

Successful Use Cases of Real-World Evidence

Transcatheter Valve Therapy STS/ACC TVT Registry

Michael Mack, M.D.

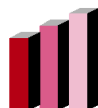
Baylor Scott& White Health

RWE

RWE

Also found in: [Wikipedia](#).

Acronym	Definition
RWE	Rot-Weiss Essen (<i>Germann football club</i>)
RWE	Ralph Waldo Emerson
RWE	Right Wing Extremist
RWE	Rheinisch-Westfälische Elektrizitätswerke (<i>German Power Supplier</i>)
RWE	Read Write Execute
RWE	Religious Witness for the Earth
RWE	Rumble World Entertainment (<i>Hawaii</i>)
RWE	Reaction Wheel Electronics
RWE	Rockford Wind Ensemble (<i>Rockford, IL</i>)
RWE	Royal Wholesale Electric (<i>various locations</i>)
RWE	Rosewater Engineering, Inc. (<i>est. 1983</i>)



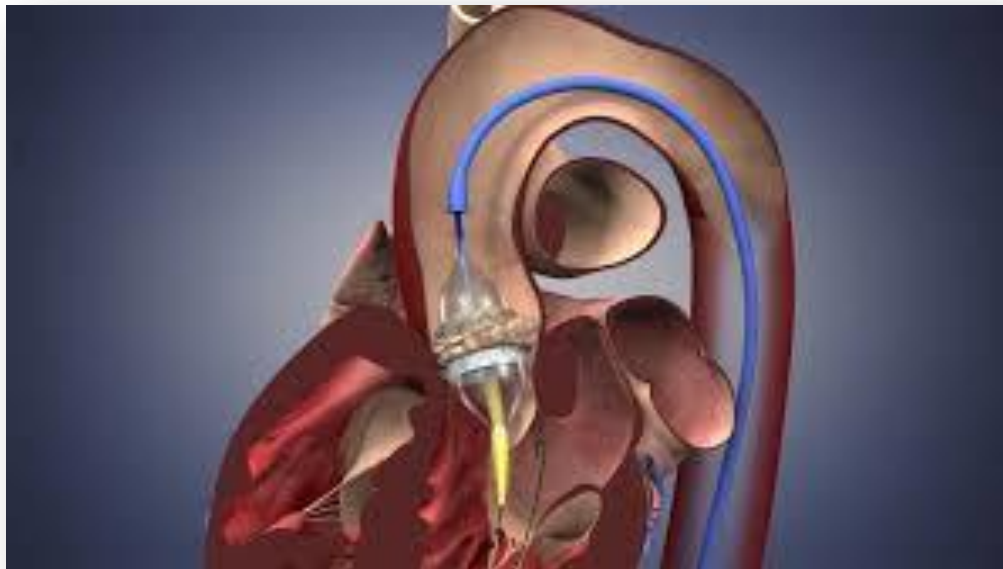
RWE- FDA Definition

- RWE refers to healthcare information derived from multiple sources outside of typical clinical research settings, including electronic health records (EHRs), claims and billing data, product and disease registries, and data gathered by personal devices and health applications.

What is TAVR?

What is the STS/ACC TVT Registry?

TAVR –Transcatheter Aortic Valve Replacement





STRENGTHENING OUR NATIONAL SYSTEM FOR MEDICAL DEVICE POSTMARKET SURVEILLANCE

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH
U.S. FOOD AND DRUG ADMINISTRATION

SEPTEMBER 2012

- UDI system incorporated into EHR
- National and international device registries
- Modernize adverse event reporting
- New methods for evidence generation, synthesis and appraisal



David Holmes
President
American
College of
Cardiology 2011

Jeff Shuren
Director CDRH
FDA

Michael Mack
President Society
of Thoracic
Surgeons 2011

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[<< Back to National Coverage Determination \(NCD\) for Transcatheter Aortic Valve Replacement \(TAVR\)](#)

National Coverage Determination (NCD) for Transcatheter Aortic Valve Replacement (TAVR) (20.32)

- TAVR approved under **“coverage with evidence development”**
- Approved for treatment of severe symptomatic aortic stenosis
- FDA approved indication and with an FDA approved device
- Two cardiac surgeons approve
- Performed in facility with
 - >50 surgical AVR'/year (~400)
 - >400 caths/50PCI/year
 - >20TAVR/year
 - Mortality <15%
 - Stroke <15%
- Multidisciplinary Heart Team
- **Mandatory national registry participation**

February 2015 Health Affairs

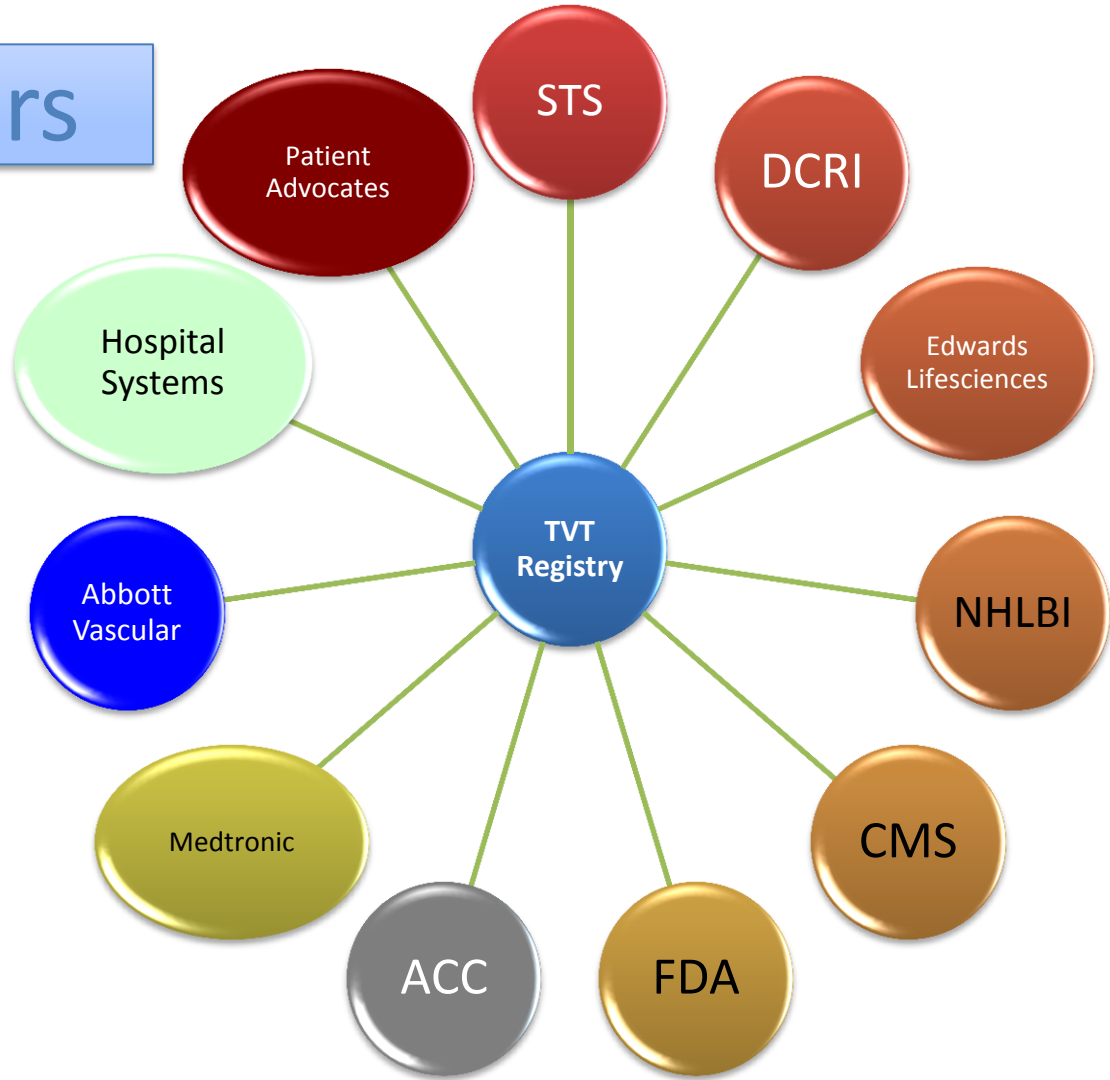
TRACKING INNOVATION

By John D. Carroll, Jeff Shuren, Tamara Syrek Jensen, John Hernandez, David Holmes, Danica Marinac-Dabic, Fred H. Edwards, Bram D. Zuckerman, Larry L. Wood, Richard E. Kuntz, and Michael J. Mack

Transcatheter Valve Therapy Registry Is A Model For Medical Device Innovation And Surveillance

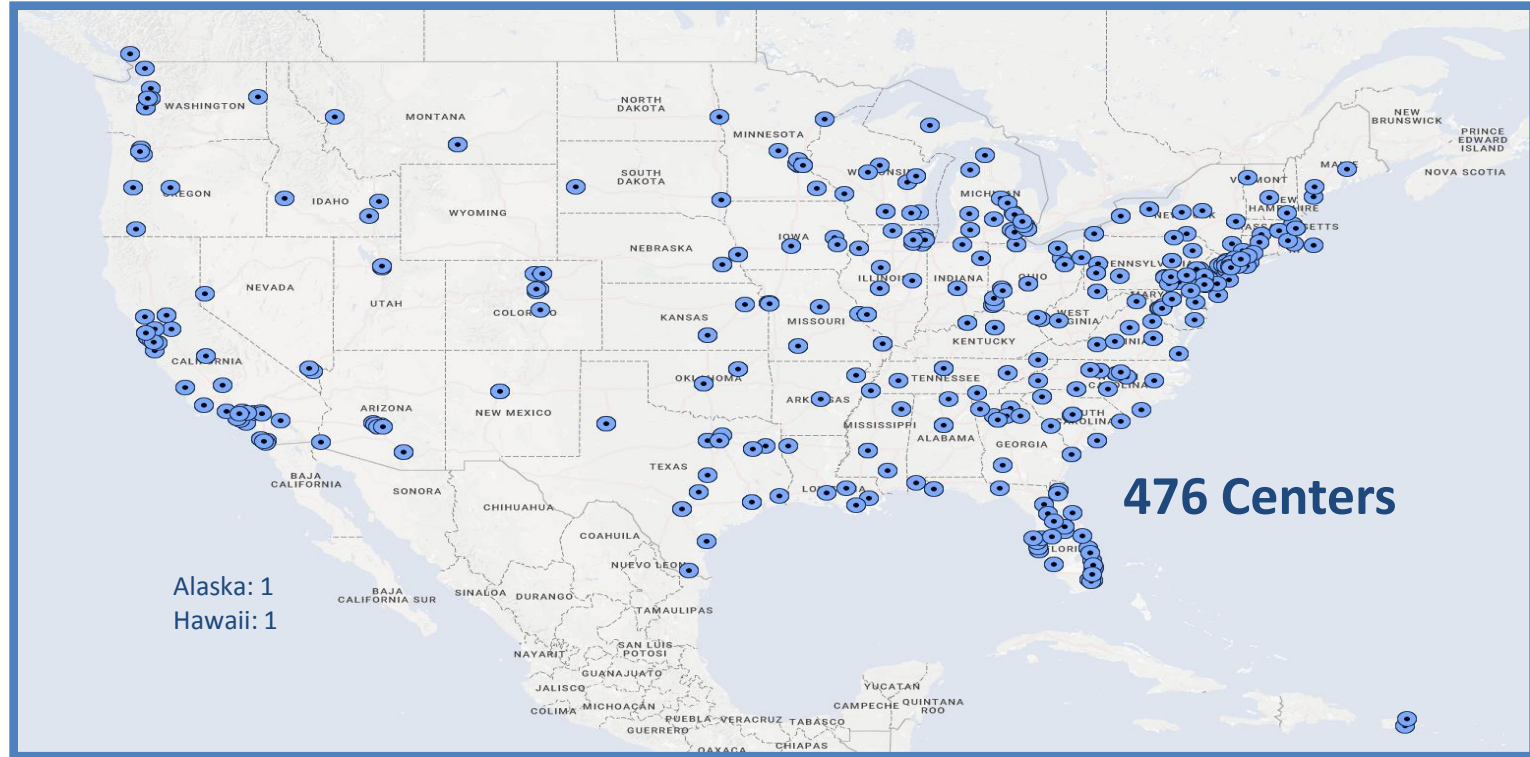
STS
ACC
FDA
CMS
Industry

The Stakeholders

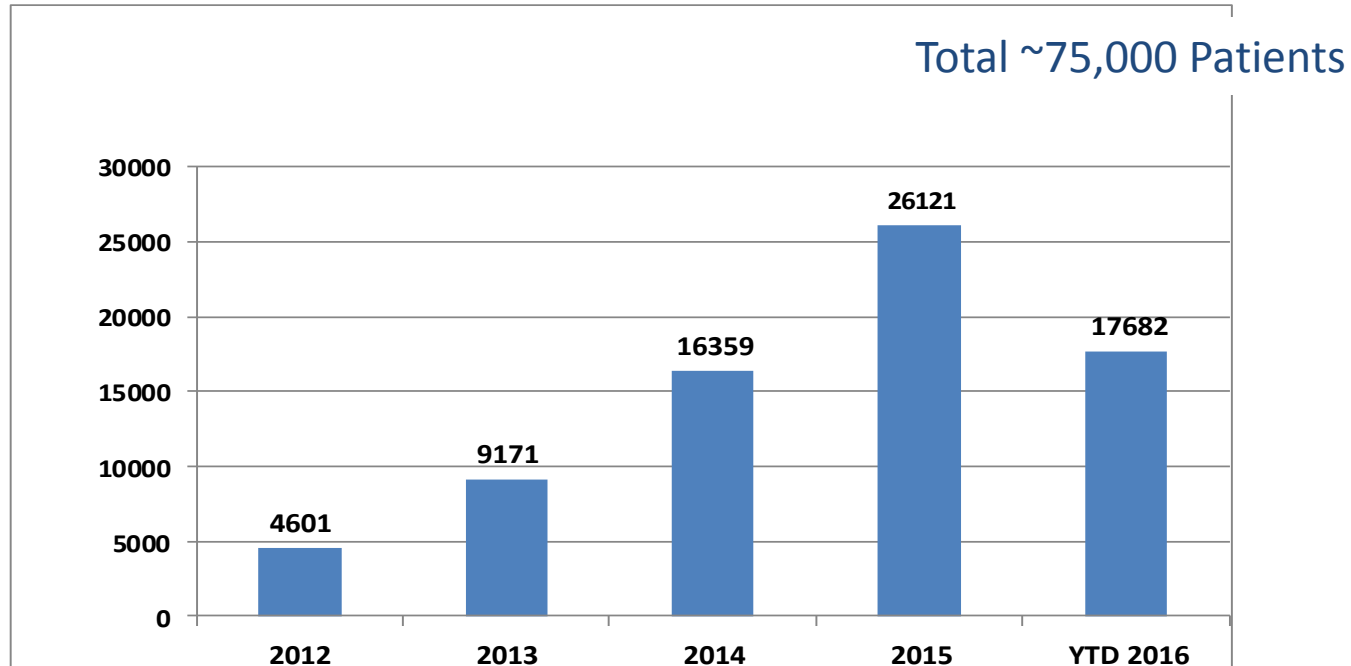


2011	2012	2013	2014	2015	2016
<u>July 2011</u> TVT Registry proposed at FDA Advisory Panel for Edwards Sapien Valve	<u>May 2012</u> CMS issued National Coverage Decision for TAVR	<u>Feb 2013</u> STS/ACC TVT Registry Launched Version 1.2	<u>June 17, 2014</u> Edwards Sapien XT FDA approval for High Risk	<u>March 30, 2015</u> Medtronic CoreValve FDA approval for ViV on tissue valve	<u>Jan 11, 2016</u> Medtronic CoreValve FDA approval for High Risk
<u>Nov 2011</u> Edwards Sapien THV FDA approval for Ext High Risk		<u>Sept 2013</u> STS/ACC TVT Registry Launched Version 1.3	<u>Aug, 7, 2014</u> CMS issued National Coverage Decision for TMVR	<u>June 17, 2015</u> Edwards Sapien 3 FDA approval for High Risk	<u>March 2, 2016</u> Edwards Sapien XT FDA approved for Pulmonic Valve
<u>Dec 2011</u> STS/ACC TVT Registry Launched Version 1.0		<u>Oct 25, 2013</u> FDA approval of Abbott MitraClip		<u>June 23, 2015</u> Medtronic Evolut R FDA approval for High Risk	<u>Aug 18, 2016</u> Edwards Sapien XT & 3 FDA approval for Intermediate Risk
				<u>Oct 9, 2015</u> Edwards Sapien XT FDA approval for VIV on tissue valve	

TAVR Centers in North America



Commercial TAVR Patients in the TVT Registry



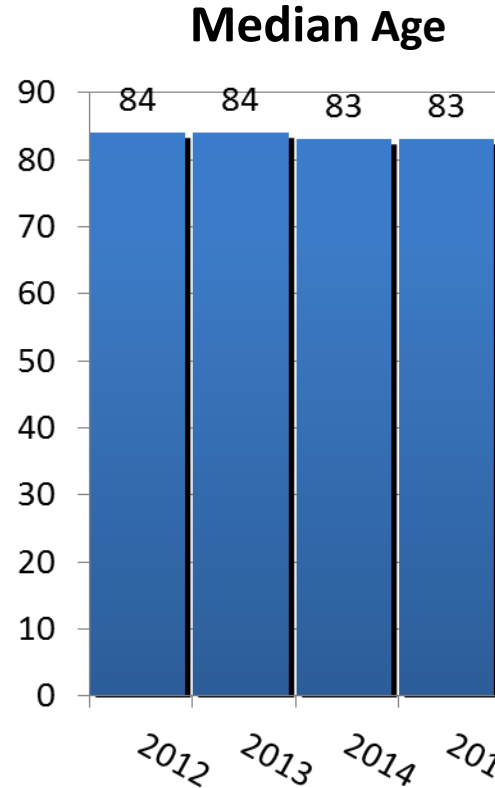
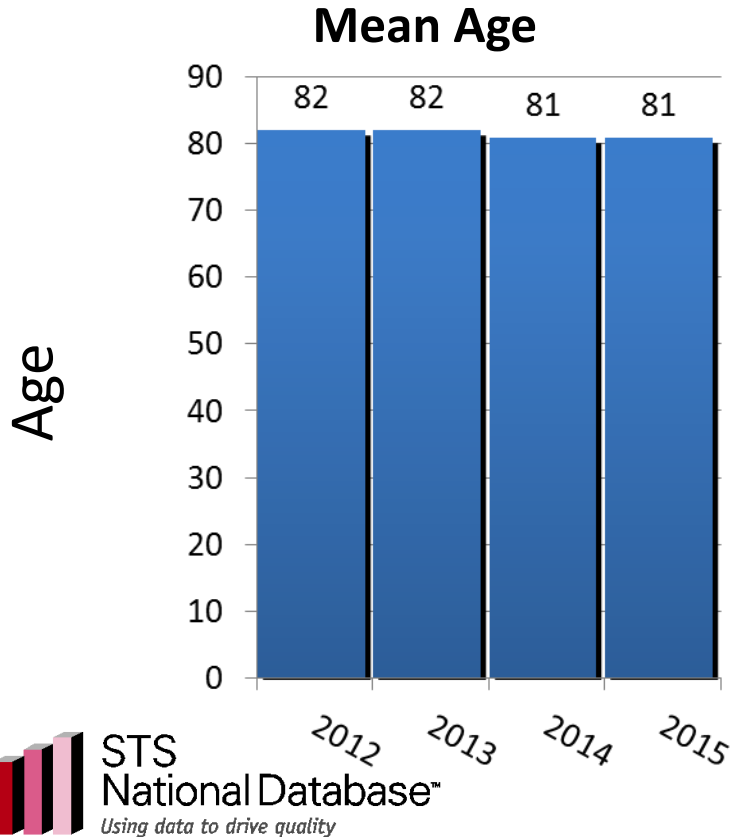
What Data Are Collected?

- Case Report Form- >400 data fields
- Demographics, provider and facility characteristics
- History/risk factors, cardiac status, and health status
- Indications for the procedure
- Pre, intra, and post procedure data and adverse events
- Quality of Life (KCCQ)
- Outcomes at 30 days and one year

What “Real World Evidence” of Medical Device Performance is Developed ?

- Near real time outcomes of virtually all devices implanted
- Risk adjusted center performance
- Long term outcomes via linkage with CMS

TAVR: Age of the Patients



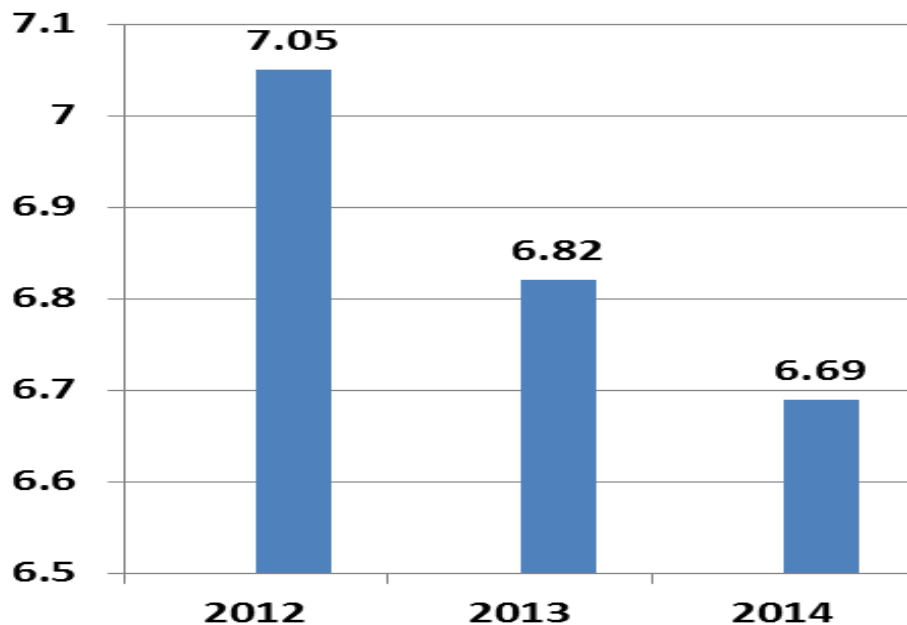
No major age “creep”, i.e. decrease in the age of the population being treated.



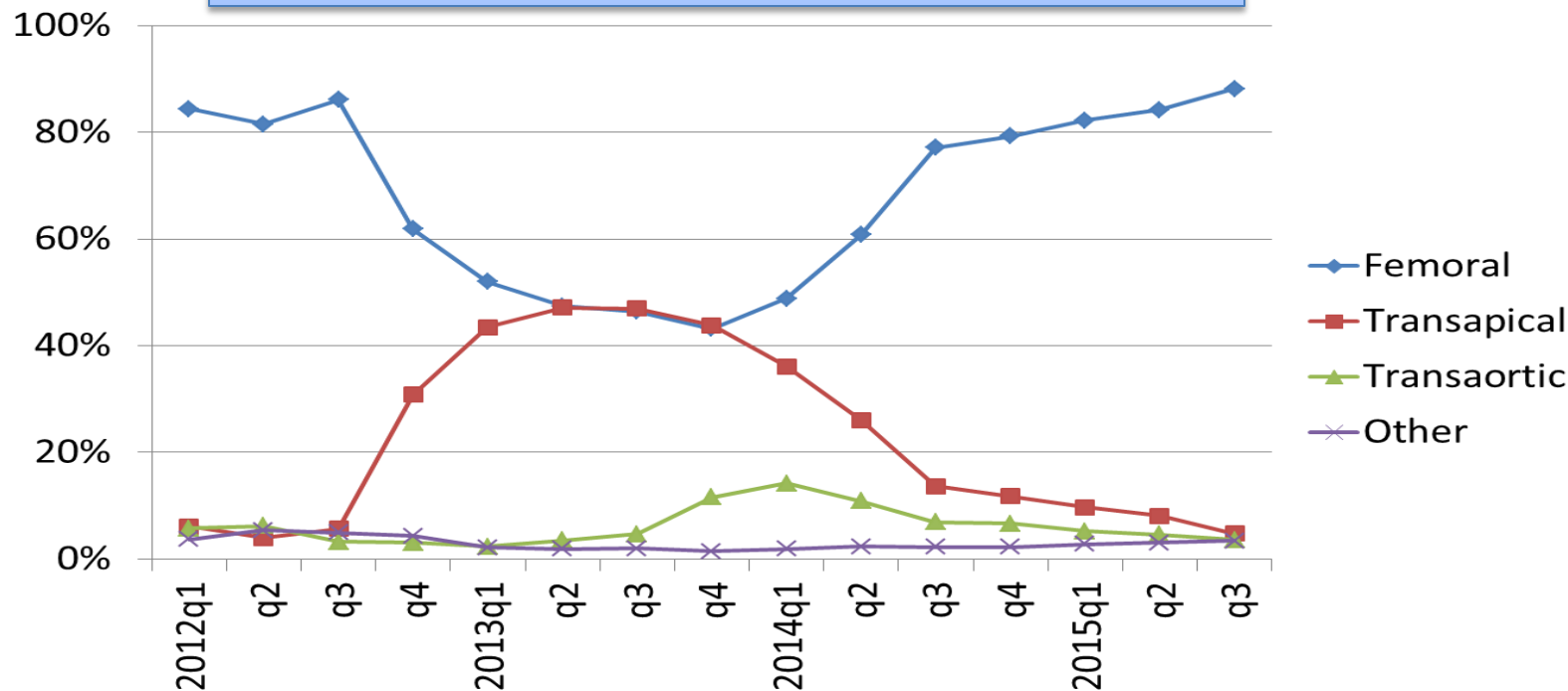
NCDR
NATIONAL CARDIOVASCULAR DATA REGISTRY

Source: STS/ACC TVT Registry Database as of Jan 17, 2016

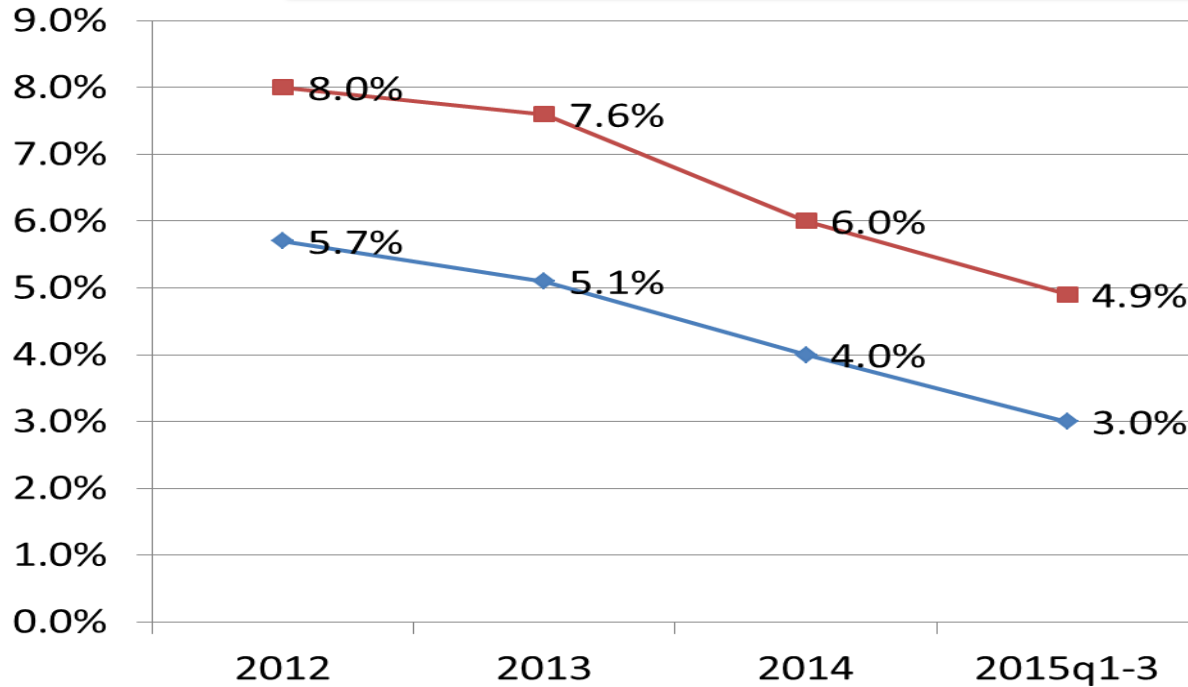
Median STS Risk Score for all TAVR Procedures



TAVR Access Site

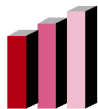


Mortality after TAVR



Almost a 50% drop
in mortality over a
3 year period.

◆ In-hospital Mortality
■ 30 day mortality



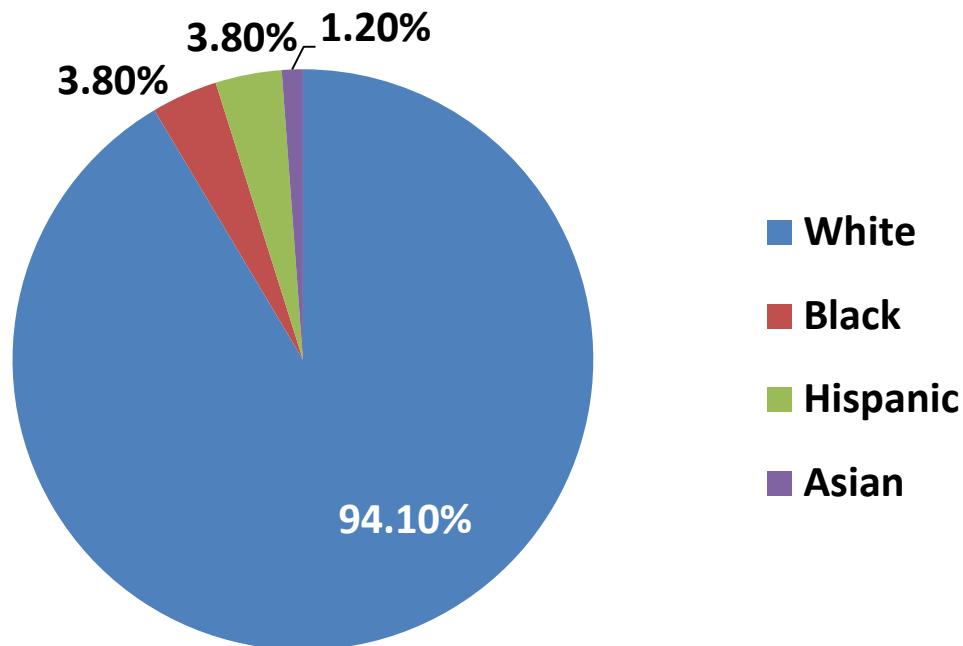
STS
National Database™ 46865 records as of 2-20-15
Using data to drive quality

Source: STS/ACC TVT Registry Database



NCDR®
NATIONAL CARDIOVASCULAR DATA REGISTRY

Racial Breakdown of Patients in TVT Registry



Data Quality Program

Event Adjudication

- Verifies and provides additional information for key events (stroke, TIA and repeat intervention, plus HF admission for MitraClip)

Audit Program

- Evaluates accuracy and reliability
- Assesses proper and complete reporting of cases
- Voluntary and self audits

Data Outlier Program

- Provides outlier alerts to registry participants

Event Adjudication

- 2170 events reviewed by clinical event team
- Summary of disagreements:
 - TIA (determined as either an ischemic stroke 20% of the time)
 - Stroke of undetermined origin (determined as ischemic stroke 1/3 of the time)
 - AV or MV re-intervention (determined as “no event 10% of the time)
 - Heart failure readmission (determined as “no event 1/3 of the time)

Real World Evidence Generation

From Patient Level Data

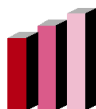
- Regulatory
 - Postmarket
 - Premarket
- Quality Improvement
- Research

“Real World Evidence” *Post Market*

- 30 day outcomes on virtually all patients (except VA)
- Quarterly data safety reports to FDA
- Nested Post Approval Studies
 - Edwards, Medtronic, Abbott Vascular
- Lifetime follow up of Partner 3 low risk patients (>10 years)

“Real World Evidence” *Pre Market*

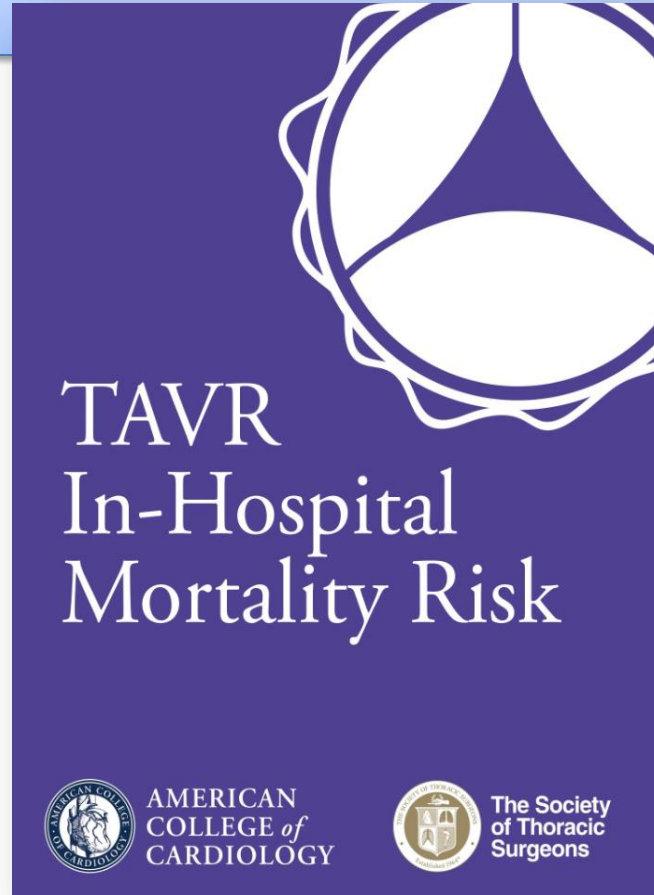
- Off label use for label expansion
 - Alternative access in inoperative patients
 - Alternative access in high risk patients
 - Valve-in-Valve in inoperable and high-risk patients
- Continued access protocols
 - Sapien 3
 - CoreValve
- IDE studies



“Real World Evidence” *Quality Improvement*

- Quarterly reports to sites benchmarked nationally
- Risk adjustment
- Risk calculator
- Appropriate use criteria performance
- Public reporting

TAVR Risk Calculator



- STS Risk Score:
 - 30 Day
- TAVR Risk Calculator:
 - In-Hospital only

Based on following evaluation

Patient Demographics

Age : 90 Years Sex : Male
Race : Hispanic or Latino

Patient Pre-Procedural Characteristics

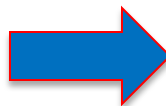
Renal Function
Glomerular Filtration Rate (calculated): 30 mL/min/1.73m²
Serum Creatinine (SCr) 2.4 mg/dL
Dialysis ✓ No
NYHA Class IV ✓ No
Severe Chronic Lung Disease ✓ Yes
Procedure Access Site ✓ Femoral



Acuity Status	Category 1
Procedure Status	Elective
Prior Cardiac arrest within 24 hrs?	✓ No
Prior cardiogenic shock within 24 hrs?	✓ No
Pre-procedure inotropes within 24 hrs?	✓ No
Pre-procedure mechanical assist device?	✓ No

Calculate Risk

Email Results



Includes 9 variables that are entered by user

Predicted Risk

Adjusted TAVR In-Hospital Mortality Risk

[Click here for info about this risk model](#)

Patient's Risk
3%

National Average
4% as of May 2015

In the United States, the average mortality of all patients undergoing this procedure is **4%**. Taking into account the patient's specific clinical condition, the statistical estimate that he might not survive the procedure is **3%**. This means that for every 100 patients having a similar clinical makeup, there would be **3** who did not survive.

The model provides an objective risk-adjusted estimate of in-hospital mortality which has real value for both patient and provider. It should be considered as one element in the evaluation process, to be considered along with the other traditional factors that determine whether the patient is an appropriate candidate for the procedure.

Steps to Establish Public Reporting

- Establish what metrics to report
- Obtain independent endorsement from NQF
- Define program policies and procedures
- Obtain consent from registry participants
- Decide what publication vehicle/display

“Real World Evidence” *Research*

- Annual Report in JACC, Annals Thoracic Surgery
- Pragmatic randomized trials
 - CLOE (NHLBI Review)
- Volume/Outcome Relationship at Clinical Sites
 - Inform CMS
- PCORI Grant
 - Management of Aortic Stenosis-*Patient Education and Decision Aids*

What “Value” Has Been Created So Far ?

- Near Real-time Reporting of Early Outcomes in Virtually All Patients
- Clinical data allowing “risk adjustment”
- One Year Outcomes by Linkage to CMS Claims
- IDE trials for label expansion
- Comparative effectiveness studies with SAVR
- QI at site level

Challenges

- Scalability
 - Beyond an expensive device (\$32K) and single payer (CMS)
- Sustainability
 - Beyond NCD
- Site Burden and Expense
 - Autopopulation from EHR's?
- Creating/Demonstrating Value
 - Does every device need to be tracked in perpetuity?

Registry Sustainability – Fit-to-Purpose Infrastructure

~~Shared Benefits of Multi-Stakeholder Partnerships~~ ACCF/STS

Databases/Registries

ACC NCDR

- CathPCI
- ICD
- IMPACT
- LAAO
- AF Ablation
- PVI

STS National Database

- STS ACS
- STS CHD
- STS Thoracic Surge

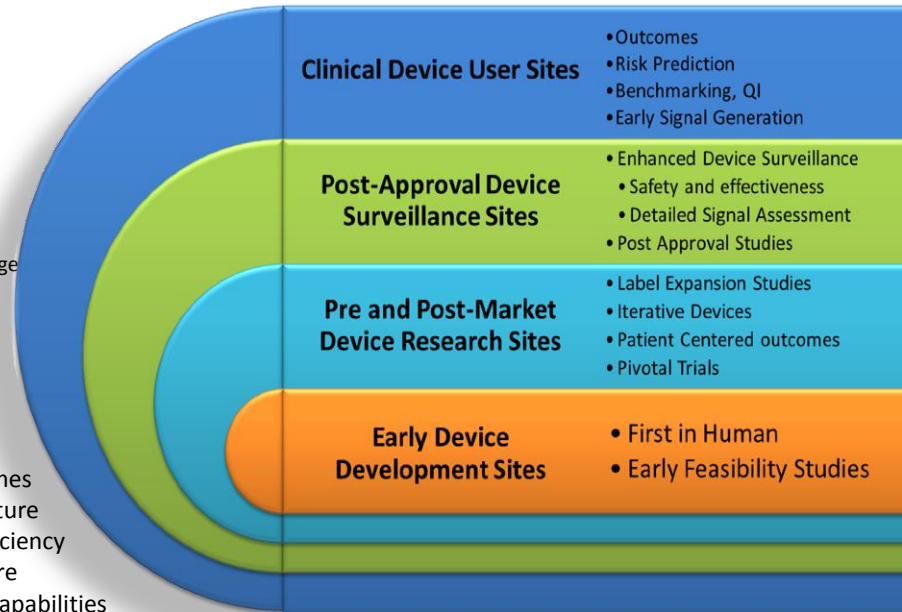
Joint STS and ACC

- TVT Aortic
- TVT Mitral
- TVT Tricuspid

Tier Criteria

- Case mix
- Volume and Outcomes
- Research Infrastructure
- IRB/Contracting Efficiency
- Clinical Infrastructure
- Dataset Needs vs. Capabilities

Tiered Site Certification*



Dataset Complexity
& Need for Multi-
Stakeholder
Support



*Sites apply for certification level desired for each database.
Free to use certification level for each database in marketing.

John Laschinger
FDA CDRH