National Cancer Institute

Colorectal Cancer Screening and Aspirin for Prevention

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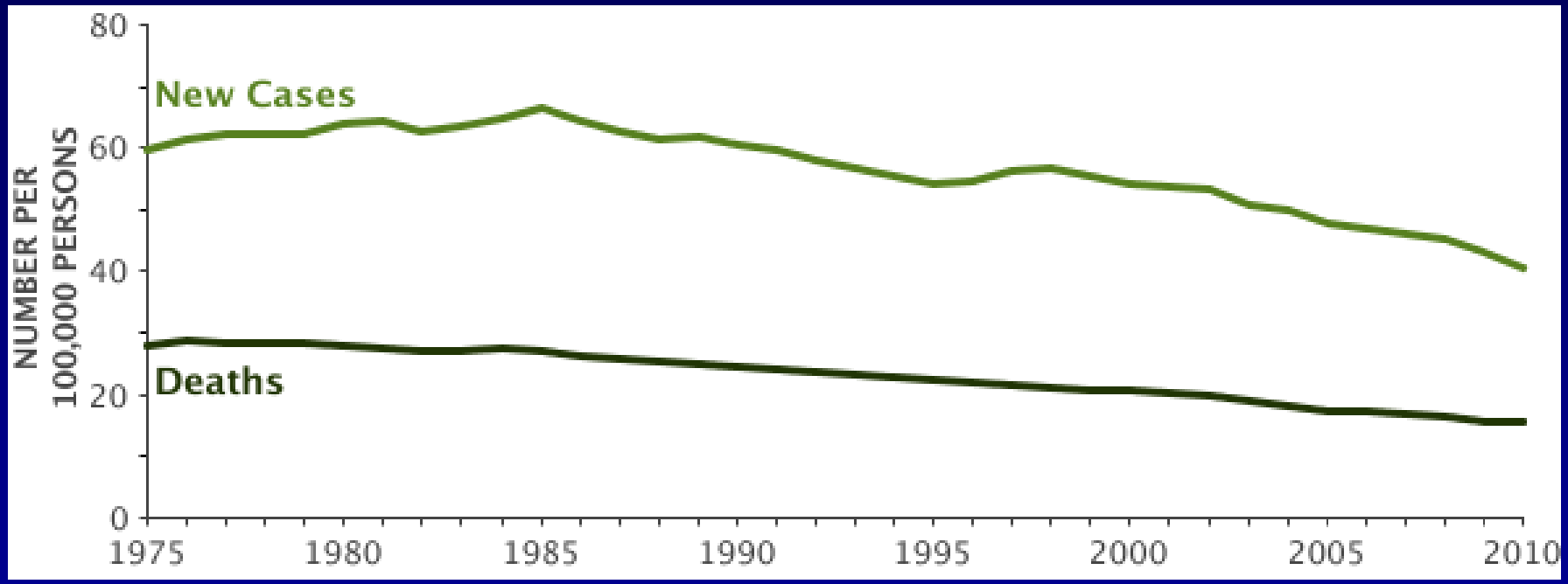
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Trends in Incidence and Mortality For Colorectal Cancer



http://seer.cancer.gov/statfacts/html/colorect.html

Outline

- What's the best colorectal cancer screening test?
- Aspirin chemoprevention
- Are endoscopy and aspirin complementary?

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- **What's the best colorectal cancer screening test?**
- **Aspirin chemoprevention**
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U.S. Preventive Services Task Force Recommendations for CRC Screening

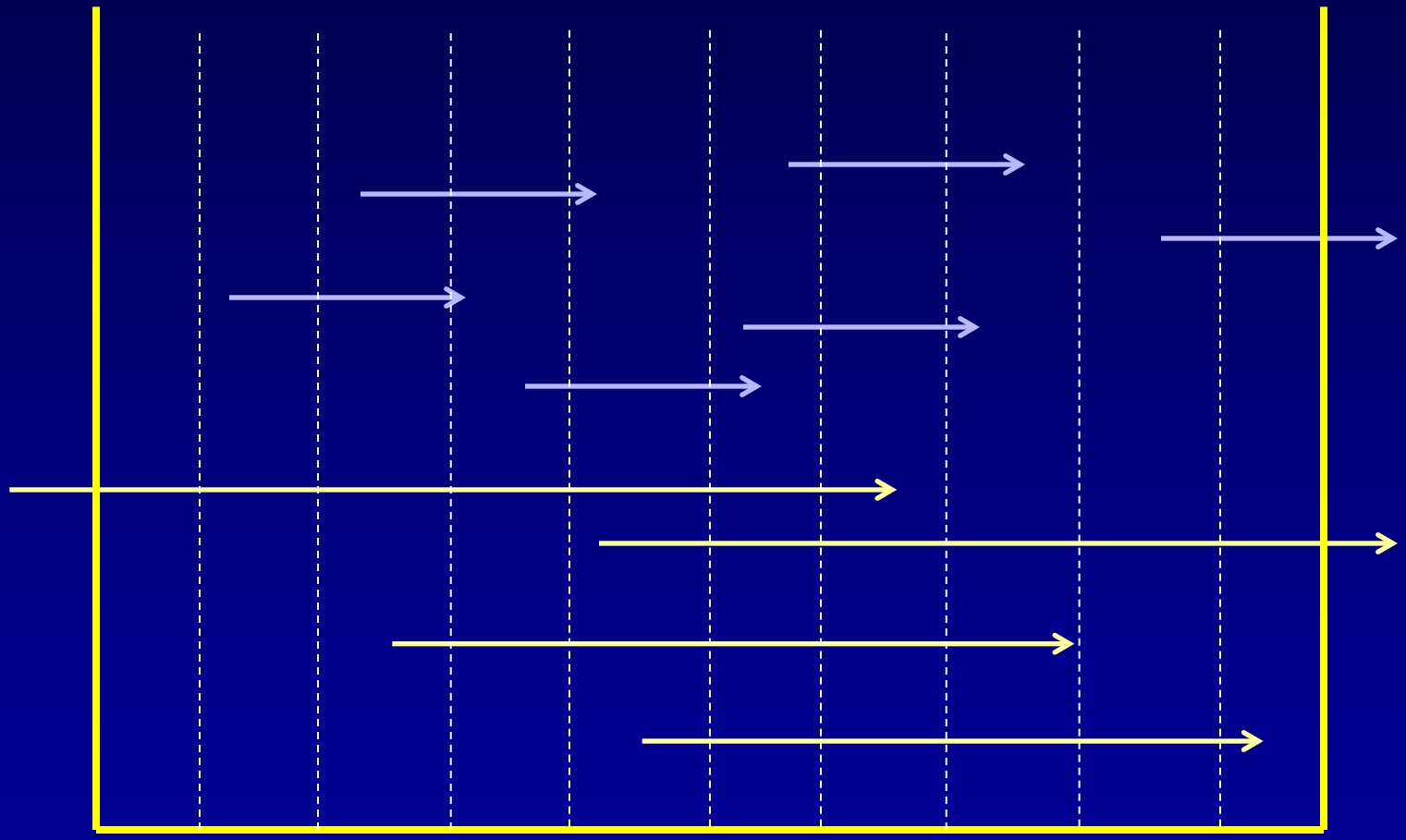
Adults Age 50-75 Years	Adults Age 76-85 Years	Adults Older than 85 Years
Screen with high-sensitivity FOBT (annual), Sigmoidoscopy (5 years) + HS-FOBT (3 years), or Colonoscopy (10 years) Grade: A	Do not screen routinely Grade: C	Do not screen Grade: D
For all populations, evidence is insufficient to assess the benefits/harms of screening with CT colonography and fecal DNA testing Grade: I (Insufficient evidence)		

Effect of Screening Intervention on Reducing Mortality from Colorectal Cancer

	Fecal Occult Blood Test	Sigmoidoscopy	Colonoscopy
Study Design	RCTs	Case-control studies; RCTs	Case-control studies, RCTs in progress
Magnitude of Effects	15%-33%	About 60%-70% for left colon	About 60%-70% for left colon; uncertain for right colon
Invasiveness	+	++	+++

http://www.cancer.gov/cancertopics/pdq/screening/colorectal/HealthProfessional

The Effect of Screening Intervals on Cancer Detection



Outcomes for the Recommendable Set of Screening Strategies/MISCAN

Beginning tests at age 50, ending tests at age 75, per 1,000 people

	No. of Colon--oscopies	Life Years Gained per 1,000 people	Incidence Reduction	Mortality Reduction
Colonoscopy	4136	230	51.9%	64.6%
Hemoccult SENSA	3350	230	49.7%	66.0%
FIT	2949	227	47.2%	64.6%
Hemoccult II	1982	194	37.1%	55.3%
Flexible Sigmoidoscopy	1911	203	46.8%	58.5%
Flexible Sig + SENSA	2870	230	51.2%	65.7%

Zauber, *Annals of Internal Medicine*
4 Nov 2008

The most effective colorectal cancer screening test is the one you are willing to take.

Compliance to FIT vs. Colonoscopy: First Round of a Spanish Randomized Trial

- Households randomly assigned to either biennial FIT or 1-time colonoscopy
- Randomization performed before invitation
- Invitation letters sent with reminders at baseline, 3 months, and 6 months
- 57,404 Randomized, 1st Round Compliance/Acceptance Rates
  - FIT 34.2 %
  - Colonoscopy 24.6%
  - OR=0.63 p <.001

Quintero, *N Eng J Med*, 23 Feb 2012

Colonoscopy vs. FIT: First Round Detection in the Spanish Randomized Controlled Trial

Table 1. Diagnostic Yield of Colonoscopy and Fecal Immunochemical Testing (FIT), According to the Intention-to-Screen Analysis.*

Colorectal Lesion	Colonoscopy (N=26,703)		FIT (N=26,599)		Odds Ratio (95% CI)†	P Value
	Subjects	Rate	Subjects	Rate		
	no.	%	*no.*	%		
Cancer	30	0.1	33	0.1	0.99 (0.61–1.64)	0.99
Advanced adenoma‡	514	1.9	231	0.9	2.30 (1.97–2.69)	<0.001
Advanced neoplasia§	544	2.0	264	1.0	2.14 (1.85–2.49)	<0.001
Nonadvanced adenoma	1109	4.2	119	0.4	9.80 (8.10–11.85)	<0.001
Any neoplasia	1653	6.2	383	1.4	4.67 (4.17–5.24)	<0.001

* The diagnostic yield was calculated as the number of subjects with true positive results divided by the number of subjects who were eligible to undergo testing. Subjects were classified according to the most advanced lesion.
† Odds ratios were adjusted for age, sex, and participating center. CI denotes confidence interval.
‡ Advanced adenoma was defined as an adenoma measuring 10 mm or more in diameter, with villous architecture (>25%), high-grade dysplasia, or intramucosal carcinoma.
§ Advanced neoplasia was defined as advanced adenoma or cancer.

Quintero, *N Eng J Med*, 23 Feb 2012

Harms/Complications in the First Round of the Spanish Randomized Trial of Colonoscopy vs. FIT

- 24 of 4,953 patients in colonoscopy group had complications (0.5%)
  - Bleeding (12)
  - Hypotension or bradycardia (10)
  - Perforation (1)
  - Desaturation (1)

- 10 of 8,983 patients in FIT group had complications (0.1%)
  - Bleeding (8)
  - Hypotension or bradycardia (2)

  (all 10 had positive FIT and received a colonoscopy)

Quintero, *N Eng J Med*, 23 Feb 2012

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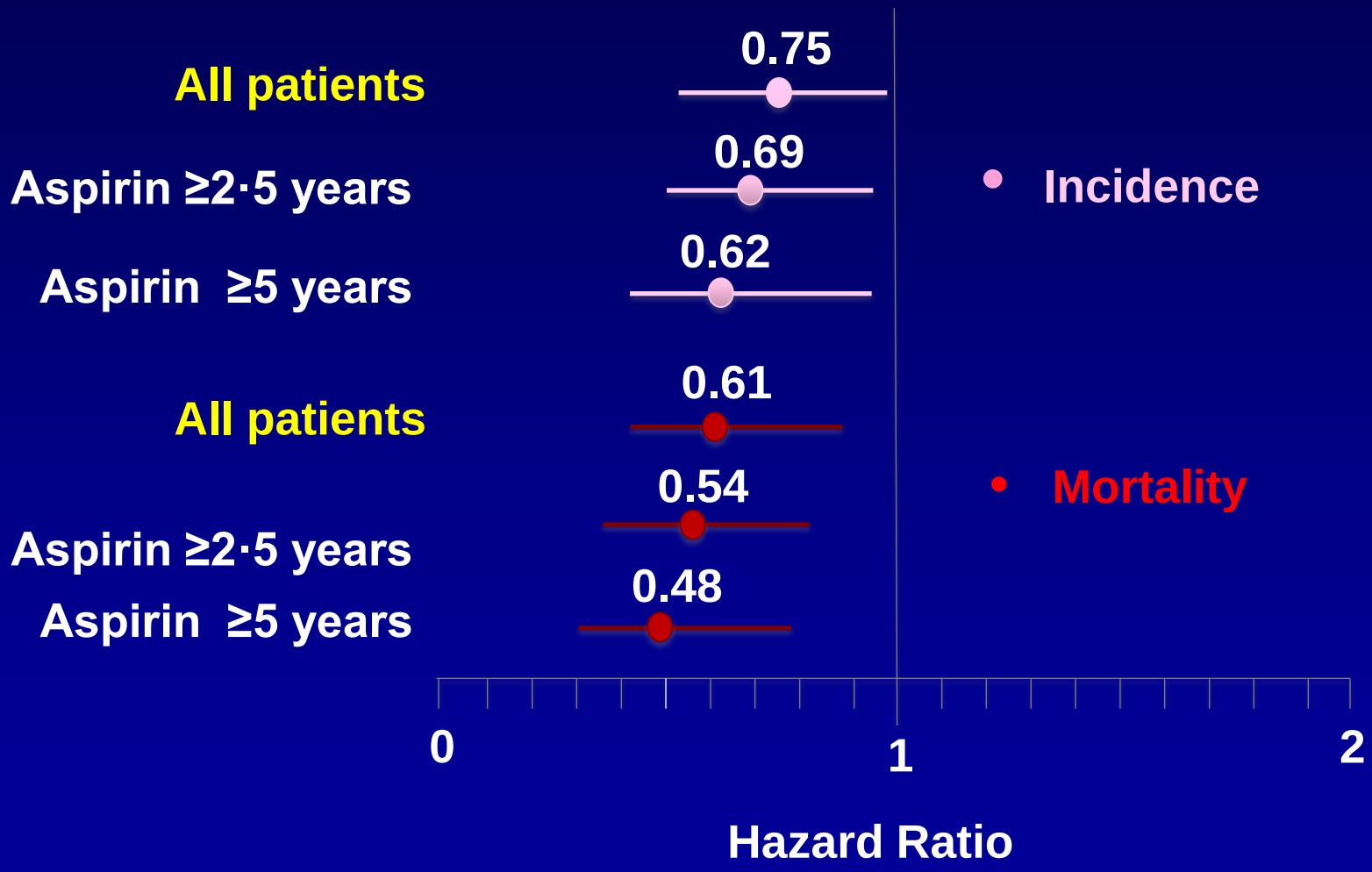
- **Aspirin chemoprevention**
- Are endoscopy and aspirin complementary?

Effect of Low-dose (75-300mg) Aspirin Versus Control on Colorectal Cancer Incidence & Mortality

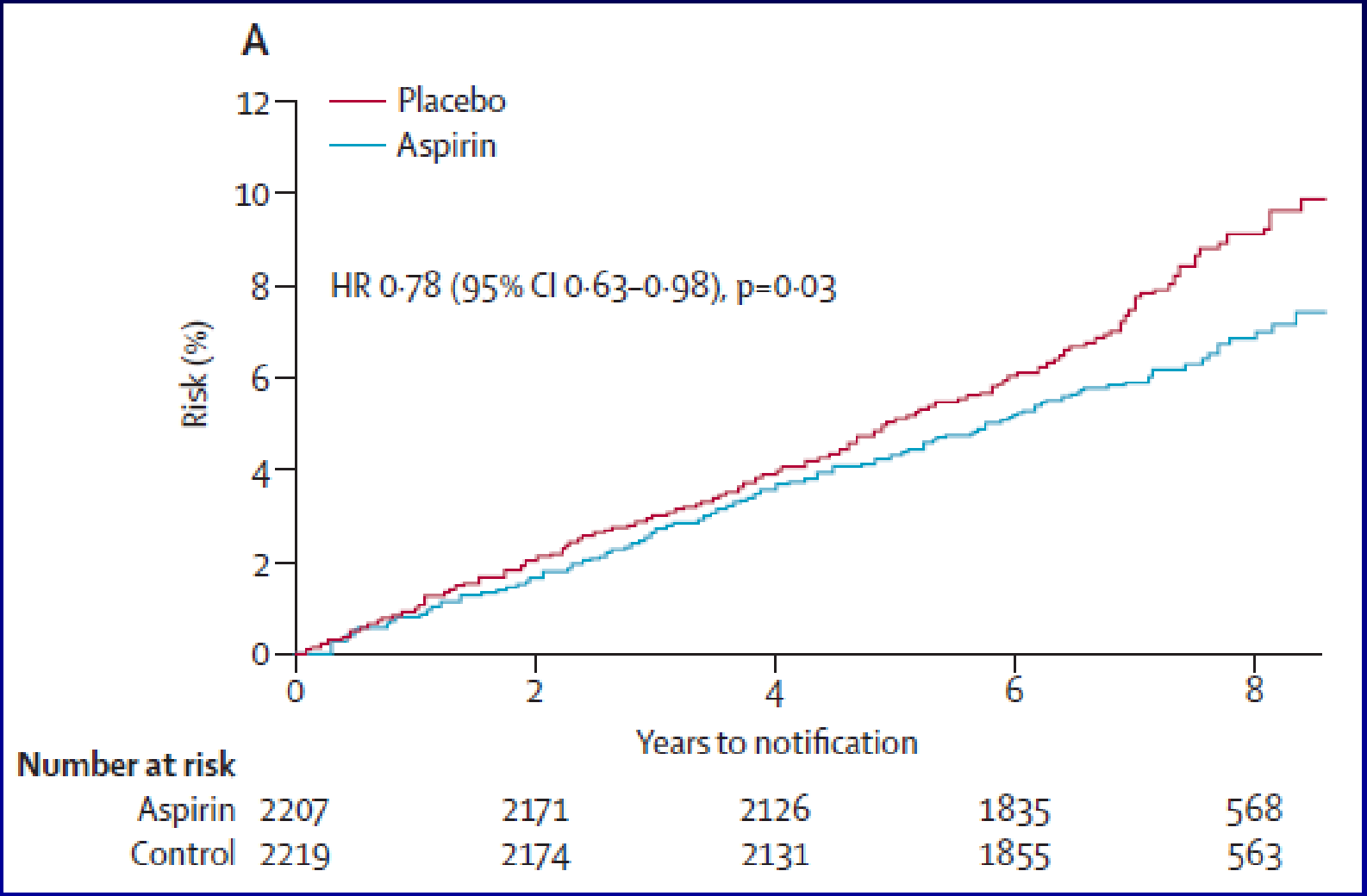


Rothwell, *Lancet,* 20 November 2010

Data from 4 randomized trials of aspirin vs. control

Effect of Aspirin on Incidence of Cancer

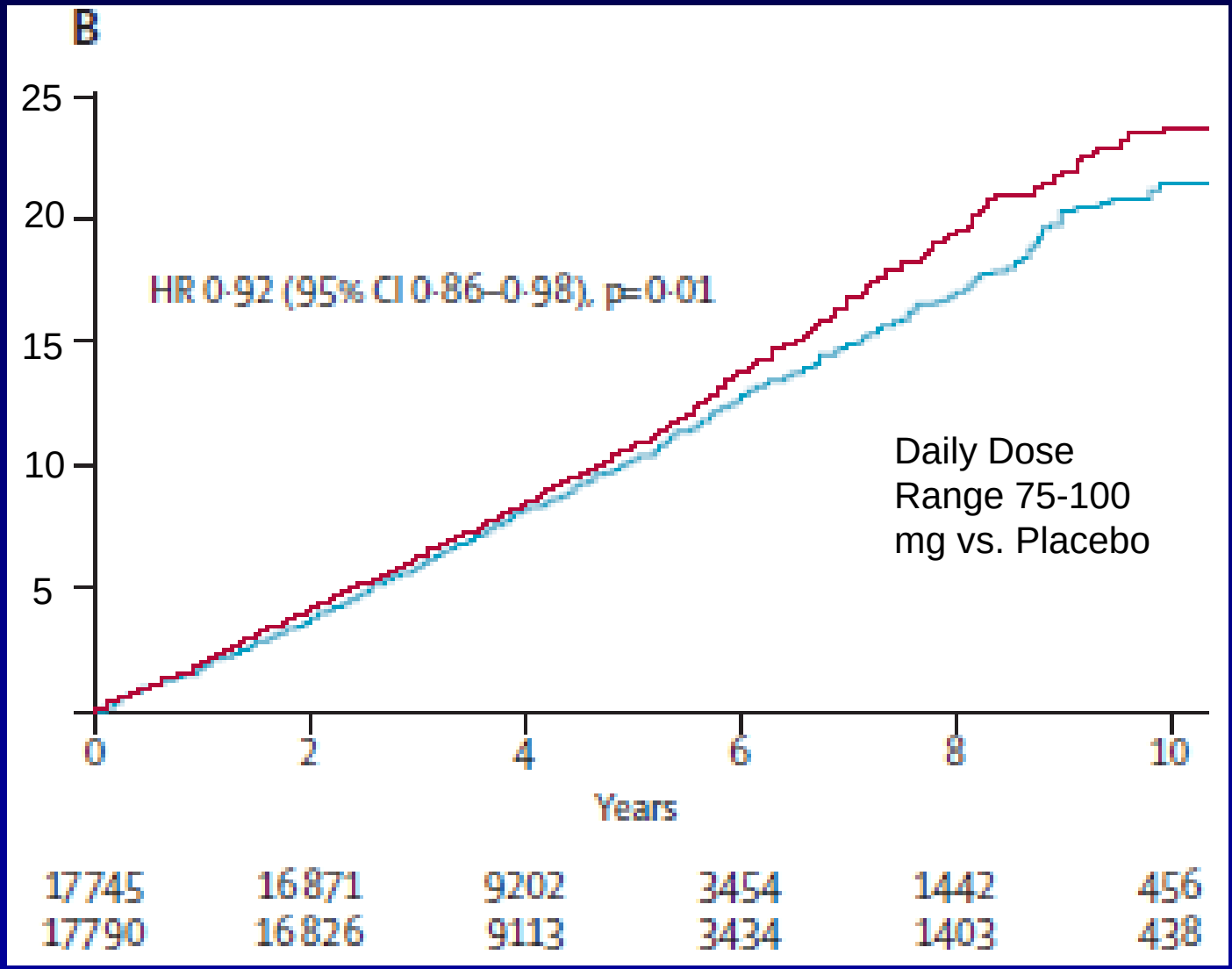
Daily Dose Range 75-100 mg, vs. Placebo



Rothwell, *Lancet,* 28 April 2012

Data from 6 randomized trials of aspirin vs. control

Effect of Aspirin on Vascular Events, Cancers, or Fatal Extra-cranial Hemorrhage



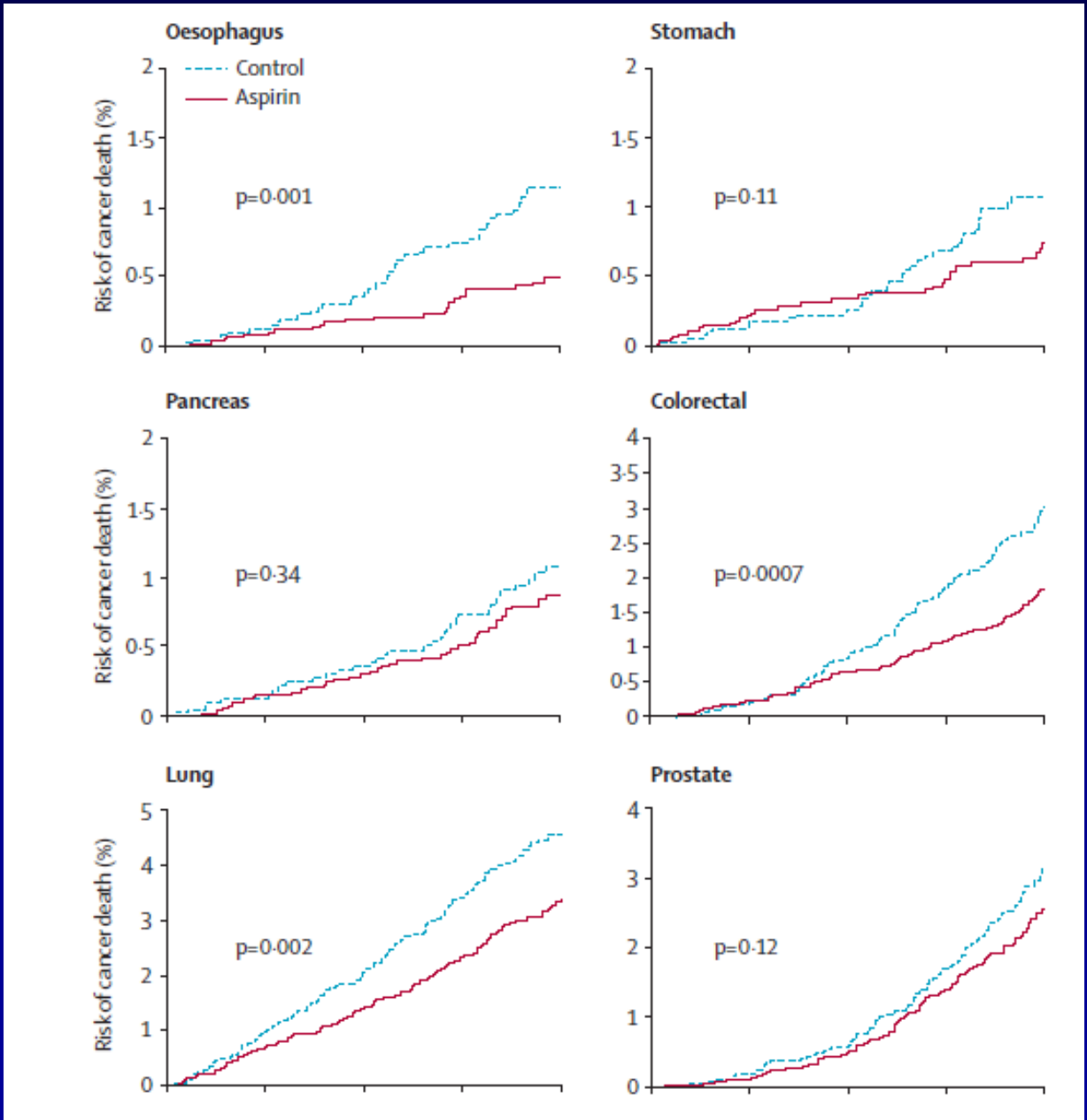
Rothwell, *Lancet,* 28 April 2012

Data from 6 randomized trials of aspirin vs. control

Screening vs. Prevention

- Screening may reduce the mortality from one disease.
- Prevention may be able to reduce the mortality from multiple diseases.

Effect of Aspirin on 20-Year Risk of Death Due to Common Cancers in 4 Long-Term Trials



Rothwell, *Lancet*,
1 Jan 2011

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Colonoscopy and Right- versus Left-sided Colorectal Cancer Death

	Odds Ratio (95% CI)		
	All Cancer	Right-Sided Cancer	Left-Sided Cancer
Attempted Colonoscopy			
None	1.00	1.00	1.00
Any	0.69 (0.63-0.74)	1.07 (0.94-1.21)	0.39 (0.34-0.45)
Completeness of Colonoscopy			
None	1.00	1.00	1.00
Complete	0.63 (0.57-0.69)	0.99 (0.86-1.14)	0.33 (0.28-0.39)
Incomplete	0.91 (0.78-1.07)	1.35 (1.07-1.69)	0.63 (0.49-0.81)

Baxter, *Ann Intern Med*, 6 Jan 2009

Differential Efficacy of Colonoscopy

Potential reasons for difference in proximal vs. distal colorectal cancer mortality reduction

- **Technical: Inadequate bowel prep**
- **Expertise/ Experience**
- **Biological**
  - **Faster growing lesions on the right**
  - **Flat and depressed adenomas on the right**

Effect of Aspirin (75-1200 mg) on Right- versus Left-sided Colorectal Cancer Incidence

	All Patients		
	Events	Hazard Ratios (95% CI)	P
All Cancers	397	0.76 (0.63-0.94)	0.01
Proximal Colon	69	0.45 (0.28-0.74)	0.001
Distal Colon	100	1.10 (0.73-1.64)	0.66
Rectum	119	0.90 (0.63-1.30)	0.58

Rothwell, *Lancet,* 20 November 2010

Data from 4 trials
of aspirin vs. control

Effect of Aspirin (75-1200 mg) on Right- versus Left-sided Colorectal Cancer Death

	All Patients		
	Events	Hazard Ratios (95% CI)	P
Fatal Cancers	240	0.66 (0.52-0.86)	0.002
Proximal Colon	41	0.34 (0.18-0.66)	0.001
Distal Colon	44	1.21 (0.66-2.24)	0.54
Rectum	70	0.80 (0.50-1.28)	0.35

Data from 4 trials of aspirin vs. control

Rothwell, *Lancet,* 20 November 2010

Remaining Uncertainties in Colorectal Screening and Prevention

- Comparative effectiveness of the available screening tests?
- Mechanism(s) of aspirin action on carcinogenesis?
- Optimal duration & age range for aspirin use
  - Aspirin in Reducing Events in Elderly (ASPREE) is examining composite disability-free survival in ≥ 70 years
- Are screening and aspirin complementary, additive?