Lipid reporting across Canada: current variability and proposed harmonized lipid profile and interpretive comments

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INTRODUCTION

- Decision limits are one of the most widely used decision-making tools in laboratory medicine. However, in some cases, even for the same analyte, different laboratories across Canada report different decision limits when differences are not warranted by analytical variation.
- Recently, the Canadian Cardiovascular Society (CCS) published the 2016 CCS Guidelines for the management of dyslipidemia in adults[1]. However, despite these guidelines, lipid reporting remains highly variable across Canada.
- The Canadian Society of Clinical Chemists (CSCC) Reference Interval Harmonization (hRI) Working Group aims to address this gap by establishing harmonized lipid reporting and supporting its implementation across the country[2].
- Harmonized lipid reporting will ensure reports obtained from different laboratories are comparable. This will improve accuracy and consistency of patient results and help standardize patient care.

AIM

- Identify gaps in lipid reporting by conducting a survey in different laboratories across Canada
- Review published reference interval studies and national guidelines for dyslipidemia and cardiovascular risk
- Propose a harmonized lipid report for adults and pediatrics

METHOD

- A lipid focus group was identified within the CSCC hRI Working Group. Lipid reports were requested from Canadian laboratories. Data examined include lipid parameters reported and flagged, decision limits and interpretative comments. Results were tabulated.
- Reference interval studies including the Canadian Health Measures Survey (CHMS)[3], Canadian Laboratory Initiative on Pediatric Reference Intervals (CALIPER)[4], Nordic Reference Interval Project (NORIP)[5] and NORIP-Pediatric[6] and recent dyslipidemia guidelines including the Canadian 2016 CCS Guidelines for the Management of Dyslipidemia[1], the European Atherosclerosis Society (EAS) and European Federation of Clinical Chemistry and Laboratory Medicine (EFLM)[7] Guidelines, National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III)[8], and the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents from the National Heart, Lung, and Blood Institute (NHLBI)[9] and NCEP[10] for pediatrics, were reviewed.
- Based on reference interval studies and guidelines, the hRI Working Group developed harmonized lipid reporting recommendations for adults and pediatrics. These recommendations will be reviewed with stakeholders including cardiologists, general practitioners, pediatricians, endocrinologists and lipid specialists to increase awareness and ensure feasibility. Recommendations will be revised accordingly by the lipid focus group.
- Recommendations will be communicated through conferences and publications and the hRI Working Group will help support implementation of recommendations in laboratories. Lipid reporting recommendations will be updated based on guideline revisions.

RESULTS

Table 1. Summary of adult lipid reporting in seven laboratories across Canada. Variation was observed in lipid parameters reported, lipid parameters flagged, decision limits, and interpretative comments. *fasting status determined by phlebotomist

Lipid Parameter	Units	Laboratory 1	Laboratory 2	Laboratory 3	Laboratory 4	Laboratory 5	Laboratory 6	Laboratory 7
Total Cholesterol	mmol/L	<5.20	No flag	2.00 – 5.19	<5.20	No flag	No flag	<5.0
Triglycerides	mmol/L	<1.70	No flag	<2.21	<1.50	0.00- 1.7	0.00- 1.7	Fasting: <1.7 Non-fasting: <2.0 Flag at ≥1.7
LDL-C (Calc)	mmol/L	No flag	No flag	1.50 – 3.40 *Comment*	<3.40 *Comment*	0.0- 3.4 mmol/L	No flag	<3.50 *Comment*
HDL-C	mmol/L	Males: ≥1.00 Females: ≥1.30	No flag	>1.19	>0.90	No flag	No flag	Males: >1.00 Females: >1.30
Non-HDL-C (Calc)	mmol/L	No flag *Comment*	No flag *Comment*	No flag *Comment*	No flag *Comment*	0.0- 4.2 mmol/L	No flag	<4.3 *Comment*
Fasting	(hrs since last meal)	Recorded	Recorded	Recorded	Recorded as fasting or non-fasting*	Recorded	Recorded	Recorded
TC/HDL Ratio		Reported, No flag	Reported, *Comment*	<4.4	Not reported	Not reported	Not reported	Not reported
Interpretation		Interpretative comment	Interpretative comment	Not included	Not included	Interpretative comment	Interpretative comment	Not included

Laboratory 2 Interpretative Comments

Lipid target values should be based on patient 10 year CVD risk assessment

	High or Intermediate CVD Risk
Primary Treatment Target	LDL-C ≤2.00 mmol/L OR ≥50% decrease in LDL-C
Alternate Treatment Target	Non-HDL ≤2.6 mmol/L OR ApoB ≤ 0.8 g/L
	Low CVD Risk
Alternate Treatment Target	≥50% decrease in LDL-C

Laboratory 1 Interpretative Comments

Treatment thresholds and targets based on 2016 CCS Guidelines

Category	Consider initiating therapy if	Treatment target
Primary prevention	High FRS (≥20%); or Intermediate FRS (10-19%) and LDL-C ≥3.5 mmol/L; or non-HDL-C ≥4.30 mmol/L; or ApoB ≥1.20 g/L; or men ≥50 and women ≥60y with ≥ 1 additional CVD risk factor	LDL-C <2.00 mmol/L or >50% decrease; or ApoB <0.80 g/L; or non-HDL-C <2.60 mmol/L
Statin indicated conditions	Clinical atherosclerosis*; abdominal aortic aneurysm; diabetes mellitus (DM) and age ≥40 y or ≥30 y with 15 years duration (DM1); DM with microvascular disease; chronic kidney disease (age ≥50 years)	LDL-C <2.00 mmol/L or >50% decrease; or ApoB <0.80 g/L; or non-HDL-C <2.60 mmol/L
Low-risk	LDL-C ≥5.00 mmol/L	LDL-C >50% decrease

*Consider target of LDL-C <1.8 mmol/L for subjects with ACS ≤3 months

Figure 1. Examples of interpretative comments reported by laboratories across Canada

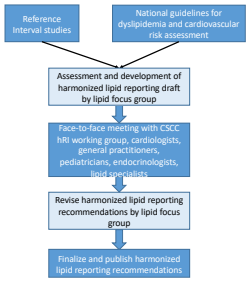

Figure 2. Process of establishing recommendations for harmonized lipid reporting in Canada

Table 2. CSCC hRI Working Group proposed harmonized lipid report and ApoB recommendation for adults (≥18 years of age)

Analyte	Decision Limit	Result Comment
Total Cholesterol	<5.20 mmol/L	Treatment thresholds and targets based on the 2016 CCS Guidelines For patients ≥40y, estimate risk using the modified Framingham Risk Score (FRS): **Low Risk (FRS <10%)** Treatment advised if LDL-C ≥5.0 mmol/L Treatment target: ≥50% reduction LDL-C **Intermediate Risk (FRS 10 - 19%)** Treatment advised if LDL-C ≥3.5 mmol/L OR Non-HDL-C ≥4.3 mmol/L OR ApoB ≥1.2 g/L OR men ≥50y and women ≥60y with ≥1 additional CV risk factor Treatment targets: LDL-C ≤2.0 mmol/L OR decrease by ≥50% OR Non-HDL-C ≤2.6 mmol/L OR ApoB ≤0.8 g/L **High Risk (FRS ≥20% or presence of high risk features)** Treatment advised in all patients Treatment targets: LDL-C ≤2.0 mmol/L OR decrease by ≥50% OR Non-HDL-C ≤2.6 mmol/L OR ApoB ≤0.8 g/L Note: If non-fasting, triglycerides <2.0 mmol/L acceptable Triglycerides >1.5 mmol/L, recommend to use non-HDL-C or ApoB as treatment target of choice If Triglycerides >4.5 mmol/L, recommend to measure lipids and lipoproteins fasted
HDL-C	>1.00 mmol/L	
LDL-C	<3.5 mmol/L	
Triglycerides	<1.7 mmol/L	
Non-HDL-C	<4.3 mmol/L	
Hours fasting	Record (h)	
ApoB	<1.2 g/L	Treatment thresholds and targets based on the 2016 CCS Guidelines **If ≥1.2 g/L** Treatment advised if Framingham Risk Score is Intermediate or High Treatment target for ApoB ≤0.8 g/L **If <1.2 g/L** Treatment target for ApoB ≤0.8 g/L

Table 3. CSCC hRI Working Group proposed harmonized lipid report and ApoB recommendation for children and adolescents (<18 years of age). *, National Heart, Lung, and Blood Institute

Analyte	Age	Decision Limit	Result Comment
Total Cholesterol	<18y	<4.40 mmol/L	Based on NHLBI 2011, and NCEP Report for Children and Adolescents Acceptable and high/low limits relative to dyslipidemia and atherosclerosis risk: Total Cholesterol Acceptable <4.40 mmol/L; High ≥5.15 mmol/L HDL-C Acceptable >1.15 mmol/L; Low <1.05 mmol/L LDL-C Acceptable <2.85 mmol/L; High ≥3.35 mmol/L Triglycerides (0-<10y) Acceptable <0.85 mmol/L; High ≥1.15 mmol/L Triglycerides (10-<18y) Acceptable <1.00 mmol/L High ≥1.45 mmol/L Non-HDL-C Acceptable <3.10 mmol/L; High ≥3.75 mmol/L
HDL-C	<18y	>1.15 mmol/L	
LDL-C	<18y	<2.85 mmol/L	
Triglycerides	<10y	<0.85 mmol/L	
	10 - <18y	<1.00 mmol/L	
Non-HDL-C	<18y	<3.10 mmol/L	
Hours fasting		Record (h)	
ApoB	<18y	<0.9 g/L	Based on NHLBI 2011, and NCEP Report for Children and Adolescents Borderline High <0.9 g/L; High ≥1.0 g/L

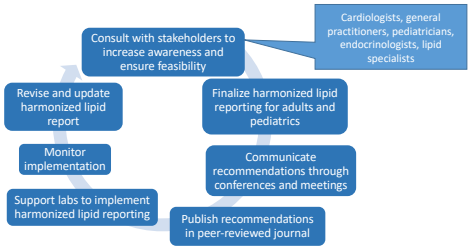

Figure 3. Continuous quality improvement plan to implement and update harmonized lipid reporting across Canada

CONCLUSIONS

- Lipid profile reports across Canada showed differences in reporting practices. Variation was noted in lipid parameters reported, lipid parameters flagged, decision limits and interpretative comments, highlighting the need for harmonization of lipid reporting across Canada.
- hRI Working Group harmonized lipid profile recommendations for adults were largely based on the Canadian 2016 CCS Dyslipidemia Guidelines[7], however, European non-fasting limits were also considered. Recommendations include: removing the TC/HDL-C ratio, recording time since last meal in hours, collecting non-fasting samples when appropriate, and basing flagging decision limits on values that suggest initiation of treatment. Pediatric lipid decision limits recommendations took NHLBI[10] reports into consideration.
- Laboratories require additional guidance to consolidate guidelines from various bodies. Recommended harmonized lipid reporting will be vetted by clinical experts prior to publication and implemented nationwide. Implementation will be monitored, and reporting recommendations will be updated based on guideline revisions.

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