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6.1.2.4 Analytical Goals for Accuracy and Precision of Plasma Creatinine Determinations Evaluated by Reference Method Measurements

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ABSTRACT

Using approaches based on "medical needs" and biological variation, goals for analytical accuracy were assessed to 0.072-0.15 expressed as relative deviations, and goals for analytical precision were estimated to 0.022-0.14 expressed as relative standard deviations. A representative clinical method was evaluated using a reference method. On this basis, it is concluded that accuracy goals are fulfilled at high but not at low levels, and that precision goals are met according to medical needs but not with respect to biological variation.

INTRODUCTION

In the present paper goals for analytical accuracy and precision for P-Creatinine are evaluated. The clinical situation is the general task of monitoring renal function. As a starting point, several approaches for assessing goals are considered. With reference to these goals, a representative clinical method is evaluated using a reference method.

MODEL FOR EVALUATION OF QUALITY SPECIFICATIONS BASED ON MEDICAL NEEDS AND BIOLOGICAL VARIATION

Models based on medical needs usually focus on the situation depicted in Figure 1.

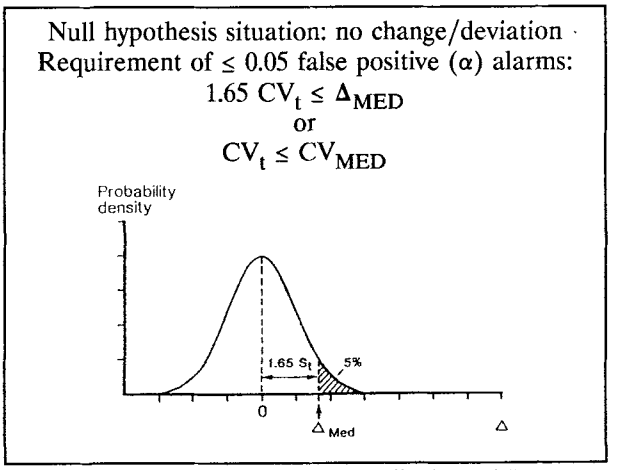

Figure 1. Model based on "medical needs".

In the so-called null hypothesis situation of no *true* change between two results or no *true* deviation from a fixed decision limit, we observe a distribution of *observed* changes or deviations because of analytical, pre-analytical and biological variations. The total standard deviation or coefficient of variation (CV_t) may be expressed as:

$$CV_t = \sqrt{CV_a^2 + CV_{pa}^2 + CV_b^2} \; (\times \sqrt{2}) \qquad \textbf{(Eq. 1)}$$

where CV_a is the analytical coefficient of variation, CV_{pa} is the pre-analytical coefficient of variation and CV_b is the biological coefficient of variation. The factor $\sqrt{2}$ is applied for differences between two results and omitted when dealing with a deviation from a fixed point (1).

Given a one-sided situation, a requirement for obtaining no more than 5 % false positive alarms is that:

$$1{,}65 \times CV_t \leq \Delta_{MED} \qquad \textbf{(Eq. 2)}$$

where Δ_{MED} is the change considered of importance by the clinicians. This is the situation that typically is used to derive analytical goals from clinical needs. For example, Skendzel et al. used this approach in their frequently cited paper (2). These authors, however, confused CV_t with CV_a, not taking biological and pre-analytical variation into account. On the basis of Eq. 2, it is possible to evaluate how much analytical bias and imprecision that are allowed in a given situation.

ANALYTICAL GOALS FOR P—CREATININE

First, analytical goals for accuracy are considered. Concerning the model based on "medical needs" we derive the goal as outlined in Figure 2.

The value for Δ_{MED} has been attained from Skendzel et al. (2), CV_a has been assigned the state of art value in Denmark with CV_{pa} equal to half the analytical standard deviation and CV_b is a published value (1). As shown in the figure, the maximum allowable inaccuracy (ΔSE_c) is obtained as a difference, 0.16, expressed as a relative value. This accuracy goal may be compared with other traditional goals:

$$2 \times CV_a = 0.072$$

as suggested by Stamm (3), and

$$0.15$$

which is used in proficiency test programs (4).

Analytical goals for accuracy
Derived from "medical needs" (Skendzel et al)

CV_{MED} = $\Delta_{MED}/1.65$ $\alpha = 0.05$
(0.16) $\Rightarrow$ $\Delta_{MED} = 0.259$

$CV_t = \sqrt{CV_a^2 + CV_{pa}^2 + CV_b^2} = 0.60$

$0.036^2 + 0.018^2 + 0.044^2$

$\Delta SE_c = \Delta_{MED} - 1.65 \times CV_t \Rightarrow \Delta SE_c = 0.160$

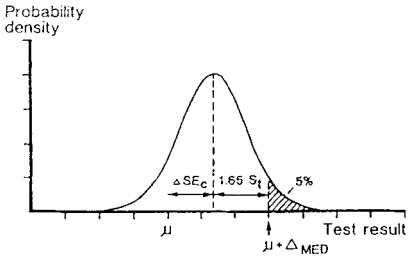

Figure 2. Analytical goals for accuracy derived from "medical needs"

Turning to analytical goals for precision (Figure 3), we may first consider the traditional one related to intra-individual biological variation, 0.022, which is a rather demanding criterion. The goal derived from "medical needs", 0.14, is a more liberal demand.

Analytical goals for precision

½ $CV_{intra\text{-}b}$ 0.022
From "medical needs" taking pre-analytical and biological variation into account:
$CV_t \leq CV_{Med}$ (0.16)

$CV_t = \sqrt{CV_a^2 + CV_{pa}^2 + CV_b^2}$
(0.16) $(1/2\ CV_a)^2\ (0.044^2)$
$\Rightarrow CV_a = 0.14$

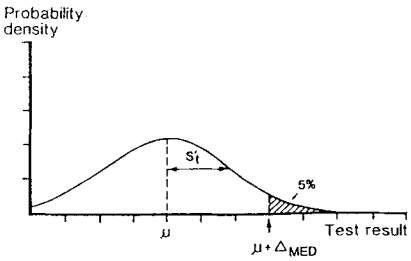

Figure 3. Analytical goals for precision.

ANALYTICAL QUALITY FOR P—CREATININE EVALUATED

The performance of a typical clinical method for P—Creatinine was evaluated using a reference method. The clinical method was based on the kinetic picrate principle (a Boehringer Mannheim test kit) and run on a Hitachi 717. The reference method was based on a combination of HPLC and enzymatic detection (5). Parallel measurement of N = 72 patient samples with values from 50 to 1 200 μmol/l yielded the following relation (least squares linear regression) (Figure 4):

$$Y = 0.94X + 16.5 \ \mu\text{mol/l}$$

where X is the reference method value and Y is the value obtained by the clinical method.

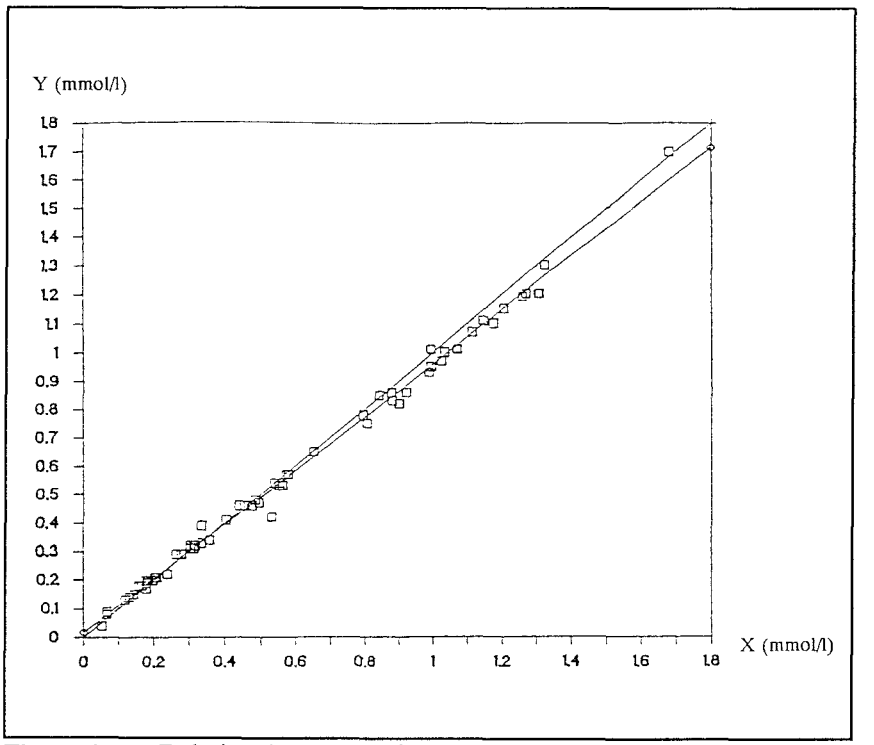

Figure 4. Relation between reference method measurements (X) and measurements by a clinical method (Y).

As shown in Table 1, the relation implies relative deviations ranging from +0.27 to -0.04.

Table 1. Examples of relations between reference method measurements (X) and measurements by the clinical method (Y).

X (μmol/l)	50	100	1 000
Y (μmol/l)	63.5	110.5	956
Rel. DEV	+0.27	+0.10	-0.04

Table 2 displays the relation between reference method values and averages of clinical laboratories observed in the surveys of the Danish Society for Clinical Chemistry using human, liquid serum pools. The relative deviations extend from +0.19 to +0.01. Table 2 also shows that the average intra-laboratory coefficients of variations range from 0.033 to 0.038.

Table 2. Results of a survey involving clinical laboratories in Denmark.

Ref. method value (μmol/l)	Average of routine methods (N = 160) (μmol/l)	Rel. DEV	Average $CV_{intra-lab}$
74.0	87.9	+0.19	0.038
126	134.2	+0.07	0.033
252	254.5	+0.01	0.036

The conclusion of the evaluation is that accuracy goals for P—Creatinine are fulfilled at moderate to high levels, and that precision goals are met according to "medical needs" but not according to biological variation ($\leq 0.022 = \frac{1}{2} CV_b$). The establishment of quality control systems designed to detect deviations from the goals has been considered previously (1).

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