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CONSENSUS STATEMENT

SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease

INTRODUCTION

Patients with ulcerative colitis or Crohn's colitis have an increased risk of colorectal cancer (CRC). Most cases are believed to arise from dysplasia, and surveillance colonoscopy therefore is recommended to detect dysplasia. Detection of dysplasia traditionally has relied on both examination of the mucosa with targeted biopsies of visible lesions and extensive random biopsies to identify invisible dysplasia. Current U.S. guidelines recommend obtaining at least 32 random biopsy specimens from all segments of the colon as the foundation of endoscopic surveillance.[1-4]

However, much of the evidence that provides a basis for these recommendations is from older literature, when most dysplasia was diagnosed on random biopsies of colon mucosa.[5] With the advent of video endoscopy and newer endoscopic technologies, investigators now report that most dysplasia discovered in patients with inflammatory bowel disease (IBD) is visible.[6,7] Such a paradigm shift may have important implications for the surveillance and management of dysplasia.

The evolving evidence regarding newer endoscopic methods to detect dysplasia has resulted in variation among guideline recommendations from organizations around the world.[1-4,8-10] We therefore sought to develop unifying consensus recommendations addressing 2 issues: (1) How should surveillance colonoscopy for detection of dysplasia be performed? (2) How should dysplasia identified at colonoscopy be managed?

DEVELOPMENT PROCESS

An international multidisciplinary group representing a wide spectrum of stakeholders and attitudes regarding IBD surveillance (Appendix 1, available online at www.giejournal.org) developed these recommendations following a process that adhered to suggested standards for guideline development from the Institute of Medicine and others and that incorporated the GRADE methodology.[11-14] Details regarding the development process are provided in Figure 1 and Appendix 2. A systematic review was performed for each focused clinical question. The search strategy is shown in Appendix 3, and the full synthesis of evidence reviewed by panelists is presented in Appendix 4. All appendices are available online at www.giejournal.org.

The strength of recommendation, provided for each recommendation, reflects the level of confidence that desirable effects of an intervention outweigh undesirable effects. Strong recommendations mean panelists are confident that the desirable effects outweigh the undesirable effects; therefore, most informed patients would choose the recommended management, and clinicians would provide the intervention to most patients. Conditional recommendations mean the desirable and undesirable effects of the intervention are closely balanced or appreciable uncertainty exists regarding the balance; therefore, informed patients' choices will vary according to their values and preferences, with many not wanting the intervention, and clinicians must ensure that patients' care is in keeping with their values and preferences.[13]

TERMINOLOGY

A subgroup of panelists developed a set of terms for colonoscopic findings in IBD surveillance to establish uniformity in communication. Descriptive phrases, modified from the Paris Classification,[15] were recommended for adoption (Table 1). Modifications included the addition of terms for ulceration and border of the lesion. It was agreed that the terms *dysplasia-associated lesion or mass (DALM), adenoma-like,* and *non-adenoma-like* should be abandoned. The term *endoscopically resectable* indicates that (1) distinct margins of the lesion could be identified, (2) the lesion appears to be completely removed on visual inspection after endoscopic resection, (3) histologic examination of the resected specimen is consistent with complete removal, and (4) biopsy specimens taken from mucosa immediately adjacent to the resection site are free of dysplasia on histologic examination.

CONSENSUS RECOMMENDATIONS AND SUMMARY OF SUPPORTING EVIDENCE

Detection of dysplasia on surveillance colonoscopy

The goal of this section is to define the optimal method(s) of detecting colon dysplasia in patients

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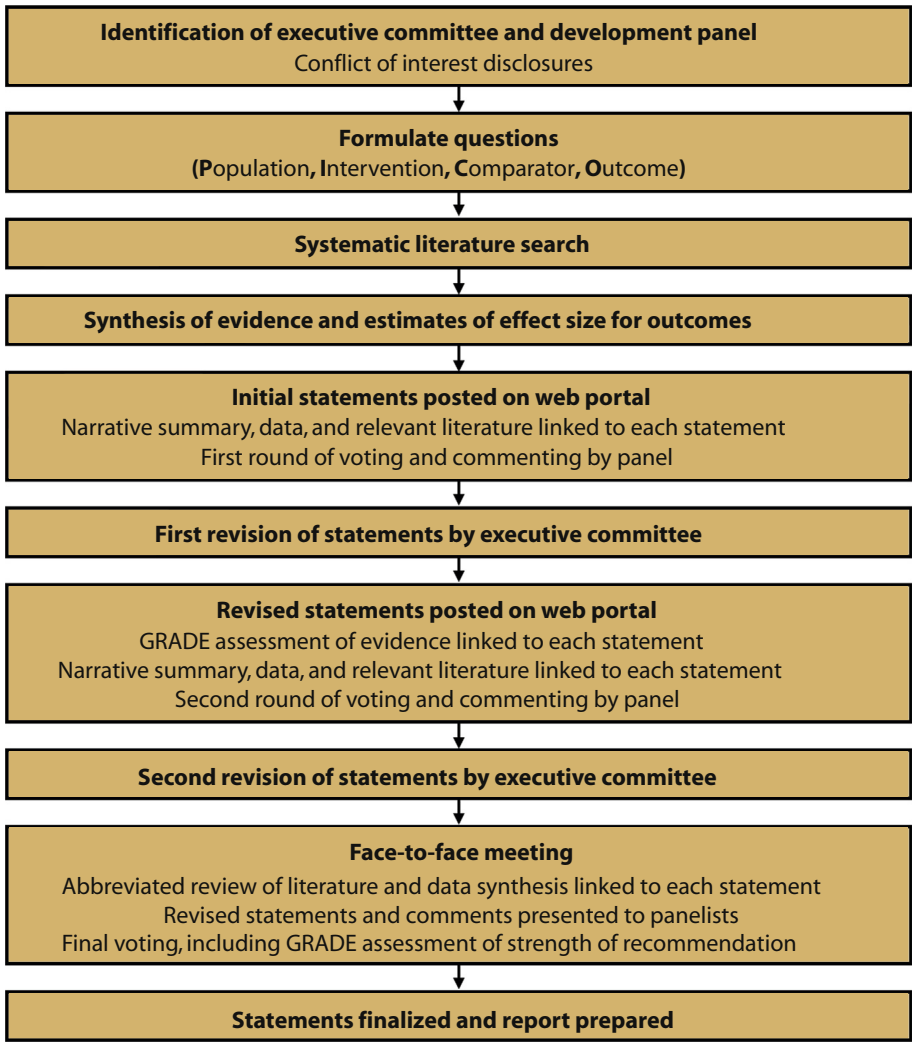


Figure 1. Development process.

with IBD. Detection of dysplasia, which is the immediate goal of surveillance colonoscopy, was chosen as the primary endpoint, with the understanding that detection of dysplasia is not clearly documented to improve clinical outcomes such as CRC incidence or mortality. Only histologic diagnoses of low-grade or high-grade dysplasia were considered; diagnoses of indefinite for dysplasia were excluded. Current guideline recommendations regarding the need for serial surveillance colonoscopy in patients with IBD were accepted, and other issues such as the appropriate surveillance interval or risk stratification[1-4,8-10] were not addressed.

Recommendations are listed in Table 2 and appear individually hereafter with the proportion of panelists in agreement, the strength of the recommendation, and the quality of evidence. A summary of the evidence and discussion regarding the recommendation follows each statement.

Statement 1: When performing surveillance with white-light colonoscopy, high definition is recommended rather than standard definition.

(80% agreement; strong recommendation; low-quality evidence)

Summary of evidence and discussion. High-definition (1080 system) endoscopy provides image signals of higher pixel density than standard definition (480 system), with faster line scanning on high-definition monitors, leading to sharper images with fewer artifacts.[16] A high-definition system includes a high-definition endoscope, processor, cabling, and monitor. A retrospective observational study found that dysplasia was discovered in approximately twice as many patients undergoing high-definition colonoscopy (n = 203) compared with a cohort undergoing standard-definition colonoscopy (n = 154): adjusted prevalence ratio = 2.2 (95% confidence interval [CI], 1.1-4.5).[17]

TABLE 1. Terminology for reporting findings on colonoscopic surveillance of patients with inflammatory bowel disease (modified from Paris Classification[15])

Term	Definition
Visible dysplasia	Dysplasia identified on targeted biopsies from a lesion visualized at colonoscopy
Polypoid	Lesion protruding from the mucosa into the lumen ≥2.5 mm
Pedunculated	Lesion attached to the mucosa by a stalk
Sessile	Lesion not attached to the mucosa by a stalk: entire base is contiguous with the mucosa
Nonpolypoid	Lesion with little (<2.5 mm) or no protrusion above the mucosa
Superficial elevated	Lesion with protrusion but <2.5 mm above the lumen (less than the height of the closed cup of a biopsy forceps)
Flat	Lesion without protrusion above the mucosa
Depressed	Lesion with at least a portion depressed below the level of the mucosa
General descriptors	
Ulcerated	Ulceration (fibrinous-appearing base with depth) within the lesion
Border	
Distinct border	Lesion's border is discrete and can be distinguished from surrounding mucosa
Indistinct border	Lesion's border is not discrete and cannot be distinguished from surrounding mucosa
Invisible dysplasia	Dysplasia identified on random (non-targeted) biopsies of colon mucosa without a visible lesion

Given that most dysplastic lesions are visible,[6,7] the improved visualization and lack of negative effects with high-definition endoscopy justified a strong recommendation for its use. In addition, patients likely would strongly desire high-definition colonoscopy because of the belief that visualization and examination are improved. The cost of purchasing new high-definition endoscopic equipment is a consideration. However, high-definition colonoscopy already is widely used in endoscopic units.

Statement 2: When performing surveillance with standard-definition colonoscopy, chromoendoscopy is recommended rather than white-light colonoscopy.

(85% agreement; strong recommendation; moderate-quality evidence)

Summary of evidence and discussion. Chromoendoscopy involves the application of dye to the colon mucosa, thereby providing contrast enhancement to improve visualization of epithelial surface detail. Methylene blue and indigo carmine, the agents most commonly used, are applied to the colon mucosa via a catheter or the colonoscope biopsy or water jet channel,[18] and accentuate the changes in epithelial surface topography.[19]

We identified 8 trials that used standard-definition colonoscopy and compared chromoendoscopy with white-light colonoscopy alone (Table 3).[20-27] The proportion of patients with dysplasia was 0% to 10% greater with chromoendoscopy in the individual studies, but the difference was not significant in any study. Meta-analysis revealed a significantly greater proportion of patients with dysplasia by using chromoendoscopy (relative risk [RR] = 1.8 [1.2-2.6] and absolute risk increase = 6% [3%-9%]). Meta-analysis of the 2 randomized, parallel-group trials also confirmed a significant increase with chromoendoscopy in the proportion of patients with dysplasia (RR = 2.3 [1.1-4.6], absolute increase = 8% [2%-15%]). The number of dysplastic lesions identified was greater with chromoendoscopy in all studies (Table 3), and in the 4 tandem studies in which all patients had both chromoendoscopy and white-light examination, the number of dysplastic areas discovered increased almost 2-fold (RR = 1.9, 1.4-2.7) with chromoendoscopy. Chromoendoscopy significantly increased the duration of colonoscopy by a mean of 11 minutes (range 9-12 minutes).

An economic analysis concluded that chromoendoscopy with targeted biopsies was less costly and more effective than white-light colonoscopy with random biopsies,[28] suggesting that chromoendoscopy should be used in place of white-light endoscopy when surveillance colonoscopy is performed. The cost-effectiveness of chromoendoscopy increased with increasing surveillance interval, suggesting that varying the surveillance interval based on the risk of CRC may be appropriate and could increase the cost effectiveness of surveillance colonoscopy. However, when surveillance is performed, even if performed less frequently than currently recommended in lower-risk patients, the best technique should be used.

Although chromoendoscopy increases the yield of dysplasia compared with standard-definition white-light colonoscopy, whether the additional lesions identified with chromoendoscopy are associated with the same increased risk for CRC as the visible and invisible dysplasia identified in older studies is not known. Data from the Surveillance, Epidemiology and End-Results Medicare-linked database of patients ≥67 years old revealed that interval cancers 6 to 36 months after colonoscopy occurred in a

TABLE 2. Summary of recommendations for surveillance and management of dysplasia in patients with inflammatory bowel disease

Detection of dysplasia on surveillance colonoscopy

1. When performing surveillance with white-light colonoscopy, high definition is recommended rather than standard definition (strong recommendation, low-quality evidence).
2. When performing surveillance with standard-definition colonoscopy, chromoendoscopy is recommended rather than white-light colonoscopy (strong recommendation, moderate-quality evidence).
3. When performing surveillance with high-definition colonoscopy, chromoendoscopy is suggested rather than white-light colonoscopy (conditional recommendation, low-quality evidence).
4. When performing surveillance with standard-definition colonoscopy, narrow-band imaging is not suggested in place of white-light colonoscopy (conditional recommendation, low-quality evidence).
5. When performing surveillance with high-definition colonoscopy, narrow-band imaging is not suggested in place of white-light colonoscopy (conditional recommendation, moderate-quality evidence).
6. When performing surveillance with image-enhanced high-definition colonoscopy, narrow-band imaging is not suggested in place of chromoendoscopy (conditional recommendation, moderate-quality evidence).

Management of dysplasia discovered on surveillance colonoscopy

7. After complete removal of endoscopically resectable polypoid dysplastic lesions, surveillance colonoscopy is recommended rather than colectomy (strong recommendation, very low-quality evidence).
8. After complete removal of endoscopically resectable nonpolypoid dysplastic lesions, surveillance colonoscopy is suggested rather than colectomy (conditional recommendation, very low-quality evidence).
9. For patients with endoscopically invisible dysplasia (confirmed by a GI pathologist) referral is suggested to an endoscopist with expertise in IBD surveillance using chromoendoscopy with high-definition colonoscopy (conditional recommendation, very low-quality evidence).

much higher proportion of patients with IBD (15.1% with Crohn's disease and 15.8% with ulcerative colitis) than patients without IBD (5.8%),[29] suggesting that clinically relevant areas of neoplasia may be missed with current colonoscopic surveillance.

Potential barriers to use of chromoendoscopy also were considered. These include the additional preparation and time required for chromoendoscopy, need to train endoscopists in this technique, need to develop quality measures and assess performance after training, procedure-related costs, and barriers to reimbursement (eg, lack of procedure code for chromoendoscopy in the United States). These issues were discussed in detail by a subgroup of the panel, and their report will appear in a separate publication.

Statement 3: When performing surveillance with high-definition colonoscopy, chromoendoscopy is suggested rather than white-light colonoscopy.

(84% agreement; conditional recommendation; low-quality evidence)

Summary of evidence and discussion. A prospective, tandem study that used high-definition colonoscopy in 75 patients with IBD found that dysplasia was identified in significantly more patients undergoing chromoendoscopy than white-light colonoscopy alone: 16 (21%) versus 7 (9%); $P = .007$.[30] Ten dysplastic lesions were identified on the initial white-light examination, and an additional 12 were discovered on the subsequent chromoendoscopic examination. Despite the significant difference in favor of chromoendoscopy, the strength of this recommendation is conditional because of its reliance on only one relatively small observational study whose primary aim was to assess chromoendoscopy training and performance.

Statement 4: When performing surveillance with standard-definition colonoscopy, narrow-band imaging (NBI) is not suggested in place of white-light colonoscopy.

(84% agreement; conditional recommendation; low-quality evidence)

Summary of evidence and discussion. Currently available endoscope-based image-enhancement technologies include NBI (Olympus, Tokyo, Japan), *i*-scan (Pentax, Tokyo, Japan), and Fuji Intelligent Chromo Endoscopy (Fujinon, Tokyo, Japan).[16] NBI, which uses filters to provide narrow bands of blue and green light wavelengths,[16] is the only one of these technologies that has been studied in IBD surveillance and thus the only one considered in this recommendation.

A randomized, crossover study of 42 patients found no significant difference between NBI and standard-definition white-light colonoscopy in the proportion of patients with dysplasia (8 [19%] vs 7 [17%]).[31] Fewer total lesions were found with NBI than with white-light colonoscopy (9 vs 12 lesions).

Given the absence of any evidence of a benefit, NBI cannot be suggested in place of standard-definition white-light colonoscopy alone. Furthermore, in the absence of evidence for *i*-scan or Fuji Intelligent Chromo Endoscopy, neither can be recommended for use in IBD surveillance.

Statement 5: When performing surveillance with high-definition colonoscopy, narrow-band imaging is not suggested in place of white-light colonoscopy.

(80% agreement; conditional recommendation; moderate-quality evidence)

Summary of evidence and discussion. Two studies comparing NBI to high-definition white-light colonoscopy were identified—a randomized, parallel-group trial in 112 patients and a randomized, crossover trial in 48 patients.[32,33]

TABLE 3. Proportion of patients with dysplasia and number of visible dysplastic lesions identified in studies comparing chromoendoscopy versus white-light colonoscopy

Study	Study type	Patients with dysplasia/all patients		RR (95% CI)	Absolute risk increase (95% CI)	No. of visible dysplastic lesions	
		Chromoendoscopy	White-light			Chromoendoscopy	White-light
Kiesslich[20]	Randomized parallel-group	13/84	6/81	2.1 (0.8-5.2)	8% (-2% to 18%)	32	10
Kiesslich[21]	Randomized parallel-group	11/80	4/73	2.5 (0.8-7.5)	8% (-1% to 17%)	19	2
Marion[24]	Prospective tandem	22/102	12/102	1.8 (0.96-3.5)	10% (0% to 20%)	35	13
Rutter[23]	Prospective tandem	7/100	2/100	3.5 (0.8-16.4)	5% (-1% to 11%)	9	2
Matsumoto[25]	Prospective tandem	12/57	12/57	1.0 (0.5-2.0)	0% (-2% to 2%)	18	8
Hlvaty[26]	Prospective tandem and additional cohort	4/30	2/45	3.0 (0.6-15.4)	9% (-5% to 23%)	6	2
Gunther[27]	Retrospective two-group	2/50	0/50	5.0 (0.3-101.6)	4% (-3% to 11%)	2	0
Chiorean[22]	Prospective tandem	No per-patient data given (N = 63)				41	18
SCENIC meta-analysis				1.8 (1.2-2.6)	6% (3%-9%)		

RR, Relative risk; *CI,* confidence interval; *SCENIC,* Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients: International Consensus Recommendations.

Neither study suggested a benefit for NBI, with the proportion of patients having dysplasia identified with NBI versus white-light colonoscopy of 5 of 56 (9%) versus 5 of 56 (9%) and 9 of 48 (19%) versus 13 of 48 (27%). In addition, NBI identified slightly fewer dysplastic lesions than white-light colonoscopy (5 vs 7 and 14 vs 16). Again, in the absence of any evidence of a benefit, NBI cannot be suggested in place of high-definition white-light colonoscopy alone.

Statement 6: When performing surveillance with image-enhanced high-definition colonoscopy, narrow-band imaging is not suggested in place of chromoendoscopy.

(90% agreement; conditional recommendation; moderate-quality evidence)

Summary of evidence and discussion. Four studies were identified comparing chromoendoscopy with NBI: two randomized, parallel-group trials; a randomized crossover trial; and a prospective, tandem study.[34-37] The proportion of patients with dysplasia was 0.1% to 22% greater with chromoendoscopy than with NBI in the individual studies, but none of the differences were significant. Meta-analysis also failed to show a significant difference: RR = 1.3 (0.8-2.1) and absolute risk difference = 6% (-1% to 14%). The mean withdrawal times were identical in one study,[36] whereas the mean procedure or withdrawal times in the other studies were 11 to 12 minutes longer with chromoendoscopy.

The results of the studies indicate that a meaningful benefit of NBI over chromoendoscopy is unlikely. Nonetheless, they do not document a benefit of chromoendoscopy over NBI.

Additional topics considered for detection of dysplasia

Random biopsies with high-definition white-light colonoscopy or chromoendoscopy. Given that high-definition white-light colonoscopy and chromoendoscopy were considered superior to standard-definition white-light colonoscopy, the panelists considered the question of whether random biopsies should be performed when endoscopists use high-definition white-light colonoscopy or chromoendoscopy. Table 4 shows the yield of targeted and random biopsies for dysplasia from pooled analyses; the evidence was graded as low quality.

Among patients with dysplasia undergoing high-definition white-light colonoscopy[17,30,32,33,36] or chromoendoscopy,[20-27,36,38] dysplasia is detected only on random biopsies in approximately 10% of patients and on targeted biopsies in the other 90%. About 1% to 1.5% of all patients undergoing surveillance would not have dysplasia detected if random biopsies were not performed. Only about one in a thousand random biopsies reveals dysplasia. Pooled results also were determined for detection of dysplasia by using standard-definition white-light colonoscopy.[6,17,20-27,31,33,39-41] The proportion of patients

TABLE 4. Pooled analyses of detection of dysplasia with targeted biopsies and with random biopsies alone in studies of high-definition white-light colonoscopy, chromoendoscopy, and standard-definition white-light colonoscopy

		High definition[17,30,32,33,36]	Chromoendoscopy [20-27,36,38]	Standard definition [6,17,20-27,31,33,39-41]
Proportion of all patients with IBD surveyed and found to have dysplasia by each modality	No. of studies (no. of patients)	4 (382)	7 (1289)	11 (1735)
	Identified on targeted biopsies	15.4% (9.3%-24.5%)*	12.4% (8.3%-18.3%)*	11.8% (8.6%-16.1%)*
	Identified on random biopsies only	1.6% (0.7%-3.6%)	1.2% (0.8%-2.0%)	2.6% (1.1%-6.0%)*
Proportion of patients with dysplasia identified by each modality	No. of studies (no. of patients)	4 (59)	7 (158)	12 (270)
	Identified on targeted biopsies	90.6% (80.1%-95.9%)	90.2% (85%-94%)	80.4% (85%-94%)*
	Identified on random biopsies only	9.4% (4.1%-19.9%)	9.8% (6%-15%)	19.6% (11.5%-31.2%)*
Proportion of all random biopsy specimens positive for dysplasia	No. of studies (no. of biopsies)	5 (8739)	11 (48,522)	11 (25,238)
	Proportion positive for dysplasia	0.2% (0.0%-1.2%)*	0.1% (0.0%-0.3%)*	0.1% (0.1%-0.3%)*

*Statistical heterogeneity with Cochran Q; $P \leq .02$ and I^2 statistic $\geq 65\%$.

with dysplasia identified only on random biopsies was approximately 20% with standard-definition colonoscopy.

Panelists did not reach consensus regarding random biopsies: 45% agreed and 30% disagreed with performing random biopsies when using high-definition white-light colonoscopy, whereas 25% agreed and 60% disagreed with performing random biopsies when using chromoendoscopy. Judgments varied regarding the importance of missing dysplasia in a small proportion of patients, and potential benefits of foregoing biopsies were considered, including a decrease in procedure time (which may offset some of the increased time required for chromoendoscopy) and a reduction in cost related to a decrease in the number of biopsy specimens submitted for histologic examination. Other recent guidelines suggest use of multiple random biopsies when using high-definition white-light colonoscopy but only targeted biopsies of visible lesions when using chromoendoscopy for detection of dysplasia.[2,8]

Other image-enhancement modalities. Autofluorescence, a technique that uses differences in emission spectra of neoplastic and nonneoplastic tissue after exposure of colon mucosa to short wavelength light,[42] has been studied in surveillance colonoscopy for patients with IBD. A tandem study found that a nonsignificantly higher proportion of patients had dysplasia detected with autofluorescence as compared with white-light colonoscopy (8/50 [16%] vs 2/50 [4%]; $P = .09$), and more dysplastic lesions were identified with autofluorescence (13 vs 3 lesions).[39] The evidence was graded low quality, and the statement "when performing surveillance with high-definition colonoscopy, autofluorescence imaging is preferred to white-light colonoscopy" was not endorsed.

Confocal laser endomicroscopy, a technique allowing real-time histologic examination of colon mucosa during endoscopy that has been studied in IBD surveillance,[21,27,42] was not included in the focused questions for guideline development because it cannot practically be used for primary examination of the entire surface area of the colon as required for IBD surveillance. Rather, its potential role would be in characterization of lesions identified during surveillance.

Management of dysplasia discovered on surveillance colonoscopy

The goal of this section is to define the optimal management of patients with IBD in whom dysplasia is identified on endoscopic surveillance. Management of endoscopically nonresectable visible lesions is not included, because such patients generally would undergo surgery.

Endoscopically resectable polypoid and nonpolypoid lesions are considered separately in these guidelines for several reasons. First, it is not clear that the risk of CRC is the same for polypoid and nonpolypoid dysplastic lesions in patients with IBD. Only recently, because of improvements in endoscopic imaging, have nonpolypoid lesions been identified regularly in patients with IBD. Consequently, little is known about the natural history of nonpolypoid lesions, although studies in patients without IBD suggest that the molecular biology of nonpolypoid

colorectal neoplasms may differ from that of polypoid colorectal neoplasms.[43] Second, the methods for endoscopic resection of polypoid and nonpolypoid lesions differ, with endoscopic resection of nonpolypoid lesions typically more difficult and often requiring advanced endoscopic skills that many endoscopists may lack. Third, confidence that the lesion has been completely removed may be lower for nonpolypoid than for polypoid lesions.

Statement 7: After complete removal of endoscopically resectable polypoid dysplastic lesions, surveillance colonoscopy is recommended rather than colectomy.

(100% agreement; strong recommendation; very low-quality evidence)

Summary of evidence and discussion. No study comparing surveillance colonoscopy and colectomy after endoscopic resection of dysplastic lesions was identified. However, 6 studies from the video-endoscopic era (1990 onward) were identified that reported CRC incidence after endoscopic removal of polypoid dysplastic lesions in >15 patients with IBD.[6,44-48] Among studies that reported the proportion of patients with low-grade versus high-grade dysplasia, most patients had low-grade dysplasia. Over mean follow-up periods of 36 to 82 months, the incidence of CRC in these studies was 19 of 311 (6%, range 2%-13%). A single study focused only on polypoid lesions with high-grade dysplasia[49] found that 0 of 9 patients followed for a mean of 76.5 months (range 52-99 months) after endoscopic resection developed CRC or flat dysplasia.

A recent systematic review of 10 studies, which followed 376 patients with IBD with resected polypoid dysplasia for a mean of 54 months, reported an annualized incidence for CRC of 0.5%.[50] The definition of an "acceptable" incidence of synchronous and metachronous CRC for physicians—and, more importantly, for patients—needs to be considered when determining management strategies.

The strength of this recommendation was considered strong despite the lack of evidence comparing the management strategies, largely based on views regarding patient preference. Stakeholders indicated that patients diagnosed with dysplasia were much more likely to refuse or delay colectomy and choose surveillance colonoscopy. They suggested that patients might accept colectomy at a later date, depending on results of subsequent surveillance procedures and further information and education about colectomy and CRC risk provided by physicians, nurses, other patients, and patient advocacy groups. These views were supported by a survey that assessed the management preferences of 199 patients with ulcerative colitis who were told that dysplasia was detected.[51] On average, patients would agree to immediate colectomy only when the risk of synchronous CRC rose to ≥73%.[51]

More intensive surveillance for patients with endoscopically resectable dysplasia than for those without dysplasia seems reasonable, and subsequent surveillance may vary based on the size and appearance of the dysplastic lesion. For example, current multi-society guidelines on colorectal polyps in patients without IBD suggest a short interval of < 1 year for flat and sessile adenomatous and serrated polyps >15 mm that are removed by using injection-assisted polypectomy and piecemeal resection if there is any question about completeness of resection.[52] Thus, patients with IBD who have larger sessile lesions removed in piecemeal fashion or via endoscopic mucosal resection or endoscopic submucosal dissection probably should return at approximately 3 to 6 months, with longer subsequent intervals (eg, yearly) if the initial repeat colonoscopy result is negative. Patients with smaller polypoid lesions resected en bloc may return at 1-year intervals.

Statement 8: After complete removal of endoscopically resectable nonpolypoid dysplastic lesions, surveillance colonoscopy is suggested rather than colectomy.

(80% agreement; conditional recommendation; very low-quality evidence)

Summary of evidence and discussion. No study comparing surveillance colonoscopy to colectomy or providing the natural history for nonpolypoid dysplastic lesions after endoscopic resection was identified.

Analogous to the polypoid lesion discussed previously, if a nonpolypoid lesion is removed completely at endoscopy, it is acceptable to follow the patient with regular surveillance colonoscopy, because most dysplasia is visible, and careful follow-up with high-definition chromoendoscopy likely would identify new or recurrent dysplastic lesions. Nonetheless, this recommendation is conditional, given the possibility that nonpolypoid lesions could confer a higher CRC risk and the greater endoscopic difficulty in assuring complete removal of these lesions. In addition, because many of the larger nonpolypoid lesions must be removed with endoscopic mucosal resection or endoscopic submucosal dissection and/or in piecemeal fashion, patients with such lesions should undergo initial follow-up surveillance colonoscopy in approximately 3 to 6 months as outlined previously for larger sessile polypoid lesions.

In contrast to the recommendation from this and other publications,[10] some recent guidelines have suggested colectomy for nonpolypoid dysplastic lesions because they considered such lesions generally not amenable to endoscopic resection.[2,8] However, variation in terminology for dysplastic lesions across publications makes comparisons difficult.

Statement 9: For patients with endoscopically-invisible dysplasia (confirmed by a GI pathologist) referral is suggested to an endoscopist with expertise in IBD surveillance using chromoendoscopy with high-definition colonoscopy.

(100% agreement; conditional recommendation; very-low-quality evidence)

Summary of evidence and discussion. No study comparing surveillance colonoscopy and colectomy for endoscopically invisible dysplasia was identified. However, 4 studies from the video-endoscopic era reported CRC incidence

after invisible dysplasia was diagnosed in >15 patients with IBD.[45,48,53,54] Over a mean follow-up of 15 to 50 months, CRC developed in 7 of 122 patients (6%, range 3%-9%).

The proportion of patients with synchronous CRC at the time invisible dysplasia is detected also is important when considering management strategies. A systematic review[55] of 20 surveillance studies and 477 patients with invisible low-grade dysplasia (which included patients from before the video-endoscope era) found that 18 of 81 patients (22%) with invisible low-grade dysplasia who had colectomy had CRC. It is uncertain what characteristics led the minority of patients with low-grade dysplasia to undergo colectomy—other unknown or unreported factors that increase the risk of CRC may have been present in some of these patients.

Colectomy has been performed more commonly when invisible high-grade dysplasia is discovered because of the reported higher risk of CRC. A 1994 systematic review found that 10 of 24 patients (42%) with non-DALM high-grade dysplasia had CRC on colectomy, whereas 15 of 47 patients (32%) who had high-grade dysplasia on subsequent surveillance examinations developed CRC.[5] Other individual studies of patients with invisible high-grade dysplasia undergoing colectomy reported since 1994 show rates of CRC ranging from 45% to 67%.[56-59]

The findings reported in older studies may be of limited relevance in the current video-endoscopic era. A 1994 review of 10 prospective studies with 1225 patients undergoing surveillance colonoscopy found that dysplasia that is not associated with a lesion accounted for 272 of 312 patients (87%) found to have dysplasia.[5] In contrast, more recent studies of chromoendoscopy or high-definition white-light colonoscopy report that invisible dysplasia accounts for about 10% of patients with dysplasia (Table 4). Thus, random biopsy specimens showing invisible dysplasia in older studies may have been taken from previously unrecognizable lesions that can now be visualized with modern endoscopic techniques.

Based on this information, general statements that the initial management step for patients with invisible low-grade or high-grade dysplasia be surveillance colonoscopy or colectomy[2,8] were not endorsed. Rather, referral to an endoscopist with expertise in IBD surveillance and image-enhanced examination using chromoendoscopy with high-definition endoscopy was considered an appropriate next step to better inform subsequent decisions regarding surveillance colonoscopy versus colectomy. If a visible dysplastic lesion is identified in the same region of the colon as the invisible dysplasia, and the lesion can be resected endoscopically, then such patients may remain in a surveillance program, as recommended previously in statements 7 and 8. Alternatively, if dysplasia is not discovered, management of such patients would be individualized after discussion of the risks and benefits of surveillance colonoscopy and colectomy. Continued intensive surveillance is an acceptable strategy if, after careful discussion, patients prefer this course.

Histologic distinctions may play a role in management decisions for patients with invisible dysplasia and no visible lesions on follow-up chromoendoscopy. Physicians may be comfortable having patients with invisible low-grade dysplasia remain in intensive surveillance while more strongly suggesting colectomy for those with invisible high-grade dysplasia. In addition, some physicians believe that multifocal invisible low-grade dysplasia is associated with higher CRC risk than unifocal low-grade dysplasia, leading to a greater likelihood of recommending colectomy, although a single study assessing this issue[54] failed to show an increased risk.

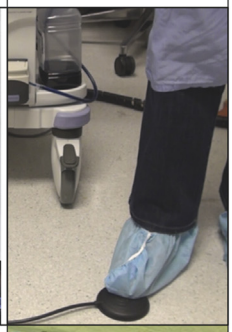
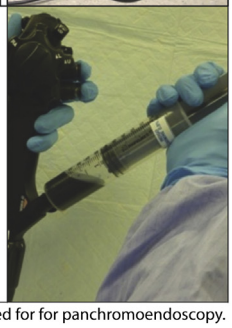
Confirmation of dysplasia by a pathologist with expertise in IBD is suggested before making management decisions. Even expert GI pathologists show no better than fair or moderate interobserver agreement on the histologic diagnosis of dysplasia, low-grade dysplasia, or high-grade dysplasia.[60-62] Diagnosis of low-grade dysplasia in Barrett's esophagus by one pathologist does not predict progression to high-grade dysplasia or cancer, but agreement among 2 or 3 pathologists significantly increases the risk of progression.[63] Similar studies are not available for IBD, but confirmation of dysplasia by a second pathologist seems appropriate before embarking on major diagnostic and therapeutic interventions.

IMPLEMENTATION OF HIGH-QUALITY ENDOSCOPIC SURVEILLANCE

Widespread implementation of high-quality endoscopic surveillance in patients with IBD will require a variety of initiatives, which will be discussed in a separate publication. Resources will be needed to train endoscopists in endoscopic surveillance and recognition of visible dysplasia with both white-light endoscopy and chromoendoscopy. These may include training courses, photographic atlases,[64-66] and video repositories.[67] Quality metrics and methods to document acceptable performance quality also should be developed. In addition, techniques such as chromoendoscopy should be standardized to allow implementation in endoscopy units, and endoscopic resection techniques for nonpolypoid lesions should be taught and disseminated.[68-70] Development of a procedure code for chromoendoscopy and reimbursement for the increased time and intensity required for chromoendoscopy would increase implementation, at least in the United States.

Performance of chromoendoscopy for surveillance of patients with IBD

Description of the technique. Surveillance colonoscopy should be performed when the disease is in remission in order to minimize potential misdiagnosis between inflammatory changes and dysplasia.[18,71,72] Clean bowel preparation is a prerequisite—the entire mucosa should be free from pus, mucus, blood, or stool. Small amounts

Purpose	Technique	Method	Dilution*	Color	
Lesion detection	Pan chromo-endoscopy	Water jet channel using auxillary foot pump or biopsy channel using spray catheter	Indigo carmine (0.8%, 5ml ampule): 2 ampules + 250ml water (0.03%) Methylene blue (1%,10ml ampule): 1 ampule + 240ml water (0.04%)		
Lesion characterization and delineation of borders	Targeted chromo-endoscopy	Syringe spray through biopsy channel	Indigo carmine (0.8%, 5ml ampule): 1 ampule + 25ml water (0.13%) Methylene blue (1%,10ml ampule): 1 ampule + 40ml water (0.2%)		

*Various dilutions ranging from 0.03-0.2% of indigo carmine and methylene blue have been reported for for panchromoendoscopy.

Figure 2. Chromoendoscopy technique.

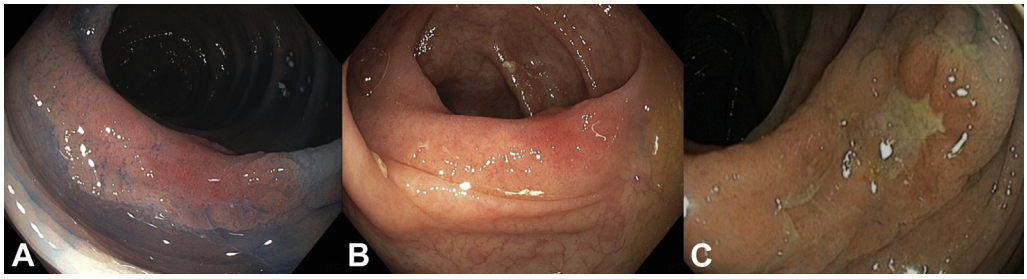


Figure 3. A, 3-cm, nonpolypoid, superficial, elevated lesion after indigo carmine chromoendoscopy. **B,** The area of the lesion before dye spray. **C,** The same lesion had likely been photographed approximately a year earlier (on fold to left of ulcer), but it was not recognized to be dysplastic. Histologic examination showed low-grade dysplasia.

of debris or fluid are washed and suctioned during insertion. Once the cecum is reached and the mucosa is cleaned, the application of either diluted indigo carmine or methylene blue dyes is initiated. We spray a total of approximately 250 mL of diluted dye (indigo carmine 0.03% to 0.1% or methylene blue 0.04 to 0.1%) circumferentially throughout the colon either through the water jet channel by using a pump or through the biopsy channel by using a spray catheter (Fig. 2). Efficient spraying of the dye through the water jet channel is typically performed by directing the stream of dye to the antigravity side of the colon.[18] When a spray catheter is used, the spray catheter is inserted through the biopsy channel until its tip protrudes 2 to 3 cm, and dye is sprayed throughout the mucosa while the colonoscope is being withdrawn.[71]

During inspection, by using the pan-chromoendoscopy technique, the endoscopist looks for areas that appear to be different from the surrounding background in color, pattern, or level. Nonpolypoid lesions may appear discolored (uneven redness), nodular or villous, slightly elevated or depressed, friable, or have an obscure vascular pattern. Polypoid lesions are easier to detect, but the dye can help delineate the lesion's border. Once a suspicious lesion is identified, we selectively spray approximately 30 mL of a more concentrated dye (indigo carmine 0.13% or methylene blue 0.2%) directly from a 60-mL syringe through the biopsy channel. With targeted chromoendoscopy, the darker blue dye can be helpful to further enhance the border and surface topography of a lesion (Fig. 3).[18] These areas should be photographed. Endoscopically resectable suspicious lesions may be removed by using polypectomy or endoscopic mucosal resection. Biopsy specimens are taken from lesions that are deemed to be unresectable. A biopsy specimen is taken from the flat area surrounding the lesion to detect dysplasia. A tattoo may be

TABLE 5. Suggested steps for implementation of chromoendoscopy into endoscopic practice

Equipment	
Colonoscope	High-definition colonoscope, monitor, and cables
Accessories	Apply dye via: Water jet channel by using water pump attached to the endoscope activated via foot pedal or Spray catheter: length 240 cm, endoscope accessory channel 2.8 mm
Contrast agent	Indigo carmine, 5-mL ampule (0.8%) Methylene blue, 10-mL ampule (1%)
Procedure and protocol	
Time allotment	Consider doubling colonoscopy time slot initially during the learning curve period.
Standard operating procedure	Complete colonoscopy to cecum. Lavage with water and suction during intubation.
	Prepare dye solution during insertion for application via the foot pump or spray. Indigo carmine (0.03%): mix 2 5-mL ampules of 0.8% indigo carmine with 250 mL water. Methylene blue (0.04%): mix one 10-mL ampule of 1% methylene blue with 240 mL water.
	If using a foot pump: once the cecum is intubated, the water irrigation can be exchanged with the contrast solution. Apply the dye solution in a circumferential technique while withdrawing the colonoscope. Direct spray to the anti-gravity side.
	If using a spray catheter: the dye spray catheter is inserted into the biopsy channel; the catheter tip should protrude 2-3 cm from the endoscope. Apply dye solution segmentally by using a rotational technique while withdrawing the colonoscope to cover the surface mucosa with dye.
	Suction any excess solution after approximately 1 minute to aid mucosal visualization.
	Focus on 20-30–cm segments sequentially with reinsertion of the endoscope to the proximal extent of each segment before slow withdrawal and mucosal visualization.
	Targeted dye spray for suspicious lesions: Prepare more concentrated dye solution for application. Indigo carmine (0.13%): mix one 5-mL ampule of 0.8% indigo carmine with 25 mL water. Methylene blue (0.2%): mix one 10-mL ampule of 1% methylene blue with 40 mL water. Spray about 30 mL directly from a 60-mL syringe through the biopsy channel.
	Remove endoscopically resectable suspicious lesions by using polypectomy or endoscopic mucosal resection.
	Do targeted biopsies of any unresectable abnormality visualized through chromoendoscopy to diagnose dysplasia.
	Do biopsies of flat area surrounding lesions to assess for dysplasia.
	Consider tattoo of suspicious dysplastic lesions arising from flat mucosa or not amenable to complete removal.
	Recommendations regarding the need to perform random, non-targeted biopsies for detection of dysplasia vary.
	If biopsies for dysplasia are not done, 2 random biopsies in every bowel segment are commonly recommended to document microscopic disease activity.

necessary to mark the location of resection or suspicious lesion. Biopsies to document disease activity may be performed during the procedure.

Available resources for self-learning. Descriptions of a systematic approach to performance of pancolonic chromoendoscopy by using either indigo carmine or methylene blue dyes with targeted biopsy for surveillance of patients with IBD are available.[18,71] In addition, endoscopic videos,[18,67] atlases,[64-66] and books[73,74] have been published recently to provide readers with information on the techniques and findings related to endoscopy in IBD. Open access of several of the materials serves to facilitate learning (http://www.youtube.com/watch?v=OARkbgwlObI, http://www.giendo.theclinics.com/issues/?elsca1=etoc&elsca2=email&elsca3=1052-5157_201407_24_3&elsca4=gastroenterology&issue_key=S1052-5157%2814%29X0003-6). Key steps for the implementation of chromoendoscopy technique into endoscopic practice are provided in Table 5.

FUTURE RESEARCH

The evidence currently available to inform decisions on appropriate colonoscopic surveillance methods to detect and manage dysplasia in patients with IBD is limited. Thus, further research would be of value for most of the issues addressed in this guideline. Suggested research includes the following: larger trials of chromoendoscopy using high-definition colonoscopy, comparison of different chromoendoscopy techniques (eg, indigo carmine vs methylene blue, concentration of dye, delivery of dye via spray catheter vs endoscopy water jet channel), a registry of endoscopists performing chromoendoscopy to

determine detection rates and learning curves, evaluation of new generations of equipment-based modalities, determination of appropriate surveillance intervals with high-definition chromoendoscopy, the natural history of visible dysplastic lesions after endoscopic resection (especially nonpolypoid lesions), and the natural history of patients with endoscopically invisible dysplasia, even after expert chromoendoscopy.

DISCLOSURE

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*Abbreviations: CRC, colorectal cancer; IBD, inflammatory bowel disease; NBI, narrow-band imaging; SCENIC, **S**urveillance for **C**olorectal **E**ndoscopic **N**eoplasia Detection and Management in Inflammatory Bowel Disease Patients: **I**nternational **C**onsensus Recommendations.*

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Loren Laine, MD[1,2]
Tonya Kaltenbach, MD[3]
Alan Barkun, MD[4]
Kenneth R. McQuaid, MD[5]
Venkataraman Subramanian, MD[6]
Roy Soetikno, MD[3]
for the SCENIC Guideline Development Panel

Current affiliations: Section of Digestive Diseases, Yale School of Medicine, New Haven, Connecticut (1), Veterans Affairs Connecticut Healthcare System, West Haven, Connecticut (2), Veterans Affairs Palo Alto Healthcare System and Stanford University School of Medicine (affiliate), Palo Alto, California (3), Division of Gastroenterology, McGill University, Montreal, Quebec, Canada (4), University of California at San Francisco, Veterans Affairs Medical Center, San Francisco, California (5), University of Leeds, Leeds, United Kingdom (6).

Reprint requests: Loren Laine, MD, Section of Digestive Diseases, Yale School of Medicine, PO Box 208019, New Haven, CT 06520.

Additional SCENIC (Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients: International Consensus Recommendations) Development Panel Members: James E. East, BSc, MBChB, MD (Res), FRCP (John Radcliffe Hospital, University of Oxford, Oxford, United Kingdom) Francis A. Farraye, MD, MSc (Boston University, Boston, Massachusetts, United States) Brian Feagan, MD, MSc (Roberts Research Institute, University of Western Ontario, Canada) John Ioannidis, MD, DSc (Stanford University, Palo Alto, California, United States) Ralf Kiesslich, MD, PhD (Johannes Gutenberg University, Mainz, Germany) Michael Krier, MD (Brooke Army Medical Center/San Antonio Military Medical Center, San Antonio, Texas, United States) Takayuki Matsumoto, MD (Iwate Medical University, Morioka, Japan) Robert P. McCabe, MD (Minnesota Gastroenterology, Minneapolis, Minnesota, United States) Klaus Mönkemüller, MD, PhD (University of Alabama, Birmingham, Alabama, United States) Robert Odze, MD (Brigham & Women's, Boston, Massachusetts, United States) Michael Picco, MD, PhD (Mayo Clinic, Jacksonville, Florida, United States) David T. Rubin, MD (University of Chicago Medicine, Chicago, Illinois, United States) Michele Rubin, RN (Society of Gastroenterology Nurses and Associates, University of Chicago Medicine, Chicago, Illinois, United States) Carlos A. Rubio, MD, PhD (Karolinska Institute and University Hospital, Stockholm, Sweden) Matthew D. Rutter, MBBS, MD, FRCP (University Hospital of North Tees, Teesside, United Kingdom) Andres Sanchez-Yague, MD (Hospital Costa del Sol, Marbella, Spain) Silvia Sanduleanu, MD, PhD (University of Maastricht, Maastricht, Netherlands) Amandeep Shergill, MD (Veterans Affairs San Francisco; University of California, San Francisco; San Francisco California, United States) Thomas Ullman, MD (Mount Sinai, New York, New York, United States) Fernando Velayos, MD (University of California, San Francisco; San Francisco, California, United States) Douglas Yakich (Crohn's and Colitis Foundation of America) Yu-Xiao Yang, MD, MSCE (University of Pennsylvania, Philadelphia, Pennsylvania, United States)

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The SCENIC international consensus statement also was reviewed and endorsed by the Asian Pacific Association of Gastroenterology, British Society of Gastroenterology, Canadian Association of Gastroenterology, European Society of Gastrointestinal Endoscopy, and Japan Gastroenterological Endoscopy Society.

APPENDIX 1. PARTICIPANTS, AFFILIATIONS, ROLES/AREAS OF FOCUS, AND POTENTIAL CONFLICTS

Participant affiliations and roles/areas of focus

Voting chair and co-chair: Loren Laine, United States, and Alan Barkun, Canada

Voting executive committee members:

Loren Laine, Yale School of Medicine, New Haven, CT and Veterans Affairs Connecticut Healthcare System, West Haven, CT, United States. Methodology (guidelines, systematic reviews), general gastroenterology

Alan Barkun, McGill University, Montreal, Quebec, Canada. Methodology (guidelines, systematic reviews), general gastroenterology

Tonya Kaltenbach, Veterans Affairs Palo Alto Health Care System, Stanford University School of Medicine (affiliate), Palo Alto, CA, United States. Methodology (systematic reviews), endoscopic imaging and resection

Kenneth R. McQuaid, Veterans Affairs San Francisco, University of California San Francisco, San Francisco, CA, United States. Inflammatory bowel disease (IBD)

Nonvoting executive committee members:

Roy Soetikno, Veterans Affairs Palo Alto Health Care System, Stanford University School of Medicine (affiliate), Palo Alto, CA, United States. IBD (endoscopy imaging and resection)

Voting participants:

James E. East, John Radcliffe Hospital, University of Oxford, Oxford, United Kingdom. IBD endoscopy imaging and resection

Francis A. Farraye, Boston University, Boston, MA, United States, IBD

Brian Feagan, Roberts Research Institute, University of Western Ontario, Canada. IBD

John Ioannidis, Stanford University, Palo Alto, CA, United States. Methodology (systematic review), internal medicine

Michael Krier, Brooke Army Medical Center/San Antonio Military Medical Center, San Antonio, TX, United States. General gastroenterology (military medicine)

Takayuki Matsumoto, Iwate Medical University, Morioka, Japan. IBD endoscopy imaging and resection

Robert P. McCabe, Minnesota Gastroenterology, Minneapolis, MN, United States. IBD and general gastroenterology (community practice)

Fabrizio Michelassi, Cornell Medical Center, New York, NY, United States. Colorectal surgeon (first vote only; scheduling conflicts prevented subsequent participation)

Klaus Mönkemüller, University of Alabama, Birmingham, AL, United States. IBD endoscopy imaging and resection

Robert Odze, Brigham & Women's, Boston, MA, United States. GI pathologist

David T. Rubin, University of Chicago Medicine, Chicago, IL, United States. IBD

Michele Rubin, Society of Gastroenterology Nurses and Associates, University of Chicago Medicine, Chicago, IL, United States. Advance practice GI nurse

Carlos A. Rubio, Karolinska Institute and University Hospital, Stockholm, Sweden. GI pathologist

Mathew D. Rutter, University Hospital of North Tees, Teesside, United Kingdom. IBD endoscopy imaging

Thomas Ullman, Mount Sinai, New York, NY, United States. IBD

Douglas Yakich, Los Angeles, CA, United States. Patient representation, Crohn's and Colitis Foundation of America

Yu-Xiao Yang, University of Pennsylvania, Philadelphia, PA, United States. Methodology (epidemiology, guidelines)

Nonvoting participants:

Ralf Kiesslich, Johannes Gutenberg University, Mainz, Germany. IBD endoscopy imaging and resection

Michael Picco, Mayo Clinic, Jacksonville, FL, United States. IBD, education/training/implementation

Andres Sanchez-Yague, Hospital Costa del Sol, Marbella, Spain. Guideline dissemination, endoscopy imaging and resection

Silvia Sanduleanu, University of Maastricht, Maastricht, Netherlands. education/training/implementation, endoscopy imaging

Amandeep Shergill, Veterans Affairs San Francisco; University of California, San Francisco; San Francisco CA, United States. Guideline dissemination

Venkataraman Subramanian, University of Leeds, Leeds, United Kingdom. Methodology (systematic review), endoscopic imaging

Fernando Velayos, University of California, San Francisco; San Francisco, CA, United States. IBD

Nonvoting ethics expert: Derek J. Jones, Montreal, Quebec, Canada, and Yidan Lu, McGill University, Montreal, Canada.

Nonvoting scribe: Sarah K. McGill, Veterans Affairs Palo Alto Health Care System, Stanford University School of Medicine, Palo Alto, CA, United States.

Participants potential conflicts:

Declaration of personal interests:

The following is a summary of the financial disclosure provided by the following participants: Alan Barkun (AB), James E. East (JE), Francis A. Farraye (FF), Brian Feagan (BF), John Ioannidis (JI), Tonya Kaltenbach (TK), Ralf Kiesslich (RK), Michael Krier (MK), Loren Laine (LL), Takayuki Matsumoto (TM), Robert P. McCabe (RM), Kenneth R. McQuaid (KMc), Fabrizio Michelassi (FM), Klaus Mönkemüller (KM), Robert Odze (RO), Michael Picco (MP), David T. Rubin (DR), Michele Rubin (MR), Carlos A. Rubio (CR), Matt D. Rutter (MRu), Andres Sanchez-Yague (AS-Y), Silvia Sanduleanu (SS), Amandeep Shergill (ASh), Roy Soetikno (RS), Venkataraman Subramanian (VS), Thomas Ullman (TU), Fernando Velayos (FV), Douglas Yakich (DY), Yu-Xiao Yang (Y-XY).

No significant financial interest to report:

JI, RK, MK, LL, TM, RM, KMc, FM, RO, MP, MR, CR, AS-Y, SS, ASh, VS, FV, DY, Y-XY.

Yes, a significant financial interest as follows:

Advisory Board: Abbvie (JE, BF), Amgen (BF), AstraZeneca (BF), Avaxia Biologics (BF), Braintree (FF), Bristol Myers Squibb (BF), Celgene (BF), Centocor (BF), Cosmo Pharmaceuticals (JE), Elan/Biogen (BF), Entera Health (FF), Ferring (BF), Genentech (TU), Janssen (FF, BF), Merck (BF), Novartis (BF), NovoNordisk (BF), Olympus (AB), Pendopharm (AB), Pfizer (BF), Prometheus (BF), Salix Pharmaceuticals (FF, BF), Takeda (BF), Teva Pharmaceuticals (BF), Tillotts Pharmaceuticals (BF), UCB Pharmaceuticals (BF).

Honorarium: Abbvie (JE, BF), Actogenix (BF), Albireo Pharmaceuticals (BF), Amgen (BF), AstraZeneca (AB, BF), Avaxia Biologics (BF), Axcan (BF), Baxter (BF), Boehringer-Ingelheim (BF), Boston Scientific (AB), Bristol Myers Squibb (BF), Calypso Biotech (BF), CDX (TU), Celgene (BF), Centocor (BF), Cook (AB, KM), Cosmo Pharmaceuticals (JE), Elan/Biogen (BF),EnGene (BF), Ferring (BF), Genentech (TU), GiCare Pharmaceuticals (BF), Gilead (BF), Given Imaging (BF), GSK (BF), Ironwood Pharmaceuticals (BF), Janssen Biotech (Centocor) (BF), Janssen (TU, BF), Kyowa Kakko Kirin (BF), Lexicon (BF), Lilly (BF), Merck (BF), Millennium (BF), Nektar (BF), Novartis (BF), NovoNordisk (BF), Olympus, (AB, MRu), Ovesco (KM), Pendopharm (AB), Prometheus Laboratories (BF), Prometheus Therapeutics and Diagnostics (BF), Pfizer (BF, TU), Receptos (BF), Roche/Genentech (BF), Salix Pharmaceuticals (BF), Serono (BF), Shire (BF), Sigmoid Pharmaceuticals (BF), Synergy Pharmaceuticals (BF), Takeda (AB, BF), Teva Pharmaceuticals (BF), Tillotts Pharmaceuticals (BF), UCB Pharmaceuticals (BF), Vertex Pharmaceuticals (BF), Warner-Chilcott (BF), Wyeth (BF), Zealand (BF), Zyngenia (BF).

Research Support: Abbott (BF), Abbvie (BF, DR), Amgen (BF), AstraZeneca (BF), Boston Scientific (AB), Bristol Myers Squibb (BF), Cook (AB), Cosmo Pharmaceuticals (JE), Cubist (FF), Elan Pharmaceuticals (DR), Genentech (BF, TU), Janssen Biotech (Centocor) (BF), Janssen (BF), Millennium (BF), Olympus (JE, RS, TK), Pfizer (BF), Prometheus Pharmaceuticals (FF, DR), Receptos (BF), Santarus (BF), Sanofi (BF), Shire (DR), Tillotts (BF), UCB Pharmaceuticals (BF), Warner Chilcott (DR).

Speaker's Bureau: Abbvie (JE, BF), AstraZeneca (AB), Cook (AB, KM), Cosmo Pharmaceuticals (JE), Janssen (BF, TU), Ovesco (KM), Olympus (RS, MRu), Pendopharm (AB), Takeda (AB, BF), UCB Pharmaceuticals (BF), Warner-Chilcott (BF).

Consultant: Abbvie (BF, DR), Actogenix (BF), Albireo Pharmaceuticals (BF), Amgen (BF), AstraZeneca (BF), Avaxia Biologics (BF), Axcan (BF), Baxter (BF), Boehringer-Ingelheim (BF), Bristol Myers Squibb (BF, DR), Calypso Biotech (BF), CDX (TU), Celgene (BF), Cook (AB), Elan/Biogen (BF, DR), EnGene (BF), Emmi (DR), Ferring (BF), Genentech (BF, TU), GiCare Pharmaceuticals (BF), Gilead (BF), Given Imaging (BF, DR), GSK (BF), Ironwood Pharmaceuticals (BF, DR), Janssen Biotech (Centocor) (FF, BF, DR, TU), Janssen (BF), Kyowa Kakko Kirin (BF), Lexicon (BF), Lifecore Biomedical (DR), Lilly (BF), Merck (BF), Nektar (BF), NovoNordisk (BF), Olympus (TK), Olympus (RS), Pfizer (BF, TU), Prometheus Pharmaceuticals (DR), Prometheus Therapeutics and Diagnostics (BF), Receptos (BF), Roche/Genentech (BF), Salix Pharmaceuticals (BF), Santarus (FF, DR), Serono (BF), Shire (BF), Sigmoid Pharmaceuticals (BF), Synergy Pharmaceuticals (BF), Takeda (BF), Teva Pharmaceuticals (BF), Tillotts (BF), Takeda-Millennium (BF, DR), Telsar Pharmaceuticals (DR), UCB Pharmaceuticals (BF, DR), Vertex Pharmaceuticals (BF, DR), Warner-Chilcott (BF), Wyeth (BF), Zealand (BF), Zyngenia (BF).

Investor: Genentech (TU)

Equipment loan: Olympus (JE), Pentax (JE).

Other:

Celgene (FF) Data Safety Monitoring Committee

Cornerstones Health, Inc (DR) Co-founder, non-profit medical education entity

Genentech (TU) investigator

Identified potential companies with interests:

1. When performing surveillance with white-light colonoscopy, high definition is recommended rather than standard definition.

EndoChoice, Fujifilm, Fujinon, Olympus, Pentax

2. When performing surveillance with standard-definition colonoscopy, chromoendoscopy is recommended rather than white-light colonoscopy.

EndoChoice, Fujifilm, Fujinon, Mauna Kea Technology—Cellvizio, Medivator, Olympus, Pentax, Akorn, Amend Chemical Company, American Regent, Baker JT, Lex Pharmaceuticals, Medsica, Professional Compounding Centers, Akorn, Amend Chemical Company, American Regent, Baker JT, Lex Pharmaceuticals, Medsica, Professional Compounding Centers

3. When performing surveillance with high-definition colonoscopy, chromoendoscopy is suggested rather than white-light colonoscopy.

EndoChoice, Fujifilm, Fujinon, Mauna Kea Technology—Cellvizio, Medivator, Olympus, Pentax, Akorn, Amend Chemical Company, American Regent, Baker JT, Lex Pharmaceuticals, Medsica, Professional Compounding Centers, Akorn, Amend Chemical Company, American Regent, Baker JT, Lex Pharmaceuticals, Medsica, Professional Compounding Centers

4. When performing surveillance with standard-definition colonoscopy, narrow band imaging is not suggested in place of white-light colonoscopy.

EndoChoice, Fujifilm, Fujinon, Mauna Kea Technology—Cellvizio, Olympus, Pentax

5. When performing surveillance with high-definition colonoscopy, narrow-band imaging is not suggested in place of white-light colonoscopy.

EndoChoice, Fujifilm, Fujinon, Mauna Kea Technology—Cellvizio, Olympus, Pentax

6. When performing surveillance with image-enhanced high-definition colonoscopy, narrow-band imaging is not suggested in place of chromoendoscopy.

EndoChoice, Fujifilm, Fujinon, Mauna Kea Technology—Cellvizio, Olympus, Pentax

7. After complete removal of endoscopically-resectable polypoid dysplastic lesions, surveillance colonoscopy is recommended rather than colectomy.

Boston Scientific, Conmed, Cook, Covidien, EndoChoice, Erbe, Johnson and Johnson, LifeCore Biomedical, Medivators, Fuji, Olympus, Pentax, Seikakagu Co, TOP, US Endoscopy, Valley Lab

8. After removal of endoscopically-resectable nonpolypoid dysplastic lesions, surveillance colonoscopy is preferred to colectomy.

Boston Scientific, Conmed, Cook, Covidien, EndoChoice, Erbe, Johnson and Johnson, LifeCore Biomedical, Medivators, Fuji, Olympus, Pentax, Seikakagu Co, TOP, US Endoscopy, Valley Lab

9. For patients with endoscopically-invisible dysplasia (confirmed by a GI pathologist) referral is suggested to an endoscopist with expertise in IBD surveillance using chromoendoscopy with high-definition colonoscopy.

Boston Scientific, Conmed, Cook, Covidien, EndoChoice, Erbe, Johnson and Johnson, LifeCore Biomedical, Medivators, Fuji, Olympus, Pentax, Seikakagu Co, TOP, US Endoscopy, Valley Lab

APPENDIX 2. DEVELOPMENT PROCESS

Development panel

A 5-member executive committee of content experts, general gastroenterologists, and methodologists oversaw the development process. The executive committee selected a multidisciplinary panel to represent a wide spectrum of stakeholders in the diagnosis and management of dysplasia in patients with inflammatory bowel disease (IBD) and to provide international viewpoints. This 21-member panel included IBD experts, general gastroenterologists, advanced endoscopists, methodologists, pathologists, a surgeon, an advanced practice IBD nurse, and a patient representative from an IBD non-profit organization. We emphasized representation from a wide spectrum of stakeholders and attitudes toward the detection and management of dysplasia in IBD. An additional 8 non-voting physicians, chosen for their expertise in areas such as endoscopic techniques or guideline dissemination/implementation, attended the meeting to provide information as requested by voting panelists. The list of participants is provided in Appendix 1.

Formulation of focused clinical questions

The participants formulated clinically pertinent focused statements related to the detection and management of dysplasia in IBD and framed each statement in terms of population, intervention, comparator, and outcome (PICO).

Systematic literature search and meta-analyses

A systematic literature search of multiple bibliographic databases (EMBASE 1980 to 2013 Week 38; Cochrane Central Register of Controlled Trials 1898 to August 2013; Ovid MEDLINE, 1946 to present, in-process and other non-indexed citations, and daily update September 24, 2013) was performed for each focused statement by the Cochrane Upper Gastrointestinal Pancreatic Diseases Review Group. Additional searches from major gastroenterology scientific meetings (eg, Digestive Disease Week, American College of Gastroenterology, United European Gastroenterology Week) for 2009-2013 and of reference lists from selected articles were also performed (Figure). The search strategy keywords were framed for the PICO-formatted focused clinical statements (Appendix 3). The search was limited to human studies without any language restriction. Two reviewers (T.K., V.S.) performed the initial title and abstract review, review of full-text articles for inclusion, and data extraction independently. Following full text review and article selection, a third person (L.L.) adjudicated any discrepancies.

By using pre-specified criteria, we excluded abstracts/articles when (1) the population did not include colonic inflammatory bowel disease; (2) the intervention or comparator did not include sigmoidoscopy or colonoscopy for the detection, diagnosis or management of colorectal neoplasia, dysplasia or early cancer; (3) the outcome did not include colorectal neoplasia, dysplasia or cancer-related detection, incidence or mortality; (4) the article type was a case report or series; (5) the article contained duplicate data; (6) the article had relevant missing data that could not be obtained despite attempts to contact corresponding authors; (7) the author had articles on the topic retracted from the literature; and (8) the studies included data from the fiberoptic endoscope era (predating 1990).

Risk of bias for individual studies was assessed independently by two reviewers (T.K., V.S.) with the QUADAS-2 tool for observational diagnostic studies and a modified Jadad score (one point added if allocation was concealed) for randomized trials; a third person (L.L.) adjudicated any discrepancies. The quality of the evidence for each statement was rated by two reviewers (L.L., A.B.) independently as very low quality, low quality, moderate quality, and high quality based on the GRADE methodology; disagreements were resolved by discussion. Quality of evidence definitions were: (1) very low quality—any estimate of effect is very uncertain; (2) low quality—further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; (3) moderate quality—further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; and (4)

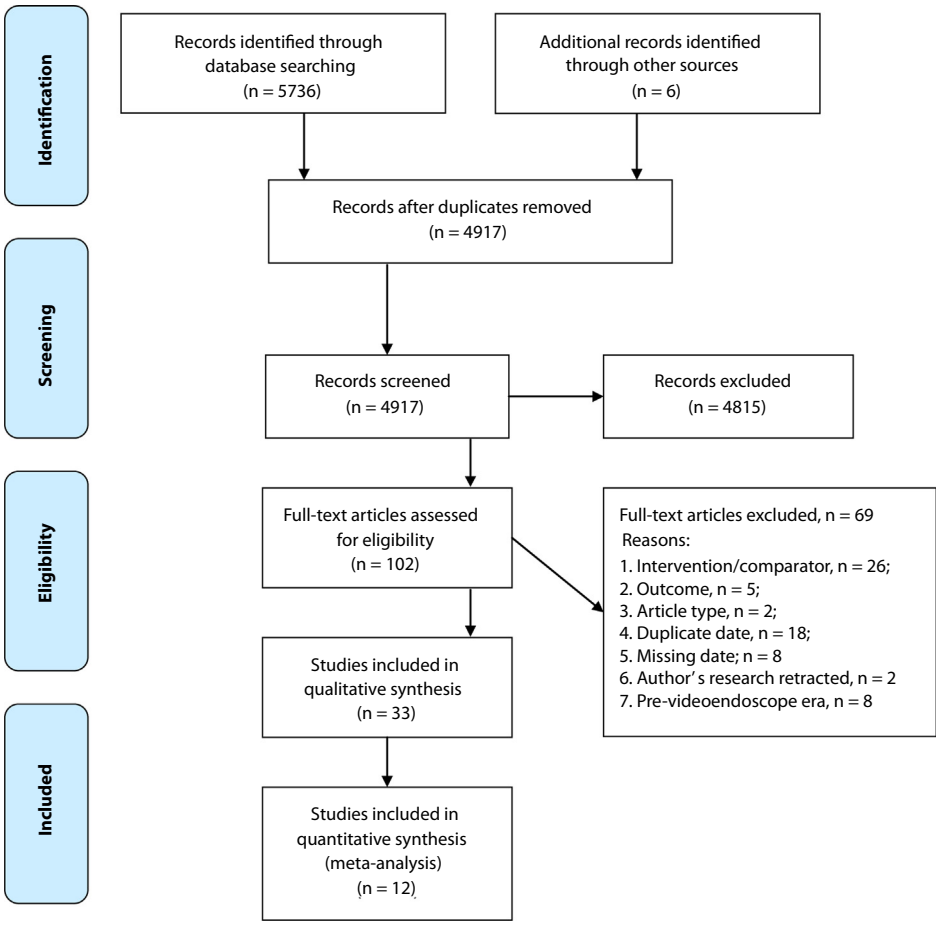


Figure. Flow diagram for systematic review and meta-analysis

high quality—further research is very unlikely to change our confidence in the estimate of effect.

Meta-analyses were performed when multiple studies relevant to a focused question were found and could be appropriately pooled. We used a fixed effect model, except in cases of significant heterogeneity when we used a DerSimonian-Laird random effects model. We used the Cochran Q test and I^2 statistic to assess heterogeneity. Significant heterogeneity was defined as a $P < .10$ for the Cochran Q test or I^2 statistic $> 50\%$. We performed the data analysis by using the Comprehensive Meta Analysis version 2.2 (Biostat, Englewood, NJ) statistical package.

We identified 4917 abstracts and selected 102 for full article retrieval based on the pre-defined inclusion criteria. We ultimately included 33 articles for qualitative synthesis for the statements (see flow diagram). We performed meta-analysis of articles for statements 2 and 6.

Consensus process for development of recommendations

We deployed an online consensus platform to facilitate most aspects of the consensus process. The panel received evidence reports for each statement. Two rounds of voting on level of agreement with the statements were conducted by using the online platform prior to a face-to-face meeting of all participants to determine consensus on the recommendations. Modifications to the wording of the statements were made as needed in response to the participants' comments after each round of voting.

We held a one and a half–day consensus conference in March 2014, where data were presented, wording of the statements was discussed and finalized, and participants voted on their level of agreement by using a 5-point scale (1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree). We defined the criterion for accepting a statement as a recommendation as $\geq 80\%$ of participants voting 4 (agree) or 5 (strongly agree). If a panel member was absent or did not vote at the time of a vote, the denominator of panelists who were present and voted was used. Once a recommendation was accepted, panelists voted on whether to label the recommendation as strong or conditional according to GRADE criteria. Wording of recommendations was based on the strength of recommendation: *recommend* was used for strong recommendations, and *suggest* was used for conditional

recommendations. Voting percentages for individual statements could vary based on the number of voting members in attendance at the time of voting on the statement. The executive committee drafted the manuscript, which was then reviewed by the voting panel members and also by the 8 non-voting physicians with expertise in areas including IBD and advanced endoscopic imaging techniques who had attended the guideline meeting to provide information to panelists. The manuscript was revised based on these comments and approved by the participants. Additional revisions for clarity and description were made in response to comments from the peer review process.

Ethics

An ethics consultant (D.J.) without personal or other conflicts of interest (COI) and an ad hoc ethics advisory committee (Y.L., T.K., A.B.) developed and implemented an ethics framework and distributed it to all participants, with set policies for declarations of interest. Mandatory written disclosures of financial conflicts of interests within 24 months before the meeting and of non-financial conflicts of interest were obtained a priori from all participants. Financial conflicts were disclosed to the entire group and included in conference materials. All potential COIs were reviewed and resolved through proportionality: depending on the judged extent of the COI by the ad hoc ethics committee, resolution was achieved through disclosure for minor COIs and recusal in the case of major COIs. No statement of related COI was deemed to be at such a high risk that recusal was required for any participant. Further information regarding disclosures is provided in Appendix 1.

Role of the funding sources

Two non-profit charitable foundations, the Maxine and Jack Zarrow Family Foundation and the William K. Warren Foundation, provided unrestricted gifts supporting the guideline development process. Focus Medical Communications administered all aspects of the meeting. The funding sources had no involvement at any stage of the development process, no representation at the consensus meeting, and no role in the drafting or approval of the manuscript.

APPENDIX 3. SEARCH STRATEGIES

MEDLINE and Cochrane Central Register of Controlled Trials

1. inflammatory bowel diseases/or colitis, ulcerative/or Crohn disease/
2. (inflammatory bowel disease* or (Crohn's or Crohn) or IBD or ileocolitis).tw.
3. (ulcerative adj2 colitis).tw.
4. or/1-3
5. colonoscopy/ or sigmoidoscopy/
6. (colonoscop* or chromocolonoscop* or sigmoidoscop* or sigmoideoscop* or proctosigmoidoscop*).tw.
7. *Colonic Polyps/di [diagnosis]
8. polypectom*.tw.
9. *Early Detection of Cancer/mt [methods]
10. Diagnostic Imaging/mt [methods]
11. Indigo Carmine/
12. Methylene Blue/
13. *Image Enhancement/
14. *Optical Imaging/mt [methods]
15. *microscopy, fluorescence/or *microscopy, fluorescence, multiphoton/
16. (fluorescence adj2 (imag* or endoscop*)).tw.
17. (autofluorescence adj2 (imag* or endoscop*)).tw.
18. Colonoscopes/
19. Narrow Band Imaging/
20. (narrow* adj3 imag*).tw.
21. NBI.tw.
22. (multiband adj2 imaging).tw.
23. (white adj2 light adj2 endoscop*).tw.
24. WLE.tw.
25. (Fuji adj4 Endoscopy).tw.
26. FICE.tw.
27. (optical adj2 filter).tw.
28. i-Scan.mp.
29. *Microscopy, Confocal/
30. chromoendoscopy.tw.
31. chromoscop*.tw.
32. *biopsy/or image-guided biopsy/or endoscopic ultrasound-guided fine needle aspiration/
33. Colectomy/
34. colectom*.tw.
35. (dye* adj2 spray*).tw.
36. or/5-35
37. 4 and 36
38. exp Population Surveillance/
39. Mass Screening/
40. (surveillance or monitor* or screen* or pattern* or epidemiolog* or detect* or recognition).tw.
41. or/38-40
42. 37 and 41

Embase

1. Crohn disease/
2. ulcerative colitis/
3. enteritis/or necrotizing enteritis/
4. (inflammatory bowel disease* or (Crohn's or Crohn) or IBD or ileocolitis).tw.
5. (ulcerative adj2 colitis).tw.
6. or/1-5
7. colonoscopy/
8. sigmoidoscopy/
9. (colonoscop* or chromocolonoscop* or sigmoidoscop* or sigmoideoscop* or proctosigmoidoscop*).tw.

10. colon polyp/di, dm, pc [diagnosis, disease management, prevention]
11. polypectomy/
12. *early diagnosis/
13. *diagnostic imaging/
14. indigo carmine/
15. methylene blue/
16. image enhancement/
17. fluorescence imaging/or autofluorescence imaging/or voltage sensitive dye imaging/
18. (fluorescence adj2 (imag* or endoscop*)).tw.
19. (autofluorescence adj2 (imag* or endoscop*)).tw.
20. exp colonoscope/
21. narrow band imaging/
22. (narrow* adj3 imag*).tw.
23. NBI.tw.
24. (multiband adj2 imaging).tw.
25. white light endoscopy/
26. (white adj2 light adj2 endoscop*).tw.
27. WLE.tw.
28. (Fuji adj4 Endoscopy).tw.
29. FICE.tw.
30. optical filter/
31. (optical adj2 filter).tw.
32. i-Scan.mp.
33. *confocal microscopy/
34. chromoendoscopy/
35. chromoendoscop*.tw.
36. chromoscop*.tw.
37. colon biopsy/or rectum biopsy/
38. image guided biopsy/
39. *colon resection/or *sigmoidectomy/
40. colectom*.tw.
41. (dye* adj2 spray*).tw.
42. or/7-41
43. 6 and 42
44. cancer epidemiology/
45. *health survey/
46. mass screening/or cancer screening/
47. (surveillance or monitor* or screen* or pattern* or epidemiolog* or detect* or recognition).tw.
48. or/44-47
49. 43 and 48
50. (animal$ not human$).sh,hw.
51. 49 not 50

APPENDIX 4. SUMMARY OF EVIDENCE REVIEWED IN DEVELOPMENT OF CONSENSUS RECOMMENDATIONS

Detection of Dysplasia

Statement 1. When performing surveillance with white-light colonoscopy, high definition is recommended rather than standard definition (Supplemental Tables 1-3).

SUPPLEMENTAL TABLE 1. Summary characteristics of study

Study	Country	Year	Enrollment period	Study design	Type	Patient no.*	No. with dysplasia
Subramanian[1]	UK	2013	2008-2010	Retrospective cohorts	High definition vs standard definition	353	32

*Study included 353 patients with 369 colonoscopies. The data are reported on the 203 patients with 209 colonoscopies in the high definition group and 154 patients with 160 in the standard definition group. Four patients had one high definition and one standard definition colonoscopy during the study period and were included in both arms.

SUPPLEMENTAL TABLE 2. Summary results, surveillance colonoscopy with high definition white light colonoscopy compared to standard definition white light colonoscopy in inflammatory bowel disease patients

Outcome	High definition white light N = 209*	Standard definition white light N = 160*	Prevalence or risk ratio (95% CI)	Summary
No. of patients with dysplasia	24 (11.5%)	8 (5.0%)	2.3 (1.0-5.1)	Surveillance colonoscopy using high definition white light detected 2.3 times more patients with dysplasia compared to standard white light.
No. of patients with endoscopically visible dysplasia	22	5	3.37 (1.28-8.89)	Targeted biopsy strategy during high definition colonoscopy was 3 times more likely to detect patients with dysplastic lesions than targeted biopsy strategy during standard white light colonoscopy.
No. of dysplastic lesions/areas	32	11	–	Surveillance colonoscopy using high definition white light detected more dysplasia compared to standard white light.

CI, Confidence interval.
*Study included 353 patients with 369 colonoscopies. The data are reported on the 209 colonoscopies n the high definition group and 160 in the standard definition group.
–, ratio cannot be calculated.

SUPPLEMENTAL TABLE 3. Quality assessment rating

QUADAS-2		Subramanian[1]
Domain 1: patient selection	Enrolled consecutive or random sample?	Yes
	Case-control design avoided?	Yes
	Inappropriate exclusion avoided?	Yes
	Bias	Low
	Applicability concerns	Low
Domain 2: index test*	Interpreted without knowledge of reference test results?	Yes
	Pre-specified threshold?	Yes
	Bias	Low
	Applicability concerns	Low
Domain 3: reference standard	Interpreted without knowledge of index test results?	Yes
	Bias	Low
	Applicability concerns	Low
Domain 4: flow and timing	Appropriate time interval between reference and index?	–
	Used same reference standard for all?	Yes
	Included all patients?	Yes
	Bias	High
	Applicability concerns	High

*We considered white light random biopsy as the reference standard. The median number of biopsy specimens taken was 14 in the high definition group and 13 in the standard definition group. The cohorts were included based on the endoscopy units' use of standard definition equipment or high definition equipment.
–, not applicable.

We identified one study on surveillance using high definition white light colonoscopy with targeted (+/- random) biopsies compared to standard definition white light colonoscopy with targeted (+/- random) biopsies that enrolled 353 patients, 32 (9.1%) of whom were later found to have dysplasia and 7 (2.0%) cancer.

Findings

1. In the detection of dysplasia and/or colorectal cancer, high definition white light colonoscopy with targeted (+/- random) biopsies compared to standard definition white light colonoscopy with targeted (+/- random) biopsies was superior.
   - Detected significantly more patients with dysplasia, prevalence ratio 2.3, 95% confidence interval (CI), 1.03-5.11
   - Detected significantly more endoscopically visible dysplasia, risk ratio: 3.4, 95% CI, 1.3-8.9
2. In the reduction of colorectal cancer incidence and mortality, high definition colonoscopy with targeted (+/- random) biopsies compared to standard definition white light colonoscopy with targeted (+/- random) biopsies could not be statistically assessed due to insufficient power and/or longitudinal data.

Statement 2: When performing surveillance with standard-definition colonoscopy, chromoendoscopy is recommended rather than white-light colonoscopy (Supplemental Tables 4-12).

We identified 8 studies on the performance of surveillance colonoscopy with a standard definition colonoscope using chromoendoscopy with targeted (+/- random) biopsies compared to white light colonoscopy with targeted (+/- random) biopsies that included a total of 785 inflammatory bowel disease patients, 82 (10.4%) of whom were later found to have dysplasia and 7 cancer (0.89%).

Findings

1. In the detection of dysplasia and/or colorectal cancer, chromoendoscopy with targeted (+/- random) biopsies compared to standard definition white light colonoscopy with targeted (+/- random) biopsies was superior.
   - Detected significantly more patients with dysplasia

   Incremental yield 6%, 95% CI, 2.8%-9.2%; relative risk 1.8, 95% CI, 1.2-2.6
   - Detected significantly more patients with endoscopically visible dysplasia

   Incremental yield 7%, 95% CI, 3.0%-10.0%; relative risk 2.3, 95% CI, 1.4-3.7
   - Detected significantly more dysplasia

   Incremental yield 15%, 95% CI, 5.0%-24.0%, relative risk 1.9, 95% CI, 1.4-2.7
   - Detected significantly more endoscopically visible dysplasia

   Incremental yield 51%, 95% CI, 42%-60%, relative risk 2.1, 95% CI, 1.6-2.8
   - Increased the procedure duration on average by 10.7 minutes, 95% CI, 9.1-12.4.

(Note: Two studies also included time for confocal laser endomicroscopy in addition to chromoendoscopy)

SUPPLEMENTAL TABLE 4. Summary characteristics of the studies

Study	Country	Year	Enrollment period	Study design	Dye type	Endoscopist no.	Patient no.	No. with dysplasia
Kiesslich[2]	Germany	2003	2001-2002	Randomized two groups	Methylene blue	Multiple	165	18
Matsumoto[3]	Japan	2003	1995-2002	Prospective tandem cohort	Indigo carmine	Single	57	12
Rutter[4]	UK	2004	2002	Prospective tandem cohort	Indigo carmine	Single	100	7
Kiesslich[5]	Germany	2007	Not stated	Randomized two groups	Methylene blue	Multiple	153	15
Marion[6]	USA	2008	Not stated	Prospective tandem cohort	Methylene blue	Multiple	102	22
Gunther[7]	Germany	2011	2006-2009	Retrospective two groups	Indigo carmine	Multiple	100*	2
Hlavty[8]	Slovakia	2011	2008-2010	Retrospective cohort	Indigo carmine	Multiple	45	6
Chiorean[9,†]	USA	2012	2006-2011	Prospective tandem cohort	Indigo carmine	Single	63	Not stated

*Excludes confocal group.
†Study is an abstract and included 100 colonoscopies.

SUPPLEMENTAL TABLE 5. Summary results, surveillance colonoscopy by using chromoendoscopy compared to standard definition white light in inflammatory bowel disease

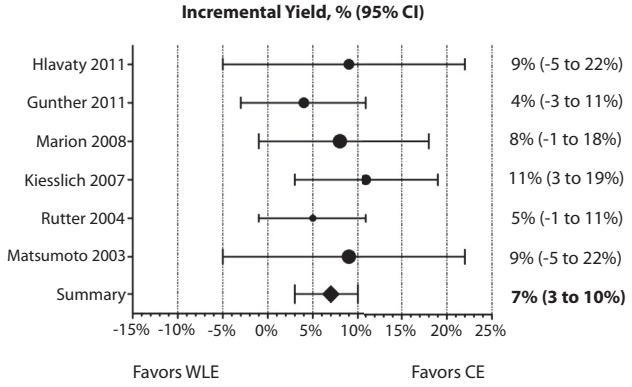
Outcome	No. of studies	No. of patients or lesions	Summary statistic (95% CI)*	Summary
No. of patients with dysplasia	7†	722	Incremental yield 6% (2.8%-9.2%) Relative risk 1.8 (1.2-2.6)	Surveillance colonoscopy using chromoendoscopy was 1.8 times more likely to detect a patient with a dysplastic lesion/area than surveillance using white light.
No. of patients with endoscopically visible dysplasia	6‡	557	Incremental yield 7% (3%-10%) Relative risk 2.3 (1.4-3.7)	Surveillance colonoscopy using chromoendoscopy was 2.3 times more likely to detect a patient with endoscopically visible dysplasia than surveillance using white light.
Detection of dysplastic lesions/areas§	4	359	Incremental yield 15% (5%-24%) Relative risk 1.9 (1.4-2.7)	Surveillance colonoscopy using chromoendoscopy was 1.9 times more likely to detect dysplastic lesions/areas than surveillance using white light colonoscopy.
Detection of endoscopically visible dysplasia	8¶	785	Incremental yield 51% (42%-60%) Relative risk 2.1 (1.6-2.8)	Surveillance colonoscopy using chromoendoscopy was 2.1 times more likely to detect endoscopically visible dysplasia than surveillance using white light.
Detection of endoscopically visible nonpolypoid dysplasia	3**	418	Incremental yield 42% (23%-61%) Relative risk 2.5 (1.2-5.3)	Surveillance colonoscopy using chromoendoscopy was 2.5 times more likely to detect endoscopically visible nonpolypoid dysplasia than surveillance using white light.

*Summary statistics calculated by using Comprehensive Meta-Analysis software.
†Includes studies 2-8.
‡Includes studies 3-8, and forest plot provided as Figure 1.
§Includes endoscopically visible (targeted) dysplasia and endoscopically invisible (random) dysplasia and could be calculated in the 4 studies with tandem design, studies 3, 4, 6, 9.
¶Includes all studies and forest plot as Figure 2.
**Includes studies 2, 4, 5.

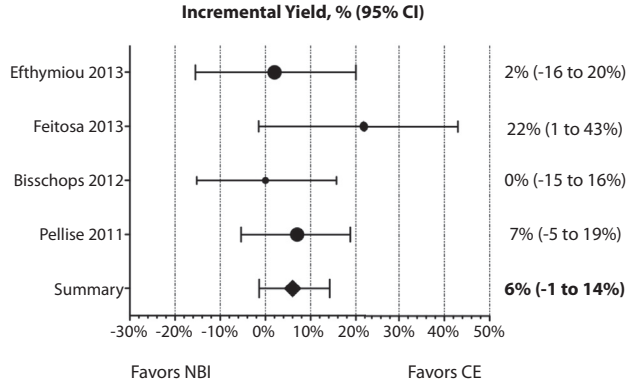
SUPPLEMENTAL TABLE 6. Individual study outcomes, incremental yield in the number of patients with dysplasia during surveillance colonoscopy comparing chromoendoscopy to white light

Type of study	No. of patients	Chromoendoscopy (No. of patients with dysplasia/no. of patients)	White light (No. of patients with dysplasia/no. of patients)	Summary statistics (95% CI)*	
				Incremental yield	Relative risk
All	722	71/503 (14.1%)	38/508 (7.5%)	6% (3% to 9%)	1.78 (1.23-2.58)
Randomized, two groups[2]	165	13/84	6/81	8% (-2% to 18%)	2.09 (0.83-5.23)
Prospective, tandem cohort[3]	57	12/57	12/57	0% (-2% to 2%)	1.0 (0.49-2.04)
Prospective, tandem cohort[4]	100	7/100	2/100	5% (-1% to 11%)	3.5 (0.75-16.44)
Randomized, two groups[5]	153	11/80	4/73	8% (-1% to 17%)	2.51 (0.84-7.53)
Prospective, tandem cohort[6]	102	22/102	12/102	10% (0% to 20%)	1.83 (0.96-3.50)
Retrospective, two groups[7]	100*	2/50	0/50	4% (-3% to 11%)	5 (0.25-101.58)
Retrospective, cohort[8]	45	4/30	2/45	9% (-5% to 23%)	3 (0.59-15.36)
Prospective, tandem cohort[9,†]	–	–	–	–	–

CI, Confidence interval; –, not stated.
*Summary statistics calculated by using Comprehensive Meta-Analysis software, by using fixed-effects model.
†Study 9 did not provide per-patient level data.



Supplemental Figure 1. Forest plot of incremental yield in the number of patients with dysplasia during surveillance colonoscopy comparing chromoendoscopy to white light. *CI,* confidence interval; *WLE,* white-light endoscopy; *CE,* chromoendoscopy.



Supplemental Figure 2. Forest plot of incremental yield in the number of patients with endoscopically visible dysplasia during surveillance colonoscopy comparing chromoendoscopy to white light. *CI,* confidence interval; *WLE,* white-light endoscopy; *CE,* chromoendoscopy.

SUPPLEMENTAL TABLE 7. Incremental yield in the number of patients with endoscopically visible dysplasia during surveillance colonoscopy comparing chromoendoscopy to white light

Type of study	No. of patients	Chromoendoscopy (No. of patients with endoscopically visible dysplasia/no. of patients)	White light (No. of patients with endoscopically visible dysplasia/no. of patients)	Incremental yield* (95% CI)	Relative risk* (95% CI)
All	557	53/419 (12.6%)	22/427 (5.2%)	7% (3% to 10%)	2.32 (1.44-3.72)
Randomized, two groups [2,†]	–	–	–	–	–
Prospective, tandem cohort[3]	57	12/57	7/57	9% (-5% to 22%)	1.71 (0.73-4.04)
Prospective, tandem cohort[4]	100	7/100	2/100	5% (-1% to 11%)	3.50 (0.75-16.44)
Randomized, two groups[5]	153	11/80	2/73	11% (3% to 19%)	5.05 (1.15-21.89)
Prospective, tandem cohort[6]	102	17/102	9/102	8% (-1% to 18%)	1.95 (0.91-4.16)
Retrospective, two groups[7]	100	2/50	0/50	4%(-3% to 11%)	5(0.25-1.58)
Retrospective, cohort[8]	45	4/30	2/45	9%(-5% to 22%)	3(0.59-15.36)
Prospective, tandem cohort[9,†]	not stated	not stated	not stated	not stated	not stated

CI, Confidence interval.
*Summary statistics calculated by using Comprehensive Meta-Analysis software, by using fixed-effects model.
†Studies 2, 9 did not have per-patient data available.

SUPPLEMENTAL TABLE 8. Incremental yield of chromoendoscopy over white light for number of dysplastic lesions/areas detected

Type of study	No. of patients	Chromoendoscopy (No. dysplastic lesions or areas detected in chromoendoscopy/total no. dysplastic lesions or areas detected)	White light (No. dysplastic lesions or areas detected in white light/total no. dysplastic lesions or areas detected)	Summary statistics (95% CI)*	
				Incremental yield	Relative risk
4 Tandem studies	322	115/115	57/115	15% (5% to 24%)	1.9 (1.4-2.7)
Prospective, tandem cohort[3]	57	21/21	15/21	9% (-10% to 30%)	1.3 (0.8-2.2)
Prospective, tandem cohort[4]	100	9/9	2/9	7% (0% to 10%)	4.5 (1-20.3)
Prospective, tandem cohort[6]	102	38/38	16/16	23% (10% to 30%)	2.5 (1.5-4.1)
Prospective, tandem cohort[9]	63	47/47	24/47	23% (10% to 40%)	1.9 (1.3-2.9)

CI, Confidence interval.
*Summary statistics calculated by using Comprehensive Meta-Analysis software, by using fixed-effects model.

SUPPLEMENTAL TABLE 9. Individual study outcomes, number of dysplastic lesions/areas during surveillance colonoscopy comparing chromoendoscopy to white light

Type of study	No. of patients	Chromoendoscopy (No. dysplastic lesions or areas detected in chromoendoscopy)	White light (No. dysplastic lesions or areas detected in white light)
All	785	180	83
Randomized, two groups[2]	165	32	12
Prospective, tandem cohort[3]	57	21	15
Prospective, tandem cohort[4]	100	9	2
Randomized, two groups[5]	153	19	6
Prospective, tandem cohort[6]	102	38	16
Retrospective, two groups[7]	100*	2	0
Retrospective, cohort[8]	45	6	2
Prospective, tandem cohort[9]	63	53	30

*Excludes confocal group.

SUPPLEMENTAL TABLE 10. Individual study outcomes, number of endoscopically visible dysplastic lesions during surveillance colonoscopy comparing chromoendoscopy to white light

Type of study	No. of patients	Chromoendoscopy (No. endoscopically visible dysplastic lesions detected in chromoendoscopy)	White light (No. endoscopically visible dysplastic lesions detected in white light)
All	785	162	57
Randomized, two groups[2]	165	32	10
Prospective, tandem cohort[3]	57	18	8
Prospective, tandem cohort[4]	100	9	2
Randomized, two groups[5]	153	19	4
Prospective, tandem cohort[6]	102	35	13
Retrospective, two groups[7]	100	2	0
Retrospective, cohort[8]	45	6	2
Prospective, tandem cohort[9]	63	41	18

Excludes confocal group.

SUPPLEMENTAL TABLE 11. Procedure duration during surveillance colonoscopy comparing chromoendoscopy to white light*

Type of study	No. of patients	Chromoendoscopy minutes ± SD	White light minutes ± SD
All	565	Mean difference (95% CI) 10.7 (9.1-12.4)	
Randomized, two groups[2]	165	44 ± 12.2	35 ± 9.3
Randomized, two groups[5]	153	42 (range 29-64)*	31 (range 18-48)
Prospective, tandem cohort[6]	102	35:32 (range 10:36-70:44)	22:11 (range 5:27-55:29)
Retrospective, two groups[7]	100	45 ± 10	35 ± 8
Retrospective, cohort[8]	45	66.1 ± 27.1†	28 ± 6.7

SD, Standard deviation; *CI,* confidence interval.
*All times are in minutes:seconds and with mean ± standard deviation unless specified.
†Included time for confocal laser endomicroscopy–directed biopsies.

SUPPLEMENTAL TABLE 12. Quality assessment rating

		Kiesslich[2]	Matsumoto[3]	Rutter[4]	Kiesslich[5]	Marion[6]	Gunther[7]	Hlavty[8]	Chiorean[9]
Jadad score*		4	–	–	4	–	–	–	–
Randomization		1			1				
Method of randomization is appropriate		1			1				
Concealed allocation		1			1				
An account of all participants		1			1				
QUADAS-2									
Domain 1: patient selection	Enrolled consecutive or random sample?	–	Yes	Yes	–	Unknown	N	Unknown	Yes
	Case-control design avoided?	–	Yes	Yes	–	Yes	Yes	Yes	Yes
	Inappropriate exclusion avoided?	–	Yes	Yes	–	Yes	Yes	Yes	Yes
	Bias	–	Low	Low	–	High	High	High	Low
	Applicability concerns		Low	Low		Low	Low	Low	Low
Domain 2: index test	Interpreted without knowledge of reference test results?	–	No	No	–	No	Yes	No	No
	Prespecified threshold?	–	Yes	Yes	–	Yes	Yes	Yes	Yes
	Bias	–	High	High	–	High	Low	High	High
	Applicability concerns		High	High		High	Low	High	High
Domain 3: reference standard†	Interpreted without knowledge of index test results?	–	Yes	Yes	–	Yes	Yes	Yes	Yes
	Bias	–	Low	Low	–	Low	Low	Low	Low
	Applicability concerns		Low	Low		Low	Low	Low	Low
Domain 4: flow and timing	Appropriate time interval between reference and index?	–	Yes	Yes	–	Yes	Yes	Yes	Yes
	Used same reference standard for all?	–	Yes	Yes	–	Yes	Yes	Yes	Yes
	Included all patients?	–	Yes	Yes	–	Yes	Yes	Yes	Yes
	Bias	–	Low	Low	–	Low	Low	Low	Low
	Applicability concerns		Low	Low		Low	Low	Low	Low

*Modified Jadad score (range 1-6). Added concealed allocation. No studies were blinded because it is not possible to blind the endoscopist to the diagnostic method.
†We considered white light colonoscopy as the reference standard and considered the reference standard to be specific but not sensitive because of sampling.
–, not applicable.

In the reduction of colorectal cancer incidence and mortality, chromoendoscopy with targeted (+/- random) biopsies compared to standard definition white light colonoscopy with targeted (+/- random) biopsies could not be adequately assessed due to insufficient power and/or longitudinal data.

Statement 3: When performing surveillance with high-definition colonoscopy, chromoendoscopy is suggested rather than white-light colonoscopy (Supplemental Tables 13-14).

We identified one study on the performance of surveillance colonoscopy with a high definition colonoscope by using chromoendoscopy with targeted (+/- random) biopsies compared to white light colonoscopy with targeted (+/- random) biopsies that enrolled 75 patients, 16 (21.3%) of whom were later found to have dysplasia and none cancer.

Findings

1. In the detection of dysplasia and/or colorectal cancer, chromoendoscopy with targeted (+/- random) biopsies compared to high definition white light colonoscopy with targeted (+/- random) biopsies was superior.
   - Detected significantly more patients with dysplasia, 21.3% (16/75) vs 9.3% (7/75)

   Incremental yield 12% ($P = .007$)
   - Detected significantly more endoscopically visible dysplasia, 100% (22/22) vs 45.4% (10/22)

   Incremental yield 16% ($P = .004$)
   - Detected significantly more patients with nonpolypoid dysplastic lesions, 9.3% vs 1.3%

   Incremental yield 8% ($P = .011$)
2. In the reduction of colorectal cancer incidence and mortality, chromoendoscopy with targeted (+/- random) biopsies compared to high definition white light colonoscopy with targeted (+/- random) biopsies could not be adequately assessed due to insufficient power and/or longitudinal data.
3. The authors aimed to study the interobserver variability in the detection of dysplastic lesions and dysplasia detection rates as well as the procedure time by using chromoendoscopy for ulcerative colitis surveillance among non-expert endoscopists.

Procedure withdrawal time was reported based on the endoscopist procedure volume:

- <5 procedures: median 31 minutes, range 15-36
- 5-14 procedures: median 18 minutes, range 13-27
- >14 procedures: median 19 minutes, range 18-22

SUPPLEMENTAL TABLE 13. Summary characteristics of the study

Study	Country	Year	Enrollment period	Study design	Dye type	Endoscopist no.	Patient no.	No. with dysplasia
Picco[10,*]	USA	2013	2009-2013	Prospective tandem	Indigo carmine	Multiple	75	16

*Personal communication with author confirmed use of high definition colonoscopies at the 3 sites.

SUPPLEMENTAL TABLE 14. Quality assessment rating

QUADAS-2		Picco[10]
Domain 1: patient selection	Enrolled consecutive or random sample?	Unknown
	Case-control design avoided?	Yes
	Inappropriate exclusion avoided?	Yes
	Bias	High
	Applicability concerns	Low
Domain 2: index test *	Interpreted without knowledge of reference test results?	No
	Prespecified threshold?	Yes
	Bias	High
	Applicability concerns	High
Domain 3: reference standard†	Interpreted without knowledge of index test results?	Yes
	Bias	Low
	Applicability concerns	Low
Domain 4: flow and timing	Appropriate time interval between reference and index?	Yes
	Used same reference standard for all?	Yes
	Included all patients?	Yes
	Bias	Low
	Applicability concerns	Low

*Personal communication with author confirmed use of high definition colonoscopies at the 3 sites.
†We considered white light colonoscopy as the reference standard and considered the reference standard to be specific but not sensitive because of sampling.

SUPPLEMENTAL TABLE 15. Summary characteristics of the studies

Study	Country	Year	Enrollment period	Study design	Image enhanced endoscopy type	Endoscopist no.	Patient no.	No. with dysplasia
Dekker[11]	Netherlands	2007	2003-2004	Randomized	Narrow band imaging	Multiple	42	11

Statement 4. When performing surveillance with standard-definition colonoscopy, narrow band imaging is not suggested in place of white-light colonoscopy (Supplemental Tables 15-16).

We identified one study on the performance of surveillance colonoscopy with a standard definition colonoscope that compared narrow band imaging with targeted (+/- random) biopsies to white light colonoscopy with targeted (+/- random) biopsies in which they randomized 42 patients, 11 (26.2%) of whom were later found to have dysplasia and 3 (7.1%) cancer.

Findings

1. In the detection of dysplasia and/or colorectal cancer, standard definition colonoscopy using narrow band imaging with targeted (+/- random) biopsies compared to white light with targeted (+/- random) biopsies was similar.
   - Showed no differences in detection rates, 8 patients with dysplasia compared to 7; $P = .705$
   - Showed no difference in procedure time, 50 ± 14.4 minutes compared to 47 ± 12.1 minutes; $P = .13$
2. In the reduction of colorectal cancer incidence and mortality, narrow band imaging with targeted (+/- random) biopsies compared to standard definition white light colonoscopy with targeted (+/- random) biopsies could not be adequately assessed due to insufficient power and/or longitudinal data.

SUPPLEMENTAL TABLE 16. Quality assessment rating

	Dekker[11]
Jadad score*	3
Randomization	1
Method of randomization is appropriate	0
Concealed allocation	1
An account of all participants	1

*Modified Jadad score (range 1-6). Added concealed allocation.

Statement 5. When performing surveillance with high-definition colonoscopy, narrow band imaging is not suggested in place of white-light colonoscopy (Supplemental Tables 17-19).

For equipment-based image enhanced endoscopy:

- 2 studies compared narrow band imaging and white light colonoscopy.
- 1 study compared auto fluorescence imaging endoscopy and white light colonoscopy.
- No studies compared other equipment-based image enhanced endoscopy methods (eg, i-scan [Pentax, Tokyo, Japan]; Fuji Intelligent Chromo Endoscopy [Fujinon, Tokyo, Japan][16]) and white light.
- Multiple studies reported on the diagnostic accuracy of equipment-based image enhanced endoscopy methods such as confocal endomicroscopy, fluorescein, or optical coherence for dysplasia but not on the detection of dysplasia.

We identified 2 studies on the performance of surveillance colonoscopy with a high definition colonoscope that compared equipment-based image enhanced endoscopy by using narrow band imaging to white light. The studies included a total of 160 IBD patients, 21 (13.1%) of whom were later found to have dysplasia and none cancer.

Findings

1. In the detection of dysplasia and/or colorectal cancer, by using a high definition colonoscope, equipment-based image enhanced endoscopy with targeted (+/- random) biopsies by using narrow band imaging compared to white light colonoscopy with targeted (+/- random) biopsies showed no significant differences. Due to the small study numbers, pooled analysis was not performed.
   - Detected similar number of patients with any grade of dysplasia

SUPPLEMENTAL TABLE 17. Summary characteristics of the studies

Study	Country	Year	Enrollment period	Study design	Image enhancement	Endoscopist no.	Patient no.	No. with dysplasia
van den Broek[12]	Netherlands	2011	2006-2009	Randomized cross-over	NBI	Multiple	48	11
Ignjatovic[13]	UK	2012	2006-2010	Randomized	NBI	Multiple	112	10

NBI, Narrow band imaging.

SUPPLEMENTAL TABLE 18. Summary results, surveillance colonoscopy with a high definition colonoscope, by using equipment-based image enhanced endoscopy with NBI compared to white light in IBD

Outcome	No. of studies	No. of patients	Results		Summary
			Study 12	Study 13	
No. of patients with dysplasia*	2	160	NBI 9 vs WL 13	NBI 5 vs WL 5	Surveillance colonoscopy with a high definition colonoscope showed no difference in the no. of patients found to have dysplasia when NBI was used compared to white light.
Detection of dysplastic lesions/areas*	2	160	NBI 15 vs WL 17	NBI 6 vs WL 7	Surveillance colonoscopy with a high definition colonoscope showed no difference in the detection of dysplasia when NBI was used compared to white light.
Detection of endoscopically visible dysplasia	2	160	NBI 14 vs WL 16	NBI 5 vs WL 7	Surveillance colonoscopy with a high definition colonoscope showed no difference in the detection of endoscopically visible dysplasia when NBI was used compared to white light.

NBI, Narrow band imaging; *IBD,* inflammatory bowel disease; *WL,* white light.
*This includes endoscopically visible (targeted) dysplasia and endoscopically invisible (random) dysplasia. It is notable that a random biopsy identified dysplasia and due to the cross-over study design is counted in both groups.

SUPPLEMENTAL TABLE 19. Quality assessment rating

	van den Broek[12]	Ignjatovic[13]
Jadad score*	4	4
Randomization	1	1
Method of randomization is appropriate	0	1
Concealed allocation	1	1
An account of all participants	1	1

*Modified Jadad score (range 1-6). Added concealed allocation. No studies were blinded as it not possible to blind the endoscopist to the diagnostic method used.

- Detected fewer dysplastic lesions

2. In the reduction of colorectal cancer incidence and mortality, by using a high definition colonoscope, equipment based image enhanced endoscopy with targeted (+/- random) biopsies by using narrow band imaging compared to white light colonoscopy with targeted (+/-) random biopsies could not be adequately assessed due to insufficient power and/or longitudinal data.

Statement 6. When performing surveillance with image-enhanced high-definition colonoscopy, narrow band imaging is not suggested in place of chromoendoscopy (Supplemental Tables 20-24).

We identified 4 studies on surveillance colonoscopy with a high definition colonoscope that compared chromoendoscopy to equipment-based image enhanced endoscopy. They included a total of 231 inflammatory bowel disease patients, 54 (23.4%) of whom were later found to have dysplasia and one cancer (0.43%). All studies compared chromoendoscopy to narrow band imaging colonoscopy.

Findings

1. In the detection of dysplasia and/or colorectal cancer, by using a high definition colonoscope, chromoendoscopy with targeted biopsies compared to equipment based

SUPPLEMENTAL TABLE 20. Summary characteristics of the studies

Study	Country	Year	Enrollment period	Study design	Image enhancement type	Endoscopist no.	Patient no.	No. with dysplasia
Pellise[14]	Spain	2011	2006-2007	Randomized cross-over	Indigo carmine vs NBI	Multiple	60	13
Bisschops[15,*]	Belgium	2012	Not stated	Randomized two groups	Methylene blue vs NBI	Multiple	93	16
Feitosa[16,†]	Brazil	2013	Not stated	Randomized two groups	Indigo carmine vs NBI	Multiple	34	4
Efthymiou[17,‡]	Australia	2013	2009-2010	Prospective tandem	Methylene blue vs NBI	Multiple	44	21

NBI, Narrow band imaging.
*Abstract.
†Data from final document (in Portuguese).
‡Only study to perform targeted and random biopsy. 3408, 468, 1220 did not perform random biopsies in either group.

SUPPLEMENTAL TABLE 21. Individual study outcomes, incremental yield in the number of patients with dysplasia during surveillance colonoscopy comparing chromoendoscopy to NBI

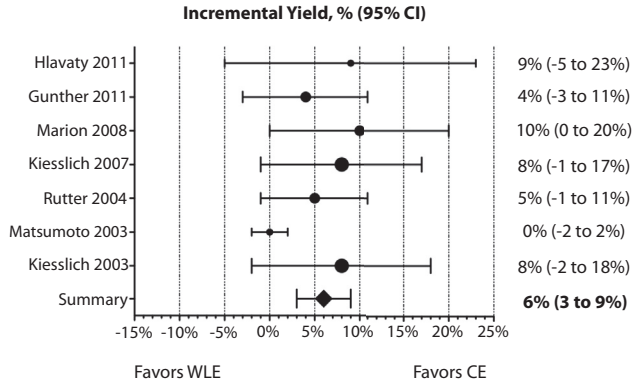
Type of study	No. of patients	Chromoendoscopy No. of patients with dysplasia/no. of patients	NBI No. of patients with dysplasia/no. of patients	Incremental yield (95% CI)*	Relative risk (95% CI)
All	231	34/174	23/161	6% (-1.4 to 14.2)	1.27 (0.78-2.06)
Randomized, cross-over[14]	60	10/60	6/60	7% (-5.4 to 18.8)	1.67 (0.65-4.30)
Randomized, two groups[15]	93	9/52	7/41	0% (-15.2 to 15.7)	1.01 (0.41-2.49)
Randomized, two groups[16]	34	4/18	0/16	22% (-1.5 to 43)	8.05 (0.47-138.87)
Prospective, tandem[17]	44	11/44	10/44	2% (-15.5 to 20.1)	1.10 (0.52-2.32)

NBI, Narrow band imaging.

SUPPLEMENTAL TABLE 22. Individual study outcomes, incremental yield in the number of endoscopically visible dysplastic lesions during surveillance colonoscopy comparing chromoendoscopy to NBI

Type of study	No. of patients	Chromoendoscopy No. endoscopically visible dysplasia	NBI No. endoscopically visible dysplasia
All	231	61	37
Randomized, cross-over[14]	60	12	10
Randomized, two groups[15]	93	25	10
Randomized, two groups[16]	34	4	0
Prospective, tandem[17]	44	20	17

NBI, Narrow band imaging.



Supplemental Figure 3. Forest plot of incremental yield in the number of patients with endoscopically visible dysplasia during surveillance colonoscopy comparing narrow band imaging to chromoendoscopy. *CI,* confidence interval; *WLE,* white-light endoscopy; *CE,* chromoendoscopy.

image enhanced endoscopy by using NBI with targeted biopsies showed no significant differences.

- Showed no significant difference in the detection of patients with dysplasia

Incremental yield of 6%, 95% CI, -1.4%-14.2%

- Showed no significant difference in the detection of dysplastic lesions, chromoendoscopy 61 vs NBI 37.
- Increased the procedure time overall, but pooled analysis is not available.

2. In the reduction of colorectal cancer incidence and mortality, by using a high definition colonoscope, chromoendoscopy with targeted biopsies compared to equipment-based image enhanced endoscopy with targeted biopsies could not be adequately assessed due to insufficient power and/or longitudinal data.

SUPPLEMENTAL TABLE 23. Procedure duration during surveillance colonoscopy comparing chromoendoscopy to NBI

Type of study	Total no. of patients (chromoendoscopy/NBI)	Chromoendoscopy, minutes, mean ± SD	NBI, minutes, mean ± SD
All	231	–	–
Randomized, cross-over[14]	60 (60/60)	26	17
Randomized, two groups[15]	93 (52/42)	26.87 ± 9.89	15.74 ± 5.62
Randomized, two groups[16]	34 (18/16)	43.6*	34.1*
Prospective, tandem[17]	44 (44/44)	13 (12-24)†	13 (12-22)†

NBI, Narrow band imaging.
*Average procedure time.
†Median and interquartile range.

SUPPLEMENTAL TABLE 24. Quality assessment rating

		Pellise[14]	Bisschops[15]	Feitosa[16]	Efthymiou[17]
Jadad score*		3	4	4	–
Randomization		1	1	1	–
Method of randomization is appropriate		1	1	1	–
Concealed allocation		0	1	1	–
An account of all participants		1	1	1	–
QUADAS-2					
Domain 1: patient selection	Enrolled consecutive or random sample?	–	–	–	Yes
	Case-control design avoided?	–	–	–	Yes
	Inappropriate exclusion avoided?	–	–	–	Yes
	Bias	–	–	–	Low
	Applicability concern				High†
Domain 2: index test	Interpreted without knowledge of reference test results?	–	–	–	Yes
	Prespecified threshold?	–	–	–	Yes
	Bias	–	–	–	Low
	Applicability concern				Low
Domain 3: reference standard‡	Interpreted without knowledge of index test results?	–	–	–	Yes
	Bias	–	–	–	Low
	Applicability concern				Low
Domain 4: flow and timing	Appropriate time interval between reference and index?	–	–	–	Yes
	Used same reference standard for all?	–	–	–	Yes
	Included all patients?	–	–	–	Yes
	Bias	–	–	–	Low
	Applicability concern				Low

*Modified Jadad score (range 1-6). Added concealed allocation. No studies were blinded as it is not possible to blind the endoscopist to the diagnostic method used.
†Study included left-sided colitis >8 years and Crohn's disease of any duration.
‡We considered chromoendoscopy as the reference standard, and consider the reference standard to be specific but not sensitive due to sampling.
–, not applicable.

Additional topic: random biopsy with chromoendoscopy surveillance colonoscopy (Supplemental Tables 25-26).

We identified 11 studies on the performance of surveillance colonoscopy by using chromoendoscopy that reported data on random biopsy. The studies included a total of 48,522 random biopsies in 1635 IBD patients. We evaluated the chromoendoscopy arms within the studies.

1. In the detection of dysplasia and/or colorectal cancer on surveillance colonoscopy using chromoendoscopy:
   - Proportion of patients surveyed who had dysplasia identified by targeted biopsies or by random biopsies alone (7 studies, 1289 patients)
     - Chromoendoscopy with targeted biopsy: 12.4% (95% CI, 8.3%-18.3%) of all patients surveyed had dysplasia identified with targeted biopsies by using chromoendoscopy; Heterogeneity: Cochran's Q 24.9 ($P < .001$) and $I^2 = 75\%$
     - Random biopsy alone: 1.2% (95% CI, 0.8%-2.0%) of all patients surveyed had dysplasia identified on random biopsies only; Heterogeneity: Cochran's Q 3.04 ($P = .80$) and $I^2 = 0\%$
   - Proportion of patients with dysplasia who had dysplasia identified by targeted biopsies or by random biopsies alone (7 studies, 158 patients with dysplasia):
     - Chromoendoscopy with targeted biopsy: 90.2% (95% CI, 85%-94%) of the patients with dysplasia had their dysplasia identified with targeted biopsy using chromoendoscopy; Heterogeneity: Cochran's Q 0.6 ($P = .97$) and $I^2 = 0\%$
     - Random biopsy alone: 9.8% (95% CI, 6%-15%) of the patients with dysplasia had their dysplasia identified on random biopsies only; Heterogeneity: Cochran's Q 0.6 ($P = .97$) and $I^2 = 0\%$
   - Proportion of random biopsies positive for dysplasia (11 studies, 48522 random biopsies):
     - Dysplasia was identified in 0.1% (95% CI, 0.0%-0.3%) of all random biopsy specimens taken; Heterogeneity: Cochran's Q 115.3 ($P < .001$) and $I^2 = 91\%$

SUPPLEMENTAL TABLE 25. Study outcomes*, random biopsies in patients who underwent chromoendoscopy surveillance

Study	Type of study*	No. of patients total	No. of patients with dysplasia	Random biopsy		
				Total no. of random biopsy specimens taken	No. of random biopsy specimens with dysplasia	No. of patients with dysplasia on random biopsy alone
Matsumoto[3]	Prospective tandem cohort	57	12	702	3	1
Rutter[4]	Prospective tandem cohort	100	9	2904	0	0
Marion[6]	Prospective tandem cohort	102	22	3264	3	2
Gunther[7]	Retrospective two groups	100	2	1811	0	0
Hlavaty[8]	Prospective cohort	30	4	1576	0	0
Mousatta[18]	Prospective cohort	900	93	27596	18	9
Picco[10]	Prospective tandem cohort	75	16	2400	3	2
Efthymiou[17]	Prospective tandem cohort	44	12	474	12	Not stated
Kiesslich[2]	Randomized two groups	84	13	2352	0	Not stated
Kiesslich[5]	Randomized two groups	80	11	1376	0	Not stated
Chiorean[9]	Prospective tandem cohort	63	Not stated	4067	6	Not stated

*Data provided are single arm or subset chromoendoscopy cohorts of the studies.

SUPPLEMENTAL TABLE 26. Quality assessment rating

		Matsumoto[3]	Rutter[4]	Marion[6]	Gunther[7]	Hlavty[8]	Mousatta[18]	Picco[10]
Jadad score		–	–	–	–	–	–	–
Randomization		–	–	–	–	–	–	–
Method of randomization is appropriate		–	–	–	–	–	–	–
Concealed allocation		–	–	–	–	–	–	–
An account of all participants		–	–	–	–	–	–	–
QUADAS-2								
Domain 1: patient selection	Enrolled consecutive or random sample?	Yes	Yes	Unknown	No	Unknown	Yes	Unknown
	Case-control design avoided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Inappropriate exclusion avoided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Bias	Low	Low	High	High	High	Low	High
	Applicability concerns	Low	Low	Low	Low	Low	Low	Low
Domain 2: index test	Interpreted without knowledge of reference test results?	No	No	No	Yes	No	No	No
	Prespecified threshold?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Bias	High	High	High	Low	High	High	High
	Applicability concerns	High	High	High	Low	High	High	High
Domain 3: reference standard*	Interpreted without knowledge of index test results?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Bias	Low	Low	Low	Low	Low	Low	Low
	Applicability concerns	Low	Low	Low	Low	Low	Low	Low
Domain 4: flow and timing	Appropriate time interval between reference and index?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Used same reference standard for all?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Included all patients?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Bias	Low	Low	Low	Low	Low	Low	Low
	Applicability concerns	Low	Low	Low	Low	Low	Low	Low

(*continued on next page*)

SUPPLEMENTAL TABLE 26. Continued

		Efthymiou[17]	Kiesslich[2]	Kiesslich[5]	Chiorean[9]
Jadad score*		–	4	4	–
Randomization		–	1	1	–
Method of randomization is appropriate		–	1	1	–
Concealed allocation		–	1	1	–
An account of all participants		–	1	1	–
QUADAS-2					
Domain 1: patient selection	Enrolled consecutive or random sample?	Yes	–	–	Yes
	Case-control design avoided?	Yes	–	–	Yes
	Inappropriate exclusion avoided?	Yes	–	–	Yes
	Bias	Low	–	–	Low
	Applicability concerns	High†		–	Low
Domain 2: index test	Interpreted without knowledge of reference test results?	Yes	–	–	No
	Prespecified threshold?	Yes	–	–	Yes
	Bias	Low	–	–	High
	Applicability concerns	Low		–	High
Domain 3: reference standard†	Interpreted without knowledge of index test results?	Yes	–	–	Yes
	Bias	Low	–	–	Low
	Applicability concerns	Low		–	Low
Domain 4: flow and timing	Appropriate time interval between reference and index?	Yes	–	–	Yes
	Used same reference standard for all?	Yes	–	–	Yes
	Included all patients?	Yes	–	–	Yes
	Bias	Low	–	–	Low
	Applicability concerns	Low	–	–	Low

*We considered white light colonoscopy as the reference standard and consider the reference standard to be specific but not sensitive due to sampling.
*Modified Jadad score (range 1-6). Added concealed allocation. No studies were blinded as it is not possible to blind the endoscopist to the diagnostic method used.
†Study included left-sided colitis >8 years and Crohn's disease of any duration.
–, not applicable.

2. In the reduction of colorectal cancer incidence and mortality, random biopsy specimens could not be adequately assessed due to insufficient power and/or longitudinal data.

Additional topic: random biopsy with high-definition white-light surveillance colonoscopy (Supplemental Tables 27-28)

We identified 5 studies on the performance of surveillance colonoscopy by using high definition white light that

SUPPLEMENTAL TABLE 27. Study outcomes, random biopsies in patients who underwent high-definition white-light surveillance

				Random biopsy		
Study	Type of study*	Total no. of patients	No. of patients with dysplasia	Total no. of random biopsy specimens taken	No. of random biopsy specimens with dysplasia	No. of patients with dysplasia on random biopsy alone
van den Broek[12]	Randomized cross over	48	14	1580	3	1
Ignjatovic[13]	Randomized two groups	56	5	1359	0	0
Subramanian[1]	Retrospective cohort	203	24	2926	5	2
Picco[10]	Prospective tandem cohort	75	16	2400	3	2
Efthymiou[17]	Prospective tandem cohort	44	12	474	12	Not stated

*Data are provided from single arm or subset high definition white light cohorts of the studies.

SUPPLEMENTAL TABLE 28. Quality assessment rating

		van den Broek[12]	Ignjatovic[13]	Subramanian[1]	Picco[10]	Efthymiou[17]
Jadad score*		4	4	–	–	–
Randomization		1	1	–	–	–
Method of randomization is appropriate		0	1	–	–	–
Concealed allocation		1	1	–	–	–
An account of all participants		1	1	–	–	–
QUADAS-2						
Domain 1: patient selection	Enrolled consecutive or random sample?	–	–	Yes	Unknown	Yes
	Case-control design avoided?	–	–	Yes	Yes	Yes
	Inappropriate exclusion avoided?	–	–	Yes	Yes	Yes
	Bias	–	–	Low	High	Low
	Applicability concerns	–	–	Low	Low	High
Domain 2: index test	Interpreted without knowledge of reference test results?	–	–	Yes	N	Yes
	Prespecified threshold?	–	–	Yes	Yes	Yes
	Bias	–	–	Low	High	Low
	Applicability concerns	–	–	Low	High	Low
Domain 3: reference standard†	Interpreted without knowledge of index test results?	–	–	Yes	Yes	Yes
	Bias	–	–	Low	Low	Low
	Applicability concerns	–	–	Low	Low	Low
Domain 4: flow and timing	Appropriate time interval between reference and index?	–	–	–	Yes	Yes
	Used same reference standard for all?	–	–	Yes	Yes	Yes
	Included all patients?	–	–	Yes	Yes	Yes
	Bias	–	–	High	Low	Low
	Applicability concerns	–	–	High	Low	Low

*Modified Jadad score (range 1-6). Added concealed allocation. No studies were blinded as it not possible to blind the endoscopist to the diagnostic method used.
†We considered white light colonoscopy as the reference standard and consider the reference standard to be specific but not sensitive due to sampling.
–, not applicable.

reported data on random biopsy. The studies included a total of 8739 random biopsy specimens in 426 IBD patients. We evaluated the high definition white light arms within the studies.

1. In the detection of dysplasia and/or colorectal cancer on surveillance colonoscopy by using high definition white light:
   - Proportion of all patients surveyed who had dysplasia identified by targeted biopsies or by random biopsies alone (4 studies, 382 patients)
     - High definition white light with targeted biopsy: 15.4% (95% CI, 9.3%-24.5%) of all patients surveyed had dysplasia identified with targeted biopsies by using high definition white light; Heterogeneity: Cochran's Q 10.3 ($P = .02$), $I^2 = 70\%$
     - Random biopsy alone: 1.6% (95% CI, 0.7%-3.6%) of all patients surveyed had dysplasia identified on random biopsies only; Heterogeneity: Cochran's Q 1.26 ($P = .73$) and $I^2 = 0\%$
   - Proportion of patients with dysplasia who had dysplasia identified by targeted biopsies or by random biopsies alone (4 studies, 59 patients with dysplasia)
     - High definition white light with targeted biopsy: 90.6% (95% CI, 80.1%-95.9%) of patients with dysplasia had their dysplasia identified with targeted biopsies by using high definition white light; Heterogeneity: Cochran's Q 0.3 ($P = .96$) and $I^2 = 0\%$
     - Random biopsy alone: 9.4% (95% CI, 4.1%-19.9%) of the patients with dysplasia had their dysplasia identified with random biopsies only; Heterogeneity: Cochran's Q 0.3 ($P = .96$) and $I^2 = 0\%$
   - Proportion of random biopsies positive for dysplasia (5 studies, 8739 random biopsy specimens)
     - Dysplasia was identified in 0.2% (95% CI, 0.0%-1.2%) of all random biopsy specimens taken; Heterogeneity: Cochran's Q 48.1 ($P < .001$) and $I^2 = 91\%$
2. In the reduction of colorectal cancer incidence and mortality, random biopsies could not be adequately assessed due to insufficient power and/or longitudinal data.

SUPPLEMENTAL TABLE 29. Individual study outcomes of random biopsies in standard definition white light surveillance

Study	Type of study*	Total no. of patients	No. of patients with dysplasia	Random biopsy		
				Total no. of random biopsy specimens taken	No. of random biopsy specimens with dysplasia	No. of patients with dysplasia on random biopsy alone
Matsumoto[3]	Prospective tandem cohort	57	12	702	7	5
Rutter[4]	Prospective tandem cohort	100	9	2904	0	0
Marion[6]	Prospective tandem cohort	102	22	3264	3	3
Gunther[7]	Retrospective two groups	100	2	1531	0	0
Hlavaty[8]	Prospective cohort	45	6	1576	0	0
Dekker[11]	Randomized cross-over	42	11	1522	9	1
van den Broek[19]	Randomized cross-over	50	10	1992	2	0
Subramanian[1]	Retrospective cohort	154	8	2080	5	3
Kiesslich[2]	Randomized two groups	81	18	2746	2	Not stated
Kiesslich[5]	Randomized two groups	73	15	2854	2	Not stated
Chiorean[9]	Prospective tandem cohort	63	Not stated	4067	6	Not stated
Jaramillo[20]	Prospective cohort	85	32	Not stated	19	16
Blonski[21]	Retrospective cohort	Not stated	49	Not stated	Not stated	7
Rutter[22]	Retrospective cohort	525	56	Not stated	Not stated	13
van den Broek[23]	Retrospective cohort	475	53	Not stated	Not stated	4

*Data are provided from single arm or subset high definition white light cohorts of the studies.

Additional topic: random biopsy with standard-definition white-light surveillance colonoscopy (Supplemental Table 29)

(We provide the following narrative summary and table for standard-definition white-light colonoscopy in order to place the chromoendoscopy and high-definition white-light results in context.)

We identified 15 studies on the performance of surveillance colonoscopy by using standard definition white light that reported data on random biopsy. The studies included over 25,238 random biopsies in 1952 IBD patients. We evaluated the standard definition white light arms within the studies.

In the detection of dysplasia and/or colorectal cancer on surveillance colonoscopy by using standard definition white light:

- Proportion of all patients surveyed who had dysplasia identified by targeted biopsies or by random biopsies alone (11 studies, 1735 patients)
  - Standard definition white light with targeted biopsy: 11.8% (95% CI, 8.6%-16.1%) of all patients surveyed had dysplasia identified with targeted biopsies by using standard definition white light; Heterogeneity: Cochran's Q 39.1 ($P < .001$) and $I^2 = 74\%$
  - Random biopsy alone: 2.6% (95% CI, 1.1%-6.0%) of all patients surveyed had dysplasia identified on random biopsies only; Heterogeneity: Cochran's Q 60.1 ($P < .001$) and $I^2 = 83\%$
- Proportion of patients with dysplasia who had dysplasia identified by targeted biopsies or by random biopsies alone (12 studies, 270 patients with dysplasia)
  - Standard definition white light with targeted biopsy: 80.4% (95% CI, 85%-94%) of the patients with dysplasia had their dysplasia identified with targeted biopsy by using standard definition white light; Heterogeneity: Cochran's Q 28.7 ($P = .001$) and $I^2 = 65\%$
  - Random biopsy alone: 19.6% (95% CI, 11.5%-31.2%) of the patients with dysplasia had their dysplasia identified on random biopsies only; Heterogeneity: Cochran's Q 28.7 ($P = .001$) and $I^2 = 65\%$
- Proportion of random biopsies positive for dysplasia (11 studies, 25,238 random biopsies)
  - Dysplasia was identified in 0.1% (95% CI, 0.1%-0.3%) of all random biopsies taken; Heterogeneity: Cochran's Q 38.3 ($P < .001$) and $I^2 = 76\%$

Additional topic: other image-enhanced endoscopy detection modalities (Supplemental Tables 30-32)

We identified one study on the performance of surveillance colonoscopy with a high definition colonoscope that compared equipment-based image enhanced endoscopy by using autofluorescence to white light. The studies included a total of 50 IBD patients, 10 (20%) of whom were later found to have dysplasia and none cancer.

Findings

1. In the detection of dysplasia and/or colorectal cancer, by using a high definition colonoscope, equipment based image enhanced endoscopy with targeted (+/- random) biopsies by using auto fluorescence imaging compared

SUPPLEMENTAL TABLE 30. Summary characteristics of the studies

First author	Country	Year	Enrollment period	Study design	Image enhancement	Endoscopist no.	Patient no.	No. with dysplasia
van den Broek[19]	Netherlands	2008	2005-2006	Randomized tandem*	Autofluorescence imaging	Multiple	50	10

*All patients underwent segmental examination using both autofluorescence imaging and white light. Patients were randomly assigned to undergo examination first by using autofluorescence imaging or white light. Random assignment was performed by a research fellow, by using a sealed opaque envelope, once the endoscopist reached the cecum.

SUPPLEMENTAL TABLE 31. Summary results, surveillance colonoscopy with a high definition colonoscope, by using autofluorescence imaging compared to white light in IBD

Outcome	Results	Summary
No. of patients with dysplasia*	AFI 10/50 vs WL 6/50	Surveillance colonoscopy with a high definition colonoscope detected dysplasia in more patients by using AFI, compared to white light.
Detection of endoscopically visible dysplasia	AFI 16/18 vs WL 13/18	Surveillance colonoscopy with a high definition colonoscope detected more dysplastic lesions by using AFI, compared to white light.

IBD, Inflammatory bowel disease; *AFI,* autofluorescence imaging; *WL,* white light.
*This includes endoscopically visible (targeted) dysplasia and endoscopically invisible (random) dysplasia.

SUPPLEMENTAL TABLE 32. Quality assessment rating

	van den Broek[19]
Jadad score*	4
Randomization	1
Method of randomization is appropriate	0
Concealed allocation	1
An account of all participants	1

*Jadad score modified to incorporate concealed allocation, and to exclude blinding, as it not logistically possible to blind endoscopist to the test.

to white light colonoscopy with targeted (+/- random) biopsies was superior. Due to the small study numbers, pooled analysis was not performed.

- Detected more patients with dysplasia
- Detected more endoscopically visible dysplastic lesions

2. In the reduction of colorectal cancer incidence and mortality, by using a high definition colonoscope, equipment based image enhanced endoscopy with targeted (+/- random) biopsies compared to white light colonoscopy with targeted (+/-) random biopsies could not be adequately assessed due to insufficient power and/or longitudinal data.

Management of Dysplasia

Statement 7: After complete removal of endoscopically-resectable polypoid dysplastic lesions, surveillance colonoscopy is recommended rather than colectomy (Supplemental Tables 33-35).

We identified no studies on surveillance colonoscopy compared to colectomy for patients identified to have endoscopically resectable polypoid dysplastic lesions.

For informational purposes

SUPPLEMENTAL TABLE 33. Summary characteristics of the studies, all retrospective in design

Study	Country	Year	Enrollment period	Type of colitis	Patient no.*	No. with polypoid dysplasia
Odze[24]	USA	2004	1990-1995	UC	34	18
Rutter[22]	UK	2004	1998-2002	UC	56	50
Blonski[21]	USA	2008	1997-2004	UC	49	6
Pekow[25]	USA	2010	1994-2008	UC	35	12
Goldstone[26]	USA	2011	1994-2006	UC	162	89
Van Schaik[27]	Netherlands	2011	1990-2006	Crohn's and UC	617	45
Kisiel[28]	USA	2012	1994-2003	UC	95	44
Subramanian[29,†]	UK	2012	1991-2011	UC	301	29
Navaneethan[30]	USA	2013	1998-2011	Crohn's and UC	102	65

UC, Ulcerative colitis.
We attempted to included only adenoma described within area of colitis.
*Excludes patients who underwent immediate colectomy.
†Abstract.

SUPPLEMENTAL TABLE 34. Study results, incidence of dysplasia or CRC during surveillance of endoscopically resectable polypoid dysplastic lesions

Enrollment period	No. with polypoid dysplasia	Follow-up, mo	Incidence of LGD	Incidence of HGD	Incidence of CRC
1990-1995[24]	18	82.1 (17-156)	15	0	1
1998-2002[22]	50	44.4 (0.08-147)	0	0	6
1997-2004[21]	6	76.5 (52-99)	0	0	0
1994-2008[25]	12	50.4	0	1	0
1994-2006[26]	89	37.5 (13.3-71.8)	0	3	4
1990-2006[27]	45	53 (7-86)	–	12	6
1994-2003[28]	44	51.4 (0.1-142)	18	0	1
1991-2011[29,*]	29	–	–	–	–
1998-2011[30]	65	36 (0.3-159)	0	1	1

LGD, Low grade dysplasia; *HGD,* high grade dysplasia; *CRC,* colorectal cancer; –, not stated.
*All studies recommend for endoscopic resection and close surveillance for polypoid dysplasia.

- We identified 9 studies on the endoscopic management of polypoid dysplastic lesions.
  - We present the studies with data from the videoendoscope era (1990 to present) in order to report findings in line with current endoscopic technology and practice.
  - All studies were retrospective and single arm.
  - Surveillance of patients with dysplasia was not standardized in detection methods (eg, performed by using standard white light without chromoendoscopy or image enhancement at various intervals) or in endoscopic removal methods.
  - Follow-up data did not account for duration of IBD.
  - Pooled analysis was not performed due to significant heterogeneity in patients, definitions, intervention, and outcome.

General descriptive summary

- Studies suggested that endoscopic resection had fairly low rates of progression or recurrent cancer on follow-up.
- Several studies suggested that rates of recurrent adenomatous endoscopically resectable lesions approached 50%, emphasizing the role of surveillance.
- Studies provide insufficient power and/or longitudinal data to report on colorectal cancer incidence and/or mortality.

SUPPLEMENTAL TABLE 35. Quality assessment rating

QUADAS-2		Odze[24]	Rutter[22]	Blonski[21]	Pekow[25]	Goldstone[26]	Kisiel[28]
Domain 1: patient selection	Enrolled consecutive or random sample?	No	No	No	No	No	No
	Case-control design avoided?*	Yes	Yes	Yes	Yes	Yes	Yes
	Inappropriate exclusion avoided?	Yes	Yes	Yes	Yes	Yes	Yes
	Bias	High	High	High	High	High	High
	Applicability concern	High	High	High	High	High	High
Domain 2: index test†	Interpreted without knowledge of reference test results?	–	–	–	–	–	–
	Prespecified threshold?	Yes	Yes	Yes	Yes	Yes	Yes
	Bias	High	High	High	High	High	High
	Applicability concern	High	High	High	High	High	High
Domain 3: reference standard†	Interpreted without knowledge of index test results?	No	No	No	No	No	No
	Bias	High	High	High	High	High	High
	Applicability concern	High	High	High	High	High	High
Domain 4: flow and timing	Appropriate time interval between reference and index?	No	No	No	No	No	No
	Used same reference standard for all?	No	No	No	No	No	No
	Included all patients?	No	No	No	No	No	No
	Bias	High	High	High	High	High	High
	Applicability concern	High	High	High	High	High	High

(*continued on next page*)

TABLE 35. Continued

	QUADAS-2	Subramanian[29]	Van Schaik[27]	Navaneethan[30]
Domain 1: patient selection	Enrolled consecutive or random sample?	No	No	No
	Case-control design avoided?*	Yes	Yes	Yes
	Inappropriate exclusion avoided?	Yes	Yes	Yes
	Bias	High	High	High
	Applicability concern	High	High	High
Domain 2: index test	Interpreted without knowledge of reference test results?	–	–	–
	Pre-specified threshold?	Yes	Yes	Yes
	Bias	High	High	High
	Applicability concern	High	High	High
Domain 3: reference standard†	Interpreted without knowledge of index test results?	No	No	No
	Bias	High	High	High
	Applicability concern	High	High	High
Domain 4: flow and timing	Appropriate time interval between reference and index?	No	No	No
	Used same reference standard for all?	No	No	No
	Included all patients?	No	No	No
	Bias	High	High	High
	Applicability concern	High	High	High

*Population included IBD patients with known dysplasia.
†We considered the index test to be endoscopic removal and surveillance and reference standard to be colectomy.
–, not applicable.

- A recent meta-analysis on the cancer risk after resection of polypoid dysplasia in patients with longstanding ulcerative colitis includes polypoid dysplasia lesions within and outside areas of colitis (Wanders LK, Dekker E, Pullens B, et al. Clin Gastroenterol Hepatol 2014;12:756-64).

Statement 8: After complete removal of endoscopically-resectable nonpolypoid dysplastic lesions, surveillance colonoscopy is suggested rather than colectomy.

We identified 0 studies on surveillance colonoscopy compared to colectomy for patients identified to have endoscopically resectable nonpolypoid dysplastic lesions.

Note: There is a growing consensus to use similar terminology to describe IBD-related superficial colon neoplasia/dysplasia and non-IBD neoplasia/dysplasia. Historic guidelines and literature have used the term *flat dysplasia* to refer to endoscopically undetectable lesions, and the term *raised dysplasia* to refer to endoscopically detectable lesions. They have used the term *flat dysplasia* to describe endoscopically detectable but only slightly raised lesions, and the acronym *DALM-dysplastic lesions or masses* to refer to more raised lesions. All of these terms resulted in inconsistent criteria in the published literature. Future studies in IBD should use the Paris Classification system for describing lesion morphology, which includes polypoid and nonpolypoid.

We did not include Hurlstone DP, Sanders DS, Atkinson R, et al. Endoscopic mucosal resection for flat neoplasia in chronic ulcerative colitis: Can we change the endoscopic management paradigm? Gut 2007;56:838-846. Other research works by this author were formally retracted.

Statement 9: For patients with endoscopically invisible dysplasia (confirmed by a GI pathologist) referral to an endoscopist with expertise in IBD surveillance by using chromoendoscopy with high definition colonoscopy is suggested (Supplemental Tables 36-38).

We identified no studies on colectomy compared to surveillance colonoscopy for patients identified as having endoscopically invisible dysplasia.

SUPPLEMENTAL TABLE 36. Summary characteristics of the studies: all USA based, retrospective, and regarding ulcerative colitis

Study	Year	Enrollment period	Patient no.*	No. with invisible dysplasia
Ullman[31]	2002	1990-1993	18	18
Ullman[32]	2003	1994-2001	137	35
Pekow[25]	2010	1994-2008	35	13
Goldstone[26]	2011	1994-2006	162	32
Navaneethan[30]	2013	1998-2011	102	37

*Excludes patients who underwent immediate colectomy.

SUPPLEMENTAL TABLE 37. Study results, surveillance of patients with endoscopically invisible dysplasia

Enrollment period	No. with invisible dysplasia	Follow-up, mo	Incidence of HGD	Incidence of CRC	Progression to dysplasia in patients with endoscopically invisible dysplasia
1990-1993[31]	18	32 (2-117)	3	1	Cumulative incidences 13% (0-29) at 1 y 26% (4-48) at 2 y 33% (9-56) at 5 y
1994-2001[32]	35	15 (4.5-50.5)	3	2	Cumulative incidence 53% (29-79) at 5 y* Progression-free survival Unifocal 71.4 mo (47-96) Multifocal 54.6 mo (35-74)
1994-2008[25]	13	50.4	1	0	Cumulative incidence 4.3 cases per 100 person years
1994-2006[26]	32	37.5	5	3	Progression-free survival 59.1 ± 12.6%†
1998-2011[30]	37	36 (0.3-159)	2	1	Higher progression to advanced neoplasia in flat compared to raised dysplasia hazard ratio 3.6 (1.3-10.6)*,†

HGD, high grade dysplasia; *CRC,* colorectal cancer.
Findings also suggest multifocal* and distal location† to be more strongly associated with progression to advanced neoplasia and cancer.
Studies overall suggest total proctocolectomy for patients with endoscopically invisible dysplasia.

Low grade dysplasia

- We identified 5 studies on the natural history of endoscopically invisible low grade dysplasia followed with surveillance.
  - We present the studies with data from the videoendoscope era (1990 to present) in order to report findings in line with current endoscopic technology and practice.
  - All (with exception of one) studies were retrospective, single arm, with small numbers and with limited follow up.

SUPPLEMENTAL TABLE 38. Quality assessment rating

	QUADAS-2	Ullman[31]	Ullman[32]	Pekow[25]	Goldstone[26]	Navaneethan[30]
Domain 1: patient selection	Enrolled consecutive or random sample?	No	No	No	No	No
	Case-control design avoided?	Yes	Yes	Yes	Yes	Yes
	Inappropriate exclusion avoided?	Yes	Yes	Yes	Yes	Yes
	Bias	High	High	High	High	High
	Applicability concern	High	High	High	High	High
Domain 2: index test	Interpreted without knowledge of reference test results?	–	–	–	–	–
	Prespecified threshold?	Yes	Yes	Yes	Yes	Yes
	Bias	High	High	High	High	High
	Applicability concern	High	High	High	High	High
Domain 3: reference standard†	Interpreted without knowledge of index test results?	No	No	No	No	No
	Bias	High	High	High	High	High
	Applicability concern	High	High	High	High	High
Domain 4: flow and timing	Appropriate time interval between reference and index?	No	No	No	No	No
	Used same reference standard for all?	No	No	No	No	No
	Included all patients?	No	No	No	No	No
	Bias	High	High	High	High	High
	Applicability concern	High	High	High	High	High

–, not applicable.

- Surveillance of patients with dysplasia was not standardized in detection methods (eg, performed by using standard white light without chromoendoscopy or image enhancement at various intervals) or in endoscopic removal methods.
- Follow-up data did not account for duration of IBD.

- A pooled analysis was thought inappropriate due to significant heterogeneity in patients, definitions, intervention, and outcome.

General descriptive summary

- The majority of studies did not recommend proctocolectomy for patients with endoscopically invisible low-grade dysplasia.
- All studies emphasized the cumulative incidence of cancer and important role of vigilant surveillance.
- Some studies reported increased cumulative incidence of cancer when endoscopically invisible dysplasia is multifocal or when it is located in the distal colon.
- Studies provide insufficient power and/or longitudinal data to report on colorectal cancer incidence and/or mortality.

- For the articles that we identified for this statement, we interpreted the report of "flat dysplasia" as endoscopically invisible dysplasia unless there were clear morphologic features described. We used this approach based on the historic guidelines and literature that have used the term *flat dysplasia* to refer to endoscopically undetectable lesions and the term *raised dysplasia* to refer to endoscopically detectable lesions.
- A recent meta-analysis on the cancer risk of low-grade dysplasia in chronic ulcerative colitis that included 20 surveillance studies totaling 508 flat low grade dysplasia or low grade dysplasia with dysplasia-associated lesions or masses. The studies predate the use of current technology of image enhanced endoscopy or even high resolution endoscopy. The authors reported a 9-fold risk of developing cancer (odds ratio [OR] 9.0, 95% CI, 4.0-20.5) and a 12-fold risk of developing any advanced lesion (OR 11.9, 95% CI, 5.2-27). The absolute risk of cancer in this meta-analysis was 14 (95% CI, 5-34) cancers/100 years patient follow-up. Meta-analysis: cancer risk of low-grade dysplasia in chronic ulcerative colitis. Thomas T, Abrams KA, Robinson RJ, et al. Aliment Pharmacol Ther 2007;25, 657-68.

High-grade dysplasia

- We identified no studies on the natural history of endoscopically invisible high-grade dysplasia followed with surveillance that reported findings during the videoendoscope era (1990 to present).

A systematic review of findings from the fiberoptic era reported a probability of finding cancer in a patient with high-grade dysplasia of 42% (10/24) if colectomy was done immediately and 32% (15/47) if colectomy was done after some follow-up: Bernstein CN, Shanahan F, Weinstein WM. Are we telling patients the truth about surveillance colonoscopy in ulcerative colitis? Lancet 1994;343,71-4. Importantly, interpretation of the data should be with caution due to significant limitations in the sensitivity of the fiberoptic technology to detect dysplasia or cancer at index colonoscopy. Furthermore, surveillance of patients with dysplasia was not standardized (eg, performed without chromoendoscopy or image enhancement at various intervals or in endoscopic removal methods). Thus, the true incidence of synchronous colorectal cancer in the setting of high grade dysplasia as well as the true natural history of endoscopically invisible high grade dysplasia is not known.

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