FIT analytical standardisation and harmonisation

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Possible conflicts of interest

• None to declare
Haemoglobin - Globin

- Antibody recognition of the tertiary structure produced by the folding of the amino acid chain in the globin protein.

FIT being used in screening and symptomatic populations

Slide from Stephen P Halloran
Qualitative and quantitative FIT
FIT laboratory challenges

- No assay standardisation
  - Different buffers
  - Different antibodies
  - Different calibration
- No primary reference material or method
- No established External Quality Assurance scheme
- No established independent Internal Quality Control
Pre-analytical Variability

Mass of faeces collected
- Stool isn’t homogenous
- “Pickers” from all manufacturers are different
- Inconsistent sampling techniques
- Instructions from manufacturers are different
- Stool consistency

Haemoglobin stability
- Storage and transit temperatures
- Buffer composition
Clinical impact of variability

• Consolidation of evidence from studies that use different FIT methods is challenging

• Screening programmes
  – Risk associated with implementing new programmes with pilot data from a different method
  – Comparison of data from different populations
    • How can we compare if different methods are used with no standardisation

• Symptomatic FIT
  – Low cut-offs recommended in eg NICE guidelines
  – Impact of variation
WEO – FIT for screening

• 2011 – “Group of 4” set up WEO Expert working group on FIT for screening

Prof Jim Allison (USA)
Prof Stephen Halloran (UK)
Prof Callum Fraser (UK)
Prof Graeme Young (Australia)

“........ FIT EWG focuses on the implementation of FIT screening around the world and provides a platform to address issues around optimisation and tailoring of FIT in CRC screening programmes”
WEO – FIT for screening

- 4 discussion documents (recommendations) published circa 2012
  
  No. 1 – FIT standardisation
  
  No. 2 – FIT Reporting Units
  
  No. 3 - Stability of Hb
  
  No. 4 – Internal Quality Control and External quality assessment
  
  No. 5 – A Standard for Faecal Immunochemical Tests for Hb Evaluation Reporting (FITTER)
### WEO – FIT for screening

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| No. 5 – A Standard for Faecal Immunochemical Tests for Hb Evaluation Reporting (FITTER) |

WEO – FIT for screening

No. 1 – FIT standardisation

No. 2 – FIT Reporting Units

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No. 4 – Internal Quality Control and External quality assessment

No. 5 – A Standard for Faecal Immunochemical TesTs for Hb Evaluation Reporting (FITTER)
WEO – FIT for screening

**No. 1 – FIT standardisation**
Different manufacturers reference to different primary reference materials and different methods
**Implication** – even if the exact same homogenous sample is run on different analysers the result could be different

**No. 3 - Stability of Hb**
Storage and transit temperatures will vary.
Buffer composition different for each manufacturer
Need consistent studies to identify impact of these variables

**No. 4 – Internal Quality Control and External quality assessment**
To ensure accuracy and precision of an assay it is important to run EQA (accuracy) and IQC (precision) materials
Challenges of finding suitable matrices and the challenge of preloading samples has meant successful EQA/IQC schemes are not yet available for labs to subscribe to
**Implication** – unable to assess if getting the correct result
WEO EWG FIT for screening – 2017

• Meeting of experts sharing research and information related to the field of FIT for screening

• 2 meetings a year – Europe and US

• Very well attended symposium of experts – clinical and scientific

• No longer the most suitable forum to work on detail of assay standardisation etc
“Advancing excellence in laboratory medicine for better healthcare worldwide”

IFCC Scientific Division;

Mission Statement
The mission of the SD is to advance the science of Clinical Chemistry and to apply it to the practice of Clinical Laboratory Medicine.

SD Strategy….

• Identify scientific and technological problems in current practice and provide solutions and guidelines on how to resolve them.
IFCC FIT Working Group
(International Federation of Clinical Chemistry)

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Initial Terms of Reference
- To attempt to standardize analysis of haemoglobin in faecal samples by immunochemistry (FIT)
- To identify all sources of pre-analytical variation and standardise if possible
- To establish external quality assurance and third party internal quality control programmes
- To determine impact of assay interference of Hb variants and other factors

First meeting held in Athens in June 2017
2nd meeting held in Barcelona in October 2017
Progress....

• To attempt to standardize analysis of haemoglobin in faecal samples by immunochemistry (FIT)
  – Ingrid Zegers (Joint Research Centre of European commission, Belgium) starting process of developing a reference material/method.
  – Survey been sent to all manufacturers represented on the group to confirm current practices and needs in terms of traceability of testing for Hb in faeces

• To identify all sources of pre-analytical variation and standardise if possible
  – Natasha Djedovic (UK) drafted summary document of pre-analytical variables for discussion and to enable priorities to be addressed

• To establish external quality assurance and third party internal quality control programmes
  – Samantha Jones (WEQAS, UK)
  – Group are drafting recommendations for EQA companies

• To determine impact of assay interference of Hb variants and other factors
  – Share papers and research
  – Discuss how to prioritise, progress and fund any research
Barcelona meeting update....
Essentialism vs Consequentialism

(Prof Patrick Bossuyt)

“the theory that the value of a marker or a medical test should be judged by the ‘trueness’ of its results”

“the theory that the value of a marker or a medical test should be judged by the value of its consequences”

FIT

Need to ensure the analytical process is:
• scientifically robust
• deficiencies understood
• Work towards improving things

IFCC working group

• patients are appropriately categorised
Photo credit: Petr Kocna