



**PHARMACY
VISION
20/20**

CSHP SEMINAR 20 • OCTOBER 21-25
Disneyland
RESORT

FOLLOW YOUR HEART BUT USE YOUR BRAIN: CARDIOLOGY UPDATES 2020

HERMAN JOHANNESMEYER, PHARM.D.

AND

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MARSHALL B. KETCHUM UNIVERSITY COLLEGE OF PHARMACY

DISCLOSURE

- Speakers have no potential conflict of interest.

LEARNING OBJECTIVES

At the end of this session, the attendees will be able to:

- Summarize the pivotal recently published cardiology articles.
- Explain the relevance of findings of these articles.
- Apply the findings of these studies to clinical practice.

ABBREVIATIONS USED

- ACC: American College of Cardiology
- AF: Atrial fibrillation
- AHA: American Heart Association
- CAD: Coronary artery disease
- cGMP: Cycling guanosine monophosphate
- CV: Cardiovascular
- CVD: Cardiovascular disease
- DAPT: Dual antiplatelet therapy
- DOAC: Direct oral anticoagulant
- DM: Diabetes mellitus
- ESRD: End-stage renal disease
- FDA: Food and Drug Administration
- HCTZ: Hydrochlorothiazide
- HF: Heart failure
- HFrEF: Heart failure with reduced ejection fraction

ABBREVIATIONS USED

- HTN: Hypertension
- MI: Myocardial infarction
- NO: Nitric oxide
- NYHA: New York Heart Association
- OAC: oral anticoagulant
- PCI: Percutaneous coronary intervention
- PE: Pulmonary embolism
- sGC: Soluble guanylate cyclase
- SGLT2: Sodium-glucose cotransporter 2
- TAVI: Transcatheter aortic valve implantation
- VTE: Venous thromboembolism
- WHO: World Health Organization
- WIIFM: What's in it for me?

TEST QUESTIONS

Q1: In patients with stable CAD, initial invasive strategy is superior to initial conservative strategy.

- A. True
- B. False

Q2: Riociguat is FDA approved for the treatment of HF.

- A. True
- B. False

TEST QUESTIONS

Q3: Which DOAC was not studied in the PAUSE Trial?

- A. Apixaban
- B. Dabigatran
- C. Edoxaban
- D. Rivaroxaban

TEST QUESTIONS

Q4: Which of the following statements most accurately reflects the findings from the DAPA-HF Trial?

- A. SGLT2 inhibitors increase the risk of volume depletion in HF patients
- B. SGLT2 inhibitors increase the risk of hypoglycemia in HF patients.
- C. Dapagliflozin has improved survival only in patients with combined DM2 + HF
- D. Dapagliflozin has improved survival in patients with HF regardless of diabetes status

STUDIES TO BE ADDRESSED

- ISCHEMIA
- TWILIGHT
- Anticoagulation in ESRD
- PAUSE
- Statins and VTE
- Caravaggio
- VICTORIA
- DAPA-HF
- HCTZ for HTN
- POPULAR TAVI

ISCHEMIA TRIAL

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

APRIL 9, 2020

VOL. 382 NO. 15

Initial Invasive or Conservative Strategy for Stable Coronary Disease

D.J. Maron, J.S. Hochman, H.R. Reynolds, S. Bangalore, S.M. O'Brien, W.E. Boden, B.R. Chaitman, R. Senior, J. López-Sendón, K.P. Alexander, R.D. Lopes, L.J. Shaw, J.S. Berger, J.D. Newman, M.S. Sidhu, S.G. Goodman, W. Ruzyllo, G. Gosselin, A.P. Maggioni, H.D. White, B. Bhargava, J.K. Min, G.B.J. Mancini, D.S. Berman, M.H. Picard, R.Y. Kwong, Z.A. Ali, D.B. Mark, J.A. Spertus, M.N. Krishnan, A. Elghamaz, N. Moorthy, W.A. Hueb, M. Demkow, K. Mavromatis, O. Bockeria, J. Peteiro, T.D. Miller, H. Szwed, R. Doerr, M. Keltai, J.B. Selvanayagam, P.G. Steg, C. Held, S. Kohsaka, S. Mavromichalis, R. Kirby, N.O. Jeffries, F.E. Harrell, Jr., F.W. Rockhold, S. Broderick, T.B. Ferguson, Jr., D.O. Williams, R.A. Harrington, G.W. Stone, and Y. Rosenberg, for the ISCHEMIA Research Group*

RELEVANT PREVIOUS TRIALS



The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

APRIL 12, 2007

VOL. 356 NO. 15

Optimal Medical Therapy with or without PCI for Stable Coronary Disease

William E. Boden, M.D., Robert A. O'Rourke, M.D., Koon K. Teo, M.B., B.Ch., Ph.D., Pamela M. Hartigan, Ph.D., David J. Maron, M.D., William J. Kostuk, M.D., Merrill Knudtson, M.D., Marcin Dada, M.D., Paul Casperson, Ph.D., Crystal L. Harris, Pharm.D., Bernard R. Chaitman, M.D., Leslee Shaw, Ph.D., Gilbert Gosselin, M.D., Shah Nawaz, M.D., Lawrence M. Title, M.D., Gerald Gau, M.D., Alvin S. Blaustein, M.D., David C. Booth, M.D., Eric R. Bates, M.D., John A. Spertus, M.D., M.P.H., Daniel S. Berman, M.D., G.B. John Mancini, M.D., and William S. Weintraub, M.D., for the COURAGE Trial Research Group*

2. *N Engl J Med* 2007;356:1503-16

ISCHEMIA

- 5179 patients with moderate or severe ischemia were randomized to
 - An initial invasive strategy and medical therapy
 - or
 - An initial medical therapy alone and angiography if medical therapy failed.

ISCHEMIA

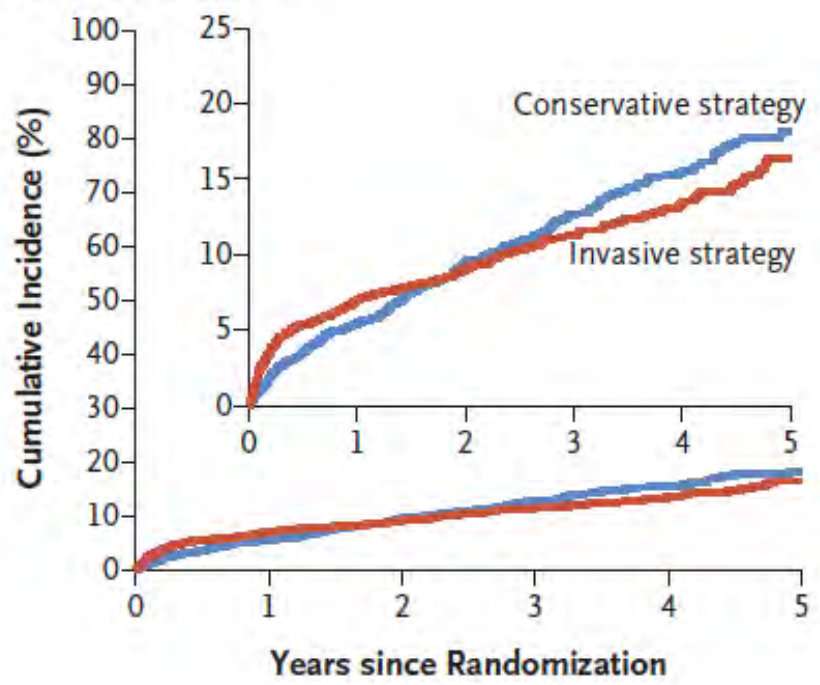
- Medical therapy consisted of intensive secondary prevention with lifestyle and pharmacologic interventions applied equally in both groups.
- Patients were followed at 1.5, 3, 6, and 12 months after randomization and every 6 months thereafter.

ISCHEMIA

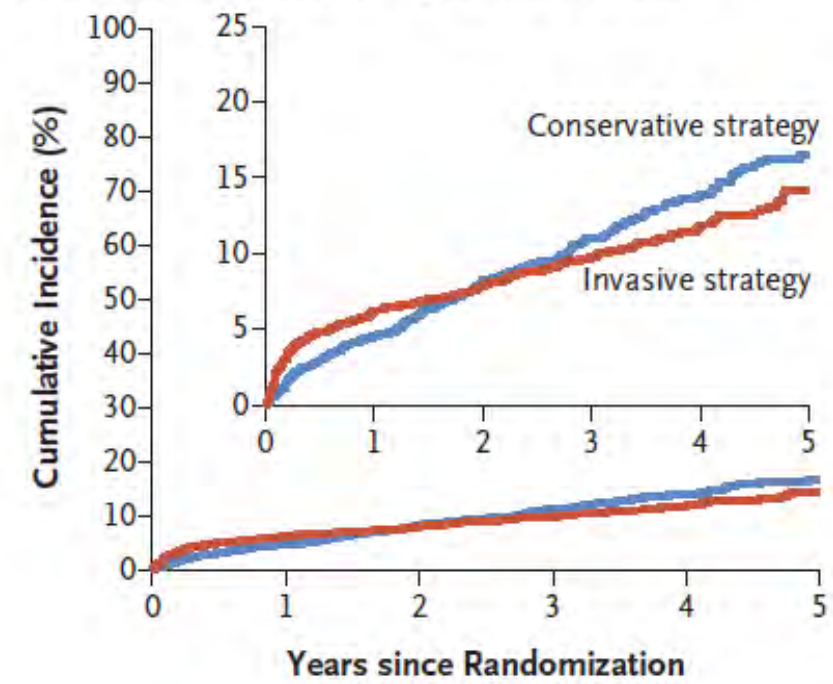
- The primary outcome was a composite of death from cardiovascular causes, myocardial infarction, or hospitalization for unstable angina, heart failure, or resuscitated cardiac arrest.
- A key secondary outcome was death from cardiovascular causes or myocardial infarction.

ISCHEMIA

Primary Composite Outcome



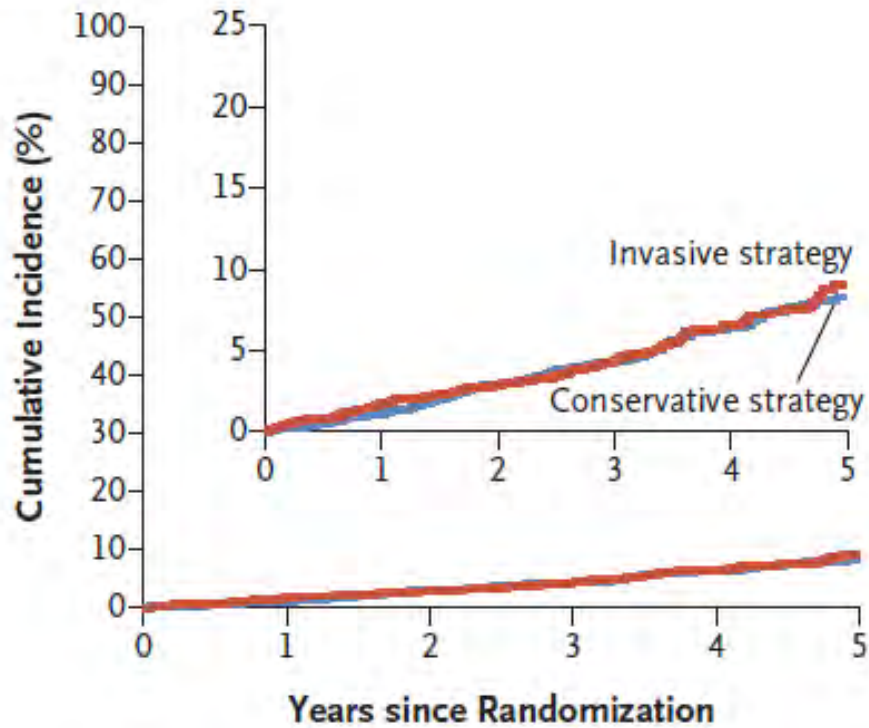
Death from Cardiovascular Causes or Myocardial Infarction



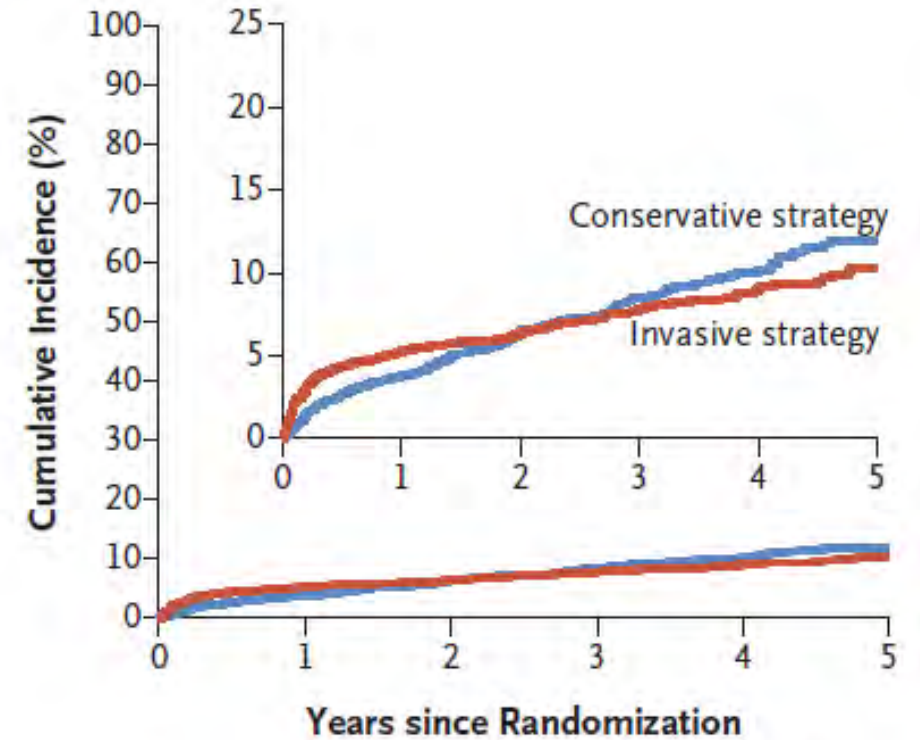
1. *N Engl J Med* 2020;382:1395-407

ISCHEMIA

Death from Any Cause



Myocardial Infarction



1. *N Engl J Med* 2020;382:1395-407

ISCHEMIA

- “Among patients with stable coronary disease and moderate or severe ischemia, we did not find evidence that an initial invasive strategy, as compared with an initial conservative strategy, reduced the risk of ischemic cardiovascular events or death from any cause over a median of 3.2 years.”

ISCHEMIA WIIFM

- Invasive strategy \approx conservative strategy
- **Stable** coronary artery disease
- Role of healthcare providers

TWILIGHT TRIAL

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

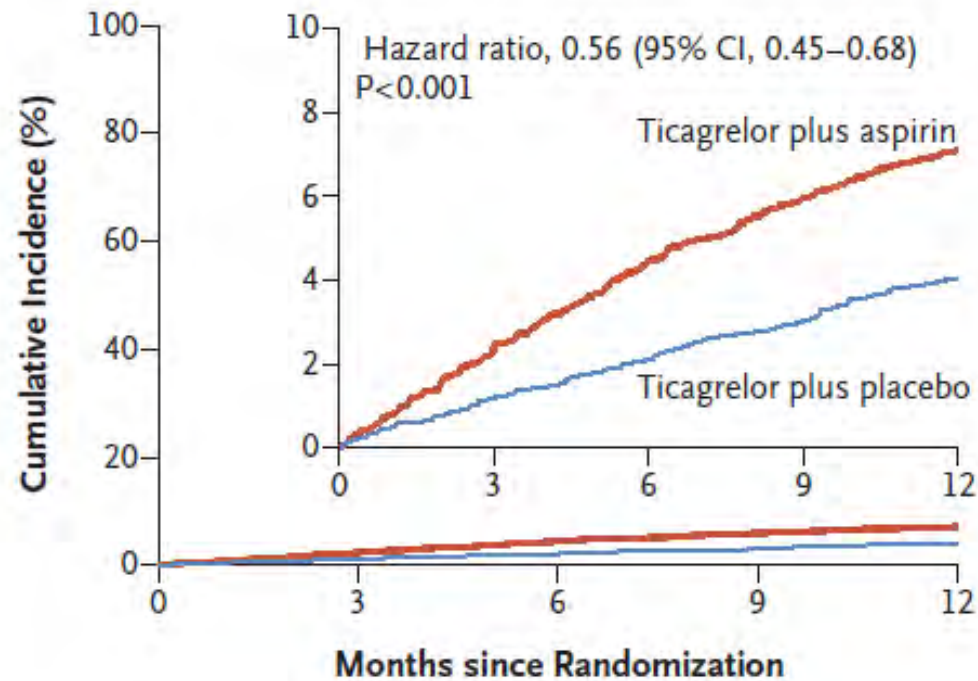
TWILIGHT

- In a double-blind trial, the effect of ticagrelor alone as compared with ticagrelor plus aspirin was examined with regard to clinically relevant bleeding among patients who were at high risk for bleeding or an ischemic event and had undergone PCI.
- After 3 months of treatment with ticagrelor plus aspirin, patients who had not had a major bleeding event or ischemic event continued to take ticagrelor and were randomly assigned to receive aspirin or placebo for 1 year.

TWILIGHT

- The primary end point was bleeding.
- The composite end point of death from any cause, nonfatal myocardial infarction, or nonfatal stroke was also evaluated.

TWILIGHT

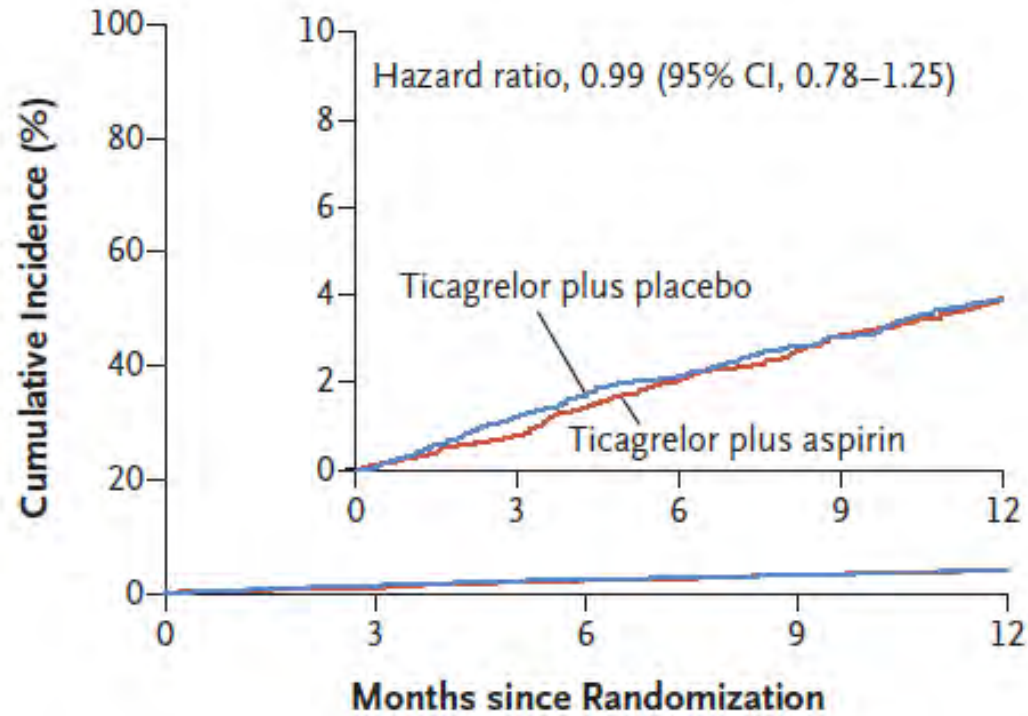


No. at Risk

Ticagrelor plus aspirin	3564	3454	3357	3277	3213
Ticagrelor plus placebo	3555	3474	3424	3366	3321

Figure 2. Kaplan–Meier Estimates of the Incidence of BARC Type 2, 3, or 5 Bleeding 1 Year after Randomization (Intention-to-Treat Population).

TWILIGHT



No. at Risk

Ticagrelor plus aspirin	3515	3466	3415	3361	3320
Ticagrelor plus placebo	3524	3457	3412	3365	3330

Figure 3. Kaplan–Meier Estimates of the Incidence of Death from Any Cause, Nonfatal Myocardial Infarction, or Nonfatal Stroke 1 Year after Randomization (Per-Protocol Population).

TWILIGHT

- “Among high-risk patients who underwent PCI and completed 3 months of dual antiplatelet therapy, ticagrelor monotherapy was associated with a lower incidence of clinically relevant bleeding than ticagrelor plus aspirin, with no higher risk of death, myocardial infarction, or stroke.”

TWILIGHT WIIFM

- Future of long-term DAPT post PCI

ANTICOAGULATION IN ESRD

Oral Anticoagulation and Cardiovascular Outcomes in Patients With Atrial Fibrillation and End-Stage Renal Disease



Sean D. Pokorney, MD, MHS,^{a,b} Eric Black-Maier, MD,^a Anne S. Hellkamp, MS,^b Daniel J. Friedman, MD,^c Sreekanth Vemulapalli, MD,^b Christopher B. Granger, MD,^b Laine Thomas, PhD,^b Eric D. Peterson, MD, MPH,^b Jonathan P. Piccini, SR, MD, MHS^{a,b}

JAMA
Network | **Open**[™]

Original Investigation | Cardiology

Association Between Use of Warfarin for Atrial Fibrillation
and Outcomes Among Patients With End-Stage Renal Disease
A Systematic Review and Meta-analysis

Mandeep S. Randhawa, MD; Rohanlal Vishwanath, BSc; Manoj P. Rai, MD; Ling Wang, PhD; Amritpal K. Randhawa, MD; George Abela, MD; Gaurav Dhar, MD

4. *J Am Coll Cardiol* 2020;75:1299-308

5. *JAMA Netw Open* 2020;3:e202175

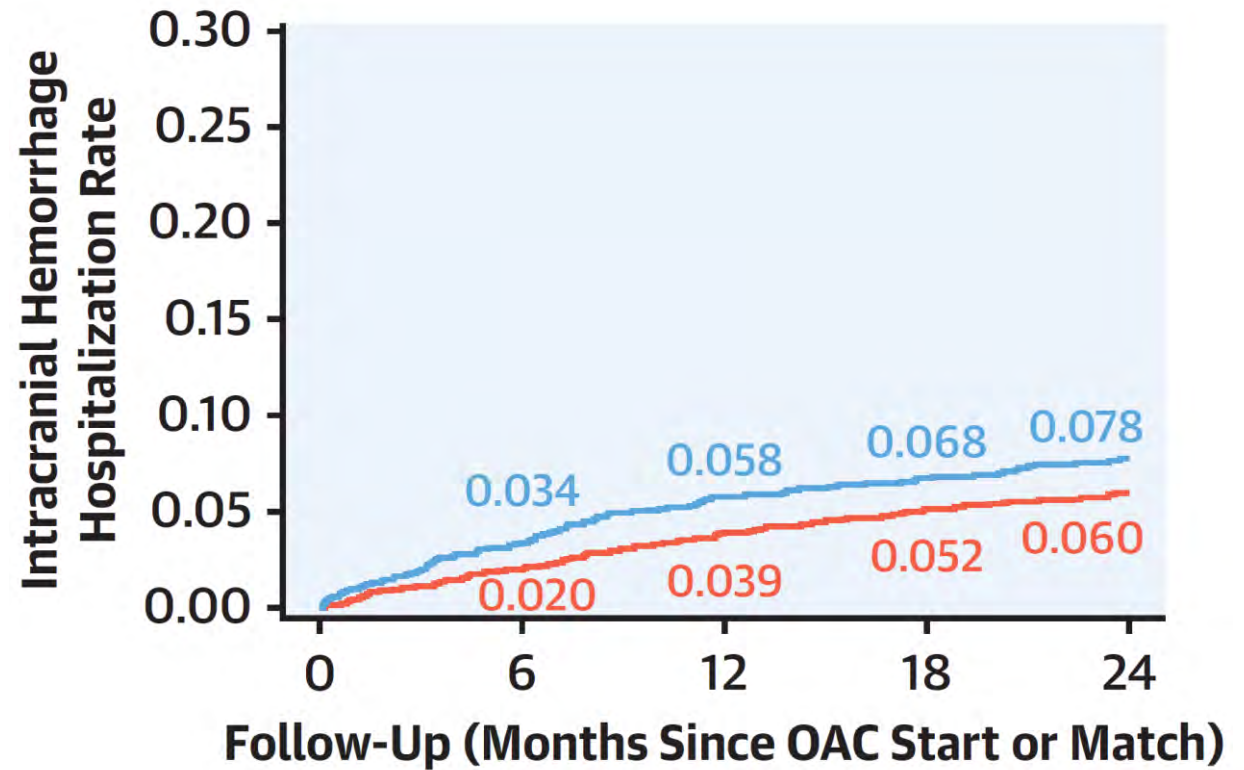
CSHP SEMINAR 2020

ANTICOAGULATION IN ESRD

- Trial 1: Medicare claims data review of 1,519 patients with AF + ESRD on anticoagulation matched to 3,018 patients AF + ESRD not on anticoagulation.
- Outcomes: Ischemic stroke, hemorrhagic stroke, hospitalization for bleeding, death.

ANTICOAGULATION IN ESRD

- Trial 1:
 - Blue = oral anticoagulant use
 - Red = no anticoagulant use

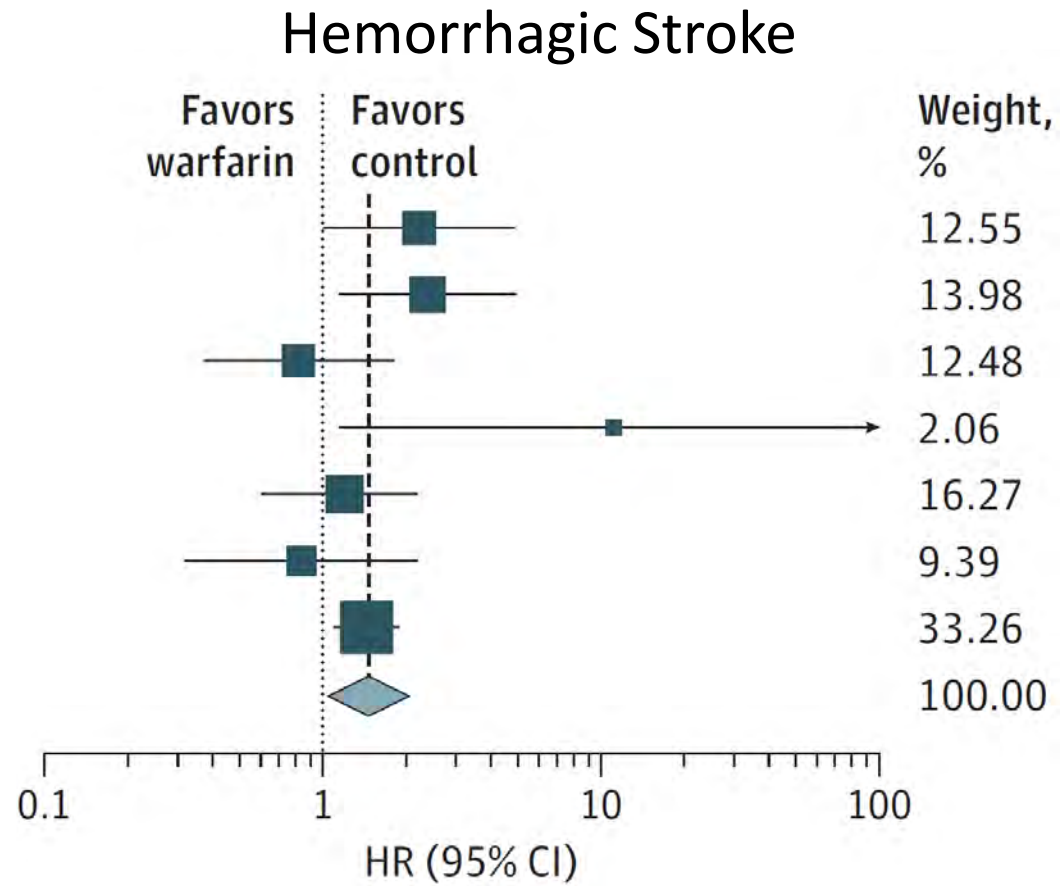


ANTICOAGULATION IN ESRD

- Trial 2: Systematic review and meta-analysis of combined ESRD + AF patients compared based on use of warfarin.
- Outcomes: Ischemic stroke, hemorrhagic stroke, major bleeding, mortality.

ANTICOAGULATION IN ESRD

- Trial 2:



ANTICOAGULATION IN ESRD

- Trial 1: “We found no association between OAC use and reduced risk of stroke or death. OAC use was associated with increased risks of hospitalization for bleeding or intracranial hemorrhage.”
- Trial 2: “...warfarin use appears to have been associated with no change in the incidence of ischemic stroke...it does appear to be associated with a significantly higher risk of hemorrhagic stroke...”

ANTICOAGULATION IN ESRD WIIFM

- Anticoagulation for patients with combined AF and ESRD appears to confer negligible therapeutic benefit and significant risk.

PAUSE TRIAL

JAMA Internal Medicine | [Original Investigation](#)

Perioperative Management of Patients With Atrial Fibrillation Receiving a Direct Oral Anticoagulant

James D. Douketis, MD; Alex C. Spyropoulos, MD; Joanne Duncan, BSc; Marc Carrier, MD, MSc; Gregoire Le Gal, MD; Alfonso J. Tafur, MD; Thomas Vanassche, MD; Peter Verhamme, MD; Sudeep Shivakumar, MD; Peter L. Gross, MD, MSc; Agnes Y. Y. Lee, MD, MSc; Erik Yeo, MD; Susan Solymoss, MD; Jeannine Kassis, MD; Geneviève Le Templier, MD; Stephen Kowalski, MD; Mark Blostein, MD; Vinay Shah, MD; Elizabeth MacKay, MD; Cynthia Wu, MD; Nathan P. Clark, PharmD; Shannon M. Bates, MDCM, MSc; Frederick A. Spencer, MD; Eleni Arnaoutoglou, MD, PhD; Michiel Coppens, MD, PhD; Donald M. Arnold, MD, MSc; Joseph A. Caprini, MD; Na Li, PhD; Karen A. Moffat, MLT; Summer Syed, MD, MSc; Sam Schulman, MD, PhD

PAUSE

- Patients with atrial fibrillation maintained on DOACs require surgical interventions with relative frequency.
- Evidence based guidance of perioperative DOAC therapy in AF has been an unmet need in the medical literature.

PAUSE

- 3007 adult patients with AF maintained on anticoagulation with either apixaban, rivaroxaban, or dabigatran who were undergoing elective surgical procedures were enrolled.
- Assigned to an open label perioperative DOAC management protocol based on specific medication used.

PAUSE

DOAC	Surgical Procedure-Associated Bleeding Risk	Preoperative DOAC Interruption Schedule					Day of Surgical Procedure (No DOAC)	Postoperative DOAC Resumption Schedule					
		Day -5	Day -4	Day -3	Day -2	Day -1		Day +1	Day +2	Day +3	Day +4		
Apixaban	High	→							→				
	Low	→											
Dabigatran etexilate (CrCl ≥50 mL/min)	High	→								→			
	Low	→											
Dabigatran etexilate (CrCl <50 mL/min) ^a	High	→								→			
	Low	→											
Rivaroxaban	High	→								→			
	Low	→											

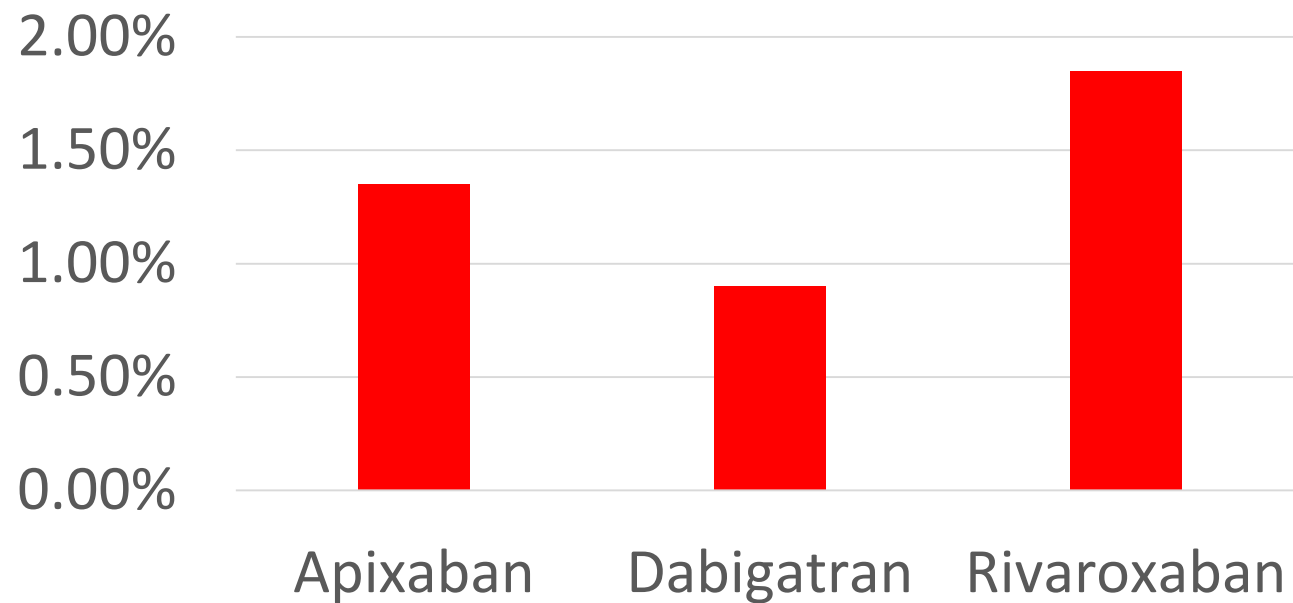
6. *JAMA Intern Med.* 2019;179:1469-78
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PAUSE

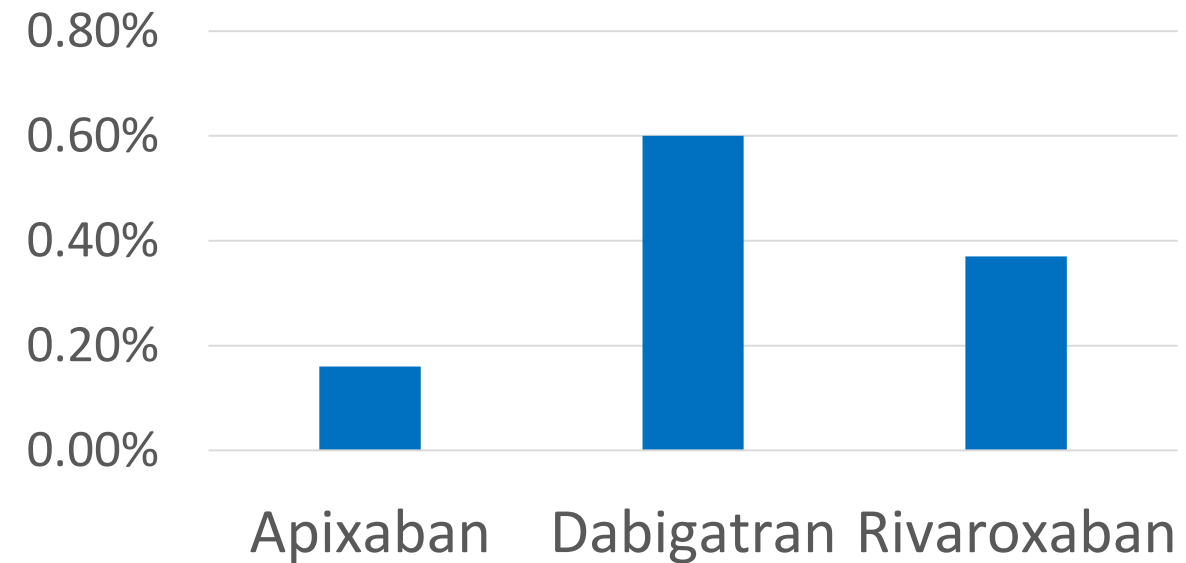
- Primary outcomes:
 - Major bleeding within 30 days.
 - Thromboembolism within 30 days.
- Multiple secondary outcomes including various clinical outcomes and residual anticoagulant level.

PAUSE

Rates of Major Bleeding- All Subjects



Rates of Arterial Thromboembolism – All Subjects



PAUSE

- “In this study, patients with AF who had DOAC therapy interruption for elective surgery or procedure, a simple standardized perioperative management strategy without heparin bridging or measurement of coagulation function was associated with low rates of major bleeding and arterial thromboembolism.”

PAUSE WIIFM

- Holding DOACs from operative -2 to +2 or +3 for high risk procedures or operative day -1 to +1 in low risk procedures is a reasonable strategy.
- Protocol must be strictly followed to ensure safety/efficacy.
- Not generalizable to edoxaban.

STATINS AND VTE

CLINICAL RESEARCH STUDY

THE AMERICAN
JOURNAL *of*
MEDICINE®

Statin Use is Associated with Reduced Risk of Recurrence in Patients with Venous Thromboembolism

Lauren K. Stewart, MD,^a Elisa J. Sarmiento, MSPH-EPAP,^b Jeffrey A. Kline, MD^{a,c}

^aDepartment of Emergency Medicine; ^bBiostatistics, Department of Emergency Medicine; ^cDepartment of Cellular and Integrative Physiology, Indiana University School of Medicine, Indianapolis.

STATINS AND VTE PREVIOUS STUDIES

Usefulness of Statins for Prevention of Venous Thromboembolism

Patricia Chaffey, PharmD^a, Mary Thompson, PharmD^a, Ajit D. Pai, BA^a, Ali R. Tafreshi, BS^b, Javad Tafreshi, PharmD^{c,*}, and Ramdas G. Pai, MD^d

Venous thromboembolism (VTE), including deep venous thrombosis and pulmonary embolism, is common with an annual incidence of 1 to 5 per 1,000, resulting in major morbidity, mortality, and increased health care costs. It is more common in the elderly, obese, those with cancer, those undergoing surgery, and those with previous VTE. Strategy to reduce its occurrence has important public health implications. Pleotropic effects of statins may have beneficial effects on a number of potential targets associated with VTE. Statins have excellent safety profile and seem to be associated with beneficial effects in VTE in case-control studies, large observational studies, meta-analyses, and a randomized trial. In conclusion, after critically reviewing the clinical data supporting statin use in the prevention of VTE, we presented clinical recommendations for the use of statins in reducing VTE occurrence, especially in high-risk situations. © 2018 Elsevier Inc. All rights reserved. (Am J Cardiol 2018;121:1436–1440)

STATINS AND VTE PREVIOUS STUDIES

Journal of Thrombosis and Haemostasis, 17: 319–328

DOI: 10.1111/jth.1430

ORIGINAL ARTICLE

Rosuvastatin use reduces thrombin generation potential in patients with venous thromboembolism: a randomized controlled trial

FERNANDA A. ORSI,^{*†} JOSEPH S. BIEDERMANN,^{‡§} MARIEKE J.H.A. KRUIP,^{‡§}
FELIX J. VAN DER MEER,[¶] FRITS R. ROSENDAAL,[†] ASTRID VAN HYLCKAMA VLIET,[†]
METTINE H. A. BOS,^{**} FRANK W. G. LEEBEEK,[§] SUZANNE C. CANNEGIETER^{†¶} and
WILLEM M. LIJFERING[†]

**Department of Clinical Pathology, School of Medical Sciences, University of Campinas (UNICAMP), Campinas, Brazil; †Department of Clinical Epidemiology, Leiden University Medical Center, Leiden; ‡Star-Medical Anticoagulation Clinic; §Department of Hematology, Erasmus University Medical Center, Rotterdam; ¶Department of Internal Medicine, Section of Thrombosis and Hemostasis, Leiden University Medical Center; and **Eindhoven Laboratory for Vascular and Regenerative Medicine, Leiden University Medical Center, Leiden, the Netherlands*

The STATins Reduce Thrombophilia (START) trial 2018

STATINS AND VTE PREVIOUS STUDIES



The NEW ENGLAND
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

NOVEMBER 20, 2008

VOL. 359 NO. 21

Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein

Paul M. Ridker, M.D., Eleanor Danielson, M.I.A., Francisco A.H. Fonseca, M.D., Jacques Genest, M.D., Antonio M. Gotto, Jr., M.D., John J.P. Kastelein, M.D., Wolfgang Koenig, M.D., Peter Libby, M.D., Alberto J. Lorenzatti, M.D., Jean G. MacFadyen, B.A., Børge G. Nordestgaard, M.D., James Shepherd, M.D., James T. Willerson, M.D., and Robert J. Glynn, Sc.D., for the JUPITER Study Group*

STATINS AND VTE

- A retrospective analysis of the Indiana Network for Patient Care database from 2004 to 2017.
- It included a total of 192,908 patients.
- Created regression model with statin use as the predictor variable and VTE recurrence as the dependent variable.
- The objective of this study was to examine the magnitude of the effect of statin therapy on VTE recurrence.

STATINS AND VTE

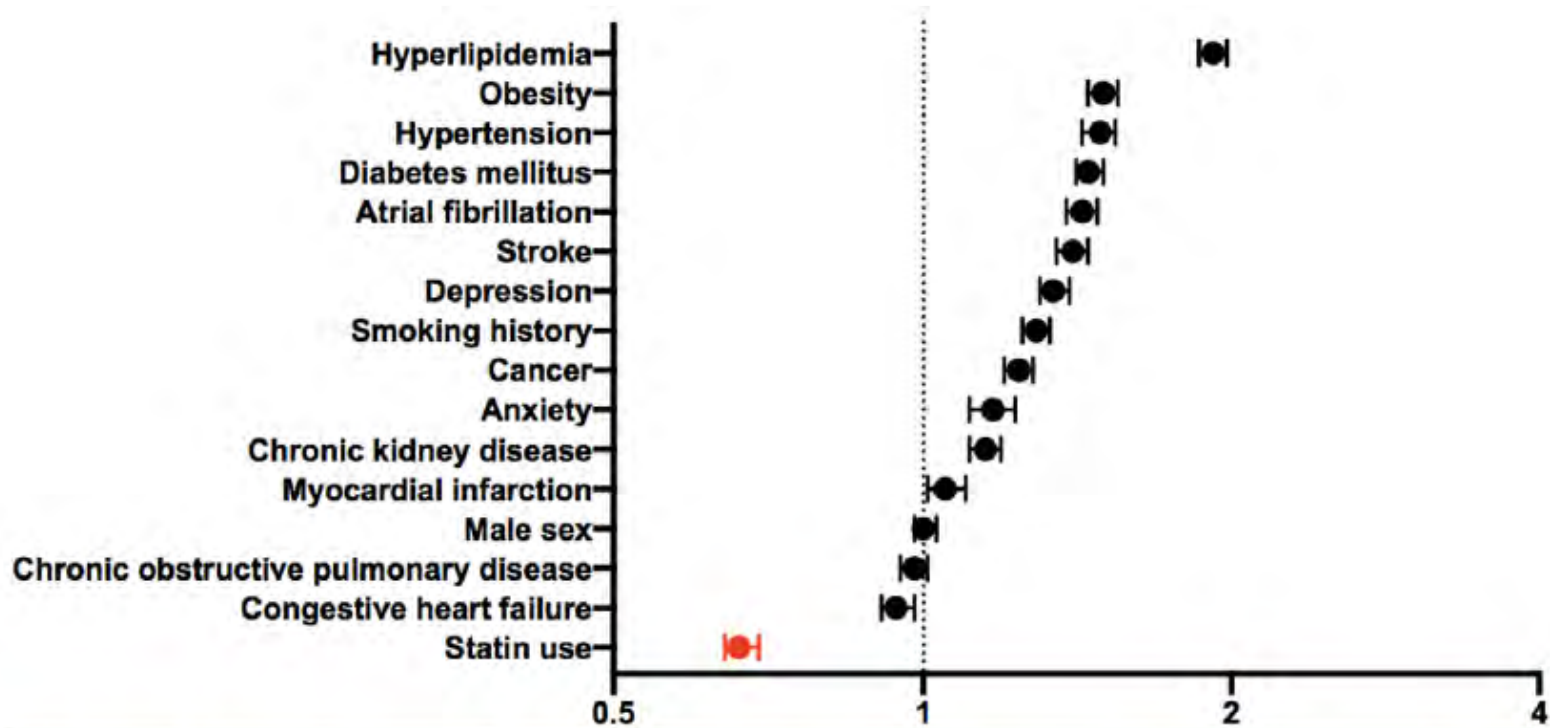


Figure Adjusted odds ratios for venous thromboembolism recurrence from multivariate logistic regression analysis.

STATINS AND VTE

- “We found that a statin prescription reduced risk of venous thromboembolism recurrence by approximately 25% after adjusting for risk factors, supporting the adjunctive role of statins in the prevention of venous thromboembolism recurrence.”

STATINS AND VTE WIIFM

- Another use for an existing medication
- Statins for non-lipid indication
- Considering to add statins for patients with VTE
- What agent and at what dose?

CARAVAGGIO TRIAL

ORIGINAL ARTICLE

Apixaban for the Treatment of Venous Thromboembolism Associated with Cancer

Giancarlo Agnelli, M.D., Cecilia Becattini, M.D., Guy Meyer, M.D.,
Andres Muñoz, M.D., Menno V. Huisman, M.D., Jean M. Connors, M.D.,
Alexander Cohen, M.D., Rupert Bauersachs, M.D., Benjamin Brenner, M.D.,
Adam Torbicki, M.D., Maria R. Sueiro, M.D., Catherine Lambert, M.D.,
Gualberto Gussoni, M.D., Mauro Campanini, M.D., Andrea Fontanella, M.D.,
Giorgio Vescovo, M.D., and Melina Verso, M.D.,
for the Caravaggio Investigators*

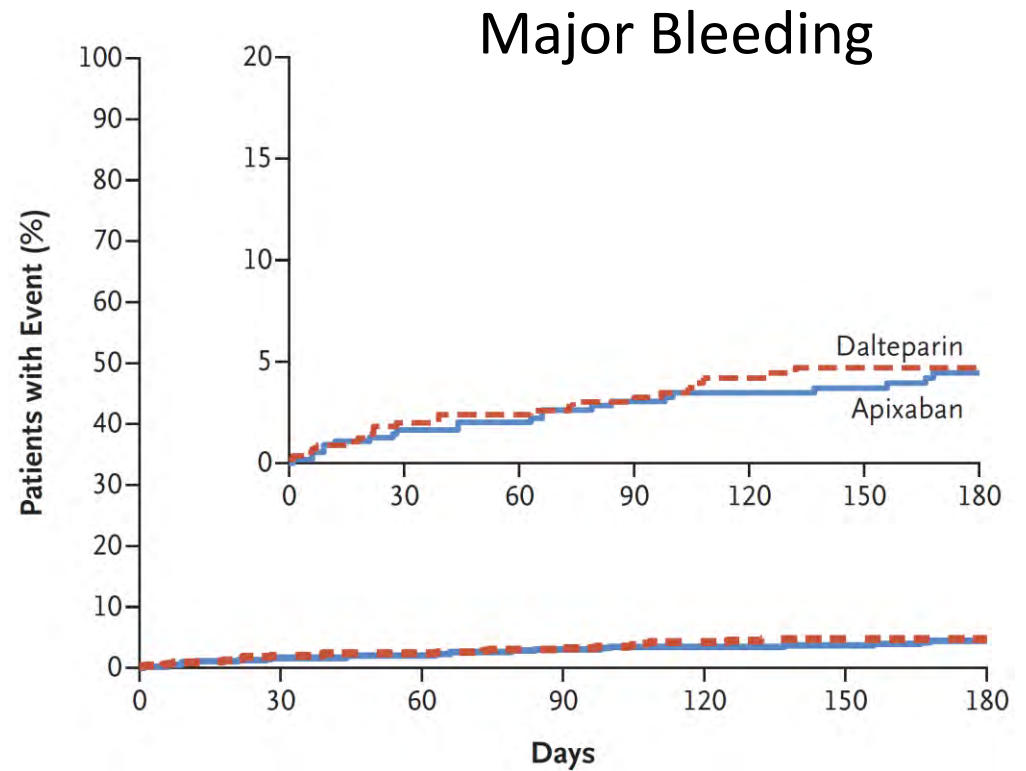
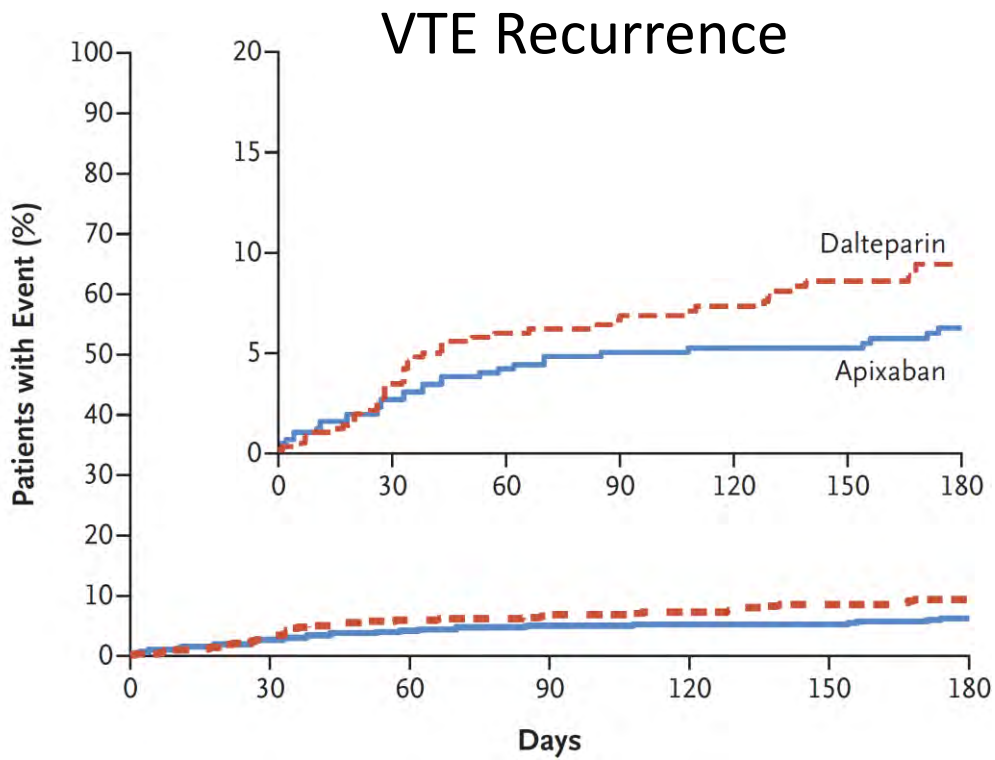
CARAVAGGIO

- Enrolled 1155 patients with cancer and newly diagnosed proximal DVT or PE.
- Patients randomized to receive DVT/PE dose apixaban or daily dalteparin x 6 months.

CARAVAGGIO

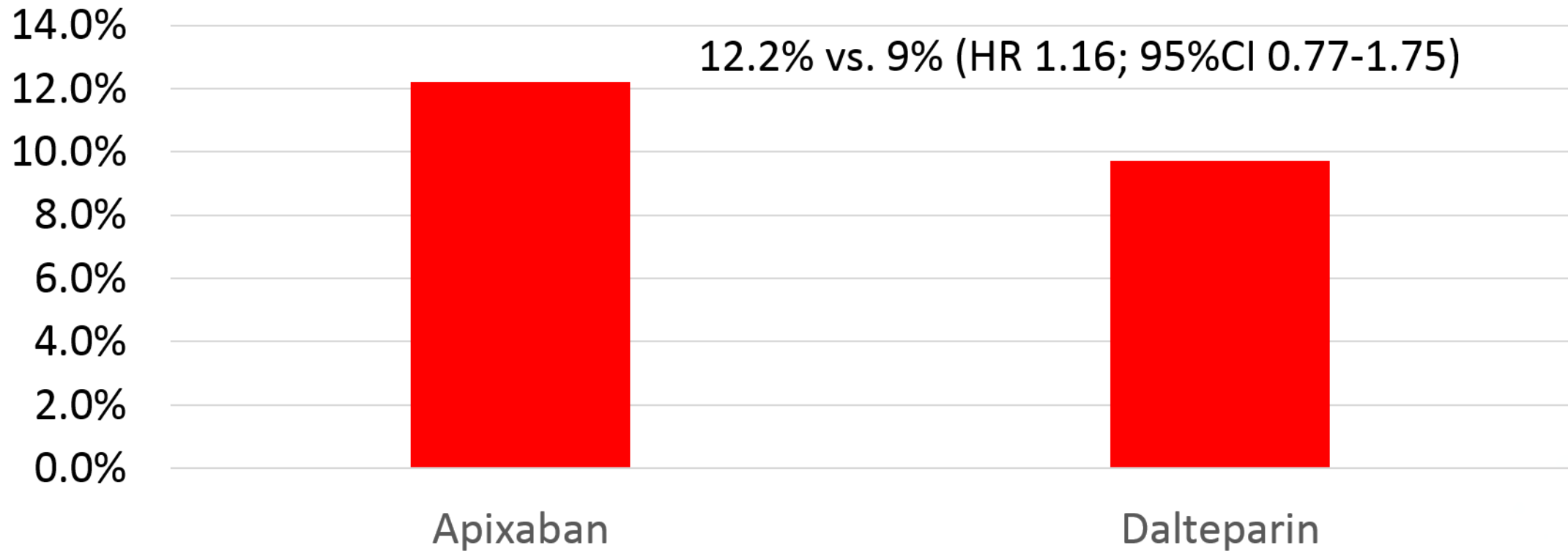
- Primary outcome was recurrence of VTE during the treatment period.
- Various secondary outcomes including:
 - Clinically overt bleeding.
 - Clinically relevant non-major bleeding.
 - All-cause mortality.

CARAVAGGIO



CARAVAGGIO

Major and Clinically Relevant Non-Major Bleeding Rates



CARAVAGGIO

- “We concluded that oral apixaban was noninferior to subcutaneous dalteparin for the treatment of cancer-associated venous thromboembolism without an increased risk of major bleeding.”

CARAVAGGIO WIIFM

- Old drug studied in new context – apixaban is an attractive option of cancer-related VTE.
- Cannot definitively exclude increased risk for bleeding with apixaban based on this study.

VICTORIA STUDY

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Vericiguat in Patients with Heart Failure and Reduced Ejection Fraction

Paul W. Armstrong, M.D., Burkert Pieske, M.D., Kevin J. Anstrom, Ph.D.,
Justin Ezekowitz, M.B., B.Ch., Adrian F. Hernandez, M.D., M.H.S.,
Javed Butler, M.D., M.P.H., M.B.A., Carolyn S.P. Lam, M.B., B.S., Ph.D.,
Piotr Ponikowski, M.D., Adriaan A. Voors, M.D., Ph.D., Gang Jia, Ph.D.,
Steven E. McNulty, M.S., Mahesh J. Patel, M.D., Lothar Roessig, M.D.,
Joerg Koglin, M.D., Ph.D., and Christopher M. O'Connor, M.D.,
for the VICTORIA Study Group*

RIOCIGUAT (ADEMPAS®)

- Riociguat was initially approved in the U.S. in 2013
- It is FDA approved for the treatment of:
 - Persistent/recurrent chronic thromboembolic pulmonary hypertension.
 - Pulmonary arterial hypertension to improve exercise capacity, improve WHO functional class, and to delay clinical worsening.

RIOCIGUAT MOA

- Riociguat is a stimulator of sGC, an enzyme in the cardiopulmonary system and the receptor for nitric oxide NO. When NO binds to sGC, the enzyme catalyzes synthesis of the signaling molecule cGMP.
- Intracellular cGMP plays an important role in regulating processes that influence vascular tone, proliferation, fibrosis, and inflammation.

RIOCIGUAT MOA

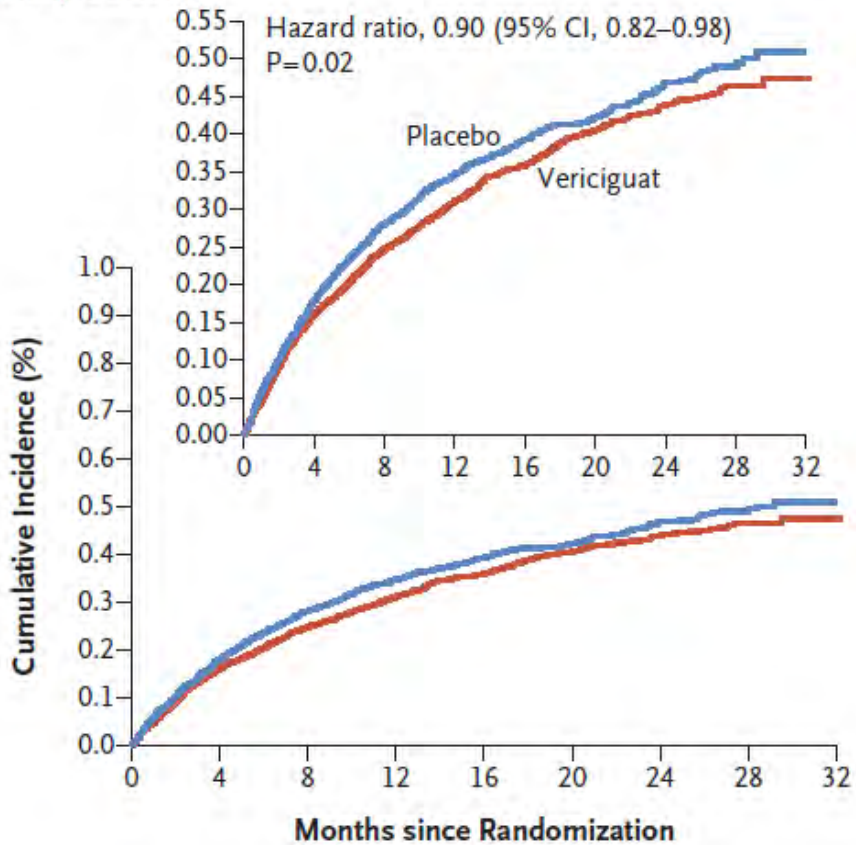
- Riociguat has a dual mode of action.
- It sensitizes sGC to endogenous NO by stabilizing the NO-sGC binding.
- It also directly stimulates sGC via a different binding site, independently of NO.
- Riociguat stimulates the NO-sGC-cGMP pathway and leads to increased generation of cGMP with subsequent vasodilation.

VICTORIA

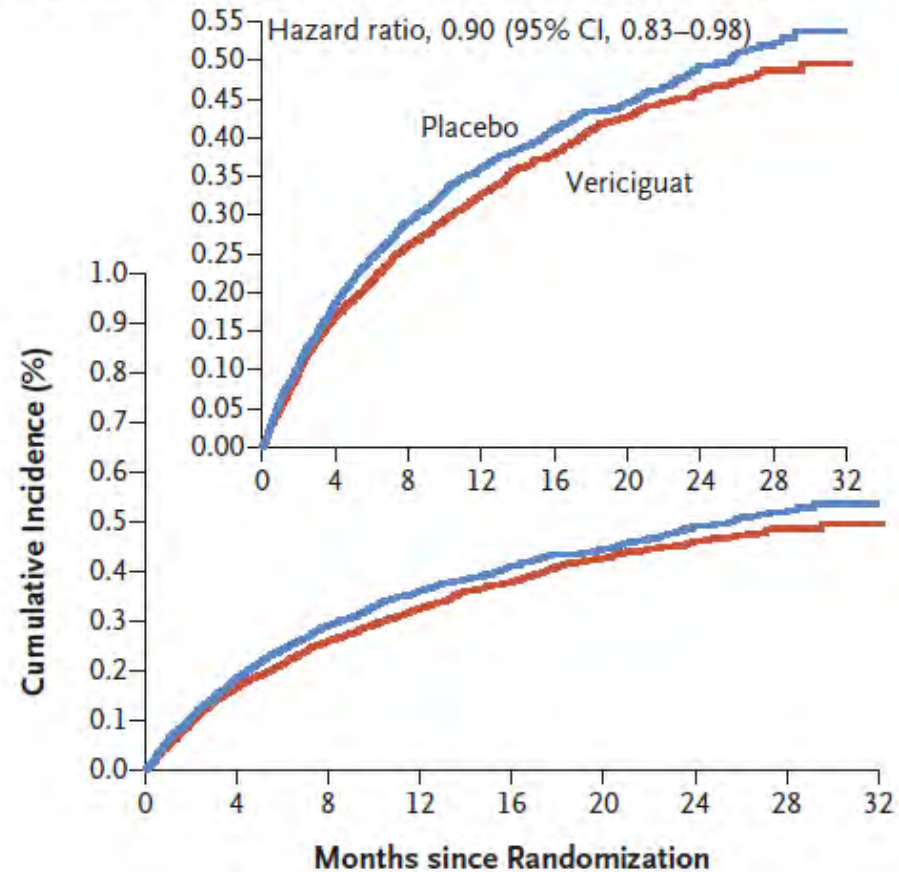
- Phase 3, randomized, double-blind, placebo-controlled
- 5050 patients with chronic HF NYHA class II, III, or IV and EF <45% to receive vericiguat or placebo
- In addition to guideline-based medical therapy.
- Primary outcome was a composite of death from CV causes or first hospitalization for HF.

VICTORIA

Primary Outcome

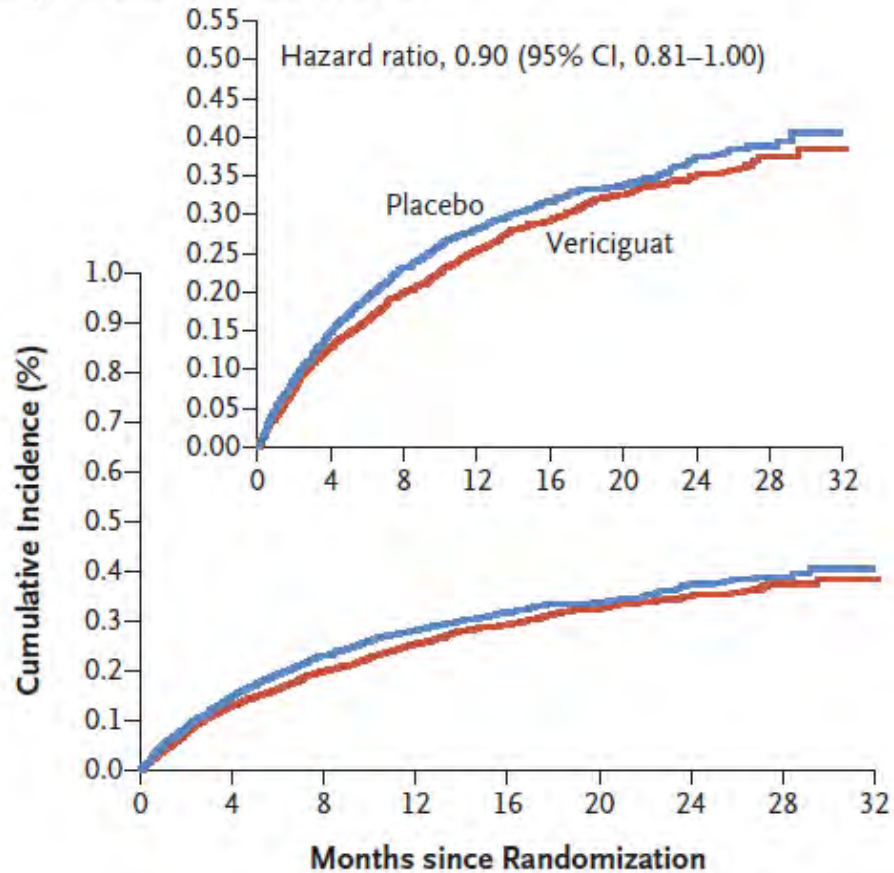


Death from Any Cause or Hospitalization for Heart Failure

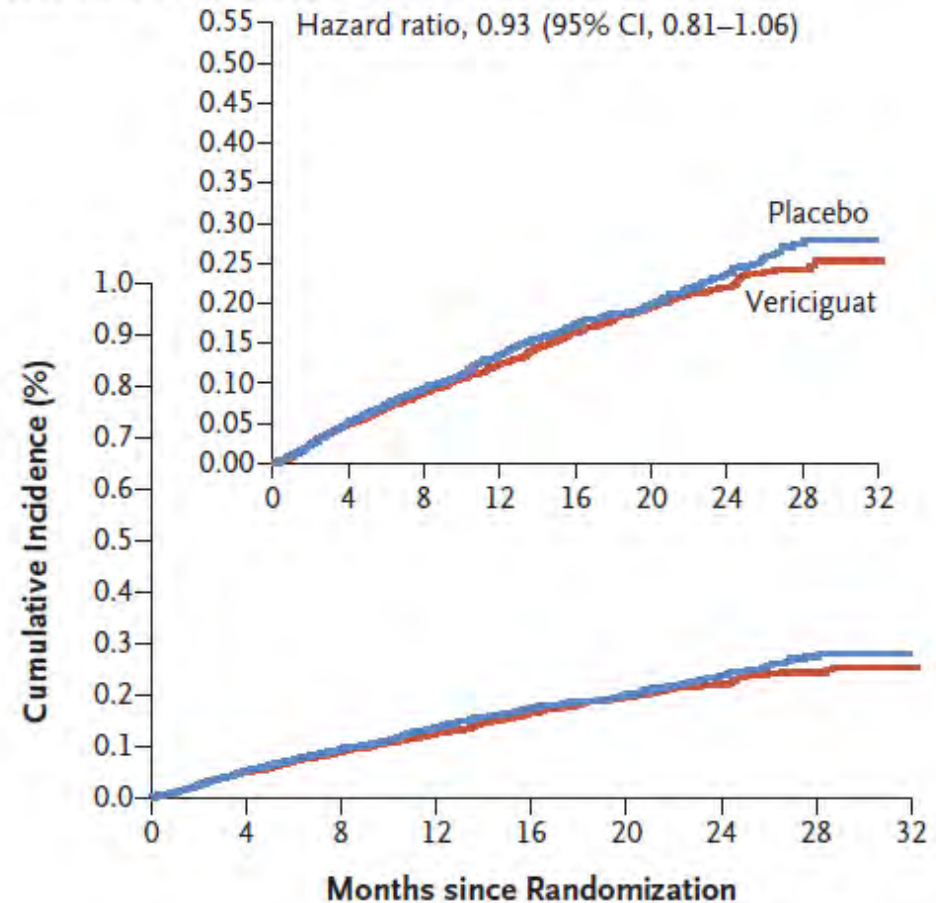


VICTORIA

Hospitalization for Heart Failure



Death from Cardiovascular Causes



VICTORIA

- Symptomatic hypotension occurred in 9.1% of the patients in the vericiguat group and in 7.9% of the patients in the placebo group (P = 0.12).
- Syncope occurred in 4.0% of the patients in the vericiguat group and in 3.5% of the patients in the placebo group (P = 0.30).

VICTORIA

- “Among patients with high-risk heart failure, the incidence of death from cardiovascular causes or hospitalization for heart failure was lower among those who received vericiguat than among those who received placebo.”

VICTORIA WIIFM

- Changing standard of care for patients with HF

DAPA-HF TRIAL

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Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

J.J.V. McMurray, S.D. Solomon, S.E. Inzucchi, L. Køber, M.N. Kosiborod, F.A. Martinez, P. Ponikowski, M.S. Sabatine, I.S. Anand, J. Böhlávek, M. Böhm, C.-E. Chiang, V.K. Chopra, R.A. de Boer, A.S. Desai, M. Diez, J. Drozd, A. Dukát, J. Ge, J.G. Howlett, T. Katova, M. Kitakaze, C.E.A. Ljungman, B. Merkely, J.C. Nicolau, E. O'Meara, M.C. Petrie, P.N. Vinh, M. Schou, S. Tereshchenko, S. Verma, C. Held, D.L. DeMets, K.F. Docherty, P.S. Jhund, O. Bengtsson, M. Sjöstrand, and A.-M. Langkilde, for the DAPA-HF Trial Committees and Investigators*

DAPA-HF

- Previous trials have shown the SGLT2 inhibitors decreased cardiovascular death and hospitalization in patients with HF.
- Effects unknown in patients without HF.

DAPA-HF

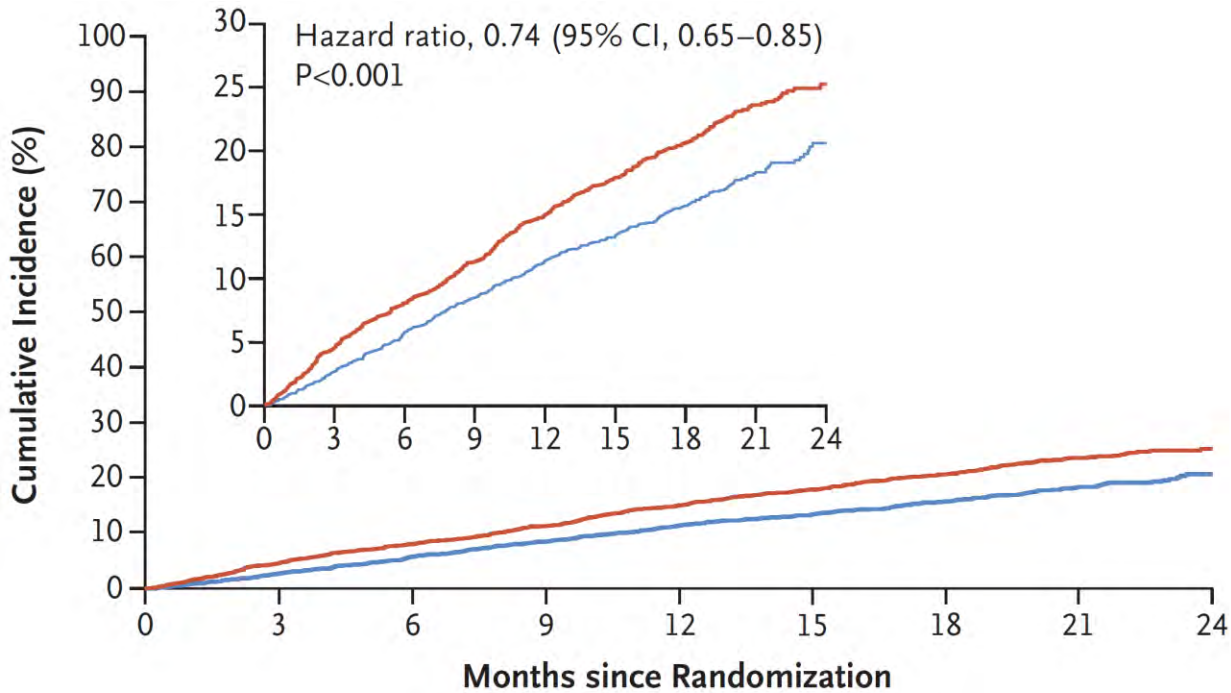
- Enrolled 4744 patients with: HFrEF + NYHA class II-IV + elevated NT-proBNP.
- Patients were randomized to receive:
 - Dapagliflozin 10 mg daily
 - or
 - Placebo daily

DAPA-HF

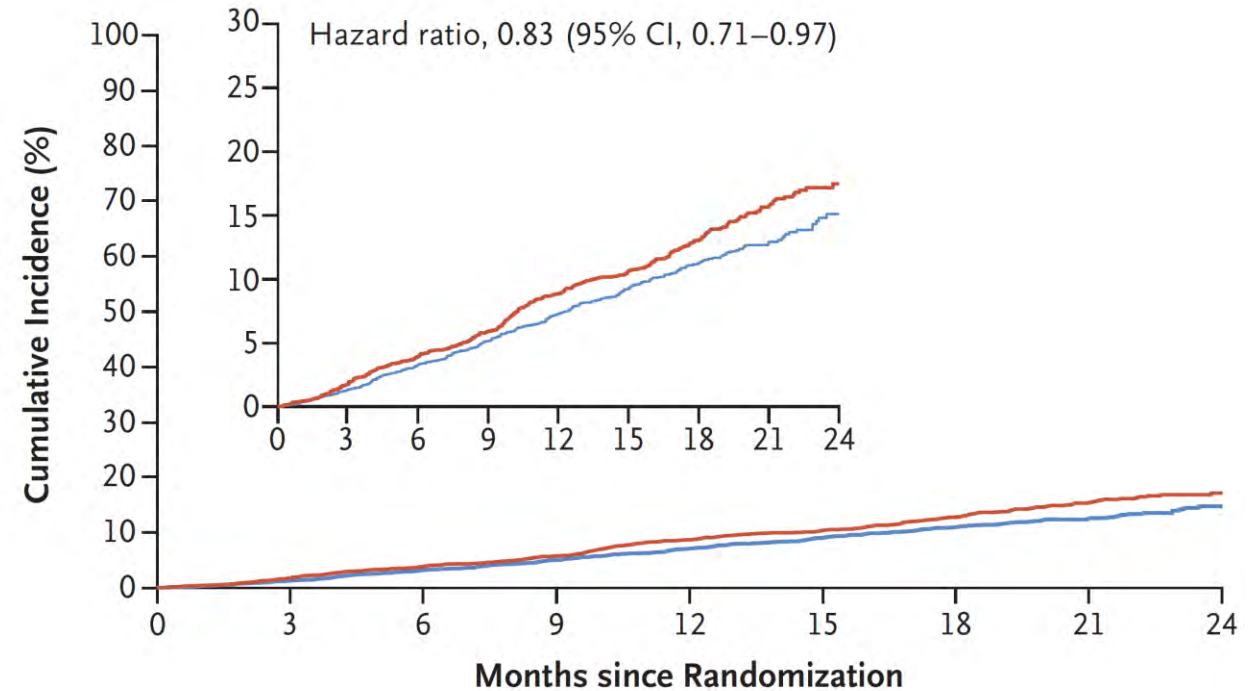
- Primary outcome was a composite of worsening HF or death from cardiovascular causes.
- Multiple secondary outcomes, including all-cause mortality.

DAPA-HF

Primary Outcome



All-Cause Mortality



DAPA-HF

- “Among patients with heart failure and a reduced ejection fraction, those who received the SGLT2 inhibitor dapagliflozin had a lower risk of worsening heart failure or death from cardiovascular causes and better symptom scores than those who received placebo, regardless of the presence or absence of diabetes.”

DAPA-HF WIIFM

- Dapagliflozin improved HF outcomes regardless of diabetes status.
- New FDA indication for the treatment of HFrEF as of May 2020.

HCTZ FOR HTN

Research

JAMA Internal Medicine | [Original Investigation](#)

Comparison of Cardiovascular and Safety Outcomes of Chlorthalidone vs Hydrochlorothiazide to Treat Hypertension

George Hripcsak, MD, MS; Marc A. Suchard, MD, PhD; Steven Shea, MD; RuiJun Chen, MD; Seng Chan You, MD; Nicole Pratt, PhD; David Madigan, PhD; Harlan M. Krumholz, MD, SM; Patrick B. Ryan, PhD; Martijn J. Schuemle, PhD

HCTZ FOR HTN PREVIOUS STUDIES

- Major Outcomes in High-Risk Hypertensive Patients Randomized to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker vs Diuretic. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA* 2002;288(23):2981-97.

HCTZ FOR HTN PREVIOUS STUDIES

- Participants were randomly assigned to receive chlorthalidone, amlodipine, or Lisinopril.
- “**Thiazide-type** diuretics are superior in preventing 1 or more major forms of CVD and are less expensive. They should be preferred for first-step antihypertensive therapy.”

HCTZ FOR HTN

- This was an observational comparative cohort study from 2001 to 2018.
- The objective was to compare the effectiveness and safety of chlorthalidone and hydrochlorothiazide as first-line therapies for hypertension in real-world practice.
- The primary outcomes were AMI, hospitalization for HF, ischemic or hemorrhagic stroke, and a composite CVD.

HCTZ FOR HTN

- “This study found that chlorthalidone use was not associated with significant cardiovascular benefits when compared with hydrochlorothiazide, while its use was associated with greater risk of renal and electrolyte abnormalities. These findings do not support current recommendations to prefer chlorthalidone vs hydrochlorothiazide for hypertension treatment in first-time users, ... further study is warranted.”

HCTZ FOR HTN WIIFM

- Continue using HCTZ for HTN

POPULAR TAVI

ORIGINAL ARTICLE

Anticoagulation with or without Clopidogrel after Transcatheter Aortic-Valve Implantation

V.J. Nijenhuis, J. Brouwer, R. Delewi, R.S. Hermanides, W. Holvoet, C.L.F. Dubois,
P. Frambach, B. De Bruyne, G.K. van Houwelingen, J.A.S. Van Der Heyden,
P. Toušek, F. van der Kley, I. Buyschaert, C.E. Schotborgh, B. Ferdinande,
P. van der Harst, J. Roosen, J. Peper, F.W.F. Thielen, L. Veenstra,
D.R.P.P. Chan Pin Yin, M.J. Swaans, B.J.W.M. Rensing, A.W.J. van 't Hof,
L. Timmers, J.C. Kelder, P.R. Stella, J. Baan, and J.M. ten Berg

POPULAR TAVI

- Patients undergoing transcatheter aortic valve implantation (TAVI) frequently have concomitant diagnoses warranting chronic anticoagulation.
- ACC/AHA guidelines recommendations regarding addition / omission of concomitant antiplatelets after valve replacement do not have a wide evidence base.

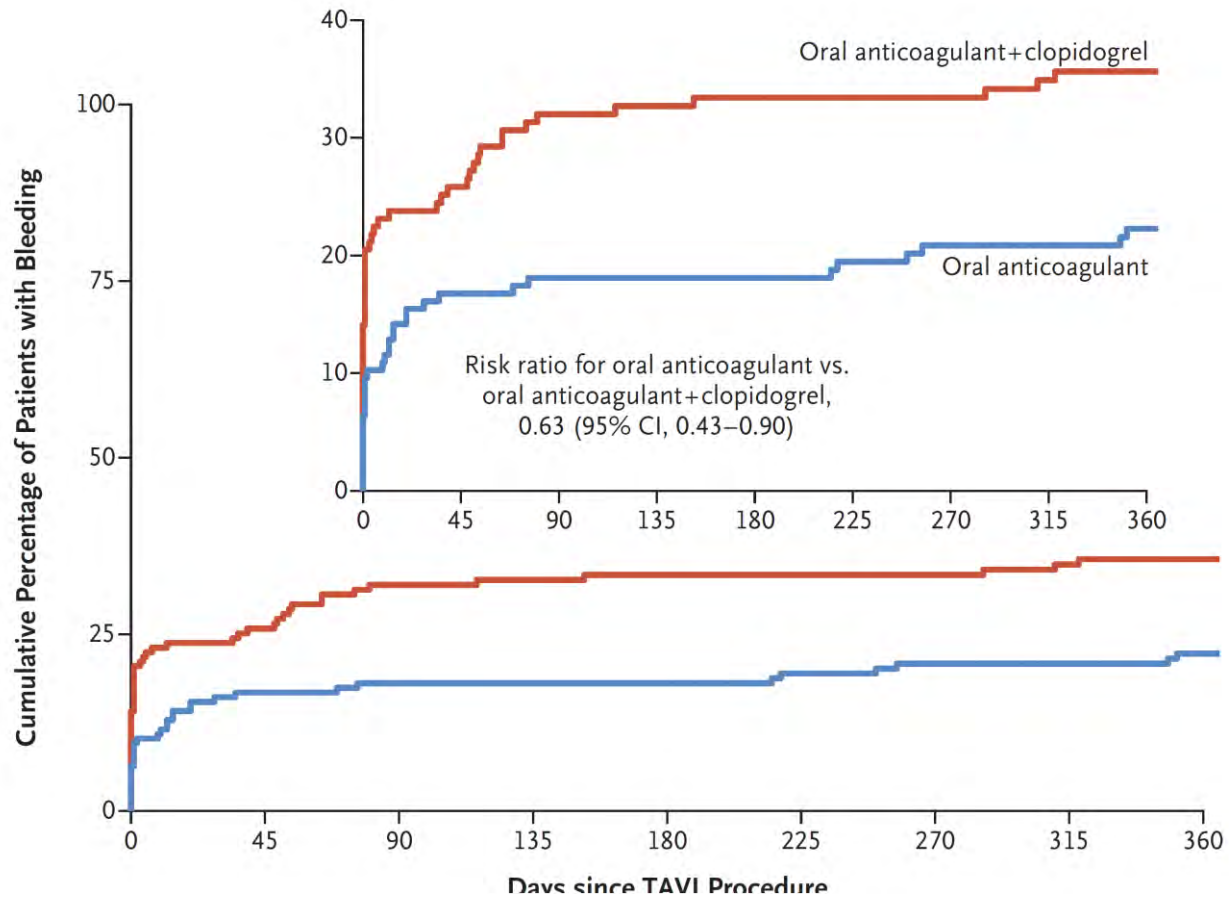
POPULAR TAVI

- 313 TAVI eligible patients previously maintained on oral anticoagulation underwent valve implantation.
- Randomly assigned to:
 - Maintain current anticoagulant + placebo.
 - Maintain current anticoagulant + clopidogrel x 3 months.

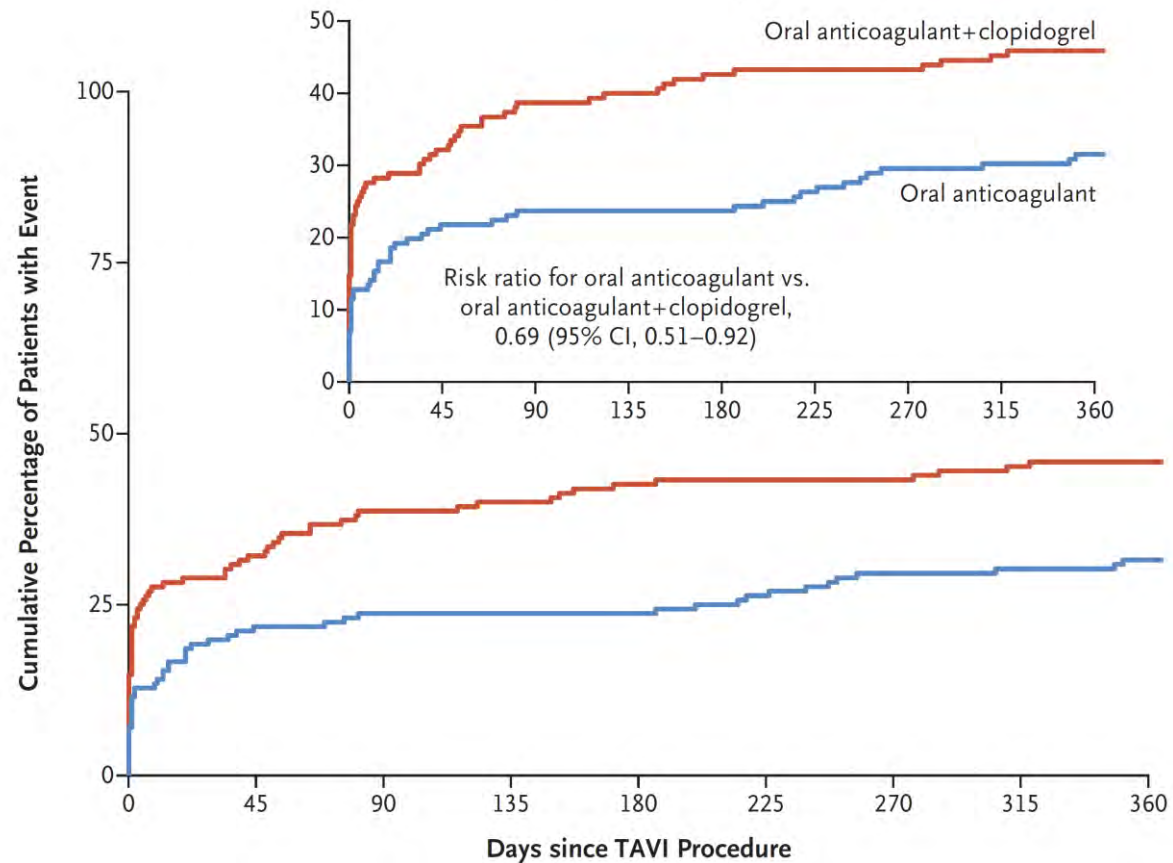
POPULAR TAVI

- Co-primary outcomes were all bleeding and non-procedure related bleeding.
- Secondary outcomes were a composite of: death from CV causes + stroke + MI +/- non-procedure related bleeding.

POPULAR TAVI



POPULAR TAVI



POPULAR TAVI

- “Among patients with long-term indications for oral anticoagulation undergoing TAVI, oral anticoagulation alone was associated with a lower incidence of serious bleeding over a period of either 1 month or 1 year than was anticoagulation plus clopidogrel.”

POPULAR TAVI WIIFM

- Lower rate of bleeding after TAVI if clopidogrel is omitted.
- Only generalizable to patients already on anticoagulants.

TEST QUESTIONS

Q1: In patients with stable CAD, initial invasive strategy is superior to initial conservative strategy.

- A. True
- B. False

Q2: Riociguat is FDA approved for the treatment of HF.

- A. True
- B. False

TEST QUESTIONS

Q3: Which DOAC was not studied in the PAUSE Trial?

- A. Apixaban
- B. Dabigatran
- C. Edoxaban
- D. Rivaroxaban

TEST QUESTIONS

Q4: Which of the following statements most accurately reflects the findings from the DAPA-HF Trial?

- A. SGLT2 inhibitors increase the risk of volume depletion in HF patients
- B. SGLT2 inhibitors increase the risk of hypoglycemia in HF patients.
- C. Dapagliflozin has improved survival only in patients with combined DM2 + HF
- D. Dapagliflozin has improved survival in patients with HF regardless of diabetes status

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