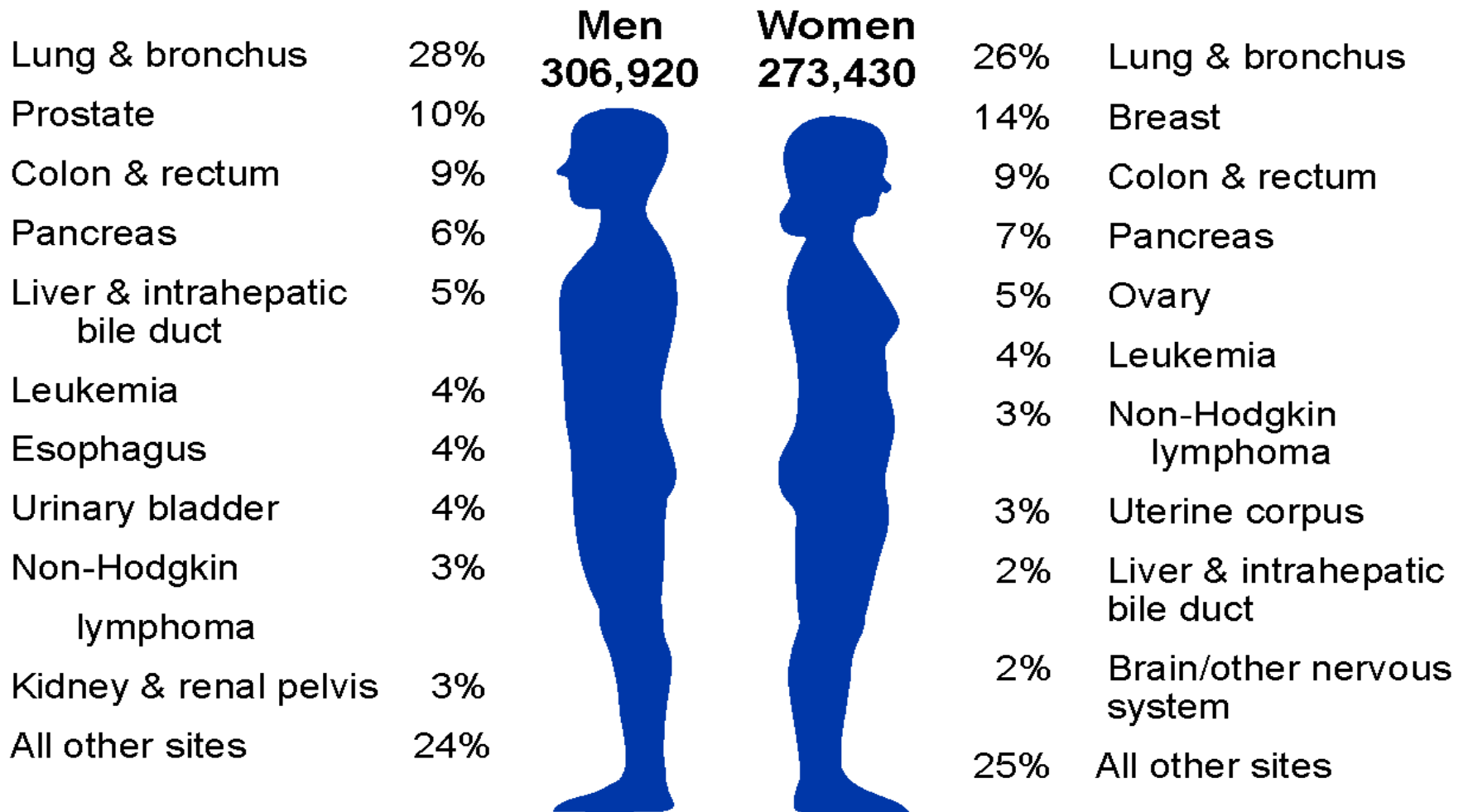


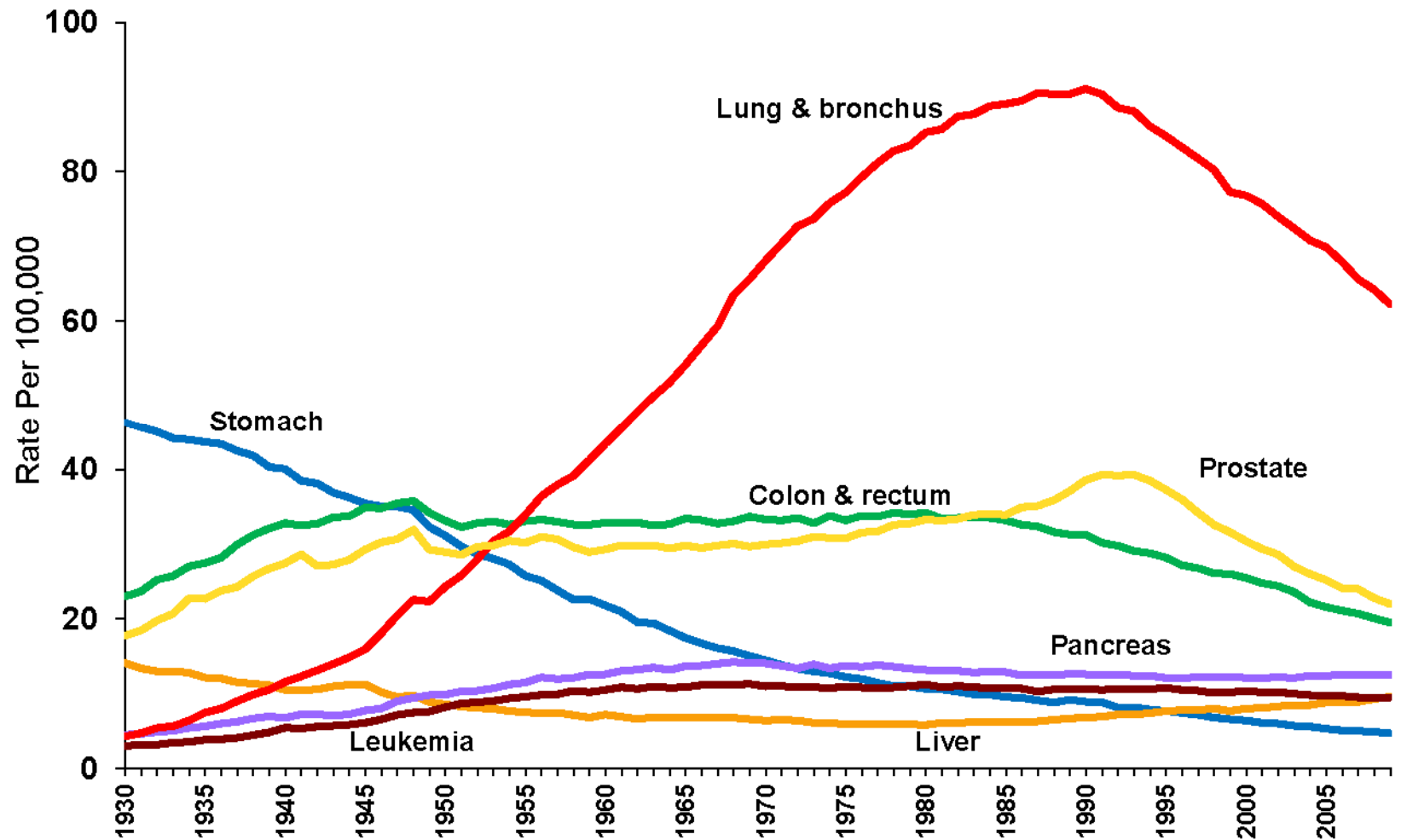
Ca del colon retto: introduzione

C. Castello

Estimated Cancer Deaths in the US in 2013



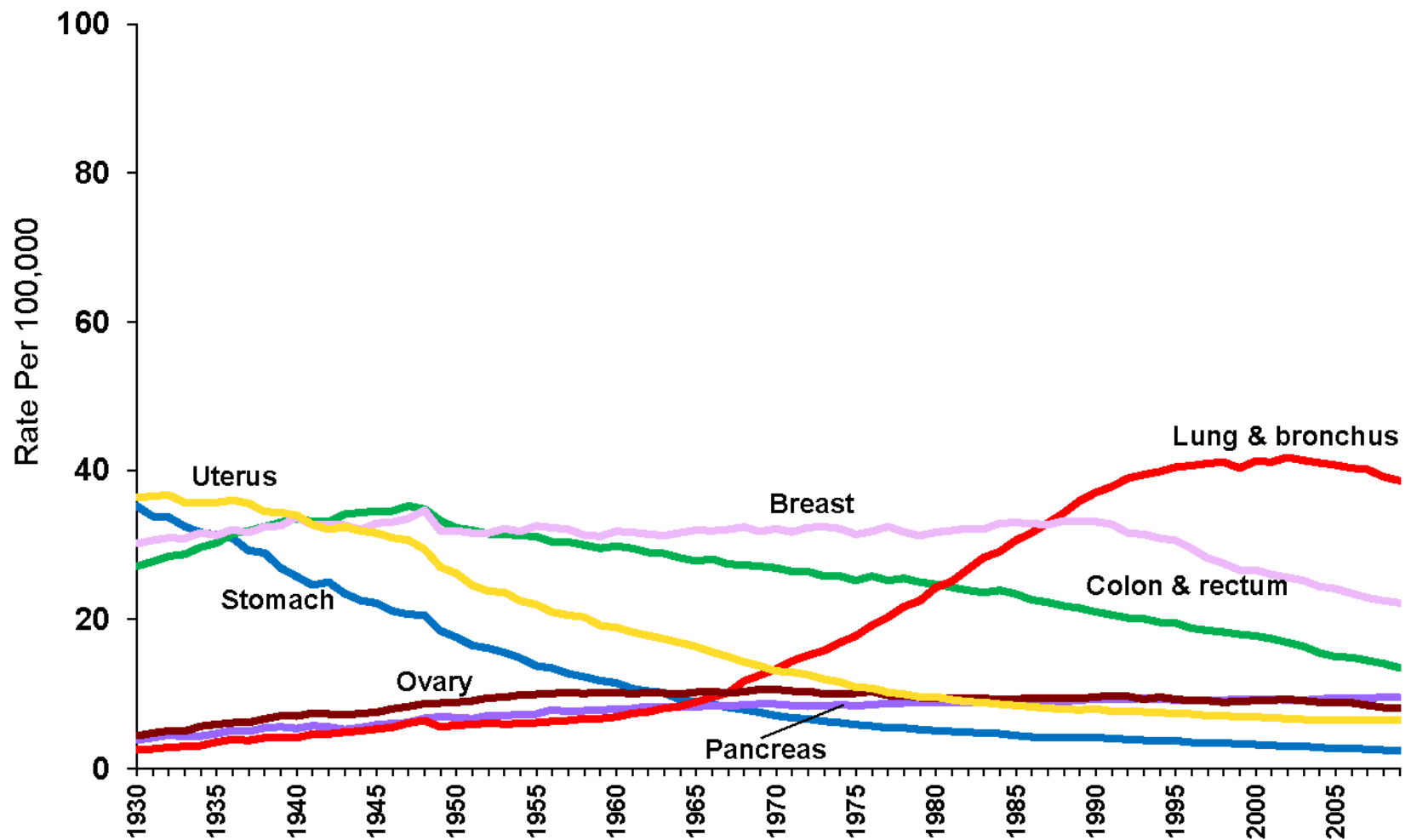
Cancer Death Rates* Among Men, US, 1930-2009



*Age-adjusted to the 2000 US standard population.

Source: US Mortality Data 1960-2009, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention.

Cancer Death Rates* Among Women, US, 1930-2009



*Age-adjusted to the 2000 US standard population.

Source: US Mortality Data 1960-2009, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention.



I nuovi casi di tumore

Sede	2011	2020	2030
VADS	9.042	10.804	11.996
Stomaco	13.695	18.648	21.367
Colon-retto	49.720	55.815	63.573
Fegato	12.695	14.443	16.559
Pancreas	10.788	12.180	13.928
Polmone	37.755	44.861	51.451
Cute melanomi	12.865	12.275	13.245
Cute non melanomi	57.586	65.642	74.577
Mammella	44.701	48.984	51.668
Utero corpo	7.465	8.207	8.985
Ovaio	4.770	5.339	5.756
Prostata	42.234	43.090	50.691
Rene vie urinarie*	11.226	12.622	14.134
Vescica**	24.472	30.311	34.906
Tiroide	12.084	9.092	9.144
Linfoma non Hodgkin	12.142	13.423	14.841
Tutti i tumori esclusi epitelomi della cute	416.486	465.003	522.861

Quali tumori più frequenti ?

Nel totale di uomini e donne
nel 2012

	Tipo di tumore	N° nuovi casi in Italia nel 2012
1°	Colon retto	50.000
2°	Mammella	46.000
3°	Polmone	38.000
4°	Prostata	36.000

Rango	Maschi			Femmine		
	anni 0-49	anni 50-69	anni 70+	anni 0-49	anni 50-69	anni 70+
1°	Testicolo (11%)	Prostata (22%)	Prostata (21%)	Mammella (41%)	Mammella (35%)	Mammella (21%)
2°	Linfoma non-Hodgkin (9%)	Colon-retto (15%)	Polmone (17%)	Tiroide (14%)	Colon-retto (13%)	Colon-retto (17%)
3°	Cute (melanomi) (8%)	Polmone (14%)	Colon-retto (15%)	Cute (melanomi) (7%)	Utero corpo (7%)	Polmone (7%)
4°	Colon-retto (8%)	Vescica* (10%)	Vescica* (11%)	Colon-retto (5%)	Polmone (6%)	Stomaco (6%)
5°	Tiroide (7%)	Vie aerodigestive superiori (5%)	Stomaco (6%)	Utero cervice (4%)	Tiroide (5%)	Pancreas (5%)

TABELLA 8. Primi cinque tumori in termini di frequenza e proporzione sul totale dei tumori incidenti (esclusi i carcinomi della cute) per sesso e fascia di età. Pool Airtum 2006-2008.

* comprende sia tumori infiltranti che non infiltranti.

Mortalità

Primi 5 cause di morte oncologica
E proporzione sul totale dei decessi per tumore per sesso e fasce d'età

Rango	Maschi			Femmine		
	anni 0-49	anni 50-69	anni 70+	anni 0-49	anni 50-69	anni 70+
1°	Polmone (15%)	Polmone (31%)	Polmone (26%)	Mammella (28%)	Mammella (21%)	Mammella (14%)
2°	Sistema nervoso centr. (11%)	Colon-retto (10%)	Colon-retto (11%)	Polmone (11%)	Polmone (14%)	Colon-retto (13%)
3°	Colon-retto (8%)	Fegato (8%)	Prostata (11%)	Colon-retto (7%)	Colon retto (10%)	Polmone (10%)
4°	Vie aerodigestive superiori (7%)	Pancreas (7%)	Stomaco (7%)	Sistema nervoso centrale (7%)	Pancreas (7%)	Pancreas (8%)
5°	Stomaco (6%)	Stomaco (6%)	Fegato (6%)	Leucemie (6%)	Ovaio (7%)	Stomaco (7%)

TABELLA 5. Primi cinque cause di morte oncologica e proporzione sul totale dei decessi per tumore per sesso e fascia di età. Pool Airtum 2006-2008.

Incidenza

Primi 5 tumori più frequenti e proporzione sul totale dei tumori per classi d'età..

EZIOLOGIA E FATTORI DI RISCHIO

Fattori ambientali

- Dieta
- Stile di vita
- Fumo
- Inquinamento ambientale

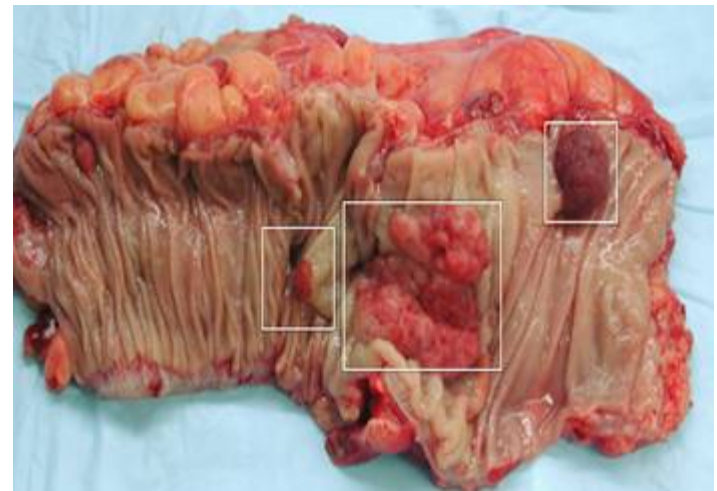


Fattori genetici:

- storia familiare della malattia
- sindromi trasmesse ereditariamente (adenomatosi poliposa familiare o FAP; sindrome di Lynch..)

Altri fattori:

- età
- presenza di polipi nel colon
- processi infiammatori cronici dell'intestino

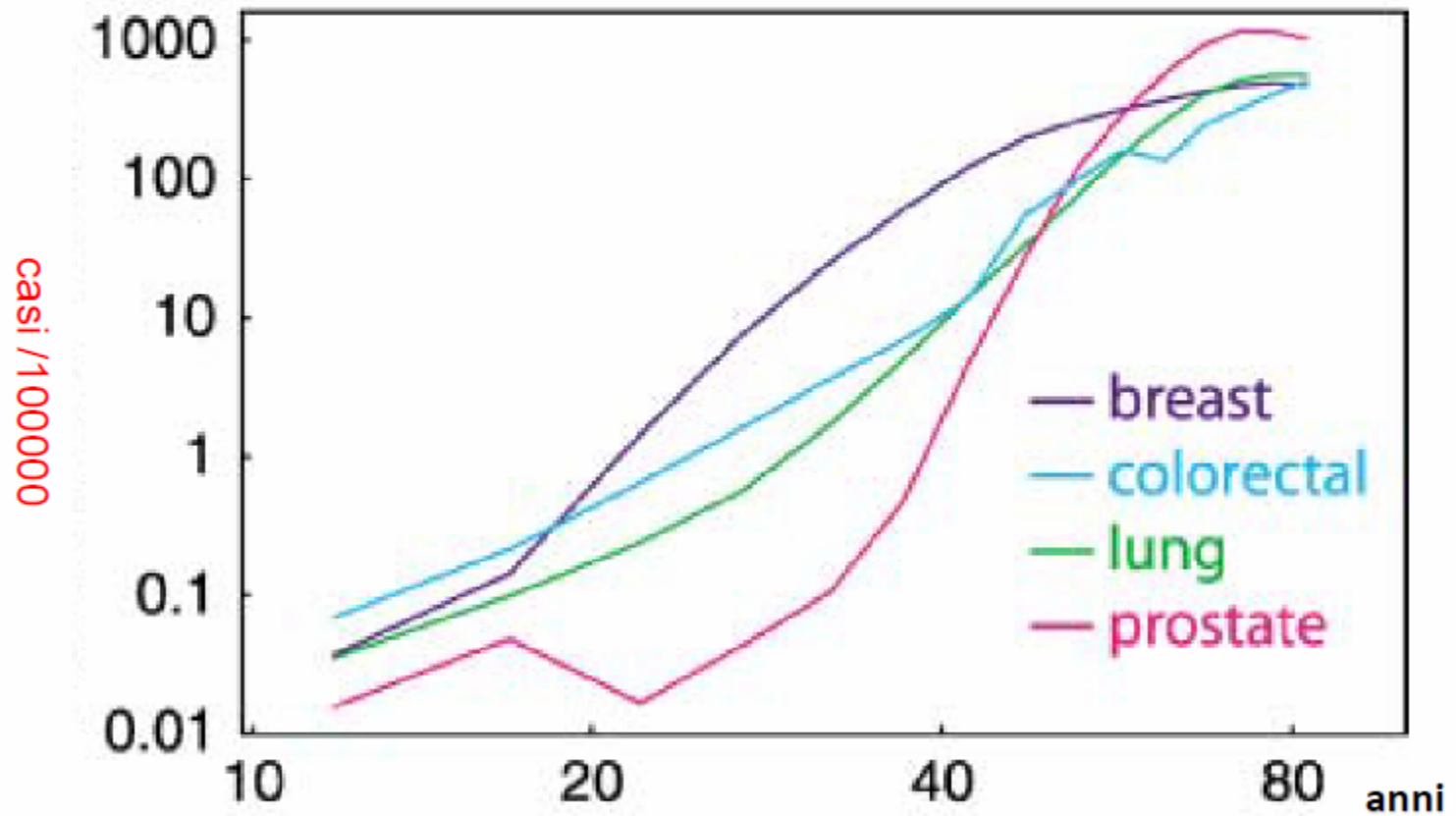


Overview of risk and preventive factors of colorectal cancer

	Risk
Sociodemographic factors	
Older age	↑↑↑
Male sex	↑↑
Medical factors	
Family history	↑↑
Inflammatory bowel disease	↑↑
Diabetes	↑
<i>Helicobacter pylori</i> infection	(↑)
Other infections	(↑)
Large bowel endoscopy	↓↓
Hormone replacement therapy	↓
Aspirin	↓
Statins	(↓)
Lifestyle factors	
Smoking	↑
Excessive alcohol consumption	↑
Obesity	↑
Physical activity	↓
Diet factors	
High consumption of red and processed meat	↑
Fruit and vegetables	(↓)
Cereal fibre and whole grain	(↓)
Fish	(↓)
Dairy products	(↓)

Età e cancro

Incidenza / 100000



PATHOGENESIS OF COLORECTAL CANCER

HNPCC, FAP



CANCER

1-5% of total

FAMILIAL CANCER



CANCER

10-20% of total

SPORADIC CANCER



CANCER

70-80% of total



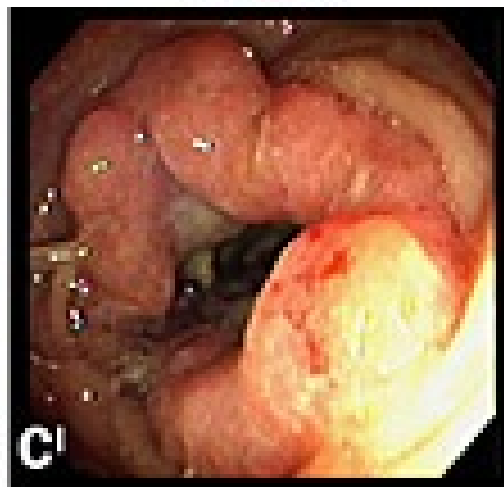
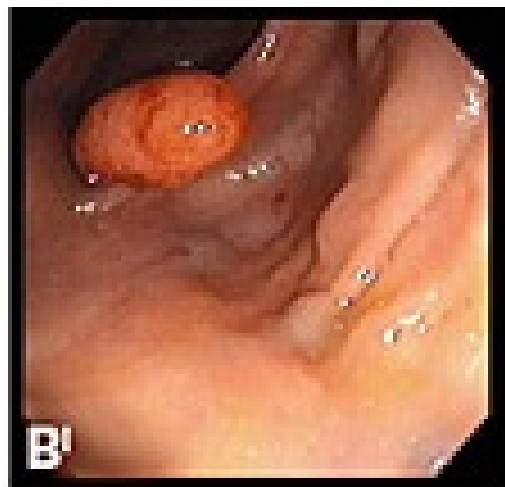
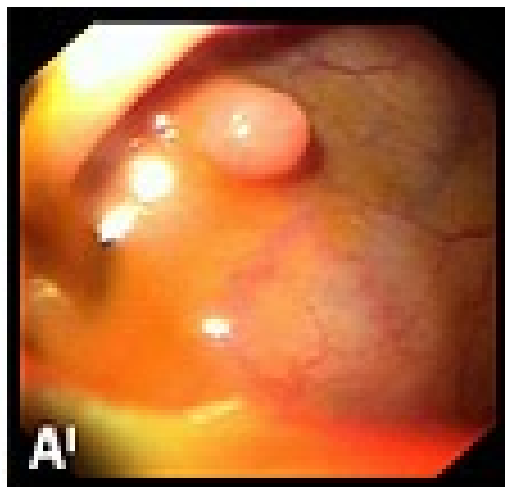
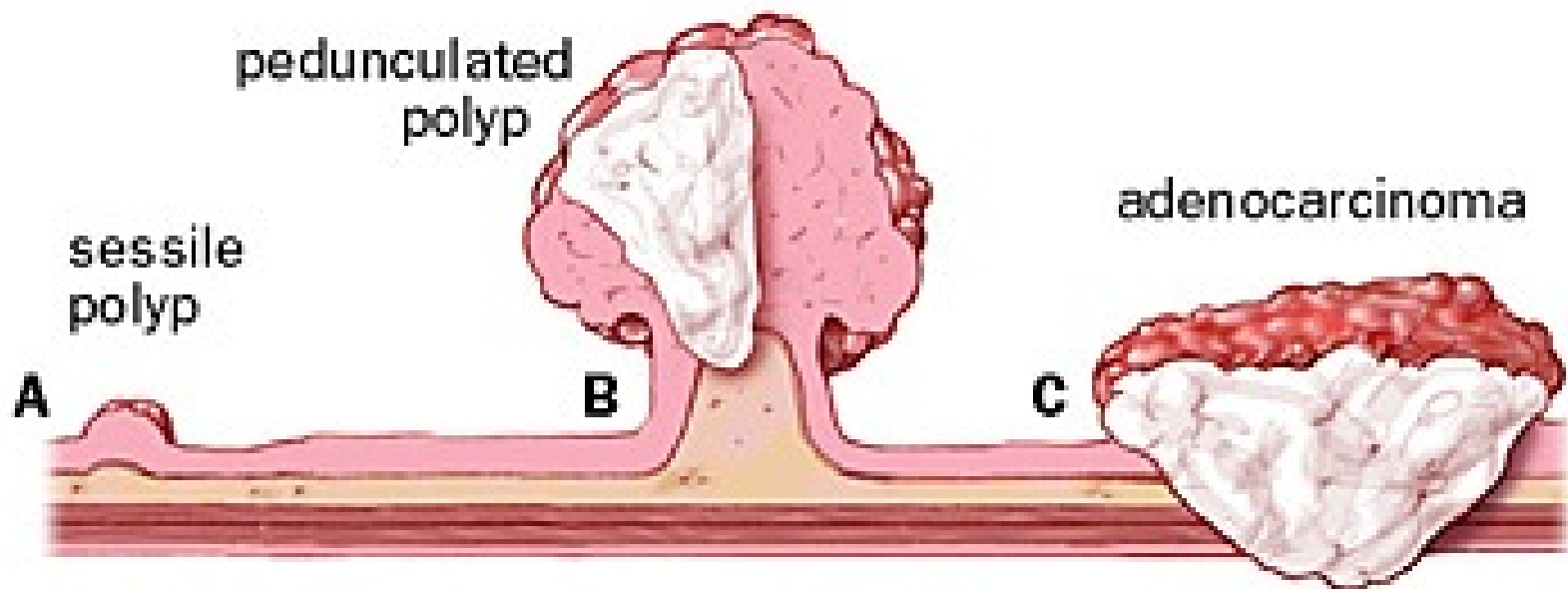
Single gene mutations (APC, MSH2, MLH1, PMS1-2)
Polygenic inheritance



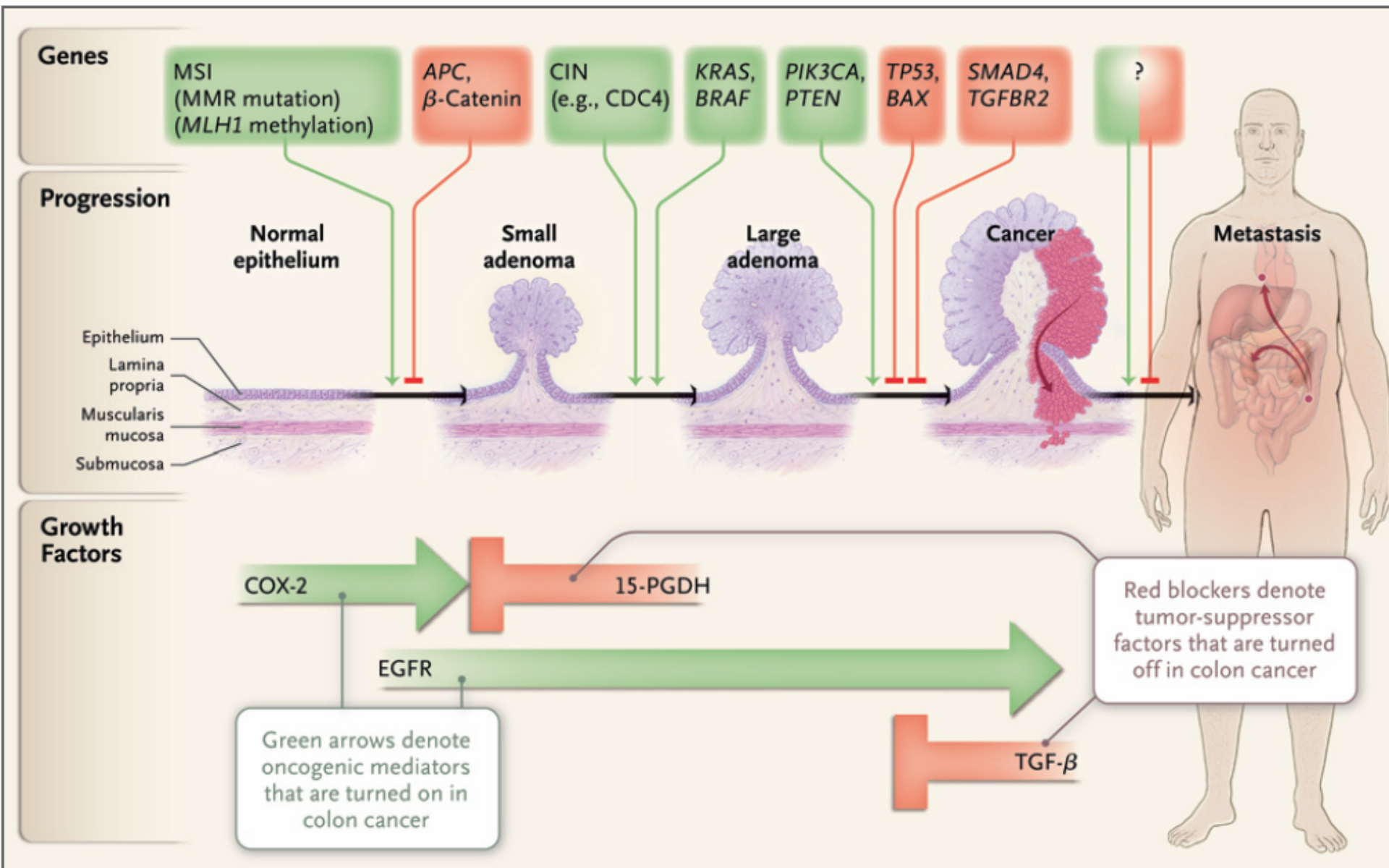
Environmental factors (diet, obesity, smoking,
alcohol, physical activity)

Sequenza adenoma-carcinoma

Lo sviluppo del cancro è un processo a stadi multipli: le cellule normali progrediscono gradualmente verso la malignità

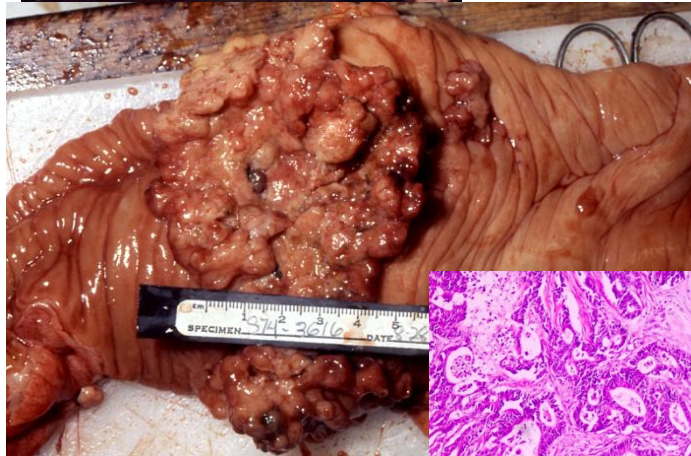
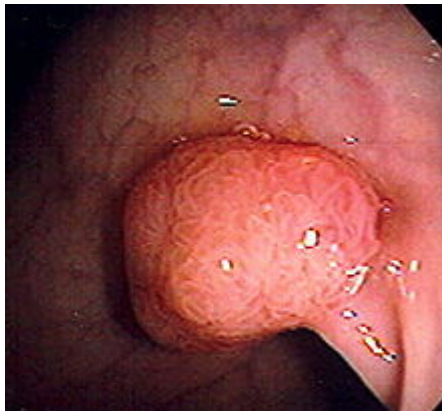


Genes and Growth Factor Pathways That Drive the Progression of Colorectal Cancer.



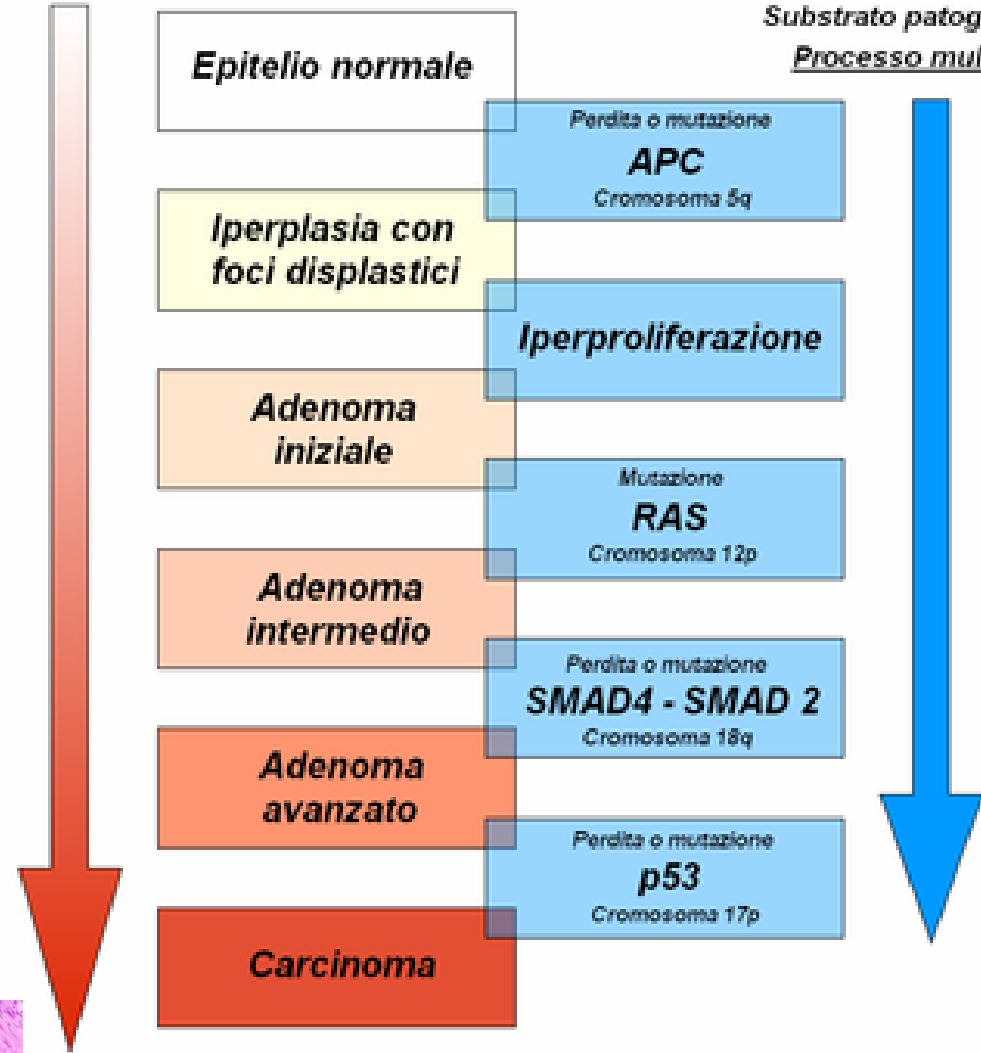
Molecular Basis of Colorectal Cancer

Markowitz SD Bertagnolli MM : NEJM 2009;361:2449



*Evoluzione
anatomo-patologica*

*Substrato patogenetico
Processo multistep*



Epitelio normale

Perdita o mutazione

APC

Cromosoma 5q

**Iperplasia con
foci displastici**

Iperproliferazione

**Adenoma
iniziale**

Mutazione

RAS

Cromosoma 12p

**Adenoma
intermedio**

Perdita o mutazione

SMAD4 - SMAD 2

Cromosoma 18q

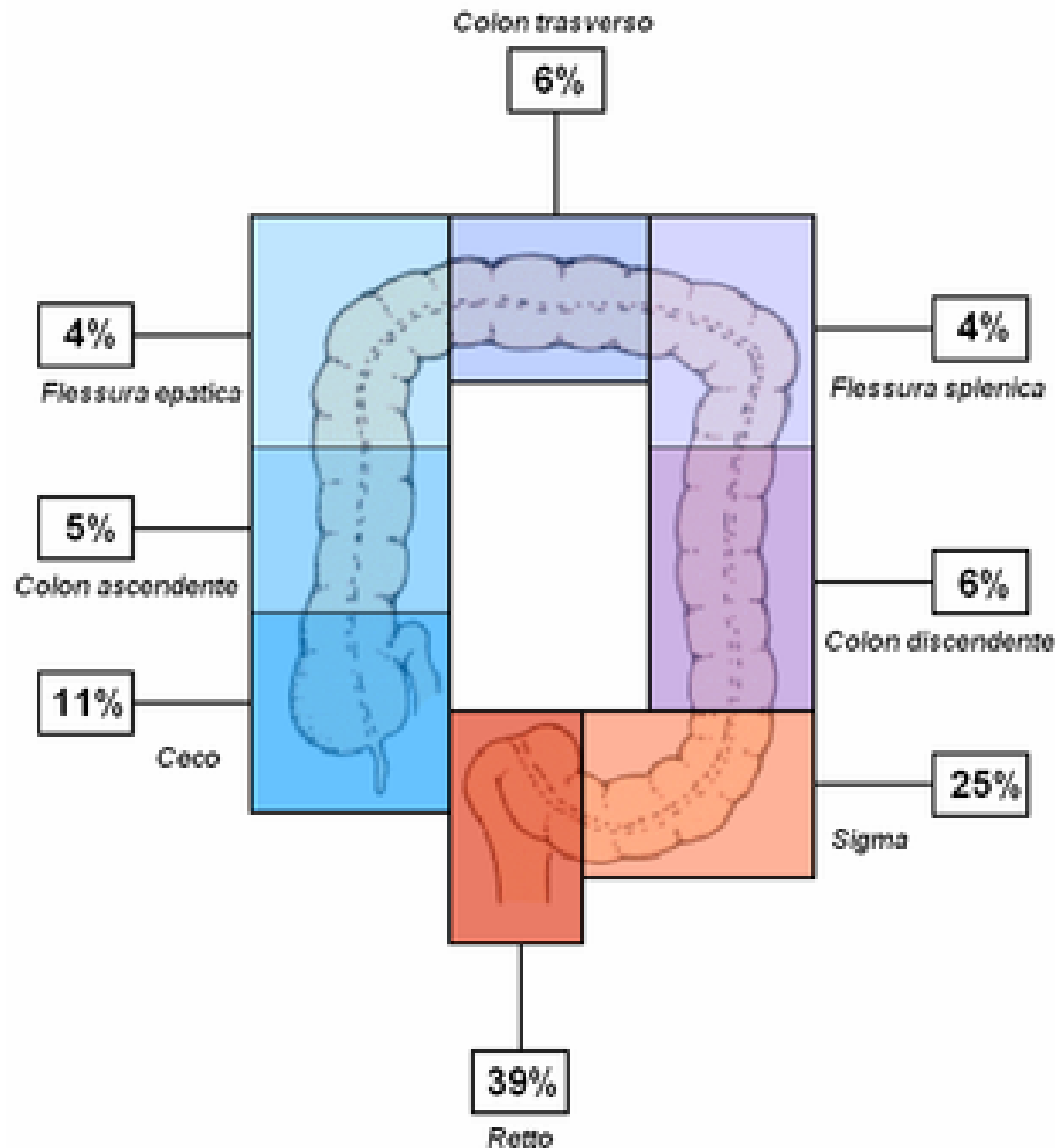
**Adenoma
avanzato**

Perdita o mutazione

p53

Cromosoma 17p

Carcinoma



Insorgenza relativa di CRC nei vari tratti del colon.

Dionigi, *Basi teoriche e Chirurgia generale - Chirurgia specialistica (4ª edizione)*, Padova, Elsevier Masson, 2006

FATTORE T

- T₁ : tumore che invade la sottomucosa.
- T₂ : “ “ “ la muscolare propria.
- T₃ : “ “ “ i tessuti pericolici e perirettali.
- T₄ : “ “ “ direttamente altri organi.

FATTORE N

- N₀ : non metastasi nei linfonodi regionali.
- N₁ : metastasi in 1-3 linfonodi pericolici o perirettali.
- N₂ : “ in 4 o più linfonodi pericolici o perirettali.
- N₃ : “ in 1 o più linfonodi lungo i tronchi vascolari.

FATTORE M

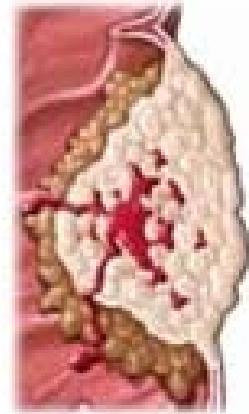
- M₀ : assenza di metastasi a distanza.
- M₁ : metastasi a distanza.



Stage I



Stage II



Stage III

STAGING

Prognosis

- ***Stage at diagnosis*** is the most important prognostic factor.
- In the USA in 2001–07, 5-year relative survival of patients diagnosed with colorectal cancer was:
 - 90·1% for patients with localised stage,
 - 69·2% for patients with regional spread,
 - 11·7% for patients with distant tumour spread
 - Overall 65%

Screening Options: Fecal Occult Blood Test

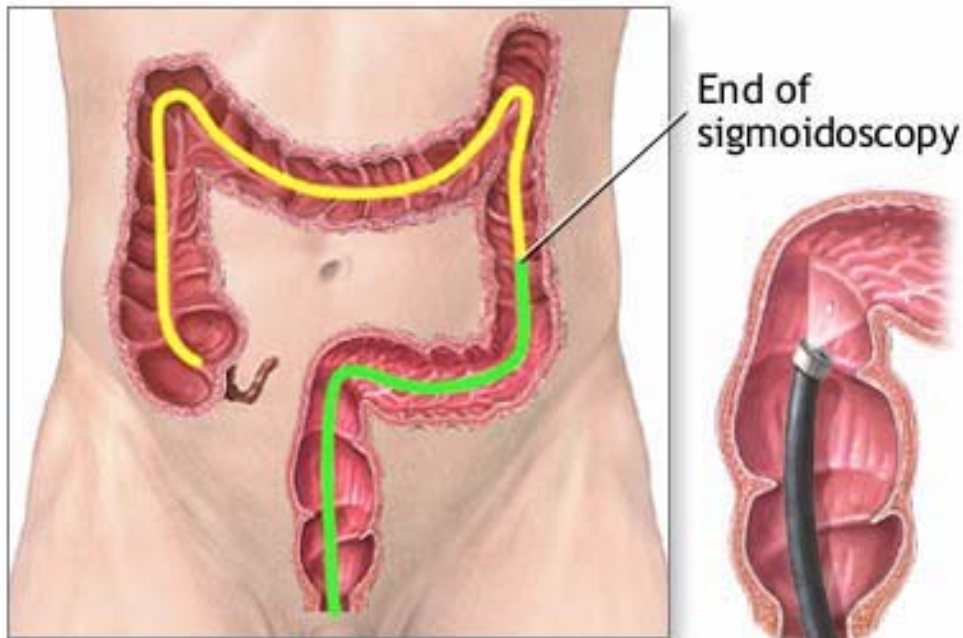
- **Stool Blood Test (FOBT or FIT):** Used to find small amounts of blood in the stool. If found further testing should be done.



<http://digestive.niddk.nih.gov/ddiseases/pubs/dictionary/pages/images/fobt.gif>

<http://www.owenmed.com/hemoccult.jpg>

Screening: Flexible Sigmoidoscopy



Colonoscopy examines the entire length of the colon; sigmoidoscopy examines only the lower third

ADAM.

<http://www.nlm.nih.gov/medlineplus/ency/images/ency/fullsize/1083.jpg>

- **Flexible Sigmoidoscopy:** A sigmoidoscope, a slender, lighted tube the thickness of a finger, is placed into lower part of colon through rectum
- It allows physician to look at inside of rectum and lower third of colon for cancer or polyps
- Is uncomfortable but not painful. Preparation consists of an enema to clean out lower colon
- If small polyp found then will be removed. If adenoma polyp or cancer found, then colonoscopy will be done to look at the entire colon

Screening: Clisma a doppio contrasto

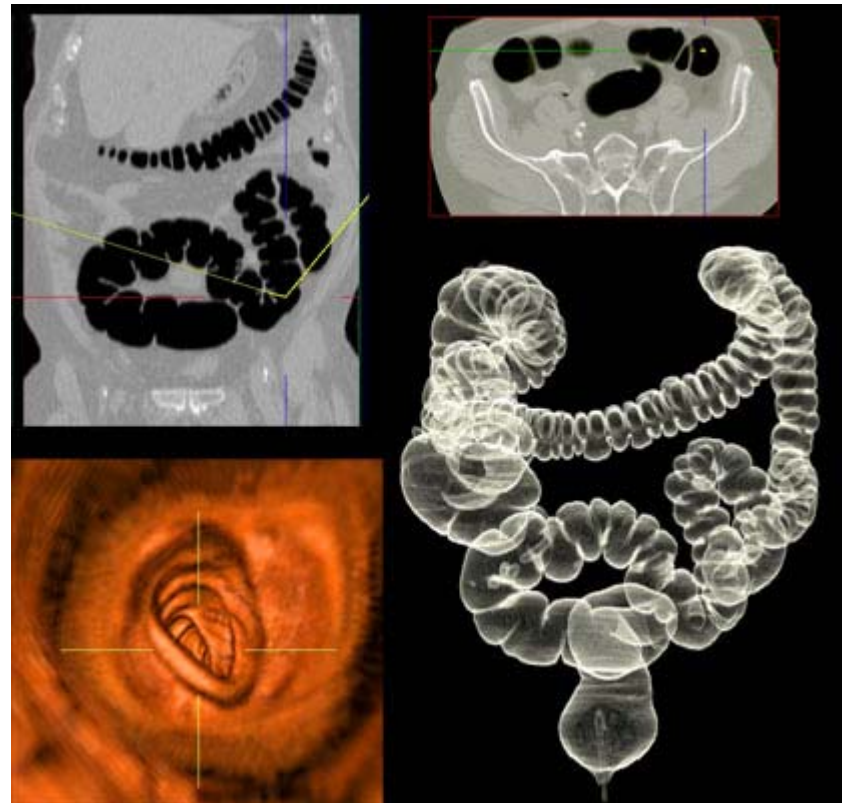


Barium enema with air contrast:

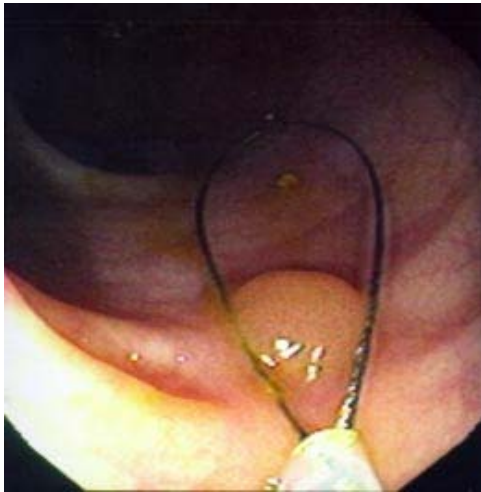
**A cancer of the ascending colon.
Tumor appears as oval shadow
at left over right pelvic bone**

Screening: Virtual Colonoscopy

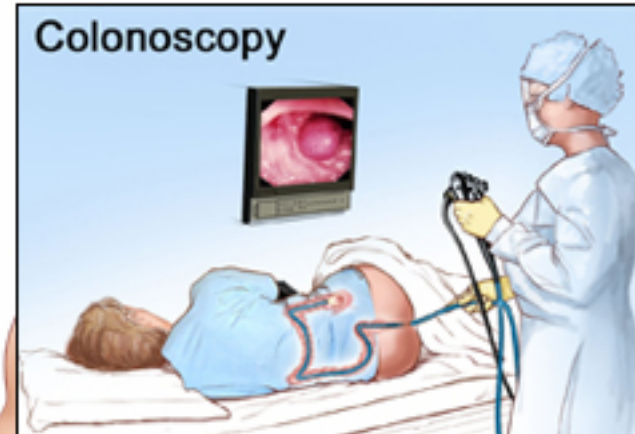
- **Virtual Colonoscopy:** Air is pumped into the colon in order for it to expand followed by a CT scan which takes hundreds of images of the lower abdomen
- Bowel prep is needed but procedure is completely non-invasive and no sedation is needed
- If abnormalities found then follow-up with colonoscopy



Screening: Colonoscopy

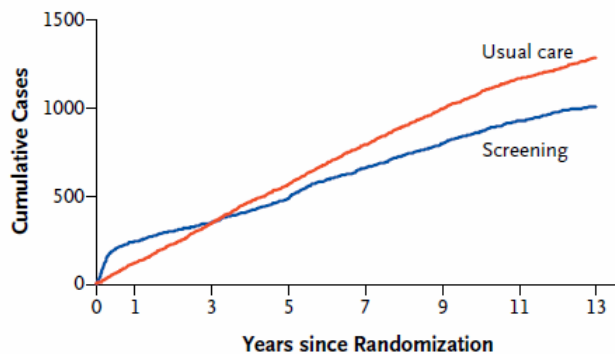


- **Colonoscopy:** A colonoscope, a long, flexible, lighted tube about the thickness of a finger, is inserted through the rectum up into the colon
- Allows physician to see the entire colon
- Bowel prep of strong laxatives to clean out colon, and the day of the procedure an enema will be given
- Procedure lasts ~15-30 minutes and are under mild sedation
- Early cancers can be removed by colonoscope during colonoscopy



Colorectal-Cancer Incidence and Mortality with Screening *Flexible Sigmoidoscopy*

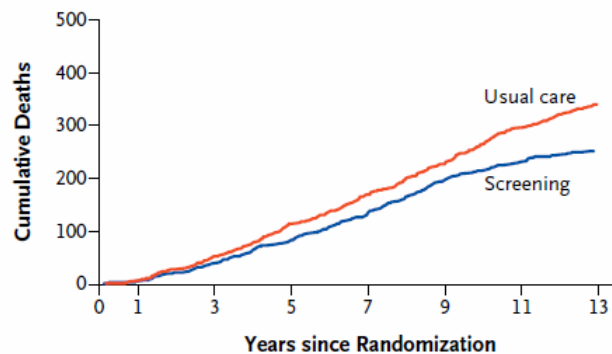
A Overall Colorectal-Cancer Incidence



No. at Risk

Screening							
Cases	242	347	487	659	797	927	1,012
Person-yr	76,520	227,007	373,895	516,773	654,740	772,625	848,403
Usual care							
Cases	119	344	564	790	998	1,169	1,287
Person-yr	76,592	227,438	374,467	517,055	654,447	771,744	847,103

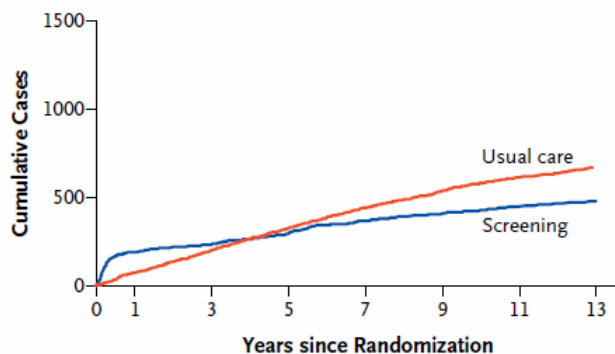
B Overall Colorectal-Cancer Mortality



No. at Risk

Screening							
Deaths	6	39	83	135	198	232	252
Person-yr	77,276	230,295	380,730	528,006	670,832	793,203	871,930
Usual care							
Deaths	6	51	114	169	228	296	341
Person-yr	77,228	230,354	380,731	527,828	670,526	792,674	871,275

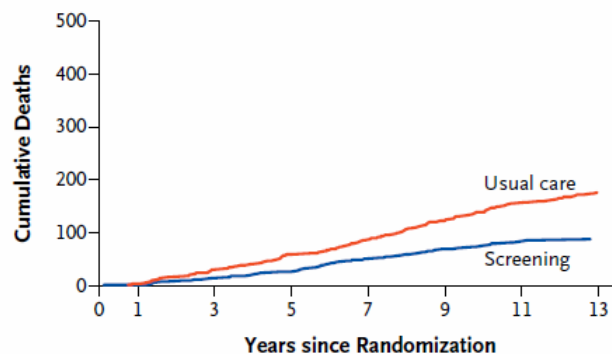
C Incidence of Distal Colorectal Cancer



No. at Risk

Screening							
Cases	190	234	295	367	407	450	479
Person-yr	76,520	227,007	373,895	516,773	654,740	772,625	848,403
Usual care							
Cases	71	200	324	439	538	617	669
Person-yr	76,592	227,438	374,467	517,055	654,447	771,744	847,103

D Mortality from Distal Colorectal Cancer

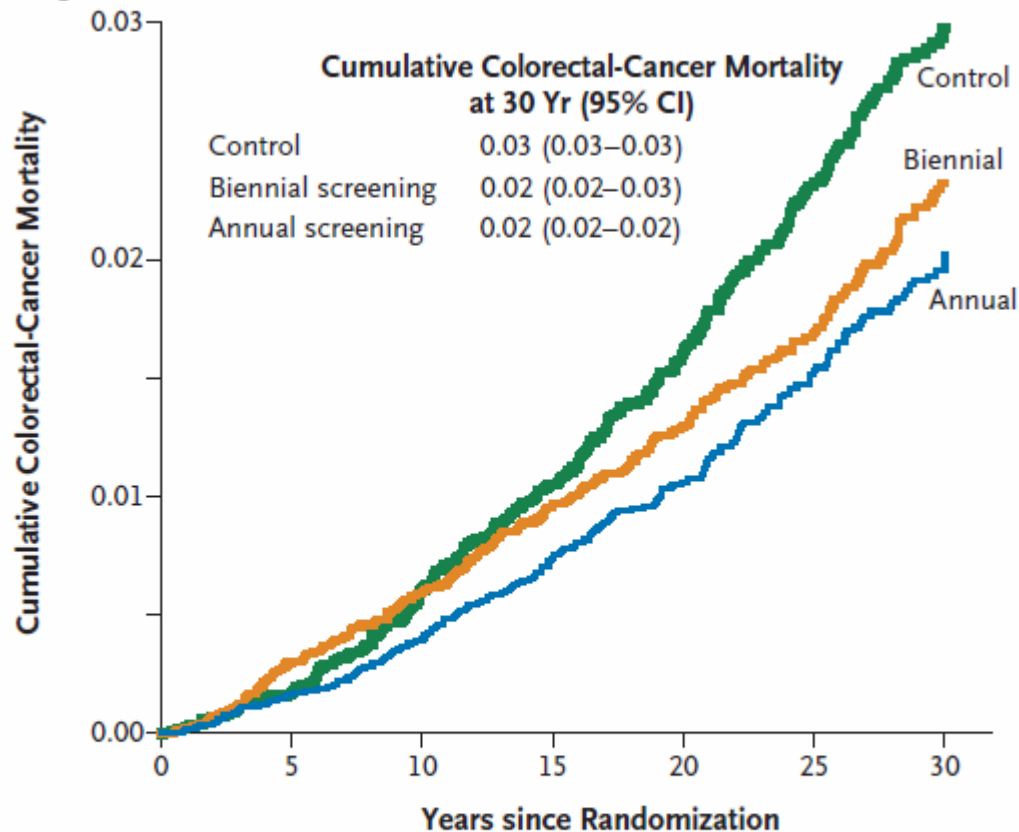


No. at Risk

Screening							
Deaths	1	14	27	51	69	84	87
Person-yr	77,276	230,295	380,730	528,006	670,832	793,203	871,930
Usual care							
Deaths	3	30	58	87	123	156	175
Person-yr	77,288	230,354	380,731	527,828	670,526	792,674	871,275

Long-Term Mortality after Screening for Colorectal Cancer

fecal occult-blood testing



No. at Risk

Control	14,497	13,103	11,320	9157	6741	4450
Biennial screening	14,635	13,243	11,445	9323	6802	4583
Annual screening	14,658	13,294	11,437	9219	6802	4498

The NEW ENGLAND JOURNAL of MEDICINE

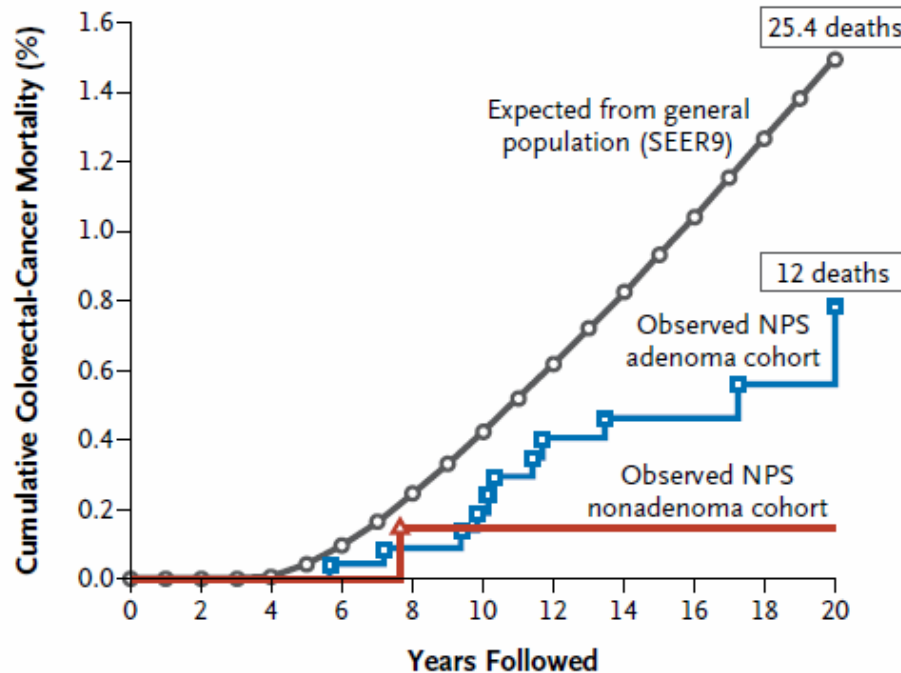
ESTABLISHED IN 1812

FEBRUARY 23, 2012

VOL. 366 NO. 8

Colonoscopic Polypectomy and Long-Term Prevention of Colorectal-Cancer Deaths

Ann G. Zauber, Ph.D., Sidney J. Winawer, M.D., Michael J. O'Brien, M.D., M.P.H., Iris Lansdorp-Vogelaar, Ph.D., Marjolein van Ballegooijen, M.D., Ph.D., Benjamin F. Hankey, Sc.D., Weiji Shi, M.S., John H. Bond, M.D., Melvin Schapiro, M.D., Joel F. Panish, M.D., Edward T. Stewart, M.D., and Jerome D. Waye, M.D.



National Polyp Study (NPS),

No. at Risk

Adenoma	2602	2358	2100	1808	1246	461
Nonadenoma	773	733	678	632	420	164

Screening Guidelines, Advantages, and Disadvantages

Screening	Guidelines	Advantages	Disadvantages
Fecal Occult Blood Test (FOBT)	Annually starting at age 50	<ul style="list-style-type: none"> -Cost effective -Noninvasive -Can be done at home 	<ul style="list-style-type: none"> -False-positive/false-negative results -Dietary restrictions -Duration of testing period
Flexible Sigmoidoscopy (FS)+FOBT	Every 5 years starting at age 50	<ul style="list-style-type: none"> -Cost effective -Can be done w/o sedation -Performed in clinic -Any polyps can be biopsied 	<ul style="list-style-type: none"> -Examines only portion of colon (additional screening may be done) -Discomfort for patient -Bowel cleansing
* Colonoscopy (preferred method b/c polyps can be biopsied and removed)	Every 10 yrs starting at age 50	<ul style="list-style-type: none"> -Patient sedated -Outpatient screening -Views entire colon and rectum -Polyps can be removed and biopsied 	<ul style="list-style-type: none"> -Bowel cleansing -Sedation may be a problem for some -Cost if uninsured -Risk of perforation
Virtual Colonoscopy (a.k.a. computed tomography colonography-CT)	Every 5 yrs starting at age 50	<ul style="list-style-type: none"> -Relatively noninvasive -No sedation needed -Can show 2- or 3-D imagery 	<ul style="list-style-type: none"> -Small polyps may go undetected -Bowel cleansing -Cost -If polyps found, colonoscopy required -Exposure to radiation -Patient discomfort

*American Cancer Society Recommendation

COLON CANCER SCREENING PLANS

The recommended colon cancer screening plan depends upon your risk of colorectal cancer.

Average risk of colorectal cancer — People with an average risk of colorectal cancer should begin screening at age 50. One of the following screening strategies is recommended :

- Colonoscopy every 10 years
- Computed tomographic colonography every 5 years
- Flexible sigmoidoscopy every five years
- Stool testing every year (for guaiac and immunochemical occult blood tests)