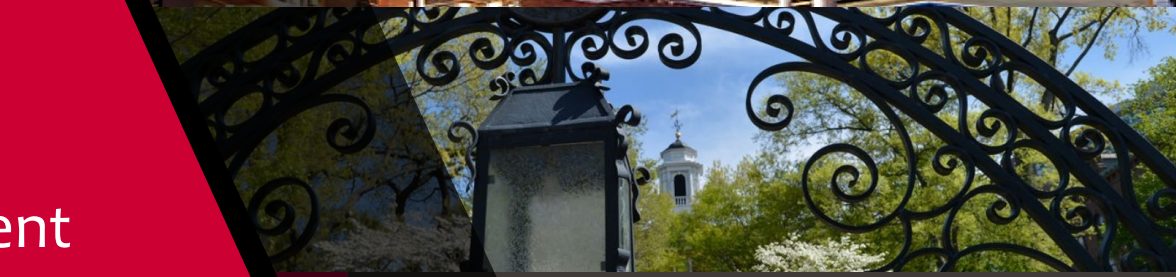
Innovation in the Treatment of Valve Disease: Does Any Disruption Remain?

Mark Russo, MD, MS
Chief, Cardiac Surgery
Director, Structural Heart Disease

Rutgers-Robert Wood Johnson Medical School



ROBERT WOOD JOHN
UNIVERSITY HOSPITAL
RUTGERS
THE STATE UNIVERSITY OF NEW JERSEY

CME Objectives

1. Outline the changing treatment paradigm for aortic stenosis

2. Understand the limitations of traditional economic analysis (e.g., cost utility analysis, cost effectiveness analysis, and cost benefit analysis)

3. Identify three sources of health-related value
   (a) meeting unmet need,
   (b) improvement of over the existing standard of care, and
   (c) raising treatment uptake.

This Project

JOURNAL OF MEDICAL ECONOMICS
2022, VOL. 25, NO. 1, 1051–1060
https://doi.org/10.1080/13696998.2022.2112442
Article 0125-FT.R2/2112442

Taylor & Francis
Taylor & Francis Group

ORIGINAL RESEARCH

OPEN ACCESS Check for updates

Cost-utility and cost-benefit analysis of TAVR availability in the US severe symptomatic aortic stenosis patient population

J. P. Sevilla[a], Jessica M. Klusty[a], Younghwan Song[b], Mark J. Russo[c], Christin A. Thompson[d], Xiayu Jiao[d], Seth J. Clancy[d] and David E. Bloom[e]

[a]Life Sciences Group, Data for Decisions, LLC, Waltham, MA, USA; [b]Department of Economics, Union College, Schenectady, NY, USA; [c]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, USA; [d]Edwards Lifesciences, Irvine, CA, USA; [e]Department of Global Health and Population, Harvard T. H. Chan School of Public Health, Boston, MA, USA

ABSTRACT

Aims: We evaluated the availability of transcatheter aortic valve replacement (TAVR) to determine its value across all severe symptomatic aortic stenosis (SSAS) patients, especially those untreated because of concerns regarding invasive surgical AVR (SAVR) and its impact on active aging.
Methods: We performed payer perspective cost-utility analysis (CUA) and societal perspective cost-benefit analysis (CBA). The CBA's benefit measure is active time: salaried labor, unpaid work, and active leisure. The study population is a cohort of US elderly SSAS patients. We compared a "TAVR available" scenario in which SSAS patients distribute themselves across TAVR, SAVR, and medical management (MM); and a "TAVR not available" scenario with only SAVR and MM. We structured each scenario with a decision-tree model of SSAS patient treatment allocation. We measured the association between health and active time in the US Health and Retirement Study and used this association to impute active time to SSAS patients given their health.
Results: The incremental cost-effectiveness ratio (ICER) and rate of return (RoR) of TAVR availability were $8,533 and 395%, respectively. CUA net monetary benefits (NMB) were $212,199 per patient and $43.4 billion population-wide. CBA NMB were $50,530 per patient and $10.3 billion population-wide.
Limitations: Among study limitations were scarcity of evidence regarding key parameters and the lack of long-term survival, health utility, and treatment cost data. Our analysis did not account for TAVR durability, retreatments, and valve-in-valve treatments.
Conclusion: Across risk-, age-, and treatment-eligibility groups, TAVR is the economically optimal treatment choice. It represents strong value-for-money per patient and population-wide. The vast majority of TAVR value involves raising treatment uptake among the untreated.

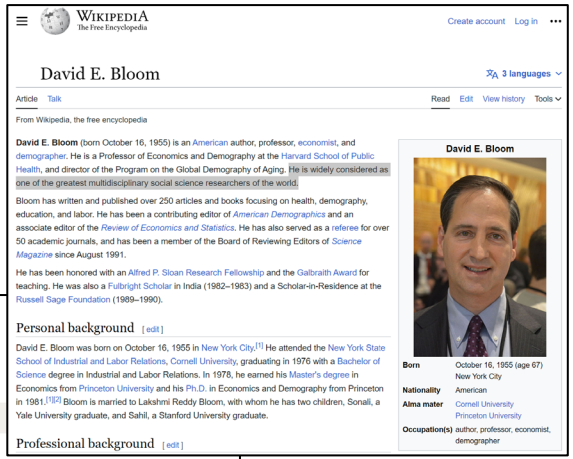
ARTICLE HISTORY
Received 2 June 2022
Revised 5 August 2022
Accepted 9 August 2022

KEYWORDS
Active aging; cost-benefit analysis; cost-utility analysis; severe symptomatic aortic stenosis; time use; transcathether aortic valve replacement

JEL CLASSIFICATION CODES
J14; I1; J; I10; I1; I; D61; D6; D

PLAIN LANGUAGE SUMMARY

Aortic stenosis (AS) is a common and lethal heart disease. Surgical treatment has long been available, but its invasiveness limits uptake. More recently, transcatheter aortic valve replacement (TAVR) has emerged as a treatment alternative. Its minimal invasiveness has significantly increased treatment rates, but economic evaluations omit this benefit, risking undervaluation. We evaluated TAVR in elderly US severe symptomatic AS patients, using payer perspective cost-utility analysis (CUA) and societal perspective cost-benefit analysis (CBA). Both CUA and CBA incorporated TAVR's impact on treatment rates. Given patient preferences for treatment options promoting active aging, our CBA used the value of active time as a benefit measure. We found that CUA/CBA net monetary benefits are $212,199/$50,530 per patient. Across risk-, age-, and treatment-eligibility groups, TAVR is the economically optimal treatment choice over surgery and medical management. It represents strong value-for-money per patient and population-wide. Increased treatment uptake accounts for the vast share of TAVR's value.



Wikipedia
The Free Encyclopedia

Create account Log in

David E. Bloom

3 languages

Article Talk Read Edit View history Tools

From Wikipedia, the free encyclopedia

David E. Bloom (born October 16, 1955) is an American author, professor, economist, and demographer. He is a Professor of Economics and Demography at the Harvard School of Public Health, and director of the Program on the Global Demography of Aging. He is widely considered as one of the greatest multidisciplinary social science researchers of the world.

Bloom has written and published over 250 articles and books focusing on health, demography, education, and labor. He has been a contributing editor of *American Demographics* and an associate editor of the *Review of Economics and Statistics*. He has also served as a referee for over 50 academic journals, and has been a member of the Board of Reviewing Editors of *Science Magazine* since August 1991.

He has been honored with an Alfred P. Sloan Research Fellowship and the Galbraith Award for teaching. He was also a Fulbright Scholar in India (1982–1983) and a Scholar-in-Residence at the Russell Sage Foundation (1989–1990).

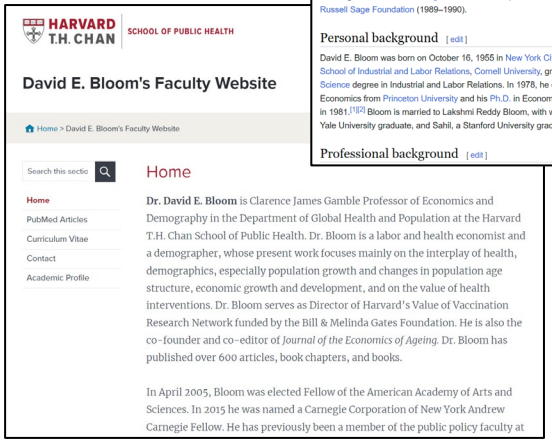
Personal background [edit]

David E. Bloom was born on October 16, 1955 in New York City.[1] He attended the New York State School of Industrial and Labor Relations, Cornell University, graduating in 1976 with a Bachelor of Science degree in Industrial and Labor Relations. In 1978, he earned his Master's degree in Economics from Princeton University and his Ph.D. in Economics and Demography from Princeton in 1981.[1][2] Bloom is married to Lakshmi Reddy Bloom, with whom he has two children, Sonali, a Yale University graduate, and Sahil, a Stanford University graduate.

Professional background [edit]

David E. Bloom

Born	October 16, 1955 (age 67) New York City
Nationality	American
Alma mater	Cornell University Princeton University
Occupation(s)	author, professor, economist, demographer



HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH

David E. Bloom's Faculty Website

Home > David E. Bloom's Faculty Website

Search this sectio

Home
PubMed Articles
Curriculum Vitae
Contact
Academic Profile

Home

Dr. David E. Bloom is Clarence James Gamble Professor of Economics and Demography in the Department of Global Health and Population at the Harvard T.H. Chan School of Public Health. Dr. Bloom is a labor and health economist and a demographer, whose present work focuses mainly on the interplay of health, demographics, especially population growth and changes in population age structure, economic growth and development, and on the value of health interventions. Dr. Bloom serves as Director of Harvard's Value of Vaccination Research Network funded by the Bill & Melinda Gates Foundation. He is also the co-founder and co-editor of *Journal of the Economics of Ageing*. Dr. Bloom has published over 600 articles, book chapters, and books.

In April 2005, Bloom was elected Fellow of the American Academy of Arts and Sciences. In 2015 he was named a Carnegie Corporation of New York Andrew Carnegie Fellow. He has previously been a member of the public policy faculty at

Sevilla et al. Cost-utility and cost-benefit analysis of TAVR availability in the US severe symptomatic aortic stenosis patient population. Journal of Medical Economics. 2022; 25:1, 1051-1060

Measuring Health Related Impact

The Problem

Conventional approaches to economically evaluating health technologies are **limited** and **often insensitive** to the **full contribution of new technologies;** they may underestimate value by capturing:

(1) only some but not all health-related impacts and
(2) little of the non-health impacts.

These limitations may have important policy implications by failing to ensure that adequate priority, resources, and attention being devoted to such technologies and disease states.

The Problem

Cost-effectiveness analysis is a way to examine both the costs and health outcomes of one or more interventions. It compares an intervention to another intervention (or the status quo) by estimating how much it costs to gain a unit of a health outcome, like a life year gained or a death prevented.

Components of Health-Related Impact

Conventional Approaches

YES

NO

a) **Meeting Unmet Need**
   - providing a treatment option for a condition, population, or indication that previously had no treatment options
     > CEA analysis versus no intervention

b) **Improvement of over the Existing Standard of Care**
   - being cost-effective relative to the existing standard of care (SoC) treatment for a condition; this involves the new technology producing sufficiently large health gains relative to the SoC to justify its higher cost
     > CEA analysis versus SoC

c) **Increasing Treatment Uptake**
   - Patients may reject the SoC despite being clinically indicated for it, thereby going untreated despite the presence of, and eligibility for, existing treatment options—because it has attributes that patients find unattractive:
     - such as long recovery,
     - perceived risks, and/or
     - significant invasiveness
   - Overcoming these negative attributes that lead such patients to finally accept treatment

Stakeholders

Payers

Patients
Cost-effectiveness

Society

Providers

Methods and Perspectives

- Cost Effectiveness Analysis
  Impact on a Patient

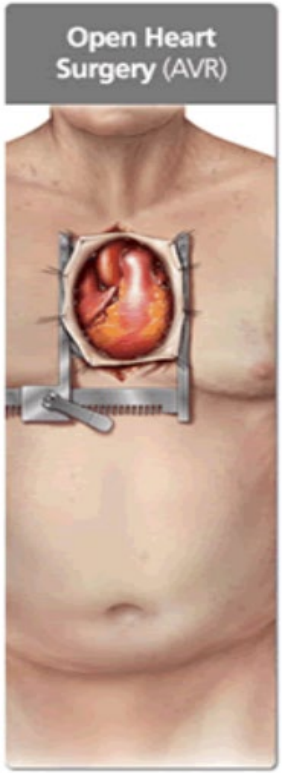
  Cost Utility

  Cost Benefit

Measuring
Non-Health Related Impact

Changing Treatment Paradigm for Aortic Stenosis

Aortic Valve Replacement: Two Options

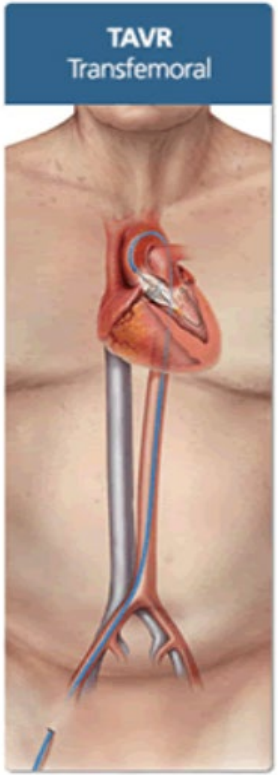


Surgical AVR (SAVR)

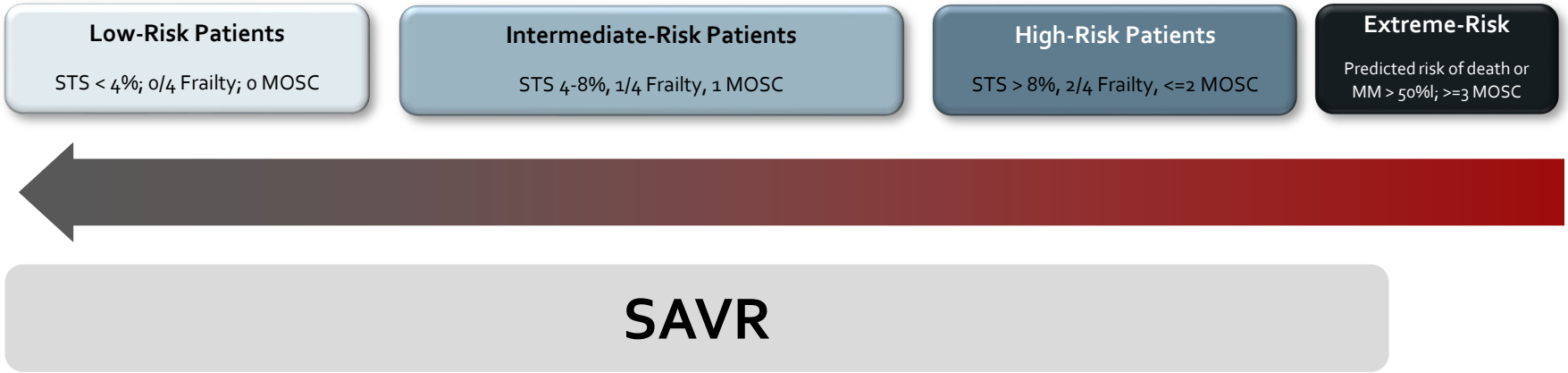
- Make an incision in the chest
- Use the heart-lung machine
- Stop the heart
- Cut the old valve and sow in a new valve
- 2 hour procedure
- Extubated in the ICU
- Discharge in 3-8 days
- Primary Advantages:
  - Reproducible
  - Known Long Term Durable

Transcatheter AVR (TAVR)

- No incision/just a puncture
- Don't stop the heart
- Don't cut out the native valve
- New valve in the inside the native valve
- 30 mins procedure
- Awake
- 80% d/ced on POD1
  - Sometimes…the same day
- Primary Advantages:
  - Expanded indications
  - Fewer Complication in Short Term
  - Rapid Recovery

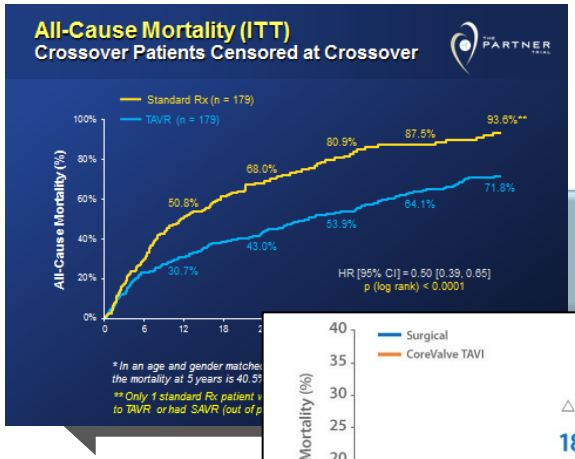


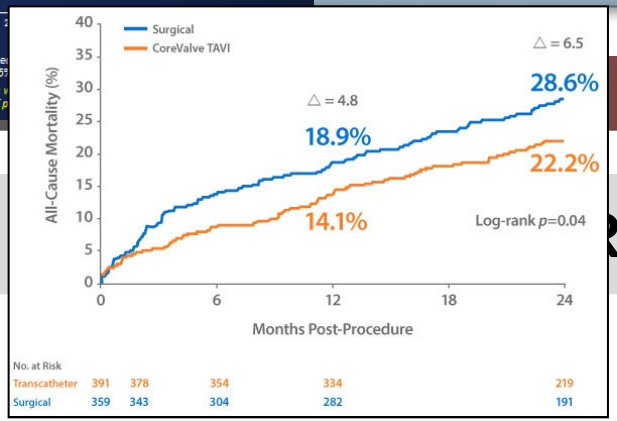
Disruption in the Treatment of Aortic Stenosis – 2010



Nishimura RA. 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 Practice Guidelines. J Thorac Cardiovasc Surg. 2014 Jul;148(1):e1-e132.

Disruption in the Treatment of Aortic Stenosis – 2012





Intermediate-Risk Patients

STS 4-8%, 1/4 Frailty, 1 MOSC

High-Risk Patients

STS > 8%, 2/4 Frailty, <=2 MOSC

Extreme-Risk

Predicted risk of death or MM > 50%l; >=3 MOSC

Phase 1

TAVR

Nishimura RA. 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 Practice Guidelines. J Thorac Cardiovasc Surg. 2014 Jul;148(1):e1-e132.

Moving Up Stream - Intermediate Risk

SAPIEN 3 Transcatheter Aortic Valve Replacement Compared with Surgery in Intermediate-Risk Patients: A Propensity Score Analysis

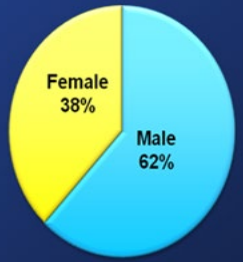
Vinod H. Thourani, MD
on behalf of The PARTNER Trial Investigators

ACC 2016 | Chicago | April 3, 2016

THE PARTNER II TRIAL

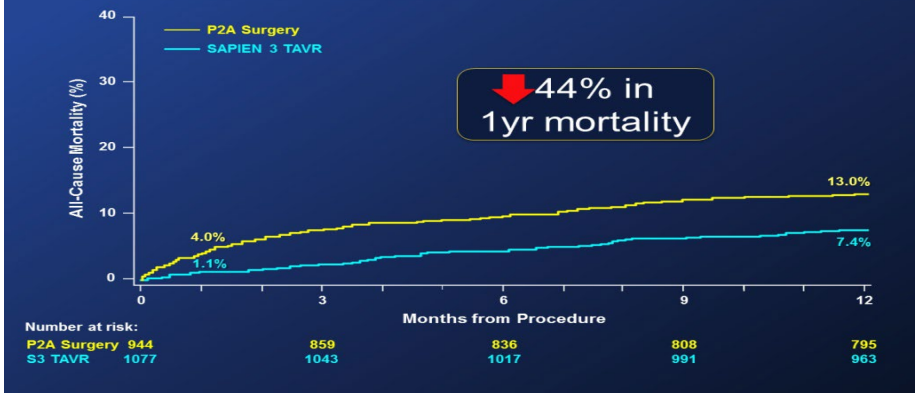
Average STS = **5.3%** (Median 5.2%)

Average Age = **81.9yrs**

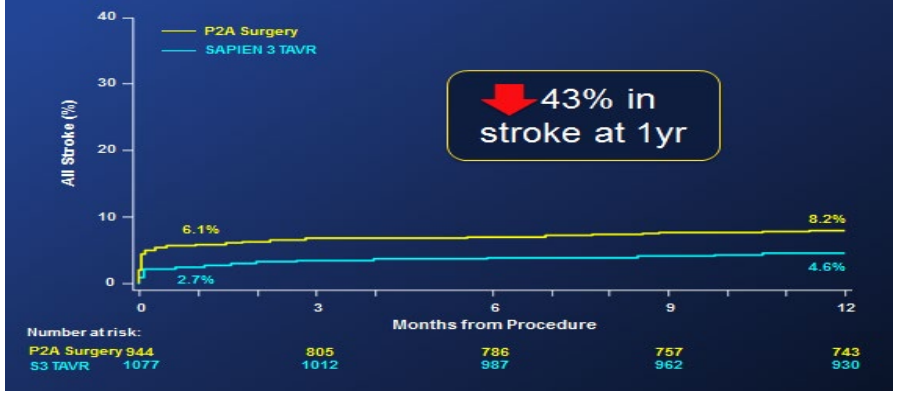


Characteristic (%)	S3i (n=1076)
NYHA Class III or IV	72.6
Previous CABG	28.0
Previous CVA	8.9
Peripheral Vascular Disease	28.3
Diabetes	34.1
COPD - O_2 Dependent	5.0
CKD - Creat. ≥ 2mg/dL	7.5
Atrial Fibrillation	36.0
Permanent Pacemaker	13.2
Frailty	8.6

Unadjusted Time-to-Event Analysis
All-Cause Mortality (AT)



Unadjusted Time-to-Event Analysis
All Stroke (AT)



Moving Up Stream - Low Risk

Mean STS:

1.9%

Mean Age:

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Repl
Balloon-Expandable Valve in Lo

M.J. Mack, M.B. Leon, V.H. Thourani, R. Makkar, S.R. Kapadia, S.C. Malaisrie, D.J. Cohen, P. Pibaro P. Blanke, M.R. Williams, J.M. McCabe, D.L. Brown, W.Y. Szeto, P. Genereux, A. Pershad, S.J. Pocock and C.R. Smith, for the PARTNER 3 Inv

Among ... risk, th ... rehosp ... than w ...
- Cor ...
- Dea ...

TAVR

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with ... Patients

v, M.D., M.D., O., D., M.D., t, M.D., D., on, M.D., M.D., lin, Ph.D., igators*

The New York Times

Tens of Thousands of Heart Patients May Not Need Open-Heart Surgery

Replacement of the aortic valve with a minimally invasive procedure called TAVR proved effective in younger, healthier patients.

THE PARTNER 3 TRIAL

Baseline Pa...

% or mean ± SD

Demographics & Vascular Disease	TAVR (N=496)	Sur... (N=...			
Age (years)	73.3 ± 5.8	73.6			
Male	67.5%	71.1%	COPD (any)	5.1%	6.2%
BMI – kg/m²	30.7 ± 5.5	30.3 ± 5.1	Pulmonary Hypertension	4.6%	5.3%
STS Score	1.9 ± 0.7	1.9 ± 0.6	Creatinine > 2mg/dL	0.2%	0.2%
NYHA Class III or IV*	31.3%	23.8%	Frailty (overall; > 2/4+)	0	0
Coronary Disease	27.7%	28.0%	Atrial Fibrillation (h/o)	15.7%	18.8%
Prior CABG	3.0%	1.8%	Permanent Pacemaker	2.4%	2.9%
Prior CVA	3.4%	5.1%	Left Bundle Branch Block	3.0%	3.3%
Peripheral Vascular Disease	6.9%	7.3%	Right Bundle Branch Block	10.3%	13.7%

*p = 0.01

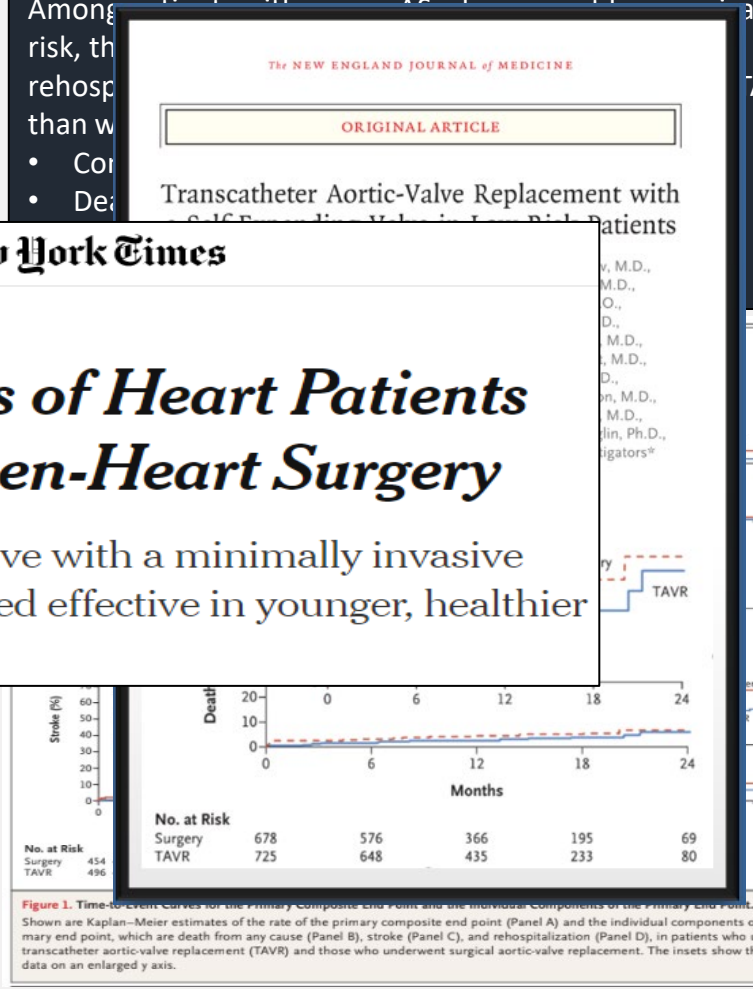


Figure 1. Time-to-Event Curves for the Primary Composite End Point and the Individual Components of the Primary End Point.
Shown are Kaplan–Meier estimates of the rate of the primary composite end point (Panel A) and the individual components of the primary end point, which are death from any cause (Panel B), stroke (Panel C), and rehospitalization (Panel D), in patients who underwent transcatheter aortic-valve replacement (TAVR) and those who underwent surgical aortic-valve replacement. The insets show the same data on an enlarged y axis.

Disruption in the Treatment of Aortic Stenosis – 2017

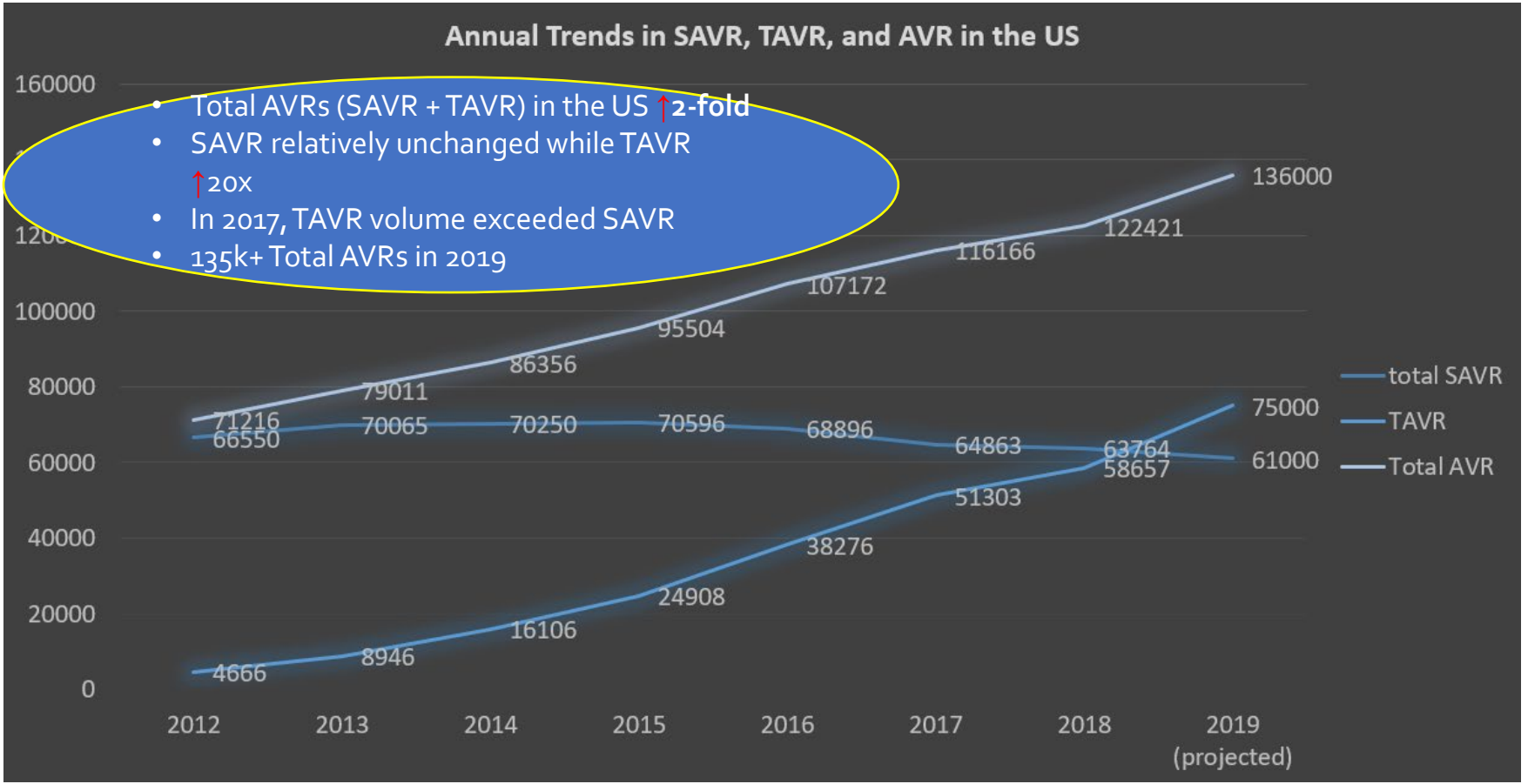
Moves upstream - Eventually it moves upstream *(eg high/intermediate risk)* disrupting an existing market, **displacing an earlier technology**

SAVR

TAVR

Phase 2

Nishimura RA. 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 Practice Guidelines. J Thorac Cardiovasc Surg. 2014 Jul;148(1):e1-e132.



Based on Bavaria, J - The Aortic Valve "Universe" in the USA

Changing Treatment Paradigm for Aortic Stenosis

Capturing population-wide value requires new methods

JOURNAL OF MEDICAL ECONOMICS
2022, VOL. 25, NO. 1, 1051–1060
https://doi.org/10.1080/13696998.2022.2112442
Article 0125-FT.R2/2112442

Taylor & Francis
Taylor & Francis Group

ORIGINAL RESEARCH

OPEN ACCESS Check for updates

Cost-utility and cost-benefit analysis of TAVR availability in the US severe symptomatic aortic stenosis patient population

J. P. Sevilla[a], Jessica M. Klusty[a], Younghwan Song[b], Mark J. Russo[c], Christin A. Thompson[d], Xiayu Jiao[d], Seth J. Clancy[d] and David E. Bloom[e]

[a]Life Sciences Group, Data for Decisions, LLC, Waltham, MA, USA; [b]Department of Economics, Union College, Schenectady, NY, USA; [c]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, USA; [d]Edwards Lifesciences, Irvine, CA, USA; [e]Department of Global Health and Population, Harvard T. H. Chan School of Public Health, Boston, MA, USA

ABSTRACT

Aims: We evaluated the availability of transcatheter aortic valve replacement (TAVR) to determine its value across all severe symptomatic aortic stenosis (SSAS) patients, especially those untreated because of concerns regarding invasive surgical AVR (SAVR) and its impact on active aging.

Methods: We performed payer perspective cost-utility analysis (CUA) and societal perspective cost-benefit analysis (CBA). The CBA's benefit measure is active time: salaried labor, unpaid work, and active leisure. The study population is a cohort of US elderly SSAS patients. We compared a "TAVR available" scenario in which SSAS patients distribute themselves across TAVR, SAVR, and medical management (MM); and a "TAVR not available" scenario with only SAVR and MM. We structured each scenario with a decision-tree model of SSAS patient treatment allocation. We measured the association between health and active time in the US Health and Retirement Study and used this association to impute active time to SSAS patients given their health.

Results: The incremental cost-effectiveness ratio (ICER) and rate of return (RoR) of TAVR availability were $8,533 and 395%, respectively. CUA net monetary benefits (NMB) were $212,199 per patient and $43.4 billion population-wide. CBA NMB were $50,530 per patient and $10.3 billion population-wide.

Limitations: Among study limitations were scarcity of evidence regarding key parameters and the lack of long-term survival, health utility, and treatment cost data. Our analysis did not account for TAVR durability, retreatments, and valve-in-valve treatments.

Conclusion: Across risk-, age-, and treatment-eligibility groups, TAVR is the economically optimal treatment choice. It represents strong value-for-money per patient and population-wide. The vast majority of TAVR value involves raising treatment uptake among the untreated.

ARTICLE HISTORY
Received 2 June 2022
Revised 5 August 2022
Accepted 9 August 2022

KEYWORDS
Active aging; cost-benefit analysis; cost-utility analysis; severe symptomatic aortic stenosis; time use; transcathether aortic valve replacement

JEL CLASSIFICATION CODES
J14; I1; J; I10; I1; I; D61; D6; D

PLAIN LANGUAGE SUMMARY

Aortic stenosis (AS) is a common and lethal heart disease. Surgical treatment has long been available, but its invasiveness limits uptake. More recently, transcatheter aortic valve replacement (TAVR) has emerged as a treatment alternative. Its minimal invasiveness has significantly increased treatment rates, but economic evaluations omit this benefit, risking undervaluation. We evaluated TAVR in elderly US severe symptomatic AS patients, using payer perspective cost-utility analysis (CUA) and societal perspective cost-benefit analysis (CBA). Both CUA and CBA incorporated TAVR's impact on treatment rates. Given patient preferences for treatment options promoting active aging, our CBA used the value of active time as a benefit measure. We found that CUA/CBA net monetary benefits are $212,199/$50,530 per patient. Across risk-, age-, and treatment-eligibility groups, TAVR is the economically optimal treatment choice over surgery and medical management. It represents strong value-for-money per patient and population-wide. Increased treatment uptake accounts for the vast share of TAVR's value.

Moving beyond conventional CEA

'Counterfactual Analysis' *evaluating TAVR's impact on the SSAS population and valuing TAVR's impact on active aging and the productive contributions of the elderly*

- TAVR available
- TAVR not available

Sevilla et al. Cost-utility and cost-benefit analysis of TAVR availability in the US severe symptomatic aortic stenosis patient population. Journal of Medical Economics. 2022; 25:1, 1051-1060

We performed
payer perspective cost-utility analysis (CUA) and
societal perspective costbenefit analysis (CBA).
The CBA's benefit measure is active time: salaried labor, unpaid work, and active leisure.

The study population is a cohort of US elderly SSAS patients.

We compared a
"TAVR available" scenario - TAVR, SAVR, and medical management (MM); vs
a "TAVR not available" scenario - with only SAVR and MM.

We structured each scenario with a decision-tree model of SSAS patient treatment allocation. We measured the association between health and active time in the US Health and Retirement Study and used this association to impute active time to SSAS patients given their health.

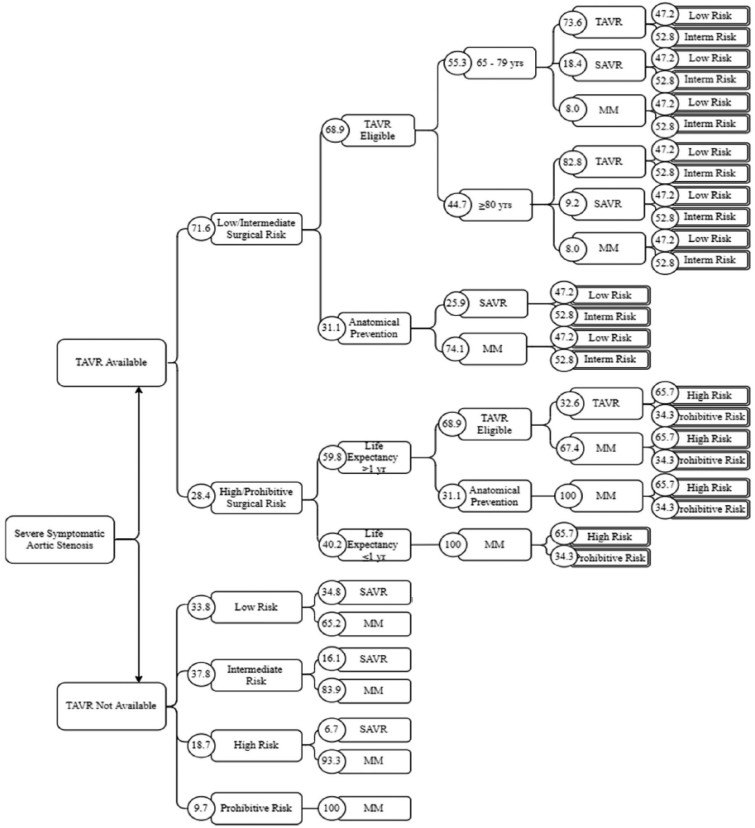


Figure 1. State-of-the-art decision tree. All lines indicate branches of the decision tree. The rectangular nodes name each branch, and the values in each associated circle indicate the percentage of the previous branch that moves into subsequent nodes. Abbreviations: MM, medical management; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

Table A1: Historical practice tree parameters and references

Parameter (Node Letter)	Value (%)	References used in parameter calculations
Overall risk proportions		
Low risk (A)	33.8	Calculations; see references below
Intermediate risk (B)	37.8	
High risk (C)	18.7	
Prohibitive risk (D)	9.7	
TAVR available		
TAVR, low risk (E)	7.1	Carroll et al. (2020)[1]
SAVR, low risk (1-E-F)	32.3	Carroll et al. (2020), Kim et al. (2018)[2]
MM, low risk (F)	60.6	Brennan et al. (2020),[3] Tang et al. (2018)[4]
TAVR, intermediate risk (G)	24.6	Carroll et al. (2020)
SAVR, intermediate risk (1-G-H)	12.1	Carroll et al. (2020), Kim et al. (2018)
MM, intermediate risk (H)	63.3	Brennan et al. (2020), Tang et al. (2018)
TAVR, high risk (J)	35.2	Carroll et al. (2020), Kim et al. (2018)
SAVR, high risk (1-J-K)	4.4	Carroll et al. (2020), Kim et al. (2018)
MM, high risk (K)	60.4	Brennan et al. (2020), Dharmarajan et al. (2017),[5] Tang et al. (2018)
TAVR, prohibitive risk (L)	24.7	Carroll et al. (2020), Kim et al. (2018)
MM, prohibitive risk (1-L)	75.3	Brennan et al. (2020), Dharmarajan et al. (2017), Tang et al. (2018)
TAVR not available		
SAVR, low risk (M)	34.8	Carroll et al. (2020), Kim et al. (2018)
MM, low risk (1-M)	65.2	Brennan et al. (2020), Tang et al. (2018)
SAVR, intermediate risk (N)	16.1	Carroll et al. (2020), Kim et al. (2018)
MM, intermediate risk (1-N)	83.9	Brennan et al. (2020), Tang et al. (2018)
SAVR, high risk (P)	6.7	Carroll et al. (2020), Kim et al. (2018)
MM, high risk (1-P)	93.3	Brennan et al. (2020), Dharmarajan et al. (2017), Tang et al. (2018)
MM, prohibitive risk (1)	100	Brennan et al. (2020), Dharmarajan et al. (2017), Tang et al. (2018)

Note: TAVR = transcatheter aortic valve replacement. SAVR = surgical aortic valve replacement. MM = medical management.

Table 1. Terminal state utilities.

Treatment	TAVR				SAVR			MM			
Risk Group	Low	Intermediate	High	Prohibitive	Low	Intermediate	High	Low	Intermediate	High	Prohibitive
Proportions	0.181	0.202	0.025	0.013	0.060	0.068	0	0.096	0.108	0.162	0.084
Age 65–79 years	0.095	0.106			0.024	0.027		0.010	0.012		
Age ≥80 years	0.086	0.096			0.010	0.011		0.008	0.009		
LE ≥1 year										0.087	0.045
LE <1 year										0.075	0.039
Costs	$155,634	$149,551	$176,043	$217,066	$185,052	$172,939	$185,702	$189,945	$73,672	$81,191	$115,509
Age 65–79 years	$165,769	$200,805			$197,976	$230,854		$239,147	$159,659		
Age ≥80 years	$117,482	$127,133			$135,966	$147,387		$46,231	$43,136		
LE ≥1 year			$176,043	$217,066						$110,820	$154,805
LE <1 year										$81,191	$51,723
QALYs	9.39	5.38	5.20	2.97	9.30	5.00	4.08	4.50	1.56	1.63	1.45
Age 65–79 years	10.54	8.92			10.46	8.40		5.74	3.59		
Age ≥80 years	5.19	3.94			5.02	3.54		1.01	0.88		
LE ≥1 year			5.20	2.97						2.25	1.99
LE <1 year										0.65	0.62
Salaried labor (h)	803	75	57	32	741	66	40	210	16	14	10
Age 65–79 years	1,315	565			1,225	521		396	189		
Age ≥80 years	72	22			63	19		8	4		
LE ≥1 year										17	13
LE <1 year										7	5
Unpaid Work (h)	13,500	7,338	7,284	4,283	13,296	6,961	5,712	6,826	2,280	2,474	2,260
Age 65–79 years	15,341	12,661			15,147	12,304		8,819	5,574		
Age ≥80 years	7,055	5,183			6,780	4,789		1,435	1240		
LE ≥1 year										3,413	3,081
LE <1 year										985	963
Active leisure (h)	9,678	4,879	4,709	2,615	9,469	4,585	3,580	4,345	1,336	1,406	1,230
Age 65–79 years	10,856	8,005			10,648	7,709		5,541	3,074		
Age ≥80 years	5,358	3,545			5,112	3,244		965	753		
LE ≥1 year										1,949	1,685
LE <1 year										555	519

This table summarizes an average patient's terminal state utilities by treatment and risk group in the shaded rows. Non-shaded rows detail any adjustments to utilities made when a patient has a differing age or life expectancy. Abbreviations. LE, life expectancy; MM, medical management; SAVR, surgical aortic valve replacement; TAVR, transcatheter aortic valve replacement.

Table 2. Cost-utility and cost-benefit analyses results.

Measure	TAVR available	TAVR not available	Incremental impact
CUA results: impact of TAVR availability on treatment costs and QALYs			
Cost	$138,010	$125,202	$12,808
QALY	4.86	3.36	1.50
Net benefit	$590,990	$378,798	$212,192
ICER	–	–	$8,533
CBA results: impact of TAVR availability on active time			
Quantity of active time			
Salaried labor (h)	287	146	141
Unpaid work (h)	6,970	4,935	2,035
Active leisure (h)	4,638	3,182	1,456
Total (h)	11,895	8,263	3,632
Value of active time			
Salaried labor ($)	$4,701	$2,095	$2,606
Unpaid work ($)	$104,780	$69,048	$35,732
Active leisure ($)	$69,626	$44,626	$25,000
Total ($)	$179,108	$115,769	$63,338
Rate of return: incremental cost of TAVR availability vs. active time gained			394.52%

Net monetary benefit is reported assuming a value of $150,000 per quality-adjusted life year. Abbreviations. CBA, cost-benefit analysis; CUA, cost-utility analysis; ICER, incremental-cost effectiveness ratio; QALY, quality-adjusted life year; TAVR, transcatheter aortic valve replacement.

Table 3. Scenario and sensitivity analyses results.

	CUA				CBA			
	ICER	Cost difference	QALY difference	RoR (%)	Salaried labor (h)	Unpaid work (h)	Active leisure (h)	Value
Base case	$8,533.37	$12,807.98	1.50	394.52	141	2,035	1,456	$63,338.19
Scenario analyses								
"Historical practice" tree	$20,173.73	$13,013.55	0.65	52.73	18	857	607	$19,876.01
30% of SSAS patients are prohibitive risk	$9,518.80	$11,326.35	1.19	340.10	110	1,607	1,154	$49,847.35
Low-risks are 50% of non-prohibitive risks	$3,964.04	$5,459.65	1.38	1,000.63	149	1,851	1,371	$60,090.47
Projection of low-risk TAVR proportion	$8,533.37	$12,807.98	1.50	394.52	141	2,035	1,456	$63,338.19
Increased high risk among SAVR patients	$7,922.09	$11,906.39	1.50	433.75	143	2,038	1,462	$63,550.21
SSAS population proportion of MM is 45%	$7,040.61	$7,195.84	1.02	552.79	106	1,387	969	$46,973.58
Attrition rates from clinical trials	$11,052.39	$25,154.45	2.28	253.62	184	3,076	2,229	$88,951.89
TAVR eligibility is 85.7%	$8,213.17	$15,440.28	1.88	414.10	179	2,549	1,827	$79,377.85
TAVR eligibility is 97%	$8,061.75	$17,210.81	2.13	423.89	204	2,894	2,077	$90,166.42
Medical futility is 12.1%	$12,533.91	$20,847.33	1.66	228.18	142	2,273	1,600	$68,417.14
Medical futility is 20%	$11,490.35	$18,587.16	1.62	260.41	142	2,206	1,559	$66,989.25
Medical futility is 60%	$5,151.86	$7,143.25	1.39	736.59	140	1,867	1,355	$59,759.43
Average wage is federal minimum wage	$8,533.37	$12,807.98	1.50	105.60	141	2,035	1,456	$26,333.44
Health utility discount 0%	$8,518.34	$12,807.98	1.50	392.77	134	2,035	1,457	$63,113.37
Sensitivity analyses								
Mortality increases by 10%	$10,132.98	$15,089.59	1.49	315.90	141	2,030	1,443	$62,757.93
Mortality decreases by 10%	$6,710.54	$10,140.14	1.51	529.90	141	2,036	1,468	$63,872.57
Health utility increases by 10%	$7,757.61	$12,807.98	1.65	394.52	141	2,035	1,456	$63,338.19
Health utility decreases by 10%	$9,481.52	$12,807.98	1.35	394.52	141	2,035	1,456	$63,338.19
Cost increases by 10%	$9,386.70	$14,088.78	1.50	349.56	141	2,035	1,456	$63,338.19
Cost decreases by 10%	$7,680.03	$11,527.18	1.50	449.47	141	2,035	1,456	$63,338.19
Predicted time increases by 10%	$8,533.37	$12,807.98	1.50	443.97	155	2,238	1,602	$69,672.01
Predicted time decreases by 10%	$8,533.37	$12,807.98	1.50	345.07	127	1,831	1,311	$57,004.37
Discount rate is 6%	$10,073.26	$12,149.63	1.21	318.88	125	1,635	1,176	$50,891.99
Discount rate is 0%	$7,275.78	$14,082.11	1.94	480.55	161	2,623	1,870	$81,753.29

Base case CUA, CBA, and RoR results are compared to the results of each scenario and sensitivity analysis. Abbreviations. CBA, cost-benefit analysis; CUA, cost-utility analysis; ICER, incremental cost-effectiveness ratio; MM, medical management; QALY, quality-adjusted life year; RoR, rate of return; SAVR, surgical aortic valve replacement; SSAS, severe symptomatic aortic stenosis; TAVR, transcatheter aortic valve replacement.

Conventional approaches to economically evaluating health technologies

Our recent work for evaluating transcatheter aortic valve replacement (TAVR) for the treatment of severe symptomatic aortic stenosis (SSAS) highlight these limitations.

In this analysis, we found that TAVR represents a strong value-for-money per patient and population-wide.

However, a vast share of its value comes from elements that are not captured by conventional methodology—this includes failing to account for raising uptake among patients who were eligible for AVR even pre-TAVR but did not undergo treatment and failure to account for the strong contribution to active aging.

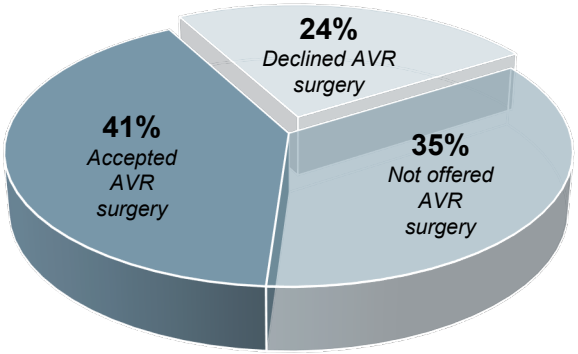
These results highlight that conventional methods fail to capture a significant proportion of the value of TAVR among SSAS patients.

TAVR Treatment

TAVR has changed the treatment paradigm for aortic stenosis

2

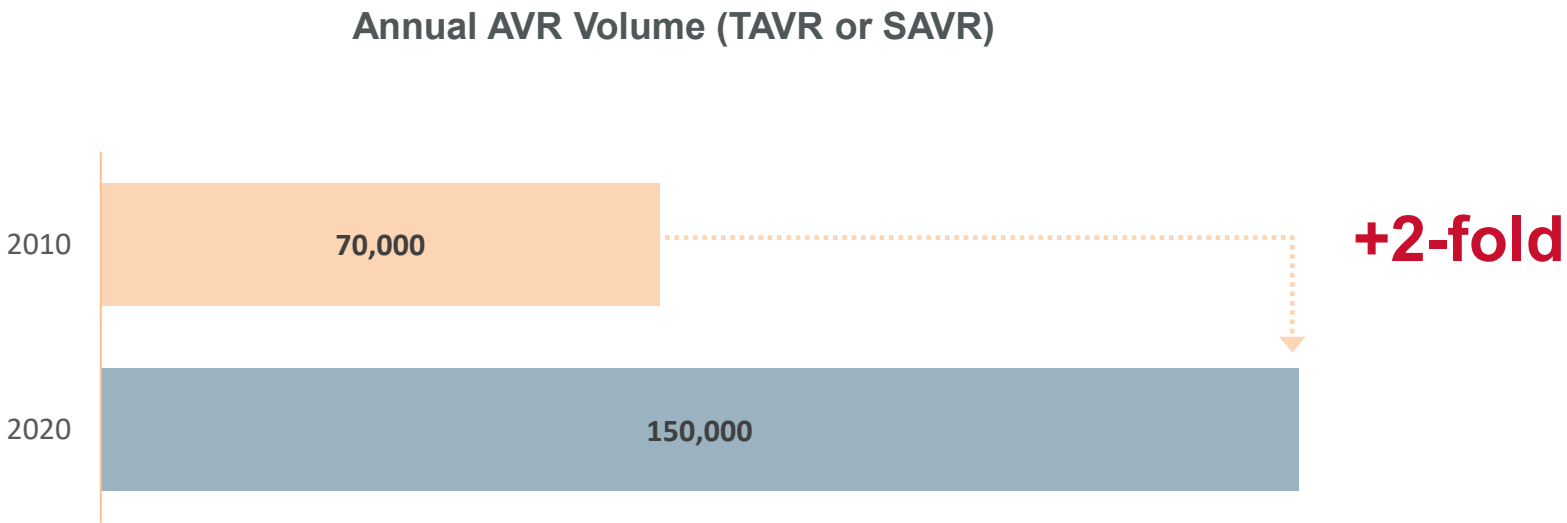
Pre-TAVR
Reasons for absence of AVR surgery in patients with severe AS



Prior to TAVR, most patients weren't offered or didn't want AVR

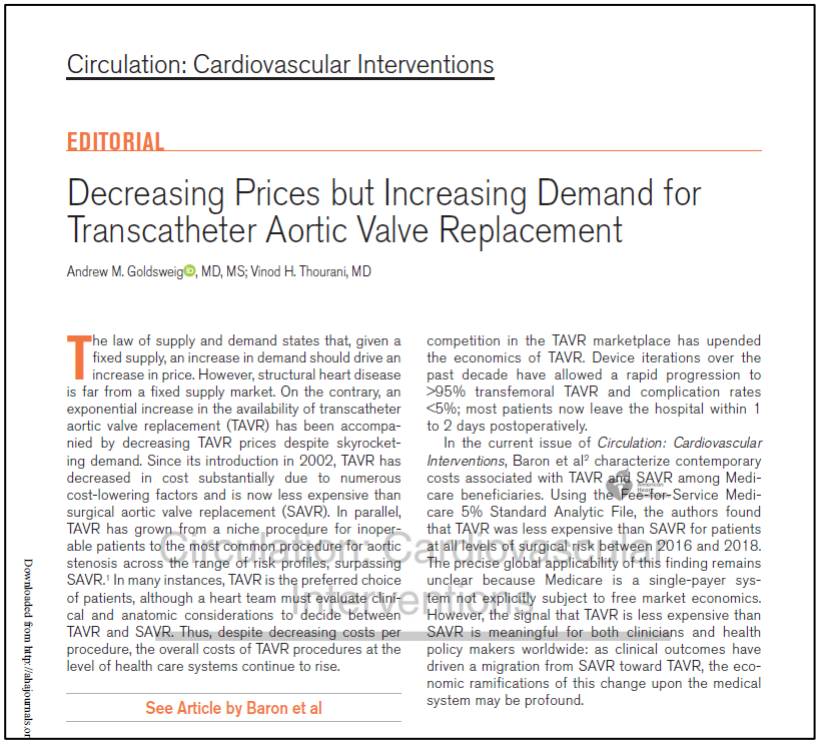
Charlson et al., Decision-Making and Outcomes in Severe Symptomatic Aortic Stenosis. The Journal of Heart Valve Disease. 2016;15:312-321 2.

TAVR availability has had a profound impact on SSAS treatment



Sevilla et al. Cost-utility and cost-benefit analysis of TAVR availability in the US severe symptomatic aortic stenosis patient population. Journal of Medical Economics. 2022; 25:1, 1051-1060

Increasing TAVR demand and systemic costs a concern despite decreasing TAVR procedure costs



Circulation: Cardiovascular Interventions

EDITORIAL

Decreasing Prices but Increasing Demand for Transcatheter Aortic Valve Replacement

Andrew M. Goldsweig, MD, MS; Vinod H. Thourani, MD

The law of supply and demand states that, given a fixed supply, an increase in demand should drive an increase in price. However, structural heart disease is far from a fixed supply market. On the contrary, an exponential increase in the availability of transcatheter aortic valve replacement (TAVR) has been accompanied by decreasing TAVR prices despite skyrocketing demand. Since its introduction in 2002, TAVR has decreased in cost substantially due to numerous cost-lowering factors and is now less expensive than surgical aortic valve replacement (SAVR). In parallel, TAVR has grown from a niche procedure for inoperable patients to the most common procedure for aortic stenosis across the range of risk profiles, surpassing SAVR.[1] In many instances, TAVR is the preferred choice of patients, although a heart team must evaluate clinical and anatomic considerations to decide between TAVR and SAVR. Thus, despite decreasing costs per procedure, the overall costs of TAVR procedures at the level of health care systems continue to rise.

See Article by Baron et al

competition in the TAVR marketplace has upended the economics of TAVR. Device iterations over the past decade have allowed a rapid progression to >95% transfemoral TAVR and complication rates <5%; most patients now leave the hospital within 1 to 2 days postoperatively.

In the current issue of *Circulation: Cardiovascular Interventions*, Baron et al[2] characterize contemporary costs associated with TAVR and SAVR among Medicare beneficiaries. Using the Fee-for-Service Medicare 5% Standard Analytic File, the authors found that TAVR was less expensive than SAVR for patients at all levels of surgical risk between 2016 and 2018. The precise global applicability of this finding remains unclear because Medicare is a single-payer system not explicitly subject to free market economics. However, the signal that TAVR is less expensive than SAVR is meaningful for both clinicians and health policy makers worldwide: as clinical outcomes have driven a migration from SAVR toward TAVR, the economic ramifications of this change upon the medical system may be profound.

"In spite of the decreasing cost of individual TAVR procedures, the aggregate costs of TAVR at the level of health care systems have increased dramatically due to rapidly climbing procedural volumes …

VINOD THOURANI
TAVR surgeon

TAVR has been extensively economically evaluated, often in connection with clinical trials

These evaluations are risk-group specific and fail to account for TAVR's population-wide value, which is realized across three groups:

1. Prohibitive risk who otherwise have no treatment options
2. Non-prohibitive risk who otherwise receive SAVR
3. Non-prohibitive risk who otherwise remain untreated, in part because of invasiveness concerns

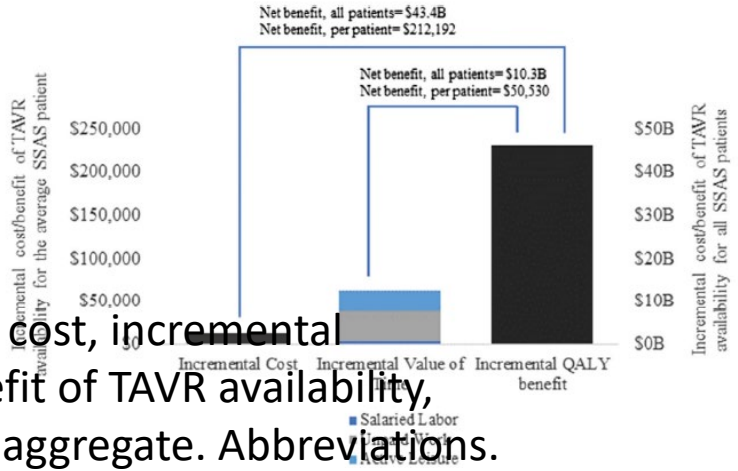


Figure 2. Incremental cost, incremental benefit, and net benefit of TAVR availability, both per-patient and aggregate. Abbreviations. B, billion; QALY, qualityadjusted life year; SSAS, severe symptomatic aortic stenosis; TAVR, transcatheter aortic valve replacement.

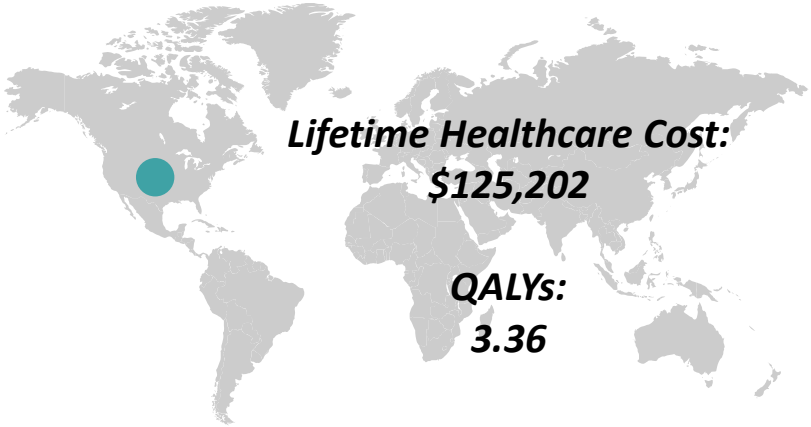
Table 4. Breakdowns by SSAS patient group: Percentage of the SSAS population and net monetary benefits.

Group	Percentage of SSAS population (%)	CUA NMB per patient	Aggregated, weighted CUA NMB	CBA NMB per patient	Aggregated, weighted CBA NMB
(1) Prohibitive-risk TAVR patients who would otherwise receive MM	1.3	$85,297.89	$1,114.23	−$33,748.6	−$440.85
(2) Non-prohibitive-risk TAVR patients who would otherwise receive SAVR	6.3	$92,125.26	$5,791.62	$36,518.84	$2,295.82
(3) Non-prohibitive-risk TAVR patients who otherwise get MM	34.5	$615,465.55	$212,594.26	$123,119.33	$42,527.91

The SSAS population contains three groups of patients who receive TAVR now that it is available, instead of receiving SAVR or MM. Each group's percentage of total SSAS patients is reported. Net monetary benefit is calculated for each group, both from a CUA and a CBA perspective. Net monetary benefit is reported per-patient and aggregated across the patient group. Abbreviations. CBA, cost-benefit analysis; CUA, cost-utility analysis; MM, medical management; NMB, net monetary benefit; SAVR, surgical aortic valve replacement; SSAS, severe symptomatic aortic stenosis; TAVR, transcatheter aortic valve replacement.

Value of TAVR to society – what if TAVR didn't exist?

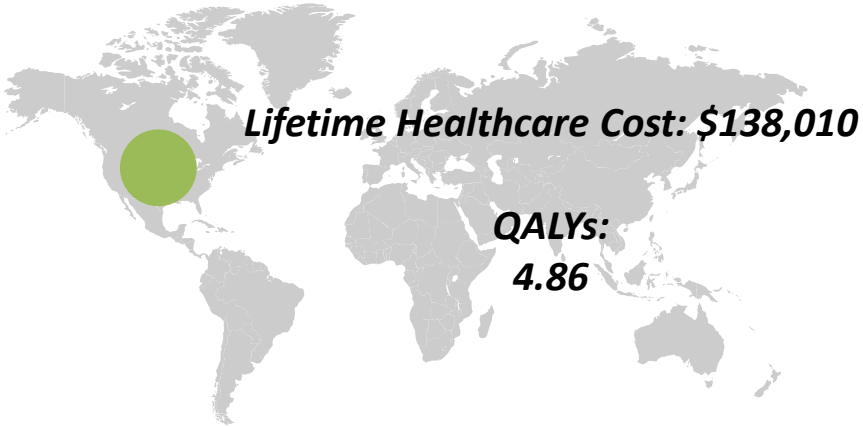
World <u>without</u> TAVR



Treatments available for SSAS:

- MM
- SAVR

World <u>with</u> TAVR



Treatments available for SSAS:

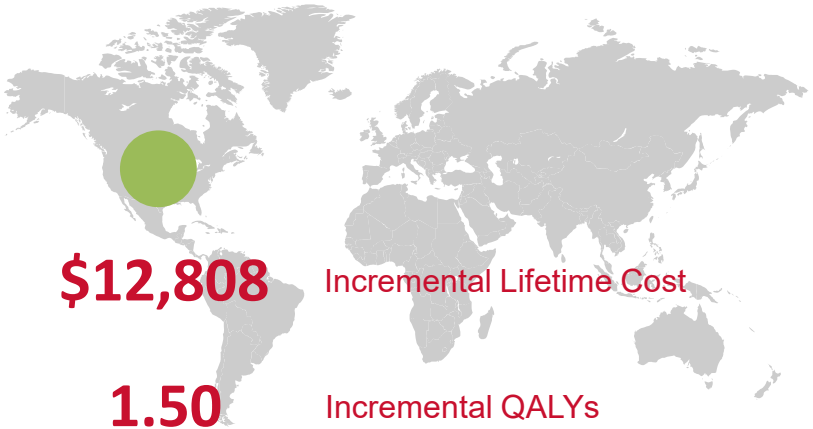
- MM
- SAVR
- TAVR

Sevilla et al. Cost-utility and cost-benefit analysis of TAVR availability in the US severe symptomatic aortic stenosis patient population. Journal of Medical Economics. 2022; 25:1, 1051-1060. QALY = Quality Adjusted Life Year.

Value of TAVR to society – per patient economic benefit

World without TAVR

World with TAVR



$12,808 Incremental Lifetime Cost

1.50 Incremental QALYs

$225,000 Monetary benefit of incremental QALYs

$212,192 Net Monetary Benefit per patient

Sevilla et al. Cost-utility and cost-benefit analysis of TAVR availability in the US severe symptomatic aortic stenosis patient population. Journal of Medical Economics. 2022; 25:1, 1051-1060. QALY = Quality Adjusted Life Year.

Value of TAVR to society – population-level economic benefit

World without TAVR

World with TAVR

306,839 QALYs gained

$43.4B Net Monetary Benefit

$8,533 Incremental Cost-Effectiveness Ratio

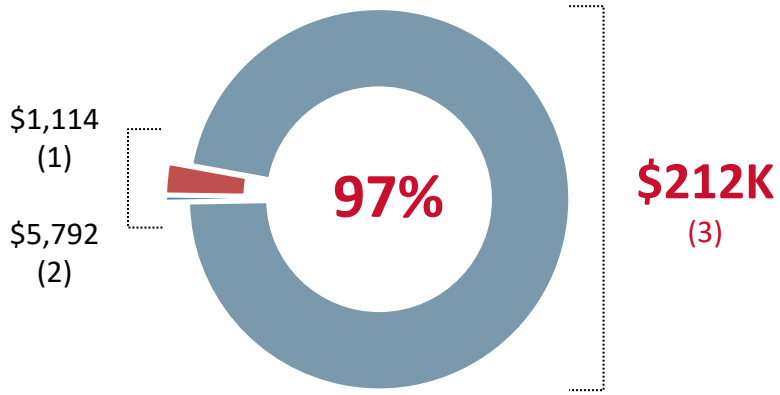
Sevilla et al. Cost-utility and cost-benefit analysis of TAVR availability in the US severe symptomatic aortic stenosis patient population. Journal of Medical Economics. 2022; 25:1, 1051-1060. QALY = Quality Adjusted Life Year.

Existing economic evaluations understate TAVR's population-wide value

SSAS patient group: percentage of the SSAS population and net monetary benefits

Groups	% of SSAS population	CUA NMB per patient
(1) Prohibitive risk, TAVR patients who would otherwise receive MM	1.3%	$85,298
(2) Non-prohibitive risk TAVR patients who would otherwise receive SAVR	6.3%	$92,125
(3) Non-prohibitive risk TAVR patients who would otherwise get MM	**34.5%**	**$615,466**

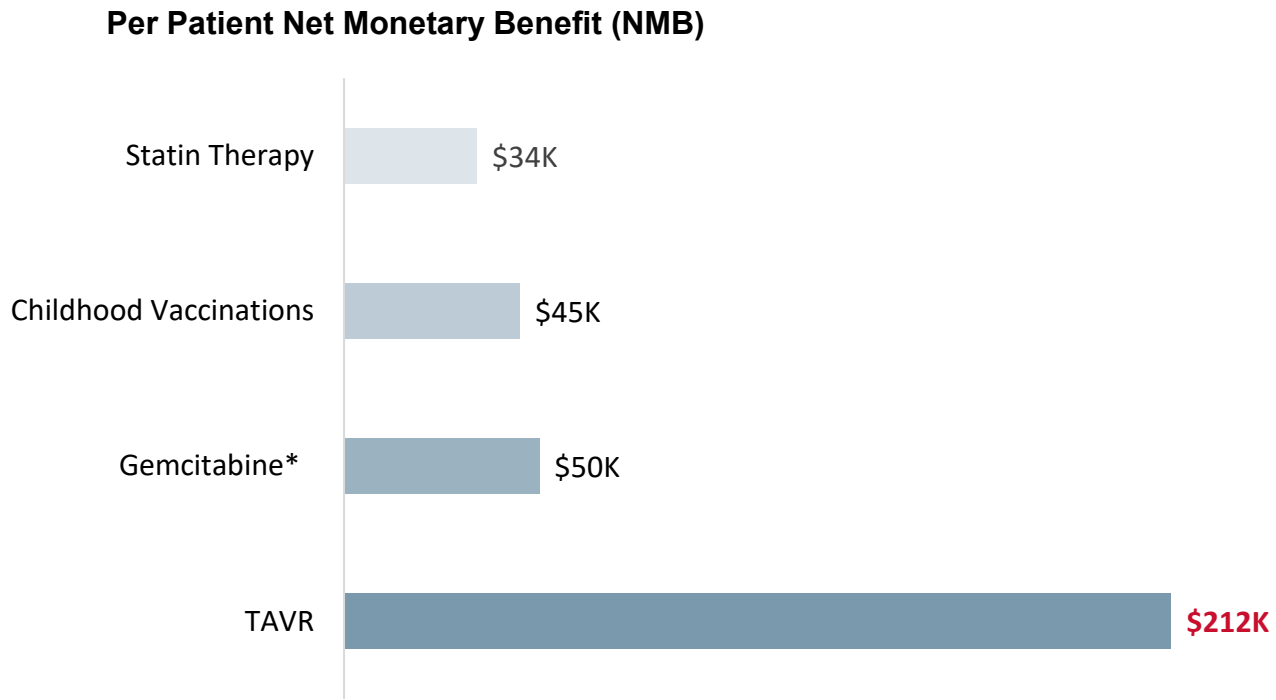
Aggregated, weighted CUA NMB (by patient group)*



- **Existing economic evaluations of TAVR focus on groups 1 and 2, and ignore 3**
- **The literature has ignored by far the most important group for which TAVR yields value**

Normalized by group size (e.g., 1.3%$85,298 = $1,114). CUA = cost-utility analysis

The Net Monetary Benefit of TAVR is higher than statin therapy, childhood vaccines and pancreatic cancer therapy



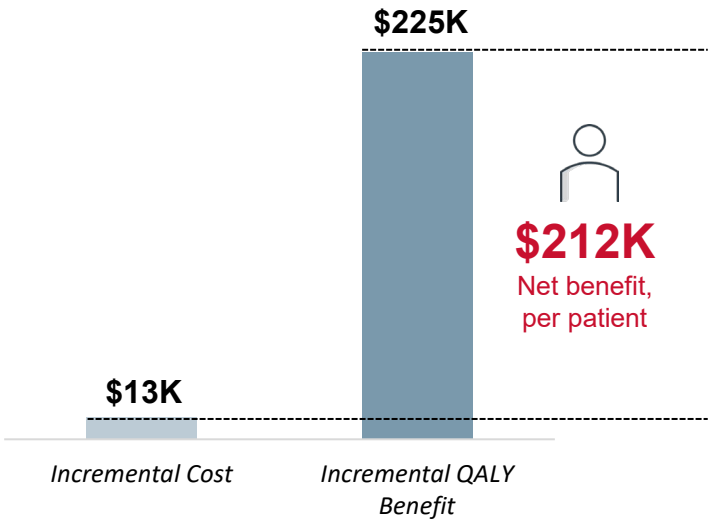
1. Grabowski et al., The Large Social Value Resulting From Use of Statins Warrants Steps to Improve Adherence and Broaden Treatment. Health Affairs. 2012;10:2276-2285
2. Philipson et al., The Social Value of Childhood Vaccination in the United States. Am J Manag Care. 2017;23(1):41-47
3. MacEwan et al., The Value of Survival Gains in Pancreatic Cancer from Novel Treatment Regimens. JMCP. 2017;23(2):206-212

*For metastatic pancreatic cancer

TAVR delivers high value for money

CUA results: impact of TAVR availability on treatment costs and QALYs

Incremental cost/benefit of TAVR availability per SSAS patient



Population-wide health gain and Net Monetary Benefit (NMB)

306,839 QALYs gained

$43.4B NMB

$8,533 ICER*

*Incremental Cost Effectiveness Ratio of TAVR availability (relative to non-availability).

Summary of base case results

CUA Results: Impact of TAVR on Average Treatment Costs and QALYs

Measure	TAVR available	TAVR not available	Incremental impact
Cost	$138,010	$125,202	**$12,808**
QALY	4.86	3.36	**1.5**
*Net Benefit**	$590,990	$378,798	**$212,192**
ICER	-	-	**$8,533**

*Net monetary benefit is reported assuming a value of $150,000 per quality-adjusted life year

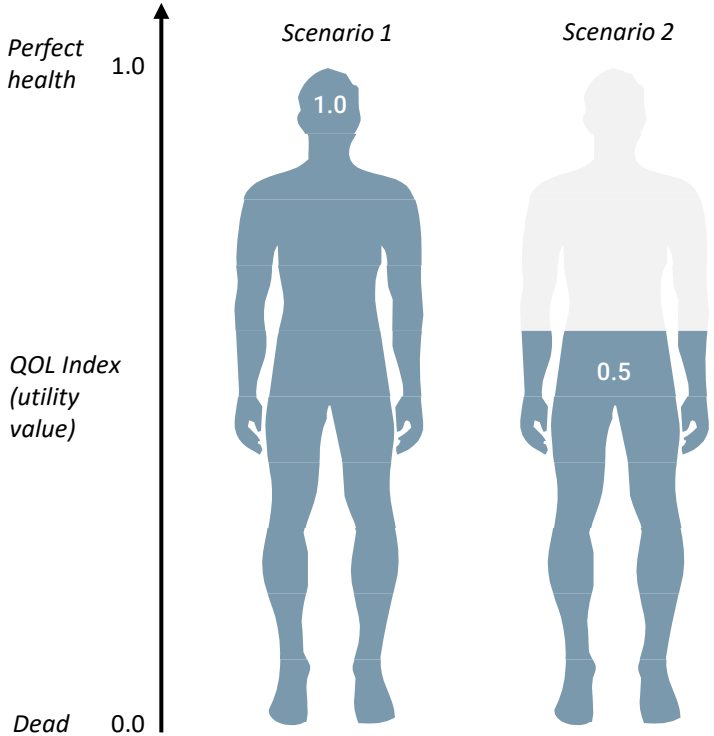
What's a Quality Adjusted Life Year (QALY)?

QALY is a measure of disease burden, including both the quantity and quality of life lived

Example:

Scenario 1
- Perfect health
- Life expectancy = 10 years
- 1.0 x 10 = **10 QALYs**

Scenario 2
- Lost sense of sight
- Quality of life index is 0.5
- Life expectancy = 10 years
- 0.5 x 10 = **5 QALYs**



Quantifying the impact of TAVR on productive time use

Salaried Labor

- Working for pay

Unpaid work

- Washing, ironing, mending clothes, **taking care of grandchildren**, yard work, preparing meals, running errands, shopping, house cleaning, money management, **volunteer work**, caring for pets, attending meetings, home improvements, vehicle maintenance, **helping friends and neighbors**, **treating the medical condition of another person**, managing medical bills

Active leisure

- Walking, participating in sports, visiting friends, neighbors and relatives, attending religious services, attending concerts, playing a musical instrument, arts and crafts, dining/eating out

Passive leisure

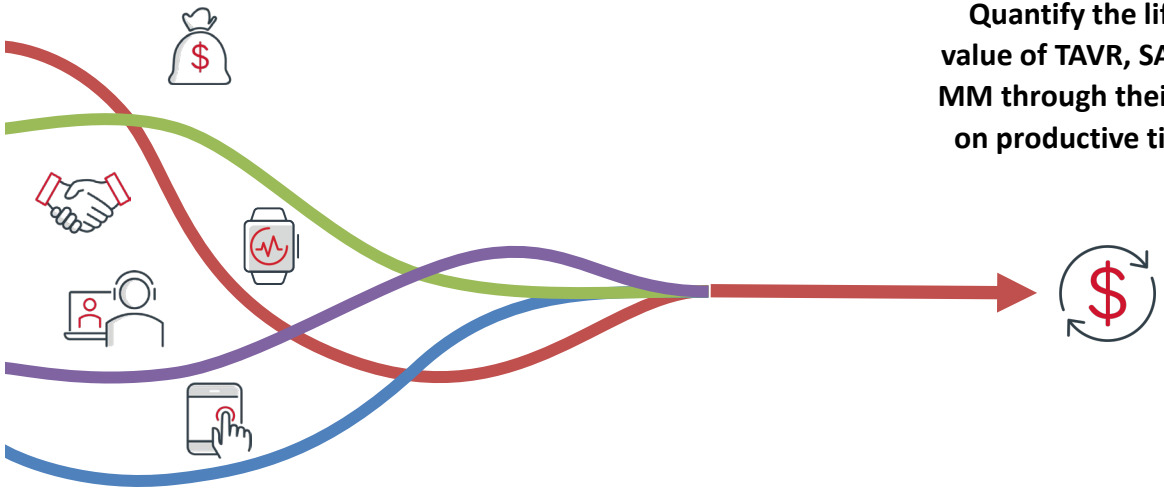
- Watching TV, reading newspapers/books, listening to music, talking on the telephone, using the computer, praying or meditating, showing affection, eating meals, playing cards

Maintenance

- Sleeping or napping, personal grooming and hygiene, managing own medical condition, doctor's visits

CBA uses ‘active time’ as a benefit measure to track TAVR’s impact on active aging

1. Quantify **time use**: hours spent on salaried labor, unpaid work, and active leisure
2. Estimate time use **over a lifetime**
3. Put a **monetary value** on these hours over the lifetime of patients



Quantify the lifetime value of TAVR, SAVR, and MM through their impact on productive time use

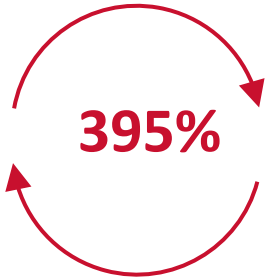
We estimated a relationship between health utility and active time from the Health and Retirement Study (HRS), then used this relationship to impute SSAS patients’ active time

TAVR availability significantly increases active time, a key metric of active aging

CBA results: impact of TAVR availability on active time

Quantity of active time	TAVR available	TAVR not available	Incremental impact
Salaried labor (h)	287	146	**141**
Unpaid work (h)	6,970	4,935	**2,035**
Active leisure (h)	4,638	3,182	**1,456**
Total (h)	11,895	8,263	**3,632**
Value of active time			
Salaried labor ($)	$4,701	$2,095	**$2,606**
Unpaid work ($)	$104,780	$69,048	**$35,732**
Active leisure ($)	$69,626	$44,626	**$25,000**

Rate of Return*

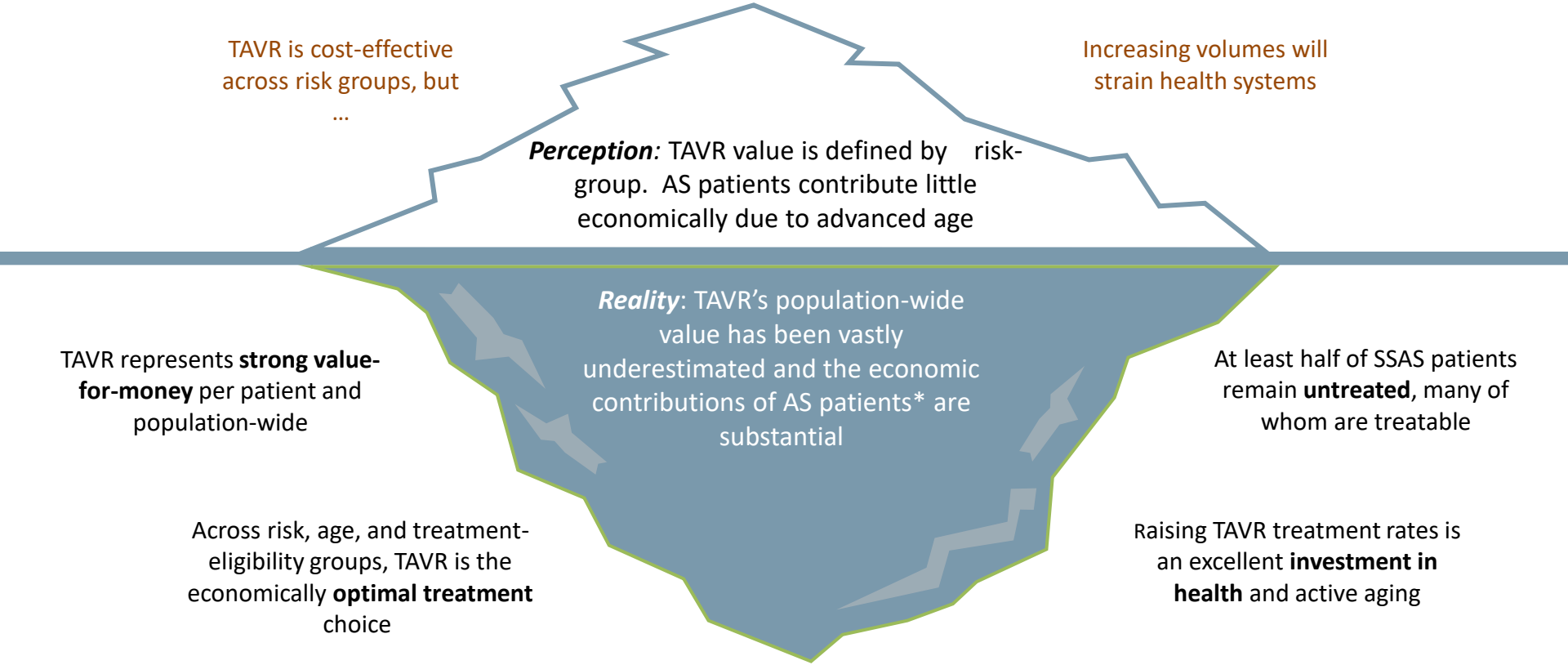


Population-wide value (NMB) of active time gained

$10.3B

*Rate of return: incremental cost of TAVR availability vs. active time gained. NMB = Net Monetary Benefit, CBA = cost-benefit analysis

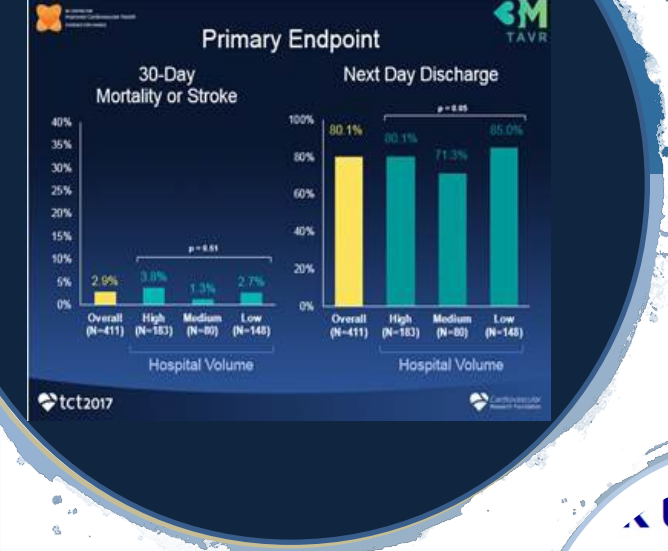
Takeaways & implications

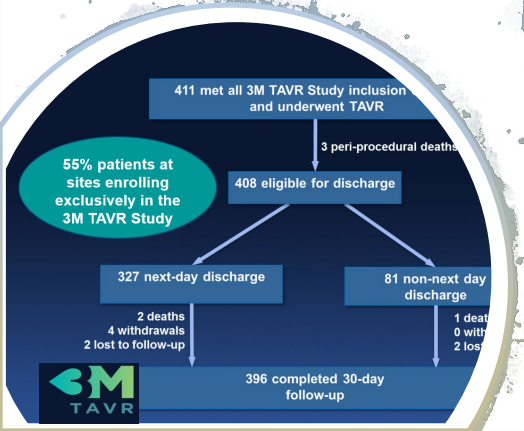


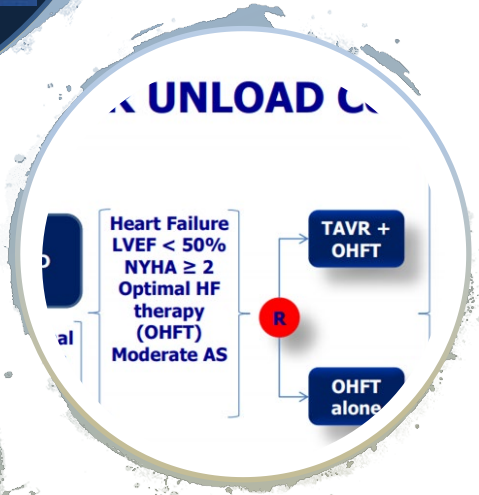
*when TAVR is available

Phase 3: the New Product or Idea Completely Redefines the Industry

Phase 3







Redefining the Market

- Minimalist Approach - 3M

Potential New Markets

- Asymptomatic Severe AS
- Moderate AS w Reduced EF
- Aortic Insufficiency

JENAVALVE