Screening and Surveillance for Colorectal Cancer

Richard Sim
Dept of Surgery
Tan Tock Seng Hospital

Background information

- Patient factors
  - age
  - functional status
  - co-morbidity

ECOG status	

- Tumour factors
  - site
  - histological type and differentiation
  - stage: T, N, M, peritoneal lavage cytology

Background information

- Treatment factors
  - surgery
    - curative
      - limited / radical
      - residual disease (R0, R1, R2)
    - palliative
      - resection / bypass -stoma
  - adjuvant chemotherapy / radiotherapy

- Post-treatment duration / progress

Aims of Follow up

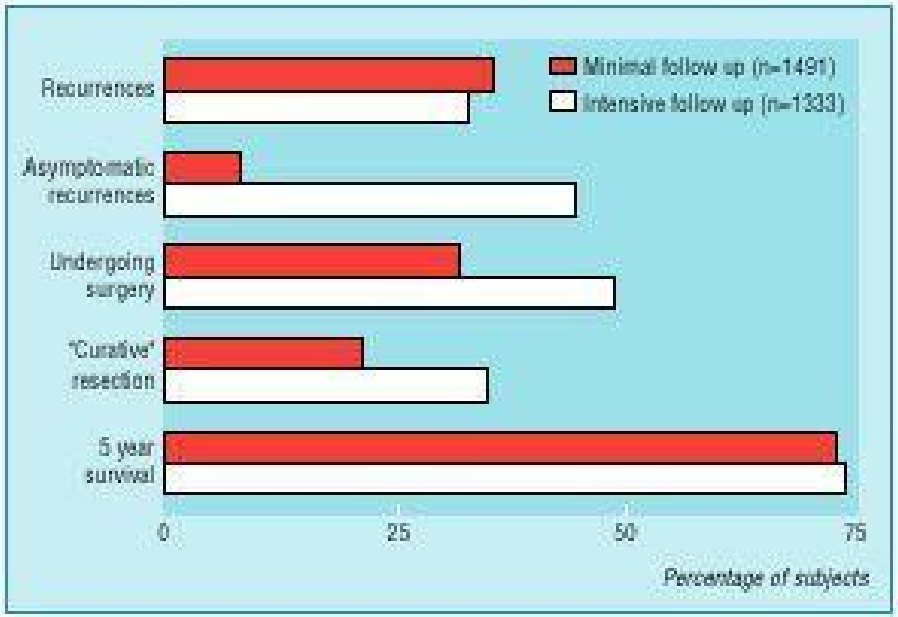
- detect recurrence
- detect metachronous tumours and pre-malignant lesions
- detect complications of treatment

How to follow up?

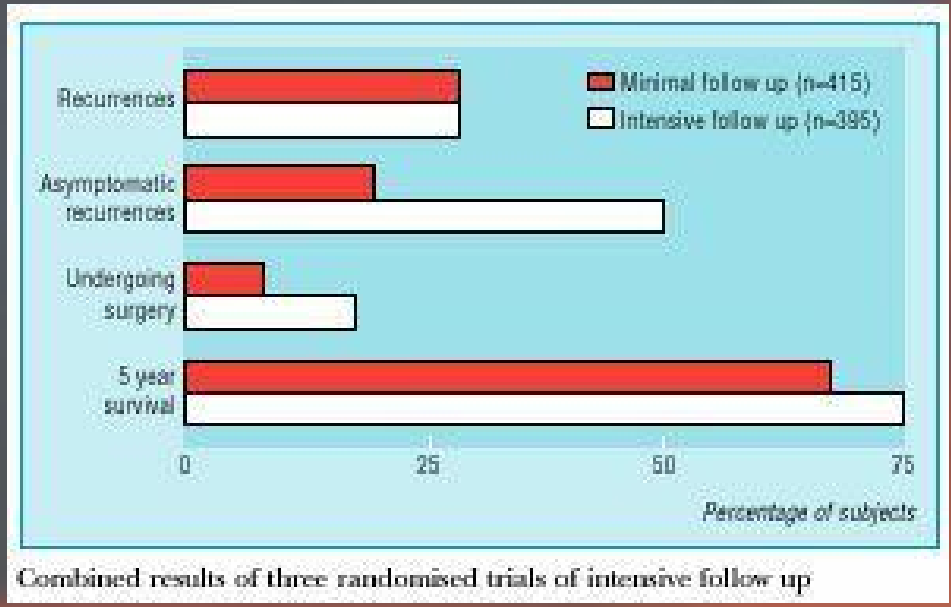
- How often and what investigations?
- Questions:
  - does intensive follow up lead to early detection?
  - does treatment of this lead to improved survival?
  - any lead time bias?
  - any side effects?
  - is it cost effective?

Colorectal Ca : benefits of FU

- 2/3 receive curative resection, 30-50% of these relapse and die of disease
- Practice
  - Wales and Trent audit (1997)
    - 57% colonoscopy 3-5 times in 5 years
    - 13% no routine testing at all
- Guidelines
  - SIGN (1997)
    - no evidence of survival benefit
- Evidence
  - RCTs : none with sufficient power
  - meta-analyses



Results of meta-analysis of seven non-randomised trials that compared intensive with minimal or no follow up (Bruinvels et al, 1994)



Combined results of three randomised trials of intensive follow up

Results of intensive follow up*

Follow up	Colonoscopy	Chest *x* ray	Liver CT
Standard (n = 158)	72	17	66
Intensive (n = 167)	577	650	674
No of extra investigations	505	633	608
No of asymptomatic recurrences resulting from extra investigations	0	0	10
No of cures resulting from extra investigations	0	1	1

CT = computed tomography.
*Data from Schoemaker et al, 1998 (see Further reading box).

Costs of follow up, suggested by recent study from Italy

- £2530 per patient over five years
- £9050 per recurrence detected
- £39 890 for each case undergoing further surgery
- £91 190 for each "cured" patient

Results of "second look" surgery according to measurement of carcinoembryonic antigen (CEA)*

CEA concentration	No of patients	No (%) of "curative" resections	% of patients free of recurrence at 1 year
Raised	345	47 (14)	2.9
Normal	672	38 (6)	1.9
Not measured	200	23 (12)	2.0

*Data from Moertel et al, 1993.

Comparison of results of trial of early versus delayed chemotherapy in patients with advanced colorectal cancer

Treatment group	No of patients	Median symptom-free survival (months)	Median survival (months)	Survival at 1 year (%)
Early	92	10	14	55
Delayed	91	2	9	38

Early chemotherapy was given when patients were asymptomatic; delayed chemotherapy was given when patients were symptomatic.
Data from the Nordic Gastrointestinal Tumor Group, 1992.

Colorectal Ca FU : Metanalysis

Study	Intensive follow up	Control follow up
Makela et al, 1995[17]	Seen in clinic 3 monthly for first 2 years, then 6 monthly: physical examination, full blood count, faecal occult blood test, carcinoembryonic antigen levels, and chest *x* ray. Yearly colonoscopy. Sigmoidoscopy 3 monthly for rectal and sigmoid cancers. Ultrasonography of liver 6 monthly. Computed tomography yearly. All followed up to 5 years	Seen in clinic 3 monthly for first 2 years, then 6 monthly: physical examination, full blood count, faecal occult blood test, carcinoembryonic antigen levels, and chest *x* ray. Yearly barium enema. Rigid sigmoidoscopy 3 monthly for rectal cancers. All followed up to 5 years
Ohlsson et al, 1995[18]	Seen in clinic 3 monthly for the first 2 years, then 6 monthly: physical examination, rigid proctosigmoidoscopy, liver function tests, carcinoembryonic antigen levels, faecal occult blood test, chest *x* ray. Colonoscopy at 3, 15, 30, and 60 months, computed tomography after abdominoperineal resection at 3, 6, 12, 18, and 24 months. All followed up to 5 years	No systematic follow up. Patients were instructed to leave samples for faecal occult blood test testing every third month during the first 2 years and then every year. All accounted for to 5 years
Schoemaker et al, 1998[19]	Seen in clinic 3 monthly for first 2 years, then 6 monthly for 5 years; physical examination, full blood count, liver function tests, and Haemoccult II. Yearly chest *x* ray and computed tomography of liver. Yearly colonoscopy. Carcinoembryonic antigen measurements were performed but not used to trigger further examinations. 94% followed up to 5 years	Seen in clinic 3 monthly for first 2 years, then 6 monthly for 5 years; physical examination, full blood count, liver function tests, carcinoembryonic antigen levels, and Haemoccult II. Carcinoembryonic antigen measurements were performed but not used to trigger further examinations. 95% followed up to 5 years
Pietra et al, 1998[20]	Seen in clinic 3 monthly for first 2 years, then 6 monthly for next 3 years, thereafter yearly; physical examination, ultrasonography of liver, carcinoembryonic antigen levels. Yearly colonoscopy, chest *x* ray, and computed tomography. All followed up to 5 years	Seen in clinic 6 monthly for first year, then yearly; physical examination, ultrasonography of liver, carcinoembryonic antigen levels. Yearly colonoscopy and chest *x* ray. All followed up to 5 years
Kjeldsen et al, 1997[21]	Physical examination, digital rectal examination, gynaecological examination, Haemoccult-II, colonoscopy, chest *x* ray, full blood count, erythrocyte sedimentation rate, liver function tests, at 6 monthly in first 3 years, then 12 monthly for next 2 years, then 5 yearly. 79% followed up to 5 years	Physical examination, digital rectal examination, gynaecological examination, Haemoccult-II, colonoscopy, chest *x* ray, full blood count, erythrocyte sedimentation rate, liver function tests, at 5 and 10 years. 73% followed up to 5 years

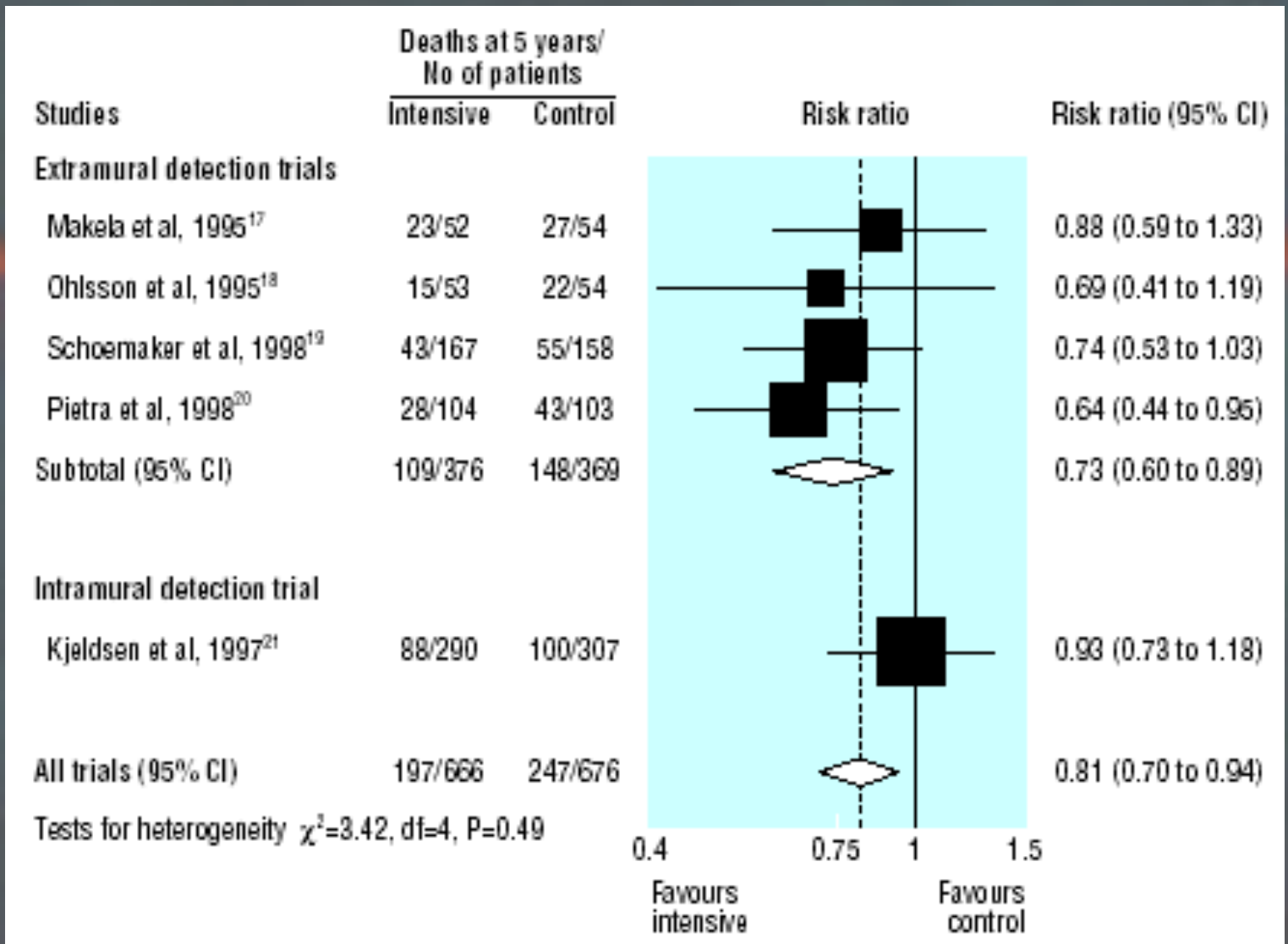


Fig 3 Pooled analysis with summary estimates (fixed effects method) for five year survival: data categorised into detection groups in accordance with a priori hypothesis (see methods)

End point	No of trials	Intensive arms	Control arms	Risk ratio (95% CI)	Test for heterogeneity P value
All site recurrences	5	212/666	224/676	0.95 (0.82 to 1.11)	0.83
Local recurrences:					
All	5	103/666	90/676	1.17 (0.91 to 1.52)	0.67
Isolated	3	65/446	42/464	1.61 (1.12 to 2.32)	0.44
Hepatic metastases:					
All	5	71/666	91/676	0.79 (0.59 to 1.04)	0.45
Isolated	3	20/323	15/315	1.13 (0.61 to 2.08)	0.53
Lung metastases	5	19/666	32/676	0.61 (0.35 to 1.05)	0.73
Intraluminal recurrences	5	18/510	15/518	1.25 (0.64 to 2.44)	0.73
Metachronous cancers	5	11/666	7/676	1.50 (0.63 to 3.54)	0.66

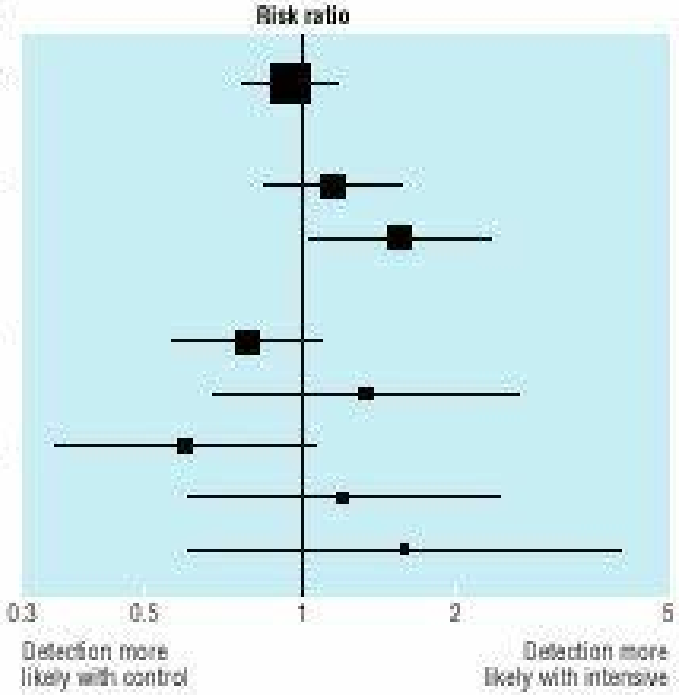


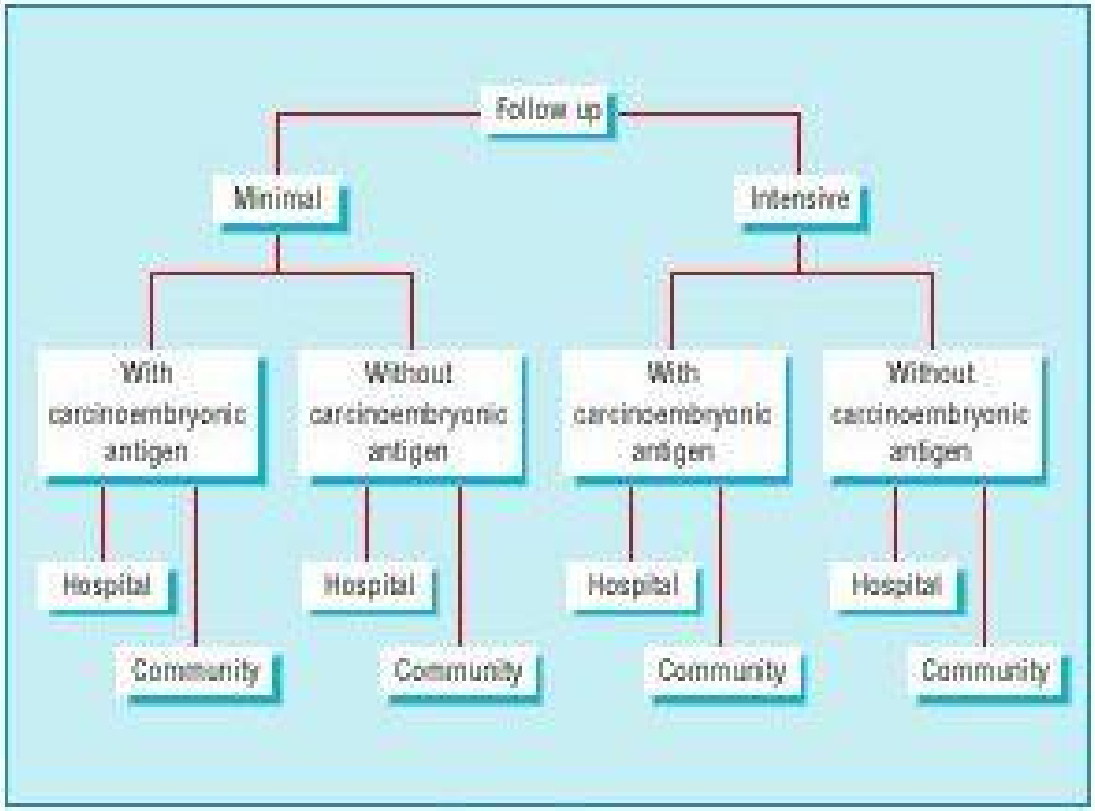
Fig 4 Pooled data and summary risk ratios (fixed effects method) for recurrences, metastases, and metachronous (second colorectal primary) cancers

Colorectal Ca FU : conclusions

- Intensive FU after curative resection improves survival at 5 years - absolute reduction in mortality of 9-13%
- Effect superior to the 5-10% benefit for adjuvant chemotherapy for Duke's C disease
- The cause of survival benefit is unclear. The components of follow up which are of most benefit are not defined
- Does not include benefits of
  - liver resection for hepatic mets
  - pelvic exenteration for recurrent pelvic disease
  - combined therapy for advanced disease
  - psychological well being

Colorectal Ca FU : conclusions

- Recurrence in all sites detected 8.5 months earlier in intensive group. No difference in overall recurrence rates between the two groups
- Intraluminal recurrence and detection of metachronous cancers were low in both groups
- It is not appropriate to follow up ALL patients intensively
- More research is required to define a suitable policy which utilises already limited resources



Suggested study outline to test three follow up strategies: intensive *v* minimalist; role of carcinoembryonic antigen; and general practitioner (community) coordinated *v* hospital coordinated

Colorectal Ca FU : recommendations

- Every 3 months for 2 years, then 6 monthly till 5 years
- Physical, rectal and pelvic examination
- FBC, LFT, CEA, FOB
- Yearly CXR, colonoscopy and CT liver

Annals of Internal Medicine 1999;131:805-12

- Reverse transcriptase polymerase chain reaction.
- Guanylyl cyclase C messenger RNA (GCC mRNA) was found in the lymph nodes of all of the 10 patients who had recurring cancer within three years of surgery. Moreover, the protein did not show up in any of the samples taken from the 11 patients who were free of disease for six years or more after surgery

Lancet 2002 Jan 19, 359(9302):219-25

- Counting alleles to predict recurrence of early-stage colorectal cancers
- Allelic imbalance is a better predictor of prognosis than histopathological stage

NEJM June 15, 2000
A Comparison of Colonoscopy and Double-Contrast Barium Enema for Surveillance after Polypectomy

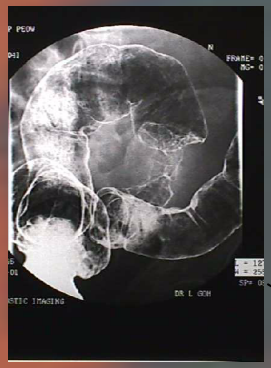
- In patients who have undergone colonoscopic polypectomy, colonoscopic examination is a more effective method of surveillance than double-contrast barium enema. (N Engl J Med 2000;342:1766-72.)

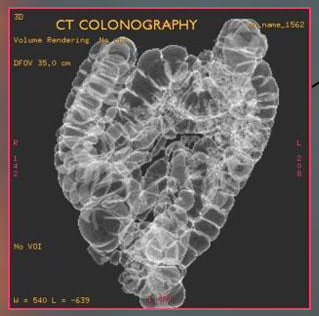
Screening

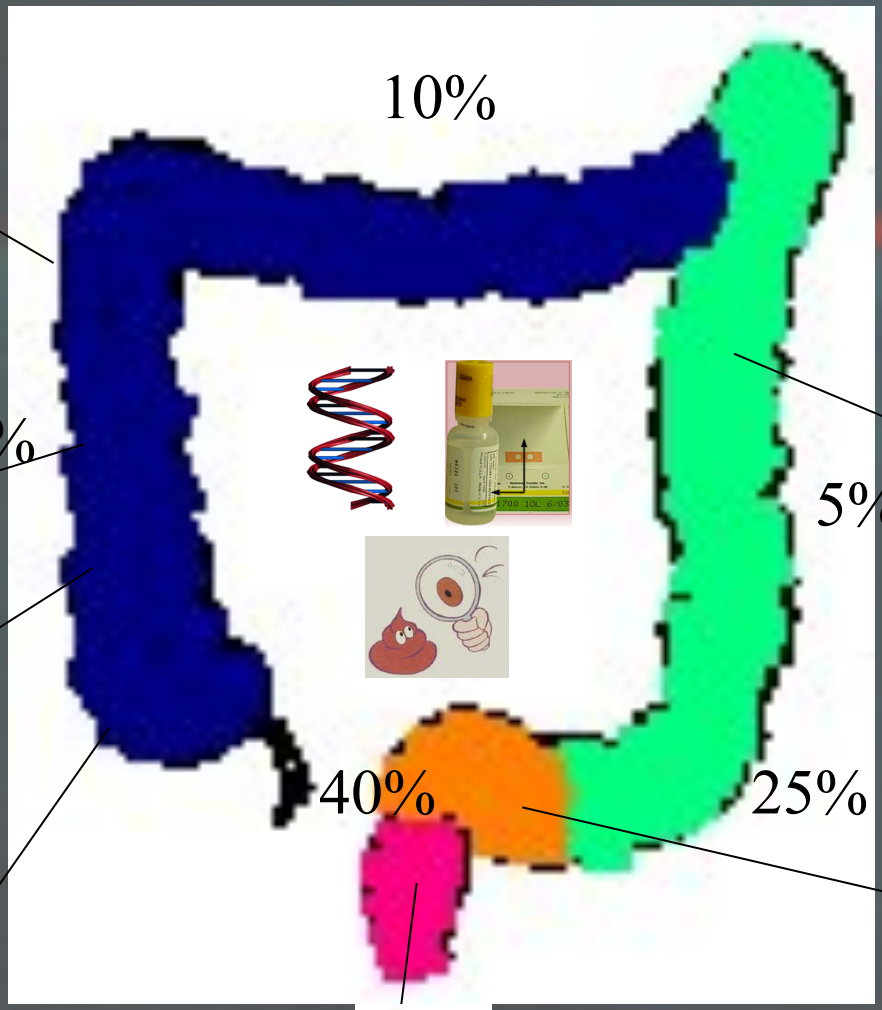
Beginning age 50

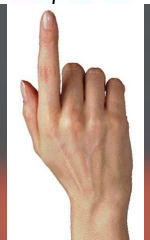
- Digital rectal examination, faecal occult blood yearly plus sigmoidoscopy every 5 years
- Barium enema every 5-10 years
- Colonoscopy every 10 years
- Stool genetic tests

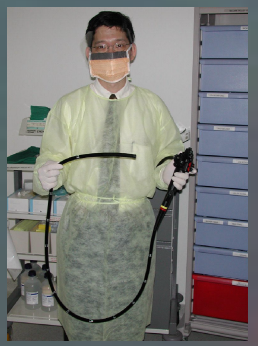
Some form of screening is better than none

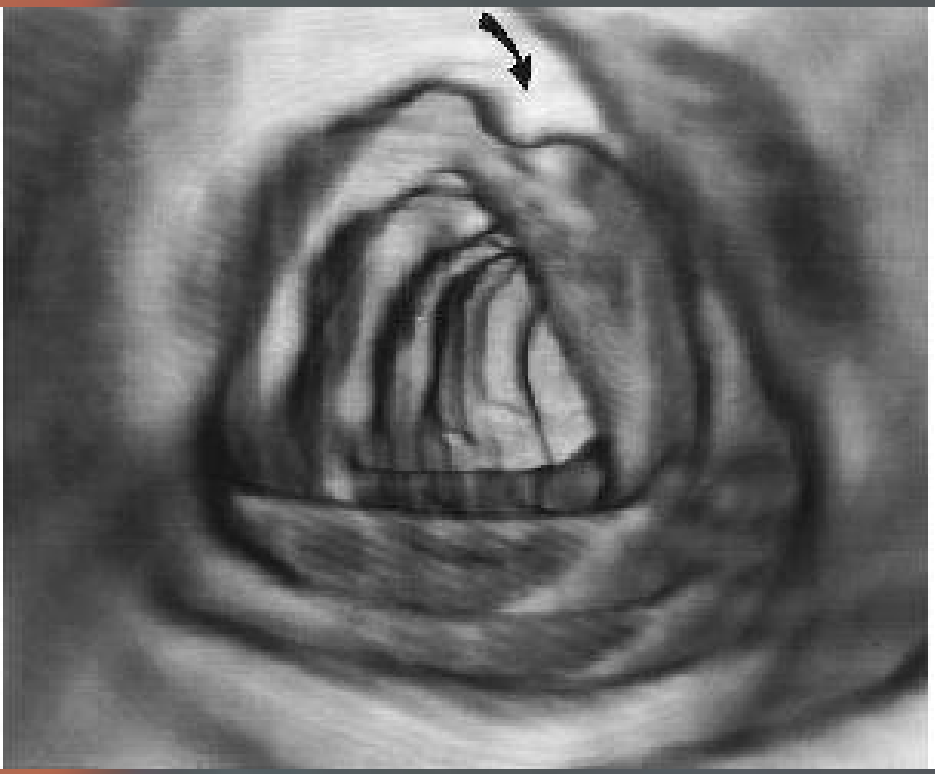


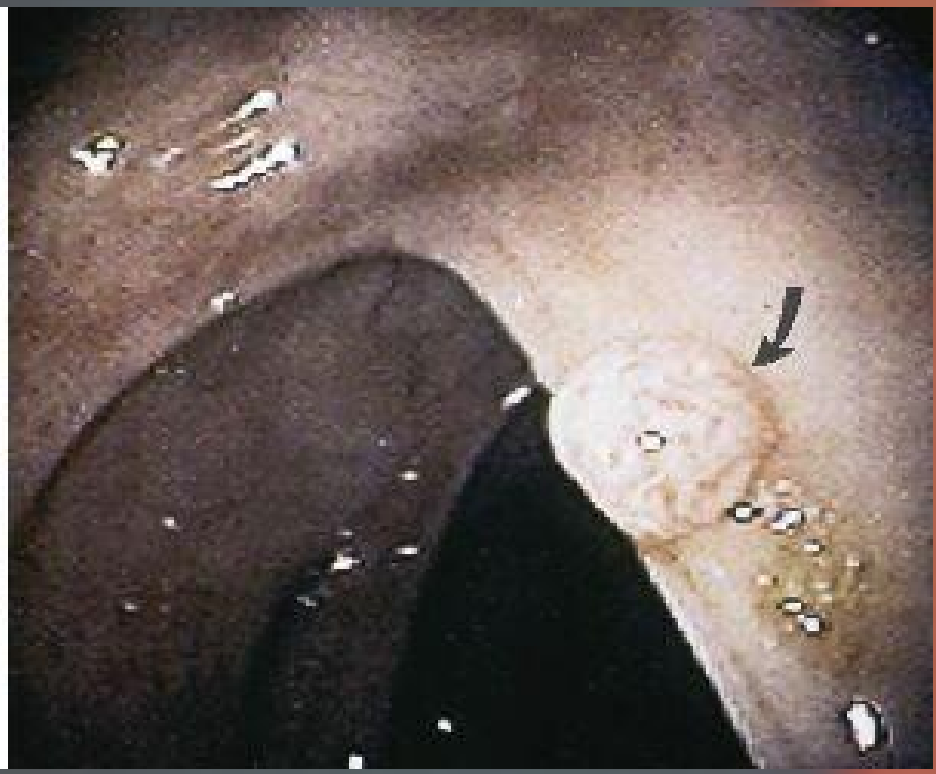

CT COLONOGRAPHY

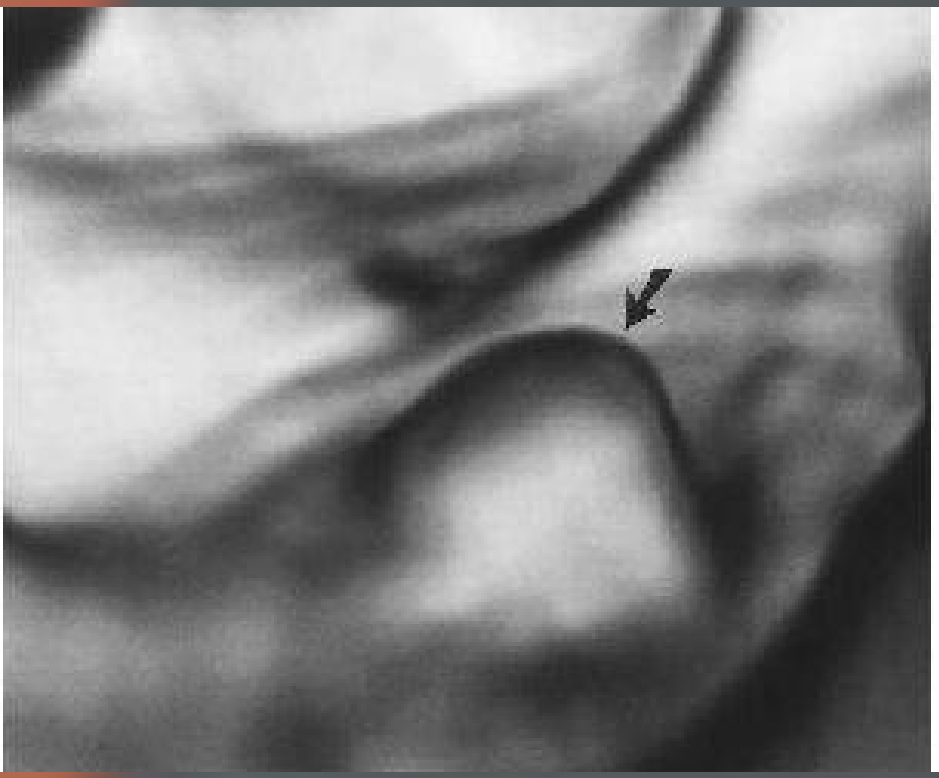

10%
20%
5%
40%
25%

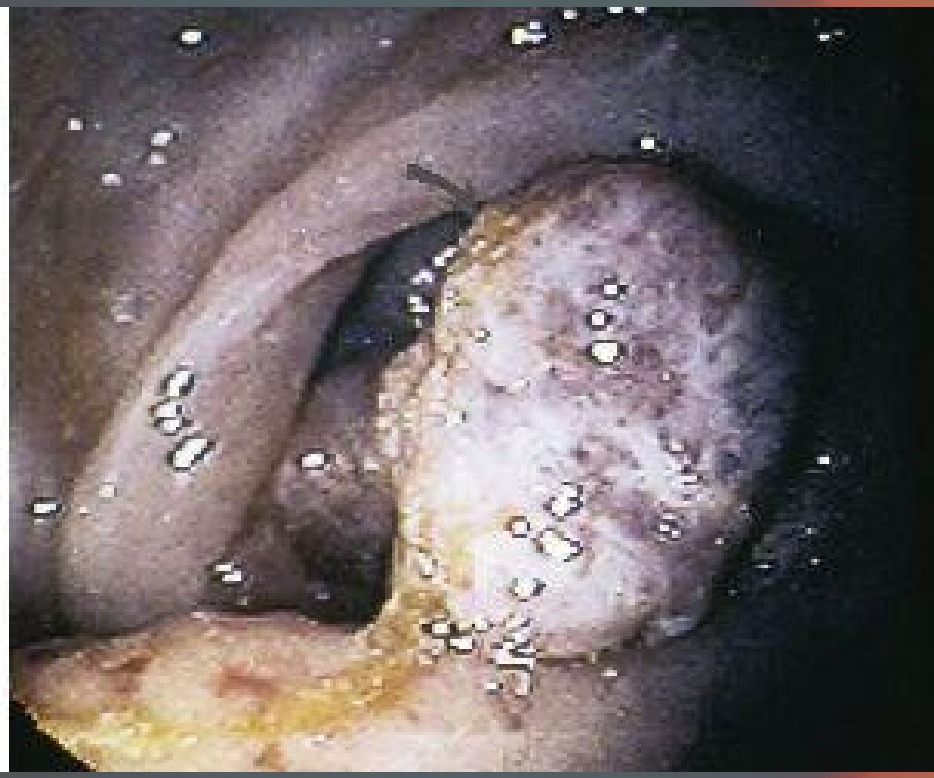













FREE
MAMMOGRAM
PLACE BOOBS HERE


Colon
Self
Exam
INSANEPICTURES.COM