

ANTIAGGREGAZIONE PIASTRINICA:

DALLA PREVENZIONE CARDIOVASCOLARE
A QUELLA CARDIO-ONCOLOGICA

07 DICEMBRE 2019

MILANO

HOTEL TOCQ
Via Alessio Di Tocqueville

ASA a bassa dose: dalla prevenzione CV a
quella cardio-oncologica?

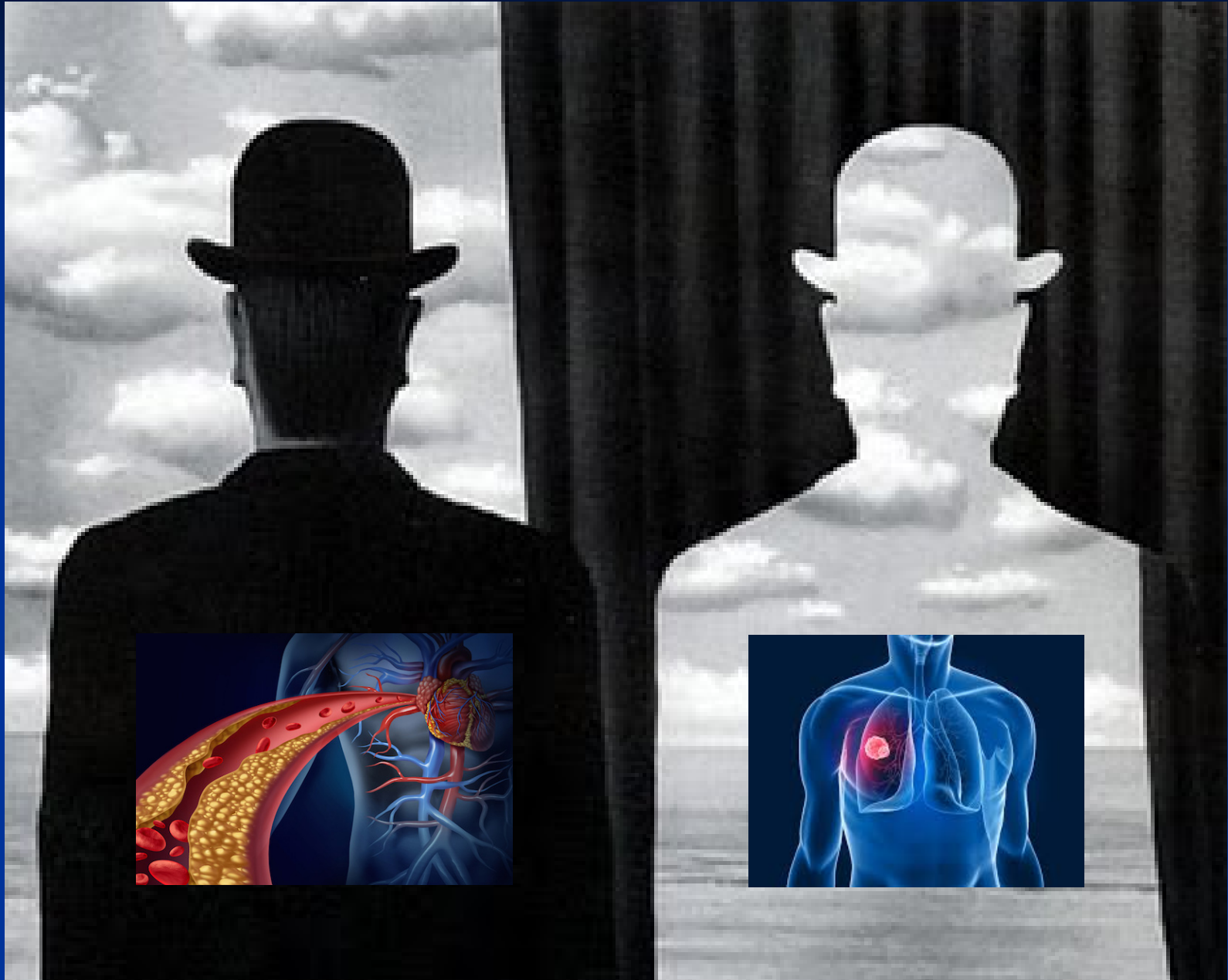
Dr Elio M. STAFFIERE



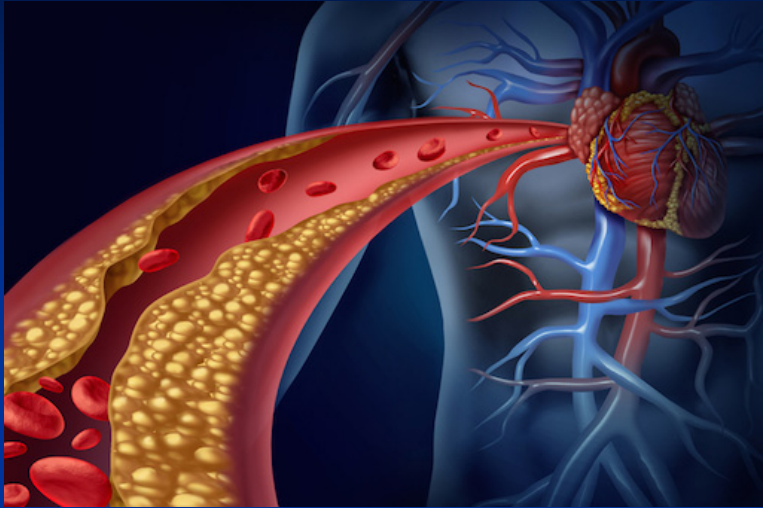
ASA: novità effervescenti



ASA: novità effervescenti



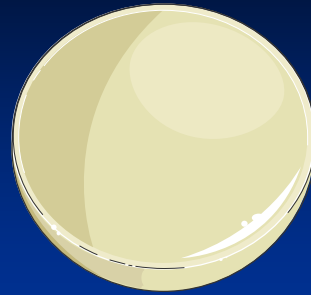
ASA: novità effervescenti



ASA: solo prevenzione CV?



ASA: solo prevenzione CV?



ASA: solo prevenzione CV?

Stili di vita e rischio di cancro



Altro 10-15%



Dieta
30-35%

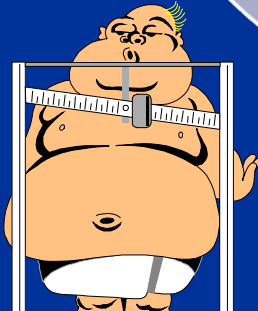


Infezioni 10-15%



Alcool 4-6%

Obesità 10-20%

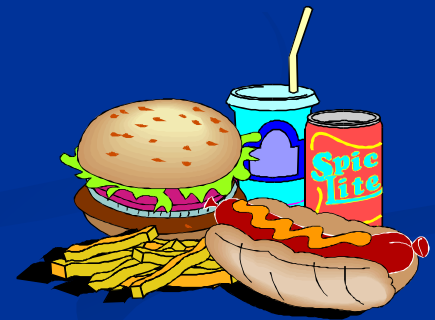
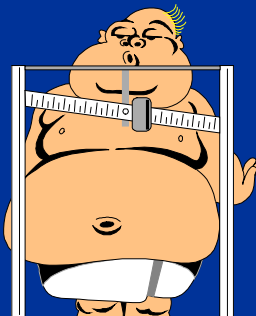


Fumo 20-30%



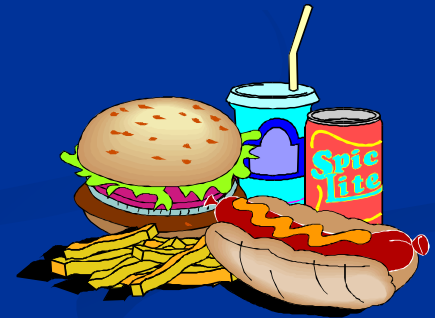
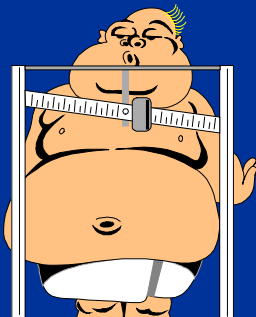
ASA: solo prevenzione CV?

Comuni fattori rischio...



ASA: solo prevenzione CV?

Comuni fattori rischio...



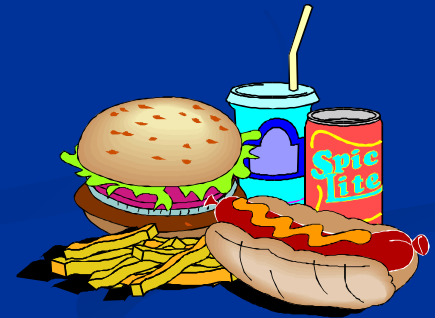
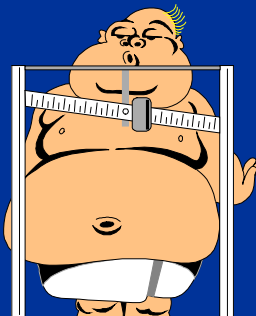
...comune destino



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Comuni fattori rischio...

comune destino ...



... comune terapia?



ASA: solo prevenzione CV?

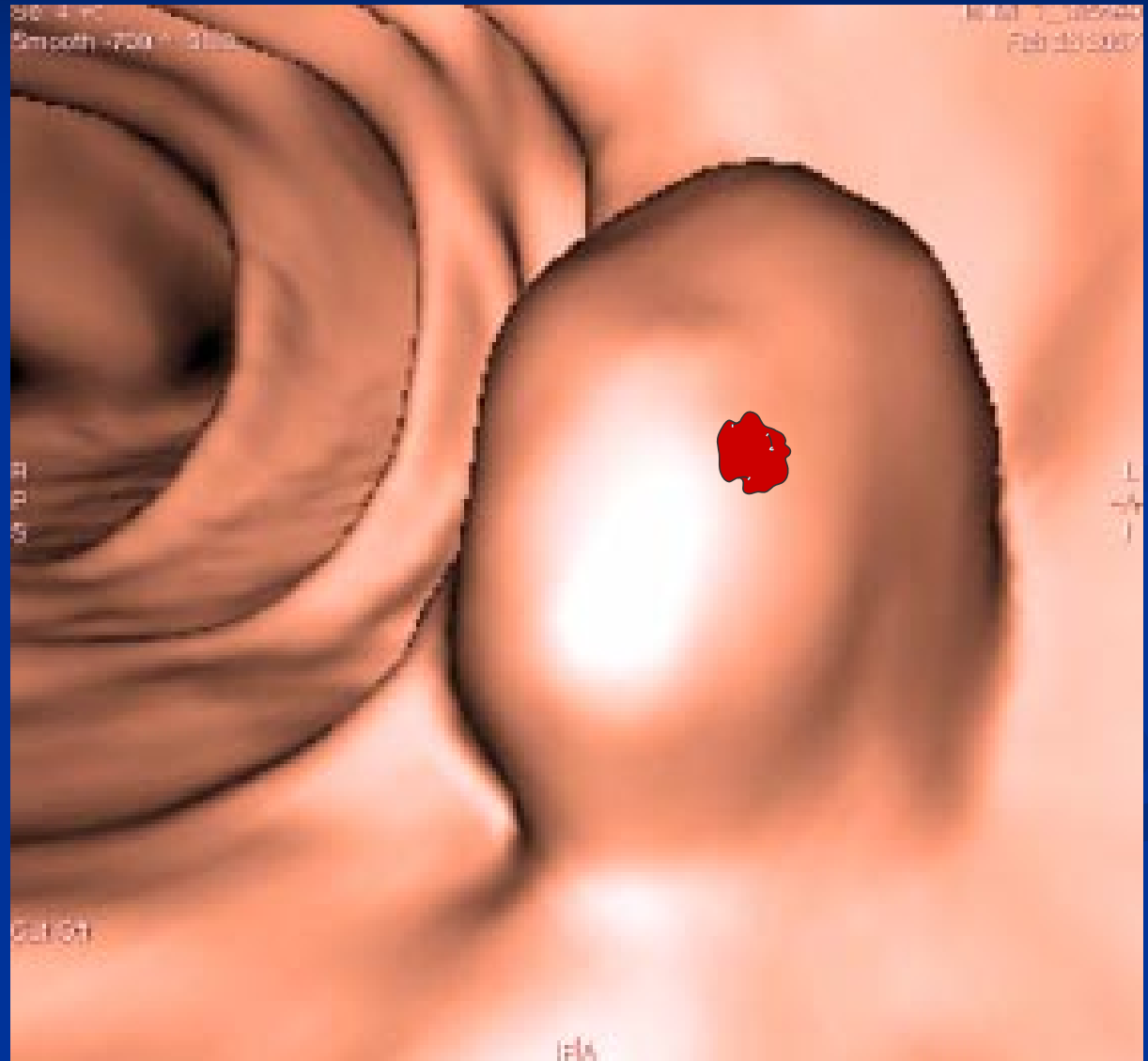
Colonrectal cancer risk, chronic illnesses, operation, and medications: case control result from Melbourne Colonrectal Cancer Study

Kune GA et al – Cancer res 1988; 88:4399-404

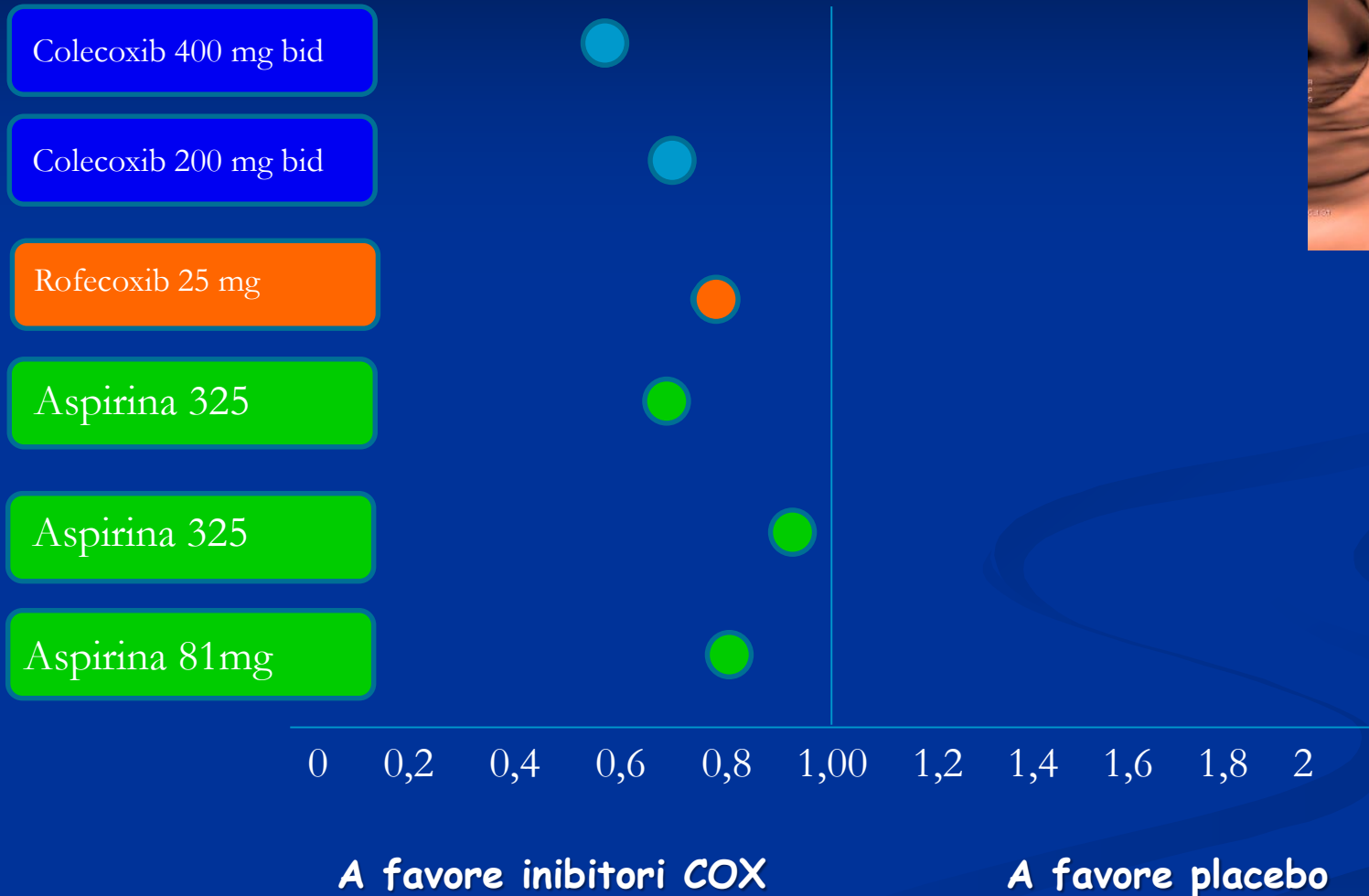
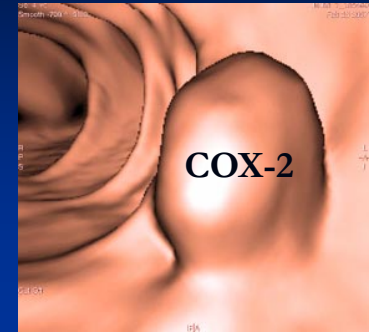
- Studio caso controllo
- 700 pz

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FANS



ASA: solo prevenzione CV?



Prevenzione primaria CV

In prevenzione
secondaria...

Gianrico Carofiglio

Ad occhi chiusi



Sellerio editore Palermo

In prevenzione
primaria...

Gianrico Carofiglio

Ragionevoli dubbi



Sellerio editore Palermo

In prevenzione
cardio-oncologica...

Gianrico Carofiglio

Testimone inconsapevole









Sellerio editore Palermo



ASA: solo prevenzione CV?

Studi prevenzione primaria

Trial	Popolazione	Età (anni)	LD-ASA dosaggio	Rischio di primo evento CVS a 10 anni
WHS (2005) ⁶	Donne apparentemente sane (n=39,876)	≥45	100mg a giorni alterni	 2.5%
HOT study (1998) ³	Uomini e donne con PAD 100–115mmHg (n=18,790)	50–80	75mg/die	 3.6%
PPP (2001) ⁵	Uomini e donne con ≥1 fattore di rischio CVS (n=4,495)	50–80+	100mg/die	 4.3%
PHS (1989) ²	Medici maschi apparentemente sani (n=22,071)	40–84	325mg a giorni alterni	 4.8%
BDT (1988) ¹	Medici maschi apparentemente sani (n=5,139)	50–78	500mg/die	 8.9%
TPT (1998) ⁴	Uomini ad alto rischio cardiovascolare (n=5,499)	45–69	75mg/die	 12.4%

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Neoplasie e ASA

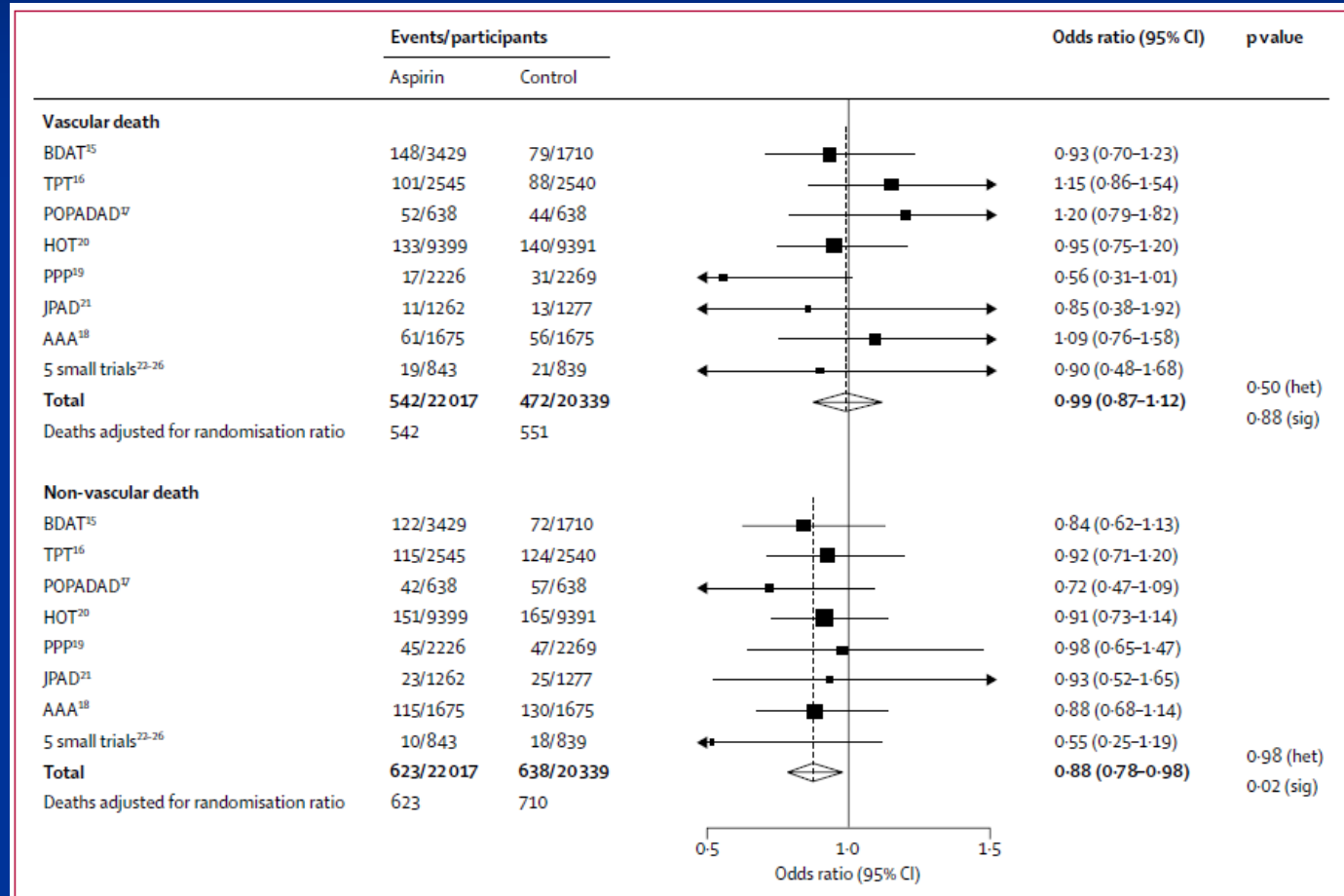


Figure 1: Meta-analysis of the effect of aspirin on risk of vascular death and non-vascular death during 12 randomised trials of daily aspirin versus control in primary prevention of vascular events



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Riduzione significativa della mortalità per cancro

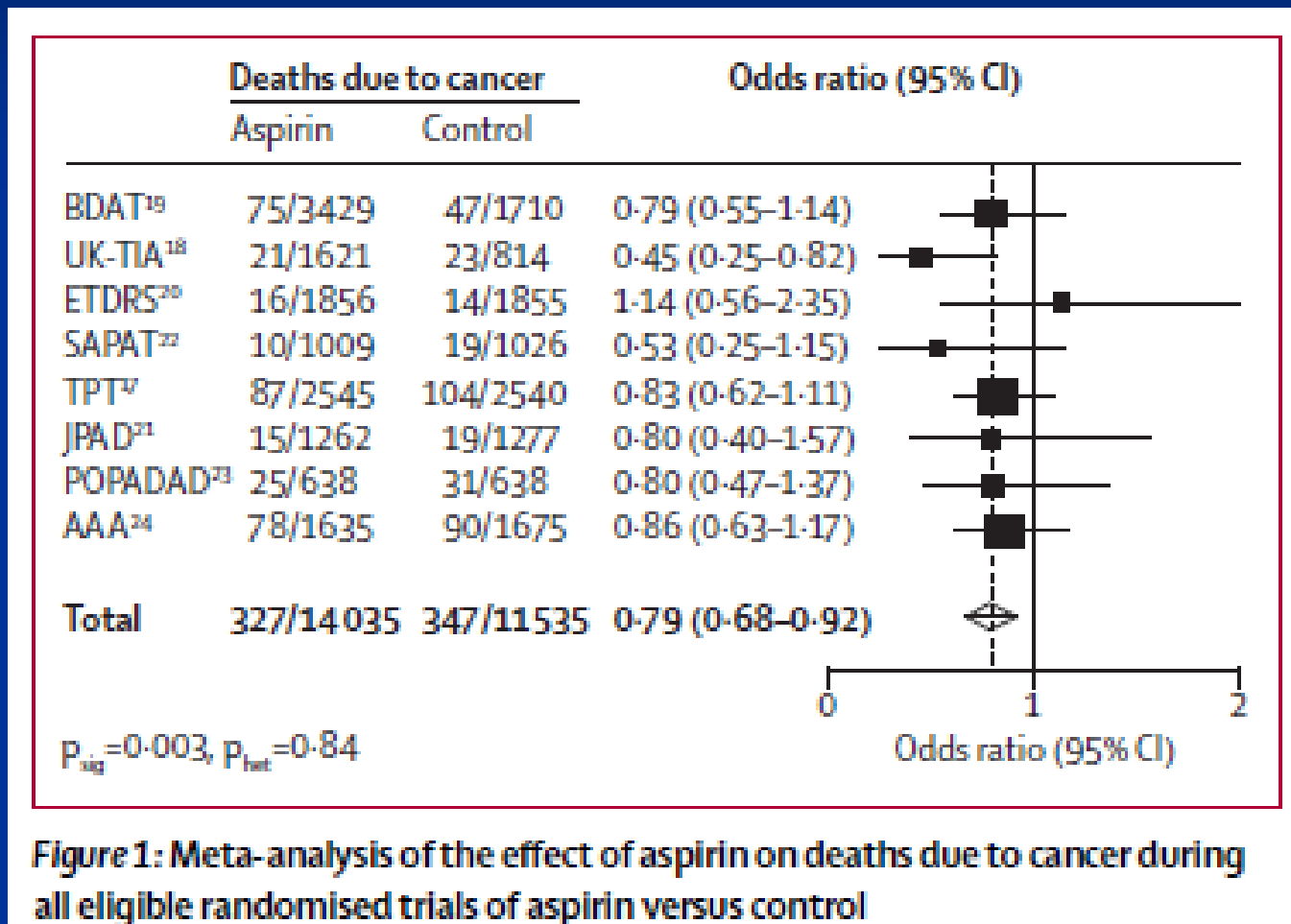


Figure 1: Meta-analysis of the effect of aspirin on deaths due to cancer during all eligible randomised trials of aspirin versus control

ASA: solo prevenzione CV?

Incidenza di cancro del colon nei 6 trials di prevenzione primaria

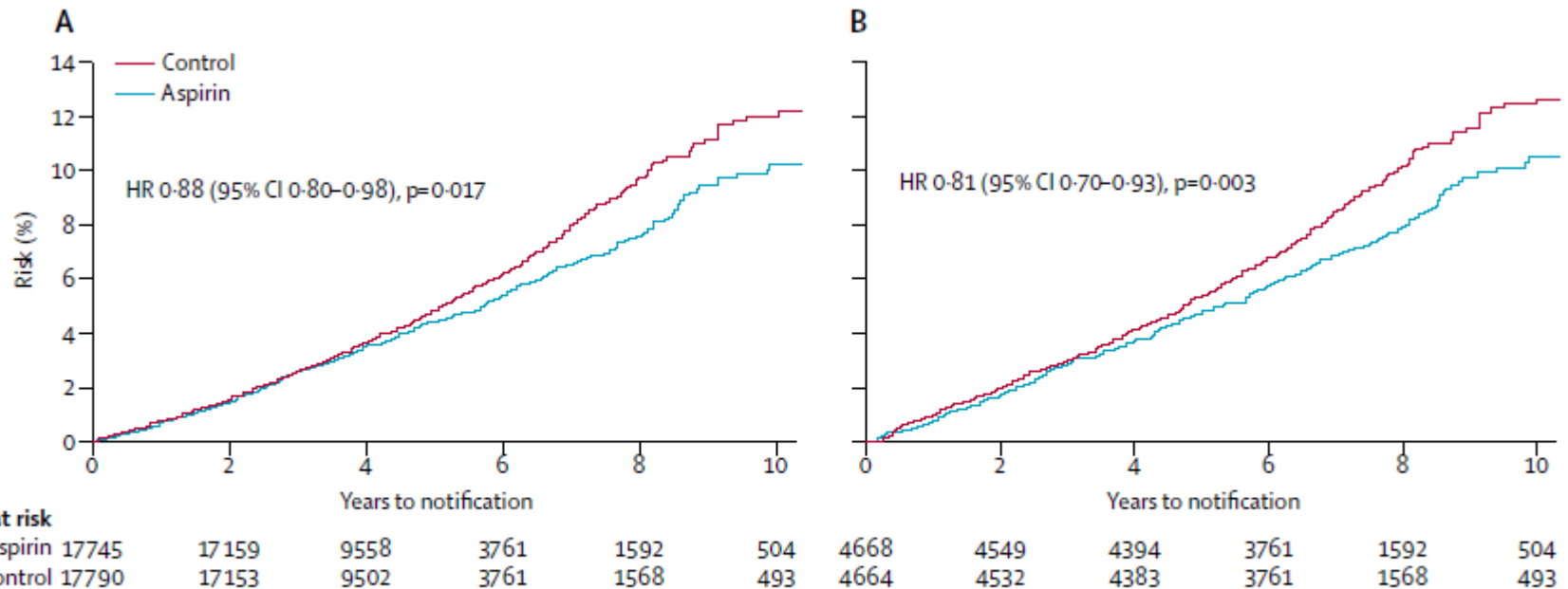


Figure 2: Pooled analysis of effect of allocation to aspirin on incidence of cancer during six randomised trials of daily low-dose (75–100mg daily) aspirin versus placebo in primary prevention of vascular events¹⁶⁻²¹

ASA: solo prevenzione CV?

Effect of daily aspirin on risk of cancer metastasis: a study of incident cancers during randomised controlled trials



Peter M Rothwell, Michelle Wilson, Jacqueline F Price, Jill F F Belch, Tom W Meade, Ziyah Mehta

www.thelancet.com Published online March 21, 2012 DOI:10.1016/S0140-6736(12)60209-8

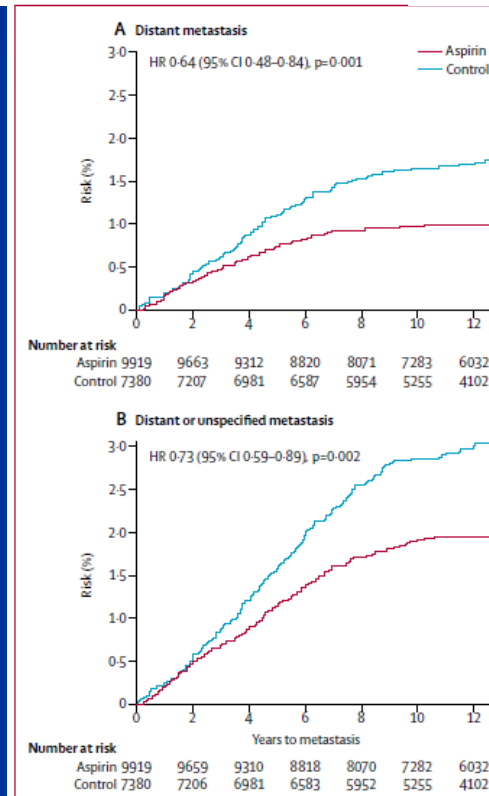


Figure 1: The effect of aspirin on risk of metastasis due to any incident cancer diagnosed during five trials of aspirin versus control

Analysis is based on time from randomisation to diagnosis of metastasis during or after the trials. Part A shows definite site-specific distant metastasis and part B also includes metastatic cancers in which the site of the metastasis was not specified. HR=hazard ratio from a Cox regression stratified by trial.

Rothwell P –
Lancet 2012; 279:1591-601



ASA: solo prevenzione CV?

RESEARCH ARTICLE

Aspirin in the Treatment of Cancer: Reductions in Metastatic Spread and in Mortality: A Systematic Review and Meta-Analyses of Published Studies

Peter C. Elwood^{1†*}, Gareth Morgan^{1,2}, Janet E. Pickering¹, Julieta Galante³, Alison L. Weightman^{1,4}, Delyth Morris¹, Mark Kelson¹, Sunil Dolwani¹

1 Cochrane Institute of Primary Care and Public Health, Cardiff University, Cardiff, United Kingdom, 2 Hywel Dda University Health Board, Llanelli SA14 8QF, United Kingdom, 3 Department of Psychiatry, University of Cambridge, Cambridge, United Kingdom, 4 Specialist Unit for Review Evidence, Cardiff University, Cardiff, United Kingdom

... ad un follow-up di 5 anni

ASA: solo prevenzione CV?

Una questione di tempo

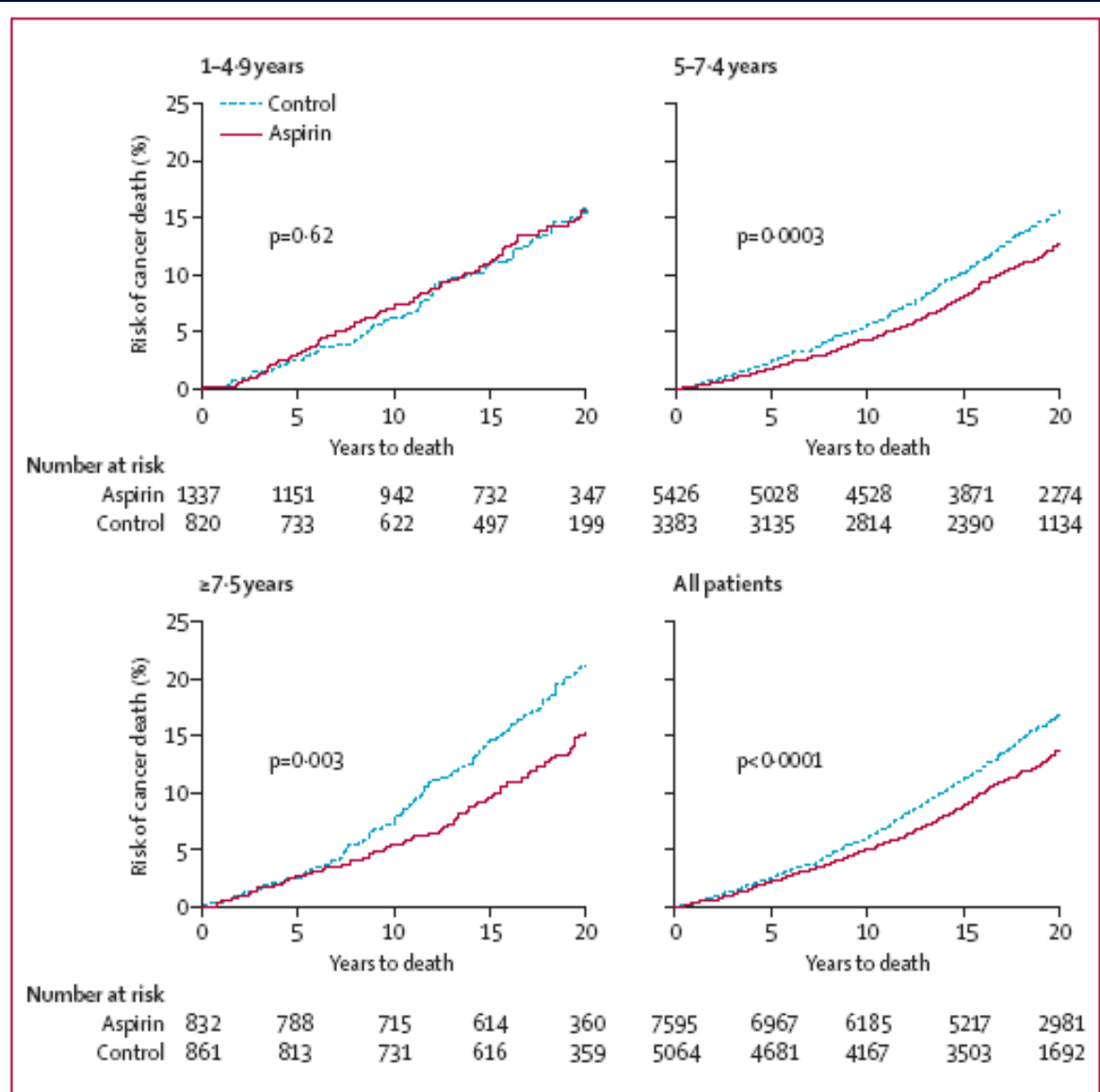


Figure 3: Effect of allocation to aspirin versus control on 20-year risk of death due to any solid cancer stratified by scheduled duration of trial treatment in three trials with long-term follow-up¹⁷⁻¹⁹
 Continuous variable interaction, p=0.01.

ASA: solo prevenzione CV?

Una questione di tempo

www.thelancet.com Published online March 21, 2012 DOI:10.1016/S0140-6736(11)61720-0

Short-term effects of daily aspirin on cancer incidence, mortality, and non-vascular death: analysis of the time course of risks and benefits in 51 randomised controlled trials



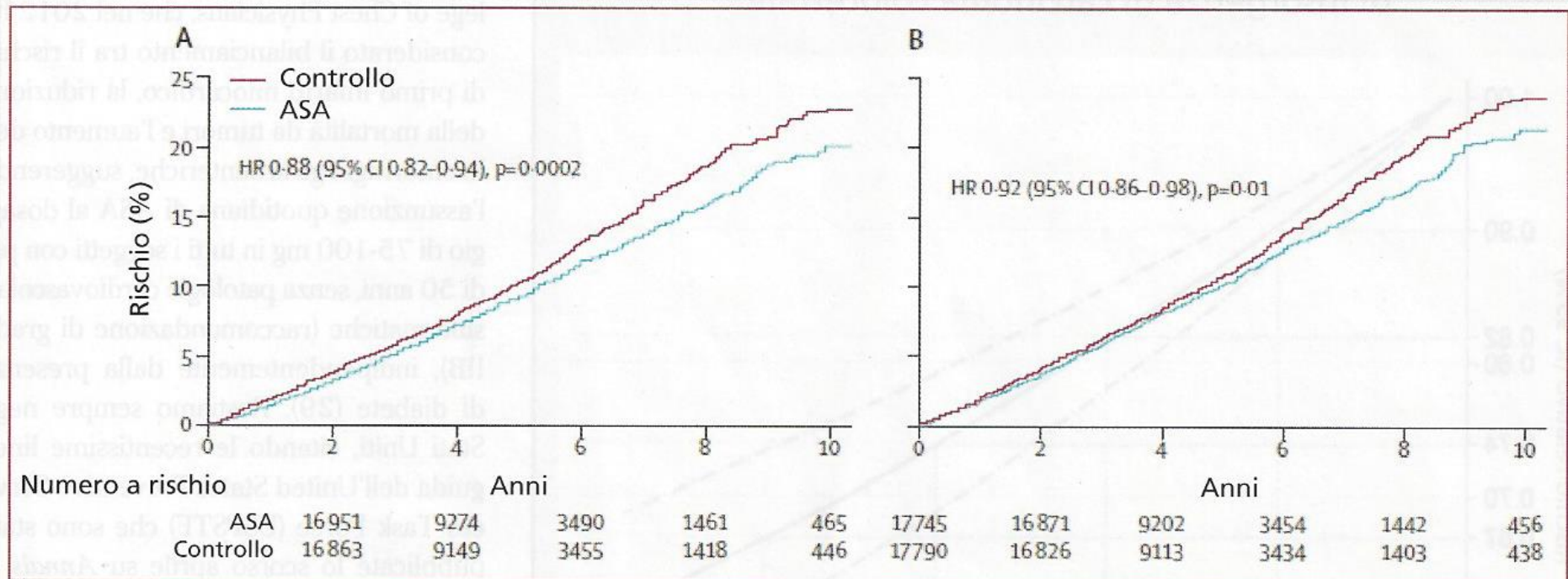
Peter M Rothwell, Jacqueline F Price, F Gerald R Fowkes, Alberto Zanchetti, Maria Carla Roncaglioni, Gianni Tognoni, Robert Lee, Jill F F Belch, Michelle Wilson, Ziyah Mehta, Tom W Meade

	Events/participants		ARR per 1000 patients per year	Odds ratio (95% CI)	P _{interaction}
	Aspirin	Control			
Cancers					
0-2-9 years	445/17745	442/17790	-0.06	1.01 (0.88-1.15)	
3-0-4-9 years	193/16463	237/16484	2.19	0.81 (0.67-0.98)	0.04
≥5 years	131/4444	184/4460	4.80	0.70 (0.56-0.88)	



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Relazione tra benefici CV e oncologici, e sanguinamenti...



ASA: solo prevenzione CV?

Effetto preventivo che Warfarin non possiede...

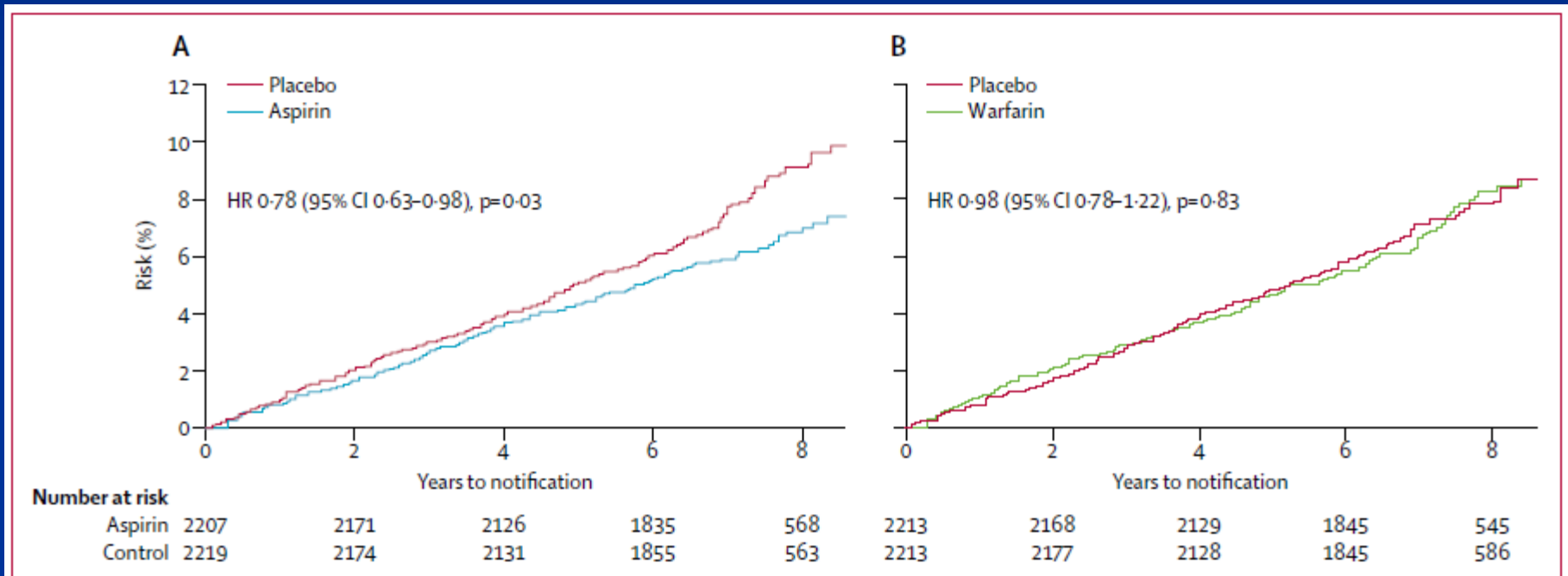


Figure 3: Effect of allocation to aspirin versus placebo (A) and warfarin versus placebo (B) on the incidence of cancer during the Thrombosis Prevention Trial¹⁶

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Quale meccanismo?



Clin Cancer Res 2004; 10:8465-71

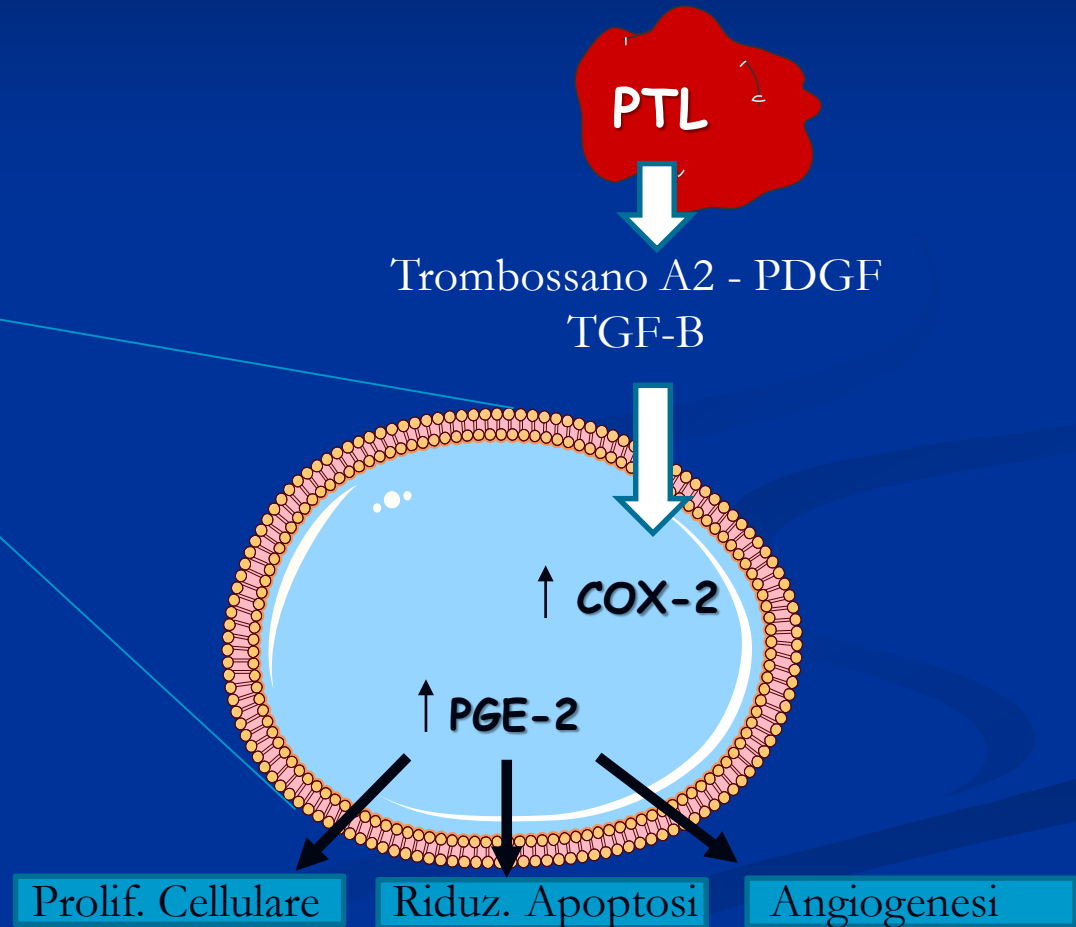
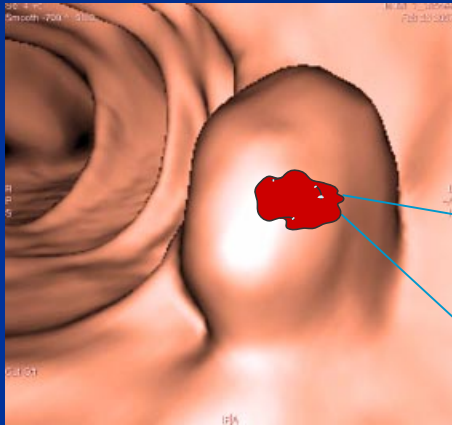


Clin Cancer Res 2001;7:861-7



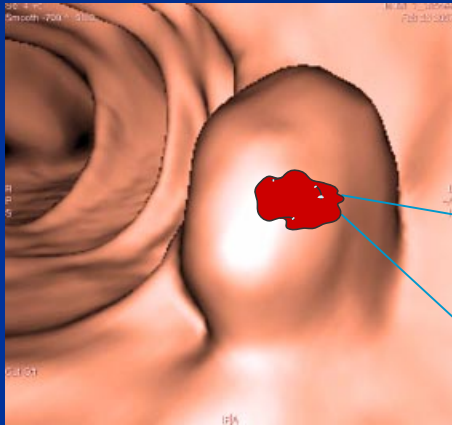
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Quale meccanismo?

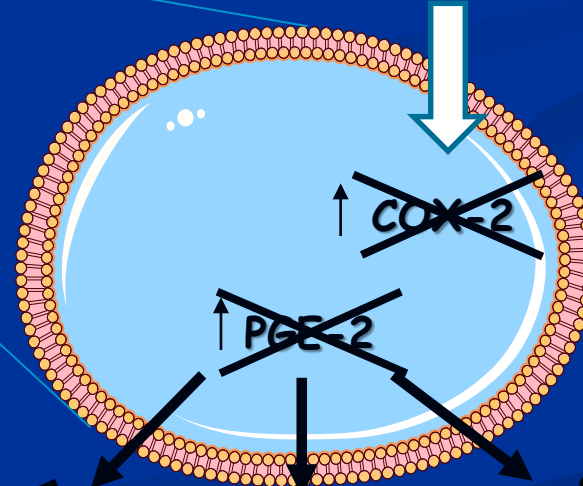


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Quale meccanismo?



Trombossano A2 - PDGF
TGF-B



~~Prolif. Cellulare~~

~~Riduz. Apoptosi~~

~~Angiogenesi~~

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In popolazioni geneticamente determinate...

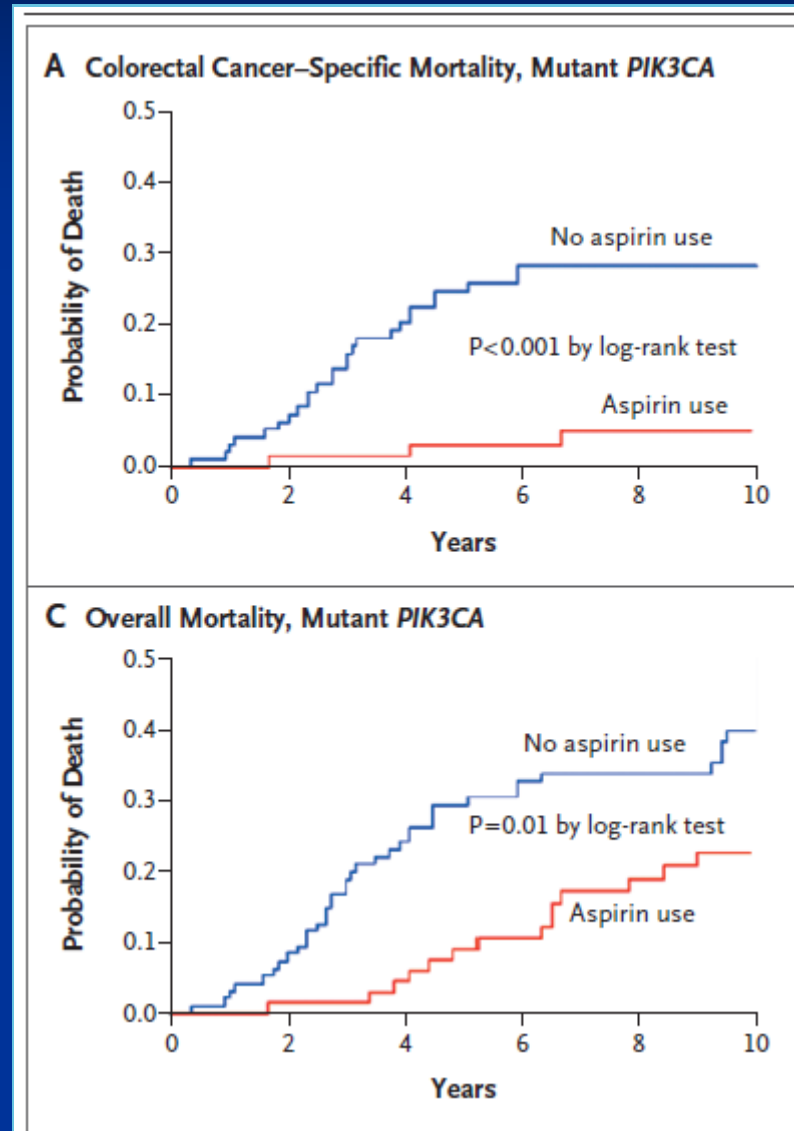
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Aspirin Use, Tumor *PIK3CA* Mutation,
and Colorectal-Cancer Survival

ASA: solo prevenzione CV?

Riduzione dell'82% della mortalità per cancro colon rettale

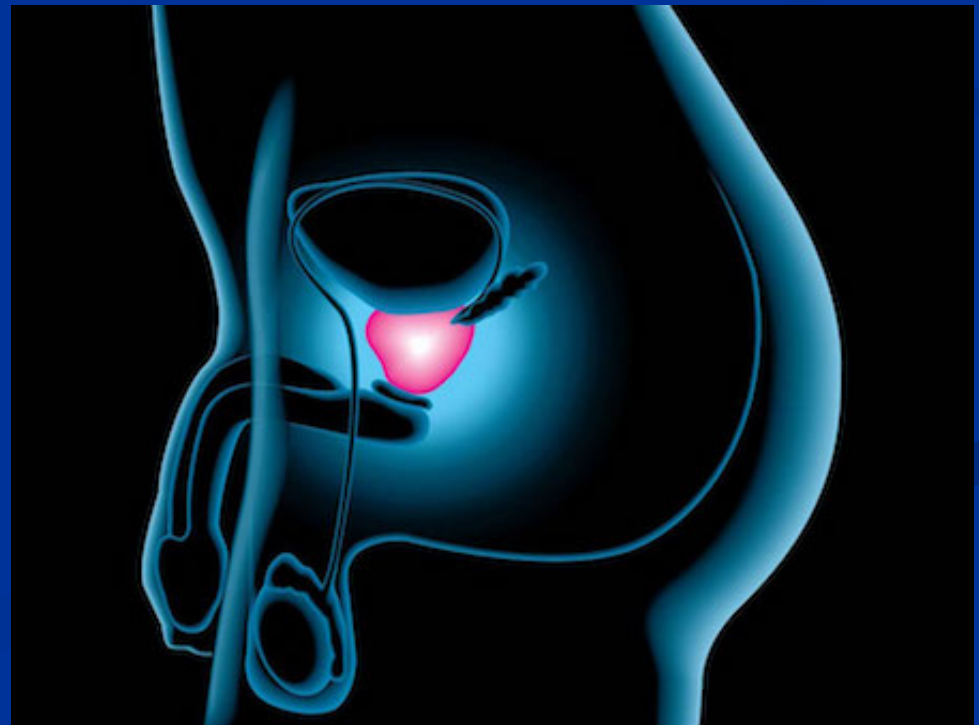


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Mahumud - Br J Cancer 2004; 90:93-99

Mahumud – Eur J Cancer Prev 2006; 15: 158-64



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IJC

International Journal of Cancer

Risk of prostate cancer in low-dose aspirin users: A retrospective cohort study

F. Lapi¹, M. Levi^{1,2}, M. Simonetti¹, M. Cancian³, D. Parretti³, I. Cricelli¹, A. Sobrero⁴ and C. Cricelli³



ASA: solo prevenzione CV?



Luo – Breast Cancer Res Treat 2012: 131:581-7



ASA: solo prevenzione CV?



Corley - Gastr – Breast Cancer Res Treat 2012:
131:581-7



ASA: solo prevenzione CV?



Wilson - Br J Cancer 2013; 108:1178-81



ASA: solo prevenzione CV?



Women Health Initiative (WHI) Cancer 2012

58.806 donne

50-79 anni



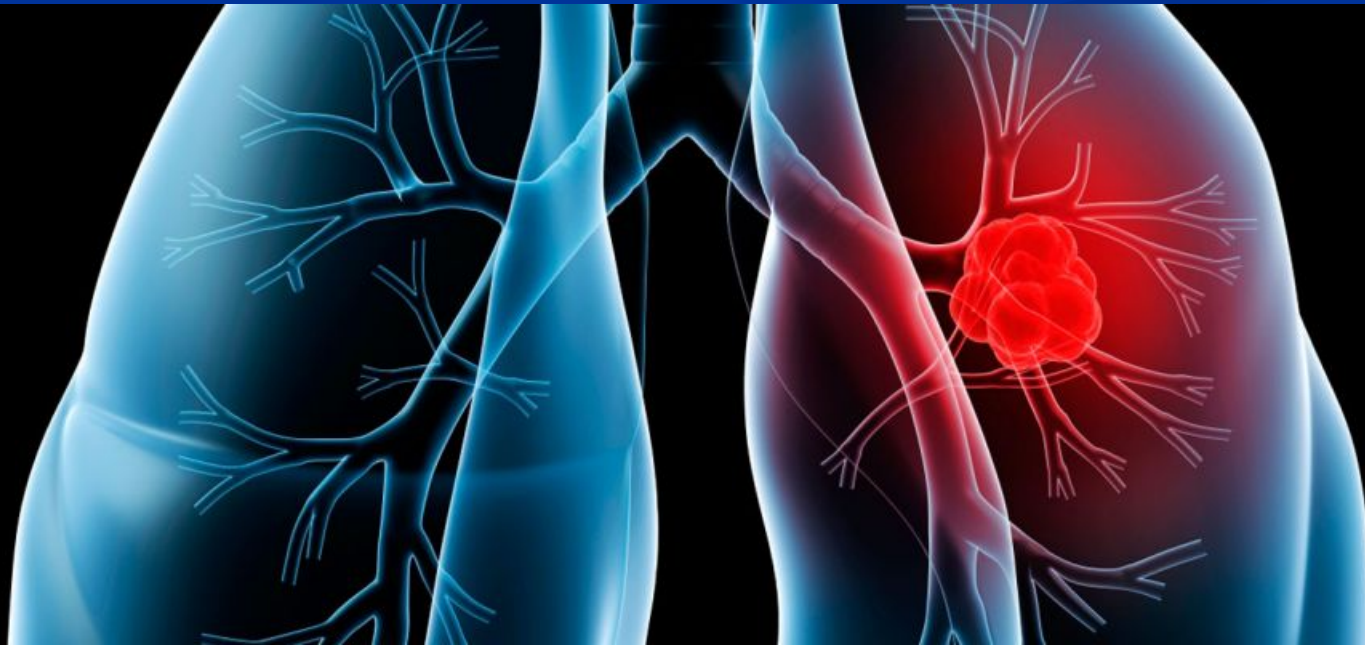
- 21%



ASA: solo prevenzione CV?



Bosetti – Ann Oncol 2012; 23(6):1403-15
Oh – Ann Oncol 2011; 22:2456-65



ASA: solo prevenzione CV?

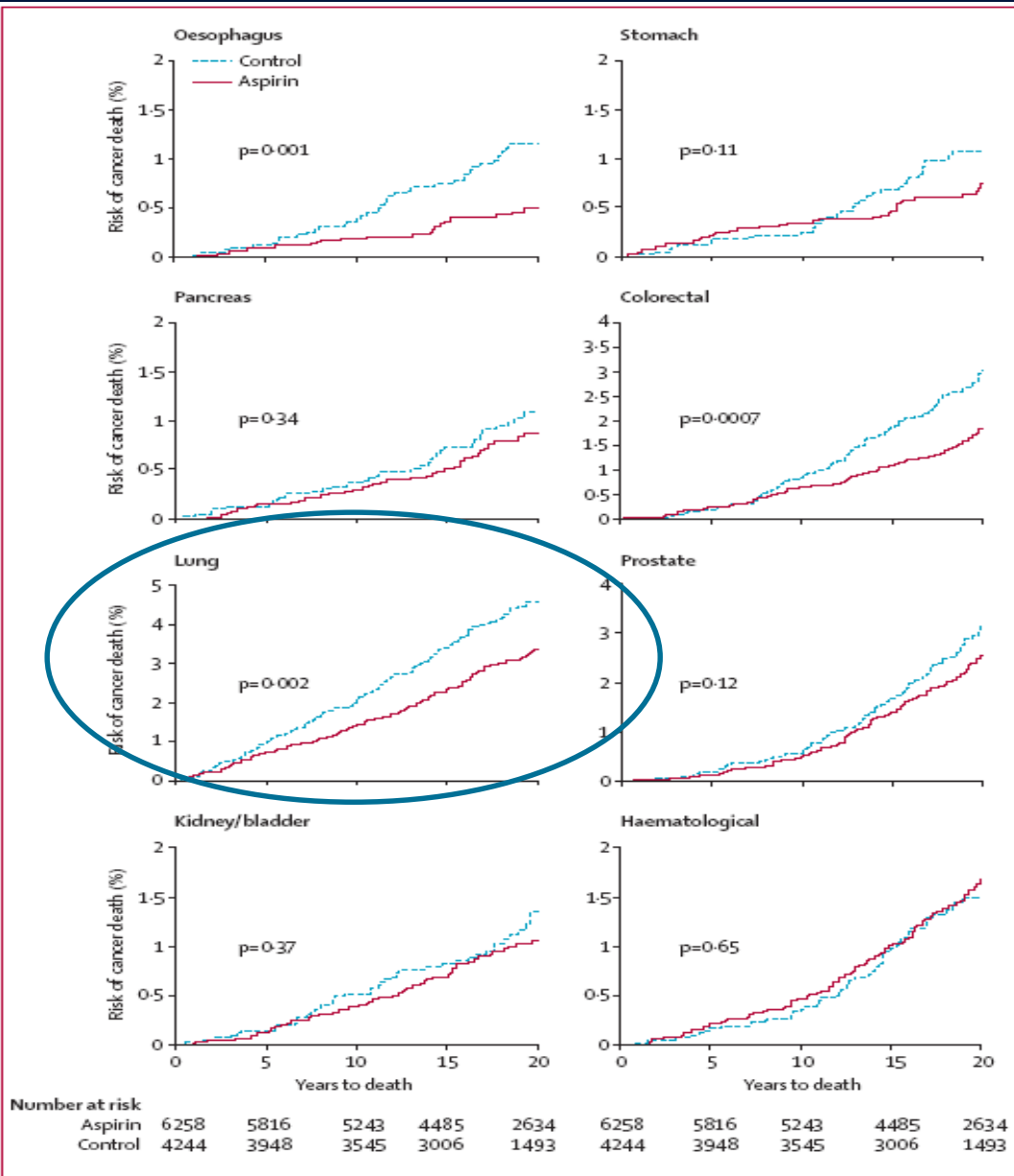


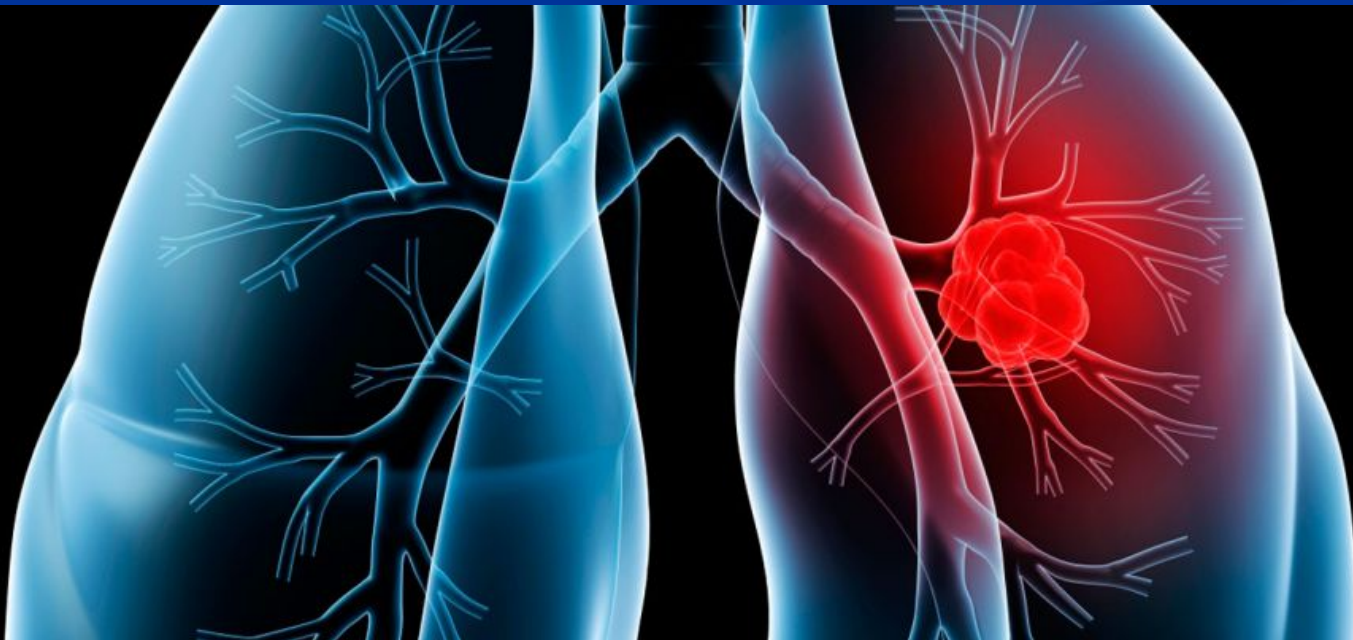
Figure 4: Effect of allocation to aspirin versus control on the 20-year risk of death due to the most common fatal cancers in the 10 502 patients with scheduled treatment duration of 5 years or longer in the three trials with long-term follow-up⁷⁻⁹



ASA: solo prevenzione CV?



Women Health Initiative (WHI) Cancer 2012

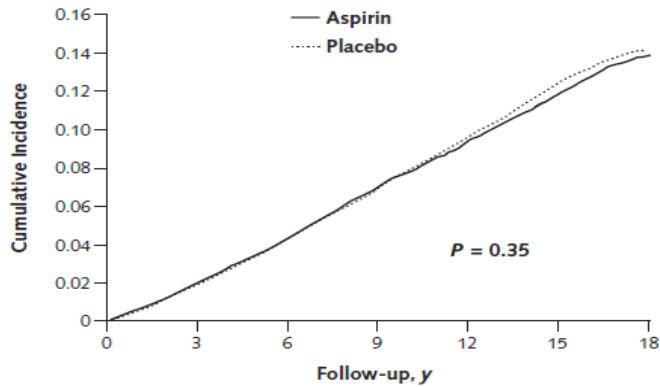


ASA: solo prevenzione CV?

Alternate-day, low-dose aspirin and cancer risk: long-term observational follow-up of a randomized trial.

Figure 2. Cumulative incidence of total (A), breast (B), colorectal (C), and lung (D) cancer from time of randomization, by random aspirin assignment, with P values from log-rank test.

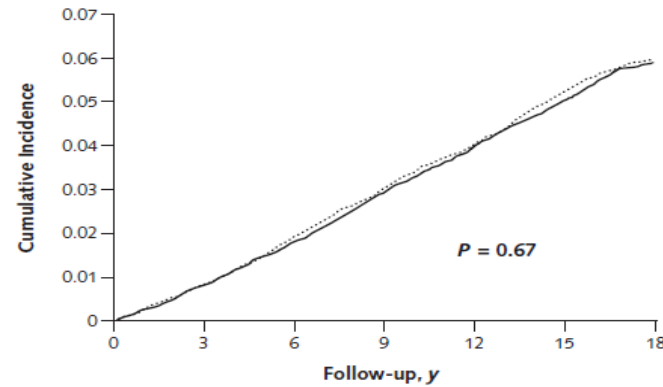
A. Total Cancer



Participants at risk, *n*

Aspirin	19 934	19 443	18 868	17 975	15 592	14 617
Placebo	19 942	19 467	18 857	17 977	15 424	14 358

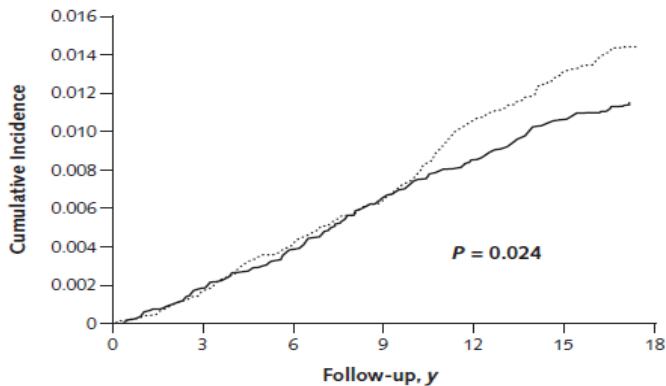
B. Breast Cancer



Participants at risk, *n*

Aspirin	19 934	19 443	18 868	17 975	15 592	14 617
Placebo	19 942	19 467	18 857	17 977	15 424	14 358

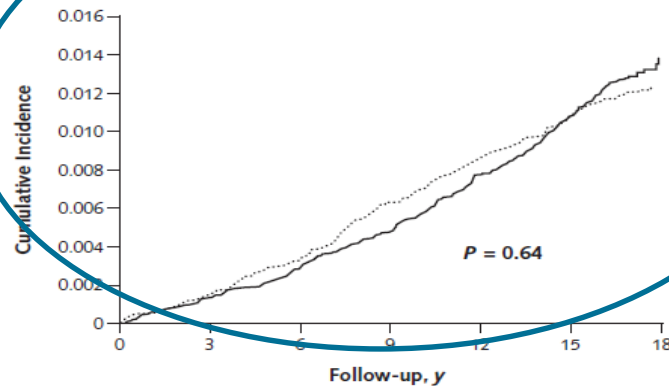
C. Colorectal Cancer



Participants at risk, *n*

Aspirin	19 934	19 443	18 868	17 975	15 592	14 617
Placebo	19 942	19 467	18 857	17 977	15 424	14 358

D. Lung Cancer



Participants at risk, *n*

Aspirin	19 934	19 443	18 868	17 975	15 592	14 617
Placebo	19 942	19 467	18 857	17 977	15 424	14 358

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Anche le linee guida iniziano a interessarsi...

2013 ESH/ESC Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

In conclusion, the prudent recommendations of the 2007 ESH/ESC Guidelines can be reconfirmed:² antiplatelet therapy, particularly low-dose aspirin, should be prescribed to controlled hypertensive patients with previous CV events and considered in hypertensive patients with reduced renal function or a high CV risk. Aspirin is not recommended in low-to-moderate risk hypertensive patients in whom absolute benefit and harm are equivalent. It is noteworthy that a recent meta-analysis has shown lower incidences of cancer and mortality in the aspirin (but not the warfarin) arm of primary prevention trials.⁶⁵⁹ If confirmed, this additional action of aspirin may lead to a more liberal reconsideration of its use. Low-dose aspirin in the prevention of pre-eclampsia is discussed in Section 6.5.3.

ASA: solo prevenzione CV?

Aspirin Therapy in Primary Cardiovascular Disease Prevention

A Position Paper of the European Society of Cardiology Working Group on Thrombosis

Fase 1: Valutare il rischio a 10 anni di eventi CV maggiori

<10%

<10-20%

>20%

Fase 2: Storia di sanguinamento senza cause reversibili, uso concomitante di altri farmaci che aumentano il rischio di sanguinamento

Considerare storia familiare di cancro GI (specialmente del colon) / valori e preferenza del paziente

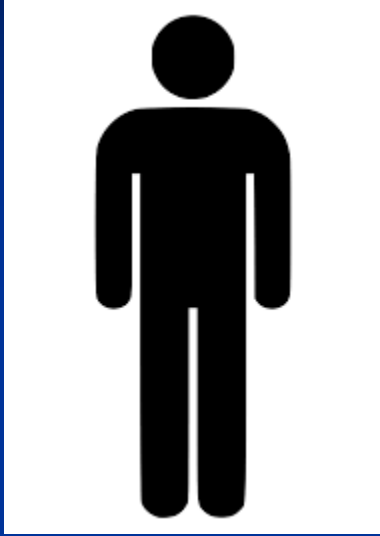
- Stop
- Avanti con cautela
- Avanti

Aspirina a basse dosi

CV: cardiovascolari; GI: gastrointestinali

J Am Coll Cardiol 2014 22; 64: 319-27

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Rischio
CV



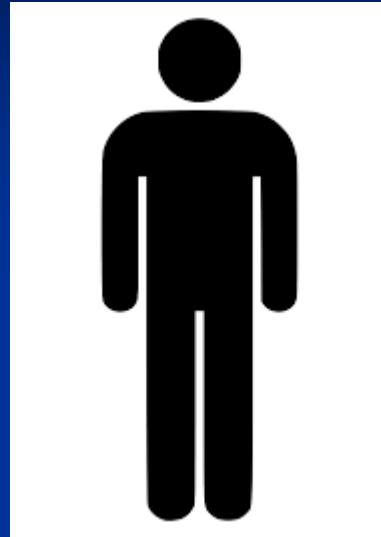
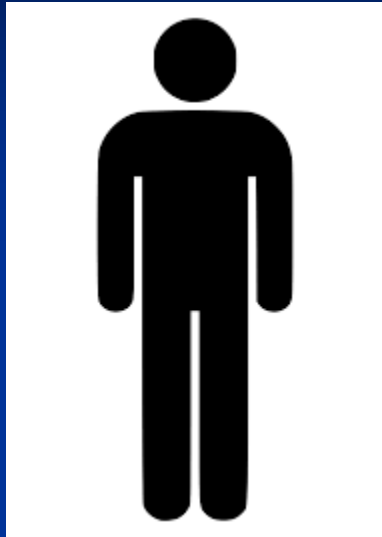
Rischio
cancro



Rischio
emorragico

SI ASA

ASA: solo prevenzione CV?



Rischio
CV



Rischio
cancro



Rischio
emorragico



Rischio
CV



Rischio
cancro

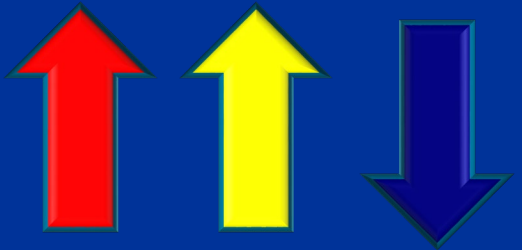
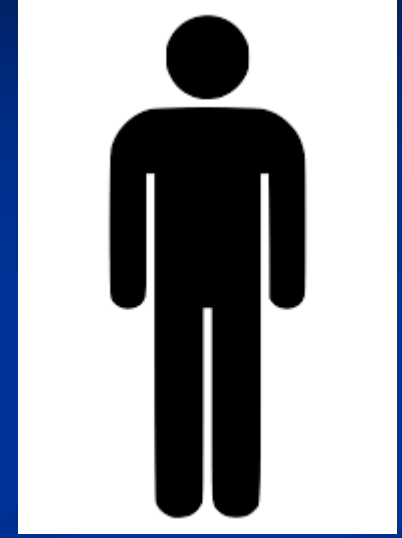
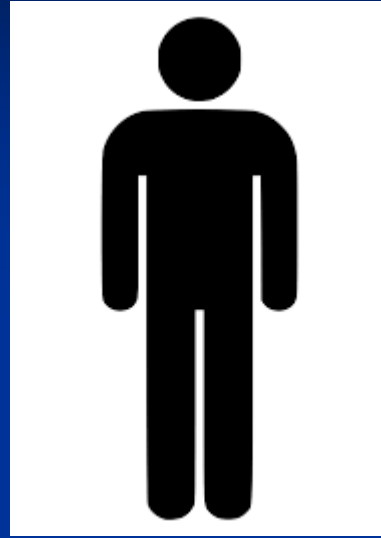
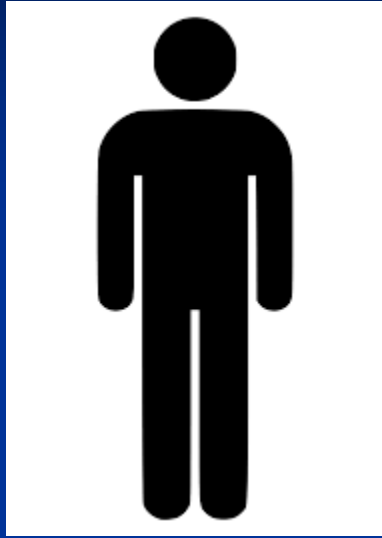


Rischio
emorragico

SI ASA

Giudizio
clinico

ASA: solo prevenzione CV?



Rischio
CV

Rischio
cancro

Rischio
emorragico



Rischio
CV

Rischio
cancro

Rischio
emorragico



Rischio
CV

Rischio
cancro

Rischio
emorragico

SI ASA

Giudizio
clinico

NO ASA

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Grazie dell'attenzione