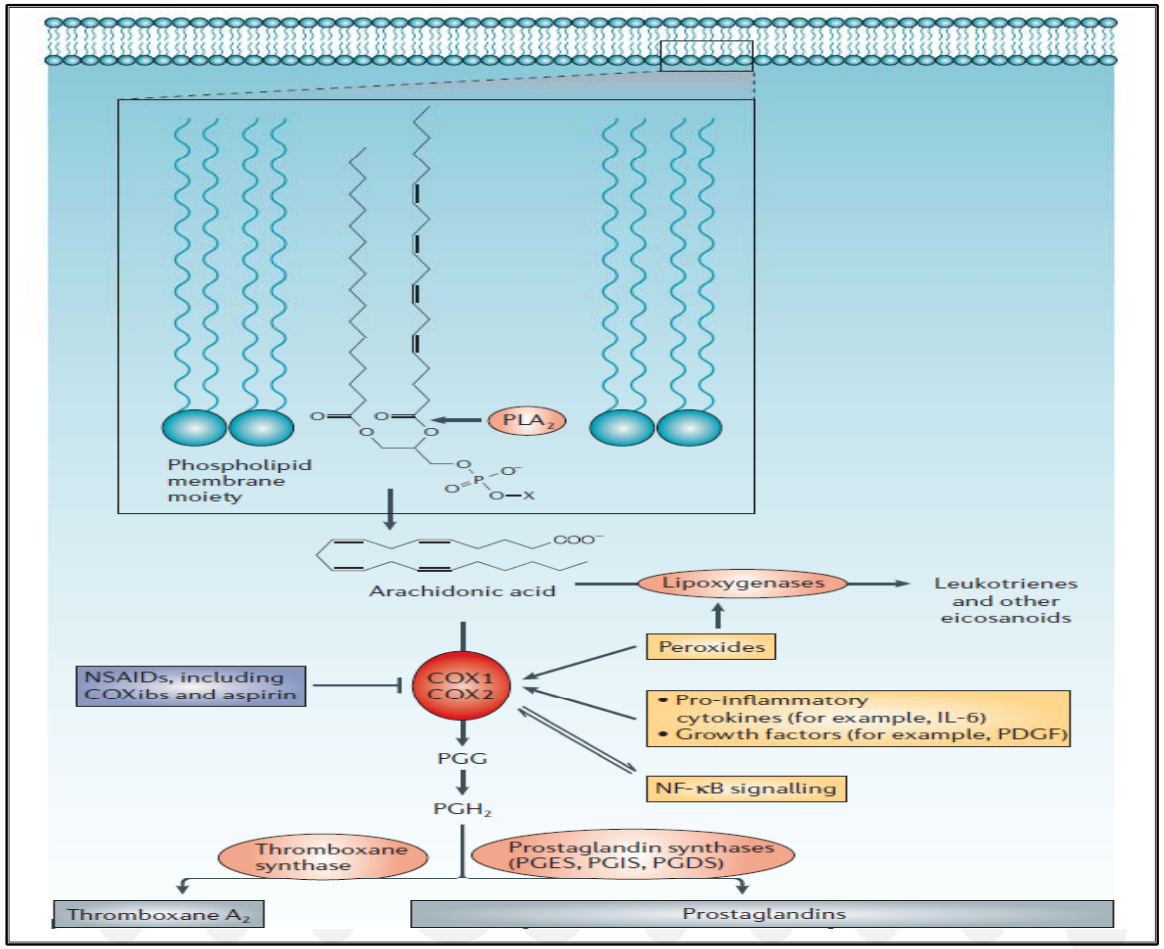
Aspirine et Cancer Colorectal

Dr David Sefrioui, 26 septembre 2013

Aspirine_Mécanismes d'action

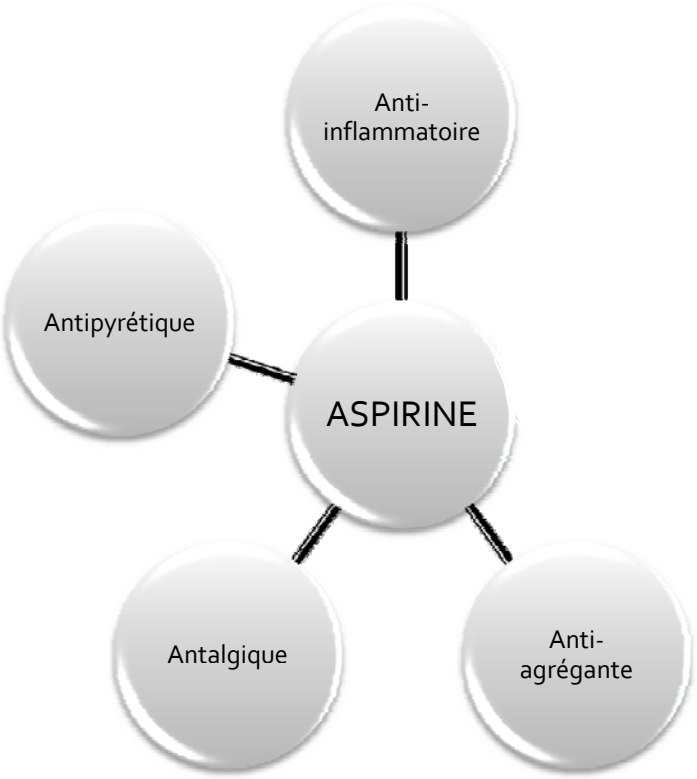


Ulrich CM et al., Nature Reviews Clancer 2011

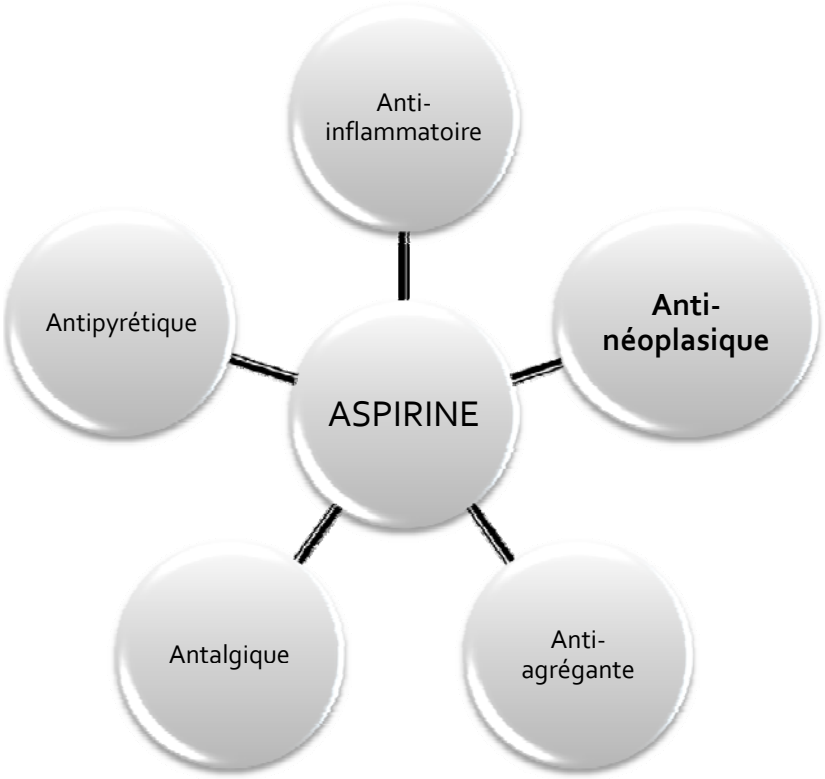
John Vane

Prix Nobel de médecine 1982

Aspirine_Propriétés pharmacologiques



Aspirine_Propriétés pharmacologiques



Colorectal Cancer Risk, Chronic Illnesses, Operations, and Medications: Case Control Results from the Melbourne Colorectal Cancer Study

Gabriel A. Kune, Susan Kune and Lyndsey F. Watson

Cancer Res 1988;48:4399-4404.

Medication	Status	Total (cases, n = 713; controls, n = 727) No. using	RR	CI	P
Aspirin and aspirin containing	Case	85			
	Control	147	0.53	0.40–0.71	<0.001

Aspirine_ Adénomes colorectaux

Prévention secondaire

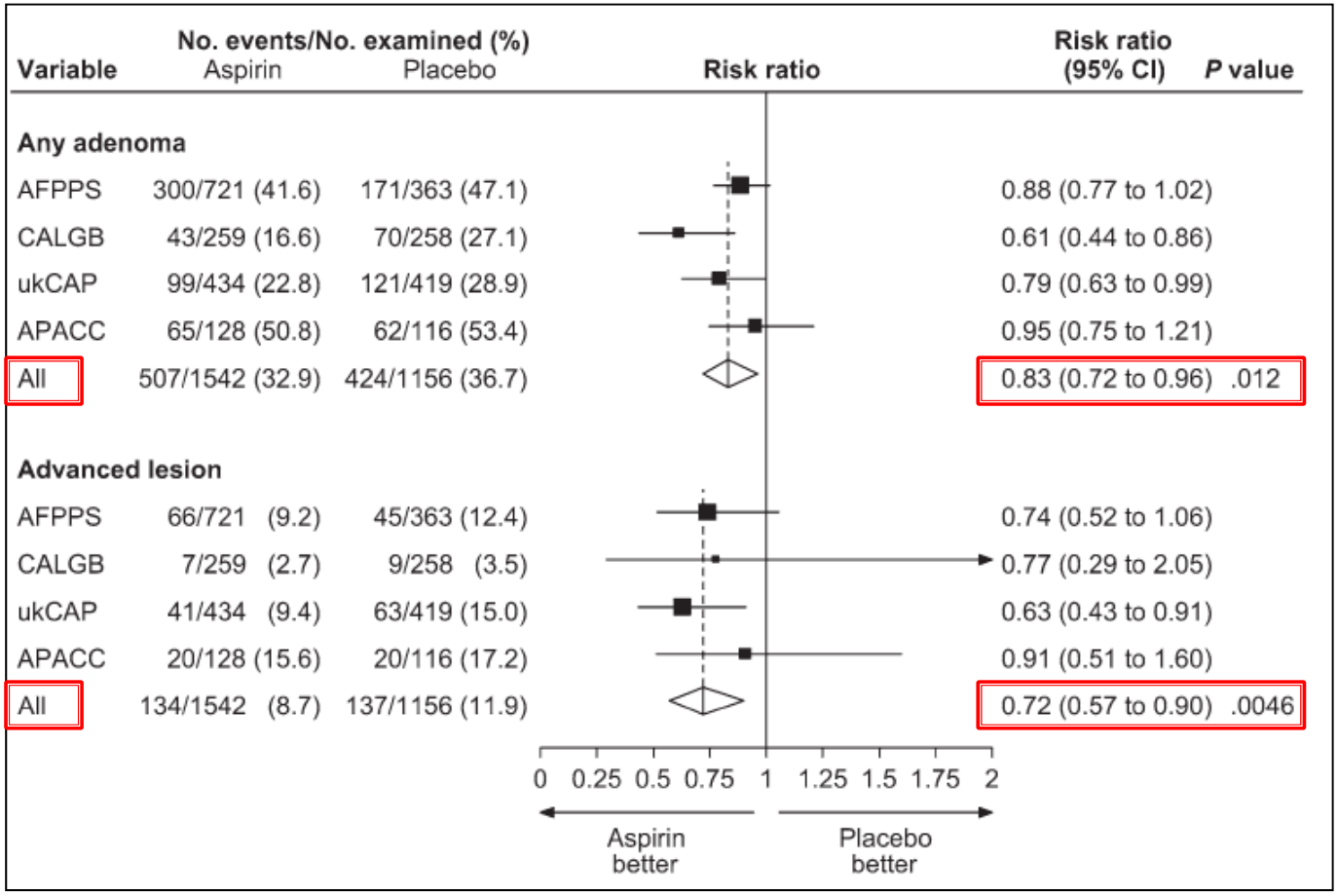
	APACC [1]	AFPPS [2]	CALGB [3]	ukCAP [4]
Design	• Randomized-controlled trial • Aspirin (160 or 300 mg/d) or placebo • Follow-up: 4 y	• Randomized-controlled trial • Aspirin (81 or 325 mg/d) or placebo • Follow-up: 3 y	• Randomized-controlled trial • Aspirin (325 mg/d) or placebo • Median follow-up: 12.8 mo	• Randomized trial • Aspirin (300 mg/d) or folate supplement (0.5 mg/d) • Follow-up: 3 y
Patients (*n*)	272	1,121	635	945
Adenoma inclusion criteria	Recent history of colorectal adenomas	Recent history of colorectal adenomas	Previous history of CRCs	Recent history of colorectal adenomas
Family history of adenomas (%)	34.6	30.4	Not reported	14.1
Risk ratio (95% CI) for any adenoma[b]	0.95 (0.75–1.21)	0.88 (0.77–1.02)	0.61 (0.44–0.86)	0.79 (0.63–0.99)
Risk ratio (95% CI) for advanced adenoma[b]	0.91 (0.51–1.60)	0.74 (0.52–1.06)	0.77 (0.29–2.05)	0.63 (0.43–0.91)

Abbreviations: APACC, Association pour la Prévention par l'Aspirine du Cancer Colorectal; AFPPS, Aspirin Folate Polyp Prevention Study; CALGB, Cancer and Leukemia Group B; ukCAP, United Kingdom Colorectal Adenoma Prevention.

[1] Benamouzig et al. Gastroenterology 2003 ; [2] Baron et al. N Engl J Med 2003 ; [3] Sandler et al., N Engl J Med 2003 ; [4] Logan et al. Gastroentrology 2008

Chan et al. Cancer Prev Res 2012

Aspirine_ Adénomes colorectaux



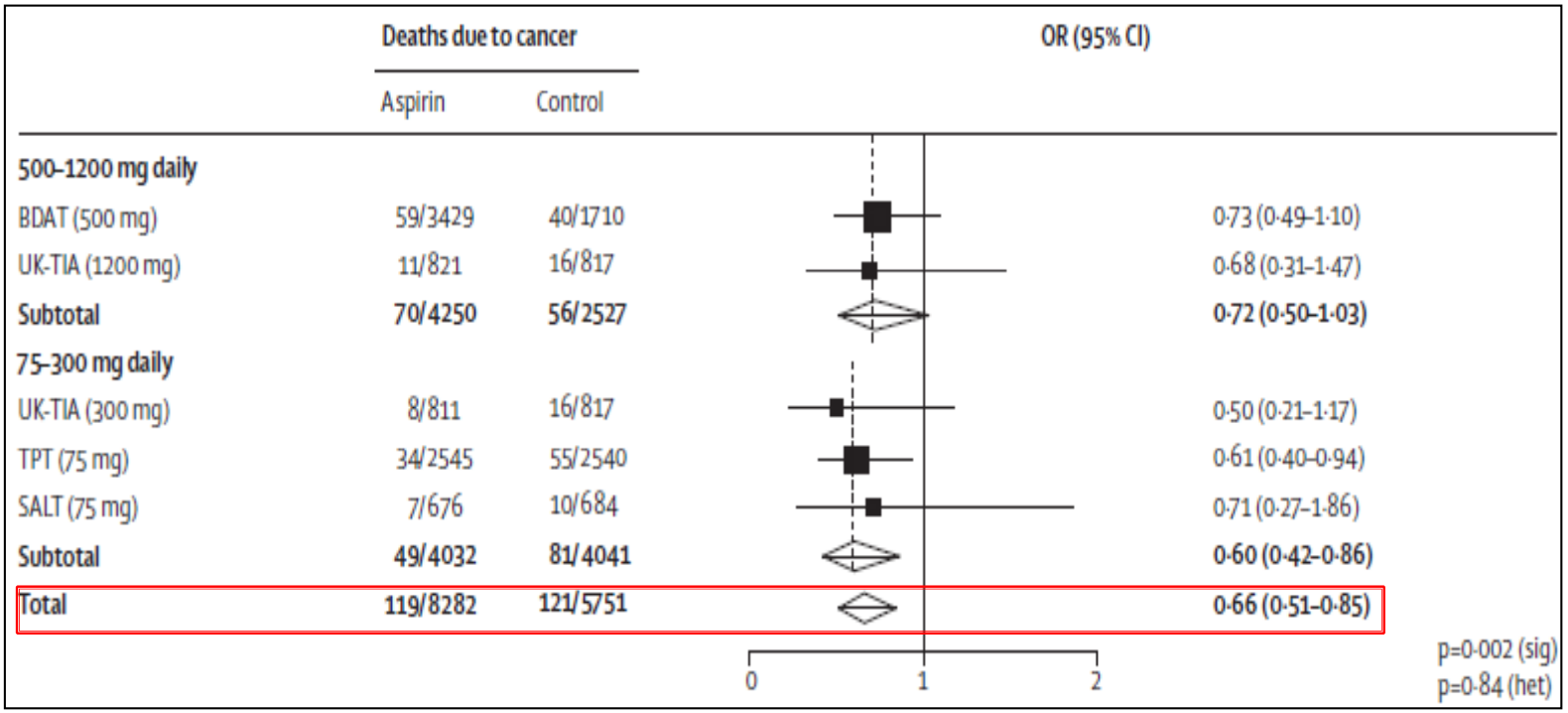
Cole BF et al., Journal of the National Cancer Institute 2009

Aspirine_ Cancer Colorectal (Prévention primaire)

	Thrombosis Prevention Trial	Swedish Aspirin Low Dose Trial	Dutch TIA Aspirin Trial*	UK-TIA Aspirin Trial	British Doctors Aspirin Trial
Aspirin comparison	75 mg daily *vs* placebo	75 mg daily *vs* placebo	283 mg *vs* 30 mg daily	300 mg *vs* 1200 mg daily *vs* placebo	500 mg daily *vs* control
Patients (active/control)	2545/2540	676/684	1231/1224	811/821/817	3429/1710
Placebo controlled and double-blind	Yes	Yes	Yes	Yes	No
Recruitment period	1989–92	1984–89	1986–89	1979–85	1978–79
Year original trial completed	1997	1990	1990	1986	1984
Median (range) duration of scheduled treatment in original trial (years)	6·9 (4·3–8·6)	2·7 (1·0–5·3)	2·6 (1·0–4·3)	4·4 (1·0–7·1)	6·0 (5·0–6·0)
Patients with scheduled duration of trial treatment ≥2·5 years (active/control)	2545/2540	444/468	648/639	684/653/702	3429/1710
Patients with scheduled duration of trial treatment ≥5 years (active/control)	2207/2219	10/9	0/0	321/312/316	3429/1710
Patients informed of treatment allocation at end of original trial	Yes	Yes	Yes	No	Open throughout
Methods of post-trial follow-up	Death certification, cancer registration	Death certification	Death certification, record review, patient contact[34]	Death certification, cancer registration	Death certification, cancer registration
Year post-trial follow-up extended to	2009	2007	2003	2006	2002
Mean (SD) age at randomisation (years)	57·5 (6·7)	66·9 (7·1)	65·3 (10·1)	60·3 (9·0)	61·6 (7·0)

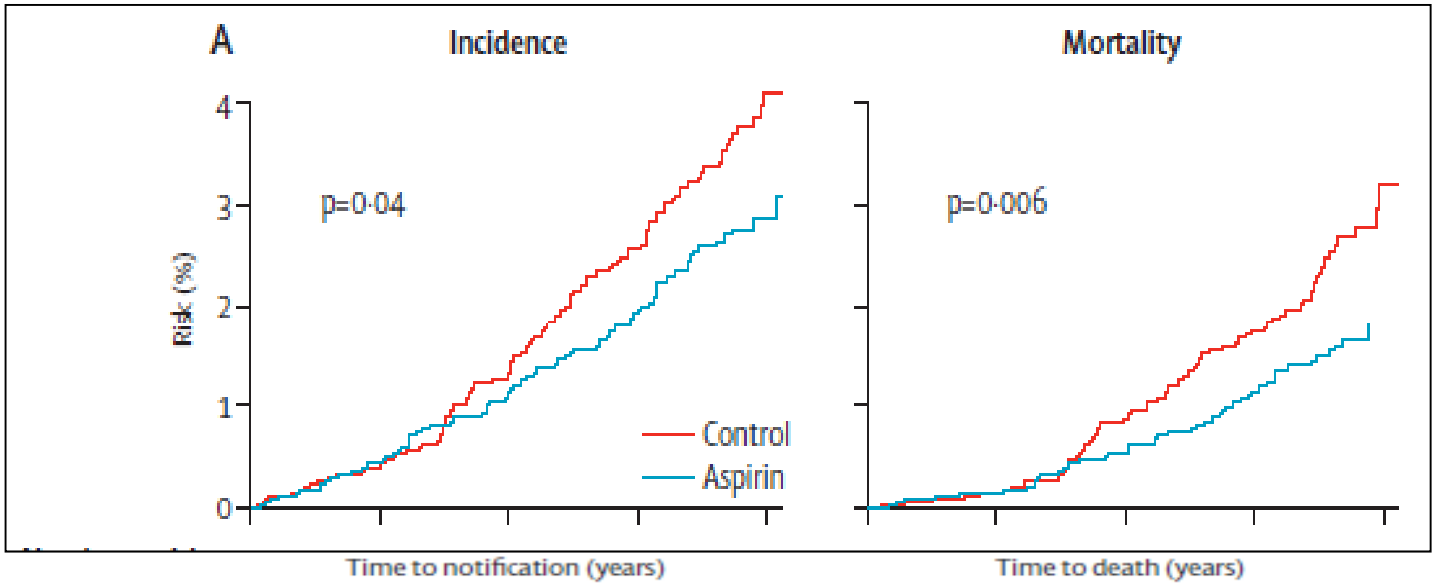
Rothwell P et al., The Lancet 2010

Aspirine_ Cancer Colorectal (Prévention primaire)



Rothwell P et al., The Lancet 2010

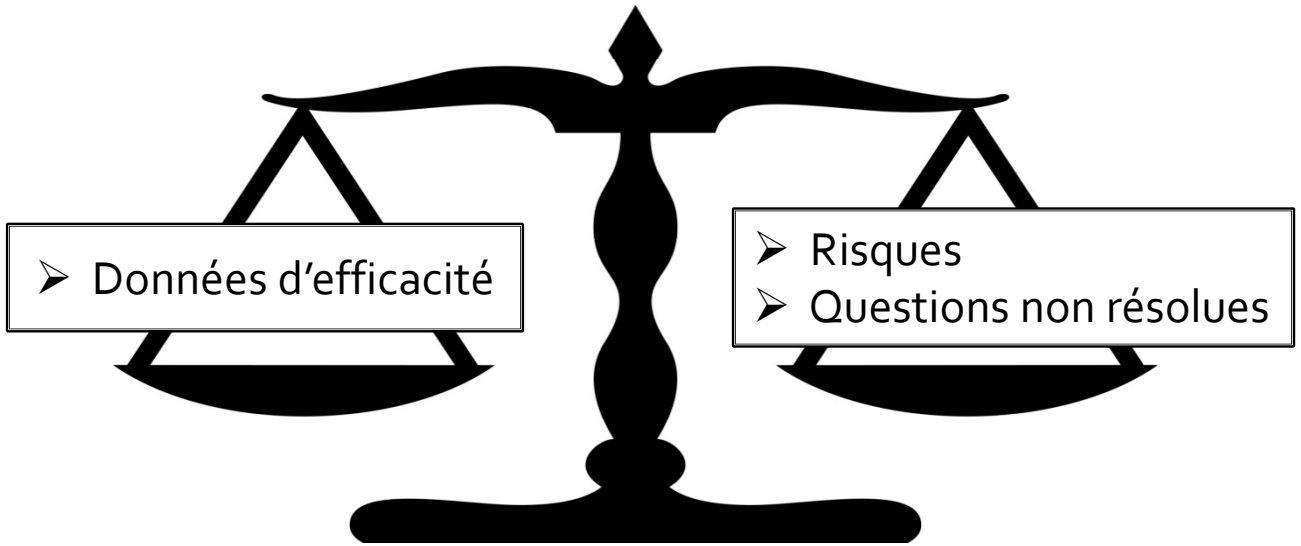
Aspirine_ Cancer Colorectal (Prévention primaire)



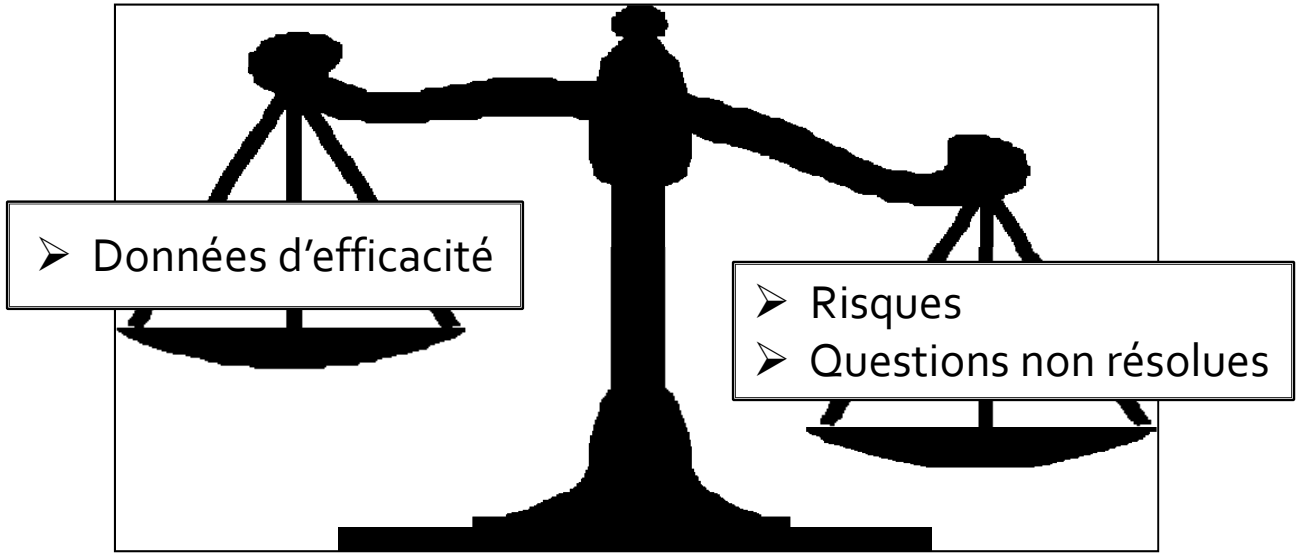
	Incidence of colorectal cancer				Mortality due to colorectal cancer			
	n/N	HR (95% CI)	ARR (95% CI)	p	n/N	HR (95% CI)	ARR (95% CI)	p
All patients	196/8073	0·75 (0·56–0·97)	1·21% (0·19–2·22)	0·02	130/8073	0·61 (0·43–0·87)	1·36% (0·44–2·28)	0·005

Rothwell P et al., The Lancet 2010

CONCLUSION



CONCLUSION



1. Risques

2. Questions non résolues :

a) Dose (75-1200 mg ?)

b) Durée (effet protecteur augmente avec la durée d'exposition)

c) Fréquence (quotidienne?)

d) Biomarqueurs ? (expression PTGS2, mutation PI3KCA...)

PERSPECTIVES

Randomized Phase II Trial of Aspirin and Difluoromethylornithine (DFMO) in Patients at High Risk of Colorectal Cancer	NCT00983580	History of CRC/ adenomas	Aspirin and difluoromethy-loorithine	325 mg/d	Phase II, RCT	August 2009	June 2015	Adenoma recurrence rate	1 y
The Systematic Evaluation of Aspirin and Fish Oil polyp prevention (SeAFOod)	SRCTN05926847	High-risk colorectal adenoma patients	Aspirin and eicosapen-taenoic acid-free fatty acid	300 mg/d	Phase III, RCT	September 2011	October 2014	Number of colorectal adenomas	1–3 y
Japan Colorectal Aspirin Polyps Prevention (J-CAPP)	UMIN000000697	Resected CRC	Aspirin	100 mg/d	Phase III, RCT	January 2007	December 2012	Newly developed tumors	2–3 y
Aspirin for Dukes C and High Risk Dukes B Colon Cancer–An International, Multi-Centre, Double-blind, Randomised, Placebo-controlled, Phase III trial (ASCOLT)	NCT00565708	Dukes B, C colon or rectal cancer	Aspirin	200 mg/d	Phase III, RCT	December 2008	December 2019	Disease-free survival	5 y
Cancer Prevention Programme Project 3 (CAPP3)	In development	Carriers of a germline mismatch repair gene defect, age 18–60 years	Aspirin	100, 300, or 600 mg daily for 5 years	Phase II/III RCT	2012	2020	Lynch syndrome cancer	At least 10 y

Aspirine_ Cancer Colorectal (Prévention secondaire)

	Stade Cancer	n	Dose aspirine	Résultats (HR ou RR)
CALGB 89809 [1]	III	830	325 mg	HR 0,45 [0,21-0,97] SSR HR 0,52 [0,19-1,46] SG
Nurses Health and Health Professinal Follow-up Study [2]	I-III	1279	325 mg	HR = 0,53 [0,33-0,86] SG CCR HR = 0,68 [0,51-0,92] SG
Dutch Cancer and Prescription Registry [3]	I-IV	4481	80 mg	RR = 0,77 [0,63-0,95] SG CCR

[1] Fuchs CS et al., Journal of Clinical Oncology 2005
[2] Chan AT et al., Journal of the American Medical Association 2009
[3] Bastiannet E et al., British Journal of Cancer 2012