COLORECTAL CANCER

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EPIDEMIOLOGY

Countries with the highest incidence rates include Australia, New Zealand, Canada, the USA, and intermediate parts of Europe.

The countries with the lowest risk include China, India, Sub-Saharian Africa and South America.

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EPIDEMIOLOGY

In Quebec, CRC is the second leading cause of cancer-related deaths among men and the third among women.

It usually develops on Polyps (more than 90% Adenomas).

Adenocarcinoma is the most common type of CRC. It makes up more than 95% of all CRC's.

From the Quebec Government official website

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EPIDEMIOLOGY

Cancer of the colon and rectum (colorectal cancer) is a major cause of cancer associated morbidity and mortality in North America, Europe and other regions where life-styles and dietary habits are similar.

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EPIDEMIOLOGY

In 2017, there will be an estimated 95,520 new cases of colon cancer and 39,910 cases of rectal cancer diagnosed in the US.[12]

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EPIDEMIOLOGY

While the numbers for **colon** cancer are fairly equal in men (47,700) and women (47,820), a larger number of men (23,720) than women (16,190) will be diagnosed with **rectal** cancer.

- (American Cancer Society : Colorectal Cancer. Facts and figures 2017-2019)

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EPIDEMIOLOGY

Estimated Canadian colorectal cancer statistics (2017)		
Category	**Males**	**Females**
New cases	14,900	11,900
Incidence rate (for every 100,000 people)*	79.6	54.9
Deaths	5,100	4,300
Death rate (for every 100,000 people)*	28.1	19.0
5-year net survival (estimates for 2006–2008)	63%	65%

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EPIDEMIOLOGY

Chances (Probability) of developing or dying from CRC:

It is estimated that about 1 in 13 Canadian men will develop colorectal cancer during his lifetime and 1 in 29 will die from it.

It is estimated that about 1 in 16 Canadian women will develop colorectal cancer during her lifetime and 1 in 34 will die from it.

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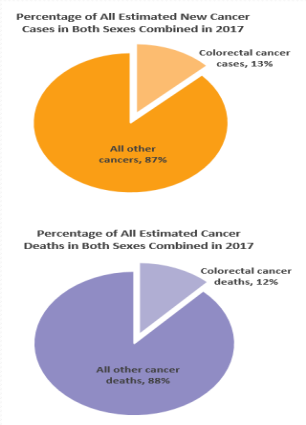
EPIDEMIOLOGY



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Potential years of life lost due to cancer, Canada, 2009

- **Lung** represents around 300,900 of potential years of life lost (PYLL) . This cancer represents 27.1% of all cancers, this is the cause of 152,200 years of life lost and 28.1% in males 148,700 and 26.1% in females.
- **Colorectal** represents 121,900 (PYLL) and 11.0% of all cancers: Males 65,100 or 12.0 %.

  Females 56,800 or 10.0%.

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Lifetime costs of colon and rectal cancer management in Canada

- Colorectal cancer is the second leading cause of cancer-related mortality among Canadians.
- The total lifetime treatment cost for the cohort of patients in 2000 was estimated to be over $333 million for colon and $187 million for rectal cancer.
- Hospitalization represented 65% and 61% of the lifetime costs of colon and rectal cancer respectively.

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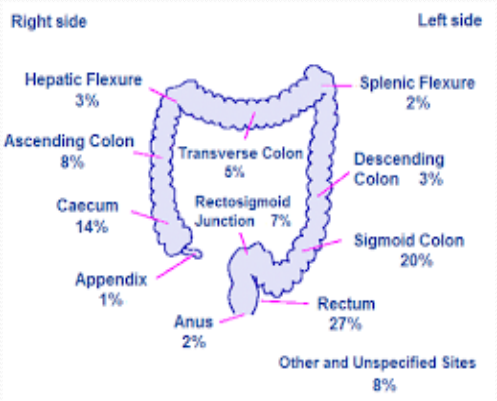
CRC Distribution



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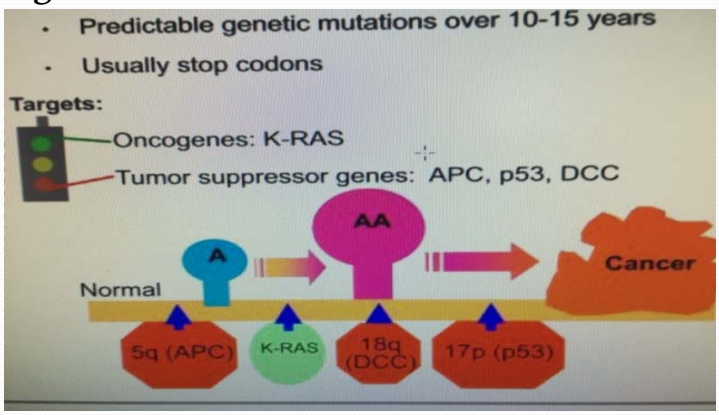
Chromosomal Instability

The Vogelstein model: Adenoma to carcinoma



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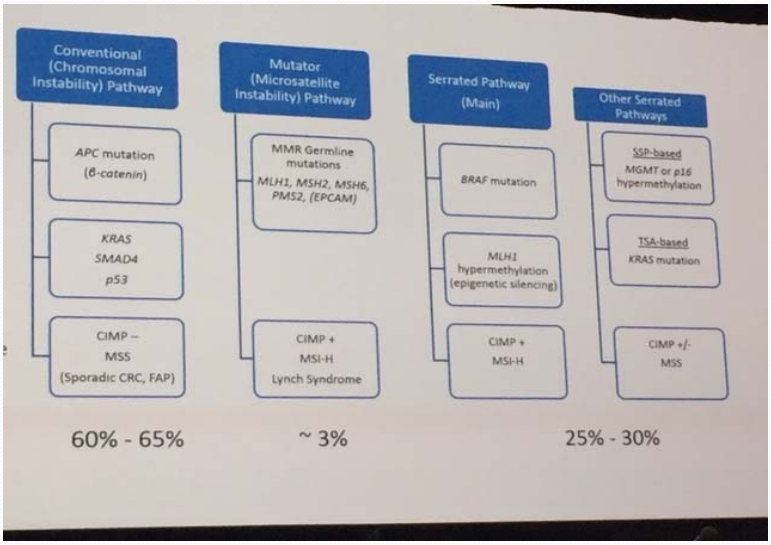

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Heredity and family history

Up to 30% of CRC patients have a family history of the disease, about 5% of which are due to an inherited genetic abnormality

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Revised Amsterdam Criteria II

There should be at least three relatives with an HNPCC-associated cancer (cancer of the colon-rectum, endometrium, small bowel, ureter, or renal pelvis) and:

- One should be a first-degree relative to the other two;
- At least two successive generations should be affected;
- At least one should be diagnosed before age 50;
- Familial adenomatous polyposis should be excluded;
- Tumors should be verified by pathological examination.

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Relative Risks for Established Colorectal Cancer Risk Factors

Factors that increase risk:	
Heredity and medical history	**Relative risk**
1 first-degree relative	2.2
More than 1 relative	4.0
Relative with diagnosis before age 45	3.9
Inflammatory bowel disease	1.7
Diabetes	1.3

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Relative Risks for Established Colorectal Cancer Risk Factors

Behavioral factors	**Relative risk**
Alcohol consumption (daily average)	
2-3 drinks	1.2
>3 drinks	1.4
Obesity (body mass index ≥30 kg/m2)	1.3
Red meat consumption (100 g/day)	1.2
Processed meat consumption (50 g/day)	1.2
Smoking (ever vs. never)	1.2

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Relative Risks for Established Colorectal Cancer Risk Factors

Factors that decrease risk:	Relative risk
Physical activity (colon)97	0.7
Dairy consumption (400 g/day)119	0.8
Milk consumption (200 g/day)119	0.9

*Relative risk compares the risk of disease among people with a particular "exposure" to the risk among people without that exposure. Relative risk for dietary factors compares the highest with the lowest consumption. If the relative risk is more than 1.0, then risk is higher among exposed than unexposed persons. Relative risks less than 1.0 indicate a protective effect.

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CRC Screening

Colorectal cancer (CRC) screening is the process of detecting early-stage CRC's and precancerous lesions in asymptomatic people with no prior history of cancer or pre-cancerous lesions.

USMSTF: 06-2017

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CRC Screening (USMSTF recommendations) 2017

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CRC Screening (USMSTF recommendations) 2017

- **We recommend**: That screening begin in non-African American, average risk persons, at age 50 years (Strong recommendation; moderate quality of evidence).

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CRC Screening (USMSTF recommendations)

We suggest: That screening begin in African Americans at age 45 years(Weak recommendation, very low quality of evidence).

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CRC Screening (USMSTF recommendations)

We recommend: That adults age< 50 years with colorectal bleeding symptoms (Hematochezia, melena with a negative UGI endoscopy, unexplained Iron deficiency anemia). Undergo colonoscopy to determine a bleeding cause, initiate treatment and complete follow up to determine resolution of bleeding (strong recommendation, moderate quality of evidence)

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CRC Screening (USMSTF recommendations)

We suggest: That persons who are up to date with screening and have negative prior screening tests particularly colonoscopy, consider stopping screening at age 75 years or when life expectancy is less than 10 years(weak recommendation, low quality of evidence)

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CRC Screening (USMSTF recommendations)

We suggest: That persons at high risk without prior screening should be considered for screening up to age 85 years depending on consideration of their age/functional status (life expectancy) and comorbidities (weak recommendation, low quality of evidence)

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Considerations When Deciding with Your Doctor Which Test Is Right for You

	Benefits	Performance and complexity	Limitations	Time interval
Visual Examinations:				
Colonoscopy:	- Examines entire colon - Biopsy, polyp removal - Can diagnose other diseases. - Required from abnormal results from other tests	**Performance:** High(for large polyps) **Complexity:** Highest	- Full bowel cleansing - Expensive - Sedation needed and a ride day of exam - patient will miss a day of work. - Highest risk of complic. compared with other tests	10 years

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Considerations When Deciding with Your Doctor Which Test Is Right for You

	Benefits	Performance and complexity	Limitations	Time interval
Visual Examinations:				
CT Colonography:	-Examines entire colon - Fairly quick -Few complications - No sedation needed - Non invasive procedure	**Performance:** High (large polyps) **Complexity:** Intermediate	- Full bowel cleansing - Can not remove polys /do biopsies. - Radiation exposure - Colonoscopy often necessary if + or dubious	**5 years**

CTC Has replaced double contrast Barium Enema. In Canada only indication is for incomplete colonoscopies. Polyps larger than 6 mm should undergo colonoscopy .

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Considerations When Deciding with Your Doctor Which Test Is Right for You

	Benefits	Performance and complexity	Limitations	Time interval
Visual Examinations:				
Flexible sigmoidoscopy:	- Fairly quick - Few complications - Minimal bowel prep. - No sedation or Gastro required	**Performance:** High for rectum, **Complexity:** Intermediate	-Partial bowel cleansing - Views only 1/3 of colon Can not remove large polyps. - Low complication rate - Better combined with annual FIT - Colono need if + - Limited availability	**5 y.**

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Considerations When Deciding with Your Doctor Which Test Is Right for You

	Benefits	Performance and complexity	Limitations	time Interval
Stool tests:				
Low-sensitivity stool tests, such as single-sample FOBT done in the doctors office or toilet bowl tests are not recommended.				
Fecal immuno-Chemical test (FIT)	- No bowel cleansing or sedation - Performed at home - Low cost - Non invasive - One sample test	**Performance:** Intermediate for CRC **Complexity:** Low	-Will miss most polyps - False positives -Slightly better if combined with FS	**1-2 y.**

Any gain in sensitivity is of interest only if specificity and positive predictive value are satisfactory.

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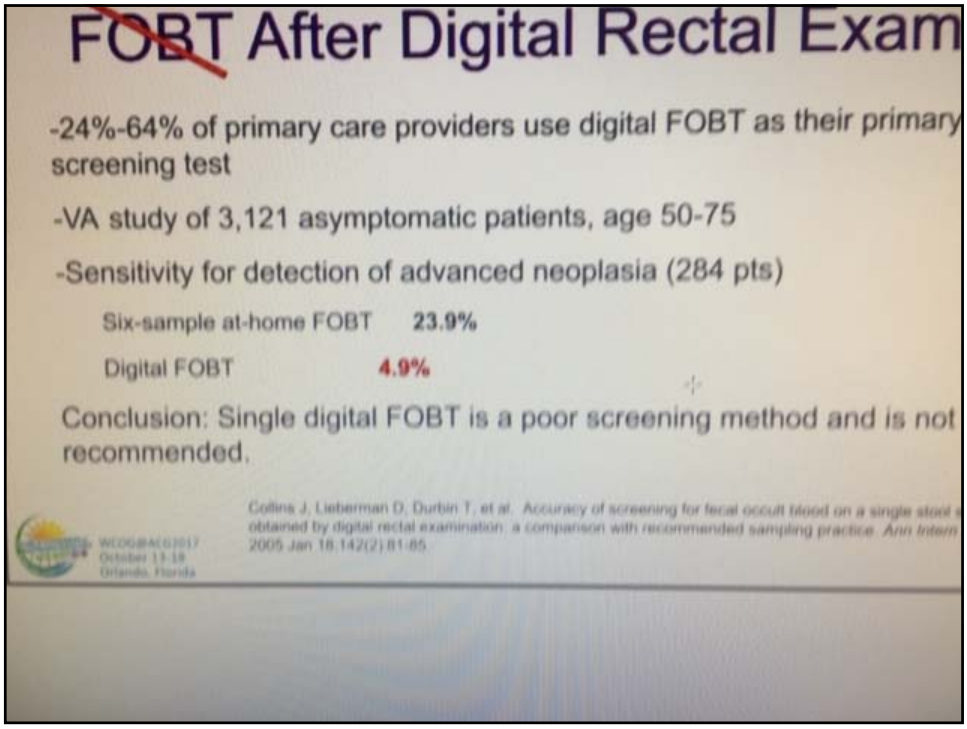

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FOBT after digital exam

Single digital FOBT is a poor screening method for colorectal neoplasia and cannot be recommended as the only test. When digital FOBT is performed as part of a primary care physical examination, negative results do not decrease the odds of advanced neoplasia. Persons with these results should be offered at-home 6-sample FOBT or another type of screening test.

Judith F. Collins, MD; David A. Lieberman, MD; Theodore E. Durbin, MD; David G. Weiss, PhD; and the Veterans Affairs Cooperative Study #380 Group*

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Fecal immunochemical test

- Advantages of FIT include its noninvasive nature, 1-time sensitivity (Only human Hb).
- for cancer of 79% in 1 meta-analysis, fair sensitivity for advanced adenomas (approximately 30%), and low 1-time cost (approximately $20).
- FIT is recommended at least every 2 years in Canada.

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FIT-DNA test

Recommendation:

- Fecal DNA testing is currently not recommended for programmatic CRC screening.
- High false positive rate
- Costs double than FIT and
- Test performance was similar to FOBT in 2 meta -analysis.

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CRC screening

- Current rates of screening for CRC in Canada are 39% of the eligible population (2017)
- The 80% by 2018 initiative:
- The National Colorectal Cancer Roundtable (NCCRT), established in 1997 by the American Cancer Society and the CDC.

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CRC screening

- The ultimate goal of the NCCRT is to increase the use of recommended CRC screening tests among appropriate populations.
- In March 2014, the NCCRT launched the 80% by 2018 initiative, an ambitious goal to reach an 80% CRC screening rate of adults 50 and older by 2018.

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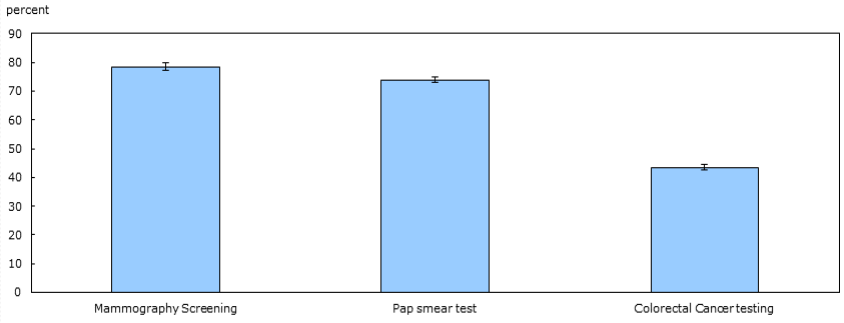
Chart 1
Meeting "The Canadian Task Force on Preventative Health Care (CTFPHC)" cancer screening guidelines, Canada, 2017



Note: The Canadian Task Force on Preventative Health Care (CTFPHC) recommends adults aged 50 to 74 receive a fecal occult blood test every two years or a sigmoidoscopy every 10 years for colorectal cancer testing. The CTFPHC recommends a mammogram every 2 to 3 years for women aged 50 to 74, and Pap test every three years for women aged 25 to 69.
Source: Canadian Community Health Survey, 2017.

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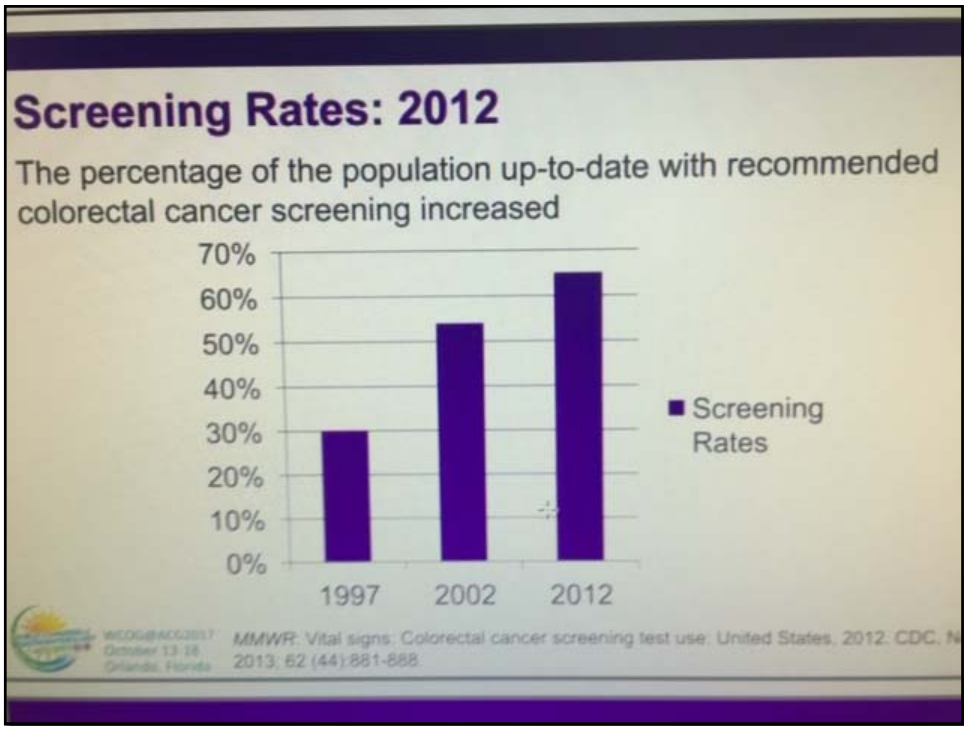

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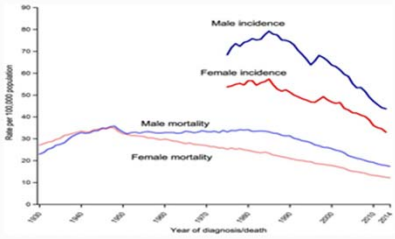
Decreasing CRC Incidence and Mortality

From R. Siegel et Al.



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Technology		Adenomas missed 1st Pass	
Traditional Forward View		30 - 40+%	
FUSE		7%	Lancet Oncol. 15 (2014), pp. 353-360
Third Eye (Original)		18%	Gastrointest Endosc. 73 (2011), pp. 480-489
Endocuff		14.7 %	Endoscopy. 2017 Aug 1. doi: 10.1055/s-0043-114412.
EndoRings		10.4%	Endoscopy 2015;47:1151-8.
G-Eye		7.5%	Endoscopy. 2015 Mar;47(3):238-44
Third eye Panoramic		-	

WCOG@ACG2017
October 13-18
Orlando, Florida

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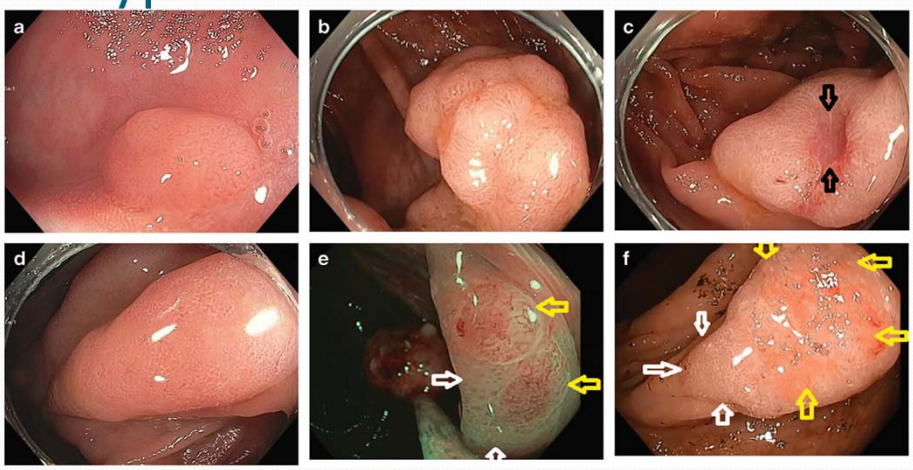
Polyps



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DEMANDE DE COLOSCOPIE LONGUE

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Histologic classification of the two major classes of colorectal polyps

Conventional adenomas:

Dysplasia grade:

- High grade
- Low grade

Villousity

- Tubular
- Tubulo-villous
- Villous

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Histologic classification of the two major classes of colorectal polyps

Serrated lesions:

1.-Hyperplastic polyps (not considered pre-cancerous)

2.-Sessile serrated polyp

- Without dysplasia
- With dysplasia

3.-Traditional serrated adenoma (SSA)

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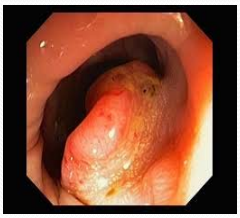
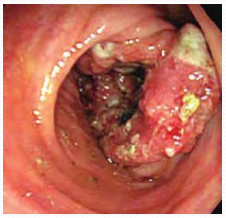
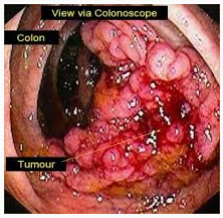
Colorectal Cancer







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

Baseline colonoscopy: Most advanced findings	Recommended surveillance interval	Quality of evidence	New evid. stron ger than 2006
No polyps	10 y	Moderate	Yes
< 10 mm H.P polyps of recto-sigmoid	10 y	Moderate	No
1-2 < 10 mm Tubular adenomas	5-10 y	Moderate	Yes
3-10 Tubular adenomas	3 y	Moderate	Yes
>10 adenomas	< 3 y	Moderate	No
1 or more Tubular adenomas >10 mm	3 y	High	Yes
Adenoma with HGD	3 y	Moderate	No

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

Baseline colonoscopy: Most advanced findings	Recommended surveillance interval	Quality of evidence	New evid. stron ger than 2006
Serrated lesions:			
Sessile serrated polyp(s) <10mm With no dysplasia	5 y	Low	N/A
Sessile serrated polyp(s)> 10 mm Or SSA with dysplasia or traditional Serrated Adenoma	3 y	Low	N/A
Serrated Adenoma Polyposis Syndrome	1 y	Moderate	N/A

NOTE. The recommendations assume that the baseline colonoscopy was complete and adequate and that all visible polyps were completely removed. GASTROENTEROLOGY 2012;143:844–857

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ACRCSP POST-POLYPECTOMY SURVEILLANCE GUIDELINES

Screening Intervals Following a Normal Colonoscopy:

Risk	Screening interval
• Average risk using	Re-screen in 10 years "average risk" strategy
• Family history of CRC/high risk polyp in one First degree relative<= 60 years at diagnostic Or 2 or more first grade relatives of any age At diagnosis.	Repeat colonoscopy in 5 y
• Known or suspected Lynch Syndrome	Repeat colonoscopy 1-2 y

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Surveillance Intervals for Adenomatous Lesions

Pathology	Screening interval	Subsequent intervals*	
Low risk Adenomas **(LRA)**	Repeat colono in 5-10 y	No adenoma :	10 y
1-2 small <10mm adenomas		LRA:	5 y
With LGD		HRA:	3 y
HRA: 3-10 adenomas or one		No adenoma:	5 y
adenoma>= 10 mm or any ade-	Repeat colono in 3 y	LRA:	5 y
noma with villous features or		HRA:	3 y
HGD			
More than 10 adenomas	Repeat colono < 3 y	No adenoma	5 y
Sessile polyps removed by piece-	Repeat colono 2-6 mo.	No adenoma	5 y
meal	to ensure complete removal	LRA	5 y
	then surveillance in 3 y	HRA	3 y

*based on findings at first surveillance colonoscopy

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Remember:

It generally takes 5-10 years for a small adenoma to develop into a malignancy; cancer may be prevented by adenoma removal (ADR index).

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Epidemiological natural history of colorectal cancer

Initial presentation of colorectal cancer (100%)

Candidate for resection
- (60 - 70%)

Non- resectable
- (30 - 40%)

Cured by surgical resection
- (30 - 45%)

Recurrent disease
- (25 - 40%)

Non- resectable
- (20 - 30%)

Potentially curable by second resection (5 - 10%)

Adapted from: Sloka JS, Hollett PD, Mathews M, McGill Journal of Medicine
http://www.medicine.mcgill.ca/mjm/issues/v07n02/orig_articles/orig_articles5.htm

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Post-Cancer Resection

The goal of follow-up after resection is to identify recurrent disease or metastases and to detect subsequent adenomas. These recommendations are generally expert consensus-based. Patients with significant co-morbidities, very advanced age or limited 5 year life expectancy are not routinely offered surveillance.

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Follow-up visits with Family Physician

Focused history and physical examination are recommended every 3 to 6 months for 2 years, and then every 6 months for a total of 5 years.

It is recommended that each follow-up visit include:

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Follow-up visits with Family Physician

- **History** to elicit gastrointestinal and constitutional symptoms, including nutritional status.
- **Physical examination** with particular attention to the abdomen, liver and rectal evaluation (or perineal inspection and palpation in those patients who have had an abdominal perineal resection).
- **Routine laboratory investigations**, such as liver chemistry, in the absence of symptoms are not useful.

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Carcinoembryonic antigen in the staging and follow-up of patients with colorectal cancer

Because of its lack of sensitivity in the early stages of colorectal cancer, CEA measurement is an unsuitable modality for population screening.

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Carcinoembryonic antigen in the staging and follow-up of patients with colorectal cancer

Frequent monitoring of CEA postoperatively may allow identification of patients with metastatic disease for whom surgical resection or other localized therapy might be potentially beneficial

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Carcinoembryonic antigen in the staging and follow-up of patients with colorectal cancer

Several authors argue that CEA surveillance is not cost-effective in terms of lives saved.

In support of this argument, there is no clear difference in survival after resection of metastatic disease with curative intent between patients in whom the second-look surgery was performed on the basis of elevated CEA levels and those with other laboratory or imaging abnormalities.

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Carcinoembryonic antigen in the staging and follow-up of patients with colorectal cancer

ASCO guidelines currently recommend every 2-3 months for at least 2 years after diagnosis.

In the follow-up of patients undergoing palliative therapy, the CEA level correlates well with response, and CEA is indicative of not only response but may also identify patients with stable disease for whom there is also a demonstrated benefit in survival and symptom relief with combination chemotherapy.

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Imaging on follow up of patients with colorectal cancer

ASCO justifies the recommendation to perform yearly CT scan of the abdomen for the first 3 years following surgery because all of the published meta-analyses showed a survival benefit for "liver imaging." Specifically, there appears to be significantly more surgical procedures performed for recurrence and a 25% lower mortality for patients undergoing liver imaging compared with non-imaging strategies.

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Colonoscopy follow up of patients with colorectal cancer

The role of follow-up colonoscopies to evaluate for anastomotic recurrence and metachronous colorectal cancers is the most widely accepted surveillance modality and it is included in most published colorectal cancer surveillance guidelines.

Colonoscopy 1-3 and 5 years after curative resection should be offered, then if no recurrence Q 5 years as to high risk population.

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