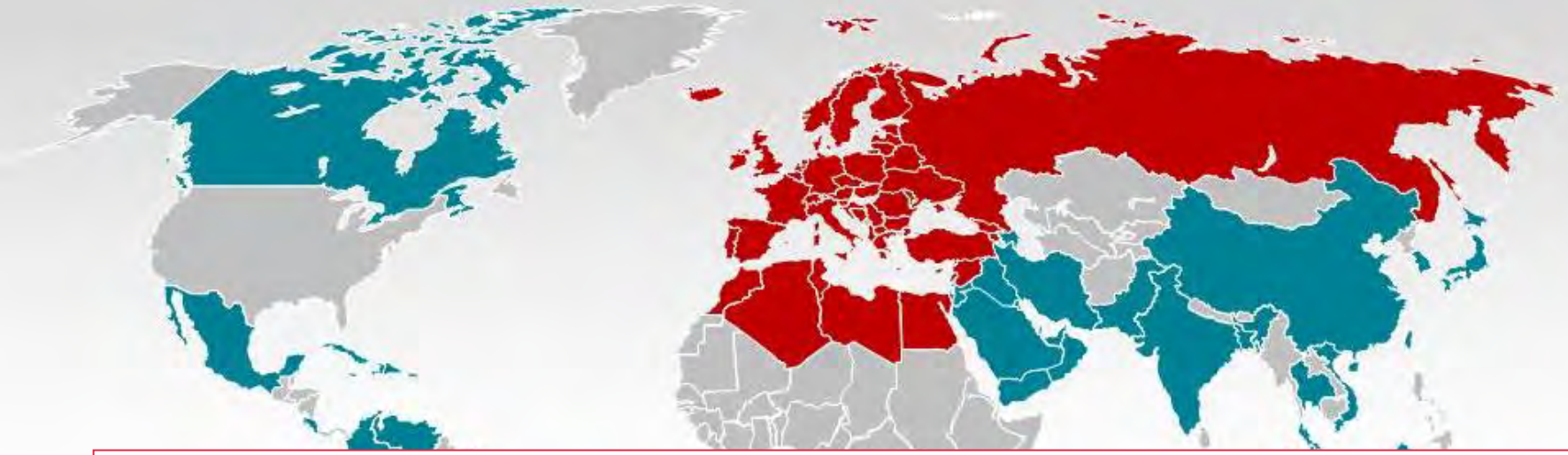

International regulatory convergence – strategic reflections from the ESC

Professor Alan G Fraser

Co-Chairman, ESC Task Force on Medical Devices

20th March 2013
IMDRF Stakeholder Forum

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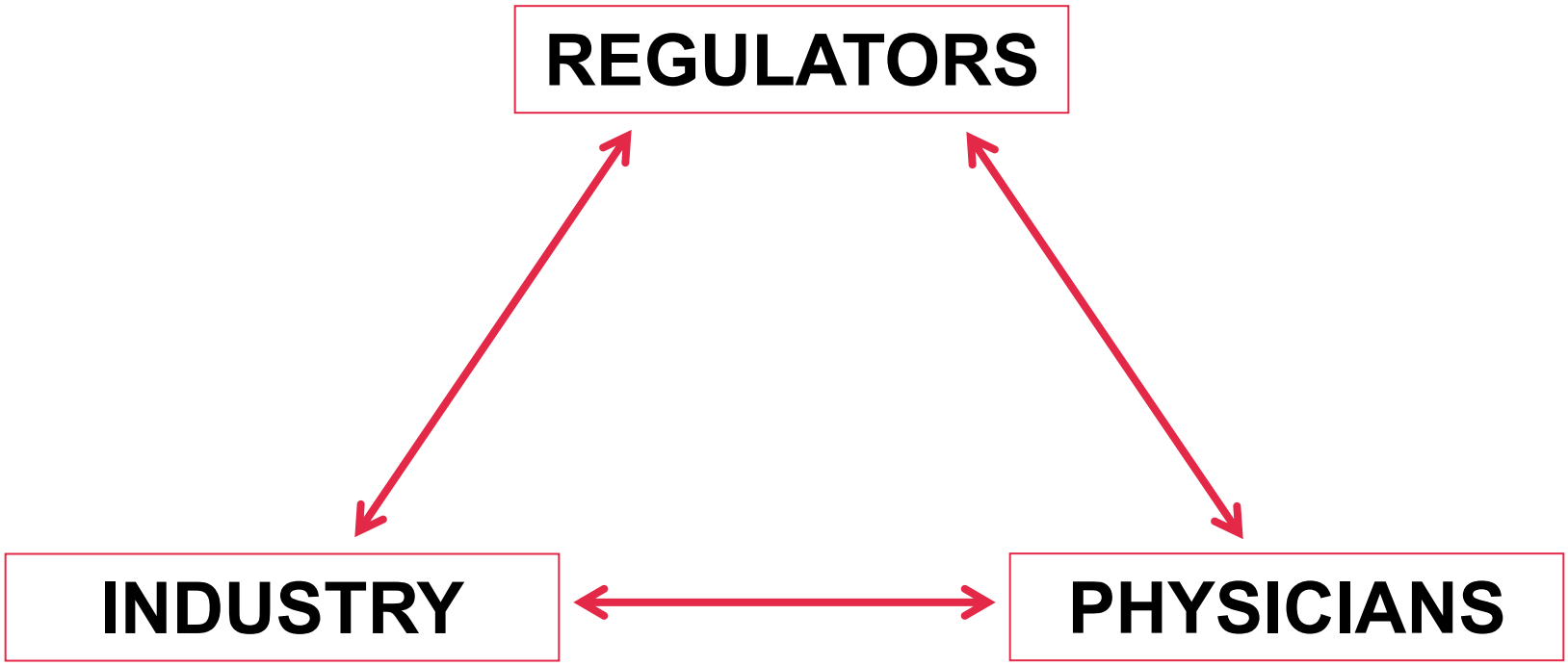
Governance of medical devices



European Heart Journal
doi:10.1093/eurheartj/ehr171

ESC REPORT

Clinical evaluation of cardiovascular devices: principles, problems, and proposals for European regulatory reform

Report of a policy conference of the European Society of Cardiology†

Alan G. Fraser*, Jean-Claude Daubert, Frans Van de Werf, N.A. Mark Estes III, Sidney C. Smith Jr, Mitchell W. Krucoff, Panos E. Vardas, and Michel Komajda, on behalf of the participants‡

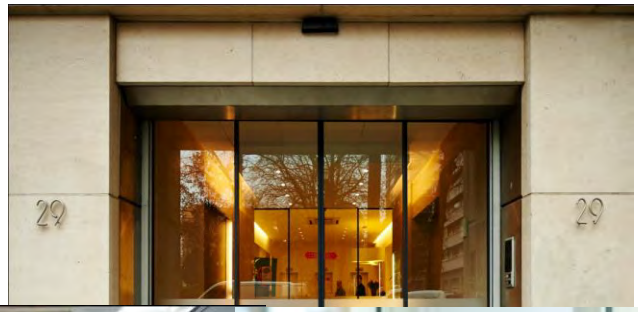
Eur Heart J 2011; 32: 1673-86

www.escardio.org

ESC Policy Conference
28-29th January 2011

27.2.13 – European Office

The European Heart Agency



www.escardio.org

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EUROPEAN COMMISSION

Brussels, 26.9.2012
COM(2012) 542 final

2012/0266 (COD)

Proposal for a

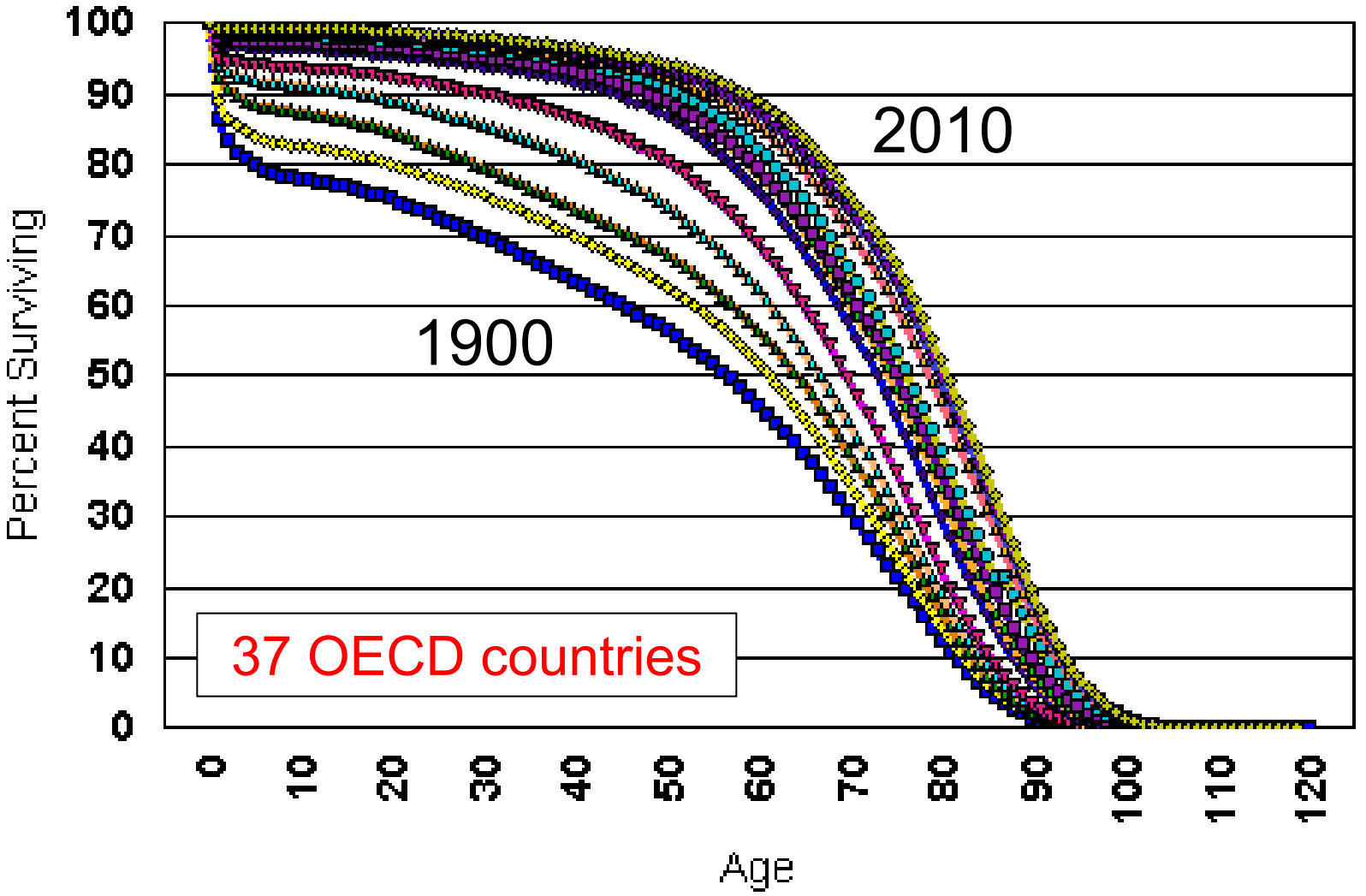
REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

on medical devices, and amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009

- Review of proposals by Rapporteur, Dagmar Roth-Behrendt
- Committee on Environment, Public Health & Food Safety 20.4.2013
  - Draft report from Rapporteur for Committee 24.4.2013
    - Deadline for amendments 3.5.2013
- Votes in European Parliament, and in European Council 2013
  - Legislation to take effect about 2019

http://ec.europa.eu/health/medical-devices/files/revision_docs/proposal_2012_542_en.pdf

The Human Mortality Database – 20th Century Trends



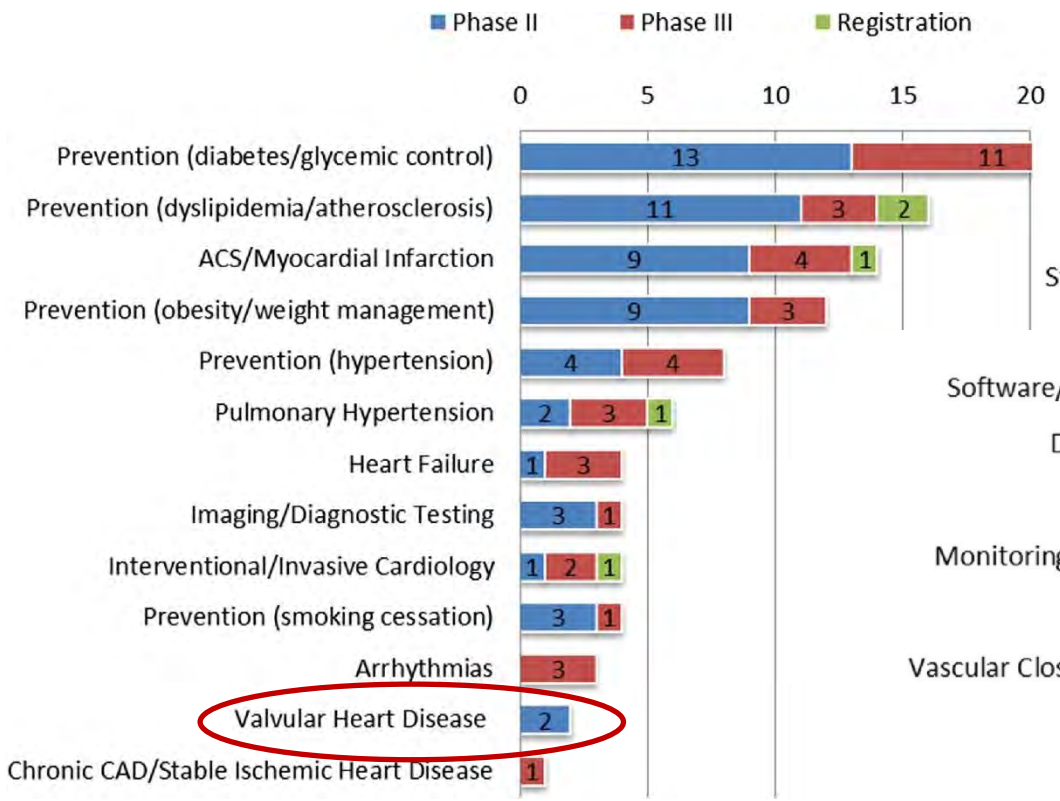
www.fis.org / from *www.mortality.org*

Cardiological and cardiac surgical devices …

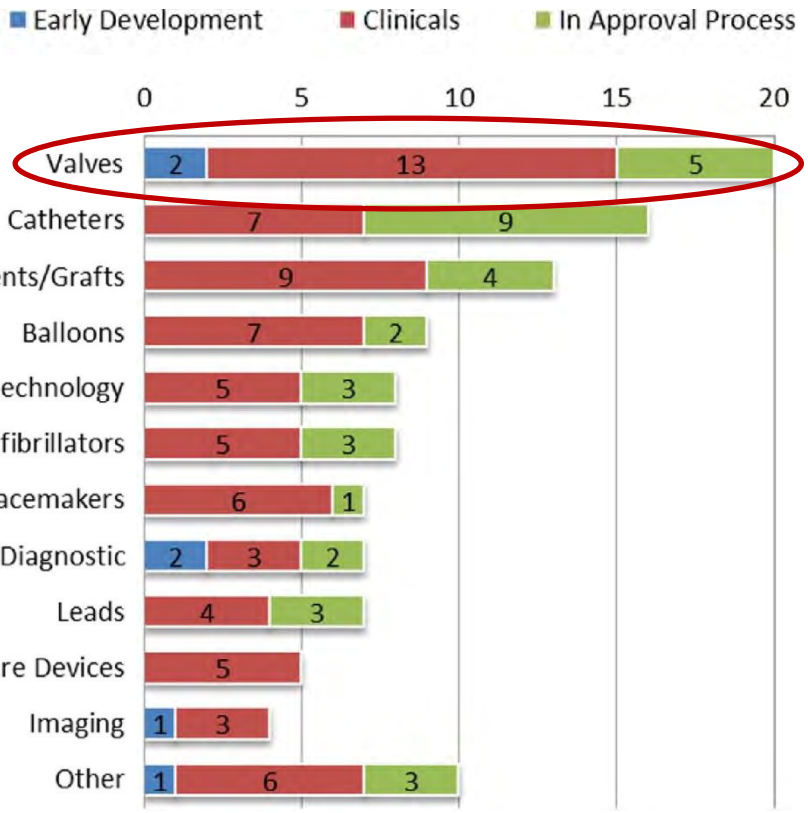
- Stethoscope
- Sphygmomanometer
- Electrocardiography
- Echocardiography
- Isotope scintigraphy
- Computed tomography
- Magnetic resonance imaging
- Invasive arteriography
- Coronary stents
- Vascular grafts
- Prosthetic heart valves
- Pacemakers
- Defibrillators
- Artificial hearts
- Cardiopulmonary bypass
- Ventilator

Cardiovascular Drugs and Devices in Development

Drugs

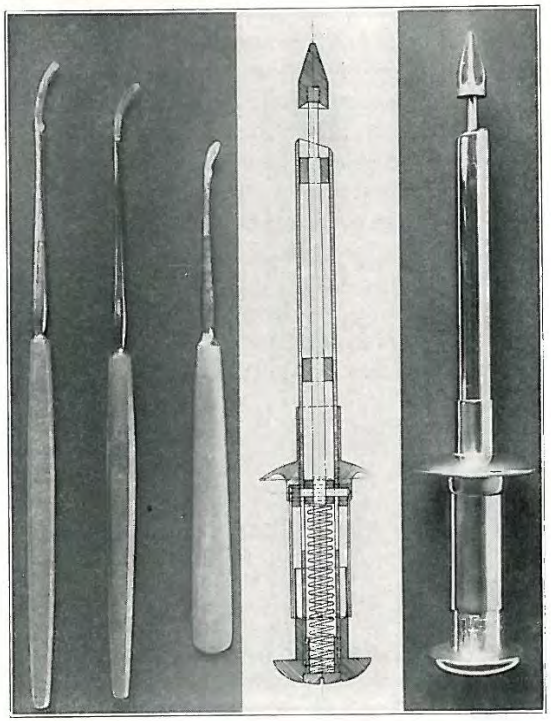


Devices



Access Communications for ACC; *Laslett LJ et al, J Am Coll Cardiol 2012; 60 Supp S: S1-S49*

THE PRESENT STATUS OF THE SURGICAL PROCEDURES IN CHRONIC VALVULAR DISEASE OF THE HEART

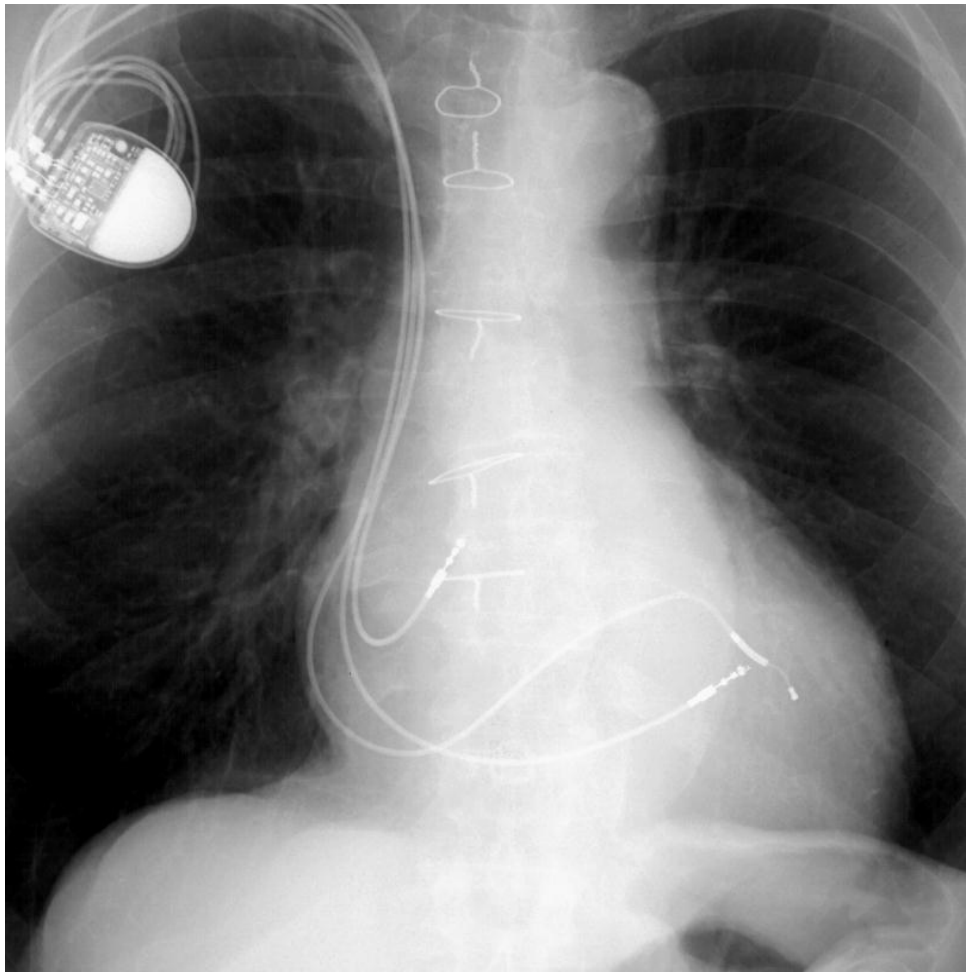


Statistical Table of Operations for Chronic Valvular Disease

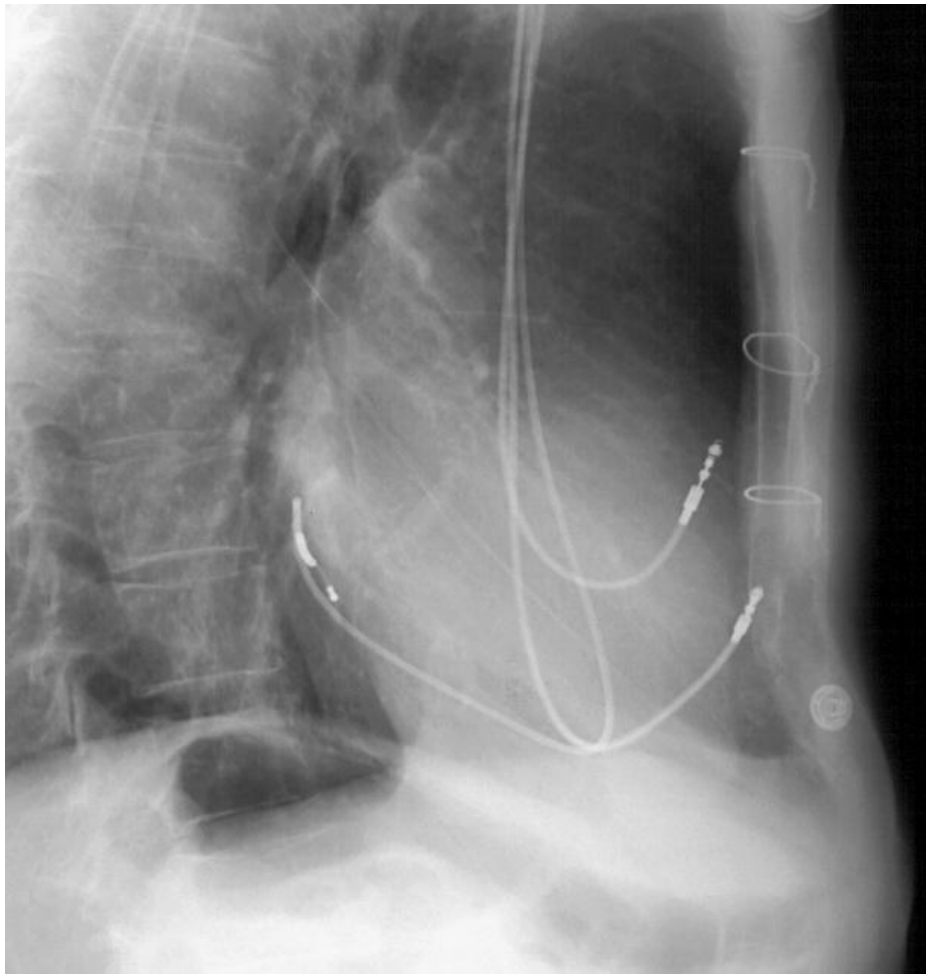
Case	Author or Operator	Date	Diagnosis	Method or Instrument	Result
1.	Doyen [1]	1913	Congenital pulmonary stenosis; patent interventricular septum	Tenotome	Died, few hours after operation
2.	Tuffier [2]	1914	Aortic stenosis	Finger dilatation	Recovery, improved
3.	Cutler and Levine: Boston M. & S. J. **188**: 1023, 1923	5/20/23	Mitral stenosis	Tenotome	Died, 4 years and 6 months after operation
4.	Allen and Graham [4]	8/ 7/23	Mitral stenosis	Cardioscope	Operative death
5.	Cutler, Levine and Beck [5]	10/ 7/23	Mitral stenosis	Tenotome	Died, 10 hours after operation
6.	Cutler, Levine and Beck [5]	1/12/24	Mitral stenosis	Tenotome	Died, 20 hours after operation
7.	Cutler, Levine and Beck [5]	2/25/24	Mitral stenosis	Cardiovalvulotome	Died, sixth day after operation
8.	Cutler, Levine and Beck [5]	6/11/24	Mitral stenosis	Cardiovalvulotome	Died, third day after operation
9.	Souttar [6]	5/ 6/25	Mitral stenosis and aortic insufficiency	Finger dilatation	Recovery, living and improved
10.	Pribram [7]	11/14/25	Mitral stenosis and aortic vegetative endocarditis	Cardiovalvulotome	Died, sixth day after operation
11.	Cutler and Beck (first report)	12/ 8/26	Mitral stenosis	Cardiovalvulotome	Died, 15 hours after operation
12.	Cutler and Beck (first report)	4/15/28	Mitral stenosis	Cardiovalvulotome	Died, 3 hours after operation
Totals:	12 cases 1 aortic stenosis, acquired 1 pulmonary stenosis, congenital 10 mitral stenosis, acquired			2 finger dilatations 4 tenotome attempts 5 cardiovalvulotome attempts 1 cardioscope attempt	Mortality, 83 per cent

Cutler EC and Beck CS, Arch Surg 1929; 18: 402-16

To Ventricular Resynchronisation



Anterior-posterior



Lateral

Jean-Claude Daubert

Cardiac Resynchronisation Therapy in Heart Failure

- ***1989:*** **Concept, atrial resynchronisation, biatrial pacing** *JC Daubert*
- ***1993:*** **Concept of ventricular resynchronisation by BiV pacing**
  LBBB and HF: *S Cazeau*
- ***1993-1999:*** **Acute hemodynamic studies with temporary pacing**
  S Cazeau, JJ Blanc, C Leclercq, A Auricchio, D Kass
- ***1993-1996:*** **Early implantations in man with existing technology**
  Epicardial (P Bakker, S Cazeau) or CS leads (JC Daubert)
- ***1997:*** **Dedicated triple-chamber devices (integrated Y adaptor)**
- ***1998-2000:*** **Observational studies of chronic CRT pacing**
- ***2000-2001:*** **Animal models** (*Christophe Leclercq, David Kass)*
- ***2001:*** **1st randomised study for proof of concept** *MUSTIC*
  With the ESC as promotor

Some Reasons for Success Story

- Original and simple (or simplistic) concept based on clinical observation
- Easy to validate in acute studies with temporary pacing
- Initial development with existing implantable technology, even suboptimal
- Limited dependence from the industry in the early phase
- Limited regulatory issues
- Support of a well-recognised professional association (ESC) to promote the first trial

BMJ

BMJ 2011;342:d3021 doi: 10.1136/bmj.d3021

Commentary: The risk of over-regulation

C Di Mario *professor*[1], S James *associate professor*[2], D Dudek *professor*[3], M Sabate *professor*[4], M Degertekin *professor*[5]

" The doctor is directly accountable to the patient and is expected to have the competency and motivation to select appropriate devices and drugs "

Continuity and innovation: the *yin* and *yang* of interventional cardiology

Carlo Di Mario[1]*, MD, PhD, FESC, *outgoing President EAPCI 2009-11*; Stephan Windecker[2], MD, PhD, FESC, *President-Elect*; Jean Fajadet[3], MD, PhD, FESC, Toulouse, France, *in-coming President 2011-13*

Cardiovascular Research Unit, Royal Brompton Hospital & Harefield Foundation Trust, London, United Kingdom; Bern University Hospital, Bern, Switzerland; Clinique Pasteur, Toulouse, France

EuroIntervention 2011;7:425-427

BMJ

Commentary: International collaboration needed on device clinical standards

Alan G Fraser *reader in cardiology*[1], Mitchell W Krucoff *professor of medicine/cardiology*[2], Ralph G Brindis *immediate past president, American College of Cardiology*[3], Michel Komajda *president, European Society of Cardiology*[4], Sidney C Smith Jr *president, World Heart Federation*[5]

Patients everywhere should be protected by similar requirements for medical devices to be safe and effective

BMJ 2011;342:d2952

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Clinical product standards

(for all Class II and Class III devices)

- Bench testing, hydrodynamics, simulations
- Appropriate biological and animal models
- Requirements for clinical evaluation
- Need for randomised clinical trials, design, duration, number of patients
- Define when equivalence acceptable
- Give limits to iterative changes
- Conditional approval
- Post-market surveillance

EUR**Observational** Research Programme

- Representative of Europe
- Conducted by ESC Constituent Bodies (Associations and Working Groups, National Cardiac Societies)
- Management centralised at EHH (EORP Department)
- In cooperation with, but independent from Industry (database management and ownership, data analysis and publication by ESC)

EACPR European Association for Cardiovascular Prevention and Rehabilitation A Registered Branch of the ESC

EACVI EUROPEAN ASSOCIATION OF CARDIOVASCULAR IMAGING A Registered Branch of the ESC

HEART FAILURE ASSOCIATION OF THE ESC

EUROPEAN Heart Rhythm ASSOCIATION A Registered Branch of the ESC

EAPCI A Registered Branch of the ESC

Acute Cardiovascular Care Association A Registered Branch of the ESC

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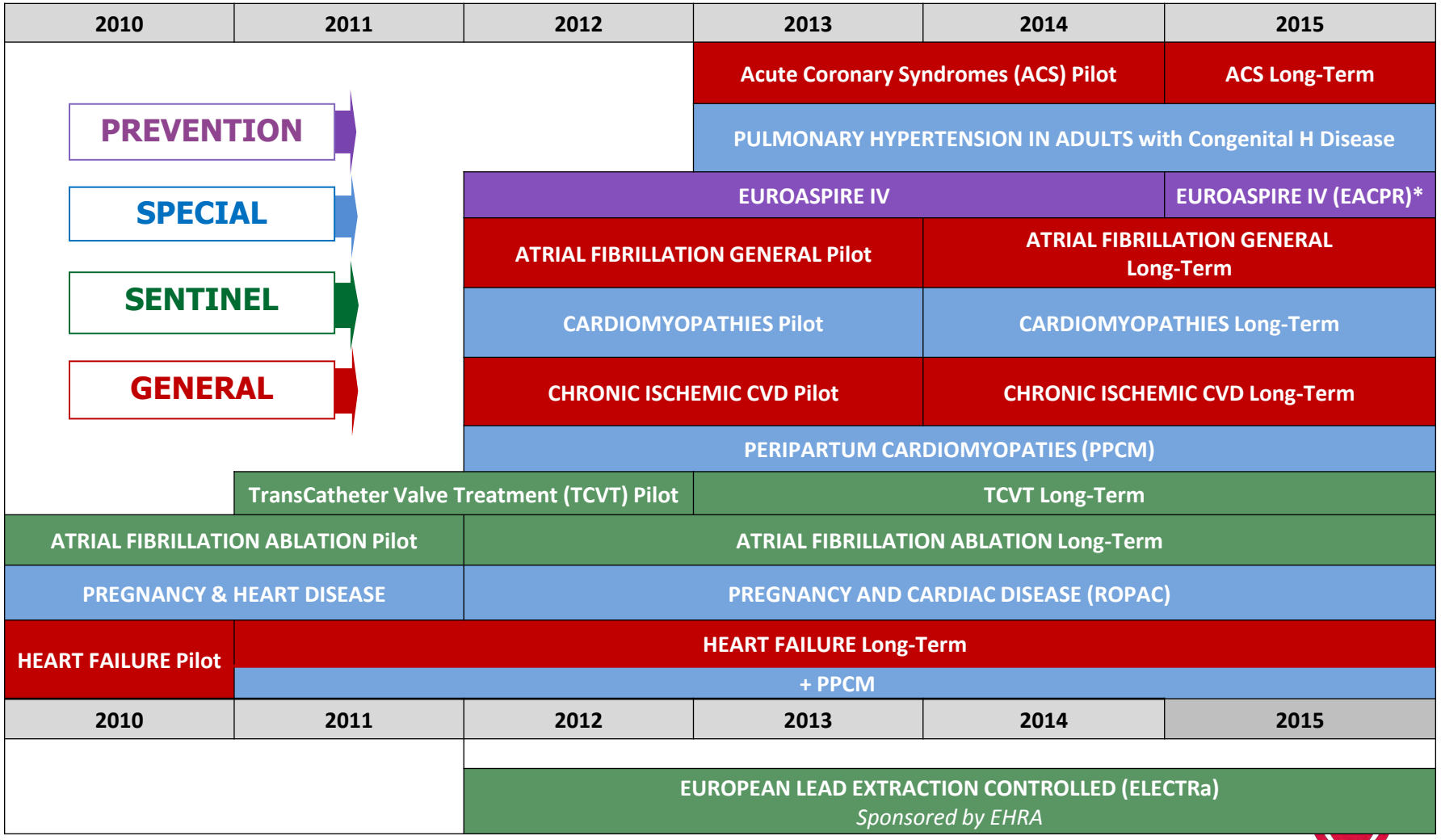
The EORP Registries 2010 – 2015



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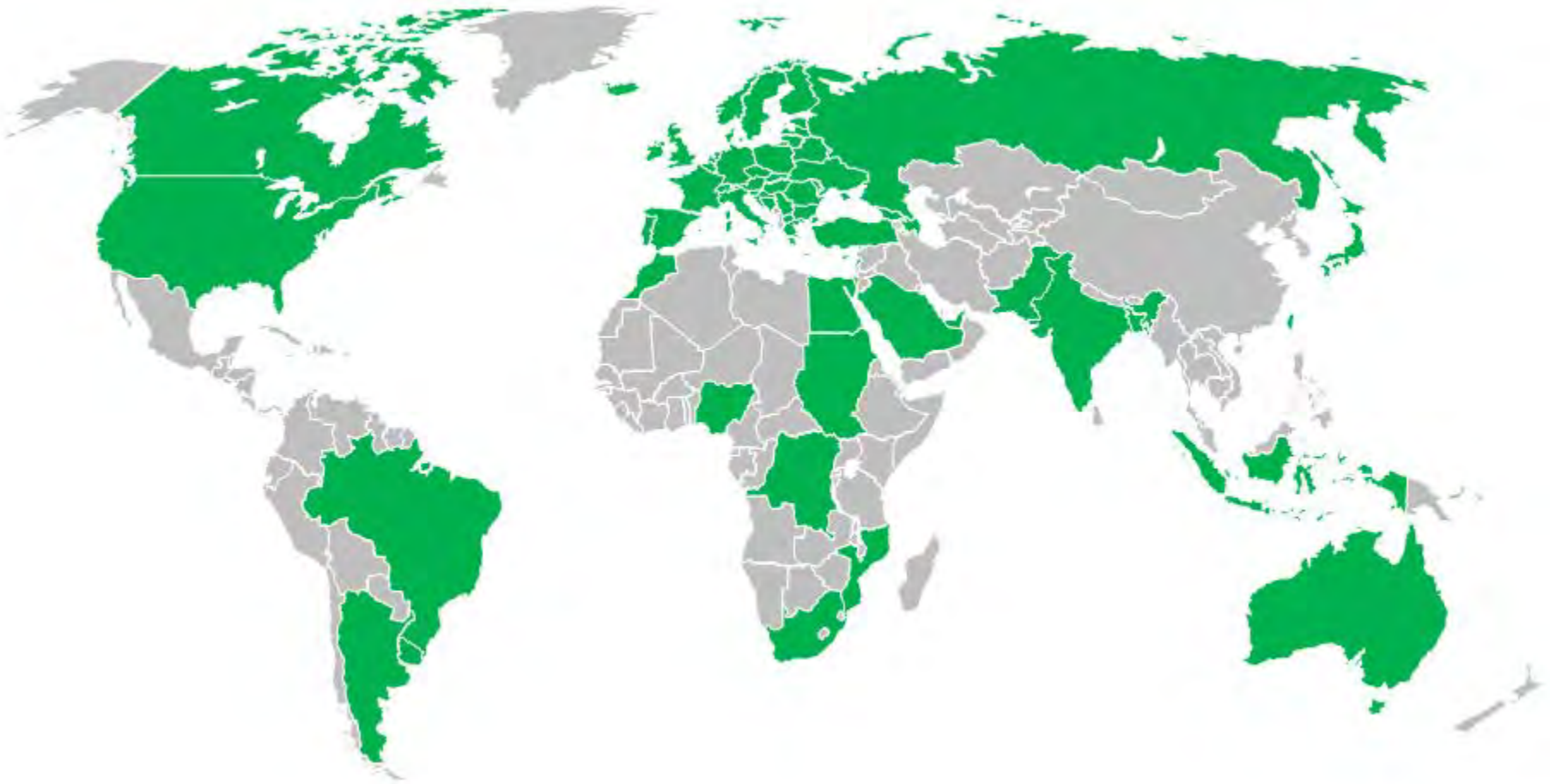
64 Countries, >1000 centres, participating in at least one EORP Registry, >50,000 patients



SWEDEHEART 2011 Annual Report

Issued 2012

RIKS-HIA
PRESENTED BY
Tomas Jernberg, Claes Held and Per Johanson

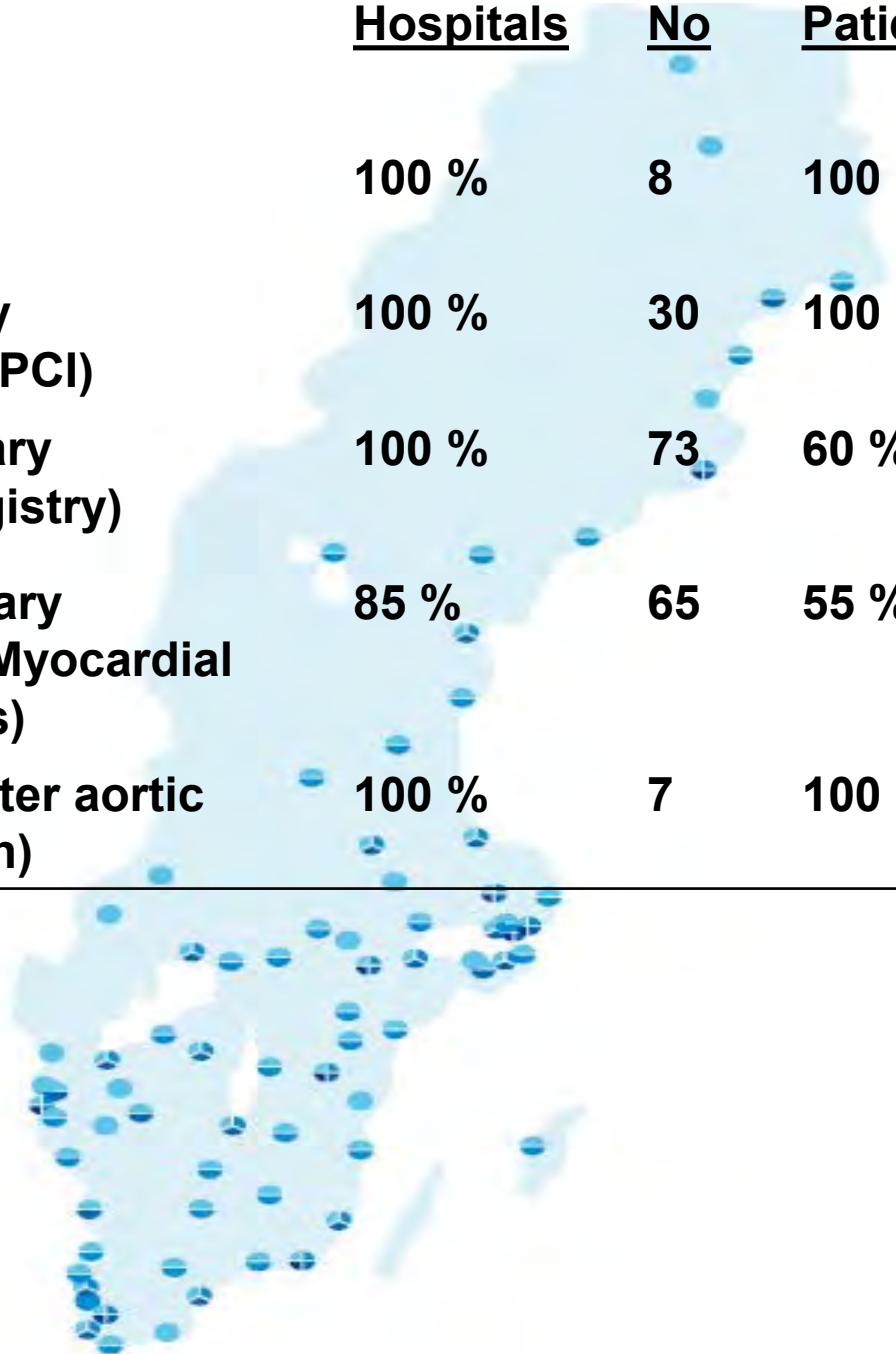
SEPHIA
PRESENTED BY
Kristina Hambraeus, Åsa Cider and Lars Svennberg

SCAAR
PRESENTED BY
Stefan James and Bo Lagerqvist

Hjärtkirurgi
PRESENTED BY
Örjan Friberg and Johan Nilsson

TAVI
PRESENTED BY
Johan Nilsson

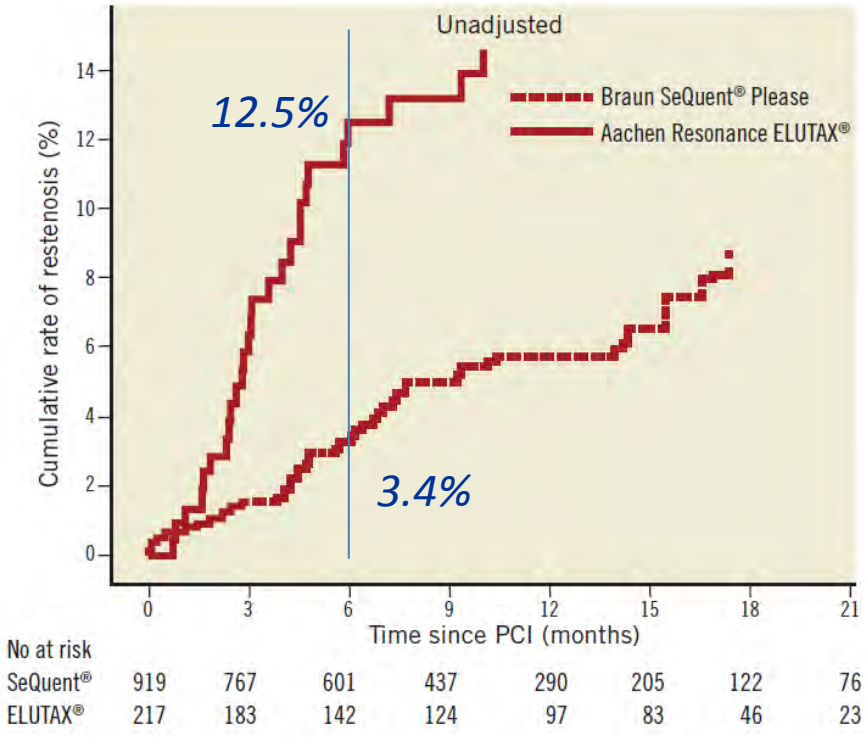
	Hospitals	No	Patients	Annual No
Thoracic surgery	100 %	8	100 %	7,000
SCAAR (Coronary angiography and PCI)	100 %	30	100 %	40,000
RIKS-HIA (Coronary intensive care registry)	100 %	73	60 %	50,000
SEPHIA (Secondary Prevention After Myocardial Infarction, <75 yrs)	85 %	65	55 %	5,500
TAVI (Trans-catheter aortic valve implantation)	100 %	7	100 %	150

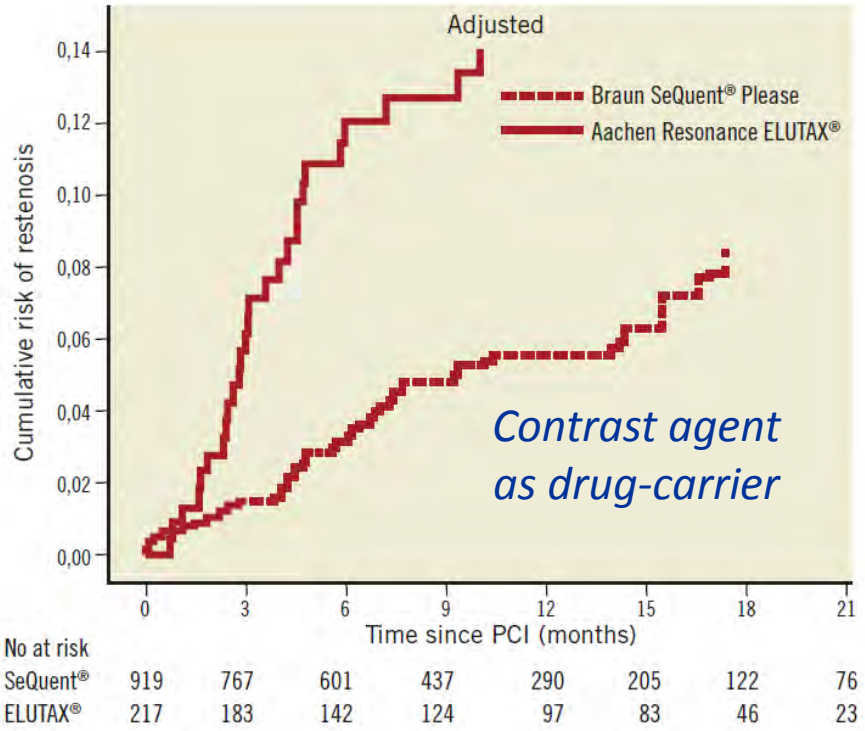


The Swedeheart registry (SCAAR)

Comparison of paclitaxel drug-eluting ***balloons***

De-novo restenosis and in-stent restenosis of bare metal stent



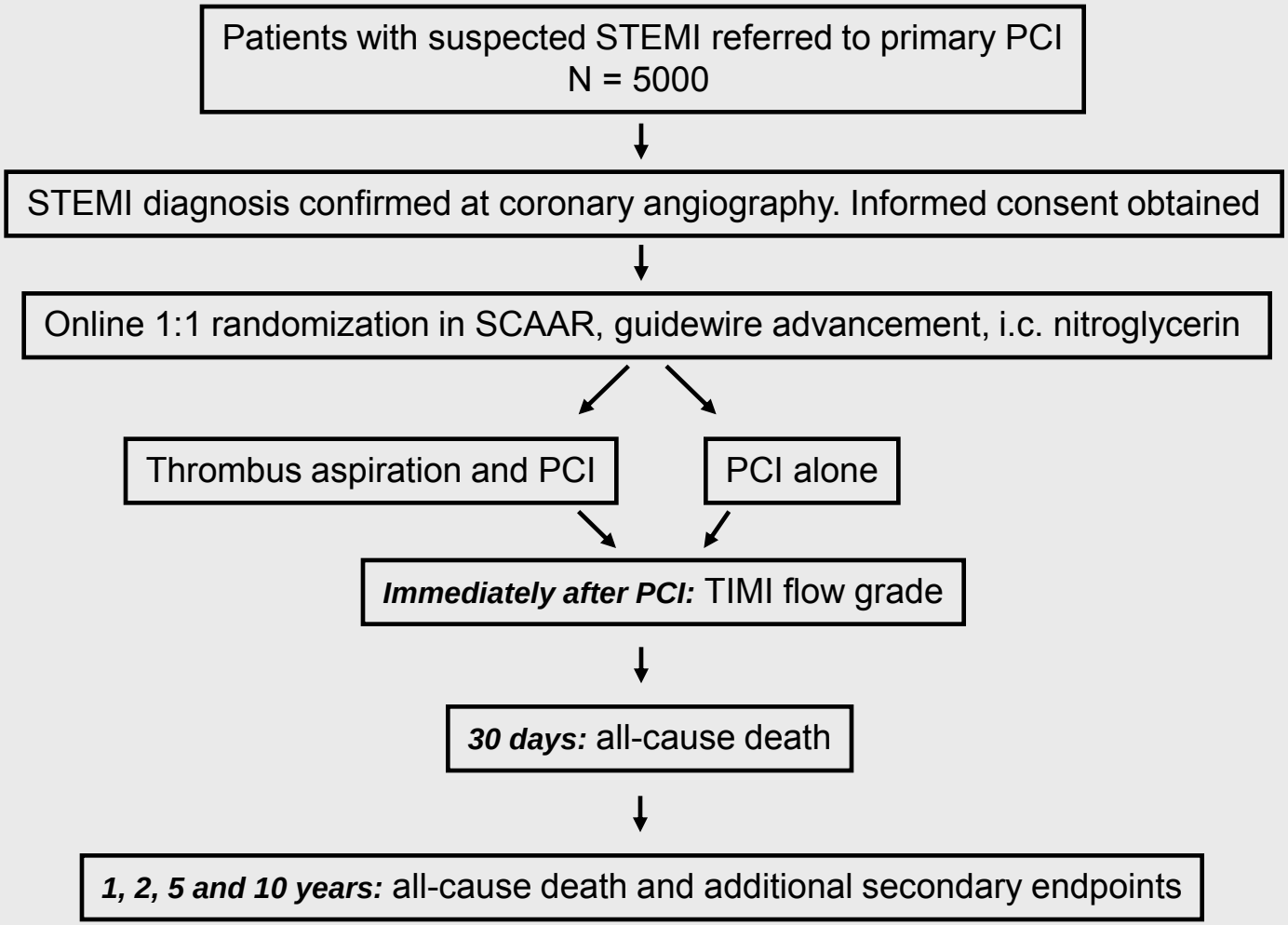


Bondesson P et al, Eurointervention 2012; 8: 444-9

TASTE trial flow chart

SCAAR SWEDEHEART

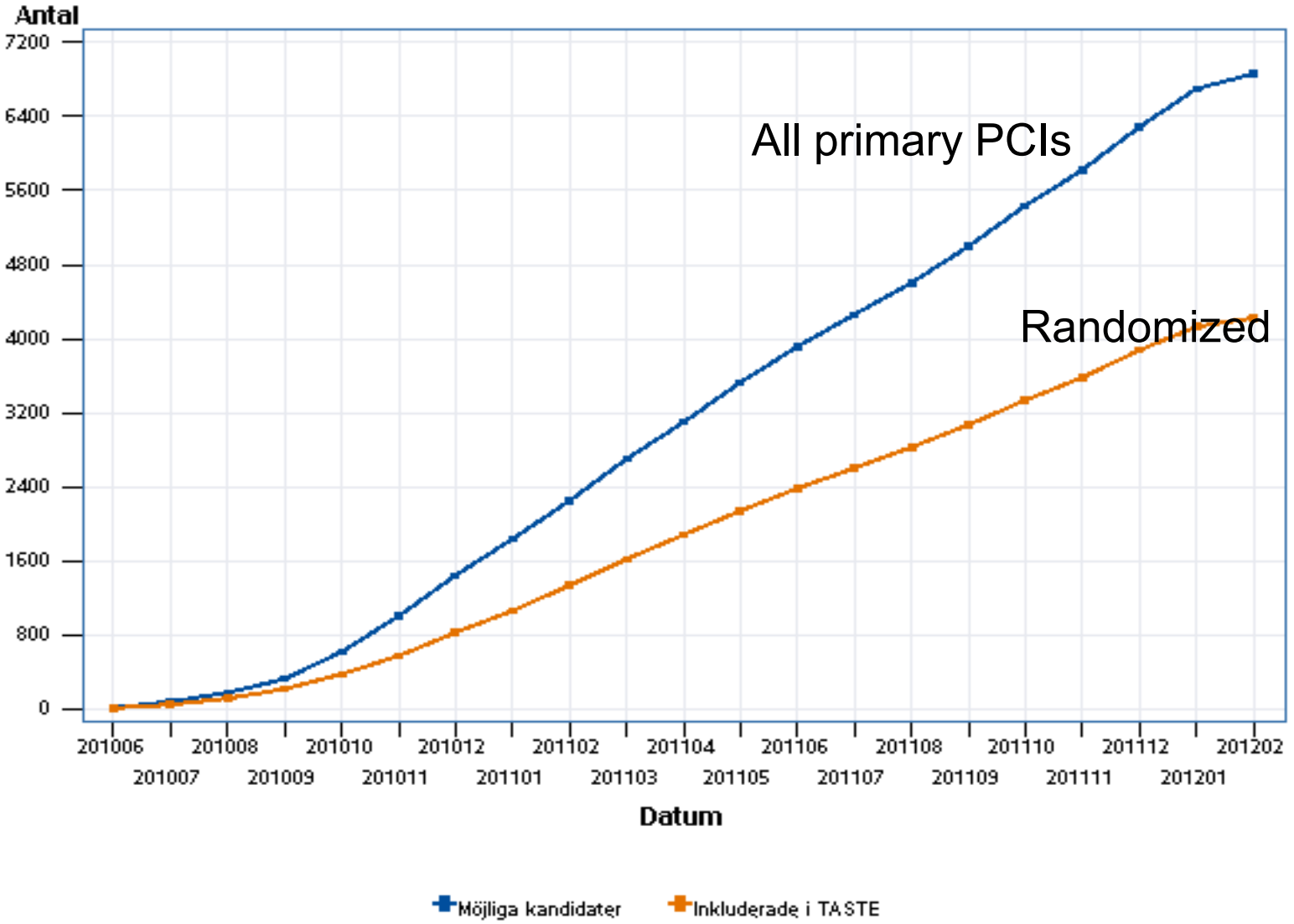
Thrombus Aspiration in ST-Elevation MI in Scandinavia



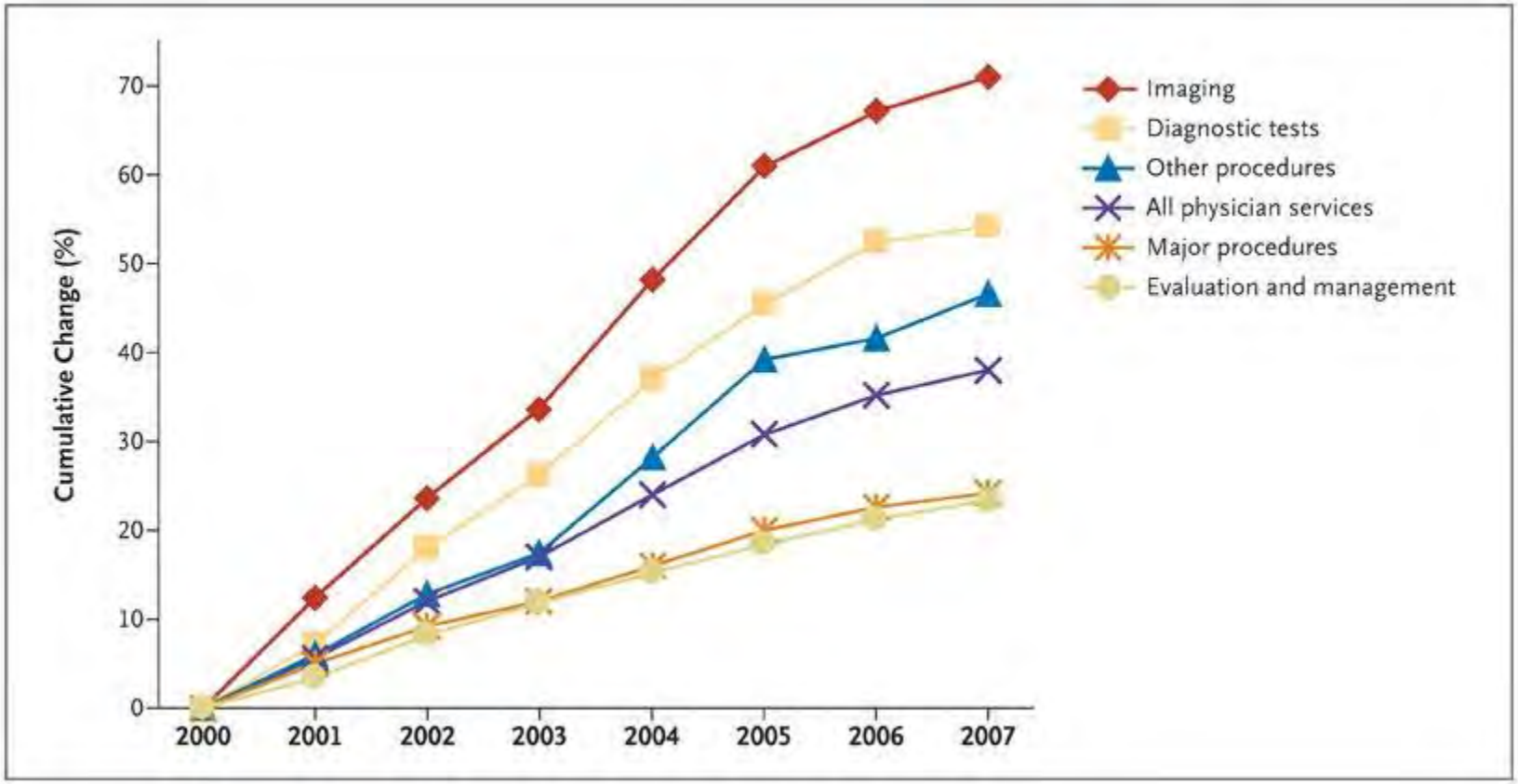
Fröbert et al, AHJ 2009

Inclusion rate

SCAAR
SWEDEHEART



The growth of diagnostic imaging and tests

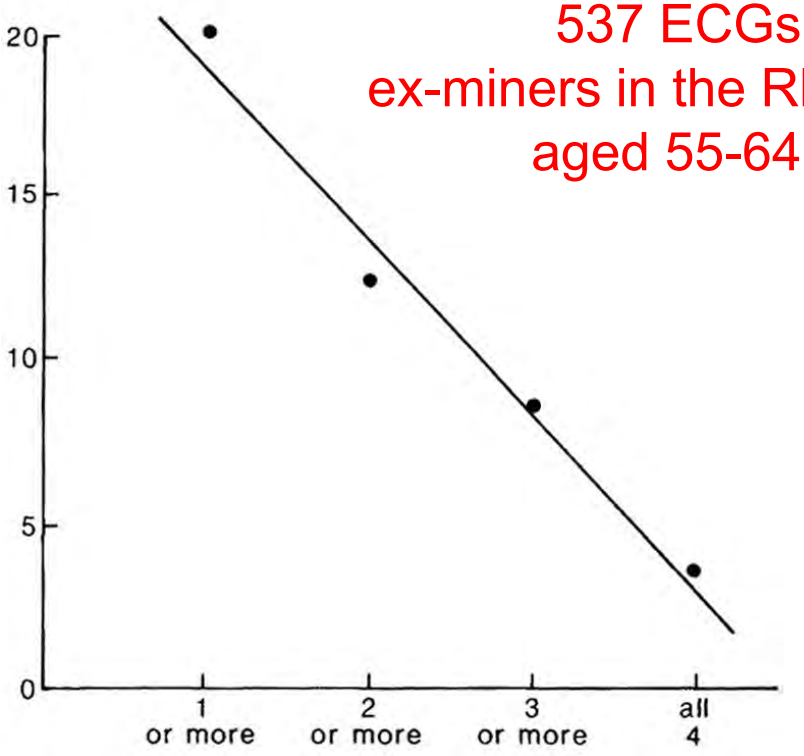


Iglehart JK, NEJM 2009; 360; 1030-37

Diagnosis of coronary artery disease

537 ECGs from
ex-miners in the Rhondda Fach
aged 55-64 years

Percentage of ECGs with concordant positive diagnosis

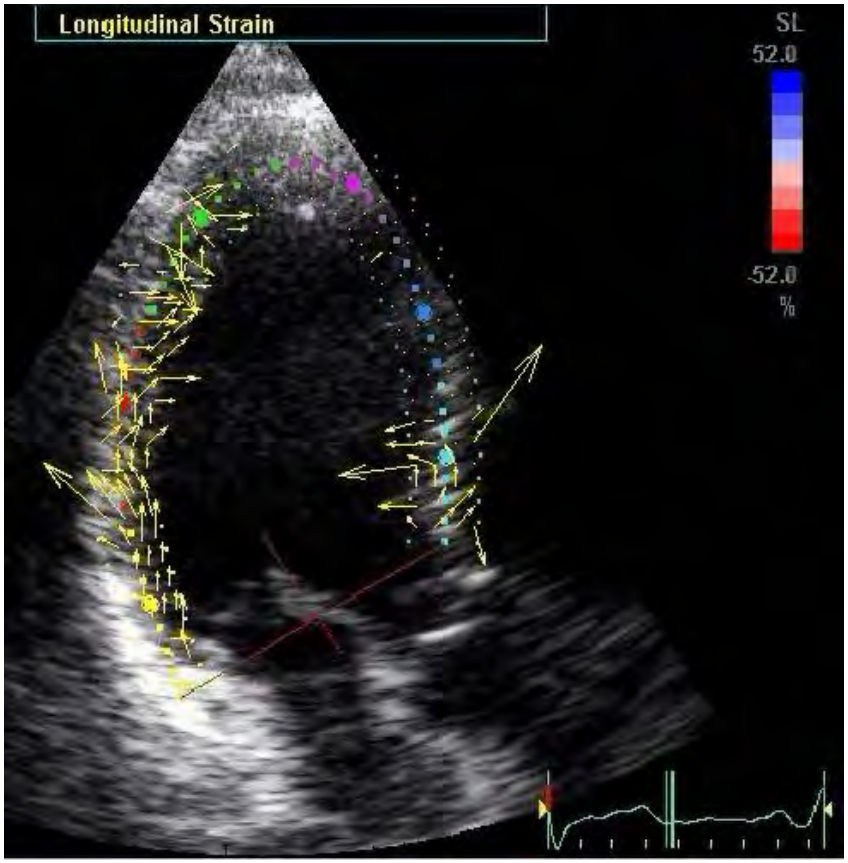


Number of observers

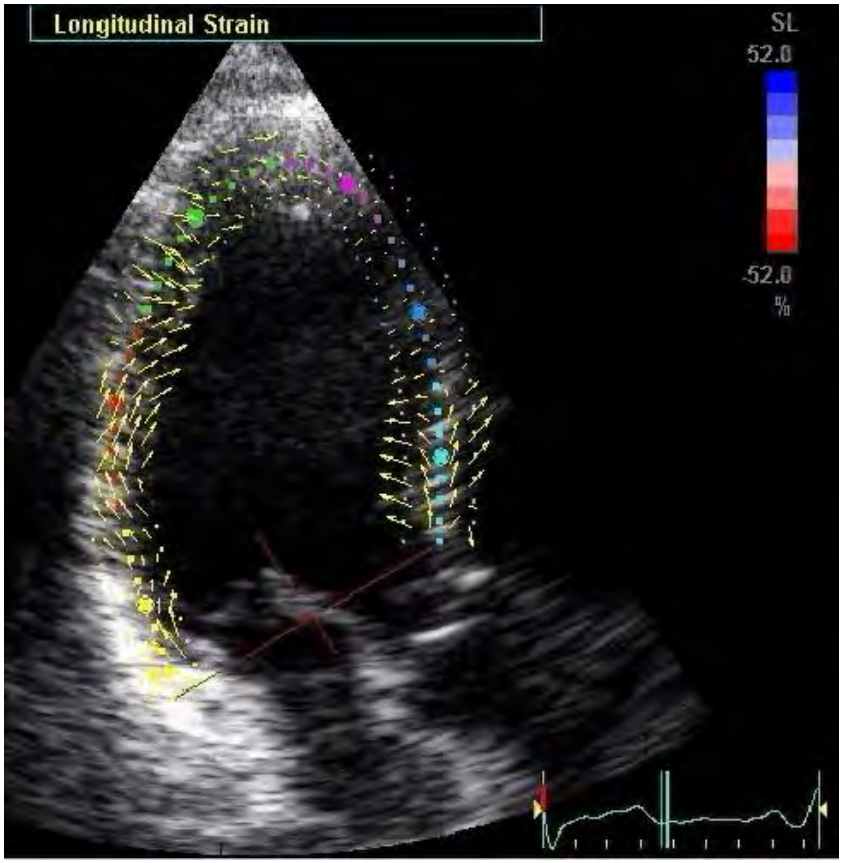
Epidemiological studies of coronary disease
Higgins IT, Cochrane AL, Thomas AJ
Br J Prev Soc Med 1963; 17: 153-65

Image processing – velocity vector imaging

“Raw” velocity field (initial estimate)

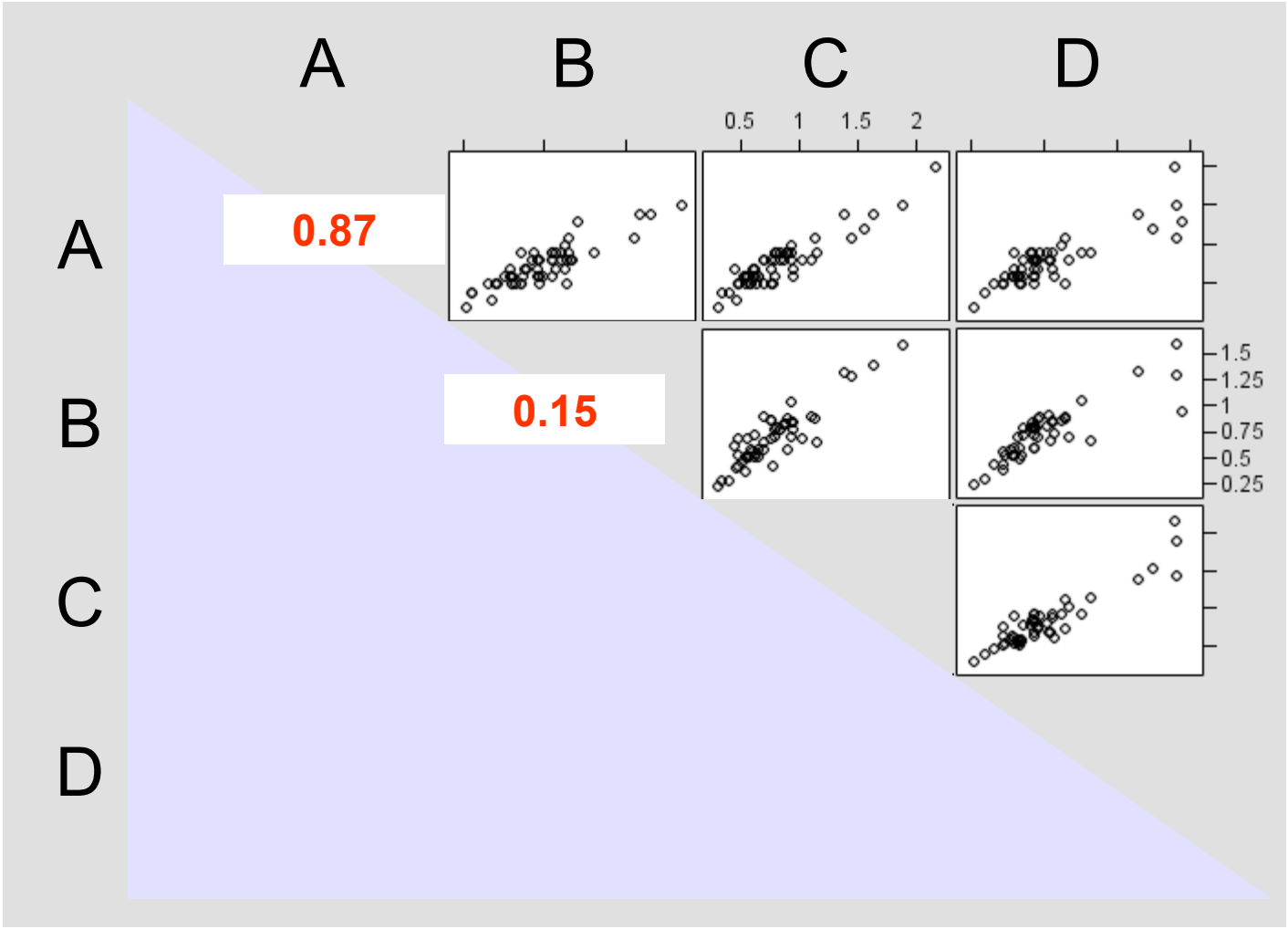


“Filtered” velocity field (after post-processing)



Courtesy of Dr MS Feinberg

60 patients studied on 4 echocardiography machines



Blood pool Doppler

R = 0.85-0.93

Myocardial strain

R = 0.02-0.35

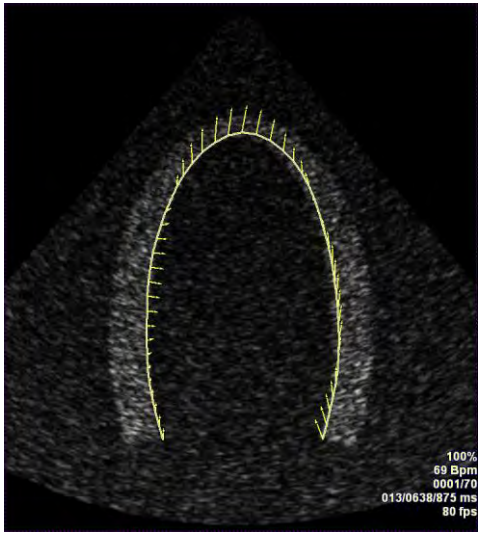
GE, Aloka, Toshiba, Acuson

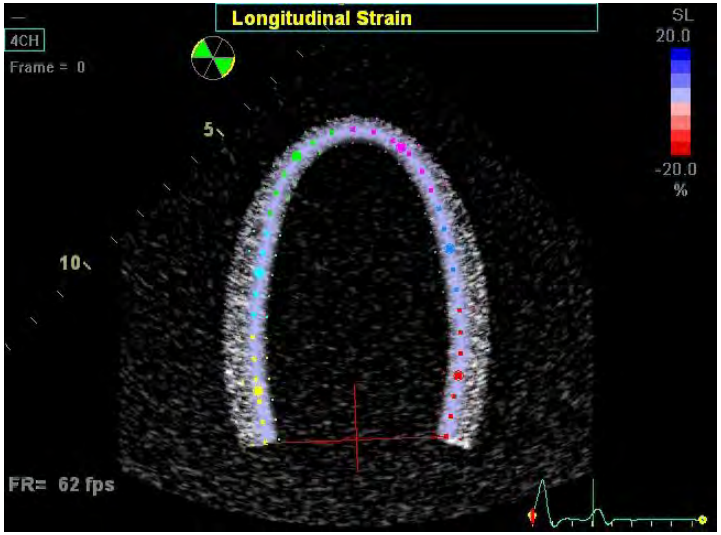
Andrew Williams et al

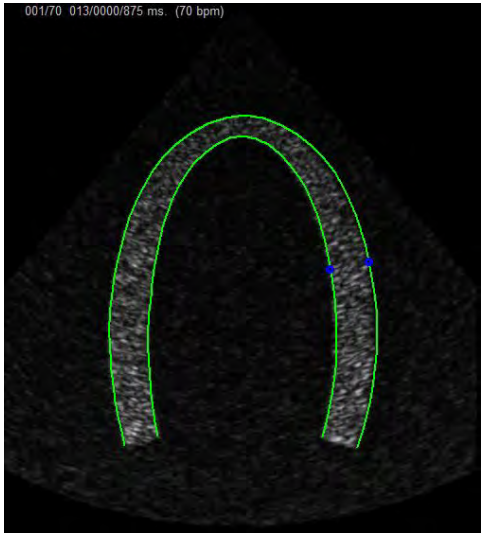
Inter-operability of deformation by speckle tracking

Joint EACVI and ASE initiative with major vendors

Vendor A **Vendor B** **Vendor C**







- Nomenclature and diagnostic targets
- Simulated data-sets
- Software revisions

Courtesy J D'hooge

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Strategic reflections from ESC for IMDRF

- Physicians need to understand medical device evaluation and practice evidence-based medicine
- Professional associations should engage in clinical product standards for medical devices, and in quality
- Convergence of evidence (systematic reviews and guidelines) and standards (safe and effective practice) but not of regulatory governance
- Flexibility for clinical need in rare or life-threatening diseases
- Independent post-market surveillance and registries
- Joint initiatives with industry for unmet needs