Colorectal Cancer Screening Committee Meeting
Program and Abstracts

June 1, 2018
Washington

Capital Hilton Hotel
Washington D.C., USA

www.worldendo.org
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, June 1, 2018 – 8.00 am – 6.00 pm
Reception 6.10 pm – 7.30 pm
Capital Hilton Hotel
1001 16th St NW, Washington, DC 20036, USA

Conveners: Linda Rabeneck, Global Chair (Canada)
Robert Schoen, Chair for the Americas (USA)

Themes:
FIT
Colonoscopy Quality
Screening and Surveillance
New Technology and New Understandings/Realizations

Goals of the meeting:
To provide updates on recent advances in CRC screening
To seek advice and comments on future initiatives
To reach consensus on controversial areas

7.30 am  Light breakfast
8.00 am  Expert Working Group meetings – parallel sessions
          Evelien Dekker (Netherlands)
          Robin Mendelsohn (USA)
          Roque Sáenz (Chile)
          Samir Gupta (USA)
          Christian von Wagner (UK)

8.00 am  Right-Sided Lesions and Interval Cancers
          Ernst Kuipers (Netherlands)

8.00 am  Colonoscopy Screening Trials
          Rodrigo Jover (Spain)

8.00 am  WEO Coalition to Reduce Inequities in CRC Screening
          Uri Ladabaum (USA)

9.45 am  Coffee break

10.15 am  FIT for Screening
          Ernest Kuipers (Netherlands)

10.15 am  Surveillance after Colorectal Neoplasia
          Rodrigo Jover (Spain)

10.15 am  Image Enhanced Endoscopy (IEE)
          Uri Ladabaum (USA)

12.00 pm  Lunch

1.00 pm  Welcome
         Linda Rabeneck & Robert Schoen

         Session 1: FIT
         Chairs: Han-Mo Chiu (Taiwan) & Robin Mendelsohn (USA)

1.05 pm  Comparison of different FIT kits in the Dutch CRC screening
         program
         Clasine de Klerk (Netherlands)

1.15 pm  Colonoscopy outcomes after different FIT haemoglobin levels in a
         surveillance program
         Erin Symonds (Australia)

1.25 pm  Reasons for non-follow up after a positive FIT in the Dutch CRC
         screening program
         Lucinda Bertels (Netherlands)

1.35 pm  Discussion

For more information please contact the WEO secretariat at: secretariat@worldendo.org
Session 2: Colonoscopy Quality  
Chairs: Seth Crockett (USA) & Adriana Safatle Ribeiro (Brazil)

1.50 pm Management of pT1 polyps  
2.00 pm Colonoscopy Upskilling

2.10 pm Key performance indicators for polypectomy: What are the prime contenders?

2.20 pm Discussion

2.35 pm Coffee break

Session 3: Screening and Surveillance  
Chairs: Peter Liang (USA) & Susan Parry (New Zealand)

2.50 pm CTC vs. Colonoscopy for surveillance after CRC  
3.00 pm Number of adenomas Needed to Remove (NNR) and Dwell time avoided – metrics for assessing screening efficiency

3.10 pm Evaluation and comparison of the effectiveness of CRC screening tests: The IARC Handbook

3.20 pm CRC screening at age 45 – What does the modeling suggest?

3.30 pm Discussion

3.50 pm IDCA - Charles Moertel Award

4.00 pm Coffee break

Session 4: New Technology and New Understandings/Realizations  
Chairs: Jaroslaw Regula (Poland) & Maria Pellisé (Spain)

4.15 pm Rates and complications of surgery for non-malignant polyps

4.25 pm Genetics in young onset CRC

4.35 pm CancerSeek: ctDNA and proteins for blood based screening for cancer

4.45 pm Deep learning for prediction of advanced neoplasia

4.55 pm Deep learning for real time histologic differentiation

5.05 pm Discussion

Celebrating 20th Years at the WEO  
Introduction by Linda Rabeneck

5.30 pm A Historical Recounting

Wrap-up & Adjourn

6.00 pm Wrap-up

6.10 pm Reception

– 7.30 pm
We thank the following partners for their support:
Friday, June 1, 2018
Time: 8.00 am – 9.45 am
Venue: Capital Hilton Hotel, Washington D.C.
Meeting room: Congressional
Chair: Evelien Dekker (Netherlands)

8.00 am  Interval cancers after the first screen round in the Netherlands: results for two cut-off levels
          (Esther Toes-Zoutendijk, Netherlands)

8.25 am  A long term surveillance program for colorectal cancer: risk of interval cancers and utility of faecal immunochemical tests
          (Erin Symonds, Australia)

8.50 am  Serrated polyp detection rates and factors associated with detection
          (Seth Crockett, USA)

9.15 am  PCCRC: where next?
          (Douglas Corley, USA)
Introduction

8.00 am  Overview/Welcome/Focus on Randomized Controlled Trials (RCTs)
(Robin Mendelsohn, USA; Roque Saenz, Chile)

Prior Randomized Controlled Colonoscopy Screening Trials

8.05 am  National Colonoscopy Study (NCS)
(Ann Zauber, USA)

8.15 am  Predictive Modeling based on NCS
(Reinier Meester, USA)

8.25 am  Discussion

Current Ongoing Randomized Controlled Colonoscopy Screening Trials:
Focus on feature of design, update on preliminary results

8.40 am  CONFIRM Trial
(Douglas Robertson, USA)

8.50 am  COLONPREV Trial
(Enrique Quintero, Spain)

9.00 am  NordiCC Trial
(Magnus Loberg, Norway)

9.10 am  SCREESCO Trial
(Rolf Hultcrantz, Sweden)

9.20 am  Discussion

9.35 am  Wrap up and future directions
Introductions
Announcement of Dr. Peter Liang as new co-lead for the Working Party

Research and Policy Perspectives

8.10 am  Snapshot of screening inequities in the United States  
(Paul Doria-Rose, USA)

8.25 am  Screening inequities in New York City  
(Peter Liang, USA)

8.40 am  Strategies to improve CRC screening rates: a meta-analysis  
(Michael Dougherty, USA)

8.55 am  General Practice provider perspectives on CRC screening and influence on non uptake  
(Lucinda Bertels, Netherlands)

9.10 am  Abnormal FIT follow up across 8 Federally Qualified Health Centers in Southern California  
(Samir Gupta, USA)

Collaborative Ideas

9.25 am  Update to summary of inequities in CRC screening in the US  
Survey/Review of published/unpublished rates of colonoscopy uptake after abnormal FIT

9.40 am  Wrap up
WEO Colorectal Cancer Screening Committee
FIT for Screening
Expert Working Group Meeting – Agenda

Friday, June 1, 2018
Time: 10.00 am – 12 pm
Venue: Capital Hilton Hotel, Washington D.C.
Meeting room: Congressional
Chair: Ernst Kuipers (The Netherlands)

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

10:20 am  A Swedish update from SCREESCO
           (Rolf Hultcrantz, Sweden)
10:30 am  Discussion

10:35 am  Effectiveness of WhatsApp reminder on compliance of colorectal cancer
           screening
           (Thomas Lam, Hong Kong)
10:45 am  Discussion

10:50 am  Do multiple negative FITs reduce risk of advanced neoplasia?
           (Erin Symonds, Australia)
11:00 am  Discussion

11:05 am  Detection in subsequent screen round in the Netherlands: results for two cut-off
           levels
           (Arthur Kooyker, The Netherlands)
11:15 am  Discussion

11:20 am  Personalizing the age to stop colorectal cancer screening in Canada based on
           comorbidity and prior screening history: model estimates of harms and benefits.
           (Jill Tinmouth, Canada)
11:30 am  Discussion

11:35 am  The Brazilian Pilot, an update
           (Adriana Safatle-Ribeiro, Brazil)
11:45 am  Discussion

11:50 am  FIT Screening History
           (Graeme Young, Australia)

11:55 am  Closing Remarks
Friday, June 1, 2018
Time: 10.15 am – 12.00 pm
Venue: Capital Hilton Hotel, Washington D.C.
Meeting room: Senate

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

10.15 am  General assumptions for surveillance guidelines: endpoints, cutoffs and comparators
(Rodrigo Jover, Spain)
Discussion 10 min

10.40 am  Surveillance: Update on US Multisociety Task Force
(Samir Gupta, USA)
Discussion 10 min

11.05 am  Performance targets for lesion detection in surveillance
(Uri Ladabaum, USA)
Discussion 10 min

11.30 am  More vs. less intensive surveillance after polypectomy:
Results from microsimulation modeling
(Reinier Meester, USA)
Discussion 10 min
Friday, June 1, 2018
Time: 10.15 am – 12.00 pm
Venue: Capital Hilton Hotel, Washington D.C.
Meeting room: Federal A+B

**Chairs:** David Hewett (Australia), Heiko Pohl (USA)

**10.15 am**  
WEO analysis on synchronous and metachronous neoplasia in diminutive polyps: implications for optical diagnosis  
(Cesare Hassan, Italy)

**10.30 am**  
Computer aided optical diagnosis of polyps  
(Michael Byrne, Canada)

**10.45 am**  
The path to unifying criteria for optical polyp diagnosis  
(Sarah McGill, USA)

**11.00 am**  
How well can image enhanced endoscopy predict deep cancer invasion?  
(Evelien Dekker, Netherlands)

**11.15 am**  
Image enhanced endoscopy for polyp detection: results, methodology, and clinical implications  
(Daniel von Renteln, Canada)

**11.30 am**  
What should the next optical polyp diagnosis study look like?  
(Discussion, Heiko Pohl, USA)

**11.45 am**  
Discussion
Faculty Overview

Drs Lucinda Bertels  
AMC - Academic Medical Center  
Amsterdam, Netherlands

Dr Michael F Byrne  
Vancouver General Hospital  
Vancouver, Canada

Dr Joshua Cohen  
Ludwig Center for Cancer Genetics and Therapeutics  
Johns Hopkins University School of Medicine  
Baltimore, MD, USA

Dr Clasine de Klerk  
Department of Gastroenterology and Hepatology  
AMC - Academic Medical Center  
Amsterdam, The Netherlands

Dr David G. Hewett  
The University of Queensland  
Brisbane, Australia

Dr Beatrice Lauby-Secretan  
International Agency for Research on Cancer  
Lyon, France

Dr Donald MacIntosh  
Dalhousie University  
Halifax, Nova Scotia, Canada

Dr Anne Peery  
University of North Carolina  
Chapel Hill, NC, USA

Dr Maria Pellise  
Gastroenterology Department (ICMDiM)  
Hospital Clinic de Barcelona  
Barcelona, Spain

Elisabeth Peterse, MSc  
Erasmus MC  
Rotterdam, Netherlands

Dr Paul Pinsky  
National Cancer Institute  
Bethesda, MD, USA

Dr Elena Stoffel  
University of Michigan  
Ann Arbor, MI, USA

Dr Erin Symonds  
Flinders Medical Centre  
Bedford Park, SA, Australia

Dr David Weinberg  
Fox Chase Cancer Center  
Philadelphia, PA, USA

Hyo-Joon Yang, MD, PhD  
Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea
Comparison of different FIT test kits in the Dutch CRC screening program

Clasine de Klerk*, Els Wieten*, Annemieke van der Steen, Christian Ramakers, Ernst Kuipers, Bettina Hansen, Iris Lansdorp-Vogelaar, Patrick Bossuyt, Evelien Dekker, Manon Spaander

Background and aims
Although different brands of fecal immunochemical tests (FIT) are currently used for colorectal cancer (CRC) screening, evidence from large studies comparing their accuracy in detecting advanced neoplasia (AN) is limited.

Methods
A large prospective cohort study was conducted within the Dutch national CRC screening program to compare the accuracy to detect AN between the two most commonly used FITs: FOB-Gold (Sentinel, Italy) and OC-Sensor (Eiken, Japan). 42,179 screening-naïve individuals aged 55-75 years were randomly selected and invited to sample both FITs from the same bowel movement. Invitation for colonoscopy followed if one or both FITs were positive (≥15 µg hemoglobin/gram feces). Equivalence in detection of AN was evaluated with a predefined margin of 0.15%.

Results
Of 42,179 invitees, 22,064 (52%) participated, and 21,078 completed both FITs. Of 2,112 participants (9.6%) with one or two positive FITs, 1,778 (84%) underwent a colonoscopy. AN was detected by FOB-Gold in 610 invitees (1.45%) and by OC-Sensor in 606 (1.44%), an absolute difference of 0.01% (95% CI: -0.06% to 0.08%). Of the 21,078 participants, 1,582 (7.5%) had a positive FOB-Gold and 1,627 (7.7%) a positive OC-Sensor (p=0.140). Relative true positive rate of FOB-Gold to OC-Sensor in detecting AN was 0.97 (CI 0.92 to 1.01) and 0.95 (CI 0.87 to 1.03) for CRC. Relative false positive rate of AN was 0.99 (CI 0.93 to 1.05).

Conclusion
FOB-Gold and OC-Sensor perform equally in detecting AN in organized CRC screening. These results are relevant for selecting a FIT in CRC screening programs worldwide.

Trial registration
Dutch National Trial Registry no. NTR5874
(http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=5874)
Colonoscopy outcomes after different FIT haemoglobin levels in a surveillance program

Erin Symonds, Charles Cock, Peter Bampton, Robert Fraser, Graeme Young

Background: Colorectal cancer (CRC) screening for individuals at elevated risk occurs through regular colonoscopic surveillance. In Australia, more than one-third of all colonoscopies are performed for surveillance, generally every 3-5 years. No significant pathology is found in >85% of these procedures suggesting this is an inefficient use of limited endoscopy resources. Previous studies suggest that faecal immunochemical test (FIT) haemoglobin (Hb) concentration predicts subsequent neoplasia in average risk populations. The aim of the current work was to determine if Hb concentrations in FIT performed between surveillance colonoscopies, indicates the risk of advanced neoplasia (CRC or advanced adenoma) in an elevated risk population.

Methods: Patients at elevated risk for CRC (due to previous adenoma or family history of CRC) were enrolled into a colonoscopy surveillance program (the Southern Cooperative Program for the Prevention of Colorectal Cancer (SCOOP)) comprising colonoscopy every 3-5 years and FIT (2 sample, Eiken OC Sensor) in the interval. Pathology findings at subsequent surveillance colonoscopy was compared between negative FIT Hb (concentrations of (i) 0μg/g faeces, or (ii) 0.1-19.9μg/g faeces), positive FIT result (≥20μg/g faeces) and individuals offered FIT but who had not done the test prior to colonoscopy.

Results: Pathology outcomes were analysed from 6,214 individuals who had completed an interval FIT, and from 1,566 who had not. Surveillance colonoscopy was performed 30.3 ± 15.3 months (mean ±SD) after negative FIT. Of those with a FIT result of 0μg/g faeces the incidence of advanced neoplasia was significantly lower compared to all other groups (Table). After adjusting for age, gender and time between FIT and colonoscopy, compared to 0μg/g faeces the odds for advanced neoplasia was significantly higher for all other Hb concentrations and for those that did not complete FIT.

Conclusions: FIT Hb concentrations predict the risk of advanced neoplasia in surveillance procedures, with absence of Hb identifying individuals at lowest risk for advanced neoplasia. This suggests Hb concentrations could be used to personalise surveillance by lengthening intervals following a FIT result of 0μg/g faeces which will reduce the burden of colonoscopic surveillance on health services.

<table>
<thead>
<tr>
<th>Findings of advanced neoplasia</th>
<th>Negative (0μg/g faeces) N=1539</th>
<th>Negative (0.1-19.9μg/g faeces) N=3750</th>
<th>Positive (≥20μg/g faeces) N=925</th>
<th>No FIT N=1566</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>9.2%</td>
<td>14.1%</td>
<td>18.5%</td>
<td>12.6%</td>
</tr>
<tr>
<td>Odds ratio (95%CI)</td>
<td>1.0</td>
<td>1.5 (1.2-1.8)</td>
<td>2.0 (1.6-2.5)</td>
<td>1.5 (1.2-1.9)</td>
</tr>
</tbody>
</table>
Reasons for non-follow up after a positive FIT in the Dutch bowel cancer screening program

Lucinda Bertels, Evelien Dekker, Kristel van Asselt, Henk van Weert, Maartje Hoogsteyns, Bart Knottnerus

Background:
Persons who receive an unfavorable result in the Dutch screening program for colorectal cancer are recommended a colonoscopy. However, in 2016, 12% (n=6578) did not undergo a colonoscopy for unknown reasons. 8% of these individuals are estimated to have colorectal cancer and 43% an advanced adenoma. In the ARCUS study (Amsterdam Research on Colonoscopy Uptake after Screening), we investigate motives of screen-positive persons for not undergoing a colonoscopy.

Methods:
21 semi structured in-depth interviews were conducted until data saturation was reached with persons who did not undergo a colonoscopy after receiving a positive FIT.

Preliminary results:
Four persons had been advised not to undergo the recommended colonoscopy because they had recently undergone one. One person underwent the colonoscopy but did not complete it. The remaining 16 interviews were thematically analyzed using open coding and constant comparison.

The motives explained by the respondents were without exception complex and multifactorial. They always included a low perception of risk, which was often related to bodily experiences such as not experiencing symptoms or to beneficial influential factors such as healthy behavior and a favorable family history. This was accompanied by one or multiple other factors such as having an alternative explanation for the blood loss, having gambled on a negative FIT or not having realized the consequences of a positive FIT, resentment against colonoscopy, aversion against the way the Dutch screening was set up, and unwillingness to visit an unknown and distant hospital. Factors less often mentioned included having other things on their mind (generally major life events), fatalism, fear of complications and distrust towards the screening organization.

Furthermore, we unexpectedly found that some women (3/10) described taking an unfavorable FIT result less serious than an unfavorable mammography in breast cancer screening.

Conclusion:
Low risk perception of colorectal cancer might be an underlying cause of non-uptake after a positive FIT, combined with one or more other factors.
The observed prevalence of early colorectal cancer (CRC) is increasing with the implementation of screening colonoscopies. Around 10% of cancers found in fecal immunochemical test-based screening programs are polyps harboring invasive cancer. Endoscopic resection of T1 is acceptable for those lesions with a low risk for lymph node metastasis whereas surgical colectomy with lymph node dissection is recommended for lesions with one or more risk factors. The risk factors of lymph node metastasis are based on surgical series and have been variable along studies and guidelines. The presence of lympho-vascular invasion, histological high-grade carcinoma and positive deep margin are broadly accepted risk factors and are included in all the guidelines. The guidelines of the Japanese Society for Cancer of the Colon and Rectum (JSCCR) and the European Society for Medical Oncology (ESMO) include two other criteria such as tumor budding and deep submucosal invasion. The decision on the therapeutic approach is very often individualized taking into consideration all these factors and patients morbidity.

Positive or unknown margins have been significantly associated with residual disease in endoscopically resected T1 CRC. Consequently, an en-bloc resection is mandatory for appropriate endoscopic treatment of pT1 polyps. Ideally, the endoscopists should suspect the presence of invasive cancer during the procedure to make the appropriate therapeutic decision and/or to tattoo the area for further surgical treatment. Unfortunately, the suspicion of covert invasive carcinoma in large polyps and/or invasive carcinoma in small polyps is clearly insufficient. Endoscopists and surgeons should be aware of the signs that can predict the presence of a focus of invasive carcinoma in a polyp. Gross morphology and surface analysis are helpful for predicting presence of invasive carcinoma. An interim analysis from the Australian cohort of large sessile lesions treated by endoscopic mucosal resection has recently shown that rectosigmoid location, combined Paris classification, surface morphology and increasing size are associated with submucosal invasion and should be considered in the treatment decision. Previous studies evaluating diagnostic accuracy of image enhanced endoscopy for predicting deep invasion have been conducted with magnification, in Eastern countries and by experienced endoscopists. Recently, a study by 58 Western endoscopists (combining university and community hospitals) who had performed an easy training program, using endoscopes without magnification has shown that in “western real-life condition”, optical diagnosis shows a very high Specificity and positive LR (96.4% and 16.3, respectively) but an unsatisfactory Sensitivity for predicting deep invasion (58.4%). Furthermore, despite the morphological criteria and optical diagnosis there is still a subgroup of lesions (12%) where it is very difficult to do an accurate in vivo prediction of endoscopic resectability. An effort has to be done in improving the diagnostic accuracy of pT1 and educating the community for suspecting these lesions.

There is scarce and heterogeneous information on the prognosis of pT1 polyps. Consequently, there are many open questions about the therapeutic decisions and surveillance strategies in these patients with early cancer.
When measurement of colonoscopy performance indicators is performed, it becomes readily apparent that the quality of colonoscopy being provided is variable.

It has been documented that there is a correlation between a colonoscopist’s adenoma detection rate (ADR) and their risk of post-colonoscopy colorectal cancer (PCCRC)\(^1,2\). As well, increasing an individual’s ADR decreases the likelihood they will have a PCCRC, implying that the effort to improve colonoscopy performance is worthwhile\(^3\).

In Canada, a national program, the Canadian Association of Gastroenterology Skills Enhancement for Endoscopy program (SEE \(^\text{TM}\)) has been developed to try and improve colonoscopy performance. This talk will briefly review this effort with progress to date and lessons learned.

1 Kaminski et al. NEJM 2010;362:1795
2 Corley et al. NEJM 2014;370:1928
3 Kaminski et al. Gastroenterol 2017;153:98
Key performance indicators for polypectomy: What are the prime contenders?

David G. Hewett, MBBS MSc PhD FRACP, The University of Queensland, Brisbane Australia

Polypectomy is fundamental to the practice of colonoscopy, and to its protective effect against colorectal cancer (CRC). Yet, like most other aspects of colonoscopy performance, polypectomy is highly operator dependent. Variation in the effectiveness of polypectomy has been documented between endoscopists, and post-colonoscopy CRC is known to occur at sites of previous polypectomy. Incomplete polypectomy contributes up to 30% of interval CRCs after colonoscopy.

Much of the variation in polypectomy performance is likely to reflect a lack of competency at fundamental polypectomy skills. Polypectomy competency varies significantly among colonoscopists, however does not correlate with established quality metrics for detection, such as adenoma detection rate and withdrawal time.

There is now a significant body of research on assessment of polypectomy competence. The most established assessment is the Directly Observed Polypectomy Skills (DOPyS) tool, which can be applied to both clinical and simulated colonoscopy. Data support its role for assessing and certifying competence at polypectomy.

However, metrics for evaluating the clinical effectiveness of polypectomy are required, and are a limitation of research on established and emerging polypectomy techniques. Frequently used outcome measures include biopsies of the margins and base of polypectomy defects, and the presence of residual neoplasia on surveillance colonoscopy. Current US quality indicators for colonoscopy do not include metrics specific to polypectomy effectiveness, only those relating to post-polypectomy complications. The 2017 ESGE guidelines include a performance measure for appropriate polypectomy technique (e.g., cold snare resection for >3mm lesions). Given the significance of incomplete polypectomy, education on polypectomy techniques and metrics of polypectomy quality are urgently needed.

References
CTC vs. Colonoscopy for surveillance after CRC

David Weinberg MD, MSc

Recommendations for surveillance after curative surgery for colorectal cancer (CRC) include a 1 year post-resection CT scan and optical colonoscopy (OC). CT colonography (CTC), when used in CRC screening, can identify colorectal polyps ≥10 mm and cancers nearly as well as OC. We recently completed a prospective study to compare the clinical and cost effectiveness of CTC compared to OC in CRC post-operative surveillance.

We enrolled 231 patients with resected stage 0–III CRC. Approximately 1 year after surgery, participants underwent CTC plus CT, followed by same-day OC. The primary outcome was CTC detection of colorectal adenomas and cancers, using OC as the standard. For the initial economic analysis, we created a simple decision tree outlining choices and outcomes at one year follow-up. Detection criteria were derived for ≥6mm or ≥10mm polyps. Relevant costs were cataloged including capital, supplies, and labor. Analyses included marginal cost of the OC strategy to detect additional polyps and number of polyps missed per 10,000 patients.

In our study 116/231 participants (50.2%) had polyps of any size or histology identified by OC, whereas 15.6% had conventional and/or serrated adenomas ≥6 mm. No intra-luminal cancers were detected. In per patient analysis, CTC detected polyps of ≥6 mm with 44.0% sensitivity (95% CI, 30.2–57.8) and 93.4% specificity (95% CI, 89.7–97.0). CTC detected polyps ≥10 mm with 76.9% sensitivity (95% CI 54.0–99.8) and 89.0% specificity (95% CI, 84.8–93.1). Similar values were found when only adenomatous polyps were considered. The negative predictive value of CTC for adenomas ≥6 mm was 90.7 (95% CI, 86.7–94.5) and for adenomas ≥10 mm the NPV was 98.6 (95% CI, 97.0–100). Using data from this trial, CTC->OC would miss 779 ≥6mm polyps per 10K patients (≥10mm: 173 per 10K). Cost to detect an additional ≥6mm polyp was $5.7K (≥10mm: $28K). Sensitivity analyses demonstrated that any improvement in CTC performance would raise the cost of OC to detect more actionable polyps. For example, meta-analytic sensitivity and specificity data for ≥6mm polyps leads to $21.6K per additional detection ($175.5K for ≥10mm). Using literature values, missed ≥6mm polyps per 10K patients would range from 154 to 950 (≥10mm: 24-283). Similar results were seen when only colorectal adenomas as opposed to all polyps were considered.

In a CRC surveillance population, CTC was inferior to OC for polyp detection. Although CTC detected adenomas with lower sensitivity than OC, a negative finding had good predictive value for the absence of large polyps. From an economic perspective, at an action threshold of ≥10mm, CTC->OC is inexpensive relative to OC.
Screening for colorectal cancer (CRC) with sigmoidoscopy reduces the incidence of CRC by detection and removal of adenomas. The number needed to screen (NNS) to prevent one incident CRC case is a measure of screening efficiency, but it is not directly associated with adenoma removal. We propose 2 new metrics for quantifying the relationship between adenoma removal and CRC prevented: number of adenomas needed to remove (NNR) and adenoma dwell time avoided (DTA).

Data from 4 randomized trials of sigmoidoscopy screening (PLCO, NORCCAP, SCORE and UKFSST) were collected to assess NNR and DTA. For each trial, NNR was computed as the number of adenomas removed from subjects in the intervention group divided by the number of CRCs prevented. DTA was computed similarly but taking into account the timing of adenoma removal; specifically, DTA equals total adenoma dwell time avoided by removal (during the period of follow-up) divided by number of CRCs prevented. Combined results across trials were assessed using standard meta-analytic techniques.

The estimated NNR for the PLCO trial was 74 (95% CI, 56–110), for the NORCCAP trial was 71 (95% CI, 44–174), for the SCORE trial was 27 (95% CI, 14–135), and for the UKFSST trial was 36 (95% CI, 28–52). The combined estimate (meta-analysis) of NNR was 52 (95% CI, 36–93) assuming heterogeneity ($P$ for heterogeneity=0.014). DTA estimates among trials ranged from 278–730 years, with a combined estimate of 500 years (95% CI, 344–833 years) assuming heterogeneity ($P$ for heterogeneity=0.035).

The reciprocal of DTA can be used to estimate the transition rate of adenomas to CRC. Therefore, a DTA of 500 years has a reciprocal of 0.002, or 0.2% transition rate per year.
The *IARC Handbooks of Cancer prevention* conduct evidence-based expert evaluations on the cancer preventive effects of agents or interventions. Colorectal cancer is the third most common cancer in men and the second most common in women. In November 2017, 23 experts from 15 countries met at the International Agency for Research on Cancer in Lyon, France to evaluate different methods of colorectal cancer screening for CRC, by assessing the benefits in reducing mortality and incidence, and the net benefit-harm ratio, taking into account medical and psychological adverse effects. Evaluations were conducted for stool-based blood tests [guaiac faecal occult blood test (gFOBT) and immunochemical fecal test (FIT)], endoscopic techniques (colonoscopy and sigmoidoscopy) and computed tomographic (CT) colonography, an imaging method based on scanning technology. The published evidence from randomized controlled trials, observational studies and modelling studies was critically reviewed and evaluated by consensus. The Handbook also covered other relevant topics, including worldwide availability of colorectal cancer screening, participation to screening, emerging techniques and screening in high-risk groups.

After review of the available evidence, the Working Group concluded that there is *sufficient evidence* that the established screening strategies (i.e., gFOBT, FIT, sigmoidoscopy and endoscopy) decrease the risk of colorectal cancer mortality; the balance of benefit to harm is positive with all techniques, although for colonoscopy the harms are more substantial than for other methods. Evidence for a reduction in colorectal cancer incidence and/or mortality following screening with CT colonography is limited due to the lack of adequate studies.

Network analyses provide indirect comparison of the effectiveness of the different methods, by using data from studies with screening compared to no screening. However, the evidence was considered to be insufficient to draw a conclusion.
CRC screening at age 45 – What does the modeling suggest?

Elisabeth F.P. Peterse, MSc; Reinier G.S. Meester, PhD; Rebecca L. Siegel, MPH; Jennifer C. Chen, MPH; Andrea Dwyer, BS; Dennis J. Ahnen, PhD; Robert A. Smith, PhD; Ann G. Zauber, PhD; Iris Lansdorp-Vogelaar, PhD

Background:
In 2016, the MISCAN-Colon model was used to inform the US Preventive Services Task Force (USPSTF) colorectal cancer (CRC) screening guidelines, which recommend screening from ages 50 to 75 years for average risk individuals. However, these models did not take into account the increase in CRC incidence below the age of 50 years. In this study, one of two microsimulation analyses to inform the update of the American Cancer Society CRC screening guideline, we re-evaluated the optimal age to start screening, age to end screening and screening interval in light of the increase in CRC incidence observed in young adults.

Methods:
We adjusted the simulated lifetime CRC incidence in the MISCAN-Colon model to reflect the observed increase in young onset incidence. In line with the strong birth cohort effect, the current generation of 40-year-olds was assumed to carry forward escalated disease risk as they age. Life-years gained (benefit), the number of colonoscopies (burden) and the ratios of incremental burden to benefit (efficiency ratio) were projected for different screening strategies. Strategies differed with respect to test modality, ages to start screening (40, 45, 50), ages to stop screening (75, 80, 85), and screening intervals (depending on screening modality). We then determined the model-recommended strategies in a similar way as we did for the USPSTF, using similar efficiency ratio thresholds to the previously accepted efficiency ratio of 39 incremental colonoscopies per life-year gained.

Results:
Because of the higher CRC incidence, model-predicted life-years gained from screening increased compared to our previous analyses for the USPSTF. Consequently, the balance of burden to benefit of screening improved, with colonoscopy screening every 10 years starting at age 45 years resulting in an efficiency ratio of 32 incremental colonoscopies per life-year gained.

Conclusion:
This decision-analytic modeling approach suggests that based on the increase in young-onset CRC incidence, screening initiation at age 45 years has a favorable balance between screening benefits and burden. Screening until age 75 years with colonoscopy every 10 years, fecal immunochemical testing annually, flexible sigmoidoscopy every 5 years, and computed tomographic colonography every 5 years was recommended by the model as these strategies provided similar life-years gained at an acceptable screening burden.
Rates and Complications of Surgery for Non-Malignant Polyps

Anne F. Peery

Increasing Rates of Surgery for Patients With Non-Malignant Colorectal Polyps in the US

Aims: We aimed to quantify and examine trends in the use of surgery for non-malignant colorectal polyps in a nationally representative sample.

Methods: We analyzed data from the HCUP National Inpatient Sample for the years 2000 through 2014. We included all adult patients who underwent elective colectomy or proctectomy and had a diagnosis of either non-malignant colorectal polyp or colorectal cancer. We compared trends in surgery for non-malignant colorectal polyps with surgery for colorectal cancer and calculated age, sex, race, region, and teaching status/bed-size specific incidence rates of surgery for non-malignant colorectal polyps.

Results: From 2000 through 2014, there were 1,230,458 surgeries for non-malignant colorectal polyps and colorectal cancer in the United States. Among those surgeries, 25% were performed for non-malignant colorectal polyps. The incidence of surgery for non-malignant colorectal polyps has increased significantly, from 5.9 in 2000 to 9.4 in 2014 per 100,000 adults (IRD, 3.56; 95% CI 3.40–3.72), while the incidence of surgery for colorectal cancer has significantly decreased, from 31.5 to 24.7 surgeries per 100,000 adults (IRD, –6.80; 95% CI, –7.11 to –6.49). The incidence of surgery for non-malignant colorectal polyps has been increasing among individuals 20–79, in men and women and including all races and ethnicities.

Conclusions: In an analysis of a large, nationally representative sample, we found that surgery for non-malignant colorectal polyps is common and has significantly increased over the last 14 years.


Morbidity and Mortality after Surgery for Non-Malignant Colorectal Polyps

Aims: We aimed to describe 30-day post-operative morbidity and mortality and to explore risk factors for adverse events in patients undergoing surgical resection for non-malignant colorectal polyps.

Methods: We analyzed data collected prospectively as part of the National Surgical Quality Improvement Program. Our analysis included 12,732 patients who underwent elective surgery for a non-malignant colorectal polyp from 2011 through 2014. We report adverse events within 30 days of the index surgery. Modified Poisson regression was used to estimate risk ratios and 95% confidence intervals.

Results: Thirty-day mortality was 0.7%. The risk of a major post-operative adverse event was 14%. Within 30 days of resection, 7.8% of patients were readmitted and 3.6% of patients had a second major surgery. The index surgery resulted in a colostomy in 1.8% and ileostomy in 0.4% of patients. Patients who had surgical resection of a non-malignant polyp in the rectum or anal canal compared with the colon had a risk ratio of 1.58 (95% CI, 1.09–2.28) for surgical site infection and 6.51 (95% CI, 4.97–8.52) for ostomy.

Conclusion: Surgery for a non-malignant colorectal polyp is associated with significant morbidity and mortality.

Colorectal cancer (CRC) incidence and mortality have declined overall; however, incidence among young individuals is rising, with 1 in 10 new CRC cases diagnosed in individuals under age 50. The relative contributions of genetic, behavioral and environmental factors to increasing CRC incidence remain largely unknown and there is a critical need to understand the biology of these tumors to improve treatments and prevention. Although hereditary cancer syndromes had previously been implicated in 3-5% of CRCs, recent studies have identified pathogenic germline variants in high and moderate penetrance cancer genes in 10% of unselected CRC cases, and 16-35% of individuals diagnosed age<50. Many germline mutation carriers lack family history of CRC in a first-degree relative, reflecting variable penetrance and expressivity. The spectrum of germline variants extends beyond Lynch Syndrome and FAP (Figure 1), justifying multigene panel genetic testing for all CRC patients age<50.

Figure 1: Genes implicated in High and Moderate Penetrance Hereditary Predisposition to Cancer

CancerSEEK: ctDNA and proteins for blood based screening for cancer

Joshua D. Cohen

The earlier diagnosis of cancer is one of the keys to reducing cancer deaths in the future. Blood tests that detect somatic mutations (“liquid biopsies”) offer the promise of exquisite specificity because they are based on driver gene mutations that are expected to be found only in abnormal clonal proliferations of cells, such as cancers. However, available evidence indicates that patients with early-stage cancers can harbor < 1 mutant template molecule per ml of plasma, which is often beyond the limit of detection of previously reported technologies that assess multiple mutations simultaneously. Yet another issue with liquid biopsies is the identification of the underlying tissue of origin. Because the same gene mutations drive multiple tumor types, liquid biopsies based on genomic analysis alone generally cannot identify the anatomical location of the primary tumor. Here we describe a non-invasive blood test for the detection of cancer which addresses these issues. The test, called CancerSEEK, utilizes combined assays for genetic alterations and protein biomarkers and has the capacity not only to identify the presence of relatively early cancers but also to localize the organ of origin of these cancers. CancerSEEK assesses mutations in 1,933 genomic positions in circulating cell-free DNA as well as the levels of 8 circulating proteins. To evaluate the performance of CancerSEEK, we applied this test to 1,005 patients with cancers of the ovary, liver, stomach, pancreas, esophagus, colorectum, lung, or breast as well as to a control cohort consisting of 812 individuals with no known history of cancer. CancerSEEK tests were positive in a median of 70% of the eight cancer types, while fewer than 1% of 812 normal individuals scored positively. The sensitivities ranged from 69% to 98% for the detection of five cancer types (ovary, liver, stomach, pancreas, and esophagus) for which there are no screening tests available for average-risk individuals. Moreover, to examine whether the CancerSEEK test can help identify a cancer’s tissue of origin, we used supervised machine learning to predict the underlying cancer type in patients with positive CancerSEEK tests. We were able to localize the source of the cancer to a small number of anatomic sites in a median of 83% of the patients scoring positive in the CancerSEEK assay. This combinatorial approach overcomes some of the fundamental obstacles facing the use of liquid biopsies for the earlier detection of cancer.
Background and Aims:
We aimed to develop deep learning models for the prediction of the risk of advanced colorectal neoplasia (ACRN) in asymptomatic adults on which colorectal cancer screening could be customized.

Methods:
Data of 26 clinical parameters from 70,336 first-time screening colonoscopy recipients were collected. A logistic regression (LR) model with 9 variables was used as a comparator. Two deep neural network (DNN) models were developed: Model 1 used the same 9 variables and Model 2 included all 26 variables. The area under the receiver operating characteristic curve (AUC), sensitivity, and specificity were compared among the models in a randomly split test set.

Results:
Compared to the LR model (AUC, 0.721; 95% confidence interval [CI], 0.680–0.762), the DNN Model 1 (AUC, 0.811; 95% CI, 0.790–0.830) and Model 2 (AUC, 0.860; 95% CI, 0.832–0.868) showed significantly improved performance (both P<.001). At the specificity of 85.1% representing primary colonoscopy screening, the sensitivity of the LR, and DNN Models 1 and 2 were 46.5%, 59.5%, and 65.4%, respectively (P=.016 and P=.001), suggesting 27.9% and 40.7% more ACRNs could be detected by the DNNs. At the sensitivity of 46.5%, the specificity values were 85.1%, 90.8%, and 94.6%, respectively (both DNNs with P<.001), suggesting number needed to colonoscopy could be reduced by 37.1% and 61.5% by the DNNs.

Conclusions:
DNNs applied to big clinical data could considerably improve the prediction of ACRNs versus the LR model, suggesting potential for further improvements utilizing large quantities and various types of biomedical information.
Deep learning, a form of Artificial Intelligence, is a rapidly growing field in all industries, including medicine. Recent advances with faster processing speed, improved algorithms, and greater access to data, have allowed for us to move from a position where computer vision could help in the analysis of perfect still images to the much more clinically applicable scenario of a real-time “moving target”.

Optical biopsy of colon polyps is one clinical space where the application of deep learning has been studied over a number of years by several groups, but only recently has shown robust performance in live colonoscopy procedures.

In this presentation, I will briefly review some of the earlier studies on machine learning for colon polyp differentiation, and then review the more recent work showing the application of types of deep learning in various endoscopic imaging technologies, including confocal laser endomicroscopy, autofluorescence imaging, and narrow-band imaging in standard non-magnification colonoscopy.

I will review the challenges to adoption of AI/deep learning for optical biopsy, and how this technology can be validated for clinical practice. The implications for the suggested “resect and discard” practice after AI- driven optical biopsy of diminutive colon polyps will be discussed, as will application of deep learning to more advanced neoplastic lesions in the colon.
INDUSTRY COOPERATION 2018

WEO wishes to thank the following industry partners for their ongoing support:

Principal Sponsor

Olympus

Major Sponsors

Fujifilm

Pentax Medical

Value from Innovation

Premium Sponsors

Boston Scientific

Eiken Chemical

CanTel Medical

General Sponsors

CBC Group

Erbe

Sentinel Diagnostics

Us Endoscopy

Supporters

Alfresa Pharma Corporation

Agen

ClinicalGenomics

Cook Medical

Exact Sciences

EpiGenomics

Kyorin Medeco Co., Ltd.

Medtronic

Medial EarlySign

Mast Group

Polymedco, Inc.

Volition
For information regarding activities of the World Endoscopy Organization, please contact the secretariat:

WEO Executive Secretariat
World Endoscopy Organization (WEO)
c/o Hamilton Services GmbH
Landwehr Str 9
80336 Munich
Germany

Tel. +49-89-9077936-12
Fax +49-89-9077936-20
secretariat@worldendo.org