The Journal Of The International Federation Of Clinical Chemistry And Laboratory Medicine
eJIFCC

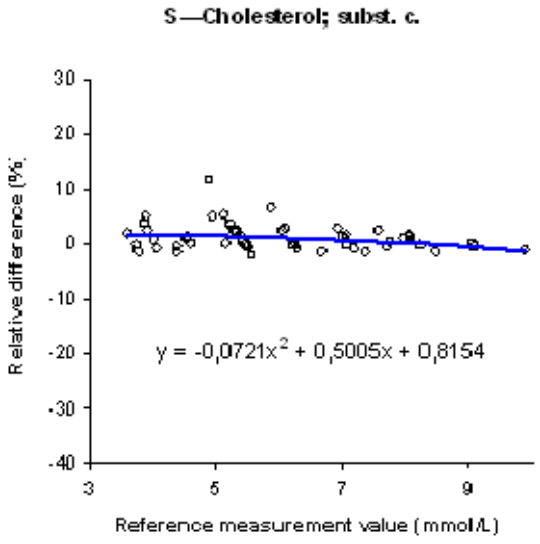
Estimating systematic error of measurement procedures of lipid quantities

Mariona García-Panyella, Sarela García-Santamarina, Xavier Fuentes-Arderiu*

Laboratori Clinic
IDIBELL-Hospital Universitari de Bellvitge,
08907 L'Hospitalet de Llobregat
Catalonia Spain

* Corresponding author: Fax +33 93 260 75 46
E-mail: xfa@csub.scs.e

Systematic error, also called *bias*, is one of the most important metrological characteristics of a measurement procedure, and its eventual change have a direct impact in the interpretation of clinical laboratory results. An estimator of systematic error is the mean of a set of replicate results of measurement obtained in a control or reference material minus a true value of the quantity intended to be measured in this material. As such a true value is by nature unobtainable, in practice a conventional true value is used. The conventional true value of the control material can be an assigned value (obtained with a primary or reference measurement procedure), a consensus value or a procedure-defined value (1).



To estimate the systematic error we can use a control material having an assigned conventional true value. The best method to assign a conventional true value is by means of a primary or reference measurement procedure, but the easier and cheaper method is using a consensus value estimated in an external quality assessment scheme (2, 3). The consensus value is usually estimated as the mean or the median, after removal of outliers, of all the results submitted by individual participants when

measuring the same particular quantity in a given control material. A choice may be made between three kinds of consensus values: (i) the overall consensus value, which includes all results independently of the method of measurement; (ii) the method related consensus value, which includes all results obtained with all measurement procedures based in the same method of measurement; and (iii) the measurement procedure ("kit") related consensus value. This choice should be made depending on the kind of quantity under measurement. Examples: for substance concentration (metabolites, ions, steroid hormones, etc.) the overall consensus value is generally used; for catalytic concentration (enzymes) the method related consensus value is generally the best choice; and for arbitrary substance concentration (tumor markers, peptide hormones, etc.) the measurement procedure (corresponding to a particular "kit") related consensus value in some cases is the only logical choice.

The reports of the external quality assessment scheme RIQAS (Randox Laboratories Ltd., UK), in the case of lipid quantities, have the three types of conventional true values for their control materials. This external quality assessment scheme is for one year; during this time, the organisers send twice a month two lyophilised control sera corresponding to different lots, but each lot may be repeated. Bearing in mind this fact, we have compared the values assigned by means of reference measurement procedures with the overall consensus values for different control materials. This comparison gives information about the differences between the two conventional true values. This information will indicate if the use of the overall consensus value is really as good as the reference measurement value to estimate the systematic error.

We have revised all the reports from the mentioned proficiency testing program received in our laboratory from the year 2000 to the present involving the measurement procedures for the quantities shown in Table 1. During this period the number of clinical laboratories participating in the proficiency-testing program oscillated between 30 and 175. For each quantity, data from all reports have been grouped when belonging to the same lot of control material and the weighed means have been estimated. Finally we have obtained from 42 to 60 couples of conventional true values.

The differences between consensus values and reference measurement values have been studied using the linear regression least squares model. The parameters of the regression line for each quantity and its significance degree are shown in Table 1. There are significant constant differences between the two types of conventional true values in cholesterol, triglycerides and in HDL-cholesterol, in addition, in three cases (cholesterol, HDL-cholesterol and apolipoprotein B) there are significant proportional differences.

We have compared the two types of conventional true values using the Bland-Altman plots (4) and we have studied the relation between the relative differences of the two conventional true values and the reference measurement values (Figure 1). It should be noted that, for the quantities taken into account, to different control materials having similar reference measurement values correspond very different relative differences. This fact suggests that the *in vitro* diagnostic industry should improve the metrological

(analytical) specificity of the measurement procedures used for the quantities taken into account.

In opinion of the Committee on Analytical Quality of IFCC (3), practical experience has shown that the consensus value usually agrees closely with the true value in proficiency testing programs with a large number of participants but it may not be valid in programs involving small numbers of laboratories. However, according to our data, the use of the consensus value instead of the reference measurement value is not appropriate to estimate the systematic error, at least for measurement procedures related to the quantities involved in this study. Thus, we think that, whenever possible, the estimation of the systematic error should be done using a control material which have a conventional true value assigned by means of a primary or reference measurement procedure. Accordingly, we encourage the manufacturers of control materials to assign, whenever possible, reference (or primary if possible) measurement values; independently of these control materials are "assayed" or "unassayed" ones.

References

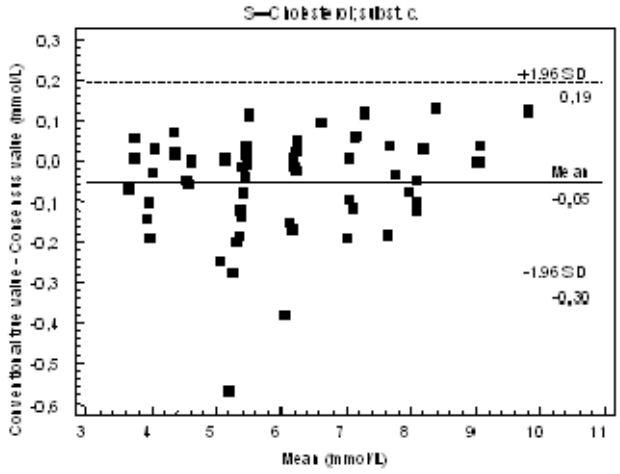
- 1. International Organization for Standardization. Clinical laboratory testing and in vitro diagnositc test systems - In vitro diagnostic medical devices - Information supplied by the manufacturer (labelling) - Part 1: General requirements and definitions. ISO/CD 18113-1. Geneva: ISO; 2005.
- 2. Counotte G, Van Dijk D, Van Loenen-Imming DC, Oussoren W, Van der Vat B, Visser RG, Boley N, Day J, Walker R. Selection, use and interpretation of proficiency testing (PT) schemes by laboratories - 2000. http://www.eurachem.ul.pt/guides/ptguide2000.pdf [Accessed 2006-05-23]
- 3. International Federation of Clinical Chemistry. Fundamentals for external quality assessment (EQA). Guidelines for improving analytical quality by establishing and managing EQA schemes. 1996. Examples from basic chemistry using limited resources. /divisions/EMD/Documents/Fundamentals-for-EQA.pdf [Accessed 2006-05-23]
- 4. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307-310.

Table 1 Parameters of the regression lines and their significance levels

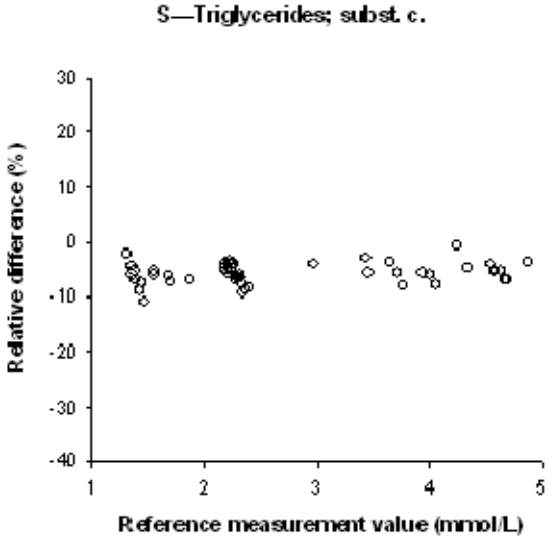
Quantities	*a*	P	*b*	*P*
S-Cholesterol; subst. c.	3,545	0,0049	-0,415	0,0385
S-Triglycerids; subst. c.	-6,627	<0,0001	0,365	0,1247
S-Cholesterol, in HDL; subst. c.	14,001	<0,0001	-9,877	<0,0001
S-Apolipoprotein B; mass c.	3,78	0,1687	-6,59	0,0024
S-Apolipoprotein A1; mass c.	4,39	0,2619	-0,66	0,7788

S = serum; subst.c. = substance concentration; mass c. = mass concentration; *a* = intercept; *b* = slope; *P* = significance level.

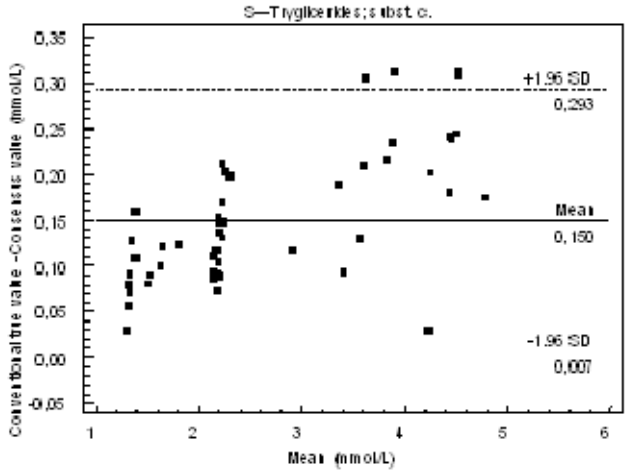
According to ISO, IFCC and IUPAC recommendations, the comma is used as the decimal sign.



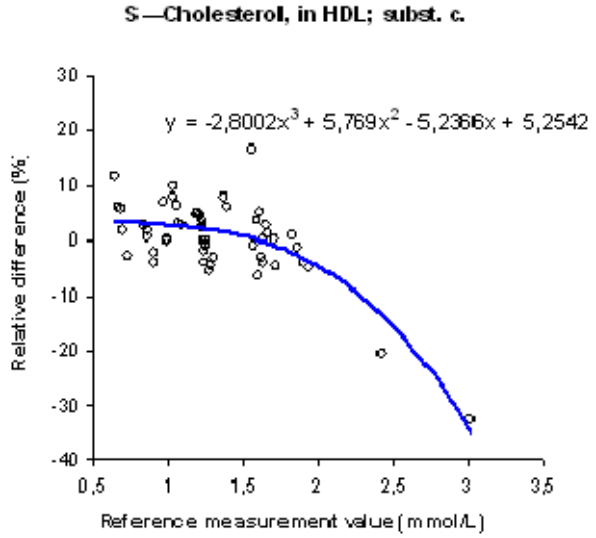
(a)



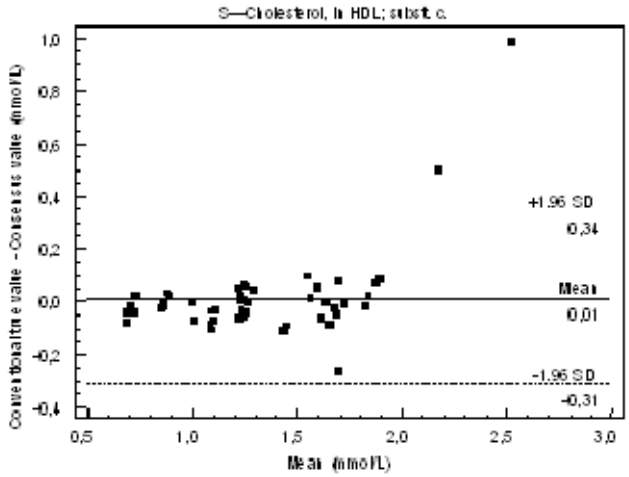
(b)



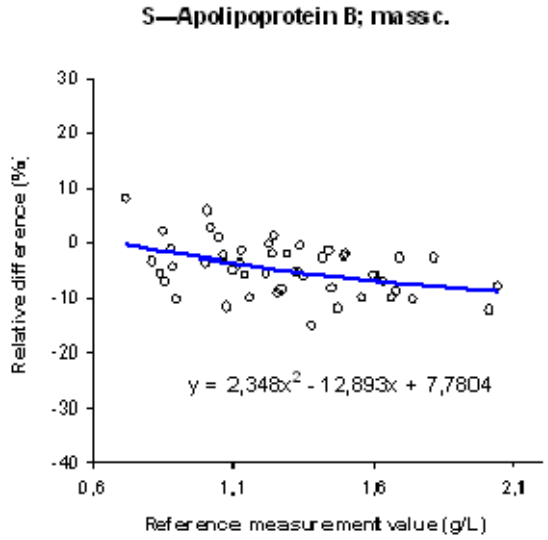
(c)


S—Cholesterol, in HDL; subst. c.
y = -2,8002x3 + 5,769x2 - 5,2366x + 5,2542
Relative difference (%)
Reference measurement value (mmol/L)

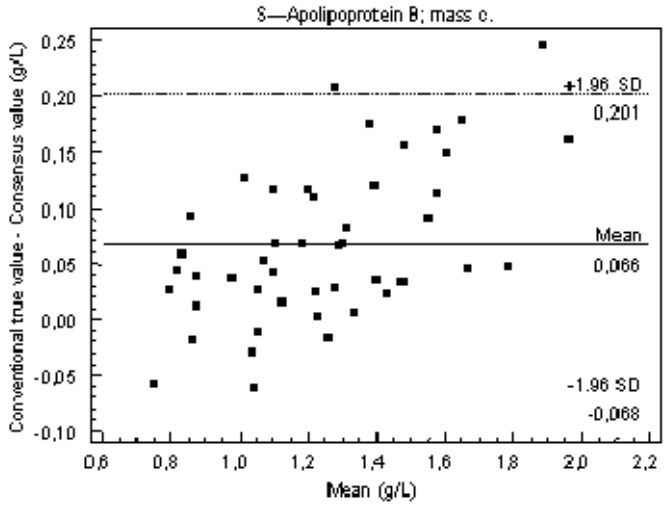
(d)


S—Cholesterol, in HDL; subst. c.
+1.96 SD
0,34
Mean
0,01
-1.96 SD
-0,31
Mean (mmol/L)

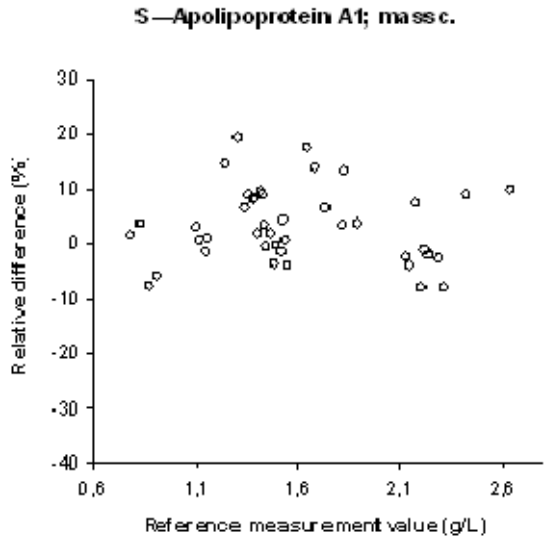
(e)


S—Apolipoprotein B; mass c.
y = 2,348x2 - 12,893x + 7,7804
Relative difference (%)
Reference measurement value (g/L)

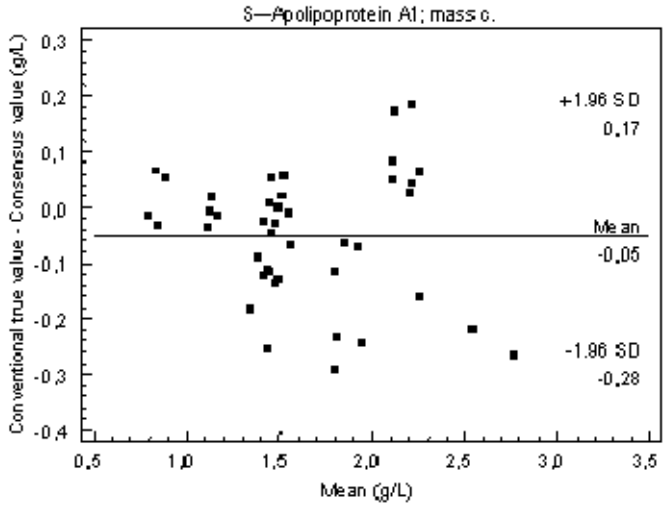
(f)


S—Apolipoprotein B; mass c.
Conventional true value - Consensus value (g/L)
Mean (g/L)
+1.96 SD
0,201
Mean
0,066
-1.96 SD
-0,068

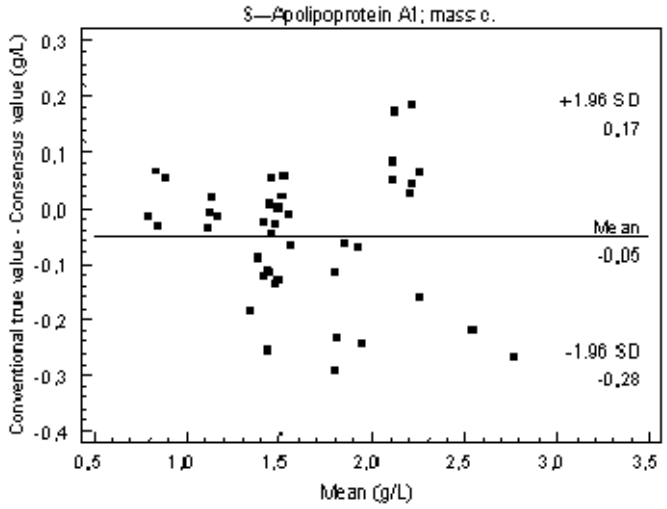
(g)


S—Apolipoprotein A1; mass c.
Relative difference (%)
Reference measurement value (g/L)

(h)


S—Apolipoprotein A1; mass c.
Conventional true value - Consensus value (g/L)
Mean (g/L)
+1.96 SD
0,17
Mean
-0,05
-1.96 SD
-0,28

(i)



(j)

Figure 1 Relation between the relative differences of the two conventional true values and the reference measurement values and Bland-Altman plots for each quantity. S = serum; subst.c. = substance concentration; mass c. = mass concentration. [According to ISO, IFCC and IUPAC recommendations, the comma is used as the decimal sign.]