Colorectal Cancer Screening Committee Meeting
Program and Abstracts

October 19, 2018
Vienna

InterContinental Hotel
Vienna, Austria
Overview of content

- Program main meeting
- Overview of supporters
- Agendas of the Expert Working Group meetings
- Faculty overview
- Abstracts (in sequence of program)
Program
WEO Colorectal Cancer (CRC) Screening Committee Meeting

Friday, October 19, 2018 – 8.00 am – 6.15 pm
InterContinental Hotel Vienna, Ballroom (Johann Strauss 1-4)
Johannesgasse 28, 1030 Vienna, Austria

Themes:
Endoscopy / Latest developments
Updates from screening programs
Blood and stools / Non-invasive testing
Trends and Risk stratification

Goals of the meeting:
To update the attendees on recent advances in CRC screening
To seek advice on future initiatives
To reach consensus on controversial areas

Expert Working Group meetings
Parallel sessions

8.00 am Surveillance after Colorectal Neoplasia
Rodrigo Jover (Spain), Uri Ladabaum (USA)
8.00 am WEO Coalition to Reduce Inequities in CRC Screening
Christian von Wagner (UK), Peter Liang (USA)
9.45 am Coffee break
10.15 am FIT for Screening
Ernst Kuipers (Netherlands), Sally Benton (UK)
10.15 am Right-Sided Lesions and Interval Cancers
Evelien Dekker (Netherlands), Matt Rutter (UK)
12.00 pm Lunch
1.00 pm Welcome
Linda Rabeneck (Canada) & Ernst Kuipers (Netherlands)

Session 1: Endoscopy / Latest developments
Chairs: Linda Rabeneck (Canada), Ernst Kuipers (Netherlands)

1.10 pm Artificial intelligence
Rodrigo Jover (Spain)
1.20 pm Prediction of lymph node metastasis (LNM) in T1 CRCs
Leon Moons (Netherlands)
1.30 pm Is there justification for levels of polyp competency?
Roland Valori (UK)
1.40 pm Can caps, cuffs, or rings improve ADR in organised screening programmes
Pradeep Bhandari (UK)
1.50 pm Discussion

Session 2: Updates from screening programs
Chairs: Jack Hardcastle (UK), Robert Steele (UK)

2.10 pm Status of the screening program in the Canton of Vaud, Switzerland
Kevin Selby (Switzerland)
2.20 pm Baseline data from the Scottish flexible sigmoidoscopy trial
Robert Steele (UK)
2.30 pm Need for colorectal cancer screening in Saudi Arabia
Samar Alhomoud (Saudi Arabia)
2.40 pm Initial findings from the Scottish Bowel Screening Program after changing to FIT
Judith Strachan (UK)
2.50 pm Discussion

Session 3: Updates from screening programs - Continued
Chairs: Rolf Hultcrantz (Sweden), Siwan Thomas-Gibson (UK)

3.10 pm Launch of the Norwegian colorectal cancer screening program
Øyvind Holme (Norway)
### Program

3.20 pm  Colorectal cancer screening in the regions of the Russian Federation  
**Stanislav Konovalov (Russia)**

3.30 pm  Screening program in Nova Scotia - performance overview  
**Donald MacIntosh (Canada)**

3.40 pm  Comparative analysis of the performance of EU screening programs  
**Carlo Senore (Italy)**

3.50 pm  Discussion

4.10 pm  **Coffee break**

4.40 pm  Incidence of colorectal cancer in young adults in Europe  
**F.E.R. (Fanny) Vuik (Netherlands)**

4.50 pm  Screening start age in light of new ACS guidelines  
**Charles Kahi (USA)**

5.00 pm  Discussion

#### Session 5: Trends and Risk stratification

Chairs: Michal Kaminski (Poland), Anna Forsberg (Sweden)

5.10 pm  Screening for colorectal cancer based on polygenic risk and family history  
**Dayna Cenin (Netherlands)**

5.20 pm  The use of an online family history questionnaire in FIT population screening  
**Victorine Roos (Netherlands)**

5.30 pm  Intelligent use of FIT  
**Stephen Halloran (UK)**

5.40 pm  Discussion

5.55 pm  Celebrating 20 Years at the WEO  
**Ernst Kuipers (Netherlands)**

6.15 pm  **Wrap-up and Adjourn**  
**Linda Rabeneck (Canada) & Ernst Kuipers (Netherlands)**

6.20 pm  **Reception**

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*For more information please contact the WEO secretariat at secretariat@worldendo.org*
We thank the following partners for their support:
WEO Colorectal Cancer Screening Committee  
Surveillance after Colorectal Neoplasia  
Expert Working Group Meeting Agenda

Friday, October 19, 2018  
Time: 8.00 am – 9.45 am  
Venue: InterContinental Hotel - Vienna, Austria  
Meeting room: Ballroom (Johann Strauss) 1+2

Chairs: Rodrigo Jover (Spain), Uri Ladabaum (USA)

WEO UPDATE OF EVIDENCES ABOUT SURVEILLANCE

8.00 am  General overview of the project  
(Rodrigo Jover, Spain)

8.25 am  Outcome measures for surveillance studies  
(Michael Bretthauer, Norway)

8.50 am  Comparators for surveillance studies  
(Matt Rutter, UK)

9.15 am  Significant thresholds in surveillance  
(Cesare Hassan, Italy)

9.40 am  Discussion (5 min)
This meeting will feature a range of presentations that will both illustrate the problem of inequalities in colorectal cancer screening and showcase examples of activities and strategies to reduce them.

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<td>Improving access to CRC screening in vulnerable populations</td>
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<td>8.25 am</td>
<td>Development and pilot-testing of a Colorectal Cancer Screening Decision</td>
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<td>Aid for individuals with low health literacy</td>
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<td>(Mirjam Fransen, Netherlands)</td>
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<td>8.40 am</td>
<td>Update of the Yorkshire bowel scope screening uptake project</td>
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<td>8.55 am</td>
<td>Interventions to increase uptake in central London</td>
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<td>(Andrew Prentice and Robert Kerrison, England)</td>
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<td>9.10 am</td>
<td>Lancashire Bowel Cancer Screening Programme: Call for a Kit Clinic</td>
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<td>(CFAKC) project- “Community engagement with a clinical twist”</td>
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<td>(Shahida Hanif &amp; Sadiq Patel, England)</td>
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<td>9.25 am</td>
<td>Closing remarks and discussion</td>
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Friday, October 19, 2018
Time: 10.15 am – 12.00 pm
Venue: InterContinental Hotel - Vienna, Austria
Meeting room: Ballroom (Johann Strauss) 1+2

Chairs: Ernst Kuipers (Netherlands), Sally Benton (UK)

**10:15 am** Welcome & Introduction from the Chair.
(Ernst Kuipers, The Netherlands)

**10:20 am** Detectability Characteristics
(Callum Fraser, UK)
**10:30 am** Discussion

**10:35 am** Comparative (cost-) effectiveness of mailed-out FIT vs invitation letter only in France
(Caroline Osoro, Netherlands)
**10:45 am** Discussion

**10:50 am** Novel stool-based protein biomarkers for improved colorectal cancer screening
(Meike de Wit, Netherlands)
**11:00 am** Discussion

**11:05 am** Dynamic changes of faecal haemoglobin to assess the risk of advanced colorectal lesions
(Josep Auge, Spain)
**11:15 am** Discussion

**11:20 am** Update on the colorectal cancer screening in East Europe and Central Asia.
(Marcis Leja and Anna Krigere, Latvia)
**11:30 am** Discussion

**11:35 am** Status of organised screening programs with FIT around the world
(Graeme Young, Australia)
**11:45 am** Discussion

**11:50 am** Closing remarks
WEO Colorectal Cancer (CRC) Screening Committee
Right-Sided Lesions and Interval Cancers
Expert Working Group Meeting Agenda

Friday, October 19, 2018
Time: 10.15 am – 12.00 pm
Venue: InterContinental Hotel - Vienna, Austria
Meeting room: Ballroom (Johann Strauss) 3+4

**Chairs:** Evelien Dekker (Netherlands), Matt Rutter (UK)

10.15 am  PCCRC in high-risk cohorts
           IBD
           (Nick Burr, UK)

10.45 am  PCCRC in high-risk cohorts
           Lynch syndrome
           (Francesc Balaguer, Spain)

11.15 am  Right-sided cancer – is it down to a field effect?
           (James East, UK)

11.45 am  Discussion
Faculty Overview

Dr Samar Alhomoud  
King Faisal Specialist Hospital & Research Centre  
Riyadh, Saudi Arabia

Professor Pradeep Bhandari  
Queen Alexandra Hospital  
Portsmouth/Hampshire, UK

Dayna Cenin  
Erasmus MC  
Rotterdam, The Netherlands

Professor Stephen P. Halloran  
Public Health England, London, UK  
University of Surrey, Guildford, UK

Dr Øyvind Holme  
Cancer Registry of Norway  
Clinical Effectiveness Research Group, University of Oslo  
Oslo, Norway

Dr Rodrigo Jover  
KaServicio de Medicina Digestiva  
Castalla, Alicante, Spain

Charles Kahi, MD, MS  
Professor of Clinical Medicine, Indiana University School of Medicine  
GI Section Chief, Roudebush VA Medical Center  
Indianapolis, Indiana, USA

Mr Stanislav Konovalov  
AGROS  
Leading expert in HTSA Plus program  
St. Petersburg, Russia

Dr Donald MacIntosh  
Dalhousie University  
Halifax, Canada

Dr Leon M.G. Moons  
UMC Utrecht  
Zeist, The Netherlands

Drs. Victorine Roos  
Amsterdam UMC  
Amsterdam, The Netherlands

Dr Kevin Selby  
Department of Ambulatory Care and Community Medicine  
University of Lausanne  
Switzerland

Dr Carlo Senore  
CPO Piemonte  
Torino, Italy

Professor Robert J. C. Steele  
Ninewells Hospital & Medical School  
Dundee, UK

Ms Judith Strachan  
NHS Tayside  
Dundee, UK

Dr Roland Valori  
Gloucestershire Hospitals  
NHS Foundation Trust  
Gloucester, UK

F.E.R. (Fanny) Vuik  
Erasmus Medical Center  
Rotterdam, The Netherlands
Artificial Intelligence in Gastrointestinal Endoscopy

Rodrigo Jover

Artificial Intelligence (AI) is considered any technique that enables computers to mimic human intelligence, using logic, rules, decision trees or machine learning. Machine learning is a part of AI that includes abstruse techniques that enables machines to improve at tasks with experience. Finally, deep learning is the subset of machine learning composed of algorithms that permit software to train itself to perform tasks like image recognition. Initial studies with AI in gastrointestinal endoscopy uses machine learning algorithms, but the revolution of AI in imaging diagnosis have come with deep learning. Deep learning allows computational models that are composed of multiple processing layers to learn representations of data with multiple levels of abstraction. These methods have dramatically improved the state-of-the-art in speech recognition, visual object recognition, object detection and many other domains such as drug discovery and genomics. Deep learning discovers intricate structure in large data sets to indicate how a machine should change its internal parameters that are used to compute the representation in each layer from the representation in the previous layer. This technology allows AI to be able to improve human performance in multiple aspects related to imaging diagnosis, such as gastrointestinal endoscopy. In the last year a number of published studies and abstract reports in the main GI meetings have demonstrated the increasing ability of AI in different aspects of GI endoscopy, such as detection and characterization of colonic polyps, quality aspects of colonoscopy or diagnosis of Barrett’s esophagus, among others. Finally, it is also important, from the gastroenterology and endoscopy community to know the limitations and pitfalls of AI as well as to define what should we expect from AI, how research in this field should be designed and which are the appropriate answers we should receive from this new and promising technology.
BACKGROUND & AIMS: Most patients with pedunculated T1 colorectal tumors referred for surgery are not found to have lymph node metastases, and were therefore unnecessarily placed at risk for surgery-associated complications. We aimed to identify histologic factors associated with need for surgery in patients with pedunculated T1 colorectal tumors.

METHODS: We performed a cohort-nested matched case-control study of 708 patients diagnosed with pedunculated T1 colorectal tumors at 13 hospitals in The Netherlands, from January 1, 2000 through December 31, 2014, followed for a median of 44 months (interquartile range, 20-80 months). We identified 37 patients (5.2%) who required surgery (due to lymph node, intramural, or distant metastases). These patients were matched with patients with pedunculated T1 colorectal tumors without a need for surgery (no metastases, controls, n = 111). Blinded pathologists analyzed specimens from each tumor, stained with H&E. We evaluated associations between histologic factors and patient need for surgery using univariable conditional logistic regression analysis. We used multivariable least absolute shrinkage and selection operator (LASSO; an online version of the LASSO model is available at: http://t1crc.com/calculator/) regression to develop models for identification of patients with tumors requiring surgery, and tested the accuracy of our model by projecting our case-control data toward the entire cohort (708 patients). We compared our model with previously developed strategies to identify high-risk tumors: conventional model 1 (based on poor differentiation, lymphovascular invasion, or Haggitt level 4) and conventional model 2 (based on poor differentiation, lymphovascular invasion, Haggitt level 4, or tumor budding).

RESULTS: We identified 5 histologic factors that differentiated cases from controls: lymphovascular invasion, Haggitt level 4 invasion, muscularis mucosae type B (incompletely or completely disrupted), poorly differentiated clusters and tumor budding, which identified patients who required surgery with an area under the curve (AUC) value of 0.83 (95% confidence interval, 0.76-0.90). When we used a clinically plausible predicted probability threshold of ≥4.0%, 67.5% (478 of 708) of patients were predicted to not need surgery. This threshold identified patients who required surgery with 83.8% sensitivity (95% confidence interval, 68.0%-93.8%) and 70.3% specificity (95% confidence interval, 60.9%-78.6%). Conventional models 1 and 2 identified patients who required surgery with lower AUC values (AUC, 0.67; 95% CI, 0.60-0.74; P = .002 and AUC, 0.64; 95% CI, 0.58-0.70; P < .001, respectively) than our LASSO model. When we applied our LASSO model with a predicted probability threshold of ≥4.0%, the percentage of missed cases (tumors mistakenly assigned as low risk) was comparable (6 of 478 [1.3%]) to that of conventional model 1 (4 of 307 [1.3%]) and conventional model 2 (3 of 244 [1.2%]). However, the percentage of patients referred for surgery based on our LASSO model was much lower (32.5%, n = 230) than that for conventional model 1 (56.6%, n = 401) or conventional model 2 (65.5%, n = 464).

CONCLUSIONS: In a cohort-nested matched case-control study of 708 patients with pedunculated T1 colorectal carcinomas, we developed a model based on histologic features of tumors that identifies patients who require surgery (due to high risk of metastasis) with greater accuracy than previous models. Our model might be used to identify patients most likely to benefit from adjuvant surgery.
Is there justification for levels of polyp competency?

Roland Valori

In 2010 the EU guideline group for quality assurance of CRC screening and diagnosis\(^1\) proposed there be four levels of polypectomy competency:

- Level 1 for FS screening
- Level 2 for symptomatic colonoscopy
- Level 3 for FIT/FOBT positive patients
- Level 4 for complex and large polyps

Since then a variety of studies have explored the feasibility and utility of creating levels of polypectomy competency. This presentation will review the justification for this approach in the context of this literature with an emphasis on quality, safety, patient centeredness and the planning and provision of services.

The key principles underpinning the presentation will be firstly that polypectomy services should be designed around the needs of patients, and secondly that the decision of what to do about polyps, especially larger polyps, should not be constrained by the availability of the appropriate expertise to remove them.

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Colorectal cancer (CRC) has historically been underused in Switzerland, with only 22% of adults up-to-date in 2012. A 2013 law authorized reimbursement by basic health insurance of either the faecal immunochemical test (FIT) every 2 years or colonoscopy every 10 years for adults aged 50 to 69 years, with no deductible in the setting of organized programs. In 2015, the Canton of Vaud launched the first large-scale, organized CRC screening program in Switzerland. The target population of approximately 180,000 eligible adults will be invited over the next 5 to 10 years.

The Vaud CRC Screening program is based on mailed invitations for inclusion via general practitioners. Participants have the choice between the OC Sensor FIT (threshold 15 µg/g), picked up at the pharmacy and returned by mail, or colonoscopy with referral to the gastroenterologist of their choice. High-risk and surveillance patients currently are not included in the program. The program emphasizes shared decision making and an equal offering of tests. Several other cantons are planning to launch organized programs within the next 1 to 3 years.
In Scotland, a biennial guaiac faecal occult blood (gFOBT)-based screening programme for all aged 50-74 has been in place since December 2009, and has recently been replaced by a FIT–based programme at a threshold of 80ugHb/g faeces. Although these strategies are unlikely to have a significant effect on the incidence of colorectal cancer (CRC), there is definitive evidence that flexible sigmoidoscopy (FS) screening at around the age of 60 does. Since there was insufficient evidence on the effect of FS at age 60 in a population already being offered biennial gFOBT or FIT screening from age 50, a RCT was carried out in Scotland to test the hypothesis that FS would be an effective adjunct to screening with gFOBT. This trial was powered primarily to study the yield of neoplastic pathology on an intention-to-treat basis rather than CRC mortality or incidence, and was carried out on a pragmatic basis, relying on routine data collection.

Between June 2014 and December 2015, 51,769 individuals were randomised to be offered FS instead of gFOBT around their 60th birthdays or to continue with the routine gFOBT algorithm. Those in the study group who did not take up the offer of FS were offered gFOBT, as were those who had a normal FS. All those who had any neoplasia detected by FS were offered a colonoscopy, as were all those with a positive gFOBT test result in both the study and control groups.

In the study group, overall uptake of FS was 17.8%. Uptake was higher in men than in women, and increased with decreasing deprivation with an overall uptake of 9.2% in the most deprived quintile (SIMD 1) and 25.7% in the least (SIMD 5) overall. The uptake of FOBT in the control group in SIMD 1 was 46.4% and 69.1% in SIMD 5, which translates to an absolute difference between the most and least deprived of 16.5% for FS and 22.7% for FOBT (p=0.02).

In those who underwent FS, the cancer detection rate was 0.13%, the adenoma detection rate was 7.27% and the total neoplasia detection rate was 7.40%. In those who underwent FS and colonoscopy in response to a positive FS, the cancer detection rate was 0.28%, the adenoma detection rate was 8.66% and the total neoplasia detection rate was 8.83%.

On an intention to screen basis, the cancer detection rate was no different in the study group and the control group. However, both the adenoma and total neoplasia detection rates were significantly higher in the study groups, with odds ratios of 5.95 (95%CI 4.69-7.56) and 5.10 (95%CI 4.09-6.35) respectively.

Thus, in a single round at age 60, despite a low uptake and neoplasia detection rate, FS did detect substantially more neoplasia than gFOBT alone in a gFOBT- screened population.
Colorectal cancer (CRC) is one of the most common cancer in Saudi Arabia, it's the first most common cancer in Saudi males & third among females according to Saudi Cancer registry (2014) accounting for 11.5% of all newly diagnosed cancer cases with an average annual age standardized rate (ASR) of 10.6/ 100,000 for males & 8.2/100,000 for females.

Although the total numbers of CRC cases are much less than other countries but the incidences are increasing as well as most of cases get diagnosed in an advance stage with only 24% of cases get diagnosed early leading to increase in the burden of cancer treatments. These incidences are expected to increase by 2040 according to the latest 2018 GLOBOCAN due several factors including longer life expectancy, increase in the population as well as changes in the life style.

Currently there is no population-based screening program in Saudi Arabia & screening is performed on an opportunistic basis therefore, efforts should be focus on planning & implementing a comprehensive strategy aiming at building a strong & effective cancer control and prevention programmes through multi-sectoral and multi-disciplinary platform approach outlying a comprehensive plan for cancer awareness, early detection programmes including screening, early diagnosis and treatment.
After an initial pilot phase, a national bowel screening programme was introduced into Scotland using the guaiac faecal occult blood test (FOBT) as the first line test in 2007. Since that time Faecal Immunochromatographic Testing (FIT) has been developed and, as it has better performance characteristics, only requires one sample and gives a quantitative estimate of the amount of haemoglobin (Hb) in faeces, it was decided to pilot this as a screening test in 2010. In this pilot, a threshold of 80ug Hb/g faeces was used and gave a positivity of 2.4%, an uptake of 58.5% and positive predictive values (PPVs) of 4.8% for cancer, 38.2% for adenoma and 23.3% for high risk adenoma. Using data from this pilot, a business case was submitted to Scottish Government, and, as a result, FIT at a threshold of 80ug Hb/g faeces replaced FOBT on 20th November 2017.

There was a complete revision of participant instructions and result letters as well as a significant number of changes to the IT system to transition from FOBT to FIT. A new laboratory to process the samples using 4 HM-Jackarc analysers (Kyowa Ltd) was commissioned and the laboratory acheived UKAS ISO 15189 accreditation for FIT.

To date, across Scotland, the uptake of FIT has been 64% compared to 53% for FOBT and the positivity has been 3.0% compared to 1.9% for FOBT. The absolute number of positive results transmitted to the NHS Boards has been 12466 for FIT compared to 6410 for FOBT, an increase of 95% (almost double).

The yield of pathology for FIT is not yet available as the pathology reports lag significantly behind the colonoscopy reports. As a snapshot, however, pathology data from the first 353 colonoscopies are available from NHS Tayside and they demonstrate a PPV of 5.4% for cancer, 44.8% for adenoma and 26.9% for high risk adenoma, which compares well with the pilot data and better adenoma detection than for FOBT.

Turnaround time to participants has greatly improved with around 95% of kits being resulted on the day of receipt meaning a much shorter time for participants having to wait for a result. This improvement has led to many favourable letters and comments.
Norway has one of the highest colorectal cancer incidence (CRC) rates in the world.

In 2016, the National Council for Prioritizing in the Health Service recommended that screening for colorectal cancer should be implemented in Norway.

The Directory of Health subsequently summoned a group of experts in spring 2017. The group recognized the equipoise with respect to effectiveness of the different screening modalities. However, as colonoscopy screening had the greatest potential for CRC incidence reduction, the Directory recommended that the goal should be primary colonoscopy screening. As in many countries, colonoscopy resources are limited also in Norway. The Directory therefore recommended that the screening program should start as a FIT-based program with gradual expansion of colonoscopy capacity with conversion to primary colonoscopy screening when endoscopic resources were sufficient. The Directory also recommended that this conversion should be introduced as a randomized trial, comparing FIT with primary colonoscopy screening.

The screening program will be introduced gradually from late 2019 with a 5 year national roll-out. Men and women 55 years of age without a previous diagnosis of CRC will be invited. The invitation will include the choice between standard screening, which comprises biennial FIT for 5 rounds, and participation in a randomized trial, comparing 5 rounds of FIT with colonoscopy.

From previous trials in Norway, it is expected that about 60% will take up the offer to get screened.

To aid in expansion of colonoscopy capacity and ensure the quality of the examinations, a centralized School of endoscopy has been established. The school offers courses for both leaders of endoscopy departments, colonoscopy teachers and endoscopists.
Colorectal cancer holds the leading positions amongst cancer diseases in all developed countries. Population mortality rate from MN in Russia is 5.7% for rectal cancer, and 7.9% for colon cancer.

In October 2017, a program of clinical examination of certain adult population groups was implemented. Clinical examination (screening) is carried out in two stages. At the first stage, a fecal occult blood test is conducted using an immunochemical method (for citizens aged 49 to 73 years). The second stage is carried out for the purpose of additional examination and includes, in particular, colonoscopy. Currently, there are several methods of fecal occult blood testing that are mainly used: manual method (immunochromatography) for detection of fecal Hemoglobin, Transferrin and etc.; semi-automated method for the quantitative determination of fecal hemoglobin; automated method for the simultaneous determination of fecal Hemoglobin and Transferrin (HTSA).

Using the method of simultaneous measurement of fecal Hb and Tf reduces the number of false-negative Hb results by 36.3%. In May 2017, fecal Transferrin was implemented into the international database and universal standard for the identification of medical and laboratory observations - LOINC, receiving the code 86271-4. The increased transferrin level indicates that lesion is mostly in the upper intestine. The increased hemoglobin level indicates that lesion is mostly in the lower intestine.

The first pilot project in Russia has been implemented in Khanty-Mansiysk region since 2011. During this time, 4 screening centers, located in 4 major cities of the region, organized the screening of 181,058 people in the framework of clinical examination using the quantitative automated method iFOBT (FIT). By using an automated method, the detectability of colon cancer on I stage has increased three times in this region. Rectum cancer detectability has increased two times. As a result, mortality rate due to colorectal cancer remained low in this region for more than 5 years.

HTSA quantitative automated method allowed to create and conduct statistics of iFOBT / FIT test results and to see the true situation in the region for this type of neoplasm.

iFOBT (FIT) quantitative automated method will significantly save public funds since detection of patients with early stages of cancer will allow to timely conduct low-cost preventive procedures, to preserve patients’ health, to improve the quality of their life and to avoid complex and expensive treatment and as a result to reduce the incidence (stage III and IV) and mortality related to colorectal cancer.
Performance of Colorectal cancer screening in the European Union Member States- Data from the second European screening report

Senore C¹, Basu P², Anttila A³, Ponti A¹, Tomatis M¹, Vale DB⁴, Ronco G¹, Soerjomataram I⁵, Primic Zakelj M⁶, Riggi E¹, Dillner J⁷, Elfstrom KM⁸, Lonnberg S⁹, Sankaranarayanan R¹⁰, Segnan N¹

¹ SSD Epidemiologia e screening – CPO, University Hospital ‘Città della Salute e della Scienza’, Turin, Italy; ² Screening Group, International Agency for Research on Cancer, Lyon, France; ³ Mass Screening Registry/Finnish Cancer Registry, Finnish Cancer Registry, Helsinki, Finland
⁴ Department of Obstetrics and Gynecology, State University of Campinas (Unicamp), Campinas, Brazil; ⁵ Section of Cancer Surveillance, International Agency for Research on Cancer, Lyon, France; ⁶ Institute of Oncology Ljubljana, Ljubljana, Slovenia; ⁷ Swedish Cervical Screening Registry, Stockholm, Sweden; ⁸ Regionalalt cancercentrum Stockholm-Gotland, Stockholm, Sweden; ⁹ Cancer Registry of Norway, Oslo, Norway; ¹⁰ Research Triangle Institute, International-India, New Delhi, India

Objective. To present comparative data about the performance of colorectal cancer (CRC) screening programs in the European Union Member States (EU MSs).

Design. Cross-sectional study. We analyzed key performance indicators - participation rate, positivity rate (PR), detection rate (DR) and positive predictive value (PPV) for adenomas and CRC, based on the aggregated quantitative data collected for the second EU screening report. We derived crude and pooled (through a random effects model) estimates to describe and compare trends across different MSs / regions and screening protocols.

Results. Participation rate was higher in countries adopting faecal immunochemical test (FIT) (range: 22.8% to 71.3%) than in those using guaiac faecal occult blood test (gFOBT) (range 4.5% to 66.6%) and it showed a positive correlation (p=0.842, p<0.001) with participation in breast cancer screening in the same areas. Compliance with referral for colonoscopy (TC) assessment ranged between 64% and 92%; TC completion rate ranged between 92% and 99%. PR and DR of advanced adenomas and CRC were higher in FIT, as compared to gFOBT programs, and, independent of the protocol, among men, older subjects and those performing their first screening. Screening performance showed a large variability.

Conclusions. These findings confirm the EU guidelines recommendation to implement organised population based programs, as opposed to opportunistic screening, as only the former can be properly monitored The variability in the results of quality indicators highlights the importance of continuous monitoring, as well as the need to promote quality improvement efforts, as recommended in the EU guidelines. The implementation of monitoring systems, ensuring availability of data for the entire process, together with initiatives aimed to enhance reproducibility of histology and quality of endoscopy, represent a priority in screening programs management.
Incidence of colorectal cancer in young adults in Europe

Fanny E.R. Vuik; Stella A.V. Nieuwenburg; Marc Bardou; I. Lansdorp-Vogelaar; Mário Dinis-Ribeiro; Maria J. Bento; Vesna Zadnik; Maria Pellisé; Laura Esteban; Michal Kaminski; Stepan Suchanek, Ondřej Ngo, Ondřej Májek, Marcis Leja, Ernst J. Kuipers; Manon C.W. Spaander

Background: In the North American population, colorectal cancer (CRC) incidence for individuals older than 50 years steadily declines, but an opposite trend has been suggested among young adults. In Europe, trends in CRC incidence among younger individuals are lacking. Therefore, the aim of this study was to analyze trends in incidence rates of young adults with CRC in the European Union over the last 25 years.

Methods: Data on age-related incidence of CRC were retrieved from national European cancer registries with a data time-frame of at least 10 years, ranging from 1990 until 2016. Young adults, defined as people between 20 to 49 years of age, with confirmed colon or rectal cancer were included. Five-year incidence- and mortality rates were collected, expressed per 100,000 person-years and corrected for age and population numbers. Trends were calculated using a Joinpoint regression analysis, and expressed as annual percent change (APC) with a 95% confidence.

Results: Data from twenty European countries were included. In adults aged 20 to 39 years of age, the overall CRC incidence rate increased by 4.9% (95%CI: 3.9–5.9) annually since 2005. For colon cancer, incidence rate increased in men by 2.2% (95%CI: 1.4–3.0) per year from 1990-2010 and with an even higher increase of 7.3% (95%CI: 2.3–12.5) per year from 2010-2016. In women the incidence rate increased by 1.5% (95%CI: 0.4–2.7) per year from 1990-2008 and increased even more by 8.9% (95%CI: 4.8–13.2) per year from 2008-2016. Incidence rate of rectal cancer increased for both men and women, respectively 2.4% (95%CI: 1.9–3.0) and 2.0% per year (95%CI: 1.2–2.8).

In adults aged 40 to 49 years, the overall CRC incidence rate increased by 1.2% per year (95%CI: 0.6–1.8) from 2002. The incidence rate of colon cancer increased in men by 0.5% (95%CI: 0.1–0.8) per year, and also in women by 0.5% (95%CI: 0.0–1.0) per year. Incidence rate of rectal cancer in men decreased by 3.9% (95%CI:-7.1– -0.7) from 1990-1997, and then increased from 1997-2016 by 1.6% (95%CI: 0.8–2.3). Rectal cancer in women increased by 8.3% (95%CI: 4.7–12.0) per year in 1990-1996, and remained stable from 1996-2016.

The overall age adjusted mortality rates for CRC did not show a significant trend in adults 20 to 39 year of age. However, mortality rates in adults 40 to 49 years of age decreased by 3.8% (95%CI: -4.4– -3.2) per year from 1990-2006, and remained stable from 2006-2016.

Conclusion: There is an increased incidence rate in CRC in young adults in Europe. The cause for this trend is still unknown. Awareness and future studies to elucidate causes for this trend are needed and may help to set up screening strategies to prevent and detect these cancers at an early and curable stage.
The American Cancer Society (ACS) has recently issued a qualified recommendation to initiate colorectal cancer (CRC) screening starting at age 45 years in average-risk individuals. The rationale for this recommendation is that (1) US epidemiologic data show an increase in CRC incidence in individuals younger than 50 years, (2) there is concern about a birth cohort effect with individuals aged 45 to 49 showing increasing CRC incidence rate ratios since 1949, and (3) updated simulation models show a favourable balance of benefit of risk from initiating screening at an earlier age.

While it is widely accepted that CRC (particularly left-sided) incidence has increased in younger individuals and has been the subject of scrutiny and research, the new ACS guidelines have been met with mixed responses from other professional societies and health care systems. On one hand, extending screening to younger average-risk individuals could decrease CRC mortality in a very vital segment of the population, including minority groups who are particularly vulnerable to CRC, and could lead to increased screening uptake in individuals aged 50 and older. On the other hand, several concerns have been raised: (1) although CRC incidence has been increasing in those younger than 50 years, the absolute risk remains low, and it is not clear whether the suspected birth cohort effect is in fact partly attributable to increased detection; (2) there are no empirical data to guide screening decisions in average-risk individuals younger than 50; (3) the models used to justify the new recommendation assume 100% adherence, which is not realistic, especially in younger individuals.

Thus, the new guideline could lead to a situation where most individuals who attend screening are younger and health-conscious, and thereby lower-risk for CRC. This could increase risk for harm from unnecessary procedures with lower potential benefit, while leading to diversion of strained resources from older individuals who are clearly at higher risk.

The ultimate goal of the new guideline is to reduce CRC incidence and mortality in individuals 45-49 years old; however, the balance of benefit and harm is not known. A pragmatic risk-stratified approach, one which targets individuals with demographic and clinical risk factors, may be effective and cost-effective.
It is universally acknowledged that screening for colorectal cancer (CRC) is an effective tool for reducing CRC related incidence and mortality. At present, implemented screening programs are age-based with additional guidelines for those with family history of CRC. However, our understanding of the underlying causes of CRC is growing, and it is now recognised that genetic susceptibility, in the form of single-nucleotide polymorphisms (SNPs), play a significant role in defining CRC risk due to their relatively high prevalence in the population. It has been suggested that this polygenic risk, coupled with family history, may provide greater discriminatory performance for risk assessment than age alone.

This provides an opportunity to stratify the population based on risk, and implement a more personalised screening regime where screening interventions are individually tailored. Such tailoring has the potential to reduce the harms of screening while maintaining or even increasing its benefits which will further improve the cost-effectiveness of screening.

Using Microsimulation Screening Analysis-Colon (MISCAN-Colon) we modelled the effects and costs of screening for CRC in a risk stratified Australian population aged 40-74 years. Individuals were categorised into one of five CRC risk groups determined by their expected distribution of polygenic risk profile and family history (first-degree relative) of CRC. Six screening scenarios were assessed: no screening; uniform biennial faecal immunochemical test screening from age 50-74 years; and four scenarios where screening start age, interval and test varied depending on risk group.

Without considering costs for risk stratification, our research suggests that screening according to risk can be cost-effective compared to uniform screening, however, the gains are small. Compared to no screening, the personalised screening scenarios that provided best value for money modified screening start age and interval (ICER $1,855/QALY gained) and start age, interval and test so that those at highest risk were offered 5-yearly colonoscopy (ICER $10,797). For personalised screening to remain cost-effective, costs for determining risk profile range between $12 and $239 depending on the screening scenario.

This research presents an early investigation of the possible impact of personalised screening for CRC based on polygenic risk and family history. Although the gains of personalised screening are currently small, and as costs fall, technology improves and more accurate risk stratification tools become available, it is likely that personalised screening will become increasingly more viable. This suggests that personalised screening is an important future consideration for policy makers and should be considered to effectively plan for future screening programs.
Adding family history of colorectal cancer to the FIT-based screening program in a Dutch colorectal cancer screening population sample

Victorine H. Roos, Frank G.J. Kallenberg, Manon van der Vlugt, Evelien J.C. Bongers, Cora M. Aalfs, Patrick M.M. Bossuyt, Evelien Dekker

Objective:
Screening for colorectal cancer (CRC) with the fecal immunochemical test (FIT) has suboptimal sensitivity for detecting advanced neoplasia. To increase the sensitivity and yield of a FIT-based screening program, FIT could be combined with other risk factors for advanced neoplasia, such as family history of CRC. We evaluated the incremental yield of adding a family history questionnaire on CRC and Lynch syndrome associated tumours to a FIT-based screening program.

Design:
In this prospective population-based CRC screening trial, we randomly selected 6,000 screening naive individuals. All were invited to complete a FIT and a validated, online family history questionnaire. Participants with a positive FIT (cut-off value 275 ng/ml) and/or a positive family history, confirmed after genetic counselling, were referred for colonoscopy. We compared the diagnostic yield in detecting advanced neoplasia per 1,000 invitees using the FIT strategy with that of the combined strategy. In addition, we evaluated the yield of the family history questionnaire in identifying persons that should undergo colonoscopy screening.

Results:
Of the 5,979 invitees, 2,379 (40%) completed both the FIT and the family history questionnaire, 1,952 (33%) completed only the FIT and 95 (2%) only the family history questionnaire. Out of 191 initially positive questionnaires, 125 (65%) participants were eligible for referral to a clinical geneticist after a telephone check. Only 50 out of 125 (40%) participants eventually underwent genetic counselling; 46 (37%) declined referral and 29 (23%) had previously received genetic counselling or colonoscopy surveillance. Based on the family history questionnaire sixteen additional colonoscopies were performed, and advanced neoplasia was detected in one individual. Overall, the diagnostic yield in detecting advanced neoplasia was 19.5 per 1,000 invitees with the FIT-only strategy and 19.6 per 1,000 invitees with the combined strategy (p-value=1.0). Genetic counselling resulted in one newly diagnosed Lynch syndrome patient, two detected gene variants of unknown clinical significance, and twenty-six patients had familial CRC, of whom fifteen were newly diagnosed.

Conclusion:
In this study in the Dutch FIT-based screening program we observed no added value of using a validated, online family history questionnaire for detecting advanced neoplasia. However, with the questionnaire we did identify persons at increased risk of developing CRC who should undergo colonoscopy screening instead of participating in the CRC screening program. [ClinicalTrials.gov ID NCT02698462].
Intelligent use of FIT

Stephen P. Halloran

Summary of presentation
We are at the beginning of a new dawn for the Faecal Immunochemical Test. The analytical specificity of FIT enabled it to be introduced at a much higher analytical sensitivity than its progenitor faecal occult blood test gFOBT that used a crude oxidation indicator. We have gradually exploited the 100-fold increase in sensitivity of FIT and employed it initially in CRC screening and more recently in primary care GI referrals. Recognising that, unlike gFOBT, FIT measures faecal blood concentration, we have begun applying different FIT concentration thresholds and exploring the use of different FIT products and systems. We are slowly exploiting the relationship between FIT concentration, test positivity and clinical sensitivity /specificity to optimise clinical outcome within available endoscopy, pathology and financial resources.

FIT is not a diagnostic test, it provides a measure of risk and its accuracy has the potential to be enhanced if combined with other measures or CRC risk. When screening we already apply a crude marker of risk when we determine the screening age range, yet we apply the same range in men and women knowing that the risk profile is different in men and women. We are beginning to see publications that explore risk markers that could supplement FIT indeed Cologuard combines FIT with other faecal markers. Family and medical history, lifestyle, age, sex, adherence to CRC screening have been subject to preliminary study as risk marker and some have combined with FIT concentration.

The new dawn for FIT-based screening will see utilisation of these risk markers not in a crude series of FIT thresholds for different ‘risk circumstances’ but as a seamless interpretation of combined CRC risk factors. Having analysed the historical data readily available in established CRC screening programmes and combining it with clinical outcome data, we will devise an algorithm that enables personalised risk referrals to colonoscopy.

We are living in an era of ‘big data’ and artificial intelligence; population-based CRC screening is an activity with big data at its core and artificial intelligence is fast infiltrating medical practice, indeed breast cancer is leading the way. The new FIT screening programmes with participation rates approaching 75% (Netherlands, Spain & Scotland) need efficient colonoscopy referrals with short waiting times and high clinical yield.

We have the information, we have the tools, we have in the WEO Screening Committee a motivated internationally informed research team… so let’s get started and design the new dawn in CRC screening!
INDUSTRY COOPERATION 2018

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