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PUBLICATION SPOTLIGHT

FOB Gold FIT solutions

FIT performance and cut-off value selection in CRC screening

In Europe, colorectal cancer (CRC) is the most prevalent of all tumours, with 471,000 cases diagnosed per year and second only to lung cancer in terms of deaths. Yet studies show that it is possible to reduce mortality significantly by adopting population-based CRC screening programmes which allow the early detection of CRC. Due to its simplicity and proven superior performance, faecal immunochemical test (FIT) is currently considered the best non-invasive faecal occult blood (FOB) test for CRC screening. Moreover, considering both positivity rate and colonoscopy capacity, the FIT cut-off can be adjusted to meet screening goals.

FOB Gold, the unique solution for FIT offered by Sysmex, is used by millions of asymptomatic and symptomatic patients and shows high sensitivity and specificity (see clinical results table below). Data from ongoing screening programmes using FOB Gold shows that 75 % of the CRC cases were early stages I and II [7, 10] and around 50 % of FOB Gold positives were advanced adenomas [10]. The performance and unique features of the FOB Gold assay supplied by Sysmex make it suitable for the widest possible range of lab settings and clinical needs.

FOB Gold is an effective rule-in test in CRC screening programmes

Clinical results table

Study	Cohort	Cut-off [µg Hb/g]	Sensitivity	Specificity	Cut-off range [µg Hb/g]
Graser *et al.* Gut (2009) 58:241–248	285 FIT / 307 colonoscopy	2.4	32 % for AA	85.8 % for AA	n/a
Chen *et al.* Clin Gastroent and Hepatol (2017) 15(10):1547–1556	1,644 frozen / 1,822 fresh samples	17	42.6 % / 35.7 % for AN	90.7 % / 94.7 % for AN	n/a
Augé *et al.* (2017) Abstract at EML, Athens	520 symptomatic / 438 surveillance	20	41.7 % / 29.6 % for AN	85.3 % / 87 % for AN	2 – 129
Niedermaier *et al.* Epidemiology (2018) 29(3):397–406	3,466	17	39 % for AN	94 % for AN	8 / 12 / 17 / 27
Augé *et al.* Clin Chem Lab Med (2018) 56(4):625–633	487	20	38 % for AN	88 % for AN	10 – 60
Gies *et al.* Gastroenterology (2018) 154(1):93–104	566	17	21.8 % for AN	96.3 % for AN	various cut-offs
Brenner *et al.* Int. J. Cancer (2017) 140:2015–2022	3,466	17	39 % for AN	93.7 % for AN	n/a
Brenner *et al.* Clin and Transl Gastroent (2017) 8(8):e111	1,822	17	35.7 % for AN	94.7 % for AN	5 – 50
Brenner *et al.* Clinical Epidem (2018) 10:381–389	3,211	17	41.2 % for AN	93.6 % for AN	10 – 50
Gies *et al.* Clin Gastroent and Hepatol (2019) 17(9):1829–1839	76 CRC / 100 without AN	17	67.1 % for CRC	96 % for CRC	5 / 10 / 20
Brenner *et al.* JAMA (2019) 321(17):1686–1692	1,059 (Placebo arm w/o Aspirin)	17	22.5 % for AN	94.8 % for AN	10.2 / 17
Niedermaier *et al.* Clin Gastroent and Hepatol (2020) Online ahead of print	435 CRC	17	84.6 % for CRC	–	10 – 40

AA = advanced adenoma (≥ 1 cm in size); AN = advanced neoplasia (CRC + AA); n/a = not applicable; reference method = colonoscopy

List of references

Screening/asymptomatic

[1] Niedermaier T et al.: *Sensitivity of fecal immunochemical test for colorectal cancer detection differs according to stage and location. Clin Gastroenterol Hepatol. (2020) Online ahead of print.*

Key message: *FOB Gold identified patients with newly diagnosed CRC with overall high sensitivity (84.6 % at a cut-off of 17 µg Hb/g) and showed a stage-specific gradient in sensitivity according to T and UICC stage, which is plausible because larger and deeper penetrating tumours are expected to be more likely to cause sufficiently strong bleeding to result in a positive FIT value.*

[2] Peng L et al.: *Risk-Adapted Cutoffs in Colorectal Cancer Screening by Fecal Immunochemical Tests. Am J Gastroenterol (2020) 00: 1–7.*

Key message: *Variations of numbers needed to scope (NNS) and positive predictive values (PPV) were present across various CRC risk groups when uniform FOB Gold cut-offs were used in screening, which leads to the conclusion that using risk-adapted cut-offs might represent an option for personalised CRC screening.*

[3] Navarro M et al.: *Fecal Hemoglobin Concentration, a Good Predictor of Risk of Advanced Colorectal Neoplasia in Symptomatic and Asymptomatic Patients. Frontiers in Medicine (2019) 6(91): 1–10.*

Key message: *FOB Gold was applied in a population-based CRC screening programme in Spain (cut-off 20 µg Hb/g) demonstrating that male gender, age and Hb concentration can be used as predictors of risk of advanced neoplasia to prioritise colonoscopy procedures.*

[4] De Klerk CM et al.: *Participation and ease of use in colorectal cancer screening: a comparison of two fecal immunochemical tests. Gastroenterology (2019) 114(3): 511–518.*

Key message: *A significant percentage of participants in the Dutch national screening programme preferred FOB Gold (36 %) over OC Sensor (5 %) – most had no preference (59 %) – whereas the rate of returned FIT samples was comparable between FOB Gold and OC Sensor (48.7 % vs 48.9 %, respectively).*

[5] Wieten E et al.: *Equal Accuracy of 2 Quantitative Fecal Immunochemical Tests in Detecting Advanced Neoplasia in an Organized Colorectal Cancer Screening Program. Gastroenterology (2018) 155: 1392–1399.*

Key message: *More than 21,000 randomly selected participants of the Dutch CRC screening programme completed the FOB Gold and OC Sensor FIT (paired design from the same stool sample). No significant differences in the power of the diagnostic performance of both FITs regarding the detection of advanced neoplasia were shown.*

[6] Brenner H et al.: *Variation of diagnostic performance of fecal immunochemical testing for hemoglobin by sex and age: results from a large screening cohort. Clinical Epidemiology (2018) 10: 381–389.*

Key message: *In real screening settings (n=3,211, ages 50 to 79) the diagnostic performance of FOB Gold was evaluated based on age and sex over a range of cut-offs. Higher sensitivity was shown for the age group 65 to 79 compared to the age group 50 to 64, as well as a lower sensitivity and higher specificity for women versus men, whereas PPV and NPV did not show significant differences between age groups; only higher NPVs were detected among women compared with men.*

[7] Solé Llop ME et al.: *Colorectal cancer screening programme in Aragon (Spain): preliminary results. Gaceta Sanitaria (2018) 32(6): 559-562.*

Key message: *FOB Gold was applied in the first year of the Aragon screening programme (2014) in patients aged 60 to 69 years, showing a positivity rate of 10.75 % and a PPV for advanced neoplasia (CRC + advanced adenoma) of 19.7 %.*

[8] Brenner H et al.: *Selecting a Cut-off for Colorectal Cancer Screening With a Fecal Immunochemical Test. Clinical and Translational Gastroenterology (2017) 8(8): e111.*

Key message: *This study shows that FOB Gold can be used for detecting advanced neoplasms (AN) within the scope of CRC screening after selection of the cut-off based on AN prevalence or colonoscopy capacity (e.g. 17 µg Hb/g revealed a positivity rate of 8.7 %, PPV of 46.5 %, Sensitivity of 35.7 % and Specificity of 94.7 %).*

[9] Toes-Zoutendijk E et al.: *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(4): 767–775.*

Key message: *Real-time monitoring of the first year of the Dutch screening programme (2014) offered the possibility to adjust the FOB Gold cut-off in order to achieve an optimal screening performance (increase from 15 to 47 µg Hb/g faeces with a decrease in the positivity rate from 10.6 % to 6.7 %).*

[10] *Erasmus MC Rotterdam, NKI/Antoni van Leeuwenhoek COLORECTAL CANCER SCREENING PROGRAMME – Monitor 2014, 2015, 2016, 2017, 2018. National Institute for Public Health and the Environment (RIVM)*

Key message: *The RIVM commissioned Erasmus MC and the Netherlands Cancer Institute (NKI)/Antoni van Leeuwenhoek Hospital to carry out national monitoring of the CRC screening programme on an annual basis.*

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