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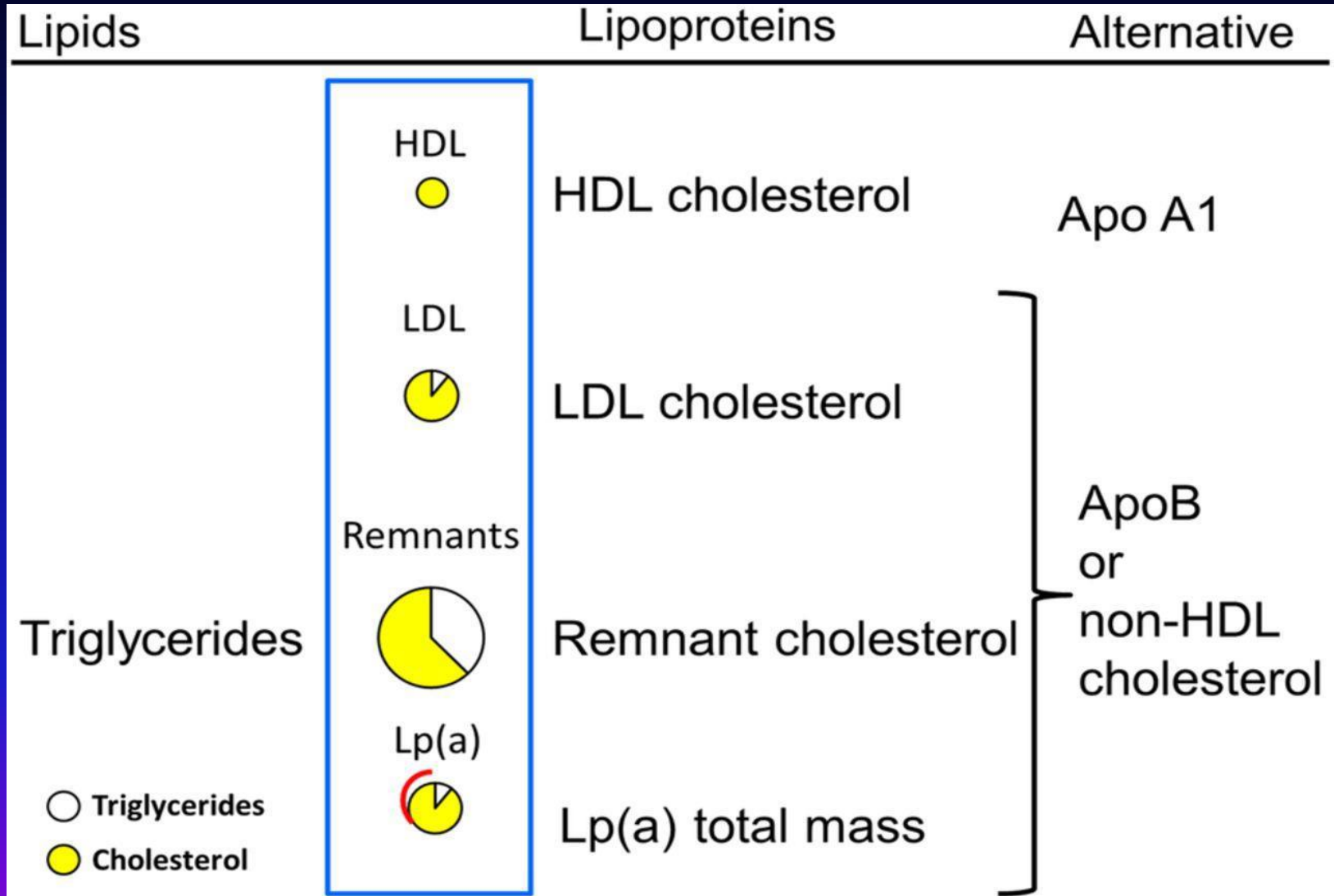
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Chennai



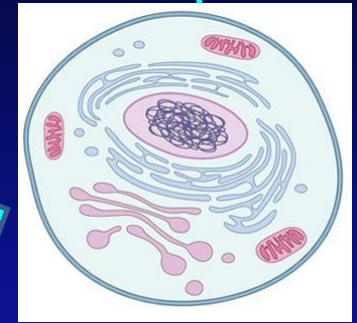
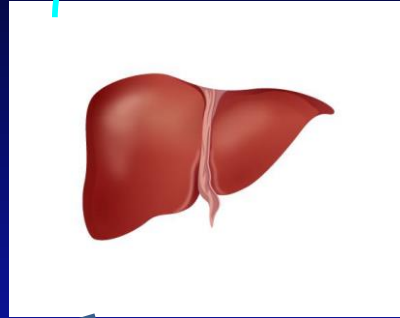
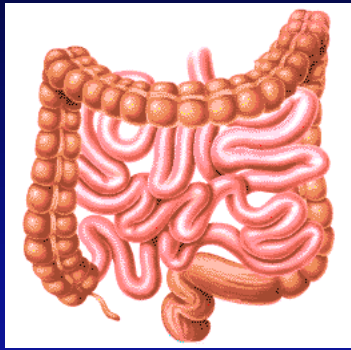
Should Non-Fasting Lipid profile
be the standard of care ?

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



Nonfasting

Fasting



Chylomicron

Chylomicron remnant

LDL

VLDL

IDL

Triglycerides

Cholesterol

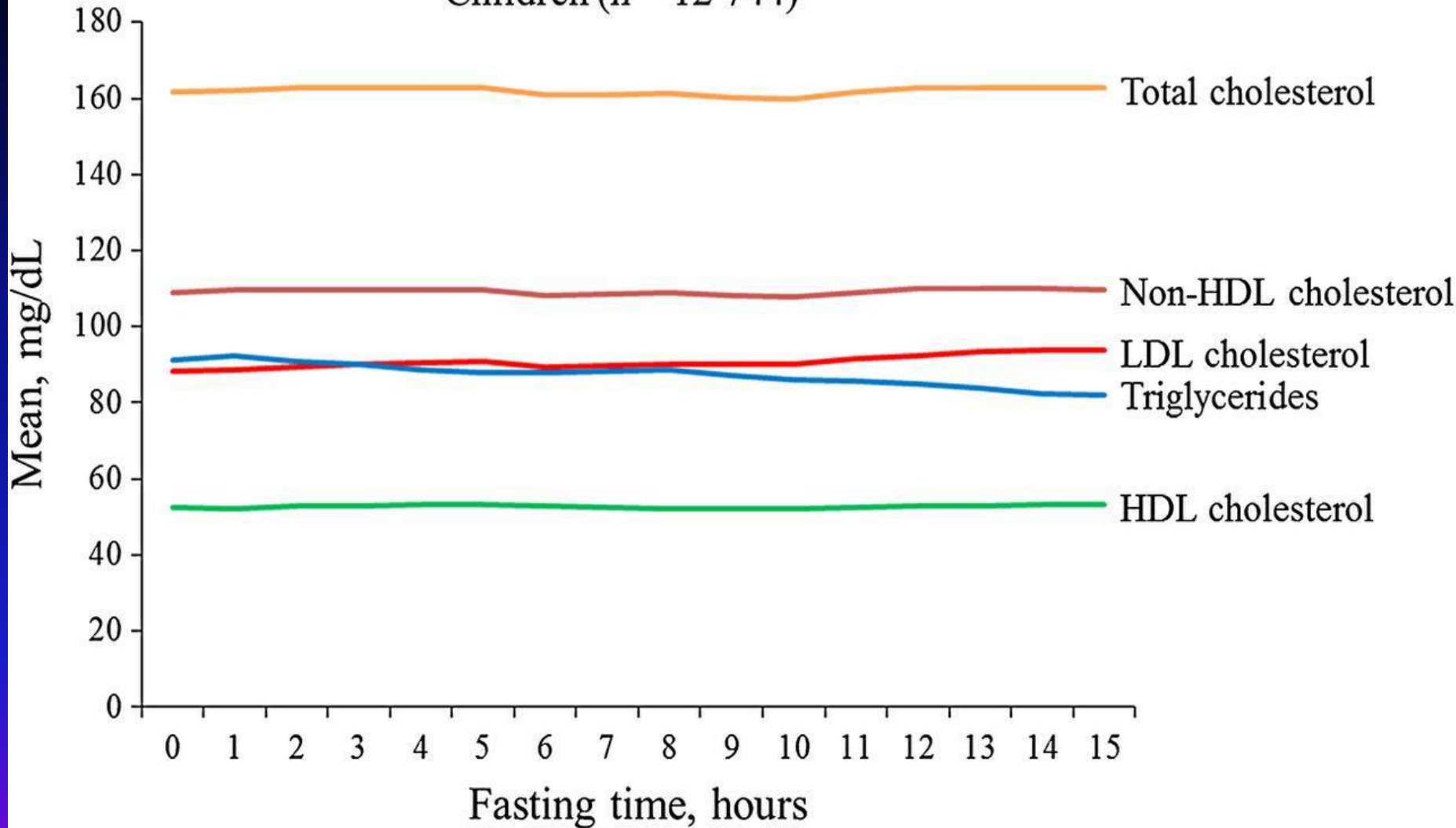
Lipoprotein lipase

Lipoprotein lipase

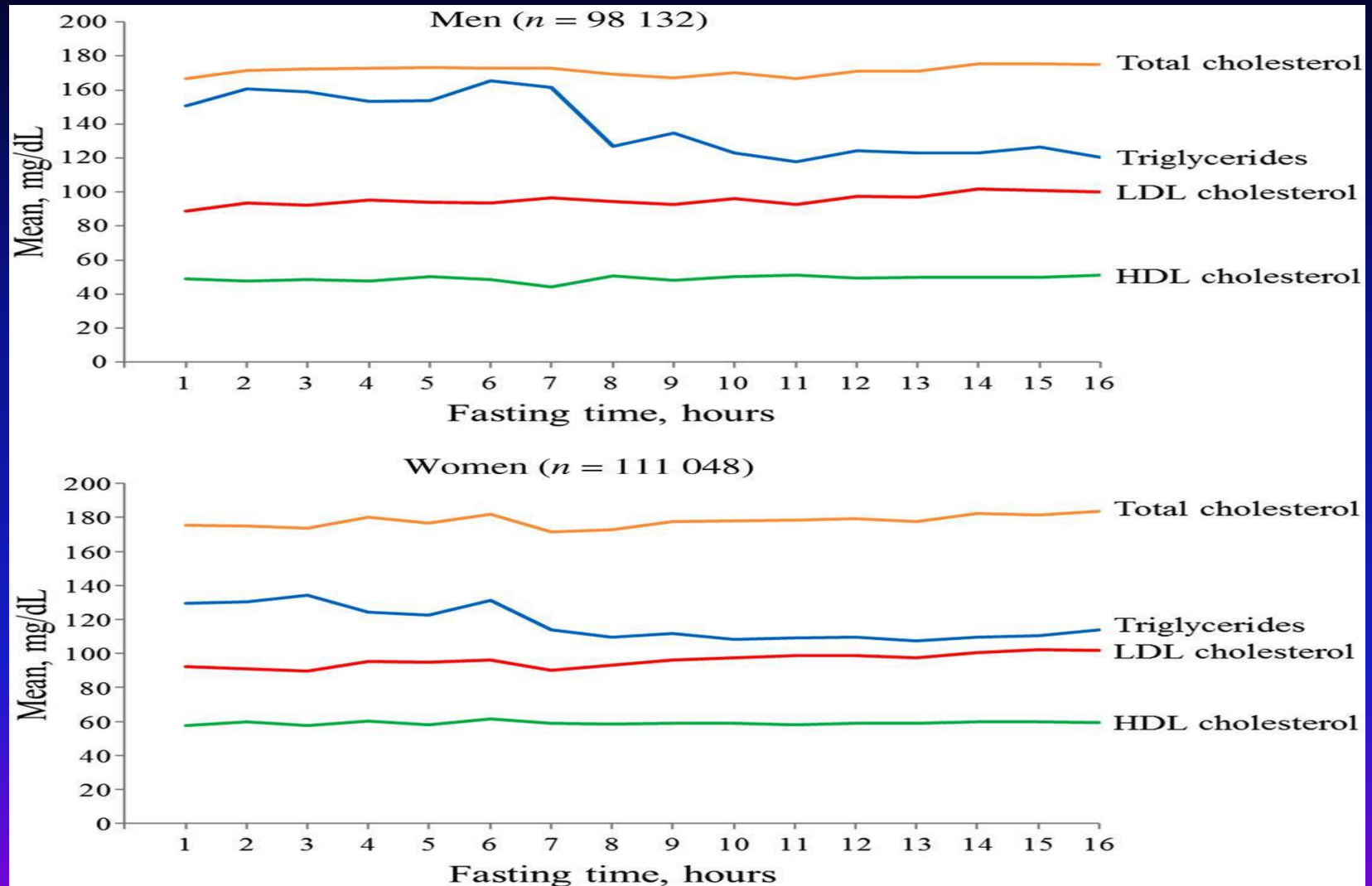
Fasting is not routinely required for assessing the
plasma lipid profile

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

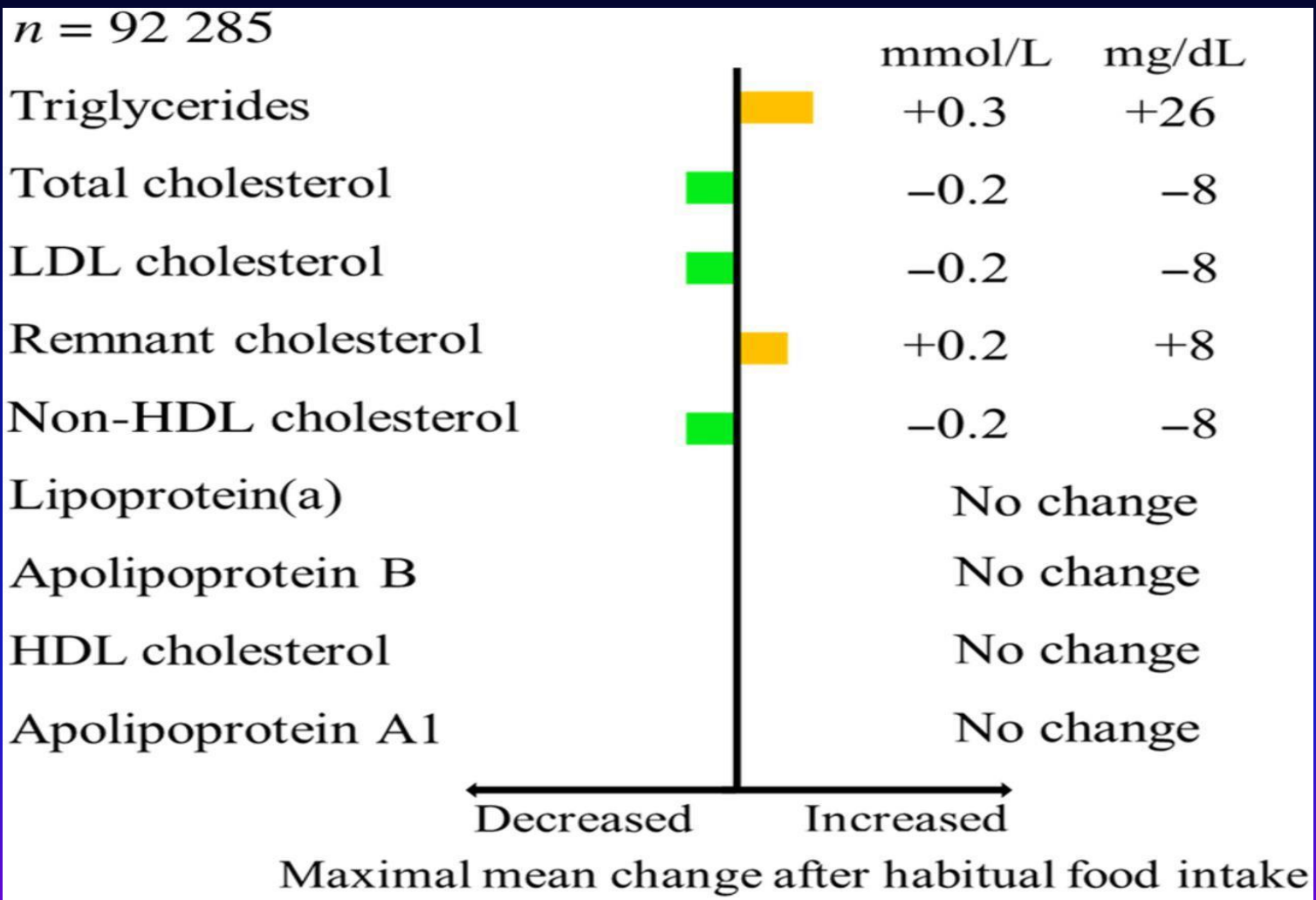
Children ($n = 12\,744$)



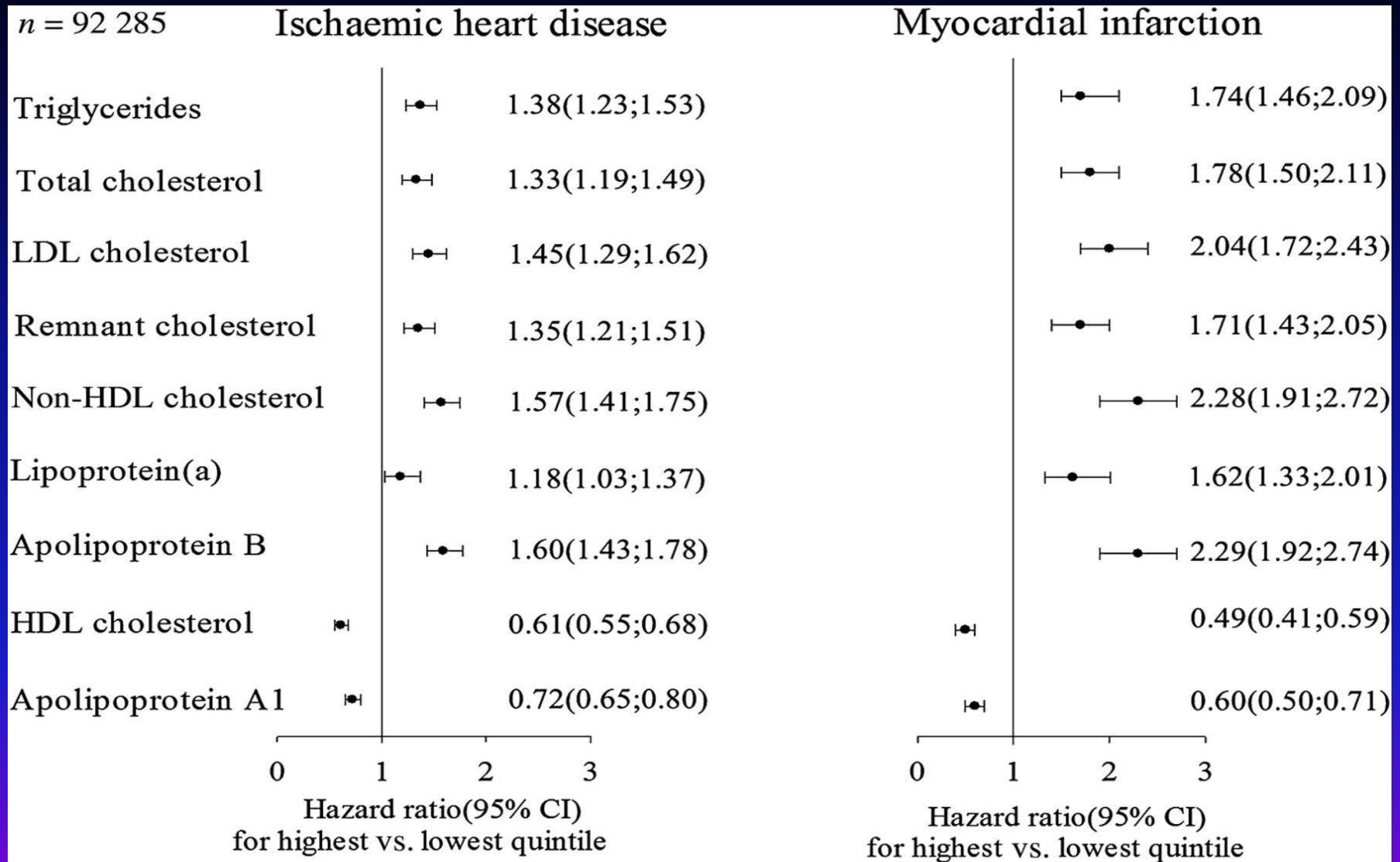
Mean concentrations of lipids and lipoproteins as a function of the period of fasting following the last meal in men and women from the Canadian general population.



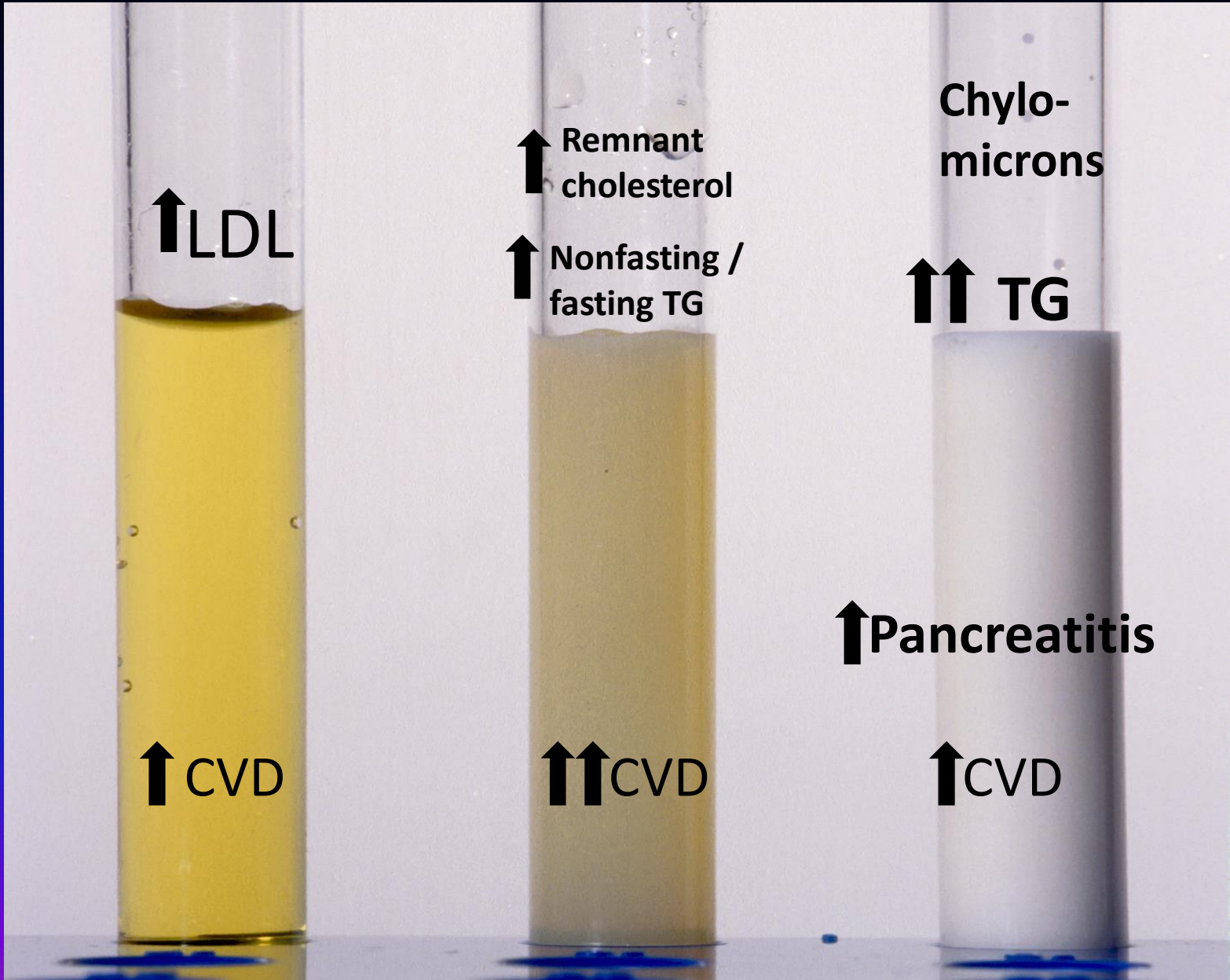
Maximal mean changes at 1–6 h after habitual food intake of lipids, lipoproteins, and apolipoproteins as part of standard and expanded lipid profiles



Risk of IHD and MI for highest vs. lowest quintile of random non-fasting lipids, lipoproteins, and apolipoproteins as part of standard and expanded lipid profiles



Copenhagen
General Population
Study





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 Langsted¹, Samia Mora², Genovefa Kolovou³, Hannsjörg Baum⁴, Eric Bruckert⁵, Gerald F. Watts⁶, Grazyna Sypniewska⁷, Olov Wiklund⁸, Jan Borén⁸, M. John Chapman⁹, Christa Cobbaert¹⁰, Olivier S. Descamps¹¹, Arnold von Eckardstein¹², Pia R. Kamstrup¹, Kari Pulkki¹³, Florian Kronenberg¹⁴, Alan T. Remaley¹⁵, Nader Rifai¹⁶, 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

Patients for non-fasting lipid profile testing

- Initial lipid profile testing in any patient
- For CV risk assessment
- Patients admitted with ACS
- In Children
 - If preferred by the patient
 - In diabetic patients
 - In the elderly
 - Patients on stable drug therapy

Non-fasting versus fasting concentrations :

lipid profile is taken in the fasting state : Traditional practice in most countries

Denmark—a non-fasting lipid profile has been the standard since 2009.

An advantage of non-fasting rather than fasting lipid profile measurements :

Blood-sampling process is simplified for Patients, Clinicians ,
Clinical Labs & hospitals

Have been used successfully in population cohort studies as well as
RCTs of statins

Increases compliance to lipid-lowering therapy and monitoring.

Non-fasting versus fasting concentrations :

Triglyceride concentrations on average only increase by 0.2–0.4 mmol / L 2–6 h after eating normal meals

These increases are clinically unimportant.

Non-fasting lipid, lipoproteins : Predict increased CV risk.

Most people eat regularly throughout the day

Non-fasting versus fasting concentrations

Recent guidelines have shifted to recommend non-fasting lipid analysis

Convenience

Supported by several studies

Fasting lipid profile testing

Can sometimes be required if :

- Non-fasting TGs >400 mg/dL
- Known HTG followed in lipid clinic
- Recovering from hypertriglyceridaemic pancreatitis
- Additional laboratory tests requested that require fasting or morning samples (e.g. fasting glucose, therapeutic drug monitoring)

Patients for fasting lipid profile testing

To establish TG assessment at baseline before starting medications that can trigger severe hypertriglyceridemia and risk of acute pancreatitis .

Steroids

Estrogens

Tamoxifen

Retinoic acid for acne

L-asparaginase used in chemotherapy.

Non-fasting versus fasting concentrations

Clinical decisions are guided by

Global risk assessment

LDL-C levels

Friedewald LDL-C equation

originally derived in fasting patients

Now increasingly utilized in the non-fasting setting to guide management to lower LDL-C.

Friedewald formula : 1972

Allows LDL-C determination by using a fasting TC, HDL-C, and Triglycerides

Friedewald Formula : $LDL-C = Total\ Cholesterol - HDL-C - TG / 5$
in mg/dl

Caveats : Cannot be used if triglycerides were ≥ 400 mg/dL & in rare type III Lipid abnormality

Friedewald formula

Provides a quick calculation

Inexpensive

Alternative that could be scaled for clinical purposes

Served as a global standard in lipid analysis over the past 4 decades.

Friedewald Formula : Limitations

Martin et al :

Sample of 1 million patients

Friedewald equation tended to underestimate LDL-C when TG levels were 150 mg/dL

Most likely occurred when TG levels exceeded 200 mg/dL

Thus the use of nonfasting samples along with guidelines that advocate decision-making based on fixed targets could affect therapy decisions.

Directly measured LDL-C

Limitations

The CDC and Prevention Lipid Standardization Program :

Does not provide certification of direct LDL -C assays as they do for TC , HDL-c and TG .

NCEP working group published recommendations for direct measurement of LDL-C while specific recommendations for manufacturers of LDL-c reagents are provided

Results from different methods cannot be used interchangeably as biases exist .

Of the several methods available , beta -quantification is most widely used .

Directly measured LDL-C

Direct measurement of LDL-C : Analytical

ultracentrifugation [Beta quantification]

Gold standard technique

Slow, Costly and really fit for only research settings.

American College of Cardiology [ACC]
Optimizing Non-Fasting Lipid Analysis
in the Era of Precision Medicine :

Mar 21, 2018

Expert Analysis

ACC :Optimizing Non-Fasting Lipid Analysis

Guidelines recommend low LDL-C in high risk and very high risk patients

Can we use non-fasting testing with the Friedewald equation ?

Friedewald equation is prone to inaccuracy.

A recent analysis showed that the equation leads to sizable errors more commonly in non-fasting samples versus fasting ones.

ACC :Optimizing Non-Fasting Lipid Analysis

The most sizable errors occur in the range of greatest clinical relevance; that is, at low LDL-C levels <70 mg/dL

This is the zone that we shoot for in the highest risk patients.

The Friedewald equation underestimates true LDL-C particularly in non-fasting patients when TG levels are raised

ACC :Optimizing Non-Fasting Lipid Analysis

Non-fasting values :

Accurate 37% of the time

81% of the time errors of 10 mg/dL observed

In those with Friedewald LDL-C <70 mg/dL

One in 12 non-fasting patients had 20-29 mg/dL errors

Compared with measured LDL-C

One in 28 patients had errors >30 mg/dL

ACC :Optimizing Non-Fasting Lipid Analysis

Novel Martin-Hopkins LDL-C method :

First to transform the Friedewald equation

From a one-size-fits-all  to an individualized approach.

It replaces the fixed factor of 5 used for the triglyceride to VLDL-C ratio

One of 180 patient-specific variables

Calculated based on serum triglyceride and Non - HDL-C concentrations.

No additional testing is required

ACC :Optimizing Non-Fasting Lipid Analysis

In fact, >97% of patients have errors <10 mg/dL, even in the non-fasting state

Cross-sectional analysis of over 1.5 million patients showed that LDL-C accuracy remains high with this new Martin-Hopkins method, regardless of fasting versus non-fasting.

How does the Martin-Hopkins calculation differ from the Friedewald calculation for LDL-C?

Provides greater customization to a patient's specific TG level by using a more "personalized" factor to calculate VLDL-C from TG

Adjustable factor, Ranges from 3.1 to 11.9

Derived from an analysis of TG -to-VLDL-C ratios in more than 1.3 million people.

How does the Martin-Hopkins calculation differ from the Friedewald calculation for LDL-C?

The factor is lowest : For patients with very low levels of TG and high levels of non-HDL-c

The factor is highest : For those with very high levels of TG and low levels of non-HDL-c.

Provides better correlation with direct LDL-C measurements.

The primary advantage of the Martin-Hopkins equation is that it is applicable to low LDL-C levels even in the presence of elevated triglyceride concentrations

Table. Concordance of Calculated (Martin-Hopkins or Friedewald) LDL-C with Direct LDL-C-based ASCVD Risk Classification

LDL-C Strata, mg/dL, TG <400 mg/dL	Concordance with Cardiovascular Risk Classification based on Directly Measured LDL-C, % (95% CI) ^a	
	Martin-Hopkins Calculation	Friedewald Calculation
Any LDL-C level	91.7 (91.6-91.8)	85.4 (85.3-85.5)
LDL-C <70		
TG 100-149	94.3 (93.9-94.7)	79.9 (79.3-80.4)
TG 150-199	92.4 (91.7-93.1)	61.3 (60.3-62.3)
TG 200-399	84.0 (82.9-85.1)	40.3 (39.4-41.3)

ASCVD, atherosclerosis cardiovascular disease

^a P < 0.001 for each comparison.

^b All individuals had triglyceride levels <400 mg/dL.



ACC :Optimizing Non-Fasting Lipid Analysis

Novel Martin-Hopkins LDL-C method :

Its accuracy and superiority to Friedewald estimation has been validated in the US and internationally in countries such as Brazil, Japan, Korea and Taiwan

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
	mg/dL ^a	mg/dL ^a
Triglycerides ^b	≥175	≥150
Total cholesterol	≥190	≥190
LDL cholesterol	≥115	≥115
Remnant cholesterol ^c	≥35	≥30
Non-HDL cholesterol ^d	≥150	≥145
Lipoprotein(a)	≥50 ^f	≥50 ^f
Apolipoprotein B	≥100	≥100
HDL cholesterol ^g	≤40	≤40
Apolipoprotein A1	≤125	≤125

Separate referral to Lipid specialist at

Life-threatening concentrations

Triglycerides

> 10 mmol/L Pancreatitis
risk?
> 880 mg/dL^a

LDL cholesterol

> 13 mmol/L HoFH?
> 500 mg/dL^a

LDL cholesterol

> 5 mmol/L
> 190 mg/dL^a HeFH?

LDL cholesterol in children

> 4 mmol/L
> 155 mg/dL^a HeFH?

Suggested implementation strategies : For use of non-fasting lipid profiles and for flagging in laboratory reports of abnormal values based on desirable concentration cut-points.

Implementation strategies in individual countries, states, and provinces for

Non-fasting lipid profiles

Key university hospitals start using non-fasting lipid profiles



National societies for cardiology, endocrinology, atherosclerosis, pediatrics, clinical chemistry, general practice, and others

Adapt non fasting lipid profiles



Journalists at key medias are invited to bring the story that fasting is no longer routinely required for lipid profile testing



Clinical chemistry laboratories no longer require fasting before lipid profile testing

Laboratory reporting on abnormal concentrations

Key university hospitals start using desirable concentration cut-points to indicate abnormal concentrations



National societies for clinical chemistry, cardiology, endocrinology, atherosclerosis, pediatrics, general practice, and others

Adapt desirable concentration cut points



Clinical chemistry laboratories use desirable concentration cut-points for lipid profile testing



National societies enforce strategy

A close-up photograph of two hands, palms up, holding a small, rectangular piece of white paper with deckled edges. The paper is held horizontally across the center of the hands. On the paper, the words "Thank You" are written in a black, elegant cursive font. The background is a solid, dark color, likely black, which makes the hands and the white paper stand out. The lighting is soft, highlighting the texture of the skin and the paper.

Thank You