SINGAPORE HEALTH & BIOMEDICAL CONGRESS 2013

ADVANCING A SHARED VISION TOWARDS HEALTHCARE 2020

Synergising Paradigms for A Patient - Centred Healthcare System , Affordable and Accessible for All

27 & 28 September 2013 I Max Atria @ Singapore Expo

Colorectal Cancer Screening

Richard Sim

Dept of Surgery

Tan Tock Seng Hospital

Original WHO criteria for screening

- 1. The condition sought should be an important health problem.
- 2. There should be an accepted treatment for patients with recognized disease.
- 3. Facilities for diagnosis and treatment should be available.
- 4. There should be a recognizable latent or early symptomatic stage.
- 5. There should be a suitable test or examination.
- 6. The test should be acceptable to the population.
- 7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
- 8. There should be an agreed policy on whom to treat as patients.
- 9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
- 10. Case-finding should be a continuing process and not a "once and for all" project.

WHO criteria for screening: synthesis of screening criteria

- 1. The screening programme should respond to a recognized need.
- 2. The objectives of screening should be defined at the outset.
- 3. There should be a defined target population.
- 4. There should be scientific evidence of screening programme effectiveness.
- 5. The programme should integrate education, testing, clinical services, and programme management.
- 6. There should be quality assurance, with mechanisms to minimize potential risks of screening.
- 7. The programme should ensure informed choice, confidentiality, and respect for autonomy.
- 8. The programme should promote equity and access to screening for the entire target population.
- 9. Programme evaluation should be planned from the outset.
- 10. The overall benefits of screening should outweigh the harm

U.S. Preventive Services Task Force

Screening for Prostate Cancer

U.S. Preventive Services Task Force Recommendation Statement

Release Date: May 2012

The U.S. Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific clinical preventive services for patients without related signs or symptoms.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

Summary of Recommendation and Evidence

The U.S. Preventive Services Task Force (USPSTF) recommends against prostate-specific antigen (PSA)-based screening for prostate cancer (D recommendation).

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

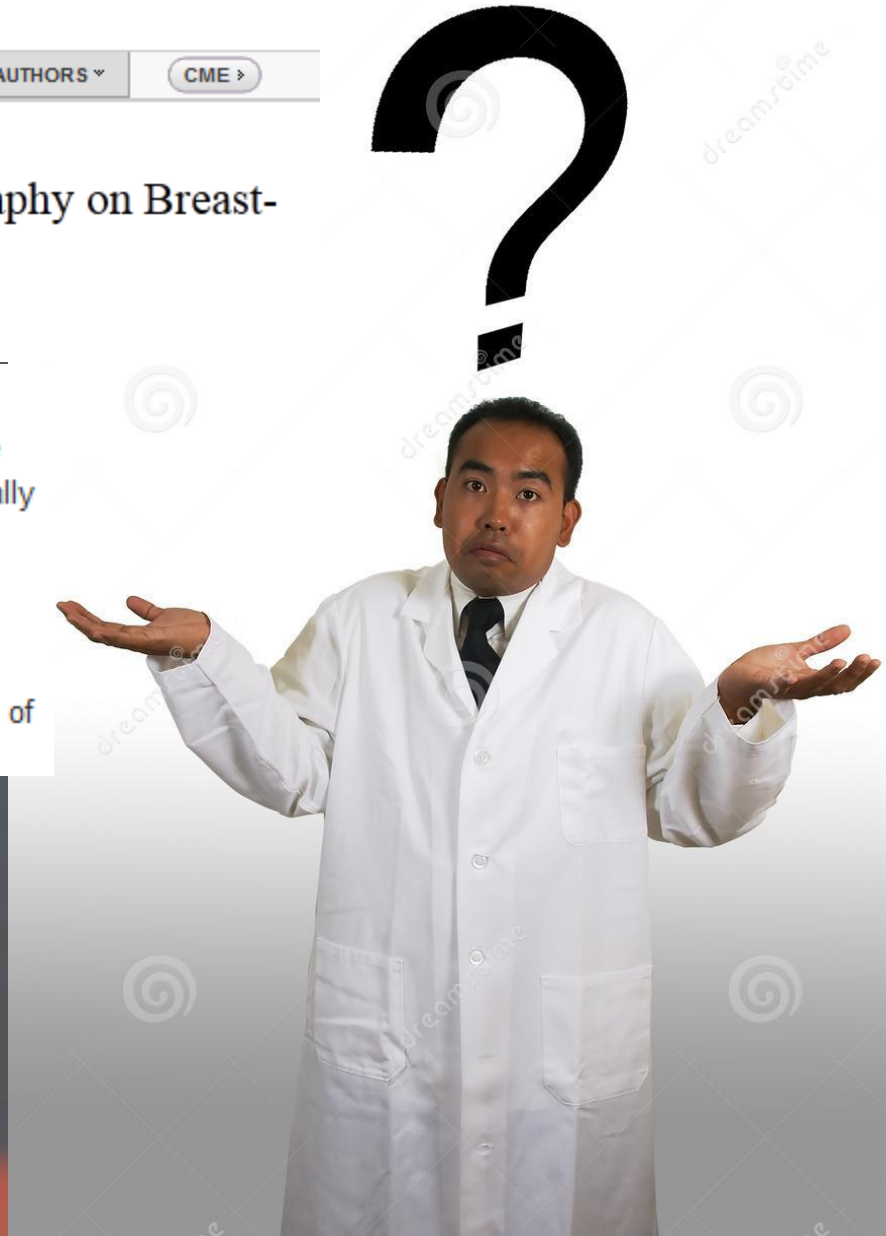
Effect of Three Decades of Screening Mammography on Breast-Cancer Incidence

Archie Bleyer, M.D., and H. Gilbert Welch, M.D., M.P.H.

N Engl J Med 2012; 367:1998-2005 | November 22, 2012 | DOI: 10.1056/NEJMoa1206809

CONCLUSIONS

Despite substantial increases in the number of cases of early-stage breast cancer detected, screening mammography has only marginally reduced the rate at which women present with advanced cancer. Although it is not certain which women have been affected, the imbalance suggests that there is substantial overdiagnosis, accounting for nearly a third of all newly diagnosed breast cancers, and that screening is having, at best, only a small effect on the rate of death from breast cancer.



Colonoscopy and sigmoidoscopy were associated with a reduced incidence of cancer of the distal colorectum; colonoscopy was also associated with a modest reduction in the incidence of proximal colon cancer. Screening colonoscopy and sigmoidoscopy were associated with reduced colorectal-cancer mortality; only colonoscopy was associated with reduced mortality from proximal colon cancer.

The NEW ENGLAND JOURNAL of MEDICINE

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

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

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

ABSTRACT

BACKGROUND

Colonoscopy and sigmoidoscopy provide protection against colorectal cancer, but the magnitude and duration of protection, particularly against cancer of the proximal colon, remain uncertain.

METHODS

We examined the association of the use of lower endoscopy (updated biennially from 1988 through 2008) with colorectal-cancer incidence (through June 2010) and colorectal-cancer mortality (through June 2012) among participants in the Nurses' Health Study and the Health Professionals Follow-up Study.

RESULTS

Among 88,902 participants followed over a period of 22 years, we documented 1815 incident colorectal cancers and 474 deaths from colorectal cancer. With endoscopy as compared with no endoscopy, multivariate hazard ratios for colorectal cancer were 0.57 (95% confidence interval [CI], 0.45 to 0.72) after polypectomy, 0.60 (95% CI, 0.53 to 0.68) after negative sigmoidoscopy, and 0.44 (95% CI, 0.38 to 0.52) after negative colonoscopy. Negative colonoscopy was associated with a reduced incidence of proxi-

From the Department of Medical Oncology, Dana–Farber Cancer Institute and Harvard Medical School (R.N., P.L., T.M., X.L., Z.R.Q., K.I., S.A.K., A.K., M.Y., Y.I., C.S.F., S.O.); the Departments of Nutrition (R.N., K.W., A.K., W.C.W., E.G.), Epidemiology (W.C.W., E.G., S.O.), and Biostatistics (B.A.R.), Harvard School of Public Health; the Channing Division of Network Medicine, Department of Medicine (K.W., W.C.W., B.A.R., C.S.F., E.G., A.T.C.), and Department of Pathology (S.O.), Brigham and Women's Hospital and Harvard Medical School; and the Division of Gastroenterology, Massachusetts General Hospital (A.T.C.) — all in Boston; the Gastrointestinal Research Group, Institute of Medical Sciences, University of Aberdeen, Aberdeen, United Kingdom (P.L.); the Department of Pathology, University of Tokyo Hospital,

The effect of screening with fecal occult-blood testing on colorectal-cancer mortality persists after 30 years but does not influence all-cause mortality. The sustained reduction in colorectal-cancer mortality supports the effect of polypectomy

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Long-Term Mortality after Screening for Colorectal Cancer

Aasma Shaukat, M.D., M.P.H., Steven J. Mongin, M.S., Mindy S. Geisser, M.S., Frank A. Lederle, M.D., John H. Bond, M.D., Jack S. Mandel, Ph.D., M.P.H., and Timothy R. Church, Ph.D.

From the Divisions of Gastroenterology (A.S., J.H.B.) and Internal Medicine (F.A.L.), Minneapolis Veterans Affairs Health Care System, and the Department of Medicine, School of Medicine (A.S., F.A.L., J.H.B.), and the Division of Environmental Health Sciences, School of Public Health (S.J.M., M.S.G., T.R.C.), University of Minnesota — both in Minneapolis; and Exponent, Menlo Park, CA (J.S.M.). Address reprint requests to Dr. Shaukat at 1 Veterans Dr., 111-D, Minneapolis, MN 55417.

N Engl J Med 2013;369:1106-14.
DOI: 10.1056/NEJMoa1300720

ABSTRACT

BACKGROUND

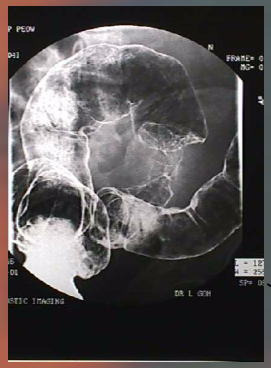
In randomized trials, fecal occult-blood testing reduces mortality from colorectal cancer. However, the duration of the benefit is unknown, as are the effects specific to age and sex.

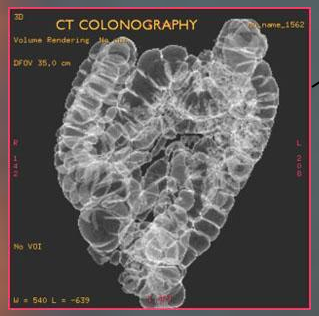
METHODS

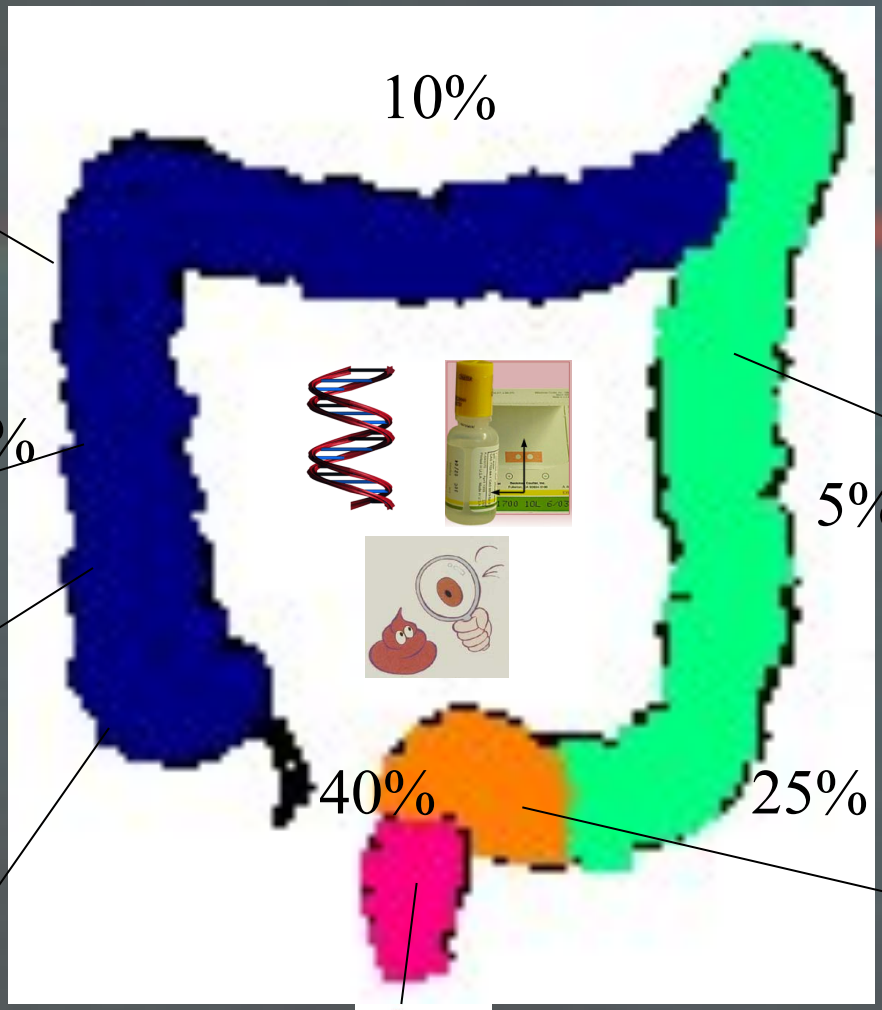
In the Minnesota Colon Cancer Control Study, 46,551 participants, 50 to 80 years of age, were randomly assigned to usual care (control) or to annual or biennial screening with fecal occult-blood testing. Screening was performed from 1976 through 1982 and from 1986 through 1992. We used the National Death Index to obtain updated information on the vital status of participants and to determine causes of death through 2008.

RESULTS

Through 30 years of follow-up, 33,020 participants (70.9%) died. A total of 732 deaths were attributed to colorectal cancer: 200 of the 11,072 deaths (1.8%) in the annual-screening group, 237 of the 11,004 deaths (2.2%) in the biennial-screening group,




CT COLONOGRAPHY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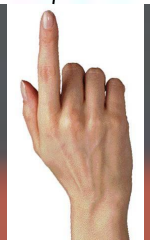


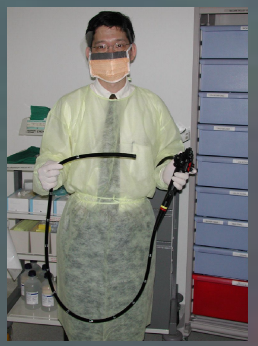


Table 1: Most commonly used screening and risk stratification systems

	USPSTF	ACG	ACS-MSTF
Beginning age	50	50 (45 for African Americans)	50
Continuing to age	75	n/a	n/a
Not for routine	76-85	n/a	n/a
Stopping age	>85	n/a	n/a
Recommended Methodologies	gFOBT or FIT, annually FSIG, every 5years or COL, every 10 years DCBE, every 5years	gFOBT or FIT, annually FSIG, every 5-10 years, or CTC every 5 years	FOBT annually or FIT annually or FSIG every 5 years or COL every 10 or years or DCBE every 5 years or CTC every 5 years or sDNA (interval uncertain)
Not recommended methodologies	sDNA CTC		

American Cancer Society recommendations for colorectal cancer early detection

People at average risk

The American Cancer Society believes that preventing colorectal cancer (and not just finding it early) should be a major reason for getting tested. Finding and removing polyps keeps some people from getting colorectal cancer. Tests that have the best chance of finding both polyps and cancer are preferred if these tests are available to you and you are willing to have them.

Beginning at age 50, both men and women at *average risk* for developing colorectal cancer should use one of the screening tests below:

Tests that find polyps and cancer

- Flexible sigmoidoscopy every 5 years*
- Colonoscopy every 10 years
- Double-contrast barium enema every 5 years*
- CT colonography (virtual colonoscopy) every 5 years*

Tests that mainly find cancer

- Fecal occult blood test (FOBT) every year*,**
- Fecal immunochemical test (FIT) every year*,**

U.S. Preventive Services Task Force

Screening for Colorectal Cancer

Release Date: October 2008

This topic page summarizes the U.S. Preventive Services Task Force (USPSTF) recommendations on screening for colorectal cancer.

Summary of Recommendations / Supporting Documents

Summary of Recommendations

- The USPSTF recommends screening for colorectal cancer (CRC) using fecal occult blood testing, sigmoidoscopy, or colonoscopy, in adults, beginning at age 50 years and continuing until age 75 years. The risks and benefits of these screening methods vary.
  Grade: A Recommendation.
- The USPSTF recommends against routine screening for colorectal cancer in adults age 76 to 85 years. There may be considerations that support colorectal cancer screening in an individual patient.
  Grade: C Recommendation.
- The USPSTF recommends against screening for colorectal cancer in adults older than age 85 years.
  Grade: D Recommendation.
- The USPSTF concludes that the evidence is insufficient to assess the benefits and harms of computed tomographic colonography and fecal DNA testing as screening modalities for colorectal cancer.
  Grade: I Statement.

Original Article

Singapore Med J 2013; 54(4): 220-223
doi: 10.11622/smedj.2013077

Opportunistic screening for colorectal neoplasia in Singapore using faecal immunochemical occult blood test

Wah Siew Tan[1], MBBS, FRCS, *Choong Leong Tang*[1,3], MBBS, FRCS, *Wen Hsin Koo*[2,3], MBBS, MRCP

INTRODUCTION The use of faecal immunochemical occult blood test (FIT) has been reported to decrease mortality from colorectal cancer. The Singapore Cancer Society (SCS) gives out FIT kits to encourage opportunistic screening of colorectal cancer. Any Singapore citizen or permanent resident aged ≥ 50 years is eligible to receive two FIT kits. Participants with at least one positive FIT are referred for further evaluation. We aimed to analyse the results of SCS data from the year 2008.

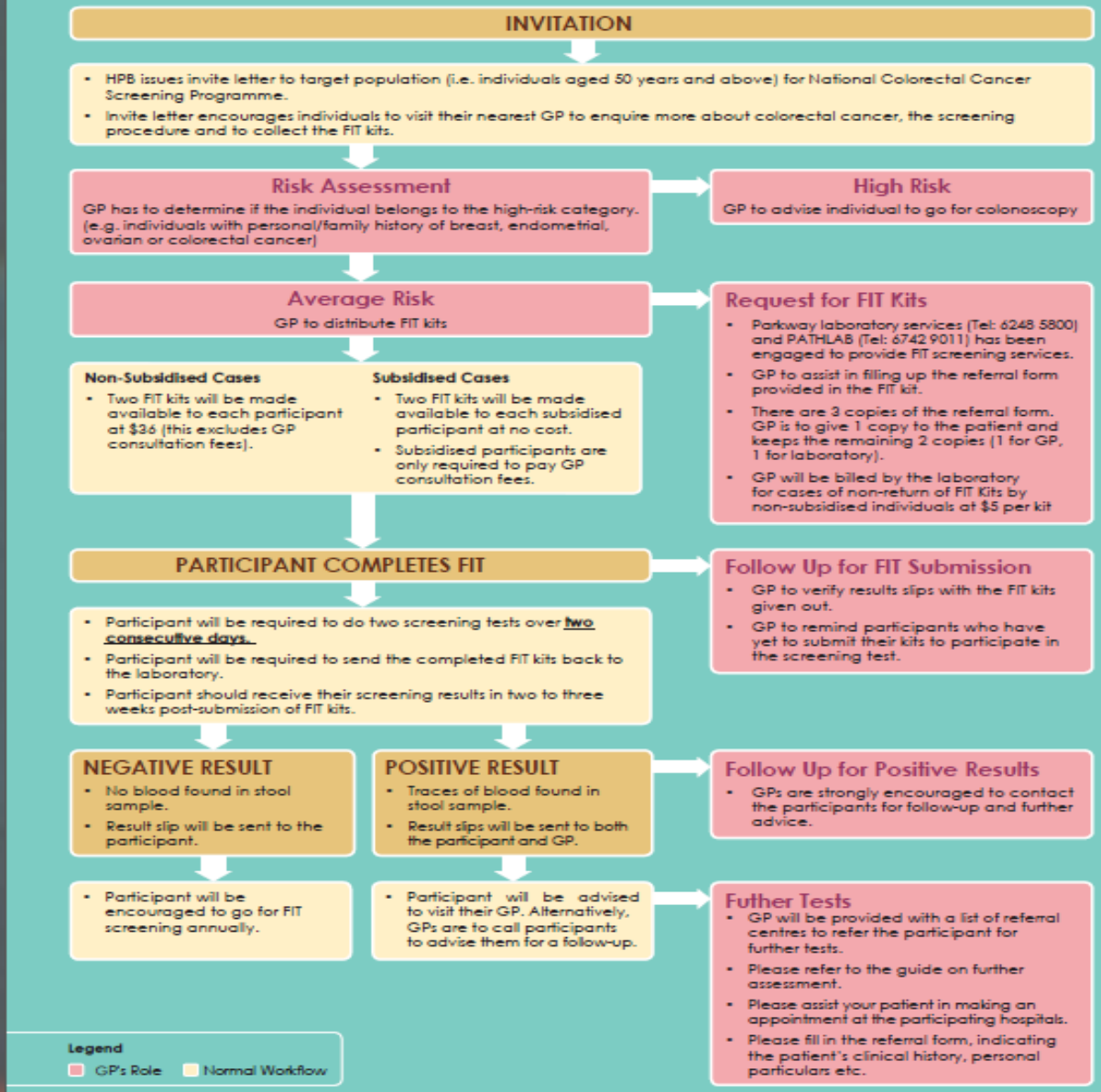
METHODS The factors evaluated included compliance, positive test rate (PR) and positive predictive value (PPV) of FIT.

RESULTS 20,989 participants received 41,978 kits in 2008. Compliance was 38.9%, with 8,156 participants returning at least one kit. 8% of participants tested positive, and 75% of these test-positive participants agreed to undergo further investigations. 33 participants had colorectal cancers, 45 had advanced polyps (≥ 1 cm) and 90 had polyps < 1 cm. Histologically, 114 polyps were adenomatous, 20 were hyperplastic and 1 was serrated. PPV of colorectal neoplasia for those who underwent further colonoscopy was 34%. Over half of the participants who had only one positive test had colorectal neoplasia.

CONCLUSION PR and PPV of FIT in our study were comparable to that in the literature. However, compliance was low and a quarter of all participants who tested positive refused further investigations. Extensive population education programmes are required to improve compliance and tackle inhibitions among the masses. It is also important to take steps to enhance the cost effectiveness of future screening programmes.

Keywords: colorectal cancer, faecal occult blood test, screening

FIT Screening Flow Chart



* To obtain the referral forms, please contact Ms Noriha at 6435 3223 or email HPB_IntegratedScreening@hpb.gov.sg. A 3-days lead time is required for the order to be processed.

Colorectal Cancer Screening (PDQ®)

Updated: 07/25/2013

Table 1. Effect of Screening Intervention on Reducing Mortality from Colorectal Cancer[a]

	Fecal Occult Blood Test	Sigmoidoscopy	Digital Rectal Exam	Colonoscopy
Study Design	RCTs	Case-control studies [1], RCTs in progress	Case-control studies	Case-control studies, RCTs in progress
Internal Validity	Good	Fair	Fair	Poor
Consistency	Good	Fair	Good	Poor
Magnitude of Effects	15%–33%	About 60%–70% for left colon	No effect	About 60%–70% for left colon; uncertain for right colon
External Validity	Fair	Fair	Poor	Fair

RCT = randomized controlled trial.

[a] *There are no data on the effect of other screening interventions (i.e., fecal occult blood test combined with sigmoidoscopy, barium enema, colonoscopy, computed tomographic colonography, and stool DNA mutation tests) on mortality from colorectal cancer.*

References

1. Thiis-Evensen E, Hoff GS, Sauar J, et al.: Population-based surveillance by colonoscopy: effect on the incidence of colorectal cancer. Telemark Polyp Study I. Scand J Gastroenterol 34 (4): 414-20, 1999. [PUBMED Abstract]

Right side versus Left side difference

- Exams were incomplete and did not reach the cecum
- Poor prep or incomplete mucosal inspection, lesions missed
- Some right-sided lesions simply grow rapidly

Table 2. Effect of Screening Intervention on Surrogate Endpoints (e.g., Stage at Diagnosis and Adenoma Detection)

	Sigmoidoscopy [2,3]	FOBT/ Sigmoidoscopy [4,5]	Barium Enema [6]	Colonoscopy [7,8]	CT Colonography [9-11]	Stool DNA Mutation Tests [12]	Immunochemical FOBT
Study Design	Case-control studies	Randomized controlled studies	Ecologic and descriptive studies	Ecologic and descriptive studies	Ecologic and descriptive studies	Studies in progress	Cross-sectional study in which iFOBT is administered to persons receiving colonoscopy
Internal Validity	Poor	Fair	Fair	Fair	Fair	Unknown	Good
Consistency	Fair	Poor	Poor	Poor	Poor	Unknown	Good
Magnitude of Effects on Surrogate Endpoints	About 45% decrease in detection rate of cancers compared with colonoscopy	No difference in diagnostic yield between sigmoidoscopy + FOBT vs. sigmoidoscopy alone	Barium enema detects about 30%–50% of cancers detected by colonoscopy	About 3% of patients with no distal adenomas have advanced proximal neoplasia. There is a threefold increase in this rate in patients with distal adenomas.	CT colonography may have similar sensitivity to colonoscopy in certain centers	Unknown	iFOBT detects >60% and ≤90% of CRCs
External Validity	Poor	N/A	N/A	N/A	Poor	Unknown	N/A

CRC = colorectal cancer; CT = computed tomography; FOBT = fecal occult blood test; iFOBT = immunochemical fecal occult blood test; N/A = not available.

Table 5: Advantages and limitations of current screening methods

Methods	Efficiency	Insufficiency or drawbacks	Reference
FOBT or FIT	Easiest, least expensive method for screening Reduces cancer mortality 15% to 33% Specificity ranging from 88% to 98%	Detects only 30–40% of CRC Detects 10% of late stage adenomas	18-24
sDNA	Sensitivity ranging from 52% to 91% Specificity ranging from 93% to 97%	Detects only late stage lesions	25-29
FSIG	Directly inspects the mucosal surface Ability to resect identified abnormalities Reduces CRC mortality	Fails to detect polyps in the proximal colon, where 40% of all cancers occur, Fails to detect 10–15% sigmoid colon cancers	30-40
COL	Directly inspects the mucosal surface Ability to resect identified abnormalities Reduces CRC mortality Ability to perform interventions for other diseases Current gold standard for detection and treatment	Invasive and time consuming Requires bowel preparation Costly Carries risk of perforation or death May miss up to 10–20% of polyps < 1 cm	41-53
DCBE	Sensitivity for detecting polyps and cancer are about 70% and 85%, respectively Less invasive procedure	Doesn't permit removal of identified abnormalities Less specific screening test	54-56
CTC	Sensitivity for detecting adenomas ≥5 mm ranging from 65-72% Sensitivity for detecting larger adenomas ranging from 80-85% Less invasive than COL	Delivers a significantly higher amount of radiation exposure (2-4 rad) than routine chest radiograph (0.5 rad)	57-62

Table 6: Comparison of the estimated costs of USPSTF recommended screening methods

N0	Screening method	Frequency	Cost/screening ($)	10-year cost ($)
1	FOBT or FIT	Annually	5-10	50-100
2	FSIG	Every 5-years	70-600	140-1,200
3	DCBE	Every 5-years	600-1000	1,200-2,000
4	COL	Every 10-years	250-5000	250-5,000

Table 3. Discounted Life-years Gained, Costs, and Costs per Life-year Gained of Established Screening Strategies for Colorectal Cancer Compared With no Screening. Source: Iris Lansdorp-Vogelaar, Amy B. Knudsen and Hermann Brenner. Cost-effectiveness of Colorectal Cancer Screening. Epidemiol Rev (2011) 33 (1): 88-100.

Study: First Author, Year (Reference No.)[a]	Annual gFOBT			Biennial gFOBT			Flexible Sigmoidoscopy Every 5 Years			Flexible Sigmoidoscopy Every 5 Years + Annual gFOBT			Colonoscopy Every 10 Years		
	LYG	Cost	Cost/ LYG	LYG	Cost	Cost/LYG	LYG	Cost	Cost/LYG	LYG	Cost	Cost/LYG	LYG	Cost	Cost/ LYG
Flanagan, 2003 (34)	0.025	328	13,100	0.016	185	11,600									
Frazier, 2000 (35)	0.042	825	19,600				0.039	751	19,500	0.059	1,523	26,000	0.048	1,514	31,700
Gyrd-Hansen, 1998 (28)	0.006	36	6,400	0.004	20	5,300									
Hassan, 2007 (44)													0.036	−10	CS
Helm, 2000 (36)				0.014	72	4,000									
Khandker, 2000 (37)	0.100	2,519	25,600				0.090	1,904	22,500	0.110	3,553	32,400	0.110	3,487	31,500
Lejeune, 2004 (38)				0.029	126	4,400									
Leshno, 2003 (39)	0.160	−158	CS							0.182	−324	CS	0.180	−26	CS
Macafee, 2008 (45)				0.009	30	3,400									
O'Leary, 2004 (40)													0.021	2,883	9,800
Pickhardt, 2007 (19)													0.046	495	10,700
Shimbo, 1994 (32)	0.013	750	56,300												
Song, 2004 (20)	0.056	508	9,100				0.048	940	19,600	0.063	1,347	21,500	0.062	1,330	21,500
Sonnenberg, 2000 (41)	0.019	285	15,100				0.036	2,059	56,600				0.080	1,355	17,000
Steele, 2004 (42)	0.008	94	11,700				0.012	132	11,400				0.019	515	26,800

PillCam COLON 2

Given Imaging Announces New Data Highlighting PillCam(R) COLON Comparability to Colonoscopy in Detecting Adenomas

Published: Tuesday, 21 May 2013 | 8:50 AM ET

Text Size

- Secondary Analysis by Dr. Rex of sub-set of PillCam COLON trial data shows sensitivity for detecting adenomas that are at least 6 mm and 10 mm to be 88% and 92% respectively and specificity to be 82% and 95% respectively -

- Additional study also validates using PillCam COLON as a useful tool for GI physicians for patients with incomplete colonoscopies -

ORLANDO, Fla., May 21, 2013 (GLOBE NEWSWIRE) -- Given Imaging Ltd, (Nasdaq:GIVN), a world leader in GI medical devices and pioneer of capsule endoscopy, today announced a secondary analysis of data from its prospective, multicenter clinical trial to assess the accuracy and safety of PillCam COLON for detecting lesions at least 6 mm in size.

Enhanced accuracy of biomarker-based tests used for CRC screening

- FIT with antibodies to colon cancer associated transcript-1 (CCAT-1)
- Colon mucosal antigens, mAb 31.1 and NPC-1
- Stool cell-based biomarkers (secreted clusterin isoform, intestinal alkaline sphingomyelinase, stool DNA, and microRNAs)
- Blood and stool-based mutation and MSI tests, serum markers, various biomarkers, and stem cell-related markers
- Application of normal colonic cell replenishment-related unique molecules

Stool DNA – methylated NDRG4, BMP3, FIT, B-actin, Kras

TOP-LINE DATA SHOW EXACT SCIENCES' COLOGUARD TEST DEMONSTRATES 92 PERCENT SENSITIVITY IN THE DETECTION OF COLORECTAL CANCER

All endpoints achieved in 10,000-patient trial of non-invasive, convenient DNA-based screening test for colorectal cancer and pre-cancerous polyps

MADISON, Wis., April 18, 2013 – Exact Sciences Corp. (Nasdaq: EXAS) today announced that preliminary analysis shows that the company's Cologuard colorectal cancer screening test met or exceeded all primary and secondary endpoints of its recently completed DeeP-C pivotal clinical trial. The clinical trial evaluated the test's use for the detection of colorectal cancer and pre-cancerous polyps.

Preliminary, top-line data show that Cologuard demonstrated 92 percent sensitivity for the detection of colorectal cancer and 42 percent sensitivity for the detection of pre-cancerous polyps, including 66 percent sensitivity for polyps equal to or greater than 2 centimeters. The test achieved a specificity of 87 percent during the trial.

Septin 9 methylated DNA

Epigenomics Provides Additional Data on the Outcome of its Head-to-Head Comparison Study of Epi proColon® to FIT

Berlin, Germany, and Seattle, WA, U.S.A., December 19, 2012 - Epigenomics AG (Frankfurt Prime Standard: ECX), the German-American cancer molecular diagnostics company, today provided detailed results from a head-to-head comparative study between its blood-based colorectal cancer (CRC) detection test Epi proColon® and fecal immunochemical testing (FIT) for which it recently reported top-line results. This trial was designed to evaluate non-inferiority of the blood based Epi proColon® assay performance in comparison to FIT.

The subjects included in the first arm of the study were average risk, asymptomatic screening patients with no history (own or familial) of CRC. These patients were identified as CRC patients in the context of screening colonoscopies performed from April-November 2012 across 70 sites in the US.

As previously reported, in this study, Epi proColon® was able to detect 73 out of 103 cancer cases, demonstrating an overall sensitivity of 71%. Clinical staging information of the disease was available for 71 of the 103 cases.

Further analysis of the data shows that Epi proColon® was able to demonstrate 61% sensitivity for 23 cases in stages 0 and 1 (FIT 61% sensitivity), 75% for 16 cases in stage 2 (FIT 75% sensitivity), 70% for 20 cases in stage 3 (FIT 85% sensitivity) and 92% in 12 stage 4 cases (FIT 64% sensitivity). In the 32 cases of unknown clinical staging, the sensitivity was 69% (57% sensitivity for FIT).

2nd Generation Septin9 Test – Epi proColon® 2.0 CE

» BETTER

Unmatched performance in non-invasive detection of colorectal cancer

» SIMPLER

Unmatched convenience for the patient

Clinical Performance Evaluation

New test configuration with three Septin9 PCRs performed on each patient sample allows for accurate colorectal cancer (CRC) detection.

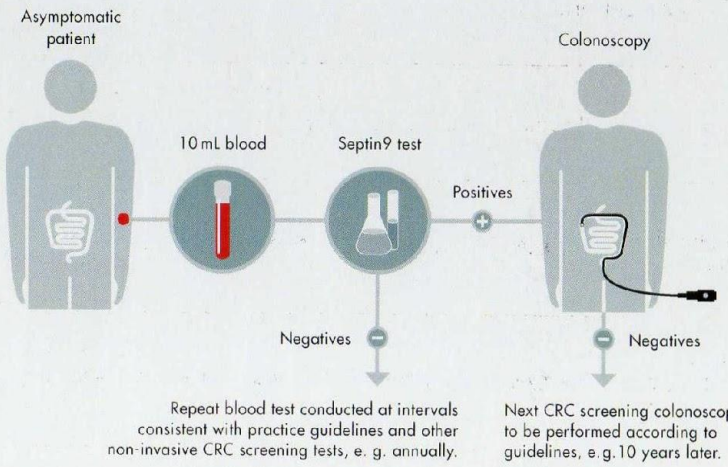
Method	Specificity	Sensitivity	Negative Predictive Value	Positive Predictive Value[4]
Epi proColon® 2.0 CE[1]	99.3%	80.6%	99.9%	45.7%
Guaiac Fecal-Occult Blood Test[2]	97.7%	37.1%	99.6%	10.1%
OC-Sensa Micro qFIT1x[3]	93.7%	69.2%	99.8%	7.5%

1) Tetzner et al. UEGW 2011 (case control); 2) Allison et al. 1996 NEJM (prospective); 3) Park et al. 2010 AmJGastro (prospective); 4) CRC with positive test result, healthy with positive test result assuming a prevalence of 0.7%; 5) Molnár et al. DDW 2012

» NO DETECTION BIAS

Similar detection rate in left and right colon

	Left Colon	Right Colon
Septin9 assay (high sens. algorithm)[5]	96.4% (54/56)	94.4% (34/36)
Guaiac Fecal-Occult Blood Test[5]	83.4% (10/12)	50.0% (5/10)



» Epi proColon® 2.0 CE detects cell-free methylated Septin9 DNA in blood plasma. The presence of methylated Septin9 DNA in plasma is associated with colorectal neoplasia.

Ann Surg. 2013 Sep;258(3):400-8. doi: 10.1097/SLA.0b013e3182a15bcc.

A Plasma MicroRNA Panel for Detection of Colorectal Adenomas: A Step Toward More Precise Screening for Colorectal Cancer.

Kanaan Z, Roberts H, Eichenberger MR, Billeter A, Ocheretner G, Pan J, Rai SN, Jorden J, Williford A, Galandiuk S.

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Abstract

OBJECTIVE: The main objective of this study was to investigate the potential use of circulating microRNAs (miRNAs) as biomarkers of colorectal (CR) adenomas.

BACKGROUND: Detection of precancerous lesions such as CR adenoma is a key to reduce CR cancer (CRC) mortality. There is a great need for accurate, noninvasive biomarkers for detection of CR adenoma and CRC. MiRNAs are non-protein-coding RNAs that regulate gene expression. Our prior work investigated the dysregulation of 5 plasma miRNAs in CRC patients. As intended, we undertook a more comprehensive plasma-miRNA screening study in patients with CR adenoma and CRC.

METHODS: We screened for 380 plasma-miRNAs using microfluidic array technology (Applied BioSystems) in a screening cohort of 12 healthy controls, 9 patients with CR adenomas, and 20 patients with CRC. A panel of the most dysregulated miRNAs ($P < 0.05$, False Discovery Rate: 5%) was then validated in a blinded cohort of 26 healthy controls, 16 patients with large adenomas, and 45 patients with CRC.

RESULTS: A panel of 8 plasma miRNAs (miR-532-3p, miR-331, miR-195, miR-17, miR-142-3p, miR-15b, miR-532, and miR-652) distinguished polyps from controls with high accuracy [area under curve (AUC) = 0.868 (95% confidence interval [CI]: 0.76-0.98)]. In addition, a panel of 3 plasma miRNAs (miR-431, miR-15b, and miR-139-3p) distinguished Stage IV CRC from controls with an [AUC = 0.896 (95% CI: 0.78-1.0)]. Receiver-operating-characteristic curves of miRNA panels for all CRC versus controls and polyps versus all CRC showed AUC values of 0.829 (95% CI: 0.73-0.93) and 0.856 (95% CI: 0.75-0.97), respectively.

CONCLUSIONS: Plasma miRNAs are reliable, noninvasive, and inexpensive markers for CR adenomas. This miRNA panel warrants study in larger cohorts. Plasma-based assays could provide better screening compliance compared to fecal occult blood or endoscopic screening.

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Table 8: Barriers and obstacles to compliance with recommended screening

#	Barriers and obstacles
1	**Physician-related**
	A. Inconsistent and frequently changing guidelines and recommendations among societies
	B. Failure to avoid common errors
	C. Patients are screened for colorectal cancer (CRC) with only a digital rectal exam.
	D. Patients are screened for CRC in the office with a single sample from a stool blood test.
	E. Patients with a history of adenomatous polyps in a first-degree relative are not Identified as people at increased risk.
	F. Providers have cultural assumptions that inhibit frank discussion, which could lead to a clear recommendation for screening.
	G. Patients with a positive FOBT, FIT, stool DNA, CT colonography, double-contrast barium enema, or flexible sigmoidoscopy never receive an order for a complete diagnostic exam.
	H. There is no follow up on patients referred for a complete diagnostic exam.
	I. Practitioners recommend screening with colonoscopy for those at average risk more often than every 10 years or CT colonography, double-contrast barium enema, or flexible sigmoidoscopy more often than every five years.
	J. Screening is started earlier than age 50 for average-risk
	K. Non adherence to ACS recommendation regarding essential elements for improved screening.
	L. Confusion about priorities and goals
	M. Lack of confidence in the efficacy and acceptability of screening tests
2	**Patient-related**
	A. Incorrectly low analysis of personal risk
	B. Fear of finding cancer
3	**System- or test-related**
	A. Inconvenience/invasiveness of some tests
	B. Insurance/reimbursement related issues
	C. Inadequate resources

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Review

Evidence-Based Guidelines for Precision Risk Stratification-Based Screening (PRSBS) for Colorectal Cancer: Lessons Learned from the US Armed Forces: Consensus and Future Directions

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Towards automated visual flexible endoscope navigation

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Abstract
Background The design of flexible endoscopes has not changed significantly in the past 50 years. A trend is observed towards a wider application of flexible endoscopes with an increasing role in complex intraluminal therapeutic procedures. The nonintuitive and nonergonomical steering mechanism now forms a barrier in the extension of flexible endoscope applications. Automating the navigation of endoscopes could be a solution for this problem. This paper summarizes the current state of the art in image-based navigation algorithms. The objectives are to find the most promising navigation system(s) to date and to indicate fields for further research.
Methods A systematic literature search was performed using three general search terms in two medical–technological literature databases. Papers were included according to the inclusion criteria. A total of 135 papers were analyzed. Ultimately, 26 were included.
Results Navigation often is based on visual information, which means steering the endoscope using the images that the endoscope produces. Two main techniques are described: lumen centralization and visual odometry. Although the research results are promising, no successful, commercially available automated flexible endoscopy system exists to date.
Conclusions Automated systems that employ conventional flexible endoscopes show the most promising prospects in terms of cost and applicability. To produce such a system, the research focus should lie on finding low-cost mechatronics and technologically robust steering algorithms. Additional functionality and increased efficiency can be obtained through software development. The first priority is to find real-time, robust steering algorithms. These algorithms need to handle bubbles, motion blur, and other image artifacts without disrupting the steering process.

Keywords Flexible endoscopy · NOTES · Computer vision · Image-based steering

Flexible endoscopes are used in a variety of clinical applications, both for diagnosis and therapy. Not much has changed in flexible endoscopy design for the past 50 years, apart from miniaturization of the cameras [1]. Flexible endoscopes come in various lengths and thicknesses, making them suitable for examining almost any hollow, tube-like structure in the human body [2]. Examples include the bowel, stomach, gall ducts, lungs, and even the salivary glands [3] and brain [4]. The most commonly performed procedures are oesophagogastroduodenoscopy (gastroscopy) and colonoscopy [2]. Generally, a flexible endoscope consists of a long, flexible tube with a light source and a lens on the tip (Fig. 1). A lens, CMOS, or CCD chip and video processor are used to convert the image to an electrical signal. The chip is mostly localized directly at the tip.

The endoscope is inserted in the organ of choice, mostly through a natural orifice. The steering mechanism is

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Conclusions

- Determine safest, most efficacious, effective and efficient algorithm
- Identify patients who need not be screened based on risk stratification by novel, cost-effective, accurate, less frequent, and readily accessible methods
- Utilize alternative strategies such as novel screening methods, biomarkers and risk stratification approaches in order to reduce costs and improve overall outcomes
- Increase education and compliance
- Improve current gold standard colonoscopy

Better Colonoscopy