ESTABLISHING ACCEPTABLE RISK

IN POINT OF CARE TESTING OF BLOOD GLUCOSE AT THE BEDSIDE

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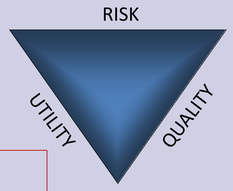


1. Describe how to prioritize between Risk, Quality, and Utility when implementing Point of Care Testing. 2. Understanding present limitations of reliability of Point of Care Testing at defined Medical Decision Points.
3. Recognize how appropriate validation procedures can mitigate risk in using Point of Care Testing.

SITUATION

Acute care of diabetic patients requires rapid and reliable measurement of blood glucose levels allowing timely response to hypoglycemic[1] and hyperglycemic states. **Point of Care Testing** [**POCT**] blood glucose measurements at the bedside provides a solution. Despite greatly improved reliability of hand held glucose meters, traditional validation procedures do not establish ***Reliability*** and ***Comparability*** at critical **Medical Decision Points** [**MDP**'s] introducing the ***Risk*** for **Systematic Diagnostic Error [SDE]** due to failure to recognize significant hypoglycemia.

PROBLEM

How do we establish ***Reliability*** and ***Comparability*** between individual **POCT** instruments and the laboratory chemical analyzer to reduce the impact of **Systematic Analytical Error**

So as to lay the ground work for establishing:

Acceptable Risk? [2]

SOLUTION

Traditional validation can be supplemented by multiple testing of single samples chosen to match the **MDP**'s used to respond to potentially significant hypoglycemia and hyperglycemia. [3]

Results can be used to measure ***Concordance*** between pairs of **POCT** instruments and between **POCT** instruments and laboratory analyzers . The resulting data can be used to determine if patients should be assigned a single **POCT** instrument and if **POCT** results at **MDP's** should be confirmed in the main laboratory prior to taking action in order to reduce **Systematic Diagnostic Error**.

IMPLEMENTATION

Implementation of concordance measurements can be achieved through a two stage approach:[4]

⇨ Validation prior to implementation of an instrument.
⇨ On going studies at periodic intervals using QC data to maintain:

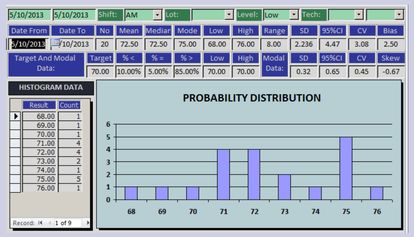
⇨ ***Reliability*** **of single test results at or near MDP's**
⇨ ***Comparability*** **between instruments.**[5]

EXAMPLE CONCORDANCE STUDIES OF TWO POCT INSTRUMENTS[5]

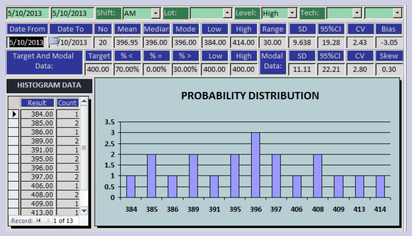
During an validation of 25 Glucose **POCT** instruments in a medium sized hospital seven were selected randomly. Two specimens of adequate volume were adjusted to 70 mg/dl and 400 mg/dl **MDP** Target Values on the laboratory's analyzer. Each **POCT** instrument was tested twenty times in a row with results logged by instrument, date, and time of test allowing for determination of any drift during the within run experiment.

Below are results at both Target Values for two of the instruments tested. Additional statistical analysis was done to estimate bias and imprecision. In this case, results were within run as opposed to between run as generated with QC testing. This means that the CV's shown below are significantly below those that would be achieved during actual use.

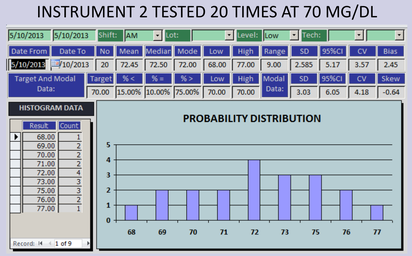
INSTRUMENT 1 TESTED 20 TIMES AT 70 MG/DL



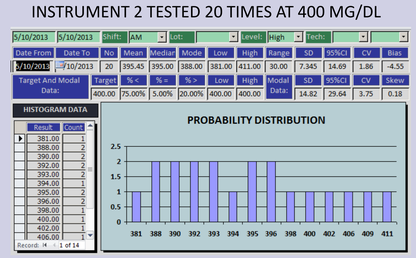
INSTRUMENT 1 TESTED 20 TIMES AT 400 MG/DL



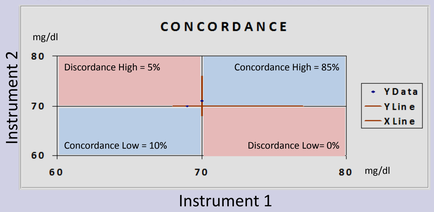
INSTRUMENT 2 TESTED 20 TIMES AT 70 MG/DL



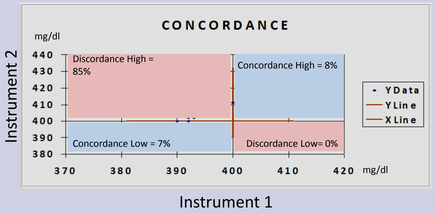
INSTRUMENT 2 TESTED 20 TIMES AT 400 MG/DL



GOOD CONCORDANCE & SIGNIFICANT UPWARD BIAS



POOR CONCORDANCE BUT LESS UPWARD BIAS



PRELIMINARY FINDINGS - SELECTED

Concordance is good at 70 mg/dl but there is a relatively high CV and upward bias.
Concordance is poor at 400 mg/dl but there is relatively low CV and mild upward bias.

This means that, for determining the presence of ***hypoglycemia*** either instrument could be substituted for the other but not for determining the presence of ***hyperglycemia***. In addition, it is clear that the patient should be evaluated for clinical signs an symptoms of hypoglycemia for results between 70 and 80 mg/dl [a grey zone] despite not having reached the MDP of 70 mg/dl.

REFERENCES – SELECTED:
1. Briscoe, VJ., Davis, SN.; **Hypoglycemia in Type 1 and Type 2 Diabetes: Physiology, Pathophysiology, and Management**; Clinical Diabetes, Vol 24 No 3, 2006 Pages 115 – 121.
2. Nichols, JH.; EP23: **Laboratory Quality Control Based on Risk Management**; Clinical Laboratory Standards Institute 1st Ed 2011
3. Bruns, DE., et. al.; **Toward a Checklist for Reporting of Studies of Diagnostic Accuracy of Medical Tests;** Clinical Chemistry, Vol 46 No 7 Pages 893-895, 2000.
4. Nichols, JH., et. al.; **Laboratory and Bedside Evaluation of Portable Glucose Meters**; American Journal of Clinical Pathology, American Society for Clinical Pathology, Vol 103 Pages 244-251, 1995.
5. Gusack, MD.; **The Case of High Correlation But Low Reliability in Point of Care Monitoring of Coumadin Therapy**; Point of Care Testing Journal Vol 10 No 4 2011 Pages 167 – 173.
6. Gusack, MD.; **An Automated System to Estimate Reliability of Analytical Laboratory Tests Using MS Access and VBA**; Alpha 20130815.

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COST BENEFIT ANALYSIS

Measuring and publishing reliability information [also known as uncertainty] can help direct the clinician to use **POCT** instruments appropriately in assessing glycemia in hospitalized diabetic patients. This activity can be fully automated requiring little additional administrative overhead from the laboratory.[5]

Publishing ***Reliability*** and ***Concordance*** information can reduce inadvertent errors in assessing patients with potentially life threatening hypoglycemia even when apparent **POCT** results do not reach established **Medical Decision Points**.

EXAMPLE RELIABILITY REPORT FOR A POCT DEVICE

POCT – GLUCOSE – A GUIDE TO SAFE USE IN DIAGNOSIS AND MANAGEMENT OF YOUR PATIENTS

==========TECHNICAL CONSIDERATIONS WHEN INTERPRETING YOUR PATIENT'S GLUCOSE==========

The technical variability of this glucometer could affect your patient's apparent glycemic test results
Based on our Validation and QC data the following should be considered before acting on any one test result

STATISTIC	CALCULATION	MDP = 70 MG/DL	MDP = 400 MG/DL
BIAS	MDP – Mean Test Result	+2.5 mg/dl	-3.00 mg/dl
IMPRECISION	CV = 100 x (SD/Mean)	3.0%	2.50%
IMPRECISION	95% CI = 1.96 x SD	±4.5 mg/dl	±19.0 mg/dl
ACTUAL RANGE	BIAS ± 95% CI	-2.0 mg/dl to + 7.0 mg/dl	-22 mg/dl to + 16.00 mg/dl

	MDP = 70 MG/DL	
AS MUCH AS 7.0 MG/DL BELOW REPORTED GLUCOSE VALUE	SAME AS REPORTED GLUCOSE VALUE	AS MUCH AS 2.0 MG/DL ABOVE REPORTED GLUCOSE VALUE
85% OF THE TIME	5% OF THE TIME	10% OF THE TIME

	MDP = 400 MG/DL	
AS MUCH AS 16.0 MG/DL BELOW REPORTED GLUCOSE VALUE	SAME AS REPORTED GLUCOSE VALUE	AS MUCH AS 22.0 MG/DL ABOVE REPORTED GLUCOSE VALUE
30% OF THE TIME	0% OF THE TIME	70% OF THE TIME

- Your patient's actual glucose will often lie significantly below 70 mg/dl when it is within 70 – 80 mg/dl
- A difference less than 9.0 mg/dl between any two test results at 70 mg/dl is probably not clinically significant
- A difference less than 38.0 mg/dl between any two test results at 400 mg/dl is probably not clinically significant

TEST LIMITATIONS

- Single Glucose results do not establish whether the patient's plasma levels are rising or falling and how rapidly.
- Single Glucose results will not identify relative hypoglycemia due to rapid fall in plasma levels over short time periods

WARNINGS

- Delay of treatment of a single Glucose results near but above the MDP of 70 mg/dl risks a hypoglycemic event.

RECOMMENDATIONS

- Confirm significantly elevated Glucose values in the laboratory before starting aggressive insulin therapy.
- Do not delay treatment of symptomatic hypoglycemia even when results do not reach the **MDP.**

CONCLUSION

Judicious use of validation and QC data can provide valuable estimates of ***Reliability*** and ***Comparability*** of **POCT** instruments upon which clinicians can better establish levels of

Acceptable Risk

Other critical issues include but are not limited to determining the most important adverse outcomes, their **Frequency**, **Severity**, and **Perception** of cost, combined with knowledge of maximum sensitivity and specificity of diagnostic methods.