Un ruolo per l'aspirina anche in ambito oncologico?

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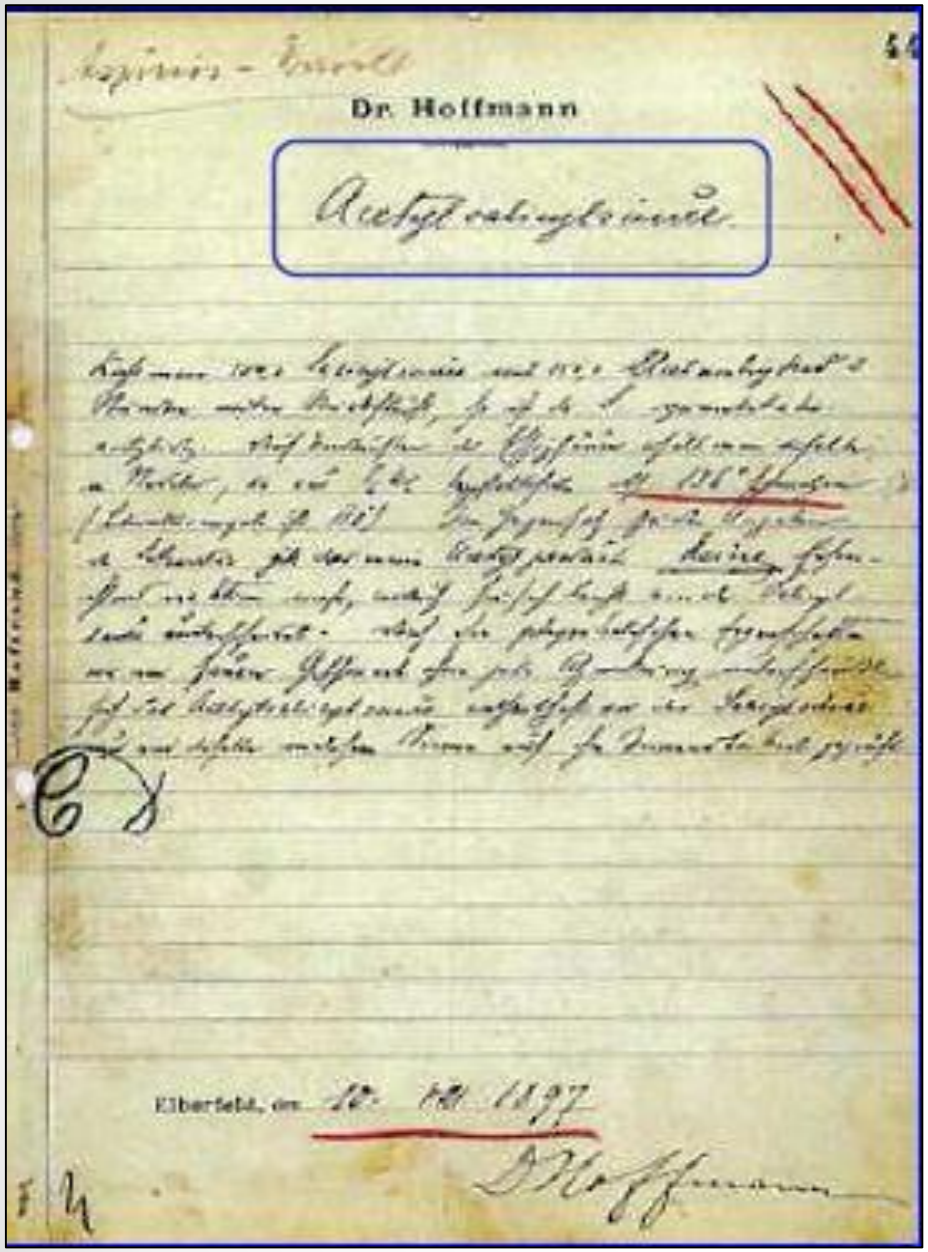
La terapia con aspirina nella prevenzione cardiovascolare primaria. Documento di consenso intersocietario italiano

Massimo Volpe[1], Maurizio Giuseppe Abrignani[2], Claudio Borghi[3], Sergio Coccheri[4], Paolo Gresele[5], Giuseppe Patti[6], Bruno Trimarco[7], Raffaele De Caterina[8]

Fase 1: Valutare il rischio a 10 anni di eventi CV maggiori	<10%	10-20%	>20%


Dr. Hoffmann

Elberfeld, den 10. VIII 1897

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The New England
Journal of Medicine

Volume 333 SEPTEMBER 7, 1995 Number 10

ASPIRIN AND THE RISK OF COLORECTAL CANCER IN WOMEN

EDWARD GIOVANNUCCI, M.D., KATHLEEN M. EGAN, M.P.H., DAVID J. HUNTER, M.D., MEIR J. STAMPFER, M.D., GRAHAM A. COLDITZ, M.D., WALTER C. WILLETT, M.D., AND FRANK E. SPEIZER, M.D.

Abstract *Background. Most data suggest that the regular use of aspirin reduces the risk of colorectal cancer, but some apparently conflicting evidence exists. The effects of the dose and the duration of aspirin consumption on the risk of colorectal cancer are not well understood.*

Methods. We determined rates of colorectal cancer according to the number of consecutive years of regular aspirin use (defined as two or more tablets per week) among women in the Nurses' Health Study who reported regular aspirin use on three consecutive questionnaires (1980, 1982, and 1984) and compared the rates in this group with the rates among women who said they did not use aspirin. Cases of cancer occurring from 1984 through 1992 (the eight years after the 1984 questionnaire) were included.

confidence interval, 0.78 to 1.45) or after five to nine years (relative risk, 0.84; 95 percent confidence interval, 0.55 to 1.28). There was a slight reduction in risk among women who took aspirin for 10 to 19 years, but it was not statistically significant (relative risk, 0.70; 95 percent confidence interval, 0.41 to 1.20). However, there was a statistically significant reduction after 20 years of consistent use of aspirin (relative risk, 0.56; 95 percent confidence interval, 0.36 to 0.90; P for trend = 0.008). The maximal reduction in risk was observed among women who took four to six tablets per week; higher doses had a similar apparent benefit. Controlling for risk factors for colorectal cancer, including diet, did not change the results, and the earlier diagnosis and removal of colorectal adenomas among aspirin users did not account for the results.

Aspirina e mortalità per cancro

Effect of daily aspirin on long-term risk of death due to cancer: analysis of individual patient data from randomised trials

Peter M Rothwell, F Gerald R Fowkes, Jill F F Belch, Hisao Ogawa, Charles P Warlow, Tom W Meade

Methods We used individual patient data from all randomised trials of daily aspirin versus no aspirin with mean duration of scheduled trial treatment of 4 years or longer to determine the effect of allocation to aspirin on risk of cancer death in relation to scheduled duration of trial treatment for gastrointestinal and non-gastrointestinal cancers. In three large UK trials, long-term post-trial follow-up of individual patients was obtained from death certificates and cancer registries.

Lancet. 2011 Jan 1;377(9759):31-41.

Aspirina e mortalità per cancro

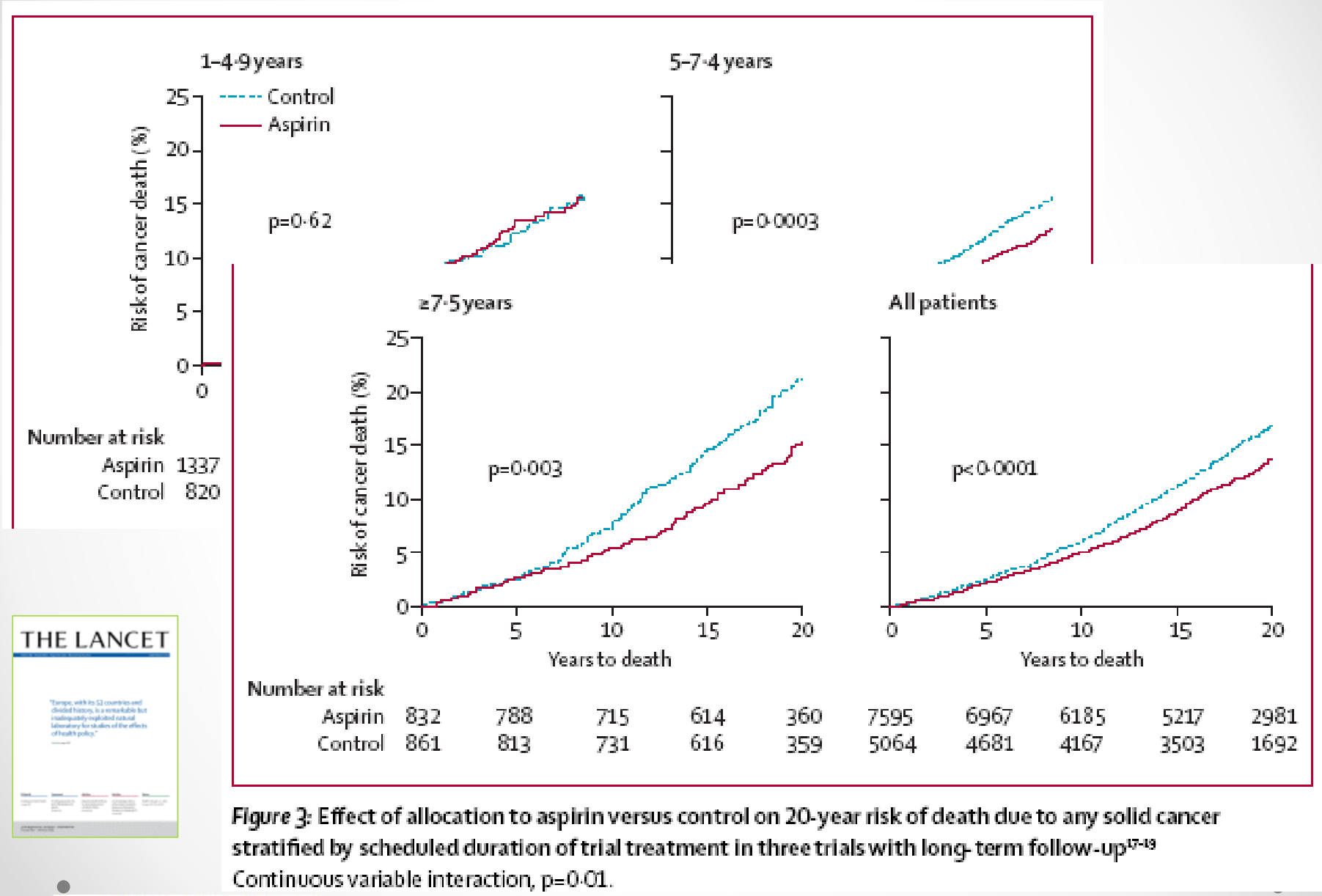

Figure 3: Effect of allocation to aspirin versus control on 20-year risk of death due to any solid cancer stratified by scheduled duration of trial treatment in three trials with long-term follow-up[17–19]
Continuous variable interaction, p=0·01.

Lancet. 2011 Jan 1;377(9759):31-41.

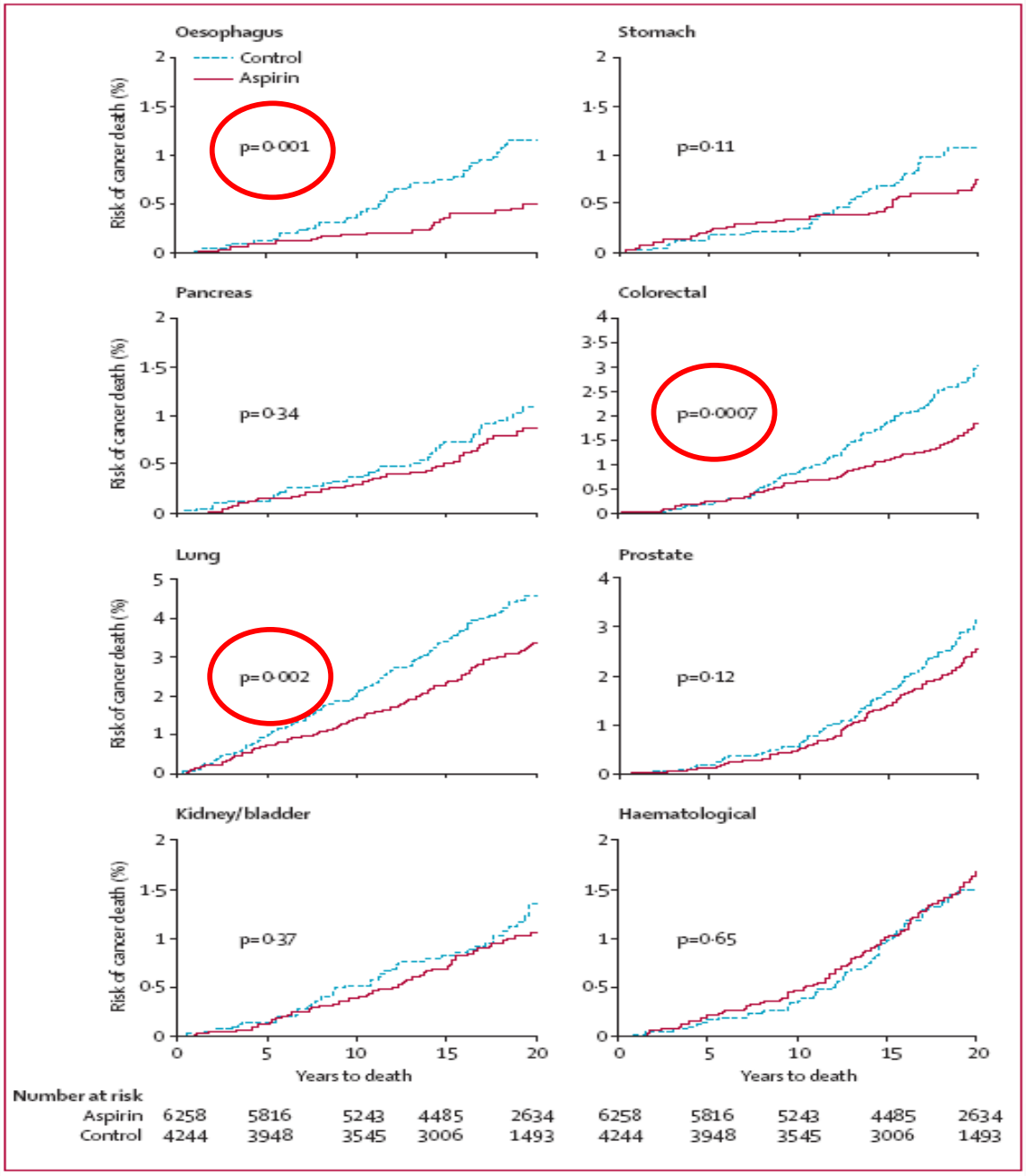

Figure 4: Effect of allocation to aspirin versus control on the 20-year risk of death due to the most common fatal cancers in the 10 502 patients with scheduled treatment duration of 5 years or longer in the three trials with long-term follow-up[17–19]

Lancet. 2011 Jan 1;377(9759):31-41.

Aspirina e mortalità per cancro

Panel: Research in context

Findings

Using individual patient data from all randomised trials of daily aspirin versus no aspirin with mean duration of scheduled trial treatment longer than 4 years, we showed that aspirin reduced risk of death due to cancer by about 20% in the trials, due mainly to a 34% reduction in cancer deaths after 5 years. By long-term post-trial follow-up of patients in three of these trials, we showed that the 20-year risk of cancer death remained about 20% lower in the aspirin groups, and that benefit increased with scheduled duration of treatment in the original trial. The latent period before an effect on deaths was about 5 years for oesophageal, pancreatic, brain, and lung cancer, but was more delayed for stomach, colorectal, and prostate cancer. For lung and oesophageal cancer, benefit was confined to adenocarcinomas.

Interpretation

These findings provide the first proof in man that aspirin reduces deaths due to several common cancers. Benefit was consistent across the different trial populations, suggesting that the findings are likely to be generalisable.

Lancet. 2011 Jan 1;377(9759):31-41.

Riduzione Incidenza di Cancro con Aspirina

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

Summary

Background Daily aspirin reduces the long-term risk of death due to cancer. However, the short-term effect is less certain, especially in women, effects on cancer incidence are largely unknown, and the time course of risk and benefit in primary prevention is unclear. We studied cancer deaths in all trials of daily aspirin versus control and the time course of effects of low-dose aspirin on cancer incidence and other outcomes in trials in primary prevention.

Methods We studied individual patient data from randomised trials of daily aspirin versus no aspirin in prevention of vascular events. Death due to cancer, all non-vascular death, vascular death, and all deaths were assessed in all eligible trials. In trials of low-dose aspirin in primary prevention, we also established the time course of effects on incident cancer, major vascular events, and major extracranial bleeds, with stratification by age, sex, and smoking status.

Published Online March 21, 2012 DOI:10.1016/S0140-6736(11)61720-0

See Online/Comment DOI:10.1016/S0140-6736(11)61654-1

See Online/Articles DOI:10.1016/S0140-6736(12)60209-8

	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)	

Riduzione Incidenza di Cancro con Aspirina

Panel: Research in context

Findings

Using all available individual patient data from randomised trials of daily aspirin versus no aspirin in prevention of vascular events, we showed that aspirin reduces the risk of non-vascular death, due mainly to fewer cancer deaths after 5 years. Using individual patient data from all randomised trials of daily low-dose aspirin in primary prevention of vascular events, we showed that aspirin also reduces cancer incidence, both in men and women and in smokers and non-smokers. The effects of aspirin on other major outcomes evolve with duration of treatment, the initial reduction in risk of major vascular events and the increase in risk of major extracranial bleeding diminishing with time, such that the reduced risk of cancer is the only significant effect from 3 years onwards.

	Number of cancers		Odds ratio (95% CI)*	p*	Absolute reduction per 1000 patient-years (95% CI)†
	Aspirin	Control			
All patients					
<3 years	445	442	1·01 (0·88 to 1·15)	0·92	−0·06 (−1·15 to 1·04)
≥3 years	324	421	0·76 (0·66 to 0·88)	0·0003	3·13 (1·44 to 4·82)
Men					
<3 years	269	284	0·94 (0·80 to 1·12)	0·49	0·60 (−0·98 to 2·18)
≥3 years	192	245	0·77 (0·63 to 0·93)	0·008	3·09 (0·85 to 5·33)
Women					
<3 years	176	158	1·13 (0·91 to 1·40)	0·28	−0·83 (−2·38 to 0·72)
≥3 years	132	176	0·75 (0·59 to 0·94)	0·01	3·19 (0·61 to 5·77)
Age <60 years					
<3 years	115	141	0·83 (0·65 to1·07)	0·14	0·92 (−0·41 to 2·25)
≥3 years	105	149	0·72 (0·56 to 0·93)	0·01	2·74 (0·69 to 4·78)
Age ≥60 years					
<3 years	330	301	1·08 (0·92 to 1·27)	0·32	−0·75 (−2·46 to 0·96)
≥3 years	219	272	0·77 (0·65 to 0·93)	0·006	3·68 (1·03 to 6·33)
Non-smokers					
<3 years	317	320	0·99 (0·85 to 1·16)	0·95	0·01 (−1·20 to 1·22)
≥3 years	202	272	0·74 (0·61 to 0·89)	0·001	3·07 (1·18 to 4·97)
Smokers					
<3 years	128	122	1·05 (0·81 to 1·35)	0·72	−0·18 (−2·90 to 2·53)
≥3 years	122	149	0·79 (0·62 to 1·02)	0·07	3·34 (−0·20 to 6·88)

*Derived from meta-analysis of individual trials by Mantel-Haenszel-Peto method. †Derived from pooled analysis of individual patient data.

Table 3: Pooled analysis of the effect of allocation to aspirin versus control on the risk of all incident cancer during trial follow-up in the six trials of low-dose aspirin in primary prevention of vascular disease,[16-21] by years to notification

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

Beneficio non correlato ad una diagnosi precoce dovuta ad aumento dei sanguinamenti

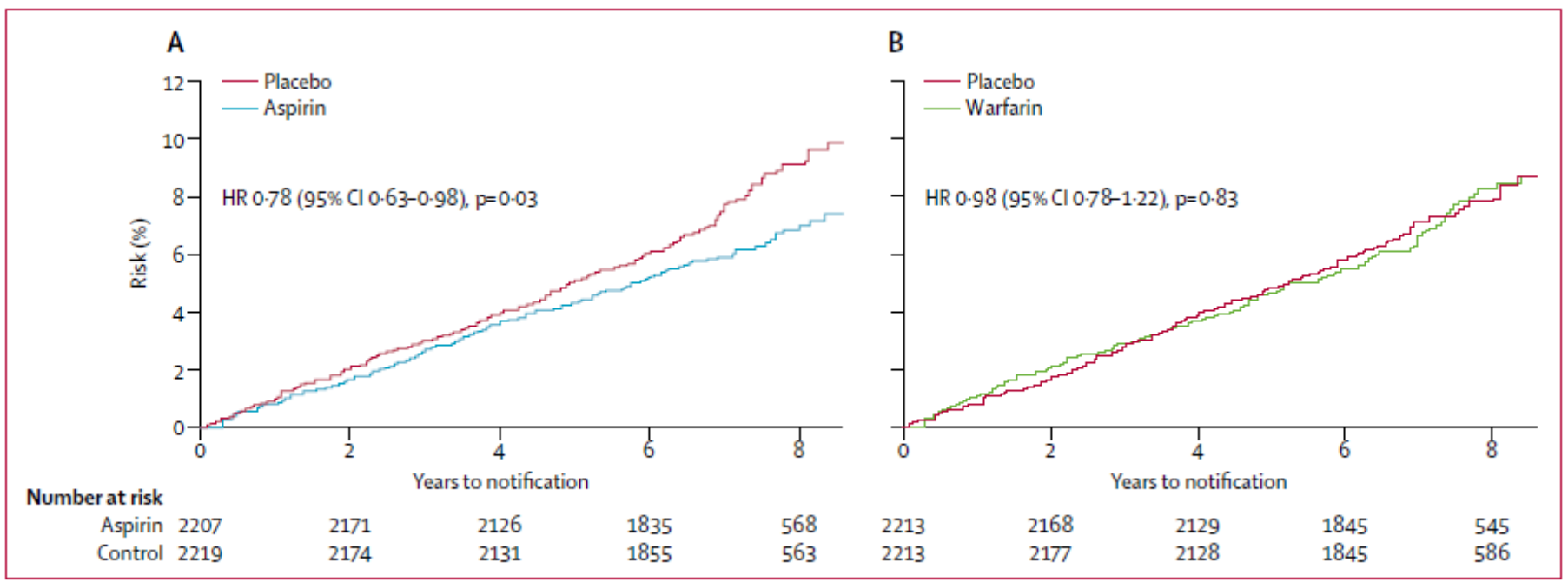

Figure 3: Effect of allocation to aspirin versus placebo (A) and warfarin versus placebo (B) on the incidence of cancer during the Thrombosis Prevention Trial[16]

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

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

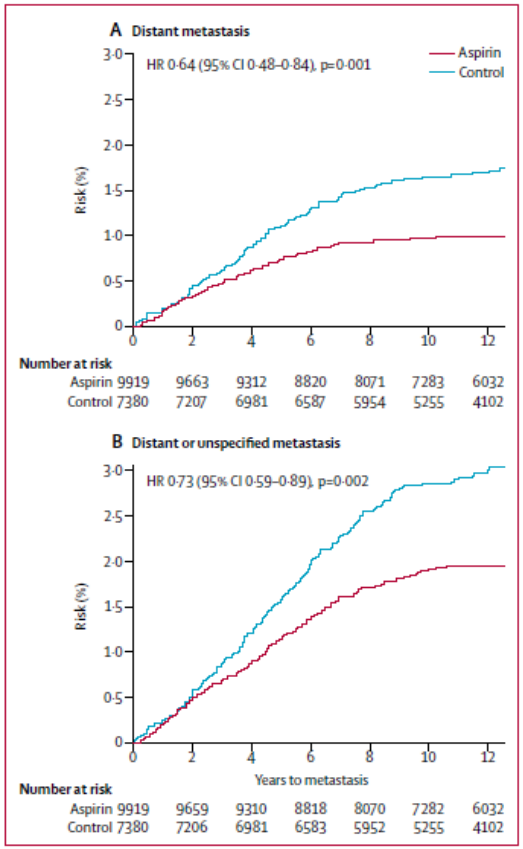

Figure 1: **The effect of aspirin on risk of metastasis due to any incident cancer diagnosed during five trials of aspirin versus control**
Analysis is based on time from randomisation to diagnosis of metastasis during or after the trials. Part A shows definite site-specific distant metastasis and part 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.

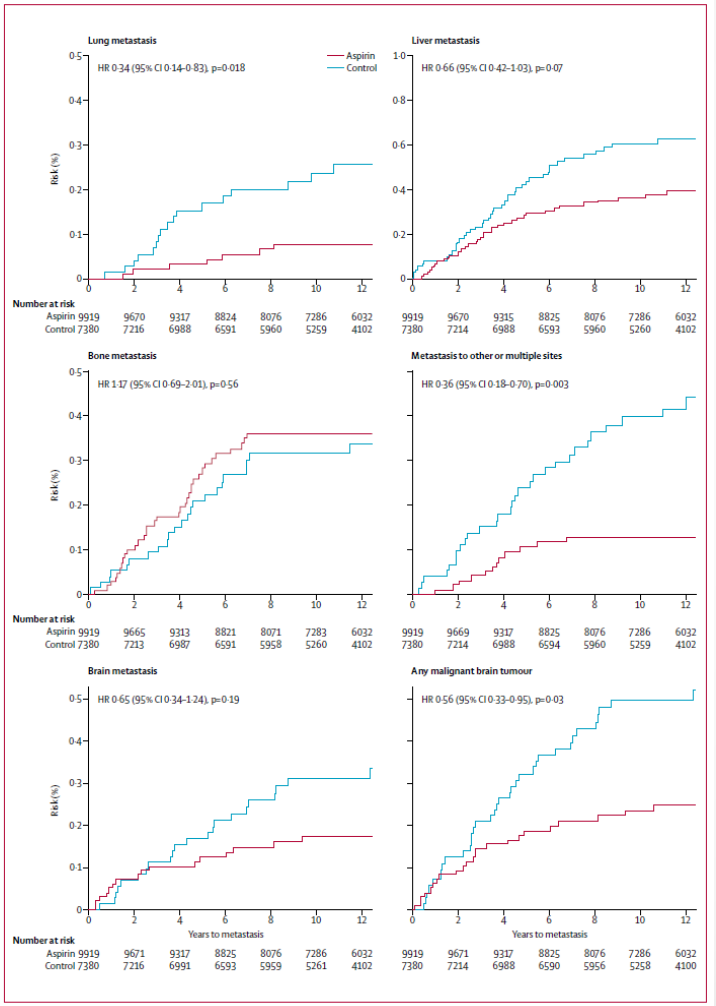

Figure 2: **The effect of aspirin on risk of definite distant metastasis due to any incident cancer diagnosed during five trials of aspirin versus control, stratified by site of metastasis**
Analysis is based on time from randomisation to diagnosis of metastasis during or after the trials. The sensitivity analysis of the effect of aspirin on risk of all malignant brain tumours is included because of the clinical inaccuracy in differentiating between a primary brain tumour and a solitary metastasis, particularly if a biopsy was not undertaken. 29 patients in the analysis of other or multiple metastasis are also included in analyses of site-specific metastasis. HR=hazard ratio from a Cox regression stratified by trial.

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

Effects of aspirin on cancer initiation and progression

Expert Rev. Anticancer Ther. 13(2), 115–117 (2013)

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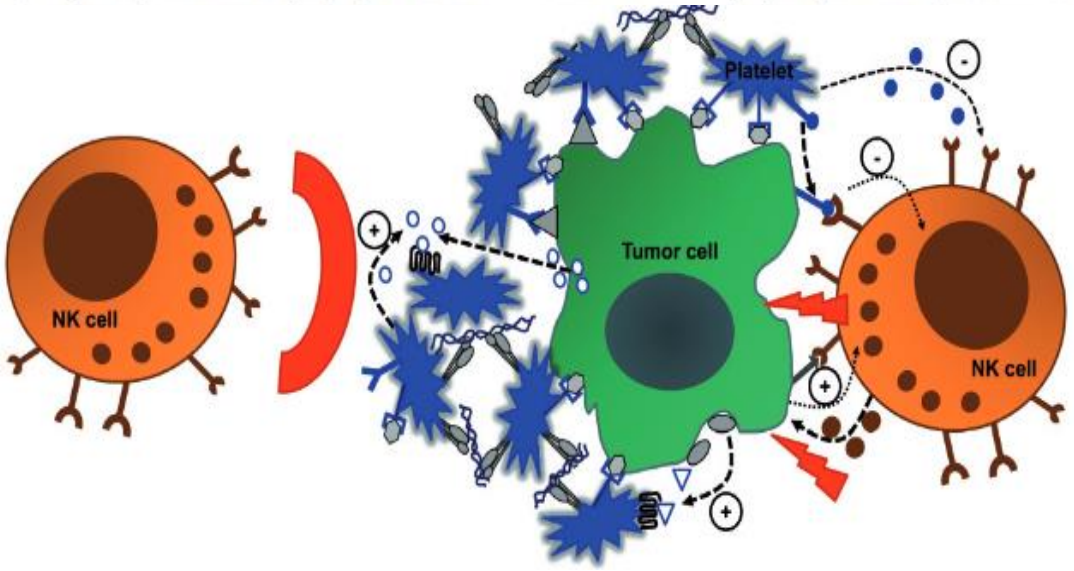
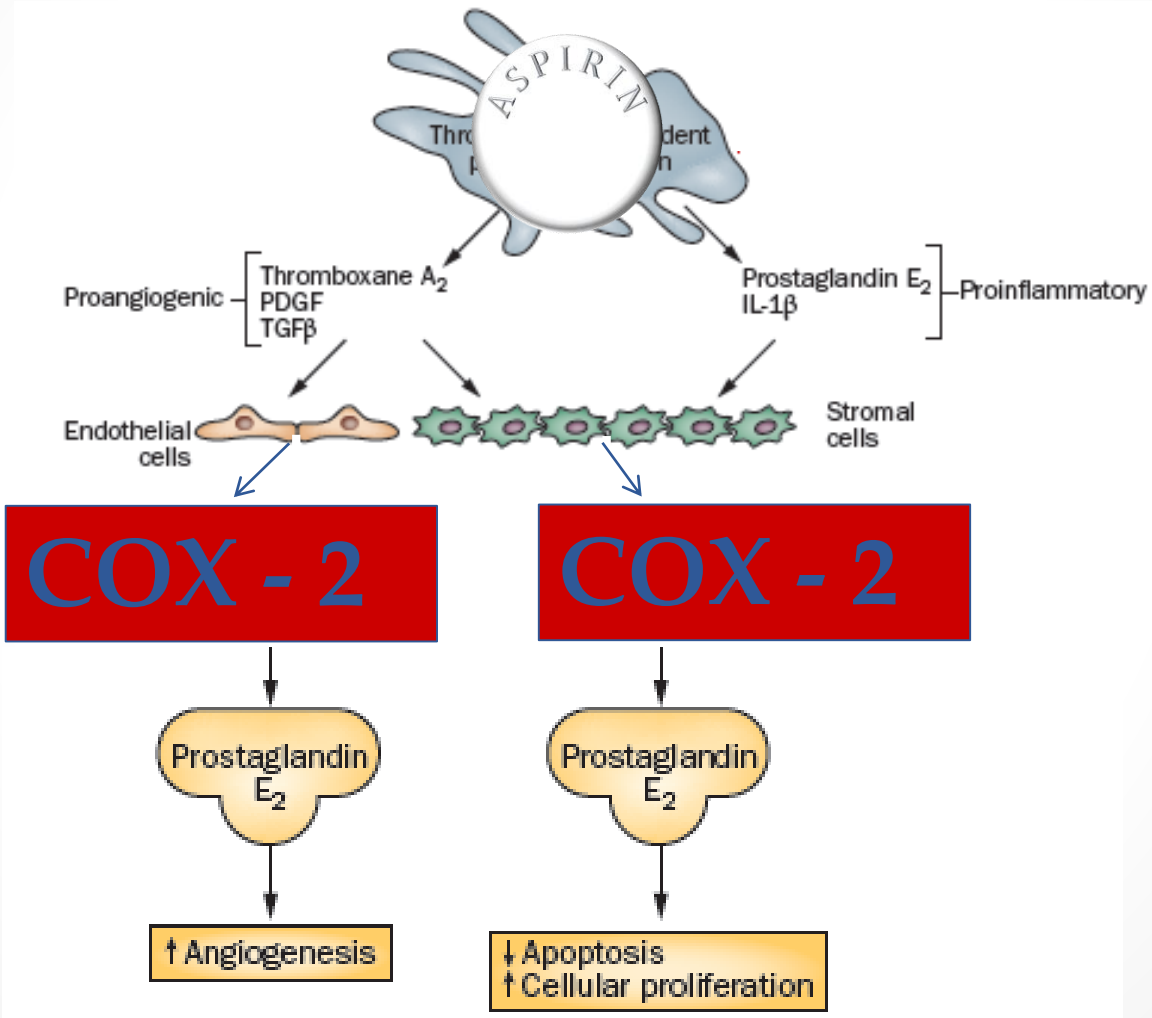
"...during metastasis, platelets surround cancer cells in the bloodstream, which protects them from immune surveillance and promotes their colonization at distant sites."

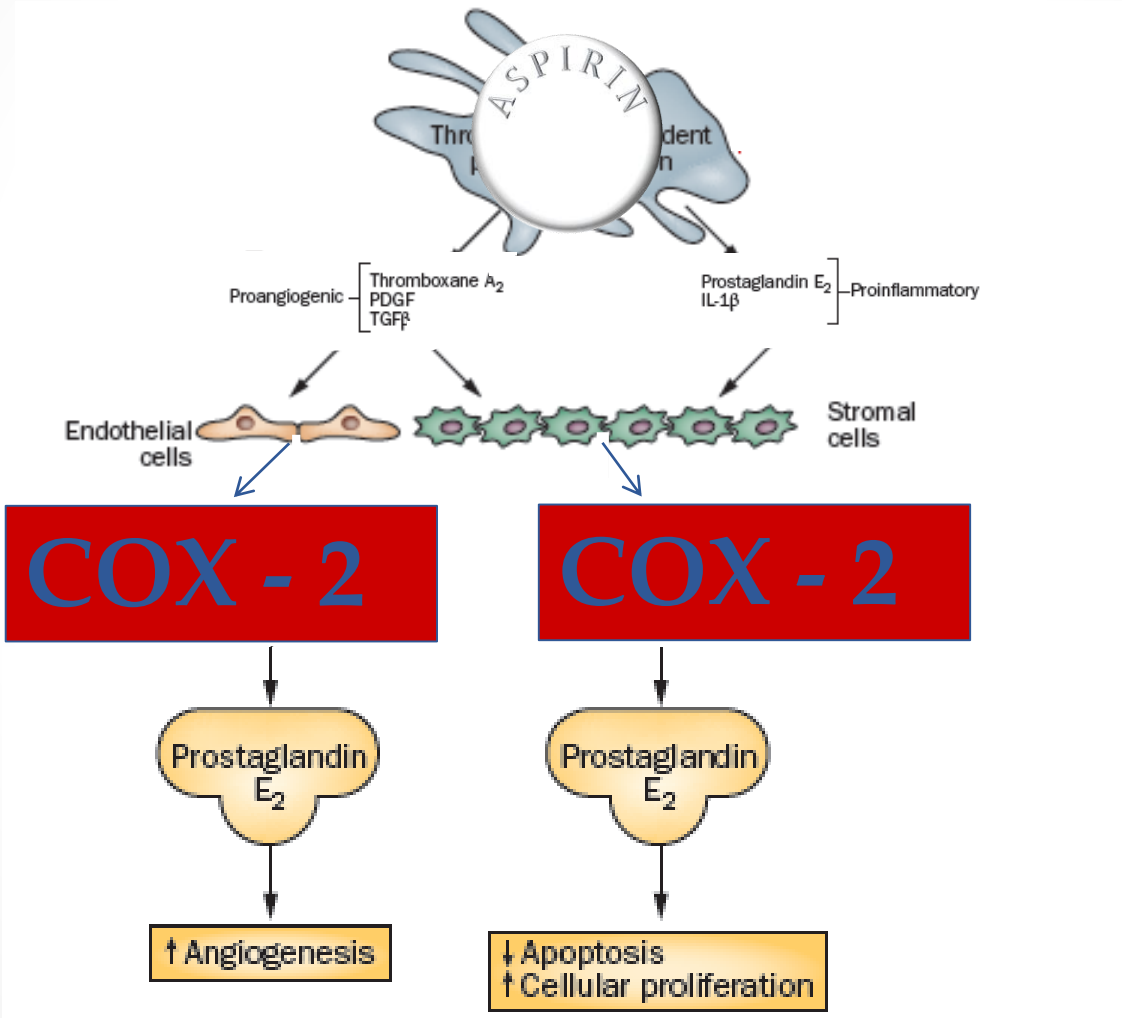


 10.1586/ERA.12.166 ISSN 1473-7140

Ipotesi di meccanismo d'azione



Ipotesi di meccanismo d'azione



Beneficio in termini di sopravvivenza

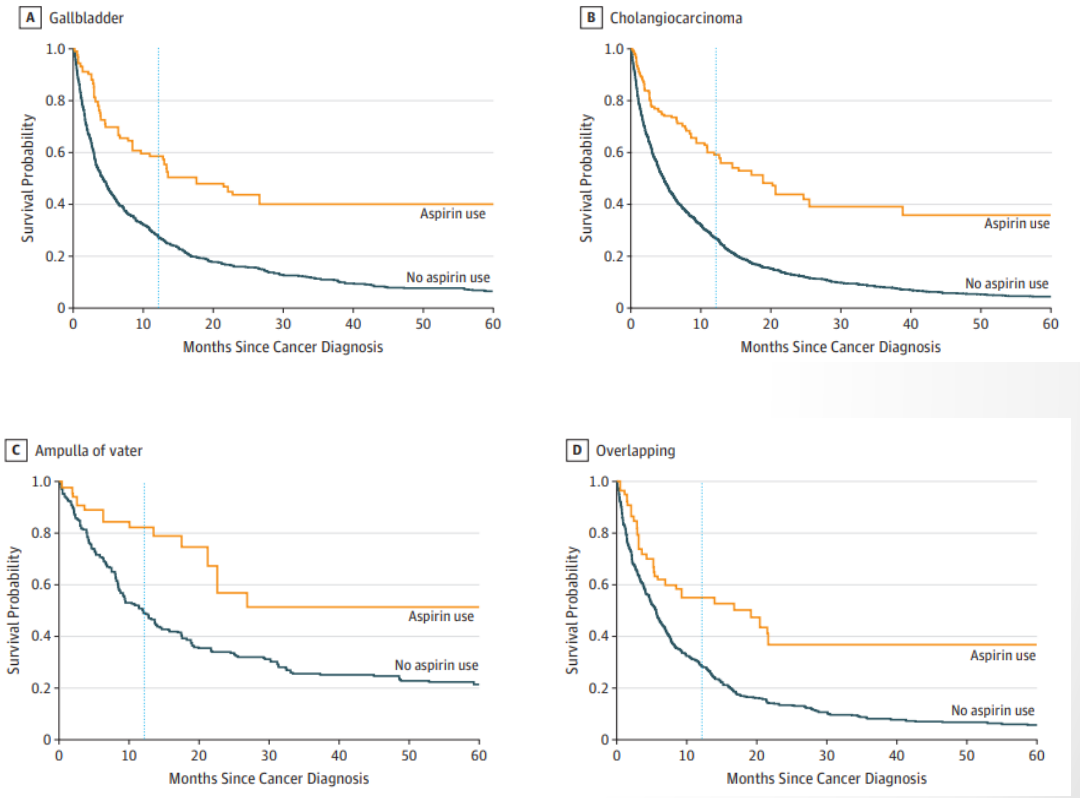
RESEARCH LETTER

Association Between Aspirin Use and Biliary Tract Cancer Survival

Biliary tract cancers (BTCs) are rare, with a worldwide incidence of less than 2 per 100 000 individuals.[1] The 5-year survival rate ranges from 5% to 15%, with a median survival of less than 1 year.[1] Between 60% and 70% of patients present with late-stage disease (eg, inoperable or metastatic tumors) owing to the lack of symptoms.[2] Consequently, there is a critical need for treatments that improve BTC survival. Aspirin has been proposed as a treatment to reduce cancer mortality because it may slow cancer growth through the inhibition of both cyclooxygenase 2, which promotes inflammation and cell proliferation,[3] and platelet aggregation, which may slow the metastatic spread of cancer.[4] We investigated the association between postdiagnosis aspirin use and BTC survival.

JAMA Oncology Published online October 17, 2019

Figure. Adjusted Survival Curves Among Postdiagnosis Aspirin Users and Nonusers by Cancer Site



Aspirina: aggiornamento RCP

GAZZETTA UFFICIALE
DELLA REPUBBLICA ITALIANA
HOME
PERMALINK

Estratto determina AAM/PPA n. 607 del 26 giugno 2018

Autorizzazione della variazione:

Variazione di tipo II: C.I.6.a) Aggiunta di una nuova indicazione terapeutica, relativamente al medicinale CARDIOASPIRIN;

Codice pratica: VN2/2017/100

E' autorizzato l'aggiornamento del riassunto delle caratteristiche del prodotto alle sezione 5.1, relativamente al medicinale «Cardioaspirin», nelle forme e confezioni sottoelencate:

AIC N. 024840074 - «100 mg compresse gastroresistenti» 30 compresse

AIC N. 024840086 - «100 mg compresse gastroresistenti» 60 compresse

AIC N. 024840098 - «100 mg compresse gastroresistenti» 90 compresse

Gli stampati corretti ed approvati sono allegati alla determinazione, di cui al presente estratto.

Titolare AIC:

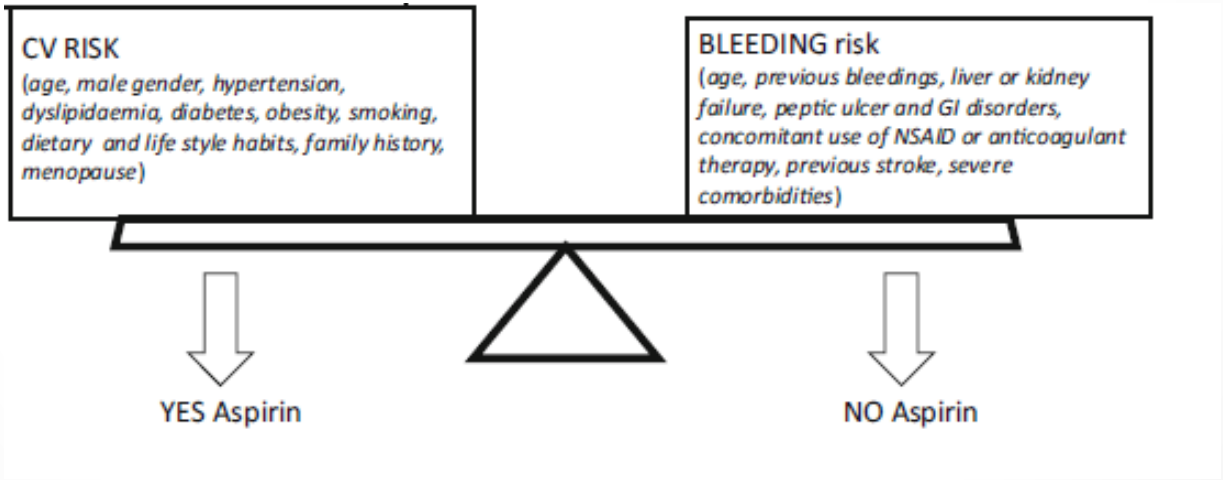
Bayer S.P.A. (codice fiscale 05849130157) con sede legale e domicilio fiscale in viale Certosa, 130, 20156 - Milano (MI) Italia

Aspirina: aggiornamento RCP

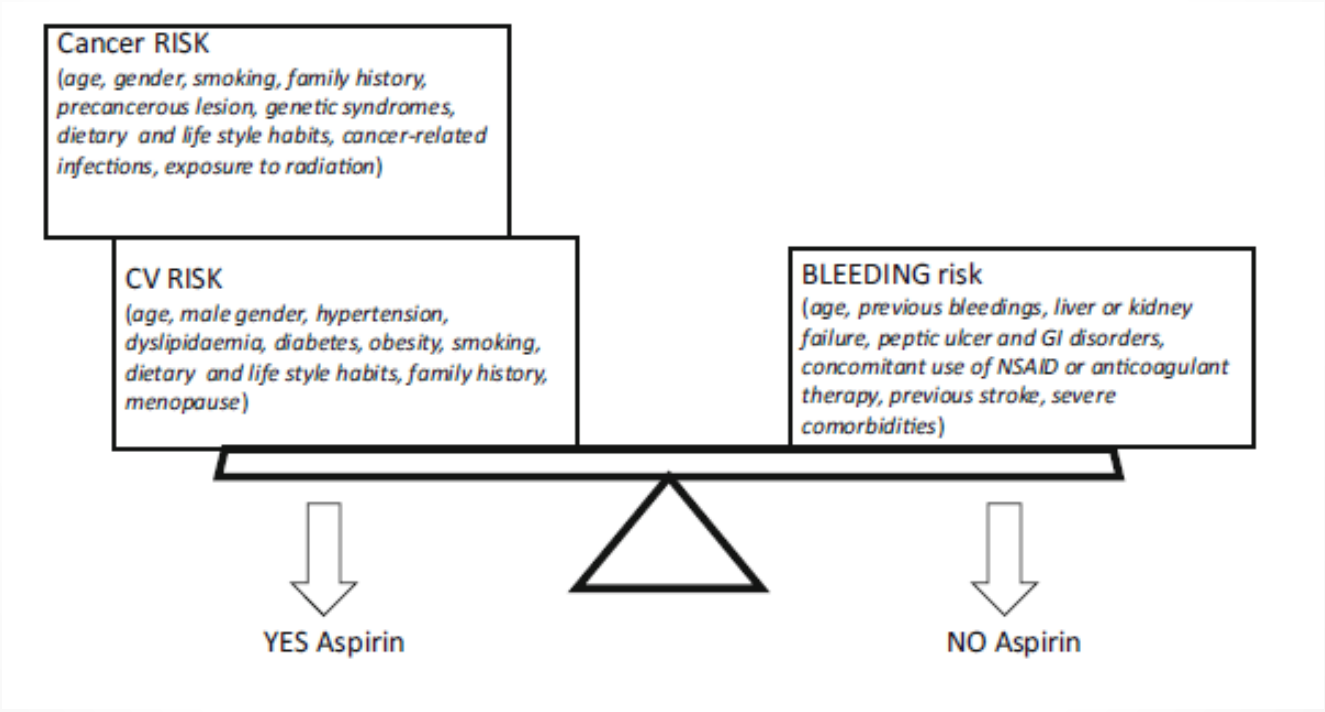
5.1 Proprietà farmacodinamiche - Categoria farmacoterapeutica: Antitrombotici.
Codice ATC:B01AC06.

Meccanismo d'azione

...L'acido acetilsalicilico ha dimostrato di inibire la cicloossigenasi-1 nella mucosa del colon retto e di ridurre la prostaglandina E2 della mucosa intestinale, fattori che, come osservato negli studi preclinici, hanno un ruolo nella genesi del cancro del colon retto (CCR). L'acido acetilsalicilico inibisce anche il rilascio, dalle piastrine attivate, di mediatori che possono favorire la crescita e la diffusione del tumore.



High Blood Press Cardiovasc Prev (2017) 24:331–339
DOI 10.1007/s40292-017-0213-4


Cancer RISK
(age, gender, smoking, family history, precancerous lesion, genetic syndromes, dietary and life style habits, cancer-related infections, exposure to radiation)
CV RISK
(age, male gender, hypertension, dyslipidaemia, diabetes, obesity, smoking, dietary and life style habits, family history, menopause)
BLEEDING risk
(age, previous bleedings, liver or kidney failure, peptic ulcer and GI disorders, concomitant use of NSAID or anticoagulant therapy, previous stroke, severe comorbidities)
YES Aspirin
NO Aspirin

TAKE HOME MESSAGGES

- L'aspirina mostra effetti favorevoli non solo in termini di riduzione di eventi cardiovascolari (prevenzione secondaria) ma anche in termini di riduzione di incidenza e diffusione di neoplasie (prevenzione primaria)
- Nei pazienti ad alto rischio di sviluppare neoplasie e a basso rischio di sanguinamento, basse dosi di aspirina sono una efficace e appropriata terapia preventiva per ridurre incidenza e diffusione di tumori solidi