


Best of DDW 2010

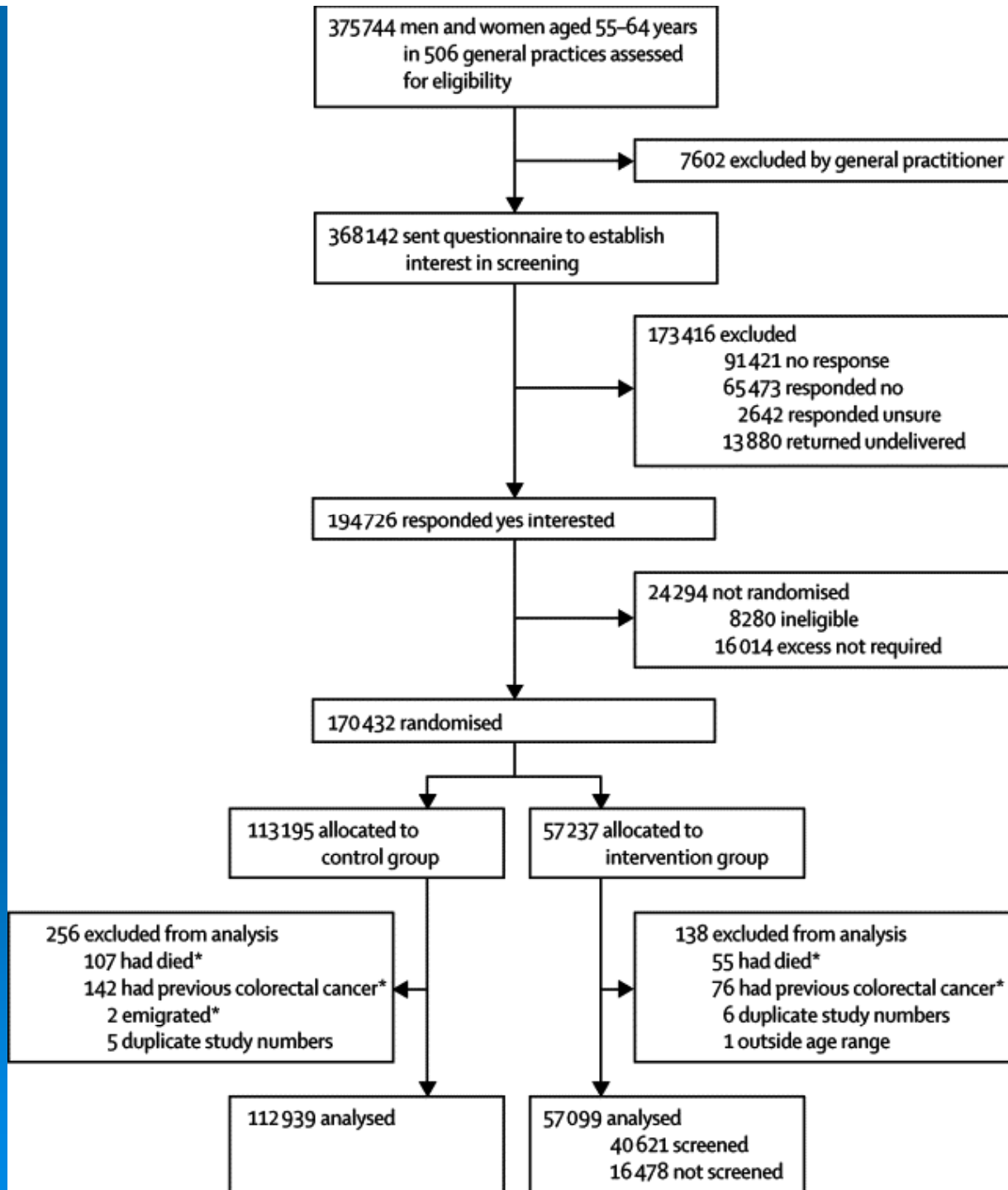
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Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial

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

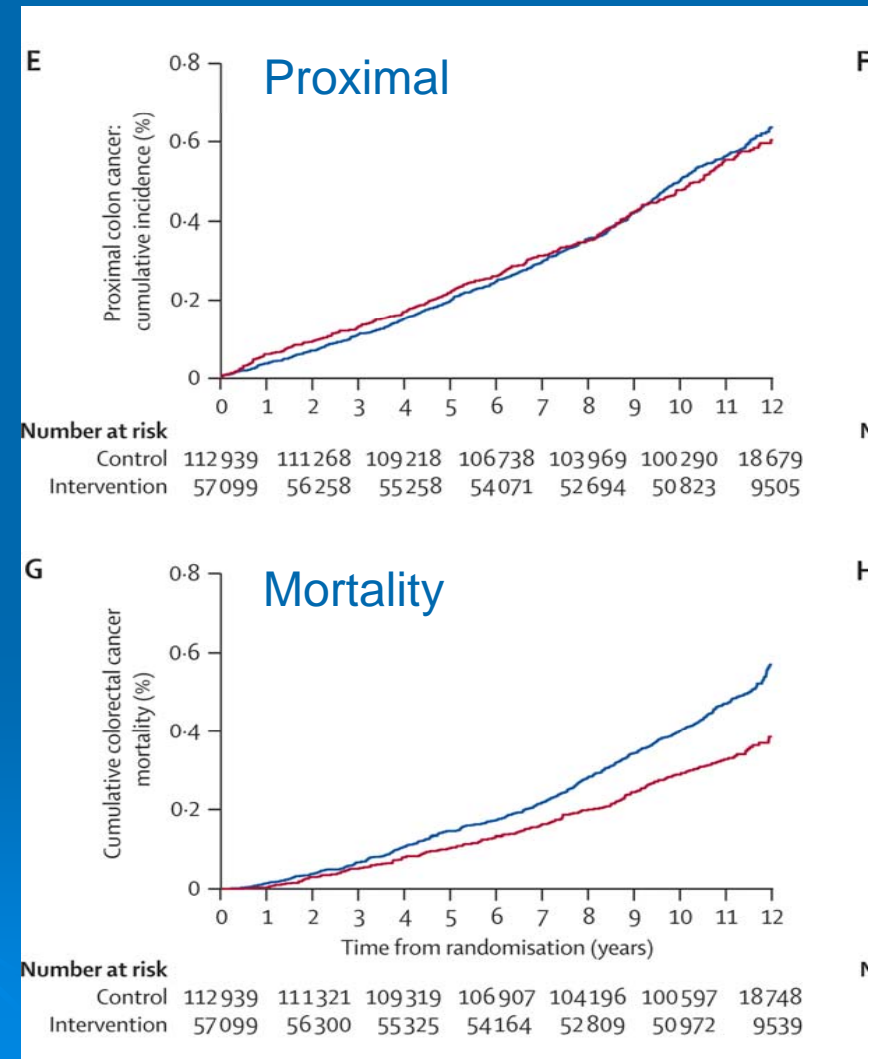
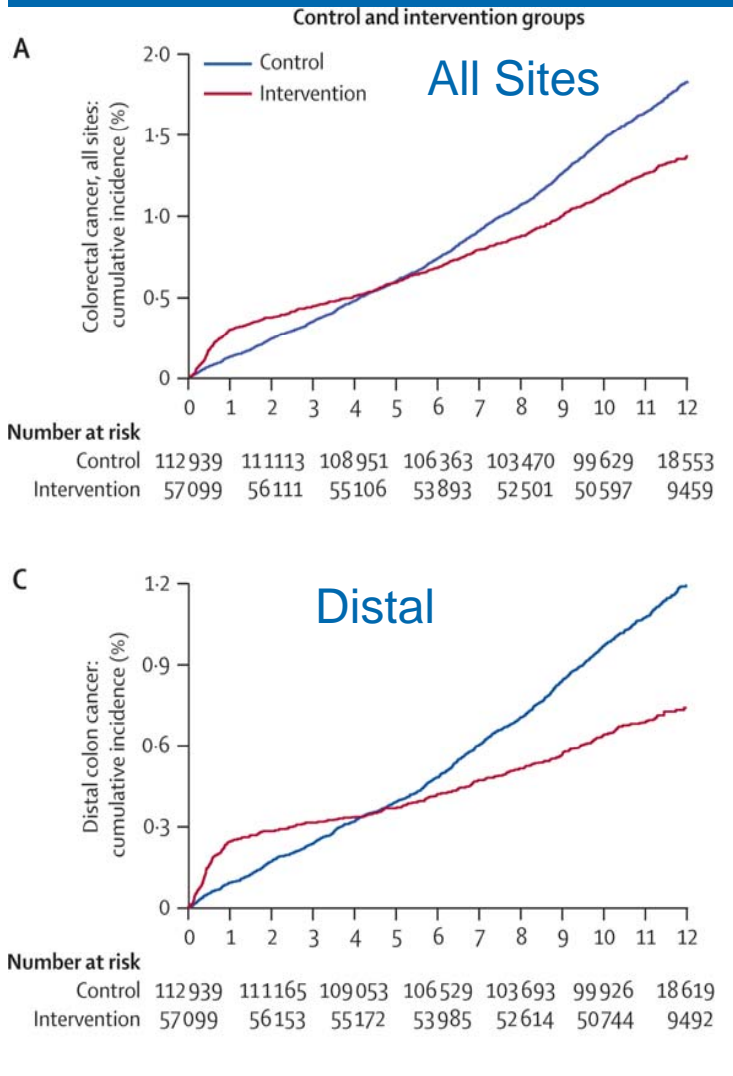
Lancet. 2010. 375:1624-33.



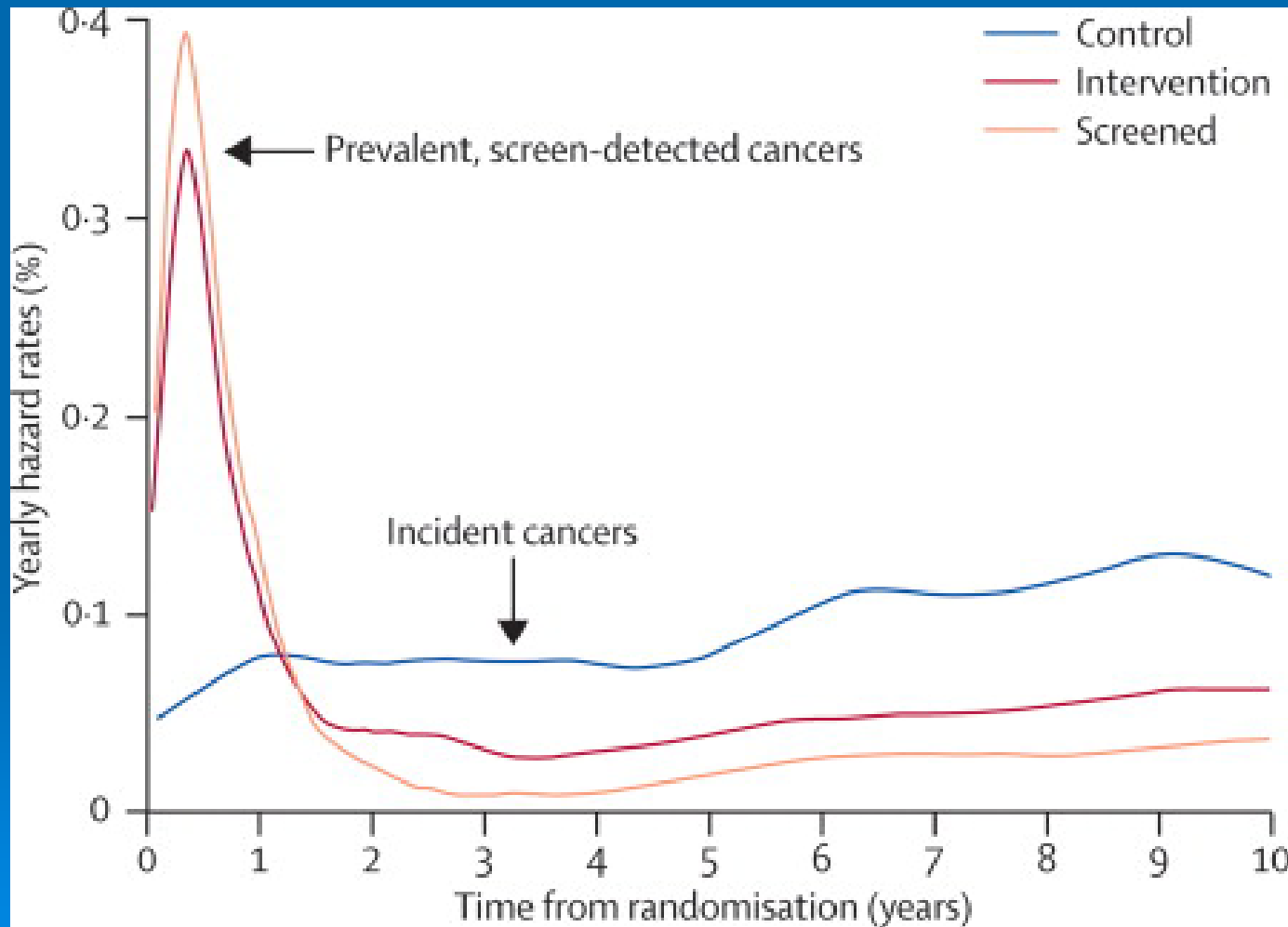
Colorectal cancer incidence and mortality

	Control N = 112,939	Intervention N = 57,099	Hazard Ratio	P-value
Incidence				
	Rate per 100,000	Rate per 100,000		
All Sites	149 (143-156)	114 (106-123)	0.77 (0.70-0.84)	<0.0001
Distal	98 (92-103)	62 (57-69)	0.64 (0.57-0.72)	<0.0001
Proximal	51 (48-56)	50 (45-56)	0.98 (0.85-1.12)	0.75
Mortality				
All Cause	1124 (1106-1143)	1093 (1067-1119)	0.97 (0.84-1.0)	0.0519
Colorectal	44 (40-48)	30 (26-35)	0.69 (0.59-0.82)	<0.0001

Kaplan-Meier Estimates of cumulative Incidence and mortality



Smoothed yearly hazard rates for distal cancer (rectum and sigmoid colon)



Cumulative incidence of and mortality from colorectal cancer, and the number needed to screen to prevent one event

	Control group (n=112 939)		Intervention group				Number of events expected in Intervention group	Number of events prevented in Intervention group	Number needed to screen to prevent one event (95% CI)
			Total (n=57 099)		Screened (n=40 621)				
	n	Rate (per 1000; 95% CI)	n	Rate (per 1000; 95% CI)	n	Rate (per 1000; 95% CI)			
Colorectal cancer diagnosis	1818	16.1 (15.4-16.9)	706	12.4(11.5-13.3)	445	11.0(10.0-12.0)	919	213	191 (145-277)
Colorectal cancer death*	538	4.8 (4.4-5.2)	189	3.3(2.9-3.8)	111	2.7(2.3-3.3)	272	83	489 (343-852)

Hazard Ratios in the Screened Group

	Hazard Ratio (95% CI) Screened vs Control
Incidence	
All Sites	0.67 (0.60-0.76)
Distal (rectum and sigmoid)	0.50 (0.42-0.59)
Proximal	0.97 (0.80-1.17)
Mortality	
All Cause	0.95 (0.91-1.00)
Colorectal Cancer	0.57 (0.45-0.72)

UK Flexible Sigmoidoscopy Study: Conclusions

➤ What this study does:

- A landmark study.
- First RCT to demonstrate the value of endoscopy at preventing incident colorectal cancers
- Shows that endoscopy is good, but not perfect
 - 50% reduction in distal CRC among those who were screened,
 - Less than is quoted from National Polyp Study

➤ What this study does not do:

- Answer questions about the value of colonoscopy
- A colonoscopy may not be twice as effective as a sigmoidoscopy

Cost Effectiveness Analysis of Hybrid Screening Strategies for Colorectal Cancer in Managed Care Setting

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DDW2010
Turning Science into Medicine



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Background

- Colorectal cancer (CRC) screening guidelines often recommend screening schedules based on a single type of test (e.g. colonoscopy every 10 years, or yearly fecal immunological test (FIT)).
- The objective of the current study is to define a hybrid screening strategy that maximizes the potential benefit, as measured by the number of CRCs averted and quality-adjusted life years (QALYs) saved, while controlling cost.

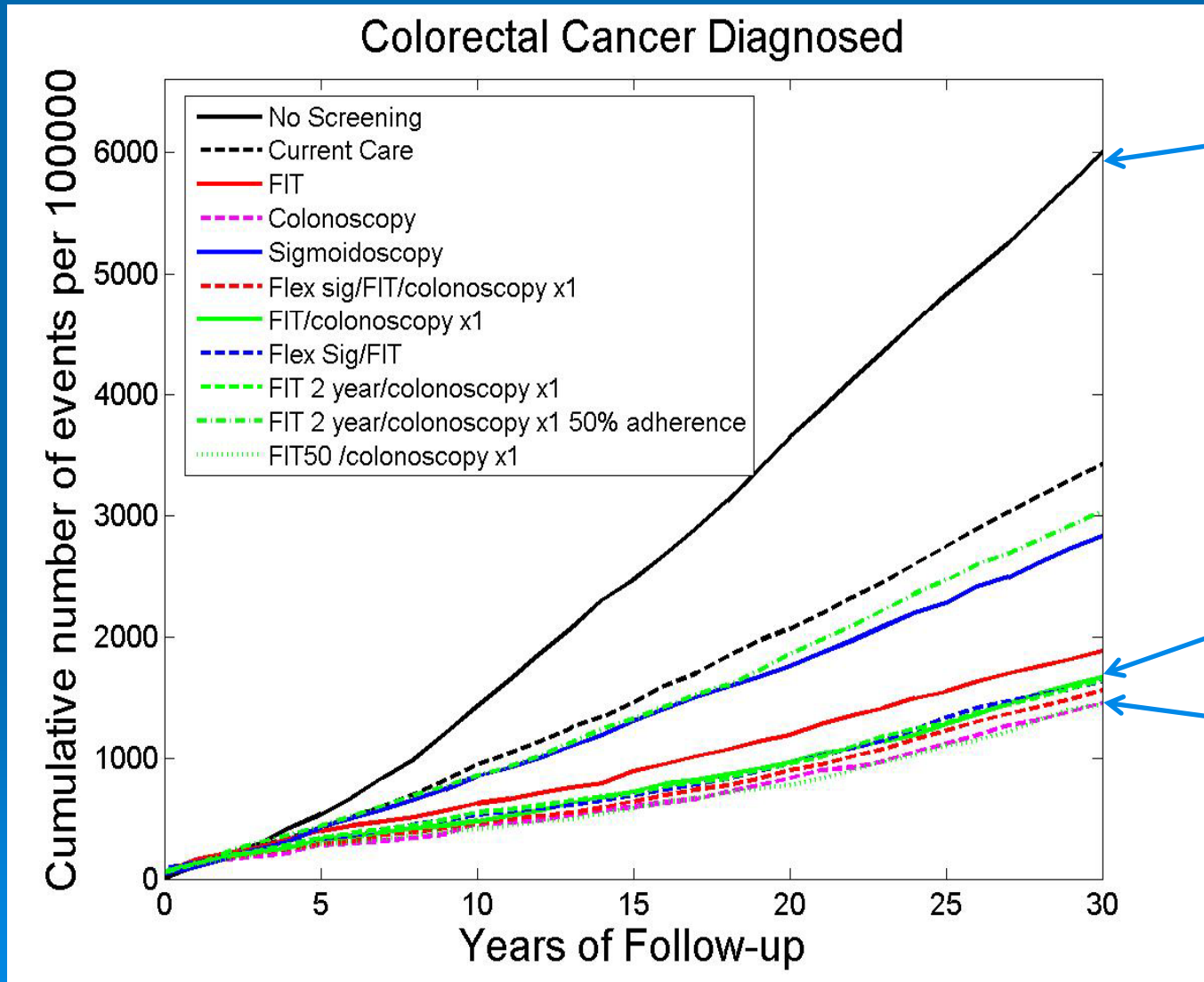
Method

- We used the Archimedes Model to evaluate the effects of different colorectal cancer screening strategies on health outcomes and costs relevant to colorectal cancer in a population representative of members of Kaiser Permanente Northern California (KPNC).
- The Archimedes Model is a large-scale simulation of human physiology, diseases, interventions, and health care systems.
- The colorectal cancer model in the Archimedes Model has been validated against several studies, including Minnesota FOBT screening trial, National Polyp Study and Cancer Prevention Study-II.
- The simulated population was a cross-section of the general U.S population, aged between 50 and 75 at the start of the simulation, and followed for a total of 30 years. Prior to the start of the simulation, there is a run-in period designed to reproduce CRC screening history in KPNC population.

CRC screening strategies considered

1. **KP current care (control arm):** This arm is designed to represent current screening practice in KPNC population (2008)
2. **FIT only:** annual screening by FIT
3. **Colonoscopy only:** colonoscopy screening every 10 years
4. **Flexible sigmoidoscopy only:** flexible sigmoidoscopy screening every 5 years
5. **Flexible sigmoidoscopy/FIT/colonoscopy x1:** (i) beginning at age 50, screen with flexible sigmoidoscopy (x1) , (ii) perform FIT beginning at age 55, and every year until age 65, (iii) at age 66, screen with colonoscopy x 1.
6. **FIT every year/colonoscopy x1:** (i) at age 50, screen with FIT every year for 15 years, (ii) at age 66, screen with colonoscopy x 1
7. **Flexible sigmoidoscopy/FIT:** beginning at age 50, screen with flexible sigmoidoscopy every 10 years concurrently with annual FIT
8. **FIT every other year/colonoscopy x1:** (i) at age 50, screen with FIT every other year for 15 years, (ii) at age 66, screen with colonoscopy x 1
9. **FIT every other year/colonoscopy x1 at 50% compliance:** (i) at age 50, screen with FIT100 every other year for 15 years, (ii) at age 66, screen with colonoscopy x 1 with only 50% compliance
10. **FIT50 every year/colonoscopy x1:** (i) at age 50, screen with FIT50 (cutoff = 50 ng Hgb/mL buffer) every year for 15 years, (ii) at age 66, screen with colonoscopy x 1

Hybrid screening strategies are effective in reducing incidence of CRC



No screening

FIT/colonoscopy x 1

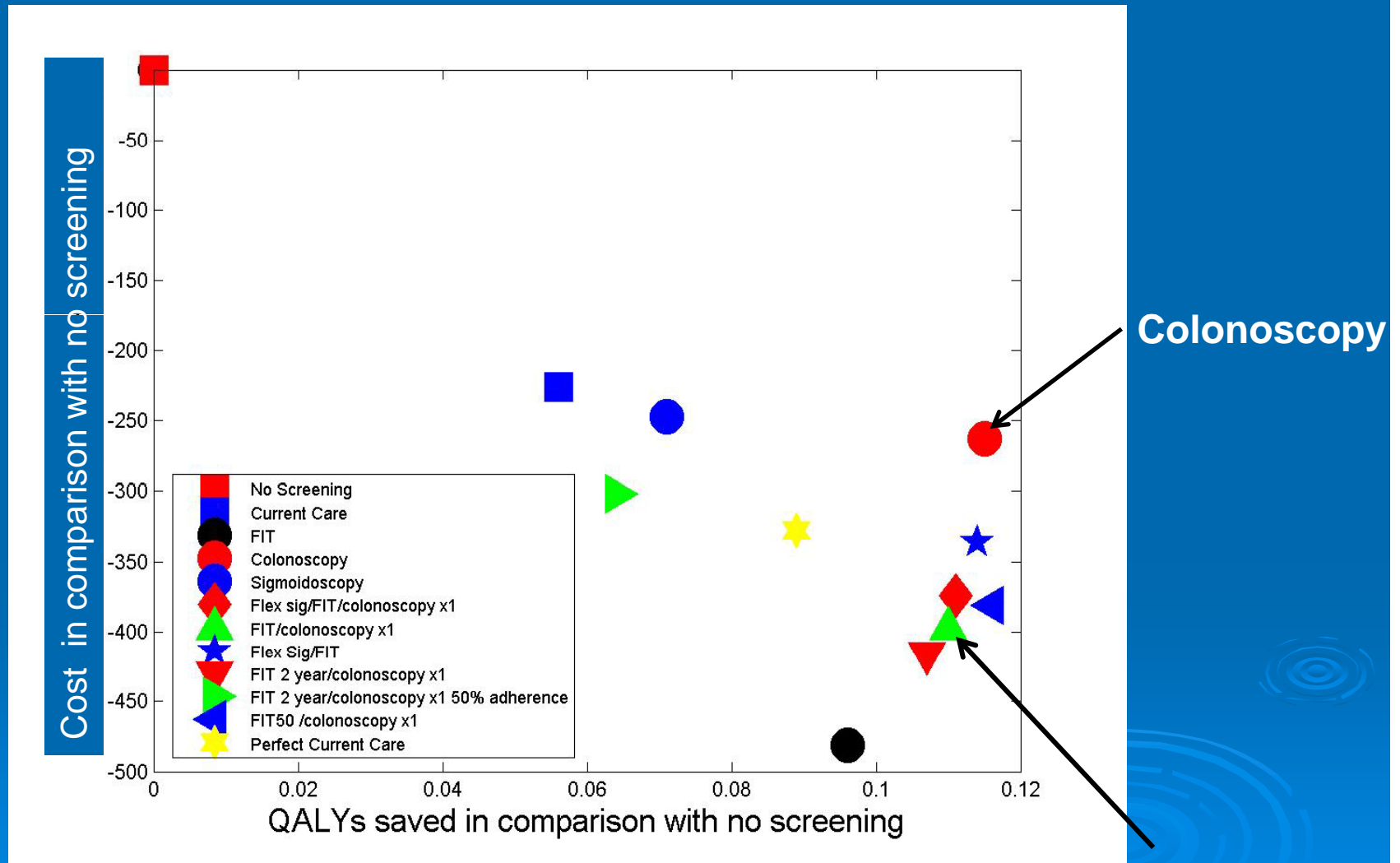
Colonoscopy

CRC screening saves money

Arms	Total cost, \$	Cost saved in comparison to no screening, \$
<i>No Screening</i>	1635	0
<i>Current Care</i>	1409	-226
<i>FIT</i>	1155	-481
<i>Colonoscopy</i>	1372	-263
<i>Sigmoidoscopy</i>	1388	-247
<i>Flex sig/FIT/colonoscopy x1</i>	1261	-374
<i>FIT/colonoscopy x1</i>	1238	-397
<i>Flex Sig/FIT</i>	1299	-336
<i>FIT 2 year/colonoscopy x1</i>	1219	-416
<i>FIT 2 year/colonoscopy x1 50% adherence</i>	1333	-302
<i>FIT50 /colonoscopy x1</i>	1254	-381

Note: Screening by FIT/colonoscopy x 1 is cost-saving in comparison to screening by colonoscopy, For a population of 100,000, screening by FIT/colonoscopy x 1 saves \$13.4 million over a period of 30 years.

Cost saved *versus* QALY saved



Note: Cost and QALYs are discounted at 3% annually.

FIT/colonoscopy x 1

Summary

- Hybrid screening strategies are comparable to the best single-test strategies in terms of decreasing incidence and mortality from CRC and reducing costs of CRC treatment.
- Screening by annual FIT between age 50 and age 65, followed by a single colonoscopy at age 66 (FIT/colonoscopy x 1) ***delivers similar health benefits, at significant cost savings***, in comparison to screening by colonoscopy at 10-year intervals between age 50 and age 75.
- The cost-effectiveness of hybrid screening strategies is sensitive to compliance with colonoscopy but less sensitive to the compliance with yearly FIT.

Method of Recommendation for Colorectal Cancer Screening Strategies Impacts Adherence

- Prospective study comparing single- vs. multiple recommendations for CRC screening in a racially/ethnically diverse population. Patients (avg. risk CRC) randomly assigned to receive a recommendation for 1) FOBT alone, 2) COL alone or 3) choice of FOBT or COL
- 1,000 subjects; 34% Latino, 30% Asian, 18% black, 15% white, and 3% other, with 53% women.
- Overall, 65.1% were adherent to CRC screening (men: 64.2%, women 65.8%; NS)
 - **38.4%** of subjects recommended COL alone
 - **67.1%** recommended FOBT alone
 - **70.0%** provided a choice between FOBT and COL adhered to screening.

Can quantitative immunochemical FOBT be used in a single sample format without compromising diagnostic yield?

Disease Status	Reference Group (100ng Hb/ml)	1st Sample only		50 ng/mL vs Reference Group P-value
	1 or 2 Positive n=272 (%)	100ng/ml n=175 (%)	50ng/ml n=196 (%)	
Cancer	5 (1.8)	4 (2.2)	4 (2.0)	Not tested
Cancer or Adv. Adenoma	80 (29.4)	53 (30.3)	62 (31.6)	0.89
Non-Advanced Adenoma	46 (16.9)	33 (18.9)	36 (18.4)	0.78

Attendance and Diagnostic Yield of One Versus Two-Sample FIT Screening; a Comparative Population-Based Colorectal Cancer Trial

	One-sample FIT n=2,493	Two Sample FIT n = 3200
Completed screening	1539 (64.4%)	1874 (61.2%)
Positive Test	106 (6.9%)	201 (10.7%)
Adv. adenoma	38	58
CRC	7	11
PPV Adv. adenoma + cancer	46% (CI: 38-55)	38% (31-45)
Detection rate Adv. Adenoma + cancer	2.9% (CI: 2.2-3.8)	3.7% (2.9 – 4.7)

van Roon, Wilschut, van Ballegooijen, et al. DDW 2010 Abstract 931

African-Americans Have the Same Prevalence and Proximal

Distribution of Adenomas As Whites in the National Colonoscopy Study

Colon Findings	African American N=182	Whites N=184	Multivariate* Odds Ratio	P Value, 95% CI
No Polyp	106 (58.6)	101 (54.5)	1.0 (ref)	N/A
Adenoma	42 (23)	43 (23)	1.01	P=0.98, (0.60-1.68)
Adv. Adenoma	10 (5.5)	12 (6.5)	1.20	P=0.68 (0.50-2.89)
Prox. Adenoma	30 (16)	31 (17)	1.03	P=0.92 (0.58-1.85)
Adv. Prox. adenoma	6 (3)	7 (4)	1.08	P=0.89 (0.34-3.41)

Close, Zauber, Mills. Abstract S1148

*Adjusted for age, sex, SES

DDW Conclusions

- Non-colonoscopy screening strategies are getting attention
- Primarily from public health oriented groups
 - Europeans, population health care focused HMOs, and underserved communities.
- The FIT is a useful and important alternative to colonoscopy, and may have higher patient acceptance than colonoscopy
- Failure to offer an alternative to colonoscopy screening will limit screening rates.