Harmonized Lipid Profile Assessment and Interpretation in Canada

Victoria Higgins

Breakfast Roundtable CSCC 2018

Wednesday June 8, 2018

7:30-8:30am

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Annual Conference of the
Canadian Society of Clinical Chemists (CSCC)

VICTORIA HIGGINS

- I have no financial relationships to disclose.

- I will not discuss off label use and/or investigational use in my presentation.

Outline

- Introduce CSCC Reference Interval Harmonization Working Group
- Reference intervals vs. decision limits
- Assess differences in lipid reporting among laboratories
- Harmonization of clinical decision limits
- Introduce the Canadian harmonized lipid reporting recommendations
  - Discuss various national cardiovascular risk assessment guidelines and origin of decision limits
- Assess decision limits with flagging rates (Alberta population)

CSCC Reference Interval Harmonization (hRI) Working Group

***Goal:** To develop evidence-based harmonized reference interval recommendations and support their implementation in laboratories across the country*

Objective 1: Review adult and pediatric RIs currently in use in clinical laboratories across Canada

Objective 2: Assess the available evidence on RIs obtained in a priori studies of healthy populations

Objective 3: Develop appropriate recommendations and guidelines on the use of harmonized RIs across Canada

Variation in RIs across Canada

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Analytical

National Survey of Adult and Pediatric Reference Intervals in Clinical Laboratories across Canada: A Report of the CSCC Working Group on Reference Interval Harmonization

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- 37 laboratories reported RIs for 7 analytes (ALT, ALP, calcium, creatinine, FT4, hemoglobin, sodium)
- 40 laboratories measured 6 analytes (all except hemoglobin) in reference samples
- High variation in reported RIs, even between laboratories using the same instrumentation, and was higher in pediatrics
- RI variation was greater than test result variation for the majority of analytes

Next Steps for the CSCC hRI WG

Create focus groups:

1. Electrolytes (sodium, potassium, chloride, total CO2, magnesium)
2. Renal function (creatinine, calcium, phosphorus)
3. Hepatic function (ALT, ALP, albumin, total protein, total bilirubin, LDH)
4. Endocrinology (glucose, HbA1c, TSH, FT4, FT3)
5. Lipids (total cholesterol, LDL-C, HDL-C, triglycerides, non-HDL-C)

Reference Intervals for Lipid Parameters

Adults

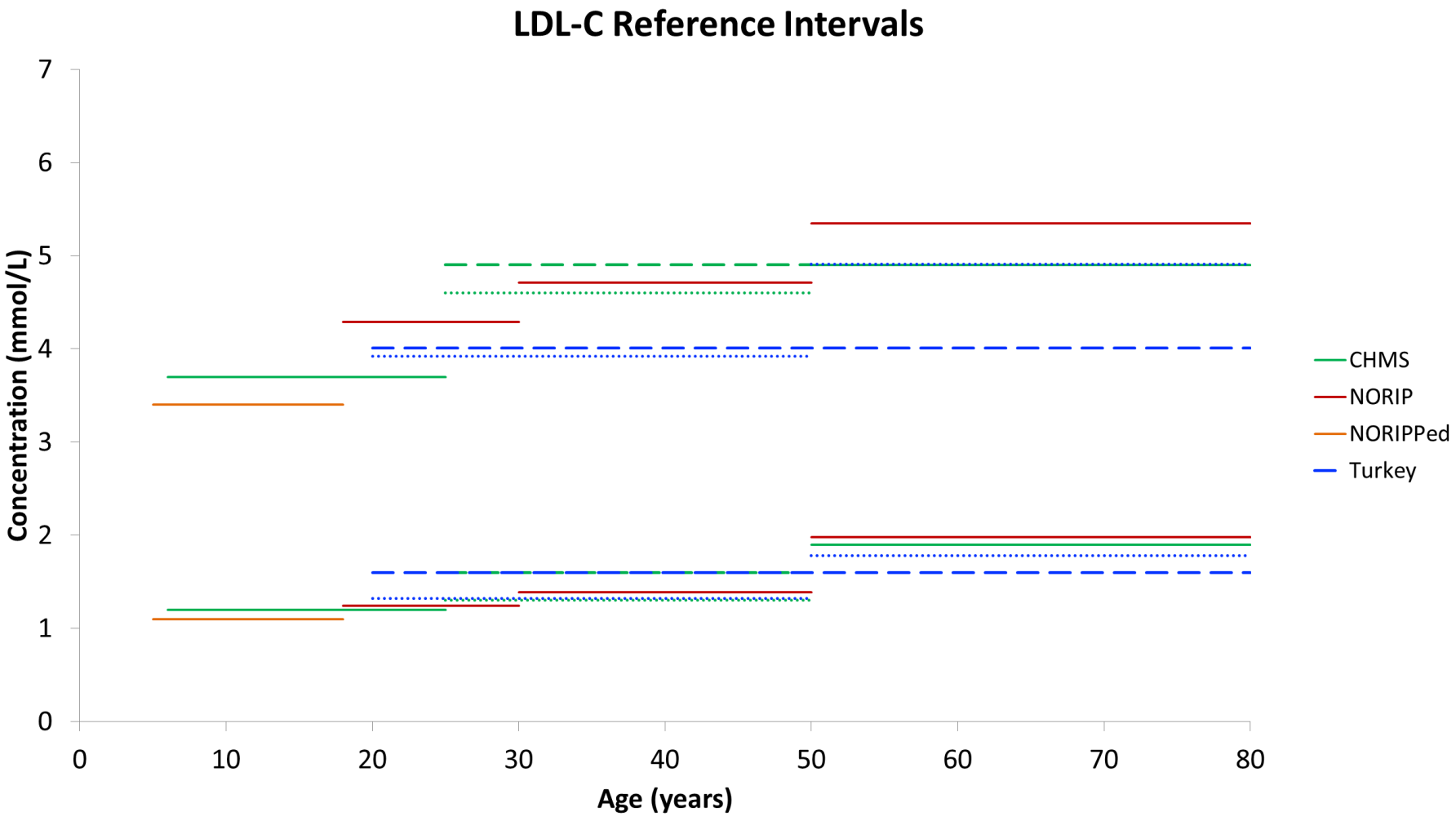
Study	Triglycerides		Total Cholesterol		HDL-Cholesterol		LDL-Cholesterol		Apolipoprotein B	
	Age (yrs) /Sex	RI (mmol/L)	Age (yrs) /Sex	RI (mmol/L)	Age (yrs) /Sex	RI (mmol/L)	Age (yrs) /Sex	RI (mmol/L)	Age (yrs) /Sex	RI (g/L)
CHMS (serum)	18-29 M/F 30-79 M 30-79 F	0.4-2.1 0.5-3.4 0.4-2.4	18-19 M/F 20-29 M/F 30-39 M/F 40-79 M/F	2.6-4.7 3.0-5.9 3.8-6.9 3.6-7.1	18-79 M 18-79 F	0.8-1.8 0.9-2.3	18-24 M/F 25-49 M 25-49 F 50-79 M/F	1.2-3.7 1.6-4.9 1.3-4.6 1.9-4.9	18-29 M/F 30-79 M/F	0.4-1.1 0.6-1.4
NORIP (serum)	18-80 M/F	0.45-2.60	18-29 M/F 30-49 M/F 50-80 M/F	2.9-6.1 3.3-6.9 3.9-7.8	18-80 M 18-80 F	0.8-2.1 1.0-2.7	18-29 M/F 30-49 M/F 50-80 M/F	1.2-4.3 1.4-4.7 2.0-5.3		
Turkey (serum)	20-79 M 20-50 F 50-79 F	0.53-3.39 0.46-2.52 0.64-3.55	20-79 M 20-50 F 50-79 F	3.20-6.42 3.20-6.38 3.93-7.92	20-79 M 20-79 F	0.85-1.52 0.95-1.56	20-79 M 20-50 F 50-79 F	1.60-4.01 1.32-3.92 1.78-4.91		

Pediatrics

Study	Triglycerides		Total Cholesterol		HDL-Cholesterol		LDL-Cholesterol		Apolipoprotein B	
	Age (yrs) /Sex	RI (mmol/L)	Age (yrs) /Sex	RI (mmol/L)	Age (yrs) /Sex	RI (mmol/L)	Age (yrs) /Sex	RI (mmol/L)	Age (yrs) /Sex	RI (g/L)
CHMS (serum)	6-18 M/F	0.4-2.1	3-5 M/F 6-15 M/F 16-18 M/F	3.1-5.6 3.0-5.3 2.6-4.7	3-5 M/F 6-14 M/F 15-18 M 15-18 F	0.8-1.9 0.9-2.1 0.8-1.8 0.9-2.3	6-18 M/F	1.2-3.7	6-13 M/F 14-18 M/F	0.5-1.0 0.4-1.1
CALIPER (serum)	0-14d M/F 15d-<1 M/F 1-18 M/F	0.93-2.93 0.60-2.92 0.50-2.23	0-14d M 0-14d F 15d-<1 M/F 1-18 M/F	1.10-2.82 1.20-3.23 1.66-6.13 2.90-5.40	0-14d M/F 15d-<1 M/F 1-<4 M/F 4-<13 M/F 13-18 M 13-18 F	0.40-1.08 0.30-1.85 0.84-1.63 0.92-1.88 0.82-1.77 0.83-1.86			0-14d M 0-14d F 15d-<1 M/F 1-<14 M/F 14-18 M/F	0.62-0.91 0.71-0.97 0.53-1.75 0.80-1.64 0.72-1.54
NORIP Ped (plasma)	5-10 M 11-18 M 5-18 F	0.34-1.58 0.34-2.54 0.34-1.95	5-18 M/F	2.7-5.5	5-13 M/F 14-18 M 14-18 F	1.0-2.3 0.8-2.0 1.0-2.3	5-18 M/F	1.1-3.4		

Reference Intervals for Lipid Parameters

Example: LDL-C



Reference Intervals (RIs) vs. Decision Limits (DLs)

RIs and DLs are often listed in the same column on reports, which can confuse the basis of terminology and the distinction between the two

Reference Intervals: The range of laboratory test results expected in a healthy reference population (commonly defined as the 2.5^{th} and 97.5^{th} percentiles)

Decision Limits: Threshold values, in which values exceeding or falling below the threshold indicating the patient is at a significantly higher risk of a clinical outcome or satisfies criteria for diagnosis of a specific disease

"When decision limits determined by national or worldwide consensus exist, these limits, rather than reference intervals should be reported" – CLSI EP28-A3c

Variability in Canadian Lipid Reports

Example 1

CODES	TEST DESCRIPTION	RESULTS	REFERENCE RANGE	OUTSIDE NORMAL LIMITS
		C H E M I S T R Y		
	HOURS FASTING	12.	hours	
	CHOLESTEROL	2.05	DESIRED: < 5.20 mmol/L	
	Patient's age not given. Interpretation based on adult values.			
	TRIGLYCERIDES	1.00	< 1.70 mmol/L	
	Patient's age not given. Interpretation based on adult values.			
	HDL CHOLESTEROL	0.98	M: >=1.00 mmol/L F: >=1.30 mmol/L	0.98
	Age / sex not given. Interpretation based on adult values.			
	LDL CHOLESTEROL CALC.	0.61	mmol/L	0.61
	NON-HDL-CHOLESTEROL(CALC	1.07	mmol/L	
	Non HDL-cholesterol is calculated from total cholesterol and HDL-cholesterol and is not affected by the fasting status of the patient.			
	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 >=60 y 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.

	TC/HDL-C RATIO	2.1		

Variability in Canadian Lipid Reports

Example 2

Cholesterol	4.65	2.00--5.19	mmol/L
Triglyceride	1.26	<2.21	mmol/L
HDL-Cholesterol	2.07	>1.19	mmol/L
CHOL:HDL Ratio	2.25	<4.4	
Non HDL-Cholesterol	2.58		mmol/L

Non HDL-cholesterol is calculated from total cholesterol and HDL-C and is not affected by the fasting status of the patient. The optimal non HDL-cholesterol level for intermediate and high risk individuals is <= 2.60 mmol/L. See Can J Cardiol 2013 vol 29 pgs 151 to 167.

LDL Cholesterol	2.01	1.50--3.40	mmol/L

The optimal LDL cholesterol level for intermediate and high risk individuals is <= 2.00 mmol/L. If triglycerides are => 1.50 mmol/L, consider monitoring of alternate lipid targets non HDL-cholesterol or apoB. For low risk individuals with LDL cholesterol => 5.00 mmol/L, target reduction of LDL cholesterol => 50 percent. See Can J Cardiol 2013 vol 29 pgs 151 to 167.

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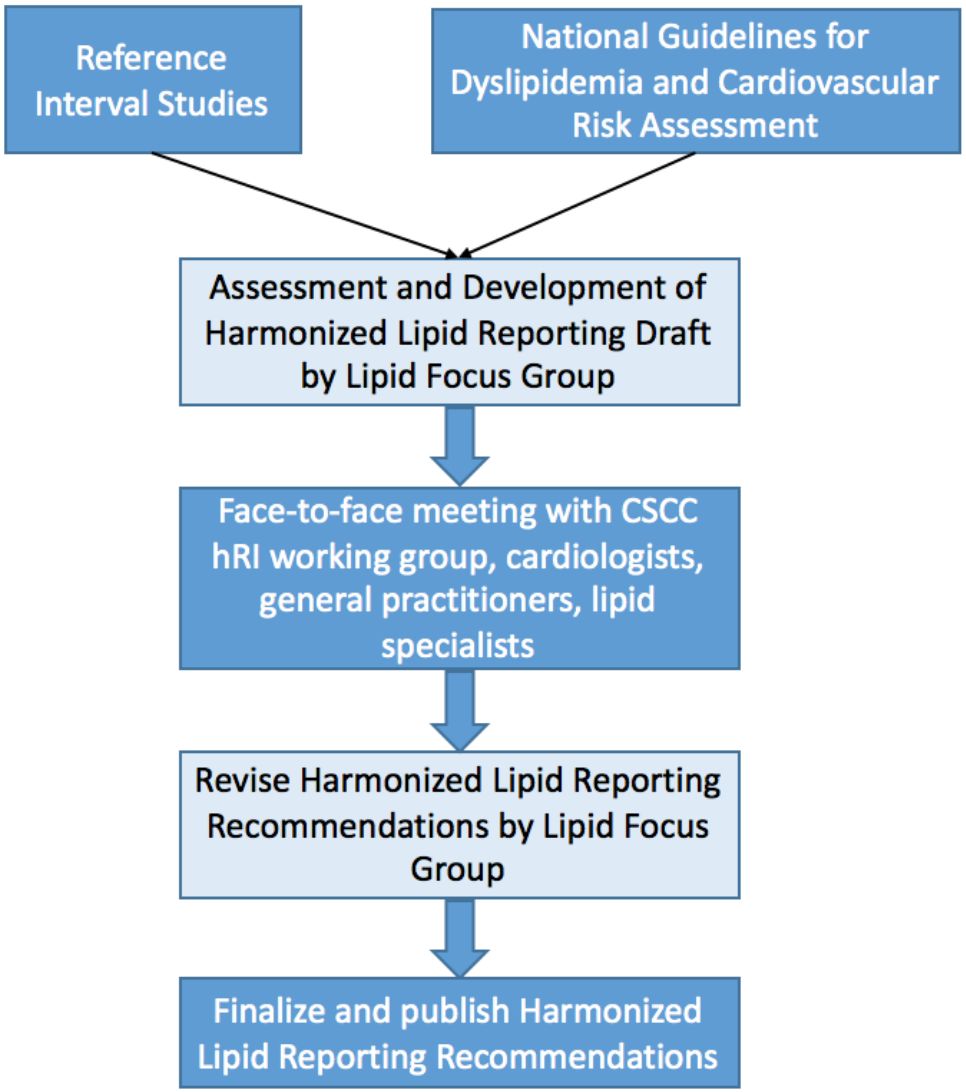
Variability in Canadian Lipid Reports

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	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	(hours 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			Interpretative comment	Interpretative comment	

Important Considerations for Harmonizing Clinical Decision Limits

- Method standardization and performance
  - Rather than requiring *de novo* establishment or verification of RIs, when adopting decision limits, reported values must not appreciably differ from those reported by a certified reference laboratory
- Harmonizing pre-analytical factors
  - Fasting vs. non-fasting
  - Seasonal variation
- Biological Variation
  - Index of individuality (II) is low for lipids
  - High RCV (e.g. 18% for cholesterol)

Process of establishing recommendations for harmonized lipid reporting in Canada



Canadian Journal of Cardiology 32 (2016) 1263–1282

Society Guidelines

2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult

Key Changes from 2012 Guidelines/Highlights:

- Lipid screening for men and women ≥ 40 years of age
- Risk assessment with FRS to determine risk category
- CLEM to calculate cardiovascular age as alternative approach
- LDL-C as primary, non-HDL-C or apoB as alternative targets
- Nonfasting lipid determination recommended as a suitable alternative to fasting levels

Canadian Journal of Cardiology 32 (2016) 1263–1282

Society Guidelines

2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult

Screening:

- Men and women ≥ 40 years of age
  - Earlier in South Asians, First Nations, those with CV risk factors (e.g. diabetes, hypertension, smoking, obesity)
- Fasting or non-fasting lipid panel (TC, LDL-C, HDL-C, TG, non-HDL-C), glucose, eGFR
  - Optional: apoB, urine albumin:creatinine ratio (if eGFR <60mL/min/1.73m^2, hypertensive, or diabetic)

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Society Guidelines

2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult

Risk Assessment:

- Cardiovascular age calculated using CLEM
- 10-year risk assessment using modified FRS (includes age, TC, HDL-C, systolic blood pressure, diabetes, smoking status, family history premature CVD)
  - Low Risk (LR, <10%) – pharmacotherapy not indicated
  - Intermediate Risk (IR, 10-19%) – additional considerations
  - High Risk (HR, ≥20%) or statin-indicated condition: statin therapy indicated

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Society Guidelines

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Treatment Target (Statin Therapy):

- Primary: LDL-C consistently <2.0 mmol/L or >50% reduction
- Secondary: apoB <0.8 g/L or non-HDL-C <2.6 mmol/L (recommended when TG > 4.5mmol/L)

Recommended Adult (>18 years) Lipid Report

Analyte	Decision Limit	Result Comment
Total Cholesterol	<5.2 mmol/L	Treatment thresholds and targets based on the 2016 CCS Guidelines For patients ≥40 years, 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≥50 and women≥60 yrs 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	>1.0 mmol/L	
LDL-C	<3.5 mmol/L	
Triglycerides	<1.7 mmol/L	
Non-HDL-C	<4.3 mmol/L	
Fasting (hours)	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 of High Treatment target for ApoB ≤ 0.8 g/L **If < 1.2 g/L** Treatment target for ApoB ≤ 0.8 g/L

Origin of Recommended Adult Lipid Decision Limits

Total Cholesterol

- Increased CHD incidence at serum cholesterol > 5.20 mmol/L (Framingham Study)

LDL-C, ApoB and non-HDL-C

- Primary prevention studies included subjects without vascular disease who on average were in the FRS IR group, but also include some HR and LR subjects
- Studies (AFCAPS/TexCAPS, WOSCOPS, ASCOTE, JUPITER) showed statin therapy reduced CVD events for subjects with
  - LDL-C≥ 3.5 mmol/L or non-HDL-C 4.3 mmol/L or ApoB≥1.2 g/L or men ≥50 yrs and women ≥60 yrs and ≥1 CVD risk factor

Triglycerides

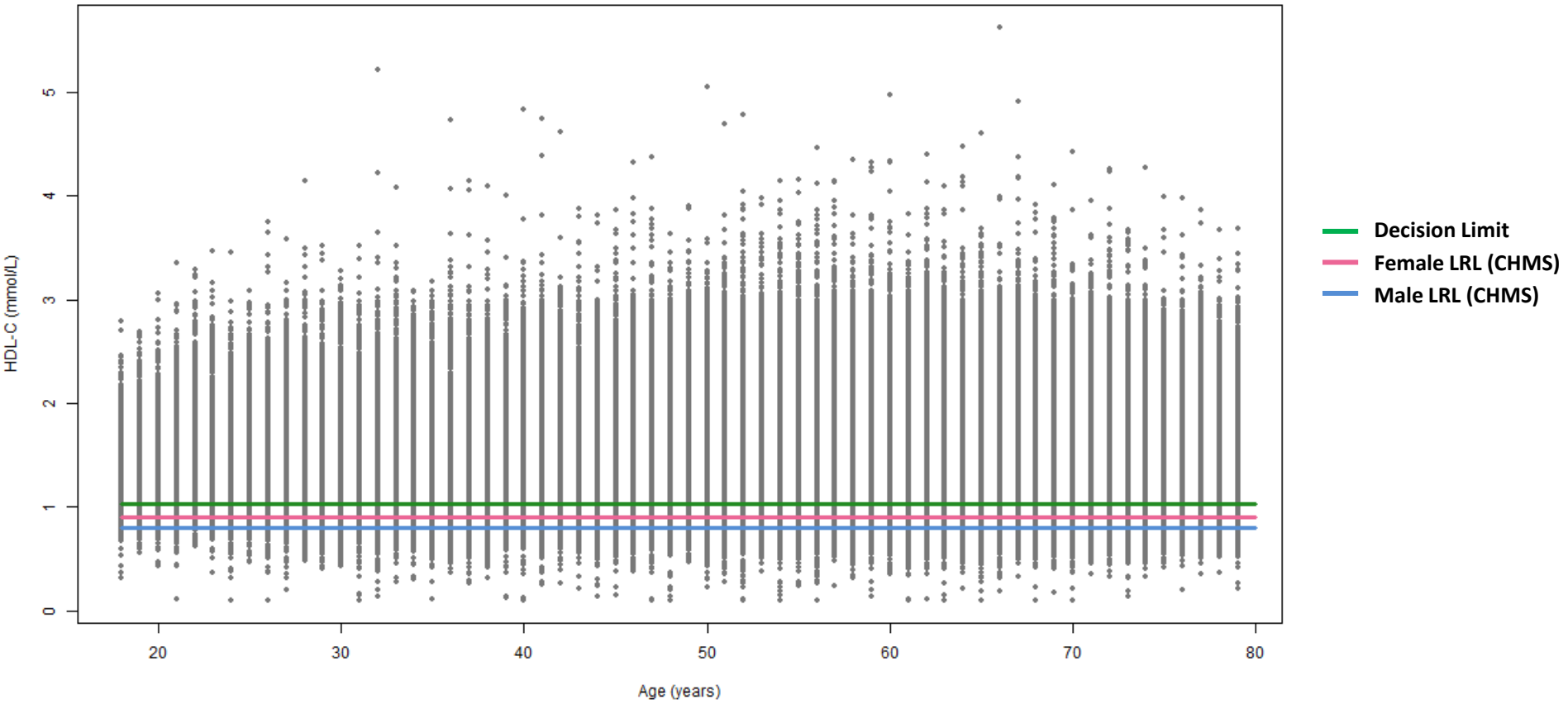
- NCEP ATP III panel reviewed studies and found when TG>1.7mmol/L, substantially increased CHD risk

HDL-C

- Population studies show continuous rise in CHD risk as HDL-C levels decline; no threshold relationship defined and therefore any categorical definition of low HCL-C is arbitrary. NCEP ATP III recommended a categorical low HDL-C defined as <1.03 mmol/L

Flagging Rates (RI vs DL)

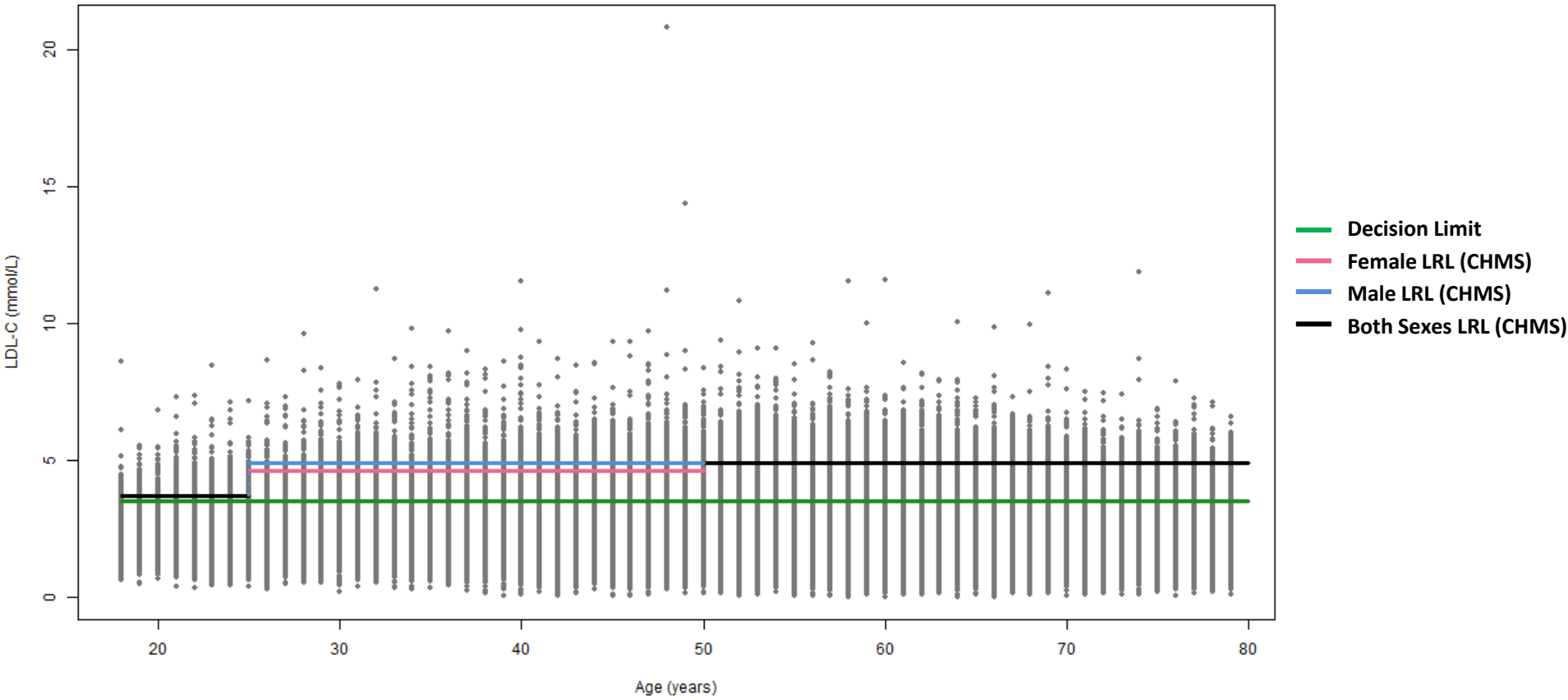
Example: HDL-C



Variable	Age Range (years)	Lower Reference Limit (LRL)	Total Flagging Rate using LRL, % (proportion)	Age Range (years)	Decision Limit (DL)	Total Flagging Rate using DL, % (proportion)
HDL-C	18-<80M 18-<80F	≥ 0.8 mmol/L ≥ 0.9 mmol/L	3.30 % (15292/462717)	18-<80	> 1.03 mmol/L	18.3 % (84643/462717)

Flagging Rates (RI vs DL)

Example: LDL-C



Variable	Age Range (years)	Lower Reference Limit (LRL)	Total Flagging Rate using URL, % (proportion)	Age Range (years)	Decision Limit (DL)	Total Flagging Rate using DL, % (proportion)
Triglycerides	18-<30 30-<80M 30-<80F	≤ 2.1 mmol/L ≤ 2.4 mmol/L ≤ 3.4 mmol/L	11.4 % (52974/463793)	18-<80	< 1.7 mmol/L	37.2 % (172630/463793)

Adult Flagging Rates (RI vs DL)

Variable	Age Range	Upper Reference Limit (URL)	Total Flagging Rate using URL, % (proportion)	Age Range (years)	Decision Limit (DL)	Total Flagging Rate using DL, % (proportion)
Total Cholesterol	18-<20 20-<30 30-<40 40-<80	≤ 4.7 mmol/L ≤ 5.9 mmol/L ≤ 6.9 mmol/L ≤ 7.1 mmol/L	3.86% (17924/463881)	18-<80	< 5.2 mmol/L	39.0% (180795/463881)
LDL-C	18-<25 25-<50M 25-<50F 50-<80	≤ 3.7 mmol/L ≤ 4.9 mmol/L ≤ 4.6 mmol/L ≤ 4.9 mmol/L	2.05% (9258/451232)	18-<80	< 3.5 mmol/L	21.7 % (97713/451232)
HDL-C	18-<80M 18-<80F	≥ 0.8 mmol/L ≥ 0.9 mmol/L	3.30 % (15292/462717)	18-<80	> 1.03 mmol/L	18.3 % (84643/462717)
Triglycerides	18-<30 30-<80M 30-<80F	≤ 2.1 mmol/L ≤ 2.4 mmol/L ≤ 3.4 mmol/L	11.4 % (52974/463793)	18-<80	< 1.7 mmol/L	37.2 % (172630/463793)

Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents (2011)

- No Canadian pediatric lipid guidelines
- Dyslipidemia associated with initiation and progression of atherosclerotic lesions in children and adolescents
- Largely used the 1992 Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents from the NCEP as a framework
- Recommend screening all children at ages 9-11 years
- Provide acceptable, borderline, and high cut points for total cholesterol, LDL-C, HDL-C, non-HDL-C, triglycerides, apoB, and apoA1

Recommended Pediatric Lipid Report

Analyte	Age	Decision Limit	Result Comment
Total Cholesterol	<18 years	< 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-<10 years) Acceptable < 0.85 mmol/L; High ≥ 1.15 mmol/L Triglycerides (10-<18 years) 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	<18 years	> 1.15 mmol/L	
LDL-C	<18 years	< 2.85 mmol/L	
Triglycerides	<10 years	< 0.85 mmol/L	
	10-<18 years	< 1.00 mmol/L	
Non-HDL-C	<18 years	< 3.10 mmol/L	
Fasting (hours)	Record (h)		

ApoB	<18 years	<0.9 g/L	Based on NHLBI 2011 and NCEP Report for Children and Adolescents Acceptable < 0.9 g/L; High ≥ 1.0 g/L

Origin of Recommended Pediatric Lipid Decision Limits

Total Cholesterol, LDL-C, HDL-C, Triglycerides

- Lipid Research Clinics (LRC) Prevalence Study (1970-1976) of US and Canadian children and adolescents (0-19 years)
- Borderline and high cut-points calculated as 75th and 95th percentiles, respectively

Non-HDL-C

- Equivalent to LDL-C recommended cut-points for CAD risk assessment
  - 2,843 serum samples from 5-17 year olds in Bogalusa Heart Study (1992-1994)
  - Regression analysis performed to determine non-HDL-C based on LDL-C

ApoB

- NHANES III (1988-1994) obtained serum samples from US population ≥ 4 years of age
- Borderline and high cut-points calculated as 75th and 95th percentiles, respectively

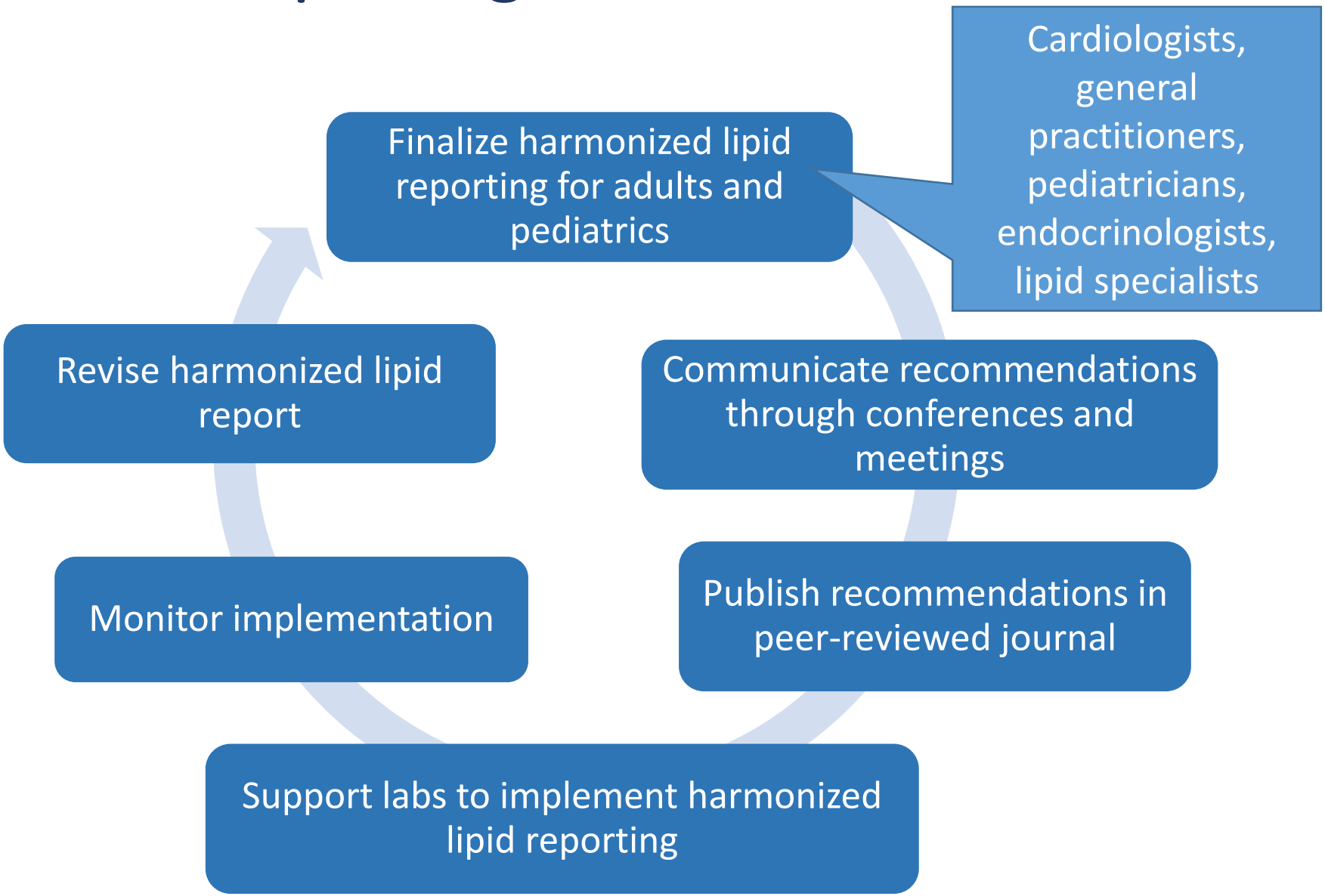
Pediatric Flagging Rates (RI vs DL)

Variable	Age Range	Upper Reference Limit (URL)	Total Flagging Rate using URL, % (proportion)	Age Range (years)	High/Low Decision Limit (DL)	Total Flagging Rate using High/Low DL, % (proportion)
Total Cholesterol	1-<18	≤ 5.9 mmol/L	**7.46%** (503/6745)	<18	< 4.4 mmol/L	**35.9%** (2423/6745)
LDL-C	1-<10M 1-<10F 10-<18	≤ 3.1 mmol/L ≤ 3.3 mmol/L ≤ 3.4 mmol/L	**6.54%** (436/6670)	<18	< 2.85 mmol/L	**19.3 %** (1290/6670)
HDL-C	1-<4 4-<13 13-<18	≥ 0.8 mmol/L ≥ 0.9 mmol/L ≥ 0.8 mmol/L	**3.06 %** (206/6738)	<18	> 1.15 mmol/L	**32.9 %** (2215/6738)
Triglycerides	1-<18	≤ 2.2 mmol/L	**8.69 %** (586/6744)	1-<10 10-<18	< 0.85 mmol/L < 1.00 mmol/L	**54.0 %** (3643/6744)
Non-HDL-C	1-<10M 1-<10F 10-<18	≤ 3.7 mmol/L ≤ 4.3 mmol/L ≤ 4.0 mmol/L	**8.22 %** (554/6738)	<18	< 3.10 mmol/L	**34.0 %** (2289/6738)

Pediatric Flagging Rates (RI vs DL)

Variable	Age Range	Upper Reference Limit (URL)	Total Flagging Rate using URL, % (proportion)	Age Range (years)	Borderline Decision Limit (DL)	Total Flagging Rate using Borderline DL, % (proportion)	Total Flagging Rate using High/Low DL, % (proportion)
Total Cholesterol	1-<18	≤ 5.9 mmol/L	**7.46%** (503/6745)	<18	< 4.4 mmol/L	**11.5%** (774/6745)	**35.9%** (2423/6745)
LDL-C	1-<10M 1-<10F 10-<18	≤ 3.1 mmol/L ≤ 3.3 mmol/L ≤ 3.4 mmol/L	**6.54%** (436/6670)	<18	< 3.35 mmol/L	**7.00 %** (467/6670)	**19.3 %** (1290/6670)
HDL-C	1-<4 4-<13 13-<18	≥ 0.8 mmol/L ≥ 0.9 mmol/L ≥ 0.8 mmol/L	**3.06 %** (206/6738)	<18	> 1.05 mmol/L	**20.5 %** (1381/6738)	**32.9 %** (2215/6738)
Triglycerides	1-<18	≤ 2.2 mmol/L	**8.69 %** (586/6744)	1-<10 10-<18	< 1.15 mmol/L < 1.45 mmol/L	**28.0 %** (1890/6744)	**54.0 %** (3643/6744)
Non-HDL-C	1-<10M 1-<10F 10-<18	≤ 3.7 mmol/L ≤ 4.3 mmol/L ≤ 4.0 mmol/L	**8.22 %** (554/6738)	<18	< 3.10 mmol/L	**12.5 %** (845/6738)	**34.0 %** (2289/6738)

Action plan to implement harmonized lipid reporting across Canada



Acknowledgements

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Felix Leung
Joseph Macri
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David Seccombe
Julie Shaw
Julia Stemp
Jennifer Taher
Dorothy Truong
Uvaraj Uddayasankar

Appendix: References

Adult Lipid Reference Intervals:

1. Adeli K., et al. *Clinical Chemistry*. 2015
2. Rustad P., et al. *Scandinavian Journal of Clinical and Laboratory Investigation*. 2004
3. Ozarda Y., et al. *Clinical Chemistry and Laboratory Medicine*. 2014

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