



Between Method/Laboratory MSMS Analyte Harmonization Using CDC Quality Control Materials

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4. Centers for Disease Control and Prevention, Atlanta, GA.

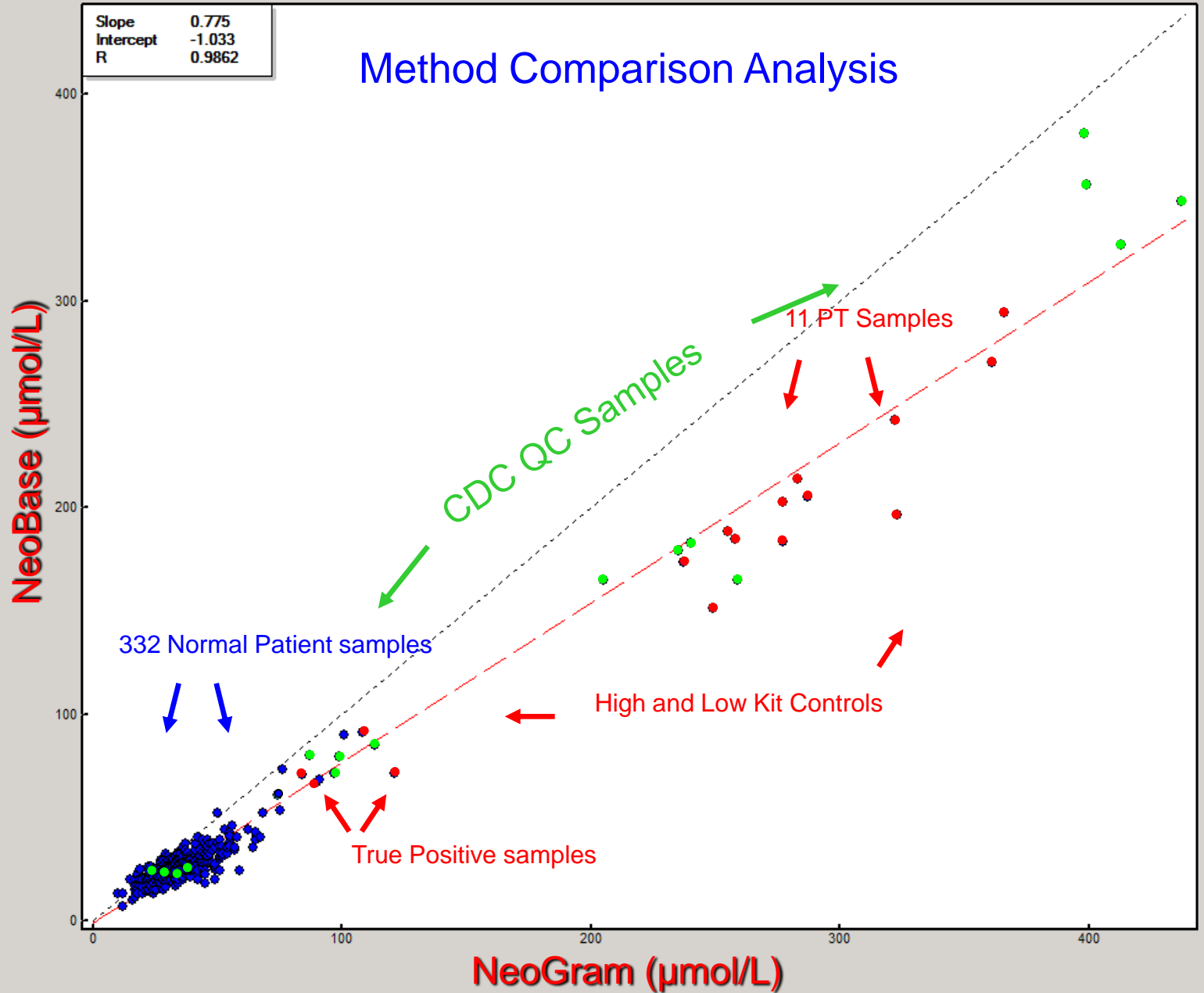
2009 Directive

- Validate PerkinElmer **NeoBase™** Non-derivatized MSMS Kit on **Waters TQD**
 - Previously PerkinElmer NeoGram® Derivatized MSMS Kit on SCIEX 2000
- Evaluate cutoffs with respect to R4 target cutoff ranges

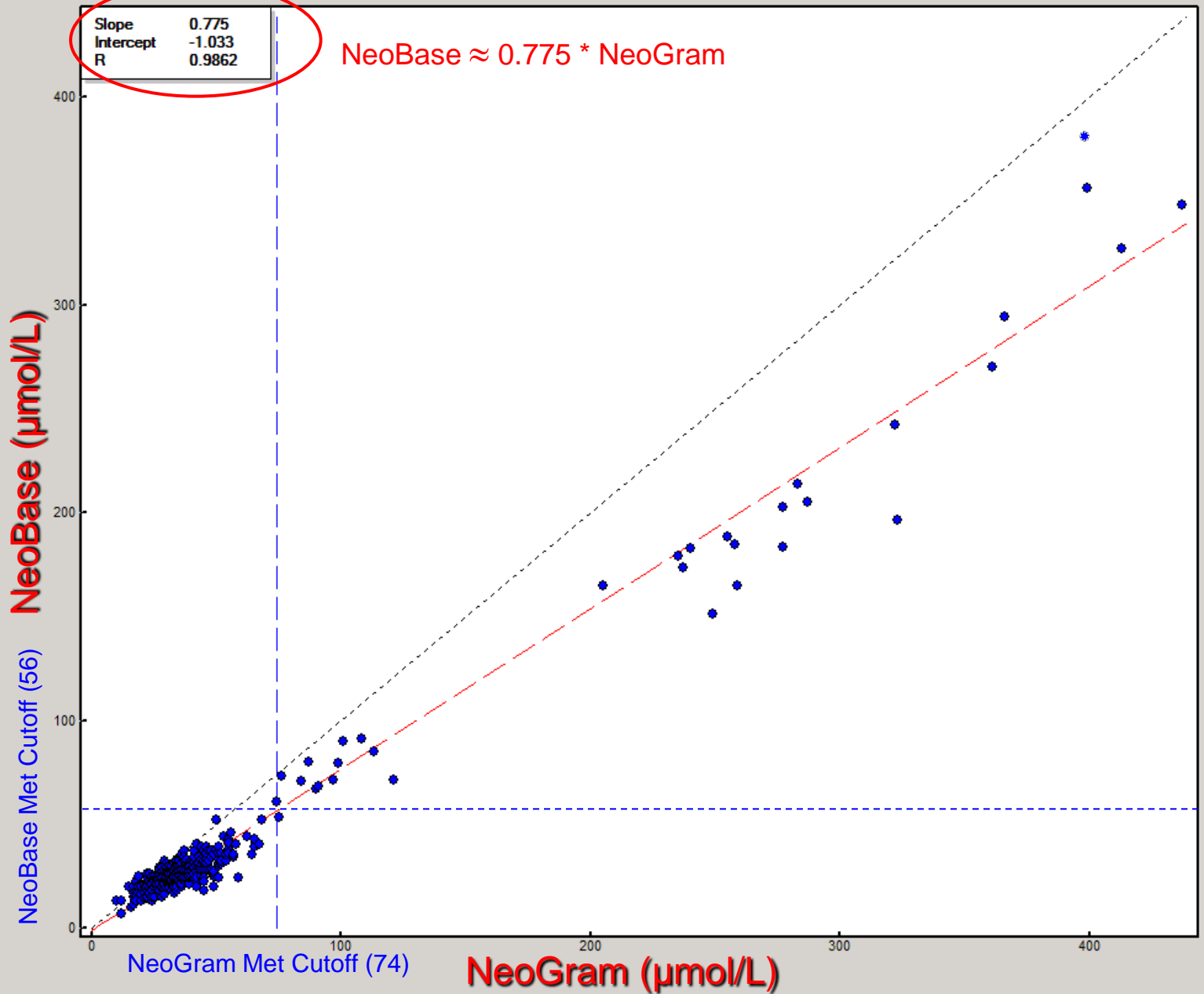
Validation Assessments

- Precision
- Linearity
- Accuracy
 - NeoBase™ Kit Controls
 - CDC Quality Control Samples
 - Cutoffs: NeoGram-NeoBase Method Comparison

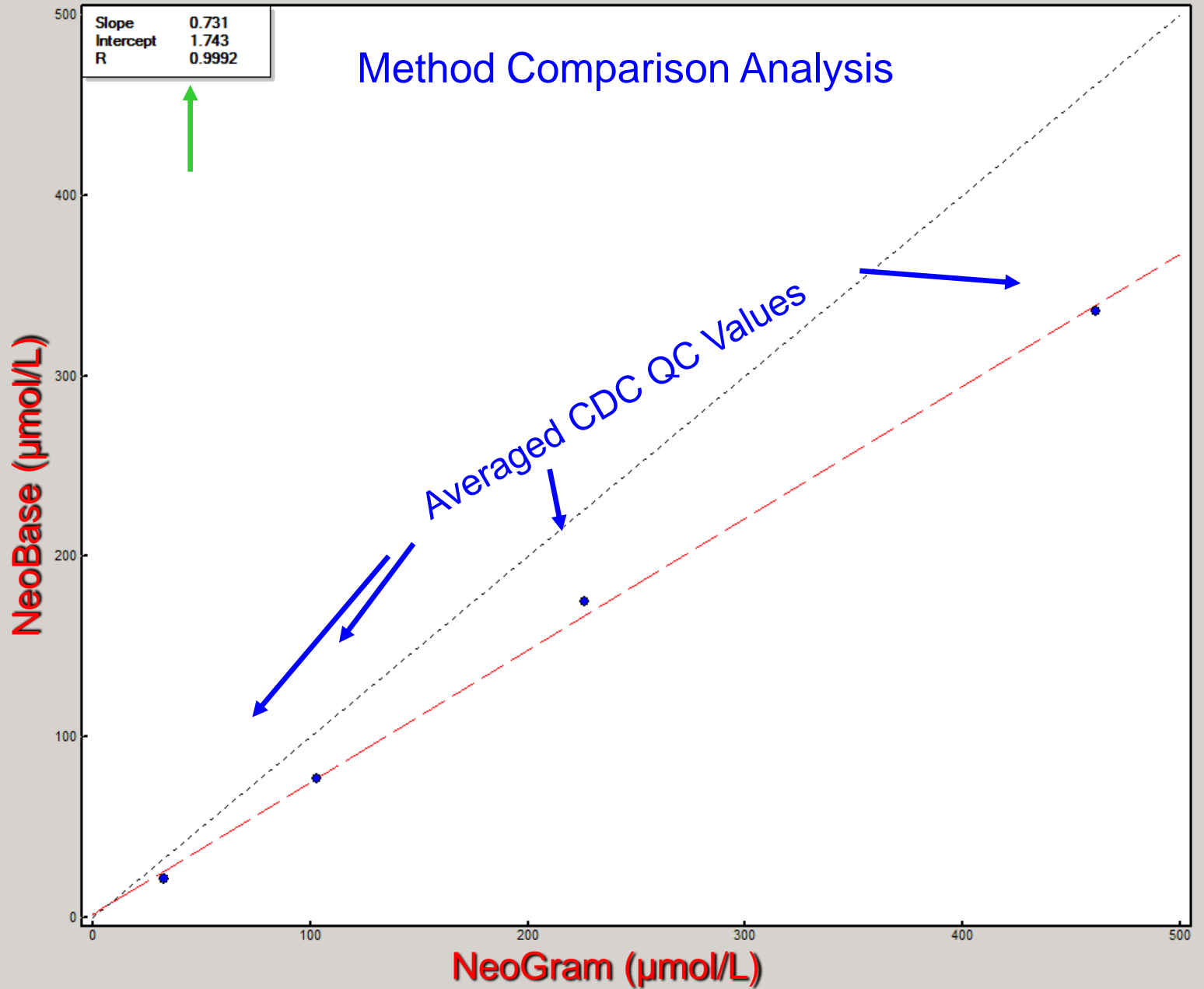
Method Comparison Analysis



Methionine (Met)

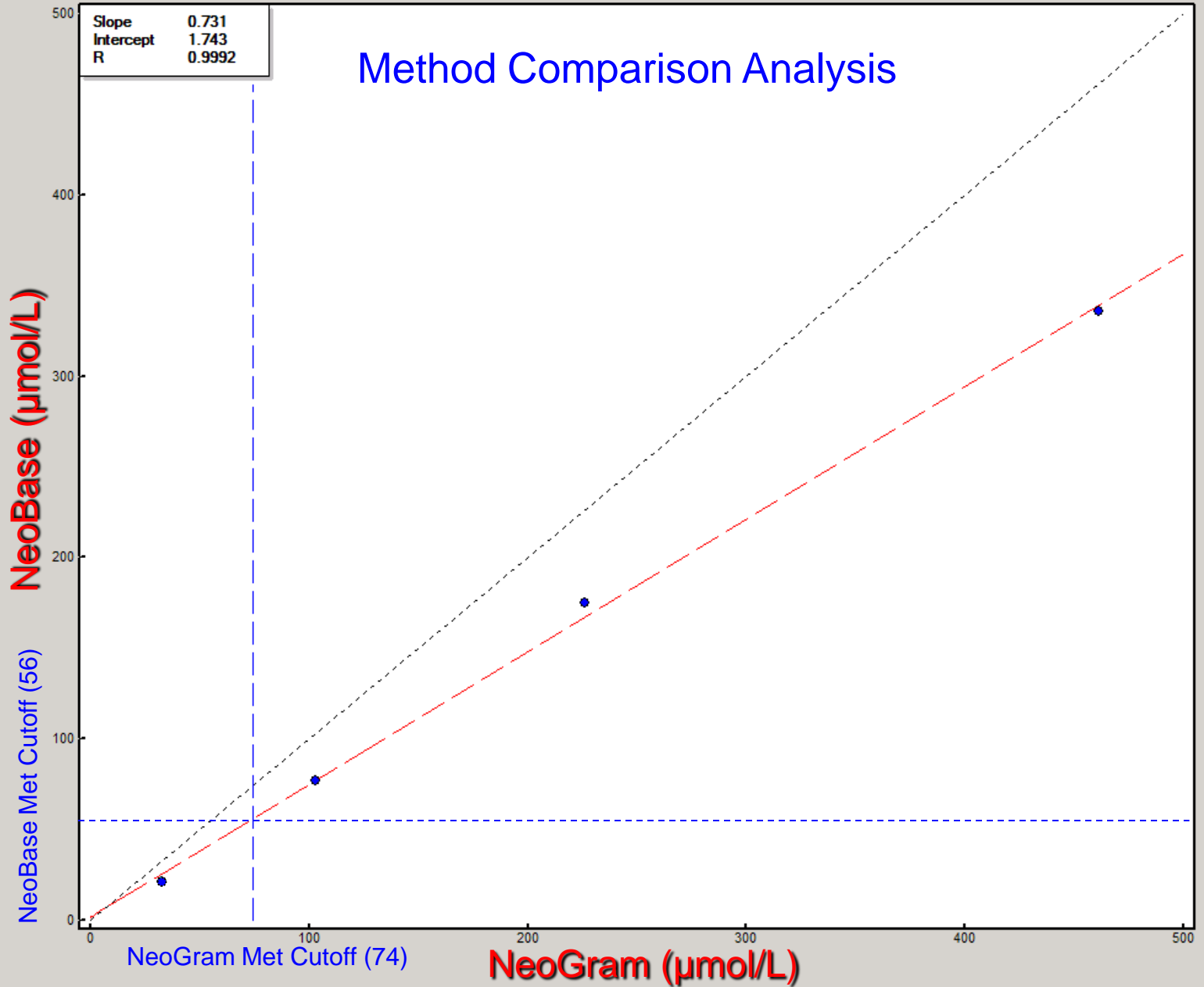


Methionine (Met)



Methionine (Met)

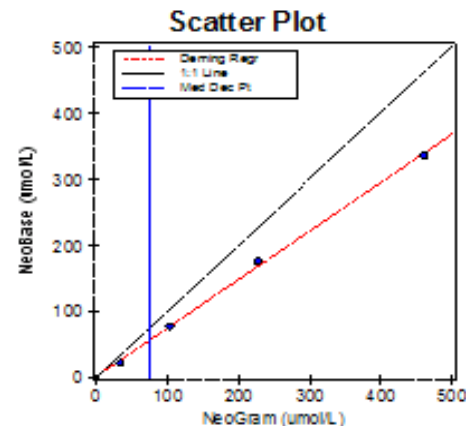
Method Comparison Analysis



Alternate (Quantitative) Method Comparison

X Method: NeoGram

Y Method: NeoBase



Regression Analysis

	Deming	Regular
Slope:	0.731 (0.721 to 0.741)	0.731 (0.721 to 0.741)
Intercept:	1.743 (-0.832 to 4.318)	1.830 (-0.744 to 4.405)
Std Err Est:	4.996	4.996

95% Confidence Intervals are shown in parentheses

Medical Decision Point Analysis

Calculated by Deming Regression ($R \geq 0.9$)

X Method MDP	Y Method Pred. MDP	95% Conf. Limits	
		Low	High
74	55.9	53.8	57.9



NeoGram Met Cutoff

Equivalent NeoBase Met Cutoff

Validation Goals

Evaluate Cutoffs

- **NeoGram/NeoBase** Method Comparison
 - All MSMS analytes cutoffs evaluated
- **Region 4** Cutoff Range Comparison:
 - Could this Method Comparison technique work for Between Laboratory **Cutoff** Comparison?

Cutoffs

Cutoff evaluation with respect to Region 4 target cutoff ranges...

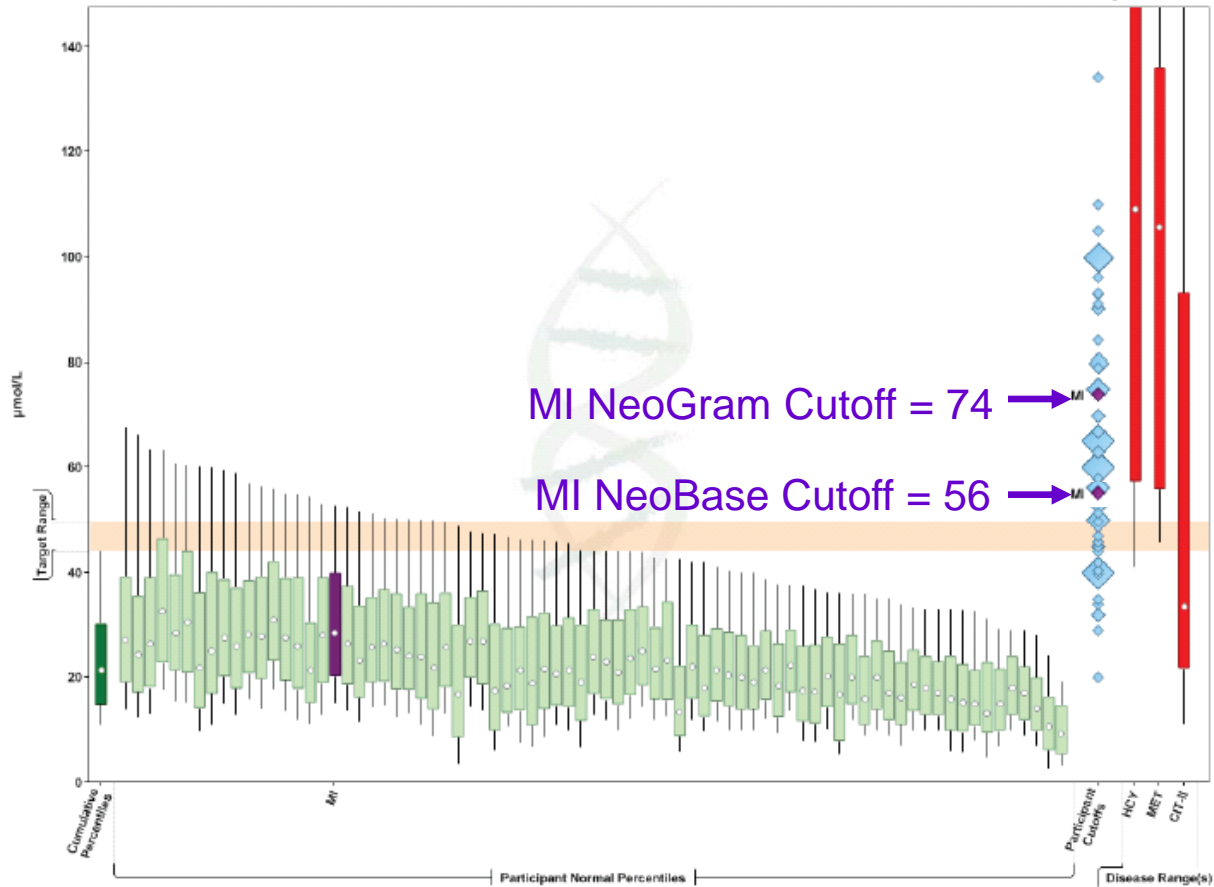
- **Why** do some of our cutoffs **not** coincide with the R4 target cutoff range?
 - Differences in the Methods
 - Extraction technique
 - Instrumentation
 - Internal Standard
 - Calibration Technique
 - Standard Calibration Material Use
 - (Traceable to National Standards)
 - Cutoffs in question are not clinically valid

Analyte Comparison Tool

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Met

◆ Cutoff marker size is proportional to the number of labs using the same value.

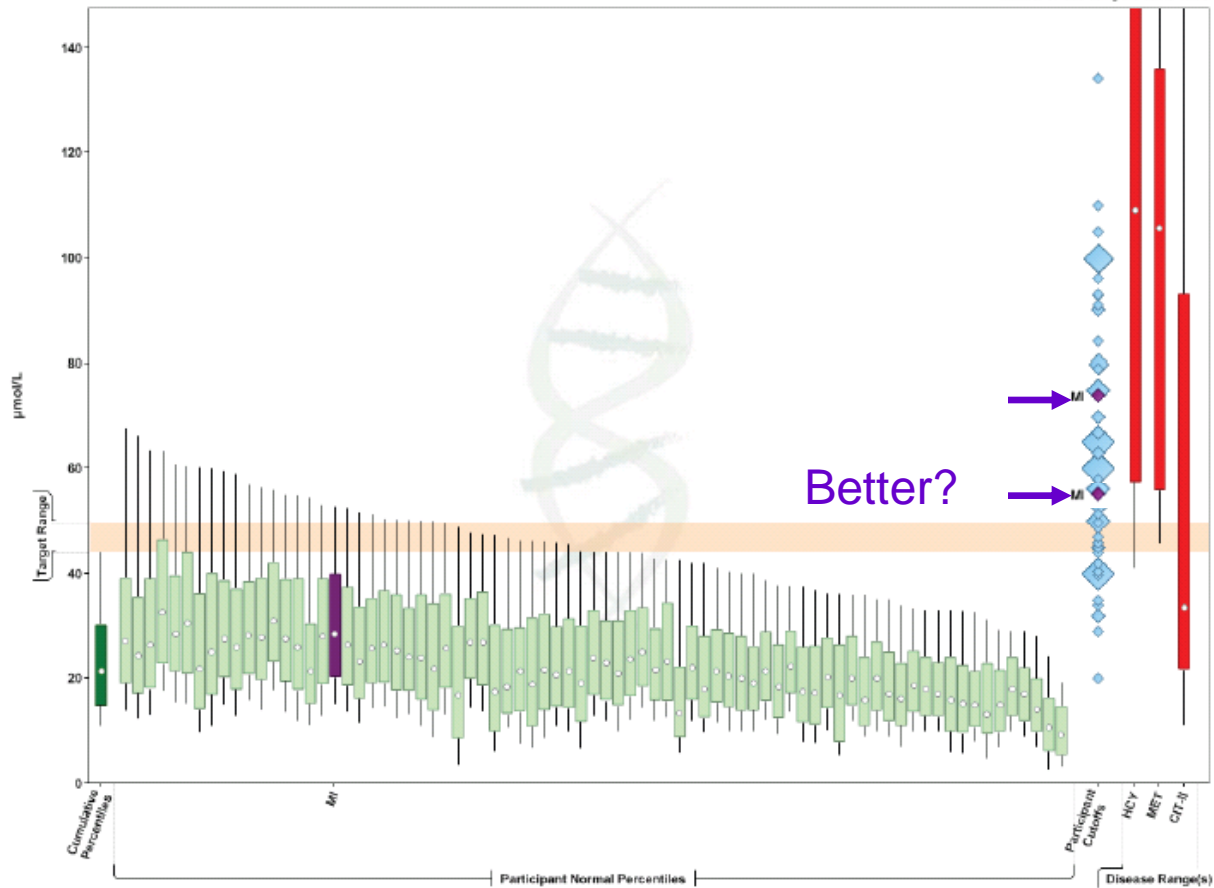


Analyte Comparison Tool

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Met

◆ Cutoff marker size is proportional to the number of labs using the same value.



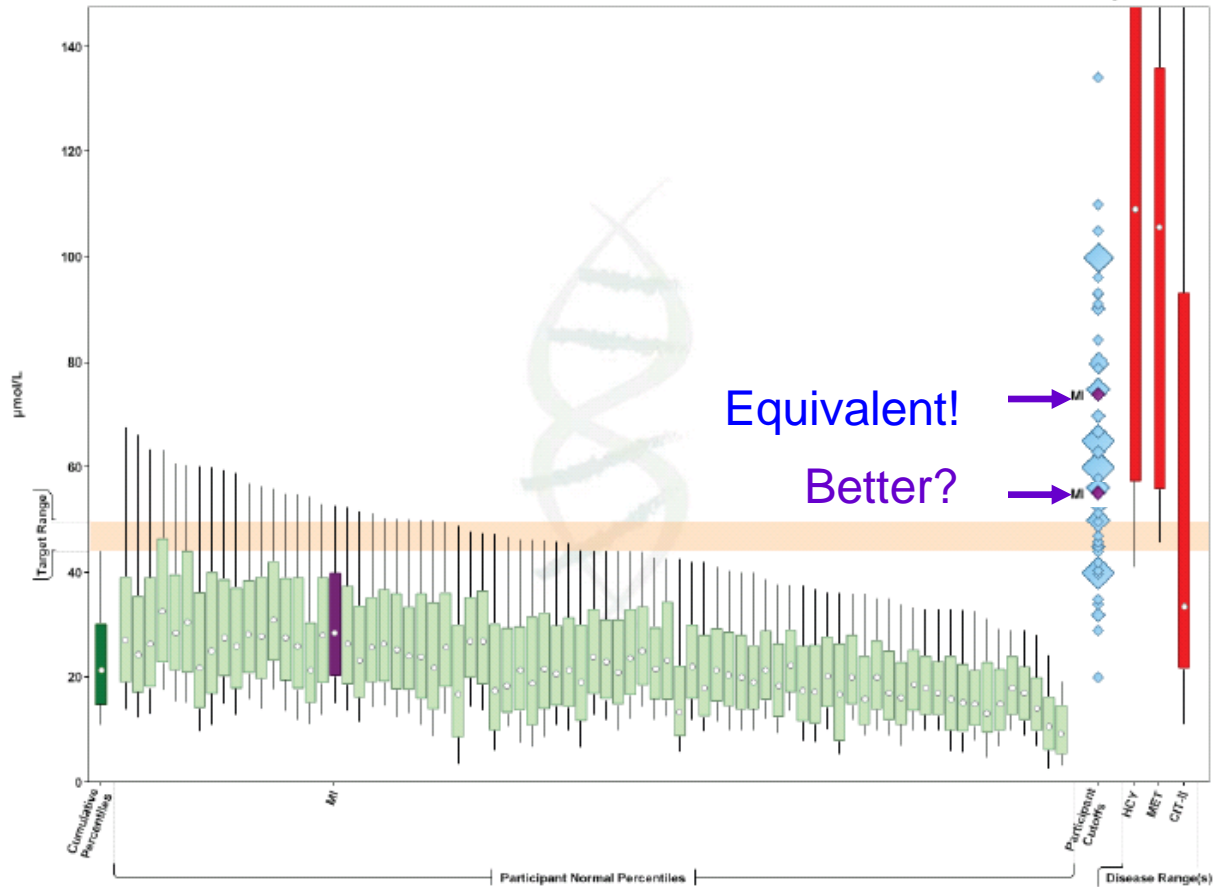
Target Range

Analyte Comparison Tool

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Met

◆ Cutoff marker size is proportional to the number of labs using the same value.



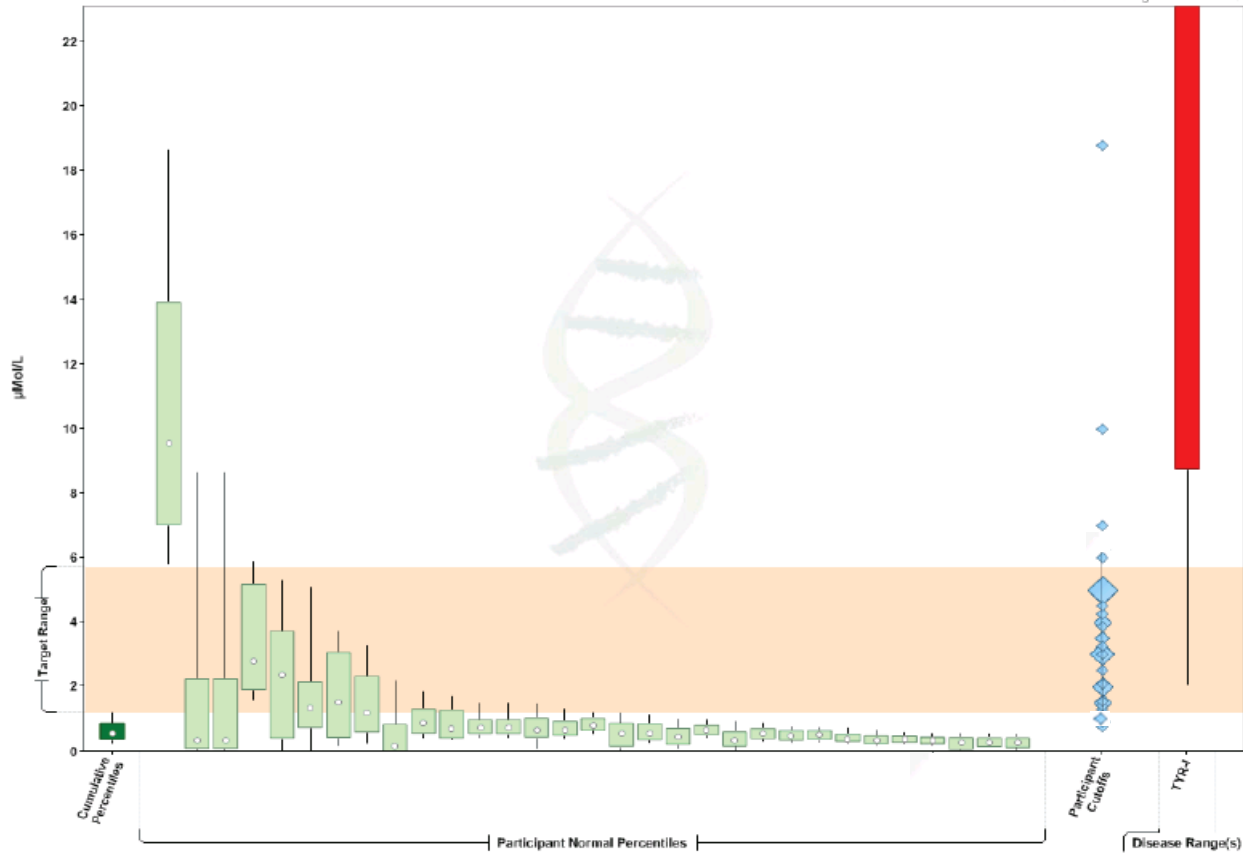
Target Range

Analyte Comparison Tool

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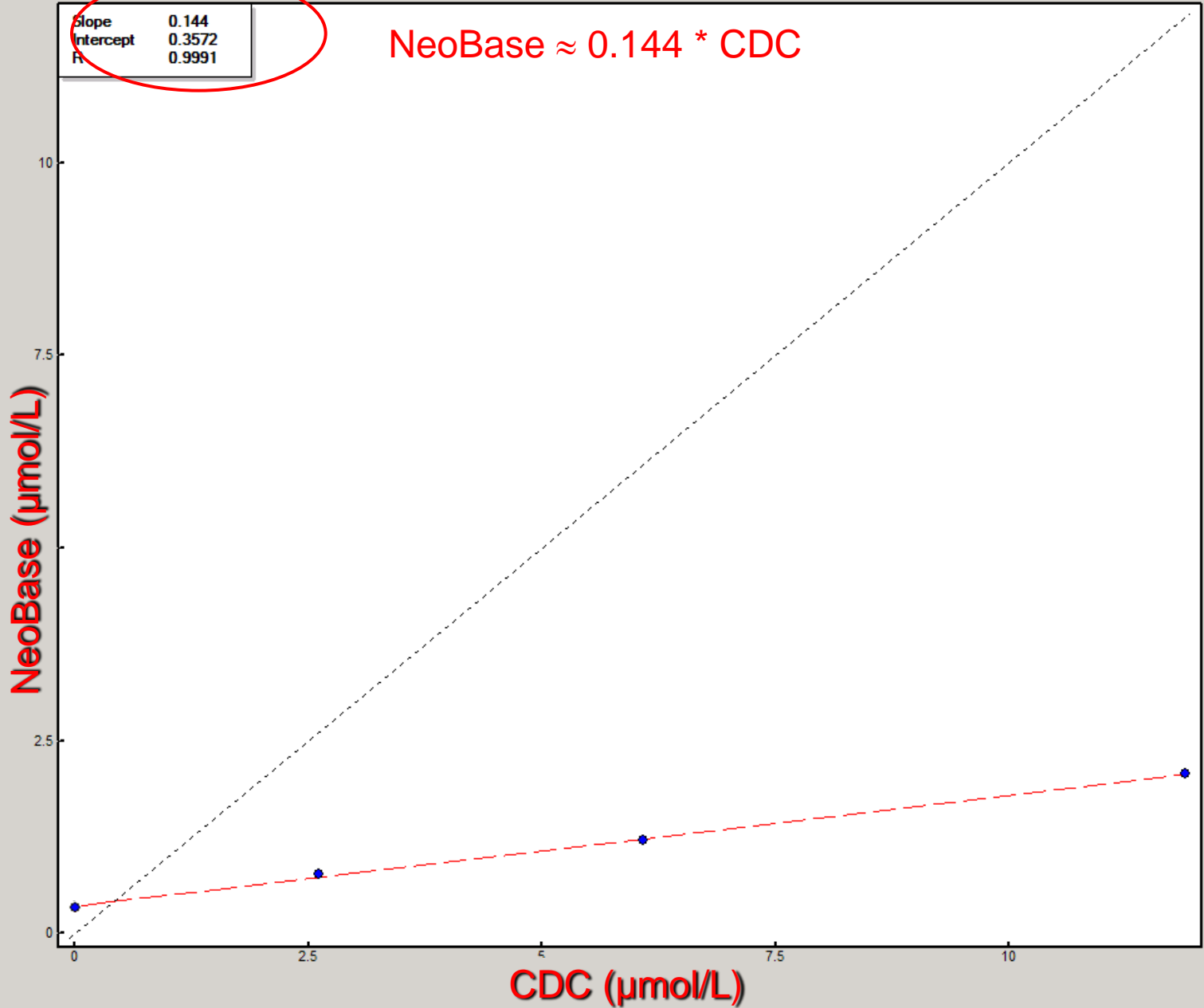
Suac

◆ Cutoff marker size is proportional to the number of labs using the same value.

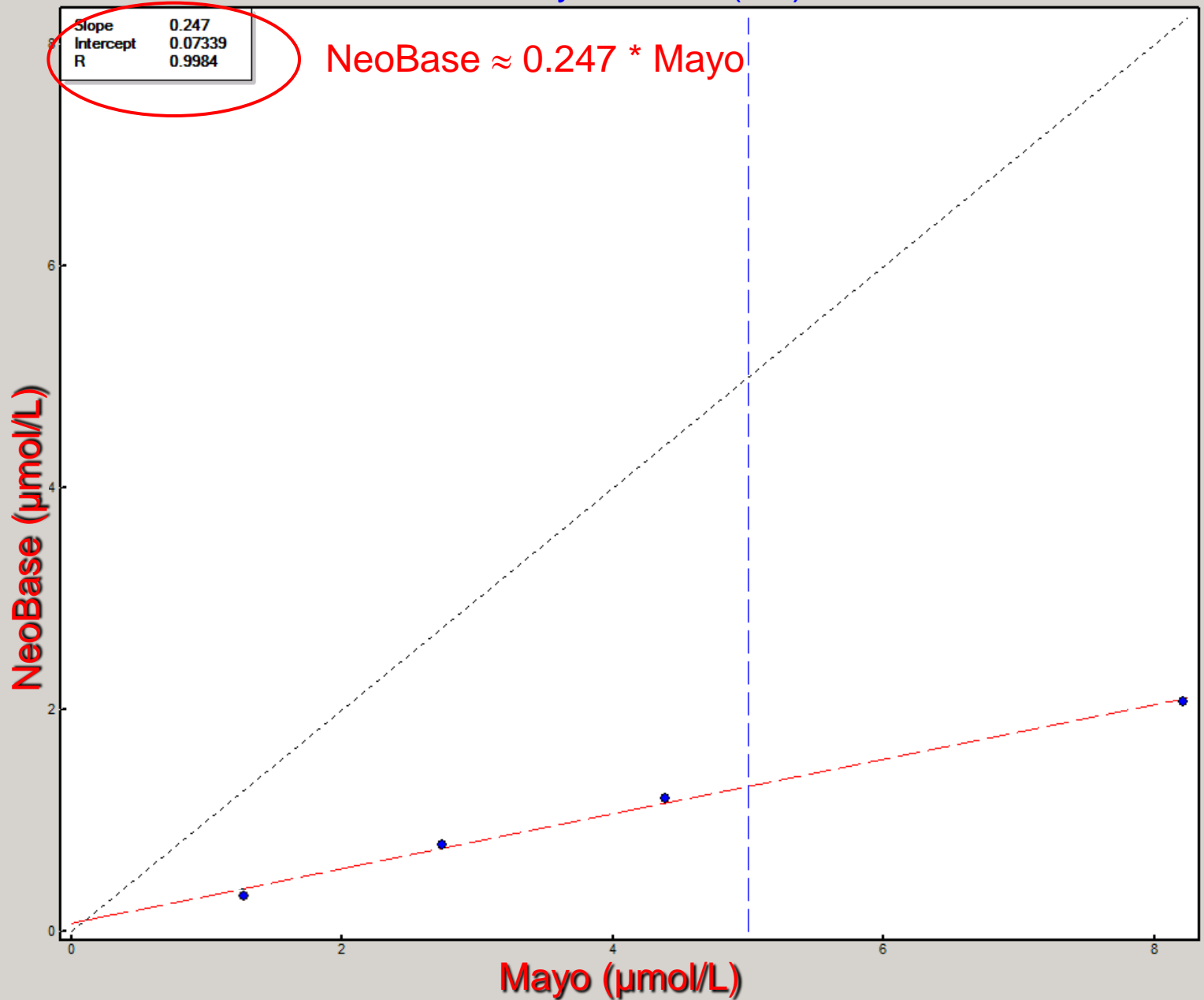


Target Range:

Succinylacetone (SA)



Succinylacetone (SA)



EP Evaluator®

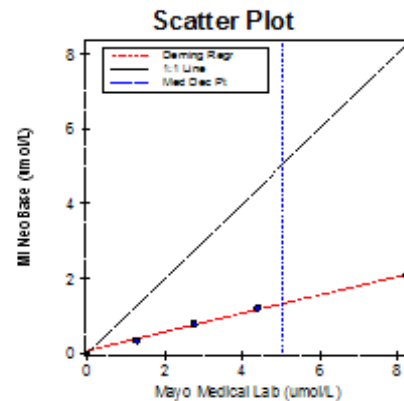
Michigan Department of Community Health – New Born Screening

SUAC w/o Patient

Alternate (Quantitative) Method Comparison

X Method: Mayo Medical Lab

Y Method: MI NeoBase



Regression Analysis

	Deming	Regular
Slope:	0.247 (0.242 to 0.251)	0.247 (0.242 to 0.251)
Intercept:	0.07339 (0.05085 to 0.09593)	0.07358 (0.05104 to 0.09612)
Std Err Est:	0.03732	0.03732

95% Confidence Intervals are shown in parentheses

Medical Decision Point Analysis

Calculated by Deming Regression ($R \geq 0.9$)

X Method MDP	Y Method Pred. MDP	95% Conf. Limits	
		Low	High
5.0	1.31	1.30	1.32



Mayo SUAC Cutoff

Equivalent NeoBase SUAC Cutoff

EP Evaluator®

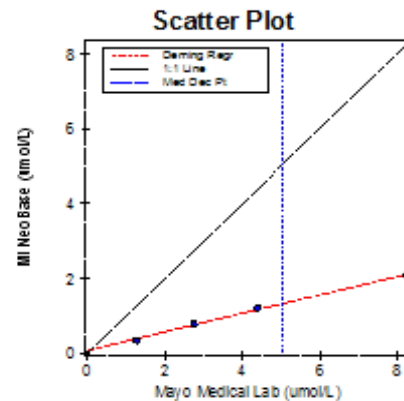
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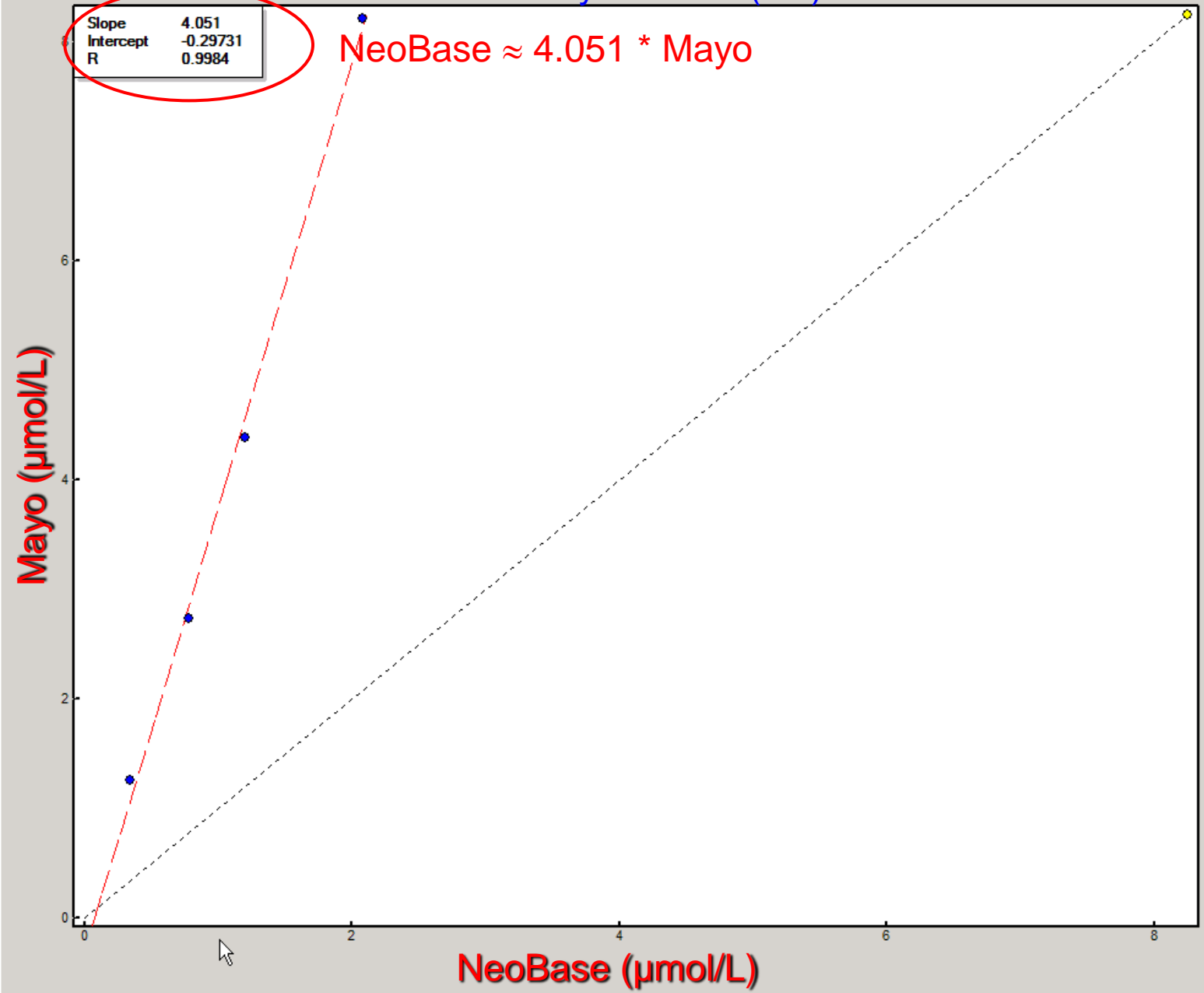
X Method MDP	Y Method Pred. MDP	95% Conf. Limits	
		Low	High
5.0	1.31	1.30	1.32



Mayo SUAC Cutoff

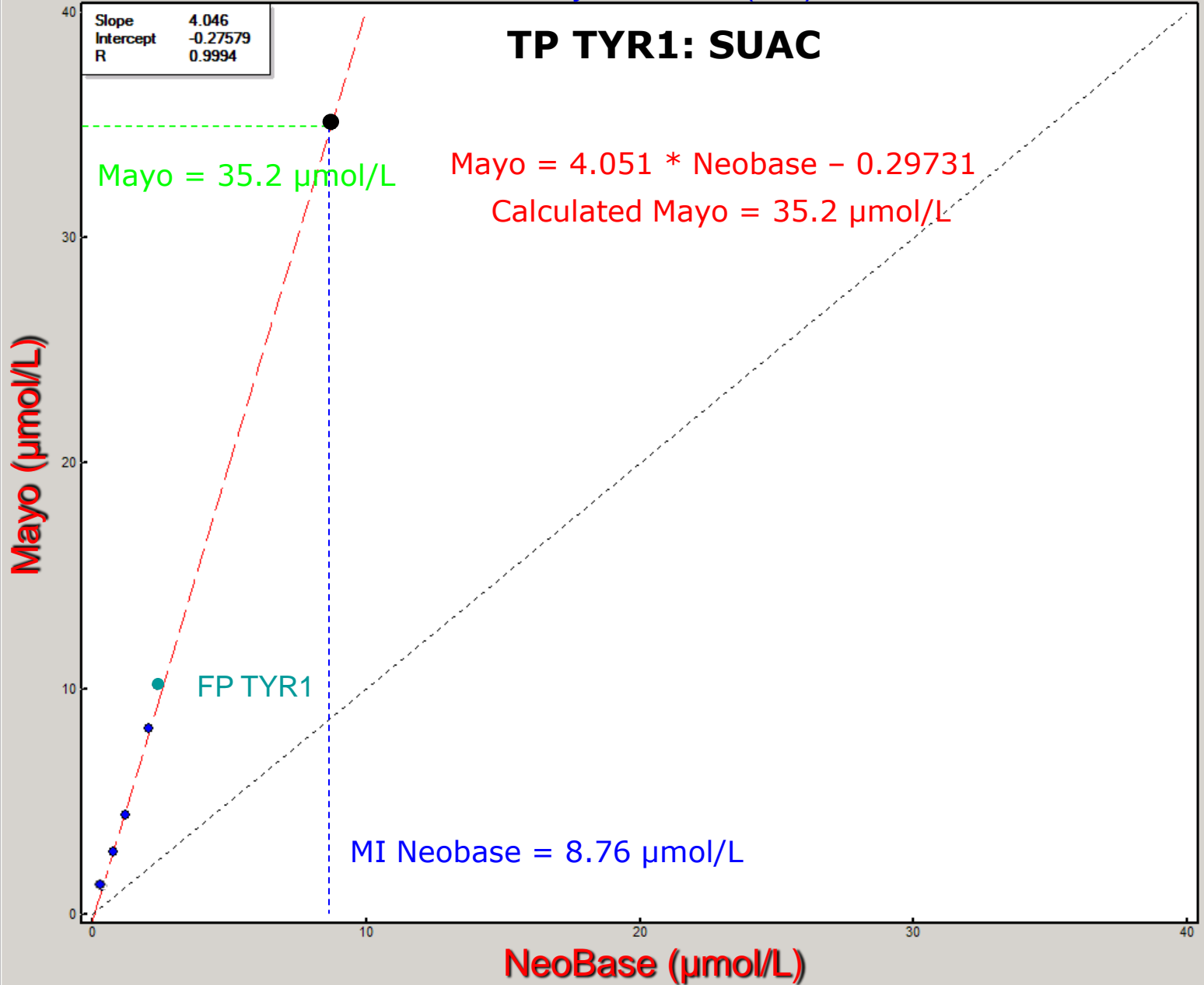
Cutoff set to 1.0 (99.99%ile = 0.82)

Succinylacetone (SA)



Succinylacetone (SA)

TP TYR1: SUAC

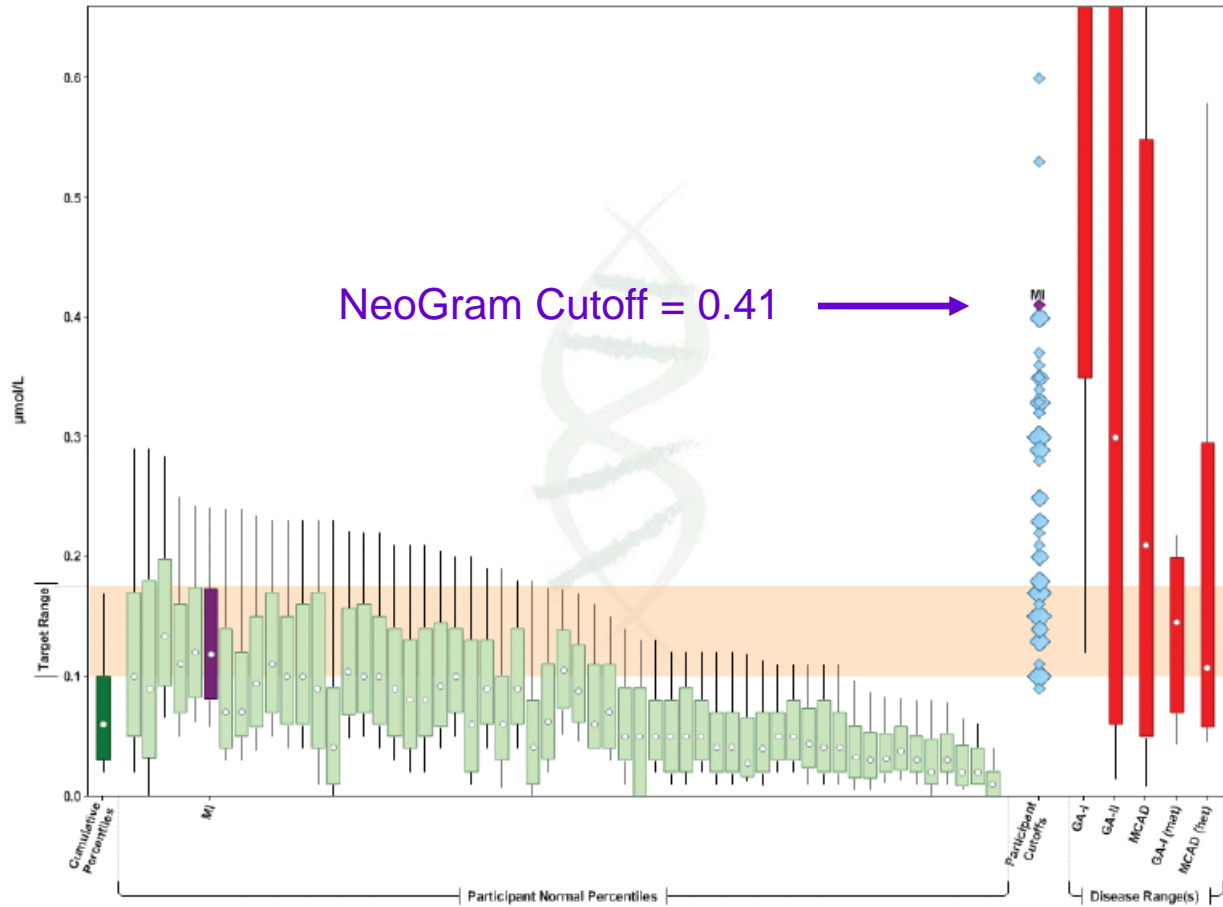


Analyte Comparison Tool

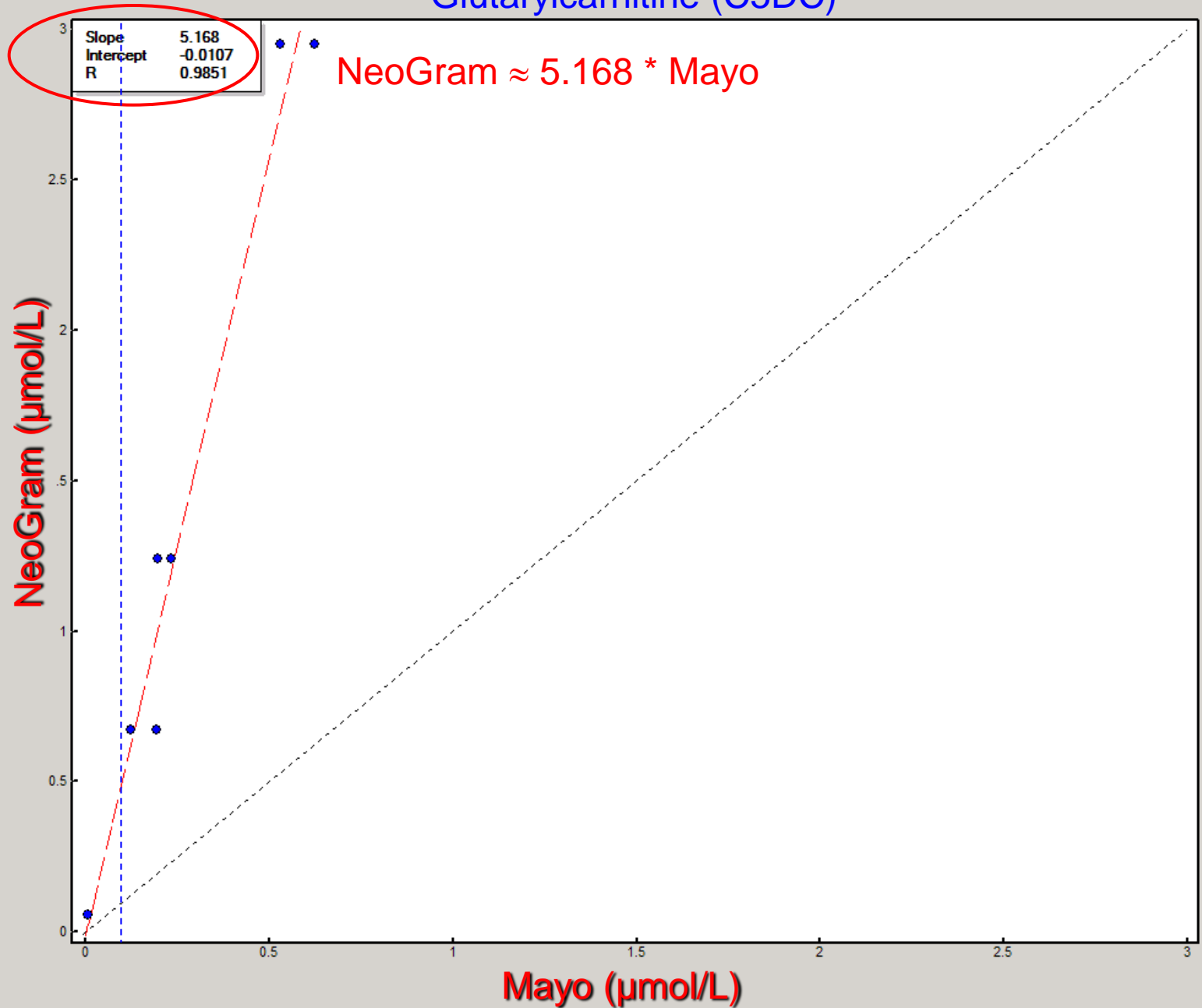
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C5DC+C10-OH

◆ Cutoff marker size is proportional to the number of labs using the same value.



Glutarylcarnitine (C5DC)



EP Evaluator®

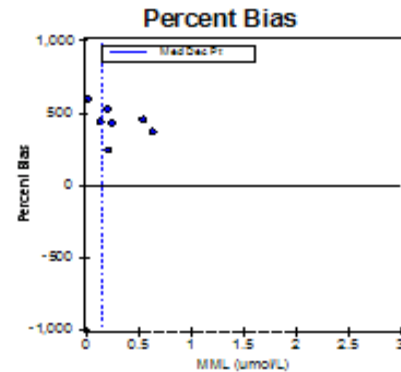
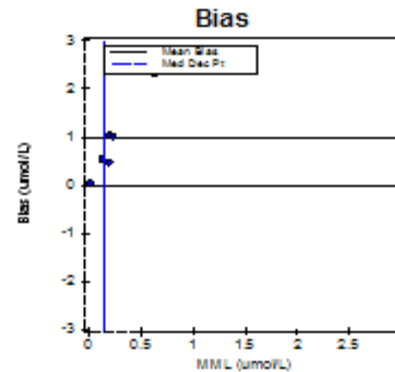
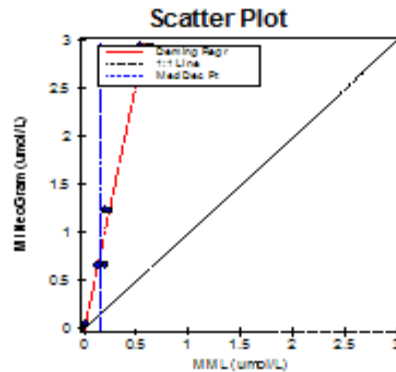
C5DC

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Alternate (Quantitative) Method Comparison

X Method: MML

Y Method: MI NeoGram



Regression Analysis

	Deming	Regular
Slope:	5.168 (4.876 to 5.460)	5.021 (4.733 to 5.309)
Intercept:	-0.0107 (-0.1040 to 0.0826)	0.0246 (-0.0674 to 0.1167)
Std Err Est:	0.1929	0.1902

95% Confidence Intervals are shown in parentheses

Medical Decision Point Analysis

Calculated by Deming Regression ($R^2=0.9$)

X Method MDP	Y Method Pred. MDP	95% Conf. Limits	
		Low	High
0.15	0.765	0.698	0.831



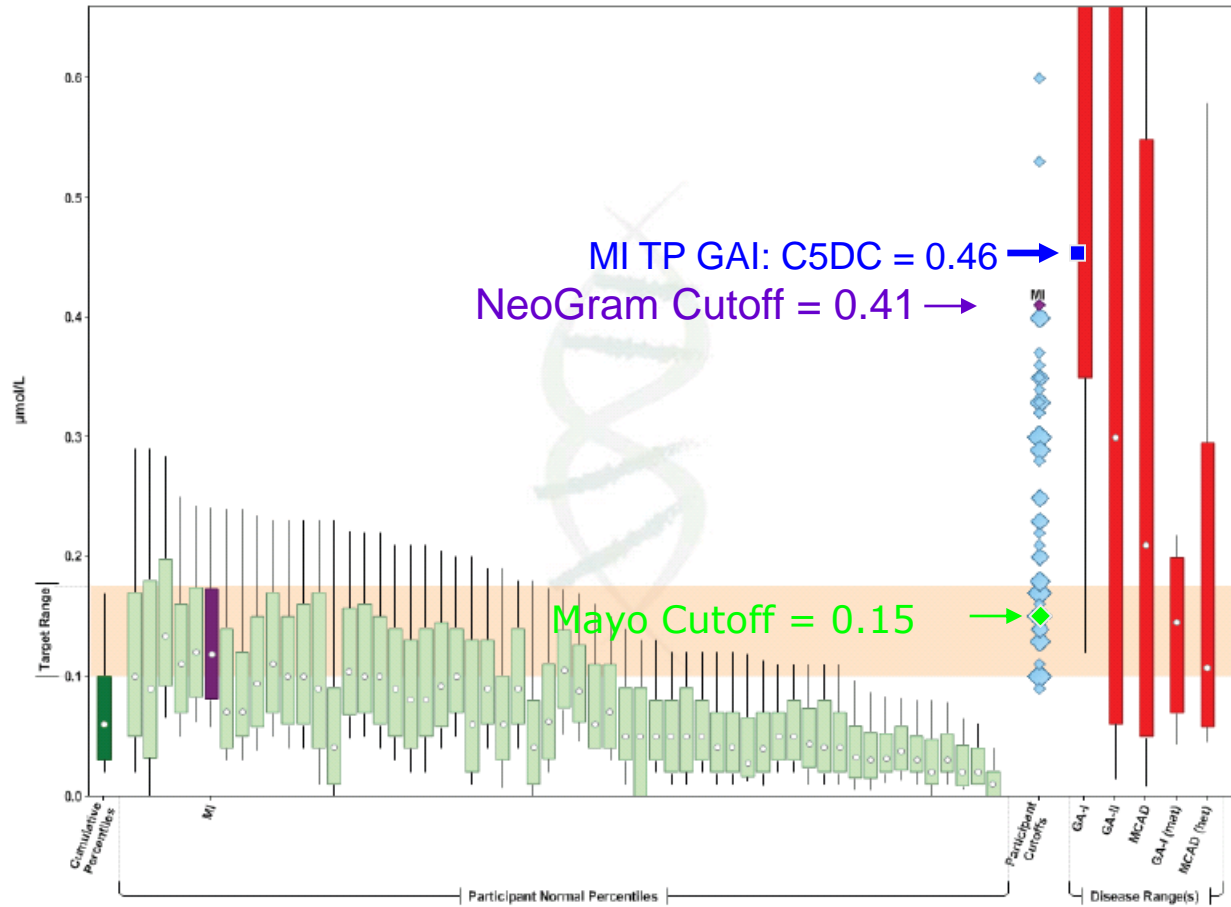
Mayo C5DC Cutoff

Equivalent NeoGram C5DC Cutoff

MI Equivalent Cutoff = 0.765 → ◆
 NeoBase C5DC 99.99%tile = 0.732 → ◆

C5DC+C10-OH

◆ Cutoff marker size is proportional to the number of labs using the same value.



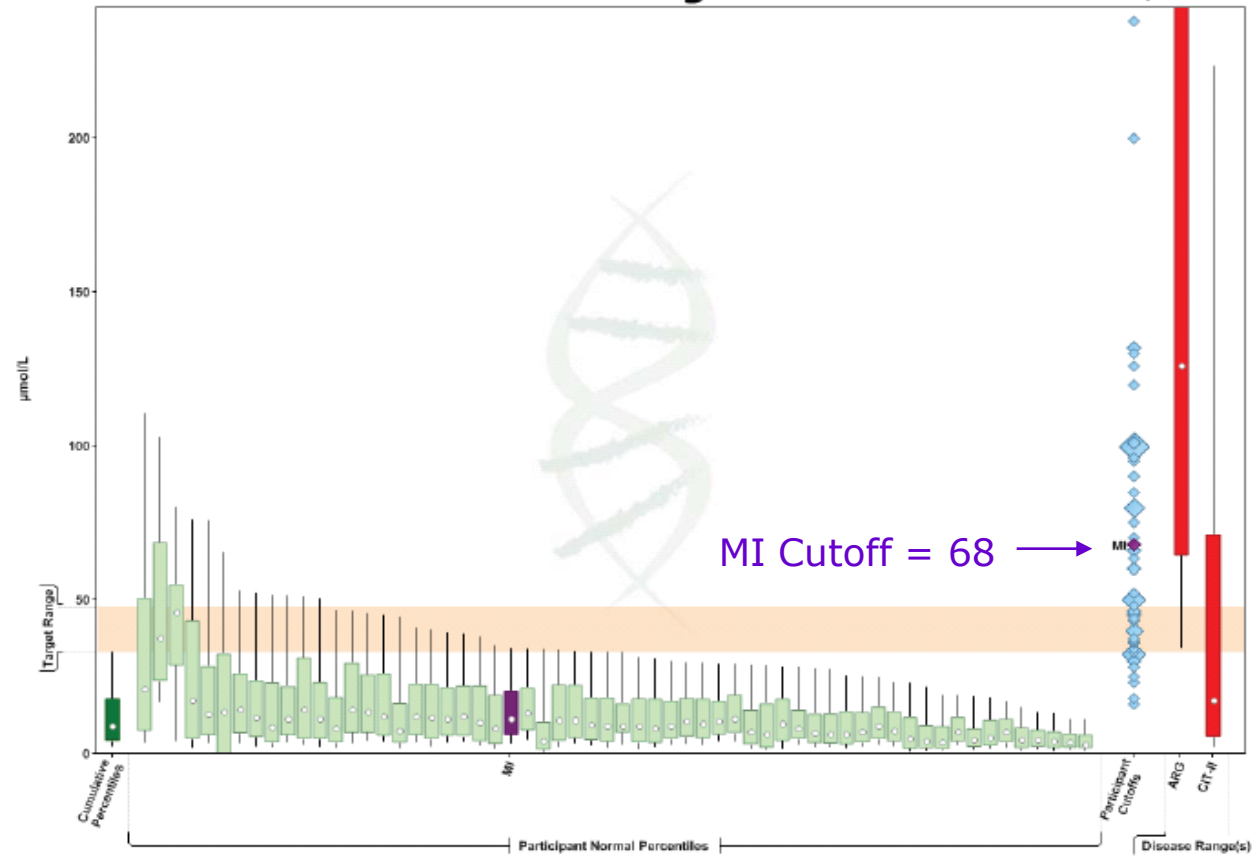
Target Range

Analyte Comparison Tool

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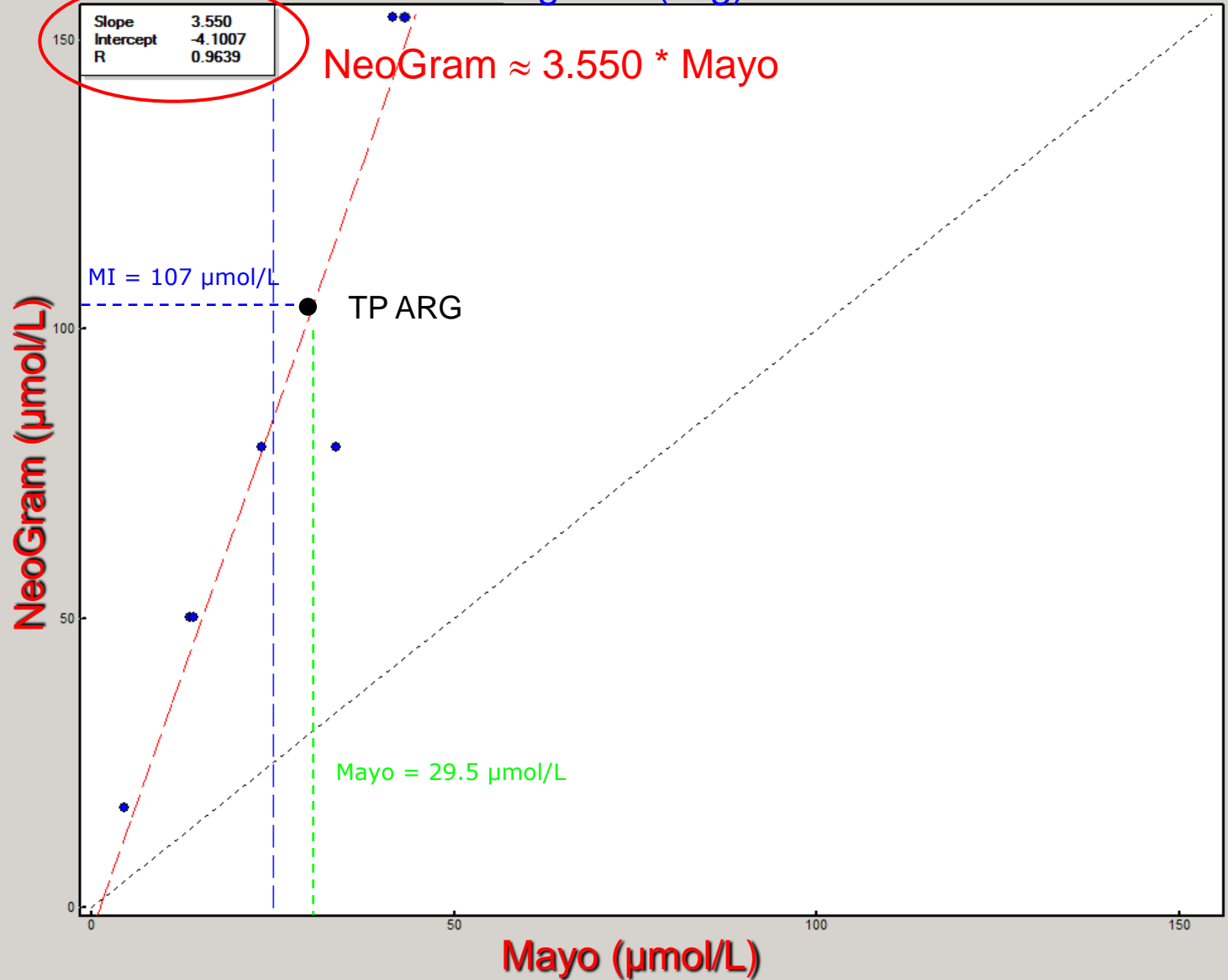
Arg

◆ Cutoff marker size is proportional to the number of labs using the same value.



Target Range

Arginine (Arg)



EP Evaluator®

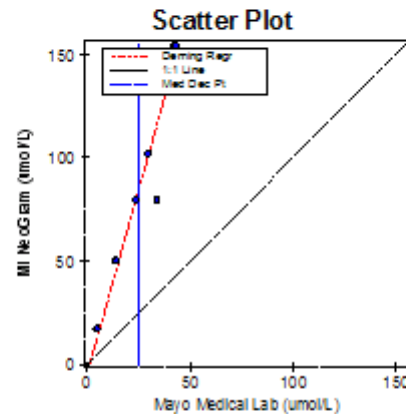
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Arg

Alternate (Quantitative) Method Comparison

X Method: Mayo Medical Lab

Y Method: MI NeoGram



Regression Analysis

	Deming	Regular
Slope:	3.551 (3.246 to 3.857)	3.319 (3.023 to 3.615)
Intercept:	-4.0952 (-12.2819 to 4.0915)	1.1319 (-6.8029 to 9.0668)
Std Err Est:	14.0499	13.6177

95% Confidence Intervals are shown in parentheses

Medical Decision Point Analysis

Calculated by Deming Regression ($R \geq 0.9$)

X Method MDP	Y Method Pred. MDP	95% Conf. Limits	
		Low	High
25	84.7	80.2	89.1



Mayo Arg Cutoff

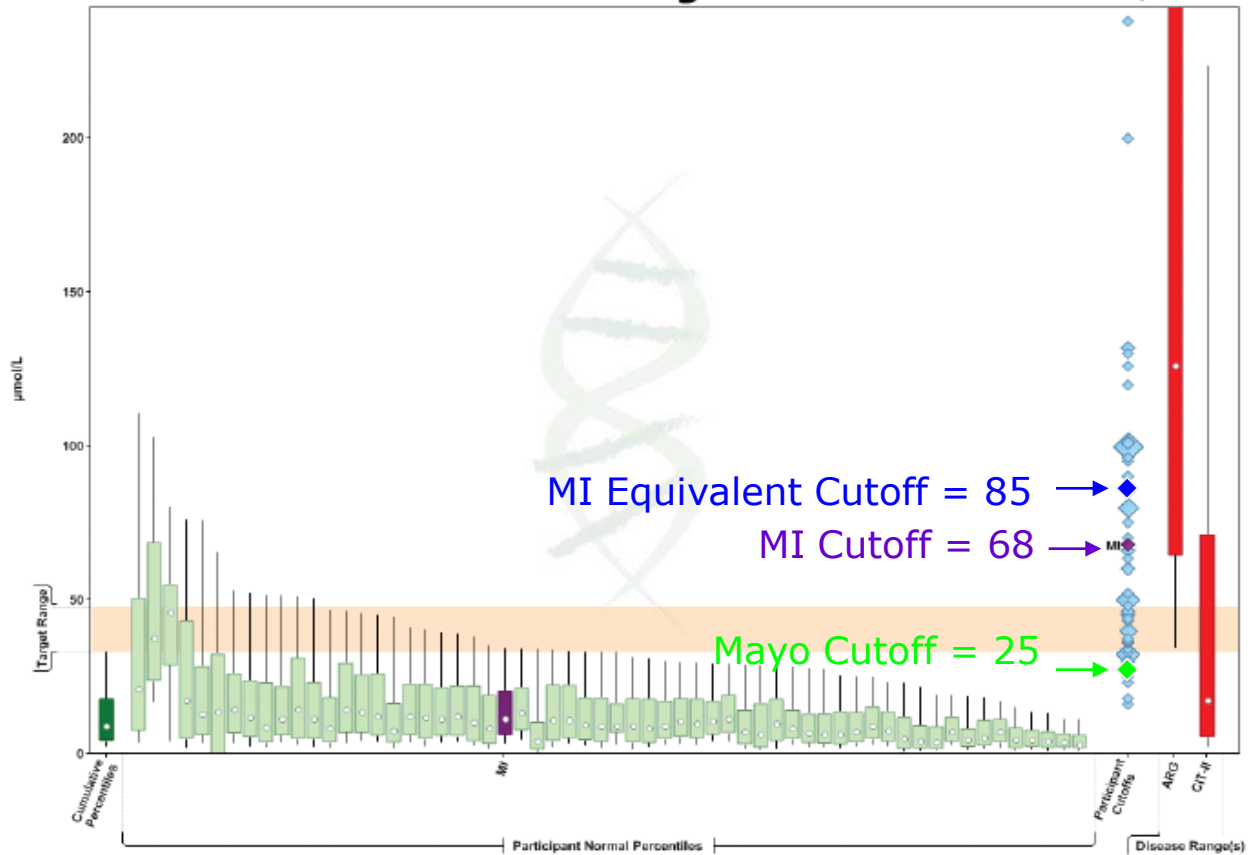
Equivalent NeoGram Arg Cutoff

Analyte Comparison Tool

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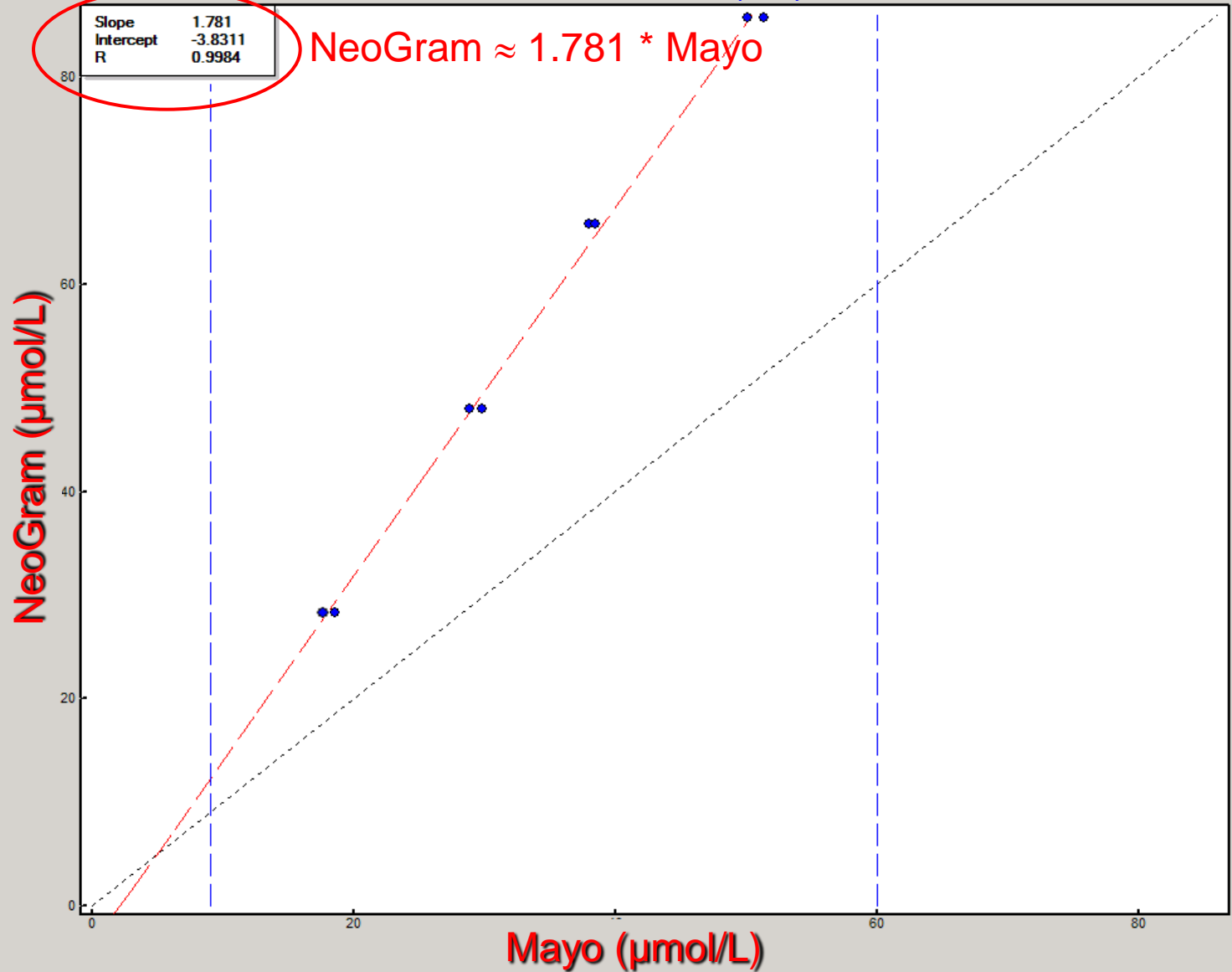
Arg

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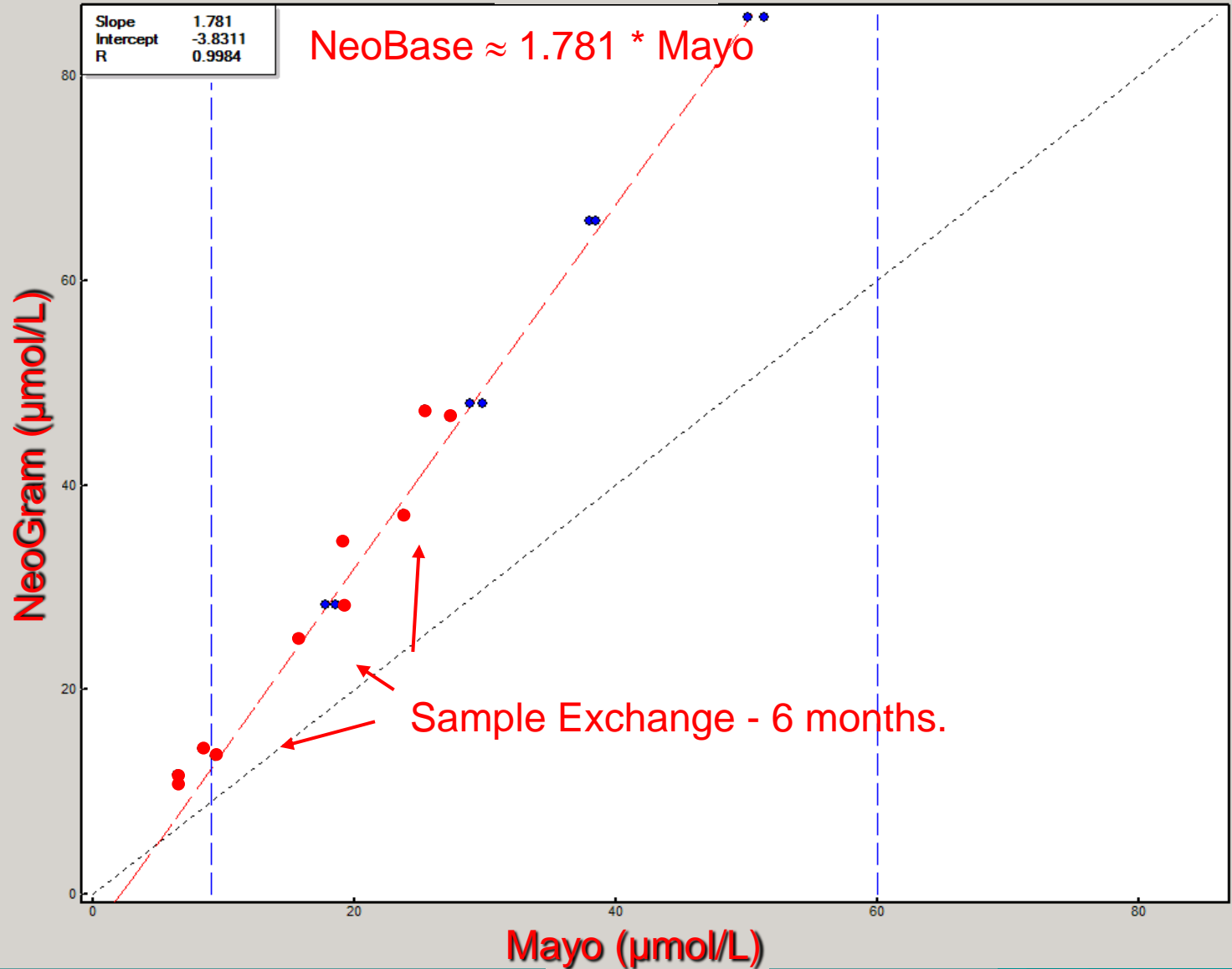


Target Range

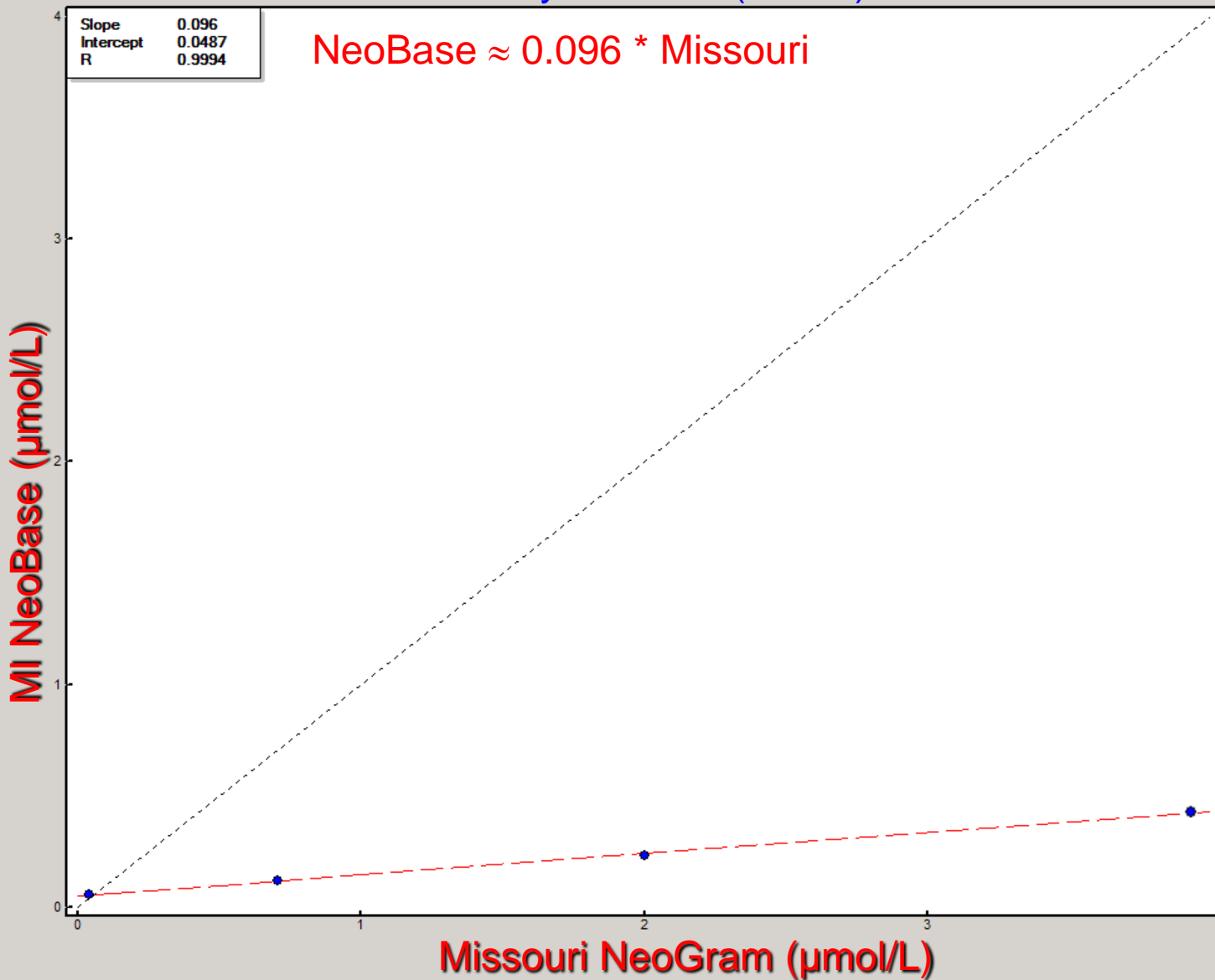
Free carnitine (C0)



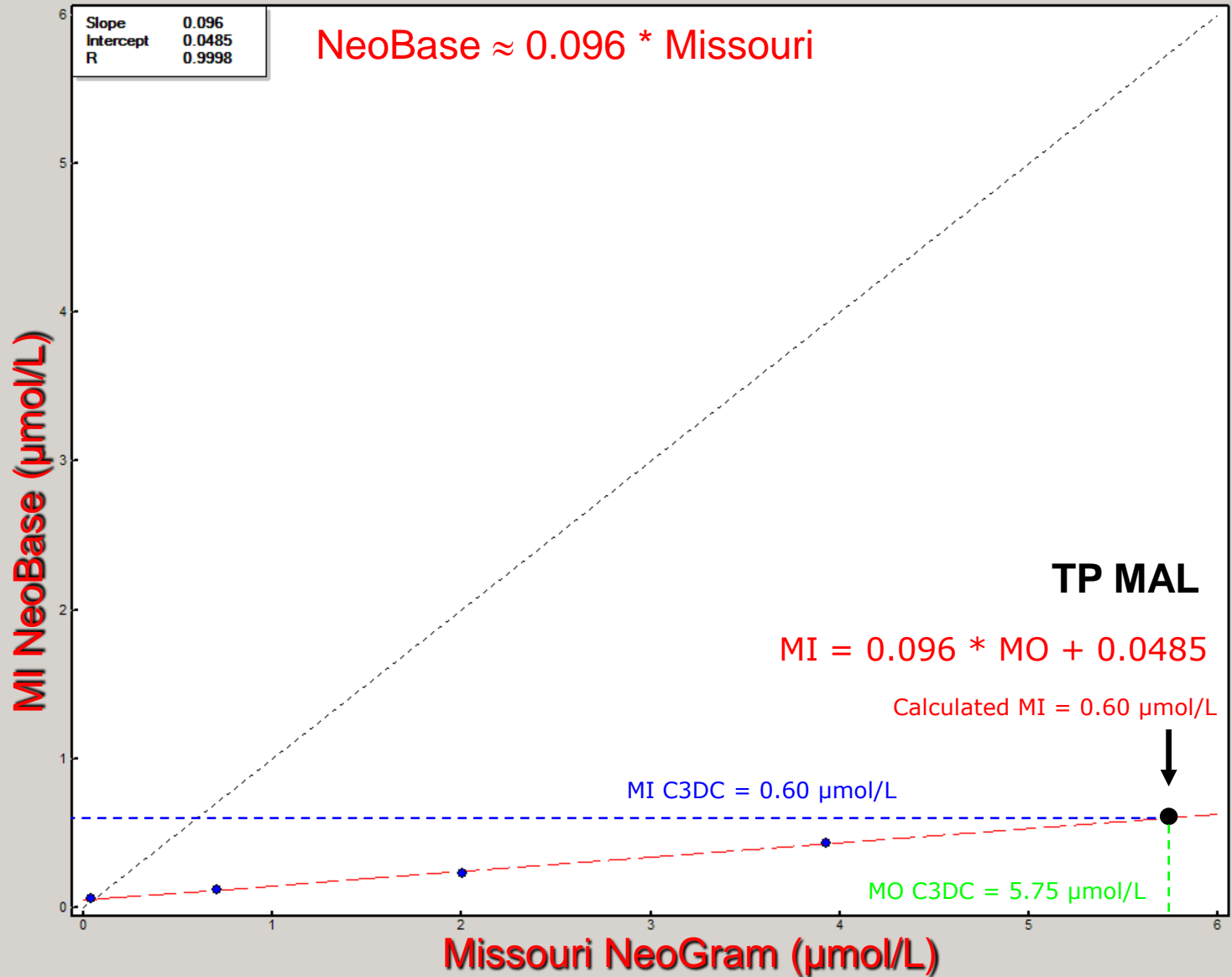
Free carnitine (C0)



Malonylcarnitine (C3DC)



Malonylcarnitine (C3DC)



Conclusions

Harmonization Using CDC Quality Control Materials:

- Allows Harmonization of Cutoffs
- Allows Harmonization of TP Analyte Concentrations

Conclusions

- Allowed for an accurate comparison of Cutoff Values between Michigan and Mayo.
- Identified that C16OH, C0, Cit, Cit/Arg, and Met cutoffs required correction.



Acknowledgements:

MI NBS Team – Eleanor Stanley

Dr. Robert Grier – CHMMC, BGL

Patrick V. Hopkins – Missouri

Marie-Thérèse Berthier, Quebec – NeoBase

Sheila Weiss/Bill Hoffman – Washington

Dr. Victor DeJesus/CDC Quality Assurance Program

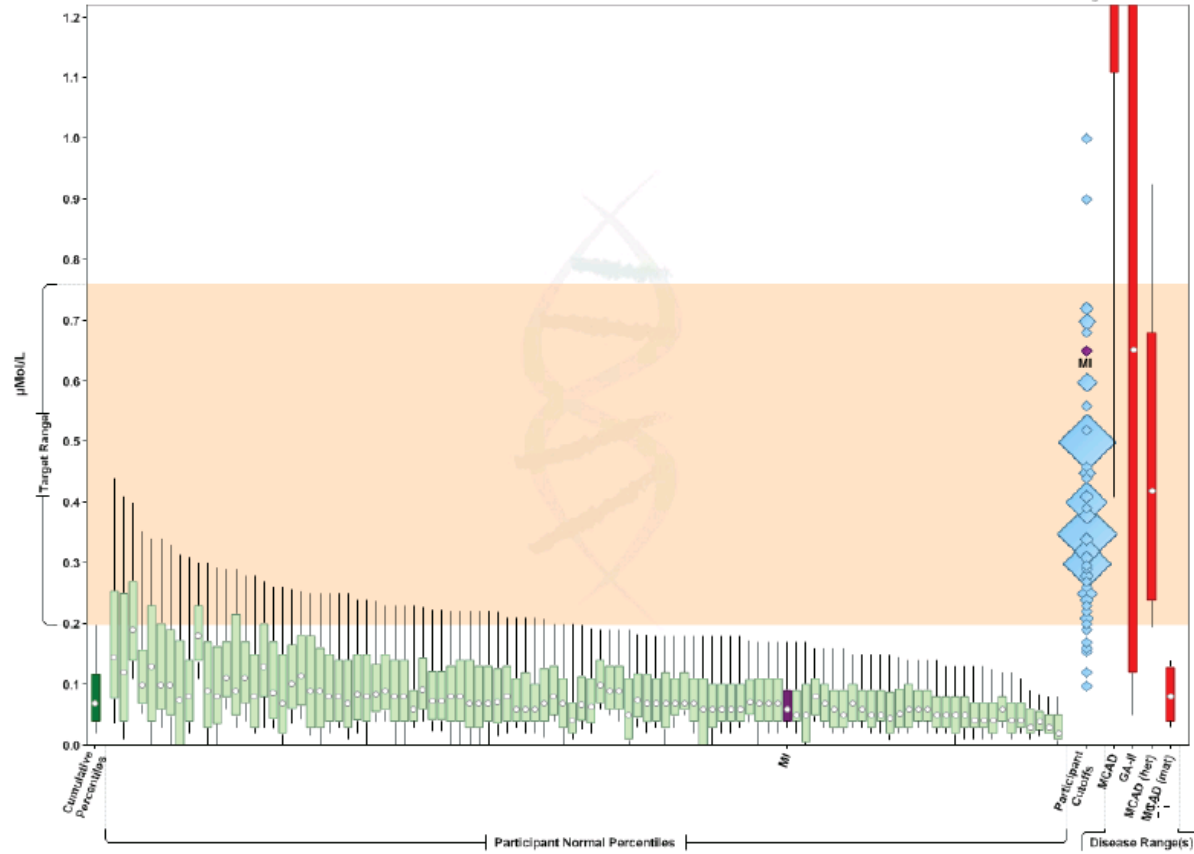
Dr. Piero Rinaldo/David McHugh - Region 4 Collaborative

Analyte Comparison Tool

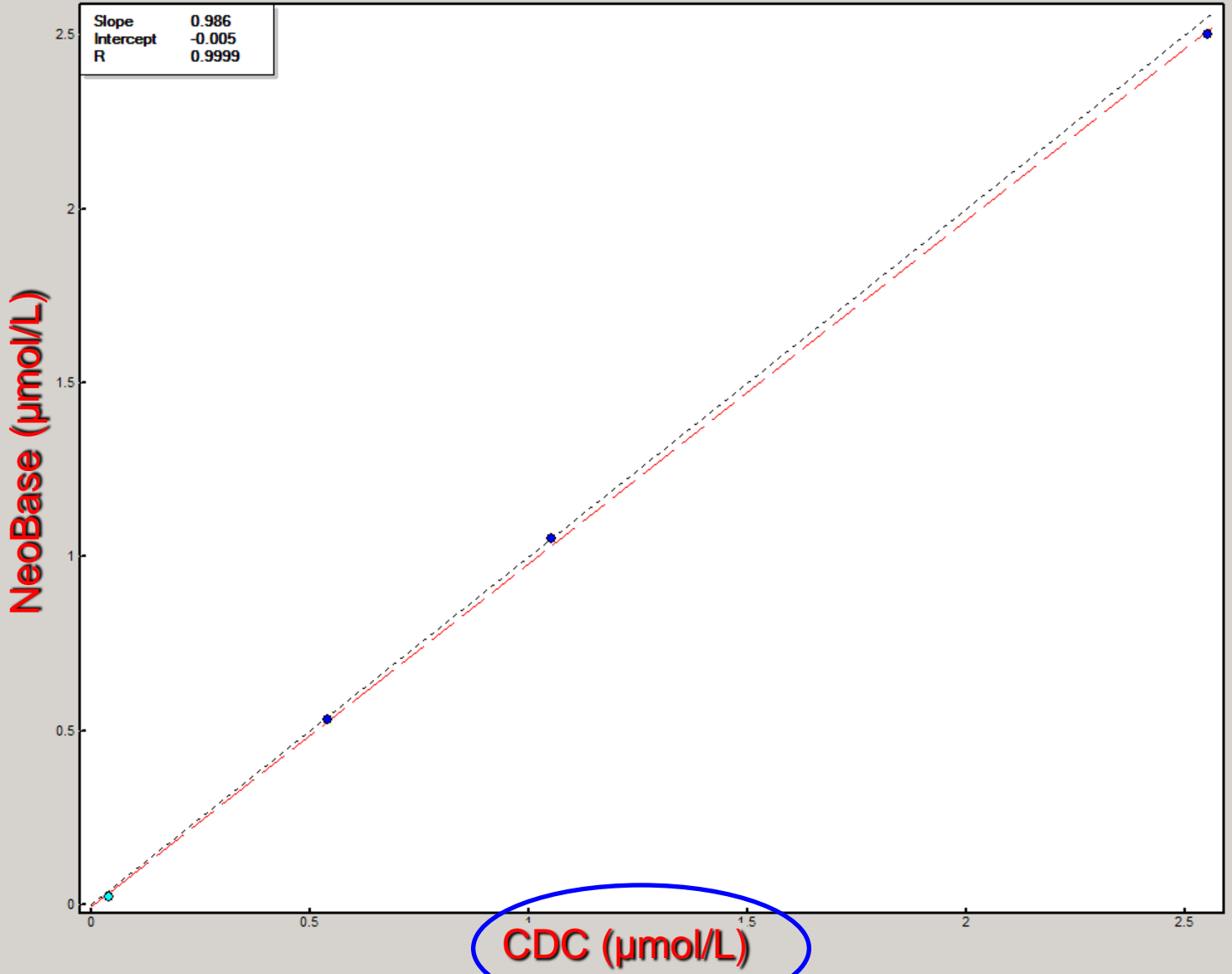
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C8

◆ Cutoff marker size is proportional to the number of labs using the same value.



C8: Scatter Plot





MS/MS COLLABORATIVE PROJECT

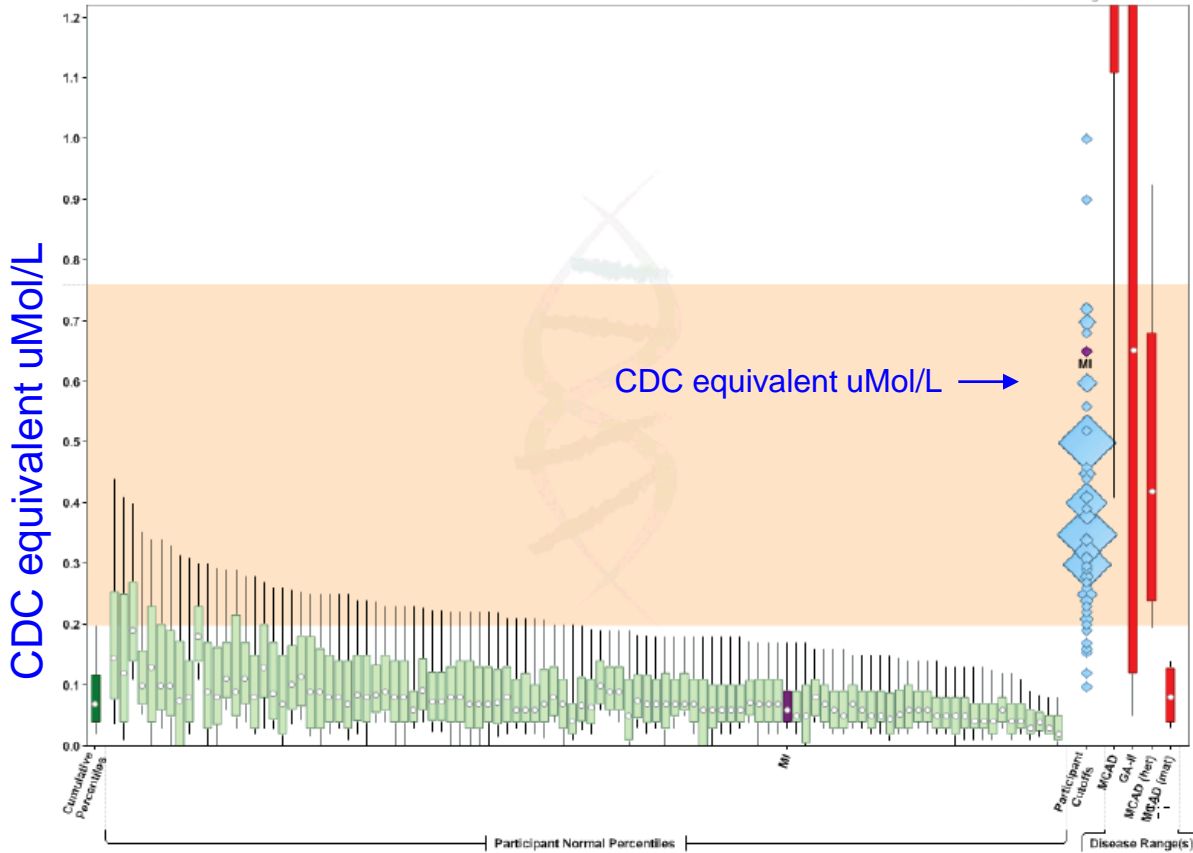


Analyte Comparison Tool

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C8

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Analyte Comparison Tool

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C8

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