Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) Focused Topic: TAVR Program Requirements

July 25, 2018

Presenter for AdvaMed: Martin B. Leon, MD

Columbia University/NY Presbyterian Hospital

Cardiovascular Research Foundation

Disclosure Statement
MEDCAC Meeting; Baltimore, MD; July 25, 2018
Martin B. Leon, MD

I, Dr. Martin B. Leon, was asked by AdvaMed to present to the Medicare Evidence Development and Coverage Advisory Committee (MEDCAC). My presentation and comments reflect my own views and experiences. In the course of developing this presentation, I solicited and received AdvaMed members' perspectives and information (including certain data analyses). AdvaMed supported my travel and accommodations to attend this MEDCAC panel.

Financial Disclosure
MEDCAC meeting; Baltimore, MD; July 25, 2018
Martin B. Leon, MD

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation / Financial Relationship	Company
• Grant / Research Support	Abbott, Boston Scientific, Edwards Lifescience, Medtronic
• Consulting Fees / Honoraria	None
• Shareholder / Equity	None

MEDCAC - TAVR Program Requirements

Caveats for this presentation

- **The public health imperative is to deliver improved access to AVR therapies with optimal clinical outcomes for all patients with severe symptomatic aortic stenosis.**
- **Data regarding the need for imposing increased minimum procedural volumes to initiate or maintain a TAVR center are imprecise and poorly validated; recommendations rely disproportionately on "expert opinions" and do not incorporate quality metrics.**
- **Future significant growth in TAVR case volume due to expanding clinical indications must be accounted for in all decisions which may adversely affect patient access.**

MEDCAC - TAVR Program Requirements

Caveats for this presentation

- **The 9 voting questions posed by MEDCAC and the Additional Topics for Discussion will be answered responsively as a supplement to this main presentation and have been made available to the panel.**
- **The purpose of this presentation is to provide needed clinical perspectives, to frame the critical issues regarding procedural volume thresholds as a central metric for TAVR site selection, and to suggest alternative quality-based approaches which will *optimize both* patient access to and clinical outcomes after TAVR procedures.**

Presentation Overview

BACKGROUND - natural history of AS, impact of TAVR on mortality, AS under-diagnosis and under-treatment by AVR

TAVR EVOLUTION & GROWTH - current treatment practices, clinical indications, and outcomes, TAVR growth expectations

TAVR VOLUME–OUTCOME RELATIONSHIPS – TVT registry and MEDPAR data, impact of volume thresholds on new/existing sites

ADDITIONAL TOPICS AND TAVR PROGRAM RECOMENDATIONS – quality vs. volume metrics, geography issues, and need for SDM

Aortic Stenosis

By JOHN ROSS, JR., M.D. AND EUGENE BRAUNWALD, M.D.

THE ADVENT of corrective operations for various forms of heart disease has placed increasing emphasis upon the need for accurate information concerning the natural history of patients with potentially correctible lesions. An understanding of the natural course assumes particular importance in the case of aortic stenosis because of the significant incidence of sudden death associated with this disease and the grave prognosis that appears to accompany the onset of certain symptoms, patients with isolated valvular aortic stenosis of rheumatic etiology and patients without a history of rheumatic fever who have isolated calcific aortic stenosis; many of the latter patients are now considered to have developed calcification and stenosis of a congenitally bicuspid valve.[1] The review will focus primarily on the prognostic significance of three major symptoms—angina pectoris, syncope, and symptoms related to left ventricular failure

From the Cardiology B
stitute, Bethesda, Maryland

Supplement V to Circulat

… the grave prognosis that appears to accompany the onset of certain symptoms

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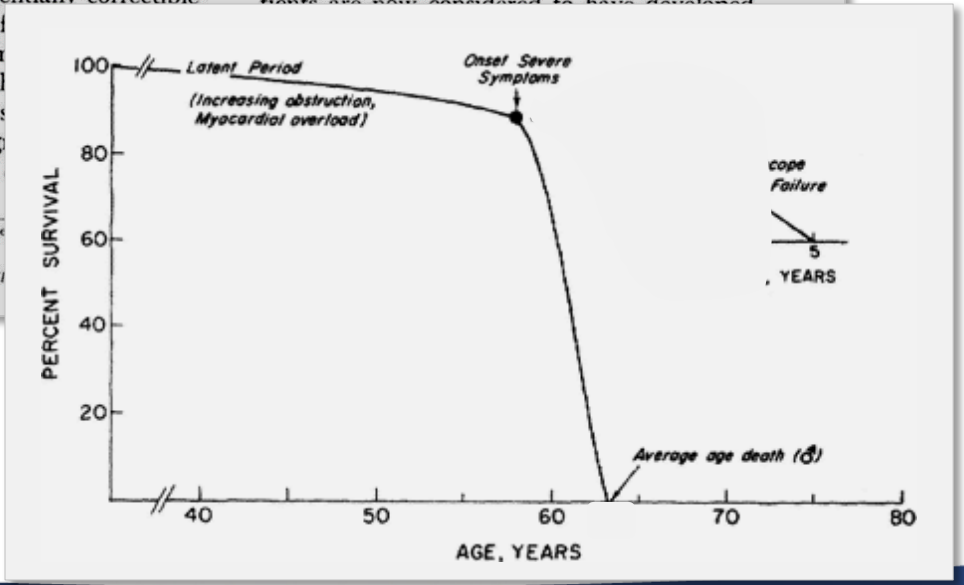
Supplement V to Circulation, Vols. XXXV



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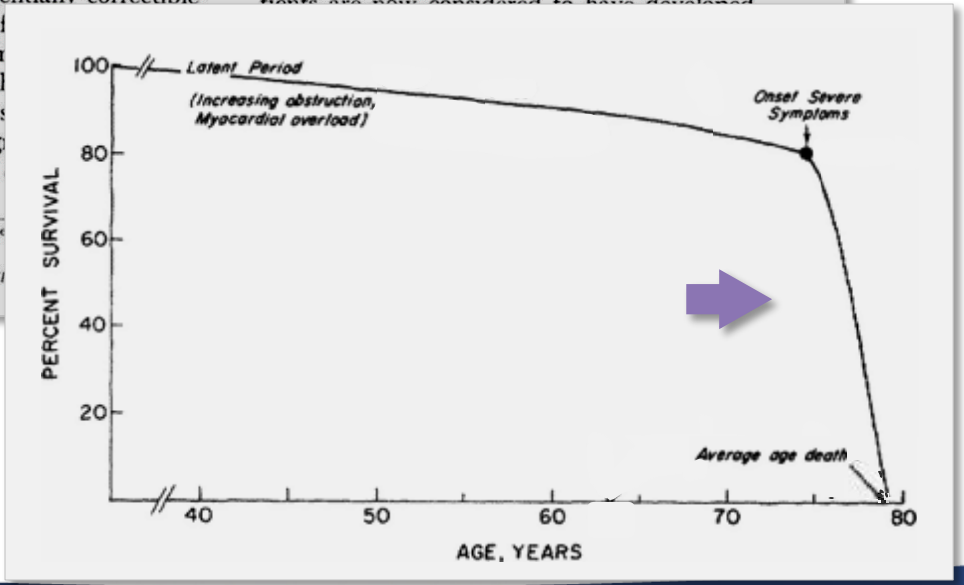
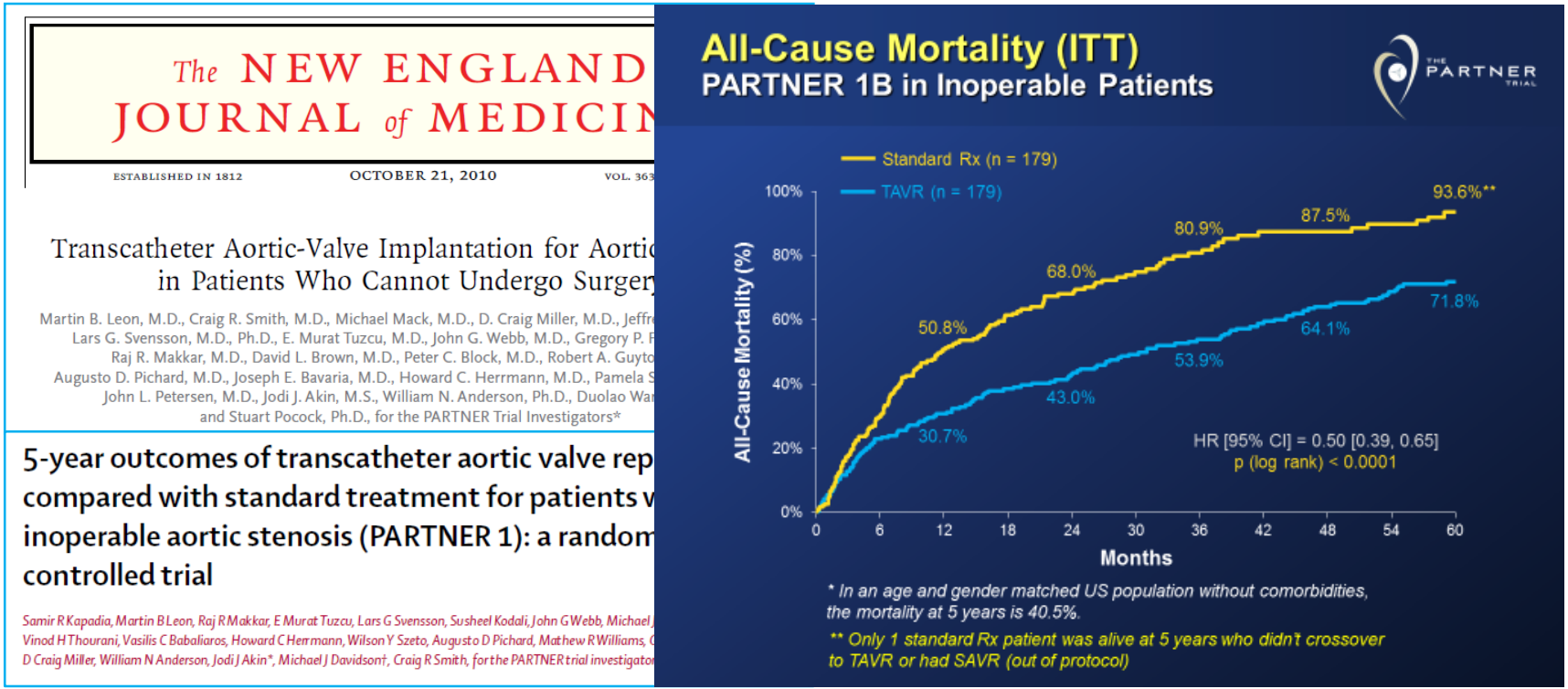
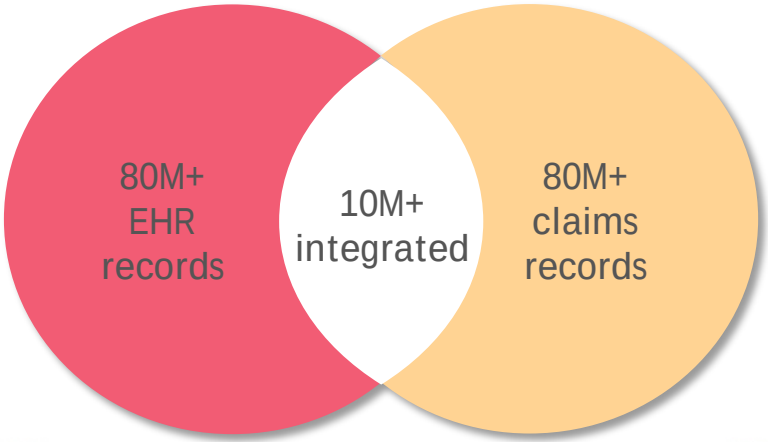




358 pts with severe symptomatic AS, randomized 1:1 standard therapy vs TAVR.
RESULTS: with TAVR, ↓20% mortality @ 1 yr, NNT = 5, median survival ↑11.1 to 27.9 mos

Real World U.S. Data – OPTUM EHR/Claims Database

- **SIZE** ~160M records: 80M EHRs and 80M claims
- **POPULATION** Older and younger patients; commercial and Medicare
- **SCOPE** Multiple institutions for national, not institution trends
- **DEPTH** Performance status, symptoms, traceability, specificity
- **RICHNESS** Patient details from Natural Language Processing on physician notes



Real World U.S. Data – OPTUM EHR/Claims Database

Characterizing the data

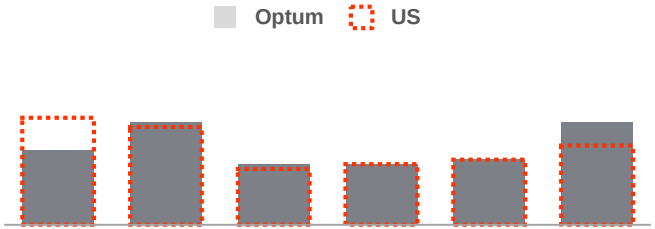
80M
Cumulative patients

10M
Patients with linked health plan data

27M
Patients with >5yrs of HER activity

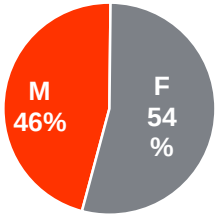
39 months
Average months of clinical observations

Age



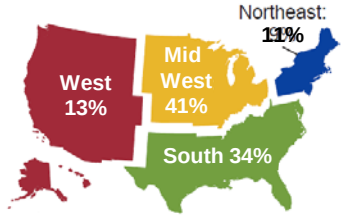
	0-17	18-34	35-44	45-54	55-64	65+
Optum #	13M	17M	10M	11M	11M	18M
Optum %	16%	22%	13%	13%	14%	22%
US Est	23%	21%	12%	14%	14%	17%

Gender



M	F
37M	43M
46%	54%
47%	53%

US Region



West	Mid-west	South	North-east
30M	8.4M	25M	9.8M
13%	41%	34%	11%
24%	21%	37%	18%

Source: Optum EHR statistics, Optum Research Data Assets (2014)

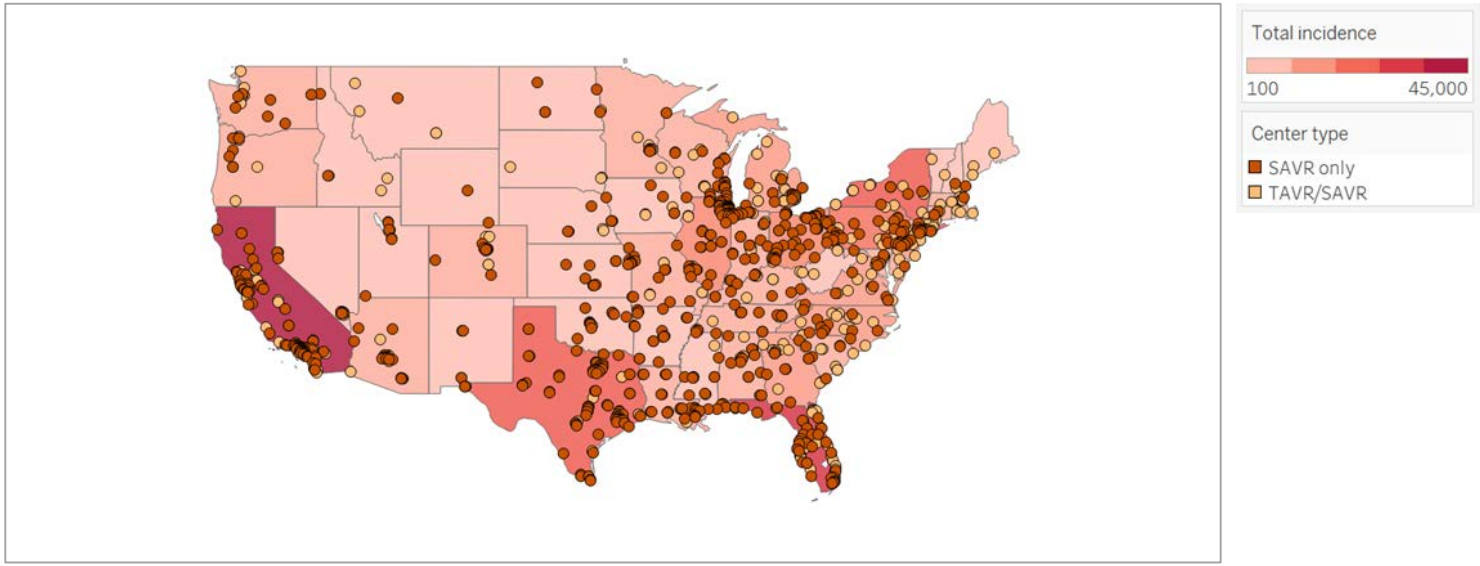
Cardiovascular Research Foundation

Columbia University Medical Center
NewYork-Presbyterian

Estimated U.S. Incidence of Severe Symptomatic AS in 2016

between 250,000 and 350,000 patients

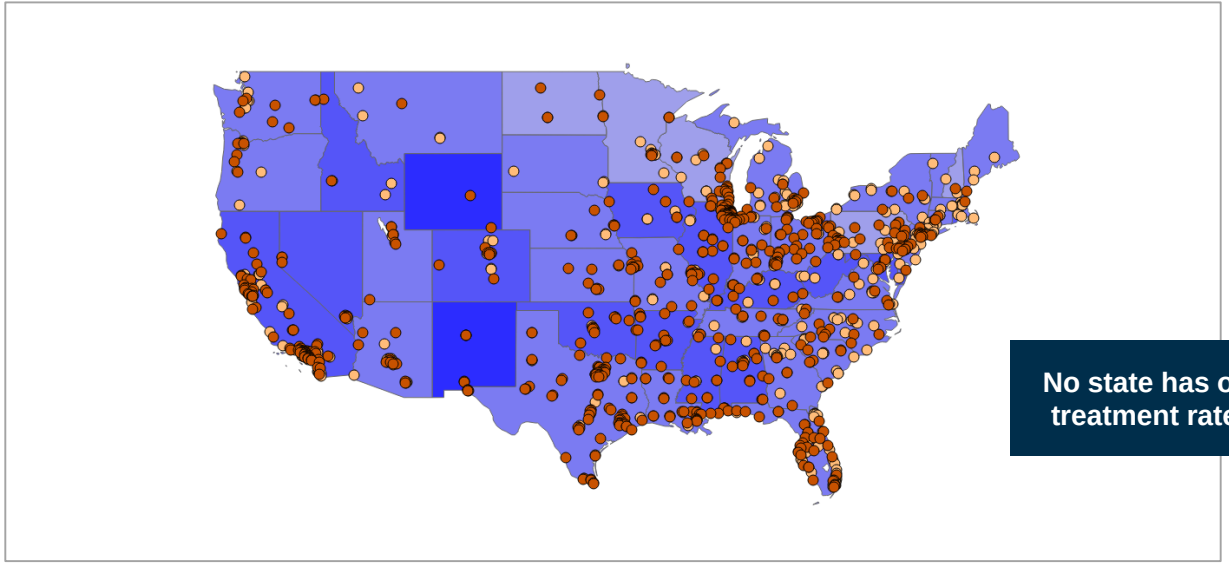
(including both diagnosed and undiagnosed)



Methods: 2016 diagnosed SSAS incidence was based on newly diagnosed SSAS patients in 2016 divided by the number of individuals seen within the calendar year in Optum in 2016. Diagnosed incidence was adjusted for undiagnosed share based on literature/disparities in diagnosis. Total SSAS incidence (diagnosed & undiagnosed) was applied to 2016 American Community Survey (ACS) 5-year Census data per state by county-level age-distributions to generate heatmaps.

AVR Treatment Penetration Relative to SSAS Incidence in 2016

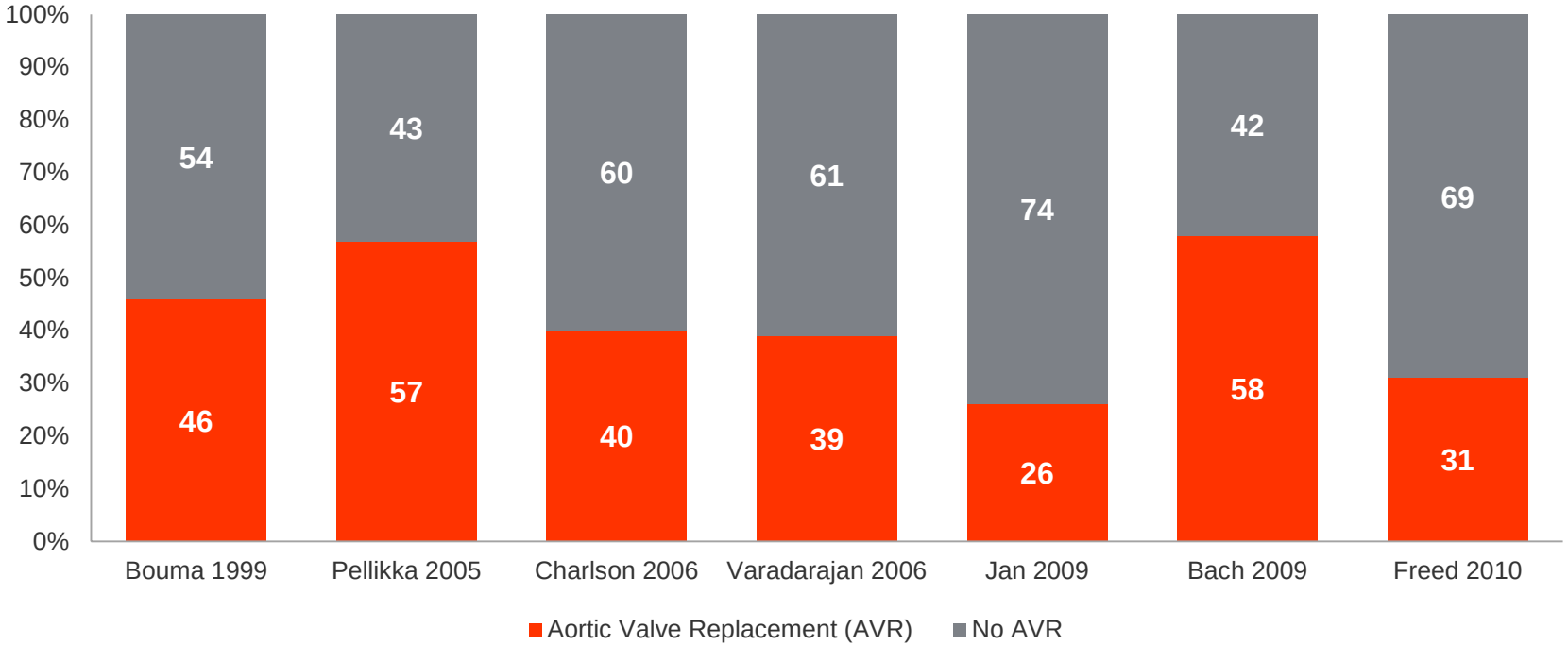
overall < 35%, despite >1,000 SAVR and >450 TAVR centers



No state has over a 40% treatment rate in SSAS

Methods: 2016 diagnosed SSAS incidence was based on newly diagnosed SSAS patients in 2016 divided by the number of individuals seen within the calendar year in Optum in 2016. Diagnosed incidence was adjusted for undiagnosed share based on literature/disparities in diagnosis. Total SSAS incidence (diagnosed & undiagnosed) was applied to 2016 American Community Survey (ACS) 5-year Census data per state by county-level age-distributions to generate heatmaps. For treatment penetration, total incidence was then overlaid with AVR volumes from 2016 inpatient SAF Medicare and adjusted for Medicare Advantage and private payer shares obtained from MEDPAR/HCUP; SAVR volumes then adjusted for SSAS-only share from STS 2016.

SSAS Under-Treatment in the Pre-TAVR Era



Source: Bouma BJ et al. Heart. 1999;82:143-148; 3. Pellikka PA et al. Circulation. 2005;111:3290-3295; Charlson E et al. J Heart Valve Dis. 2006;15:312-321; Varadarajan P et al. Ann Thorac Surg. 2006;82:2111-2115; Jan F et al. Circulation. 2009;120;S753; Bach DS et al. Circ Cardiovasc Qual Outcomes. 2009;2:533-539; Freed BH et al. Am J Cardiol. 2010;105:1339-1342.

A Large AVR Treatment Gap After Diagnosis

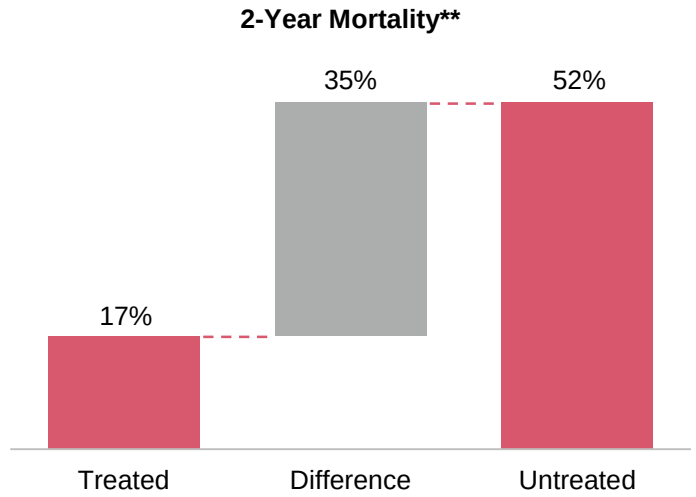
Resulting in Increased Mortality for Untreated Patients

1 Less than half of newly diagnosed SSAS patients are treated

Of a cohort of SSAS patients in 2016:

46% of newly diagnosed patients treated (TAVR & SAVR)

2 The under treatment of SSAS results in significant excess mortality



Source: *Based on Optum cohort of patients diagnosed in 6 month period between 2015 and 2016. **Optum cohort diagnosed in 2014 and 2015 with 2 year follow-up.

Factors Impacting AVR Treatment Likelihood

Patient Demographics, Co-morbidities, and Symptoms

Treated patients younger, male, and white

Age

Treated patients are 3 years younger

Gender

Men treated 29% more frequently than women

Race

Whites treated 34% more frequently than blacks or Asians

Comorbidities & symptoms with weak link to AVR rate

Limited trends observed in comorbidities and AVR rate

No association between symptom type and AVR rate

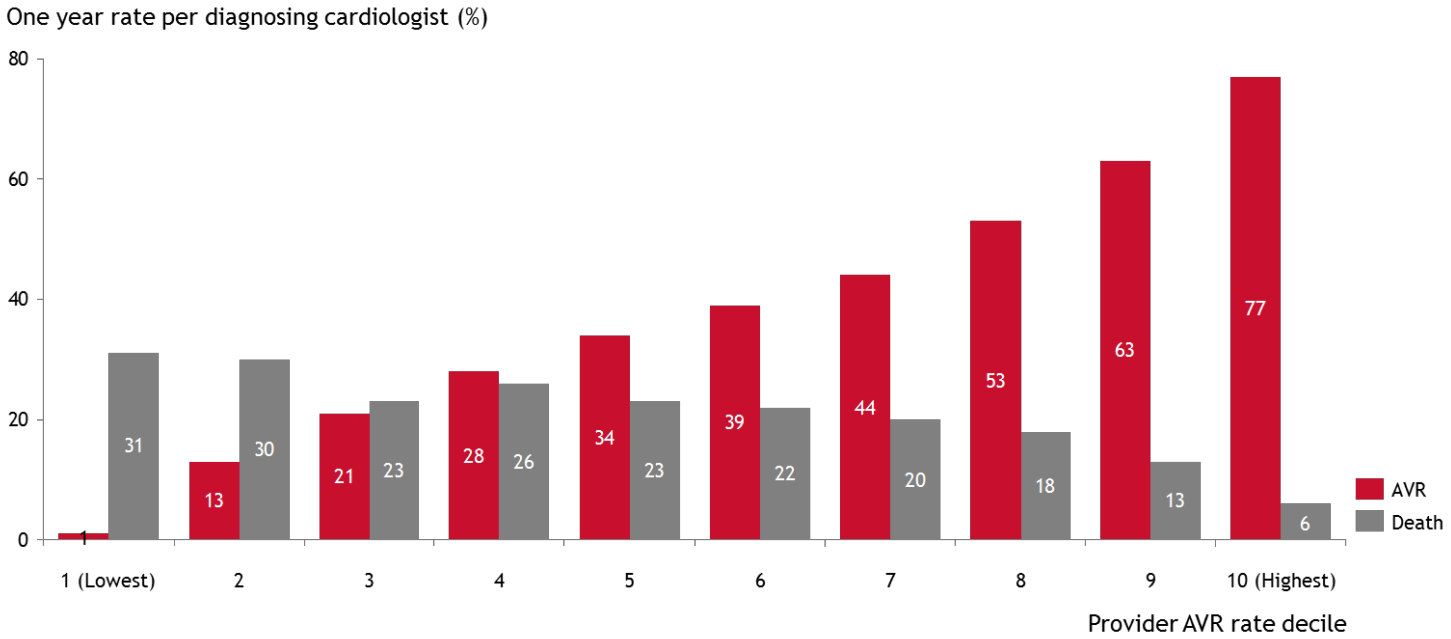
Symptom burden also with weak association to AVR

70% of treated and untreated patients have a previous history of AS

Note: ssAS cohort identified by selecting patients diagnosed between Oct '15-March '16 with sAS with a history of cardinal symptoms or HF in the 6 months prior to diagnosis (n=3197). Only patients in validated systems in the integrated delivery network were to reduce the risk of out of system care or incomplete records. Patients were tracked a 1 year period to evaluate treatment rate. Treatments were assessed by using SAVR/TAVR ICD9/10 procedure codes or CPT4 codes. Patient characteristics including symptoms assessed using physician notes and ICD 9/10 diagnosis codes. Patient comorbidities were evaluated the year before diagnosis; symptom status was assessed in the 6 months prior to diagnosis. Previous AS history was obtained any time prior to diagnosis from physician notes.

Diagnosing Cardiologists AVR Treatment Rate

Marked variability and striking impact on mortality in SSAS patients



Notes: Identified a cohort of 25,329 patients diagnosed with sAS between 2007-2016 and a history of cardinal symptoms/HF and an identifiable diagnosing cardiologist. Evaluated patients the year before diagnosis for their baseline status using ICD-9/10 codes, CPT4 codes, & Optum NLP. Identified diagnosing cardiologists based on providers linked to the first note instance of severe aortic stenosis. Only included patients diagnosed by cardiologists with at least two diagnosed ssAS cases in 2007-2016. Patients were clustered by diagnosing provider. Additional multivariate regression was performed to control for the year of diagnosis finding diagnosing cardiologist still had a significant impact of treatment likelihood even when controlling for the year of diagnosis.

Factors Impacting AVR Treatment Likelihood

Mulitvariate logic modeling

Elderly

Hazard ratio (HR) 0.46

ssAS patients 80+ are 54% less likely to receive AVR even when controlling for other patient factors (95% CI: 0.42, 0.50)

Blacks

HR 0.68

Black ssAS patients 32% less likely to receive AVR even when controlling for other patient factors (95% CI: 0.56, 0.81)

Women

HR 0.82

Female ssAS patients 18% less likely to receive AVR even when controlling for other patient factors (95% CI: 0.77, 0.87)

Diagnosing Cardiologist

MOR 2.35

ssAS patients have a 235% likelihood of a different outcome (i.e. receiving AVR or not) if they were to be diagnosed by another randomly selected cardiologist

Notes: Identified a cohort of 25,329 patients diagnosed with sAS between 2007-2016 and a history of cardinal symptoms/HF and an identifiable diagnosing cardiologist. Evaluated patients the year before diagnosis for their baseline status using ICD-9/10 codes, CPT4 codes, & Optum NLP. Identified diagnosing cardiologists based on providers linked to the first note instance of severe aortic stenosis. Only included patients diagnosed by cardiologists with at least two diagnosed ssAS cases in 2007-2016. Patients were clustered by diagnosing provider. Additional multivariate regression was performed to control for the year of diagnosis finding diagnosing cardiologist still had a significant impact of treatment likelihood even when controlling for the year of diagnosis.

MEDCAC - TAVR Program Requirements

Background - Key Points

- **Untreated SSAS has a grave prognosis (worse than most cancers) and is dramatically impacted by AVR therapy (NNT = 5).**
- **There is a wide gap between SSAS incidence and AVR treatment due to both under-diagnosis and under-treatment after diagnosis (treatment penetration rates are <40% in ALL states in the U.S.)**
- **Under-treatment bias is affected by multiple factors: elderly age, female sex, blacks (non-white ethnicities), and the diagnosing cardiologist.**
- **Current ACCESS to AVR (SAVR+TAVR) is sub-optimal and will worsen as case volumes increase in the future.**

Presentation Overview

BACKGROUND - natural history of AS, impact of TAVR on mortality, AS under-diagnosis and under-treatment by AVR

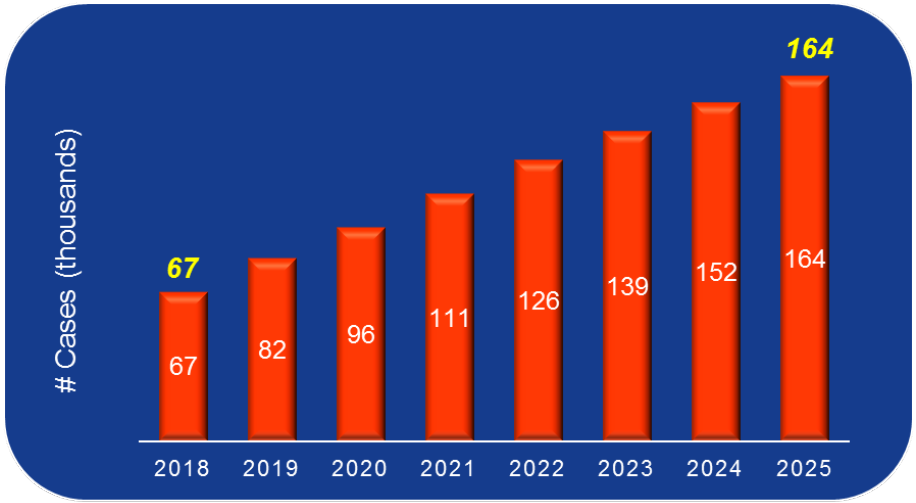
TAVR EVOLUTION & GROWTH - current treatment practices, clinical indications, and outcomes, TAVR growth expectations

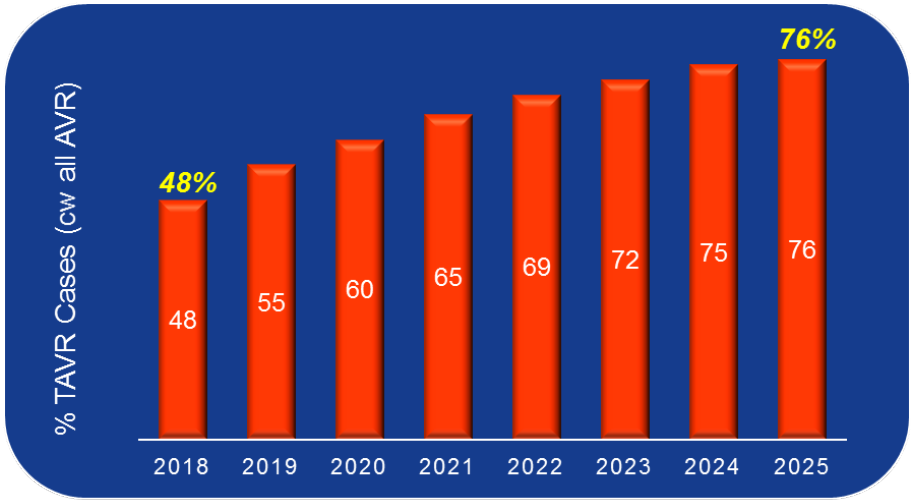
TAVR VOLUME–OUTCOME RELATIONSHIPS – TVT registry and MEDPAR data, impact of volume thresholds on new/existing sites

ADDITIONAL TOPICS AND TAVR PROGRAM RECOMENDATIONS – quality vs. volume metrics, geography issues, and need for SDM

Estimated U.S. TAVR Growth

(2018 – 2025)





US TAVR Market will Increase 2.5X

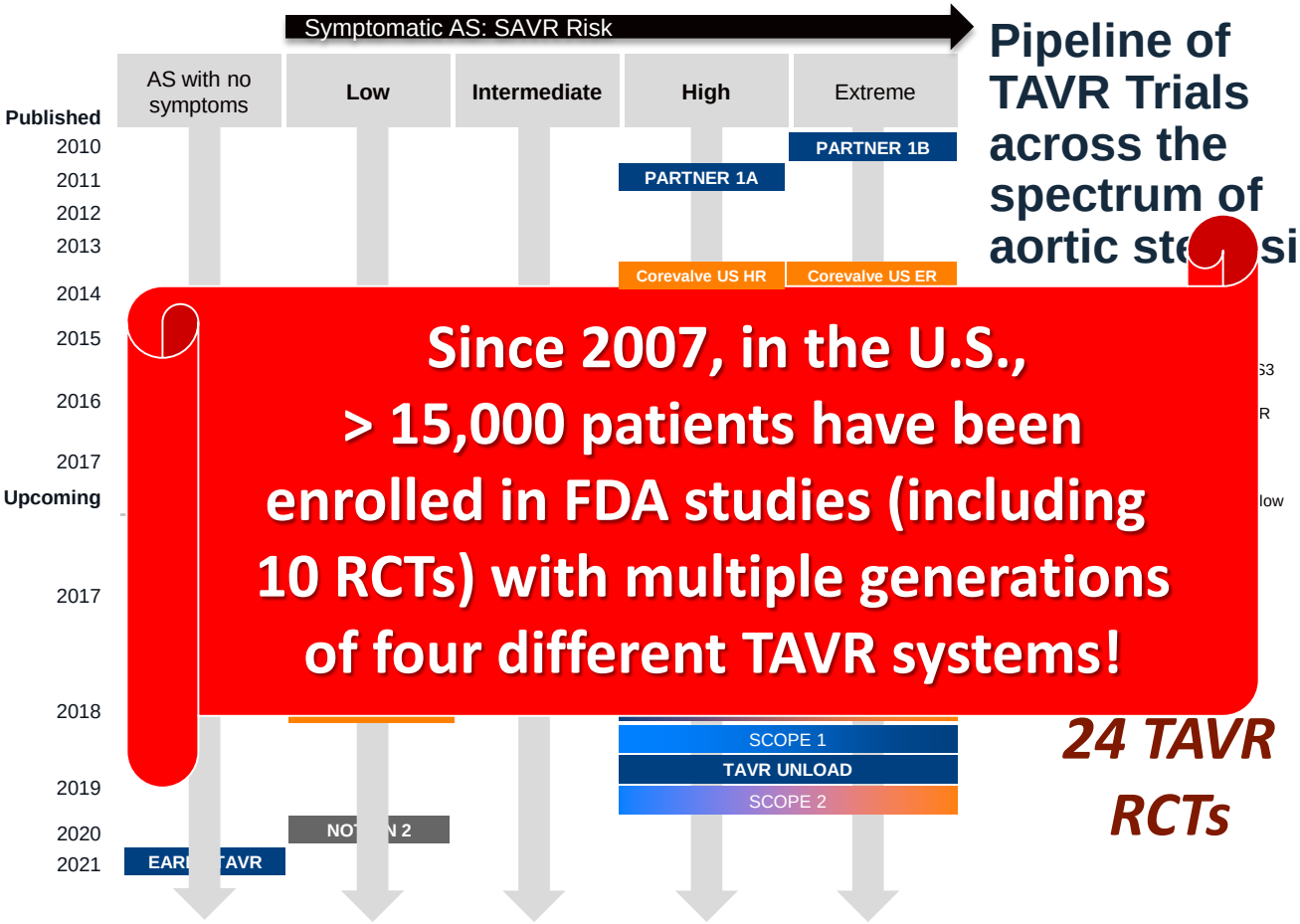
In 2025, >75% of all AVR in US will be TAVR

Global Growth of TAVR

The "drivers" of TAVR growth have been…

1. **acceptance of the multi-disciplinary heart team concept**
2. **commitment to evidence-based medicine clinical research**
3. **rapid technology advancement**
4. **simplification of the procedure**
5. ***ALL resulting in a striking reduction in complications and improved clinical outcomes!***

Pipeline of TAVR Trials across the spectrum of aortic stenosis



Since 2007, in the U.S., > 15,000 patients have been enrolled in FDA studies (including 10 RCTs) with multiple generations of four different TAVR systems!

24 TAVR RCTs

TAVR Guidelines

The "New" AHA/ACC Focused Update

2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Severe AS Symptomatic

Surgical Risk Strata

Low	Intermediate	High	Prohibitive
SAVR	**SAVR or TAVR**	**SAVR or TAVR**	**TAVR**
IB	IIa B	IA	IA

The "New" ESC/EACTS VHD Report

2017 ESC/EACTS Guidelines for the management of valvular heart disease

The Task Force for the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

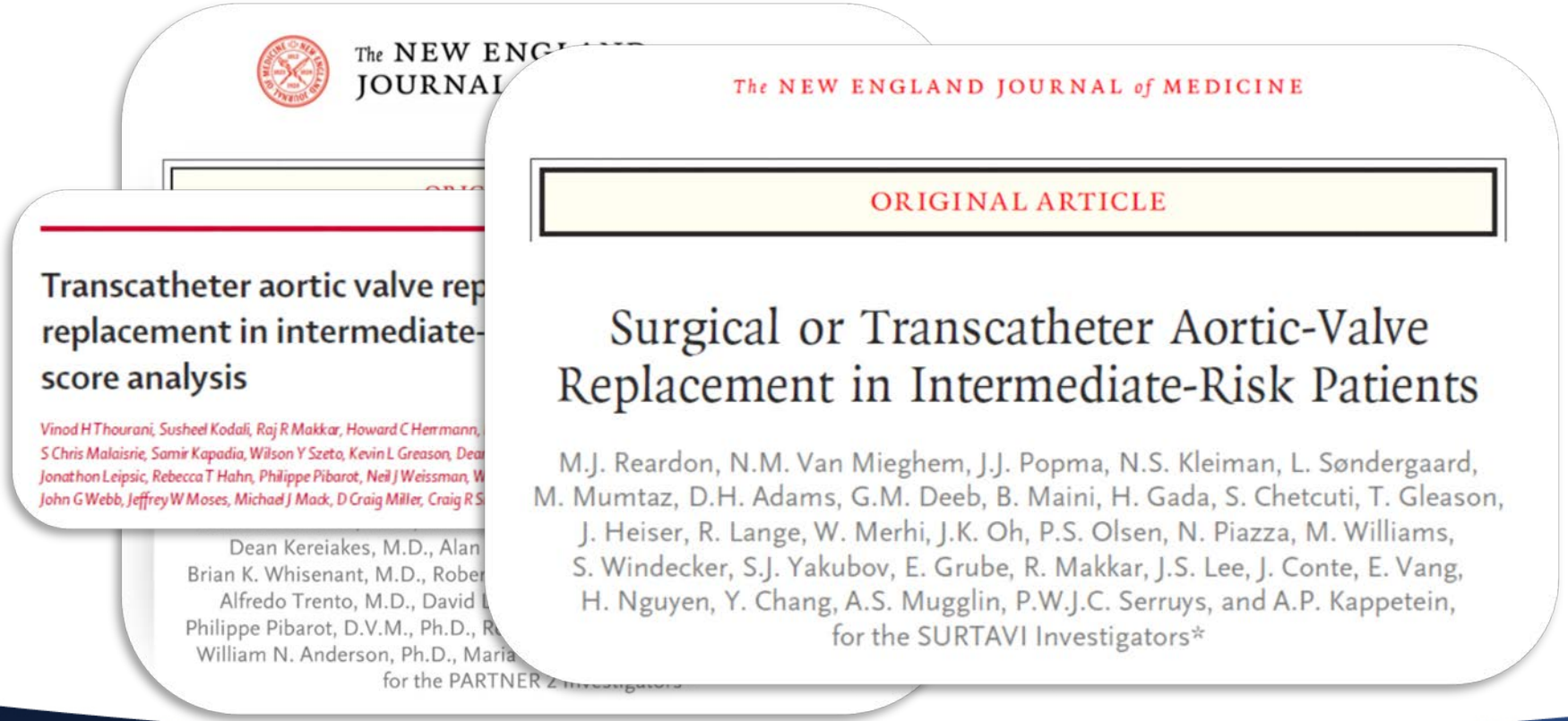
Severe AS Symptomatic

Surgical Risk Strata

Low	Intermediate or High	Prohibitive
SAVR	**SAVR or TAVR**	**TAVR**
IB	IB	IB

Rigorous clinical evidence has supported the expanded use of TAVR as an alternative to surgery in all tested populations!

Recent TAVR Studies in Intermediate-Risk Patients



Recent TAVR Studies in Intermediate-Risk Patients

Key Findings

Surgery better

Vascular complications
PVR

Non-inferior

Mortality

Strokes

TAVR better

AKI
Severe bleeding
New onset AF
Valve area
30-day QOL
30-day 6MWT
ICU/hospital LOS
Days alive OOH

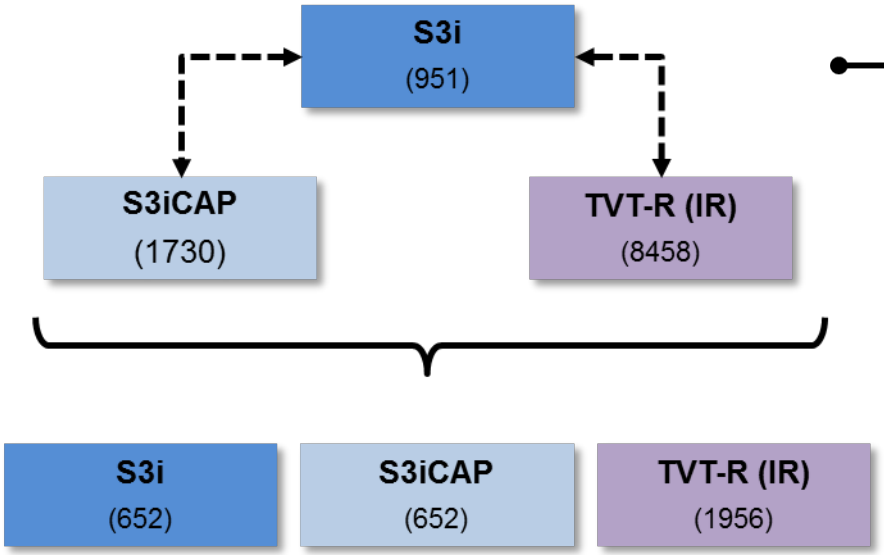
Recent TAVR Studies in Intermediate-Risk Patients

Recent TAVR Studies in Intermediate-Risk Patients

	S3i	S3iCAP	TVT-R (IR)
Study Design	• Prospective • Safety and effectiveness clinical study	• Prospective • Safety and effectiveness in expanded population using TVT-R	• Retrospective • Real world data using TVT-R
# Patients	1077	1814	8781
Enrollment Period	Feb'14 – Sep'14	Jan'15 – Aug'16	Jun'15 – Jul'17
# Sites	**51**	**60**	**453**
Study Conduct	• CEC adjudication of all events • DSMB monitoring of all events • Echo and CT Core Labs	• Independent medical reviewers adjudicated death, stroke, reintervention • Monitored death, stroke, reintervention • No Core Labs	• DCRI cardiologists adjudicated death, stroke and reintervention • Annual audits • No Core Labs

Recent TAVR Studies in Intermediate-Risk Patients

EuroPCR study methodology

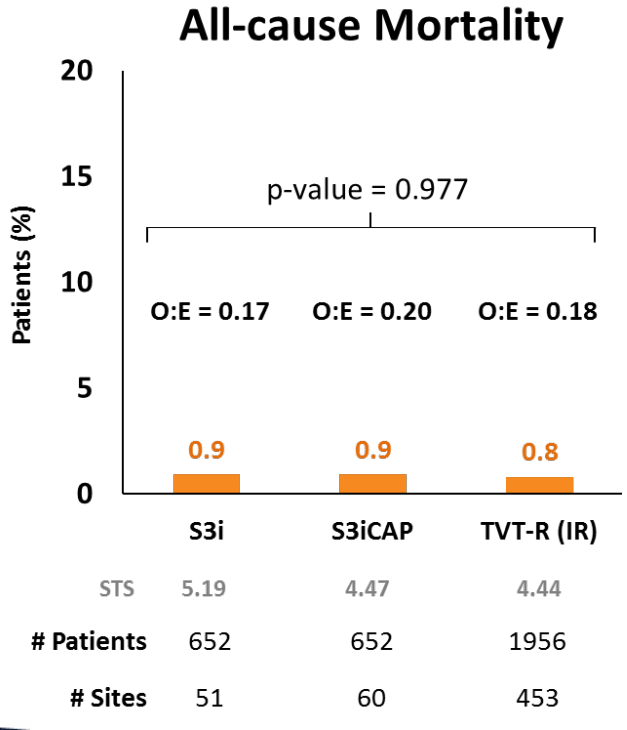


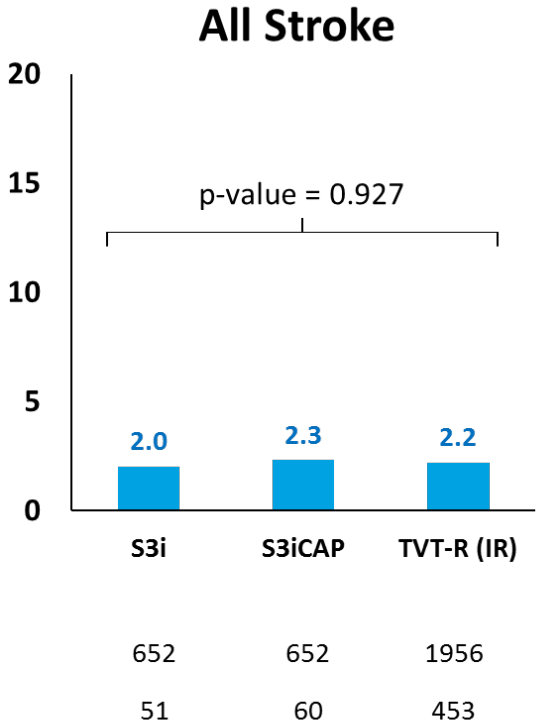
Propensity Matched Analysis

- **1:1:3 subject selection**
- Transfemoral population
- **24 baseline covariates**
  - Missing values: imputed using Markov Chain Monte Carlo method
- **Logistic regression model**
- S3i used as control

Recent TAVR Studies in Intermediate-Risk Patients

Propensity matched, TF patients, AT, 30-day outcomes





Recent TAVR Studies in Intermediate-Risk Patients

Propensity matched, TF patients, AT, 30-day outcomes

	S3i N = 652	S3iCAP N = 652	TVT-R (IR) N = 1956	Overall P-value
All-Cause Mortality %	0.9	0.9	0.8	0.977
All Stroke %	2.0	2.3	2.2	0.927
New Pacemaker %	11.1	12.0*	10.2*	0.356
Major Vasc Complications %	6.9	5.8*	4.0*	0.007
Length of Stay Median [IQR]	3.0 [2.0, 4.0]	2.0* [2.0, 3.0]	2.0* [2.0, 3.0]	<0.001
PVL (Mod/Sev) %	4.6	4.3*	1.3*	<0.001

Expanding TAVR Clinical Indications

Based upon ongoing and future studies

- Bioprosthetic aortic valve failure
- Low-risk patients (? all-comers)
- Low-flow, low-gradient AS
- Bicuspid AV disease
- AS + concomitant disease (CAD, MR, AF)
- Severe asymptomatic AS
- Moderate AS + CHF
- High-risk AR

MEDCAC - TAVR Program Requirements

TAVR Evolution & Growth - Key Points

- **TAVR has been a breakthrough therapy with rapid evolution of technology, procedural factors, and expanded clinical indications with expected continued 2.5X growth between now and 2025 which will strain the capacities of many centers, threatening to limit TAVR access.**
- **In the current environment of strict adherence to evidence-based medicine principles, careful site selection, rigorous site training, and continuous monitoring/oversight, clinical outcomes have stabilized and are excellent across the spectrum of TAVR sites under the current NCD (2012) case volume requirements (e.g. outcomes in intermediate-risk patients in the TVT registry).**

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Two Joint Society Expert Consensus Documents have been drafted with significant health policy and patient access implications

2017 AATS/ACC/ASE/SCAI/STS Expert Consensus System of Care Draft Documents (Operator and Institutional TAVR Requirements and Optimizing Care for VHD Patients)

MULTISOCIETY EXPERT CONSENSUS SYSTEMS OF CARE DOCUMENT

2017 AATS/ACC/ASE/SCAI/STS Expert Consensus Systems of Care Document
A Proposal to Optimize Care for Patients with Valvular Heart Disease

A Joint Report of the American Association for Thoracic Surgery, American College of Cardiology, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons

WRITING COMMITTEE

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Michael J. Mack, MD, FACC*
Laura Mauri, MD, MSc, FACC*
William R. Miranda, MD*
Thoralf M. Sundt, III, MD, FACC†

MULTISOCIETY EXPERT CONSENSUS SYSTEMS OF CARE DOCUMENT

2017 AATS/ACC/SCAI/STS Expert Consensus Systems of Care Document: Operator and Institutional Requirements for Transcatheter Aortic Valve Replacement

A Joint Report of the American Association for Thoracic Surgery, the American College of Cardiology, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons

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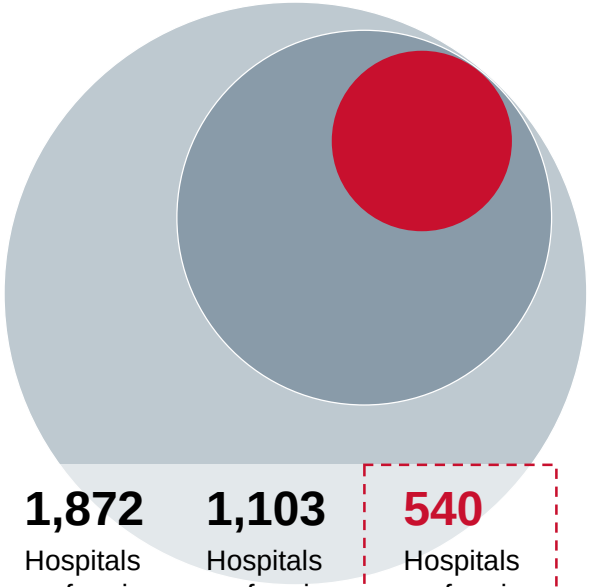
Dharam J. Kumbhani, MD, SM, FACC, FSCAI†
D. Craig Miller, MD, FACC, FACS*
A. Allen Seals, MD, FACC†
Richard J. Shemin, MD, FACC, FACS§
Thoralf M. Sundt, III, MD, FACC, FACS*
Vinod H. Thourani, MD, FACC, FACS§

TAVR Access Relative to Hospitals Performing PCI and Surgical AVR

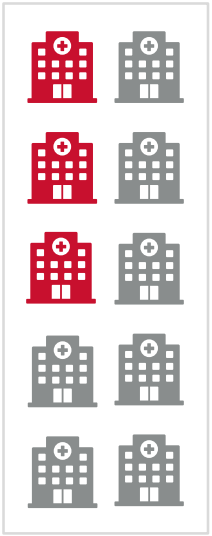


1,872
Hospitals performing PCI

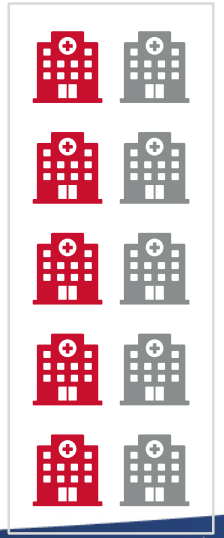
1,103
Hospitals performing Surgical AVR

540
Hospitals performing TAVR

29%
PCI hospitals performing TAVR in 2017



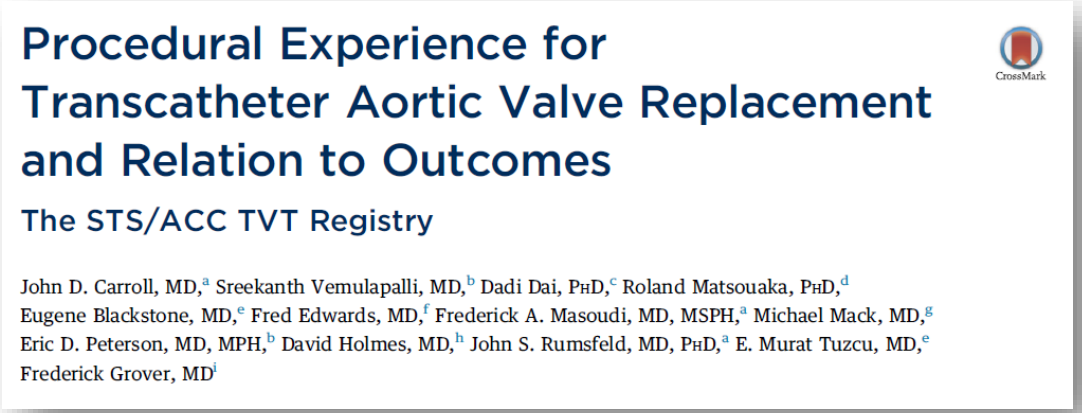
49%
Surgical AVR hospitals performing TAVR in 2017



Data Source: FY 2017 MedPAR.

Does TAVR Volume = Outcomes?

The TVT Registry



Procedural Experience for Transcatheter Aortic Valve Replacement and Relation to Outcomes

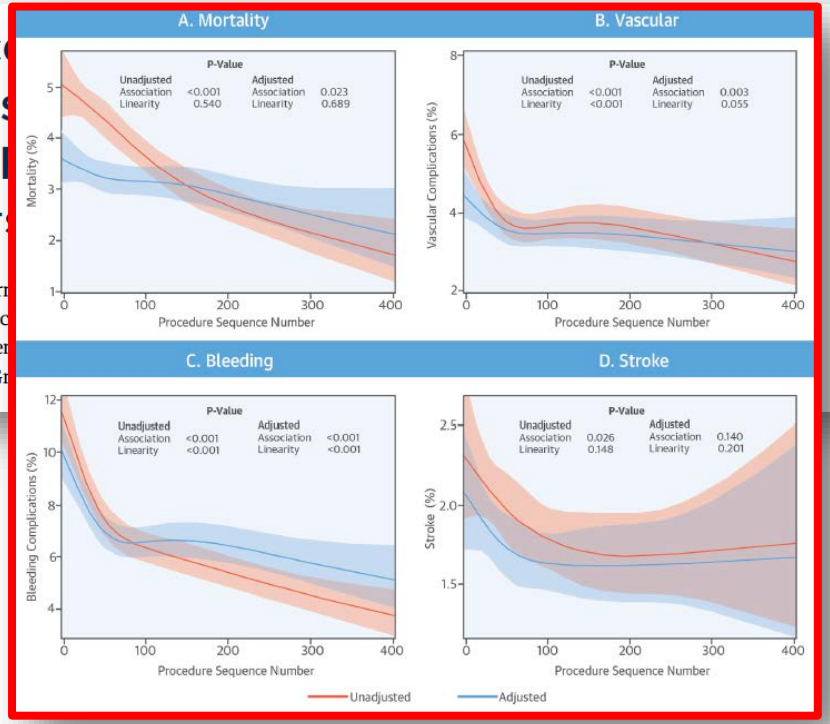
The STS/ACC TVT Registry

John D. Carroll, MD,[a] Sreekanth Vemulapalli, MD,[b] Dadi Dai, PhD,[c] Roland Matsouaka, PhD,[d] Eugene Blackstone, MD,[e] Fred Edwards, MD,[f] Frederick A. Masoudi, MD, MSPH,[a] Michael Mack, MD,[g] Eric D. Peterson, MD, MPH,[b] David Holmes, MD,[h] John S. Rumsfeld, MD, PhD,[a] E. Murat Tuzcu, MD,[e] Frederick Grover, MD[i]

- **Early U.S. experience (2011 – 2015), consecutive case sequence analysis at 395 hospitals with 42,988 commercial TAVR cases using Sapien, Sapien XT, and CoreValve**
- **Mean age 83 yo, mean STS 6.6% (38% >8%), 30% trans-apical**
- **Unadjusted and risk-adjusted outcomes for in-hospital mortality, strokes, vascular complications, and bleeding**

Does TAVR Volume = Outcomes?

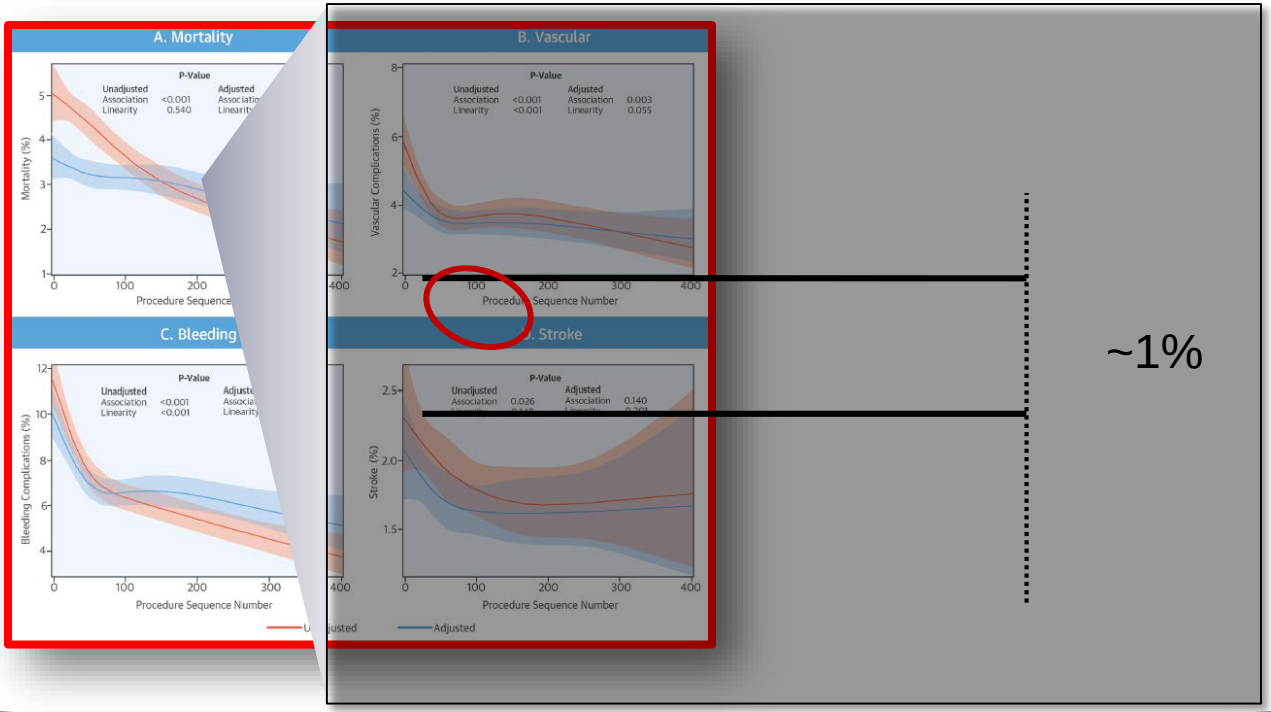
The TVT Registry



Carroll JD et al. J Am Coll Cardiol 2017;70:29-41

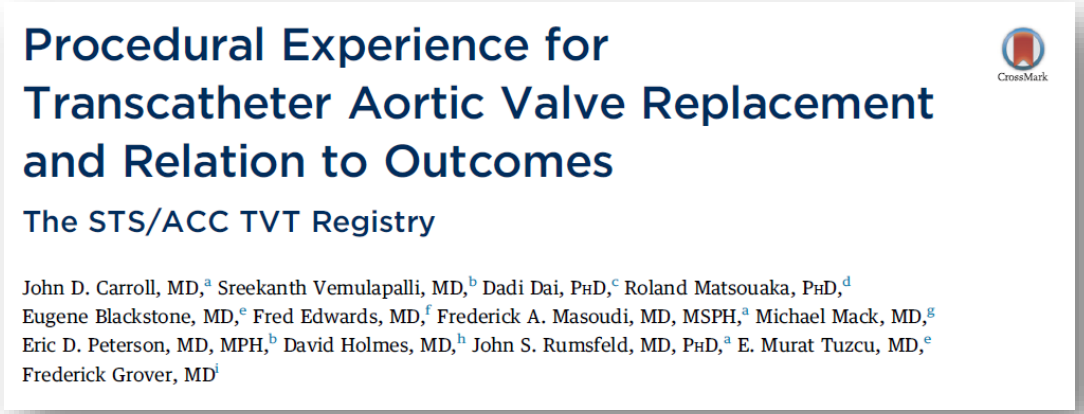
Does TAVR Volume = Outcomes?

Adjusted mortality difference (0-300 cases)



Does TAVR Volume = Outcomes?

The TVT Registry



Procedural Experience for Transcatheter Aortic Valve Replacement and Relation to Outcomes

The STS/ACC TVT Registry

John D. Carroll, MD,[a] Sreekanth Vemulapalli, MD,[b] Dadi Dai, PhD,[c] Roland Matsouaka, PhD,[d] Eugene Blackstone, MD,[e] Fred Edwards, MD,[f] Frederick A. Masoudi, MD, MSPH,[a] Michael Mack, MD,[g] Eric D. Peterson, MD, MPH,[b] David Holmes, MD,[h] John S. Rumsfeld, MD, PhD,[a] E. Murat Tuzcu, MD,[e] Frederick Grover, MD[i]

- From 1st case to the 400th case, increasing site volume was associated with a decline in the risk-adjusted outcomes for mortality (p=0.02), vascular complications (p<0.003) and bleeding (p<0.001), but not for strokes (p=0.14).
- In the TF subgroup, there was no association between site volume and outcomes in risk-adjusted mortality (p=0.15), and in both unadjusted and adjusted strokes.

Does TAVR Volume = Outcomes?

The TVT Registry

Procedural Experience for Transcatheter Aortic Valve Replacement and Relation to Outcomes

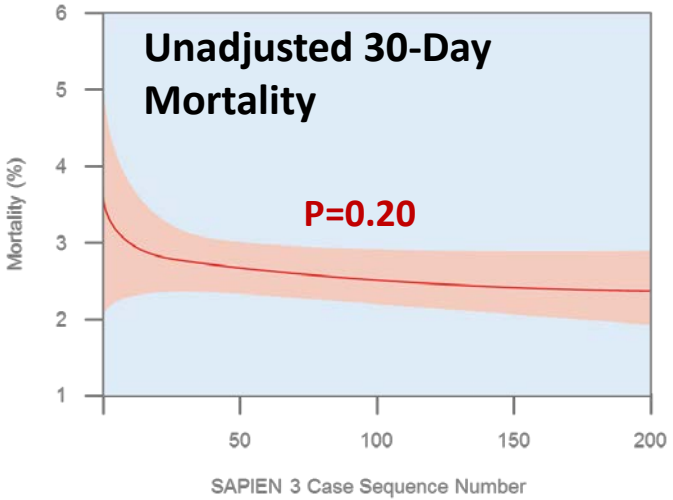
The STS/ACC TVT Registry

John D. Carroll, MD,[a] Sreekanth Vemulapalli, MD,[b] Dadi Dai, PhD,[c] Roland Matsouaka, PhD,[d] Eugene Blackstone, MD,[e] Fred Edwards, MD,[f] Frederick A. Masoudi, MD, MSPH,[a] Michael Mack, MD,[g] Eric D. Peterson, MD, MPH,[b] David Holmes, MD,[h] John S. Rumsfeld, MD, PhD,[a] E. Murat Tuzcu, MD,[e] Frederick Grover, MD[i]

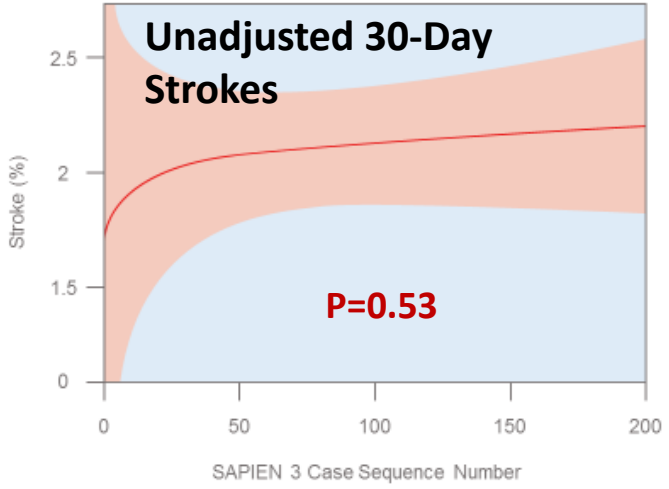
CONCLUSIONS The initial adoption of TAVR into practice in the United States showed that increasing experience was associated with better outcomes. This association, whether deemed a prolonged learning curve or a manifestation of a volume-outcome relationship, suggested that concentrating experience in higher volume heart valve centers might be a means of improving outcomes. (STS/ACC Transcatheter Valve Therapy Registry [TVT Registry]; NCT01737528)
(J Am Coll Cardiol 2017;70:29–41)

Does TAVR Volume = Outcomes?

The TVT Sapien 3 Experience (0-200 cases)



# of Sites:	375	147	47	18	12
Age	81.9	81.8	82.1	83.5	81.6
STS Score	7.1	7.1	7.4	7.7	7.8
% TF	96.4	92.9	91.7	93.6	92.3



# of Sites:	375	147	47	18	12
Age	81.9	81.8	82.1	83.5	81.6
STS Score	7.1	7.1	7.4	7.7	7.8
% TF	96.4	92.9	91.7	93.6	92.3

Cardiovascular Research Foundation

SOURCE: TVT Registry; Edwards analysis of SAPIEN 3 data through Feb 2017

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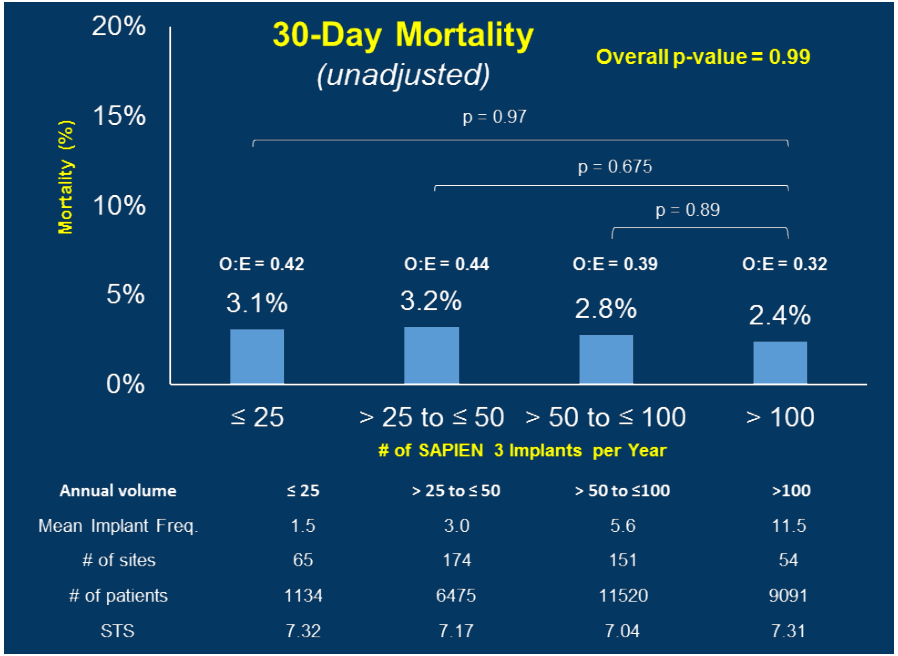
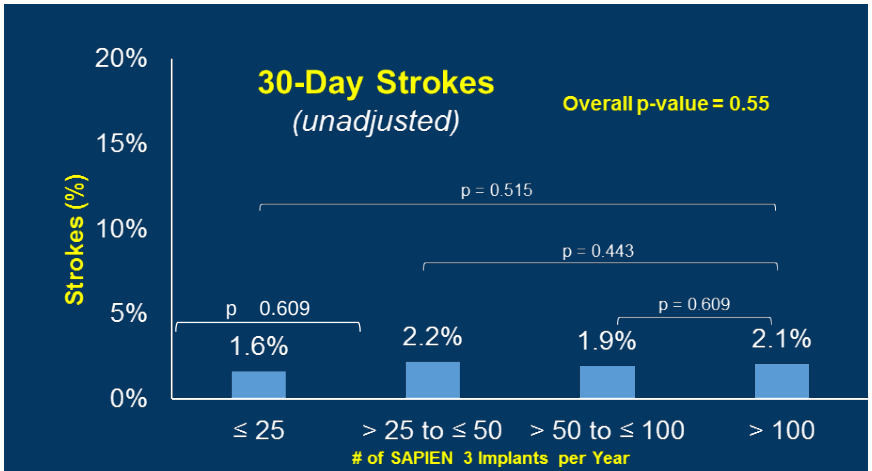
Does TAVR Volume = Outcomes?

TVT Sapien 3 Hospital Volume vs. Outcomes



Annual volume	≤ 25	> 25 to ≤ 50	> 50 to ≤100	>100
Mean Implant Freq.	1.5	3.0	5.6	11.5
# of sites	65	174	151	54
# of patients	1134	6475	11520	9091
STS	7.32	7.17	7.04	7.31



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Cardiovascular Research Foundation

SOURCE: TVT Registry; Edwards analysis of SAPIEN 3 data through Feb 2017

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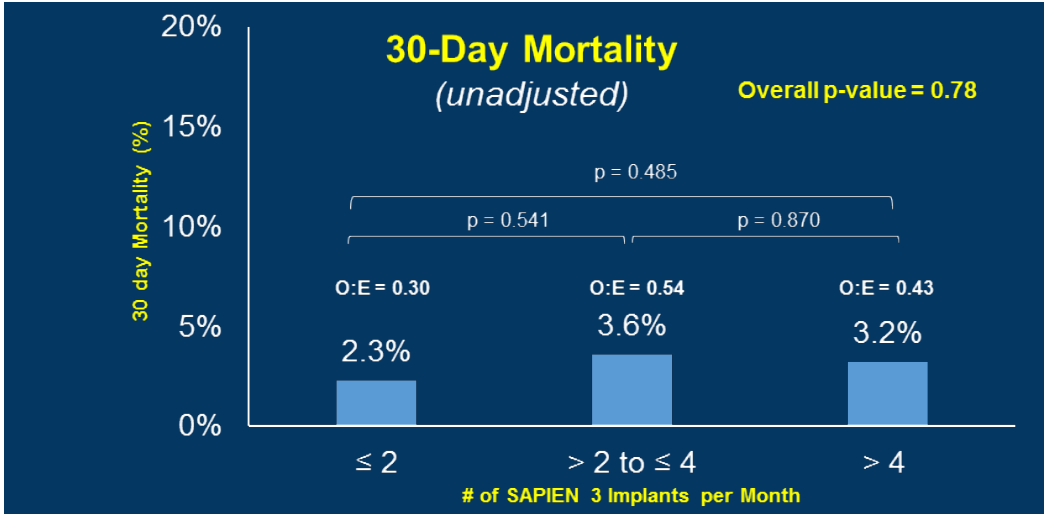
Does TAVR Volume = Outcomes?

New TVT TAVR Hospitals with Sapien 3



Monthly volume	≤ 2	> 2 to ≤ 4	> 4
# of sites	7	25	21
Mean Implant Freq	1.7	3.2	7.1
# of patients	96	570	543
STS	7.53	6.65	7.49

Cardiovascular Research Foundation

SOURCE: TVT Registry; Edwards analysis of SAPIEN 3 data through Feb 2017

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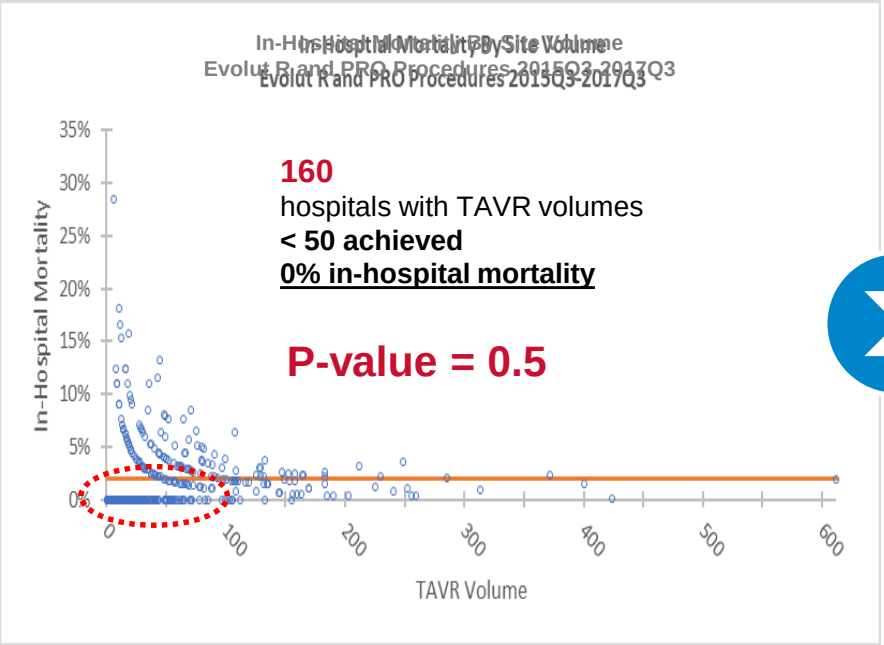
Does TAVR Volume = Outcomes?

TVT Evolut R/PRO TAVR Hospital Volume vs. Outcomes

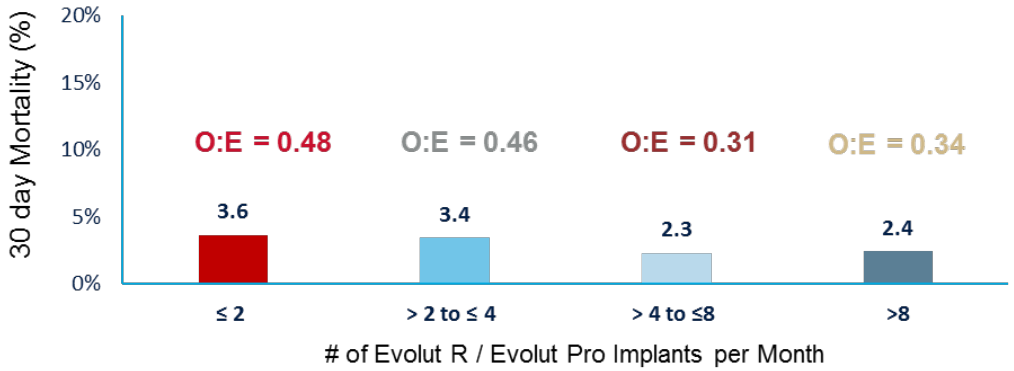


1. The correlation between TAVR volume and in-hospital mortality is not statistically significant
2. Certain low volume centers achieve excellent outcomes
3. Certain high volume centers achieve worse outcomes than low volume centers

Source: TVT Registry; Medtronic analysis includes all procedures through Q32017

Does TAVR Volume = Outcomes?

TVT Evolut R/PRO TAVR Hospital Volume vs. Outcomes

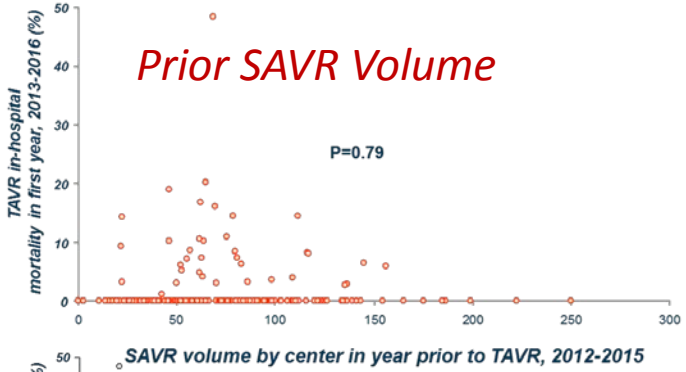


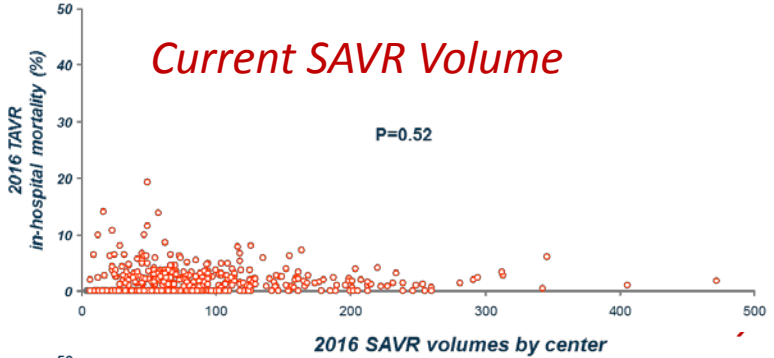
Monthly volume	≤ 2	> 2 to ≤ 4	> 4 to ≤8	>8
# of sites	295	50	31	10
Mean Implant Freq	1.4 ± 0.8	3.8 ± 0.6	6.4 ± 1.0	12.8 ± 4.2
# of patients	8552	4693	5087	3427
STS	7.5 ± 5.4	7.4 ± 5.2	7.5 ± 5.1	7.1 ± 5.4

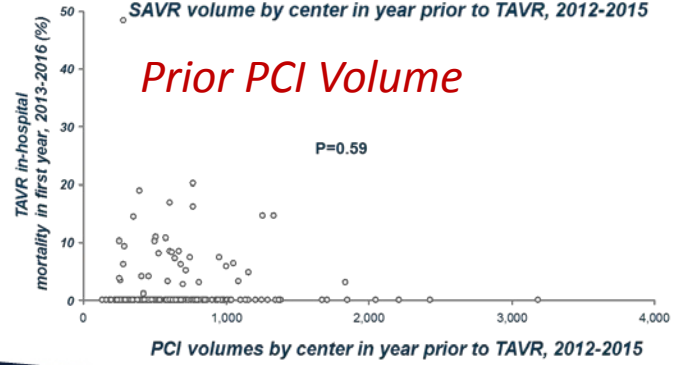
Source: TVT Registry; Medtronic analysis includes all procedures through Q32017

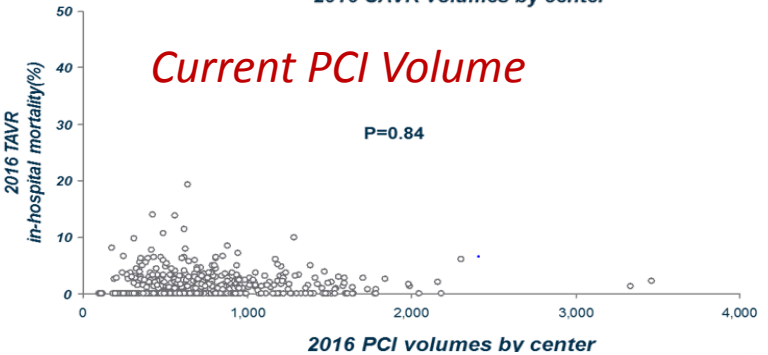
MEDPAR Data Analyses

Prior/Current SAVR/PCI Volume vs. TAVR Mortality









Cardiovascular Research Foundation

Data Source: 2012 2016 100% inpatient SAF Medicare. SAVR center volumes based on Medicare Fee For Service claims adjusted for Medicare Advantage and private payer share from MEDPAR/HCUP.

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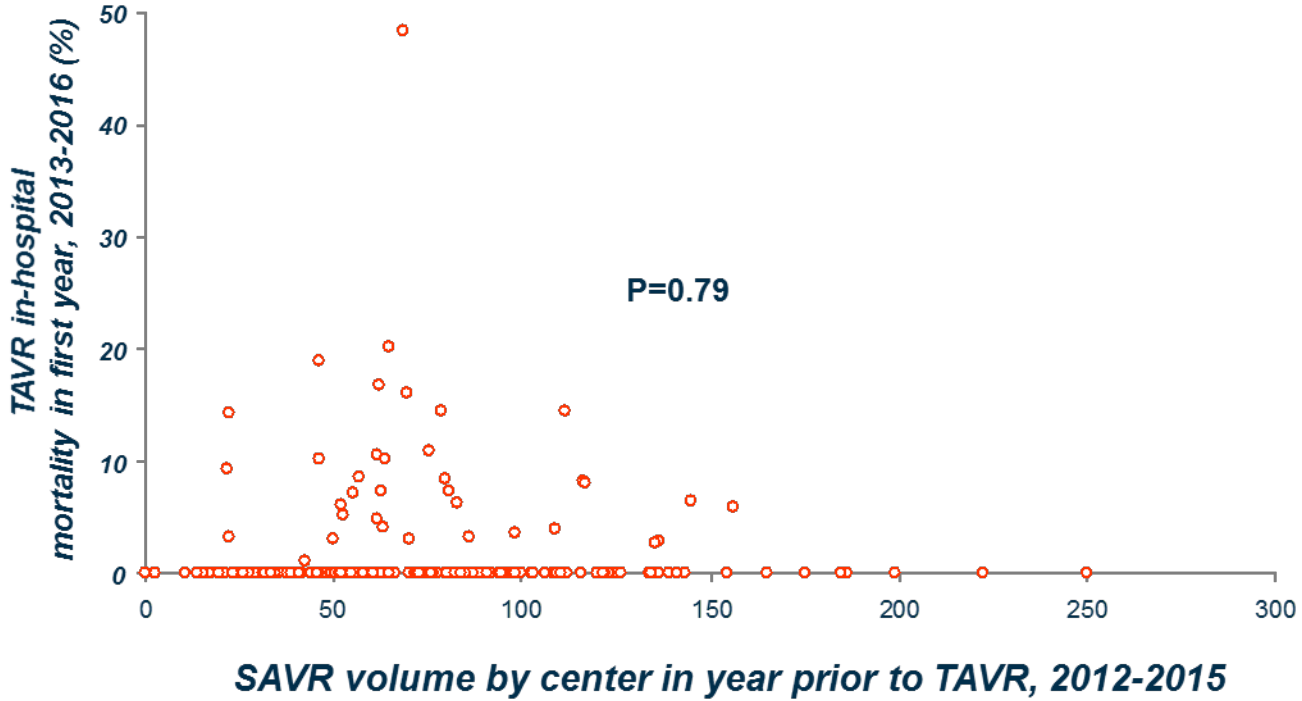
MEDPAR Data Analyses

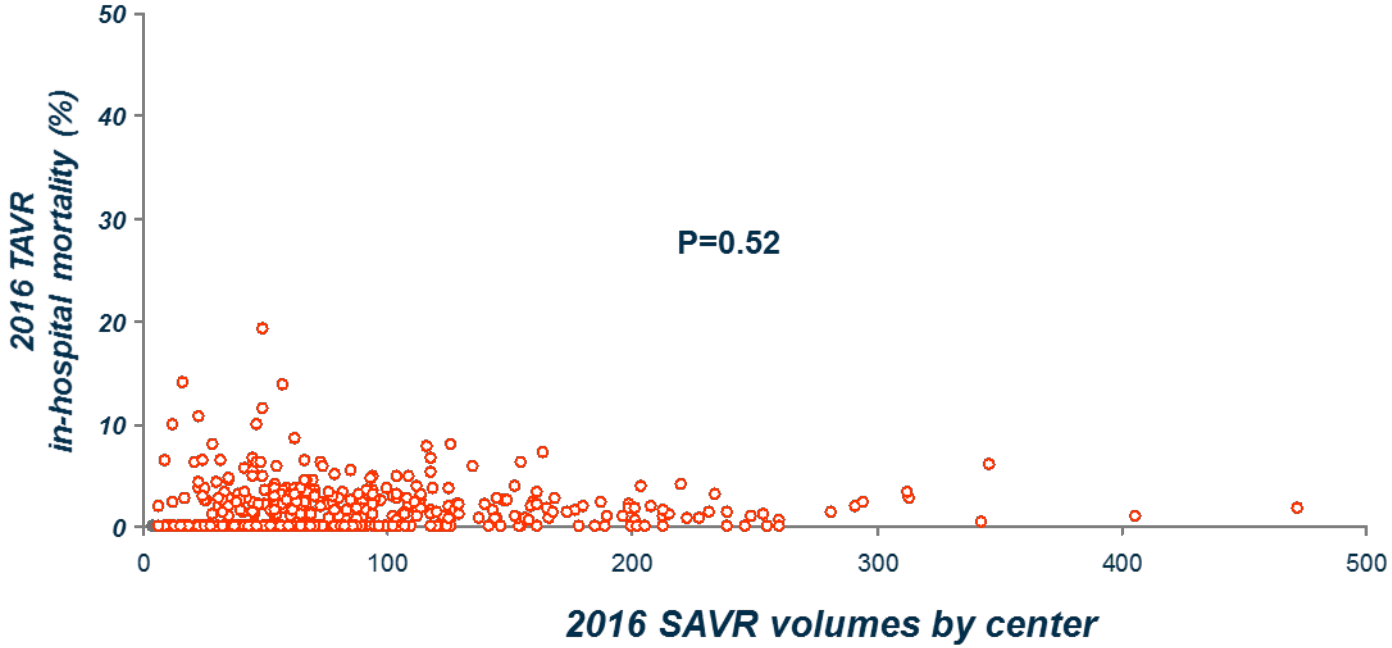
Prior SAVR Volume vs. TAVR Mortality



Data Source: 2012 2016 100% inpatient SAF Medicare. SAVR center volumes based on Medicare Fee For Service claims adjusted for Medicare Advantage and private payer share from MEDPAR/HCUP.

MEDPAR Data Analyses

Current SAVR Volume vs. TAVR Mortality



Cardiovascular Research Foundation

Data Source: 2012 2016 100% inpatient SAF Medicare. SAVR center volumes based on Medicare Fee For Service claims adjusted for Medicare Advantage and private payer share from MEDPAR/HCUP.

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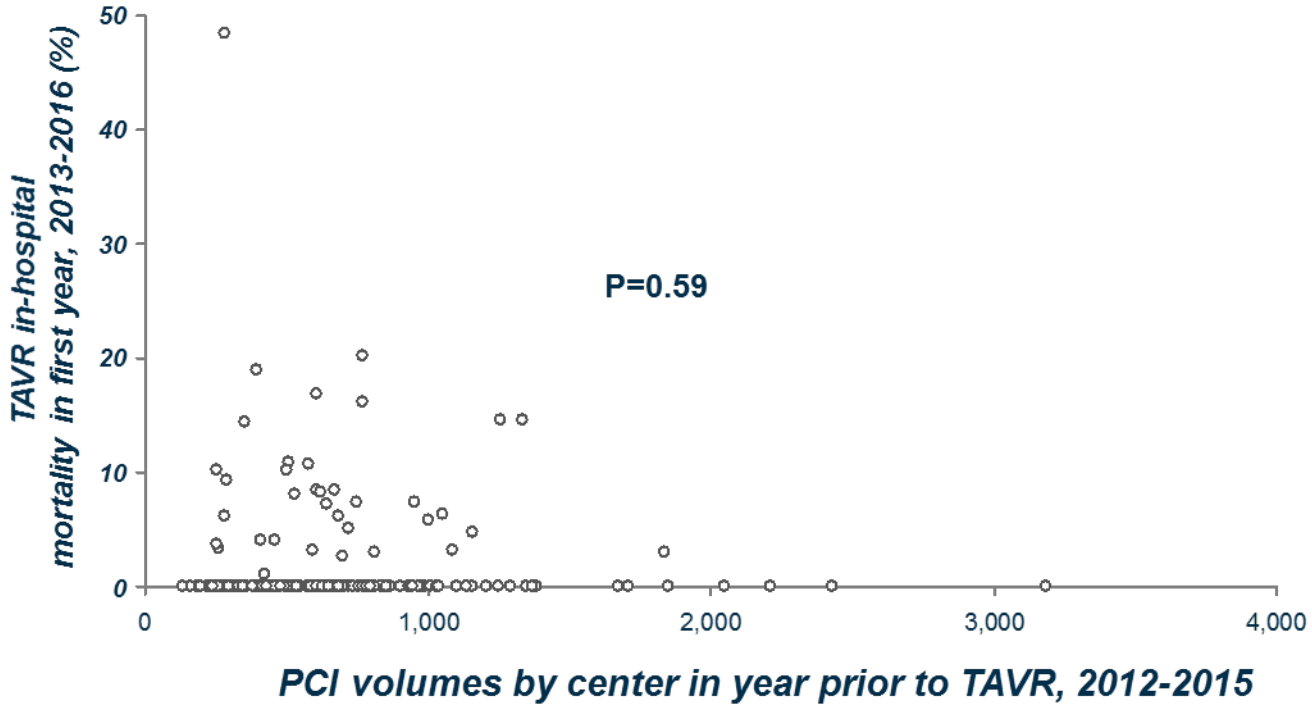
MEDPAR Data Analyses

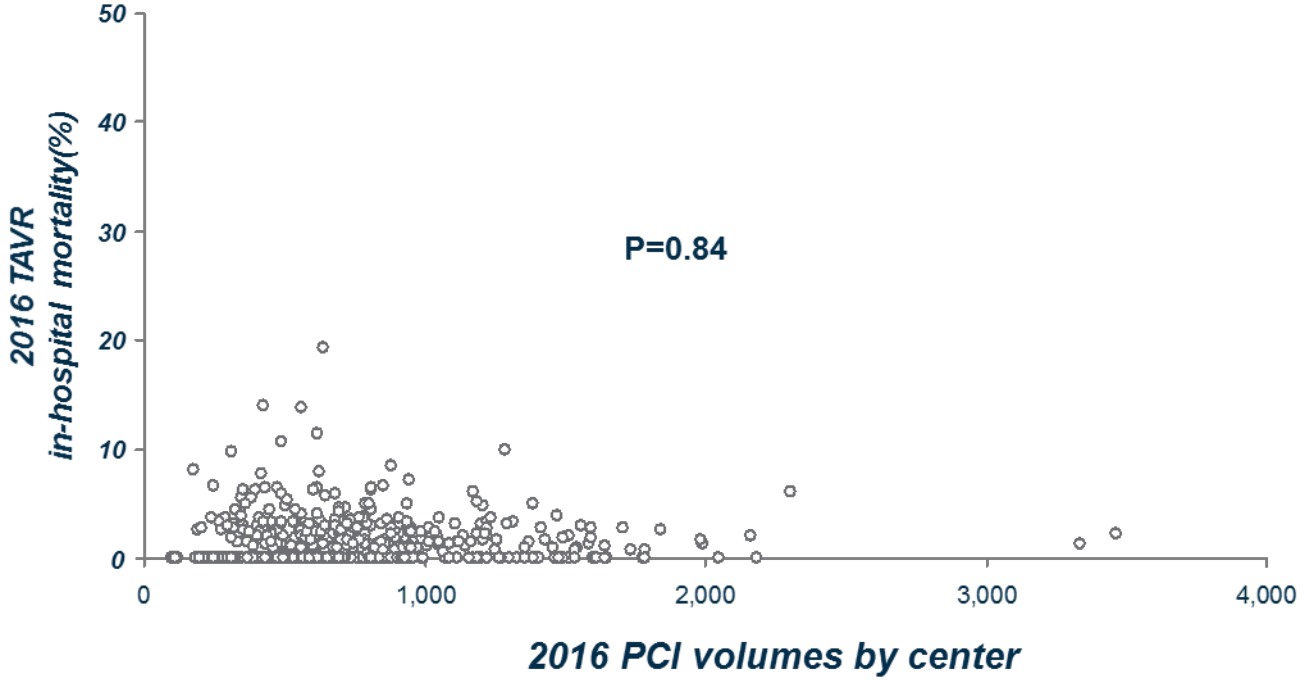
Prior PCI Volume vs. TAVR Mortality



Data Source: 2012 2016 100% inpatient SAF Medicare. SAVR center volumes based on Medicare Fee For Service claims adjusted for Medicare Advantage and private payer share from MEDPAR/HCUP.

MEDPAR Data Analyses

Current PCI Volume vs. TAVR Mortality



Cardiovascular Research Foundation

Data Source: 2012 2016 100% inpatient SAF Medicare. SAVR center volumes based on Medicare Fee For Service claims adjusted for Medicare Advantage and private payer share from MEDPAR/HCUP.

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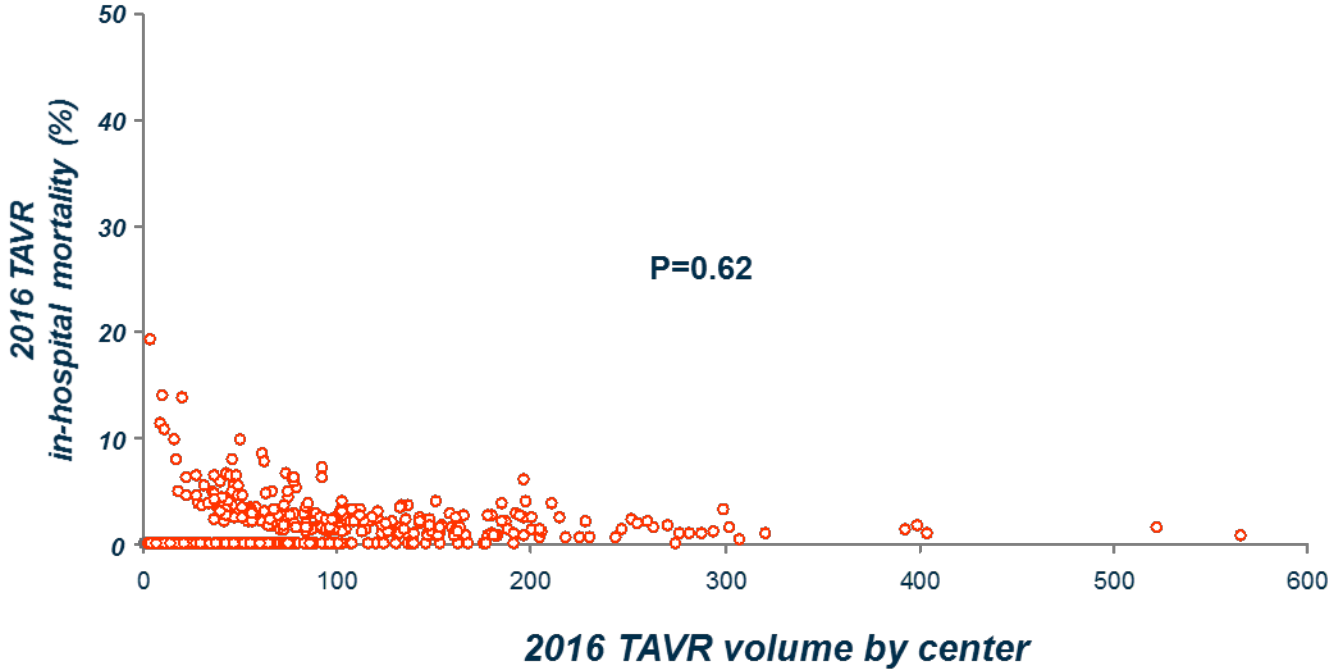
MEDPAR Data Analyses

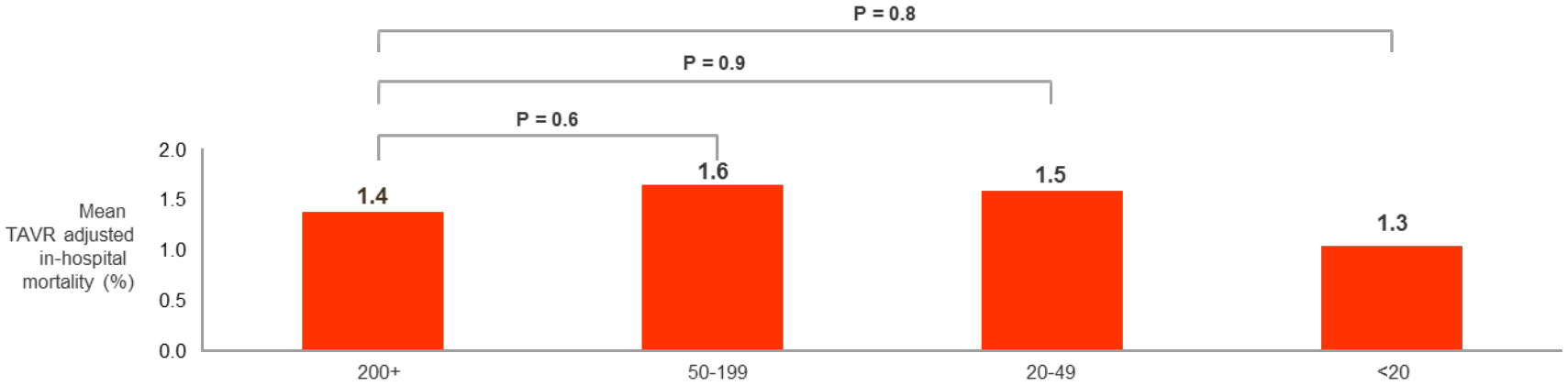
Current TAVR Volume vs. TAVR Mortality



Data Source: 2012 2016 100% inpatient SAF Medicare. SAVR center volumes based on Medicare Fee For Service claims adjusted for Medicare Advantage and private payer share from MEDPAR/HCUP.

MEDPAR Data Analyses

Current TAVR Volume vs. TAVR Mortality



2016 TAVR center volumes

# of centers	33	261	134	62
95% confidence interval	(1.14, 1.70)	(1.36, 1.78)	(1.05, 1.89)	(0.29, 2.23)
Percent of TAVR volumes (adjusted)	7%	53%	27%	13%

Cardiovascular Research Foundation

***Data Source*: 2016 100% SAF Medicare. Center volumes based on Medicare Fee For Service claims adjusted for Medicare Advantage and private pay share from MEDPAR/HCUP. Risk adjustment methodology in supplement.**

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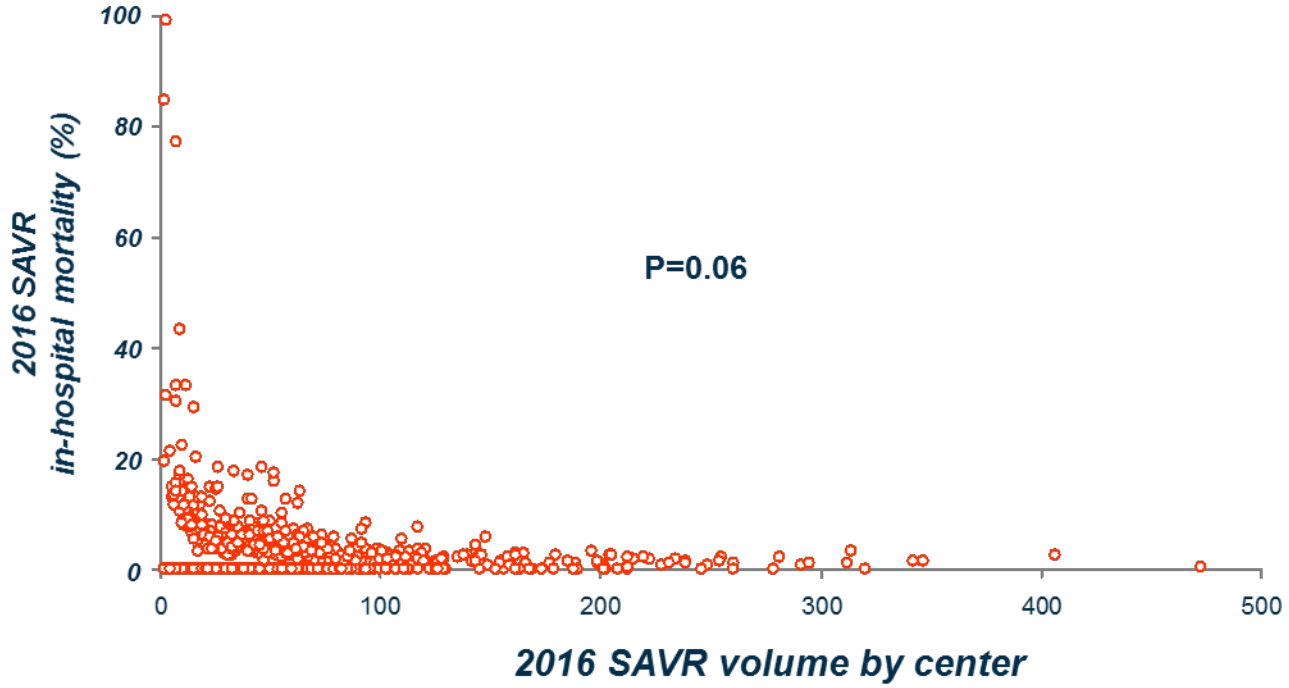
MEDPAR Data Analyses

Current SAVR Volume vs. SAVR Mortality



Cardiovascular Research Foundation

Data Source: 2012 2016 100% inpatient SAF Medicare. SAVR center volumes based on Medicare Fee For Service claims adjusted for Medicare Advantage and private payer share from MEDPAR/HCUP.

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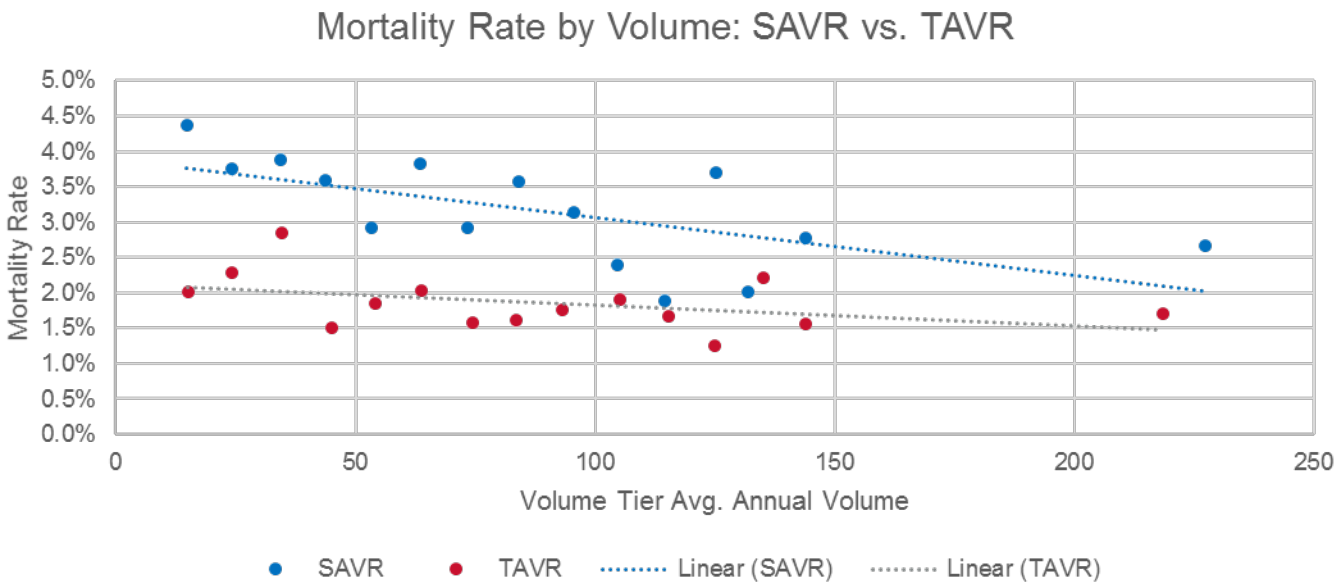
MEDPAR Data Analyses

Current SAVR/TAVR Volume vs. Mortality



Cardiovascular Research Foundation

Data Source: 2012 2016 100% inpatient SAF Medicare. SAVR center volumes based on Medicare Fee For Service claims adjusted for Medicare Advantage and private payer share from MEDPAR/HCUP.

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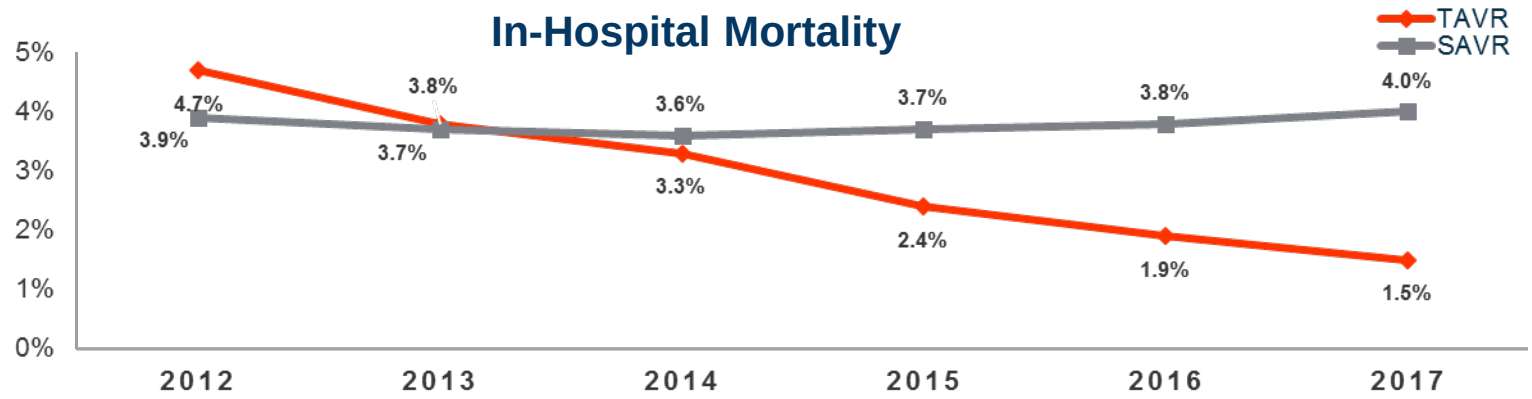
MEDPAR Data Analyses

SAVR/TAVR Mortality Trends Over time



N	SAVR	26,321	26,287	26,066	25,310	32,318	29,183
	TAVR	3,964	6,426	10,112	17,385	26,615	33,618
Age	SAVR	76	76	75	75	74	73
	TAVR	83	83	83	83	82	81
Charlson Index	SAVR	2.23	2.22	2.22	2.24	2.17	2.33
	TAVR	3.30	3.24	3.32	3.25	3.10	3.13

Cardiovascular Research Foundation

Data Source: 2012 2016 100% inpatient SAF Medicare. SAVR center volumes based on Medicare Fee For Service claims adjusted for Medicare Advantage and private payer share from MEDPAR/HCUP.

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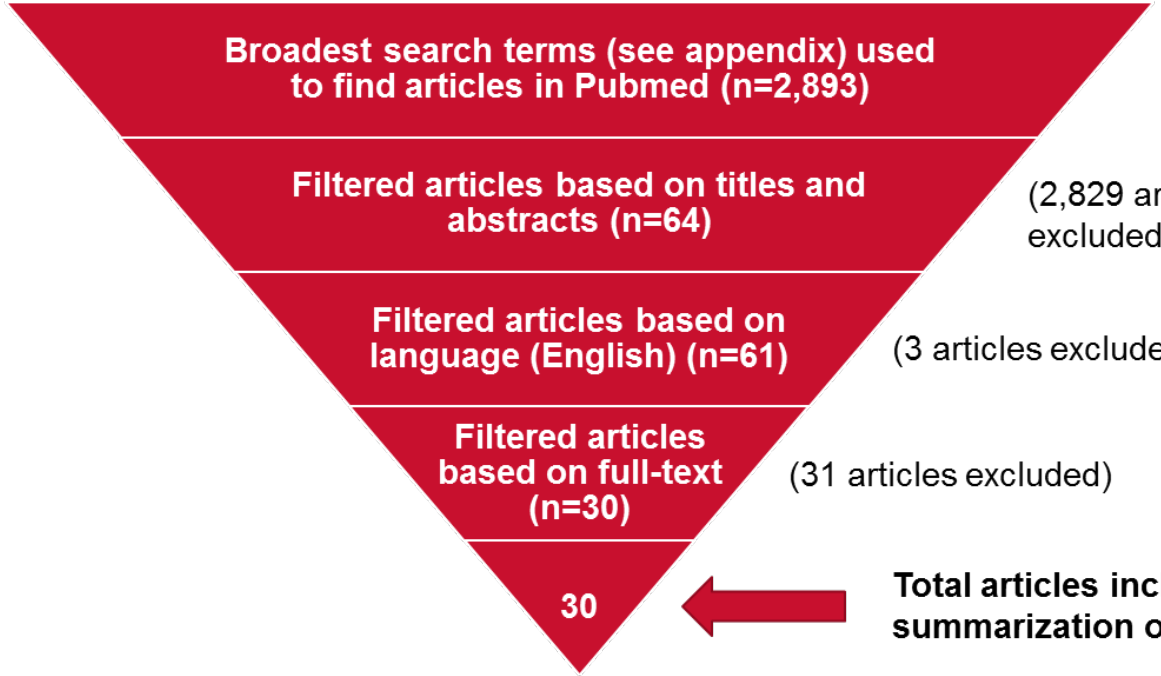
AVR Volume-Outcome Literature Search



See references slide for a full citation of the 30 articles included in the summarization of evidence

AVR Volume-Outcome Literature Search

Summary of Results

- **SAVR Volume – TAVR Outcomes:** only 2 studies and no relationship between SAVR volume and TAVR outcomes; 2 other studies indicated that increasing TAVR volume was associated with improved SAVR outcomes
- **PCI Volume – TAVR Outcomes:** no manuscripts and only 1 abstract showing no association between PCI volumes and TAVR outcomes
- **TAVR Volume – TAVR Outcomes:** 26 studies, 7 reported no relationship, 19 reported that as TAVR volumes increased, adverse TAVR outcomes decreased; the 19 reports showing a relationship were limited by small sample sizes (n=7), poor control of confounders (n=8), early (before 2016) time bias (n=19), and NONE assessed specific recommended volume thresholds

TAVR Program Volume Requirements

Existing TAVR Programs

	Current 2012 NCD	Draft Multi-Society Consensus
Institutional Surgical volume	• ≥ 20 SAVR/year, or 40 in 2 years	• ≥ 30 SAVR/year, or 60 in 2 years
Institutional PCI volume	• ≥ 1000 cath/ year, at least 400 are PCI	• 300 PCI/year
Institutional TAVR volume	• ≥ 20 TAVR/year, or 40 in 2 years	• ≥ 50 TAVR/year, or 100 in 2 years

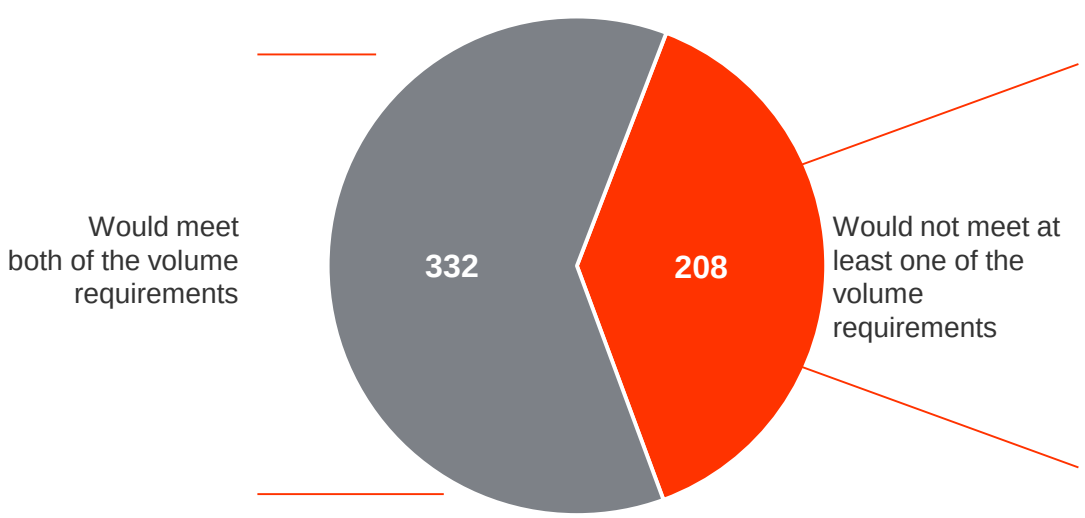
TAVR Program Volume Requirements

New TAVR Programs

	Current 2012 NCD	Draft Multi-Society Consensus
Institutional Surgical volume	• ≥ 50 SAVR (incl. 10 High Risk) • 2 physicians with cardiac surgery privileges	• ≥ 40 SAVR (or 80 in 2 years) • 2 hospital-based cardiac surgeons who each spend 50% of their time at the hospital with the intended TAVR program
Institutional PCI volume	• ≥ 1000 catheterizations/ year, of which at least 400 are PCI	• 300 PCI/year
Cardiac surgeon experience	• ≥ 100 career SAVR (incl. 10 high-risk); or • ≥ 25 AVRs in one year; or • ≥ 50 AVRs in 2 year	• ≥ 100 career SAVR (incl. 10 high-risk); or • ≥ 25 AVRs in one year; or • ≥ 50 AVRs in 2 year
Interventional cardiologist experience	• 100 structural procedures lifetime; or • 30 left-sided structural procedures/yr (60% BAV)	N/A
TAVR Proceduralist experience	N/A	• 100 TF-TAVR lifetime, including 50 TAVR as primary operator • Board eligible or certified in IC or CT Surgery • Certification of device-specific training on device(s) to be used

Impact of Increased Volume Requirements on Existing TAVR Hospitals

Scenario: Existing TAVR hospitals subject to 50 TAVR / 30 SAVR annual volume requirement



Reasons for TAVR Center not meeting Volume Requirements

161 TAVR sites close because of TAVR volumes

8 TAVR sites close because of SAVR volumes

39 TAVR sites close because of both SAVR and TAVR volumes

39% Decrease in TAVR Centers in the U.S.

Cardiovascular Research Foundation

Data Source: FY 2017 MedPAR. Site volume estimates inflated to reflect missing Medicare Advantage and private payer claims.

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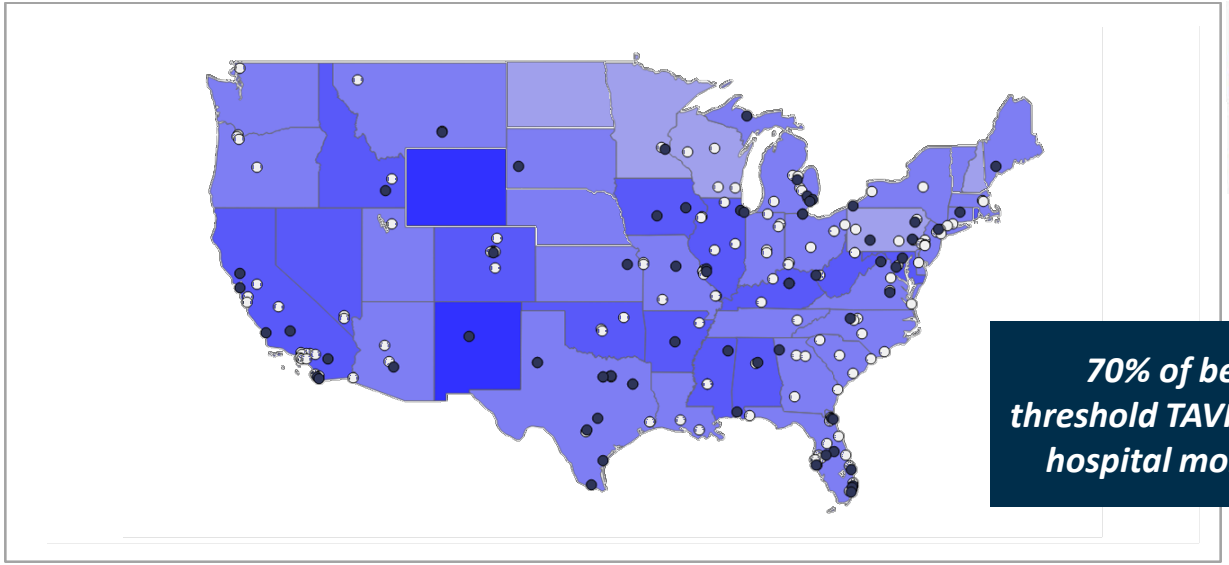
Impact of Increased Volume Requirements on Existing TAVR Hospitals

Scenario: Existing TAVR hospitals subject to 50 TAVR / 30 SAVR annual volume requirement

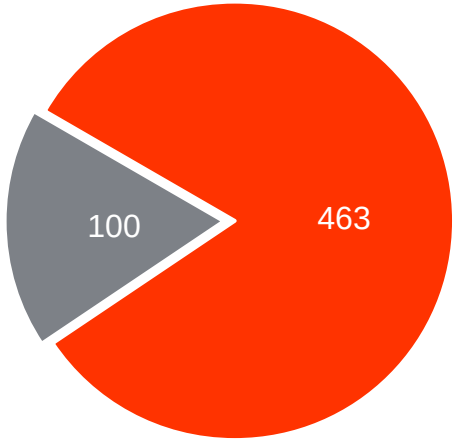


70% of below volume threshold TAVR sites had 0% in-hospital mortality in 2016!

Methods: *Methods:* 2016 diagnosed SSAS incidence was based on newly diagnosed SSAS patients in 2016 divided by the number of individuals seen within the calendar year in Optum in 2016. Diagnosed incidence was adjusted for undiagnosed share based on literature/disparities in diagnosis. Total SSAS incidence (diagnosed & undiagnosed) was applied to 2016 American Community Survey (ACS) 5-year Census data per state by county-level age-distributions to generate heatmaps. For treatment penetration, total incidence was then overlaid with AVR volumes from 2016 inpatient SAF Medicare and adjusted for Medicare Advantage and private payer shares obtained from MEDPAR/HCUP; SAVR volumes then adjusted for SSAS-only share from STS 2016. Modeled impact with 50 TAVR/30 SAVR annual volume requirement scenario.

Impact of Volume Requirements on Current SAVR ONLY Sites Eligibility for TAVR

Scenario: SAVR only hospitals subject to 40 SAVR prior year volume requirement



< 25% SAVR ONLY Sites Would be TAVR Eligible

Cardiovascular Research Foundation

Data Source: FY 2017 MedPAR. Site volume estimates inflated to reflect missing Medicare Advantage and private payer claims.

Columbia University Medical Center
NewYork-Presbyterian

MEDCAC - TAVR Program Requirements

TAVR Volume – Outcome Relationships - Key Points

- **TAVR outcomes have not been affected by either surgery or PCI volumes (MEDPAR data)**
- **The TVT registry had indicated an association between TAVR volumes and TAVR outcomes in the early analyses (2012-2015) which is difficult to dissociate with learning curve issues related to a new therapy.**
- **Recent TVT registry analyses (newer devices, after 2015) have shown no volume threshold outcome relationships with Sapien 3 or Evolut R/PRO.**
- **Scenario testing clearly indicates that arbitrarily increasing the TAVR/SAVR volume requirements will adversely affect patient access.**

Presentation Overview

BACKGROUND - natural history of AS, impact of TAVR on mortality, AS under-diagnosis and under-treatment by AVR

TAVR EVOLUTION & GROWTH - current treatment practices, clinical indications, and outcomes, TAVR growth expectations

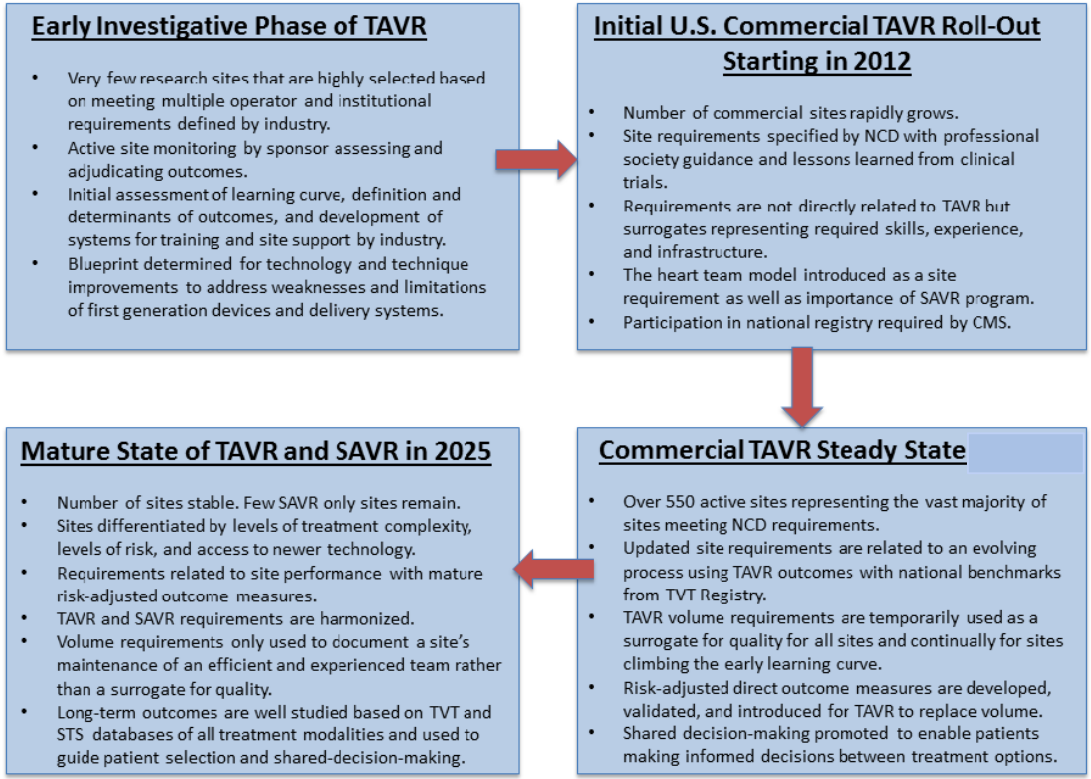
TAVR VOLUME–OUTCOME RELATIONSHIPS – TVT registry and MEDPAR data, impact of volume thresholds on new/existing sites

ADDITIONAL TOPICS AND TAVR PROGRAM RECOMENDATIONS – quality vs. volume metrics, geography issues, and need for SDM

Consensus Document Statements

- *"While this document specifically addresses TAVR requirements, it should be placed in a larger context and specifically address the broader goal of optimizing the care of all patients with severe aortic valve disease."*
- *"The primary objective of this updated document is to promote standards that will help centers achieve high quality outcomes for patients who have clinically significant aortic valve disease."*
- *"The TVT Registry has gathered data from over 100,000 patients who have received TAVR. These data are now focused in three new directions within the draft document.*
  1. *Emphasis on direct measures of quality of care*
  2. *Emphasis on the care of all patients with aortic valve disease rather than only those receiving TAVR*
  3. *Emphasis on the incorporation of SDM "*

Consensus Document Statements



Consensus Document Statements

- The narrative from the consensus document makes good sense with clear goals to rely on quality metrics rather than crude site volume thresholds to determine TAVR (and surgery) performance and site readiness as a new or existing TAVR center.
- The main difference in opinions is the need for acceleration in timing to the quality metric platform, without a burdensome and arbitrary increased volume transition period of 7 years – which will limit patient access!

"Steady State" and "Mature State" should be combined, as TAVR has already demonstrated excellent outcomes at the current NCD volume thresholds!

1. Direct Measures of Quality of Care

- Should begin with direct quality measures (using the TVT database)…
  - Raw in-hospital mortality outcomes compared to national benchmarks
  - Risk-adjusted outcomes (specifically in-hospital and 30-day mortality)
- Evolve over time to other validated outcome measures, including composite endpoints (hard events and quality of life measures)
- The methodology has already been developed for surgery outcomes with the STS database, accounting for low-volume center statistical considerations

Quality Measurement in Adult Cardiac Surgery: Part 2—Statistical Considerations in Composite Measure Scoring and Provider Rating

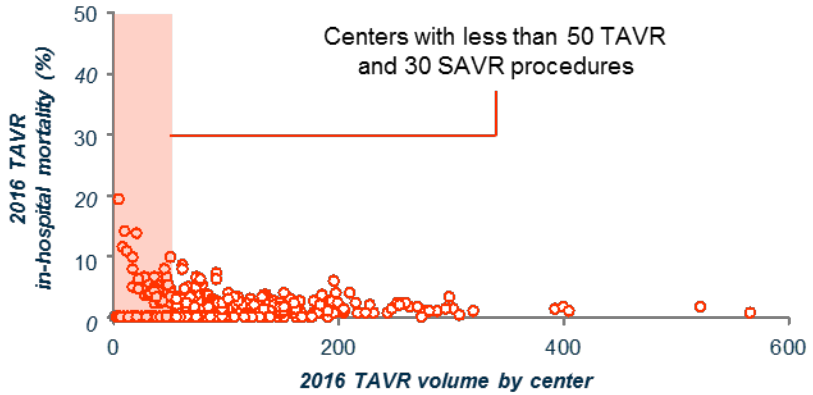
Sean M. O'Brien, PhD,[a] David M. Shahian, MD,[b†] Elizabeth R. DeLong, PhD,[a] Sharon-Lise T. Normand, PhD,[c] Fred H. Edwards, MD,[d] Victor A. Ferraris, MD,[e] Constance K. Haan, MD,[d] Jeffrey B. Rich, MD,[f] Cynthia M. Shewan, PhD,[g] Rachel S. Dokholyan, MPH,[a] Richard P. Anderson, MD,[h] and Eric D. Peterson, MD, MPH[a]

The Society of Thoracic Surgeons Isolated Aortic Valve Replacement (AVR) Composite Score: A Report of the STS Quality Measurement Task Force

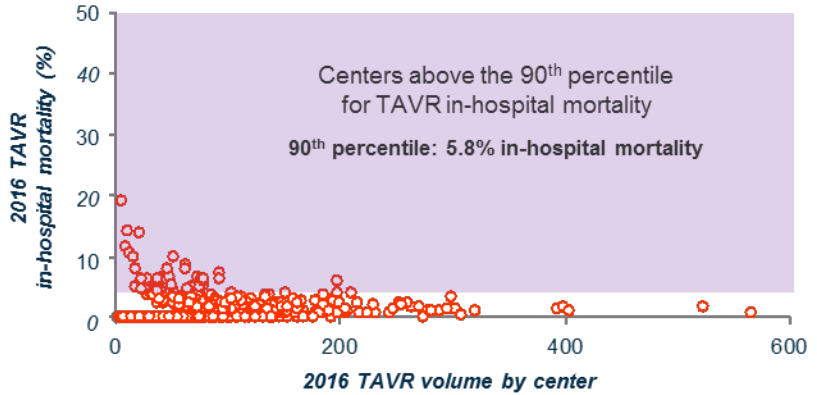
David M. Shahian, MD, Xia He, MS, Jeffrey P. Jacobs, MD, J. Scott Rankin, MD, Karl F. Welke, MD, Giovanni Filardo, PhD, MPH, Cynthia M. Shewan, PhD, and Sean M. O'Brien, PhD

Outcome Thresholds, NOT Volume Thresholds, Will Lead to Better Patient Care

Comparing system impact with volume vs. outcome thresholds



- **65%** drop in sites with TAVR 0% in-hospital mortality (78)
- **43%** of TAVR centers below threshold (211)
- **16%** patients at below volume centers (6622)
- Change in-hospital mortality from **2.0%** to **1.98%** **(<5% improvement)**



- **0%** drop in sites with TAVR 0% in-hospital mortality (225)
- **10%** of TAVR centers below threshold (50)
- **5%** patients at below volume centers (2078)
- Change in hospital mortality from **2.0%** to **1.7%** **(15% improvement)**

1. Lives saved calculated based on comparing original in-hospital mortality and then calculating new overall mortality based on the in-hospital mortality of the centers still in the system (excludes displaced centers and patients which are assessed on the next slide). Data Source: 2016 100% inpatient SAF Medicare. TAVR/SAVR volumes based on Medicare Fee-For-Service and adjusted Medicare Advantage and private payer shares from MEDPAR/HCUP.

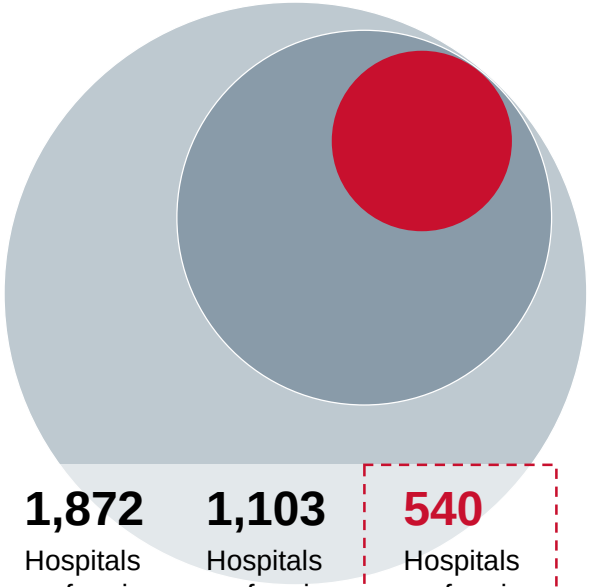
Outcome-based vs. Volume-based Requirements

	Volume-based Volumes as a proxy for outcomes	**Outcomes-based** Directly focus on key care metrics
Implementation ease	**High:** Obtainable from claim submissions	**Mid:** Registry required with potential need for adjustment
System impact	No adjustment for outcomes (i.e. small volume, high performance centers remove)	Size independent (i.e. high performing, low volume centers can be retained)
Effect on outcomes variation	No direct impact	Directly reduced
Ease of improvement	**Low:** Doubling volumes difficult especially in areas with low patient or high center density	**High:** Centers can implement policies to improve outcomes on current volumes

2. Emphasis on ALL AS Patients and Therapies

- All forms of treatment should be available and offered to AS patients, including TAVR, surgery, medical care, and palliative case, as appropriate for the clinical circumstances and directed by a multi-disciplinary heart team.
- The dilemma of SAVR ONLY centers in the U.S. (currently one-half of all AS AVR treatment centers) creates care-giver and referral biases resulting in disparities in optimal AS treatment.
- Increased volume threshold requirements will further limit patient access to TAVR as a treatment alternative at a time when the aging population and expanded clinical indications will demand more (not less) access to TAVR!
- Decreased access to TAVR will result in prolonged AVR treatment wait-times and geography-based constraints which will negatively impact AS outcomes.

TAVR Access Relative to Hospitals Performing PCI and Surgical AVR

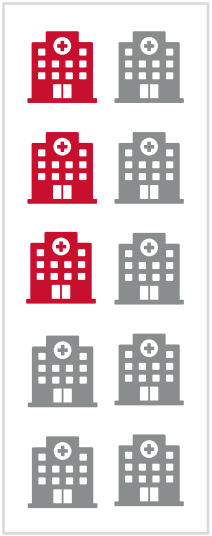


1,872
Hospitals performing PCI

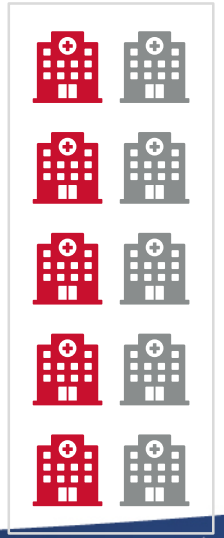
1,103
Hospitals performing Surgical AVR

540
Hospitals performing TAVR

29%
PCI hospitals performing TAVR in 2017



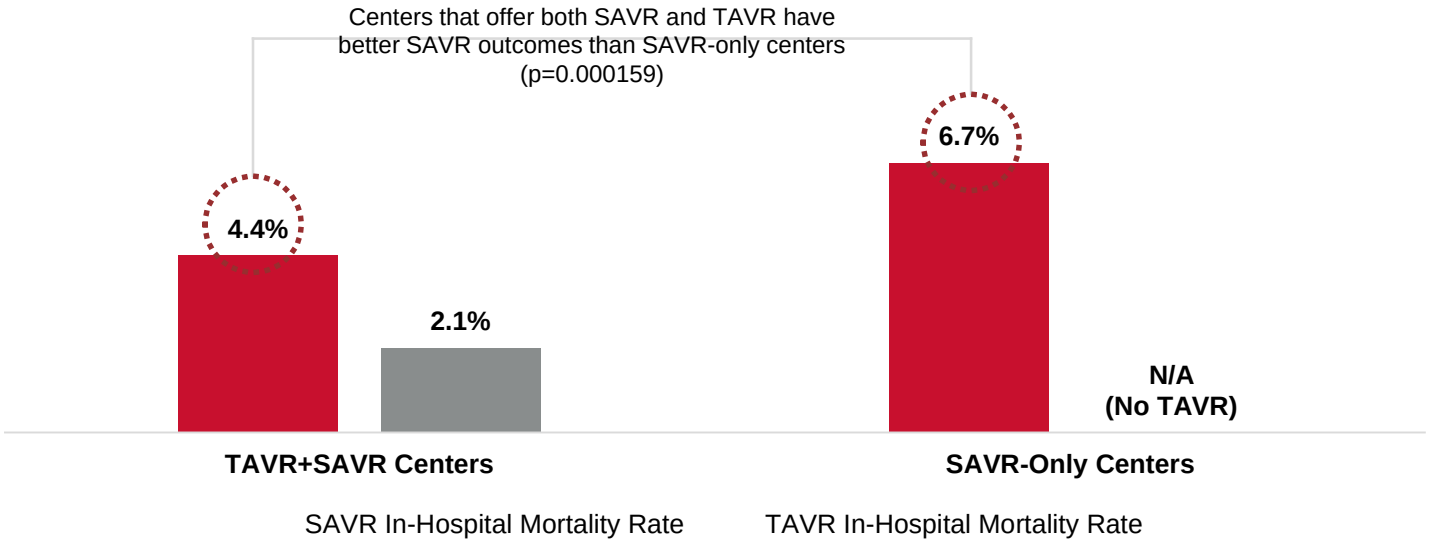
49%
Surgical AVR hospitals performing TAVR in 2017



Data Source: FY 2017 MedPAR.

SAVR Outcomes in Centers With and Without TAVR Programs

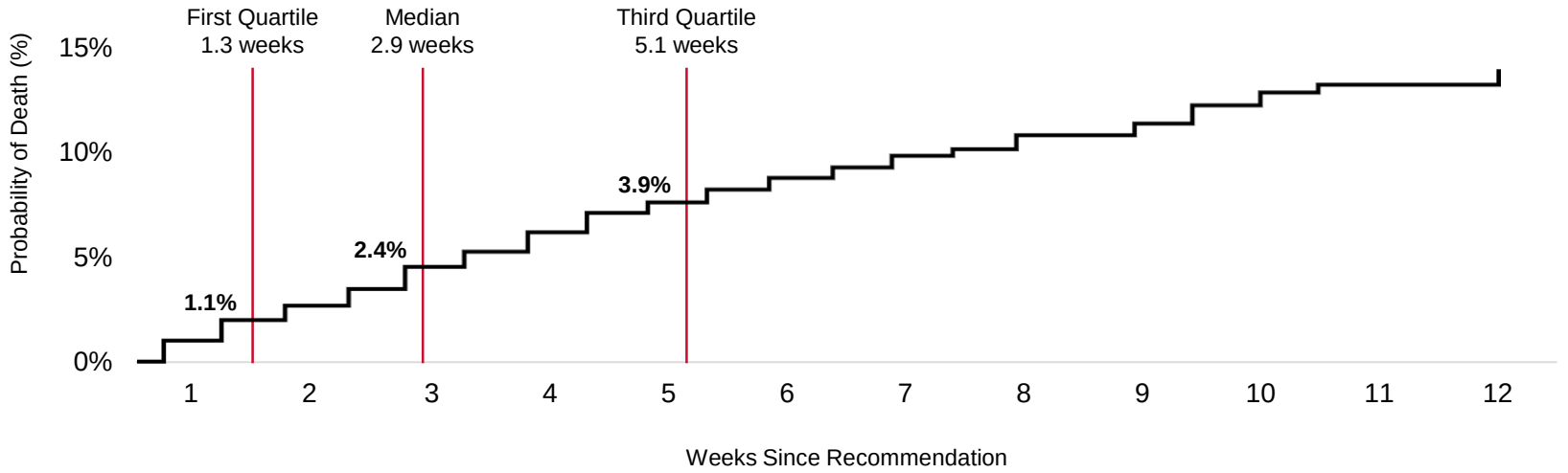
TAVR and SAVR Mortality Rates at SAVR-Only Centers Vs. TAVR+SAVR Centers



Data Source: 2016 100% SAF Medicare.

Delay to AVR Treatment Results in Increased Mortality after Diagnosis of SSAS

First 12 Weeks Since TAVR Recommended: Cumulative Probability of Death without Intervention



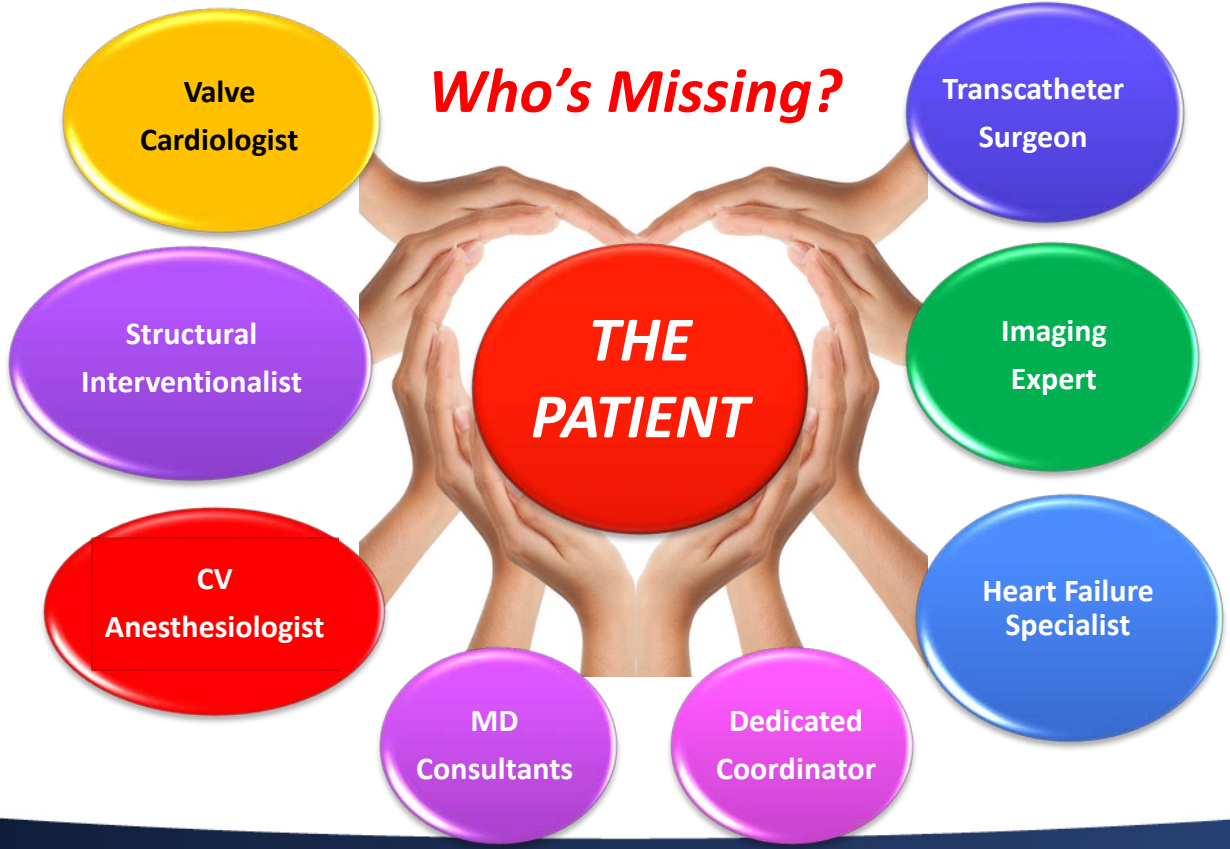
Distance – Outcome Relationships

- **A systematic review of the association between patient travel time/travel distance to healthcare services and health outcomes found:**
  - **77%** of studies reported a ***distance decay*** association. (i.e., patient living further away from healthcare facilities had worse health outcomes (survival, length of stay, and non-attendance at follow-up) than patients who lived closer
  - This associa wide range of diseases, ir CABG and non-emergent c


Are differences in travel time or distance to healthcare for adults in global north countries associated with an impact on health outcomes? A systematic review

Charlotte Kelly,[1,2] Claire Hulme,[1] Tracey Farragher,[1] Graham Clarke[3]

The Heart Team 3.0



3. Incorporating Shared Decision-Making (SDM)

- The profound influence of a shared decision-making process and declared communication aids is now being embedded into patient management discussions, informed consents, FDA approval clinical trials, and CMS coverage determinations.

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- The profound influence of a shared decision-making process and declared communication aids is now being embedded into patient management discussions, informed consents, FDA approval clinical trials, and CMS coverage determinations.

Health Expectations
An International Journal of Public Participation in Health Care and Health Policy

doi: 10.1111/hex.12393

Patient-defined goals for the treatment of severe aortic stenosis: a qualitative analysis

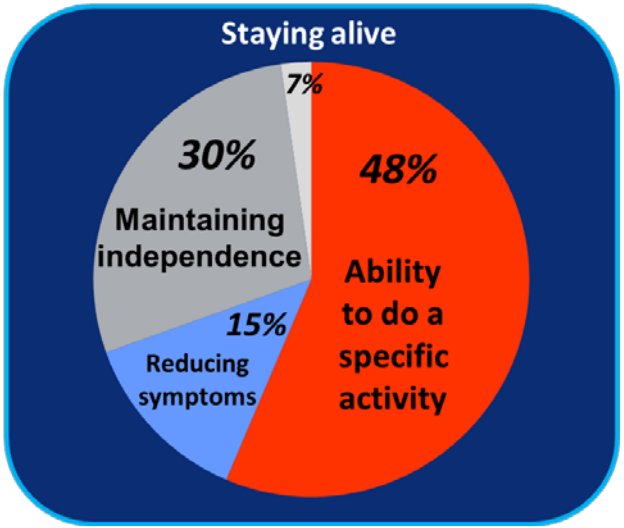
Megan Coylewright MD MPH,*† Roseanne Palmer MSN RN,‡ Elizabeth S. O'Neill MPH,§ John F. Robb MD¶ and Terri R. Fried MD**††

*Assistant Professor of Medicine, ‡Transcatheter Aortic Valve Replacement Program Coordinator, §Research Fellow, ¶Professor of Medicine, Section of Cardiology, Department of Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH, †Assistant Professor of Health Policy and Clinical Practice, The Dartmouth Institute for Health Policy and Clinical Practice, Geisel School of Medicine at Dartmouth, Lebanon, NH, **Professor of Medicine, Department of Internal Medicine, School of Medicine, Yale University, New Haven, CT, ††Investigator, Clinical Epidemiology Research Center, Veterans Affairs Connecticut Healthcare System, West Haven, CT, USA

- ***"What matters most to you?"***
- ***"What do you hope to accomplish with treatment?"***
- ***"What to do you want to do, that you cannot now?"***

3. Incorporating Shared Decision-Making (SDM)

- The profound influence of a shared decision-making process and declared communication aids is now being embedded into patient management discussions, informed consents, FDA approval clinical trials, and CMS coverage determinations.



- *"What matters most to you?"*
- *"What do you hope to accomplish with treatment?"*
- *"What to do you want to do, that you cannot now?"*

3. Incorporating Shared Decision-Making (SDM)

- The profound influence of a shared decision-making process and declared communication aids is now being embedded into patient management discussions, informed consents, FDA approval clinical trials, and CMS coverage determinations.
- The concept of shared decision-making becomes distorted in an environment when patient access to all therapies is further limited, especially a therapy like TAVR, wherein secondary endpoints such as rapid return to normal daily activities, improved early QOL, and reduced procedure-related discomfort are clear and meaningful benefits to patients.
- Currently, the high prevalence of SAVR ONLY centers for AS is problematic for SDM; in the future, if SDM is to be coveted, then the goal must be to reduce SAVR ONLY centers for the treatment of AS patients!

MEDCAC - TAVR Program Requirements

Additional Topics & Recommendations - Key Points

- **The consensus document thoughtfully addresses the need for quality metrics, patient access to all AS therapies and SDM processes.**
- **However, arbitrary implementation of increased volume requirements and the delay in introducing quality metrics are counter to the above mentioned principles and will significantly limit access to TAVR.**
- **The limitations in access to TAVR will create a 'distance decay' and delayed wait times, serving to worsen clinical outcomes.**
- **Shared decision-making (SDM), a vital component of future clinical interactions, will be eroded by available therapy disparities.**

‘Compromise’ AVR Volume Recommendations

- In the spirit of maintaining and hopefully improving BOTH patient access to ALL therapies and achieving optimal clinical outcomes for ALL AS patients:
- Quality metrics should supersede arbitrary volume thresholds as a general principle.
  - Surgery volumes should be eliminated as a criteria for new and existing TAVR centers and be replaced by a quality metric, such as having and maintaining a “2 star rating” (defined by the STS).
  - PCI volumes should be adjusted to 250 cases per year to maintain necessary infra-structure and skills, until such time that the NCDR database quality metrics can also be incorporated.
  - TAVR volumes should be maintained at the current NCD levels of 20 cases per year or 40 over two years to maintain necessary infra-structure and skills.

‘Compromise’ AVR Volume Recommendations

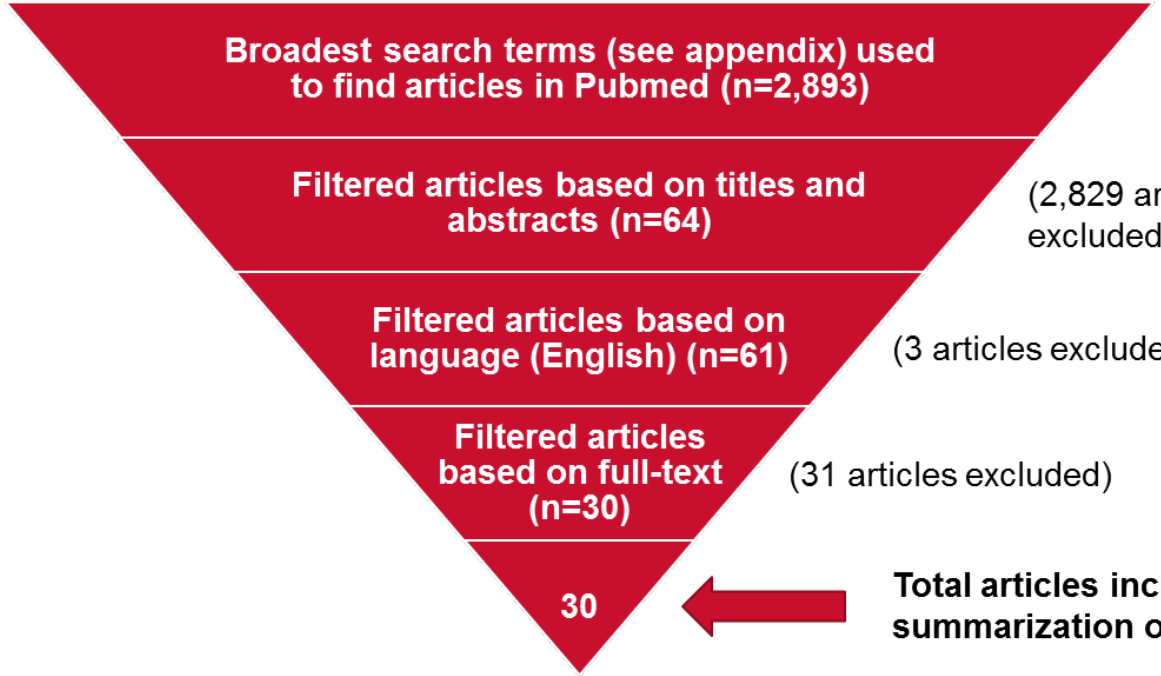
- The reasons to justify maintaining TAVR volume thresholds are the following:
  - Current clinical outcomes have been carefully scrutinized and by all standards have both stabilized and are excellent in most TAVR centers.
  - Both TVT and MEDPAR data indicate that with current generation TAVR systems an adjustment in TAVR volume thresholds is **NOT** indicated.
  - An arbitrary increase in TAVR volume requirements will undoubtedly impact patient access to TAVR which will result in worsening outcomes for AS patients.
- TAVR quality metrics should be integrated into the proposed new NCD to rapidly replace the need for volume requirements and to more closely monitor the clinical outcomes of ALL TAVR centers (esp. the lower volume centers), with corrective measures for poor performance, installed as needed.

Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) Focused Topic: TAVR Program Requirements July 25, 2018

APPENDIX

1. AVR Volume – Outcome Literature Search
2. Voting Question Responses

AVR Volume-Outcome Literature Search



See references slide for a full citation of the 30 articles included in the summarization of evidence

SAVR Volume = TAVR Outcomes?

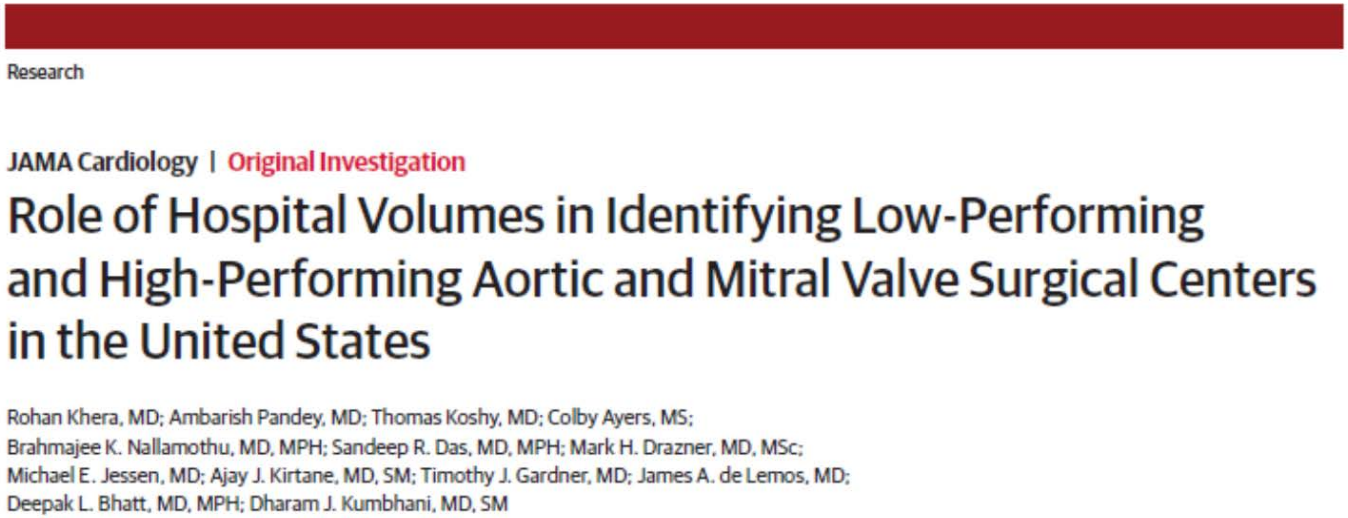
- Only 2 studies assessed the relationship between SAVR volume and concurrent TAVR outcomes; neither found a significant association[1,2]

- 2 studies assessed the impact of TAVR volume on SAVR outcomes, and found significant decrease in morbidity and mortality of SAVR with increasing TAVR volume[3,4]

1. De biasi AR et al. Cardiology 2016 2. Mccarthy FH et al. Circ Cardiovasc Interv 2015
2. 3. Hawkins RB et al. Ann Thorac Surg 2017 4. Singh V et al. Am J Cardiol 2015

SAVR Volume = SAVR Outcomes?

- **Substantial literature supporting an inverse linear relationship between SAVR Volume and SAVR outcomes. However…**



Research

JAMA Cardiology | Original Investigation

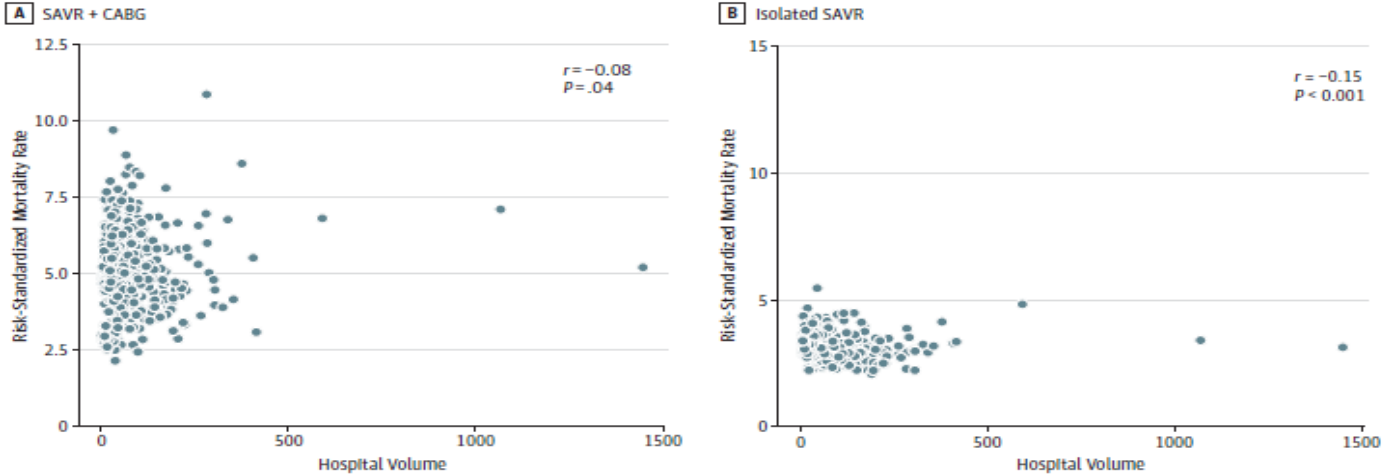
Role of Hospital Volumes in Identifying Low-Performing and High-Performing Aortic and Mitral Valve Surgical Centers in the United States

Rohan Khera, MD; Ambarish Pandey, MD; Thomas Koshy, MD; Colby Ayers, MS; Brahmajee K. Nallamothu, MD, MPH; Sandeep R. Das, MD, MPH; Mark H. Drazner, MD, MSc; Michael E. Jessen, MD; Ajay J. Kirtane, MD, SM; Timothy J. Gardner, MD; James A. de Lemos, MD; Deepak L. Bhatt, MD, MPH; Dharam J. Kumbhani, MD, SM

SAVR Volume = SAVR Outcomes?

- **Despite a significant p-value, correlation between SAVR volume and risk-stratified mortality was very weak (r = - 0.08 for SAVR+CABG and - 0.15 for Isolated SAVR)**

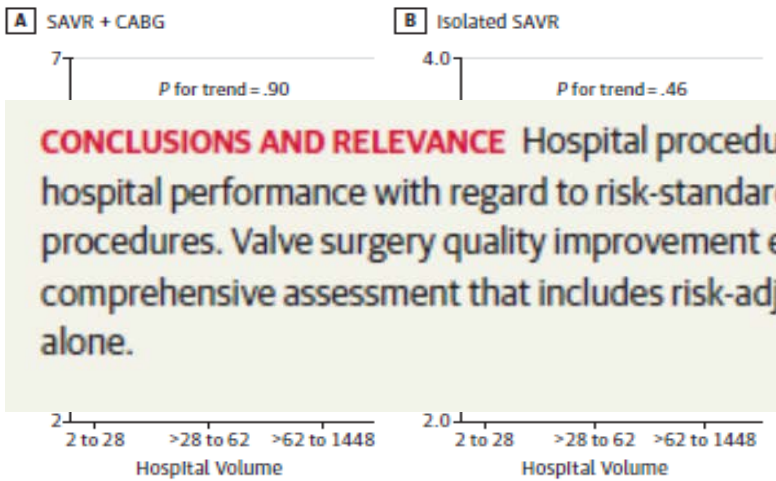
Figure 1. Spearman Rank Correlation Plots for Annual Hospital Volume



SAVR Volume = SAVR Outcomes?

- **No association was observed between volume-based tertiles and risk-stratified mortality rate**

Figure 2. Median Risk-Standardized Mortality Rate Across Annual Hospital Volume–Based Tertiles



CONCLUSIONS AND RELEVANCE Hospital procedure volume alone frequently misclassifies hospital performance with regard to risk-standardized outcomes after aortic and MV surgical procedures. Valve surgery quality improvement endeavors should focus on a more comprehensive assessment that includes risk-adjusted outcomes rather than hospital volume alone.

"If these volume-based (low, medium, and high) tertiles were used to categorize hospitals for

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PCI Volume = TAVR Outcomes?

- 0 full manuscripts
- 1 abstract

PCI volume and TAVR outcomes - no association found

Relationship between PCI volume and TAVR outcomes

Annual Hospital PCI Volume	Overall	< 400	≥400	P value
In-hospital mortality	4.9	5.2	4.7	0.124
Unadjusted OR (95% CI)		Referent	0.89 (0.78-1.02)	0.124
Adjusted OR (95% CI)		Referent	0.98 (0.62-1.54)	0.923
Vascular complications	6.7	6.9		
Unadjusted OR (95% CI)		Referent	0.96	
Adjusted OR (95% CI)		Referent	1.13	
Bleeding requiring transfusion	13.0	13.3		
Unadjusted OR (95% CI)		Referent	0.97 -	
Adjusted OR (95% CI)		Referent	1.01 (- 58)	
Neurological complications	1.5	0.9	1.7	<0.001
Unadjusted OR (95% CI)		Referent	1.85 (1.36-2.49)	<0.001
Adjusted OR (95% CI)		Referent	1.91 (0.90-4.06)	0.090

"The CMS requirement of 400 PCIs per year **does not seem to be necessary - to warrant optimal TAVR outcomes**. The skillsets needed to **perform PCI may not fully translate to TAVR**, which is a very distinct procedure."

Patel, Nileshkumar, Impact of Annual Hospital Percutaneous Coronary Intervention Volume on Transcatheter Aortic-Valve Replacement Outcomes. Poster presented at TCT 2017

TAVR Volume = TAVR Outcomes?

- 26 studies assessed the relationship between institutional TAVR volumes and outcomes in TAVR patients.
- Outcomes included mortality (or a composite measure including mortality), LOS, vascular complications, bleeding, regurgitation, hospital readmissions, and acute kidney injury
  - 19 studies reported that as institutional TAVR volumes increase, adverse TAVR outcomes decrease significantly
  - 7 studies reported no relationship

TAVR Volume = TAVR Outcomes?

Key Limitations of the 19 TAVR Studies Showing a Volume-Outcome Association

1. ***Limited generalizability due to small sample size***
   - **7 studies at single sites with low patient volumes**
2. ***Lack of control of important confounders***
   - **8 studies used bivariate analyses not controlling for important patient-level, operator-level, and institution-level confounding variables**
3. ***Early time bias (most cases before 2016)***
   - **Rapid evolution in TAVR technology limits the generalizability from studies prior to 2016**
     - **All 19 studies included procedures performed prior to 2016**
     - **10 studies were limited to procedures performed during first year of commercial approval in the US (2012); unable to distinguish procedural learning curve from volume-outcome relationships**
4. ***Difficulty in determining appropriate threshold of procedure volumes***
   - **Threshold of prior procedures required to maintain a current TAVR program was difficult to determine[1] and None of the studies assessed or reported a specific threshold**

Morche J, Mathes T, Pieper D. Relationship between surgeon volume and outcomes: a systematic review of systematic reviews. Systematic Reviews. 2016; 5: 204.

Voting Questions
MEDCAC on procedural volume requirements for hospitals to maintain and start TAVR programs

Martin B. Leon, MD

Columbia University Medical Center
Cardiovascular Research Foundation
New York City

on behalf of AdvaMed

July 25th, 2018

Hospital requirements to begin TAVR programs

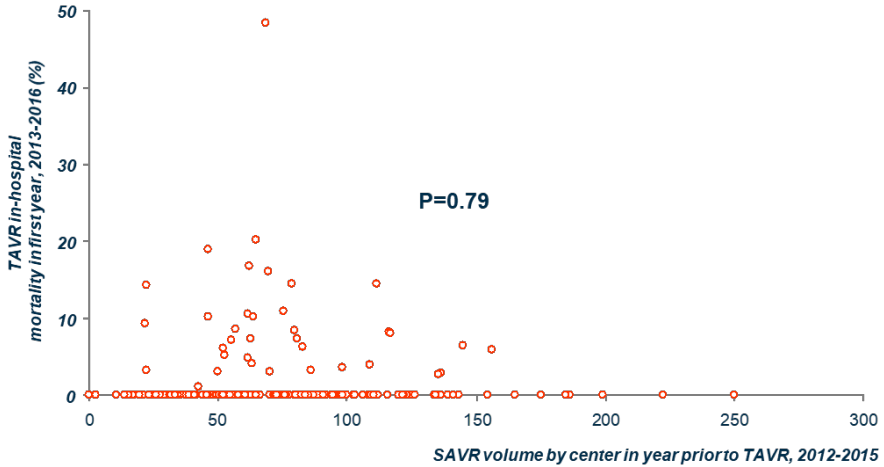
1

How confident are you that there is sufficient evidence that a certain threshold of **SAVR procedural volumes** must be required for **hospitals without previous TAVR experience to begin** TAVR programs?

Low Confidence *Intermediate* *High Confidence*

1. How confident are you that there is sufficient evidence that a certain threshold of SAVR procedural volumes must be required for hospitals without previous TAVR experience to begin TAVR programs?

- **The presence of an active cardiac surgery program would ensure a familiarity with severe aortic stenosis patients and surgical procedures.**
- **We find insufficient evidence supporting a specific volume threshold of SAVR procedures that is associated with the successful initiation of a TAVR program.**
- **In fact, an analysis of the 2012-2016 100% SAF Medicare database revealed NO ASSOCIATION (p=0.79) between SAVR procedural volume in the year prior to beginning a TAVR program and TAVR outcomes.**



Data Source: 2012-2016 100% inpatient SAF Medicare. SAVR center volumes based on Medicare Fee-For-Service claims adjusted for Medicare Advantage and private payer share from MEDPAR/HCUP.
See backup slides for risk adjustment methodology for TAVR mortality.

Hospital requirements to begin TAVR programs

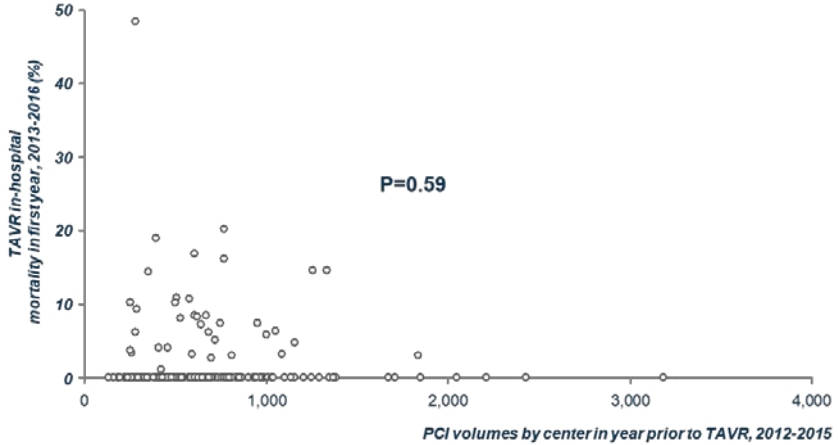
2

How confident are you that there is sufficient evidence that a certain threshold of **PCI procedural volumes** must be required for **hospitals without previous TAVR experience to begin** TAVR programs?

Low Confidence *Intermediate* *High Confidence*

2. How confident are you that there is sufficient evidence that a certain threshold of PCI procedural volumes must be required for hospitals without previous TAVR experience to begin TAVR programs?

- **The presence of an active interventional cardiology program would ensure a familiarity with coronary artery disease management and the indications for and technical aspects of PCI procedures.**
- **We find no evidence supporting a specific volume threshold of PCI procedures for hospitals that is associated with the successful initiation of a TAVR program.**
- **In fact, an analysis of the 2012-2016 100% SAF Medicare database revealed NO ASSOCIATION (p=0.59) between PCI procedural volume in the year prior to beginning a TAVR program and TAVR outcomes.**



Data Source: 2012-2016 100% inpatient SAF Medicare. PCI center volumes based on Medicare Fee-For-Service claims adjusted for Medicare Advantage and private payer share from MEDPAR/HCUP; also adjusted for outpatient share from 5% Medicare sample. See backup slides for risk adjustment methodology for TAVR mortality.

Hospital requirements to begin TAVR programs

3

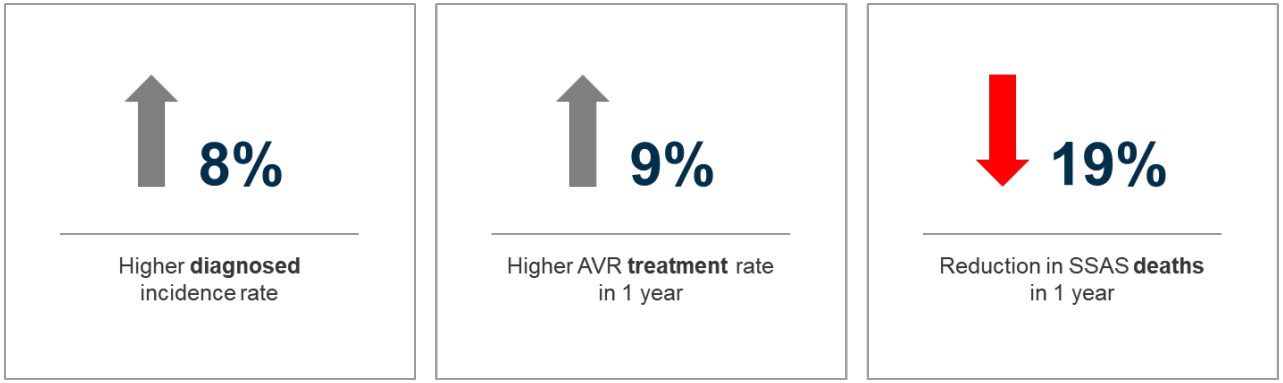
How confident are you that the **benefits** of meeting procedural (i.e., SAVR, PCI) volume requirements to **begin a TAVR program** outweigh the **harms** of limiting access to TAVR to only hospitals that meet volume requirements?

Low Confidence *Intermediate* *High Confidence*

3. How confident are you that the benefits of meeting procedural (i.e., SAVR, PCI) volume requirements to begin a TAVR program outweigh the harms of limiting access to TAVR to only hospitals that meet volume requirements?

- **Given the lack of evidence supporting a specific minimum volume requirement of PCI and SAVR procedures to begin a TAVR program, the harms of limiting access to TAVR far outweighs the benefits.**
- **In fact, the addition of new TAVR centers has been associated with higher diagnosis rates, higher AVR treatment rates, and lower mortality.**

Impact from 370 TAVR centers in 2014 to 470 TAVR centers in 2016

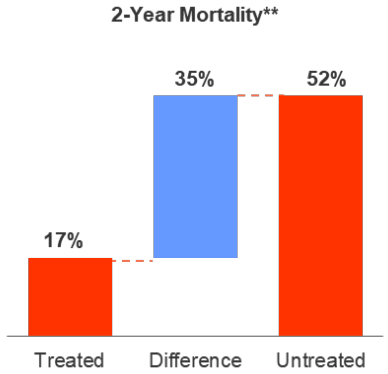


Specific methods: Access over time analysis: SSAS patients in Optum diagnosed in 2014 and 2016 were followed for 1 year to evaluate outcomes. Treatment rate, untreated mortality, and TAVR rate were compared in each scenario. Source: Optum EHR

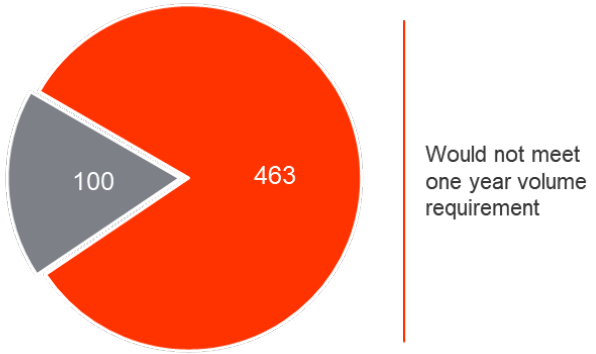
3. How confident are you that the benefits of meeting procedural (i.e., SAVR, PCI) volume requirements to begin a TAVR program outweigh the harms of limiting access to TAVR to only hospitals that meet volume requirements?

- **Since less than half of newly diagnosed SSAS* patients are treated and untreated SSAS patients have a two year mortality rate of 52%, reduced access to TAVR by limiting or decreasing the number of TAVR sites will negatively impact AS mortality.**
- **If increased volume requirements were to be implemented, less than 25% of current SAVR-ONLY sites may be eligible as approved TAVR sites in the future.**

The under treatment of SSAS results in significant excess mortality



Scenario: SAVR only hospitals subject to 40 SAVR annual volume requirement



Data Source: FY 2017 MedPAR. Site volume estimates inflated to reflect missing Medicare Advantage and private payer claims.

Source: *Based on Optum cohort of patients diagnosed in 6 month period between 2015 and 2016. **Optum cohort diagnosed in 2014 and 2015 with 2 year follow-up. *** 2016 100% SAF Medicare
† Kapadia S. et al Lancet 2015 Jun 20;385(9986):2485-91.

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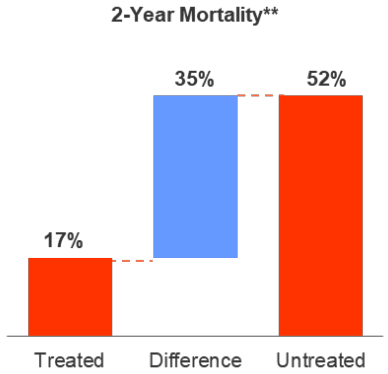
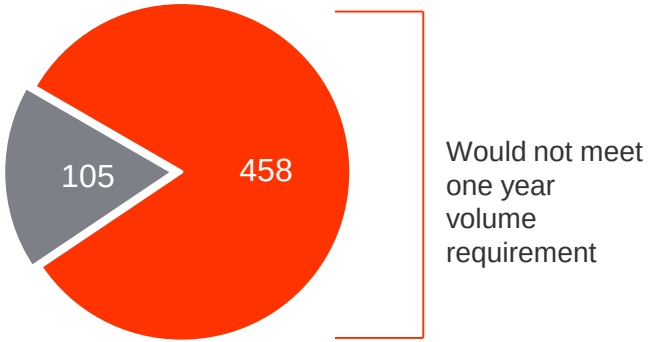


Scenario: SAVR only hospitals subject to 30 SAVR annual volume requirement



Data Source: FY 2017 MedPAR. Site volume estimates inflated to reflect missing Medicare Advantage and private payer claims.

Source: *Based on Optum cohort of patients diagnosed in 6 month period between 2015 and 2016. **Optum cohort diagnosed in 2014 and 2015 with 2 year follow-up. *** 2016 100% SAF Medicare
† Kapadia S. et al Lancet 2015 Jun 20;385(9986):2485-91.

Hospital requirements to maintain TAVR programs

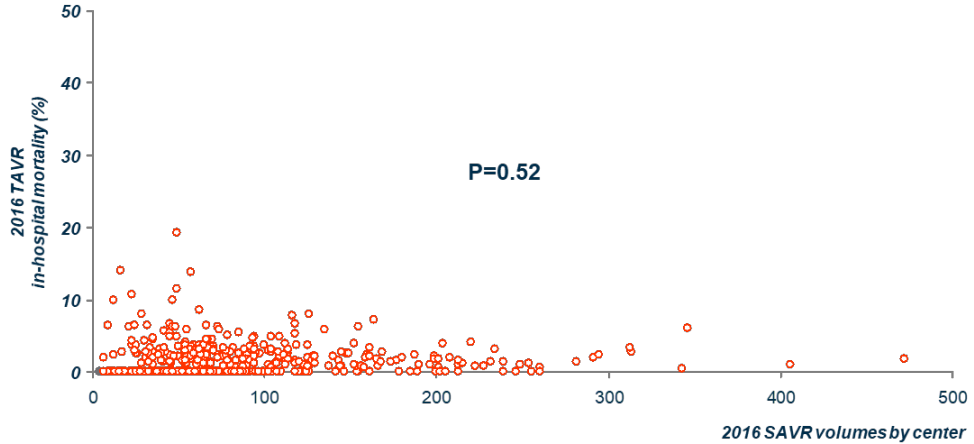
4

How confident are you that there is sufficient evidence that a certain threshold of **SAVR procedural volumes** must be required for **hospitals with TAVR experience to maintain** TAVR programs?

Low Confidence *Intermediate* *High Confidence*

4. How confident are you that there is sufficient evidence that a certain threshold of SAVR procedural volumes must be required for hospitals with TAVR experience to maintain TAVR programs?

- **The presence of an active heart team and cardiac surgery program would ensure a process, infrastructure and commitment to a comprehensive aortic valve program.**
- **We find insufficient evidence supporting a specific volume threshold of SAVR procedures that is associated with improved TAVR outcomes at existing TAVR programs.**
- **In fact, an analysis of the 2016 100% SAF Medicare database revealed NO ASSOCIATION (p=0.52) between SAVR procedural volume and TAVR outcomes.**



Data Source: 2012-2016 100% inpatient SAF Medicare. SAVR center volumes based on Medicare Fee-For-Service claims adjusted for Medicare Advantage and private payer share from MEDPAR/HCUP.
See backup slides for risk adjustment methodology for TAVR mortality. Note: Centers with volumes above 600 excluded for graphical presentation but included in correlation calculation.

Hospital requirements to maintain TAVR programs

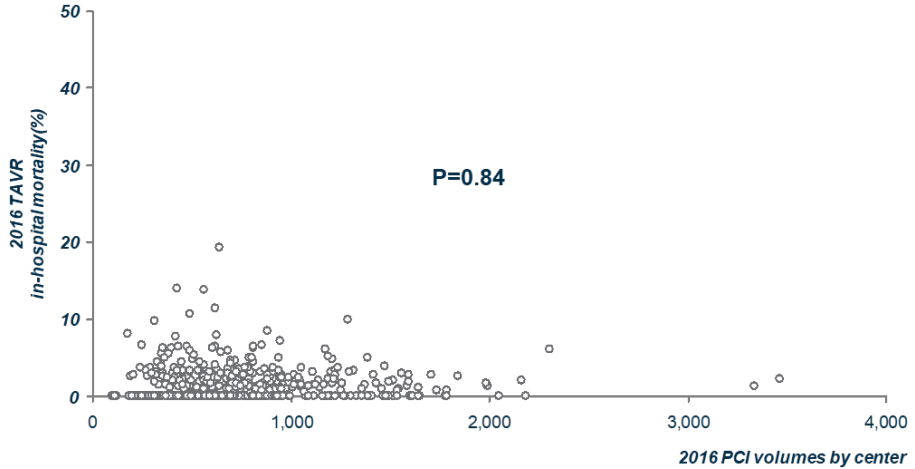
5

How confident are you that there is sufficient evidence that a certain threshold of **PCI procedural volumes** must be required for **hospitals with TAVR experience to maintain** TAVR programs?

Low Confidence *Intermediate* *High Confidence*

5. How confident are you that there is sufficient evidence that a certain threshold of PCI procedural volumes must be required for hospitals with TAVR experience to maintain TAVR programs?

- **The presence of an active heart team and interventional cardiology program would ensure a process, infrastructure and commitment to a comprehensive aortic valve program.**
- **We find no evidence supporting a specific volume threshold of PCI procedures that is associated with improved TAVR outcomes at existing TAVR programs.**
- **In fact, an analysis of the 2016 100% SAF Medicare database revealed NO ASSOCIATION (p=0.84) between PCI procedural volume and TAVR outcomes.**



Data Source: 2012-2016 100% inpatient SAF Medicare. PCI center volumes based on Medicare Fee-For-Service claims adjusted for Medicare Advantage and private payer share from MEDPAR/HCUP; also adjusted for outpatient share from 5% Medicare sample. See backup slides for risk adjustment methodology for TAVR mortality.

Looking specifically at PCI volume and TAVR outcomes and no association is found

Relationship between PCI volume and TAVR outcomes

Annual Hospital PCI Volume	Overall	< 400	≥400	P value
In-hospital mortality	4.9	5.2	4.7	0.124
Unadjusted OR (95% CI)		Referent	0.89 (0.78-1.02)	0.124
Adjusted OR (95% CI)		Referent	0.98 (0.62-1.54)	0.923
Vascular complications	6.7	6.9		
Unadjusted OR (95% CI)		Referent	0.96	
Adjusted OR (95% CI)		Referent	1.13	
Bleeding requiring transfusion	13.0	13.3		
Unadjusted OR (95% CI)		Referent	0.97 -	
Adjusted OR (95% CI)		Referent	1.01 (- 58)	
Neurological complications	1.5	0.9	1.7	<0.001
Unadjusted OR (95% CI)		Referent	1.85 (1.36-2.49)	<0.001
Adjusted OR (95% CI)		Referent	1.91 (0.90-4.06)	0.090

"The CMS requirement of 400 PCIs per year **does not seem to be necessary - to warrant optimal TAVR outcomes**. The skillsets needed to **perform PCI may not fully translate to TAVR**, which is a very distinct procedure."

Patel, Nileshkumar, Impact of Annual Hospital Percutaneous Coronary Intervention Volume on Transcatheter Aortic-Valve Replacement Outcomes. Poster presented at TCT 2017

Hospital requirements to maintain TAVR programs

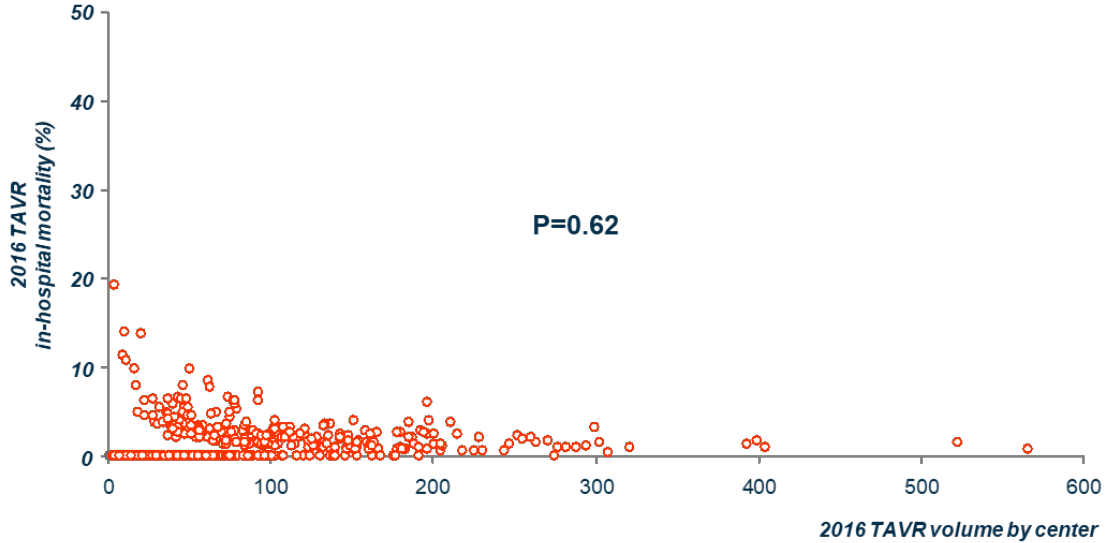
6

How confident are you that the **benefits** of meeting procedural (i.e., SAVR, TAVR, PCI) volume requirements to **maintain a TAVR program** outweigh the **harms** of limiting access to TAVR to only hospitals that meet volume requirements?

Low Confidence *Intermediate* *High Confidence*

6. How confident are you that the benefits of meeting procedural (i.e., SAVR, TAVR, PCI) volume requirements to maintain a TAVR program outweigh the harms of limiting access to TAVR to only hospitals that meet volume requirements?

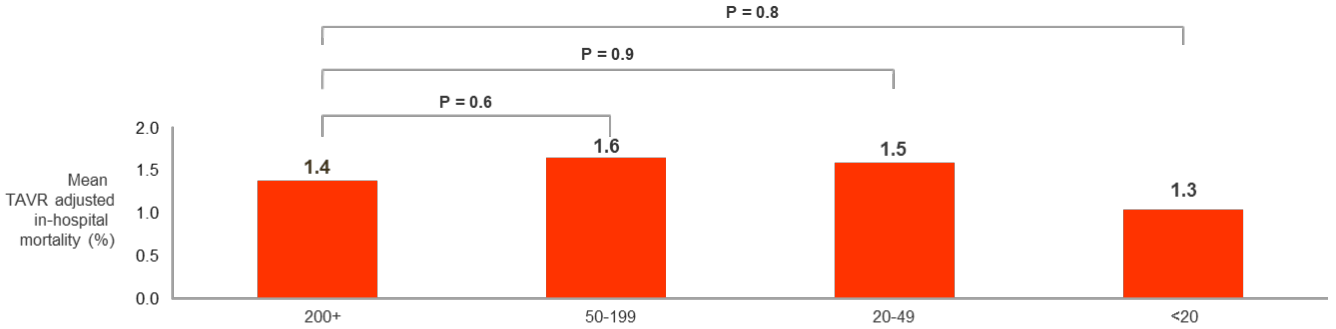
- **Given the lack of evidence supporting a specific minimum volume requirement of PCI, SAVR and TAVR procedures to maintain a TAVR program, the harms of limiting access to TAVR far outweighs the benefits.**
- **In fact, an analysis of the 2016 100% SAF Medicare database revealed NO ASSOCIATION (p=0.62) between TAVR procedural volume and TAVR outcomes.**



Data Source: 2012-2016 100% in-patient SAF Medicare. Center volumes based on Medicare Fee-For-Service claims adjusted for Medicare Advantage and private payer share from MEDPAR/HCUP. See backup slides for risk adjustment methodology for TAVR mortality. Note: Center volumes above 600 excluded for graphic purposes but included in correlation calculation.

6. How confident are you that the benefits of meeting procedural (i.e., SAVR, TAVR, PCI) volume requirements to maintain a TAVR program outweigh the harms of limiting access to TAVR to only hospitals that meet volume requirements?

- **A separate analysis of the 2016 100% SAF Medicare database shows similar outcomes across different TAVR center volume cohorts.**
- **40% of TAVR procedures were performed at centers with less 50 TAVR annual volume, and as a group, they achieved excellent outcomes.**
- **More stringent volume requirements will limit the addition of new TAVR centers, creating further capacity constraints for existing TAVR centers.**

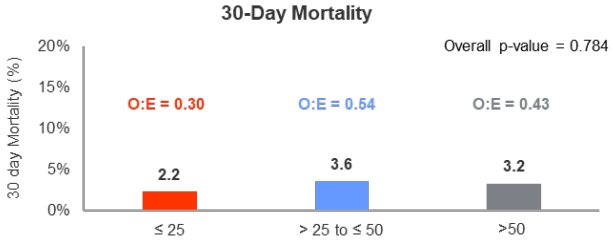


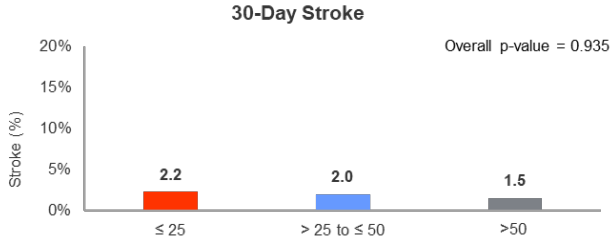
2016 TAVR center volumes				
# of centers	33	261	134	62
95% confidence interval	(1.14, 1.70)	(1.36, 1.78)	(1.05, 1.89)	(0.29, 2.23)
Percent of TAVR volumes (adjusted)	7%	53%	27%	13%

Data Source: 2016 100% SAF Medicare. Center volumes based on Medicare Fee-For-Service claims adjusted for Medicare Advantage and private pay share from MEDPAR/HCUP. See backup slides for risk adjustment methodology.

6. How confident are you that the benefits of meeting procedural (i.e., SAVR, TAVR, PCI) volume requirements to maintain a TAVR program outweigh the harms of limiting access to TAVR to only hospitals that meet volume requirements?

- **An analysis of the TVT Registry for the Edwards SAPIEN 3 TAVR system shows excellent outcomes across all TAVR center volume cohorts.**





# of SAPIEN 3 Implants per Month

Monthly volume	≤ 25	> 25 to ≤ 50	> 50
# of sites	7	25	21
Mean Implant Freq	1.7	3.2	7.1
# of patients	96	570	543
STS	7.53	6.65	7.49

# of SAPIEN 3 Implants per Month

Monthly volume	≤ 25	> 25 to ≤ 50	> 50
# of sites	7	25	21
Mean Implant Freq	1.7 ± 0.3	3.2 ± 0.6	7.1 ± 3.4
# of patients	96	570	543
STS	7.53 ± 9.1	6.65 ± 4.5	7.49 ± 4.7

TVT Registry; Edwards analysis of SAPIEN 3 valve data through Feb 2017

Operator requirements to begin TAVR Programs

7

To **begin performing TAVR**, how confident are you that there is sufficient evidence that a certain threshold of SAVR and TAVR procedural volumes must be required for the principle cardiovascular surgeon on a TAVR heart team?

Low Confidence *Intermediate* *High Confidence*

7. To begin performing TAVR, how confident are you that there is sufficient evidence that a certain threshold of SAVR and TAVR procedural volumes must be required for the principle cardiovascular surgeon on a TAVR heart team?

- **We find no evidence supporting a specific volume threshold for principle cardiovascular surgeon is associated with the successful initiation of a TAVR program.**
- **The current training programs for TAVR in the U.S. are intense and rigorous. Requirements to be considered a possible TAVR center include the demonstration of procedural proficiency in (1) cardiac surgery (specifically aortic valve disease management and therapy), (2) interventional cariology with specific skills in vascular access and closure and PCI, (3) structural heart disease management including balloon aortic valvuloplasty, and (4) cardiac imaging with advanced capabilities in echocardiography and MSCT acquisition and interpretation. Moreover, new TAVR centers MUST have a functional Heart Valve Team with multi-disciplinary expertise and a designated heart valve clinic for case screening.**
- **The principle cardiovascular surgeon on the TAVR heart team must spend a significant portion of his/her time at the TAVR site hospital and take co-leadership responsibilities for case screening, involvement in case procedures, and post-operative management.**

Operator requirements to begin TAVR Programs

8

To **begin performing TAVR**, how confident are you that there is sufficient evidence that a certain threshold of structural heart disease procedural volumes must be required for the principle interventional cardiologist on a TAVR heart team?

Low Confidence *Intermediate* *High Confidence*

8. To begin performing TAVR, how confident are you that there is sufficient evidence that a certain threshold of structural heart disease procedural volumes must be required for the principle interventional cardiologist on a TAVR heart team?

- **We find no evidence supporting that a specific volume threshold of structural heart procedures for the principle interventional cardiologist is associated with the successful initiation of a TAVR program.**
- **The current training programs for TAVR in the U.S. are intense and rigorous. Requirements to be considered a possible TAVR center include the demonstration of procedural proficiency in (1) cardiac surgery (specifically aortic valve disease management and therapy), (2) interventional cariology with specific skills in vascular access and closure and PCI, (3) structural heart disease management including balloon aortic valvuloplasty, and (4) cardiac imaging with advanced capabilities in echocardiography and MSCT acquisition and interpretation. Moreover, new TAVR centers MUST have a functional Heart Valve Team with multi-disciplinary expertise and a designated heart valve clinic for case screening.**
- **The principle interventional cardiologist on the TAVR heart team must spend a significant portion of his/her time at the TAVR site hospital and take co-leadership responsibilities for case screening, involvement in case procedures, and post-operative management. As indicated above, the principle interventional cardiologist must be proficient with significant experience in vascular access and closure, PCI procedures, and structural heart disease procedures including balloon aortic valvuloplasty.**

Heart team requirements to maintain TAVR Programs

9

To **maintain proficiency**, how confident are you that there is sufficient evidence that a certain threshold of TAVR procedural volumes must be required for:

- The **principle cardiovascular surgeon** on a TAVR heart team?
- The **principle interventional cardiologist** on a TAVR heart team?
- The **combined experience** of the principle cardiovascular surgeon and interventional cardiologist on a TAVR heart team?

1 2 3 4 5

Low Confidence *Intermediate* *High Confidence*

9. To maintain proficiency, how confident are you that there is sufficient evidence that a certain threshold of TAVR procedural volumes must be required for:

a) The principle cardiovascular surgeon on a TAVR heart team?

b) The principle interventional cardiologist on a TAVR heart team?

c) The combined experience of the principle cardiovascular surgeon and interventional cardiologist on a TAVR heart team?

- **We find no evidence supporting a specific volume threshold for principle cardiovascular surgeon, interventional cardiologist and combined experience of principle cardiovascular surgeon and interventional cardiologist on a TAVR heart team that is associated with maintaining TAVR outcomes.**
- **Existing TAVR programs in the U.S. are under continuous scrutiny with multiple layers of oversight to achieve sufficient case volumes to maintain a high-quality heart team environment and TAVR clinical outcomes. Participation in the national TVT registry and site hospital quality assurance examinations are routinely required. Attributes to maintain an existing TAVR center include the demonstration of procedural proficiency in (1) cardiac surgery (specifically aortic valve disease management and therapy), (2) interventional cariology with specific skills in vascular access and closure and PCI, (3) structural heart disease management including balloon aortic valvuloplasty, and (4) cardiac imaging with advanced capabilities in echocardiography and MSCT acquisition and interpretation. Moreover, TAVR centers MUST continue to demonstrate the highest standards of a functional Heart Valve Team with multi-disciplinary expertise and a designated heart valve clinic for case screening.**

Additional discussion topics

10

Do hospital volume requirements create unintended barriers to TAVR based on any of the following:

- Geographic location (both rural and urban)
- Gender
- Ethnicity
- Race
- Socioeconomic status
- Provider preference (i.e. when a patient prefers to work with their long time/trusted physician whose hospital does not meet volume requirements instead of transferring to one that does with an unknown physician team)
- Hospital setting (community hospital vs. academic medical center/tertiary referral center)

Low Confidence *Intermediate* ***High Confidence***

10. Do hospital volume requirements create unintended barriers to TAVR based on any of the following:
- Geographic location (both rural and urban)
- Gender
- Ethnicity
- Race
- Socioeconomic status
- Provider preference
- Hospital setting

- **Increased TAVR access is associated with better care.**
- **Hospital volume requirements do create significant unintended barriers to TAVR.**
- **Rural residence, elderly (patients age 80+), females, minorities, lower socioeconomic status communities already struggle to access proper care in many instances. Further volume requirements may create additional barriers that negatively impact patient access to TAVR.**
- **Further volume requirements may disproportionately impact non-academic/community hospitals.**

Increased TAVR access associated with better care

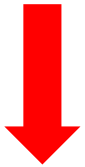
Impact from 370 TAVR centers in 2014 to 470 TAVR centers in 2016

8%

Higher **diagnosed** incidence rate

9%

Higher AVR **treatment** rate in 1 year



19%

Reduction in SSAS **deaths** in 1 year

Specific methods: Access over time analysis: SSAS patients in Optum diagnosed in 2014 and 2016 were followed for 1 year to evaluate outcomes. Treatment rate, untreated mortality, and TAVR rate were compared in each scenario. Source: Optum EHR

Hospital volume requirements create unintended barriers to TAVR for all of the following undertreated patients

Considerations	Unintended Barriers
Geographic Location	• 42 additional miles to travel for patients* • 25% increase in in-hospital mortality (some of the displaced patients would be sent to centers with worse outcomes)* • Centers receiving displaced patients will need a 62% increase in capacity*
Gender	• Compared to male patients, female patients benefit more from TAVR than SAVR • Increased TAVR access over time has improved care for female patients, further restricting access could mitigate or reverse progress
Ethnicity/Race	• Currently, only 6% of patients diagnosed with SSAS are minorities and only 4% of patients treated with AVR are minorities • Increased TAVR access over time has improved care for minority patients, further restricting access could mitigate or reverse progress
Socioeconomic	• Higher median income is associated with greater probability of receiving TAVR • 66% of centers below volume threshold are in states where over 15% of the population is below the poverty line**
Provider Preference	• Many patients prefer their local hospitals over traveling • Patients over 65 avoid traveling for care
Hospital Setting	• More stringent volume requirements will disproportionately impact non-academic/community hospitals • 16 sole community TAVR programs serve over 2 million patients over 65

See appendix slides for data and analytics. *On average, based on displaced patient volumes being allocated to nearest distance open TAVR center.
**Modeled impact with 50 TAVR/30 SAVR annual volume requirement scenario.

MEDCAC Questions	Confidence in the Evidence
1. Begin: SAVR volume requirements	★
2. Begin: PCI volumes requirements	★
3. Begin: Benefits outweigh harm of volume requirements	★
4. Maintain: SAVR volume requirements	★
5. Maintain: PCI volumes requirements	★
6. Maintain: Benefits outweigh harm of volume requirements	★
7. Begin: Operator, cardiovascular surgeon volume requirements	★
8. Begin: Operator, interventional cardiologist volume requirements	★
9. Maintain: Heart team volume requirements	★
10. Additional: Volume requirements create unintended barriers to TAVR	★★★★★

Low Confidence — High Confidence

Appendix

Optum: 160M+ EHR & claims database
Dataset leverages patient health information from across US

Characterizing the data

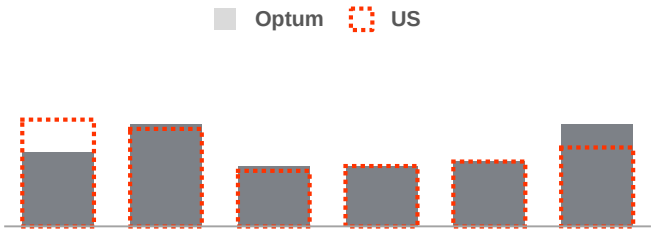
80M
Cumulative patients

10M
Patients with linked health plan data

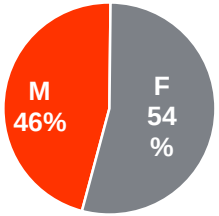
27M
Patients with >5yrs of HER activity

39 months
Average months of clinical observations

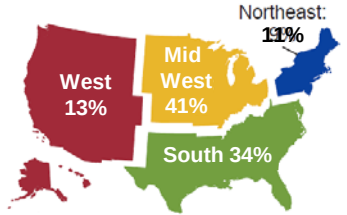
Age



Gender



US Region



	0-17	18-34	35-44	45-54	55-64	65+	M	F	West	Mid-west	South	North-east
Optum #	13M	17M	10M	11M	11M	18M	37M	43M	30M	8.4M	25M	9.8M
Optum %	16%	22%	13%	13%	14%	22%	46%	54%	13%	41%	34%	11%
US Est	23%	21%	12%	14%	14%	17%	47%	53%	24%	21%	37%	18%

Source: Optum EHR statistics, Optum Research Data Assets (2014)

Methodology for adjusting in-hospital mortality

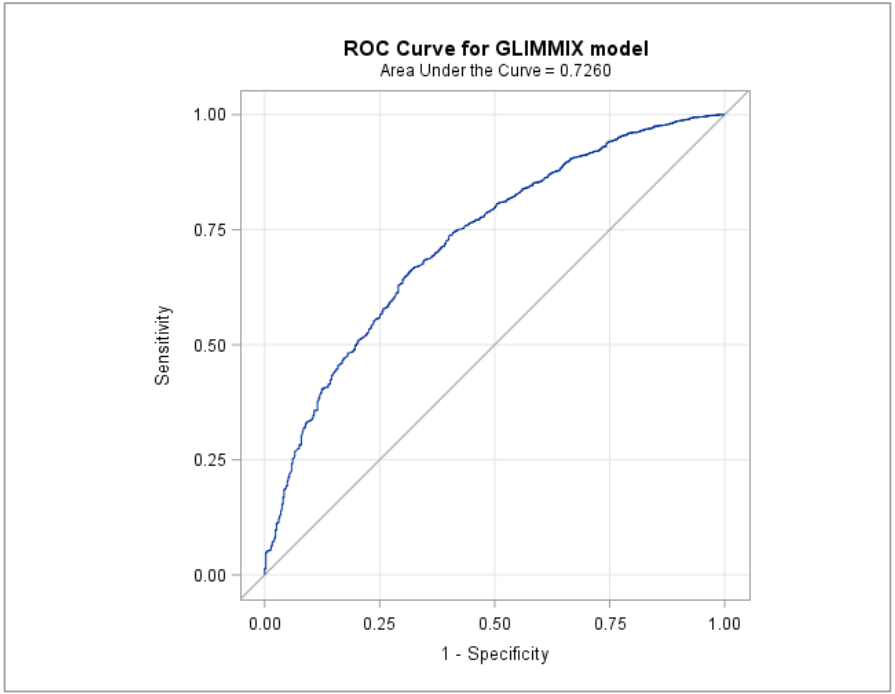
- Identified inpatient primary and secondary claims and relevant cardiac procedures on the index admission used to develop a risk adjusted model (RAM) for inpatient mortality
- Categorized ICD9/10 codes in HCC categories
- Model covariates were selected via lasso with forced demographic variables in order to incorporate as many predictors as possible to improve model fit, prediction and power
- Fit the hierarchical models to the data for each condition separately using in-hospital mortality associated with the index procedure (i.e. SAVR or TAVR) as the outcome
- Utilized standardization (ratio of observed/expected *standard; the standard rate was from all hospitals in this population, expected rate is calculated from the model) to adjust mortality[1]
  - Output is akin to showing if this ‘hospital taken on the risk profile of an “average” hospital, what would mortality look like ’
  - Leverages semi-Bayesein methods to adjust for small volumes with clustered model
- Separate models were run for SAVR, TAVR, and PCI
- Pressure tested results with marginal GEE model to further control for small centers[2]

1 Drye 2013, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3319769/
2 Truong 2017, https://link.springer.com/article/10.1186/s13063-017-2248-1

Backup: Covariates and AUC for risk-adjustment model

Variables in the final model

- Gender
- Race
- Region
- Age (categorical)
- CCI (categorical)
- CABG
- MVR/r
- TVR/r
- MAZE
- PCI
- Sepsis
- Metatstatic cancer
- Protein calorie malnutrition
- Liver disease
- Immunity disorders
- Drug/alcohol dependence
- MS
- CHF
- Heart arrhythmias
- Vascular disease
- COPD
- Chronic lung
- Renal disease
- Head injury
- Facility (cluster)



- **Geographic & wait-time barriers**
- Disparity in elderly
- Disparity in women
- Disparity in race
- Disparity in income
- Disparity in community vs. academic

Volume thresholds with multiple negative impacts on patients

If patients displaced under the 50 TAVR/30 SAVR volumes scenario are moved to the next nearest TAVR center

25% increase 30 day in-hospital mortality: Some of the displaced patients would be sent to centers with worse outcomes

42 additional miles to travel[1]
Patients, on average, will have increased distance to care with some even having to go to another state

Average 62% increase in capacity required[1]
Centers receiving displaced patients will have to significantly increase volumes and resources

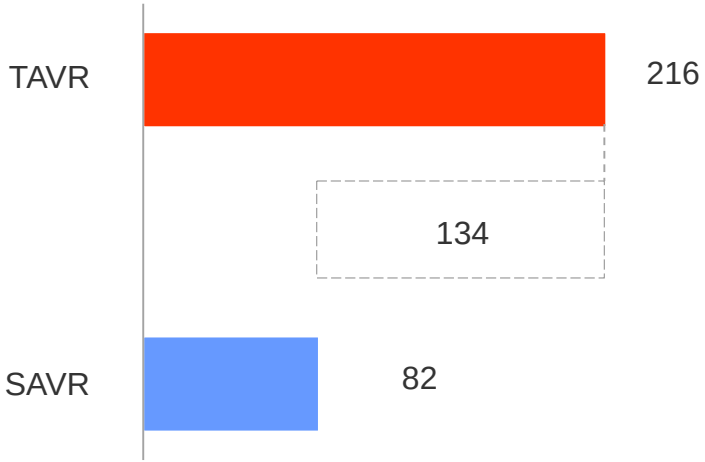
Volume based approach reduces overall system quality while imposing additional patient and center burdens

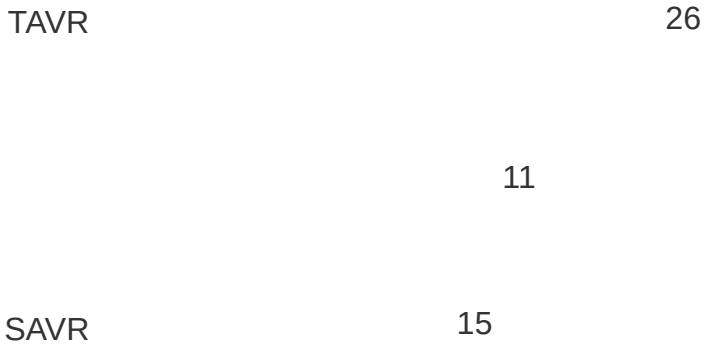
1. On average, based on displaced patient volumes being allocated to nearest distance open TAVR center.

Data Source: 2016 100% SAF Medicare. TAVR volumes based on Medicare Fee-For-Service and adjusted Medicare Advantage and private pay shares.

Within the current landscape, TAVR patients face substantially greater burden between diagnosis and treatment

2016: Days between AS diagnosis & treatment for SAVR vs. TAVR

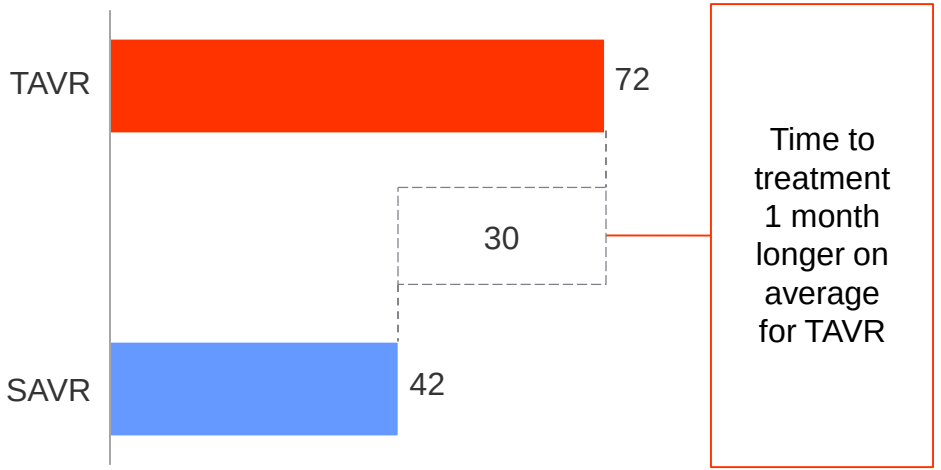




Source: : FY 2016 MedPAR - 2016 IQVIA Patient Claims Analysis.

Additional center restrictions could impede timely access to care

2016: Days between SSAS diagnosis & treatment for SAVR vs TAVR



Aortic Stenosis Patients Can't Wait

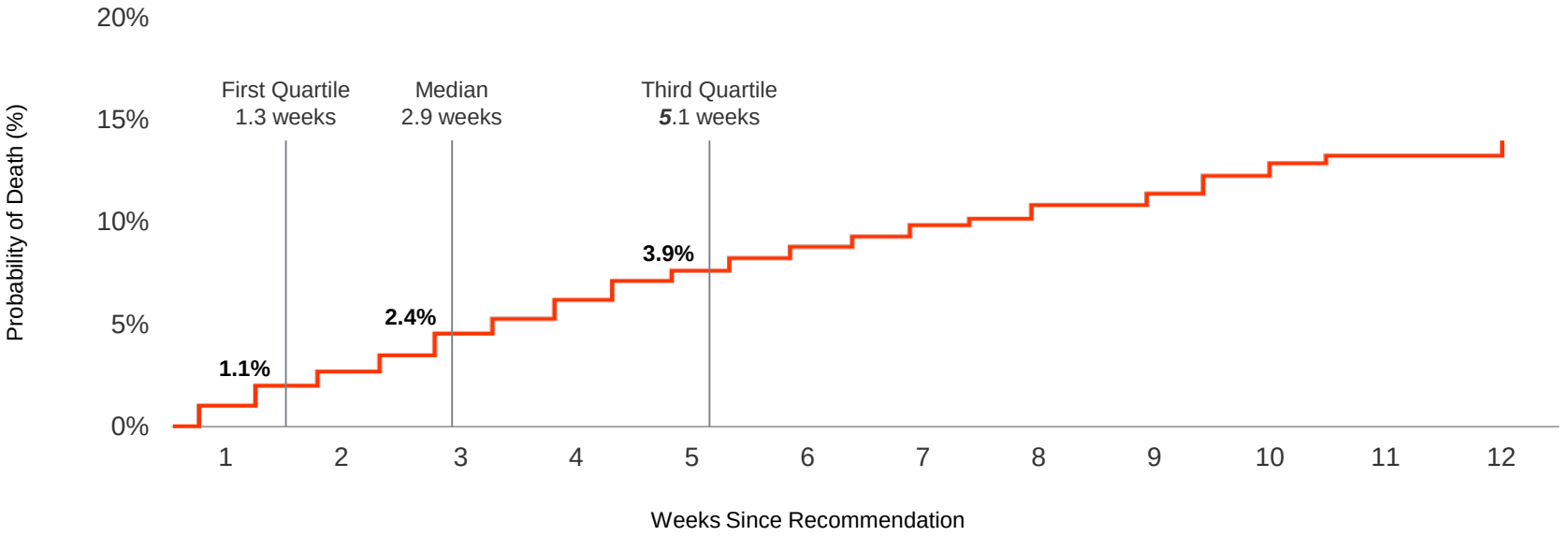
3.7%
Mortality while waiting for valve replacement at 1 month*

11.6%
Mortality while waiting for valve replacement at 6 months*

Source: 2016 Optum data, BCG EHR analytics. *Malaisrie et al. Mortality while waiting for Aortic Valve Replacement. Ann Thorac Surg 2014,98:1564-71

The risk of mortality increases with every week a patient has to wait for TAVR treatment

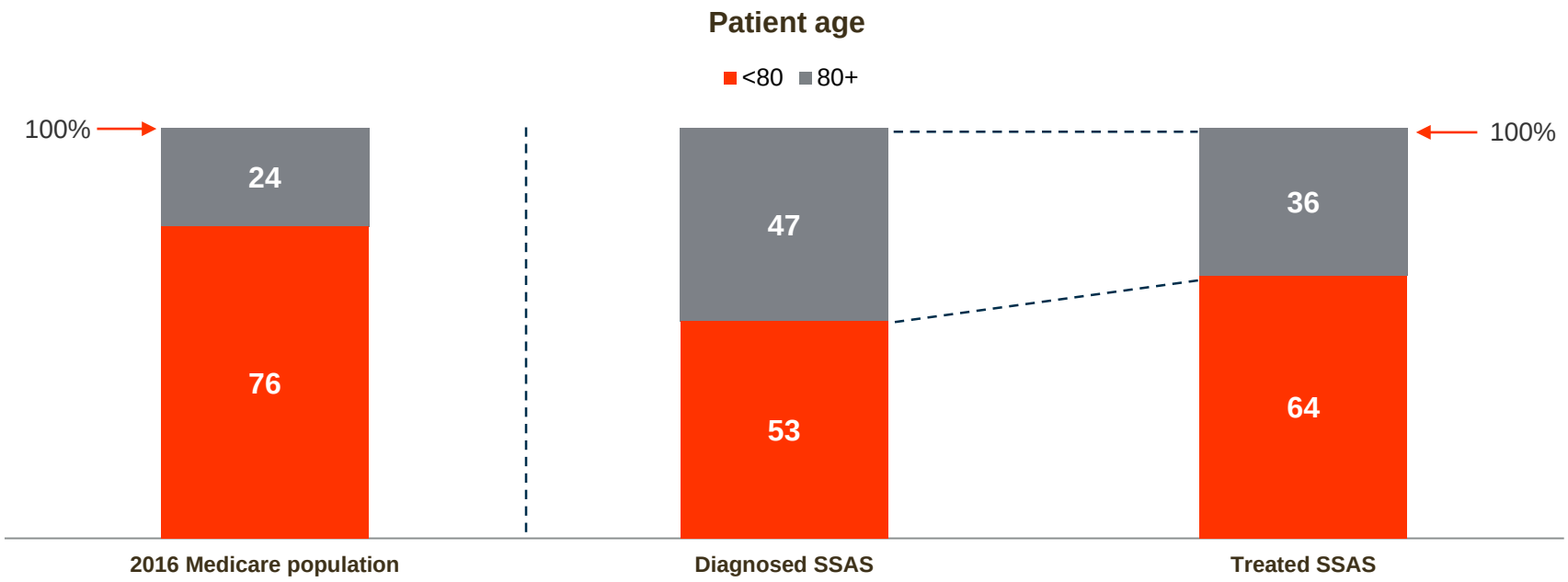
First 12 Weeks Since Recommendation: Cumulative Probability of Death without Intervention



Malaisrie.SC. Mortality Awaiting Aortic Valve Replacement. STS 2014;

- Geographic & wait-time barriers
- **Disparity in elderly**
- Disparity in women
- Disparity in race
- Disparity in income
- Disparity in community vs. academic

Medicare patients aged 80+ currently are disproportionately undertreated



Source: Medicare breakdown, Kaiser Family Foundation. Diagnosis and treatment based on Optum EHR 2016.

Increased TAVR access has improved care for the elderly

Key metric	TAVR% (treated within 1 year)	AVR% (treated within 1 year)	Mortality% (untreated and died within 1 year)
% change in key outcomes **from 2014 to 2016**	91%	23%	-17%
% change in key outcomes comparing **fast vs. slow[1] systems in 2016**	143%	65%	-48%

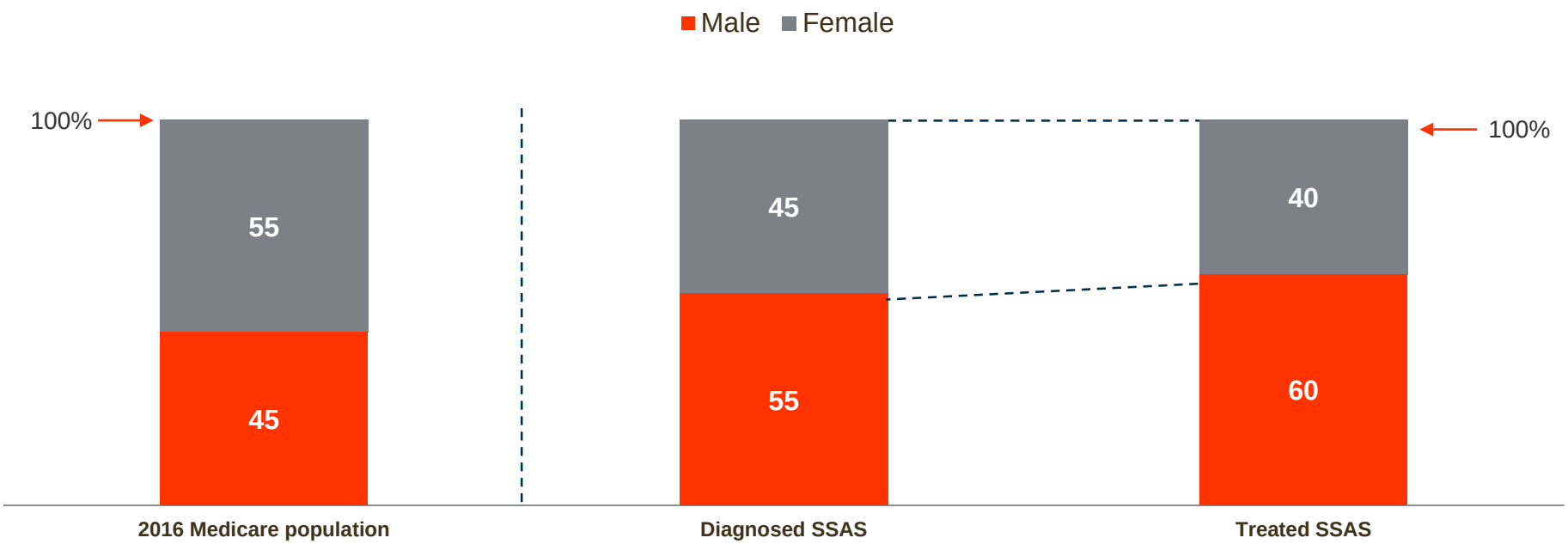
Access over time: Outcomes for elderly patients has **improved** with increased TAVR access

Speed to TAVR: Faster systems with **significant decrease in untreated mortality** in elderly patients with SSAS

Fast system <90 days to TAVR, slow system >90 days to TAVR. Source: Optum EHR. Specific methods: Access over time analysis: SSAS patients in Optum diagnosed in 2014 and 2016 were followed for 1 year to evaluate outcomes. Treatment rate, untreated mortality, and TAVR rate were compared in each scenario. Speed to TAVR analysis: SSAS patients diagnosed from Oct 2015-March 2016 were stratified by healthcare system. Systems with less than 90 days between diagnosis and TAVR were categorized as 'fast'; those with over 90 days to TAVR from diagnosis were categorized as 'slow'. Patients were followed for 1 year to evaluate outcomes. Treatment rate, untreated mortality, and TAVR rate were compared in each scenario.

- Geographic & wait-time barriers
- Disparity in elderly
- **Disparity in women**
- Disparity in race
- Disparity in income
- Disparity in community vs. academic

Female patients are currently disproportionately undertreated



Source: Medicare breakdown, Kaiser Family Foundation. Diagnosis and treatment based on Optum EHR 2016.

Increased TAVR access has improved care for female patients

Key metric	TAVR% (treated within 1 year)	AVR% (treated within 1 year)	Mortality% (untreated and died within 1 year)
% change in key outcomes from 2014 to 2016	67%	15%	-17%
% change in key outcomes comparing fast vs. slow[1] systems in 2016	117%	39%	-41%

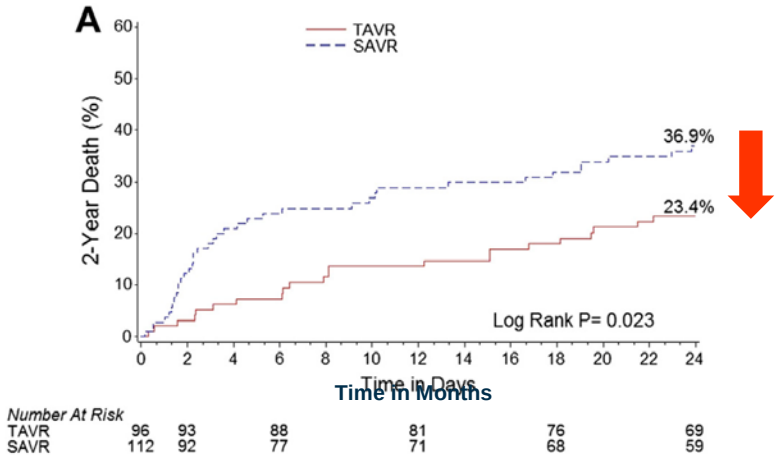
Access over time: Outcomes for women with SSAS has **improved** with increased TAVR access

Speed to TAVR: Faster systems **with significant decrease in untreated mortality** in female patients with SSAS

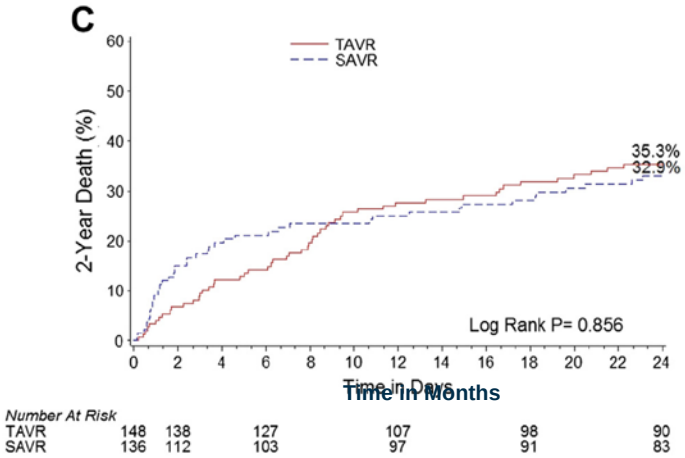
Fast system <90 days to TAVR, slow system >90 days to TAVR. Source: Optum EHR. Specific methods: Access over time analysis: SSAS patients in Optum diagnosed in 2014 and 2016 were followed for 1 year to evaluate outcomes. Treatment rate, untreated mortality, and TAVR rate were compared in each scenario. Speed to TAVR analysis: SSAS patients diagnosed from Oct 2015-March 2016 were stratified by healthcare system. Systems with less than 90 days between diagnosis and TAVR were categorized as 'fast'; those with over 90 days to TAVR from diagnosis were categorized as 'slow'. Patients were followed for 1 year to evaluate outcomes. Treatment rate, untreated mortality, and TAVR rate were compared in each scenario.

Reducing access to TAVR has a disproportionate negative impact on women

Female



Male

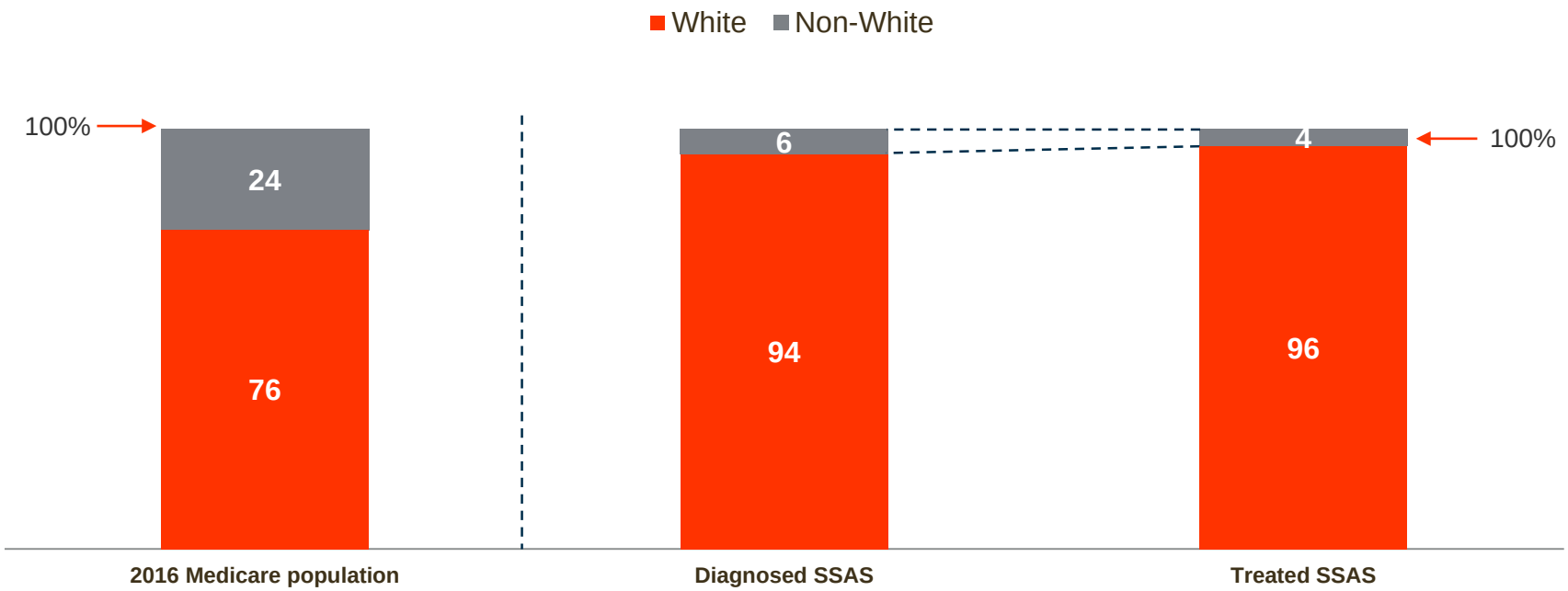


Compared to male patients, female patients benefit more from TAVR than SAVR, even with older generation devices.

Williams M. et al. JACC 2014;63:1522-8

- Geographic & wait-time barriers
- Disparity in elderly
- Disparity in women
- **Disparity in race**
- Disparity in income
- Disparity in community vs. academic

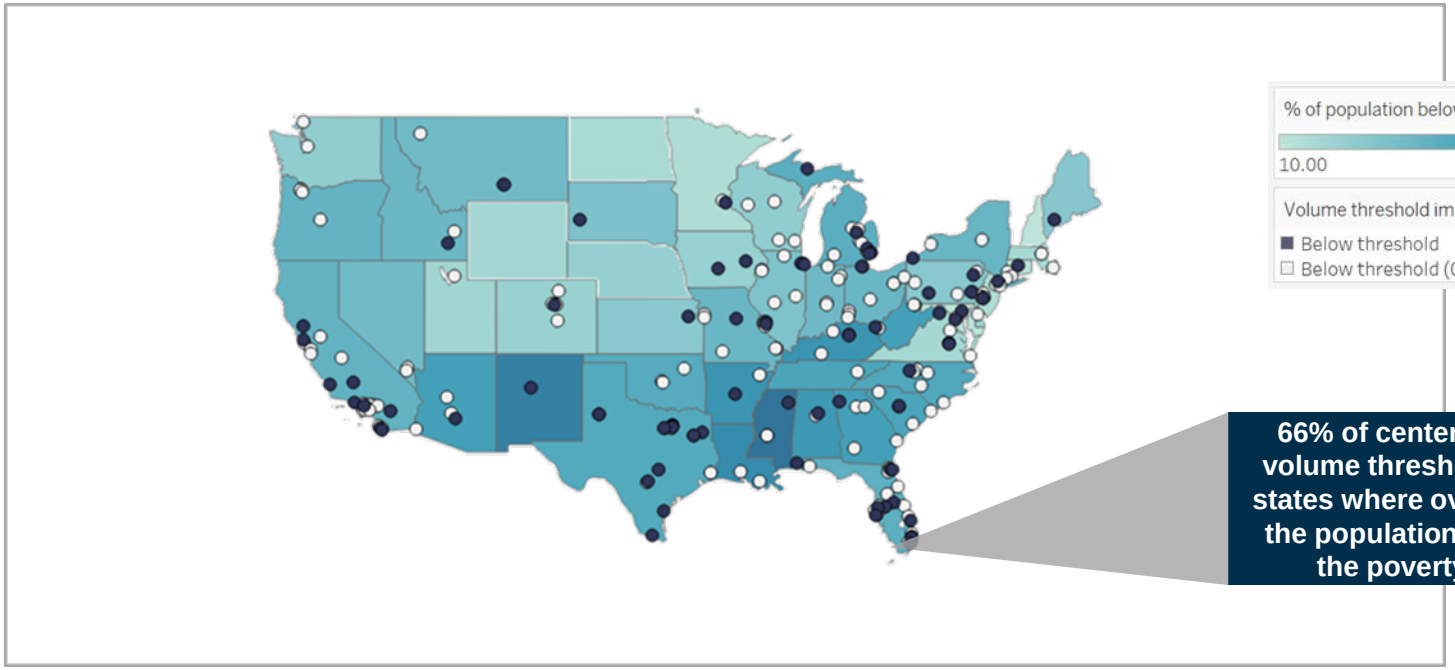
Minorities are significantly underdiagnosed and undertreated



Source: Medicare breakdown, Kaiser Family Foundation. Diagnosis and treatment based on Optum EHR 2016.

- Geographic & wait-time barriers
- Disparity in elderly
- Disparity in women
- Disparity in race
- **Disparity in income**
- Disparity in community vs. academic

More stringent volume requirements disproportionately impacts states with over 15% of the population below the poverty line

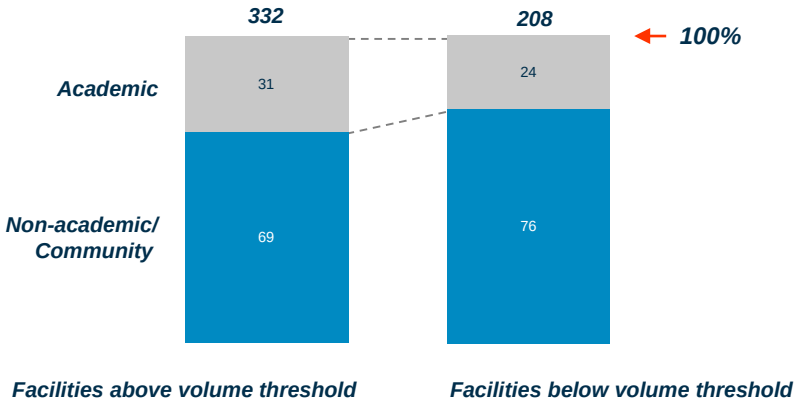


Source: 2016 100% Inpatient SAF Medicare; AVR volumes based on Medicare Fee-For-Service and adjusted Medicare Advantage and private pay shares.
American Community Survey 2016 5-year data used for % of population below poverty line. Modeled impact with 50 TAVR/30 SAVR annual volume requirement scenario.

- Geographic & wait-time barriers
- Disparity in elderly
- Disparity in women
- Disparity in race
- Disparity in income
- **Disparity in community vs. academic**

More stringent volume requirements disproportionately impacts non-academic/community hospitals

With a 50 TAVR/30 SAVR annual volume requirement scenario

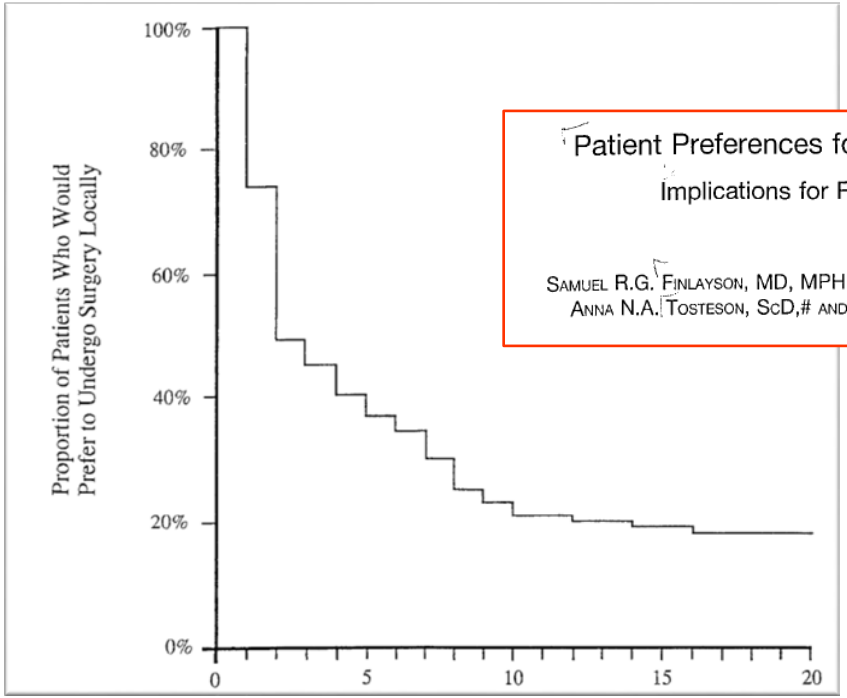


1. Academic centers are hospitals that include a major teaching unit a of medical school and/or graduate level medical education, Non-academic are hospitals not meeting above criteria.
2. Sole Community Hospitals are small rural hospitals for which 'by reason of factors such as isolated location, weather conditions, travel conditions, or absence of other hospitals, are the sole source of inpatient hospital services reasonably available in a geographic area to Medicare beneficiaries. Data Source: FY 2017 MedPAR proposed rule file, count of all (FFS + MA) Medicare TAVR and SAVR,
and crude estimate of all-payer TAVR and SAVR based on national average market share from 2015 HCUP. Modeled impact with 50 TAVR/30 SAVR annual volume requirement scenario.

Patients prefer local hospitals vs traveling

"Many patients prefer to undergo surgery locally even when travel to a regional center would result in lower operative mortality risk."

If local operative mortality risk were 6% but regional risk were 3% 45% of patients would still prefer their local hospital.



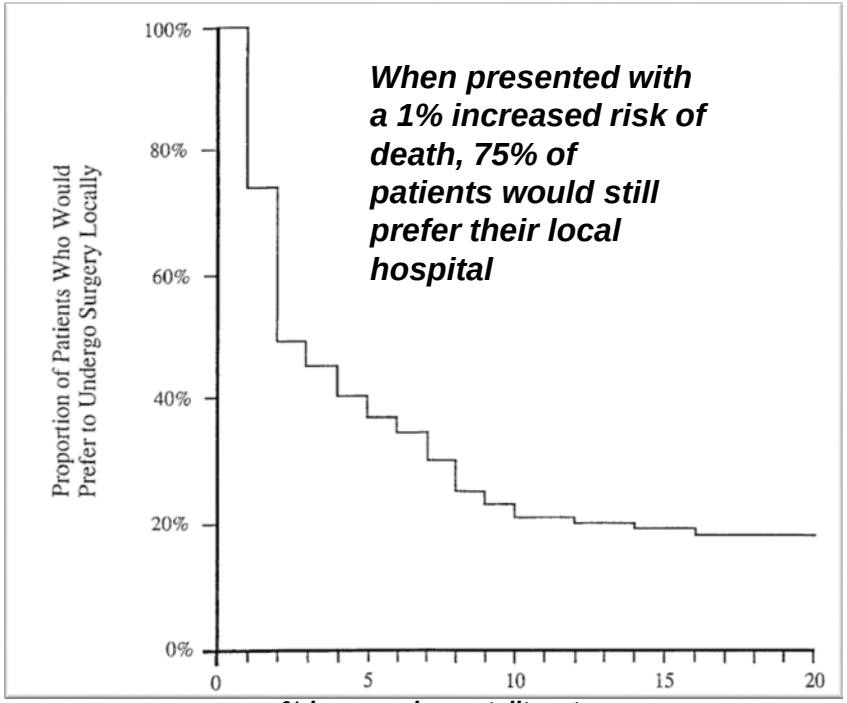
Patient Preferences for Location of Care

Implications for Regionalization

SAMUEL R.G. FINLAYSON, MD, MPH,*† JOHN D. BIRKMEYER, MD,*‡#
ANNA N.A. TOSTESON, ScD,# AND ROBERT F. NEASE, JR, PhD¶

Finlayson, S. R., et al. (1999)Patient preferences for location of care: implications for regionalization." Med Care 37(2): 204-209.

Patients prefer local hospitals to travelling for care



20.3% of their decision to seek surgical care was determined by travel time

Travel time was more than 2x as important than following a referral or hospital affiliation

Source: The Advisory Board

SOURCE: *Finlayson, S. R., et al. (1999)Patient preferences for location care: implications for regionalization." Med Care 37(2): 204-209.

Socioeconomic and racial disparities would widen with volume requirements and reduction in TAVR centers

Every $10,000 increase in income, the odds of receiving TAVR increased by 10% ***(p = 0.05)***

Non-blacks were significantly more likely to receive TAVR than blacks
(odds ratio [OR] 2.812, confidence interval [CI] 1.007-7.853; p = 0.048)

After echo, blacks were more likely to decline AVR, be lost to follow-up, and not be referred to cardiology
(OR 4.41, CI 1.43-13.64; p = 0.010)

Sleder A. Socioeconomic and Racial Disparities: a Case-Control Study of Patients Receiving Transcatheter Aortic Valve Replacement for Severe Aortic Stenosis. Journal for Racial Health Disparities. 2017