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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INTRODUCTION

- > Harmonization in laboratory medicine includes all aspects of the total testing process
- > Harmonization is required to ensure data obtained from different laboratories are comparable
- > Healthcare professionals are often unaware of the profound variation in laboratory test interpretation
- Canadian Society of Clinical Chemists (CSCC) Reference Interval Harmonization (hRI) Working Group formed to address the need for hRIs in Canada
- First aim of the Working Group was to assess adult and pediatric RIs currently in use in Canadian clinical laboratories

OBJECTIVE

To assess the variation in reference intervals in Canadian laboratories through a national survey.

METHODS

3-part survey disseminated to Canadian laboratories:

A. General Statements: Participants stated their agreement or disagreement with 3 statements regarding RI variation **B.** Reference Intervals: Participants provided lower reference limit (LRL), upper reference limit (URL), units, age range, sex, and instrument manufacturer for 7 analytes: alanine aminotransferase (ALT), alkaline phosphatase (ALP), calcium, creatinine, free thyroxine (FT4), hemoglobin and sodium

C. Reference Sample: Reference pooled human serum samples (provided by CEQAL) were assigned target values and shipped to participating laboratories to measure 6 analytes: ALT, ALP, calcium, creatinine, FT4 and sodium



"There are gaps and inconsistencies in adult/geriatric reference intervals used in Canadian laboratories."

"There are gaps and inconsistencies in pediatric reference intervals used in Canadian laboratories."

Figure 1: Responses to **(A)** statement 1 and **(B)** statement 2 by Canadian laboratories

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Figure 3: Variation in reference intervals for alkaline phosphatase (ALP) used in clinical laboratories across Canada for a (A) child, (B) adolescent, and (C) adult



Figure 4: Variation in reference intervals for creatinine used in clinical laboratories across Canada for a (A) child, (B) adolescent, and (C) adult



across Canada for ALP.



across Canada for creatinine

Table 1: Comparing variation and bias between reference intervals and reference sample results for ALP

Instrument	CV (Reference Sample)	CV (URL)	% Bias to Target (Reference Sample)	% Bias to ARM (URL)
All	6.6%	41.9%		
Abbott	3.8%	52.3%	-4.3%	-11.7%
Beckman	5.2%	35.7%	-20.2%	25.2%
Ortho	2.1%	43.2%	-7.5%	15.0%
Roche	2.8%	23.1%	-11.1%	-25.9%
Siemens	3.1%	41.1%	-5.2%	19.5%

CONCLUSION

There is a critical lack of harmonization in laboratory RIs across Canada, particularly for the pediatric population. The variation in RIs is greater than the variation in test results and cannot be explained by the bias in results obtained from different instrument manufacturers.





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