



# Serum creatinine assays: performance against requirements for GFR estimation



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## Background

- The Australasian Creatinine Consensus Working Group has recommended a total error for serum creatinine measurement of  $\pm 15\%$  for suitability for use in estimation of GFR with the MDRD formula<sup>1</sup>.
- Total error must include variation due to imprecision from the following sources:
  - within instrument
  - between different instruments of the same type
  - between different methods
  - variation in assay specificity.
- Results from QAP programs may be sub-optimal for assessing creatinine assay performance due to possible matrix effects given the limitations in analytical specificity of Jaffe creatinine assays.

## Aims

- To assess the total error of serum creatinine measurements for common methods in routine use in Australia using pools of patient samples.
- To assess the suitability of results from the RCPA-AACB Quality Assurance Program for comparing serum creatinine assays.

## Methods

- 11 pools of serum or heparin plasma were prepared covering a range of creatinine concentrations.
- Aliquots were sent to 13 laboratories and run on 20 different instruments.
- Major suppliers represented included Abbott, Beckman-Coulter, Dade-Behring and Roche (see table below for full details).
- Laboratories analysed the samples and returned the results together with creatinine results from the then current RCPA-AACB General Chemistry Quality Assurance Program.
- Sample and QAP data was analysed for total variation of the results and method bias compared to the group mean.

Supplier	Instrument	Principle	Number
Abbott Architect	c8000	Jaffe	1
Beckman-Coulter	CX3	Jaffe	1
Dade-Behring	RxL	Jaffe	1
Dade-Behring	Expand	Jaffe	1
Dade-Behring	ARx	Jaffe	1
Dade-Behring	ARx	Enzymatic *	1
Ortho Clinical Diagnostics	V250	Enzymatic	2
Ortho Clinical Diagnostics	V950	Enzymatic	1
Roche	Modular	Jaffe	6
Roche	Integra	Jaffe	2
Roche	Integra	Enzymatic	1
Roche	Hitachi 917	Enzymatic	1
Roche	Hitachi 917	Jaffe	1

\* Using Randox enzymatic reagents

Table. Suppliers, equipment and reagents. With the exception of the Randox reagents noted, the instrument manufacturers reagents were used.

## Results 1

- The raw data for all patient samples is shown in figure 1 as a difference plot compared with the  $\pm 15\%$  limits.
- COMMENT:** All results are within the  $\pm 15\%$  target.
- Figure 2 shows the scatter of the lines of best fit for each instrument.
- COMMENT:** By comparison with the total variation (seen in figure 1) it can be seen that the between-method and between-instrument is a significant contributor to total error.
- Figure 3 shows the scatter due to between instrument variation (taken from the lines of best fit for each creatinine concentration) and the total scatter from the raw data.
- COMMENT:** This display confirms the importance of between-instrument and between-method variation as a component of total variation.

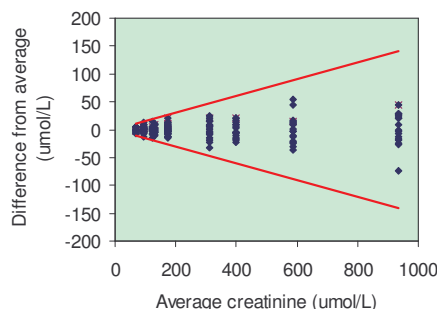


Figure 1: Difference plot of all results (raw data – average result for that sample) plotted against sample average. The red lines show + and – 15% differences.

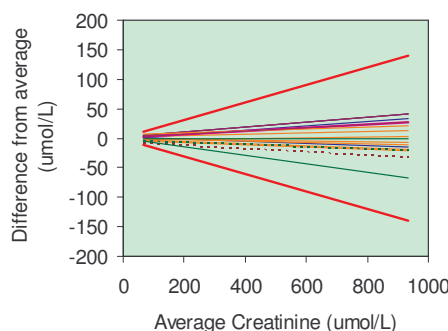


Figure 2: Lines of best fit for each analyser from the difference plot in figure 1. Each colour represents results from a different manufacturer. The red lines show + and – 15% differences.

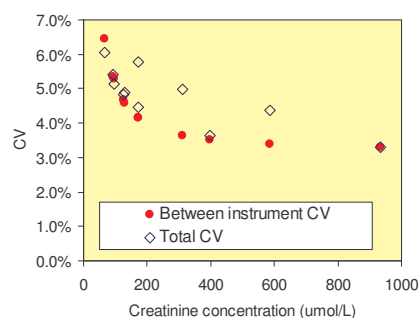


Figure 3. CVs for between instrument variation (taken from lines of best fit) and for total variation (taken from individual data points).

## Results 2

- The between-analyser CVs for the patient samples are compared with the between-analyser CVs for the QAP material in figure 4.
- COMMENT:** It can be seen that the scatter for QAP results is considerably higher than for patient data at both low and high creatinine concentrations.
- The slopes of the lines of best fit for QAP data are compared with the slopes for patient data in figure 5.
- COMMENT:** It can be seen that the QAP material produces a much wider scatter of slopes than the patient material – consistent with a matrix effect.

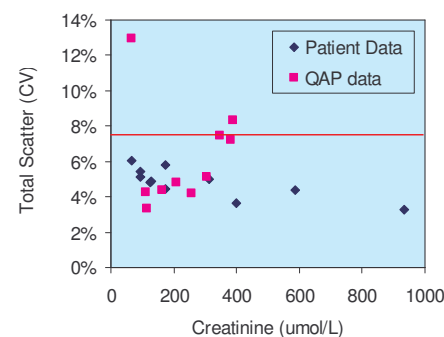


Figure 4: Between-analyser CV for patient data and QAP data plotted against creatinine concentration. The red line is a CV of 7.5% corresponding to a scatter of  $\pm 15\%$ .

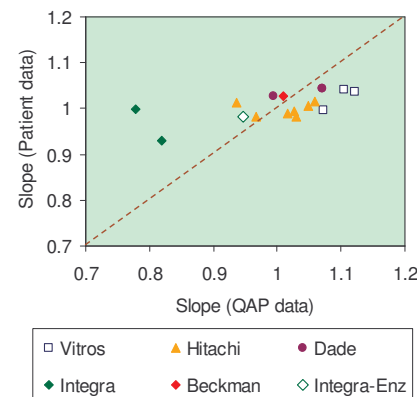


Figure 5: Slopes of lines of best for patient samples plotted against slopes for QAP material. Each is the slope against the average results.

## Conclusions

- Current assays, when assessed using patient material, are likely to meet total error requirements for application of the MDRD equation.
- Note that this does not exclude assay non-specificity.
- QAP material is not suitable for comparing total error when different methods are used.

## Acknowledgement

I acknowledge the support of the NSW QC Subcommittee and thank the various laboratories for their enthusiastic response in performing the assays.

(1) Medical Journal of Australia 2005;183:138-141.