Appendix: evidence tables and meta-analysis

Supplementary Table 1.

Key question	In Korea, is the incidence rate of colorectal cancer increasing?					
Study	Design	Sample size	Criteria	Definition	Results	Conclusion
Jung et al.,[1] 2010, Korea	Korea central cancer registry Nationwide hospital-based discharge recording system	General population	Korean, colorectal cancers	Crude incidence rate (CR) Age-standardized incidence rate (ASR) Annual percent change (APC)	-2006, per 100,000 CR: 40.0 ASR: 32.0 -2007, per 100,000 CR: 41.8 ASR: 32.3 -APC: 6.6% (p<0.05)	The incidence rates have continued to increase for colorectal cancer in Korea
Jung et al.,[2] 2009, Korea	Korea central cancer registry Nationwide hospital-based discharge recording system	General population	Korean, colorectal cancers	CR ASR APC	-2005, per 100,000 CR: 36.2 ASR: 29.8 -APC: 6.8% (p<0.005)	The incidence rates have continued to increase for colorectal cancer in Korea
Shin et al.,[3] 2005, Korea	Korea central cancer registry Nationwide hospital-based discharge recording system	General population	Korean, colorectal cancers	CR ASR	-1999-2001, per 100,000 Male (M), CR: 24.2 ASR: 27.3 Female (F), CRL 19.6 ASR: 16.7	
Key question	In Korea, is the incidence rate of colorectal adenomas increasing?					
Study	Design	Sample size	Criteria	Definition	Results	Conclusion
Park et al.,[4] 2009, Korea	Multicenter Prospective cohort July 2003 to June 2004	n=3,951 M/F, 2,374/1,577 (60.1%) 52.1±11.6 yr	<Inclusion> -asymptomatic Korean <Exclusion> -symptoms of lower gastrointestinal tract disease -family history of colorectal cancer or adenomatous polyps in first-degree relatives -personal history of colorectal cancer, polyps, or IBD -history of colorectal examination within the previous 10 yr or colorectal surgery	Colorectal neoplasm: adenoma or invasive cancer Advanced adenoma: adenoma with a diameter of 10 mm or more, a villous adenoma, or adenoma with high grade dysplasia	Neoplasm: 33.2% Adenoma : 33.1% Advanced adenoma: 2.1%	The overall prevalence of colorectal neoplasm in asymptomatic average-risk Koreans was comparable with that in Western countries.

Key question	In Korea, is the incidence rate of colorectal adenomas increasing?					
Study	Design	Sample size	Criteria	Definition	Results	Conclusion
Choe et al.,[5] 2007, Korea	Retrospective Cross-sectional analysis March 1998 to May 2004	*n*=5,086 M/F, 3,583/1,500 (70.5%) 49.3±9.8 yr >50 yr, *n*=2,435 M/F, 1,623/812 (66.7%)	<Inclusion> -asymptomatic Korean -20 yr of age or older <Exclusion> -symptoms of lower gastrointestinal tract disease -family history of colorectal cancer or adenomatous polyps in first-degree relatives -personal history of colorectal cancer, polyps, or IBD -history of colorectal examination within the previous 10 yr or colorectal surgery	Colorectal neoplasm: adenoma or invasive cancer Advanced adenoma: adenoma with a diameter of 10 mm or more, a villous adenoma, or adenoma with high grade dysplasia	-Total Neoplasm: 21.9% Adenoma : 21.8% Advanced adenoma: 2.4% Invasive cancer 0.2% ->50 yr old Neoplasm: 30.2% Adenoma : 29.8% Advanced adenoma: 3.7% Invasive cancer: 0.3	The overall prevalence of colorectal neoplasm in asymptomatic average-risk Koreans was comparable with that in Western countries. The prevalence of advanced neoplasm in Koreans was lower than that seen in Westerners of equal age.

Key question	Based on studies of screening tests, are prevalence rates of colorectal cancers or colorectal adenomas higher in average-risk groups aged 50 or more compared to those aged less than 50?					
Study	Design	Sample size	Criteria	Definition	Results	Conclusion
Jung et al.,[1] 2010, Korea	Korea central cancer registry Nationwide hospital-based discharge recording system	General population	Korean, colorectal cancers	CR	-2008, CR per 100,000 40-49 yr: 28.8 50-59 yr: 82.5 60-65 yr: 174.5 Over 70 yr: 245.7	The incidence of colorectal cancer is rapidly increasing over 50 yr old in Korea.
Park et al.,[4] 2009, Korea	Prospective cohort, multiinstitutional	*n*=3,951 M, 2,374 (60.1%) ≥50 yr, 2,307 < 50 yr, 1,644	<Inclusion> -Undergoing colonoscopy as a screening <Exclusion> - symptoms of lower gastrointestinal tract disease, including rectal bleeding, changes in bowel habits, or lower abdominal pain that required medical evaluation - family history of colorectal cancer or adenomatous polyps in first-degree relatives - personal history of colorectal cancer, polyps, or inflammatory bowel disease - history of colorectal examination (including sigmoidoscopy, colonoscopy, or barium enema) within the previous 10 yr, or colorectal surgery - subjects whose colonoscopy failed to reach the cecum were excluded from the analysis.	-Adenoma - Advanced adenoma: 1 cm or larger in size, villous histologic features, high-grade dysplasia -Advanced neoplasm: advanced adenoma or invasive cancer	-Adenoma ≥50 yr: 40.5% < 50 yr: 22.6% -Advanced adenoma ≥50 yr: 2.5% < 50 yr: 1.6% -Invasive cancer ≥50 yr: 0.2% < 50 yr: 0.0%	The prevalence of colorectal neoplasm in asymptomatic-average-risk Koreans is more common in 50 yr or older than 50 yr or younger

Key question	Based on studies of screening tests, are prevalence rates of colorectal cancers or colorectal adenomas higher in average-risk groups aged 50 or more compared to those aged less than 50?					
Study	Design	Sample size	Criteria	Definition	Results	Conclusion
Rundle et al.,[6] 2008, USA	Retrospective cohort	Age, 40-49; yr, 553; M, 417 (75%) Age, 50-59; yr, 352; M, 271 (77%)	<Inclusion> -Colonoscopy screening performed on individuals ages 40-49 yr as well as individuals ages 50-59 yr during the 27-month period from January 2004 through March 2006 <Exclusion> -Colonoscopies that did not reach the cecum as well as colonoscopies for which the clinical indication was other than for screening purposes (e.g., anemia, abdominal pain, or diarrhea). -a family history of colon cancer or a personal history of inflammatory bowel disease or any malignancy other than skin cancer	-Adenoma - Advanced adenoma: 1cm or larger in size, villous histologic features, high-grade dysplasia	-Adenoma Age 40-49 yr: 14% Age 50-59 yr: 16% -Advanced adenoma Age 40-49 yr: 2% Age 50-59 yr: 4% -Colorectal cancer Age 40-49 yr: 0% Age 50-59 yr: 0.3%	The prevalence of total adenomas was similar in individuals ages 40-49 and in those 50-59 yr, although the prevalence of advanced neoplasia in the 50-59 yr age group may be higher than that in the 40-49 yr age group.
Choe et al.,[5] 2007, Korea	Retrospective cohort	*n*=5,086 M, 3583 (70.5%) Mean age, 49.3 ≥50 yr, 2,435 < 50 yr, 2,651	<Inclusion> -Health Promotion Center at Asan Medical Center for a screening colonoscopy as part of a routine health check-up <Exclusion> -symptoms of colorectal disease, including rectal bleeding, lower abdominal pain, or changes in bowel habits -personal history of colorectal cancer, colorectal polyps, or inflammatory bowel disease -history of colon examination (sigmoidoscopy, colonoscopy, or barium enema) within the previous 10 yr, or colonic surgery -family history of colorectal cancer or polyps in first-degree relatives. -subjects who had an incomplete colonoscopy were excluded from the analysis.	-Adenoma - Advanced adenoma: 1cm or larger in size, villous histologic features, high-grade dysplasia -Advanced neoplasm: advanced adenoma or invasive cancer -Invasive cancer: invasion of malignant cells beyond the muscularis mucosa	-Adenoma ≥50 yr: 29.8% < 50 yr: 14.3% -Advanced adenoma ≥50 yr: 3.7% < 50 yr: 1.1% -Invasive cancer ≥50 yr: 0.3% < 50 yr: 0.04%	Colonoscopy is a useful modality for colorectal cancer screening in Korea.

Key question	Based on studies of screening tests, are prevalence rates of colorectal cancers or colorectal adenomas higher in average-risk groups aged 50 or more compared to those aged less than 50?					
Study	Design	Sample size	Criteria	Definition	Results	Conclusion
Byeon et al.,[7] 2007, Asian	Prospective cohort, multinational, multicenter	*n*=860 Mean age, 54.4 M, 471(54.8%) ≥50 yr, 565 < 50 yr, 298	<Inclusion> -consecutive asymptomatic subjects above the age of 16 yr, who were undergoing colonoscopy as a screening procedure referred to 17 centers from 11 Asian cities <Exclusion> -subjects who had undergone colorectal imaging (including sigmoidoscopy, colonoscopy, or barium enema) within the previous 5 yr, -those with a history of colorectal surgery -those colonoscopic examinations that failed to reach the cecum -Subjects with symptoms of lower-GI tract disease, including rectal bleeding, a change in bowel habits, or lower abdominal pain that required medical evaluation -those with a history of colorectal disease, such as polyp, cancer, or inflammatory bowel disease	-Adenoma - Advanced adenoma: 1cm or larger in size, villous histologic features, high-grade dysplasia -Invasive cancer: invasion of malignant cells beyond the muscularis mucosa	-Overall neoplasm (p<0.001) ≥50 yr: 23.9% < 50 yr: 11.2% -Advanced neoplasm (p=0.001) ≥50 yr: 5.8% < 50 yr: 2.0%	The overall prevalence of advanced colorectal neoplasm in asymptomatic Asians is comparable with the West.
Eisele et al.,[8] 2007, Germany	Prospective cohort	*n*=618 M, 100% Age 40-49 yr, 285 Age 50-59 yr, 333	<Inclusion> -screening colonoscopy, volunteers who had no family history of colorectal neoplasms and reported normal stool habits <Exclusion>	-Adenoma - Advanced adenoma: 1 cm or larger in size, villous histologic features, high-grade dysplasia -Invasive cancer: invasion of malignant cells beyond the muscularis mucosa	-Adenoma 50-59 yr: 35.7% 40-49 yr: 26.7% -Advanced adenoma 50-59 yr: 10.2% 40-49 yr: 3.2% -Invasive cancer 50-59 yr: 0.0% 40-49 yr: 0.0%	By using high-resolution endoscopes we found an unexpectedly large number of neoplastic lesions in the colon even in a relatively young average-risk population.
Regula et al.,[9] 2006, Poland	Cross-sectional analysis, mlticenter	*n*=50,148 Age 40-49 yr, 7,106 M, 2,646 (37%) Age 50-66 yr, 43,042 M, 15366 (36%)	<Inclusion> -50 to 66 yr of age and in good general health and colorectal cancer was not suspected -40 to 49 yr of age were also eligible if they had a family history of cancer of any type	-Adenoma - Advanced adenoma: 1cm or larger in size, villous histologic features, high-grade dysplasia -Invasive cancer: invasion of malignant cells beyond the muscularis mucosa	-Adenoma 40-49 yr: 6.1% 50-66 yr: 8.9% -Advanced adenoma 40-49 yr: 3.0% 50-66 yr: 5.0% -Invasive cancer	The age of more than 49 yr was an independent predictors of advanced neoplasia

Key question	Based on studies of screening tests, are prevalence rates of colorectal cancers or colorectal adenomas higher in average-risk groups aged 50 or more compared to those aged less than 50?					
Study	Design	Sample size	Criteria	Definition	Results	Conclusion
			<Exclusion> -recent changes in bowel habits, anemia, unexplained weight loss, bleeding in the lower gastrointestinal tract not attributable to hemorrhoids (although people with small amounts of apparently fresh blood during defecation and known hemorrhoids were eligible), -hereditary nonpolyposis colorectal cancer or familial adenomatous polyposis, inflammatory bowel disease -colonoscopy within the preceding 10 yr		40-49 yr: 0.4% 50-66 yr: 0.9% OR (95% CI) for advanced neoplasia, $p<0.001$ 50-54 yr vs. 40-49: 1.82 (1.38-2.40) 55-59 yr vs. 40-49:: 2.38 (1.81-3.14) 60-66 yr vs. 40-49: 2.91 (2.21-3.83)	
Strul et al.,[11] 2006, Israel	Retrospective cohort	*n*=1,177 40-49 yr, 183 M, 49.2% 50-75 yr, 917 M, 47.5% 76-80 yr, 77 M, 37.7%	<Inclusion> -average-risk men and women aged 40-80 yr who underwent a complete colonoscopy in the outpatient clinic <Exclusion> -Suggestive symptoms of neoplasia: Rectal bleeding, change in bowel habits, abdominal pain, or unexplained weight loss during the previous six months; -Laboratory abnormalities: A positive fecal occult blood testing (FOBT), elevated CEA or iron deficiency anemia (in Israel, a complete blood count is practically done in all subjects prior to routine endoscopic procedures, including screening colonoscopy. Patients with hemoglobin value below the normal range are checked for iron and/or ferritin levels); -Imaging abnormalities: Suspected CR lesion or evaluation of metastatic spread; -Personal history of CR adenoma or carcinoma at any time; -Family history of CR adenoma or carcinoma in first-degree relatives aged ≤70 yr or in ≥2 family relatives at any	-Adenoma - Advanced adenoma: 1cm or larger in size, villous histologic features, high-grade dysplasia -Invasive cancer: invasion of malignant cells beyond the muscularis mucosa	-Adenoma 40-49 yr: 8.7% 50-75 yr: 15.8% 76-80 yr: 14.3% -Advanced adenoma 40-49 yr: 1.1% 50-75 yr: 5.5% 76-80 yr: 11.7% -Invasive cancer 40-49 yr: 0.0% 50-75 yr: 1.2% 76-80 yr:: 2.6%	Primary screening colonoscopy should be considered in health programs for the average-risk population, beginning at the age of 50 yr

Key question	Based on studies of screening tests, are prevalence rates of colorectal cancers or colorectal adenomas higher in average-risk groups aged 50 or more compared to those aged less than 50?					
Study	Design	Sample size	Criteria	Definition	Results	Conclusion
			age; -Inflammatory bowel disease (ulcerative colitis or Crohn's disease); -Severe co-morbidity (e.g., malignancy, cardiopulmonary, renal or hepatic failure); -Colonoscopy, sigmoidoscopy, or barium enema within the previous 5 yr; or -Unsatisfactory bowel cleansing or incomplete examination, when the cecum was not intubated.			

Key question	Among average-risk adults aged 50 yr and older, do colorectal cancer incidence rates and mortality rates decrease in groups who had received a FOBT for colorectal cancer screening compared to groups who had not?					
Study	Design	Sample size	Inclusion/Exclusion criteria	Definition	Results	Conclusion
Morikawa et al.,[11] 2005, Japan	FIT(Fujirebio Inc: original version of HemeSelect) (1 time sample)	*n*=21,805	Inclusion criteria: asymptomatic adults Exclusion criteria: :symptoms of disease of the lower gastrointestinal tract including visible rectal bleeding, recent change in bowel habits, or lower abdominal pain that normally would require a medical evaluation.	Advanced colonic neoplasia was defined as adenomas 10 mm or more in diameter, adenomas with high-grade dysplasia, or invasive cancer.	**Sensitivity (95%CI)** Cancer:65.8% (55.4, 76.3) Adenoma(>10mm): 20.0% (16.6, 23.4) High grade dysplasia: 32.7% (24.3, 41.2) Advanced neoplasm: 27.1%(23.9,30.3) **Specificity (95%CI):** Cancer: 94.6%(94.3-94.9) Advanced neoplasm: 95.1%(94.8, 95.4) Other not shown	the sensitivity of FIT is relatively low, compared with that of CFS.
Allison et al.,[12] 2007, USA	Diagnostic cohort study -high sensitive guaiac based fecal occult blood testing (gFOBT) (Hemoccult-Sensa) (3 samples) -sigmoidoscopy -I-FOBT (FlexSure-OBT) (3 samples) -sigmoidoscopy	*n*=5,841	-Inclusion criteria : Asymptomatic person >50 yr old -Exclusion criteria : Age <50 (*n*=60) or >80 Sigmoidoscopy ≤5 yr ago Colonoscopy ≤5 yr ago History of IBD History of colon polyps History of colorectal cancer Family history of colorectal cancer Positive FOBT in last 12 months *not mutually exclusive		**<gFOBT>** **- Distal advanced adenoma (>10 mm)** Sensitivity (95% CI) :41.3% (32.7, 50.4) Specificity (95% CI) : 90.6% (89.8, 91.4) PPV (95% CI): 8.9% (6.8, 11.6) **-Distal cancer** Sensitivity (95% CI) :64..3% (35.6, 86.0) Specificity (95% CI) : 90.1% (89.3, 90.8) PPV (95% CI): 1.5% (0.8, 3.0) **<FIT>** **Distal advanced adenoma (>10 mm)** Sensitivity (95% CI): 29.5% (21.4, 38.9) Specificity (95% CI): 97.3% (96.8, 97.7) PPV (95% CI):19.1% (13.7, 25.9)	FIT & FOBT have low sensitivity and high specificity for detecting left-sided adenoma**.**

Key question	Among average-risk adults aged 50 yr and older, do colorectal cancer incidence rates and mortality rates decrease in groups who had received a FOBT for colorectal cancer screening compared to groups who had not?					
Study	Design	Sample size	Inclusion/Exclusion criteria	Definition	Results	Conclusion
					Distal cancer Sensitivity (95% CI) :81.8% (47.8, 96.8) Specificity (95% CI) : 96.9% (96.4, 97.4) PPV (95% CI): 5.2% (2.6, 10.0)	
Smith et al.,[13] 2006, Austrailia	-Prospective cohort study -sensitive gFOBT (Hemoccult II Sensa) (3 consecutive samples) FIT (Insure) (2 consecutive samples) -colonoscopy	*n*=2351	Inclusion criteria: 50-75 yr Average risk group	significant adenoma :high grade dysplasia, villous change, ≥10 mm, serrated histology or >3 polyps	**-Positive rate of gFOBT (**Hemoccult II Sensa) Cancer: 47.1% Multiple polyp: 12.5% High grade dysplasia: 25% Villous: 36.4% Serrated: 0 ≥10 mm: 33.3% Total significant adenoma: 24.2% **-Positive rate of FIT (Insure)** Cancer: 82.4% Multiple polyp: 50% High grade dysplasia: 25% Villous: 54.5% Serrated: 0 ≥10 mm: 44.4% Total significant adenoma: 44.4%	gFOBT only detected 47.1% of cancer and 24.2% of advanced adenomas. The sensitivity of FIT for advanced adenoma is 44.4%, but 82.4% for .cancer.
Allison et al.,[14] 1996, USA	Diagnostic cohort study gFOBT (Hemoccult II/ Hemoccult II Sensa) (3 samples -colonoscopy	*n*=8104	Inclusion criteria: 50 yr of age or older Not average risk		**-Sensitivity for polyp (>10 mm)** Hemoccult II (95% CI): 30.8% (21.6, 41.1) Hemoccult II Sensa (95% CI): 68.6% (59.2, 77.9) **-Specificity for polyp (>10 mm)** Hemoccult II (95% CI): 98.1% (97.7, 98.4) Hemoccult II Sensa (95% CI): 87.5% (86.7, 88.2)	Sensitive gFOBT is more sensitive and less specific test compared with gFOBT. But still low sensitive test for screening advanced colorectal adenoma.,
Park et al.,[15] 2010, Korea	-Cross sectional study -gFOBT: hemoccult II test (3 samples) -qFIT: OC-SENSA MICRO (3 samples) -colonoscopy	*n*=770	-Inclusion criteria: asymptomatic, average-risk people between 50 and 75 yr of age -Exclusion criteria no colonoscopy performed No stool sample submitted Incomplete colonoscopy and no further evaluation IBD Infectious colitis Bleeding hemorrhoid	-Advanced adenoma: tubular adenoma ≥10 mm, or tubulovillous or villous adenomas, or with high grade dysplasia -Intramucosal carcinoma or carcinoma *in situ*	**-Prevalence of colonic adenoma (by CFS)** : 36.1% (278 pts) **-Prevalence of advanced adenoma (by CFS)** **:**7.7% (59 pts) Cancer (by CFS): 1.7% (13 pts) **<gFOBT>** **Advanced adenoma** Sensitivity (95% CI): 13.6% (6.0, 25.0) Specificity (95% CI): 92.4% (90.2, 94.3) **Cancer** Sensitivity (95% CI): 30.8% (9.1, 61.4) Specificity (95% CI): 92.4% (90.2, 94.2)	The FIT and gFOBT provides a low sensitivity for detecting advanced adenoma, But FIT provides a comparable sensitivity for detecting colon cancer.

Key question	Among average-risk adults aged 50 yr and older, do colorectal cancer incidence rates and mortality rates decrease in groups who had received a FOBT for colorectal cancer screening compared to groups who had not?					
Study	Design	Sample size	Inclusion/Exclusion criteria	Definition	Results	Conclusion
					<FIT> **advanced adenoma** (Using the 100 ng/mL cut point and 3-sample) Sensitivity (95% CI): 33.9% (22.1, 47.4) Specificity (95% CI): 90.6% (88.2, 92.6) **Cancer** Sensitivity (95% CI): 92.3% (64.0, 99.8) Pecificity (95% CI): 90.1% (87.7, 92.1)	
Lieberman et al.,[16] 2001, USA	-Cross sectional study -gFOBT: hemoccult II test (3 samples) rehydrated. -colonoscopy	*n*=2,885	-Inclusion criteria: asymptomatic, average-risk people between 50 and 75 yr of age	-advanced adenoma: tubular adenoma ≥10 mm, or tubulovillous or villous adenomas, or with high grade dysplasia	**-Prevalence of advanced adenoma (by CFS)** **:** 10.6% (306 pts) **-Prevalence of colonic cancer (by CFS)** **:** 0.8% (24 pts) **-gFOBT for advanced adenoma** Sensitivity: 23.9% (73/306) Specificity: 93.6% (2,413/2,579) **-gFOBT for cancer** Sensitivity: 50% (12/24) Specificity: 92.1% (2,634/2,861)	The gFOBT provides a low sensitivity for detecting advanced adenoma and cancer.
Imperiale et al.,[17] 2004, USA	-Cross sectional study -gFOBT: hemoccult II test (3 samples) not rehydrated. -compare with fecal DNA & colonoscopy	*n*=4,404	asymptomatic persons at average risk for colorectal cancer		**-Positive rate of gFOBT (**Hemoccult II) Adenocarcinoma: 12.9% (5.1-28.9) Advanced adenoma: 10.7% (8.0-14.1) Small polyp(<10 mm): 4.8% (3.4-6.7)	The traditional gFOBT provides a low sensitivity for detecting cancer or advanced adenoma

Key question	**In average-risk adults aged 50 yr and older, is FIT superior to the traditional gFOBT as a colorectal cancer screening test?**					
Study	**Design**	**Sample size**	**Inclusion/Exclusion criteria**	**Definition**	**Results**	**Conclusion**
Smith et al.,[13] 2006, Austrailia	-Prospective cohort study -Sensitive gFOBT (Hemoccult II Sensa) (3 consecutive samples) FIT(Insure) (2 consecutive samples) -Colonoscopy	*n*=2351 Performed CFS=161	Inclusion criteria: 50-75 yr Average risk group	Significant adenoma :highgrade dysplasia, villous change, ≥10 mm, serrated histology or ≥3 polyps	**-Positive rate of gFOBT (**Hemoccult II Sensa) Cancer: 47.1% Multiple polyp: 12.5% High grade dysplasia: 25% Villous: 36.4% Serrated: 0 ≥10 mm: 33.3% Total significant adenoma: 24.2% **-Positive rate of FIT (Insure)** Cancer: 82.4% Multiple polyp: 50% High grade dysplasia: 25% Villous: 54.5% Serrated: 0 ≥10 mm: 44.4% Total significant adenoma: 44.4%	**FIT is more sensitive** for adenomas than a sensitive GFOBT.

Key question	In average-risk adults aged 50 yr and older, is FIT superior to the traditional gFOBT as a colorectal cancer screening test?					
Study	**Design**	**Sample size**	**Inclusion/Exclusion criteria**	**Definition**	**Results**	**Conclusion**
Park et al.,[15] 2010, Korea	-Cross sectional study -qFIT: OC-SENSA MICRO (3 samples) -gFOBT: hemoccult II test (3 samples) -Colonoscopy	*n*=770	-Inclusion criteria: asymptomatic, average-risk people between 50 and 75 yr of age -Exclusion criteria No colonoscopy performed No stool sample submitted Incomplete colonoscopy and no further evaluation IBD Infectious colitis Bleeding hemorrhoid	-Advanced adenoma : tubular adenomas with diameters of ≥ 10 mm, or tubulovillous or villous adenomas, or those with high grade dysplasia regardless of size. -Intramucosal carcinoma or ca *in situ*	**-Prevalence of colonic adenoma (by CFS)**: 36.1% (278 pts) **-Prevalence of advanced adenoma (by CFS):** 7.7% (59 pts) **-Cancer (by CFS)** : 1.7% (13 pts) **-<gFOBT>** **Advanced adenoma** Sensitivity (95% CI): 13.6% (6.0, 25.0) Specificity (95% CI): 92.4% (90.2, 94.3) **Cancer** Sensitivity (95% CI): 30.8% (9.1, 61.4) Specificity (95% CI): 92.4% (90.2, 94.2) **-<FIT>** **Advanced adenoma** (Using the 100 ng/mL cut point and 3-sample) Sensitivity (95% CI): 33.9% (22.1, 47.4) Specificity (95% CI): 90.6% (88.2, 92.6) **Cancer** Sensitivity (95% CI): 92.3% (64.0, 99.8) Specificity (95% CI): 90.1% (87.7, 92.1)	**The qFIT provides a higher sensitivity for detecting colon cancer than gFOBT,** and has an acceptable specificity that significantly reduces the need for CFS evaluation in the screened population.
Rozen et al.,[18] 2009, Israel	Observational Study -gFOBT; Hemoccult-II SENSA (3 samples) FIT: OC-MICRO -colonoscopy	*n*=330	Aged 50-75 yr, average risk	-Significant neoplasm: CRC or advanced adenoma -FIT(+): ≥50 ng/mL	**-gFOBT for significant (advanced) neoplasm** **:** Sensitivity (95% CI): 53.0% Specificity (95% CI): 59.0% **-FIT for advanced adenoma** **:** Sensitivity (95% CI): 75.0% Specificity (95% CI): 87.0%	quantified I-FOBT had significantly better specificity than G-FOBT for significant neoplasms,
Wong et al.,[19] 2003, China	Cross sectional study -sensitive gFOBT (Hemoccult-Sensa) (3 samples) -I-FOBT (FlexSure-OBT) -colonoscopy	*n*=135 (performed CFS=135)	-Exclusion criteria: a previously positive faecal occult blood test,, history of overt GI bleeding, active rectal bleeding, menstruation, haematuria and known IBD .	Significant neoplasm : adenoma ≥1.0 cm or cancer	**Hemoccult SENSA** Sensitivity for significant neoplasm:10/11 (91%), Specificity : 70% positive predictive value : 10/56 (18%) **FlexSure OBT.** Sensitivity for significant neoplasm:9/11(82%), Specificity :94% positive predictive value :9/19 (47%)	**The positive predictive value of the FIT** for the detection of significant colorectal neoplasia was 29% **better** than that of the sensitive gFOBT.

Key question	In average-risk adults aged 50 yr and older, is two or more times of FIT superior to one time of FIT as a colorectal cancer screening test?					
Study	Design	Sample size	Inclusion/Exclusion criteria	Definition	Results	Conclusion
Park et al.,[15] 2010, Korea	-Cross sectional study -qFIT: OC-SENSA MICRO (3 samples) -gFOBT: hemoccult II test (3 samples) -Colonoscopy	*n*=770	-Inclusion criteria: asymptomatic, average-risk people between 50 and 75 yr of age -Exclusion criteria No colonoscopy performed No stool sample submitted Incomplete colonoscopy and no further evaluation IBD Infectious colitis Bleeding hemorrhoid	-Advanced adenoma : tubular adenomas with diameters of ≥10 mm, or tubulovillous or villous adenomas, or those with high grade dysplasia regardless of size. -Intramucosal carcinoma or carcinoma *in situ* : designated as having high-grade dysplasia.	-Prevalence of colonic adenoma (by CFS): 36.1% (278 pts) -Prevalence of advanced adenoma (by CFS): 7.7% (59 pts) **Cancer (by CFS)**: 1.7% (13 pts) **-FIT for advanced adenoma** (Using the 100 ng/mL cut point) 1) 1 sample Sensitivity (95% CI): 23.7% (13.6, 36.6) Specificity (95% CI): 94.0% (91.9, 95.6) 2) 2 samples Sensitivity (95% CI): 27.6% (16.7, 40.9) Specificity (95% CI): 92.4% (90.2, 94.2) 3) 3 samples Sensitivity (95% CI): 34.5% (22.5, 48.1) Specificity (95% CI): 90.4% (88.0, 92.5) **-FIT for cancer** (Using the 100 ng/mL cut point) 1) 1 sample Sensitivity (95% CI): 69.2% (38.6, 90.9) Specificity (95% CI): 93.7% (91.7, 95.3) 2) 2 samples Sensitivity (95% CI): 84.6% (54.6, 98.1) Specificity (95% CI): 92.2% (90.0, 94.0) 3) 3 samples Sensitivity (95% CI): 84.6% (54.6, 98.1) Specificity (95% CI): 89.8% (87.3, 91.9) - In this study, we showed that two samples and a 118 ng/mL of threshold provides the best discrimination for CRC in an average-risk Korean population.	The more tests analyzed per patient improve sensitivity, but decrease specificity.
Rozen et al.,[18] 2009, Israel	Observational study: FIT:OC-MICRO gFOBT: :Hemoccult SENSA	*n*=330	Inclusion criteria: patients scheduled for CFS Exclusions for preparing the HOS or I-FOBT were visible rectal bleeding, haematuria, menstruation, known diagnosis of inflammatory bowel disease and non co-operation with preparing a faecal test.	-Significant neopl asms: CRC or AAP; this latter category included adenomas ≥10 mm in diameter or having ≥20% villous histology or having any amount of HGD independent of size. - FIT level (+): >50 ngHb⁄mL - number of colonoscopy examinations: resulting from a positive test and needed to identify the significant neoplasm found at colonoscopy examination.	**-FIT for significant neoplasm** -1 sample Sensitivity (CI): 53.1 (35.8-70.4) Specificity (CI): 94.0 (91.3-96.7) PPV, 48.6%; NPV, 94.9 No. CFS needed: 2.1 - 2 samples Sensitivity (CI): 68.8 (52.7-84.8) Specificity (CI): 91.9 (88.9-95.0) PPV, 47.8%; NPV, 96.5% No. CFS needed: 2.1 - 3 samples Sensitivity (CI): 75.0 (60.0-90.0) Specificity (CI): 86.9 (83.1-90.7) PPV, 38.1%; NPV, 97.0% No. CFS needed: 2.8	Requesting two I-FOBTs improve sensitivity without increasing the number of colonoscopies needed. (but would increase costs, possibly reduce Compliance)

Key question	In average-risk adults aged 50 yr and older, is two or more times of FIT superior to one time of FIT as a colorectal cancer screening test?					
Study	Design	Sample size	Inclusion/Exclusion criteria	Definition	Results	Conclusion
			in preparing a fecal test, and incomplete colonoscopy examination		**FIT for advanced neoplasm (*n*=149)** -1 sample Sensitivity (CI): 41.6 (33.7-49.5) Specificity (CI): 93.3 (92.1-94.6) - 2 samples Sensitivity (CI): 55.0 (47.0-63.0) (vs. 1, $p<0.001$) Specificity (CI): 90.2 (88.7-91.7) - 3 samples Sensitivity (CI): 61.1 (53.2-68.9) (vs. 1, $p<0.001$) (vs. 2, $p<0.004$) Specificity (CI): 87.8 (86.2-89.4) **FIT for advanced adenoma (*n*=129)** -1 sample Sensitivity (CI): 36.4 (28.1-44.7) Specificity (CI): 93.3 (92.1-94.6) - 2 samples Sensitivity (CI): 48.8 (40.2-57.5) (vs. 1, $p<0.01$) Specificity (CI): 90.2 (88.7-91.7) - 3 samples Sensitivity (CI): 55.0 (46.5-63.6) (vs. 1, $p<0.01$) (vs. 2, $p=0.08$) Specificity (CI): 87.8 (86.2-89.4)	
Grazzini et al.,[21] 2009, Italy	Cross sectional study FIT: OC-Hemodia	*n*=20,596	Inclusion criteria: aged 50-69 yr involved in CRC population based screening programmes	-FIT level (+): >100 ngHb⁄mL -Significant neoplasia :cancer + advanced adenoma	**FIT for cancer** -1 sample, detection rate: 2.8 (/1000 screened subject) PPV -2 samples, detection rate: 3.4 (/1000 screened subject) **FIT for significant nedplasm** -1 sample, detection rate: 18.4 (/1000 screened subject)	Repeated tests seem to have a greater impact on adenomas rather than on cancer detection rate.

Key question	In average-risk adults aged 50 yr and older, is two or more times of FIT superior to one time of FIT as a colorectal cancer screening test?					
Study	Design	Sample size	Inclusion/Exclusion criteria	Definition	Results	Conclusion
					-2 samples, detection rate: 23.1 (/1000 screened subject) (1 vs. 2: p<0.006)	

Key question	In average-risk groups aged 50 or more, can CT colonography be recommended for colorectal cancer screening and polyp detection?								
Study	**Setting**	**Reference standard operator characteristics CT test characteristics**	**Patient characteristics**	**Prevalence and yield of polyps**	**Sensitivity (95% CI)**	**Specificity (95% CI)**	**Positive predictive value**	**Comments**	**Conclusion**
Mulhall et al.,[22] 2005	Meta-analysis		***n***: 6,393 from 33 studies **Average risk**: only 4 studies **High risk**: 29 studies		**Pooled per-patient sensitivity**: All sizes: 70% (53.0, 87.0) <6 mm: 48% (25.0, 70.0) 6-9 mm: 70% (55.0, 84.0) >9 mm: 85% (79.0, 91.0) **I^2 statistics**: <6 mm: 96.7% 6-9 mm: 93.1% >9 mm: 85.2%	**Pooled per-patient specificity**: All sizes: 86% (84.0, 88.0) <6 mm: 91% (89.0, 95.0) 6-9 mm: 93% (91.0, 95.0) >9 mm: 97% (96.0, 97.0) **I^2 statistics**: <6 mm: 47.1% 6-9 mm: 50% >9 mm: 41.8%		**Source of heterogeneity**: 1. Collimation width: 1mm increse in collimation decreases sensitivity by 4.9% 2. Type of scanner: multidetector (95% sensitivity)>single detector (82% sensitivity) 3. Mode of interpretation: 2D (81.9%)<2D+3D (91%)<3D (99%)	CTC is highly specific, but the range of reported sensitivities is wide. Patient or scanner characteristics do not fully account for this variability, but collimation, type of scanner, and mode of imaging explain some of the discrepancy.
Halligan et al.,[23] 2005	Systemic review, Meta-analysis		***n***: 4,181 from 24 studies **Average risk**: only 3 studies **High risk**: 21 studies	**Per-patient prevalence of polyps or cancers:** 15-72%	**Pooled per-patient sensitivity**: All sizes: 45-97% ≥5 mm: 86% (75.0, 93.0) ≥10 mm: 93% (73.0, 98.0) **Pooled per-polyp sensitivity**: All sizes: not reported due to heterogeneity ≥5 mm: 70% (63.0, 76.0) ≥10 mm: 77% (70.0, 83.0) **Sensitivity for cancer detection**: 96% (91.0, 99.0)	**Pooled per-patient specificity**: All sizes: 26-97% ≥5 mm: 86% (76.0, 93.0) ≥10 mm: 97% (95.0, 99.0)		**Source of heterogeneity**: 1. Size of the polyps: greater heterogeneity of the study results was noted for small polyps (<5 mm) 2. Incorporation bias: consensus assessment>independent assessment 3. Absence of generally accepted reporting format	CTC seems sufficiently to be sensitive and specific in the detection of large and medium polyps. It is especially sensitive in the detection of symptomatic cancer.
Chaparro et al.,[24] 2009	Meta-analysis		***n***: 10,546 from 47 studies **Average risk**: only 6 studies **High risk**: 41 studies		**Pooled per-patient sensitivity**: All sizes: 69% (66.0, 72.0) 6-9 mm: 60% (56.0, 65.0) >9 mm: 83% (70.0, 85.0) I^2 >50% **Pooled per-polyp sensitivity**: All sizes: 66% (64.0, 68.0) 6-9 mm: 59% (56.0, 61.0) >9 mm: 76% (73.0, 79.0) I^2 >50%	**Pooled per-patient specificity**: All sizes: 83% (81.0, 84.0) 6-9 mm: 90% (89.0, 91.0) >9 mm: 92% (92.0, 93.0) **I^2 statistics**: All sizes: 89% 6-9 mm: 21% >9 mm: 62%		**Source of heterogeneity**: Sensitivity 1. Colon preparation regimen: NaP: 83.3%>other than NaP: 62% 2. Fecal tagging: Yes: 88%>No: 59% 3. Collimation width: <5 mm: 72% > ≥5 mm: 65% 4. Reconstruction thickness: <3 mm: 64% > ≥3 mm: 58% 5. Mode of interpretation: 3D:83% > 2D±3D: 64% 6. Radiation dose: >100 mA: 79% > <100 mA: 63% 7. Risk of population: average risk: 82% > high risk: 65%	CTC is highly specific for the detection of colorectal polyps and tumors. Some studies reported high sensitivities, but the results of the studies were highly heterogeneous, while the studied variables explained only part of this discrepancy.
Graser et al.,[25] 2009	Single center, Prospective cohort study	Same day CTC and OC (100%). OC was performed by 1/6 experienced colonoscopists and 1/3 experienced radiologists (with >300 CTC cases) prospectively reviewed the CT data using primary 3D reading State-of-the art 64-rows MDCT CO_2 (n=227) or manual air (n=80) insufflation Use of Buscopan Use of fluid tagging 0.6 mm collimation; 0.5 mm reconstruction interval; 120 kVp/70 mAs for supine & 30 mAs for prone	***n***: 307 **Mean age**: 60.5 yr **F**: 45% **Race/Ethnicity**: NR **SES**: NR **Average risk**: 100% FOBT, FIT, Flexible sigmoidoscopy, colonoscopy 와 direct 하게 비교한 study 임. Incomplete colonoscopy: 2/311 (0.64%)	**Per-patient prevalence** Patients with ≥1 adenoma of any size: 36.8% (113/307) **Yield** **<6 mm polyp**: Adenomatous 147 Nonadenomatous 271 **6-9 mm polyp**: Adenomatous 41 Nonadenomatous 15 **≥10 mm polyp**: Adenomatous 33 Nonadenomatous 4	**Of adenomas per-polyp** All sizes: 84.1% (76.0, 90.3) >5 mm: 91.3% (79.2, 97.6) >9 mm: 92% (74.0, 99.0) Advanced neoplasia: 96.7% (82.8, 99.9)	**Of adenomas per-polyp** All sizes: 47.4% (40.2, 54.7) >5 mm: 93.1% (89.3, 95.9) >9 mm: 97.9% (95.4, 99.2) Advanced neoplasia: 39.4% (33.6, 45.4)	**PPV** Of adenomas per-patient All sizes: 48.2% (41.1, 55.4) >5 mm: 70.0% (56.8, 81.2) >9 mm: 79.3% (60.3, 92.0) Advanced neoplasia: 14.7% (10.1, 20.5) **NPV** Of adenomas per-patient All sizes: 83.6% (75.4, 90.0) >5 mm: 98.4% (95.9, 99.6) >9 mm: 99.3% (97.4, 99.0) Advanced neoplasia: 99.1% (95.0, 100)	**Sensitivity/specificity for adenomas >9 mm** Colonoscopy 100%/98.6% Sigmoidoscopy 68%/99.6% FOBT 23.8%/89.8% FIT 33.3%/85.6% FOBT+FS 76.2%/89.4% FIT+FS 71.4%/85.2% **Sensitivity/specificity For advanced neoplasia** Colonoscopy 100%/43% Sigmoidoscopy 83.3%/59.6% FOBT 20%/89.6% FIT 32%/85.8% FOBT+FS 80%/57%	High-resolution and low-dose CTC is feasible for CRC screening and reaches sensitivities comparable with colonoscopy for adenomas > 5 mm (91.3%)

Key question: In average-risk groups aged 50 or more, can CT colonography be recommended for colorectal cancer screening and polyp detection?

Study	Setting	Reference standard operator characteristics CT test characteristics	Patient characteristics	Prevalence and yield of polyps	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value	Comments	Conclusion
Johnson et al.,[26] 2008	15 study centers, Feb. 2005-Dec. 2006 Multicenter RCT	Same day CTC and OC in 99%. For cases in which lesions ≥10 mm were detected on CTC but not on colonoscopy, patients underwent repeated colonoscopy within 90 day. 15 high-quality radiologists who had the highest scores on the qualifying examination reviewed CTC data. Primary 2D (*n*=1280) or 3D (*n*=1251) reading. State-of-the art ≥16 rows MDCT, CO_2 insufflation Use of glucagon 0.5-1 mm collimation; 1 mm reconstruction interval; 120 kVp/50 mAs	***n***: 2531 **Mean age**: 58.3 yr **F**: 52% **Race/Ethnicity**: White 81.7% Black 13% American indian or Alaskan native 0.9% Asian 2.3% Native Hawaiian 0.27% Unknown or missing 1.8% **SES**: NR **Average risk**: 88.9% (2,249/2,531) **Personal or family history**: 11.1% (282/2,531)	**Per-patient prevalence** Patients with no polyp: 64.4% (1,629/2,531) Patients with polyp <5 mm: 20.2% (512/2,531) Patients with 5-9 mm polyp: 10.2% (258/2,531) Patients with polyp ≥10 mm: 5.2% (132/2,531) **Yield** **5-9 mm polyp**: Adenomatous 246 Nonadenomatous 146 **≥10 mm polyp**: Adenomatous 128 Nonadenomatous 27	**Of adenomas per-patient** ≥5 mm: 65% (58.0, 73.0) ≥6 mm: 78% (71.0, 85.0) ≥7 mm: 84% (78.0, 91.0) ≥8 mm: 87% (80.0, 93.0) ≥9 mm: 90% (83.0, 96.0) ≥10 mm: 90% (84.0, 96.0) **Of adenomas per-polyp** ≥5 mm: 59% (54.0, 64.0) ≥6 mm: 70% (64.3, 75.2) ≥7 mm: 75% (68.9, 80.3) ≥8 mm: 80% (73.9, 85.3) ≥9 mm: 82% (74.6, 87.3) ≥10 mm: 84% (77.0, 89.7)	**Of adenomas per-patient** ≥5 mm: 89% (85.1, 92.3) ≥6 mm: 88% (84.0, 92.0) ≥7 mm: 87% (83.1, 91.4) ≥8 mm: 87% (82.5, 90.9) ≥9 mm: 86% (81.7, 90.2) ≥10 mm: 86% (81.3, 90.0)	**PPV** Of adenomas per-patient ≥5 mm: 45% (38.9, 51.3) ≥6 mm: 40% (33.5, 46.3) ≥7 mm: 35% (29.9, 39.7) ≥8 mm: 31% (25.6, 35.5) ≥9 mm: 25% (20.9, 29.2) ≥10 mm: 23% (19.4, 27.3) **NPV** Of adenomas per-patient ≥5 mm: 95% (94.1, 96.5) ≥6 mm: 98% (97.1, 98.4) ≥7 mm: 99% (98.0, 99.2) ≥8 mm: 99% (98.4, 99.4) ≥9 mm: 99% (99.0, 99.8) ≥10 mm: 99% (99.1, 99.8)	30 lesions ≥10 mm were detected in 27 pts on CTC but were not detected on the initial colonoscopy. Fifteen of these 27 pts, with 18 reported lesions, returned for a second colonoscopy. Five of 18 lesions were confirmed on the second colonoscopy (9 mm inflammatory polyp, 10 mm tubular adenoma, 11 mm tubular adenoma, 14 mm inflammatory polyp, and 35 mm tubulovillous adenoma with dysplasia)	In asymptomatic adults, CTC screening identified 90% of subjects with adenomas or cancers ≥10 mm
Kim et al.,[27] 2008	Single center, Prospective cohort study	OC with segmental unblinding Same day CTC and OC. Colon preparation: 4 L PEG (*n*=172) 90 mL NaP (*n*=69) No fecal tagging 16-row MDCT 120 kVp/50 (supine) & 120 mAs (prone) IV contrast injection 1.25 mm collimation 3D fly-through with 2D confirmation (Viatronix V3D) 1 of 2 experienced radiologists interpreted CTC. 1/5 board certified gastroenterologists performed OC.	***n***: 241 **Mean age**: 57.6 yr **F**: 49.4% **Race/Ethnicity**: NR **SES**: NR **Average risk**: 95% (229/241) **Family history of CRC**: 5% (12/241)	**Prevalence** Any size adenoma: 192 in 95 pts (39.4%) Advanced adenomas: 25 17 ≥10 mm 7 villous adenoma <10 mm 1 tubular adenoma with HG **Yield** **Any size polyp**: Adenomatous 192 Nonadenomatous 203 **≤5 mm**: Adenomatous 122 Nonadenomatous 172 **6-9 mm**: Adenomatous 53 Nonadenomatous 26 **≥10 mm**: Adenomatous 17 Nonadenomatous 5	**Any polyp** **Per-patient sensitivity** **Overall**: 55.3 (47.3, 63.0) **≥6 mm**: 68.5 (55.2, 79.3) **≥8 mm**: 73.3 (55.5, 85.8) **≥10 mm**: 86.7 (62.2, 96.3) **Per-polyp sensitivity** **Overall:** 44.4 (39.3, 49.0) **≥6 mm:** 60.4 (50.6, 69.4) **≥8 mm:** 70.5 (55.8, 81.9) **≥10 mm:** 72.7 (51.8, 86.8) **Adenomas** **Per-patient sensitivity** Overall: 61.1 (50.0, 70.3) ≥6 mm: 72.7 (57.2, 85.0) ≥8 mm: 78.3 (56.3, 92.5) ≥10 mm: 90.0 (55.5, 99.7) **Per-polyp sensitivity** Overall: 49.5 (42.5, 56.5) ≥6 mm: 64.3 (51.9, 75.4) ≥8 mm: 74.3 (56.7, 87.5) ≥10 mm: 76.5 (50.1, 93.2)	**Any polyp** **Per-patient specificity** **Overall**: 34.1 (25.2, 44.3) **≥6 mm**: 88.8 (84.3, 92.5) **≥8 mm**: 95.3 (91.5, 97.4) **≥10 mm**: 97.3 (94.3, 98.7)		**≥6 mm polyps** Dry versus wet preparation Sensitivity / Specificity Dry 66.7% / 75.0% Wet 69.4% / 94.7% - Wet preparation with PEG shows significantly higher specificity than dry preparation **Sensitivity according to morphology** ≥6 mm / ≥10 mm Flat 37.5% / 0% Sessile 64.1% / 70% Pedunculated 84.6% / 100%	Per-patient sensitivity & specificity for polyps ≥10 mm of CTC is 86.7% and 72.7%. But, dry preparation may decrease specificity and PPV. Flat morphology is difficult to be detected by CTC.
An et al.,[28] 2008	Single center, Prospective cohort study	Colon preparation: NaP (*n*=623) Mg citrate (*n*=392) Fecal tagging (87.7%, 890) 16-row MDCT 90-120 kVp/13-45 mAs 2 mm/1 mm ST/RI 3D fly-through with 2D confirmation (Terarecon, Brilliance workstation, Rapidia) 1 of 2 experienced radiologists interpreted CTC	***n***: 1,015 **Mean age**: 51 yr **F**: 40% **Race/Ethnicity**: NR **SES**: NR **Average risk**: 100%	**Diagnostic yield for advanced neoplasm**: 1.5% (15/1,015)	—		**Per-patient PPV** C2 / C3 / C4 Any Neoplasm 74% / 90% / 100% 45% / 70% / 100% **Per-polyp PPV** Of all polyps ≥6 mm: 69% (57, 80) ≥7 mm: 71% (57, 83) ≥8 mm: 74% (57, 87) ≥9 mm: 76% (59, 89) ≥10 mm: 92% (73, 99) **Per-polyp PPV** Of neoplastic polyp ≥6 mm: 43% (31, 56) ≥7 mm: 46% (32, 61) ≥8 mm: 45% (29, 62) ≥9 mm: 47% (30, 65) ≥10 mm: 58% (37, 78)	Of 1,015 patients, CTC yields 21 (2.1%) C0, 916 C1 (90.2%), 54 C2 (5.3%), 23 C3 (2.3%), and 1 C4 (0.1%) categories. **OC referal rate** **Actual rate:** 5.3% (54/1,015) **Maximum (C0, C2-4):** 9.8% (99/1,015) **C3 or C4**: 2.4% (24/1,015) **Incomplete colonoscopy** (*n*=1), **CTC complications:** symptomless extraluminal air (*n*=1) which spontaneously resolved at follow-up CT. **Radiation dose:** 0.8-1.0 mSv for both scanning	A successful screening CTC program can be reproduced in an Asian population

Key question	In average-risk groups aged 50 or more, can CT colonography be recommended for colorectal cancer screening and polyp detection?								
Study	**Setting**	**Reference standard operator characteristics CT test characteristics**	**Patient characteristics**	**Prevalence and yield of polyps**	**Sensitivity (95% CI)**	**Specificity (95% CI)**	**Positive predictive value**	**Comments**	**Conclusion**
Kim et al.,[29] 2007	Prospective cohort Single institution, US Recruitment through referrals for screening colonoscopy	45 mL sodium phosphate (most patients) 250 mL 2.1% w/v barium+60 mL gastrografin 8- or 16-row MDCT 120 kVp/25-75 mAs 1.25 mm collimation 3D fly-through with 2D confirmation (Viatronix V3D) 1 of 5 experienced radiologists interpreted CTC 1/10 board certified gastroenterologists performed OC	**OC group** ***n***: 3,163 **Mean age**: 58.1 yr **F**: 55.6% **Race/Ethnicity**: NR **SES**: NR **Asymptomatic:** 98% **Family history:** 8.4% **CTC group** ***n***: 3,120 **Mean age**: 57.0 yr **F**: 56% **Race/Ethnicity**: NR **SES**: NR **Asymptomatic:** 97.8% **Family history:** 5.1%	**% of patients who use OC** OC group: 100% (3,163/3,163) CTC group: 7.9% (246/3,120) **Total No. of removed polyp** OC group: 2,434 CTC group: 561 **No. of advanced adenomas** ≥10 mm OC/CTC 103/103 6-9 mm OC/CTC 11/5 ≤5 mm OC/CTC 3/1 **No. of invasive carcinoma** OC/CTC 4/14 **% patients /w invasive carcinoma** OC/CTC 0.1%/0.4% **Total No. of advanced lesions** OC/CTC 121/123 **% patients /w advanced lesions** OC/CTC 3.4%/3.2%	—				**Rates of+screening results** size threshold: CTC/OC ≥10 mm: 164 (5.3%)/134 (4.2%) ≥6 mm: 404 (12.9%)/424 (13.4%) overall: 404 (12.9%)/1,189 (37.6%)	CTC (3.2%) shows similar detection rates for advanced neoplasia to optical colonoscopy (3.4%), with considerably smaller number of polypectomies and complications. These findings support the use of CTC as a primary screening test before therapeutic colonoscopy.
Johnson et al.,[30] 2007	Mayo Clinic, MN. Comparison of primary 2D and 3D interpretation and slice thickness of 1.25 vs. 2.5 mm. 3D software allows for 360 degree panoramic display with virtual unfolding and dissecting of the colon along the longitudinal axis.	OC Same day CTC and OC Three radiologists who all had >1,000 colonoscopy-verified CT colonography examinations. 6 weeks between the two readings of an exam by the same reader. Performed by staff gastroenterologists or supervised by staff gastroenterologists and colorectal surgeons 1.25 and 2.5 mm collimation; 1.25 mm reconstruction interval; Multi detector; No contrast; Voxtool 5.4.46, GE Healthcare	***n***: 452 **Mean age:** 65 yr (41-82) **Female:** 44% **Race/Ethnicity:** White 85% Asian 12% Hispanic 3% African American 1% Native American 0.2% **SES:** NR **Asymptomatic**: 100%	**Prevalence at least 1 adenomatous lesion** ≥10 mm: 5.8% (26/452) 6-9 mm: 6.6% (30/452) **Yield** Adenoma ≥10 mm: 26 Adenoma 6-9 mm: 38	**Per-Patient ≥10 mm** **2D** Reviewer 1 83% (5/6) Reviewer 2 70% (7/10) Reviewer 3 78% (7/9) **3D** Reviewer 1 50% (4/8) Reviewer 2 83% (5/6) Reviewer 3 83% (10/12) **2D & 3D Review:** 95% (18/19) **Per-Patient 6-9 mm** **2D** Reviewer 1 40% (4/10) Reviewer 2 25% (2/8) Reviewer 3 83% (10/12) **3D** Reviewer 1 33% (4/12) Reviewer 2 60% (6/10) Reviewer 3 100% (8/8) **2D & 3D Review:** 71% (10/14)	**Per-Patient ≥10 mm** **2D** Reviewer 1 99% (134/135) Reviewer 2 98% (137/140) Reviewer 3 97% (143/147) **3D** Reviewer 1 97% (134/138) Reviewer 2 99% (142/144) Reviewer 3 97% (137/141) **2D & 3D Review:** 98% (205/210) **Per-Patient 6-9 mm** **2D** Reviewer 1 92% (120/131) Reviewer 2 99% (140/142) Reviewer 3 95% (137/144) **3D** Reviewer 1 93% (125/134) Reviewer 2 96% (134/140) Reviewer 3 94% (136/145) **2D & 3D Review:** 91% (196/215)		Asymptomatic population but did include persons with previous colonic resection Study initiated prior to standard tagging procedures and mechanical insufflation that are commonly used in clinical practice today. Limited power due to multiple analyses and not primarily addressing overall accuracy. Per lesion sensitivity of colonoscopy for lesions ≥10 mm: 77%	1.25 mm thin slice CTC with primary 2D and 3D interpretation shows 95% per-patient sensitivity and 98% specificity for ≥10 mm adenomatous polyps
Macari et al.,[31] 2004	Veterans Affairs Hospital in New York. Recruited from gastro clinic	OC with no unblinding during procedure to verify finding on CT that were not seen during CTC Same day CTC and OC. Performed by a gastroenterologist with 5 yr experience or fellow under supervision of the gastroenterologist. 2D with 3D confirmation of any abnormality; 4×1 mm collimation; 1 mm reconstruction interval; Multidetector; No contrast; Vitrea 2	***n***: 68 **Mean age:** 55 yr **F:** 0% **Race/Ethnicity:** NR **SES:** NR **Average risk:** 100%	**Prevalence** Any polyp: 57% (39/68 patients) Largest polyp 1-5 mm: 23 patients 6-9 mm: 13 ≥10 mm: 3 **Yield** 1-5 mm: 78 6-9 mm: 17 ≥10 mm: 3	**Per polyp** Any size: 21.4 (14.2, 31.1) 1-5 mm: 11.5 (5.4, 23.3) 6-9 mm: 52.9 (29.1, 75.5) ≥10 mm: 100 (36.8, 100)	**Per patient** Any size: 89.7 (72.7, 97.8) ≥10 mm: 98.5 (91.7, 99.9)	NR	100% male population seen in a VA medical center. Small sample size. All had negative FOBT results and no prior history. False positives of CT were not verified during colonoscopy, rather assumed to be residual fecal material. No per-patient sensitivity, only per-polyp.	CTC shows 100% per-polyp and 98.5% per-patient sensitivity for polyps ≥10 mm

Key question: In average-risk groups aged 50 or more, can CT colonography be recommended for colorectal cancer screening and polyp detection?

Study	Setting	Reference standard operator characteristics CT test characteristics	Patient characteristics	Prevalence and yield of polyps	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value	Comments	Conclusion
Pickhardt et al.,[32] 2003	Military Medical Centers in Bethesda, MD; Washington, DC; San Diego, CA Recruited consecutive patients who were primarily referred for screening colonoscopy	OC with segmental unblinding, Same day CTC and OC. Performed by 1/17 experienced colonoscopists. 1 of 6 board-certified radiologists prospectively reviewed the CT data. All had completed training and read at least 25 studies. Two had interpreted more than 100. Flythrough 3D with 2D correlation of any abnormality; 1.25-2.5 mm collimation; 1 mm reconstruction interval; Multidetector; Oral contrast; Viatronix V3D 1.2	***n***: 1,233, **Mean age**: 57.8 yr, **F**: 41%, **Race/Ethnicity**: NR, **SES**: NR, **Average risk**: 97.4% (1,201/1,233), **Family history**: 2.6% (32/1,233)	**Prevalence** **≥10 mm**: 3.9% **≥8 mm**: 6.7% **≥6 mm**: 13.6% **Yield** **Any size polyp:** Adenomatous 554 Nonadenomatous 756 **≤5 mm:** Adenomatous 344 Nonadenomatous 622 **6-9 mm:** Adenomatous 159 Nonadenomatous 103 **≥10 mm:** Adenomatous 51 Nonadenomatous 31	**Of adenomas per patient** ≥6: 88.7 (82.9, 93.1) ≥7: 90.9 (83.9, 95.6) ≥8: 93.9 (86.3, 98.0) ≥9: 93.0 (83.0, 98.1) ≥10: 93.8 (82.8, 98.7) **Of adenomas per polyp** ≥6: 85.7 (80.2, 90.1) ≥7: 89.5 (83.0, 94.1) ≥8: 92.6 (85.4, 97.0) ≥9: 91.8 (81.2, 97.3) ≥10: 92.2 (81.1, 97.8)	**Of adenomas per patient** ≥6: 79.6 (77.0, 82.0) ≥7: 87.4 (85.3, 89.2) ≥8: 92.2 (90.5, 93.7) ≥9: 94.9 (93.5, 96.1) ≥10: 96.0 (94.8, 97.1)	**PPV** Of adenomas per patient ≥6: 40.7% ≥7: 41.3% ≥8: 46.1% ≥9: 46.9% ≥10: 48.9% (Calculated) **NPV** Of adenomas per patient ≥6: 97.8% ≥7: 99.0% ≥8: 99.5% ≥9: 99.6% ≥10: 99.7% (Calculated)	Uses rigorous methods that are unlikely to be found in general practice (type of bowel prep, stool tagging, electronic fluid cleansing). Screening conducted at military medical centers. Large sample size that includes 41% women. Ethnic diversity unknown. Incomplete optical colonoscopy: 0.6% (8/1,253) Inadequate preparation: 0.5% (6/1,253) Failure of CT colographic system: 0.5% (6/1,253)	CTC shows 93.8% per-patient and 92.2% per-polyp sensitivity for adenomas ≥10 mm which is greater than those (87.5% and 88.2%) of colonoscopy.
Macari et al.,[33] 2000	New York City Patient recruitment: NR	OC with no unblinding during procedure to verify findings on CT that were not seen during colonoscopy. Same day CT colonography and optical colonoscopy. **Method 1**: 2D with 3D on abnormal areas. **Method 2**: 2D then 3D Two radiologists with training in CTC examined each data set with different methods. 2D and 3D; 5 mm collimation; 2.5 mm reconstruction interval; Single detector; No contrast; Advantage/Navigator	***n***: 42 **Mean age:** 56 yr **F:** 45% **Race/Ethnicity:** NR **SES:** NR **Asymptomatic**: 100% **Family history**: 29%	**Prevalence** Any polyp: 31% (13/42) **Yield** 1-5 mm: 10 6-9 mm: 5 >10 mm: 1	**Method 1: per-polyp** 38% **Method 2: per-polyp** 38% **For polyps ≥6 mm** 67% **For polyps ≥7 mm** 100%	**Method 1: per-polyp** 100% **Method 2: per-polyp** 96%	**PPV** **Method 1: per-polyp** 100% **Method 2: per-polyp** 86% **NPV** **Method 1: per-polyp** 73% **Method 2: per-polyp** 72%	Patient recruitment to University medical center unknown. Population included 45% women, but the ethnic distribution is unknown. Small sample size. 2 false positives in one patient were attributed to residual stool.	CTC with primary 2D or combined 2D and 3D methods shows 67% per-polyp sensitivity for polyps ≥6 mm and 100% for polyps ≥10 mm.

Key question: In average-risk groups aged 50 or more, is CT colonography more risky than colonoscopy?

Study	Setting/Study Design	Patient Characteristics	Procedure	Perforation	Radiation Dose	Other Adverse Effects
Benson et al.,[34] 2010	Prospective case-control, Single center	**OC group** ***n***: 1,700 **Mean age**: 58.8 yr **Average risk**: 100% **CTC group** ***n***: 1,307 **Mean age**: 56.7 yr **Average risk**: 100%	**Total colonoscopy:** 1,700 **Total CT colonography:** 1,307	**Total perforations:** CTC group: 0% OC group: 0%	NR	CTC group: 0% OC group: 0%
Graser et al.,[25] 2009	Prospective Cohort, Single center	***n***: 307 **Mean age**: 60.5 yr **Average risk**: 100% ***n***: 2531 **Mean age**: 58.3 yr	**Total colonoscopy:** 307 **Total CT colonography:** 307	**Total perforations:** CTC group: 0% OC group: 0%	**Mean radiation dose:** 4.5 mSv (range, 3.5-6.1 mSv) Supine: 3.2 mSv Prone: 1.3 mSv	0% for both CTC and OC CTC group: 0.04% (1/2,531), severe

Key question	In average-risk groups aged 50 or more, is CT colonography more risky than colonoscopy?					
Study	Setting/Study Design	Patient Characteristics	Procedure	Perforation	Radiation Dose	Other Adverse Effects
Johnson et al.,[26] 2008	Prospective Cohort, Multicenter (15) study	**Average risk**: 88.9% (2,249/2,531) **Personal or family history**: 11.1% (282/2,531)	**Total CT colonography:** 2,531 **Total colonoscopy:** 2,531	**Total perforations:** CTC group: 0% OC group: 0%	NR	nausea & vomiting OC group: 0.08% (2/2,531) Hematochezia in 1 *E. coli* bacteremia in 1
Kim et al.,[29] 2007	Prospective Cohort, Single center	**OC group** ***n***: 3,163 **Mean age**: 58.1 yr **Asymptomatic**: 98% **Family history**: 8.4% **CTC group** ***n***: 3,120 **Mean age**: 57.0 yr **Asymptomatic**: 97.8% **Family history**: 5.1%	**Total CT colonography:** 3,120	**Total perforations:** 0/3,120 (0%) No perforations from 246 (7.9%) follow-up therapeutic OC	NR	0 from 246 (7.9%) follow-up therapeutic OC
Pickhardt et al.,[35] 2006	Retrospective Cohort, International (5 countries), multicenter (16) study	**Mean age:** NR **Symptomatic**: 46.6%	**Total CT colonography:** 21,923 Screening (asx): 11,707 Diagnostic (sx): 10,216 **Total incomplete procedures**: NR	**Total perforations:** 2/21,923 (0.009%) Screening: 0/11,707 (0%) Diagnostic: 2/10,216 (0.02%)	NR	Exacerbated acute renal failure: 2/21,923 (0.009%) Chest pain (not MI): 1/21,923 (0.0045%)
Edwards et al.,[36] 2004	Prospective Cohort, Australia, Randomly selected population from voting database	**Age (range):** 50-54 and 65-69 **Symptomatic:** 0%	**Total CT colonography:** 340 **Total incomplete procedures:** NR	**Total perforations:** 0%	<5 mSv	**CTC-related (*n*=7):** Mild nausea (*n*=3), abdominal pain (*n*=2), flushing and sweating (*n*=2); **Preparation-related (*n*=4):** Syncope (*n*=3), presyncopal episode (*n*=1) from magnesium citrate/NaP
Sosna et al.,[37] 2006	Retrospective Cohort, Israel, Multicenter (11) study	**Mean age:** 59.9 yr **Symptomatic:** NR	**Total CT colonography:** 11,870 **Total incomplete procedures:** NR	**Total perforations:** 7/11,870 (0.06%) Screening: 1/11,870 (0.008%) Diagnostic: 6/11,870 (0.05%)	NR	NR
Pickhardt et al.,[32] 2003	Prospective Cohort, Multicenter (3) study	**Mean age:** 57.8 yr **Symptomatic:** 0%	**Total CT colonography:** 1,247 **Total incomplete procedures:** 6/1,253 (99.5%)	**Total perforations:** NR	NR	Reported no adverse effects

Key question	What is the incidence of the extracolonic findings in CT colonography?			
Study/Study design	Patient characteristics	Tube current	Description of extracolonic findings (as reported in study)	Work-up of extracolonic findings (with final disposition at end of study)
Veerappan et al.,[38] 2010, Retrospective Cohort	*n*: 2,277, Asymptomatic: >99%, Follow-up: NR	100 mAs	46% (1,037/2,277) participants with 520 extracolonic findings 34.6% (787/2,277): potentially important finding (C-RADS E4) 9.3% (211/2,277): probably unimportant finding (C-RADS E3) 1.7% (39/2,277): clinically unimportant finding (C-RADS E2)	8.7% (199/2,277; 167 patients with E3 lesions and 32 patients with E4 lesions) patients had additional diagnostic studies 19 surgeries were performed
Kimberly et al.,[39] 2009	*n*: 136, Asymptomatic: 90.4% Follow-up: up to 45 mo (med, 38mo)	180 mA/80 mA	98% (134/136) participants with 423 extracolonic findings 15.7% (25/136) participants had 25 ECFs of high importance 24.5% (35/136) participants had 53 ECFs of moderate importance 51.7% (74/136) participants had 345 ECFs of low importance	10.3% (14/136) patients had additional diagnostic studies
Flicker et al.,[40] 2008	*n*: 376 Follow-up: 18 mo for E3, 1.5mo for E4 lesions	80-10 0mAs	72.3% (272/376) participants with 520 extracolonic findings 3.3% (17/520): potentially important finding (C-RADS E4) 10.8% (56/520): probably unimportant finding (C-RADS E3) 86% (447/520): clinically unimportant finding (C-RADS E2)	2.7% (14/520) lesions had additional diagnostic studies
Johnson et al.,[26] 2008, Prospective Cohort	*n*: 2,531 88.9% average risk, Follow-up: NR	50 mAs	66% participants with any extracolonic finding	16% were deemed to require either additional evaluation or urgent care (27% chest, 18% GI tract, 45% GU system, 6% vascular system, 3% MSK system)
Pickhardt et al.,[41] 2008, Prospective Cohort	*n*: 2,195 Asymptomatic, Follow-up: up to 18 mo	Low dose	9.3% (204 of 2,195) at least "moderate" or "high" clinical significance	7.2% (157 of 2,195) recommended to have additional diagnostic evaluation 6.1% (133 of 2,195) had additional diagnostic evaluation 2.5% (55 of 2,195) with confirmed diagnosis of an unsuspected condition of at least "moderate" importance 1.0% (22 of 2,195) required surgical procedures as follow-up
Kim et al.,[29] 2007, Prospective Cohort	*n*: 3,120 98% asymptomatic Follow-up: NR	25-75 mAs	2.2% (70 of 3,120): potentially important finding (C-RADS E4) 8.5% (265 of 3,120): probably unimportant finding (C-RADS E3) 47.8% (1,490 of 3,120): clinically unimportant finding (C-RADS E2)	7.7% (241 of 3,120) recommended to have additional diagnostic evaluation 0.3% (8 of 3,120) persons with extracolonic malignancy (treatment NR)
Pickhardt et al.,[42] 2007, Prospective Cohort	N: 2014 Asymptomatic Follow-up: unclear duration	25-75 mAs	Only evaluated extracolonic GI tumors 0.5% (10 of 2,014) persons with focal extracolonic GI tumors	0.5% (10 of 2,014) had further diagnostic evaluation 0.3% (7 of 2,014) required surgical resection 0.05% (1 of 2,014) required endoscopic resection All GI tumors found to be benign
Chin et al.,[43] 2005, Prospective Cohort	*n*: 432 Asymptomatic Follow-up: 2 yr	79-96 mAs	27.3% (118 of 432) persons with any extracolonic findings 7.4% (32 of 432) persons with clinically relevant extracolonic findings	7.4% (32 of 432) required further diagnostic evaluation: 1.8% (8 of 432) cancer or aneurysms 5.5% (24 of 432) benign lesions 1.4% (6 of 432) ongoing follow-up at 2 y, none required treatment at 2 y
Gluecker et al.,[44] 2003, Prospective Cohort	*n*: 681 Asymptomatic Follow-up: at least 12 mo	40-70 mAs	69% (469/681) persons with any extracolonic finding 10% (71/681) persons with findings of "high" clinical importance 27% (183/681) persons with findings of "moderate" clinical importance	Total 94 follow-up diagnostic procedures 15 follow-up diagnostic procedures in 183 persons with "moderate" findings 1% (9 of 681) needed treatment
Pickhardt et al.,[32] 2003, Prospective Cohort	*n*: 1245 Asymptomatic Follow-up: NR	100 mAs	4.5% (56/1,245) persons with findings of "high" clinical importance >13% (169/1,245) persons with findings of "moderate" clinical importance	0.4% (5 of 1,245) extracolonic malignancy (treatment NR)
Ginnerup Pederson et al.,[45] 2003, Prospective Cohort	*n*: 75 Asymptomatic, Follow-up: 6 mo	70 mAs	65% (49/75) persons with any extracolonic finding 12% (9/75) persons with extracolonic findings warranting additional workup	11% (8 of 75) had further diagnostic evaluation 3% (2 of 75) had surgery due to findings or complications of workup
Hara et al.,[46] 2000, Prospective Cohort	*n*: 264 Asymptomatic but 162 undergoing surveillance Follow-up: 7-22 mo	70 mAs	41% (109 of 264) with any extracolonic findings 11% (30 of 264) persons with extracolonic findings of "high" clinical importance 17% (46 of 264) persons with extracolonic findings of "moderate" clinical importance	6.8% (18 of 264) had further diagnostic evaluation 1.9% (5 of 264) had surgery due to malignant or nonmalignant findings 1.5% (4 of 264) required ongoing follow-up

C-RADS, Colonography Reporting and Data System; GI, gastrointestinal; NR, not reported.

Key question	In average-risk groups aged 50 or more, can screening colonoscopy decrease colorectal cancer incidence and its related mortality?					
Study	Design	Sample size	Criteria	Definition/Intervention	Results	Conclusion
Rabeneck et al.,[47] 2010, Canada	Population-based cohort study from 4 sources	- study cohort 2,412,077 persons	- 50-90 yr - Exclusion Previous diagnosis of CRC Previous diagnosis of UC or CD	- 14 yr follow-up of a cohort exposed to different intensities of colonoscopy use	- Mean age 64 yr - 53.7% women - colonoscopy rates increased in all regions during 1993-2006. - 1% increase in complete colonoscopy rate, the hazard of death decreased by 3%	Increased colonoscopy use was associated with mortality reduction from CRC
Baxter et al.,[48] 2009, Canada	Population-based case-control study	10,292 case patients 51,460 controls		- Case 52 to 90 yr who received a CRC diagnosis -Control Five controls matched by age, sex, geographic location, and socioeconomic status *Screening could not be differentiated from diagnostic procedures.	- Colonoscopy 719 patients (7.0%) 5031 controls (9.8%) - Case pts were less likely to have undergone any attempted colonoscopy (adjusted conditional OR, 0.69 [CI, 0.63 to 0.74]; $p<0.001$) or complete colonoscopy (adjusted conditional OR, 0;63 [CI, 0.57 to 0.69], $p<0.001$) - Complete colonoscopy was strongly associated with fewer deaths from left-sided CRC (adjusted conditional OR, 0.33 [CI, 0.28 to 0.39]) but not from right-sided CRC (adjusted conditional OR, 0.99 [CI, 0.86 to 1.14]).	- In usual practice, colonoscopy is associated with **fewer deaths** from CRC. - This association is primarily limited to deaths from cancer developing in the **left side** of the colon.
Kahi et al.,[49] 2009, US	Cohort study	715 patients		- Comparison of the observed CRC rates with expected rates from the SEER data	- 715 patients (mean age, 61 6.5 yr; 59% male; 95% Caucasian) with 10,492 patient-yr of follow-up. -12 cases of CRC: 5 found at baseline and 7 found after a median follow-up period of 8 yr (range, 3-16 yr). - When the first 2 yr of follow-up were excluded, 7 incident cases of CRC (95% CI, 2-13) over 9,075 person-yr of follow-up. - a relative risk reduction in CRC incidence of 67% The expected number based on SEER data was 21. The incidence rate was 0.77 cases per 1000 person yr, and the standardized incidence ratio was 0.33 (95% CI, 0.10-0.62) - a relative reduction in CRC death: 65% 3 patients died from CRC (95% CI, 0-9) The expected number of deaths based on SEER data: 9. The mortality rate was 0.29 per 1,000 person-yr the standardized mortality ratio was 0.35 (95% CI, 0.0-1.06)	CRC incidence and mortality were reduced after screening colonoscopy.

Key question	In average-risk groups aged 50 or more, can screening colonoscopy decrease colorectal cancer incidence and its related mortality?					
Study	Design	Sample size	Criteria	Definition/Intervention	Results	Conclusion
Winawer et al.,[50] 1993, US	Cohort study	- 1,418 patients who had a complete colonoscopy which one or more adenomas of the colon or rectum were removed.		- periodic colonoscopy during an average follow-up of 5.9 yr - the incidence of colorectal cancer was compared with that in 3 reference groups (2 cohorts in which colonic polyps were not removed or one general population registry)	- 97% followed clinically for a total of 8401 person-yr - 80% returned for scheduled colonoscopies - 5 early stage CRC were detected.(No of CRC in 3 reference groups 48.3, 43.4, and 20.7) - Reduction in the incidence of CRC 90%, 88%, and 76%	Colonoscopic polypectomy resulted in a lower-than-expected incidence of CRC.

Key question	When the index colonoscopy for colorectal cancer screening and polyp detection is negative in an average-risk group aged 50 or more, is there any significant difference in colorectal cancer incidence between cases where a follow-up colonoscopy was performed five yr or longer afterwards and cases where a follow-up colonoscopy was performed within 5 yr?					
Study	Design	Sample size	Criteria	Definition	Results	Conclusion
Brenner et al.,[51] 2010, Germany	State wide cohort study/ tofill out standardized questionnaires, and examine CS finding	*n*=3,234 M/F=1,556/1,678 (35.5%)	<Inclusion criteria>: -residents of Saarland state - aged 55 or older <Exclusion criteria> :Recruited after screening CS Questionnaired returned after screening CS History of IBD Unknownif previous CS Unknown findings, detected polyps, unknown yr of last CS, last CS in the same yr in previous CS group	Advanced adenoma: at least 1 adenoma with at least 1 of the following features: _1 cm in size, tubulovillous or villous components, high-grade dysplasia)	-Findings in pt with no previous CS (*n*=2,701) CRC: 41 (1.5%) Advanced adenoma (AA) 267(9.9%) -Findings in pt with previous CS (*n*=533) 1+yr ago: CRC:0/ AA:25 (4.7) 1-5 yr : 0/ 5(4.4) 6-10 yr: 0/ 6(3.6) 11-15 yr: 0/ 5(4.3) 16+yr: 0/ 9(6.7) - Standardized prevalence ratio (95% CI) CRC: 0.00 (0-0.55) Advanced adenoma: 0.42 (0.25-0.68) -Adjusted prevalence ratios for detecting AA among pts with a negative colonoscopy(vs. no previous CS) : 0.38 (95% CI, 0.16-0.90) conducted 1-5 yr ago 0.34 (95% CI, 0.15-0.74) 6-10 yr ago 0.38 (95% CI, 0.16-0.90) 11-15 yr ago 0.53 (95% CI, 0.27-1.04) >16 yr ago,	The low risk of CRC and advanced adenomas after a negative colonoscopy supports suggestions that screening intervals be extended to >10 yr.

Key question	When the index colonoscopy for colorectal cancer screening and polyp detection is negative in an average-risk group aged 50 or more, is there any significant difference in colorectal cancer incidence between cases where a follow-up colonoscopy was performed five yr or longer afterwards and cases where a follow-up colonoscopy was performed within 5 yr?					
Study	Design	Sample size	Criteria	Definition	Results	Conclusion
Imperiale et al.,[52] 2008, USA	Cross sectional study Using data in cohort study of the Lilly Colorectal Cancer Prevention Program	1,256 (51.6% of initial negative CS 5 yr ago) were rescreened : mean interval (±SD)-5.34±1.34 yr	Inclusion criteria: - rescreened persons with initial negative colonoscopy 5 yr before. -initially participants in Eli Lilly colonoscopy screening program -50 yr of age or older, -asymptomatic,	Advanced adenoma : a tubular adenoma 1 cm or larger in diameter, a polyp with a villous component of at least 25%, or a polyp with high-grade dysplasia.	Mean age: 56.7 yr M:56.7% findings of CS at 5 yr - CRC: 0 One or more adenomas: 201(16.0%). Advanced adenomas: 19 in 16 person(1.3%) 10 adenoma (52.6%) in distal to the splenic flexure -Advanced adenoma in pt with no polyps at baseline :1.1% (12 of 1,057) with hyperplastic polyps :2.0% (4 of 199) (p=0.30) - Men with any adenoma: RR, 1.88; 95% CI (1.42-2.51) with advanced adenoma: RR, 3.31; 95% CI (1.02-10.8) (compared to women) - Number of persons with normal baseline screening CS who would need to be rescreened at 5 yr to detect one advanced adenoma M: 55 (32-102) Women: 182 (63-909)	-Among persons with no colorectal neoplasia on initial screening colonoscopy, the 5-yr risk of colorectal cancer is extremely low. -The risk of advanced adenoma is also low, although it is higher among men than among women. -support a rescreening interval of 5 yr or longer after a normal colonoscopic examination.
Lakoff et al.,[53] 2008, Canada	Prospective cohort study	110,402 individuals with a negative complete colonoscopy	Inclusion criteria: -Ontario residents aged 50 to 80 yr who had a negative colonoscopy (1992,1.1-1997.12.31) -no prior history of CRC,IBD, or recent colonic resection before the index colonoscopy. -Each individual was followed up through December 31.2005.		-1,461 CRC (1.3%) during 14 yr -RR of CRC overall/distal CRC was significantly lower than Ontario population. RR of distal CRC at 14 yr later: 0.21 (95% CI, 0.05-0.36). (vs. Ontario population) -RR of proximal CRC was significantly lower than the Ontario population mainly after 7 yr of follow-up. cf. The finding reported here that in the negative complete colonoscopy cohort the RR for proximal CRC was not decreased until after yr 7 is important. One possible explanation is that colonoscopy misses lesions in the proximal colon that can evolve into cancer in the first 8 yr of follow-up evaluation. cf. In the negative complete colonoscopy cohort, in yr 1 the percentage of an incident CRC was higher than in subsequent yr. The most likely explanation is that some patients in the negative complete colonoscopy cohort had a cancer that was missed.	Over a 14-yr follow-up period, negative complete colonoscopy was associated with a subsequent reduced incidence of CRC overall, and of incident CRC in the distal colon. However, the reduction in incidence of proximal CRC occurred, mainly after 7 yr of follow-up. (an important limitation of colonoscopy in usual clinical Practice).

Key question	When the index colonoscopy for colorectal cancer screening and polyp detection is negative in an average-risk group aged 50 or more, is there any significant difference in colorectal cancer incidence between cases where a follow-up colonoscopy was performed five yr or longer afterwards and cases where a follow-up colonoscopy was performed within 5 yr?					
Study	Design	Sample size	Criteria	Definition	Results	Conclusion
Leung et al.,[54] 2009,China	Prospective cohort study	511 pts. underwent repeat-screening colonoscopy at the endof 5 yr. (620 ptsunderwent baseline CS)	Inclusion criteria: -aged between 50 and 70 yr asymptomatic -no family history of colorectal cancer. -Participants who had completed a full baseline-screening colonoscopy Exclusion criteria: -previous colonoscopy or prior colonic surgery -pt who had severe co-morbidities -those who were older than 75 ys at f/u CS	Advanced neoplasia :presence of any one of the following features-adenomas larger than 10 mm in diameter, with villous histology, or with highgrade dysplasia or invasive carcinoma	-401 pts : no baseline neoplasia (370: no baseline polyps/31: hyperplastic polyps at baseline CS) on rescreeing in these pts -24.6 %: at least one adenoma 1.4 %: advanced neoplasia - number needed to rescreen for one advanced neoplasia in subjects with no baseline polyp : 74 pts (95 % CI, 32-168) - prevalence of advanced neoplasia at 5 yr in subjects with baseline-advanced neoplasia : 20.7 % (RR, 19.6; 95 % CI, 5.2-74.1; vs. subjects with no baseline polyp). - independent factors for development of advanced neoplasia at 5 yr : presence of baseline-advanced neoplasia (OR, 13.1; 95 % CI, 4.1-41.7) and age in yr (OR, 1.11; 95 % CI, 1.01-1.22).	The risk of advanced neoplasia is suffi cientl y low 5 yr after a normal screening colonoscopy in Chinese subjects.
Singh et al.,[55] 2010, USA	Prospective cohort study	A total of 45,985 individuals (18,606 men; 27,379 women)	-Inclusion criteria: All individuals 40 yr or older with negative CS from Manitoba's provincial physicians ' billing claims database. (1989.4.1-2006.6.30) -Exclusion criteria: Individuals with less than 5 yr of coverage by the provincial health plan, earlier CRC, IBD, resective colorectal		-followed up for 229,090 person-yr.(6 mo- >10 yr) -After a negative colonoscopy, In men: 40-50% risk reduction of CRC diagnosis In women: similar to that of women in the general population in the first 3 yr 40 -50% risk reduction after 3 yr -independent predictors for early/missed CRC (cancers occurring within 3 yr): Older subject age performance of index CS by non-	Women may have a higher rate of missed / early CRCs after negative colonoscopy. Predictors of missed / early CRCs after negative CS include older age and performance of index CS by a non-gastroenterologist.

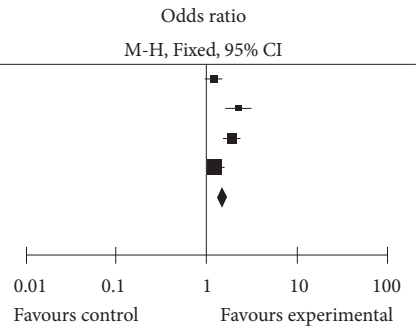
Key question	When the index colonoscopy for colorectal cancer screening and polyp detection is negative in an average-risk group aged 50 or more, is there any significant difference in colorectal cancer incidence between cases where a follow-up colonoscopy was performed five yr or longer afterwards and cases where a follow-up colonoscopy was performed within 5 yr?					
Study	Design	Sample size	Criteria	Definition	Results	Conclusion
			surgery, Follow-up of less than 6 months after the index colonoscopy		gastroenterologists (ex. Family practice HR, 3.01; 95% CI, 1.42-6.37)	
Singh et al,[56] 2006, USA	Restrospective cohort study	*n*=35,975 (1989.4.1-2003.12.31)	Exclusion criteria: Patients with a history of colorectal cancer prior to the index colonoscopy, IBD, resective colorectal surgery, and CS/SFS within the 5 yr before the index colonoscopy	Right-sided colon cancers:cancer in the cecum,ascending colon, and hepatic flexure. Left-sided cancers :cancer in the descending and sigmoid colon.	-Standardized incidence rates (SIRs) (vs. provincial population) : 0.69 (95% CI, 0.59-0.81) at 6 mo 0.66 (95% CI, 0.56-0.78) at 1 yr, 0.59 (95% CI, 0.48-0.72) at 2 yr, 0.55 (95% CI, 0.41-0.73) at 5 yr, 0.28 (95% CI, 0.09-0.65) at 10 yr. -The proportion of colorectal cancer located in the right colon was significantly higher in the colonoscopy cohort than the rate in the Manitoba population (47% vs. 28%; p<.001).	The risk of developing colorectal cancer remains decreased for more than 10 yr following the performance of a negative CS. There is a needto improve the early detection rate of right-sided colorectal neoplasia in usual clinical practice.
Bressler et al.,[57] 2007, Canada	Retrospective cohort study	12,487 pts after exclusion in study cohort -data from the Canadian Institute for Health Information, the Ontario Health Insurance Program, and Ontario Cancer Registry	Inclusion criteria: - >20 yr of age) with a new diagnosis of CRC (1997.4.1-2002.3.31) -who had a colonoscopy within the 3 yr before their diagnosis. Exclusion criteria: -IBD - <20 yr old -those who did not have a CS inserted to the site of the CRC within 3 yr - those who had a flexible SFS between the date of the last colonoscopy and the diagnosis	Patients with new or missed cancers : those whose most recent colonoscopy was 6 to 36 months before diagnosis.	-diagnosis of CRC : 3,288 (right sided) 777 (transverse) 710 (splenic flexure/descending) 7,712 (rectal or sigmoid) -The rates of new or missed cancers : 5.9% (right sided), 5.5% (transverse), 2.1% (splenic flexure/descending), 2.3% (rectal or sigmoid), - Independent risk factors (in men and women) : older age, OR, 1.04, (95% CI, 1.02-1.05) diverticular disease, OR, 6.88 (5.00-9.47) right-sided or transverse CRC, OR, 2.52 (1.84-3.45) colonoscopy by an internist or family physician : OR, 1.77 (1.14-2.74) colonoscopy in an office. OR, 3.07 (2.02-4.66)	Because having an office colonoscopy and certain patient, procedure, and physician characteristics are independent risk factors for new or missed CRC, physicians must inform patients of the small risk (2% to 6%) of these cancers after colonoscopy.

Key question	When the index colonoscopy for colorectal cancer screening and polyp detection is negative in an average-risk group aged 50 or more, is there any significant difference in colorectal cancer incidence between cases where a follow-up colonoscopy was performed five yr or longer afterwards and cases where a follow-up colonoscopy was performed within 5 yr?					
Study	Design	Sample size	Criteria	Definition	Results	Conclusion
Rex et al.,[58] 1996, USA	Observational study	154 pts with flu CS at a mean of 66 months after the initial negative CS (subset of initial screeing CS study in average risk persons)	Inclusion criteria: who had f/u CS after initial negative CS Exclusion criteria: person who refuse the study	Regular nonsteroidal anti-inflammatory drug (NSAID) use: defined as one or more aspirin or NSAID tablets at least four times per week for at least 2 yr.	-41 (27%): at least one adenoma, -only 1 person:an adenoma >1 cm. -cancer/severe dysplasia/villous or tubulovillous histology: all negative -Hyperplastic polyps at the initial examination did not predict incident adenomas. Absent at first exam : adenoma in 22% Present : in 28% -Regular NSAID was associated with a decreased rate of incident adenomas. Regular use: adenoma in 18%	In average-risk persons, the interval between screening examinations can be safely expanded beyond 5 yr, provided the initial examination is a carefully performed complete CS that is negative for colonic adenomas or cancer.
Matsuda et al.,[59] 2009, Japan	Multicenter Retrospective Cohort Study	5,309 pts	Inclusion criteria : over 40 yr who were referred for initial total colonoscopy Exclusion criteria: familial or personal history of FAP, HNPCC, IBD, a personal history of polypectomy or invasive CRC or a sessile adenoma with a base >30 mm		-initial negative CS: 2,006 pts -median follow-up period: 5.2 yr (3.0-12.3). - cumulative incidence of new lesion : 2.6% (lesion of rt colon: 46% of new lesion) - advanced ca.: 7/2006 (0.3%)	
Lieberman et al.,[60] 2007, USA	Case-control study (cohort study)	1,171 with neoplasia, 501 neoplasia-free controls	Inclusion criteria: -age 50 to 75 yr who had screening CS (1994-1997) -who did not have lower gastrointestinal tract symptoms, prior history of colon disease, or structural examination of the colon within 10 yr.	Advanced neoplasia was defined as tubular adenoma greater than >10 mm, adenoma with villous histology, adenoma with high-grade dysplasia, or invasive cancer.	-F/U colonoscopy within 5.5 yr : 895 (76.4%) with neoplasia 298 (59.5%) without neoplasia at baseline -7/298 (2.4%) without neoplasia had interval advanced neoplasia. 1/298 (0.3%) had cancer. -Risk of HD/cancer per 1000 person-yr f/u (95% CI) : 0.7 with no neoplasia -RR in baseline neoplasia : 1.92 (95% CI, 0.83-4.42) with 1- 2 TA <10 mm, 5.01 (95% CI, 2.10-11.96) with ≥3 TA <10 mm, 6.40 (95% CI, 2.74-14.94) with TA >10 mm, 6.05 (95% CI, 2.48-14.71) for VA 6.87 (95% CI, 2.61-18.07) for adenoma with HD	There is a strong association between results of baseline screening colonoscopy during 5.5 yr of surveillance. Patients with 1 or 2 tubular adenomas less than 10mm represent a low-risk group compared withother patients with colon neoplasia.

Study or subgroup	2 tests Events	2 tests Total	1 test Events	1 test Total	Weight	Odds ratio M-H, Fixed, 95% CI
Park 2010[15]	213	770	182	770	15.1%	1.24 (0.98, 1.55)
Rosen 2009[18]	227	330	175	330	6.3%	1.95 (1.42, 2.68)
Rosen 2010[20]	925	1,682	700	1,682	36.1%	1.71 (1.50, 1.96)
Grazzini 2009[21]	476	20,596	379	20,596	42.5%	1.26 (1.10, 1.45)
Total (95% CI)		23,378		23,378	100.0%	1.46 (1.34, 1.60)
Total events	1,841		1,436			

Heterogeneity: Chi^2=14.94, df=3 (p=0.002); I^2=80%

Test for overall effect: Z=8.74 (p<0.00001)

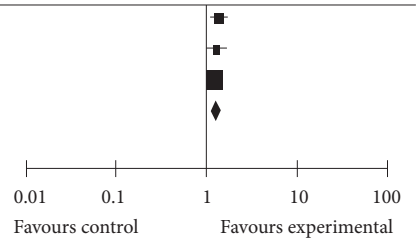


A 1 test vs. 2 tests

Study or subgroup	3 tests Events	3 tests Total	2 test Events	2 test Total	Weight	Odds ratio M-H, Fixed, 95% CI
Park 2010[15]	266	770	213	770	25.0%	1.38 (1.11, 1.71)
Rosen 2009[18]	248	330	227	330	10.1%	1.37 (0.98, 1.93)
Rosen 2010[20]	1,026	1,682	925	1,682	64.8%	1.28 (1.12, 1.47)
Total (95% CI)		2,782		2,782	100.0%	1.31 (1.18, 1.47)
Total events	1,540		1,365			

Heterogeneity: Chi^2=0.40, df=2 (p=0.82); I^2=0%

Test for overall effect: Z=4.88 (p<0.00001)



B 2 test vs. 3 tests

Supplementary Fig. 1. Detection rate of FIT for advanced colorectal neoplaisa according to the number of samples.

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