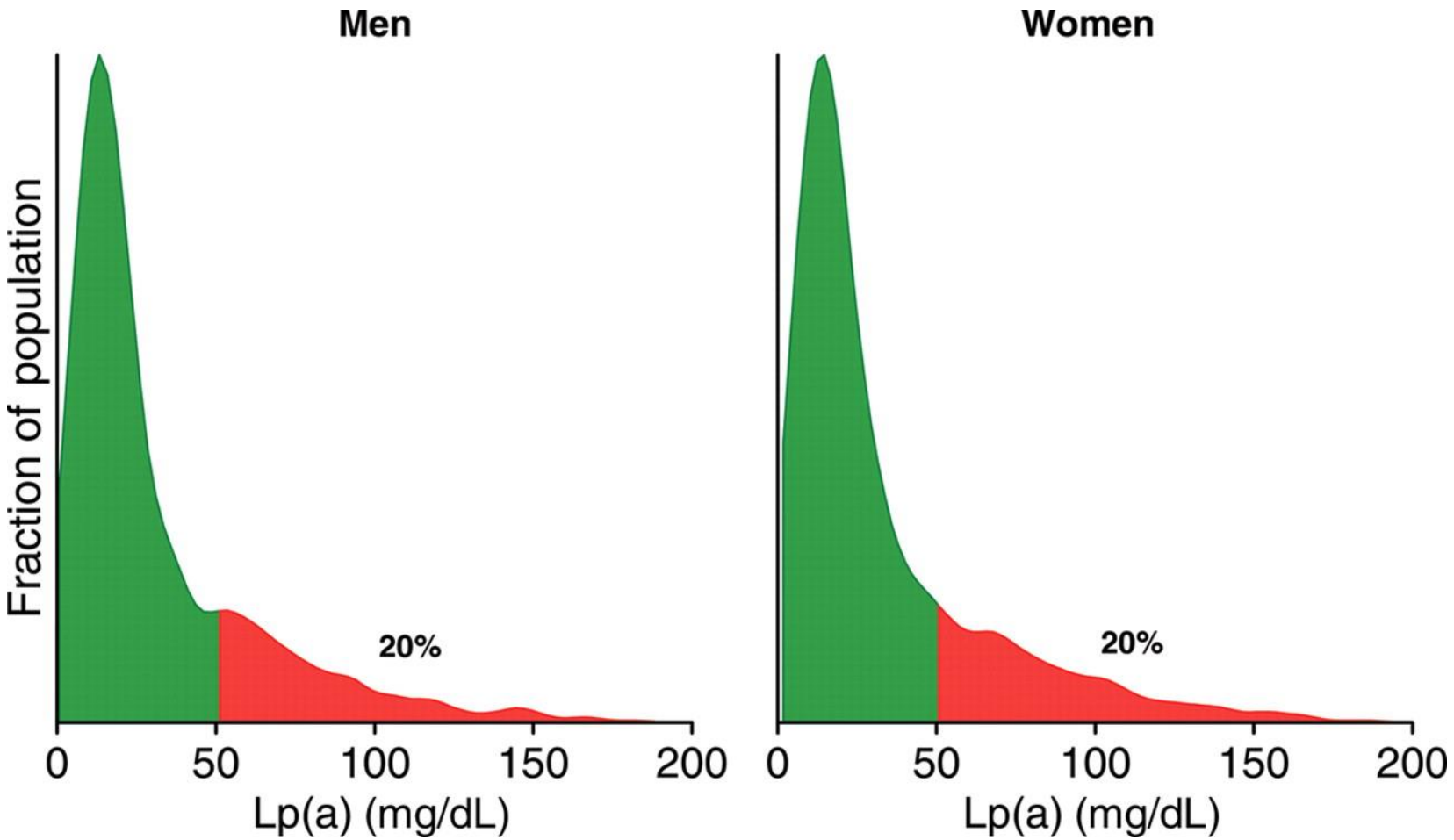
European Heart Journal

Copenhagen General Population Study



Nordestgaard 2010

Typical distributions of lipoprotein(a) levels in the general population.



Nordestgaard B G et al. Eur Heart J 2010;31:2844-2853

Copenhagen General Population Study

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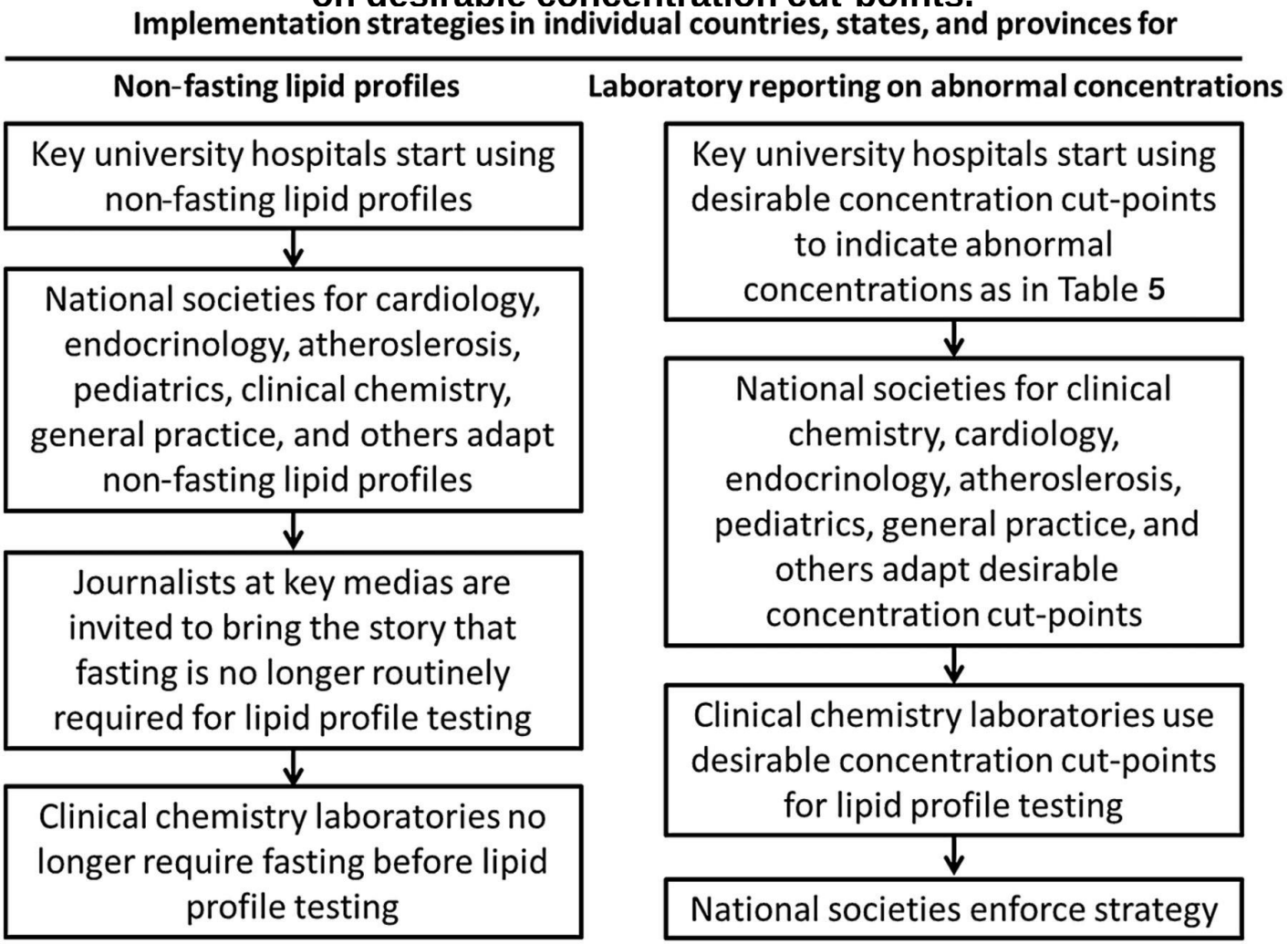
Implementation strategies in individual countries, states, and provinces for

Nonfasting lipid profiles	Laboratory reporting on abnormal concentrations
Key university hospitals start using nonfasting lipid profiles	Key university hospitals start using desirable concentration cut-points to indicate abnormal concentrations as in Table 4
National societies for cardiology, endocrinology, atheroslerosis, pediatrics, clinical chemistry, general practice and others adapt nonfasting lipid profiles	National societies for clinical chemistry, cardiology, endocrinology, atheroslerosis, pediatrics, general practice and other adapt desirable concentration cut-points
Journalists at key medias are invited to bring the story that fasting is no longer routinely required for lipid profile testing	Clinical chemistry laboratories use desirable concentration cut-points for lipid profile testing
Clinical chemistry laboratories no longer require fasting before lipid profile testing	National societies enforce strategy

Nordestgaard et al. EAS EFLM joint Consensus Panel. Eur Heart J 2016; online April 26

Suggested implementation strategies in individual countries, states, and/or provinces for use of non-fasting lipid profiles and for flagging in laboratory reports of abnormal values based on desirable concentration cut-points.



Børge G. Nordestgaard et al. Eur Heart J 2016;eurheartj.ehw152

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Disclosures

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Nordestgaard et al. EAS EFLM joint Consensus Panel. Eur Heart J 2016; online April 26