Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Maron DJ, Hochman JS, Reynolds HR, et al. Initial invasive or conservative strategy for stable coronary disease. N Engl J Med 2020;382:1395-407. DOI: 10.1056/NEJMoa1915922

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Table of Contents

Contents

I. ISCHEMIA Committee, CCC, Trial-Related Personnel

Past and Current Committee Members

Leadership Committee

Judith S. Hochman (Chair)
David J. Maron (Co-Chair)
William Boden (Co-Principal Investigator)
Bruce Ferguson (Co-Principal Investigator)
Robert Harrington (Co-Principal Investigator)
Gregg W. Stone (Co-Principal Investigator)
David Williams (Co-Principal Investigator)

Executive Committee

Judith S. Hochman (Chair)
David J. Maron (Co-Chair)
Karen P. Alexander
Sripal Bangalore
Jeffrey Berger
William Boden
Robert Harrington
Daniel Mark
Sean M. O'Brien
Harmony R. Reynolds
Yves Rosenberg
Leslee J. Shaw
John Spertus
Gregg W. Stone

Steering Committee

Judith S. Hochman (Chair)
David J. Maron (Co-Chair)
Members of Executive Committee
Christie Ballantyne*
Daniel Berman
Rafael Beyar*
Balram Bhargava
Chris Buller*
Antonio (Tony) Carvalho**
Bernard R. Chaitman
Rafael Diaz*
Rolf Doerr
Vladimir Dzavik
Bruce Ferguson
Shaun Goodman
Gilbert Gosselin

Rory Hachamovitch*
Christian Hamm*
Claes Held
Malte Helm*
Kurt Huber*
Lixin Jiang
Matyas Keltai
Shun Kohsaka
Irene Lang*
Renato Lopes
Jose Lopez-Sendon
Aldo Maggioni
John Mancini
C. Noel Bairey Merz
James Min
Eric Peterson*
Michael H. Picard
Witold Ruzyllo
Joseph Selvanayagam
Roxy Senior
Tali Sharir
Gabriel Steg
Hanna Szwed
Frans Van de Werf*
William Weintraub
Harvey White
David Williams

Optimal Medical Therapy Committee
William Boden (Co-Chair)
David J. Maron (Co-Chair)
Christie Ballantyne
Sripal Bangalore
Karen Calfas **
Bernard R. Chaitman
Mary Ann Champagne
Michael Davidson
Jerome Fleg
Peter A. McCullough
Jonathan Newman
Peter Stone

Optimal Revascularization Therapy Planning Committee
Gregg W. Stone (Chair)

Subcommittee: CABG
Bruce Ferguson (Co-Chair)
Philippe Menasche (Co-Chair)
Sripal Bangalore
Michael Davidson**
Stephen Fremes
Robert Guyton
Michael Mack
Fred Mohr
Anupama Rao
Joe Sabik
Oz Shapira
David Taggart
James Tatoulis

Subcommittee: PCI
David Williams (Co-Chair)
Sripal Bangalore
Jim Blankenship
Sorin Brener
Chris Buller
Antonio Colombo
Bernard de Bruyne
Philippe Généreux
Robert Harrington
Dean Kereiakes
Thierry Lefevre
Jeffrey Moses

Clinical Events
Endpoint Definition Panel
Bernard R. Chaitman (Chair)
Karen P. Alexander
Judith S. Hochman
Ken Mahaffey
David J. Maron
Gregg W. Stone
Harvey White
Clinical Event Review Committee
Bernard R. Chaitman (Chair)
Salvador Cruz-Flores
Nicholas Danchin
Eli Feen
Mario J. Garcia

Paul Hauptman
Abhay A. Laddu
Eugene Passamani
Ileana L. Pina
Maarten Simoons
Hicham Skali
Kristian Thygesen
David Waters

CEC Administrative Group

Karen P. Alexander
Patricia Endsley*
Gerard Esposito
Jeffrey Kanters
John Pownall
Dimitrios Stournaras

ISCHEMIA Imaging Committee

Leslee J. Shaw (Chair)
Daniel Berman
Matthias Friedrich
Rory Hachamovitch
Raymond Kwong
John Mancini
James Min
Dana Oliver
Michael H. Picard
Harmony R. Reynolds

Biostatistics Planning Committee

Frank Harrell (Chair)
Jeffrey Blume
Kerry Lee
Sean M. O'Brien

BioRepository Committee

Jeffrey Berger (Chair)
Claes Held
Iftikhar Kullo
Bruce McManus
Kristin Newby

EQOL Committee

Daniel Mark (Co-Chair)
John Spertus (Co-Chair)

David Cohen
William Weintraub

Recruitment for Women & Minorities
C. Noel Bairey Merz (Chair)
Raffaele Bugiardini
Jelena Celutkiene
Jorge Escobedo
Angela Hoye
Radmila Lyubarova
Deirdre Mattina
Jesus Peteiro
Harmony R. Reynolds
Paola Smanio

Publications
David J. Maron (Chair)
Karen P. Alexander
Sripal Bangalore
Jeffrey Berger
William Boden
Robert Harrington
Judith S. Hochman
Sean M. O'Brien
Harmony R. Reynolds
Yves Rosenberg
Gregg W. Stone

Publication Subcommittees

Economics
Daniel Mark (Chair)
John Spertus

QOL
John Spertus (Chair)
Daniel Mark

Stress Testing
Leslee J. Shaw (Chair)
Dan Berman
Bernard R. Chaitman
Jerome Fleg
Raymond Kwong
Michael H. Picard
Harmony R. Reynolds
Roxy Senior

CCTA

James Min (Chair)
Jonathan Leipsic
John Mancini

Angiography/Optimal Revascularization Therapy

Gregg W. Stone (Chair)
Ziad Ali (Co-chair)
Sripal Bangalore
T. Bruce Ferguson
David Williams
(Philippe Genereux, former Chair, Angiography Subcommittee)*

Optimal Medical Therapy

William Boden (Co-Chair)
David J. Maron (Co-Chair)
Jerome Fleg
Jonathan Newman

Biorepository

Jeffrey Berger (Chair)

CEC

Bernard R. Chaitman (Chair)
Karen P. Alexander

CKD

Sripal Bangalore (Chair)
Karen P. Alexander
Jerome Fleg
Judith S. Hochman
David J. Maron
Roy Mathew
Sean M. O'Brien
Harmony R. Reynolds
Mandeep Sidhu

CIAO

Harmony R. Reynolds (Chair)

DSMB Members

Lawrence Friedman (Chair)
Jeffrey Anderson
Jessica Berg *
David DeMets
C. Michael Gibson
Gervasio Lamas
Nicole Deming
Jonathan Himmelfarb
Pamela Ouyang

Pamela Woodard

Independent Statistical Analysis Center for DSMB Reporting

Frank Harrell
Samuel Nwosu

NHLBI Program Staff

Project Office
Yves Rosenberg (Project Officer)
Jerome Fleg
Ruth Kirby
Statisticians
Neal Jeffries

ISCHEMIA Clinical Coordinating Center (CCC)

Study Leadership
Judith S. Hochman (Study Chair, Director of CCC)
David J. Maron (Study Co-Chair, Co-Director of CCC, US Country Leader)
CCC Faculty
Sripal Bangalore (Optimal Revascularization Therapy CCC Director, Regional Leader)
Jeffrey Berger (Director of the Biorepository, Regional Leader)
William Boden (US-VA Regional Leader)
Jonathan Newman (Optimal Medical Therapy CCC Director, Regional Leader)
Harmony R. Reynolds (Associate Director of CCC, CCC Imaging Lead, Regional Leader)
Mandeep Sidhu (US-VA Regional Co-Leader)
Program Directors
Jean E. Denaro***
Stephanie Mavromichalis
Project Managers
Kevin Chan
Gia Cobb*
Aira Contreras
Diana Cukali*
Stephanie Ferket*
Andre Gabriel*
Antonietta Hansen*
Arline Roberts
Clinical Research Associates
Michelle Chang
Sharder Islam*
Graceanne Wayser*
Solomon Yakubov*
Michelle Yee

Clinical Trial Assistants
Caroline Callison
Isabelle Hogan
Albertina Qelaj*
Charlotte Pirro*
Kerrie Van Loo
Brianna Wisniewski*
Grants and Finance Administration
Margaret Gilsenan (Grants Manager)
Bevin Lang
Samaa Mohamed
Publications Team
Jihyun Lyo (Publications Manager)
Nadia Gakou
Data Analyst
Vincent Setang*
Mark Xavier*

Statistical and Data Coordinating Center (SDCC)

Sean M. O'Brien (Principal Investigator)
Karen P. Alexander (Co-Principal Investigator)
Akshay Bagai*
Samuel Broderick
Michelle Crowder
Derek Cyr
Patricia Endsley
Jyotsna Garg
Xiangqiong Gu
Robert
Harrington*
Lisa Hatch
Anne Heath*
Zhen Huang
Jeffrey Kanters
Kerry Lee*
Jeff Leimberger
Jill Marcus
Courtney Page
Wanda Parker*
Wayne Pennachi
John Pownall
Frank Rockhold
Susanna Stevens
Allegra Stone

Dimitrios
Stournaras
Omar Thompson
Sheri Ussery
Jennifer White*
Mary (Kaye)
Williams
Weibing Xing
Songlin Zhu

Economics and Quality of Life Coordinating Center (EQOL CC)

Duke Clinical Research Institute, Durham, NC
Daniel B. Mark (Principal Investigator)
Kevin Anstrom
Khaula Baloch
Janet Blount
Patricia Cowper
Linda Davidson-Ray
Laura Drew
Tina Harding
J David Knight
Diane Minshall Liu
Betsy O'Neal
Thomas Redick

Saint Luke's Mid America Heart Institute, Kansas City, MO
John Spertus (Principal Investigator)
Philip Jones
Karen Nugent
Grace Jingyan Wang

ISCHEMIA Imaging Coordinating Center (ICC)

Leslee J. Shaw (Principal Investigator)
Lawrence Phillips
Abhinav Goyal
Holly Hetrick
Dana Oliver
Nuclear Core Lab
Daniel Berman (Director)
Sean W. Hayes (Co-Director)
John D. Friedman
R. James Gerlach
Mark Hyun
Romalisa Miranda-Peats

Piotr Slomka
Louise Thomson
CMR Core Lab
Raymond Y. Kwong (Director)
Matthias Friedrich (Director)*
Francois Pierre Mongeon (Co-Director)
Steven Michael
Echo Core Lab
Michael H. Picard (Director)
Judy Hung
Marielle Scherrer-Crosbie
Xin Zeng

ECG/ETT CoreLab

Bernard R. Chaitman (Director)
Jane Eckstein
Bandula Guruge
Mary Streif

Angiographic Core Lab

Ziad Ali (Director)
Philippe Genereux (Director)*
Maria A. Alfonso
Maria P. Corral
Javier J. Garcia
Jennifer Horst
Ivana Jankovic
Maayan Konigstein
Mitchel B. Lustre*
Yolayfi Peralta
Raquel Sanchez

CCTA Core Lab

James Min (Director)
Reza Arsanjani
Matthew Budoff
Kimberly Elmore
Millie Gomez
Cameron Hague
Niree Hindoyan
Jonathan Leipsic
GB John Mancini
Rine Nakanishi
M. Barbara Srichai-Parsia

Eunice Yeoh
Tricia Youn

Academic Research Organizations (AROs)

Associazione Nazionale Medici Cardiologi Ospedalieri (ANMCO) -Italy & Switzerland
Aldo P. Maggioni (Country Leader)
Francesca Bianchini
Martina Ceseri
Andrea Lorimer
Marco Magnoni
Francesco Orso
Laura Sarti
Martinia Tricoli*
Brazilian Clinical Research Institute (BCRI) - Brazil
Antonio Carvalho (Country Leader)**
Renato Lopes (Country Leader)
Lilian Mazza Barbosa
Tauane Bello Duarte
Tamara Colaiácovo Soares
Julia de Aveiro Morata
Pedro Carvalho
Natalia de Carvalho Maffei
Flávia Egydio*
Anelise Kawakami*
Janaina Oliveira*
Elissa Restelli Piloto*
Jaqueline Pozzibon*
Canadian Heart Research Centre (CHRC) - Canada
Shaun Goodman (Country Leader)
Diane Camara
Neamat Mowafy
Caroline Spindler
China Oxford Centre for International Health Research - China
Lixin Jiang (Country Leader)
Hao Dai
Fang Feng
Jia Li
Li Li*
Jiamin Liu
Qiulan Xie
Haibo Zhang
Jianxin Zhang
Lihua Zhang
Liping Zhang

Ning Zhang
Hui Zhong
Estudios Clínicos Latino America (ECLA) - Argentina
Rafael Diaz*
Claudia Escobar
Maria Eugenia Martin*
Andrea Pascual*
Foundation for Biomedical Research of La Paz University Hospital (FIBHULP) - Spain
José Lopez-Sendon (Country Leader)
Paloma Moraga
Victoria Hernandez
Almudena Castro
Maria Posada*
Sara Fernandez
José Luis Narro Villanueva
Rafael Selgas
French Alliance for Cardiovascular Trials (FACT) - France
Gabriel Steg (Country Leader)
Helene Abergel
Jean Michel Juliard
Green Lane Coordinating Centre Ltd. (GLCC) -Malaysia, New Zealand, Singapore, Taiwan, Thailand
Harvey White (Country Leader)
Caroline Alsweiler
*KU Leuven Research & Development - Belgium**
Frans Van de Werf (Country Leader)
Kathleen Claes
Kaatje Goetschalckx
Ann Luyten
Valerie Robesyn
South Australian Health and Medical Research Institute Ltd (SAHMRI) - Australia
Joseph B. Selvanayagam (Country Leader)
Deirdre Murphy

Contract Research Organizations (CROs) for ISCHEMIA Trial

FOCUS Clinical Research Center d.o.o. Belgrade - Serbia
Nevena Garcevic
Jelena Stojkovic
iProcess Global Research Inc. - India
Asker Ahmed
Richa Bhatt
Nitika Chadha*
Vijay Kumar*
Sadath Lubna*
Pushpa Naik

Shruti Pandey*
Karthik Ramasamy*
Mohammed Saleem
Pratiksha Sharma
Hemalata Siddaram*

**past members / past organizations*
***deceased*

II. Site Personnel

Country (No.Randomizations)	Investigator(s)	Study Coordinator(s)	City & State (if applicable)	Institution (No. Randomizations)
*United States (853) Country Leader David J. Maron, MD Regional Leader for VA Sites William E. Boden, MD				
	Kreton Mavromatis, MD Jason Linefsky, MD	John Doan, MD Raven Lee, CCRP Risha Patel So Yang Cho	Decatur, GA	Atlanta VA Medical Center (139)
	Todd Miller, MD	Susan Milbrandt Dawn Shelstad	Rochester, MN	Mayo Clinic (50)
	Subhash Banerjee, MD	Preeti Kamath, BDS, MHA, CCRP Ishita Tejani, BDS, MS, MSPH	Dallas, TX	V.A. North Texas Health Care System (35)
	Harmony R. Reynolds, MD Jonathan D. Newman, MD, MPH Sripal Bangalore, MD Robert M. Donnino, MD Lawrence M. Phillips, MD Muhamed Saric, MD, PhD	Stanley E. Cobos, BA Kirsten J. Quiles, MS Raven R. Dwyer, MPH Dalisa Espinosa, MBS	New York, NY	NYU Langone Medical Center-Bellevue Hospital (26)
	Khaled Abdul-Nour, MD	Allison Schley, BS Heather Golden Hermine Osseni, MS	Detroit, MI	Henry Ford Health System (21)
	Peter H. Stone, MD	Charlene Wiyarand Peter Douglass, BA Hayley Pomeroy, BA Alexandra Craft, BA	Boston, MA	Brigham & Women's Hospital, Harvard Medical School (21)

	Bethany Harvey, BA		
James J. Jang, MD Gennie Yee, MD	Olivia Anaya Phoebe Goold, RN	San Jose, CA	Kaiser Permanente San Jose (18)
Steven Weitz, MD	Steven Giovannone Lori Pritchard, RN	Schenectady, NY	Cardiology Associates of Schenectady P.C. (17)
Suzanne Arnold, MD James Henry O'Keefe, Jr, MD (PI from 2012-2016)	Rosann Gans, RN Paul Kennedy, RN	Kansas City, MO	Saint Luke's Hospital (17)
Michael D. Shapiro, DO	Shobana Ganesan, PhD David Schlichting, LPN Aynun Naher	Portland, OR	Oregon Health & Science University (17)
Mohammad El-Hajjar, MD Mandeep S. Sidhu, MD, MBA Steven A. Fein, MD Mikhail T. Torosoff, MD, PhD Radmila Lyubarova, MD Sulagna Mookherjee, MD Krzysztof Drzymalski, MD Edward O. McFalls, MD, PhD Santiago A. Garcia, MD	Wendy L. Stewart, MS Kristin M. Salmi, BS	Albany, NY	Albany Medical Center Hospital (16)
Stefan C. Bertog, MD Rizwan A. Siddiqui, MD Areef Ishani, MD Ronnell A. Hansen, MD	Debra K. Johnson, RN Rebekah R. Herrmann, RN	Minneapolis, MN	Minneapolis VAMC (15)
Michel Georges Khouri, MD	Kristine Arges Melissa LeFevre Jennifer Tomfohr	Durham, NC	Duke University Medical Center (15)
Jonathan L. Goldberg, MS, MD	Kimberly Ann Byrne Taissa Zappernick	Cleveland, OH	Louis Stokes Cleveland Veterans Affairs Medical Center (14)
Richard Goldweit, MD	Sallie Canada Meghana Kakade Patricia Mieses	Englewood, NJ	Englewood Hospital and Medical Center (13)
	Stanley E. Cobos, BA Raven R. Dwyer, MPH	Brooklyn, NY	NYU-HHC Woodhull Hospital (12)

Ronny A. Cohen, MD	Dalisa Espinosa, MBS		
Brooks Mirrer, MD	Kirsten J. Quiles, MS		
Victor Navarro, MD	Magdalena Rantinella, BS		
	Jessica Rodriguez, BS		
	Olivia Mancilla, BS		
David E. Winchester, MD, MS	Susan Stinson, RN	Gainesville, FL	Malcom Randall VAMC (11)
Marvin Kronenberg, MD	Terry Weyand		
Philip Rogal, MD	Sherron C. Crook	Nashville, TN	Vanderbilt University Medical Center (11)
Christopher McFarren, MD			
	Jean Ho		
John F. Heitner, MD	Saadat Khan	Brooklyn, NY	New York - Presbyterian/Brooklyn Methodist Hospital (10)
	Mahmoud Mohamed		
	Mary R. Soltau, RN		
	Delsa K. Rose, RN		
Ira M. Dauber, MD	Rebecca J. Wimmer, RN	Littleton, CO	South Denver Cardiology Associates, P.C. (10)
	Kathy E. Siegel, RN		
	Susan Derbyshire		
Charles Cannan, MD	Michelle Dixon	Portland, OR	Providence Heart and Vascular Institute (10)
	Gerald Leonard		
	Ciarra Heard, LVN		
Sriram Sudarshan, MD	Viviana Gabriel, LVN	Wichita Falls, TX	Wichita Falls Heart Clinic (9)
	Sukie Desire		
Puja K. Mehta, MD			
Michael McDaniel, MD	Fauzia Rashid, PhD		
Stamatios Lerakis, MD	Senait Asier	Atlanta, GA	Emory University (9)
Arshed Quyyumi, MD	Keyur Patel		
Nanette K. Wenger, MD			
Chester M. Hedgepeth, MD, PhD	Jennifer Gillis, APRN		
Heather Hurlburt, MD	Megan Manocchia, RN	Warwick, RI	Kent Hospital (9)
Alan Rosen, MD	Susan Moore, RN		
	Elizabeth Congdon		
	Gail Brandt		
Zakir Sahul, MD	Nora Marchelletta	Ypsilanti, MI	Michigan Heart, PC (9)
	Kristina Wippler		
David Booth, MD	Yvonne Taul, RN	Lexington, KY	University of Kentucky (8)
Steve Leung, MD	Jennifer Isaacs, MS		

Ahmed Abdel-Latif, MD, PhD Hassan Reda, MD Khaled Ziada, MD	Viktoria Bulkley, RN Caroline Rodgers		
Sampoornima Setty, MD	Kimberly E. Halverson, RHIT Christine Roraff, RN Jonean Thorsen, RN	La Crosse, WI	Gundersen Lutheran Medical Center (8)
Rajat S. Barua, MD, PhD	Amarachi Ojajuni Oni Olurinde Kamalakar Surineni	Kansas City, MO	Kansas City VA Medical Center (8)
Fadi Hage, MD Christiano Caldeira, MD James E. Davies, MD Massoud Leesar, MD Jaekyeong Heo, MD Amy Iskandrian, MD Firas Al Solaiman, MD Satinder Singh, MD	Badhma Valaiyapathi, MD	Birmingham, AL	UAB Vascular Biology and Hypertension Program (8)
Khaled Dajani, MD	Carol M. Kartje, BSN	Maywood, IL	Loyola University Medical Center (8)
Mohammad El-Hajjar, MD Paul Der Mesropian, MD Joseph Sacco, MD Brian McCandless, MD Marisa Orgera, MD Mandeep S. Sidhu, MD, MBA (2012-2016)	Michele Rawlins, NP Jennifer Thomson, MA	Albany, NY	Samuel Stratton VA Medical Center of Albany NY (7)
Imran Arif, MD Hanan Kerr, MD	Mary Colleen Rogge, RN Julie Bunke , BA Kendra Unterbrink , PA Jacqueline Fannon, RN Cynthia Burman, NP	Cincinnati, OH	Cincinnati VA Medical Center (7)
Jorge F. Trejo (Gutierrez), MD Gerald Fletcher, MD Gary E. Lane, MD Lynn M. Neeson, DNP Pragnesh P. Parikh, MD	Marcia F. Dubin, CCRP	Jacksonville, FL	Mayo Clinic Florida (7)

Peter M. Pollak, MD Brian P. Shapiro, MD Kevin Landolfo, MD Anthony Gemignani, MD Daniel O'Rourke, MD	Sarah Beaudry, RN	White River Junction, VT	VAMC-White River Junction (7)
Judith L. Meadows, MD	Stephanie A. Tirado, RN Janet Halliday Pamela Julian	West Haven, CT	VA Connecticut Healthcare System (7)
Jason T. Call, MD	Stephanie, M. Lane, RN, BSN, CCRN Jennifer L. Stanford, RN, MSN	Winchester, VA	Winchester Cardiology and Vascular Medicine, PC (7)
Joseph Hannan, MD Robert Bojar, MD Deepti Kumar, MD John Mukai, MD	Patricia Arsenault, RN Pamela Sigel, RN	Worcester, MA	Saint Vincent Hospital at Worcester Medical Center (7)
Edward T. Martin, MS, MD	Miriam Brooks	Tulsa, OK	Oklahoma Heart Institute (7)
Gabriel Vorobiof, MD	Ladda Douangvila Rubine Gevorgyan Fatima Ranjbaran, RN	Los Angeles, CA	Ronald Reagan UCLA Medical Center (7)
Alec Moorman, MD	Bryn Smith, BS Carly Ohmart	Seattle, WA	University of Washington Medical Center (7)
Scott Kinlay, MBBS, PhD Robert J. Hamburger, MD Thomas P. Rocco, MD Deepak L. Bhatt, MD, MPH Kevin Croce, MD, PhD Jacquelyn A Quin, MD Jati Anumpa, MD Marco Zenati, MD, MSc David P Faxon, MD	Samantha Ly, MA Margot C. Quinn, BA Sara Temiyasathit, PhD Jacquelyn Do, MPH Desiree Tobin, MPH	West Roxbury, MA	VA Boston Healthcare System (6)
Glenn Rayos, MD	Jennifer Langdon Marcia Werner Bayer	Daytona Beach, FL	Daytona Heart Group (6)
Ashraf Seedhom, MD Lance Sullenberger, MD	Amanda O'Malley Erin Orvis	Albany, NY	Capital Cardiology Associates (6)
Gregory Kumkumian, MD	Mandy Murphy, RN Ann Greenberg, RN	Bethesda, MD	NIH Heart Center at Suburban Hospital (6)

	Margaret Iraola, RN		
Steven P. Sedlis, MD Robert M. Donnino, MD Jeffrey Lorin, MD	Leandro C.Maranan, CCRC	New York, NY	VA New York Harbor Health Care System (6)
Jacqueline E. Tamis-Holland, MD Robert Kornberg, MD Robert Leber, MD Souheil Saba, MD Michael W. Lee, MD	Ammy Malinay, RN	Ridgewood, NJ	Mount Sinai Saint Luke's Hospital (6)
Delano R. Small, MD Wassim Nona, MD Patrick B. Alexander, MD Iram Rehman, MD	Candice P. Edillo, RN	Southfield, MI	Providence - Providence Park Hospital (6)
Umesh Badami, MD	Ann Ostrander, RN Stephanie Wasmiller, RN	Saginaw, MI	Covenant Medical Center, Inc. (5)
Kevin Marzo, MD	Wendy Drewes, RN Dipti Patel, RN	Mineola, NY	NYU Winthrop (5)
Inga H. Robbins, MD Howard A. Levite, MD Sanjay Shetty, MD Mayuri Patel, MD	Jackie M White, RN, BSN CCRC Alison Hallam	Pomona, NJ	AtlantiCare Regional Medical Center (5)
Glenn S. Hamroff, MD	Benjamin J Spooner, RPA-C Linda M Hollenweger, LPN,CCRC	Cortlandt Manor, NY	NYP Medical Medical Group Hudson Valley Cardiology (5)
Raymond W. Little, MD Brandi D. Zimbelman, FNP-C Charles Y. Lui, MD	Holly Little Tiffany Little	Houston, TX	Houston Heart & Vascular Associates (5)
Brigham R. Smith, MD Daniel P. Vezina, MD, MSC Lillian L. Khor, MBBCh, MSc Josephine D. Abraham, MD, MPH David A. Bull, MD	Nona A Eskelson, RN	Salt Lake City, UT	Salt Lake City VA Medical Center (4)
Stephen H. McKellar, MD, MSc David Booth, MD John Kotter, MD	Yvonne Taul, RN Caroline Rodgers, RN	Lexington, KY	Lexington VA Medical Center (4)

Ahmed Abdel-Latif, MD, PhD Bob Hu, MD Arthur J. Labovitz, MD Michael Berlowitz, MD Philip Rogal, MD Christopher McFarren, MD Fadi Matar, MD Christiano Caldeira, MD David J. Maron, MD	Jennifer Isaacs, MS Viktoria Bulkley Renee Kaneshiro Bonnie J. Kirby, RN, MSN Nhi N. Tran, MS Catherine Jahrsdorfer, RN, BSN	Palo Alto, CA Tampa, FL	Palo Alto Medical Foundation Research Institute (4) University of South Florida (4)
Fatima Rodriguez, MD, MPH Ingela Schnittger, MD William F. Fearon, MD	Reem Yunis, PhD Jhina Patro	Stanford, CA	Stanford University School of Medicine (4)
Prakash Deedwania, MD Kiran Reddy, MD	Antonia Vega	Fresno, CA	UCSF - Fresno Community Regional Medical Center (4)
Joseph Sweeny, MD	Hugo Bloise-Adames Santa Jimenez Nicole Saint Vrestil Reyna Bhandari	New York, NY	Icahn School of Medicine at Mount Sinai (4)
Christopher Spizzieri, MD	Danielle Schade Roxanne Yost	Camp Hill, PA	Holy Spirit Hospital Cardiovascular Institute (4)
Claudia P Hochberg, MD	Paula Beardsley Denise Fine	Boston, MA	Boston Medical Center (4)
William D. Salerno, MD	Jana Tancredi, RN, MA/MSN, CCRN Patricia Arakelian Susan Mathus Deborah O'Neill	Saddle Brook, NJ	Hackensack University Medical Center (4)
Ray Wyman, MD	Joy Burkhardt, CCRP Suellen Hosino, RN, BSN, CCRP	Torrance, CA	Torrance Memorial Medical Center (4)
Amer Zarka, MD Anil V. Shah, MD	Oksana A. Lubyanaya, BA Jose D. Salas, BS Maria Aguirre Manu Dhawan Diana Parra Tri Tran	Santa Ana, CA	Coastal Heart Medical Group (4)

Thomas Haldis, DO	Catherine Weick, BSRT(R)(VI) Katie Fowler-Lehman, BSN Natalie Spitzer, BSN Casey Riedberger Catherine Weick	Fargo, ND	Sanford Health (4)
Jeffrey A. Kohn, MD	Stanley E. Cobos, BA Raven R. Dwyer, MPH Dalisa Espinosa, MBS Kirsten J. Quiles, MS	New York, NY	NYU New York Medical Associates (4)
Saket Girotra, MD	Carrie Drum, RN Kimberly Miller-Cox, RN Amy Ollinger, RN	Iowa City, IA	University of Iowa Hospitals and Clinics (4)
Omar Almousalli, MD	Elizabeth Capasso-Gulve Alaine Melanie Loehr Marlowe Mosley	Fairview Heights, IL	Advanced Heart Care Group (4)
Mayil S. Krishnam, MD Jeffrey C. Milliken, MD Pranav M. Patel, MD Arnold H. Seto, MD Kevin T. Harley, MD Michael A. Gibson, MD Byron J. Allen, MD	Shirin Heydari, MS Andrea M. Lundeen, MA Edgar Karanjah, MD Wanda C. Marfori, MD Eduardo Hernandez-Rangel, MD Pam Singh	Orange, CA	University of California Irvine Medical Center (3)
Rita Coram, MD	Anne Marie Webb, BSN Ellie Fridell, BS Heidi Wilson, BS	Louisville, KY	University of Louisville (3)
Sabu Thomas, MD, MSc Ronald G Schwartz, MD, MS Wei Chen, MD, MS	Angela Kim, BS Patrick Wilmot, BS	Rochester, NY	University of Rochester (3)
Mahfouz El Shahawy, MD	Ramona Stevens	Sarasota, FL	Cardiovascular Center of Sarasota (3)
James Stafford, MD	Loriane Black	Baltimore, MD	University of Maryland Medical Center (3)
William B. Abernethy, MD	Amber B. Hull, RN Olivia J. Lim, RN Helen C. Tucker Natasha C. Putnam, RN Linda L. Hall	Asheville, NC	Asheville Cardiology Associates (3)

Andrew Zurick, MD	Tia Cauthren Trish Tucker Hollie Horton Jan Orga	Nashville, TN	Saint Thomas Hospital (3)
Thomas M. Meyer, MD Ronald G. Morford, MD	Joyce R. White, MSN NP-C Cynthia Baumann, RN	Lynchburg, VA	Stroobants Cardiovascular Center (3)
Bruce Rutkin, MD	Vidya Seeratan	Manhasset, NY	Northwell Health - Manhasset (3)
Sabahat Bokhari, MD	Magnolia Jimenez	New York, NY	Columbia University Medical Center (3)
Seth I. Sokol, MD Jay Meisner, MD Ihab Hamzeh, MD	Cidney Schultz, RN Jeanne Russo, RN	Bronx, NY	Jacobi Medical Center (3)
Arunima Misra, MD Matthew Wall Jr., MD Veronica Lenges De Rosen, MD Mahboob Alam, MD	Zohra Huda, RN, BSN, CCRP Araceli Boan	Houston, TX	Baylor College of Medicine (3)
Michael C. Turner, MD Thomas J. Mulhearn, MD	Christine R Hinton	Lake Charles, LA	Cardiovascular Specialists of Southwest Louisiana (3)
Arnold P. Good, MD	Beth A. Archer, BSN, RN Julia S. Dionne, BA Cheryl A. Allardyce, BSN, RN Lindsey N. Sikora, BSN, RN Jennifer H. Czerniak, RN Jennifer A. Mull, MSN, RN Elizabeth Ferguson Frances Laube	Columbus, OH	Ohio Health Grant Medical Center (3)
Nicolas W. Shammas, MD, MS	Gail A Shammas, BSN, RN Lori Christensen Holly Park	Davenport, IA	Midwest Cardiovascular Research Foundation (3)
Robert Chilton, MD	Joan Hecht	San Antonio, TX	Audie Murphy V.A. (2)
Patricia K. Nguyen, MD	Davis Vo, BS James Hirsch	Palo Alto, CA	VA Palo Alto Healthcare System (2)
Matthew Jezior, MD	Jody Bindeman Sara Salkind	Bethesda, MD	Walter Reed National Military Medical Center (2)
	Dalisa Espinosa, MBS Lori-Ann Desimone, BSN	Providence, RI	Miriam Hospital (2)

Paul C. Gordon, MD Thomas Crain, MD	Lina Felix-Stern Jassira Gomes Catherine Gordon, BSN		
Robert Stenberg, MD	Aimee Mann Theresa McCreary	Johnstown, PA	Conemaugh Valley Memorial Hospital (2)
Ronald P. Pedalino, MD	Stanley E. Cobos, BA Raven R. Dwyer, MPH Dalisa Espinosa, MBS Kirsten J. Quiles, MS	Brooklyn, NY	NYU-HHC Kings County Hospital Center (2)
Joseph Wiesel, MD	Stanley E. Cobos, BA Raven R. Dwyer, MPH Dalisa Espinosa, MBS Kirsten J. Quiles, MS	Flushing, NY	New York University - Langone Cardiovascular Associates (2)
George J. Juang, MD	Candace Gopaul, BS Karen Hultberg Tauqir Huk Afshan Hussain	Brooklyn, NY	Coney Island Hospital (2)
Mohammed Al-Amoodi, MD	Yesenia Zambrano, BS Sarah Medina Rodriguez Trudie Milner	Yuma, AZ	Yuma Regional Medical Center (2)
David Wohns, MD	Abbey Mulder, RN Stacie Van Oosterhout, MEd	Grand Rapids, MI	Spectrum Health (2)
Ellis W. Lader, MD	Martha Meyer, RN, MSN	Kingston, NY	Mid Valley Cardiology (1)
Michael Mumma, MD	Nancy L. Clapp, RN, BA, CCRC Heather Barrentine Jenne M. Jose, PA	Sarasota, FL	Sarasota Memorial Hospital (1)
Lekshmi Dharmarajan , MD	Stanley E. Cobos, BA Raven R. Dwyer, MPH Dalisa Espinosa, MBS Kirsten J. Quiles, MS Jenne Manchery	Bronx, NY	NYU-HHC Lincoln Medical and Mental Health Center (1)
Joseph F.X. McGarvey Jr, MD	Vera McKinney, RN Linda Schwarz, RN	Doylestown, PA	Doylestown Health Cardiology (1)
Thomas R. Downes, MD (till Dec. 2016) Gary J. Luckasen, MD (from Dec. 2016)	Scott M. Kaczkowski Adam J. Jaskowiak	Loveland, CO	Medical Center of the Rockies (1)
Benjamin Cheong, MD	Joel Klitch Debra Dees	Houston, TX	Baylor St. Luke's Medical Center (1)

	Srinivasa Potluri, MD	Precilia Vasquez	Plano, TX	Baylor Research Institute at Legacy Heart Center (1) **
	Ronald A. Mastouri, MD Jeffery A. Breall, MD, PhD George E. Revtyak, MD Jonathan W. Bazeley, MD	Elise L. Hannemann, RN,CCRC Judy Mae Foltz, RN,CCRC Emily DeRosa	Indianapolis, IN	Indiana University/Krannert Institute of Cardiology (1)
	Dayuan Li, MD	Beth Jorgenson Joyce Riestenberg-Smith	St. Paul, MN	HealthEast Saint Joseph's Hospital (1)
	Kenneth Giedd, MD		New York, NY	Beth Israel Medical Center (1)
	Wayne Old, MD	Rebecca Bariciano	Chesapeake, VA	Cardiovascular Associates, Ltd. (1)
	Francis Burt, MD		Bethlehem, PA	Saint Luke's Hospital and Health Network (1)
	Kozhaya Sokhon, MD	Jessica Waldron Michelle Mayon	Sugar land, TX	Medicus Alliance Clinical Research Org., Inc. (1)
	Deepika Gopal, MD		Plano, TX	The Heart Hospital Baylor (1)
	Uma S. Valeti, MD	Gretchen Ann Peichel, RN	Minneapolis, MN	University of Minnesota (1)
	Jon Kobashigawa, MD	Brandy Starks Lucilla Garcia Maria Thottam	Beverly Hills, CA	Cedars Sinai Medical Center (1)
India (941) Country Leader Balram Bhargava, DM				
	Sajeev Chakanalil Govindan, MD, DNB, DM, PhD Rajesh Gopalan Nair, MD, DNB, DM Cholenahally Nanjappa Manjunath, MD, DM Nagaraja Moorthy, MD, DM Satvic Cholenahally Manjunath, MD,DM Suryaprakash Narayanappa, MBBS	Anjali Anand, MSc Janitha Raj, B.Tech Reshma Ravindran, MSc Rajalekshmi VS, MSc, MScCRRA Nandita Nataraj, BE(Biotech) PGDICRCDM Soundarya Nayak, BE(Biotech) PGDICRCDM Mahevamma Mylarappa, GNM (General Nursing)	Calicut Bangalore	Government Medical College (208) Sri Jayadeva Institute of Cardiovascular Sciences and Research (149)

Neeraj Pandit, MD, DM	Sheromani Bajaj		
Ranjit Kumar Nath, MD, DM	Vandana Yadav, Msc,PGDACR Girish Mishra, Msc, PGDACR	New Delhi	Dr Ram Manohar Lohia Hospital (101)
S.K. Dwivedi, DM	Roma Tewari, PG		
V.S. Narain, DM	Meenakshi Mishra, PG		
Sharad Chandra, DM	Shivali Patel	Lucknow	King George's Medical University, Department of Cardiology (100)
	Suman Singh, PG		
Gurpreet S. Wander, DM Rohit Tandon, MD Sarju Ralhan, M.Ch (CTVS) Naved Aslam, DM	Baljeet Kaur, MSc (Biotechnology) Sonika Gupta , MBA, B. Pharmacy	Ludhiana	Hero DMC Heart Institute, Dayanand Medical College and Hospital (83)
Abhishek Goyal, DM Balram Bhargava, DM G.Karthikeyan, DM S.Ramakrishnan, DM Sandeep Seth, DM Rakesh Yadav, DM Sandeep Singh, DM Ambuj Roy, DM Neeraj Parakh, DM Sunil Kumar Verma, DM Rajiv Narang, DM Sundeep Mishra, DM Nitish Naik, DM Gautam Sharma, DM Shiv Kumar Choudhary, M.Ch Chetan Patel, DNB Gurpreet Gulati, MD Sanjeev Sharma, MD V K Bahl, DM	Chandini Suvarna, BDS	New Delhi	All India Institute Of Medical Sciences (67)
Anoop Mathew, MD Eapen Punnoose, MD	Binoy Mannekkattukudy Kurian	Kolenchery	MOSC Medical College Hospital (39)
Milind Avdhoot Gadkari, MD Siddharth Gadage, MD DNB	Sheetal Rupesh Karwa, BHMS Suvarna Kolhe, MSc	Pune	KEM Hospital Pune (35)

Tapan Umesh Pillay, BHMS MSc			
Santhosh Satheesh, MBBS, MD, DM	R. J. Vindhya, B.Sc. (Bio-Technology), MSc(Bio-Informatics)	Pondicherry	Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER) (31)
	Peeyush Jain, MD		
	Ashok Seth, MD		
	Zile Singh Meharwal, MD		
Atul Mathur, MD	Atul Verma, MD		
Upendra Kaul, MD	Mona Bhatia, MD	New Delhi	Fortis Escort Heart Institute (31)
	Ankush Sachdeva, MD		
	Thounaojam Indira Devi, RN		
	Nungshi Jungla, RN		
Johann Christopher, MD, DNB	K. Manjula Rani, MSc.		
Rajeev Menon, MD, DNB	M. Sowjanya Reddy, BSc	Hyderabad	Gurunanak CARE Hospital (27)
Nirmal Kumar, MD, DNB	K. Preethi, BSc		
Abraham Oomman, MD,DM,DNB	Rinu R sidh, MSc(Clinical Research)		
Robert Mao, MD, DM	Ramakrishnan T., B.Tech(Biotechnology)	Chennai	Apollo Research and Innovation (23)
Hilda Solomon, PhD	Rajesh Francis, MSc(Clinical Research)		
Sudhir Naik, MD, DM			
Sajeeda Parveen Khan, MBBS, (Dip.Card)	Vamshi Priya P., MSc	Hyderabad	Apollo Research & Innovations (13)
Johann Christopher, MD	Kotiboinna Preethi	Hyderabad	CARE Nampally (11)
Nirmal Kumar, MD			
	Shweta Hande, BHMS, PGDCR		
Purvez Grant, MD	Poonam Sonawane, B.ScMicrobiology, ACCR	Pune	Ruby Hall Clinic,Grant Medical Foundation (10)
	Abhishek Dubey		Fortis Healthcare Fl.t
Ranjan Kachru, MD	Kavita Rawat	New Delhi	Lt. Rajan Dhall Hospital (4)
Ajit Kumar VK, MD, DM			
Sanjay Ganapathi, MD, DM		Trivandrum	Sree Chitra Tirunal Institute for Medical Sciences and Technology (3)
Jayakumar K, MS, M.Ch	Vineeth CP		

	Harikrishnan Sivadasanpillai, MD, DM Bijulal Sasidharan, MD, DM Kapilamoorthy TR, MD Johann Christopher, MD Praneeth Polamuri, MD	Manas Chacko, RN Suresh Babu Sowjanya Reddy Manjula Rani	Hyderabad	CARE Hospital (3)
	Upendra Kaul, MD	Priyadarshani Arambam Bebek Singh	New Delhi	Batra Hospital and Medical Research Centre (BHMRC) (3)
United Kingdom (539)				
Country Leaders				
Roxy Senior, MBBS, MD, DM Keith AA Fox, MBChB *(past)*				
Country Coordinators				
Grace M. Young , MSc, BSc (Hons)				
Kathryn Carruthers *(past)*				
	Roxy Senior, MBBS, MD, DM Ahmed Elghamaz, MB BCh Sothinathan Gurunathan, MBChB Nikolaos Karogiannis, MBBS Benoy N Shah, MD, MBBS, BSc (Hons) Richard HJ Trimlett, MBBS, CCST Michael B Rubens, LRCP, MRCS, MBBS, DMRD Edward D Nicol, MD, BMedSci, MBBS, DTM&H Tarun K Mittal, MD	Grace M. Young , MSc, BSc (Hons) Christopher Kinsey Raisa Kavalakkat, MSc, BSc, RN Jo Evans, RN Ikraam Hassan, RN	Harrow	Northwick Park Hospital Harrow/ Royal Brompton Hospital London (202)
	Reinette Hampson, BSc (Hons), BA (Hons) Reto Andreas Gamma, MBBS	Sarah Williams, RN Kim Holland, RN Karen Swan, RN	Chelmsford	Broomfield Hospital (39)
	Mark A de Belder, MD Jeet Thambyrajah, MD	Bev Atkinson, RN	Middlesbrough	The James Cook University Hospital, Middlesbrough (37)

Thuraia Nageh, BSc(Hons) MBBS MD MRCP John R Davies, MBBS, PhD Steven J. Lindsay, MD	Swapna Kunhunny, MRes Clin Res, BSc (N), RN Craig Atkinson, RN	Westcliffe on Sea	Southend University Hospital (34)
John Kurian, MD Haqeel Jamil, MD Osama Raheem, MD	Carita Krannila, RN Manitha Vinod, RN	Bradford	Bradford Royal Infirmary (20)
Angela Hoye, MD	Lisa Chaytor Leanne Cox Julie Morrow Kay Rowe	Cottingham	The University of Hull/Castle Hill Hospital (19)
Patrick Donnelly, MD Bernardas Valecka, MD	Stephanie Kelly, RN Susan Regan, RN Dawn Turnbull	Belfast	South Eastern Health and Social Care (17)
Anoop Chauhan, MD	Catherine Fleming Arijit Ghosh Karen Gratrix Stephen Preston	Blackpool	Blackpool Teaching Hospitals (16)
Craig Barr, MD	Anne Cartwright	Dudley	Russells Hall Hospital (15)
Khaled Alfakih, MBBS, MD Jonathan Byrne, PhD Ian Webb, PhD, MA	Abigail Knighton, BSc., PG Dip. Katherine Martin, RGN, Dip. N, MSc	London	King's College NHS Foundation Hospital (14)
Peter Henriksen, PhD, MB ChB, BSc(Hons)	Laura Flint, RGN James Harrison, BSc(Hons), PG dip	Edinburgh	Royal Infirmary of Edinburgh (13)
Peter OKane, MD	Nicki Lakeman Anja Ljubez	Bourneouth	Royal Bournemouth Hospital (13)
Ramesh de Silva, MB ChB, MD		Bedford	Bedford Hospital NHS Trust (11)
Dwayne S. G. Conway, MD	Judith Wright Donna Exley	Wakefield	Pinderfields Hospital (11)
Alexander A Sirker, MB BChir, PhD	Mervyn Andiapen, RN Amy J. Richards, BSc	London	University College London Hospitals NHS Foundation Trust BartsHealth NHS Trust (11)

Stephen P Hoole, MD	Lisa Wong, MSc	Cambridge	Papworth Hospital (10)
Fraser N. Witherow, MD	Melanie J. Munro, RGN	Dorchester	Dorset County Hospital (8)
Nicola Johnston, MB, Bch BAO, MRCP, MD			
Mark Harbinson, MB, Bch BAO, MRCP, MD	Michelle McEvoy, RN	Belfast	Belfast Trust (7)
Simon Walsh, MB, Bch BAO, MD	Caroline Brown, RN		
Hanna Douglas, MB, Bch BAO, MRCP, MD			
Matthew Luckie, MD	Thabitha Charles Laurel Kolakaluri Hannah Phillips	Manchester	Central Manchester University Hospital (7)
Jolanta Sobolewska, MD	Louise Morby, RN Karen Hallett, RN Carolyn Corbett, RN Lynne Winstanley	Oldham	The Pennine Acute Hospitals NHS Trust (6)
Paramjit Jeetley, MD Niket Patel, MD Tushar Kotecha, MBChB, Mpharm	Angelique Smit, RN	London	Royal Free London NHS Foundation Trust (6)
Christopher Travill, MBBS, MD Iqbal Karimullah, MBBS Mahmud Al-Bustami, MBBS	Susan Gent, SRN RGN Nafisa Hussain, BSc	Luton	Luton and Dunstable University Hospital NHS FT (5)
Denise Braganza, MD Robert Henderson, MD	Fiona Haines Joanne Taaffe Jane Burton	Peterborough	Peterborough City Hospital (5)
Kate Pointon, MBBS Surendra Naik, PhD Thomas Mathew, MBBS, MD, DM	Maria Colton Rachel King	Nottingham	Nottingham University Hospitals (4)
Colin Berry, BSc MB ChB, PhD Damien Collison, MB ChB Giles Roditi, MB ChB	Ammani Brown, MSc BA RN Andrew Docherty, RN Lisa McCloy, RN Kate Robb, RN Craig Paterson, PhD Wenda Crawford, RN Joanne Kelly, RN	Clydebank	University of Glasgow (4)

		Lorraine McGregor, RN		
	Andrew J Moriarty, BSc MB PhD	Anne Mackin, RN, BSc	Craigavon	Cardiovascular Research Unit, Craigavon Area Hospital (2)
	Jason D. Glover, MBBS Jiwan Pradhan, MBBS Ghada Mikhail, MD	Janet P Knight, RN	Basingstoke	Hampshire Hospitals NHS Foundation Trust (2)
	Darrel P. Francis, MD, MA	Tuhina Bose	London	Imperial College Healthcare NHS Trust (1)
*Canada (447) Country Leaders Vladimir Dzavik, MD Shaun Goodman, MD, MSc Gilbert Gosselin, MD				
		Anna Proietti, RN		
	Gilbert Gosselin, MD	Myriam Brousseau, RN Magalie Corfias, RN Patricia Blaise Luc Harvey	Montreal, QC	Montreal Heart Institute (90)
	Ariel Diaz, MD			
	Philippe Rheault, MD Miguel Barrero, MD			
	Carl-Éric Gagné, MD	Patricia Alarie		
	Yanek Pépin-Dubois, MD	Linda Arcand		
	Ricardo Costa, MD	Isabelle Roy	Trois-Rivieres, QC	Centre Hospitalier de Regional Trois-Rivieres (71)
	Ying Tung Sia, MD	Estelle Montpetit		
	Catherine Lemay, MD Alejandro Gisbert, MD Pierre Gervais, MD			
	Alain Rheault, MD			
		Katia Drouin, RN		
	Denis Carl Phaneuf, MD Gilbert Gosselin, MD	Christine Bergeron, RN Christine Shelley	Terrebonne, QC	CISSSL - Hopital Pierre-Le Gardeur (42)
		Christine Masson		
	Pallav Garg, MBBS, MSc	Sandy Carr, RN Catherine Bone, RN	London, ON	London Health Sciences Centre (35)
	Benjamin J.W. Chow, MD	Ermina Moga	Ottawa, ON	University of Ottawa Heart Institute (29)

Renee C. Hessian, MD Rob S. Beanlands, MD Richard F. Davies, MD	Janetta Kourzenkova Olga Walter		
Kevin R. Bainey, MD, MSc Asim N. Cheema, MD, PhD Akshay Bagai, MD, MHS Ron Wald, MDCM, MPH	Norma Hogg, RN Suzanne Welsh, RN	Edmonton, AB	University of Alberta (28)
Shaun Goodman, MD, MSc John Joseph Graham, MRCP, MB ChB, BSc Mark Peterson, MD, FRCSC, PhD Chi-Ming Chow, MD, CM, MSc Beth Abramson, MD, MSc	Khrystyna Kushniriuk, HBSc, MD Mohammed Hussain Olugbenga Bello	Toronto, ON	St. Michael's Hospital (27)
Asim Nazir Cheema, MD Mohammad Tariq Vakani, MD	Ishba Syed, MBBS Mohammed Hussain, BSc(H) Khrystyna Kushniriuk, MBBS	Mississauga, ON	Dixie Medical Group (24)
James Cha, MD	Judy Otis, CRC Rebecca Otis, CRC Michelle M Seib, RN	Oshawa, ON	Dr. James Cha (21)
Andrew G Howarth, MD, PhD	Sandra M Rivest, RN Rosa Sandonato, BSCN	Calgary, AB	University of Calgary (15)
Graham Wong, MD	Jackie Chow Andrew Starovoytov Naomi Uchida Ngaire Meadows	Vancouver, BC	Vancouver General Hospital (15)
Amar Uxa, MD	Nadia Asif Suzana Tavares	Toronto, ON	University Health Network (14)
Paul Galiwango, MD Saleem Kassam, MD Ashok Mukherjee, MD A. Joseph Ricci, MD	Bev Bozek, RN, CCRC Maria Shier Lori-Ann Larmand Amir Janmohamed	Scarborough, ON	Scarborough Cardiology Research (9)
Andy Lam, MD	Brenda Hart Jane Marucci Sharon Tai	East Grimsby, ON	West Lincoln Memorial Hospital (8)

		Sonya Brons, RN Chris Beck, RN		
	Shamir Mehta, MD	Glenda Wong, RN Krystal Etherington Thippeekaa Arumairajah Maria Aprile	Hamilton, ON	Hamilton General Hospital (7)
	Jacob Udell, MD	Sara Karlsson Susan Webber	Toronto, ON	Women's College Hospital (7)
	Philippe Généreux, MD	Chantale Mercure	Montréal, QC	Centre Intégré Universitaire de Santé et de Services Sociaux du Montréal (2)
	Adnan Hameed, MD	Nancy Aedy Fran Farquharson	St. Catharines, ON	Saint Catharines General Hospital (2)
	Ledjalem Daba, MD	Anam Siddiqui	Vaughan, ON	Northwest GTA Cardiovascular and Heart Rhythm Program (1)
Brazil (399)				
Country Leaders				
Antonio Carlos Carvalho, MD, PhD				
Renato D. Lopes, MD, PhD				
	Whady Hueb, MD			
	Paulo Cury Rezende, MD Expedito Eustáquio Ribeiro Silva, MD Alexandre Ciappina Hueb, MD	Myrthes Emy Takiuti, RN	Sao Paulo	Heart Institute (InCor) University of São Paulo (127)
	Paola Emanuela Poggio Smanio, MD, PhD Alexandre Schaan de Quadros, MD	Leonardo Pizzol Caetano, PhD	São Paulo	Instituto Dante Pazzanese de Cardiologia (98)
	Renato Abdala Karam Kalil, MD José Luiz da Costa Vieira, MD Gabriel Grossmann, MD Pedro Píccaro de Oliveira, MD Leonardo Bridi, MD	Aline Peixoto Deiro Alice Manica Muller Maria Antonieta Pereira de Moraes Bruna Maria Ascoli Sílvia Zottis Poletti	Porto Alegre	Instituto de Cardiologia de Porto Alegre (41)
	Simone Savaris, MD João V Vitola, MD, PhD Rodrigo J Cerci, MD, Msc	Sandra S. Zier, BSc	Curitiba	Quanta Diagnostico & Terapia (33)

Fabio R Farias, MD, Msc Miguel M Fernandes, MD, PhD José Antonio Marin-Neto, MD, PhD André Schmidt, MD, PhD Moysés de Oliveira Lima Filho, MD, PhD Ricardo Mendes Oliveira, MD João Reynaldo Abbud Chierice, MD Carísi A. Polanczyk, MD Mariana V. Furtado, MD Luis F. Smidt, MD Antonio Carlos Carvalho, MD Gustavo Pucci, MD Flavio Lyra, MD	Vilmar Veiga Jr, BSc Diego Franca da Cunha Guilherme G Rucatti, PsyD Fernanda Igansi, BSc Mauren P Haeffner, BSc Viviane Almeida Gabriela Sanchez de Souza	Ribeirao Preto Porto Alegre Sao Paulo	Hospital das Clinicas da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo (31) Hospital de Clínicas de Porto Alegre (12) Unifesp - Hospital Sao Paulo (9)
Alvaro Rabelo Alves Junior, MD	Mayana Almeida Viviane dos Santos	Salvador	Fundacao Bahiana de Cardilogia (9)
Marianna D. A. Dracoulakis, MD, PhD Rodolfo G. S. D Lima, MD	Natalia S Oliveira, RN	Salvador	Hospital da Bahia (8)
Estevao Figueiredo, MD	Bruna Edilena Paulino Azevedo Marco Bizzaro Santos	Belo Horizonte	Hospital Lifecenter (8)
Paulo Ricardo Caramori, MD	Amanda Germann Vitor Gomes Rosa Homem Ellen Magedanz	Porto Alegre	Hospital Sao Lucas da Pontificia Universidade Catolica do Rio Grande do Sol (7)
Rogerio Tumelero, MD	Rosane Laimer Alexandre Tognon	Fundo	Hospital Sao Vicente de Paulo (5)
Frederico Dall'Orto, MD		Pocos de Caldas	Hospital Maternidade e Pronto Socorro Santa Lucia (4)
Claudio T. Mesquita, MD Alexandre S. Colafranseschi, MD Amarino C. Oliveira Jr., MD	Roberta P Santos, RN	Botafogo	Hospital Pró-Cardíaco (3)

	Luiz A. Carvalho, MD Isabella C. Palazzo, MD Andre S. Sousa, MD Expedito Eustáquio Ribeiro da Silva, MD, PhD Pedro Gabriel Melo de Barros e Silva, MD, PhD Luciana de Pádua Silva Baptista, MD, PhD Marcelo Jamus Rodrigues, MD Marcos Valério Coimbra de Resende, MD, PhD	Mariana Yumi Okada, RN Ana Paula Batista, RN Aline Nogueira Rabaça, BS	Sao Paulo	Hospital TotalCor (2)
	Jose Francisco Saraiva, MD	Larissa Miranda Trama Talita Silva Camila Thais de Souza Ormundo Carla Vicente	Sao Paulo	Hospital Celso Pierro (1)
	Costantino Costantini, MD, PhD	Caroline Pinheiro Daniele Komar	Curitiba	Hospital Cardiologico Costantini (1)
Poland (333) Country Leaders Witold Ruzyllo, MD Hanna Szwed, MD, PhD Country Coordinator Radoslaw Pracon, MD, PhD				
	Marcin Demkow, MD, PhD Radoslaw Pracon, MD, PhD Cezary Kepka, MD PhD Anna Teresinska, MD PhD Karolina Kryczka, MD PhD Jan Henzel, MD PhD Mateusz Solecki, MD PhD Edyta Kaczmarska, MD PhD	Olga Walesiak Katarzyna Malinowska	Warsaw	Coronary and Structural Heart Diseases Department, Institute of Cardiology (127)
	Tomasz Mazurek, MD, PhD	Jakub Maksym, MD Karolina Wojtera, MD	Warszawa	Medical University of Warsaw (48)

	Anna Fojt, MD Ewa Szczerba, MD		
Jaroslaw Drozdz, PhD Bartosz Czarniak, MD Malgorzata Frach (formerly Stasiak), MD Konrad Szymczyk, MD Iwona Niedzwiecka, MD Sebastian Sobczak, MD Tomasz Ciurus, MD Piotr Jakubowski, MD Magdalena Misztal-Teodorczyk, MD Dawid Teodorczyk, MD Aleksandra Fratczak, MD Marcin Szkopiak, MD Patrycja Lebioda, MD Michal Wlodarczyk, MD Anna Plachcinska, MD Jacek Kusmierek, MD Magdalena Miller, MD Halina Marciniak, MD Karolina Wojtczak-Soska, MD Katarzyna Łuczak, MD Tomasz Tarchalski, MD Anna Cichocka-Radwan, MD Hanna Szwed, MD, PhD Grazyna Anna Szulczyk, MD	Marta Swiderek, MA Ewelina Wojtala, MA Jaroslaw Karwowski, MD	Lodz Warsaw	Cardiology Clinic, Medical University in Lodz (43) National Institute of Cardiology, Warsaw (35)
Adam Witkowski, MD, PhD Krzysztof Kukuła, MD, PhD Małgorzta Celińska-Spodar, MD		Warsaw	Department of Interventional Cardiology & Angiology, Institute of Cardiology (20)

	Joanna Zalewska, MD Grzegorz Gajos, MD, PhD Krzysztof Bury, MD, PhD		Krakow	Department of Coronary Disease, John Paul II Hospital, Jagiellonian University Medical College (16)
	Piotr Pruszczyk, MD, PhD Marek Roik, MD, PhD	Andrzej Łabyk, MD Agnieszka Szramowska, MD Olga Zdończyk, MD	Warszawa	Department of Internal Medicine and Cardiology, Infant Jesus Teaching Hospital, Medical University of Warsaw (15)
	Krystyna Łoboz-Grudzień, MD, PhD Leszek Sokalski, MD, PhD Barbara Brzezińska, MD, PhD	Joanna Jaroch, MD, PhD	Wrocław	T.Marciniak Hospital (11)
	Maciej Lesiak, Professor, MD Magdalena Łanocha, MD		Poznan	Szpital Kliniczny Przemienienia Pańskiego (10)
	Krzysztof W. Reczuch, MD	Adam Kolodziej, MD	Wroclaw	Military Hospital / Medical University (4)
	Zbigniew Kalarus, MD Andrzej Swiatkowski, MD Mariola Szulik, MD		Zabrze	Medical University of Silesia, School of Medicine with the Division of Dentistry, Department of Cardiology, Congenital Heart Diseases and Electrotherapy, Silesian Center for Heart Diseases (3)
	Wlodzimierz J. Musial, MD	Marta Marcinkiewicz-Siemion, MD	Bialystok	University Hospital in Bialystok (1)
Russia (303) Country Coordinator Olga Bockeria, MD, PhD				
	Leo Bockeria, MD, PhD Karen Petrosyan, MD, PhD Tatiana Trifonova, MD	Olga Bockeria, MD, PhD Zalina Kudzoeva, MD Nodira Aripova, MD	Moscow	National Medical Research Center for Cardiovascuar Surgery (113)
	Alexander M. Chernyavskiy, MD, PhD Evgeniy I. Kretov, MD Igor O. Grazhdankin, MD	Ivan A. Naryshkin, MD Alena Kuleshova, MD Dastan Malaev, MD	Novosibirsk	E.Meshalkin National Medical Research Center of the Ministry of Health of the Russian Federation (101)

	Leonid L. Bershtein, MD, PhD Sergey A. Sayganov, MD, PhD Anastasia M. Kuzmina-Krutetskaya, MD Elizaveta V. Zbyshevskaya, MD, PhD Nana O. Katamadze, MD, PhD Elena A. Demchenko, MD, PhD Pavel S. Kozlov, MD Vikentiy Y. Kozulin, MD Ekaterina I. Lubinskaya, MD	Irina Subbotina Victoria Gumerova Olga B. Nikolaeva, MD	Saint Petersburg	North-Western State Medical University (50) Federal Almazov North-West Medical Research Centre (39)
*Spain (286) Country Leader Jose Luis Lopez-Sendon, MD, PhD Country Coordinator Almudena Castro, MD				
	Jose Lopez-Sendon, MD, PhD Almudena Castro, MD Elena Refoyo Salicio, MD Gabriela Guzman, MD Gabriel Galeote, MD Silvia Valbuena, MD	Virginia Fernández-Figares, Pharm	Madrid	Hospital La Paz. IdiPaz (118)
	Jesús Peteiro, MD, PhD María Dolores Martínez-Ruíz, MD Ruth Pérez-Fernández, MD José J Cuenca-Castillo, MD Xacobe Flores-Ríos, MD Óscar Prada-Delgado, MD Gonzalo Barge-Caballero, MD	Moisés Blanco-Calvo, PhD Encarnación Alonso-Álvarez, BSc Paula García-González, BSc	A Coruna	Complexo Hospitalario Universitario A Coruña (CHUAC) Sergas, Department of Cardiology. INIBIC A Coruña. CIBER-CV. Universidad de A Coruña, Spain (112)
	Jose Ramon Gonzalez Juanatey, MD, PhD	Jose Seijas Amigo, Pharm	Santiago de Compostela	Hospital Clinico Universitario de Santiago (17)

	Miguel Souto Bayarri, MD, PhD Virginia Pubull Nuñez, MD Raymundo Ocaranza Sanchez, MD, PhD Belen Cid Alvarez, MD Carlos Peña Gil, MD, PhD Amparo Martinez Monzonis, MD Alessandro Sionis, MD Montserrat Vila Perales, MD Josep Maria Padró, MD Antonio Serra Peñaranda, MD Joan García Picart, MD Antonino Ginel Iglesias, MD Xavier Garcia-Moll Marimon, MD Guillem Pons Lladó, MD Francesc Carreras Costa, MD Vicente Miro, MD	Ana Fernández Martínez, RN	Barcelona	Hospital de la Santa Creu i Sant Pau (11)
	Jose L Diez, MD Pilar Calvillo, MD F. Marin Ortuño, MD, PhD	Begoña Igual, MD	Valencia	Hospital Universitario y Politecnico La Fe (10)
	M. Valdés Chávarri, MD, PhD A. Tello Montolliu, MD, PhD E. Pinar Bermudez, MD, PhD G. De La Morena, MD, PhD	M. Quintana Giner, MD A.I. Romero Aniorte, MD JM. Rivera Caravaca, MD	Murcia	HUVA, Hospital Clínico Universitario Virgen De La Arrixaca (8)
	Montserrat Gracida Blancas, MD	Olga Cañavate Sonia Guerrero Silvia Riera	Barcelona	Hospital De Bellvitge (4)
	Jose Enrique Castillo Luena, MD	Jose Enrique Castillo Luena Maria Lasala	Zaragoza	Hospital Universitario Miguel Servet (4)
	Francisco Fernandez-Aviles, MD	Maria Lorenzo Olga Sobrino Alexandra Vazquez	Madrid	Hospital General Universitario Gregorio Maranon (2)
China (246)				

Country Leader
Lixin Jiang, MD, PhD

Jiyan Chen, MD	Haojian Dong Peiyu He Chunli Xia Junqing Yang Qi Zhong	Guangzhou	Guangdong General Hospital (102)
Yongjian Wu, MD, PhD	Yanmeng Tian, MD Dongze Li	Beijing	Chinese Academy of Medical Sciences, Fuwai Hospital (17)
Yitong Ma, MD Yining Yang, MD	Xiaomei Li Xiang Ma Zixiang Yu Qian Zhao	Urumqi	First Affiliated Hospital of Xinjiang Medical University (15)
Zheng Ji, MD	Chunguang Li Lei Zhang Yu Zhao Bolin Zhu	Tangshan	Tangshan Gongren Hospital (15)
Xinchun Yang, MD	Mulei Chen Hongjie Chi Yang Wang Jing Zhang	Beijing	Beijing Chao-yang Hospital, Capital Medical University (12)
Wenhua Lin, MD	Rui Jing Jingjing Liu	Tianjing	TEDA International Cardiovascular Hospital (12)
Hesong Zeng, MD	Qiang Zhou, MD Chang Xu, MD Zhuxi Li, MD Junhua Li, MD Luyang Xiong, MD Dan Gao	Wuhan	Tongji Medical College (11)
Xin Fu, MD	Dengke Jiang Ran Leng Xutong Wang Qianqian Yuan Lili Zhang	Zhengzhou	The First Affiliated Hospital of Zhengzhou University (11)
Bin Yang, MD	Ziliang Bai Jianhua Li Jie Qi Fei Wang Haitao Wang Bin Yang Zhou Yue Zhulin Zhang	Taiyuan	Shanxi Cardiovascular Hospital (10)

	Songtao Wang, MD	Yumei Dong Jiajia Mao Bin Zhang Xiuhong Li	Qingdao	Qingdao Fuwai Hospital (8)
	Gong Cheng, MD	Xiaowei Yao Nier Zhong Ning Zhou	Xian	Shanxi Provincial People's Hospital (6)
	Yulan Zhao, MD	Yaping Huang, MS Panpan Zhou, MS	Zhengzhou	The Second Affiliated Hospital of Zhengzhou University (6)
	Xuehua Fang, MD	Wei Su	Beijing	Liangxiang Hospital, Beijing Fangshan District (6)
	Qiutang Zeng, MD	Yu Kunwu Yudong Peng Xin Su	Wuhan	Wuhan Union Hospital, Tongji Medical College, Huazhong Science and Tech University (3)
	Xi Su, MD	Chen Wang Yunhai Zhao	Wuhan	Wuhan Asia Heart Hospital (3)
	Qingxian Li, MD	Yaming Geng Yanfu Wang	Jining	Affiliated Hospital of Jining Medical University (3)
	Shao-ping Nie, MD, PhD	Jing-yao Fan, MD Si-ting Feng, MD,PhD Xiao Wang, MD,PhD Yan Yan, MD,PhD Hui-min Zhang, MD,PhD	Beijing	Beijing Anzhen Hospital (2)
	Qin Yu, MD	Lingping Chi Fang Liu	Dalian	Affiliated Zhongshan Hospital of Dalian University (2)
	Jian'an Wang, MD	Han Chen Jun Jiang Huajun Li Jian'an Wang	Hangzhou	The Second Affiliated Hospital Zhejiang University School of Medicine (1)
	Shuyang Zhang, MD, PhD Zhenyu Liu, MD	Yechen Han, MM Lihong Xu, RN Zhenyu Liu Gang Chen Rongrong Hu	Beijing	Peking Union Medical College Hospital (1)
*Italy (139) Country Leader Aldo P. Maggioni, MD				
	Gian Piero Perna, MD	Francesca Pietrucci, PhD	Ancona	

Marco Marini, MD Gabriele Gabrielli, MD Stefano Provasoli, MD Edoardo Verna, MD	Anna Di Donato	Varese	Cardiology and CCU - Ospedali Riuniti Ancona (54) Ospedale di Circolo e Fondazione Macchi (23)
Lorenzo Monti, MD Barbara Nardi, MD		Rozzano	Humanitas Research Hospital, Rozzano (MI) (17)
Antonio Di Chiara, MD	Francesca Pezzetta, MD	Tolmezzo	Azienda Servizi Sanitaria n.3 Alto Friuli-Collinare-Medio Friuli (9)
Andrea Mortara, MD	Valentina Casali, MD	Monza	Policlinico di Monza, Monza MB (8)
Marcello Galvani, MD Filippo Ottani, MD	Chiara Attanasio	Forli	Ospedale “G.B. Morgagni – L. Pierantoni” Forli (AUSL della Romagna) (8)
Marco Sicuro, MD	Gianpiero Leone, MD Francesco Pisano, MD Cristina Bare, BSc	Aosta	Ospedale Regionale Umberto Parini (5)
Paolo Calabro, MD Tiziana Formisano, MD	Fabio Fimiani	Napoli	AORN Dei Colli "V. Monaldi" UOC Cardiologia Università della Campania "L.Vanvitelli" (4)
Giuseppe Tarantini, MD Umberto Cucchini, MD Anto Luigi Andres, MD	Alberto Barioli, MD Federica Ramani	Padua	University of Padua-Cardiology Clinic (3)
Emanuela Racca, MD	Fabrizio Rolfo, MD Cecilia Goletto	Cuneo	Azienda Ospedaliera S. Croce e Carle (3)
Carlo Briguori, MD	Francesca De Micco	Naples	Clinica Mediterranea (2)
Roberto Amati, MD William Vergoni, MD	Stefano Di Marco, MD Martina Tricoli	Pescia	UO Cardiologia Ospedale SS Cosma e Damiano (2)
Aldo Russo, MD Raffaele Fanelli, MD	Massimo Villella, MD	San Giovanni Rotondo	IRCCS "Casa Sollievo della Sofferenza" (1)

*Singapore (61)

Country Leader

Harvey Douglas White, MD

Country Coordinator

Caroline Alsweiler				
	Kian-Keong Poh, MD Ping Chai, MD Titus Lau, MD Joshua P. Loh, MD Edgar L. Tay, MD Kristine Teoh, MD Lynette L. Teo, MD Ching-Ching Ong, MD Raymond C. Wong, MD Poay-Huan Loh, MD Theodoros Kofidis, MD Wan Xian Chan, MD Koo Hui Chan, MD David Foo, MBBS	Sik-Yin V Tan, BSc Winnie C Sia, BSc Audrey W Leong, BSc	Singapore	National University Heart Center Singapore (33)
	Jason Loh Kwok Kong, MD Ching Min Er, MD Fahim Haider Jafary, MD	Li Hai Yan, RN	Singapore	Tan Tock Seng Hospital (22)
	Terrance Chua, MD	Nasrul Ismail Min Tun Kyaw Deborah Yip	Singapore	National Heart Centre Singapore (6)
Germany (54)				
Country Leader				
Rolf Doerr, MD				
	Rolf Doerr, MD Juergen Stumpf, MD Klaus Matschke, MD, PhD Gregor Simonis, MD, PhD Clemens T. Kadalie, MD Udo Sechtem, MD Peter Ong, MD	Dorit Grahl Franziska Guenther Kerstin Bonin Ina Wenzelburger Susanne Gruensfelder, RN	Dresden Stuttgart	Praxisklinik Herz und Gefaesse (29) Robert-Bosch-Krankenhaus (22)

	P. Christian Schulze, MD, PhD Bjoern Goebel, MD Karsten Lenk, MD		Jena	University Hospital Jena (2)
	Georg Nickenig, MD	Jan-Malte Sinning, MD Marcel Weber, MD Nikos Werner, MD	Bonn	Universitatsklinikum Bonn (1)
Austria (50)				
Country Leaders				
Irene Marthe Lang, MD				
Kurt Huber, MD				
	Herwig Schuchlenz, MD Stefan Weikl, MD	Gudrun Steinmaurer	Graz	LKH Graz West Austria (35)
	Irene Marthe Lang, MD	Max-Paul Winter, MD Tijana, Andric, MD	Vienna	Medical University of Vienna, Department of Cardiology (8)
	Kurt Huber, MD Gabriele, Jakl-Kotauschek, MD	Maximilian, Tscharre, MD Claudia, Wegmayr, MSc Bernhard, Jäger, MD Florian, Egger, MD	Vienna	Wilhelminen Hospital Vienna (7)
Hungary (49)				
Country Leader				
Matyas Keltai, MD, PhD, DSc				
	Andras Vertes, MD	Judit Sebo, MD Zoltan Davidovits, MD Laszlone Matics	Budapest	Eszszk- Szent Istvan Hospital (20)
	Albert Varga, MD, PhD	Gergely Ágoston, MD	Szeged	University of Szeged (12)
	Geza Fontos, MD	Gabor Dekany, MD	Budapest	George Gottsegen National Institute of Cardiology (9)
	Bela Merkely, MD, PhD, DSc	Andrea Bartykowszki, MD Pal Maurovich-Horvat, MD, PhD, MPH	Budapest	Heart and Vascular Center, Semmelweis University (8)
	Gabor Kerecsen, MD	Agnes Jakal	Budapest	Military Hospital, Budapest (1)
Serbia (47)				
	Sasa Hinic, MD, BSc	Jelena Djokic, MD	Belgrade	

	Marija Zdravkovic, MD, PhD Vladan Mudrenovic, MD Bogdan Crnokrak, MD Branko D. Beleslin, MD, PhD			University Hospital Center Bezanijska Kosa (13)
	Nikola N. Boskovic, MD Marija T. Petrovic, MD Milan R. Dobric, MD Zeljko Z. Markovic, MD, PhD Ana S. Mladenovic, MD, PhD	Ana D. Djordjevic-Dikic, MD, PhD Vojislav L. Giga, MD, PhD Jelena J. Stepanovic, MD, PhD	Belgrade	Faculty of Medicine, University of Belgrade; Cardiology Clinic, Clinical Center of Serbia (10)
	Nada Cemerlic-Adjic, MD	Lazar Velicki, MD Ljiljana Pupic	Sremska Kamenica	Institute of Cardiovascular Diseases Vojvodina, Sremska Kamenica, Serbia and Faculty of Medicine, University of Novi Sad (9)
	Goran Davidović, MD, PhD Rada Vučić, MD	Stefan M. Simović, MD	Kragujevac	Clinical Center Kragujevac (7)
	Milica Nikola Dekleva, MD PhD	Miroslav Stevo Martinovic, MD Gordana Stevanovic	Belgrade	University Clinical Hospital Zvezdara (6)
	Goran Stankovic, MD	Milan Dobric	Belgrade	Clinical Center of Serbia (1)
	Svetlana Apostolovic, MD	Sonja Salinger Martinovic Dragana Stanojevic	Nis	Clinic for Cardiovascular Diseases, Clinical Center Nis (1)
Mexico (46)				
	Jorge Escobedo, MD Rubén Baleón-Espinosa, MD Arturo S Campos-Santaolalla, MD Elihú Durán-Cortés, MD José M Flores-Palacios, MD Andrés García-Rincón, MD Moisés Jiménez-Santos, MD Joaquín V Peñafiel, MD José A Ortega-Ramírez, MD	Ramon de Jesús-Pérez, RN	Benito Juarez	Instituto Mexicano del Seguro Social (35)

	Aquiles Valdespino-Estrada, MD			
	Erick Alexánderson Rosas, MD	María Fernanda Canales Brassetti, MD Diego Adrián Vences Anaya, MD María Pérez García Isabel Estela Carvajal Juarez , MD Magdalena Madero Rovalo, MC Erick Donato Morales Rodríguez, MD	Mexico City	Instituto Nacional de Cardiología "Ignacio Chávez" (11)

Australia (45)

Country Leaders

Joseph B. Selvanayagam, MBBS (Hons), DPhil

Jamie Rankin, MBBS *(past)*

Country Coordinator

Deirdre Murphy

	Joseph B. Selvanayagam, MBBS (Hons), DPhil Majo X. Joseph, MBBS	Sau Lee, PhD Prince Thomas, RN Melissa D Chaplin, RN	Adelaide	Flinders Medical Centre (30)
	Suku T. Thambar, MBBS	Stephanie C Boer, B Biotechnology (Honours)	New Lambton Heights	John Hunter Hospital (8)
	John F. Beltrame, MD	Jeanette K. Stansborough, RN Marilyn Black, RN	Woodville South	The Queen Elizabeth Hospital (5)
	Graham S. Hillis, PhD	Michelle M. Bonner, B. Nursing Kim F. Ireland, RN Clare Venn-Edmonds, RN	Perth	Royal Perth Hospital (2)

France (42)

Country Leader

Philippe-Gabriel Steg, MD

Country Coordinators

Helene Abergel

Jean-Michel Juliard

	Christophe Thuaire, MD	Corine Thobois, RN Emilie Tachot, RN	Chartres	C.H. Louis Pasteur (21)

	Téodora Dutoiu, MD	Christophe Laure, RN		
		Christel Vassaliere, RN		
	Philippe Gabriel Steg, MD	Helene Abergel, MSc		
	Jean-Michel Juliard, MD	Axelle Fuentes, MSc	Paris	Bichat Hospital (9)
	Michel S. Slama, MD	Ludivine Eliahou, MD	Clamart Cedex	Antoine-Beclere Hospital (5)
	Rami El Mahmoud, MD	Olivier Dubourg, MD Pierre Michaud, MD	Boulogne	Ambroise Pare Hospital (2)
	Eric Nicollet, MD	Sarah Hadjih	Corbeil-Essonnes Cedex	Centre Hospitalier Sud Francilien (2)
	Pascal Goube, MD	Patricia Brito		
	Gilles Barone-Rochette, MD	Gilles Barone-Rochette	Grenoble	Grenoble University Hospital (2)
	Alain Furber, MD	Charles Cornet, MD, PhD	Angers Cedex 9	Centre Hospitalier Universitaire d'Angers (1)
	Loïc Bière, MD	Jeremy Rautureau, MD, PhD		
Lithuania (39)				
		Agne Juceviciene, MD		
		Irma Kalibataite-Rutkauskiene, MD		
		Laura Keinaite		
	Aleksandras Laucevicius, MD	Monika Laukyte	Vilnius	Vilnius University Hospital Santariskes Clinic (39)
	Jelena Celutkiene, MD	Gelmina Mikolaitiene		
		Akvile Smigelskaite, MD		
		Ilona Tamasauskiene, MD		
		Agne Urboniene, MD		
*Netherlands (37)				
	Elvin Kedhi MD, PhD			
	Jorik Timmer, MD	Ilse Bouwhuis	Zwolle	Isala Klinieken (25)
	Rik Hermanides, MD	Lia Nijmeijer		
	Eliza Kaplan, MD			
	Robert K. Riezebos, MD, PhD			
	Pouneh Samadi, MD	Jeannette, J. M. Schoep, RN	Amsterdam	Cardio Research Hartcentrum OLVG (11)
	Elise van Dongen, MD	Elisabeth, M. Janzen, RN		
	Sander R. Niehe, MD			
	Harry Suryapranata, MD	Sandra Ahoud	Nijmegen	Radboudumc (1)

	Stijn van Vugt, MD, PhD			
Portugal (33)				
	Ruben Ramos, MD			
	Duarte Cacela, MD			
	Ana Santana, MD			
	Antonio Fiarresga, MD			
	Lidia Sousa, MD			
	Hugo Marques, MD			
	Lino Patricio, MD	Mafalda Selas		
	Luis Bernanrdes, MD	Filipa Silva		
	Pedro Rio, MD	Cláudia Freixo	Lisbon	Hospital de Santa Marta (25)
	Ramiro Carvalho, MD			
	Rui Ferreira, MD			
	Tiago Silva, MD			
	Ines Rodrigues, MD			
	Pedro Modas, MD			
	Guilherme Portugal, MD			
	Jose Fragata, MD			
	Fausto J. Pinto, PhD	Inês Zimbarra Cabrita, PhD		
	Miguel Nobre Menezes, MD	Andreia Rocha, MSc		
	Guilhermina Cantinho Lopes, MD	Francisca Patuleia Figueiras, PhD		
	Ana Gomes Almeida, PhD	Andreia Coelho, BSc	Lisbon	Santa Maria University Hospital, Cardiology Department, CHLN (6)
	Pedro Canas Silva, MD	Marta Capinha		
	Angelo Nobre, MD	Maria Inês Caetano		
	Ana Rita Francisco, MD	Susana Silva		
	Nuno Ferreira, MD			
	Ricardo L. Lopes, MD		Vila Nova de Gaia	Centro Hospitalar de Vila Nova de Gaia/Espinho, EPE (2)
Argentina (29)				
Country Leader				
Rafael Diaz, MD *(past)*				
	Luis Guzman, MD	Veronica Tinnirello	Cordoba	Instituto Medico DAMIC (11)

	Julio César Figal, MD			
	Oscar Méndiz, MD Claudia Cortés, MD Roberto René Favaloro, MD	Matías Nicolás Mungo	Ciudad Autonoma de Buenos Aires	Fundación Favaloro (10)
	Carlos Alvarez, MD	Marina Garcia	Bahia Blanca	Hospital Italiano Regional del Sur Bahia Blanca (3)
	Javier Courtis, MD Gabriela Zeballos, MD	Valeria Godoy	Cordoba	Clinica Romagosa and Clinica De La Familia (2)
	Lilia Schiavi, MD	Maria Victoria Actis	Cordoba	Clinica Del Prado (2)
	Mariano Rubio, MD	Graciela Scaro, MD	Cordoba	Clínica Privada Vélez Sarsfield (1)
*New Zealand (28)				
Country Leader				
Harvey Douglas White, MD				
Country Coordinator				
Caroline Alsweiler				
	Gerard Patrick Devlin, MD Raewyn Fisher, MD	Liz Low, RN Jayne Scales, RN Kirsty Abercrombie, RN	Hamilton	Waikato Hospital (22)
	Ralph Alan Huston Stewart, MCChB, MD Harvey Douglas White, MD Jocelyne Benatar, MD	Leah Howell , RN Cathrine Patten, RN	Auckland	Auckland City Hospital (6)
*Macedonia (28)				
	Sasko Kedev, MD, PhD Irena Peovska Mitevska, MD, PhD Elizabeta Srbinovska Kostovska, MD, PhD Hristo Pejkov, MD, PhD		Skopje	University Clinic of Cardiology (28)
*Sweden (23)				
Country Leader				
Claes Held, MD, PhD				
	Claes Held, MD, PhD Kai Eggers, MD, PHhD		Uppsala	Uppsala University (18)

	Gunnar Frostfelt, MD, PhD Nina Johnston, MD, PhD Maciej Olsowka, MD Axel Åkerblom, MD, PhD Inga Soveri, MD, PhD	Christina Björklund, RN Maria Andreasson, RN Marie Essermark, RN		
	Johannes Aspberg, MD	Liselotte Persson	Stockholm	Karolinska Institutet at Danderyd Hospital (5)
Israel (15)				
Country Leaders				
Rafael Beyar, MD, MD, DSc, MPH				
Tali Sharir, MD				
Country Coordinator				
Eugenia Nikolsky, MD				
	Tali Sharir, MD Dan Elian, MD	Or Harel, MA	Tel-Aviv	Assuta Medical Centers (9)
	Arthur Kerner, MD Samia Massalha, MD	Margalit Bentzvi Ludmila Helmer	Haifa	Rambam Medical Center (6)
Japan (14)				
Country Leader				
Shun Kohsaka, MD				
	Keiichi Fukuda, MD, PhD Shun Kohsaka, MD	Ikuko Ueda, PhD Jun Fujita, MD Akemi Furukawa, RN	Shinjuku-ku	Keio University (7)
	Satoshi Yasuda, MD, PhD	Kanae Hirase, RN Toshiyuki Nagai, MD, PhD Fumiyuki Otsuka, MD, PhD	Suita-shi	National Cerebral and Cardiovascular Center (4)
	Shigeyuki Nishimura, MD	Shintaro Nakano	Hidaka	Saitama Medical University (3)
*Belgium (7)				
Country Leader				
Frans Van de Werf, MD, PhD				
Country Coordinator				
Kaatje Goetschalckx, MD				

	Kaatje Goetschalckx, MD Frans Van de Werf, PhD, MD Kathleen Claes, PhD, MD	Valerie Robesyn	Leuven	University Hospital Leuven (7)
*Taiwan (7)				
Country Leader				
Harvey Douglas White, MD				
Country Coordinator				
Caroline Alsweiler				
	Chung-Lieh Hung, MD Chun-Ho Yun, MD			
	Charles Jia-Yin Hou, MD Jen-Yuan Kuo, MD			
	Hung-I Yeh, MD, PhD Ta-Chuan Hung, MD Jiun-Yi Li , MD, PhD			
	Chen-Yen Chien, MD, PhD Cheng-Ting Tsai, MD Chun-Chieh Liu, MD Fa-Chang Yu, MD	Yi-Hsuan Yang	Taipei City	Mackay Memorial Hospital (7)
	Yueh-Hung Lin, MD			
	Wei-Ren Lan, MD			
	Chih-Hsuan Yen, MD Jui-Peng Tsai, MD			
	Kuo-Tzu Sung, MD			
*South Africa (7)				
	Mpiko Ntsekhe, MD			
	Shaheen Pandie, MD Charle A Viljoen, MD Marianne De Andrade, MD	Constance Philander (Nee Talliard), ND Noloyiso Mtana, RN	Cape Town	Groote Schuur Hospital / University of Cape Town (7)
*Switzerland (7)				
Country Leader				

Aldo P. Maggioni, MD				
	Tiziano Moccetti, MD M.Grazia Rossi, MD	Adriana Anesini, RN Simona Maspoli, RN Manuela Mombelli, RN	Lugano	Cardiocentro (7)
Egypt (6)				
	Magdy Abdelhamid, MD Ahmed Adel, MD Ahmed Kamal, MsC Hossam Mahrous, MD Sameh El Kaffas, MD Hussien El Fishawy, MD	Ahmed Talaat, MD	Cairo	Cairo University (6)
Romania (5)				
	Calin Pop, MD, PhD Matei Claudia, MD, PhD Bogdan A. Popescu, MD, PhD		Bucharest	Emergency County Hospital Baia Mare (4)
	Carmen Ginghina, MD, PhD Dan Deleanu, MD, PhD Vlad A. Iliescu, MD, PhD	Monica Rosca, MD, PhD Carmen C. Beladan, MD, PhD	Bucharest	Emergency Institute of Cardiovascular Diseases "Prof. Dr. C. C. Iliescu" (1)
*Saudi Arabia (5)				
	Mouaz H. Al-Mallah, MD MSc Ahmed Aljzeeri, MD Hani Najm, MD Ali Alghamdi, MD	Sarah Zahrani, RN	Central Province	King AbdulAziz Cardiac Center (5)
*Peru (4)				
	Walter Enrique Mogrovejo Ramos, MD	Marco Antonio Monsalve Davila, RN	Mirafloes	Instituto Neuro Cardiovascular De Las Americas (4)
Thailand (3)				
Country Leader				
Harvey Douglas White, MD				
Country Coordinator				
Caroline Alsweiler				
	Srun Kuanprasert, MD		Chiang Mai	

	Arintaya Prommintikul, MD Weerachai Nawarawong, MD Surin Woragidpoonpol, MD Thitipong Tepsuwan, MD Noppon Taksaudom, MD Chataroon Rimsukcharoenchai, MD Juntima Euathrongchit, MD Yutthaphan Wannasopha, MD Sukit Yamwong, MD Piyamitr Sritara, MD Suthara Aramcharoen, MD Krissada Meemuk, MD	Supatchara Khwakhong, RN Anong Chaiyasri, RN Warangkana Mekara, RN Supap Kulthawong, RN Anong Amaritakomol, RN Pachara Panpunuan, RN	Bangkok	Maharaj Nakorn Chiang Mai Hospital (2) Ramathibodi Hospital (1)
*Malaysia (2) Country Leader Harvey Douglas White, MD Country Coordinator Caroline Alsweiler	Ahmad Khairuddin, MD Hafidz Abd Hadi, MD Shaiful Azmi Yahaya, MD	Noor Syamira Mokhtar, RN Nor Asiah Basri, RN Irni Yusnida, RN Humayrah Hashim	Kuala Lumpur	Institut Jantung Negara (2)

** Countries participated in Economics Quality of Life (EQoL) Questionnaires*

***This site received one participant in transfer that was randomized at another site*

III. Supplementary Methods

Required Quality Metrics for Participating Sites

A site must meet the following criteria to qualify for participation in the ISCHEMIA trial, as determined by site-reported data collected via the survey qualification process:

1. Access to a Stress Imaging Modality- Must be able to transmit images digitally
2. Access to a CT Scanner- Must be able to produce >64 slices and must perform 1 scan/week
3. PCI site and operator requirements are as follows:
    a. PCI Site Criteria
        i. Must be willing to establish an ISCHEMIA trial HEART TEAM of cardiovascular interventionalists and surgeons that can evaluate randomized patients on an ongoing basis in a collaborative, multidisciplinary fashion
        ii. Average number of annual PCI cases over the last 3 years for the primary PCI location ≥400/year
        iii. EXCLUDING CASES WITH TOTAL OCCLUSION AND STEMI:
            1.Average procedural success rate over the last 3 years >95%:
            2.Average rate of emergency CABG over the last 3 years <0.6%:
            3.Average rate of in-hospital mortality over the last 3 years <1.5%
    b. PCI Operator Criteria
        i. Average number of annual PCI cases for the operator over the last 3 years ≥75cases/year. If the volume is <75 per year, total number of lifetime PCI cases must be >1500 cases:
4. CABG Site and Operator requirements are as follows:
    a. CABG Site Criteria
        i. Average annual total procedures with CABG over the last 3 years ≥125/year
        ii. Average annual cardiac surgical procedures (open heart) over the last 3 years ≥300/year
        iii. AND [either 1, 2 or 3]
            1. Non-risk adjusted in-hospital mortality for all isolated CABG procedures over the last 3 years ≤3.0%
            2. Non-risk adjusted in-hospital mortality for isolated elective CABG procedures over the last 3 years ≤2.0%
            3. (For US Sites participating in STS Registry): Risk adjusted operative mortality for isolated CABG procedures over the last 3 years ≤2.7%
    b. CABG Operator Criteria:
        i. Average number of annual total procedures with CABG for the surgeon over the last 3 years ≥75 cases/year
        ii. Lifetime total procedures with CABG ≥750 cases

Sites that qualified for participation in the EXCEL trial[1] qualified for participation in ISCHEMIA.
[[1]Stone GW, Sabik JF, Serruys PW, et al. Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronaray Disease. N Engl J Med 2017;376:1089.]

Guidelines for Sites on How to Achieve Revascularization of All Ischemic Territories

These revascularization guidelines apply to participants randomized to the invasive management strategy and participants in the conservative management strategy who undergo cardiac catheterization due to failure of guideline-based medical therapy, such as those who experience a myocardial infarction (MI), hospitalization for unstable angina, resuscitated cardiac arrest, or hospitalization for heart failure, or who have angina that is refractory to maximal medical therapy. In such participants in every case revascularization should be performed using the principles of revascularization therapy as outlined below.

Each site should have a "Heart Team" which includes a non-invasive/imaging cardiologist(s) (or a general internist), an interventional cardiologist, and a cardiovascular surgeon. The heart team will collectively decide on the method of revascularization for each ISCHEMIA participant randomized to the invasive strategy.

1. Revascularization Strategy
Revascularization will be performed based on findings from the diagnostic catheterization as well as other relevant clinical information. While the selection of percutaneous coronary intervention (PCI) vs. coronary artery bypass graft surgery (CABG)—or medical therapy only in cases of non-obstructed coronary arteries, diffuse small vessel disease, etc.—will be left to the discretion of the treating team per local standards and expertise. Several general principles should be followed:

- The revascularization modality selected should have the greatest likelihood to safely and effectively relieve significant ischemia in all viable myocardial territories of at least moderate size. In general, non-ischemic and/or non-viable myocardium, as demonstrated by ancillary imaging, will not be a target for revascularization
- Decisions regarding viability testing and revascularization decisions determined by such testing should be based on routine clinical practice

1a. Revascularization by PCI
PCI should be performed with a goal of relieving all areas of significant ischemia (i.e., ischemia that would be detected by noninvasive imaging or by fractional flow reserve (FFR) testing in the catheterization laboratory).

For participants with ischemia in the lesion distribution on noninvasive testing or by FFR:

a. PCI is recommended for lesions with visually estimated diameter stenosis (DS) ≥50% and a reference vessel diameter of ≥2.25 mm
b. PCI is not recommended for lesions with visually estimated DS <50% and a reference vessel diameter of ≥2.25 mm unless FFR ≤0.80
c. The decision whether to perform PCI of a lesion with reference vessel diameter <2.25 mm, which is causing ischemia, should be individualized according to the judgment of the operator. However, in general PCI is recommended if it supplies at least a moderate amount of myocardium

For participants with no ischemia on noninvasive testing in the distribution of a stenotic artery:

PCI is recommended for lesions with visually estimated DS ≥80% and a reference vessel diameter of ≥2.25 mm

a. PCI is not recommended for lesions with visually estimated DS <80% and a reference vessel diameter of ≥2.25 mm unless FFR ≤0.80
b. If FFR is not available, intravascular ultrasound (IVUS) criteria of minimal luminal area ≤4 mm2 + plaque burden ≥60% should be applied
c. Although FFR (strongly preferred) or IVUS is required to guide PCI decisions of lesions with DS <80% with no evidence of ischemia with noninvasive testing, there may be situations in which PCI is acceptable without such testing (e.g. ruptured plaque)

1b. Revascularization by CABG

Anatomy (% stenosis and epicardial coronary artery architecture) has typically guided decision-making in surgical revascularization. Given the absence of intraoperative FFR or IVUS, the assessment of ischemic regions must rely on preoperative testing and FFR/IVUS at diagnostic catheterization. Anatomically, all coronary arteries with ≥70% stenosis and >1.5 mm in diameter should be revascularized unless these territories are known not to be ischemic on the basis of other noninvasive or invasive testing. Functionally, all ischemic myocardial areas (subtended by coronary arteries with visually assessed ≥50% diameter stenosis) should be grafted. For important left main stenosis, all participants should have at least one bypass graft to the left anterior descending coronary artery system and a second graft to circumflex coronary artery system.

Prior to performing PCI or CABG, the Heart Team should review each participant and determine the strategy of revascularization for the individual participant. The strategy will include a plan of which lesions/vessels will be attempted based on the considerations described above.

2. Complete “Ischemic Revascularization” vs. Complete “Anatomic Revascularization”

Complete anatomic revascularization is defined for PCI as revascularization of all vessels ≥2.25 mm reference vessel diameter with a DS ≥70%; for CABG, revascularization of all vessels >1.5 mm reference vessel diameter with a DS ≥70%.

Complete ischemic revascularization is defined for PCI as revascularization of all vessels ≥2.25 mm that have been demonstrated to result in ischemia by noninvasive imaging or FFR (see above); for CABG, grafting of all areas of significant ischemia based on preoperative testing or FFR of intermediate lesions at diagnostic catheterization, as well as making every effort to revascularize areas subtended by occluded coronaries unless the myocardium is demonstrated to be nonviable.

The goal of revascularization in ISCHEMIA is complete ischemic revascularization rather than complete anatomic revascularization. For assessment of the completeness of ischemic revascularization, physiologic significance “trumps” anatomic severity. For example, if the angiographic DS is ≥70% but the FFR is >0.80, that lesion does not require treatment for ischemic revascularization to be considered to be complete, however, may be indicated for bypass grafting based on surgical anatomic criteria and judgment.

3. Role of the Angiographic Core Lab
The angiographic core lab will analyze coronary angiograms according to the definitions of complete ischemic revascularization and complete anatomic revascularization for all participants randomized to the invasive strategy.

Following CABG or PCI, the angiographic core lab will determine the extent of revascularization by review of post-procedural angiograms and other relevant clinical data including operative notes, which will be routinely submitted for evaluation.
The angiographic core lab will also analyze cases requested by the Clinical Events Committee or Clinical Coordinating Center related to suspected outcome events.

4. Criteria to Select PCI vs. CABG
In general, the decision between PCI and CABG will be determined according to local hospital standards and practices. Guidelines from professional societies and appropriateness criteria should be incorporated into the decision process.1-3 It is desirable for the study's Heart Team (interventional cardiologist and cardiac surgeon) to discuss each case after diagnostic angiography to reach a consensus on the best revascularization technique. The overriding goal is to select the approach that the heart team believes will provide the most complete relief of ischemia with the lowest chance of procedure-related death, MI, or stroke.

It is recognized, however, that in some cases of non-complex coronary artery disease that the performance of "ad hoc" PCI after diagnostic angiography may be preferred by participants and physicians.4, 5 Whenever possible, the Heart Team should record an opinion on each participant regarding the best mode of revascularization, reaching a consensus where possible, and recording disagreement if not possible.

In general, the following principles should be followed when selecting between PCI and CABG:
a. For participants with 1- or 2-vessel disease, revascularization may be performed by either PCI or CABG depending on the complexity of the coronary anatomy and other considerations:

- If PCI is selected, ad hoc PCI is permitted if the anticipated success rate is >95% with major complication rate <1% (and renal function is normal)
- Staged PCI for 2-vessel disease should be considered if the estimated glomerular filtration rate is <60 ml/min
- CABG is recommended for severe diffuse disease, marked calcification or vessel tortuosity, complex branch lesions, complex chronic total occlusions supplying viable myocardium, or situations otherwise unfavorable for PCI
- For both PCI and CABG, every attempt will be made for the selected revascularization procedure to be performed within one week following randomization. While this will not always be feasible, the target in all cases is for Cath and revascularization (if it is to occur) to be performed within 30 days

b. For participants with 3-vessel or unprotected left main disease:

- Ad hoc PCI is strongly discouraged and is not permitted in participants with unprotected left main (LM) disease. The catheterization procedure should be terminated after the diagnostic portion is complete. A SYNTAX score should be calculated, and the case

discussed by the Heart Team and participant to reach a consensus decision as to whether PCI vs. CABG is most appropriate for that particular participant

- The SYNTAX score has been found to be prognostically useful in selecting patients with 3-vessel and LM disease who may have comparable or even improved outcomes with PCI utilizing drug-eluting stents compared to CABG. Conversely, the two- and three-year outcomes for intermediate and high SYNTAX score patients are significantly better with CABG 6-8 9
- In the SYNTAX study, approximately a third of patients with 3-vessel and LM disease were referred for CABG because of advanced disease. In the remaining patients—felt to be suitable for CABG or PCI by the interventionalist/surgeon team, and depending on local expertise and experience—as a general guideline:
  - PCI is recommended for SYNTAX score 0 to 22 (low)
  - CABG is recommend for SYNTAX score ≥33 (high)
  - PCI or CABG may be performed for SYNTAX score 23 to 32 (intermediate); if in doubt, CABG is recommended

c. Non-Coronary Factors

Diabetes, renal insufficiency, and low left ventricular ejection fraction are by themselves not sufficient criteria to determine selection of PCI vs. CABG. Some,10 but not all11 meta-analyses have found improved late survival in patients with diabetes managed with CABG rather than PCI. A recent randomized trial of stents vs. CABG in diabetic patients found comparable short-term mortality between the two modalities.12 However, in the larger more recent randomized trial—the FREEDOM trial—CABG significantly reduced rates of death and myocardial infarction as compared with PCI, with a higher rate of stroke.13 Of note, 86% of patients in this trial had triple vessel disease, with a mean of 5.7 lesions per patient. Thus, these trial results primarily apply to outcomes of patients with very advanced coronary artery disease. Nonetheless, patients with diabetes often have more diffuse disease than patients without diabetes which is better managed with CABG. Focal, discrete atherosclerotic disease in patients with diabetes may be treated by PCI. If there is equipoise between PCI and CABG in patients with diabetes, in general CABG should be preferred.

d. Chronic Total Occlusion

An artery with a chronic total occlusion (CTO) supplying viable myocardium with significant ischemia should be revascularized. A well-formed collateral supply is not adequate to protect the patient from ischemia. PCI is an acceptable first choice if the anticipated procedural success rate is reasonably high (>70%) and complication rate low (<1%), and a drug eluting stent (DES) can be placed; otherwise CABG should be performed.

Definitions of Outcomes

Death

All deaths will be adjudicated and classified as cardiovascular, non- cardiovascular or undetermined. Cardiovascular deaths are defined as all deaths excluding those for which the principal and underlying cause is solely non-cardiovascular. Any death for which a cardiovascular contributing cause is suspected will also be considered a cardiovascular death.

Myocardial Infarction

Two versions of MI will be adjudicated in ISCHEMIA: a primary definition and secondary definition. Each definition includes a hierarchy of markers and threshold values as well as a set of rules for diagnosing MI when one or more key elements of the medical record are missing.

The Primary Definition is based upon the Universal Definition of MI, but relies upon site-reported MI decision limits for troponin (which may or may not be the same as the manufacturer 99%URL), and has selected unique marker criteria for MI after PCI or CABG (Type 4a, 5).

The Secondary Definition is also based upon the Universal Definition of Myocardial Infarction, but specifically uses the 99%URL from the assay manufacturer's package insert (which may or may not be the site's MI decision limit) and uses the same supporting criteria (eg. angiographic and ECG) as the UMI definition.

All MI events will be classified based on the Universal MI classification system as follows:

- Type 1: Spontaneous MI
- Type 2: Secondary MI
- Type 3: Sudden Death MI
- Type 4a: MI related to PCI
- Type 4b: MI related to stent thrombosis
- Type 4c: MI related to stent restenosis
- Type 5: MI related to CABG
- Silent MI

Spontaneous MI (Types 1, 2, 4b, 4c)

Diagnosis of spontaneous MI will be satisfied by a clinical setting consistent with acute myocardial ischemia and any one or more of the following criteria:

Marker elevation, as outlined below and at least 1 of the following:

- Symptoms of ischemia, usually lasting > 20 minutes in duration
- New ischemic ST and/or T wave and/or Q-wave ECG changes, or new LBBB, as described below
- Imaging evidence of new loss of viable myocardium in comparison to the baseline imaging test
- Angiographic evidence of intracoronary thrombus, stent thrombosis (4b) or high-grade in-stent restenosis (≥50%) (4c)

Marker data not available and at least 2 of the following:

- New ischemic ST and/or T wave and/or Q-wave ECG changes, or new LBBB, as described below
- Imaging evidence of new loss of viable myocardium in comparison to the baseline imaging test
- Angiographic evidence of intracoronary thrombus.

Autopsy evidence of a fresh myocardial infarction as stand-alone criterion

Spontaneous MI Marker Criteria

Troponin, including high-sensitivity troponin, is the preferred biomarker and takes precedence over CK-MB for both definitions.

Primary Definition: Preferentially uses a troponin threshold value reported as MI Decision Limit or the Upper Limit of Normal (ULN). Marker elevation is defined as troponin > ULN/MI decision limit. If troponin is not done or not available, then CK-MB > ULN will qualify. If both troponin and CK-MB are not done or not available, then CK > 2 x ULN will qualify.

Secondary Definition: Preferentially uses a troponin threshold reported by the manufacturer, namely, the manufacturer 99th percentile. Marker elevation is defined as troponin > 99th percentile. If the troponin 99th percentile is not reported, then troponin > ULN will qualify. If troponin is not done or not available, then CK-MB > ULN will qualify. If both troponin and CK-MB are not done or not available, then CK > 2 x ULN will qualify.

Spontaneous MI ECG Criteria

ECG criterion is considered to be met if any of the following:

ST elevation: New ST elevation at the J-point in two contiguous leads with the cutpoints: ≥ 0.2 mV in men >age 40 and ≥ 0.25mV in men <40 years or ≥ 0.15 mV in women in leads V2–V3 and/or ≥ 0.1 mV in other leads, or new LBBB.

Any new Q-wave in leads V2–V3 ≥ 0.02 seconds or QS complex in leads V2 and V3 or Q-wave ≥ 0.03 seconds and ≥ 0.1 mV deep or QS complex in leads I, II, aVL, aVF, or V4–V6 in any two leads of a contiguous lead grouping (I, aVL, V6; V4–V6; II, III, and aVF) or R-wave ≥ 0.04 seconds in V1–V2 and R/S ≥ 1 with a concordant positive T- wave in the absence of a conduction defect.

ST depression and/or T-wave changes, new horizontal or down-sloping ST depression ≥ 0.05 mV in two contiguous leads; and/or T-wave inversion ≥ 0.1 mV in two contiguous leads. The ST-T wave criteria only apply in the absence of findings that would preclude ECG analysis such as LBBB, LVH with repolarization abnormalities, pre-excitation and pacemakers.

Silent MI

This event includes evidence of new silent Q-wave MI detected during routine protocol or clinically obtained ECG follow-up. Silent MI events will be classified as a type 1 MI.

Sudden death MI (Type 3)

MI events in which a presentation consistent with infarction is present but the patient dies before the biomarkers are drawn or within the first few hours of the event before the biomarkers become positive. Sudden unexpected cardiac death, including cardiac arrest, often with symptoms suggestive of myocardial ischemia, accompanied by presumably new ST-segment elevation, or new LBBB, or evidence of fresh thrombus in a coronary artery by angiography and/or at autopsy, but death occurring before blood samples could be obtained, or at a time before the appearance of cardiac biomarkers in the blood.

PCI-Related MI (Type 4a)

Primary Definition

CK-MB is the preferred biomarker and takes precedence over troponin. For subjects with normal baseline biomarker level pre-PCI, peri-PCI MI requires a rise in CK-MB to >5-fold the ULN (or a rise in troponin to >35 times the MI Decision Limit/ULN, when CK- MB is unavailable) within 48 hours post-PCI. If pre-PCI cardiac markers (CKMB or cTn) are elevated, they must be stable or falling as indicated by two samples at least 6 h apart. The post-PCI CKMB level should reflect a rise of >20% over pre-PCI levels. In addition to biomarker criteria, peri-PCI MI requires at least one of the following:

- Post- procedure angiographic TIMI 0/1 flow in a major coronary artery or a side branch with reference vessel diameter ≥2.0 mm which had TIMI 2-3 flow at baseline, or TIMI 2 flow in a major coronary artery or a side branch with reference vessel diameter ≥3.0 mm which had TIMI 3 flow at baseline or Type C dissection (NHLBI classification) or greater in the target vessel.
- New ECG changes (ST segment elevation or depression >0.1mV in 2 contiguous leads), new pathologic Q-waves in ≥2 contiguous leads, or new persistent LBBB present on a post-PCI ECG obtained at least 30 minutes and up to 48 hours post procedure in the absence of any intervening coronary event between the time of the PCI procedure and the ECG showing changes.

NOTE: A type 4a MI will be diagnosed with a rise in CK-MB to >10-fold the ULN (or when CK-MB is unavailable, a rise in troponin to >70 times the MI Decision Limit/ULN) as a stand-alone criterion. If biomarkers are missing, a type 4a MI will be diagnosed if BOTH ECG criteria (new ST elevation or depression, Q-wave criteria, or new and persistent LBBB) AND angiographic criteria above are present. If pre-PCI cardiac markers are missing, they will be assumed to be normal in those without a preceding event.

Secondary Definition

Elevation of troponin values >5 X 99th percentile URL within 48 hours post-PCI in patients with normal baseline troponin values pre-PCI AND a rise of troponin values >20% if the baseline values are elevated pre-PCI and are stable or falling. If the troponin 99th percentile is not available, the MI Decision Limit / ULN may be used. If troponins are not available, CKMB elevation >5 X ULN will be used.

In addition to biomarker criteria, peri-PCI MI requires at least one of the following:

- Symptoms suggestive of myocardial ischemia (≥20 min)

- New ischemic ST changes or new pathological Q waves. (see “ECG Criteria” above) Note the UMI definition uses ≥0.05 mV of STD whereas the ISCHEMIA definition uses ≥ 0.1mV for PCI related ECG criteria
- Angiographic evidence of a flow limiting complication, such as loss of patency of a side branch, persistent slow-flow or no re-flow, embolization, or Type C dissection (NHLBI classification) or greater in the target vessel.
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

NOTE: A type 4a MI will be diagnosed with a rise in troponin to >70 times the 99th percentile URL (or, when troponin is unavailable, a rise in CK-MB to >10 times the ULN) as a stand-alone criterion. If biomarkers are missing, a type 4a MI will be diagnosed if BOTH ECG criteria (new ST elevation or depression, Q-wave criteria, or new and persistent LBBB) AND angiographic criteria above are present. If pre- PCI cardiac markers are missing, they will be assumed to be normal in those without a preceding event.

CABG-Related MI (Type 5)

Primary Definition

CK-MB is the preferred serum biomarker and takes precedence over cardiac troponin. For subjects with normal baseline biomarker level pre-CABG, peri-CABG MI requires a rise in CK-MB to >10-fold the ULN (or a rise in troponin to >70 times MI Decision Limit/ULN when CK-MB is unavailable) within 48 hrs post-CABG. In addition to biomarker criteria, peri-CABG MI requires at least one of the following:

- A new substantial wall motion abnormality by cardiac imaging (CEC assessed), except new septal and apical abnormalities. The CEC will have latitude in determining whether a new wall motion abnormality is “substantial” in the context of the clinical event.
- New pathologic Q-waves in ≥2 contiguous leads or new persistent LBBB is present on post CABG ECG obtained day 3 post CABG, or hospital discharge, whichever comes earlier in the absence of any intervening coronary event between the time of the CABG procedure and the ECG showing changes.

NOTE: A type 5 MI will be diagnosed with a rise in CK-MB to >15-fold the ULN (or when CK-MB is unavailable a rise in troponin to >100 times the MI Decision Limit/ULN) as a stand-alone criterion. If biomarkers are missing, an MI will be diagnosed if the ECG criteria (New pathologic Q waves or new persistent LBBB) AND new substantial wall motion abnormality are BOTH present. If pre-CABG cardiac markers are missing, they will be assumed to be normal in those without a preceding event.

Secondary Definition

Elevation of troponin values >10 X 99th percentile URL within 48 hrs post-CABG in patients with normal baseline troponin values (≤ 99th percentile URL). If the troponin 99th percentile is not available, the ULN may be used. If troponins are not available, CKMB elevation >10 X ULN will be used. In addition to biomarker criteria, peri-CABG MI requires at least one of the following:

- New pathologic Q waves or new LBBB
- Angiographic evidence of new graft or new native coronary artery occlusion.
- Imaging evidence of new loss of viable myocardium.

NOTE: A type 5 MI will be diagnosed with a rise in troponin to >100 times the 99th percentile URL (or when troponin is unavailable a rise in CK-MB to >15 times the ULN) as a stand-alone criterion. If biomarkers are missing, an MI will be diagnosed if the ECG criteria (New pathologic Q waves or new persistent LBBB) AND new substantial wall motion abnormality are BOTH present. If pre-CABG cardiac markers are missing, they will be assumed to be normal in those without a preceding event.

Complicated MI and Large MI

Complicated MI: Prognostically important MIs may also be identified as those with complications such as hemodynamic instability, cardiogenic shock, drop in EF >10% from baseline, electrical instability with life-threatening VT or VF, or heart failure complicating MI. Complicated myocardial infarctions may typically require ICU care, invasive support (eg. intubation, IABP, PA catheters) and intravenous medications (eg. inotropes or antiarrhythmics.) CEC adjudicators will identify complicated MIs based upon the information available to them in the eCRF and source documents.

- Hemodynamic instability: requiring fluids, inotropic or vasopressor support to maintain end-organ perfusion. May progress to shock if also accompanied by end-organ underperfusion.
- Shock: Compromise of end-organ perfusion due to hemodynamic instability and sustained hypotension. Often manifested by hypotension, increased creatinine, shock liver, and decreased mentation.
- Life-threatening VT or VF: Requiring antiarrhythmics or defibrillation to return sinus rhythm. Transient runs of VT (eg. during reperfusion) are not associated with hemodynamic instability are not usually considered life-threatening.
- Decreased EF ≥ 10%: EF assessment during the event which indicates a drop from prior assessments (eg. EF 30% from previous EF 55%)
- HF in the setting of an MI is defined on the basis of the physician's decision to treat HF with an intravenous (IV) diuretic, IV inotropic agent or IV vasodilator and at least 1 of the following:
    - Presence of pulmonary edema or pulmonary vascular congestion on chest radiograph believed to be of cardiac cause.
    - Rales greater than 1/3 up the lung fields believed to be due to HF.
    - Pulmonary Capillary Wedge Pressure (PCWP) or left ventricular end diastolic pressure (LVEDP) greater than 18 mmHg.
    - Dyspnea, with documented paO2 less than 80 mmHg on room air or O2 saturation less than 90% on room air, without significant lung disease

Large MI: The size of MI will be assessed by examining peak levels of cardiac biomarkers as a continuous function.

Hospitalization for Unstable Angina

Prolonged ischemic symptoms at rest (usually ≥10 minutes in duration), or accelerating pattern of chest pain that occurs with a lower activity threshold (CCS class III or IV) considered to be myocardial ischemia upon final diagnosis resulting in an unscheduled visit to a healthcare facility resulting in an overnight stay generally within 24 hours of the most recent symptoms, cardiac biomarkers not meeting MI criteria, and at least one of the following:

- New or worsening ST or T wave changes on resting ECG* (core laboratory assessed)
- Angiographic evidence of a ruptured/ulcerated plaque, or thrombus in an epicardial coronary artery believed to be responsible for the ischemic symptoms/signs (core laboratory assessed).

*ECG Criteria:
ST segment shifts and T-wave changes: New horizontal or down-sloping ST depression ≥0.05 mV in two contiguous leads; and/or T inversion ≥0.1 mV in two contiguous leads, or new ST segment elevation ≥0.1mV in 2 contiguous leads. The ST-T wave criteria only apply in the absence of findings that would preclude ECG analysis such as LBBB, LVH with repolarization abnormalities, pre-excitation and pacemakers.

Resuscitated Cardiac Arrest

Resuscitated cardiac arrest is defined as successful resuscitation for documented cardiac arrest out-of-hospital (or ER) in a patient subsequently admitted to hospital, and then discharged. A patient who is successfully resuscitated but dies before hospital discharge of complications related to the cardiac arrest (e.g., anoxic encephalopathy, septic shock), will be classified as a coronary heart disease death. An uncomplicated procedure-related cardiac arrest with prompt resuscitation and without adverse sequelae will not be counted as an event. Events that meet the MI criteria will be categorized as MI.

Hospitalization for Heart Failure

While patients may have multiple simultaneous disease processes, for the outcome event of heart failure requiring hospitalization, the diagnosis of congestive heart failure would need to be the primary process. Heart failure (HF) requiring hospitalization is defined as an event that meets the following criteria:

a. Requires hospitalization defined as an admission to an inpatient unit or a visit to an emergency department that result in at least a 24 hour stay (or a date change if the time of admission/discharge is not available).

AND

b. Clinical symptoms of heart failure, including at least one of the following: New or worsening
   - Dyspnea
   - Orthopnea
   - Paroxysmal nocturnal dyspnea
   - increasing fatigue/worsening exercise tolerance

AND

c. Physical signs of heart failure, including at least two of the following:
    1. Edema (> 2+ lower extremity)
    2. Pulmonary rales (pulmonary edema not occurring as the consequence of an arrhythmia in the absence of worsening heart failure. If pulmonary edema complicates acute MI event should be coded as MI)
    3. Jugular venous distension
    4. Tachypnea (respiratory rate > 20 breaths/minute)
    5. Rapid weight gain
    6. S3 gallop
    7. Increasing abdominal distension or ascites
    8. Hepatojugular reflux
    9. Radiological evidence of worsening heart failure
    10. A right heart catheterization within 24 hours of admission showing a pulmonary capillary wedge pressure (pulmonary artery occlusion pressure) ≥ 18 mm Hg and/or a cardiac output < 2.2 L/min/m2

NOTE: Biomarker results (e.g., brain natriuretic peptide (BNP)> 500 or Pro-NT BNP > 2500) consistent with congestive heart failure will be supportive of this diagnosis, but the elevation in BNP cannot be due to other conditions such as cor pulmonale, pulmonary embolus, primary pulmonary hypertension, or congenital heart disease. Increasing levels of BNP, although not exceeding the ULN, may also be supportive of the diagnosis of congestive heart failure in selected cases (e.g. morbid obesity).

AND

d. Need for additional/increased therapy
   Initiation of, or an increase in, treatment directed at heart failure or occurring in a patient already receiving maximal therapy for heart failure and including at least one of the following:
    1. Initiation of or a significant augmentation in oral therapy for the treatment of congestive heart failure
    2. Initiation of intravenous diuretic, inotrope, or vasodilator therapy
    3. Uptitration of intravenous therapy, if already on therapy
    4. Initiation of mechanical or surgical intervention (mechanical circulatory support, heart transplantation or ventricular pacing to improve cardiac function), or the use of ultrafiltration, hemofiltration, or dialysis that is specifically directed at treatment of heart failure.

AND

e. No other non-cardiac etiology (such as chronic obstructive pulmonary disease, hepatic cirrhosis, acute renal failure, or venous insufficiency) and no other cardiac etiology (such as pulmonary embolus, cor pulmonale, primary pulmonary hypertension, or congenital heart disease) for signs or symptoms are identified.

Stroke

Stroke is defined as the rapid onset of a new neurologic deficit attributed to an obstruction in cerebral blood flow and/or cerebral hemorrhage with no apparent non-vascular cause (eg. trauma, tumor, or infection). Available neuroimaging studies will be considered to support the clinical impression and to determine if there is a demonstrable lesion compatible with an acute stroke.

Classification:

Transient Ischemic Attack

A Transient Ischemic Attack is defined as an acute episode of focal cerebral, spinal, or retinal dysfunction caused by an ischemia of central nervous system tissue which resolves within 24 hrs and without neuroimaging evidence of acute infarction.

Ischemic Stroke

Ischemic stroke is defined as an acute episode of focal cerebral, spinal, or retinal dysfunction caused by an infarction of central nervous system tissue.

Signs/ symptoms ≥ 24 hrs regardless of neuroimaging findings:

Ischemic stroke can be defined clinically- by persistence of signs and symptoms ≥ 24 hrs, usually supported by evidence of infarction on neuroimaging (CT or MRI) although very early neuroimaging (usually with CT) may not demonstrate the infarction.

Signs/ symptoms < 24 hrs with neuroimaging evidence of infarction:

Ischemic stroke can be defined by neuroimaging- where neuroimaging (usually MRI diffusion weighted or flair images) confirms the presence of acute infarction even if signs/ symptoms resolve within 24 hrs.

Patients admitted for an acute stroke treated with thrombolysis or interventions that have no residual neurologic symptoms after treatment will be classified as an ischemic stroke.

Ischemic Stroke with Symptomatic Hemorrhagic Conversion

Hemorrhagic conversion may be a consequence of ischemic stroke and may be symptomatic, resulting in neurologic deterioration, or asymptomatic. Symptomatic Hemorrhagic Conversion is defined neuroimaging evidence of hemorrhage within the area of infarction associated with clinical deterioration (eg. increase in NIHSS of ≥ 4 points) or death, symptoms to hemorrhage related mass effect, or symptoms out of proportion to what would be expected from the ischemic stroke or cerebral edema alone. When an Ischemic Stroke with Symptomatic Hemorrhagic Conversion is identified, the date and time of stroke onset will refer to the first onset of the Ischemic Stroke and will not be counted as two events.

Hemorrhagic Stroke

Hemorrhagic stroke is defined as an acute episode of focal or global cerebral or spinal dysfunction caused by a non-traumatic intraparenchymal, intraventricular, or subarachnoid hemorrhage.

Undetermined- or Uncertain type- of Stroke

Undetermined stroke is defined as a stroke with insufficient information to allow categorization as Ischemic Stroke or Hemorrhagic Stroke. If possible, speculate on the stroke subtype and note in Comments. This is not to signify an indeterminate event where there is insufficient evidence to suspect a stroke had occurred.

SUPPLEMENTARY STATISTICAL METHODS

Pre-Specified Primary Cox Model

Outcome differences by treatment group were assessed in accordance with the statistical analysis plan using the Cox proportional-hazards model. To improve power and interpretability, the Cox model for each outcome was adjusted for a set of pre-specified baseline covariates (age, sex, estimated glomerular filtration rate [eGFR], ejection fraction, and diabetes). Continuous variables (age, eGFR, and ejection fraction) were modeled as restricted cubic splines with 2 degrees of freedom. For some patients ejection fraction was available in a categorical (35-45, 45-55, 55+) but not continuous form. We used a multiple imputation procedure to convert these patients' categorical ejection fraction values into continuous. Missing covariate data were rare and were handled within the same multiple imputation procedure with categorical ejection fraction.

Competing Risks

The application of the Cox model accounted for the competing risk of death in the analysis of non-fatal outcomes and the competing risk of non-cardiovascular death in the analysis of outcomes that include cardiovascular but not non-cardiovascular death. We modeled the cause-specific hazard of the outcome of interest semi-parametrically under the proportional hazards assumption and left the form of the cause-specific hazard function of the competing event type unspecified. This was equivalent to treating patients with competing risk events as censored.

Assessment of Proportional Hazards

The underlying assumption of proportional hazards for the Cox model was assessed graphically and by including time by treatment interaction terms. The statistical analysis plan specified that results presentation would emphasize alternative nonparametric analyses if the proportional hazards assumption was violated. Indeed, the proportional hazards assumption was not met for the primary outcome ($p < 0.0001$ for test of time x treatment interaction) and for several secondary outcomes. Under non-proportional hazards, the p-value generated by the Cox model for testing the hypothesis of no difference in covariate-specific hazard rates by treatment group maintains its type-I error rate validity but is less powerful compared to the case where the proportional hazards assumption is satisfied.

Nonparametric Cumulative Incidence Function Estimator

Cumulative event probability curves were estimated by the Kaplan-Meier method for outcomes not subject to competing risks and by a nonparametric cumulative incidence function estimator for outcomes that were subject to competing risks. Non-fatal outcomes such as myocardial infarction and heart failure are subject to the competing risk of death because the occurrence of such an event may be prevented by death. Cardiovascular death is also subject to competing risks because a cardiovascular death may be prevented by non-cardiovascular death. In general,

outcomes not subject to competing risks were all-cause death and composite outcomes that include all-cause death as a component outcome. Outcomes subject to competing risks are all the others. The cumulative incidence function estimator for competing risk data reduces to the Kaplan-Meier as a special case when it is applied to outcomes that are not subject to competing risks.

Considerations for Crossing Event Rate Curves

For outcomes that are measured by time until the outcome occurs, there is no single number that can fully and uniquely capture the difference between treatment groups. This is because the magnitude of difference varies depending on the choice of time point for assessing a difference and the measurement scale (e.g. relative versus absolute differences). From a very general perspective, the "effect" of being randomized to invasive versus conservative treatment on a time-to-event outcome is the set of curves describing the event's probability of occurrence by time t over time in each treatment group. If these curves cross, then judgments about which treatment is "better" may depend heavily on the choice of summary metric. Such a determination is further complicated by the progressively greater statistical uncertainty accompanying estimates at later time points due to fewer patients being followed. In light of these challenges, the investigators' analysis and reporting philosophy was to report the data in a manner that provides readers with the full spectrum of relevant estimates and uncertainty measures. In particular, we sought to avoid a presentation style that causes study interpretation to be dominated by the investigators' own subjective preferences about the choice of a single summary metric. The ability to provide text descriptions of multiple summary metrics was partly constrained by the Journal's length requirements.

Difference in Event Rate at a Specified Time Point

In accordance with the SAP, cumulative outcome event rates and differences in these event rates were tabulated at annual time points and presented with 95% confidence intervals. . Differences at 6 months were also tabulated to reflect early differences arising from procedural complications as assigned revascularization procedures were completed by then.

Restricted Mean Event-Free Time

This metric is derived from the cumulative event rate curves and is interpreted as the per-person average number of days spent "event-free" during the time point between randomization and a designated time point which we selected as 5 years. A caveat about restricted mean event-free time is that it is heavily influenced by the proportion of patients who are event-free for the full 5 years. If this proportion is close to 1 (e.g. rare outcome events) then the average event-free time will necessarily be close to 5 and the difference between groups will necessarily be small. This feature is not necessarily undesirable as it correctly reflects the fact that rare events tend to have a limited impact on the average days spent event-free over the follow-up period.

BAYESIAN COMPETING RISKS NON-PROPORTIONAL HAZARDS SURVIVAL ANALYSIS

Overview

The goal of this analysis is to provide a framework for making probability statements about the direction and magnitude of the unknown treatment effect. We use the phrase "event probability curve" to describe the unknown probabilities that generated the study data. Our goal was to quantify the probability that curves for the invasive and conservative groups differ by an amount that is clinically meaningful. Separate parallel analyses were performed for three outcomes: (1) the primary outcome, (2) the major secondary outcome of CV death or MI, and (3) all-cause death.

Bayesian Background

Bayesian analysis uses the language of probability to express beliefs about unknown quantities and clinical hypotheses in light of prior beliefs and the current study data. [1,2] The output of a Bayesian analysis is a posterior probability distribution describing the relative likelihood of different numerical estimates of unknown quantities. The posterior distribution of a parameter of interest can be summarized graphically in the form of a histogram or tabulated by presenting the probability that the true parameter is above or below some chosen numerical value. The Bayesian analog of a confidence interval (known as a credible) has a direct and intuitively appealing interpretation as an interval containing the true value with a specified probability e.g. 95%.

Statistical Model

We originally planned to perform Bayesian analysis using the Cox proportional hazards model. Because the proportional hazards assumption underlying the Cox model was violated, we instead present a post-hoc Bayesian analysis using a flexible piecewise-exponential hazards (non-proportional hazards) model. The piecewise exponential approach was selected because it lends itself to simple and efficient Bayesian Markov Chain Monte Carlo (MCMC) computation and because it is flexible enough to accommodate a variety of shapes for the unknown cause-specific hazard function.[3] To implement the piecewise exponential modeling approach, follow-up time was divided into 14 intervals (0 to 14 days, 14 to 30 days, 30 to 60 days, 60 to 90 days, 90 to 180 days, 180 to 365 days, 1 to 1.5 years, 1.5 to 2 years, 2 to 2.5 years, 2.5 to 3 years, 3 to 3.5 years, 3.5 to 4 years, 4 to 5 years, 5 to 6 years, and beyond 6 years). The cause-specific hazard function for the event of interest was then approximated as a constant function within each treatment group and time interval. Additional details are in the Technical Details section which is immediately after the results.

Prior Distribution

Bayesian analysis requires the specification of a probability distribution representing prior information about the set of unknown model parameters before observing the study data. Because prior information about model parameters was limited, our goal was to choose a

noninformative prior that would allow inferences to be driven by the current study data. The prior assumed that hazard rate parameters describing risk with each time interval in the CON group followed independent gamma distributions and that log-hazard ratios comparing INV to CON within each time interval followed independent diffuse normal distributions. To explore sensitivity to the choice of prior distribution we performed sensitivity analyses by using alternative specifications for the parameters of the gamma distributions and by assuming that log-hazard ratios follow an autoregressive AR(1) prior making them a priori dependent instead of independent. The choice of parameters of the gamma distributions had a negligible impact and these results are not shown. The choice between an independent versus AR(1) prior for log hazard ratios had a small but noticeable impact on calculated probabilities and we report results for both choices of prior.

Results

Figures: In the Figures S10a through S10i, we summarize evidence about the direction and magnitude of the difference in event rates at 1, 3, and 5 years in the form of a Bayesian posterior probability distribution. Event rates are expressed as proportions ranging from 0 to 1. The probability that the true difference in proportions is within a narrow interval is proportional to the height of the bar covering that interval.

Tables: Tables S12a through S12f summarize evidence about cumulative event rates and differences in these event rates at annual time points. Event rates are expressed as percentages ranging from 0% to 100%. The Bayesian point estimate (posterior mean) of the difference in event rates is presented along with a 95% Bayesian credible interval (CrI). For each time point, we report Bayesian probabilities that express the likelihood that the difference at that time point favors INV or CON by any amount, by at least 1 percentage point, or by at least 3 percentage points.

Technical Details for Bayesian Analysis

Model

In order to account for competing risk of non-cardiovascular mortality in the analysis of the primary outcome and the CV death or MI outcome, we assumed that outcome events and competing non-cardiovascular deaths could be described by a continuous time multi-state model with states corresponding to: (1) alive and event free, (2) died event free from non-cardiovascular mortality, and (3) event has occurred. All patients were assumed to begin in State 1. The joint distribution of sojourn time in State 1 and the state entered upon leaving State 1 was assumed to be determined by a set of hazard functions (aka transition intensity functions) which were assumed to differ by treatment group. Hazard functions describing transitions into State 3 (event) were approximated as piecewise constant functions with jumps at months 0.5,1, 2, 3, 6, 12, 18, 24, 30, 36, 42, 48 and 60. Hazard functions describing transitions into State 2 (competing non-cardiovascular death) were approximated as step functions with jumps at months 12, 24, 36 and 48. Parameters to be estimated were:

- 14 hazard rate parameters describing transitions into State 3 (event) in CON

- $\lambda_{\text{con},1}^{\text{event}}, \lambda_{\text{con},2}^{\text{event}}, \ldots, \lambda_{\text{con},14}^{\text{event}}$
- 14 hazard rate parameters describing transitions into State 3 (event) in INV
  - $\lambda_{\text{inv},1}^{\text{event}}, \lambda_{\text{inv},2}^{\text{event}}, \ldots, \lambda_{\text{inv},14}^{\text{event}}$
- 5 hazard rate parameters describing transitions into State 2 (competing non-CV death) in CON
  - $\lambda_{\text{con},1}^{\text{ncvdeath}}, \lambda_{\text{con},2}^{\text{ncvdeath}}, \ldots, \lambda_{\text{con},5}^{\text{ncvdeath}}$
- 5 hazard rate parameters describing transitions into State 2 (competing non-CV death) in INV
  - $\lambda_{\text{inv},1}^{\text{ncvdeath}}, \lambda_{\text{inv},2}^{\text{ncvdeath}}, \ldots, \lambda_{\text{inv},5}^{\text{ncvdeath}}$

In order to estimate these parameters we assumed that the number of patients experiencing the outcome event of interest and the number of patients experiencing the competing non-CV death event within each treatment group and time interval were independent Poisson random variables. Specifically, we assumed that:

$$Y_{\text{inv},j} \sim \text{ind. Poisson}\left(N_{\text{inv},j}\lambda_{\text{inv},j}^{\text{event}}\right)$$
$$Y_{\text{con},j} \sim \text{ind. Poisson}\left(N_{\text{con},j}\lambda_{\text{con},j}^{\text{event}}\right)$$
$$D_{\text{inv},j} \sim \text{ind. Poisson}\left(N_{\text{inv},j}\lambda_{\text{inv},j}^{\text{ncvdeath}}\right)$$
$$D_{\text{con},j} \sim \text{ind. Poisson}\left(N_{\text{con},j}\lambda_{\text{con},j}^{\text{ncvdeath}}\right)$$

where $N_{\text{inv},j}$ and $N_{\text{con},j}$ are the person-days of follow-up in time interval j in the invasive and conservative groups, respectively, $Y_{\text{inv},j}$ and $Y_{\text{con},j}$ are the number of patients experiencing the outcome event of interest in the j-th interval in the invasive and conservative groups, respectively, and $D_{\text{inv},j}$ and $D_{\text{con},j}$ are the number of patients with a competing CV death in the j-th interval in the invasive and conservative groups, respectively. The assumption that outcome events and deaths follow independent Poisson distributions is a consequence of the multi-state modeling assumptions described above combined with the assumptions that hazard rate functions are piecewise constant and that censoring times are independent of death or outcome events.

Prior Specification

To simplify notation we use subscript 1 in place of INV and 2 in place of CON. Thus, the analysis requires specification of a prior distribution for the collection of parameters:

$\lambda_{1,1}^{\text{event}}, \lambda_{1,2}^{\text{event}}, \ldots, \lambda_{1,14}^{\text{event}}$ (hazard rates for events in INV)
$\lambda_{2,1}^{\text{event}}, \lambda_{2,2}^{\text{event}}, \ldots, \lambda_{2,14}^{\text{event}}$ (hazard rates for events in CON)
$\lambda_{1,1}^{\text{ncvdeath}}, \lambda_{1,2}^{\text{ncvdeath}}, \ldots, \lambda_{1,5}^{\text{ncvdeath}}$ (hazard rates for non-CV deaths in INV)
$\lambda_{2,1}^{\text{ncvdeath}}, \lambda_{2,2}^{\text{ncvdeath}}, \ldots, \lambda_{2,5}^{\text{ncvdeath}}$ (hazard rates for non-CV deaths in INV)

Define $\beta_j^{\text{event}} = \log(\lambda_{1,j}^{\text{event}}/\lambda_{2,j}^{\text{event}})$ and $\beta_j^{\text{ncvdeath}} = \log(\lambda_{1,j}^{\text{ncvdeath}}/\lambda_{2,j}^{\text{ncvdeath}})$ to be the log-hazard ratio for INV versus CON in the j-th time interval for events and competing non-CV deaths, respectively. We implemented the analysis using 2 choices for the prior distribution as follows.

Prior #1 (primary)

We specified independent gamma priors for the hazard rates in the INV group and vague independent normal priors for the set of log-hazard ratios. The prior distribution was:

$$\lambda_{2,j}^{\text{event}} \sim \text{ind. Gamma}(0.001,1.0), \qquad j = 1,\dots,14$$
$$\beta_j^{\text{event}} \sim \text{ind. Normal}(\text{mean} = 0, \text{variance} = 10^5), \qquad j = 1,\dots,14.$$
$$\lambda_{2,j}^{\text{ncvdeath}} \sim \text{ind. Gamma}(0.001,1.0), \qquad j = 1,\dots,5$$
$$\beta_j^{\text{ncvdeath}} \sim \text{ind. Normal}(\text{mean} = 0, \text{variance} = 10^5), \qquad j = 1,\dots,5.$$

Prior #2 (sensitivity analysis using autoregressive AR(1) prior on log-hazard ratios)

$$\lambda_{2,j}^{\text{event}} \sim \text{ind. Gamma}(0.001,1.0), \qquad j = 1,\dots,14$$
$$\beta_1^{\text{event}} \sim \text{ind. Normal}(\text{mean} = 0, \text{variance} = 10^5)$$
$$\beta_j^{\text{event}} \sim \text{ind. Normal}\big(\text{mean} = 0.9999984\beta_{j-1}, \text{variance} = 0.31419\big), \quad j = 2,\dots,14$$
$$\lambda_{2,j}^{\text{ncvdeath}} \sim \text{ind. Gamma}(0.001,1.0), \qquad j = 1,\dots,5$$
$$\beta_1^{\text{ncvdeath}} \sim \text{ind. Normal}(\text{mean} = 0, \text{variance} = 10^5)$$
$$\beta_j^{\text{ncvdeath}} \sim \text{ind. Normal}\big(\text{mean} = 0.9999984\beta_{j-1}, \text{variance} = 0.31419\big), \quad j = 2,\dots,5$$

Parameters of the autoregressive prior were chosen to ensure that the ratio of hazard ratios in two consecutive time intervals would fall between 1/3 and 3 with 95% prior probability.

Computation

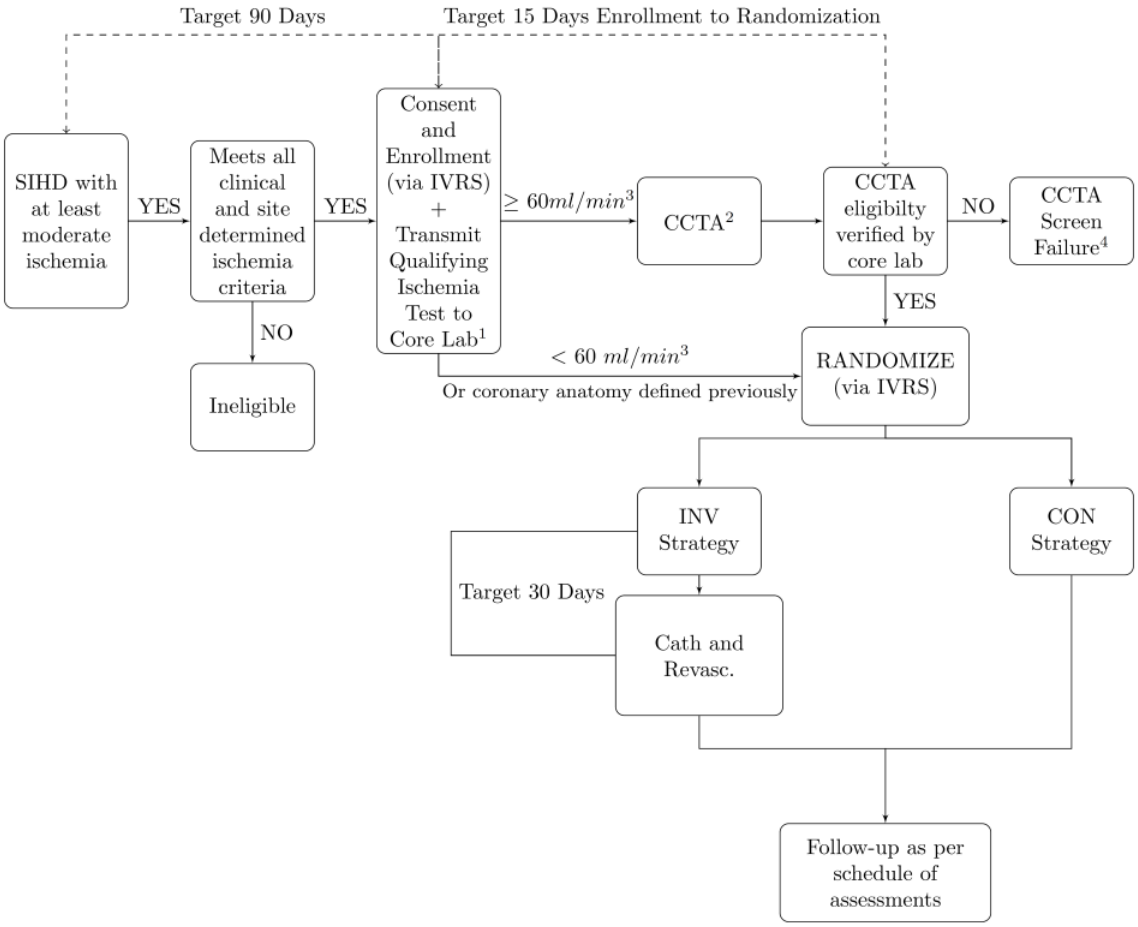
Posterior means and other summaries of the posterior distribution were calculated using Markov Chain Monte Carlo (MCMC) simulations as implemented in WinBUGS software and validated with the SAS PROC MCMC procedure. To reduce Monte Carlo error and ensure convergence, we generated 2,000,000 sets of simulated parameter values and retained every 20th sample for a final set of 100,000 randomly sampled sets of parameter values.

References

1. Jaynes ET. Confidence intervals vs Bayesian intervals. In Foundations of probability theory, statistical inference, and statistical theories of science, Vol II, 1976 (pp. 175-257). D. Reidel Publishing Company. Dordrecht Holland.
2. Gelman A, Carlin JB, Stern HS, Dunson DB, Vehtari A, Rubin DB. Bayesian data analysis. Chapman and Hall/CRC; 2013 Nov 27.
3. Ibrahim JG, Chen MH, Sinha D. Bayesian survival analysis. Springer, New York, 2001.

IV. Supplementary Figures

Figure S1. Study Flow



[1] See MOO for measures to ensure randomization of participants who meet ischemia eligbility.

[2] CCTA will not be performed in participants with eGFR<60 ml/min or in participants who have had invasive angiography or CCTA within the prior 12 months (the number of patients enrolled with recent invasive angiography or CCTA may be capped)

[3] Participants with eGFR<60 ml/min with no clinical or ischemia testing characteristics suggestive of significant left main coronary artery stenosis are eligible to be randomized. Participants with eGFR<30 or on dialysis are included in the CKD ancillary trial. Some participants with eGFR≥60 may not undergo CCTA (see 6.5 and MOO). Some participants with eGFR<60 may undergo CCTA based on physician preference. Allowance of participants with exceptions to performance of CCTA relative to eGFR.

[4] CCTA screen failure due to no obstructive CAD will be enrolled in an ancillary study at participating sites. (CIAO-ISCHEMIA)

SIHD: Stable ischemic heart disease
CCTA: Coronary computed tomography angiography
IVRS: Interactive Voice Response Systems
INV: Invasive
CON: Conservative
MOO: Manual of Operations
eGFR: Estimated glomerular filtration rate
CKD: Chronic Kidney Disease
CIAO-ISCHEMIA: Ancillary study. Changes in Ischemia and Angina over One year among ISCHEMIA trial screen failures with no obstructive coronary artery disease on CT angiography.
CAD: Coronary artery disease

Figure S2. Cross-Sectional Screening Data

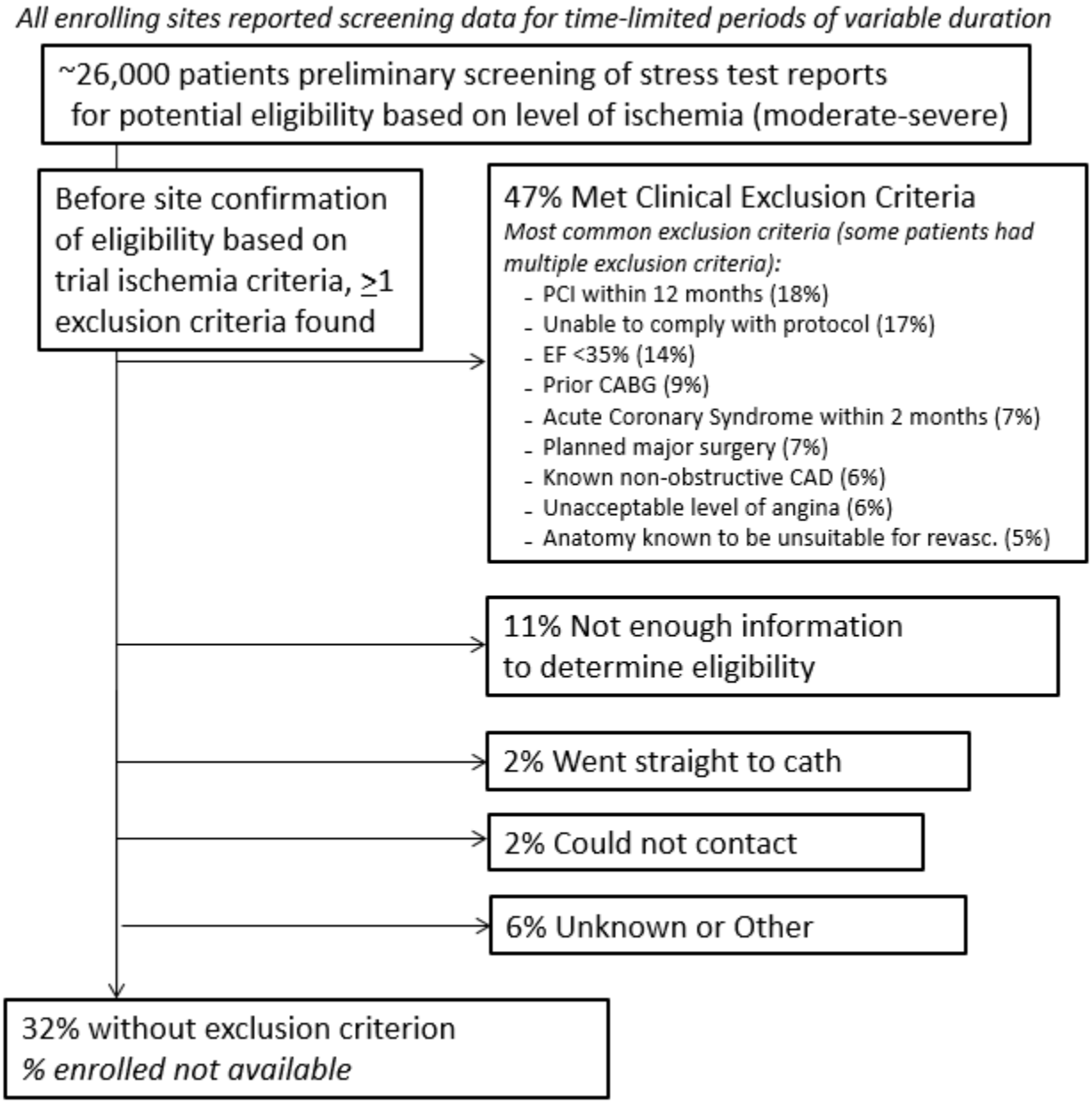
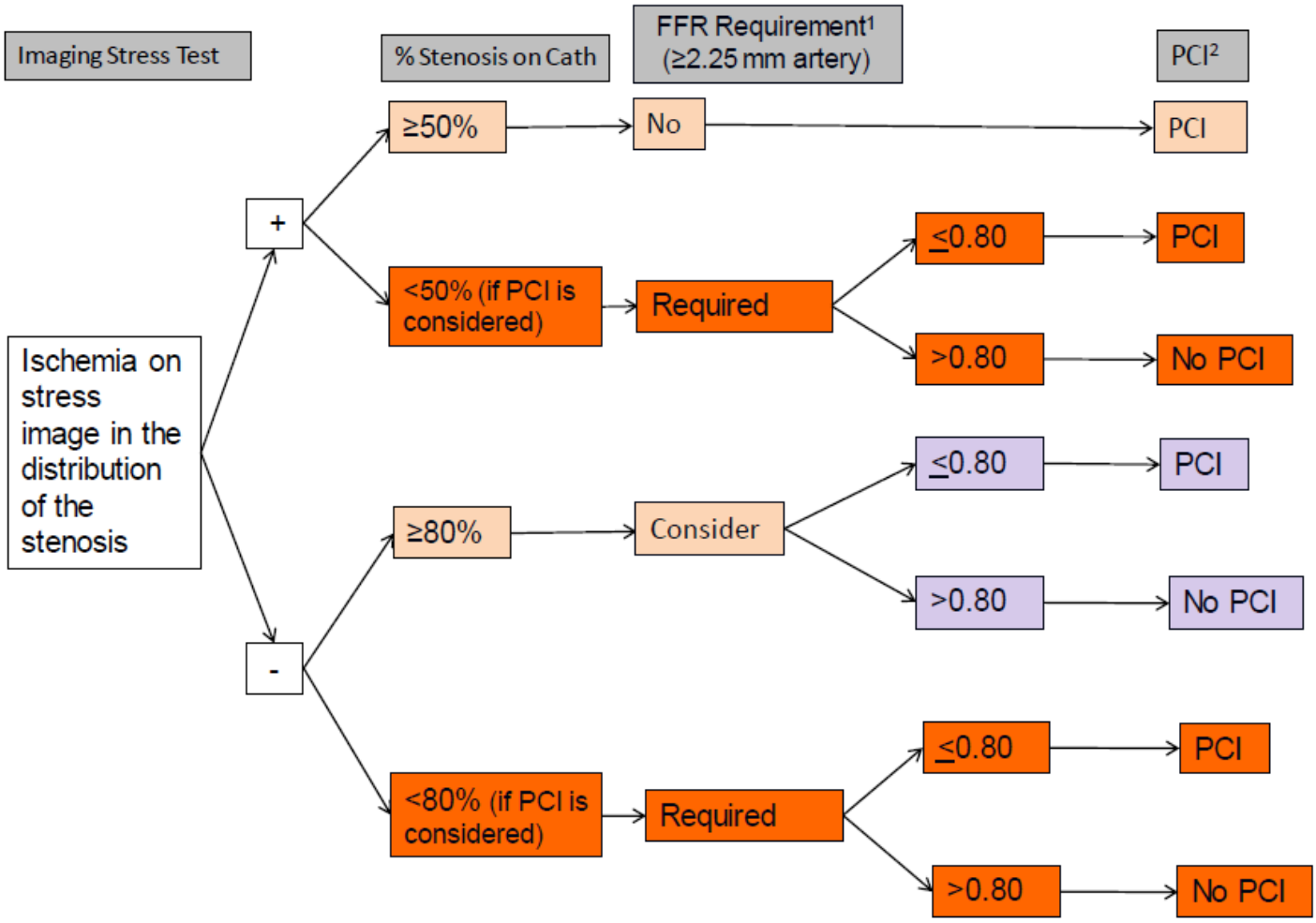


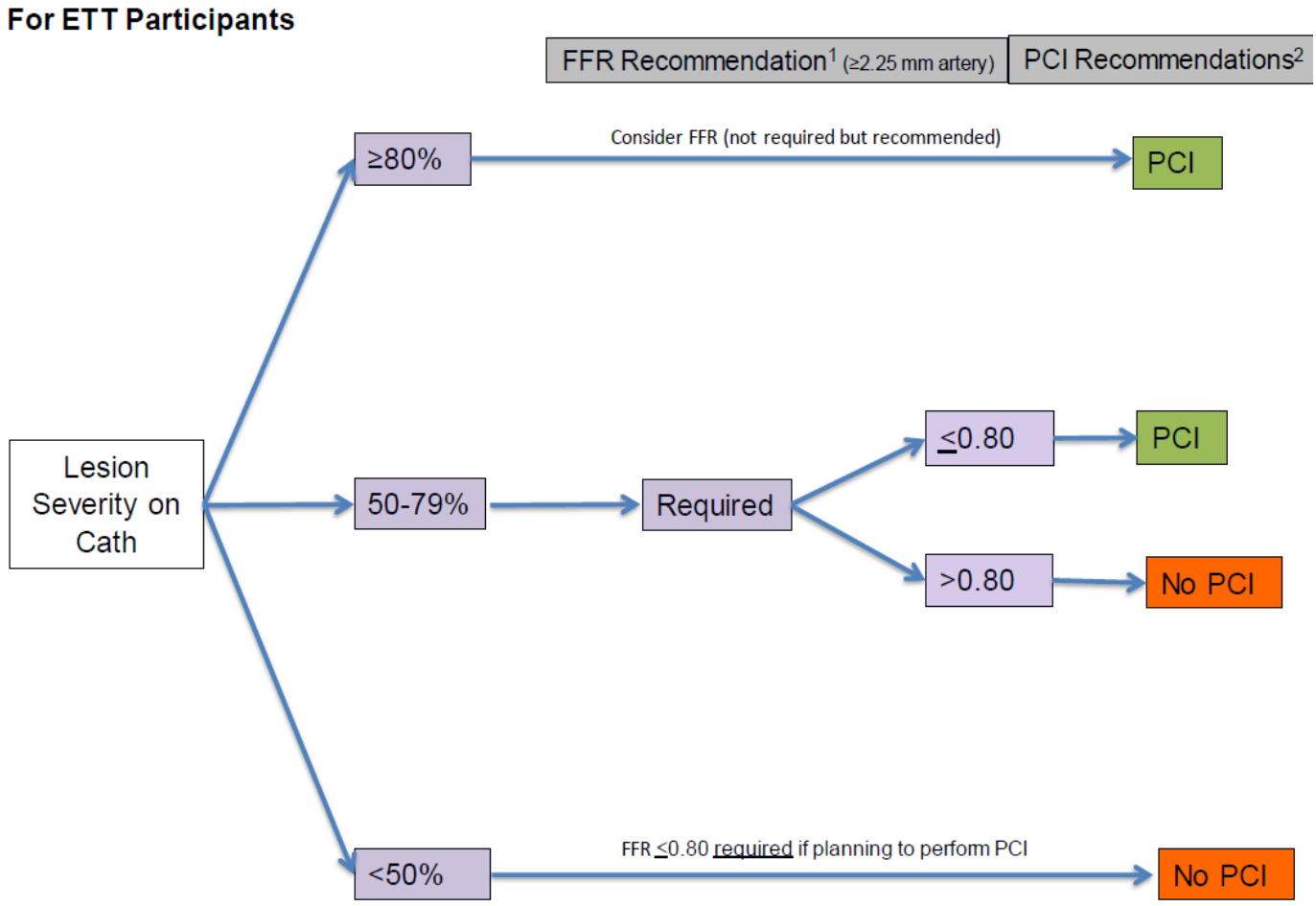
Figure S3a. Fractional Flow Reserve Algorithm After Stress Imaging



[1]The use of instantaneous wave-free ratio (iFR) instead of FFR (where available) was permitted, using a cutoff of ≤0.89 for physiologic significance.
[2]PCI based on anatomic feasibility and clinical considerations

Reprinted from American Heart Journal, 2018;201:124-135, ISCHEMIA Trial Research Group, Maron DJ, Hochman JS, O'Brien SM, Reynolds HR, Boden WE, Stone GW, Bangaore S, Spertus JA, Mark DB, Alexander KP, Shaw L, Berger JS, Ferguson TB Jr, William DO, Harrington RA, Rosenberg Y, International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial: Rationale and Design, 2018, with permission from Elsevier

Figure S3b. Fractional Flow Reserve Algorithm After Non-Imaging Exercise Stress Test

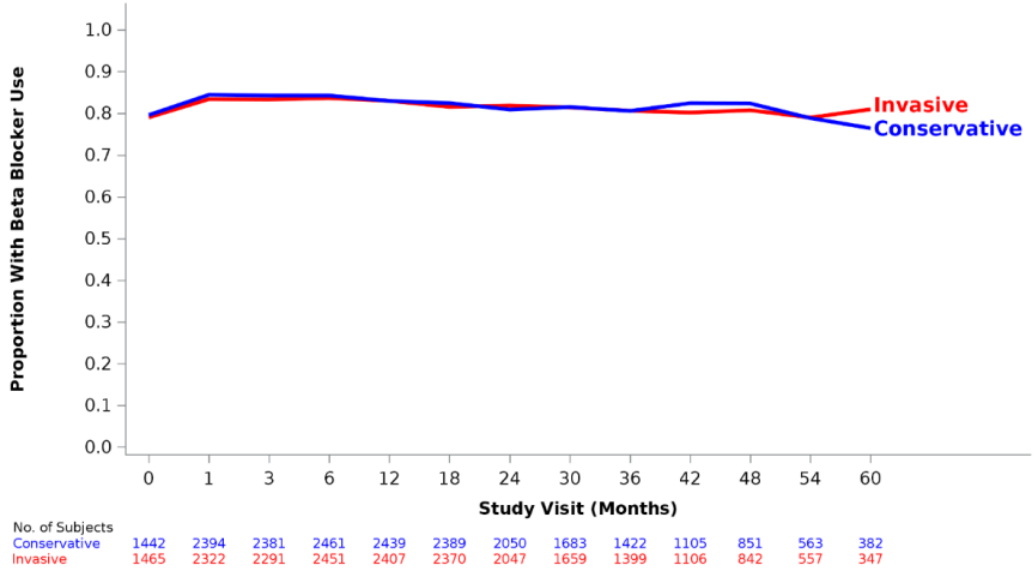


[1]The use of instantaneous wave-free ratio (iFR) instead of FFR (where available) was permitted, using a cutoff of ≤0.89 for physiologic significance.
[2]PCI based on anatomic feasibility and clinical considerations

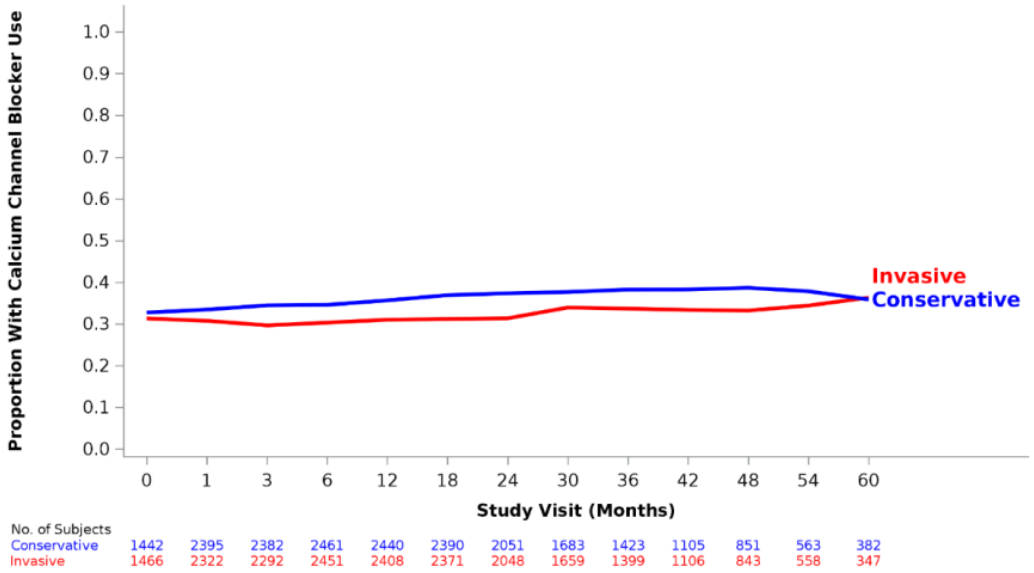
Reprinted from American Heart Journal, 2018;201:124-135, ISCHEMIA Trial Research Group, Maron DJ, Hochman JS, O'Brien SM, Reynolds HR, Boden WE, Stone GW, Bangaore S, Spertus JA, Mark DB, Alexander KP, Shaw L, Berger JS, Ferguson TB Jr, William DO, Harrington RA, Rosenberg Y, International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial: Rationale and Design, 2018, with permission from Elsevier

Figure S4. Medication Use During the Trial

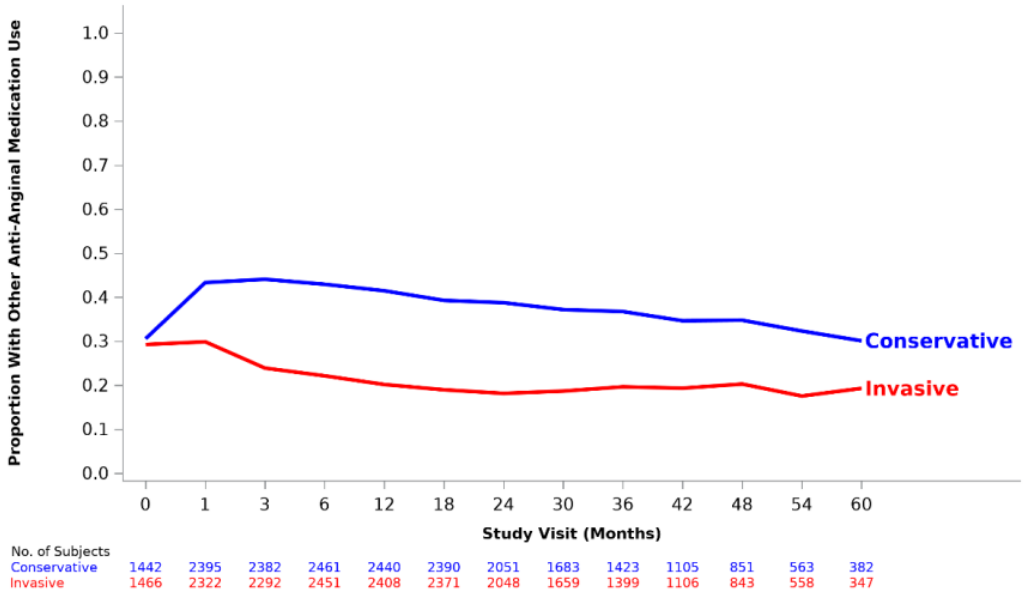
Beta Blockers



Calcium Channel Blockers

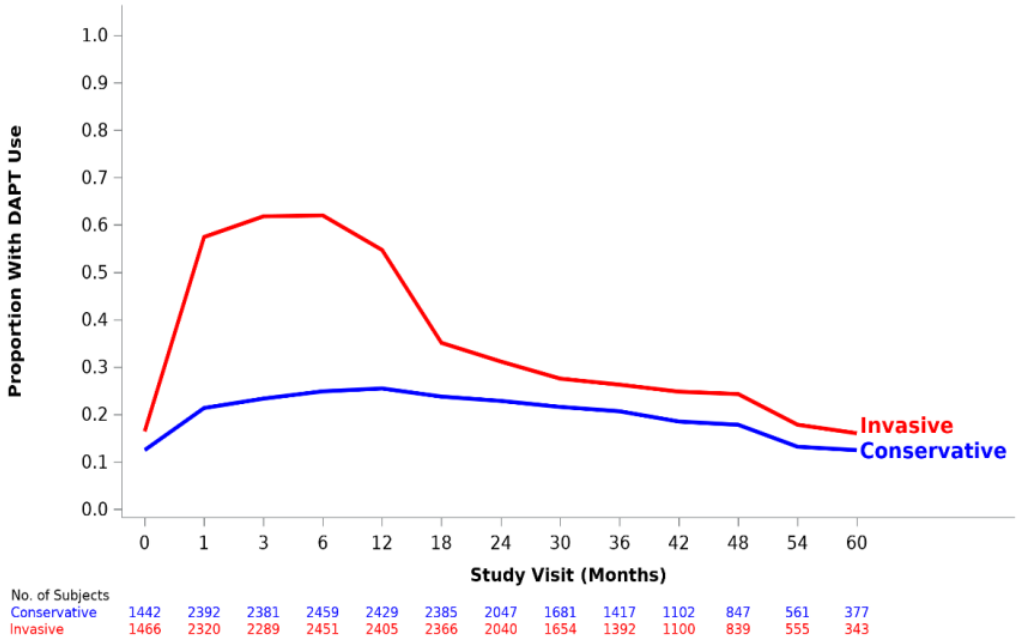


Other Anti-Anginal Medication



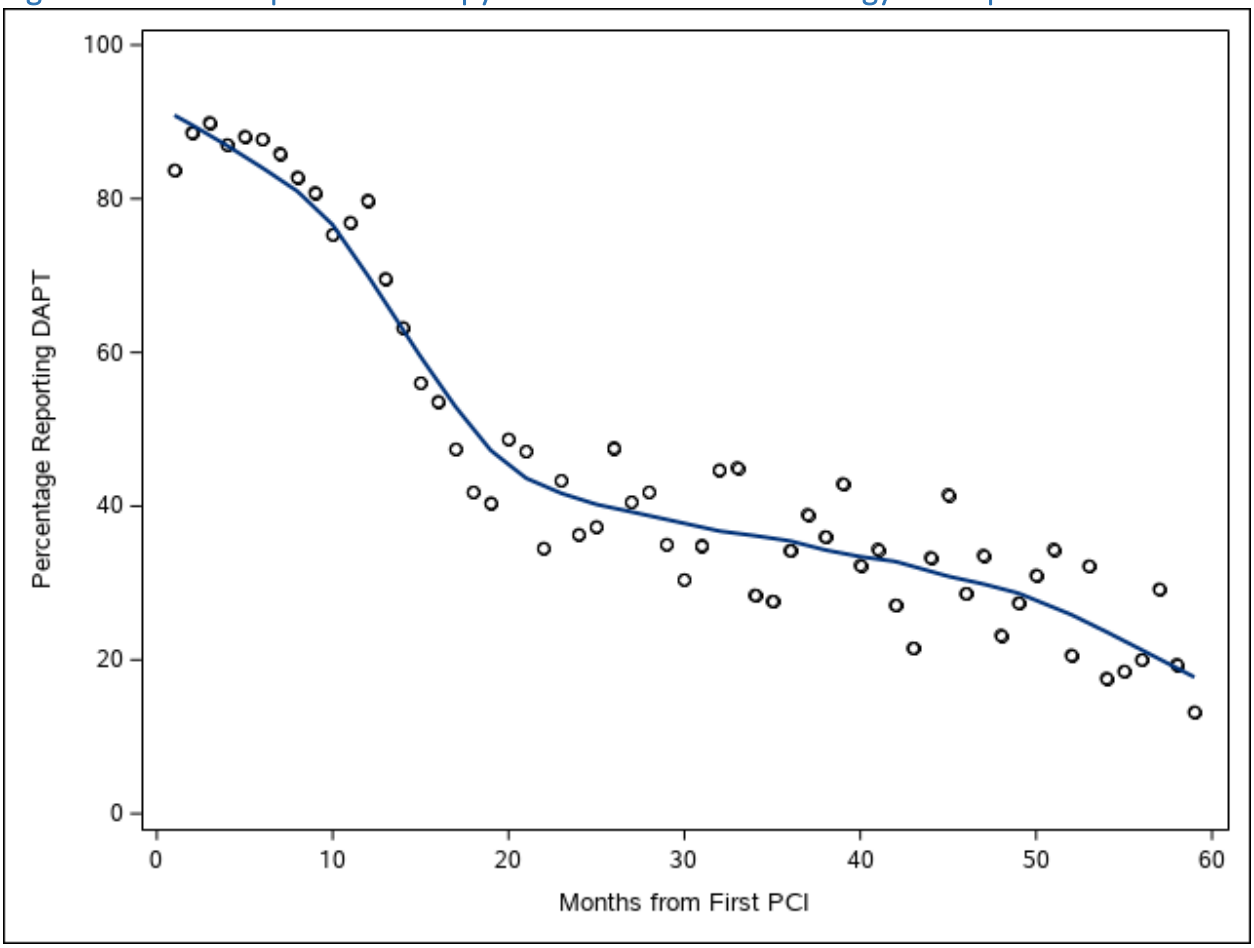
Includes long-acting nitrates

Dual Antiplatelet (DAPT)



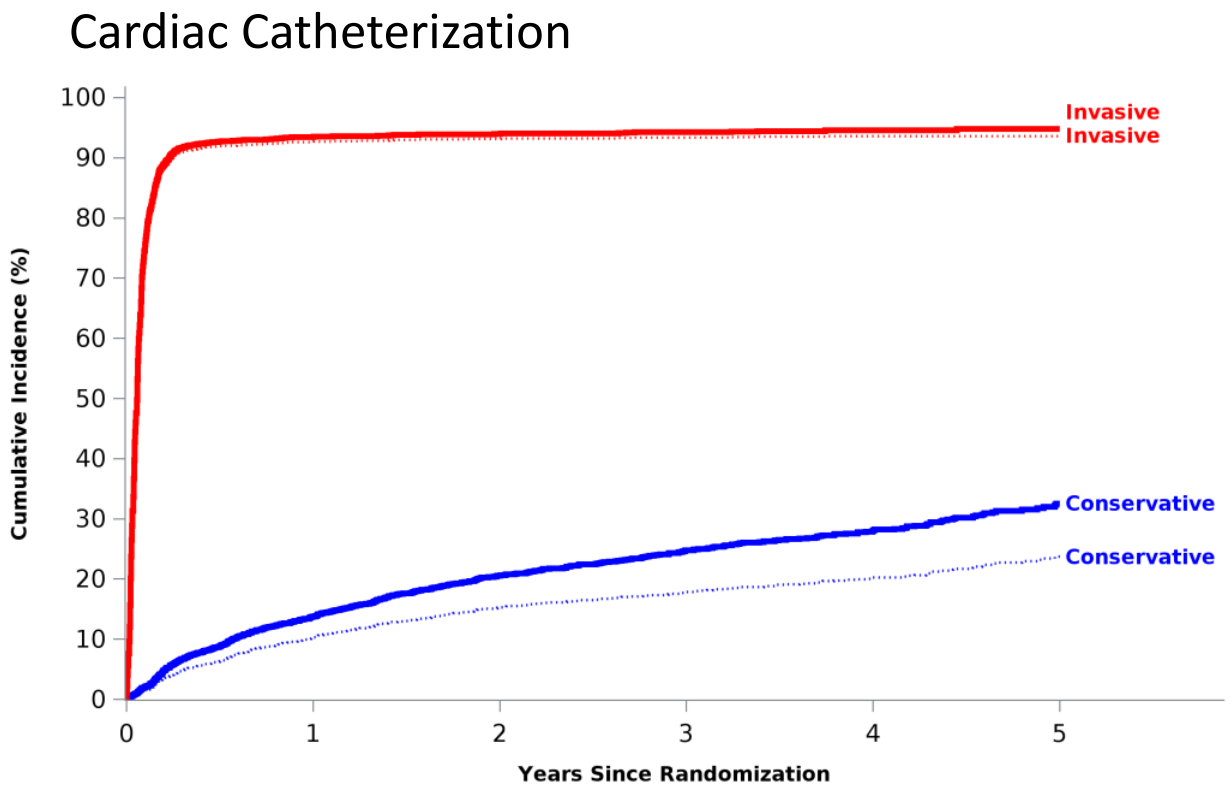
DAPT use is defined as the use of aspirin and another antiplatelet medication.

Figure S5. Dual Antiplatelet Therapy After PCI in Invasive Strategy Participants



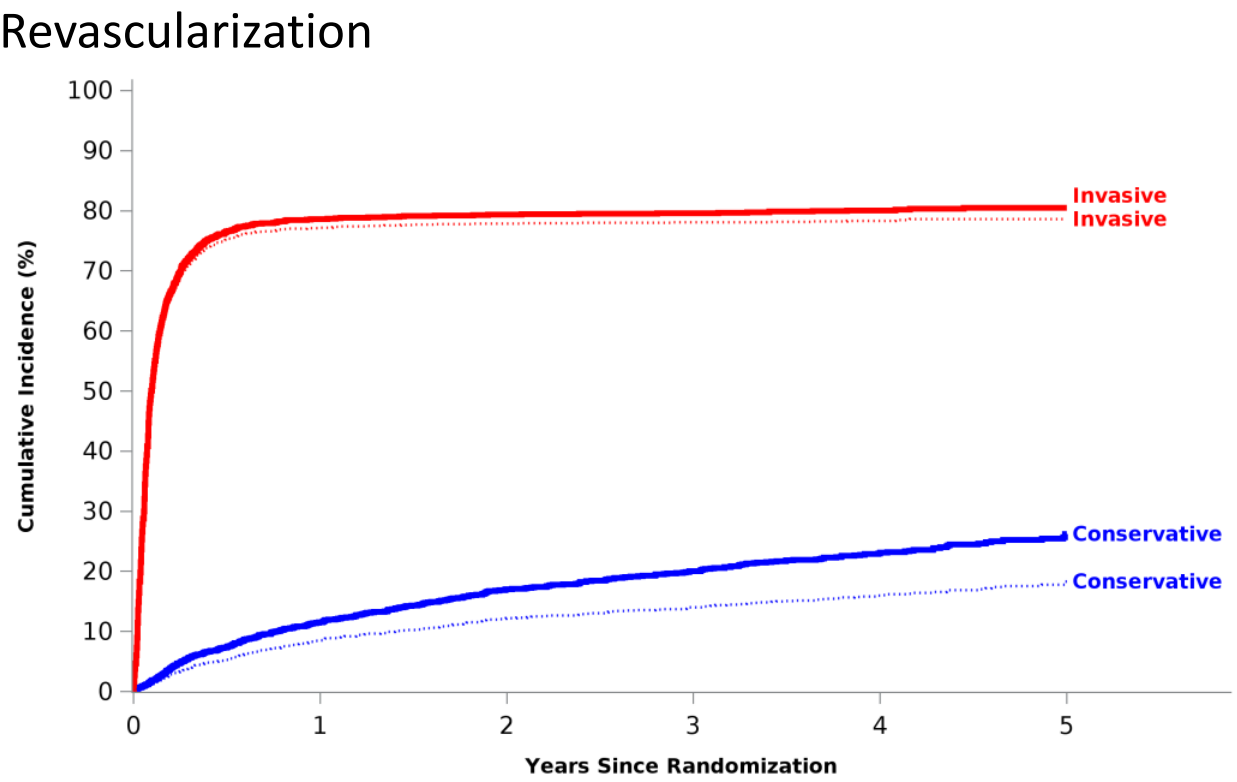
Due to timing of visits when current medication use was collected and varying DAPT duration, it does not reflect 100% DAPT use, which we believe was universal. Collection of information at follow-up visits may have occurred after completion of prescribed course of DAPT.

Figure S6a. Cumulative Incidence Plot of Cardiac Catheterization by Treatment Group.



The dotted lines represent procedures not preceded by outcome events.When counting catheterizations performed prior to randomization that were not repeated prior to CABG in INV participants, 95% of INV patients had a catheterization prior to a primary outcome event.
A total of 2475/2588 (96%) of INV participants had catheterization or revascularization for any reason, consistent with protocol adherence.

Figure S6b. Cumulative Incidence Plot of Revascularization by Treatment Group.



The dotted lines represent procedures not preceded by outcome events.

Figure S7. Estimated Instantaneous Hazard Rates

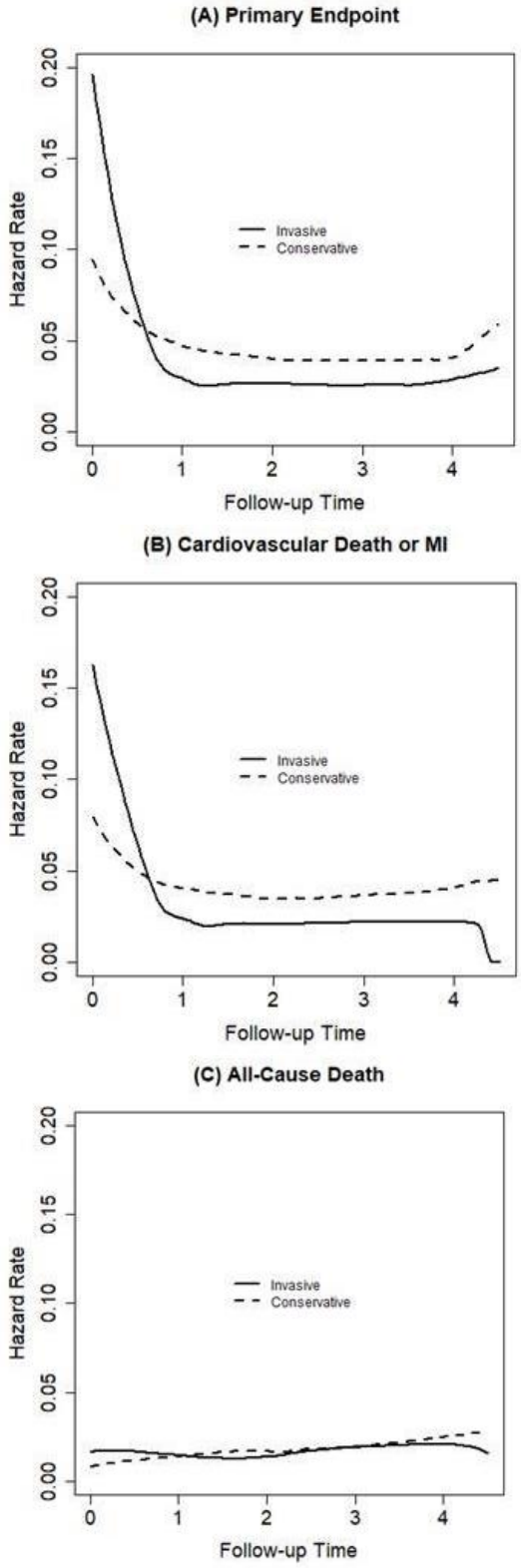


Figure S8. The following figures are time-to-event curves shown in Figure 2, Individual components of the primary outcome not shown in Figure 2, and other outcomes including net clinical benefit. These figures have insets displaying the half width of the confidence interval for the difference between treatment groups. Overlap of the lines and shading indicates that the 95% CI for the difference includes zero. are also shown.

Additional Analyses to be Reported Separately

As stated in the SAP, additional pre-specified secondary outcomes will be analyzed, and they will be reported separately:

(a) Composite of cardiovascular death or complicated MI as defined in the CEC charter
(b) Complicated MI as defined in the CEC charter
(c) Large MI

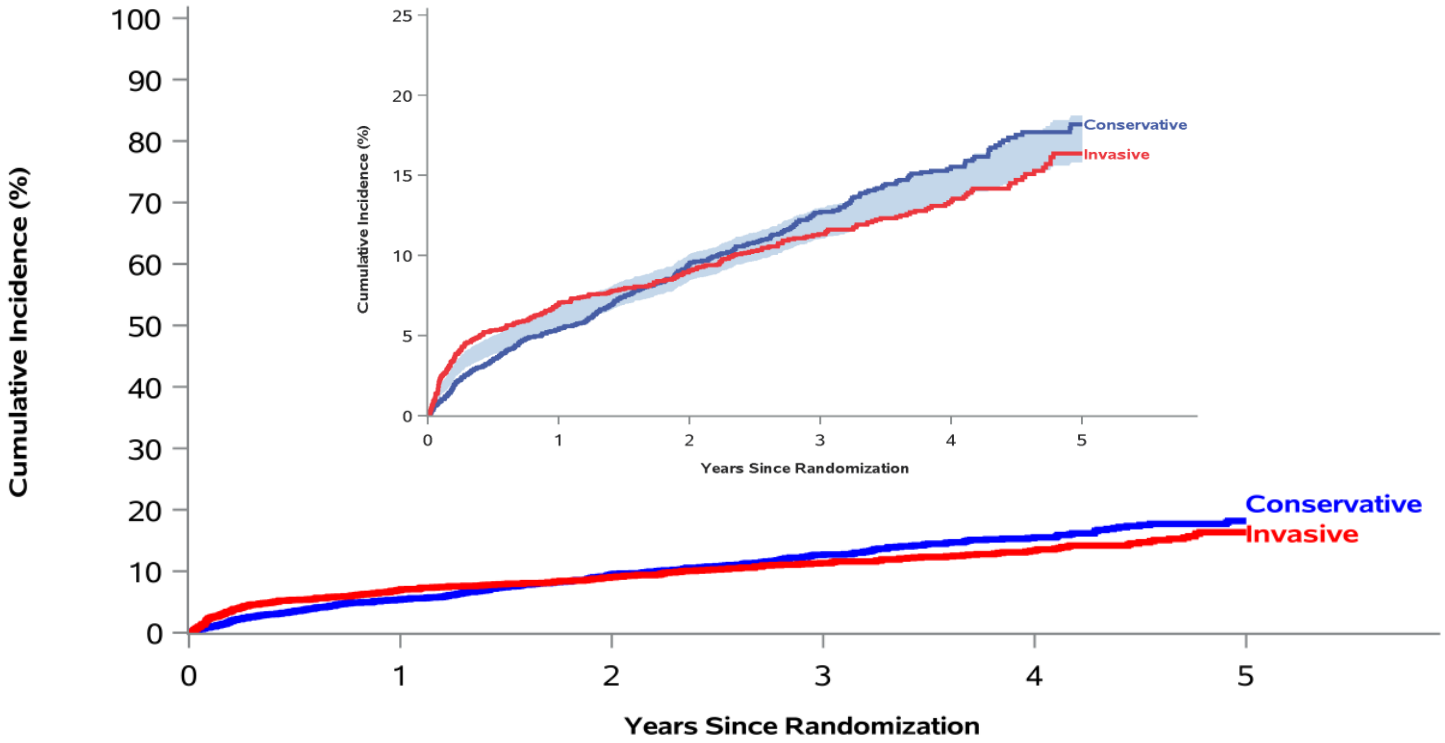
Other outcomes as defined in the SAP to be reported separately to aid interpretation of the trial's primary and secondary analyses include:

(a) Composite of all-cause death or nonfatal MI
(b) Composite of all-cause death, nonfatal MI, or stroke
(c) Composite of all-cause death, nonfatal MI, or hospitalization for resuscitated cardiac arrest, unstable angina or heart failure
(d) Composite of all-cause death, nonfatal MI, stroke, hospitalization for unstable angina, heart failure or resuscitated cardiac arrest

Figure S8. Rates of the Primary Outcome Components and Other Outcomes

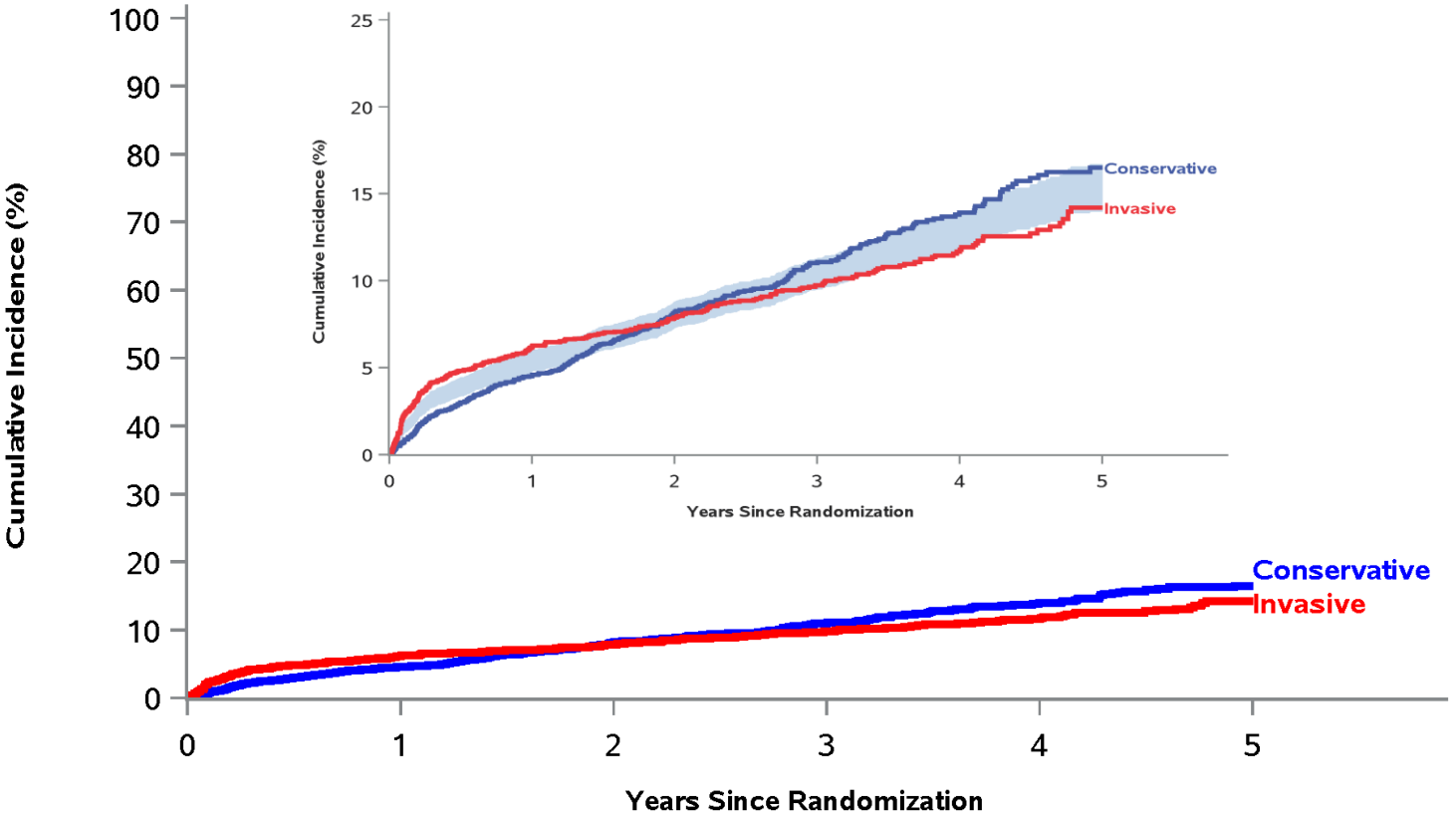
Shading in inset figures indicates the half width of the confidence interval for the difference. Overlap of the lines and shading indicates that the 95% CI for the difference includes zero.

Primary Outcome (composite of Cardiovascular Death, Myocardial Infarction, or Hospitalization for Unstable Angina, Heart Failure, or Resuscitated Cardiac Arrest)



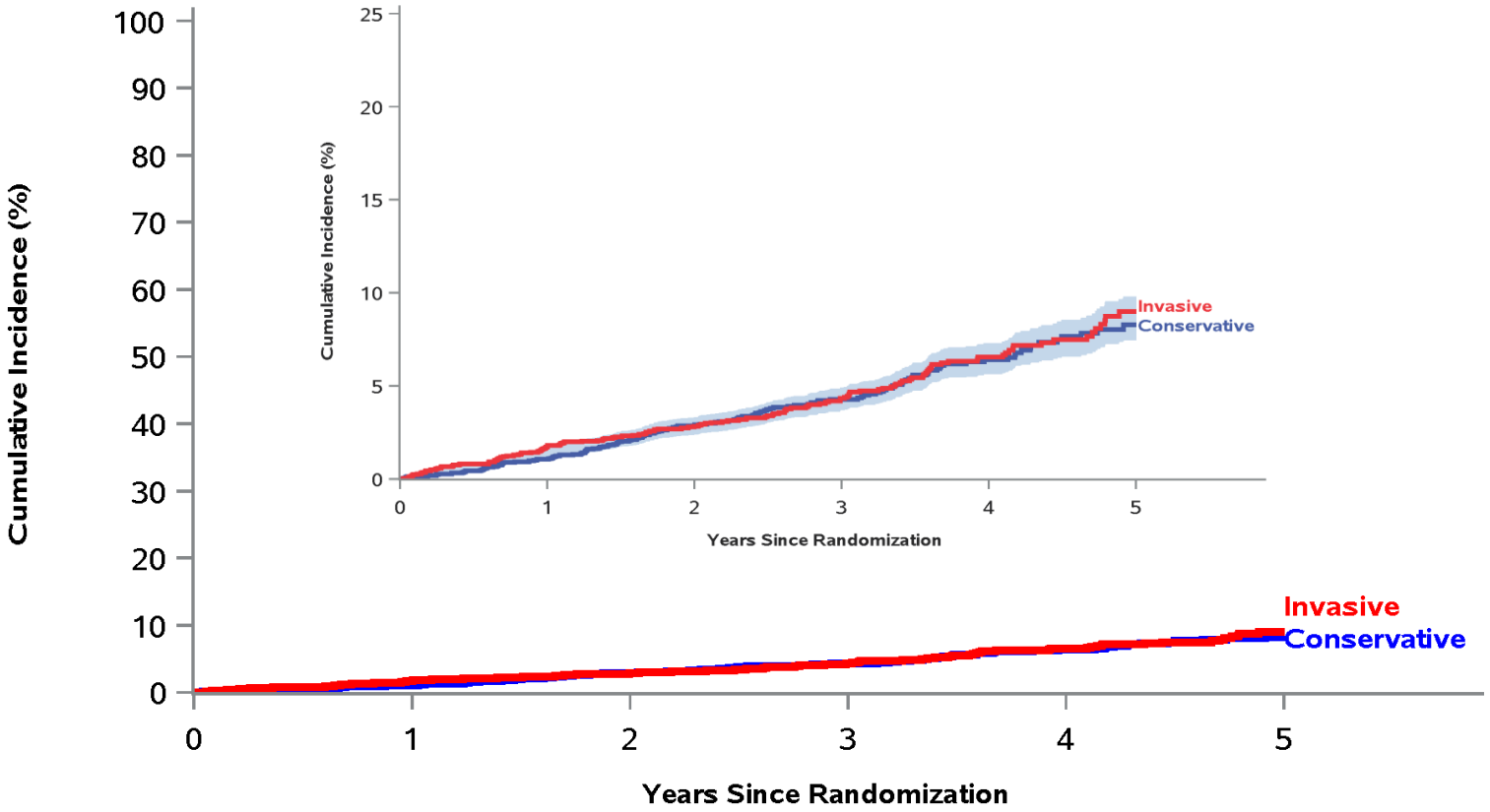
No. at Risk						
Conservative	2591	2431	1907	1300	733	293
Invasive	2588	2364	1908	1291	730	271

Cardiovascular Death or Myocardial Infarction



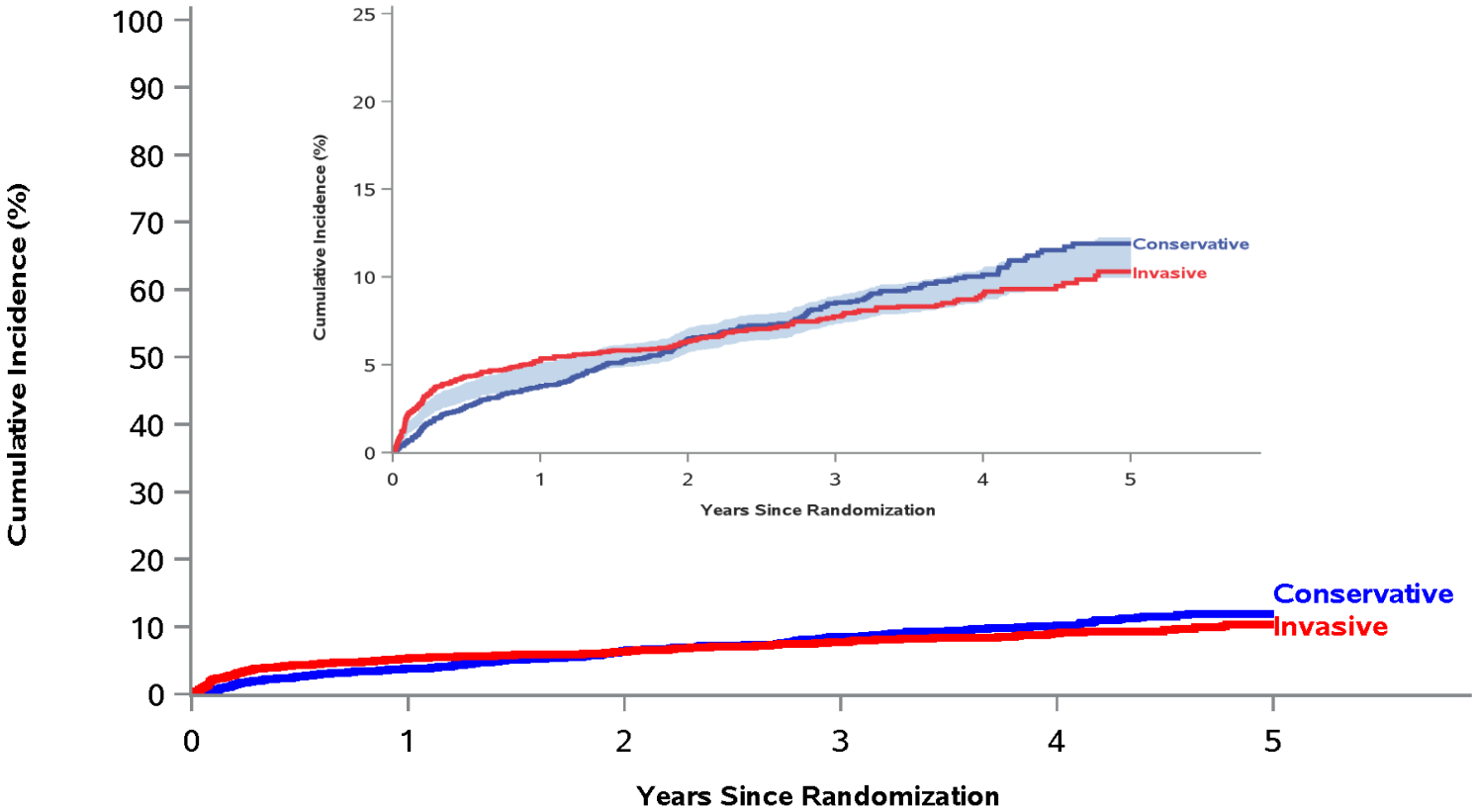
No. at Risk						
Conservative	2591	2453	1933	1325	746	298
Invasive	2588	2383	1933	1314	742	282

All-cause Mortality



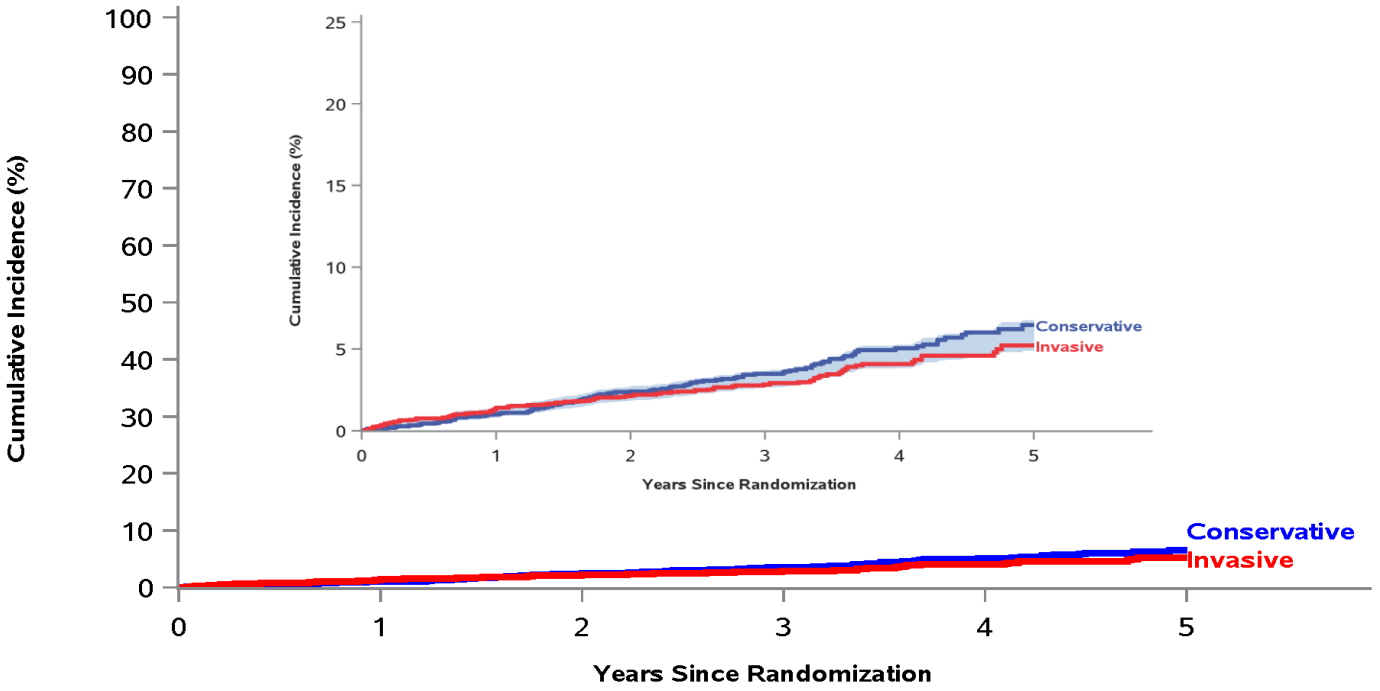
No. at Risk						
Conservative	2591	2548	2065	1445	844	349
Invasive	2588	2518	2061	1431	827	317

Myocardial Infarction



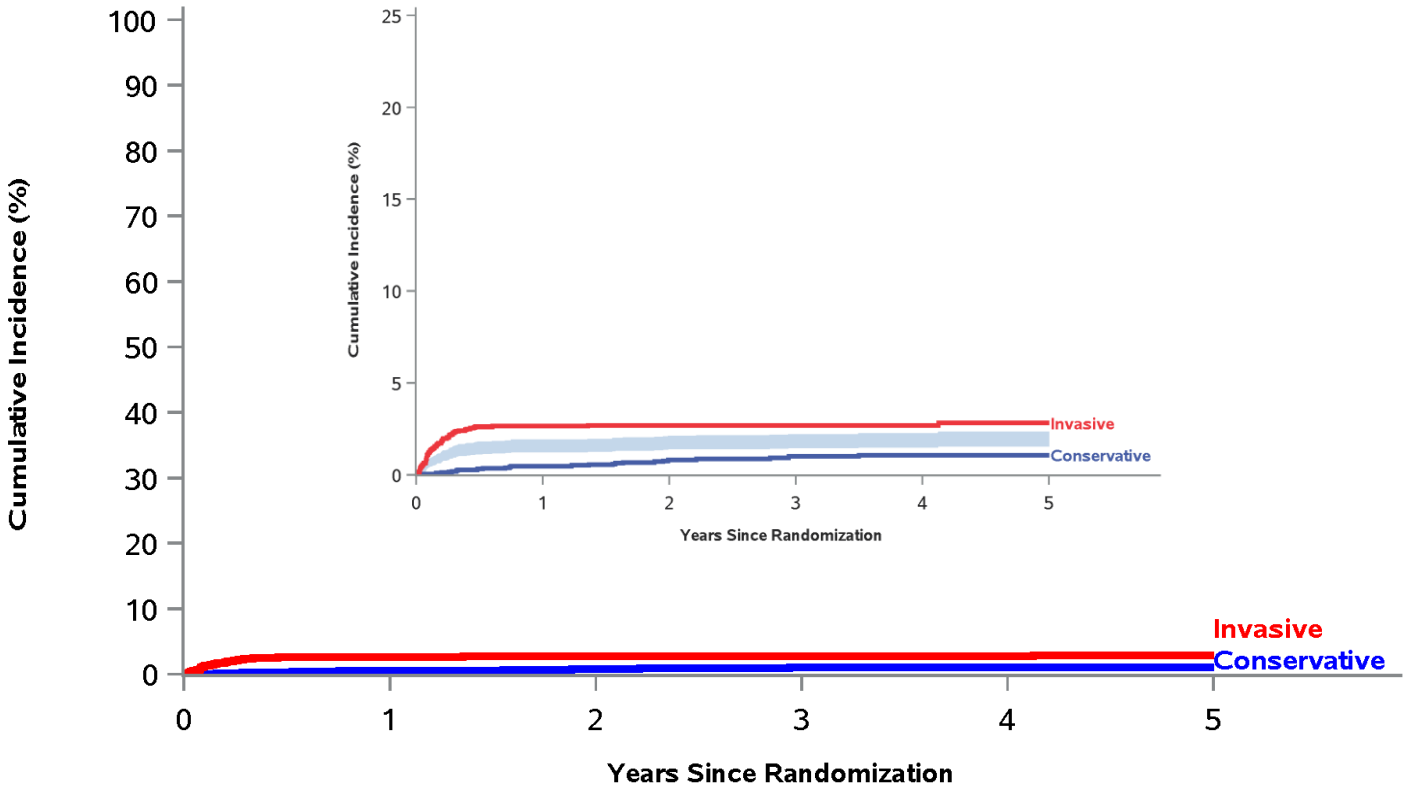
No. at Risk						
Conservative	2591	2452	1931	1321	747	298
Invasive	2588	2379	1931	1313	742	283

Cardiovascular Death



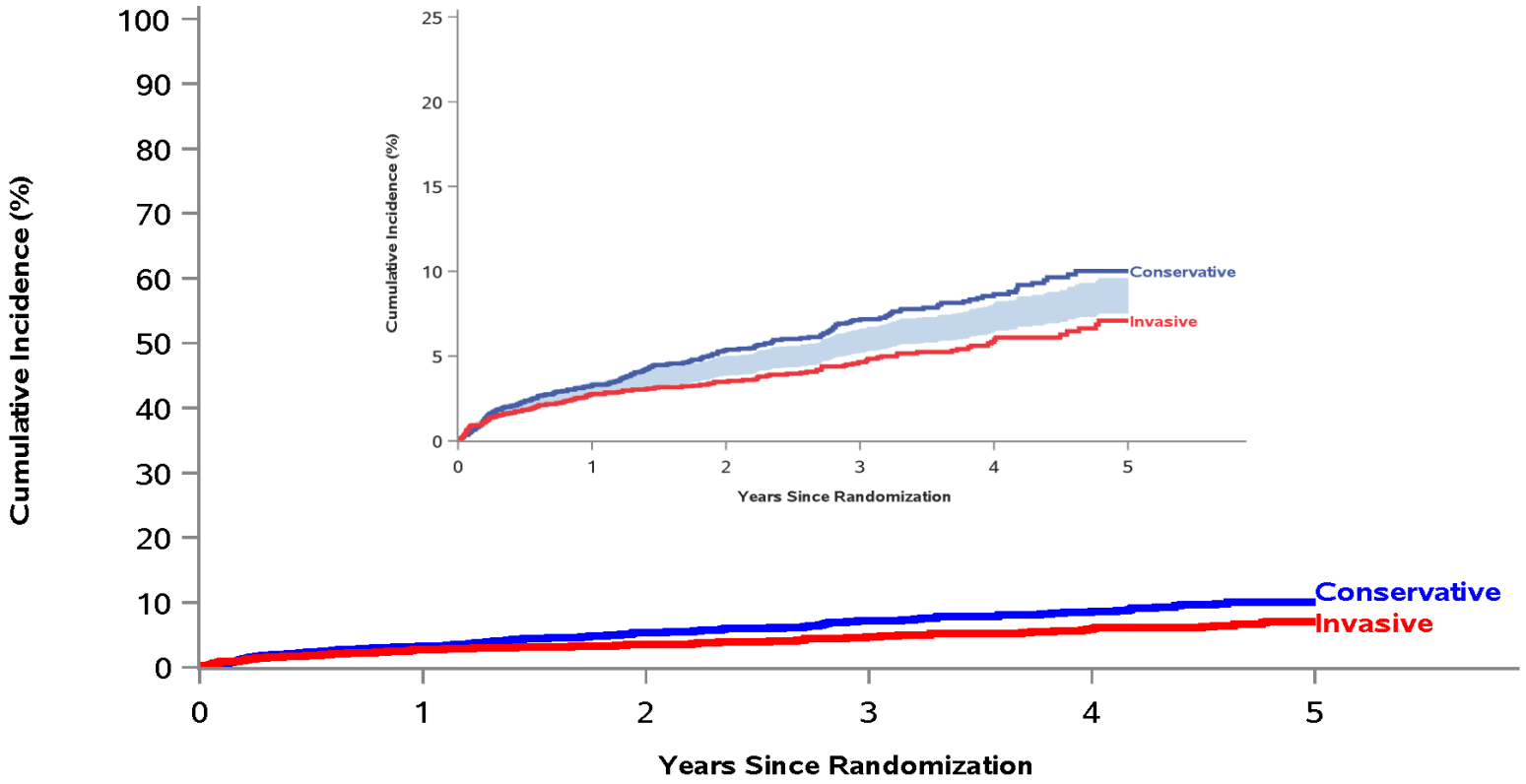
No. at Risk						
Conservative	2591	2548	2065	1445	844	349
Invasive	2588	2518	2061	1431	827	317

Procedural MI



No. at Risk						
Conservative	2591	2529	2035	1419	828	342
Invasive	2588	2439	2000	1380	794	304

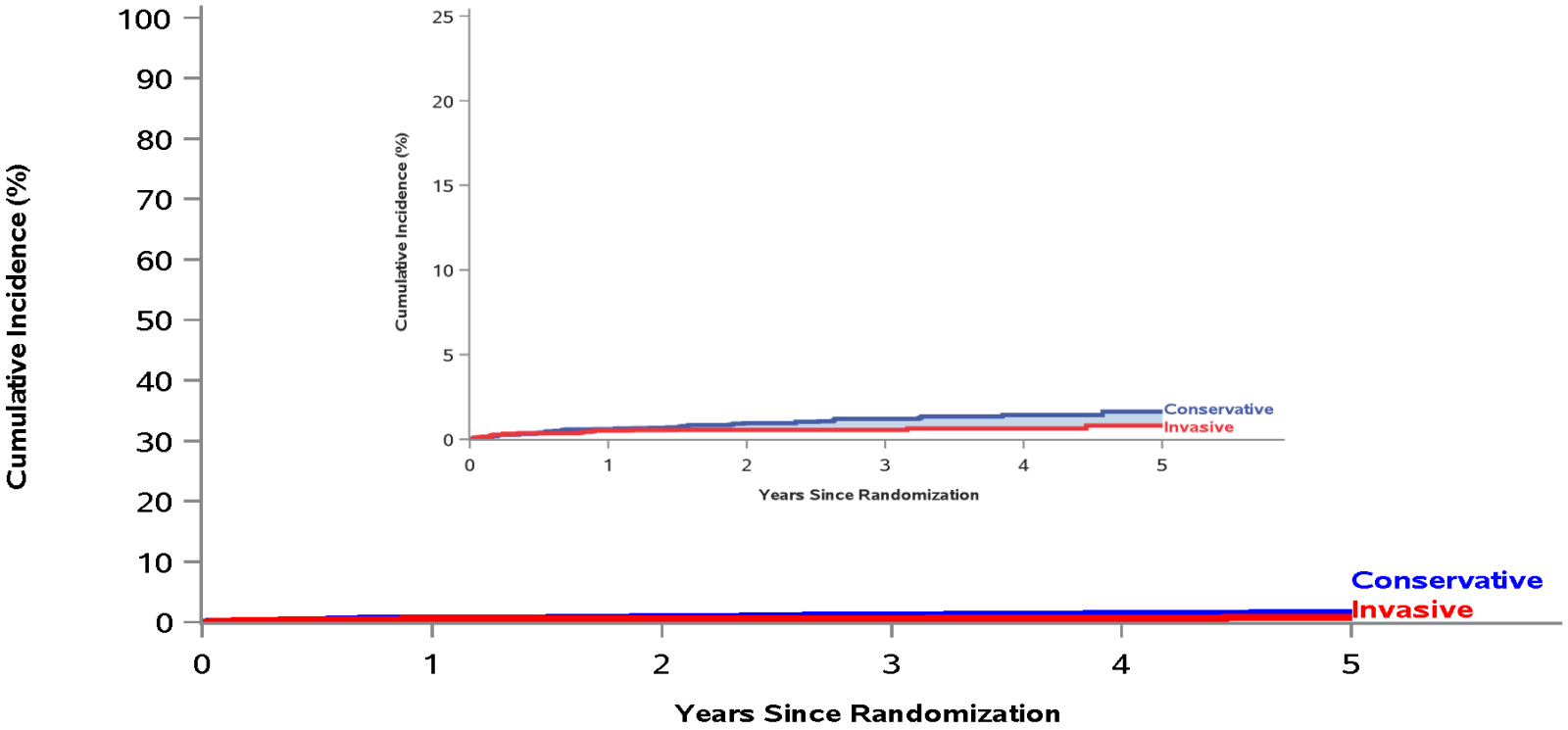
Non-procedural MI



No. at Risk						
Conservative	2591	2464	1951	1340	762	303
Invasive	2588	2438	1987	1355	768	291

HR_{adj} for invasive vs. conservative: 0.67 (95% CI: 0.53 to 0.83). Diagnosis of nonprocedural MI was defined as Type 1, 2, 4b, or 4c myocardial infarction. See Definitions of Outcomes in Supplementary Methods.

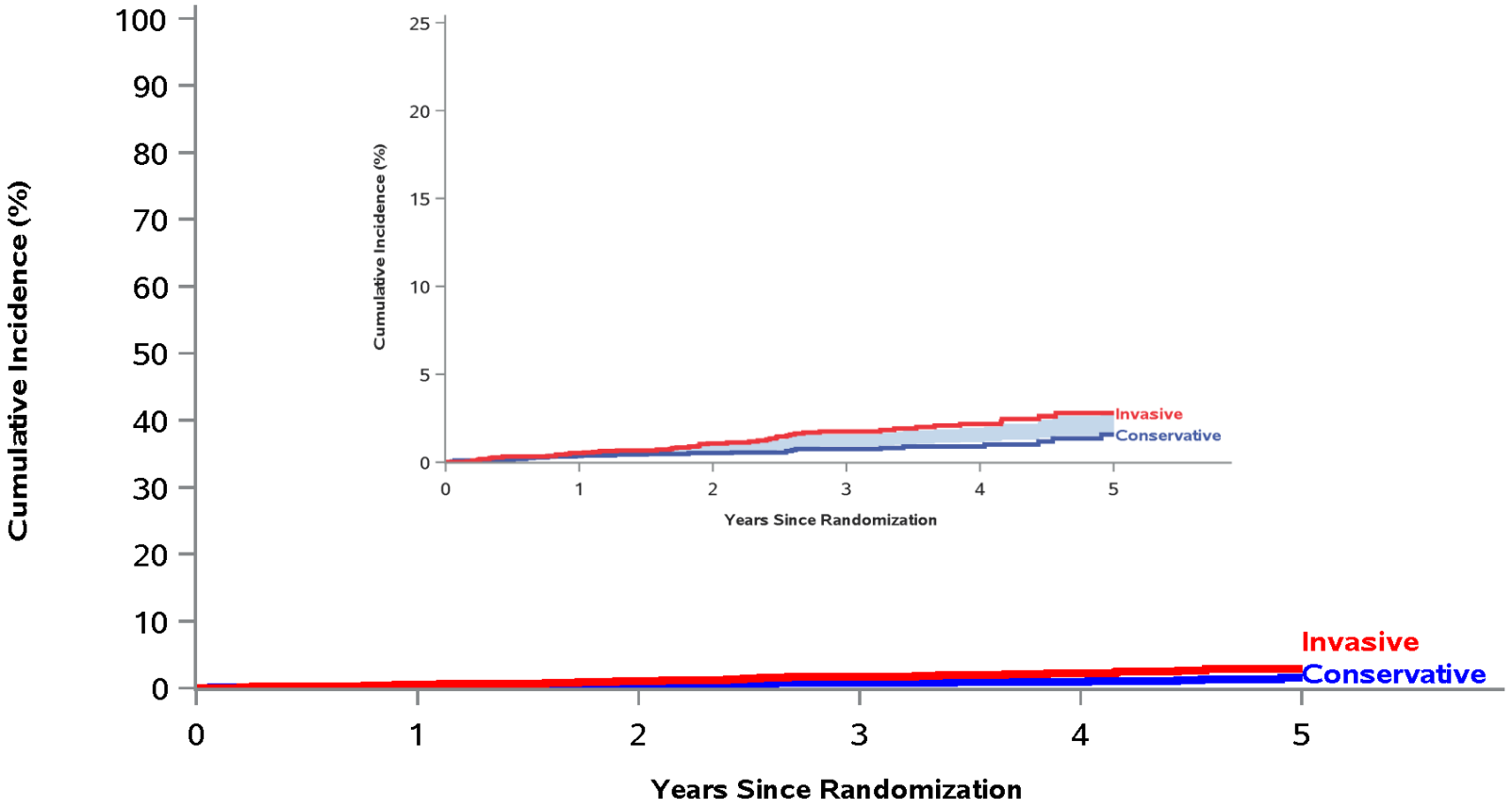
Hospitalization for unstable angina



No. at Risk						
Conservative	2591	2526	2034	1417	826	342
Invasive	2588	2491	2042	1409	812	308

HR_{adj} for invasive vs. conservative: 0.50 (95% CI: 0.27 to 0.91).

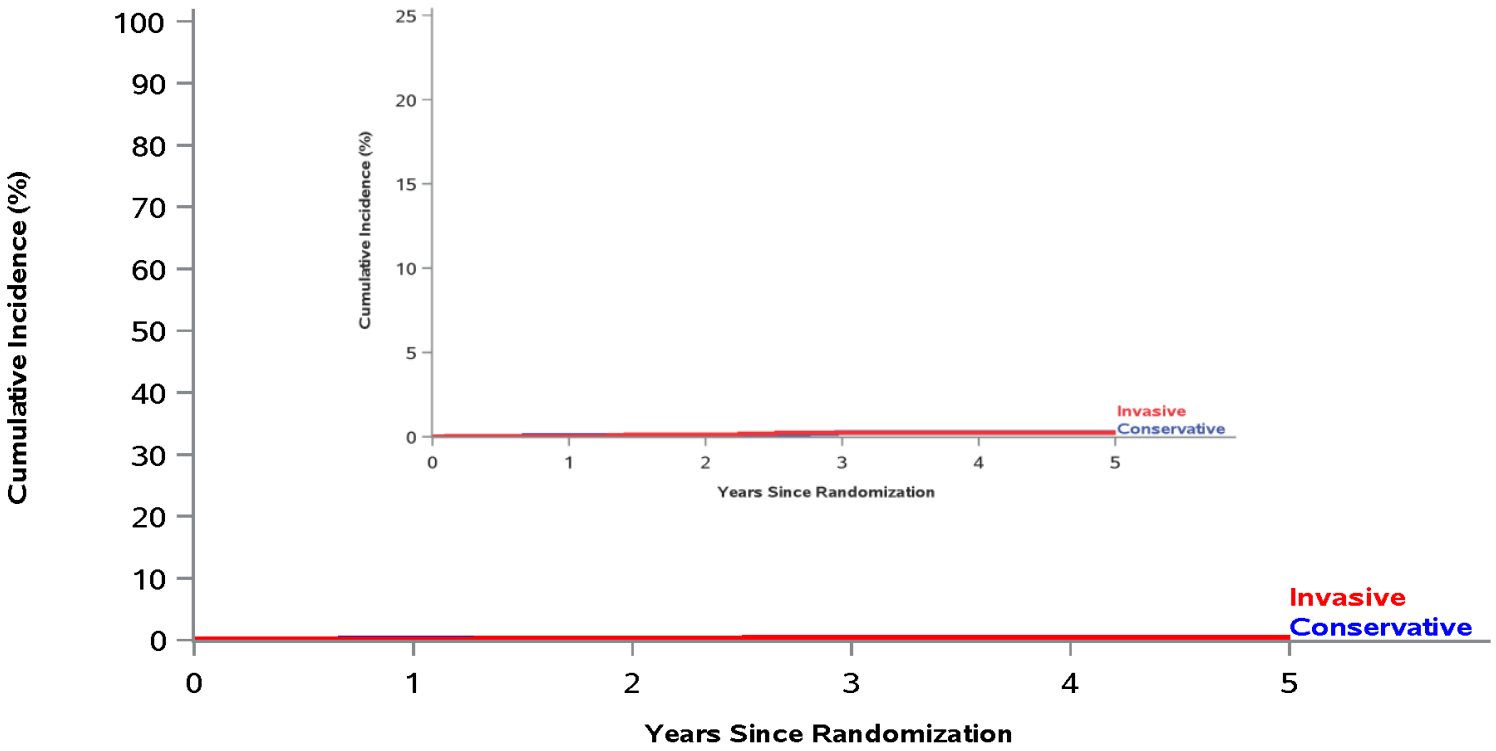
Hospitalization for heart failure



No. at Risk						
Conservative	2591	2535	2044	1424	834	345
Invasive	2588	2494	2031	1397	807	302

HR_{adj} for invasive vs. conservative: 2.23 (95% CI: 1.38 to 3.61).

Hospitalization for resuscitated cardiac arrest

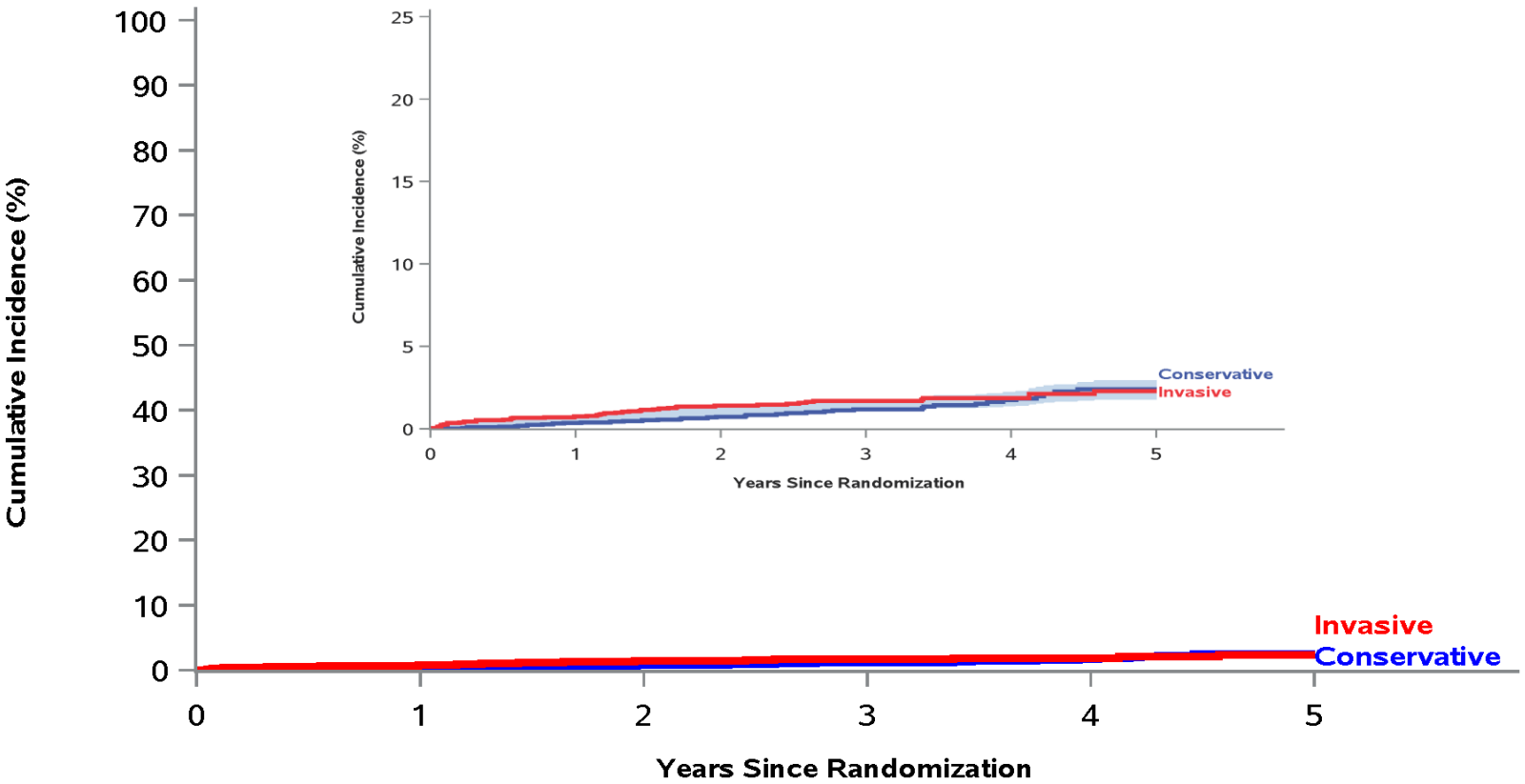


No. at Risk

Conservative	2591	2540	2050	1429	836	346
Invasive	2588	2503	2048	1413	817	311

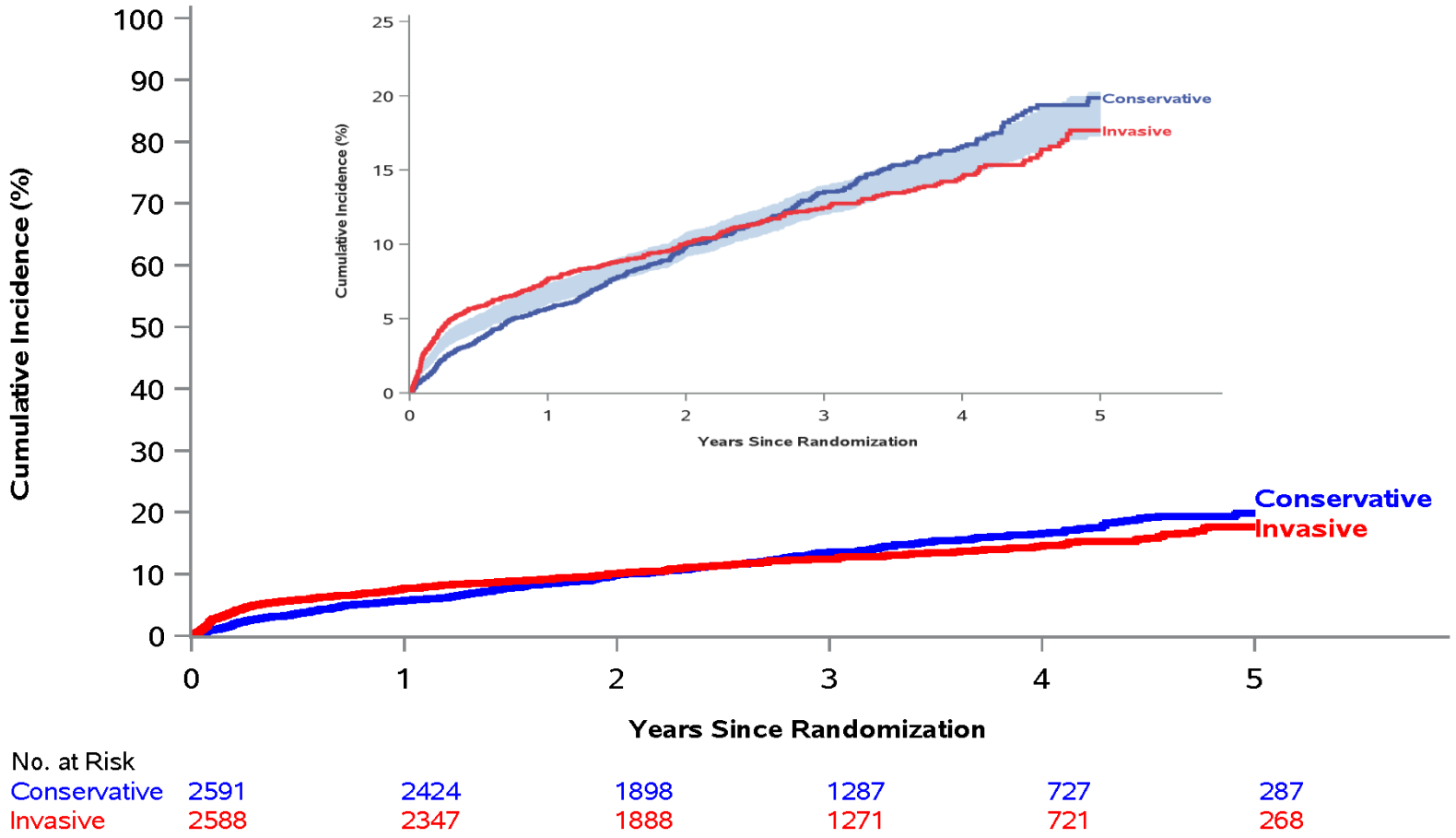
HR_{adj} for invasive vs. conservative: 1.01 (95% CI: 0.29 to 3.49).

Stroke



No. at Risk						
Conservative	2591	2533	2038	1416	831	341
Invasive	2588	2486	2027	1391	807	309

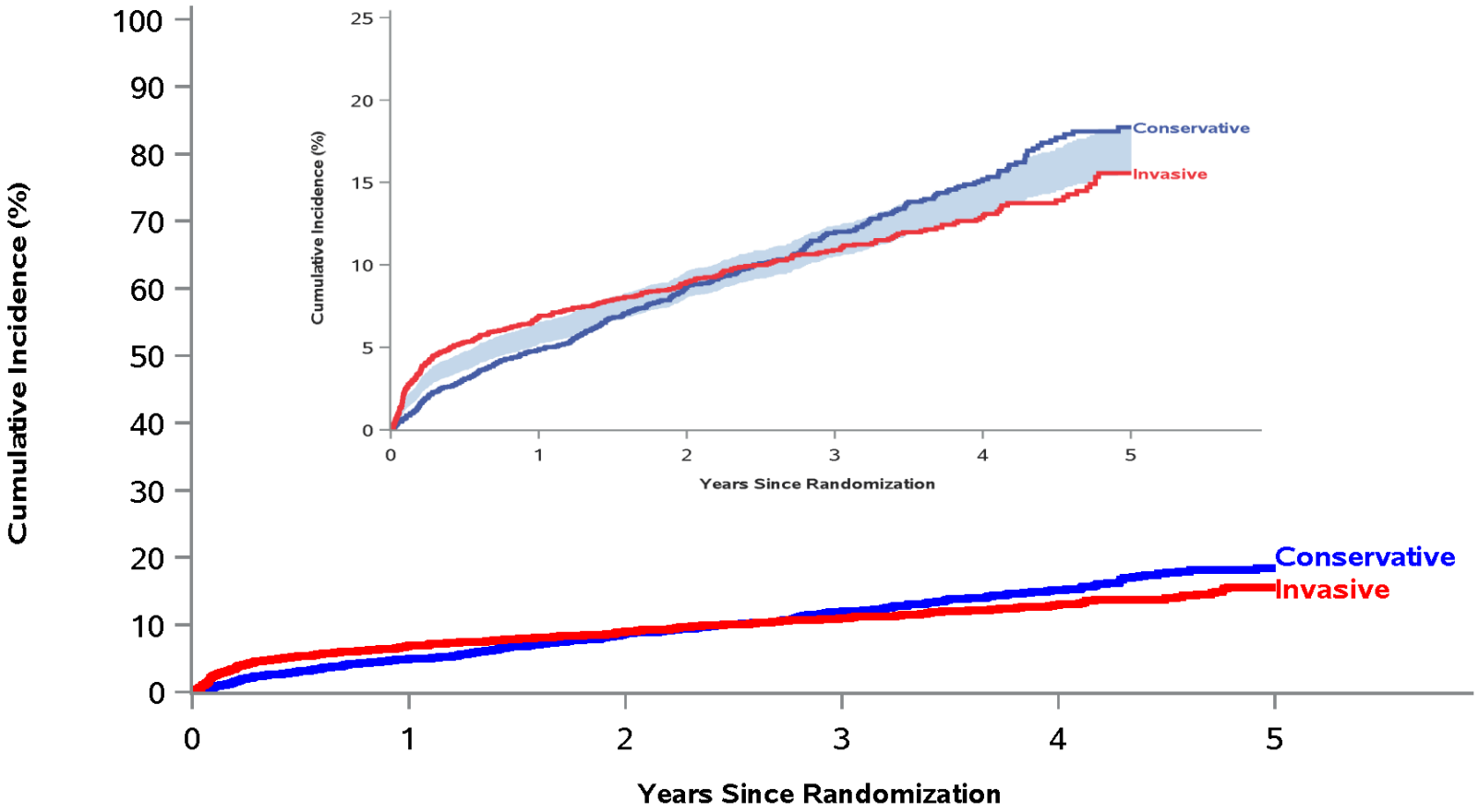
Net Clinical Benefit: CV Death, MI, UA, HF, RCA, Stroke



No. at Risk						
Conservative	2591	2424	1898	1287	727	287
Invasive	2588	2347	1888	1271	721	268

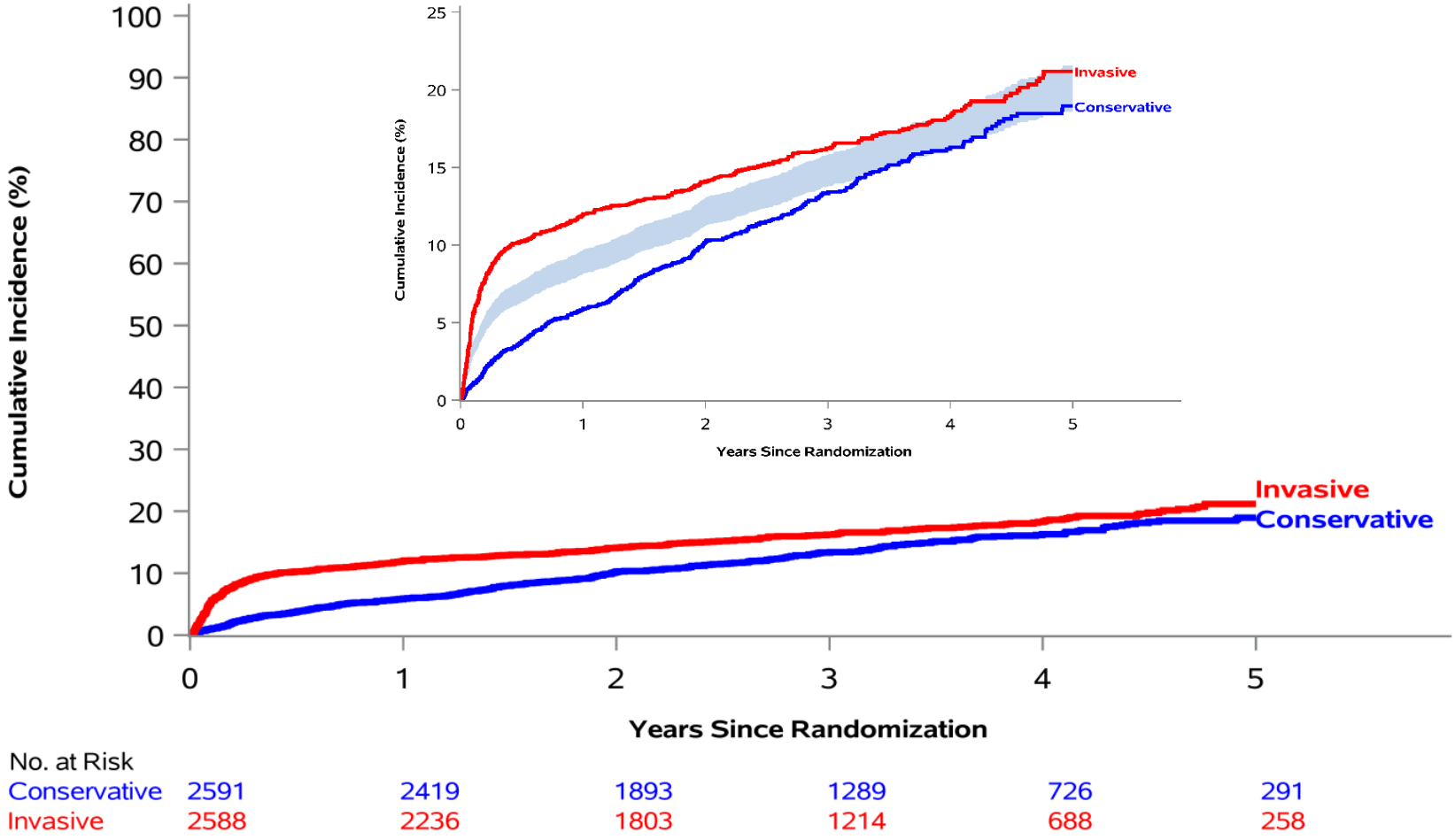
Net clinical benefit: cardiovascular death; myocardial infarction; hospitalization for unstable angina, heart failure, resuscitated cardiac arrest; or stroke.

CV Death/MI/Stroke



No. at Risk						
Conservative	2591	2445	1922	1310	740	291
Invasive	2588	2366	1912	1292	733	279

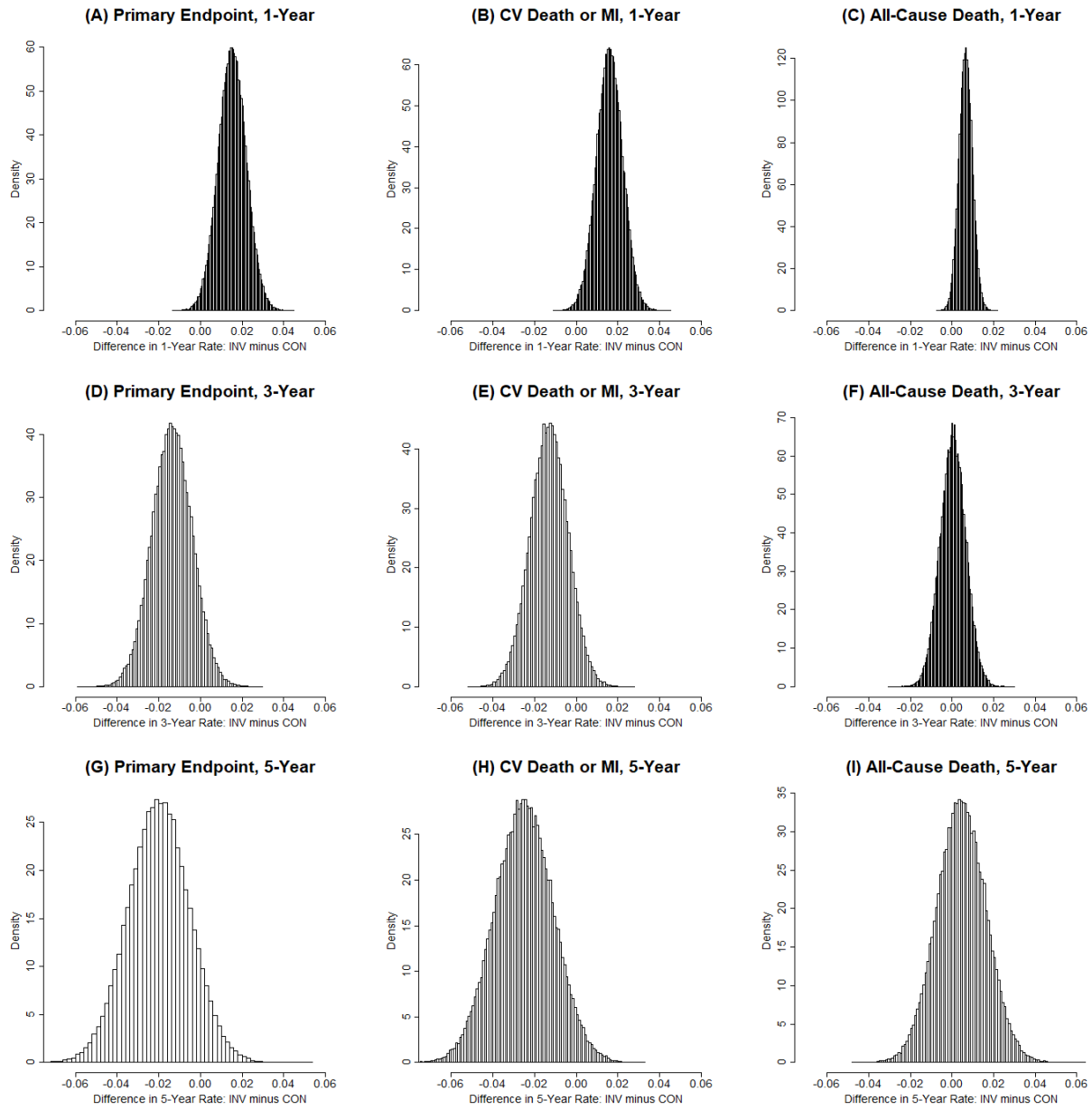
Figure S9. Time-to-Event Curves for the Primary Composite Outcome Using the Secondary Definition of MI



No. at Risk						
Conservative	2591	2419	1893	1289	726	291
Invasive	2588	2236	1803	1214	688	258

Shading in inset figure indicates the half width of the confidence interval for the difference. Overlap of the lines and shading indicates that the 95% CI for the difference includes zero.

Figures S10a-10i. Posterior Distribution of Difference in Cumulative Event Rate at 1, 3, and 5 Years



Note: Cumulative event rates are expressed as proportions ranging from 0 to 1.

Interpretation: The probability that the true difference falls in a narrow interval is proportional to the height of the bar around that interval.

V. Supplementary Tables

Table S1. Participant Eligibility Criteria

* ISCHEMIA Protocol Version 2.0

Inclusion Criteria (at enrollment)

1. At least moderate ischemia on a qualifying stress test
2. Participant is willing to give informed consent
3. Age ≥ 21 years

Exclusion Criteria

1. LVEF <35%
2. History of unprotected left main stenosis ≥50% on prior CCTA or prior cardiac catheterization (if available)
3. Finding of "no obstructive coronary artery disease" (<50% stenosis in all major epicardial vessels) on prior CCTA or prior catheterization, performed within 12 months
4. Coronary anatomy unsuitable for either PCI or CABG
5. Unacceptable level of angina despite maximal medical therapy
6. Very dissatisfied with medical management of angina
7. History of noncompliance with medical therapy
8. Acute coronary syndrome within the previous 2 months
9. PCI within the previous 12 months
10. Stroke within the previous 6 months or spontaneous intracranial hemorrhage at any time
11. History of ventricular tachycardia requiring therapy for termination, or symptomatic sustained ventricular tachycardia not due to a transient reversible cause
12. NYHA class III-IV heart failure at entry or hospitalization for exacerbation of chronic heart failure within the previous 6 months
13. Non-ischemic dilated cardiomyopathy or hypertrophic cardiomyopathy
14. End stage renal disease on dialysis or estimated glomerular filtration rate <30 ml/min (not an exclusion criterion for CKD ancillary trial, see CKD ancillary trial)
15. Severe valvular disease or valvular disease likely to require surgery or percutaneous valve replacement during the trial
16. Allergy to radiographic contrast that cannot be adequately pre-medicated, or any prior anaphylaxis to radiographic contrast
17. Planned major surgery necessitating interruption of dual antiplatelet therapy (note that patients may be eligible after planned surgery)
18. Life expectancy less than the duration of the trial due to non-cardiovascular comorbidity
19. Pregnancy (known to be pregnant; to be confirmed pre-CCTA and/or randomization, if applicable)
20. Patient who, in the judgment of the patient's physician, is likely to have significant unprotected left main stenosis (those who are able to undergo CCTA will have visual assessment of the left main coronary artery by the CCTA core laboratory)

21. Enrolled in a competing trial that involves a non-approved cardiac drug or device
22. Inability to comply with the protocol
23. Exceeds the weight or size limit for CCTA or cardiac catheterization at the site
24. Canadian Cardiovascular Society Class III angina of recent onset, or angina of any class with a rapidly progressive or accelerating pattern
25. Canadian Cardiovascular Society Class IV angina, including unprovoked rest angina
26. High risk of bleeding which would contraindicate the use of dual antiplatelet therapy
27. Cardiac transplant recipient
28. Prior CABG, unless CABG was performed more than 12 months ago and coronary anatomy has been demonstrated to be suitable for PCI or CABG to accomplish complete revascularization of ischemic areas (CCC approval required)

Table S2. Ischemia Eligibility Criteria by Stress Test Modality

Stress Test Modality	Diagnostic criteria
Nuclear perfusion via SPECT or PET	≥10% myocardium ischemic[1]
Echocardiography	≥3/16 segments with stress-induced severe hypokinesis or akinesis
Cardiac Magnetic Resonance	Perfusion: ≥12% myocardium ischemic, and/or Wall motion: ≥3/16 segments with stress-induced severe hypokinesis or akinesis
Exercise Test without Imaging[2] (criteria 1-4 must all be met)	1. Clinical history of typical angina or typical angina during the exercise test 2. Absence of resting ST-segment depression ≥1.0 mm or confounders that render exercise ECG non-interpretable (LBBB, LVH with repolarization, pacemaker, etc.) 3. As compared to the baseline tracing, additional exercise-induced horizontal or downsloping ST-segment depression ≥1.5 mm in 2 leads *or* ≥2.0 mm in any lead; ST-segment elevation ≥1mm in a non-infarct territory. 4. Either of the following: a. Workload at which ST-segment criteria are met is not to exceed completion of stage 2 of a standard Bruce protocol or 7 METs if a non-Bruce protocol is used *or* b. ST segment criteria are met at <75% of the maximum predicted HR *Note: Anatomic eligibility must be confirmed*

SPECT denotes single photon emission computed tomography; PET denotes positron emission tomography; ECG denotes electrocardiogram; LBBB denotes left bundle branch block; LVH denotes left ventricular hypertrophy; HR denotes heart rate; MET denotes metabolic equivalent of task;

Ischemia criteria across imaging modalities were selected to achieve a projected rate of CV death or MI of 5% per year.

[1]An expanded definition of moderate ischemia required all of the following: 1. History of typical angina, or chest pain during exercise stress. 2. Heart rate ≤75% predicted maximum. 3. Workload not greater than stage 2 of Bruce Protocol or 7 METs. 4. Nuclear imaging: ≥5% ischemic myocardium; Echocardiography: ≥2 segments with dobutamine- or exercise-induced severe hypokinesis or akinesis. The result was inclusion of 26 of 5179 randomly assigned patients who were enrolled after stress myocardial perfusion imaging and 30 of 5179 randomly assigned patients who were enrolled after stress echocardiography.

[2]Non-imaging exercise test criteria were developed to approximate severe ischemia, taking into account the potentially higher false positive rate. Anatomic eligibility confirmation was required and CCTA eligibility criteria were more stringent for participants enrolled using non-imaging

exercise stress tests, requiring ≥70% stenosis in the proximal or mid left anterior descending, proximal or mid right coronary artery, or proximal left circumflex (or circumflex equivalent).

Adapted from American Heart Journal, 2018:124-135, ISCHEMIA Trial Research Group, Maron DJ, Hochman JS, O'Brien SM, Reynolds HR, Boden WE, Stone GW, Bangaore S, Spertus JA, Mark DB, Alexander KP, Shaw L, Berger JS, Ferguson TB Jr, William DO, Harrington RA, Rosenberg Y, International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial: Rationale and Design, 2018, with permission from Elsevier

Table S3. Guideline-Based Medical Therapy Goals

RISK FACTOR	GOALS
Behavioral	
Smoking	Smoking cessation[1]
Physical activity	≥30 minutes of moderate intensity ≥5 times/week
Saturated fat	<7% calories
Physiological	
Blood pressure	Systolic blood pressure <130 mm/Hg[1,2]
LDL cholesterol	LDL-C <70 mg/dl (1.8 mmol/L)[1]
Body Mass Index (kg/m^2)	Initial BMI — Weight Loss Goal 25-27.5 — BMI <25 >27.5 — 10% relative weight loss
Diabetes	<8%.[3] A more stringent HbA1c goal (such as <7%) may be appropriate for selected individuals.[4]
Pharmacological agents	**Indications**
Aspirin	All participants, 75-162 mg daily[1]
Statin	All participants, maximum tolerated dose of high-intensity statin (atorvastatin 40-80 mg or rosuvastatin 20-40 mg)[1]
ACEi/ARB	Use for hypertension, diabetes, eGFR <60 or LVEF <40%[1]
Beta blocker	Use for history of MI or LVEF <40%[1]
P2Y12 receptor antagonist	Use for participants with contraindication to aspirin; In combination with aspirin for participants who receive PCI (duration depends on BMS vs. DES); post-MI/ACS for 1 year
Ezetimibe	Use for participants unable to reach LDL-C goal on maximally tolerated statin dose in countries without access to evolocumab provided to trial participants
Evolocumab	Use for participants unable to reach LDL-C goal on maximally tolerated statin dose in countries with access to evolocumab provided to trial participants

BMI denotes body mass index; HbA1c denotes hemoglobin A1c; MI denotes myocardial infarction; ACEi/ARB denotes angiotensin converting enzyme inhibitor/angiotensin receptor blocker; eGFR denotes estimated glomerular filtration rate; LVEF denotes left ventricular ejection fraction; MI denotes myocardial infarction; PCI denotes percutaneous coronary intervention; BMS denotes bare metal stent; DES denotes drug-eluting stent; ACS denotes acute coronary syndrome; LDL-C denotes low-density lipoprotein cholesterol.

[1] This risk factor goal is included in the trial's definition of guideline-based medical therapy.

[2] This risk factor goal changed from <140 mmHg to <130 mmHg in April 2018.

[3] Appropriate for participants with a history of severe hypoglycemia, advanced microvascular or macrovascular complications, extensive comorbid conditions, and those with longstanding diabetes in whom a goal of <7% is difficult to attain.
[4] May be appropriate for participants with a short duration of diabetes and a long life expectancy if this can be achieved without significant hypoglycemia or other adverse effects of treatment.

Reprinted from American Heart Journal, 2018;201:124-135, ISCHEMIA Trial Research Group, Maron DJ, Hochman JS, O'Brien SM, Reynolds HR, Boden WE, Stone GW, Bangaore S, Spertus JA, Mark DB, Alexander KP, Shaw L, Berger JS, Ferguson TB Jr, William DO, Harrington RA, Rosenberg Y, International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial: Rationale and Design, 2018, with permission from Elsevier

Table S4. Industry Support

MEDICATIONS AND DEVICES PROVIDED BY INDUSTRY		
Company Name	**Product**	**Country**
Abbott, Abbott Vascular	XIENCE Everolimus Eluting Coronary Stent System	ALL
Abbott (previously St. Jude Medical)	PressureWire™ Certus and PressureWire™ Aeris; RadiAnalyzer™ Xpress Measurement System	Argentina; Australia; Austria; Belgium; Brazil; Canada; China; Egypt; France; Hungary; India; Israel; Lithuania; Malaysia; Netherlands; New Zealand; Poland; Russia; Saudi Arabia; Serbia; Singapore; South Africa; Spain; Taiwan; Thailand; UK; United Arab Emirates; USA
Amgen	Repatha® (evolocumab)	Canada; Germany; Spain; USA
Arbor Pharmaceuticals	Nitrolingual® Pumpspray (nitroglycerin lingual spray)	Canada *(distributor Pohl Boskamp);* USA
	Edarbi® (azilsartan medoxomil)	USA
	Edarbyclor® (azilsartan medoxomil/chlorthalidone)	USA
AstraZeneca	Crestor® (rosuvastatin calcium) Brilinta® (ticagrelor)	Brazil; Canada; China; Mexico;Singapore;USA
Espero Pharmaceuticals	GoNitro™ (nitroglycerin) sublingual powder	USA
Medtronic	Resolute Integrity DES	ALL
Merck & Co.	Zetia® (ezetimibe) Vytorin® (ezetimibe and simvastatin)	Argentina; Brazil; USA
Omron	Pedometers	ALL
Philips (previously Volcano Corporation)	Prime Wire Prestige PLUS Imaging Consoles	Austria, Belgium, Canada, France, Germany, Italy, Japan, Netherlands, Poland, Portugal, South Africa, Spain, Sweden, UK, USA
Sunovion Pharmaceuticals	Niaspan® (extended-release niacin)	Canada

Reprinted from American Heart Journal, 2018;201:124-135, ISCHEMIA Trial Research Group, Maron DJ, Hochman JS, O'Brien SM, Reynolds HR, Boden WE, Stone GW, Bangaore S, Spertus JA, Mark DB, Alexander KP, Shaw L, Berger JS, Ferguson TB Jr, William DO, Harrington RA, Rosenberg Y, International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial: Rationale and Design, 2018, with permission from Elsevier

Table S5. Baseline Stress Test and Coronary CT Angiography Results

	Total (N=5179)	INV (N=2588)	CON (N=2591)
Stress test modality			
Stress imaging	75.5% (3909/5179)	75.3% (1949/2588)	75.6% (1960/2591)
Severe	44.8% (1746/3901)	43.6% (848/1947)	46.0% (898/1954)
Moderate	41.0% (1601/3901)	42.0% (818/1947)	40.1% (783/1954)
Mild	8.2% (318/3901)	8.4% (163/1947)	7.9% (155/1954)
None	5.8% (226/3901)	5.8% (112/1947)	5.8% (114/1954)
Uninterpretable	0.3% (10/3901)	0.3% (6/1947)	0.2% (4/1954)
Exercise stress test	24.5% (1270/5179)	24.7% (639/2588)	24.4% (631/2591)
Severe	83.0% (1051/1266)	83.8% (534/637)	82.2% (517/629)
Moderate	8.0% (101/1266)	8.6% (55/637)	7.3% (46/629)
Mild	2.7% (34/1266)	2.0% (13/637)	3.3% (21/629)
None	2.2% (28/1266)	1.9% (12/637)	2.5% (16/629)
Uninterpretable	4.1% (52/1266)	3.6% (23/637)	4.6% (29/629)
Coronary anatomy by CCTA			
Vessels ≥ 50% stenosis by CCTA[1]			
0	0.1% (4/2986)	0.1% (2/1490)	0.1% (2/1496)
1	23.3% (697/2986)	24.2% (360/1490)	22.5% (337/1496)
2	31.4% (938/2986)	29.1% (434/1490)	33.7% (504/1496)
3	45.1% (1347/2986)	46.6% (694/1490)	43.6% (653/1496)
Specific native vessels with ≥ 50% stenosis by CCTA[1,2]			
Left main	1.0% (40/3845)	1.1% (21/1926)	1.0% (19/1919)
Left anterior descending	86.8% (3190/3677)	86.6% (1591/1837)	86.9% (1599/1840)
Proximal left anterior descending	46.8% (1749/3739)	46.3% (865/1870)	47.3% (884/1869)
Left circumflex	67.4% (2354/3495)	67.7% (1184/1749)	67.0% (1170/1746)
Right coronary artery	68.8% (2311/3359)	70.0% (1178/1684)	67.6% (1133/1675)

[1]Includes study (N=3765) and nonstudy (N=148) CCTAs. Randomized participants with any study or nonstudy CCTA: 3913. These numbers represent 50% stenosis criteria for all stress test modalities.
[2]Includes participants with a prior coronary artery bypass graft surgery.
CCTA denotes coronary computed tomography angiography.

Table S6. Baseline and On-Trial Physiologic Measurements, Risk Factors, and Medications by Treatment Group

Variables	Baseline Total (N=5179)	Last Visit Total (N=5179)	Baseline		Last Visit	
			INV (N=2588)	CON (N=2591)	INV (N=2588)	CON (N=2591)
Systolic blood pressure						
N	5150	4962	2572	2578	2463	2499
Median	130.0	129.0	130.0	130.0	129.0	128.0
(Q1, Q3)	(120.0, 142.0)	(120.0, 138.0)	(120.0, 142.0)	(120.0, 142.0)	(120.0, 138.0)	(120.0, 138.0)
Diastolic blood pressure						
N	5150	4962	2572	2578	2463	2499
Median	77.0	74.0	77.0	77.0	74.0	74.0
(Q1, Q3)	(70.0, 81.0)	(69.0, 80.0)	(70.0, 81.0)	(70.0, 81.0)	(69.0, 80.0)	(68.0, 80.0)
Total cholesterol (mg/dL)						
N	5074	4892	2522	2552	2422	2470
Median	154.3	131.0	154.7	154.0	130.7	131.0
(Q1, Q3)	(129.2, 185.6)	(114.0, 154.0)	(130.0, 186.0)	(129.0, 185.6)	(113.3, 153.0)	(114.0, 154.7)
HDL cholesterol (mg/dL)						
N	5023	4888	2503	2520	2420	2468
Median	42.5	43.0	42.5	42.5	43.0	42.9
(Q1, Q3)	(36.0, 50.7)	(36.0, 52.0)	(36.0, 51.0)	(36.0, 50.3)	(36.0, 52.0)	(36.0, 51.4)
LDL cholesterol (mg/dL)						
N	4940	4883	2464	2476	2416	2467
Median	83.0	64.0	83.0	83.0	64.0	64.0
(Q1, Q3)	(63.0, 111.0)	(51.0, 81.2)	(63.0, 111.0)	(63.0, 109.5)	(51.0, 81.2)	(51.0, 81.6)
Triglycerides (mg/dL)						
N	4984	4885	2482	2502	2418	2467
Median	124.0	111.5	124.0	124.0	110.0	113.0
(Q1, Q3)	(91.2, 177.0)	(82.0, 153.0)	(91.0, 178.0)	(92.0, 175.0)	(82.0, 152.0)	(81.4, 155.0)
HbA1c (%)						
N	3439	3789	1716	1723	1869	1920
Median	6.3	6.3	6.3	6.3	6.3	6.3
(Q1, Q3)	(5.8, 7.4)	(5.8, 7.3)	(5.8, 7.5)	(5.8, 7.4)	(5.8, 7.4)	(5.8, 7.2)
Body mass index						
N	5124	4895	2564	2560	2428	2467
Median	27.7	27.5	27.7	27.7	27.7	27.5
(Q1, Q3)	(25.0, 31.3)	(24.7, 31.1)	(25.0, 31.2)	(24.9, 31.6)	(24.7, 30.9)	(24.7, 31.2)
Current smoking	12.4% (640/5174)	9.7% (467/4829)	12.3% (319/2587)	12.4% (321/2587)	9.6% (230/2402)	9.8% (237/2427)
Medications						
Aspirin or aspirin alternative	96.1% (4872/5068)	96.9% (4663/4814)	96.6% (2443/2530)	95.7% (2429/2538)	96.9% (2316/2390)	96.8% (2347/2424)
Clopidogrel	26.0% (1345/5175)	27.0% (1348/4997)	28.2% (730/2586)	23.8% (615/2589)	30.0% (744/2483)	24.0% (604/2514)
Anticoagulant	4.0% (203/5131)	6.9% (342/4992)	4.4% (114/2567)	3.5% (89/2564)	7.3% (182/2482)	6.4% (160/2510)

Variables	Baseline Total (N=5179)	Last Visit Total (N=5179)	Baseline		Last Visit	
			INV (N=2588)	CON (N=2591)	INV (N=2588)	CON (N=2591)
Antiplatelet or anticoagulant	100% (4978/4978)	100% (4845/4845)	100% (2499/2499)	100% (2479/2479)	100% (2409/2409)	100% (2436/2436)
Statin	94.8% (4904/5174)	95.2% (4755/4997)	94.4% (2441/2586)	95.2% (2463/2588)	95.0% (2361/2484)	95.3% (2394/2513)
High-intensity statin	40.9% (1911/4670)	66.0% (3223/4881)	40.1% (933/2328)	41.8% (978/2342)	66.3% (1604/2421)	65.8% (1619/2460)
Ezetimibe	4.1% (212/5175)	24.4% (1222/4998)	4.1% (105/2586)	4.1% (107/2589)	24.2% (602/2484)	24.7% (620/2514)
Ace inhibitor / ARB	66.0% (3416/5175)	69.4% (3469/4996)	65.2% (1685/2586)	66.9% (1731/2589)	69.2% (1718/2483)	69.7% (1751/2513)
Adherent to Medications[1]	73.9% (3672/4967)	81.5% (3991/4896)	73.7% (1823/2473)	74.1% (1849/2494)	82.7% (2012/2434)	80.4% (1979/2462)

[1]As assessed by Morisky-Greene-Levine medication adherence scale. (Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Medical Care 1986;24:67-74). A summary binary variable was created by coding those who responded strongly agree, agree, don't know, or refuse to any of the 4 questions in the survey as nonadherent; otherwise, patients were coded as adherent.
Aspirin alternative denotes P2Y12 inhibitor.
Antiplatelet denotes aspirin or P2Y12 inhibitor.

Table S7a. Frequency and Timing of the First Catheterization and Revascularization for Participants Randomized to the INV Treatment[1] Intent-to-Treat Population

	Statistic	INV (N=2588)
First Catheterization[2] or Revascularization Done	% (n / N)	95.6% (2475/2588)
First Catheterization or Revascularization Done Within 6 Weeks of Randomization	% (n / N)	80.3% (2079/2588)
First Catheterization or Revascularization Done Within 3 Months of Randomization	% (n / N)	92.1% (2383/2588)
First Catheterization or Revascularization Done Within 12 Months of Randomization	% (n / N)	94.9% (2457/2588)
First Catheterization or Revascularization Done by the Time of the 6-week Visit	% (n / N)	87.2% (2257/2588)
Days From Randomization to First Catheterization or Revascularization	n	2475
	Mean (Stand. Dev.)	31.8 (73.9)
	Median (Q1, Q3)	19 (10, 32)
	Min, Max	1, 1623
First Revascularization Done	% (n / N)	79.4% (2054/2588)
First Revascularization Done Within 6 Weeks of Randomization	% (n / N)	54.9% (1420/2588)
First Revascularization Done Within 3 Months of Randomization	% (n / N)	69.3% (1794/2588)
First Revascularization Done Within 12 Months of Randomization	% (n / N)	78.1% (2021/2588)
First Revascularization Done by the Time of the 6-week Visit	% (n / N)	63.3% (1639/2588)
Days From Randomization to First Revascularization	n	2054
	Mean (Stand. Dev.)	54.4 (127.8)
	Median (Q1, Q3)	27 (14, 51)
	Min, Max	1, 2144

1 The purpose of this table is to summarize participants' level of adherence to the INV strategy as measured by the completion and timeliness of a post-randomization catheterization and/or revascularization procedure.

2 The first catheterization is done within 6 weeks of randomization if the date of the first catheterization is prior to the date that is exactly 6 weeks after randomization. The first catheterization is done by the time of the 6-week visit if the date of the first catheterization is prior to the date of the visit that is indicated as being the 6-week follow-up visit. The 6-week follow up visit may not occur exactly 6 weeks after randomization as the visit can happen at any time between randomization and 2 months after randomization.

23 invasive strategy participants had a primary outcome event prior to their first catheterization.

42 invasive strategy participants had a primary outcome event prior to their first revascularization.

When counting catheterizations performed prior to randomization that were not repeated prior to CABG in INV participants, a total of 2475/2588 (96%) of INV participants had catheterization or revascularization for any reason, consistent with protocol adherence. The proportions of participants undergoing angiography and revascularization differ from the cumulative incidence function rates which account for censoring.

Table S7b. Unadjusted Cumulative Incidence Function Estimates (Accounting for Competing Risk of Death) of First Cardiac Catheterization for Conservative Strategy Participants by Indications for the Procedure

	Any Reason	Suspected but Not Confirmed Event (MIUA, HF, RCA)	Confirmed Event (MIUA, HF, RCA)	OMT Failure / Refractory Angina	Non-adherence / Other
First Catheterization	667	177	180	100	210
≤ 30 days	1.9%	0.5%	0.5%	0.2%	0.7%
≤ 45 days	2.4%	0.7%	0.6%	0.2%	0.9%
≤ 60 days	3.6%	1.0%	0.9%	0.6%	1.1%
≤ 90 days	5.8%	1.2%	1.7%	1.2%	1.7%
≤ 180 days	8.7%	2.1%	2.5%	1.6%	2.6%
≤ 1 year	13.8%	3.8%	3.5%	2.6%	4.0%
≤ 2 years	20.6%	5.8%	5.3%	3.5%	6.0%
≤ 3 years	24.8%	6.7%	6.9%	3.8%	7.3%
≤ 4 years	28.1%	7.4%	7.8%	4.1%	8.7%
≤ 5 years	32.5%	8.4%	8.8%	4.4%	11.0%
First Catheterization Not Preceded by Confirmed Primary Endpoint Event	487	177	0	100	210
≤ 30 days	1.4%	0.5%		0.2%	0.7%
≤ 45 days	1.7%	0.7%		0.2%	0.9%
≤ 60 days	2.7%	1.0%		0.6%	1.1%
≤ 90 days	4.1%	1.2%		1.2%	1.7%
≤ 180 days	6.2%	2.1%		1.6%	2.6%
≤ 1 year	10.3%	3.8%		2.6%	4.0%
≤ 2 years	15.3%	5.8%		3.5%	6.0%
≤ 3 years	17.9%	6.7%		3.8%	7.3%
≤ 4 years	20.3%	7.4%		4.1%	8.7%
≤ 5 years	23.7%	8.4%		4.4%	10.9%

The proportions of participants undergoing angiography and revascularization differ from the cumulative incidence function rates which account for censoring.

Table S7c. Unadjusted Cumulative Incidence Function Estimates (Accounting for Competing Risk of Death) of First Revascularization for Conservative Strategy Participants by Indications for the Procedure

	Any Reason	Suspected but Not Confirmed Event (MIUA, HF, RCA)	Confirmed Event (MIUA, HF, RCA)	OMT Failure / Refractory Angina	Non-adherence / Other
First Revascularization	544	151	162	47	184
≤ 30 days	1.4%	0.3%	0.4%	0.2%	0.6%
≤ 45 days	2.2%	0.5%	0.6%	0.2%	0.8%
≤ 60 days	3.0%	0.7%	0.9%	0.3%	1.1%
≤ 90 days	4.7%	1.1%	1.4%	0.6%	1.6%
≤ 180 days	7.3%	1.8%	2.1%	0.8%	2.7%
≤ 1 year	11.6%	3.1%	3.0%	1.3%	4.1%
≤ 2 years	17.0%	4.7%	4.8%	1.6%	5.9%
≤ 3 years	20.1%	5.7%	6.1%	1.6%	6.7%
≤ 4 years	23.1%	6.5%	7.0%	1.9%	7.7%
≤ 5 years	26.2%	7.3%	7.9%	2.4%	8.7%
First Revascularization Not Preceded by Confirmed Primary Endpoint Event	382	151	0	47	184
≤ 30 days	1.0%	0.3%		0.2%	0.6%
≤ 45 days	1.6%	0.5%		0.2%	0.8%
≤ 60 days	2.2%	0.7%		0.3%	1.1%
≤ 90 days	3.3%	1.1%		0.6%	1.6%
≤ 180 days	5.2%	1.8%		0.8%	2.7%
≤ 1 year	8.5%	3.1%		1.3%	4.1%
≤ 2 years	12.2%	4.7%		1.6%	5.9%
≤ 3 years	14.0%	5.7%		1.6%	6.7%
≤ 4 years	16.1%	6.5%		1.9%	7.7%
≤ 5 years	18.3%	7.2%		2.4%	8.7%

The proportions of participants undergoing angiography and revascularization differ from the cumulative incidence function rates which account for censoring.

Table S8. Angiographic Characteristics and Procedural Data for First Procedure

Parameter	Invasive Strategy Participants (N=2588)
Angiographic Characteristics	
Number of Native Vessels With ≥50% Stenosis (QCA)	
0	6.4% (151/2371)
1	22.3% (529/2371
2	31.7% (751/2371)
3	39.6% (940/2371)
Native Vessels With ≥ 50% Stenosis (QCA)	
Left Main	3.8% (95/2473)
Left Anterior Descending (LAD)	76.5% (1859/2430)
Proximal LAD	36.2% (895/2473)
Left Circumflex	62.0% (1512/2440)
Right Coronary Artery	63.7% (1536/2410)
FFR use	20.3% (481/2372)
Revascularization Characteristics	
Mode of Revascularization	
PCI	74.2% (1524/2054)
Stent use	93.0% (1418/1524)
DES use	97.9% (1357/1386)
1st generation	1.9% (26/1355)
2nd generation	98.1% (1329/1355)
Stent not deliverable	5.4% (83/1524)
Balloon angioplasty only	1.5% (23/1524)
CABG	25.8% (530/2054)
Internal mammary artery use	91.9% (486/529)
Intended Management Strategy After First Diagnostic Catheterization in Participants with a Catheterization But No Revascularization During Follow-up	421
Medical Therapy Only	88.1% (371/421)
No Obstructive Coronary Artery Disease	52.5% (221/421)
Anatomy Not Suitable for Any Mode of Revascularization	26.4% (111/421)
Patient Preference	6.7% (28/421)
Other	2.6% (11/421)
Intent to Perform PCI / CABG / Hybrid	11.6% (49/421)
Undecided	0.0% (0/421)
Unknown	0.2% (1/421)

Diameter stenosis ≥50% by quantitative coronary angiography (among 2474 angiograms received in the core laboratory). Most participating centers had FFR capabilities at the time of their first participant enrollment. Sites without this capability were provided a loaner console from St. Jude Medical, Inc. or Volcano Corp. and were trained to use FFR prior to participant enrollment. The decision to perform FFR was based on visual estimation of stenosis.

QCA denotes quantitative coronary angiography

LAD denotes left anterior descending
SYNTAX Score denotes a scoring system derived from the Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial
FFR denotes fractional flow reserve
PCI denotes percutaneous coronary intervention
CABG denotes coronary artery bypass graft surgery

Table S9. Total Number of Catheterization and Revascularization Procedures by Treatment Group

	All Subjects (N=5179)	INV (N=2588)	CON (N=2591)
Total Number of Invasive Coronary Angiograms	3718	2887	831
Average Per Participant	0.7	1.1	0.3
Total Number of Revascularizations (PCI or CABG)	3125	2450	675
Average Per Participant	0.6	0.9	0.3
Total Number of PCI Procedures[1]	2350	1873	477
Total Number of CABG Procedures	775	577	198
Total Number of Catheterization Lab Visits	4352	3397	955
Average Per Participant	0.8	1.3	0.4

[1] A PCI procedure may include more than one treated vessel in the same Catheterization Lab visit.

Table S10. Outcomes by Treatment Group Using the Primary Definition of MI

Estimated Cumulative Event Rates and Differences

Cardiovascular Death	**INV (N=2588)**	**CON (N=2591)**	**Estimated Difference (95% CI)**
Patients with events	92	111	
6-month cumulative event rate	0.7%	0.4%	0.3% (-0.1% to 0.7%)
1-year cumulative event rate	1.3%	1.0%	0.4% (-0.2% to 0.9%)
2-year cumulative event rate	2.2%	2.4%	-0.3% (-1.1% to 0.6%)
3-year cumulative event rate	2.8%	3.5%	-0.6% (-1.7% to 0.4%)
4-year cumulative event rate	4.1%	5.0%	-1.0% (-2.3% to 0.4%)
5-year cumulative event rate	5.2%	6.5%	-1.3% (-3.1% to 0.6%)
Restricted mean event-free time[1]	4.87 years	4.85 years	7.4 days (-7.2 days to 21.9 days)
Cox model HR[2]: 0.87 (95% CI: 0.66 to 1.15)			
Procedural MI	**INV**	**CON**	**Estimated Difference (95% CI)**
Patients with events	70	24	
6-month cumulative event rate	2.6%	0.3%	2.3% (1.6% to 2.9%)
1-year cumulative event rate	2.6%	0.5%	2.2% (1.5% to 2.9%)
2-year cumulative event rate	2.7%	0.8%	1.9% (1.2% to 2.6%)
3-year cumulative event rate	2.7%	1.0%	1.7% (0.9% to 2.4%)
4-year cumulative event rate	2.7%	1.1%	1.6% (0.8% to 2.4%)
5-year cumulative event rate	2.8%	1.1%	1.7% (0.9% to 2.5%)
Restricted mean event-free time	4.87 years	4.96 years	-33.6 days (-46.0 days to -21.2 days)
Non-procedural MI[3]	**INV**	**CON**	**Estimated Difference (95% CI)**
Patients with events	130	196	
6-month cumulative event rate	1.8%	2.3%	-0.5% (-1.2% to 0.3%)
1-year cumulative event rate	2.7%	3.3%	-0.6% (-1.5% to 0.4%)
2-year cumulative event rate	3.5%	5.4%	-1.9% (-3.0% to -0.8%)
3-year cumulative event rate	4.6%	7.1%	-2.5% (-3.9% to -1.1%)
4-year cumulative event rate	5.9%	8.7%	-2.8% (-4.5% to -1.1%)
5-year cumulative event rate	7.1%	10.0%	-2.9% (-5.0% to -0.8%)
Restricted mean event-free time	4.79 years	4.70 years	34.6 days (14.6 days to 54.6 days)
Hospitalization for Unstable Angina	**INV**	**CON**	**Estimated Difference (95% CI)**
Patients with events	16	32	
6-month cumulative event rate	0.4%	0.3%	0.0% (-0.3% to 0.3%)
1-year cumulative event rate	0.5%	0.6%	-0.1% (-0.5% to 0.3%)
2-year cumulative event rate	0.5%	1.0%	-0.4% (-0.9% to 0.1%)
3-year cumulative event rate	0.5%	1.2%	-0.6% (-1.2% to -0.1%)
4-year cumulative event rate	0.6%	1.4%	-0.8% (-1.4% to -0.2%)
5-year cumulative event rate	0.8%	1.6%	-0.8% (-1.6% to -0.1%)
Restricted mean event-free time	4.97 years	4.95 years	8.6 days (0.4 days to 16.7 days)
Cox model HR: 0.50 (95% CI: 0.27 to 0.91)			

Hospitalization for Heart Failure	**INV**	**CON**	**Estimated Difference (95% CI)**
Patients with events	51	25	
6-month cumulative event rate	0.3%	0.2%	0.2% (-0.1% to 0.4%)
1-year cumulative event rate	0.5%	0.3%	0.2% (-0.2% to 0.5%)
2-year cumulative event rate	1.1%	0.5%	0.6% (0.1% to 1.1%)
3-year cumulative event rate	1.7%	0.7%	1.0% (0.3% to 1.7%)
4-year cumulative event rate	2.2%	0.9%	1.3% (0.5% to 2.1%)
5-year cumulative event rate	2.8%	1.6%	1.2% (-0.0% to 2.4%)
Restricted mean event-free time	4.93 years	4.97 years	-13.5 days (-22.5 days to -4.6 days)
Cox model HR: 2.23 (95% CI: 1.38 to 3.61)			
Resuscitated Cardiac Arrest	**INV**	**CON**	**Estimated Difference (95% CI)**
Patients with events	5	5	
6-month cumulative event rate	0.0%	0.0%	-0.0% (-0.1% to 0.1%)
1-year cumulative event rate	0.0%	0.1%	-0.0% (-0.2% to 0.1%)
2-year cumulative event rate	0.1%	0.1%	-0.0% (-0.2% to 0.2%)
3-year cumulative event rate	0.2%	0.2%	-0.0% (-0.3% to 0.3%)
4-year cumulative event rate	0.2%	0.2%	-0.0% (-0.3% to 0.3%)
5-year cumulative event rate	0.2%	0.2%	-0.0% (-0.3% to 0.3%)
Restricted mean event-free time	4.99 years	4.99 years	-0.0 days (-3.6 days to 3.5 days)
Cox model HR: 1.01 (95% CI: 0.29 to 3.49)			
Stroke	**INV**	**CON**	**Estimated Difference (95% CI)**
Patients with events	45	38	
6-month cumulative event rate	0.5%	0.1%	0.4% (0.1% to 0.7%)
1-year cumulative event rate	0.7%	0.4%	0.4% (-0.0% to 0.8%)
2-year cumulative event rate	1.4%	0.7%	0.7% (0.1% to 1.2%)
3-year cumulative event rate	1.7%	1.2%	0.5% (-0.2% to 1.2%)
4-year cumulative event rate	1.8%	1.7%	0.1% (-0.7% to 1.0%)
5-year cumulative event rate	2.3%	2.4%	-0.1% (-1.3% to 1.0%)
Restricted mean event-free time	4.93 years	4.95 years	-6.9 days (-16.8 days to 3.1 days)
Primary Endpoint or Stroke	**INV**	**CON**	**Estimated Difference (95% CI)**
Patients with events	346	376	
6-month cumulative event rate	5.8%	3.5%	2.3% (1.1% to 3.4%)
1-year cumulative event rate	7.6%	5.7%	1.9% (0.6% to 3.3%)
2-year cumulative event rate	10.1%	9.9%	0.2% (-1.5% to 1.8%)
3-year cumulative event rate	12.5%	13.5%	-1.0% (-3.0% to 1.0%)
4-year cumulative event rate	14.4%	16.6%	-2.2% (-4.5% to 0.1%)
5-year cumulative event rate	17.7%	19.8%	-2.2% (-5.2% to 0.8%)
Restricted mean event-free time	4.45 years	4.44 years	4.3 days (-23.9 days to 32.5 days)
CV death, MI, or Stroke	**INV**	**CON**	**Estimated Difference (95% CI)**
Patients with events	306	342	
6-month cumulative event rate	5.3%	3.0%	2.3% (1.2% to 3.4%)
1-year cumulative event rate	6.9%	4.9%	2.0% (0.7% to 3.2%)

2-year cumulative event rate	9.0%	8.7%	0.2% (-1.3% to 1.8%)
3-year cumulative event rate	10.9%	11.9%	-1.0% (-2.9% to 0.8%)
4-year cumulative event rate	12.9%	15.2%	-2.3% (-4.5% to -0.1%)
5-year cumulative event rate	15.6%	18.3%	-2.8% (-5.6% to 0.1%)
Restricted mean event-free time	4.51 years	4.49 years	5.7 days (-21.1 days to 32.6 days)

[1]Defined as the per-person average time spent event-free over the time period between randomization and 5 years. This average is close to 5 years because most patients do not experience outcome events in that timeframe.
[2]Hazard ratio for invasive versus conservative according to the Cox proportional hazards model (pre-specified primary analysis). Adjusted for age, sex, estimated glomerular filtration rate, ejection fraction, and diabetes. Hazard ratios are reported for outcomes that appear to satisfy proportional hazards.
[3]Diagnosis of non-procedural MI was defined as Type 1, 2, 4b, or 4c myocardial infarction. See Definitions of Outcomes in Supplementary Methods.
INV denotes invasive strategy; CON denotes conservative strategy; CV denotes cardiovascular; MI denotes myocardial infarction; HR denotes hazard ratio; CI denotes confidence interval

Table S11. Outcomes by Treatment Group Using the Secondary Definition of MI

Primary Outcome Using Secondary MI Definition	**INV (N=2588)**	**CON (N=2591)**	**Estimated Difference (95% CI)**
Patients with events	446	369	
6-month cumulative event rate	10.2%	3.7%	6.5% (5.2% to 7.9%)
1-year cumulative event rate	11.9%	5.9%	6.0% (4.5% to 7.6%)
2-year cumulative event rate	14.1%	10.2%	3.9% (2.0% to 5.7%)
3-year cumulative event rate	16.2%	13.3%	2.9% (0.8% to 4.9%)
4-year cumulative event rate	18.3%	16.3%	2.0% (-0.4% to 4.3%)
5-year cumulative event rate	21.2%	19.0%	2.2% (-0.7% to 5.2%)
Restricted mean event-free time[1]	4.25 years	4.44 years	-68.7 days (-99.4 days to -38.0 days)
CV death or MI Using Secondary MI Definition	**INV**	**CON**	**Estimated Difference (95% CI)**
Patients with events	406	331	
6-month cumulative event rate	9.7%	3.2%	6.5% (5.2% to 7.9%)
1-year cumulative event rate	11.2%	5.0%	6.1% (4.6% to 7.6%)
2-year cumulative event rate	12.9%	8.9%	4.0% (2.3% to 5.7%)
3-year cumulative event rate	14.7%	11.7%	3.0% (1.1% to 5.0%)
4-year cumulative event rate	16.8%	14.7%	2.1% (-0.2% to 4.4%)
5-year cumulative event rate	19.1%	17.3%	1.9% (-0.9% to 4.7%)
Restricted mean event-free time	4.31 years	4.50 years	-69.9 days (-99.4 days to -40.4 days)
Myocardial Infarction Using Secondary MI Definition	**INV**	**CON**	**Estimated Difference (95% CI)**
Patients with events	343	250	
6-month cumulative event rate	9.3%	2.8%	6.5% (5.2% to 7.8%)
1-year cumulative event rate	10.3%	4.3%	6.0% (4.6% to 7.5%)
2-year cumulative event rate	11.5%	7.2%	4.3% (2.7% to 5.9%)
3-year cumulative event rate	12.9%	9.1%	3.7% (1.9% to 5.5%)
4-year cumulative event rate	14.2%	10.9%	3.2% (1.2% to 5.3%)
5-year cumulative event rate	15.4%	12.7%	2.7% (0.3% to 5.1%)
Restricted mean event-free time	4.40 years	4.61 years	-78.0 days (-105.7 days to -50.2 days)
Procedural MI Using Secondary MI Definition	**INV**	**CON**	**Estimated Difference (95% CI)**
Patients with events	211	44	
6-month cumulative event rate	7.7%	0.6%	7.2% (6.1% to 8.2%)
1-year cumulative event rate	8.0%	0.9%	7.1% (6.0% to 8.2%)
2-year cumulative event rate	8.0%	1.4%	6.6% (5.5% to 7.8%)
3-year cumulative event rate	8.1%	1.7%	6.4% (5.2% to 7.6%)
4-year cumulative event rate	8.2%	2.0%	6.2% (5.0% to 7.4%)
5-year cumulative event rate	8.4%	2.0%	6.4% (5.2% to 7.7%)
Restricted mean event-free time	4.60 years	4.93 years	-118.6 days (-138.8 days to -98.3 days)

Non-procedural MI[2] Using Secondary MI Definition	**INV**	**CON**	**Estimated Difference (95% CI)**
Patients with events	134	200	
6-month cumulative event rate	1.9%	2.4%	-0.5% (-1.3% to 0.3%)
1-year cumulative event rate	2.8%	3.5%	-0.7% (-1.6% to 0.3%)
2-year cumulative event rate	3.6%	5.6%	-2.0% (-3.1% to -0.8%)
3-year cumulative event rate	4.8%	7.3%	-2.5% (-3.9% to -1.1%)
4-year cumulative event rate	6.0%	8.9%	-2.8% (-4.5% to -1.1%)
5-year cumulative event rate	7.3%	10.2%	-2.9% (-5.0% to -0.8%)
Restricted mean event-free time	4.79 years	4.69 years	35.5 days (15.3 days to 55.8 days)
Primary Outcome or Stroke Using Secondary MI Definition	**INV**	**CON**	**Estimated Difference (95% CI)**
Patients with events	469	393	
6-month cumulative event rate	10.6%	3.8%	6.8% (5.4% to 8.2%)
1-year cumulative event rate	12.5%	6.2%	6.4% (4.8% to 7.9%)
2-year cumulative event rate	15.0%	10.6%	4.4% (2.5% to 6.2%)
3-year cumulative event rate	17.1%	14.1%	3.0% (0.9% to 5.1%)
4-year cumulative event rate	19.2%	17.4%	1.8% (-0.6% to 4.2%)
5-year cumulative event rate	22.3%	20.6%	1.7% (-1.4% to 4.7%)
Restricted mean event-free time	4.21 years	4.41 years	-70.9 days (-102.2 days to -39.5 days)
CV Death, MI, or Stroke Using Secondary MI Definition	**INV**	**CON**	**Estimated Difference (95% CI)**
Patients with events	431	359	
6-month cumulative event rate	10.1%	3.3%	6.8% (5.5% to 8.2%)
1-year cumulative event rate	11.7%	5.4%	6.4% (4.9% to 7.9%)
2-year cumulative event rate	13.9%	9.5%	4.4% (2.7% to 6.2%)
3-year cumulative event rate	15.7%	12.6%	3.1% (1.1% to 5.1%)
4-year cumulative event rate	17.7%	16.0%	1.7% (-0.6% to 4.1%)
5-year cumulative event rate	20.3%	19.1%	1.2% (-1.7% to 4.1%)
Restricted mean event-free time	4.27 years	4.46 years	-70.5 days (-100.7 days to -40.2 days)

[1]Defined as the per-person average time spent event-free over the time period between randomization and 5 years. This average is close to 5 years because most patients do not experience outcome events in that timeframe.
[2]Diagnosis of non-procedural MI was defined as Type 1, 2, 4b, or 4c myocardial infarction. See Definitions of Outcomes in Supplementary Methods.
INV denotes invasive strategy; CON denotes conservative strategy; CV denotes cardiovascular; MI denotes myocardial infarction; HR denotes hazard ratio; CI denotes confidence interval

Tables S12a-S12f. Bayesian Probability Tables

PRIMARY OUTCOME

S12a. Prior #1 (Primary analysis): Diffuse independent normal prior on regression coefficients

	Cumulative Incidence By Treatment Group (95% CrI)			Bayesian Probability of Difference (Δ) Between Cumulative Incidence Rates					
				Difference Favoring INV			Difference Favoring CON		
Years	INV	CON	Difference (Δ)	Pr(Δ<0%)	Pr(Δ< -1%)	Pr(Δ< -3%)	Pr(Δ> 0%)	Pr(Δ> 1%)	Pr(Δ> 3%)
1	7.0%	5.4%	1.5% (0.2% - 2.9%)	1.1%	<0.1%	<0.1%	98.9%	78.7%	1.5%
2	9.0%	9.5%	-0.5% (-2.1% - 1.1%)	71.9%	25.9%	0.1%	28.1%	3.5%	<0.1%
3	11.3%	12.7%	-1.4% (-3.3% - 0.5%)	92.2%	65.0%	4.5%	7.8%	0.7%	<0.1%
4	13.4%	15.4%	-2.1% (-4.3% - 0.1%)	96.7%	82.9%	20.6%	3.3%	0.3%	<0.1%
5	16.3%	18.3%	-2.0% (-4.9% - 0.9%)	91.4%	75.4%	24.5%	8.6%	2.0%	<0.1%

S12b. Prior #2: (Sensitivity analysis) Autoregressive normal AR(1) prior on regression coefficients

	Cumulative Incidence By Treatment Group (95% CrI)			Bayesian Probability of Difference (Δ) Between Cumulative Incidence Rates					
				Difference Favoring INV			Difference Favoring CON		
Years	INV	CON	Difference (Δ)	Pr(Δ<0%)	Pr(Δ< -1%)	Pr(Δ< -3%)	Pr(Δ> 0%)	Pr(Δ> 1%)	Pr(Δ> 3%)
1	6.9%	5.5%	1.4% (0.1% - 2.7%)	1.5%	<0.1%%	<0.1%%	98.5%	74.3%	0.9%
2	9.1%	9.4%	-0.4% (-1.9% - 1.2%)	67.4%	21.5%	0.1%	32.6%	4.4%	<0.1%%
3	11.3%	12.7%	-1.3% (-3.2% - 0.5%)	92.3%	64.0%	4.1%	7.7%	0.7%	<0.1%%
4	13.4%	15.4%	-2.0% (-4.2% - 0.1%)	96.9%	82.9%	19.2%	3.1%	0.3%	<0.1%%
5	16.3%	18.3%	-2.0% (-4.8% - 0.7%)	92.6%	76.8%	24.0%	7.4%	1.5%	<0.1%%

CrI = Credible interval

Δ = Difference in cumulative event rates

Δ< 0% denotes the hypothesis that the difference favors INV by any amount

Δ< -1% denotes the hypothesis that the difference favors INV by at least 1 percentage point

Δ< -3% denotes the hypothesis that the difference favors INV by at least 3 percentage points

Δ> 0% denotes the hypothesis that the difference favors CON by any amount

Δ> 1% denotes the hypothesis that the difference favors CON by at least 1 percentage point

Δ> 3% denotes the hypothesis that the difference favors CON by at least 3 percentage points

CV DEATH OR MI

S12c. Prior #1 (Primary analysis): Diffuse independent normal prior on regression coefficients

	Cumulative Incidence By Treatment Group (95% CrI)			Bayesian Probability of Difference (Δ) Between Cumulative Incidence Rates					
				Difference Favoring INV			Difference Favoring CON		
Years	INV	CON	Difference (Δ)	Pr(Δ<0%)	Pr(Δ< -1%)	Pr(Δ< -3%)	Pr(Δ> 0%)	Pr(Δ> 1%)	Pr(Δ> 3%)
1	6.2%	4.6%	1.6% (0.4% - 2.8%)	0.5%	<0.1%	<0.1%	99.5%	83.5%	1.3%
2	7.9%	8.2%	-0.3% (-1.8% - 1.2%)	66.3%	18.7%	<0.1%	33.7%	4.1%	<0.1%
3	9.7%	11.0%	-1.3% (-3.1% - 0.5%)	92.6%	63.2%	3.1%	7.4%	0.5%	<0.1%
4	11.8%	13.8%	-2.1% (-4.2% - 0.1%)	97.2%	83.7%	19.2%	2.8%	0.2%	<0.1%
5	14.2%	16.7%	-2.5% (-5.3% - 0.2%)	96.4%	86.0%	36.3%	3.6%	0.6%	<0.1%

S12d. Prior #2: (Sensitivity analysis) Autoregressive normal AR(1) prior on regression coefficients

	Cumulative Incidence By Treatment Group (95% CrI)			Bayesian Probability of Difference (Δ) Between Cumulative Incidence Rates					
				Difference Favoring INV			Difference Favoring CON		
Years	INV	CON	Difference (Δ)	Pr(Δ<0%)	Pr(Δ< -1%)	Pr(Δ< -3%)	Pr(Δ> 0%)	Pr(Δ> 1%)	Pr(Δ> 3%)
1	6.1%	4.6%	1.5% (0.3% - 2.7%)	0.8%	<0.1%%	<0.1%%	99.2%	78.7%	0.8%
2	7.9%	8.1%	-0.2% (-1.7% - 1.2%)	61.8%	15.5%	<0.1%%	38.2%	5.2%	<0.1%%
3	9.7%	11.0%	-1.3% (-3.0% - 0.5%)	92.2%	61.5%	2.5%	7.8%	0.6%	<0.1%%
4	11.8%	13.8%	-2.1% (-4.1% - 0.0%)	97.5%	84.4%	18.6%	2.5%	0.2%	<0.1%%
5	14.1%	16.7%	-2.6% (-5.2% - 0.0%)	97.4%	88.4%	38.3%	2.6%	0.4%	<0.1%%

CrI = Credible interval

Δ = Difference in cumulative event rates

Δ< 0% denotes the hypothesis that the difference favors INV by any amount

Δ< -1% denotes the hypothesis that the difference favors INV by at least 1 percentage point

Δ< -3% denotes the hypothesis that the difference favors INV by at least 3 percentage points

Δ> 0% denotes the hypothesis that the difference favors CON by any amount

Δ> 1% denotes the hypothesis that the difference favors CON by at least 1 percentage point

Δ> 3% denotes the hypothesis that the difference favors CON by at least 3 percentage points

ALL-CAUSE DEATH

S12e. Prior #1 (Primary analysis): Diffuse independent normal prior on regression coefficients

	Cumulative Incidence By Treatment Group (95% CrI)			Bayesian Probability of Difference (Δ) Between Cumulative Incidence Rates					
				Difference Favoring INV			Difference Favoring CON		
Years	INV	CON	Difference (Δ)	Pr(Δ<0%)	Pr(Δ< -1%)	Pr(Δ< -3%)	Pr(Δ> 0%)	Pr(Δ> 1%)	Pr(Δ> 3%)
1	1.7%	1.0%	0.7% (0.0% - 1.3%)	1.9%	<0.1%	<0.1%	98.1%	14.9%	<0.1%
2	2.8%	2.9%	-0.1% (-1.0% - 0.9%)	55.8%	2.5%	<0.1%	44.2%	1.3%	<0.1%
3	4.3%	4.3%	0.1% (-1.1% - 1.3%)	46.5%	4.3%	<0.1%	53.5%	6.0%	<0.1%
4	6.6%	6.4%	0.2% (-1.4% - 1.9%)	40.0%	7.5%	<0.1%	60.0%	17.7%	0.1%
5	8.9%	8.5%	0.5% (-1.8% - 2.8%)	34.9%	10.7%	0.2%	65.1%	32.1%	1.6%

S12f. Prior #2: (Sensitivity analysis) Autoregressive normal AR(1) prior on regression coefficients

	Cumulative Incidence By Treatment Group (95% CrI)			Bayesian Probability of Difference (Δ) Between Cumulative Incidence Rates					
				Difference Favoring INV			Difference Favoring CON		
Years	INV	CON	Difference (Δ)	Pr(Δ<0%)	Pr(Δ< -1%)	Pr(Δ< -3%)	Pr(Δ> 0%)	Pr(Δ> 1%)	Pr(Δ> 3%)
1	1.6%	1.1%	0.5% (-0.1% - 1.1%)	4.4%	<0.1%%	<0.1%%	95.6%	5.9%	<0.1%%
2	2.9%	2.9%	-0.0% (-0.9% - 0.9%)	51.7%	1.7%	<0.1%%	48.3%	1.3%	<0.1%%
3	4.3%	4.3%	-0.0% (-1.2% - 1.1%)	53.1%	5.4%	<0.1%%	46.9%	3.9%	<0.1%%
4	6.5%	6.4%	0.1% (-1.5% - 1.7%)	43.1%	8.0%	<0.1%%	56.9%	14.3%	<0.1%%
5	8.9%	8.5%	0.3% (-1.8% - 2.5%)	37.6%	11.3%	0.1%	62.4%	27.8%	0.9%

CrI = Credible interval

Δ = Difference in cumulative event rates

Δ< 0% denotes the hypothesis that the difference favors INV by any amount

Δ< -1% denotes the hypothesis that the difference favors INV by at least 1 percentage point

Δ< -3% denotes the hypothesis that the difference favors INV by at least 3 percentage points

Δ> 0% denotes the hypothesis that the difference favors CON by any amount

Δ> 1% denotes the hypothesis that the difference favors CON by at least 1 percentage point

Δ> 3% denotes the hypothesis that the difference favors CON by at least 3 percentage points