

Analytic Performance of Glucose Meters: State of the Art

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Outline

1. Introduction
2. Common Interferences
3. Tight Glycemic Control and Meters
4. Accuracy and Reproducibility
 - Allowable Error Criteria
 - Past and Current Performance
 - Our Institution's Data
 - Newer Meters
 - What should allowable error be?
5. Conclusions

1. Introduction

- Smaller
- Many
 - ADA lists 30 home use meters (2008)
- > \$6 billion/year market
- Growth of ~10% per year
- ~ 30% of 2006 laboratory testing revenue in U.S.

<http://www.diabetes.org/diabetes-forecast/RG07/RG07BGMonitors.pdf>,

Frost and Sullivan 2005, G-2 Reports, Oct 2007

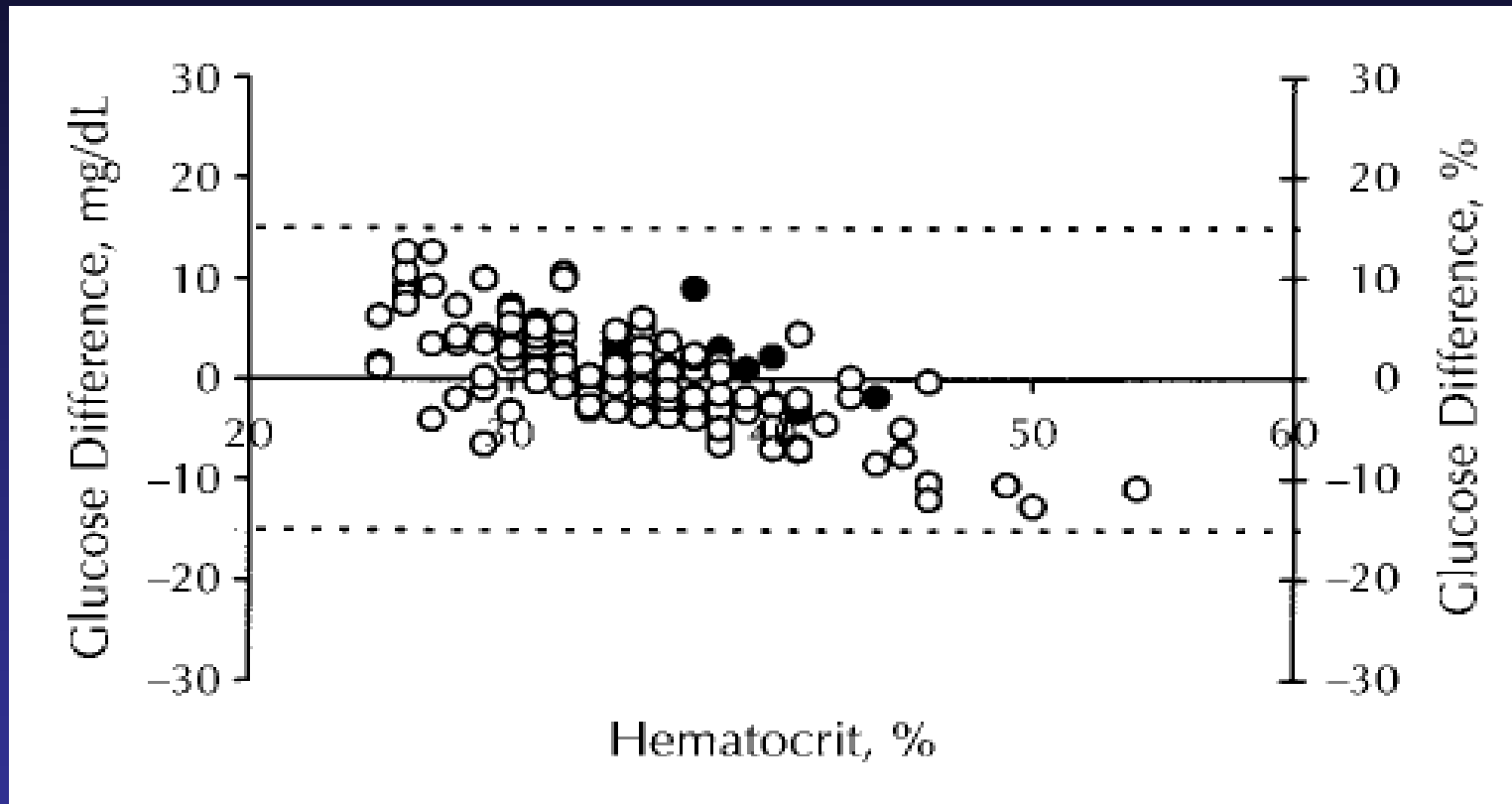
Recent Improvements

- “No wipe” strips
- Sample Volume Detection
- Smaller sample size
- Data storage and capture (LIS)
- QC lockouts
- Alternate Site Testing
 - Time lag issue (*Diabetes Care 2003;26:829*)

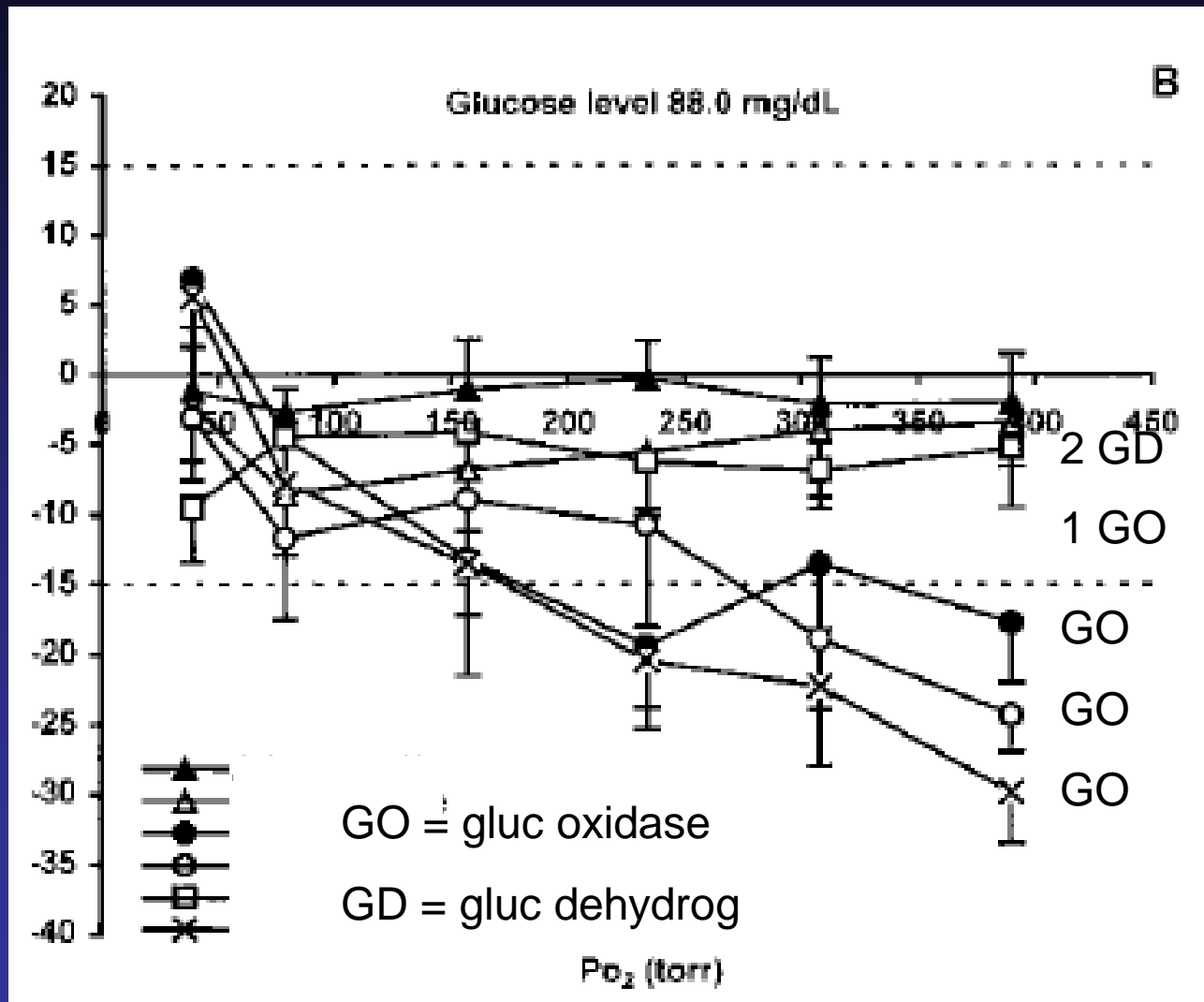
2. Interferences

- Most Methods
 - Hematocrit effect
 - Anemia = higher glucose
 - Polycythemia = lower glucose
 - Reducing agents (ascorbate, acetaminophen)
 - Effects vary by method
 - Some newer meters correct for hematocrit and reducing agents (*Clin Chim Acta 2005;356:178*)

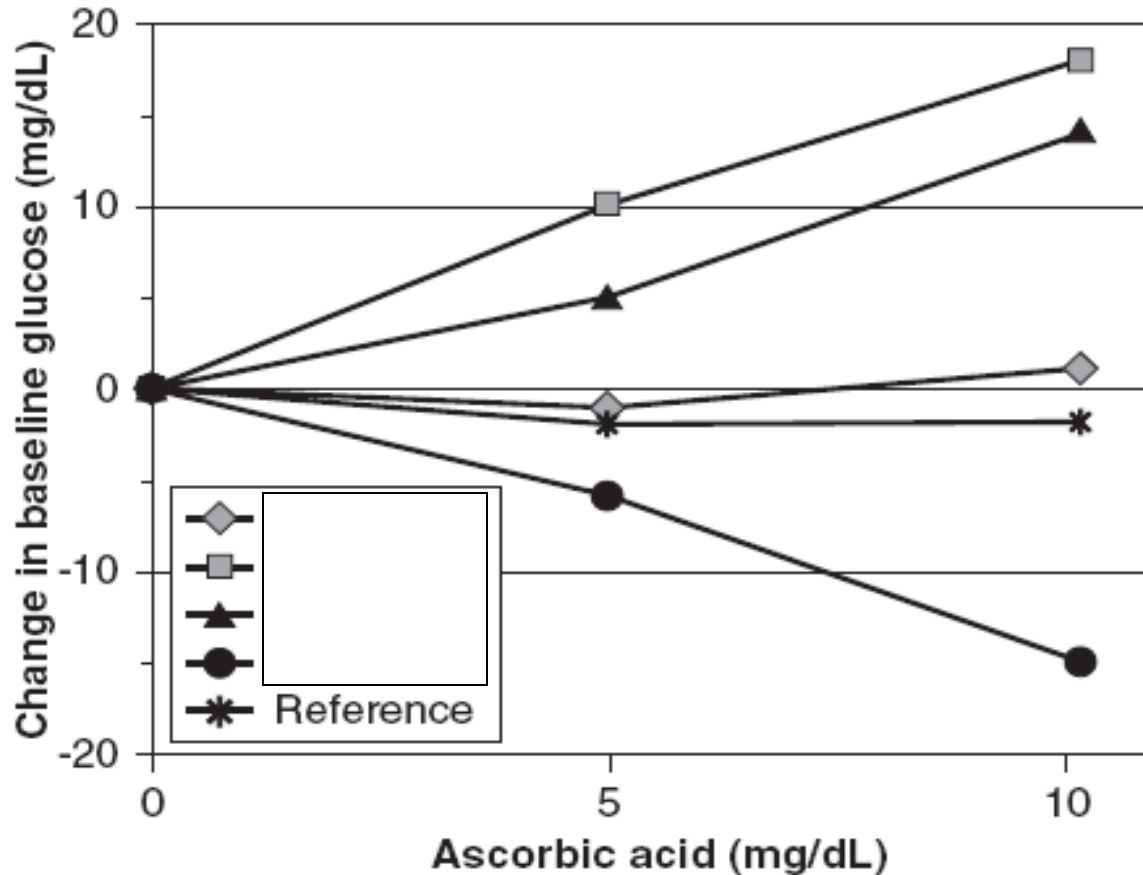
Hematocrit Effect



Oxygen Effect



Reducing Substances



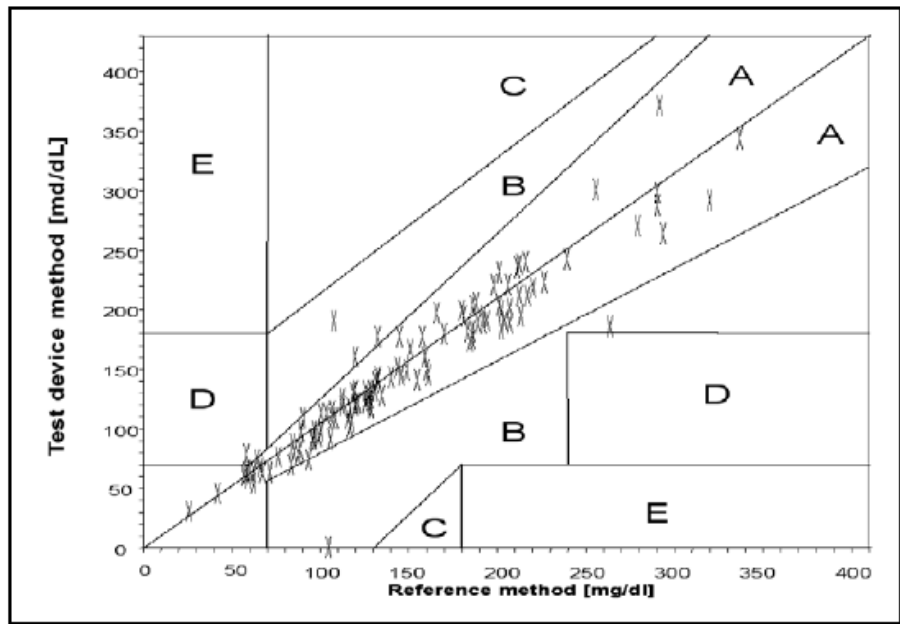
Glucose = 70 mg/dL

- Glucose Dehydrogenase Methods
 - Maltose containing agents (IVIg)
 - Peritoneal dialysis (icodextrin)
- Marked false increases in glucose

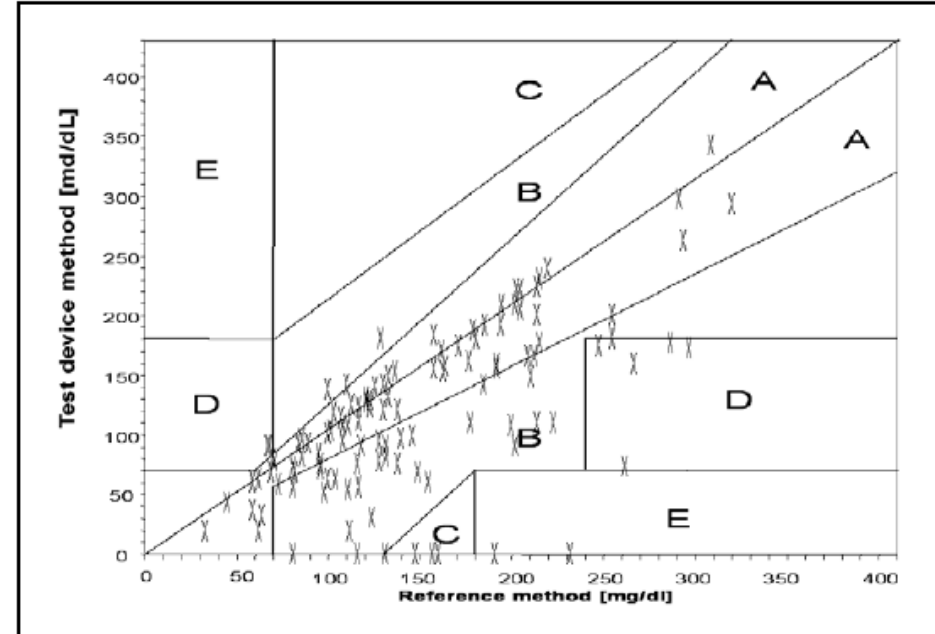
K Dungan et. al. Diabetes Care 2007; 30:403. (A good review of interferences)

User Induced Errors

Per Package Insert



Strip Manipulation



3. Tight Glycemic Control

- Most critical care areas have protocols to keep glucose below 130 mg/dL (7.8 mmol/L)
- Frequent glucose values
- IV insulin adjustment
 - Small changes in glucose can lead to doubling or having insulin infusion rates
- Barnes-Jewish Hospital (Wash U)
 - 2000 – ~ 250,000 strips/year
 - 2009 - ~ 550,000 strips used
 - Nearly ½ in Critical Care Units

Glucose Methods in TGC?

- Original Van den Berghe Study (2001) used Blood Gas Instrument Method and Arterial Blood
- 2006 Van den Berghe Study Used Hemocue Glucose Meter and Capillary Blood

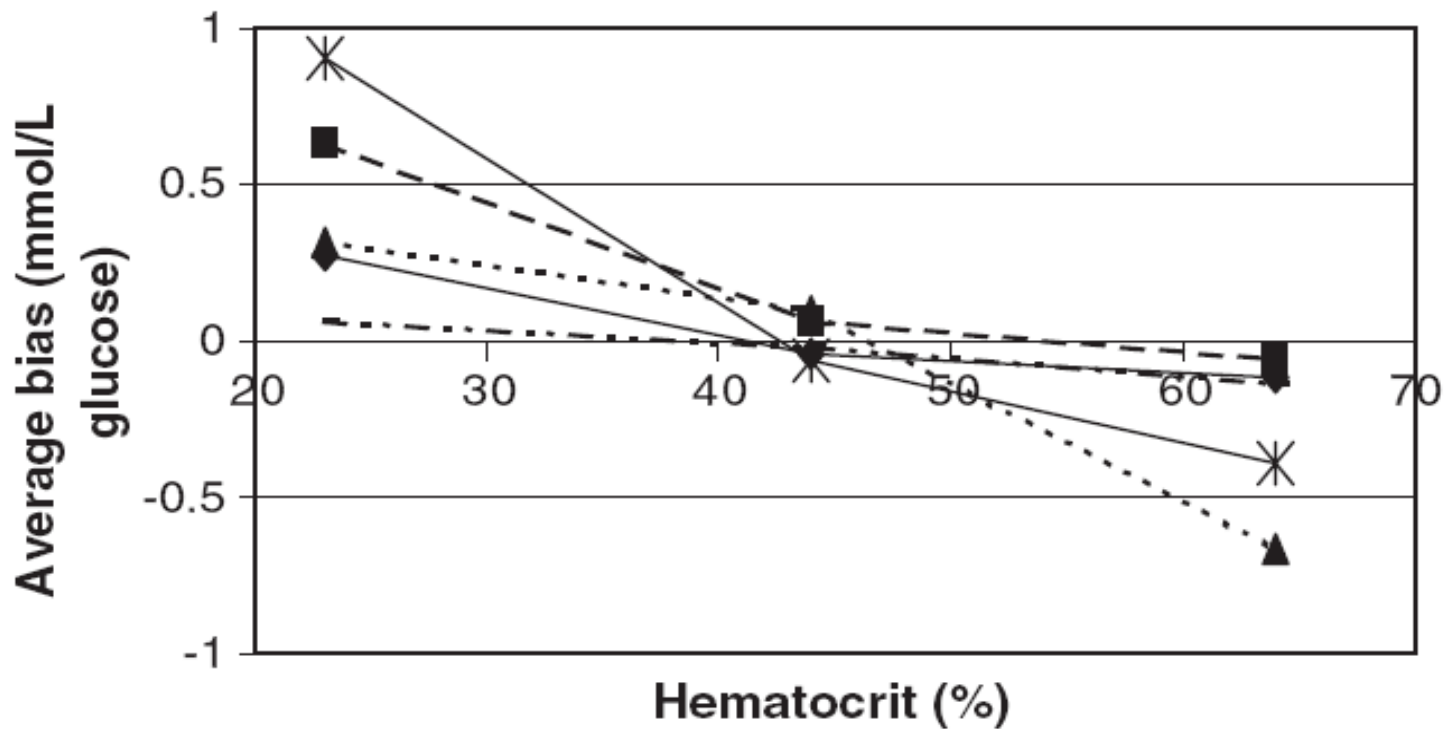
- Glucose Method is Provided in Only 10 of the 27 Studies in the JAMA Meta-Analysis
 - 8 were meters
 - 2 were the Van den Berghe studies
 - 17 do not say

JAMA 2008;300:2725

- NICE-SUGAR – Can't Tell!

N Engl J Med 2009;360:1283

Does Anemia Lead to Overestimation of Glucose?



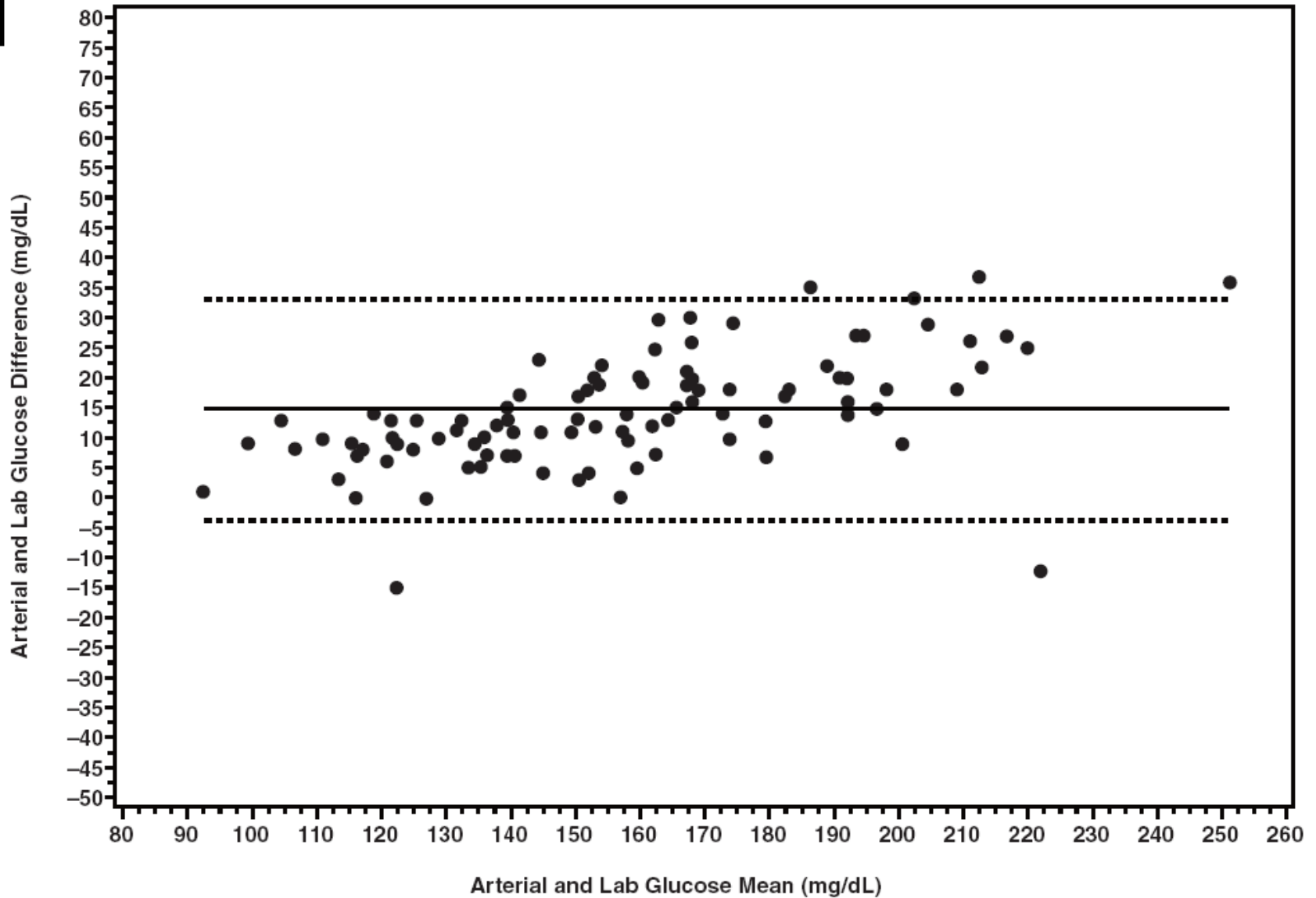
Glucose = 4.3 mmol/L (77 mg/dL)

Sample Type?

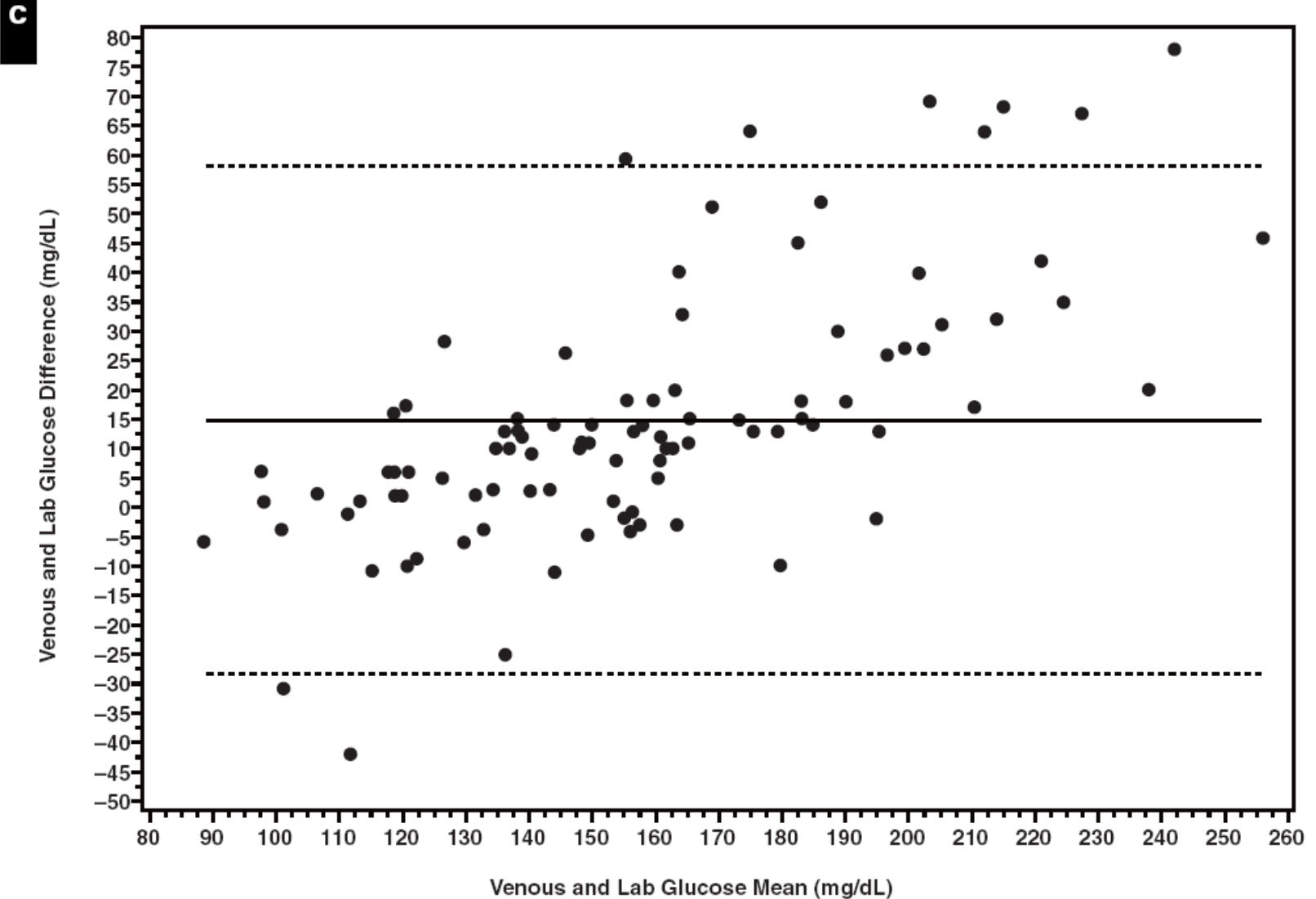
- 20 Cardiovascular Surgery Pts
- IV Insulin
- First five hourly samples
- Art., Ven., and Cap. compared to main lab
- Cap. samples matched well (149 vs. 151 mg/dL)

Arterial vs. Lab

B



Venous vs. Lab



Tight Glycemic Control – Are Glucose Meters Up to The Task?

- They are not for diagnosis

Clin Chem 2009;55:18.

4. Accuracy and Reproducibility

- Allowable Error Criteria
- Where we are Now
- Which Criteria to Use?
- Suggestion for TGC Use

Allowable Error Criteria

CLIA

10% or 6 mg/dL (greater of) – Main Lab/ABG Methods

ADA

Total Analytic Error < 5% **(all values)**

CAP WBG Survey

20% or 12 mg/dL (greater of)

CLIS

20% (> 75 mg/dL); 15 mg/dL (< 75 mg/dL) **(95% of Values)**

ISO 15197

20% (> 75 mg/dL); 15 mg/dL (< 75 mg/dL) **(95% of Values)**

FDA

20% (> 100 mg/dL); 12 mg/dL (< 100 mg/dL) **(95%)**

Clarke Error Grid

Six Home Meters, 1993 - 98

- Hemocue as Reference Method
- RN Performed
- n = 1973

*Frequency of SMBG Measurements for 2 Levels of Accuracy**

Meter	No. of Measurements	Level of Accuracy	
		±10.5% n (%)	±15.5% n (%)
1	425	309 (73)	364 (86)
2	160	97 (61)	137 (86)
3	476	329 (69)	400 (84)
4	784	494 (63)	623 (80)
5	78	47 (60)	66 (85)
6	50	34 (68)	38 (76)

CDC Study of 5 Common Meters

- Single Med Tech Operator
 - 93 subjects, 12 samples obtained (2 each meter and for reference method)
 - “Aged” and “fresh” strips used for total %CV
- Total CVs = 6.3 – 11.3%
- Difference Between Meters Varied With Concentration and Meter Pairs
 - 1 - 32% average differences observed

Four Common Meters

- CVs of 1.4 – 8.7%
 - n = 54, nine health care operators, six replicates
 - Venous whole blood, three concentrations
 - Worst CVs at low glucose (< 60 mg/dL)
- Bias vs. Hexokinase Reference Method
 - Slopes of 0.88, 0.97, 1.00 and 1.12

Which Criteria to Use?

TABLE 5. NUMBER (%) OF SPECIMENS FALLING OUTSIDE VARIOUS CRITERIA FOR THE FOUR METERS

<i>Criteria</i>	<i>Meter A</i>	<i>Meter B</i>	<i>Meter C</i>	<i>Meter D</i>
NCCLS (C30-A) ⁵³	122 (26%)	11 (2.4%)	7 (1.5%)	28 (6.1%)
ADA (1987) ¹⁸	247 (54%)	23 (5.0%)	15 (3.3%)	71 (15%)
ADA (1996) ⁵⁴	423 (92%)	233 (51%)	194 (42%)	299 (65%)
FDA (1998) ²¹	116 (25%)	4 (0.9%)	6 (1.3%)	23 (5.0%)
ISO 15197 (2001) ²²	112 (26%)	11 (2.4%)	7 (1.5%)	25 (5.4%)

TABLE 6. NUMBER (%) OF SPECIMENS FALLING INTO EACH OF THE CATEGORIES OF CLARKE GLUCOSE ERROR GRID ANALYSIS

<i>Zone</i>	<i>Categories</i>	<i>Meter A</i>	<i>Meter B</i>	<i>Meter C</i>	<i>Meter D</i>
A	Accurate	339 (74%)	450 (97.6%)	454 (98%)	435 (94%)
B	No error in treatment	117 (25%)	5 (1.1%)	5 (1%)	22 (5%)
C	Overtreat	1 (0%)	1 (0%)	1 (0%)	1 (0%)
D	Failure to detect	5 (1%)	6 (1.3%)	2 (0%)	4 (1%)
E	Wrong treatment	0 (0%)	0 (0%)	0 (0%)	0 (0%)

CAP 2009 WBG

No. Results	Mean	S.D.	C.V.	Median	Low Value	High Value
243	102.8	7.8	7.6	102	82	123
4407	99.5	5.3	5.3	100	<u>83</u>	116
64	98.2	6.1	6.2	99	84	113
72	113.1	15.8	14.0	119	71	134
26	117.4	3.5	3.0	117	112	125
59	76.4	4.4	5.7	76	68	85
33	74.7	2.1	2.8	75	71	79
21	<u>124.0</u>	8.2	6.6	127	104	136
3550	107.9	6.5	6.0	108	<u>88</u>	128
155	105.3	4.0	3.8	105	95	117
37	76.4	2.4	3.2	77	71	82
30	122.2	4.1	3.4	122	116	134
29	76.6	2.6	3.4	77	72	81
33	76.3	2.9	3.8	76	69	83
2198	<u>78.2</u>	3.7	4.7	78	67	89
8670	78.4	3.8	4.8	78	<u>67</u>	90

- **BJH Glucose Meters**

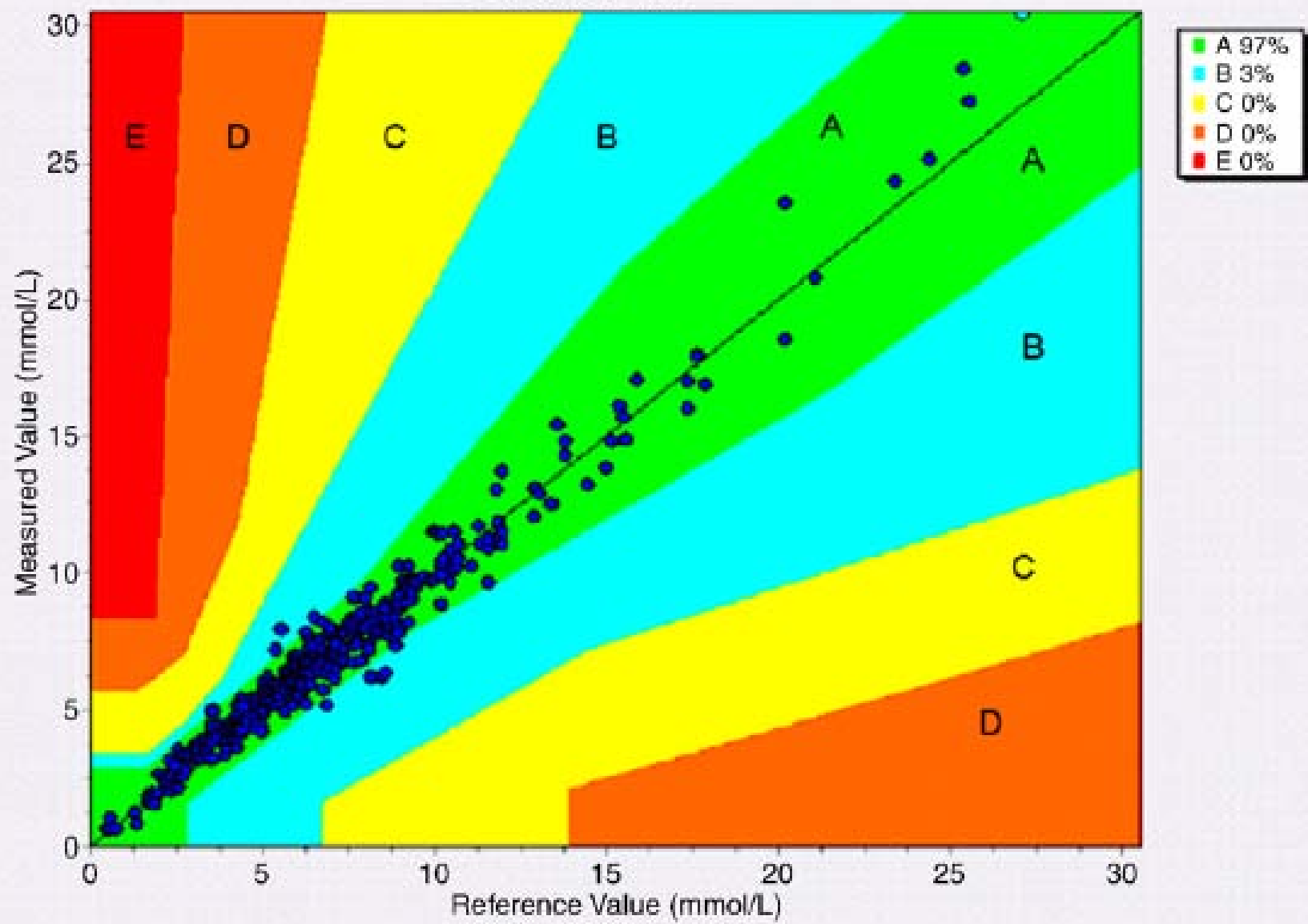
- One sample performed on 40 meters
- Mean value = 167
- Range: 153 – 210
- %CV = 8.4%
- **95% C.I. = 139 - 195**

Newer Meter

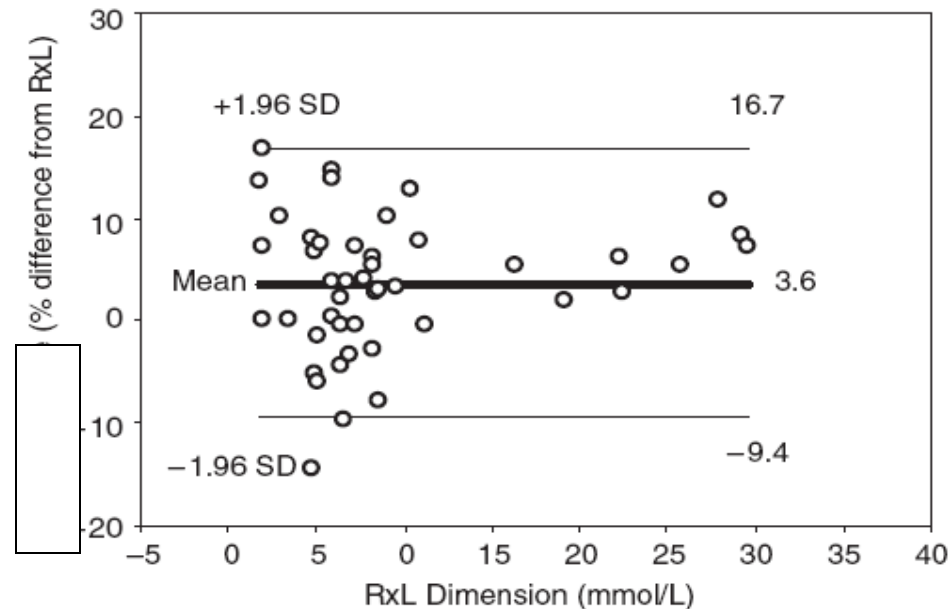
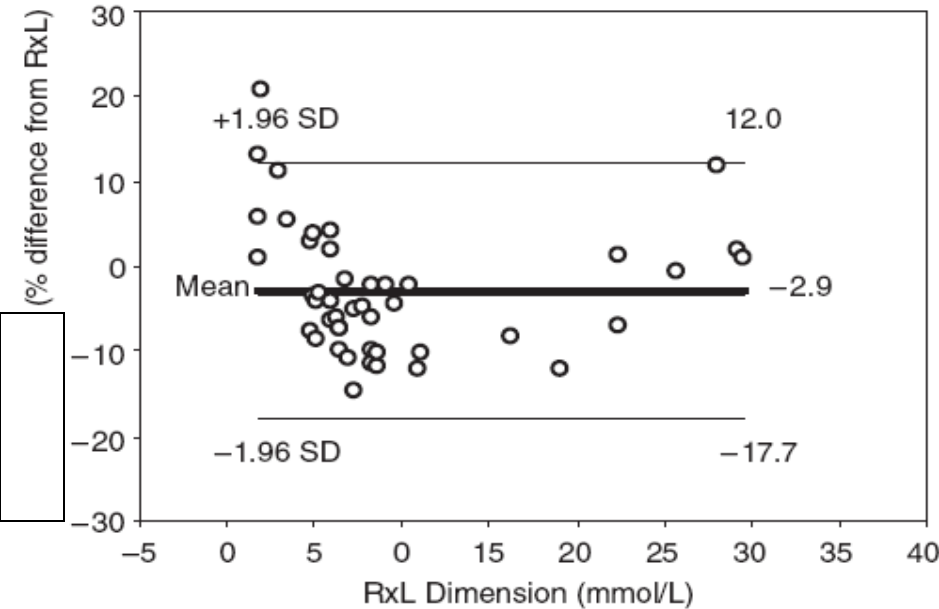
- 6 “units”, 20 nurses
- Precision
 - Venous and Arterial WB, aqueous
 - All CVs < 5%
- No effects from extreme hematocrits
- No interference from reducing substances
- $y = 1.01x + 1.8$ (n = 386)

a

Consensus Grid



Two Newer Meters



- Imprecision 2.2 – 3.2%
- Small Bias, most within 10% (n = 45)

Biologic Variability-Based Criteria

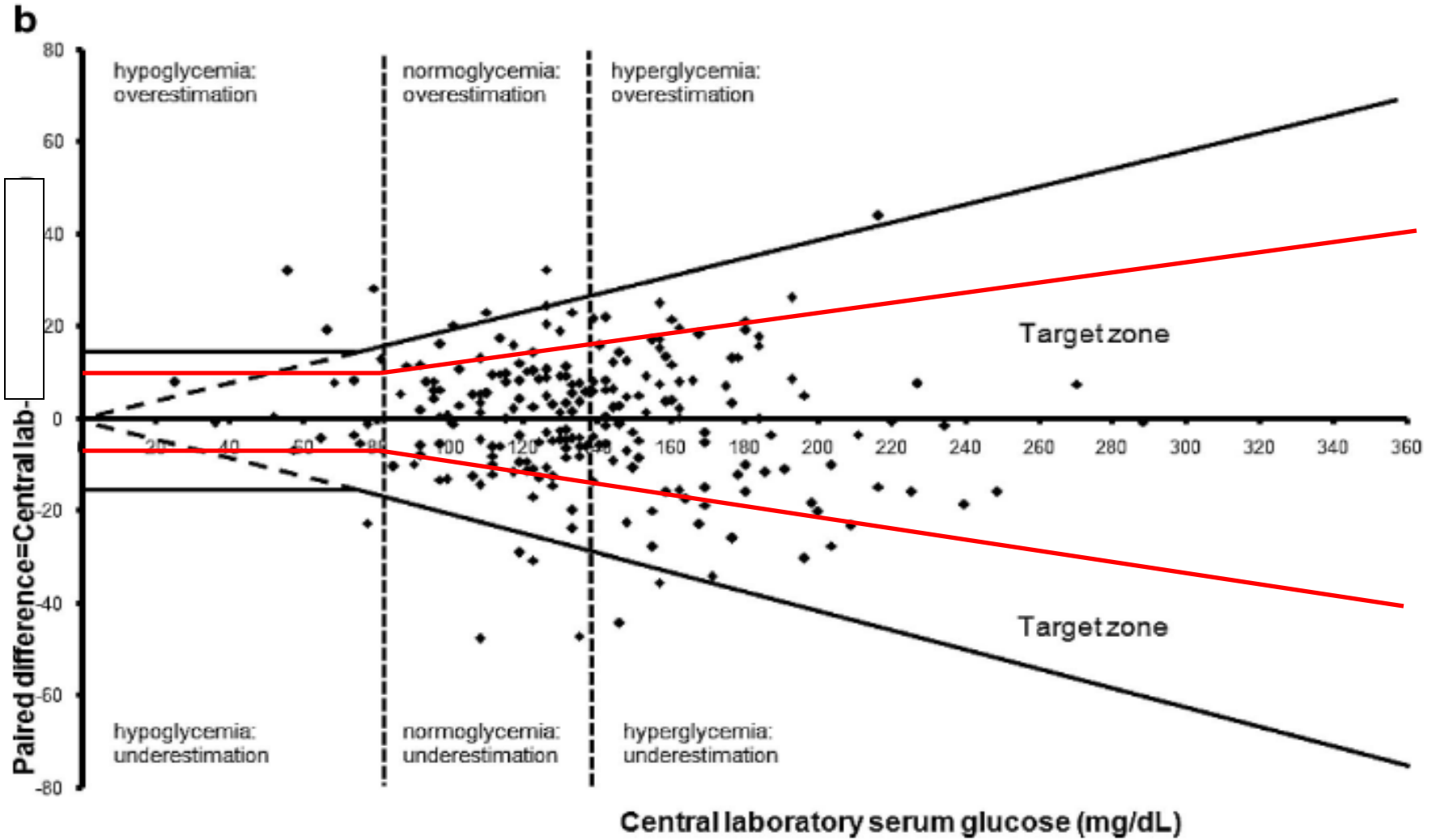
- Fasting Glucose
 - Within Subject % $CV_w = 6.5\%$
 - Between Subject % $CV_b = 7.7\%$
- Desirable Quality Specs
 - Precision $< 0.5 CV_w$
 - Bias $< 0.25 (CV_w^2 + CV_b^2)^{1/2}$
 - TAE < 1.65 Imprecision + Bias ($p < 0.05$)
- For Glucose TAE would be $\leq 7.9\%$

Ricos, Scand J Clin Lab Invest 1999;59:491

Fraser CG, Crit Rev Lab Sci 1989;27:409

Suggestion

- 10% or 10 mg/dL (< 100 mg/dL) seems consistent with newer meters and with biologic based criteria
- A new TGC Error Grid? (*J Diab Sci Tech* 2010:75)
 - 95% of values within 10% or 10 mg/dL (A)
 - 99 % of values within 15% or 12 mg/dL (B)
 - <1% of values exceed 20% or 15 mg/dL (C)



Summary

- Newer Meters Appear to be Getting Better
 - Imprecision often $< 5\%$
 - Bias improving
- Clearly can do better than current ISO/CLSI criteria
- Can they meet 10 – 15% allowable error?
- What About -
 - Interferences?
 - Sample Type?
 - User Error?
- Patients receiving a dangerous drug should have best analytic method available
- There are alternatives to meters if necessary (cost?)