Cardiology Pearls for the Hospitalist

Krishan Soni, MD, MBA, FACC
Assistant Professor of Medicine
Division of Cardiology

SCHOOL OF MEDICINE * UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

Disclosures

No Conflicts of Interest

No Financial Disclosures

Credit to Dr. Lucas Zier (UCSF) for several slides in this presentation

Krishan.soni@ucsf.edu

Objectives

Prevention

1. Understand the use of aspirin in the prevention of coronary artery disease (CAD)

Coronary Artery Disease

2. Be familiar with contemporary data regarding surgery versus stents for left main and triple vessel disease
3. Be aware of updates in dual antiplatelet therapy (DAPT) after coronary stenting procedures
4. Develop an approach to triple therapy in patients requiring antiplatelet and anticoagulant agents

Structural Heart Disease (if time allows)

5. Define the expanding role of Transcatheter Aortic Valve Replacement (TAVR) in the management of aortic stenosis

Cardiology Pearls for the Hospitalist

- Major Society Guideline Updates 2016-2019

- Clinical Trials Published 2016-2019

Acronyms

- **ACS**: Acute Coronary Syndrome
- **BMS:** Bare Metal Stent
- **CAD**: Coronary Artery Disease
- **CABG:** Coronary Artery Bypass Graft Surgery
- **DAPT**: Dual Antiplatelet Therapy
- **DES:** Drug Eluting Stent
- **PCI**: Percutaneous Coronary Intervention
- **SIHD**: Stable Ischemic Heart Disease
- **VKA**: Vitamin K Antagonist
- **TAVR**: Transcatheter Aortic Valve Replacement

Strength of Guideline Recommendations

CLASS I (STRONG) — **Benefit >>> Risk**

Suggested phrases for writing recommendations:

- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS IIa (MODERATE) — **Benefit >> Risk**

Suggested phrases for writing recommendations:

- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK) — **Benefit ≥ Risk**

Suggested phrases for writing recommendations:

- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS III: No Benefit (MODERATE) — **Benefit = Risk**

(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:

- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — **Risk > Benefit**

Suggested phrases for writing recommendations:

- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

Outline

Prevention

1. Aspirin and prevention of coronary artery disease (CAD)

Coronary Artery Disease

1. Surgery versus stents for left main and triple vessel disease
2. Dual antiplatelet therapy (DAPT) after coronary stenting
3. Triple therapy in patients requiring antiplatelet and anticoagulant agents

Structural Heart Disease

1. Expanding role of Transcatheter Aortic Valve Replacement (TAVR) in the management of aortic stenosis

Primary Prevention: Aspirin

Primary Prevention: Aspirin

ARRIVE Trial

Clinical Question:

What is the clinical benefit of 100 mg per day of aspirin in reducing the risk of cardiovascular death, myocardial infarction, unstable angina, stroke, or transient ischemic attack in patients at moderate risk of cardiovascular events without diabetes?

Use of aspirin to reduce risk of initial vascular events in patients at moderate risk of cardiovascular disease (ARRIVE): a randomised, double-blind, placebo-controlled trial

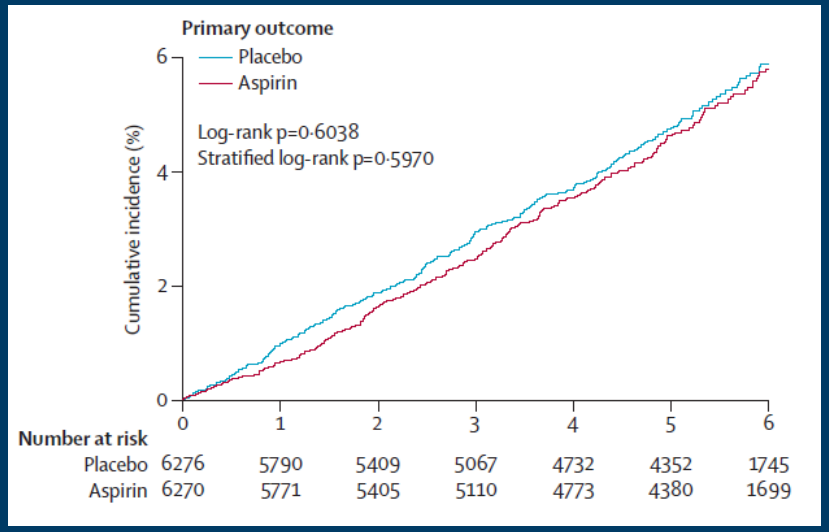
J Michael Gaziano, Carlos Brotons, Rosa Coppolecchia, Claudio Cricelli, Harald Darius, Philip B Gorelick, George Howard, Thomas A Pearson, Peter M Rothwell, Luis Miguel Ruilope, Michal Tendera, Gianni Tognoni; the ARRIVE Executive Committee

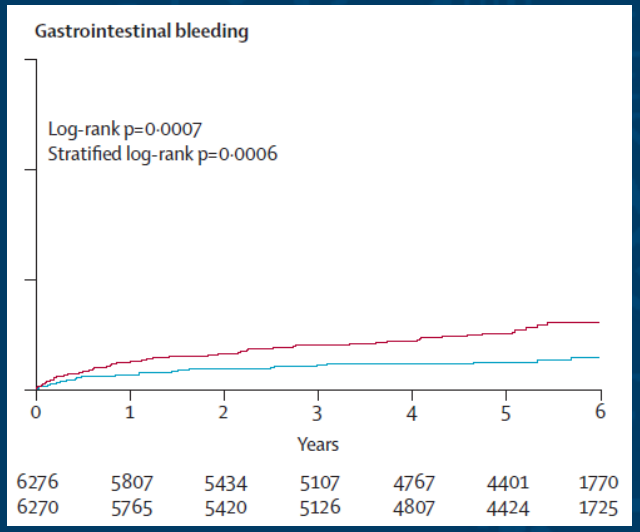
Gaziano JM, Brotons C, Coppolecchia R, et al., on behalf of the ARRIVE Executive Committee. Use of aspirin to reduce risk of initial vascular events in patients at moderate risk of cardiovascular disease (ARRIVE): a randomised, double-blind, placebo-controlled trial. Lancet 2018;Aug 26:

Primary Prevention: Aspirin

ARRIVE Trial

	Aspirin	Placebo	p Value
Composite Outcome of Cardiovascular Death, Myocardial Infarction, Unstable Angina, Stroke, or TIA	4.3%	4.5%	p = 0.60
Gastrointestinal Bleeding	0.97%	0.43%	p = 0.0007



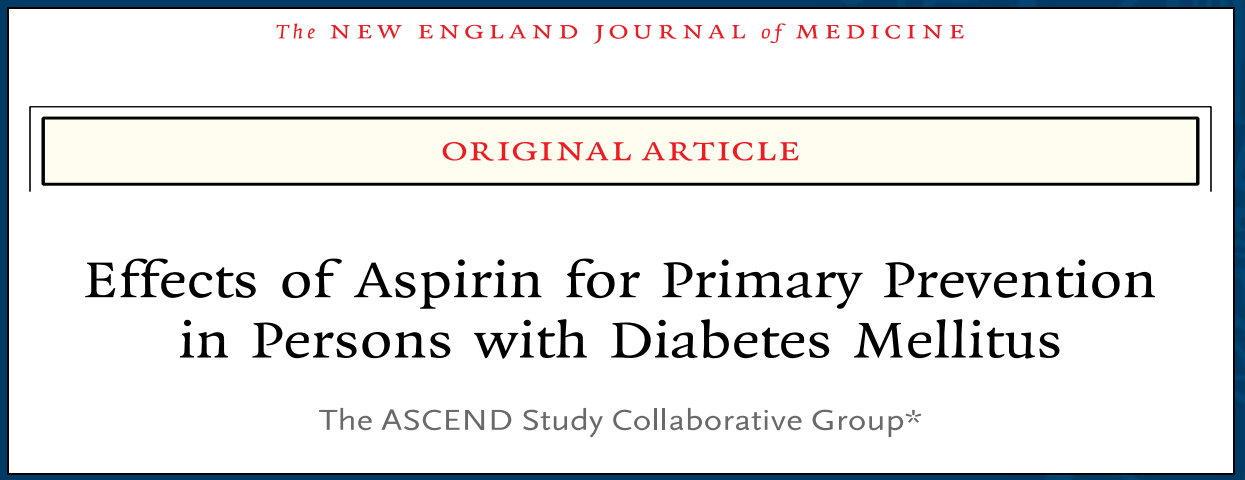


Primary Prevention: Aspirin

ASCEND Trial

Clinical Question:

What is the clinical benefit of 100 mg per day of aspirin in reducing the risk of vascular death, myocardial infarction, or stroke/transient ischemic attack in patients with known diabetes but no history of cardiovascular disease?

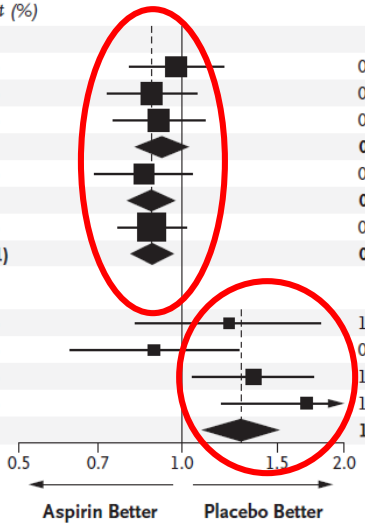


The ASCEND Study Collaborative Group. Effects of Aspirin for Primary Prevention in Persons With Diabetes Mellitus. N Engl J Med 2018;379:1529-39.

Primary Prevention: Aspirin
ASCEND Trial

	Aspirin	Placebo	p Value
Composite Outcome of Cardiovascular Death, Myocardial Infarction, Stroke, or TIA	8.5%	9.6%	p = 0.01
Major Bleeding	4.1%	3.2%	p = 0.003

Type of Event	Aspirin (N=7740)	Placebo (N=7740)	Rate Ratio (95% CI)	P Value
	no. of participants with event (%)			
Vascular Outcomes				
Nonfatal myocardial infarction	191 (2.5)	195 (2.5)	0.98 (0.80–1.19)	
Nonfatal presumed ischemic stroke	202 (2.6)	229 (3.0)	0.88 (0.73–1.06)	
Vascular death excluding intracranial hemorrhage	197 (2.5)	217 (2.8)	0.91 (0.75–1.10)	
Any serious vascular event excluding TIA	**542 (7.0)**	**587 (7.6)**	**0.92 (0.82–1.03)**	
TIA	168 (2.2)	197 (2.5)	0.85 (0.69–1.04)	
Any serious vascular event including TIA	**658 (8.5)**	**743 (9.6)**	**0.88 (0.79–0.97)**	**0.01**
Any arterial revascularization	340 (4.4)	384 (5.0)	0.88 (0.76–1.02)	
Any serious vascular event or revascularization	**833 (10.8)**	**936 (12.1)**	**0.88 (0.80–0.97)**	
Major Bleeding				
Intracranial hemorrhage	55 (0.7)	45 (0.6)	1.22 (0.82–1.81)	
Sight-threatening bleeding in eye	57 (0.7)	64 (0.8)	0.89 (0.62–1.27)	
Serious gastrointestinal bleeding	137 (1.8)	101 (1.3)	1.36 (1.05–1.75)	
Other major bleeding	74 (1.0)	43 (0.6)	1.70 (1.18–2.44)	
Any major bleeding	**314 (4.1)**	**245 (3.2)**	**1.29 (1.09–1.52)**	**0.003**

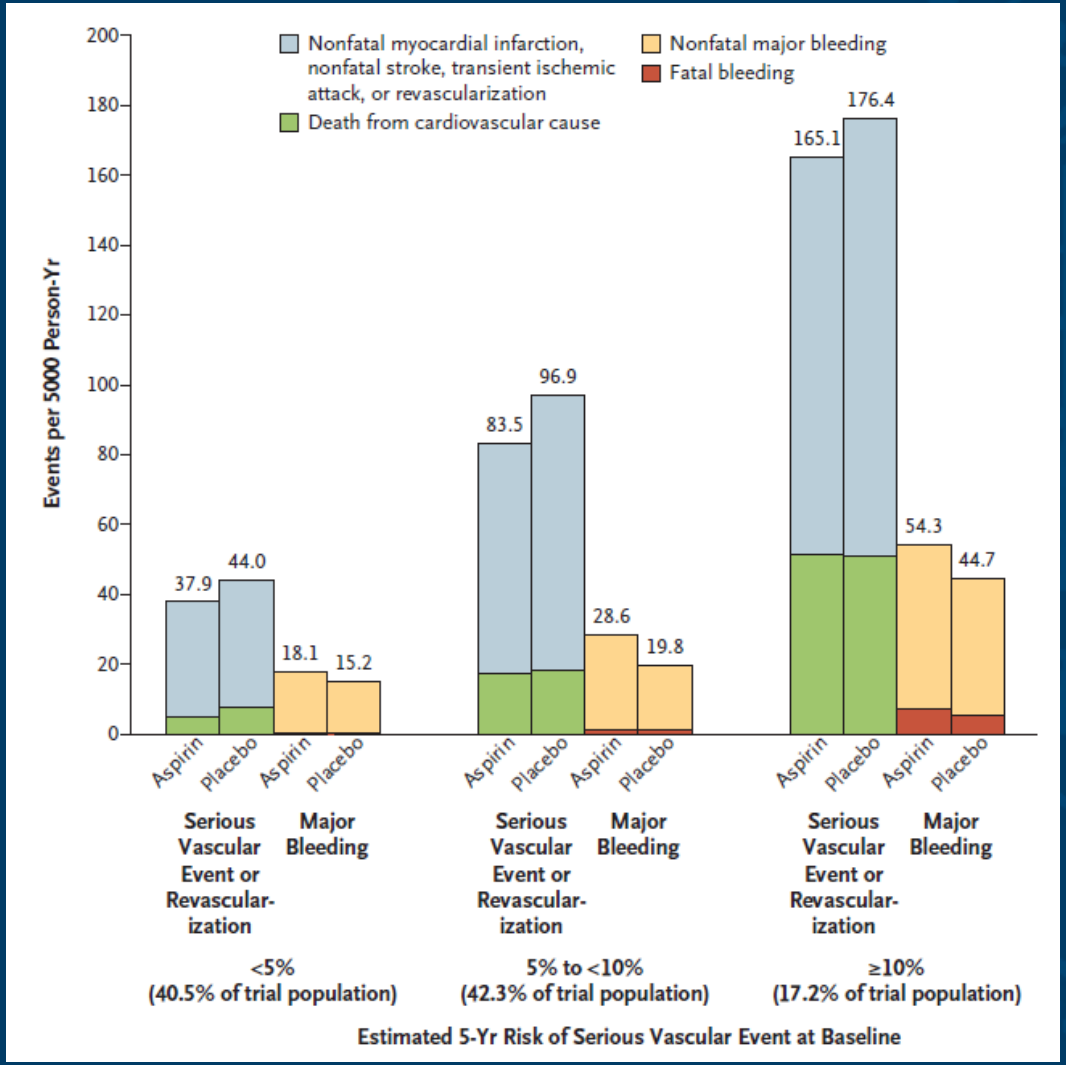


Vascular Events Better

Bleeding worse

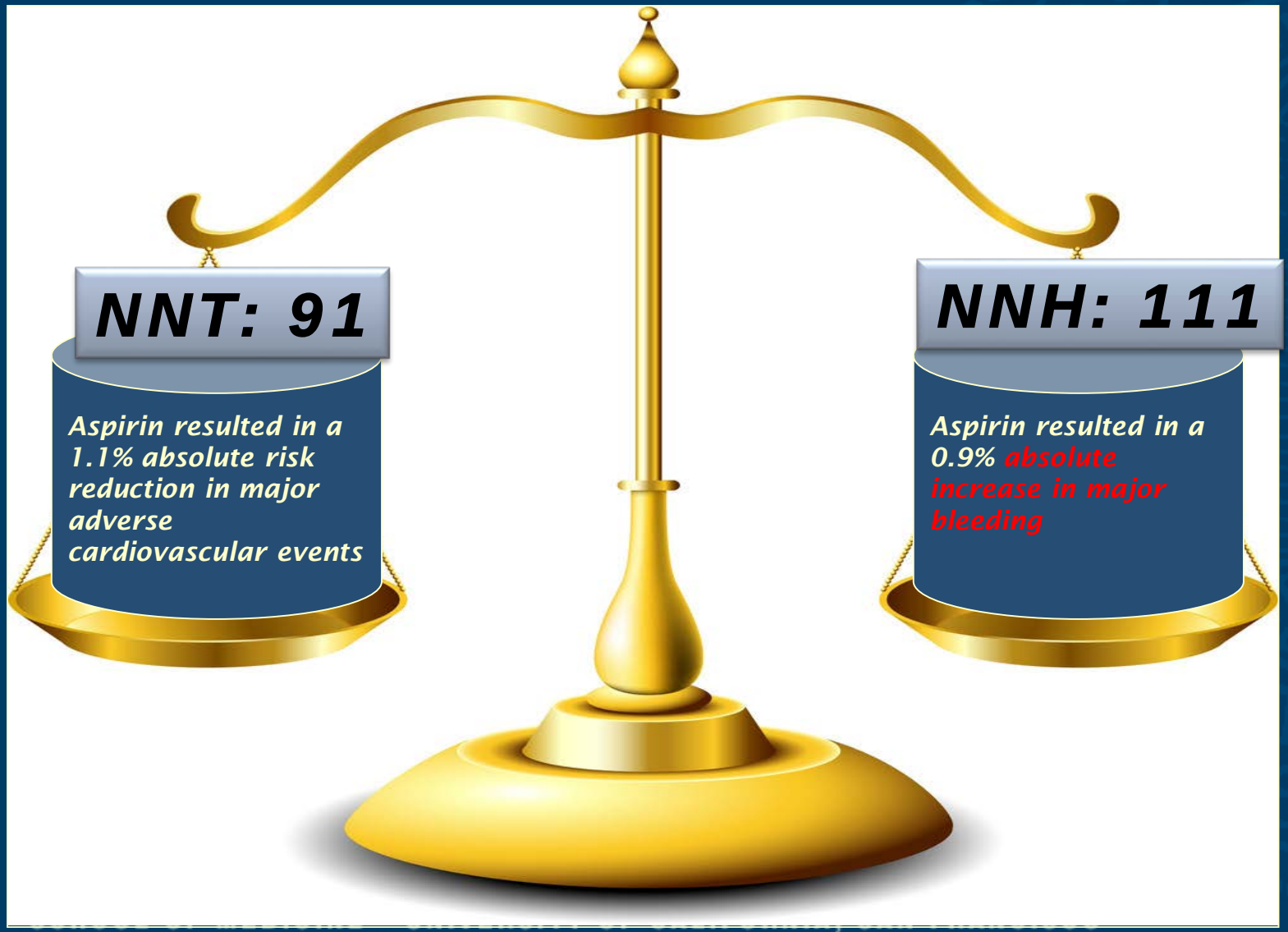
Primary Prevention: Aspirin

ASCEND Trial



Primary Prevention: Aspirin

ASCEND Trial



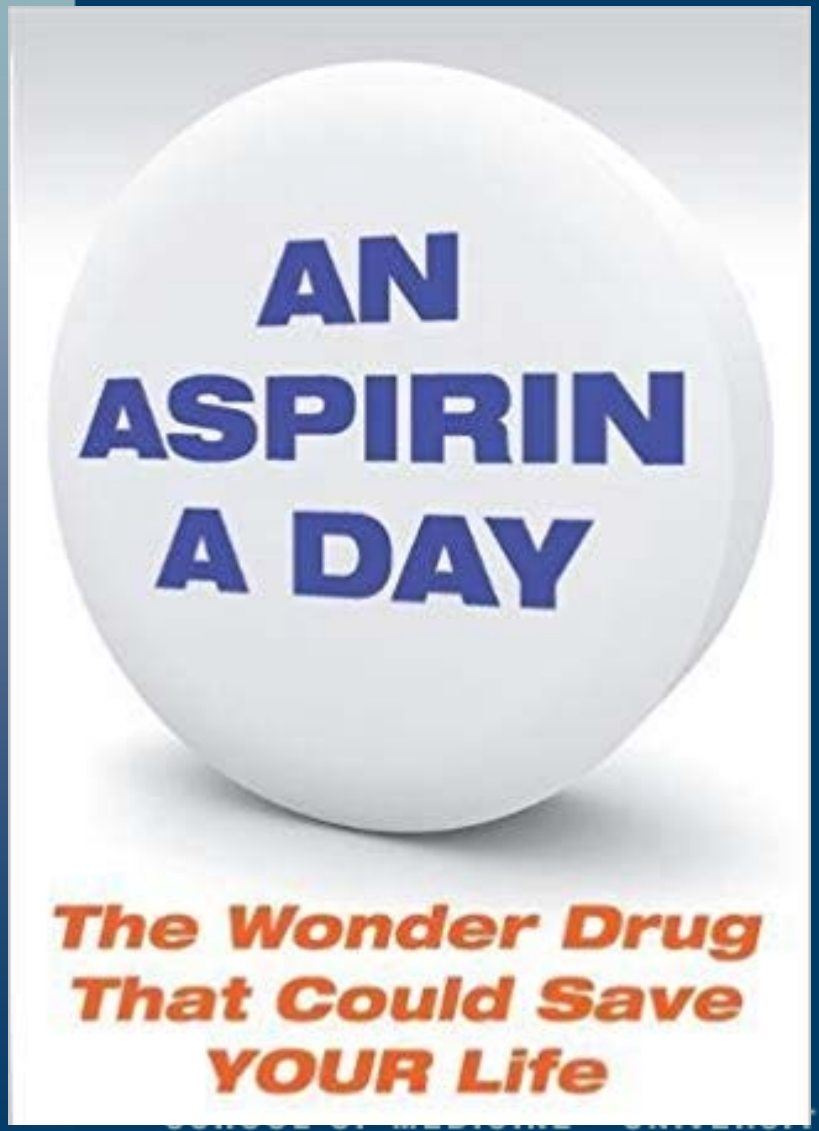
Primary Prevention: Aspirin
ASCEND Trial

What about cancer?...

	Aspirin	Placebo	p Value
Gastrointestinal Cancer	2.0%	2.0%	p = 1
All Cancer	11.6%	11.5%	p = 0.98

No Benefit in Reducing Fatal or Non-Fatal Cancer

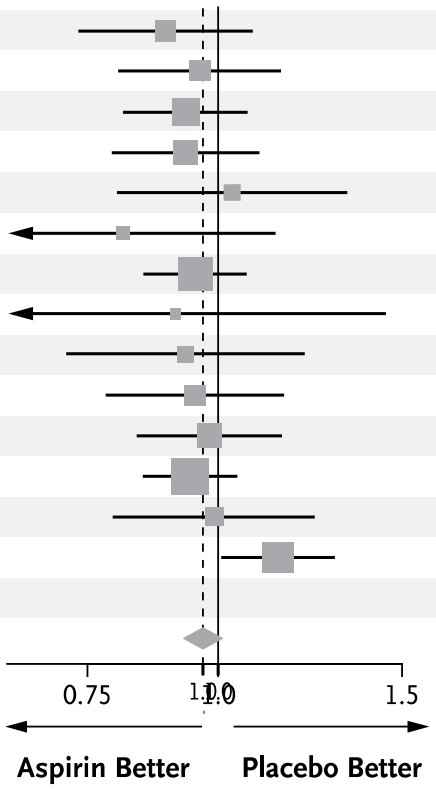
Primary Prevention: Aspirin



Primary Prevention: Aspirin

Aspirin and All Cause Mortality in 14 Primary Preventions Trials

Trial (year)	Aspirin	Placebo	Hazard Ratio for All-Cause Mortality (95% CI)
	no. of deaths/total no. of participants		
BMDT (1988)	270/3429	151/1710	0.89 (0.74–1.08)
PHS (1989)	217/11,037	227/11,034	0.96 (0.80–1.14)
ETDRS (1992)	340/1856	366/1855	0.93 (0.81–1.06)
HOT (1998)	284/9399	305/9391	0.93 (0.79–1.09)
TPT (1998)	113/1268	110/1272	1.03 (0.80–1.32)
PPP (2001)	62/2226	78/2269	0.81 (0.58–1.13)
WHS (2005)	609/19,934	642/19,942	0.95 (0.85–1.06)
JPAD (2008)	34/1262	38/1277	0.91 (0.57–1.43)
POPADAD (2008)	94/638	101/638	0.93 (0.72–1.21)
AAA (2010)	176/1675	186/1675	0.95 (0.78–1.15)
JPPP (2014)	297/7220	303/7244	0.98 (0.84–1.15)
ASCEND (2018)	748/7740	792/7740	0.94 (0.85–1.04)
ARRIVE (2018)	160/6270	161/6276	0.99 (0.80–1.24)
ASPREE (2018)	558/9525	494/9589	1.14 (1.01–1.29)
Overall (I^2=0%, P=0.67)			**0.97 (0.93–1.01)**



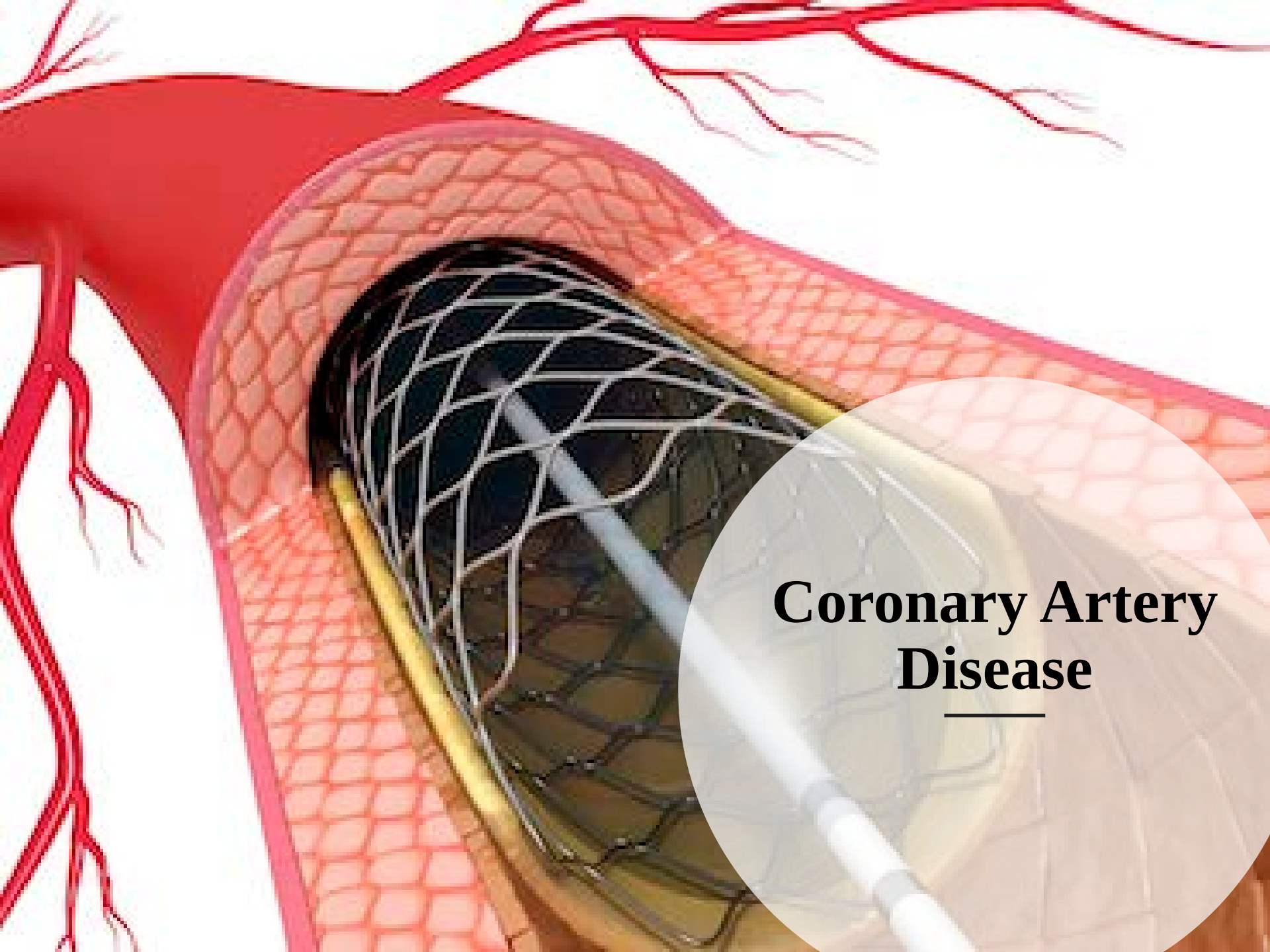
Primary Prevention: Aspirin

An aspirin a day…

Should not routinely be prescribed to patients without prior cardiovascular events due to a lack of clinical benefit and/or increased risk of bleeding that offsets the reduction in cardiovascular events

Primary Prevention: Aspirin

2019 AHA/ACC Guidelines



Coronary Artery Disease

Outline

Prevention

1. Aspirin and prevention of coronary artery disease (CAD)

Coronary Artery Disease

1. Surgery versus stents for left main and triple vessel disease
2. Dual antiplatelet therapy (DAPT) after coronary stenting
3. Triple therapy in patients requiring antiplatelet and anticoagulant agents

Structural Heart Disease

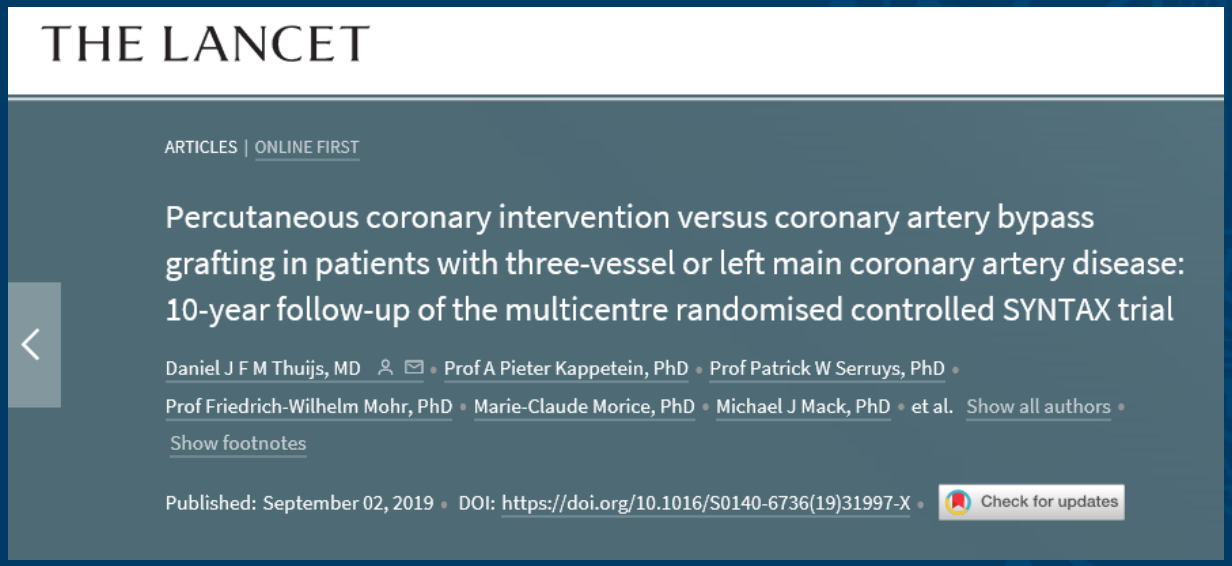
1. Expanding role of Transcatheter Aortic Valve Replacement (TAVR) in the management of aortic stenosis

Stable Ischemic Heart Disease

Syntaxes Trial

Clinical Question:

What is the long term (10 year) mortality benefit of bypass surgery (CABG) vs coronary stenting (PCI) in patients with severe three vessel or left main disease?



THE LANCET

ARTICLES | ONLINE FIRST

Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial

Daniel J F M Thuijs, MD • Prof A Pieter Kappetein, PhD • Prof Patrick W Serruys, PhD • Prof Friedrich-Wilhelm Mohr, PhD • Marie-Claude Morice, PhD • Michael J Mack, PhD • et al. Show all authors • Show footnotes

Published: September 02, 2019 • DOI: https://doi.org/10.1016/S0140-6736(19)31997-X • Check for updates

Thuijs DJFM, Kappetein AP, Serruys PW, et al. SYNTAX Extended Survival Investigators. Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial. Lancet 2019;Sep 2

Stable Ischemic Heart Disease

Syntaxes Trial

All Cause Mortality at 10 Years	**PCI** n = 903	**CABG** n = 897	**HR** (95% CI)
All Patients	244	211	1.17 (0.97-1.41)
Left Main Disease	93	98	0.90 (0.68-1.20)
Three Vessel Disease	151	113	1.41 (1.10-1.80)

Patients who do better with CABG

- *Three vessel disease*
- *Complex Anatomy*
- *Diabetes*

PCI and CABG "equivalent"

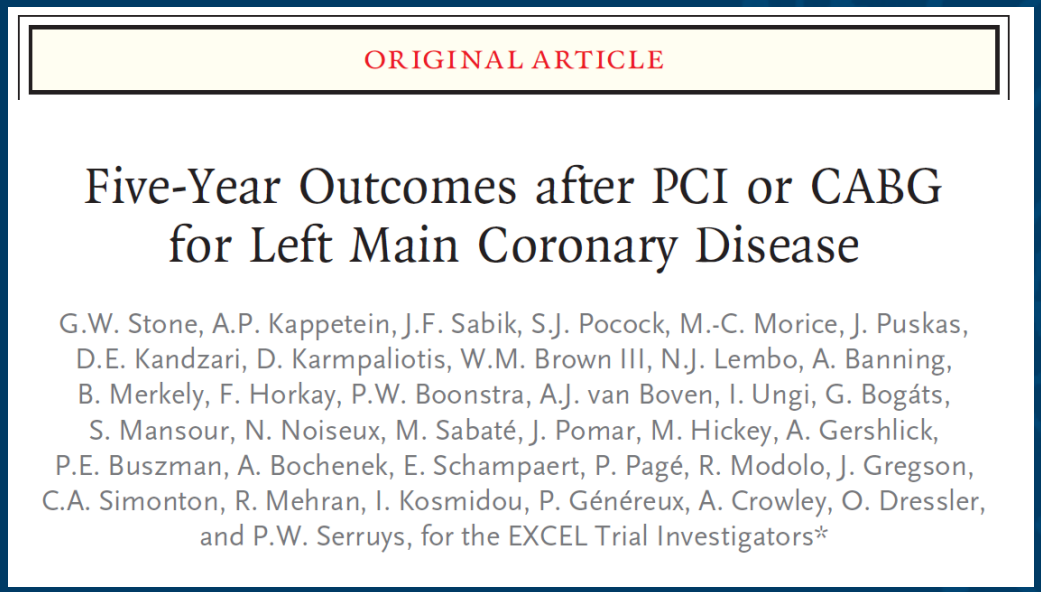
- *Left Main Disease*

Stable Ischemic Heart Disease

Excel Trial

Clinical Question:

What is the long term (5 year) benefit (death, stroke, myocardial infarction) of bypass surgery (CABG) vs coronary stenting (PCI) in patients with left main disease?



ORIGINAL ARTICLE

Five-Year Outcomes after PCI or CABG for Left Main Coronary Disease

G.W. Stone, A.P. Kappetein, J.F. Sabik, S.J. Pocock, M.-C. Morice, J. Puskas, D.E. Kandzari, D. Karmpaliotis, W.M. Brown III, N.J. Lembo, A. Banning, B. Merkely, F. Horkay, P.W. Boonstra, A.J. van Boven, I. Ungi, G. Bogáts, S. Mansour, N. Noiseux, M. Sabaté, J. Pomar, M. Hickey, A. Gershlick, P.E. Buszman, A. Bochenek, E. Schampaert, P. Pagé, R. Modolo, J. Gregson, C.A. Simonton, R. Mehran, I. Kosmidou, P. Généreux, A. Crowley, O. Dressler, and P.W. Serruys, for the EXCEL Trial Investigators*

Stone GW, et al. Five Year Outcomes after PCI or CABG for Left Main Coronary Disease. NEJM 2019;Sep 28

Stable Ischemic Heart Disease

Excel Trial

5 Year Outcome	PCI n = 903	CABG n = 897	CI
Death, Stroke or MI	22%	19.2%	[-0.9 to 6.5]
Death from any cause	13.0%	9.9%	[0.2 to 6.1]
Definite cardiovascular death	5.0%	4.5%	[-1.4 to 2.5]
Myocardial infarction	10.6%	9.1%	[-1.3 to 4.2]
Cerebrovascular events	**3.3%**	**5.2%**	[-2.4 to 0.9]
Ischemia driven revascularization	**16.9%**	**10.0%**	[3.7 to 10]

Takeaway: In patients with left main coronary artery disease of low or intermediate anatomical complexity, there was **no significant difference** between PCI and CABG with respect to the rate of the composite outcome of death, stroke, or myocardial infarction at 5 years.

Stable Ischemic Heart Disease

Summary

- For patients with left main coronary artery disease, PCI and CABG offer similar long term mortality benefits
  - Cerebrovascular events are higher after CABG
  - Need for coronary revascularization is higher after PCI
- For patients with triple vessel coronary artery disease, CABG remains superior

Outline

Prevention

1. Aspirin and prevention of coronary artery disease (CAD)

Coronary Artery Disease

1. Surgery versus stents for left main and triple vessel disease
2. Dual antiplatelet therapy (DAPT) after coronary stenting
3. Triple therapy in patients requiring antiplatelet and anticoagulant agents

Structural Heart Disease

1. Expanding role of Transcatheter Aortic Valve Replacement (TAVR) in the management of aortic stenosis

Current recommendations for antiplatelet therapy in patients with CAD

ACC/AHA FOCUSED UPDATE

2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease

ESC European Society of Cardiology

European Heart Journal (2017) **0**, 1–48
doi:10.1093/eurheartj/ehx419

ESC GUIDELINES

2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS

Aspirin dosing in patients with Coronary Artery Disease

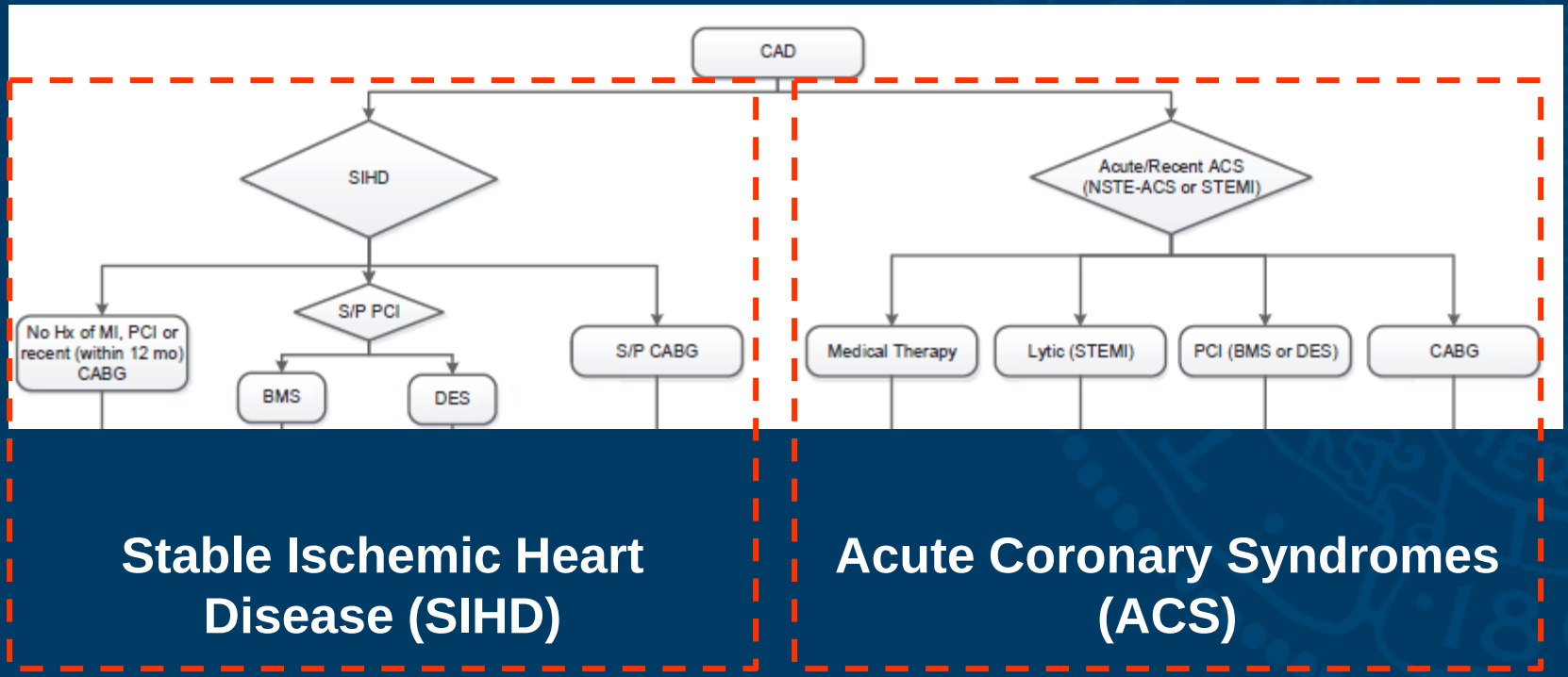
Aspirin Dosing in Patients Treated With DAPT

COR	LOE	Recommendation
I	B-NR	In patients treated with DAPT, a daily aspirin dose of 81 mg (range, 75 mg to 100 mg) is recommended.

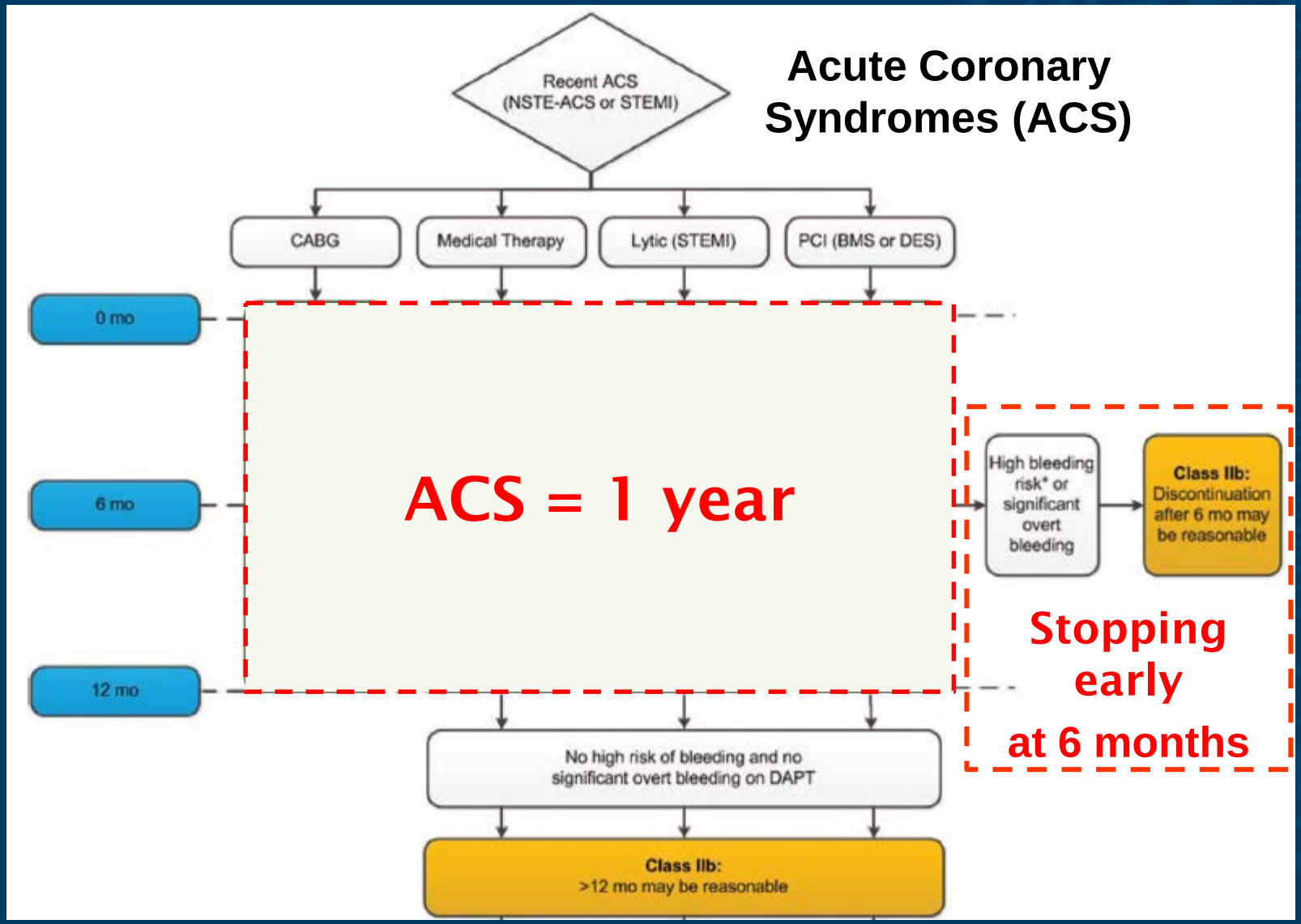
- ***Higher doses of aspirin are associated with bleeding and no increased anti-ischemic benefit***

Duration of dual antiplatelet therapy (DAPT)

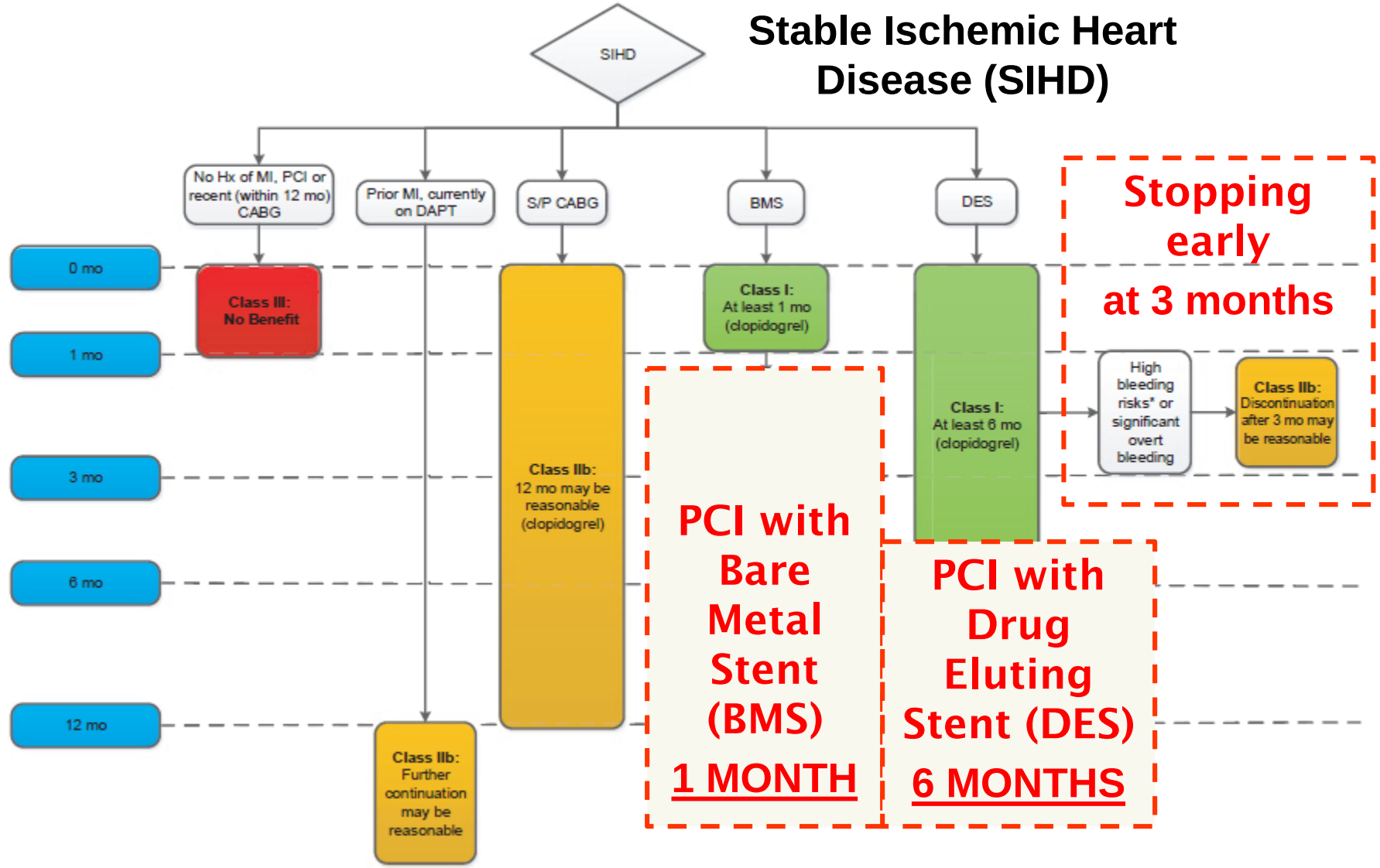
- Duration of DAPT depends on:
  - Underlying condition
  - Treatment provided



Duration of dual antiplatelet therapy (DAPT) in patients with ACS



Duration of dual antiplatelet therapy (DAPT) in patients with SIHD

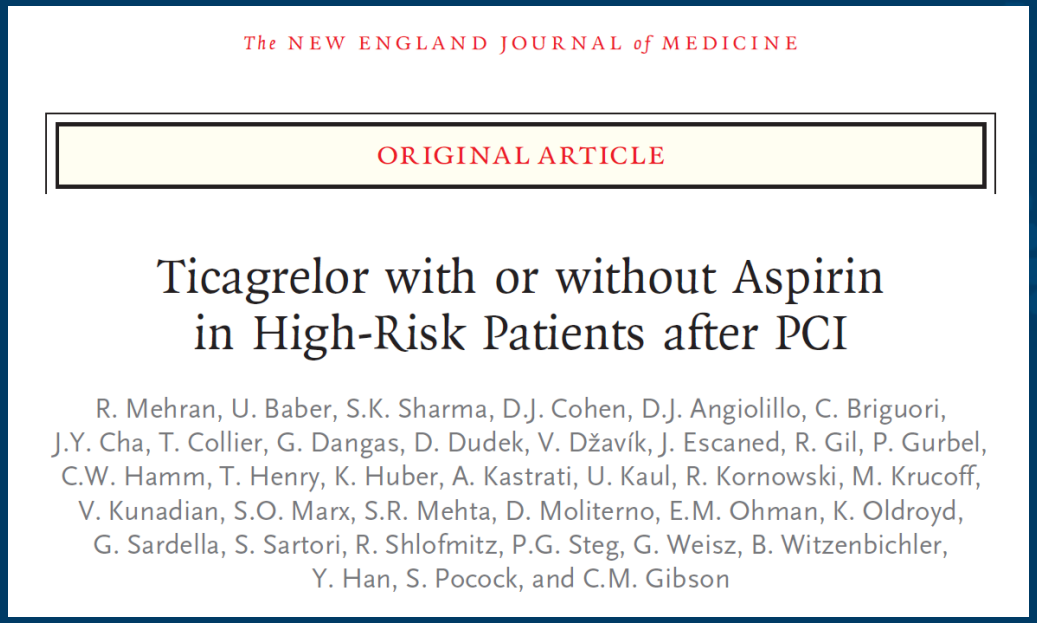


Duration of Antiplatelet Therapy

TWILIGHT Trial

Clinical Question:

Can aspirin be safely discontinued from the dual antiplatelet regimen after three months in patients undergoing PCI?



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ticagrelor with or without Aspirin in High-Risk Patients after PCI

R. Mehran, U. Baber, S.K. Sharma, D.J. Cohen, D.J. Angiolillo, C. Briguori, J.Y. Cha, T. Collier, G. Dangas, D. Dudek, V. Džavík, J. Escaned, R. Gil, P. Gurbel, C.W. Hamm, T. Henry, K. Huber, A. Kastrati, U. Kaul, R. Kornowski, M. Krucoff, V. Kunadian, S.O. Marx, S.R. Mehta, D. Moliterno, E.M. Ohman, K. Oldroyd, G. Sardella, S. Sartori, R. Shlofmitz, P.G. Steg, G. Weisz, B. Witzenbichler, Y. Han, S. Pocock, and C.M. Gibson

Mehran R, et al. Ticagrelor with or without Aspirin in High-Risk Patients after PCI. NEJM 2019;Sep 26

Regimen:

Aspirin 81 + Ticagrelor x 12 months

OR

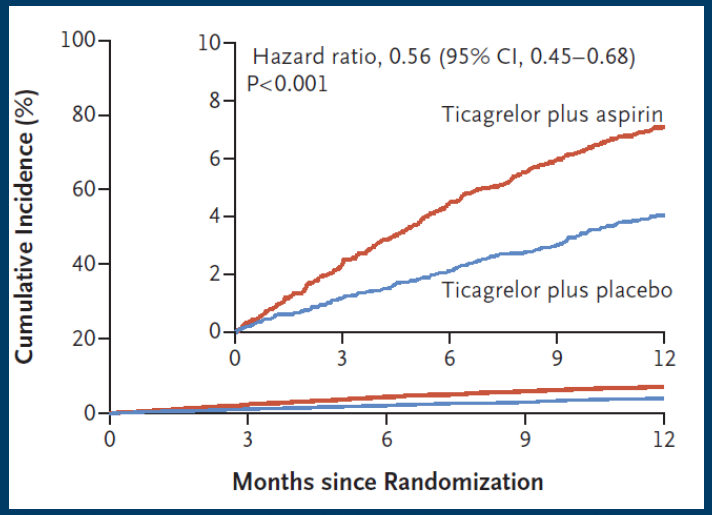
Aspirin 81+ ticagrelor x 3 months, then ticagrelor + placebo x 9 months

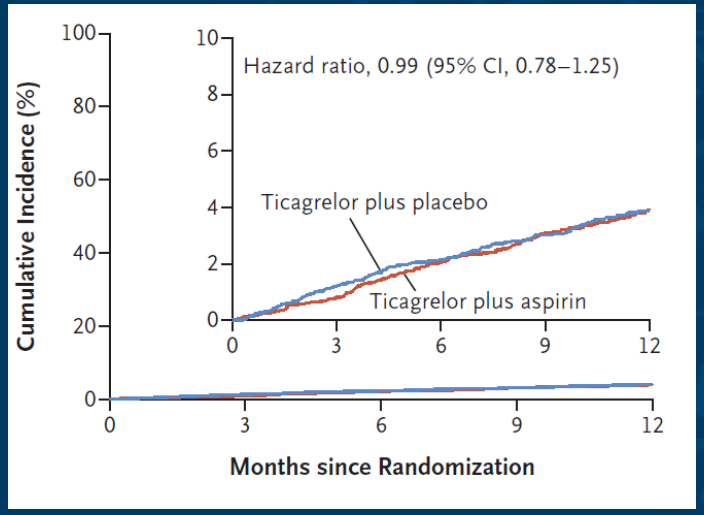
Duration of Antiplatelet Therapy

TWILIGHT Trial

	ASA + Ticagrelor (12 months)	ASA (3 mos) Ticagrelor (12 months)	HR P-value
Bleeding	7.1%	4.0%	0.56 P<0.001
Composite • Death (any cause) • Nonfatal MI • Nonfatal stroke	3.9%	3.9%	0.99 P <0.001 (non-inferiority)

Bleeding





Composite

Antiplatelet Therapy Summary

- Dose of Aspirin for all patients with CAD is **81 mg daily**
- Guideline Duration of DAPT:
  - ACS Patients: **1 YEAR for ALL** (with/without stent)
  - SIHD (Stable Ischemic Heart Disease) Patients:
    - **Drug Eluting Stent (DES): 6 MONTHS**
    - **Bare Metal Stent (BMS): 1 MONTH**
- New trials (TWILIGHT) show that shorter durations of aspirin therapy (3 months) and after coronary stenting may be effective and result in lower bleeding risk.

Outline

Prevention

1. Aspirin and prevention of coronary artery disease (CAD)

Coronary Artery Disease

1. Surgery versus stents for left main and triple vessel disease
2. Dual antiplatelet therapy (DAPT) after coronary stenting
3. Triple therapy in patients requiring antiplatelet and anticoagulant agents

Structural Heart Disease

1. Expanding role of Transcatheter Aortic Valve Replacement (TAVR) in the management of aortic stenosis

Triple Therapy: The conundrum

- Long-term treatment with oral anticoagulants is necessary in patients with:
  - Mechanical heart valves
  - Many with atrial fibrillation
- 20–30% of these patients have concomitant ischemic heart disease that requires PCI with stenting and subsequent antiplatelet therapy.
- The combination of oral anticoagulants and antiplatelets is associated with a high annual risk (4–16%) of fatal and non-fatal bleeding episodes.

Dewilde, Lancet 2013

What is the indication for triple therapy?

Dual Antiplatelet (DAPT)	Anticoagulation
▪ Recent ACS (<1 year) ▪ Recent PCI (< 6 months) ▪ Chronic Ischemic heart disease ▪ Stroke ▪ Peripheral vascular disease	▪ Atrial fibrillation ▪ Mechanical heart valves ▪ Deep venous thrombosis ▪ Pulmonary embolism ▪ Other indications

- Need to balance risk of thrombotic / ischemic events with bleeding

- Use risk scores to help assess:
  - $CHADS_2VASC$ for stroke risk in AF
  - HAS-BLED for bleeding risk

Multiple medical options for therapy

Dual Antiplatelet (DAPT)	Oral Anticoagulation

▪ Aspirin
▪ $P2Y_{12}$ Inhibitors
  ▪ Clopidogrel
  ▪ Ticagrelor
  ▪ Prasugrel
	▪ Coumadin
	▪ Dabigatran
	▪ Rivaroxaban
	▪ Apixaban
	▪ Edoxaban

- What is the safety and efficacy of each medication?
- What combinations offer the greatest reduction in ischemic / thrombotic events?
- Which combinations have the lowest bleeding risk?

Four recent trials:

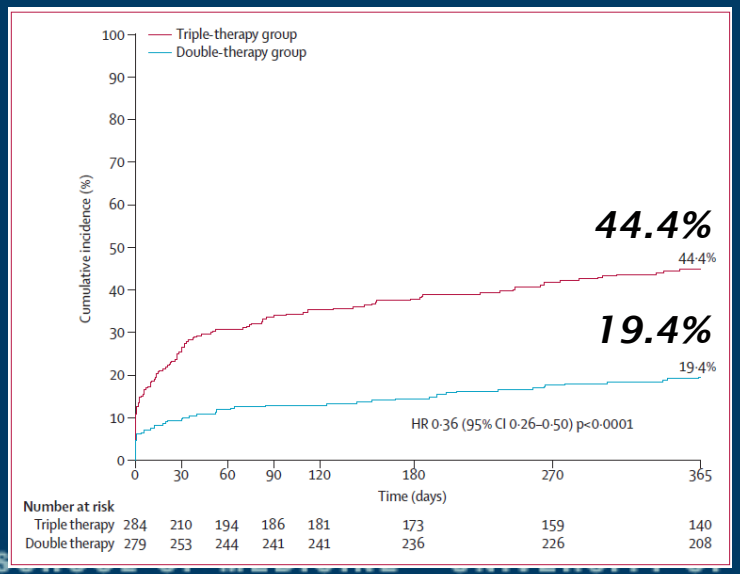
- WOEST (2013)
- PIONEER AF (2016)
- RE DUAL PCI (2017)
- AUGUSTUS (2019)

What's the update on triple therapy? Recent studies

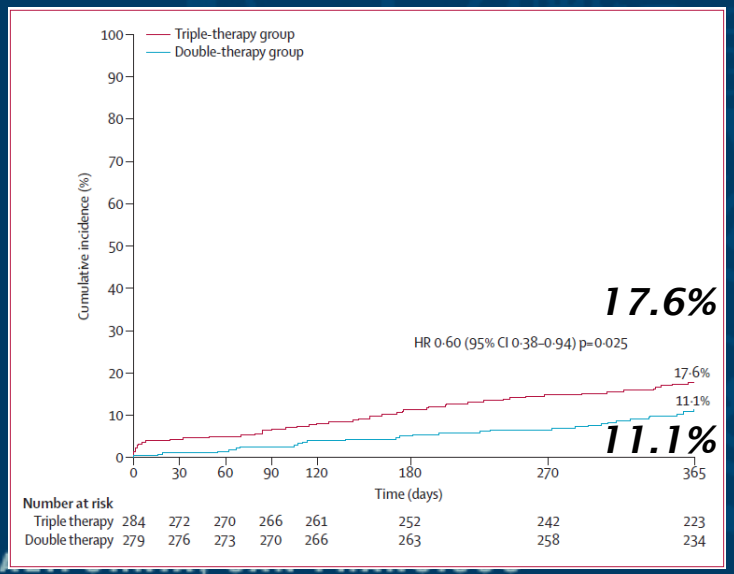
***WOEST Trial* (Lancet 2013)**

- RCT, Europe, 2008-2011
- 573 patients on anticoagulation undergoing PCI
- Randomized to:
  - ***Double Therapy: Clopidogrel + Coumadin***
  - ***Triple Therapy: Clopidogrel + Aspirin + Coumadin***

Any bleeding at 1 year



Incidence of death, MI, stroke, stent thrombosis, revascularization



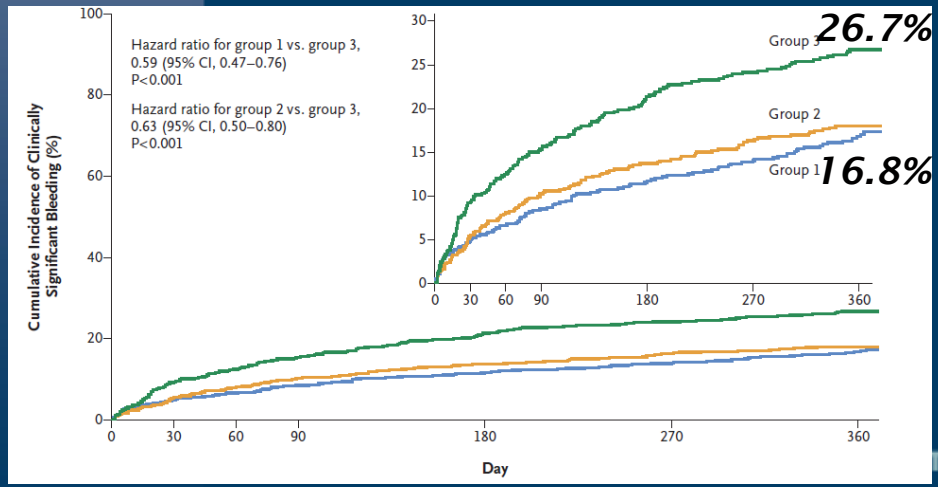
Dewilde, Lancet 2013

What's the update on triple therapy? Recent studies

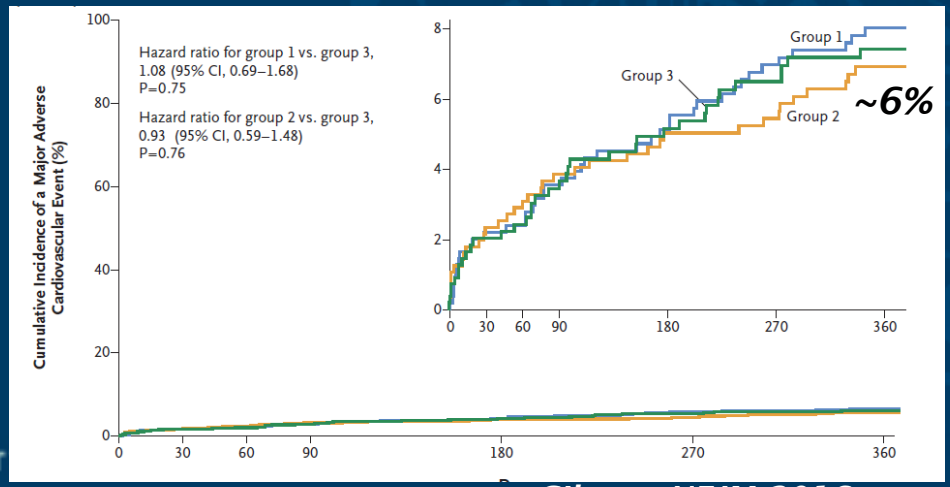
PIONEER AF PCI (NEJM 2016)

- RCT
- 2124 patients with nonvalvular AF undergoing PCI
- Randomized to:
  - **(1) Rivaroxaban 15 mg Daily + $P2Y_{12}$**
  - **(2) Rivaroxaban 2.5 mg BID + Aspirin + $P2Y_{12}$**
  - **(3) Coumadin + Aspirin + $P2Y_{12}$**

Any bleeding at 1 year



Incidence of death, MI, stroke, stent thrombosis



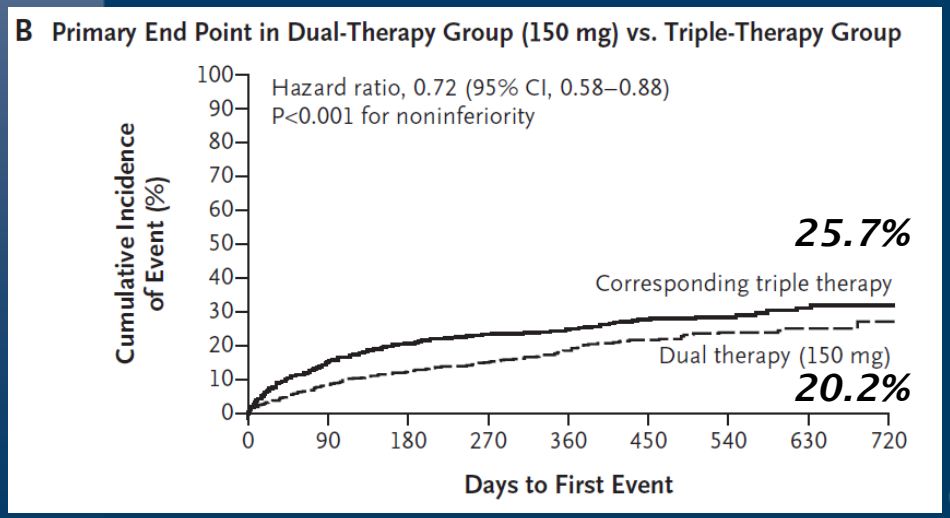
Gibson, NEJM 2016

What's the update on triple therapy? Recent studies

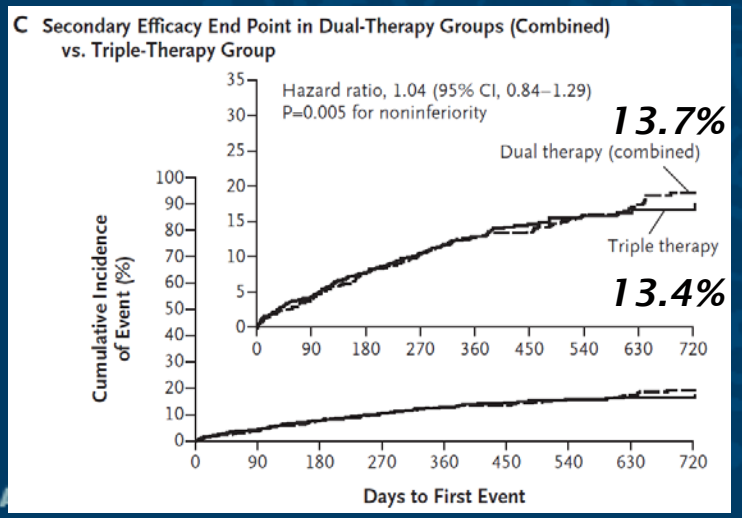
***REDUAL PCI* (NEJM 2017)**

- RCT
- 2725 patients with AF undergoing PCI
- Randomized to:
  - ***(1) Coumadin + $P2Y_{12}$ + aspirin***
  - ***(2) Dabigatran 110 mg BID + $P2Y_{12}$***
  - ***(3) Dabigatran 150 mg BID + $P2Y_{12}$***

Major or clinically relevant bleeding at 2 years



Incidence of death, MI, stroke, systemic embolism, unplanned revascularization



Cannon, NEJM 2017

What's the update on triple therapy? Summary of recent studies

Preferred options in United States

			Bleeding	Thrombosis
WOEST				
Coumadin	+ Clopidogrel		19%	11%
Coumadin	+ Clopidogrel	+ Aspirin	44%	18%
PIONEER AF PCI				
Rivaroxaban 15 mg Daily	+ $P2Y_{12}$		17%	6.5%
Rivaroxaban 2.5 mg BID	+ $P2Y_{12}$	+ Aspirin	18%	5.6%
Coumadin	+ $P2Y_{12}$	+ Aspirin	27%	6.0%
RE DUAL PCI				
Dabigatran 110 mg BID	+ $P2Y_{12}$		15%	13%
Dabigatran 150 mg BID	+ $P2Y_{12}$		20%	13%
Coumadin	+ $P2Y_{12}$	+ Aspirin	26%	14%

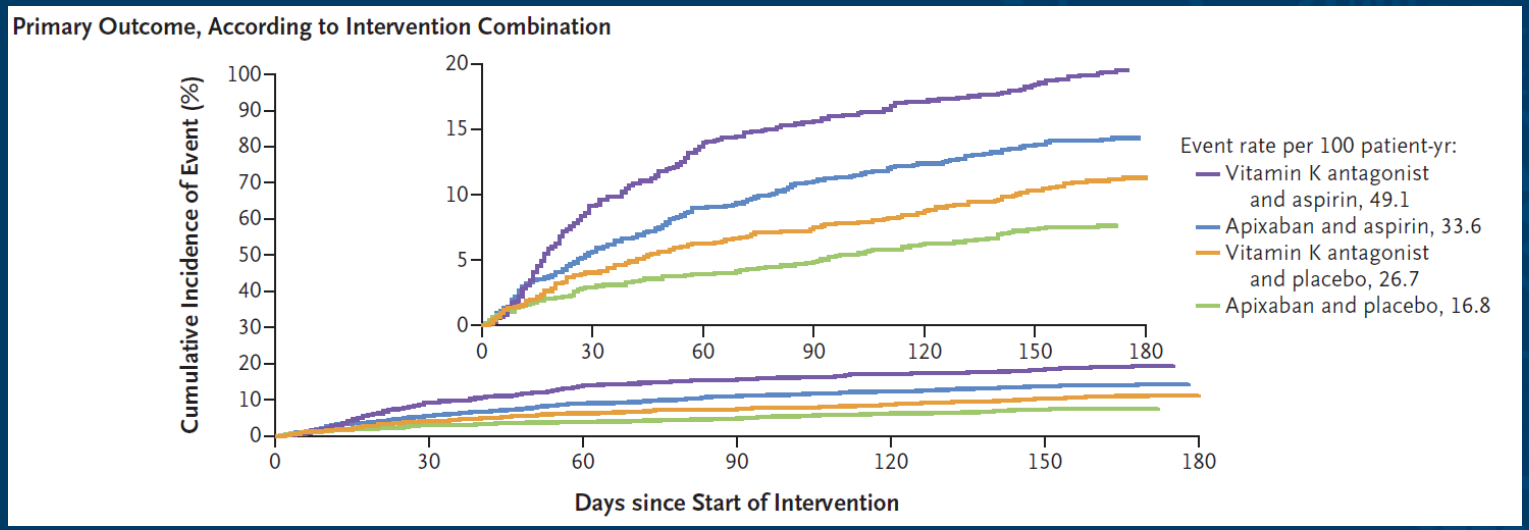
What's the update on triple therapy?

New in 2019: AUGUSTUS

***AUGUSTUS* (NEJM 2019)**

- RCT, 2x2 factorial design
- 4614 patients with AF undergoing PCI
- Factors:
  - ***Apixaban vs. Vitamin K antagonist***
  - ***Aspirin vs. Placebo***

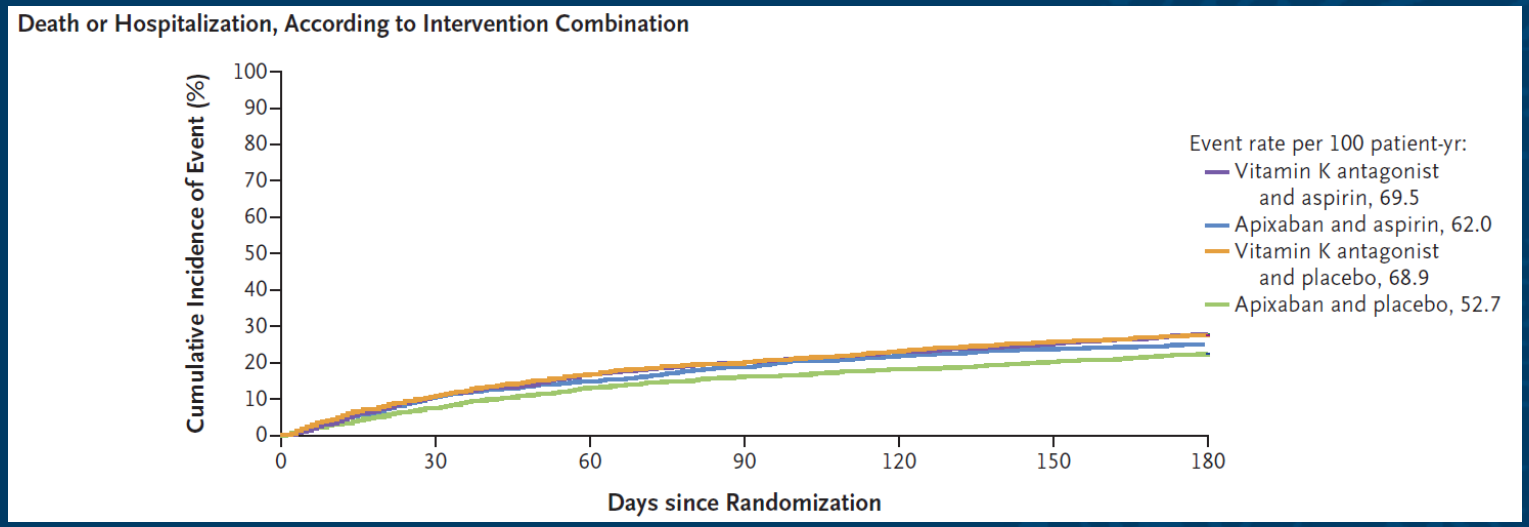
Major or clinically relevant non major bleeding



Lopes, NEJM 2019

What's the update on triple therapy?
AUGUSTUS

Composite of Death or Hospitalization



TAKEAWAY: In patients with atrial fibrillation and a recent acute coronary syndrome or PCI treated with a P2Y12 inhibitor, an antithrombotic regimen that included **apixaban, without aspirin, resulted in less bleeding and fewer hospitalizations** without significant differences in the incidence of ischemic events than regimens that included a vitamin K antagonist, aspirin, or both.

Lopes, NEJM 2019

Key points regarding triple therapy

- Recent studies have shown safety and efficacy of:
  - Any DOAC over Coumadin
  - DOAC + P2Y12 alone without Aspirin
- European Guidelines (2017) suggest DOAC
- US (Cardiology) Guidelines are still catching up

KEY TAKEAWAYS

- If a patient is a candidate for a DOAC, then a DOAC is strongly preferred over Coumadin

- For patients who require anticoagulation and antiplatelet therapy, aspirin can be safely removed from the regimen.

Long Term Anticoag and Antiplatelet

AFIRE Trial

Clinical Question:

What is the safest and most effective medical regimen for patients with atrial fibrillation and **chronic** coronary artery disease (angiography with no intervention or PCI/CABG > 1 year prior)?

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 19, 2019 VOL. 381 NO. 12

Antithrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease

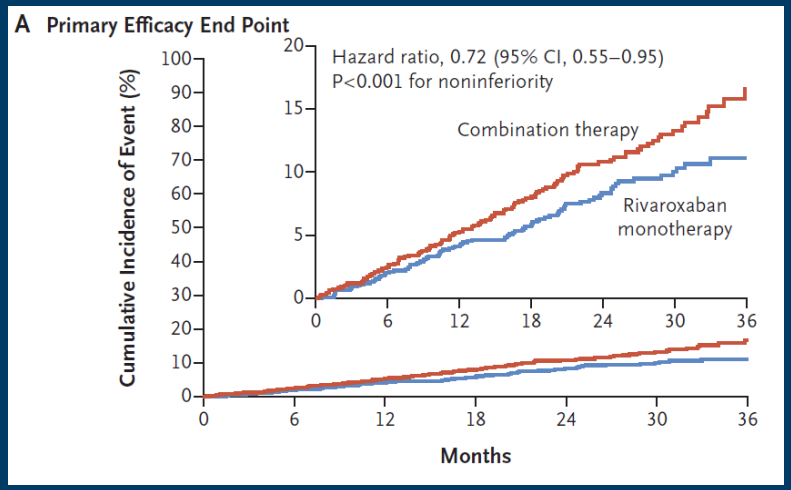
Satoshi Yasuda, M.D., Ph.D., Koichi Kaikita, M.D., Ph.D., Masaharu Akao, M.D., Ph.D., Junya Ako, M.D., Ph.D., Tetsuya Matoba, M.D., Ph.D., Masato Nakamura, M.D., Ph.D., Katsumi Miyauchi, M.D., Ph.D., Nobuhisa Hagiwara, M.D., Ph.D., Kazuo Kimura, M.D., Ph.D., Atsushi Hirayama, M.D., Ph.D., Kunihiko Matsui, M.D., M.P.H., and Hisao Ogawa, M.D., Ph.D., for the AFIRE Investigators*

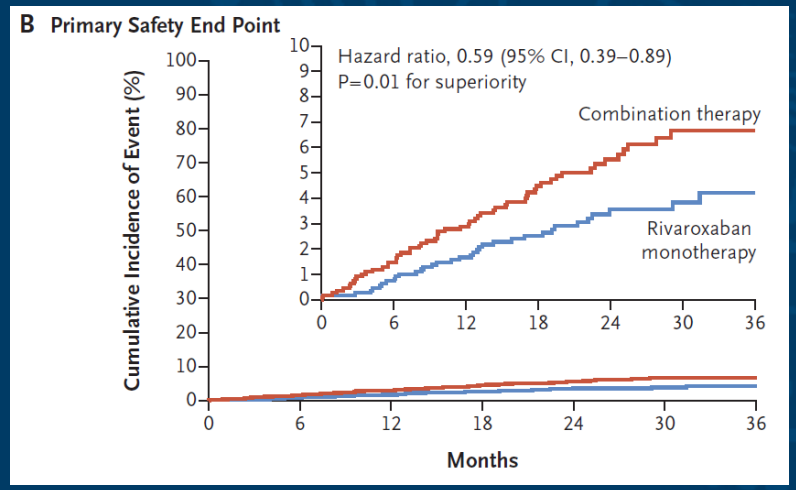
Yasuda, S, et al . Antithrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease. NEJM 2019;Sept 19: 1103.

Long Term Anticoag and Antiplatelet

AFIRE Trial

	Rivaroxaban + Placebo	Rivaroxaban + antiplatelet	p Value
Composite Outcome of Stroke, Embolism, Myocardial Infarction, Unstable Angina requiring revasc, or Death	4.14%	5.75%	p = <0.001
Major Bleeding	1.62%	2.76%	p = 0.01





Long Term Anticoag and Antiplatelet

AFIRE Trial

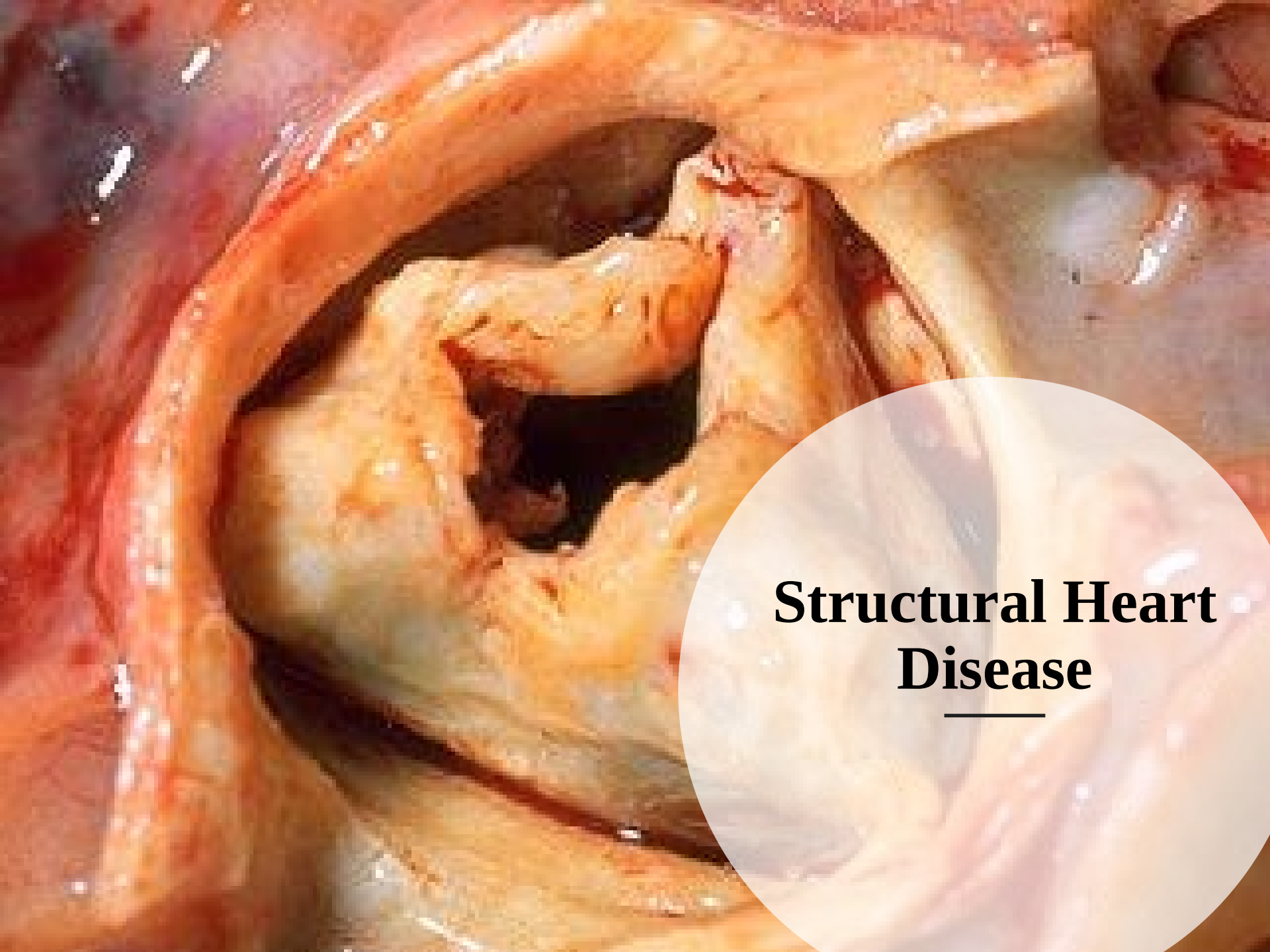
- Patients with atrial fibrillation and stable coronary artery disease more than 1 year after revascularization or in those with angiographically confirmed coronary artery disease not requiring revascularization

- Rivaroxaban monotherapy was **noninferior** to combination with respect to cardiovascular events and death from any cause

- Rivaroxaban monotherapy was **superior** with respect to major bleeding.

Doc, Should I still take my aspirin?

	Aspirin?	Therapy in 2019
Primary Prevention	**NO**	**Lifestyle**
After Acute Coronary Syndrome ▪ Recent MI / PCI	**As short as 3 months**	**P2Y12 for 1 Year Limited Aspirin**
Atrial fibrillation + ACS ▪ Recent MI / PCI	**NO**	**DOAC indefinitely Limited P2Y12**
Atrial fib and Chronic Coronary Disease ▪ Prior MI/PCI > 1 year	**Probably not**	**DOAC indefinitely +/- long term Antiplatelet**



Structural Heart Disease

Outline

Prevention

1. Aspirin and prevention of coronary artery disease (CAD)

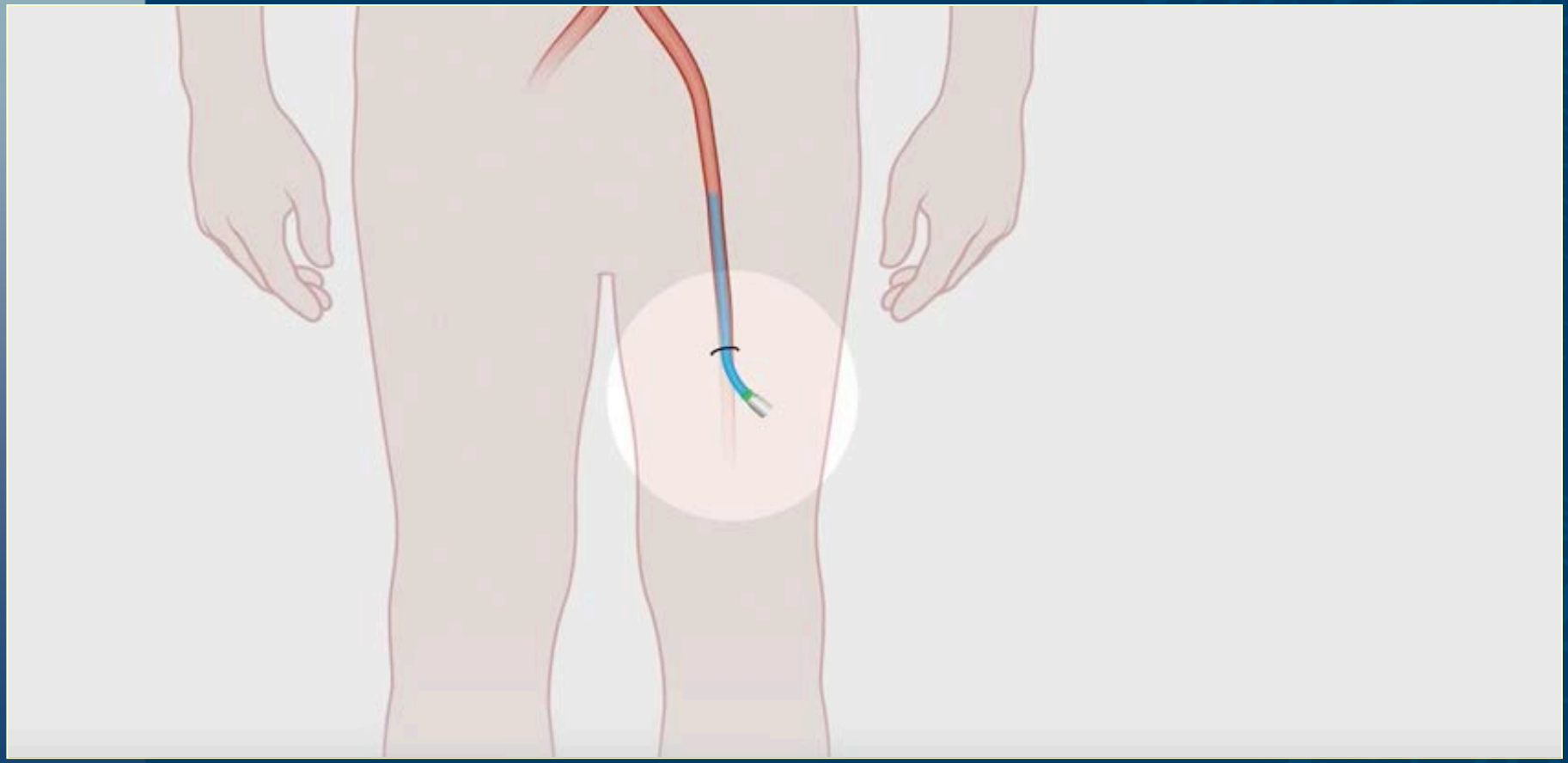
Coronary Artery Disease

1. Surgery versus stents for left main and triple vessel disease
2. Dual antiplatelet therapy (DAPT) after coronary stenting
3. Triple therapy in patients requiring antiplatelet and anticoagulant agents

Structural Heart Disease

1. Expanding role of Transcatheter Aortic Valve Replacement (TAVR) in the management of aortic stenosis

Structural Heart Disease: TAVR



Structural Heart Disease: TAVR

Domains of Aortic Valve Intervention Risk Assessment…

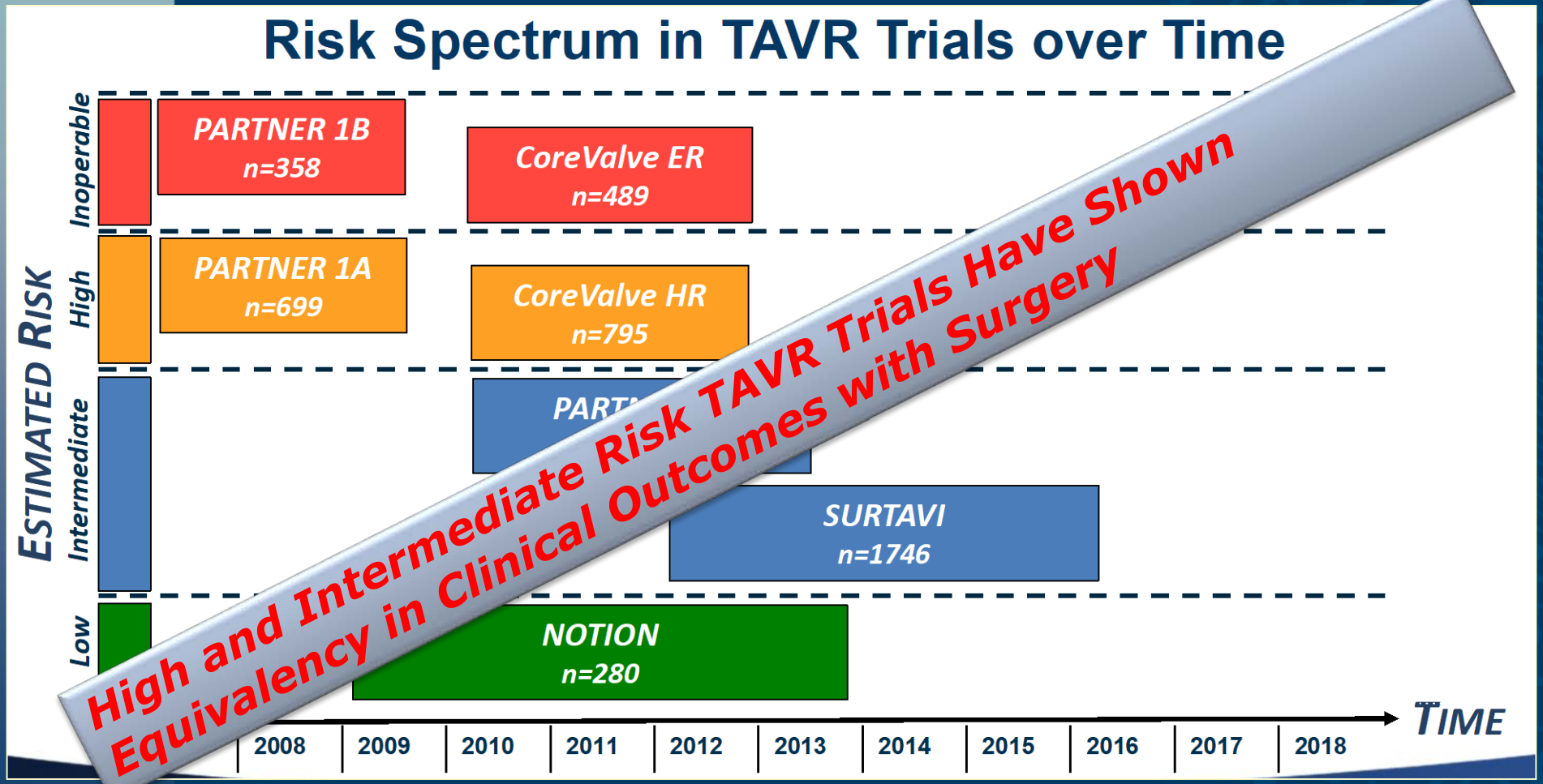
Surgical Mortality
(STS Prom Risk Calculator)

Major Organ System Compromise Not Likely to be Improved Post procedurally

Frailty Assessment

Procedure Specific Impediments
(ex. Morbid Obesity)

Structural Heart Disease: TAVR



Structural Heart Disease: Low Risk TAVR
PARTNER 3 Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients

M.J. Mack, M.B. Leon, V.H. Thourani, R. Makkar, S.K. Kodali, M. Russo, S.R. Kapadia, S.C. Malaisrie, D.J. Cohen, P. Pibarot, J. Leipsic, R.T. Hahn, P. Blanke, M.R. Williams, J.M. McCabe, D.L. Brown, V. Babaliaros, S. Goldman, W.Y. Szeto, P. Genereux, A. Pershad, S.J. Pocock, M.C. Alu, J.G. Webb, and C.R. Smith, for the PARTNER 3 Investigators*

Mack, Michael J., et al. "Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients." New England Journal of Medicine (2019).

Structural Heart Disease: Low Risk TAVR
PARTNER 3 Trial

Clinical Question:

What is the clinical benefit of TAVR compared with SAVR in reducing the risk of death from any cause, stroke, or rehospitalization at one year after the procedure?

Structural Heart Disease: Low Risk TAVR
PARTNER 3 Trial

	TAVR	SAVR	p Value
Composite of Death From Any Cause, Stroke, or Rehospitalization at 1 Year After the Procedure	8.5%	15.1%	p < 0.001 for Non Inferiority p = 0.001 for Superiority
Key Secondary Endpoints •New Onset Atrial Fibrillation •Length of Hospitalization •Stroke at 30 days	 5% 3% 0.6%	 39.5% 8% 2.4%	 p < 0.001 p < 0.001 p = 0.02

Structural Heart Disease: TAVR Summary

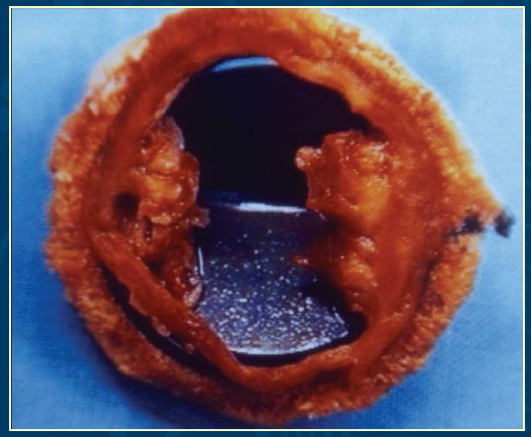
Transcatheter Aortic Valve Replacement…

Is equivalent to surgical aortic valve replacement in high, intermediate, and low risk patients with severe aortic stenosis and may be superior to surgical aortic valve replacement in low risk patients

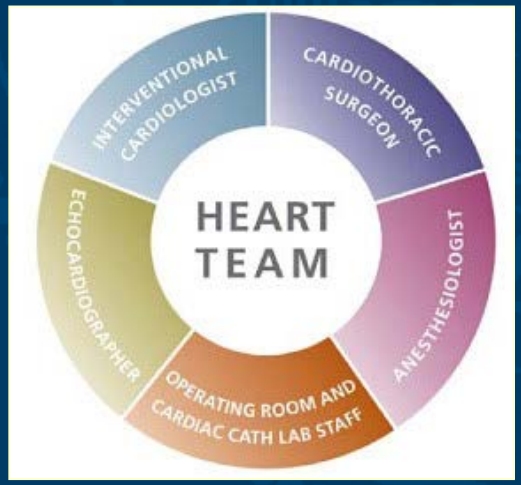
Structural Heart Disease: TAVR Summary

But…

Long term valve durability remains unknown especially in younger patients



Referral to a high volume center with a multidisciplinary heart team remains critical



What have we learned?

Primary Prevention

- Aspirin should not routinely be prescribed to patients without prior cardiovascular events

Stable Ischemic Heart Disease

- For patients with left main coronary artery disease, PCI and CABG offer similar long term mortality benefits

- For patients with triple vessel coronary artery disease, CABG remains superior

What have we learned?

Dual Antiplatelet Therapy

- Guideline based duration of DAPT is currently 12 months after ACS and 6 months after PCI with medicated stents in stable ischemic disease
- Dropping aspirin early (at 3 months) may be safe

Triple Therapy

- DOACs offer lower bleeding risk compared with Coumadin when used in combination with antiplatelet agents
- Aspirin can usually be safely dropped when anticoagulation and DAPT are indicated
- Long term monotherapy with DOAC may be safe in patients with AF and Stable CAD

What have we learned?

Structural Heart Disease

- TAVR is equivalent to surgical aortic valve replacement in high, intermediate, and low risk patients with severe aortic stenosis and may be superior to surgical aortic valve replacement in low risk patients


Questions?

Thank You!

Questions:

Email Krishan Soni @

Krishan.soni@ucsf.edu

415-476-6541

Additional Reading

Provided for your reference, but will not be covered during the session

Oral Antiplatelet Agents

	Aspirin	Clopidogrel	Prasugrel	Ticagrelor
Indication	ACS Post PCI Stroke PVD	ACS Post PCI Stroke PVD	Post PCI	ACS Post PCI
Dose **Load** **Maintenance**	325 mg **81 mg DAILY**	300-600 mg **75 mg DAILY**	60 mg **10 mg DAILY**	180 mg **90 mg BID**
Class	NSAID	2nd gen thienopyridine (PRODRUG)	2nd gen thienopyridine (PRODRUG)	CTPT
Mechanism	IRREVERSIBLE COX 1	IRREVERSIBLE $P2Y_{12}$	IRREVERSIBLE $P2Y_{12}$	REVERSIBLE $P2Y_{12}$
Peak Effect	1-3 hours	6 hours	4 hours	2 hours
CYP Metabolism	NA	2C19	3A4	3A4/5
FDA Approval		*1997*	*2009*	*2011*
Generic Approved	✚	✚	*2017*	*9/2018*

Which $P2Y_{12}$ agent will the cardiologist recommend?

COR	LOE	RECOMMENDATIONS
IIa	B-R	In patients with ACS (NSTE-ACS or STEMI) treated with DAPT after coronary stent implantation and in patients with NSTE-ACS treated with medical therapy alone (without revascularization), it is reasonable to use ticagrelor in preference to clopidogrel for maintenance $P2Y_{12}$ inhibitor therapy (53,71,72).
IIa	B-R	In patients with ACS (NSTE-ACS or STEMI) treated with DAPT after coronary stent implantation who are not at high risk for bleeding complications and who do not have a history of stroke or TIA, it is reasonable to choose prasugrel over clopidogrel for maintenance $P2Y_{12}$ inhibitor therapy (54,55).
III: Harm	B-R	Prasugrel should not be administered to patients with a prior history of stroke or TIA (54).

For Medically Managed ACS

Reasonable to choose **Ticagrelor** over **Clopidogrel**

For ACS with PCI

Reasonable to choose **Ticagrelor** or **Prasugrel** over **Clopidogrel**

Other pearls regarding $P2Y_{12}$ inhibitors

- Ticagrelor
  - can cause dyspnea (14%) and bradycardia (6%)
- Prasugrel
  - may be less effective (more bleeding) in patients < 60 kg and > 75 years of age
  - should not be given until after invasive angiography (Class III)
  - do not give to patients with a history of TIA or stroke (Class III)