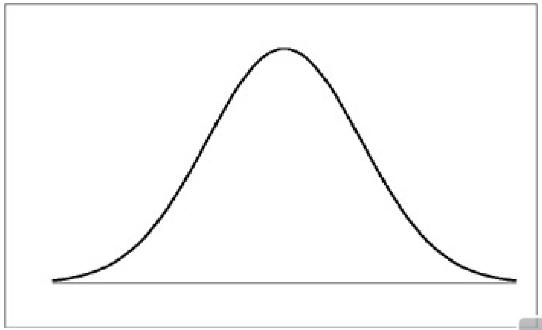
Quality Control and Statistics

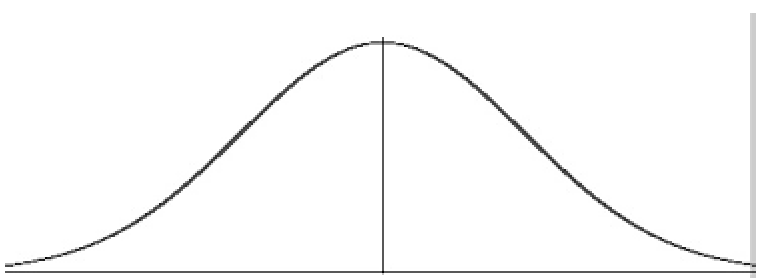
Lab Statistics

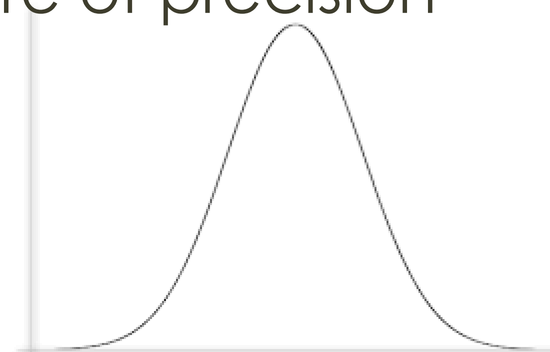
- Medical Lab Scientists rely on data
  - How to interpret numbers
    - "Descriptive Statistics"
  - Mean Median and Mode
    - These numbers describe the overall data set
    - In Gaussian distribution these are all the same



Lab Statistics

- After we know what the data set is, we must know more about how it is spread out
- $\sigma = \sqrt{\frac{\sum(\bar{x}-x_n)^2}{n-1}}$
- CV = $\frac{\sigma}{\bar{x}} \times 100$ Measure of precision





Lab Statistics

- Not every data set will have “normal distribution” about the mean
  - It is important to see when data sets do not fit this curve

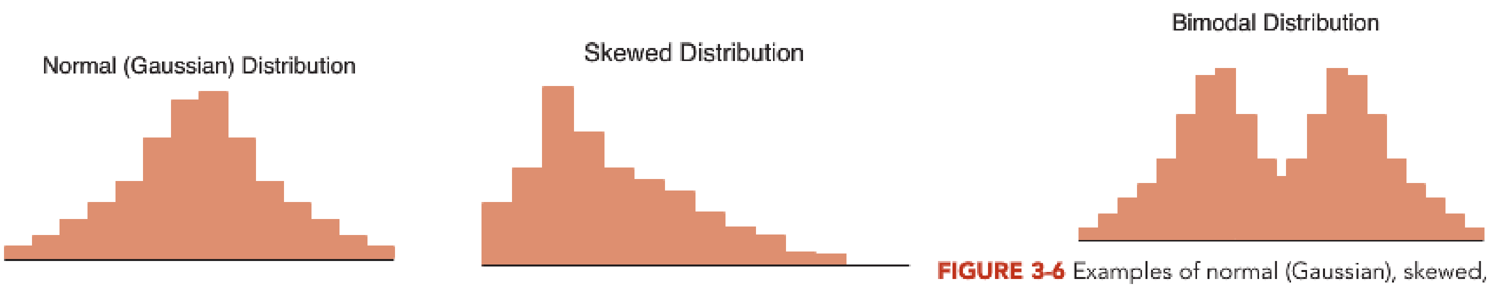
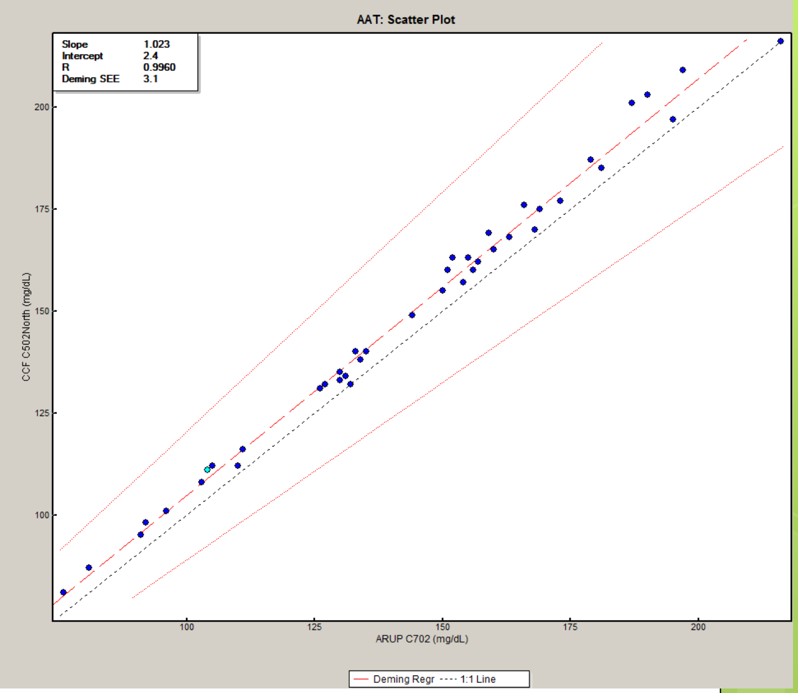


FIGURE 3-6 Examples of normal (Gaussian), skewed, and bimodal distributions. The type of statistical analysis that is performed to analyze the data depends on the distribution (shape).

Lab Statistics

- Much of what we know about how well methods work is based off of a “reference method”
  - The best known method produces a “known” or “true” value that is taken to be 100% accurate

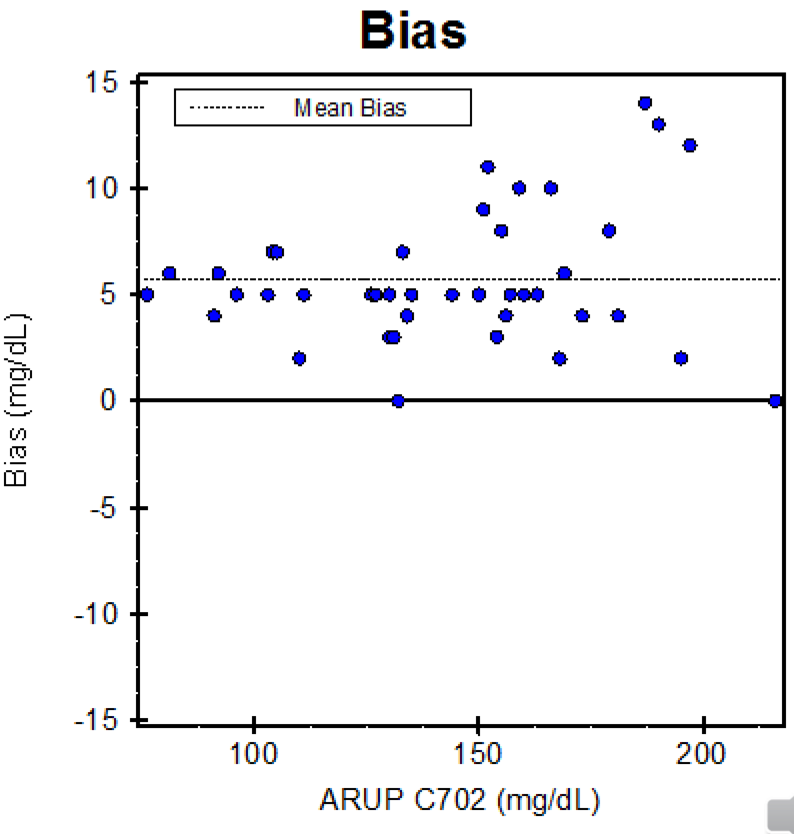
Lab Statistics



- Correlation Coefficient (r)
  - Strength of relationship
    - Should be >.98
- Any deviation from the 1:1 line (reference method) is due to error
  - Random error- unpredictable but ever present
  - With increasing sample size the impact of random error is decreased

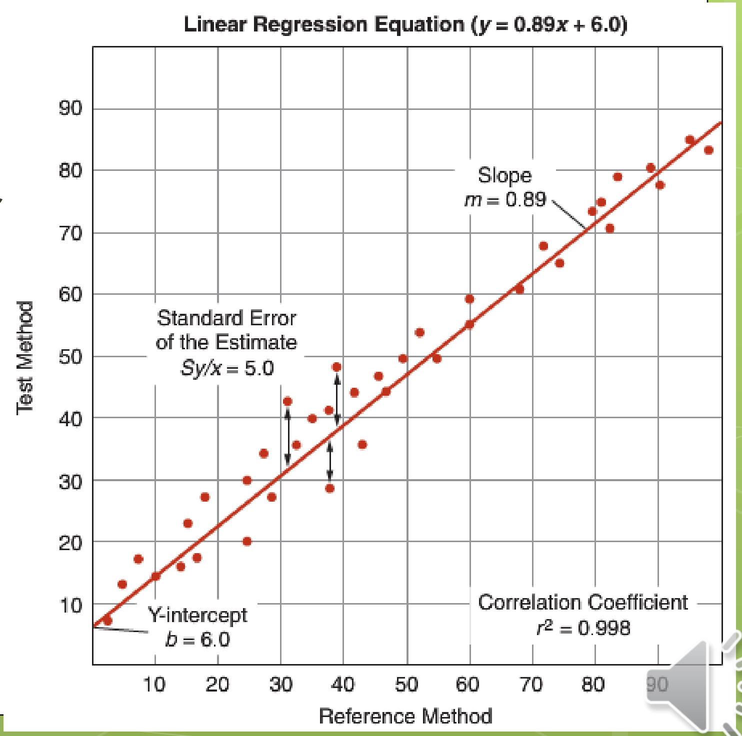
Lab Statistics

- Bias
  - It can be difficult to see a bias if it is subtle or not present across measuring range
  - This one is kind of obvious



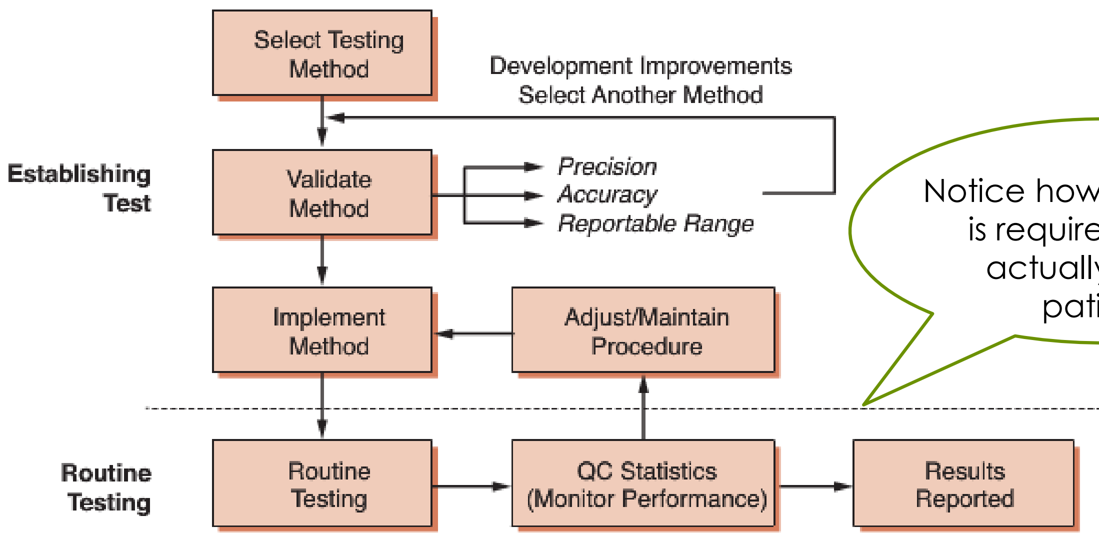
Lab Statistics

- Systematic error- consistently moves measurements in one direction
  - Constant systematic error
    - Y-intercept constant +6
  - Proportional systemic error
    - Slope indicates underestimation
    - As value increases so does difference



Lab Statistics

- Why test the test?
  - Method evaluation and validation



Notice how much work is required before actually testing patients

FIGURE 3-10 A flowchart on the process of method selection, evaluation, and monitoring. (Adapted from Westgard JO, Quam E, Barry T. *Basic QC Practices: Training in Statistical Quality Control for Healthcare Laboratories*. Madison, WI: Westgard Quality Corp.; 1998.)

Lab Statistics

- How to choose a method
  - The ability of a method to diagnose disease (or exclude one) is what we care about when selecting a method
  - Sensitivity vs specificity
    - Trade-off, as sensitivity increases *generally* the specificity will decrease

Lab Statistics

- Understanding Sensitivity and specificity

	People who we *know* have a condition	**People who we *know* do not have a condition**
People who tested positive	True Positives	False positives
People who tested negative	False negatives	True Negatives

Lab Statistics

- Sensitivity: True positives / (true positives + false negatives)
- Specificity: True negatives /(true negatives + false positives)
- Next level of statistics PPV and NPV
  - PPV-if you test positive what is the likelihood you have a condition
  - NPV- if you do not test positive how sure are we that you don’t have disease

Lab Statistics

- PPV = True positives / (True + False positives)
- NPV = True negative / (True + False negatives)

Lab Statistics

- Evaluate this method for spec. sens. PPV and NPV

	People having heart attacks	People not having heart attacks
cTnT > 0.030 ng/mL	254	15
cTnT < 0.030 ng/mL	7	812

Sensitivity: 97% Specificity:98% PPV: 94% NPV: 99%

Quality Control or QC

- Reliability (what do we want in a method)
  - Repeatable
  - Accurate
  - Precise
  - Trustworthy
  - Consistent

Quality

- Every lab must establish Quality Assurance Plan (QAP)
  - This must detect, control, and prevent occurrence of errors
- Quality Assurance is more than QC
  - Covers preanalytic, analytic, and post analytic phases

Quality

- Preanalytic controls
  - Physicans must order
  - Patient prep. i.e. fasting, 24 hr collection etc
  - Patient ID
  - Specimen acquisition, transport, processing and storage

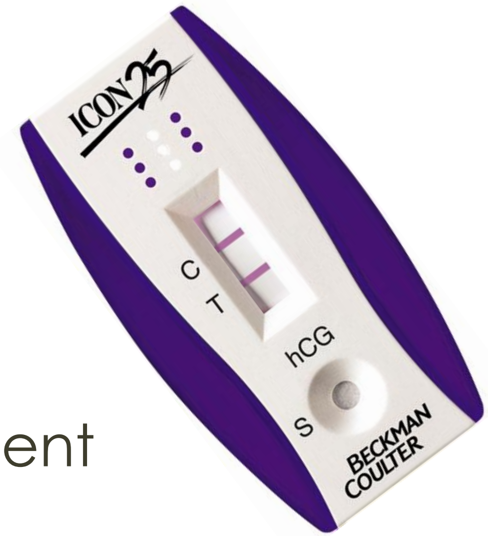
Quality

- Analytic controls
  - What methodologies are chosen
  - Standardization and calibration techniques
  - Documentation of linearity and variability
  - Monitoring insturmentation, reagents
    - This is where QC comes in

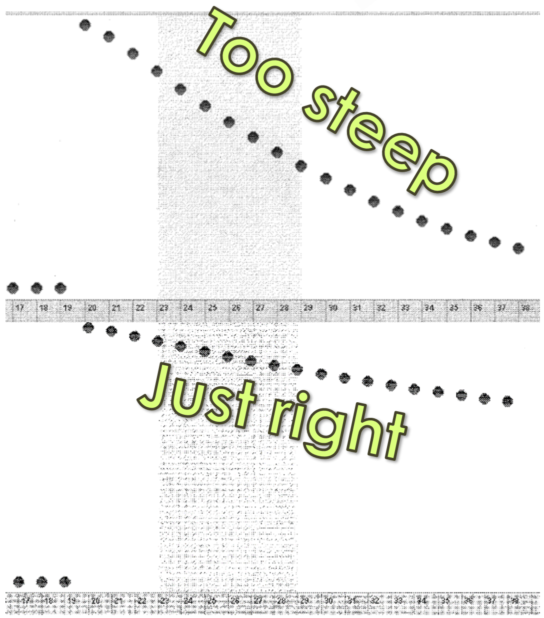
Quality

- Postanalytic controls
  - Notify of critical values
  - HIPAA maintained
  - Maintain records of values

Quality Control

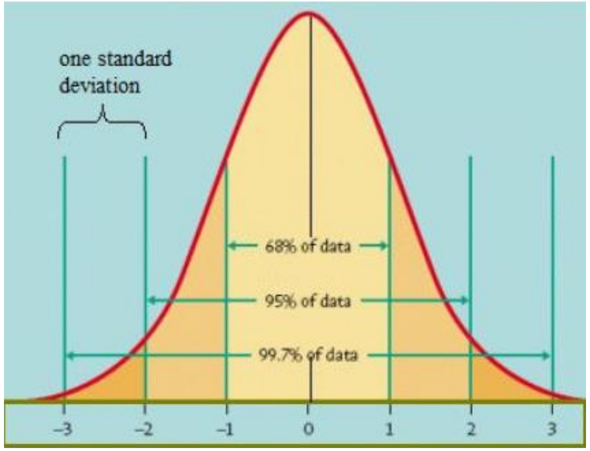


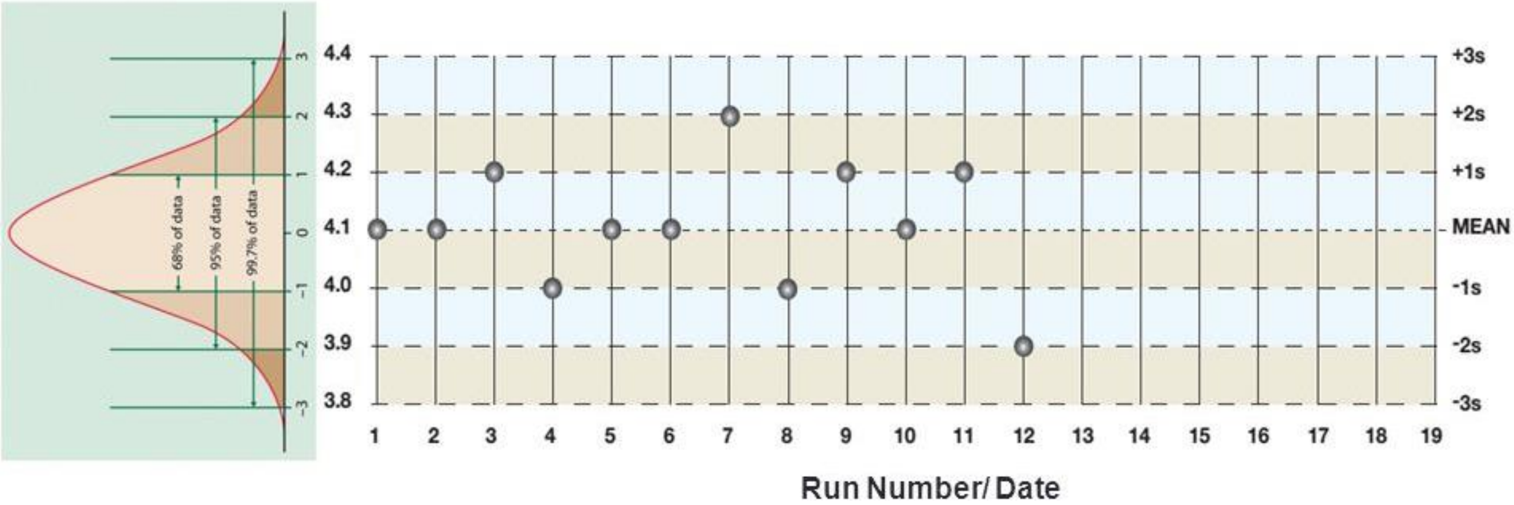
- Regular monitoring of tests
  - Analyze controls along with patient specimens
    - Internal QC
      - Monitor linearity
      - Ensure test limits met
    - External QC
      - Prof. Testing
      - QC samples



Quality Control

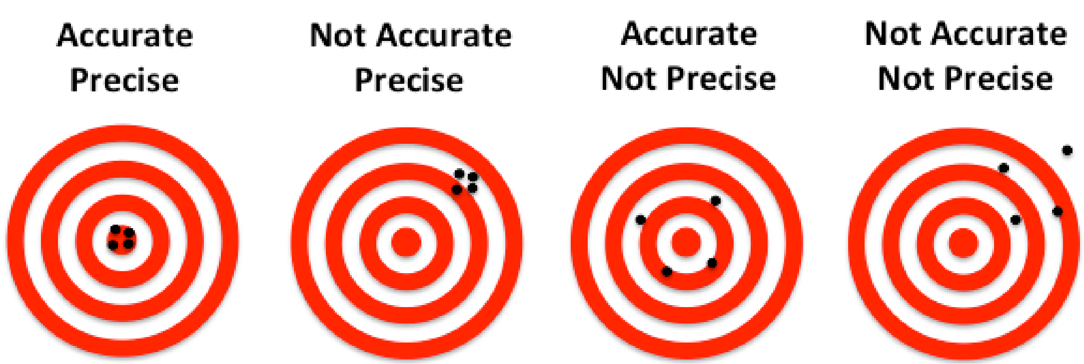
- Standard Deviation
  - Material assayed for 20 days
  - Establish mean and SD





Quality Control

- Accuracy and Precision
  - Accuracy: Closeness of agreement between measured value of analyte and its TRUE value
  - Precision: Ability to produce same value for replicate measurements



Quality Control

- Materials to measure accuracy:
  - Calibrator
  - Standards
  - Assayed Material
  - Reestablish the true values
- Materials to measure precision:
  - Unassayed QC
  - Patients from other instruments

ACCURACY

cobas®

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CalCheck 5 Lot: 183507

Reagent Pack Lot 120341 for Elecsys 2010, MODULAR ANALYTICS E170, **cobas e** 411, **cobas e** 601 and **cobas e** 602 analyzers
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Level	Value	Range	Unit
Check 1	≤ 0.010	≤ 0.010	µIU/mL
Check 2	1.97	1.62 - 2.32	µIU/mL
Check 3	48.0	40.8 - 55.2	µIU/mL
Check 4	81.0	68.9 - 93.2	µIU/mL
Check 5	> 100	90.1 - > 100	µIU/mL

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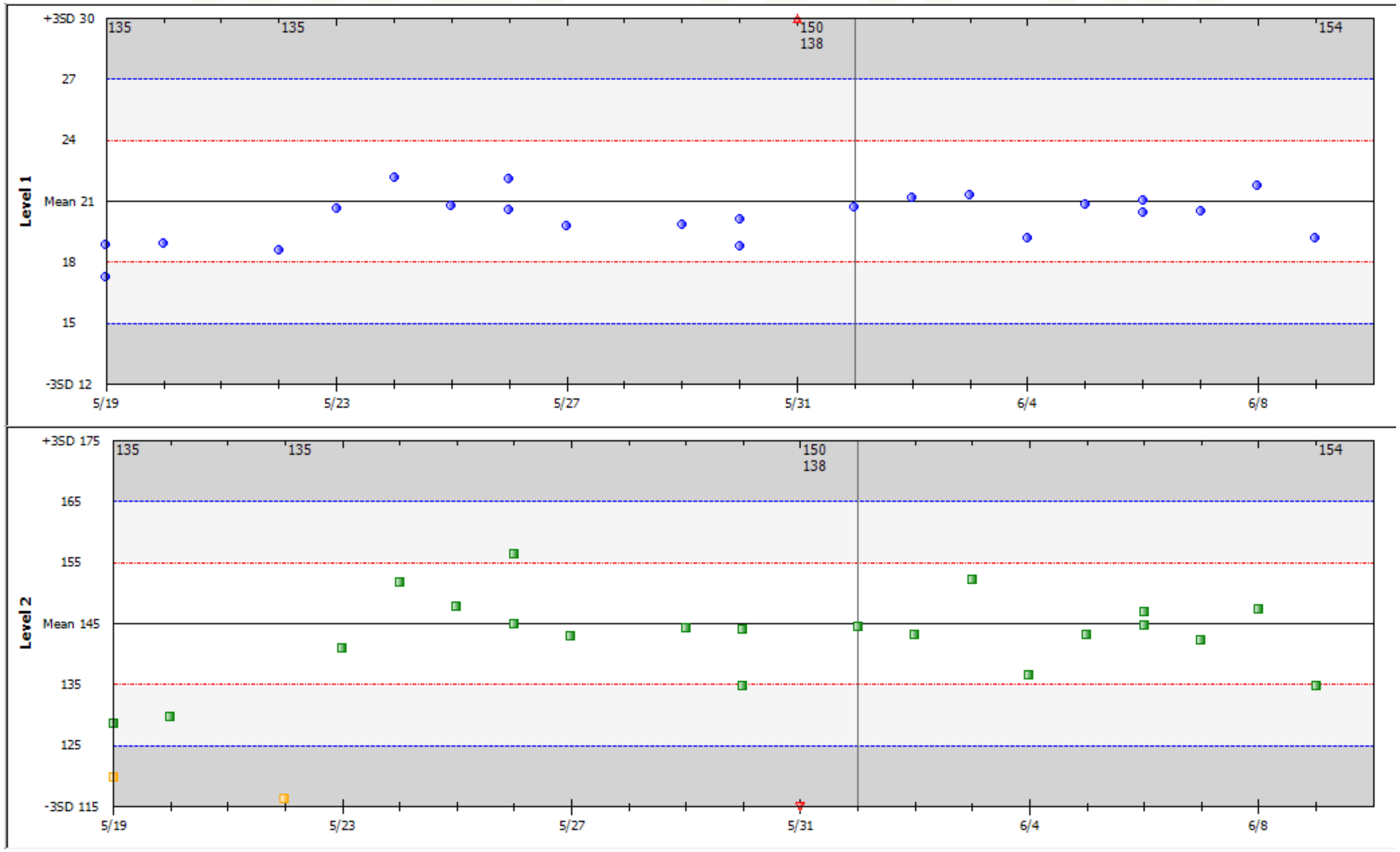
PRECISION

CHEM	TBIL	ALB	BUN	CA	CHOL	CL	CO2	CREAT	GLU	HDL	K	MG	NA	PHOS	TP	TRIG	TECH ID
LIMITS ±	0.2 or 20%	0.4 or 10%	2 or 9%	0.4 or 5%	4 or 10%	2 or 5%	3 or 15%	0.04 or 10%	6or 10%	4 or 15%	0.5	0.2 or 10%	4	0.2 or 10%	0.2 or 5%	4 or 5%	
N756A/N1			20	7.6		103	24	1.50	103	31	7.1		144		6.2		cn
N756B/N2	0.5	3.1	22	7.7	114	102	23	1.56	107		7.1	2.0	144	3.4		105	cn
N766A/N3			21	7.7		104	23	1.49	106	30	7.2		146		6.0		cn
N766B/N4	0.5	3.2	21	7.4	110	104	23	1.49	107		7.2	2.0	145	3.4		104	cn
S756A/S1			20	7.7		104	22	1.45	105	30	7.2		145		6.0		cn
S756B/S2	0.5	3.1	21	7.6	110	105	22	1.49	105		7.1	1.9	146	3.4		98/101	cn
S766A/S3			20	7.6		104	22	1.52	106	30	7.1		145		5.8/5.9		cn
S766B/S4	0.5	3.2	21	7.6	112	104	22	1.53	105		7.2	1.9	145	3.3		100	cn
VAR.	~~0~~	0.1	2	0.3	4	<5%	2	<10%	4	1	0.1	0.1	2	0.1	~~6%~~ 5%	~~7%~~ 5%	

PRECISION



Level 1
+3SD 30
27
24
Mean 21
18
15
-3SD 12
135
135
150
138
154
5/19
5/23
5/27
5/31
6/4
6/8
Level 2
+3SD 175
165
155
Mean 145
135
125
-3SD 115
135
135
150
138
154
5/19
5/23
5/27
5/31
6/4
6/8

QC values

- Abnormal and normal values
- Range representative of assay
- Calculating the SDs
  - $\sigma = \sqrt{\frac{\sum(\bar{x}-x_n)^2}{n-1}}$
  - CV = $\frac{\sigma}{\bar{x}} \times 100$ (a universal SD language)
- Measures of precision

QC Values

- How is CV useful?
  - Example:
    - Potassium QC
      Level 1: $\bar{x}$ = 2.6 σ = 0.1CV = 3.85%
      Level 3: $\bar{x}$ = 7.7 σ = 0.2CV = 2.60%
    - Cholesterol QC
      Level 1: $\bar{x}$ = 105 σ = 5 CV = 4.76%
      Level 3: $\bar{x}$ = 273 σ = 9 CV = 3.30%

Practice

- Let's evaluate the precision of 2 methods:

	Method 1	Method 2
$\overline{x}$	100 units	138 units
σ	25 units	31 units
CV?	25	23

More precise

Less precise

Control Situations

- What does it take to be out of control?
  - Any value greater than ±3 SD
  - Both Levels greater than ±2 SD
  - One Control < ±2 SD and another between ±2-3 SD
    - This is acceptable once every 20 days under LJ rules
  - Trends: In/decreasing for 6 consecutive days on both levels
  - Shift: All controls on one side of mean for 6 consecutive days on both levels

Shifts & Trends

- Why shift?
  - Improper storage of standard
  - New standard prepared incorrectly
  - Reagent shifted to new level of activity (enzymes at a different temperature)
  - Timer is not working properly
  - Different lot of reagent or standard

Shifts & Trends

- Why Trend?
  - Gradual deterioration of standard or reagent
  - Continued temp. instability (evap, damage)
  - Protein accumulation

QC

- What is it good for?
  - Alerts tech a problem exists
    - Does not ID problem
    - Does not fix problem
  - Troubleshooting *should* ID and fix the problem

Other QC

- Cumulative Summary Control Chart
  - Used in coagulation-hematology
- Moving Averages
  - Also used in heme, how stable the average for patient analytes is, if it is moving too much it's a problem
- Westgard Multi-Rule Control Chart
  - The Modern interpretation of LJ charts

Westgard Rules

- 1_{2S}-Warning, 1 control >2 SD
- 1_{3S}- Fail 1 control >3 SD
- 2_{2S}- Fail 2 consecutive controls > 2 SD
  - Also if *both levels* are >2 SD once
- R_{4S}- Range between levels greater than 4 SD
- 4_{1S}-Fail when 4 consecutive exceed same SD
- 10_{x}-Fail when 10 consecutive are on same side of mean