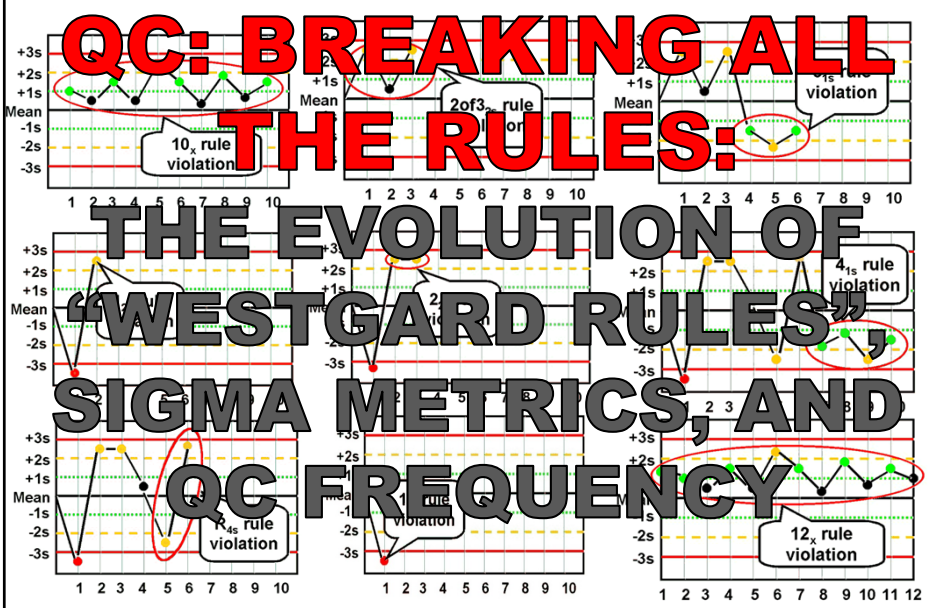
QC: BREAKING ALL THE RULES: THE EVOLUTION OF "WESTGARD RULES", SIGMA METRICS, AND QC FREQUENCY



STEN WESTGARD, WESTGARD QC

1

WESTGARD QC

HOW DO WE IMPROVE HEALTHCARE?

- **Recognize where we are**
  - QC skill deficits
  - Manufacturer failures
- **Adopt tools for assessment and improvement**
  - Six Sigma Equation
  - Method Decision Chart
  - OPSpecs chart / Westgard Sigma Rules
- **See the impact of using these tools**
  - Global benchmarking
  - Individual case studies
  - Savings of time, money, and improved patient outcomes

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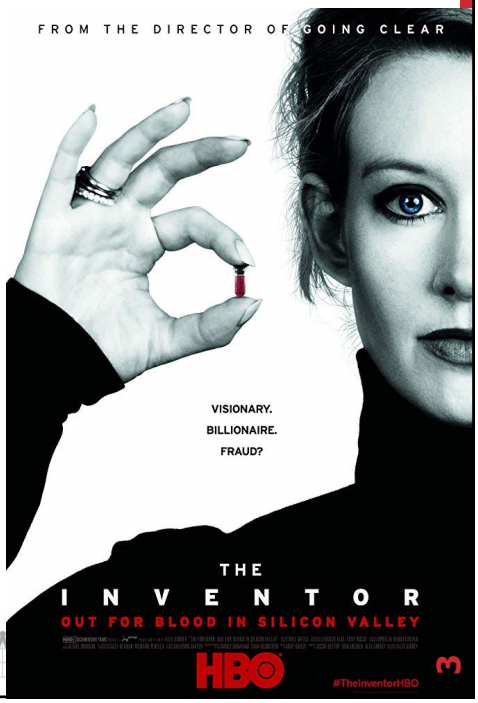
2

WESTGARD QC

"I spent many long nights independently doing training on QC systems and Westgard Rules when I worked at Theranos.

"Before reporting Theranos… to CMS, I tried to collect and present lots of evidence on how our QC systems were severely failing and it wasn't just my opinion, but violated basic QC procedures, Westgard Rules, and was far from Six Sigma laboratory principles. I was fortunate to be a young scientist who stumbled upon all the content you developed and was able to leverage it to understand how a company was endangering patients…"

-- Erika Cheung



3

WESTGARD QC

REAL WORLD EXAMPLE SHOWS NEED FOR IMPROVED SQC PLANNING

Survey Report: "Quality Control practices for chemistry and immunochemistry in a cohort of 21 large academic medical centers."

- Rosenbaum MW, Flood JG,… Lewandrowski KB
- Am J Clin Pathol 2018 (August);150:96-104
- *"We observed significant variation and unexpected similarities in practice across laboratories, including QC frequency, cutoffs, number of levels analyzed, and other features."*

MGH 1811 · Stanford Medicine · Mayo Clinic · Johns Hopkins Medicine · The Johns Hopkins Hospital · NYP · Cleveland Clinic · Northwestern Memorial Hospital · NYU Langone Medical Center · UCSF Health

4

WESTGARD QC "TOP 21" MEDICAL CENTERS QC PRACTICES

"There was wide variation in the frequency of running CHEM QC, ranging from daily (n=3, 14%) to every 2 hours (N=2, 10%);

- Intermediate intervals included every 4 hours (n=3, 14%), 6 hours (n=1, 5%), 8 hours (n=6, 29%), and 12 hours (n=6, 29%).

"Most hospitals used a QC rule of 2 SD (n=16, 76%)…"

MGH 1811 · Stanford Medicine · Mayo Clinic · Johns Hopkins Medicine · The Johns Hopkins Hospital · NYP · NYU Langone Medical Center · Cleveland Clinic · Northwestern Memorial Hospital · UCSF Health

5

"WESTGARD RULES"

THE ORIGINAL

THE FIRST INNOVATION IN QUALITY CONTROL FOR LABORATORIES

6

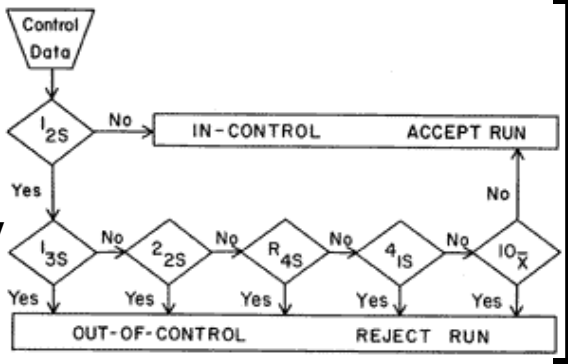
WESTGARD QC

THE ORIGINAL "WESTGARD RULES"

Maximize error detection from few measurements

Attempt to balance work with practicality

Classic laboratory workaround



Westgard JO, Barry PL, Hunt MR, Groth T. A multi-rule Shewhart chart for quality control in clinical chemistry. Clin Chem 1981;27:493-501.

https://www.westgard.com/mltirule.htm
https://www.westgard.com/westgard-rules.htm

QC

7

"WESTGARD RULES"

THE PRESENT

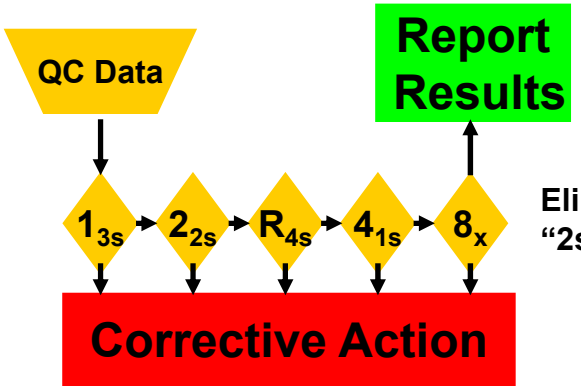
Are we weary and wary of the 2s "warning rule"?

OPTIMIZED MULTIRULES FOR TODAY'S INFORMATICS

8

WESTGARD QC

MODERN MULTIRULE QC PROCEDURE (N=2)



Eliminate the "2s Warning" rule

WWQC

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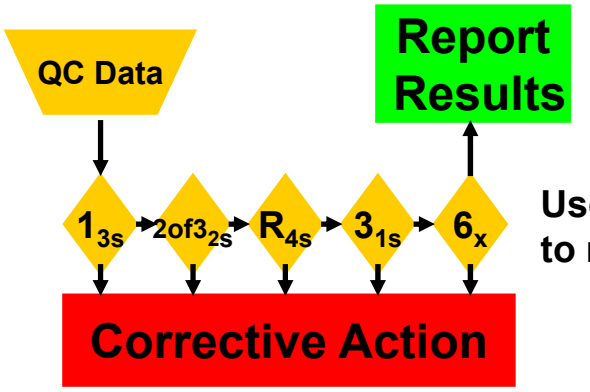
WESTGARD QC

MODERN MULTIRULE QC PROCEDURE (N=3)



Use rules suited to multiples of 3

WWQC

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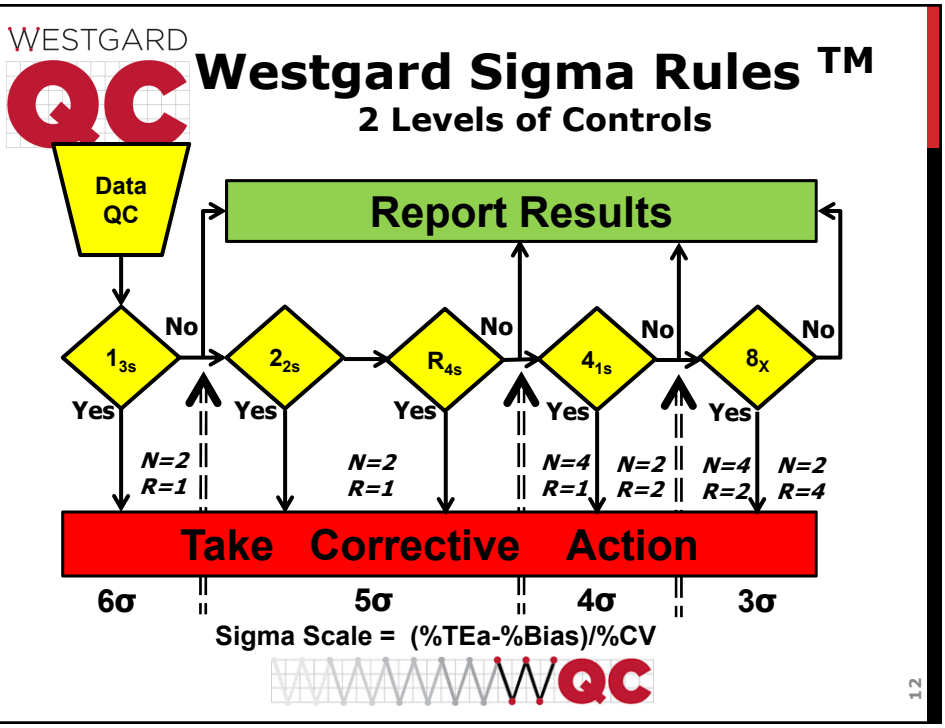
“WESTGARD RULES”

THE FUTURE

SIX SIGMA QUALITY INTEGRATED INTO QUALITY ASSESSMENT AND CONTROL

11



WESTGARD QC

SIX SIGMA: TELLS US WE HAVE A TARGET TO HIT

Defects Per Million (DPM)

Scale of 0 to 6 (Sigma short-term scale)

2

3 **3 Sigma is minimum for any business or manufacturing process** (66,807 dpm)

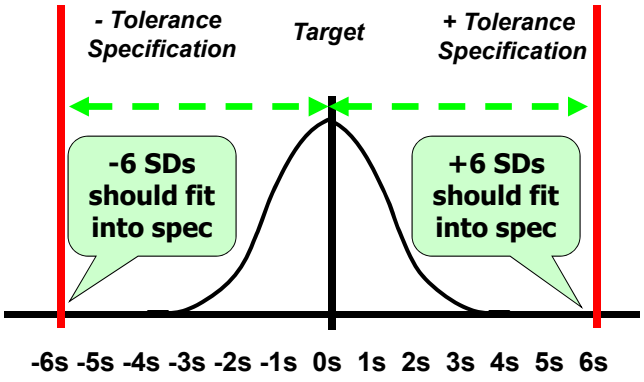
4

5

6 **World Class Performance (3.4 DPM)**

WESTGARD QC

WHAT DOES SIX SIGMA ACTUALLY MEAN?



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WESTGARD QC

TEST QUALITY REQUIREMENTS: WHERE TO FIND THEM

Total Allowable Errors (TEa)

- **CLIA**
- **PT/EQA groups**
- **RCPA**
- **Rilibak**
- **Biologic Variation Database "Ricos Goals"**
- **EFLM goals**
- ***SIGMA VP PROGRAM***

http://www.westgard.com/biodatabase1.htm

	Analyte	Biological Variation		Desirable specification		
		CVw	CVg	I(%)	B(%)	TE(%)
S-	11-Desoxycortisol	21.3	31.5	10.7	9.5	27.1
S-	17-Hydroxyprogesterone	19.6	50.4	9.8	13.5	29.7
U-	4-hydroxy-3-methoximandelate (VMA)	22.2	47.0	11.1	13.0	31.3
S-	5' Nucleotidase	23.2	19.9	11.6	7.6	26.8
U-	5'-Hydroxyindolacetate, concentration	20.3	33.2	10.2	9.7	26.5
S-	a1-Acid Glycoprotein	11.3	24.9	5.7	6.8	16.2
S-	a1-Antichymotrypsin	13.5	18.3	6.8	5.7	16.8
S-	a1-Antitrypsin	5.9	16.3	3.0	4.3	9.2
S-	a1-Globulins	11.4	22.6	5.7	6.3	15.7
U-	a1-Microglobulin, concentration, first morning	33.0	58.0	16.5	16.7	43.9
P-	a2-Antiplasmin	6.2	---	3.1	---	---
S-	a2-Globulins	10.3	12.7	5.2	4.1	12.6
S-	a2-Macroglobulin	3.4	18.7	1.7	4.8	7.6
U-	a2-Microglobulin output, first morning	29.0	32.0	14.5	10.8	34.7
P-	a-aminobutryic acid	24.7	32.3	12.4	10.2	30.5
S-	a-Amylase	8.7	28.3	4.4	7.4	14.6
S-	a-Amylase (pancreatic)	11.7	29.9	5.9	8.0	17.7
U-	a-Amylase (pancreatic)	39.0	78.4	19.5	21.9	54.1
U-	a-Amylase concentration, random	94.0	46.0	47.0	26.2	103.7
P-	a-Carotene	24.0	65.0	12.0	17.3	37.1
S-	a-Carotene	48.0	65.0	24.0	20.2	59.8
S-	a-Fetoprotein(non hepatic carcinoma)	12.2	45.6	6.1	11.8	21.9
S-	a-Tocopherol	13.8	15.0	6.9	5.1	16.5

Quality Requirements

- Minimum analytical quality requirements
- Minimum Specifications from Biological Variation database
- Optimal Biological Variation database specifications
- Rilibak - German Guidelines for Quality
- Biological Variation in Patients with Disease
- CLIA Requirements for Analytical Quality
- Clinical Quality Requirements
- European Biologic Goals
- Biological Variation Database references
- Biological Variation Database reference list
- RCPA (Australasian) Quality Requirements
- Quality Requirements for Dogs, Cats, and Horses?
- 1999 Stockholm Consensus Statement

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WESTGARD QC

HOW DO WE MEASURE (SIX) SIGMA PERFORMANCE?

Measure Variation – Use existing data

- Can we measure imprecision (CV)?
- Can we measure inaccuracy (bias)?
- ***Capture this data at critical medical decision levels***

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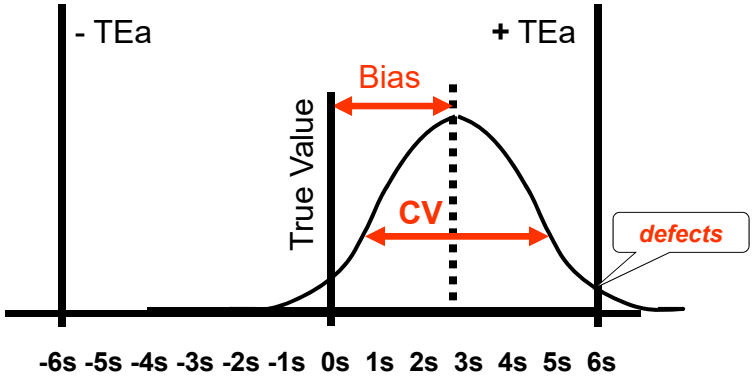
WESTGARD QC

SIGMA METRIC EQUATION FOR ANALYTICAL PROCESS PERFORMANCE

Sigma-metric = (TE_a – Bias)/CV



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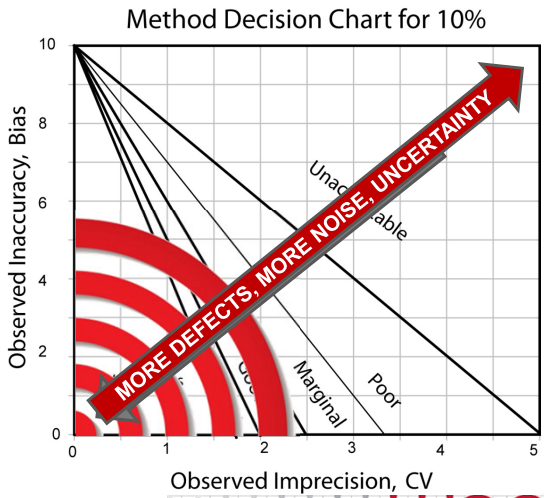
WESTGARD QC

VISUAL DISPLAY OF SIGMA-METRICS: METHOD DECISION CHART



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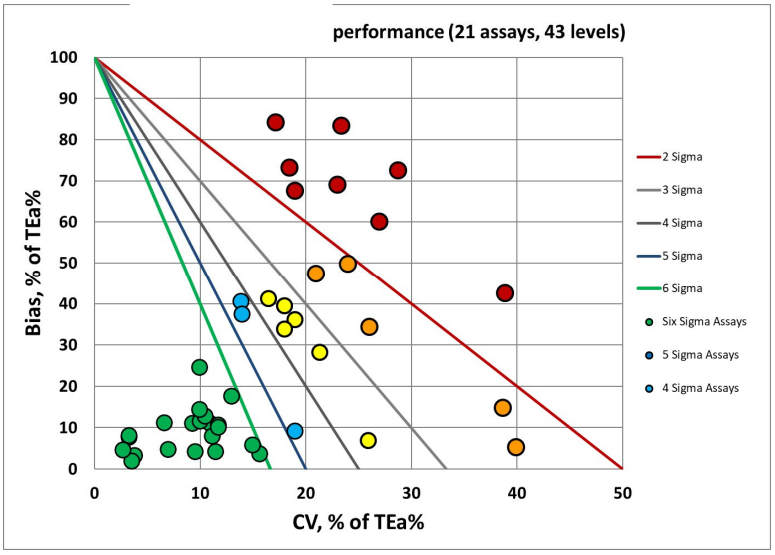
WESTGARD QC

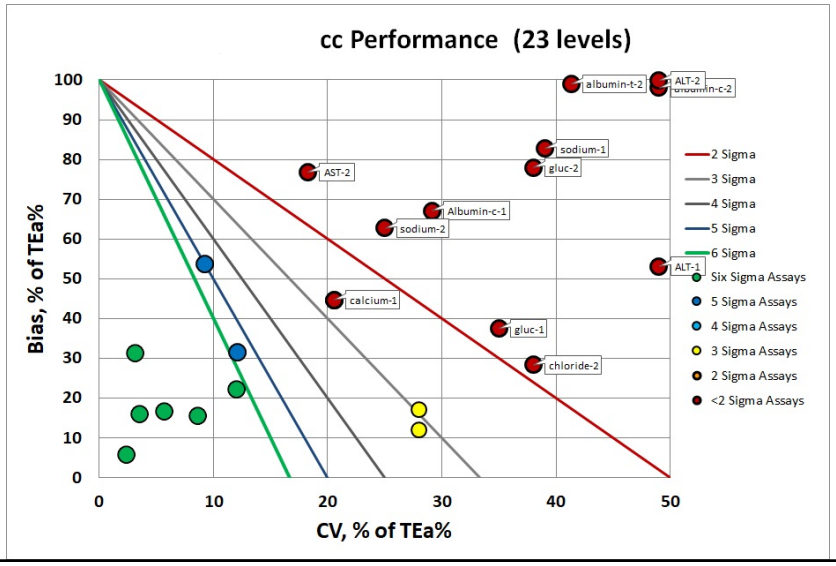
FROM PACKAGE INSERT DATA!



19

WESTGARD QC

PERFORMANCE AND SUITABILITY OF Y OPEN CLINICAL CHEMISTRY ANALYZER ANNE-MARIE DUPUY, MAELLE PLAWECKI, ANNE-SOPHIE BARGNOUX, STEPHANIE BADIOU, MARTINE DELAGE, MANUELA LOTIERZO, JEAN-PAUL CRISTOL.ANN CLIN LAB SCI. 2018 JUL;48(4):511-516.



20

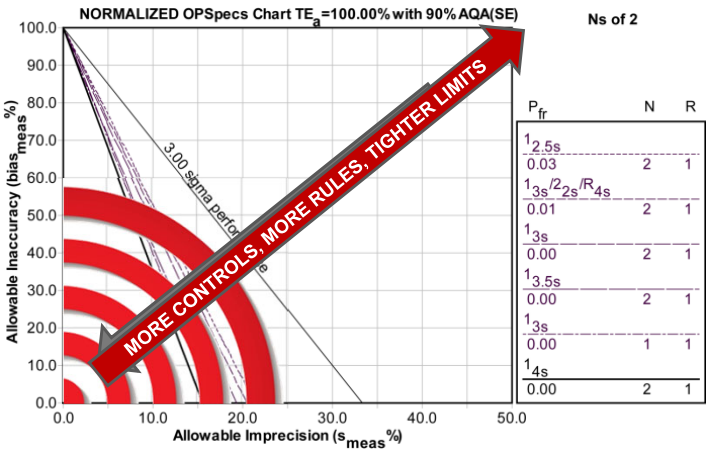
WHY ISN'T THE FDA (OR SOMEONE) PROTECTING THE PATIENT FROM POOR QUALITY?

"Conclusion 7-1. The 510(k) clearance process is not intended to evaluate the safety and effectiveness of medical devices with some exceptions. The 510(k) process cannot be transformed into a premarket evaluation of safety and effectiveness as long as the standard for clearance is substantial equivalance to any previously cleared device."

Institute of Medicine 2011: Medical Devices and the Public's health: the FDA 510(k) Clearance Process at 35 years, prepublication copy

21

CHOOSING QC RULES: THE OPSPECS CHART

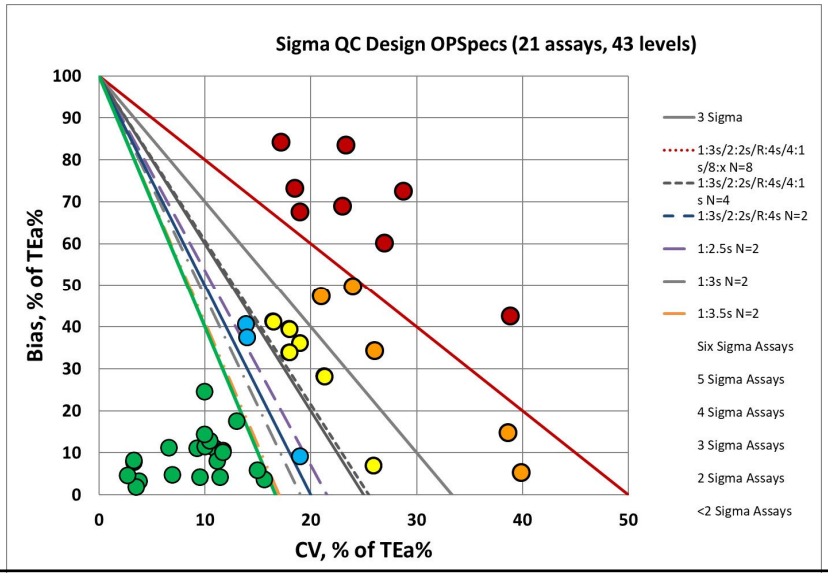


Free download at http://www.westgard.com/downloads/

22

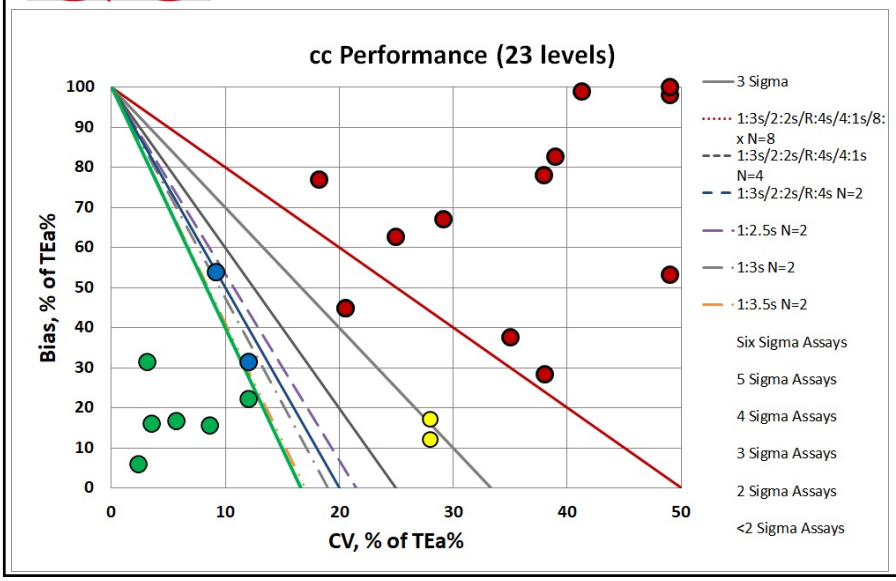
WESTGARD QC

FROM PACKAGE INSERT

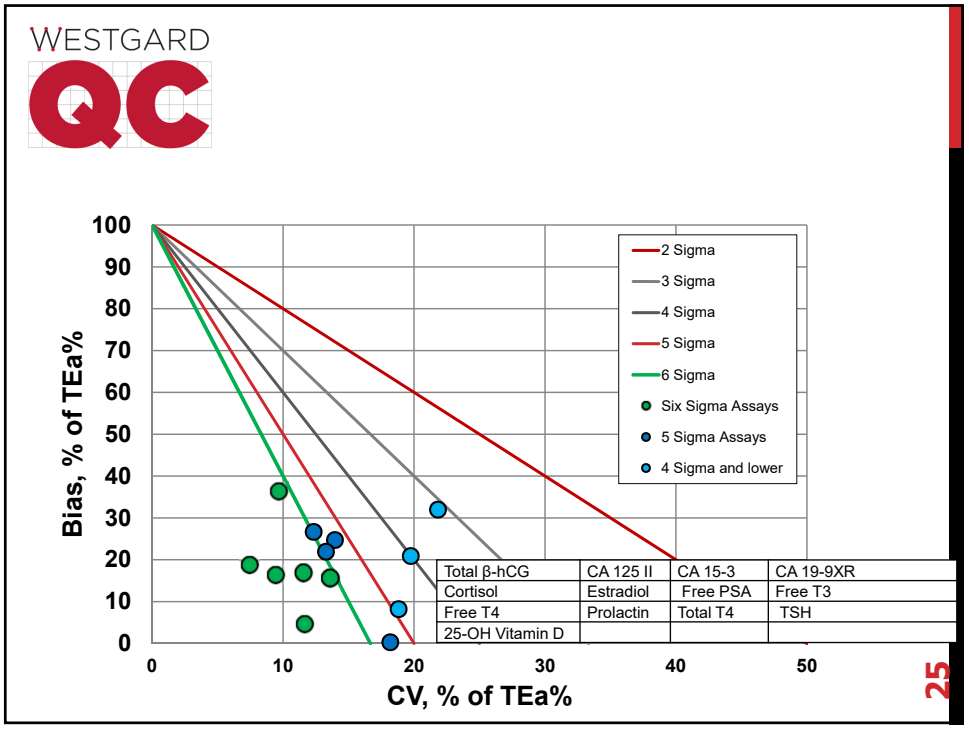


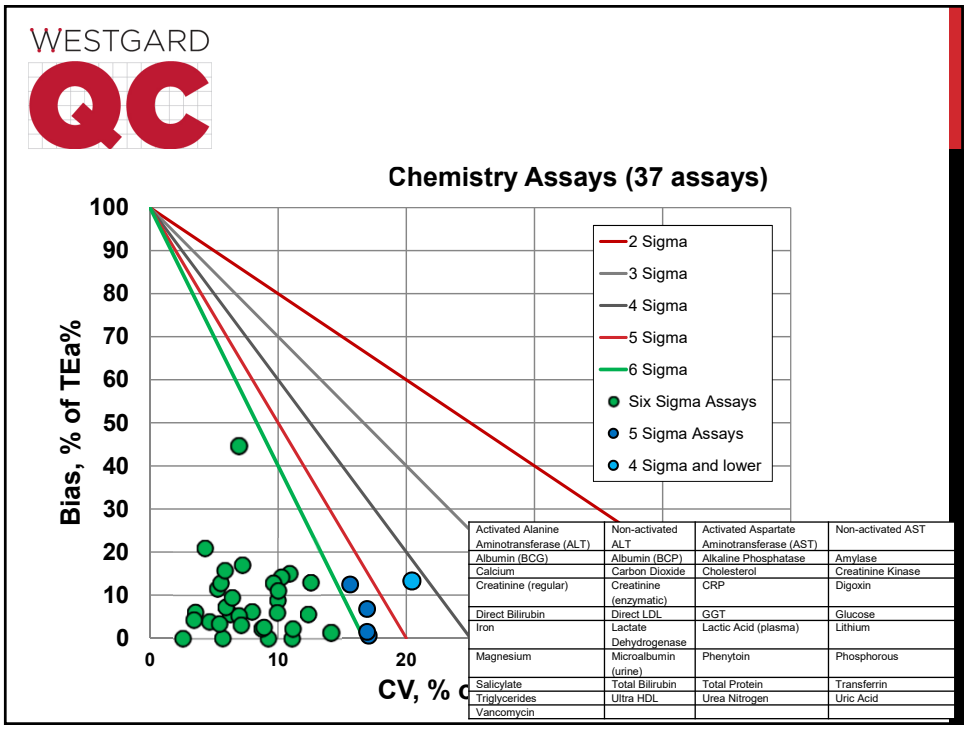
23

WESTGARD QC



24


WESTGARD
QC
Bias, % of TEa%
CV, % of TEa%
2 Sigma
3 Sigma
4 Sigma
5 Sigma
6 Sigma
Six Sigma Assays
5 Sigma Assays
4 Sigma and lower
Total β-hCG
CA 125 II
CA 15-3
CA 19-9XR
Cortisol
Estradiol
Free PSA
Free T3
Free T4
Prolactin
Total T4
TSH
25-OH Vitamin D


WESTGARD
QC
Chemistry Assays (37 assays)
Bias, % of TEa%
CV, % o
2 Sigma
3 Sigma
4 Sigma
5 Sigma
6 Sigma
Six Sigma Assays
5 Sigma Assays
4 Sigma and lower
Activated Alanine Aminotransferase (ALT)
Non-activated ALT
Activated Aspartate Aminotransferase (AST)
Non-activated AST
Albumin (BCG)
Albumin (BCP)
Alkaline Phosphatase
Amylase
Calcium
Carbon Dioxide
Cholesterol
Creatinine Kinase
Creatinine (regular)
Creatinine (enzymatic)
CRP
Digoxin
Direct Bilirubin
Direct LDL
GGT
Glucose
Iron
Lactate Dehydrogenase
Lactic Acid (plasma)
Lithium
Magnesium
Microalbumin (urine)
Phenytoin
Phosphorous
Salicylate
Total Bilirubin
Total Protein
Transferrin
Triglycerides
Ultra HDL
Urea Nitrogen
Uric Acid
Vancomycin

QC FREQUENCY

RUN LENGTH

CAN WE DEVELOP A DATA-DRIVEN WAY TO DETERMINE QC FREQUENCY?

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WESTGARD QC

HOW DO WE CURRENTLY DETERMINE QC FREQUENCY?

Planet-based
QC Frequency:
Once per 24 hours

LUNACY:
Once per month
QC Frequency

Personnel-based
(staff)
QC Frequency:
Once per shift
2-3 / day

OUR GOAL:
Patient-based
Performance-base
QC Frequency

WQC

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WE CAN CHOOSE METHODS, QC RULES, AND CONTROLS: NOW HOW ABOUT RUN LENGTH?

Curt Parvin (of Bio-Rad) concepts

- Ref: Parvin CA. Assessing the impact of the frequency of Quality Control testing on the quality of reported patient results. Clin Chem 2008;54:2049-54.
- **Max E(Nuf)** [maximum number of expected unacceptable patient results] seeks to find the point at which the *maximum* risk to the patient is *minimized*. Usually set at 1, so that only 1 patient is impacted by an analytical error.

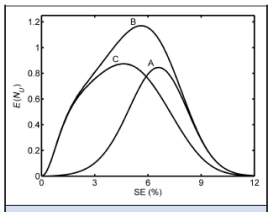

Fig. 2. The expected increase in the number of unacceptable patient results reported, $E(N_U)$, as a function of the magnitude of a systematic out-of-control error condition, SE, given as a percentage of the true concentration.
Curves are labeled to match the corresponding cases in Fig. 1. In all cases a $\bar{x}_{1.5ES}/s_{2.8S}$ QC rule is evaluated with 2 QC samples per batch (per QC event) and 50 patient specimens per batch (between QC events).

error conditions. The maximum value attained by $E(N_U)$ corresponds to the worst-case situation for the

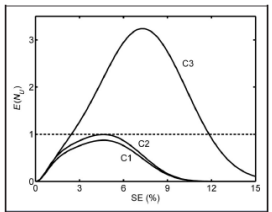

Fig. 3. The expected increase in the number of unacceptable patient results reported, $E(N_U)$, as a function of the magnitude of a systematic out-of-control error condition for different QC utilization rates assuming a continuous-mode testing process with bracketed QC.
Curves C1 and C2 reflect a $\bar{x}_{1.5ES}/s_{2.8S}$ QC rule with 2 QC samples per QC event. For curve C1, 50 patient specimens are evaluated between QC events, and for curve C2, 57 patient specimens are evaluated between QC events. Curve C3 represents a $1_{2.5S}$ QC rule with 1 QC sample measured at each QC event and 50 patient specimens evaluated between QC events. The false-rejection probability of the QC rules is 0.01 in all cases.

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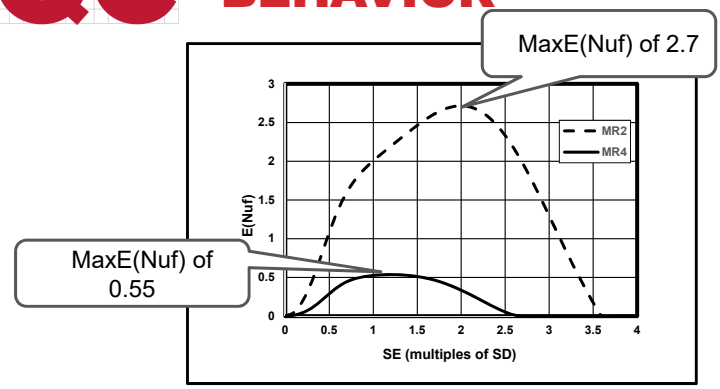
EXPECTED SQC BEHAVIOR



Small errors difficult to detect, so E(Nuf) increases

Large errors readily detected by SQC, E(Nuf) decreases

Leads to a maximum that is the worst case condition

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WESTGARD QC

NEW GRAPHICAL TOOLS NOW AVAILABLE FOR PARVIN'S PATIENT RISK MODEL

Nomograms relating Sigma quality to MaxE(Nuf) for various SQC procedures

- Yago & Alcover. Clin Chem 2016;62:959-965.
  - Single-rule SQC procedures
- Bayat. Clin Chem Lab Med. 2017 Oct 26;55(11):1702-1708
  - Multi-rule SQC procedures
- Bayat, Westgard, & Westgard. J Appl Lab Med 2017
  - Graphical tools to support CLSI C24-Ed4 guidance
- Westgard, Bayat & Westgard. J Diabetes Sci Technol. 2018 Jul;12(4):780-785.
  - Selecting a Risk-Based QC Procedure for a HbA1c Total QC Plan
- Westgard, Hassan & Westgard Clinical Chemistry Feb 2018, 64 (2) 289-296;
  - Planning Risk-Based SQC Schedules for Bracketed Operation of Continuous Production Analyzers

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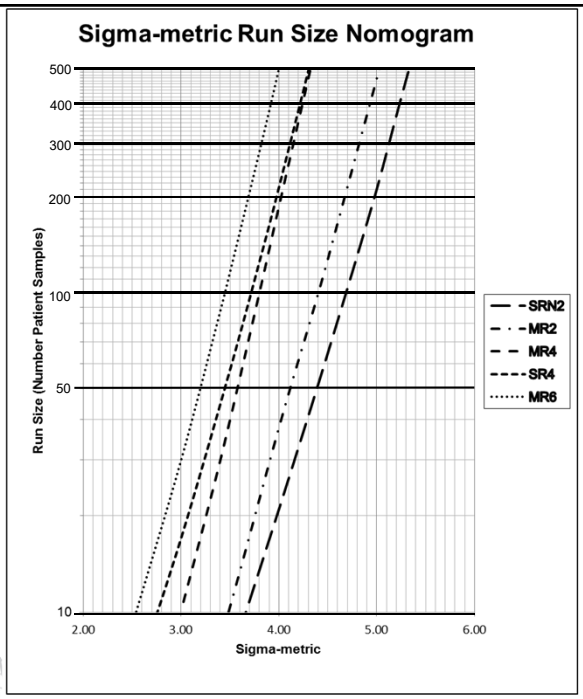
WESTGARD QC

NEWEST WESTGARD TOOL: QUANTITATIVE RISK ASSESSMENT OF TESTING?

SIGMA QC FREQUENCY NOMOGRAM



WESTGARD QC

SIX SIGMA TOOLS FOR QC DESIGN AND FREQUENCY

Sigma-metric	Control Rule	N	QC Frequency	Controls per 1000
Six Sigma	1:3s	2	1 per **1000** patients	2
Five Sigma	1:3s/2:2s/R:4s	2	1 per **450** patients	10
Four Sigma	1:3s/2:2s/R:4s/4:1s	4	1 per **200** patients	20
Three Sigma	1:3s/2:2s/R:4s/4:1s/10:x	8	1 per **45** patients	120
≤ Two Sigma	1:3s/2:2s/R:4s/4:1s/10:x	8,12,??	1 per ?? patients	600

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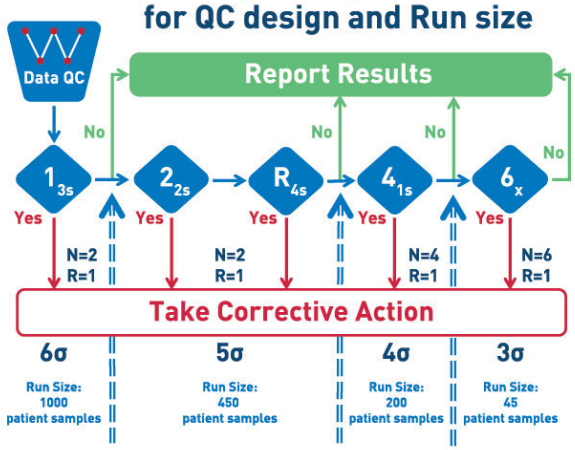
WESTGARD QC

Westgard Sigma Rules® for QC design and Run size



WESTGARDQC Sigma Scale = (%TEa-%Bias)/%CV

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WHAT ARE THE OUTCOMES OF SIX SIGMA IMPLEMENTATION?

Dr. Joseph Litten

First Sigma VP laboratory in the USA

Control Material Savings

- Approximately 45% savings in control material
  - Approximately **$10,000** annual savings

Reagent and Supplies Savings

- Approximately 45% savings in reagents and supplies for running controls
  - Chemistry: **$8,000**

ValleyHealth
Winchester Medical Center

J. Litten and J. Householder; Practical Applications of Sigma Metrics to Evaluate Assay Quality, 2013 AACC Poster.

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ADDITIONAL SAVINGS FROM VALLEY HEALTH SIX SIGMA IMPLEMENTATION: REDUCTIONS IN QC EVENTS

Labor Savings

- Savings from running QC q12 hour versus q8 hour
  - ~$11,000 per year (1 hour per day) 0.175 FTE

- Less investigation of QC failures
  - **Over 85% fewer QC failures to investigate**

2014: ran 185,964 QCs, 5 insts, 70 analytes

- Assays <5 Sigma = 14.7% outlier rate (3,272) [27,336]
- Assays >5 Sigma = 2.1% outlier rate (896) [3,905]
- Assay >6 Sigma = 0.7% outlier rate (836) [1,302]

J. Litten and J. Householder; Practical Applications of Sigma Metrics to Evaluate Assay Quality, 2013 AACC Poster.

WESTGARD QC

STILL MORE SIMILAR OUTCOMES OF SIGMA-METRICS & REDESIGN OF QC

HUKM Hospital, Malaysia

- **14.2% reduction in reagent and control material costs**
- **91% reduction of false rejections**
- **>250 hours saved** (295 to 26) **in troubleshooting false rejects**
- **>$9,000 annual savings in control materials**

ChiMei Hospitals, Tainan, Taiwan

- **>85% in control costs**
- **>$50,000 annual savings in reduced reagent and control consumption**
- **>200 hours saved in troubleshooting** (240 hours down to 35 hours)

Hanita, O. Reducing False Quality Control Failure Rate with Implementation of Six-Sigma Statistical Quality Control Management Program. Poster from 2016 AACC Annual Meeting.

Hung, HY et al. Laboratory Labor and Cost Efficiency Improvement with the Implementation of Six Sigma Statistical Quality Control Management, Poster from Chi Mei Medical Center, Tainan, Taiwan

WQC

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UNDERSTANDING THE IMPACT OF LABORATORY PERFORMANCE ON OUTCOMES IN A SCREENING POPULATION FOR CARDIOVASCULAR DISEASE IN TAIWAN

[1]ChiMei Medical Center, Tainan, Taiwan; [2]Abbott Diagnostics, Wiesbaden, Germany; [3]ChiMei Medical Center, Health Management Center, Tainan, Taiwan

ISPOR 7th Asia-Pacific Conference, 3-6 September 2016, Singapore

Introduction

Risk scores for cardiovascular disease (CVD) events based on laboratory values have been established in primary prevention programs [1]. The performance of laboratory test systems may lead to discordant treatment decisions in some cases. The goal of this study was to investigate the impact of laboratory diagnostic system performance on outcomes in a screening population for CVD in Taiwan.

Methods

Data were collected from 1,396 people (Age >=40 years) enrolled for CVD screening between January and April 2015 in Tainan (Table 1).

A time-to-event microsimulation model was developed (Figure 1). Starting with screening, each individual was classified into risk categories based on observed values for LDL-, HDL-, total cholesterol, and a 10-years CVD risk score. Patients with observed values of LDL≥190mg/L, 70<LDL<190 and a risk score ≥7.5%, and diabetic patients with LDL between 70 and 190 plus a risk score between 5 and 7.5% were referred for treatment. They received lipid lowering drugs thus reducing risk for a CVD event. Individuals not assigned to treatment remained in the "No treatment"- state until the next screening cycle after 1-4 years, the occurrence of a CVD event, or death.

Minimum and optimum test specifications as suggested in literature were tested against a control scenario assuming perfect performances (Table 2).

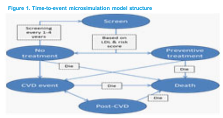
Samples were bootstrapped from the cohort with 100,000 iterations. Model followed a lifetime horizon and a health system perspective. Results were expressed in costs, quality 1-

Strategy	Total -C Bias, %	Total -C CV, %	HDL-C Bias, %	HDL-C CV, %	LDL-C Bias, %	LDL-C CV, %	Source
Mimimun (MIN)	6.2	4.5	8.4	5.5	8.2	5.9	[16,17]
Optimum (OPT)	2.1	1.5	2.8	1.8	2.7	2.9	
Control (CON)	0.0	0.0	0.0	0.0	0.0	0.0	Assumption

Table 1. Characteristics of screening cohort (n=1,396)

Variable	Mean (SE)
Sex (% women)	35.9
Age, years*	52.9 (40-85)
BMI	24.2 (0.1)
Pulse	72.9 (0.3)
BPSys (mmHg)	116.5 (0.5)
BPDia (mmHg)	74.2 (0.3)
GLUC_FAST	100.8 (0.8)
TCHOL (mg/dL)	202.2 (1.0)
HDL-C (mg/dL)	54.7 (0.4)
LDL-C (mg/dL)	132.1 (0.9)

Figure 1. Time-to-event microsimulation model structure



Variable	Value	Distribution	Source
Setting, risk & events			
CVD risk (10 years)	Risk based equations		[1]
In-hospital mortality from stroke	10.1	Beta	[2]
In-hospital mortality from AMI	6.5	Beta	[3]
Mortality from stroke at 1 year, %	12.0	Weibull	[2]
Mortality from MI at 1 year, %	6.0	Weibull	[4]
Mortality (non-CVD)	Age-, sex-specific lifetable	Weibull	[5]
Annual risk for recurrent CVD, %	6.8	Weibull	[4]
Risk reduction under treatment, % (95%CI)	65 (58, 73)	Uniform	[6]
CVD event type (Stroke vs. MI), %	76	Beta	[7]
Smoking prevalence Male, % (95%CI)	31 (28.0, 35.2)	Uniform	[8]
Smoking prevalence Female, % (95%CI)	3.4 (2.8, 4.2)	Uniform	[8]
Laboratory results	Mean from cohort	Normal	Assumption
Screening cycle, years	1 to 4	Uniform	Assumption
Utility			
Baseline	0.936	Beta	[9]
Lipid lowering treatment, Mean (SD)	0.934 (0.001)	Beta	[10]
MI (disutility), Mean (SD)	0.080 (0.048)	Beta	[9]
Stroke (disutility), Mean (SD)	0.242 (0.039)	Beta	[9]
Post MI	0.799 (0.010)	Beta	[9]
Post stroke	0.576 (0.010)	Beta	[9]
Costs, NT$[1,2]			
Screening & visit	5,585	Uniform	[11]
Permanent lipid lowering treatment	15,639	Uniform	[12]
Stroke	74,832	Uniform	[13]
Post-stroke	45,630	Uniform	[14]
MI	189,497	Uniform	[15]
Post MI	82,897	Uniform	[14]
Annual discount rate for costs and utility, %	3.0		

Table 3. Model input assumptions.
(1) All costs adjusted for inflation with a 3% rate to 2015 New Taiwan dollar.(2) A range of ±25% was used to create upper and lower bounds.

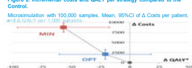
Results

Results in terms of incremental values compared to the control scenario are summarized in Table 2.

Analytical measurement uncertainty caused by CV and bias resulted in discordant management in some cases. The MIN and OPT strategy led to different decisions in 14.1% and 4.1%, respectively. Patients who had not received preventive treatment based on erroneous results had a higher risk for CVD events at an earlier time. The observed strategies showed a small but significantly ... per 1,000 subjects (95%CI 43, 220), whereas a non-significant trend was observed for the OPT performance. Loss in QALY resulting from unnecessary treatment, earlier and increased risk for events, or increased mortality was found to be significant for MIN but not for OPT.

CVD related life-time costs were significantly higher compared to CON for MIN (+NT$ 8,753) and OPT (+NT$ 2,075).

Figure 2. Incremental costs and QALY per strategy compared to the Control.
Microsimulation with 100,000 samples. Mean, 95%CI of Δ Costs per patient, and Δ QALY per 1,000 subjects.



Outcome value	MIN vs. CON Mean	MIN vs. CON (95%CI)	OPT vs. CON Mean	OPT vs. CON 95%CI	MIN vs.OPT Mean	MIN vs.OPT 95%CI
Δ Costs per patient, NT$	8753	(7516; 9990)	2075	(844; 3307)	6678	

The "Minimum" and "Optimum" strategy led to higher costs compared to the Control for 32% and 27%, respectively (Fig. 3).

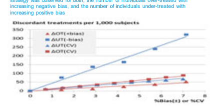
As revealed from a sensitivity analysis, for each increase in percent point of CV, negative or positive bias 22, 43 or 7 individuals per 1,000 screened subjects would be either over- or under-treated compared to the control (Fig. 4, Tab. 3). Negative bias particularly increased the risk for denying preventive treatment, and would affect six times more patients than positive bias.

Incremental costs per patients caused from discordant management decisions and related consequences would accrue to NT$786 (96%CI 734,838), NT$762 (612,912) and NT$699 (668;729) per percent increase in negative bias, positive bias and ...

Variable	Response	Coeff.	(95%CI)	R-Sq, %
(-) bias	ΔUT, per 1,000 subjects	43.3	(40.6; 45.9)	
	ΔCosts, NT$	786	(734;838)	

Figure 3. Distribution of incremental costs (IC) per strategy.

Figure 4. Impact of increasing Bias and CV on discordant treatments.
OT: Over-treated; UT: Under-treated. No significant deviation from the Control strategy was observed for both, the number of individuals over-treated with increasing negative bias, and the number of individuals under-treated with increasing positive bias



Conclusions

- Analytical measurement uncertainty may impose a higher risk for missing prevention opportunities.
- The selection of high performance diagnostic systems plus a strict quality control management in the laboratory conforming to the optimum specification is critical to consistently providing high and efficient quality of care.

Limitations

Results are limited to the information derived from the cohort. Risk scores may not accurately estimate the actual risk. Patient characteristics were sampled from distributions in order to reflect variability and uncertainty. The model assumed a stable lipid status over the time span of the simulation.

Acknowledgement

We thank Roger Low and Sten Westgard for motivation and fruitful discussions.

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WESTGARD QC

HEALTH ECONOMICS OUTCOMES OF OPTIMAL SIX SIGMA QUALITY

HEOR Focus: impact of individual risk categorization and 10-year CVD score. Samples bootstrapped from [historical database] cohort with 100,000 iterations. Model followed a lifetime horizon and a health system perspective.

Tests included:

- LDL
- HDL
- total cholesterol

Variables studied:

- Minimum (low Sigma) test performance
- Optimum (high Sigma) test performance

Outcomes assessed:

- Costs of patient care
- Over- and under-treatment of patient
- Quality-adjusted life-years (QALY) of patient

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WESTGARD QC

HOW SIX SIGMA METHODS IMPACT QC AND PATIENT OUTCOMES

Impact of both CV and Bias on Discordant Management:

Minimum (low Sigma) causes 14.1% of patients to incur discordant health management

Optimum (high Sigma) causes 4.1% of patients to incur discordant health management

LOSS OF LIFE YEARS PER 1,000 PATIENTS:

Minimum (low Sigma) causes 131 Life Years Loss

Optimum (high Sigma) causes no statistically significant loss of life versus perfect scenario.

CVD LIFETIME COSTS PER PATIENT:

MIN (+NT$ 8,753) vs. OPT (+NT$ 2,075).

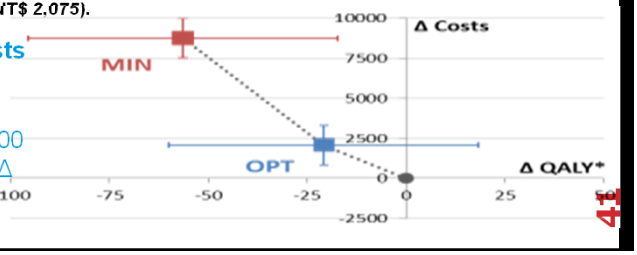

Figure 2. Incremental costs and QALY per strategy compared to the Control. Microsimulation with 100,000 samples. Mean, 95%CI of Δ Costs per patient, and Δ QALY per 1,000 subjects.

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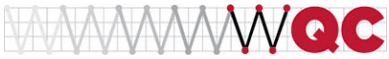
WESTGARD QC

CONCLUSION

QC must evolve with the laboratory and instruments

Six Sigma tools allow the laboratory to

- **Select the RIGHT rules**
- **Run the RIGHT number of controls**
- **Run controls at the RIGHT frequency**
- **Most importantly, enable the RIGHT patient outcomes**



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