

# Boston Scientific

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## Diversity in Medical Device Trials: Experiences From the Field

Paul Underwood, MD, FACC  
Medical Director, Interventional Cardiology/Structural Heart

**CLOSE**THE**GAP**  
Health Equity for Life

# Clinical Trials: Assessing Safety and Efficacy for a Diverse Population

## Today's Objectives

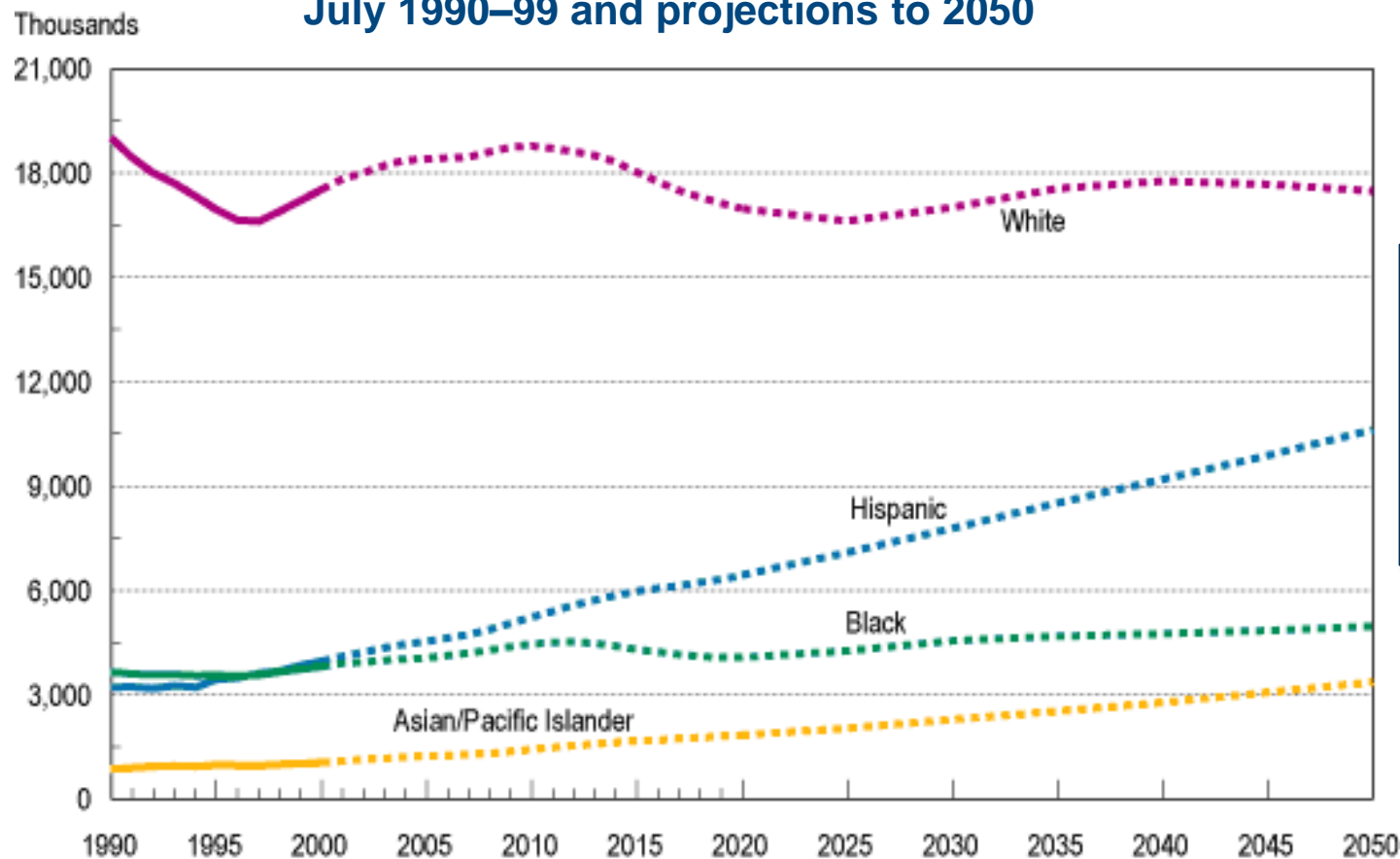
- Share with FDA and the public an example of how one company, Boston Scientific, has operationalized the principle of diversity in clinical data collection.

## Background

- Product performance data must be reflective of the population at risk.
- The approach to demographic subgroup analyses in implantable medical devices has evolved over time (FDASIA 907).
- Barriers to clinical trial participation in implantable medical devices are similar to those encountered in other therapeutic areas.
- Disparities in clinical trial enrollment mirror the disparities in treatment.
- Analysis of premarket and post-market data can assure safety and efficacy are met in the entire population.

# Diversity of the U.S. Population

U.S. population 18–24 years old, by race/ethnicity:  
July 1990–99 and projections to 2050



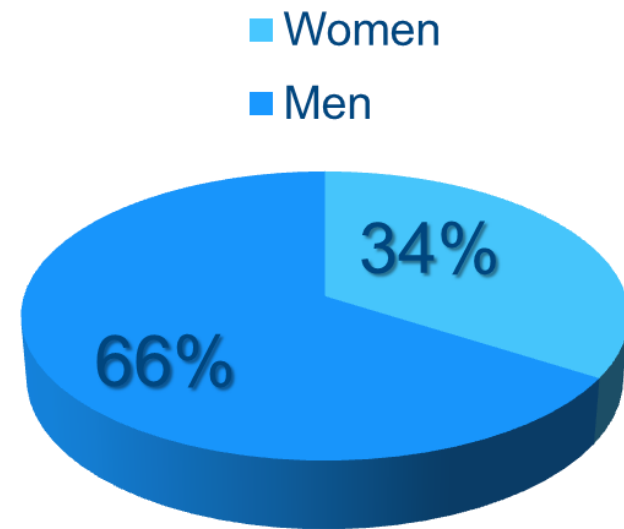
People of color are expected to represent over half (52%) of the U.S. population by 2050

NOTE: Hispanics may be of any race

U.S. Census Bureau, 2009 National Projections supplement to the 2008 National Projections, August 14, 2008

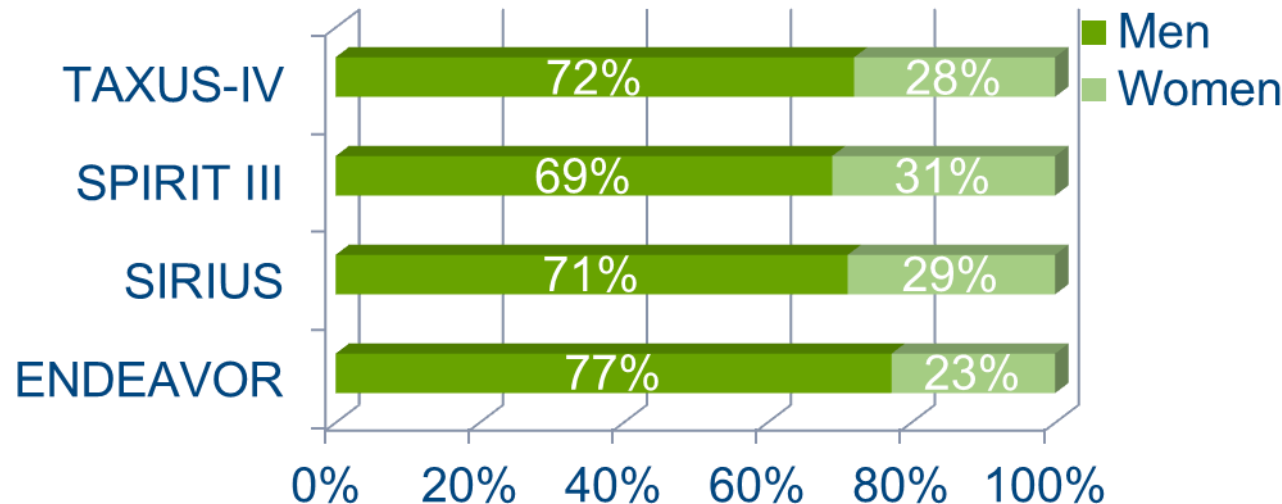
# Disparities in Clinical Practice are Mirrored in Clinical Research

## Women comprise 30% of PCI procedures and PCI clinical trial enrollment



### PCI Procedures 2009

Patients: N=596,000



## Gender Representation in PCI Clinical Trials

National Hospital Discharge Survey/National Center for Health Statistics, 2009 Estimates are based on a sample of inpatient records from short-stay hospitals in the United States.

Heart Disease and Stroke Statistics-2012 Update. *Circulation*. <http://circ.ahajournals.org/content/125/1/e2>  
Einstein et al. 2009. "4-Year Follow-Up From the ENDEAVOR II Trial." *JACC: Cardiovascular Interventions*, 2(12): 1178-87.

Holmes et al. 2004. "Analysis of 1-Year Clinical Outcomes in the SIRIUS Trial." *Circulation*, 109:634-640.

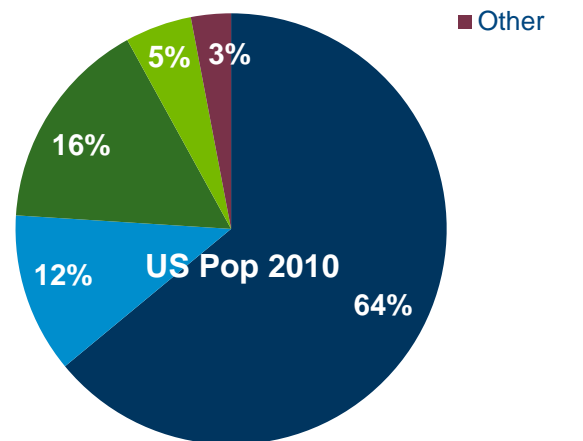
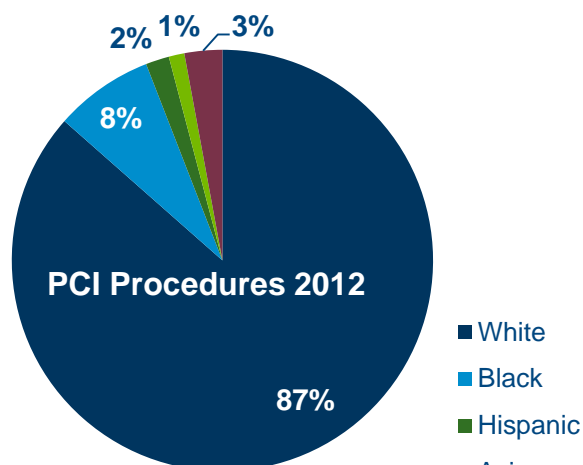
Stone et al. 2009. "Everolimus-and Paclitaxel-Eluting Stents." *Circulation*, 119:680-686.

Lansky et al. 2005. "Gender Differences After Paclitaxel-Eluting Stents." *JACC*, 45(8): 1180-5.

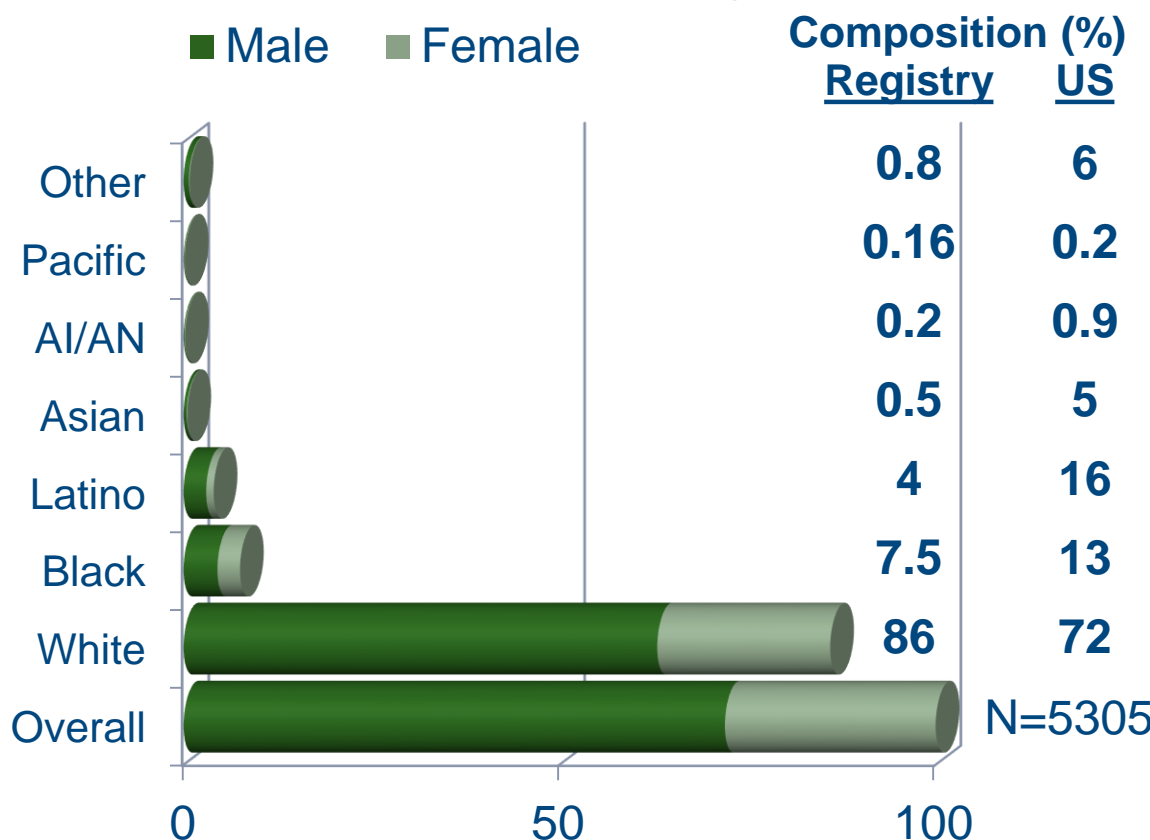
Morice, MC. 2008. "XIENCE V SPIRIT WOMEN clinical trial: characterization of the female population undergoing stent implantation. *Women's Health*, 4(5):439-443.

# Disparities in Clinical Practice are Mirrored in Clinical Research

**White people comprise ~80% of PCI procedures and PCI clinical trial enrollment**

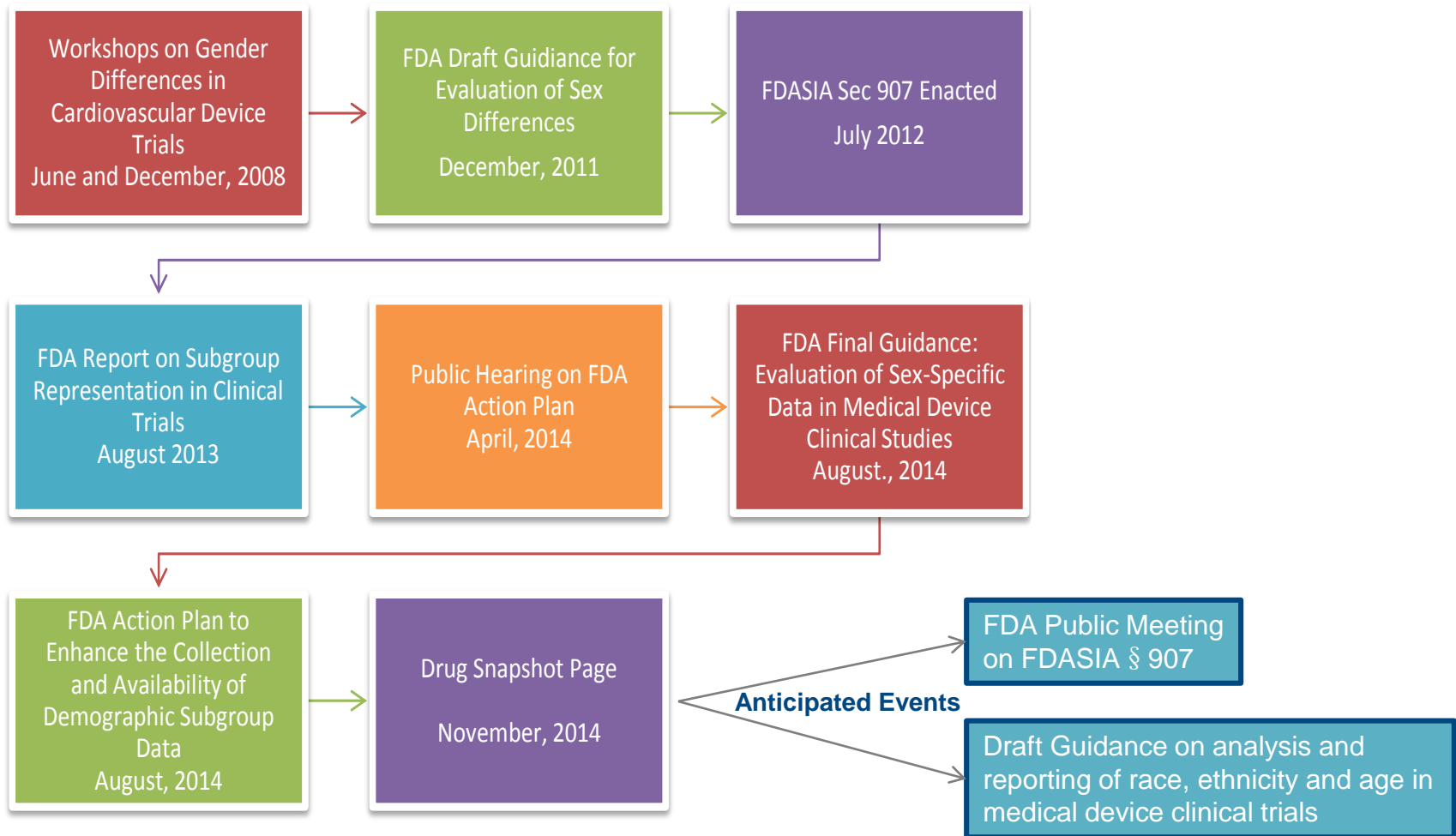


**Boston Scientific ION and LIBERTE Post-Market Studies:  
Pooled Patient Demographics**



MedPar 2012, 2013 Master Hospital file & US 2010 Census

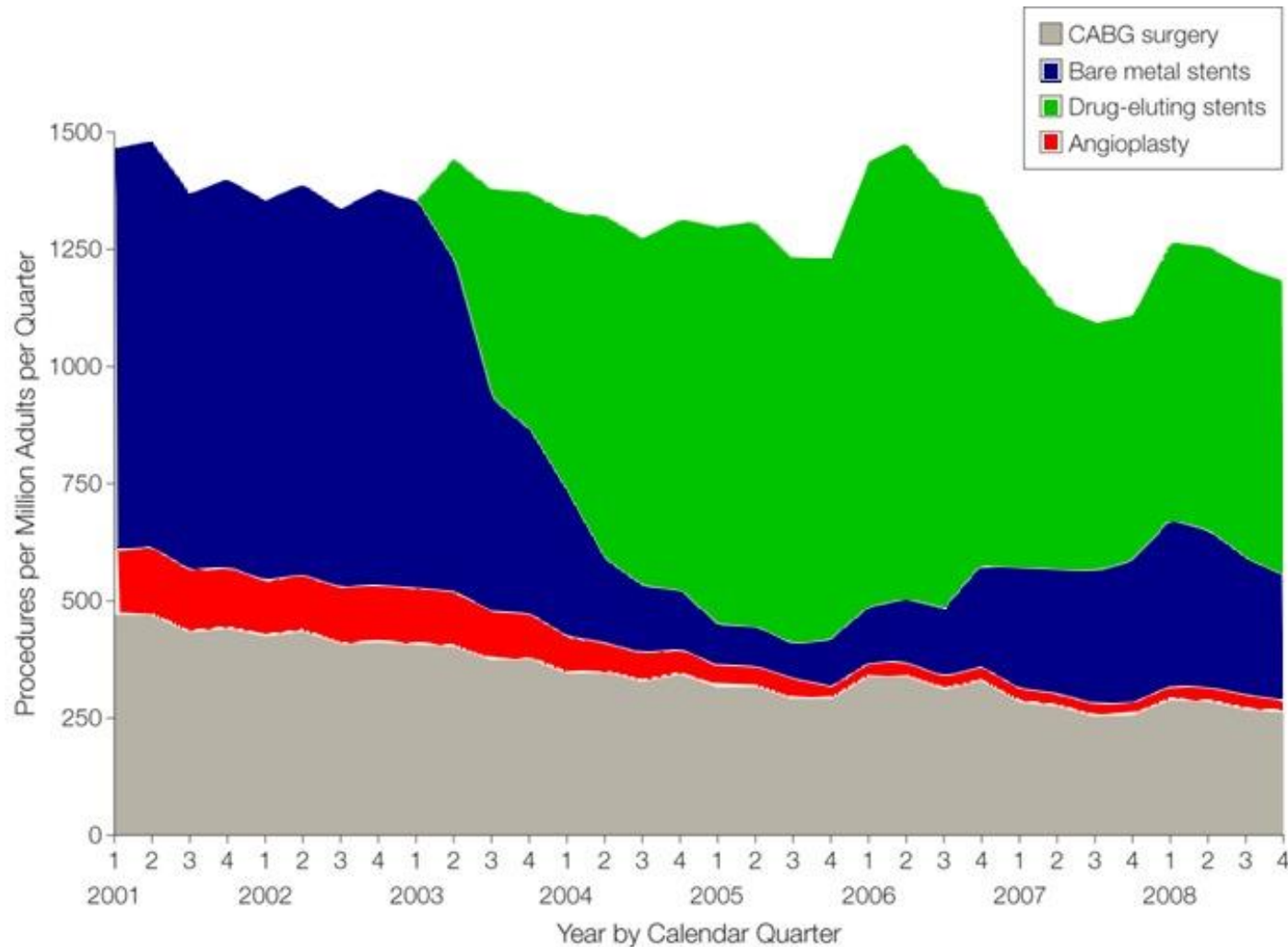
# FDA Safety and Innovation Act Sec. 907 Timeline





# Drug Eluting Stent Thrombosis

# Coronary Revascularization Trends in the United States, 2001-2008

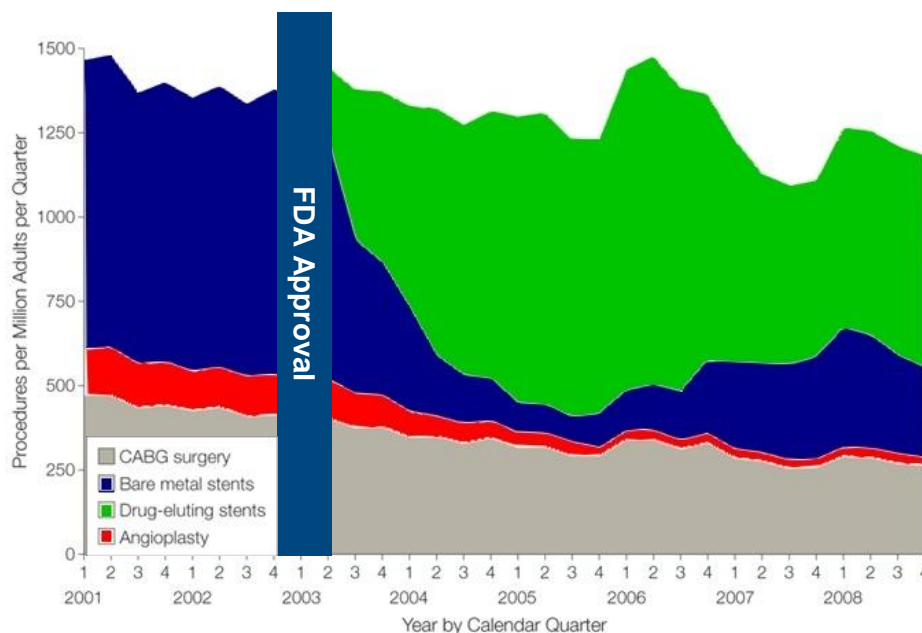




# Drug Eluting Stent Approval

## 2003 FDA approves first drug eluting stent

- Pivotal pre-market study of 1,100 patients in the SIRIUS trial

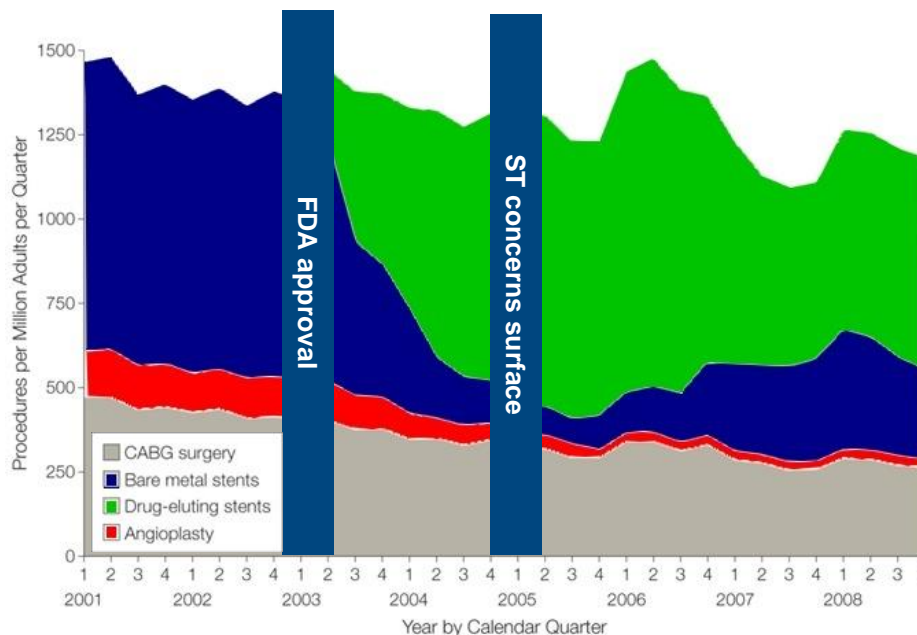


Moses JW et al; SIRIUS Investigators. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. N Engl J Med. 2003

# DES Late Stent Thrombosis (ST) Observations

## 2005 concerns regarding DES late stent thrombosis surface

- Rare (~1.5%), catastrophic event (up to 50% mortality)
- Swedish Coronary Angiography and Angioplasty Registry ~20,000 pts
- Numerous meta-analyses and scholarly reports on DES outcomes.

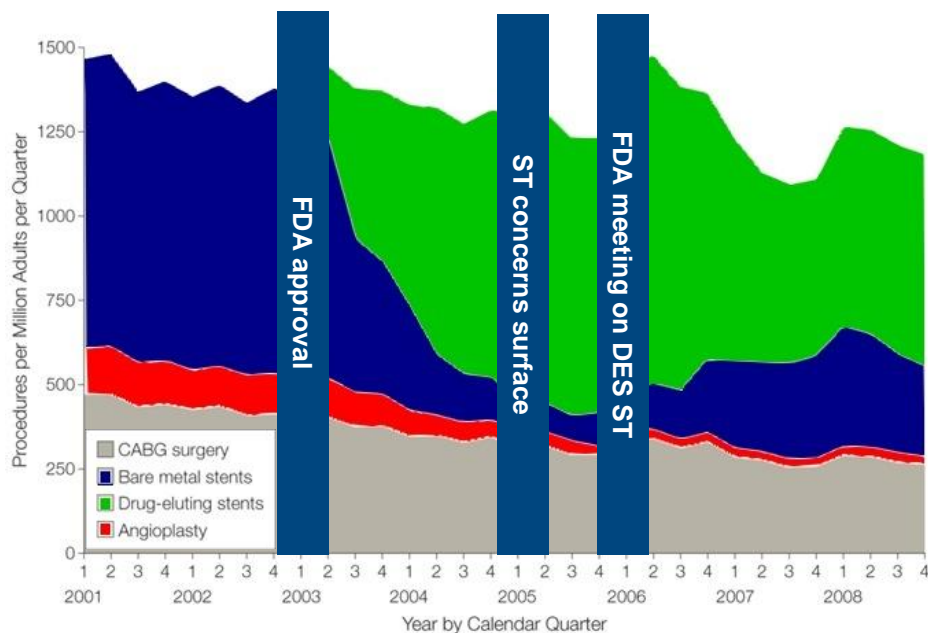


Lagerqvist B et al. Long-term outcomes with drug-eluting stents versus bare-metal stents in Sweden. N Engl J Med 2007

# FDA panel addresses DES stent thrombosis

2006 FDA convenes meeting regarding dual antiplatelet therapy (DAPT) duration

- DAPT duration extended to 1 year for DES.

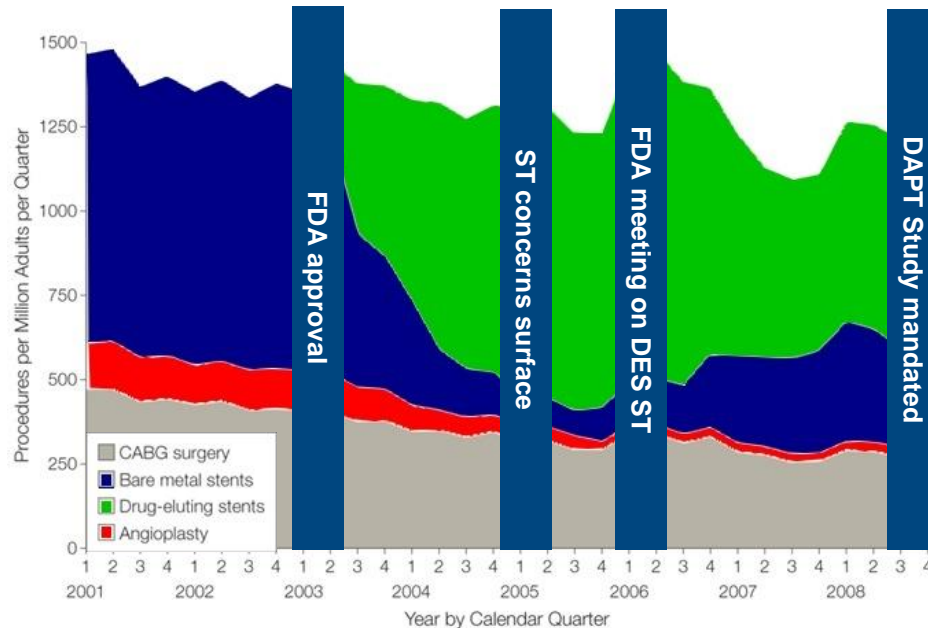


Weighing DES Safety and Efficacy  
New Insights from TCT 2006

# FDA mandates Dual AntiPlatelet Therapy Study

## 2009 FDA Critical Path Initiative launches DAPT Study

- Unprecedented collaboration between 4 DES, 4 antiplatelet drug manufacturers and Harvard Clinical Research Institute.
- 2014 Primary endpoint announced: 11,648 pts; 30 vs 12 month DAPT following DES lowers ST and MI but raises bleeding rate.

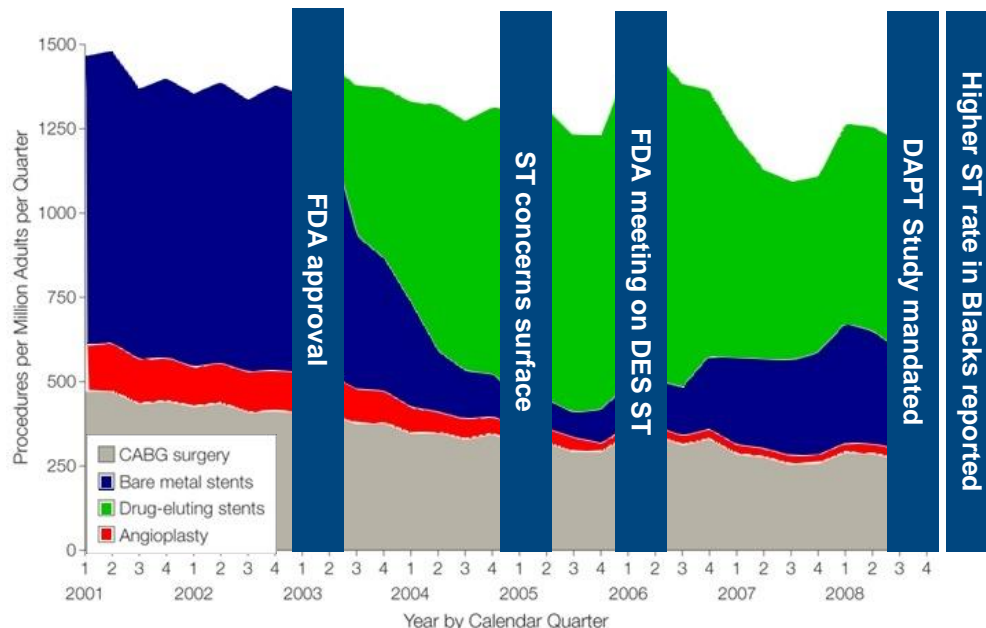


Kereiakes DJ, et al Dual Antiplatelet Therapy (DAPT) Study Investigators. Antiplatelet therapy duration following bare metal or drug-eluting coronary stents: the dual antiplatelet therapy randomized clinical trial. JAMA. 2015

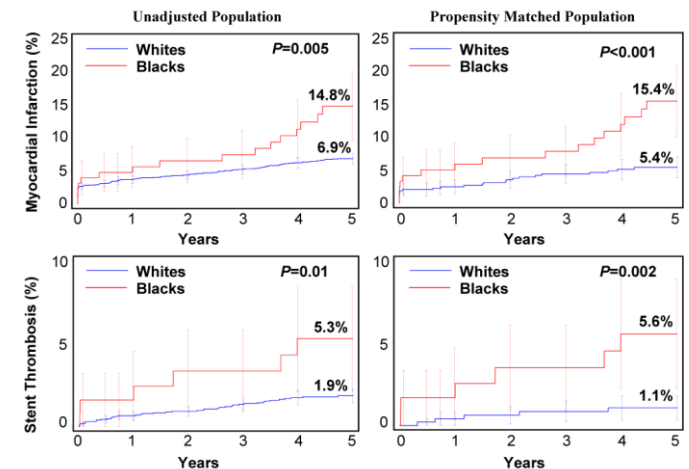
# Higher ST rate in African Americans observed in real-world registries

## 2009 Washington Hospital Center reports double rate of ST in Blacks

- 2012 Taxus Ethnicity meta-analysis confirmed registry data using randomized control trial data from robust Taxus database.



## Black vs. White: Risk of MI and Stent Thrombosis

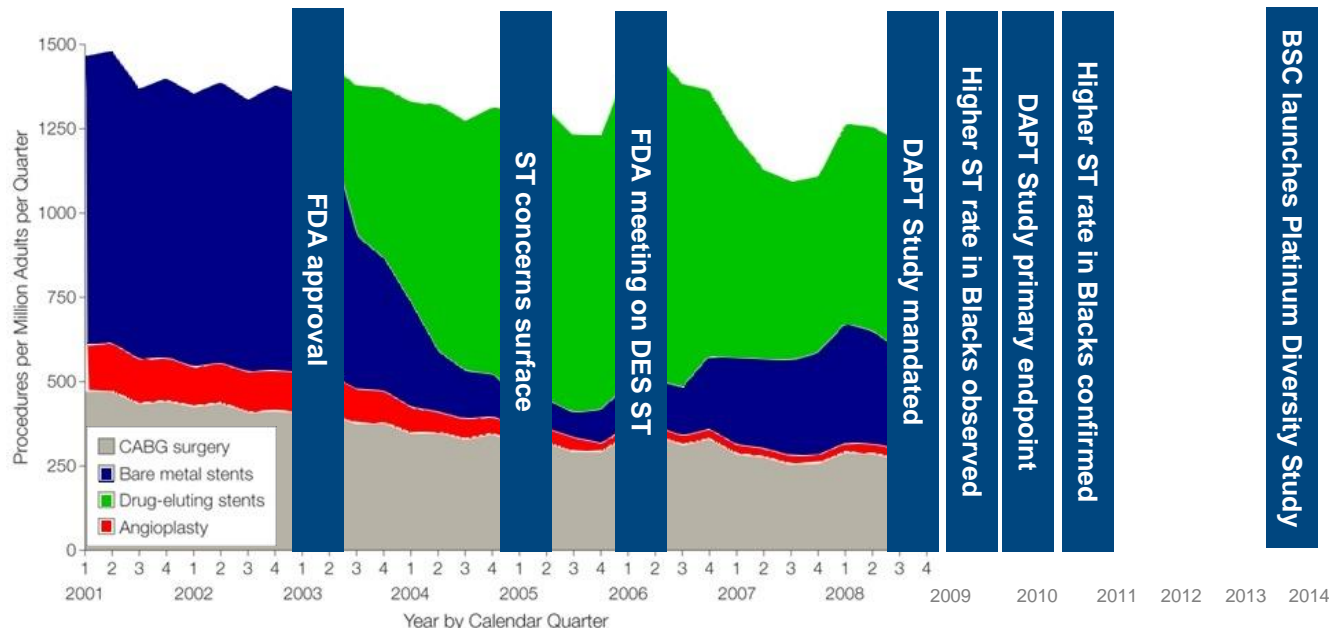


Batchelor et al. J Interv Cardiol 2012

# Post-market study focused on women and minorities

## 2014 Boston Scientific launches Platinum Diversity study of women and minorities receiving DES

- Enrollment completed 3 months ahead of expected.
- Results expected late 2016.



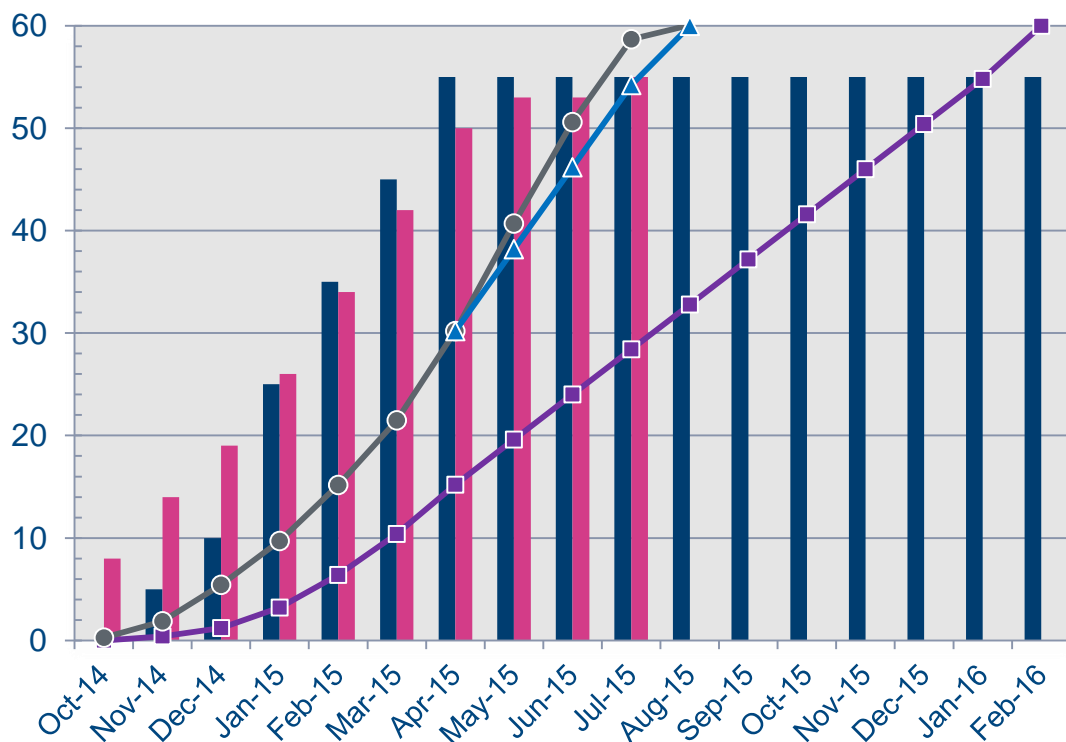


# PLATINUM Diversity: Enrollment



Boston  
Scientific

## Enrollment & Site Ramp-up



■ Total Sites - Planned

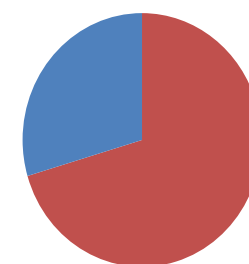
■ Total Sites - Actual

— Total Patients - Original Projection

— Total Patients - Actual

— Total Patients - New Projection

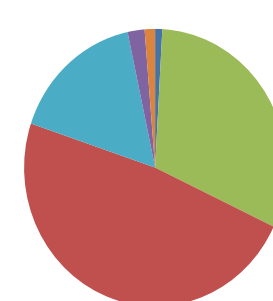
## By Gender



■ Women - 71%

■ Men - 29%

## Both Genders



■ American Indian or Alaska Native - 1%

■ Black of African heritage - 31%

■ Caucasian - 48%

■ Hispanic or Latino - 16.5%

■ Multiple - 2%

The background of the slide features a complex, abstract pattern of thin, light blue lines and curves. These lines intersect and overlap, creating a sense of movement and depth. The pattern is most dense on the left side and fades towards the right. The overall color scheme is a range of light blues, from very pale to a slightly darker shade where the lines are more concentrated.

# What have we learned?

# Potential Barriers to Research Participation

## Patient Pathway

**Patients not aware and/or not asked to participate**

**Patient misunderstands potential risks and benefits**

**Patient initially interested but does not enroll**

**Patient cannot execute participation logistics**

### Physician Sources

- Physicians ask women and minorities less often
- Female symptoms misdiagnosed
- Women and minorities not referred to specialist or treated in a setting with no access to research

- Poor physician communication

- Patient does not meet criteria or has too many comorbidities to be a good candidate

- Clinic inefficiencies create patient burden

### Patient Sources

- Patients not aware of opportunities
- No (or limited) access to internet
- Women are older than men at disease onset

- Patients misunderstand risks and benefits
- Lack of patient educational materials
- Cultural biases
- Intimidated by terminology ("clinical trial" vs. "health research")

- Patient or family intimidated by consent form or trial materials
- Insurance coverage creates financial burden
- Comorbidities reduce interest
- No time, logistical burden, or caregiving responsibilities

- Caregiving responsibilities
- Cost of travel, lost wages, or child care
- Extra clinic visits
- No time
- No transportation

1

## **Increase awareness around participation opportunities**

- Patient-focused awareness around the benefits of participation
- Make it easier for patients and physicians to locate research opportunities (e.g. database)
- Tools to increase awareness of participation opportunities among PCPs and General Cardiologists
- Leverage physician societies and social networks to encourage women and minorities to participate (through interaction with their peers who have participated, etc)

2

## **Examine trial design elements/protocols and propose changes to increase the number of women and minorities who qualify**

3

## **Reduce the perceptions and misperceptions around participation risk**

- Patient education materials that describe the research process as well as the benefits of participation
- Education for investigators and trial coordinators on how to more effectively approach and communicate with female and minority patients

4

## **Leverage current investigator database to understand patient demographics with respect to clinical practice**

- Understand characteristics of demographic enrollment (which sites provide diverse enrollment, where do diverse patients reside, who manages the subgroup in question)
- Close the Gap approach

Each of these opportunities requires participation from multiple stakeholders

- **Pre-market data collection representative of investigator clinical practice**
  - Sufficient safety and efficacy data to allow device approval for broad population.
  - Assures device availability to general public is not delayed by lengthy enrollment timelines.
- **Post-market surveillance to provide data for subgroup analysis**
  - Variances in safety or efficacy may be identified during post-market clinical experience
  - Statistically relevant sample related to specific demographic subgroup are available for evaluation.
- **Additional analytic modalities to focus on specific subgroups**
  - Meta-analyses
  - Collaborative partnerships (e.g. NIH, CMS, HCRI)
  - Hypothesis generating studies
- **Leveraged data from existing sources such as SSED and Clinicaltrials.gov should be kept within the context from which the data were collected.**
- **Boston Scientific appreciates FDA's openness to share internal practices and thinking. Interactive initiatives supporting FDASIA 907 action plan allow industry and FDA to align on key concepts which will result in better decision making and compliance.**