Overview of HBD Activity 2003-2019

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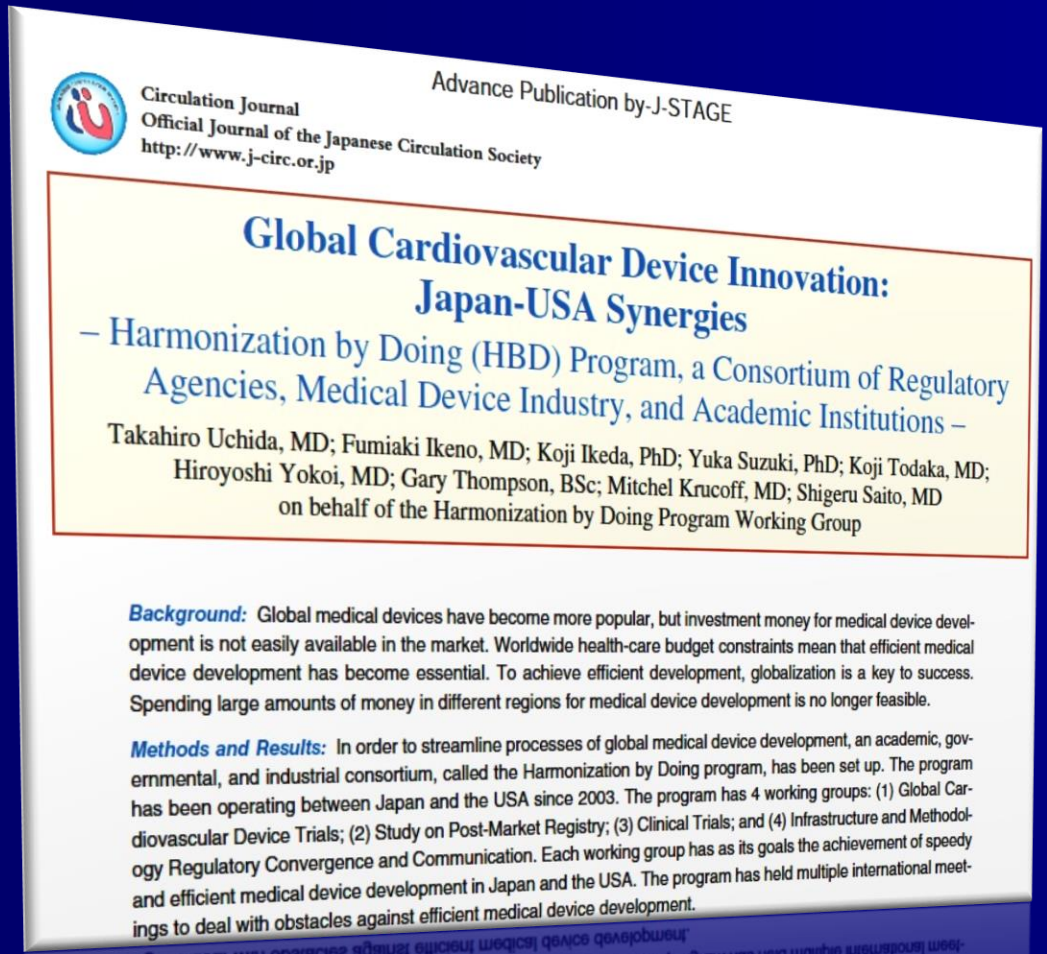


Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

Advance Publication by-J-STAGE

Global Cardiovascular Device Innovation: Japan-USA Synergies

– Harmonization by Doing (HBD) Program, a Consortium of Regulatory Agencies, Medical Device Industry, and Academic Institutions –

Takahiro Uchida, MD; Fumiaki Ikeno, MD; Koji Ikeda, PhD; Yuka Suzuki, PhD; Koji Todaka, MD; Hiroyoshi Yokoi, MD; Gary Thompson, BSc; Mitchel Krucoff, MD; Shigeru Saito, MD
on behalf of the Harmonization by Doing Program Working Group

Background: Global medical devices have become more popular, but investment money for medical device development is not easily available in the market. Worldwide health-care budget constraints mean that efficient medical device development has become essential. To achieve efficient development, globalization is a key to success. Spending large amounts of money in different regions for medical device development is no longer feasible.

Methods and Results: In order to streamline processes of global medical device development, an academic, governmental, and industrial consortium, called the Harmonization by Doing program, has been set up. The program has been operating between Japan and the USA since 2003. The program has 4 working groups: (1) Global Cardiovascular Device Trials; (2) Study on Post-Market Registry; (3) Clinical Trials; and (4) Infrastructure and Methodology Regulatory Convergence and Communication. Each working group has as its goals the achievement of speedy and efficient medical device development in Japan and the USA. The program has held multiple international meetings to deal with obstacles against efficient medical device development.

HBD

Program History

Uchida T et al, Circulation Journal 2013

September 2003
The Era of Global Regulatory Harmonization

TCT 2003: 15th Annual Transcatheter Cardiovascular Therapeutics

September 15 - 19, 2003; Washington, DC

David Feigal MD
Director, CDRH 1999-2004

The Maureen and Mike Mansfield Foundation

Promoting Understanding and Cooperation in U.S.-Asia Relations since 1983

Program Overview

The Mansfield Fellowship Program—named after Mike Mansfield, former U.S. Ambassador to Japan, Senate Majority Leader, U.S. Senator and U.S. Congressman from Montana—is a first-of-its-kind program for both the United States and Japan. The two-year Fellowships enable U.S. federal government employees to develop an in-depth understanding of Japan, learn how its government works, and establish relationships with their counterparts in the government of Japan as well as in the business, professional and academic communities.

DUKE UNIVERSITY MEDICAL CENTER

December 2003

FDA U.S. Food and Drug Administration

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

Department of Health and Human Services

FDA Home Page | CDRH Home Page | Search | A-Z Index

FDA > CDRH > International Issues > Japan - U.S. "Harmonization By Doing" HBD Pilot Program Initiative

Questions?

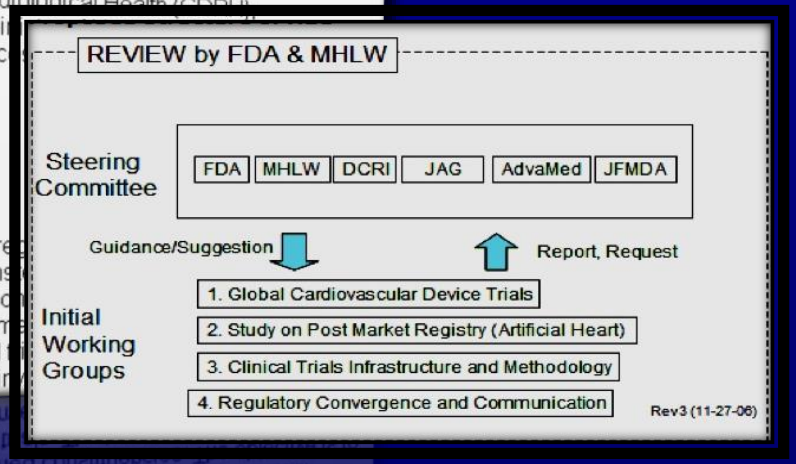
Japan - U.S. "Harmonization By Doing" HBD Pilot Program Initiative

"Harmonization by Doing," commonly known as HBD, is an international effort to develop global clinical trials and address regulatory barriers that may be impediments to timely device approvals. This process is a cooperative effort to move both Japan and the U.S. toward international regulatory harmonization. Participants in this process include:

- U.S. Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH)
- Japan 's Pharmaceutical and Food Safety Bureau (PFSB) of the Mi
(MHLW) and its review agency, the Pharmaceutical and Medical Devic
- Duke Clinical Research Institute (DCRI),
- Japanese academic community, and
- Japanese and U.S. medical device industry.

What is the HBD initiative?

The HBD initiative is a pilot project launched in December 2003 that seeks re
and MHLW-PMDA premarket review of device cardiovascular technology. Ins
to harmonization, HBD will utilize parallel development, application submissio
device projects by FDA and MHLW-PMDA in conjunction with the above-nam
eliminate redundancies, added costs, and time delays inherent in sequential
to create guidance and discuss policy but to develop common protocols for in



Pharmaceuticals and Medical Devices Agency, Japan

2003-2004: Japan MHLW launches PMDA

April 2004: PMDA Adopts Early Consultation

DUKE UNIVERSITY MEDICAL CENTER

HBD Foundational Principles

1) Balanced stakeholder leadership/participation
2) Pre-competitive collaboration, dialogue & trust
3) “Small steps to big changes”
4) Emphasis on “doing” (POC projects & deliverables)
5) Barrier elimination supporting global regulatory harmonization pathways

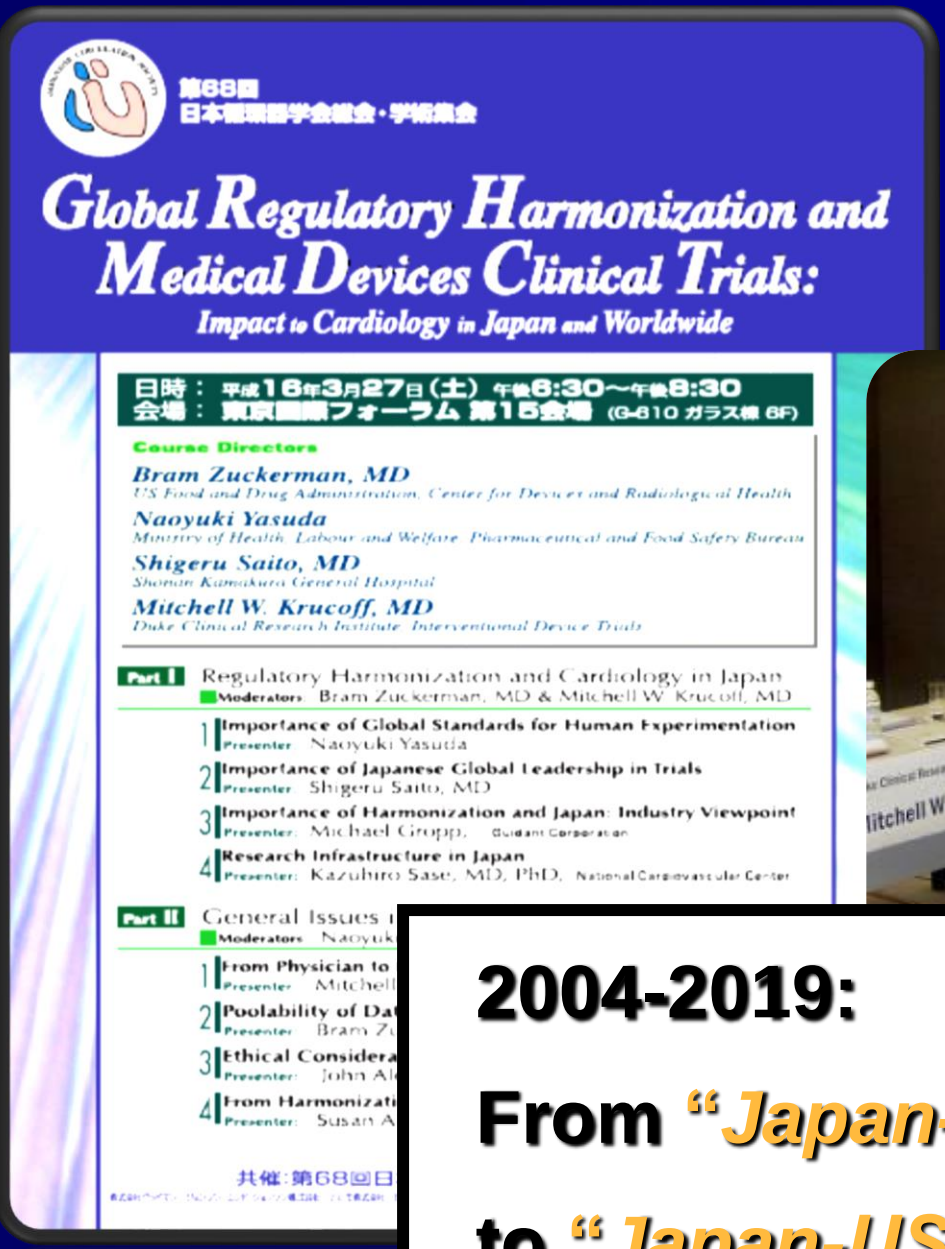
HBD

Proof Of Concept (POC) Projects

HBD POC's

Educational Programs & Thinktanks

Japan Circulatory Society
March 2004
Tokyo, Japan



2004-2019:

From “*Japan-USA Barriers*”

to “*Japan-USA Synergies*”

, CIT, PS, ned, CR

Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

December 2004: Kamakura Public Forum

Attention to the Patient's Perspective

Medical Technology Leadership Forum
Washington D.C.
April 2005

DUKE UNIVERSITY MEDICAL CENTER

CRI Duke Clinical Research Institute

October 2007

Tomiko Tawaragi

MHLW

HBD POC's

Harmonized Regulatory Processes

Regulatory Convergence:
Ethics, Methods and Science of Human Studies

Regulatory Focus, April 2010

Regulatory Focus, January 2013

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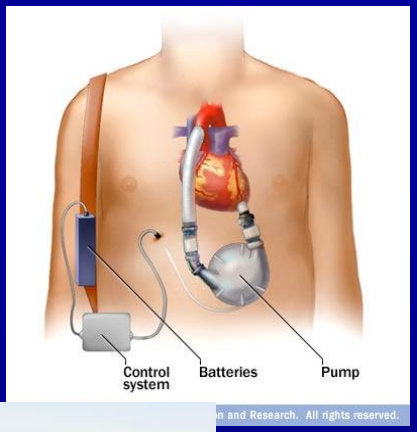
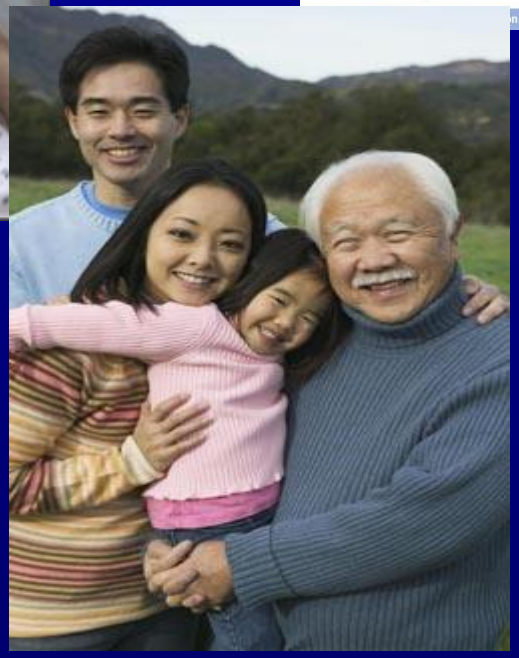
HBD POC's

Post-market Surveillance Registries

Linking Post-Market Surveillance: LVADS





JACC

JOURNAL of the AMERICAN COLLEGE of CARDIOLOGY

J Am Coll Cardiol, 2010; 56:738-740, doi:10.1016/j.jacc.2010.05.021
© 2010 by the American College of Cardiology Foundation

INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support): A New Paradigm for Translating Registry Data Into Clinical Practice

Marissa A. Miller, Karen Ulisney, and J. Timothy Baldwin

JMACS

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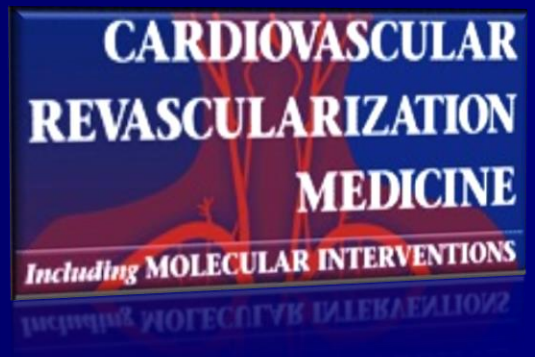
HBD POC's

Global Clinical Trials

2005: Endeavor Japan (Medtronic)



The clinical evaluation of the Endeavor zotarolimus-eluting coronary stent in Japanese patients with de novo native coronary artery lesions: primary results and 3-year follow-up of the Endeavor Japan study☆☆☆

Shigeru Saito ✉, Ross Prpic, Jeffery J. Popma, John Alexander, Mitchell W. Krucoff, on behalf of the ENDEAVOR Japan Investigators

Cardiovascular Revascularization Medicine
Volume 12, Issue 5, Pages 273–279, September–October, 2011

- Identical inclusion/exclusion
- Identical endpoints
- Identical core laboratories
- Enhanced poolability
- Enhanced interpretability

2007: SPIRIT III Japan (Abbott Vascular): *Enhanced poolability & interpretability*

JIC JOURNAL OF INVASIVE CARDIOLOGY

Mid-Term Results of Everolimus-Eluting Stent in a Japanese Population Compared With a US Randomized Cohort: SPIRIT III Japan Registry With Harmonization by Doing

Wednesday, 08/29/12 | 9993 reads

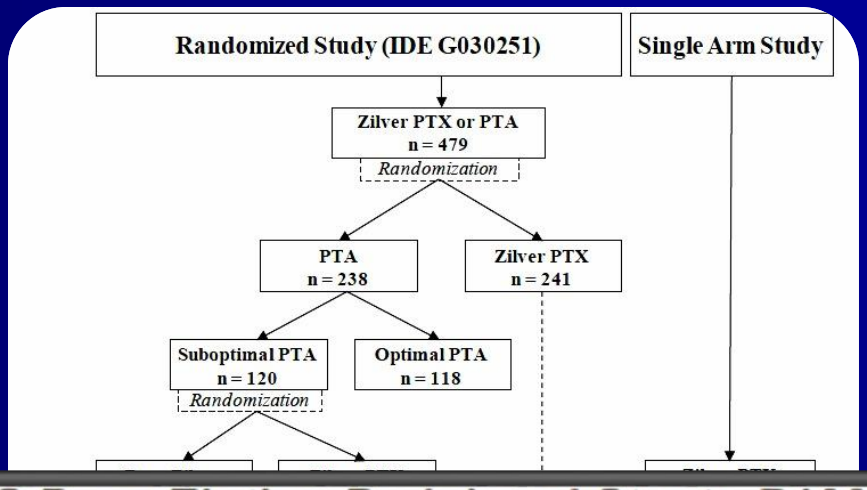
Author(s):

Shigeru Saito, MD[1], Shigeru Nakamura, MD[2], Kenshi Fujii, MD[3], Masato Nakamura, MD[4], Takaaki Isshiki, MD[5], Haruo Hirayama, MD[6], Tadashi Kikuchi, MD, PhD[7], Hiroshi Fujita, MD[8], Hiroshi Nonogi, MD, PhD[9], Kazuaki Mitsudo, MD[10], Takeshi Kimura, MD[11], Keiichi Igarashi, MD[12], Kumiko Saito, MS, MPH[13], Alexandra J. Lansky, MD[14], Gregg W. Stone, MD[14], Yasuhiro Honda, MD[15], Katsuhisa Waseda, MD, PhD[16], Peter J. Fitzgerald, MD, PhD[15], Krishnankutty Sudhir, MD, PhD[16]

Issue Number:
Volume 24 - Issue 9 - September 2012

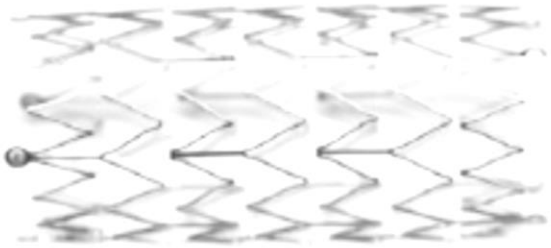
- *Concomitant enrollment*
- Identical inclusion/exclusion
- Identical endpoints
- Identical core laboratories

2009: Zilver PTX (Cook Medical)
Single protocol global RCT



Zilver® PTX® Drug-Eluting Peripheral Stent - P100022

This is a brief overview of information related to FDA's approval to market this product. See the links below to the Summary of Safety and Effectiveness Data (SSED) and product labeling for more complete information on this product, its indications for use, and the basis for FDA's approval.



Product Name: Zilver® PTX Drug-Eluting Peripheral Stent
PMA Applicant: Cook, Inc.
Address: 750 Daniels Way, P.O. Box 489, Bloomington, IN 47402-0489
Approval Date: November 14, 2012
Approval Letter: http://www.accessdata.fda.gov/cdrh_docs/pdf10/p100022a.pdf

HARMONEE Study: Coronary DES Japan-USA RCT

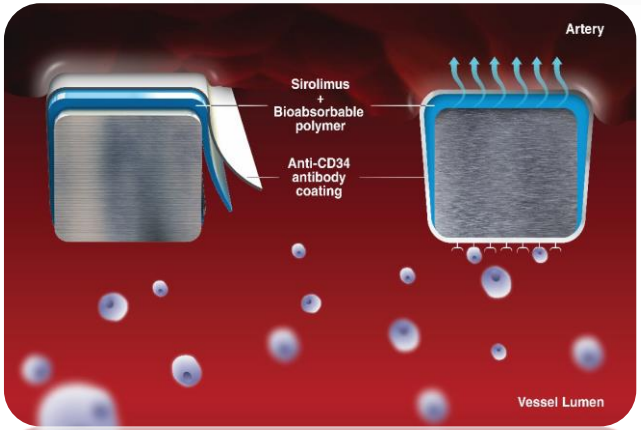
ESC European Society of Cardiology
European Heart Journal (2018) 0, 1–9 doi:10.1093/eurheartj/ehy275
CLINICAL RESEARCH
Interventional cardiology

Japan-United States of America Harmonized Assessment by Randomized Multicentre Study of OrbusNEich's Combo StEnt (Japan-USA HARMONEE) study: primary results of the pivotal registration study of combined endothelial progenitor cell capture and drug-eluting stent in patients with ischaemic coronary disease and non-ST-elevation acute coronary syndrome

Shigeru Saito[1], Mitchell W. Krucoff[2]*, Shigeru Nakamura[3], Roxana Mehran[4], Akiko Maehara[5], Hussein R. Al-Khalidi[2], Stephen M. Rowland[6], Gudaye Tasissa[2], Debbie Morrell[6], Diane Joseph[2], Yumiko Okaniwa[7], Yoshisato Shibata[8], Barry D. Bertolet[9], Mark D. Rothenberg[10], Philippe Généreux[11], Hiram Bezerra[12], and David F. Kong[2]

Rationale and design of the Japan-USA harmonized assessment by randomized, multicenter study of OrbusNEich's combo StEnt (Japan-USA HARMONEE): Assessment of a novel DES platform for percutaneous coronary revascularization in patients with ischemic coronary disease and non–ST-elevation acute coronary syndrome

David F. Kong, MD, Shigeru Saito, MD, Shigeru Nakamura, MD, Roxana Mehran, MD, Stephen M. Rowland, PhD, Allison Handler, MHSc, Hussein R. Al-Khalidi, PhD, and Mitchell W. Krucoff, MD *Durham, NC; Kamakura, Sapporo, Kyoto, Japan; New York, NY; and Fort Lauderdale, FL*

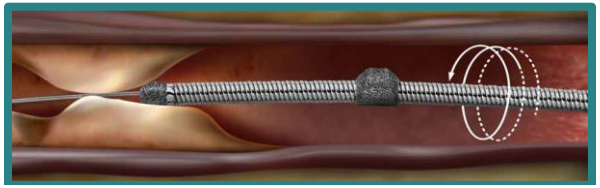


The COMBO Plus Dual Therapy Stent

Kong DF et al Am Heart J 2017;187:112-121

Saito S, Krucoff MW et al. European Heart Journal (2018) 0, 1–9 doi:10.1093/eurheartj/ehy275

COAST Study (CSI)



Diamondback 360® Coronary OAS Micro Crown

- To evaluate the performance of the Coronary OAS Micro Crown in treating *de novo*, severely calcified coronary lesions
  - Prospective, single-arm, multi-center Investigational Device Exemption (IDE) study conducted in Japan and the USA
  - Harmonization by Doing (regulatory collaboration between Japan and the USA)

100 patients enrolled

USA	74 patients 12 sites
Japan	26 patients 5 sites

1-year follow-up completed* (93/100)

*6 subjects died and 1 subject lost to follow-up

HBD POC's

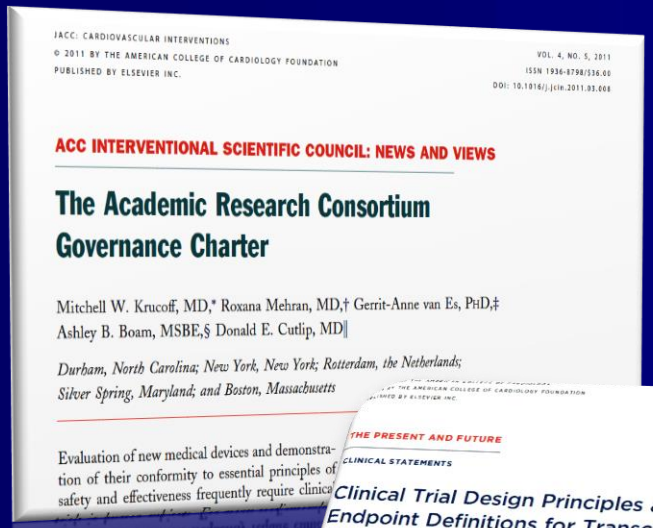
Present Into Future Directions

HBD

"Harmonization By Data":

- *Consensus definitions*
- *Minimum core data sets*
- *Data quality*
- *Data structure & interoperability*

The Academic Research Consortium (ARC):
Pragmatic consensus definitions for device evaluation


JACC: CARDIOVASCULAR INTERVENTIONS
© 2011 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER INC.
VOL. 4, NO. 5, 2011
ISSN 1936-8798/$36.00
DOI: 10.1016/j.jcin.2011.03.008

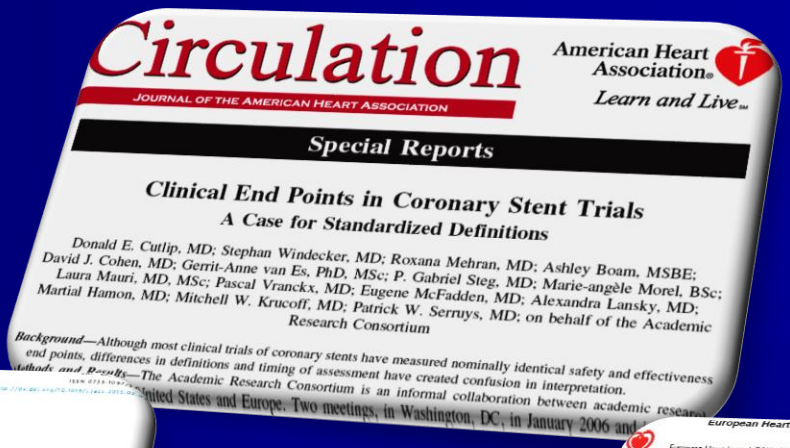
ACC INTERVENTIONAL SCIENTIFIC COUNCIL: NEWS AND VIEWS

The Academic Research Consortium Governance Charter

Mitchell W. Krucoff, MD,* Roxana Mehran, MD,† Gerrit-Anne van Es, PhD,‡ Ashley B. Boam, MSBE,§ Donald E. Cutlip, MD‖

Durham, North Carolina; New York, New York; Rotterdam, the Netherlands; Silver Spring, Maryland; and Boston, Massachusetts

Evaluation of new medical devices and demonstration of their conformity to essential principles of safety and effectiveness frequently require clinica


Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
American Heart Association
Learn and Live

Special Reports

Clinical End Points in Coronary Stent Trials
A Case for Standardized Definitions

Donald E. Cutlip, MD; Stephan Windecker, MD; Roxana Mehran, MD; Ashley Boam, MSBE; David J. Cohen, MD; Gerrit-Anne van Es, PhD, MSc; P. Gabriel Steg, MD; Marie-angèle Morel, BSc; Laura Mauri, MD, MSc; Pascal Vranckx, MD; Eugene McFadden, MD; Alexandra Lansky, MD; Martial Hamon, MD; Mitchell W. Krucoff, MD; Patrick W. Serruys, MD; on behalf of the Academic Research Consortium

Background—Although most clinical trials of coronary stents have measured nominally identical safety and effectiveness end points, differences in definitions and timing of assessment have created confusion in interpretation.
Methods and Results—The Academic Research Consortium is an informal collaboration between academic research
United States and Europe. Two meetings, in Washington, DC, in January 2006 and

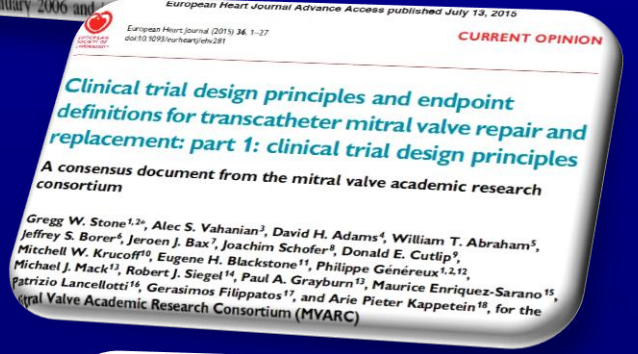

THE PRESENT AND FUTURE
CLINICAL STATEMENTS

Clinical Trial Design Principles and Endpoint Definitions for Transcatheter Mitral Valve Repair and Replacement: Part 1: Clinical Trial Design Principles

A Consensus Document From the Mitral Valve Academic Research Consortium

Gregg W. Stone, MD,*† Alec S. Vahanian, MD,‡ David H. Adams, MD,§ William T. Abraham, MD,‖ Jeffrey S. Borer, MD,¶ Jeroen J. Bax, MD, PhD,# Joachim Schofer, MD,** Donald E. Cutlip, MD,†† Mitchell W. Krucoff, MD,‡‡ Eugene H. Blackstone, MD,§§ Philippe Généreux, MD,*‖‖ Paul A. Grayburn, MD,¶¶ Maurice Enriquez-Sarano, MD,*** Michael J. Mack, MD,††† Patrizio Lancellotti, MD, PhD,‡‡‡ Gerasimos Filippatos, MD,§§§ Arie Pieter Kappetein, MD, PhD,‖‖‖ for the Mitral Valve Academic Research Consortium (MVARC)

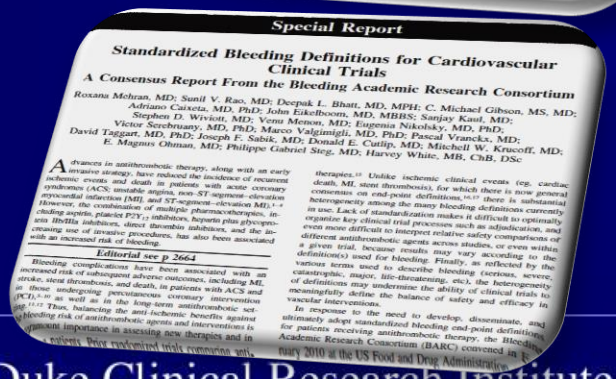
- Coronary
- Bleeding
- Aortic valve
- Mitral valve
- Neurologic


European Heart Journal Advance Access published July 13, 2015
European Heart Journal (2015) 36, 1–27
doi:10.1093/eurheartj/ehv281
CURRENT OPINION

Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: part 1: clinical trial design principles

A consensus document from the mitral valve academic research consortium

Gregg W. Stone[1,2*], Alec S. Vahanian[3], David H. Adams[4], William T. Abraham[5], Jeffrey S. Borer[6], Jeroen J. Bax[7], Joachim Schofer[8], Donald E. Cutlip[9], Mitchell W. Krucoff[10], Eugene H. Blackstone[11], Philippe Généreux[1,2,12], Michael J. Mack[13], Robert J. Siegel[14], Paul A. Grayburn[13], Maurice Enriquez-Sarano[15], Patrizio Lancellotti[16], Gerasimos Filippatos[17], and Arie Pieter Kappetein[18], for the Mitral Valve Academic Research Consortium (MVARC)


Special Report

Standardized Bleeding Definitions for Cardiovascular Clinical Trials

A Consensus Report From the Bleeding Academic Research Consortium

Roxana Mehran, MD; Sunil V. Rao, MD; Deepak L. Bhatt, MD, MPH; C. Michael Gibson, MS, MD; Adriano Caixeta, MD, PhD; John Eikelboom, MD, MBBS; Sanjay Kaul, MD; Stephen D. Wiviott, MD; Yeni Menon, MD; Eugenia Nikolsky, MD, PhD; Victor Sorrentuney, MD, PhD; Marco Valgimigli, MD, PhD; Pascal Vranckx, MD; David Taggart, MD, PhD; Joseph F. Sabik, MD; Donald E. Cutlip, MD; Mitchell W. Krucoff, MD; E. Magnus Ohman, MD; Philippe Gabriel Steg, MD; Harvey White, MB, ChB, DSc

Advances in antithrombotic therapy, along with an early invasive strategy, have reduced the incidence of recurrent ischemic events and death in patients with acute coronary syndromes (ACS; unstable angina, non–ST-segment–elevation myocardial infarction [MI], and ST-segment–elevation MI).[1–4] However, the combination of multiple pharmacotherapies, including aspirin, platelet $P2Y_{12}$ inhibitors, heparin plus glycoprotein IIb/IIIa inhibitors, direct thrombin inhibitors, and the increasing use of invasive procedures, has also been associated with an increased risk of bleeding.

Editorial see p 2664

Bleeding complications have been associated with an increased risk of subsequent adverse outcomes, including MI, stroke, stent thrombosis, and death, in patients with ACS and in those undergoing percutaneous coronary intervention (PCI).[5–10] as well as in the long-term antithrombotic setting.[11,12] Thus, balancing the anti-ischemic benefits against the bleeding risk of antithrombotic agents and interventions is of paramount importance in assessing new therapies and in patients. Prior randomized trials comparing anti-

therapies.[13] Unlike ischemic clinical events (eg, cardiac death, MI, stent thrombosis), for which there is now general consensus on end-point definitions,[14–17] there is substantial heterogeneity among the many bleeding definitions currently in use. Lack of standardization makes it difficult to optimally organize key clinical trial processes such as adjudication, and even more difficult to interpret relative safety comparisons of different antithrombotic agents across studies, or even within a given trial, because results may vary according to the definition(s) used for bleeding. Finally, as reflected by the various terms used to describe bleeding (serious, severe, catastrophic, major, life-threatening, etc), the heterogeneity of definitions may undermine the ability of clinical trials to meaningfully define the balance of safety and efficacy in vascular interventions.

In response to the need to develop, disseminate, and ultimately adopt standardized bleeding end-point definitions for patients receiving antithrombotic therapy, the Bleeding Academic Research Consortium (BARC) convened in February 2010 at the US Food and Drug Administration


European Heart Journal (2011) 32, 205–217
doi:10.1093/eurheartj/ehq406
CLINICAL RESEARCH
Valvular medicine

Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium†

Martin B. Leon*, Nicolo Piazza, Eugenia Nikolsky, Eugene H. Blackstone, Donald E. Cutlip, Arie Pieter Kappetein, Mitchell W. Krucoff, Michael Mack, Roxana Mehran, Craig Miller, Marie-angèle Morel, John Petersen, Jeffrey J. Popma, Johanna J.M. Takkenberg, Alec Vahanian, Gerrit-Anne van Es, Pascal Vranckx, John G. Webb, Stephan Windecker, and Patrick W. Serruys

Columbia University Medical Center, Center for Interventional Vascular Therapy, 173 Fort Washington Avenue, Heart Center, 3rd floor, New York, NY 10032, USA.
Received 30 July 2010; revised 30 September 2010; accepted 6 October 2010

Peripheral ARC (PARC)

THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

Evaluation and Treatment of Patients With Lower Extremity Peripheral Artery Disease

Consensus Definitions From Peripheral Academic Research Consortium (PARC)

Manesh R. Patel, MD,* Michael S. Conte, MD,† Donald E. Cutlip, MD,‡§ Nabil Dib, MD,‖ Patrick Geraghty, MD,¶ William Gray, MD,#** William R. Hiatt, MD,†† Mami Ho, MD, PhD,‡‡ Koji Ikeda, PhD,§§ Fumiaki Ikeno, MD,‖‖ Michael R. Jaff, DO,¶¶ W. Schuyler Jones, MD,* Masayuki Kawahara, MD,‡ Robert A. Lookstein, MD,## Roxana Mehran, MD,# ## Sanjay Misra, MD,*** Lars Norgren, MD,††† Jeffrey W. Olin, MD,## Thomas J. Povsic, MD, PhD,* Kenneth Rosenfield, MD,‡‡‡ John Rundback, MD,§§§ Fadi Shamoun, MD,‖‖‖ James Tcheng, MD,* Thomas T. Tsai, MD,¶¶¶ Yuka Suzuki, PhD,### Pascal Vranckx, MD,**** Bret N. Wiechmann, MD,†††† Christopher J. White, MD,‡‡‡‡ Hiroyoshi Yokoi, MD,§§§§ Mitchell W. Krucoff, MD*

ABSTRACT

The lack of consistent definitions and nomenclature across clinical trials of novel devices, drugs, or biologics poses a significant barrier to accrual of knowledge in and across peripheral artery disease therapies and technologies. Recognizing this problem, the Peripheral Academic Research Consortium, together with the U.S. Food and Drug Administration

Patel MR et al, JACC 2015: 65:931-41

Circulation

WHITE PAPER

Defining High Bleeding Risk in Patients Undergoing Percutaneous Coronary Intervention

A Consensus Document From the Academic Research Consortium for High Bleeding Risk

ABSTRACT: Identification and management of patients at risk undergoing percutaneous coronary intervention are o importance, but a lack of standardization in defining this limits trial design, data interpretation, and clinical decision The Academic Research Consortium for High Bleeding Ris is a collaboration among leading research organizations, r authorities, and physician-scientists from the United State Europe focusing on percutaneous coronary intervention–r Two meetings of the 31-member consortium were held in DC, in April 2018 and in Paris, France, in October 2018. T were organized by the Cardiovascular European Research behalf of the ARC-HBR group and included representative Food and Drug Administration and the Japanese Pharmac Medical Devices Agency, as well as observers from the pha and medical device industries. A consensus definition of p bleeding risk was developed that was based on review of evidence. The definition is intended to provide consistency population for clinical trials and to complement clinical de and regulatory review. The proposed ARC-HBR consensus represents the first pragmatic approach to a consistent de high bleeding risk in clinical trials evaluating the safety an of devices and drug regimens for patients undergoing per coronary intervention.

ESC European Society of Cardiology

European Heart Journal (2019) **0**, 1–22
doi:10.1093/eurheartj/ehz372

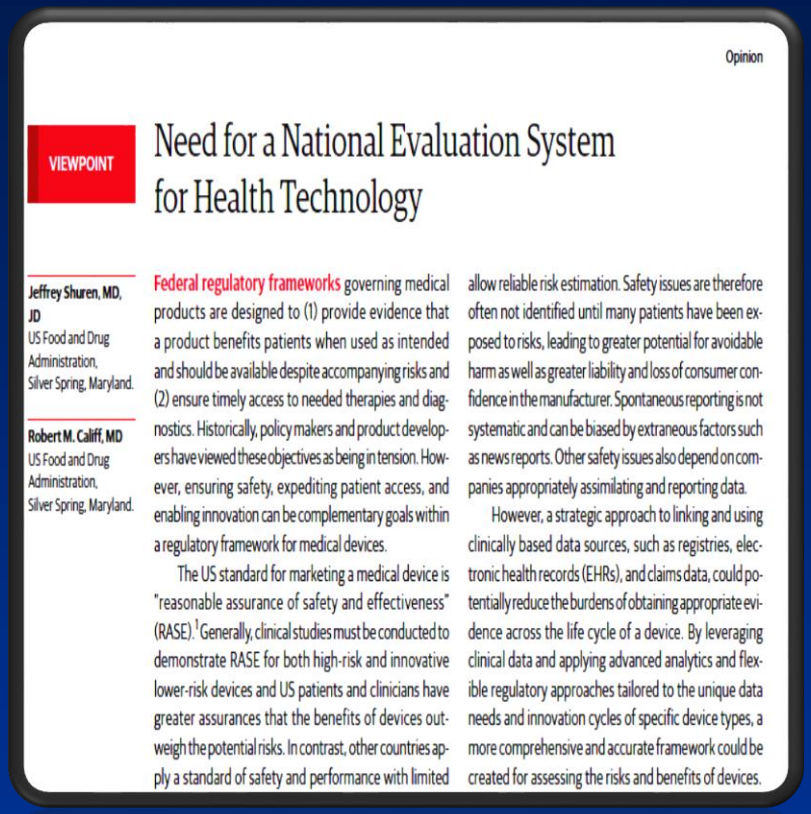
CURRENT OPINION

Defining high bleeding risk in patients undergoing percutaneous coronary intervention: a consensus document from the Academic Research Consortium for High Bleeding Risk

Philip Urban[1,2]*, Roxana Mehran[3], Roisin Colleran[4], Dominick J. Angiolillo[5], Robert A. Byrne[4], Davide Capodanno[6,7], Thomas Cuisset[8], Donald Cutlip[9], Pedro Eerdmans[10], John Eikelboom[11], Andrew Farb[12], C. Michael Gibson[13,14], John Gregson[15], Michael Haude[16], Stefan K. James[17], Hyo-Soo Kim[18], Takeshi Kimura[19], Akihide Kohishi[20], John Laschinger[12], Martin B. Leon[21,22], P.F. Adrian Magee[12], Yoshiaki Mitsutake[20], Darren Mylotte[23], Stuart Pocock[15], Matthew J. Price[24], Sunil V. Rao[25], Ernest Spitzer[26,27], Norman Stockbridge[12], Marco Valgimigli[28], Olivier Varenne[29,30], Ute Windhoevel[2], Robert W. Yeh[31], Mitchell W. Krucoff[25,32], Marie-Claude Morice[2]

PCR By and For you PCRonline.com

Real World Evidence:
Data Structure, Quality & Capture
Coordinated Registry Networks (CRNs) & NEST



Opinion

VIEWPOINT

Need for a National Evaluation System for Health Technology

Jeffrey Shuren, MD, JD
US Food and Drug Administration, Silver Spring, Maryland.

Robert M. Califf, MD
US Food and Drug Administration, Silver Spring, Maryland.

Federal regulatory frameworks governing medical products are designed to (1) provide evidence that a product benefits patients when used as intended and should be available despite accompanying risks and (2) ensure timely access to needed therapies and diagnostics. Historically, policy makers and product developers have viewed these objectives as being in tension. However, ensuring safety, expediting patient access, and enabling innovation can be complementary goals within a regulatory framework for medical devices.

The US standard for marketing a medical device is "reasonable assurance of safety and effectiveness" (RASE).[1] Generally, clinical studies must be conducted to demonstrate RASE for both high-risk and innovative lower-risk devices and US patients and clinicians have greater assurances that the benefits of devices outweigh the potential risks. In contrast, other countries apply a standard of safety and performance with limited allow reliable risk estimation. Safety issues are therefore often not identified until many patients have been exposed to risks, leading to greater potential for avoidable harm as well as greater liability and loss of consumer confidence in the manufacturer. Spontaneous reporting is not systematic and can be biased by extraneous factors such as news reports. Other safety issues also depend on companies appropriately assimilating and reporting data.

However, a strategic approach to linking and using clinically based data sources, such as registries, electronic health records (EHRs), and claims data, could potentially reduce the burdens of obtaining appropriate evidence across the life cycle of a device. By leveraging clinical data and applying advanced analytics and flexible regulatory approaches tailored to the unique data needs and innovation cycles of specific device types, a more comprehensive and accurate framework could be created for assessing the risks and benefits of devices.

JAMA Published online July 11, 2016

VIEWPOINT

Bridging Unmet Medical Device Ecosystem Needs With Strategically Coordinated Registries Networks

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MDEpiNet Science and Infrastructure Center, Weill Cornell Medical College, New York, New York.

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Harvard T. H. Chan School of Public Health, Boston, Massachusetts; and MDEpiNet Methodology Center, Harvard Medical School, Boston, Massachusetts.

In June 2014, the Medical Device Epidemiology Network (MDEpiNet) Public Private Partnership,[1] on behalf of the US Food and Drug Administration Center for Devices and Radiologic Health (CDRH), convened the Medical Device Registries Task Force (MDRTF) (see eAppendix in the Supplement). The task force was launched to address the CDRH's commitments[2,3] to strengthen the medical device postmarket surveillance system using existing resources and under current authorities and to develop an integrated system that efficiently and effectively achieves its basic functions, from timely identification of postmarket signals to facilitating premarket device clearance and approval.

The MDRTF included broad stakeholder representation and was mandated to examine the objectives and logistics of leveraging existing electronic registries and information repositories in support of a national system. This work was done in parallel with efforts at the Engelberg Center at the Brookings Institution, which in 2015 reported recommendations from their planning board for a "national medical device surveillance system." These recommendations depicted a system that "supports optimal patient care by leveraging the experiences of patients to inform decisions about medical device safety

The MDRTF recognized that most existing registries, electronic health records (EHRs), and data sources do not contain all the elements necessary for device evaluations, including device and procedural details, patient descriptors, or long-term outcomes. However, the MDRTF recognized that such limitations could be mitigated through interoperability solutions that strategically link complementary registries and data sources to produce networks for which the data composite could support robust device evaluation. The MDRTF termed this structure the strategically *coordinated registries network*, or CRN—with the recognition that many key elements in such networks (such as EHRs, administrative claims data, or mobile device outputs) are not registries per se. The MDRTF recommends strategic CRNs as the foundational architectural construct for the national system that will augment national registry development and unique device identifier implementation rather than replace them.

The proposed CRN structure could provide novel, important attributes to the national system. Creation of CRNs could encourage efficient "dual-purpose" leveraging of existing registries, EHRs, administrative data resources, and lessons learned from existing linked-registry models such as the Transcatheter Value Therapy[6] registry administra-

Krucoff MW, Normand SL et al, JAMA 2015

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NEST
National Evaluation System for health Technology
Coordinating Center

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National Evaluation System for health Technology Coordinating Center (NESTcc) Selects Medical Device Real-World Evidence Demonstration Projects

February 2, 2018

Projects support NESTcc's mission to establish fu

Arlington, VA – (January 29, 2018) – The **National Eva**
selected eleven **demonstration projects** for their pote
real-world evidence (RWE) generation across the medic
explores diverse aspects of evidence generation metho
healthcare systems, device types, and manufacturers.

Projects mainly focused on Pre-Market requirements:

- Lung-RADS Assist: Artificial Intelligence Model Verification, Reporting, and Monitoring
- Registry Assessment of Peripheral Interventional Devices (RAPID) - Superficial femoral and Popliteal Evidence Development (SPEED) as first device evaluation project
- SAFE STEMI for Seniors: An International CRN-based Prospective Randomized IDE Study of Labelling for Diagnostic and Therapeutic Devices Used in Seniors Suffering Heart Attack

Projects mainly focused on Post-Market requirements (including Post-Approval Studies):

- Developing and Implementing Sustainable Real-World Evidence Infrastructure for in vitro Diagnostics (IVDs) Through Systemic Harmonization and Interoperability for Enhancement of Laboratory Data (SHIELD)
- Electrophysiology Predictable and Sustainable Implementation of National Registries (EP PASSION)
- Feasibility Study to Evaluate the use of mHealth as Data Source in Post-Market Surveillance
- Post-Market Medical Device Surveillance with a Novel mHealth Platform
- Use of EHR-Based Data Network to Support Evidence Generation Across the Total Product Life Cycle (TPLC)
- Use of linked implantable device/Medicare data to assess association between device diagnostics and patient outcomes

Projects mainly focused on Surveillance:

- ICD Registry DELTA Active Surveillance Pilot Study
- Vascular Implant Surveillance and Interventional Outcomes Network (VISION)

https://nestcc.org/demo-announcement/

Registry Assessment of Peripheral Interventional Devices (*RAPID*): *Core Minimum Data Set* for Device Evaluation

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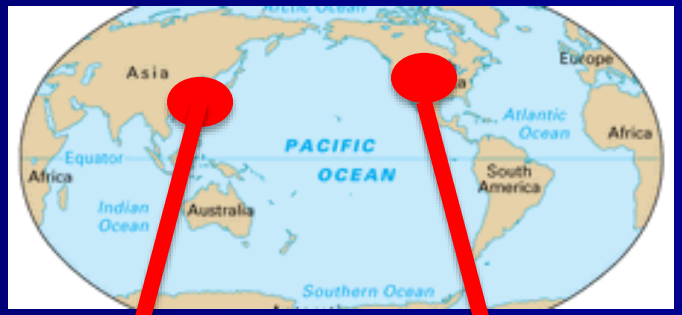
Robert Thatcher
CEO 4C Medical

Mitchell W. Krucoff, M.D.
Duke University Medical Center/Duke Clinical Research Institute

RAPID Minimum Core Elements for PAD Devices:
Trans-Pacific Co-publication



Circ J 2018; 82: 316–322
doi:10.1253/circj.CJ-17-1156

REVIEW

Registry Assessment of Peripheral Interventional Devices (RAPID)

— Registry Assessment of Peripheral Interventional Devices Core Data Elements —

W. Schuyler Jones, MD; Mitchell W. Krucoff, MD; Pablo Morales, MD; Rebecca W. Wilgus, RN, MSN; Anne H. Heath, BA; Mary F. Williams, BS; James E. Tcheng, MD; J. Danica Marinac-Dabic, MD, PhD; Misti L. Malone, PhD; Terrie L. Reed, MS; Rie Fukaya, MMedSc; Robert Lookstein, MD; Nobuhiro Handa, MD; Herbert D. Aronow, MD, MPH; Daniel J. Bertges, MD; Michael R. Jaff, DO; Thomas T. Tsai, MD, MSc; Joshua A. Smale, BS; Margo J. Zaugg, BSN; Robert J. Thatcher, MBA; Jack L. Cronenwett, MD; Durham, NC; Silver Spring, Md; Tokyo, Japan; New York, NY; Providence, RI; Burlington, Vt; Newton, Mass; Denver, Colo; Tempe, Ariz; Santa Clara, Calif; Minneapolis, Minn; Lebanon, NH

Background: The current state of evaluating patients with peripheral artery disease and more specifically of evaluating medical devices used for peripheral vascular intervention (PVI) remains challenging because of the heterogeneity of the disease process, the multiple physician specialties that perform PVI, the multitude of devices available to treat peripheral artery disease, and the lack of consensus about the best treatment approaches. Because PVI core data elements are not standardized across clinical care, clinical trials, and registries, aggregation of data across different data sources and physician specialties is currently not feasible.

Jones WS, Krucoff MW et al, Circ J 2018: 82:316-22

SPECIAL COMMUNICATIONS

Registry Assessment of Peripheral Interventional Devices (RAPID): Registry assessment of peripheral interventional devices core data elements

W. Schuyler Jones, MD,[a] Mitchell W. Krucoff, MD,[a] Pablo Morales, MD,[b] Rebecca W. Wilgus, RN, MSN,[a] Anne H. Heath, BA,[a] Mary F. Williams, BS,[a] James E. Tcheng, MD,[a] J. Danica Marinac-Dabic, MD, PhD,[b] Misti L. Malone, PhD,[b] Terrie L. Reed, MS,[b] Rie Fukaya, MMedSc,[c] Robert A. Lookstein, MD,[d] Nobuhiro Handa, MD,[c] Herbert D. Aronow, MD, MPH,[e] Daniel J. Bertges, MD,[f] Michael R. Jaff, DO,[g] Thomas T. Tsai, MD, MSc,[h] Joshua A. Smale, BS,[i] Margo J. Zaugg, BSN,[j] Robert J. Thatcher, MBA,[k] and Jack L. Cronenwett, MD,[l] *Durham, NC; Silver Spring, Md; Tokyo, Japan; New York, NY; Providence, RI; Burlington, Vt; Newton, Mass; Denver, Colo; Tempe, Ariz; Santa Clara, Calif; Minneapolis, Minn; and Lebanon, NH*

ABSTRACT

Objective: The current state of evaluating patients with peripheral artery disease and more specifically of evaluating medical devices used for peripheral vascular intervention (PVI) remains challenging because of the heterogeneity of the disease process, the multiple physician specialties that perform PVI, the multitude of devices available to treat peripheral artery disease, and the lack of consensus about the best treatment approaches. Because PVI core data elements are not standardized across clinical care, clinical trials, and registries, aggregation of data across different data sources and physician specialties is currently not feasible.

Jones WS, Krucoff MW et al, J Vasc Surg 2018: 67:637-45

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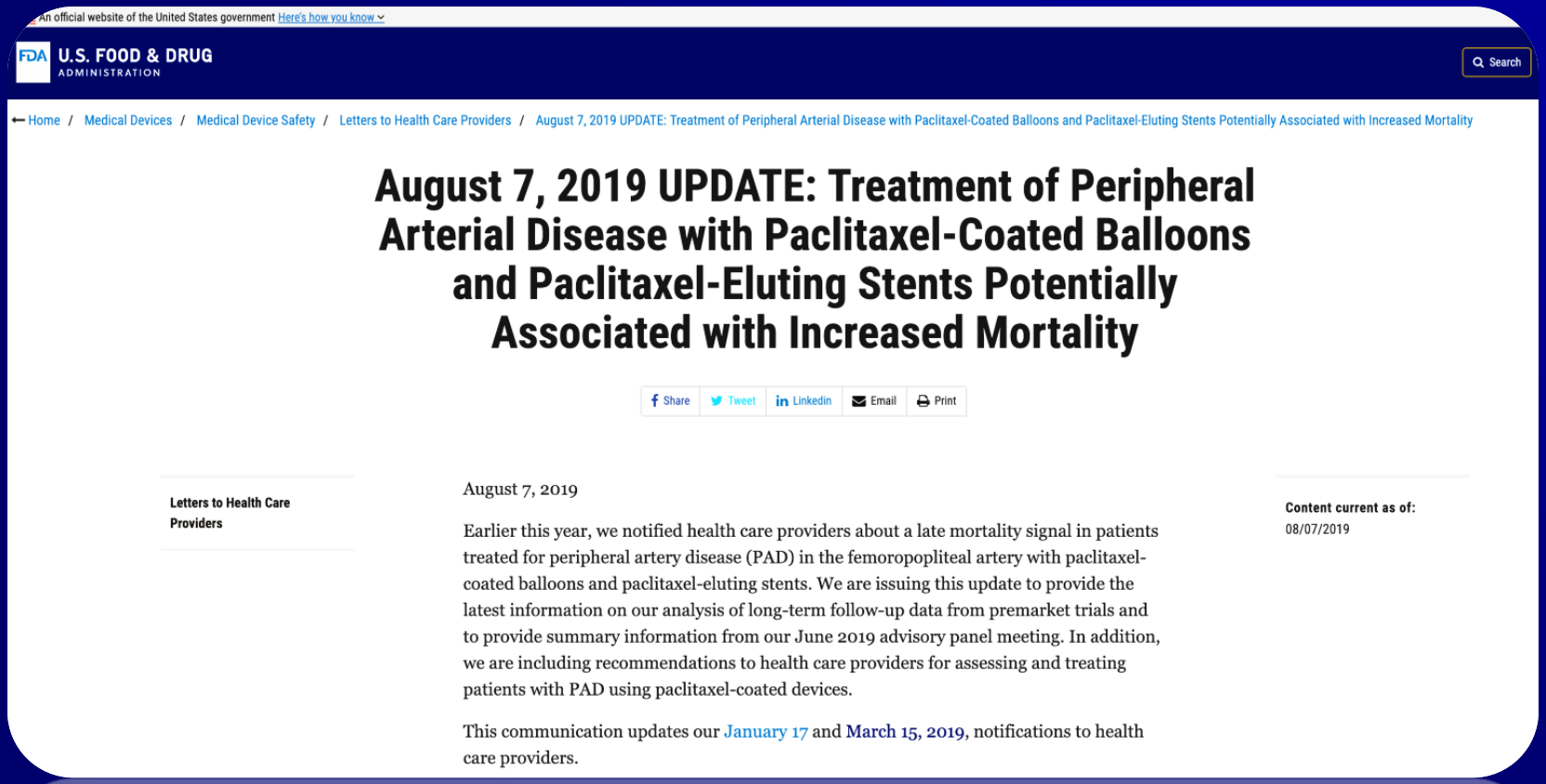
Late Mortality Safety Signal Discernment for Paclitaxel Delivery Devices in PAD



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Home / Medical Devices / Medical Device Safety / Letters to Health Care Providers / August 7, 2019 UPDATE: Treatment of Peripheral Arterial Disease with Paclitaxel-Coated Balloons and Paclitaxel-Eluting Stents Potentially Associated with Increased Mortality

August 7, 2019 UPDATE: Treatment of Peripheral Arterial Disease with Paclitaxel-Coated Balloons and Paclitaxel-Eluting Stents Potentially Associated with Increased Mortality

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Letters to Health Care Providers

August 7, 2019

Earlier this year, we notified health care providers about a late mortality signal in patients treated for peripheral artery disease (PAD) in the femoropopliteal artery with paclitaxel-coated balloons and paclitaxel-eluting stents. We are issuing this update to provide the latest information on our analysis of long-term follow-up data from premarket trials and to provide summary information from our June 2019 advisory panel meeting. In addition, we are including recommendations to health care providers for assessing and treating patients with PAD using paclitaxel-coated devices.

This communication updates our January 17 and March 15, 2019, notifications to health care providers.

Content current as of:
08/07/2019

https://www.fda.gov/medical-devices/letters-health-care-providers/august-7-2019-update-treatment-peripheral-arterial-disease-paclitaxel-coated-balloons-and-paclitaxel

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CRI Duke Clinical Research Institute

RAPID PTX Pathways Program

Working Groups

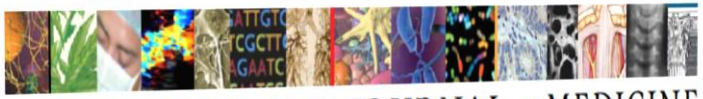
- Lean CRF
- SMART CRF
- Patient Preference Science
- Signal Discernment Biostatistics & Epi
- Independent Programs & Projects

Partner Collaborations

- FDA PTX Team
- Industry collaborative
- Professional societies collaborative

The Randomized Registry Trial — The Next Disruptive Technology in Clinical Research?

Michael S. Lauer, M.D., and Ralph B. D'Agostino, Sr., Ph.D.



The NEW ENGLAND JOURNAL of MEDICINE
September 2013

Embedding a randomized clinical trial into an ongoing registry infrastructure: Unique opportunities for efficiency in design of the Study of Access site For Enhancement of Percutaneous Coronary Intervention for Women (SAFE-PCI for Women)

Connie N. Hess, MD, MHS,[a] Sunil V. Rao, MD,[a] David F. Kong, MD,[a] Laura H. Aberle, BSPH,[a] Kevin J. Anstrom, PhD,[a] C. Michael Gibson, MD,[b] Ian C. Gilchrist, MD,[c] Alice K. Jacobs, MD,[d] Sanjit S. Jolly, MD,[c] Roxana Mehran, MD,[f] John C. Messenger, MD,[g] L. Kristin Newby, MD, MHS,[a] Ron Waksman, MD,[h] and Mitchell W. Krucoff, MD[a] *Durham, NC; Boston, MA; Hershey, PA; Ontario, Canada; New York, NY; Denver, CO; and Washington, DC*

A Registry-Based Randomized Trial Comparing Radial and Femoral Approaches in Women Undergoing Percutaneous Coronary Intervention

The SAFE-PCI for Women (Study of Access Site for Enhancement of PCI for Women) Trial

Sunil V. Rao, MD,* Connie N. Hess, MD, MHS,* Britt Barham, BA,* Laura H. Aberle, BSPH,* Kevin J. Anstrom, PhD,* Tejan B. Patel, MD,† Jesse P. Jorgensen, MD,‡ Ernest L. Mazzaferri Jr., MD,§ Sanjit S. Jolly, MD,‖ Alice Jacobs, MD,¶ L. Kristin Newby, MD,* C. Michael Gibson, MD,# David F. Kong, MD,* Roxana Mehran, MD,** Ron Waksman, MD,†† Ian C. Gilchrist, MD,‡‡ Brian J. McCourt,* John C. Messenger, MD,§§ Eric D. Peterson, MD, MPH,* Robert A. Harrington, MD,‖‖ Mitchell W. Krucoff, MD*

Hess C et al, Am Heart J 2013

Rao S et al JACC Cardiovascular Int 7(8)2014

Lauer M et al, NEJM 2013

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IMDRF Essential Principles for Device Evidence: Registry Infrastructure and Analytic Methodologies

IMDRF/Registry WG/N46 FINAL:20

IMDRF International Medical Device Regulators Forum

Final Document

Title: Tools for Assessing the Usability of Registries in Support of Regulatory Decision-Making

Authoring Group: Patient Registries Working Group

Date: 27 March 2018

Yuan Lin, IMDRF Chair

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IMDRF/Registry WG/N42FINAL:20

IMDRF International Medical Device Regulators Forum

FINAL DOCUMENT

Title: Methodological Principles in the Use of International Medical Device Registry Data

Authoring Group: IMDRF Patient Registries Working Group

Date: 16 March 2017

Kimby Barton, IMDRF Chair

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http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-180327-usability-tools-n46.pdf

http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170316-methodological-principles.pdf

ESC European Society of Cardiology
European Heart Journal (2019) **40**, 2745–2759
doi:10.1093/eurheartj/ehz599

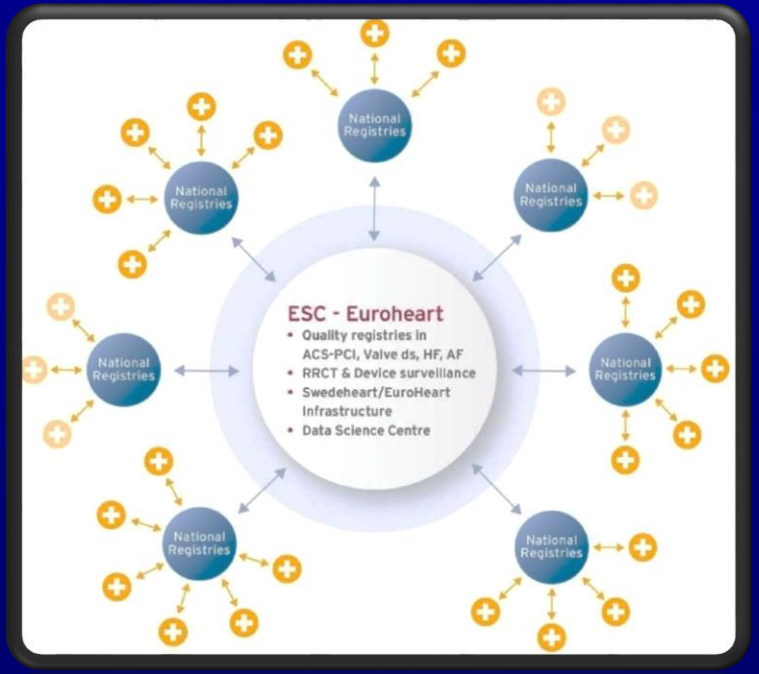
EuroHeart: European Unified Registries On Heart Care Evaluation and Randomized Trials

An ESC project to develop a new IT registry system which will encompass multiple features of cardiovascular medicine

In July 2019, the ESC Board agreed to co-ordinate and sponsor the development of the European Unified Registries On Heart care Evaluation And Randomized Trials (EuroHeart) for supporting assessment and improvement of quality of cardiovascular care in Europe based on continuous recording of individual patient data. EuroHeart will offer a common IT- and dataset infrastructure, which will allow participating countries to undertake continuous quality improvement, with the added value of providing a platform for observational and randomized research and post-marketing surveillance of new devices and pharmacotherapies. The national quality development programme, infrastructure, and the database will belong to each participating country. The EuroHeart will have the potential to stepwise include most ESC countries, which could either adopt the proposed EuroHeart com- infrastructure or align already existing systems to the EuroHeart Practice Guidelines. The EORP provides important information on the development of the treatment of cardiovascular disease in Europe but has been criticized concerning data quality, representativeness and coverage regarding common diseases. In 2018, it was agreed that there was a need to further develop ESC-generated observational data and simultaneously expand the scope of the registry programme to also include a quality development programme, long-term monitoring of medical devices and pragmatic RCTs and under instruction of the ESC Board, the principles and pilot phase of European Unified Registries On Heart care Evaluation And Randomized Trials (EuroHeart) project were developed in 2019.

This article presents a summary of the EuroHeart programme.

Improving the quality of observational data



European Heart Journal (2019) 40, 2745–2759

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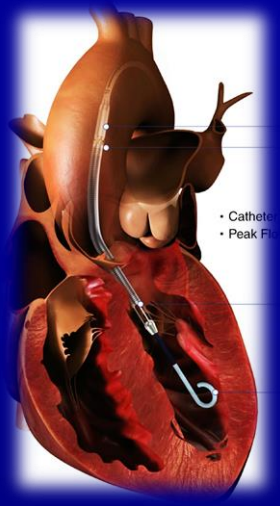
Cardiogenic Shock Devices



Cardiac Safety Research Consortium

Clinical and regulatory landscape for cardiogenic shock: A report from the Cardiac Safety Research Consortium ThinkTank on cardiogenic shock☆

Marc Samsky, MD,[a] Mitchell Krucoff, MD,[b] Andrew D. Althouse, PhD,[c] William T. Abraham, MD,[d] Philip Adamson, MD, MSc,[e] Fernando Aguel,[f] Seth Bilazarian,[g] George D. Dangas, MD,[h] Ian C Gilchrist, MD,[i] Timothy D. Henry, MD, FACC, MSCAI,[j] Judith S. Hochman, MD,[k] Navin K. Kapur, MD, FAHA,[l] John Laschinger, FACC,[m] Roy G. Masters, MD, FRCSC,[n] Eric Michelson, MD,[o] David A. Morrow, MD, MPH,[p] Valarie Morrow, MD,[q] E. Magnus Ohman, MD,[r] Ileana Pina, MD, MPH,[s] Senatore,[v] Norman Stockbridge, MD, MD,[z] and Sunil Rao, MD[aa]

Cardiogenic shock (CS) is a leading ca
associated with acute myocardial infa
Improved prehospital emergency care a
fusion from initially systemic lytics to no

Shock III at CRT
Saturday Feb 22, 2020
Washington D.C.

Samsky M, Krucoff M et al Am Heart J November 2019

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HB *Doing*

Early Feasibility Studies (EFS)

Early Feasibility Studies: Can We Do Together? 2013-2017-2019

Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies

Guidance for Industry and Food and Drug Administration Staff

Document issued on: October 1, 2013

EFS in Japan: PMDA View

Sara Takahashi
Reviewer
Office of Medical Devices III
Pharmaceuticals and Medical Devices Agency (PMDA), Japan

tct2017 Cardiovascular Research Foundation

4C MEDICAL

Percutaneous Mitral Valve EFS POC

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https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm279103.pdf

HB *Doing*

HBD for Children

Introduction and achievement of HBD-for-Children

Yasuko Nakamura

Reviewer, Office of Medical Devices III

Pharmaceuticals and Medical Devices Agency (PMDA)

Japan-USHBD East 2017 Think Tank Meeting

Heart on Hearts

HBD-for-Children

Progress and Challenges

Satoshi Yasukochi, MD
Nagano Children's Hospital
JSPCCS vice-president

December 7th, 2017
National Center for Global Health and Medicine (NCGM)

POC candidates

	Covered CP Stent	Medtronic Melody Transcatheter Pulmonary Valve	AMPLATZER muscular VSD occluder
industry	NuMED	Medtronic	ST.JUDE MEDICAL
			

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Future directions

- International approaches to safety signal discernment PTX in PAD
- Real World Evidence
- HBD for Children
- Early Feasibility Studies: mitral valve
- High Bleeding Risk PCI patients
- Multi-national collaboration: Inter^{2}Nest
- Vascular shunts
- Billing data for event ascertainment ?
- Cardiogenic shock ?

HBD

Together We Have Made a Pretty Big Splash!

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