UEG Week 2014

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How Good Should Quantitative FIT Analyses Be?

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Defining Analytical Quality Specifications

Expert Working Group (EWG) – 'FIT for Screening'
Short Discussion Document No. 4 –
Internal Quality Control & External Quality Assessment.

This document provides recommendations that will ensure acceptable international analytical performance in CRC screening, enable screening programmes to provide evidence that analysis is of adequate quality and enable and encourage publications that describe the use of FIT to include standardised information about analytical performance and quality.

http://www.worldendo.org/fit-ewg-publications.html

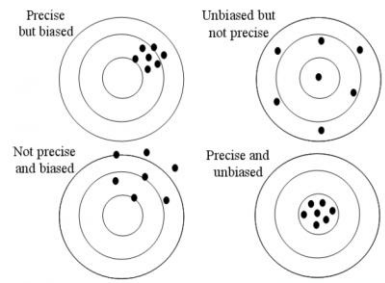
Performance Characteristics

Analytical performance characteristics are of two types:

- ***Practicability*** **-** include throughput, turnaround time of results, sample volume, stability of samples, stability of reagents and calibrators, skills required, and space and services.
- ***Reliability*** - include bias (a measure of how close the result is to a true value), precision (a measure of the random variation of the analytical method), working range (the range in which a valid result is obtained without any manipulation of sample or reagents), detection limit (the least amount that can be detected) and limit of quantitation (least measured to defined level of quality).

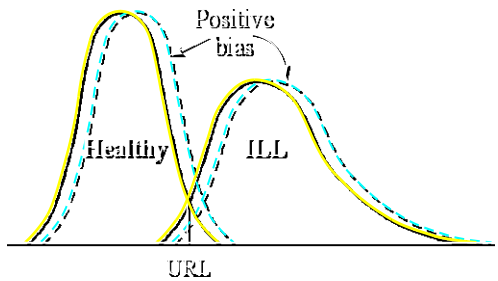
The analytical quality needed for FIT has received little attention.

Precision and Bias of a Measurement System



Both bias and precision have many effects on test results and their interpretation – need to define what is "acceptable" - AQS.

Effect of Bias on Clinical Characteristics



Consequence of Bias

POSITIVE	*NEGATIVE*
More false positives	Fewer false positives
Fewer false negatives	More false negatives
Higher sensitivity	Lower sensitivity
Lower specificity	Higher specificity

The Consensus Conference

Strategies to Set Global Quality Specifications in Laboratory Medicine

ifcc International Federation of Clinical Chemistry and Laboratory Medicine

IUPAC International Union of Pure and Applied Chemistry

World Health Organization

What Exists for Quantitative FIT?

1. Evaluation of the effect of analytical performance on clinical outcomes in specific clinical settings. **No**
2. Evaluation of the effect of analytical performance on clinical decisions. **No**
3. Published professional recommendations. **No**
4. Performance goals set by PT or EQAS organisers. **No**
5. Goals based on ***the current state of the art as in*** PT or EQAS or ***publications***. **Possible**

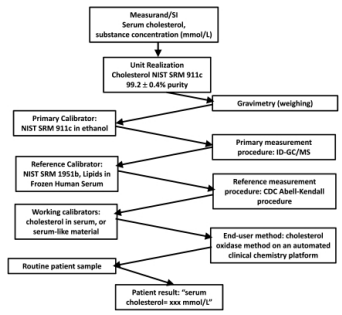
What is Acceptable Bias?

Zero! If bias exists and is known, then the results should be adjusted so as to be bias-free.

This really is the remit of manufacturers who should ensure "traceability".

"Faecal haemoglobin" should be just that!

Precision, in contrast, is inherent in analysis and cannot be eliminated – AQS needed!



Sources of Data on Precision

Manufacturers' IfU – usually "conservative"

Manufacturers' IQC materials

Kyowa Medex Co Ltd (150ADB)

Low	18-26	thus CV allowable = [(8/22)/3] x100]	=12.2%
High	75-111	thus CV allowable = [(36/93)/3] x100]	=12.9%

Eiken Chemical Co Ltd (01001)

Low	124-186	thus CV allowable = [(62/155)/3] x100]	=13.3%
High	504-756	thus CV allowable = [(252/630)/3] x100]	=13.3%

Sources of Data on Precision

Evaluations

GMEC

Carroll MRR, Piggott C, Pearson S, Seaman HE, Halloran SP. Evaluation of quantitative faecal immunochemical tests for haemoglobin. Guildford Medical Device Evaluation Centre (GMEC), Guildford, UK, 2013.

http://www.worldendo.org/fit-ewg-publications.html

Florence

Rubeca T, et al.

Sample	Number	Mean (µg/g)	SD (µg/g)	CV (%)
C1	64	61	3.8	6.7
C2	64	194	6.9	3.5

Sources of Data on Precision

Publications

The combined weighted CV obtained for the two analysers over the course of the study were 3.5 % at ca. 155 ng haemoglobin/mL buffer (n = 444) and 3.8 % at ca. 650 ng haemoglobin/mL buffer (n = 452).
McDonald PJ, et al. CCLM 2012;50:935.

The combined weighted coefficient of variation obtained was 4.0% at 25 µg hemoglobin/g feces (n = 594) and 4.1% at 90 µg hemoglobin/g feces (n = 594).
Auge JM, et al. Gastroenterology 2014;147:628.

A Standard for Faecal Immunochemical TesTs for Haemoglobin Evaluation Reporting (FITTER)
http://www.worldendo.org/fit-ewg-publications.html

What is Acceptable Precision? What Next?

We know the current state of the art. Should we assume current analytical standards meet clinical needs? Should we do no more. Should we suggest a "round number"?

Investigate the effect of performance on outcomes and set objective analytical quality specifications –
BUT – who decides what are acceptable outcomes?

Set up a Working Party of this EWG to prepare a discussion document for consideration by the EWG at a future meeting? Providers of data? Volunteers?