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 ≥ 10 μg/g. 20 322 FIT positive subjects underwent colonoscopy. Cut-off ≥ 10 μg/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 positivity 8 - 11%
Adenoma detection approx. 50%
CRC detection - 6.7

FIT 200 ng/ml (40 µg/g)

gFOBT positivity 3 - 5%
CRC detection - 3.1

FIT 50 ng/ml (10 µg/g)

Adenoma detection approx. 30%
CRC detection - 4.7

Effort to increase
Sensitivity and Higher financial efficiency

High false positivity
Decrease number of colonoscopies

5
SETTING THE CUT-OFF VALUE FIT TEST - FIT OPTIMISATION

Determine **sensitivity** - rate of detected neoplasma /CRC
Determine specificity - the numbers of 'unnecessary' colonoscopies
Decide required **capacity of GE centers and screening costs**

Accuracy and reliability of Hb analysis in stool

Standardization of FIT analysis
Transferability of FIT analysis results
External quality control of FIT analysis
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.
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

EQA Korea 2015
235 participants (29%)
7 different analyzers
Results in ng/ml

POSITIVE SAMPLE
NEGATIVE SAMPLE

cut-off

Eiken Micro  Eiken Diana  Eiken Io  Alfresa NS-1000  Alfresa NS-C  Kyowa HM-Jack  Kyowa HM-Jack Arc

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
FIT EXTERNAL QUALITY ASSESSMENT IN CZECH REPUBLIC

April 2016

Data from cycle FOB 2016-01

- **Eiken OC-Sensor**
  - Sample A: 50 µg/g
  - Sample B: 140 µg/g
  - CV: 8.10%

- **Sentinel FOBGold**
  - Sample A: 30 µg/g
  - Sample B: 80 µg/g
  - CV: 8.85%

1.6x higher

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 %

Toes-Zoutendijk E, van Leerdam ME, Dekker E et all. : Real-Time Monitoring of Results During First Year of Dutch Colorectal Cancer Screening Program and Optimization by Altering Fecal Immunochemical Test Cut-Off Levels. Gastroenterology 2017;152:767–775
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 – 5.5
- 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