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RESEARCH ARTICLE

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Sigma metrics application for validated and non-validated detecting systems performance assessment

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Abstract

Background: Sigma metrics provide an objective and quantitative methodology for analytical quality evaluation of clinical laboratory. This study investigated the testing performance of validated systems and non-validated systems based on sigma metrics, and explored the major parameters affecting the system performance.

Methods: Sigma metrics were evaluated by six biochemistry assays based on Beckman and Mindray validated and non-validated systems through crossing the reagents and analyzers. Imprecision and bias were assessed for all assays based on trueness programs organized by National Centre for Clinical Laboratory. Total error allowance obtained from the Chinese Ministry of Health Clinical Laboratory Centre Industry Standard (WS/T403-2012).

Results: The imprecision for all systems meets the quality specifications except TP assay (2.19%) detected by Mindray non-validated system, and the bias for four assays measured by non-validated systems cannot fulfill the criterion, including lactate dehydrogenase (LDH), total protein (TP), triglycerides (TG), and glucose (GLU). Higher biases were detected in six assays at different levels among non-validated and validated systems. Systems performed poorly or unacceptably for TP assay with sigma metrics lower than 3 except Mindray non-validated system. The sigma metrics for other assays with four systems were greater than 3 except the LDH evaluated on Mindray non-validated systems.

Conclusion: Non-validated systems may introduce performance uncertainty compared with validated systems based on sigma metrics evaluation, and lower bias was provided by validated systems. The performance of non-validated systems should be evaluated thoroughly in the clinical laboratory before they were adopted for routine use.

KEYWORDS

non-validated systems, performance, sigma metrics, validated systems

1 | INTRODUCTION

Laboratory results play a fundamental role in clinical decision-making, so the analytical quality must be guaranteed for proper treatment and the error rates must be controlled for patients' safety.[1,2] The examination results are influenced by the in vitro diagnosis detecting systems comprehensively, which consist of analyzers, corresponding assay reagents, calibrators and relevant clinical laboratories, etc Matched or validated analytical systems are the preferred choices for laboratories, where commercial kit methods are ready to be apply on a dedicated instrument.[3] The manufacturer/method developer verifies and claims the performance characteristics of the validated systems or examination procedure, which only need to be simply validated by the laboratories.[4] However, given limited test revenue of dedicated systems and cost containment, laboratories are forced to seek additional operational efficiency by using the existing analyzers whenever possible.[5,6] Some clinical laboratories adopt instruments, reagents and calibrators provided by different manufacturers, and such combinations form unmatched or non-validated systems.[7] In this case, the laboratories should carry out comprehensive and sufficient performance verification including trueness, precision, uncertainty, specificity, sensitivity, detection limit, and quantitation limit.[4] Of all these performances, trueness and precision are the most important parameters.

Sigma metrics provide an objective and quantitative methodology for analytical quality evaluation of clinical laboratories and can be calculated with defined tolerance limit, measuring process variation and analytical bias, which integrates total error allowance (TEa), estimated trueness and precision.[8,9] Sigma metrics have already been demonstrated to be a useful tool for all parts of the quality control (QC) design process, through which laboratories can easily visualize performance, establish individual internal quality control criteria, and evaluate the performance of analytical systems on a universal scale.[10-12]

Previously, our study has demonstrated that there were five analytes with marginal or poor performance ($\sigma < 4$) in 9 "non-validated or kit" reagents which was worse performance than that of 2 analytes in 27 original manufacturer reagents on the Beckman AU5800 chemistry analyzer.[13] Cao et al have reported that non-validated reagent system has relatively lower sigma metrics level than validated reagent system,[7] but the causes for performance differences were not elucidated. Thus, we hypothesized that sigma performance was influenced by bias and precision differently, and mainly due to the inaccuracy of non-validated system compared with validated system.

In this study, we evaluated the sigma metrics of six biochemistry assays in four detecting systems (2 validated systems and 2 non-validated systems through crossing the reagents and analyzers) to explore performance difference and the major parameters affecting the analytical quality among validated and non-validated systems.

2 | MATERIALS AND METHODS

2.1 | Materials

This study was conducted in the clinical chemistry laboratory of the Peking University Shenzhen Hospital for assessment of Beckman AU5800 chemistry analyzer (Beckman Coulter) and BS-2000 biochemical analyzer (Mindray), respectively. Six routine chemistry analytes were evaluated, including alanine aminotransferase (ALT, without pyridoxal-5-phosphate), LDH, GLU (hexokinase method), TP, TC, and TG. Two kinds of reagents for the assays were obtained from Beckman Coulter (ALT: Lot AUZ5916; LDH: Lot AUZ5921;GLU: Lot AUZ5707; TP: Lot AUZ6045;TC: Lot AUZ5738; TG: Lot AUZ5760) and Mindray (ALT: Lot 140118012; LDH: Lot 142718005; GLU: Lot 141419001; TP: Lot 140818009; TC: Lot 141618012; TG: Lot 141718007). All assays were calibrated by Beckman coulter System Calibrator (Lot 1120N) for Beckman reagents, and calibrated by Mindray Multi Sera Calibrator for Mindray reagents (Lot 059118003). For bias and imprecision assessment, trueness verification materials with assigned values were provided by National Centre for Clinical Laboratory (Peking, China) for ALT and LDH (Level 1 lot: 201901, Level 2 lot: 201902), TC and TG (Level 1 lot: 201911, Level 2 lot: 201912), and GLU and TP (Level 1 lot: 201921, Level 2 lot: 201922).

3 | Methods

3.1 | Detecting systems establishment

The four evaluated detecting systems were summarized in Table 1, including Beckman AU5800, Mindray BS-2000 validated systems, and two non-validated detecting systems. The analyzers were calibrated based on the standard protocols recommended by the manufacturers.

TABLE 1 Systems establishment

System	Analyzer	Regent	Calibrator	Comments
1	Beckman AU5800	Beckman	Beckman	Beckman verified system
2	Beckman AU5800	Mindray	Beckman	Beckman non-verified system
3	Mindray BS-2000	Mindray	Mindray	Mindray verified system
4	Mindray BS-2000	Beckman	Mindray	Mindray non-verified system

3.2 | Sample preparation

The trueness verification materials were fresh human mixed serum prepared by National Center for Clinical Laboratories (NCCL, China). All specimens were transported on dry ice and stored at −80°C freezer immediately once received by our laboratory. The samples were thawed completely at room temperature for 20 minutes and mixed gently before testing on the four detecting systems. Two levels of materials were provided for each assay and three separated aliquots for each level. One aliquot of each level was measured under repeatability condition for five times, and the three aliquots were evaluated on March 27, April 3, and April 10, 2019, respectively.

3.3 | Imprecision evaluation

The precision and bias assessment were conducted based on trueness verification protocol organized by NCCL, China in 2019, which was designed according to to the procedure of CLSI EP 15-A2,[14] measuring each sample with three replicates in five runs. Two levels of specimens were measured for each assay (ALT, LDH, GLU, TP, TC, TG). All tests were conducted on four detecting systems, respectively. The system imprecision was calculated and expressed as coefficient of variation (% CV).

3.4 | Bias calculation

According to the trueness verification scheme, a total of 15 results were obtained for each level; the mean value of the 15 results was regarded as the laboratory testing results (excluding outlier more than three standard deviations with the mean). The target values for the trueness verification materials were assigned by using reference measurement procedures. The bias was assessed for each analyte according to the deviation (ratio) of detected results from the assigned values provided by NCCL.

3.5 | Sigma calculation

The TEa values implying the tolerance limits were taken from the Chinese Ministry of Health Clinical Laboratory Center Industry Standard (WS/T403-2012).[15] Sigma metrics were calculated as follows:

$$\text{Sigma metrics} = (\text{TEa} - |\text{Bias}|)/\text{CV}\ (\%)$$

3.6 | Statistical analyses

Data were analyzed using R software. Results are presented as means (95% CI) with N = 15. The bias significance was determined by the *t* test, and *P* value <0.05 was regarded as a significant difference among validated and non-validated systems.

4 | RESULTS

Imprecision and bias were estimated for six biochemistry assays using the four detecting systems. Testing results and sigma metrics were calculated and summarized in Table 2. Acceptable TEa, bias (1/2TEa) and CVs were also presented in Table 2 based on WS/T403-2012. Results showed that, firstly, the imprecision for all systems meets the quality specifications except TP assay at high concentration (2.19%) detected by Mindray instrument with Beckman reagent; the Beckman non-validated systems showed better performance than the validated systems with GLU and TC assays at both low and high levels; and the imprecision of Mindray non-validated systems increased for LDH assay compared with Mindray validated systems at two concentrations (3.49% vs 1.49% and 2.74% vs 1.89% among non-validated and validated systems at two levels). Secondly, the bias for four assays cannot fulfill the criterion, including LDH, TP, and TG measured by Mindray non-validated system, TP tested by Beckman validated system, and GLU measured by Beckman non-validated system; the bias for validated system showed a better performance than non-validated system for most assays, but individual non-validated system provided more optimal bias. For example, the bias for TP assay detected by Beckman validated system versus non-validated system was −0.74% vs 0.1% and −2.41% vs 0.47% at low and high levels, and bias for ALT assay tested by Mindray validated versus non-validated system was 2.58% vs 1.13 and 3.85% vs 2.74 at low and high levels. Figure 1(A-I) showed the bias comparison of validated and non-validated systems for all assays with two concentration.

The Sigma Method Decision Chart, a normalized Method Decision Chart, plotting the methods performance was showed in Figure 2. The sigma metrics for ALT assay were World-Class quality for all systems. The systems performed well for LDH assay with sigma metrics higher than 4 except the detecting system constructed by Beckman reagent with Mindray instrument (1.9 and 2.9 for low and high concentration, respectively). For GLU assay, the Mindray reagent with Beckman instrument achieved World-Class quality at both low and high concentration, and sigma metrics were higher than 3 for other systems. The TP assay performance was poor and unacceptable for Beckman validated system and Mindray validated and non-validated systems, and Beckman non-validated system reached best performance with sigma greater than 3. For TC and TG assays, three systems achieved World-Class quality except the Beckman non-validated system (Sigma > 3.0) and Mindray non-validated system (Sigma > 4), respectively.

5 | DISCUSSION

In this study, the sigma metrics and imprecision varied among systems and assays, and validated systems provided lower bias than the non-validated systems for most assays. Uncertain parameters may exist on non-validated systems, which were untraceable and may lead to greater deviation or inaccurate results. When such modified

TABLE 2 Sigma metrics calculation for six assays on four detecting systems

Assay	Reagent manufacturer	Verified Analyzer	TEa% WT/S 2012	Bias%	CV%	Bias%		CV%		Sigma	
						Level 1	Level 2	Level 1	Level 2	Level 1	Level 2
ALT	Beckman	Y	16	6	6	−0.48	2.22	1.1	1.3	14.11	10.6
	Mindray	N				4.75	2.81	1.06	0.57	10.61	23.14
	Mindray	Y				2.58	3.85	1.47	1.94	9.12	6.26
	Beckman	N				1.13	2.74	1.64	1.6	9.06	8.31
LDH	Beckman	Y	11	4	4	−1.41	0.26	0.8	1.3	11.99	8.26
	Mindray	N				−0.87	−3.09	0.8	1.23	12.66	6.43
	Mindray	Y				−1.61	−2.45	1.49	1.89	6.29	4.53
	Beckman	N				−4.27	−3.14	3.49	2.74	1.93	2.87
GLU	Beckman	Y	7	2	3	0.83	0.87	1.84	0.98	3.35	6.26
	Mindray	N				−2.34	−2.04	0.52	0.45	8.96	11.02
	Mindray	Y				0.41	1.42	1.74	0.91	3.78	6.14
	Beckman	N				1.76	0.57	1.62	1.69	3.23	3.8
TP	Beckman	Y	5	2	2	−0.74	−2.41	1.9	1.9	2.24	1.36
	Mindray	N				0.1	0.47	1.27	1.05	3.86	4.31
	Mindray	Y				−1.05	−0.81	1.32	1.6	2.99	2.61
	Beckman	N				−4.26	−3.28	1.78	2.19	0.41	0.78
TC	Beckman	Y	9	4	3	2.25	2.11	0.77	0.99	8.77	6.96
	Mindray	N				2.34	1.69	2.05	2.4	3.25	3.04
	Mindray	Y				−1.04	−1.21	0.68	0.59	11.71	13.2
	Beckman	N				−1.23	1.54	0.93	0.83	8.35	8.99
TG	Beckman	Y	14	5	5	0.84	0.24	1.22	0.93	10.79	14.8
	Mindray	N				−1.85	−1.66	1.27	1.03	9.57	11.98
	Mindray	Y				0.84	1.47	1.11	0.75	11.9	16.6
	Beckman	N				6.41	3.95	1.62	1.86	4.68	5.4

Abbreviations: ALT, alanine aminotransferase; CV, coefficient of variation; GLU, glucose; LDH, lactate dehydrogenase; TC, total cholesterol; TG, triglycerides; TP, total protein; TEa, total error allowance; N indicates the analyzer is not produced by the same manufacturer as reagent and calibrator; Y indicates the analyzer is produced by the same manufacturer as reagent and calibrator.

procedures are applied to clinical laboratories, particular attention should be given to the analytical performance differentia caused by bias. Traceability relates a measurement result to a known reference value based on an unbroken chain of calibration, which transfers the degree of trueness of a reference material, and/or reference measurement procedure to the next lower metrological order until routine procedure. The traceability is established and documented by the assay manufacturer for commercial methods, which could be adopted by clinical laboratories directly without requiring validation traceability, but the non-validated systems are modified measurement procedures, and the measurements cannot be traced to the available reference and may lead to non-comparable results.[16,17] The potential sources affecting the precision of results in the detecting system include sample pipetting, reagent pipetting, photometer drift, frequency of calibration, lot-to-lot variation of reagent, and calibrators.[18] Lower imprecision represents more stability of analytical process.[19]

The bias relies on the estimation of measure and concentrations of materials with known concentrations or target value.[20] In this study, the materials are fresh human mixed serum obtained from NCCL, which are commutable for all detecting methods, and the target values are assigned by reference methods and materials.[21] The results showed that the bias for four assays did not meet the WS/T403-2012 criterion, including LDH, TP, and TG assays detected by Beckman non-validated systems and GLU assay detected by Mindray non-validated systems. A national trueness verification scheme to evaluate serum creatinine assays performance in China, the disappointing sigma metrics of the theses assays (including matched reagent and unmatched reagent) were also mainly due to the unacceptable analytical bias.[22] However, the performance of precision in validated and non-validated system was different from that in bias. There was no significant trend changes between validated and non-validated system, and there is only one level TP of Mindray non-validated system did not meet the quality specifications. Therefore, when considering both bias and precision, the performance of validated and non-validated system was evaluated by sigma metric, and the results were often more confusing. In this

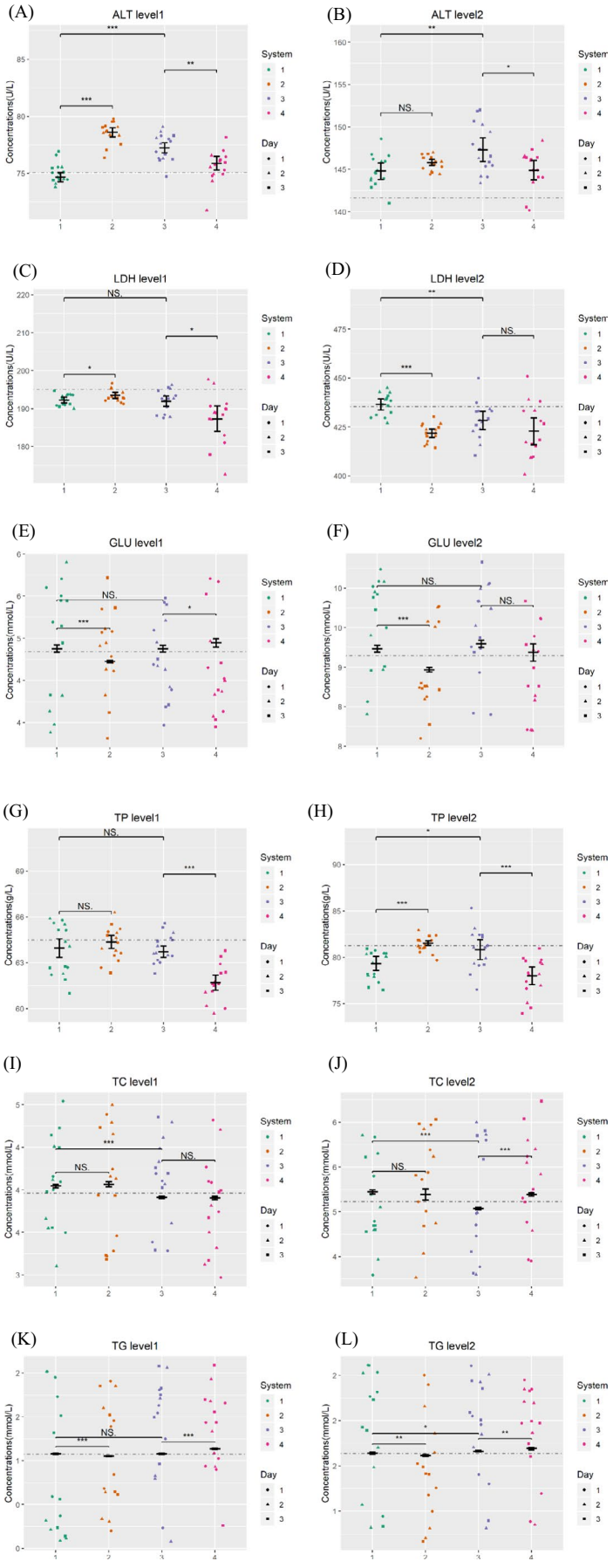

FIGURE 1 Bias comparison of validated and non-validated systems for all assays with two concentrations. Note: System 1-4 represents the Beckman validated system, Beckman non-validated system, Mindray validated system, and Mindray non-validated system. Day 1-3 represents the time course according to the trueness verification protocol. The horizontal lines correspond to the means (95% CI), - - - represents the target value of trueness material, *represents $P < .05$, ** represents $P < .01$, *** represents $P < .005$. ALT, alanine aminotransferase, U/L; LDH, lactate dehydrogenase, U/L; GLU, glucose, mmol/L; TP, total protein g/L.;TG, triglycerides, mmol/L; TC, total cholesterol, mmol/L

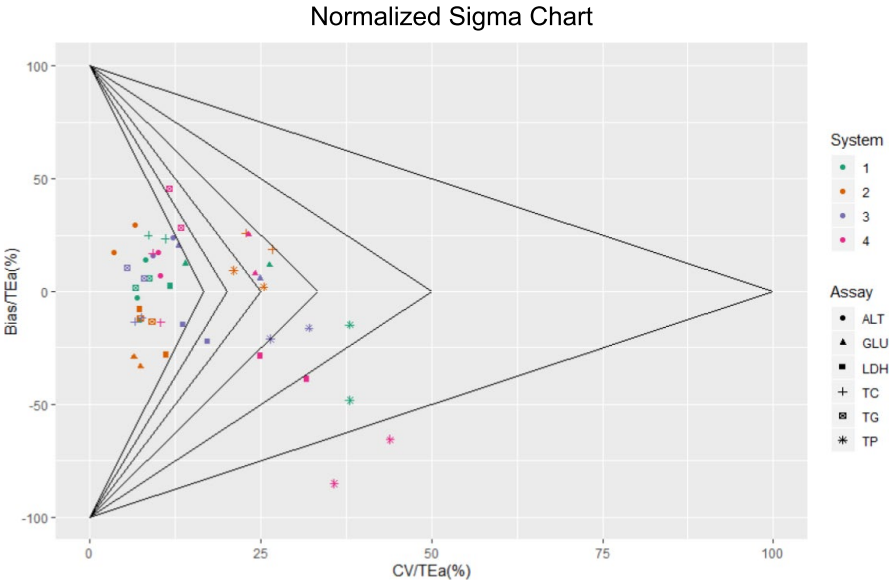

FIGURE 2 Normalized method decision chart demonstrating the Sigma values for the six assays. Note: System 1-4 represents the Beckman validated system, Beckman non-validated system, Mindray validated system, and Mindray non-validated system. X-axis and Y-axis display the imprecision and bias as percentages of the TEa

study, among the four detecting systems of six assays, the sigma metrics for ALT assay were all greater than 6, and for the other assays, the lowest sigma metrics were all distributed in non-validated systems. The Mindray validated systems qualities were unacceptable for LDH and TP assays with $\sigma < 3$, and for GLU assay, the system displayed lowest sigma values at two concentration, respectively; the Beckman and Mindray non-validated systems provided inferior sigma metrics for TC and TG assays respectively with $\sigma < 6$.

Unexpectedly, Beckman validated system and Mindray validated and non-validated systems provided poor and unacceptable quality for TP assay with sigma values varied from 0.41 to 2.99, which may be affected by the stringent TEa of 5%. TEa is the analytical quality requirement for laboratory tests, and existing resources of TEa goals are not harmonious and standardized now, and different sources of TEa impact the estimation of Sigma metrics.[23] Similar situation was found in Westgard's study and they proved that the sigma metrics of same albumin assay ranged from negative to 32, and the quality would be classified to unacceptable or even well above world class depending on the TEa targets chosen from different sources.[24] Meanwhile, Beckman non-validated system achieved the best sigma metrics with good and marginal quality for TP assay, which showed a different varying trend with other assays, the bias and imprecision for Beckman non-validated system were both decreased compared with validated system. We speculated following reasons might explain the phenomenon. First of all, the non-validated system was not traceable, and may generate random results, and lead to decreased bias accidentally. Secondly, the precision was evaluated in a short period of time which reflected mainly analyzer variation regardless of the factors such as lot-to-lot variation of reagent, and reagent stability and frequency of calibration. So, compared with the Beckman validated systems, when the same reagent was used on the Mindray analyzer, the non-validated system imprecision for TP assays was decreased. A similar reduction in precision had occurred in ALT and GLU assays.

In this study, the Beckman and Mindray validated systems offered satisfied performance for the six assays we assessed, and the non-validated systems, constituted by crossing the reagents and analyzers, broke the traceability chain and result in significantly bias increasing. Nevertheless, due to the uncertainty of precision changes, the sigma metrics varied among systems and assays. One limitation of this study was that the precision was evaluated according to trueness verification scheme within 3 days, which could result in lower CV% and higher sigma metric for performance estimation. Reliable precision assessment should be obtained from long term CV% estimation. Another limitation was the target value for ALT-pyridoxal phosphate (pp) was assigned by using International Federation of Clinical Chemistry (IFCC) reference measurement procedures for the measurement of catalytic activity concentrations of AST and ALT at 37°C, the ALT reagents evaluated in our study had no pyridoxal phosphate activation (ALT no pp, ALT-npp), and the target values for ALT-npp were calculated as the robust means of reported data by all laboratories, which cannot be used for trueness verification.[25] Sigma metrics reflected the detecting system performance directly with assessment of bias and imprecision, but cannot represent the other performance characteristics include analytical range, detection limit, analytical specificity, and reagent carryover.

6 | CONCLUSION

In conclusion, our study presented that non-validated systems may introduce performance uncertainty compared to validated systems based on sigma metrics evaluation, and lower bias was provided by validated systems. The performance of non-validated systems should be evaluated thoroughly in the clinical laboratory before they are adopted for routine use. Besides, the practical value of our study was intended to remind reagent manufactures to establish

measurement traceability chains and ensure the laboratory results comparability.

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CONFLICT OF INTERESTS

No potential conflicts of interest were disclosed.

AUTHOR CONTRIBUTIONS

Yong Xia, Mingyang Li, and Bowen Li conceived and designed the study. Hao Xue and Yu Lin acquired the data. Jie Li involved in statistical analysis and interpreted the data. Ling Ji supervised the study. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

All data relevant to the study are included in the article.

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REFERENCES

1. Price CP. Evidence-based laboratory medicine: supporting decision-making. *Clin Chem*. 2000;46(8 Pt 1):1041-1050.
2. Smith AF, Shinkins B, Hall PS, Hulme CT, Messenger MP. Toward a framework for outcome-based analytical performance specifications: a methodology review of indirect methods for evaluating the impact of measurement uncertainty on clinical outcomes. *Clin Chem*. 2019;65(11):1363-1374.
3. Carl A, Edward RA, David E, Tietz N. *Text book of Clinical Chemistry and Molecular Diagnostics*. In Philadelphia, PA: WB Saunders; 2013.
4. Standardization ISO. Medical laboratories requirements for quality and competence. Geneva: ISO. 2012.
5. Ledue TB, Collins MF, Ritchie RF. Development of immunoturbidimetric assays for fourteen human serum proteins on the Hitachi 912. *Clin Chem Lab Med*. 2020;40(5):520-528.
6. Whicher J, Johnson M. The present state of protein analysis and interpretation. *Clin Chem Lab Med*. 2001;39(11):1017-1018.
7. Cao S, Qin X. Application of Sigma metrics in assessing the clinical performance of validated versus non-validated reagents for routine biochemical analytes. *Biochem Med (Zagreb)*. 2018;28(2):20709.
8. Westgard JO, Westgard SA. Six sigma quality management system and design of risk-based statistical quality control. *Clin Lab Med*. 2017;37(1):85-96.
9. Westgard S, Bayat H, Westgard JO. Analytical Sigma metrics: a review of Six Sigma implementation tools for medical laboratories. *Biochem Med (Zagreb)*. 2018;28(2):20502.
10. Xia J, Chen SF, Xu F, Zhou YL. Quality specifications of routine clinical chemistry methods based on sigma metrics in performance evaluation. *J Clin Lab Anal*. 2017;32(3):e22284.
11. Mao X, Shao J, Zhang B, Wang Y. Evaluating analytical quality in clinical biochemistry laboratory using Six Sigma. *Biochem Med (Zagreb)*. 2018;28(2):20904.
12. Westgard JO, Bayat H, Westgard SA. Planning risk-based SQC schedules for bracketed operation of continuous production analyzers. *Clin Chem*. 2018;64(2):289-296.
13. Xia Y, Xue H, Yan C, et al. Risk analysis and assessment based on Sigma metrics and intended use. *Biochem Med (Zagreb)*. 2018;28(2):20707.
14. Wang X, Wen D, Wang W, Suo M, Hu T. Application of biological variation and six sigma models to evaluate analytical quality of six HbA1c analyzers and design quality control strategy. *Artif Cells Nanomed Biotechnol*. 2019一本书;47(1):3598-3602.
15. People's Republic of China Health Industry Standard (WS/T403-2012); 2012. Available at: http://www.clinet.com.cn/sigmapv/ Accessed November 20th 2017.
16. Standardization ISO. In vitro Diagnostic Medical Devices—Measurement of Quantities in Biological Samples Metrological Traceability of Values Assigned to Calibrators and Control Materials. Geneva, Switzerland: International Organization for Standardization. 2003.
17. Vesper HW, Thienpont LM. Traceability in laboratory medicine. *Clin Chem*. 2009;55(6):1067-1075.
18. Ramamohan V, Abbott JT, Yih Y.Effect of uncertainty in calibration on the correlation structure of the rheumatoid factor immunoassay calibration function. Paper presented at: 2015 Winter Simulation Conference (WSC) 18.
19. Westgard JO, Burnett RW. Precision requirements for cost-effective operation of analytical processes. *Clin Chem*. 1990;36(9):1629-1632.
20. CLSI. *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline*. In Wayne, PA: Clinical and Laboratory Standards Institute; 2010.
21. Li R, Wang T, Gong L, et al. Comparative analysis of calculating sigma metrics by a trueness verification proficiency testing-based approach and an internal quality control data inter-laboratory comparison-based approach. *J Clin Lab Anal*. 2019;33(9):e22989.
22. Kang F, Zhang C, Wang W, Wang Z. Sigma metric analysis for performance of creatinine with fresh frozen serum. *Scand J Clin Lab Invest*. 2016;76(1):40-44.
23. Westgard S, Bayat H, Westgard JO. Analytical Sigma metrics: a review of Six Sigma implementation tools for medical laboratories. *Biochem Med (Zagreb)*. 2018;28(2):20502.
24. Hens K, Berth M, Armbruster D, Westgard S. Sigma metrics used to assess analytical quality of clinical chemistry assays: importance of the allowable total error (TEa) target. *Clin Chem Lab Med*. 2014;52(7):973-980.
25. Wang Y, Wang J, Zhao H, et al. Assessment of enzyme measurement procedures in China through a trueness verification program. *Clin Chim Acta*. 2016;461:98-102.

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