

Colorectal adenoma & carcinoma

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순서

- Epidemiology
- Mortality
- Colon polyp
- Colorectal carcinogenesis
- Screening target
- Screening method
- Screening guideline review

Epidemiology

International Agency for Research on Cancer



GLOBOCAN 2012: Estimated Cancer Incidence,
Mortality and Prevalence Worldwide in 2012



ABOUT

DATA SOURCES AND METHODS

FACT SHEETS

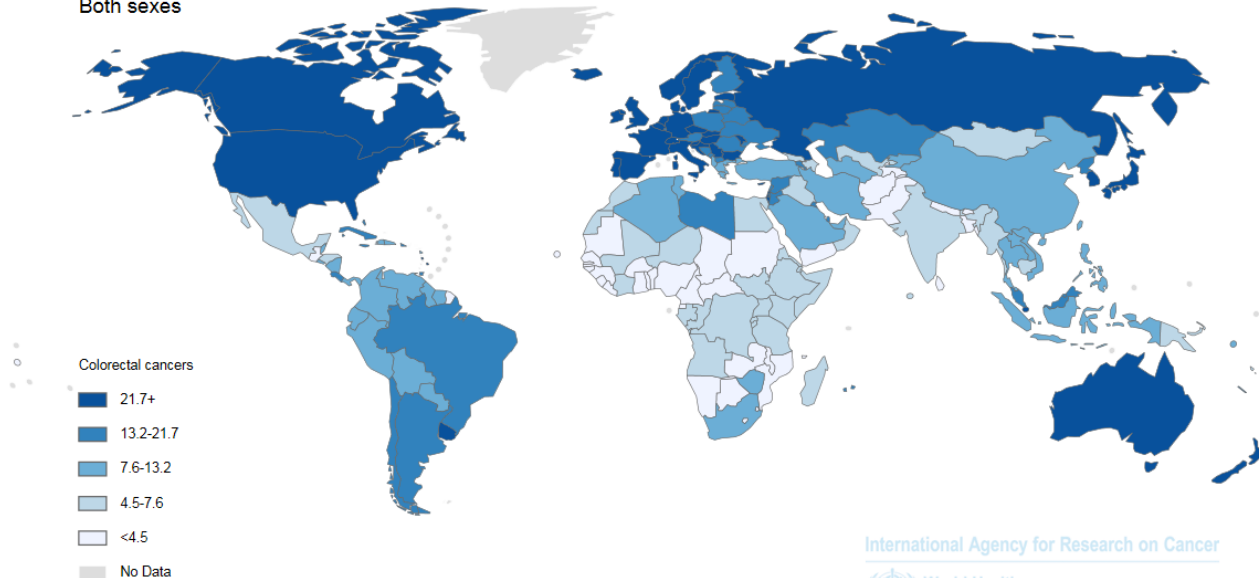
ONLINE ANALYSIS

HELP

SIMPLE MAPS

Region: World Type: Incidence Indicator: ASR Site: Colorectum Sex: Both sexes

Incidence ASR
Both sexes



International Agency for Research on Cancer



Source: GLOBOCAN 2012 (IARC)

About 1.4 million new cases of CRC were diagnosed in 2012 (9.7% of all cancer diagnoses worldwide)

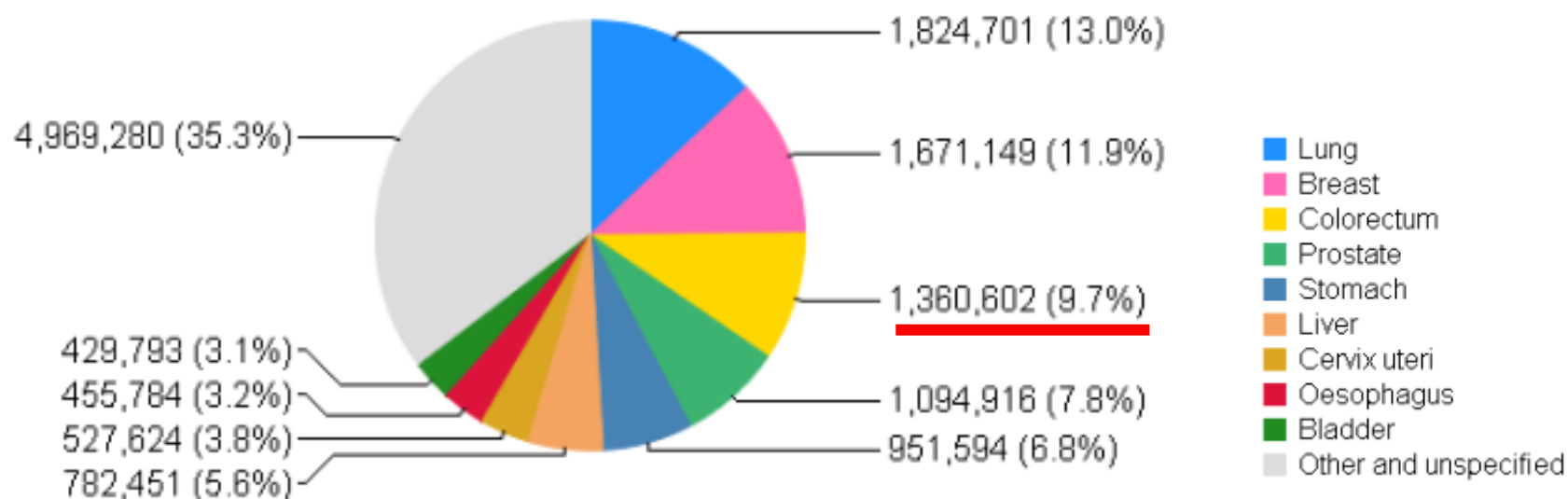
Age-standardized rate per 100,000

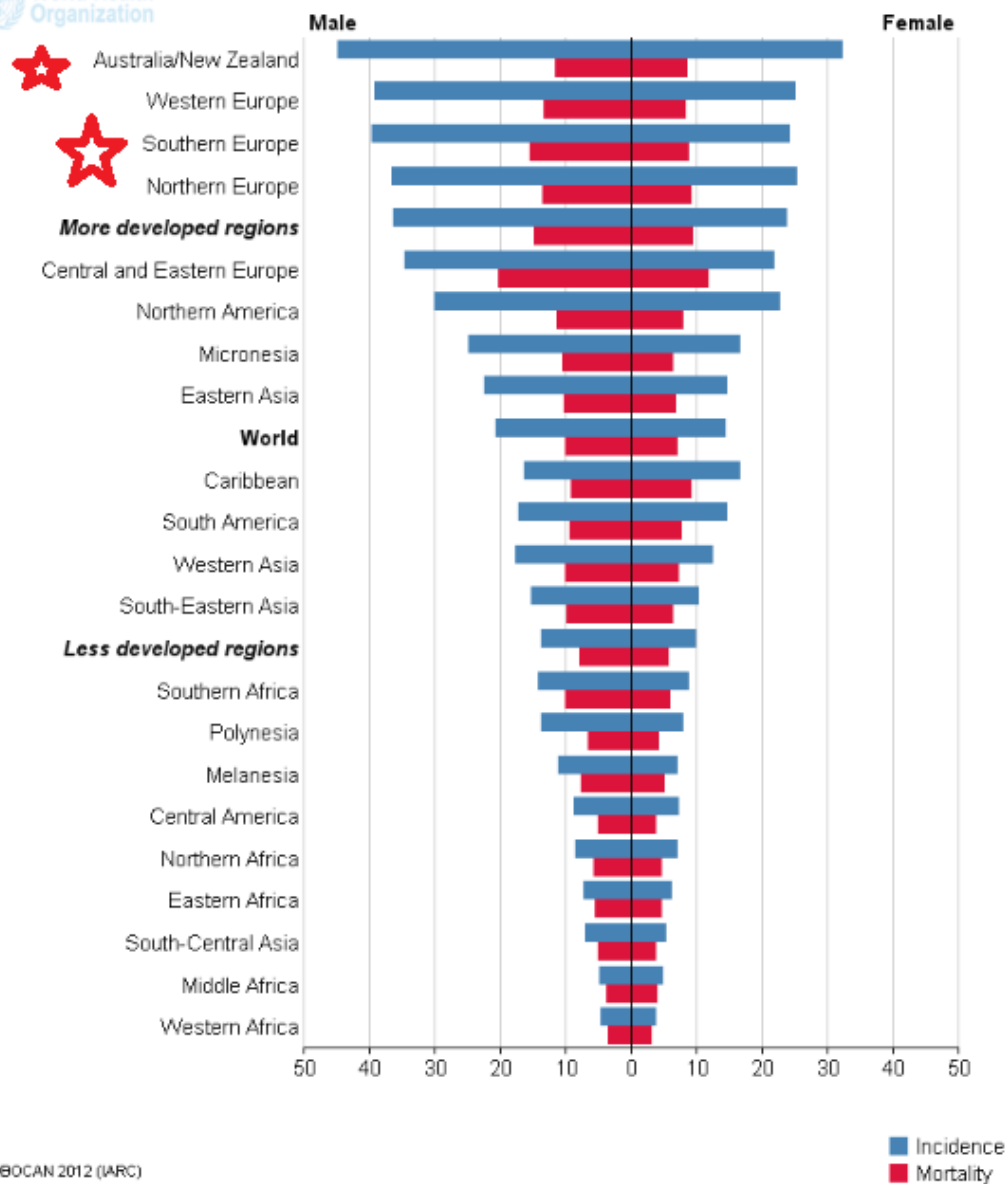
Trends in ASR of selected cancers in worldwide

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Incidence

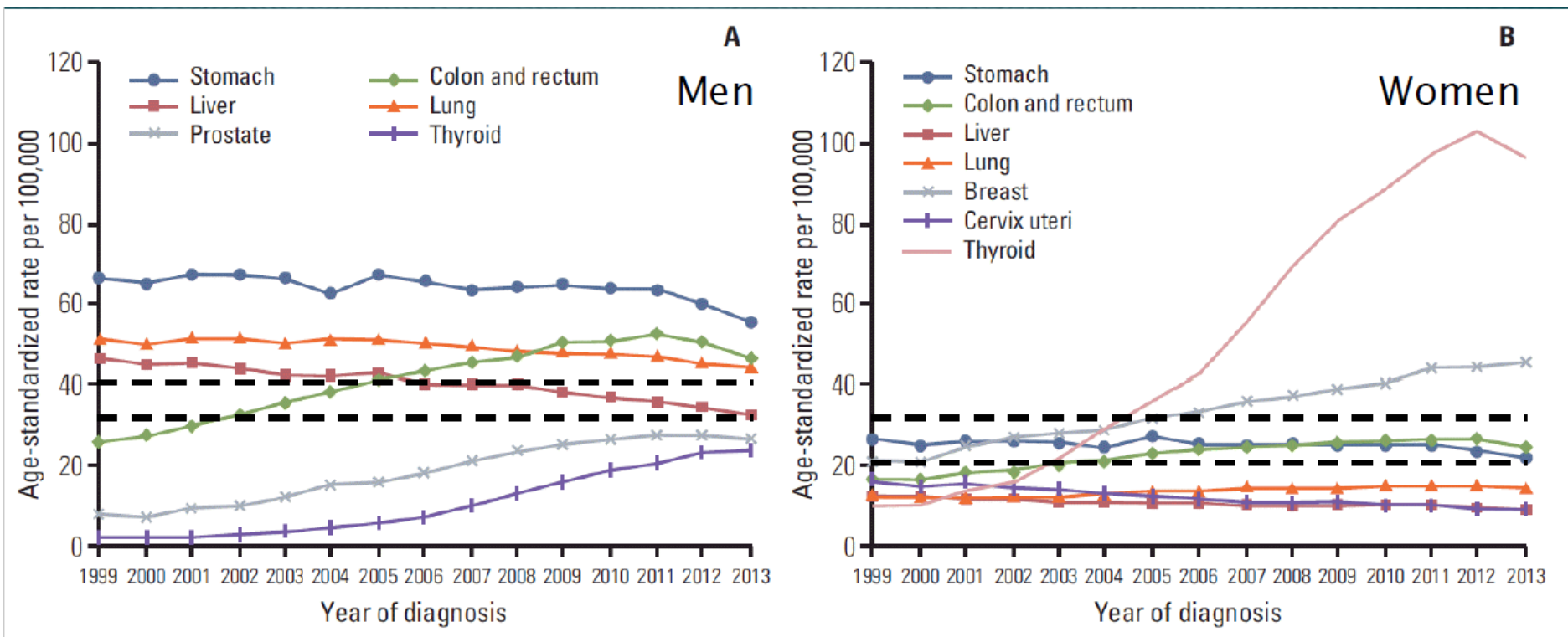




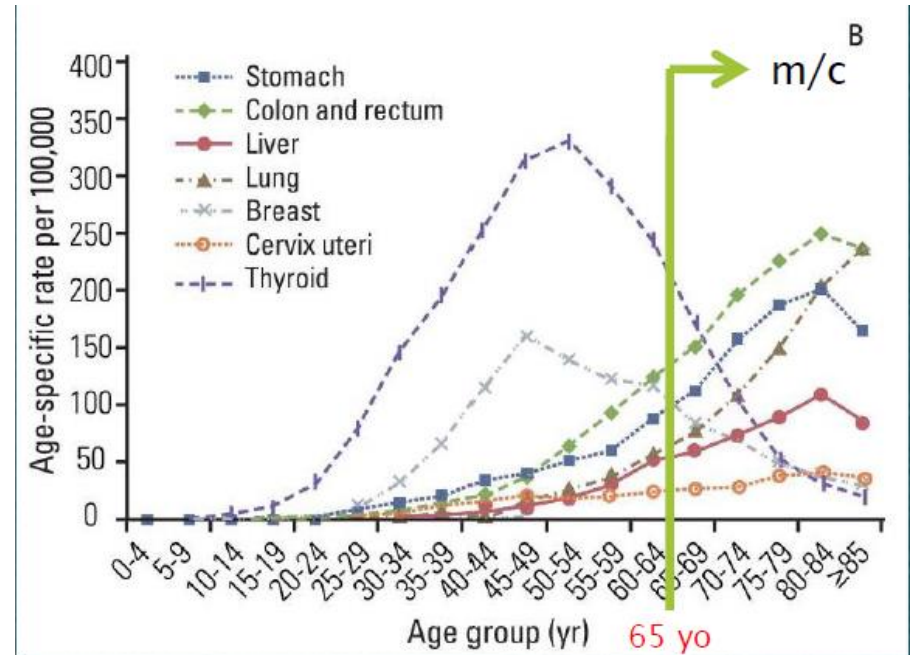
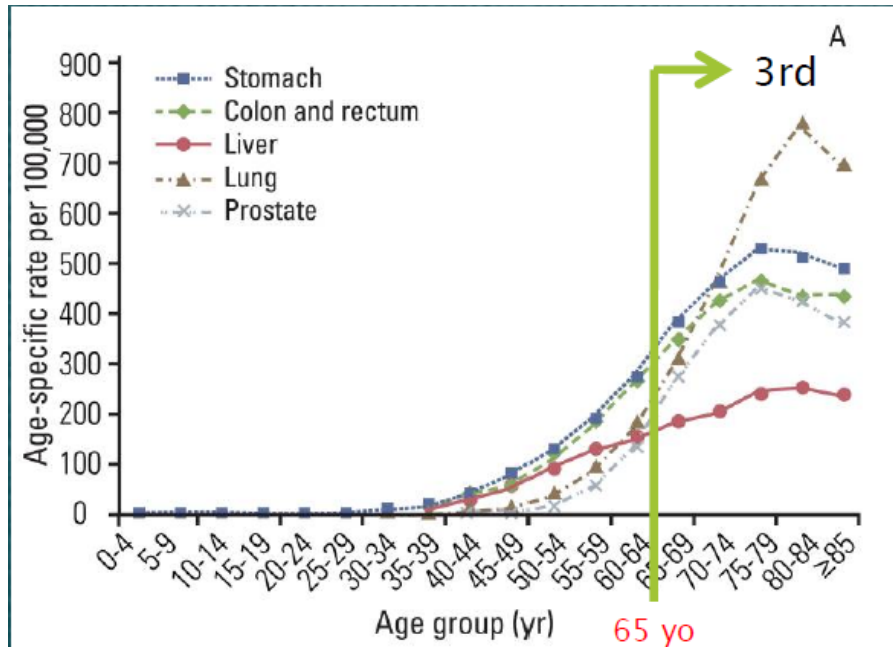
GLOBOCAN 2012 (IARC)

Estimated age-standardised rates (World) per 100,000

Trends in ASR of selected cancers in KOREA from 1999 to 2013



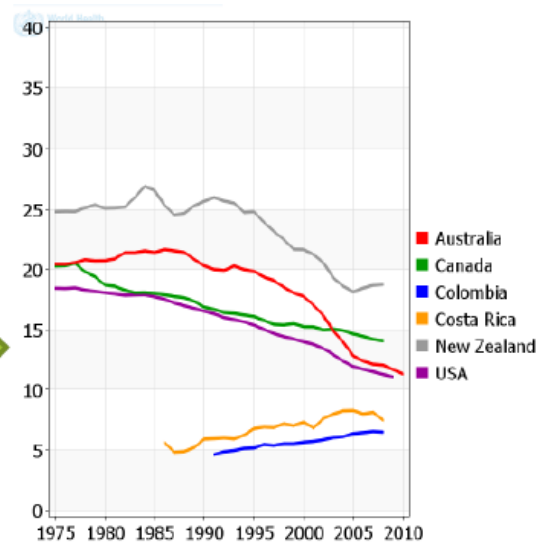
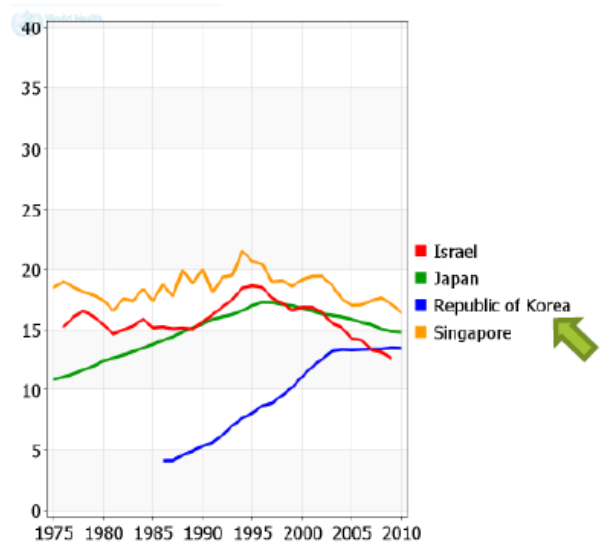
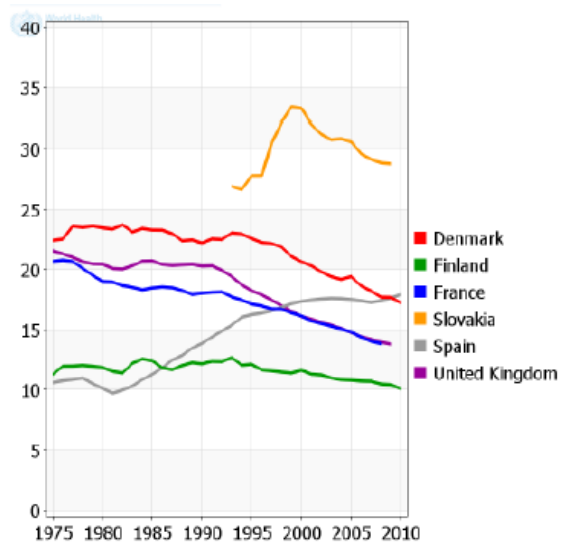
Age specific incidence of CRC in KOREA



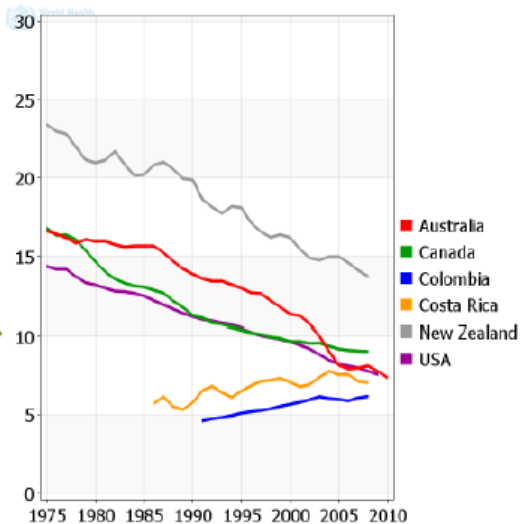
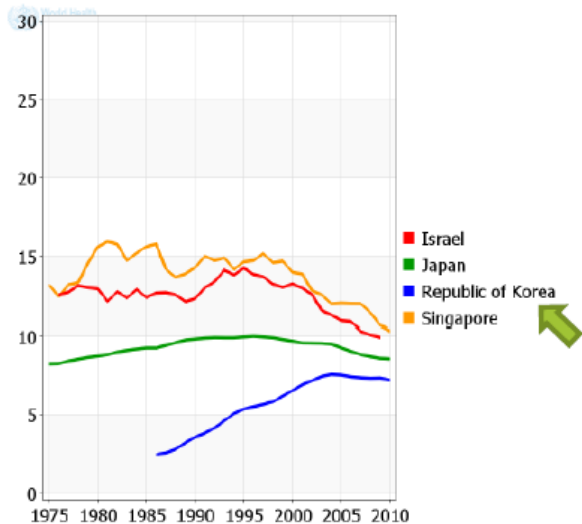
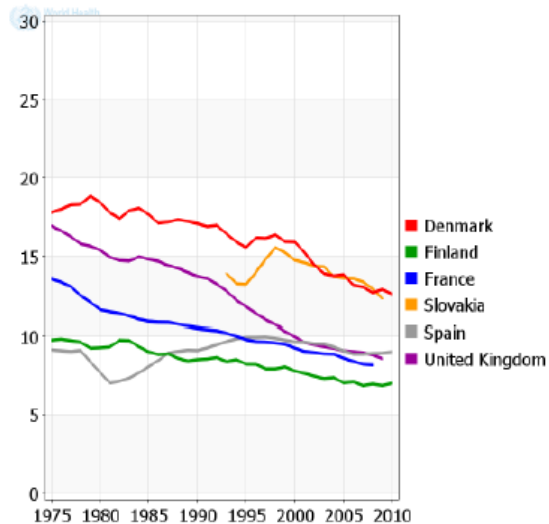
Projected age-specific incidences of major cancers during 2012 in Korea.
(A) Male. (B) Female.

Mortality

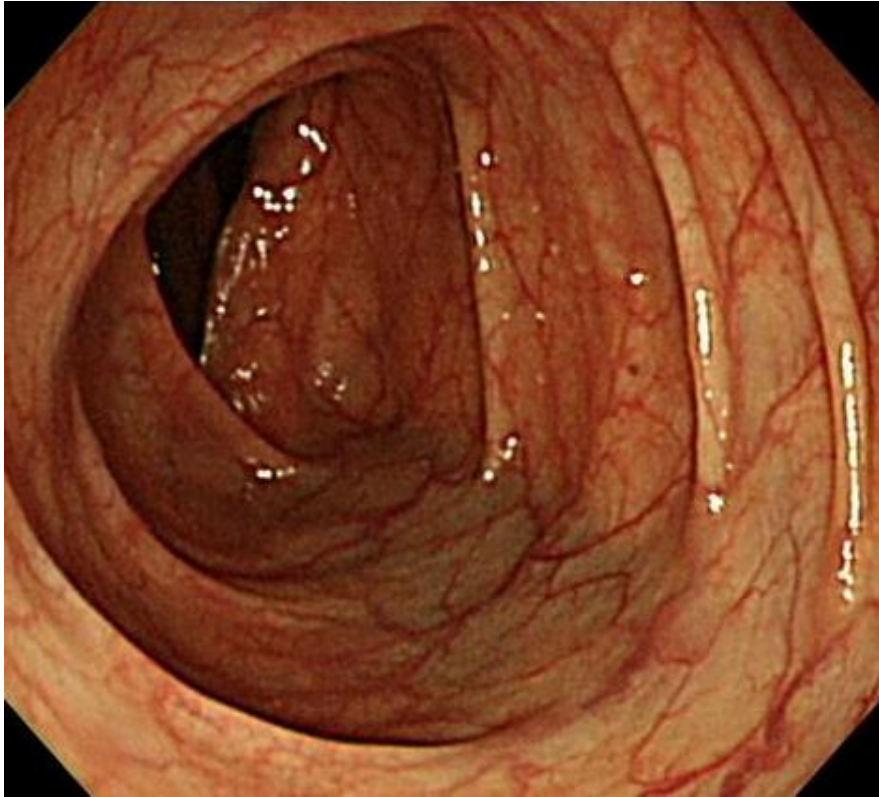
- Declined progressively since the mid-1980s in USA
 - Detection and removal of colonic polyps
 - Detection of CRCs at an earlier stage
 - Widespread implementation of CRC screening
 - Effective adjuvant therapy
- Mortality rates continue to increase in many countries with more limited resources and health infrastructure, particularly in Central and South America and Eastern Europe



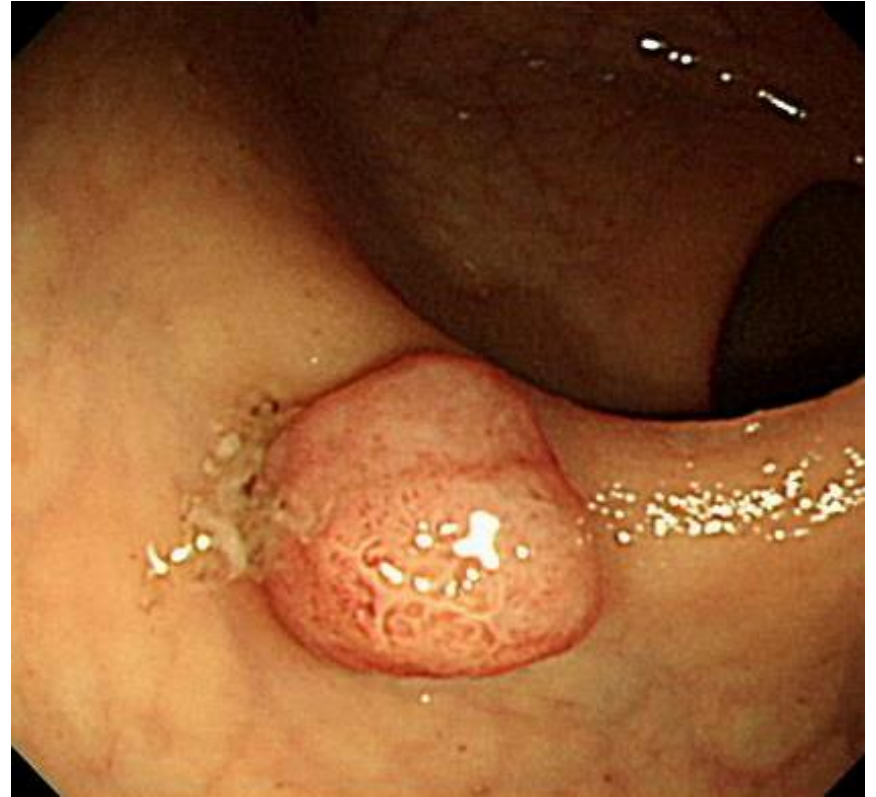
/10⁵ men



/10⁵ women



정상 대장 점막



용종(polyp): 튀어나온 병변

Colon polyp

- Polyp ??
 - Protuberance into the lumen above the surrounding colonic mucosa
- Classification
 - By histologic findings
 - Neoplastic vs Non-neoplastic

Neoplastic

Premalignant polyp:

Tubular **adenoma**

Tubulovillous **adenoma**

Villous **adenoma**

Carcinoma in situ:

High-grade dysplasia

Intraepithelial cancer

Intramucosal cancer

Invasive carcinoma:

Submucosal cancer

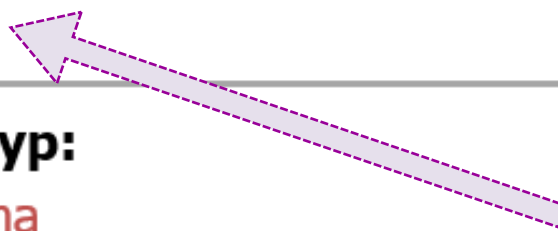
Non-neoplastic

Mucosal tag

Hyperplastic

Inflammatory

Juvenile

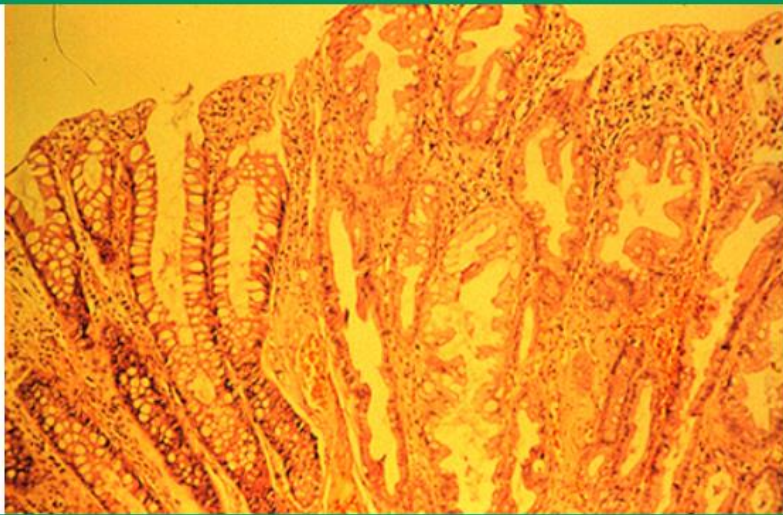


Serrated polyp

Table 2. Histologic Classification of the Two Major Classes of Colorectal Polyps

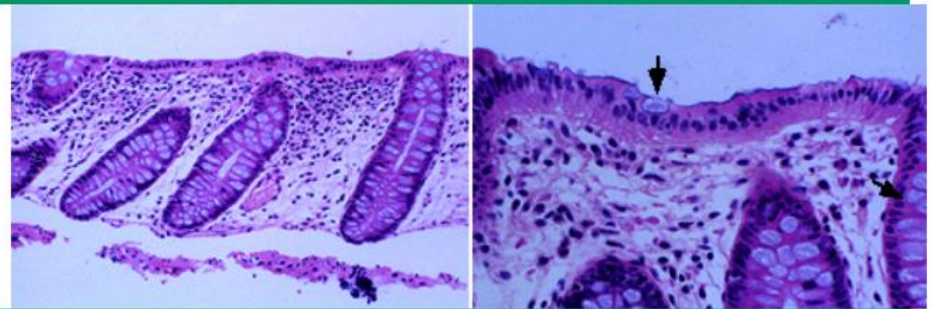
• Serrated	I. Conventional adenomas	
	a. Dysplasia grade	
• 36% of	i. High grade	
• 과거 h	ii. Low grade	polyp
	b. Villousity	
	i. Tubular	
	ii. Tubulovillous	
• Heterc	iii. Villous	potential
	II. Serrated lesions	
	a. Hyperplastic polyps (not considered precancerous)	
• 종류	b. Sessile serrated polyp	
– Hyp	i. Without cytologic dysplasia	
– Tra	ii. With cytologic dysplasia	
– Ses	c. Traditional serrated adenoma	

Hyperplastic colonic polyp



Medium power view of a hyperplastic colonic polyp shows a serrated surface contour and marked luminal infolding of the crypt epithelium.

Normal colon



Low (left) and high (right) power views of a biopsy of a normal colon. Low power reveals straight crypts and mild lamina propria mononuclear cell infiltration. High power shows the surface enterocytes with interspersed goblet cells (arrows).

Courtesy of Robert Odze, MD

Graphic 81083 Version 1.0

Hyperplastic polyp

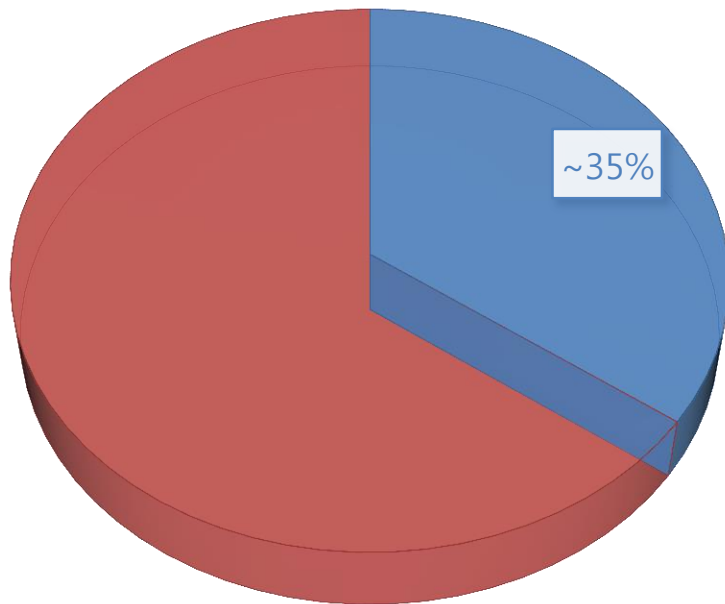
- Typically located in the rectosigmoid and are less than 5mm size
- Normal cellular components, No dysplasia
- Risk of cancer
 - Small rectosigmoid hyperplastic polyps (x)
 - Systemic review (18 studies) with distal HP
 - 21 ~ 25 % proximal neoplasm
 - Four studies
 - 1.3 (95% CI 0.9-1.8) relative risk of proximal neoplasia

Carcinogenesis

- 3 patterns
 - Sporadic disease
 - Accounts for 70% of all CRC
 - Over age 50
 - No family history
 - Inherited predisposition
 - Fewer than 10%
 - Subdivided existence of polyposis (FAP, MAP ...)
 - Familial
 - Accounts for 25% of cases
 - Inherited 의 경우만큼 risk 가 높지는 않음
 - 2명 이상의 1촌의 CRC 발병, CRC 진단된 1촌의 나이가 55세 미만일 경우 risk 가 증가

Screening

- Risk 에 대한 평가



1. CRC with genetic susceptibility
 - <6% : high penetrance susceptibility (HNPCC, FAP, MYH ...)
 - Majority : co-inheritance of multiple low-risk variants

2. Sporadic CRC

3. IBD

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	3.10 – 6.02
One FDR with an advanced adenoma	1.99	1.55 – 2.55
Second degree relative (SDR)		
One second or third DR with CRC	1.50	
Two second-degree relatives with CRC	2.30	

60세 이전 CRC or advanced adenoma를 진단받은 FDR or SDR 가 있을 경우
: 40세 혹은 가장 어린 나이에 발병한 직계 가족보다 10년 먼저 5년 주기로 대장내시경 검사 시행

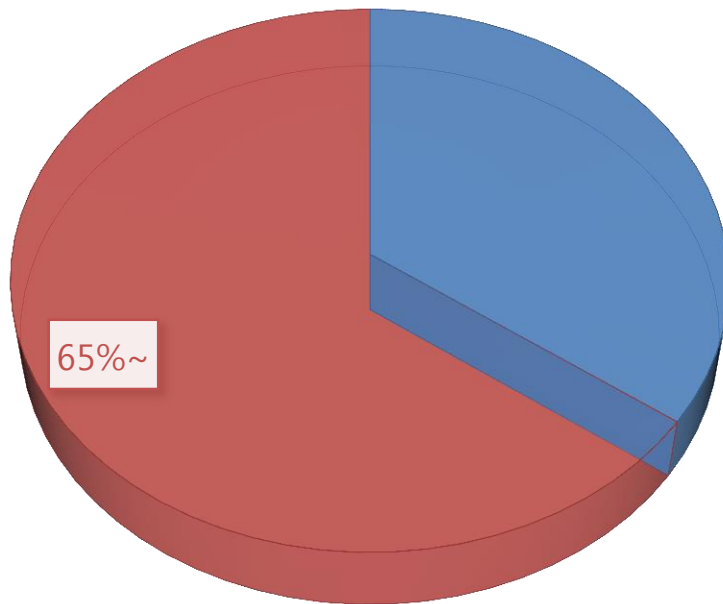
60세 이후 CRC or Advanced adenoma를 진단받은 FDR 이 있을 경우
: 40세부터 대장내시경 시행

60세 이후 CRC or Advanced adenoma를 진단받은 SDR 이 있을 경우
: Average risk

advanced adenoma
- a lesion more than 1 cm in size or having high-grade dysplasia or villous elements

Screening

- Risk 에 대한 평가



1. CRC with genetic susceptibility
 - <6% : high penetrance susceptibility (HNPCC, FAP, MYH ...)
 - Majority : co-inheritance of multiple low-risk variants

2. Sporadic CRC
 - d/t environmental factors (lifestyle and diet)

3. IBD

Table 1. Dietary and lifestyle factors thought to exert adverse effects on colorectal neoplasia

Factor	WCRF assessment (1997)*	Authors' 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
Glycaemic load	N/A	Possible
Total fat	Possible	Insufficient
Iron	Possible	Insufficient

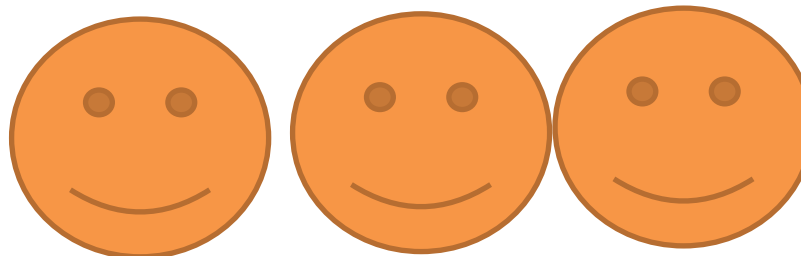
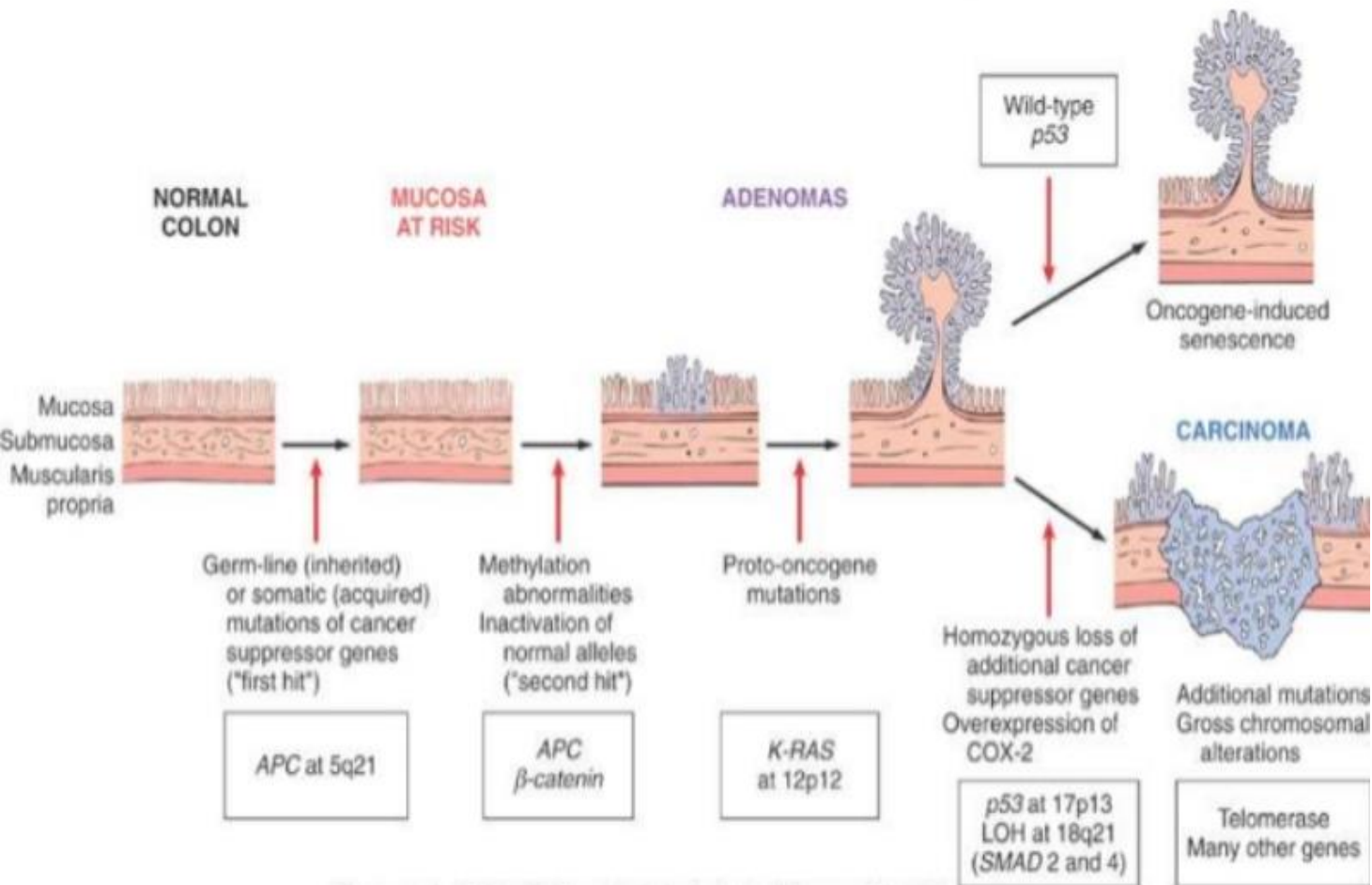
Factor	WCRF assessment (1997)	Authors' current assessment
High physical activity	Convincing (colon only)	Convincing (colon only)
Normal BMI (>18 to <25)	Possible (colon only)	Convincing (colon only)
Dietary fibre	Possible	Probable
Vegetables (total)	Convincing	Possible
Brassica vegetables	N/A	Possible†
Fish	No relationship	Possible†
Folate	Insufficient	Probable†
Calcium	No relationship	Insufficient
Vitamin D	Insufficient	Insufficient
Selenium	No relationship	Possible
Antioxidant nutrients	Insufficient	Insufficient
Flavonoids	N/A	Insufficient

Table 2. Dietary and lifestyle factors thought to exert protective effects against colorectal neoplasia

BMI, body-mass index.

* 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; † Evidence suggests effects depend on the individual's genetic profile.

Adenoma-carcinoma sequence



Screening
→ Prevention & early detection

1. CRC with genetic susceptibility

2. Sporadic 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%

- 앞서 언급한 risk 에 따라
 - 위험 인자가 있다면 high risk 군으로 분류하고 surveillance (감시) 를 시행
 - 위험 인자가 없다면 Average-risk 군으로 분류하고 Screening (선별검사)를 시행
- 대장암 연관 증상이 있을 경우는 바로 diagnostic test (진단검사) 를 시행

Diagnostic tool

Table 2. Screening Tests for Colorectal Cancer

Screening Test	Sensitivity	Specificity	Cost	Interval	Patient Information
gFOBT	Variable	Variable	Low	Annual	Two samples from 3 consecutive stools at home Low risk <u>Positive result requires follow-up colonoscopy</u>
iFOBT	Variable	Variable	Medium	Annual	Stool sample Low risk <u>Positive result requires follow-up colonoscopy</u>
sDNA	Variable	High	High	Uncertain	Adequate stool sample (30-g minimum) Low risk <u>Positive result requires follow-up colonoscopy</u>
DCBE	Low	Low	Low	5 y	Complete bowel preparation Risks include perforation and bleeding <u>Positive result requires follow-up colonoscopy</u>
Flexible sigmoidoscopy	Medium	Medium	High	5 y	Complete bowel preparation Low risk <u>Positive result requires follow-up colonoscopy</u>
Colonoscopy	High	High	High	10 y	Complete bowel preparation Risks include perforation and bleeding
CTC	Medium	Medium	High	5 y	Complete bowel preparation Low risk <u>Polyps require follow-up colonoscopy</u>

CTC = computed tomography colonography; DCBE = double-contrast barium enema; gFOBT = guaiac-based fecal occult blood test; iFOBT = immunochemical-based fecal occult blood test; sDNA = stool DNA panel.

FIT vs gFOBT

gFOBT (Guaiac fecal occult blood test)	FIT (Fecal immunochemical tests)
<ul style="list-style-type: none"> • 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 	<ul style="list-style-type: none"> • Method : Antibody detection of globin • No dietary interference • Detects only colonic bleeding when occult

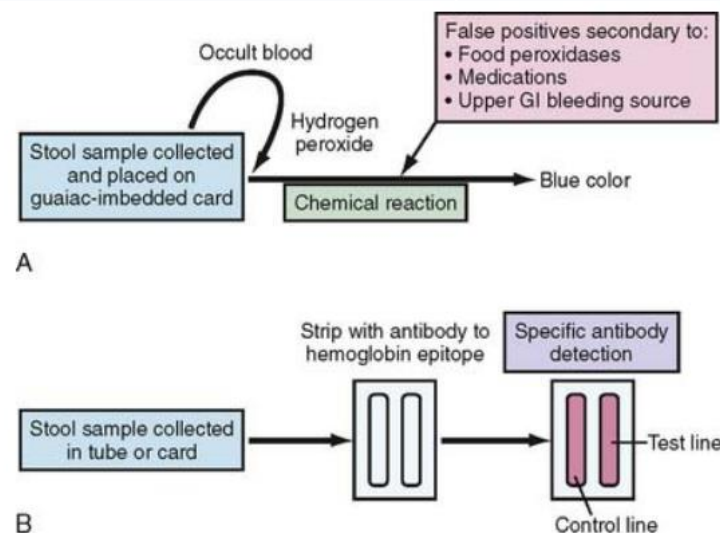
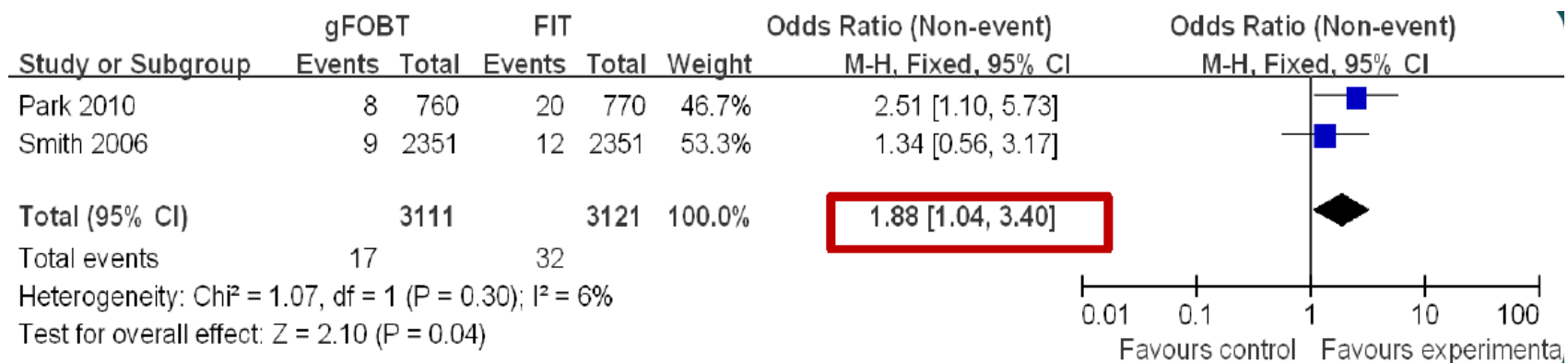


Figure 7-1 Schematic of the g-FOBT (A) and i-FOBT (B) blood detection reactions. g-FOBT, guaiac-based fecal occult blood test; i-FOBT, immunochemical fecal occult blood test.



CONSENSUS GUIDELINE

Colorectal Cancer Screening: Recommendations for Physicians and Patients From the U.S. Multi-Society Task Force on Colorectal Cancer



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Recommendations

1. We recommend colonoscopy every 10 years or annual FIT as first-tier options for screening the average-risk persons for colorectal neoplasia (strong recommendation; moderate-quality evidence).
2. We recommend that physicians performing screening colonoscopy measure quality, including the adenoma detection rate (strong recommendation, high-quality evidence).
3. We recommend that physicians performing FIT monitor quality (strong recommendation, low-quality evidence). The recommended quality measurements for FIT programs are detailed in a prior publication.⁸⁶
4. We recommend CT colonography every 5 years or FIT-fecal DNA every 3 years (strong recommendation, low-quality evidence) or flexible sigmoidoscopy every 5 to 10 years (strong recommendation, high-quality evidence) in patients who refuse colonoscopy and FIT.
5. We suggest that capsule colonoscopy (if available) is an appropriate screening test when patients decline colonoscopy, FIT, FIT-fecal DNA, CT colonography, and flexible sigmoidoscopy (weak recommendation, low-quality evidence).
6. We suggest against Septin9 for CRC screening (weak recommendation, low-quality evidence).

Recommendations

1. We recommend that screening begin in non-African American average-risk persons at age 50 years (strong recommendation; moderate-quality evidence).
2. We suggest that screening begin in African Americans at age 45 years (weak recommendation, very-low-quality evidence).
3. We recommend that adults age <50 years with colorectal bleeding symptoms (hematochezia, unexplained iron deficiency anemia, melena with a negative upper endoscopy) undergo colonoscopy or an evaluation sufficient to determine a bleeding cause, initiate treatment, and complete follow-up to determine resolution of bleeding (strong recommendation, moderate-quality evidence).
4. 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 evidence).
5. We suggest that persons without prior screening should be considered for screening up to age 85, depending on consideration of their age and comorbidities (weak recommendation, low-quality evidence).

대장암 검진 권고안

손대경¹ · 김민주² · 박윤희³ · 서민아⁴ · 신애선⁵ · 이희영⁶ · 임종필⁷ · 조현민⁸ · 홍성필⁹ · 김백희¹⁰ · 김용수¹¹ · 김정욱¹² · 김현수¹³ · 남정모¹⁴ · 박동일¹⁵ · 엄준원¹⁶ · 오순남¹⁷ · 임환섭³ · 장희진¹ · 함상근¹⁸ · 정지혜⁴ · 김수영¹⁹ · 김열⁴ · 이원철²⁰ · 정승용²¹ | 국립암센터 ¹대장암센터, ²영상의학과, ³가톨릭관동대학교 의과대학 진단검사의학교실, ⁴국립암센터 국가암관리사업본부, ⁵서울대학교 의과대학 예방의학교실, ⁶분당서울대병원 공공의료사업단, ⁷서울대학교 의과대학 내과학교실, ⁸가톨릭대학교 성빈센트병원 외과, ⁹연세대학교 의과대학 내과학교실, ¹⁰고려대학교 의과대학 병리학교실, ¹¹한양대학교 의과대학 영상의학교실, ¹²중앙대학교 의과대학 내과학교실, ¹³연세대학교 원주의과대학 내과학교실, ¹⁴연세대학교 의과대학 예방의학교실, ¹⁵성균관대학교 의과대학 강북삼성병원 내과학교실, ¹⁶고려대학교 안산병원 외과, ¹⁷가톨릭대학교 의과대학 방사선과학교실, ¹⁸한전병원 가정의학과, ¹⁹한림대학교 의과대학 강동삼성병원 가정의학과, ²⁰가톨릭대학교 의과대학 예방의학교실, ²¹서울대학교 의과대학 외과학교실

The Korean guideline for colorectal cancer screening

Table 1. Key questions for developing the guidelines for colorectal cancer screening

Screening method	Key question
Colonoscopy	Is there enough evidence of screening benefit?
	What is the optimal screening interval?
	What is the optimal age to start and stop screening?
	What is the incidence of harms of screening?
Fecal occult blood test	Is there enough evidence of screening benefit?
	What is the optimal screening interval?
	What is the optimal age to start and stop screening?
	What is the incidence of harms of screening?
Double-contrast barium enema	Is there enough evidence of screening benefit?
	What is the optimal screening interval?
	What is the optimal age to start and stop screening?
	What is the incidence of harms of screening?
Computed tomographic colonography	Is there enough evidence of screening benefit?
	What is the optimal screening interval?
	What is the optimal age to start and stop screening?
	What is the incidence of harms of screening?

Table 3. Summaries of current recommendations or guidelines for colorectal cancer screening

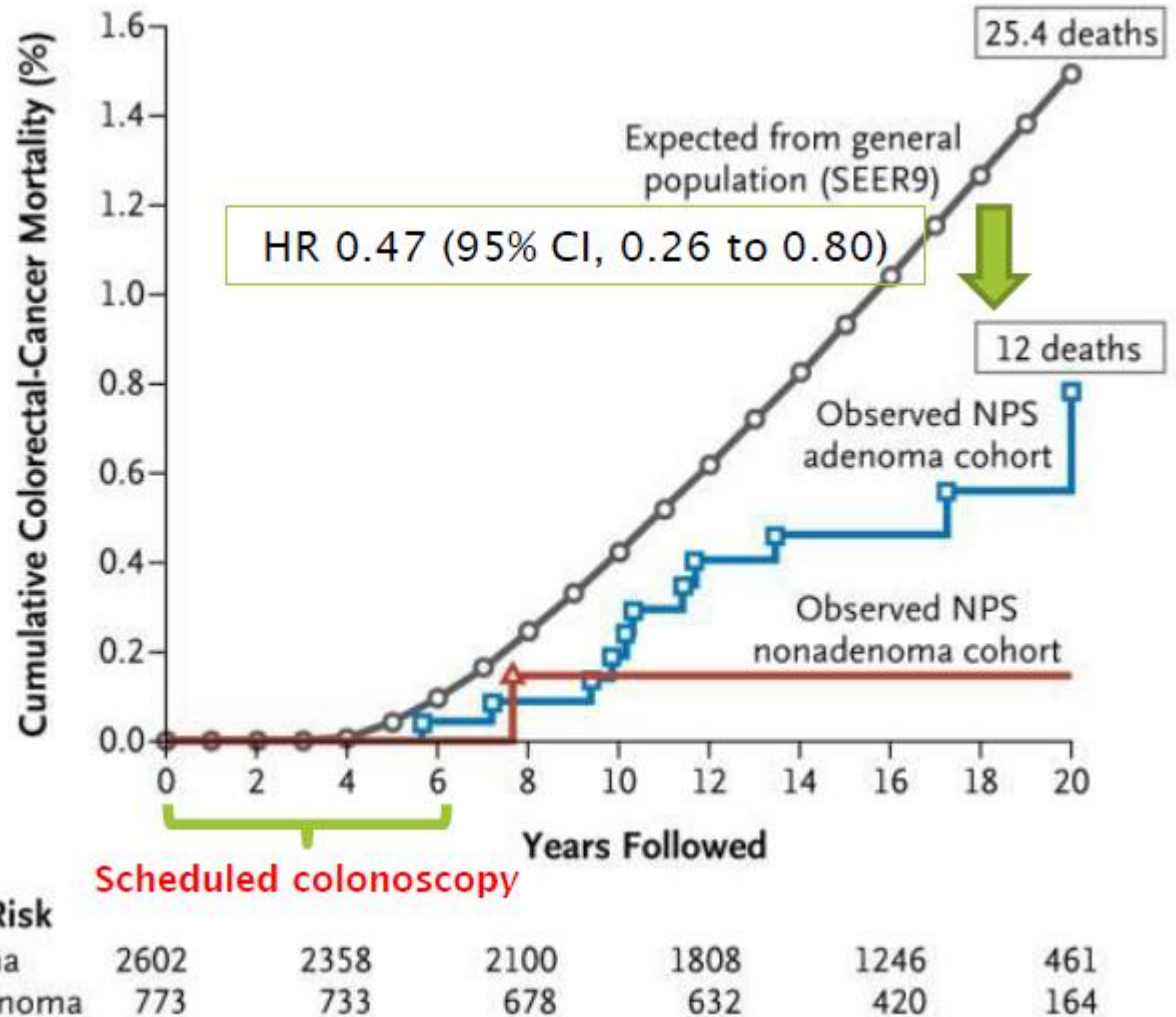
Guideline	Age (yr)	Methods	Interval (yr)
Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement (2008) [4]	50-75	FOBT	1
		Sigmoidoscopy + FOBT	5 (FOBT 3)
		Colonoscopy	10
	76-85	Do not screen routinely	
	Older than 85	Do not screen	
European guidelines for quality assurance in colorectal cancer screening and diagnosis (2012) [8]	45-80	gFOBT	1-2
	(-)	FIT	(-)
	55-64	Sigmoidoscopy	10
	50-74	Colonoscopy (limited evidence)	10
A joint Guidelines from the American Cancer Society, the US Multi-Society Task Force in Colorectal Cancer, and the American College of Radiology (2008) [5]	50 and older	Tests that find polyps and cancer	
		Sigmoidoscopy	5
		Colonoscopy	10
		Double-contrast barium enema	5
		CT colonography	5
		Tests that primarily find cancer	
		FIT	1
		gFOBT	1
		Stool DNA test	3
Diagnosis and management of colorectal cancer SIGN (2011) [6]	(-)	gFOBT	(-)
Korean Guidelines for Colorectal Cancer Screening and Polyp Detection (2012) [7]	50 and older	FOBT (FIT better than gFOBT)	(-)
		CT colonography	(-)
		Double-contrast barium enema	(-)
		Colonoscopy	5

FOBT, fecal occult blood test; gFOBT, guaiac-based FOBT; FIT, fecal immunochemical test; CT, computed tomography.

대장내시경

Table 3. Deaths from Colorectal Cancer

Follow-up Time	No.
All	2602
<10 yr	2602
≥10 yr	2031



- 이득에 대한 권고수준 (전체 중등도)
 - 사망률 : Moderate (중등도)
 - 발생률 : Moderate (중등도)
 - 조기 발견율 : Very low (매우 낮음)
- 위해
 - 중대한 합병증(천공 0-0.04% , 출혈 0-0.27%, 심혈관계 0-0.1%)은 전체 0-0.47%
 - 경미한 합병증 (복부통증 또는 불편감 0.9-48.5%, 경미한 출혈 0.12-0.4%, 경미한 심혈관계 이상 0.058-55.6%, 기타 항문통증 및 어지러움) 은 전체 0.19-55.6%
 - 사망 : 0-0.06%
 - 중간암 (다음 검사전까지 5년 이내 암발생) : 4.6-5.4%
- 이득과 위해를 비교한 선별검사로서의 역할
 - 선별검사로서의 이득의 크기는 작음

분변잠혈검사

- 이득
 - 대장암 사망률 근거수준 “높음”
 - 대장암 발생률 근거수준 “낮음”
- 주기
 - 2년 주기로 시행한 대상군에 비해 1년 주기로 시행한 경우 사망률의 감소율이 높았지만 유의한 통계학적 차이는 없음
 - 2012년 국내 대장암 선별검사 가이드라인의 경우 주기에 대한 언급은 없던 상태였고 2차에 걸친 논의 후 1년 또는 2년으로 결정

- 시행연령
 - 여러 가이드라인을 검토하여 국내에서 45-80 세로 결정
 - 80세 이상의 연령대에 대해서는 이득과 위험을 비교할만한 근거 불충분
- 위해
 - 현재 국내에서는 2004년 부터 FIT 를 시행하고 있는 상태로 guaiac 검사법에 비하여 위양성, 위음성이 낮은 것을 고려하여 위해 근거수준은 "매우 낮음" 으로 결정
- 종합 : 이득과 위해의 비교 결과 이득의 크기가 "중등도" 라고 판단하여 45-80 세 무증상 성인을 대상으로 1-2년 마다 분변잠혈검사를 기본적인 대장암 선별검사로 시행하는 것을 권고

이중조영 바륨 관장술

- 이득
 - 사망률을 낮춘다는 연구 결과는 확인불가
- 주기 및 시행연령
 - 연구결과 확인 불가
- 위해
 - 합병증 (0.01%), 사망률 (0.0018%)
- 종합
 - 이득과 위해를 비교할 만한 근거가 매우 부족한 상태로 근거 불충분함으로 결정

CT 대장조영술

- 이득
 - 연구결과 불충분
- 주기 및 시행연령
 - 연구결과 불충분
- 위해
 - 9개의 연구에서 주요 합병증과 사망은 발생하지 않음
 - 11개 기관에서 시행된 11,870 건의 CT 대장조영술 분석 시 7건의 천공이 발생하였다고 보고된 문헌이 있음
- 종합
 - 이득과 관련된 보고는 없었고 위해는 크지 않았으나 이를 비교할 만한 근거는 매우 부족하여 근거 불충분함으로 결정

Thank you

