

Is aspirin ready for colorectal cancer chemoprevention ?

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Aspirin and Colorectal carcinogenesis

Animal experiments

- Aspirin inhibits:
 - colon cancer xenograft in mouse model
 - chemically-induced colonic carcinogenesis in rodents
 - carcinogenesis related to APC gene mutations in the Min mouse model and APC (Δ^{474}) mice

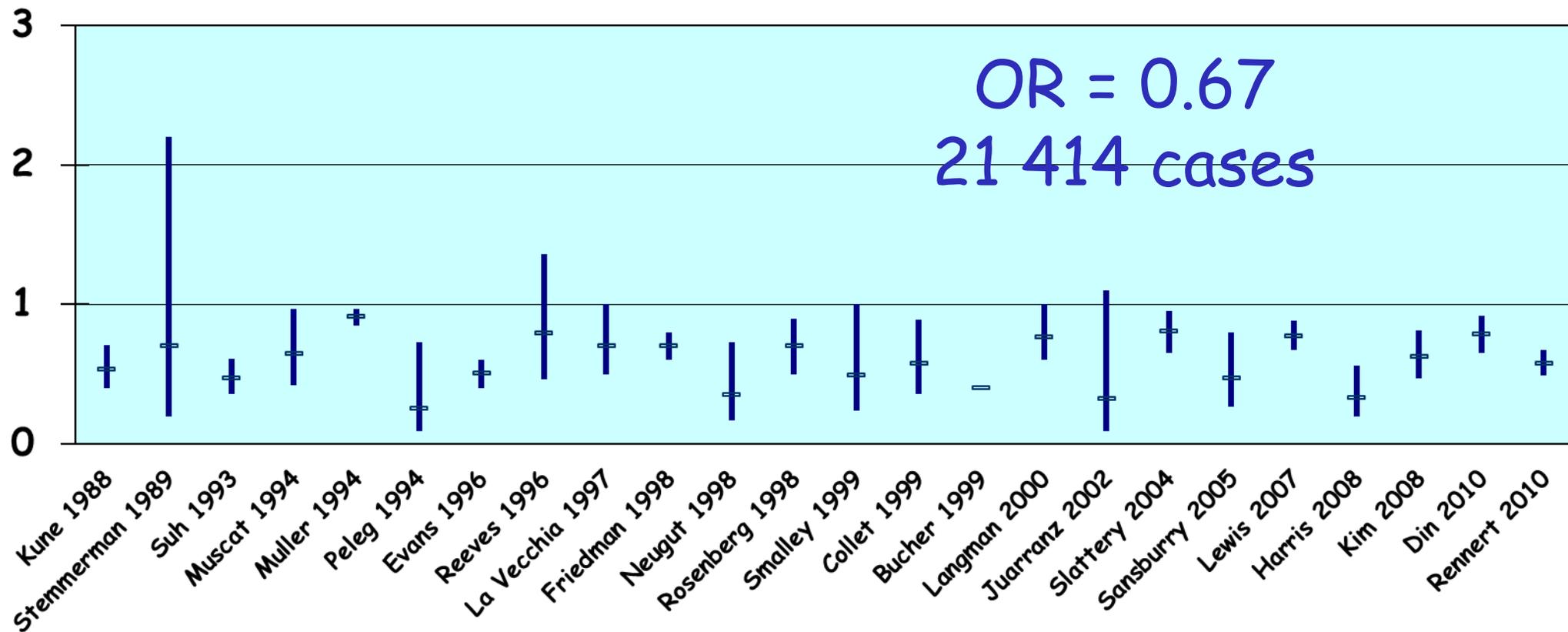
Aspirin and Colorectal carcinogenesis

Animal experiments

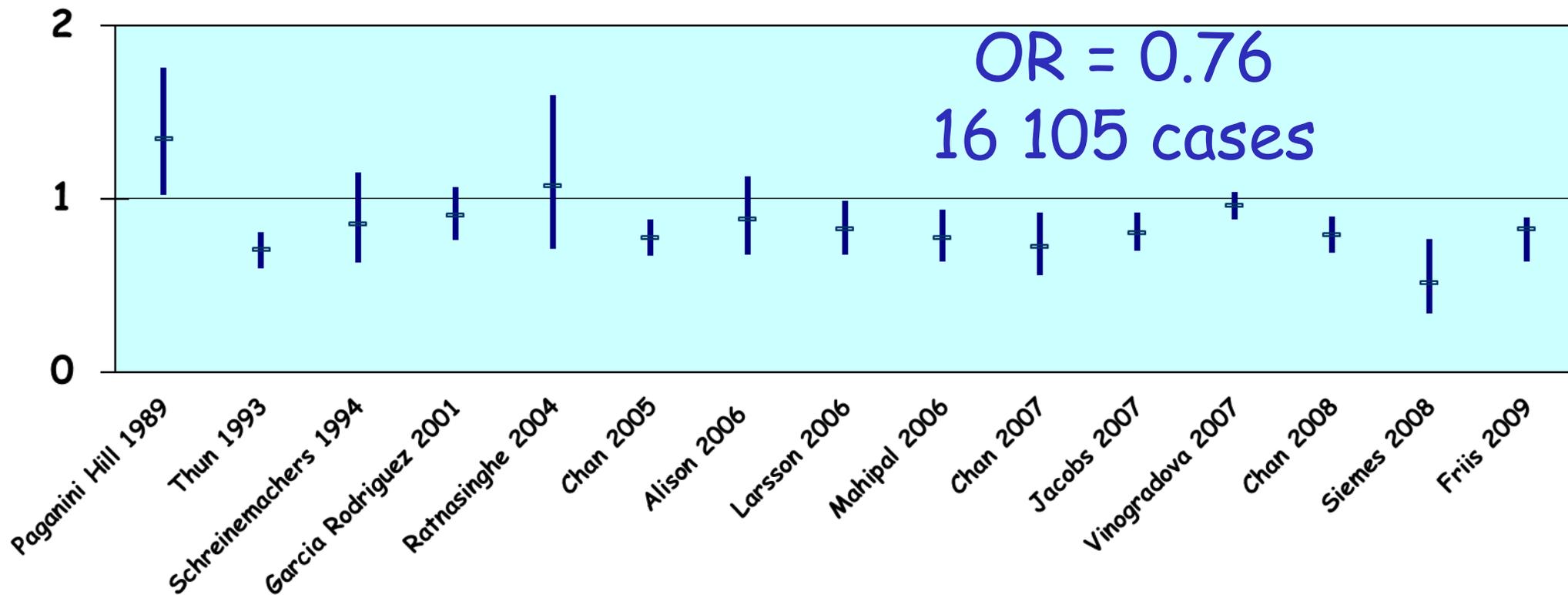
- Number of animals with tumors
- Number of tumors per animal
- Early step of carcinogenesis: Aberrant crypt foci
- Before and after carcinogen administration

- Low and high dose
- Reversible

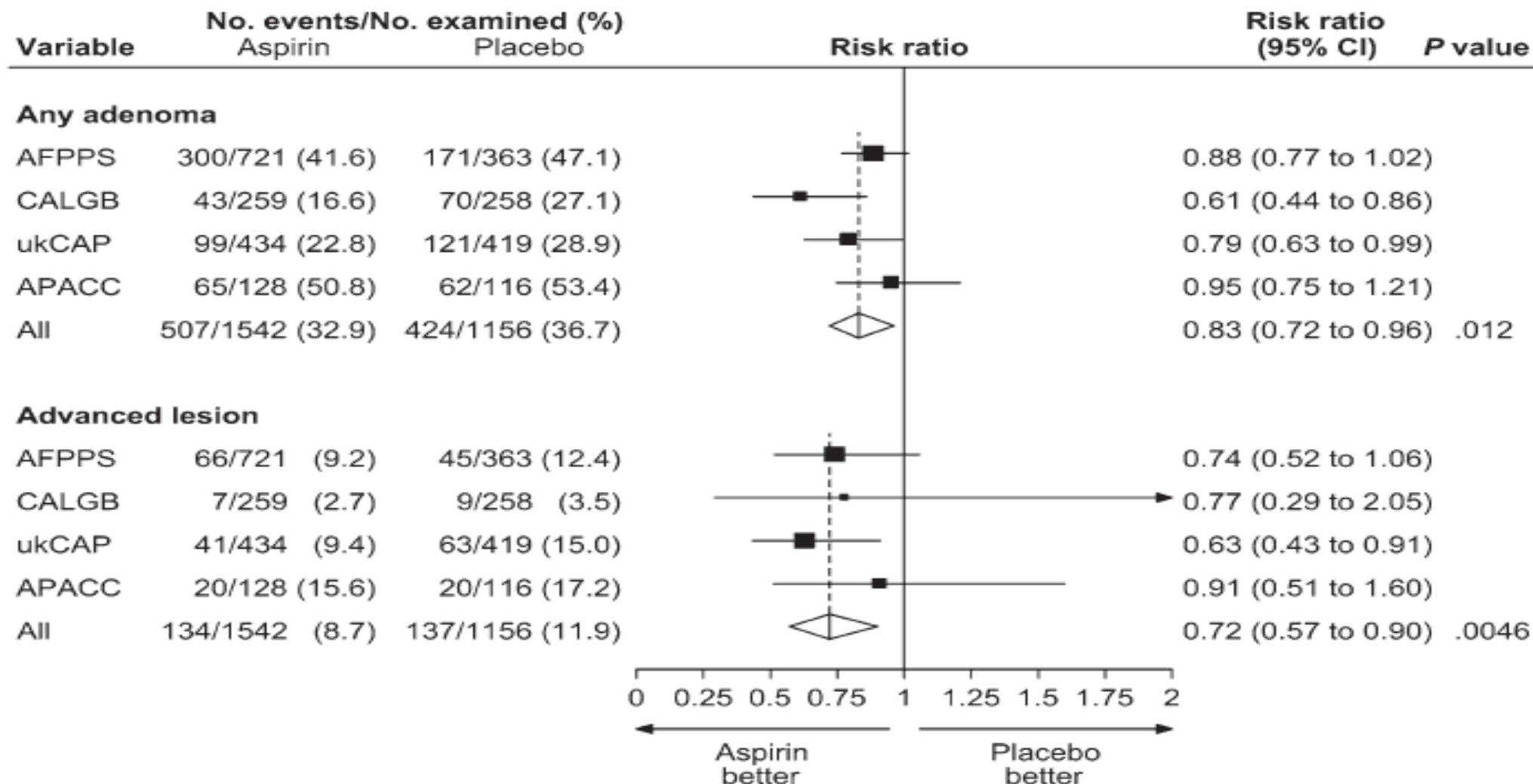
Colorectal cancer & aspirin : Case-control studies



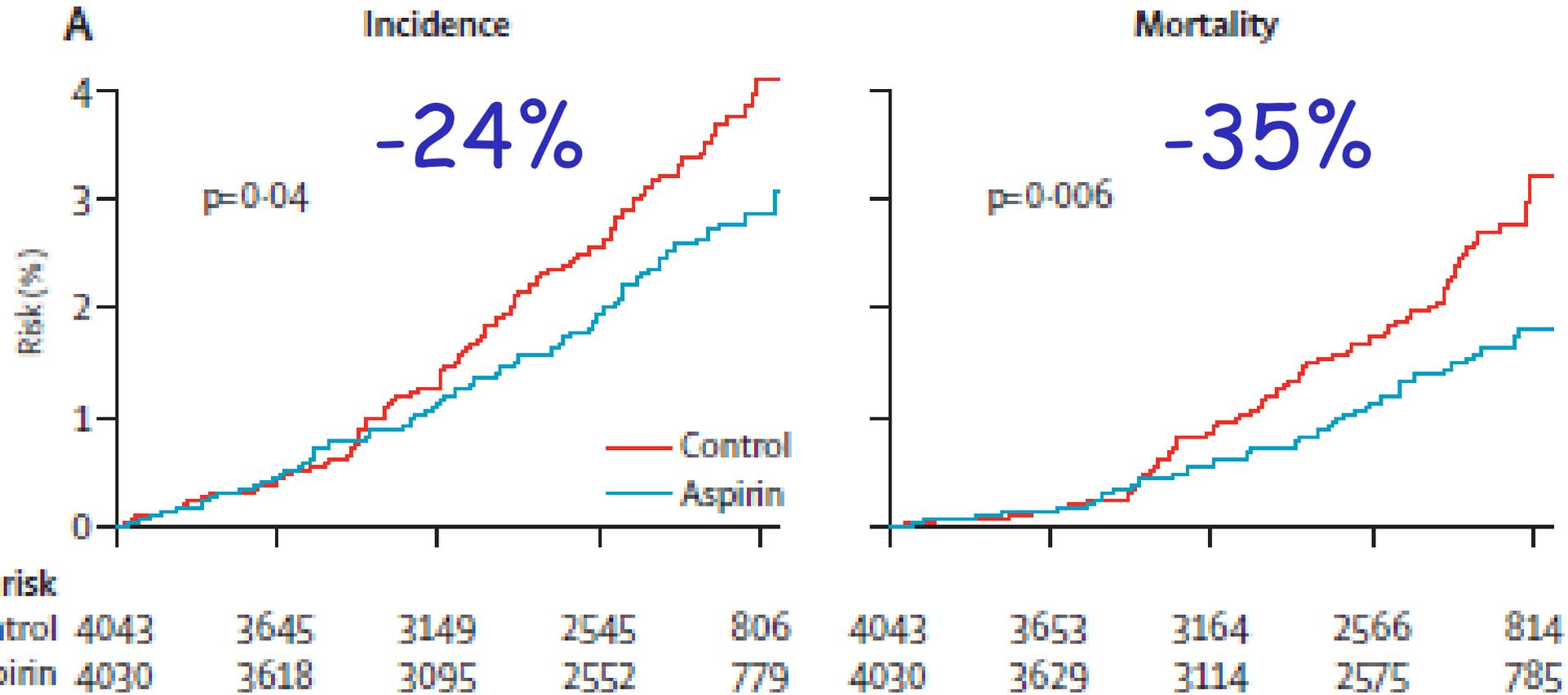
Colorectal cancer & aspirin : Cohort studies



Aspirin RCTs : adenomas



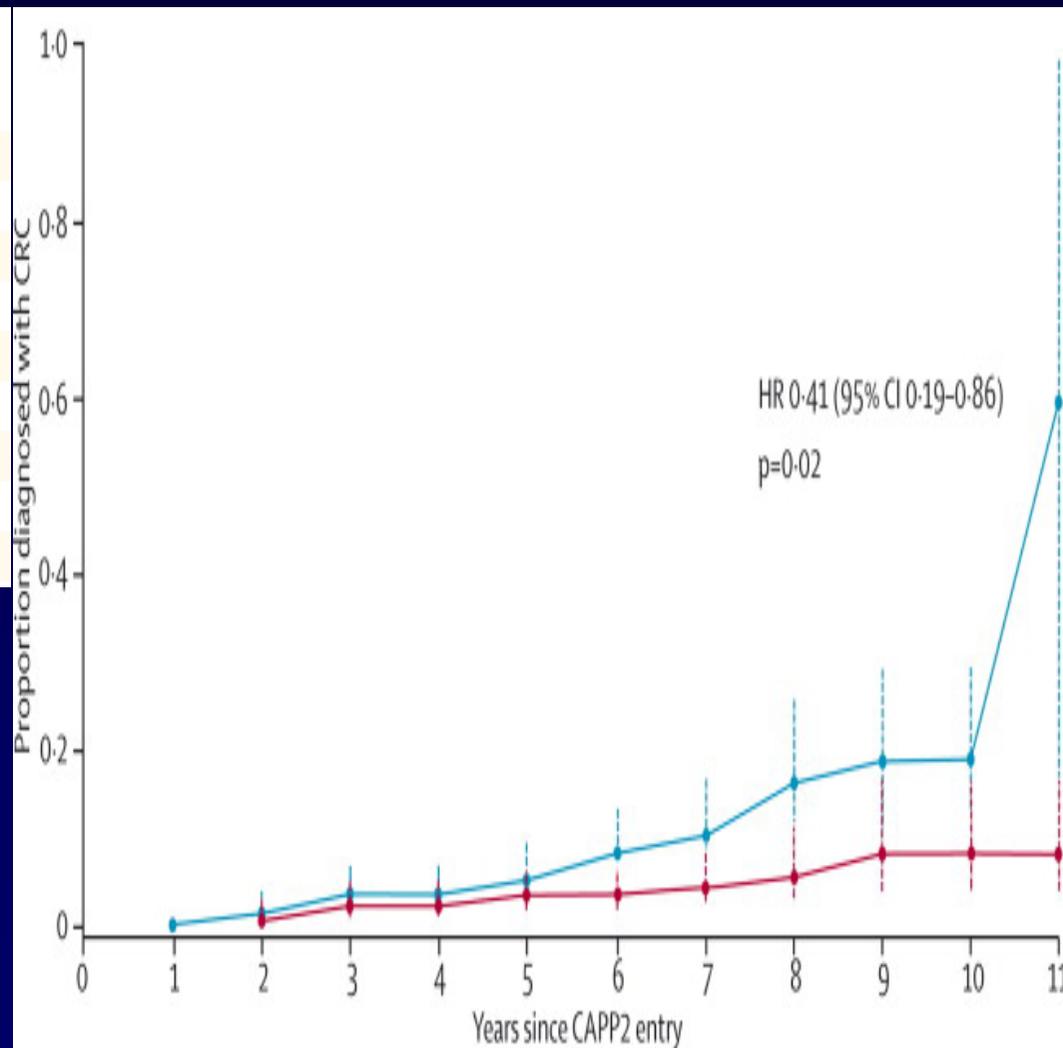
Aspirin RCTs : Colorectal cancer Secondary prevention



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Lynch & aspirin : CAPP2

Variable	Aspirin (N=350)	Placebo (N=343)	P Value
Development of neoplasia — no. of patients (%)			
No neoplasia	284	278	
Neoplasia	66 (18.9)	65 (19.0)	0.96
Adenoma only	56 (16.0)	55 (16.0)	0.96
Colorectal cancer only	5 (1.4)	7 (2.0)	0.54
Adenoma and colorectal cancer	5 (1.4)	3 (0.9)	0.45
Advanced adenoma or colorectal cancer	26 (7.4)	34 (9.9)	0.33
Neoplastic burden — mm ³			
Mean	8.7	9.4	0.7
Range	0.4–68	1–70	



600 mg per day during 29 months

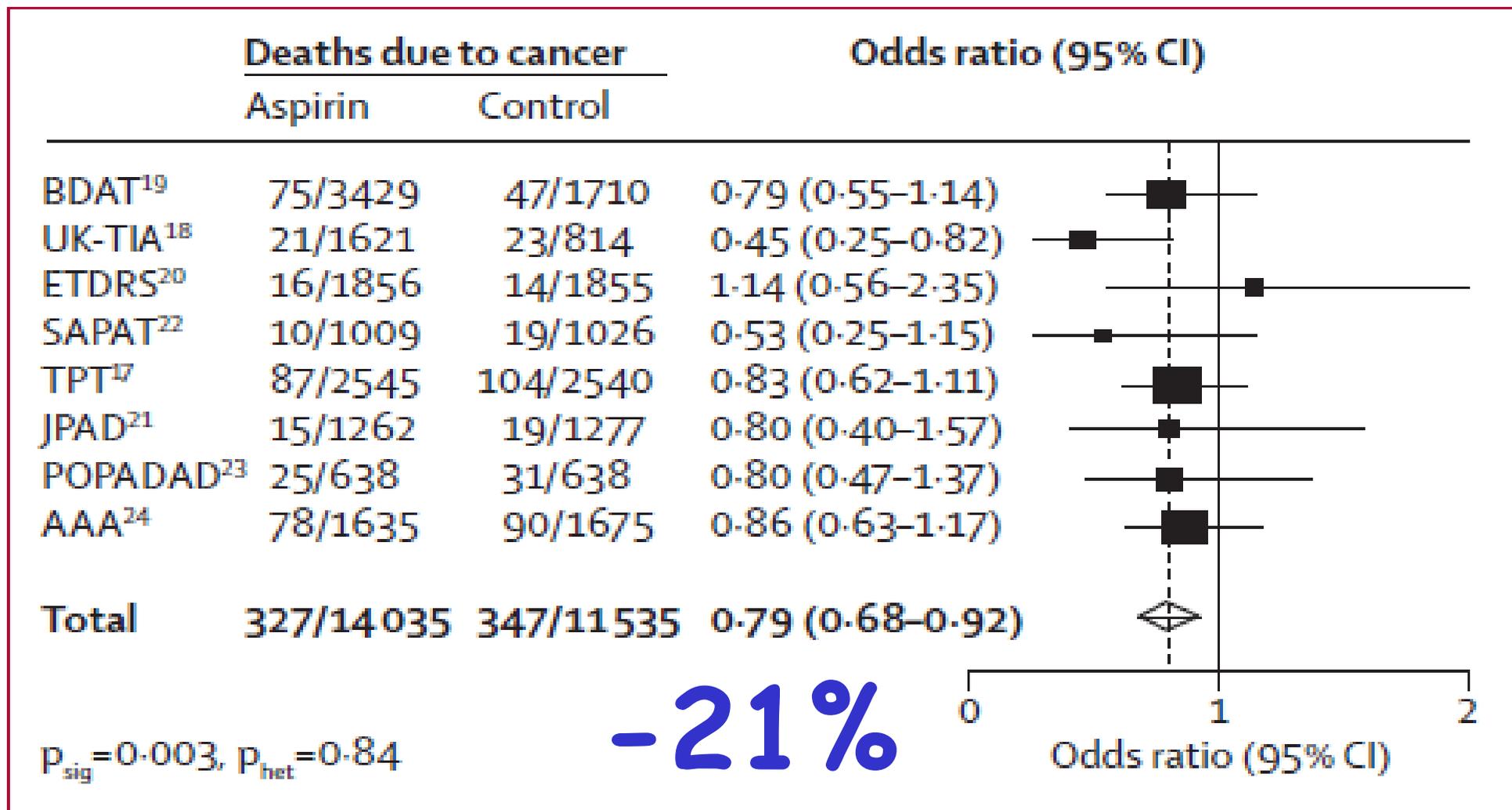
Burn, NEJM 2008 & Lancet 2011

Aspirin & other cancers

Case-control and cohort studies

Cancer	Studies (n)	Cases (n)	RR	95% CI
Oesophagus (SCC)	11	2193	0.61	0.50-0.76
Oesophagus/cardia (AdenoK)	11	3721	0.64	0.52-0.78
Gastric	13	4519	0.67	0.54-0.83
Pancreas	10	7877	0.91	0.83-1.01
Lung	20	16 219	0.91	0.84-0.99
Endometrial	9	3481	0.92	0.82-1.02
Breast	32	52 926	0.90	0.85-0.95
Ovarian	15	8940	0.91	0.81-1.01
Prostate	24	37 452	0.90	0.85-0.96
Bladder	9	6982	0.95	0.83-1.07
Kidney	10	5338	1.14	0.95-1.37

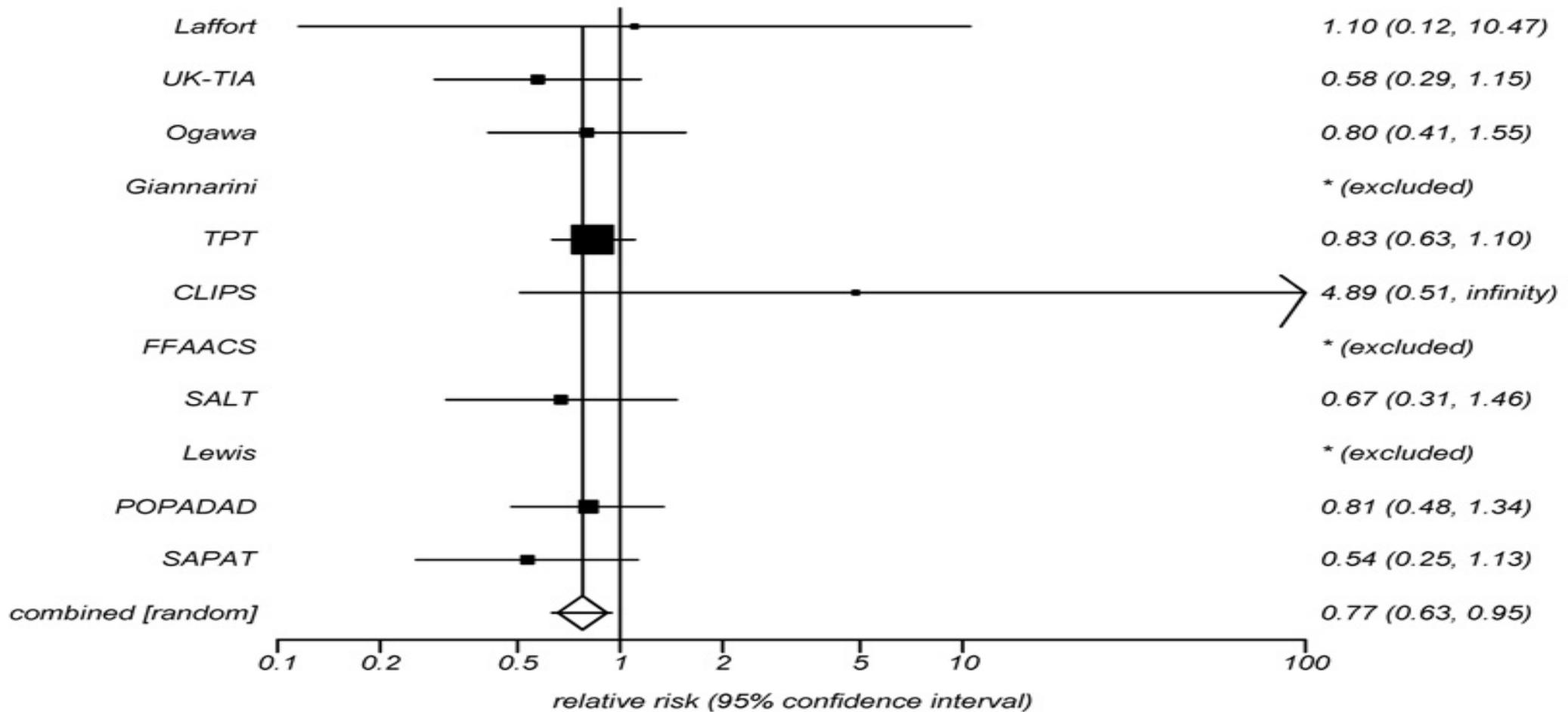
Aspirin RCTs : all cancer mortality



RCTs : all cancer mortality

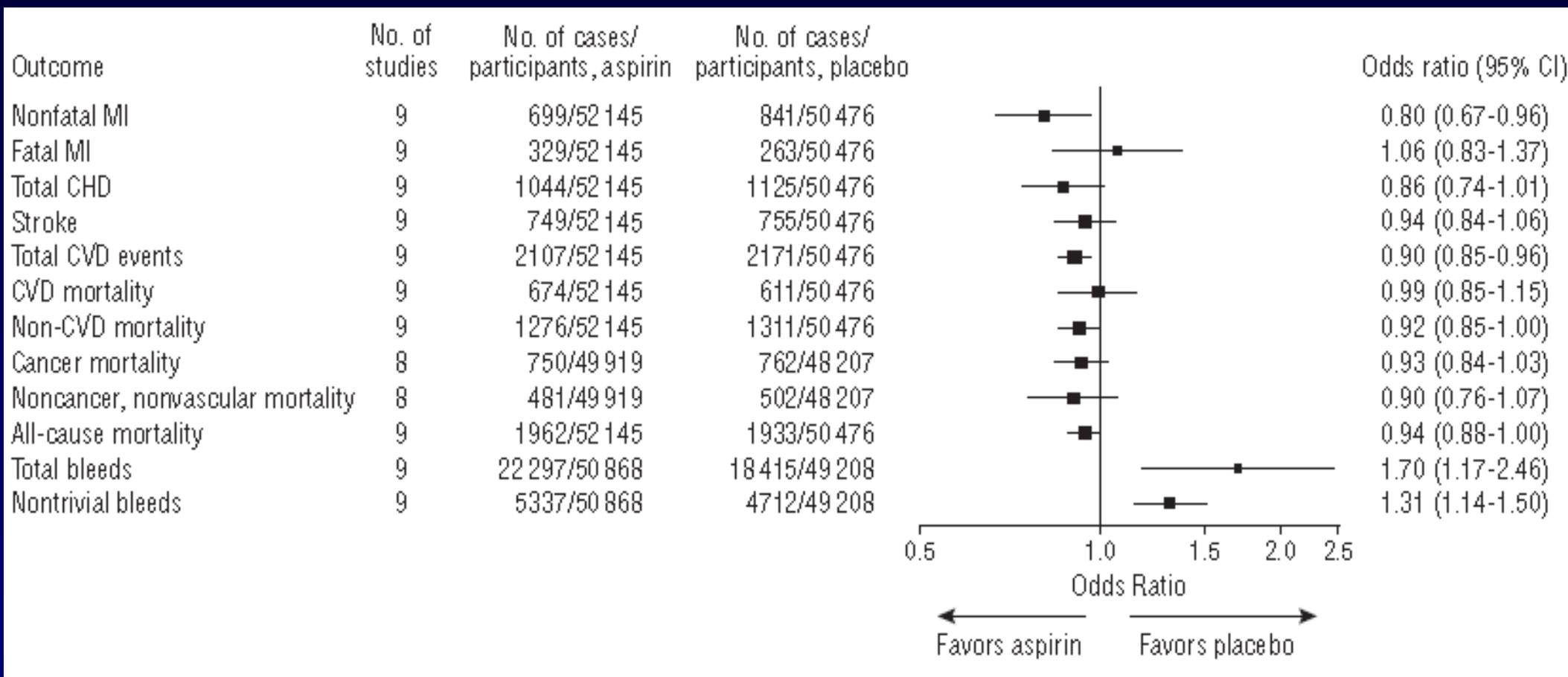
Secondary prevention

Relative risk meta-analysis plot (random effects)



RCTs : vascular and all cancer mortality

Primary prevention

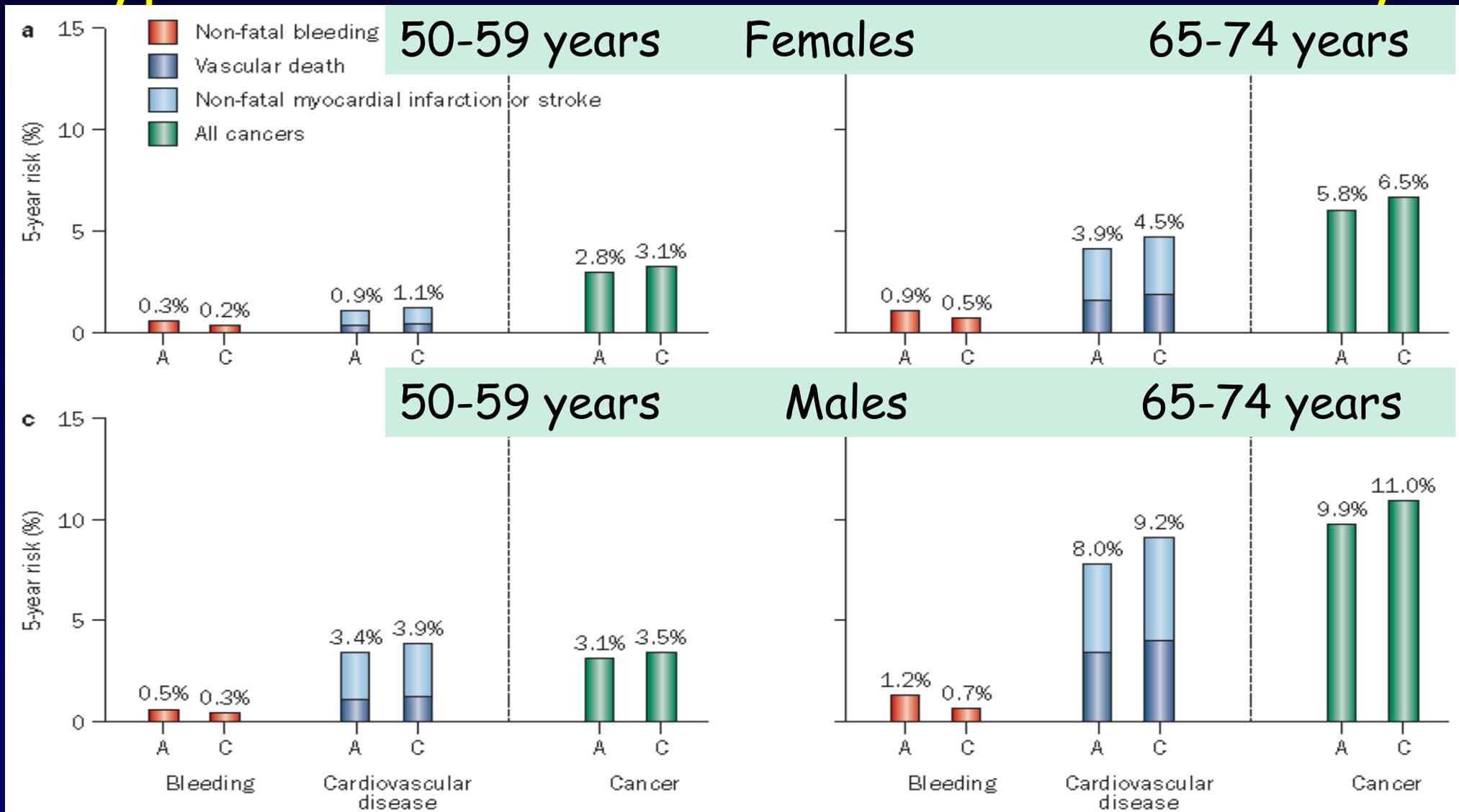


Major aspirin safety issues

- GI ulcers
- GI Bleeding +
 - Significant GI bleeding : HR = 1.55 (CI 1.27-1.90)
 - 1 to 2 significant bleeds / 1000 person-years
 - Lower risk for low dose aspirin ?
- Intracranial bleeding ++
 - HR = 1.43 (CI 0.85-2.42)
 - 1 or 2 / 10 000 person-years

Risk-benefit issues

Hypothesis : 10% reduction in cancer mortality

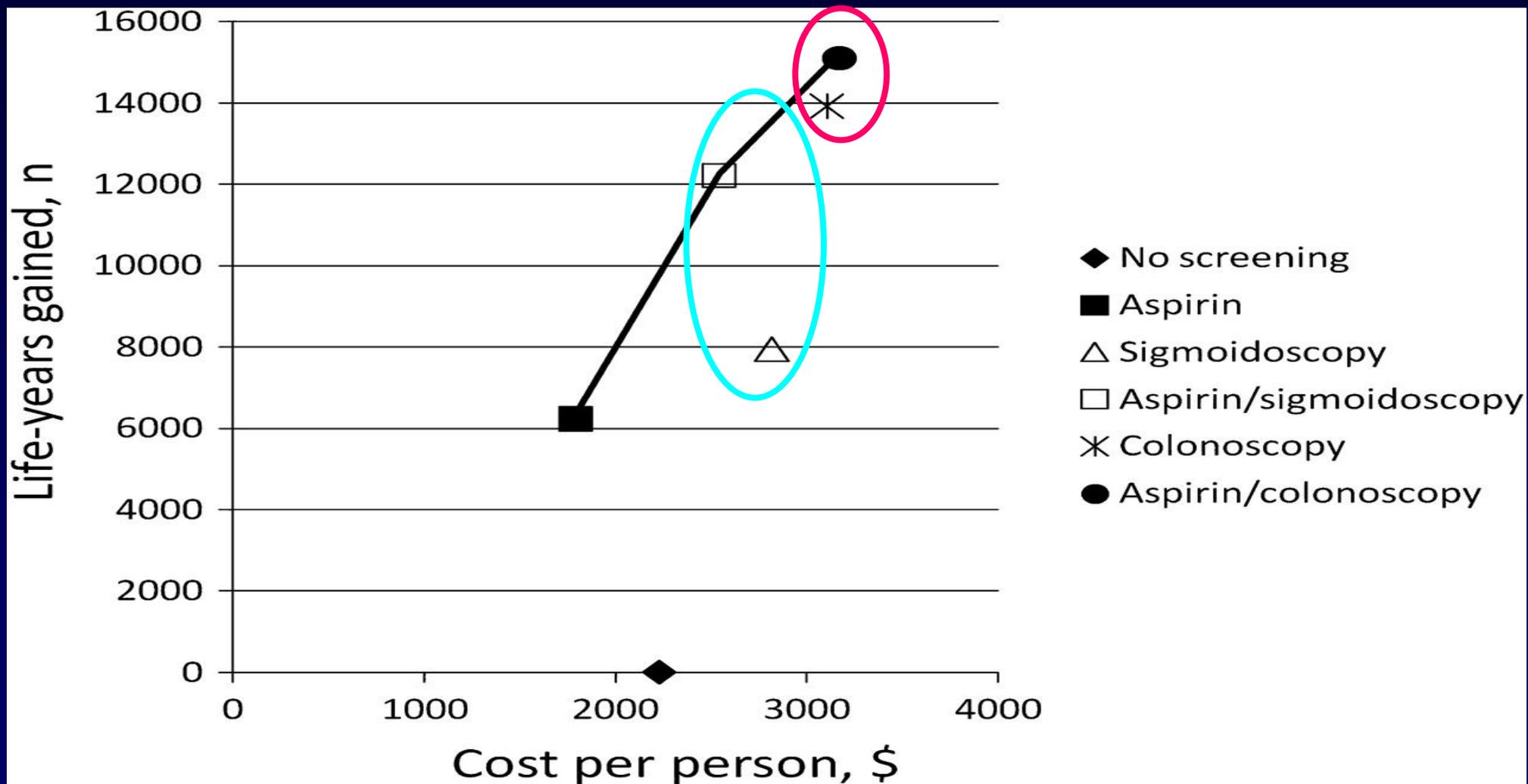


Is aspirin protection predated by endoscopy ?

Benefit for a cohort of 100 000 subjects included in 20 years prevention programmes

	No screening	Aspirin	Sigmoidoscopy	Sigmoidoscopy + Aspirin	Colonoscopy	Colonoscopy + Aspirin
CRC cases	5903	3858	4078	2487	1759	1105
CRC prevent. rate		35%	31%	58%	68%	78%
CRC deaths	2842	1458	1503	779	803	477
Life-years gained		+ 6232	+ 7945	+ 12 215	+ 13 922	+ 15 108

Is aspirin protection predated by endoscopy?

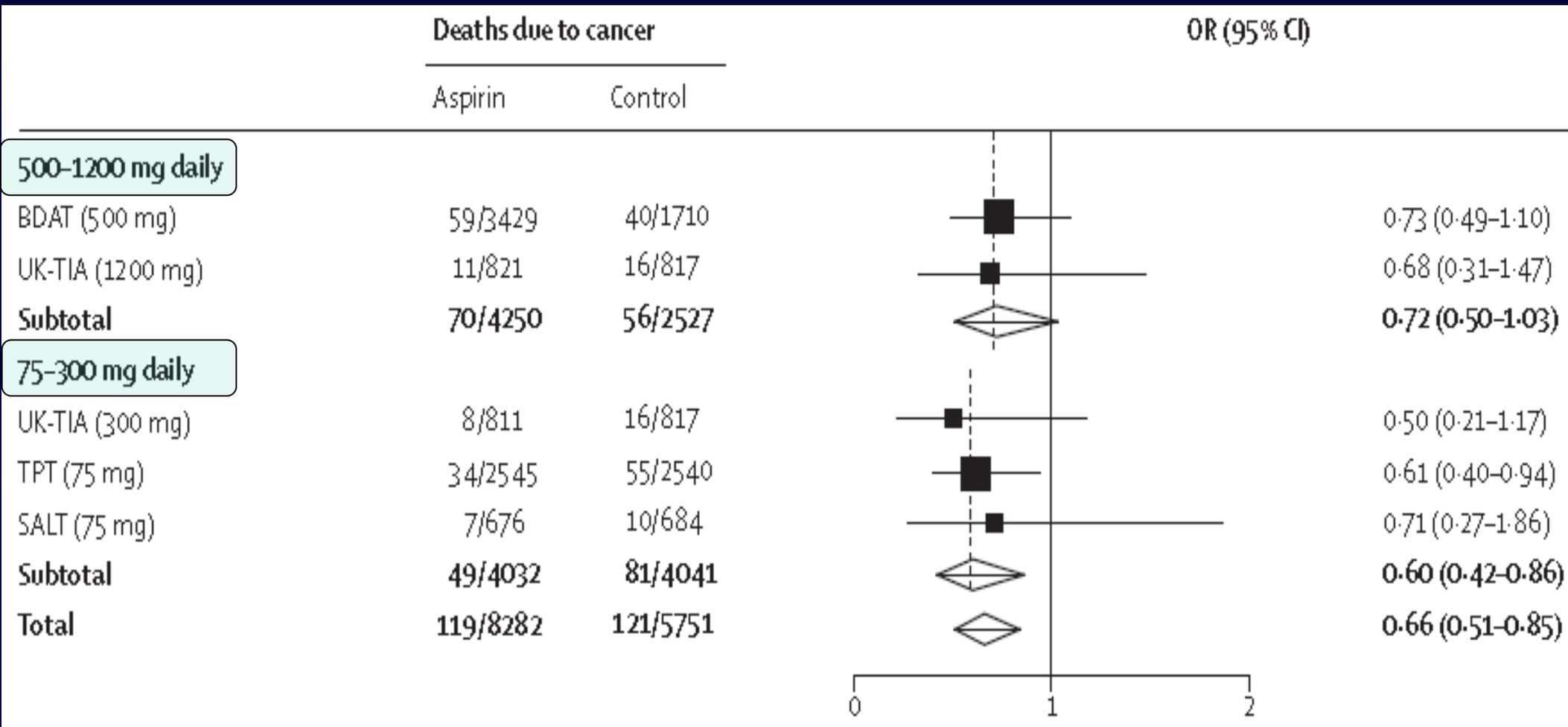


Colorectal cancer chemoprevention

- Aspirin is effective
- Aspirin is efficient
- Modalities & targets ?

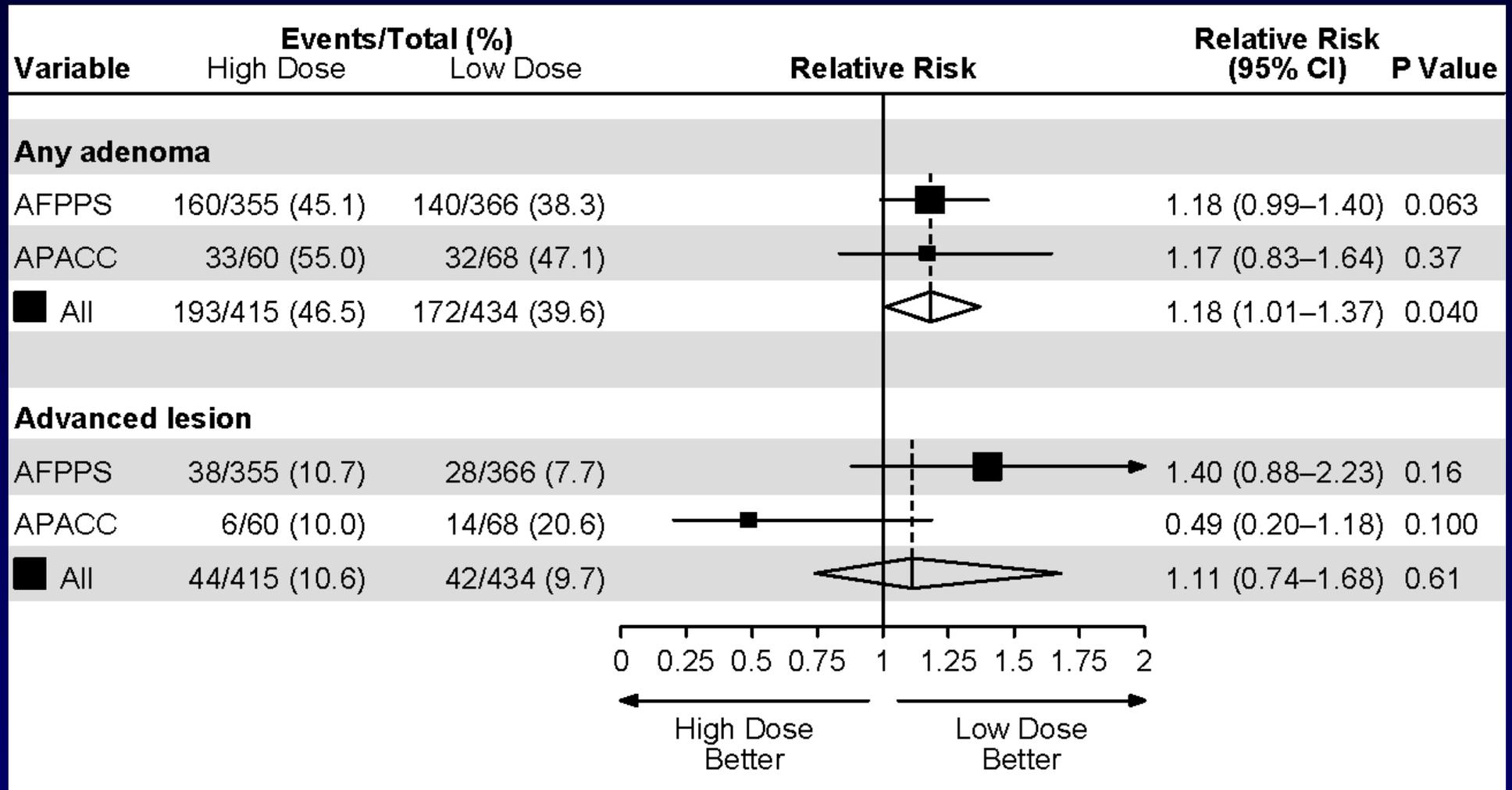
Aspirin Dose in RCTs

Low dose better ?

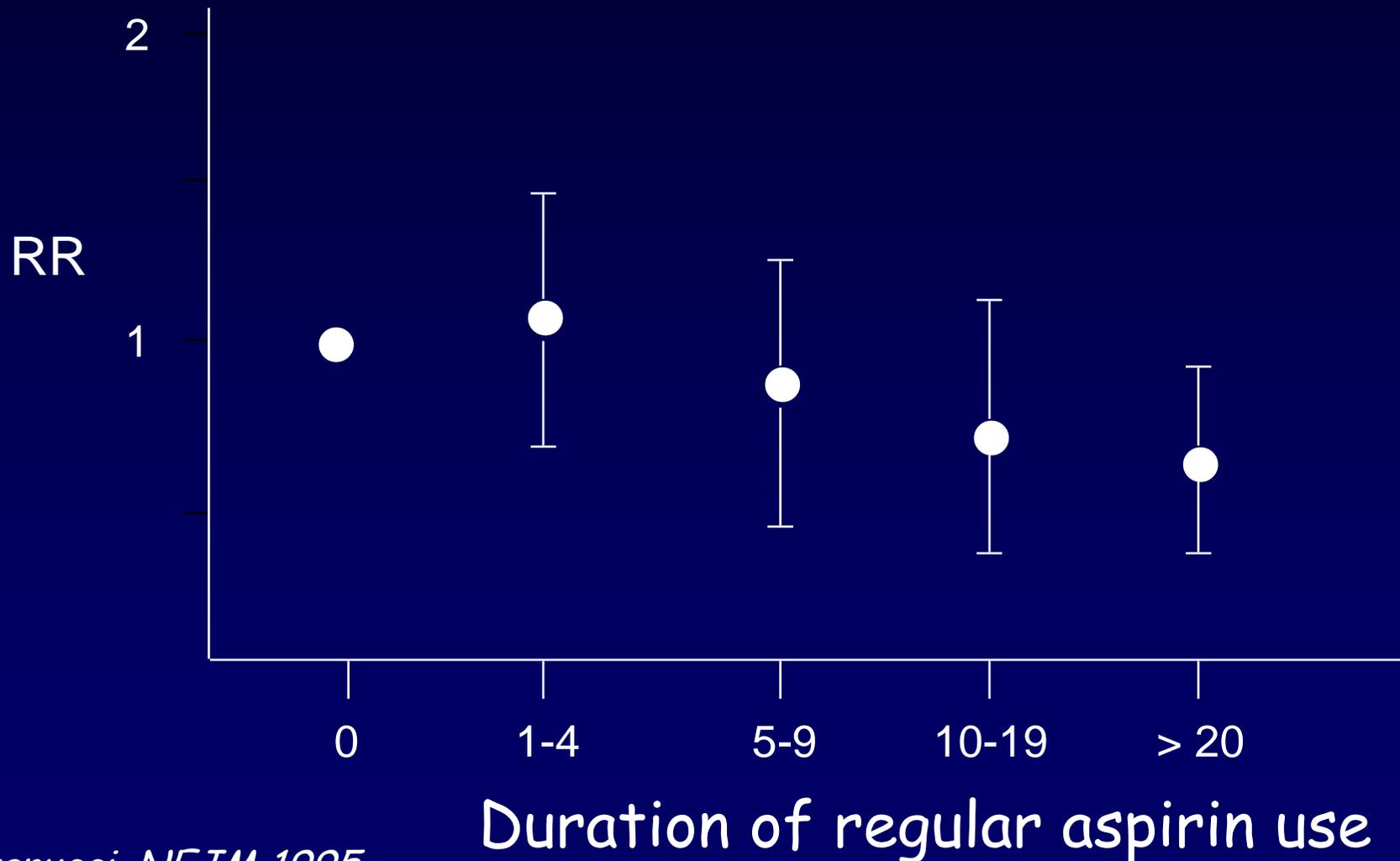


Aspirin Dose in RCTs

Low dose better ?



How long to treat: A long term effect



Aspirin prevention modalities ?

Dose ?	Yes : the lower (75-300 mg)
Treatment duration ?	Yes : the longest possible
Target population ?	Primary prevention ? Secondary prevention ? None ?

Aspirin targets

- Discussed on a personal basis in :
- Healthy people with increased vascular risk
 - 10 year risk > 10%
- Healthy people with increased cancer risk
- People with vascular conditions
- People with advanced colorectal adenomas, particularly those with proximal lesions

« Standard risk » ?



- Age
- Sex
- BMI
- Exercice
- Diet
- Tobacco

- Vascular risk factors

