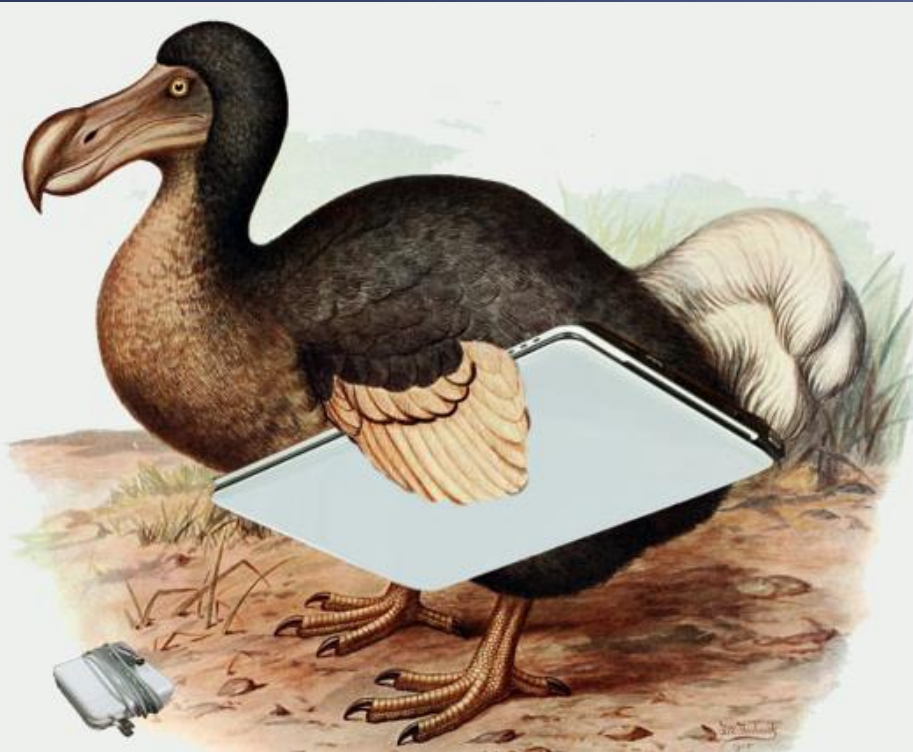


New Technology From Bench to Clinical Practice

Alexandra J Lansky, MD

Yale University School of Medicine
University College of London

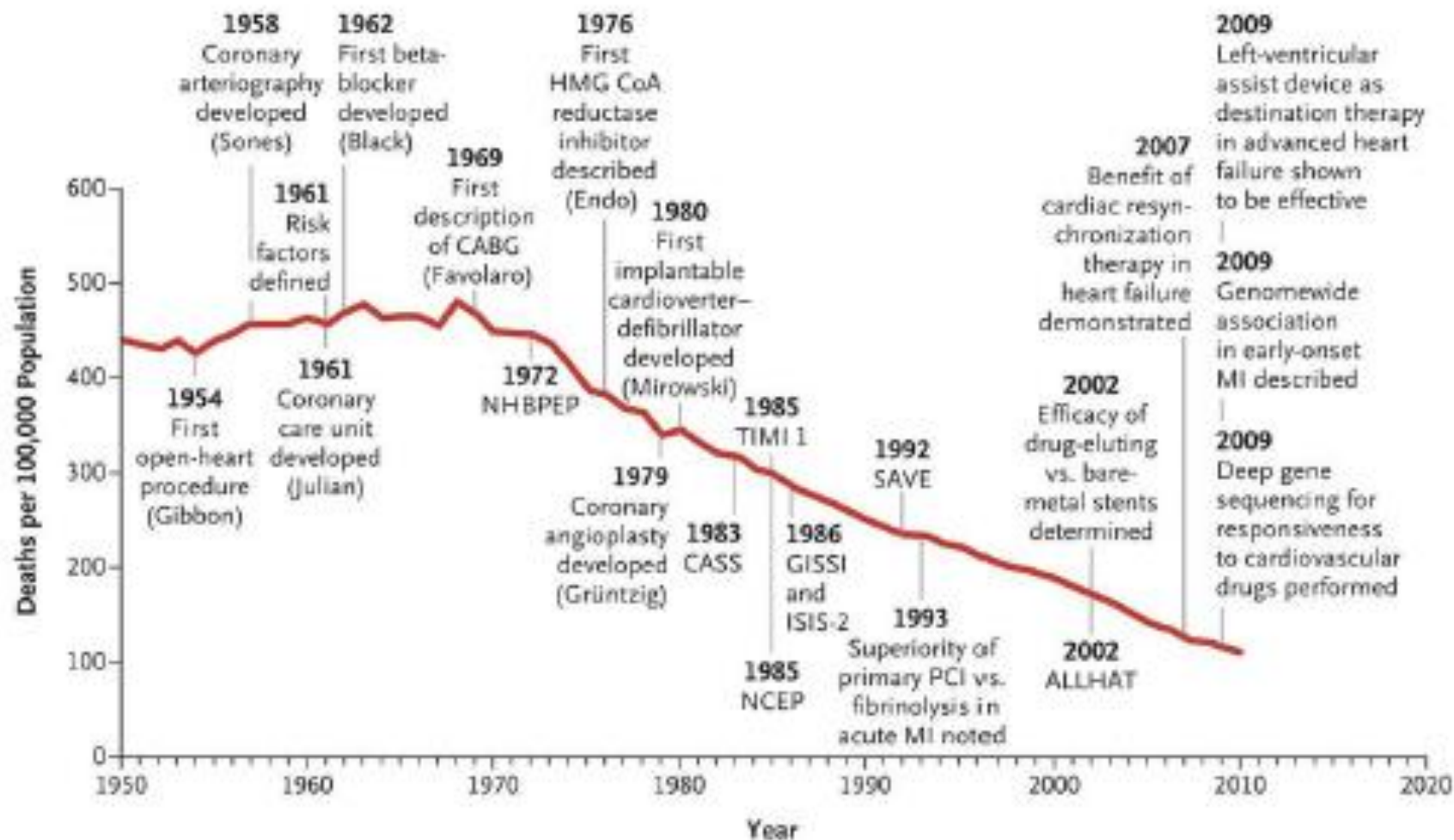
Innovation is inevitable... Do you want to part of it?



It is not the strongest species that survives, nor the most intelligent, but rather the one most adaptable to change.

----- Charles Darwin

Decline in CV mortality relative to Scientific Advances



Medical Innovation

Technology Progress

30 yrs of iterative AMI therapies

- progressive improvements in “core” product performance
- incremental (continuous) or radical (discontinuous)
- comprises most technology advances

Sustaining Technologies

<10 yrs of breakthrough TAVI therapy

- new market applications
- with improved performance, rapidly supplants standard conventional technology
- more risky, but can change treatment paradigms

Disruptive Technologies

Medical Device Development Costs have Increased...

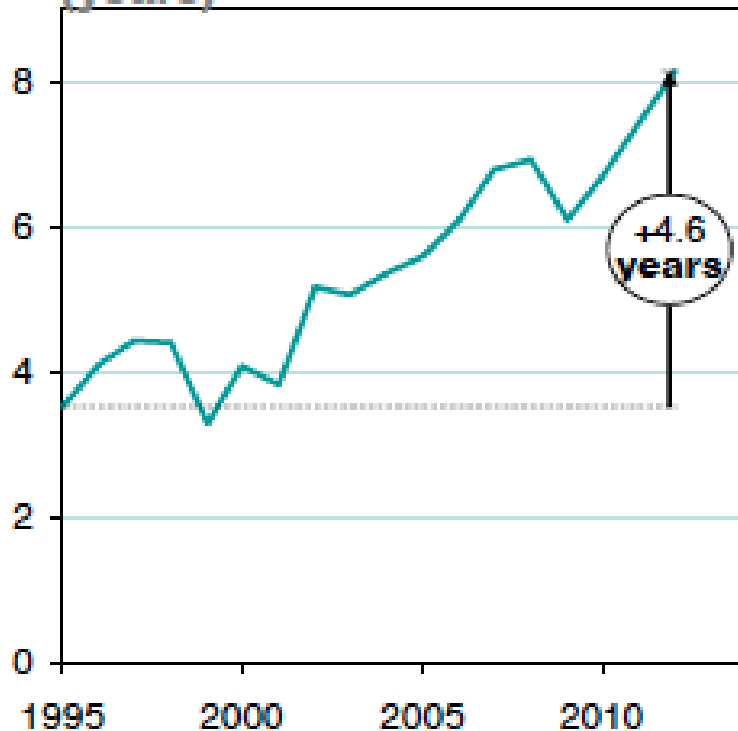
- Greater Evidence Requirements
 - Regulatory pathway; Reimbursement, Physicians, Patients
- Greater Emphasis on Safety
 - More Bench testing
 - More Preclinical Testing
 - Larger Clinical trials, better outcomes
- Greater Emphasis on Economic Benefit
 - National or 3rd party Payers

Time and Cost to Build Companies has Grown

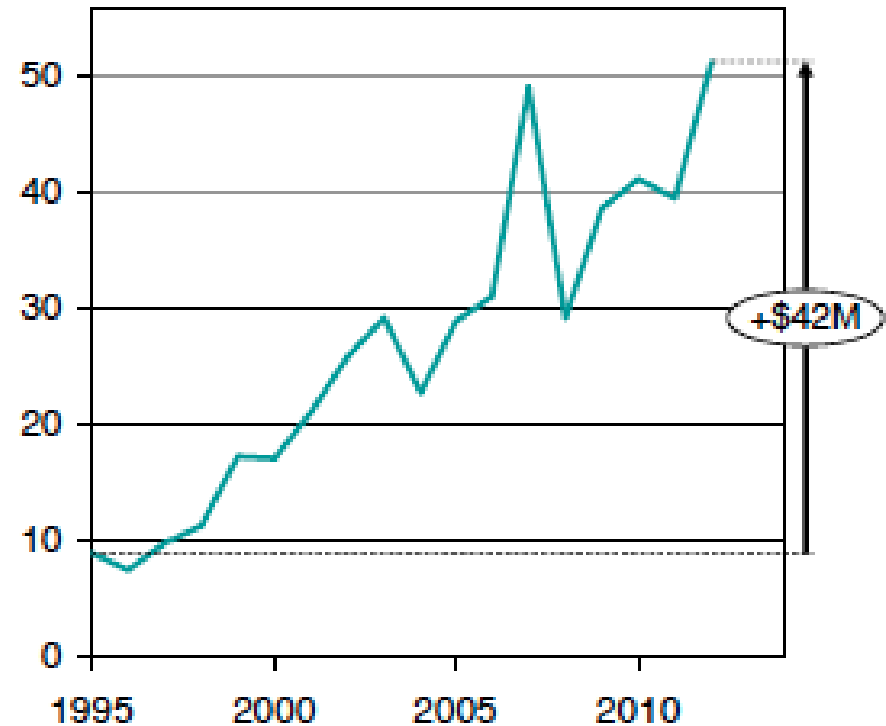
Time to exit VC backed device co has doubled at 4x investment

Median Time to Acquisition of US Venture-Backed HC Companies by Year of Exit

(years)



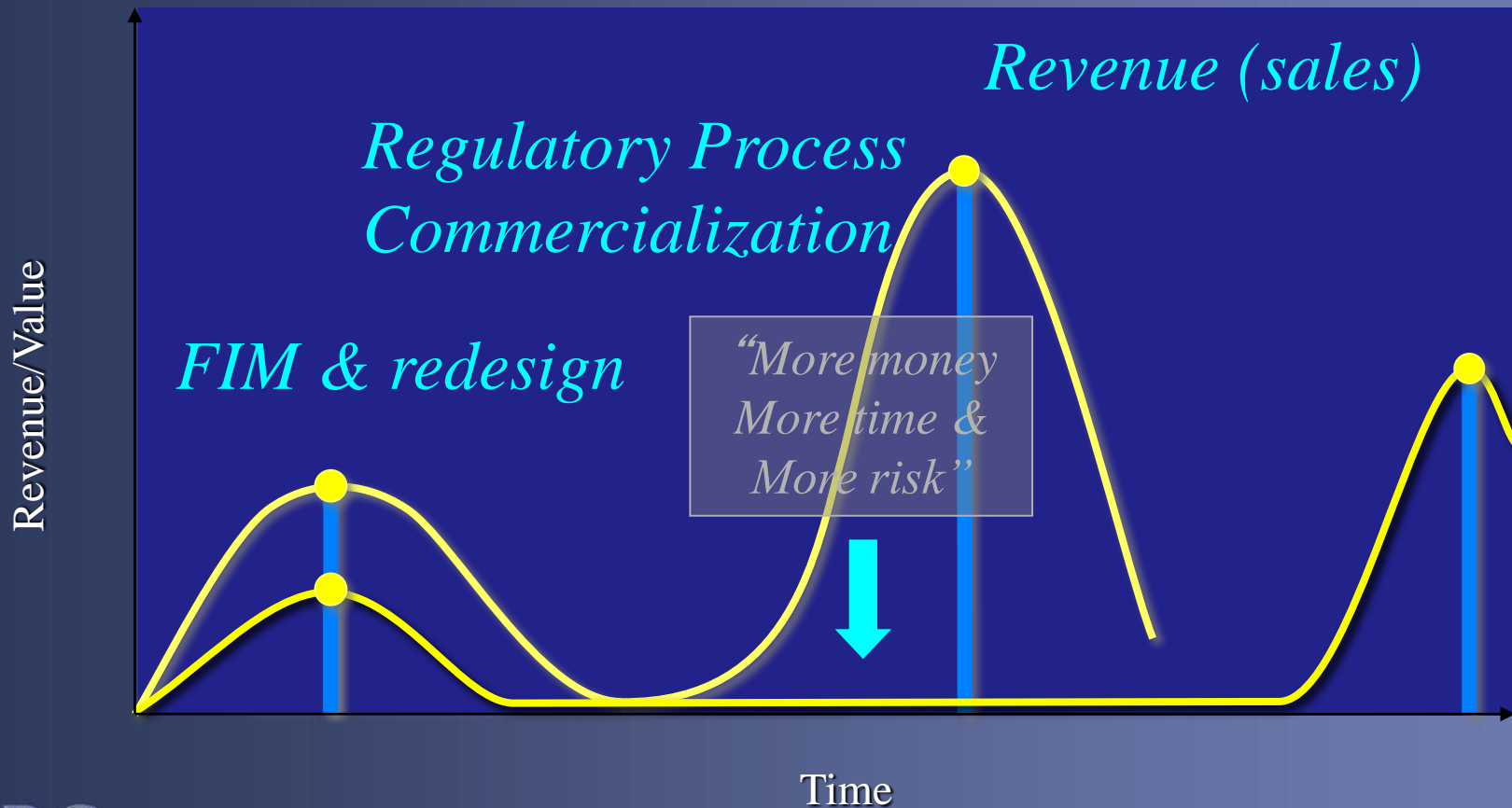
Average Equity Raised to Acquisition by Year of Exit (\$Millions)



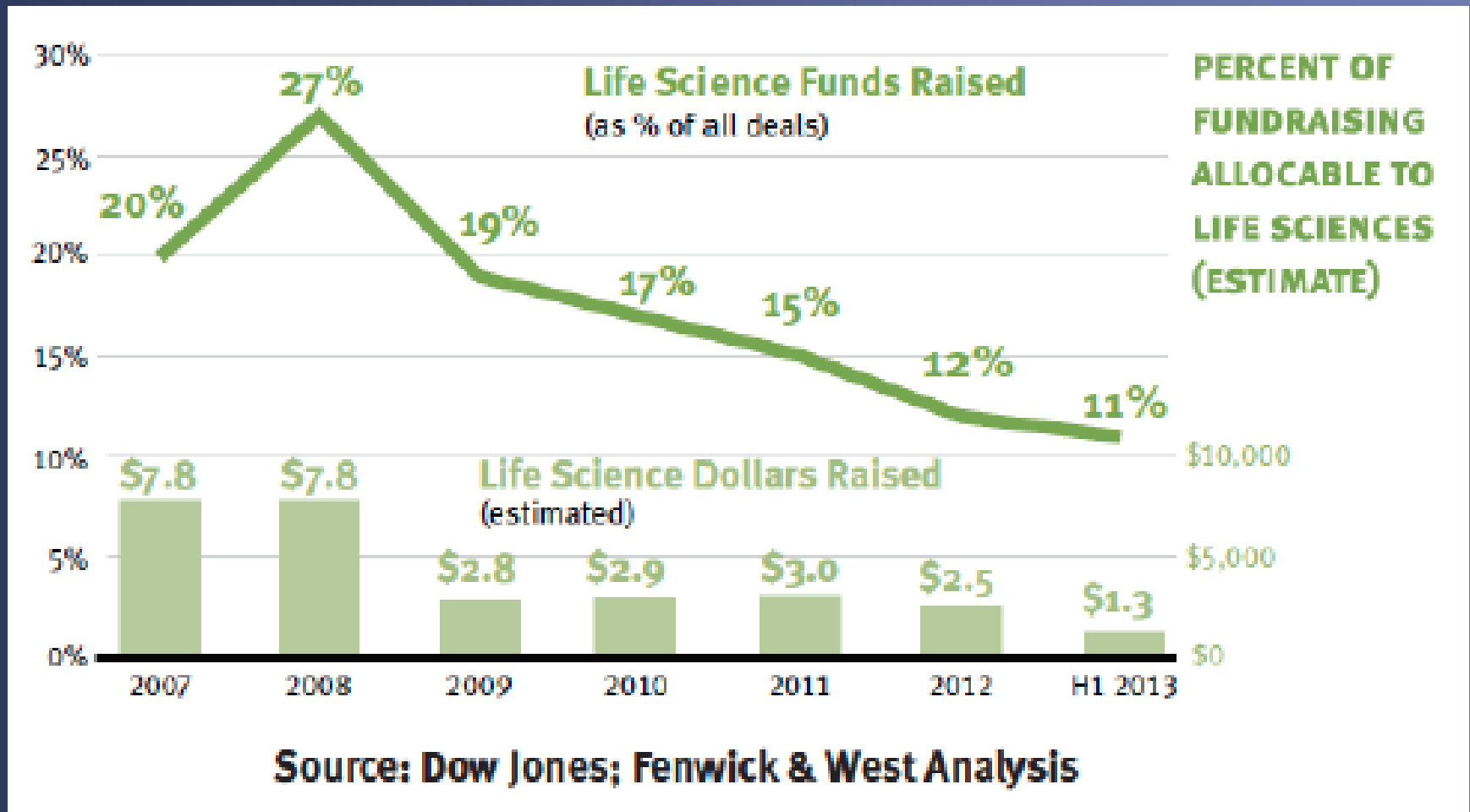
VentureSource; August 2012

Medical Device Cycle

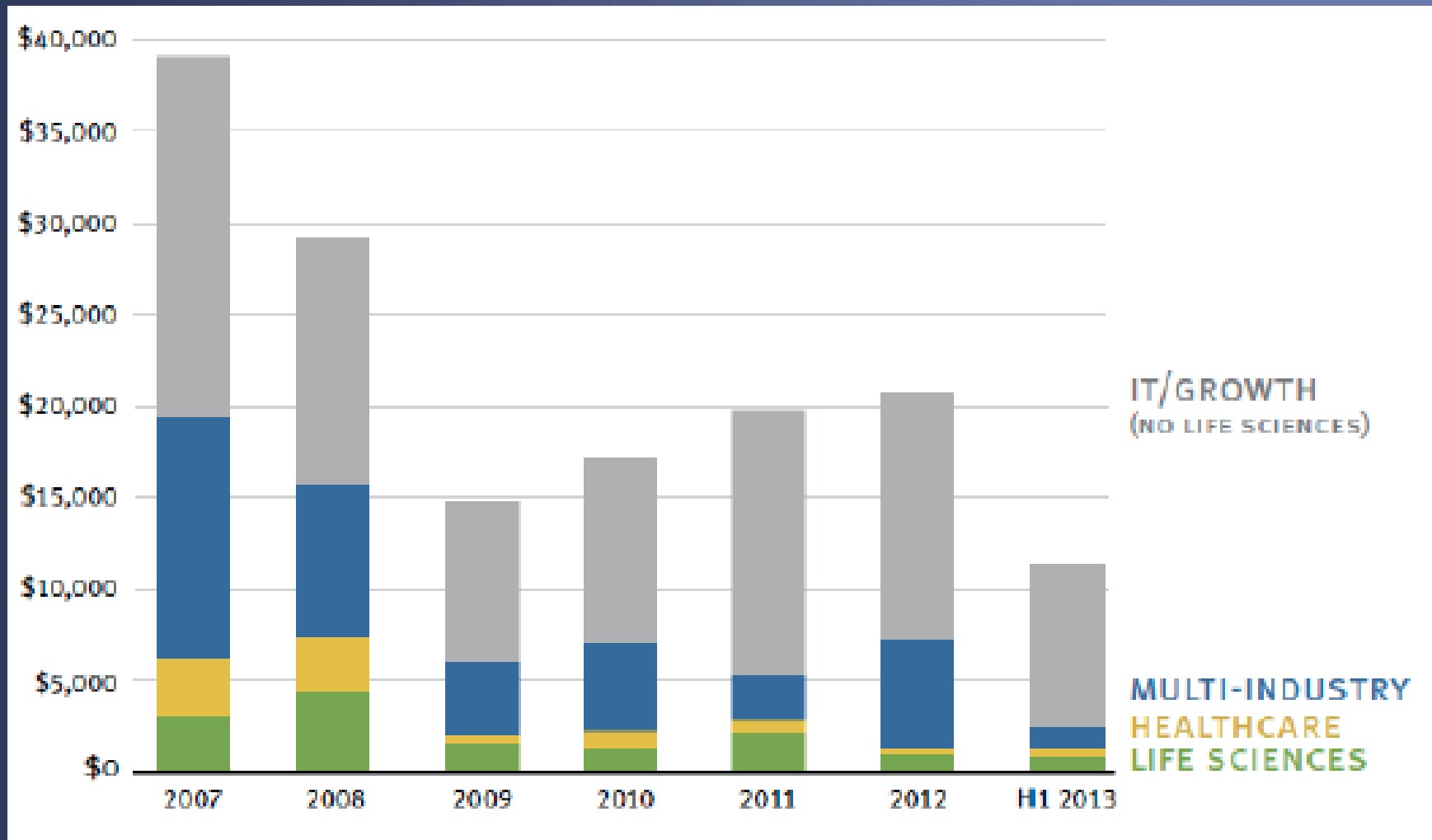
Changing Landscape



LifeScience VC Funds Trends



VC Fundraising by Sector



The Changing US Landscape...

Development
Implementation
+
Innovation

Off Shore

Off Shore

Taiwan
India
China
Singapore

Israel
Switzerland

Private
Innovation
Centers

MedTech of the past

- Technology that improved healthcare
- Focused on the physician as the decision maker
- Good margins supporting R&D and sales
- Funding of internal high risk R&D
- Early stage investments in external high risk technologies
- Venture money readily available

MedTech of today

- Decreases in reimbursement rates
- Hospital best pricing, “Bundling”
- Restricted use of premium devices
- “Finding efficiencies”, “Restructuring”, “reducing risk”
- Modest early stage organic R&D investment
- Less investment in early stage companies
- Less venture money available

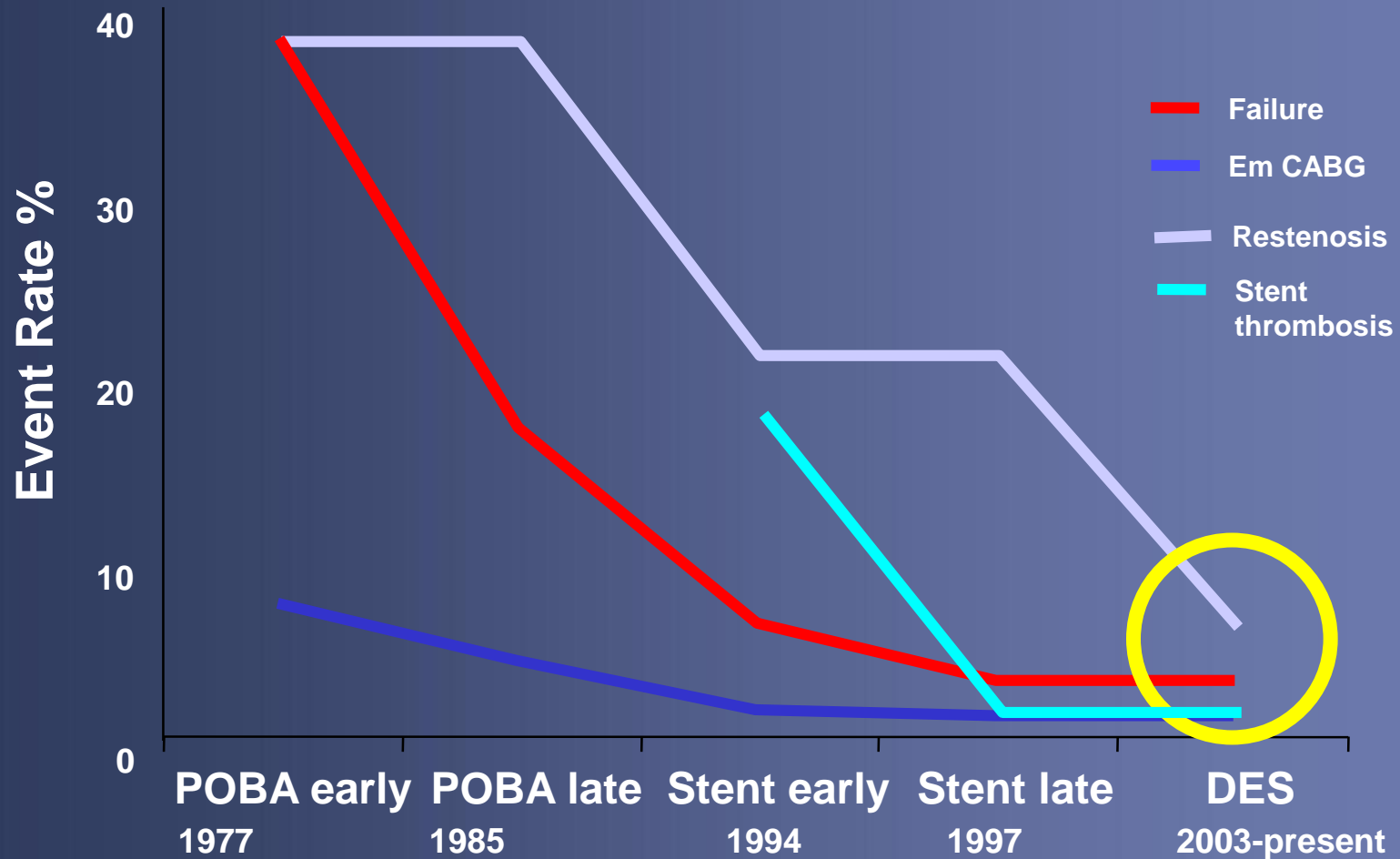
The Game Has Changed....



- “its not good enough to be better. You must be cheaper

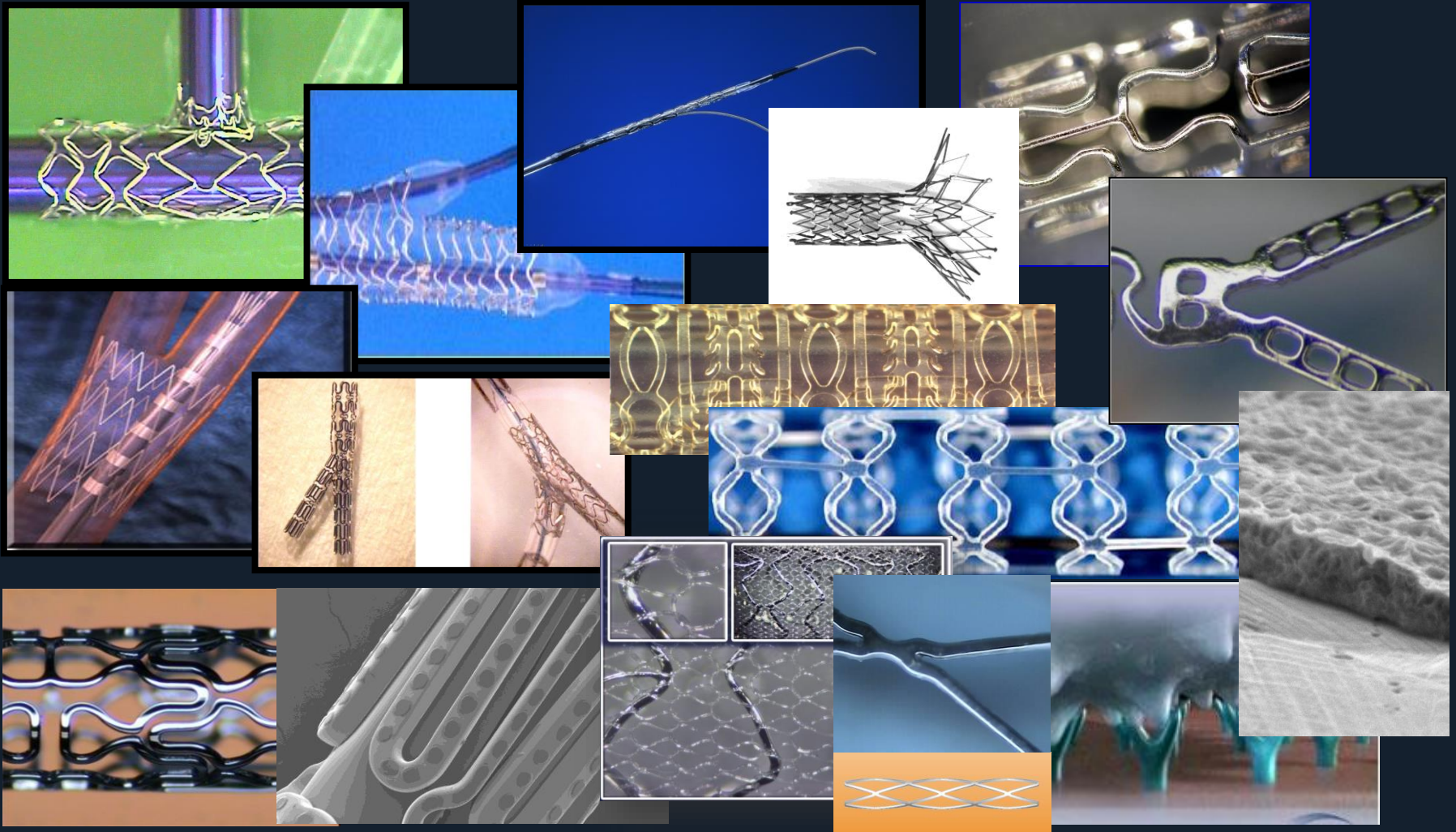
Some Procedural Trends...

PCI: Incremental Improvements



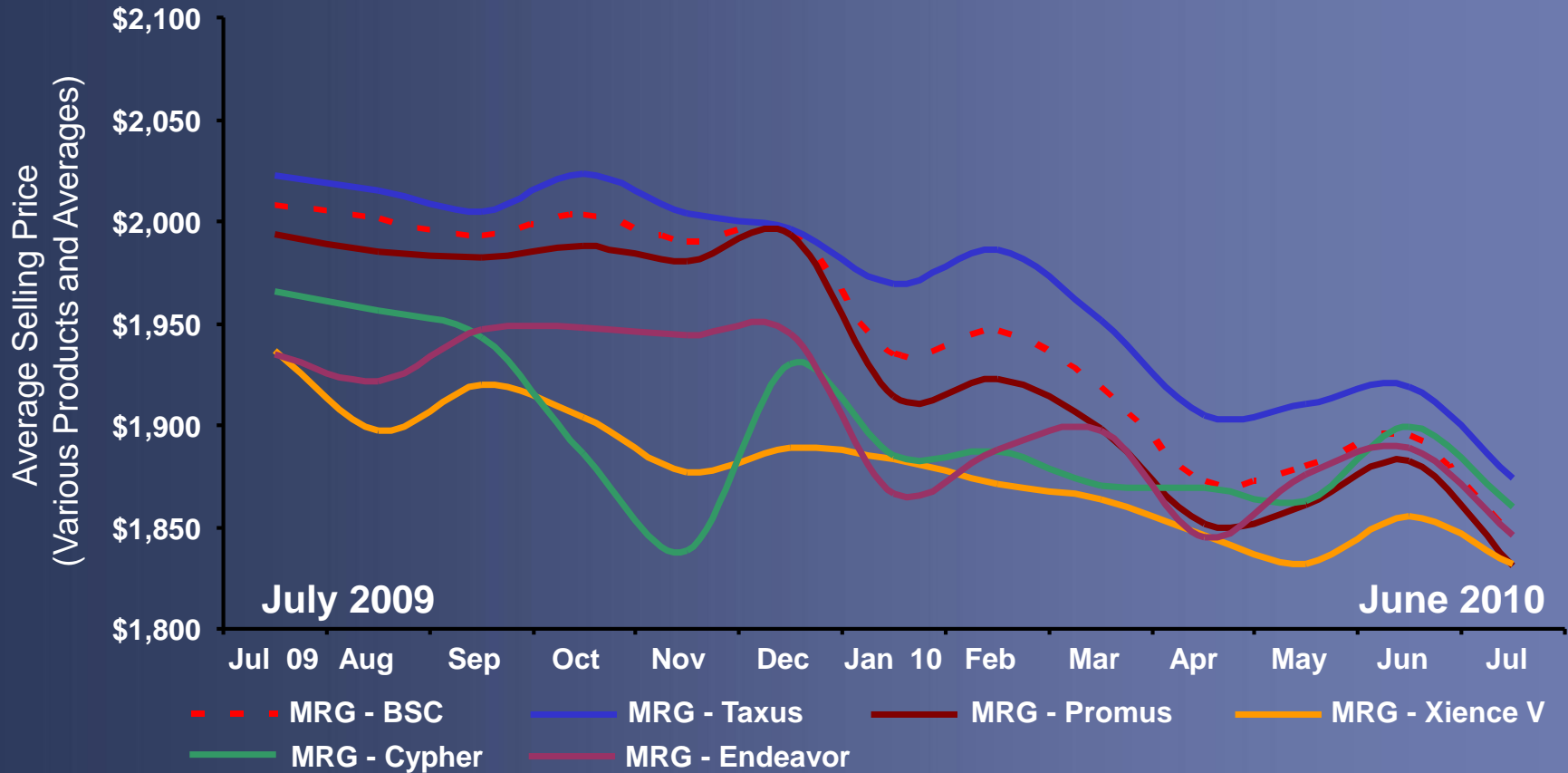
Boston Scientific internal estimates

The DES Technology Explosion

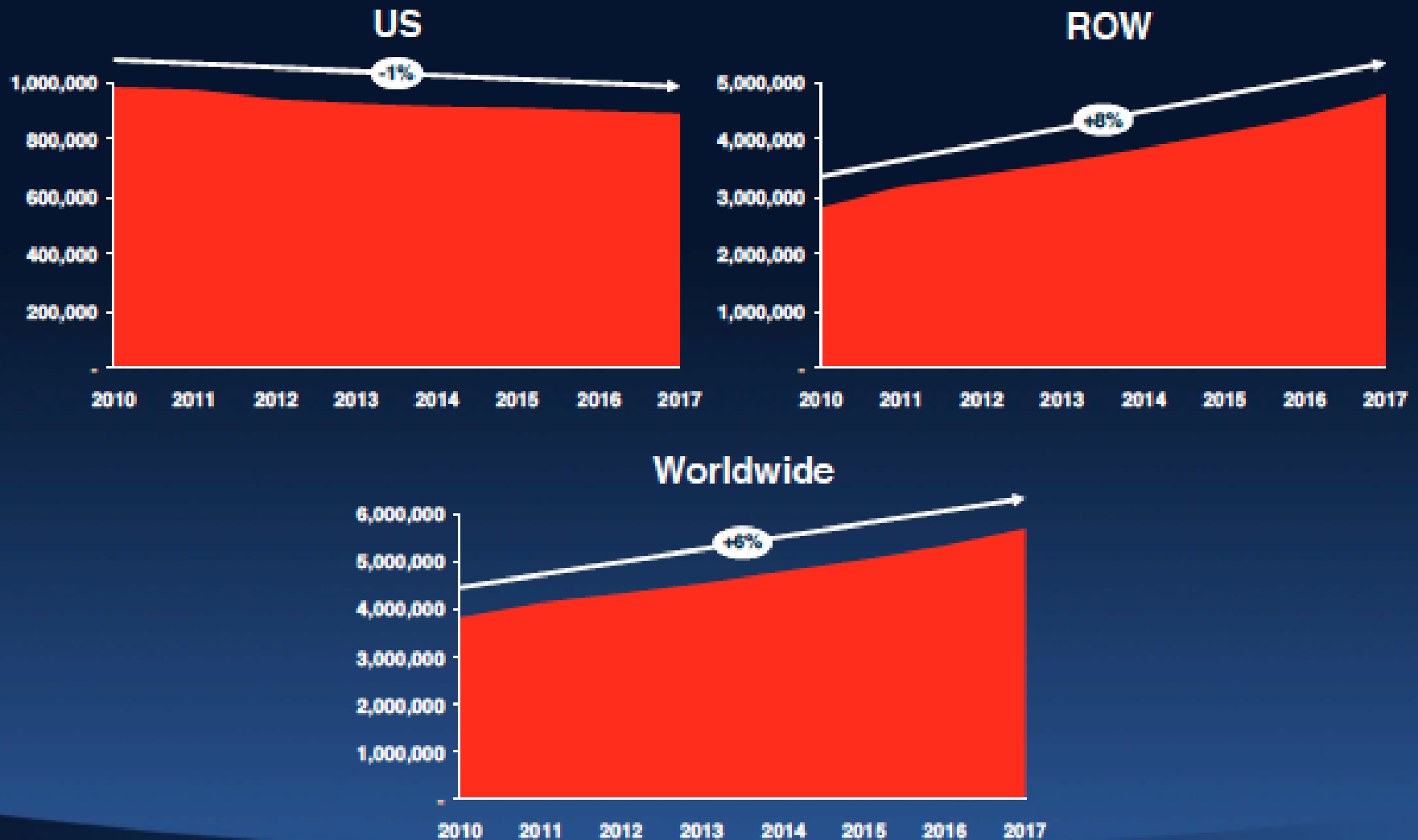


DES Average Selling Price (US)

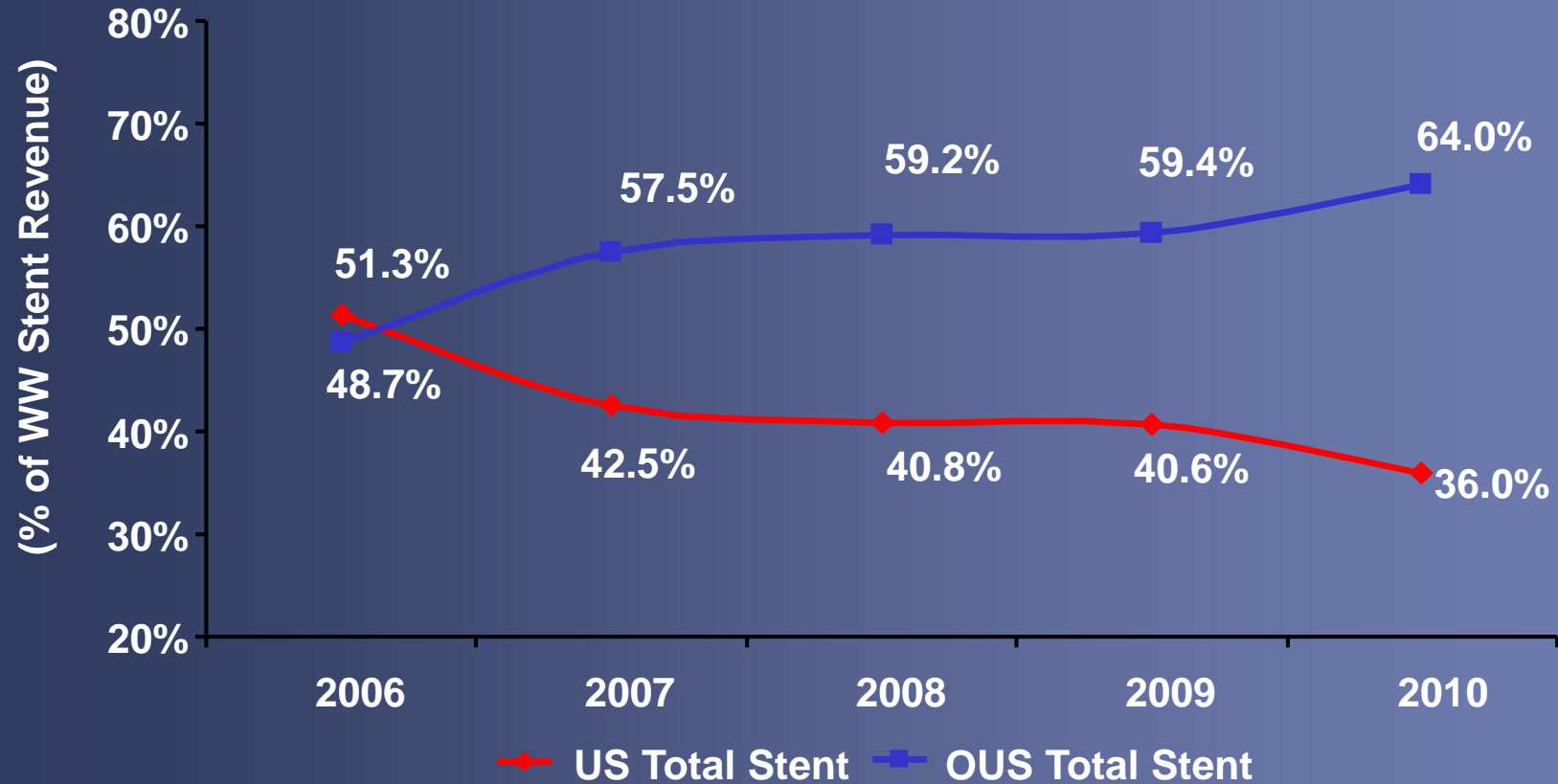
Price Erosion



PCI Procedures (2010-2017)

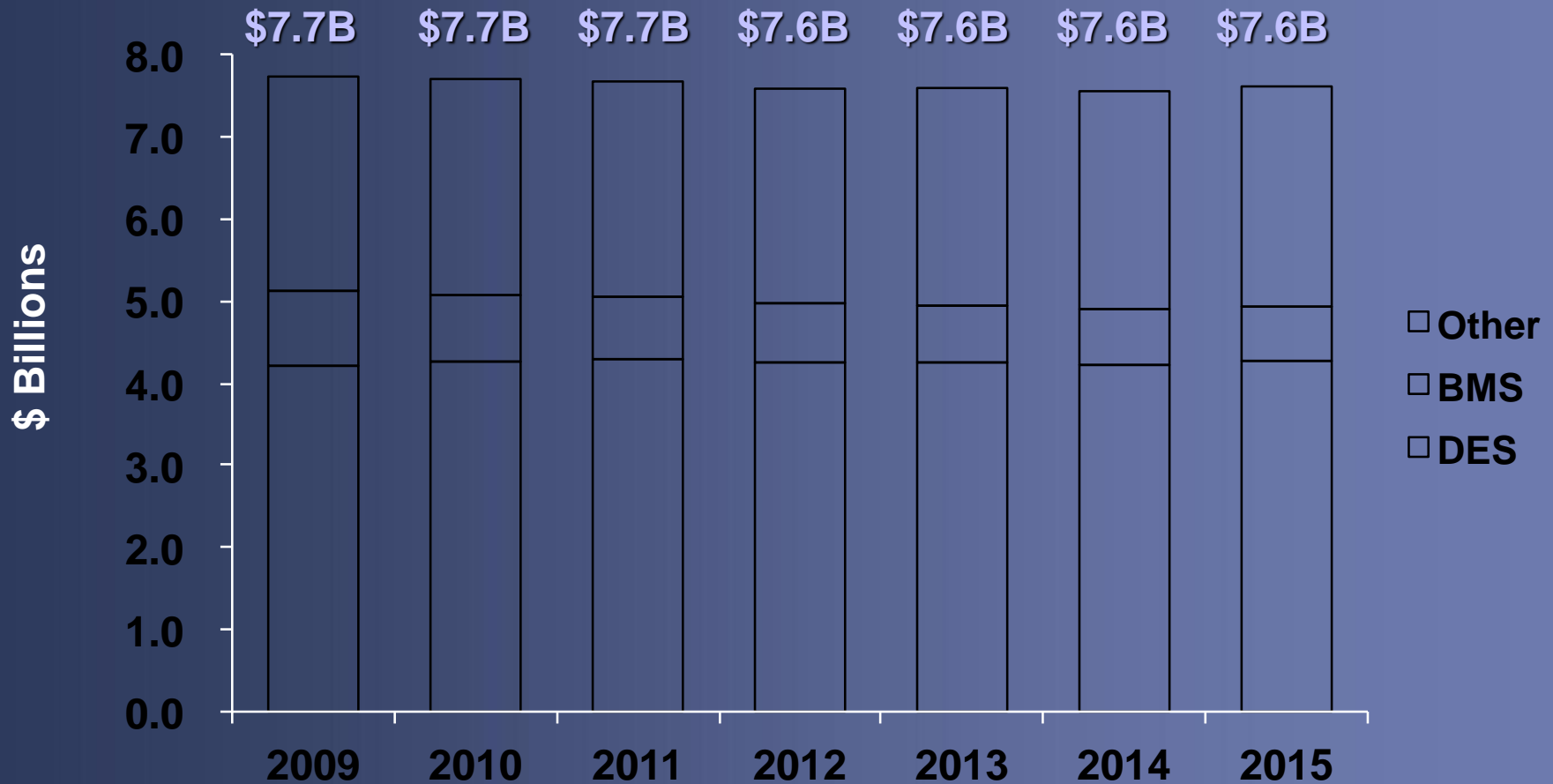


World Wide Stent Market (DES + BMS) Revenue



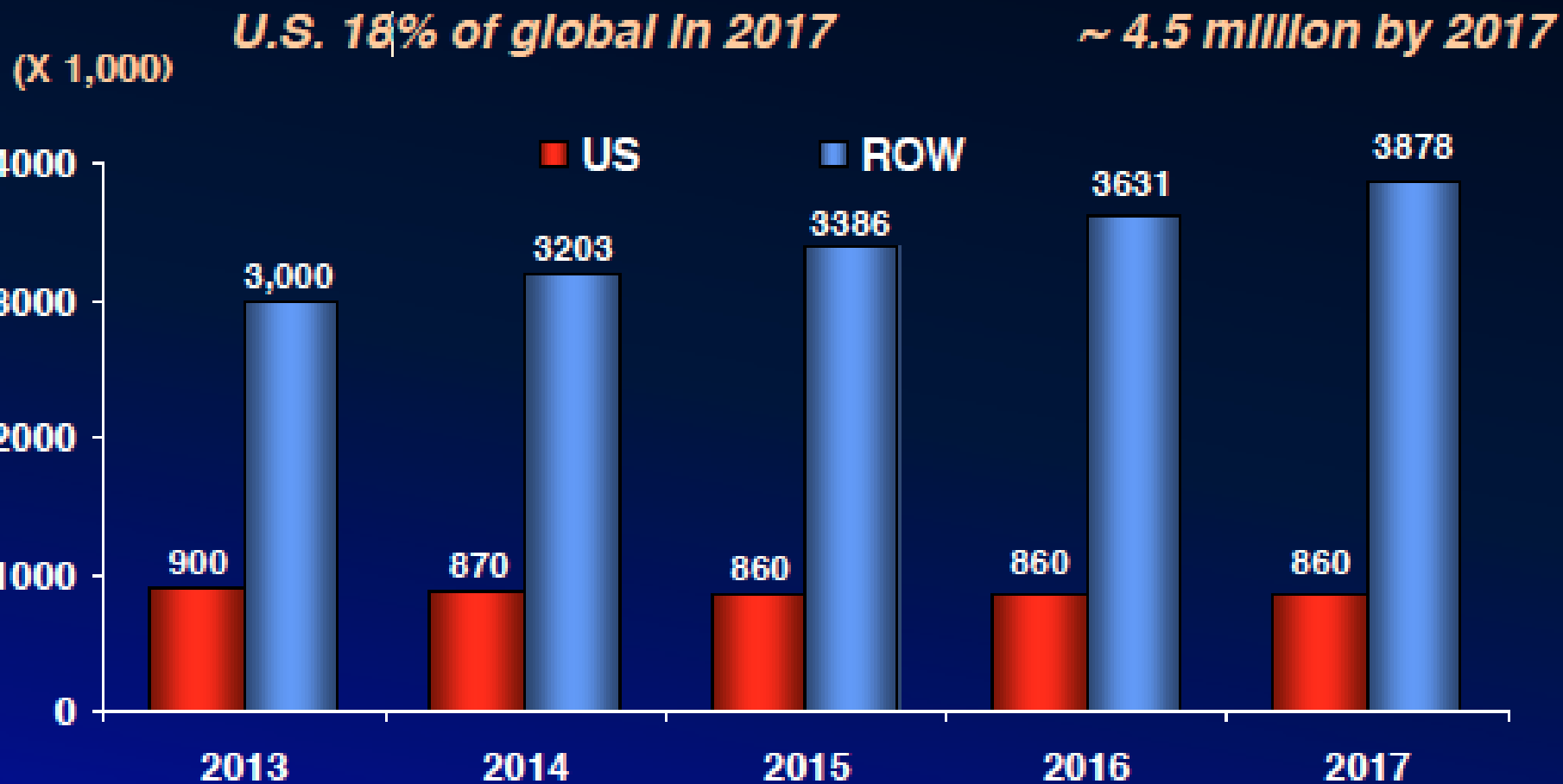
Sources: MRG Synergy, MRG Marketrack,
Earnings Calls, Industry sources

IC WW Market Revenues *Static*



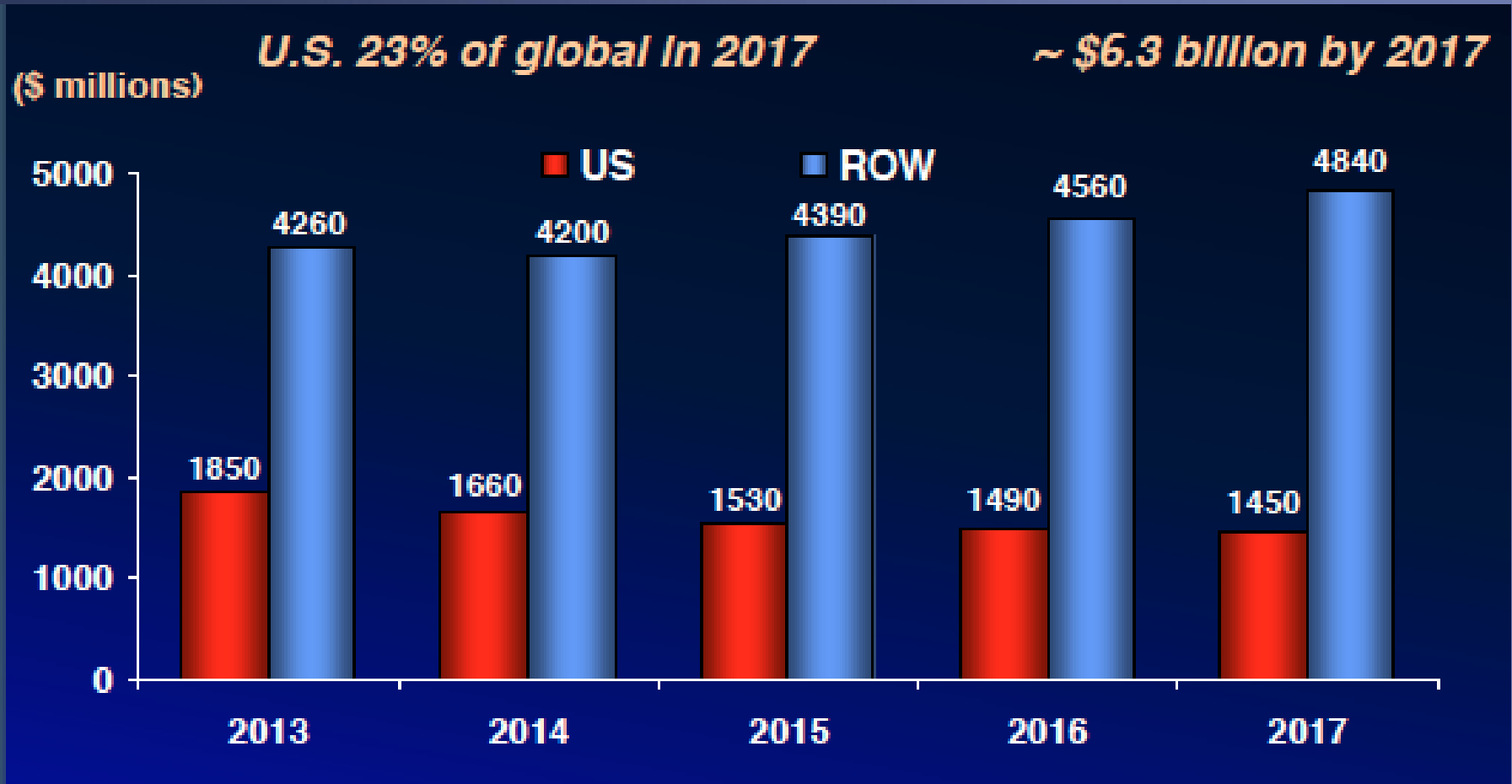
PCI Procedures

Growth from 2013 - 2017



PCI Revenue (\$ millions)

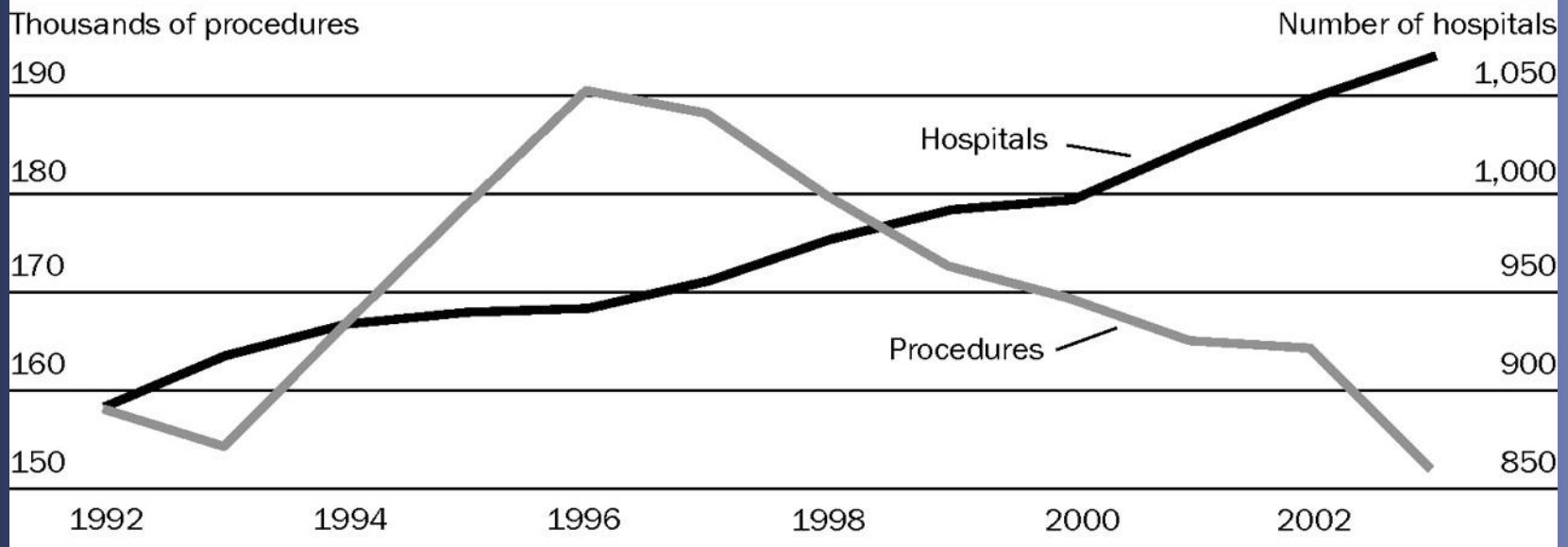
Growth from 2013 - 2017



Annual Number Of Coronary Artery Bypass Graft (CABG) Procedures And Number Of Hospitals Performing CABG In The United States, 1992–2003.

EXHIBIT 1

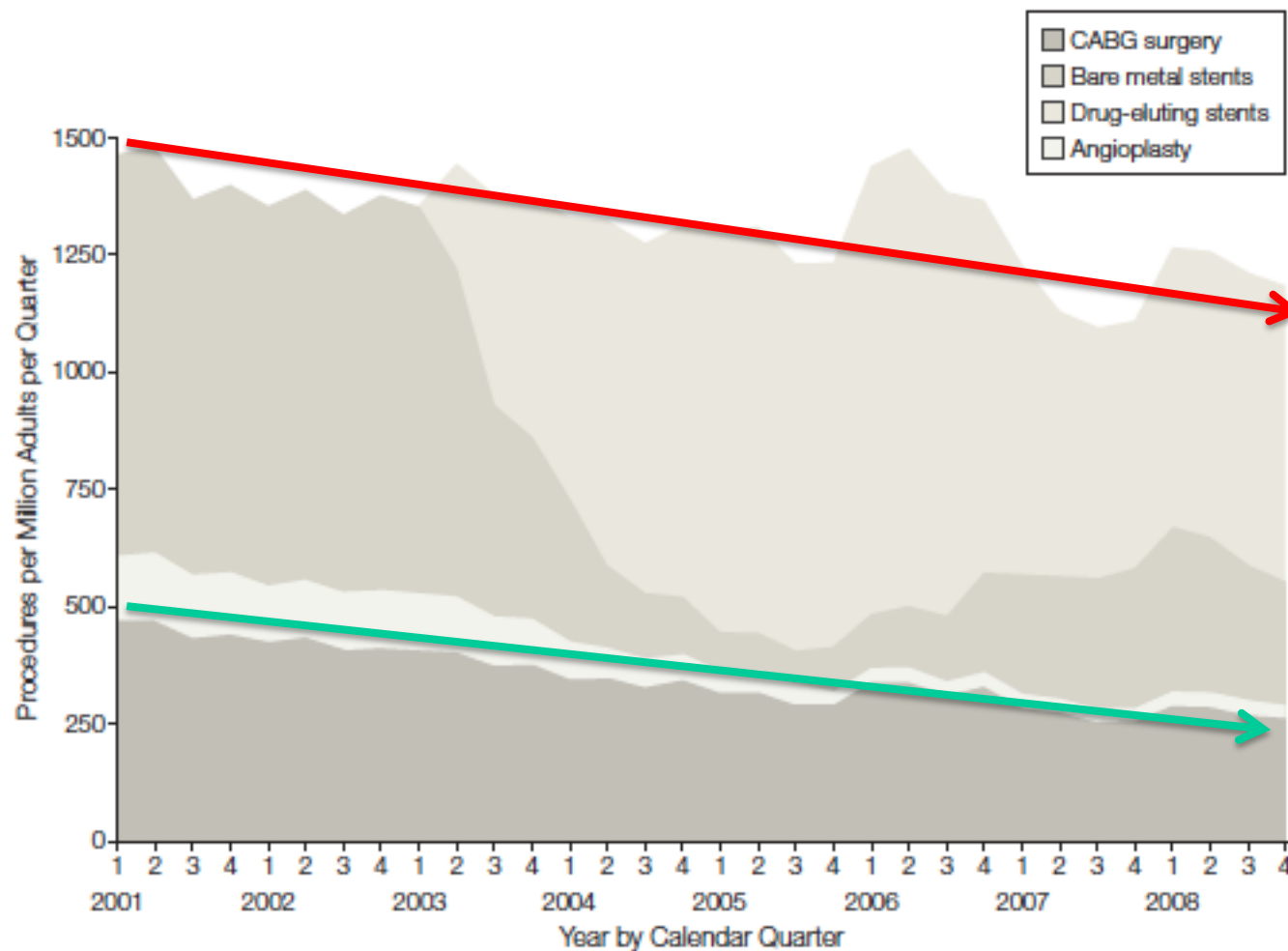
Annual Number Of Coronary Artery Bypass Graft (CABG) Procedures And Number Of Hospitals Performing CABG In The United States, 1992–2003



SOURCE: Authors' analysis based on Medicare data.

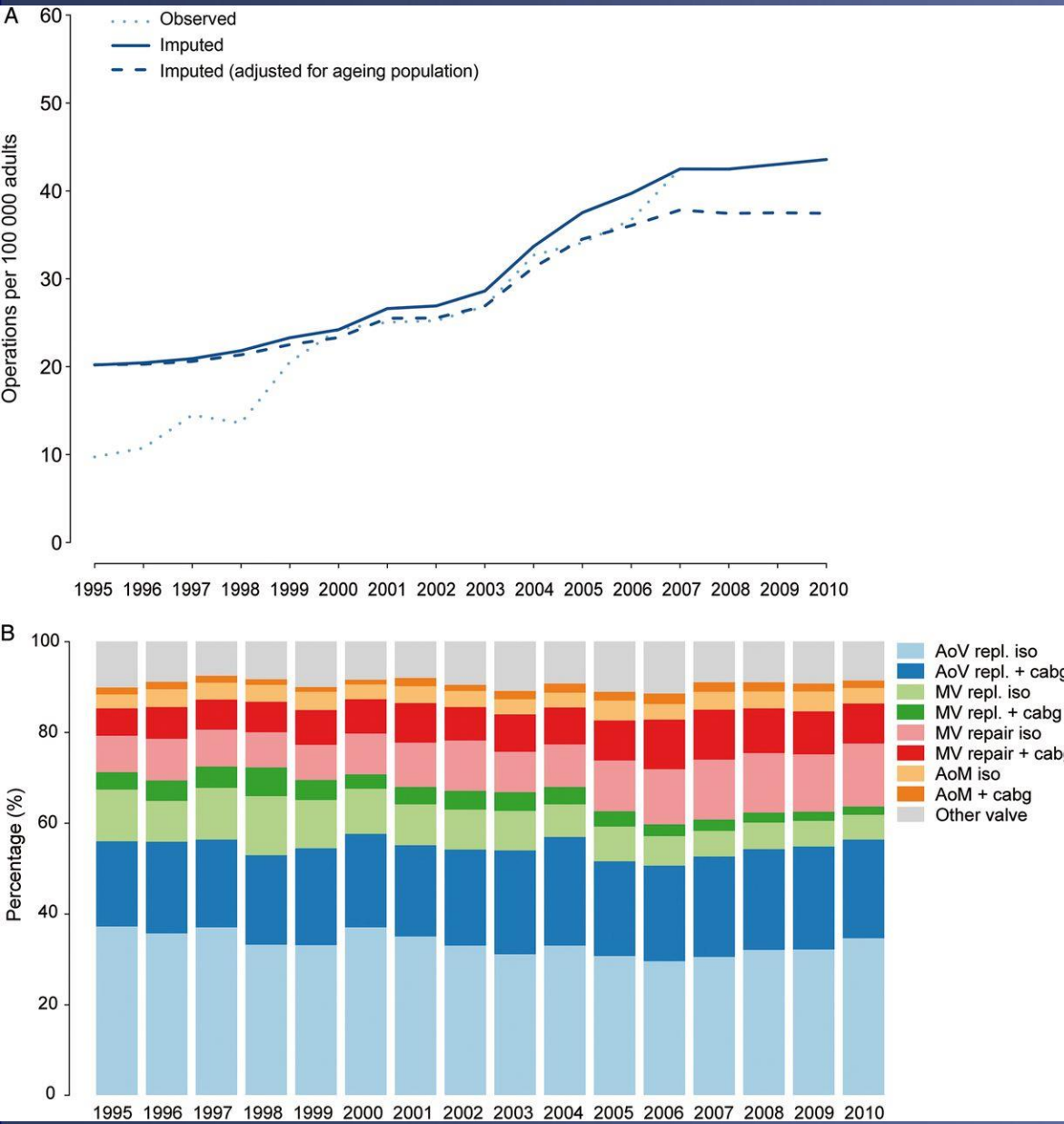
NOTES: The number of CABG procedures are the total number of Medicare CABG claims submitted every year during the period of the analysis nationwide. The number of CABG hospitals are all hospitals performing Medicare CABG during the year. Number of procedures relates to the left-hand y axis and is shown by the gray line; number of hospitals relates to the right-hand y axis and is shown by the black line.

Figure 1. Revascularization Procedure Rates of CABG Surgery, Bare Metal Stents, Drug-Eluting Stents, and Angioplasty per Million Adults per Quarter Between 2001 and 2008



CABG indicates coronary artery bypass graft.

Annual number and distribution of type of valve surgery from 1995 to 2010 in Netherlands.



Siregar S et al. Eur J Cardiothorac Surg
 2014;46:386-397



The New Innovation Ecosystem

- Healthcare cost challenges continue to increase
- Regulatory and clinical expectations continue to increase, increasing cost
- More involved and informed patients increase expectations
- Reduced investment risk taking
- Greater emphasis on cost effectiveness

Doom and Gloom?

**Catalyst for Change!
New Opportunities**

The New Challenge is Cost Effectiveness...



- Reduce hospitalization stays
- Reduce complications in hospital
- Facilitate conversion from in/out pt. Rx
- Reduce readmissions
- Improve patient compliance

*The Goal: Same day discharge
after major cardiac procedure...
and eternal life!*

YCRG

Yale Cardiovascular Research Group



Understanding Macro Trends to Focus R&D Efforts

Value-Based Healthcare



Trend toward value-oriented healthcare means companies need to focus on creating value for the customer and related stakeholders

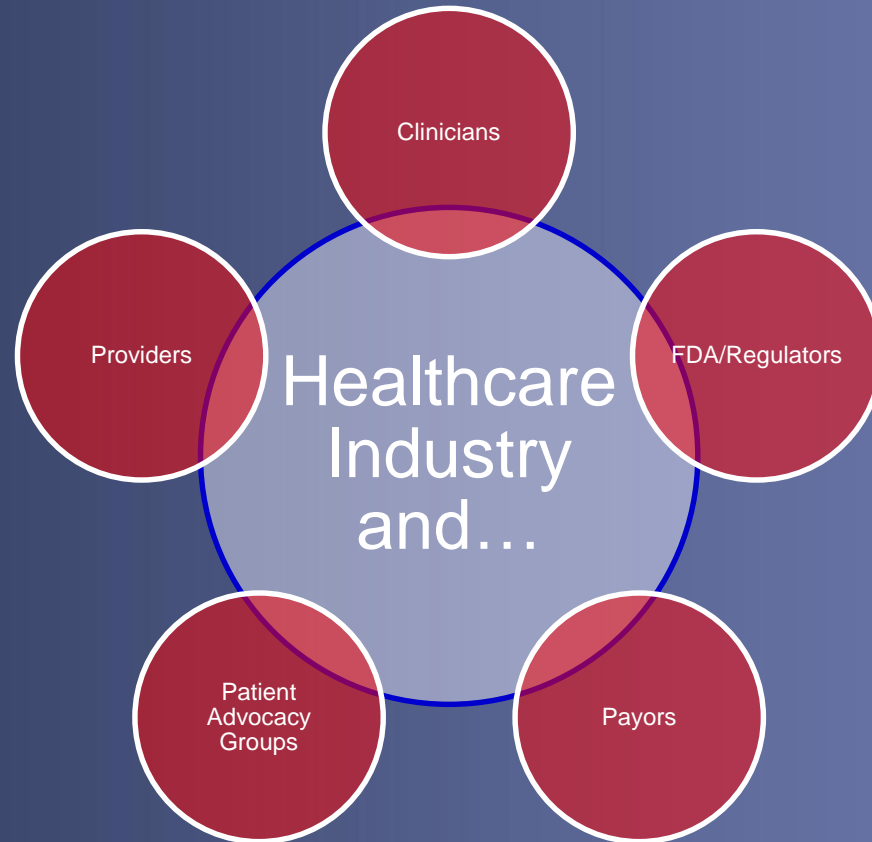
Delivering Complete Solutions



As a result, R&D efforts and collaborations are focused more on **providing a complete service or solution** and less on a new breakthrough product

Patients, Physicians, Payors and other stakeholders are becoming more sophisticated, requiring R&D groups to find ways to innovate in ways that address these needs

Future Will Demand More Up-Front Collaboration Between a Range of Stakeholders

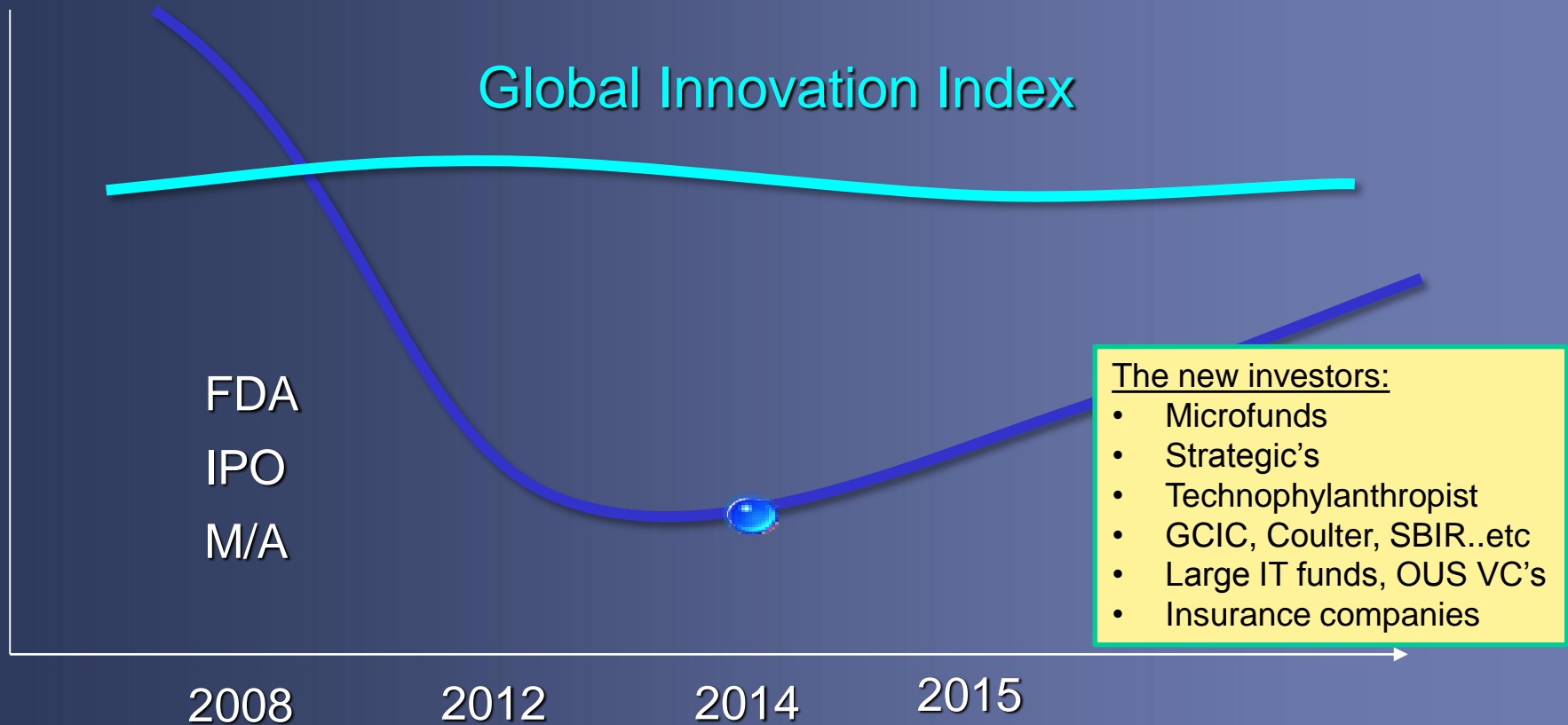


We must ensure we keep the channels of communication open and supportive in order to harmonize requirements and continue bringing innovative products to the marketplace

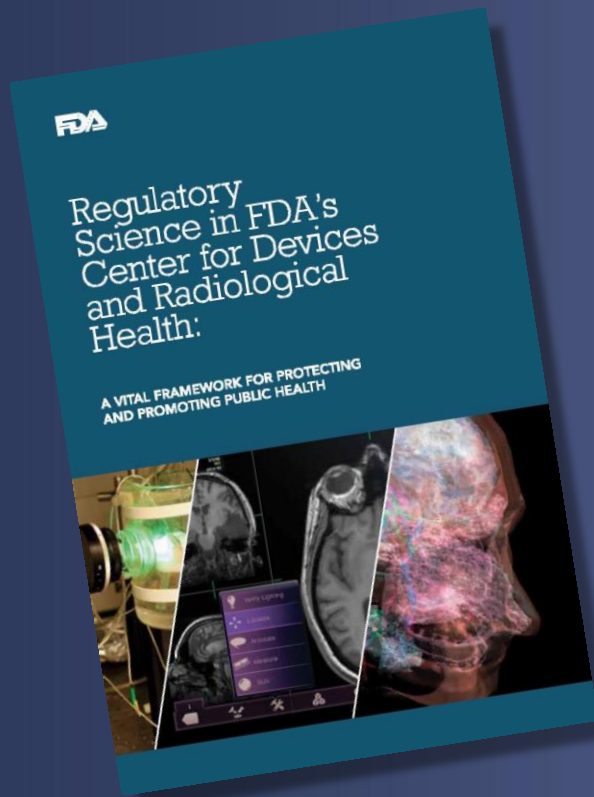
“The Cycle” of VC Healthcare Landscape

- Innovation does not stop, just “ole school” VC’s do -

No. of VC’s



FDA Enlightenment Regulatory Science



The science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of FDA-regulated products

- *Benefits patients by speeding the rate of important technologies reaching market*
- *Reduces time and resources needed for device development, assessment, and review.*

For example:

- *Can lead to quicker, more efficient device approvals*
- *Can decrease the size and duration of pre-market clinical trials*

FDA Strategic Plan, August 2011
Advancing Regulatory Science at FDA

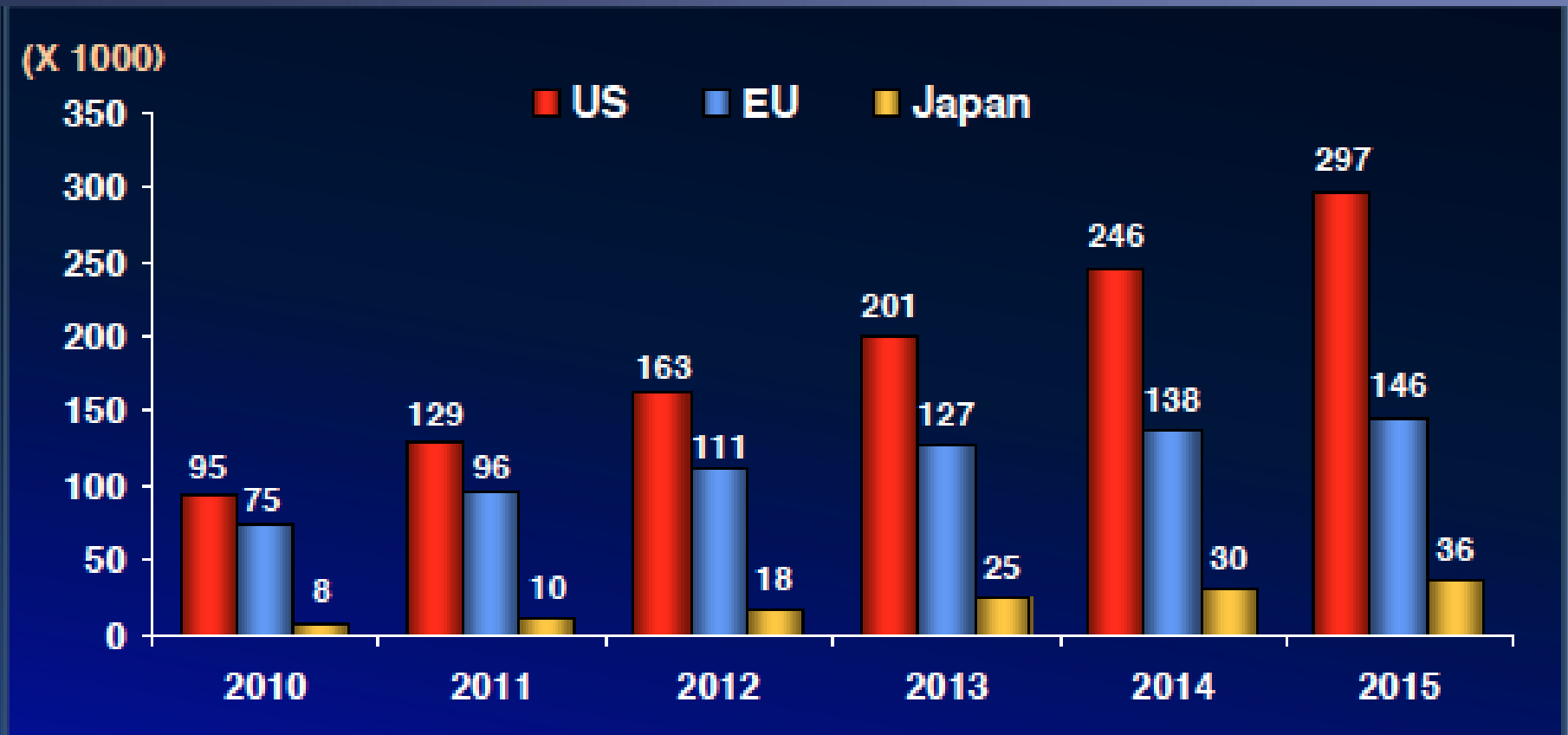
Faster, Safer, More Cost-effective

New Innovation Opportunities

Areas of Growth

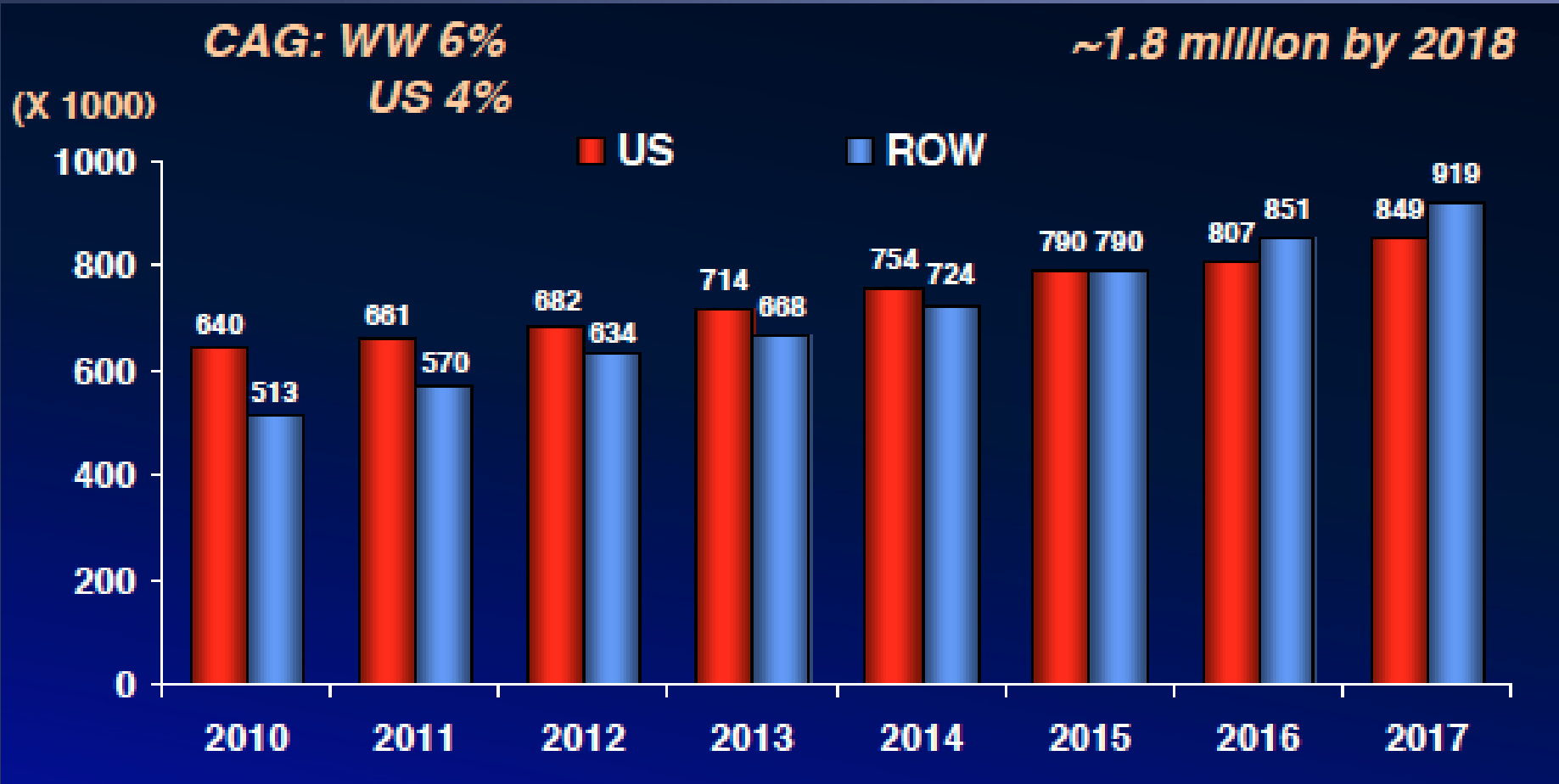
Invasive FFR Procedures

Growth from 2010 - 2017



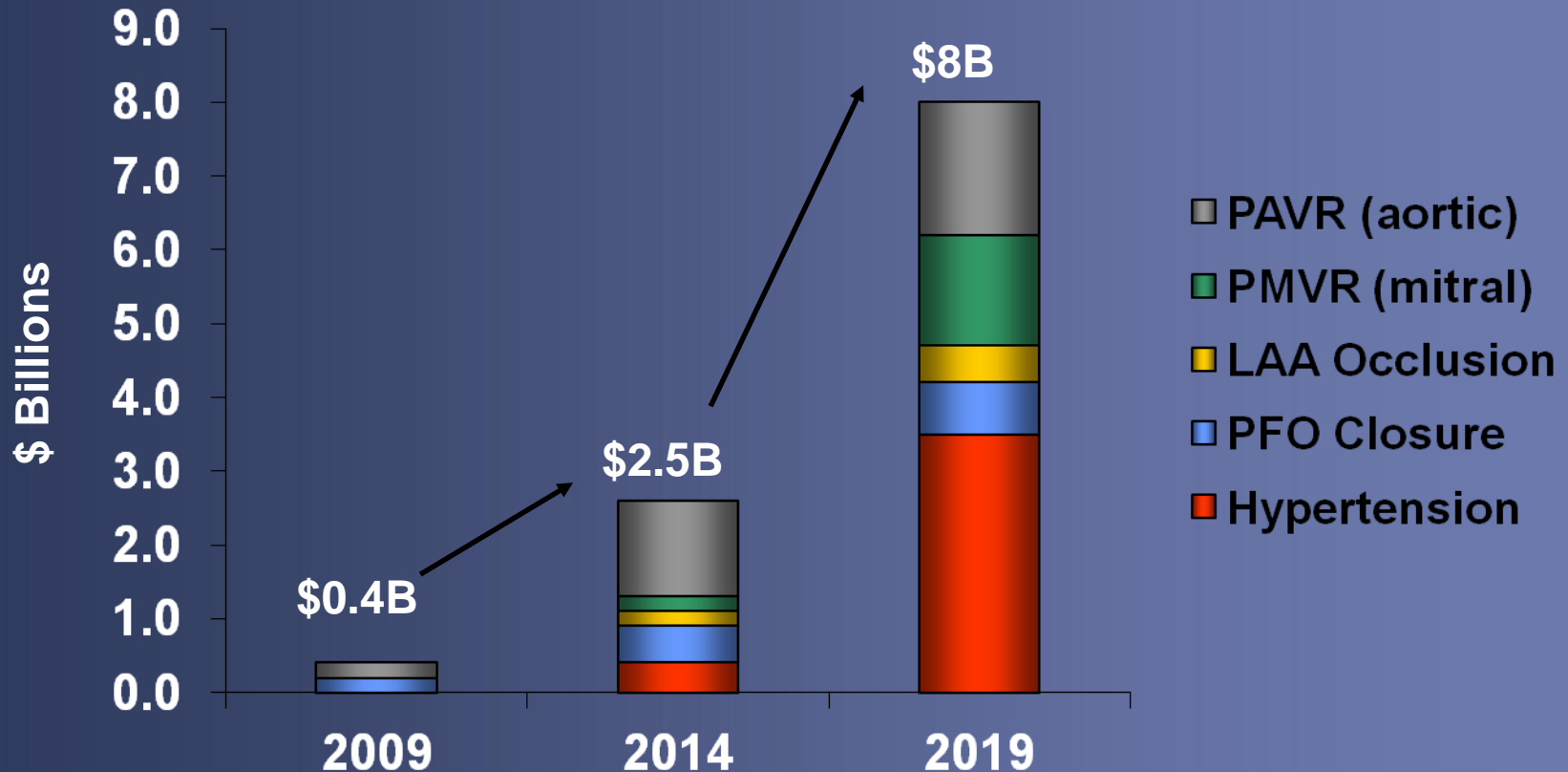
Peripheral Vascular Procedures

Growth from 2010 - 2017



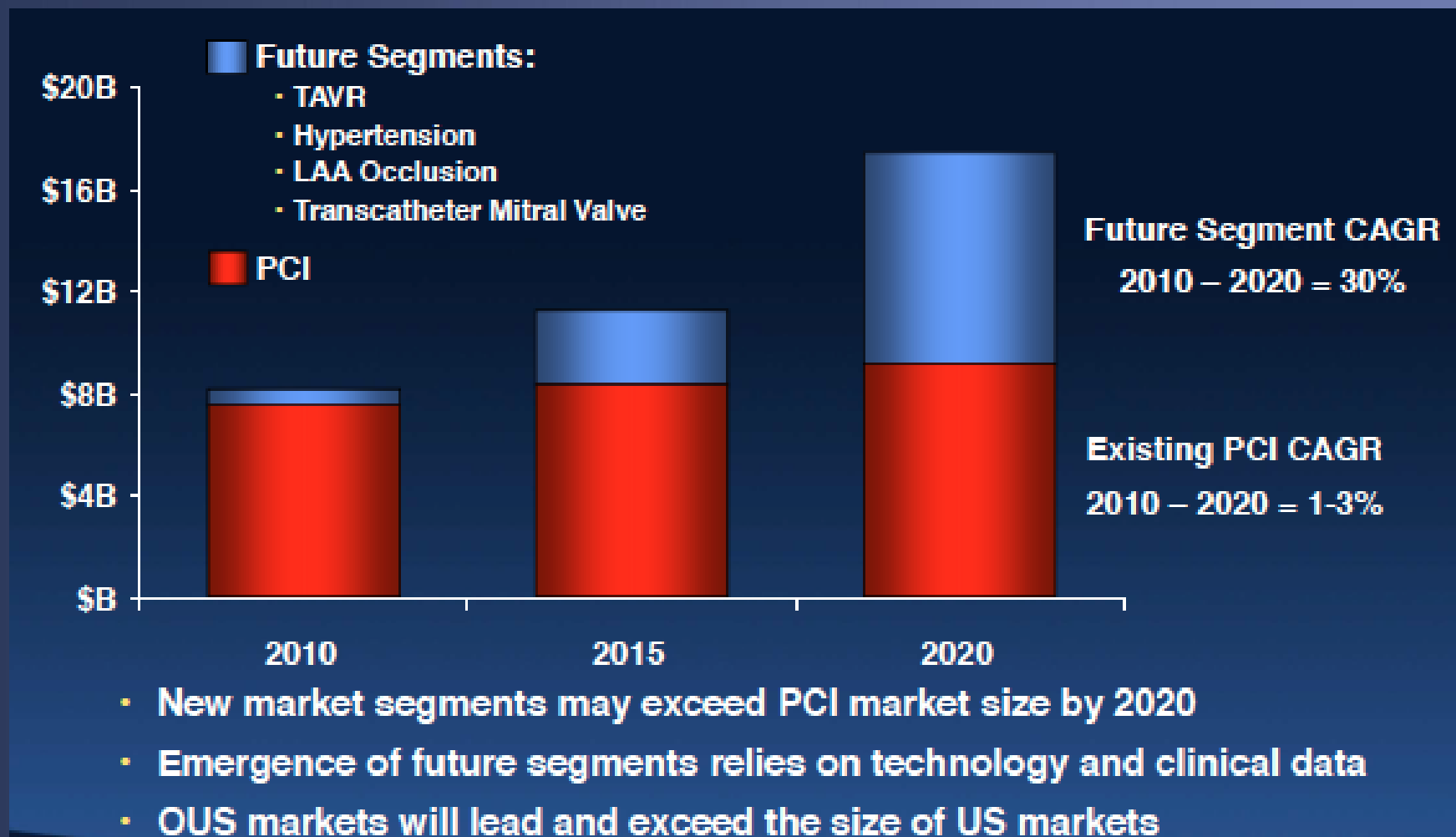
The Future Growth of IC Markets

Driven by New Segments



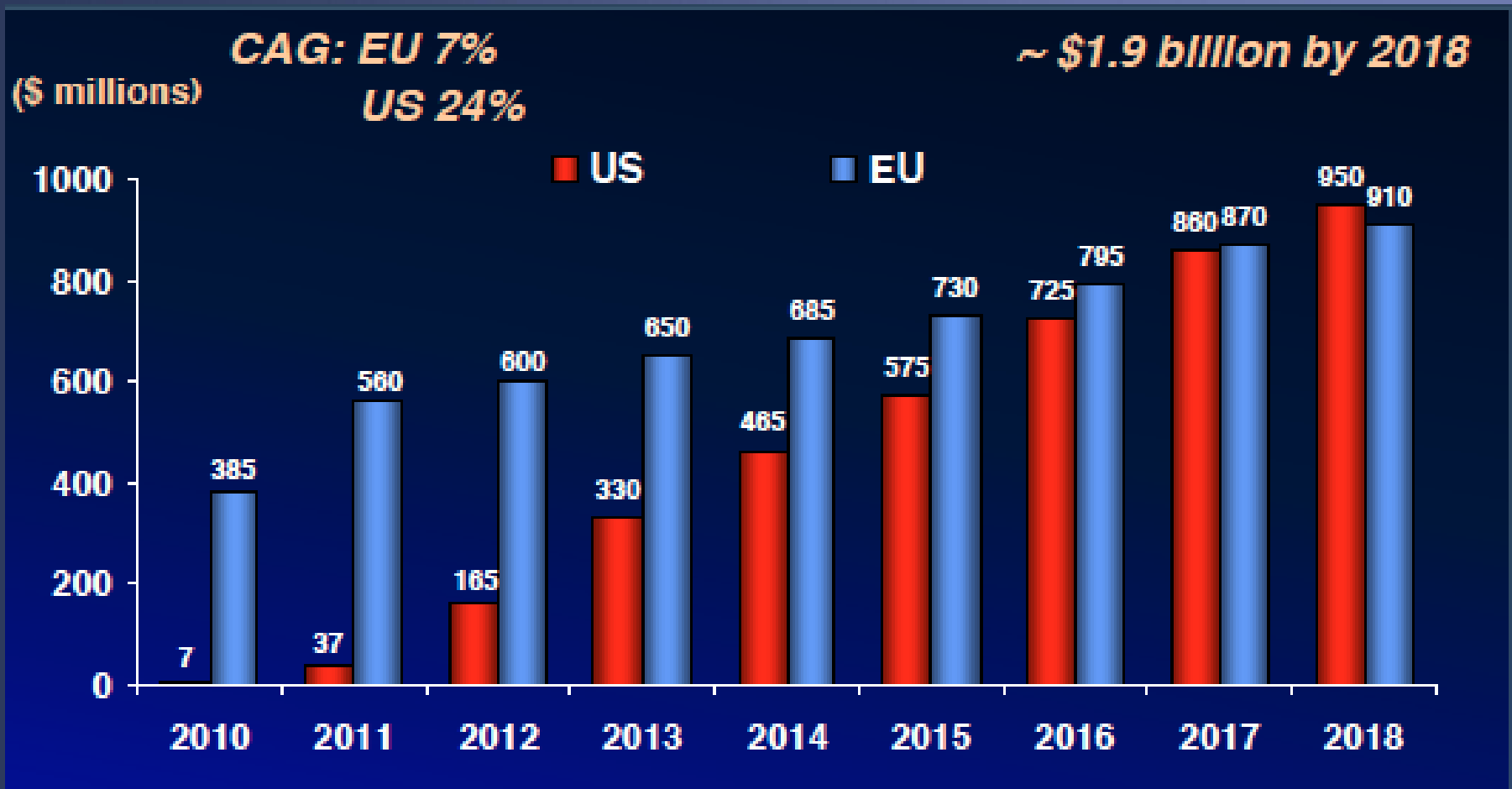
Boston Scientific Internal Estimates

WW Cardiology Market Trends



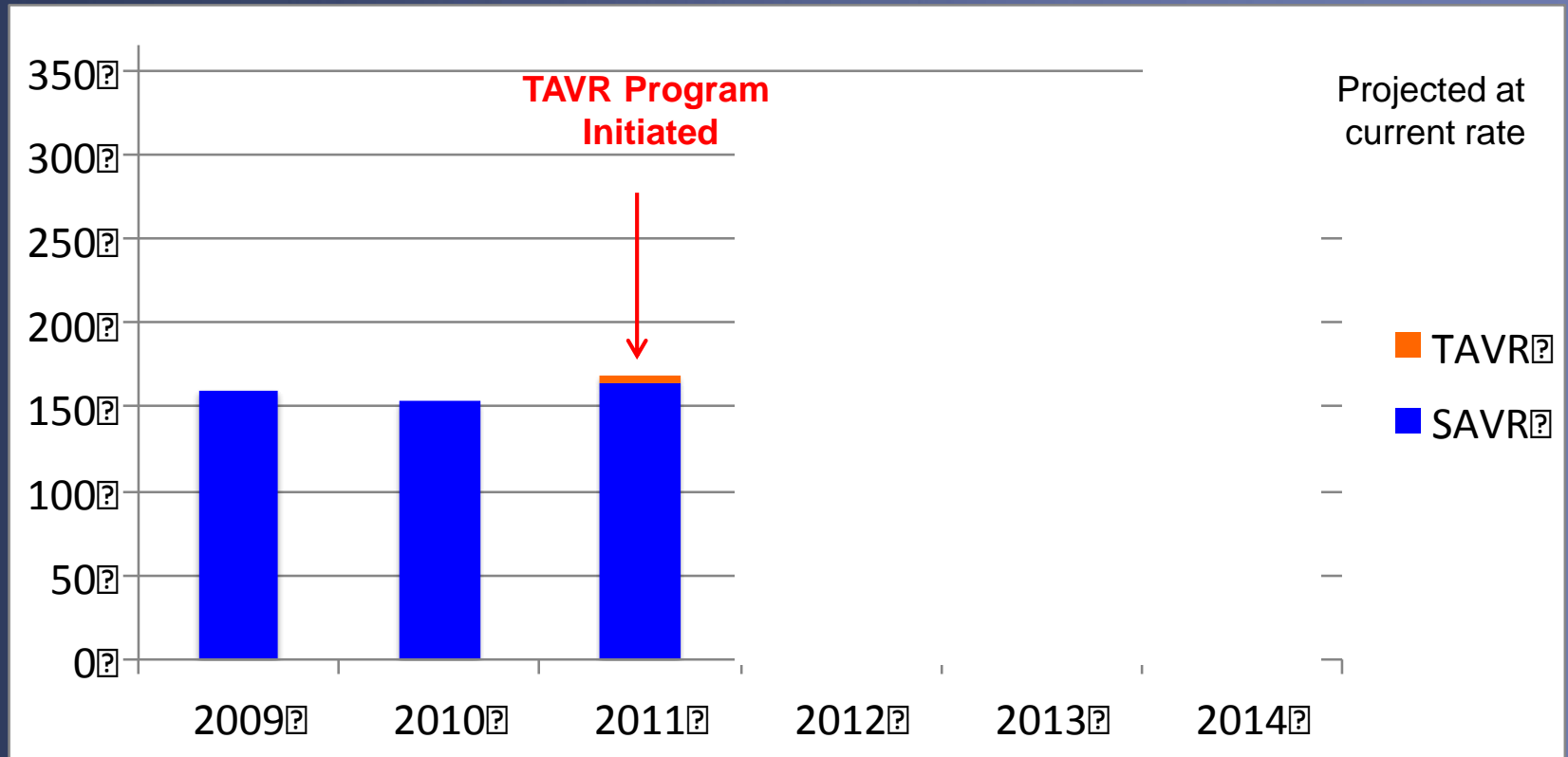
TAVR Revenue (\$millions)

Growth (2010-2018)



Impact of TAVR on SAVR Volume at Yale

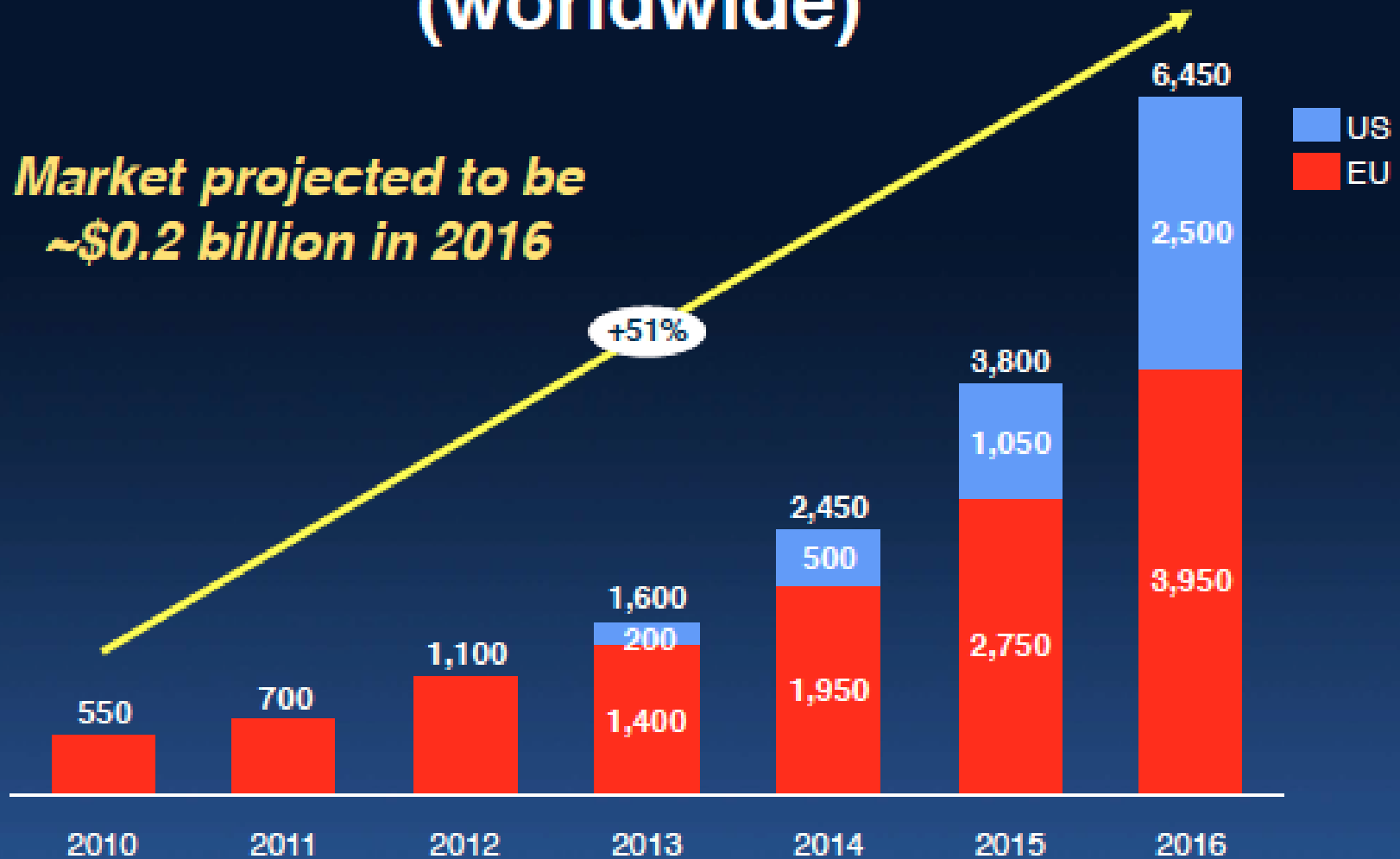
(Total SAVR: including SAVR only, CABG/SAVR, and SAVR + other valve)



2013 represented over a 40% increase in total AVRs as compared to prior 3 year average

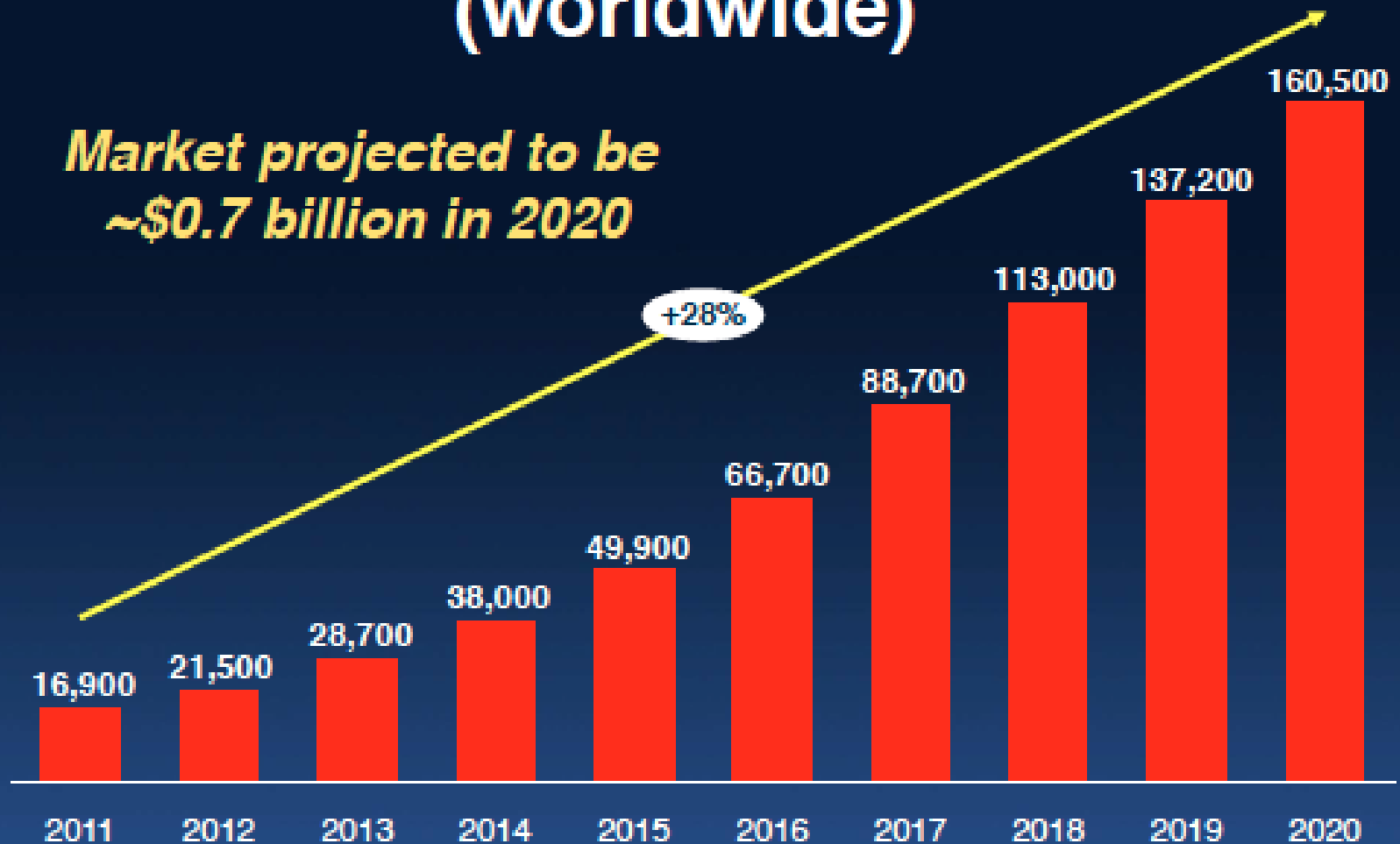
Mitral Valve Repair Procedures (worldwide)

*Market projected to be
~\$0.2 billion in 2016*



LAA Closure Procedures (worldwide)

*Market projected to be
~\$0.7 billion in 2020*



Rules of Engagement: Heart Team



Future Opportunities

Congestive Heart Failure

Heart Failure

A Growing Global Concern

Prevalence and Incidence

- 5.1M US heart failure patients in 2010¹
- 15 M EU heart failure patients in the ESC 51-member countries²
 - Overall 2-3% prevalence²

Mortality

- For AHA/ACC stage C/D patients diagnosed with HF:
 - 30% will die in the first year. 3-5
 - 60% will die within 5 years.⁵

Readmission

- 25% at 30 days
- 50% at 6 months

HF prevalence in the US is projected to increase 46% from 2012 to 2030, resulting in > 8M people ≥ 18 years of age with HF.⁶

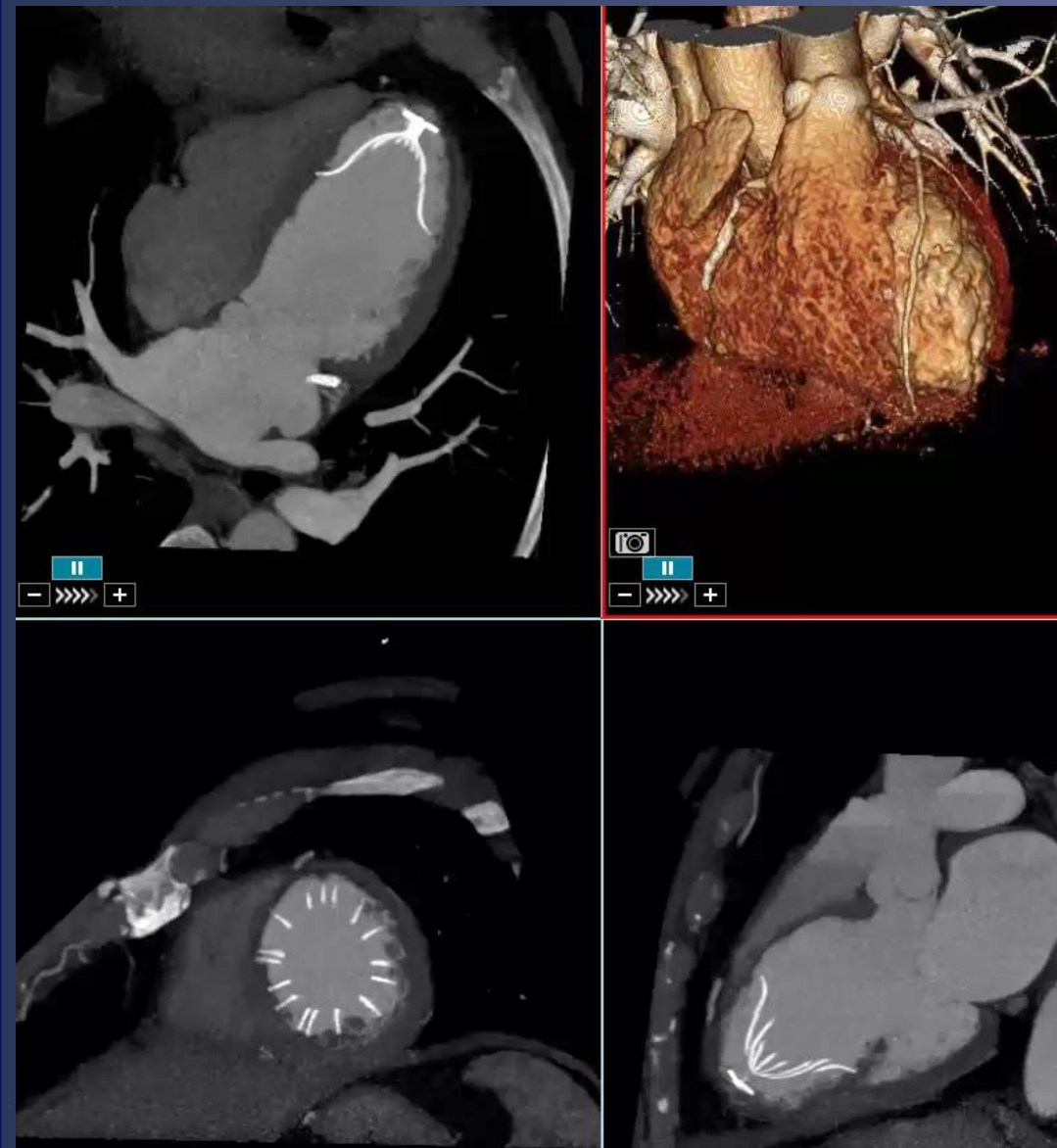
1. AHA 2014 Statistics at a Glance, 2014
2. The European Society of Cardiology, ESC HF Guideline, 2008
3. Curtis et al, Arch Intern Med, 2008.
4. Roger et al. JAMA, 2004.
5. Cowie et al, EHJ, 2002.
6. Heidenreich PA et al. Circ Heart Failure 2013.

Next Big Breakthrough

New CHF Therapies

- Sensors to monitor therapy
- LV remodeling devices
- Contractility Modulation
- Micro VADS
- Inter-atrial shunt implants

Percutaneous Ventricular Restoration



Treatment Goal

Improved hemodynamics by

- Partition scar
- LV Volume reduction
- LVED pressure reduction
- Restors LC Conical shape
- Preserves torsional contraction
- No arrhythmias

CardioMEMS™ HF System

Simple PA artery implant
Continuous PA pressure monitoring (RF powered, no battery)
PA measures transmitted to MD

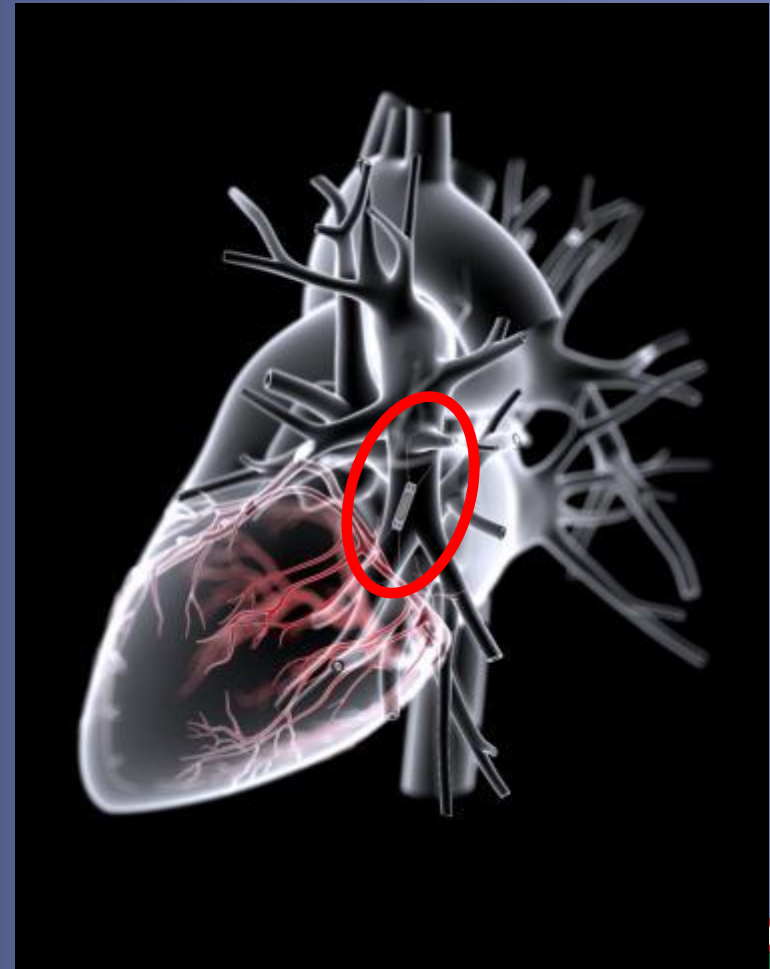


CHAMPION Trial

550 Randomized pts with HF

- 30% reduction in rehospital at 6 mos
- 38% reduction in hops over entire trial period

Target location for pulmonary artery pressure sensor



Future Opportunities

Digital Healthcare

From Fitness to... Chronic Disease Management



SAMSUNG



APPLE



Consumer Paths...will be patient paths



**Congestive
Heart Failure**



Diabetes



Hypertension



Pediatrics



- *Decrease 30 day re-hospitalization for heart failure patients*
- *Prevent episodes of hypoglycemia for diabetic patients*
- *Decrease ER visits for childhood asthma exacerbations*

New Realities of Innovation

- Accept the fact that the innovation ecosystem has changed FOREVER – “Adapt and Evolve” embracing more minimally invasive therapies
- The physician scientist and academic community must re-organize emphasizing multi-disciplinary cooperation, better communication, and accept industry as welcome and indispensable partners driving innovation
- Regulatory hurdles –have become global (US, China, Japan, even EU is getting tougher)
- Financial constraints are global–Affect physician salaries, hospital reimbursement and industry revenues

New Realities of Innovation

- FDA pathways are opening up— more communication, early feasibility program, more flexible pathways
- Extension of therapies to chronic disease - emphasizing compliance, early detection, out-patient management of common disease with yet un met needs and solutions
- Focus on health economic imperatives –create new opportunities for innovation by integrating healthcare and IT

Time for a make over?

