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.
   - o Detected significantly more patients with dysplasia, prevalence ratio 2.3, 95% confidence interval (CI), 1.03-5.11
   - o 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.
   - o 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
   - o 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
   - o Detected significantly more dysplasia
   Incremental yield 15%, 95% CI, 5.0%-24.0%, relative risk 1.9, 95% CI, 1.4-2.7
   - o Detected significantly more endoscopically visible dysplasia
   Incremental yield 51%, 95% CI, 42%-60%, relative risk 2.1, 95% CI, 1.6-2.8
   - o 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

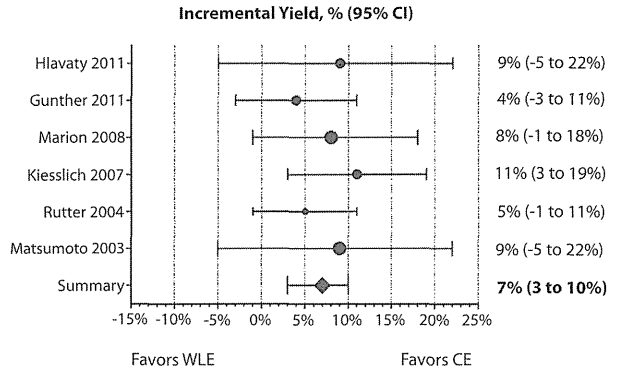
Outcome	No. of studies	No. of patients or lesions	Summary statistic (95% CI)*	Summary
No. of patients with dysplasia	7†	722	Incremental yield 6% (2.8%-9.2%) Relative risk 1.8 (1.2-2.6)	Surveillance colonoscopy using chromoendoscopy was 1.8 times more likely to detect a patient with a dysplastic lesion/area 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.

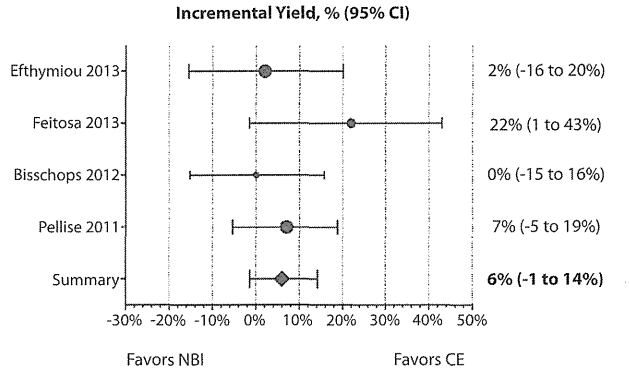
SUPPLEMENTAL TABLE 6. Individual study outcomes, incremental yield in the number of patients with dysplasia during surveillance colonoscopy comparing chromoendoscopy to white light

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.

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.

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 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 colonoscopy 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

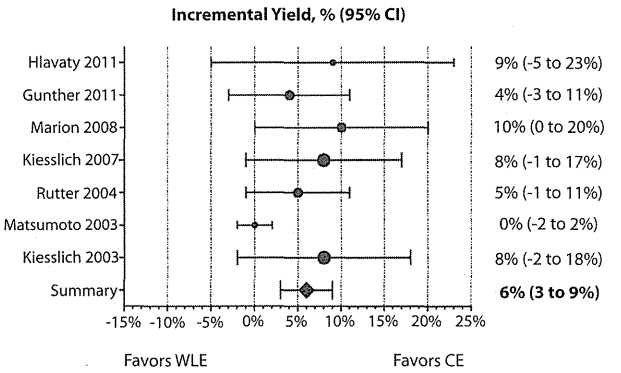
Type of study	No. of patients	Chromoendoscopy No. of patients with dysplasia/no. of patients	NBI No. of patients with dysplasia/no. of patients	Incremental yield (95% CI)*	Relative risk (95% CI)
All	231	34/174	23/161	6% (-1.4 to 14.2)	1.27 (0.78-2.06)
Randomized, cross-over[14]	60	10/60	6/60	7% (-5.4 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 $I^2 = 91\%$

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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.

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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.