Bias in Laboratory Medicine: The Dark Side of the Moon

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Supplemental Method

Practical examples of bias calculation in clinical laboratories

Bias can be evaluated using a four-step procedure:

Step 1. Determine the reference or assigned value.

Step 2. Measure the sample n times (n = 10 is reasonable).

Step 3. Calculate the mean, SD, SE, and 95% confidence interval (CI) of the measurand. Bias is the difference between the mean of the repeated measurements and the reference or assigned value.

Step 4. Use a suitable statistical test such as the *t*-test to evaluate the significance of bias. A practical method, which is based on visually inspecting the CIs rather than conducting strict statistical analysis, can also be utilized. If the 95% CIs of the mean and assigned value overlap, bias can be considered insignificant; otherwise, the bias is considered significant.

Supplemental Table S1. Numerical example for bias of glucose (mg/dL). The mean of the peer group from EQAS is accepted as the target value

Laboratory data		**Peer group**	**Bias (%)**
Repeated measurements	Measurement results		
1	120		
2	117		
3	125		
4	119		
5	117		
6	121		
7	120		
8	116		
9	124		
10	123		
Mean	120.2	115.1	5.1 (4.4%)*
SD	3.08	4.01	
n	10	90	Bias is significant
SE	0.98	0.42	
CI (95, %)	118.3 – 122.1	114.3 – 115.9	CIs do not overlap

*Bias is significant; thus, corrective or preventive action is necessary.

Abbreviations: EQAS, External Quality Assessment Scheme; CI, confidence interval.

Supplemental Table S2. Numerical example for bias of cholesterol (mg/dL). The mean of the peer group from EQAS is taken as the target value.

Laboratory data		**Peer group**	**Bias (%)**
Repeated measurements	Measurement results		
1	146		
2	150		
3	153		
4	143		
5	147		
6	150		
7	144		
8	148		
9	149		
10	143		
Mean	147.3	150.1	- 2.8 (- 1.9%)*
SD	3.34	5.08	
n	10	120	Bias is not significant
SE	1.05	0.46	
CI (95, %)	145.2 – 149.4	149.2 – 151.0	CIs overlap

*Bias is not significant; thus, corrective or preventive action is not necessary.

Abbreviations: EQAS, External Quality Assessment Scheme; CI, confidence interval.

Supplemental Table S3. Calculation of acceptable bias for glucose and cholesterol based on biological variation data

Measurands	CV_I (SD_I)*	CV_G (SD_G)*	Optimum B_A	Desirable B_A	Minimum B_A	Calculated B_A
Glucose	5.0 (5.8)	8.1 (9.3)	1.4	2.7	4.1	5.1
Cholesterol	5.3 (8.0)	16.7 (25.1)	3.3	6.6	9.9	2.8

*Both CV_I and CV_G were taken from the European Federation of Clinical Chemistry and Laboratory Medicine database [70]. CV_I and CV_G were converted to SD for the corresponding target values of the measurands.

The following equations can be used to calculate the optimum, desirable, and minimum bias for glucose and cholesterol

$$Optimum\ B_A < 0.125(CV_I^2 + CV_G^2)^{1/2}$$

$$Desirable\ B_A < 0.250(CV_I^2 + CV_G^2)^{1/2}$$

$$Minimum\ B_A < 0.375(CV_I^2 + CV_G^2)^{1/2}$$

Abbreviation: B_A, acceptable bias.