Screening for colorectal cancer (CRC) is effective. Randomized controlled trials (RCTs) have demonstrated that fecal blood tests and endoscopic screening (with flexible sigmoidoscopy) are effective. Primary screening with colonoscopy has been shown to reduce CRC incidence and mortality in uncontrolled cohort and case–control studies.

After screening is completed, there are important questions about the interval of follow-up exams. This discussion will review newly updated information about intervals after a negative baseline exam and after an exam with neoplasia. The sections are based on the most advanced finding of the baseline colonoscopy.

Baseline Exam Negative for Neoplasia: Average Risk
Guidelines have recommended a 10-year interval, based largely on three lines of evidence. First, the natural history of the adenoma-carcinoma sequence suggests that it takes at least 10 years to progress from normal tissue to adenoma to CRC. Second, RCTs using flexible sigmoidoscopy have demonstrated a protective effect of at least 10 years. Third, cohort and case-control studies of colonoscopy show a durable reduced incidence and mortality of 10 years or more.

However, there are concerns about reports of interval cancer, defined as CRC occurring within 3-5 years after a baseline colonoscopy. Analyses of cancer registries reveal that 2-9% of patients with CRC had a prior colonoscopy within 3-5 years, without a diagnosis of CRC. In studies of adenoma-bearing patients who have all polyps removed, the risk of CRC within 3 years is 0.3-0.9% (1-3 per 1,000 person-years of follow-up). It is likely that many or most of the interval CRCs are related to exam quality: either lesions are missed on baseline exam, or polyps are incompletely removed. Recent studies have shown that the adenoma detection rate is inversely related to the risk of interval CRC. Interval CRC tend to be located in the proximal colon, and have some biologic characteristics associated with the serrated polyp pathway. Endoscopists should carefully examine the proximal colon to detect these lesions. Quality of the baseline exam is critical to reducing the likelihood of interval CRC.

New evidence supports a 10-year interval after negative baseline screening. Six studies since 2007 found that the rate of advanced neoplasia at 5 years after a negative baseline colonoscopy is low, averaging around 2%. If the baseline colonoscopy was complete with good bowel prep, the risk of developing an interval cancer or advanced neoplasia is low, and a 10-year interval is recommended. There is no evidence that average-risk individuals with rectal or sigmoid hyperplastic polyps have a higher risk of CRC.

Family History of CRC; Negative Baseline Colonoscopy
Individuals with a first degree relative (FDR) with CRC have a higher personal risk of CRC, particularly if the FDR was less than 60 years of age at the time of diagnosis. For these individuals with FDR less than 60 years of age, the recommended interval for screening should be 5 years.

Baseline Exam with 1-2 Tubular Adenomas < 10 mm
There is a growing body of evidence that this is a low-risk group. Three studies were able to compare 5-year risk of advanced neoplasia in the following groups: no adenoma versus 1-2 tubular adenomas less than 10 mm. There is a small numerical increase in risk, but it was statistically non-significant in each of the studies. The absolute risk of advanced neoplasia at 5 years is 2.4-5.3%. The current recommendation is a 5-10 year interval. However, these data support a surveillance interval of longer than 5 years for most patients, assuming the baseline exam was of high quality.

Baseline Exam with 3-10 Adenomas
There is growing evidence that multiplicity of adenomas is associated with a higher risk of advanced neoplasia at surveillance. The absolute risk of advanced neoplasia at 3-5 years is 15-24% in individuals with three or more adenomas. The available studies include patients with diminutive (1-5 mm), small (5-9 mm), and larger polyps, and do not answer the following question: what if all adenoma are 5 mm or less? Based on the current available evidence, a 3-year surveillance interval is recommended. Individuals with 10 or more adenomas should be examined at a shorter interval (less than 3 years), because of the high likelihood that lesions are missed at the baseline exam.

Baseline Exam with ≥ 1 Adenomas > 10 mm, with Villous Histology or High-grade Dysplasia
There is strong evidence that these individuals represent a high-risk group. Compared to patients with no neoplasia at baseline, the relative risk is increased 5-6 fold. Compared to patients with tubular adenomas < 10 mm at baseline, these patients have a 2- to 3-fold higher risk of advanced neoplasia during surveillance. The absolute risk is around 16% at 3 years.
The recommended surveillance interval is 3 years. This assumes a complete removal of all lesions at baseline. If lesions were removed piecemeal, or there is uncertainty about completeness of polypectomy, exams should be repeated within 1 year.

Patients with CRC at baseline (with complete exam of colon) should have follow-up at 1 year after resection of CRC. Patients with CRC who had an incomplete baseline exam due to obstructive tumor should have a clearing exam of the remaining colon within 3-6 months of the CRC resection.

Baseline Exam with Serrated Polyps
Approximately 20-30% of CRC arise through a molecular pathway characterized by CPG island methylation. Methylation can result in silencing of a key mismatch repair gene (MLH1), which can promote carcinogenesis. The natural history of serrated lesions is uncertain for several reasons. There is substantial inter-observer variability in interpretation of histopathology, leading to misclassification. A second problem is failed endoscopic detection. These lesions are very flat, located in the proximal colon, often covered by mucus, and represent a significant challenge for endoscopic detection.

Therefore, recommendations for surveillance are based on very weak evidence, subject to change with more data. For individuals with hyperplastic polyposis, follow-up at 1 year is recommended until all polyps have been removed. For those with serrated polyps < 10 mm with no cytological dysplasia, follow-up is recommended at 5 years, similar to low-risk adenomas (LRA). Patients with larger (> 10 mm) serrated lesions, or lesions with cytological dysplasia, follow-up is recommended at 3 years, similar to high-risk adenomas (HRA).

Surveillance after the First Follow-up Colonoscopy
Three studies have performed “serial” surveillance (Table 1). Distinctions are made for patients with LRA adenomas at baseline (defined as one tubular adenoma < 10 mm at baseline) and HRA (size > 10 mm, or advanced histology).

Summary
Most recommendations for surveillance are now supported by stronger evidence. The age for stopping surveillance should be individualized based on expected time horizon and consideration of risk and benefit. There is now substantial evidence that if the bowel prep is inadequate at baseline, the exam should be repeated to complete the exam. Endoscopists should monitor the quality of bowel preps, and the frequency of repeat examinations as a quality indicator. Quality of endoscopy is an important element of the surveillance recommendation. All endoscopists should monitor key indicators as part of a colonoscopy screening and surveillance program.

### Table 1

<table>
<thead>
<tr>
<th>Baseline Colonoscopy</th>
<th>First Surveillance</th>
<th>Interval for Second Surveillance (Years)</th>
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</thead>
<tbody>
<tr>
<td>LRA</td>
<td>HRA</td>
<td>3</td>
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<tr>
<td>LRA</td>
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<td>5</td>
</tr>
<tr>
<td>No adenoma</td>
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<td>10</td>
</tr>
<tr>
<td>HRA</td>
<td>HRA</td>
<td>3</td>
</tr>
<tr>
<td>LRA</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>No adenoma</td>
<td></td>
<td>5 (weak evidence)</td>
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</tbody>
</table>

### REFERENCES