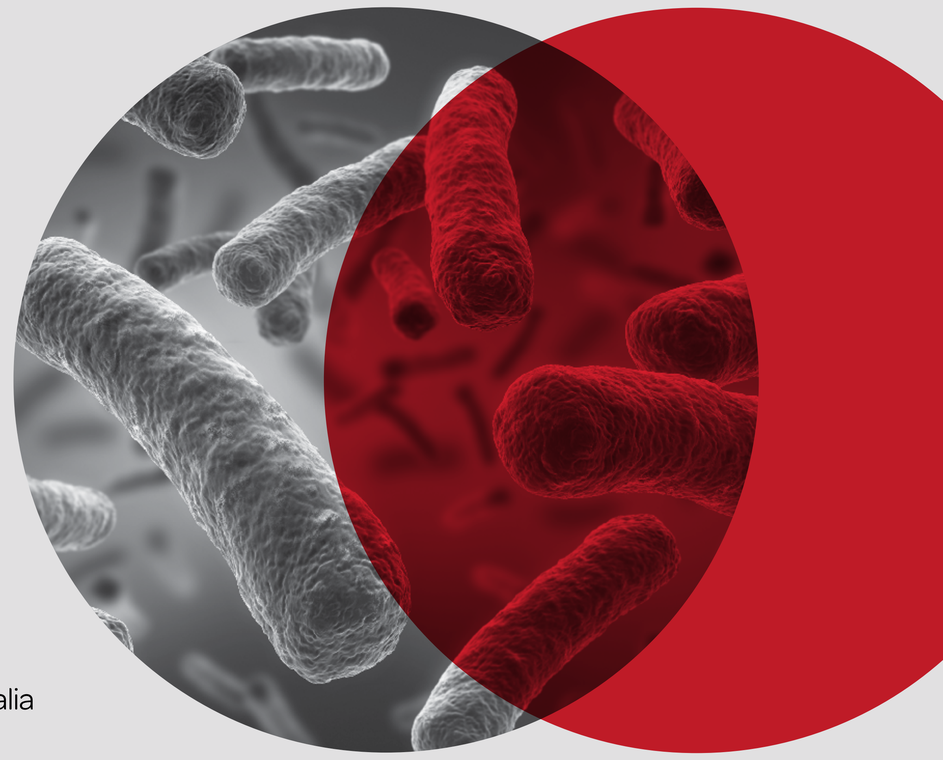
One Size Doesn't Fit All: Lessons from a Procalcitonin External Quality Assurance Program



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Introduction

Sepsis accounts for approximately 20% of global deaths, and early diagnosis is a critical factor in intervention. Procalcitonin (PCT) is an established biomarker for bacterial infection and algorithms utilising PCT measurement and antibiotic therapy in various clinical scenarios have been proposed[1]. A recent review of PCT EQAs, including the RCPAQAP's PCT program, has highlighted variable performance between assays[2]. If this is the case; the use of generic algorithms may not be appropriate if method variation occurs at clinical decision limits. This study aims to assess method variation in PCT reporting in the RCPAQAP's PCT program.

Method

Data submitted for the 2019, 2020 and 2021 RCPAQAP PCT program were reviewed. Material for this program is commercially sourced lyophilised serum (Aalto Scientific Ltd, USA). Quantitative data were assessed using a two-way analysis of variance with Tukey's multiple comparison test for each survey (based on instrument manufacturer with sufficient sample sizes). The sensitivity and specificity of the semi-quantitative PCT method to identify low (<0.5ng/mL) and high (≥2.0 ng/mL, ≥10.0 ng/mL) risk/likelihood of sepsis was also assessed compared to the quantitative results.

Results and Discussion

Roche Diagnostics instruments were the dominant group reporting for quantitative PCT, followed by Abbott (Table 1). The semi-quantitative Thermo Scientific BRAHMS PCT-Q labs comprised 24%, 25%, and 17% in 2019, 2020 and 2021 respectively.

A significant increase in CV% was observed in 2020 and 2021 (average ~19%) program years compared to 2019 (13%) (p=0.0119) (Figure 1). This increase coincided with changes in methods used within the program, an increase in Beckman Coulter and Siemens instruments users reported in 2020/2021.

At PCT levels <0.5 ng/mL, no difference was observed between Roche/Abbott, Roche/bioMerieux, Abbott/bioMerieux or Beckman Coulter/Siemens, however significant differences were observed for all other comparisons (Roche/Beckman Coulter, Roche/Siemens, and bioMerieux/Siemens p<0.001; Abbott/Beckman Coulter, Abbott/Siemens, and Beckman Coulter/bioMerieux p<0.0001).

At PCT levels 1.0–2.0 ng/mL, all methods performed significantly different to one another (p<0.0001) except bioMerieux and Siemens which were not significantly different (Abbott/Siemens and Beckman Coulter/bioMerieux p<0.01; all other comparisons p<0.0001).

At PCT levels 5–10 ng/mL, Beckman Coulter/Siemens and Roche/Abbott were not significantly different from one another while all other comparisons were significantly different (Beckman Coulter/bioMerieux p<0.05; Abbott/bioMerieux and bioMerieux/Siemens p<0.001; all other comparisons p<0.0001).

At 10 ng/mL, all methods had significant variation from one another (Beckman Coulter/bioMerieux p<0.01; Beckman Coulter/Siemens p<0.001, all other comparisons p<0.0001) except Roche and Abbott which were not significantly different.

For PCT levels >10 ng/mL, no difference was observed between Roche/Abbott while significant differences were observed for all other comparisons (Beckman Coulter/bioMerieux p<0.001, all other comparisons p<0.0001).

In general, the PCT concentrations reported by Beckman Coulter, bioMerieux, and Siemens were higher compared to Abbott and Roche instrument users (Figure 2).

The sensitivity and specificity of the semi-quantitative PCT method to identify low and high risk of sepsis were calculated. For PCT levels <0.5 ng/mL (low risk of sepsis), the average sensitivity was 99% and average specificity 30% with 57–85% of semi-quantitative users reporting a higher PCT range. For PCT levels >2.0 ng/mL (high risk of sepsis), an average sensitivity of 83% and average specificity of 80% was calculated with 8–38% of semi-quantitative users reporting a different PCT range to the quantitative mean.

Conclusion

This review of the RCPAQAPs 2019–2021 PCT program data clearly demonstrates method variation in the quantitation of PCT at all levels. Validation of PCT decision intervals for bacterial infections, including sepsis, and algorithms for antibiotic use may be required. Variable performance of the semi-quantitative method, both at low and high PCT concentrations, brings into question the clinical utility of this point-of-care test. A limitation of these findings is the unproven commutability of the EQA material. Future RCPAQAP PCT programs should include PCT levels at common clinical decision points 0.5 and 1.0 ng/mL to allow further review of method variation.

Table 1. Method breakdown for the RCPAQAP Procalcitonin Program (2019–2021).
** Semi-quantitative method (Thermo Scientific BRAHMS PCT-Q)

	Procalcitonin Method (% program participants)						
	Abbott	Beckman Coulter	bioMerieux	Ortho-Clinical	Roche	Siemens	Thermo Scientific**
2019	20	2	14	0	39	0	24
2020	18	6 ⇧	11	2	29	8 ⇧	25
2021	19	11 ⇧	8	3	33	8	17

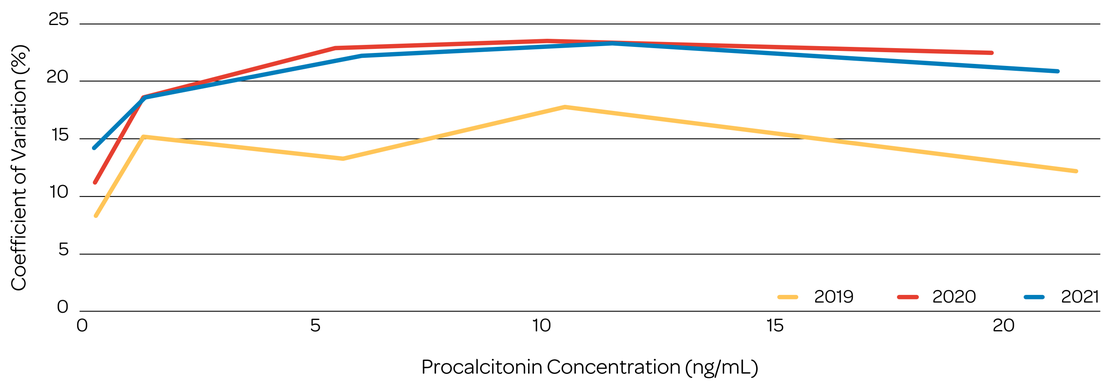

Figure 1. Coefficients of Variation for the RCPAQAP Procalcitonin Program (2019–2021).

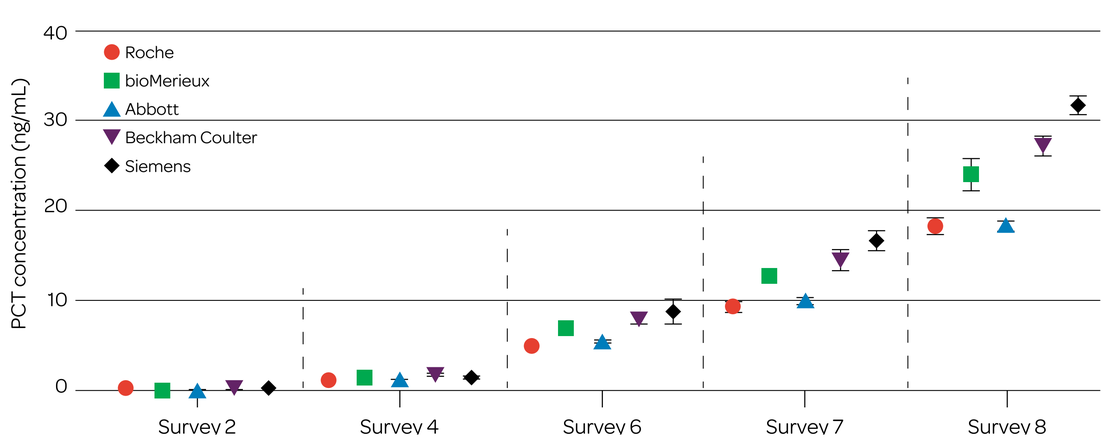

Figure 2. Method variation in PCT reporting in the 2021 RCPAQAP Procalcitonin Program.

References:

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