Who Should be on Aspirin and Why ?

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Disclosures

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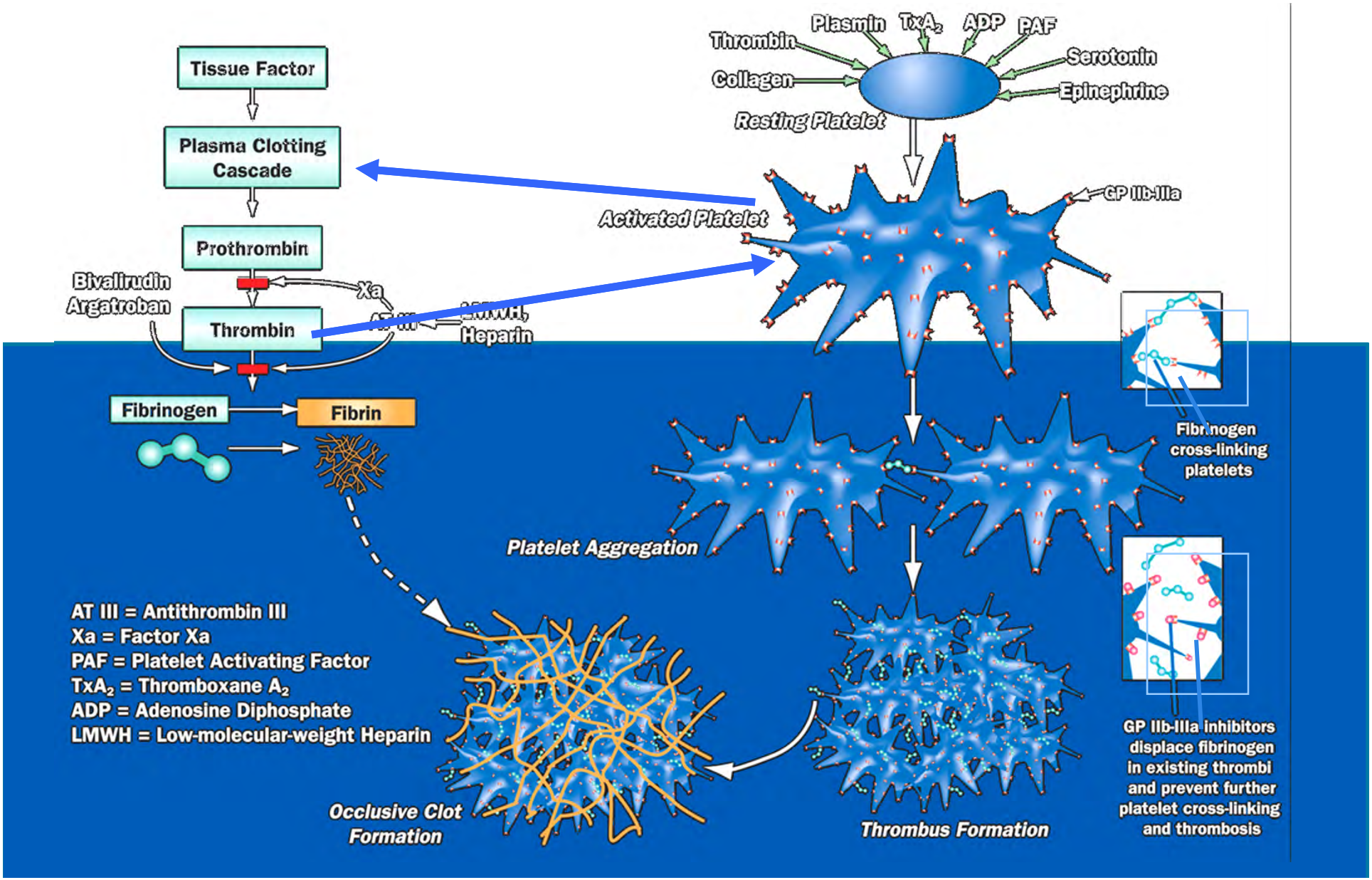
Who Should be on Aspirin and Why ?

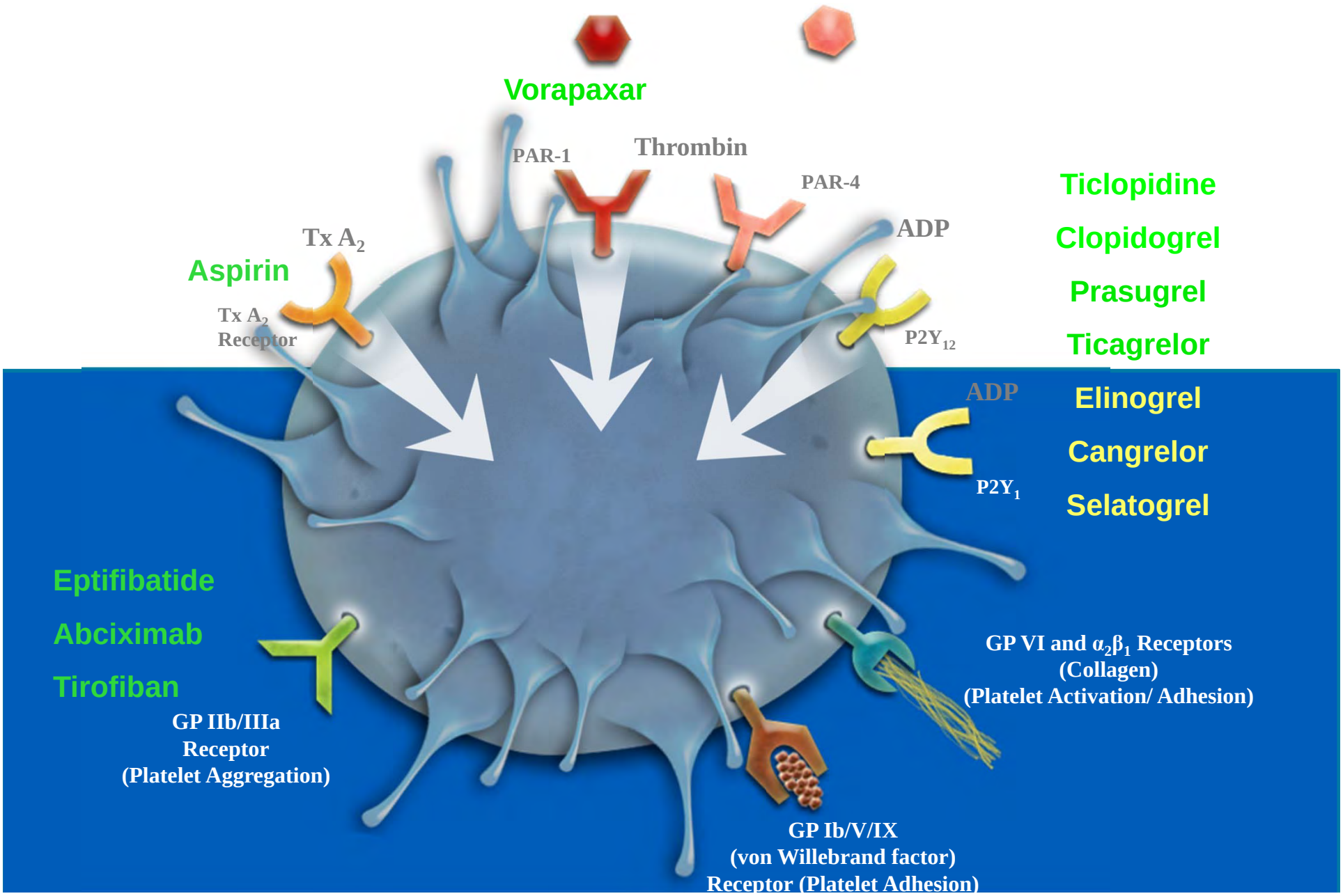
1. Why did we get here?
2. Proactive or Reactive
3. As an Adjuvant

Clot Formation

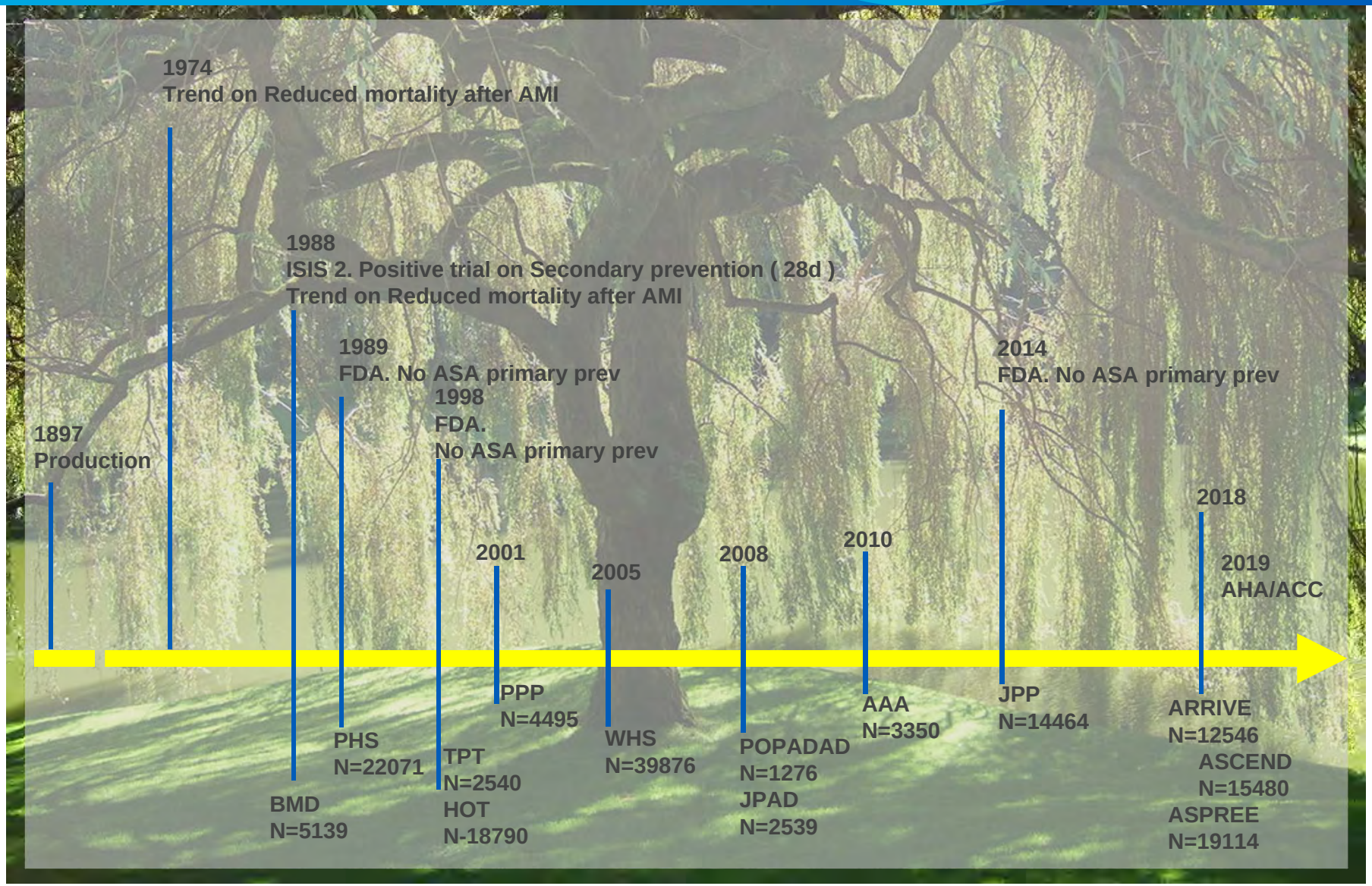
The Inseparable Relation Between Platelet Function and Coagulation



Platelet Activation Pathways



Why did we get here



ACC/AHA CLINICAL PRACTICE GUIDELINE

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

COR	LOE	Recommendations
IIb	A	1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk.[54.6-1–54.6-8]
III: Harm	B-R	2. Low-dose aspirin (75-100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults >70 years of age.[54.6-9]
III: Harm	C-LD	3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding.[54.6-10]

Circulation. 2019;140:e596–e646


CNN Center
7:57 AM ET
SANJAY GUPTA MD
NEW DEVELOPMENTS
STUDIES: LOW-DOSE ASPIRIN RISK MAY OUTWEIGH BENEFITS
Dr. Sanjay Gupta | On Twitter: @drsanjaygupta
CNN
4:57 AM PT

Primary Prevention vs Secondary Prevention

A 63 YOM former smoker with HTN and DM, SP CABG is on ASA 81 daily. Has no history of major bleeding. He heard about the new guidelines.

Doctor, I stopped using asa.

a) I agree, CNN is right

b) Please resume asa

Who Should be on Aspirin and Why ?

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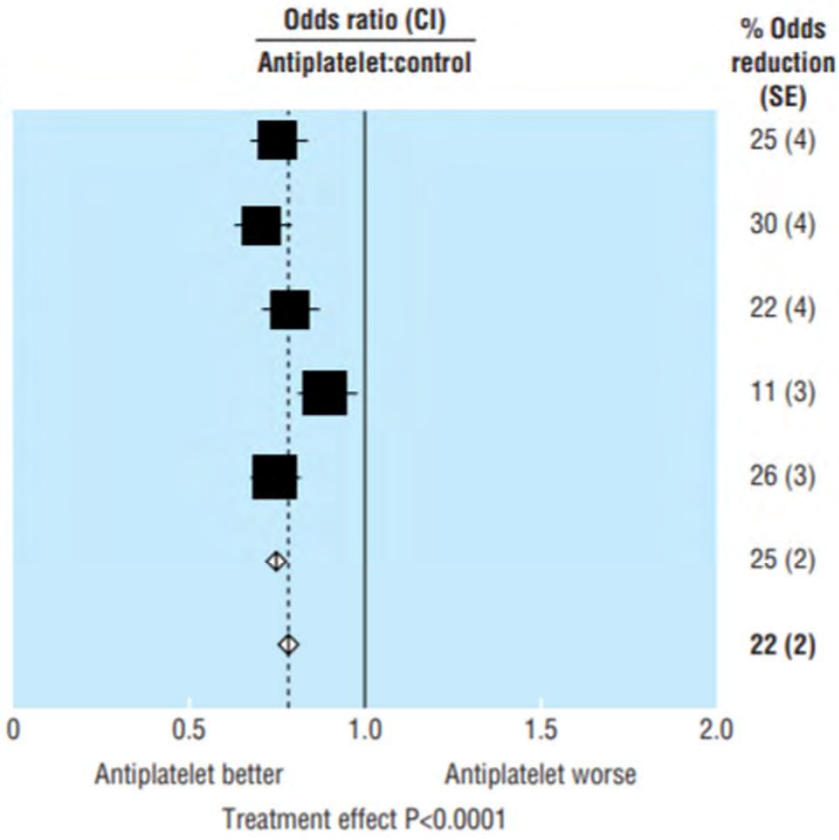
REACTIVE ASA Arterial

Category of trial	No of trials with data	No (%) of vascular events: Allocated antiplatelet	No (%) of vascular events: Adjusted control	Observed-expected	Variance	% Odds reduction (SE)
Previous myocardial infarction	12	1345/9984 (13.5)	1708/10 022 (17.0)	-159.8	567.6	25 (4)
Acute myocardial infarction	15	1007/9658 (10.4)	1370/9644 (14.2)	-181.5	519.2	30 (4)
Previous stroke/transient ischaemic attack	21	2045/11 493 (17.8)	2464/11 527 (21.4)	-152.1	625.8	22 (4)
Acute stroke	7	1670/20 418 (8.2)	1858/20 403 (9.1)	-94.6	795.3	11 (3)
Other high risk	140	1638/20 359 (8.0)	2102/20 543 (10.2)	-222.3	737.0	26 (3)
Subtotal: all except acute stroke	188	6035/51 494 (11.7)	7644/51 736 (14.8)	-715.7	2449.6	25 (2)
All trials	**195**	**7705/71 912 (10.7)**	**9502/72 139 (13.2)**	**-810.3**	**3244.9**	**22 (2)**

Heterogeneity of odds reductions between:

5 categories of trial: χ^2=21.4, df=4; P=0.0003

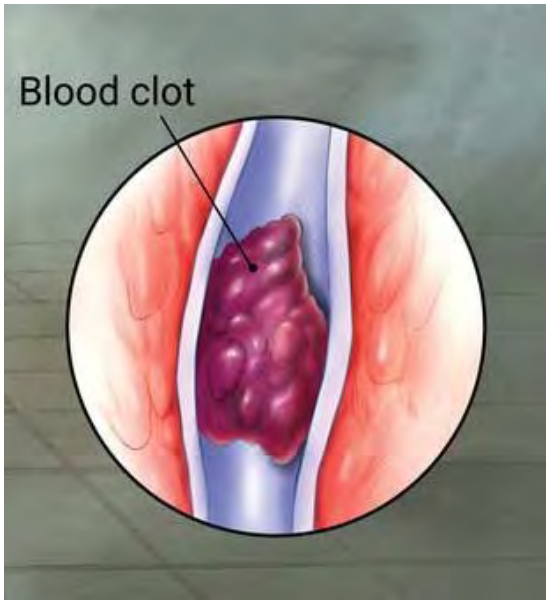
Acute stroke *v* other: χ^2=18.0, df=1; P=0.00002



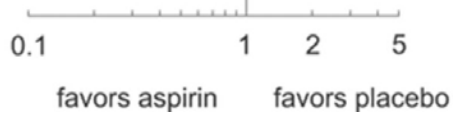
For MACE/MALE secondary prevention the ASA benefit outweighs the Bleed risk

BMJ 2002;324:71–86

REACTIVE ASA VTE



Subgroup	Event rate/year (%) Placebo (*n*=608)	Aspirin (*n*=616)	Hazard ratio (95% CI)	*P*
Venous thromboembolism	112 (7.5)	81 (5.1)	0.65 (0.49–0.86)	0.003
Major vascular events	129 (8.7)	91 (5.7)	0.63 (0.48–0.83)	<0.001
Net clinical benefit	144 (9.8)	103 (6.5)	0.64 (0.50–0.83)	<0.001
Pulmonary embolism	42 (2.6)	27 (1.7)	0.63 (0.39–1.02)	0.06
Deep-vein thrombosis	85 (5.5)	59 (3.6)	0.63 (0.45–0.88)	0.006
All-cause mortality	23 (1.4)	20 (1.2)	0.82 (0.45–1.52)	0.53
Major bleeding	7 (0.4)	9 (0.5)	1.31 (0.48–3.53)	0.60



For VTE secondary prevention, MAY also consider ASA

Primary Prevention vs Secondary Prevention

A 62 YOWF with HTN, 6 y of DM and hypothyroidism. Has been taking asa 81 mg for 5 y. She has no Hx of PAD or CAD.

She heard about the new guidelines.

Doctor, I stopped using asa.

a)I agree, CNN is right

b)Please resume asa

PROACTIVE ASA MACE

Benefits and Risks of Low-Dose Aspirin in Primary Prevention Trials

Risk of Serious Vascular Events *vs.* Bleeding Risk

LOW-RISK

NNT= 500-1,000

NNH= 500-1,000

Consider aspirin evaluating potential benefits and risks

MODERATE-RISK

ASCEND NNT= 91; NNH= 112

ARRIVE NNT=126; NNH= 196

ASPREE NNT=100; NNH=100

HIGH-RISK

NNT= ≤100

NNH= 500-1,000

Use aspirin routinely unless contraindicated

TRIAL	NNT	NNH	NNH/NNT
COMPASS	77	83	1.07
PEGASUS TIMI 54	79	106	1.34
ASCEND	91	112	1.38
ARRIVE	126	196	1.55
ASPREE	100	100	1

	Guideline	Recommendation
2016	USPSTF	Recommend low-dose aspirin use for the primary prevention of CVD and CRC in adults aged 50 to 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years (grade B)
2016	ESC	Recommend against initiating aspirin in individuals without overt cardiovascular disease (class III)
2016	EASD	Antiplatelet therapy (e.g., with aspirin) is not recommended for people with DM who do not have CVD (class IIIA)
2019	AHA/ACC	Recommend against aspirin in individuals older than 70 years and provide a weak recommendation (class IIb) that aspirin might be considered among adults aged 40–70 years
2019	NICE	Recommend against aspirin for the primary prevention of CVD. Consider prescribing aspirin in people with a high risk of stroke or myocardial infarction
2019	ADA	Recommend aspirin therapy (75–162 mg/day) for primary prevention strategy in those with diabetes who are at increased cardiovascular risk, after a discussion with the patient on the benefits versus increased risk of bleeding. Aspirin is not recommended for those at low risk of ASCVD (such as men and women aged ≤50 years with diabetes with no other major ASCVD risk factors) as the low benefit is likely to be outweighed by the risks of bleeding

ARRIVE

ASPREE

ASCEND

ARRIVE Trial

Primary endpoint occurred

4·29% for ASA

4·48% for placebo

HR 0·96; 95% CI 0·81–1·13; p=0·6038

Gastrointestinal bleeding

0·97% for ASA

0·46% for placebo

HR 2·11; 95% CI 1·36–3·28; p=0·0007

Male patients

- ***55 years and older***
- ***and had between two and four risk factors***

Female patients

- ***60 years or older***
- ***and had three or more risk factors.***

Average cardiovascular risk (10-y risk of CHD 10–20%)

" The event rate was much lower than expected, which is probably reflective of contemporary risk management strategies, making the study more representative of a low-risk population".

Lancet 2018; 392: 1036–46

ASPREE

Rate of cardiovascular disease
10.7 events per 1000 person-years in the aspirin
11.3 events per 1000 person-years in the placebo

HR 0.95; 95%CI 0.83 to 1.08

Major hemorrhage
8.6 events per 1000 person-years
6.2 events per 1000 person-years

HR 1.38; 95% CI, 1.18 to 1.62

- ***70 years of age or older (or ≥65 y-o among blacks and Hispanics in the US).***

Free of: CAD, CVD, AF, Dementia or physical disability, high bleed risk

Composite of Death, Dementia, Physical disability was not different

N Engl J Med 2018;379:1509-18.

ASCEND

Serious vascular events

Aspirin	8.5%
Placebo	9.6%
RR	0.88; 95%CI 0.79 to 0.97

Major bleeding

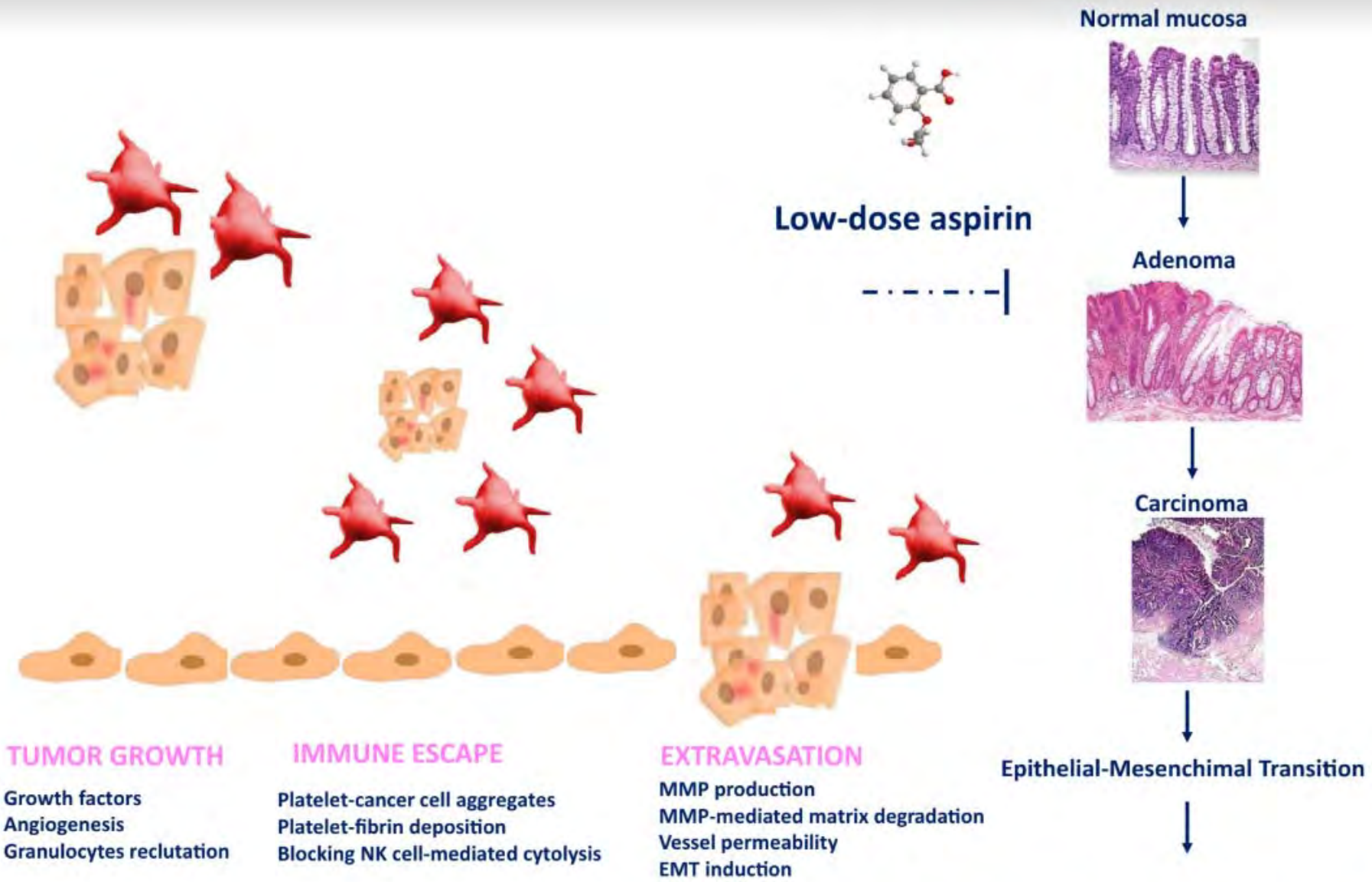
Aspirin	4.1%
Placebo	3.2%

RR 1.29; 95% CI, 1.09 to 1.52
(Most of the excess being gastrointestinal bleeding)

- ***40 years of age***
- ***Diabetes mellitus (any type)***
- ***No known cardiovascular disease***

Outcomes on cancer are still expected.

N Engl J Med 2018;379:1529-39.


Normal mucosa
Low-dose aspirin
Adenoma
Carcinoma
Epithelial-Mesenchimal Transition
TUMOR GROWTH
Growth factors
Angiogenesis
Granulocytes reclutation
IMMUNE ESCAPE
Platelet-cancer cell aggregates
Platelet-fibrin deposition
Blocking NK cell-mediated cytolysis
EXTRAVASATION
MMP production
MMP-mediated matrix degradation
Vessel permeability
EMT induction
Invasive and metastatic cancer cells

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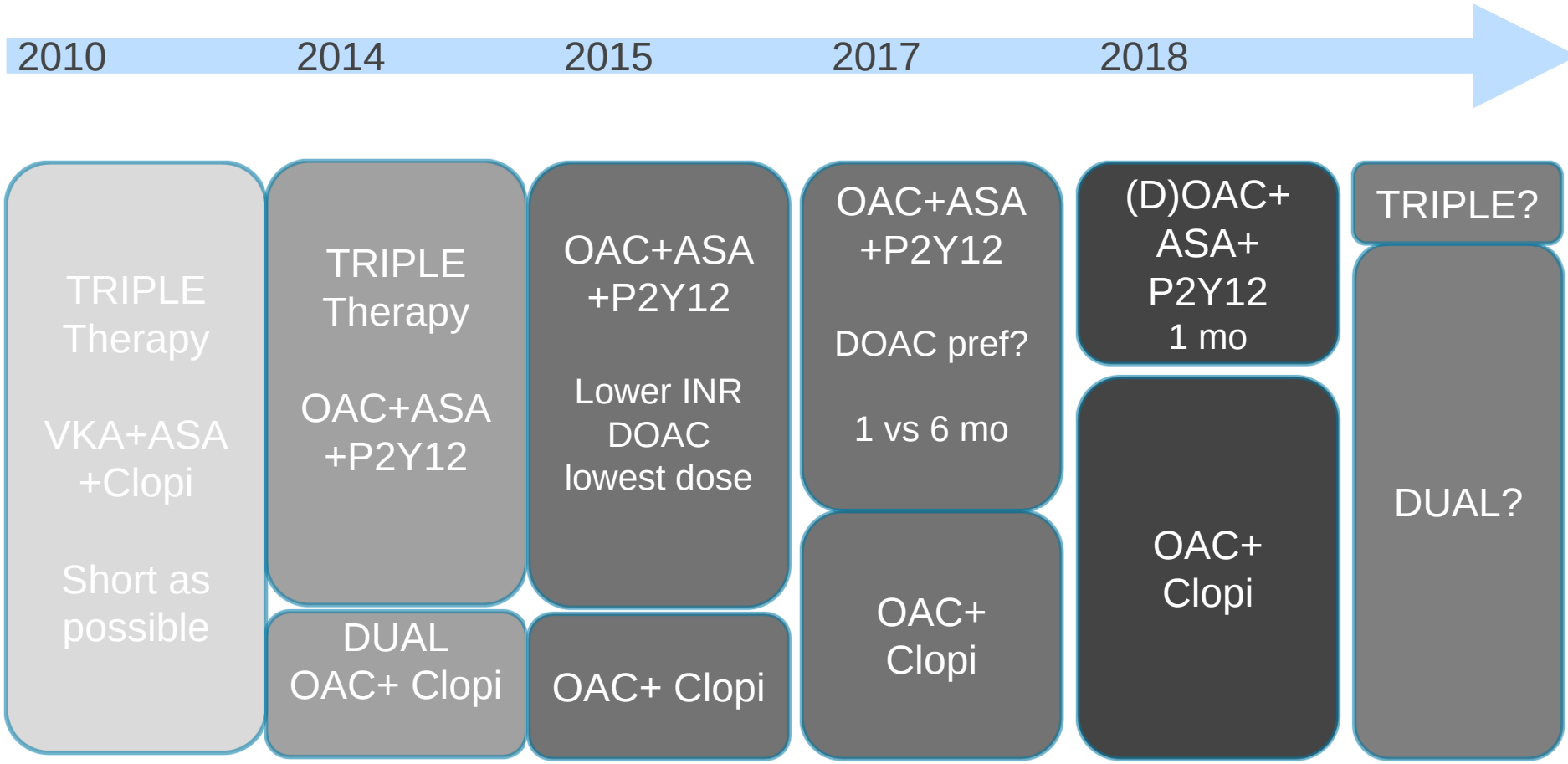
A 66 YO Hispanic male with atrial fibrillation, DM, HTN arrives to the office 3 w after LAD DES due to NSTEMI. Has no Hx of stroke

He is currently on Apixaban 5 mg BID + Clopidogrel 75 mg daily and ASA 81.

a) Stop asa

b) Continue asa

In Triple Therapy ?



Saito et al Journal of Cardiology 2019

W + DAPT	Apix + DAPT
W + P2Y12	Apix + P2Y12

DAPT

P2Y12

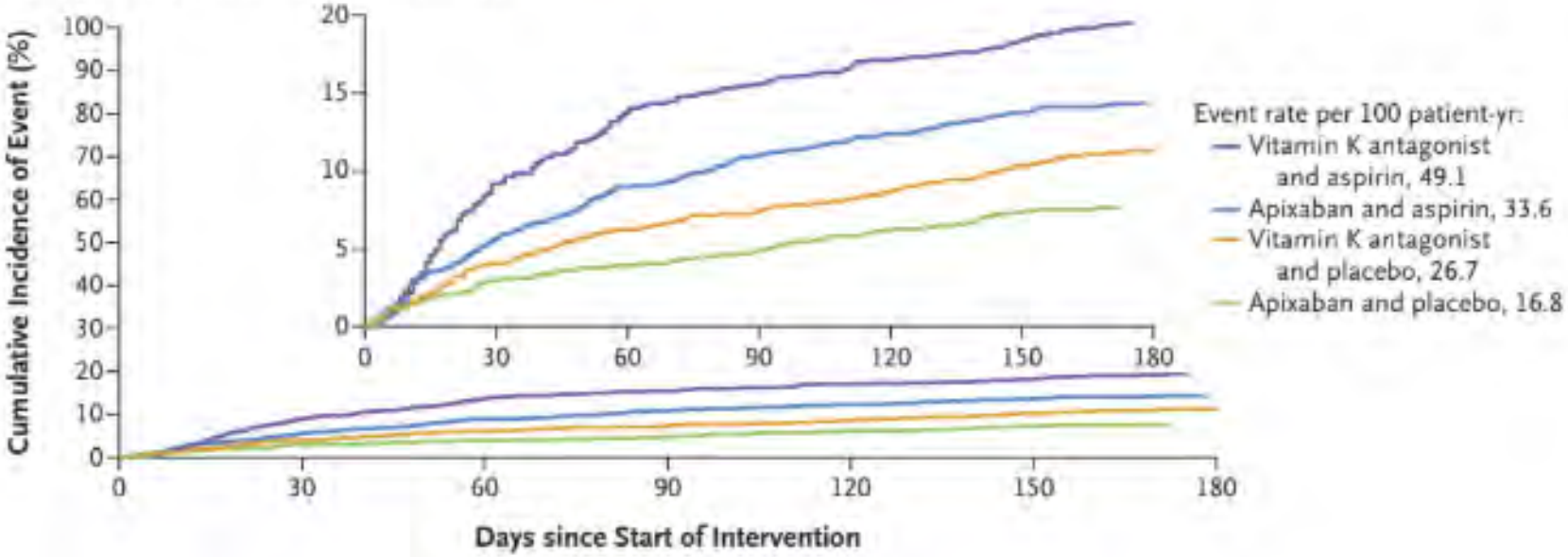
Warf Apix

Outcome	Apixaban	Vitamin K Antagonist	Hazard Ratio (95% CI)	P Value for Superiority
Anticoagulation-regimen comparison				
ISTH major or clinically relevant nonmajor bleeding†				
No. of patients with event/total no. (%)	241/2290 (10.5)	332/2259 (14.7)	—	—
Event rate per 100 patient-yr	24.7	35.8	0.69 (0.58–0.81)	<0.001
Death or hospitalization				
No. of patients with event/total no. (%)	541/2306 (23.5)	632/2308 (27.4)	—	—
Event rate per 100 patient-yr	57.2	69.2	0.83 (0.74–0.93)	0.002
Death or ischemic event‡				
No. of patients with event/total no. (%)	154/2306 (6.7)	163/2308 (7.1)	—	—
Event rate per 100 patient-yr	14.3	15.3	0.93 (0.75–1.16)	NS
Antiplatelet-regimen comparison	**Aspirin**	**Placebo**		
ISTH major or clinically relevant nonmajor bleeding				
No. of patients with event/total no. (%)	367/2277 (16.1)	204/2279 (9.0)	—	—
Event rate per 100 patient-yr	40.5	21.0	1.89 (1.59–2.24)	<0.001
Death or hospitalization§				
No. of patients with event/total no. (%)	604/2307 (26.2)	569/2307 (24.7)	—	—
Event rate per 100 patient-yr	65.7	60.6	1.08 (0.96–1.21)	NS
Death or ischemic event				
No. of patients with event/total no. (%)	149/2307 (6.5)	168/2307 (7.3)	—	—
Event rate per 100 patient-yr	13.9	15.7	0.89 (0.71–1.11)	NT

N Engl J Med 2019; 380:1509-1524

NorthShore University HealthSystem

Primary Outcome, According to Intervention Combination



No. at Risk							
Vitamin K antagonist and aspirin	1123	962	881	838	800	776	467
Apixaban and aspirin	1145	1036	975	937	903	880	485
Vitamin K antagonist and placebo	1126	1007	947	917	883	851	528
Apixaban and placebo	1143	1075	1044	1007	975	947	536

Patients in the apixaban group had a lower incidence of death or hospitalization than those in the vitamin K antagonist group (23.5% vs. 27.4%; hazard ratio, 0.83; 95% CI, 0.74 to 0.93; P=0.002)

Similar incidence of ischemic events.

Patients in the aspirin group had an incidence of death or hospitalization and of ischemic events that was similar to that in the placebo group.

NorthShore University HealthSystem

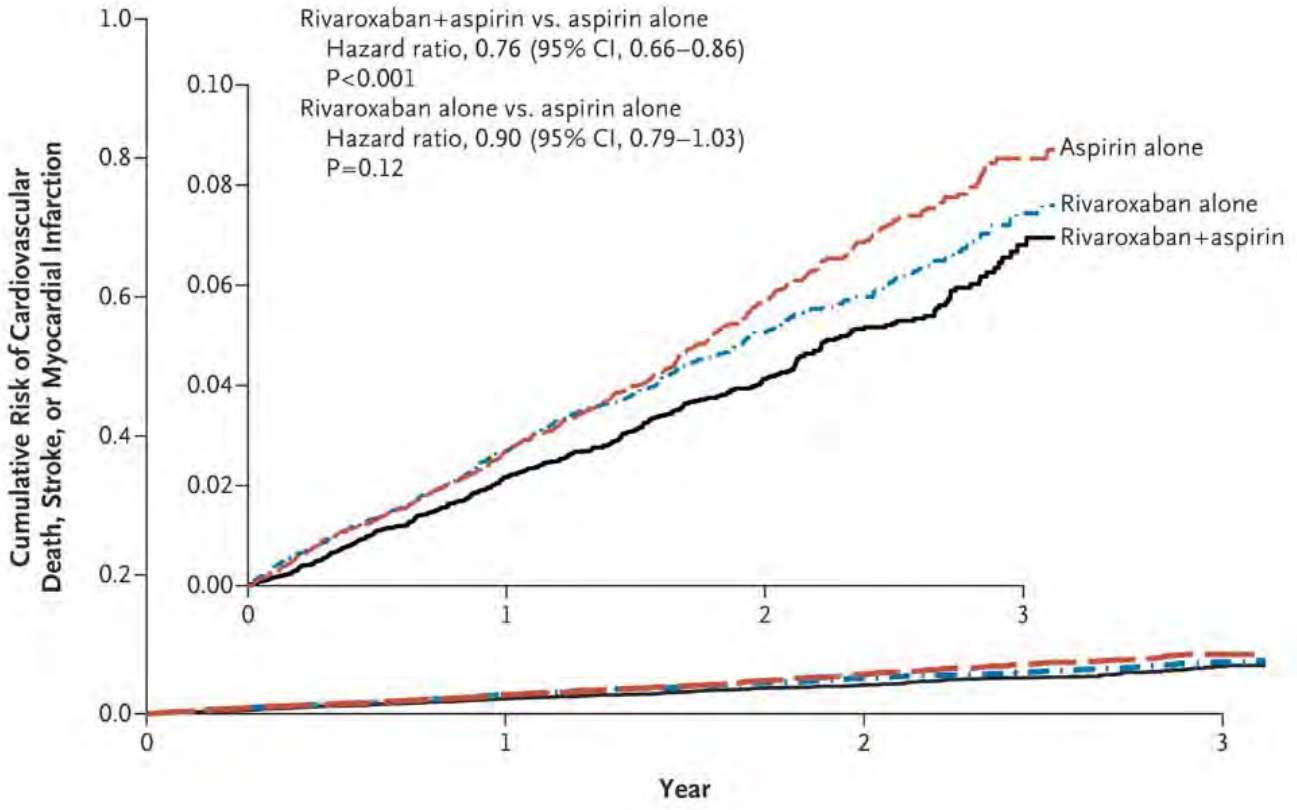
A 66 YO Hispanic male with CAD SP CABG 5 y ago, DM, HTN arrives to the office. He has a Hx of CLI and is SP SFA stent 1y ago, still claudicates but does not have rest pain.

He is on Rivaroxaban 2.5 and asa low dose

a) Stop asa

b) Continue asa

COMPASS



No. at Risk				
Aspirin alone	9126	7808	3860	669
Rivaroxaban alone	9117	7824	3862	670
Rivaroxaban+aspirin	9152	7904	3912	658

N Engl J Med 2017; 377:1319-1330

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