Monte Carlo simulation as a possible approach to determine the standard deviation for proficiency assessment for an external quality assessment programme in clinical chemistry

G. Chew, P S. Cheow, Q. Liu, R. Shin, T L. Teo, T K. Lee

Chemical Metrology Laboratory, Chemical Metrology Division, Applied Sciences Group, Health Sciences Authority (HSA), Singapore

WHY READ THIS POSTER

- This work may be of interest to providers of external quality assessment (EQA) programme in clinical chemistry using assigned values based on reference methods (e.g. isotope dilution mass spectrometry).
- We demonstrated how the ***Monte Carlo Simulation (MCS) technique*** can be used to determine the ***standard deviation for proficiency assessment, σ***.
- The major determinant of MCS ***σ*** or ***CV*** is the repeatability of a reference laboratory.
- The MCS technique was found to give a ***CV*** comparable to the ***prescribed CV*** determined from the pooled robust CV of previous EQA programmes.
- MCS may be used to determine ***σ*** or ***CV*** for ***new analytes*** in future EQA programmes.

INTRODUCTION

- Monte Carlo Simulation (MCS) was previously used by Wong (2005) to simulate participating laboratories' results in an EQA programme to determine the impact of various factors[1].
- In this work, we are interested to ***simulate*** an EQA programme in which 10,000 laboratories participate, using Microsoft EXCEL.
- MCS is used to perform random sampling from the probability density function (PDF) of the input variables (assigned value, sample homogeneity, repeatability of a reference laboratory and method precision) to determine ***σ for which 95 % of the participating laboratories obtained acceptable z-scores***.

METHOD

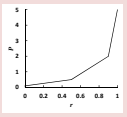
Assign parameters of input variables

- Assigned value, T_v
- Sample homogeneity, S_H expressed as a coefficient of variation (CV).
- Repeatability of a reference laboratory[2], P, expressed as a CV.

Generate random variables

- Value of analyte in sample received by laboratory i, m_i = NORMINV(RAND(), T_v, T_v*S_H)
- Method precision distribution[1], S_{Pi}: IF(r_i < 0.5,0.8*r_i + 0.1, IF(r_i < 0.9,3.75*r_i - 1.375, IF(r_i <=1, 30*r_i - 25)))* P

where r_i is a uniformly distributed random number between 0 and 1.



Implementation of Monte Carlo Simulation using Microsoft EXCEL

Input variables	Symbol	Value
Assigned value	T_v	0.957
Sample homogeneity	S_H	0.0025
Repeatability of a reference lab	P	0.0225
MCS CV (%)		3.3
MCS σ		0.031581

Lab #	Value of as received by laboratory i m_i	Method Precision r_i	Method Precision S_{Pi}
1	0.95984	0.25240	0.006793
2	0.95566	0.03968	0.002964
3	0.95992	0.58928	0.018783
4	0.95563	0.67539	0.026048
⋮	⋮	⋮	⋮
N	m_N	r_N	S_{PN}

Output	Symbol	Value
No. of labs with acceptable z- scores		9474
Proportion of labs with acceptable z-scores	Y	0.95

Measurement result reported by laboratory x_i	z-score z_i
0.962507071	0.17
0.956210445	-0.03
0.956247586	-0.02
0.930251575	-0.85
⋮	⋮
x_N	z_N

Determine MCS σ

- Measurement result reported by laboratory, x_i = NORMINV (RAND(), m_i, m_i * S_{Pi})
- Initial value of $MCS\ CV$ (%) = 150*P
- MCS σ = T_v . $MCS\ CV/100$
- Calculate *z*-score from result reported by laboratory and MCS σ . $z_i = \frac{x_i - T_v}{\sigma_{MCS}}$
- Carry out further iterations of MCS σ until proportion of participating laboratories with acceptable *z*-scores, Y = 95% (COUNTIFS(*range*,">=-2",*range*,"<=2")/N)
- When the number of Monte Carlo trials, N = 10,000, variability is about 0.2 % for ten repeated simulations of Y.

RESULTS AND DISCUSSION

Comparison of *z*-score distribution between prescribed and MCS CV for participating laboratories in the HSA 2013 EQA programme at three different concentration levels (n > 60).

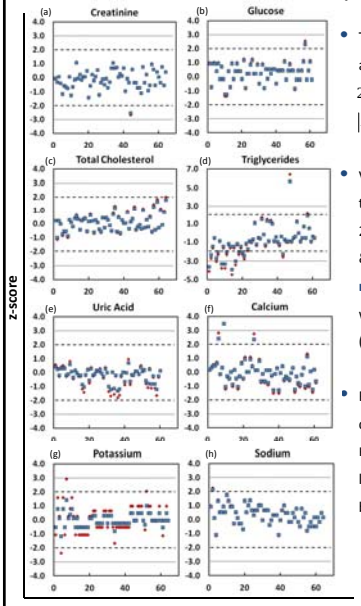


Fig. 1. *z*-Score distribution for the analytes (a) creatinine (b) glucose (c) total cholesterol (d) triglycerides (e) uric acid (f) calcium (g) potassium and (h) sodium using the prescribed (♦) and MCS σ (■). The prescribed CVs were determined from the pooled robust CV of the participating laboratories' data collected over several cycles of the programmes organised in 2011 and 2012, rounded up to the nearest 1.0 %.

- The classification of *z*-scores is as follows: $|z| \le 2$ (acceptable); $2 < |z| \le 3$ (questionable) and $|z| > 3$ (unacceptable).
- Variations of the MCS CV against the prescribed CV are less than 20% for all analytes (Columns 4 & 5 of Table 1) resulting in **minor changes** to the *z*-score, with the exception of potassium (Fig. 1 g).
- For potassium, the *z*-scores changed by about 50 %. However, only three out of > 60 laboratory results were affected by the change in classification.

Table 1. Repeatability of a reference laboratory, worldwide reproducibility, MCS CV and prescribed CV for each analyte.

Analyte	Repeatability of a reference laboratory (%)	Worldwide reproducibility based on Biorad QC data^(%)	MCS CV determined using our proposed simulation technique (%)	Prescribed CV used in HSA 2013 EQA programme (%)
Creatinine	4.30	8.10	6.3	6.0
Glucose	2.22	4.21	3.3	3.0
Total cholesterol	2.34	5.49	3.4	3.0
Triglycerides	2.29	6.29	3.4	3.0
Uric Acid	3.77	4.17	5.5	4.0
Calcium	2.37	3.37	3.5	3.0
Potassium	**2.81**	**2.84**	4.1	2.0
Sodium	1.43	1.67	2.1	2.0

^Data was computed from the Unity Worldwide report based on the Biorad Multiqual Liquid Assay obtained from August 2012 to June 2014. The worldwide reproducibility (pooled CV obtained from different concentrations, instruments, methods and laboratories) is almost two times that of the repeatability of a reference laboratory (pooled CV obtained from different concentrations but measured on the same instrument and method in a single laboratory) for a majority of analytes except ***potassium***.

- The repeatability of a reference laboratory (Column 2) should ideally be less than the worldwide reproducibility (Column 3). Column 2 is used in the MCS technique to determine the CV (Column 4) which is compared against the prescribed CV (Column 5).
- The MCS CV has to be ***calculated with caution***. The repeatability of the reference laboratory is an important factor in the determination of MCS CV.

REFERENCES

1. Wong, S., Evaluation of the use of consensus values in proficiency testing programmes. *Accredit. Qual. Assur.* **2005**, *10* (8), 409-414.
2. Ramamohan, V., Yih, Y., Abbott, J.T., Klee, G.G., Category-specific uncertainty modelling in clinical laboratory measurement processes. *Clin. Chem. Lab. Med.* **2013**, *51*(12), 2273-2280.

CONTACTS

Corresponding author: Dr Gina Chew (Email: Gina_CHEW@hsa.gov.sg Tel: +65 67751605 ext 105)
Presenter: Ms Cheow Pui Sze (Email: CHEOW_Pui_Sze@hsa.gov.sg Tel: +65 67751605 ext 112)

Health Sciences Authority. All Rights Reserved