

Faut il prescrire de l'aspirine pour prévenir et pour traiter le cancer colorectal ?

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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

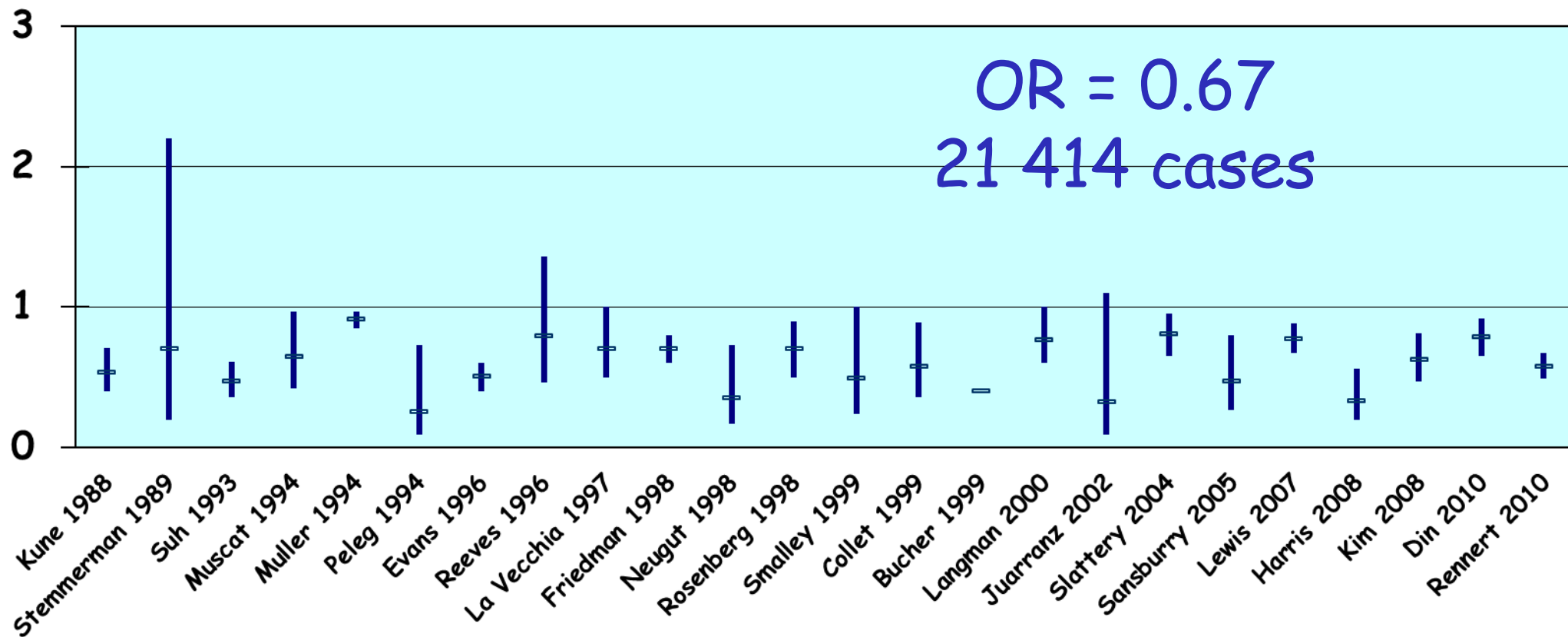
Aspirin and Colorectal carcinogenesis

Animal experiments

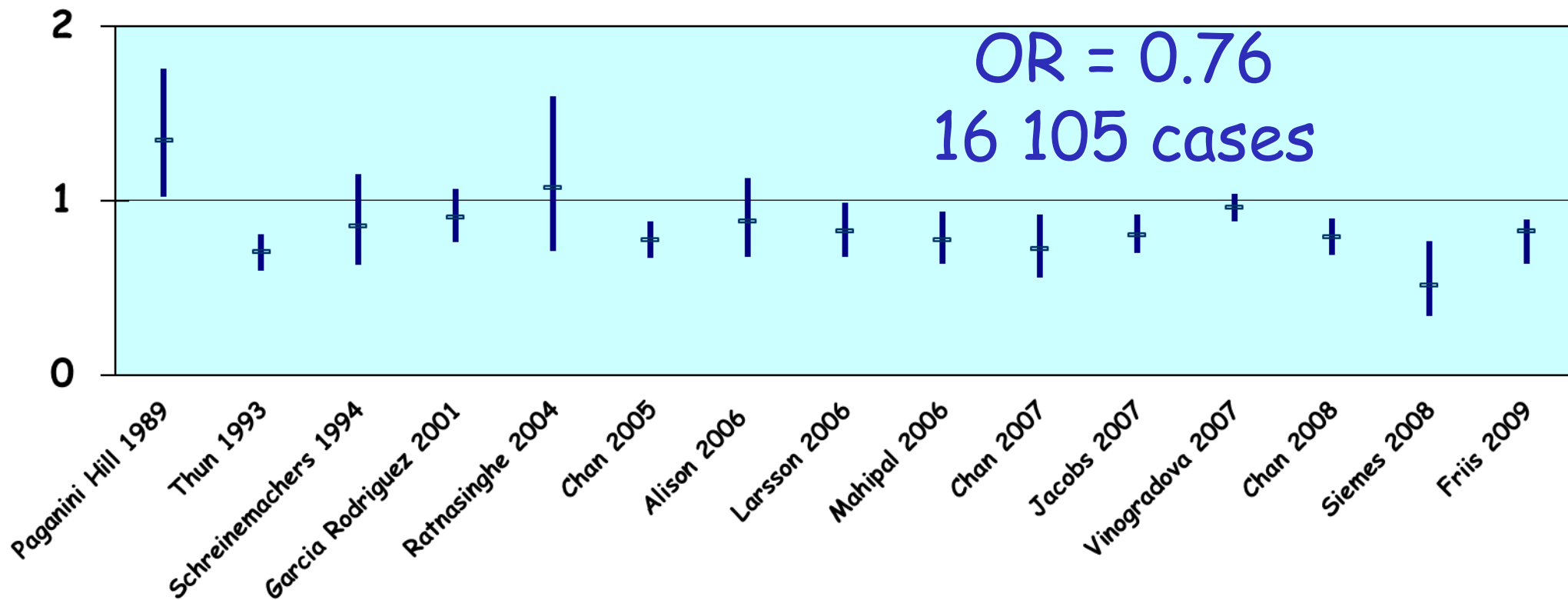
- Number of animals with tumors
- Number of tumors per animal
- Early step of carcinogenesis: Aberrant crypt foci
- Before and after carcinogen administration

- Low and high dose
- Reversible

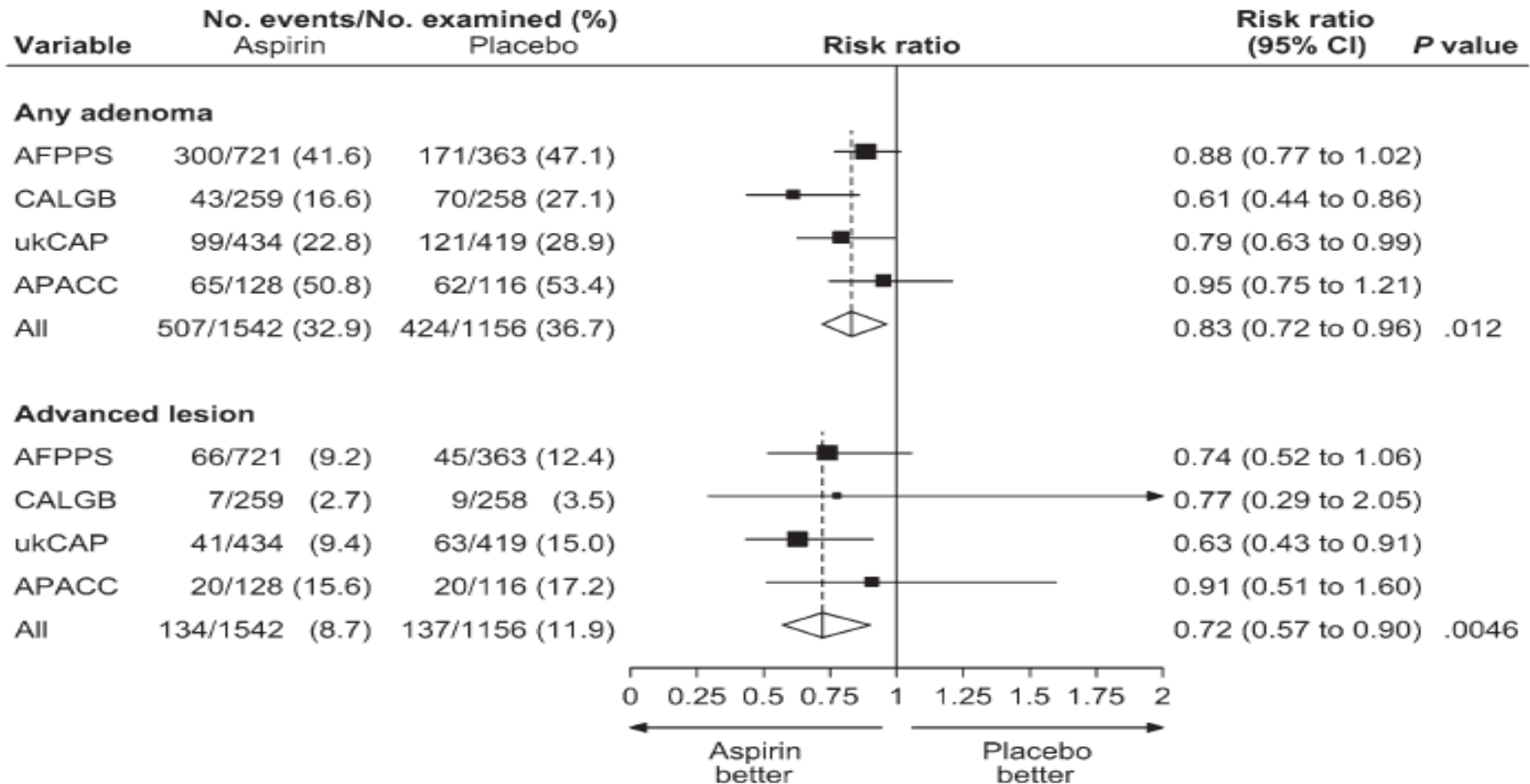
Colorectal cancer & aspirin : Case-control studies



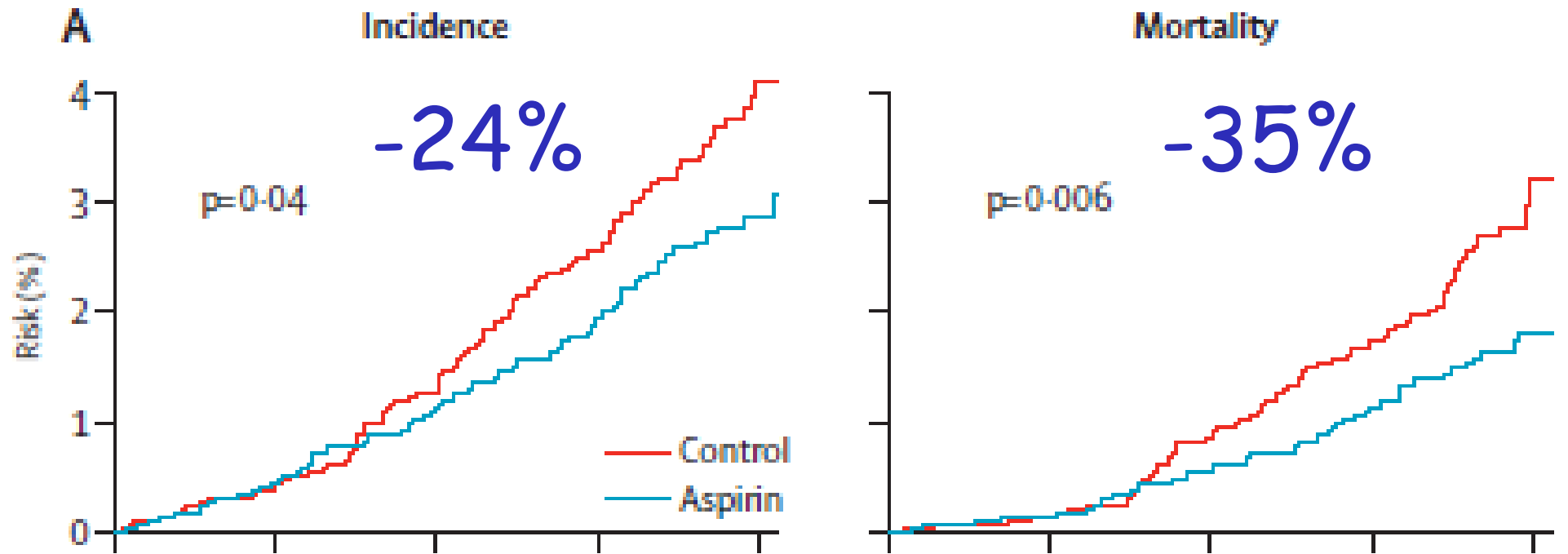
Colorectal cancer & aspirin : Cohort studies



Aspirin RCTs : adenomas



Aspirin vascular RCTs : Colorectal cancer



Number at risk

Control	4043	3645	3149	2545	806	4043	3653	3164	2566	814
Aspirin	4030	3618	3095	2552	779	4030	3629	3114	2575	785

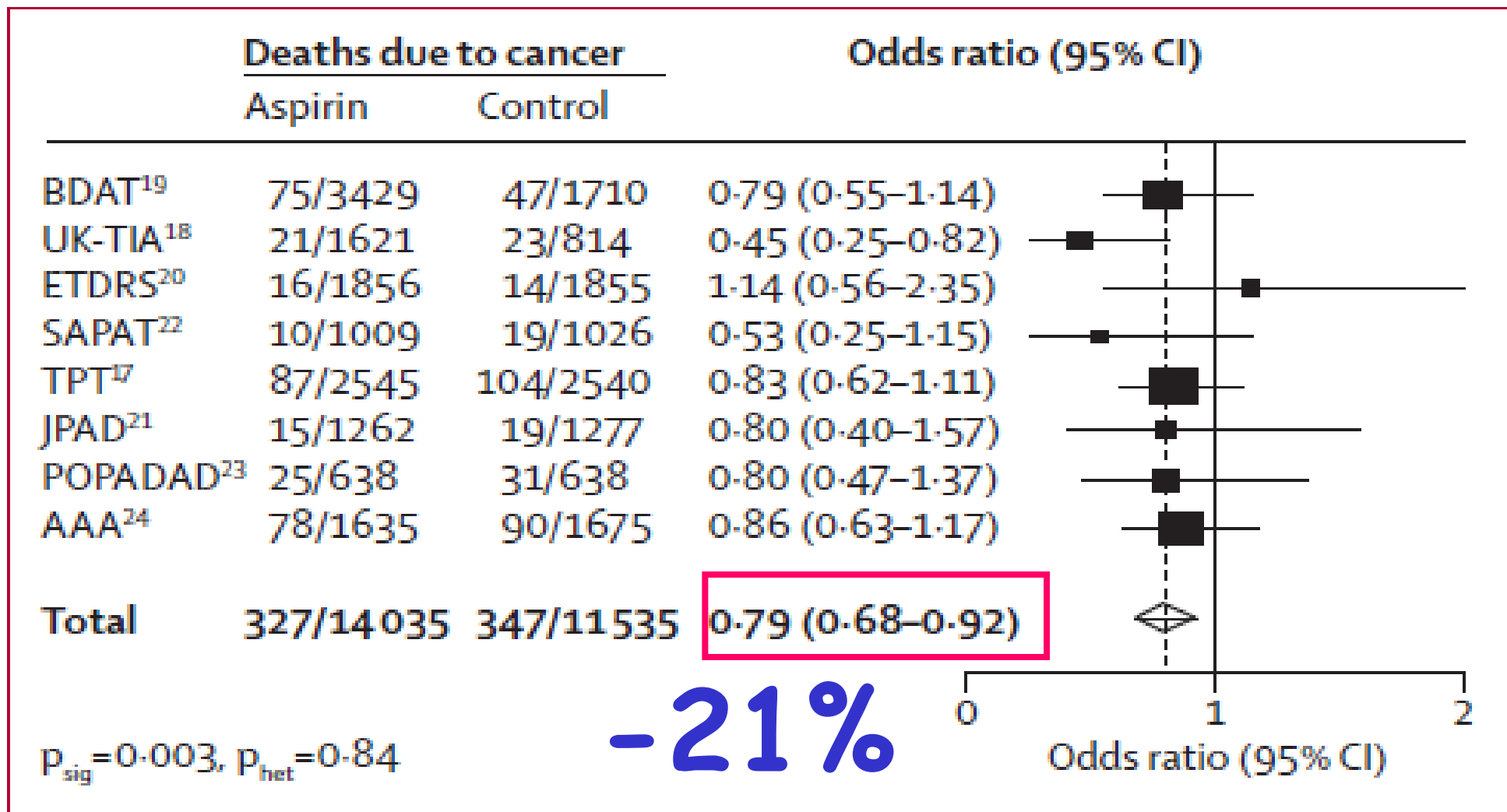
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Aspirin & other cancers

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



Adjuvant aspirin after colorectal cancer in patients : overall mortality

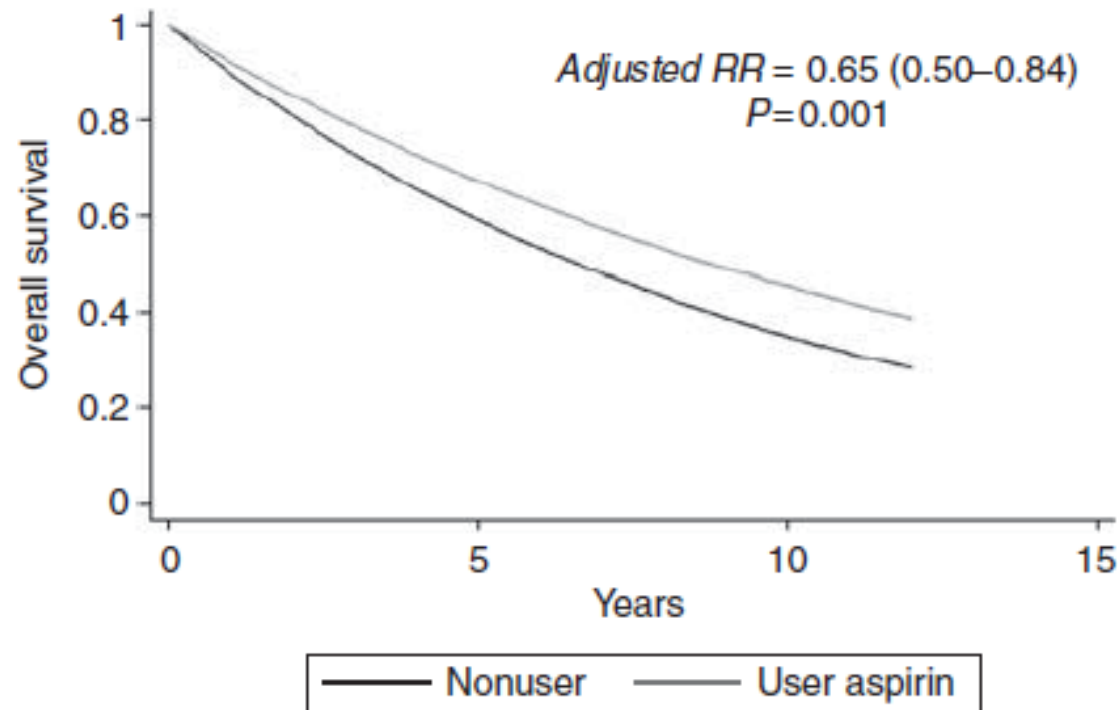


Figure 1 Survival curve for overall survival in colon cancer patients according to non-user/user of aspirin.

Adjuvant aspirin after colorectal cancer in patients > 70 years

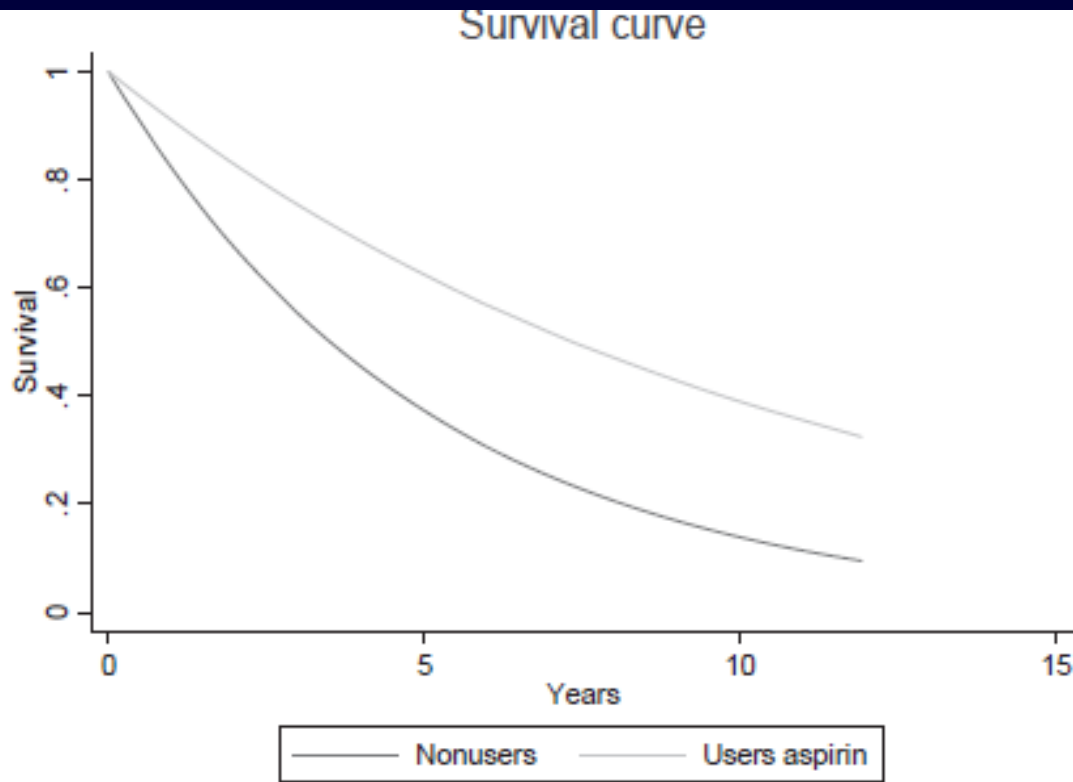
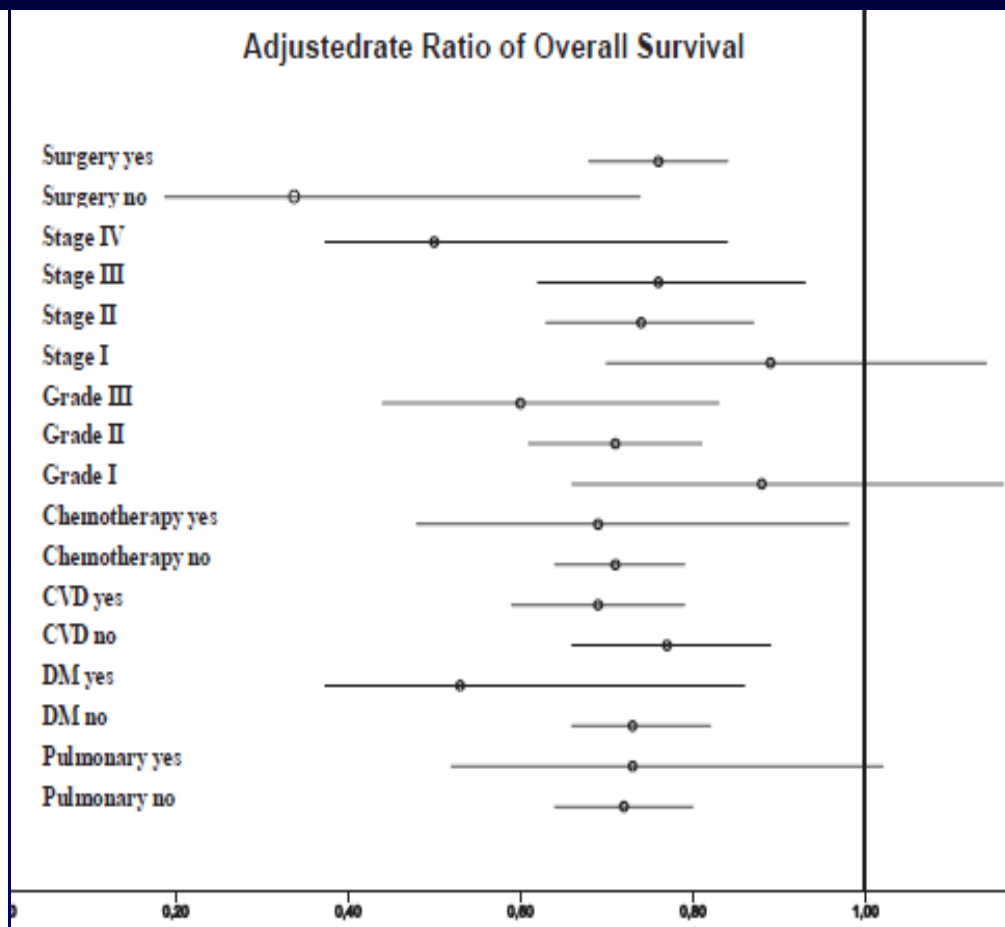
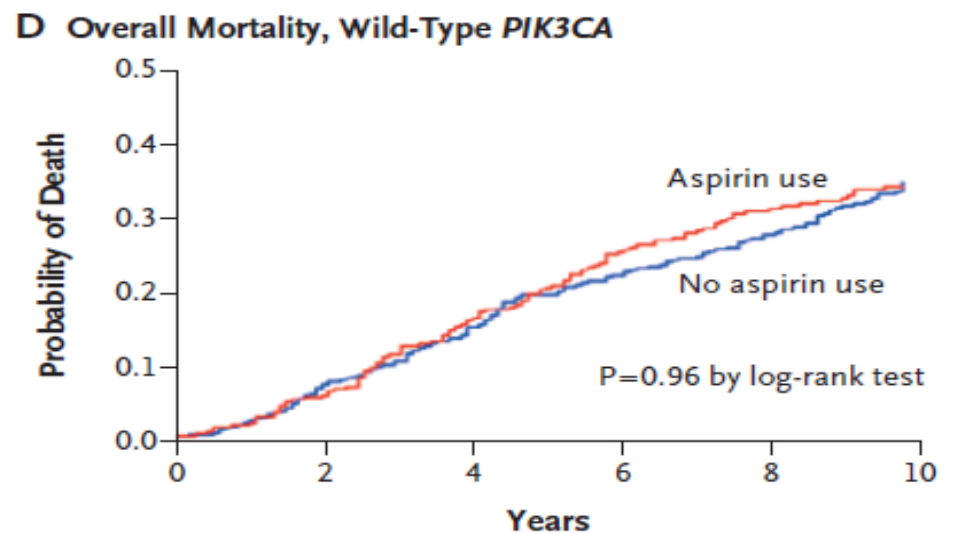
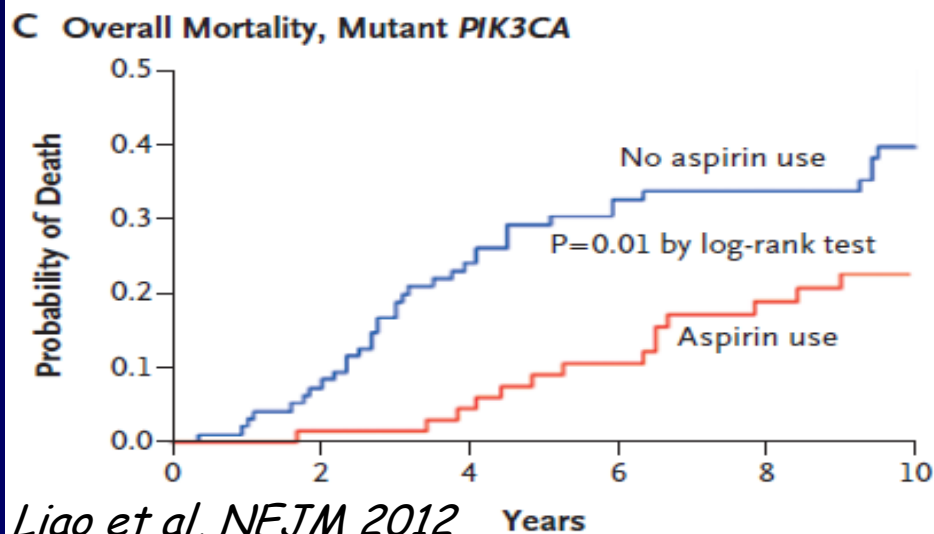
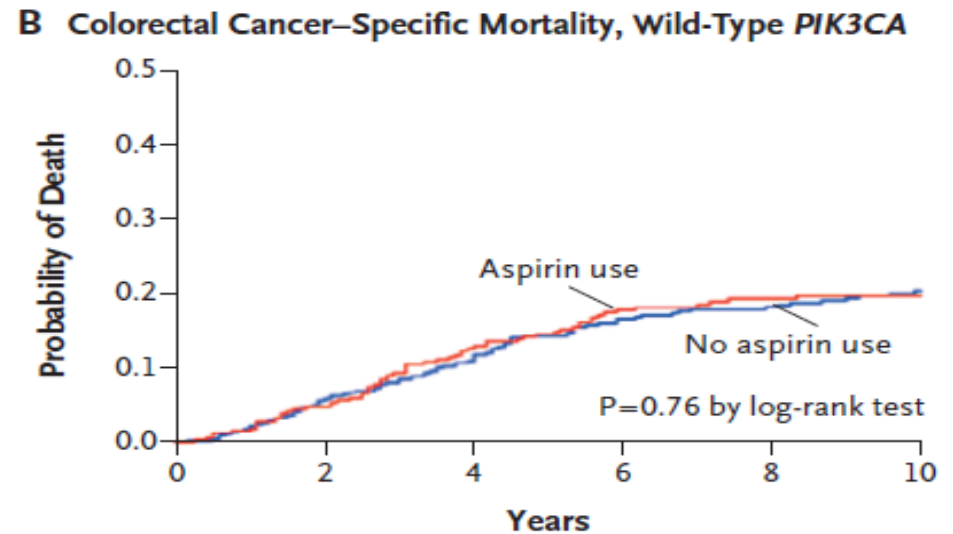
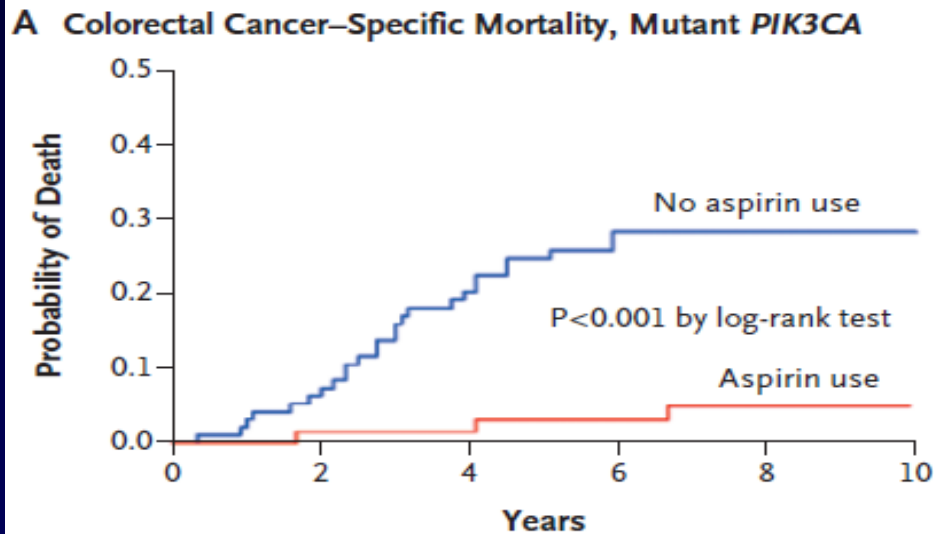


Figure 1. Survival curve for overall survival in older adults with colon cancer according to use of aspirin.



Adjuvant aspirin in colorectal cancer : a PI3K mutation effect

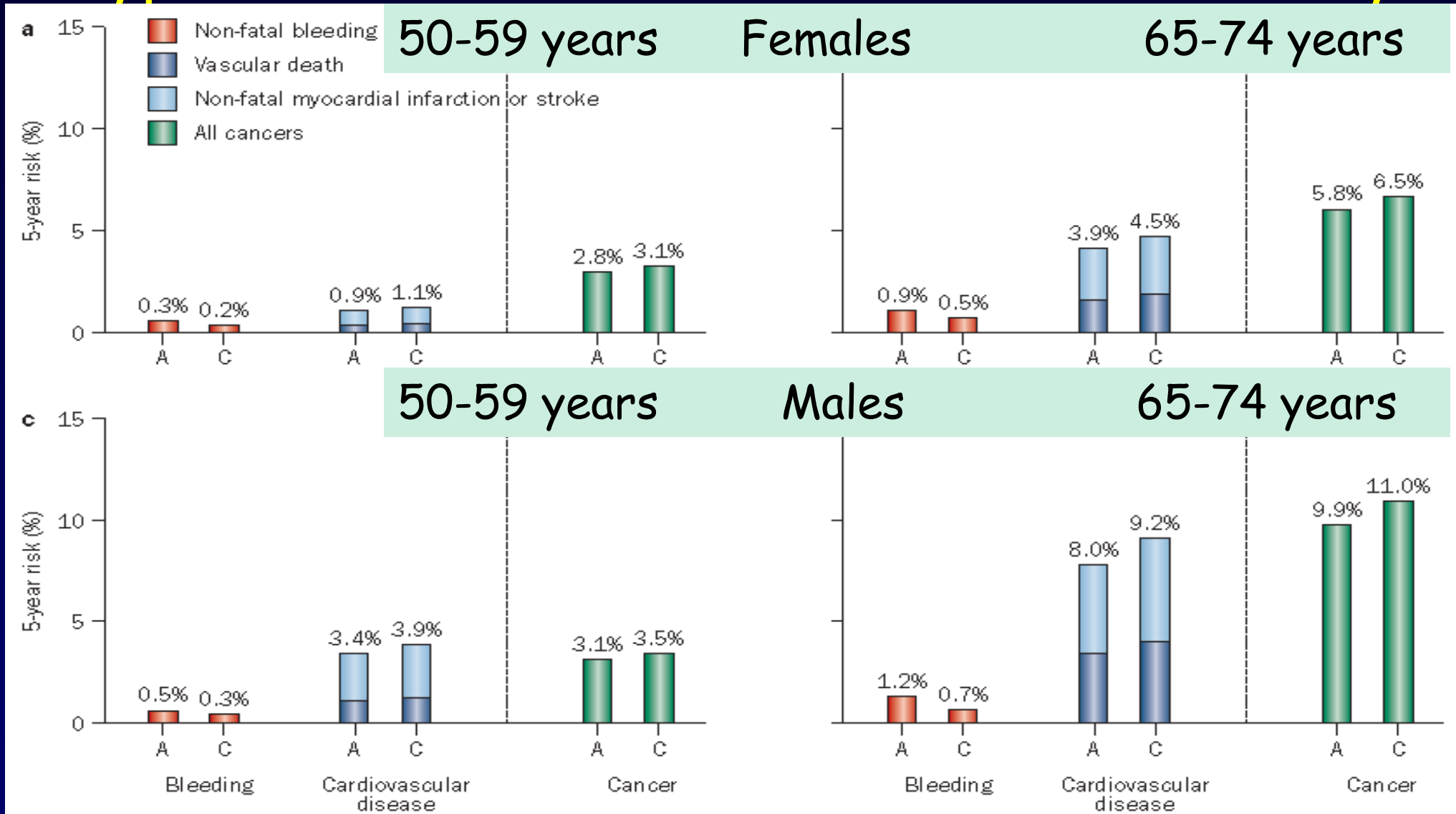


Major aspirin safety issues

- 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

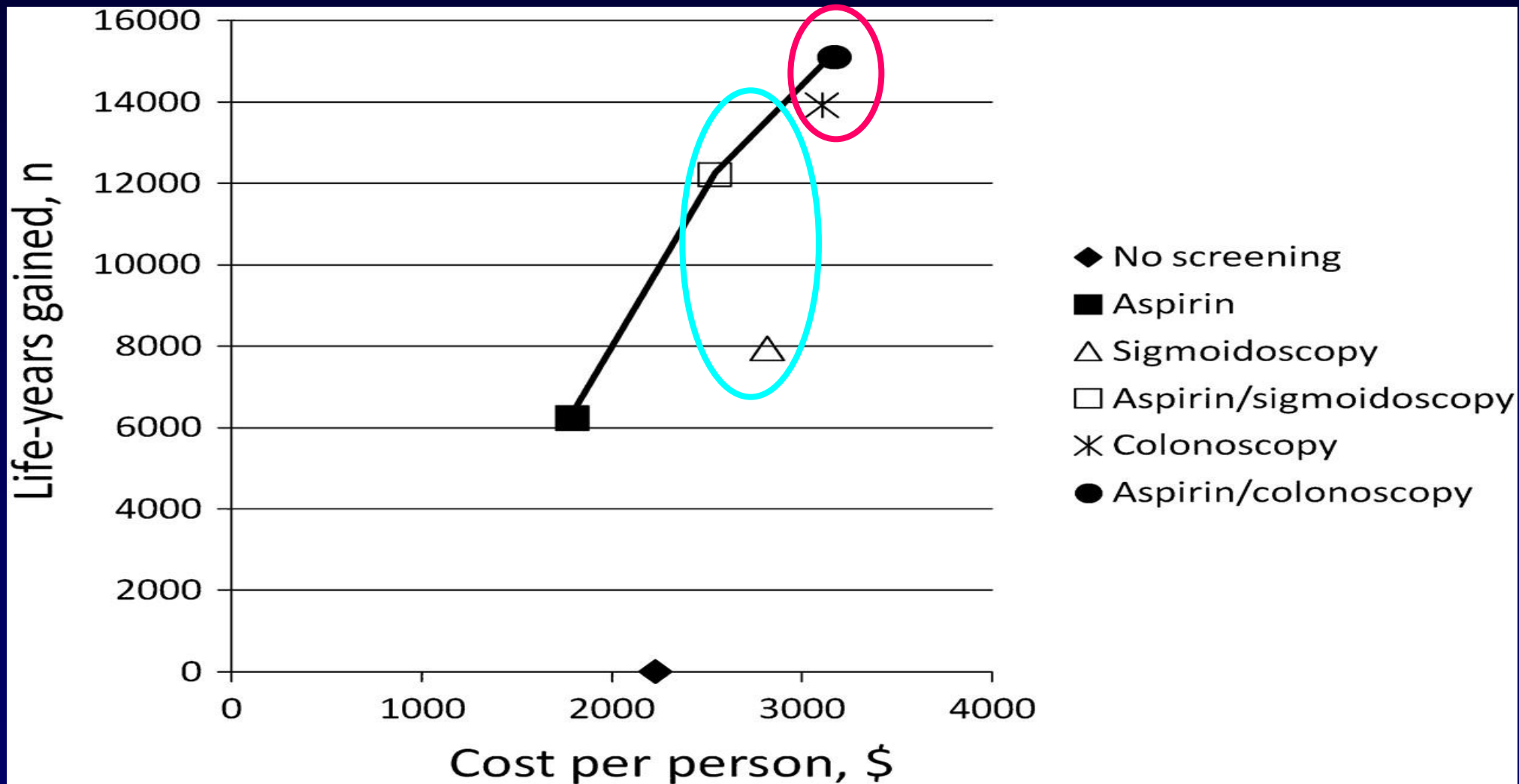


Is aspirin protection predated by endoscopy ?

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?



Aspirin prevention modalities ?

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

Aspirin effect in high risk patients

- Reductions in colon cancer risk associated with aspirin use were not significantly modified by :
 - Body mass index
 - Physical activity
 - Plasma C-peptide level