HARMONISATION OF THE DILUTION FACTOR IN THE FACTOR VIII INHIBITOR TEST IMPROVES THE BETWEEN-LABORATORY COMPARABILITY

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Piet Meijer [1], Lotte Keetels [2],Moniek de Maat [1,3], Bert Verbruggen [1], Matthijs van Leeuwen [2].

1. ECAT Foundation, Voorschoten, The Netherlands; 2. University of Nijmegen, Dept. of Behavioural Psychology, Nijmegen, The Netherlands; 3. Erasmus University Medical Center, Rotterdam, The Netherlands

Introduction and Objectives:

The comparability of Factor VIII Inhibitor test results is hampered by a large between-laboratory variation (30-60%) in the surveys of the external quality assessment programme (EQAP) of the ECAT Foundation[1]. In a small study it has recently been suggested that harmonisation of the dilution factor of the patient sample advances the between-laboratory comparability of test results[2]. Previous communication to participants in the ECAT programme about the appropriate use of the dilution factor learned that the majority of participants did not follow these recommendations. Therefore we conducted a study to investigate how laboratories can be challenged to change their dilutions procedure.

Materials and Methods:

One month prior to a regular survey in the EQAP of the ECAT the participants were informed on the optimal dilution procedure. The total of 273 participants were divided into three equal groups. One group received a standard letter (control group), one group received a flyer with an attention-grabbing lay-out (intervention group) and one group received the standard letter in a flyer format (mixed group). The purpose of the three different methods of information was to determine how the method of providing information influenced the implementation of the required improvement. In the EQA survey two inhibitor samples were used: sample 1: 10 BU/mL (to be measured in 10 times dilution) and sample 2: 1 BU/mL (to be measured undiluted). Participants reported there obtained results together with the dilution factor used.

Recommended Dilution Factors:

Inhibitor range (BU/mL)	Dilution Factor
0.0 – 2.0	Undiluted
2.1 - 6.0	1 + 2
6.1 – 20.0	1 + 9
20.1 – 60.0	1 + 29

RESULTS

Use of recommended dilutions factors:

The table below shows the percentage of participants using the recommended dilution factors in regular ECAT surveys and the project-related survey.

	Low inhibitor (1 BU/mL)	High Inhibitor (10 BU/mL)	Both samples
Regular surveys	37.1%	2.4%	1.0%
Project survey	49.8%	17.9%	14.4%
	p = 0.002	p < 0.001	p < 00.1

The table below shows the relationship between the way laboratories were informed about the recommended dilution factors and the percentage of laboratories using these dilution factors.

	Low inhibitor (1 BU/mL)	High Inhibitor (10 BU/mL)	Both samples
Intervention group	51.9%	20.8%	18.2%
Mixed group	40.3%	15.6%	10.4%
Control group	57.3%	17.3%	14.7%
	p = 0.098	p = 0.694	P=0.381

These data show that clear instructions to participants may help to increase the number of laboratories using the appropriate dilution factors. On the other hand, specific attention-grabbing techniques have no significant benefit over regular information techniques.

The effect of recommended dilutions factors on the between-laboratory variation:

The table below shows between-laboratory variation (%) with and without using the recommended dilution factors (DF).

	Low inhibitor (1 BU/mL)	High Inhibitor (10 BU/mL)
Regular surveys	35 – 55%	30 – 40%
Project survey		
Overall	36.9%	33.6%
Recommended DF	30.0%	27.8%
Suboptimal DF	46.7%	35.1%
	p < 0.001	p = 0.039

The table below shows the relationship between the way laboratories were informed about the recommended dilution factors and the between-laboratory variation (%).

	Low inhibitor (1 BU/mL)	High Inhibitor (10 BU/mL)
Intervention group	34.1%	32.0%
Mixed group	43.0%	39.3%
Control group	33.9%	31.7%
	p < 0.025	p < 0.035

These data show that the intervention and control group did show a desirable effect, but the mixed group did not.

Conclusion:

The between-laboratory variation improved significantly when the recommended dilution factors are used. It is important that laboratories are clearly informed about the proper dilutions factors to be used for different inhibitor levels. However, the way of informing laboratory professionals seems to have no major effect on the implementation of test improvements.

References:

1. Meijer, P. and B. Verbruggen, *The between-laboratory variation of factor VIII inhibitor testing: the experience of the external quality assessment program of the ECAT foundation.* Semin Thromb Hemost, 2009. **35**(8): p. 786-93.
2. Verbruggen, B., et al., *The factor VIII inhibitor assays can be standardized: results of a workshop.* J Thromb Haemost, 2011. **9**(10): p. 2003-8.