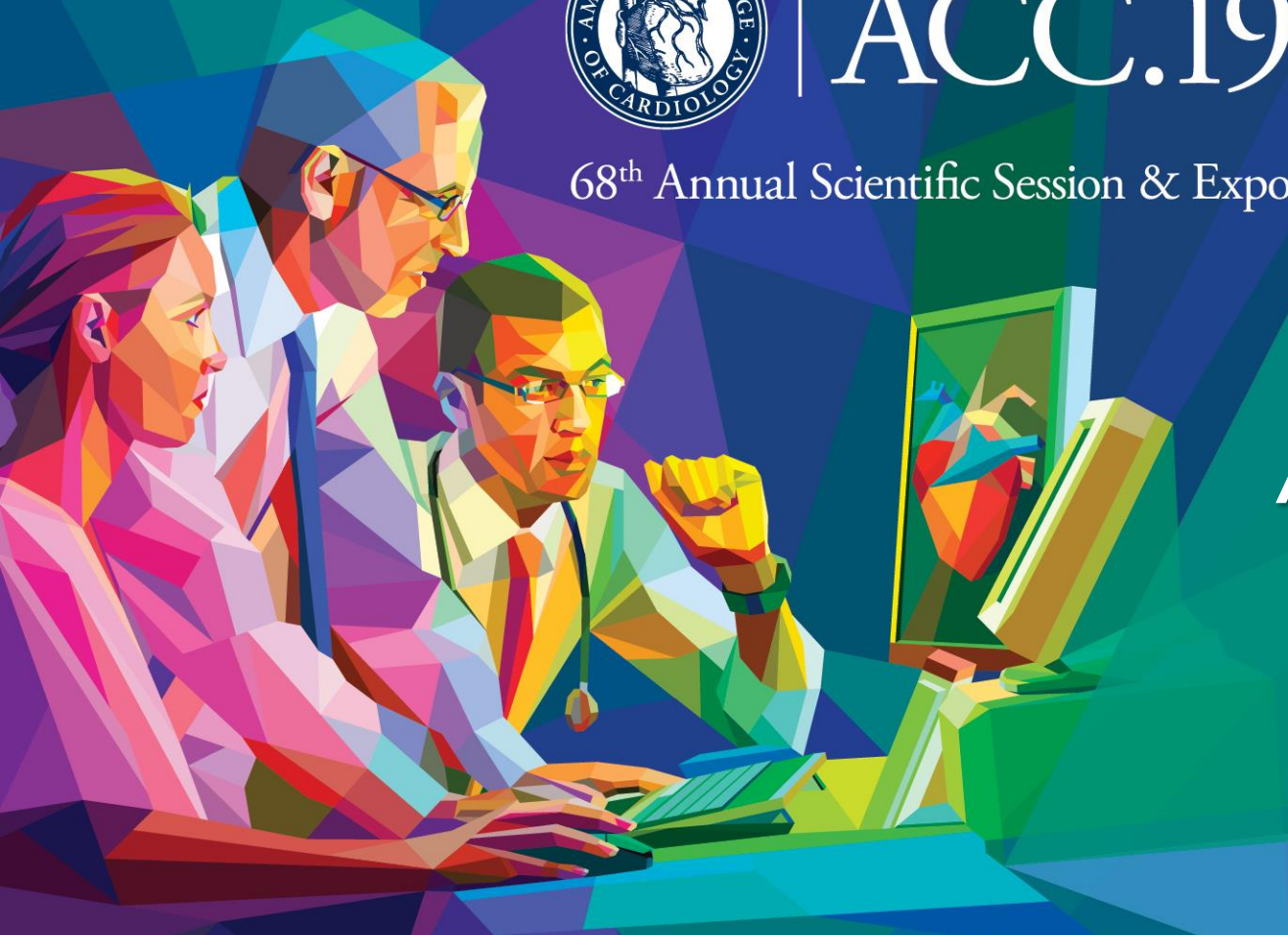
ACC.19

68th Annual Scientific Session & Expo



NEW ORLEANS
MARCH 16 - 18
2019

Best of ACC.19

ACC.19 Late Breaking Clinical Trials

Andrew M. Kates, MD, FACC
Chair ACC.19/ACC.20
Professor of Medicine
Washington University School of Medicine
St. Louis, MO USA

ACC Vision Statement

A world where

- *Global impact*
- *Imagining a better future*

innovation and knowledge

- *ACC is THE trusted knowledge source*
- *Seamlessly integrated in clinician workflow at point-of-care*
- *Easily consumed, shared and updated*

- *Leverage technology*
- *Creator and facilitator of tools and processes*
- *Adapt and stay relevant*

optimize

- *Reduce variations in care delivery*
- *Increase personalization of care*

cardiovascular care and outcomes

- *CV Team-based Care*
- *Shared decision-making*
- *Unifies patient-clinician*

- *Reductions in mortality, life extension, quality of life and quality of care*
- *Clinician, patient and family wellbeing*

ACC'S GLOBAL IMPACT & REACH

AMERICAN COLLEGE of CARDIOLOGY

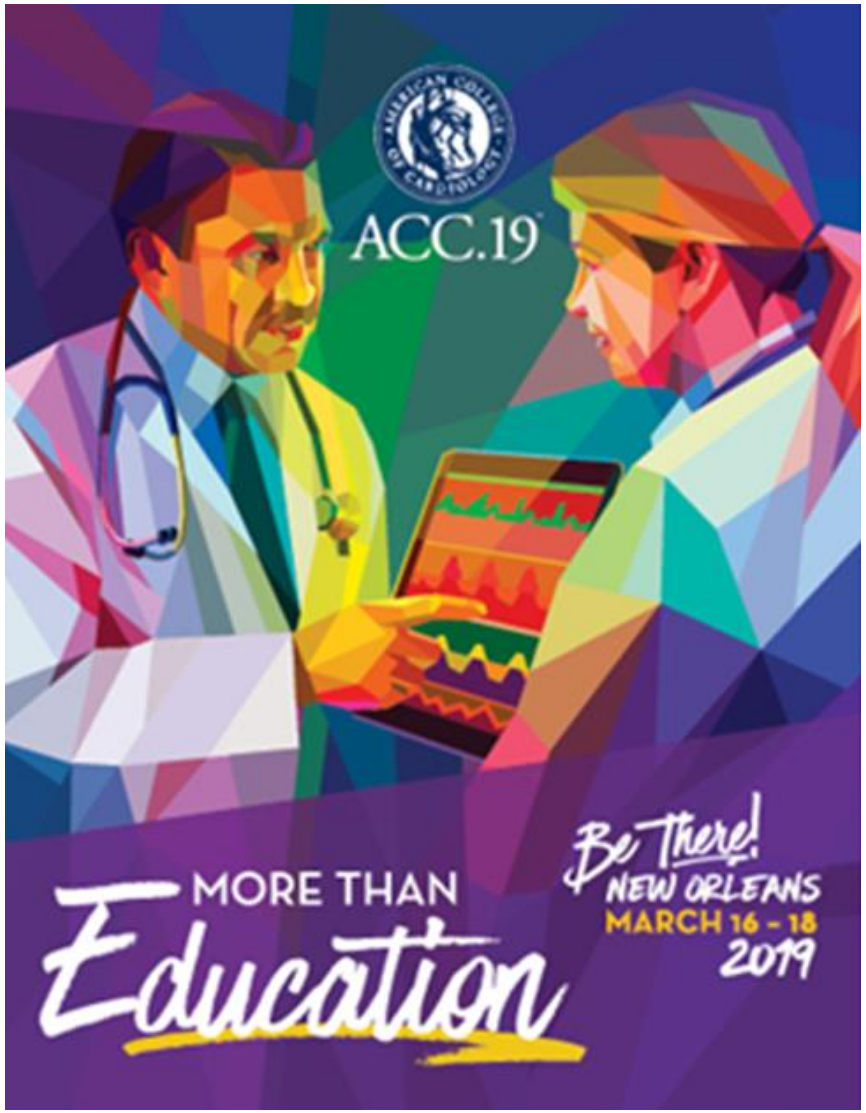
AMERICAN COLLEGE of CARDIOLOGY

52,000 Members Worldwide

ACC.19 in NEW ORLEANS!

Education at ACC.19

- **1,520** Faculty from around the world providing education
- **363** Education sessions
- **11** Pathways
- **15** Guideline-related sessions



Research at ACC.19

- 3,143 Abstracts accepted for oral and poster presentations
- 21 LBCTs (5 sessions)
- 15 Featured Clinical Research Trials (3 sessions)

Practice-Changing Science at ACC.19

- **Opening LBCT session featured Apple Heart Study**

- PARTNER 3
- TAVR/SAVR in Patients with Low Risk of Surgical Mortality
- AUGUSTUS
- CLEAR Wisdom
- DECLARE
- PANACHE
- REDUCE-IT
- INFINITY
- ALCOHOL-AF
- Depression in ACS and Heart Failure

Results of a Large-scale, App-based Study to Identify Atrial Fibrillation Using a Smartwatch: The Apple Heart Study

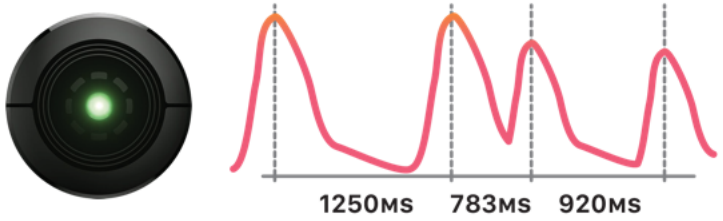
Mintu Turakhia MD MAS and Marco Perez MD

on behalf of the Apple Heart Study Investigators

Introduction

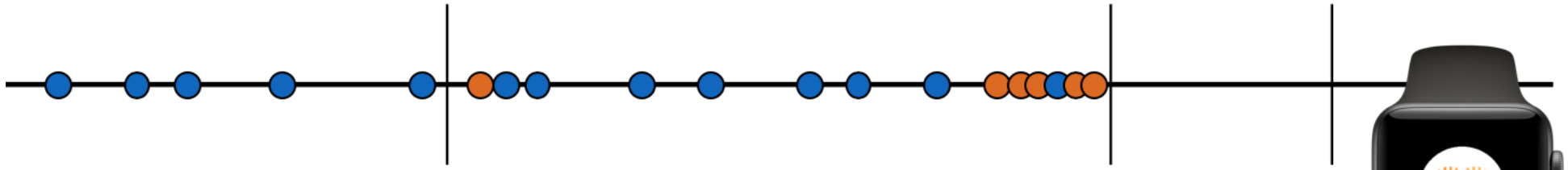
- Optical sensor detects pulse waveform passively to measure heart rate
- Detection of pulse irregularity may be useful to identify atrial fibrillation (AF)

Irregular Pulse Notification Algorithm



Algorithm results

- Regular pulse
- Suggestive of Afib



Tachogram = Periodic spot measurements

5 confirmations ⇒ notify user

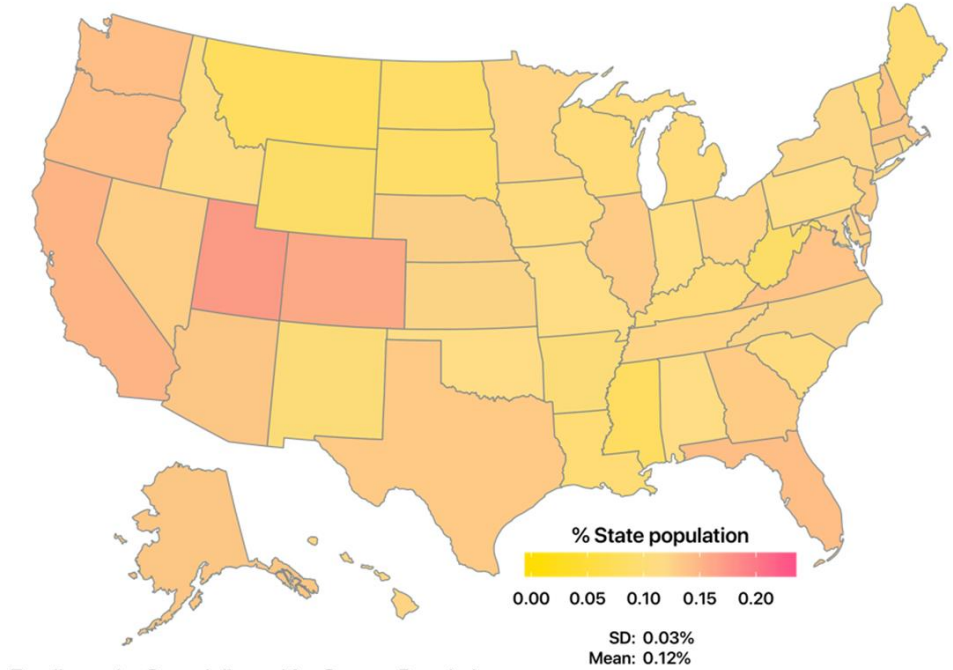
Positive triggers frequent measurements

Not confirmed ⇒ return to usual sampling

The algorithm does not use the watch ECG feature

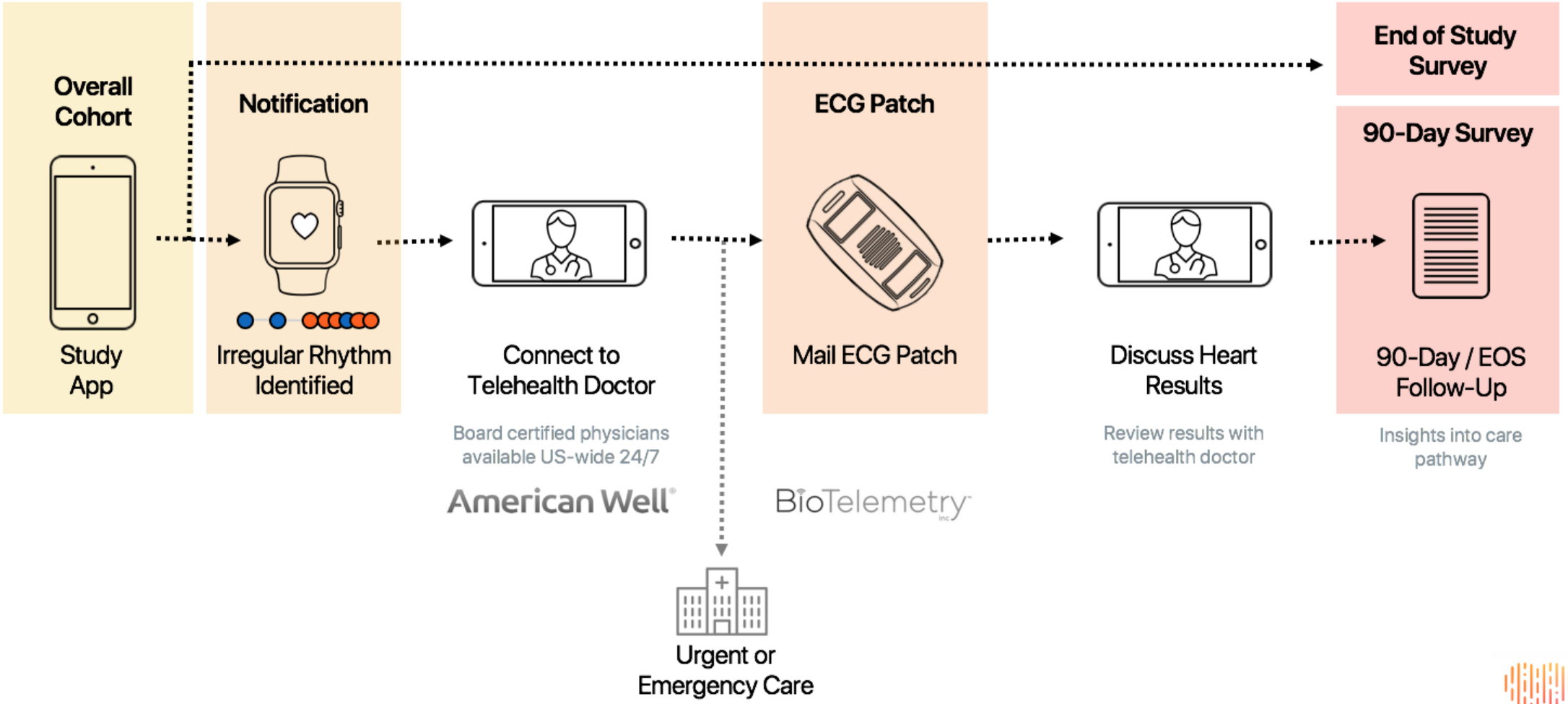
Study Design

- Prospective, Single Arm, Open Label, Non-Significant Risk Study
- Subject: 419,297 individuals
  - 24,626 Age ≥65 years
  - November 2017-February 2019
- Inclusion criteria
  - Age ≥22 years
  - iPhone (5S or higher), Watch (Series 1-3)
- Exclusion criteria
  - Known atrial fibrillation or flutter
  - Anticoagulation

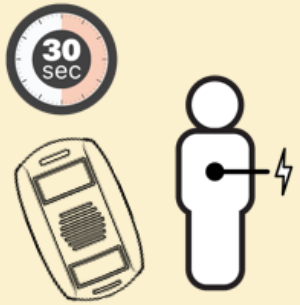


Enrollment by State Adjusted for Census Population

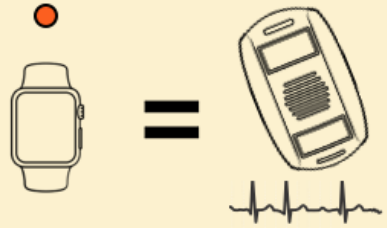
Prospective, Single Arm, Open Label, Non-Significant Risk Study



Primary Endpoints

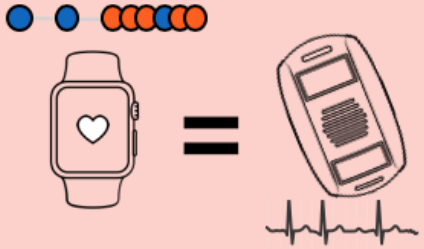


Afib > 30 seconds
on ECG patch
in patients ≥ 65 years



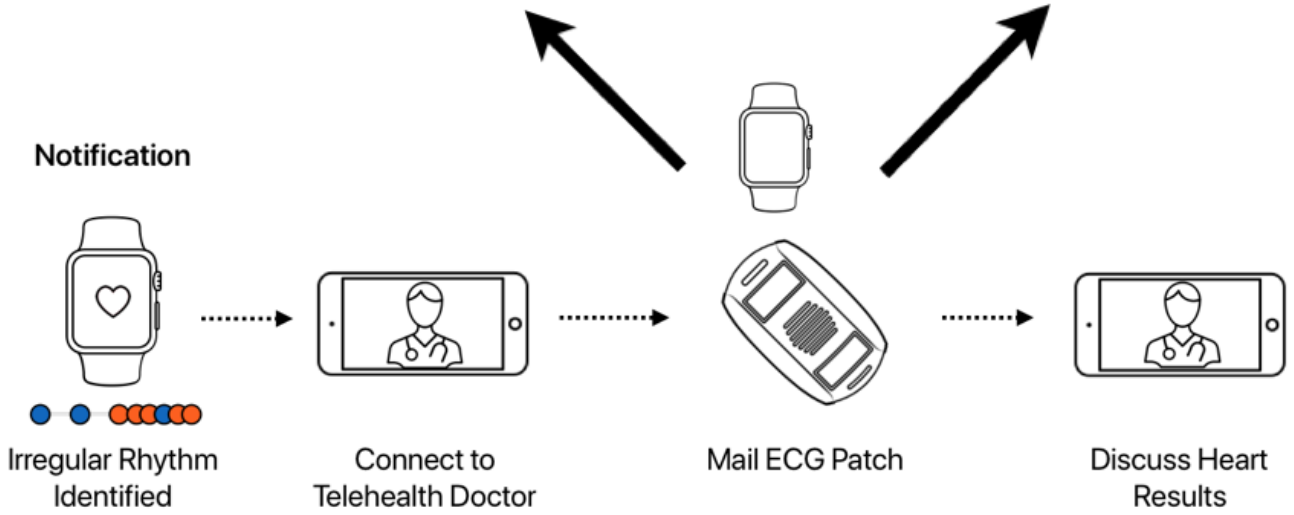
Simultaneous Afib on
ECG Patch and
individual tachogram

Secondary Endpoints

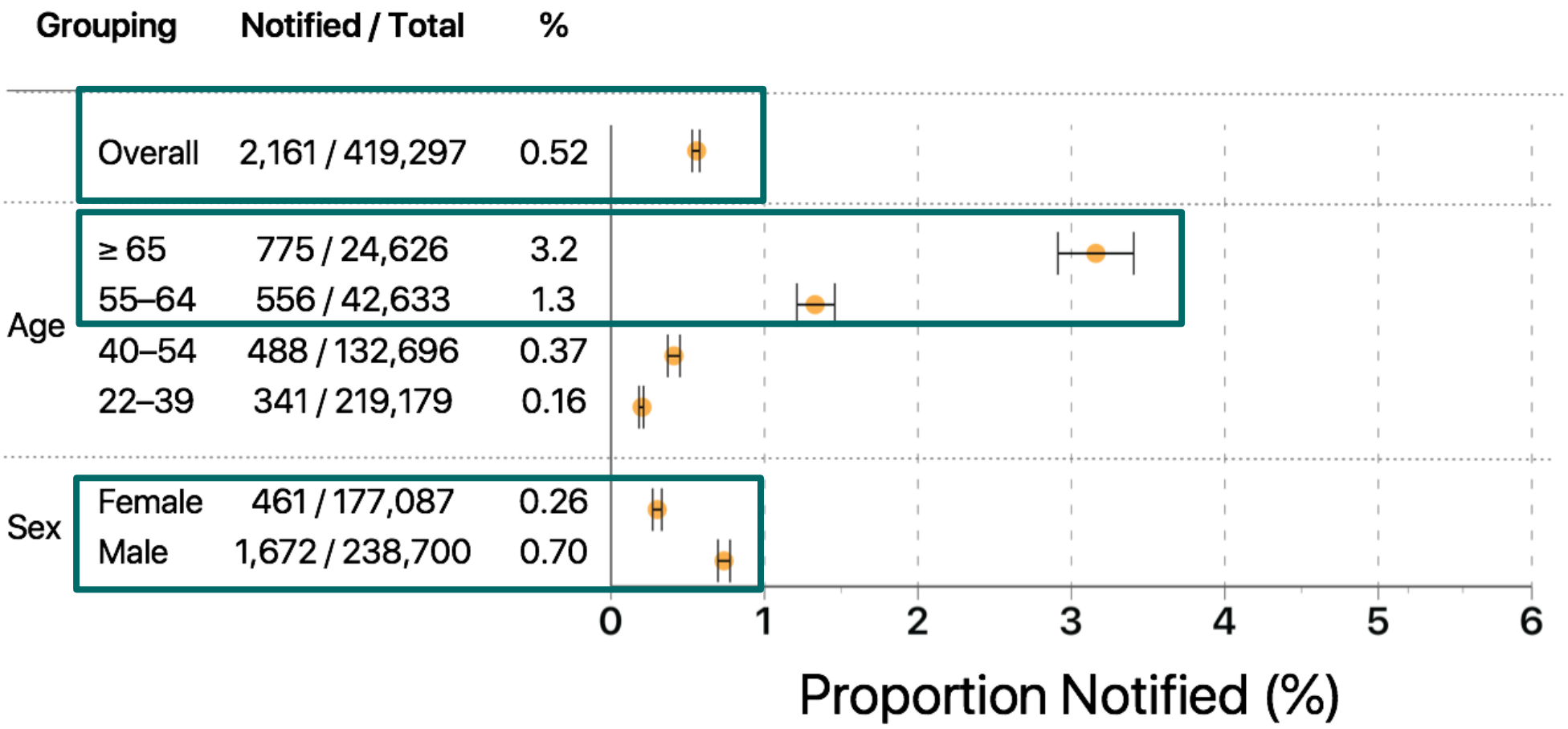


Simultaneous Afib on
ECG Patch w/ notification

Self-reported contact
w/ health care provider

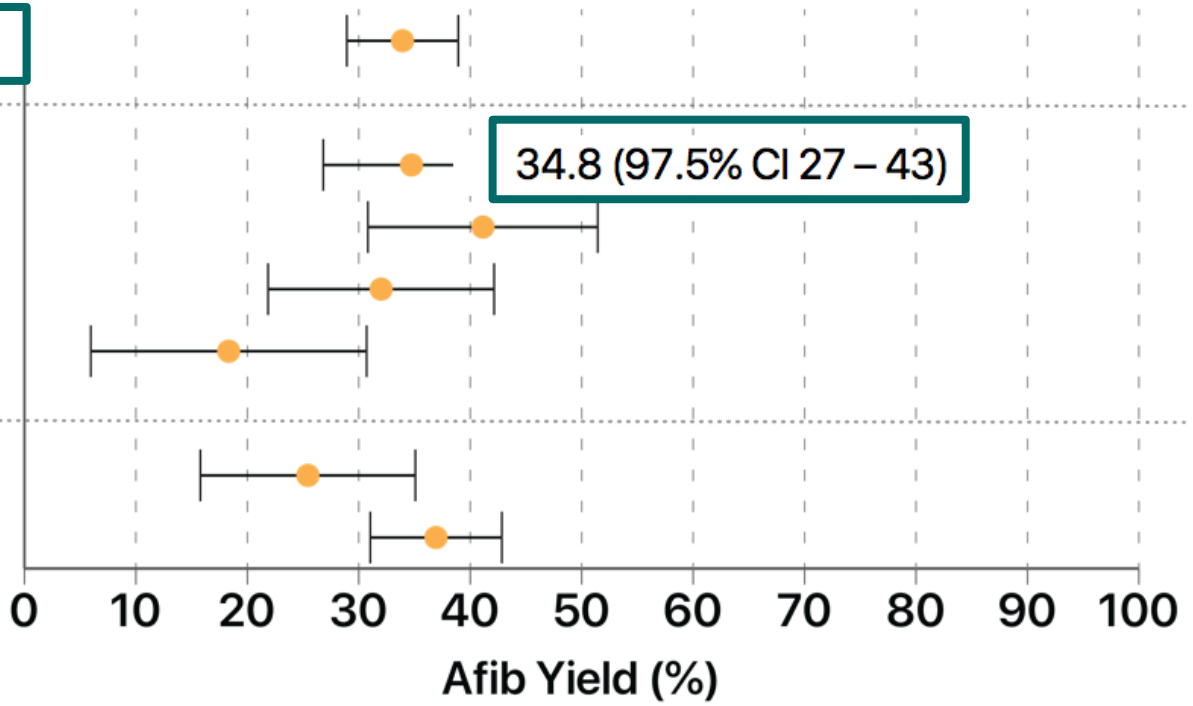


Results: Irregular Pulse Notification



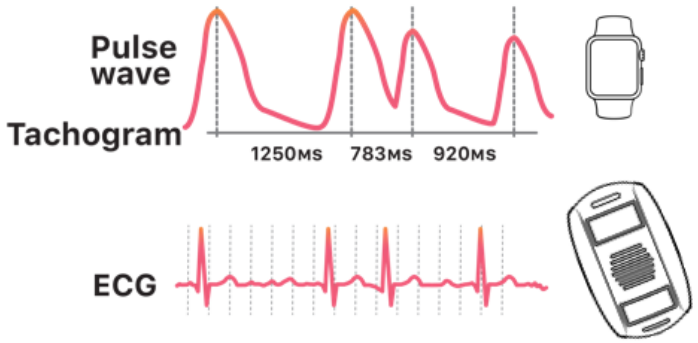
Results: AF Detected on ECG Patch

Grouping		Observed AF / Total	%
	Overall	153 / 450	34.0
Age	≥ 65	63 / 181	34.8
	55–64	47 / 114	41.2
	40–54	34 / 106	32.1
	22–39	9 / 49	18.4
Sex	Female	26 / 102	25.5
	Male	124 / 335	37.0



Positive Predictive Values

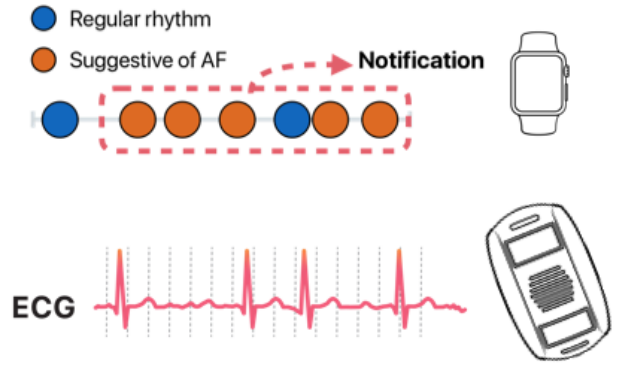
Irregular Tachograms



Afib on ECG Patch	Total Positive Tachograms	PPV* (97.5% CI)
1,489	2,089	**0.71** (0.69–0.74)

* Decision rule for lower bound of CI ≥ 0.7 and upper bound ≥ 0.75 not met

Irregular Pulse Notifications

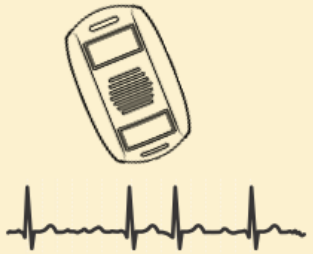


Afib on ECG Patch	Total Positive Notifications	PPV (95% CI)
72	86	**0.84** (0.76–0.92)

Conclusion

Operational success
419,297 in 8 months

Irregular pulse notification rates were low
Overall: 0.52% (0.49-0.54)



ECG patch 13 days later
34% had Afib

Positive predictive values
Tachogram: 0.71 (0.69-0.74)
Notification: 0.84 (0.76-0.92)

Contact Non-Study Provider within 90 days : 57%

Exposure to the app was safe

Potential Impact

- Use of wearable technology expected to increase
- Notification PPV of 0.84 supports ability of Apple Watch algorithm to correctly identify AF among those notified
- Findings may inform decision to seek advice of healthcare provider

PARTNER 3

Transcatheter or Surgical Aortic Valve Replacement in Low Risk Patients with Aortic Stenosis

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

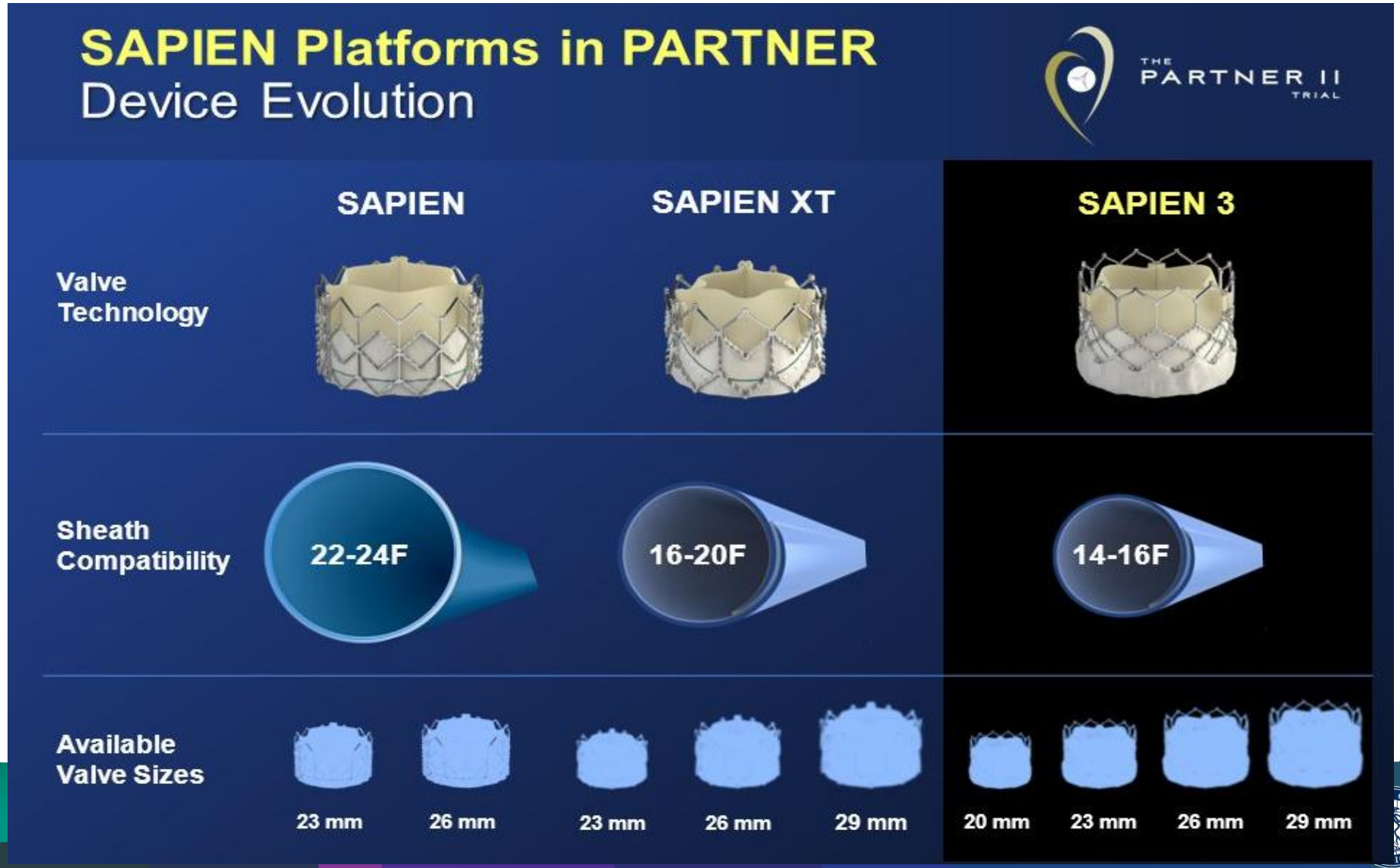
M.J. Mack, M.B. Leon, V.H. Thourani, R. Makkar, S.K. Kodali, M. Russo, S.R. Kapadia, S.C. Malaisrie, D.J. Cohen, P. Pibarot, J. Leipsic, R.T. Hahn, P. Blanke, M.R. Williams, J.M. McCabe, D.L. Brown, V. Babaliaros, S. Goldman, W.Y. Szeto, P. Genereux, A. Pershad, S.J. Pocock, M.C. Alu, J.G. Webb, and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

Martin B. Leon, MD &
Michael J. Mack, MD
on behalf of the PARTNER 3 Trial Investigators

Introduction

- Previous PARTNER studies with SAPIEN valves have shown
  - TAVR was *superior* to standard therapy in extreme-risk patients
  - TAVR *non-inferior* to surgery in high- and intermediate-risk patients.
- Technology enhancements and procedural refinements have reduced complications and improved clinical outcomes after TAVR.
- Majority of patients with aortic stenosis (AS) treated with surgery have low surgical risk profiles
  - TAVR vs. surgery in such patients has not been investigated in rigorous clinical trials.

SAPIEN Valve Evolution



Study Design

- To compare the safety and effectiveness of TAVR versus conventional surgery (SAVR) in patients with severe symptomatic aortic stenosis (AS) who are at *low surgical risk*.
- Multicenter, randomized trial of TAVR with 3rd generation balloon-expandable SAPIEN 3 valve compared with SAVR
- Subjects:
  - 1,000 patients with severe AS
  - Low surgical risk: STS-PROM <4%
  - 71 centers
  - Exclusion criteria: frailty, bicuspid aortic valve, other anatomical features that would increase risk of TAVR or SAVR
- Primary endpoint: all-cause death, stroke, or rehospitalization at 1 year

Results: Baseline Characteristics

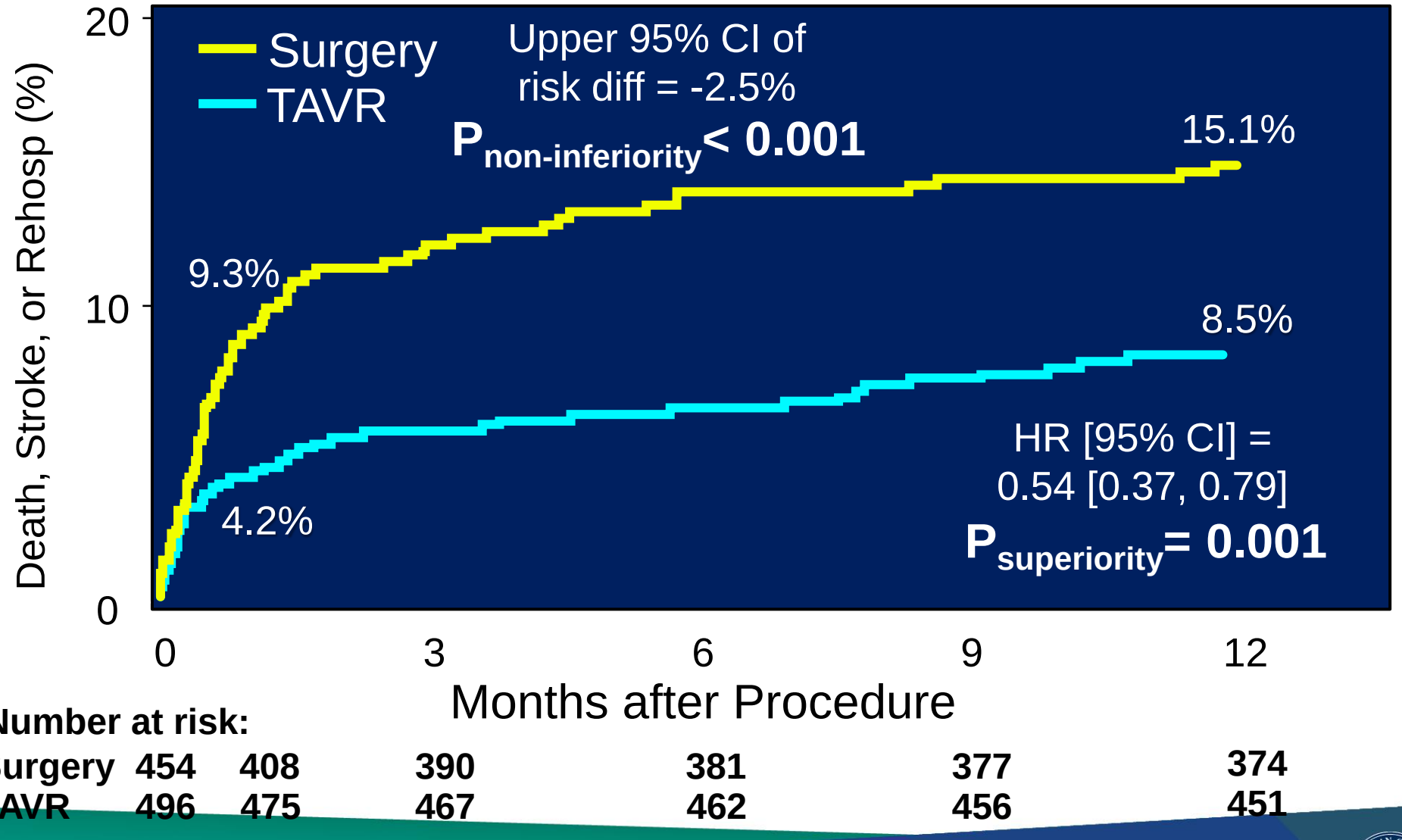
- Mean age: 73 years
- STS-PROM score: 1.9%
- CAD: 28%
- Diabetes: 30%
- Men: 67.5% (TAVR) -71.1% (SAVR)

Results: Procedural Complications In-Hospital

Complication	TAVR (N=496)	Surgery (N=454)	P-value
In-hospital Death	0.4% (2)	0.9% (4)	0.43
≥ 2 Transcatheter Valves Implanted*	0.2% (1)	NA	NA
Valve Embolization	0	NA	NA
Aortic Dissection	0	NA	NA
Annular Rupture	0.2% (1)	NA	NA
Ventricular Perforation	0.2% (1)	0.4% (2)	0.61
Coronary Obstruction	0.2% (1)	0.4% (2)	0.61
Access Site Infections	0.4% (2)	1.3% (6)	0.16

*Valve-in-valve

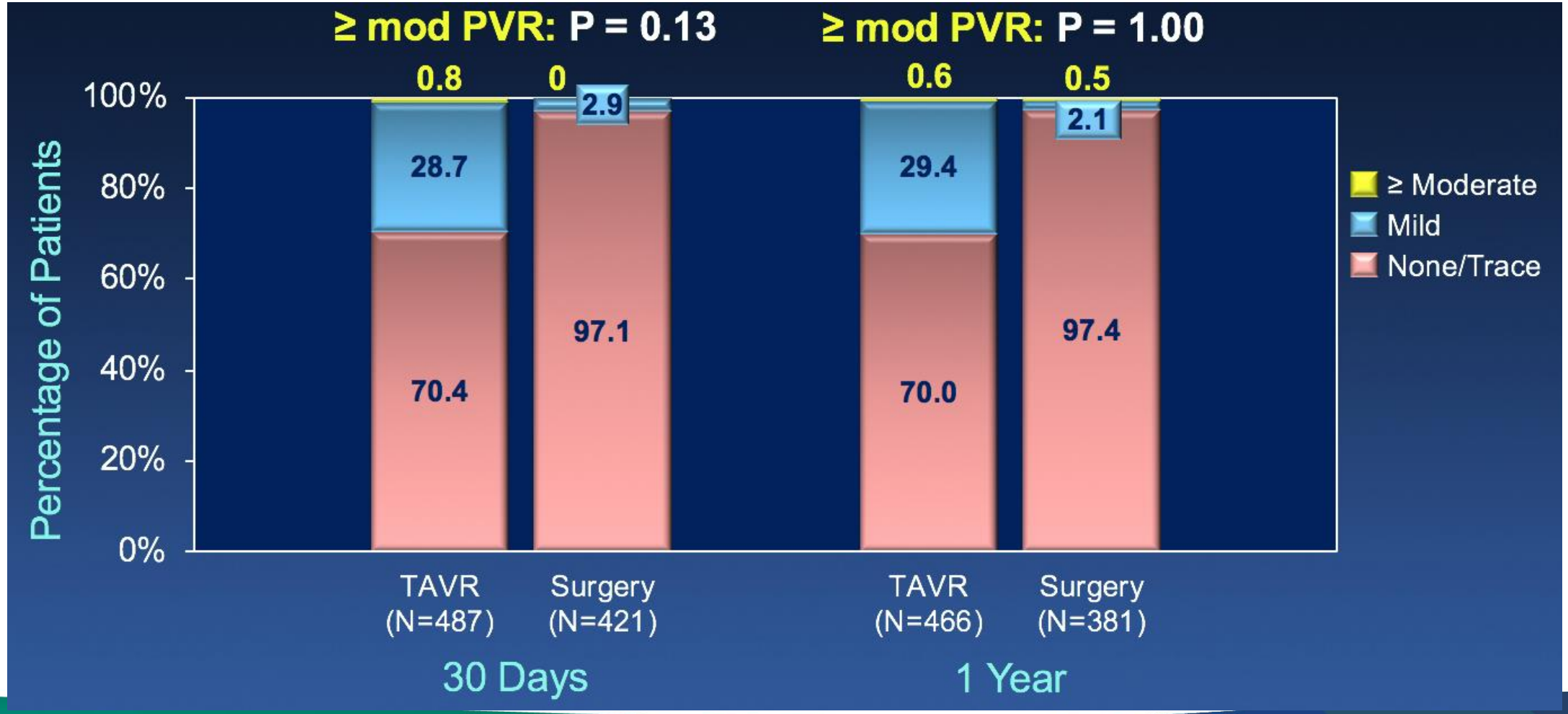
Results: Primary Endpoint



Number at risk:

Surgery	**454**	**408**	**390**	**381**	**377**	**374**
TAVR	**496**	**475**	**467**	**462**	**456**	**451**

Paravalvular Regurgitation



Conclusions – PARTNER 3

In severe symptomatic AS patients at low surgical risk, TAVR compared to surgery:

- At 1-year, significantly reduced primary endpoint (death, stroke, or rehospitalization) by 46%
- At 30 days, TAVR resulted in lower rate of stroke, new onset AF, and poor treatment outcome (death and quality of life)
- Shorter index hospitalization
- No difference in vascular complications, pacemaker, moderate/severe AR

Primary Results From the Evolut Low Risk Trial

Michael J. Reardon, MD, FACC
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Vascular Institute, Houston, TX
For the Evolut Low Risk Trial Investigators

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients

Jeffrey J. Popma, M.D., G. Michael Deeb, M.D., Steven J. Yakubov, M.D., Mubashir Mumtaz, M.D., Hemal Gada, M.D., Daniel O'Hair, M.D., Tanvir Bajwa, M.D., John C. Heiser, M.D., William Merhi, D.O., Neal S. Kleiman, M.D., Judah Askew, M.D., Paul Sorajja, M.D., Joshua Rovin, M.D., Stanley J. Chetcuti, M.D., David H. Adams, M.D., Paul S. Teirstein, M.D., George L. Zorn III, M.D., John K. Forrest, M.D., Didier Tchétché, M.D., Jon Resar, M.D., Antony Walton, M.D., Nicolo Piazza, M.D., Ph.D., Basel Ramlawi, M.D., Newell Robinson, M.D., George Petrossian, M.D., Thomas G. Gleason, M.D., Jae K. Oh, M.D., Michael J. Boulware, Ph.D., Hongyan Qiao, Ph.D., Andrew S. Mugglin, Ph.D., and Michael J. Reardon, M.D., for the Evolut Low Risk Trial Investigators*

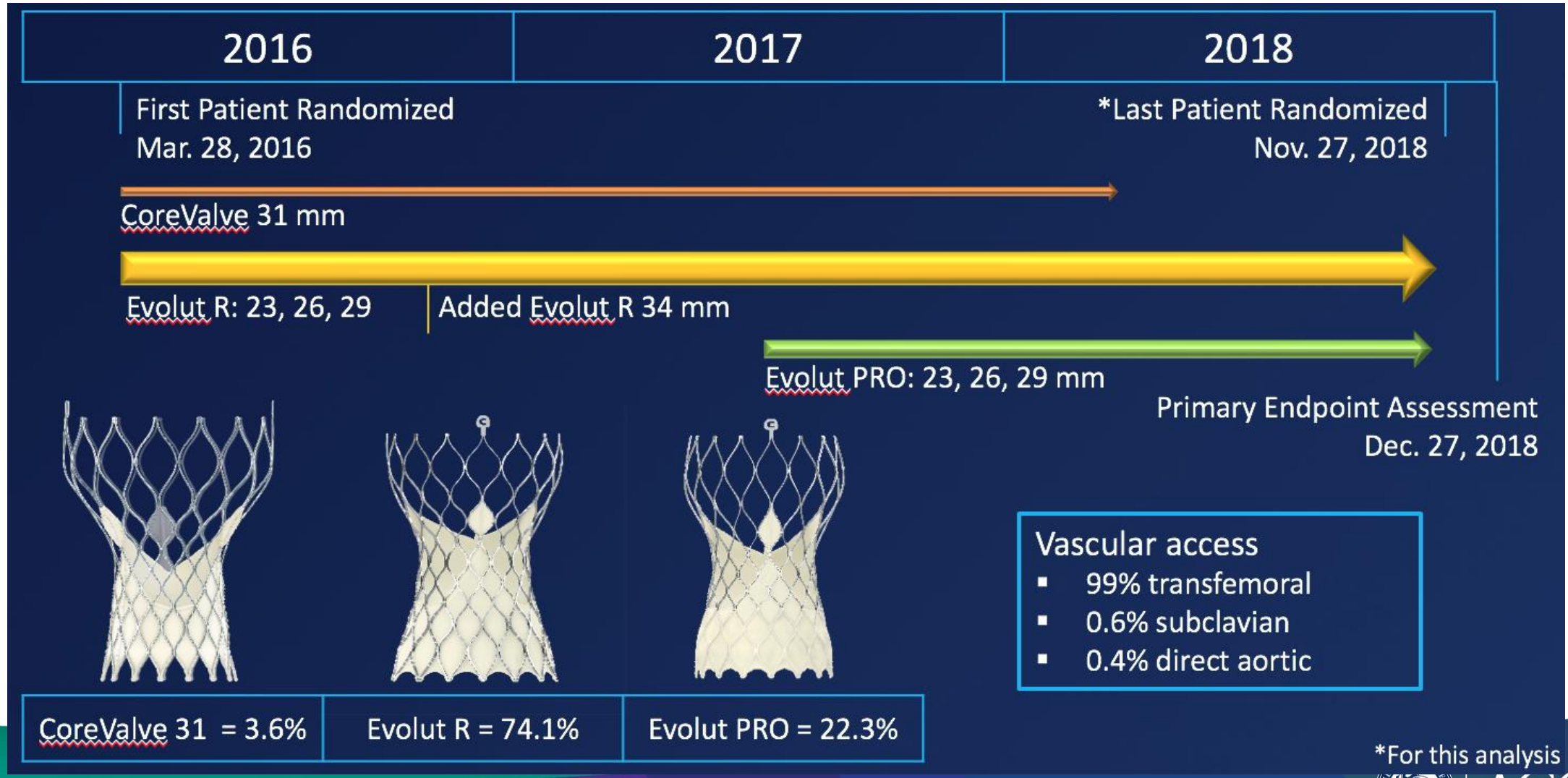
Background

- Prior randomized controlled trials of Evolut self-expanding valves in patients with severe aortic stenosis across a spectrum of surgical risk.
  - In *high-risk* patients, TAVR was superior to SAVR for the primary endpoint to 2 years and similar at 5 years with self-expanding TAVR valve
  - SURTAVI *intermediate-risk* trial showed non-inferiority at interim analysis

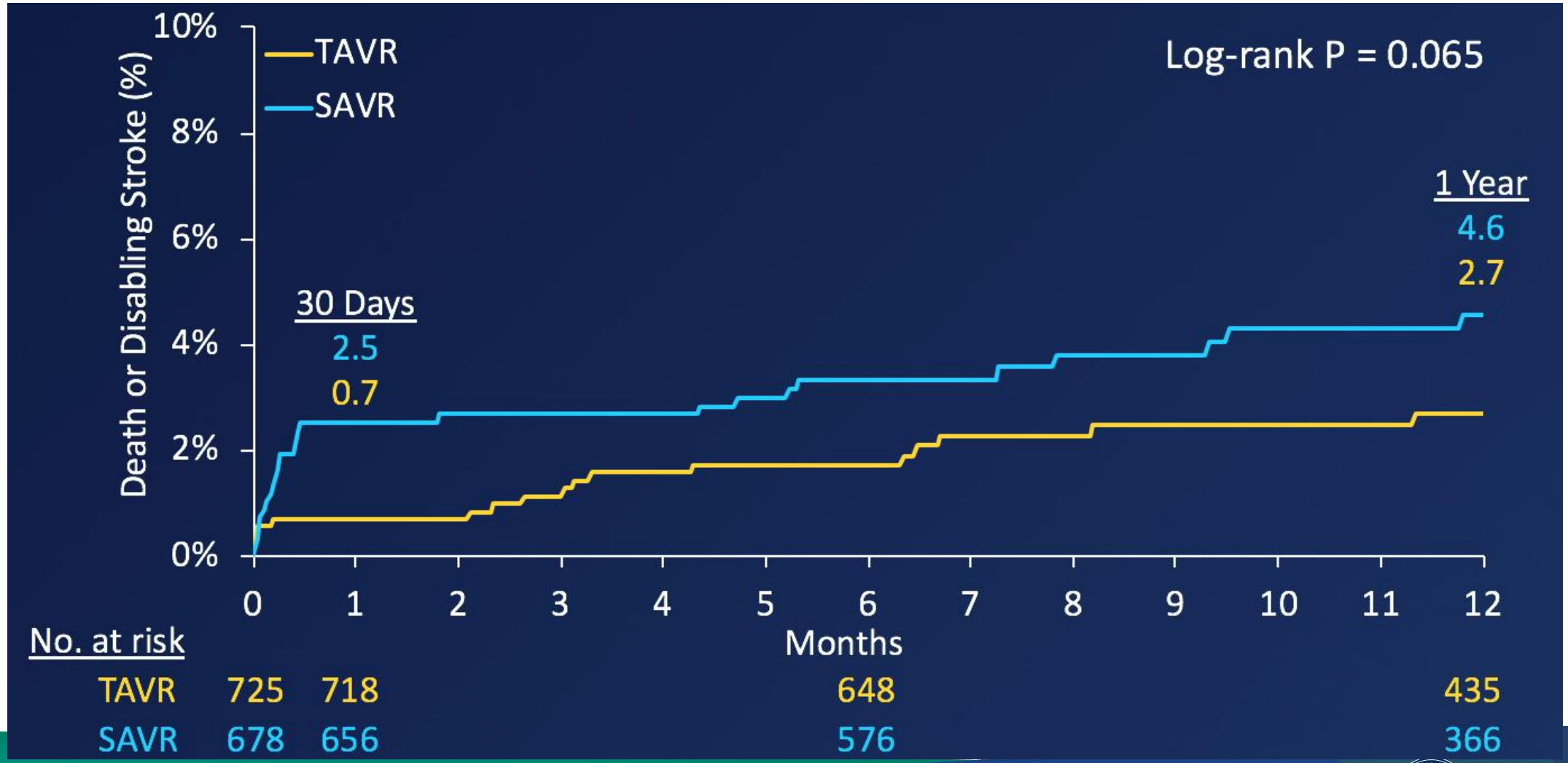
Study Design

- Assess the safety and efficacy of TAVR with the Evolut self-expanding supra-annular valve compared with SAVR in patients with a low predicted risk of 30-day surgical mortality
- Multinational, randomized, non-inferiority clinical trial
- Subjects
  - 1403 patients
  - Mean age 74 years
  - Mean STS-PROM 1.9%
  - 64% men, 36% women
- Primary safety and effectiveness endpoint
  - Composite of death or disabling stroke at 24 months

Study Time and Valve Evolution



Results – Primary endpoint



Hierarchical Secondary Endpoints

All Noninferiority and Superiority Endpoints Met

Evolut™ Low Risk Trial

	TAVR	SAVR	Difference TAVR–SAVR	Posterior Probability
Noninferiority (margin)			(90% BCI)	
Mean gradient at 12 months (5 mmHg)	8.6 ± 3.7	11.2 ± 4.9	-2.6 (-3.1, -2.1)	> 0.999 ✓
Mean EOA at 12 months (0.1 cm^2)	2.3 ± 0.7	2.0 ± 0.6	0.3 (0.2, 0.4)	> 0.999 ✓
Mean NYHA class change (12 months –Baseline) (0.375)	0.9 ± 0.7	1.0 ± 0.7	-0.1 (-0.2, 0.0)	> 0.999 ✓
Mean KCCQ change (12 months –Baseline) (5)	22.2 ± 20.3	20.9 ± 21.0	1.3 (-1.2, 3.8)	> 0.999 ✓
Superiority			(95% BCI)	
Mean gradient at 12 months, mmHg	8.6 ± 3.7	11.2 ± 4.9	-2.6 (-3.2, -2.0)	> 0.999 ✓
Mean EOA at 12 months, cm^2	2.3 ± 0.7	2.0 ± 0.6	0.3 (0.2, 0.4)	> 0.999 ✓
Mean KCCQ change (30 Days–Baseline)	20.0 ± 21.1	9.1 ± 22.3	10.9 (8.6, 13.2)	> 0.999 ✓

Clinical Outcomes at 30 days

Evolut™ Low Risk Trial

Bayesian rates as %	TAVR (N=725)	SAVR (N=678)	(95% BCI for Difference)
30-Day composite safety end point*	5.3	10.7	(-8.3, -2.6)
All-cause mortality	0.5	1.3	(-1.9, 0.2)
Disabling stroke*	0.5	1.7	(-2.4, -0.2)
Life-threatening or disabling bleeding*	2.4	7.5	(-7.5, -2.9)
Acute kidney injury, stage 2-3*	0.9	2.8	(-3.4, -0.5)
Major vascular complication	3.8	3.2	(-1.4, 2.5)
Atrial fibrillation*	7.7	35.4	(-31.8, -23.6)
Permanent pacemaker implant*	17.4	6.1	(8.0, 14.7)
All-cause mortality or disabling stroke*	0.8	2.6	(-3.2, -0.5)
All stroke	3.4	3.4	(-1.9, 1.9)
Aortic valve reintervention	0.4	0.4	(-0.8, 0.7)

* Significantly favors TAVR; * significantly favors SAVR

BCI = Bayesian credible interval.

Conclusions - Evolut Low Risk Trial

- TAVR with self-expanding valves was noninferior to SAVR in patients with severe aortic stenosis at ***low*** surgical risk
- At 30 days, TAVR showed a better safety and recovery profile than SAVR
  - Less death or disabling stroke, less disabling stroke, shorter length of stay
  - Better quality of life while SAVR had fewer pacemakers implanted and less residual aortic regurgitation.
- At 1 year, both groups had excellent survival
  - TAVR showed fewer disabling strokes and heart failure rehospitalizations
  - Superior hemodynamics manifest by lower gradients and larger EOAs.

"This is a historic moment, and of all of us here should remember it as such…We will talk to our grandchildren about this — that we were here at the time this incredible advance in the care of patients with aortic stenosis was presented."

-Eugene Braunwald

Potential Impact of PARTNER-3 and EVOLUT

- Increased referrals for TAVR in low-risk surgical patients with aortic stenosis
- TAVR, through 1-year, may be preferred therapy in low-risk surgical aortic stenosis patients
- TAVR vs. SAVR in aortic stenosis patients should be a shared-decision making process, respecting patient preferences, understanding knowledge gaps (esp. in younger patients), and considering clinical and anatomic factors
- Longer-term outcomes data needed

Apixaban vs VKA and Aspirin vs Placebo in Patients with Atrial Fibrillation and ACS/PCI: *The AUGUSTUS Trial*

Renato D. Lopes, MD, PhD
on behalf of the AUGUSTUS Investigators

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Antithrombotic Therapy after Acute Coronary Syndrome or PCI in Atrial Fibrillation

Renato D. Lopes, M.D., Ph.D., Gretchen Heizer, M.S., Ronald Aronson, M.D., Amit N. Vora, M.D., M.P.H., Tyler Massaro, Ph.D., Roxana Mehran, M.D., Shaun G. Goodman, M.D., Stephan Windecker, M.D., Harald Darius, M.D., Jia Li, Ph.D., Oleg Averkov, M.D., Ph.D., M. Cecilia Bahit, M.D., Otavio Berwanger, M.D., Ph.D., Andrzej Budaj, M.D., Ph.D., Ziad Hijazi, M.D., Ph.D., Alexander Parkhomenko, M.D., Ph.D., Peter Sinnaeve, M.D., Ph.D., Robert F. Storey, M.D., Holger Thiele, M.D., Dragos Vinereanu, M.D., Ph.D., Christopher B. Granger, M.D., and John H. Alexander, M.D., M.H.S., for the AUGUSTUS Investigators*

Background

- Optimal antithrombotic regimen for patients with atrial fibrillation (AF) who have an acute coronary syndrome (ACS) or require percutaneous coronary intervention (PCI) is unclear
- Limited data with apixaban in patients with AF requiring DAPT
- Data on the independent effects of aspirin in this population are needed

New Eng J Med. 2019 March 17. DOI: 10.1056/NEJMoa1817083

Study Hypothesis

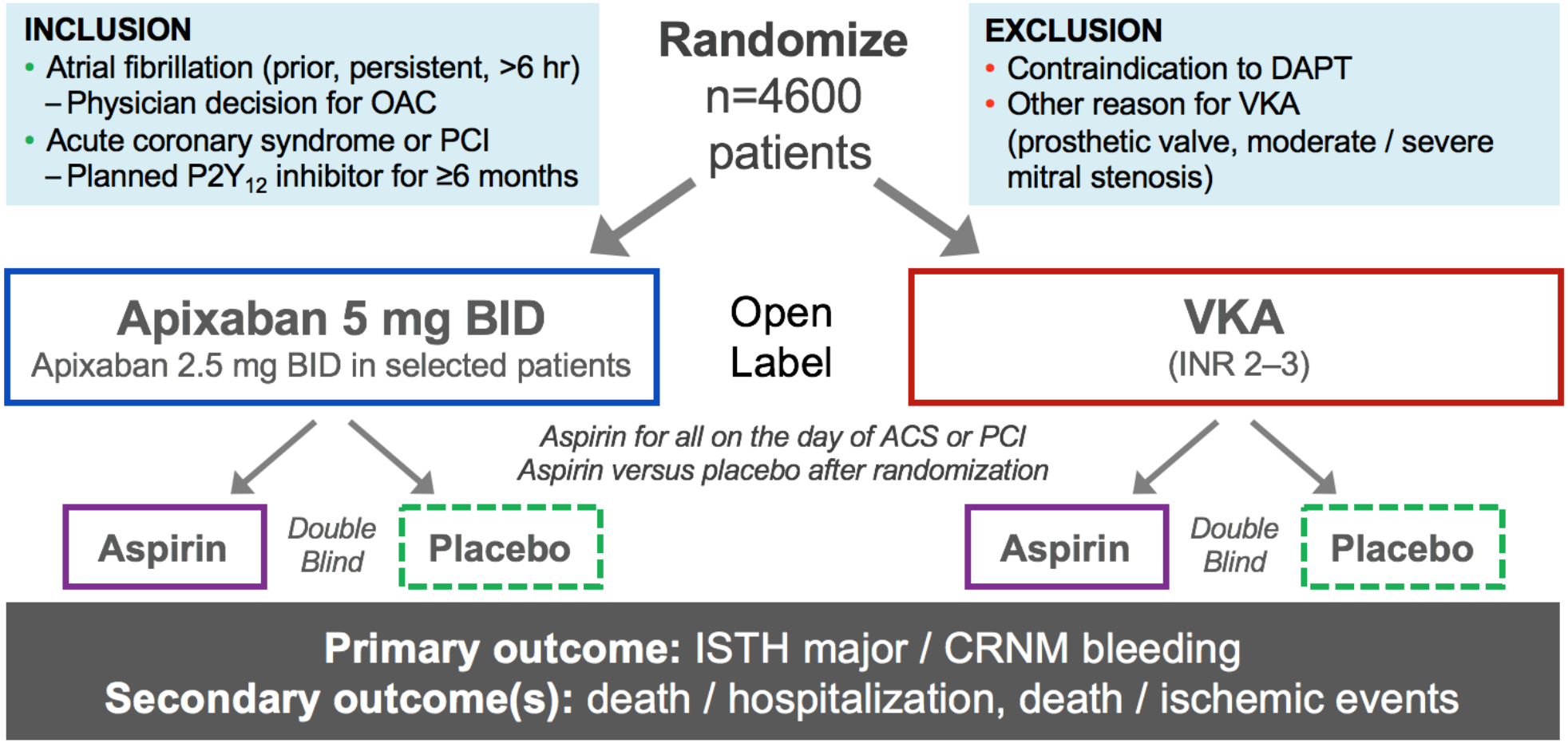
In patients with AF and ACS or PCI on a $P2Y_{12}$ inhibitor

1. Apixaban is non-inferior to vitamin K antagonists for International Society on Thrombosis and Haemostasis (ISTH) major or clinically relevant non-major (CRNM) bleeding

2. Aspirin is inferior to placebo for ISTH major or CRNM bleeding in patients on oral anticoagulation (OAC)

New Eng J Med. 2019 March 17. DOI: 10.1056/NEJMoa1817083

Trial Design



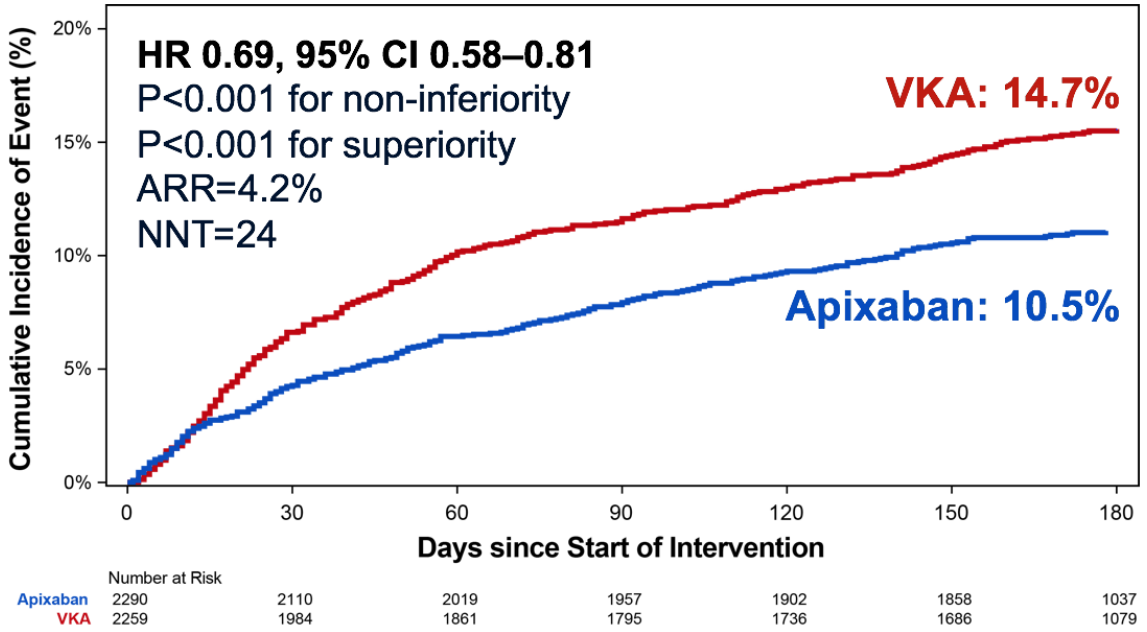
New Eng J Med. 2019 March 17. DOI: 10.1056/NEJMoa1817083

Results: Baseline Characteristics

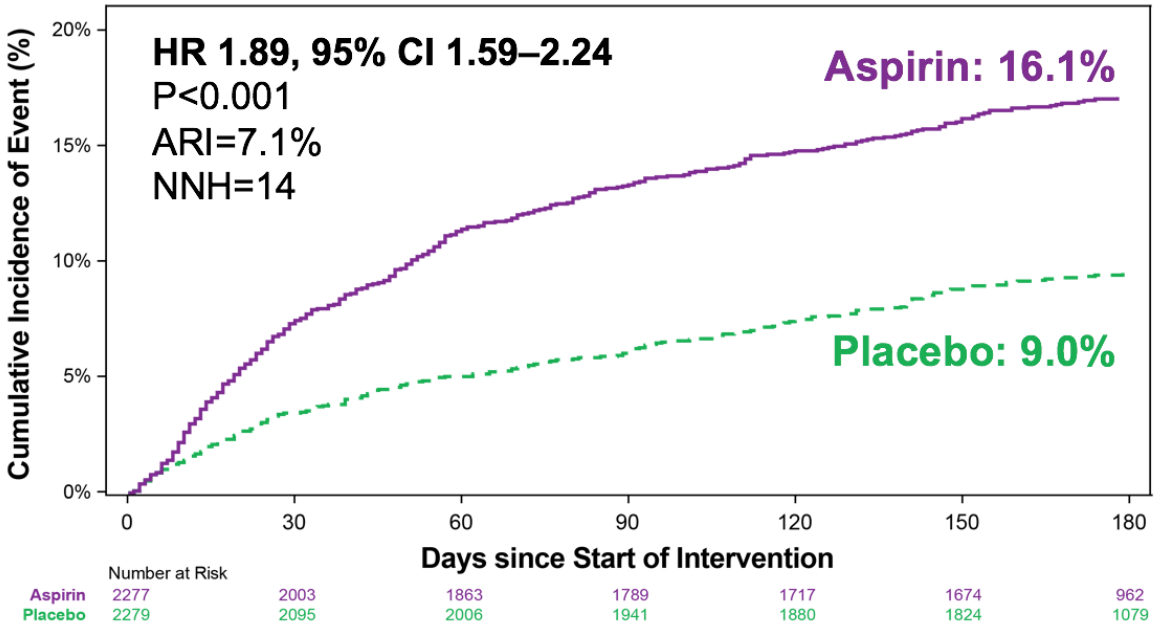
	Total (N=4614)
Age, median (25^{th}, 75^{th}), years	70.7 (64.2, 77.2)
Female, %	29.0
CHA_2DS_2-VASc score, mean (SD)	3.9 (1.6)
HAS-BLED score, mean (SD)	2.9 (0.9)
Prior OAC, %	49.0
$P2Y_{12}$ inhibitor, %	
Clopidogrel	92.6
Prasugrel	1.1
Ticagrelor	6.2
Number of days from ACS/PCI to randomization, mean (SD)	6.6 (4.2)
Qualifying index event, %	
ACS and PCI	37.3
ACS and no PCI	23.9
Elective PCI	38.8

New Eng J Med. 2019 March 17. DOI: 10.1056/NEJMoa1817083

Major / CRNM Bleeding
Apixaban vs. VKA

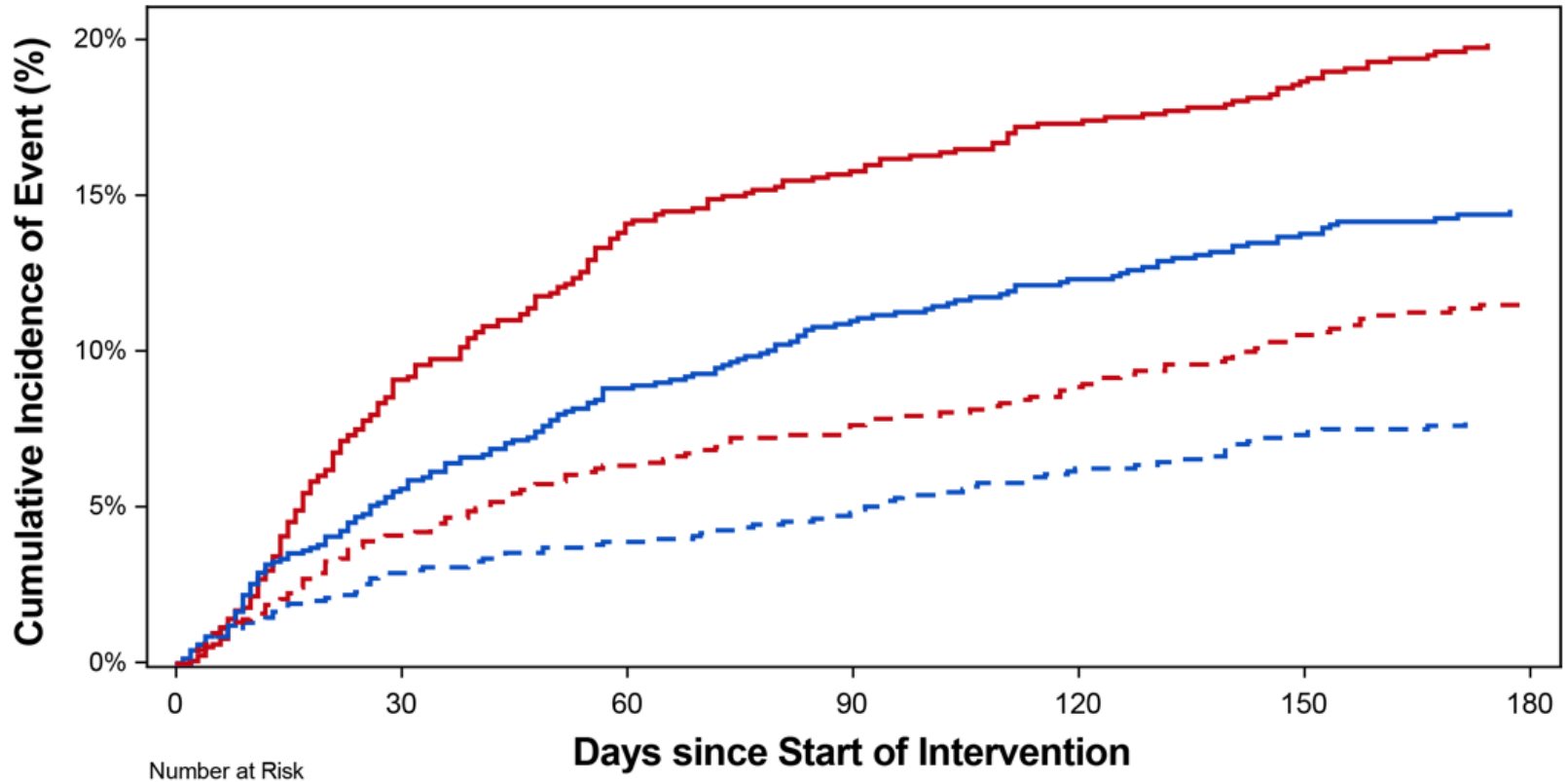


Major / CRNM Bleeding
Aspirin vs. Placebo



New Eng J Med. 2019 March 17. DOI: 10.1056/NEJMoa1817083

Major / CRNM Bleeding



Number at Risk							
Apixaban and Aspirin	1145	1036	975	937	903	880	485
Apixaban and Placebo	1143	1075	1044	1007	975	947	536
VKA and Aspirin	1123	962	881	838	800	776	467
VKA and Placebo	1126	1007	947	917	883	851	528

VKA + Aspirin (18.7%)

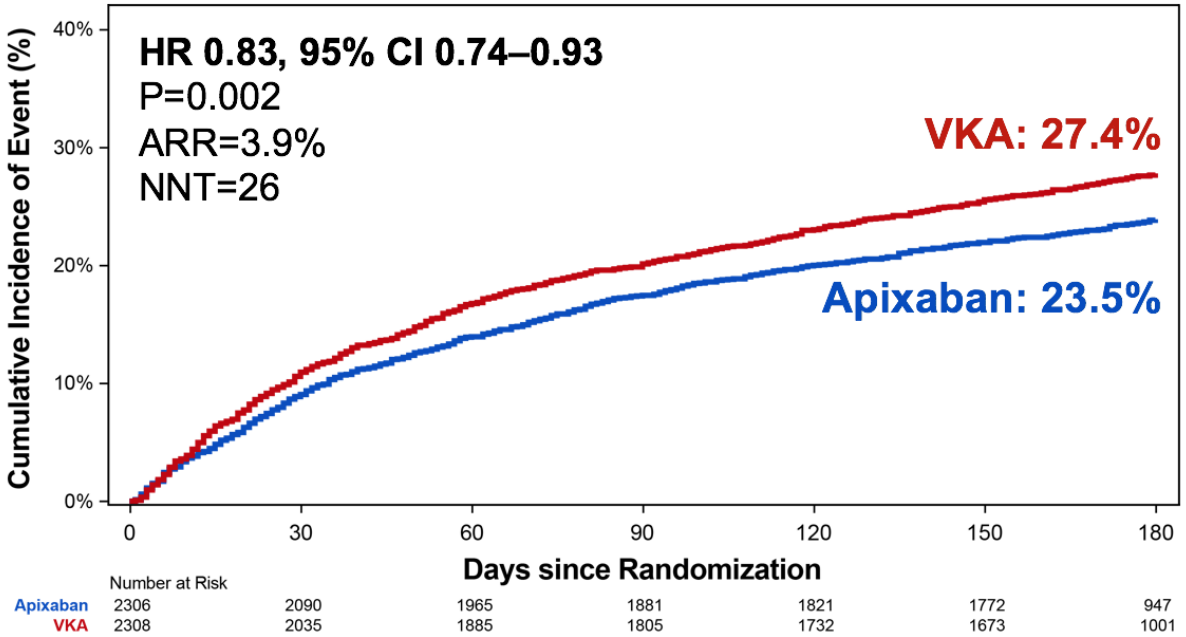
Apixaban + Aspirin (13.8%)

VKA + Placebo (10.9%)

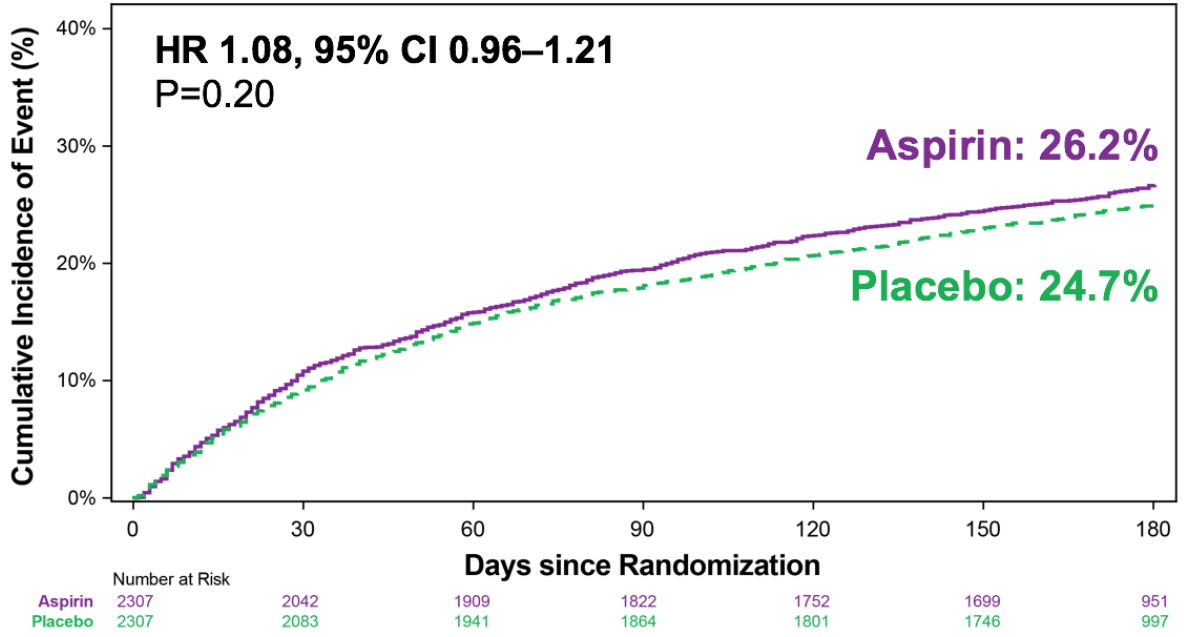
Apixaban + Placebo (7.3%)

Apixaban + Placebo vs. VKA + Aspirin: 11.4% absolute risk reduction (NNT=9)

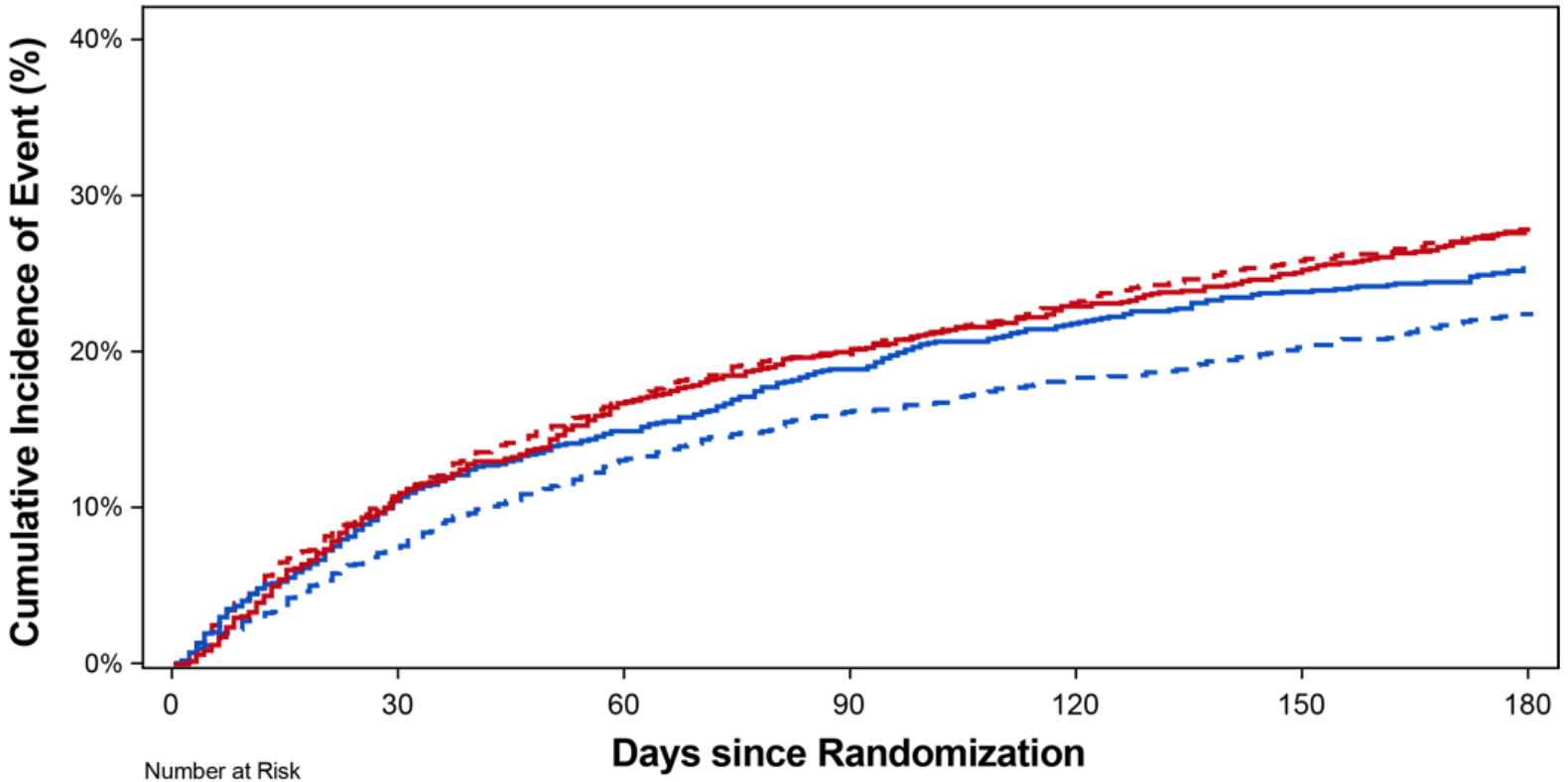
Death / Hospitalization
Apixaban vs. VKA



Death / Hospitalization
Aspirin vs. Placebo



Death / Hospitalization



Number at Risk

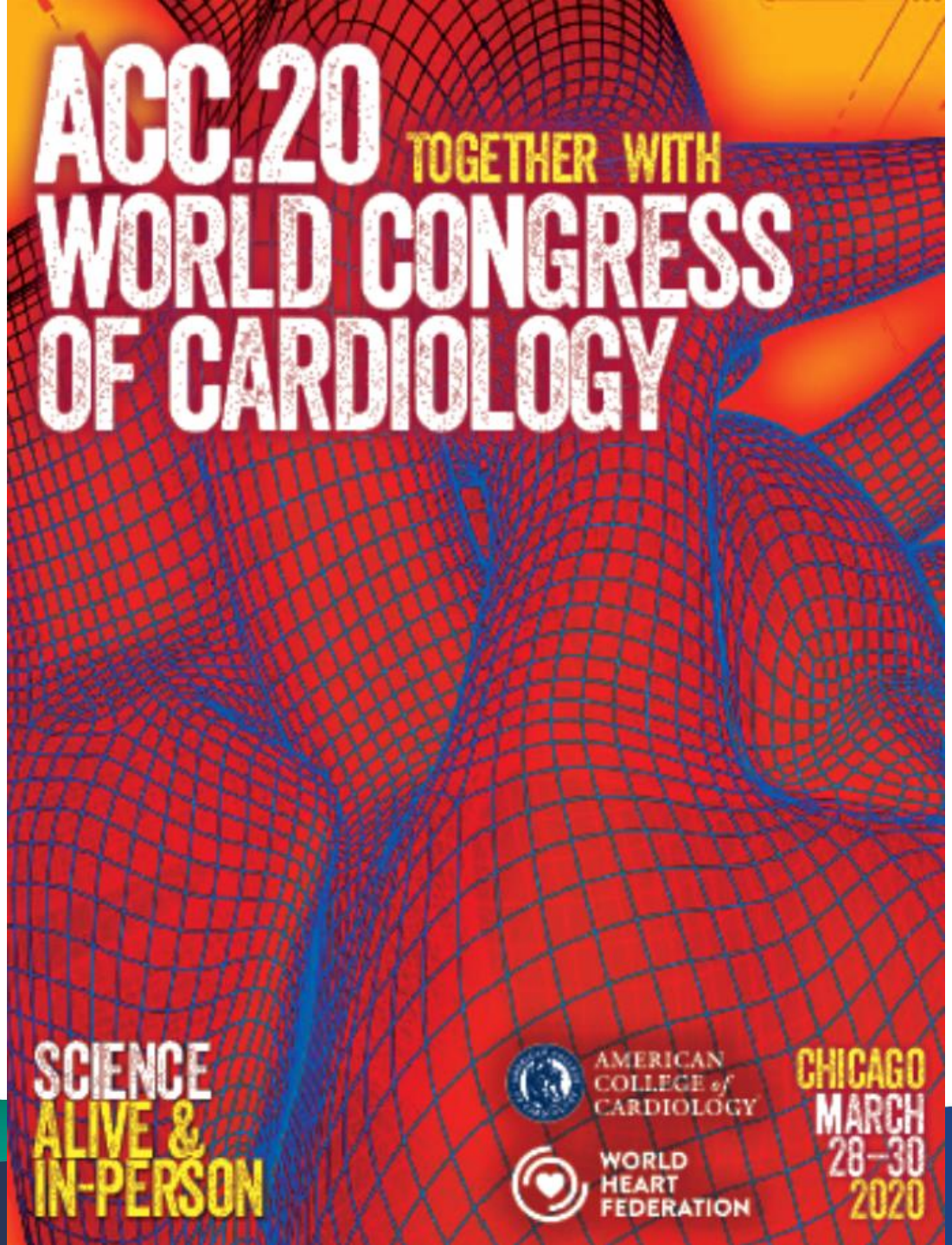
Apixaban and Aspirin	1153	1026	970	923	888	863	459
Apixaban and Placebo	1153	1064	995	958	933	909	488
VKA and Aspirin	1154	1016	939	899	864	836	492
VKA and Placebo	1154	1019	946	906	868	837	509

VKA + Aspirin (27.5%)
VKA + Placebo (27.3%)
Apixaban + Aspirin (24.9%)
Apixaban + Placebo (22.0%)

Apixaban + Placebo vs. VKA + Aspirin:
5.5% absolute risk reduction (NNT=18)

AUGUSTUS

- Conclusions:
  - In patients with AF and a recent ACS or PCI treated with a $P2Y_{12}$ inhibitor, antithrombotic regimen that included apixaban **without** aspirin resulted in
    - Less bleeding and fewer hospitalizations
    - No significant difference in ischemic events compared with regimens that included a vitamin K antagonist, aspirin, or both
- Potential Impact
  - Limited role for triple therapy in patients with AF and ACS or recent PCI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2020

Long-term Outcome of Partial Oral Treatment of Endocarditis: The POET trial

Henning Bundgaard, MD, Professor
Copenhagen University Hospital, Denmark
On behalf of the investigators

Background

- Infectious endocarditis is treated with IV antibiotics for up to 6 weeks (sometimes while hospitalized)
  - High in-hospital complication and mortality rates
  - Hospital stays *per se* may cause complications

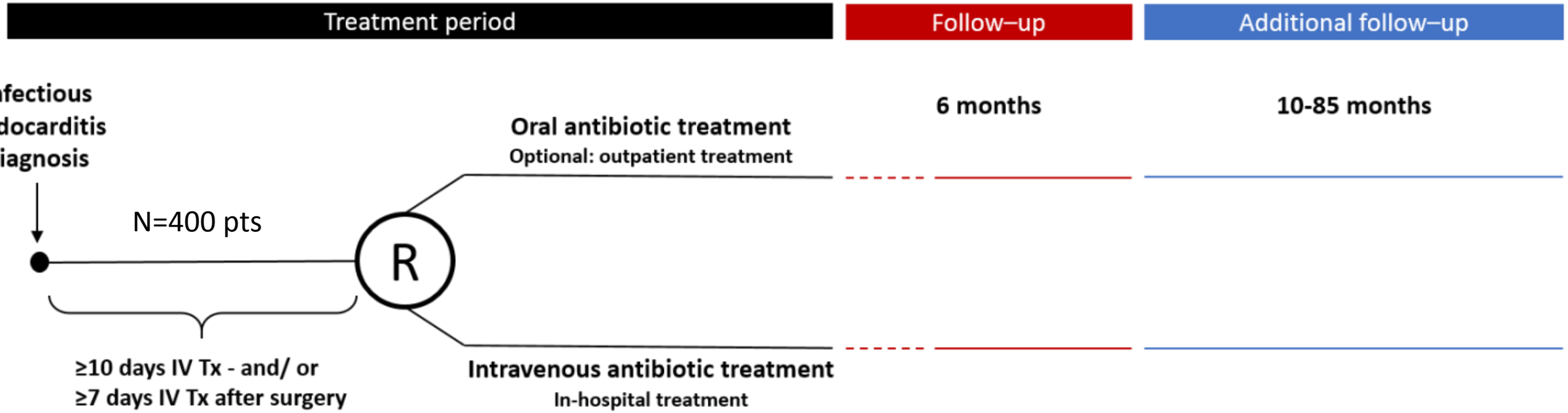
Study Design

- Objective: To determine whether in stabilized patients with left-sided endocarditis change to orally administered antibiotics has similar efficacy and safety as continued IV antibiotics
- Non-inferiority randomized trial
- Nationwide including all Danish Heart centers
- Subjects: stabilized patients with left-sided endocarditis
  - Streptococcus spp, Enterococcus faecalis, Staphylococcus aureus, or coagulase-negative staphylococci

Trial Design and Endpoint

Left-sided endocarditis based on the modified Duke criteria caused by:

Streptococci or *Enterococcus faecalis or Staphylococcus aureus or* Coagulase-negative staphylococci



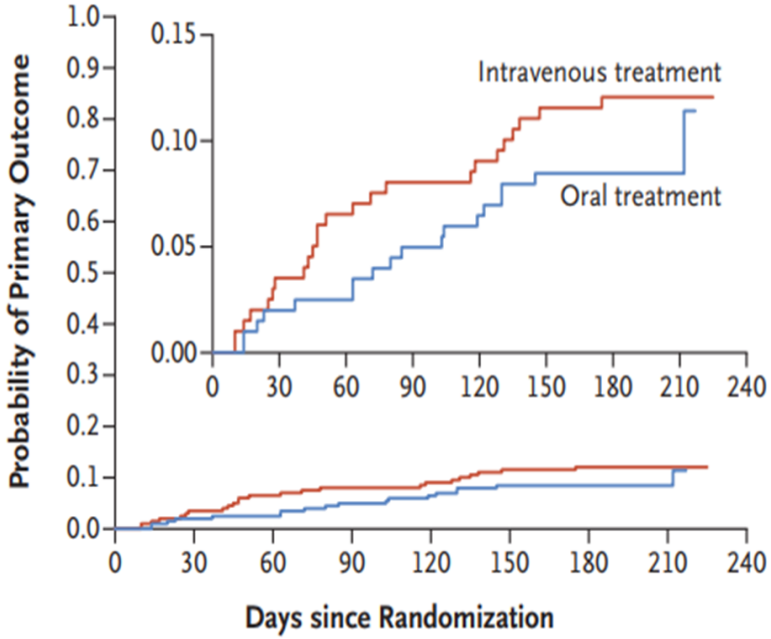
Endpoint: A composite endpoint ≤ 6 months:

All cause mortality, Unplanned cardiac surgery, Embolic events confirmed by imaging, Relapse of bacteremia with the primary pathogen

Results

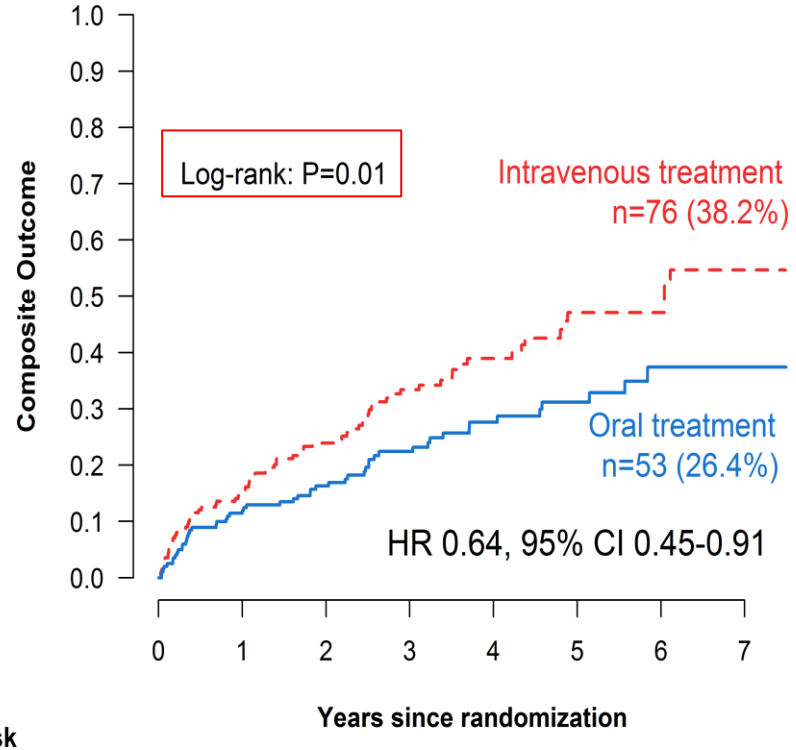
6 Months

Difference 3.1%, 95% CI: -3.4% - 9.6%,



No. at Risk									
Intravenous treatment	199	192	186	183	181	176	174	28	0
Oral treatment	201	197	196	191	188	184	183	36	0

Long Term



No. at Risk								
Intravenous treatment	199	169	127	89	57	34	21	4
Oral treatment	201	177	138	100	67	43	25	6

POET

- Conclusions
  - Efficacy and safety of changing to oral antibiotic treatment was non-inferior to continued IV antibiotic treatment in short term and long term:
    - Across co-morbidities, native vs prosthetic valve, and surgically vs conservatively treatment
  - Oral antibiotics may safely be administered during approximately
    - Half of the recommended antibiotic treatment period/ As outpatient treatment
  - > 50% of patients with endocarditis may be candidates for partial oral antibiotic treatment
- Potential Impact
  - Transition from IV to oral antibiotics earlier in stable patients with left-sided endocarditis
  - Ongoing patient evaluation still needed to determine if surgical valve replacement needed

Reduction in Total Ischemic Events in the Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial

Deepak L. Bhatt, MD, MPH, on behalf of the **REDUCE-IT** Investigators

reduce-it

JACC
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

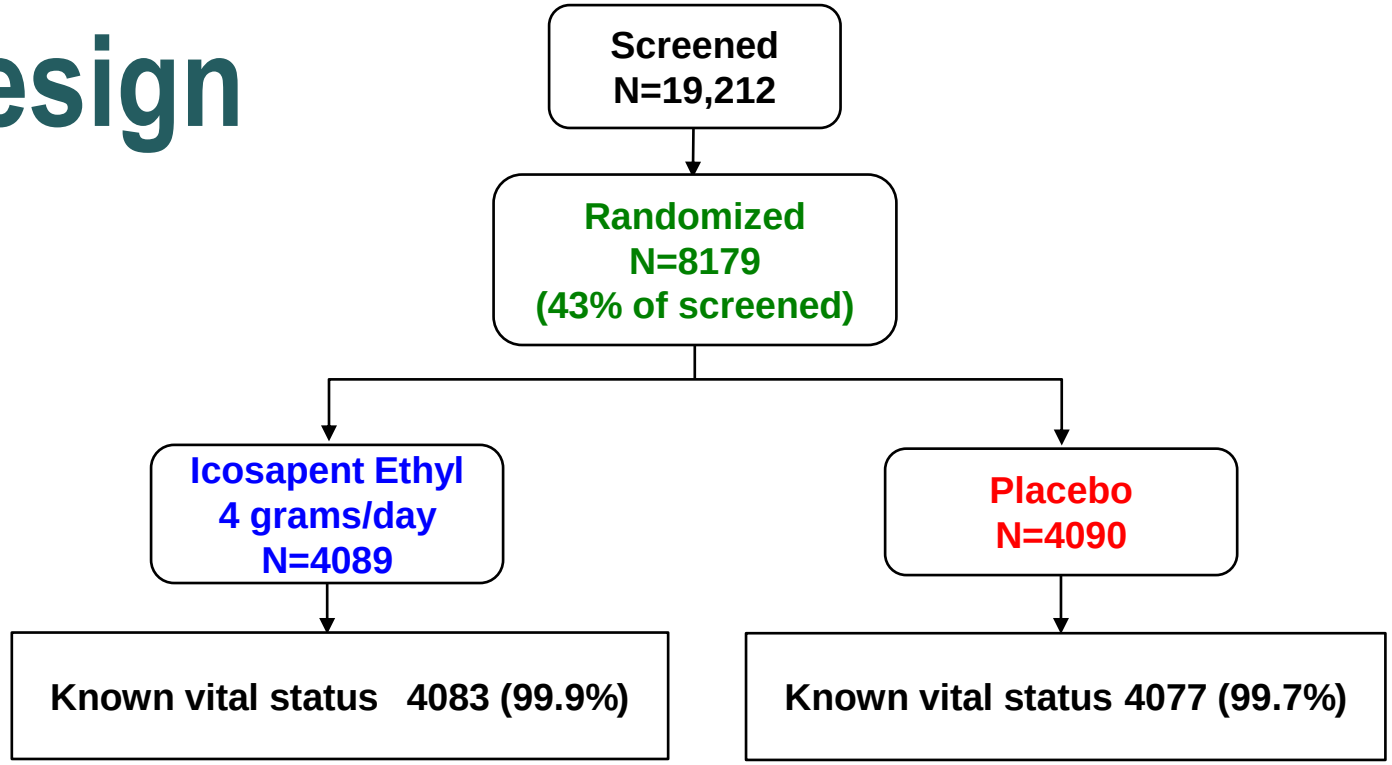
Effects of Icosapent Ethyl on Total Ischemic Events: From REDUCE-IT

Deepak L Bhatt, MD, MPH, Ph. Gabriel Steg, MD, Michael Miller, MD, Eliot A. Brinton, MD, Terry A. Jacobson, MD, Steven B. Ketchum, PhD, Ralph T. Doyle, Jr., BA, Rebecca A. Juliano, PhD, Lixia Jiao, PhD, Craig Granowitz, MD, PhD, Jean-Claude Tardif, MD, John Gregson, PhD, Stuart J. Pocock, PhD, Christie M. Ballantyne, MD, on Behalf of the REDUCE-IT Investigators*

Study Design

- Randomized, double blind trial
- Subjects:
  - 8,179 subjects
  - ≥45 years of age with established cardiovascular disease *(secondary prevention cohort)*
    - or
  - ≥50 years old with type 2 or type 1 diabetes mellitus and at least one additional cardiovascular risk factor *(primary prevention cohort)*
  - Fasting TG levels ≥135 mg/dL (1.5 mmol/L) and <500 mg/dL (5.6 mmol/L)
  - LDL-C >40 mg/dL (1 mmol/L) and ≤100 mg/dL (2.6 mmol/L) on stable statin therapy (± ezetimibe) for ≥4 weeks prior to randomization
- Compare icosapent ethyl 4 g/day vs. placebo

Study Design



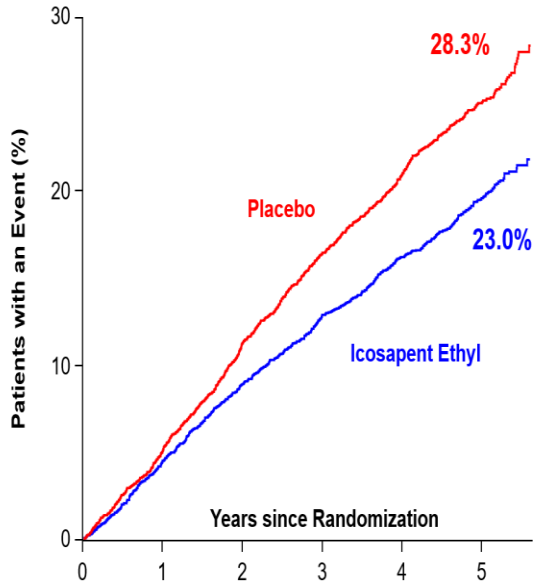
Median trial follow up duration was 4.9 years

Primary Endpoint Events: CV death, nonfatal MI, nonfatal stroke, coronary revascularization, hospitalization for unstable angina

Key Secondary Endpoint Events: CV death, nonfatal MI, nonfatal stroke

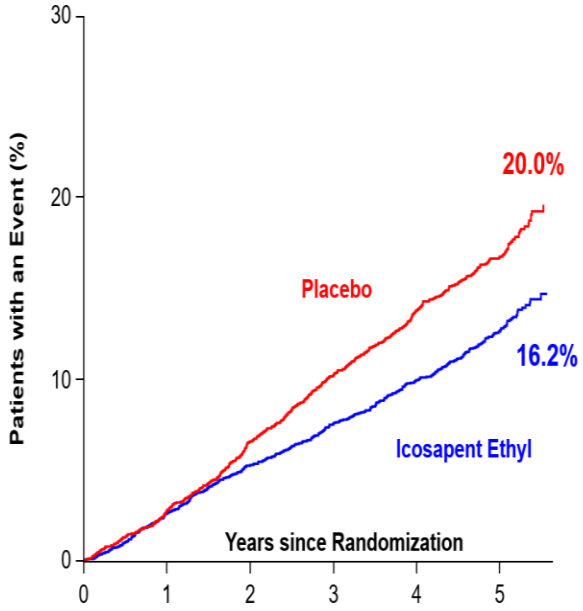
Topline Results: First Events
Presented AHA 2018

Results: Primary End Point
(1st event CV Death, MI, Stroke, Coronary Revasc, Unstable Angina)



Hazard Ratio, 0.75
(95% CI, 0.68–0.83)
RRR = 24.8%
ARR = 4.8%
NNT = 21 (95% CI, 15–33)
P=0.00000001

Key Secondary End Point:
CV Death, MI, Stroke

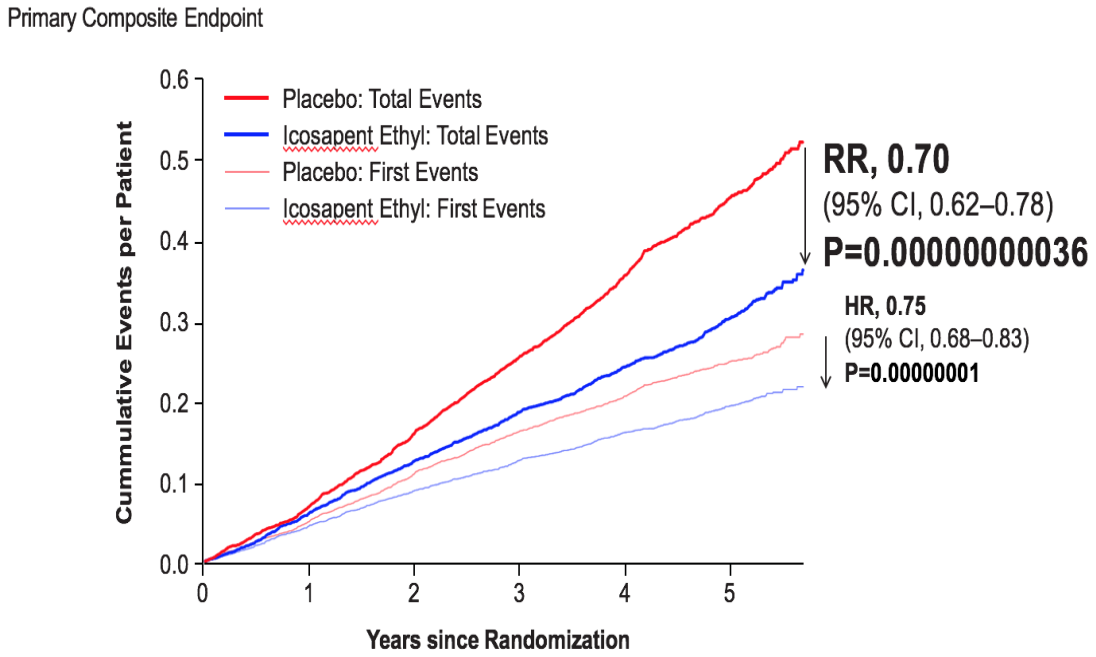


Hazard Ratio, 0.74
(95% CI, 0.65–0.83)
RRR = 26.5%
ARR = 3.6%
NNT = 28 (95% CI, 20–47)
P=0.0000006

Results: Total Events

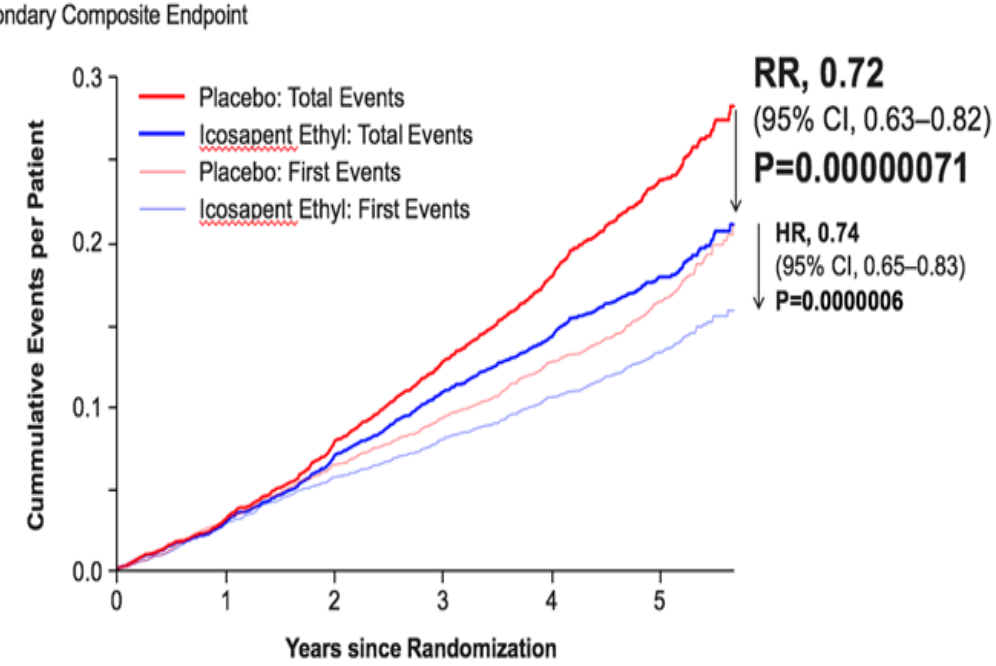
Total (First and Subsequent) Events

Primary: CV Death, MI, Stroke, Coronary Revasc, Unstable Angina

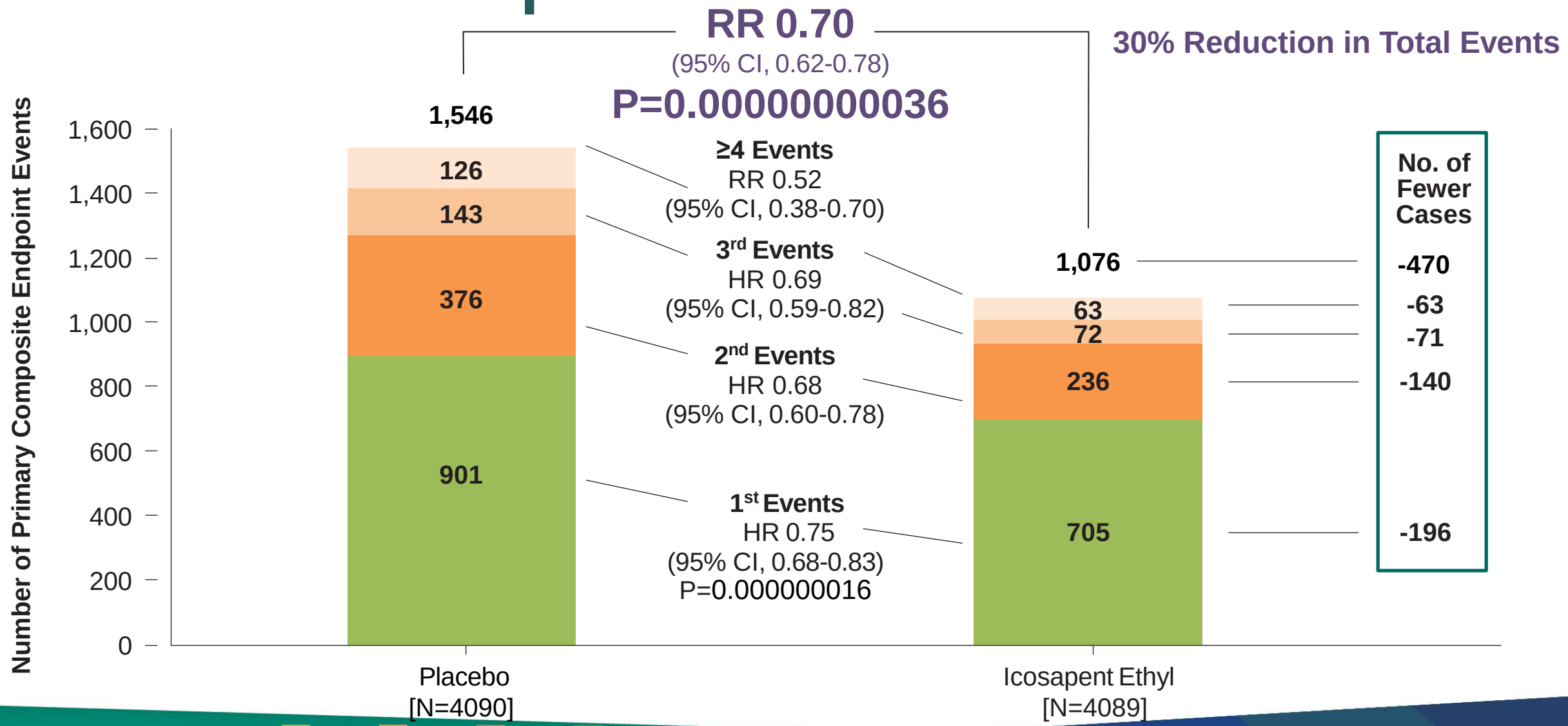


Total (First and Subsequent) Events

Key Secondary: CV Death, MI, Stroke



First and Subsequent Events



Bhatt DL, Steg PG, Miller M, et al. *J Am Coll Cardiol*. 2019.

Note: WLW method for the 1st events, 2nd events, and 3rd events categories; Negative binomial model for ≥4th events and overall treatment comparison.

REDUCE-IT

- Conclusions
  - Icosapent ethyl 4g/day significantly reduced overall **total** CV events by 30% vs placebo
    - 25% reduction in first cardiovascular events
    - 32% reduction in second cardiovascular events
    - 31% reduction in third cardiovascular events
    - 48% reduction in fourth or more cardiovascular events
  - Demonstrates
    - Large burden of ischemic events in statin-treated patients with baseline triglycerides $\geq$100 mg/dL
    - Potential role of icosapent ethyl in reducing residual risk
- Potential Impact
  - Reduce residual risk for CV events in patients with CAD (or diabetes and risk factors for CAD) with elevated triglycerides on statin + ezetimibe

Effect of Dapagliflozin on Heart Failure and Mortality in Type 2 Diabetes Mellitus

Results from the DECLARE-TIMI 58 Trial

Eri T. Kato, Michael G. Silverman, Ofri Mosenzon, Thomas A. Zelniker, Avivit Cahn, Remo H.M. Furtado, Julia Kuder, Sabina A. Murphy, Deepak L. Bhatt, Lawrence A. Leiter, Darren K. McGuire, John P.H. Wilding, Marc P. Bonaca, Christian T. Ruff, Akshay S. Desai, Shinya Goto, Peter A. Johansson, Ingrid Gause-Nilsson, Per Johanson, Anna Maria Langkilde, Itamar Raz, Marc S. Sabatine and Stephen D. Wiviott

On behalf of the DECLARE-TIMI 58 Investigators

doi/pdf/10.1161/CIRCULATIONAHA.119.039996

Study Design

- 17,160 patients with Type 2 diabetes and with established or multiple risk factors for ASCVD
  - randomized to dapagliflozin 10mg vs placebo

- Prespecified analysis planned to examine the clinical benefit of dapagliflozin in patients with and without HFrEF

doi/pdf/10.1161/CIRCULATIONAHA.119.039996

Baseline Characteristics

	HFrEF (n=671)	Not HFrEF (n=16,489)	
		HF without known rEF (n=1,316)	No hx of HF (n=15,173)
Age, yr, median (IQR)	63 (58, 68)	65 (60, 69)	64 (60, 68)
Male (%)	84	57	62
HbA1c, %, median (IQR)	8.1 (7.4, 9.2)	8.2 (7.5, 9.3)	8.0 (7.3, 9.0)
History of hypertension (%)	87	96	90
LVEF, %, median (IQR)	38 (30, 40)	55 (50, 61)	60 (55, 65)
Main etiology of HF (%)			
Ischemic	63	50	NA
Non-Ischemic	15	15	NA
Unknown	21	36	NA
Established ASCVD (%)	86	62	37
eGFR, mL/min/1.73m^2, median (IQR)	83 (66, 95)	86 (70, 96)	89 (76, 97)

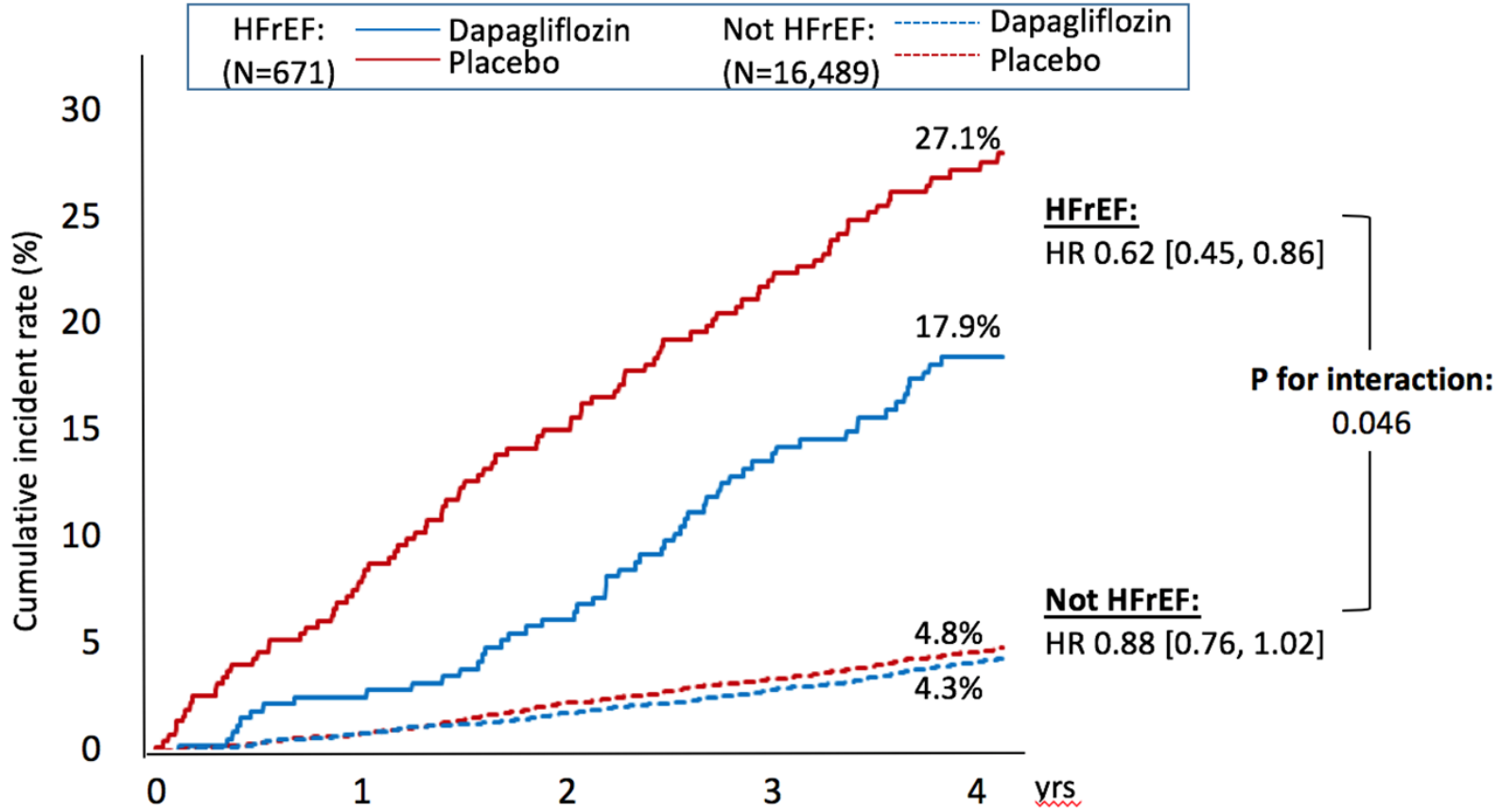
doi/pdf/10.1161/CIRCULATIONAHA.119.039996

Baseline Medications

	HFrEF (n=671)	Not HFrEF (n=16,489)	
		HF without known rEF (n=1,316)	No hx of HF (n=15,173)
ACEi or ARB (%)	88	85	81
Beta-blocker (%)	88	77	49
Diuretic (%)	67	63	37
Loop	46	35	7
Thiazide	13	18	23
Mineralocorticoid receptor antagonist (%)	30	14	2

doi/pdf/10.1161/CIRCULATIONAHA.119.039996

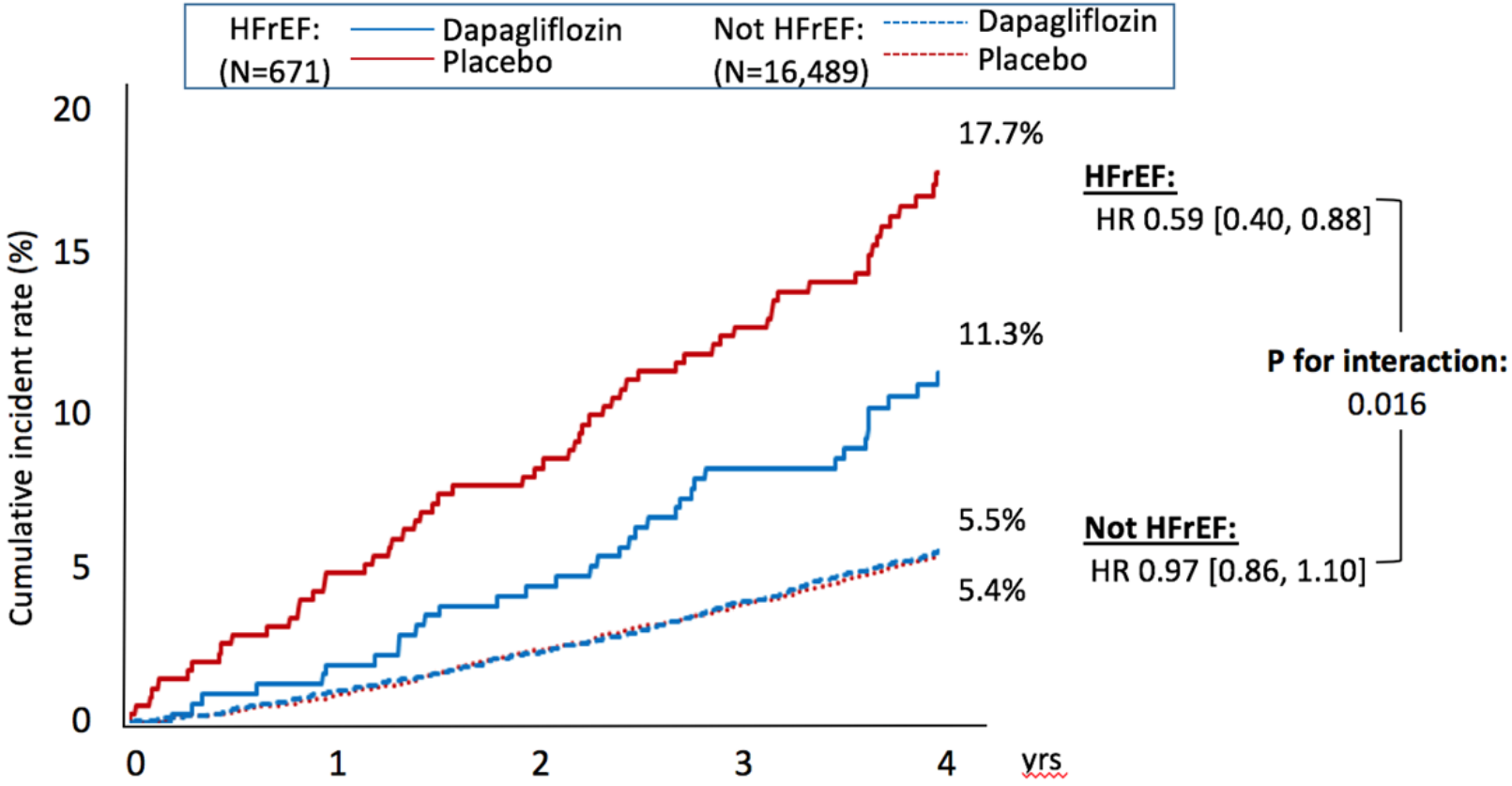
Results: CV Death/Heart Failure Hospitalizations



Not HFrEF defined as pts with HF without known reduced EF and pts without hx of HF

doi/pdf/10.1161/CIRCULATIONAHA.119.039996

Results: All-Cause Mortality



Not HFrEF defined as pts with HF without known reduced EF and pts without hx of HF

doi/pdf/10.1161/CIRCULATIONAHA.119.039996

Safety Analysis

		Dapagliflozin (%)	Placebo (%)	HR (95% CI)	P-interaction
Serious adverse event	*HFrEF*	56.9	58.8	0.87 (0.71-1.07)	0.754
	Not HFrEF	35.7	38.4	0.91 (0.87-0.96)	
Symptoms of volume depletion	*HFrEF*	7.5	5.6	1.52 (0.79-2.93)	0.204
	Not HFrEF	2.5	2.6	0.96 (0.79-1.18)	
Acute renal failure	*HFrEF*	8.2	14.0	0.57 (0.34-0.96)	0.240
	Not HFrEF	3.4	4.6	0.78 (0.66-0.91)	

doi/pdf/10.1161/CIRCULATIONAHA.119.039996

DECLARE-TIMI 58

- Conclusions
  - Treatment with dapagliflozin resulted in a lower rate of hospitalization for HF vs placebo in a broad spectrum of patients including those with preserved EF.
  - Dapagliflozin reduced CV death (NNT4y=19) and all-cause mortality (NNT4y=16) in patients with HFrEF, but not in those without HFrEF
  - These benefits were seen with similar safety profile for dapagliflozin regardless of HF status
- Potential Impact
  - SGLT2 inhibitors may provide an even greater benefit with lower CV death and mortality in patients with HFrEF

doi/pdf/10.1161/CIRCULATIONAHA.119.039996

Coronary Angiography after Cardiac Arrest without STEMI: The COACT trial

On behalf of the **COACT investigators**

Jorrit Lemkes, MD, Interventional cardiologist

Amsterdam UMC, Vrije Universiteit Amsterdam, the Netherlands

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Coronary Angiography after Cardiac Arrest without ST-Segment Elevation

J.S. Lemkes, G.N. Janssens, N.W. van der Hoeven, L.S.D. Jewbali, E.A. Dubois, M. Meuwissen, T.A. Rijpstra, H.A. Bosker, M.J. Blans, G.B. Bleeker, R. Baak, G.J. Vlachojannis, B.J.W. Eikemans, P. van der Harst, I.C.C. van der Horst, M. Voskuil, J.J. van der Heijden, A. Beishuizen, M. Stoel, C. Camaro, H. van der Hoeven, J.P. Henriques, A.P.J. Vlaar, M.A. Vink, B. van den Bogaard, T.A.C.M. Heestermans, W. de Ruijter, T.S.R. Delnoij, H.J.G.M. Crijns, G.A.J. Jessurun, P.V. Oemrawsingh, M.T.M. Gosselink, K. Plomp, M. Magro, P.W.G. Elbers, P.M. van de Ven, H.M. Oudemans-van Straaten, and N. van Royen

COACT - Introduction

- Out of Hospital Cardiac Arrest (OHCA) is a leading cause of death in Europe and the United States
  - Poor outcomes
  - Mortality remains 40% among patients with ROSC
- Most frequent cause of cardiac arrest is ischemic heart disease
  - CAD has been reported in up to 70% of patients after OHCA
  - Guidelines recommend immediate coronary angiography with PCI in patients who present with STEMI and cardiac arrest (class 1 LOE B)
- In patients with cardiac arrest *without* ST-elevation, guidelines also recommend emergency angiography (weak recommendation, very-low-quality evidence)
  - Based on observational data
  - No randomized trials have been performed

New Eng J Med. 2019 March 18. DOI: 10.1056/NEJMoa1816897

COACT

- Study Hypothesis: immediate coronary angiography will improve survival

Inclusion criteria

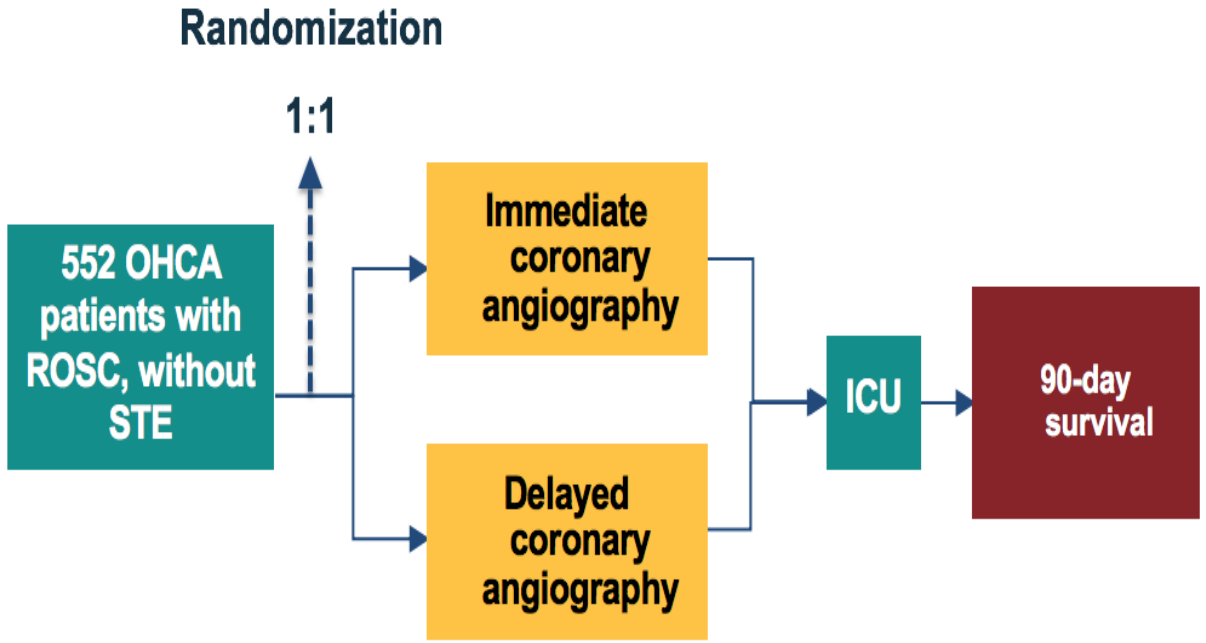
- Age >18 years
- Comatose patients (Glasgow coma score <8) with ROSC after OHCA
- Ventricular tachycardia or ventricular fibrillation as initial arrest rhythm
  - Including patients treated with an AED

Exclusion criteria

- Signs of STEMI on ECG in ED
- Hemodynamic instability unresponsive to medical therapy
- Refractory ventricular arrhythmia
- Obvious/suspected non-coronary cause of arrest
- Suspected/confirmed acute intracranial bleeding or acute stroke

New Eng J Med. 2019 March 18. DOI: 10.1056/NEJMoa1816897

Study Design



Primary endpoint:

- Survival at 90 days

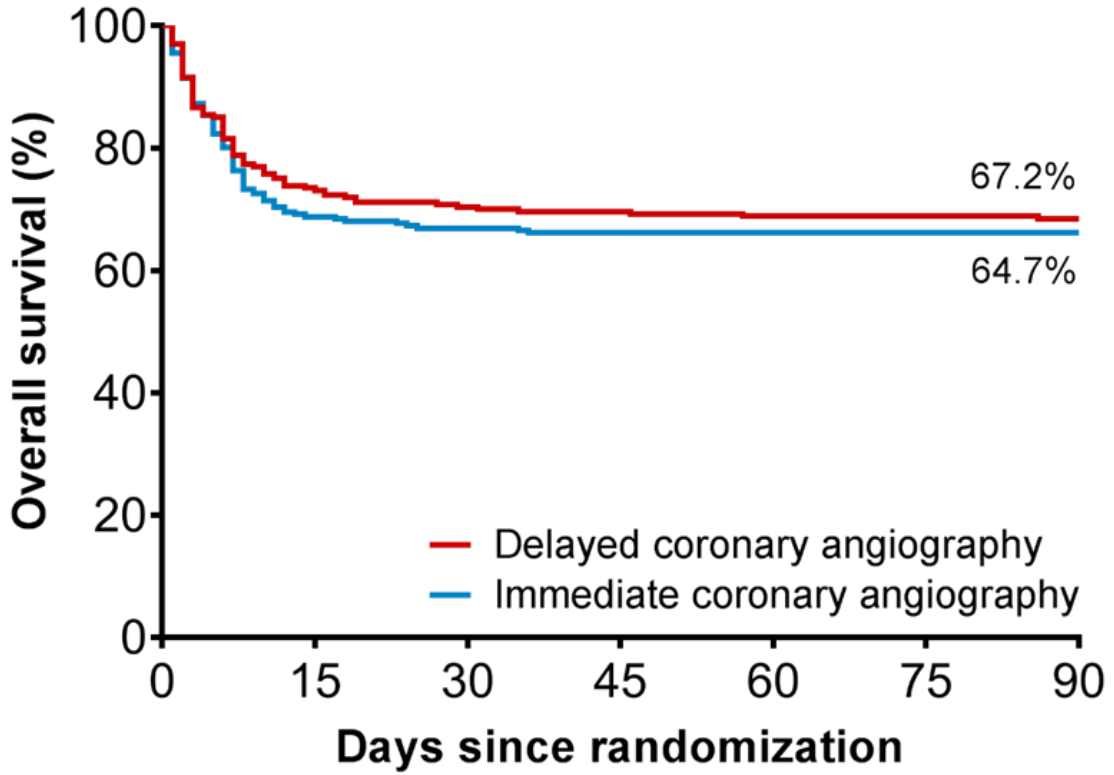
Secondary endpoints:

- Survival at 90 days with good cerebral performance or moderate disability
- TIMI major bleeding
- Recurrence of ventricular tachycardia
- Occurrence of acute kidney injury/ need for renal-replacement therapy
- Time to target temperature
- Duration of inotropic/catecholamine support
- Duration of mechanical ventilation
- Myocardial injury
- Markers of shock

New Eng J Med. 2019 March 18. DOI: 10.1056/NEJMoa1816897

Results – Overall Survival

Primary endpoint: Survival at 90 days



No. at risk							
Immediate	273	183	178	176	176	176	176
Delayed	265	191	183	181	179	179	178

New Eng J Med. 2019 March 18. DOI: 10.1056/NEJMoa1816897

COACT

- Conclusions
  - In patients with ROSC after OHCA without signs of STEMI, immediate coronary angiography was not found to improve survival at 90 days compared to delayed coronary angiography.
  - Patients allocated to immediate coronary angiography reached target temperature later as compared to delayed coronary angiography
  - No significant difference in myocardial injury between the two treatment groups
- Potential Impact
  - Rates for immediate coronary angiography may decline for patients with OHCA in the absence of STEMI

New Eng J Med. 2019 March 18. DOI: 10.1056/NEJMoa1816897

One-Month Dual Antiplatelet Therapy Followed by Clopidogrel Monotherapy versus Standard 12-Month Dual Antiplatelet Therapy with Clopidogrel After Drug-Eluting Stent Implantation:

Hirotoshi Watanabe

on behalf of STOPDAPT-2 investigators

Objective

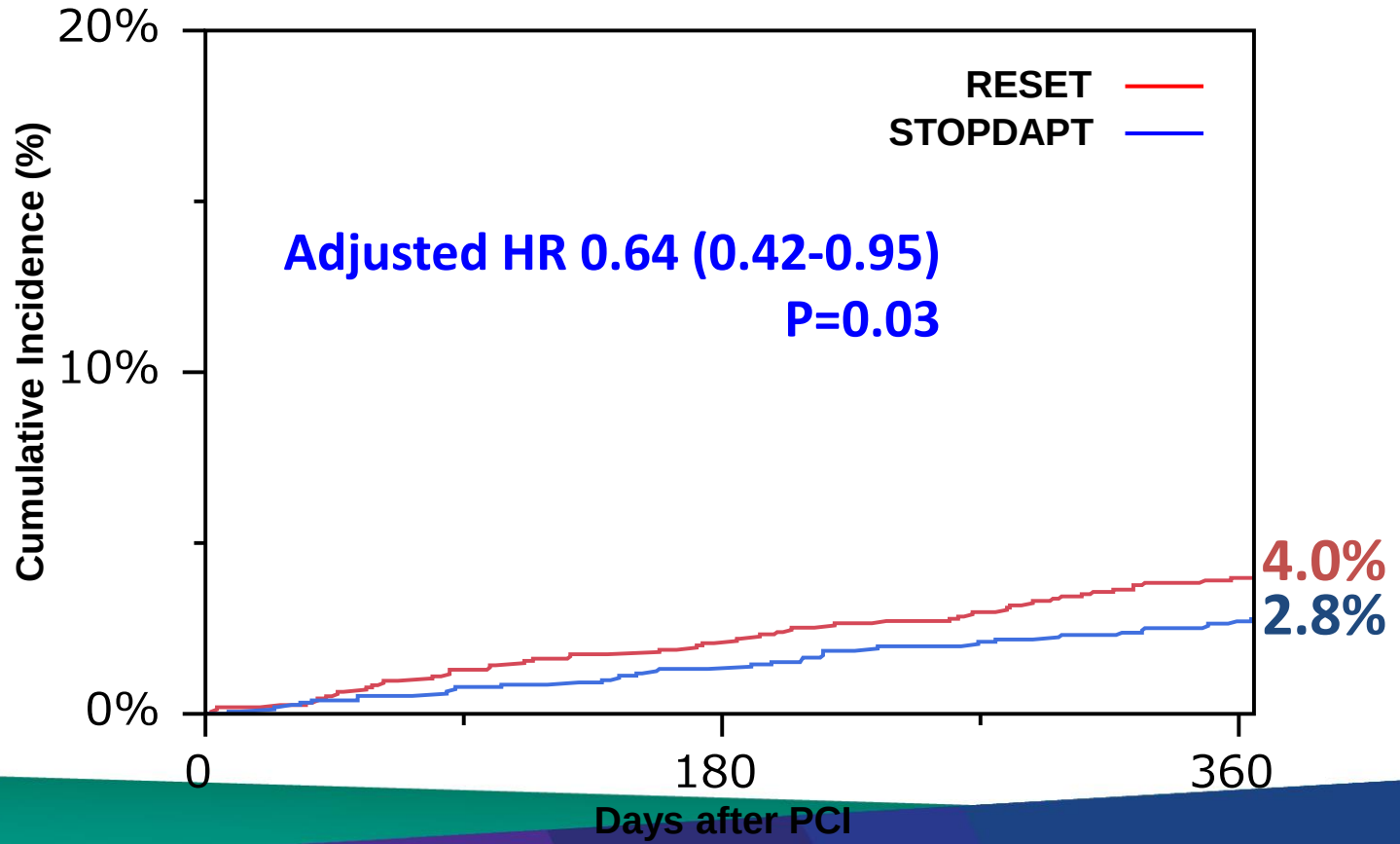
- Explore the safety and efficacy of the experimental regimen of
  - 1-month DAPT followed by clopidogrel monotherapy
  - Compared with standard 12-month DAPT with aspirin and clopidogrel
- After implantation of cobalt-chromium everolimus-eluting stents (CoCr-EES (Xience^{TM} series))

STOPDAPT

Prospective multicenter open-label single arm trial evaluating 3-month DAPT after CoCr-EES implantation

Primary Endpoint

Cardiovascular death, MI, Stroke, Definite ST, and Bleeding

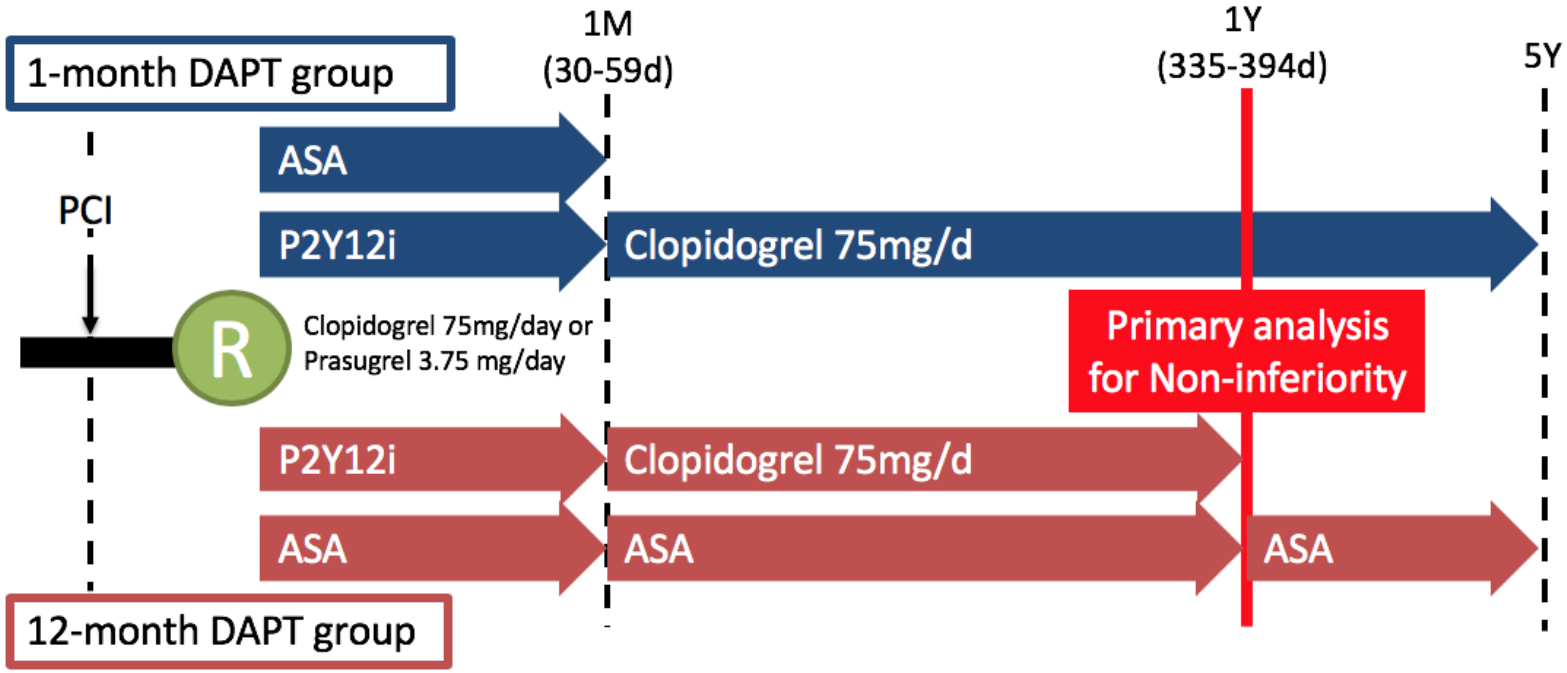


Cardiovasc Interv Ther 2016; 31: 196–209.

Study Design

STOPDAPT-2:

Prospective multicenter open-label randomized trial comparing 1-month versus 12-month DAPT after CoCr-EES implantation with limited exclusion criteria.



Inclusion criteria:

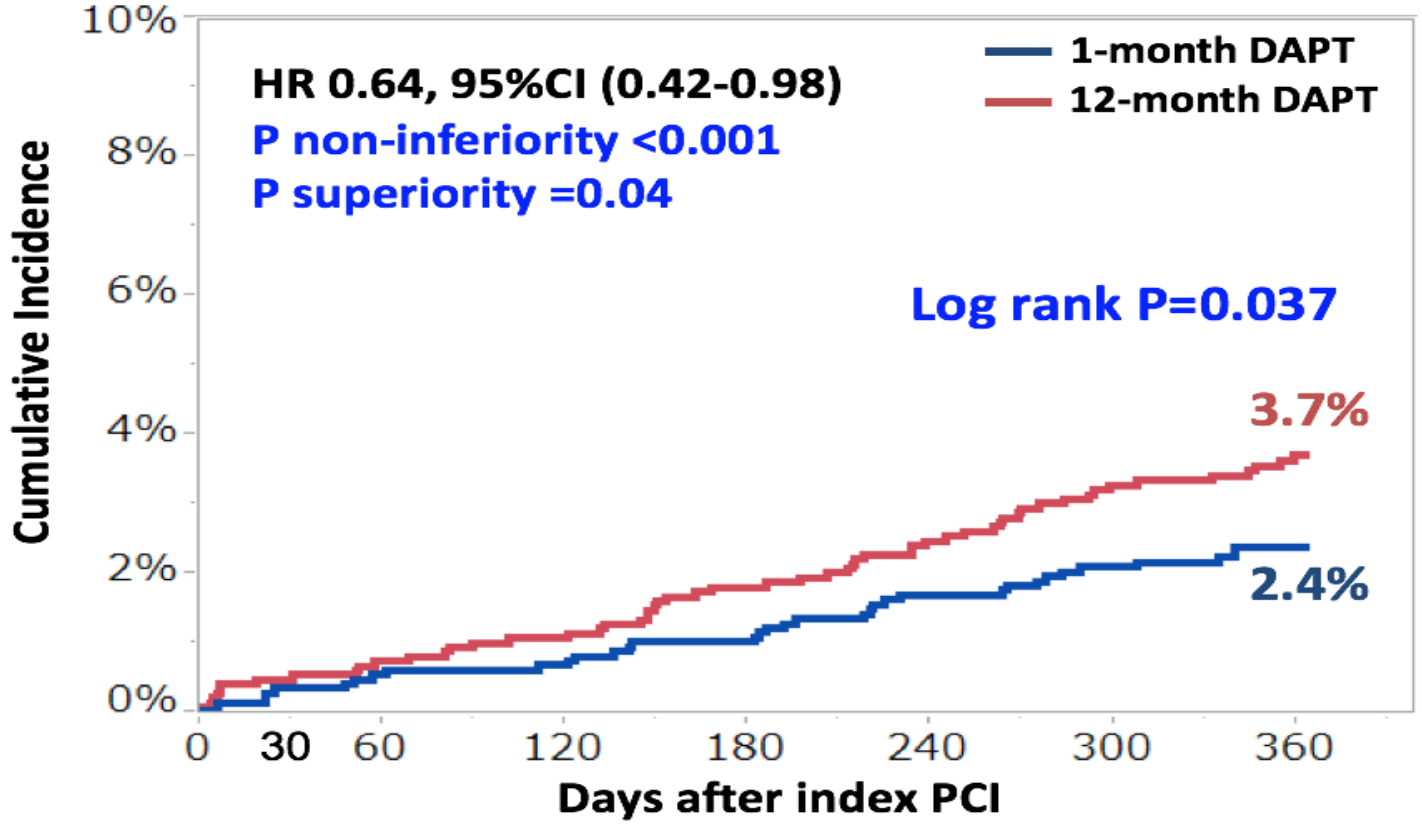
- Patients undergoing PCI in setting of acute coronary syndrome

Primary endpoint:

- A composite of cardiovascular death, MI, Definite ST, Stroke, or TIMI major/minor bleeding

Results: Primary Net Benefit

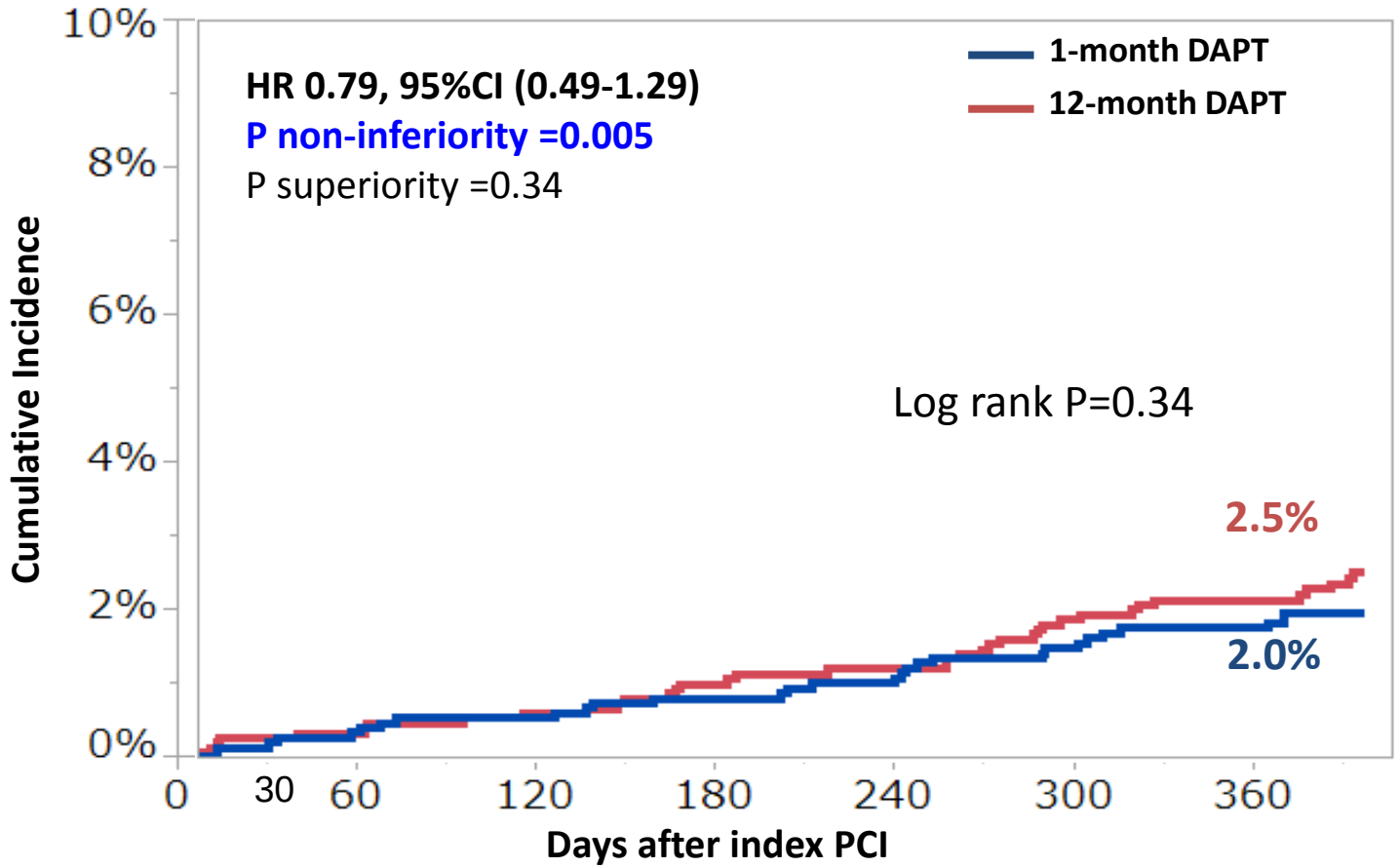
CV Death/MI/ST/Stroke/TIMI Major/Minor bleeding



No. at risk								
12-month DAPT	1509	1501	1486	1481	1469	1458	1442	1159
1-month DAPT	1500	1494	1479	1475	1468	1453	1441	1151

Major secondary ischemic endpoint

CV death/MI/ST/Stroke

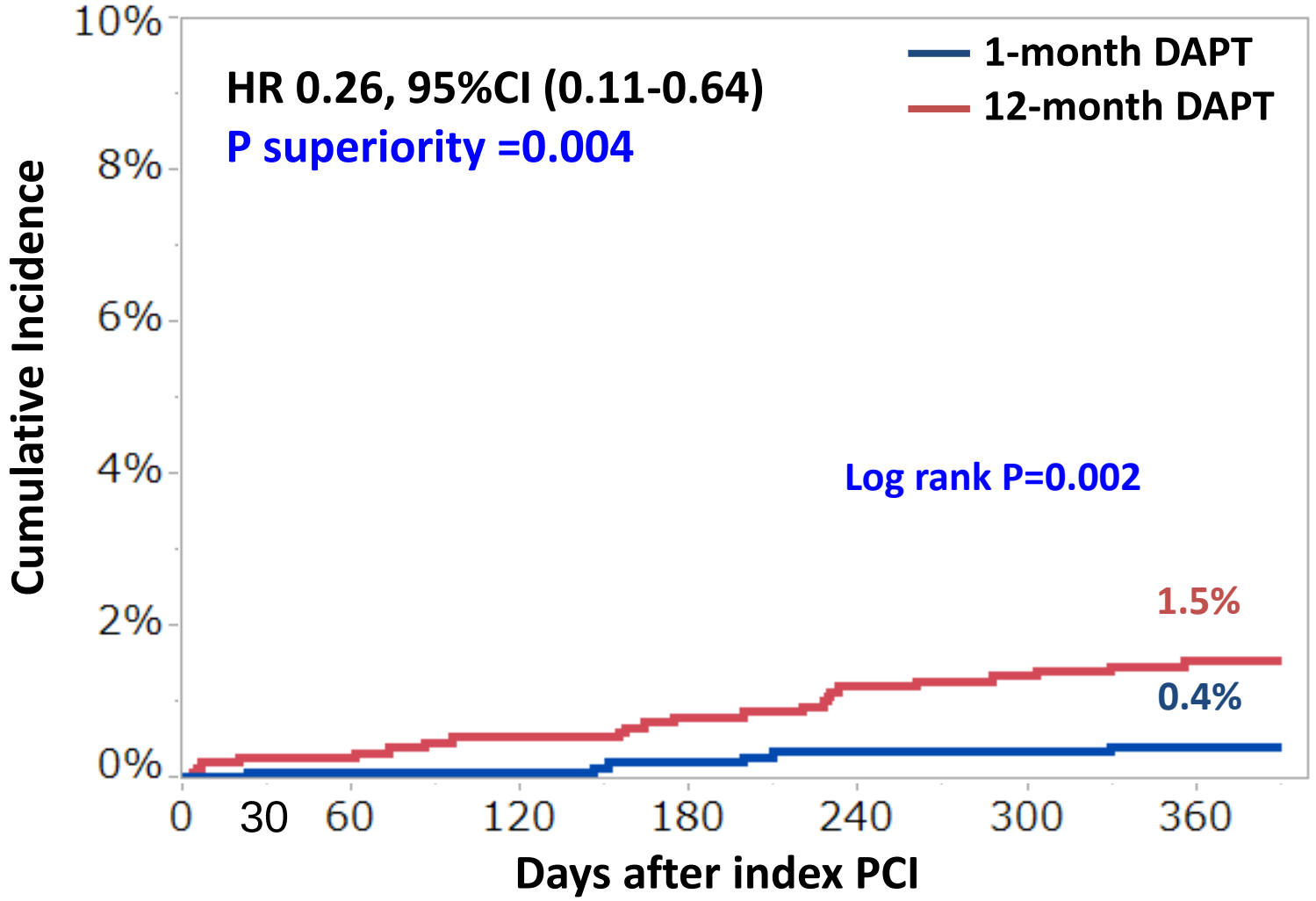


Days after index PCI

No. at risk								
12-month DAPT	1509	1504	1490	1488	1479	1473	1458	1172
1-month DAPT	1500	1495	1480	1476	1471	1458	1446	1157

Major secondary bleeding endpoint

TIMI major/minor bleeding



No. at risk								
12-month DAPT	1509	1504	1491	1487	1480	1471	1462	1180
1-month DAPT	1500	1495	1483	1481	1477	1467	1457	1166

STOPDAPT-2

- Conclusions
  - One-month DAPT followed by clopidogrel monotherapy provided a net clinical benefit for ischemic and bleeding events over 12-month DAPT with aspirin and clopidogrel after CoCr-EES implantation
  - Benefit driven by significant reduction in bleeding events without increase in ischemic events
- Potential Impact
  - Shorter duration (1-3 months) of DAPT following PCI followed by P2Y12 monotherapy may be a reasonable strategy in many patients

The World-Wide Randomized Antibiotic Envelope Infection Prevention Trial (WRAP-IT) to Reduce CIED Infection

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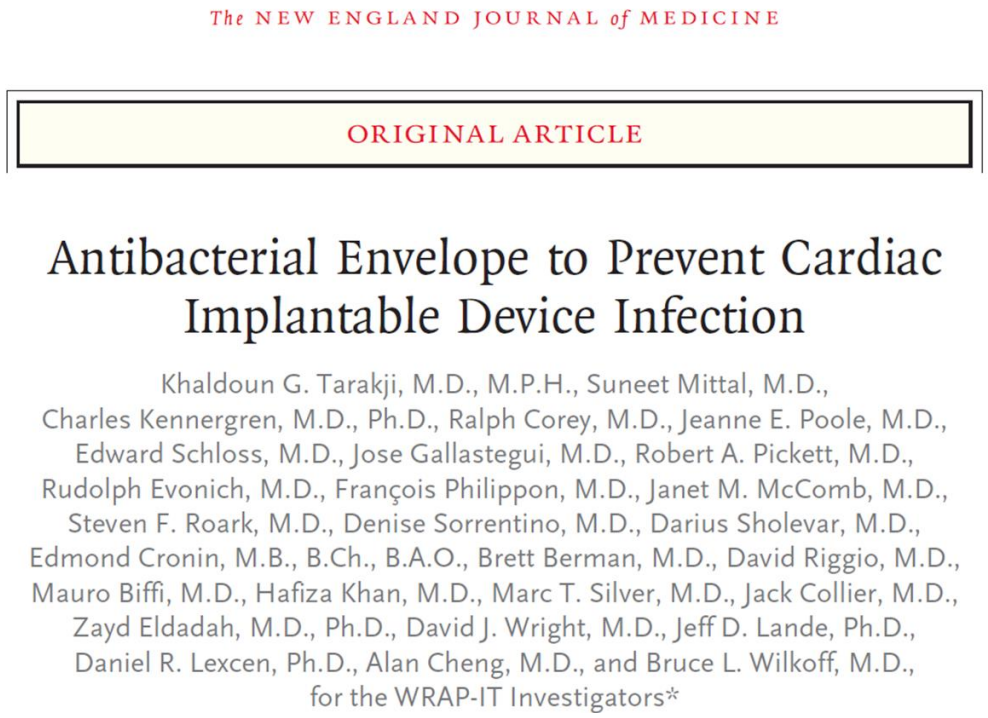
Cleveland Clinic, Cleveland, OH
For the WRAP-IT Investigators



TYRX Absorbable Antibacterial Envelope

- Single-use device
- Absorbable multifilament knitted mesh
- Polymer-controlled antibiotic elution
- Locally delivered minocycline and rifampin sustained for 7 days
- Fully absorbed in ~9 weeks

New Eng J Med. 2019 March 18.doi/pdf/10.1056/NEJMoa1901111

Objective

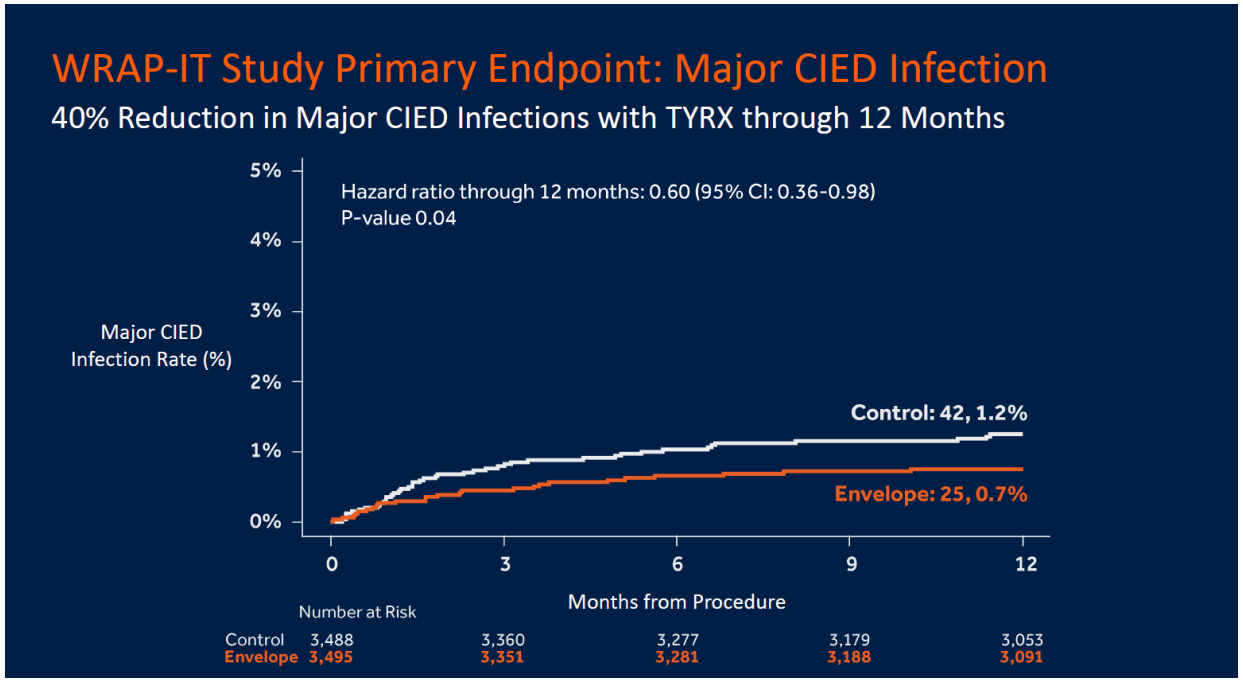
- To evaluate safety and effectiveness of the TYRX envelope in reducing CIED infections in addition to standard infection prevention strategies

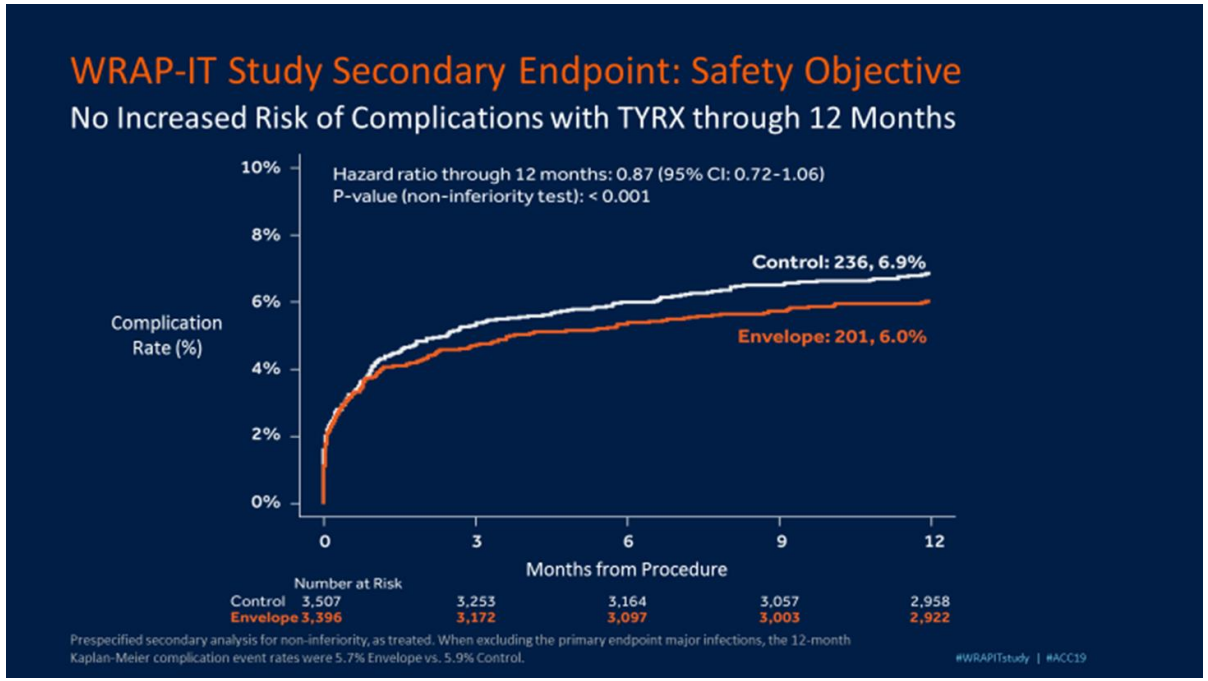
Study Design

- Prospective, randomized, controlled, multicenter, global trial
- Study patients (6,983 pts, 25 countries)
  - Cardiac implantable electronic device (CIED) generator replacement, system upgrade, or revision
  - Initial CRT-D
- Randomized 1:1 to TYRX envelope vs control
- Primary endpoint:
  - Rate of major CIED infections through 1 year post-procedure
  - TYRX vs control

New Eng J Med. 2019 March 18.doi/pdf/10.1056/NEJMoa1901111

Results

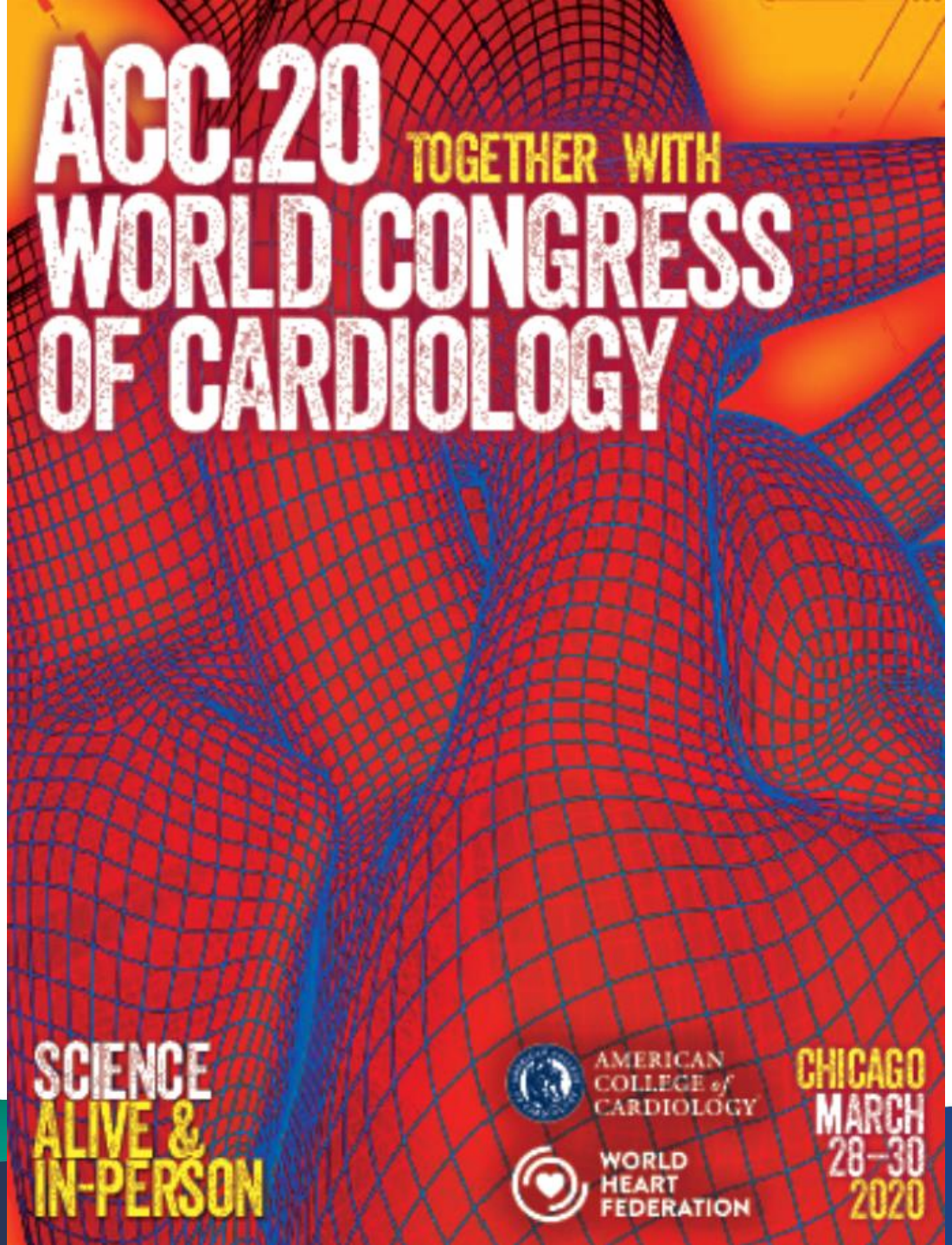




New Eng J Med. 2019 March 18.doi/pdf/10.1056/NEJMoa1901111

WRAP-IT

- Conclusions
  - TYRX envelope significantly reduced major CIED infections by 40%, without increasing complications
  - Reduced major pocket infections reduced by 61%
- Potential impact
  - Increasing role for absorbable antibacterial envelope compared to standard infection prevention strategies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