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How Good Should Quantitative FIT Analyses Be?

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Defining, in numerical terms, how good quantitative FIT should be has been addressed previously by the Expert Working Group (EWG) on 'FIT for Screening in 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. See: www.worldendo.org/fit-ewg-publications.html

Analytical performance characteristics are of two types. 1. Practicability – includes throughput, turnaround time for results, sample volume, stability of samples, stability of reagents and calibrators, skills required, and space and services. 2. Reliability – includes 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 amount measured to defined level of quality). Bias and precision have many effects on numerical test results and their interpretation. For example, positive bias leads to more false positives, fewer false negatives, higher sensitivity and lower specificity, while negative bias leads to fewer false positives, more false negatives, lower sensitivity and higher specificity. There is a need to define what is acceptable bias and precision, namely, analytical quality specifications. It is impossible to undertake quality control, quality assessment, quality assurance or quality improvement unless the desired quality is defined

The setting of analytical quality specifications in laboratory medicine has been a topic of discussion and debate for over 50 years. Fifteen years ago, as the subject matured and a profusion of recommendations appeared, many of them from expert groups, it was realised by a number of leading professionals that there was a need for a global consensus on the setting of such specifications. The Stockholm Conference held in 1999 on ''Strategies to Set Global Analytical Quality Specifications in Laboratory Medicine'' achieved this and advocated the ubiquitous application of a hierarchical structure of approaches. The hierarchy has five levels, namely: 1. Evaluation of the effect of analytical performance on clinical outcomes in specific clinical settings; 2. Evaluation of the effect of analytical performance on clinical decisions in general; 3. Published professional recommendations from expert bodies; 4. Performance goals set by regulatory bodies or organizers of external quality assessment (EQA) schemes; 5. Goals based on the current state of the art. This approach has been much used since its wide promulgation.

It is widely recognised that the goal for bias is zero! If bias exists and is known, then the results should be adjusted so as to be bias-free. However, bias is considered to fall within the remit of

manufacturers who should ensure “traceability” and “faecal haemoglobin” should be just that! Precision, in contrast, is inherent in analysis and can be minimised through a variety of strategies, but not eliminated, so that quality specifications are needed. There are many data in the literature on the precision achieved. Should it be assumed that the current analytical standards meet clinical needs? Should no more be done? Should the effect of performance on outcomes be used to set objective analytical quality specifications, but who decides what acceptable outcomes are? Should a Working Party of this EWG prepare a discussion document for consideration by the EWG at a future meeting?