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L'ACIDO ACETILSALICILICO IN PREVENZIONE PRIMARIA. A CHI?

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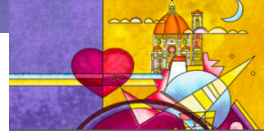
ASPIRIN and PRIMARY PREVENTION



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1. Low-dose **aspirin** and upper gastrointestinal bleeding in **primary** versus secondary cardiovascular **prevention**: a population-based, nested case-**control** study.
   Lin KJ, De Caterina R, García Rodríguez LA.
   Circ Cardiovasc Qual Outcomes. 2014 Jan;7(1):70-7. doi: 10.1161/CIRCOUTCOMES.113.000494. Epub 2013 Nov 19.
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2. Low-dose **aspirin** in **primary prevention**: cardioprotection, chemoprevention, both, or neither?
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3. A short-term risk-benefit analysis of occasional and regular use of low-dose **aspirin** in

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Aspirin for **primary** stroke **prevention** in elderly patients with [J Gen Fam Med. 2017]

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2016 European Guidelines on cardiovascular disease prevention in clinical practice

Recommendations for antiplatelet therapy

Recommendations	Class[a]	Level[b]	Ref[c]
Antiplatelet therapy is not recommended in individuals without CVD due to the increased risk of major bleeding.	III	B	464

3a.10.1 Antiplatelet therapy in individuals without cardiovascular disease

Prevention in individuals without overt CV or cerebrovascular disease was investigated using long-term aspirin vs. control in a systematic review of six trials including 95 000 individuals. A risk reduction from 0.57% to 0.51%/year of serious vascular events was found by the Antithrombotic Trialists' Collaboration.[464] Major gastrointestinal and extracranial bleeds increased by 0.03%/year. The risk of vascular mortality was not changed by treatment with aspirin. In a recent Japanese study,[470] patients 60–85 years of age presenting with hypertension, dyslipidaemia or DM were randomized to treatment with 100 mg aspirin or placebo. The 5 year cumulative primary outcome event rate (death from CV causes) was not significantly different between the groups, but treatment with aspirin significantly increased the risk of extracranial haemorrhage requiring transfusion or hospitalization ($P = 0.004$). In individuals with multiple risk factors, clo-

Recommendations for management of diabetes

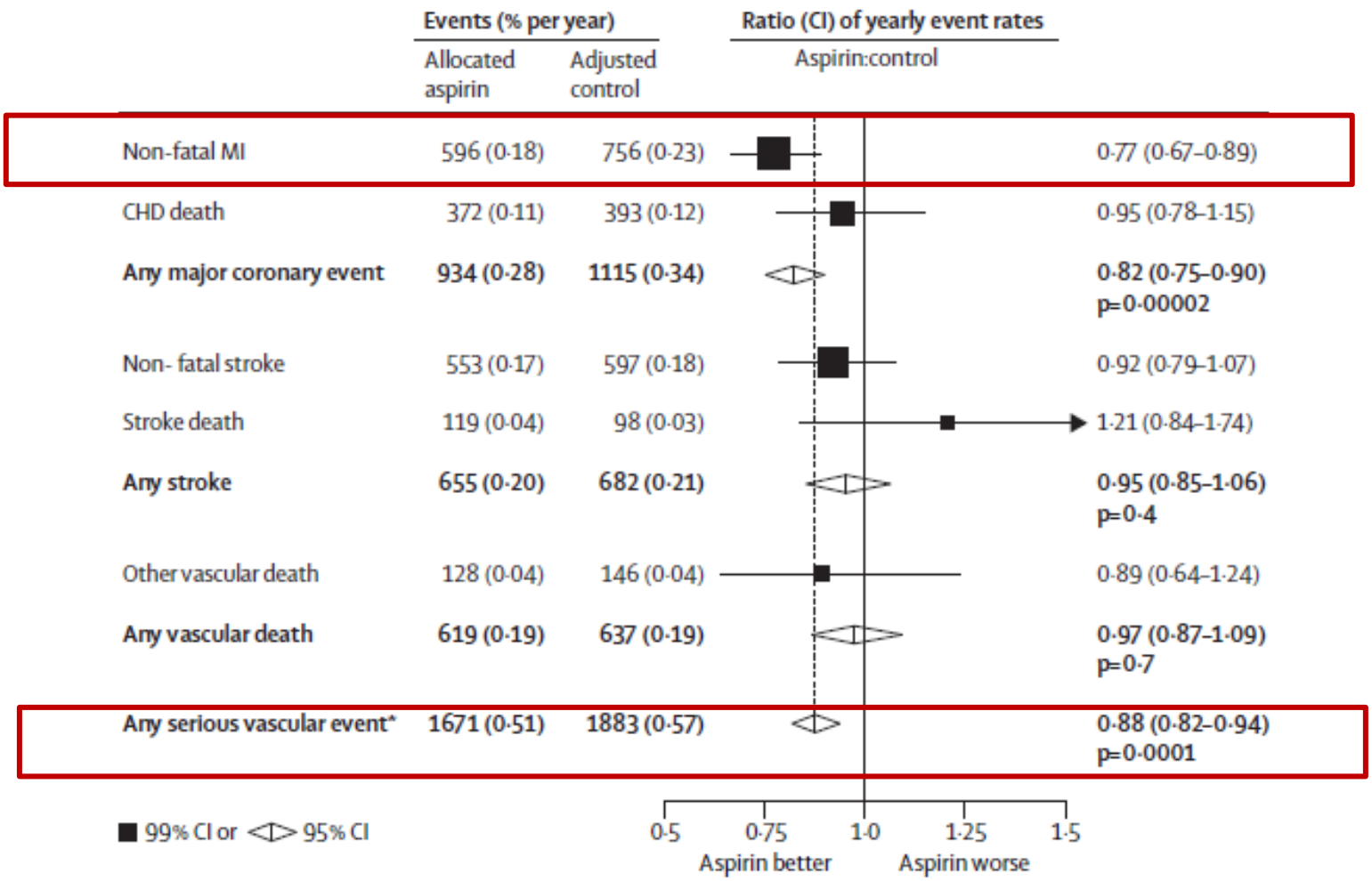
Recommendations	Class[a]	Level[b]	Ref[c]
Antiplatelet therapy (e.g. with aspirin) is not recommended for people with DM who do not have CVD.	III	A	398

Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials

Antithrombotic Trialists' (ATT) Collaboration*

Antithrombotic Trialists´ (ATT) Collaboration. Lancet. 2009;373: 1849–60.

Aspirin and specific CV events



Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials

Antithrombotic Trialists' (ATT) Collaboration*

Antithrombotic Trialists´ (ATT) Collaboration. Lancet. 2009;373: 1849–60.

Aspirin and Bleeding risk

	Number of events (aspirin vs control)		Rate ratio (95% CI) (aspirin vs control)			Yearly absolute difference (% per year)	
	Primary prevention (660 000 person-years)	Secondary prevention (43 000 person-years)	Primary prevention	Secondary prevention	p value for heterogeneity	Primary prevention	Secondary prevention
Major coronary event	934 vs 1115	995 vs 1214	0·82 (0·75–0·90)	0·80 (0·73–0·88)	0·7	−0·06	−1·00*
Non-fatal MI	596 vs 756	357 vs 505	0·77 (0·69–0·86)	0·69 (0·60–0·80)	0·5	−0·05	−0·66
CHD mortality	372 vs 393	614 vs 696	0·95 (0·82–1·10)	0·87 (0·78–0·98)	0·4	−0·01	−0·34
Stroke	655 vs 682	480 vs 580	0·95 (0·85–1·06)	0·81 (0·71–0·92)	0·1	−0·01	−0·46*
Haemorrhagic	116 vs 89	36 vs 19	1·32 (1·00–1·75)	1·67 (0·97–2·90)	0·4	0·01	..†
Ischaemic	317 vs 367	140 vs 176	0·86 (0·74–1·00)	0·78 (0·61–0·99)	0·5	−0·02	..†
Unknown cause	222 vs 226	304 vs 385	0·97 (0·80–1·18)	0·77 (0·66–0·91)	0·1	−0·001	..†
Vascular death	619 vs 637	825 vs 896	0·97 (0·87–1·09)	0·91 (0·82–1·00)	0·4	−0·01	−0·29
Any serious vascular event	1671 vs 1883 (0·51% vs 0·57% per year)	1505 vs 1801 (6·69% vs 8·19% per year)	0·88 (0·82–0·94)	0·81 (0·75–0·87)	0·1	−0·07	−1·49*
Major extracranial bleed	335 vs 219	23 vs 6	1·54 (1·30–1·82)	2·69 (1·25–5·76)	0·2	0·03	..†

MI=myocardial infarction. CHD=coronary heart disease. Non-fatal MI definitions vary; see methods. *Major coronary event rates (percent per year, aspirin vs control) 6·0 vs 7·4 in post-MI trials and 2·4 vs 3·0 in post-cerebral vascular disease trials; corresponding rates of stroke (mainly of unknown cause) 0·6 vs 0·8 in post-MI trials and 3·9 vs 4·7 in post-cerebral vascular disease trials (webappendix pp 14–18). †Stroke causes, and extracranial bleeds, very incompletely reported.

Table 2: Comparison of proportional and absolute effects of aspirin in primary and secondary prevention trials

Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials

Antithrombotic Trialists' (ATT) Collaboration*

Antithrombotic Trialists´ (ATT) Collaboration. Lancet. 2009;373: 1849–60.

95000 individuals, low average risk

	Dates of recruitment	Participating countries	Year of main publication	Number of participants	Mean duration of follow-up (years)	Target population	Eligible age range (years) at entry	Aspirin regimen	Randomised factorial comparison	Placebo control
British Doctors' Study[10]	Nov 1978–Nov 1979	UK	1988	5139	5·6	Male doctors	19–90	500 mg daily	None	No
US Physicians' Health Study[11]	Aug 1981–Apr 1984	USA	1988	22071	5·0	Male doctors	45–73	325 mg alternate days	β carotene *vs* placebo	Yes
Thrombosis Prevention Trial[9]	Feb 1989–May 1994	UK	1998	5085	6·7	Men with risk factors for CHD	45–69	75 mg daily	Warfarin *vs* placebo	Yes
Hypertension Optimal Treatment Trial[12]	Oct 1992–May 1994	Europe, North and South America, Asia	1998	18790	3·8	Men and women with DBP 100–115 mm Hg	50–80	75 mg daily	Three blood pressure regimens	Yes
Primary Prevention Project[13]	June 1993–Apr 1998	Italy	2001	4495	3·7	Men and women with one or more risk factors for CHD	45–94	100 mg daily	Vitamin E *vs* open control	No
Women's Health Study[14]	Sep 1992–May 1995	USA	2005	39876	10·0	Female health professionals	≥45	100 mg alternate days	Vitamin E *vs* placebo	Yes

CHD=coronary heart disease. DBP=diastolic blood pressure.

Table 1: **Design and eligibility criteria of primary prevention trials**

Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial

Hansson L et al. Lancet. 1998;351: 1755-62.

Summary

Background Despite treatment, there is often a higher incidence of cardiovascular complications in patients with hypertension than in normotensive individuals. Inadequate reduction of their blood pressure is a likely cause, but the optimum target blood pressure is not known. The impact of acetylsalicylic acid (aspirin) has never been investigated in patients with hypertension. We aimed to assess the optimum target diastolic blood pressure and the potential benefit of a low dose of acetylsalicylic acid in the treatment of hypertension.

Methods 18 790 patients, from 26 countries, aged 50–80 years (mean 61·5 years) with hypertension and diastolic blood pressure between 100 mm Hg and 115 mm Hg (mean 105 mm Hg) were randomly assigned a target diastolic blood pressure. 6264 patients were allocated to the target pressure ⩽90 mm Hg, 6264 to ⩽85 mm Hg, and 6262 to ⩽80 mm Hg. Felodipine was given as baseline therapy with the addition of other agents, according to a five-step regimen. In addition, 9399 patients were randomly assigned 75 mg/day acetylsalicylic acid (Bamycor, Astra) and 9391 patients were assigned placebo.

Findings Diastolic blood pressure was reduced by 20·3 mm Hg, 22·3 mm Hg, and 24·3 mm Hg, in the ⩽90 mm Hg, ⩽85 mm Hg, and ⩽80 mm Hg target groups, respectively. The lowest incidence of major cardiovascular events occurred at a mean achieved diastolic blood pressure of 82·6 mm Hg; the lowest risk of cardiovascular mortality occurred at 86·5 mm Hg. Further reduction below these blood pressures was safe. In patients with diabetes mellitus there was a 51% reduction in major cardiovascular events in target group ⩽80 mm Hg compared with target group ⩽90 mm Hg (p for trend=0·005). Acetylsalicylic acid reduced major cardiovascular events by 15% (p=0·03) and all myocardial infarction by 36% (p=0·002), with no effect on stroke. There were seven fatal bleeds in the acetylsalicylic acid group and eight in the placebo group, and 129 versus 70 non-fatal major bleeds in the two groups, respectively (p<0·001).

Interpretation Intensive lowering of blood pressure in patients with hypertension was associated with a low rate of cardiovascular events. The HOT Study shows the benefits of lowering the diastolic blood pressure down to 82·6 mm Hg. Acetylsalicylic acid significantly reduced major cardiovascular events with the greatest benefit seen in all myocardial infarction. There was no effect on the incidence of stroke or fatal bleeds, but non-fatal major bleeds were twice as common.

Lancet 1998; **351:** 1755–62

See Commentary page

Introduction

The background and rationale of the Hypertension Optimal Treatment (HOT) Study have been presented previously in some detail.[1] In brief, it is well documented that treatment of hypertension reduces cardiovascular morbidity and mortality.[2,3] However, it is obvious that treated patients with hypertension remain at a greater risk of developing cardiovascular complications than matched normotensive individuals.[4,5] One possible explanation could be that the blood pressure of the patients with

Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice

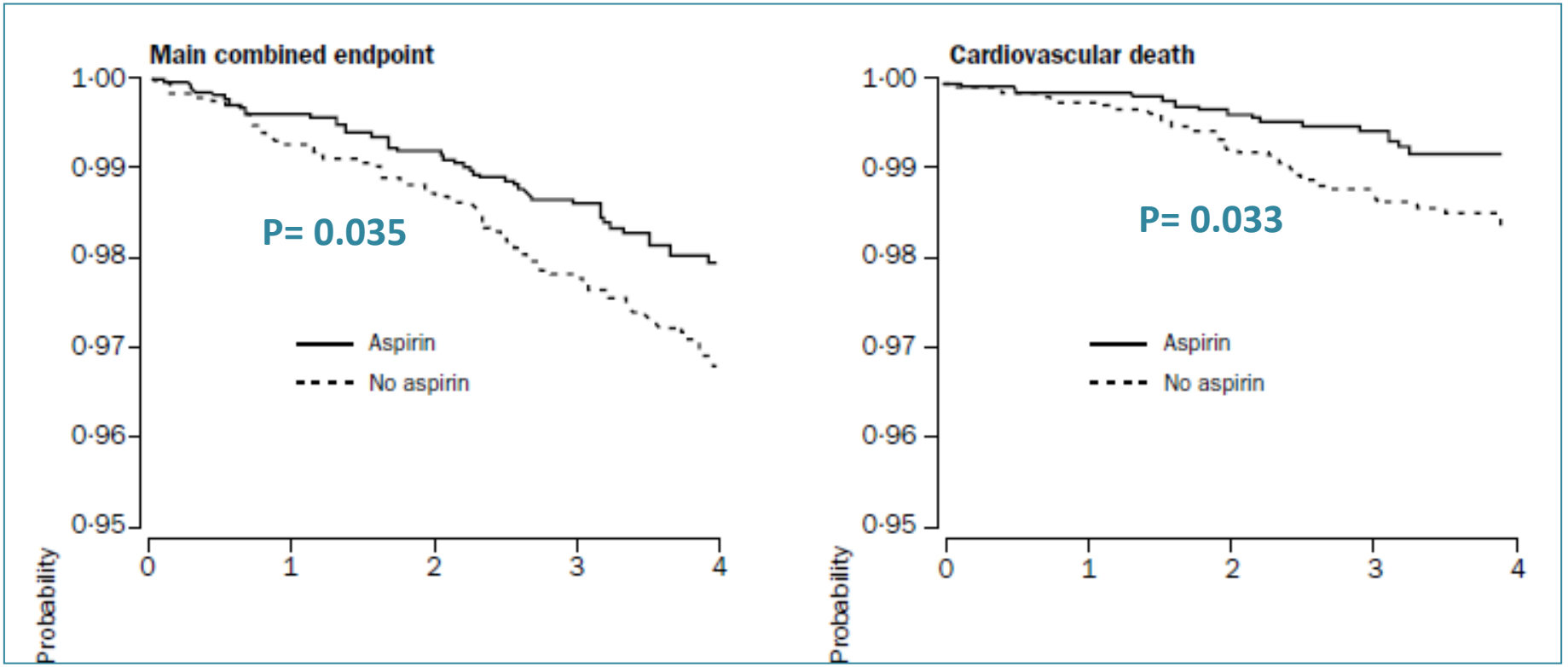
Primary Prevention Project (PPP). Lancet. 2001;357: 89-95.

- 4495 patients with at least one major risk factor mean age 64 years; 57,7% W
- 30% one risk factor, 39% two risk factors, 30% three or more risk factors

	Aspirin (n=2226)	No aspirin (n=2269)	Relative risk (95% CI)
Main combined endpoint (cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke)	45 (2·0%)	64 (2·8%)	0·71 (0·48–1·04)
Total cardiovascular events or diseases*	141 (6·3%)	187 (8·2%)	0·77 (0·62–0·95)
All deaths	62 (2·8%)	78 (3·4%)	0·81 (0·58–1·13)
Cardiovascular	17 (0·8%)	31 (1·4%)	0·56 (0·31–0·99)
Non-cardiovascular	45 (2·0%)	47 (2·0%)	0·98 (0·65–1·46)
All myocardial infarction	19 (0·8%)	28 (1·2%)	0·69 (0·38–1·23)
Non-fatal myocardial infarction	15 (0·7%)	22 (1·0%)	0·69 (0·36–1·33)
All stroke	16 (0·7%)	24 (1·1%)	0·67 (0·36–1·27)
Non-fatal stroke	15 (0·7%)	18 (0·8%)	0·84 (0·42–1·67)
Angina pectoris	54 (2·4%)	67 (3·0%)	0·82 (0·58–1·17)
Transient ischaemic attack	28 (1·3%)	40 (1·8%)	0·71 (0·44–1·15)
Peripheral-artery disease	17 (0·8%)	29 (13%)	0·60 (0·33–1·08)
Revascularisation procedure	20 (0·9%)	29 (1·3%)	0·70 (0·40–1·24)

Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice

Primary Prevention Project (PPP). Lancet. 2001;357: 89-95.



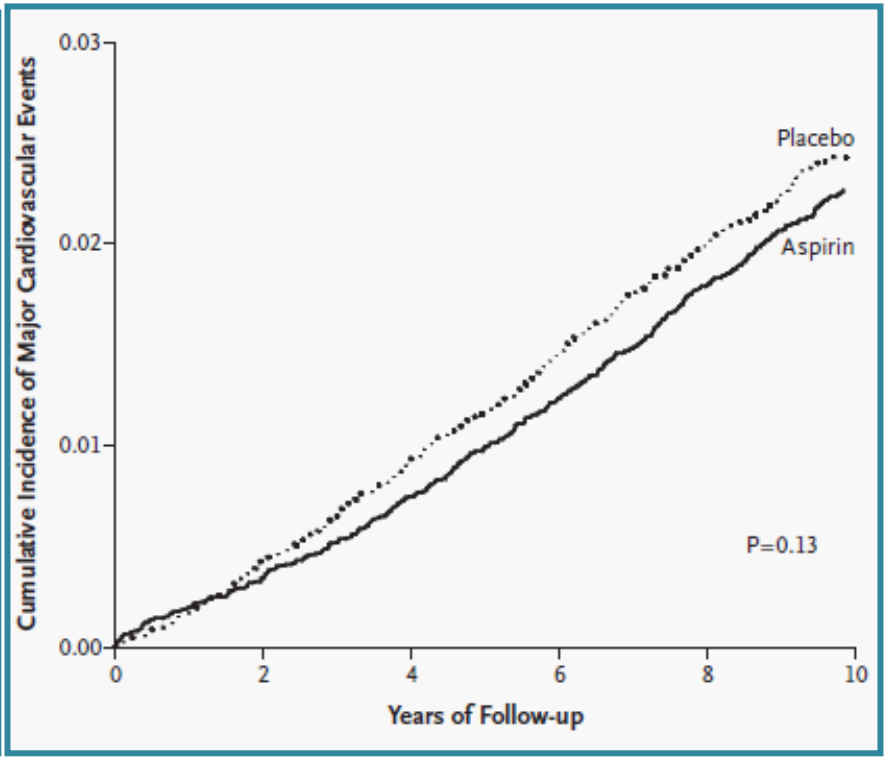
cardiovascular events (from 8·2 to 6·3%; 0·77 [0·62–0·95]). Severe bleedings were more frequent in the aspirin group than the no-aspirin group (1·1% *vs* 0·3%; p<0·0008). Vitamin E showed no effect on any prespecified endpoint. Analyses were by intention-to-treat.

clear-cut evidence derived from other studies, thus favouring the integrity of the trial more than the rights of the patients,[19,20] our trial was stopped on the basis of evidence of an aspirin benefit in cardiovascular primary prevention documented by two large trials.[15,16] The consistency of the results of the planned interim analysis

A Randomized Trial of Low-Dose Aspirin in the Primary Prevention of Cardiovascular Disease in Women

Ridker PM, et al. N Engl J Med 2005;352:1293–304.

Characteristic	Aspirin (N=19,934)	Placebo (N=19,942)
Hyperlipidemia (%)§		
Yes	29.9	29.1
No	70.1	70.9
Diabetes (%)		
Yes	2.7	2.5
No	97.3	97.5
Parental history of myocardial infarction before 60 yr of age (%)		
Yes	13.0	12.9
No	87.0	87.1
10-yr risk of coronary heart disease (%)¶		
<5.0%	84.4	84.6
5.0 to 9.9%	11.8	11.3
≥10.0%	3.9	4.1
No. of risk factors (%)‖		
0	41.8	42.4
1	34.1	34.1
2	18.0	17.2
≥3	6.2	6.3



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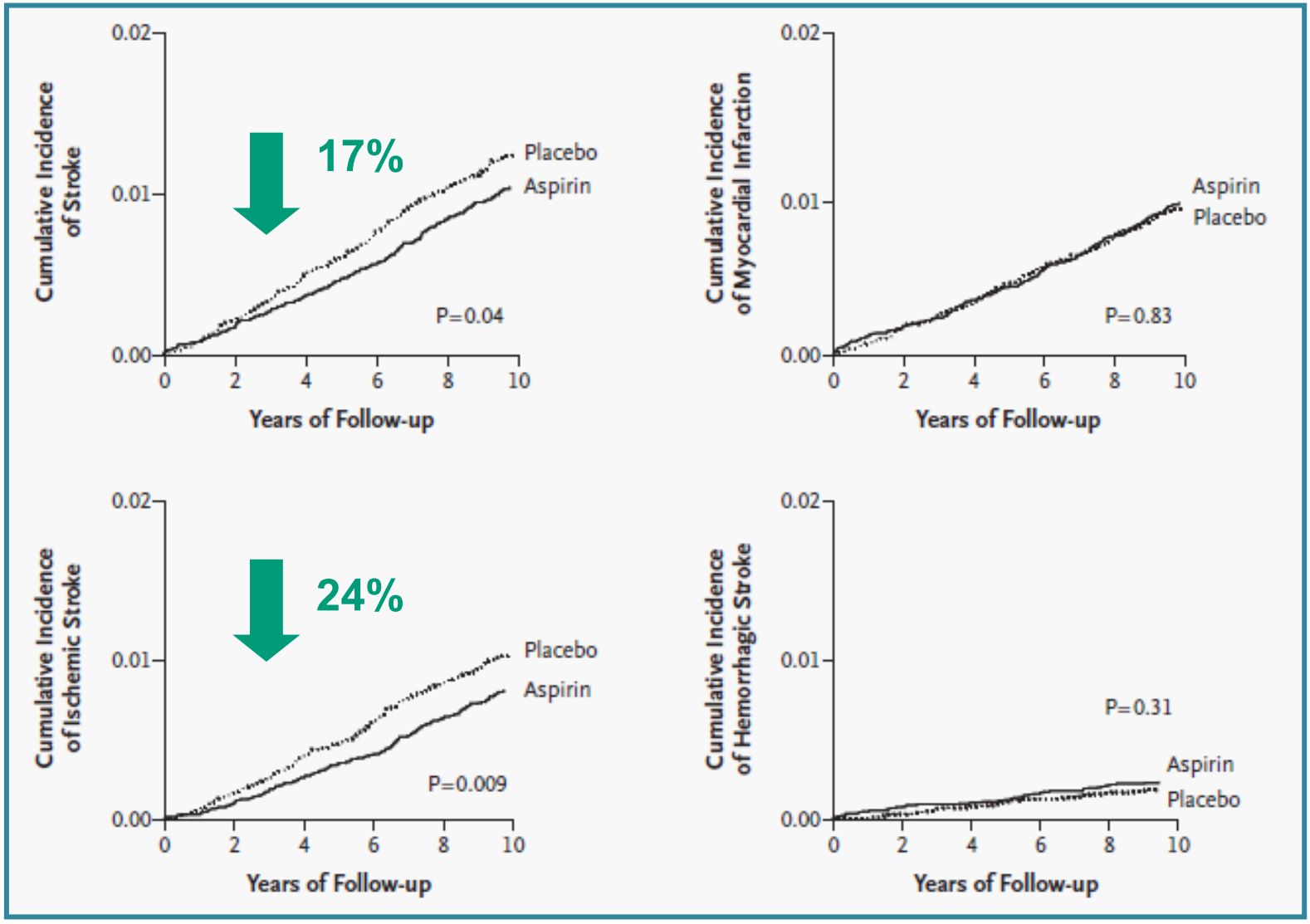
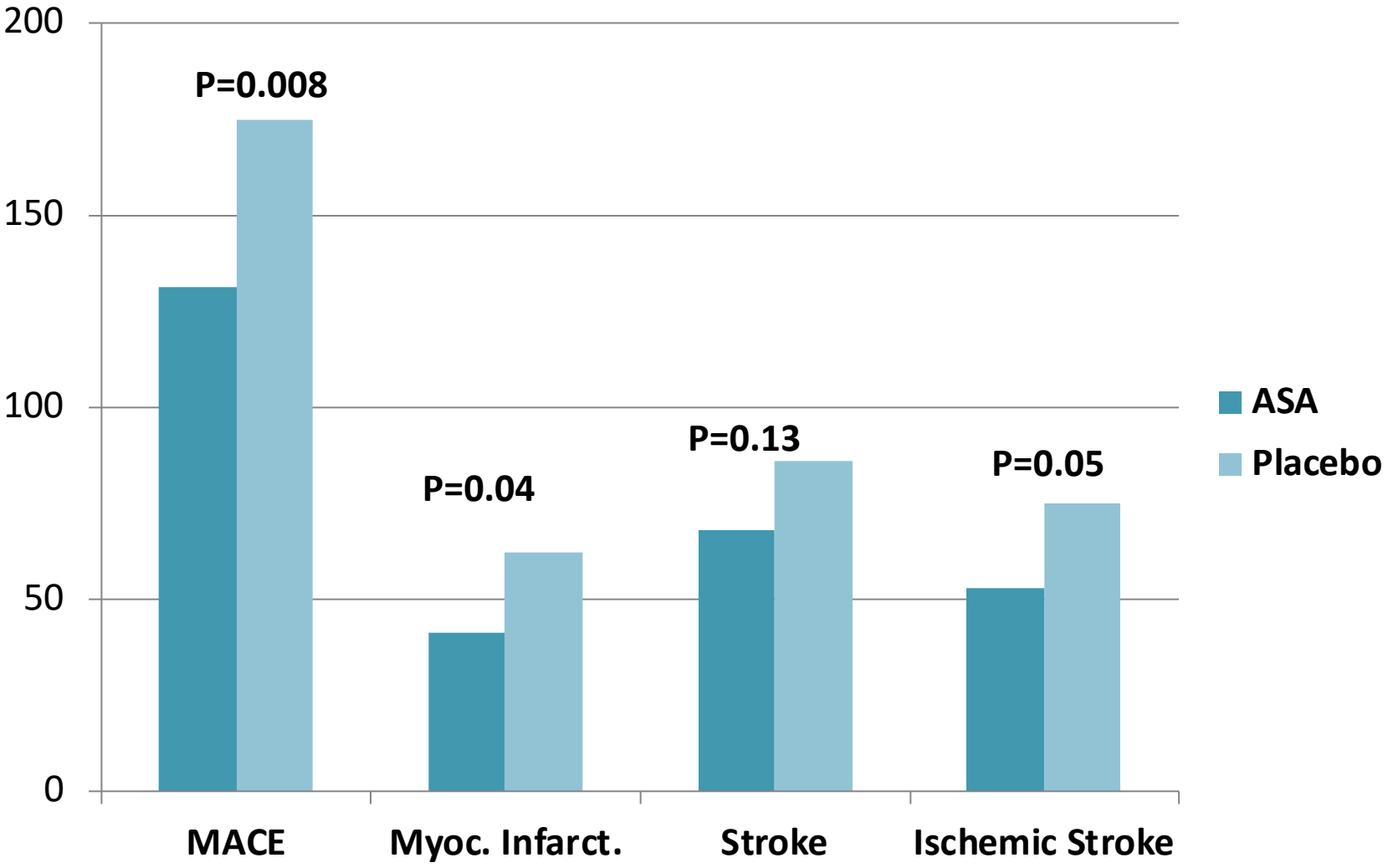


A Randomized Trial of Low-Dose Aspirin in the Primary Prevention of Cardiovascular Disease in Women

Ridker PM, et al. N Engl J Med 2005;352:1293–304.

In the subgroup of women ≥ 65 years



RECENT TRIALS

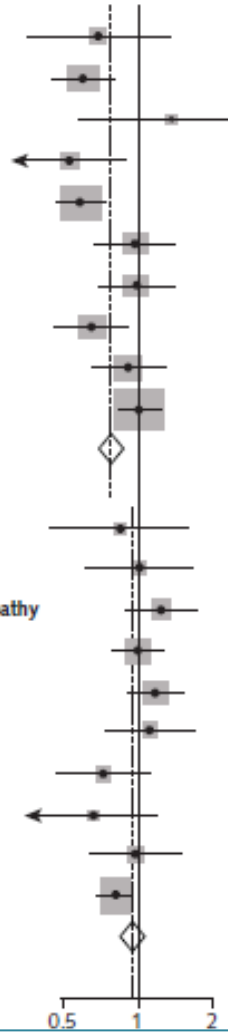
TRIAL	N° of subjects	Aspirin dose	Results
Aspirin for Asymptomatic Atherosclerosis Trial (AAAT)	3,350 patients with PAD (ABI < 0.95)	100 mg	No significant reduction of MACE
Japanese Primary prevention Project (JPPP)	14,464 patients with cardiovascular risk factors	100 mg	No significant reduction of MACE
Early Treatment Diabetic Retinopathy Study (ETDRS)	3,711 patients with DM	650 mg	**Support the use of ASA for diabetic in primary prevention**
Japanese Primary Prevention of Atherosclerosis with Aspirin in Diabetes (JPAD)	2,539 patients with type 2 DM	81-100 mg	No significant reduction of MACE
Prevention of Progression of Arterial Disease and Diabetes (POPADAD)	1,276 patients with diabetes	100 mg	No evidence to support use of ASA in diabetic in primary prevention

Aspirin for the Primary Prevention of Cardiovascular Events: A Systematic Evidence Review for the U.S. Preventive Services Task Force

U.S. Preventive Services TASK FORCE

JM Guirguis-Blake, Annals of Internal Medicine, 2016; 164: 804-813

Study, Year (Reference)	Aspirin Dose, *mg/d*	Follow-up, *mo*	Population Description	RR (95% CI)	Events, *n/N* IG	Events, *n/N* CG
Nonfatal MI						
PPP, 2001 (38)	100	43.2	Men and women with ≥1 risk factor for CVD	0.69 (0.36–1.33)	15/2226	22/2269
HOT, 1998 (34)	75	45.6	Men and women with hypertension	0.60 (0.45–0.81)	68/9399	113/9391
JPAD, 2008 (35)	100	52.4	Men and women with diabetes	1.35 (0.57–3.19)	12/1262	9/1277
JPPP, 2014 (39)	100	60.2	Men and women with ≥1 risk factor for CVD	0.53 (0.31–0.91)	20/7220	38/7244
PHS I, 1989 (30)	162.5	60.2	Men physicians	0.59 (0.47–0.74)	129/11 037	213/11 034
BMD, 1988 (36)	500	72	Men physicians	0.97 (0.67–1.41)	80/3429	41/1710
POPADAD, 2008 (31)	100	80.4	Men and women with diabetes and ABI ≤0.99	0.98 (0.69–1.40)	55/638	56/638
TPT, 1998 (24)	75	81.6	Men at high risk for ischemic heart disease	0.65 (0.45–0.92)	47/1268	73/1272
AAA, 2010 (33)	100	98.4	Men and women with ABI ≤0.95	0.91 (0.65–1.28)	62/1675	68/1675
WHS, 2005 (37)	50	121.2	Women health professionals	1.01 (0.83–1.24)	184/19 934	181/19 942
Overall: I^2 = 61.9%; P = 0.005)				0.78 (0.71–0.87)		
Nonfatal stroke						
PPP, 2001 (38)	100	43.2	Men and women with ≥1 risk factor for CVD	0.84 (0.42–1.07)	15/2220	18/2209
JPAD, 2008 (35)	100	52.4	Men and women with diabetes	1.01 (0.60–1.72)	27/1262	27/1277
ETDRS, 1992 (32)	650	60	Men and women with diabetes and diabetic retinopathy	1.26 (0.89–1.80)	67/1856	53/1855
JPPP, 2014 (39)	100	60.2	Men and women with ≥1 risk factor for CVD	1.00 (0.77–1.31)	109/7220	109/7244
PHS I, 1989 (30)	162.5	60.2	Men physicians	1.20 (0.91–1.59)	110/11 037	92/11 034
BMD, 1988 (36)	500	72	Men physicians	1.13 (0.72–1.77)	61/3429	27/1710
POPADAD, 2008 (31)	100	80.4	Men and women with diabetes and ABI ≤0.99	0.71 (0.45–1.12)	29/638	41/638
TPT, 1998 (24)	75	81.6	Men at high risk for ischemic heart disease	0.64 (0.34–1.20)	18/1280	25/1272
AAA, 2010 (33)	100	98.4	Men and women with ABI ≤0.95	0.97 (0.62–1.52)	37/1675	38/1675
WHS, 2005 (37)	50	121.2	Women health professionals	0.81 (0.67–0.97)	198/19 934	244/19 942
Overall: I^2 = 25.1%; P = 0.212)				0.95 (0.85–1.06)		



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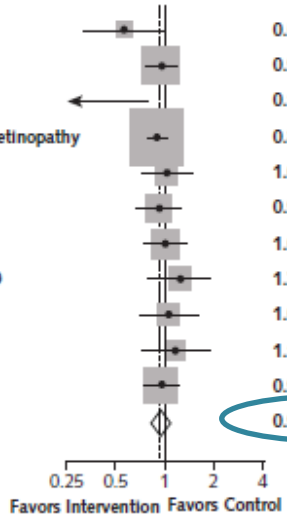
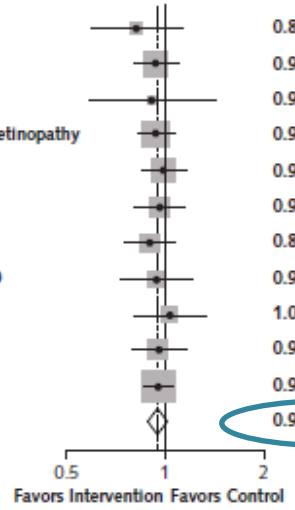
U.S. Preventive Services TASK FORCE

JM Guirguis-Blake, Annals of Internal Medicine, 2016; 164: 804-813

Study, Year (Reference)	Aspirin Dose, *mg/d*	Follow-up, *mo*	Population Description	RR (95% CI)	Events, *n/N* IG	Events, *n/N* CG
CVD mortality						
PPP, 2001 (38)	100	43.2	Men and women with ≥1 risk factor for CVD	0.56 (0.31–1.01)	17/2226	31/2269
HOT, 1998 (34)	75	45.6	Men and women with hypertension	0.95 (0.75–1.20)	133/9399	140/9391
JPAD, 2008 (35)	100	52.4	Men and women with diabetes	0.10 (0.01–0.79)	1/1262	10/1277
ETDRS, 1992 (32)	650	60	Men and women with diabetes and diabetic retinopathy	0.89 (0.76–1.04)	244/1856	275/1855
JPPP, 2014 (39)	100	60.2	Men and women with ≥1 risk factor for CVD	1.02 (0.71–1.47)	58/7220	57/7244
PHS I, 1989 (30)	162.5	60.2	Men physicians	0.92 (0.66–1.28)	66/11 037	72/11 034
BMD, 1988 (36)	500	72	Men physicians	1.01 (0.74–1.37)	119/3429	59/1710
POPADAD, 2008 (31)	100	80.4	Men and women with diabetes and ABI ≤0.99	1.23 (0.80–1.89)	43/638	35/638
TPT, 1998 (24)	75	81.6	Men at high risk for ischemic heart disease	1.05 (0.69–1.61)	42/1268	40/1272
AAA, 2010 (33)	100	98.4	Men and women with ABI ≤0.95	1.17 (0.72–1.89)	35/1675	30/1675
WHS, 2005 (37)	50	121.2	Women health professionals	0.95 (0.74–1.22)	120/19 934	126/19 942
Overall: (I^2 = 8.8%; P = 0.360)				0.94 (0.86–1.03)		



All-cause mortality						
PPP, 2001 (38)	100	43.2	Men and women with ≥1 risk factor for CVD	0.81 (0.58–1.13)	62/2226	78/2269
HOT, 1998 (34)	75	45.6	Men and women with hypertension	0.93 (0.79–1.09)	284/9399	305/9391
JPAD, 2008 (35)	100	52.4	Men and women with diabetes	0.91 (0.57–1.43)	34/1262	38/1277
ETDRS, 1992 (32)	650	60	Men and women with diabetes and diabetic retinopathy	0.93 (0.81–1.06)	340/1856	366/1855
JPPP, 2014 (39)	100	60.2	Men and women with ≥1 risk factor for CVD	0.98 (0.84–1.15)	297/7220	303/7244
PHS I, 1989 (30)	162.5	60.2	Men physicians	0.96 (0.80–1.14)	217/11 037	227/11 034
BMD, 1988 (36)	500	72	Men physicians	0.89 (0.74–1.08)	270/3429	151/1710
POPADAD, 2008 (31)	100	80.4	Men and women with diabetes and ABI ≤0.99	0.93 (0.72–1.21)	94/638	101/638
TPT, 1998 (24)	75	81.6	Men at high risk for ischemic heart disease	1.03 (0.80–1.32)	113/1268	110/1272
AAA, 2010 (33)	100	98.4	Men and women with ABI ≤0.95	0.95 (0.78–1.15)	176/1675	186/1675
WHS, 2005 (37)	50	121.2	Women health professionals	0.95 (0.85–1.06)	609/19 934	642/19 942
Overall: (I^2 = 0.0%; P = 0.996)				0.94 (0.89–0.99)		



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U.S. Preventive Services TASK FORCE

JM Guirguis-Blake, Annals of Internal Medicine, 2016; 164: 804-813

US Preventive Services Task Force 2016[17]

Use aspirin for adults aged 50-59 y with 10-y ASCVD risk ≥10%, not at increased risk of bleeding, life expectancy of ≥10 y, and willing to take aspirin for ≥10 y

Individualize the decision for adults aged 60-69 y with 10-y ASCVD risk 10%, not at increased risk of bleeding, life expectancy of ≥10 y, and willing to take aspirin for ≥10 y

No recommendation for adults aged <50 y or ≥70 y

Bleeding Risks With Aspirin Use for Primary Prevention in Adults: A Systematic Review for the U.S. Preventive Services Task Force

U.S. Preventive Services TASK FORCE

E.P. Whitlock, Annals of Internal Medicine, 2016; 164: 826-835

Table 1. Sensitivity Analyses for Bleeding in CVD Primary Prevention Trials

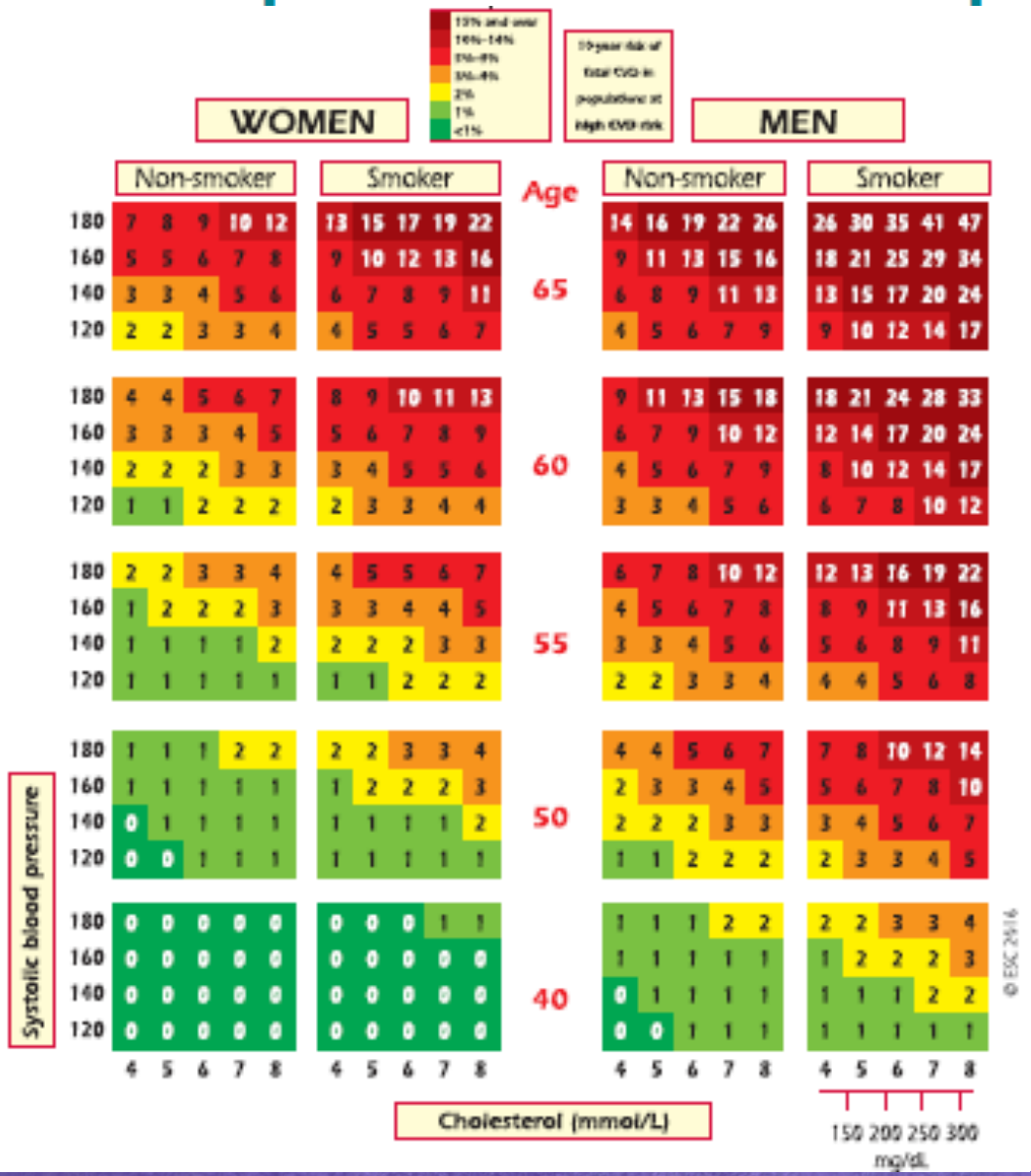
Study, Year (Reference)	Dose	Studies, *k*	Participants, *n*	Pooled OR (95% CI)	Included Trials
Major GI or extracranial bleeding					
Whitlock et al (main analysis), 2015 (5)*	Any	7	94 307	1.59 (1.32–1.91); I^2 = 22.2%	HOT, JPAD, PHS, BMD, TPT, AAA, WHS
	≤100 mg	5	67 097	1.58 (1.29–1.95); I^2 = 28.6%	HOT, JPAD, TPT, AAA, WHS
ATT Collaboration, 2009 (15)†	Any	6	95 456	1.54 (1.30–1.82)§; chi square = 3.1	BMD, PHS, TPT, HOT, PPP, WHS
De Berardis et al (cohort study), 2012 (22)*‡	≤300 mg	1	372 850	1.55 (1.46–1.65)‖	NA
Hemorrhagic stroke					
Guirguis-Blake et al (meta-analysis), 2015 (11)	Any	9	113 264	1.33 (1.03–1.71); I^2 = 0%	PPP, HOT, JPAD, JPPP, PHS, BMD, TPT, AAA, WHS
	≤100 mg	7	86 054	1.27 (0.96–1.68); I^2 = 0%	PPP, HOT, JPAD, JPPP, TPT, AAA, WHS
ATT Collaboration (IPD meta-analysis), 2009 (15)	Any	6	95 456	1.32 (1.00–1.75)§; chi square = 4.7	BMD, PHS, TPT, HOT, PPP, WHS
Intracranial hemorrhage, including hemorrhagic stroke					
Whitlock et al (main analysis), 2015 (5)	Any	10	114 540	1.34 (1.07–1.70); I^2 = 0%	PPP, TPT, HOT, JPAD, PHS, JPPP, BMD, POPADAD, AAA, and WHS
	≤100 mg	8	87 330	1.30 (1.00–1.68); I^2 = 0%	PPP, TPT, HOT, JPAD, JPPP, POPADAD, AAA, and WHS
De Berardis (cohort study), 2012 (22)‡	≤300 mg	1	372 850	1.54 (1.43–1.67)‖	NA

Table 3. Major Risk Factors for Gastrointestinal Bleeding and Related Complications

Risk Factor	Adjusted Relative Risk Increase
History of upper GI disorder	
Dyspepsia/pain	2
Prior GI hospitalization	3
Peptic ulcer (uncomplicated)	3 to 6
Peptic ulcer with GI bleeding/perforation	10
Age >60 y	Exponential
Male sex	2
Medications	Variable
NSAID use (current or recent)	1.1 to 2
Aspirin (≤325 mg/d)	1.5 to 2
Other antiplatelets/anticoagulants	1.3 to 2
Other	Variable (generally <2)
Smoking	
Excess alcohol	
Hypertension	
Diabetes	
Increased BMI	
Renal or liver disease	

Mora S et al, JAMA, 2016; 316:709-10.

2016 European Guidelines on cardiovascular disease prevention in clinical practice



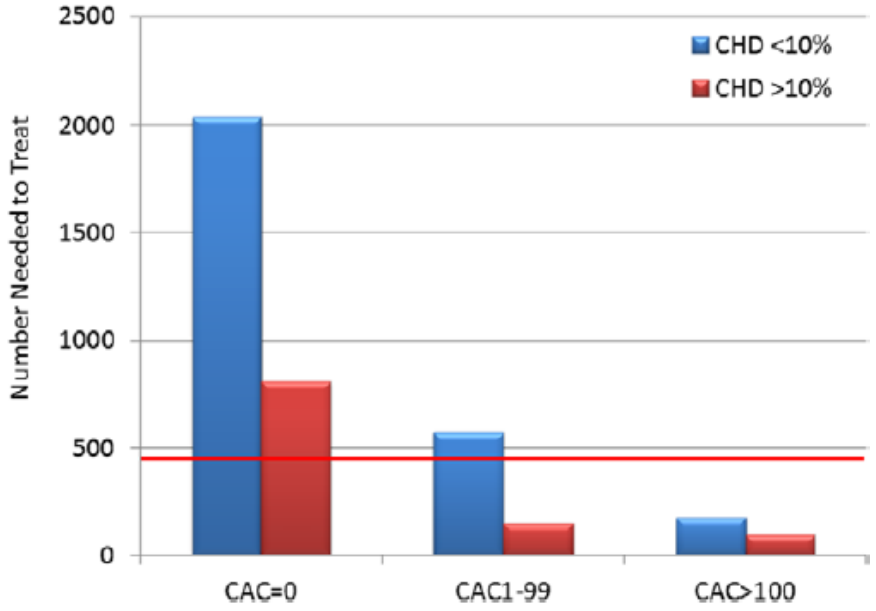
Very high-risk	Subjects with any of the following: • Documented CVD, clinical or unequivocal on imaging. Documented clinical CVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented CVD on imaging includes significant plaque on coronary angiography or carotid ultrasound. It does NOT include some increase in continuous imaging parameters such as intima–media thickness of the carotid artery. • DM with target organ damage such as proteinuria or with a major risk factor such as smoking or marked hypercholesterolaemia or marked hypertension. • Severe CKD (GFR <30 mL/min/1.73 m2). • A calculated SCORE ≥10%.
High-risk	Subjects with: • Markedly elevated single risk factors, in particular cholesterol >8 mmol/L (>310 mg/dL) (e.g. in familial hypercholesterolaemia) or BP ≥180/110 mmHg. • Most other people with DM (with the exception of young people with type 1 DM and without major risk factors that may be at low or moderate risk). • Moderate CKD (GFR 30–59 mL/min/1.73 m²). • A calculated SCORE ≥5% and <10%.
Moderate-risk	SCORE is ≥1% and <5% at 10 years. Many middle-aged subjects belong to this category.
Low-risk	SCORE <1%.

Use of Coronary Artery Calcium Testing to Guide Aspirin Utilization for Primary Prevention: Estimates From the Multi-Ethnic Study of Atherosclerosis

high risk for CHD although the majority of CHD events occur in individuals who are at low to intermediate risk.

Methods and Results—To estimate the potential of coronary artery calcium (CAC) scoring to guide aspirin use for primary prevention of CHD, we studied 4229 participants from the Multi-Ethnic Study of Atherosclerosis who were not on aspirin at baseline and were free of diabetes mellitus. Using data from median 7.6-year follow-up, 5-year number-needed-to-treat estimations were calculated by applying an 18% relative CHD reduction to the observed event rates. This was contrasted to 5-year number-needed-to-harm estimations based on the risk of major bleeding reported in an aspirin meta-analysis. Results were stratified by a 10% 10-year CHD Framingham Risk Score (FRS). Individuals with CAC≥100 had an estimated net benefit with aspirin regardless of their traditional risk status (estimated 5-year number needed to treat of 173 for individuals <10% FRS and 92 for individuals ≥10% FRS, estimated 5-year number needed to harm of 442 for a major bleed). Conversely, individuals with zero CAC had unfavorable estimations (estimated 5-year number needed to treat of 2036 for individuals <10% FRS and 808 for individuals ≥10% FRS, estimated 5-year number needed to harm of 442 for a major bleed). Sex-specific and age-stratified analyses showed similar results.

Conclusions—For the primary prevention of CHD, Multi-Ethnic Study of Atherosclerosis participants with CAC≥100 had favorable risk/benefit estimations for aspirin use while participants with zero CAC were estimated to receive net harm from aspirin. (***Circ Cardiovasc Qual Outcomes*. 2014;7:453-460.**)

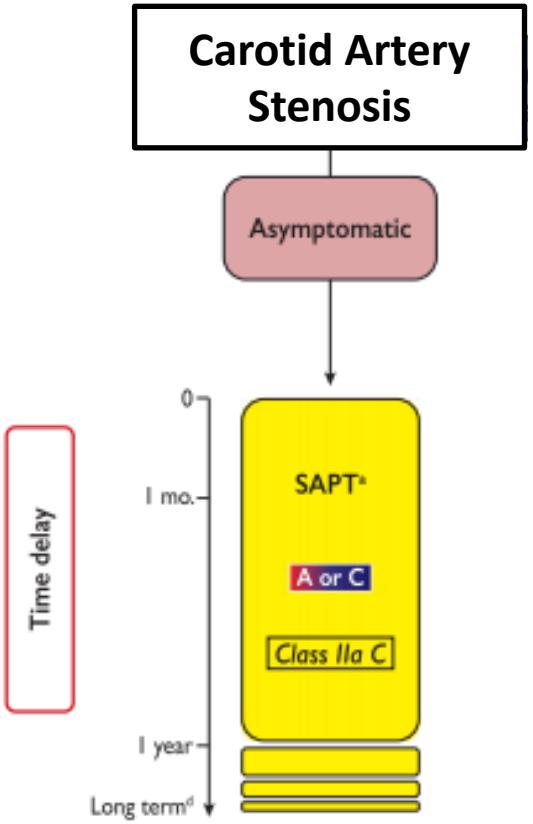


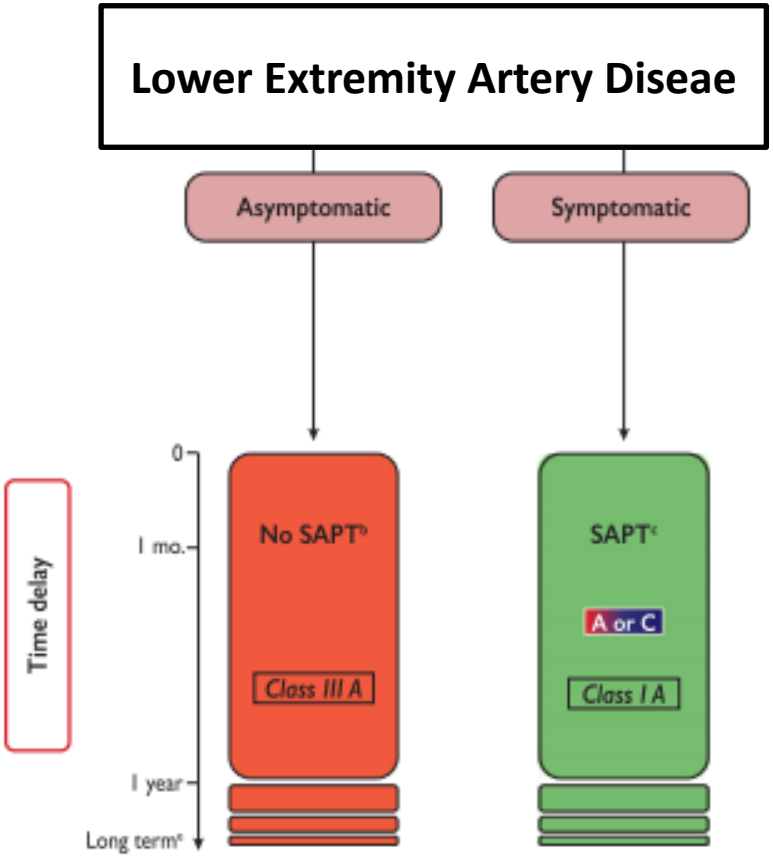
Peripheral Artery Disease

9.1. For persons with asymptomatic carotid stenosis, we suggest aspirin 75 to 100 mg daily over no aspirin therapy (Grade 2B).

2.1. For persons with asymptomatic peripheral arterial disease (PAD), we suggest aspirin 75 to 100 mg daily over no aspirin therapy (Grade 2B).

ACCP Guidelines, Chest 2012



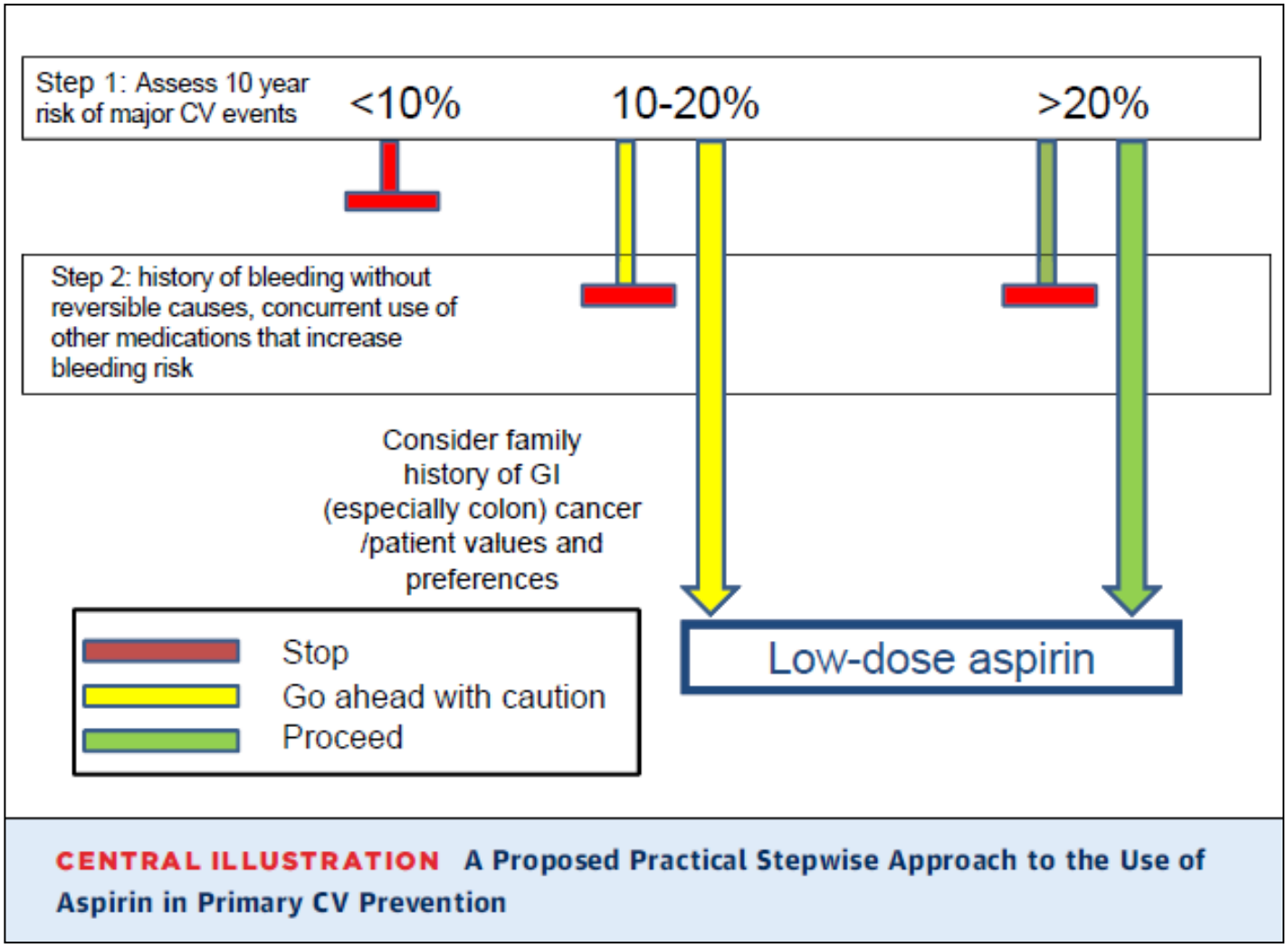


ESC Guidelines, EHJ 2017

Aspirin Therapy in Primary Cardiovascular Disease Prevention

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

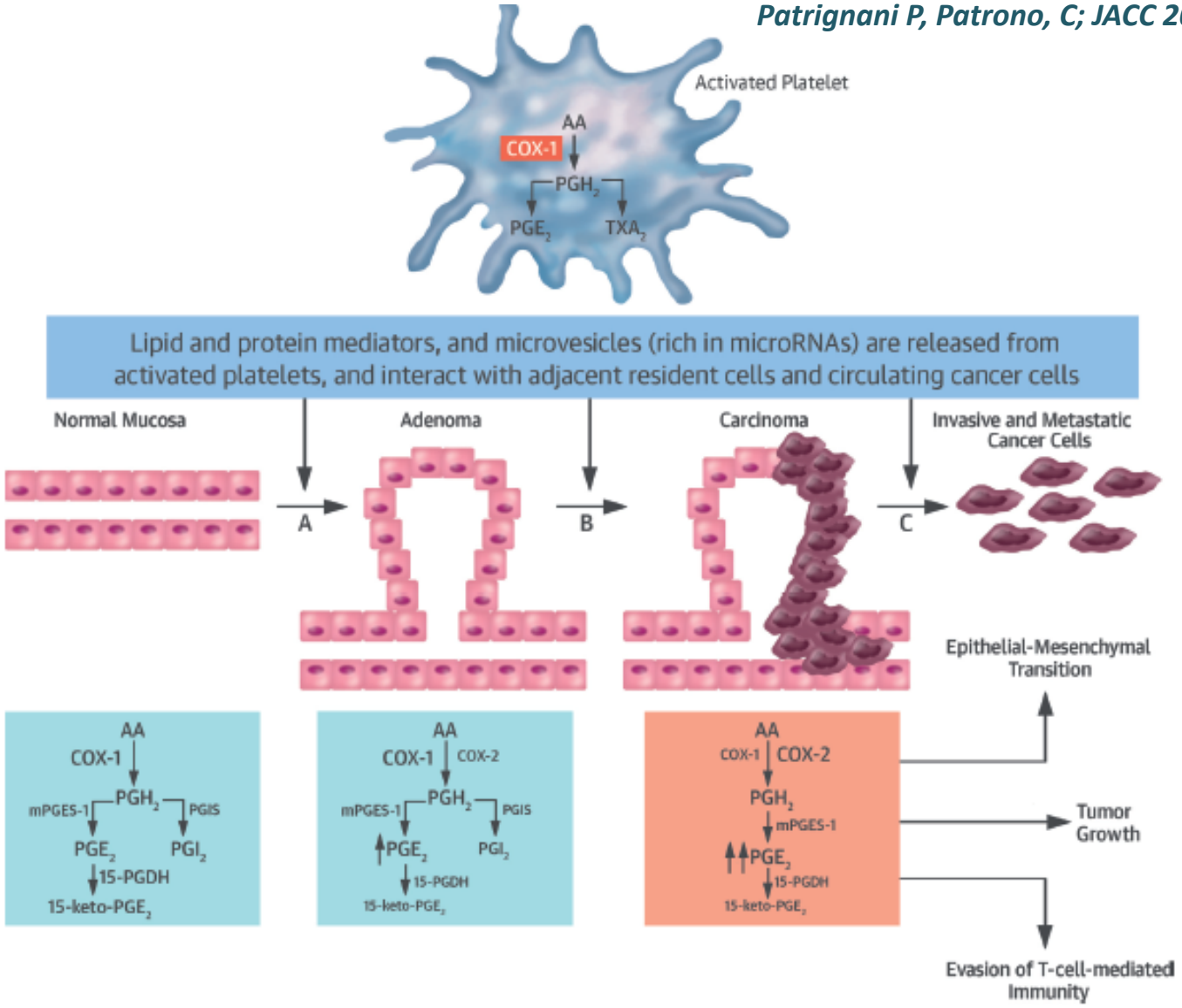
Halvorsen et al, J Am Coll Cardiol 2014



CENTRAL ILLUSTRATION **A Proposed Practical Stepwise Approach to the Use of Aspirin in Primary CV Prevention**

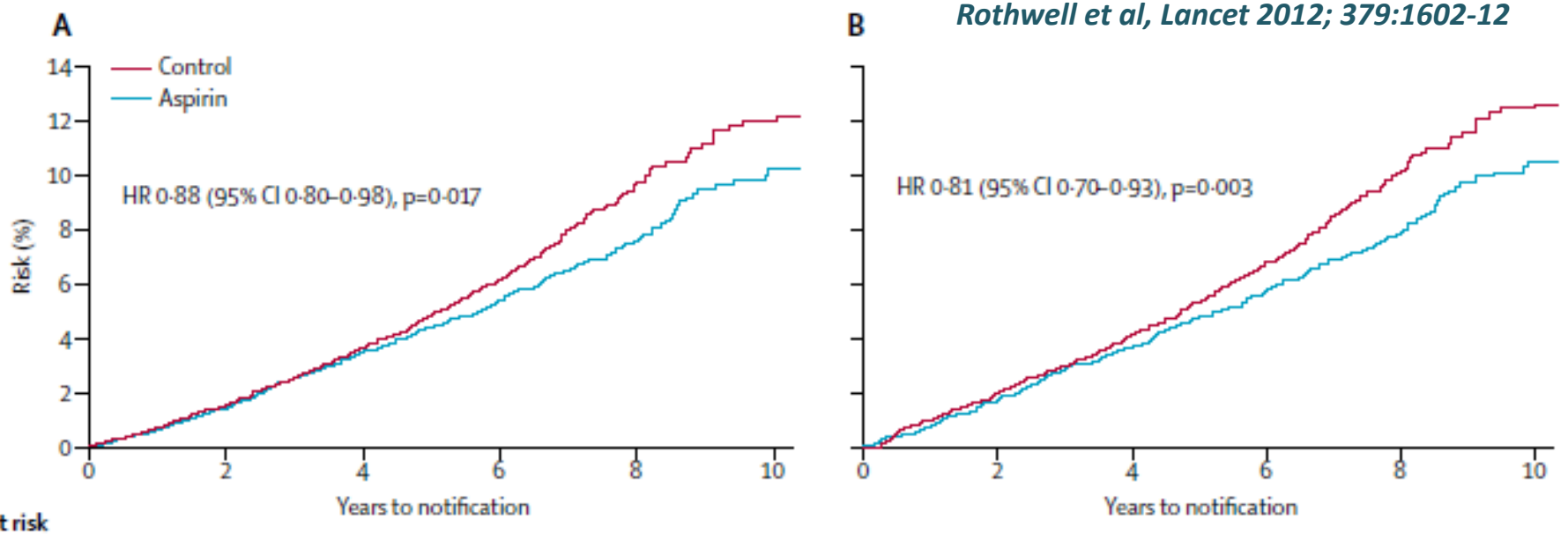
Aspirin and Cancer

Patrignani P, Patrono, C; JACC 2016; 68: 967-976



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

Rothwell et al, Lancet 2012; 379:1602-12



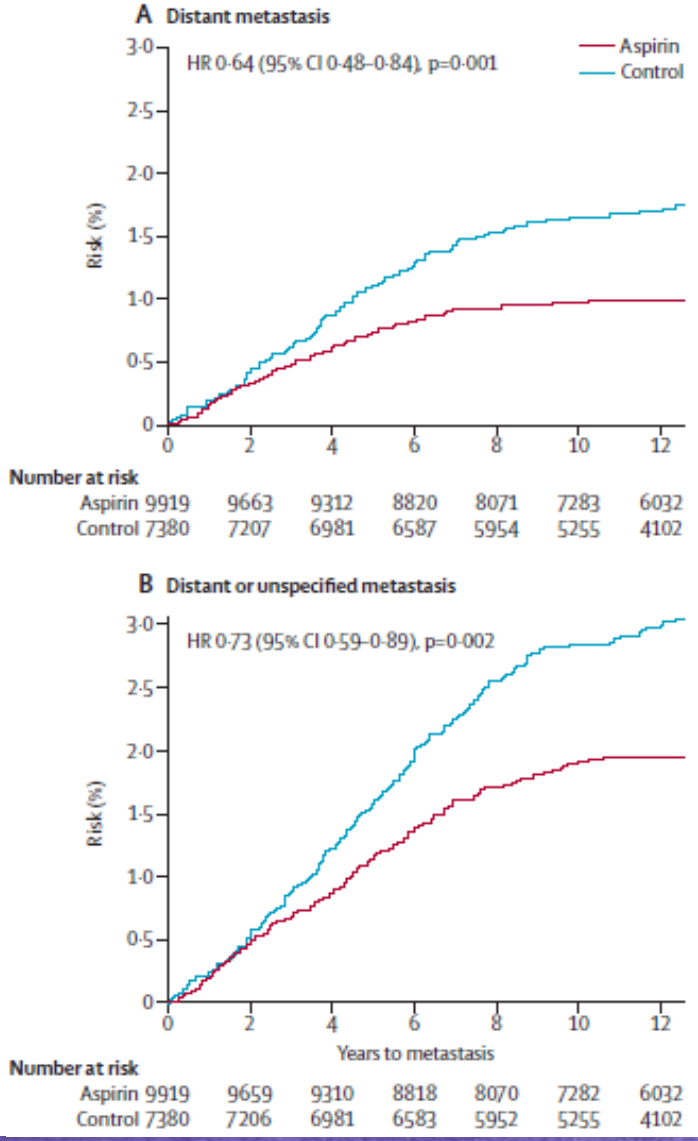
Number at risk

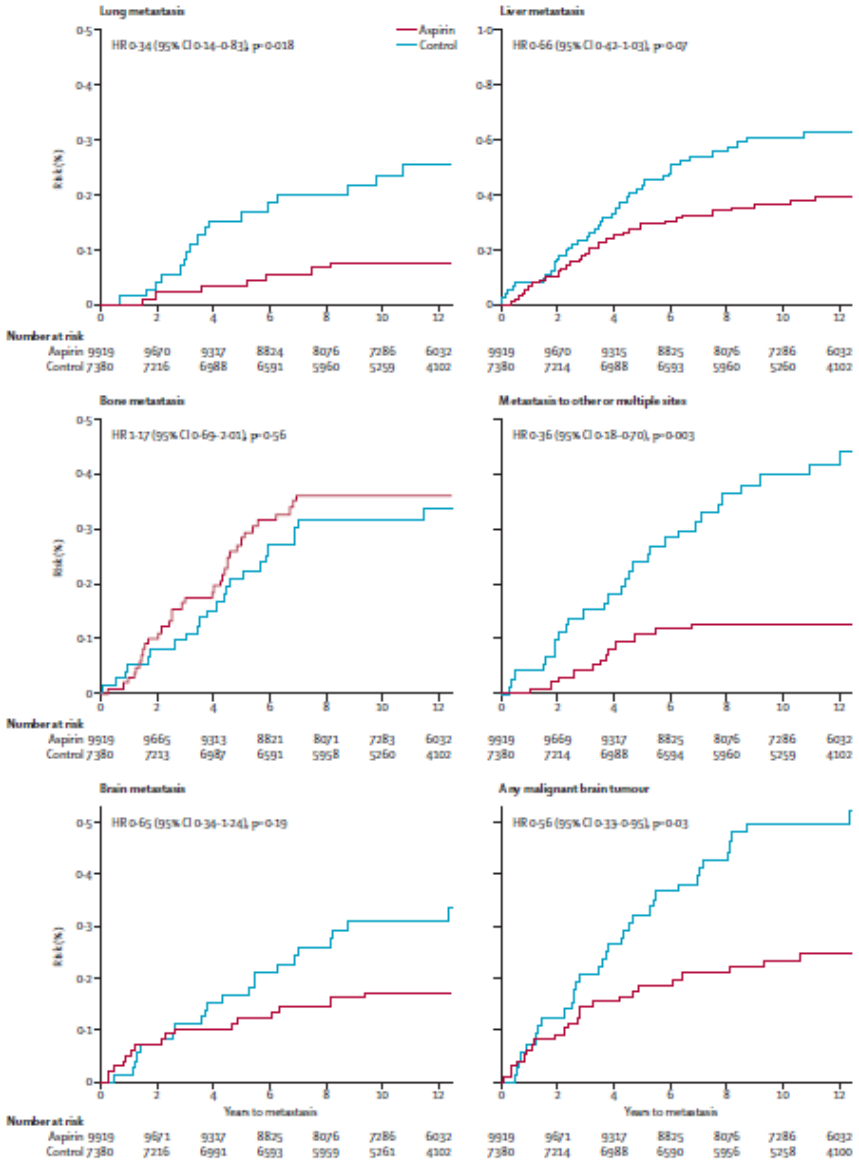
Aspirin	17745	17159	9558	3761	1592	504	4668	4549	4394	3761	1592	504
Control	17790	17153	9502	3761	1568	493	4664	4532	4383	3761	1568	493

	Number of deaths		Odds ratio (95% CI)	p
	Aspirin	Control		
Cancer death only*				
0–2·9 years	292	325	0·90 (0·76–1·06)	0·18
3·0–4·9 years	161	173	0·93 (0·75–1·16)	0·51
≥5 years	92	145	0·63 (0·49–0·82)	0·0005
Unknown	17	21	..	..
Total	562	664	0·85 (0·76–0·96)	0·008

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

Rothwell et al, Lancet 2012; 379:1591-601

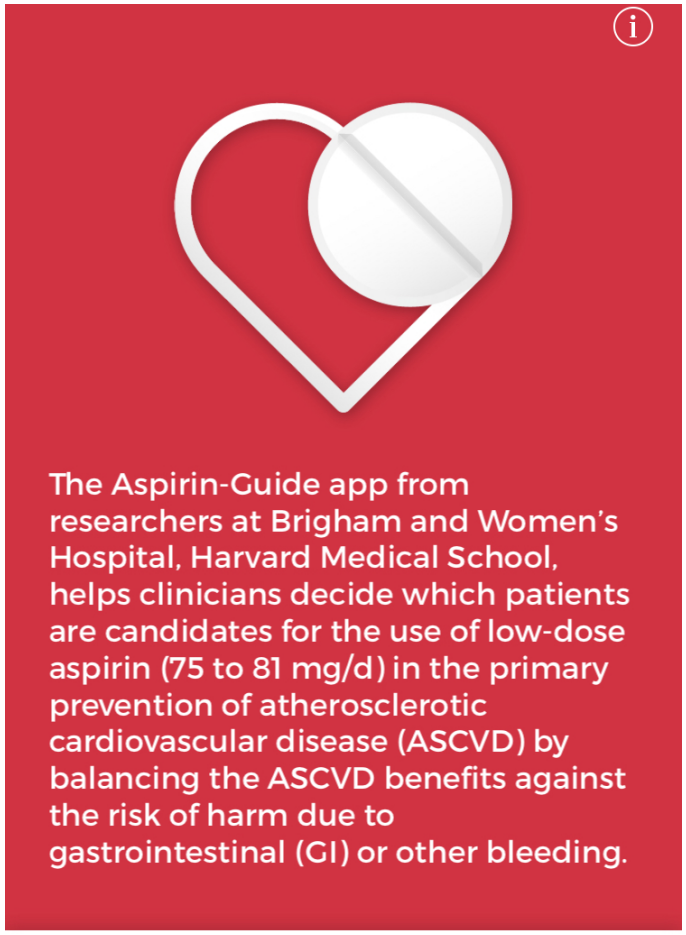




Take home messages

- Aspirin in primary prevention represents a unique opportunity to reduce morbidity and mortality due to both cardiovascular disease and cancer
- Cardiovascular risk can be viewed as a continuum, increasing from young totally healthy individuals to high risk primary prevention patients
- It is essential to estimate the individual baseline profile carefully balancing ischemic and bleeding risk

Aspirin Guide APP



- ✓ **Previous Cardiovascular Events?**
- ✓ **Controindications to ASA (bleeding, allergy)?**
- ✓ **Age**
- ✓ **Sex**
- ✓ **Race**
- ✓ **Current Smoking**
- ✓ **High blood pressure: medication and values**
- ✓ **Diabetes**
- ✓ **Statins or other cholesterol lowering medication**
- ✓ **Total Cholesterol level, HDL Cholesterol level**
- ✓ **Atrial fibrillation or anticoagulation therapy**
- ✓ **Hystory of peptic ulcer**
- ✓ **Hystory of upper GI pain or dyspepsia**
- ✓ **Use of NSAIDs or corticosterodis**