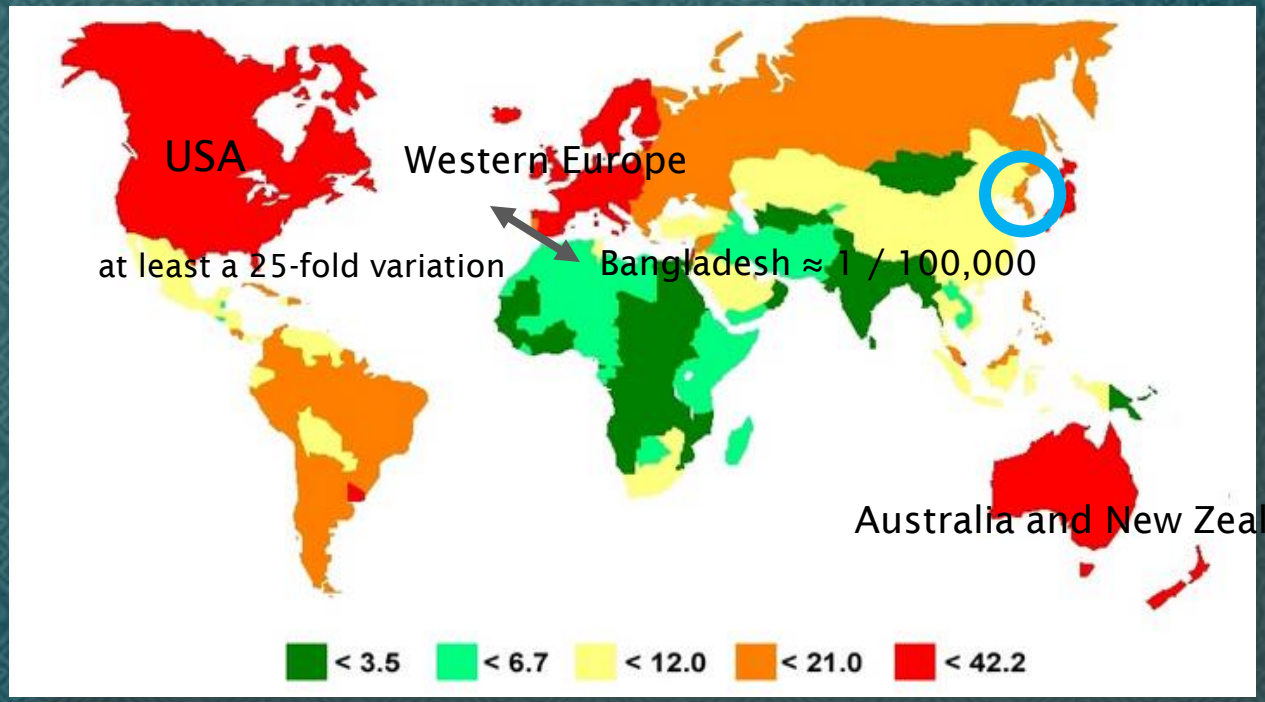
대장암과 대장용종

홍 성 노

삼성서울병원 소화기내과

Distribution of Colorectal Cancer (CRC) Worldwide (GLOBOCAN 2002)

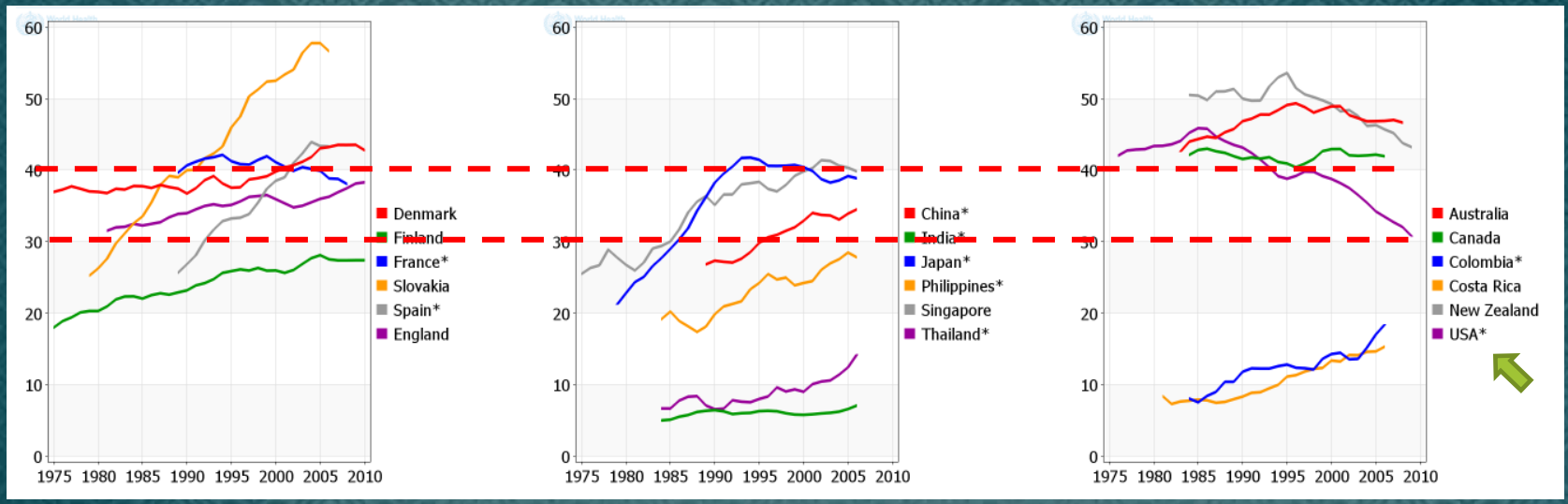
About 1 million new cases of CRC were diagnosed in 2002 (9.4% of all cancer diagnoses worldwide)



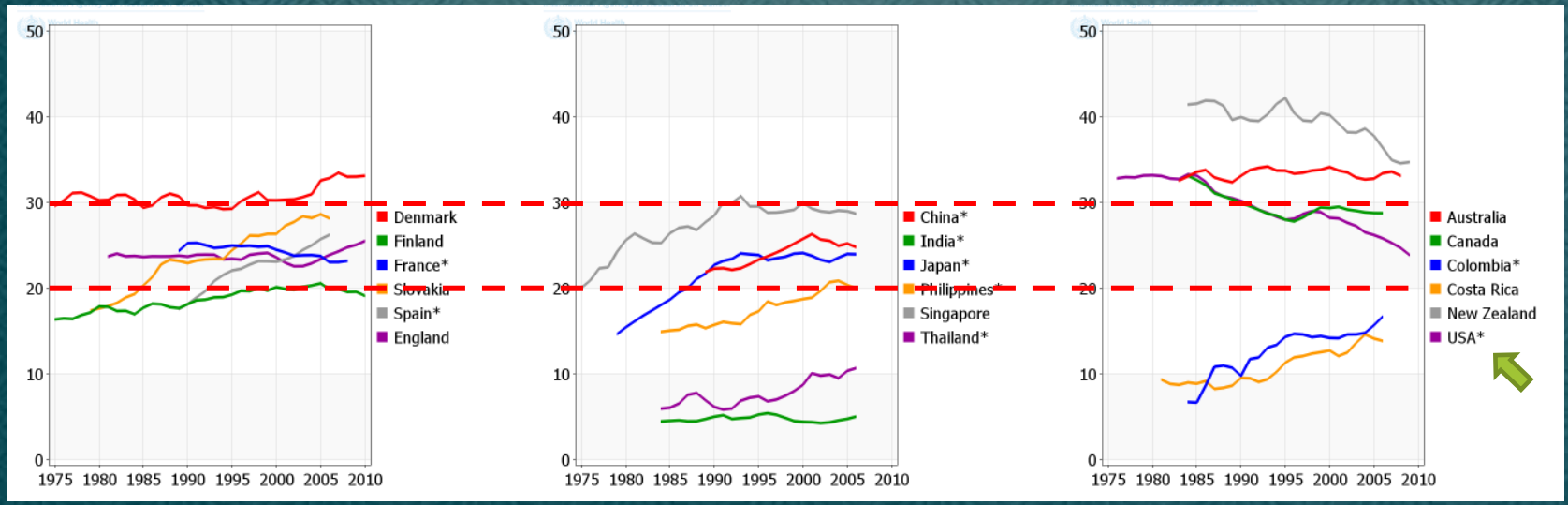
Age-standardized rate per 100,000

- Overall the average rate of colorectal cancer amongst males in countries defined by the WHO as 'less developed' is around **20%** of that in the industrialized west.

Trends in incidence of colorectal cancer in selected countries (GLOBOCAN 2012)

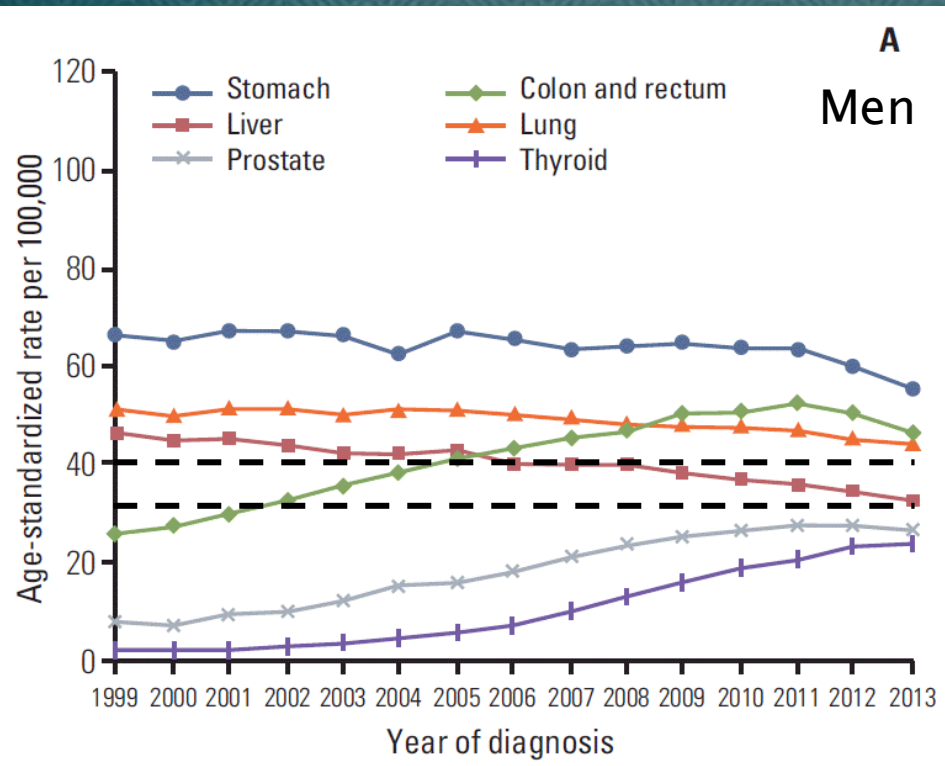


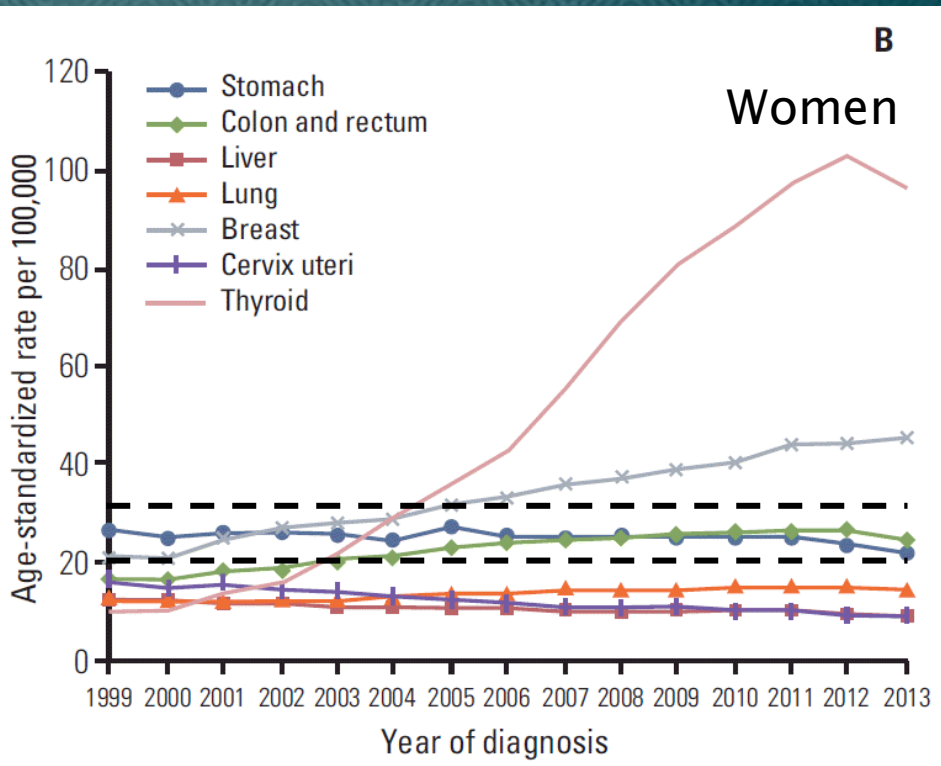
/10^5 men



/10^5 women

Trends in age-standardized incidences of selected cancers from 1999 to 2013 in Korea





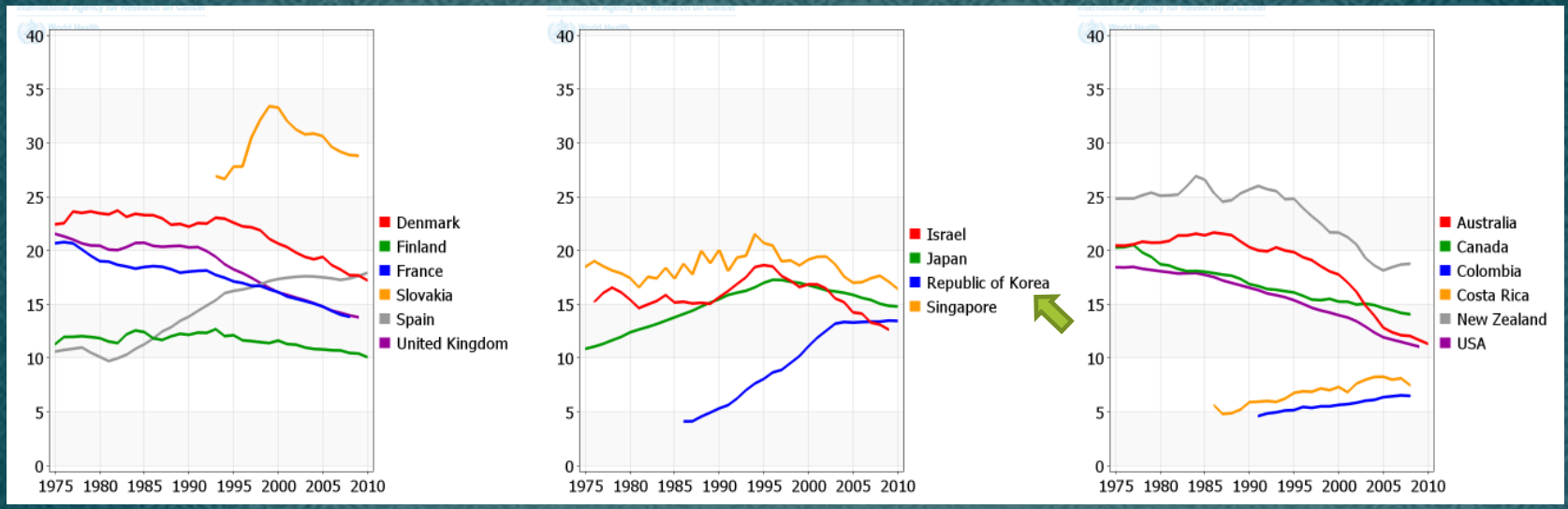
Cancer Res Treat 2016; 48

Colonic Epithelial Tumors	Risk of malignant transformation (% of LN metastasis)	WHO (Western viewpoint)
Non-neoplastic lesion		
Hyperplastic polyp	No	K635
Neoplastic lesion		
Adenoma, low grade dysplasia		D12
Adenoma, high grade dysplasia	Low (<1)	D01
Carcinoma in situ		D01
Intraepithelial carcinoma		D01
Intramucosal carcinoma (lamina propria invasion)		D01
Colorectal cancer (invasion to submucosa)		
SM invasion < 1000 μm	Intermediate (1-4.8)	C18, C19, C20
SM invasion > 1000 μm, poorly diff., lymphovascular inv., and budding	High (10)	

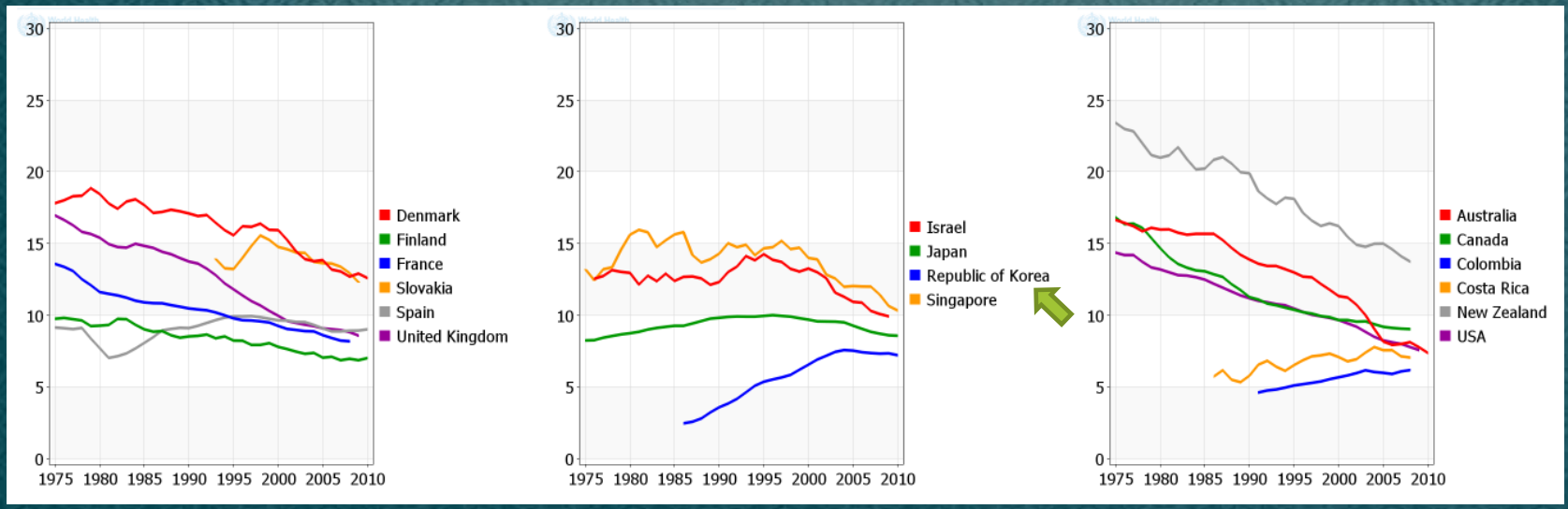
Traditional Japanese Viewpoint

Gastrointest Endosc 2009;70:1182-99.

Trends in mortality from colorectal cancer in selected countries (GLOBOCAN 2012)

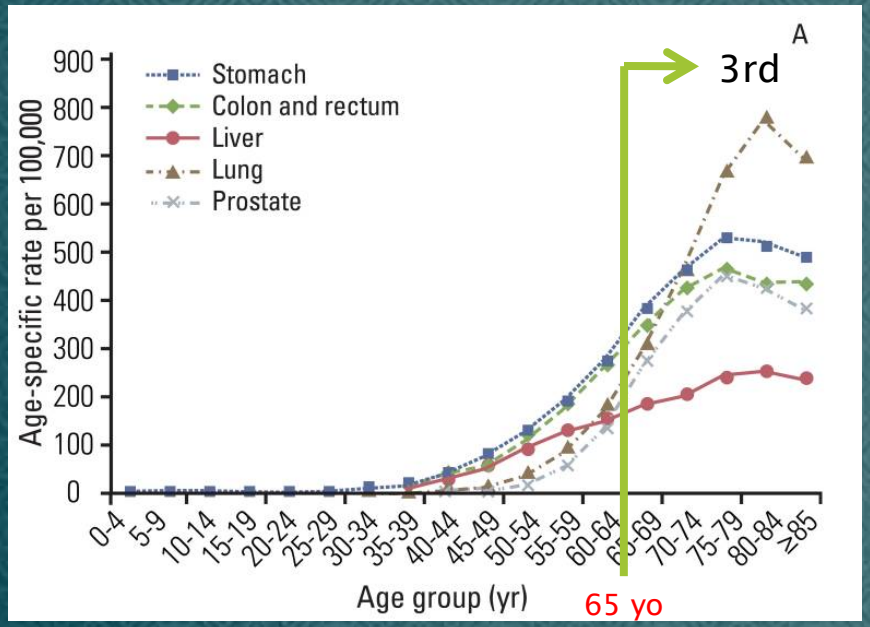


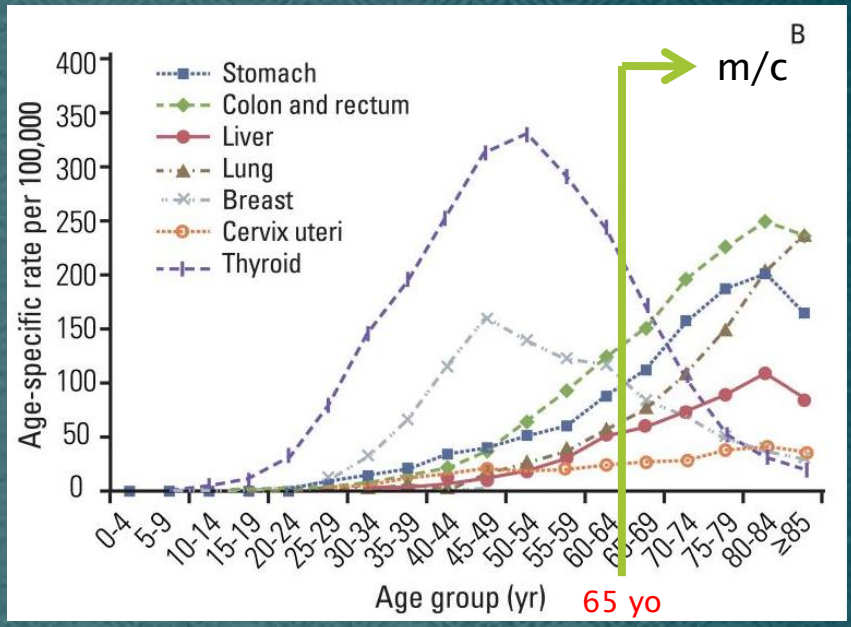
/10^5 men



/10^5 women

Age-specific incidences of CRC

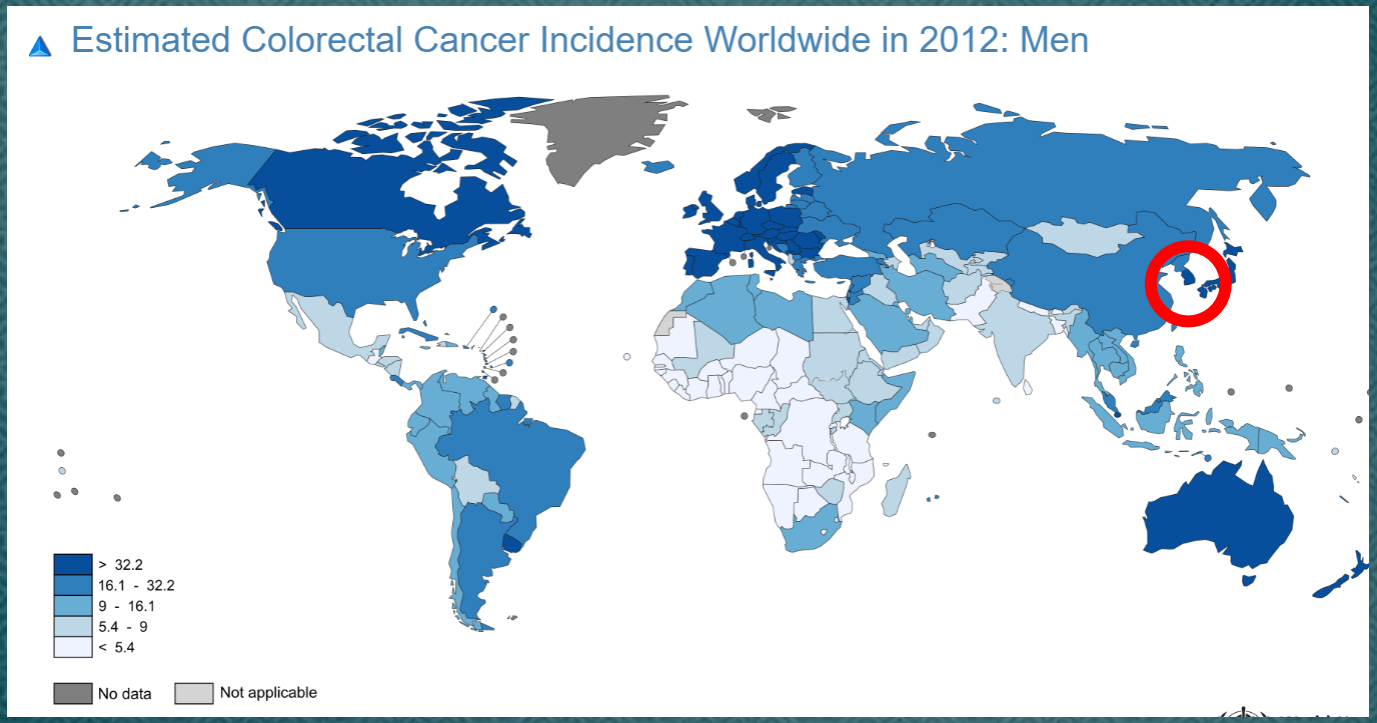




Projected age-specific incidences of major cancers during 2012 in Korea. (A) Male. (B) Female.

Cancer Res Treat 2012; 44: 25-31.

Distribution of Colorectal Cancer (CRC) Worldwide (GLOBOCAN 2012)



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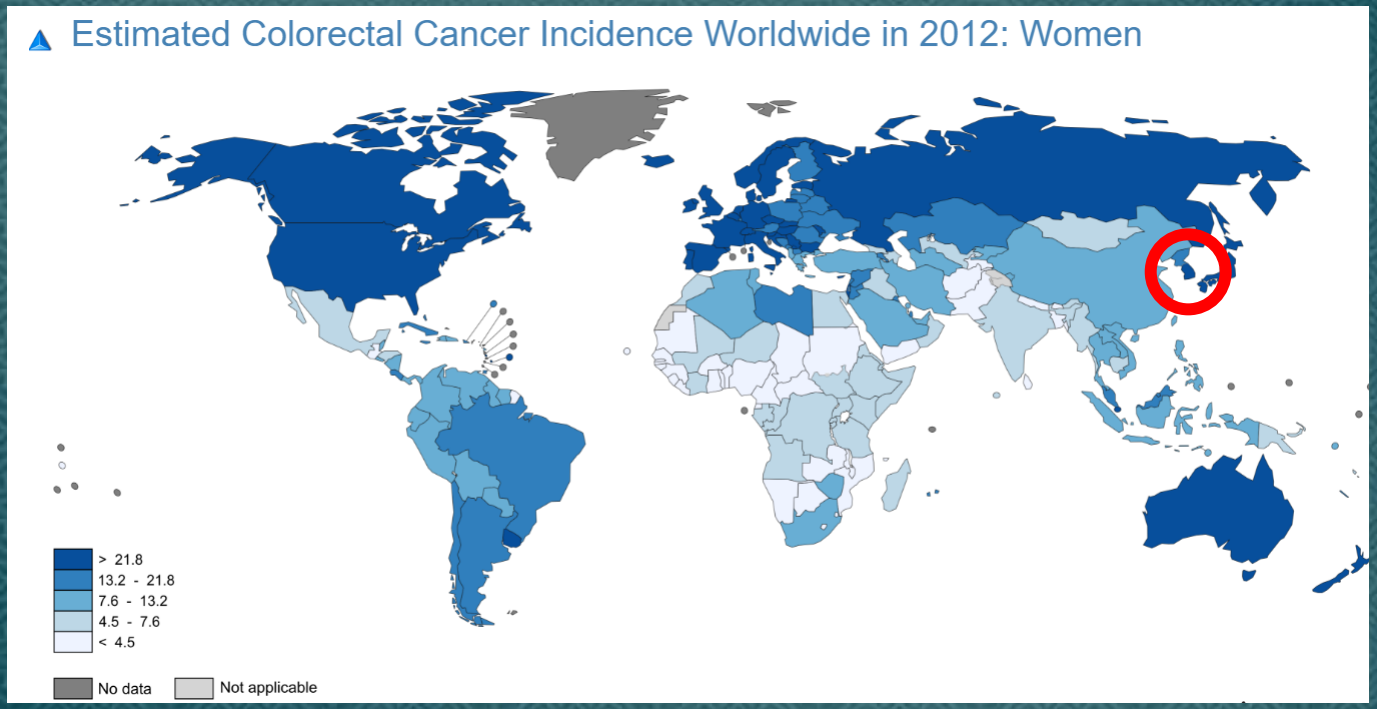
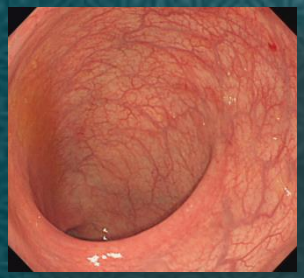
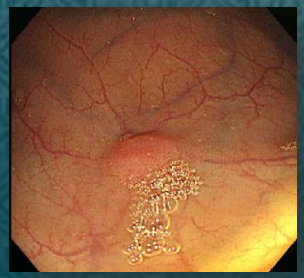
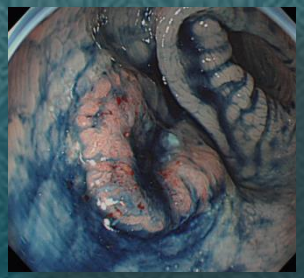
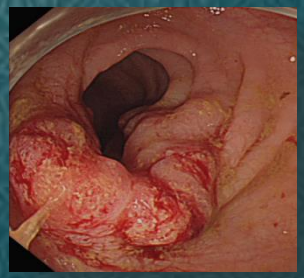


Carcinogenesis of colorectal cancer: Opportunity for CRC Screening

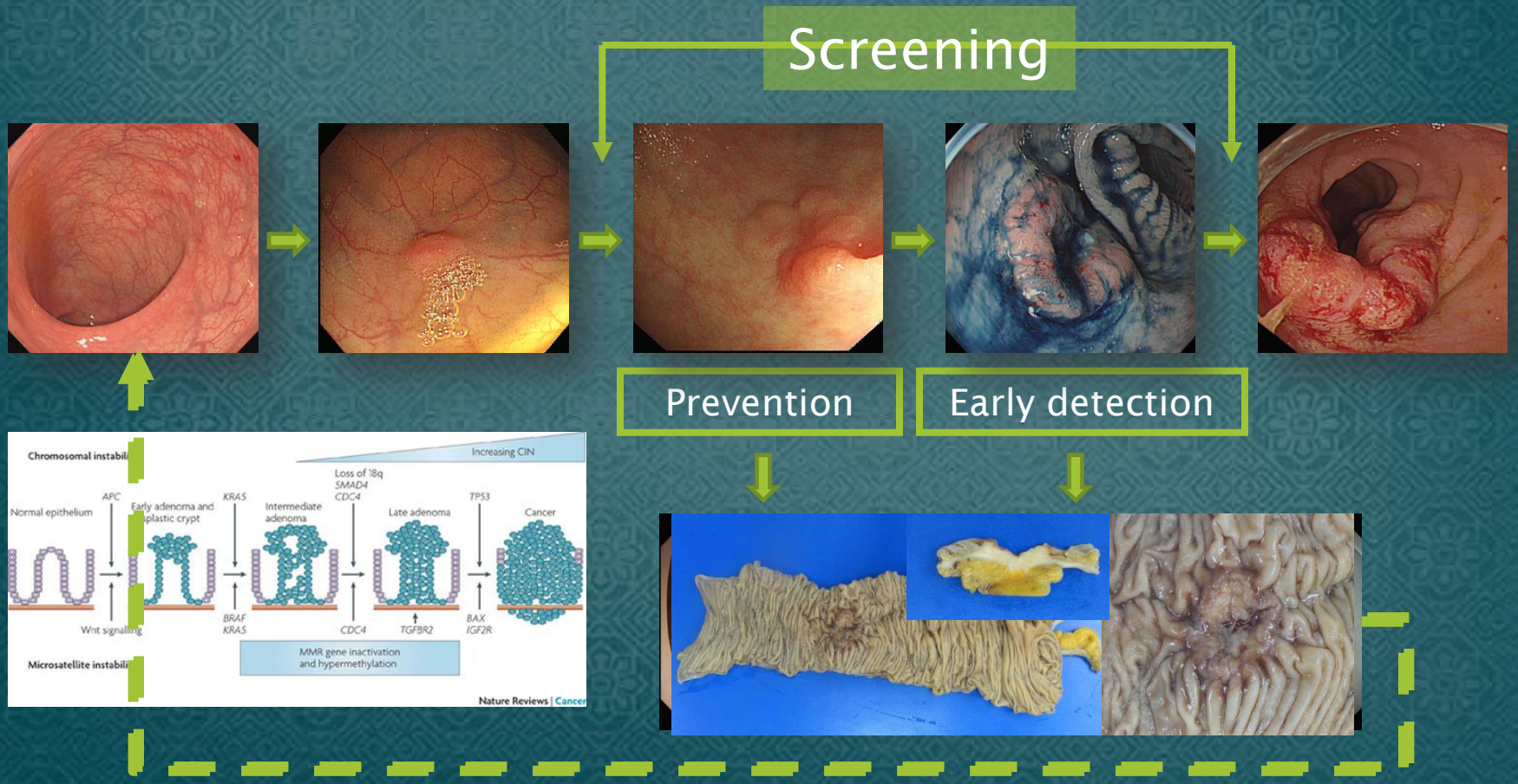



Colorectal Carcinogenesis

Colorectal Carcinogenesis

- Adenoma-Carcinoma sequence



대장암은 예방 가능한 암

- 대장암은 예방 가능한 암이란 인식과 이에 대한 관심 증가

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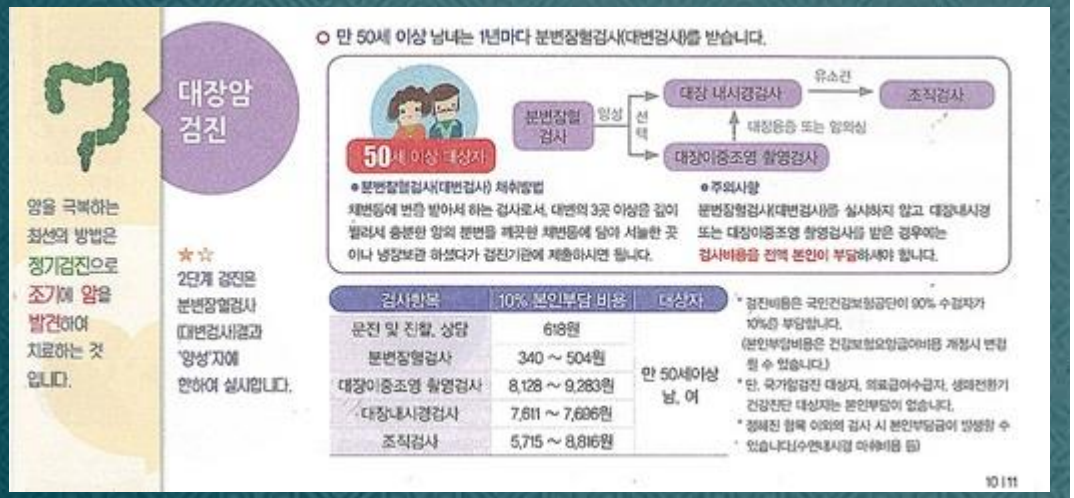
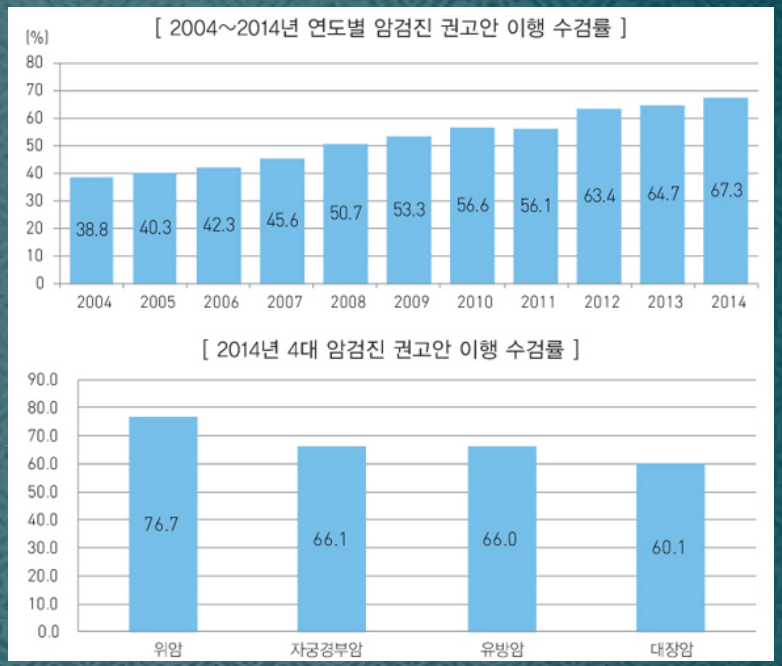
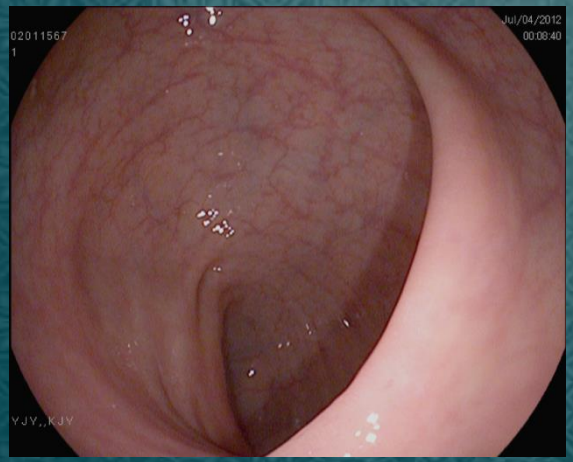


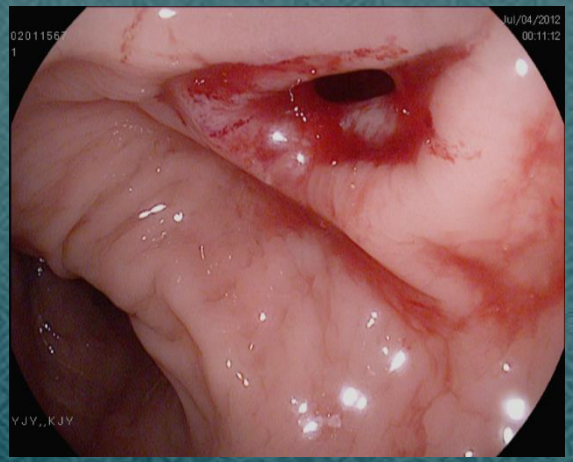


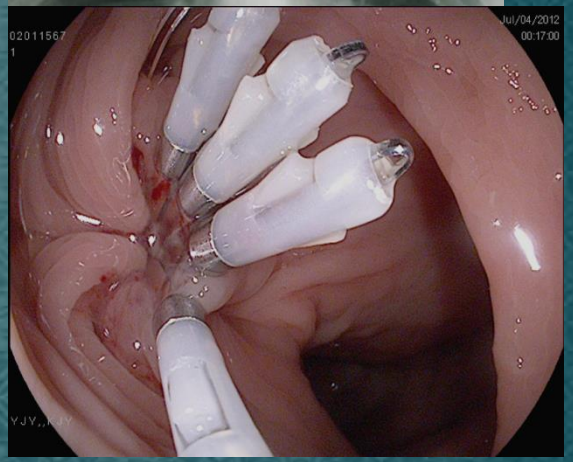
「2014년 암검진 수검행태 조사」

38/M

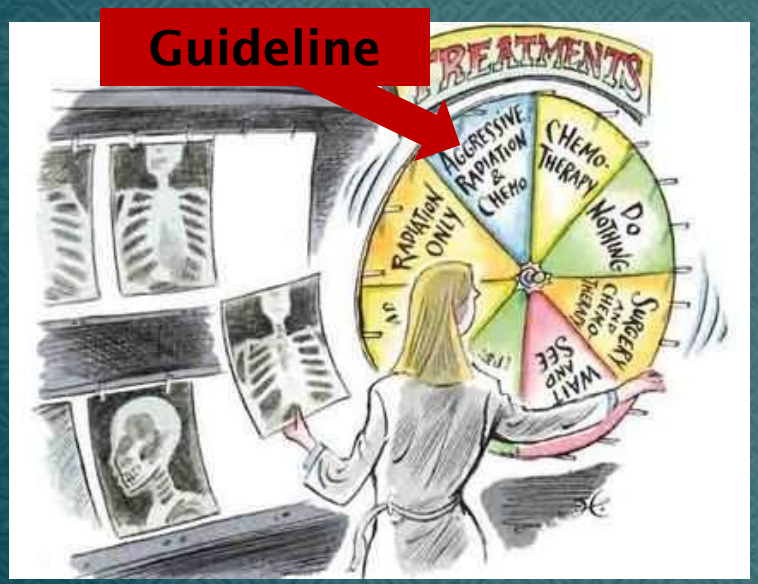
- 대장암 가족력 (-)
- 과거력: 대장질환(-)
- 소화기 증상 (-)
- 직장 건강검진 대장내시경검사





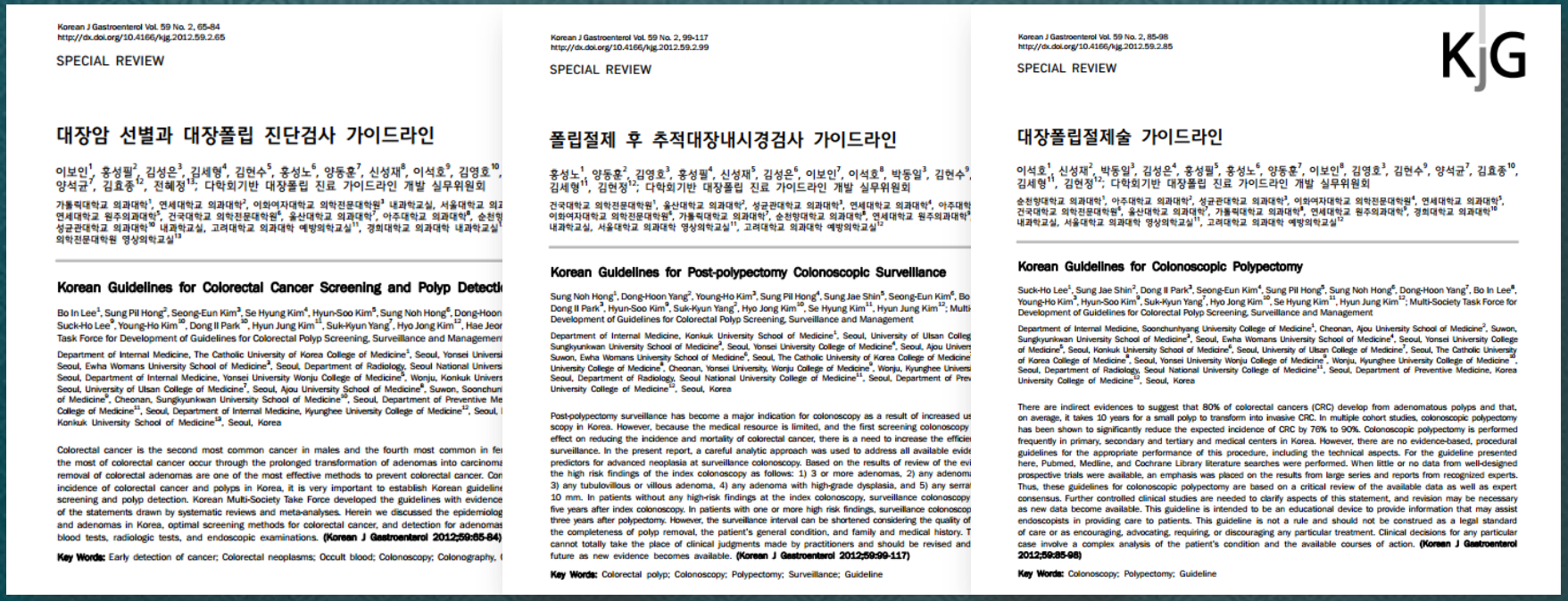


Evidence-based medicine



Evidence-based health care can improve those odds, save lives and cut health care costs

2012 대장폴립의 진료 가이드라인



Korean J Gastroenterol Vol. 59 No. 2, 65-84
http://dx.doi.org/10.4166/kjg.2012.59.2.65

SPECIAL REVIEW

대장암 선별과 대장폴립 진단검사 가이드라인

이보인[1], 홍성필[2], 김성은[3], 김세형[4], 김현수[5], 홍성노[6], 양동훈[7], 신성재[8], 이석호[9], 김영호[10], 양석균[7], 김효종[12], 전혜정[13]; 다학회기반 대장폴립 진료 가이드라인 개발 실무위원회

가톨릭대학교 의과대학[1], 연세대학교 의과대학[2], 이화여자대학교 의학전문대학원[3] 내과학교실, 서울대학교 의과
연세대학교 원주의과대학[5], 건국대학교 의학전문대학원[6], 울산대학교 의과대학[7], 아주대학교 의과대학[8], 순천
성균관대학교 의과대학[10] 내과학교실, 고려대학교 의과대학 예방의학교실[11], 경희대학교 의과대학 내과학교실
의학전문대학원 영상의학교실[13]

Korean Guidelines for Colorectal Cancer Screening and Polyp Detecti

Bo In Lee[1], Sung Pil Hong[2], Seong-Eun Kim[3], Se Hyung Kim[4], Hyun-Soo Kim[5], Sung Noh Hong[6], Dong-Hoon
Suck-Ho Lee[8], Young-Ho Kim[10], Dong Il Park[10], Hyun Jung Kim[11], Suk-Kyun Yang[7], Hyo Jong Kim[12], Hae Jeor
Task Force for Development of Guidelines for Colorectal Polyp Screening, Surveillance and Management

Department of Internal Medicine, The Catholic University of Korea College of Medicine[1], Seoul, Yonsei Universi
Seoul, Ewha Womans University School of Medicine[3], Seoul, Department of Radiology, Seoul National Universi
Seoul, Department of Internal Medicine, Yonsei University Wonju College of Medicine[5], Wonju, Konkuk Univers
Seoul, University of Ulsan College of Medicine[7], Seoul, Ajou University School of Medicine[8], Suwon, Soonchuni
of Medicine[9], Cheonan, Sungkyunkwan University School of Medicine[10], Seoul, Department of Preventive Me
College of Medicine[11], Seoul, Department of Internal Medicine, Kyunghee University College of Medicine[12], Seoul,
Konkuk University School of Medicine[13], Seoul, Korea

Colorectal cancer is the second most common cancer in males and the fourth most common in fe
the most of colorectal cancer occur through the prolonged transformation of adenomas into carcinoma
removal of colorectal adenomas are one of the most effective methods to prevent colorectal cancer. Cor
incidence of colorectal cancer and polyps in Korea, it is very important to establish Korean guideline
screening and polyp detection. Korean Multi-Society Take Force developed the guidelines with evidence
of the statements drawn by systematic reviews and meta-analyses. Herein we discussed the epidemiolog
and adenomas in Korea, optimal screening methods for colorectal cancer, and detection for adenomas
blood tests, radiologic tests, and endoscopic examinations. **(Korean J Gastroenterol 2012;59:65-84)**

Key Words: Early detection of cancer; Colorectal neoplasms; Occult blood; Colonoscopy; Colonography,

Korean J Gastroenterol Vol. 59 No. 2, 99-117
http://dx.doi.org/10.4166/kjg.2012.59.2.99

SPECIAL REVIEW

폴립절제 후 추적대장내시경검사 가이드라인

홍성노[1] 양동훈[2], 김영호[3], 홍성필[4], 신성재[5], 김성은[6], 이보인[7], 이석호[8], 박동일[3], 김현수[9],
김세형[11], 김현정[12]; 다학회기반 대장폴립 진료 가이드라인 개발 실무위원회

건국대학교 의학전문대학원[1], 울산대학교 의과대학[2], 성균관대학교 의과대학[3], 연세대학교 의과대학[4], 아주대학
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내과학교실, 서울대학교 의과대학 영상의학교실[11], 고려대학교 의과대학 예방의학교실[12]

Korean Guidelines for Post-polypectomy Colonoscopic Surveillance

Sung Noh Hong[1], Dong-Hoon Yang[2], Young-Ho Kim[3], Sung Pil Hong[4], Sung Jae Shin[5], Seong-Eun Kim[6], Bo
Dong Il Park[7], Hyun-Soo Kim[8], Suk-Kyun Yang[7], Hyo Jong Kim[10], Se Hyung Kim[11], Hyun Jung Kim[12]; Multi
Development of Guidelines for Colorectal Polyp Screening, Surveillance and Management

Department of Internal Medicine, Konkuk University School of Medicine[1], Seoul, University of Ulsan Colleg
Sungkyunkwan University School of Medicine[2], Seoul, Yonsei University College of Medicine[4], Seoul, Ajou Univers
Suwon, Ewha Womans University School of Medicine[6], Seoul, The Catholic University of Korea College of Medicine
University College of Medicine[8], Cheonan, Yonsei University, Wonju College of Medicine[9], Wonju, Kyunghee Univers
Seoul, Department of Radiology, Seoul National University College of Medicine[11], Seoul, Department of Prev
University College of Medicine[12], Seoul, Korea

Post-polypectomy surveillance has become a major indication for colonoscopy as a result of increased us
scopy in Korea. However, because the medical resource is limited, and the first screening colonoscopy
effect on reducing the incidence and mortality of colorectal cancer, there is a need to increase the efficie
surveillance. In the present report, a careful analytic approach was used to address all available evid
predictors for advanced neoplasia at surveillance colonoscopy. Based on the results of review of the evi
the high risk findings of the index colonoscopy as follows: 1) 3 or more adenomas, 2) any adenom
3) any tubulovillous or villous adenoma, 4) any adenoma with high-grade dysplasia, and 5) any serra
10 mm. In patients without any high-risk findings at the index colonoscopy, surveillance colonoscopy
five years after index colonoscopy. In patients with one or more high risk findings, surveillance colonoscop
three years after polypectomy. However, the surveillance interval can be shortened considering the quality of
the completeness of polyp removal, the patient's general condition, and family and medical history. T
cannot totally take the place of clinical judgments made by practitioners and should be revised and
future as new evidence becomes available. **(Korean J Gastroenterol 2012;59:99-117)**

Key Words: Colorectal polyp; Colonoscopy; Polypectomy; Surveillance; Guideline

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KJG

SPECIAL REVIEW

대장폴립절제술 가이드라인

이석호[1], 신성재[2], 박동일[3], 김성은[4], 홍성필[5], 홍성노[6], 양동훈[7], 이보인[8], 김영호[3], 김현수[9], 양석균[7], 김효종[10],
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Korean Guidelines for Colonoscopic Polypectomy

Suck-Ho Lee[1], Sung Jae Shin[2], Dong Il Park[3], Seong-Eun Kim[4], Sung Pil Hong[5], Sung Noh Hong[6], Dong-Hoon Yang[7], Bo In Lee[8],
Young-Ho Kim[9], Hyun-Soo Kim[9], Suk-Kyun Yang[7], Hyo Jong Kim[10], Se Hyung Kim[11], Hyun Jung Kim[12]; Multi-Society Task Force for
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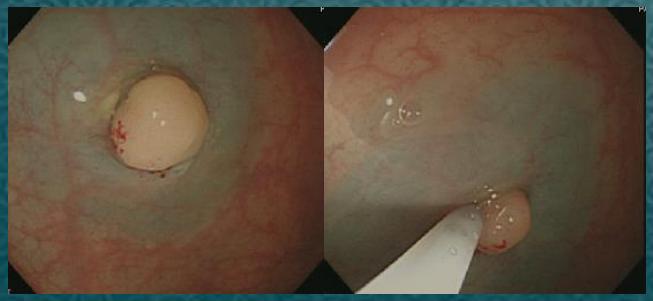
Seoul, Department of Radiology, Seoul National University College of Medicine[11], Seoul, Department of Preventive Medicine, Korea
University College of Medicine[12], Seoul, Korea

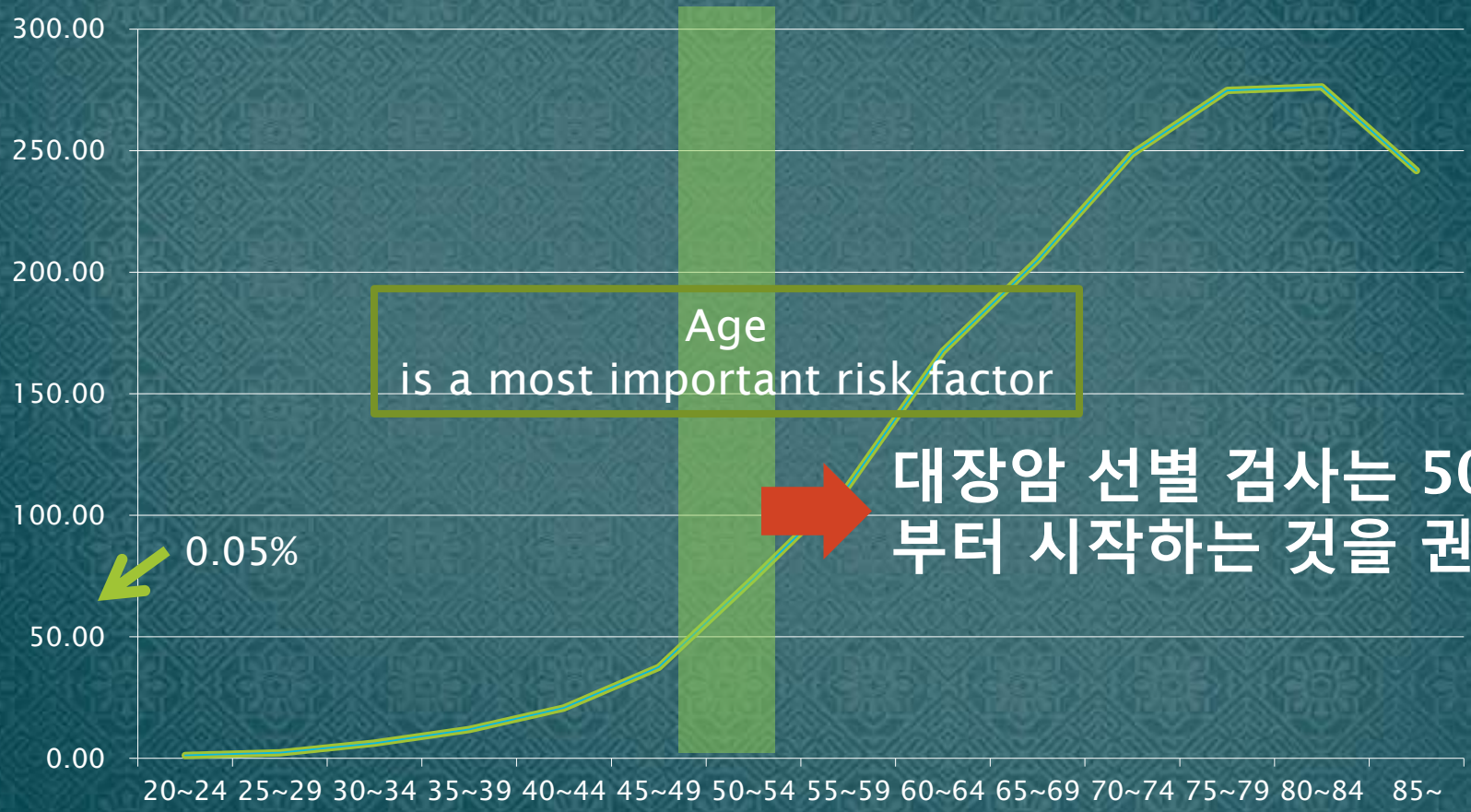
There are indirect evidences to suggest that 80% of colorectal cancers (CRC) develop from adenomatous polyps and that, on average, it takes 10 years for a small polyp to transform into invasive CRC. In multiple cohort studies, colonoscopic polypectomy has been shown to significantly reduce the expected incidence of CRC by 76% to 90%. Colonoscopic polypectomy is performed frequently in primary, secondary and tertiary and medical centers in Korea. However, there are no evidence-based, procedural guidelines for the appropriate performance of this procedure, including the technical aspects. For the guideline presented here, Pubmed, Medline, and Cochrane Library literature searches were performed. When little or no data from well-designed prospective trials were available, an emphasis was placed on the results from large series and reports from recognized experts. Thus, these guidelines for colonoscopic polypectomy are based on a critical review of the available data as well as expert consensus. Further controlled clinical studies are needed to clarify aspects of this statement, and revision may be necessary as new data become available. This guideline is intended to be an educational device to provide information that may assist endoscopists in providing care to patients. This guideline is not a rule and should not be construed as a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment. Clinical decisions for any particular case involve a complex analysis of the patient's condition and the available courses of action. **(Korean J Gastroenterol 2012;59:85-98)**

Key Words: Colonoscopy; Polypectomy; Guideline

Who Should Get Screened?



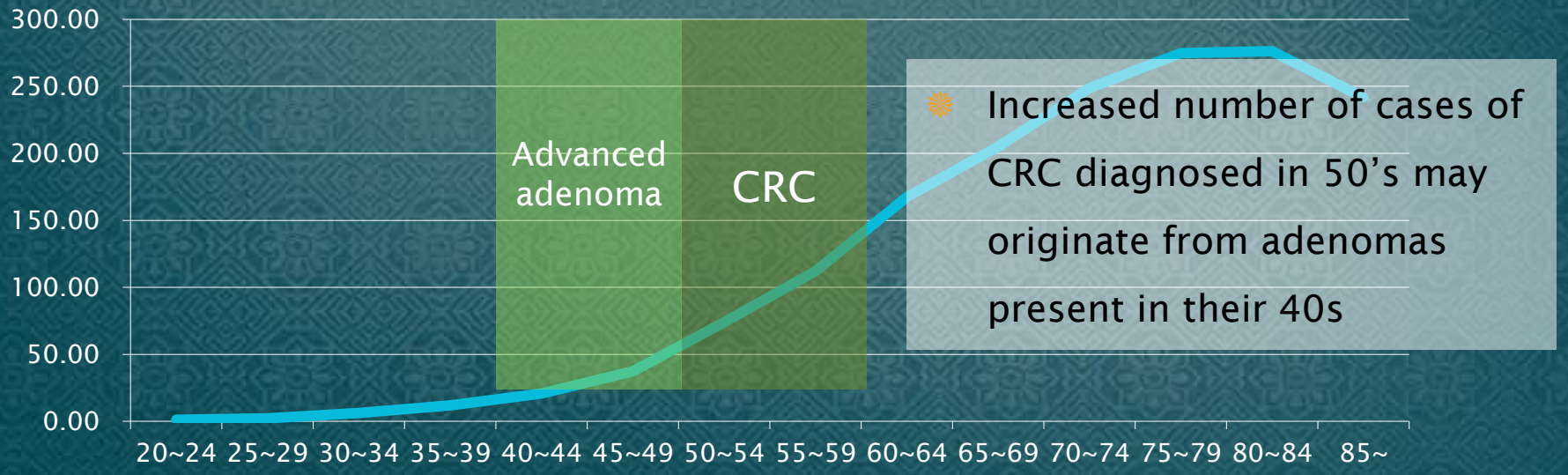
CRC incidence per 100,000 in Korean



Colorectal Carcinogenesis

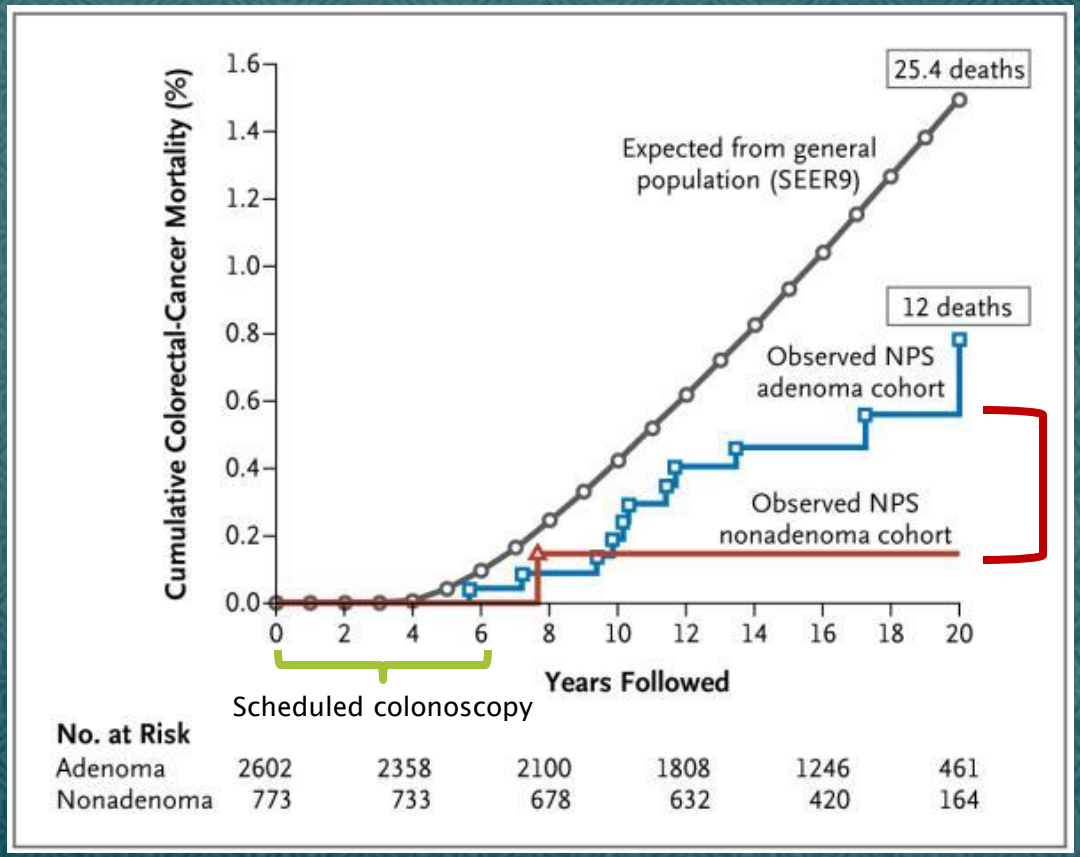
10% for 5-10 years ≈ 1% / year

Stryker. Gastroenterology 1987



Individuals with an increased risk of CRC under 50 years of age

1. Past history of colorectal neoplasia



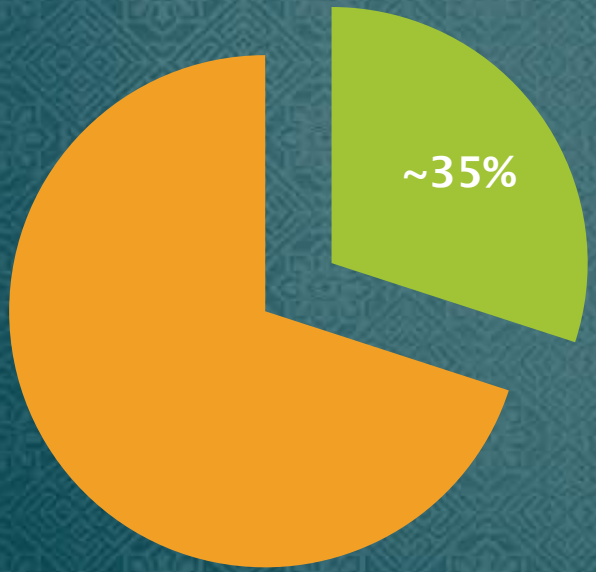
Zauber et al. NEJM 2012

Individuals with an increased risk of CRC under 50 years of age

Genetic counseling

2. Genetic predisposition of CRC

Potentially **HIGH (>50%)** Risk of CRC



- CRC with genetic susceptibility
  - < 6%
    : High-penetrance susceptibility
    - HNPCC, FAP, MYH …
  - Majority
    : co-inheritance of multiple low-risk variants

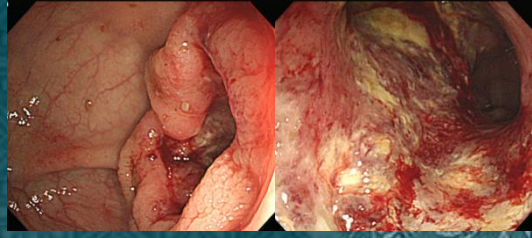
Family history

- Sporadic CRC

d/t Environmental factors (lifestyle and diet)

3. Inflammatory bowel disease

Familial risk of CRC



Familial setting			RR	95%CI
First degree relative (FDR)				
	One FDR with CRC		2.25	2.00- 2.53
		<45 y	3.87	2.40- 6.22
		45-59 y	2.25	1.85-2.72
		≥ 60 y	1.82	1.47-2.25
	Only two FDRs		3.76	2.56-5.51
	Two or more FDRs with CRC		4.25	3.01-6.02
	One FDR with an **adenoma**<60y		1.99	1.55 - 2.55
Second degree relative				
	One second or third DR with CRC		1.50	
	Two second-degree relatives with CRC		2.30	

40세
혹은
가장 어린 나이에 발병한 직계 가족 보다 **10년 먼저**
→ 대장내시경검사

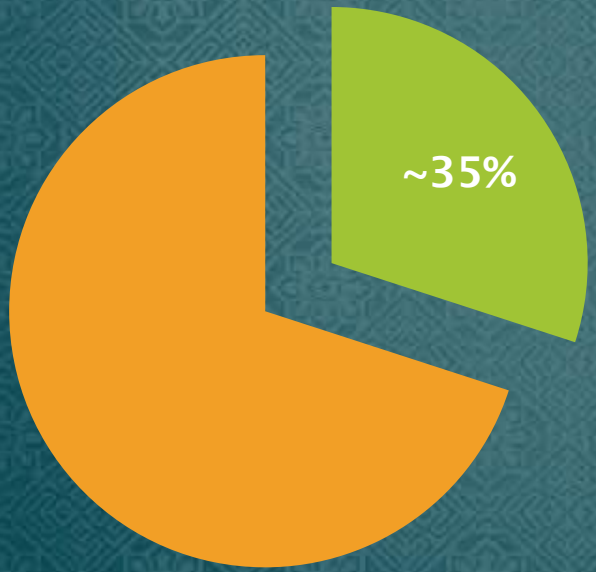
40세
→ 대장내시경검사

50세
= average-risk

Johns, Am J Gastroenterol 2001

Individuals with an increased risk of CRC under 50 years of age

2. Genetic predisposition of CRC



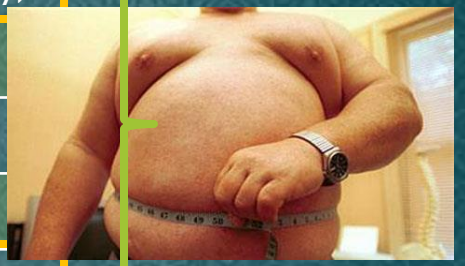
- CRC with genetic susceptibility
  - < 6%
    : High-penetrance susceptibility
    - HNPCC, FAP, MYH …
  - Majority
    : co-inheritance of multiple low-risk variants
- Sporadic CRC

d/t Environmental factors (lifestyle and diet)

3. Inflammatory bowel disease

Dietary and lifestyle factors thought to exert adverse effects on colorectal neoplasia

Factor	World Cancer Research Fund (1997)*	Current assessment†
Low physical activity	Convincing (colon only)	Convincing (colon only)
High body mass	Possible (colon only)	Convincing (colon only)
Red meat	Probable	Probable
Processed meat	Possible	Probable
Heavily cooked meat	Possible	Possible
Glycemic load	N/A	Possible
Total fat	Possible	Insufficient
Iron	Possible	Insufficient



Obesity

* Table adapted from World Cancer Research Fund. Food, Nutrition and the Prevention of Cancer: a Global Perspective. Washington DC: American Institute for Cancer Research; 1997

† Table adapted from Jonhson et al. Aliment Pharmacol Ther 2007

Individuals with an increased risk of CRC under 50 years of age

2. Genetic predisposition of CRC

3. Inflammatory bowel disease
   - Meta-analysis (Eaden et al. Gut 2001)
     : CRC risk after 10, 20, and 30 yrs of IBD = 2%, 8%, and 18%
   - Calculated incidence rate ratios for CRC in IBD patients
     - Crohn's disease = 2.64 (95%CI 1.69–4.12)
     - Ulcerative colitis = 2.75 (95%CI 1.91–3.97)

     Bernstein et al. Cancer 2001
   - Korean Multi-center study (Kim et al. JGH 2009)
     : Cumulative risk of UC-ass. CRCs for 10, 20, and 30 yrs
     = 0.7%, 7.9%, and 33.2%

Individuals with an increased risk of CRC under 50 years of age

- **Summary of AGA Guidelines 2010**

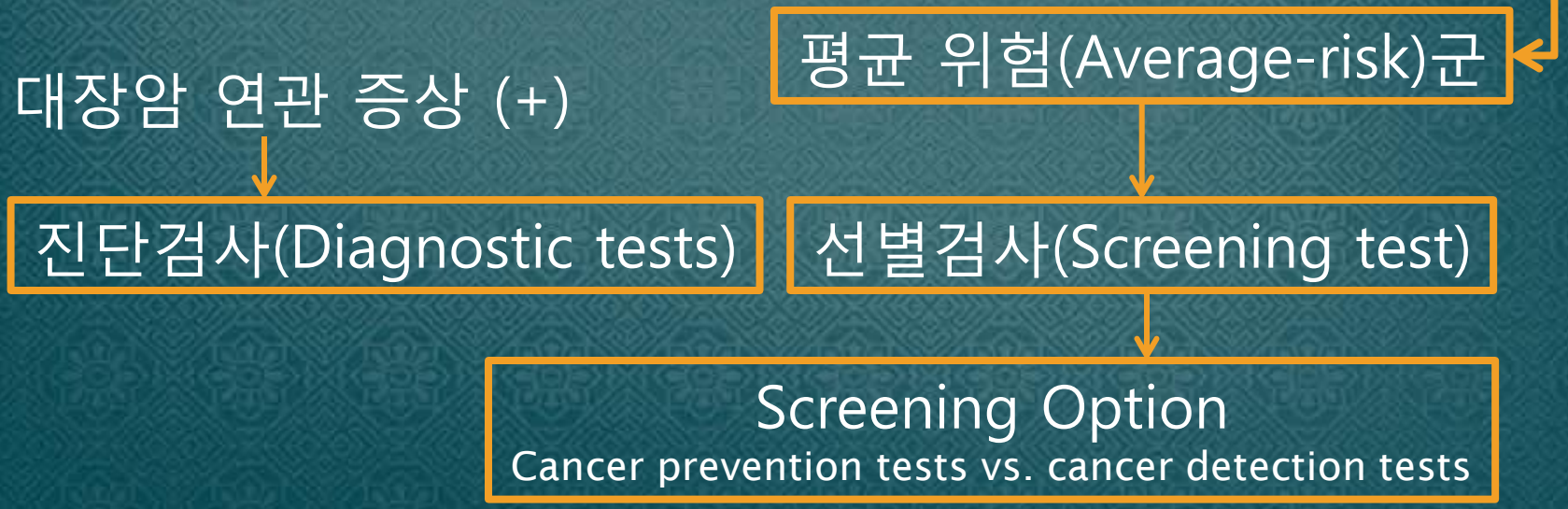
1. **Screening colonoscopy 8 years after onset of symptoms**
2. **Left-sided/extensive colitis: start surveillance within 2 yrs after initial screening**
3. **Repeat surveillance every 1-3 years**
4. **Biopsies should be taken of each anatomic section of the colon**
5. **Patients with PSC: start annual surveillance after this diagnosis**
6. **Ideally, surveillance colonoscopy should be performed when remission is achieved**
7. **A positive family history in first-degree relatives, ongoing active inflammation, anatomic abnormalities, or multiple inflammatory pseudopolyps may benefit from more frequent surveillance colonoscopies**

대장암 발생 위험 구분
Stratification of risk of CRC

- 대장암의 발생 위험은 개인마다 다름

- 고려 사항
  - 첫째, 이전에 대장샘종이나 대장암의 과거력 (-)
  - 둘째, 대장암과 대장샘종의 가족력 (-)
  - 셋째, 염증성 장질환과 같은 대장 질환 유무 (-)

- 대장암 연관 증상 (+)



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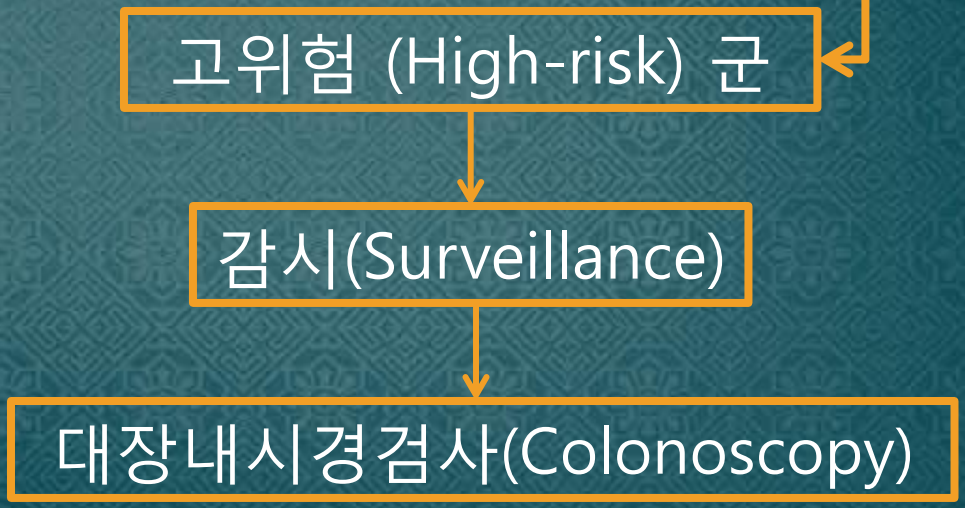
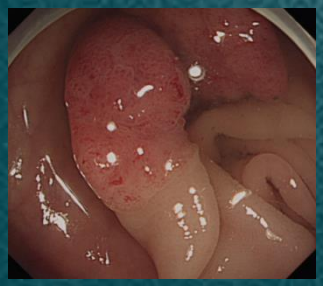
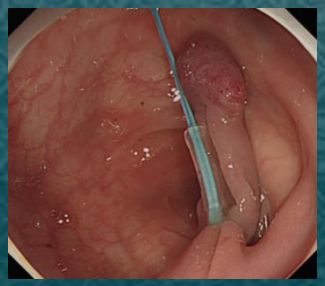
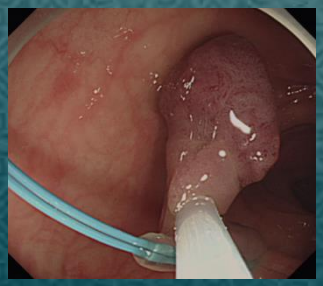
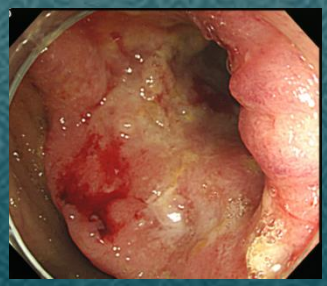
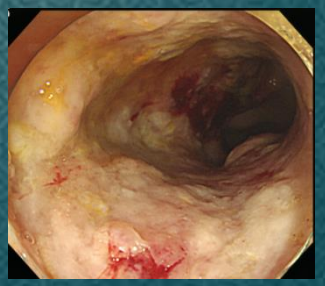


Screening Option

Cancer prevention tests vs. cancer detection tests

Cancer prevention tests vs. Cancer detection tests

No symptom

Occult tumor bleeding (+)
Tumor cell shedding

Imaging tests

High sensitivity for detection CRC and polyp

Polyp detection and removal

Cancer prevention tests

Stool test

Cancer detection tests

Screening Tests for CRC

Screening Test	Sensitivity	Specificity	Cost	Patient Information
guaiac-based FOBT	Variable	Variable	Very Low	• 3 consecutive stool sample at home • Low risk • (+) → follow-up colonoscopy
Fecal Immuno-chemical Tests (FIT)	Variable	Variable	Low	• Stool sample • Low risk • (+) → follow-up colonoscopy
stool DNA panel	Variable	High	N/A	• Adequate stool sample (≥30g) • Low risk • (+) → follow-up colonoscopy
Double-contrast barium enema (DCBE)	Low	Low	Medium	• Complete bowel preparation • Risk (+) : perforation, bleeding • (+) → follow-up colonoscopy
Flexible sigmoidoscopy	Medium	Medium	Medium	• Complete bowel preparation • Low risk • (+) → follow-up colonoscopy
Colonoscopy	High	High	High	• Complete bowel preparation • Risk (+) : perforation, bleeding
CT colonography (CTC)	Medium	Medium	High	• Complete bowel preparation • Low risk • (+) → follow-up colonoscopy

Adopted from Screening for Colorectal Cancer from American College of Physicians. Ann Intern Med. 2012

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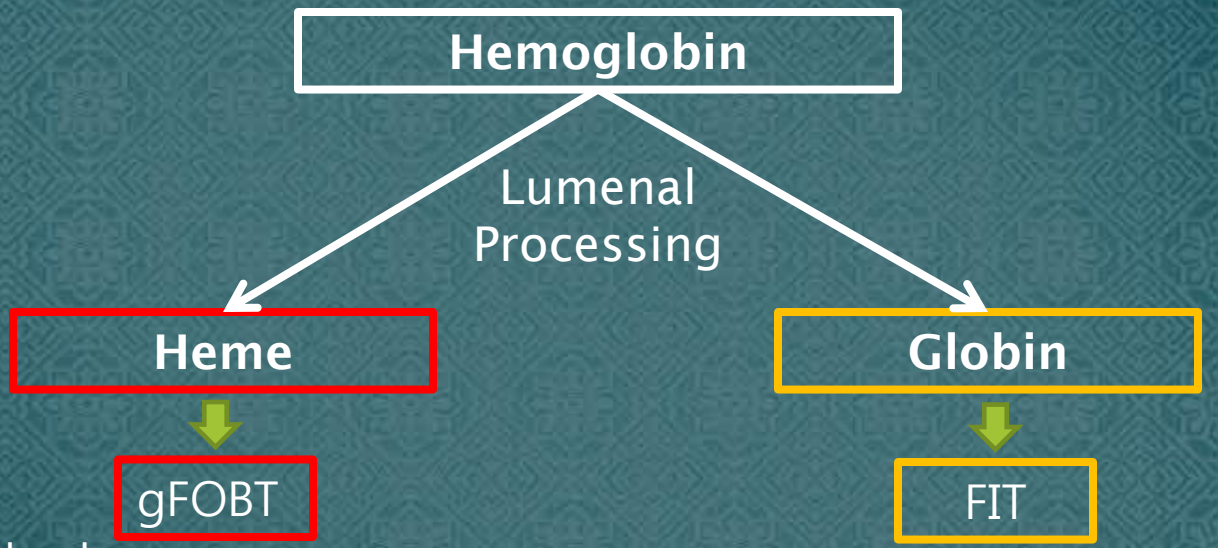
Fecal Immunochemical Tests (FIT) vs. Guaiac Fecal Occult Blood Test (gFOBT)



- Method

Guaiac (colorless) —Heme / H_2O_2→ "Oxidized" Guaiac (Blue color)

- Interfered with plant peroxidases and red meat; Vit C
- Detects bleeding from entire GIT

- Methid
  : Antibody detects Globin
- No dietary interference
- Detects only colonic bleeding when occult

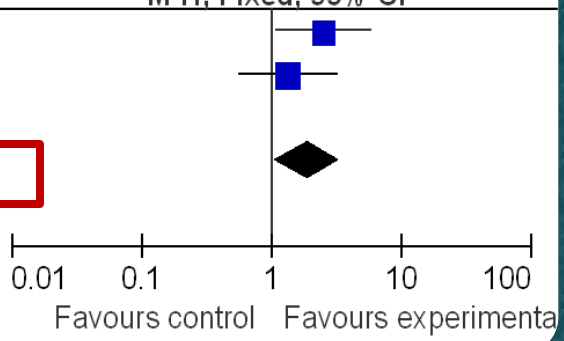
Fecal Immunochemical Tests (FIT) vs. Guaiac Fecal Occult Blood Test (gFOBT)

* Meta-analysis: 대장암 진단능력

Study or Subgroup	gFOBT Events	gFOBT Total	FIT Events	FIT Total	Weight	Odds Ratio (Non-event) M-H, Fixed, 95% CI
Park 2010	8	760	20	770	46.7%	2.51 [1.10, 5.73]
Smith 2006	9	2351	12	2351	53.3%	1.34 [0.56, 3.17]
Total (95% CI)		**3111**		**3121**	**100.0%**	**1.88 [1.04, 3.40]**
Total events	17		32			

Heterogeneity: Chi² = 1.07, df = 1 (P = 0.30); I² = 6%

Test for overall effect: Z = 2.10 (P = 0.04)



대변잠혈검사는 대장암의 선별검사로 적당한가?

* Four randomized controlled trials

Study	Screening vs. control	Mean FU time	Absolute risk reduction	RR (95% CI)
UK	76466/76384	11 years	11/100,000	0.87 (0.78-0.97)
Denmark	30967/30966	17 years	16/100,000	0.84 (0.71-0.99)
USA	31157/15394	18 years	27/100,000	0.75 (0.62-0.91)
Sweden	34144/31164	15.5 years	11/100,000	0.84 (0.71-0.99)

* FOBT screening
  * overall: 17% risk reduction of CRC mortality
  * actually attended at least one screening: 25% risk reduction

Hardcastle JD et al. Lancet. 1996;348:1472

Kronborg O et al. Lancet. 1996;348:1467

Mandel JS et al. J Natl Cancer Inst. 1999;91:434

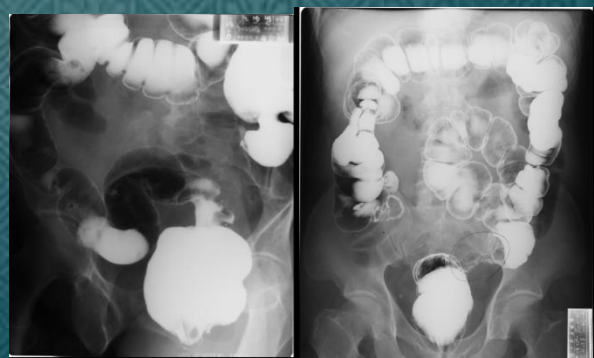
Mandel JS et al. N Engl J Med. 2000;343:1603

Double-contrast barium enema는 대장암 선별검사로 적당한가?

- 대장암 진단 민감도: 85%~97%
- 대장 폴립
  - 민감도
    - ≥ 10 mm: 48%
    - 6-9 mm: 53%
    - 진행 샘종: 75% (6/8 on DCBE)
  - 특이도: 82.3%

이중조영바륨관장술이 대장암 연관 사망률을 낮출 수 있는지에 대한 연구는 제한적

Zauber AG et al. Author reply. N Engl J Med. 2000;343:1729-1730.



Flexible sigmoidoscopy는 대장암 선별검사로 적당한가?

Articles

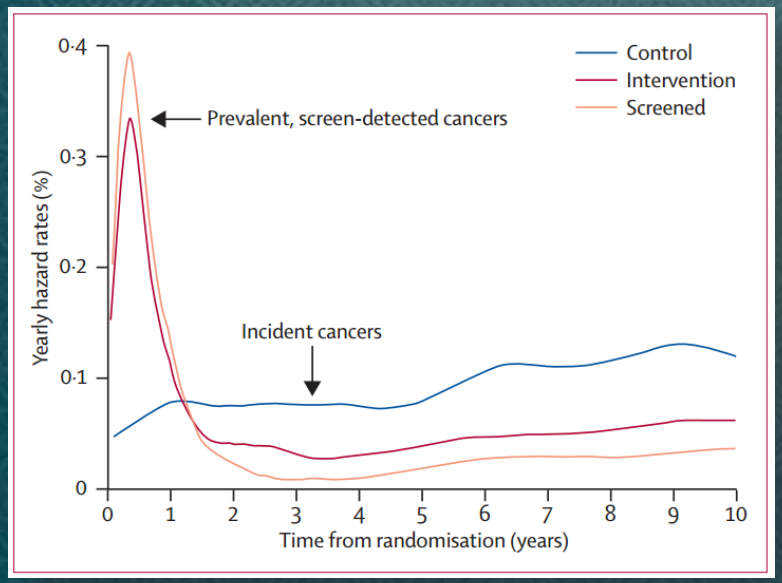
Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial

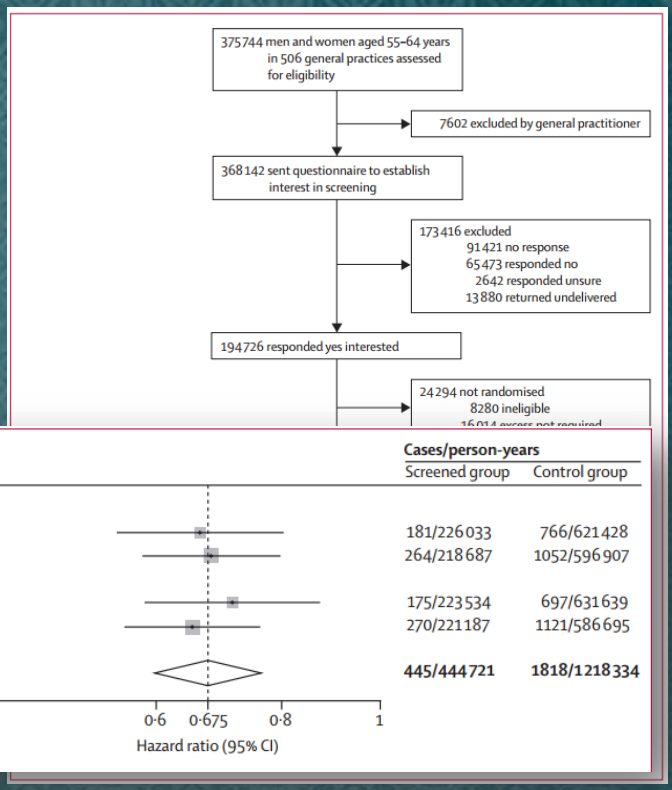
Wendy S Atkin, Rob Edwards, Ines Kralj-Hans, Kate Wooldrage, Andrew R Hart, John M A Northover, D Max Parkin, Jane Wardle, Stephen W Duffy, Jack Cuzick, UK Flexible Sigmoidoscopy Trial Investigators

Lancet 2010; 375: 1624–33
Published Online
April 28, 2010

Summary

Background Colorectal cancer is the third most common cancer worldwide and has a high mortality rate. We tested the hypothesis that only one flexible sigmoidoscopy screening between 55 and 64 years of age can substantially reduce colorectal cancer incidence and mortality.





- Flexible sigmoidoscopy is a safe and practical test and, when offered only once between ages 55-64 yrs, confers a substantial and longlasting benefit.

Flexible sigmoidoscopy는 대장암 선별검사로 적당한가?

- Limitation
  - Isolated proximal CRN
    → Can not prevent proximal CRC
  - If (+) finding
    → f/u colonoscopy
  - Low preference of patients and endoscopists
  - Cost compared to colonoscopy

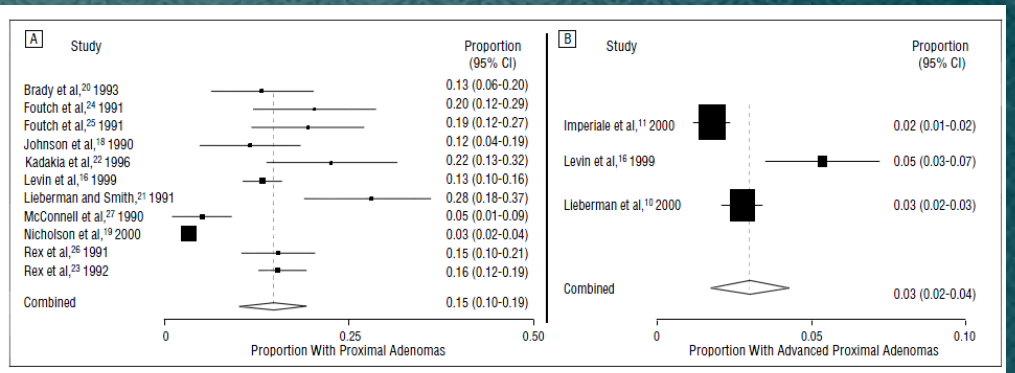


Figure 4. Summary plots of the proportion of patients without distal adenomatous polyps who have isolated proximal adenomas. A, The results for any isolated proximal adenoma. B, The results for isolated advanced proximal adenomas. Pooled estimates are derived from the random-effects model. CI indicates confidence interval.

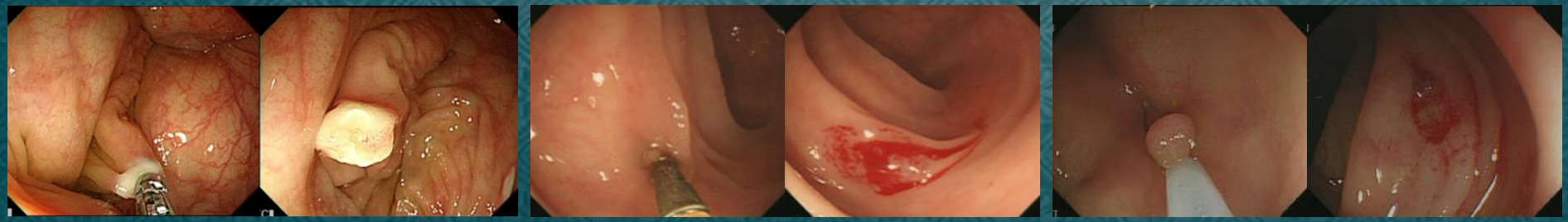
Table 3. Pooled Estimate of the Prevalence of Isolated Proximal Neoplasms

	Any Adenoma, % (95% CI)		Advanced Adenoma, % (95% CI)	
Inclusion Criterion	Random Effects	Fixed Effects	Random Effects	Fixed Effects
Published articles before July 2000	14.6 (9.7-19.4)	6.7 (5.8-7.6)	3.0 (1.6-4.3)	2.4 (1.9-2.8)
Published articles before July 2000 plus abstracts	15.2 (10.6-19.8)	7.1 (6.2-8.0)	3.1 (2.2-4.1)	2.6 (2.2-3.0)
Published articles before July 2000 plus article after July 2000	14.0 (10.2-17.8)	8.4 (7.7-9.1)	2.4 (1.1-3.7)	1.3 (1.1-1.6)
Published articles before July 2000 plus abstracts and article after July 2000	14.6 (11.0-18.2)	8.6 (7.9-9.3)	2.8 (1.7-3.9)	1.5 (1.3-1.8)

Abbreviation: CI, confidence interval.

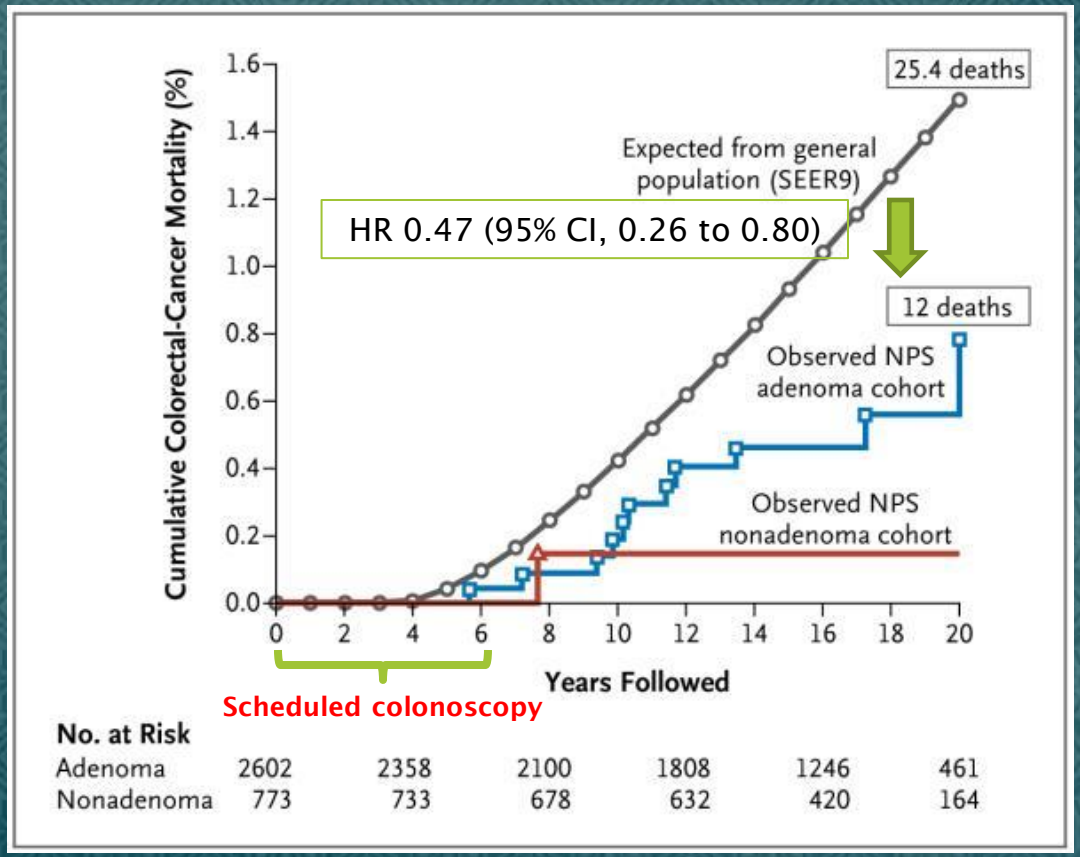
Lewis et al. Arch Intern Med 2003

Preferred CRC prevention test: Colonoscopy



Colonoscopic polypectomy and long-term prevention of CRC deaths

* National polyp study : long-term effect (23yrs) of colonoscopic polypectomy



Zauber et al. NEJM 2012

Limitations of Colonoscopy

1. Interval CRC after polypectomy or negative findings on baseline colonoscopy
   - NCI Pooling Project
     : overall rate of interval cancer = 1.1–2.7/1000 person-years of f/u
2. Important lesions are missed at baseline colonoscopy
   - CT colonography studies
     - Up to 17% of lesions ≥10mm are missed in optical colonoscopy
3. Adenomas may be incompletely removed at the time of baseline colonoscopy
   - Study of patients with large sessile polyps (>2 cm)
     - 17.6% had residual adenomatous tissue when reexamined.

Limitations of Colonoscopy

4. Interval CRC may biologically differ from prevalent CRC
   - Interval lesions are more likely located in the proximal colon, be MSI unstable, and have CpG island methylator phenotype
   - De-novo cancer

5. Quality of baseline colonoscopy is associated with risk of interval cancer
   - Large Polish study
     - if the ADR in screening examinations < 20%, a significantly higher risk of interval cancer occurred in the next 5 years