Quantitative immunochemical tests: evidence on accuracy and implementation considerations in the Czech MUDr. Petr Kocna, CSc.
Quantitative FIT are replacing traditional guaiac FOBT in population screening programs for many reasons.

- Quantitative FIT achieves 90% sensitivity for CRC detection and is therefore at least 3 times more sensitive than guaiac test.

- Quantitative FIT needs to be optimised for population screening with professional, epidemiological and economic aspects.

- Quantitative FIT offer much more than just FOBT+/FOBT- results, and FIT cut-off could significantly modify the screening programs.

- Quantitative FIT are developed over 20 years, and over the past 20 years there are 5189 publications in MEDLINE (09/2017).
Quantitative one FIT test (NS-Plus, Alfresa) with cut-off $\geq 10 \mu g/g$

20 322 FIT positive subjects underwent colonoscopy.

Cut-off $\geq 10 \mu g/g$ with all adenoma detection exceeds national recommendations and endoscopic sources need to be considered.
FIT ANALYSIS, FAECAL Hb CONCENTRATION, CUT-OFF

HEALTHY SUBJECTS

ADENOMA LOW-RISK

ADENOMA HIGH-RISK

COLORECTAL CANCER

Probability

0 10 20 30 40 50 60 70 80 90 100 110 120 140 160 μg/g

cut-off FIT

cut-off gFOBT
FIT 100 ng/ml
(20 μg/g)

FIT 200 ng/ml
(40 μg/g)

FIT 50 ng/ml
(10 μg/g)

FIT positivity 8 - 11%
Adenoma detection
approx. 50%
CRC detection - 6,7

Adenoma detection
approx. 30%
CRC detection - 4,7

gFOBT positivity 3 - 5%
CRC detection - 3,1

High false positivity
Decrease number of colonoscopies

Effort to increase
Sensitivity and
Higher financial
efficiency
Standardization of FIT analysis
Transferability of FIT analysis results
External quality control of FIT analysis

Accuracy and reliability of Hb analysis in stool

Determine sensitivity - rate of detected neoplasma /CRC
Determine specificity - the numbers of 'unnecessary' colonoscopies
Decide required capacity of GE centers and screening costs
Faecal immunochemical tests for Hb are replacing traditional guaiac faecal occult blood tests in population screening programs for many reasons.

Many available faecal immunochemical test devices use a range of sampling methods, differ with sampling methods, buffer volume and characteristics, Hb stability and results are expressed by different way.

The current lack of consistency in units for Hb concentration is particularly problematic because apparently similar Hb concentrations obtained with different devices can lead to very different clinical interpretations.

Consistent adoption of an internationally accepted method for reporting results would facilitate comparisons of outcomes from these tests. We propose a simple strategy for reporting faecal Hb concentration.
First WG-FIT Meeting
Euromedlab Athens 14. June 2017

IFCC
Scientific Division Working Group
Fecal Immunochemical Testing (WG-FIT)

To harmonise and/or standardise analysis of haemoglobin in faecal samples by immunochemistry (FIT)
- External quality control in Korea - in 2015
- EQA analysis was conducted 3x during the year - 1,250 participants
- Qualitative tests - 569 participants (71%) - 9 different methods
- Qualitative tests provide false-positive results
- The success of the qualitative samples for negative sample was only 11%

- Quantitative FIT test - 235 participants (29%) - 7 different analyzers
- Totally different results depending on the technique used - in ng/ml

FIT REALIZED BY GENERAL PRACTITIONER IN CZECH - 2014

QUESTIONNAIRE
FOR PRACTITIONERS
n = 522

- g-FOBT 3%
- Laboratory FIT 7.5%
- POCT FIT 23.5%

Qualitative FIT 66% - 13 different methods - rapid tests

External quality assessment Hb determination in the stool started in January 2012, as a part of the national EQA programme provided by SEKK member of EQALM accredited ISO/IEC 17043:2010. 90 users in the Czech Republic. EQA in Czech Republic - 2 liquid samples, twice per year.
Data from cycle FOB 2016-01

- FOB Gold analysis
  - Sample A: 50 μg/g
  - Sample B: 140 μg/g

- OC-Sensor analysis
  - Sample A: 30 μg/g
  - Sample B: 80 μg/g

CV - 8.10 %
CV - 8.85 %

1.6x higher

April 2016

Eiken OC-Sensor
Sentinel FOB Gold


**Screening with cut-off** 15 μg/g according to OC-Sensor - Eiken study

**Predicted positivity** - 6.3%

**Screening done with the test** FOB Gold - Sentinel

**FIT test positivity** - 12.2%

**Cut-off has been modified to** 47 μg/g to effort positivity 6.3%
Epidemiology of colorectal cancer: comparison of Czech regions

FIT positivity in individual districts could be significantly affected by the FIT method used

Test positivity

- < 5.0
- 5.0 – 6.5
- 6.5 – 8.0
- 8.0 – 9.5
- > 9.5

Total positivity (2016): - 7.2 %
Range between districts: 4.0 - 13.3 %

Májek O., Suchánek Š. Quality-assured immunochemical testing – proposal for a pilot project in the Czech Republic
European Digestive Cancer Days, Prague - 26. September 2017
TAKE HOME MESSAGE

- Efforts to change qualitative FIT to quantitative FIT
- Efforts to change units from ng/ml to $\mu$g/g of stool
- Standardization of FIT methods according to IFCC committee
- Essential requirement for FIT external quality control
- Personalized approach to FIT analysis of Hb in faeces
- Screening programs modifications using FIT values