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Guidelines for Colonoscopy Surveillance After Screening and Polypectomy: A Consensus Update by the US Multi-Society Task Force on Colorectal Cancer

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Screening for colorectal cancer (CRC) in asymptomatic patients can reduce the incidence and mortality of CRC. In the United States, colonoscopy has become the most commonly used screening test. Adenomatous polyps are the most common neoplasm found during CRC screening. There is evidence that detection and removal of these cancer precursor lesions may prevent many cancers and reduce mortality.[1] However, patients who have adenomas are at increased risk for developing metachronous adenomas or cancer compared with patients without adenomas. There is new evidence that some patients may develop cancer within 3–5 years of colonoscopy and polypectomy—so-called interval cancers.

Ideally, screening and surveillance intervals should be based on evidence showing that interval examinations prevent interval cancers and cancer-related mortality. We have focused on the interval diagnosis of advanced adenomas as a surrogate marker for the more serious end point of cancer incidence or mortality. In 2006, the United States Multi-Society Task Force (MSTF) on CRC issued a guideline on postpolypectomy surveillance,[2] which updated a prior 1997 guideline. A key principle of the 2006 guideline was risk stratification of patients based on the findings at the baseline colonoscopy. The surveillance schema identified 2 major risk groups based on the likelihood of developing advanced neoplasia during surveillance: (1) low-risk adenomas (LRAs), defined as 1–2 tubular adenomas <10 mm, and (2) high-risk adenomas (HRAs), defined as adenoma with villous histology, high-grade dysplasia (HGD), ≥10 mm, or 3 or more adenomas. The task force also published recommendations for follow-up after resection of CRC.[3]

More recently, the British Society of Gastroenterology updated their 2002 surveillance guideline in 2010.[4] Their risk stratification differs from the US guideline, dividing patients into 3 groups: low risk (1–2 adenomas <10 mm), intermediate risk (3–4 small adenomas or one ≥10 mm), and high risk (>5 small adenomas or ≥3 with at least one ≥10 mm). They recommend that the high-risk group undergo surveillance at 1 year because of concerns about missed lesions at baseline. US guidelines place emphasis on performing a high-quality baseline examination. In 2008, the MSTF published screening guidelines for CRC, which included recommendations for the interval for repeat colonoscopy after negative findings on baseline examination.[5]

New issues have emerged since the 2006 guideline, including risk of interval CRC, proximal CRC, and the role of serrated polyps in colon carcinogenesis. New evidence suggests that adherence to prior guidelines is poor. The task force now issues an updated set of surveillance recommendations. During the past 6 years, new evidence has emerged that endorses and strengthens the 2006 recommendations. We believe that a stronger evidence base will improve adherence to the guidelines. The 2012 guidelines are summarized in Table 1 and are based on risk stratification principles used in the 2006 guideline. The ensuing discussion reviews the new evidence that supports these guidelines. This guideline does not address surveillance after colonoscopic or surgical resection of a malignant polyp.

Methodology

Literature Review

We performed a MEDLINE search of the postpolypectomy literature under the subject headings of colonoscopy, adenoma, polypectomy surveillance, and adenoma surveillance, limited to English language articles from 2005 to 2011. Subsequently, additional articles were gleaned from references of the reviewed articles. Relevant studies include those in which outcomes addressed the relationship between baseline examination

Abbreviations used in this paper: CI, confidence interval; CIMP, CpG island methylator phenotype; CRC, colorectal cancer; CT, computed tomography; FDR, first-degree relative; FOBT, fecal occult blood test; HGD, high-grade dysplasia; HP, hyperplastic polyp; HR, hazard ratio; HRA, high-risk adenoma; LRA, low-risk adenoma; MSTF, Multi-Society Task Force; NCI, National Cancer Institute; OR, odds ratio; PPT, Polyp Prevention Trial; RR, relative risk; TVA, tubulovillous adenoma; USPSTF, United States Preventive Services Task Force.

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Table 1. 2012 Recommendations for Surveillance and Screening Intervals in Individuals With Baseline Average Risk

Baseline colonoscopy: most advanced finding(s)	Recommended surveillance interval (*y*)	Quality of evidence supporting the recommendation	New evidence stronger than 2006
No polyps	10	Moderate	Yes
Small (<10 mm) hyperplastic polyps in rectum or sigmoid	10	Moderate	No
1–2 small (<10 mm) tubular adenomas	5–10	Moderate	Yes
3–10 tubular adenomas	3	Moderate	Yes
>10 adenomas	<3	Moderate	No
One or more tubular adenomas ≥10 mm	3	High	Yes
One or more villous adenomas	3	Moderate	Yes
Adenoma with HGD	3	Moderate	No
Serrated lesions			
Sessile serrated polyp(s) <10 mm with no dysplasia	5	Low	NA
Sessile serrated polyp(s) ≥10 mm OR Sessile serrated polyp with dysplasia OR Traditional serrated adenoma	3	Low	NA
Serrated polyposis syndrome[a]	1	Moderate	NA

NOTE. The recommendations assume that the baseline colonoscopy was complete and adequate and that all visible polyps were completely removed.

NA, not applicable.

[a]Based on the World Health Organization definition of serrated polyposis syndrome, with one of the following criteria: (1) at least 5 serrated polyps proximal to sigmoid, with 2 or more ≥10 mm; (2) any serrated polyps proximal to sigmoid with family history of serrated polyposis syndrome; and (3) >20 serrated polyps of any size throughout the colon.

findings and the detection of CRC, advanced adenoma, or any adenoma during the follow-up period. Studies used in the final analysis are summarized in Table 2 by specific category. We also reviewed studies with results of more than one surveillance examination to determine the downstream risk that may be associated with the baseline findings. A key goal was to determine if the risk of subsequent neoplasia was reduced once a patient had negative findings on colonoscopy or had low-risk adenomas. We excluded studies that included patients with inflammatory bowel disease or prior history of CRC. This review applies to average-risk individuals and excluded patients with hereditary syndromes associated with CRC.

Table 2. New Papers Since 2005 With Surveillance Outcomes After Baseline Colonoscopy

Category: baseline colonoscopy finding	No. of papers meeting criteria (reference no.)
Exposure to colonoscopy: 1. Risk of CRC 2. Risk of proximal vs distal CRC	6 (18–22, 52)
Exposure to colonoscopy: rate of CRC within 10 y	4 (18, 20, 21, 52)
No polyps at baseline: rates of advanced neoplasia	6 (14, 47–51)
HPs	1 (61)
Small adenomas <10 mm	7 (7, 14, 51, 64–67)
Advanced adenomas	3 (7, 14, 66)
Adenoma with HGD	3 (7, 14, 71)
Serrated polyps	2 (72, 73)
Family history of CRC or polyps	1 (59)
Multiple rounds of surveillance	3 (67, 77, 78)
Poor bowel preparation	2 (68, 82)
Surveillance after FOBT	2 (84, 85)
Miscellaneous risk factors	
Smoking	1 (58)
Aspirin/nonsteroidal anti-inflammatory drugs	4 (54–57)

Levels of Evidence

There are no high-quality randomized controlled trials of polyp surveillance performed in the past 6 years. All studies are either retrospective or prospective observational, cohort, population-based, or case-control studies. We have adopted a well-accepted rating of evidence[6] that relies on expert consensus about whether new research is likely to change the confidence level of the recommendation (Table 3).

Process

The task force is composed of gastroenterology specialists with a special interest in CRC, representing the 3 major gastroenterology professional organizations: American College of Gastroenterology, American Gastroenterological Association Institute, and American Society for Gastrointestinal Endoscopy. We recognize that inherent bias can be introduced when a group of experts in the field review evidence and provide recommendations. In addition to the task force, the practice committees of the American Gastroenterological Association Institute and the

Table 3. Rating Evidence

Rating of evidence	Impact of potential further research
High quality	Very unlikely to change confidence in the estimate of effect
Moderate quality	Likely to have an important impact on confidence and may change estimate of effect
Low quality	Very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate
Very low quality	Any estimate of effect is very uncertain

American College of Gastroenterology and the governing board of the American Society for Gastrointestinal Endoscopy reviewed and approved this document.

Format of the Report

The report includes statements that summarize new, relevant literature since 2005. This is followed by recommendations for surveillance based on the most advanced finding of the baseline colonoscopy examination. For each baseline finding (or lack of finding), there is a recommendation, background section, summary of new evidence since 2006, and discussion of unresolved issues and areas for further research.

Terms and Definitions

Low-risk adenoma (LRA) refers to patients with 1–2 tubular adenomas <10 mm in diameter. High-risk adenoma (HRA) refers to patients with tubular adenoma ≥10 mm, 3 or more adenomas, adenoma with villous histology, or HGD. Advanced neoplasia is defined as adenoma with size ≥10 mm, villous histology, or HGD.

Throughout the document, statistical terms are used. The odds ratio (OR) is the ratio of the odds of an event occurring in one group to the odds of it occurring in another group. Generally there is a referent group (OR = 1.0) that is compared with another group. Relative risk (RR) is used frequently in the statistical analysis of binary outcomes where the outcome of interest has relatively low probability. The RR is different from the OR, although it asymptotically approaches it for small probabilities. The OR has much wider use in statistics, because logistic regression, often associated with clinical trials, works with the log of the OR, not RR. In survival analysis, the hazard ratio (HR) is the ratio of the hazard rates corresponding to the conditions described by 2 sets of explanatory variables in a defined period. For example, in a drug study, the treated population may die at twice the rate per unit time as the control population. The HR would be 2, indicating higher hazard of death from the treatment.

Results of Literature Review

New Evidence on Limitations of Colonoscopic Surveillance

New evidence documents the risk of developing interval CRC after polypectomy or negative findings on baseline colonoscopy. New data have emerged on the risk of interval cancer after colonoscopy. Data from studies in which patients had adenomas detected and removed were analyzed in a pooling project funded by the National Cancer Institute (NCI) (hereafter referred to as the NCI Pooling Project).[7] These include randomized controlled trials to evaluate chemoprevention[8–13] and cohort studies.[1,14,15] The overall rate of interval cancer was 1.1–2.7 per 1000 person-years of follow-up.

Interval cancers have also been reported in patients with baseline examinations negative for neoplasia. Studies from Ontario[16] and Manitoba[17] used cancer registries to identify patients with cancer and then linked these patients to claims data to determine if there had been a prior colonoscopy. These studies suggest that up to 9% of cancers in the registry were interval cancers, with the patients having had a colonoscopy in the 6 to 36 months before diagnosis of CRC. These studies did not include data on completion rates and quality of prior colonoscopy.

Several studies[18–22] have suggested that patients who develop cancer after colonoscopy are more likely to have proximal compared than distal cancers (Table 4). One hypothesis is that some endoscopists may be more likely to miss lesions in the proximal colon compared with the distal colon. This could be due to quality of bowel preparation, failure to fully examine the proximal colon, differences in proximal polyp/cancer morphology, the skill of the endoscopist, and variable quality of colonoscopy. Serrated polyps and some classic adenomatous polyps in the proximal colon may be challenging to detect if they are flat, covered with mucus, or behind folds. Most prior studies of colonoscopy have failed to report on the quality of the colonoscopy examinations. A second hypothesis is that neoplastic lesions of the proximal colon may biologically differ from distal lesions and progress to malignancy with a short dwell time. The serrated pathway has a predilection for the proximal colon. These lesions may be associated with BRAF or k-ras mutations, and CPG island methylation, which can lead to silencing of mismatch repair genes (MLH1), which could result in more rapid progression to malignancy in some individuals.[23]

Concerns about interval cancer may impact physician behavior with regard to surveillance intervals and may contribute to early repeat examinations in some cases.

Important lesions are missed at baseline colonoscopy. Considerable evidence suggests that important lesions may be missed at colonoscopy. Studies that have compared computed tomography (CT) colonography and optical colonoscopy use a method of segmental unblinding to assess the sensitivity of colonoscopy. As each segment is examined, the endoscopist is informed of findings at CT. If the CT revealed a polyp and colonoscopy did not, the region is reexamined; if a polyp(s) is found on the second look, it is considered a missed lesion by colonoscopy. These studies suggest that up to 17% of lesions ≥10 mm are missed with optical colonoscopy.[24–29] Recent studies suggest that most interval cancers are due to missed lesions at baseline colonoscopy.[30,31] Missed lesions are directly related to the quality of the examination.

Adenomas may be incompletely removed at the time of baseline colonoscopy. If adenoma removal is not complete, residual neoplastic tissue could progress to malignancy. New studies have found that 19%–27% of interval cancers occur in the same portion of the colon as the site of prior polypectomy. In a study of patients with large sessile polyps (>2 cm), 17.6% had residual adenomatous tissue when reexamined.[30,32–35]

Interval CRC may biologically differ from prevalent CRC. When interval CRCs are compared with prevalent CRC, interval lesions are more likely located in the proximal colon, be microsatellite unstable, and have CpG island methylator phenotype (CIMP). It has been proposed that the mismatch repair defects associated with microsatellite unstable tumors can lead to a rapid accumulation of mutations and accelerated tumor growth.[36,37]

Table 4. Risk of CRC After Colonoscopy: Case-Control or Observational Studies

Study	Location and type of study	n	Follow-up (*y*)	CRC risk	Risk over 10 y[a]	Notes: proximal vs distal[b]
Singh et al, 2006[18]	Manitoba Cohort/claims data	35,975 with colonoscopy compared with expected rates of CRC in population	10	Incidence: SIR, 0.55 (0.41–0.73)	SIR: 1 y, 0.66 2 y, 0.59 5 y, 0.55 10 y, 0.28	Proximal CRC more common in patients with interval CRC (47%) vs those with prevalent CRC (28%)
Lakoff et al, 2008[20]	Ontario Cohort/claims data	110,402 with negative colonoscopy compared with rates in population	Up to 14		Incidence RR: 2 y, 0.80 5 y, 0.56 10 y, 0.45 14 y, 0.25	No reduction in proximal CRC risk until year 8 of follow-up
Baxter et al, 2009[21]	Ontario Case-control claims data	10,292 CRC cases vs 51,460 cancer-free controls; measured exposure to colonoscopy	Median, 7.8	Mortality: OR, 0.69 (0.63–0.74)		Proximal CRC: OR, 0.99 Distal CRC: OR, 0.33 (0.28–0.39)
Brenner et al, 2011[22]	Germany Case-control	1688 CRC cases vs cancer-free controls; exposure to colonoscopy	10	Incidence: OR, 0.23 (0.19–0.27)		Proximal CRC: OR, 0.44 (0.35–0.55) Distal CRC OR, 0.16 (0.12–0.20)
Brenner et al, 2011[52]	Germany Case-control	1945 CRC cases vs 2399 controls	Up to 20		Incidence OR: 1–2, 0.14 3–4, 0.12 5–9, 0.26[c] 10–19, 0.28	

SIR, standardized incidence ratio.
[a]Based on interval since prior colonoscopy.
[b]Prevalent CRC, diagnosis of CRC at time of initial colonoscopy; interval CRC, diagnosis of CRC at time of follow-up colonoscopy, at some interval after baseline examination.
[c]At 5–9 years: OR of 0.61 in smoker, OR of 0.66 with positive family history.

Quality of baseline colonoscopy is associated with risk of interval cancer. An underlying premise of recommendations for surveillance is that the baseline colonoscopy was performed with high quality, which minimizes the risk of missed lesions. Since 2002, quality indicators for reporting and performance have been published.[38–40] There is now evidence of a clear relationship between specific quality indicators and the risk of interval cancer after colonoscopy. Variation in adenoma detection rate among endoscopists has been reported.[16,41] A large Polish study found that if the adenoma detection rate in screening examinations was <20%, a significantly higher risk of interval cancer occurred in the next 5 years.[42] In Ontario, investigators compared endoscopists with high and low polyp detection rates, finding that interval cancers were less likely when the colonoscopy was performed by an endoscopist with high polyp detection rates.[16] The same investigators compared endoscopists with high (>95%) and low (<80%) cecal intubation rates and similarly found that interval cancers were less common among the patients who had colonoscopy performed by higher-performance endoscopists. These new data reinforce the importance of colonoscopy quality and its impact on surveillance.

There is growing interest in using adherence to polyp surveillance recommendations as an indicator of endoscopy quality.[40] There is evidence that guideline adherence is variable and overall far from consistent with national guideline recommendations. Surveys of primary care and specialty physicians revealed that many recommend frequent surveillance colonoscopy for low-risk patients, despite recommendations for lengthened surveillance intervals.[43,44] A recent study reported on actual surveillance performance after colonoscopy.[45] Approximately 25% of patients with no adenomas at baseline had a repeat colonoscopy within 5 years, and more than 40% of patients with small adenomas had one or more examinations within 5 years. The study also revealed evidence for underutilization of surveillance in some higher-risk patients with advanced neoplasia at baseline. Roughly 40% of such patients did not have surveillance within 5 years. Overutilization exposes patients to the cost and risk of unnecessary procedures. Underutilization could result in higher-risk patients developing cancer.

Recommendations for Surveillance

Baseline examination: no adenomas or polyps.

2008 recommendation for next examination	10 years
2012 recommendation for next examination	No change
Quality of evidence	Moderate – stronger than 2008

Background. The foundation of the 10-year interval is based on indirect, observational data discussed in prior guidelines.[5]

New information since 2008. The United Kingdom sigmoidoscopy randomized controlled trial demonstrated a reduction in CRC incidence and mortality at 10 years in patients who received one-time sigmoidoscopy compared with controls—a benefit limited to the distal colon.[46] This is the first randomized study to show the effectiveness of endoscopic screening, an effect that appears to have at least a 10-year duration.

Table 5. Prevalence of Advanced Neoplasia After Negative Findings on Colonoscopy

Study	N (type of cohort)	Interval after baseline (*y*)	Advanced neoplasia (%)
Lieberman et al, 2007[14]	291 (veterans, male)	5	2.4
Imperiale et al, 2008[47]	1256 (US, men and women)	5	1.3
Leung et al, 2009[48]	370 (Chinese men and women)	5	1.4
Brenner et al, 2010[49]	115 (men and women)	5	4.4
Miller et al, 2010[50]	US veterans (99% male)	5–10	
	5-y follow-up: n = 86		7.0
	6- to 10-y follow-up: n = 111		3.6
Chung et al, 2011[51]	1242 Korean men and women)	5	2.0

Risk of advanced adenomas at follow-up colonoscopy. Several prospective observational studies[14,47–51] in different populations have shown that the risk of advanced adenomas within 5 years after negative findings on colonoscopy is low (1.3%–2.4%) relative to the rate on initial screening examination (4%–10%). In these studies, interval cancers within 5 years were rare (Table 5).

Risk of cancer during surveillance. Case-control and observational studies[18,20,21,52] have suggested that patients with prior colonoscopy have either reduced CRC incidence or mortality, with a duration of effect of 10 years or more (Table 4). A large case-control study from Germany compared patients undergoing true screening colonoscopy with unscreened controls, finding a durable risk reduction with colonoscopy for at least 10 years.[53] Other studies that have included higher-risk patients (lower gastrointestinal symptoms or positive fecal occult blood test [FOBT] result) have reported higher rates of interval cancers,[18,53] which may be due to a higher likelihood of cancer at baseline compared with asymptomatic screening cohorts.

Other risk factors. There are new data about the possible impact of nonsteroidal anti-inflammatory drugs (reduced risk) and smoking (no effect) on risk of adenomas during surveillance.[54–58] There is insufficient evidence to tailor recommendations based on these risk factors.

Recommendation. There is now stronger evidence to support the 10-year interval after negative findings on baseline colonoscopy for average-risk individuals, assuming that the baseline colon examination is complete with a good bowel preparation.

Individuals with a first-degree relative (FDR) with CRC or HRA have an increased lifetime risk of developing CRC, particularly if the FDR was younger than 60 years at the time of diagnosis.[59] If colonoscopy is performed and the finding is normal, the recommended interval for repeat screening should be 5 years if the FDR was younger than 60 years and 10 years if the FDR was 60 years or older.

Unresolved issues and areas for further research. The reports of interval cancer after negative findings on colonoscopy have raised concerns about the 10-year interval recommendation. The new prospective studies are reassuring and show that the risk of advanced neoplasia is very low at 5 years. However, one Canadian population-based study suggests that the highest risk of interval CRC is within 1–5 years of the baseline examination, when it is most likely that missed lesions will progress and lead to diagnosis of CRC.[18] These data emphasize the importance of performing high-quality examinations to reduce the likelihood of missed lesions. Future studies should make every effort to document quality indicators.

Baseline examination: no adenomas; distal small (<10 mm) hyperplastic polyps.

2006 recommendation for next examination	10 years
2012 recommendation for next examination	No change
Quality of evidence	Moderate

Background. There is considerable evidence that patients with only rectal or sigmoid hyperplastic polyps (HPs) appear to represent a low-risk cohort. Earlier literature focused on whether the finding in the distal colon was a marker of risk for advanced neoplasia elsewhere. Most studies show no such relationship.[2] Most evidence suggests that small lesions (<10 mm) limited to the rectum and sigmoid are benign.

New information since 2006. Distal HPs are a common finding at screening colonoscopy.[60] HPs accounted for 50% of polyps 1–5 mm, 27.9% of polyps 6–9 mm, and 13.7% of polyps >10 mm.

Laiyemo et al[61] followed up 437 participants of the Polyp Prevention Trial (PPT) who had baseline HPs coexisting with adenomas. Neither proximal nor distal HPs were associated with an increased risk of recurrent adenomas at 3 years after the baseline examination. There are no other new studies of follow-up colonoscopy in patients with baseline distal HPs.

Recommendation. Prior and current evidence suggests that distal HPs <10 mm are benign and nonneoplastic. If the most advanced lesions at baseline colonoscopy are distal HPs <10 mm, the interval for colonoscopic follow-up should be 10 years.

Unresolved issues and areas for further research. Future research should include patients with distal HPs in analyses of surveillance outcomes.

Baseline examination: 1–2 tubular adenomas <10 mm.

2006 recommendation for next examination	5- to 10-year interval
2012 recommendation for next examination	No change
Quality of evidence	Moderate – evidence stronger than 2006

Background. Prior evidence suggested that patients with LRAs had a lower risk of developing advanced adenomas during follow-up compared with patients with HRAs. An independent meta-analysis and systematic review in 2006 confirmed the findings of the MSTF.[63] At that time, the consensus on the task force was that "observations of cohort studies supports an interval of at least 5 years in this low-risk group; however we reasoned that based on the data from Atkin et al[62]. . .that a 10 year interval, similar to that used in the average-risk population, also would be acceptable."

New information since 2006. There are new studies[7,14,50,51,63–66] confirming that individuals with LRAs represent a low-risk group (Table 6). Laiyemo et al[64] used the 2006 guideline to predict risk for advanced neoplasia during surveillance in the PPT, comparing high-risk with low-risk patients. The probability of recurrence of advanced adenoma was 0.09 among patients with HRAs at baseline and 0.05 among those with LRAs at baseline (RR, 1.68; 95% confidence interval [CI], 1.19–2.38).

The NCI Pooling Project analyzed data from 8 prospective studies in which patients with baseline adenomas were followed up over 3–5 years and had repeat colonoscopy.[7] Compared with patients with LRAs, ORs were increased in patients with 3 or more adenomas, size ≥10 mm, and villous histology. The VA Cooperative Study 380[14] compared risk of advanced neoplasia at 5 years in 298 patients with no baseline neoplasia (2.4%) and 496 patients with 1–2 tubular adenomas <10 mm (4.6%), with an adjusted RR of 1.92 (0.83–4.42) not reaching statistical significance.

Korean investigators followed up patients for 5 years after baseline colonoscopy.[51] HRAs were found in 2.0% of 1242 patients with no baseline neoplasia compared with 2.4% in 671 patients with LRAs (adjusted HR, 1.14 [0.61–2.17]). The Prostate Lung Colorectal Ovarian Cancer study[67] compared rates of advanced neoplasia during 6–7 years of follow-up after baseline colonoscopy. Among 318 patients with no adenoma at baseline, the risk of advanced neoplasia during surveillance was similar to those with LRAs (5.3%).

Recommendation. Data published since 2006 endorse the assessment that patients with 1–2 tubular adenomas with low-grade dysplasia <10 mm represent a low-risk group. Three new studies suggest that this group may have only a small, nonsignificant increase in risk of advanced neoplasia within 5 years compared with individuals with no baseline neoplasia.

The evidence supports a surveillance interval of longer than 5 years for most patients. We recognize that quality of the bowel preparation may result in a less than optimal

Table 6. Follow-up of Patients With Adenomas at Baseline Colonoscopy

Reference	Type of study	Rate or risk of advanced adenoma during surveillance
Saini et al, 2006[63]	Meta-analysis: 5 studies stratified by index findings	Baseline RR: ≥3 vs 1–2 adenomas, 2.52 Villous vs TA, 1.26 Adenoma >10 mm vs ≤10 mm, 1.39 HGD vs low-grade dysplasia, 1.84
Laiyemo et al, 2008[64]	PPT N = 1905	Baseline RR: LRA, 1.00 (ref) HRA, 1.68 (1.19–2.38)
Lieberman et al, 2007[14]	N = 895 with baseline neoplasia	Baseline rate of AA at 5 y: 1–2 TA <10 mm, 6.1% TA >10 mm, 15.5% ≥3 adenomas, 15.9% Villous adenoma/TVA, 16.1%
Martinez et al, 2009[7]	Pooling 8 studies	Baseline OR: Size >10 mm, 1.56 ≥3 adenomas, 1.32 Proximal adenoma, 1.68 Villous adenoma/TVA, 1.40
Miller H et al, 2010[50]	VA cohort	Baseline rate of AA at follow-up: LRA 5 y (n = 77), 5.2% LRA 6–10 y (n = 81), 6.2% HRA 5 y (n = 23), 26.1%
Miller J et al, 2010[65]	Cohort N = 88	Baseline rate of AA at follow-up: 1–2 small tubular adenomas, 4.5%
Chung et al, 2011[51]	Cohort	Baseline rate of AA at follow-up: LRA (n = 671), 2.4% HRA (n = 539), 12.2%
Cottet et al, 2011[66]	Cohort, population-based registry, France; 7.7-y follow-up	Baseline rate of CRC at follow-up: LRA (n = 3236), 0.8%; SIR, 0.68 HRA (n = 1899), 2.8%; SIR, 2.23

AA, advanced adenoma; TA, tubular adenoma; SIR, standardized incidence ratio.

examination in some portions of the colon. In a recent report, when the bowel preparation was inadequate,[68] the miss rates for adenoma and advanced adenoma at 1 year were 35% and 36%, respectively. Factors associated with finding an adenoma on subsequent examination included lack of cecal intubation (OR, 3.62; 95% CI, 2.50–5.24) and finding a polyp at the baseline examination (OR, 1.55; 95% CI, 1.17–2.07). In these circumstances, a 5-year interval might still be prudent.

Unresolved issues and areas for further research. Most studies have not subclassified patients whose largest polyp is diminutive (1–5 mm) versus small (6–9 mm) on screening examinations. Improvements in colonoscopy have resulted in higher detection rates for diminutive polyps. Future study is needed to stratify risk for individuals with LRAs <6 mm and LRAs 6–9 mm in diameter.

Baseline examination: 3–10 adenomas.

2006 recommendation for next examination	3-year interval
2012 recommendation for next examination	No change
Quality of evidence	Moderate: if any polyp ≥6 mm Low: if all polyps <6 mm Evidence stronger than 2006

Background. Two independent meta-analyses in 2006 found that patients with 3 or more adenomas at baseline had an increased RR for adenomas during surveillance, ranging from 1.7 to 4.8.[3,63] Other studies show that patients with multiple adenomas are more likely to have adenomas detected at 1 year, suggesting that lesions may be more likely to be missed on the baseline examination when multiple polyps are present. These data form the basis of the recommendation for a 3-year interval, similar to the recommendation for large polyps and those with advanced histology. The earlier studies did not stratify multiplicity based on size. Many of the studies of multiplicity include patients with larger polyps. It was not possible to determine if the risk level was different if all polyps were <6 mm versus >6 mm.

New information since 2006. Two new studies reported outcomes in patients with multiple adenomas. The NCI Pooling Project[7] analysis found that with each additional adenoma, there is a linear increase in risk for both advanced and nonadvanced neoplasia (Table 7).

The VA study (which contributed data to the pooling project) also provided a second referent group: patients with no baseline neoplasia.[14] The risk of advanced neoplasia at 5 years was 2.4% in the nonneoplasia referent group, 4.6% if patients had 1–2 tubular adenomas <10

Table 7. NCI Pooling Project (8 Studies): Risk of Advanced Adenoma at 3–5 Years Based on Number of Polyps at Baseline Colonoscopy[7]

Baseline adenoma no.	% with advanced adenoma at follow-up (95% CI)	Adjusted OR (95% CI)
1	8.6 (7.8–9.3)	1.00 (referent)
2	12.7 (11.3–14.1)	1.39 (1.17–1.66)
3	15.3 (12.9–17.6)	1.85 (1.46–2.34)
4	19.6 (15.3–19.3)	2.23 (1.71–3.40)
5+	24.1 (19.8–28.5)	3.87 (2.76–5.42)
P trend		<.0001

From Martinez et al.[7]

mm (RR, 1.92; 95% CI, 0.83–4.42), and 11.9% if they had 3 or more tubular adenomas <10 mm (RR, 5.01; 95% CI, 2.10–11.96). The VA study shows that even if all of the adenomas are <10 mm, there is increased risk of advanced neoplasia with multiplicity of adenomas.

Recommendation. The new information from the VA study and the NCI Pooling Project support the previous recommendation that patients with 3 or more adenomas have a level of risk for advanced neoplasia similar to other patients with advanced neoplasia (adenoma >10 mm, adenoma with HGD). There are insufficient new data to support a change in the prior recommendation.

Unresolved issues and areas for further research. Historically, some older studies had lower rates of adenoma detection compared with modern studies. In a recent review[69] of screening studies (n = 18), the prevalence of adenomas in average-risk cohorts was 30.2% (range, 22.2%–58.2%). In more recent screening studies using modern technology (such as high-definition white light), adenoma detection rates of 40% or more have been reported.[70] Therefore, it is very likely that there was misclassification of some patients in earlier studies; patients reported to have 1–2 adenomas may have had additional adenomas that were not detected.

There remains some doubt about whether patients who have 3–5 diminutive adenomas (all <6 mm) really have an increased risk of interval advanced neoplasia during surveillance. However, there is little doubt that if patients have 3 or more adenomas, and at least one is advanced, the risk of having advanced neoplasia during surveillance is high. In the VA study, these patients had a nearly 10-fold increased RR compared with patients with no neoplasia and a 5-fold increased RR compared with those with 1–2 small tubular adenomas.[14]

Further research is needed to determine the level of risk of advanced neoplasia if a patient has 3–5 adenomas all <6 mm at the baseline examination. These new studies should use modern colonoscopic technology to determine an accurate number of adenomas at baseline.

Baseline examination: >10 adenomas.

2006 recommendation for next examination	<3-year interval
2012 recommendation for next examination	No change
Quality of evidence	Moderate-high

Background. These patients represent a small proportion of patients undergoing screening examinations. The 2006 guideline noted that such patients should be considered for hereditary syndromes. The recommendation for early follow-up is based on clinical judgment because there is little evidence.

New evidence since 2006. There are no new studies that single out this small group of patients for analysis. The NCI Pooling Project notes a marked increased risk of advanced neoplasia among patients with 5 or more adenomas at baseline.

Recommendation. There is no basis for changing the recommendation to consider follow-up in less than 3 years after a baseline colonoscopy.

Baseline examination: one or more tubular adenomas ≥10 mm.

2006 recommendation for next examination	3-year interval
2012 recommendation for next examination	No change
Quality of evidence	High – evidence stronger than 2006

Background. The 2006 guideline reviewed data related to adenoma size, demonstrating that most studies showed a 2- to 5-fold increased risk of advanced neoplasia during follow-up if the baseline examination had one or more adenomas ≥10 mm.

New information since 2006. The NCI Pooling Project analyzed polyp size as a risk factor for development of interval advanced neoplasia (Table 6).[7] Compared with patients with adenomas <5 mm, those with baseline polyp(s) 10–19 mm had an increased risk of advanced neoplasia (15.9% vs 7.7%; OR, 2.27; 95% CI, 1.84–2.78). If the baseline polyp was 20 mm or more, the risk of advanced neoplasia at follow-up was 19.3% (OR, 2.99; 95% CI, 2.24–4.00). In the VA Cooperative Study 380, the referent group was patients with no neoplasia.[14] The risk of advanced neoplasia within 5.5 years was 2.4% in the no neoplasia group and 15.5% in patients with baseline adenomas >10 mm (RR, 5.01; 95% CI, 2.10–11.96).

Recommendation. The new information provides additional data showing that patients with one or more adenomas ≥10 mm have an increased risk of advanced neoplasia during surveillance compared with those with no neoplasia or small (<10 mm) adenomas. There is no basis for changing the recommended 3-year surveillance interval. This recommendation assumes that the examination was of high quality and complete removal of neoplastic tissue occurred at baseline. This group represents a small proportion of all patients with adenomas. If there is question about complete removal (ie, piecemeal resection), early follow-up colonoscopy is warranted.

Table 8. Clinical Features of Serrated Lesions of the Colorectum

World Health Organization classification	Prevalence	Shape	Distribution	Malignant potential
Hyperplastic polyp	Very common	Sessile/flat	Mostly distal	Very low
Sessile serrated adenoma/polyp	Common	Sessile/flat	80% proximal	
No dysplasia				Low
Dysplastic				Significant
Traditional serrated adenoma	Uncommon	Sessile or pedunculated	Mostly distal	Significant

Baseline examination: one or more adenomas with villous features of any size.

2006 recommendation for next examination	3-year interval
2012 recommendation for next examination	No change
Quality of evidence	Moderate

Background. The 2006 guideline regarded adenomas with villous histology to be HRA.

New information since 2006. The NCI Pooling Project analyzed polyp histology as a risk factor for development of interval advanced neoplasia (Table 6).[7] Compared with patients with tubular adenomas, those with baseline polyp(s) showing adenomas with villous or tubulovillous histology (TVA) had increased risk of advanced neoplasia during follow-up (16.8% vs 9.7%; adjusted OR, 1.28; 95% CI, 1.07–1.52). The level of risk was lower than that associated with size or multiplicity. In the VA Cooperative Study 380, the referent group was patients with no neoplasia.[14] The risk of advanced neoplasia within 5.5 years was 2.4% in the no neoplasia group and 16.1% in patients with baseline adenomas >10 mm (RR, 6.05; 95% CI, 2.48–14.71).

Recommendation. The new information provides additional data showing that patients with one or more adenomas with villous histology have an increased risk of advanced neoplasia during surveillance compared with those with no neoplasia or small (<10 mm) tubular adenomas. There is no basis for changing the recommended 3-year surveillance interval.

Unresolved issues and areas for further research. The available studies do not separately identify patients whose most advanced polyp is a TVA or villous adenoma <10 mm in size. Future studies should stratify risk based on both pathology and polyp size.

Baseline examination: one or more adenomas with HGD.

2006 recommendation for next examination	3-year interval
2012 recommendation for next examination	No change
Quality of evidence	Moderate

Background. The 2006 guideline concluded that the presence of HGD in an adenoma was associated with both villous histology and larger size, which are both risk factors for advanced neoplasia during surveillance.

New information since 2006. In a univariate analysis from the NCI Pooling Project,[7] HGD was strongly associated with risk of advanced neoplasia during surveillance (OR, 1.77; 95% CI, 1.41–2.22). The NCI Pooling Project did not find that HGD was independently associated with an increased risk of metachronous advanced neoplasia (OR, 1.05; 95% CI, 0.81–1.35) after adjustments for size and histology, which are known confounders. Toll et al[71] followed up 83 patients with HGD over a median of 4 years, during which 7% developed new HGD or CRC.

Recommendation. The presence of an adenoma with HGD is an important risk factor for development of advanced neoplasia and CRC during surveillance. There is no basis for changing the recommended 3-year surveillance interval.

Baseline examination: serrated polyps.

2006 recommendation for next examination	None
2012 recommendation for next examination	See Table 1
Quality of evidence	Low

Background. A total of 20%–30% of CRCs arise through a molecular pathway characterized by hypermethylation of genes, known as CIMP.[23] Precursors are believed to be serrated polyps (Table 8). Tumors in this pathway have a high frequency of BRAF mutation, and up to 50% are microsatellite unstable. CIMP-positive tumors are overrepresented in interval cancers, particularly in the proximal colon. The principal precursor of hypermethylated cancers is probably the sessile serrate polyp (synonymous with sessile serrated adenoma; Table 8). Sessile serrated polyps sometimes have foci of cytological dysplasia, which indicates a more advanced lesion in the polyp-cancer sequence.

These polyps are difficult to detect at endoscopy. They may be the same color as surrounding colonic mucosa, have indiscrete edges, are nearly always flat or sessile, and may have a layer of adherent mucus and obscure the vascular pattern.

New information since 2006. The clinical implications of serrated polyps are uncertain. Recent studies show that proximal colon location or size >10 mm may be markers of risk for synchronous advanced adenomas elsewhere in the colon.[72,73] Surveillance after colonoscopy was evaluated in one study, which found that coexisting serrated polyps and HRA is associated with a higher risk of advanced neoplasia at surveillance.[72] This study also found that if small proximal serrated polyps are the only finding at baseline, the risk of adenomas during surveillance is similar to that of patients with LRA.

Table 9. Multiple Rounds of Colonoscopy Surveillance

		Advanced neoplasia at second surveillance (%)		
Baseline colonoscopy	First surveillance	Pinsky et al, 2009, Prostate Lung Colorectal Ovarian Cancer study[67]	Laiyemo et al, 2009, PPT[77]	Robertson et al, 2009[78]
HRA	HRA	19.3	30.6	18.2
	LRA	6.7	8.9	13.6
	No adenoma	5.9	4.8	12.3
LRA	HRA	15.6	6.9	20.0
	LRA	5.7	4.7	9.5
	No adenoma	3.9	2.8	4.9
No adenoma	HRA	11.5		
	LRA	4.7		
	No adenoma	3.1		

NOTE. HRA is defined as 3 or more adenomas, tubular adenoma ≥10 mm, adenoma with villous histology, or HGD. LRA is defined as 1–2 tubular adenomas <10 mm.

Recommendation. Prior surveillance guidelines did not comment on surveillance intervals if proximal serrated polyps are found at baseline colonoscopy. There are no longitudinal studies available on which to base surveillance intervals after resection. Our recommendation is based on low-quality evidence and will require updating when new data are available. The current evidence suggests that size (>10 mm), histology (a sessile serrated polyp is a more significant lesion than an HP; a sessile serrated polyp with cytological dysplasia is more advanced than a sessile serrated polyp without dysplasia), and location (proximal to the sigmoid colon) are risk factors that might be associated with higher risk of CRC. A sessile serrated polyp ≥10 mm and a sessile serrated polyp with cytological dysplasia should be managed like HRA (Table 1). Serrated polyps that are <10 mm and do not have cytological dysplasia may have lower risk and can be managed like LRA.

Unresolved issues and areas for further study. There is considerable variation in detection rate by different endoscopists[74,75] and histologic interpretation by pathologists[76] that makes it challenging to evaluate the natural history of serrated polyps. It is likely that many patients are misclassified because of one or both of these factors. Because of this interobserver variation in pathologic interpretation, some experts endorse a position that all proximal colon serrated lesions ≥10 mm should be considered sessile serrated polyps, even if the pathologic interpretation is HP. Further study is needed to reduce interobserver variability in diagnosis and determine natural history.

Other Issues Related to Colon Surveillance

Surveillance after the first follow-up colonoscopy. The follow-up of patients after they undergo surveillance has been uncertain. It is not clear if risk continues to be increased if surveillance colonoscopy reveals an LRA or no neoplasia. There are 3 new cohort studies that have followed up patients over several surveillance cycles to determine the risk of advanced neoplasia over time.[67,77,78] These studies all have important limitations, because many patients did not receive a second surveillance, which could lead to selection bias, and intervals were irregular. Data from these studies are summarized in Table 9. These data suggest that the detection of an advanced adenoma is an important risk factor for finding advanced adenoma at the next examination. Once patients have a low-risk lesion or no adenoma, the risk of advanced neoplasia at the next examination is lower. Patients with LRA at baseline and no adenomas at first surveillance have a very low risk (2.8%–4.9%) of having advanced adenomas at the second surveillance examination 3–5 years later. Although the evidence is weak due to incomplete follow-up of the cohorts, it is consistent across 3 longitudinal studies.

Recommendation. We believe that patients with LRA at baseline and negative findings at first surveillance can have their next surveillance examination at 10 years. Patients who have HRA at any examination appear to remain at high risk and should have shorter follow-up intervals for surveillance. A summary of these recommendations is outlined in Table 10.

When should surveillance stop? There is considerable new evidence that the risk of colonoscopy increases with advancing age.[79,80] Both surveillance and screening should not be continued when risk may outweigh benefit. The United States Preventive Services Task Force (USPSTF) determined that screening should not be continued

Table 10. Recommendations for Polyp Surveillance After First Surveillance Colonoscopy

Baseline colonoscopy	First surveillance	Interval for second surveillance (*y*)
LRA	HRA	3
	LRA	5
	No adenoma	10
HRA	HRA	3
	LRA	5
	No adenoma	5[a]

[a]If the findings on the second surveillance are negative, there is insufficient evidence to make a recommendation.

after age 85 years[81] because risk could exceed potential benefit. Patients with HRA are at higher risk for developing advanced neoplasia compared with average-risk screenees. Therefore, the potential benefit of surveillance could be higher than for screening in these individuals. For patients aged 75–85 years, the USPSTF recommends against continued routine screening but argues for individualization based on comorbidities and findings of any prior colonoscopy. This age group may be more likely to benefit from surveillance, depending on life expectancy.

It is the opinion of the MSTF that the decision to continue surveillance should be individualized, based on an assessment of benefit, risk, and comorbidities.

When should colonoscopy be repeated if there is a poor bowel preparation at baseline colonoscopy? Poor-quality bowel preparations that obscure visualization of the colon may be associated with missed lesions at the baseline colonoscopy.[68,82] Current quality indicators for colonoscopy call for monitoring the quality of bowel preparation,[39] with the goal of achieving preparations adequate for detection of lesions >5 mm. There is now substantial evidence[83] that splitting the dose of bowel preparation results in better quality, and this practice is strongly encouraged by the MSTF.

If the bowel preparation is poor, the MSTF recommends that in most cases the examination should be repeated within 1 year. Alternative methods of imaging, such as CT colonography, also require excellent bowel preparation for an adequate examination. If the bowel preparation is fair but adequate (to detect lesions >5 mm) and if small (<10 mm) tubular adenomas are detected, follow-up at 5 years should be considered.

Positive FOBT (guaiac FOBT or fecal immunochemical test) result before scheduled surveillance. If patients have an adequate baseline colonoscopy, surveillance colonoscopy should be based on the current guidelines. Patients should not have interval fecal blood testing if colonoscopy is planned. The role of interval fecal testing is uncertain.[84] A recent study from Australia found that interval fecal immunochemical test led to diagnosis of cancers before the scheduled surveillance.[85] However, this study included patients with baseline cancer and did not provide information about the findings or quality of the baseline examination, which may have been important risk factors for interval pathology.

In clinical practice, patients may have had an interval FOBT performed. A decision to perform an early colonoscopy due to positive fecal test result could be based on careful review of the baseline examination. If this examination was not complete or somewhat compromised by fair bowel preparation, it may be quite reasonable to perform an early examination. There are no data to support the practice of a routine early examination and no evidence that these patients have a higher than expected risk of cancer or advanced adenoma.

Interval fecal testing should not be a substitute for high-quality performance of colonoscopy. The task force recommends that interval fecal testing not be performed within the first 5 years after colonoscopy. There is currently insufficient evidence to support this practice. The likelihood of false-positive test results is high, which would result in unnecessary early colonoscopies.

If fecal blood test is performed in the first 5 years after colonoscopy, there is insufficient evidence to make a recommendation. If the patient does have an interval-positive FOBT result, the clinician's judgment to repeat colonoscopy could consider the prior colonoscopy findings, completeness of examination and bowel preparation, and family history. Despite the low likelihood of significant pathology if the baseline examination was high quality, we recognize that there may be concerns about missed lesions at the baseline examination. Potential medical-legal issues often lead to repeat examination. Future studies of this subject should carefully document the quality of the baseline examination and determine rates of significant pathology.

Development of new symptoms during the surveillance interval (minor rectal bleeding, diarrhea, constipation). Patients may develop new problems within 3–5 years after colonoscopy that might otherwise be indications for colonoscopy. If patients develop significant lower gastrointestinal bleeding as defined by clinical judgment, they may need further evaluation.

Change in bowel habits, abdominal pain, or minor rectal bleeding are common symptoms that may occur after completion of a colonoscopy. This creates a clinical dilemma: should colonoscopy be repeated before the scheduled surveillance examination? The likelihood of finding significant pathology after a prior complete and adequate colonoscopy is uncertain but likely to be low. However, if the colonoscopy will answer an important clinical question, it may be valuable to repeat.

The consensus of the task force is that there is insufficient evidence to make a recommendation.

Should surveillance be modified based on lifestyle risk factors for CRC? There is considerable new evidence that risk of recurrent adenomas may be reduced by taking aspirin or nonsteroidal anti-inflammatory drugs.[11,54–57] We believe there is insufficient evidence to recommend any change in surveillance intervals in patients who are taking these medications.

Should surveillance be modified based on patient race, ethnicity, or sex? CRC age-adjusted risk varies based on patient demographic characteristics. However, there is no new evidence that that the surveillance interval should be altered once patients have had colonoscopy and polypectomy based on these factors.

Discussion

The 2006 MSTF guideline provided a valuable framework for polyp surveillance based on the histology and number of polyps detected at the baseline examination. We find that new data since 2006 support these recommendations.

The current guideline recommendations apply only to high-quality baseline examinations.

Quality indicators[37–39] for reporting and performance have been well documented and should become part of routine endoscopic practice. Several key performance indicators, such as cecal intubation rate and adenoma detection rate, are associated with rates of interval cancer.[16,42] The task force believes that quality indicators must be measured as an essential part of a colonoscopy screening and surveillance program.

The 2006 guideline posed several important questions, some of which are now addressed:

What are the reasons that guidelines are not followed more closely? The utilization of colonoscopy for surveillance has an important impact on resource utilization and health care costs. New evidence suggests that surveillance is often overutilized, which increases cost and risk to patients and the health care system. Reasons for poor adherence to guidelines are unclear. We speculate that concerns about interval cancer after colonoscopy may result in some overutilization during surveillance. Incorporation of the guidelines as quality indicators of colonoscopy may improve adherence.

Will emerging studies with longer colonoscopy follow-up times support the safety of lengthening surveillance intervals? New evidence from 3 longitudinal studies in which patients have undergone multiple surveillance examinations has identified a low-risk group that may require little or no surveillance after 2 examinations.[65,77,78]

What is the role of family history in predicting advanced adenomas and CRC? There is some new evidence that individuals with an FDR with CRC or HRA have an increased risk of developing HRA or CRC.[59]

What roles will chromoendoscopy, magnification endoscopy, narrow band imaging, and CT colonography play in postpolypectomy surveillance? The role of new endoscopic technologies has not been studied in surveillance cohorts, although there are ongoing studies of CT colonography. The technical endoscopic enhancements may increase the likelihood of detecting small polyps. Chromoendoscopy and narrow band imaging may enable endoscopists to accurately determine if lesions are neoplastic, and if there is a need to remove them and send material to pathology. At this point, these technologies do not have an impact on surveillance intervals.

What is the usefulness of FOBT in postpolypectomy surveillance? A new study[85] found that a positive fecal immunochemical test performed at some interval before scheduled surveillance colonoscopy, may help identify patients who may benefit from early surveillance. This study did not evaluate baseline findings or examination quality to determine their relationship to development of interval CRC. The question of interval testing to detect interval CRC is important and merits further study.

What is the importance of the serrated polyp pathway and detection of serrated adenomas and proximal HPs? The current guideline reviews new information about serrated polyps and makes recommendations for follow-up.

What is the appropriate surveillance of patients who had an adenoma removed in piecemeal resection? Flat and sessile adenomatous and serrated polyps >15 mm are increasingly removed using injection-assisted polypectomy and piecemeal resection technique. There are insufficient data upon which to base a recommendation. However, the MSTF recommends consideration of a short interval for repeat colonoscopy (<1 year) if there is any question about completeness of resection of neoplastic tissue.

The MSTF believes that the evidence supporting these recommendations for screening and surveillance intervals has become stronger in the past 6 years. We have highlighted areas of uncertainty that require further research. The guidelines are dynamic and will be revised in the future based on new evidence. This new evidence should include information about the quality of the baseline examinations. The task force recommends that all endoscopists monitor key quality indicators as part of a colonoscopy screening and surveillance program.

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Reprint requests

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Conflicts of interest

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