Bowel Cancer Screening and Interventions: Colonoscopy

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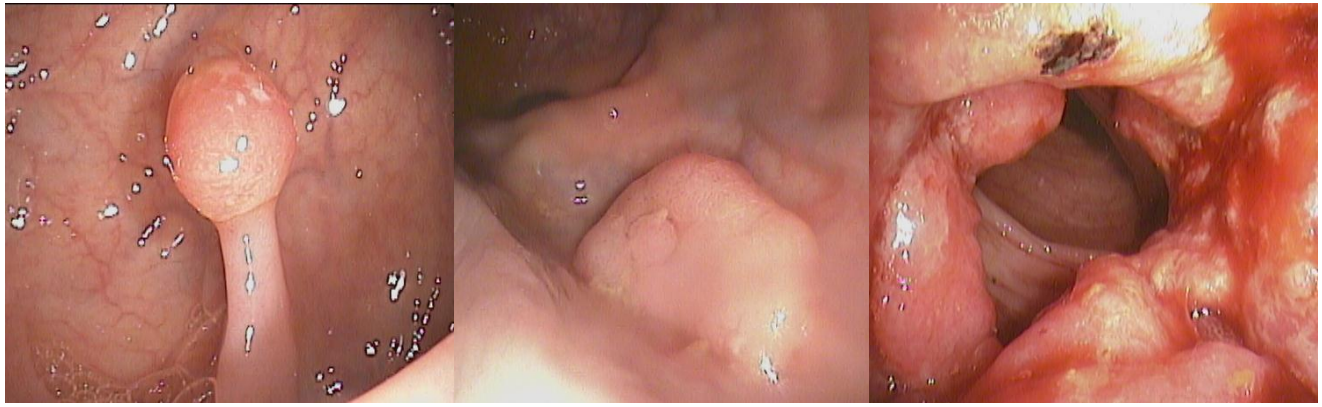
Rotorua GP CME June 2015



DYING OF EMBARRASSMENT: NZ TOPS BOWEL CANCER RATES

NEW ZEALAND HERALD. WEDNESDAY, JAN 22, 2014

Outline

- Scope of the problem
- Bowel cancer screening
  - Waitemata Bowel Screening Pilot
  - role of colonoscopy
- Surveillance colonoscopy
  - previous polyp
  - previous colorectal cancer
- Quality colonoscopy

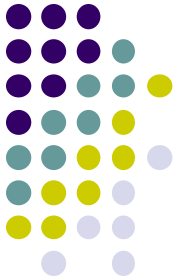
Colon Cancer

Scope of the Problem

- Most common cancer in NZ
  - 3030 new cases in 2011
  - 14.4% of all cancers
  - cumulative risk 5.6% by age 75 years (1:18)
  - 1:16 men or 1:21 women
  - risk of CRC rises with age
  - low risk <40 years
  - >90% of cases over 50 years
  - [commonest cancer in men – prostate; women – breast]
- 2nd commonest cause of cancer death in NZ
  - 1191 deaths in 2011
  - 13.4% of all cancer deaths

NZ Cancer Registry, MOH 2014

Rationale for Bowel Cancer Screening and Surveillance

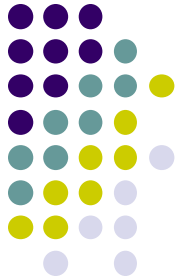


- Early stage disease has better prognosis
- The majority of CRCs evolve through either:
  - adenoma-carcinoma pathway
  - serrated pathway
  - progression typically over quite a long course (5-10 years)
- High risk groups are well established
  - family history of colorectal cancer
  - genetic colorectal cancer syndromes
  - personal history of colonic polyps
  - personal history of colorectal cancer
  - personal history of inflammatory bowel disease

➔ Opportunity for early detection

➔ For the average risk population costs per life-year gained (LYG) is less than $US50,000 compared to no screening for FOBT, sigmoidoscopy and colonoscopy Epidemiologic Reviews 2011;33:88-100

Screening Test Options



- Faecal occult blood testing
- Faecal DNA testing
- Flexible sigmoidoscopy
- Colonoscopy
- (Double contrast barium enema)
- Virtual colonoscopy
- Capsule endoscopy
- Serum-based DNA methylation biomarkers

Screening Test Options

gFOBT/iFOBT:
- supported by RCTs
- 13% to 33% reduction in CRC mortality

FLEXIBLE SIGMOIDOSCOPY:
- supported by RCTs
- 22% to 31% reduction in CRC mortality
- no or minimal reduction in right sided CRC

COLONOSCOPY:
- supported by observational studies, RCTs in progress
- allows direct visualisation of the whole colon
- polypectomy can interrupt the progression of precancerous polyps to cancer
- allows determination of appropriate surveillance interval based on index examination
- less frequent intervals between examinations
- increasing acceptability and tolerability

Screening Test Options

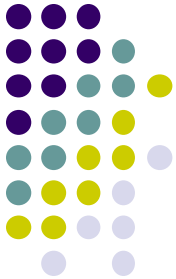
- Faecal occult blood testing
- Faecal DNA testing
- Flexible sigmoidoscopy
- Colonoscopy
- (Double contrast barium enema)
- Virtual colonoscopy
- Capsule endoscopy
- Serum-based DNA methylation biomarkers

NOT BEEN SHOWN TO BE COST-EFFECTIVE

Faecal occult blood testing

	Mechanism	Notes
Guaiac test Haemoccult Haemoccult II Haemoccult II Sensa	Detects heme and haemoglobin, due to its inherent pseudoperoxidase activity Sensitivity ↑ with rehydration but ↓ specificity	False positive: red meats, plant peroxidases, aspirin False negative: Vitamin C. Do not detect porphyrin and thus relative specific for lower GI bleeding.
Immunochemical tests (FIT)	Antibody specific to intact human haemoglobin	More specific for lower GI bleeding. No dietary restrictions. Quantitative so allows selection of an optimal cut-off value
Heme-porphyrin assays	Detects all 3 components of faecal blood: Hb, heme derived porphyrins and intact heme	Not widely used. Detects upper and lower GI bleeding, plus dietary porphyrins and animal haems

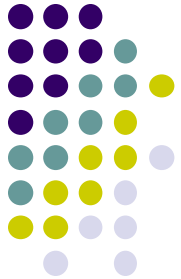
RCTs using gFOBTs for CRC Screening



	Minnesota	Funen	Nottingham
Population	Volunteers	Population based	Population based
Size	3 groups of 15,000	2 groups of 31,000	2 groups of 76,000
Age range	50-80 years	45-75 years	50-74 years
Method	Annual or biennial*	Biennial	Biennial
Colonoscopy rate	38% and 28%	4.3%	4%
Mortality reduction	33%	18%	15% (13%)
Absolute reduction	22 per 100,000 PY	16 per 100,000 PY	10 per 100,000 PY
NNT	4,545	6,250	10,000
*rehydrated	NEJM 1993	Lancet 1996	Lancet 1996 & Gut 2012 (20yr FU)

iFOBT associated with higher compliance and higher diagnostic yield of advanced neoplasia

Waitemata Bowel Screening Pilot



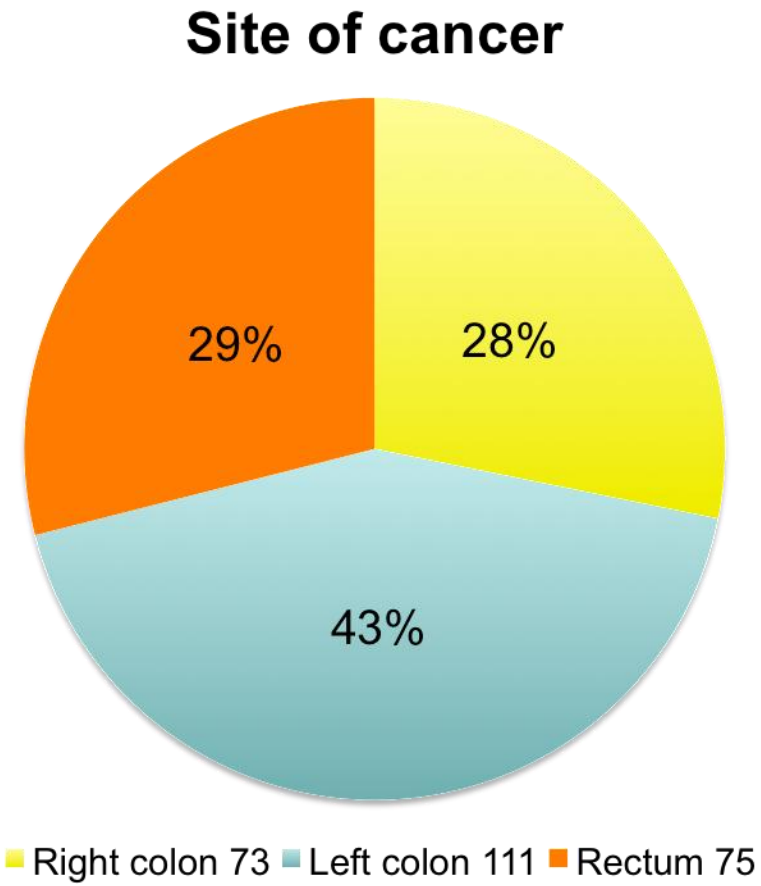
- Men and women aged 50 to 74 years
  - 137,000 eligible over 2 years
- 4-year pilot, October 2011 to December 2015
- Biennial iFOBT
- Colonoscopy offered if iFOBT positive

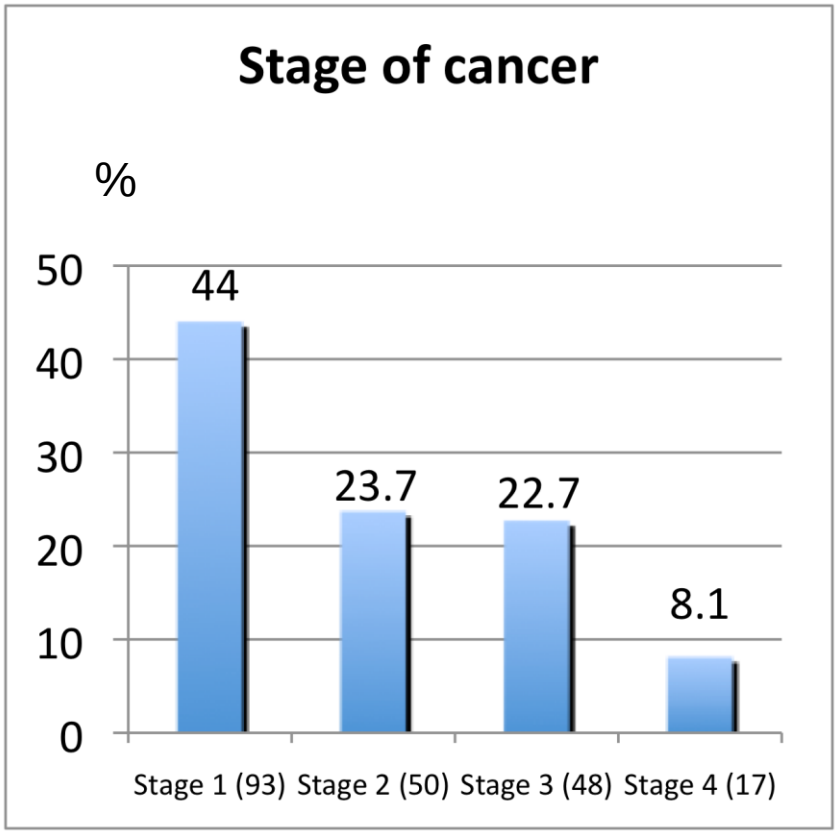
WBSP Monitoring Indicators

	Round 1	Round 2	Target
Participation	55.6%	50.2%	60%
iFOBT positivity	7.5%	5.7%	6-8%
Colonoscopy if iFOBT +ve	95.8% (96.1%)*	94.1% (94.6%)*	>90%
Colonoscopy <11 weeks	99.3% at Dec 2014		95%
Caecal intubation rate	97%	97%	>95%
Complications[#]	3.7		<10 per 1000
CRC detection rate	3.1	1.4	1.8-9.5 per 1000
Advanced adenoma detection rate	15.9	7.5	-
Adenoma detection rate	36.9	22.8	13.3-22.3 per 1000
PPV +ve iFOBT for cancer	4.4%	2.7%	4.5%-8.6%
PPV +ve iFOBT for advanced adenoma	24.2%	15.4%	-
PPV +ve iFOBT for adenoma	56.1%	46.5%	9-6-40.3%

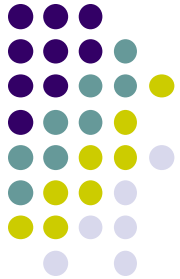
MOH April 2015

WBSP cancers





Waitemata Bowel Screening Program – Resource Implications



- About 2,000 extra colonoscopies per annum
- Detected cancer comprise 19% of the total colon cancer surgical workload
- Surveillance colonoscopy
  - 2192 pts referred to mid October 2014
    - Less than 1 year 5%
    - 1 year surveillance 19%
    - 3 year surveillance 52%
    - 5 year surveillance 23%
  - Cancer follow-up

Personal Communication, Dr Mike Hulme-Moir 2015

Indications for Colonoscopy

- Symptoms
- Screening high risk groups
  - family history of colorectal cancer
  - genetic colorectal cancer syndromes
  - personal history of colonic polyps
  - personal history of colorectal cancer
  - personal history of inflammatory bowel disease
- Implicit component of any FOBT screening program
- Average risk population?

Colonoscopy and polypectomy protects against colon cancer

National polyp study

- 76% reduction in incidence of CRC in a cohort of patients who underwent colonoscopy and polypectomy compared to SEER reference group
- 53% reduction in CRC mortality after a median of 16 years compared to SEER reference group

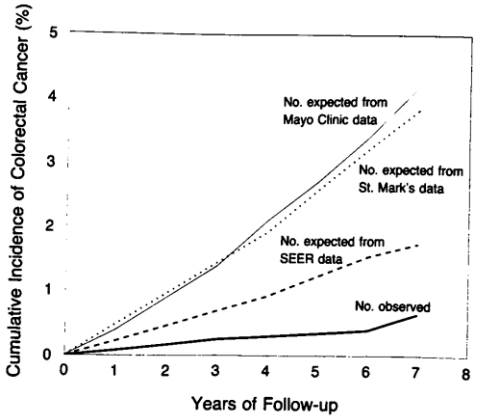


Figure 1. Cumulative Incidence of Colorectal Cancer in the National Polyp Study Cohort.

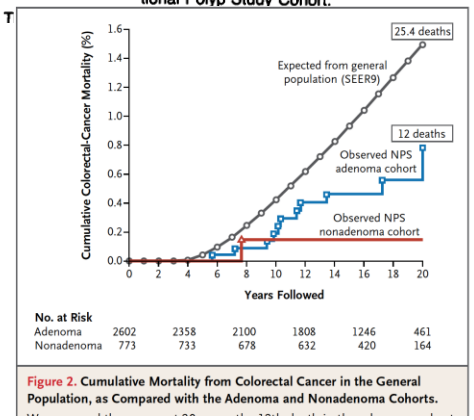


Figure 2. Cumulative Mortality from Colorectal Cancer in the General Population, as Compared with the Adenoma and Nonadenoma Cohorts.

NEJM 1993;329:1977-81
NEJM 2012;366:687-96

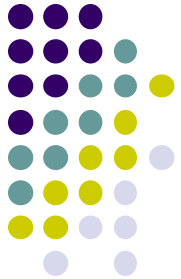
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 19, 2013 VOL. 369 NO. 12

Long-Term Colorectal-Cancer Incidence and Mortality after Lower Endoscopy

Reiko Nishihara, Ph.D., Kana Wu, M.D., Ph.D., Paul Lochhead, M.B., Ch.B., Teppei Morikawa, M.D., Ph.D., Xiaoyun Liao, M.D., Ph.D., Zhi Rong Qian, M.D., Ph.D., Kentaro Inamura, M.D., Ph.D., Sun A. Kim, M.D., Ph.D., Aya Kuchiba, Ph.D., Mai Yamauchi, Ph.D., Yu Imamura, M.D., Ph.D., Walter C. Willett, M.D., Dr.P.H., Bernard A. Rosner, Ph.D., Charles S. Fuchs, M.D., M.P.H., Edward Giovannucci, M.D., Sc.D., M.P.H., Shuji Ogino, M.D., Ph.D., and Andrew T. Chan, M.D., M.P.H.

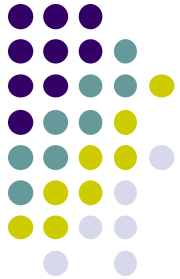
Long-Term Colorectal Cancer Incidence and Mortality after Lower Endoscopy



- Nurses's Health Study and Health Professional Follow-up Study
- 88,902 participants
- Follow-up 22 years
- Participants were asked whether they had undergone either sigmoidoscopy or colonoscopy
- Medical records and pathology reports reviewed
- 1,815 incident colorectal cancers
- 474 deaths from colorectal cancers

NEJM 2013;369:1095-105

Long-Term Colorectal Cancer Incidence and Mortality after Lower Endoscopy



- Hazard ratios for CRC
  - 0.57 (0.45-0.72) after polypectomy
  - 0.60 (0.53-0.68) after negative sigmoidoscopy
  - 0.44 (0.38-0.52) after negative colonoscopy
- Reduced incidence of proximal CRC
  - 0.73 (0.57-0.92) after negative colonoscopy
- Hazard ratio for death from CRC
  - 0.59 (0.45-0.76) after screening sigmoidoscopy
  - 0.32 (0.24-0.45) after screening colonoscopy
- Reduced mortality from proximal CRC
  - 0.47 (0.29-0.76) after screening colonoscopy

NEJM 2013;369:1095-105

Effect of screening sigmoidoscopy and screening colonoscopy on colorectal cancer incidence and mortality: systematic review and meta-analysis of randomised controlled trials and observational studies

OPEN ACCESS

BMJ 2014;348:g2467

Hermann Brenner *professor of epidemiology*[1 2], Christian Stock *senior researcher in epidemiology*[1 3], Michael Hoffmeister *senior researcher in epidemiology*[1]

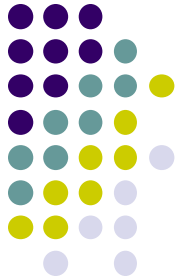
Effect of screening sigmoidoscopy and screening colonoscopy on colorectal cancer incidence and mortality: systematic review and meta-analysis of randomised controlled trials and observational studies

BMJ 2014;348:g2467

Examination	Incidence*			Mortality*		
	Any site	Proximal	Distal	Any site	Proximal	Distal
Sigmoidoscopy 4 randomised trials 10 observational studies	0.51 (0.39-0.65)	0.76 (0.65-0.90)	0.36 (0.26-0.50)	0.53 (0.30-0.97)	0.96 (0.74-1.23)	0.34 (0.19-0.69)
Colonoscopy 6 observational studies	0.31 (0.12-0.77)	0.44 (0.15-1.31)	0.21 (0.03-1.53)	0.32 (0.23-0.43)	0.47 (0.29-0.76)	0.18 (0.10-0.31)

* Relative risk

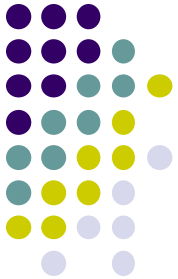
Screening Colonoscopy: High Risk Groups



	Risk CRC	Description
Category 1	2-fold	One first degree relative with CRC >55 years
Category 2	3-6 fold	One first degree relative with CRC <55 years Two first degree relatives on the same side of the family diagnosed at any age
Category 3	50% +	•FAP, HNPCC or other familial CRC syndrome •One first-degree relative plus two or more first- or second-degree relatives, all on the same side of the family, with a diagnosis of CRC, at any age •Two first-degree relatives, or one first-degree relative plus one or more second-degree relatives, all on the same side of the family, with a diagnosis of CRC and one such relative − was diagnosed with CRC under the age of 55 years, or − developed multiple bowel cancers, or − developed an extracolonic tumour suggestive of hereditary non-polyposis colorectal cancer (i.e., endometrial, ovarian, stomach, small bowel, upper renal tract, pancreas or brain) •At least one first- or second-degree family member diagnosed with CRC in association with multiple bowel polyps •A personal history or one first-degree relative with CRC diagnosed under the age of 50, •particularly where colorectal tumour immunohistochemistry has revealed loss of mismatch repair gene (hMLH1 or hMSH2)

NZGG 2012

Screening Colonoscopy: High Risk Groups - Action

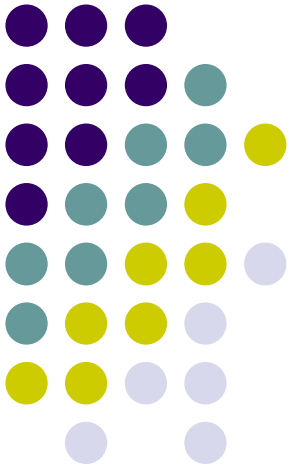


	Risk CRC	Description
Category 1	2-fold	No screening recommendations
Category 2	3-6 fold	Offer colonoscopy every 5 years commencing age 50 (or from an age 10 years before the earliest age at which CRC was diagnosed in the family, which ever come first)
Category 3	50%+	Refer to Genetic Services or NZ Familial Gastrointestinal Cancer Service Timing of 1st colonoscopy dependent on cancer syndrome and genetic testing e.g. HNPCC – begin age 20 to 25 years or 10 years before the youngest case in the immediate family

NZGG 2012

Polyp Follow-up

Guidelines



Five-Year Colon Surveillance After Screening Colonoscopy

Gastroenterology 2007;133:1077=1085

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Table 4. Relative Risk of Advanced Neoplasia Within 5.5 Years Based on Baseline Finding

Baseline finding (n with examination)	No advanced neoplasia, n (%)	Advanced neoplasia, n (%)	RR[a]	95% CI	*P* value	Cancer n (%)	HGD/cancer per 1000 person-yr (95% CI)
No neoplasia (298)	291 (97.6)	7 (2.4)	1.00			1 (0.3)	0.7 (0–2.0)
Tub Ad <10 mm (622)	584 (93.9)	38 (6.1)	2.56	1.16–5.67	.02	4 (0.6)	1.5 (0–2.9)
1 or 2 (496)	473 (95.4)	23 (4.6)	1.92	0.83–4.42	.13	3	1.4 (0–2.9)
>3 (126)	111 (88.1)	15 (11.9)[b]	5.01	2.10–11.96	< .001	1	1.9 (0–5.5)
Tub Ad >10 mm (123)	104 (84.6)	19 (15.5)	6.40	(2.74–14.94)	< .001	1 (0.8)	6.4 (0–13.5)
Villous adenoma (81)	68 (83.9)	13 (16.1)	6.05	(2.48–14.71)	< .001	1 (1.2)	6.2 (0–14.7)
HGD (46)	38 (82.6)	8 (17.4)	6.87	(2.61–18.07)	< .001	2 (4.4)	26.0 (3.2–48.8)
Cancer (23)	15 (65.2)	8 (34.8)	13.56	(5.54–33.18)	< .001	5 (21.7)	74.8 (14.9–134.7)
Number of adenomas[c] at baseline (n)							
1 or 2 (617)	577	40 (6.5)				7 (1.1)	3.3 (1.2–5.5)
3 or 4 (145)	122	23 (15.9)				2 (1.4)	6.6 (0.1–13.0)
5–9 (64)	53	11 (17.2)				3 (4.7)	13.1 (0.0–27.9)
10+ (8)	7	1 (12.5)				0	0.0

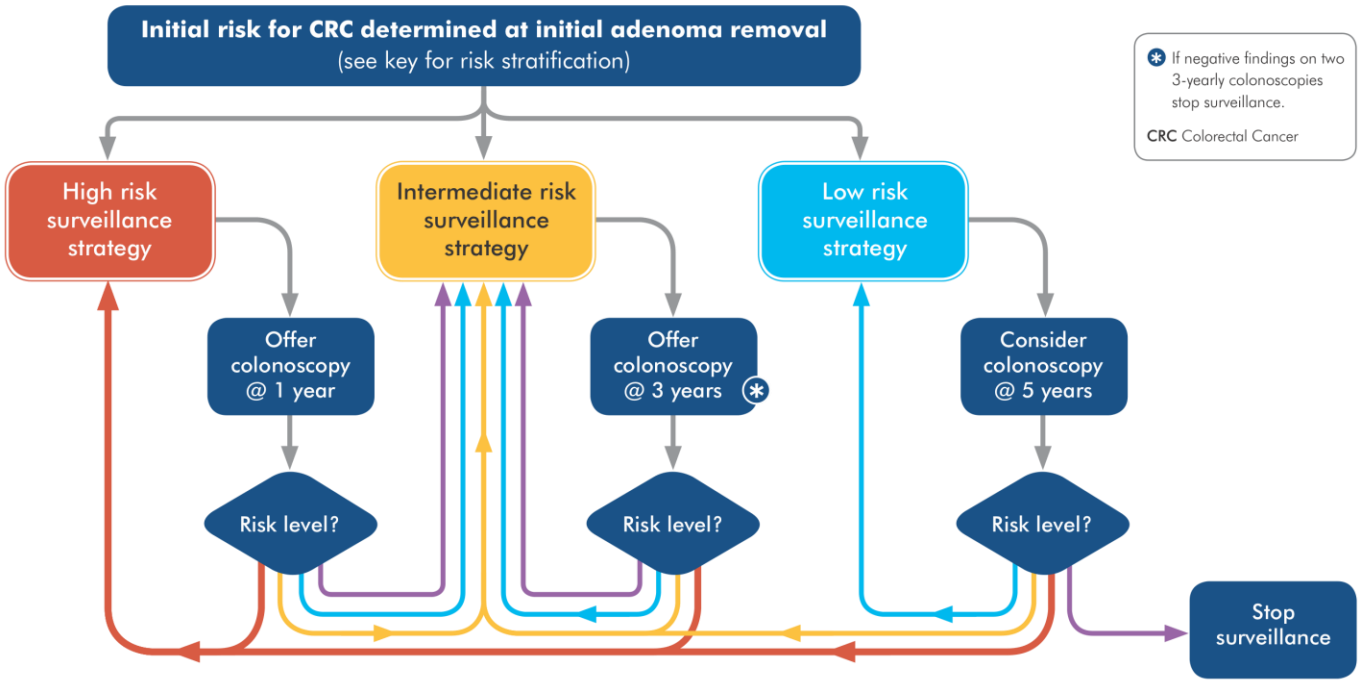
NOTE. Advanced neoplasia defined as tubular adenoma ≥10 mm, adenoma with villous histology or high-grade dysplasia, or invasive cancer. HGD, high-grade dysplasia; Tub Ad, tubular adenomas.

[a]Adjusted for age and family history.

[b]Compared with patients with 1 or 2 tubular adenomas <10 mm at baseline, patients with 3 or more had a higher rate of advanced neoplasia ($P < .002$).

[c]Adenoma number, irrespective of size and histology; not included in the multivariate model.

Figure 1 Colonoscopic surveillance strategy: people with adenomas



Key: Risk stratification

High risk for CRC

Five or more adenomas smaller than 10 mm

or

three or more adenomas if one is 10 mm or larger

Intermediate risk for CRC

Three or four adenomas smaller than 10 mm

or

one or two adenomas if one is 10 mm or larger

or

histological polyps with villous features

or

polyps with high grade dysplasia

Low risk for CRC

One or two adenomas smaller than 10 mm

Negative finding

No adenomas found

NZGG 2012

Assumes complete colonoscopy, adequate bowel prep and complete polyp resection

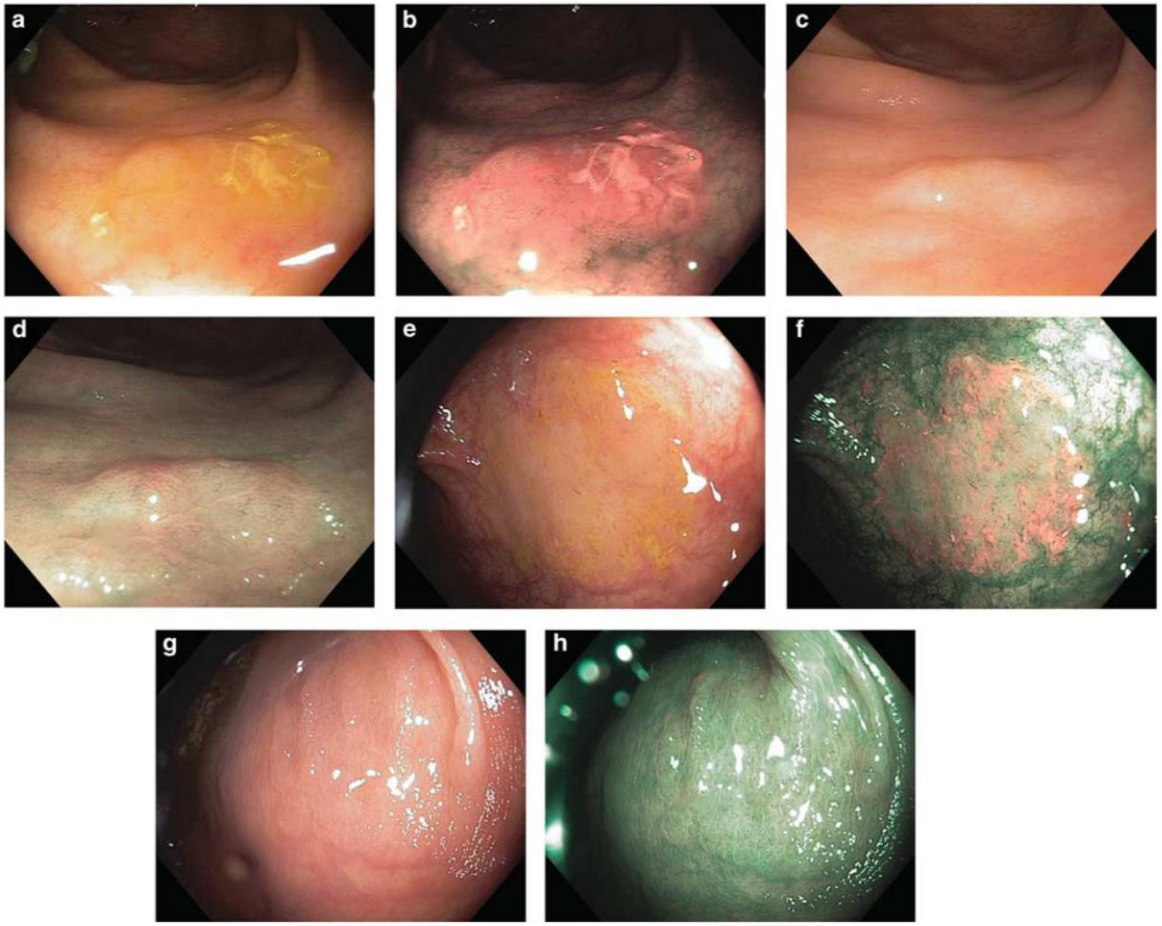
Multi-Society Task Force on Colorectal Cancer Colon Polyp Surveillance: Clinical Decision Tool

<table>
<tr><th colspan="3">No polyps, or hyperplastic polyps in rectum/sigmoid</th></tr>
<tr><td colspan="3">Repeat in 10 years</td></tr>
<tr><th colspan="3">Neoplasia found</th></tr>
<tr><th>Serrated polyps/lesions</th><th>High risk adenomas</th><th>Low risk adenomas</th></tr>
<tr><td rowspan="2">Serrated polyposis
Repeat in 1 year</td><td>> 10 Adenomas
Repeat in less than 3 years</td><td rowspan="4">1–2 Tubular adenomas < 10 mm
Repeat in 5–10 years</td></tr>
<tr><td rowspan="2">3–10 Adenomas
Repeat in 3 years</td></tr>
<tr><td rowspan="2">≥ 10 mm or With dysplasia or traditional serrated adenoma
Repeat in 3 years</td></tr>
<tr><td>Villous adenoma(s) or tubular adenoma(s) ≥ 10 mm
Repeat in 3 years</td></tr>
<tr><td rowspan="2">< 10 mm in Proximal colon and without dysplasia
Repeat in 5 years</td><td>Adenoma(s) with high grade dysplasia
Repeat in 3 years</td></tr>
</table>

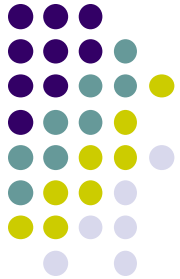
These recommended intervals assume a complete exam to cecum, adequate bowel prep, and complete removal of polyps at the baseline exam.

Gastroenterology 2014;146:305-6

Sessile serrated polyps

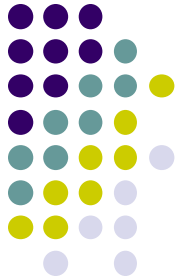


Surveillance:
Post Colon Cancer Resection



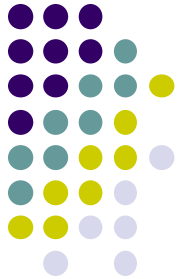
- Clear colon of synchronous disease
- First follow-up colonoscopy 1 year
- If first follow-up negative next exam in 3-5 years
- If patient under 50 years consider closer intervals
- CEA
- Consider annual CT scan and CXR

Surveillance: Post Rectal Cancer Resection



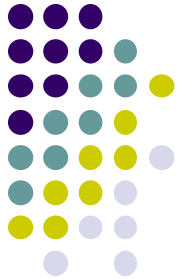
- Best approach may depend on how the cancer was treated
- Lower local recurrence rates associated with total mesorectal excision and with neoadjuvant radiation/chemotherapy
- If risk of local recurrence high
  - Consider flexi-sigmoidoscopy or rectal EUS every 3-6 months for first 2 years'
- Other surveillance same as for colon cancer

Surveillance: Inflammatory Bowel Disease



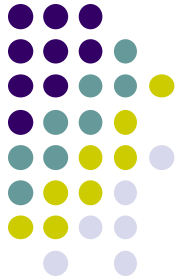
- Risk
  - Individuals with longstanding (>8-10 years) extensive ulcerative colitis have an increased risk of CRC
  - Studies suggest 2% by 10 years, 8% by 20 years and 18% by 30 years.
  - Individuals with total or extensive colitis are at greater risk of developing CRC than those with left sided or colitis affecting only rectum and sigmoid
  - Individuals with longstanding extensive Crohn's disease have a similar risk
- Recommendation
  - Refer individuals with UC and CR of 8-10 years duration for colonoscopy with serial biopsies to define disease extent and to examine for dysplasia OR chromoendoscopy and directed biopsy

Limitations of Colonoscopy



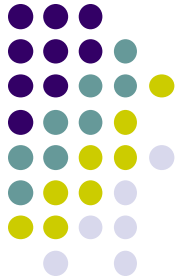
- Colonoscopy and polypectomy prevents about 80% of colorectal cancers
  - WINAWER SJ ET AL. THE NATIONAL POLYP STUDY N ENGL J MED 1993;329:1977–81.
  - CITARDA F ET AL. ITALIAN STUDY GUT 2001;48:812–5.
  - THIIS-EVENSEN E ET AL. TELEMARK POLYP STUDY SCAND. J GASTROENTEROL 1999;34:414–20.
- Less protective against proximal CRC
- Missed adenomas
  - Tandem colonoscopy studies (Rex 6%)
  - CT colonoscopy studies (Pickhardt 12% and Van Gelder 17%)
- Missed cancers i.e. neoplasia within 3 years of a clear colonoscopy
  - 0.63% - pooled data from 8 US prospective colonoscopy studies after median follow-up of 4 years
  - 2.9% - Dutch community-based study of CRC diagnosed within 5 years of colonoscopy
  - ROBERTSON ET AL. Gut 2014;63:949-956 and CHANTAL ET AL. Gut 2014;63:957-963
- Complications
  - bleeding, perforation etc

Possible causes of Missed Cancer after Colonoscopy



- Biological variation in growth rates of tumours
- Incomplete removal of polyps
  - technical limitations in detection
  - hidden mucosa
- Flat polyps
- Incomplete colonoscopy
- Inadequate bowel preparation
- Suboptimal examination technique

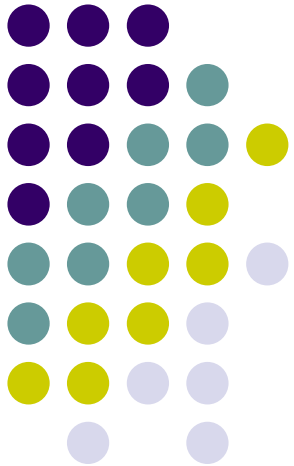
Quality Colonoscopy



- Bowel preparation
  - split prep
  - runway time
- Caecal intubation rate
  - >95% (?>98%)
- Polyp detection rate
  - Adenoma detection rate
    - Males >25% and females >15%
  - Adenoma per colonoscopy
    - Males >0.50 and females >0.20
  - Serrated lesion detection rate
  - Careful inspection
  - Withdrawal time
  - Training
  - High definition imaging
- Adherence to recommended screening and surveillance intervals

Colonoscopy Audit

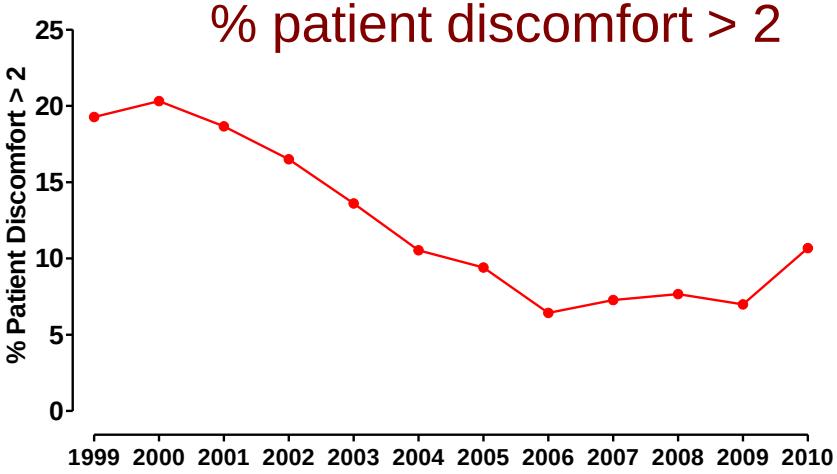
Endoscopy Auckland and
MercyAscot Endoscopy



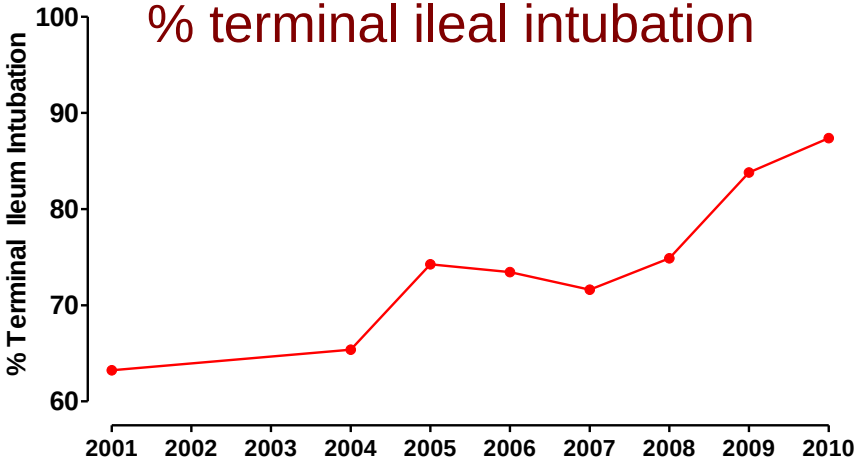
TRENDS

% adjusted caecal intubation rate

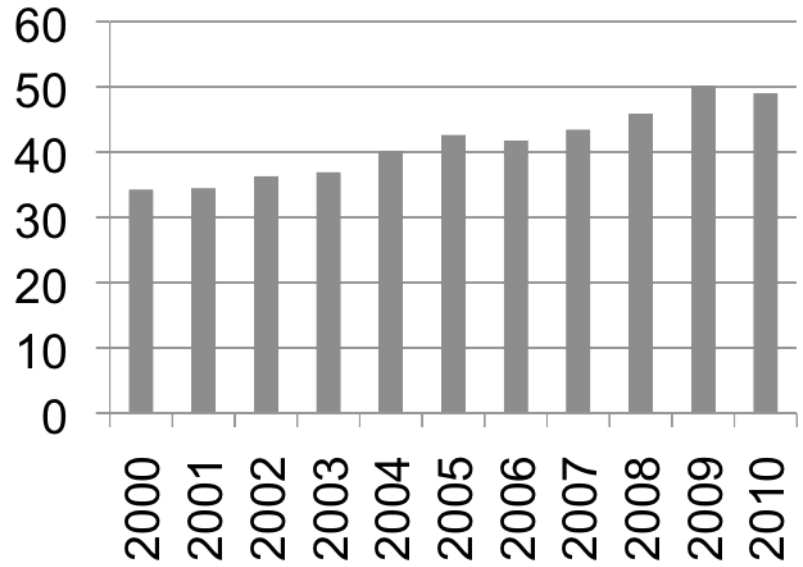
% patient discomfort > 2



% terminal ileal intubation

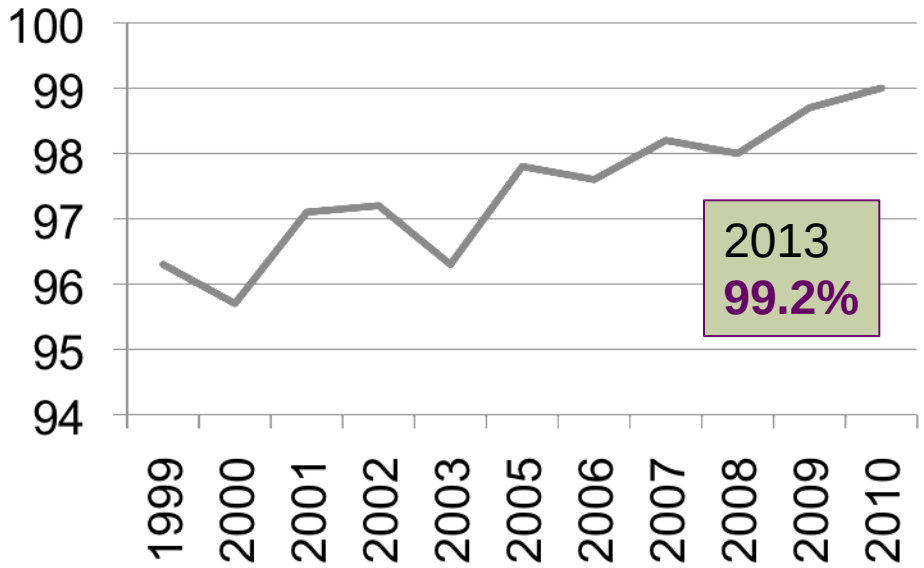


% polyps

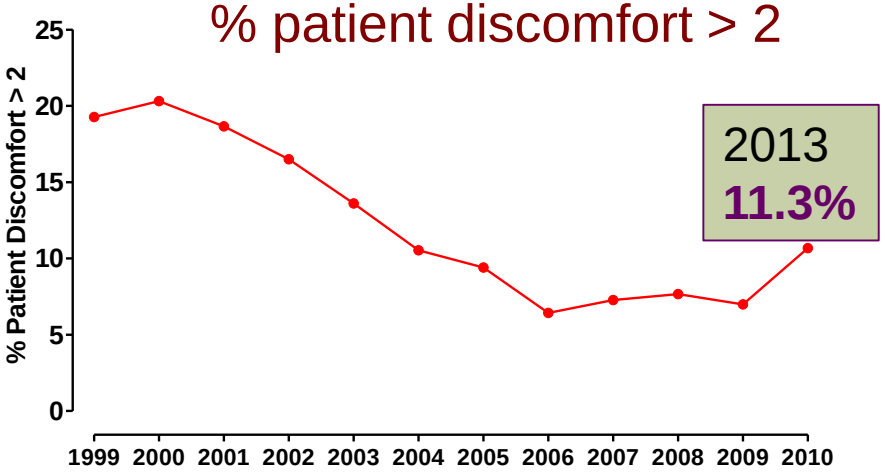


TRENDS

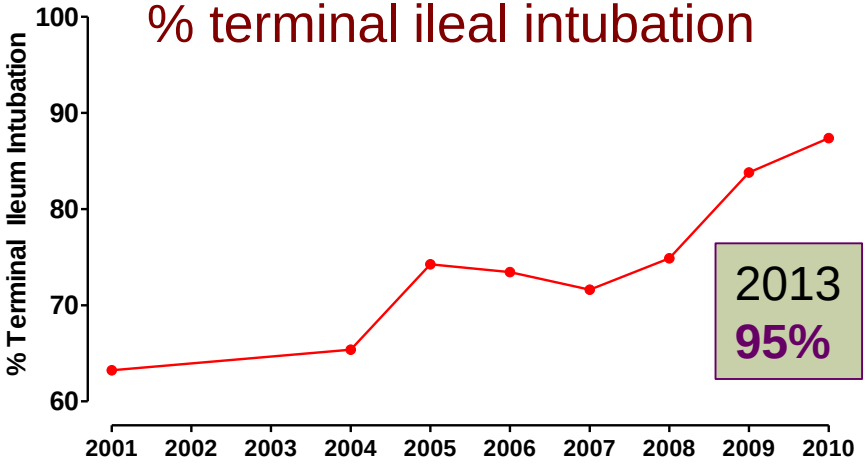
% adjusted caecal intubation rate



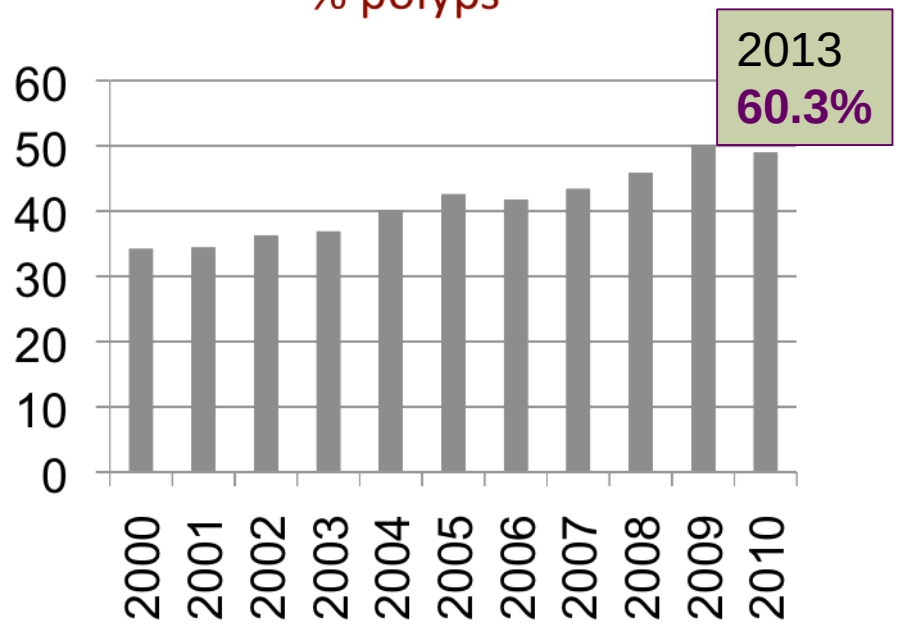
% patient discomfort > 2



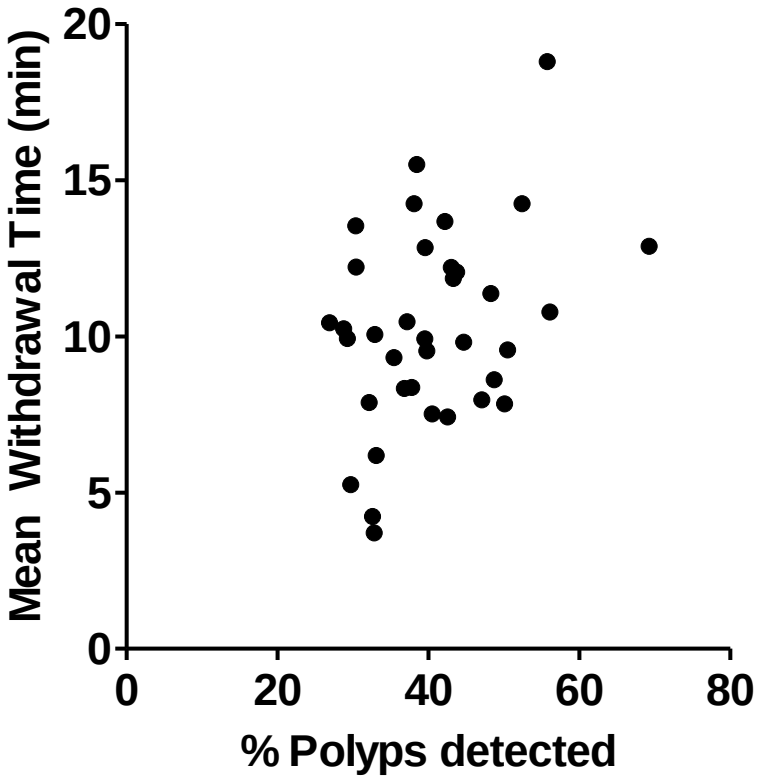
% terminal ileal intubation



% polyps

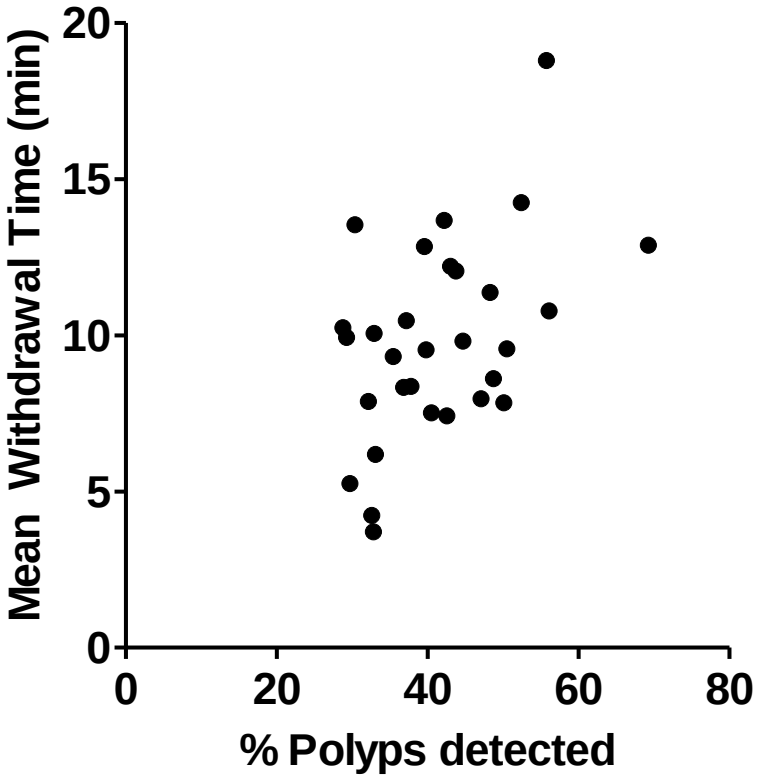


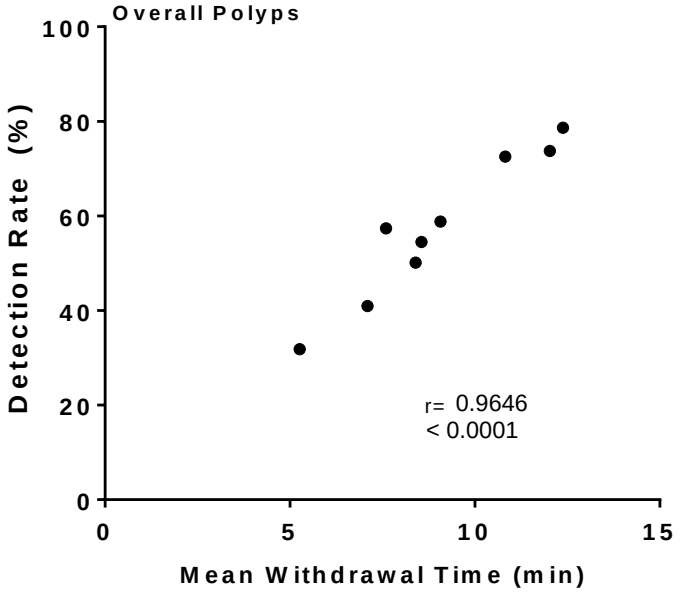
All Endoscopists (n=65,642 procedures)

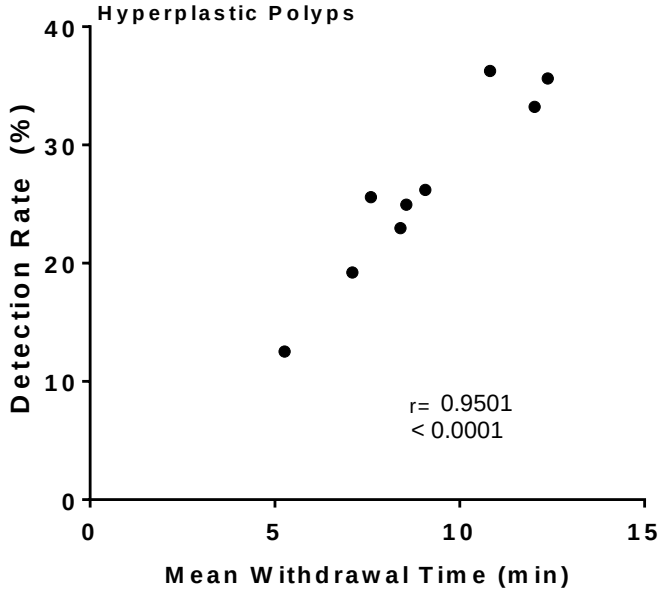


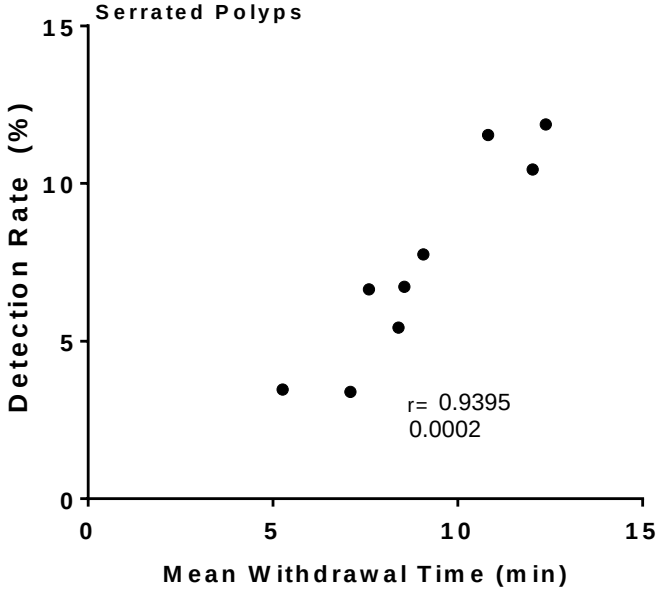
Excluding endoscopists with < 100 Procedures
(n=65,433 procedures 7 endoscopists excluded)

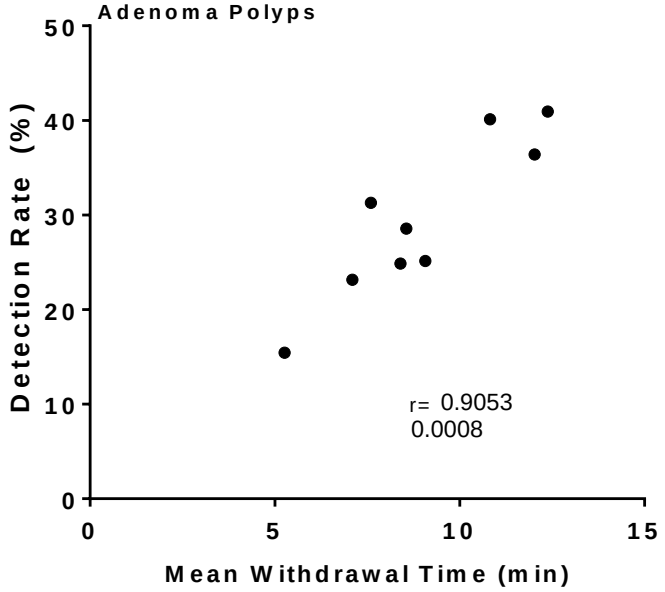
r = 0.42
P = 0.03




Overall Polyps
Detection Rate (%)
100
80
60
40
20
0
0
5
10
15
Mean Withdrawal Time (min)
r= 0.9646
< 0.0001


Hyperplastic Polyps
Detection Rate (%)
40
30
20
10
0
0
5
10
15
Mean Withdrawal Time (min)
r= 0.9501
< 0.0001


Serrated Polyps
Detection Rate (%)
15
10
5
0
0
5
10
15
Mean Withdrawal Time (min)
r= 0.9395
0.0002


Adenoma Polyps
Detection Rate (%)
50
40
30
20
10
0
0
5
10
15
Mean Withdrawal Time (min)
r= 0.9053
0.0008

Effect of a Time-Dependent Colonoscopy Withdrawal Protocol on Adenoma Detection During Screening Colonoscopy.

Barclay CGH 2008;6:1091-1098

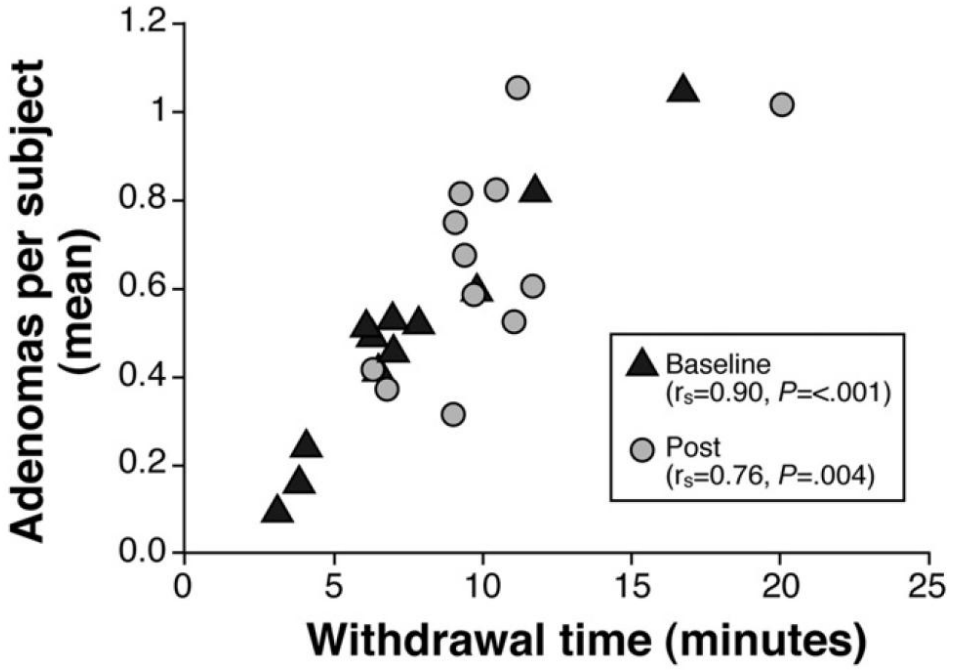


Figure 2. Physician adenoma detection rates versus colonoscopic withdrawal times in examinations without polyp removal. Baseline: r_s = 0.90; $P < .001$; postintervention: r_s = 0.76; $P = .004$.

Take home message

- Screening for colorectal cancer is effective
  - average risk
  - high risk
- Make sure your patient with a history of bowel cancer or polyps has appropriate surveillance
- Make sure your patient gets a quality colonoscopy

Have you had a colonoscopy?

Self colonoscopy in the sitting position.

Thank you