Advanced imaging for detection and differentiation of colorectal neoplasia: updated ESGE guideline.

Authors

Raf Bisschops, University Hospitals Leuven, Department of Gastroenterology and Hepatology, TARGID, KU Leuven, Belgium

James E. East
1Translational Gastroenterology Unit, Nuffield Department of Medicine, Experimental Medicine Division, John Radcliffe Hospital, University of Oxford, Oxford, UK
2 Oxford National Institute for Health Research Biomedical Research Centre, Oxford, UK

Cessare Hassan
Digestive Endoscopy,'Nuovo Regina Margherita Hospital, Rome, Italy

Yark Hazewinkel

Department of Gastroenterology and Hepatology, Amsterdam University Medical Center, location Academic Medical Center, University of Amsterdam, the Netherlands

Michal F. Kaminski
1. Department of Gastroenterological Oncology, the Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland

2. Department of Gastroenterology, Hepatology and Oncology, Medical Center for Postgraduate Education, Warsaw, Poland

3. Institute of Health and Society, University of Oslo, Oslo, Norway

Helmut Neumann
Department of Medicine I, University Medical Center Mainz, Mainz, Germany

Maria Pellisé

Department of Gastroenterology. Institut clinic de Malalties Digestives I Metabòliques. Hospital Clinic of Barcelona.

Institut d'Investigacions Biomediques August Pi i Sunyer (IDIBAPS). Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd).

Universitat de Barcelona, Barcelona, Spain

* = contributed equally to the manuscript

Giulio Antonelli

Marco Bustamante Balen

Gastrointestinal Endoscopy Unit, Digestive Diseases Department, La Fe Polytechnic University Hospital, Valencia, Spain; 2 Gastrointestinal Endoscopy Research Group, La Fe Health Research Institute

Emmanuel Coron

CHU Nantes, Université Nantes, Institut des Maladies de l'Appareil Digestif (IMAD), F-44000 Nantes, France

Georges Cortas

Division of Gastroenterology

University of Balamand Faculty of Medicine

St. George Hospital University Medical Center

Beirut, Lebanon

Marietta Iacucci

Institute of Translational of Medicine, Institute of immunology and immunotherapy and

NIHR Biomedical Research Centre, University of Birmingham and University Hospitals

Birmingham NHS Foundation Trust, UK

Mori Yuichi

Digestive Disease Center, Showa University Northern Yokohama Hospital, Yokohama, Japan

Gaius Longcroft-Wheaton

Nastazja Pilonis

1. Department of Gastroenterological Oncology, the Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland

2. Department of Gastroenterology, Hepatology and Oncology, Medical Center for Postgraduate Education, Warsaw, Poland

Ignasi Puig

1. Digestive Diseases Department. Althaia Xarxa Assistencial Universitària de Manresa, Manresa, Spain. 2. Medicine Department. Facultat de Ciències de la Salut, Universitat de Vic-Universitat Central de Catalunya (UVic-UCC), Manresa, Spain

Jeanin E. van Hooft

Department of Gastroenterology and Hepatology, Amsterdam University Medical Centers, University of Amsterdam, Cancer Center Amsterdam, Meibergdreef 9, Amsterdam, The Netherlands

Evelien Dekker

Department of Gastroenterology and Hepatology, Amsterdam University Medical Center, location Academic Medical Center, University of Amsterdam, the Netherlands

Funding (exactly as worded here please):

James E. East was funded by the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre. The views expressed are those of the author(s) and not necessarily those of the National Health Service, the NIHR or the Department of Health.
Raf Bisschops was funded by a grant of the Research Foundation Flanders (FWO).

Yark Hazewinkel: no funding

Yuichi Mori was funded by the Japan Society for the Promotion of Science

Marietta Iacucci receives funding support from National Institute for Health Research (NIHR)Birmingham Biomedical Research Centre Birmingham. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health

Helmut Neumann: no funding.

Emmanuel Coron : no funding

This guideline is an official statement of the European Society of Gastrointestinal Endoscopy (ESGE). It is a revision of the previously published guideline addressing the role of advanced endoscopic imaging for detection and differentiation of colorectal neoplasia [1] .

Main recommendations

1. **ESGE suggest that high definition endoscopy, dye or virtual chromoendoscopy, as well as add-on devices can be used in average risk patients to increase the endoscopist's adenoma detection rate. However, their routine use must be balanced against costs and practical considerations. (Weak recommendation, high quality of evidence)**
2. **ESGE recommends the routine use of high definition systems in individuals with Lynch syndrome. (Strong recommendation, high quality of evidence)**
3. **ESGE recommends the routine use of dye-based pancolonic chromoendoscopy or virtual chromoendoscopy with targeted biopsies for neoplasia surveillance in patients with long-standing colitis. (Strong recommendation, moderate quality of evidence).**
4. **ESGE suggests that virtual chromoendoscopy and dye-based chromoendoscopy can be used, under strictly controlled conditions, for real-time optical diagnosis of diminutive (≤ 5 mm) colorectal polyps and replace histopathological diagnosis. The optical diagnosis has to be reported using validated scales, must be adequately photodocumented, and can be performed only by experienced endoscopists who are adequately trained, as defined in the ESGE curriculum, and audited (weak recommendation, high quality of evidence).**
5. **ESGE recommends the use of HD white light endoscopy in combination with (virtual) chromoendoscopy to predict the presence and depth of any submucosal invasion in non-pedunculated colorectal polyps prior to any treatment. (Strong recommendation, moderate quality of evidence).**
6. **ESGE recommends the use of virtual or dye-based chromoendoscopy in addition to white light endoscopy for the detection of residual neoplasia at a piecemeal polypectomy scar site (Strong recommendation, moderate quality evidence).**
7. **ESGE suggests the possible incorporation of computer-aided diagnosis (detection and characterisation of lesions) to colonoscopy, if acceptable and reproducible accuracy for colorectal neoplasia is demonstrated in high quality multi-centre in vivo clinical studies. Possible significant risks with implementation, specifically endoscopist deskilling and over-reliance on AI, non-representative training datasets, and hacking, need be considered. (weak recommendation, low quality of evidence).**

Introduction

Colonoscopy is the key examination technique in a colorectal cancer screening program for detection and treatment of early precursor lesions and timely diagnosis of colorectal cancer (CRC)[2,3]. The quality of colonoscopy, which depends on both bowel preparation and examination technique is the main determining factor that drives the protective effect of this invasive examination to decrease the disease burden on society[4–6]. Over the last fifteen years, several new techniques to improve polyp detection and characterisation have been developed and studied[7]. For all these techniques, the possible financial burden, learning curve and additional cost need to be balanced against the potential benefit. In general, a point of potential bias in the available literature lies in the fact that it is impossible to blind the endoscopist to the technique that is being studied. Therefore, even the setting of a fully randomized trial, there is always a potential bias in favour of any technique that mau effect the performance of the endoscopists, even subconsciously. This update of the previously

published guideline aims to put the new evidence that became available over the last 5 years into perspective and provide statements on what the possible role of advanced techniques may be in polyp detection or characterisation in the average risk and high risk population. The potential role of artificial intelligence in the detection and characterisation of colorectal lesions, including possible hazards of its implementation, has been addressed for the first time. We also refer for training in optical diagnosis of diminutive polyps, detection of colitis associated neoplasia and prediction of invasion of larger polyps to the standardised ESGE training curriculum. Although this work is in progress, we anticipate that the curriculum will be available in 2020 and want to include this standard in the guideline as a prerequisite for obtaining cognitive skills in CE for lesion characterisation and detection.

Methods

The ESGE commissioned this guideline (chair J.v.H.) and appointed a guideline leader (R.B), who invited the listed authors to participate in the project development. The key questions were prepared by the coordinating team (R.B; E.D; J.E. E; M.P;M.K; C.H; H.N) and were then approved by the other members. The coordinating team formed task force subgroups, based on the statements of the previous guideline, each with its own leader, and divided the key topics among these task forces (Appendix 1) with a specific focus on the update of literature and revision of the statements . The guideline was developed during September 2018 and June 2019. The work included telephone conferences, a face to face meeting and online discussions and additional Delphi voting if necessary. In addition to the five TFs in the previous GL, we included a sixth task force to address the role of artificial intelligence (AI) in the detection and characterisation of colorectal polyps. The TFs conducted a literature search of the following techniques: high definition endoscopy, chromoendoscopy or dye-based endoscopy, virtual chromoendoscopy (NBI, i- SCAN, FICE and BLI), autofluorescence endoscopy (AFI) and add-on devices. The techniques which are under development or without clear clinical implementation since the time of the publication of the previous guidelines were not included (i.e. confocal endomicroscopy, endocytoscopy, optical coherence tomography). Key questions were formulated using PICO methodology [8].

The literature search was conducted through the Medline (via Pubmed) and the Cochrane Central Register of Controlled Trials up to June 2019. New evidence on each key question was summarized in the tables using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. Grading depends on the balance between the benefits and risk or burden of any health intervention [9]. (Appendix 2). Further details on guideline development have been reported before [10].

The results of the search were presented to all members of the guideline committee during a meeting in Prague on April 1st 2019. After this meeting drafts were made by the chairs of each TF and distributed between the TF members for revision and online discussion. Statements were created by consensus or Delphi voting of two rounds for task force 2.

In July 2019, a draft prepared by R.B. and the chairs of all TFs was sent to all group members. After agreement of all members had been obtained, the manuscript was reviewed by a two external reviewers and was sent for further comments to the ESGE national societies and individual members. After this, the manuscript was submitted to the journal Endoscopy for publication. The journal subjected the manuscript to peer review, and the manuscript was amended to take into account the reviewers' comments. The final revised manuscript was agreed upon by all the authors. This

Guideline was issued in 2019 and will be considered for update in 2024. Any interim updates will be noted on the ESGE website: http://www.esge.com/esge-guidelines.html.

Evidence and statements

Evidence statements are compared to the ones in the previous guideline (2014). The previous statements are written in Italic and the new statements in bold. The statements are grouped according to the different TFs.

TF 1: Detection of colorectal neoplasia in the average risk population

Previous statements:

- *ESGE suggests the routine use of high definition white-light endoscopy systems for detecting colorectal neoplasia in average risk populations (weak recommendation, moderate quality evidence).*
- *ESGE does not recommend routine use of virtual pancolonic chromoendoscopy, AFI, or add-on devices for detecting colorectal neoplasia in average risk populations (strong recommendation, high quality evidence).*

New statement

ESGE suggests that high definition endoscopy, dye or virtual chromoendoscopy, as well as add-on devices can be used in average risk patients to increase the endoscopist's adenoma detection rate. However, their routine use must be balanced against costs and practical considerations. (Weak recommendation, high quality of evidence)

The term of average risk population refers to patients undergoing screening colonoscopy outside of the setting of colitis or hereditary syndromes. Colorectal cancer screening is performed on a large scale in Europe, and therefore a small increase in adenoma detection may have a significant effect on health care outcome of colorectal cancer [11]. Nonetheless, because of the widespread use of colonoscopy for colorectal cancer screening, the cost and practicality of advanced imaging techniques or add-on devices has to be taken into consideration to avoid too much financial or organisational burden.

High Definition Endoscopy

A 2011 meta-analysis of five studies including 4,422 average risk patients showed a 3.5% (95% Confidence Interval (CI) 0.9%–6.1%) incremental yield from high definition white-light endoscopy (HD-WLE) over standard definition white-light endoscopy (SD-WLE) for the detection of patients with at least one adenoma [12]. There were no differences between HD-WLE and SD-WLE for high-risk adenomas. We postulate that the difference in the fields of view of the endoscopes that were used is unlikely to account for the increased yield observed with HD-WLE because three randomized controlled trials (RCTs) from two centers found no significant difference in polyp detection rates between SD-WLE endoscopies with 140° and 170° fields of view[13–15].
Also in a two-center RCT published after the meta-analysis [16], the proportion of participants in whom adenomas were detected with HD-WLE was higher as compared with SD-WLE (45.7%

vs. 38.6%; p=0.166). The difference was significant for patients with flat adenomas (9.5% vs. 2.4%; p=0.003) and right-sided adenomas (34.0% vs. 19.0%; p=0.001).
A recent RCT [17] comparing HD-WLE with SD-WLE in 1855 patients has shown a significant increase in detection of sessile serrated lesions, also precursors for CRC (8.2% vs. 3.8%), as well as adenocarcinomas (2.6% vs. 0.5%). However, in this study no difference in ADR or PDR was seen.
Two recent multicenter RCTs [18,19] have postulated that two generations of improvements in colonoscopes are necessary to significantly increase ADR. The two RCTs compared the latest generation HD-WLE colonoscopes from one company (Olympus 190C) against SD next to last colonoscopes (Olympus 160C) both in a hospital [18] and in a private-practice [19] setting. Results from both trials were not fully concordant. In the hospital setting, a significant decrease in adenoma miss rates for HD colonoscopes was found (16.6%; 95%CI 13.0%-20.1% vs. 30.2%; 95%CI, 25.9%-34.6%; p=<0,001) as well as a significant increase in ADR (43.8% vs. 36.5%; p=0.03). [18] In the private-practice setting [19] however, ADR difference in favor of the latest generation colonoscope did not reach statistical significance (32% vs. 28%; p=0.10]. The detection of diminutive polyps (<5mm) was significantly increased (22.5% vs 15.6%; p=0,0002) for HD-WLE, as well as the adenoma per patient rate (all adenomas/all patients): 0.57 vs. 0.47; p= < 0.001. Details on the mentioned RCTs are available in appendix 3.
Cost–effectiveness of using HD-WLE in routine practice was not studied. High-definition colonoscopes are available from all major manufacturers.
Based on the above results with moderate to high quality evidence we can conclude that HD systems may be of benefit to improve polyp and adenoma detection, although trial results are not entirely consistent.

Virtual chromoendoscopy

NBI

Four meta-analyses and one Cochrane systematic review of RCTs compared detection of colorectal lesions in average risk populations using WLE and NBI [20–24]. When considering HD-WLE vs HD-NBI, none of these showed a significant difference in adenoma detection rate between the two technologies. HD-NBI showed a small increase in detection rate when compared to SD-WLE only.
A very recent meta-analysis [25] comprised data of 4,491 individual patients from 11 RCTs. In this study, HD-NBI showed a significant increase in unadjusted odds ratio for adenoma detection compared to HD-WLE: OR 1.14; 95% CI 1.01–1.29; p= 0.04 (ADR: HD-WLE 42.3% vs. 45.2% HD NBI). When sub-analyses were performed, NBI showed an increased detection only when preparation was best (compared to average). Moreover, it was only the second generation NBI, with a brighter light, that significantly increased ADR, and not the first-generation (OR for second-generation NBI 1.28; 95% CI, 1.05–1.56; p=0.02).
We can therefore concluded that the additional value of NBI in polyp detection is rather marginal, taking into consideration the marginal significance in the meta-analysis. The introduction of better imaging quality with HD systems has probably a more important role.

i-SCAN/FICE/BLI/LCI

One meta-analysis, published in 2014 and including 5 studies with 3032 patients [23], compared HD-FICE and HD-i-SCAN vs. HD-WLE in the detection of adenomas and found no additional detection with these advanced techniques. (RR 1.09 95%CI: 0.97-1.23).

A RCT published after the meta-analysis [26] showed a favorable result for i-SCAN technology, with a significantly higher ADR in the i-SCAN group compared to the HD-WLE colonoscopy group (47.2% vs. 37.7%; p = 0.01). This result, however, was mainly due to an increased rate of diminutive, flat and right-sided adenomas.
Data on BLI and LCI for the detection of colorectal lesions are preliminary. Recent RCTs on LCI showed an increased per-patient ADR compared to HD-WLE (37% vs. 28%) [27], as well as a reduction in the miss rate in the right colon [28]. The single recent RCT on BLI [29] showed an increased mean adenoma per patient rate (1.27±1.73 vs. 1.01±1.36; p=0.008), but no increase in ADR or PDR compared to HD-WLE.
Details on the mentioned studies are available in appendix 4.
In conclusion, data on advanced imaging with these techniques is scarce and the beneficial effect in terms of incremental polyp detection seems to be clinically marginal.

Autofluorescence imaging endoscopy

One meta-analysis published in 2015 [30] including six RCTs and 1199 patients evaluated AFI for the detection of colorectal neoplasia in average risk patients, and showed no significant difference in ADR or PDR by AFI or WLE (ADR: OR 1.01; 95%CI 0.74–1.37; p=0.96) (PDR:OR 0.86; 95%CI 0.57–1.30; p=0.71), with no significant heterogeneity among the studies (p=0.67; I^2=0).
One recently published RCT [31] focused on the role of updated AFI in the detection of flat lesions and showed a significant increase in the detection of right-sided flat lesions (adenomas and carcinoma, not SSPs) (0.87 [0.78-0.97] vs 0.53 [0.46-0.61]), but no increase in overall ADR or PDR. Details on the mentioned studies are available in appendix 5.
Based on the findings of the meta-analysis there seems to be no major additional value of AFI for polyp detection in the average risk population. In addition the system is not commercialized.

Add-on devices

In 2018, two network meta-analyses investigating the efficacy of add-on devices (cap, Endocuff, Endorings) to improve ADR were published [32,33].
One network metanalysis including 25 RCTs and 16,103 patients [32] showed an overall slight increase in ADR for add-on devices compared to standard colonoscopy (SC): 39.3% vs 35.1%, RR 1.13; 95%CI 1.03-1.23; p=0.007). When considering the single devices, both Endocuff vs HD-WLE and Endorings vs. SC showed a small but significant improvement in ADR, these however would be of benefit mostly for already high-performing endoscopists. The use of a short transparent cap at the tip of the endoscope resulted in a statistically insignificant increase in ADR compared to HD-WLE (37% vs 34.3%, RR, 1.07; 95% CI, 0.96-1.19; p=0.19). However, the considerable heterogeneity (I^2=89%) should lead to cautious interpretation of these results. Subgroup analysis revealed a substantial increase of ADR and PDR of lesions ≤5mm (RR 1.53, 95%CI 1.13-1.71 and RR 1.38, 95%CI 1.10-1.43 respectively).
The second network meta-analysis [33] included 10 studies reporting on 6,047 patients and showed, in contrast to the latter, an overall increase in ADR for Endocuff in comparison to HD-WLE (OR 1.36; 95%CI 1.12-1.60; p=0.001), that was only significant in low performing endoscopists (OR 1.85; 95%CI 1.35-2.53; p=0.0001, for ADR <25%) when a subgroup analysis was performed.
Most RCTs do not report cost effectiveness data and this aspect has not yet been evaluated systematically. Details on the mentioned studies are available in appendix 6.

Based on the available data, the evidence for general use of add-on devices is rather weak and cost effectiveness has never been well assessed. It might however have a role in low performers to assist them in reaching the important ADR threshold of 25 % [4].

Dye-based Chromoendoscopy

A recently updated Cochrane systematic review of 2016 [34] analyzed seven RCTs (total 2727 patients) that assessed the role of dye-based CE in detecting colorectal lesions outside the setting of polyposis or colitis. Pancolonic CE significantly increased the number of patients with at least one polyp detected (OR 1.87; 95%CI 1.51–2.30) and of those with at least one neoplastic polyp (adenoma or carcinoma) detected (OR 1.53; 95%CI 1.31-1.79). Limitations of the systematic review were the lack of blinding in the RCTs, and the significant heterogeneity observed between the studies. Indeed, quality of evidence was graded as low in this review.
Since the publication of this Cochrane systematic review, two large multicenter RCTs have been published. The first [35], including 1065 patients, showed an increase in the mean adenoma per patient rate (0.79 vs. 0.64; p=0.005), but not in ADR (40.4 % vs. 37.5 %; OR 1.13; 95 %CI 0.87 - 1.48; p = 0.35) or sessile serrated lesion detection rate, using routine pancolonic CE compared to HD-WLE.
A recent, phase 3, multicenter RCT [36] has evaluated the role of a novel pH- and time-dependent per-oral methylene blue formulation (MB-MMX) that is delivered in pills taken during the bowel preparation phase. This RCT enrolled 1205 patients undergoing screening or surveillance colonoscopy and found an increased overall ADR in the MB-MMX group compared to placebo (56.29 vs 47.81% (OR, 1.46; 95% CI, 1.09–1.96). The MB-MMX group showed a higher number of patients with adenomas ≤5mm (37.11% vs. 30.90%; OR, 1.36; 95% CI, 1.01–1.83). Details of the aforementioned studies are available in appendix 7.
We can conclude that chromoendoscopy increases ADR and PDR, however it's systematic implementation may be hampered in daily practice due to practical considerations and additional costs. The use of MB-MMX may help to overcome these.

TF 2 : Detection of colorectal neoplasia in high risk population with hereditary syndromes

Previous statements :

- *ESGE recommends the routine use of high definition pancolonic chromoendoscopy in patients with known or suspected Lynch syndrome (conventional chromoendoscopy, NBI, i-SCAN) or serrated polyposis syndrome (conventional chromoendoscopy, NBI) (strong recommendation, low quality evidence).*
- *ESGE does not make any recommendation for the use of advanced endoscopic imaging in patients with suspected or known familial adenomatous polyposis (FAP) including attenuated and MUTYHassociated polyposis (insufficient evidence to make a recommendation).*

New statements

- **ESGE recommends the routine use of high definition systems in individuals with Lynch syndrome. (Strong recommendation, high quality of evidence)**

- **ESGE suggests that the use of virtual chromoendoscopy may be of benefit in individuals with Lynch syndrome undergoing colonoscopy; however its routine use must be balanced against costs, training and other practical considerations (weak recommendation, moderate quality of evidence).**
- **ESGE suggests the use of high-definition systems and dye-based chromoendoscopy in the diagnosis and surveillance of individuals with serrated polyposis syndrome; however routine use must be balanced against costs, training and practical considerations. (weak recommendation, moderate quality of evidence)**
- **ESGE does not recommend the systematic use of dye-based nor virtual chromoendoscopy for FAP, MUTYH-associated polyposis or hamartomatous polyposis (strong recommendation, moderate quality of evidence)**

Lynch syndrome

Lynch syndrome is the most common cause of hereditary colorectal cancer (CRC). It is an autosomal dominant disorder caused by germline mutations in the DNA Mismatch Repair (MMR) genes (i.e., *MLH1, MSH2, MSH6, PMS2 and EpCAM*). An accelerated progression from adenoma to CRC has been described, and often the adenomas display advanced histology features (i.e., high-grade dysplasia or a villous component), are frequently flat in morphology, and located in the proximal colon compared with sporadic adenomas. An intensive surveillance strategy with annual or biennial colonoscopy starting at early ages has reduced both the incidence and mortality associated with CRC. A high detection rate for these aggressive adenomas is especially important to minimize the risk of interval CRC.

In total, seven studies comparing indigo carmine CE with WLE in patients with Lynch Syndrome are published [37–42]. Three mono-centric studies with a small number of patients in a back-to-back design showed that CE was superior to SD-WLE with an adenoma miss rate ranging from 61%-74%[37,38,41]. A recent back-to-back multicenter study, where the second pass was performed by a different endoscopist in order to minimize the second inspection bias, showed again superiority of SD-CE over SD-WLE (ADR of 41% and 23%, respectively; adenoma miss rate 52%). Nevertheless, the study had no comparator arm, was slightly underpowered (ß-risk of 26%) and the withdrawal time during CE was twice that of WLE [39]. All these results are methodologically flawed by the back-to-back design that may lead to an overestimation of the effect of CE over WLE.

There are three trials with a control arm. A study by Stoffel et al included 54 patients in four centres[40]. After the first pass with SD-WLE, 28 patients were randomised to a second pass with CE and 27 to a second pass with an intensive 20 minutes inspection, showing no significant difference in adenoma miss rate.

Very recently, 2 well-powered randomised, multicentre, controlled studies with a comparator arm were published. Haanstra et al showed no differences in neoplasia detection rate between CE and WLE in 246 Lynch patients neither at baseline (27% vs. 30% respectively; p=0.56) nor in the 2 year follow-up colonoscopy (26% vs. 28% respectively; p =0.81) [42]. This study is limited by the fact that CE was applied only proximal to splenic flexure and that the study extended over a very long recruitment period (10 years) which may entail important variability in procedure performances and ability for detecting colorectal lesions. Rivero-Sánchez et al performed a study with only HD endoscopes and high detector endoscopists in 256 Lynch patients in 14 different hospitals, and showed that ADR was statistically not different between HD-CE than HD-WLE (34.4% [95% CI; 26.4%–43.3%] vs. 28.1% [95% CI;

21.1%–36.4%], p=0.28) [43]. In both trials, CE was more time-consuming and detected more clinically irrelevant lesions. Details on the mentioned studies are available in appendix 8.

In Lynch patients, 3 mono-center back-to-back studies were performed with HD virtual CE, which appeared to be superior to HD-WLE for polyp detection. [44,45]. East et al showed in a non-randomized back-to-back study in 62 Lynch patients that during a second inspection, with NBI additional adenomas were detected in 17/62 (27%) patients. In this study, 26/62 (42%) patients had at least one adenoma detected that was missed during the first inspection with WLE [44]. Bisschops et al showed in a randomized crossover study in 61 Lynch patients that the adenoma miss rate was significantly lower when I-scan was used in comparison to HD-WLE (12% vs. 62%) [45]. Both studies were conducted by a single expert endoscopist and in the second study, the ADR was relatively low for HD-WLE inspection (19%). On the other hand, virtual CE appears to be inferior to dye-based CE in two back-to-back studies. In a German cohort study the incremental yield of CE vs. SD-WLE (n=47) and NBI (n=62) was assessed, showing a higher detection with CE during second inspection [41]. Very recently, a study comparing NBI to CE in a back-to-back design has been published as an abstract. This multicentre French study in 138 Lynch patients showed an adenoma miss rate of 48% for the third generation of HD-NBI (Exera III, 190 series) when followed by a second pass with dye-based CE by the same endoscopist. The authors concluded that although NBI colonoscopy is less time consuming, cannot be recommended to replace dye-based CE in Lynch syndrome patients [46].
Finally, one study in 75 patients compared AFI, with the Xillix-system (XillixTechnologies Corporation, Richmond, BC, Canada), to WLE in a crossover trial, showing a better detection of adenomas for AFI (92% vs. 68% for WLE).[47] Details on the mentioned studies are available in appendix 9.

In conclusion, evidence suggests a benefit of dye-based CE in Lynch Syndrome patients at the expense of longer procedure times. However, most of the studies were performed with SD endoscopes, had a small and heterogeneous sample size and a non-randomized back-to-back design that may have lead to a bias in favour to dye-based CE. Recent evidence from two well-powered multicenter trials with a parallel design have shown no differences in ADR between WLE and dye-based CE. This possibly implies that a thorough inspection by high detectors and using high definition endoscopes might decrease the advantageous effect of dye-based CE in Lynch patients. These two RCTs are the reason for a slight discrepancy between the recommendations in this guideline and the recently published guideline on the management of polyposis syndromes, that included also dye based CE as a suggestion. However the new evidence was not available at the time of development of the other guideline [48]. On the other hand, two studies have reported superiority of virtual CE (NBI and i-Scan) over WLE. Conversely, other two studies have shown that dye-based CE was superior to virtual CE. Most of these studies have methodological limitations such as back-to-back design, the second pass performed by the same expert endoscopist or with a low ADR in the first pass.

Taking this in consideration ESGE recommends at least the use of HD endoscopes in Lynch patients and suggests in addition that in view of the evidence that advanced imaging techniques like virtual chromoendoscopy can be useful.

Serrated Polyposis Syndrome (SPS)

Serrated polyposis syndrome (SPS) has emerged as the most frequent colorectal polyposis syndrome. This entity is associated with an increased risk of CRC and is often grouped with the hereditary polyposis syndromes although no underlying gene defect has been identified yet.

Although recent studies show an increase in SPS prevalence [49–51]attributed to a major clinical and pathological awareness and better endoscopic diagnostic accuracy[52,53], SPS remains an underdiagnosed entity [54]. SPS diagnosis depends directly on the capacity for detecting serrated lesions (SLs), which are often easily overlooked due to their imperceptibility [51]. In a FIT-based CRC screening program, a reassessment colonoscopy within one-year after a screening colonoscopy tripled the number of patients diagnosed with SPS. Use of CE, either dye-based or virtual, at reassessment colonoscopy was associated with a higher detection rate of serrated lesions, but not of adenomas [55].

Recently, a multicenter randomized back to back study evaluated the usefulness of dye-based CE with indigo carmine for the detection of colonic polyps in SPS patients under surveillance [56]. Patients were randomly assigned to a group: one received 2 HD white-light endoscopy examinations (n=43) and the other received HD-white light endoscopy followed by 0.4% indigo carmine CE (n=43). This study demonstrated a significantly higher additional polyp detection rate in the HD-CE group (0.39; 95%CI 0.35-0.44) than in the HD-WLE group (0.22; 95%CI 0.18-0.27; p< 0.001). HD-CE detected more serrated lesions than HD-WLE (40% vs. 24%; p=0.001), serrated lesions proximal to the sigmoid (40% vs.21%, p= 0.001) and serrated lesions >5mm proximal to the sigmoid (37% vs. 18%; p=0.013). Over 70% of additional serrated lesions detected by CE were hyperplastic polyps and at least two-thirds of them were located proximal to the sigmoid colon. Detection of adenomas and serrated lesions >10 mm did not differ significantly between groups. The additional detection rate for SSP was higher in the HD-CE group (0.29 in HD-CE vs. 0.13 in HD-WL; p=0.059) but not statistically significant. In a multivariate logistic regression analysis, only use of HD-CE was independently associated with an increase in polyp detection throughout the colon.

The role of virtual CE (i.e. NBI) in SPS has been evaluated in two randomised crossover studies. A first single-centre study including 22 patients showed that NBI had a lower polyp miss rate than high-resolution WLE (10% vs. 36%), however this was not confirmed in a second multicentre study including 52 SPS patients (20% vs. 29%; p=0.065).[57,58] The authors explained this contradictory result by the fact that the pilot study was performed by a single endoscopist, at a single institution and with older equipment.

A recent multicentre prospective randomised controlled trial evaluated the usefulness of Endocuff assisted colonoscopy in the SPS surveillance, showing no increase in detection of sessile serrated lesions, adenomas or polyps overall [59]. Details on the mentioned studies are available in appendix 10.

Thus, based on the abovementioned single RCT, the use of dye-based CE improves polyp detection and could be considered in the surveillance of SPS patients. However, its routine use must be balanced against practical considerations.

TF 3 : Detection and differentiation of colorectal neoplasia in IBD

Patients with long-standing or extensive ulcerative colitis (UC) or Crohn's disease are at an increased risk of developing CRC compared to the average risk population. Accordingly, regular and extensive surveillance colonoscopies are recommended [60,61]. In this context, advanced endoscopic imaging may be of benefit by (I) increasing the detection rate of neoplasia, (II) improving the differentiation

of lesions (colitis associated neoplasia, sporadic neoplasia, and non-neoplastic lesions) and (III) reducing the number of unnecessary biopsies.

Previous statements :

- *ESGE recommends the routine use of 0.1% methylene blue or 0.1%–0.5% indigo carmine pancolonic chromoendoscopy with targeted biopsies for neoplasia surveillance in patients with long-standing colitis. In appropriately trained hands, in the situation of quiescent disease activity and adequate bowel preparation, non-targeted four quadrant biopsies can be abandoned (strong recommendation, high-quality evidence).*
- *ESGE found insufficient evidence to recommend for or against the use of virtual chromoendoscopy or autofluorescence imaging (AFI) for the detection of colorectal neoplasia in inflammatory bowel disease (insufficient evidence to make a recommendation).*

New statement :

- **ESGE recommends the routine use of dye-based pancolonic chromoendoscopy or virtual chromoendoscopy with targeted biopsies for neoplasia surveillance in patients with long-standing colitis, in the situation of quiescent disease activity and adequate bowel preparation. (Strong recommendation, moderate quality of evidence).**
- **ESGE recommends that after obtaining proper training in chromoendoscopy, as defined in the ESGE curriculum, in the situation of quiescent disease activity and adequate bowel preparation, non-targeted four-quadrant biopsies can be abandoned (strong recommendation, high quality of evidence).**
- **ESGE suggests that In case of high risk patients with a personal history of colonic neoplasia, tubular appearing colon, strictures and primary sclerosing cholangitis, chromoendoscopy targeted biopsies can be combined with four-quadrant non-targeted biopsies every 10 cm in the colon (weak recommendation, low quality evidence).**

In general, surveillance of long standing colitis can only be accurately performed in the absence of disease activity and with an adequate bowel preparation. Indeed, all imaging studies mentioned below only apply to patients with longstanding colitis undergoing surveillance in the setting of quiescent disease activity and adequate bowel preparation. The use of dye-based or virtual CE is technically cumbersome in the presence of active colitis, in the presence of multiple inflammatory or post-inflammatory polyps and poor bowel preparation.

SD-WLE or HD-WLE versus dye-based CE

Overall, in 8 prospective studies comparing dye-based CE with SD-WLE, the former consistently increased the proportion of patients found with dysplasia with a factor 2.08–3.26 [62–66]. A meta-analysis showed a pooled incremental yield of CE with random biopsies over SD-WLE with random biopsies for the detection of patients with neoplasia of 7% (95%CI 3.2%–11.3%). Moreover, the difference in proportion of lesions detected by targeted biopsies only was 44% (95%CI 28.6%–59.1 %) in favour of dye-based CE. This finding has been confirmed by a new retrospective cohort study including 78 patients with ulcerative colitis[67] in which CE visualized dysplastic lesions in 50 patients, including 34 new lesions not visualized on the index SD-WLE examination . A prospective longitudinal study included 55 patients with UC and identified 44 dysplastic lesions in 24 patients; 6 were detected by random biopsy, 11 by WLE, and 27 by CE [68]. CE and targeted WLE were more likely than random biopsies to detect dysplasia, and CE was superior to SD-WLE (OR 2.4; 95%CI, 1.4-

4.0). One retrospective cohort study including 2242 colonoscopies demonstrated equal dysplasia detection rate for CE and WLE with random biopsies (11% vs 10%,p=0.80) [69].

Most recently CE was evaluated for neoplasia detection and characterization in long-standing colitis in more real life setting other than a randomized controlled trial with only expert endoscopists [70]. In this muticenter prospective cohort study including 350 patients, 41.5 % of colonoscopies were performed with SD endoscopes. Overall dysplasia miss rate for combined HD and SD WLE was 40/94 (57.4% incremental yield for CE). CE-incremental detection yield for dysplasia was comparable between SD and HD (51.5% vs. 52.3%, p=0.30) and statistically not different between expert and non-expert endoscopists (18.5% vs 13.1% p=0.2).

Although this last study did not show a difference between SD and HD-CE detection of neoplasia, the additional value of HD endoscopy in detecting UC related neoplasia became more recently clear and seems to indicate that CE increases detection when SD endoscopy is used. A recent meta-analysis of 10 studies (494 patients) compared dye-based CE with SD-WLE and HD-WLE [71]. Six of them were RCTs (3 on SD-WLE and 3 on HD-WLE). The proportion of patients diagnosed with dysplasia using CE was 17% as compared with 11% for WLE. When analyzed separately, CE was more effective at identifying dysplasia than SD-WLE (RR 2.12; 95%Cl 1.15-3.91), however CE was not more effective as compared with HD-WLE (RR 1.36; 95%C, 0.84-2.18). Based on this meta-analysis, non-RCTs demonstrated a benefit of CE over SD-WLE and HD-WLE, whereas RCTs showed a small benefit of CE over SD-WLE, but not over HD-WLE. In addition two other meta-analyses comparing different advanced techniques point in the same direction. One recent systematic review comparing CE to other techniques (SD-WLE, HD-WLE, HD-NBI or HD-I-scan), included 10 randomized trials with 1500 participants [72]. CE was associated with higher detection of patients with dysplasia as compared with other techniques. However, subgroup analyses confirmed this effect only in comparison with SD-WLE (RR 2.12; 95%CI, 1.15-3.91). These findings have been confirmed by another network meta-analysis including only 8 parallel-group RCTs with 924 patients [73] and comparing HD-WLE, SD-WLE, SD-CE, HD-CE and HD-NBI for detection of neoplasia in longstanding colitis. The network analysis did not find any single technique to be statistically superior. CE was probably more effective than SD-WLE for detecting any dysplasia (OR 2.37, 95% CI 0.81-6.94). Finally, a recent RCT compared HD-WLE (n=90) alone with HD dye-based CE (n=90) and virtual CE with I-scan (n=90) for detection of neoplastic lesions during IBD surveillance colonoscopy in a prospective RCT [74]. HD-WLE neoplasia detection rate (25.5%) was non-inferior either to dye-based (24.4%) and virtual CE (15.5%) for detection of all neoplastic lesions (p=0.91).

Details on the mentioned studies with SD endoscopy and HD endoscopy are available in appendix 11 and 12.

Limitations of dye-based CE in the context of long-standing colitis surveillance need to be mentioned. There is no proof that better detection of neoplasia by CE results in the reduction of CRC mortality or decreased risk of interval CRC. Data on cost–effectiveness is also limited, however reduced number of colonoscopies and histological samples could be achieved by the risk stratification [75]. One study assessed the cost-effectiveness of CE in comparison with WLE or no endoscopy for CRC surveillance in patients with UC using a decision-analytic state-transition (Markov) model with Monte Carlo simulation [76]. CE was found to be more effective and less expensive than WLE at all surveillance intervals. However, compared with no surveillance, CE was cost-effective only at 7-year surveillance intervals, with an incremental cost effectiveness ratio of $77,176. At the sensitivity levels >0.23 for dysplasia detection and cost <$2200, CE was the most cost-effective strategy, regardless of the level

of sensitivity of WLE. The estimated population lifetime risk of developing CRC ranged from 2.5% (annual CE) to 5.9% (CE every 10 years).

Virtual CE

Three RCTs compared NBI in all cases with HD-WLE for the detection of neoplasia in long-standing inflammatory bowel. Regardless of the generation of NBI and the level of definition of colonoscopes used, virtual CE did not significantly increased the detection rate of neoplastic lesions as compared with WLE [77–79]. However, virtual CE with targeted biopsies alone yielded neoplasia detection rates comparable to WLE with targeted and random four-quadrant biopsies (mean number of biopsies per patient of 0.5 to 3.5 in NBI with targeted biopsies only and 24.6 to 38.3 in WLE with targeted and random biopsies). Two RCTs compared a HD-NBI system with high definition dye-based CE, both without non targeted biopsies, for the detection of neoplasia in long-standing UC. The first, single-center, crossover RCT comparing neoplasia miss rates with HD-NBI and HD dye-based CE [80] , showed a considerably higher miss rate of neoplastic lesions with HD-NBI as compared with HD dye-based CE (31.8% and 13.6 %, respectively). However, this study was not adequately powered to show a statistical significance. The second is a recent multicenter RCT that compared HD-CE with HD-NBI in 131 patients with UC in a 1:1 randomisation [81]. Mean numbers of neoplastic lesions per colonoscopy were 0.47 for CE and 0.32 for NBI (p=0.992). The neoplasia detection rate did not differ significantly between CE and NBI (21.2% vs. 21.5%, respectively). The per lesion neoplasia detection was 17.4% for CE and 16.3% for NBI (p=0.793) and the total procedural time was on average 7 min shorter in the NBI group. One study compared I-scan as virtual CE with HD-WLE and dye-based HD-CE. There was no significant difference between three groups of patients with neoplasia detection (15.5%, 25.5% and 24.4% respectively). Although 10% non-inferiority was just passed statistically, caution should be exerted as the difference may still be clinically relevant [74]. A recent meta-analysis has highlighted the potential role of virtual CE for dysplasia detection in IBD. For the comparison NBI vs WLE, 4 studies with 305 patient were included. The analysis showed no difference in per patient neoplasia (OR 0.97, 95%CI 0.62-1.53) and per neoplastic lesion detection (OR 0.94,95%CI 0.63-1.4) [82].

Two studies (1 RCT) compared HD-WLE with AFI for the detection of colorectal neoplasia in inflammatory bowel disease [79,83]. A pilot study [83] showed that protruding lesions with a low AFI signal were significantly more likely to be neoplastic than lesions with a high AFI signal (45.0% vs. 13.3 %, respectively, p=0.043). In the RCT, the miss rate for neoplastic lesions was statistically significantly lower with AFI compared with HD-WLE (0% vs. 50%, p=0.036) [79]. It should be noted that inadequate bowel preparation and active inflammation interrupt tissue AFI, resulting in discoloration on AFI and resembling neoplasia. Another recent RCT confirmed that AFI did not meet criteria for proceeding to a large non-inferiority trial and that the existing AFI imaging technology should not be further investigated as an alternative dysplasia surveillance method [84]. Details on the mentioned studies are available in appendix 13.

Role of biopsies

A limited diagnostic yield of four quadrant biopsies in comparison to targeted biopsies was already shown in the previous guidelines. A pooled sensitivity for the detection of neoplasia with CE targeted biopsies only was 86% (range 71%–100%) [37,62,63,65,66,85–87]. The median numbers of targeted and targeted plus random biopsies were 1.3 (range 0.28–14.2) and 34.3 (range 7.0–42.2), respectively. Therefore, a number of biopsies needed during dye-based CE surveillance of long-standing colitis can be significantly reduced if targeted biopsies are taken. The yield and clinical impact of random biopsies were also assessed in a retrospective analysis of 1010 colonoscopies [88]. Overall, 11722 random biopsies (median 29) were taken in 466 surveillance colonoscopies. Neoplasia

was detected in 88 colonoscopies: in 75 (85%) by targeted biopsies, in 8 (9.1%) by both targeted and random biopsies and in 5 (5.7%) colonoscopies by random biopsies in 4 patients (7.5%). In 94% of colonoscopies neoplasia was macroscopically visible. A RCT comparing the rates of neoplasia detection by targeted vs. random biopsies in 246 patients with UC found the mean number of biopsies to contain neoplastic tissue per colonoscopy to be 0.211 (24 of 114) in the target group and 0.168 (18 of 107) in the random group [89]. Neoplasia was detected in 11.4% of patients in the target group and 9.3% of patients in the random group (p=0.617). Another, non-randomized study evaluating different surveillance strategies in 454 IBD patients showed a neoplasia detection rate of 8.2% in the random biopsy group compared to 19.1% in the targeted biopsy group [90]. Recently, a study with 1000 colonoscopies showed neoplasia in 82 patients diagnosed by targeted biopsies or removed lesions [91]. Dysplasia was detected by random biopsies in 7 patients and in 12 additional patients by random biopsies only. The yield of neoplasia by random biopsies only was 0.2% per-biopsy, 1.2% per-colonoscopy and 12.8% per-patient with neoplasia. Dysplasia detected by random biopsies was associated with a personal history of neoplasia, a tubular appearing colon and the presence of primary sclerosing cholangitis. It may therefore be careful and advisable to combine random biopsies with dye-based or virtual CE targeted biopsies in these high risk patients. . In addition, since it may be difficult to relocate small lesions with dysplasia, it may be advisable in case of lesions < 10 mm to resect the lesion entirely to facilitate patient management. Details on the mentioned studies are available in appendix 14.

In conclusion, the literature on advanced imaging in detection of colitis associated neoplasia is large but also heterogeneous as illustrated by the several meta-analysis. Although several meta-analysis have been performed on the same literature and sometimes seem to contradict each other, the additional value of dye based CE seems reasonable to accept. Recent evidence with HD endoscopes point to the fact that also virtual chromoendoscopy may be equally effective. Although the Spanish real-life study [70] did not show a clear difference in dysplasia detection between expert and non-expert (18.5% vs. 13.1%, p=0.20) and did not observe a significant learning curve for CE, it is conceivable that lesion recognition by virtual CE is facilitated by previous dye based CE. In fact, all investigators involved in the virtual CE trials had previous experience with dye based CE. In standard risk patients, the evidence clearly points to abandoning non-targeted random biopsies. The additional value of using virtual CE lies than in the fact that it is time saving (7 min less on average than dye CE [81]) and may facilitate surveillance in case of poorer bowel preparation

Neoplastic versus non-neoplastic lesions

- *ESGE recommends taking biopsies from flat mucosa surrounding neoplastic lesions and taking biopsies from or resecting all suspicious lesions identified at neoplasia surveillance in long-standing colitis, because there is no evidence that nonmagnified conventional or virtual chromoendoscopy can reliably differentiate between colitis-associated and sporadic neoplasia or between neoplastic and non-neoplastic lesions (strong recommendation, low to moderate quality evidence).*

New statement

- **ESGE recommends using advanced imaging to assess the borders of lesions in previously colitic mucosa, to assess resectability. If optical diagnosis is used for lesion characterization of visible lesions, ESGE recommends that the suspicion of neoplasia should be confirmed**

by classical histology in case of colitis surveillance (strong recommendation, low quality of evidence).

Lesions can be well delineated with HD endoscopes and advanced imaging techniques. In a RCT, comparing dye based HD-CE with HD-NBI, no dysplasia was found in biopsies taken next to a visible lesion, even when the lesion was flat [81]. This means that if lesions can be well delineated, that resectability can be defined. However the proportion of neoplasia per suspicious lesion detected during colitis surveillance is in general rather low and lies around 15 % [70,81]. This means that the majority of lesions found are regenerative changes and non-neoplastic. Especially when they are larger, resection may harbour unnecessary risks . The question therefore arises whether optical diagnosis could be used to differentiate neoplastic from non-neoplastic lesions. Modified pit pattern classifications has been used in three dye-based CE studies to differentiate between neoplastic and non-neoplastic lesions in long-standing IBD [37,62,65] with high sensitivity and specificity (93%–100% and 88%– 97%, respectively). Kawasaki et al. evaluated the efficacy of the Japanese magnifying colonoscopic classifications (JNET) for UC-associated neoplasia [92]. Lesions JNET type IIA, IIB and III correlated with the histopathological findings of low-grade dysplasia (LGD),high-grade dysplasia (HGD)/superficially submucosally invasive cancer and massively and massively submucosal invasive (mSM) carcinoma, respectively. Lesions of Kudo types III/IV, VI low irregularity, and VI high irregularity/VN by pit pattern classification were correlated with the histopathological findings of LGD/HGD, HGD, and mSM carcinoma, respectively. One more recent study evaluated the endoscopic features of HGD in 62 patients with UC [93]. HGD imaged with CE and magnifying endoscopy was frequently associated with a flat/superficial elevated area and red colour. However, magnifying endoscopes are still not widely spread and total procedure times were on average 9–11 minutes longer. Recently, a Spanish multicentre trial showed that predictive factors for neoplasia for dye based CE are Kudo pit pattern III-V, sessile morphology, loss of a innominate lines and location in the right colon [70].

Previous studies evaluating the role of non-magnified NBI in differentiating neoplastic and non-neoplastic lesions in patients with long-standing colitis suggested that a tortuous pit pattern and a high vascular pattern intensity may help to distinguish neoplastic and non-neoplastic lesions in longstanding IBD [94,95]. However, in two RCTS, the sensitivity and specificity of NBI in predicting histology were insufficient [79,96]. A more a recent multicenter interobserver study [97] showed a median sensitivity, specificity, negative predictive value, and positive predictive value for diagnosing neoplasia based on the presence of pit pattern other than I or II of 77%, 68%, 88%, and 46%, respectively. Diagnostic accuracy was significantly higher when a diagnosis was made with a high level of confidence (77% vs. 21%, $p<0.001$). The agreement for differentiation between non-neoplastic patterns (I, II) and neoplastic patterns (IIIL, IIIS, IV, or V) was moderate and significantly better for NBI in comparison with HD-CE ($\kappa = 0.653$ vs. 495, $p<0.001$). Another multi-centre, RCT compared AFI with CE for dysplasia detection in 210 patients with long-standing UC [98]. Overall sensitivity for real-time prediction of dysplasia was 76.9% for ETMI, and 81.6% for CE. Overall negative predictive value for ETMI was 96.9% and 94.7% for CE. Two-hundred and five lesions in UC were analyzed with virtual CE (FICE) in another study by Cassinotti et al. [99]. Sensitivity, specificity, positive and negative likelihood ratios of the Kudo classification were 91%, 76%, 3.8, and 0.12, respectively. Recently Aladrén et al aimed to analyze results of a CE screening program in Spain and to assess the possibility of identifying low-risk dysplastic lesions by their endoscopic appearance in order to avoid histological analysis [100]. Correlation between dysplasia and Kudo pit patterns predictors of dysplasia (≥ III) was low while Kudo I and II lesions were correctly identified with a high negative predictive value of 92 %, even by non-experts. Recently a group of international experts developed and validated a new classification FACILE (Frankfurt Advanced Chromoendoscopic Ibd

LEsions) using images from all endoscopic platforms that may improve performance in both trainees and experienced operators. The four characteristics that predicted neoplastic lesions were morphology of non-polypoid/polypoid lesion, irregular surface pattern, vessel architecture and signs of inflammation within the lesion, without using Kudo pit pattern [101]. Details on the mentioned studies are available in appendix 15.

Based on these studies we can say that optical diagnosis to a certain extend may help to identify typically non-neoplastic lesions with type I or II pit pattern, but that the overall diagnostic accuracy, even in expert hands is insufficient. Resection of small lesions < 10 mm with a neoplastic pit pattern is probably safe and maybe more practical to determine patient management in case neoplasia is found. However in larger lesions, with sessile morphology or in the right colon [70], a biopsy should always be taken to confirm or rule out dysplasia.

Task force 4: Differentiation between neoplastic and non-neoplastic small colorectal polyps.

Previous statement

> *ESGE suggests that virtual chromoendoscopy (NBI, FICE, i-SCAN) and dye-based chromoendoscopy can be used, under strictly controlled conditions, for real-time optical diagnosis of diminutive (≤ 5 mm) colorectal polyps to replace histopathological diagnosis. The optical diagnosis has to be reported using validated scales, must be adequately photodocumented, and can be performed only by experienced endoscopists who are adequately trained and audited (Weak recommendation, high quality of evidence).*

Changed statement

- **ESGE suggests that virtual chromoendoscopy and dye-based chromoendoscopy can be used, under strictly controlled conditions, for real-time optical diagnosis of diminutive (≤ 5 mm) colorectal polyps to replace histopathological diagnosis. The optical diagnosis should be reported using a validated scale, must be adequately photo-documented, and can be performed only by experienced endoscopists who are adequately trained, as defined in the ESGE curriculum, and audited (Weak recommendation, high quality of evidence).**

The vast majority of polyps detected during colonoscopy are diminutive (1–5 mm) or small (6-9 mm) in size. Diminutive polyps represent approximately 60% of all polyps detected and the risk that these lesions incur advanced pathology or cancer is very low [102–104]. However, based on current management protocols, all removed polyps, including diminutive polyps, are submitted for histological analysis. This is expensive and generates a large burden of work for pathologists and histopathology departments. Instead of sending diminutive polyps for histological evaluation, a real-time optical diagnosis by the endoscopist would allow diminutive polyps to be discarded after resection, and non-neoplastic polyps located in the rectum and sigmoid to be left in situ. Furthermore, optical diagnosis could be used to determine the interval for the next surveillance colonoscopy. The primary goal of this strategy is to reduce the number of polyps submitted for histopathological evaluation, which may lead to cost-savings.

The optical diagnosis strategy also raises several concerns. First, when diminutive polyps are discarded, advanced histological features (high-grade dysplasia, tubulovillous or villous morphology)

or invasive growth, i.e. a cancer, are not diagnosed as such. This could lead to a setting of suboptimal treatment and/or inappropriate surveillance intervals. However, risk estimates for advanced pathology within diminutive polyps are low, ranging from 0.1% to 12%, with most estimates at the lower end of this range [105–134]. Details on the mentioned studies are available in appendix 16. The rate of cancer in diminutive polyps is even lower, although not completely negligible, ranging from 0% to 0.6%, with most estimates again at the lower end of the range. To further reduce the risk of missing cancer, it is recommended that an optical diagnosis should be avoided in suspicious lesions (e. g. depressed lesions, Paris classification 0-IIc) [135]. The question whether undiagnosed advanced histological features within diminutive polyps would lead to inappropriate surveillance recommendations was recently addressed in a large study [103]. In this study, data of 12 cohorts (5 FIT cohorts and 7 colonoscopy screening cohorts) were combined, resulting in a total cohort of 64.344 individuals with 51.510 diminutive polyps. Advanced histological features were observed in 5.6% and cancer in 0.07% of all diminutive polyps. The risk of finding metachronous advanced neoplasia did not significantly differ between patients with 1 or 2 non-advanced diminutive or small adenomas (low-risk patients) compared with patients with diminutive polyps with advanced histological features detected at baseline colonoscopy. This indicates that diminutive polyps with advanced histological features do not increase the risk for metachronous advanced neoplasia and therefore seem not to interfere with a correct surveillance recommendation. Details on the mentioned studies are available in appendix 16.

A second concern is that an incorrect optical diagnosis could result in a patient being incorrectly considered at low risk for metachronous advanced neoplasia and/or that neoplastic lesions in the rectosigmoid are left in situ. For this reason, the ASGE published the Preservation and Incorporation of Valuable Endoscopic Innovation (PIVI) document in which they attempted to set standards against which a technology should be assessed in order to be deemed suitable for applying. A policy of resect and discard should have ≥90% agreement in assignment of post-polypectomy surveillance intervals when compared with decisions based on pathology assessment and a policy of leaving suspected non-neoplastic polyps in place should have a ≥90% negative predictive value, when used with high confidence [136]. A meta-analysis published in 2015 [137], including 20 NBI studies [138–157], 8 I-SCAN studies [155,158–163] and 8 FICE studies [164–171], all in-vivo studies and published between 2008 and 2014, showed that the pooled NPV of NBI for adenomatous polyp histology was 91% (95% CI 88%–94%). The agreement in assignment of post-polypectomy surveillance intervals with NBI was 89% (95% CI 85%-93%). Importantly, subgroup analysis indicated that the pooled NPV and the surveillance agreement was only greater than 90% for academic medical centers, for experts and when the optical assessment was made with high confidence. Comparable results were observed for I-SCAN. For FICE the pooled NPV in this meta-analysis was 80% (95% CI 76%–85%). Dye-based CE shows similar accuracy in differentiating between neoplastic and non-neoplastic polyps, but because of inconvenience and costs associated with the use of dyes it is unlikely that this technique will be adopted in routine clinical practice [164,166]. From 2015 onwards, real-time differentiating studies, performed in academic centres as well as in community hospitals, have shown conflicting results in achieving the above mentioned PIVI thresholds [125,172–179]. This variability in performance may be explained by a lack of rigorous training and/or performance measurement. However, in those studies in which the endoscopists where adequately trained prior to the study, PIVI thresholds were also not always met [125,174,179]. In conclusion, performance levels of endoscopists in correctly predicting histology of diminutive polyps remain highly variable, underlining the necessity of a training, auditing and performance monitoring system in case an optical diagnosis strategy is implemented. How this possibly could effected by implementation of artificial intelligence in the

future is at this stage also unclear (see TF 6). Details on the mentioned studies are available in appendix 17.

During real-time optical diagnosis, validated optical diagnostic scales, such as the widely used NBI International Colorectal Endoscopic (NICE) classification or the Workgroup serrated polyps and polyposis (WASP) classification (which includes also SSLs) should be used to improve the diagnostic accuracy [145,174,180]. No universal training system for differentiation between neoplastic and non-neoplastic colorectal polyps has been established yet. Several teaching modules, mostly computer-based, have been studied and some of them are showing promising results with respect to improving the interobserver agreement, however in a substantial number of studies the interobserver agreement was still moderate after training [180–188]. Details on the mentioned studies are available in appendix 18.

There are currently no data to suggest what kind of documentation is needed for implementation of the optical diagnosis strategy. As in this situation an endoscopic picture rather than a histology slide becomes the record of a diminutive polyp, it seems logical that those images are stored. At least one or two images must be stored as evidence of adenoma detection and also for review of the optical diagnosis [136]. However, this strategy poses significant challenges at present, especially with regard to logistics and the available disk space on servers in endoscopy units.

Implementation of the optical diagnosis strategy would be cost-effective, with good evidence from large modeling studies to support this [157,170,189–193]. However, concerns associated with the data used for model analysis include: (i) the use of different screening programs for CRC used in these models may not be simply extrapolated to the various screening programs in use in Europe; (ii) the assumptions are derived from studies that are mainly performed by experts; and (iii) the costs for implementation of the resect and discard policy (training for and photo documentation of real-time diagnosis) are not included. It is therefore unclear if these results of these modeling studies can be reproduced in a real-time daily practice and this should be further investigated in a real-time (multicenter) setting.

Task force 5: Role of advanced imaging in treatment of colorectal neoplasia.

Predicting deep submucosal invasion.

Previous statement :

- *ESGE suggests the use of conventional or virtual (NBI) magnified chromoendoscopy to predict the risk of invasive cancer and deep submucosal invasion in lesions such as those with a depressed component (0-IIc according to the Paris classification) or nongranular or mixed-type laterally spreading tumors (weak recommendation, moderate quality evidence)*

New statement :

- **ESGE recommends the use of HD white light endoscopy in combination with (virtual) chromoendoscopy to predict the presence and depth of any submucosal invasion in non-pedunculated colorectal polyps prior to any treatment. (Strong recommendation, moderate quality of evidence).**

When endoscopic resection is considered for colonic lesions, it is important to assess the lesion accurately and attempt to predict the presence and depth of SM invasion, as this will aid in determining the correct treatment strategy (piecemeal endoscopic resection e.g. EMR, en-bloc endoscopic resection e.g. ESD or FTRD, or surgery). White light characterization, virtual and dye-based CE without magnification and with magnification help to predict the presence and depth of SM invasion.

The morphology, size, location and recognition of gross morphological malignant features is the first step in the characterisation of colonic lesions with white-light endoscopy and may help to suspect malignancy. SM invasion has been shown elsewhere to be higher in certain morphologies (LST-NG pseudo-depressed lesions, LST nodular mixed type, and also in sessile polyps), increased size, and the rectum location [194,195]. A large prospective study of colonic lesions showed that the risk of 'COVERT' SM invasion was predicted by rectosigmoid location (odds ratio, 1.87; P = .01), combined Paris classification, surface morphology (odds ratios, 3.96-22.5), and increasing size (odds ratio, 1.16/10 mm; P = .012) [196]. In particular rectosigmoid Paris 0-Is and 0-IIa+Is non-granular lesions had a high risk of SM invasion whereas proximally located Paris 0-Is or 0-IIa granular lesions a very low risk. In addition, non-lifting sign, chicken skin sign, edge retraction, depressed areas, folds convergence, induration, ulceration, polyp over polyp, redness, tumour fullness and spontaneous bleeding have been reported to be associated with SM invasion, also in lesions < 10 mm, but none of them was definitive [194,197]. A systematic review and meta-analysis showed that sensitivity of these features for predicting deep SM invasion range from 18% to 68% and specificities from 80% to 98%.[198] The recognition of demarcated areas (clearly visualized zone between two morphological areas of a lesion, e.g., depression, large nodule, or reddened area) is also a key point to identify zones that deserve close observation because they are associated with an increased risk of SM invasion [199].

On closer inspection of the target colonic lesion, detection and characterisation of a demarcated area where a regular neoplastic pit/vascular pattern (e.g. Kudo IV, NICE II, Sano II) becomes disordered (e.g. Kudo V, NICE III, Sano III), often associated with a visible depression (Paris classification 0-IIa+c) due to a fibrotic reaction in the submucosa, is a specific marker of submucosal invasion within colonic lesions.

There are only 3 prospective studies evaluating in vivo CE without magnification. The OPTICAL study [200] prospectively assessed 343 large non-pedunculated colorectal polyps with NBI using the Hiroshima classification without magnification. Forty-seven cancers were identified (36 T1 and 11 ≥T2), of which only 11 contained superficial sm1 invasion (23.4% of all malignant polyps). Sensitivity and specificity for optical diagnosis of T1 CRC were 78.7% (95%CI 64.3%-89.3%) and 94.2% (95%CI 90.9%-96.6%), and 63.3% (95%CI 43.9%-80.1%) and 99.0% (95%CI 97.1%-100.0%) for optical diagnosis of endoscopically unresectable lesions (i.e., ≥T1 CRC with deep invasion), respectively. Obvious advanced cancers were excluded, but 11 out of 47 were still advanced cancers (7 T2 and 4 T3), which might have increased the sensitivity.

In a Spanish multicenter prospective study including 2,123 lesions >10 mm using NBI and without magnification, the NICE classification system identified lesions with deep invasion with 58.4% sensitivity (95%CI 47.5%–68.8%) and 96.4% specificity (95% CI 95.5%–97.2%). [194] In addition, a conditional inference tree that included all variables found that NICE classification was the most accurate for identification of lesions with deep invasion (0<0.001). However, pedunculated morphology (p< 0.007), ulceration (p=0.026), depressed areas (p<0 .001), or nodular-mixed type (p<0

.001) also affected accuracy of identification (Figure 1). Therefore, virtual CE without magnification is useful for predicting deep SM invasion when a non-pedunculated NICE type 3 polyp is ulcerated and is useful to rule it out when a NICE type 1 or 2 lesion has no depressed area nor nodules. Results were comparable for identifying lesions that were endoscopically not resectable for oncological reasons (with any risk factor for lymph node metastasis). This is consistent with previous Japanese studies showing a higher prevalence of deep SM invasion in demarcated areas.[199] Therefore, magnification is especially needed in non-ulcerated NICE type 3 lesions or when a demarcated area (nodule, redness, or depression) is present in a NICE type 1 or 2 lesion.

Without magnification, there is only one study assessing the Kudo pit pattern for predicting SM invasion [196]. Sensitivity and specificity of the Kudo pit pattern type V were 40.4% (95%CI, 33.3%–47.8%) and 97.5% (95%CI, 96.7%–98.1%) in 2106 lateral spreading lesions > 20 mm.

In Japan, magnified NBI CE has been shown to have a sensitivity of 77% (95%CI 0.68%–0.84%) and a specificity of 98% (95%CI 95%–99%) in 13 studies using different classification systems [198]. Recently, type 3 JNET classification has shown a sensitivity of 55.4% (95%CI 48.7%-62.1%) and a specificity of 99.8% (95%CI 99.6%-100.0%) in retrospective assessment of 2,933 images [201]. Studies with similar results showed that JNET Type 2B included a wide variety of colorectal tumours ranging from low grade dysplasia to deep SM lesions and therefore the sensitivity of JNET type 3 is low [202–207]. The authors suggest that direct observation of the Kudo pit pattern with crystal violet should be performed in JNET 2B lesions.

The above mentioned systematic review and meta-analysis showed a sensitivity of 81% (95%CI 75%–87%) and a specificity of 95% (95%CI 89%–97%) for magnified CE in 17 studies [198]. All the studies were performed in Asian countries, mainly Japan, with crystal violet. A retrospective study conducted in Brazil by a single experienced endoscopist included 123 lesions with a suspicion of SM invasion by another endoscopist. Magnifying CE with pit pattern classification had 73.3% sensitivity and 100% specificity [208].

Details on the mentioned studies are available in appendix 19.

In summary, WLE may raise suspicion for SM invasion, virtual CE without magnification is useful to rule out the presence of deep SM invasion when no demarcated area is present, and magnifying CE may allow the differentiation between deep and superficial submucosal invasion in highly suspicious lesions as those containing demarcated areas. Based on the recent evidence, a 4-step strategy incorporating the different roles of WLE, non-magnifying virtual CE, magnifying virtual CE and magnifying dye-based CE in predicting SM invasion has been proposed, but it should be first validated [209]. In the near future, it seems likely that AI, directed to a demarcated area by a human observer, will significantly improve both sensitivity and specificity (see section below).

Defining the borders of colorectal lesions.

Unchanged statement :

- ***ESGE recommends the use of virtual or dye-based chromoendoscopy to define the margins of large nonpolypoid or otherwise indistinct lesions before or during endoscopic resection (strong recommendation, very low quality of evidence).***

No new evidence has become available regarding this statement. Because of the better contrast, the entire extent of the lesion can be better appreciated with additional imaging techniques to safeguard a complete resection of a lesion. Especially in IBD related neoplasia demarcation of a lesion can be challenging and is facilitated by CE.

Previous statement :

- *ESGE recommends the use of virtual or conventional chromoendoscopy in addition to white light endoscopy for the detection of residual neoplasia at a piecemeal polypectomy scar site (strong recommendation, low quality evidence).*

New statements :

- **ESGE recommends the use of virtual or dye-based chromoendoscopy in addition to white light endoscopy for the detection of residual neoplasia at a piecemeal polypectomy scar site (Strong recommendation, moderate quality evidence).**
- **ESGE suggests that routine biopsy of post-polypectomy scar can be abandoned providing that standardized imaging protocol with virtual chromoendoscopy is used by a sufficiently trained endoscopist (Weak recommendation, moderate quality evidence).**

Follow-up after endoscopic resection of lesions.

Endoscopic piecemeal polypectomy has emerged as a safe and effective method of removing large sessile or non-polypoid colorectal lesions however, due to a relatively high rate of adenoma recurrence estimated at 15%-30%, [210,211] it is recommended to perform a surveillance colonoscopy at 4 to 6 months after endoscopic resection [212,213]. It has been shown that using HD-WLE alone allows for the identification of 69% to 83% of recurrences revealed by performing targeted and random biopsies [141,214]. Recent studies provided new evidence for the efficacy of the advanced endoscopic imaging in the detection of post-polypectomy/post-EMR scars and residual/recurrent colorectal neoplasia. A prospective single-centre study which analysed 183 scars after a median of 3.9 months from the endoscopic polypectomy, showed a significantly higher sensitivity for endoscopic residual neoplasia detection for a combination of HD-WLE and NBI compared with HD-WLE alone (93.3% vs. 66.7%). Negative predictive value (NPV) for combination of HD-WLE and NBI was 98.6% (95%CI 95.1%-99.8%) [215]. Another prospective multicentre study, which evaluated 255 colorectal scars after a median of 7 months following a colorectal piecemeal-EMR, showed a NPV of 100% (95%CI 98%-100%) and sensitivity of 100% (95%CI 93%-100%) for NBI with near focus imaging [216]. However, slightly lower values were observed in a study of 112 scars, which showed that the accuracy of NBI for the detection of residual neoplasia at the resection site as compared to WLE was 86.8% and 81.6% (p=0.15), respectively [217]. This study has however several limitations, including single operator, high recurrence rates and non-blinded pathologist. Another study comparing the combination of HD-WLE and virtual or dye-based CE against histological verification in recurrence assessment revealed biopsy evidence of residual/recurrent lesions in 16 of 228 macroscopically inconspicuous polypectomy scars (7%) [218]. This study had however very high rates of recurrence (31.7%) and used argon plasma coagulation to complete/ascertain complete resection in 50% of patients. High sensitivity and negative predictive value (93-100%) of HD-WLE combined with virtual CE in identifying residual and/or recurrent colorectal neoplasia justifies abandoning biopsy of macroscopically normal EMR or piecemeal polypectomy scars.

Task force 6: Role of artificial intelligence in detection and characterization of colorectal polyps

New statement:

ESGE suggest the possible incorporation of computer-aided diagnosis (detection and characterisation of lesions) to colonoscopy, if acceptable and reproducible accuracy for colorectal neoplasia is demonstrated in high quality multi-centre in vivo clinical studies. Possible significant risks with implementation, specifically endoscopist deskilling and over-reliance on AI, non-representative training datasets, and hacking, need be considered. (Weak recommendation, low quality of evidence).*

*N.B. the field of AI is changing very rapidly and it is likely this statement may need to be modified as new data emerges. The ESGE plans an addendum to this section of the guideline in the near future.

Computer aided diagnosis in medical imaging has been revolutionized they the advent of artificial intelligence “deep learning” based on neural networks that simulate to some degree the workings of the human brain. It seems likely that such systems will have a major place in clinical practice in the future with more than 20 systems, in particular in radiology and pathology, receiving regulatory approval [219]. Video endoscopy provides a further opportunity for the application of AI systems to support and enhance clinical practice and endoscopist performance; however despite the potential benefits, there are also risks with clinical AI adoption.

AI interaction with the endoscopist

There are a number of ways that AI can support clinicians in endoscopy. We consider two major scenarios below for colonoscopy, looking at lesion detection and lesion characterization; however there are a number of ways that the endoscopist can interact with the computer aided diagnosis system. This can be active, where we find a polyp and ask the AI system to confirm our diagnosis as a “second reader”, or passive where AI is running continuously in the background for example for polyp detection, reading alongside the endoscopist, a “concurrent read”. There may be situations where the AI acts completely autonomously to make a decision without any endoscopist input, in a situation where the way the AI output is determined is unknown [220] [Figure 2]. The European Union has recently proposed that algorithms “black boxes” are deconvoluted before they can be used for patient care [221]. There are similarities in endoscopist AI interaction with how we think about self-driving cars where humans can monitor the environment but can be aided by automated speed control and breaking. Self-driving also allows for the AI system to monitor the environment with limited human input or even be fully autonomous; however it seems unlikely that fully autonomous “black box” AI will feature widely in medicine [219].

Diagnostic performance of AI detection for colonic polyp detection

Substantial variation between endoscopists in terms of polyp detection and effectiveness in preventing CRC with colonoscopy exists [4,11]. This variability has been attributed to many factors, but a significant factor seems to be due to missing polyps that could potentially have been recognized [179,222–225]. Limitations in human visual perception and other human biases such as fatigue, distraction, level of alertness during examination increases such recognition errors and way of mitigating them may be the key to improve polyp detection and further reduction in mortality from CRC. Computer-aided detection (CAD) could address these limitations [226] Recent advances in

artificial intelligence (AI), deep learning (DL), and computer vision have shown potential to assist polyp detection during colonoscopy. Preliminary studies of DL-based CAD systems have been reported sensitivities from 70% to 90% and specificities from 60% to 90% for detecting polyps [227–232]. There is insufficient data to establish whether there is effective detection of sessile serrated lesions or relatively flat and prepressed lesions (Paris 0-II). Although CAD could be useful for polyp detection in clinical practice [228], some limitations remain. One of the major limitations with current CAD schemes is a relatively large number of false-positive detections, which could adversely affect the application of CAD in clinical practice. A large rate of false positives is likely to confound the endoscopists task of images interpretation and lower colonoscopy efficiency. In addition, endoscopists may lose their confidence in CAD as a useful tool. The speed of CADs for image analysis and output presentation may also be an issue. Fast processing times for image analysis and on-screen labelling are required, so that the endoscopists is alerted in real time regarding the presence of a polyp.

Details on the mentioned studies are available in appendix 20.

Diagnostic performance of AI in polyp characterisation

AI for characterization of colorectal lesions might have potential advantages to (I) improve the learning phase of endoscopists (II) predict neoplastic and non-neoplastic tissue (e.g. resect and discard strategy) and (III) for guidance of endoscopic therapy (e.g. prediction of sm infiltration). So far, no randomized controlled trials are available for this rapidly emerging technology. Specifically, no data is yet available on the effect of AI for the learning curve of endoscopists. Regarding prediction of adenomatous and hyperplastic polyp histology, recent data has highlighted that AI, based on deep learning models, can accurately predict polyp histology with sensitivities and negative predictive values exceeding 90% [233]. Similar results have also been shown for AI based on traditional machine learning [234,235]. AI based on machine learning has also been evaluated for predicting the need for additional surgery after endoscopic resection of T1 colorectal cancer showing that it could significantly reduce unnecessary additional surgery [236]. Finally AI based on a deep learning model has been used to assist in diagnosis of SM colorectal cancer showing an accuracy of 81% [237,238]. Beyond colonic polyps there may be a role for AI in scoring inflammation in inflammatory bowel disease with preliminary data supporting distinguishing Mayo 0-1 versus higher levels of inflammation Mayo 2-3), area under ROC 0.98 [239]. In addition, it may potentially help to automatically register quality indicators for colonoscopy (withdrawal time, caecal intubation, bowel preparation).

Details on the mentioned studies are available in appendix 21.

The role of add on standalone systems versus AI which is integrated into commercially available endoscopy systems remains unclear; however either approach seems to have significant potential to enhance practice and facilitate optical diagnosis or DISCARD type strategies [220].

Risks of adoption of AI in clinical practice

Whilst many previous publications exclusively mentioned strength and advantage of the use of artificial intelligence for medicine, there are potential drawbacks of AI for colonoscopy. Among previously conducted seven prospective studies on AI for colonoscopy [231,234,240–244] , there has been no study which addressed the downsides of AI as one of the main outcome measures except for the assessment of the time required for the use of AI, with results varying from an increase 35-47 seconds per polyp assessed with AI [234] to no additional burden to withdrawal time [231].

Apart from the colonoscopy field, recent review articles warned unintended consequences that possibly arise from the use of AI for health care[219,245], namely overreliance on AI, deskilling, biased datasets for machine learning, and the risk of hacking of AI, all of which seem to be applicable to AI for colonoscopy. Overreliance on the capabilities of AI comprises two disadvantages: in the short term, endoscopists' diagnosis can be affected by incorrect predictions of AI. Some previous studies on decision support systems for mammography [246] and electrocardiography [247] demonstrated a negative effect in practice. According to these studies, experienced radiologists and residents, respectively tended to adopt wrong decisions when they were given a wrong prediction by AI.

Biased data for machine learning should be addressed when AI for colonoscopy is widely implemented into clinical practice. Currently, no AI systems for colonoscopy used learning data from different countries where status of colonic mucosa, morphologic pattern of polyps, and quality of bowel preparation may differ significantly. Similarly, differences in endoscopic technology between Asia and UK and the rest of the world (e.g. Lucera Elite vs Exera III, Olympus) or between endoscopy manufacturers may significantly affect performance of AI if the training set did not include a full range of data. In this regard, international validation should be required before global use of the developed AI. Unintended outcomes are possible from small, unrepresentative data sets e.g. IBM Watson for Oncology [248], which if adopted widely in healthcare systems can have very broad negative consequences.

The risk of hacking is also an inevitable concern for such a computational device. Once the computer in which AI is installed is deliberately hacked, it can harm patients at a large scale. Use of AI which provides wrong histological prediction of the polyps due to malware could lead to serious consequences, such as leaving neoplastic polyps in situ.

In addition to these general concerns, the outputs from CAD, especially when they were inaccurate, might distract the concentration of the endoscopists, leading to missing/mischaracterization of polyps, because endoscopists need to pay more attention to both outputs of CAD and their own prediction when using CAD [249]. On the other hand, no serious adverse event such as perforation has been reported due to such distraction according to two prospective studies [234,243]. Detection algorithms may produce many false positives which require careful mucosal inspection which can increase time and mental load when performing colonoscopy leading to distraction. There is also an assumption that effects of CAD (e.g. improved adenoma detection) will automatically lead to a reduction of missed CRC according to the association studies of ADR and post-colonoscopy colorectal cancers [11]; however changes in ADR produced by AI are in effect improvements in detection of polyps within the visual field. AI cannot detect polyps in non-inspected mucosa. Therefore if improved ADR is in fact a surrogate measure of enhanced mucosal visualisation, with better re-inspection of flexures, suctioning and pressing down mucosal folds, not changed by application of AI, the link between enhancement of ADR and fewer missed cancers may not hold true.

Although there is limited evidence that supports the risks of the use of AI for colonoscopy, various risks of AI such as prolonged procedure time, overreliance on AI, and distraction caused by AI should be considered, and quality assurance measures instituted [250,251]. Future prospective studies should assess the impact of these downsides of AI in addition to its efficacy.

Disclaimer: These ESGE guidelines represent a consensus of best practice based on the available evidence at the time of preparation. They may not apply in all situations and should be interpreted in the light of specific clinical situations and resource availability. Further controlled clinical studies may

be needed to clarify aspects of the statements, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance to these recommendations. ESGE guidelines are intended to be an educational device to provide information that may assist endoscopists in providing care to patients. They are not rules and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment.

Conflict of interest

To be subtracted from previously submitted forms

Acknowledgement of reviewers

TO BE ADDED BY EO

References

1 Kamiński M, Hassan C, Bisschops R, *et al.* Advanced imaging for detection and differentiation of colorectal neoplasia: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2014;**46**:435–57. doi:10.1055/s-0034-1365348

2 Stock C, Brenner H. Utilization of lower gastrointestinal endoscopy and fecal occult blood test in 11 European countries: evidence from the Survey of Health, Aging and Retirement in Europe (SHARE). *Endoscopy* 2010;**42**:546–56. doi:10.1055/s-0029-1244127

3 Chen C, Stock C, Jansen L, *et al.* Trends in colonoscopy and fecal occult blood test use after the introduction of dual screening offers in Germany: Results from a large population-based study, 2003-2016. *Prev Med (Baltim)* 2019;**123**:333–40. doi:10.1016/j.ypmed.2019.03.048

4 Kaminski MF, Regula J, Kraszewska E, *et al.* Quality Indicators for Colonoscopy and the Risk of Interval Cancer. *N Engl J Med* 2010;**362**:1795–803. doi:10.1056/NEJMoa0907667

5 Kaminski M, Thomas-Gibson S, Bugajski M, *et al.* Performance measures for lower gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. *Endoscopy* 2017;**49**:378–97. doi:10.1055/s-0043-103411

6 Clark BT, Rustagi T, Laine L. What level of bowel prep quality requires early repeat colonoscopy: systematic review and meta-analysis of the impact of preparation quality on adenoma detection rate. *Am J Gastroenterol* 2014;**109**:1714–23; quiz 1724. doi:10.1038/ajg.2014.232

7 East J, Vleugels J, Roelandt P, *et al.* Advanced endoscopic imaging: European Society of Gastrointestinal Endoscopy (ESGE) Technology Review. *Endoscopy* 2016;**48**:1029–45. doi:10.1055/s-0042-118087

8 Richardson WS, Wilson MC, Nishikawa J, *et al.* The well-built clinical question: a key to evidence-based decisions. *ACP J Club*;**123**:A12-3.http://www.ncbi.nlm.nih.gov/pubmed/7582737 (accessed 17 Jun 2019).

9 Atkins D, Best D, Briss PA, *et al.* Grading quality of evidence and strength of recommendations. *BMJ* 2004;**328**:1490. doi:10.1136/bmj.328.7454.1490

10 Dumonceau J-M, Hassan C, Riphaus A, *et al.* European Society of Gastrointestinal Endoscopy (ESGE) Guideline Development Policy. *Endoscopy* 2012;**44**:626–9. doi:10.1055/s-0031-1291747

11 Corley DA, Levin TR, Doubeni CA. Adenoma Detection Rate and Risk of Colorectal Cancer and Death. *N Engl J Med* 2014;**370**:2539–41. doi:10.1056/NEJMc1405329

12 Subramanian V, Mannath J, Hawkey CJ, *et al.* High definition colonoscopy vs. standard video endoscopy for the detection of colonic polyps: A meta-analysis. *Endoscopy* 2011;**43**:499–505. doi:10.1055/s-0030-1256207

13 Deenadayalu VP, Chadalawada V, Rex DK. 170° Wide-angle colonoscope: Effect on efficiency and miss rates. *Am J Gastroenterol* 2004;**99**:2138–42. doi:10.1111/j.1572-0241.2004.40430.x

14 Fatima H, Rex DK, Rothstein R, *et al.* Cecal Insertion and Withdrawal Times With Wide-Angle Versus Standard Colonoscopes: A Randomized Controlled Trial. *Clin Gastroenterol Hepatol* 2008;**6**:109–14. doi:10.1016/j.cgh.2007.10.009

15 Rex DK, Chadalawada V, Helper DJ. Wide angle colonoscopy with a prototype instrument:

Impact on miss rates and efficiency as determined by back-to-back colonoscopies. *Am J Gastroenterol* 2003;**98**:2000–5. doi:10.1111/j.1572-0241.2003.07662.x

16 Rastogi A, Early DS, Gupta N, *et al.* Randomized, controlled trial of standard-definition white-light, high-definition white-light, and narrow-band imaging colonoscopy for the detection of colon polyps and prediction of polyp histology. *Gastrointest Endosc* 2011;**74**:593–602. doi:10.1016/j.gie.2011.04.050

17 Roelandt P, Demedts I, Willekens H, *et al.* Impact of endoscopy system, high definition, and virtual chromoendoscopy in daily routine colonoscopy: a randomized trial. *Endoscopy* 2019;**51**:237–43. doi:10.1055/a-0755-7471

18 Pioche M, Denis A, Allescher HD, *et al.* Impact of 2 generational improvements in colonoscopes on adenoma miss rates: results of a prospective randomized multicenter tandem study. *Gastrointest Endosc* 2018;**88**:107–16. doi:10.1016/j.gie.2018.01.025

19 Zimmermann-Fraedrich K, Groth S, Sehner S, *et al.* Effects of two instrument-generation changes on adenoma detection rate during screening colonoscopy: results from a prospective randomized comparative study. *Endoscopy* 2018;**50**:878–85. doi:10.1055/a-0607-2636

20 Dinesen L, Chua TJ, Kaffes AJ. Meta-analysis of narrow-band imaging versus conventional colonoscopy for adenoma detection. *Gastrointest Endosc* 2012;**75**:604–11. doi:10.1016/j.gie.2011.10.017

21 Jin XF, Chai TH, Shi JW, *et al.* Meta-analysis for evaluating the accuracy of endoscopy with narrow band imaging in detecting colorectal adenomas. *J Gastroenterol Hepatol* 2012;**27**:882–7. doi:10.1111/j.1440-1746.2011.06987.x

22 Nagorni A, Bjelakovic G, Petrovic B. Narrow band imaging versus conventional white light colonoscopy for the detection of colorectal polyps. *Cochrane database Syst Rev* 2012;**1**:CD008361. doi:10.1002/14651858.CD008361.pub2

23 Omata F, Ohde S, Deshpande GA, *et al.* Image-enhanced, chromo, and cap-assisted colonoscopy for improving adenoma/neoplasia detection rate: A systematic review and meta-analysis. Scand. J. Gastroenterol. 2014;**49**:222–37. doi:10.3109/00365521.2013.863964

24 Pasha SF, Leighton JA, Das A, *et al.* Comparison of the yield and miss rate of narrow band imaging and white light endoscopy in patients undergoing screening or surveillance colonoscopy: A meta-analysis. Am. J. Gastroenterol. 2012;**107**:363–70. doi:10.1038/ajg.2011.436

25 Atkinson NSS, Ket S, Bassett P, *et al.* Narrow-band Imaging for Detection of Neoplasia at Colonoscopy: a Meta-analysis of Data From Individual Patients in Randomized Controlled Trials. *Gastroenterology* Published Online First: April 2019. doi:10.1053/j.gastro.2019.04.014

26 Kidambi TD, Terdiman JP, El-Nachef N, *et al.* Effect of I-scan Electronic Chromoendoscopy on Detection of Adenomas During Colonoscopy. *Clin Gastroenterol Hepatol* 2019;**17**:701-708.e1. doi:10.1016/j.cgh.2018.06.024

27 Min M, Deng P, Zhang W, *et al.* Comparison of linked color imaging and white-light colonoscopy for detection of colorectal polyps: a multicenter, randomized, crossover trial. *Gastrointest Endosc* 2017;**86**:724–30. doi:10.1016/j.gie.2017.02.035

28 Paggi S, Mogavero G, Amato A, *et al.* Linked color imaging reduces the miss rate of neoplastic lesions in the right colon: a randomized tandem colonoscopy study. *Endoscopy* 2018;**50**:396–402. doi:10.1055/a-0580-7405

29 Ikematsu H, Sakamoto T, Togashi K, *et al.* Detectability of colorectal neoplastic lesions using a novel endoscopic system with blue laser imaging: a multicenter randomized controlled trial. *Gastrointest Endosc* 2017;**86**:386–94. doi:10.1016/j.gie.2017.01.017

30 Zhao Z-Y, Guan Y-G, Li B-R, *et al.* Detection and miss rates of autofluorescence imaging of adenomatous and polypoid lesions during colonoscopy: a systematic review and meta-analysis. *Endosc Int Open* 2015;**3**:E226–35. doi:10.1055/s-0034-1391708

31 Takeuchi Y, Sawaya M, Oka S, *et al.* Efficacy of autofluorescence imaging for flat neoplasm detection: a multicenter randomized controlled trial (A-FLAT trial). *Gastrointest Endosc* 2019;**89**:460–9. doi:10.1016/j.gie.2018.11.012

32 Facciorusso A, Del Prete V, Buccino RV, *et al.* Comparative Efficacy of Colonoscope Distal Attachment Devices in Increasing Rates of Adenoma Detection: A Network Meta-analysis. Clin. Gastroenterol. Hepatol. 2018;**16**:1209-1219.e9. doi:10.1016/j.cgh.2017.11.007

33 Clelia, M.; Frazzoni, L.; Fuccio, L.; Bhandari, P;Thayalasekaran, S; Hassan, C; Marmo R. Mucosal flattening assisted colonoscopy (FAC) for improving adenoma detection rate: a systematic review with pairwise and network meta-analysis. *United Eur Gastroenterol J* 2018;**6**:A195.

34 Brown SR, Baraza W, Din S, *et al.* Chromoscopy versus conventional endoscopy for the detection of polyps in the colon and rectum. *Cochrane database Syst Rev* 2016;**4**:CD006439. doi:10.1002/14651858.CD006439.pub4

35 Lesne A, Rouquette O, Touzet S, *et al.* Adenoma detection with blue-water infusion colonoscopy: a randomized trial. *Endoscopy* 2017;**49**:765–75. doi:10.1055/s-0043-105073

36 Repici A, Wallace MB, East JE, *et al.* Efficacy of Per-oral Methylene Blue Formulation for Screening Colonoscopy. *Gastroenterology* 2019;**156**:2198-2207.e1. doi:10.1053/j.gastro.2019.02.001

37 Hurlstone DP, Karajeh M, Cross SS, *et al.* The role of high-magnification-chromoscopic colonoscopy in hereditary nonpolyposis colorectal cancer screening: a prospective "back-to-back" endoscopic study. *Am J Gastroenterol* 2005;**100**:2167–73. doi:10.1111/j.1572-0241.2005.41481.x

38 LECOMTE T, CELLIER C, MEATCHI T, *et al.* Chromoendoscopic Colonoscopy for Detecting Preneoplastic Lesions in Hereditary Nonpolyposis Colorectal Cancer Syndrome. *Clin Gastroenterol Hepatol* 2005;**3**:897–902. doi:10.1016/S1542-3565(05)00403-9

39 Rahmi G, Lecomte T, Malka D, *et al.* Impact of chromoscopy on adenoma detection in patients with Lynch syndrome: a prospective, multicenter, blinded, tandem colonoscopy study. *Am J Gastroenterol* 2015;**110**:288–98. doi:10.1038/ajg.2014.423

40 Stoffel EM, Turgeon DK, Stockwell DH, *et al.* Missed adenomas during colonoscopic surveillance in individuals with Lynch Syndrome (hereditary nonpolyposis colorectal cancer). *Cancer Prev Res (Phila)* 2008;**1**:470–5. doi:10.1158/1940-6207.CAPR-08-0098

41 Hüneburg R, Lammert F, Rabe C, *et al.* Chromocolonoscopy detects more adenomas than white light colonoscopy or narrow band imaging colonoscopy in hereditary nonpolyposis colorectal cancer screening. *Endoscopy* 2009;**41**:316–22. doi:10.1055/s-0028-1119628

42 Haanstra JF, Dekker E, Cats A, *et al.* Effect of chromoendoscopy in the proximal colon on colorectal neoplasia detection in Lynch syndrome: a multicenter randomized controlled trial. *Gastrointest Endosc* 2019;**0**. doi:10.1016/j.gie.2019.04.227

43 Rivero Sanchez , C. Arnau Colell , F. Balaguer , J.M. Herrero Rivas , D. Remedios Espino , M.V

Alvarez Sanchez , E. Albeniz Arbizu , P. Calvo Aranda , J. Gordillo , I. Puig , J. Lopez Vicente , A. Huerta Madrigal, M. Lopez-Ceron, I. Salces, B. Penas Garci MPU. HIGH-DEFINITION WHITE-LIGHT COLONOSCOPY VERSUS CHROMOENDOSCOPY FOR SURVEILLANCE OF LYNCH SYNDROME. A MULTICENTER, RANDOMIZED AND CONTROLLED STUDY (ENDOLYNCH STUDY). *United Eur Gastroenterol J* 2018;**6**:A117 OP295.

44 East JE, Suzuki N, Stavrinidis M, *et al.* Narrow band imaging for colonoscopic surveillance in hereditary non-polyposis colorectal cancer. *Gut* 2008;**57**:65–70. doi:10.1136/gut.2007.128926

45 Bisschops R, Tejpar S, Willekens H, *et al.* Virtual chromoendoscopy (I-SCAN) detects more polyps in patients with Lynch syndrome: a randomized controlled crossover trial. *Endoscopy* 2017;**49**:342–50. doi:10.1055/s-0042-121005

46 Cellier C, Perrod G, Colas C, *et al.* Back-to-Back Comparison of Colonoscopy With Virtual Chromoendoscopy Using a Third-Generation Narrow-Band Imaging System to Chromoendoscopy With Indigo Carmine in Patients With Lynch Syndrome. *Am J Gastroenterol* 2019;:1. doi:10.14309/ajg.0000000000000386

47 Ramsoekh D, Haringsma J, Poley JW, *et al.* A back-to-back comparison of white light video endoscopy with autofluorescence endoscopy for adenoma detection in high-risk subjects. *Gut* 2010;**59**:785–93. doi:10.1136/gut.2008.151589

48 van Leerdam ME, Roos VH, van Hooft JE, *et al.* Endoscopic management of polyposis syndromes: European Society of Gastrointestinal Endoscopy (ESGE) guideline. *Endoscopy* Published Online First: 23 July 2019. doi:10.1055/a-0965-0605

49 Moreira L, Pellisé M, Carballal S, *et al.* High prevalence of serrated polyposis syndrome in FIT-based colorectal cancer screening programmes. *Gut* 2013;**62**:476–7. doi:10.1136/gutjnl-2012-303496

50 Biswas S, Ellis AJ, Guy R, *et al.* High prevalence of hyperplastic polyposis syndrome (serrated polyposis) in the NHS bowel cancer screening programme. *Gut* Published Online First: 31 July 2012. doi:10.1136/gutjnl-2012-303233

51 Hazewinkel Y, López-Cerón M, East JE, *et al.* Endoscopic features of sessile serrated adenomas: validation by international experts using high-resolution white-light endoscopy and narrow-band imaging. *Gastrointest Endosc* Published Online First: 21 February 2013. doi:10.1016/j.gie.2012.12.018

52 Kahi CJ, Li X, Eckert GJ, *et al.* High colonoscopic prevalence of proximal colon serrated polyps in average-risk men and women. *Gastrointest Endosc* 2012;**75**:515–20. doi:10.1016/j.gie.2011.08.021

53 Abdeljawad K, Vemulapalli KC, Kahi CJ, *et al.* Sessile serrated polyp prevalence determined by a colonoscopist with a high lesion detection rate and an experienced pathologist. *Gastrointest Endosc* 2015;**81**:517–24. doi:10.1016/j.gie.2014.04.064

54 Vemulapalli KC, Rex DK. Failure to recognize serrated polyposis syndrome in a cohort with large sessile colorectal polyps. *Gastrointest Endosc* 2012;**75**:1206–10. doi:10.1016/j.gie.2012.01.033

55 Rivero-Sanchez L, Lopez-Ceron M, Carballal S, *et al.* Reassessment colonoscopy to diagnose serrated polyposis syndrome in a colorectal cancer screening population. *Endoscopy* 2016;**49**:44–53. doi:10.1055/s-0042-115640

56 López-Vicente J, Rodríguez-Alcalde D, Hernández L, *et al.* Panchromoendoscopy Increases Detection of Polyps in Patients With Serrated Polyposis Syndrome. *Clin Gastroenterol Hepatol*

2018;**0**. doi:10.1016/j.cgh.2018.10.029

57 Boparai KS, Mathus-Vliegen EMH, Koornstra JJ, *et al.* Increased colorectal cancer risk during follow-up in patients with hyperplastic polyposis syndrome: a multicentre cohort study. *Gut* 2010;**59**:1094–100. doi:10.1136/gut.2009.185884

58 Hazewinkel Y, Tytgat KMAJ, van Leerdam ME, *et al.* Narrow-band imaging for the detection of polyps in patients with serrated polyposis syndrome: a multicenter, randomized, back-to-back trial. *Gastrointest Endosc* 2015;**81**:531–8. doi:10.1016/j.gie.2014.06.043

59 Rivero-Sánchez L, López Vicente J, Hernandez Villalba L, *et al.* Endocuff-assisted colonoscopy for surveillance of serrated polyposis syndrome: a multicenter randomized controlled trial. *Endoscopy* 2019;**51**:637–45. doi:10.1055/a-0925-4956

60 Cairns SR, Scholefield JH, Steele RJ, *et al.* Guidelines for colorectal cancer screening and surveillance in moderate and high risk groups (update from 2002). *Gut* 2010;**59**:666–89. doi:10.1136/gut.2009.179804

61 Van Assche G, Dignass A, Bokemeyer B, *et al.* Second European evidence-based consensus on the diagnosis and management of ulcerative colitis Part 3: Special situations. *J Crohn's Colitis* 2013;**7**:1–33. doi:10.1016/J.CROHNS.2012.09.005

62 Kiesslich R, Fritsch J, Holtmann M, *et al.* Methylene blue-aided chromoendoscopy for the detection of intraepithelial neoplasia and colon cancer in ulcerative colitis. *Gastroenterology* 2003;**124**:880–8. doi:10.1053/gast.2003.50146

63 Kiesslich R, Goetz M, Lammersdorf K, *et al.* Chromoscopy-guided endomicroscopy increases the diagnostic yield of intraepithelial neoplasia in ulcerative colitis. *Gastroenterology* 2007;**132**:874–82. doi:10.1053/j.gastro.2007.01.048

64 Subramanian V, Mannath J, Ragunath K, *et al.* Meta-analysis: the diagnostic yield of chromoendoscopy for detecting dysplasia in patients with colonic inflammatory bowel disease. *Aliment Pharmacol Ther* 2011;**33**:304–12. doi:10.1111/j.1365-2036.2010.04525.x

65 Hlavaty T, Huorka M, Koller T, *et al.* Colorectal cancer screening in patients with ulcerative and crohn's colitis with use of colonoscopy, chromoendoscopy and confocal endomicroscopy. *Eur J Gastroenterol Hepatol* 2011;**23**:680–9. doi:10.1097/MEG.0b013e32834791b4

66 Günther U, Kusch D, Heller F, *et al.* Surveillance colonoscopy in patients with inflammatory bowel disease: comparison of random biopsy vs. targeted biopsy protocols. *Int J Colorectal Dis* 2011;**26**:667–72. doi:10.1007/s00384-011-1130-y

67 Deepak P, Hanson GJ, Fletcher JG, *et al.* Incremental diagnostic yield of chromoendoscopy and outcomes in inflammatory bowel disease patients with a history of colorectal dysplasia on white-light endoscopy. *Gastrointest Endosc* 2016;**83**:1005–12. doi:10.1016/j.gie.2015.09.021

68 Marion JF, Waye JD, Israel Y, *et al.* Chromoendoscopy Is More Effective Than Standard Colonoscopy in Detecting Dysplasia During Long-term Surveillance of Patients With Colitis. *Clin Gastroenterol Hepatol* 2016;**14**:713–9. doi:10.1016/j.cgh.2015.11.011

69 Mooiweer E, van der Meulen-de Jong AE, Ponsioen CY, *et al.* Chromoendoscopy for Surveillance in Inflammatory Bowel Disease Does Not Increase Neoplasia Detection Compared With Conventional Colonoscopy With Random Biopsies: Results From a Large Retrospective Study. *Am J Gastroenterol* 2015;**110**:1014–21. doi:10.1038/ajg.2015.63

70 Carballal S, Maisterra S, López-Serrano A, *et al.* Real-life chromoendoscopy for neoplasia detection and characterisation in long-standing IBD. *Gut* 2018;**67**:70–8. doi:10.1136/gutjnl-

2016-312332

71 Feuerstein JD, Rakowsky S, Sattler L, *et al.* Meta-analysis of dye-based chromoendoscopy compared with standard- and high-definition white-light endoscopy in patients with inflammatory bowel disease at increased risk of colon cancer. *Gastrointest Endosc* Published Online First: April 2019. doi:10.1016/j.gie.2019.04.219

72 Iannone A, Ruospo M, Wong G, *et al.* Chromoendoscopy for Surveillance in Ulcerative Colitis and Crohn's Disease: A Systematic Review of Randomized Trials. *Clin Gastroenterol Hepatol* 2017;**15**:1684-1697.e11. doi:10.1016/j.cgh.2016.11.021

73 Bessissow T, Dulai PS, Restellini S, *et al.* Comparison of Endoscopic Dysplasia Detection Techniques in Patients With Ulcerative Colitis: A Systematic Review and Network Meta-analysis. *Inflamm Bowel Dis* 2018;**24**:2518–26. doi:10.1093/ibd/izy188

74 Iacucci M, Kaplan GG, Panaccione R, *et al.* A Randomized Trial Comparing High Definition Colonoscopy Alone With High Definition Dye Spraying and Electronic Virtual Chromoendoscopy for Detection of Colonic Neoplastic Lesions During IBD Surveillance Colonoscopy. *Am J Gastroenterol* 2018;**113**:225–34. doi:10.1038/ajg.2017.417

75 Elsadani NN, East JE, Walters JRF. New 2010 British Society of Gastroenterology colitis surveillance guidelines: costs and surveillance intervals. *Gut* 2011;**60**:282–3. doi:10.1136/gut.2010.225466

76 Konijeti GG, Shrime MG, Ananthakrishnan AN, *et al.* Cost-effectiveness analysis of chromoendoscopy for colorectal cancer surveillance in patients with ulcerative colitis. *Gastrointest Endosc* 2014;**79**:455–65. doi:10.1016/j.gie.2013.10.026

77 Ignjatovic A, East JE, Subramanian V, *et al.* Narrow Band Imaging for Detection of Dysplasia in Colitis: A Randomized Controlled Trial. *Am J Gastroenterol* 2012;**107**:885–90. doi:10.1038/ajg.2012.67

78 Dekker E, van den Broek FJ, Reitsma JB, *et al.* Narrow-band imaging compared with conventional colonoscopy for the detection of dysplasia in patients with longstanding ulcerative colitis. *Endoscopy* 2007;**39**:216–21. doi:10.1055/s-2007-966214

79 van den Broek FJC, Fockens P, van Eeden S, *et al.* Endoscopic tri-modal imaging for surveillance in ulcerative colitis: randomised comparison of high-resolution endoscopy and autofluorescence imaging for neoplasia detection; and evaluation of narrow-band imaging for classification of lesions. *Gut* 2008;**57**:1083–9. doi:10.1136/gut.2007.144097

80 Pellisé M, López-Cerón M, Rodríguez de Miguel C, *et al.* Narrow-band imaging as an alternative to chromoendoscopy for the detection of dysplasia in long-standing inflammatory bowel disease: a prospective, randomized, crossover study. *Gastrointest Endosc* 2011;**74**:840–8. doi:10.1016/j.gie.2011.05.013

81 Bisschops R, Bessissow T, Joseph JA, *et al.* Chromoendoscopy versus narrow band imaging in UC: a prospective randomised controlled trial. *Gut* 2018;**67**:1087–94. doi:10.1136/gutjnl-2016-313213

82 Har-Noy O, Katz L, Avni T, *et al.* Chromoendoscopy, Narrow-Band Imaging or White Light Endoscopy for Neoplasia Detection in Inflammatory Bowel Diseases. *Dig Dis Sci* 2017;**62**:2982–90. doi:10.1007/s10620-017-4772-y

83 Matsumoto T, Nakamura S, Moriyama T, *et al.* Autofluorescence imaging colonoscopy for the detection of dysplastic lesions in ulcerative colitis: a pilot study. *Colorectal Dis* 2010;**12**:e291-7. doi:10.1111/j.1463-1318.2009.02181.x

84 Vleugels JLA, Rutter MD, Ragunath K, *et al.* Chromoendoscopy versus autofluorescence imaging for neoplasia detection in patients with longstanding ulcerative colitis (FIND-UC): an international, multicentre, randomised controlled trial. *lancet Gastroenterol Hepatol* 2018;**3**:305–16. doi:10.1016/S2468-1253(18)30055-4

85 Matsumoto T, Nakamura S, Jo Y, *et al.* Chromoscopy might improve diagnostic accuracy in cancer surveillance for ulcerative colitis. *Am J Gastroenterol* 2003;**98**:1827–33. doi:10.1111/j.1572-0241.2003.07580.x

86 Rutter MD, Saunders BP, Schofield G, *et al.* Pancolonic indigo carmine dye spraying for the detection of dysplasia in ulcerative colitis. *Gut* 2004;**53**:256–60. doi:10.1136/gut.2003.016386

87 Marion JF, Waye JD, Present DH, *et al.* Chromoendoscopy-targeted biopsies are superior to standard colonoscopic surveillance for detecting dysplasia in inflammatory bowel disease patients: a prospective endoscopic trial. *Am J Gastroenterol* 2008;**103**:2342–9. doi:10.1111/j.1572-0241.2008.01934.x

88 van den Broek FJC, Stokkers PCF, Reitsma JB, *et al.* Random biopsies taken during colonoscopic surveillance of patients with longstanding ulcerative colitis: low yield and absence of clinical consequences. *Am J Gastroenterol* 2014;**109**:715–22. doi:10.1038/ajg.2011.93

89 Watanabe T, Ajioka Y, Mitsuyama K, *et al.* Comparison of Targeted vs Random Biopsies for Surveillance of Ulcerative Colitis-Associated Colorectal Cancer. *Gastroenterology* 2016;**151**:1122–30. doi:10.1053/j.gastro.2016.08.002

90 Gasia MF, Ghosh S, Panaccione R, *et al.* Targeted Biopsies Identify Larger Proportions of Patients With Colonic Neoplasia Undergoing High-Definition Colonoscopy, Dye Chromoendoscopy, or Electronic Virtual Chromoendoscopy. *Clin Gastroenterol Hepatol* 2016;**14**:704-712.e4. doi:10.1016/j.cgh.2015.12.047

91 Moussata D, Allez M, Cazals-Hatem D, *et al.* Are random biopsies still useful for the detection of neoplasia in patients with IBD undergoing surveillance colonoscopy with chromoendoscopy? *Gut* 2018;**67**:616–24. doi:10.1136/gutjnl-2016-311892

92 Kawasaki K, Nakamura S, Esaki M, *et al.* Clinical usefulness of magnifying colonoscopy for the diagnosis of ulcerative colitis-associated neoplasia. *Dig Endosc* 2019;**31 Suppl 1**:36–42. doi:10.1111/den.13382

93 Sugimoto S, Naganuma M, Iwao Y, *et al.* Endoscopic morphologic features of ulcerative colitis-associated dysplasia classified according to the SCENIC consensus statement. *Gastrointest Endosc* 2017;**85**:639-646.e2. doi:10.1016/j.gie.2016.11.013

94 East JE, Suzuki N, von Herbay A, *et al.* Narrow band imaging with magnification for dysplasia detection and pit pattern assessment in ulcerative colitis surveillance: a case with multiple dysplasia associated lesions or masses. *Gut* 2006;**55**:1432–5. doi:10.1136/gut.2005.087171

95 Matsumoto T, Kudo T, Jo Y, *et al.* Magnifying colonoscopy with narrow band imaging system for the diagnosis of dysplasia in ulcerative colitis: a pilot study. *Gastrointest Endosc* 2007;**66**:957–65. doi:10.1016/j.gie.2007.04.014

96 van den Broek FJC, Fockens P, van Eeden S, *et al.* Narrow-band imaging versus high-definition endoscopy for the diagnosis of neoplasia in ulcerative colitis. *Endoscopy* 2011;**43**:108–15. doi:10.1055/s-0030-1255956

97 Bisschops R, Bessissow T, Dekker E, *et al.* Pit pattern analysis with high-definition chromoendoscopy and narrow-band imaging for optical diagnosis of dysplasia in patients with

ulcerative colitis. *Gastrointest Endosc* 2017;**86**:1100-1106.e1. doi:10.1016/j.gie.2017.09.024

98 Vleugels JLA, Rutter MD, Ragunath K, *et al.* Diagnostic Accuracy of Endoscopic Trimodal Imaging and Chromoendoscopy for Lesion Characterization in Ulcerative Colitis. *J Crohn's Colitis* 2018;**12**:1438–47. doi:10.1093/ecco-jcc/jjy129

99 Cassinotti A, Buffoli F, Fociani P, *et al.* Virtual Chromoendoscopy With FICE for the Classification of Polypoid and Nonpolypoid Raised Lesions in Ulcerative Colitis. *J Clin Gastroenterol* 2019;**53**:269–76. doi:10.1097/MCG.0000000000000974

100 Aladrén BS, González-Lama Y, García-Alvarado M, *et al.* Even non-experts identify non-dysplastic lesions in inflammatory bowel disease via chromoendoscopy: results of a screening program in real-life. *Endosc Int open* 2019;**7**:E743–50. doi:10.1055/a-0839-4514

101 Iacucci M, McQuaid K, Gui XS, *et al.* A multimodal (FACILE) classification for optical diagnosis of inflammatory bowel disease associated neoplasia. *Endoscopy* 2019;**51**:133–41. doi:10.1055/a-0757-7759

102 Regula J, Rupinski M, Kraszewska E, *et al.* Colonoscopy in Colorectal-Cancer Screening for Detection of Advanced Neoplasia. *N Engl J Med* Published Online First: 2006. doi:10.1056/nejmoa054967

103 Vleugels JLA, Hassan C, Senore C, *et al.* Diminutive Polyps With Advanced Histologic Features Do Not Increase Risk for Metachronous Advanced Colon Neoplasia. *Gastroenterology* Published Online First: 2019. doi:10.1053/j.gastro.2018.10.050

104 Pickhardt PJ, Kim DH. Colorectal cancer screening with CT colonography: Key concepts regarding polyp prevalence, size, histology, morphology, and natural history. Am. J. Roentgenol. 2009. doi:10.2214/AJR.08.1709

105 Tsai FC, Strum WB. Prevalence of advanced adenomas in small and diminutive colon polyps using direct measurement of size. *Dig Dis Sci* Published Online First: 2011. doi:10.1007/s10620-011-1598-x

106 Kolligs FT, Crispin A, Graser A, *et al.* Risk factors for advanced neoplasia within subcentimetric polyps: Implications for diagnostic imaging. *Gut* Published Online First: 2013. doi:10.1136/gutjnl-2011-300111

107 Lieberman D, Moravec M, Holub J, *et al.* Polyp Size and Advanced Histology in Patients Undergoing Colonoscopy Screening: Implications for CT Colonography. *Gastroenterology* Published Online First: 2008. doi:10.1053/j.gastro.2008.06.083

108 Butterly LF, Chase MP, Pohl H, *et al.* Prevalence of clinically important histology in small adenomas. *Clin Gastroenterol Hepatol* Published Online First: 2006. doi:10.1016/j.cgh.2005.12.021

109 Church JM. Clinical Significance of Small Colorectal Polyps. *Dis Colon Rectum* Published Online First: 2004. doi:10.1007/s10350-003-0078-6

110 Weston AP, Campbell DR. Diminutive Colonic Polyps: Histopathology, Spatial Distribution, Concomitant Significant Lesions, and Treatment Complications. *Am J Gastroenterol* Published Online First: 1995. doi:10.1111/j.1572-0241.1995.tb08002.x

111 Pickhardt PJ, Choi JR, Hwang I, *et al.* Computed Tomographic Virtual Colonoscopy to Screen for Colorectal Neoplasia in Asymptomatic Adults. *N Engl J Med* Published Online First: 2003. doi:10.1056/nejmoa031618

112 Nusko G, Mansmann U, Altendorf-Hofmann A, *et al.* Risk of invasive carcinoma in colorectal

adenomas assessed by size and site. *Int J Colorectal Dis* Published Online First: 1997. doi:10.1007/s003840050103

113 Aldridge AJ, Simson JNL. Histological assessment of colorectal adenomas by size. Are polyps less than 10 mm in size clinically important? *Eur J Surg* Published Online First: 2001. doi:10.1080/11024150152707770

114 Ignjatovic A, East JE, Guenther T, *et al.* What is the most reliable imaging modality for small colonic polyp characterization? Study of white-light, autofluorescence, and narrow-band imaging. *Endoscopy* Published Online First: 2011. doi:10.1055/s-0030-1256074

115 Gschwantler M, Kriwanek S, Langner E, *et al.* High-grade dysplasia and invasive carcinoma in colorectal adenomas: A multivariate analysis of the impact of adenoma and patient characteristics. *Eur J Gastroenterol Hepatol* Published Online First: 2002. doi:10.1097/00042737-200202000-00013

116 Kudo S ei, Takemura O, Ohtsuka K. Flat and Depressed Types of Early Colorectal Cancers: From East to West. Gastrointest. Endosc. Clin. N. Am. 2008. doi:10.1016/j.giec.2008.05.013

117 Gupta N, Bansal A, Rao D, *et al.* Prevalence of advanced histological features in diminutive and small colon polyps. *Gastrointest Endosc* Published Online First: 2012. doi:10.1016/j.gie.2012.01.020

118 Sakamoto T, Matsuda T, Nakajima T, *et al.* Clinicopathological features of colorectal polyps: Evaluation of the 'predict, resect and discard' strategies. *Color Dis* Published Online First: 2013. doi:10.1111/codi.12210

119 Chiu HM, Chang LC, Shun CT, *et al.* Current management of diminutive colorectal polyps in Taiwan. *Dig Endosc* Published Online First: 2014. doi:10.1111/den.12260

120 Oka S, Tanaka S, Nakadoi K, *et al.* Endoscopic features and management of diminutive colorectal submucosal invasive carcinoma. *Dig Endosc* Published Online First: 2014. doi:10.1111/den.12275

121 Suna N, Koksal AS, Yildiz H, Parlak E, Kuzu UB, Yuksel M, Aydinli O, Turhan N, Sakaogullari SZ YZ. Prevalence of advanced histologic features in diminutive colon polyps. *Acta Gastroenterol Belg 2015, 78287-291*

122 Ponugoti PL, Cummings OW, Rex DK. Risk of cancer in small and diminutive colorectal polyps. *Dig Liver Dis* Published Online First: 2017. doi:10.1016/j.dld.2016.06.025

123 Iwai T, Imai K, Hotta K, Ito S, Yamaguchi Y, Kawata N, Tanaka M, Kakushima N, Takizawa K IH. Endoscopic prediction of advanced histology in diminutive and small colorectal polyps Title. *J Gastroenterol Hepatol 2018*

124 Turner KO, Genta RM, Sonnenberg A. Lesions of all types exist in colon polyps of all sizes. *Am J Gastroenterol* Published Online First: 2018. doi:10.1038/ajg.2017.439

125 Vleugels JLA, Dijkgraaf MGW, Hazewinkel Y, *et al.* Effects of Training and Feedback on Accuracy of Predicting Rectosigmoid Neoplastic Lesions and Selection of Surveillance Intervals by Endoscopists Performing Optical Diagnosis of Diminutive Polyps. *Gastroenterology* Published Online First: 2018. doi:10.1053/j.gastro.2018.01.063

126 von Renteln D, Kaltenbach T, Rastogi A, *et al.* Simplifying Resect and Discard Strategies for Real-Time Assessment of Diminutive Colorectal Polyps. *Clin Gastroenterol Hepatol* Published Online First: 2018. doi:10.1016/j.cgh.2017.11.036

127 Jeong YH, Kim KO, Park CS, *et al.* Risk factors of advanced adenoma in small and diminutive

colorectal polyp. *J Korean Med Sci* Published Online First: 2016. doi:10.3346/jkms.2016.31.9.1426

128 Shapiro R, Ben-Horin S, Bar-Meir S, *et al.* The risk of advanced histology in small-sized colonic polyps: Are non-invasive colonic imaging modalities good enough? *Int J Colorectal Dis* Published Online First: 2012. doi:10.1007/s00384-012-1409-7

129 Chaput U, Alberto SF, Terris B, *et al.* Risk factors for advanced adenomas amongst small and diminutive colorectal polyps: A prospective monocenter study. *Dig Liver Dis* Published Online First: 2011. doi:10.1016/j.dld.2011.02.002

130 Denis B, Bottlaender J, Weiss AM, *et al.* Some diminutive colorectal polyps can be removed and discarded without pathological examination. *Endoscopy* Published Online First: 2011. doi:10.1055/s-0030-1255952

131 Graser A, Stieber P, Nagel D, *et al.* Comparison of CT colonography, colonoscopy, sigmoidoscopy and faecal occult blood tests for the detection of advanced adenoma in an average risk population. *Gut* Published Online First: 2009. doi:10.1136/gut.2008.156448

132 Bretagne JF, Manfredi S, Piette C, *et al.* Yield of high-grade dysplasia based on polyp size detected at colonoscopy: A series of 2295 examinations following a positive fecal occult blood test in a population-based study. *Dis Colon Rectum* Published Online First: 2010. doi:10.1007/DCR.0b013e3181c37f9c

133 Tae WY, Dong IP, Kim YH, *et al.* Clinical significance of small colorectal adenoma less than 10mm: The KASID study. *Hepatogastroenterology* 2007.

134 Rex DK, Overhiser AJ, Chen SC, *et al.* Estimation of impact of american college of radiology recommendations on CT colonography reporting for resection of high-risk adenoma findings. *Am J Gastroenterol* Published Online First: 2009. doi:10.1038/ajg.2008.35

135 Update on the paris classification of superficial neoplastic lesions in the digestive tract. *Endoscopy* 2005;**37**:570–8. doi:10.1055/s-2005-861352

136 Rex DK, Kahi C, O'Brien M, *et al.* The American Society for Gastrointestinal Endoscopy PIVI (Preservation and Incorporation of Valuable Endoscopic Innovations) on real-time endoscopic assessment of the histology of diminutive colorectal polyps. *Gastrointest Endosc* Published Online First: 2011. doi:10.1016/j.gie.2011.01.023

137 ASGE Technology Committee, Abu Dayyeh BK, Thosani N, *et al.* ASGE Technology Committee systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting real-time endoscopic assessment of the histology of diminutive colorectal polyps. *Gastrointest Endosc* Published Online First: 2015. doi:10.1016/j.gie.2014.12.022

138 East JE, Suzuki N, Stavrinidis M, *et al.* Narrow band imaging with magnification for the characterization of small and diminutive colonic polyps: Pit pattern and vascular pattern intensity. *Endoscopy* Published Online First: 2008. doi:10.1055/s-2008-1077586

139 Rogart JN, Jain D, Siddiqui UD, *et al.* Narrow-band imaging without high magnification to differentiate polyps during real-time colonoscopy: improvement with experience. *Gastrointest Endosc* Published Online First: 2008. doi:10.1016/j.gie.2008.04.035

140 Coe SG, Thomas C, Crook J, *et al.* Colorectal surveillance interval assignment based on in vivo prediction of polyp histology: Impact of endoscopic quality improvement program. *Gastrointest Endosc* Published Online First: 2012. doi:10.1016/j.gie.2012.03.007

141 Shahid MW, Buchner AM, Heckman MG, *et al.* Diagnostic accuracy of probe-based confocal

laser endomicroscopy and narrow band imaging for small colorectal polyps: A feasibility study. *Am J Gastroenterol* Published Online First: 2012. doi:10.1038/ajg.2011.376

142 Hewett DG, Huffman ME, Rex DK. Leaving distal colorectal hyperplastic polyps in place can be achieved with high accuracy by using narrow-band imaging: An observational study. *Gastrointest Endosc* Published Online First: 2012. doi:10.1016/j.gie.2012.04.446

143 Paggi S, Rondonotti E, Amato A, *et al.* Resect and discard strategy in clinical practice: A prospective cohort study. *Endoscopy* Published Online First: 2012. doi:10.1055/s-0032-1309891

144 Sakamoto T, Matsuda T, Aoki T, *et al.* Time saving with narrow-band imaging for distinguishing between neoplastic and non-neoplastic small colorectal lesions. *J Gastroenterol Hepatol* Published Online First: 2012. doi:10.1111/j.1440-1746.2011.06854.x

145 Dg H, Kaltenbach T, Sano Y. Validation of a simple classification system for endoscopic diagnosis of small colorectal polyps using narrow-band imaging. *Gastroenterol Endosc* Published Online First: 2012. doi:10.11280/gee.54.3642

146 Repici A, Hassan C, Radaelli F, *et al.* Accuracy of narrow-band imaging in predicting colonoscopy surveillance intervals and histology of distal diminutive polyps: Results from a multicenter, prospective trial. *Gastrointest Endosc* Published Online First: 2013. doi:10.1016/j.gie.2013.01.035

147 Singh R, Jayanna M, Navadgi S, *et al.* Narrow-band imaging with dual focus magnification in differentiating colorectal neoplasia. *Dig Endosc* Published Online First: 2013. doi:10.1111/den.12075

148 Ladabaum U, Fioritto A, Mitani A, *et al.* Real-time optical biopsy of colon polyps with narrow band imaging in community practice does not yet meet key thresholds for clinical decisions. *Gastroenterology* Published Online First: 2013. doi:10.1053/j.gastro.2012.09.054

149 Wallace MB, Crook JE, Coe S, *et al.* Accuracy of in vivo colorectal polyp discrimination by using dual-focus high-definition narrow-band imaging colonoscopy. *Gastrointest Endosc* Published Online First: 2014. doi:10.1016/j.gie.2014.05.305

150 van den Broek FJC, Fockens P, Van Eeden S, *et al.* Clinical Evaluation of Endoscopic Trimodal Imaging for the Detection and Differentiation of Colonic Polyps. *Clin Gastroenterol Hepatol* Published Online First: 2009. doi:10.1016/j.cgh.2008.10.025

151 Sano Y, Ikematsu H, Fu KI, *et al.* Meshed capillary vessels by use of narrow-band imaging for differential diagnosis of small colorectal polyps. *Gastrointest Endosc* Published Online First: 2009. doi:10.1016/j.gie.2008.04.066

152 Rex DK. Narrow-Band Imaging Without Optical Magnification for Histologic Analysis of Colorectal Polyps. *Gastroenterology* Published Online First: 2009. doi:10.1053/j.gastro.2008.12.009

153 Ignjatovic A, East JE, Suzuki N, *et al.* Optical diagnosis of small colorectal polyps at routine colonoscopy (Detect InSpect ChAracterise Resect and Discard; DISCARD trial): a prospective cohort study. *Lancet Oncol* Published Online First: 2009. doi:10.1016/S1470-2045(09)70329-8

154 Henry ZH, Yeaton P, Shami VM, *et al.* Meshed capillary vessels found on narrow-band imaging without optical magnification effectively identifies colorectal neoplasia: a North American validation of the Japanese experience. *Gastrointest Endosc* Published Online First: 2010. doi:10.1016/j.gie.2010.01.048

155 Lee CK, Lee SH, Hwangbo Y. Narrow-band imaging versus I-Scan for the real-time histological prediction of diminutive colonic polyps: A prospective comparative study by using the simple unified endoscopic classification. *Gastrointest Endosc* Published Online First: 2011. doi:10.1016/j.gie.2011.04.049

156 Kuiper T, Marsman WA, Jansen JM, *et al.* Accuracy for Optical Diagnosis of Small Colorectal Polyps in Nonacademic Settings. *Clin Gastroenterol Hepatol* Published Online First: 2012. doi:10.1016/j.cgh.2012.05.004

157 Gupta N, Bansal A, Rao D, *et al.* Accuracy of in vivo optical diagnosis of colon polyp histology by narrow-band imaging in predicting colonoscopy surveillance intervals. *Gastrointest Endosc* Published Online First: 2012. doi:10.1016/j.gie.2011.08.002

158 Chan JL, Lin L, Feiler M, *et al.* Comparative effectiveness of i-SCAN™ and high-definition white light characterizing small colonic polyps. *World J Gastroenterol* Published Online First: 2012. doi:10.3748/wjg.v18.i41.5905

159 Schachschal G, Mayr M, Treszl A, *et al.* Endoscopic versus histological characterisation of polyps during screening colonoscopy. *Gut* Published Online First: 2014. doi:10.1136/gutjnl-2013-304562

160 Hoffman A, Sar F, Goetz M, *et al.* High definition colonoscopy combined with i-Scan is superior in the detection of colorectal neoplasias compared with standard video colonoscopy: A prospective randomized controlled trial. *Endoscopy* Published Online First: 2010. doi:10.1055/s-0030-1255713

161 Pigò F, Bertani H, Manno M, *et al.* I-Scan high-definition white light endoscopy and colorectal polyps: Prediction of histology, interobserver and intraobserver agreement. *Int J Colorectal Dis* Published Online First: 2013. doi:10.1007/s00384-012-1583-7

162 Hong SN, Choe WH, Lee JH, *et al.* Prospective, randomized, back-to-back trial evaluating the usefulness of i-SCAN in screening colonoscopy. *Gastrointest Endosc* Published Online First: 2012. doi:10.1016/j.gie.2011.11.040

163 Hoffman A, Kagel C, Goetz M, *et al.* Recognition and characterization of small colonic neoplasia with high-definition colonoscopy using i-Scan is as precise as chromoendoscopy. *Dig Liver Dis* Published Online First: 2010. doi:10.1016/j.dld.2009.04.005

164 Togashi K, Osawa H, Koinuma K, *et al.* A comparison of conventional endoscopy, chromoendoscopy, and the optimal-band imaging system for the differentiation of neoplastic and non-neoplastic colonic polyps. *Gastrointest Endosc* Published Online First: 2009. doi:10.1016/j.gie.2008.10.063

165 Buchner AM, Shahid MW, Heckman MG, *et al.* Comparison of Probe-Based Confocal Laser Endomicroscopy With Virtual Chromoendoscopy for Classification of Colon Polyps. *Gastroenterology* Published Online First: 2010. doi:10.1053/j.gastro.2009.10.053

166 Pohl J, Lotterer E, Balzer C, *et al.* Computed virtual chromoendoscopy versus standard colonoscopy with targeted indigocarmine chromoscopy: A randomised multicentre trial. *Gut* Published Online First: 2009. doi:10.1136/gut.2008.153601

167 Dos Santos CEO, Lima JCP, Lopes CV, *et al.* Computerized virtual chromoendoscopy versus indigo carmine chromoendoscopy combined with magnification for diagnosis of small colorectal lesions: A randomized and prospective study. *Eur J Gastroenterol Hepatol* Published Online First: 2010. doi:10.1097/MEG.0b013e32833a5d63

168 Kim YS, Kim D, Chung SJ, *et al.* Differentiating Small Polyp Histologies Using Real-Time

Screening Colonoscopy With Fuji Intelligent Color Enhancement. *Clin Gastroenterol Hepatol* Published Online First: 2011. doi:10.1016/j.cgh.2011.05.021

169 dos Santos CEO, Malaman D, Lopes CV, *et al.* Digital Chromoendoscopy for Diagnosis of Diminutive Colorectal Lesions. *Diagn Ther Endosc* Published Online First: 2012. doi:10.1155/2012/279521

170 Longcroft-Wheaton GR, Higgins B, Bhandari P. Flexible spectral imaging color enhancement and indigo carmine in neoplasia diagnosis during colonoscopy: A large prospective UK series. *Eur J Gastroenterol Hepatol* Published Online First: 2011. doi:10.1097/MEG.0b013e328349e276

171 Longcroft-Wheaton G, Brown J, Cowlishaw D, *et al.* High-definition vsstandard-definition colonoscopy in the characterization of small colonic polyps: Results from a randomized trial. *Endoscopy* Published Online First: 2012. doi:10.1055/s-0032-1310004

172 Paggi S, Rondonotti E, Amato A, *et al.* Narrow-band imaging in the prediction of surveillance intervals after polypectomy in community practice. *Endoscopy* Published Online First: 2015. doi:10.1055/s-0034-1392042

173 Patel SG, Schoenfeld P, Kim HM, *et al.* Real-Time Characterization of Diminutive Colorectal Polyp Histology Using Narrow-Band Imaging: Implications for the Resect and Discard Strategy. *Gastroenterology* Published Online First: 2016. doi:10.1053/j.gastro.2015.10.042

174 Bae JH, Lee C, Kang HY, *et al.* Improved Real-Time Optical Diagnosis of Colorectal Polyps Following a Comprehensive Training Program. *Clin Gastroenterol Hepatol* Published Online First: 2019. doi:10.1016/j.cgh.2019.02.019

175 Klare P, Haller B, Wormbt S, *et al.* Narrow-band imaging vshigh definition white light for optical diagnosis of small colorectal polyps: A randomized multicenter trial. *Endoscopy* Published Online First: 2016. doi:10.1055/s-0042-110650

176 Vu HT, Sayuk GS, Hollander TG, *et al.* Resect and Discard Approach to Colon Polyps: Real-World Applicability Among Academic and Community Gastroenterologists. *Dig Dis Sci* Published Online First: 2015. doi:10.1007/s10620-014-3376-z

177 Chandran S, Parker F, Lontos S, *et al.* Can we ease the financial burden of colonoscopy? Using real-time endoscopic assessment of polyp histology to predict surveillance intervals. *Intern Med J* Published Online First: 2015. doi:10.1111/imj.12917

178 Kaltenbach T, Rastogi A, Rouse R V., *et al.* Real-time optical diagnosis for diminutive colorectal polyps using narrow-band imaging: The VALID randomised clinical trial. *Gut* Published Online First: 2015. doi:10.1136/gutjnl-2014-307742

179 Rees CJ, Rajasekhar PT, Wilson A, *et al.* Narrow band imaging optical diagnosis of small colorectal polyps in routine clinical practice: the Detect Inspect Characterise Resect and Discard 2 (DISCARD 2) study. *Gut* 2017;**66**:887–95. doi:10.1136/gutjnl-2015-310584

180 IJspeert JEG, Bastiaansen BAJ, Van Leerdam ME, *et al.* Development and validation of the WASP classification system for optical diagnosis of adenomas, hyperplastic polyps and sessile serrated adenomas/polyps. *Gut* Published Online First: 2016. doi:10.1136/gutjnl-2014-308411

181 dos Santos C, Perez H, Mönkemüller K, *et al.* Observer agreement for diagnosis of colorectal lesions with analysis of the vascular pattern by image-enhanced endoscopy. *Endosc Int Open* Published Online First: 2015. doi:10.1055/s-0034-1391667

182 Bisschops R, Hassan C, Bhandari P, *et al.* BASIC (BLI Adenoma Serrated International

Classification) classification for colorectal polyp characterization with blue light imaging. *Endoscopy* Published Online First: 2018. doi:10.1055/s-0043-121570

183 Repici A, Ciscato C, Correale L, *et al.* Narrow-band Imaging International Colorectal Endoscopic Classification to predict polyp histology: REDEFINE study (with videos). *Gastrointest Endosc* Published Online First: 2016. doi:10.1016/j.gie.2016.02.020

184 Rastogi A, Rao DS, Gupta N, *et al.* Impact of a computer-based teaching module on characterization of diminutive colon polyps by using narrow-band imaging by non-experts in academic and community practice: A video-based study. *Gastrointest Endosc* Published Online First: 2014. doi:10.1016/j.gie.2013.07.032

185 Sinh P, Gupta N, Rao DS, *et al.* Community gastroenterologists can learn diminutive colon polyp histology characterization with narrow band imaging by a computer-based teaching module. Dig. Endosc. 2015. doi:10.1111/den.12403

186 Dos Santos CEO, Daniele Malaman, Naohisa Yoshida, Júlio C. Pereira-Lima, Fernanda Q. Onófrio, Rafaelle G. Furlan FIT and OM. Blue laser imaging: a new image-enhanced endoscopy for the diagnosis of colorectal lesions. *Eur J Gastroenterol* 2018;**30**:1514–20.

187 Smith SCL, Saltzman J, Shivaji UN, Lethebe BC, Cannatelli R; Birmingham Colonic Polyp Characterisation Group, Ghosh S IMA. A randomized controlled study of the prediction of diminutive/small colorectal polyp histology using didactic vs. computer based self-learning module in gastroenterology trainees. *Dig Endosc* 2019;:epub.

188 Iacucci M, Trovato C, Daperno M, *et al.* Development and validation of the SIMPLE endoscopic classification of diminutive and small colorectal polyps *. *Endoscopy* Published Online First: 2018. doi:10.1055/s-0044-100791

189 Kessler WR, Imperiale TF, Klein RW, *et al.* A quantitative assessment of the risks and cost savings of forgoing histologic examination of diminutive polyps. *Endoscopy* Published Online First: 2011. doi:10.1055/s-0030-1256381

190 Vleugels J, Greuter M, Hazewinkel Y, *et al.* Implementation of an optical diagnosis strategy saves costs and does not impair clinical outcomes of a fecal immunochemical test-based colorectal cancer screening program. *Endosc Int Open* Published Online First: 2017. doi:10.1055/s-0043-113565

191 Picot J, Rose M, Cooper K, *et al.* Virtual chromoendoscopy for the real-time assessment of colorectal polyps in vivo: A systematic review and economic evaluation. *Health Technol Assess (Rockv)* Published Online First: 2017. doi:10.3310/hta21790

192 Solon C, Klausnitzer R, Blissett D, *et al.* Economic value of narrow band imaging versus white light endoscopy for the characterization of diminutive polyps in the colon: systematic literature review and cost-consequence model. *J Med Econ* Published Online First: 2016. doi:10.1080/13696998.2016.1192550

193 Hassan C, Pickhardt PJ, Rex DK. A resect and discard strategy would improve cost-effectiveness of colorectal cancer screening. *Clin Gastroenterol Hepatol* Published Online First: 2010. doi:10.1016/j.cgh.2010.05.018

194 Puig I, López-Cerón M, Arnau A, *et al.* Accuracy of the Narrow-Band Imaging International Colorectal Endoscopic Classification System in Identification of Deep Invasion in Colorectal Polyps. *Gastroenterology* 2019;**156**:75–87. doi:10.1053/j.gastro.2018.10.004

195 Bogie R, Veldman M, Snijders L, *et al.* Endoscopic subtypes of colorectal laterally spreading tumors (LSTs) and the risk of submucosal invasion: a meta-analysis. *Endoscopy* 2018;**50**:263–

82. doi:10.1055/s-0043-121144

196 Burgess NG, Hourigan LF, Zanati SA, *et al.* Risk Stratification for Covert Invasive Cancer Among Patients Referred for Colonic Endoscopic Mucosal Resection: A Large Multicenter Cohort. *Gastroenterology* 2017;**153**:732-742.e1. doi:10.1053/j.gastro.2017.05.047

197 Bugajski M, Kaminski MF, Orlowska J, *et al.* Suspicious macroscopic features of small malignant colorectal polyps. *Scand J Gastroenterol* 2015;**50**:1261–7. doi:10.3109/00365521.2015.1024280

198 Backes Y, Moss A, Reitsma JB, *et al.* Narrow Band Imaging, Magnifying Chromoendoscopy, and Gross Morphological Features for the Optical Diagnosis of T1 Colorectal Cancer and Deep Submucosal Invasion: A Systematic Review and Meta-Analysis. *Am J Gastroenterol* 2017;**112**:54–64. doi:10.1038/ajg.2016.403

199 Matsuda T, Fujii T, Saito Y, *et al.* Efficacy of the invasive/non-invasive pattern by magnifying chromoendoscopy to estimate the depth of invasion of early colorectal neoplasms. *Am J Gastroenterol* 2008;**103**:2700–6. doi:10.1111/j.1572-0241.2008.02190.x

200 Backes Y, Schwartz MP, Ter Borg F, *et al.* Multicentre prospective evaluation of real-time optical diagnosis of T1 colorectal cancer in large non-pedunculated colorectal polyps using narrow band imaging (the OPTICAL study). *Gut* 2019;**68**:271–9. doi:10.1136/gutjnl-2017-314723

201 Sumimoto K, Tanaka S, Shigita K, *et al.* Clinical impact and characteristics of the narrow-band imaging magnifying endoscopic classification of colorectal tumors proposed by the Japan NBI Expert Team. *Gastrointest Endosc* 2017;**85**:816–21. doi:10.1016/j.gie.2016.07.035

202 Komeda Y, Kashida H, Sakurai T, *et al.* Magnifying Narrow Band Imaging (NBI) for the Diagnosis of Localized Colorectal Lesions Using the Japan NBI Expert Team (JNET) Classification. *Oncology* 2017;**93 Suppl 1**:49–54. doi:10.1159/000481230

203 Minoda Y, Ogino H, Chinen T, *et al.* Objective validity of the Japan Narrow-Band Imaging Expert Team classification system for the differential diagnosis of colorectal polyps. *Dig Endosc* 2019;:den.13393. doi:10.1111/den.13393

204 Iwatate M, Sano Y, Tanaka S, *et al.* Validation study for development of the Japan NBI Expert Team classification of colorectal lesions. *Dig Endosc* 2018;**30**:642–51. doi:10.1111/den.13065

205 Sumimoto K, Tanaka S, Shigita K, *et al.* Diagnostic performance of Japan NBI Expert Team classification for differentiation among noninvasive, superficially invasive, and deeply invasive colorectal neoplasia. *Gastrointest Endosc* 2017;**86**:700–9. doi:10.1016/j.gie.2017.02.018

206 Sakamoto T, Nakajima T, Matsuda T, *et al.* Comparison of the diagnostic performance between magnifying chromoendoscopy and magnifying narrow-band imaging for superficial colorectal neoplasms: an online survey. *Gastrointest Endosc* 2018;**87**:1318–23. doi:10.1016/j.gie.2017.12.021

207 Kobayashi S, Yamada M, Takamaru H, *et al.* Diagnostic yield of the Japan NBI Expert Team (JNET) classification for endoscopic diagnosis of superficial colorectal neoplasms in a large-scale clinical practice database. *United Eur Gastroenterol J* 2019;:205064061984598. doi:10.1177/2050640619845987

208 Kawaguti FS, Franco MC, Martins BC, *et al.* Role of Magnification Chromoendoscopy in the Management of Colorectal Neoplastic Lesions Suspicious for Submucosal Invasion. *Dis Colon Rectum* 2019;**62**:422–8. doi:10.1097/DCR.0000000000001343

209 Puig I, Mármol C, Bustamante M. Endoscopic imaging techniques for detecting early colorectal cancer. *Curr Opin Gastroenterol* 2019;**35**:432–9. doi:10.1097/MOG.0000000000000570

210 Moss A, Williams SJ, Hourigan LF, *et al.* Long-term adenoma recurrence following wide-field endoscopic mucosal resection (WF-EMR) for advanced colonic mucosal neoplasia is infrequent: results and risk factors in 1000 cases from the Australian Colonic EMR (ACE) study. *Gut* 2015;**64**:57–65. doi:10.1136/GUTJNL-2013-305516

211 Belderbos TDG, Leenders M, Moons LMG, *et al.* Local recurrence after endoscopic mucosal resection of nonpedunculated colorectal lesions: systematic review and meta-analysis. *Endoscopy* 2014;**46**:388–402. doi:10.1055/s-0034-1364970

212 Atkin WS, Valori R, Kuipers EJ, *et al.* European guidelines for quality assurance in colorectal cancer screening and diagnosis. First Edition--Colonoscopic surveillance following adenoma removal. *Endoscopy* 2012;**44 Suppl 3**:SE151-63. doi:10.1055/s-0032-1309821

213 Lieberman DA, Rex DK, Winawer SJ, *et al.* Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology* 2012;**143**:844–57. doi:10.1053/j.gastro.2012.06.001

214 Khashab M, Eid E, Rusche M, *et al.* Incidence and predictors of "late" recurrences after endoscopic piecemeal resection of large sessile adenomas. *Gastrointest Endosc* 2009;**70**:344–9. doi:10.1016/j.gie.2008.10.037

215 Desomer L, Tutticci N, Tate DJ, *et al.* A standardized imaging protocol is accurate in detecting recurrence after EMR. *Gastrointest Endosc* 2017;**85**:518–26. doi:10.1016/j.gie.2016.06.031

216 Kandel P, Brand EC, Pelt J, *et al.* Endoscopic scar assessment after colorectal endoscopic mucosal resection scars: when is biopsy necessary (EMR Scar Assessment Project for Endoscope (ESCAPE) trial). *Gut* 2019;:gutjnl-2018-316574. doi:10.1136/GUTJNL-2018-316574

217 Riu Pons F, Andreu M, Gimeno Beltran J, *et al.* Narrow band imaging and white light endoscopy in the characterization of a polypectomy scar: A single-blind observational study. *World J Gastroenterol* 2018;**24**:5179–88. doi:10.3748/wjg.v24.i45.5179

218 Knabe M, Pohl J, Gerges C, *et al.* Standardized long-term follow-up after endoscopic resection of large, nonpedunculated colorectal lesions: a prospective two-center study. *Am J Gastroenterol* 2014;**109**:183–9. doi:10.1038/ajg.2013.419

219 Topol EJ. High-performance medicine: the convergence of human and artificial intelligence. *Nat Med* 2019;**25**:44–56. doi:10.1038/s41591-018-0300-7

220 East JE, Rees CJ. Making optical biopsy a clinical reality in colonoscopy. *lancet Gastroenterol Hepatol* 2018;**3**:10–2. doi:10.1016/S2468-1253(17)30366-7

221 No Title. https://ec.europa.eu/digital-single-market/en/news/ethics-guidelines-trustworthy-ai.

222 Mahmud N, Cohen J, Tsourides K, *et al.* Computer vision and augmented reality in gastrointestinal endoscopy. *Gastroenterol Rep* 2015;**3**:179–84. doi:10.1093/gastro/gov027

223 Lee CK, Park D Il, Lee S-H, *et al.* Participation by experienced endoscopy nurses increases the detection rate of colon polyps during a screening colonoscopy: a multicenter, prospective, randomized study. *Gastrointest Endosc* 2011;**74**:1094–102. doi:10.1016/j.gie.2011.06.033

224 Buchner AM, Shahid MW, Heckman MG, *et al.* Trainee participation is associated with increased small adenoma detection. *Gastrointest Endosc* 2011;**73**:1223–31. doi:10.1016/j.gie.2011.01.060

225 Aslanian HR, Shieh FK, Chan FW, *et al.* Nurse Observation During Colonoscopy Increases Polyp Detection: A Randomized Prospective Study. *Am J Gastroenterol* 2013;**108**:166–72. doi:10.1038/ajg.2012.237

226 Mori Y, Kudo S, Berzin T, *et al.* Computer-aided diagnosis for colonoscopy. *Endoscopy* 2017;**49**:813–9. doi:10.1055/s-0043-109430

227 Urban G, Tripathi P, Alkayali T, *et al.* Deep Learning Localizes and Identifies Polyps in Real Time With 96% Accuracy in Screening Colonoscopy. Published Online First: 2018. doi:10.1053/j.gastro.2018.06.037

228 Wang Y, Tavanapong W, Wong J, *et al.* Polyp-Alert: Near real-time feedback during colonoscopy. *Comput Methods Programs Biomed* 2015;**120**:164–79. doi:10.1016/j.cmpb.2015.04.002

229 Mori Y, Kudo S-E, Mohmed HEN, *et al.* Artificial intelligence and upper gastrointestinal endoscopy: Current status and future perspective. *Dig Endosc* 2018;:den.13317. doi:10.1111/den.13317

230 Kudo S, Mori Y, Misawa M, *et al.* Artificial intelligence and colonoscopy: Current status and future perspectives. *Dig Endosc* Published Online First: 27 February 2019. doi:10.1111/den.13340

231 Wang P, Berzin TM, Glissen Brown JR, *et al.* Real-time automatic detection system increases colonoscopic polyp and adenoma detection rates: a prospective randomised controlled study. *Gut* 2019;:gutjnl-2018-317500. doi:10.1136/gutjnl-2018-317500

232 Figueiredo P, Figueiredo I, Pinto L, *et al.* Polyp detection with computer-aided diagnosis in white light colonoscopy: comparison of three different methods. *Endosc Int Open* 2019;**07**:E209–15. doi:10.1055/a-0808-4456

233 Byrne MF, Chapados N, Soudan F, *et al.* Real-time differentiation of adenomatous and hyperplastic diminutive colorectal polyps during analysis of unaltered videos of standard colonoscopy using a deep learning model. *Gut* 2019;**68**:94–100. doi:10.1136/gutjnl-2017-314547

234 Mori Y, Kudo S, Misawa M, *et al.* Real-Time Use of Artificial Intelligence in Identification of Diminutive Polyps During Colonoscopy. *Ann Intern Med* 2018;**169**:357. doi:10.7326/M18-0249

235 Misawa M, Kudo S-E, Mori Y, *et al.* Accuracy of computer-aided diagnosis based on narrow-band imaging endocytoscopy for diagnosing colorectal lesions: comparison with experts. *Int J Comput Assist Radiol Surg* 2017;**12**:757–66. doi:10.1007/s11548-017-1542-4

236 Ichimasa K, Kudo S, Mori Y, *et al.* Artificial intelligence may help in predicting the need for additional surgery after endoscopic resection of T1 colorectal cancer. *Endoscopy* 2018;**50**:230–40. doi:10.1055/s-0043-122385

237 Ito N, Kawahira H, Nakashima H, *et al.* Endoscopic Diagnostic Support System for cT1b Colorectal Cancer Using Deep Learning. *Oncology* 2019;**96**:44–50. doi:10.1159/000491636

238 Lui TKL, Wong KKY, Mak LLY, *et al.* Endoscopic prediction of deeply submucosal invasive carcinoma with use of artificial intelligence. *Endosc Int open* 2019;**7**:E514–20. doi:10.1055/a-0849-9548

239 Ozawa T, Ishihara S, Fujishiro M, *et al.* Novel computer-assisted diagnosis system for endoscopic disease activity in patients with ulcerative colitis. *Gastrointest Endosc* 2019;**89**:416-421.e1. doi:10.1016/j.gie.2018.10.020

240 Kominami Y, Yoshida S, Tanaka S, *et al.* Computer-aided diagnosis of colorectal polyp histology by using a real-time image recognition system and narrow-band imaging magnifying colonoscopy. *Gastrointest Endosc* 2016;**83**:643–9. doi:10.1016/j.gie.2015.08.004

241 Rath T, Tontini G, Vieth M, *et al.* In vivo real-time assessment of colorectal polyp histology using an optical biopsy forceps system based on laser-induced fluorescence spectroscopy. *Endoscopy* 2016;**48**:557–62. doi:10.1055/s-0042-102251

242 Kuiper T, Alderlieste Y, Tytgat K, *et al.* Automatic optical diagnosis of small colorectal lesions by laser-induced autofluorescence. *Endoscopy* 2014;**47**:56–62. doi:10.1055/s-0034-1378112

243 Klare P, Sander C, Prinzen M, *et al.* Automated polyp detection in the colorectum: a prospective study (with videos). *Gastrointest Endosc* 2019;**89**:576-582.e1. doi:10.1016/j.gie.2018.09.042

244 Aihara H, Saito S, Inomata H, *et al.* Computer-aided diagnosis of neoplastic colorectal lesions using 'real-time' numerical color analysis during autofluorescence endoscopy. *Eur J Gastroenterol Hepatol* 2013;**25**:488–94. doi:10.1097/MEG.0b013e32835c6d9a

245 Cabitza F, Rasoini R, Gensini GF. Unintended Consequences of Machine Learning in Medicine. *JAMA* 2017;**318**:517. doi:10.1001/jama.2017.7797

246 Povyakalo AA, Alberdi E, Strigini L, *et al.* How to discriminate between computer-aided and computer-hindered decisions: a case study in mammography. *Med Decis Making* 2013;**33**:98–107. doi:10.1177/0272989X12465490

247 Tsai TL, Fridsma DB, Gatti G. Computer decision support as a source of interpretation error: the case of electrocardiograms. *J Am Med Inform Assoc* 2003;**10**:478–83. doi:10.1197/jamia.M1279

248 Ross, C. & Swetlitz I. IBM's Watson supercomputer recommended 'unsafe and incorrect' cancer treatments, internal documents show. Stat News. 2018.https://www.statnews.com/2018/07/25/ibm-watson-recommended-unsafeincorrect-treatments/

249 Mori Y, Kudo S. Detecting colorectal polyps via machine learning. *Nat Biomed Eng* 2018;**2**:713–4. doi:10.1038/s41551-018-0308-9

250 Vinsard DG, Mori Y, Misawa M, *et al.* Quality assurance of computer-aided detection and diagnosis in colonoscopy. *Gastrointest Endosc* Published Online First: 26 March 2019. doi:10.1016/j.gie.2019.03.019

251 Rajkomar A, Dean J, Kohane I. Machine Learning in Medicine. *N Engl J Med* 2019;**380**:1347–58. doi:10.1056/NEJMra1814259

Appendices (all online only)

APPENDIX 1 : Task forces

TASK FORCE 1 : Detection of colorectal neoplasia in average risk population Chair : C. Hassan; members : M. Bustamante Balén , G. Cortas, M. Kaminski, G. Antonelli
TASK FORCE 2: Detection of colorectal neoplasia in high risk population : Fap, aFAP, Lynch, Peutz Jeghers, SPS Chair : M. Pellisé; members : R. Bisschops, G. Cortas, J. East, Y. Hasewinkel, M. Iacucci
TASK FORCE 3 : Detection and Differentiation of colorectal neoplasia in IBD Chair : H. Neumann; members : R. Bisschops, M. Iacucci, M. Pellisé
TASK FORCE 4: Differentiation between neoplastic and non-neoplastic small colorectal polyps. Chair : E. Dekker & Y. Hazewinkel; M Bustamante Balén, E. Corron, C. Hassan, M. Iacucci, I.Puig del Castillo , G Longcroft-Wheaton
TASK FORCE 5 : Role of advanced imaging in treatment of colorectal neoplasia Chair : M. Kaminski; members : E. Corron, M. Iacucci, H. Neumann, P. Pelissé, I.Puig del Castillo
TASK FORCE 6 : Role of artificial intelligence in detection and characterisation of colorectal polyps. Chair : J. East; members : R. Bisschops, C. Hassan, H. Neumann, Y. Mori

APPENDIX 2

GRADE SYSTEM @ Thieme : please use the previous tables that was used in the previous guideline

Appendix e2 a Levels of evidence according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system [8].

Evidence level	
High quality	One or more well-designed and well-executed randomized controlled trials (RCTs) that yield consistent and directly applicable results. This also means that further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality	RCTs with important limitations (i. e. biased assessment of the treatment effect, large loss to follow-up, lack of blinding, unexplained heterogeneity), indirect evidence originating from similar (but not identical) populations of interest, and RCTs with a very small number of participants or observed events. In addition, evidence from well-designed controlled trials without randomization, well-designed cohort or case–control analytic studies, and multiple time series with or without intervention are in this category. It also means that further research will probably have an important effect on our confidence in the estimate of effect and may change the estimate.
Low quality	Observational studies would typically be rated as low quality because of the risk for bias.[1] It also means that further research is very likely to have an important effect on our confidence in the estimate of effect and will probably change the estimate.
Very low quality[2]	Evidence is conflicting, of poor quality, or lacking, and hence the balance of benefits and harms cannot be determined. Any estimate of effect that is very uncertain as evidence is either unavailable or does not permit a conclusion.

[1] Quality of evidence based on observational studies may be rated as moderate or even high, depending on circumstances under which evidence is obtained from observational studies. Factors that may contribute to upgrading the quality of evidence include a large magnitude of the observed effect, a dose–response association, or the presence of an observed effect when all plausible confounders would decrease the observed effect.

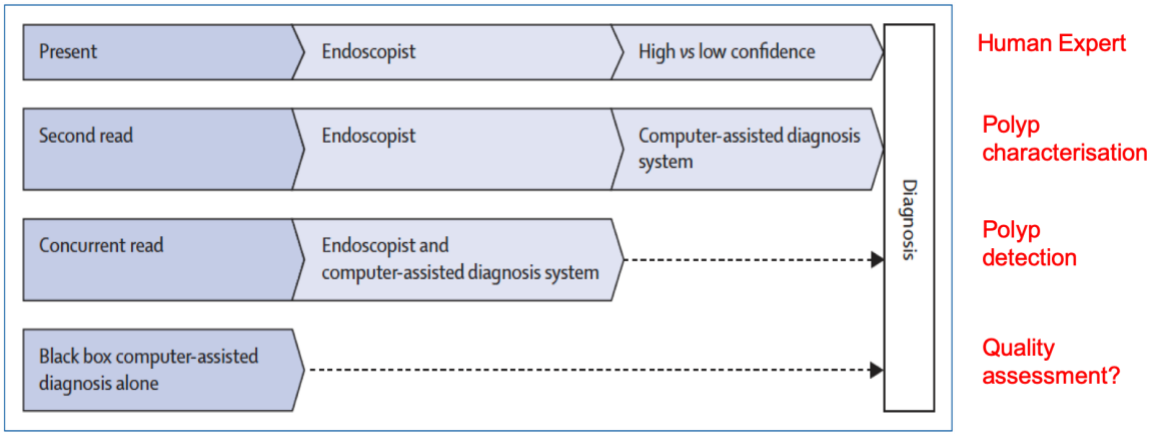
[2] Insufficient evidence to determine for or against routinely providing a service.

Appendix e2 b Strength of recommendations according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system [8].

Strength of recommendation	
Strong	Benefits clearly outweigh risks and burden or vice-versa. Usually stated as "we recommend".
Weak	Benefits closely balanced with risks and burden. Usually stated as "we suggest".

ALL OTHER APPENDICES SUBMITTED SEPERATELY (tables of evidence)

FIGURE 2 (task force 6)



Adapted from: East JE and Rees CJ. Lancet Gastroenterol Hepatol. 2018 Jan;3(1):10-12. [Needs to be redrawn by Endoscopy Graphics team – I can provide original powerpoint]

Figure 1. Proposed algorithm to guide therapeutic decisions for colorectal polyps > 10 mm assessed with NBI without magnification

. [Needs to be redrawn by Endoscopy Graphics team ask ignasi if we can use this figure]