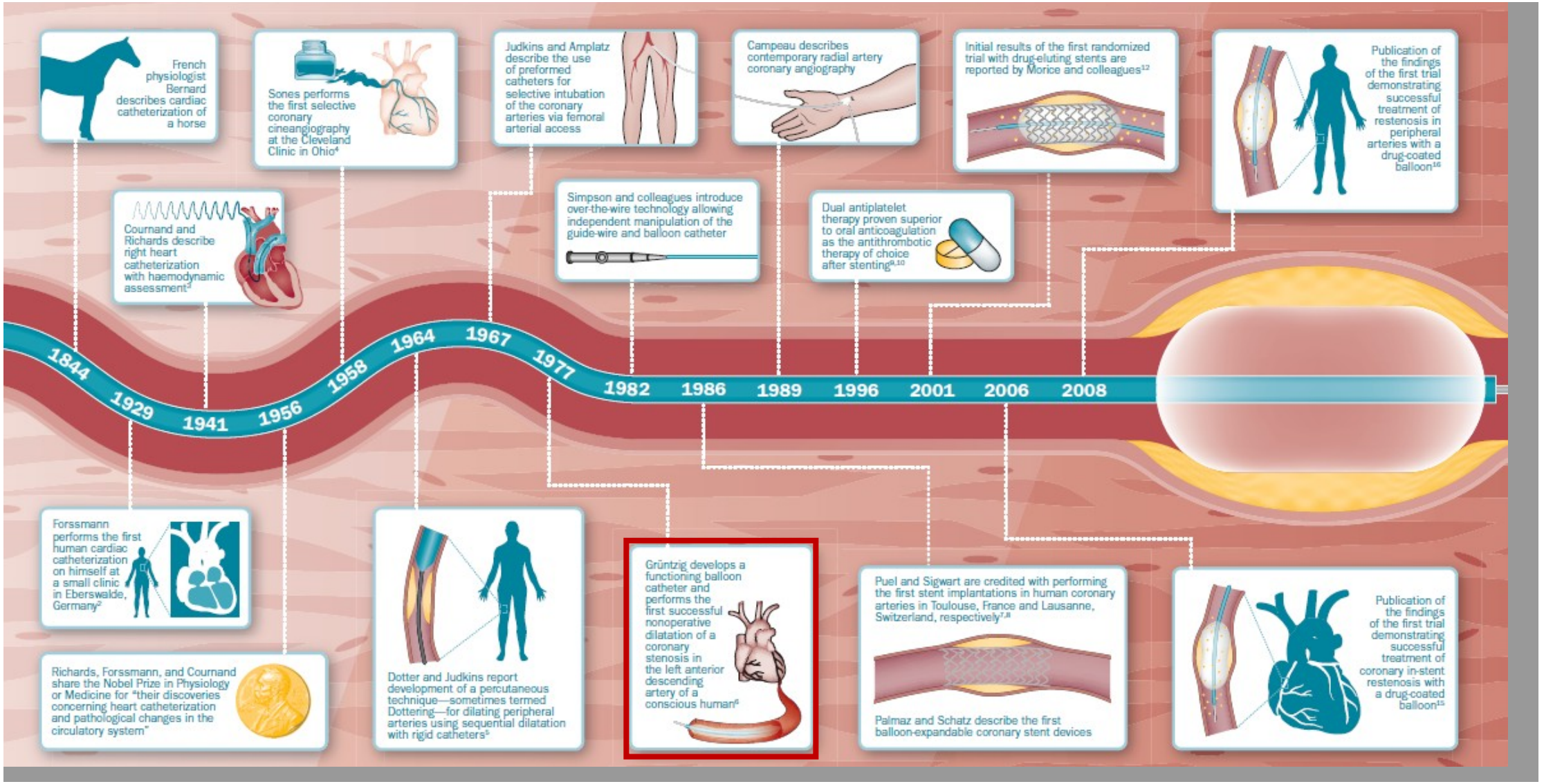
CORE-MD

Coordinating Research and Evidence for Medical Devices

Evaluation of Coronary Stents

Monday 3 April 2023

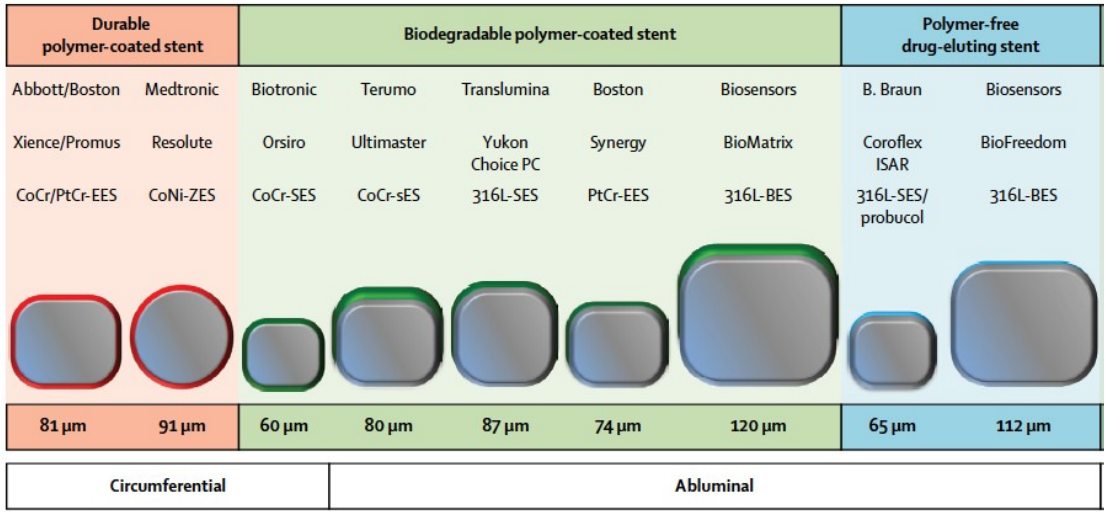
Prof Robert Byrne
RCSI University, Dublin, IRELAND

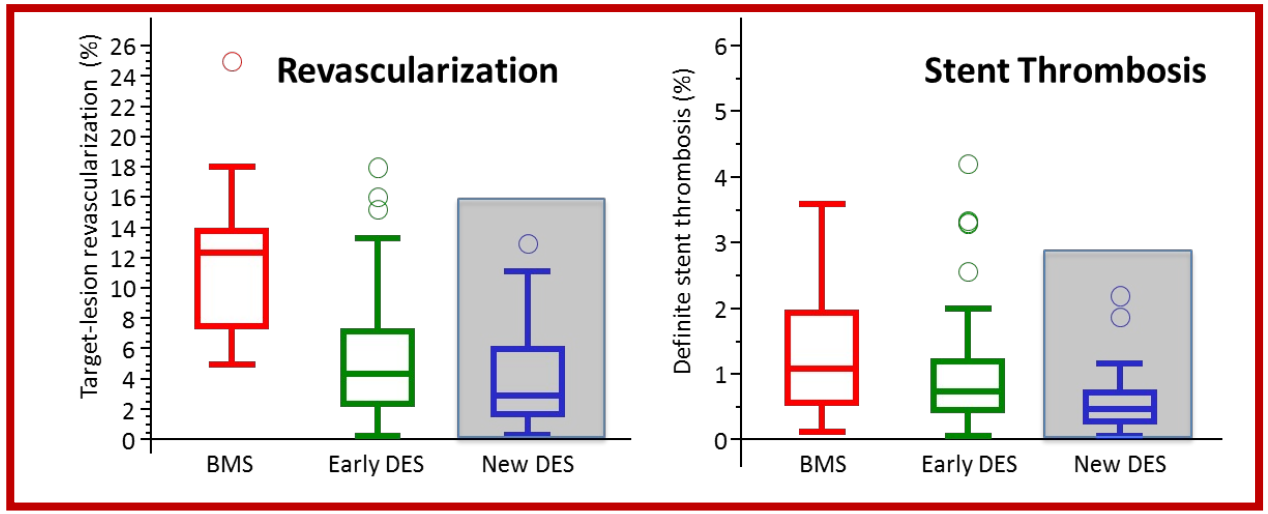


A brief history of catheter intervention

Byrne, Kastrati | Nat Rev Cardiol 2015

Drug-eluting stents: breakthrough technology

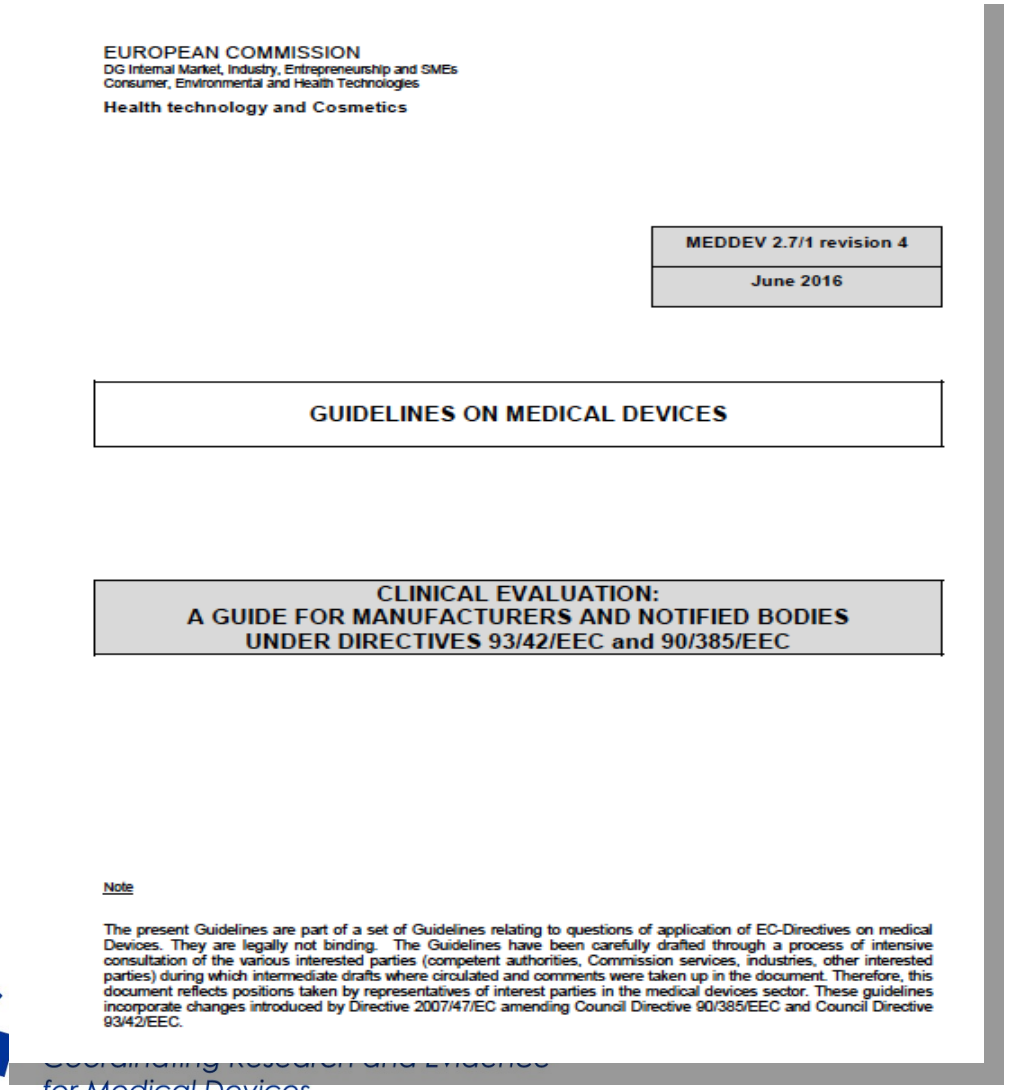




Recommendations	Class	Level
DES are recommended over BMS for any PCI irrespective of: • clinical presentation, • lesion type, • planned non-cardiac surgery, • anticipated duration of DAPT, • concomitant anticoagulant therapy.	I	A

Byrne, Stone, Ormiston, Kastrati | Lancet 2017; ESC Stent Task Force Report 2015

EC Guidance Documents



EUROPEAN COMMISSION
DG Internal Market, Industry, Entrepreneurship and SMEs
Consumer, Environmental and Health Technologies

Health technology and Cosmetics

MEDDEV 2.7/1 revision 4

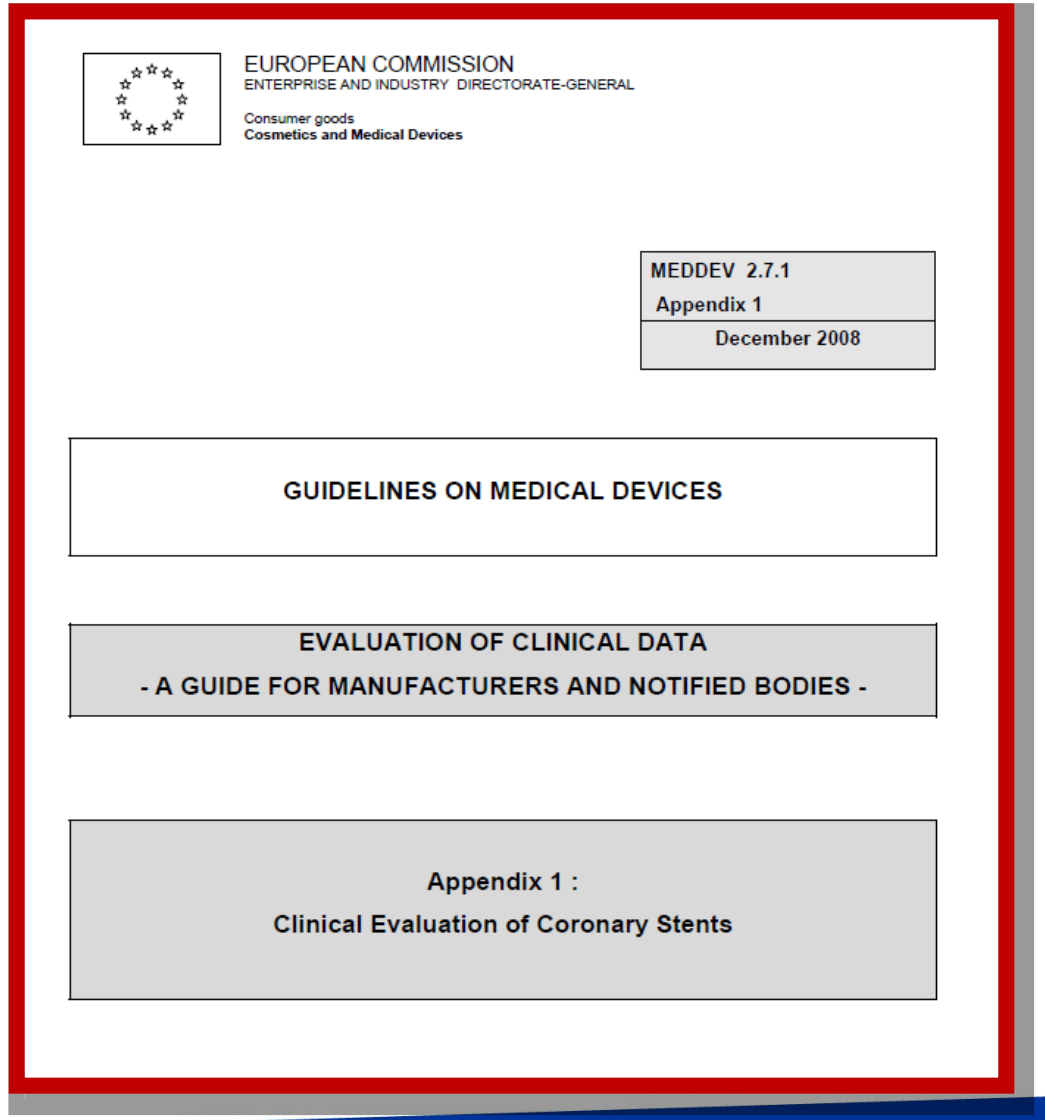
June 2016

GUIDELINES ON MEDICAL DEVICES

CLINICAL EVALUATION:
A GUIDE FOR MANUFACTURERS AND NOTIFIED BODIES
UNDER DIRECTIVES 93/42/EEC and 90/385/EEC

Note

The present Guidelines are part of a set of Guidelines relating to questions of application of EC-Directives on medical Devices. They are legally not binding. The Guidelines have been carefully drafted through a process of intensive consultation of the various interested parties (competent authorities, Commission services, industries, other interested parties) during which intermediate drafts where circulated and comments were taken up in the document. Therefore, this document reflects positions taken by representatives of interest parties in the medical devices sector. These guidelines incorporate changes introduced by Directive 2007/47/EC amending Council Directive 90/385/EEC and Council Directive 93/42/EEC.



EUROPEAN COMMISSION
ENTERPRISE AND INDUSTRY DIRECTORATE-GENERAL

Consumer goods
Cosmetics and Medical Devices

MEDDEV 2.7.1
Appendix 1

December 2008

GUIDELINES ON MEDICAL DEVICES

EVALUATION OF CLINICAL DATA
- A GUIDE FOR MANUFACTURERS AND NOTIFIED BODIES -

Appendix 1 :
Clinical Evaluation of Coronary Stents

for Medical Devices

The only medical device-specific guidance in Europe!

European Heart Journal Advance Access published June 12, 2015

European Heart Journal
doi:10.1093/eurheartj/ehv203

SPECIAL ARTICLE

Report of a European Society of Cardiology-European Association of Percutaneous Cardiovascular Interventions task force on the evaluation of coronary stents in Europe: executive summary

**Robert A. Byrne[1], Patrick W. Serruys[2], Andreas Baumbach[3], Javier Escaned[4], Jean Fajadet[5], Stefan James[6], Michael Joner[7], Semih Oktay[8], Peter Jüni[9], Adnan Kastrati[1], George Sianos[10], Giulio G. Stefanini[11], William Wijns[12], and Stephan Windecker[11]*

[1]Deutsches Herzzentrum München, Technische Universität München, Munich, Germany; [2]Erasmus Medical Center Rotterdam, Rotterdam, The Netherlands; [3]Bristol Heart Institute, Bristol, UK; [4]Interventional Cardiology, Hospital San Carlos, Madrid, Spain; [5]Interventional Cardiology, Clinique Pasteur, Toulouse, France; [6]Clinical Research Center, Uppsala University, Uppsala, Sweden; [7]CVPath Institute, Inc., Gaithersburg, USA; [8]Cardio Med Device Consultants, Baltimore, USA; [9]Institute of Primary Health Care (BIHAM), University of Bern, Bern, Switzerland; [10]AHEPA University Hospital, Thessaloniki, Greece; [11]Swiss Cardiovascular Center Bern, Bern University Hospital, Bern, Switzerland; and [12]Cardiovascular Center O.L.V.Z., Aalst, Belgium

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Coordinating Research and Evidence for Medical Devices

ESC-EAPCI Task Force on Coronary Stents

Systematic review of 158 RCTs

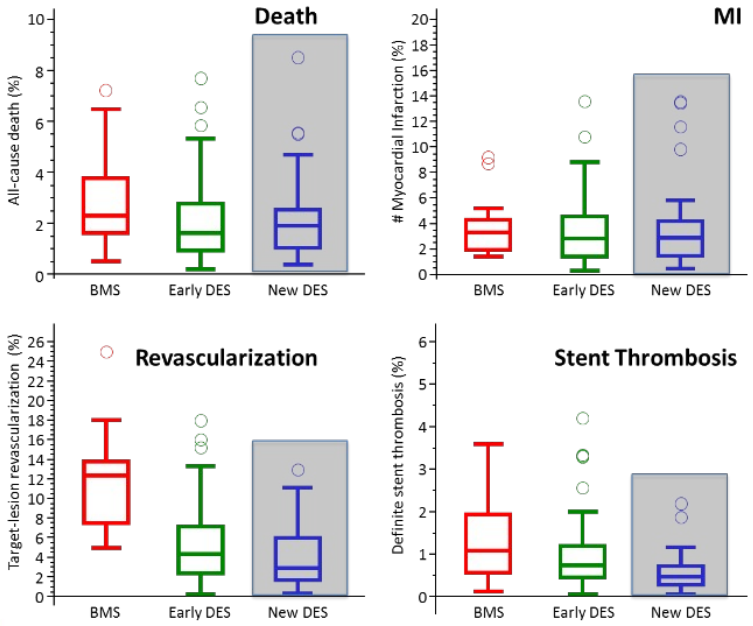
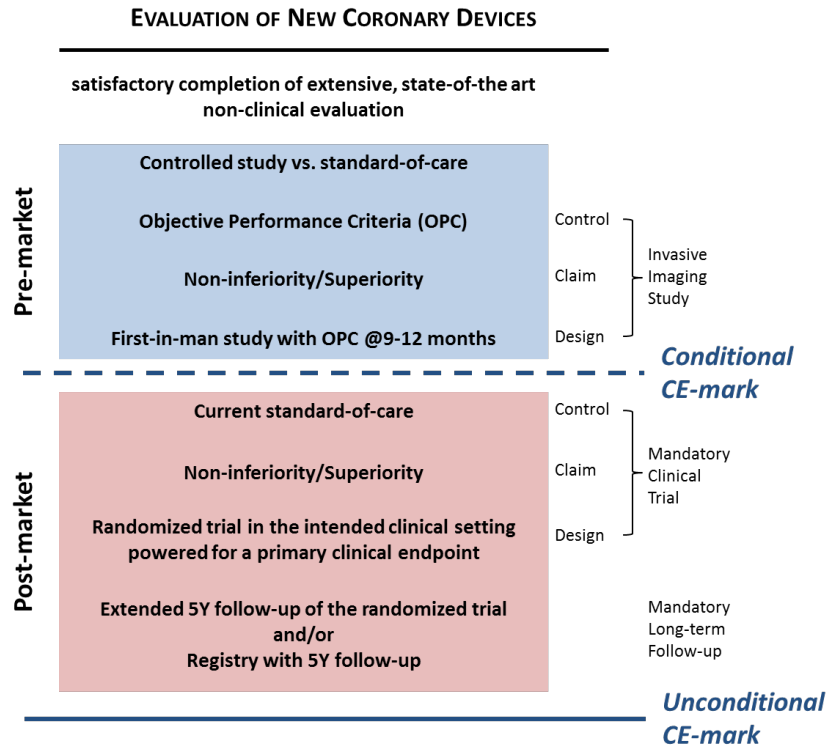


Table 6 Checklist for non-clinical studies performed according to Good Laboratory Practice standards

Test modalities	Most relevant documents
Bioengineering	
• Risk analysis • Bench testing • Material characterization • Stent dimensional and functional attributes • Delivery system dimensional and functional attributes • Coating component characterization ○ Medicinal substance characterization ○ Complete characterization of ○ Biodegradation in BRS • Biocompatibility	• EMEA/CHMP/EWP/110540/2007: Guideline on the clinical and non-clinical evaluation during the consultation procedure on medicinal substances contained in drug-eluting (medicinal substance eluting) coronary stents • MEDDEV 2.1/3 rev 3 • Guidance for Industry and FDA Staff—Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems (April 2010) • Select Updates for Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems—Draft Guidance for Industry and Food and Drug Administration Staff (August 2013) • FDA Coronary Drug-Eluting Stents—Non-clinical and Clinical Studies (March 2008) • FDA Coronary Drug-Eluting Stents: Companion Document—Non-clinical and Clinical Studies (March 2008)
Toxicity	• ISO 10993 Biological Evaluation of Medical Devices
Safety studies	
• *In vivo* information ○ Angiography ○ Device deployment procedures ○ Device acute performance ○ Complications ○ Final angiography and intravascular imaging at follow-up ○ Clinical information and blood work ○ Necropsy information • Histopathology ○ Histomorphometry ○ Assessment of inflammation ○ Assessment of thrombus formation ○ Characterization of strut degradation in BRS ○ Characterization of tissue composition during degradation in BRS • Intravascular imaging ○ Morphometric assessment ○ Judgement of strut coverage ○ Characterization of strut degradation in BRS ○ Assessment of thrombus formation	• EMEA/CHMP/EWP/110540/2007: Guideline on the clinical and non-clinical evaluation during the consultation procedure on medicinal substances contained in drug-eluting (medicinal substance-eluting) coronary stents • MEDDEV 2.1/3 rev 3 • ANSI/AAMI/ISO 25539-2:2012: Cardiovascular implants—Endovascular devices—Part 2: Vascular stents • FDA Coronary Drug-Eluting Stents—Non-clinical and Clinical Studies (March 2008) • FDA Coronary Drug-Eluting Stents: Companion Document—Non-clinical and Clinical Studies (March 2008) • FDA Guidance for Industry and FDA Staff: General Considerations for Animal Studies for Cardiovascular Devices (2010) • Tearney *et al.*[38] • Prati *et al.*[42]
Pharmacokinetic studies	
• *In vitro* pharmacokinetics • *In vivo* pharmacokinetics • Establishment of *in vitro–in vivo* correlations	• EMEA/CHMP/EWP/110540/2007: Guideline on the clinical and non-clinical evaluation during the consultation procedure on medicinal substances contained in drug-eluting (medicinal substance-eluting) coronary stents • MEDDEV 2.1/3 rev 3 • FDA Coronary Drug-Eluting Stents—Non-clinical and • Clinical Studies (March 2008) • FDA Coronary Drug-Eluting Stents: Companion Document—Non-clinical and Clinical Studies (March 2008)
Biochemical analysis of degradation products in BRS	
• Definition of degradation products • *In vitro* degradation profile • *In vivo* degradation profile • Establishment of *in vitro – in vivo* correlations	• Use of International Standard ISO-10993, 'Biological Evaluation of Medical Devices Part 1: Evaluation and Testing • ISO/TS 12417:2011 • ISO/DIS 12417-1 • ISO/TR 37137:2014 • ISO/TS 17137:2014

BRS, bioresorbable stent.



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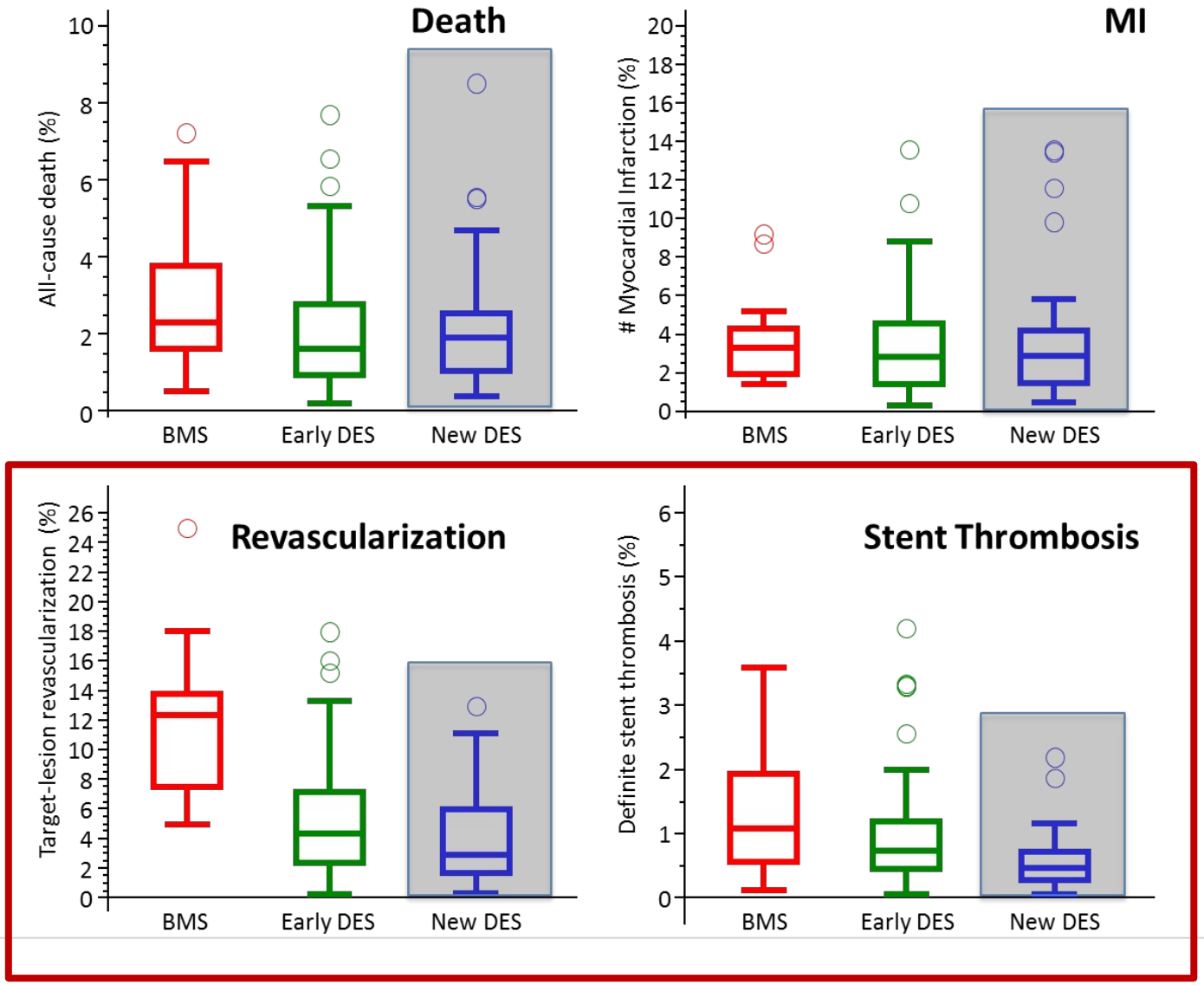
Systematic review of 158 RCTs



Systematic review of 158 RCTs | ESC-EAPCI Stent Task Force | *Eur Heart J* 2015

CHECKLIST for non-clinical testing

Table 6 Checklist for non-clinical studies performed according to Good Laboratory Practice standards

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  ○ Biodegradation in BRS
• Biocompatibility
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Toxicity	
	• ISO 10993 Biological Evaluation of Medical Devices
Safety studies	

• *In vivo* information
  ○ Angiography
  ○ Device deployment procedures
  ○ Device acute performance
  ○ Complications
  ○ Final angiography and intravascular imaging at follow-up
  ○ Clinical information and blood work
  ○ Necropsy information
• Histopathology
  ○ Histomorphometry
  ○ Assessment of inflammation
  ○ Assessment of thrombus formation
  ○ Characterization of strut degradation in BRS
  ○ Characterization of tissue composition during degradation in BRS
• Intravascular imaging
  ○ Morphometric assessment
  ○ Judgement of strut coverage
  ○ Characterization of strut degradation in BRS
  ○ Assessment of thrombus formation
	• EMEA/CHMP/EWP/110540/2007: Guideline on the clinical and non-clinical evaluation during the consultation procedure on medicinal substances contained in drug-eluting (medicinal substance-eluting) coronary stents
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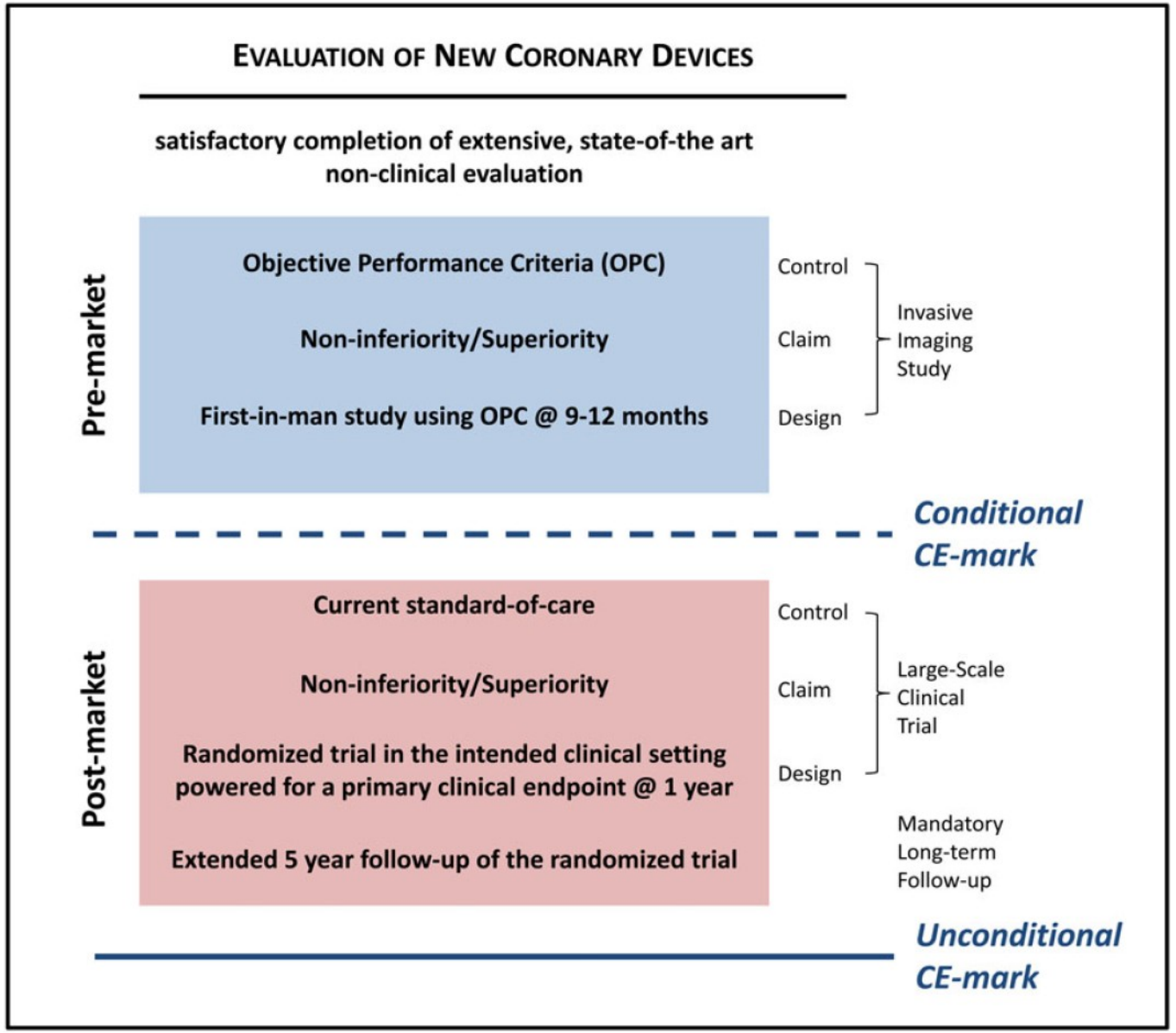
BRS, bioresorbable stent.

EAPCI
European Association of Percutaneous Cardiovascular Interventions

ESC


EVALUATION OF NEW CORONARY DEVICES
satisfactory completion of extensive, state-of-the art non-clinical evaluation
Pre-market
Objective Performance Criteria (OPC)
Non-inferiority/Superiority
First-in-man study using OPC @ 9-12 months
Control
Claim
Design
Invasive Imaging Study
Conditional CE-mark
Post-market
Current standard-of-care
Non-inferiority/Superiority
Randomized trial in the intended clinical setting powered for a primary clinical endpoint @ 1 year
Extended 5 year follow-up of the randomized trial
Control
Claim
Design
Large-Scale Clinical Trial
Mandatory Long-term Follow-up
Unconditional CE-mark

ESC European Society of Cardiology

European Heart Journal (2018) **39**, 1591–1601
doi:10.1093/eurheartj/ehx488

FAST TRACK CLINICAL PAPER
Interventional cardiology

Report of an ESC-EAPCI Task Force on the evaluation and use of bioresorbable scaffolds for percutaneous coronary intervention: executive summary

Robert A. Byrne[1,2], Giulio G. Stefanini[3], Davide Capodanno[4], Yoshinobu Onuma[5], Andreas Baumbach[6], Javier Escaned[7], Michael Haude[8], Stefan James[9], Michael Joner[1,2], Peter Jüni[10], Adnan Kastrati[1,2], Semih Oktay[11], William Wijns[12,13], Patrick W. Serruys[14,15], and Stephan Windecker[16]*

[1]Deutsches Herzzentrum München, Technische Universität München, Germany; [2]DZHK (German Centre for Cardiovascular Research), Partner Site Munich Heart Alliance, Munich, Germany; [3]Division of Cardiology, Cardio Center, Humanitas Research Hospital, Rozzano, Milan, Italy; [4]Cardio-Thoracic-Vascular Department, Ferrarotto Hospital, University of Catania, Italy; [5]Department of Interventional Cardiology Erasmus Medical Center Rotterdam, The Netherlands; [6]Department of Cardiology, St Bartholomew's Hospital, William Harvey Research Institute, and Queen Mary University of London, London, UK; [7]Interventional Cardiology, Hospital San Carlos, Madrid, Spain; [8]Medical Clinic I, Städtische Kliniken Neuss, Lukaskrankenhaus GmbH, Neuss, Germany; [9]Clinical Research Center, Uppsala University, Uppsala, Sweden; [10]Applied Health Research Centre, Li Ka Shing Knowledge Institute of St Michael's Hospital, University of Toronto, Toronto, Ontario, Canada; [11]Cardio Med Device Consultants, Baltimore, USA; [12]Saolta University Healthcare Group, Galway, Ireland; [13]The Lambe Institute for Translational Medicine and Curam, National University of Ireland, Galway, Ireland; [14]Erasmus University, Rotterdam, the Netherlands; [15]International Centre for Circulatory Health, National Heart and Lung Institute, Imperial College London, London, UK; and [16]Cardiovascular Center Bern, Bern University Hospital, Bern, Switzerland

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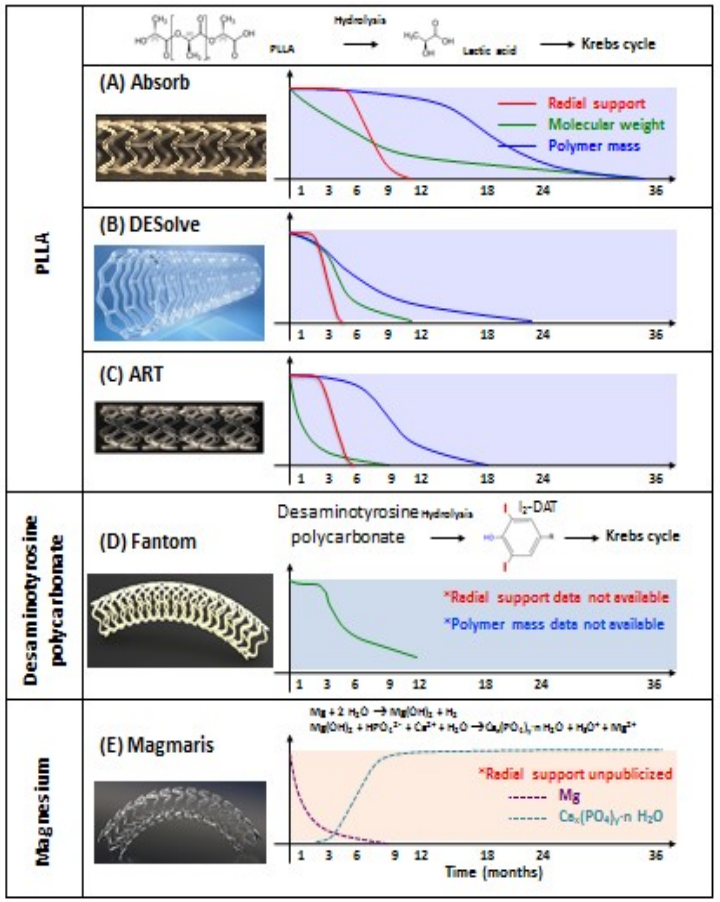
ESC-EAPCI Task Force on Bioresorbable Scaffolds



Target lesion failure

Target lesion failure

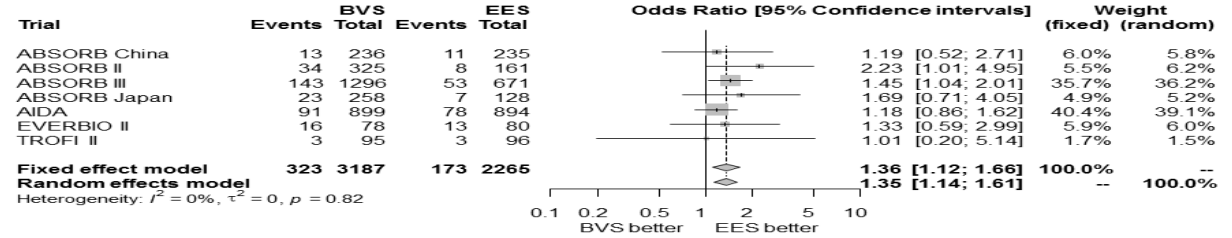


Figure 1-A

Scaffold thrombosis (def/prob)

Definite or probable stent/scaffold thrombosis

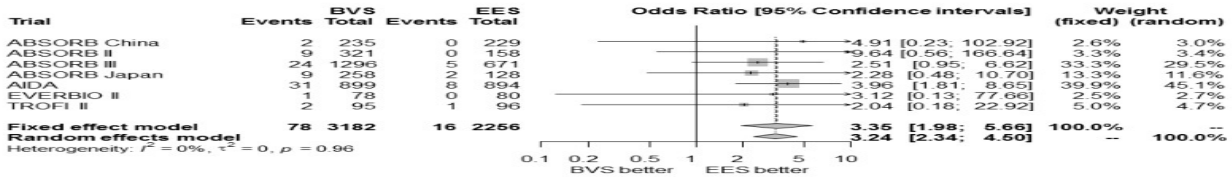


Figure 1-B

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Coordinating Research and Evidence for Medical Devices

Take Home Messages | Evaluation of Coronary Stents

- Common Specifications are an important component of the regulatory process for high risk medical devices under EU MDR
- Unmet need exists for a device specific guidance document or Common Specification for coronary stents
- Drug-eluting stents are a mature technology with standardized endpoints for clinical trials and well established
- Development of objective performance criteria for coronary stents would facilitate single arm clinical investigations for novel coronary stents

CORE-MD, Coordinating Research and Evidence for Medical Devices, aims to translate expert scientific and clinical evidence on study designs for evaluating high-risk medical devices into advice for EU regulators.

For more information, visit: www.core-md.eu

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945260

ESC

EFORT – JOINT EFFORTS

Biomedical Alliance in Europe

European Academy of Paediatrics
Paediatric Section of U.E.M.S

EPF European Patients Forum

LUMC Leiden University Medical Center

University of Oxford

Region Uppsala

RCSI University of Medicine and Health Sciences

INSELSPITAL
UNIVERSITÄTSSPITAL BERN
HÔPITAL UNIVERSITAIRE DE BERNE

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Politecnico Milano 1863

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An tÚdarás Rialáia Táirgí Sláinte
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Ministry of Health, Welfare and Sport

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Austrian Institute for Health Technology Assessment GmbH

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Coordinating Research and Evidence for Medical Devices