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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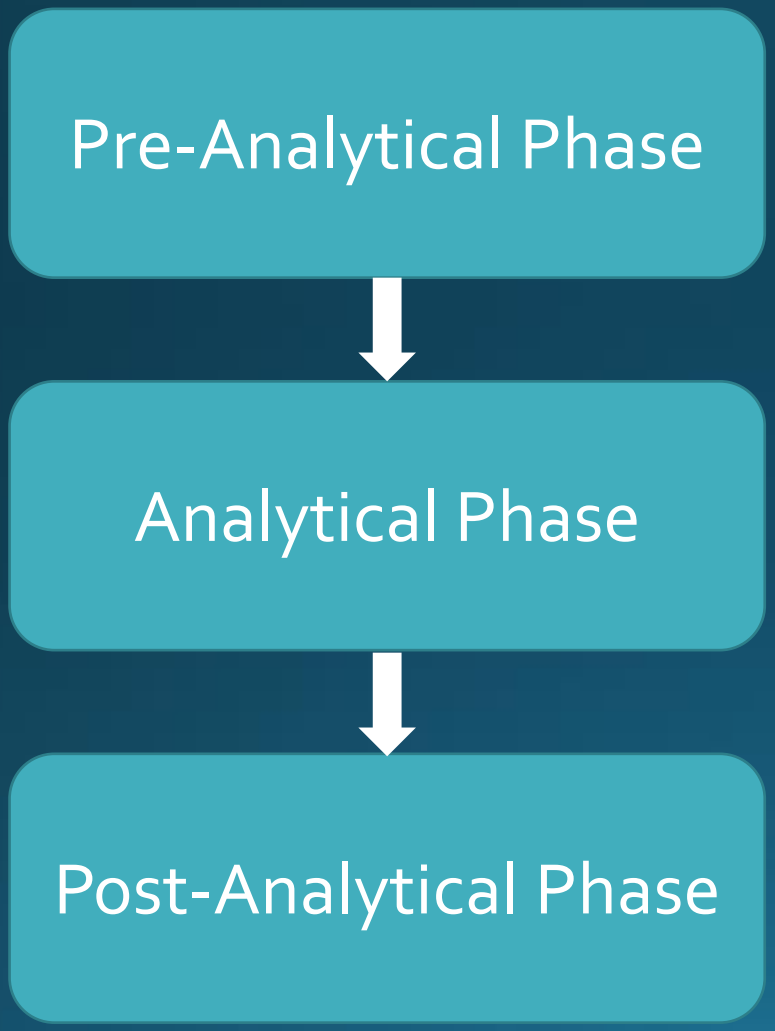
Speaker Financial Disclosure Information

I have nothing to disclose.

Scope of Harmonization in Laboratory Medicine



- Test requests
- Sample collection
- Handling and transportation

- Analytical method
- Calibration
- Quality control

- Reporting terminology and units
- Report formats
- Reference intervals
- Interpretive comments

Scope of Harmonization in Laboratory Medicine

Pre-Analytical Phase

- Test requests
- Sample collection
- Handling and transportation

Analytical Phase

- Analytical method
- Calibration
- Quality control

Post-Analytical Phase

- Reporting terminology and units
- Report formats
- **Reference intervals**
- Interpretive comments

Drivers for Reference Interval Harmonization

- Consistent test result interpretation across laboratories
- Electronic medical records
- Direct access to test results by patients

Optimize and standardize patient care to improve patient safety

Harmonized Reference Interval Initiatives

- Nordic Reference Interval Project (NORIP)
- Australasian Harmonised Reference Intervals (AHRIP and AHRIA)
- UK Pathology Harmony Project
- Canadian Society of Clinical Chemists (CSCC) Reference Interval Harmonization (hRI) Working Group

CSCC hRI Working Group

Goal

To establish evidence-based harmonized reference intervals and support their implementation in laboratories across the country.

Objectives

1. Assess variation in adult and pediatric RIs currently in use in Canadian clinical laboratories
2. Develop a model and methodology for establishing harmonized reference intervals
3. Establish appropriate recommendations and guidelines on the use of hRIs across Canada

CSCC hRI Working Group

Objective 1: Assess variation in adult and pediatric RIs currently in use in Canadian clinical laboratories

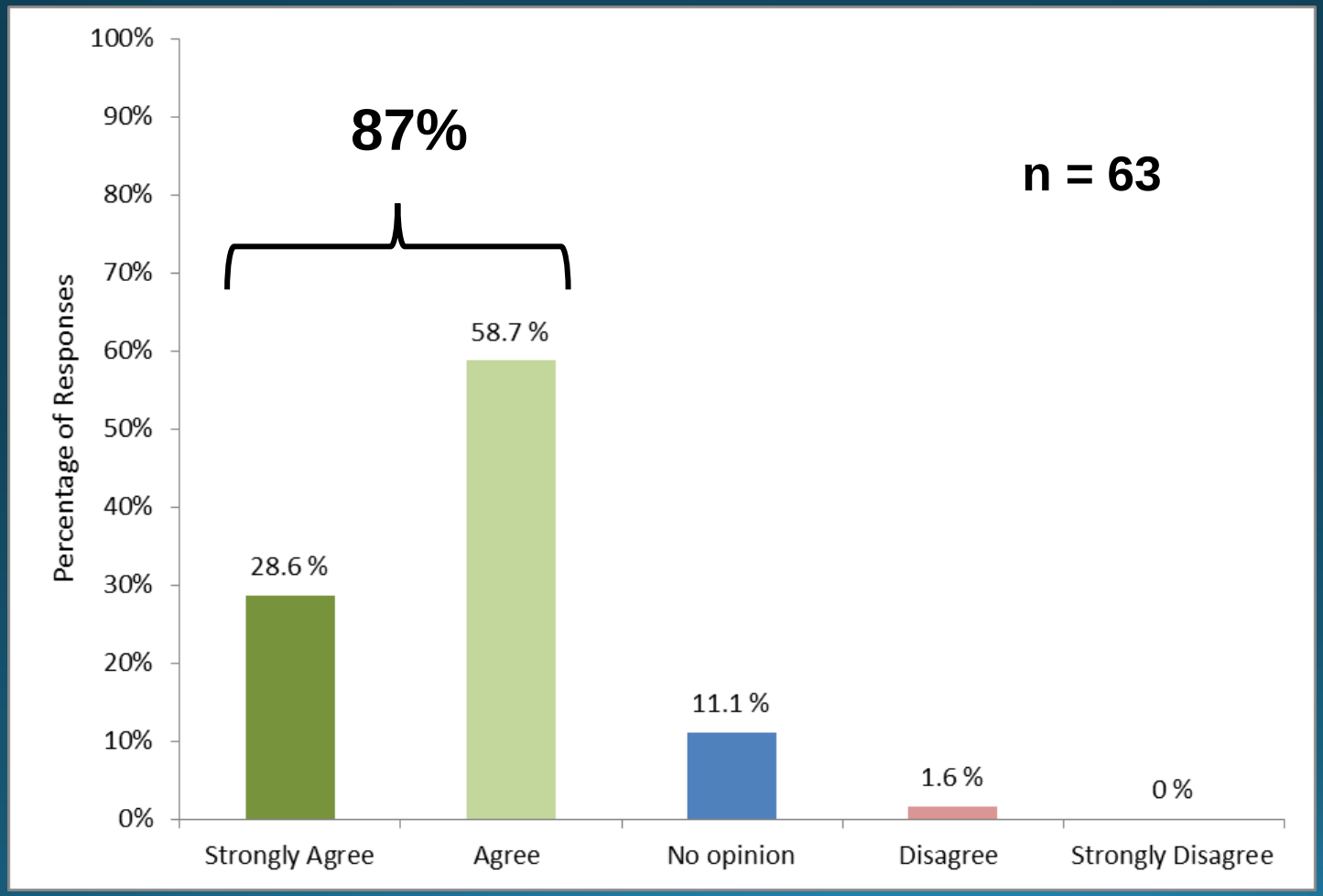
Approach

➢Create and disseminate survey to clinical laboratories across Canada (May/April 2016)

- 3 survey questions to assess awareness of need for hRIs
- Report reference intervals for 7 analytes
  - ALP, ALT, calcium, creatinine, FT4, hemoglobin, sodium
- Analyze a reference sample for 6 analytes
  - ALP, ALT, calcium, creatinine, FT4, sodium

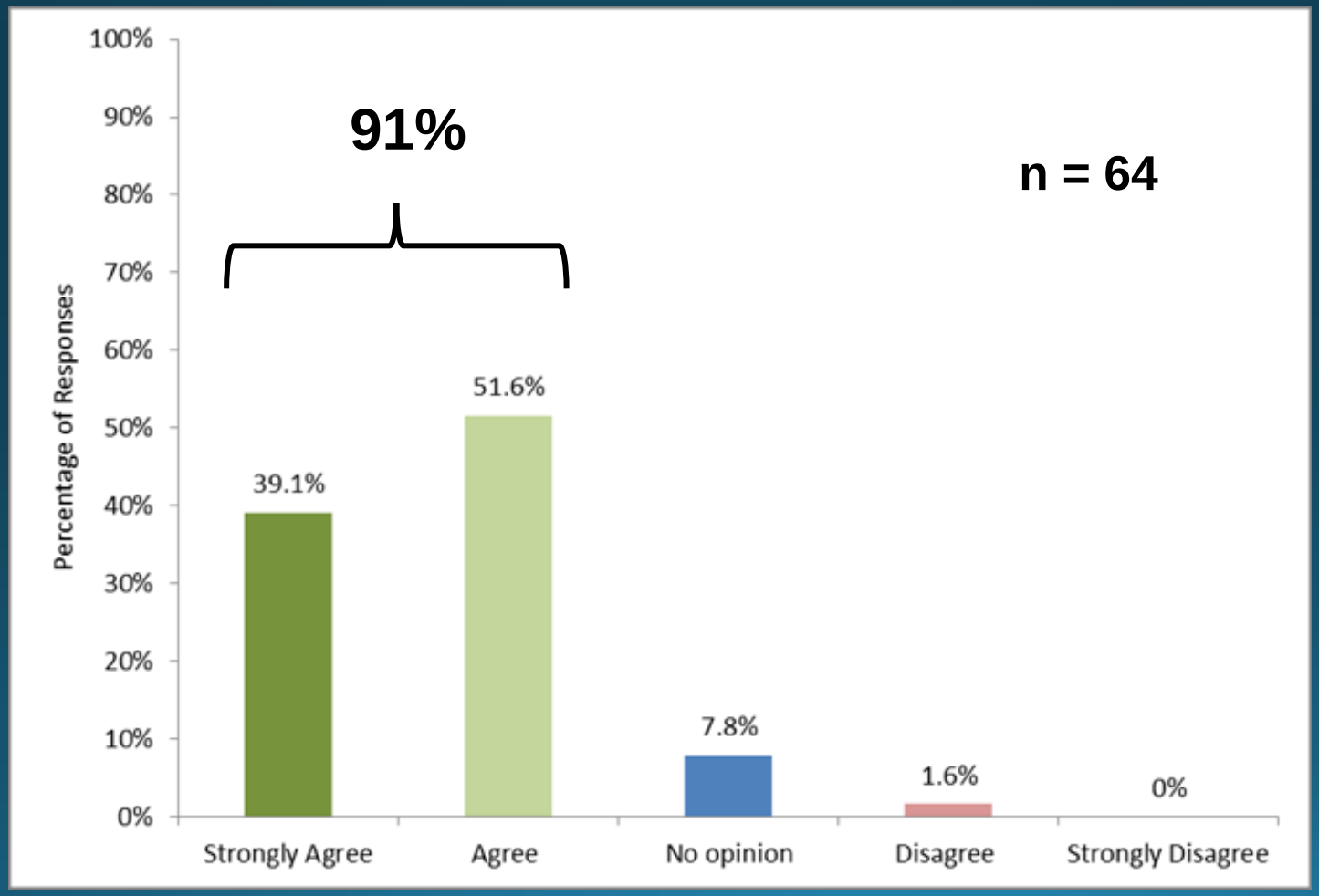
hRI Survey Question 1

"There are significant gaps and inconsistencies in adult/geriatric reference intervals and decision limits currently used in clinical laboratories in Canada."



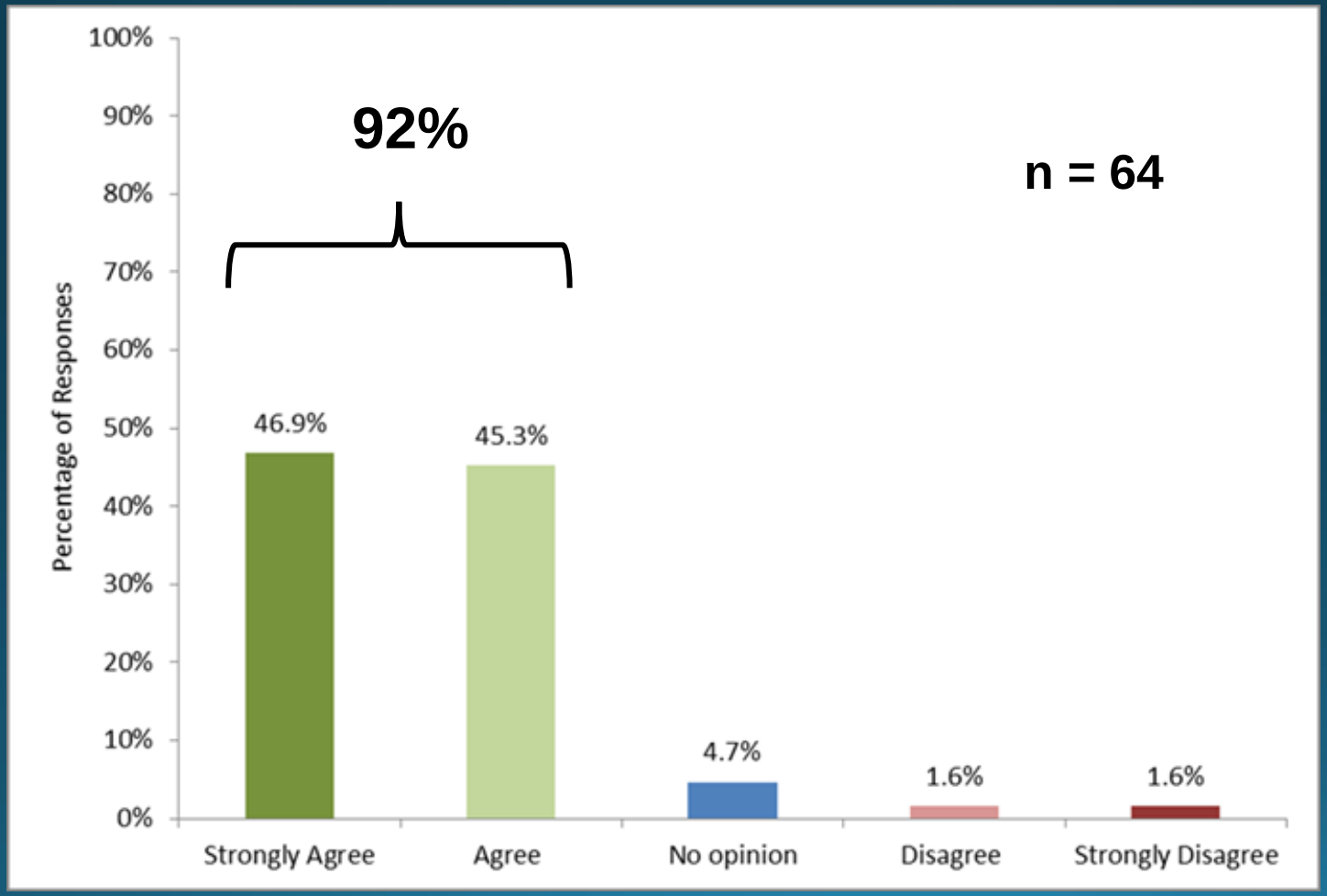
hRI Survey Question 2

"There are significant gaps and inconsistencies in pediatric reference intervals and decision limits currently used in clinical laboratories in Canada."

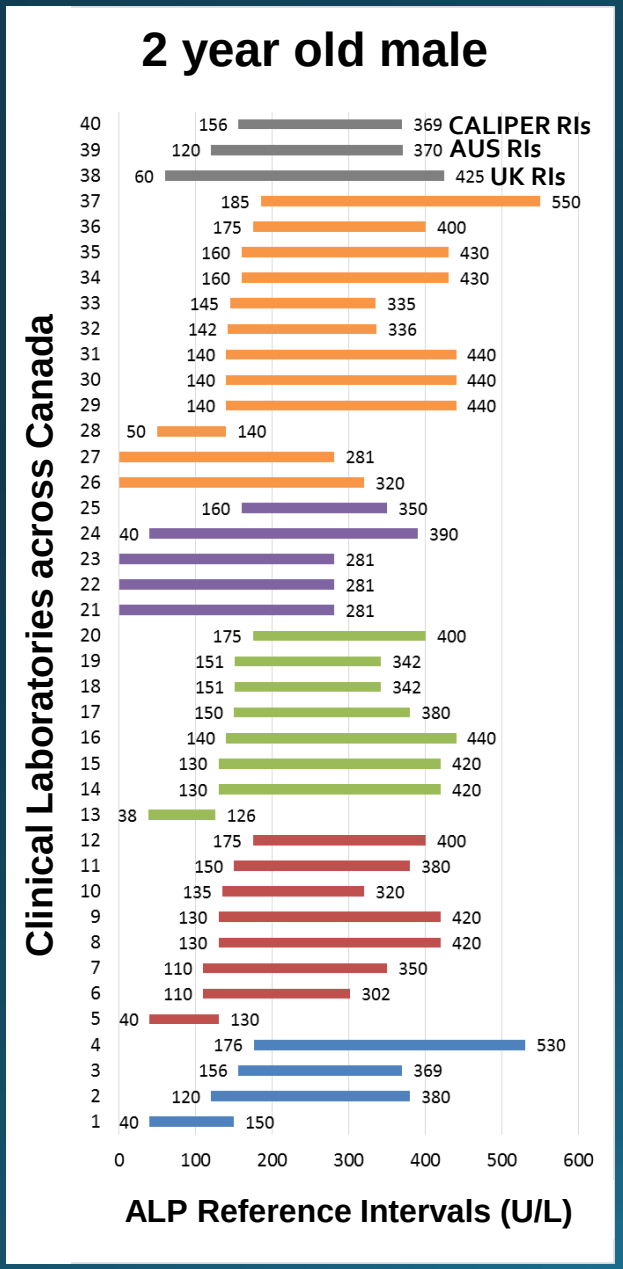


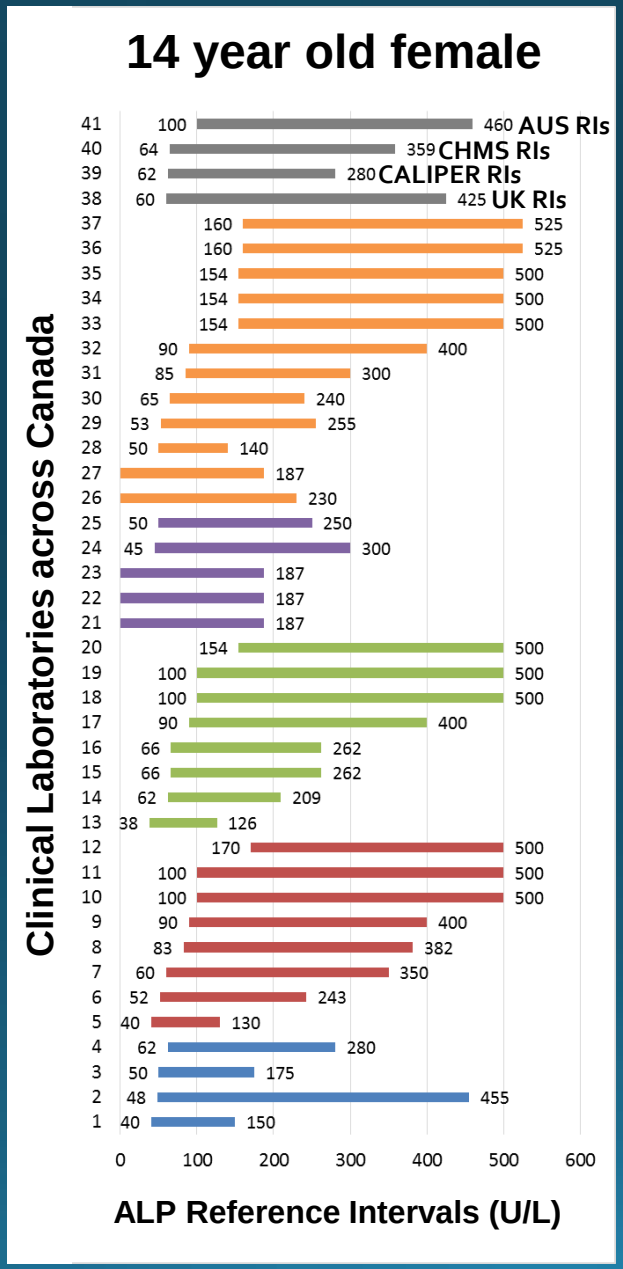
hRI Survey Question 3

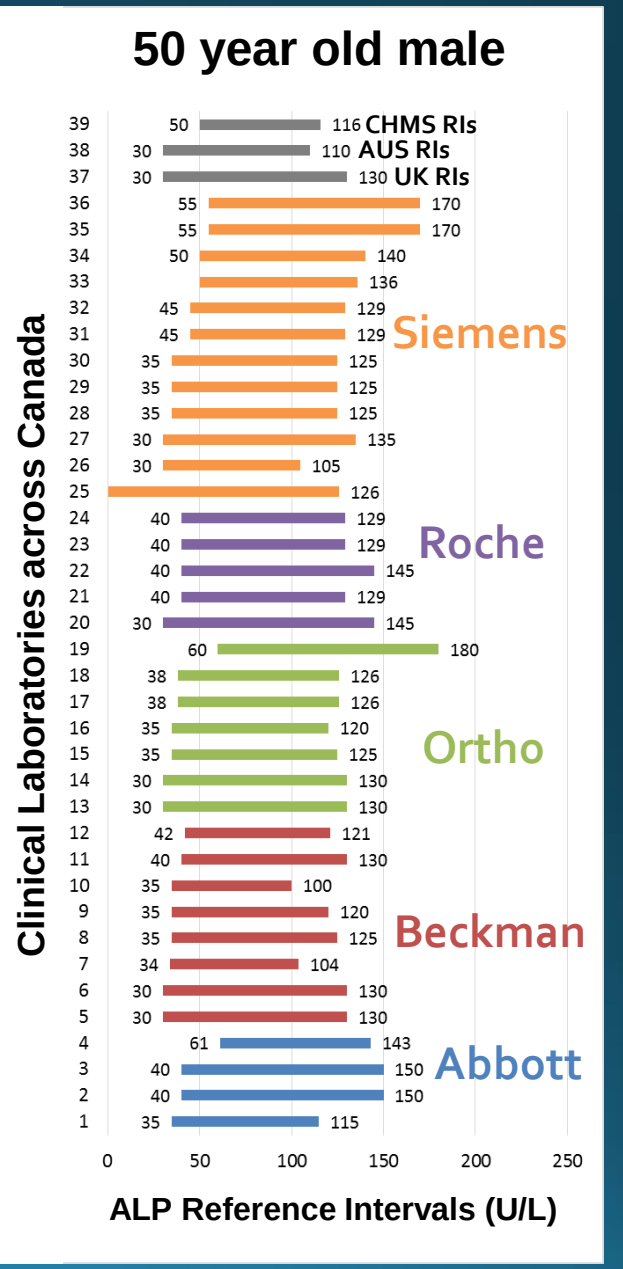
"There is a need for harmonized reference intervals and decision limits in clinical laboratories across Canada."



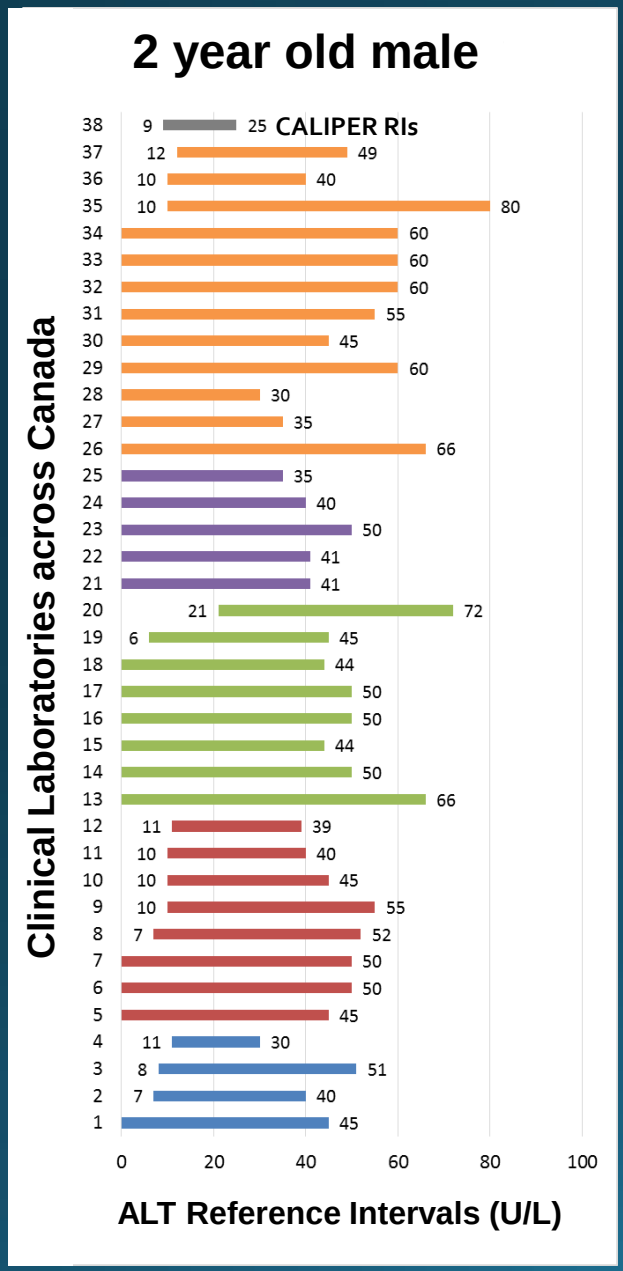
ALP Reference Intervals

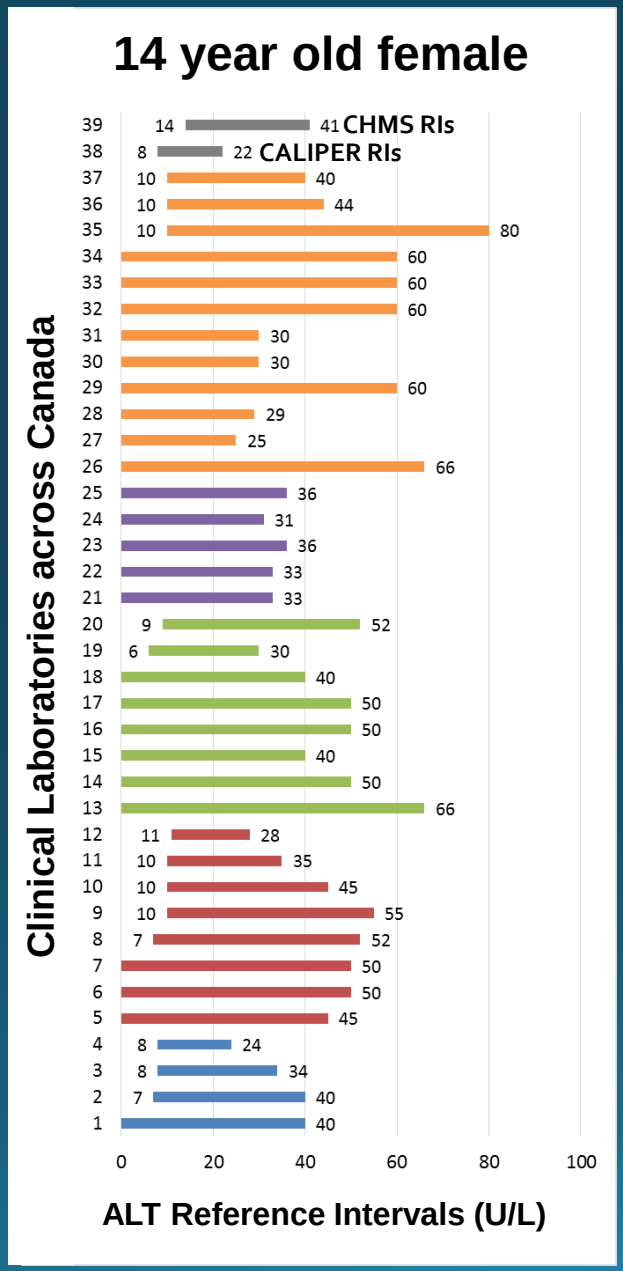


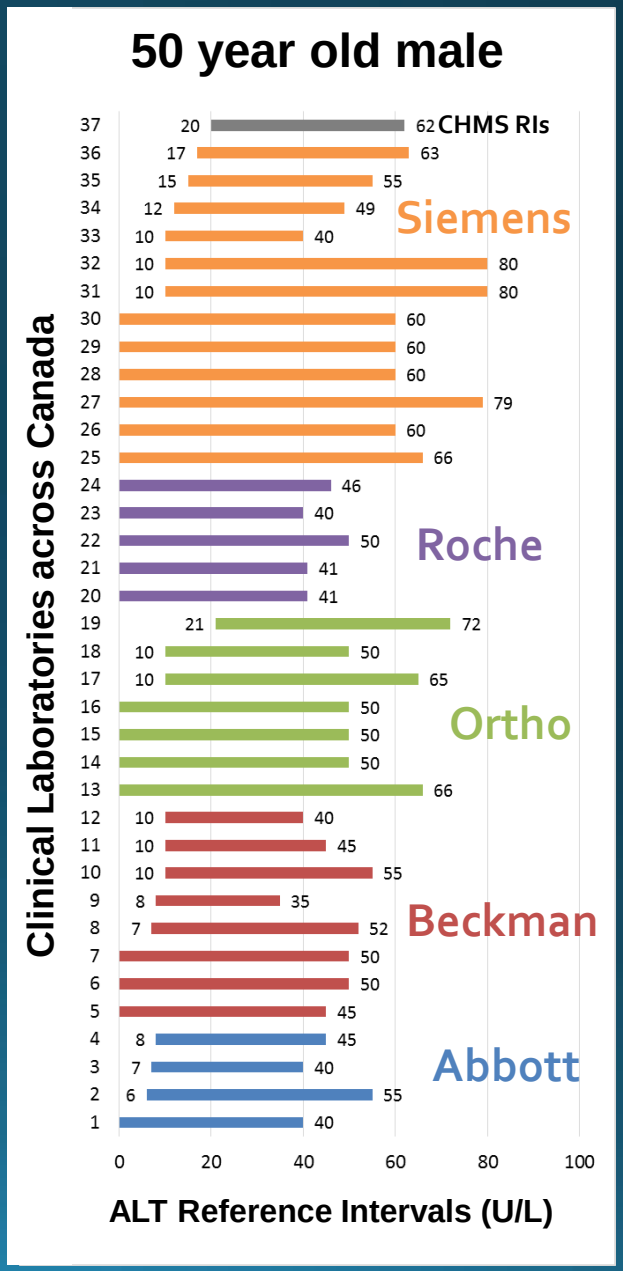




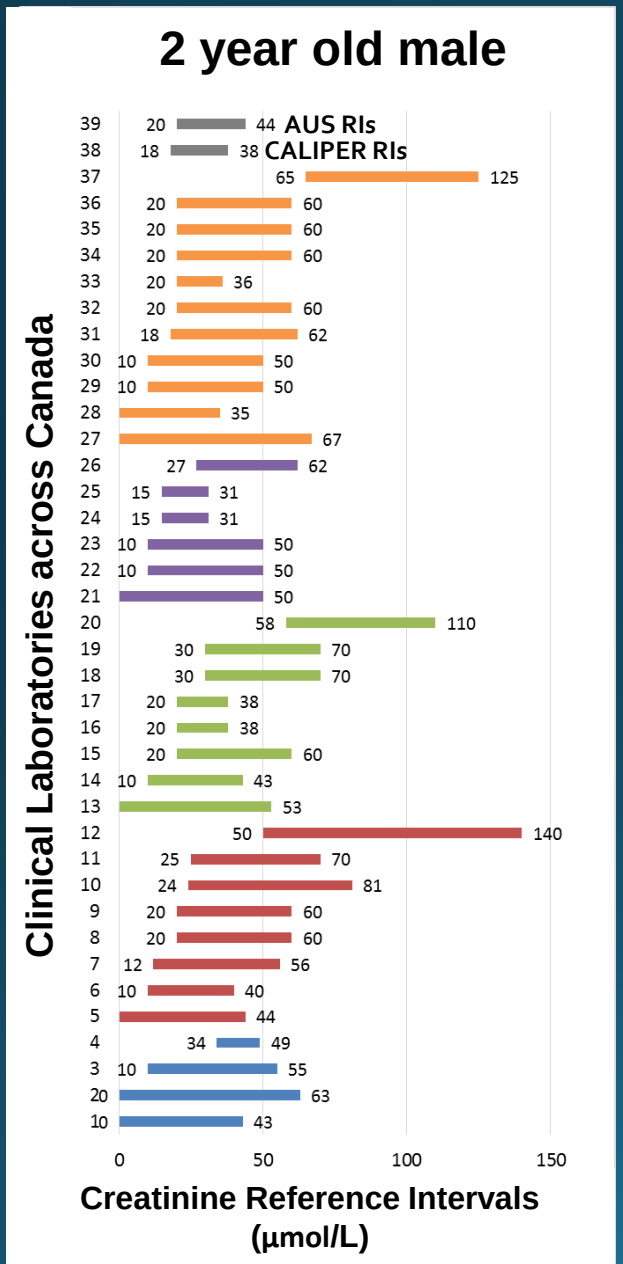
ALT Reference Intervals

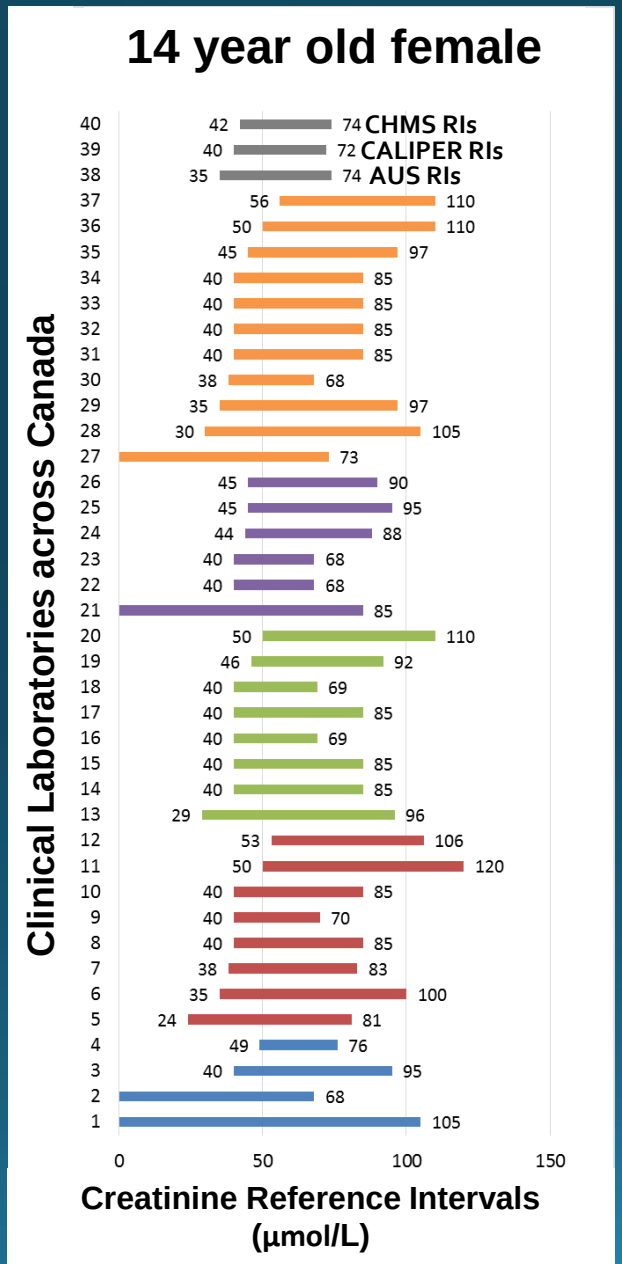


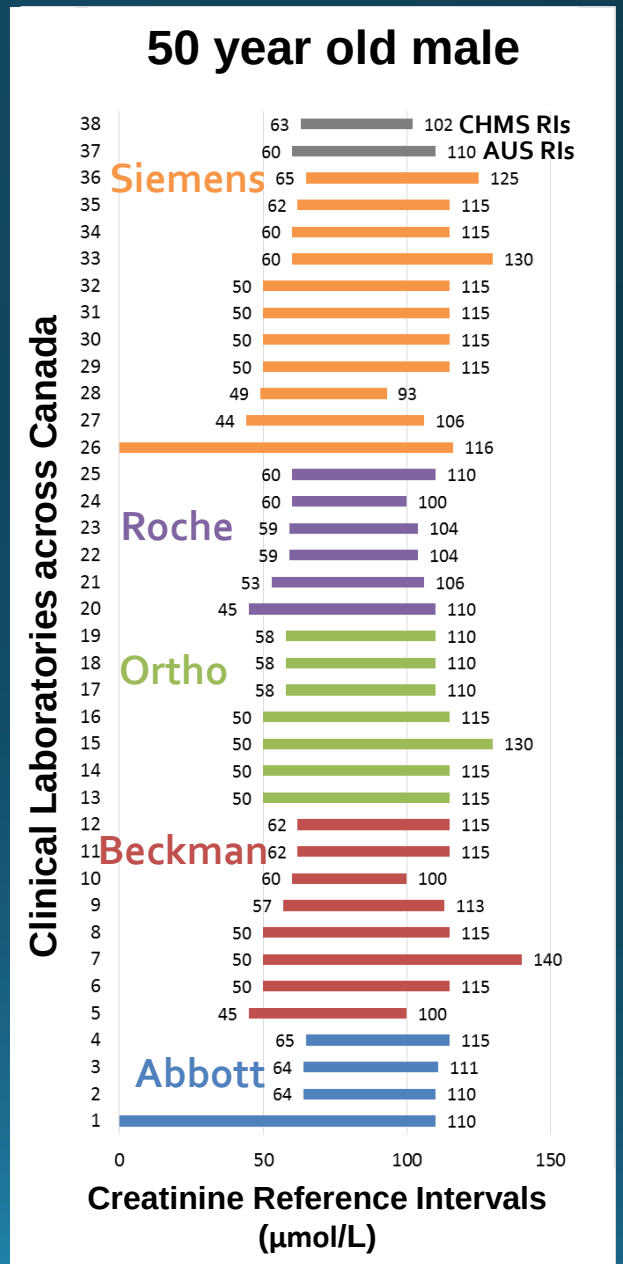




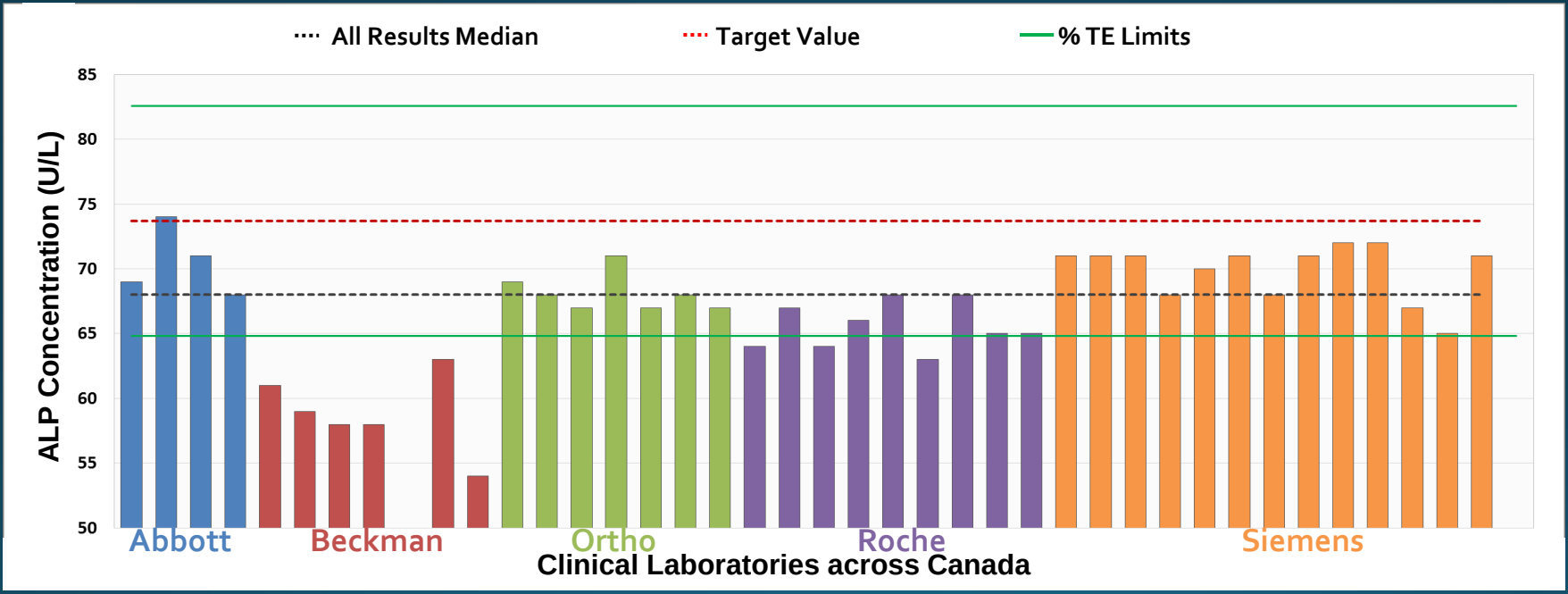
Creatinine Reference Intervals



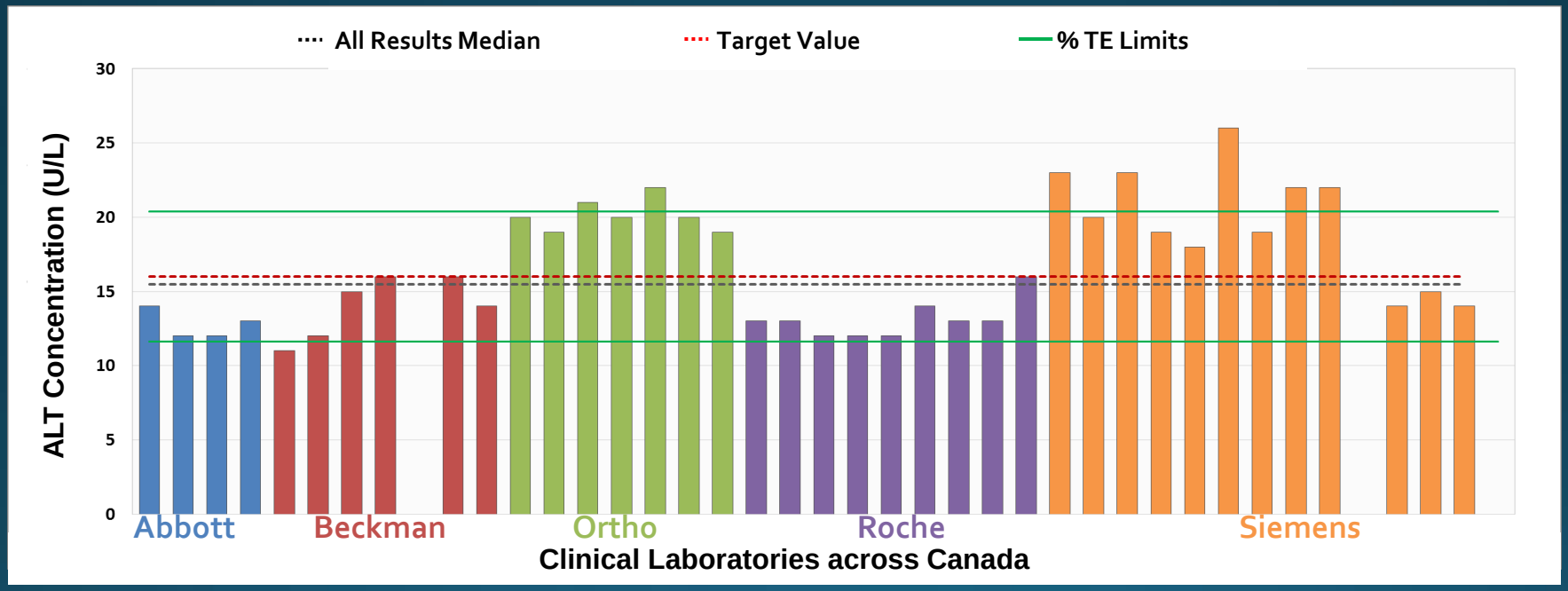




ALP Reference Sample Results



ALT Reference Sample Results



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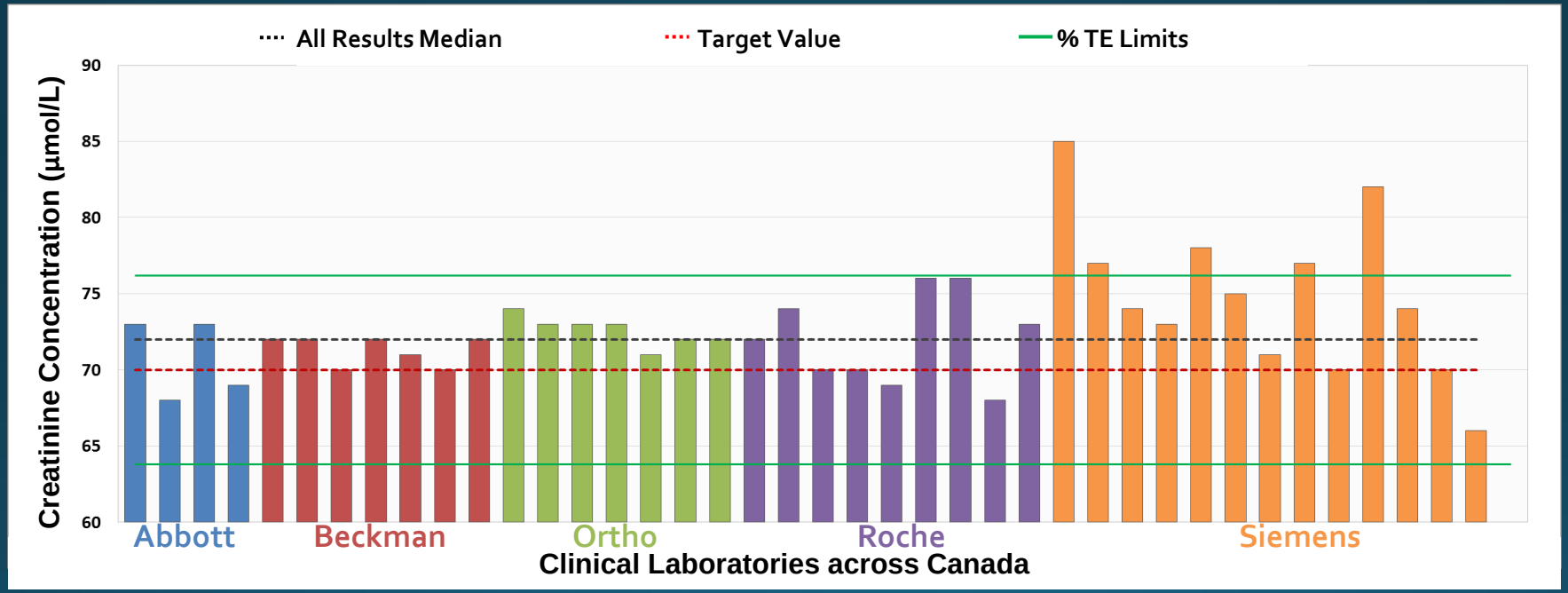


Comparing *variation* between reference intervals and reference sample results

Example: ALP

Reference Interval Variation

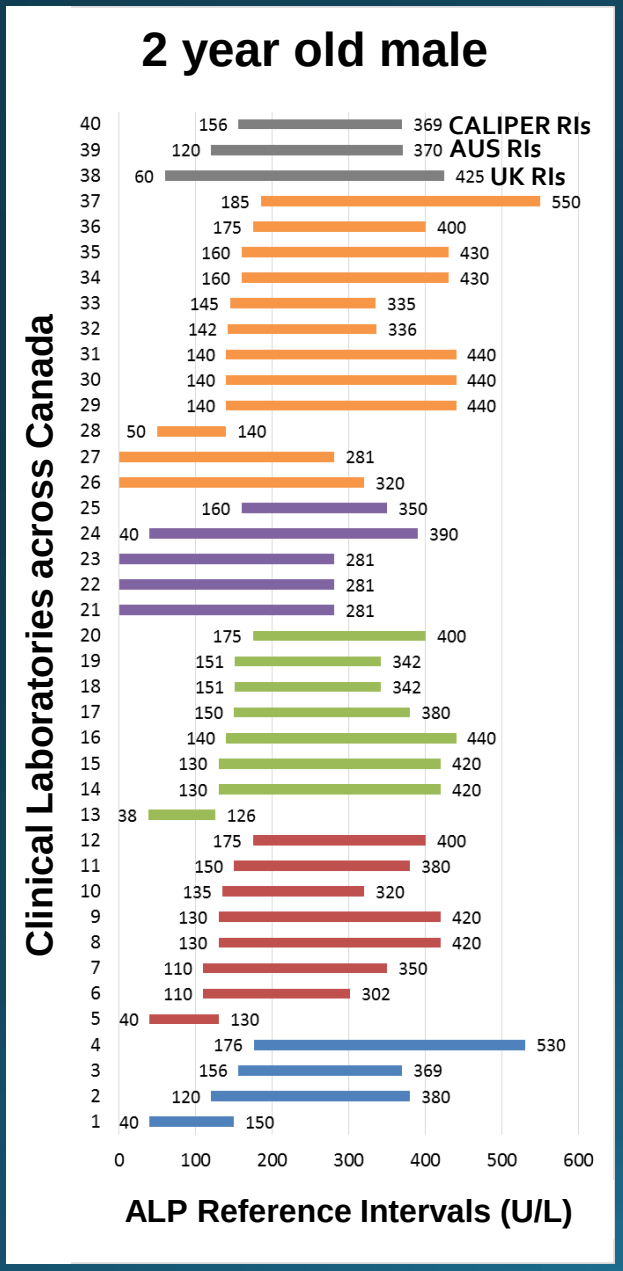
14 year old female

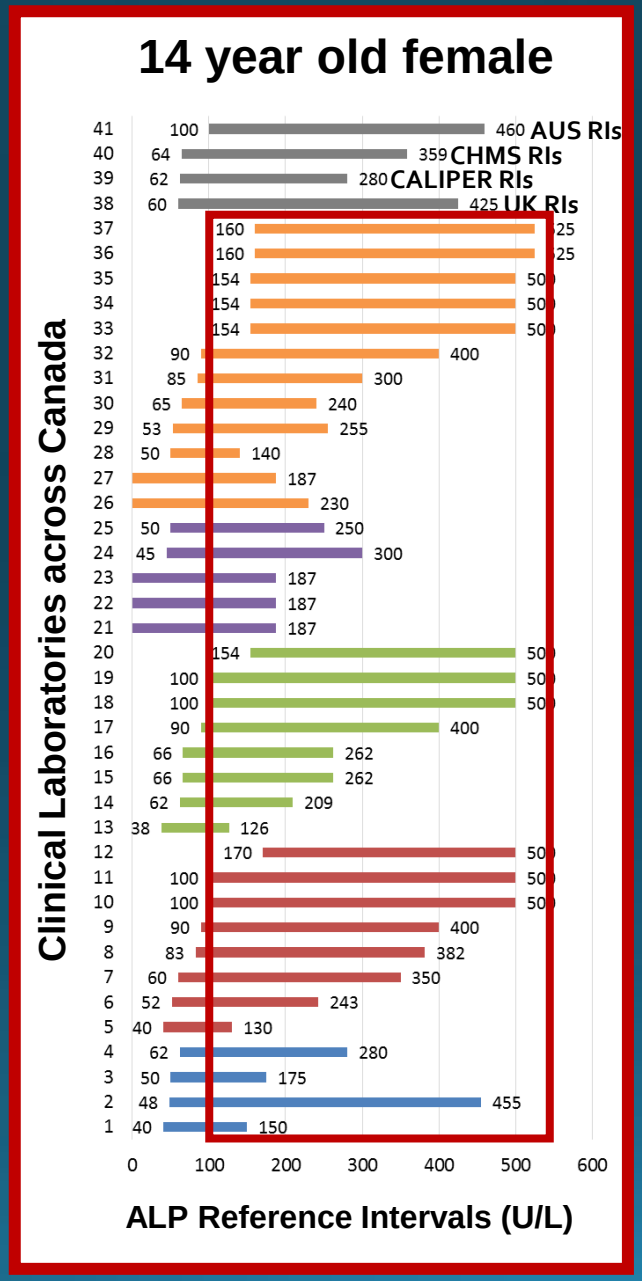
Instrument	n	% V (Upper Reference Limit)
All	37	41.9%
Abbott	4	52.3%
Beckman	8	35.7%
Ortho	8	43.2%
Roche	5	23.1%
Siemens	12	41.1%

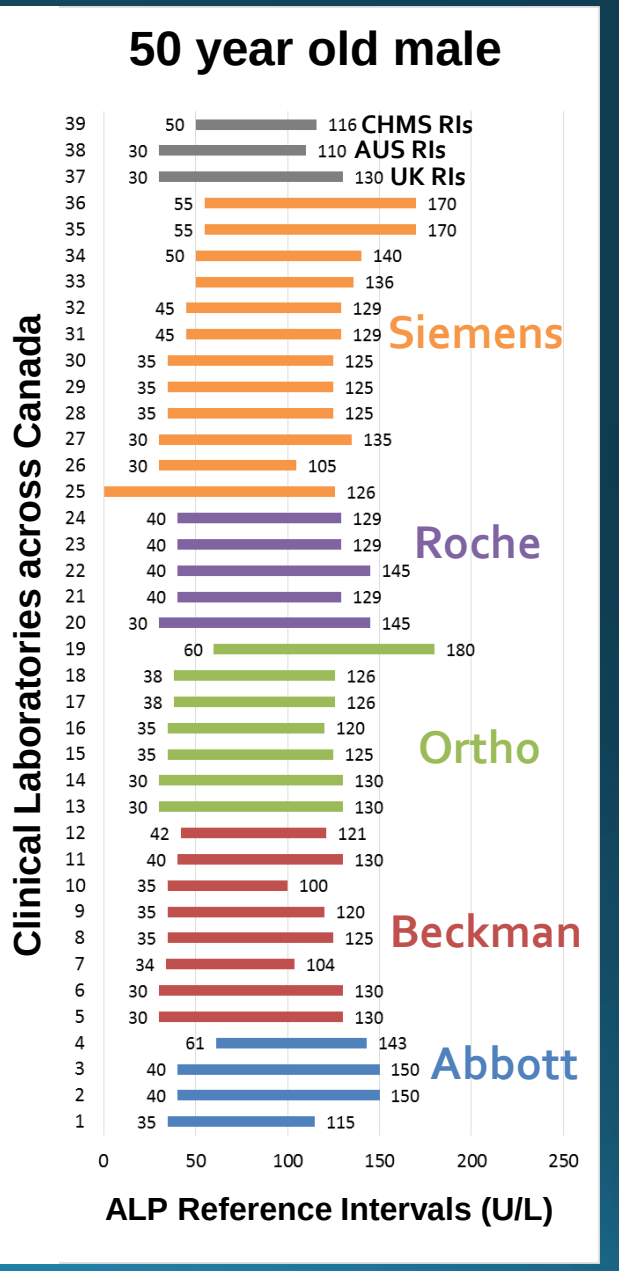
% Variation calculated as:

$$\frac{\text{SD (reported URLs)}}{\text{Mean (reported URLs)}} \times 100\%$$

ALP Reference Intervals







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Reference Sample Result Variation

Instrument	n	%CV
All	39	6.6%
Abbott	4	3.8%
Beckman	6	5.2%
Ortho	7	2.1%
Roche	9	2.8%
Siemens	13	3.1%

Reference limits for all analytes had higher between-laboratory variation than was seen for the sample results, except sodium.

Comparing *bias* between reference intervals and reference sample results

Example: ALP

Reference Interval Bias

14 year old female

Instrument	n	% Bias to ARM (URL)
Abbott	4	-11.7%
Beckman	8	25.2%
Ortho	8	15.0%
Roche	5	-25.9%
Siemens	12	19.5%

ARM: All Results Median
URL: Upper Reference Limit

% Bias calculated as:

$$\frac{\text{Deviation from ARM}}{\text{ARM}} \times 100\%$$

Comparing *bias* between reference intervals and reference sample results

Example: ALP

Reference Interval Bias

14 year old female

Instrument	n	% Bias to ARM (URL)
Abbott	4	-11.7%
Beckman	8	**25.2%**
Ortho	8	**15.0%**
Roche	5	-25.9%
Siemens	12	**19.5%**

Reference Sample Result Bias

Instrument	n	% Bias to target
Abbott	4	-4.3%
Beckman	6	**-20.2%**
Ortho	7	**-7.5%**
Roche	9	-11.1%
Siemens	13	**-5.2%**

ARM: All Results Median

URL: Upper Reference Limit

The variation in reference intervals across instruments cannot be explained by the bias of the results obtained on instruments by different manufacturers

CSCC hRI Survey Conclusions

- Reference limits for all analytes had higher between-laboratory variation than was seen for reference sample results, except sodium
- Reference interval variation across instruments cannot be explained by the bias of the results obtained on instruments by different manufacturers

There is a critical need for harmonized reference intervals in Canada

CSCC hRI Working Group

Goal

To establish evidence-based harmonized reference intervals and support their implementation in laboratories across the country.

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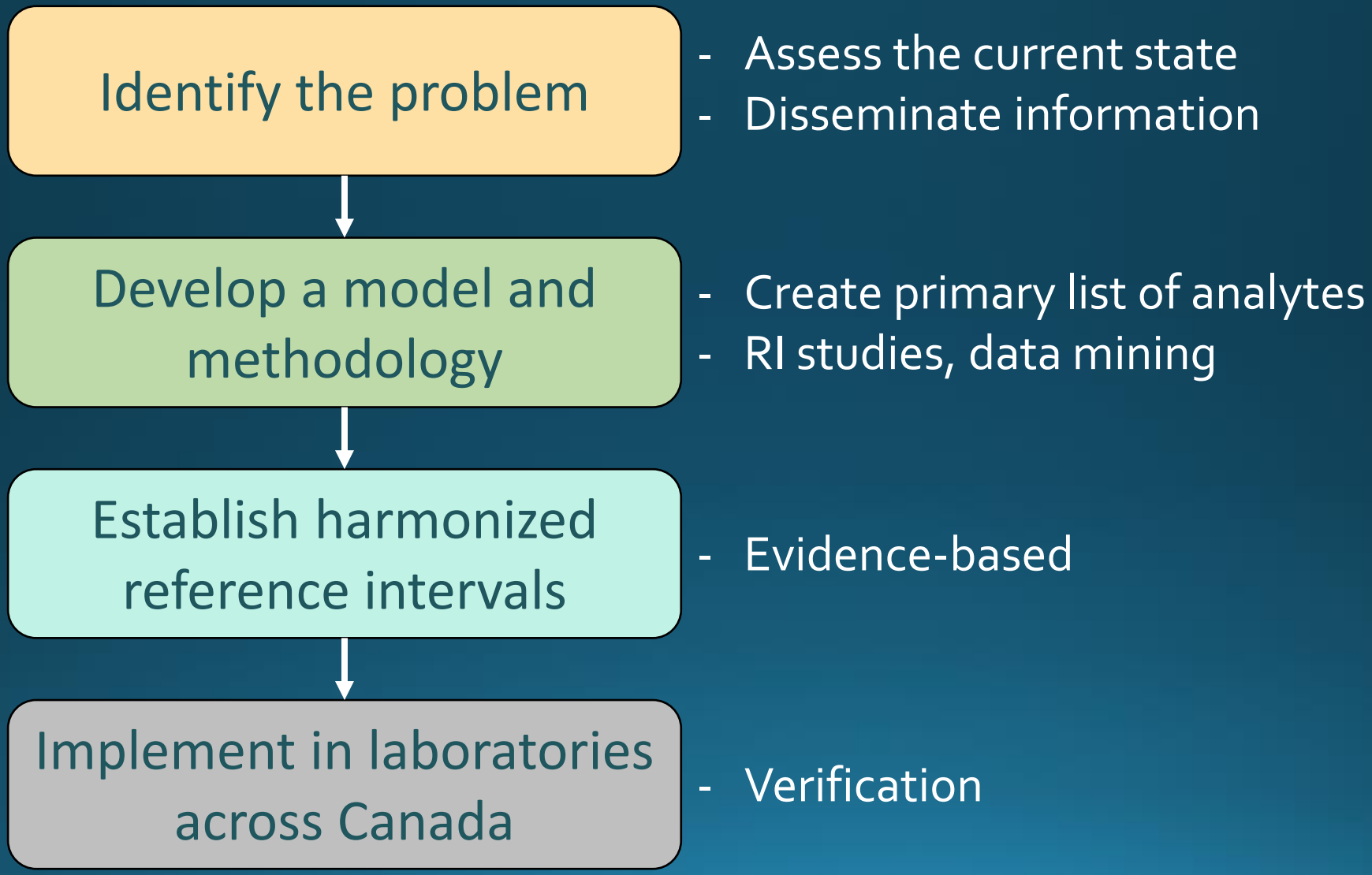
Canadian Reference Interval Databases

- Canada has unique opportunity
- Two robust, evidence-based reference interval databases established from the healthy Canadian population
  - Pediatrics – CALIPER (0-<19 years)
  - Pediatrics, Adults, Geriatrics – CHMS (3-<80 years)

CALIPER
'ARM' us with the knowledge to help others

Statistics Canada Statistique Canada

Canadian Harmonized Reference Intervals



Acknowledgements

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