Association of Black Cardiologists, Inc.
Saving the Hearts and Minds of a Diverse America

ABC 2023 Roundtable Pre-Reads

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Saving the Hearts and Minds of a Diverse America

ABC Roundtable:
Addressing Disparities in Contemporary Care of the Minority Patient with Valvular Heart Disease
Summary Recommendations

Developed in collaboration with participants of the Addressing Disparities in Contemporary Care of the Minority Patient with Valvular Heart Disease Roundtable

June 2017

Executive Summary

Valvular heart disease (VHD) is a degenerative condition characterized by improper heart valve functioning, either due to stenosis (narrowing of the heart valve) or regurgitation (leaky heart valve). For several years, the standard of care for the treatment of VHD has been open heart surgery, but more recently minimally invasive transcatheter procedures, such as transcatheter aortic valve replacement (TAVR) or transcatheter mitral valve repair, are now commonly used for appropriate patients. Despite the fact that new and emerging technologies are now widely available in most major hospitals, there still exists a major gap regarding access by minority patients to these life-saving procedures. Minority and underserved patients receive far fewer treatments for VHD, despite comparable surgical and transcatheter outcomes [1, 2]. Valvular heart conditions, poor socioeconomic status, bias within the healthcare system, lack of awareness about the benefits of treatment and quick recovery time, and mistrust of medical providers are all barriers that can contribute to treatment disparities among minorities and underserved patients [3, 4]. Although these barriers often link to disparities across multiple chronic disease states, the Association of Black Cardiologists convened an interdisciplinary roundtable specifically focused on VHD due to the disease's grave prognosis when these lifesaving procedures are not given. [4, 5]. This group came together to address the urgency of developing solutions for eradicating preventable differences in VHD outcomes. While many barriers were identified, roundtable participants elected to prioritize barriers with immediately actionable solutions.

Introduction

According to The Centers for Disease Control and Prevention (CDC), 20th century advances in medical treatment and public health strategies contributed to an unprecedented 30-year increase in average life expectancy in the United States. Recent successes in protecting health and promoting longevity have provided many opportunities for overcoming the challenges of an aging American society [6]. Nevertheless, amid America's transforming population landscape of aging and diverse individuals, a widening gap exists between lower income minorities and other underserved patients in terms of disproportionate access to care and treatment for chronic diseases [7]. For example, forty-two percent of African American men, and over 45% of African American women aged 20 and older, have high blood pressure [8, 9]. Chronic high blood pressure increases the likelihood of heart failure, a primary risk factor for valvular heart disease (VHD). Advanced age and other chronic diseases, such as diabetes, chronic kidney disease, obesity, and physical inactivity,

increase risk for VHD and complicate treatment [10, 11]. The average age at diagnosis for minorities with VHD is far younger than whites [2]. Additionally, having low income increases the widening disparities gap around receiving appropriate care and treatment [6, 12, 13]. Older white patients access VHD medical services at greater rates through major market insurance programs like Medicare that are unavailable to younger minorities. Avoidance of care and treatment, which is often seen in minority and underserved valvular heart disease patients, substantially contributes to chronic disease disparities, decreased quality of life and potentially early death within these population groups [12]. Early detection based on national screening and treatment guidelines can identify risk factors (i.e. chronic hypertension, obesity) at younger ages to prevent VHD's inherent effects.

Roundtable Proceedings

As an organization committed to the identification and mitigation of detrimental effects of cardiovascular disease, the Association of Black Cardiologists (ABC) convened a roundtable of 21 diverse clinical and industry professionals from government, providers, advocacy organizations, academia, and communications, in conjunction with the Cardiovascular Research Technologies (CRT) 2017 meeting. Participants worked to develop solutions that mitigate health disparities among minorities and underserved patients living with VHD through strategic priorities. Topics included the review of the disease landscape and health disparity findings (i.e. disease burden statistics by population), understanding clinical and government perspectives on research gaps, understanding patient and advocacy perspectives, awareness-building and communication perspectives for strategies appropriate to educate patients and providers, and consensus-building and prioritizing solutions of greatest impact. The diverse group of stakeholders enriched the capacity to comprehensively address access to care and treatment differences amongst minority and underserved populations.

Understanding the Barriers

Although a breadth of barriers was discussed, roundtable participants specifically acknowledged the lack of awareness about both the disease state and less invasive options, such as transcatheter aortic valve replacement (TAVR), significant research gaps, and limited minority participation in clinical trials, as the most adverse barriers that impact minority and underserved VHD patients. Understanding barriers better situates the roundtable for developing appropriate solutions.

1. **African Americans are more likely to decline lifesaving treatment for Valvular Heart Disease.** Chiefly important to the roundtable was addressing why minority and underserved patients are more likely to decline life-saving treatment for VHD. It is not fully understood why these patients may be declining treatment or exploring treatment options. On the basis of their patient interactions, roundtable participants highlighted the burden of having, or treating, a chronic disease like VHD as a consideration for declined treatment. Minorities have earlier onset of VHD, therefore hindering their daily activities or ability to earn income. When patients are the primary income earners, they may not be able to afford the loss of earnings due

to extensive recovery, or forgo responsibilities as a caregiver to a child or other relative(s). Other factors may also play a role. Minorities and underserved patients typically involve family members in their care-seeking decisions [14]. Improving and broadening understanding among providers about these patient considerations could improve shared-decision making and better help patients and their families choose appropriate treatment options.

2. **Unfamiliarity with the TAVR subject matter and uneven access to TAVR.** Approved by the FDA in 2011, transcatheter aortic valve replacement (TAVR) is a minimally-invasive treatment for severe aortic stenosis that offers the potential to reduce procedural morbidity, mortality, and cost of surgical valve replacement or repair, while accelerating patient recovery and quality of life. Nationally, the average TAVR patient is aged 83 years, male and largely white (96%) [1]. Young minorities represent a population that is not eligible for major market carriers, like Medicare, due to typical age of onset. Among all patients treated with TAVR, a similar (3-yr) survival rate, similar risks, and comparable outcomes were noted [3, 4, 15]. Surgical treatment affords most patients a healthier, longer life [3, 10, 16]. However, minorities and underserved patients are infrequently referred for cardiovascular surgical treatment as compared to whites [17], creating uneven access to TAVR.

   While all the reasons for patients opting out of TAVR are not yet clearly understood, roundtable participants believe that anecdotal reports from patients, combined with the low percentage of treatment for minority and underserved patients, suggest meaningful patient and provider educational gaps. Frequently, facilities that are approved to conduct transcatheter procedures exclude facilities that minorities typically seek treatments. The Food and Drug Administration's SNAPSHOT program specifies which patient populations participate in clinical trials for FDA approved medications. However, devices like TAVR do not apply to SNAPSHOT, which creates ambiguity about minority and unserved patient access to TAVR and other devices. The National Institute of Health is bound by the 1993 Revitalization Act, a public law which requires a certain proportion of minority participation in clinical studies and trials in federally funded research. However, privately sponsored trials are not bound by these rules and may circumvent the parameters. The goal of diversifying the participants in clinical trials to increase access and awareness is commendable, but advancements are still necessary [19] to increase minority access to TAVR, similar emerging technologies, and knowledge about these devices. Roundtable participants believe that improving economic incentives for centers of excellence has the potential to encourage greater recruitment of historically underrepresented populations.

3. **Patients' and providers' lack of understanding about valvular heart disease and its prevalence.** Roundtable participants identified another important barrier as patients' and providers' lack of understanding about valvular heart disease and its prevalence. Patients typically learn about VHD at the time of diagnosis with limited knowledge about the disease state. Today, over 500,000 patients have severe aortic stenosis and more than 800,000 people live with aortic stenosis. Severe cases typically seen in minorities (14% of cases) and underserved patients necessitate intervention, surgical or catheter-based treatment to eliminate

risk factors for VHD and preserve the strength and functionality of the heart muscle [11, 16]. Minorities are at increased risk for VHD's poor outcomes due to earlier onset (ages 65-70), more comorbidities that complicate treatment, and higher mortality risk. Additionally, and despite these higher risks for poor outcomes, minorities often have higher treatment refusal rates, as compared to whites. Yet, little is known about why patient's refuse life-saving procedures. [3, 4, 9]. If left untreated, valvular heart disease has a grave prognosis; fifty percent of people die within two years and only 20% live five years post diagnosis [16].

Every patient deserves educational opportunities to promote appropriate care-seeking behaviors. General and specialty providers require enhanced education on VHD risk factors and cultural competence to omit missed diagnoses in atypical patients (i.e. younger minorities). Effective and efficient action is necessary to enhance clinical awareness about the risks of VHD in minorities and underserved patients to eliminate health disparities.

Solutions

In addition to the immediate solutions identified below, roundtable participants also explored future solutions, such as insurance/coverage improvements, better aligned incentives and greater diversity in the provider workforce and selection of facilities approved to conduct transcatheter procedures. However, roundtable participants emphasized the importance of focusing on immediately actionable items, which are described in more detail below.

1. **Conduct patient outreach pre-survey/TAVR or post-refusal of treatment.** Additional research regarding patient expectation of treatment options, patient social influences in deciding on treatment options, and barriers to accepting treatment could provide the gateway to bridging the TAVR and/or surgical denial gap for minority patients. Receiving information pre-TAVR or surgery allows providers to address patient concerns and properly navigate shared-decision making with patients and caregivers. Post-refusal patient outreach and research allows providers and other medical stakeholders to follow-up with patients about treatment after possible initial shock of diagnosis. This provides an active outlet for providers to continue to learn about the most adverse barriers and best options for a patient on an individual level. Another source of research and outreach support is public health surveillance data, electronic health records or insurance claims data. These sources for collecting VHD care and treatment patterns for minority patients can be helpful in shedding light on the unclear causes for minorities opting out of surgical treatment. Understanding the causes can enhance provider understanding and promote interpersonal relations and care practices. Studies show that minorities and underserved patients frequently partner with family members when they seek care [15, 18, 20]. Both patient and family member surveys may prove viable in dissecting reasons for treatment denial. Companion provider surveys can gauge clinical awareness for VHD symptoms in minorities and understand treatment referral patterns. The aforementioned information can also help develop appropriate, informed, and effective strategies to increase patient and provider awareness through health education materials and national initiatives.

2. **Develop a taskforce to increase education and awareness.** Patient education is a pivotal step in optimizing treatment in minorities and underserved patient populations. The primary objective is to encourage partnerships for strengthening communication and awareness around valvular heart disease. Recommended strategies include convening a taskforce of varying clinical, industry and community organizations to address disparities, conducting focus groups for understanding care and treatment-seeking behavior (and use this as basis for communication), and enacting diverse communication modalities that reach underserved patients where they are (i.e. digital platforms), as well as understanding who they are (via providers). Powerful and impactful stakeholder messaging is essential to effectively reach minority and underserved patients, their caregivers and the providers that care for and treat them. Supporting partnerships and information sharing between clinical, industry and community members can have far-reaching implications for eradicating differential care and treatment access among minorities and the underserved who are living with valvular heart disease.

3. **Develop national campaign to address disparities.** Roundtable participants expressed the need for a national awareness campaign as an initial strategy in an ongoing effort to raise the profile for valvular heart disease. Greater attention to VHD is vitally important due to high mortality rates among minorities and the significant impact on elderly patients across all racial groups [13, 20]. Unlike typical VHD patients, minority and underserved patients experience early onset, between ages 65-70, and are not necessarily elderly. Death of these VHD patients can leave families without a caregiver or breadwinner and communities without important figures. Minority and underserved families more often consist of one income-earner per household, and have higher risk factors for VHD [3-5, 9, 20]. A social marketing campaign is an effective public health practice for reaching large groups within a targeted audience to encourage behavior change, and gain greater insight into their care-seeking behaviors [21, 22]. Roundtable participants emphasized key communication techniques for education, awareness, and other general communication considerations. As a first step to building an effective campaign, roundtable participants believe that additional research to understand population characteristics is essential to promote health behavior change through messages and modalities that resonate—especially among minority and underserved populations.

Call to Action

As stakeholders in the patient and cardiovascular spaces, we believe it is crucial to address healthcare access and treatment disparities in minorities and underserved patients with valvular heart disease, as these patients experience high mortality rates with low treatment rates. By crafting collaborative and diverse solutions, we aim to increase disease state and treatment awareness of VHD among minority patients, and encourage treatment. We encourage collaboration in progressing key solutions identified in the *ABC Roundtable: Addressing Disparities in Contemporary Care of the Minority Patient with Valvular Heart Disease*.

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Disclaimer
This document does not necessarily represent the opinions, policies, or recommendations of the FDA.

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About the Association of Black Cardiologists (ABC)
Founded in 1974, the Association of Black Cardiologists, Inc., (ABC) is a nonprofit organization with an international membership of 1,700 health professionals, lay members of the community (Community Health Advocates), corporate members, and institutional members. ABC is dedicated to eliminating the disparities related to cardiovascular disease in all people of color and seeks to promote the prevention and treatment of cardiovascular disease, including stroke, in blacks and other minorities and to achieve health equity for all through the elimination of disparities. The association's aggressive goal is to reduce cardiovascular disease 20% by 2025.

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Understanding Clinical and Industry Perspectives on TAVR in the US

Association of Black Cardiologists Inc.
Structural Heart Roundtable
February 24, 2023

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The better the question. The better the answer.
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Building a better working world

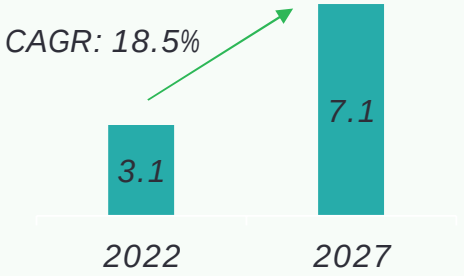
Content

1. *Clinical perspectives of TAVR*
2. *Industry perspective of TAVR*

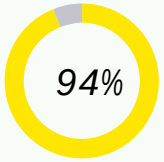
1 Clinical perspectives of TAVR

The global TAVR market is ~US$3bn as of 2022 and is expected to reach US$7bn by 2027, with North America contributing ~22%; TAVR constituted 56% of all AVR's in the US in 2019

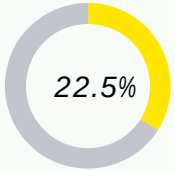
Global TAVR Market (US$bn)



Globally, over **400,000** people have undergone TAVR procedure as of 2019

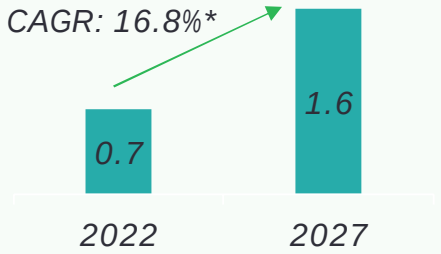


Increase in number of people undergoing AVR from 2012 to 2019 primarily due to greater disease awareness and an aging population



North America's share in global TAVR market

US TAVR Market



*North American market includes US and Canada

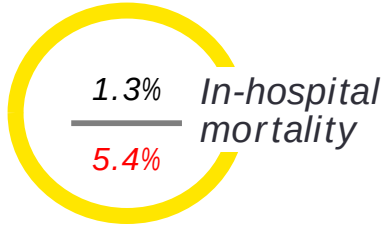
- In 2019, total of ~130K AVR were performed, with TAVR procedures constituting 56% (~73K) while 44% (~58K) received surgical valve replacement (SAVR)
- In 2021, ~92K TAVR were performed in US
- An estimated 76% of all aortic valve replacements will be done by TAVR by 2025

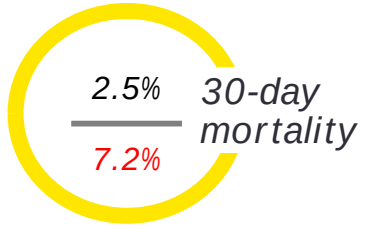
TAVR available in **50** US states (2020)

730 TAVR sites in US (2020)

Average of **84** TAVR procedures performed per site (2019)

Extreme and high-risk patients were the largest cohort undergoing TAVR till 2018; in 2019 intermediate-risk became the largest cohort after expanded FDA approval





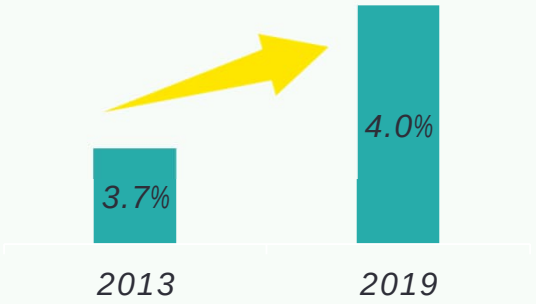
Refer slide notes for sources

Note: 'AVR' mentioned in the slide includes both TAVR and SAVR

Figures in 2019
Figures in 2011-2013

Despite TAVR's increased usage, treatment rates remain low for Black, Indigenous and People of Color (BIPOC) patients compared to White patients; the gap has narrowed marginally in recent years

% of BIPOC patients who have received TAVR for AS in US has increased marginally



Number of BIPOC patients receiving TAVR increased from ~504 in 2013 to 2,948 in 2019

As of 2021, 62% of cardiologists in US are White

BIPOC cardiologists accounts for only 5%

<2% of enrolled patients in TAVR studies are BIPOC

Refer slide notes for sources

Racial differences in use of aortic valve replacement (AVR) for treatment of AS

According to a study (based on 2007-2017 Optum's EHR data of ~32K AS patients), the AVR racial gap has narrowed due to rapid increase of TAVR use among BIPOC patients, however the likelihood of receiving AVR is still lower in BIPOC vs. White patients

Key stats highlighted in the study:

Overall rate of AVR increased from 20.1% to 37.1% (2011-16)

Likeliness to receive AVR is lower (22.9%) in BIPOC vs White patients (31%)

During 2015 to 2016, AVR White/ BIPOC utilization gaps were decreased from 35.2% to 29.5% because of greater uptake of TAVR in BIPOC (53.4%) than White patients (47.3%)

AS: Aortic stenosis
AVR mentioned in the slide includes both TAVR and SAVR

BIPOC and other minorities face multiple barriers for accessing TAVR; elective admissions to hospital, insurance and socioeconomic status are significant contributors to TAVR use gap

According to American College of Cardiology's retrospective analysis^ of 2019 National Inpatient Sample (NIS) data of US adults, there is ~12% gap exists in TAVR use between BIPOC and White patients. Below are the major contributing factors:

Factors contributing to TAVR gaps	% contribution	Supporting facts
Access to TAVR performing institutions and providers	56%	• ZIP codes with higher proportions of BIPOC patients have lower rates of TAVR procedures • In 2018, 98% of new TAVR centres opened were in metropolitan areas • BIPOC patients are less likely be referred to tertiary hospitals and tend to go to community hospitals, lacking TAVR facilities • BIPOC patients with aortic valve disease had 54% lower odds of being referred for AVR than White patients due to increased burden of comorbidities
Participants age	61%	• Approximately half of the gap in TAVR use was due to the older age of White patients diagnosed with and referred for AS
Insurance status	4.3%	• As of 2021, there was a higher percentage of uninsured BIPOC patients (10.9%) vs White patients (7.2%) • White TAVR patients were more likely to have private insurance than BIPOC patients (63% vs. 43%) while 49.3% BIPOC patients had Medicare coverage
Socio-economic status	4.1%	• Median annual wage for BIPOC workers is ~30% or $10,000, lower than that of White workers ◦ As Medicare study revealed that for each 1% increase of BIPOC patients in a zip code, the number of TAVR procedures per 100,000 Medicare beneficiaries decreased by 1.1% • Sociodemographic factors such as education level, living conditions, employment status influence access to health care, disadvantaging large numbers of BIPOC patients • BIPOC patients were more likely to refuse AVR (33%) compared to Caucasians due to poor understanding of risk-benefits, and mistrust with their predominantly Caucasian physician • In BIPOC patients, medical decisions are often reached by consensus of several family members, increasing complexity of alignment for consent for advanced medical procedures • Studies suggest that when physician demographics are more representative of patients they treat, decision making is more participatory, translating to greater patient satisfaction and better outcomes

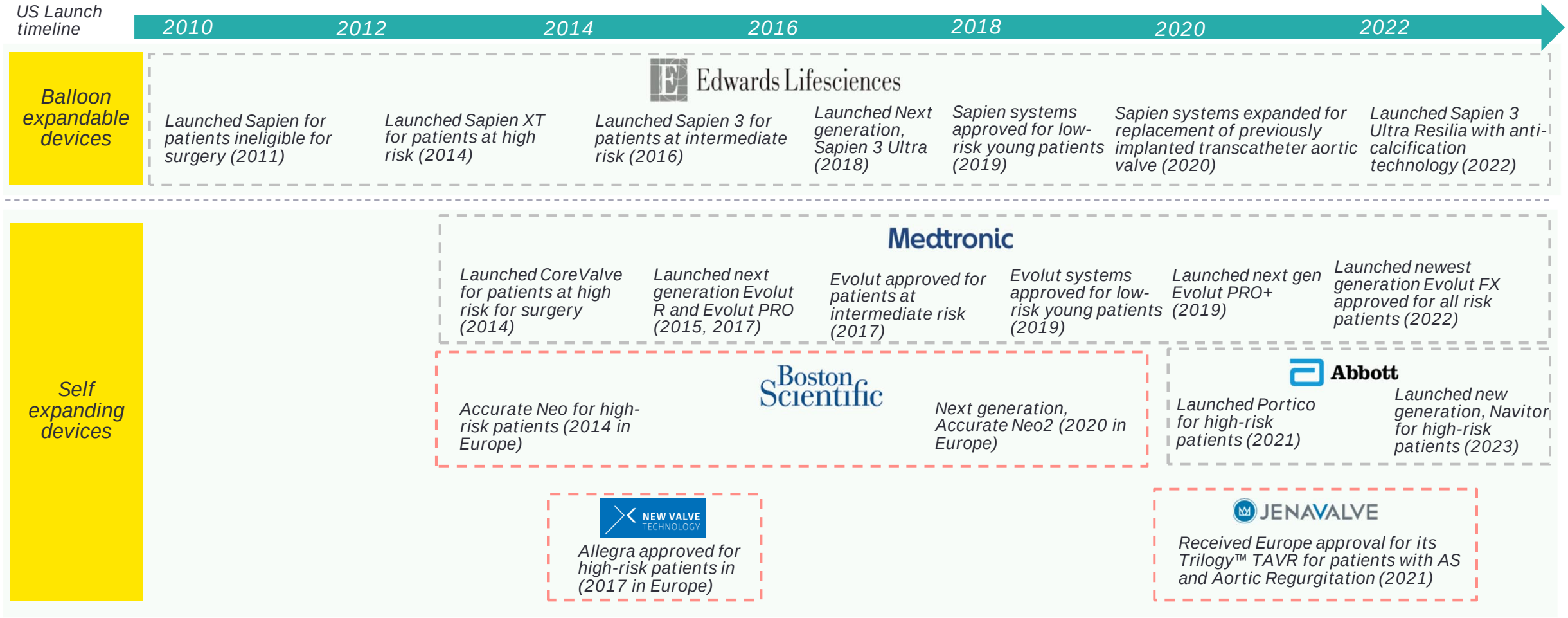
^Access to full study not available

Refer slide notes for sources

2 *Industry perspectives of TAVR*

Currently, there are 3 key players in the US TAVR market: Edward Lifesciences leading since 2011, Medtronic joining in 2014 and Abbott becoming the 3rd competitor with 2021 approval

Market evolution: Since the first launch of TAVR in high-risk inoperable AS patients, the TAVR systems have expanded to low-risk patients (including high and intermediate); alternate access sites (including transapical and transaortic); Valve-in-valve use for failed surgical prosthetic valves, and expanded to AR (aortic regurgitation) patients, along with continuous launch of next generation systems to reduce paravalvular leak*



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Available in US, Europe

Currently under trials in US, launched in Europe

**Devices approved for valve in valve use include: Edwards' Sapien 3 and Sapien XT, and Medtronic CoreValve, Evolut R, Evolut PRO*

Note: Boston Scientific launched the mechanically expandable devices, Lotus Edge in 2019 in US, however discontinued in 2020 due to design and delivery challenges

Multiple newer companies are developing innovative TAVR systems such as ready-to-use systems, and durable valves designed for lifetime and TAVR for less severe AS patients

*TAVR system pipeline^*

Company	Innovation in TAVR	Description
Edwards Lifesciences	• *TAVR for less severe patients and more durable TAVR*	• *Edward is evaluating TAVR systems (in clinical trials) for less severe patients such as moderate AS and asymptomatic AS; along with developing next generation Sapien 4 system based on RESILIA tissue with advanced anti-calcification technology*
Boston Scientific	• *Device for prevent stroke due to TAVR*	• *BS is evaluating its SENTINEL™ Cerebral Protection System which is designed to capture and remove embolic debris stemming from TAVR before it can reach the brain and potentially prevent stroke*
Colibri Heart Valve	• *Ready-to-use pre mounted TAVR systems*	• *Colibri is developing TAVR, a pre-mounted, pre-crimped and pre-packaged device that is designed to be shipped ready to use*
Genesis MedTech / JC Medical	• *TAVR systems for both AS and AR*	• *JS Medical (recently acquired by Genesis) is developing TAVR, J-Valve for treatment of both regurgitation and stenosis patients. Currently under clinical trials in US and Canada; available in China*
FOLDAX	• *Durable valves designed to last a lifetime*	• *Foldax is developing TAVR incorporating a new, proprietary biopolymer – LifePolymer™ with innovative valve designs intended to resist calcification, to withstand stresses and strains, and restore patient quality of life without lifelong use of anticoagulants*
P&F PRODUCTS & FEATURES	• *Ready-to-use pre mounted TAVR systems*	• *P&F is developing TRICVALVE® TAVR device which are fully pre-mounted with specially prepared bovine pericardium, thus reducing preparation steps and procedure time*

^Not exhaustive in nature
Refer slide notes for sources

In addition to TAVR, companies are also developing transcatheter valve replacement devices for mitral & tricuspid valves; the first TMVR device was approved in 2020

	Transcatheter Mitral Valve Replacement (TMVR) System	*Transcatheter Tricuspid Valve Replacement (TTVR) systems*
Approved	Abbott: *World's first Transcatheter Mitral Valve approved in Europe. Abbott's Tendyne TMVR system received CE mark clearance in 2020*	*Transcatheter Tricuspid Valve Replacement (TTVR) systems are under clinical trials while few repair devices have been approved in US and Europe*
	There are several transcatheter mitral repair devices approved in US and Europe, such as Abbott MitraClip and MitraClip G4	*There are several transcatheter tricuspid valve repair devices approved in Europe such as Abbott's TriClip and TriClip G4, Edwards' Pascal & CardioBand. In US only Edwards' Pascal is approved*
*Pipeline^*	neovasc: *Neovasc filed Tiara TMVR System for European CE mark in 2020*	Medtronic: *Medtronic's Intrepid TTVR System is under clinical trial and has received FDA's breakthrough device designation*
	Medtronic: *Medtronic's Intrepid TMVR System is under clinical trial*	Edwards Lifesciences: *Edward's EVOQUE and SAPIEN XT TTVR Systems are under clinical trial*
	Edwards Lifesciences: *Edward's EVOQUE, SAPIEN M3 and CardiAQ TMVR Systems are under clinical trial*	OrbusNeich: *OrbusNeich's TricValve System is under clinical trial*
	4C MEDICAL: *4C medical's AltaValve TMVR System is under clinical trial*	

^Not exhaustive
Refer slide notes for sources

MedTech companies have historically preferred ex-US countries to conduct heart device clinical studies and secure approval due to less stringent ex-US regulatory requirements

However, the US FDA has taken multiple initiatives to boost US feasibility studies resulting in accelerated approval timelines

Historically, lenient requirements led companies to prioritise ex-US markets

By the time FDA approved Edward's Sapien in 2011, it had already been approved in 40 countries, including most of Europe since 2007

Since 2010, growth in device clinical trials in US had fallen behind other countries, including Brazil, China, France, Germany and India

Europe has less stringent^ requirements for studies and hence quicker approval timelines than FDA (However, the new MDR in Europe might impact this regulatory timelines)*

Consequently, US authorities took multiple initiatives

Reduced investigational device exemptions (IDE) review time (2015)

- *Center for Devices and Radiological Health (CDRH) reduced review time to IDE (required to initiate clinical study) from a ~ 442 days in 2011 to 30 days in 2015*

Faster approval based on real world evidence (2016) :

- *FDA expanded approval of Sapien 3 in 2016 for valve in valve procedure, based on real world data from the Transcatheter Valve Therapy (TVT) registry*

Development of 'Regulatory Toolkit' (2016) :

- *CDRH developed guidance for sponsors giving more clarity on the amount of data required to support early feasibility/first-in-human studies (EFS) approval*
- *CDRH has developed division-level teams to help sponsors prepare EFS application*

Launch of breakthrough device program (2018)

- *Breakthrough device program offers several advantages (timely communication, priority review etc.) to speed up market availability*

Trends towards improvement

"First" approvals by FDA

In Aug 2019, FDA becomes the first regulatory body in the world to expand TAVR indication to low-risk patients

Narrowing gap of approval times for next generation devices

Abbott received approval for Navitor in Europe in May 2021 and in US in Jan 2023 (difference of ~1.5 years vs. 4 years in 2011)

Refer slide notes for sources

^Approval times achieved in Europe are quicker than in the United States largely due to the use of notified bodies (NB), also European requirements require demonstration that the device is safe and performs in a manner consistent with the manufacturer's intended use. Furthermore, a risk/benefit analysis is provided. While FDA requires demonstration of safety and effectiveness within the context of a specific indication

**EU has implemented new MDR (medical device regulation) effective since 2021, which has increased the scope of general safety and performance requirements, technical documentation, and clinical data and evaluation requirements and also increased post-market product surveillance*

Despite similar procedure cost, TAVR is found to provide more economic benefit for patients & payers vs. SAVR due to its benefit of better quality of life and reduced long-term costs

Despite higher TAVR valve costs compared to SAVR valve costs (US$32K vs US$5-6K), there is no major difference in the total cost of procedure

Procedure cost over time	TAVR	SAVR
• In 2012, median Medicare payments per procedure for TAVR were slightly lower than SAVR (a difference of ~$1K)	~$49K	~$50K
• In 2016, total two-year TAVR cost is slightly lower vs SAVR (a difference of ~$2K)	~$67K	~$69K

Additionally, TAVR's cost effectiveness drives further value benefits in both quality of life and survival

As per PARTNER 3 study analysis (2016-17)

- *TAVR leads to reduction of about 4.5 days in total hospital length of stay, and 2 days reduction in ICU stay*

4.5 days *Shorter hospital stays*

- *Two-year quality-adjusted life expectancy was greater with TAVR than SAVR (1.71 vs. 1.66 QALY) driven by early benefits in both quality of life and survival*

0.05 *Higher QALY* with TAVR vs SAVR*

**QALY: Quality adjusted life years*

- *According to a study published in 2019, TAVR is cost effective when compared with SAVR for AS patients at intermediate or high surgical risk*

In addition, iterative improvements in the TAVR device and delivery system over the last 10 years and improved procedural planning and operator experience led to lower rates of peri-procedural complications (i.e., major bleeding, disabling stroke, and vascular complications), that are associated with increased length of stay

Summary of cost-effectiveness of TAVR (vs. SAVR) by different patient population

Population	Δ Costs	Δ Life Expectancy	Incremental cost-effectiveness ratio (ICER)*	
Extreme Risk	↑↑↑	↑↑↑	Intermediate to High economic Value	TAVR is cost effective when compared with SAVR for AS patients at high surgical risk
Very High Risk	Similar	Slight ↑	Dominant/High economic value	
High Risk	↑↑	↑↑	Intermediate to High economic value	
Intermediate Risk	↓↓	↑	Dominant	TAVR is projected to be economically dominant because of both greater QALY and lower long-term costs than SAVR

Refer slide notes for sources

**Based on American Heart Association and American College of Cardiology guidelines ICER < $50,000/QALY gained represents high economic value; ICER between $50,000 and $150,000/QALY represents intermediate economic value; ICER > $150,000/QALY represents low economic value*

Various long-term studies have shown durability benefits (lower structural deterioration) and lower composite risk of death, myocardial infarction and stroke in TAVR vs. SAVR

Multiple clinical trials have demonstrated equivalence or superiority of TAVR over SAVR across the spectrum of surgical risk, providing basis for fundamental paradigm shifts in AS management

*Results of studies comparing TAVR vs. SAVR^*

Study name	Patients evaluated	Publishing date	Follow up time	Endpoint evaluated	Results: TAVR	Results: SAVR
SURTAVI and CoreValve US High-Risk Pivotal Trial (Link)	~2K with high and intermediate risk	2022	5 years	Structural valve deterioration	2.57%	4.38%
NOTION trial (Link)	~280 with low surgical risk	2019	8 years	Risks for all-cause mortality, stroke, or myocardial infarction	54.5%	54.8%
				Risk of structural valve deterioration	13.9%	28.3%
PARTNER 3 trial (Link)	~1K with low surgical risk	2019	1 year	Rate of composite death, stroke, or rehospitalization	8.5%	15.1%
NCT02701283 (Link)	~1.4K with low surgical risk	2019	2 years	Rate of composite death, stroke	5.3%	6.7%

^Not exhaustive
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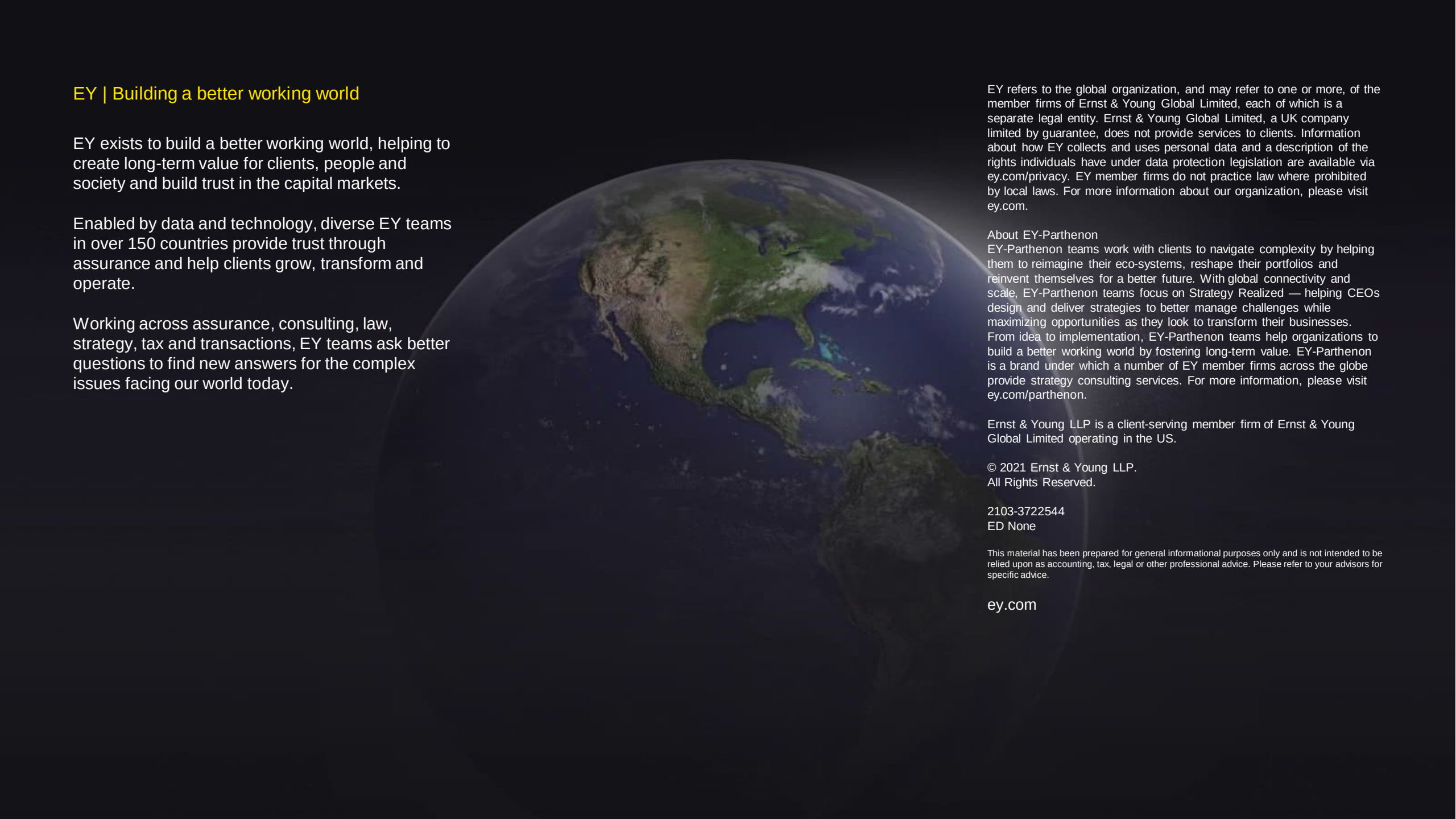

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How biopharma companies can drive greater diversity in clinical trials

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By accelerating representative diversity in clinical trial enrollment, biopharma companies enable better patient outcomes and promote growth.

As we continue to examine the deep inequities in health and health care in the US, the racial and ethnic diversity of clinical trials is top of mind for industry stakeholders as well as the Food and Drug Administration (FDA) and other public health organizations. While health inequities have been illuminated by the pandemic over the past 18 months, the need to improve participation in clinical trials by Black and Latinx people, women, elderly people and other underrepresented groups has been understood for many years.

In 2017, the National Institutes of Health (NIH) convened a group of leaders, as mandated by the 21st Century Cures Act, for a workshop on inclusion across the lifespan that resulted in two papers published in the Journal of the American Medical Association (JAMA).[1] The papers highlight gaps in trial participation by key groups, the impact that this has had in several key areas and the criticality of improving clinical trial diversity as a matter of public health. This work, along with growing prioritization of health equity issues overall, has pushed the biopharma industry toward innovation in clinical trial design. However, to drive lasting change and a more inclusive long-term approach to biopharma research and development, we must first understand why diversity in clinical trial enrollment is so important.

Current state of clinical trial diversity

Despite the disproportionate impact of conditions such as cancer, heart disease and diabetes on Black, Latinx and other vulnerable populations, most participants in biopharma studies and clinical research are of European ancestry. For example, one recent study reviewed 230 clinical trials in oncology over a recent 10-year period, finding that only 145 trials (63%) included any information about the participant's race and only 18 (8%) broke down participants by race.[2]

In addition, a 2018 data collation on clinical trials that led to FDA approvals between 1994 and 2014 revealed the median percentage of Black participants per trial ranged from 1.8% to 3.5%.[3] For Asian participants, the range was 0% to 7%, and for any group unspecified or not described as White, Black or Asian, it was 1.4% to 3.4%.[4] This is a nonrepresentative reflection of the population at large[5] and skews even further from the actual burden of cancers by race.[6]

Similarly, today's genomic databases primarily contain DNA samples from people of European ancestry. For instance, a 2019 study revealed that participation in genome-wide association studies, 78% of participants were European, 10% were Asian, 2% were African, 1% were Hispanic, and all other ethnicities represented less than 1%.[7] Ultimately, this lack of diversity impairs objective analysis of drug efficacy in communities of color and impedes our understanding of the influence of genetics on disease management.

There is also an acute need for biopharma to understand specific nuances around how some conditions manifest in patients of color. This creates greater institutional awareness around the social determinants of

health (i.e., the economic, environmental and social conditions that impact health) and has the potential to help drive better health for underrepresented populations as researchers uncover nuanced information on the differential impact of novel treatments in different races, communities and ethnicities. Examples of these nuances include but are not limited to the following:

- Even though asthma is the most common chronic childhood disease in the world,[8] disproportionately affecting Black, Puerto Rican and Native American people,[9] drug trials conducted to demonstrate the efficacy of asthma treatment have not adequately represented the populations most impacted by the disease.[10] In the US, Black and Puerto Rican children — who also have the highest prevalence of asthma nationwide — respond least well to lifesaving asthma medications such as albuterol and experience higher rates of hospitalization, poorer health outcomes and more deaths.[11] There are many underlying causes for these disparities, but recent studies demonstrate that genetic risk factors are linked to higher rates of asthma and poor response to bronchodilator medications in these populations.[12]

- Systemic lupus erythematosus (SLE) is an autoimmune disease that affects the skin, joints and several other organs. SLE also disproportionately impacts Black, Latinx and Asian patients, who are at increased risk of developing severe manifestations from the disease.[13] Despite this fact, there is insufficient medical literature describing the manifestations of SLE (and other skin diseases such as psoriasis and atopic dermatitis) on pigmented skin. For example, a 2018 study found that just 4.5% of images in medical textbooks showed disease manifestations on dark skin.[14] Hence, most medical and nursing students, along with many experienced clinicians, are unaware of how these skin diseases affect entire populations. This impedes clinicians' ability to effectively diagnose and treat skin diseases in people with pigmented skin, augmenting delayed or missed diagnoses and adverse outcomes in this demographic.[15]

- The incidence rate for inflammatory bowel disease (IBD), a chronic gastrointestinal condition, is rising three times faster among Asian, Latinx and Black patients than among White patients.[16] Studies demonstrate that Black IBD patients tend to be diagnosed later, are less likely to receive recommended biologics and immunomodulators, and are less likely to be referred to a specialist, resulting in more serious consequences from the disease.[17] The relevant literature suggests that these clinical trials have not comprised the racial and ethnic diversity needed to enable a better understanding of the efficacy of approved IBD drugs in Asian, Latinx and Black patients, since most published studies on the epidemiology and progression of IBD in the US were performed with predominantly White participants.[18]

How EY can help

EY Center for Health Equity

Health equity is the state in which health outcomes and health care costs are not determined by race, ethnicity or socioeconomic status.

Read more

Practices are starting to change, but much work still needs to be done

In one promising example, the COVID-19 vaccines with emergency use authorization from the FDA have demonstrated that diverse enrollment in clinical trials is both possible and effective.[19] By developing these vaccines with greater racial and ethnic diversity among clinical trial subjects from the very beginning, biopharma and government stakeholders have achieved a more accurate representation of the actual US population among trial participants. The scientific benefits of this approach, which drives both economic and societal value, cannot be overstated.

Along with biopharma companies, the Pharmaceutical Research and Manufacturers of America (PhRMA), NIH and FDA have recently taken significant steps to enhance racial and ethnic diversity in clinical trials.[20] These measures include developing guidance to drive more inclusive research and promote relationship-building in underserved communities. For example, one biopharma company has created a clinical trial diversity alliance "to advance the representation of diverse patient populations in the company's oncology clinical trials, test recruitment and retention approaches, and establish best practices that can be leveraged across the industry to help achieve health equity for people with cancer."[21] Adopting and scaling these strategies across all drugs and therapeutics is essential to enhance the positive impact these therapeutics are designed to achieve.

The path forward

Biopharma organizations need to continue to prioritize initiatives that address health equity, with improving clinical trial participation and recruiting being a critical starting point.

There are three key actions that will help drive this effort:

1. Focus on creating a culture of equity and inclusion across your business

- Prioritize diversity, equity and inclusion (DEI) principles and competencies across all functions within the business to facilitate greater understanding of the cultural nuances that enable effective, diverse clinical trials and inform evidence-based treatment for all racial and ethnic groups
- Develop specific goals and compliance metrics for diverse representation in all self-sponsored clinical trials that seek to inform efficacy of new therapeutics across all races and ethnicities
- Invest in strategies that drive more diverse genomic databases and collaborate with leaders in academia to develop precision medicine for at-risk and understudied populations

2. Challenge partners to prioritize DEI-related goals

- Devise communication strategies to set expectations for diverse clinical trial enrollment at all partnering clinical trial site organizations

- Provide investigators and clinicians with resources and content to mitigate biases in the development and/or administration of clinical trials
- Create customized content for communities of color that promotes the safety, benefits and value of diverse clinical trial enrollment

3. Leverage technology

- Use artificial intelligence and machine learning to mine structural, social, biological and behavioral population data to identify larger portfolios of diverse candidates that meet criteria for clinical trials
- Utilize digital platforms to connect more diverse participants with clinical trial sites and investigators, and electronically track real-time enrollment at clinical trial sites to drive visibility and accountability for diverse participation

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Summary

To drive drug approval for therapeutics that benefit all populations, biopharma companies must commit to more strategic participation that enables diverse, representative enrollment in their clinical trials. Aligning on this imperative by redesigning clinical trial business models that drive equal therapeutic value throughout the diversity of humanity will deliver equitable health outcomes for us all.

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JACC FOCUS SEMINAR: RACE, ETHNICITY, AND HEART DISEASE

JACC FOCUS SEMINAR

Valvular Heart Disease in Relation to Race and Ethnicity

JACC Focus Seminar 4/9

Julio A. Lamprea-Montealegre, MD, PhD,[a] Shakirat Oyetunji, MD,[b] Rodrigo Bagur, MD, PhD,[c] Catherine M. Otto, MD[d]

ABSTRACT

Valvular heart disease (VHD) is a major global public health problem. Many regions of the world continue to grapple with the adverse consequences of untreated rheumatic heart disease, a condition that is largely preventable with timely access to diagnosis and treatment. In turn, middle- and high-income countries have experienced a rise in the prevalence of calcific aortic and mitral disease, owing in part to population aging. This public health problem is further compounded by high rates of infective endocarditis, which is associated with substantial morbidity and mortality. Yet, considerations of race and ethnicity have not taken center stage in VHD research. This is despite evidence of major health care disparities in socioeconomic and medical risk factors, access to diagnosis, and provision of appropriate treatment. In this paper, the authors review differences in the etiology, diagnosis, and treatment of VHD within the context of race, ethnicity, and health care disparities. (J Am Coll Cardiol 2021;78:2493–2504) © 2021 by the American College of Cardiology Foundation.

Race has been defined as "a social construct primarily based on phenotype, ethnicity, and other indicators of social differentiation that results in varying access to power and social and economic resources" (1). As such, the unique use of discrete self-identified race and ethnicity categories as proxies for genomic variation and ancestral background has profound limitations (2). Conversely, racial and ethnic categories are more useful in understanding systematic differences in the burden of cardiovascular disease caused by social determinants of health that include economic stability, access to quality education, social and community context, and access to quality health care. In addition, structural racism, which is pervasive in the U.S. health care system (1), is a major determinant of health care disparities. These disparities encompass "differences in health care quality, access, and outcomes adversely affecting members of racial and ethnic minority groups and other socially disadvantaged populations" (3). Finding solutions to overcome these disparities must be an integral component of the quest to improve cardiovascular health (4).

The past decade has seen major breakthroughs in the diagnosis and treatment of valvular heart disease (VHD). Multimodality imaging has offered new opportunities for improved diagnosis and staging. In turn, transcatheter interventions for valve repair and replacement have changed the landscape of treatment options, especially for high-risk patients. However, there is mounting evidence that inequitable access to health care has systematically prevented

Listen to this manuscript's audio summary by Editor-in-Chief Dr Valentin Fuster on JACC.org.

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

AS = aortic stenosis

BAV = bicuspid aortic valve

DOAC = direct oral anticoagulant

ECG = electrocardiography

IDU = injection drug use

IE = infective endocarditis

MVP = mitral valve prolapse

RHD = rheumatic heart disease

SAVR = surgical aortic valve replacement

TAVR = transcatheter aortic valve replacement

VHD = valvular heart disease

VKA = vitamin K antagonist

racial and ethnic minorities from fully benefiting from these advancements. Recent calls have been made to intensify research efforts to identify and overcome determinants of existing racial and ethnic health care disparities in VHD (5). Accordingly, this review will summarize the available literature on VHD according to its etiology, diagnosis, and treatment within a context of race, ethnicity, and health care disparities (**Central Illustration**).

HIGHLIGHTS

- Disparities based on race and ethnicity are pervasive in the care of patients with VHD.
- Surgical and transcatheter treatments are widely underutilized among racial and ethnic minorities.
- Future research should address barriers to diagnosis and treatment of VHD among members of racial and ethnic minority groups.

EPIDEMIOLOGY OF VHD

The epidemiology of VHD differs depending on the etiology, which can be classified in valve disorders with a strong genetic basis, valve disorders with strong influence from environmental factors, and calcific valve disease, which is strongly influenced by both genetic and environmental factors.

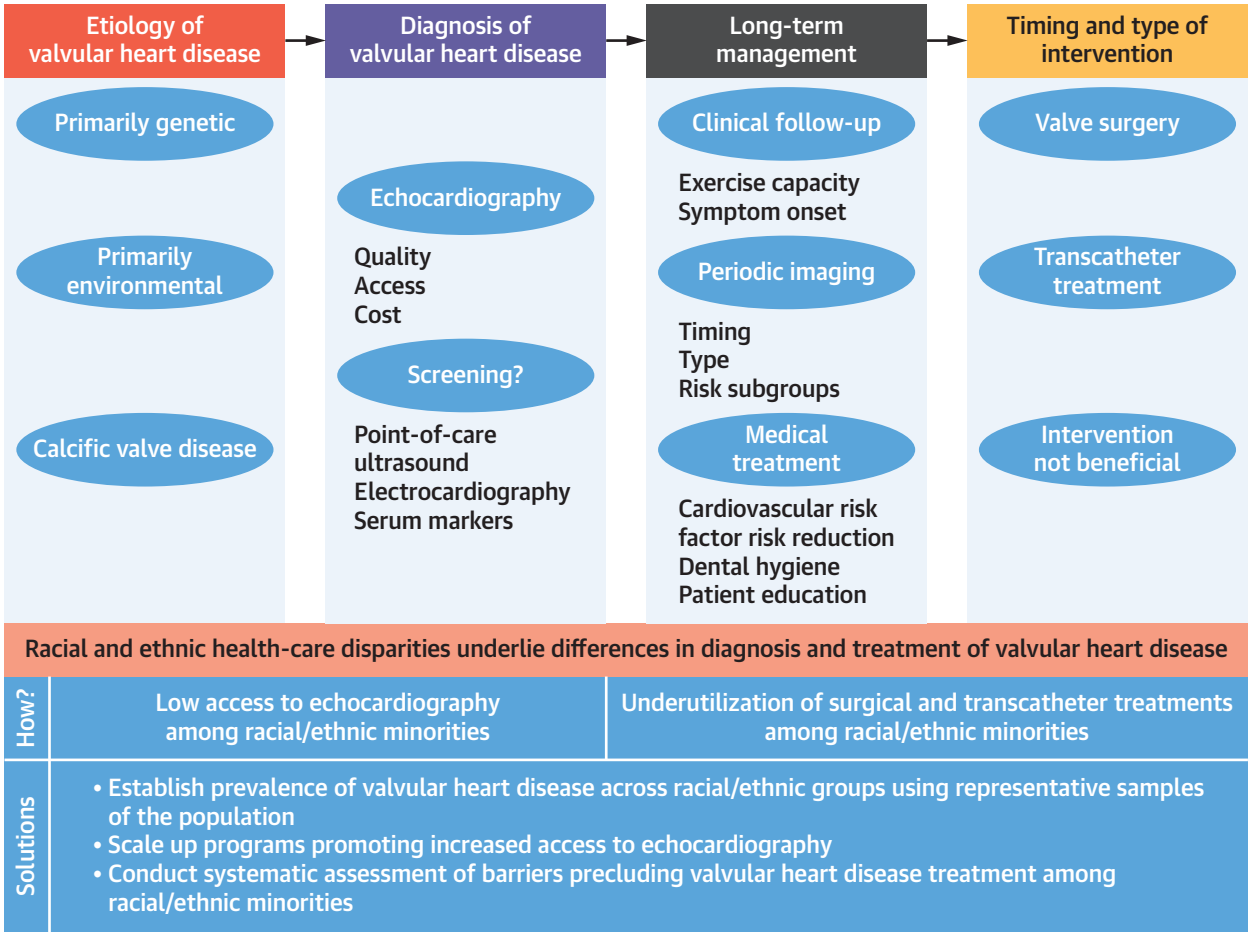
VHD WITH STRONG GENETIC BASIS. Mitral valve prolapse (MVP) and bicuspid aortic valve (BAV) are relatively frequent valve disorders with familial clustering and high heritability (6,7). Prevalence estimates in nonprobabilistic samples of population-based studies range from 2%-3% for MVP and from 0.5%-1.5% for BAV (8). In MVP, prevalence estimates have been remarkably similar across racially and ethnically diverse studies including the Framingham Offspring Heart Study of mainly White participants, the Strong Heart Study of American Indian participants, and a multiethnic population-based study of South Asian, European, and Chinese participants (8-10). For BAV, one retrospective study from a single academic medical center reported higher prevalence of BAV in White than in Black patients (1.1% and 0.17%, respectively) (11). Yet, the nonprobabilistic nature of the sample and the possibility of referral bias preclude the generalizability of these results.

VHD WITH STRONG ENVIRONMENTAL DETERMINANT. The Global Burden of Disease study estimated that there were >33 million cases of rheumatic heart disease (RHD) with >300,000 deaths in 2015 (12). Because RHD can be prevented by timely access to antibiotic treatment and quality health care, few diseases exemplify the effect of social inequities and health care disparities as RHD. Only 5 countries (India, Pakistan, China, Indonesia, and the Democratic Republic of Congo) account for nearly 75% of global cases (11). Prevalence estimates of RHD vary widely between geographic regions, with the highest global prevalence observed in certain countries in Oceania and South Asia, which have age-standardized prevalence rates exceeding 1,000 cases per 100,000 individuals (12). Although the overall prevalence of RHD is very low in high-income countries, marked disparities within countries continue to exist disproportionally affecting socioeconomically disadvantaged populations (13).

INFECTIVE ENDOCARDITIS. Over the past decades, the epidemiology of infective endocarditis (IE) in high-income countries has shifted from cases associated with RHD to IE associated with calcific valve disease, prosthetic valve endocarditis, and cardiac device-related endocarditis (14). In the United States, the opiate epidemic has also led to increased incidence of IE secondary to injection drug use (IDU), mainly affecting young and middle-aged Americans (15). Although data about racial or ethnic disparities in IE associated with IDU are lacking, overdose mortality from IDU disproportionally affects American Indian and Alaska Natives compared with other racial and ethnic groups (16).

CALCIFIC VALVE DISEASE. Calcific aortic and mitral valve disease is the most prevalent valve disease in high-income countries (17). Some studies have reported a lower prevalence of AS in patients from racial and ethnic minorities compared with White patients. An analysis from the nationwide Healthcare Cost and Utilization Project database reported significantly lower odds of a diagnosis of AS in Black, Hispanic, and Asian patients compared with White patients (18). Similarly, in a large retrospective study of echocardiographic records form a single academic medical center, Black patients were found to have 60% lower odds of severe AS than White patients (19). Because racial and ethnic minorities have historically had lower access to diagnostic imaging and cardiac procedures (20,21), these observed differences in prevalence based on hospital data may be representative of differential access to AS diagnosis and treatment, rather than of biological differences in

CENTRAL ILLUSTRATION **Racial and Ethnic Health Care Disparities in Valvular Heart Disease Etiology, Diagnosis, and Treatment**



Lamprea-Montealegre, J.A. et al. J Am Coll Cardiol. 2021;78(24):2493–2504.

disease occurrence. Therefore, studies with representative samples of the general population must be conducted to estimate the population-wide prevalence of calcific valve disease across racial and ethnic groups.

DIAGNOSIS OF VHD

In most patients, the initial diagnosis of VHD is made based on echocardiography requested for other indications or the onset of cardiac symptoms, in conjunction with a murmur on auscultation. Unfortunately, numerous studies have shown that physical examination is not reliable for identifying patients with VHD and accuracy is not improved by additional training or experience (22). For example, in a study of 251 asymptomatic patients >65 years of age with no known VHD, echocardiography demonstrated mild VHD in 68% and significant VHD in 14% of participants. However, the sensitivity of auscultation was only 32% for mild and 44% for severe VHD (23). Simple tests including chest radiography and electrocardiography (ECG) are rarely helpful for diagnosis of VHD, although the presence of ECG criteria for left ventricular hypertrophy, in the absence of a history of hypertension, should prompt further evaluation (24). Deep learning analysis of ECG for diagnosis of aortic stenosis has been proposed and might allow population-based screening if validated in other studies (25).

Echocardiography is the key to diagnosis of the presence and severity of VHD, supplemented by additional testing in specific clinical situations (**Table 1**). Although there are little data, racial and

TABLE 1 Evaluation of Patients With Known or Suspected VHD

Reason	Test	Indication
Initial evaluation: All patients with known or suspected valve disease	TTE[a]	Establishes chamber size and function, valve morphology and severity, and effect on pulmonary and systemic circulation
	History and physical	Establishes symptom severity, comorbidities, valve disease presence and severity, and presence of HF
	ECG	Establishes rhythm, LV function, and presence or absence of hypertrophy
Further diagnostic testing: Information required for equivocal symptom status, discrepancy between examination and echocardiogram, further definition of valve disease, or assessing response of the ventricles and pulmonary circulation to load and to exercise	Chest x-ray film	Important for the symptomatic patient; establishes heart size and presence or absence of pulmonary vascular congestion, intrinsic lung disease, and calcification of aorta and pericardium
	TEE	Provides high-quality assessment of mitral and prosthetic valve, including definition of intracardiac masses and possible associated abnormalities (eg, intracardiac abscess, LA thrombus)
	CMR	Provides assessment of LV volumes and function, valve severity, and aortic disease
	PET CT	Aids in determination of active infection or inflammation
	Stress testing	Gives an objective measure of exercise capacity
	Catheterization	Provides measurement of intracardiac and pulmonary pressures, valve severity, and hemodynamic response to exercise and drugs
Further risk stratification: Information on future risk of the valve disease, which is important for determination of timing of intervention	Biomarkers	Provide indirect assessment of filling pressures and myocardial damage
	TTE strain	Helps assess intrinsic myocardial performance
	CMR	Assesses fibrosis by gadolinium enhancement
	Stress testing	Provides prognostic markers
	Procedural risk	Quantified by STS (Predicted Risk of Mortality) and TAVR scores
	Frailty score	Provides assessment of risk of procedure and chance of recovery of quality of life
Preprocedural testing: Testing required before valve intervention	Dental examination	Rules out potential infection sources
	CT coronary angiogram or invasive coronary angiogram	Gives an assessment of coronary anatomy
	CT: Peripheral	Assesses femoral access for TAVR and other transcatheter procedures
	CT: Cardiac	Assesses suitability for TAVR and other transcatheter procedures

Reprinted with permission from Otto et al (27). [a]TTE is the standard initial diagnostic test in the initial evaluation of patients with known or suspected VHD.

CMR = cardiac magnetic resonance; CT = computed tomography; ECG = electrocardiogram; HF = heart failure; LA = left atrial; LV = left ventricular; PET = positron emission tomography; STS = The Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography; VHD = valvular heart disease.

ethnic inequities are likely in terms of access to echocardiography. In addition, financial constraints and potential implicit biases in referral for diagnostic imaging even when patients do present with symptoms are likely.

The ability of primary care providers to identify which patients would benefit from echocardiography is low. For example, in a study from Brazil, remote reading of screening echocardiograms obtained by providers with minimal training showed aortic stenosis in 5.4% and mitral regurgitation in 8.9% of patients who had not been identified as having a clinical indication for echocardiography (26). All these factors may contribute to racial and ethnic disparities in diagnosis of VHD, with diagnosis being made later in the disease course when outcomes after intervention are often suboptimal. Indications for echocardiography across all racial and ethnic groups are the presence of any diastolic murmur, a loud systolic murmur, or any systolic murmur if cardiac symptoms are present, including the subtle onset of reduced exercise capacity (27).

The 2015 American Society of Echocardiography and European Association of Cardiovascular Imaging guidelines for chamber quantification established reference values for measures of chamber size, aortic root, and ascending aorta indexed for sex and body size (28). A limitation of these normative values is that the data that were used for their derivation comprised mainly White participants in the United

TABLE 2 Medical Therapy Recommendations for Patients With VHD

VHD	Recommendations	Racial/Ethnic Knowledge Gaps
Medical treatment of cardiovascular risk factors	In patients at risk for developing AS and in patients with asymptomatic AS, hypertension should be treated according to GDMT In all patients with calcific AS, statin therapy is indicated	Access to CVD preventive therapies and attainment of cardiovascular risk factor control across race/ethnic groups
IE antibiotic prophylaxis before dental procedures	1. Prosthetic cardiac valves 2. Prosthetic material used for valve repair 3. Previous IE 4. Unrepaired cyanotic heart disease or repaired congenital heart disease, with residual shunts or valvular regurgitation at the site of or adjacent to the site of a prosthetic patch or device 5. Cardiac transplant with valve regurgitation due to structurally abnormal valve	Utilization of guideline-recommended antibiotic prophylaxis across race/ethnic groups Rates of IE in patients with indication to receive antibiotic prophylaxis across race/ethnic groups
Anticoagulation for AF in native VHD (except rheumatic mitral stenosis)	VKA or DOAC in patients with AF and CHA_2DS_2-VASc score ≥2	Differential utilization of VKA vs DOACs across race/ethnic groups
Anticoagulation for AF in rheumatic mitral stenosis	Long-term VKA anticoagulation	Time at target INR across race/ethnic groups Complications from VKA across race/ethnic groups
Antithrombotic therapy for bioprosthetic valves	VKA or DOAC if atrial fibrillation before procedure or after 3 months of valve implantation VKA if new onset AF within 3 months of valve implantation Aspirin 75-100 mg in patients without AF	Time at target INR across race/ethnic groups Complications from VKA across race/ethnic groups Utilization of antiplatelet agents across race/ethnic groups
Antithrombotic therapy for mechanical valves	Anticoagulation with a VKA and INR monitoring Aspirin 75-100 mg in addition to anticoagulation with a VKA	Time at target INR across race/ethnic groups Complications from VKA across race/ethnic groups

Reprinted with permission from Otto et al (27).

ACC = American College of Cardiology; AHA = American Heart Association; AF = atrial fibrillation; AS = aortic stenosis; CHA_2DS_2-VASc = congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack or thromboembolism, vascular disease, age 65-74 years, sex category; CVD = cardiovascular disease; DOAC = direct oral anticoagulant; GDMT = guideline-directed medical therapy; IE = infective endocarditis; INR = international normalized ratio; VKA = vitamin K antagonist.

States and Europe. The World Alliance Societies of Echocardiography Normal Values Study, which enrolled a multiethnic and racially diverse population across 15 countries (29), did not find evidence of differences in left ventricular dimensions and volumes between White and Black participants. The largest source of variability in left ventricular volumes was found between countries even after indexing for body surface area. The authors concluded that nationality should be considered for defining ranges of normality. With computed tomographic imaging, different thresholds for abnormal valve calcification have been established for men vs women, but there are no data on racial and ethnic differences.

Given the limited accuracy of clinical history and physical examination for identification of patients with VHD, screening with point-of-care cardiac ultrasound studies by providers with limited training in image acquisition has been proposed for populations with a high prevalence of RHD (30). Screening of >1,000 students in Uganda identified border RHD in 3.3% and definite RHD in 1.2% (31). In a study of >12,000 Brazilian students (median age 12.9 years, 55% female), the overall prevalence of RHD was 4.0%, with higher prevalence in girls (4.9% vs 4.0%; $P = 0.02$) but no differences between students at public schools, private schools, and primary care centers (30).

Screening for calcific valve disease in older adults has received less attention. In a UK-based study of 2,500 individuals 65 years of age or older, echocardiography identified VHD in 51% of participants, including aortic sclerosis in 34%, mitral regurgitation in 22%, aortic regurgitation in 15%, and significant aortic stenosis in 1.3%. Although data on racial or ethnic differences were not provided, the likelihood of undiagnosed VHD was twice as likely in the 2 most deprived socioeconomic quintiles (32).

The role of family screening for VHD with a strong genetic component remain controversial. Screening of first-degree relatives of patients with a bicuspid valve identifies another affected individual in about 20%-30% of families (33). Early identification of a bicuspid valve exposes the patient to a lifetime of periodic imaging even though most do not develop valve dysfunction until the fifth to seventh decade of life due to superimposed calcific valve disease. A minority of patients with a bicuspid valve have

TABLE 3 Racial and Ethnic Differences in Number of Valve Admissions and Procedures

Diagnosis or Procedure	White	Black	Hispanic	First Author, Year (Ref. #)
Admission for AS[a]	26	9.5	–	Alqahtani, 2018 (38)
% with SAVR[b]	11.3%	6.7%	–	
Admission for AS[c]	90%	10%	–	Yeung, 2013 (39)
% with SAVR[c]	53%	39%	–	
TAVR[d]	43.1	18.0	21.2	Alkhouli, 2019 (42)
TEER[d]	5.0	3.2	3.2	Alkhouli, 2019 (42)

[a]Cases per 100,000 patient-years in 2014. [b]Ratio of aortic valve replacement to AS-related admissions. [c]Sample of 880 patients with severe AS from 2004 to 2010 at Barnes-Jewish Hospital. [d]Procedures per 100,000 U.S. population >65 years of age from the National (Nationwide) Inpatient Sample (2011-2016).

AS = aortic stenosis; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement; TEER = transcatheter edge-to-edge repair.

significant regurgitation that requires intervention earlier in life, but these patients typically are diagnosed based on the presence of a diastolic murmur. One concern suggesting that early diagnosis of bicuspid valve disease may be beneficial is the associated aortopathy, with a small subset of patients having progressive aortic dilation and a higher risk of aortic dissection. There are no data on whether there are racial or ethnic differences in the risk of adverse aortic outcomes in patients with bicuspid aortic valve disease that would affect timing and type of imaging follow-up.

TREATMENT OF VHD

MEDICAL TREATMENT. There are no known medical therapies to prevent progression of VHD. However, the updated American College of Cardiology/American Heart Association 2020 valve guidelines recommend blood pressure management according to guideline-directed medical therapy in all patients at high risk for AS and in patients with asymptomatic AS (**Table 2**) (27). In addition, statins are recommended for all patients with calcific AS. The basis for these recommendations is that AS is a strong marker of risk for atherosclerotic cardiovascular disease including obstructive coronary artery disease and for cardiovascular mortality unrelated to progression of VHD. Therefore, clinical care should seek to attain optimal cardiovascular risk factor control in this population. In the general population, however, there are profound disparities in the control of cardiovascular risk factors and in the access to statins across race and ethnic groups (34,35). Indeed, compared with White patients, Black and Hispanic patients are substantially less likely to utilize a statin for secondary cardiovascular disease prevention (35).

There is a paucity of data regarding racial and ethnic differences in utilization of guideline-recommended antibiotic prophylaxis for IE or in the utilization of antiplatelet and anticoagulation therapies for VHD (**Table 2**). The updated American College of Cardiology/American Heart Association valve guidelines recommended direct oral anticoagulants (DOACs) as an alternative to vitamin K antagonists (VKAs) in patients with atrial fibrillation (AF) and native valve disease excluding rheumatic mitral stenosis and in patients with AF who received a bioprosthetic valve more than 3 months before (27). Yet, it is not known whether utilization of DOACs differs by race and ethnicity in patients with VHD. In patients with AF without known VHD, DOACs are prescribed less often to Black patients compared with White patients (36). In addition, for patients with AF on VKAs, the median time in therapeutic anticoagulation range has been shown to be much lower in Black and Hispanic patients than in White patients (36). New basic science insights into the cellular and molecular pathophysiology of valve calcification suggest that therapies targeted at these pathways might be effective. It will be essential that future clinical trials of potential therapies include racially and ethnically diverse patient populations.

TABLE 4 Racial and Ethnic Differences in Valve Procedure Outcomes

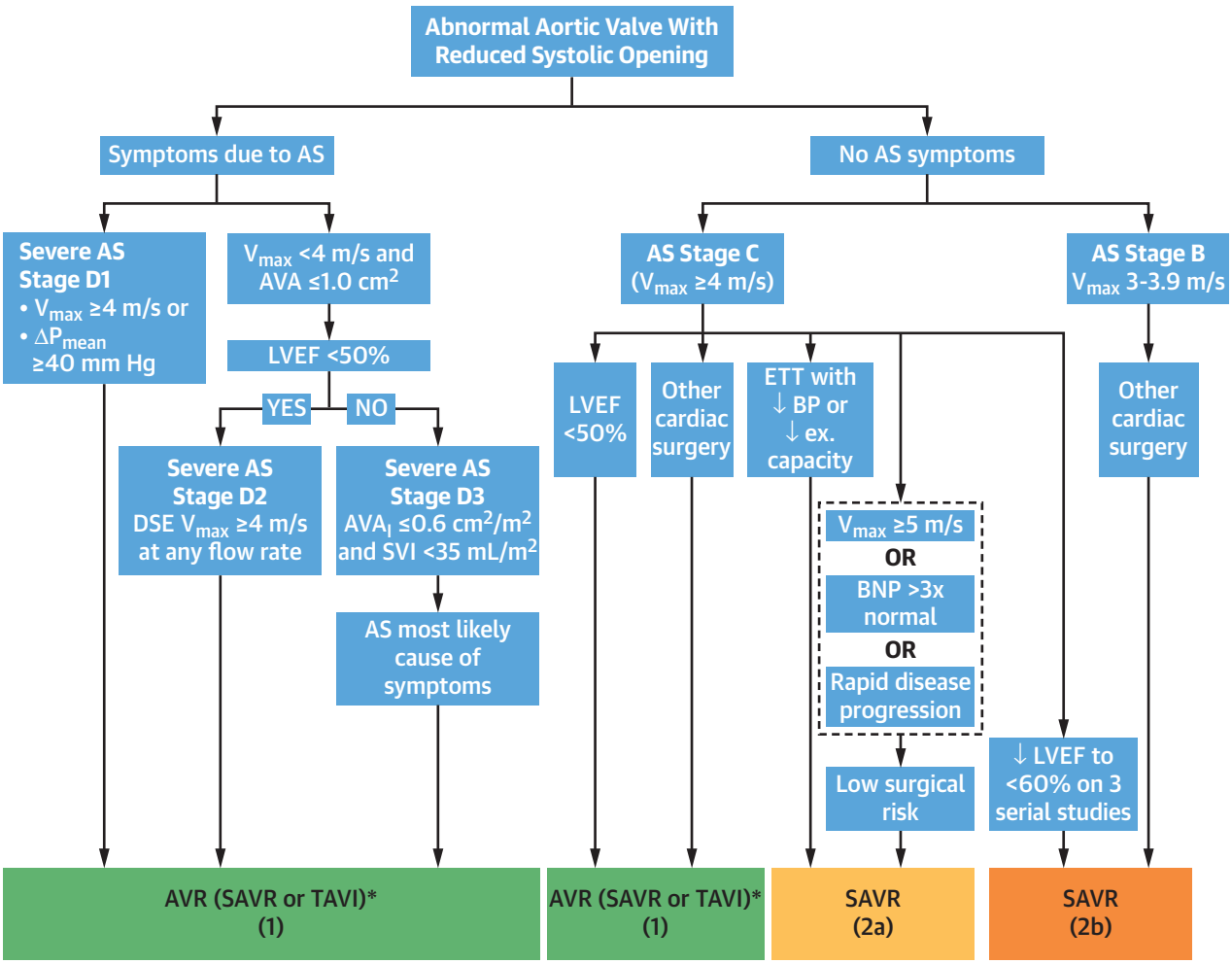
Procedure	Outcome	White	Black	Hispanic	First Author, Year (Ref. #)
SAVR	Death	4.7	6.4[a]	–	Alqahtani, 2018 (38)
	Propensity matched	3.7	4.7		
	Stroke	2.7	3.9[a]	–	
	Propensity matched	3.1	3.4		
	Pacer	7.3	7.7	–	
	Propensity matched	5.2	6.6		
	Vascular complications	5.0	5.0	–	
	Propensity matched	3.8	3.6		
SAVR	Death	49	50		Yeung, 2013 (39)
TAVR	Death	2.8	2.1	3.3	Alkhouli, 2019 (42)
	Stroke	2.3	2.6	2.3	
	Pacer	12.6	13.0	15.4[a]	
	Vascular complications	7.0	6.6	9.5[a]	
Mitral TEER	Death	2.25	1.6	1.9	Alkhouli, 2019 (42)
	Stroke	0.8	1.6	0.9	
	Vascular complications	4.7	2.4	2.7	

Values are %. [a]$P < 0.001$ compared with White patients.

Abbreviations as in Table 3.

SURGICAL TREATMENT. Health care disparities in the surgical management of VHD across racial and ethnic groups have been documented (37). In a study of 96,278 patients admitted for AS from 2003 to 2014, Black patients were less likely to undergo surgical aortic valve replacement (SAVR) than were White patients (6.7% vs 11.3%; $P < 0.001$) (**Table 3**) (38). Black patients, compared with White patients,

FIGURE 1 **Timing of Intervention for AS (American College of Cardiology/American Heart Association Guidelines)**

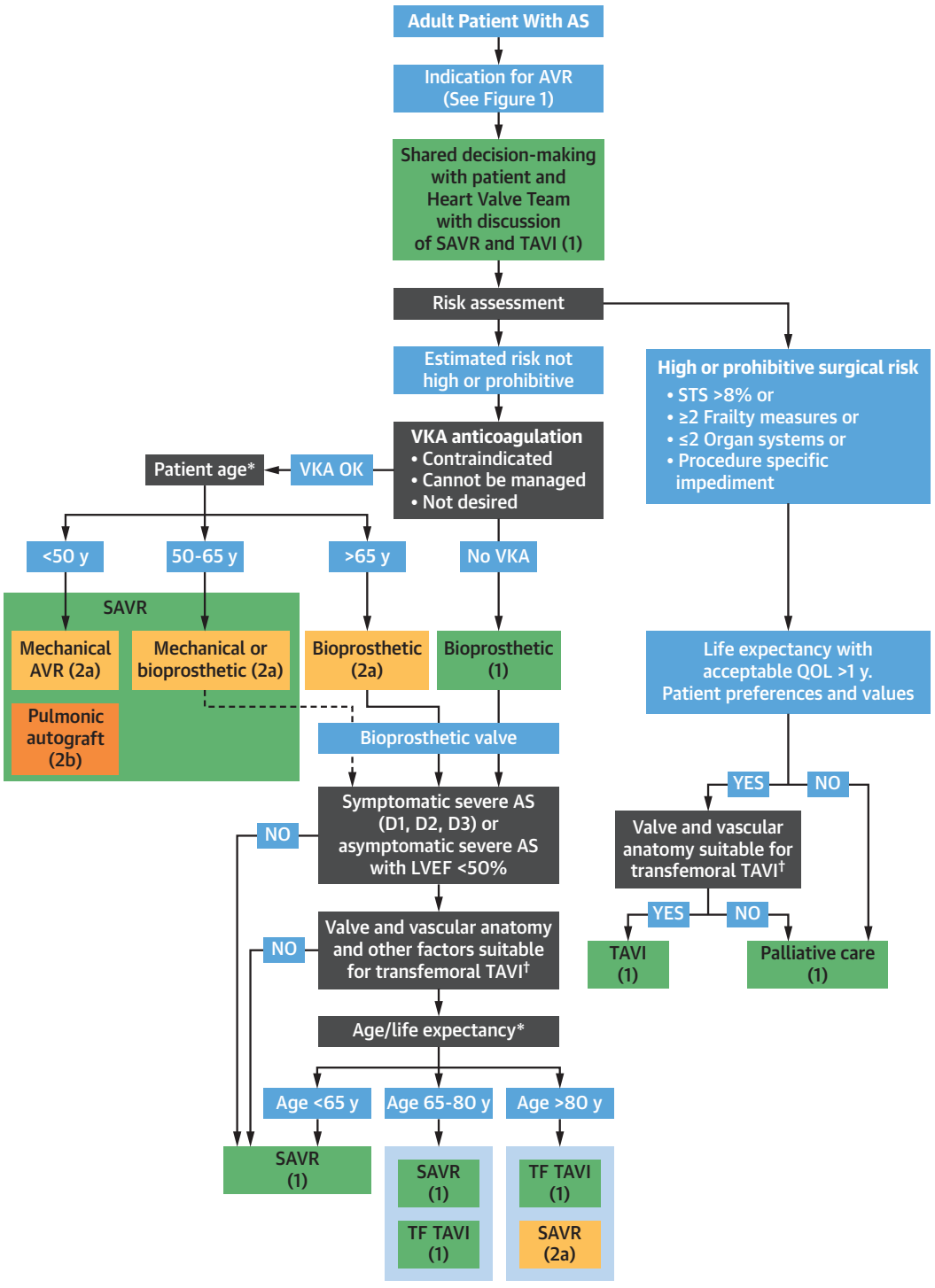


*See **Figure 2** for recommendations regarding the choice of SAVR vs TAVI. Reprinted with permission from Otto et al (27). AS = aortic stenosis; AVA = aortic valve area; AVAi = aortic valve area index; AVR = aortic valve replacement; BNP = B-type natriuretic peptide; BP = blood pressure; DSE = dobutamine stress echocardiography ETT = exercise treadmill test; LVEF = left ventricular ejection fraction; ΔP_{mean} = mean systolic pressure gradient between left ventricle and aorta; SAVR = surgical aortic valve replacement; SVI = stroke volume index; TAVR = transcatheter aortic valve replacement; V_{max} = maximum velocity.

also had longer hospitalizations (12 days vs 10 days; $P < 0.001$) and higher rates of nonhome discharge (32% vs 27%; $P < 0.04$) (38). Similar findings were reported in a single-center retrospective study of 880 patients with severe AS, with Black patients undergoing SAVR less frequently than White patients (39% vs 53%; $P = 0.02$) (39). In both studies, survival after valve surgery did not significantly differ between Black and White patients (**Table 4**).

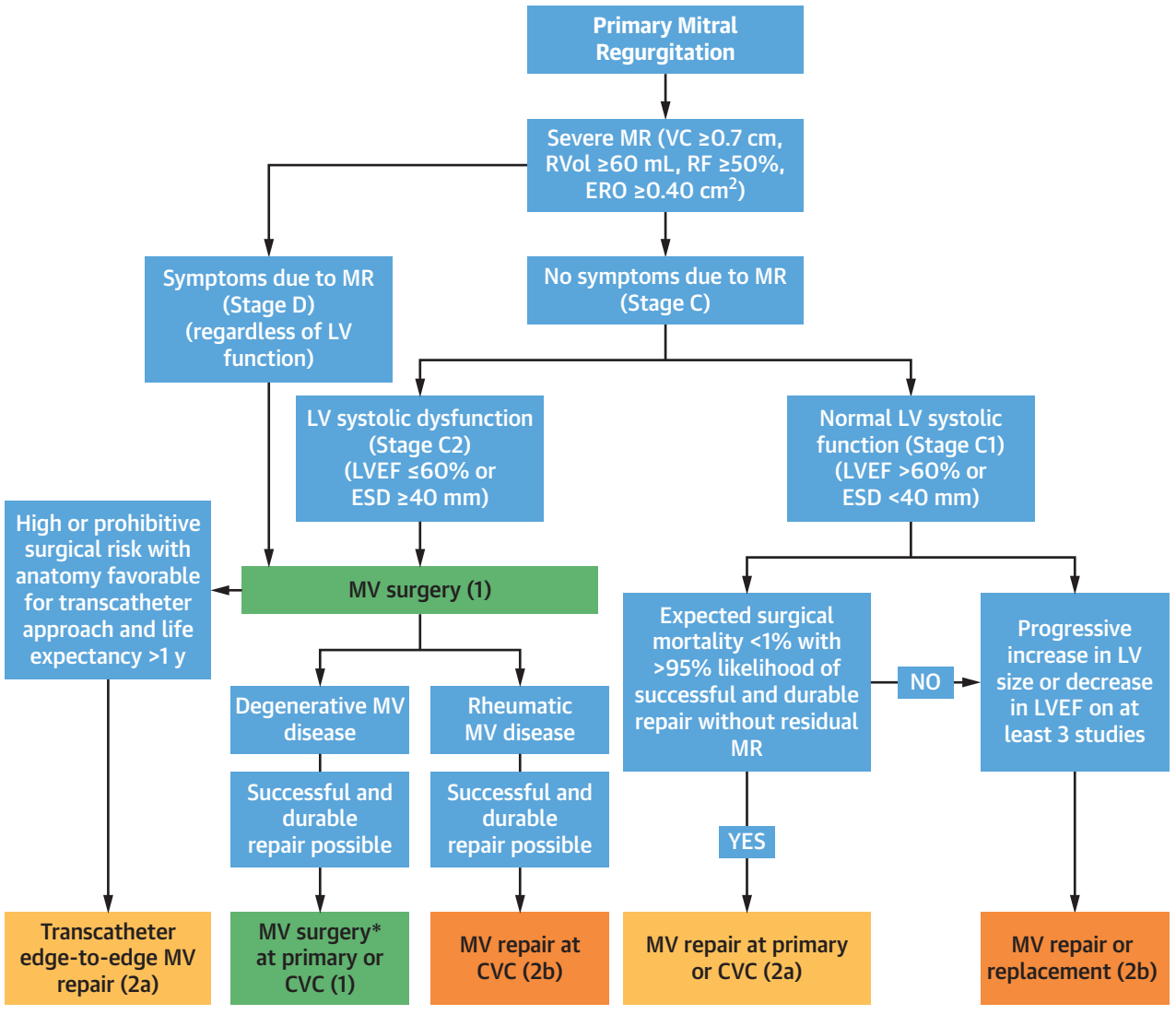
Less is known about racial and ethnic disparities in mitral valve surgery. A retrospective study of 2 medical centers comprising 1,425 patients found significant differences in the indication and types of procedures between Black and White patients between 1996 and 2003 (40). Black individuals represented 8.6% of patients and presented for mitral valve surgery at a significantly younger age than White individuals (45 vs 60 years of age). White patients more commonly had degenerative mitral disease, and Black patients had significantly higher incidence of endocarditis and rheumatic mitral disease and were less likely to undergo mitral valvuloplasty. The authors of this study concluded that the decreased rates of mitral valvuloplasty in Black patients may have an effect on long-term outcome, and improved screening will facilitate earlier

FIGURE 2 **Choice of SAVR Vs TAVR When AVR Is Indicated for Valvular AS (American College of Cardiology/American Heart Association Guidelines)**



*Approximate ages, based on U.S. Actuarial Life Expectancy tables, are provided for guidance. †Placement of a transcatheter valve requires vascular anatomy that allows transfemoral delivery and the absence of aortic root dilation that would require surgical replacement. Valvular anatomy must be suitable for placement of the specific prosthetic valve, including annulus size and shape, leaflet number and calcification, and coronary ostial height. Reprinted with permission from Otto et al (27). QOL = quality of life; STS = The Society of Thoracic Surgeons; TF = transfemoral; VKA = vitamin K antagonist; other abbreviations as in Figure 1.

FIGURE 3 **Intervention for Primary MR (American College of Cardiology/American Heart Association Guidelines)**



*See Prosthetic Valve section (11.1.2) in Otto et al (27) for choice of mitral valve replacement if mitral valve repair is not possible. Reprinted with permission from Otto et al (27). CVC = Comprehensive Valve Center; ERO = effective regurgitant orifice; ESD = end-systolic dimension; MR = mitral regurgitation; MV = mitral valve; MVR = mitral valve replacement; RF = regurgitant fraction; RVol = regurgitant volume; VC = vena contracta; other abbreviations as in Figure 1.

referral, increasing the potential for mitral valvuloplasty.

Isolated tricuspid valve surgery remains rare compared with the overall prevalence of moderate-to-severe tricuspid insufficiency, which is estimated to affect approximately 1.6 million persons in the United States (41). Health care disparities have been well documented, with approximately 60% of patients undergoing tricuspid valve surgery being White, compared with 10% being Black patients and 6% being Hispanic patients. The in-hospital mortality after tricuspid valve surgery remains high, at approximately 9%, but there are no available data to compare outcomes across race and ethnicity groups (41).

TRANSCATHETER TREATMENT. There are enormous health care disparities across racial and ethnic groups in the utilization of transcatheter aortic valve replacement (TAVR) and other structural heart interventions. In a study based on the National (Nationwide) Inpatient Sample, utilization rates and outcomes of structural heart intervention hospitalizations from 2011 to 2016 in the United States, rates of

TAVR among White patients were 43.1 per 100,000 compared with 21 and 18 per 100,000 among Hispanic and Black patients, respectively (**Table 4**) (42). Similarly, in the 2020 Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry, which reported data on 276,316 patients who underwent TAVR, <10% of procedures were performed among racial and ethnic minority groups (43). Health care disparities extend to transcatheter mitral edge-to-edge-repair. In the National (Nationwide) Inpatient Sample registry, rates of transcatheter mitral edge-to-edge-repair among White patients were 5 per 100,000, compared with 3.2 per 100,000 among Black and Hispanic patients (42).

The 2020 American College of Cardiology/American Heart Association valve guidelines have updated decision algorithms for the selection of patients indicated to undergo a valve intervention and for the choice between surgical and transcatheter treatments (**Figures 1 to 3**) (27). Critical components of these recommendations include shared decision making between the patient and the heart valve team, individualized risk assessment, ascertainment of eligibility for anticoagulation with a VKA, and establishing a balance between life expectancy and estimated valve durability. The first decision point is choosing between a mechanical valve, which does not deteriorate but requires long-term VKA anticoagulation, and a bioprosthetic valve, which avoids the need for VKA anticoagulation but has limited durability. When a bioprosthetic valve is appropriate, the second decision point is the choice between surgical valve replacement and transcatheter valve replacement. Overall, outcomes at 2 years are similar with both approaches, but there are only limited data on longer-term durability of transcatheter valves, making this option less appropriate in younger patients with a longer life expectancy. There are no data addressing racial or ethnic differences in patient outcomes after SAVR or TAVR or long-term valve durability.

For the successful population-wide implementation of these guidelines, VHD research should systematically identify and overcome barriers accounting for the profound health care disparities across racial and ethnic groups in the utilization of surgical and transcatheter treatments, as well as recording data to allow identification of any racial or ethnic differences in outcomes. To accomplish this, integration of implementation science methods to VHD research is urgently needed. Barriers accounting for the low utilization of VHD surgical and transcatheter treatments among racial and ethnic minorities are likely multifactorial, encompassing patient, provider, and system levels. Higher prevalence of comorbid conditions among racial and ethnic minorities including poorly controlled diabetes and hypertension may affect eligibility for treatment (34). In addition, ineffective patient communication and lack of racial concordance may also play a role. For example, it has been reported that White patients are substantially less likely to refuse valve interventions compared with Black patients (39). In a randomized study using video vignettes (44), Black participants who viewed a race-concordant physician, compared with a race-discordant physician, were more likely to perceive coronary bypass grafting surgery as necessary (4.05 vs 3.72; $P = 0.03$) and more likely to undergo the procedure (2.43 vs 2.09; $P = 0.004$). Patient-centered communication style reduced, but did not eliminate, the impact of race concordance. Presumably, results would be similar for surgical valve procedures. This suggests that Black patients are more likely to follow recommendations from Black physicians and underscores the importance of a diverse physician workforce.

Decreased referral rates may also account for the lower rates of SAVR and TAVR among racial and ethnic minorities. Even after echocardiographic diagnosis of severe AS, Black patients had over 4-fold higher odds than non-Black patients of declining AVR, being lost to follow-up, and not being referred to cardiology (45). Implicit bias likely plays a role in this observation. An analysis of 404,277 subjects with a subsample of 2,535 medical doctors who took the Harvard Race Attitude Implicit Association Test (46) showed an implicit preference for White patients relative to Black patients, with 7 of 10 of the physicians showing a White male preference. White, Asian, and Hispanic physicians also self-reported mild levels of explicit anti-Black bias.

These observations indicate that the quest to overcome health care disparities in VHD must incorporate strategies that account for their structural nature.

FUTURE RESEARCH OPPORTUNITIES

Globally, the prevalence of VHD will continue to increase in the coming decades due to population aging, unhealthy lifestyle behaviors, and consequent higher rates of calcific valve disease. Although limited, available evidence suggests that the rise in prevalence will be coupled with substantial health care disparities across racial and ethnic groups. Moving forward, future research should focus in 3 main areas. First, high-quality studies using

representative samples of the population should be conducted to assess the prevalence of calcific valve disease across racial and ethnic groups. This could serve as an objective measure of the diagnostic and treatment gaps experienced by racial and ethnic minorities and as a benchmark to assess improvements in VHD care. Second, approaches to guaranteeing equitable access to echocardiography are needed, as this is currently a major determinant of disparities in timely diagnosis and referral of VHD. Third, VHD research should incorporate implementation science methods to systematically identify and overcome barriers to access to medical treatment and surgical and transcatheter therapies among racial and ethnic minorities. The current unacceptably low rates of surgical and transcatheter interventions among racial and ethnic minorities should be a call to action to put health care disparities at the forefront of VHD research and care.

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STATE-OF-THE-ART REVIEW

Racial and Ethnic Differences in Treatment and Outcomes of Severe Aortic Stenosis

A Review

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ABSTRACT

Aortic stenosis (AS) is among the most common valvular heart diseases encountered in the United States. In this review the authors examine differences between racial and ethnic groups in the epidemiology and management of severe AS, explore potential explanations for these findings, and discuss the implications for improving the delivery of care to racially and ethnically diverse populations. Underrepresented racial and ethnic groups experience a paradoxically lower prevalence or incidence of AS relative to white subjects, despite having a higher prevalence of traditional risk factors. Historically, UREGs with severe AS have had lower rates of both surgical and transcatheter aortic valve replacement and experienced more post-surgical complications, including, bleeding, worsening heart failure, and rehospitalization. Last, UREGs with severe AS have an increased risk for morbidity and mortality relative to white patients. To date much of the research on AS has examined black-white differences, so there is a need to understand how other racial and ethnic groups with severe AS are diagnosed and treated, with examination of their resulting outcomes. Overall, racial and ethnic disparities in health care access and care delivery are a public health concern given the changing demographics of the U.S. population. These differences in AS management and outcomes highlight the need for additional research into contributing factors and appropriate interventions to address the lower rates of aortic valve replacement and higher morbidity and mortality among UREGs. (J Am Coll Cardiol Intv 2020;13:149–56) © 2020 by the American College of Cardiology Foundation.

Aortic stenosis (AS) is the most common valvular heart disease globally and the third most common cardiovascular disease after hypertension and coronary artery disease (1,2). Risk factors associated with AS include hypertension, tobacco use, hyperlipidemia, renal insufficiency, diabetes mellitus, atherosclerosis, congenital bicuspid aortic valve (AV), congestive heart failure, and advanced age (3–7). The prevalence of AS is 12.4% in persons ≥75 years of age and affects approximately 2.7 million and 4.9 million people in North America and Europe, respectively (8).

AS is a progressive disease with high mortality and an average life expectancy of 1 year after the onset of symptoms such as angina, dyspnea, and heart failure or syncope (9,10). Severe AS affects 3.4% of the elderly population, with approximately 75.6% of these patients experiencing symptoms (8). In North America alone, it is estimated that there will be 0.8 million and 1.4 million patients with symptomatic

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ABBREVIATIONS AND ACRONYMS

aOR = adjusted odds ratio

AS = aortic stenosis

AV = aortic valve

AVR = aortic valve replacement

CI = confidence interval

HR = hazard ratio

SAVR = surgical aortic valve replacement

TAVR = transcatheter aortic valve replacement

UREG = underrepresented racial and ethnic group

severe AS in 2025 and 2050 respectively (8). An analysis of Medicare data from 2003 estimated that the total annual cost of medically managed severe, symptomatic AS is between $600 million and $1.3 billion per year, representing a substantial financial burden to the health care system (11). Management of symptomatic AS has evolved over time from medical therapy and balloon angioplasty to surgical AV replacement (SAVR). More recently, transcatheter AV replacement (TAVR) has been successful in reducing morbidity and mortality in the highest risk patients (5,12,13), and eligibility is expanding to moderate and low surgical risk patients.

To date, few studies have examined differences in the prevalence, management, and outcomes of severe AS in racially and ethnically diverse populations. Moreover, most studies of severe AS have focused largely on data from black and white racial groups; thus, data from Asian and Hispanic populations with severe AS are limited. Given the changing demographics of the U.S. population, understanding the public health impact of AS across racial and ethnic groups is necessary. In this review, our objectives were to examine the prevalence and incidence of severe AS among racially/ethnically diverse populations, analyze the management of

HIGHLIGHTS

- Data on the management and outcomes of diverse populations with severe AS are lacking.
- Underrepresented racial/ethnic groups have lower rates of AVR and worse outcomes.
- Studies assessing reasons for lower AVR and strategies/interventions are needed.

TABLE 1 Cited Studies on the Prevalence, Management, or Outcomes of Severe Aortic Stenosis in Underrepresented Racial and Ethnic Groups

First Author, Year (Ref. #)	Title	Study Design	Major Findings
Alkhouli et al., 2019 (27)	Racial Disparities in the Utilization and Outcomes of TAVR: TVT Registry Report	RCS, from ACC/STS TVT Registry using CMS data in a subset of patients for outcomes	TAVR rates were lower among nonwhites relative to whites, but no differences in adjusted 30-day or 1-yr mortality.
Alqahtani et al., 2018 (24)	Effect of Race on the Incidence of Aortic Stenosis and Outcomes of Aortic Valve Replacement in the United States	Retrospective propensity-matched cohort study of patients ≥60 yrs of age with diagnoses of AS who underwent AVR	Blacks undergo AVR less than whites. After AVR, in-hospital mortality is similar, but blacks have higher costs and longer hospitalizations than whites.
Aronow et al., 2001 (14)	Comparison of Echocardiographic Abnormalities in African-American, Hispanic, and White Men and Women Aged >60 Years	Prospective cohort study analyzing the prevalence of echocardiographic findings in black, Hispanic, and white men and women age ≥60 yrs in long-term health care facilities	The overall prevalence of AS was higher in white men and women relative to blacks and Hispanics.
Brennan et al., 2019 (23)	Race and Sex-Based Disparities Persist in the Treatment of Patients With Severe, Symptomatic Aortic Valve Stenosis	Retrospective claims linked database study using hierarchical logistic regression models to determine the propensity of AVR and TAVR among women and racial and ethnic minorities	Blacks were less likely to undergo AVR relative to whites but underwent TAVR at a similar rate.
Beydoun et al., 2016 (1)	Sex, Race, and Socioeconomic Disparities in Patients With Aortic Stenosis (From a Nationwide Inpatient Sample)	Cross-sectional study of the Healthcare Cost and Utilization Project Nationwide Inpatient Sample to examine sex, racial, and socioeconomic disparities in AS-related health in patients age ≥50 yrs	AS prevalence was ~2% and was higher among men, whites, and higher income groups; length of stay for AS hospitalization varied by sex, race, and income.
Chandra et al., 2012 (7)	Bicuspid Aortic Valve: Inter-Racial Difference in Frequency and Aortic Dimensions	RCS of 229 patients from echocardiography database with BAV (65% black, 31% white) to assess patient characteristics and risk factors and AV morphology and function	Smaller aortic dimensions were observed in blacks despite more risk factors, suggesting race as a potential disease modifier in the development of BAV.
Cruz Rodriguez et al., 2017 (18)	Comparison of Frequency of Referral to Cardiothoracic Surgery for Aortic Valve Disease in Blacks, Hispanics, and Whites	RCS of clinical and echocardiographic data of 952 patients with AV disease (423 white, 376 black, and 153 Hispanic) to assess referral to CTS as function of race/ethnicity	Blacks were less likely to be referred to CTS for treatment of AS relative to whites; there was no difference in referral of Hispanics.
Minha et al., 2015 (13)	Outcome Comparison of African-American and Caucasian Patients with Severe Aortic Stenosis Subjected to Transcatheter Aortic Valve Replacement: A Single-Center Experience	Prospective cohort study of 469 consecutive patients with severe, symptomatic AS (10.8% black, 74.5% white) who underwent TAVR at a single center from 2007 to 2013	TAVR procedures in black patients were less frequently performed; black patients referred for TAVR shared similar risks and outcomes compared with whites.

Continued on the next page

severe AS as a function of race/ethnicity, and compare morbidity and mortality among patients with severe AS according to race/ethnicity.

METHODS

STUDY SELECTION. In accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, a search of PubMed, Scopus, and Web of Science was performed using a mixture of the following terms as Medical Subject Headings or their equivalent: "aortic valve stenosis or aortic stenosis," "minority," "ethnic groups," "African Americans," "blacks," "Hispanics," "Latinos," "Mexican American," "Asian," "Pacific Islander," "Asian American," "Native American," "Indian," "Caucasian," "European American," "disparity," and "bias." The search strategy focused on studies in English from January 2001 to December 2018. Our initial findings were supplemented with manual searches of the bibliographies of relevant papers. Several independent reviewers (J.B.W., T.J., C.M., G.S.A.Y., K.L.T., F.E.U., L.R.J.) appraised a selection of both full publications and abstracts of randomized controlled trials, observational studies, and systematic reviews and meta-analyses. We identified 31 published papers and abstracts focused on diverse racial and ethnic populations with severe AS; 15 were ultimately included (Table 1). Our search strategy is outlined in the Consolidated Standards of Reporting Trials diagram in Figure 1.

RESULTS

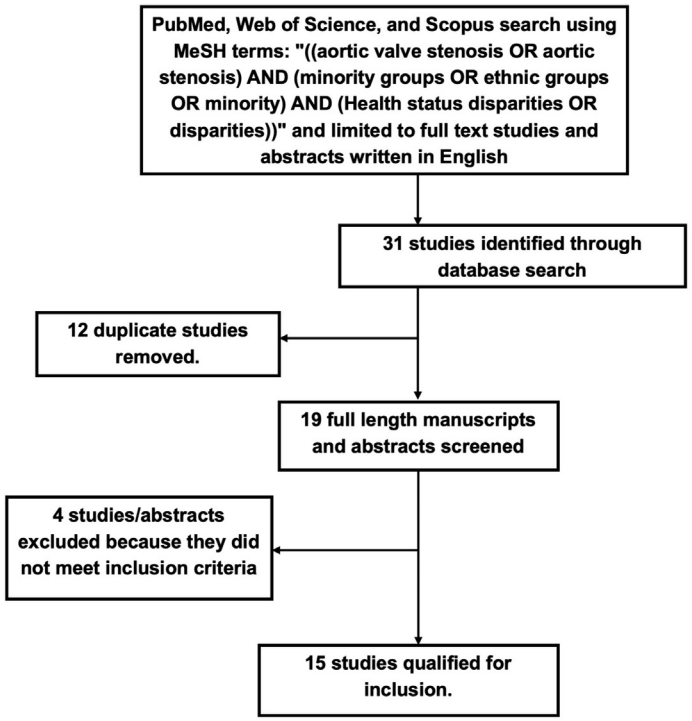
RACIAL AND ETHNIC DIFFERENCES IN PREVALENCE OF SEVERE AS. AS is a progressive, degenerative process that results in clinically significant narrowing of the valve and resultant outflow obstruction. The most common cause of AS in the United States is

TABLE 1 Continued

First Author, Year (Ref. #)	Title	Study Design	Major Findings
Patel et al., 2014 (5)	Racial differences in the Prevalence of Severe Aortic Stenosis	RCS of echocardiographic data from the Synthetic Derivative at Vanderbilt University Medical Center to assess the association of race with severe AS	Blacks patients have a significantly lower risk of developing severe AS compared with whites.
Sleder et al., 2017 (16)	Socioeconomic and Racial Disparities: A Case-Control Study of Patients Receiving Transcatheter Aortic Valve Replacement for Severe Aortic Stenosis	Retrospective case-control study of 67 patients with severe AS who underwent TAVR from 2013 to 2014	The odds of undergoing TAVR increased by 10% with every $10,000 increase in income; nonblacks were significantly more likely to undergo TAVR than blacks, with no differences in comorbidities between groups.
Stamou et al., 2012 (29)	Effects of Gender and Ethnicity on Outcomes After Aortic Valve Replacement	RCS of Massachusetts Cardiac Surgery Database, which identified 6,809 adults ≥18 yrs of age who underwent isolated AVR or AVR with CABG	Ethnicity and sex were not associated with greater 30-day and 1-yr mortality after AVR or AVR with CABG; there were no differences in postoperative outcomes between ethnic groups.
Taylor et al., 2005 (12)	Relationship Between Race and Mortality and Morbidity After Valve Replacement Surgery	RCS of 3,137 black and 46,249 white patients who underwent MVR alone or AVR alone from 1999 through 2002 in the Society of Thoracic Surgeons National Cardiac Database	There was evidence of an association between race and certain complications, but overall race did not appear to be a significant predictor of operative mortality after isolated AVR or MVR.
Yankey et al., 2018 (22)	Aortic Valve Replacement and Outcomes in Patients with Severe Aortic Stenosis: Is It Black or White?	Abstract for RCS of patients from a single center between 1999 and 2013 who met criteria for AVR on the basis of echocardiographic indices plus EF <50%, evidence of heart failure, or need for CABG	There were no significant racial differences in all-cause mortality; black patients were less likely to receive AVR; risk was attenuated after adjustment for demographics and comorbidities.
Yeung et al., 2013 (17)	Racial Differences in Rates of Aortic Valve Replacement in Patients with Severe Aortic Stenosis	RCS of rates of AVR in 880 patients (10% AA, 90% EA) from a single center between 2004 and 2010	AA patients had a higher prevalence of comorbidities; AA patients underwent AVR less frequently than EA patients and refused treatment more often; among those who received intervention, AA and EA patients had similar 3-yr survival.
Yoon et al., 2016 (28)	Clinical Outcomes Following Transcatheter Aortic Valve Replacement in Asian Population	Prospective cohort study of a multicenter, international Asian TAVR registry examining patients with AS who underwent TAVR in Asian countries	TAVR clinical outcomes in observed Asian population were comparable with those previously published in trials and observational studies.

AA = African American; ACC = American College of Cardiology; AS = aortic stenosis; AV = aortic valve; AVR = aortic valve replacement; BAV = bicuspid aortic valve; CABG = coronary artery bypass grafting surgery; CMS = Centers for Medicare and Medicaid Services; EA = European American; EF = ejection fraction; MVR = mitral valve replacement; RCS = retrospective cohort study; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement; TVT = Transcatheter Valve Therapy.

FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses Flowchart Documenting Search Strategy, Exclusions, and Final Numeric Selection of Papers for the Review



Thirty-one total papers and abstracts were identified. Twelve were excluded for duplication, along with 2 abstracts published >2 years previously and not published as full-length papers and two papers that did not focus on prevalence, management, or outcomes as a function of race or ethnicity. Fifteen papers and abstracts were ultimately included. MeSH = Medical Subject Headings.

calcific AV disease, which shares many risk factors with the development of atherosclerosis, including older age, male sex, hypertension, and tobacco use. AS can also be caused by congenital bicuspid valve and rheumatic heart disease, which are less common in developed countries. The overall prevalence of severe AS (AV area <1.0 cm^2 or AV index ≤0.60 cm^2/m^2 or AV velocity ≥40 mm Hg) in the United States is approximately 2% to 7% of the general population (2,13). The overall estimated prevalence of AS in elderly patients is reported to range from 2.6% to 22.8%, with severe AS prevalent in 1.2% to 6.1% (8).

Several cohort studies have analyzed the epidemiology of AS in various racial and ethnic populations. An analysis of data from the Healthcare Cost and Utilization Project Nationwide Inpatient Sample found that relative to white patients, the diagnosis of AS was less prevalent in underrepresented racial and ethnic groups (UREGs) with adjusted odds ratios (aORs) of 0.68 in black patients (95% confidence interval [CI]: 0.66 to 0.71), 0.79 in Hispanics (95% CI: 0.76 to 0.84), and 0.68 in Asians (95% CI: 0.64 to 0.74) (1). Data support the relative underdetection of AS among UREGs. Patel et al. (5) identified a cohort of 272,429 patients with echocardiographic data from the Synthetic Derivative at Vanderbilt University Medical and found that severe AS was observed in 0.29% of black and 0.91% of white patients; after multivariate adjustment, black patients remained significantly less likely to be diagnosed with severe AS relative to white patients (aOR: 0.41; 95% CI: 0.33 to 0.50).

Using a large echocardiography database of 40,878 patients, Chandra et al. (7) discovered, in their sample of 183 patients with bicuspid AV, that blacks had a lower prevalence relative to Caucasians (0.17% vs. 1.1%; $p = 0.001$) of this anomaly. Patel et al. (5), in an analysis of echocardiographic records in a large patient cohort, found that blacks were less likely to have severe AS secondary to calcific disease or congenital bicuspid disease, with aORs of 0.47 (95% CI: 0.36 to 0.61) and 0.13 (95% CI: 0.02 to 0.80), respectively. In a study analyzing the echocardiographic findings of 2,805 black, Hispanic, and white men and women living in a long-term care facility, there were no differences in echocardiographic AS indexes by race or ethnicity (14).

In an effort to examine the genetics underlying the development of phenotypically significant AS, Thanassoulis et al. (15) conducted a genomewide association study using patients from the CHARGE (Cohorts for Heart and Aging Research in Genomic Epidemiology) consortium (15). Researchers isolated a single-nucleotide polymorphism (rs10455872) in the lipoprotein(a) locus that reached significance for AV calcification (odds ratio: 2.05; $p = 9.0 \times 10^{-10}$). This finding was successfully replicated in cohorts of European white, black, and Hispanic patients ($p < 0.05$ for all comparisons). In prospective analyses, the lipoprotein(a) genotype was linked to incident AS (hazard ratio [HR]: 1.68; 95% CI: 1.32 to 2.15), as well as AV replacement (AVR) (HR: 1.54; 95% CI: 1.05 to 2.27). Further research in the field of AS genetics is important to potentially identify additional genetic loci associated with the phenotypic development of AS and severe AS physiology and the conceivable variable expression in different racial and ethnic groups.

It is known that UREGs relative to white patients possess higher rates of traditional AS risk factors, such as congestive heart failure, chronic kidney disease, smoking, hypertension, obesity, and diabetes mellitus (1,4,5,12,13,16–18). The paradox whereby

UREGs cluster more AS risk factors relative to whites but display a lower burden of disease has been observed in other cardiovascular diseases, most notably with atrial fibrillation (19,20). A lower incidence of bicuspid AV, lower likelihood of developing calcific AS, and potential racial and ancestry variations in AS genetic risk predilection may, in part, explain variances in AS prevalence. However, the mechanism behind this finding has yet to be completely elucidated (**Central Illustration**).

RACIAL DIFFERENCES IN MANAGEMENT OF SEVERE AS. SAVR. Approximately 67,500 SAVR procedures are performed annually in the United States (21). Few studies have examined racial/ethnic differences in SAVR procedures. However, those that have consistently demonstrate that UREGs are less likely to undergo SAVR compared with white patients (12,17,22,23). Yeung et al. (17) found that blacks underwent SAVR significantly less often than whites (39% vs. 53%; $p = 0.02$) (17). Similarly, Alqahtani et al. (24) analyzed data from 96,278 patients who underwent SAVR between 2003 and 2014 and found that among patients admitted for AS, black patients were less likely to undergo SAVR than white patients (6.7% vs. 11.3%; $p < 0.001$) (24).

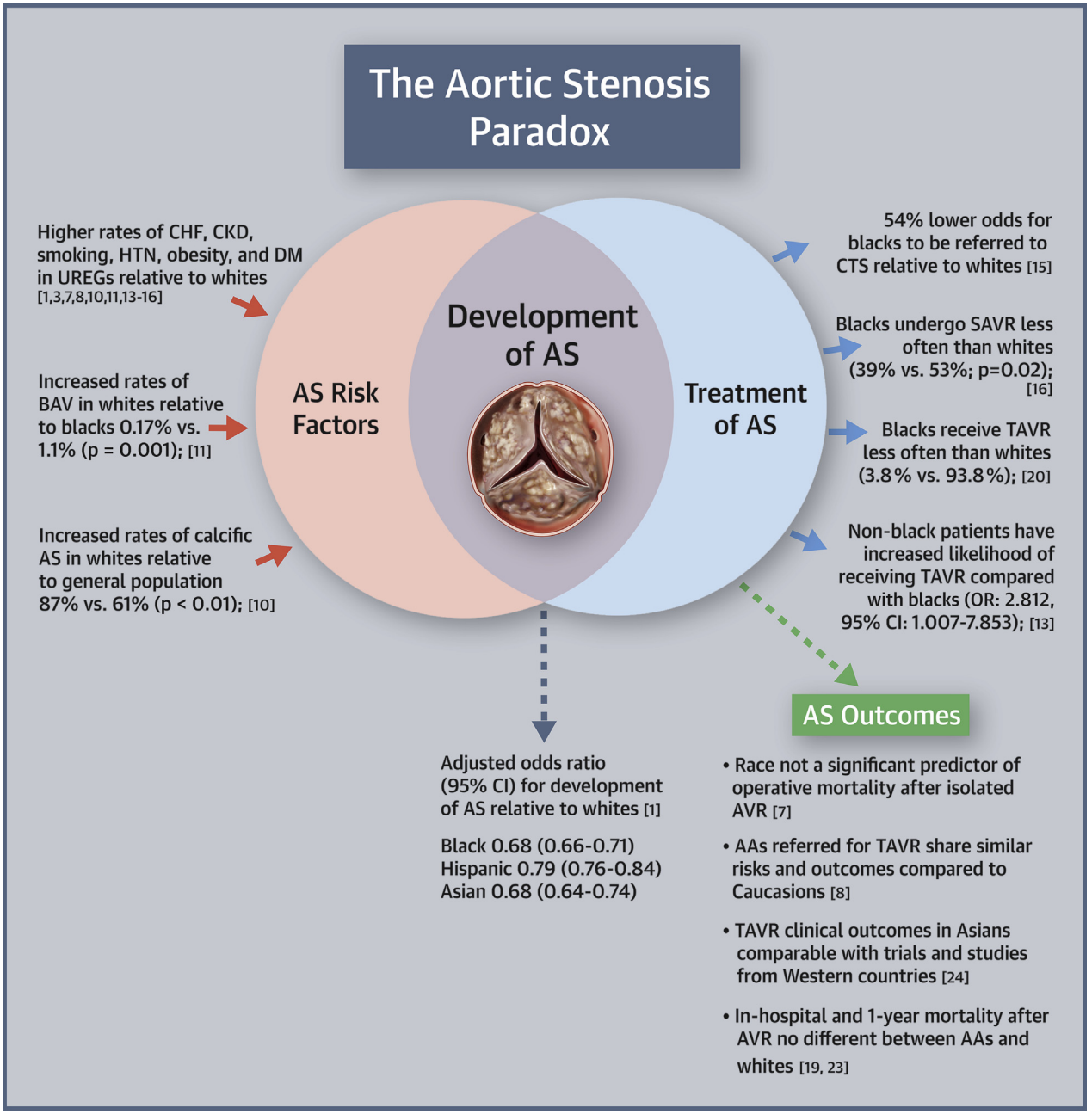
There is a paucity of research examining the reasons for racial and ethnic differences in AVR. Racial and ethnic differences in referral to specialists may in part explain differences in AVR rates. Cruz Rodriguez et al. (18), after adjusting for age, sex, aortic calcification, AV area, or stage of AS, found that black patients with AV disease had a 54% lower odds of being referred to cardiothoracic surgery (aOR: 0.46; 95% CI: 0.31 to 0.67) relative to white patients. Hispanics were 10% less likely to be referred for cardiothoracic surgical evaluation, but this value did not reach statistical significance. Additional hypotheses for differences in cardiothoracic surgery referral rates and SAVR procedures include dissimilarities in socioeconomic and cultural influences and black patients' more often declining intervention (17,18). Consistent with other invasive procedures, black patients may decline SAVR because of misconceptions about the surgical procedure or lack of insight regarding their disease prognosis (8,18,25). Consequently, shared decision making may represent an opportunity to address racial and ethnic disparities in SAVR.

Additionally, UREGs may be less likely to undergo SAVR because of an increased burden of comorbidities. This was observed by Yeung et al. (17) in blacks with AVA <1 cm^2, who were found to have higher rates of hypertension (82% vs. 67%; $p < 0.01$), diabetes mellitus (45% vs. 32%; $p = 0.02$), chronic kidney disease (28% vs. 17%; $p = 0.01$), and end-stage renal disease (18% vs. 2%; $p < 0.001$) relative to whites. Yeung et al. (17) also found that noncardiac comorbidities were the most common reasons preventing patients from undergoing major cardiovascular surgery. Assessing surgical risk through tools validated in diverse populations may determine the cogency of this explanation.

TAVR. Over the past decade, TAVR has emerged as an effective and safe alternative for treatment of symptomatic severe AS in patients at high surgical risk (26). However, several studies have demonstrated that racial and ethnic disparities also exist in the use of TAVR. Data from the Society of Thoracic Surgeons/American College of Cardiology TVT (Transcatheter Valve Therapy) Registry revealed from 2012 to 2014, blacks underwent TAVR less often than whites (3.8% vs. 93.8%) (25). Similarly, in a retrospective case-control study, Sleder et al. (16) observed that nonblack patients had an increased likelihood of undergoing TAVR compared with black patients (odds ratio: 2.812; 95% CI: 1.007 to 7.853; $p = 0.048$). Moreover, the odds of undergoing TAVR increased by 10% for every $10,000 increase in income ($p = 0.05$). Last, in a more recent analysis of the TVT Registry from 2011 to 2016 by Alkhouli et al. (27), relative to white patients, black, Hispanic, and other nonwhite groups remained underrepresented among patients undergoing TAVR in the United States. The reasons for this difference in TAVR receipt are likely multifactorial, with a complex interplay of socioeconomic, cultural, and patient- and provider-centric factors. Specifically, patients' mistrust of physicians and the health system, patients' denial or misunderstanding of the grave risks associated with untreated AS, and the lack of access to care and qualified services all likely play a role in differences in receipt of TAVR procedures (9). Brennan et al. (23), using records from the claims-linked Optum database (2014 to 2017), found that among 20,577 patients (3.3% black, 0.7% Asian, and 6.9% other) with severe symptomatic AS, blacks (odds ratio: 0.77; 95% CI: 0.63 to 0.95) but not Asians were less likely to undergo AVR relative to whites but had a similar propensity for TAVR. These findings suggest TAVR use among UREGs may be different among the broader community, and underuse may be diminishing over time.

OUTCOMES IN PATIENTS WITH SEVERE AS BY RACE AND ETHNICITY. Without AVR, patients with symptomatic, severe AS have a 50% mortality risk at 2 years (10) (**Figure 2**). Patients who undergo AVR have significantly better survival at 1 and 3 years (10,17). Alqahtani et al. (24) found in black relative to white

CENTRAL ILLUSTRATION **The Aortic Stenosis Paradox**



Wilson, J.B. et al. J Am Coll Cardiol Intv. 2020;13(2):149–56.

This diagram depicts the "aortic stenosis (AS) paradox," whereby underrepresented racial and ethnic groups (UREGs) cluster more AS risk factors relative to whites but display a lower burden of disease. Complicating this picture is the differential use of aortic valve replacement (AVR) by race and outcomes among those with severe AS. AA = African American; BAV = bicuspid aortic valve; CHF = congestive heart failure; CI = confidence interval; CKD = chronic kidney disease; CTS = cardiothoracic surgery; DM = diabetes mellitus; HTN = hypertension; OR = odds ratio; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement.

patients, blacks had a higher crude mortality rate after AVR (6.4% vs. 4.7%; p < 0.001), longer hospitalizations (12 ± 12 days vs. 10 ± 9 days; p < 0.001), increased costs of hospitalization ($55,631 ± $37,773 vs. $52,521 ± $38,040; p < 0.001), and higher rates of discharge to skilled nursing facilities or nursing homes (32.1% vs. 27.2%; p = 0.004).

Yeung et al. (17) found that black and white patients had similar 3-year survival rates after AVR (49% [95% CI: 38% to 60%] vs. 50% [95% CI: 45% to 54%]; p = 0.31). Taylor et al. (12) found that after adjusting for risk factors that black race was not associated with increased operative mortality after SAVR but was linked to several complications including prolonged intubation and ventilation, longer post-operative stay, and higher reoperation rates for bleeding after SAVR compared with white patients. In a cohort of 469 patients undergoing TAVR, post-procedural mortality risk was not found to differ by race, although black relative to white patients had higher rates of hemodynamic instability and use of intra-aortic balloon pumps (13). In a contemporary subset of 29,351 patients from the TVT Registry with Centers for Medicare and Medicaid Services linkage, 1-year adjusted mortality rates were similar in blacks and Hispanics compared with whites but lower among patients of Asian, Native American, or Pacific Islander race. Black and Hispanic patients had more heart failure hospitalizations compared with whites (27).

In a recent study by Yankey et al. (22), among patients with severe AS, blacks had lower rates of AVR relative to white patients (26.6% vs. 40.3%; HR: 0.70; 95% CI: 0.50 to 0.98; p = 0.036) and comparable 1-year mortality rates (25.7% vs. 23.4%, respectively; HR: 1.01; 95% CI: 0.71 to 1.45) (22).

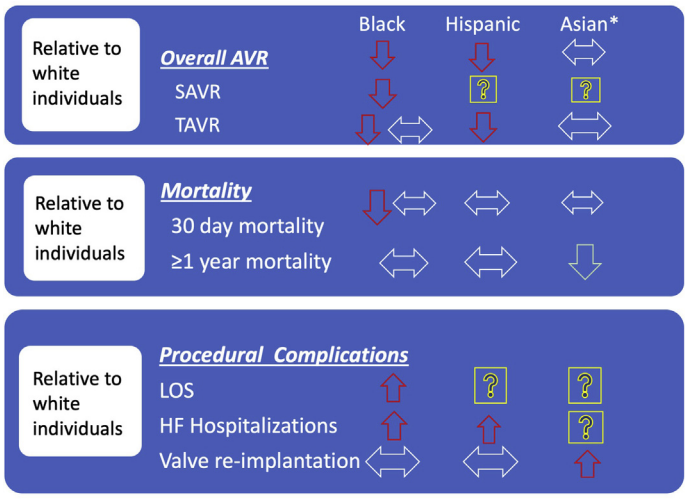
In Asians, Yoon et al. (28) showed in 848 patients who underwent TAVR that the procedural success rate was 97.5% and 30-day and 1-year mortality rates were 2.5% (p = 0.12) and 10.8% (p = 0.40), respectively, among the lowest reported rates among observational studies. They also observed that the rates of stroke, serious vascular complications, major bleeding, and acute kidney injury were in line with the clinical outcomes observed in other previously published trials.

FUTURE DIRECTIONS AND UNANSWERED QUESTIONS

Few studies have examined racial and ethnic patterns in the prevalence, management, and outcomes of patients with severe symptomatic AS. The majority of this research has focused on differences between black and white patients, thus limited data exist in other nonwhite racial and ethnic groups. Given the changing demographics of the U.S. population, further investigation of treatment and management considerations for diverse populations is necessary to address the significant morbidity and mortality of AS for all. In an era of more personalized medicine, studies of genetics and epigenetics in the development of AS are needed. Additionally, an increased focus on inclusion of UREGs in registries and clinical trials is essential to better understand possible risks and benefits of treatment in at risk populations. Last, investigating the epidemiology and natural history of AS in diverse populations will lend insight into the development of screening programs, increased access to care, and appropriate referral and intervention to ameliorate differences in outcomes.

STUDY LIMITATIONS. The data presented were obtained from a collection of nonrandomized studies of various designs, each with separate techniques for data analysis, which because of their heterogeneity may reduce the generalizability of our findings. In addition, there is a paucity of data on severe AS in patients of Hispanic ethnicity and other nonwhite

FIGURE 2 Outcomes of Patients With Severe Aortic Stenosis by Race and Ethnicity



*The Asian racial group is the only underrepresented population to have a published separate transcatheter aortic valve replacement (TAVR) registry. **Symbols** represent less than, greater than, equal to, or unknown for each respective racial/ethnic group relative to white patients for the stated outcome. For black patients, there are several outcomes for which the data suggest more than 1 comparative outcome with white patients, thus there are multiple indicators. AVR = aortic valve replacement; HF = heart failure; LOS = length of stay; SAVR = surgical aortic valve replacement.

races, which limits our review findings. Finally, although we conducted a systematic search and review of the available published research, the omission of relevant data, including unpublished data, cannot be completely excluded.

CONCLUSIONS

Among the limited published data, black and other nonwhite racial and ethnic groups relative to white patients with severe symptomatic AS appear to have a lower incidence and prevalence, experience a lower receipt of SAVR and TAVR, and have either similar or worse short- and long-term outcomes. Racial and ethnic disparities in AVR are likely multifactorial and may in part be explained by differences in subspecialty referral rates and uninformed patient refusal. Future research into these racial/ethnic disparities will help bridge the gap in equitable health care delivery.

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KEY WORDS aortic stenosis, disparities research, outcomes, race and ethnicity, valvular disease

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THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

STS-ACC TVT Registry of Transcatheter Aortic Valve Replacement

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ABSTRACT

The STS-ACC TVT Registry (Society of Thoracic Surgeons–American College of Cardiology Transcatheter Valve Therapy Registry) from 2011 to 2019 has collected data on 276,316 patients undergoing transcatheter aortic valve replacement (TAVR) at sites in all U.S. states. Volumes have increased every year, exceeding surgical aortic valve replacement in 2019 (72,991 vs. 57,626), and it is now performed in all U.S. states. TAVR now extends from extreme- to low-risk patients. This is the first presentation on 8,395 low-risk patients treated in 2019. In 2019, for the entire cohort, femoral access increased to 95.3%, hospital stay was 2 days, and 90.3% were discharged home. Since 2011, the 30-day mortality rate has decreased (7.2% to 2.5%), stroke has started to decrease (2.75% to 2.3%), but pacemaker need is unchanged (10.9% to 10.8%). Alive with acceptable patient-reported outcomes is achieved in 8 of 10 patients at 1 year. The Registry is a national resource to improve care and analyze TAVR's evolution. Real-world outcomes, site performance, and the impact of coronavirus disease 2019 will be subsequently studied. (STS/ACC Transcatheter Valve Therapy Registry [TVT Registry]; NCT01737528) (J Am Coll Cardiol 2020;76:2492–516) © 2020 by The Society of Thoracic Surgeons and the American College of Cardiology Foundation.

This state-of-the-transcatheter aortic valve replacement (TAVR) in the United States report presents the data submitted to the ACC-STS TVT Registry (Society of Thoracic Surgeons [STS]-American College of Cardiology [ACC] Transcatheter Valve Therapy Registry), from 276,316 patients who have undergone TAVR in the United States from 2011 to 2019. The Registry has been the national repository of data on new transcatheter valve therapies, including a TAVR module, to capture all procedures that use U.S. Food and Drug Administration (FDA)-approved TAVR devices (1,2). The first

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC* author instructions page.

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HIGHLIGHTS

- The STS-ACC TVT Registry documents the growth of TAVR in the United States.
- Low-risk patients and valve-in-valve procedures are rapidly growing subsets of TAVR procedures.
- The Registry will continue to gather data on the demographics and outcomes of TAVR procedures and allow assessment of the impact of the COVID-19 on patients and health systems involved in this procedure.

TAVR device approval occurred in late 2011 for patients with symptomatic, severe aortic stenosis deemed at extreme risk for surgical aortic valve replacement (SAVR). Subsequently, label expansion and new device approvals have extended access to TAVR to patients deemed to be at high risk (2012), intermediate risk (2016), and low risk (2019) for SAVR, as well as to patients with degenerated surgically implanted aortic tissue valves (3). The TAVR National Coverage Determination (NCD) from the Centers for Medicare & Medicaid Services (CMS), first released in 2012 and updated in 2019, links reimbursement to submission of patient-level data on all patients receiving commercially approved TAVR to a qualified national registry with the goal of gathering additional evidence on this transformative therapy (4). The Registry has been approved for this purpose (NCT01737528) and has been operational since 2011 (5). The timelines for FDA approvals of TAVR, CMS release of TAVR NCDs, and relevant Registry events are presented in **Table 1**.

METHODS

DATA SOURCE. Using the Registry database, we report the year-by-year data from hospital sites performing TAVR, including procedure volumes, patient characteristics, procedure characteristics, and outcomes (**Table 2**). The data collection form (DCF) and data definitions for the TAVR module are available at the Registry's website (6). Deadlines for submission of data from each calendar quarter are communicated to sites, but sites occasionally modify and submit data after deadlines, and this results in small changes in the subsequent summary statistics. The coronavirus disease 2019 (COVID-19) pandemic has impaired submission of data from some sites in 2020.

Patient-level data for the baseline and in-hospital time point are available for all patients treated through the end of 2019. Thirty-day outcome data are available for patients treated on/before September 30, 2019. All 1-year outcomes are for patients treated on/before September 30, 2018. One-year follow-up also uses data links to the CMS database with CMS performing the linkage using direct patient identifiers. Complete 1-year post-TAVR data using the CMS linkage are available for Medicare fee-for-service patients treated through calendar year 2017. Partial 2018 1-year post-TAVR data using the CMS linkage are available for patients treated on/before March 31, 2018. More recent CMS-linked data are currently not available.

The Registry has approval from a central institutional review board (IRB, Advarra, Columbia, Maryland), and sites have received a waiver of informed consent under the Common Rule based on the IRB finding that the Registry constitutes a minimal risk to the patient. Because the societies, as sponsors of the Registry, have IRB approval and a waiver of informed consent, and because the data are already routinely collected, individual sites participating in the Registry do not need to obtain local IRB approval before enrolling in the Registry.

DATA QUALITY. Data quality was assessed at 3 stages. First, confidential Data Quality Reports are sent to all sites after their quarterly data submission. The Data Quality Reports inform sites whether their data pass rigorous electronic quality checks on completeness. Second, all data are subsequently transferred to Duke Clinical Research Institute (DCRI) where additional quality checks occur. Clinicians at DCRI independently adjudicate stroke, transient ischemic attack, and repeat aortic valve intervention using source documentation. Third, yearly audits are performed in conjunction with a Quality Innovation Network Quality Improvement Organization contractor (7). Every year, approximately 10% of randomly selected sites are audited by nurse auditors trained by the ACC. The data included in the results section, tables, and figures of this report have been reviewed and finalized for analysis by the DCRI.

DATA PRESENTATION. The tables and figures contain data from all TAVR procedures performed at sites active through 2019. Data elements collected during the pre-procedure evaluation, procedure-related hospitalization, and follow-up at 30 days and 1 year are reported from all patients with the time

ABBREVIATIONS AND ACRONYMS

ACC = American College of Cardiology
AR = aortic regurgitation
aRD = adjusted risk difference
CMS = Centers for Medicare & Medicaid Services
COVID-19 = coronavirus disease 2019
CPB = cardiopulmonary bypass
DCF = data collection form
FDA = U.S. Food and Drug Administration
IQR = interquartile range
IRB = institutional review board
KCCQ = Kansas City Cardiomyopathy Questionnaire
LOS = length of stay
NCD = National Coverage Determination
NYHA = New York Heart Association
OHS = open heart surgery
SAVR = surgical aortic valve replacement
STS = Society of Thoracic Surgeons
TAVR = transcatheter aortic valve replacement
V-in-V = valve-in-valve

TABLE 1 Timeline for FDA TAVR Approvals, CMS National Coverage Determinations, and Associated TVT Registry Events

Date	Event
2011 May–November	STS and ACC commit to designing and operating the TVT Registry for TAVR with support and guidance from FDA, CMS, and involved medical device companies. Data elements are chosen by all stakeholders. Agreement is reached to incorporate patient-reported health status (KCCQ) and measures of frailty. Follow-up at 30 days and 1 year is mandated. Use of the Registry for post-approval studies proposed and supported by FDA.
2011 July	At FDA panel, the use of a professional society registry is proposed to gather patient-level data and use for post-approval studies in TAVR.
2011 August	First draft of a data collection form (DCF) for TAVR to be used in the Registry.
2011 September	VARC-2 meeting with harmonization of data elements in the Registry with VARC definitions.
2011 November	FDA approval of Edwards SAPIEN (Edwards Lifesciences, Irvine, California) using femoral access for inoperable patients with severe aortic stenosis.
2011 November	First 2 patients at Columbia University receive TAVR post-FDA approval and are first 2 patients to be entered into the Registry.
2011 December	The Registry is operational using data version 1.2.
2012 May	CMS issues National Coverage Decision establishing the first CMS coverage policy for TAVR under CED and requires patient-level data to be entered into a national registry.
2012 October	FDA approval of Edwards SAPIEN expands TAVR indication to high-risk patients using femoral or other forms of access.
2013 February	FDA and CMS approval of Investigational Device Exemption study (Alternative Access Approaches for Transcatheter Aortic Valve Replace [TAVR] in Inoperable Patients With Aortic Stenosis; NCT01787084), sponsored by the STS and ACC using the TVT Registry for prospective gathering of off-label alternative access cases.
2013 September	FDA updates approval of Edwards SAPIEN for inoperable patients for all forms of vascular access.
2013 December	PCORI funds 3-yr grant: Optimizing Health Outcomes in Patients with Symptomatic Aortic Valve Disease, Principal Investigator Matthew Brennan of Duke. Grant compares SAVR and TAVR outcomes using Registry data.
2014 January	FDA approval of Medtronic CoreValve (Medtronic, Dublin, Ireland) for extreme-risk patients.
2014 June	Version 2.0 of the TAVR DCF released by the Registry.
2014 June	FDA approval of Medtronic CoreValve expands indication to high-risk patients.
2014 June	FDA approval of Edwards SAPIEN XT for high-risk and inoperable patients using femoral and alternative access delivery systems.
2015 March	FDA approval of Medtronic CoreValve for aortic V-in-V for degenerated surgically implanted bioprosthetic valves, in high- and extreme-risk patients.
2015 June	FDA approval of Edwards SAPIEN 3 for high-risk and inoperable patients.
2015 June	FDA approval of Medtronic CoreValve Evolut R System for high- and extreme-risk patients.
2015 October	FDA approval of Edwards SAPIEN XT for aortic V-in-V for high-risk patients.
2016 April	In-Hospital TAVR Mortality Risk model released as an app for clinicians by the Registry.
2016 August	FDA approval of Edwards SAPIEN XT and SAPIEN 3 for intermediate-risk patients.
2017 May	FDA approval of Edwards SAPIEN 3 for aortic and mitral V-in-V for high-risk and inoperable patients.
2018 January	TVT Registry adds cerebral protection using the Sentinel device (currently Boston Scientific) to the TAVR DCF.
2018 July	Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) Focused Meeting Topic: TAVR Program Requirements.
2018 December	FDA approval of Edwards SAPIEN 3 Ultra for mitral V-in-V.
2019 April	FDA approval of Boston Scientific Lotus Edge for high- and extreme-risk patients.
2019 June	CMS issues updated NCD for TAVR under CED.
2019 August	FDA approval for SAPIEN 3, SAPIEN 3 Ultra, CoreValve Evolut R, and CoreValve Evolut PRO for low-risk patients.
2020 February	National Quality Forum votes 17 to 0 to endorse the TAVR 30-day risk-adjusted mortality model developed by the Risk Model Subcommittee of the TVT Registry. COVID-19 pandemic begins, having an impact on all programs, most only performing TAVR with urgent clinical indications.
2020 March	Casper, Wyoming, performs their first TAVR, which signifies TAVR programs being present in all 50 U.S. states. Late-breaking presentation at ACC 2020: "A Composite Metric For Benchmarking Site Performance In Transcatheter Aortic Valve Replacement: Results From The STS/ACC TVT Registry." This performance metric was developed by the Risk Model Subcommittee of the TVT Registry.
2020 April	STS-ACC TVT Registry presents webinar "Rebooting Your Valve Program Post-COVID."
2020 July	STS-ACC TVT Registry presents webinar "The COVID Pandemic and Clinical Trials in New Transcatheter Treatments for Valvular Heart Disease."
2020	The Registry's 30-day composite metric will be included in future reports to all sites.
2021	Voluntary public reporting for TAVR sites begins using Registry data.
2021	Version 3.0 of DCF to be released.
2021	Appropriate use criteria for TAVR will be included in Registry's reports to all sites.

ACC = American College of Cardiology; CED = Coverage with Evidence Development; CMS = Centers for Medicare & Medicaid Services; COVID-19 = coronavirus disease 2019; DCF = data collection form; FDA = U.S. Food and Drug Administration; KCCQ = Kansa City Cardiomyopathy Questionnaire; NCD = National Coverage Determination; PCORI = Patient-Centered Outcomes Research Institute; SAVR = surgical aortic valve replacement; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement; TVT = Transcatheter Valve Therapy; VARC = Valve Academic Research Consortium; V-in-V = valve-in-valve.

of the most recent results as clarified in the preceding text. Data results presented in the text are median values with interquartile ranges (IQR) in parentheses.

Trends for many data elements are presented graphically with year-to-year comparisons. Other trends are presented as changes from early TAVR experience (defined as patients treated from late 2011 up until the end of 2013) compared with current TAVR experience (defined as patients treated in 2019).

ANALYSIS BY RISK GROUPS. Understanding the factors affecting trends is influenced by the

expansion of approved indications over time to include increasingly lower-risk patients. Unlike prior Registry reports, when the patient population was more homogenous with only patients with high to extreme risk for SAVR receiving TAVR, the patient population now receiving TAVR encompasses a broad spectrum of surgical risk profiles, that is, from low to extreme risk (8,9). Although surgical risk category is no longer a determinant of candidacy for TAVR in the United States, national trends, as well as a program's performance, can be better understood by evaluating outcomes within different patient risk categories.

Therefore, data from all patients were categorized into 3 subgroups on the basis of traditional SAVR risk: high or extreme risk, intermediate risk, and low risk. We employed the treatment team's assessment of surgical risk, which reflects important patient characteristics, such as frailty, that are not captured in the STS calculator for isolated SAVR risk (10).

Not unexpectedly, some patients receiving TAVR were classified as intermediate and low risk before the FDA-approved expansion of indications to these risk groups. The small number of patients reported in the intermittent-risk category treated before FDA approval in mid-2016 and in the low-risk category treated before FDA approval in mid-2019, therefore, represent off-label cases.

ANALYSIS OF SITE VOLUMES. Yearly site volumes were calculated based on site-reported volumes for each year and the number of months a site was performing TAVR in the first year of the site's activation. Because new sites were being opened each year and may have started performing TAVRs after the first month of the year, there needed to be a calculation of annualized volumes for new sites. See the legend of **Table 3** for details.

ANALYSIS OF VALVE-IN-VALVE TAVR. Aortic valve-in-valve (V-in-V) procedures represented a form of TAVR that is captured in the Registry. There are several forms of V-in-V performed, and different relevant data elements in the DCF are defined in the data dictionary (6). A planned or pre-procedure indication for V-in-V may be for either degeneration of a surgically implanted tissue valve (TAVR-in-SAVR) or dysfunction of a TAVR valve (TAVR-in-TAVR). Separately, a data element captures an urgent or intraprocedure indication for TAVR-in-TAVR that may occur with acute TAVR dysfunction or deployment of the initial TAVR valve too low or high with resultant aortic regurgitation (AR) and/or unstable anchoring. This is captured in the data element concerning Valve-in-Valve Procedure Status with the option being "Immediate Intraprocedure."

TAVR SYSTEM USED. Data are collected on the TAVR technology used during the procedure, including the type of TAVR valve implanted. As shown in **Table 1**, there have been different TAVR valve models from 3 different manufacturers that have received FDA approval from 2011 through 2019. The TAVR valves currently approved have 3 different modes of deployment: balloon-expandable, self-expanding, and mechanically expanding.

MISSING DATA. Missing data for reported data elements are quantified in **Table 2** and Supplemental Tables 1 to 3. The results of 30-day and 1-year outcomes for only those patients with submitted data for that element are denoted in the tables as the nonmissing dataset. The nonmissing dataset is used in the Results and in the figures.

RESULTS

From 2011 through 2019, 276,316 patients underwent TAVR with data submitted to the Registry. Data are from 49 sites (a site in Wyoming opened in 2020), as well as cases from the 2 sites in the District of Columbia and 2 sites in Puerto Rico, a U.S. territory. **Table 2** presents demographics, clinical characteristics, procedure performance, and in-hospital, 30-day, and 1-year outcomes. These data were compiled by a data run on June 17, 2020, at DCRI. In the Supplemental Appendix are 3 tables of similar data elements but categorized by SAVR risk as assigned by the local heart team, including high or extreme risk (n = 179,397) (Supplemental Table 1), intermediate risk (n = 84,108) (Supplemental Table 2), and low risk (n = 11,534) (Supplemental Table 3).

OVERVIEW OF TAVR HOSPITAL SITES AND CASE VOLUME. TAVR sites. The number of U.S. TAVR sites at the end of August 2020 was 715. The year-by-year trend in the number of U.S. hospital sites performing TAVR is shown as part of the **Central Illustration**. With the opening of a site in Wyoming in March 2020, TAVR programs exist in all 50 U.S. states. The geographic distribution of U.S. TAVR sites is shown in **Figure 1A,** and **Figure 1B** show the number of TAVR sites per state. The only TAVR sites in the United States not included in the Registry are those in a few military hospitals and the Veterans Authority (VA) medical system: as of mid-2019 there were 8 VA TAVR programs.

TAVR volume versus SAVR volume. The annual volume of TAVR have increased every year since 2011, and in 2019, TAVR volume (n = 72,991) exceeded all forms of surgical AVR (n = 57,626). **Figure 2** displays

TABLE 2 Demographics, Patient Characteristics, Procedure Characteristics, and Outcome for All Patients Receiving Commercial TAVR in the United States From 2011 Through 2019

	Level	Overall (N = 276,316)	≤2013 (N = 13,723)	2014 (N = 16,312)	2015 (N = 25,085)	2016 (N = 38,035)	2017 (N = 51,002)	2018 (N = 59,168)	2019 (N = 72,991)	p Value
Demographics										
Age, yrs*	n [median]	276,316 [81.00]	13,723 [84.00]	16,312 [83.00]	25,085 [83.00]	38,035 [82.00]	51,002 [81.00]	59,168 [81.00]	72,991 [80.00]	<0.0001
	25th	75.00	78.00	77.00	77.00	76.00	75.00	75.00	73.00	
	75th	86.00	88.00	88.00	87.00	87.00	86.00	86.00	85.00	
	Missing, %	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	
Sex	Missing	32 (0.01)	2 (0.01)	1 (0.01)	7 (0.03)	3 (0.01)	8 (0.02)	2 (0.00)	9 (0.01)	<0.0001
	Male	149,657 (54.16)	6,704 (48.85)	8,587 (52.64)	13,250 (52.82)	20,533 (53.98)	27,701 (54.31)	32,171 (54.37)	40,711 (55.78)	
	Female	126,627 (45.83)	7,017 (51.13)	7,724 (47.35)	11,828 (47.15)	17,499 (46.01)	23,293 (45.67)	26,995 (45.62)	32,271 (44.21)	
White	No	19,831 (7.18)	794 (5.79)	1,021 (6.26)	1,465 (5.84)	2,674 (7.03)	3,625 (7.11)	4,603 (7.78)	5,649 (7.74)	<0.0001
	Yes	256,485 (92.82)	12,929 (94.21)	15,291 (93.74)	23,620 (94.16)	35,361 (92.97)	47,377 (92.89)	54,565 (92.22)	67,342 (92.26)	
Black/African American	No	265,310 (96.02)	13,219 (96.33)	15,670 (96.06)	24,134 (96.21)	36,547 (96.09)	48,972 (96.02)	56,725 (95.87)	70,043 (95.96)	0.0126
	Yes	11,006 (3.98)	504 (3.67)	642 (3.94)	951 (3.79)	1,488 (3.91)	2,030 (3.98)	2,443 (4.13)	2,948 (4.04)	
Asian	No	272,622 (98.66)	13,550 (98.74)	16,104 (98.72)	24,819 (98.94)	37,515 (98.63)	50,343 (98.71)	58,310 (98.55)	71,981 (98.62)	0.0018
	Yes	3,694 (1.34)	173 (1.26)	208 (1.28)	266 (1.06)	520 (1.37)	659 (1.29)	858 (1.45)	1,010 (1.38)	
Native American/Alaskan native	No	275,515 (99.71)	13,683 (99.71)	16,267 (99.72)	25,024 (99.76)	37,937 (99.74)	50,845 (99.69)	59,007 (99.73)	72,752 (99.67)	0.0478
	Yes	801 (0.29)	40 (0.29)	45 (0.28)	61 (0.24)	98 (0.26)	157 (0.31)	161 (0.27)	239 (0.33)	
Native Hawaiian/Pacific Islander	No	275,858 (99.83)	13,699 (99.83)	16,282 (99.82)	25,033 (99.79)	37,982 (99.86)	50,930 (99.86)	59,069 (99.83)	72,863 (99.82)	0.9387
	Yes	458 (0.17)	24 (0.17)	30 (0.18)	52 (0.21)	53 (0.14)	72 (0.14)	99 (0.17)	128 (0.18)	
Hispanic or Latino ethnicity	Missing	5,587 (2.02)	323 (2.35)	277 (1.70)	486 (1.94)	752 (1.98)	988 (1.94)	1,279 (2.16)	1,482 (2.03)	<0.0001
	No	257,745 (93.28)	12,924 (94.18)	15,403 (94.43)	23,602 (94.09)	35,598 (93.59)	47,579 (93.29)	54,949 (92.87)	67,690 (92.74)	
	Yes	12,984 (4.70)	476 (3.47)	632 (3.87)	997 (3.97)	1,685 (4.43)	2,435 (4.77)	2,940 (4.97)	3,819 (5.23)	
History and risk factors										
% predicted mortality (STS SAVR model)*	n [median]	276,282 [5.22]	13,720 [6.91]	16,309 [6.65]	25,079 [6.26]	38,031 [5.73]	50,994 [5.12]	59,165 [4.89]	72,984 [4.38]	<0.0001
	25th	3.31	4.56	4.37	4.11	3.71	3.35	3.17	2.72	
	75th	8.36	10.66	10.08	9.72	8.97	8.07	7.80	7.17	
	Missing, %	0.01	0.02	0.02	0.02	0.01	0.02	0.01	0.01	
% predicted mortality (TVTTAVR Model)*	n [median]	276,302 [3.18]	13,717 [4.55]	16,312 [3.99]	25,084 [3.51]	38,035 [3.30]	50,997 [3.10]	59,168 [3.04]	72,989 [2.88]	<0.0001
	25th	2.35	3.18	2.88	2.60	2.46	2.33	2.28	2.14	
	75th	4.42	6.99	6.07	4.96	4.52	4.21	4.10	3.93	
	Missing, %	0.01	0.04	0.00	0.00	0.00	0.01	0.00	0.00	
5-m gait speed	Missing	389 (0.14)	76 (0.55)	32 (0.20)	39 (0.16)	50 (0.13)	48 (0.09)	65 (0.11)	79 (0.11)	<0.0001
	Slowest	71,522 (25.88)	2,862 (20.86)	4,752 (29.13)	7,731 (30.82)	10,610 (27.90)	13,154 (25.79)	15,088 (25.50)	17,325 (23.74)	
	Slow	94,576 (34.23)	2,824 (20.58)	5,181 (31.76)	8,595 (34.26)	13,509 (35.52)	18,100 (35.49)	21,094 (35.65)	25,273 (34.62)	
	Normal	69,613 (25.19)	1,446 (10.54)	2,862 (17.55)	4,974 (19.83)	8,575 (22.55)	13,313 (26.10)	16,411 (27.74)	22,032 (30.18)	
	Walk test not performed	40,216 (14.55)	6,515 (47.48)	3,485 (21.36)	3,746 (14.93)	5,291 (13.91)	6,387 (12.52)	6,510 (11.00)	8,282 (11.35)	
Hostile chest	Missing	283 (0.10)	79 (0.58)	29 (0.18)	12 (0.05)	30 (0.08)	44 (0.09)	45 (0.08)	44 (0.06)	<0.0001
	No	257,884 (93.33)	12,370 (90.14)	15,017 (92.06)	23,171 (92.37)	35,049 (92.15)	47,542 (93.22)	55,588 (93.95)	69,147 (94.73)	
	Yes	18,149 (6.57)	1,274 (9.28)	1,266 (7.76)	1,902 (7.58)	2,956 (7.77)	3,416 (6.70)	3,535 (5.97)	3,800 (5.21)	
Home oxygen	Missing	263 (0.10)	78 (0.57)	23 (0.14)	20 (0.08)	28 (0.07)	30 (0.06)	43 (0.07)	41 (0.06)	<0.0001
	No	250,963 (90.82)	11,758 (85.68)	14,252 (87.37)	22,195 (88.48)	34,292 (90.16)	46,455 (91.08)	54,349 (91.86)	67,662 (92.70)	
	Yes	25,090 (9.08)	1,887 (13.75)	2,037 (12.49)	2,870 (11.44)	3,715 (9.77)	4,517 (8.86)	4,776 (8.07)	5,288 (7.24)	

Continued on the next page

TABLE 2 Continued

	Level	Overall (N = 276,316)	≤2013 (N = 13,723)	2014 (N = 16,312)	2015 (N = 25,085)	2016 (N = 38,035)	2017 (N = 51,002)	2018 (N = 59,168)	2019 (N = 72,991)	p Value
Porcelain aorta	Missing	498 (0.18)	50 (0.36)	55 (0.34)	42 (0.17)	54 (0.14)	67 (0.13)	103 (0.17)	127 (0.17)	<0.0001
	No	266,126 (96.31)	12,692 (92.49)	15,220 (93.31)	23,704 (94.49)	36,449 (95.83)	49,307 (96.68)	57,438 (97.08)	71,316 (97.71)	
	Yes	9,692 (3.51)	981 (7.15)	1,037 (6.36)	1,339 (5.34)	1,532 (4.03)	1,628 (3.19)	1,627 (2.75)	1,548 (2.12)	
Baseline KCCQ-12 performed	Missing	214 (0.08)	128 (0.93)	22 (0.13)	19 (0.08)	10 (0.03)	14 (0.03)	6 (0.01)	15 (0.02)	<0.0001
	No	26,897 (9.73)	5,837 (42.53)	2,134 (13.08)	2,487 (9.91)	3,273 (8.61)	3,867 (7.58)	4,106 (6.94)	5,193 (7.11)	
	Yes	249,205 (90.19)	7,758 (56.53)	14,156 (86.78)	22,579 (90.01)	34,752 (91.37)	47,121 (92.39)	55,056 (93.05)	67,783 (92.86)	
Baseline KCCQ-12 score, among performed*	n [median]	248,863 [43.75]	7,737 [37.50]	14,112 [39.06]	22,526 [39.58]	34,687 [42.19]	47,075 [44.79]	55,021 [44.79]	67,705 [46.88]	<0.0001
	25th	26.04	21.88	22.92	22.92	25.00	27.08	27.08	28.47	
	75th	63.54	55.73	58.33	59.37	61.98	64.58	64.58	67.19	
	Missing, %	0.14	0.27	0.31	0.23	0.19	0.10	0.06	0.12	
NYHA functional class within 2 weeks	Missing	2,186 (0.79)	170 (1.24)	152 (0.93)	231 (0.92)	268 (0.70)	358 (0.70)	374 (0.63)	633 (0.87)	<0.0001
	Class I	9,363 (3.39)	451 (3.29)	512 (3.14)	673 (2.68)	983 (2.58)	1,644 (3.22)	2,052 (3.47)	3,048 (4.18)	
	Class II	61,394 (22.22)	1,882 (13.71)	2,386 (14.63)	3,876 (15.45)	6,650 (17.48)	11,303 (22.16)	14,708 (24.86)	20,589 (28.21)	
	Class III	166,232 (60.16)	8,180 (59.61)	10,007 (61.35)	15,643 (62.36)	24,270 (63.81)	31,295 (61.36)	35,418 (59.86)	41,419 (56.75)	
	Class IV	37,141 (13.44)	3,040 (22.15)	3,255 (19.95)	4,662 (18.58)	5,864 (15.42)	6,402 (12.55)	6,616 (11.18)	7,302 (10.00)	
Procedure information										
TAVR in SAVR, prior SAVR and no prior TAVR	No	260,933 (94.43)	13,480 (98.23)	15,902 (97.49)	23,792 (94.85)	35,763 (94.03)	47,943 (94.00)	55,542 (93.87)	68,511 (93.86)	<0.0001
	Yes	15,383 (5.57)	243 (1.77)	410 (2.51)	1,293 (5.15)	2,272 (5.97)	3,059 (6.00)	3,626 (6.13)	4,480 (6.14)	
TAVR in TAVR, prior TAVR and no prior SAVR	No	275,912 (99.85)	13,711 (99.91)	16,295 (99.90)	25,046 (99.84)	37,978 (99.85)	50,921 (99.84)	59,080 (99.85)	72,881 (99.85)	0.2505
	Yes	404 (0.15)	12 (0.09)	17 (0.10)	39 (0.16)	57 (0.15)	81 (0.16)	88 (0.15)	110 (0.15)	
Procedure location	Missing	247 (0.09)	15 (0.11)	12 (0.07)	21 (0.08)	46 (0.12)	42 (0.08)	48 (0.08)	63 (0.09)	<0.0001
	Hybrid OR suite	161,081 (58.30)	8,233 (59.99)	10,352 (63.46)	15,792 (62.95)	23,265 (61.17)	29,834 (58.50)	33,706 (56.97)	39,899 (54.66)	
	Hybrid cath lab suite	75,281 (27.24)	3,511 (25.58)	4,188 (25.67)	6,806 (27.13)	10,260 (26.98)	13,644 (26.75)	15,709 (26.55)	21,163 (28.99)	
	Cath lab	38,575 (13.96)	1,833 (13.36)	1,736 (10.64)	2,448 (9.76)	4,384 (11.53)	7,292 (14.30)	9,397 (15.88)	11,485 (15.73)	
	Other	1,132 (0.41)	131 (0.95)	24 (0.15)	18 (0.07)	80 (0.21)	190 (0.37)	308 (0.52)	381 (0.52)	
Procedure status	Missing	226 (0.08)	17 (0.12)	21 (0.13)	15 (0.06)	27 (0.07)	46 (0.09)	49 (0.08)	51 (0.07)	<0.0001
	Elective	251,569 (91.04)	12,258 (89.32)	14,849 (91.03)	22,683 (90.42)	34,520 (90.76)	46,472 (91.12)	54,009 (91.28)	66,778 (91.49)	
	Urgent	23,613 (8.55)	1,418 (10.33)	1,415 (8.67)	2,315 (9.23)	3,368 (8.86)	4,324 (8.48)	4,909 (8.30)	5,864 (8.03)	
	Emergency	765 (0.28)	25 (0.18)	19 (0.12)	60 (0.24)	104 (0.27)	138 (0.27)	171 (0.29)	248 (0.34)	
	Salvage	143 (0.05)	5 (0.04)	8 (0.05)	12 (0.05)	16 (0.04)	22 (0.04)	30 (0.05)	50 (0.07)	
Procedure indication	Missing	300 (0.11)	22 (0.16)	13 (0.08)	19 (0.08)	36 (0.09)	61 (0.12)	60 (0.10)	89 (0.12)	<0.0001
	Primary AS	256,976 (93.00)	13,196 (96.16)	15,700 (96.25)	23,552 (93.89)	35,514 (93.37)	47,339 (92.82)	54,605 (92.29)	67,070 (91.89)	
	Primary AI	1,864 (0.67)	54 (0.39)	79 (0.48)	164 (0.65)	259 (0.68)	373 (0.73)	422 (0.71)	513 (0.70)	
	Mixed AS/AI	7,164 (2.59)	297 (2.16)	273 (1.67)	644 (2.57)	824 (2.17)	1,275 (2.50)	1,634 (2.76)	2,217 (3.04)	
	Failed bioprosthetic valve	10,012 (3.62)	154 (1.12)	247 (1.51)	706 (2.81)	1,402 (3.69)	1,954 (3.83)	2,447 (4.14)	3,102 (4.25)	

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the annual number of TAVR, isolated SAVR, and other operations involving SAVR, using data from the STS National Database. Annual TAVR volume exceeded isolated SAVR volume in 2016 after TAVR was approved for intermediate surgical risk patients. Annual TAVR volume exceeded all forms of SAVR volume in 2019, coinciding with FDA approval of TAVR for low-risk patients. For the first time, SAVR volume has clearly declined in 2019 as quantified in the legend of Figure 2.

TAVR volume:V-in-V. Elective or planned V-in-V TAVR has increased from 305 cases between 2011 and

TABLE 2 Continued

	Level	Overall (N = 276,316)	≤2013 (N = 13,723)	2014 (N = 16,312)	2015 (N = 25,085)	2016 (N = 38,035)	2017 (N = 51,002)	2018 (N = 59,168)	2019 (N = 72,991)	p Value
Valve sheath access site	Missing	959 (0.35)	107 (0.78)	92 (0.56)	110 (0.44)	130 (0.34)	158 (0.31)	151 (0.26)	211 (0.29)	<0.0001
	Femoral	248,985 (90.11)	7,833 (57.08)	11,335 (69.49)	21,733 (86.64)	35,028 (92.09)	47,780 (93.68)	55,743 (94.21)	69,533 (95.26)	
	Axillary	2,282 (0.83)	8 (0.06)	40 (0.25)	105 (0.42)	249 (0.65)	477 (0.94)	697 (1.18)	706 (0.97)	
	Transapical	11,356 (4.11)	4,693 (34.20)	3,107 (19.05)	1,520 (6.06)	891 (2.34)	590 (1.16)	342 (0.58)	213 (0.29)	
	Transaortic	4,884 (1.77)	710 (5.17)	1,415 (8.67)	932 (3.72)	552 (1.45)	475 (0.93)	459 (0.78)	341 (0.47)	
	Subclavian	4,993 (1.81)	4 (0.03)	229 (1.40)	501 (2.00)	864 (2.27)	1,127 (2.21)	1,158 (1.96)	1,110 (1.52)	
	Transiliac	288 (0.10)	93 (0.68)	58 (0.36)	46 (0.18)	49 (0.13)	18 (0.04)	8 (0.01)	16 (0.02)	
	Transseptal	41 (0.01)	10 (0.07)	2 (0.01)	4 (0.02)	5 (0.01)	3 (0.01)	9 (0.02)	8 (0.01)	
	Transcarotid	1,469 (0.53)	6 (0.04)	16 (0.10)	58 (0.23)	147 (0.39)	196 (0.38)	384 (0.65)	662 (0.91)	
	Transcaval	123 (0.04)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	2 (0.00)	121 (0.17)	
	Other	936 (0.34)	259 (1.89)	18 (0.11)	76 (0.30)	120 (0.32)	178 (0.35)	215 (0.36)	70 (0.10)	
Heart team reason for procedure	Missing	748 (0.27)	74 (0.54)	47 (0.29)	42 (0.17)	62 (0.16)	107 (0.21)	115 (0.19)	301 (0.41)	<0.0001
	Patient preference /other	529 (0.19)	474 (3.45)	55 (0.34)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	
	Inoperable or extreme/high risk	179,397 (64.92)	13,164 (95.93)	15,552 (95.34)	23,712 (94.53)	33,284 (87.51)	31,049 (60.88)	31,038 (52.46)	31,598 (43.29)	
	Intermediate risk	84,108 (30.44)	11 (0.08)	573 (3.51)	1,078 (4.30)	4,318 (11.35)	18,863 (36.98)	26,568 (44.90)	32,697 (44.80)	
	Low risk	11,534 (4.17)	0 (0.00)	85 (0.52)	253 (1.01)	371 (0.98)	983 (1.93)	1,447 (2.45)	8,395 (11.50)	
Cardiopulmonary bypass used	Missing	445 (0.16)	50 (0.36)	31 (0.19)	38 (0.15)	67 (0.18)	96 (0.19)	67 (0.11)	96 (0.13)	<0.0001
	No	273,259 (98.89)	13,108 (95.52)	15,867 (97.27)	24,695 (98.45)	37,643 (98.97)	50,572 (99.16)	58,790 (99.36)	72,584 (99.44)	
	Yes	2,612 (0.95)	565 (4.12)	414 (2.54)	352 (1.40)	325 (0.85)	334 (0.65)	311 (0.53)	311 (0.43)	
Conversion to open heart surgery	Missing	502 (0.18)	33 (0.24)	34 (0.21)	61 (0.24)	94 (0.25)	89 (0.17)	75 (0.13)	116 (0.16)	<0.0001
	No	274,203 (99.24)	13,498 (98.36)	16,079 (98.57)	24,816 (98.93)	37,746 (99.24)	50,671 (99.35)	58,815 (99.40)	72,578 (99.43)	
	Yes	1,611 (0.58)	192 (1.40)	199 (1.22)	208 (0.83)	195 (0.51)	242 (0.47)	278 (0.47)	297 (0.41)	
Procedure aborted	Missing	331 (0.12)	20 (0.15)	16 (0.10)	43 (0.17)	52 (0.14)	49 (0.10)	64 (0.11)	87 (0.12)	<0.0001
	No	273,635 (99.03)	13,306 (96.96)	16,094 (98.66)	24,828 (98.98)	37,719 (99.17)	50,564 (99.14)	58,695 (99.20)	72,429 (99.23)	
	Yes	2,350 (0.85)	397 (2.89)	202 (1.24)	214 (0.85)	264 (0.69)	389 (0.76)	409 (0.69)	475 (0.65)	
Other procedure performed concurrently	Missing	16,444 (5.95)	12,147 (88.52)	3,325 (20.38)	120 (0.48)	194 (0.51)	204 (0.40)	241 (0.41)	213 (0.29)	<0.0001
	No	238,179 (86.20)	1,487 (10.84)	12,274 (75.25)	23,065 (91.95)	34,856 (91.64)	47,048 (92.25)	53,587 (90.57)	65,862 (90.23)	
	Yes—PCI	4,910 (1.78)	19 (0.14)	218 (1.34)	475 (1.89)	805 (2.12)	977 (1.92)	1,097 (1.85)	1,319 (1.81)	
	Yes—other	16,783 (6.07)	70 (0.51)	495 (3.03)	1,425 (5.68)	2,180 (5.73)	2,773 (5.44)	4,243 (7.17)	5,597 (7.67)	
Valve-in-valve procedure	Missing	359 (0.13)	35 (0.26)	24 (0.15)	26 (0.10)	56 (0.15)	73 (0.14)	72 (0.12)	73 (0.10)	<0.0001
	No	258,064 (93.39)	13,058 (95.15)	15,426 (94.57)	23,362 (93.13)	35,445 (93.19)	47,584 (93.30)	55,142 (93.20)	68,047 (93.23)	
	Yes	17,893 (6.48)	630 (4.59)	862 (5.28)	1,697 (6.76)	2,534 (6.66)	3,345 (6.56)	3,954 (6.68)	4,871 (6.67)	
Valve-in-valve procedure status	Missing	96 (0.54)	3 (0.48)	2 (0.23)	2 (0.12)	3 (0.12)	3 (0.09)	34 (0.86)	49 (1.01)	<0.0001
	Elective	15,898 (88.85)	305 (48.41)	472 (54.76)	1,360 (80.14)	2,308 (91.08)	3,127 (93.48)	3,704 (93.68)	4,622 (94.89)	
	Immediate intraprocedure	1,899 (10.61)	322 (51.11)	388 (45.01)	335 (19.74)	223 (8.80)	215 (6.43)	216 (5.46)	200 (4.11)	
Discharge										
Discharge location, among survivors	Missing	55 (0.02)	5 (0.04)	5 (0.03)	6 (0.02)	5 (0.01)	15 (0.03)	9 (0.02)	10 (0.01)	<0.0001
	Home	227,739 (84.12)	8,100 (62.40)	10,681 (68.25)	18,398 (75.51)	30,623 (82.15)	43,455 (86.65)	51,421 (88.22)	65,061 (90.32)	
	Extended care/TCU/ rehab	31,163 (11.51)	3,917 (30.17)	3,933 (25.13)	4,434 (18.20)	4,749 (12.74)	4,666 (9.30)	4,707 (8.08)	4,757 (6.60)	
	Other acute care hospital	1,067 (0.39)	104 (0.80)	96 (0.61)	126 (0.52)	200 (0.54)	167 (0.33)	188 (0.32)	186 (0.26)	
	Nursing home	9,492 (3.51)	739 (5.69)	830 (5.30)	1,258 (5.16)	1,525 (4.09)	1,624 (3.24)	1,750 (3.00)	1,766 (2.45)	
	Hospice	623 (0.23)	72 (0.55)	70 (0.45)	68 (0.28)	77 (0.21)	113 (0.23)	100 (0.17)	123 (0.17)	
	Left against medical advice	88 (0.03)	2 (0.02)	3 (0.02)	10 (0.04)	9 (0.02)	13 (0.03)	18 (0.03)	33 (0.05)	
	Other	516 (0.19)	42 (0.32)	32 (0.20)	64 (0.26)	90 (0.24)	95 (0.19)	95 (0.16)	98 (0.14)	

Continued on the next page

TABLE 2 Continued

	Level	Overall (N = 276,316)	≤2013 (N = 13,723)	2014 (N = 16,312)	2015 (N = 25,085)	2016 (N = 38,035)	2017 (N = 51,002)	2018 (N = 59,168)	2019 (N = 72,991)	p Value
Mortality										
Discharge mortality status	Missing	14 (0.01)	6 (0.04)	0 (0.00)	1 (0.00)	0 (0.00)	5 (0.01)	0 (0.00)	2 (0.00)	<0.0001
	Alive	270,743 (97.98)	12,981 (94.59)	15,650 (95.94)	24,364 (97.13)	37,278 (98.01)	50,148 (98.33)	58,288 (98.51)	72,034 (98.69)	
	Deceased	5,559 (2.01)	736 (5.36)	662 (4.06)	720 (2.87)	757 (1.99)	849 (1.66)	880 (1.49)	955 (1.31)	
30-day death (30 day)	Missing	15,300 (5.99)	1,165 (8.49)	1,066 (6.54)	1,500 (5.98)	2,085 (5.48)	2,323 (4.55)	2,653 (4.48)	4,508 (8.64)	<0.0001
	No	232,248 (90.89)	11,654 (84.92)	14,338 (87.90)	22,553 (89.91)	34,818 (91.54)	47,299 (92.74)	55,070 (93.07)	46,516 (89.11)	
	Yes	7,980 (3.12)	904 (6.59)	908 (5.57)	1,032 (4.11)	1,132 (2.98)	1,380 (2.71)	1,445 (2.44)	1,179 (2.26)	
30-day death (30 day), nonmissing	No	232,248 (96.68)	11,654 (92.80)	14,338 (94.04)	22,553 (95.62)	34,818 (96.85)	47,299 (97.17)	55,070 (97.44)	46,516 (97.53)	<0.0001
	Yes	7,980 (3.32)	904 (7.20)	908 (5.96)	1,032 (4.38)	1,132 (3.15)	1,380 (2.83)	1,445 (2.56)	1,179 (2.47)	
1-yr death (1 yr)	Missing	41,150 (21.86)	3,521 (25.66)	4,085 (25.04)	6,239 (24.87)	8,774 (23.07)	10,095 (19.79)	8,436 (19.13)	-	<0.0001
	No	124,118 (65.93)	7,724 (56.29)	9,585 (58.76)	15,440 (61.55)	24,874 (65.40)	35,317 (69.25)	31,178 (70.71)	-	
	Yes	22,979 (12.21)	2,478 (18.06)	2,642 (16.20)	3,406 (13.58)	4,387 (11.53)	5,590 (10.96)	4,476 (10.15)	-	
1-yr death (1 yr), nonmissing	No	124,118 (84.38)	7,724 (75.71)	9,585 (78.39)	15,440 (81.93)	24,874 (85.01)	35,317 (86.33)	31,178 (87.45)	-	<0.0001
	Yes	22,979 (15.62)	2,478 (24.29)	2,642 (21.61)	3,406 (18.07)	4,387 (14.99)	5,590 (13.67)	4,476 (12.55)	-	
Alive and well										
Baseline and 1-yr KCCQ complete, among 1-yr survivors (1 yr)	No	39,604 (31.91)	4,195 (54.31)	3,293 (34.36)	5,062 (32.78)	7,478 (30.06)	10,422 (29.51)	9,154 (29.36)	-	<0.0001
	Yes	84,514 (68.09)	3,529 (45.69)	6,292 (65.64)	10,378 (67.22)	17,396 (69.94)	24,895 (70.49)	22,024 (70.64)	-	
Alive and well, among 1-yr survivors with complete KCCQ (1 yr)	No	17,786 (21.05)	816 (23.12)	1,502 (23.87)	2,417 (23.29)	3,772 (21.68)	5,049 (20.28)	4,230 (19.21)	-	<0.0001
	Yes	66,728 (78.95)	2,713 (76.88)	4,790 (76.13)	7,961 (76.71)	13,624 (78.32)	19,846 (79.72)	17,794 (80.79)	-	
Nonfatal endpoints, in-hospital										
Any stroke	No	271,240 (98.19)	13,402 (97.90)	15,945 (97.79)	24,572 (98.00)	37,326 (98.15)	50,053 (98.15)	58,112 (98.22)	71,830 (98.41)	<0.0001
	Yes	5,009 (1.81)	288 (2.10)	360 (2.21)	502 (2.00)	702 (1.85)	944 (1.85)	1,056 (1.78)	1,157 (1.59)	
AV reintervention	No	275,792 (99.83)	13,651 (99.72)	16,258 (99.71)	25,000 (99.70)	37,973 (99.86)	50,942 (99.89)	59,081 (99.85)	72,887 (99.86)	<0.0001
	Yes	457 (0.17)	39 (0.28)	47 (0.29)	74 (0.30)	55 (0.14)	55 (0.11)	87 (0.15)	100 (0.14)	
PCI	No	275,248 (99.64)	13,595 (99.31)	16,224 (99.50)	24,982 (99.63)	37,900 (99.66)	50,836 (99.68)	58,949 (99.63)	72,762 (99.69)	<0.0001
	Yes	1,001 (0.36)	95 (0.69)	81 (0.50)	92 (0.37)	128 (0.34)	161 (0.32)	219 (0.37)	225 (0.31)	
Pacemaker (v1.3)	No	206,564 (90.02)	1,699 (90.90)	11,862 (87.05)	18,346 (86.77)	29,024 (88.98)	40,000 (90.12)	46,695 (90.62)	58,938 (91.66)	<0.0001
	Yes	22,911 (9.98)	170 (9.10)	1,765 (12.95)	2,798 (13.23)	3,594 (11.02)	4,386 (9.88)	4,833 (9.38)	5,365 (8.34)	
Dialysis	No	263,496 (99.30)	12,839 (98.03)	15,389 (98.37)	23,797 (99.04)	36,101 (99.28)	48,794 (99.46)	56,596 (99.52)	69,980 (99.56)	<0.0001
	Yes	1,850 (0.70)	258 (1.97)	255 (1.63)	231 (0.96)	260 (0.72)	263 (0.54)	274 (0.48)	309 (0.44)	
VARC degree of bleeding	No VARC Bleed	256,188 (94.26)	11,866 (88.34)	14,848 (91.99)	23,074 (93.12)	35,365 (94.24)	47,510 (94.71)	55,261 (95.08)	68,264 (95.29)	<0.0001
	Major bleed	9,072 (3.34)	721 (5.37)	676 (4.19)	963 (3.89)	1,286 (3.43)	1,543 (3.08)	1,786 (3.07)	2,097 (2.93)	
	LT/disabling bleed	6,541 (2.41)	845 (6.29)	617 (3.82)	742 (2.99)	874 (2.33)	1,110 (2.21)	1,073 (1.85)	1,280 (1.79)	
RBC/whole blood transfusion	Missing	705 (0.26)	77 (0.56)	52 (0.32)	62 (0.25)	113 (0.30)	123 (0.24)	119 (0.20)	159 (0.22)	<0.0001
	No	235,797 (85.34)	7,557 (55.07)	11,265 (69.06)	19,501 (77.74)	32,136 (84.49)	44,840 (87.92)	53,352 (90.17)	67,146 (91.99)	
	Yes	39,814 (14.41)	6,089 (44.37)	4,995 (30.62)	5,522 (22.01)	5,786 (15.21)	6,039 (11.84)	5,697 (9.63)	5,686 (7.79)	
Major vascular access site complications (v1.3)	No	261,585 (98.79)	2,201 (98.43)	16,109 (98.80)	24,740 (98.67)	37,571 (98.80)	50,394 (98.82)	58,505 (98.88)	72,065 (98.74)	0.7639
	Yes	3,210 (1.21)	35 (1.57)	196 (1.20)	334 (1.33)	457 (1.20)	603 (1.18)	663 (1.12)	922 (1.26)	

Continued on the next page

TABLE 2 Continued

	Level	Overall (N = 276,316)	≤2013 (N = 13,723)	2014 (N = 16,312)	2015 (N = 25,085)	2016 (N = 38,035)	2017 (N = 51,002)	2018 (N = 59,168)	2019 (N = 72,991)	p Value
30-day follow-up										
Follow-up assessment, among 30-day survivors (30-day)	No	29,835 (12.05)	2,753 (21.48)	2,370 (15.39)	3,265 (13.57)	4,776 (12.94)	5,512 (11.11)	6,087 (10.55)	5,072 (9.94)	<0.0001
	Yes	217,713 (87.95)	10,066 (78.52)	13,034 (84.61)	20,788 (86.43)	32,127 (87.06)	44,110 (88.89)	51,636 (89.45)	45,952 (90.06)	
Nonfatal endpoints										
Stroke (30-day)	Missing	15,940 (6.24)	1,301 (9.48)	1,169 (7.17)	1,592 (6.35)	2,203 (5.79)	2,494 (4.89)	2,725 (4.61)	4,456 (8.54)	<0.0001
	No	233,754 (91.48)	12,081 (88.03)	14,722 (90.25)	22,898 (91.28)	34,958 (91.91)	47,313 (92.77)	55,125 (93.17)	46,657 (89.38)	
	Yes	5,834 (2.28)	341 (2.48)	421 (2.58)	595 (2.37)	874 (2.30)	1,195 (2.34)	1,318 (2.23)	1,090 (2.09)	
Stroke (30-day), nonmissing	No	233,754 (97.56)	12,081 (97.25)	14,722 (97.22)	22,898 (97.47)	34,958 (97.56)	47,313 (97.54)	55,125 (97.66)	46,657 (97.72)	<0.0001
	Yes	5,834 (2.44)	341 (2.75)	421 (2.78)	595 (2.53)	874 (2.44)	1,195 (2.46)	1,318 (2.34)	1,090 (2.28)	
AV reintervention (30-day)	Missing	16,341 (6.39)	1,332 (9.71)	1,195 (7.33)	1,639 (6.53)	2,278 (5.99)	2,563 (5.03)	2,790 (4.72)	4,544 (8.70)	<0.0001
	No	238,615 (93.38)	12,345 (89.96)	15,059 (92.32)	23,351 (93.09)	35,678 (93.80)	48,362 (94.82)	56,253 (95.07)	47,567 (91.12)	
	Yes	572 (0.22)	46 (0.34)	58 (0.36)	95 (0.38)	79 (0.21)	77 (0.15)	125 (0.21)	92 (0.18)	
AV reintervention (30-day), nonmissing	No	238,615 (99.76)	12,345 (99.63)	15,059 (99.62)	23,351 (99.59)	35,678 (99.78)	48,362 (99.84)	56,253 (99.78)	47,567 (99.81)	<0.0001
	Yes	572 (0.24)	46 (0.37)	58 (0.38)	95 (0.41)	79 (0.22)	77 (0.16)	125 (0.22)	92 (0.19)	
PCI (30-day)	Missing	16,342 (6.40)	1,331 (9.70)	1,197 (7.34)	1,638 (6.53)	2,270 (5.97)	2,561 (5.02)	2,794 (4.72)	4,551 (8.72)	0.0014
	No	238,047 (93.16)	12,293 (89.58)	15,022 (92.09)	23,340 (93.04)	35,606 (93.61)	48,241 (94.59)	56,096 (94.81)	47,449 (90.89)	
	Yes	1,139 (0.45)	99 (0.72)	93 (0.57)	107 (0.43)	159 (0.42)	200 (0.39)	278 (0.47)	203 (0.39)	
PCI (30-day), nonmissing	No	238,047 (99.52)	12,293 (99.20)	15,022 (99.38)	23,340 (99.54)	35,606 (99.56)	48,241 (99.59)	56,096 (99.51)	47,449 (99.57)	0.0014
	Yes	1,139 (0.48)	99 (0.80)	93 (0.62)	107 (0.46)	159 (0.44)	200 (0.41)	278 (0.49)	203 (0.43)	
Pacemaker (30-day) (v1.3)	Missing	11,866 (5.62)	172 (9.18)	882 (6.47)	1,200 (5.67)	1,756 (5.38)	1,970 (4.44)	2,240 (4.35)	3,646 (7.96)	<0.0001
	No	174,815 (82.85)	1,515 (80.89)	10,856 (79.64)	16,941 (80.10)	26,840 (82.27)	37,396 (84.25)	43,668 (84.75)	37,599 (82.06)	
	Yes	24,333) (11.53)	186 (9.93)	1,894 (13.89)	3,009 (14.23)	4,029 (12.35)	5,023 (11.32)	5,620 (10.91)	4,572 (9.98)	
Pacemaker (30-day) (v1.3), nonmissing	No	174,815 (87.78)	1,515 (89.07)	10,856 (85.15)	16,941 (84.92)	26,840 (86.95)	37,396 (88.16)	43,668 (88.60)	37,599 (89.16)	<0.0001
	Yes	24,333 (12.22)	186 (10.93)	1,894 (14.85)	3,009 (15.08)	4,029 (13.05)	5,023 (11.84)	5,620 (11.40)	4,572 (10.84)	
Dialysis (30-day)	Missing	15,428 (6.29)	1,257 (9.57)	1,119 (7.15)	1,545 (6.43)	2,135 (5.87)	2,409 (4.91)	2,643 (4.65)	4,320 (8.61)	<0.0001
	No	227,953 (92.93)	11,606 (88.40)	14,262 (91.13)	22,244 (92.54)	33,950 (93.35)	46,364 (94.50)	53,932 (94.83)	45,595 (90.86)	
	Yes	1,916 (0.78)	266 (2.03)	270 (1.73)	248 (1.03)	283 (0.78)	289 (0.59)	295 (0.52)	265 (0.53)	
Dialysis (30-day), nonmissing	No	227,953 (99.17)	11,606 (97.76)	14,262 (98.14)	22,244 (98.90)	33,950 (99.17)	46,364 (99.38)	53,932 (99.46)	45,595 (99.42)	<0.0001
	Yes	1,916 (0.83)	266 (2.24)	270 (1.86)	248 (1.10)	283 (0.83)	289 (0.62)	295 (0.54)	265 (0.58)	
Acute kidney injury (30-day)	Missing	5,075 (2.07)	247 (1.88)	174 (1.11)	263 (1.09)	454 (1.25)	884 (1.80)	1,480 (2.60)	1,573 (3.13)	<0.0001
	None	235,600 (96.05)	12,222 (93.09)	14,914 (95.29)	23,158 (96.34)	35,257 (96.95)	47,453 (96.72)	54,663 (96.12)	47,933 (95.52)	
	Stage I	690 (0.28)	103 (0.78)	92 (0.59)	83 (0.35)	95 (0.26)	119 (0.24)	110 (0.19)	88 (0.18)	
	Stage II	403 (0.16)	79 (0.60)	42 (0.27)	67 (0.28)	50 (0.14)	63 (0.13)	51 (0.09)	51 (0.10)	
	Stage III	3,529 (1.44)	478 (3.64)	429 (2.74)	466 (1.94)	512 (1.41)	543 (1.11)	566 (1.00)	535 (1.07)	
Major vascular access site complication (30-day) (v1.3)	Missing	15,121 (6.20)	217 (9.68)	1,188 (7.28)	1,637 (6.53)	2,259 (5.94)	2,538 (4.98)	2,769 (4.68)	4,513 (8.65)	0.8946
	No	225,683 (92.48)	1,986 (88.58)	14,910 (91.41)	23,082 (92.02)	35,282 (92.76)	47,811 (93.74)	55,660 (94.07)	46,952 (89.94)	
	Yes	3,243 (1.33)	39 (1.74)	214 (1.31)	366 (1.46)	494 (1.30)	653 (1.28)	739 (1.25)	738 (1.41)	
Major vascular access site complication (30-day) (v1.3), nonmissing	No	225,683 (98.58)	1,986 (98.07)	14,910 (98.59)	23,082 (98.44)	35,282 (98.62)	47,811 (98.65)	55,660 (98.69)	46,952 (98.45)	0.8946
	Yes	3,243 (1.42)	39 (1.93)	214 (1.41)	366 (1.56)	494 (1.38)	653 (1.35)	739 (1.31)	738 (1.55)	
In-hospital/30-day VARC major or LT/disabling bleed (v1.3)	Missing	17,695 (7.25)	222 (9.90)	1,231 (7.55)	1,779 (7.09)	2,595 (6.82)	3,156 (6.19)	3,606 (6.09)	5,106 (9.78)	<0.0001
	No	211,290 (86.58)	1,765 (78.72)	13,649 (83.67)	21,405 (85.33)	33,026 (86.83)	44,839 (87.92)	52,333 (88.45)	44,273 (84.81)	
	Yes	15,062 (6.17)	255 (11.37)	1,432 (8.78)	1,901 (7.58)	2,414 (6.35)	3,007 (5.90)	3,229 (5.46)	2,824 (5.41)	

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TABLE 2 Continued

	Level	Overall (N = 276,316)	≤2013 (N = 13,723)	2014 (N = 16,312)	2015 (N = 25,085)	2016 (N = 38,035)	2017 (N = 51,002)	2018 (N = 59,168)	2019 (N = 72,991)	p Value
NYHA and KCCQ, follow-up										
30-day NYHA functional class (30-day)	Missing	59,149 (23.89)	4,195 (32.72)	3,826 (24.84)	6,065 (25.22)	8,956 (24.27)	11,713 (23.60)	13,317 (23.07)	11,077 (21.71)	<0.0001
	Class I	98,630 (39.84)	4,133 (32.24)	5,239 (34.01)	8,561 (35.59)	14,153 (38.35)	20,375 (41.06)	24,011 (41.60)	22,158 (43.43)	
	Class II	71,909 (29.05)	3,366 (26.26)	4,851 (31.49)	7,349 (30.55)	11,040 (29.92)	14,218 (28.65)	16,519 (28.62)	14,566 (28.55)	
	Class III	15,932 (6.44)	965 (7.53)	1,266 (8.22)	1,788 (7.43)	2,462 (6.67)	2,999 (6.04)	3,546 (6.14)	2,906 (5.70)	
	Class IV	1,928 (0.78)	160 (1.25)	222 (1.44)	290 (1.21)	292 (0.79)	317 (0.64)	330 (0.57)	317 (0.62)	
30-day NYHA functional class (30-day), nonmissing	Class I	98,630 (52.35)	4,133 (47.92)	5,239 (45.25)	8,561 (47.59)	14,153 (50.64)	20,375 (53.75)	24,011 (54.07)	22,158 (55.47)	<0.0001
	Class II	71,909 (38.17)	3,366 (39.03)	4,851 (41.90)	7,349 (40.86)	11,040 (39.50)	14,218 (37.51)	16,519 (37.20)	14,566 (36.46)	
	Class III	15,932 (8.46)	965 (11.19)	1,266 (10.93)	1,788 (9.94)	2,462 (8.81)	2,999 (7.91)	3,546 (7.99)	2,906 (7.27)	
	Class IV	1,928 (1.02)	160 (1.86)	222 (1.92)	290 (1.61)	292 (1.04)	317 (0.84)	330 (0.74)	317 (0.79)	
30-day KCCQ score status (30-day)	Missing	64,533 (26.07)	6,937 (54.11)	4,827 (31.34)	6,654 (27.66)	9,609 (26.04)	11,699 (23.58)	13,149 (22.78)	11,658 (22.85)	<0.0001
	Nonmissing	183,015 (73.93)	5,882 (45.89)	10,577 (68.66)	17,399 (72.34)	27,294 (73.96)	37,923 (76.42)	44,574 (77.22)	39,366 (77.15)	
30-day KCCQ score (30-day), among complete*	n, n [median]	183,015 [80.21]	5,882 [71.88]	10,577 [73.96]	17,399 [76.04]	27,294 [79.17]	37,923 [81.25]	44,574 [81.25]	39,366 [82.29]	<0.0001
	25th	60.42	52.08	52.78	56.25	59.72	61.98	62.50	64.06	
	75th	93.06	87.50	88.54	90.62	92.19	93.75	93.75	94.79	
	Missing, %	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	
1-yr KCCQ score status (1 yr)	Missing	74,384 (45.01)	5,906 (52.52)	6,789 (49.66)	10,569 (48.75)	15,199 (45.17)	19,311 (42.52)	16,610 (41.93)	-	<0.0001
	Nonmissing	90,884 (54.99)	5,339 (47.48)	6,881 (50.34)	11,110 (51.25)	18,449 (54.83)	26,101 (57.48)	23,004 (58.07)	-	
1-yr KCCQ score (1 yr), among complete*	n [median]	90,884 [84.38]	5,339 [80.73]	6,881 [80.21]	11,110 [82.29]	18,449 [83.33]	26,101 [85.42]	23,004 [86.11]	-	<0.0001
	25th	65.97	62.50	61.46	63.54	65.28	67.19	68.75	-	
	75th	95.83	93.75	93.75	93.75	94.79	95.83	96.88	-	
	Missing, %	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-	
Echocardiogram outcomes										
In-hospital/30-day aortic insufficiency (30-day)	Missing	12,883 (5.04)	2,034 (14.82)	1,458 (8.94)	1,700 (6.78)	1,997 (5.25)	1,924 (3.77)	2,037 (3.44)	1,733 (3.32)	<0.0001
	None/trace/mild	235,208 (92.05)	10,758 (78.39)	13,779 (84.47)	21,948 (87.49)	34,820 (91.55)	48,108 (94.33)	56,119 (94.85)	49,676 (95.16)	
	Moderate/severe	7,437 (2.91)	931 (6.78)	1,075 (6.59)	1,437 (5.73)	1,218 (3.20)	970 (1.90)	1,012 (1.71)	794 (1.52)	
In-hospital/30-day aortic insufficiency (30-day), nonmissing	None/trace/mild	235,208 (96.94)	10,758 (92.04)	13,779 (92.76)	21,948 (93.86)	34,820 (96.62)	48,108 (98.02)	56,119 (98.23)	49,676 (98.43)	<0.0001
	Moderate/severe	7,437 (3.06)	931 (7.96)	1,075 (7.24)	1,437 (6.14)	1,218 (3.38)	970 (1.98)	1,012 (1.77)	794 (1.57)	
In-hospital/30-day AV mean gradient	Missing	14,424 (5.64)	2,365 (17.23)	1,688 (10.35)	1,919 (7.65)	2,219 (5.83)	2,159 (4.23)	2,188 (3.70)	1,886 (3.61)	<0.0001
	<10	118,869 (46.52)	5,659 (41.24)	9,018 (55.28)	13,317 (53.09)	16,737 (44.00)	22,925 (44.95)	27,306 (46.15)	23,907 (45.80)	
	10-20	107,782 (42.18)	5,102 (37.18)	5,071 (31.09)	8,735 (34.82)	16,675 (43.84)	22,696 (44.50)	26,196 (44.27)	23,307 (44.65)	
	≥20	14,453 (5.66)	597 (4.35)	535 (3.28)	1,114 (4.44)	2,404 (6.32)	3,222 (6.32)	3,478 (5.88)	3,103 (5.94)	
In-hospital/30-day AV mean gradient (30-day), nonmissing	<10	118,869 (49.30)	5,659 (49.82)	9,018 (61.67)	13,317 (57.49)	16,737 (46.73)	22,925 (46.94)	27,306 (47.92)	23,907 (47.51)	<0.0001
	10-20	107,782 (44.70)	5,102 (44.92)	5,071 (34.68)	8,735 (37.71)	16,675 (46.56)	22,696 (46.47)	26,196 (45.97)	23,307 (46.32)	
	≥20	14,453 (5.99)	597 (5.26)	535 (3.66)	1,114 (4.81)	2,404 (6.71)	3,222 (6.60)	3,478 (6.10)	3,103 (6.17)	
Change in AVMG from post-procedure to 1 yr (1 yr)	Missing	90,218 (54.59)	7,678 (68.28)	8,695 (63.61)	12,658 (58.39)	18,548 (55.12)	23,045 (50.75)	19,594 (49.46)	-	0.4675
	Change <10	71,494 (43.26)	3,444 (30.63)	4,804 (35.14)	8,546 (39.42)	14,294 (42.48)	21,319 (46.95)	19,087 (48.18)	-	
	Change ≥10	3,556 (2.15)	123 (1.09)	171 (1.25)	475 (2.19)	806 (2.40)	1,048 (2.31)	933 (2.36)	-	
Change in AVMG from post-procedure to 1 yr (1 yr), nonmissing	Change <10	71,494 (95.26)	3,444 (96.55)	4,804 (96.56)	8,546 (94.73)	14,294 (94.66)	21,319 (95.31)	19,087 (95.34)	-	0.4675
	Change ≥10	3,556 (4.74)	123 (3.45)	171 (3.44)	475 (5.27)	806 (5.34)	1,048 (4.69)	933 (4.66)	-	

Continued on the next page

TABLE 2 Continued

	Level	Overall (N = 276,316)	≤2013 (N = 13,723)	2014 (N = 16,312)	2015 (N = 25,085)	2016 (N = 38,035)	2017 (N = 51,002)	2018 (N = 59,168)	2019 (N = 72,991)	p Value
Length of stay										
Length of stay*	n [median]	276,316 [3.00]	13,723 [7.00]	16,312 [6.00]	25,085 [4.00]	38,035 [3.00]	51,002 [2.00]	59,168 [2.00]	72,991 [2.00]	<0.0001
	25th	2.00	4.00	4.00	3.00	2.00	2.00	1.00	1.00	
	75th	6.00	10.00	9.00	8.00	6.00	5.00	4.00	3.00	
	Missing, %	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	

Values are n (%) unless otherwise indicated. Data run at Duke Clinical Research Institute on June 17, 2020. Registry population includes index TAVR procedure per patient, started on/before December 31, 2019. (30 day) indicates all 30-day outcomes among procedures started on/before September 30, 2019. (1 yr) indicates all 1-year outcomes among procedures started on/before September 30, 2018. (v1.3) indicates field is new in DCF version 1.3 or with additional/revised options; subset on procedures started on/after October 1, 2013. p values do not correspond to the table exactly as it is presented here. More appropriately, p values were calculated by comparing only nonmissing row values. p values are based on chi-square rank-based group means score statistics for all categorical row variables (equivalent to Kruskal-Wallis test for row variables with 3+ levels and Wilcoxon test for 2 levels). *p values are based on chi-square 1 degree of freedom rank correlation statistics for all continuous/ordinal row variables. All tests treat the column variable as an ordinal.

AI = aortic insufficiency; AS = aortic stenosis; AV = aortic valve; AVMG = aortic valve mean gradient; LT = life-threatening; NYHA = New York Heart Association functional; OR = operating room; PCI = percutaneous coronary intervention; RBC = red blood cells; TCU = transitional care unit; other abbreviations as in Table 1.

2013 to 4,508 in 2019. Immediate or urgent V-in-V during TAVR has decreased from 322 cases between 2011 and 2013 to 208 in 2019. Figure 3 demonstrates the trends in the annual procedural volume of these 2 categories of aortic V-in-V.

Elective V-in-V is predominantly TAVR-in-SAVR with only a small number of elective TAVR-in-TAVR. As shown in Table 2, the pre-procedure indication of TAVR-in-TAVR was infrequent with a total of only 404 patients having been treated in all years. The annual number of planned TAVR-in-TAVR has slowly been increasing, with 110 treated in 2019. This compares with 15,382 patients having planned TAVR-in-SAVR, with 4,480 treated in 2019 alone. Thus, all forms of elective V-in-V were performed in 15,898 in the period 2011 to 2019.

Separately, immediate intraprocedure TAVR-in-TAVR was performed in 1,899 cases over the period 2011 to 2019.

There is an additional relevant data element called Procedure Indication that lists the spectrum of stenosis, insufficiency, and mixed hemodynamic abnormalities but also includes the option of Failed Bioprosthetic Valve. The volumes for the later are significantly less than the volumes for both TAVR-in-SAVR and TAVR-in TAVR categories, probably due to data entry personnel choosing the option that describes the hemodynamic abnormality of the SAVR or TAVR valve rather than the Failed Bioprosthetic Valve option.

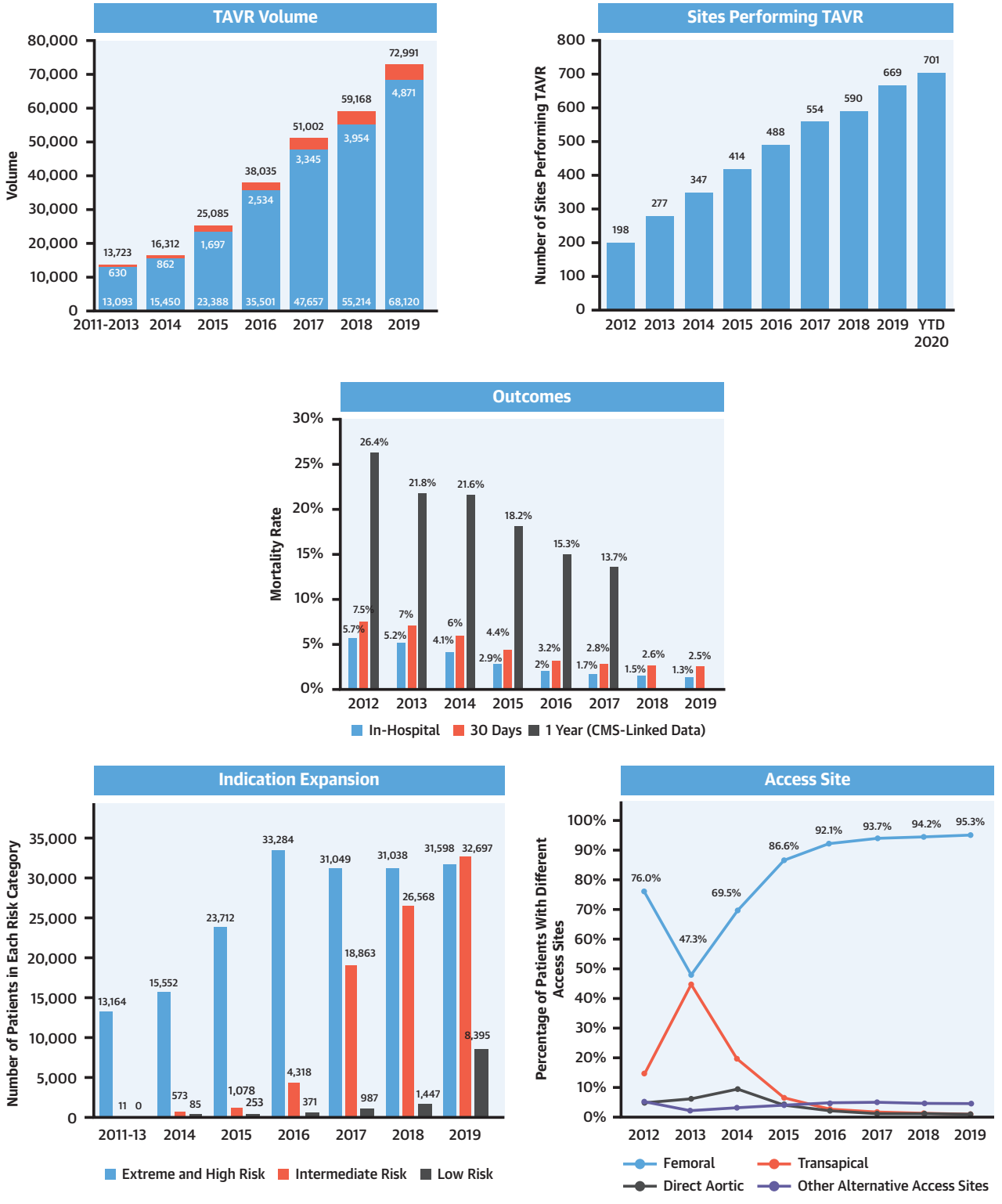
Procedure volume by site. The number of TAVR procedures performed per site varies markedly. Table 3 shows the annual trends in mean, median, range, and first and third quartiles of annual TAVR volume per site and the number of sites performing fewer than 50 TAVRs in a given year. The 50-case annual threshold is aligned with the Joint Report of the American Association for Thoracic Surgery, ACC, Society for Cardiovascular Angiography and Interventions, and STS expert consensus document published in 2019 (11). The number of sites performing TAVR has steadily increased, the total annual volume of TAVRs has increased, and the mean annual procedural volume per site has now increased in 2019 to 110 with a median of 84

TABLE 3 Year-to-Year Site TAVR Volume Statistics

	2012	2013	2014	2015	2016	2017	2018	2019
Total sites with at least 1 TAVR	198	277	347	414	488	554	590	669
Total of sites' TAVR volumes: annualized	6,482.1	10,103.6	17,392.7	26,282.6	39,516.0	52,298.9	60,172.6	73,411.0
Minimum of site's TAVR volume	1	3	5	4	4	5	8	1
Maximum of site's TAVR volume	168	136	235	275	424	571	559	688
Mean of site's TAVR volume	32.7	36.5	50.1	63.5	81.0	94.8	102.0	109.7
1st quartile of sites' TAVR volume	20.7	22	25	30	38	45	49	50
Median of sites' TAVR volume	27	30.86	39	48	61	70.5	76	84
3rd quartile of sites' TAVR volume	38.4	44	62	80	101	122	127	137
Number of sites with <50 TAVRs	167	224	219	214	191	171	153	161

All site yearly transcatheter aortic valve replacement (TAVR) volumes reported here are annualized as follows: For a given year, site TAVR annualized yearly volume = 12 × (total site TAVRs in given year / # of months). If site's first TAVR is before given year, then # months = 12, and annualized volume is just the total site TAVRs in given year. If site's first TAVR is in given year, then # of months = total months on/after site's first TAVR month in given year. If site's first TAVR is after given year, then site is excluded from all metric calculations for given year.

CENTRAL ILLUSTRATION **The State of Transcatheter Aortic Valve Replacement: Trends in the United States From 2011 to 2019**



Carroll, J.D. et al. J Am Coll Cardiol. 2020;76(21):2492-516.

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(IQR: 50 to 137). In 2019, 161 sites performed <50 cases.

PATIENT CHARACTERISTICS. Demographics. In 2019, the median age of individuals undergoing TAVR was 80 years (IQR: 73 to 85 years), compared with 84 in the years immediately following the initial FDA approval (Table 2). The median age in high/extreme risk patients in 2019 was 81 years (IQR: 74 to 87 years), for the intermediate-risk patients 80 years (IQR: 74 to 84 years), and for the low-risk cohort 75 years (IQR: 70 to 81 years) (Supplemental Tables 1 to 3). There has been a small shift from equal male/female distribution of 48.8%/51.1% in the early TAVR period to a predominance of males in 2019 of 55.8%/44.2%. For all years, patients undergoing TAVR were predominantly of white race. In the first half of 2019, 4.0% were Black/African American, and 5.2% were of Hispanic or Latino ethnicity.

Patient risk categorization. There has been a substantial evolution in the clinical characteristics of patients undergoing TAVR driven by the expansion of approved indications for TAVR. The median 30-day STS PROM (Predicted Risk of Mortality) has steadily fallen from 6.9% (IQR: 4.6% to 10.7%) in 2013 to 4.4% (IQR: 2.7% to 7.2%) in 2019 (Figure 4).

The year-by-year results of the local heart team's assessment of SAVR risk in patients undergoing TAVR are shown in the Central Illustration. The annual number of patients deemed high/extreme risk initially increased but then stabilized, but remains substantial; this group accounts for approximately 31,000 to 33,000 procedures in each of the last 4 years. The volume of intermediate-risk patients steadily has increased to 32,697 procedures in 2019. The number of patients deemed low risk is starting to increase, with 8,395 patients treated in 2019 representing 11.5% of all TAVR patients.

Comorbid conditions. Patients undergoing TAVR often have other comorbid conditions. The burden of comorbidity has declined with expansion of TAVR into lower-risk populations (Table 2). Gait speed was still abnormal in 69.8% of TAVR patients in 2019. Hostile chest and porcelain aorta, although substantially less common than in the early TAVR experience, were noted in 5.2% and 2.1% of patients, respectively, in 2019. Those using supplemental oxygen has declined from 13.8% to 7.2%.

Functional class. The proportion of patients with New York Heart Association (NYHA) functional class IV symptoms before TAVR has declined from 22.2% to 10.0% from early TAVR experience to 2019. The majority of patients have NYHA functional class III symptoms, in a proportion that has been relatively stable from early TAVR (59.6%) to 2019 (56.75%). There has been a substantial increase in the proportions of patients with NYHA functional class II symptoms, from 13.7% during the early TAVR period to 28.2% in the first half of 2019.

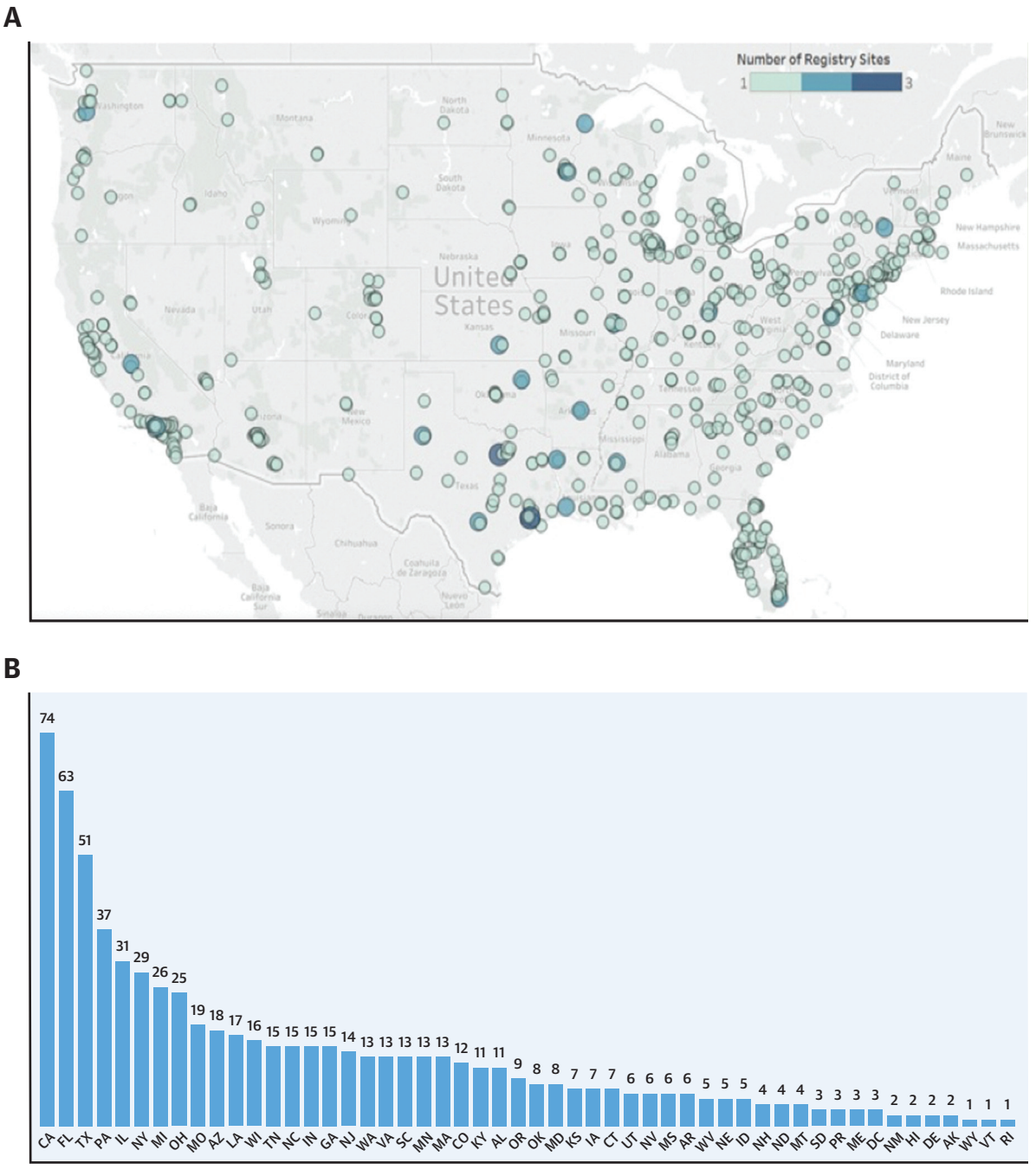
Patient-reported health status at baseline. Patient-reported health status at baseline is shown in Table 4. The Kansas City Cardiomyopathy Questionnaire (KCCQ) provides a measure of the patient's perception of their health status, including symptoms, impact on physical and social function, and their quality of life. During the early TAVR experience the median score was 44 (IQR: 26 to 64) and, over subsequent years, has slowly increased (Table 2). In 2019, baseline KCCQ scores were available in 67,783 patients representing 93% of patients undergoing TAVR. For all TAVR patients in 2019, the median baseline score was 47 (IQR: 28 to 67). In 2019, the median baseline KCCQ summary score for those patients classified by the heart team as high/extreme risk was 41 (IQR: 23 to 60), intermediate risk was 49 (IQR: 32 to 69), and low risk was 58 IQR: 39 to 78).

Procedure indication. The dominant indication for TAVR was severe native valve aortic stenosis. Since the early period of TAVR to 2019, this has minimally changed from 96.2% to 91.9%. Other indications in 2019 include failed bioprosthetic valve (4.25%), mixed aortic stenosis/AR (3.0%), and primary AR (0.7%). There are no FDA-approved TAVR technologies for AR, and these cases, therefore, represent off-label use of TAVR valves.

CENTRAL ILLUSTRATION Continued

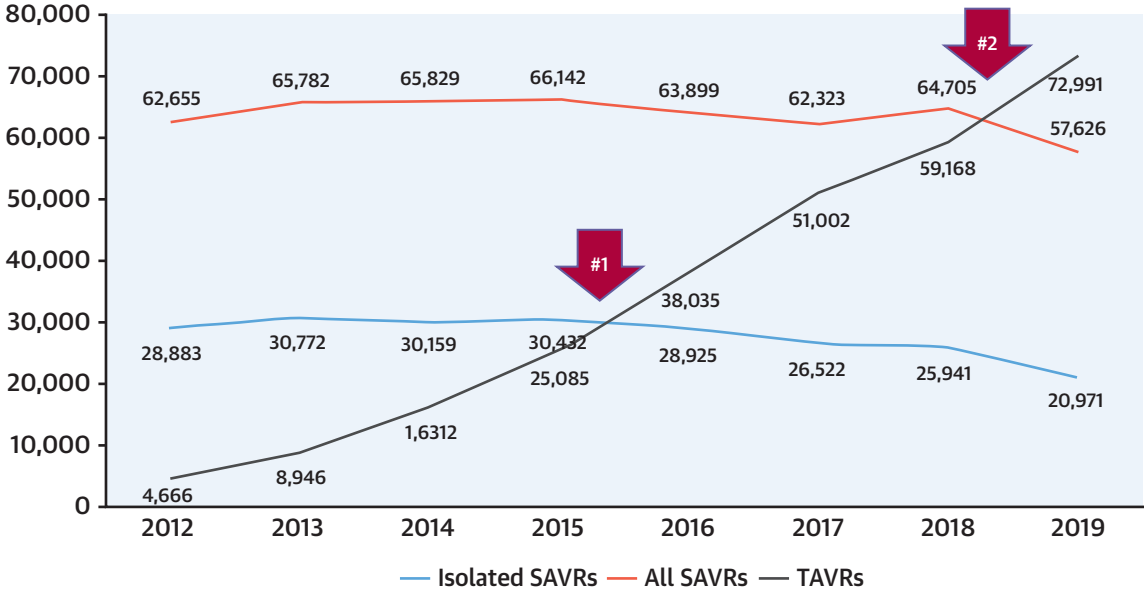
TAVR Volume: volume of transcatheter aortic valve replacement (TAVR) for native aortic valve disease (**blue** with value at base of column) and for failure of prosthetic aortic valves **(red with value in white below)** between 2011 and 2019. The **value above each column** is the total number of TAVRs performed in that year. Sites Performing TAVR: number of sites, that is, hospitals, performing TAVR from 2012 through the end of May 2020. Indication Expansion: yearly number of patients undergoing TAVR categorized by surgical aortic valve replacement risk profile. The heart team's assessment of patient risk was used for categorization: extreme- and high-risk patients **(blue)**, intermediate-risk patients **(red)**, and low-risk patients **(black)**. Access Site: yearly (2012 to 2019) proportions of TAVR procedures by access site, including femoral **(blue)**, transapical **(red)**, direct aortic **(gray)**, and other approaches (**purple**: subclavian, carotid, and transcaval) approaches. Outcomes: mortality rates between 2012 and 2019, according to ascertainment time: **blue** = in-hospital; **red** = 30 days; **black** = 1 year. This figure uses Centers for Medicare & Medicaid (CMS)–linked data for 1-year mortality, available with complete data only for patients treated through 2017.

FIGURE 1 **Location of TAVR Sites**



(A) Location of TAVR sites. U.S. map of 48 states and the location of sites through March 2020. **Color codes** indicate >1 site in close proximity. Both Hawaii and Alaska have sites. **(B)** Distribution of TAVR sites in states. The number of TAVR sites in each of the U.S. states is shown in decreasing order of number of sites. Abbreviations for each State are from the U.S. Postal Service. TAVR = transcatheter aortic valve replacement.

FIGURE 2 Annual Volumes of TAVR and SAVR



The volume of isolated surgical aortic valve replacement (SAVR) **(blue line)**, all forms of SAVR (SAVR + coronary artery bypass grafting, Bentall procedures, and SAVR plus other surgical procedures, **red line**), and transcatheter aortic valve replacement (TAVR) **(gray line)** are shown from 2012 until 2018. The 2 **red arrows** denote transition points: **Arrow #1**—the volume of TAVR first exceeded isolated SAVR between 2015 and 2016 with the beginning of a decline in isolated SAVR volume that in 2019 was 9,801 fewer cases than the peak in 2013. TAVR in intermediate-risk patients was approved in 2016. **Arrow #2**—the volume of TAVR exceeded all forms of SAVR between 2018 and 2019 with a 1-year decline in 2019 from 2018 of 7,079 for all types of SAVR cases. TAVR for low-risk patients was approved in 2019. Source of SAVR data is the Society of Thoracic Surgeons National Database. AVR = aortic valve replacement.

Procedure status. Procedures in 2019 were predominantly classified as elective (91.4%); procedures were considered urgent in 8.0%, emergent in 0.3%, and salvage in 0.07%.

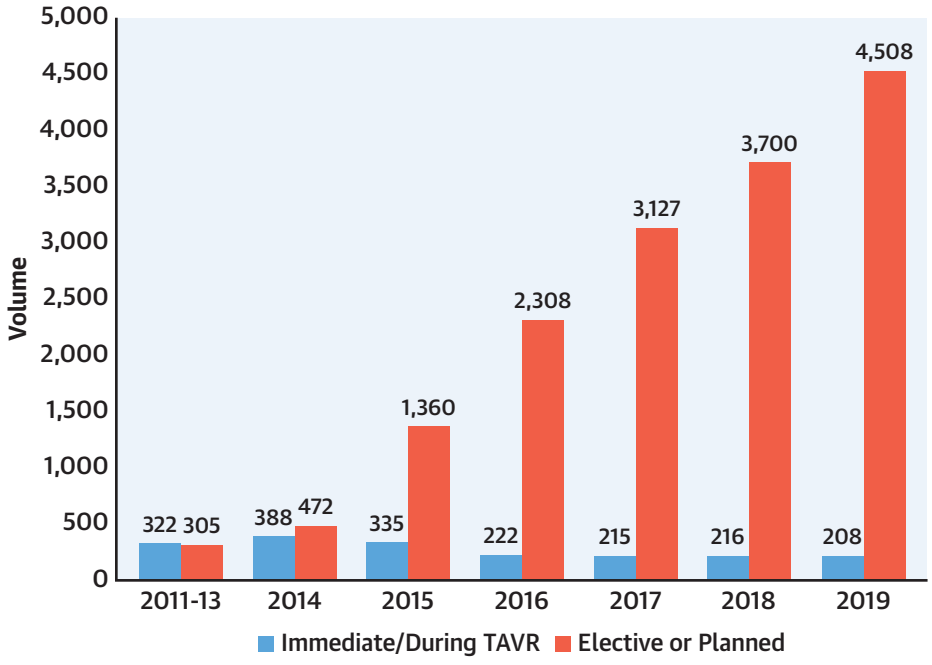
Location. The hybrid operating room was used for 54.7% of TAVR procedures in 2019. The use of either a hybrid or regular catheterization laboratory increased slightly from 38.9% in early TAVR experience to 44.7% in 2019.

Anesthesia. A recent report from the Registry documented an increase in the use of conscious sedation from 33% in 2016 to 64% in early 2019, with a large variability in the use of general anesthesia with a few centers using only general anesthesia (12). Furthermore, Registry data demonstrated that the use of conscious sedation compared with general anesthesia was associated with a small, but statistically significantly, lower risk of in-hospital mortality (adjusted risk difference [aRD] 0.2%; $p = 0.010$), 30-day mortality (aRD 0.5%; $p < 0.001$), hospital length of stay (LOS, adjusted difference 0.8 days; $p < 0.001$), and more frequent discharge to home (aRD 2.8%; $p < 0.001$) (12).

Access site. The vascular access site for TAVR has evolved substantially, as shown in the **Central Illustration and Figure 5**. First, there has been a steady increase in the use of femoral access, from 57.1% in the early TAVR period to 95.3% in 2019 (**Table 2**). In 2019, the high/extreme-risk cohort had femoral access in 93.65% compared with 96.2% in the intermediate-risk cohort and 97.8% in low-risk patients. In 2013, there was a transient drop in the percentage of patients having femoral access because of the FDA expansion of indications to include alternative access.

A second trend has been the change in the types of alternative access used (**Figure 5**). In the early TAVR experience, transapical and direct aortic approaches were predominantly employed, but in 2019, only 213 patients (0.3%) had transapical access and 341 (0.5%) had direct aortic access. In 2019, axillary-subclavian was the most commonly employed alternative approach, that is, 1,816 cases (2.5%). Carotid access has increased to 662 cases (0.9%). Transcaval access was added as an option in April of 2019, and 121 cases were subsequently

FIGURE 3 Volume of Valve-in-Valve TAVR



The annual volume of 2 forms of valve-in-valve TAVR are displayed for 2011 to 2019 The first is when valve-in-valve is performed immediately during TAVR due to malfunction with a first TAVR valve. This is urgent TAVR-in-TAVR. The second is elective or planned valve-in-valve predominantly for degeneration of a surgical bioprosthesis, although elective TAVR-in-TAVR will increase with large numbers of patients with TAVR valves implanted in the last 9 years. TAVR = transcatheter aortic valve replacement.

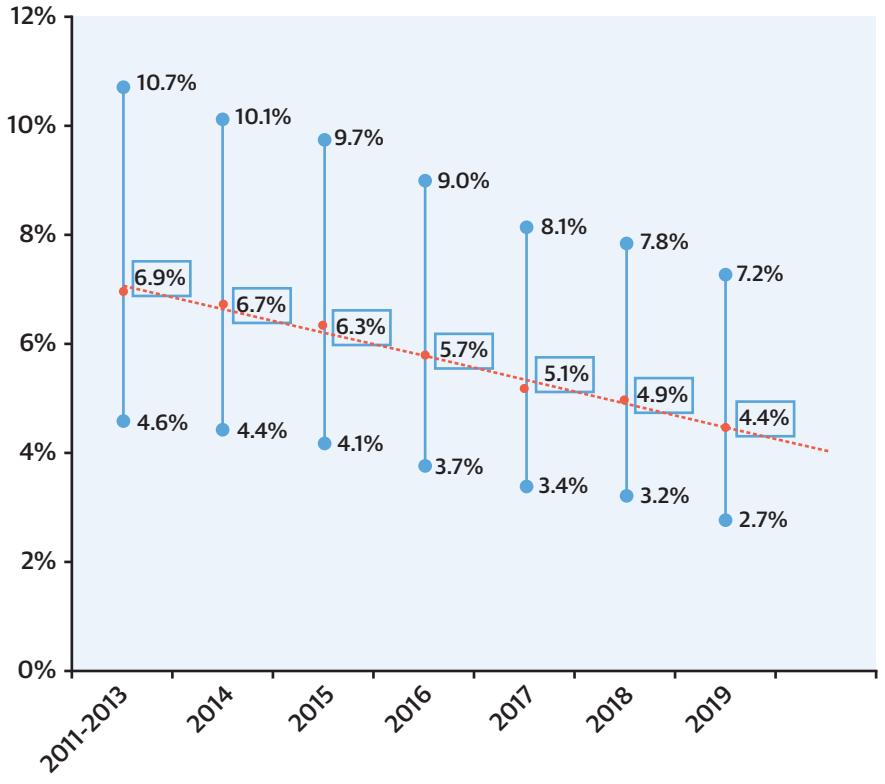
reported. Previously transcaval was included in the "other' category.

Use of bypass and conversion to open heart surgery. The use of cardiopulmonary bypass (CPB) has steadily decreased from 4.1% to 0.4%. The use of CPB is currently surprisingly similar in the high/extreme-risk cohort (0.5%), intermediate-risk cohort (0.35%), and low-risk cohort (0.4%). Conversion to open heart surgery (OHS) has declined from 1.4% to 0.4% since TAVR was initially approved. Conversion to OHS is currently similar in the high/extreme-risk cohort (0.4%), intermediate-risk cohort (0.4%), and low-risk cohort (0.5%). These findings suggest that CPB and OHS are most likely required due to unexpected complications that occur at similar rates across the spectrum of patient risk, although it is not known to what extent patients in each risk category have expressed their decision to not be converted to OHS if problems arise during their TAVR.

Second valve and percutaneous coronary intervention. The need for immediate V-in-V procedure has declined (Figure 3). Percutaneous coronary intervention is infrequently performed during TAVR procedures (1.8% in 2019).

Use of adjunctive techniques. Three important adjunctive techniques and technologies have become part of clinical practice and were added as data elements to the DCF in 2018 and 2019 (Table 1). Volume data captured by the Registry regarding these novel approaches to prevent TAVR-related complications are presented in Table 5. First, the Sentinel device (currently Boston Scientific, Marlborough, Massachusetts) was FDA-approved in December 2017 for cerebral protection. From January 2018 until the end of 2019, Sentinel has been used in 11,877 patients. Second, bioprosthetic or native aortic scallop intentional laceration to prevent iatrogenic coronary artery obstruction (BASILICA) was performed in 41 patients undergoing native valve TAVR and 125 patients undergoing V-in-V TAVR in 2018 to 2019. Finally, intentional fracture of the sewing ring of surgically implanted bioprosthetic valves using a high-pressure, noncompliant balloon was performed in 332 patients during V-in-V TAVR in 2018 to 2019. Dedicated reports on the safety and effectiveness of these 3 adjunctive techniques will be forthcoming from the Registry.

FIGURE 4 Risk Profile of Patients



The median (value in **blue box**), 25th, and 75th quartile values of the Society of Thoracic Surgeons (STS) 30-day predicted risk of mortality (PROM) score for isolated surgical aortic valve replacement for patients undergoing transcatheter aortic valve replacement through 2019. The decline in STS PROM values coincides with expansion of TAVR indication to intermediate- and low-risk patients.

TAVR system used in 2019. For native valve TAVR, 72.3% were balloon-expandable valves, 26.7% were self-expanding valves, and 1.0% were the recently approved mechanically expanded valves. For V-in-V TAVR, 53.3% were self-expanding valves, 46.5% were balloon-expandable valves, and 0.2% were mechanically expanded valves. Sites did not report complete valve delivery systems and valve type data in 2.6% patients submitted to the Registry, including patients who had aborted procedures.

Hospital LOS. LOS has declined from a median of 7 days (IQR: 4 to 10 days) to 2 days (IQR: 1 to 3 days) for all patients (**Figure 6**). In 2019, patients deemed by the heart team to be high/extreme risk had a median LOS of 2 days (IQR: 1 to 5 days), intermediate-risk patients also had LOS of 2 days (IQR: 1 to 3 days), whereas those in the low-risk cohort had a median LOS of only 1 day (IQR: 1 to 2 days).

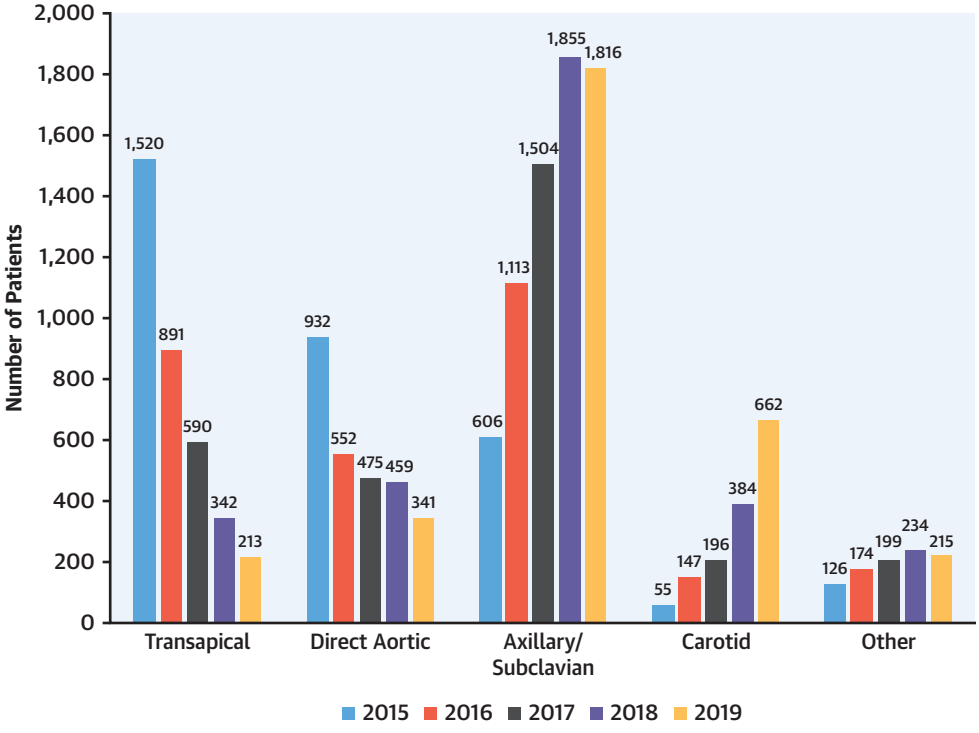
Patient disposition. In 2019, the majority of patients (90.3%) are discharged home, 6.6% to rehabilitation or extended care facility, and 2.45% to a nursing home. Patients during the early period of TAVR were often discharged to another facility (**Figure 7**).

OUTCOMES. Mortality. The year-by-year decline in mortality from the early TAVR experience to 2019 has been steady and dramatic, with in-hospital mortality falling from 5.4% to 1.3%, and 30-day mortality decreasing from 7.2% to 2.5%. These trends are shown in the **Central Illustration**.

Shown in Supplemental Table 1, the 30-day mortality for those deemed high/extreme risk has declined from 7.15% to 3.8%, and 1-year mortality has decreased from 24.3% to 16.6% from the early TAVR experience to 2018.

In-hospital, 30-day, and 1-year mortality rates were assessed in patients treated in 2018 and broken down by risk cohort (Supplemental Tables 1 to 3). All patients treated in 2018 (n = 59,168) had an in-hospital mortality rate of 1.5%, 30-day rate of

FIGURE 5 Forms of Alternative Access



Since 2015, there has been evolution of the preferred alternative access sites. This figure shows year-by-year trends of different forms of alternative access that have been used, typically when femoral access is not feasible. The other category includes iliac, transseptal, and transcaval approaches to alternative access. The dramatic shift away from central forms of alternative access (transapical and direct aortic) coincides with the rise of more peripheral forms of alternative access (axillary-subclavian and carotid).

2.6%, and 1-year rate of 12.55% (for the 35,654 patients with 1-year data). Comparing mortality rates for those classified in 2018 as high/extreme (n = 30,993) and intermediate (n = 26,566) showed the following trends: in-hospital mortality rates were 2.1% and 0.8%, 30-day mortality rates were 3.65% and 1.4%, and 1-year mortality rates were 16.6% and 8.3%, respectively.

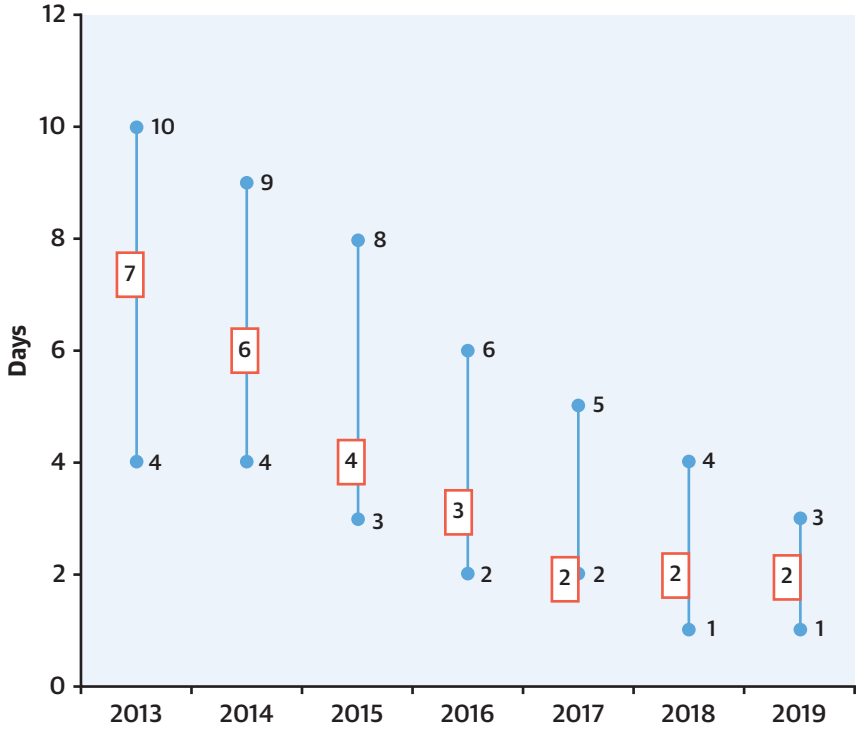
Stroke. In-hospital stroke rates (Figure 8) have decreased slightly from early TAVR (2.1%) to more recent experience in 2019 (1.6%), as well as 30-day stroke rates (2.75% vs. 2.3%). In-hospital and 30-day stroke rates in 2019 for the high/extreme-risk cohort were 1.9% and 2.7%, intermediate-risk cohort were 1.3% and 1.9%, and the low-risk cohort were 1.3% and 1.9%. The 30-day stroke rate for those classified as high-extreme risk has not declined from the early TAVR experience (2.8%) to 2019 (2.7%).

Permanent pacemaker. Figure 9 demonstrates that permanent pacemaker implantation during the index TAVR hospitalization peaked in 2015 at 13.2% and by 2019 was 8.3%. However, this decrease occurred in the context of shorter hospital LOS (Figure 6). The 30-day pacemaker rate in the early TAVR experience was 10.9%, peaked in 2015 at 15.1%, and then slowly declined, but in 2019 was still substantial at 10.8% and not different from the early TAVR experience. A substantial proportion of pacemaker insertions occurred between hospital discharge and 30 days for all patients and over all years of data collection. For example, in 2019, the in-hospital versus 30-day pacemaker rate was 9.5% versus 11.8% in the high/extreme-risk cohort, 7.9% versus 10.3% in the intermediate-risk cohort, and 6.15% versus 8.2% in the low-risk cohort.

Dialysis. The need for in-hospital dialysis as a result of TAVR has declined from 1.97% during the early TAVR experience to 0.4% in 2019. The need for in-hospital dialysis in 2019 for the high/extreme-risk cohort was 0.7%, the intermediate-risk cohort was 0.3%, and the low-risk cohort was 0.1%.

Bleeding. The use of blood transfusion has declined from 18.2% during the early TAVR experience to 5.8%. Rates of life-threatening/disabling bleeding

FIGURE 6 Length of Hospital Stay



Median length of stay values in **red boxes** between 2013 and 2019. The **bars** represent the 25th and 75th percentiles.

during index hospitalization declined from 6.3% in the early TAVR experience to 1.8% in 2019. In 2019, the high/extreme-risk cohort had an in-hospital life-threatening/disabling bleeding rate of 2.3%, whereas the intermediate-risk cohort rate was 1.45%, and the low-risk cohort rate was 1.2%. The in-hospital life-threatening/disabling bleeding rate for those at high/extreme risk has declined from 6.3% during the early TAVR experience to 2.3% for 2019.

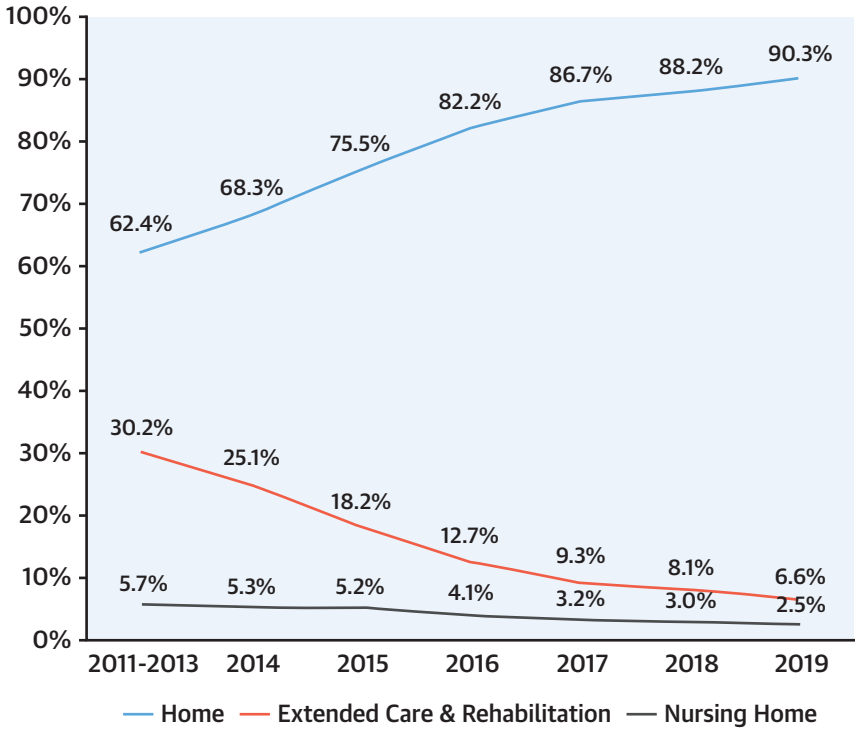
Vascular complications. Thirty-day major vascular access site complications have declined from 1.6% to 1.3% (Table 2). The 2019 rate was highest in the high/extreme-risk cohort at 1.5%, than in the intermediate-risk cohort at 1.1%, and least in the low-risk cohort at 0.7%. The 30-day major vascular access site complications for those at high/extreme risk has decreased slightly from the early TAVR experience (1.9%) to 2019 (1.8%). Vascular complication rates need to be interpreted in the context of the major shift to predominantly femoral access over the years.

Aortic regurgitation (includes paravalvular leaks). Moderate/severe AR 30-days post-TAVR was present in 8.0% of patients in the early TAVR experience and has fallen to 1.6% in 2019. In 2019, the rate in the high/extreme-risk cohort was 1.7%, in the intermediate-risk cohort 1.4%, and in the low-risk cohort 1.4%. The 30-day rate of moderate/severe AR for those classified as high-extreme risk has decreased from the early TAVR experience (8.1%) to 2019 (1.75%).

High aortic mean gradient early post-TAVR. The proportion of patients with mean gradients ≥20 mm Hg, either in-hospital or at 30 days, has increased (5.3% before and during 2013 vs. 6.2% in 2019) (Table 2). In 2019, the proportion of patients with the 20 mm Hg or greater gradient in the high/extreme-risk cohort was 6.1%, in the intermediate-risk cohort 6.0%, and in the low-risk cohort 8.2%.

Higher aortic mean gradient at 1 year. An increase in aortic valve mean gradient from post-procedure to 1 year of 10 mm Hg or greater occurred in 3.45% for year 2013 and was detected in 4.7% of patients treated in 2018, in those with 1-year data available. The rate for patients treated in 2018 for the high/extreme-risk cohort was 4.8%, 4.55% in the intermediate-risk cohort, and 4.1% in the low-risk cohort.

FIGURE 7 Discharge Disposition



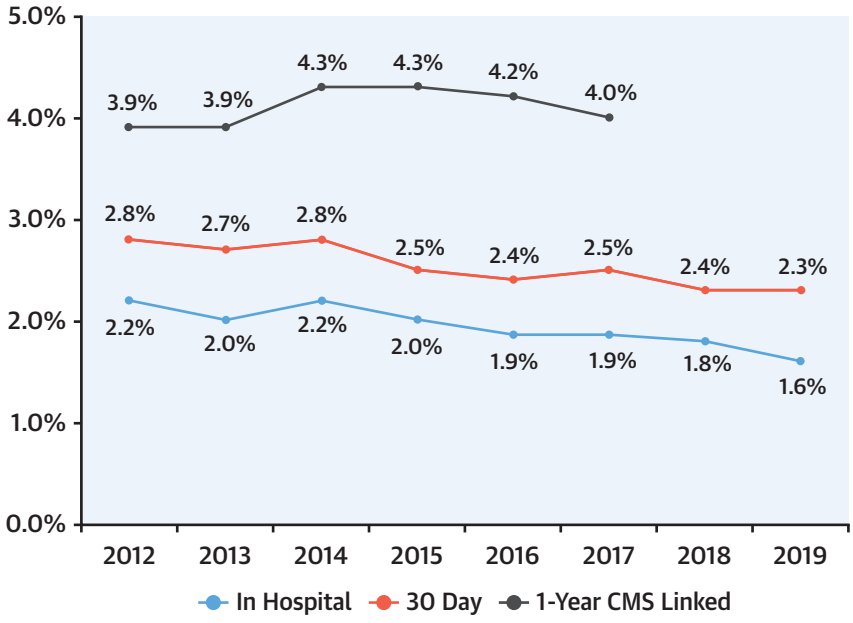
Proportions of patients discharged directly to home **(blue)**, to a rehabilitation facility **(red)**, and to a nursing home **(gray)** between 2011 and 2019.

1 year alive and well. Table 4 shows the baseline, 30-day, and 1-year KCCQ data of patients treated in 2018. Substantial improvements in KCCQ scores are demonstrated following TAVR. The percentage of patients with complete data for this metric is 71%.

The percentage of patients treated in 2018 achieving a favorable outcome at 1 year, defined as being alive, with a 1-year KCCQ score of ≥60 and no decline of ≥10 points versus baseline score, are presented in Table 4. This stringent definition of a favorable outcome was achieved in 80.7% of all patients, including 77.7% of high/extreme-risk, 83.6% of intermediate-risk, and 85.8% of low-risk patients.

A first look at real-world results in low-risk patients. This report provides an opportunity to perform a preliminary assessment of patients having TAVR who were classified by the local heart team as being low risk for SAVR. As noted in Table 1, FDA approved TAVR in low-risk patients in August of 2019. The 2 published trials of TAVR in low-risk patients included 496 and 725 patients, respectively, who were randomized to TAVR and received the treatment, that is, in the as-treated cohort (13,14). In 2019, there were 8,395 patients entered into the Registry who were classified as low risk with 1,294 treated in the first half of 2019 and 7,101 treated in the second half. The demographics of low-risk patients in the Registry were similar to those enrolled in the trial with a median age of 75 years (IQR: 70 to 81 years) as compared with mean ages of 73 and 74 years in the 2 trials. In the Registry, 65% were male versus 67.5% and 66% in the 2 trials, and 93% were white versus 92% in the 1 trial reporting race. The Registry patients had a median STS PROM score of 2.3 (IQR: 1.6 to 3.45) versus 1.9 and 1.9 in the 2 trials. In the Registry, 48.9% were NYHA functional class III or IV compared with 31.2% and 25.1%. Registry patients had femoral access in 97.8%; by study design, all patients in the 2 low-risk trials had femoral access. Median LOS for Registry patients was 1 day (IQR: 1 to 2 days) compared with a mean LOS of 3 days in 1 of the trials, with the caveat that the 2 trials treated patients in 2016 to 2018. In-hospital mortality for the Registry patients was 0.5% compared with 0.4% in 1 trial. Thirty-day mortality was 0.4% and 0.5% in the 2 trials. At the time of this report, comparisons between

FIGURE 8 Stroke Rates After TAVR



Yearly average rate of stroke after TAVR from 2012 through 2019. In-hospital rates are in **blue**, 30-day in **red**, and 1-year in **gray** (1-year values are from CMS-linked data, unavailable after 2017). There has been a small, slow, downward trend in stroke rates. CMS = Centers for Medicare & Medicaid; TAVR = transcatheter aortic valve replacement.

low-risk patients in the Registry and those in the 2 trials are limited because 30-day follow-up is incomplete for the majority of Registry patients treated in the second half of 2019, and in the 2 low-risk trials, 30-day outcomes are reported more comprehensively than in-hospital outcomes.

DISCUSSION

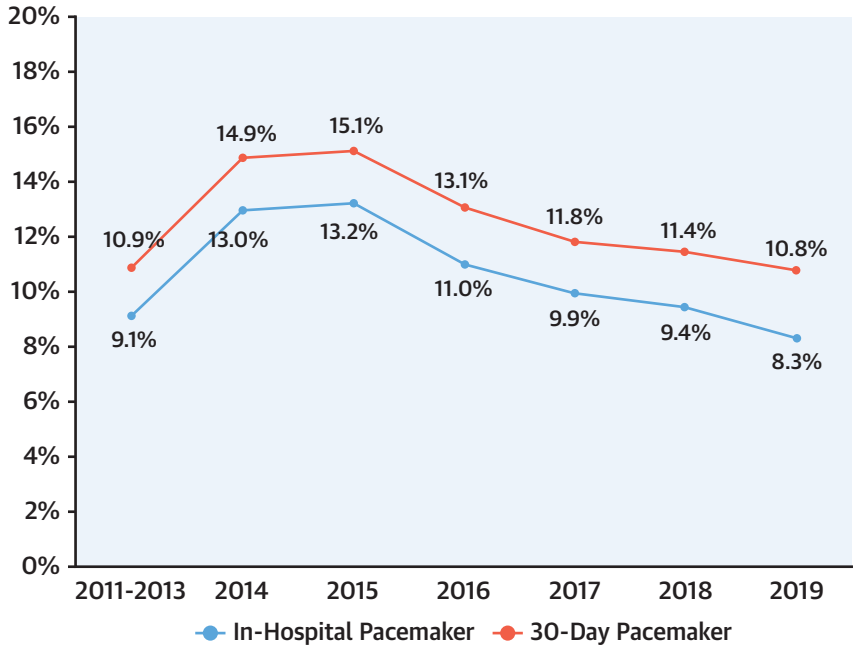
Multiple temporal trends including some of historic proportions are identified from these data and comprehensively describe the current state of TAVR in the United States, up until the onset of the COVID-19 pandemic. The rapid growth in the number of sites and case volume, the broader spectrum of patients treated, TAVR becoming the dominant form of AVR, and the lower procedure burden with fewer complications are all well-documented in these data. The dramatic decrease in LOS, the high percentage of patients being discharged directly to home, and 8 of 10 patients, including high-extreme risk patients, achieving at 1 year the "alive and well" patient-reported outcome are all testaments to the on-going reduced burden of TAVR treatment and achievement of benefits to patients including those who are elderly with a heavy dose of comorbid conditions.

This report from the Registry, using a huge volume of observational data, documents these changes and other substantial advances in TAVR. The logical next question is what accounts for these changes. The field has many dynamic elements that may be considered, including improvements in TAVR technology and techniques, adjunctive technologies, the level of heart team experience, and changes in the patient risk profiles.

In Table 6, 10 highlights from this report are listed along with associated next steps in using the Registry to perform a deeper dive to identify associations and areas for further trials and improvements in care. As noted, the impact of COVID-19 and the extent and timing of a subsequent recovery will depend on a myriad of factors including geographical differences in COVID-19 penetration, local policies having an impact on the resumption of nonemergent procedures, and patients' willingness to access the medical system out of fears of COVID-19 infectivity (12).

The indications for TAVR in the United States are outlined in FDA approvals. Beginning in 2021, the Registry will start to collect and report data on appropriate use criteria as defined by a professional society consensus document (15). The consensus document was written before TAVR being approved

FIGURE 9 Pacemaker Rates After TAVR



Annual proportion of patients without a previous permanent pacemaker who received a permanent pacemaker during TAVR procedure hospitalization **(blue)** or within 30 days **(red)** from 2011 to 2013 until 2019. TAVR = transcatheter aortic valve replacement.

for low-risk patients and, therefore, will need to be updated. In general, patients receiving TAVR have native aortic stenosis in 91.5% and failed prosthetic aortic valves in 4.5% in 2019. Only 3.55% were reported to be NYHA functional class I, that is, asymptomatic.

The increasing incidence of TAVR V-in-V procedures (6.7% of all TAVRs in 2019) must be considered when interpreting the overall, that is, in all TAVR, Registry results. TAVR V-in-V procedures have a high rate of initial success (16) but increase the risk several-fold for severe prosthesis-patient mismatch, which in turn has been associated with an increase in short-term mortality and heart failure rehospitalization (17), as well as an associated with higher gradients and mortality, particularly in small surgical prostheses (18). These procedures may also pose different risks for other outcomes, including stroke, pacemaker, and paravalvular regurgitation compared with TAVR performed in a native annulus.

PATIENT-REPORTED OUTCOMES: KCCQ ASSESSMENT. The Registry uniquely incorporates patient-reported outcomes and has used the KCCQ tool administered to patients at baseline, 30-days post-TAVR, and 1-year post-TAVR. The results as displayed in **Table 4** show the substantial impact of aortic valve disease on patients pre-TAVR with a median baseline KCCQ of 45 in 2018. The increase to a median value of 81 took only 30 days post-TAVR to be manifest, and by 1-year, the median KCCQ was 86, albeit this reflects the results only among survivors.

The percentage of patients currently undergoing TAVR having a favorable 1-year outcome of being both alive and well has increased to approximately 8 of 10 patients from a previous report during the early TAVR experience when only 6 of 10 achieved this metric of success (7). Even patients deemed high/extreme risk have now achieved this key 1-year metric in 78%, which is also noteworthy because of the large number of patients who continue to be treated in this risk category.

OUTCOMES BY RISK CATEGORIES. By analyzing outcomes based on the heart team's assessment of SAVR risk, a better understanding emerges of factors that are related to key outcomes, with the caveat that these are observational data, and the causes of trends can be suggested, but not proven.

This risk-based analysis also suggests the major degree to which the rates of some TAVR outcomes metrics are associated with patient factors. The rates of mortality, bleeding, stroke, and the need for a

TABLE 4 KCCQ Scores Pre- and Post-TAVR in Patients Treated in 2018

Patient Cohort According to Heart Team's Assessment	Total Number of Patients	Baseline KCCQ Summary Score	30-Day KCCQ Summary Score	1-Year KCCQ Summary Score	% of Patients With Both Baseline and 1-Year KCCQ Complete*	% of Patients at 1 Year With Favorable Outcome†
All patients	59,130	45 (27–65)	81 (63–94)	86 (69–97)	70.75	80.66
High/prohibitive risk	30,993	41 (24–60)	78 (58–92)	82 (64–95)	68.68	77.74
Intermediate risk	26,566	49 (31–69)	84 (68–96)	89 (73–98)	72.89	83.59
Low risk	1,454	53 (34–74)	88 (72–97)	92 (80–98)	76.31	85.79

Values are median (interquartile range) unless otherwise indicated. *Among 1-year survivors. †Favorable outcome is defined as alive with reasonable quality of life (Kansas City Cardiomyopathy Questionnaire [KCCQ] ≥60) and no significant decline (≥10 points) from baseline. †Favorable outcome is defined as alive with reasonable quality of life (Kansas City Cardiomyopathy Questionnaire [KCCQ] ≥60) and no significant decline (≥10 points) from baseline.

TAVR = transcatheter aortic valve replacement.

permanent pacemaker are all associated with the heart team's risk categorization of their patients. On the other hand, the degree of post-TAVR aortic regurgitation, high residual gradient, and an increased valve gradient at 1 year do not. Likewise, the rates of needing CPB and conversion to OHS are similar across all risk groups, but fortunately very low in current TAVR practice.

In addition, this risk-based analysis provides insight into the extent to which TAVR outcomes have improved over the years independent of patient risk. Specifically, rates of mortality (30-day and 1-year), bleeding, and moderate/severe AR post-TAVR have declined substantially among patients in the high/extreme-risk category. This implies a substantial improvement in the quality of care.

Although TAVR is now approved in the United States for patients in all SAVR risk categories, it remains useful for heart teams to continue to perform comprehensive pre-procedural assessment of patient characteristics and the associated risk categories. Identification of patients at higher risk for complications may potentially modify the nature of procedure performance and post-procedure care. In addition, heart teams better understand their program's performance compared with national benchmarks of quality metrics and case mix.

CHANGES IN PROCEDURE PERFORMANCE. Multiple dynamic factors of TAVR performance are also identified and quantified. Two major shifts involve anesthesia and vascular access that are often interconnected.

Conscious sedation. The shift from general anesthesia to conscious sedation is noteworthy because it is typically accompanied by no longer routinely using transesophageal echocardiography, intubation, and other invasive monitoring techniques (16).

Shifts in vascular access. The ability to treat most patients, 95% of all patients, with transfemoral access has been associated with lower bleeding rates, reduced LOS, and discharges to home. In those requiring alternative access, there has been a dramatic shift to subclavian-axillary access, plus other approaches less commonly used, and away from transapical and direct aortic approaches.

MAJOR COMPLICATIONS. The infrequent need for CPB and conversion to OHS represent another reason TAVR has become lower risk. But the occasional occurrence of emergency transitions to mechanical support and OHS during TAVR, across all risk groups, justifies that all patients undergo TAVR in facilities with teams capable of performing these potentially life-saving procedures.

TABLE 5 Novel Adjunctive Technologies and Technique Captured in the STS/ACC TVT Registry

Procedure	Primary Goal	Target Population	Total Number Performed in 2018–2019	Total Number Performed in 2018	Total Number Performed in 2019
Cerebral protection using Sentinel device	Prevention of embolic debris causing stroke	Native valve TAVR	11,877	4,136	7,741
		V-in-V TAVR	961	306	655
Fracture of surgical valve ring	Reduction of patient-prosthetic mismatch: high post-V-in-V gradient	V-in-V TAVR	332	71	261
Laceration of aortic valve leaflet (BASILICA)	Prevention of coronary obstruction post-TAVR	Native valve TAVR	41	0	41
		V-in-V TAVR	125	1	124

Abbreviations as in Table 1.

TABLE 6 10 Data Highlights and Potential STS-ACC TVT Registry Actions to Answer Resultant Questions

Key Findings in This State of TAVR Report From the Registry	Associated Issues and Questions for Registry Monitoring, Analysis, and Hypothesis Generation
1. Growth: TAVR growth has continued every year since 2011, and the increase in 2019 was the largest yearly increase, with 13,823 more cases performed than the previous year. TAVR used in a valve-in-valve fashion has increased in parallel.	Data on the impact of COVID-19 on TAVR volumes are currently being collected to be reported in late 2020. The Registry will monitor anticipated further growth from: 1) low-risk patients; 2) population aging; and 3) lack of any therapy that prevents valve degeneration.
2. TAVR has become the dominant form of AVR in the United States.	Isolated SAVR volume has decreased 32% from its peak in 2013 to 2019 with expanded TAVR indications. Defining the patient and clinical situations when SAVR should be preferred is needed remains. Linkage of the Registry with the STS database is needed.
3. Early indications from the Registry on TAVR in low-risk patients suggest parallels with the pivotal clinical trials.	In 2020, the Registry will have more data on the degree to which real-world outcomes for TAVR in low-risk patients are similar to those in the clinical trials.
4. Valve-in-valve also has grown, with its greatest increase in volume in 2019, and has been driven primary by TAVR-in-SAVR.	The Registry will also be critical in assessing the safety and effectiveness of TAVR-in-TAVR as degeneration of TAVR valves becomes manifest.
5. The steady increase in the number of hospital sites has now exceeded 700.	Access to TAVR has thus improved at least from a geographical perspective.
6. Black patients receiving TAVR have increased from 504 during the early TAVR period to 2,948 in 2019. Yet there has been no change in only 4% of all patients receiving TAVR being Black.	The Registry does not have a means to study underlying issues that may account for health care disparities versus disease prevalence. But the Registry can monitor the impact of efforts to increase access and reduce disparities.
7. The percentage of sites performing <50 cases per year is substantial at 161 of 669 sites when last analyzed.	The Registry in 2020 to 2021 will incorporate a validated and reliable 30-day composite outcome metric for use to assess site performance and will remain essential to monitoring quality, changes over time, and the impact of local and national efforts to improve outcomes.
8. This report demonstrates improvements in numerous outcomes. The analysis of TAVR outcomes by patient risk subgroup is presented for the first time and allows insight into the association of patient risk categories.	This form of analysis and algorithmic risk-adjusted outcomes will continue to be important to understand trends in TAVR and quantify associations with other determinants of outcomes.
9. This Registry report clearly documents the major shifts in vascular access, the high percentage of femoral access attained in all risk groups, and the major shifts in alternative access approaches.	The observational nature of the Registry cannot determine what alternative approach may be superior to others, but it can help formulate hypotheses to be tested in trials that potentially can be imbedded in the Registry.
10. The Registry now captures novel adjunctive techniques such as cerebral protection, laceration of valve leaflets, and fracture of previously implanted tissue valves.	Research proposals using Registry data will assess the safety and effectiveness of these techniques.

Abbreviations as in Table 1.

Clinical challenges remain, and the volume of patients classified as high/extreme risk remains substantial; these data should focus attention on strategies to further improve outcomes. It is noteworthy that there has been a decline in rates of stroke and perhaps in the need for permanent pacemaker, but these declines are small.

Stroke. The self-reported rates of stroke are low, but underreporting of clinically mild strokes is a known phenomenon (19). A small decline in stroke rates appears associated with the addition of large numbers of patients in the intermediate-risk category and, more recently, low-risk patients. An analysis suggests stroke rates are related to risk category. Further reports from the Registry on stroke and the impact of the use of cerebral protection are forthcoming; issues of ascertainment bias will confound site-reported stroke rates, and the multivariable analysis of patient and procedure factors on stroke rates will be important.

Need for permanent pacemaker. Pacemaker rates remain high. It is perplexing that there has been only a small decline in recent years with the inclusion of large numbers of patients in the intermediate-risk category despite the finding that pacemaker rates are related to patient risk category. This issue is clinically problematic, given the short hospital LOS after TAVR and an increasing proportion of patients require a pacemaker after hospital discharge, during which time, there is some risk of sudden death and other complications due to conduction system block.

CONCLUSIONS

The Registry, as an example of an innovative national learning health care system, provides in this report, and in the numerous previous publications using Registry data, a comprehensive observational warehouse of patient-level data from over a quarter of a million patients, with analyses that provide great insight into the state of TAVR in the United States. TAVR is the dominant form of AVR, with sites in all 50 states. Outcomes out to 1 year have steadily improved. Further growth is expected with recovery of the health care system in the new world of COVID-19.

AUTHOR RELATIONSHIP WITH INDUSTRY

Dr. Carroll has been a local investigator for clinical trials sponsored by Edwards Lifesciences, Medtronic, and Abbott; and has been a consultant to Abbott. Dr. Mack has had nonremunerative positions of clinical trial leadership at Edwards Lifesciences, Medtronic, and Abbott. Dr. Vemulapalli has received grants/contracts from the American College of Cardiology, Society of Thoracic Surgeons, National Institutes of Health, Patient Centered Outcomes Research Institute, Food and Drug Administration (NESTcc), Boston Scientific, and Abbott Vascular; and has been a consultant/Advisory Board member for Boston Scientific, Janssen, and HeartFlow. Dr. Herrmann has received institutional research grants from Abbott Vascular, Bayer, Boston Scientific, Edwards Lifesciences, and Medtronic; and has received consulting fees from Abbott Vascular, Edwards Lifesciences, and Medtronic. Dr. Gleason has been a member of the Medical Advisory Board for Abbott. Dr. Hanzel has been the local site principal investigator for trials sponsored by Edwards Lifesciences, Abbott, and Boston Scientific. Dr. Deeb has been the local site principal investigator in the Medtronic International TAVR clinical trials. Dr. Thourani has been an advisor to or received research grants from Abbott Vascular, Boston Scientific, Edwards Lifesciences, Gore Vascular, and JenaValve. Dr. Cohen has received research grant support from Edwards Lifesciences, Medtronic, Boston Scientific, and Abbott; and has received consulting income from Edwards Lifesciences, Medtronic, Boston Scientific, and Abbott. Dr. Desai has been an advisor to or received research grants from Gore, Medtronic, and Terumo. Dr. Kirtane has received institutional funding to Columbia University and/or Cardiovascular Research Foundation from Medtronic, Boston Scientific, Abbott Vascular, Abiomed, CSI, CathWorks, Siemens, Philips, and ReCor Medical (in addition to research grants, institutional funding includes fees paid to Columbia University and/or Cardiovascular Research Foundation for speaking engagements and/or consulting); and has received travel expenses/meals from Medtronic, Boston Scientific, Abbott Vascular, Abiomed, CSI, CathWorks, Siemens, Philips, ReCor Medical, Chiesi, OpSens, Zoll, and Regeneron. Dr. Masoudi has had a contract with the American College of Cardiology for his role as chief scientific advisor, NCDR. Dr. Brindis is senior medical officer, EXTERNAL AFFAirs-ACC National Cardiovascular Data Registry. Dr. Bavaria has been a local investigator for TAVR clinical trials sponsored by Edwards Lifesciences, Medtronic, Abbott, and Boston Scientific; and has been a consultant to Edwards Lifesciences and Abbott. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS aortic stenosis, outcomes, registry, TAVR, valvular heart disease

APPENDIX For supplemental tables, please see the online version of this paper.

Journal of the American Heart Association

EDITORIAL

Racial Disparity in the Treatment of Aortic Stenosis

J. James Edelman, MD, PhD; Vinod H. Thourani, MD

In this issue of Journal of the American Heart Association (JAHA), Czarny and colleagues compare the incidence of aortic stenosis (AS) in Black, Hispanic, and White patients admitted to a hospital in Maryland using the Maryland Health Services Cost Review Commission administrative database.[1] Despite that Black patients had a higher incidence of acute hospitalizations and rate of inpatient echocardiography, they were half as likely to have any diagnosis of AS compared with White patients. Black patients were younger and had a greater burden of comorbidities and lower median income than White and Hispanic patients. In the cohort of patients with any AS diagnosis, Black patients were less likely to undergo treatment with either surgical or transcatheter aortic valve replacement (TAVR) than White patients. Of the cohort with any diagnosis of mitral regurgitation, Black patients were less likely to undergo surgical or transcatheter mitral valve replacement than White patients. Interestingly, in the 2537 patients admitted with a primary diagnosis of AS, 13.2% were Black (29.1% of the overall Maryland population ≥50 years is Black), but race no longer predicted likelihood of treatment with surgical aortic valve replacement or TAVR. The authors conclude that racial inequity exists in the rates of surgical aortic valve replacement or TAVR because of numerous complex and multifactorial mechanisms.

See Article by Czarny et al.

Racial inequality in the diagnosis, treatment, and outcomes of cardiovascular disease has been well documented. We agree with Czarny and his esteemed colleagues that the cause of racial disparity in the management of AS is complex and multifactorial. Potential targets to correct inequality require increased understanding of the true prevalence of AS among different races, improved access to health care, and an improvement in the relationship and trust between the healthcare system and people from diverse racial and ethnic groups.

The incidence of AS has been debated and may be lower in Black than in White patients; however, Black patients suffer the risk factors for AS at a greater frequency than White patients.[2] Age is a major risk factor for AS, and it is possible that Black patients become more unwell with other illnesses before their AS becomes severe enough to require treatment. AS is most commonly a disease managed as an outpatient, with referral for treatment on an elective basis. Barriers of access to primary health care reduce the opportunity for patients have valvular disease diagnosed before the development of heart failure. Those who present to hospital with their first presentation of AS are more likely to be suffering end-stage disease. In the study by Czarny and colleagues, Black patients presented to the hospital for acute admissions more frequently than White patients.[1]

Black patients are underrepresented in TAVR. In the recently published STS-ACC TVT (Society of Thoracic Surgeons, American College of Cardiology Transcatheter

Key Words: Editorials ■ aortic stenosis ■ race and ethnicity

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For Disclosures, see page 2.

JAHA is available at: www.ahajournals.org/journal/jaha

Valve Therapies) Registry for all commercial TAVR performed in the United States, only 3.98% were performed in Black patients.[3] This increased slightly from the period before 2013 (3.67%) to 2019 (4.04%). Hispanic patients represented 5.2% of all TAVR recipients. In US Census data, people of Black and Hispanic race/ethnicity represent 8% and 9% of the population >65 years of age, respectively.[4] An analysis of STS-ACC TVT Registry data from 2011 to 2016 reported TAVR mortality outcomes that were no different between White, Black, and Hispanic patients, but repeat hospitalizations at 1 year were higher in Black patients.[4]

Unfortunately, Black patients and other ethnic minorities are underrepresented in studies for new technology in the treatment of AS. Of the major TAVR trials, only PARTNER 3 reported the rate of non-White patients: 7.7% for TAVR and 9.9% for surgical aortic valve replacement.[5] The reason for underrepresentation of ethnic groups in trials is not clear; investigator bias, which is less likely, and the presence of comorbidities occurring at higher rates in Black patients that may exclude them from participation or refusal to consent are some viable possibilities. A mistrust of health care and research by minorities groups likely persists because of a history of unethical studies in the United States.[6]

The study by Czarny is limited by the use of an administrative database, which without clinical data (such as the results of echocardiography) lacks the granularity required to assess true differences in prevalence and treatment of AS among racial groups. It nonetheless supports the growing weight of evidence that racial bias exists in the treatment of AS and adds to the growing interest in the amelioration of this divide. The TVT Steering committee has commenced a task force to investigate the cause of racial disparity in the treatment of AS and to suggest strategies to address it. A better understanding of the true prevalence of AS in people from diverse racial and ethnic groups will assist in better public health strategies for screening. Measures to address access to health care must go beyond purely funding and address underlying mistrust, socioeconomic disparity, and systemic racism.

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Disclosures

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SPECIAL REPORT

Priorities for Patient-Centered Research in Valvular Heart Disease: A Report From the National Heart, Lung, and Blood Institute Working Group

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ABSTRACT: Over the past decade, the field of valvular heart disease (VHD) has rapidly transformed, largely as a result of the development and improvement of less invasive transcatheter approaches to valve repair or replacement. This transformation has been supported by numerous well-designed randomized trials, but they have centered almost entirely on devices and procedures. Outside this scope of focus, however, myriad aspects of therapy and management for patients with VHD have either no guidelines or recommendations based only on expert opinion and observational studies. Further, research in VHD has often failed to engage patients to inform study design and identify research questions of greatest importance and relevance from a patient perspective. Accordingly, the National Heart, Lung, and Blood Institute convened a Working Group on Patient-Centered Research in Valvular Heart Disease, composed of clinician and research experts and patient advocacy experts to identify gaps and barriers to research in VHD and identify research priorities. While recognizing that important research remains to be done to test the safety and efficacy of devices and procedures to treat VHD, we intentionally focused less attention on these areas of research as they are more commonly pursued and supported by industry. Herein, we present the patient-centered research gaps, barriers, and priorities in VHD and organized our report according to the "patient journey," including access to care, screening and diagnosis, preprocedure therapy and management, decision making when a procedure is contemplated (clinician and patient perspectives), and postprocedure therapy and management. It is hoped that this report will foster collaboration among diverse stakeholders and highlight for funding bodies the pressing patient-centered research gaps, opportunities, and priorities in VHD in order to produce impactful patient-centered research that will inform and improve patient-centered policy and care.

Key Words: aortic valve ■ heart valve ■ heart valve surgery ■ mitral valve ■ patient-centered care ■ shared decision making ■ transcatheter valve implantation

There has been an explosion in valvular heart disease (VHD) research over the past few decades with a shift in the evidence base from expert opinion alone, with virtually no randomized clinical trials (RCTs), to numerous RCTs addressing the safety and efficacy of devices to relieve stenosis or reduce regurgitation.[1–3] However, many guideline recommendations for VHD are still only supported by expert opinion and observational studies. Further, as is true of many areas of cardiovascular research, studies of patients with

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Nonstandard Abbreviations and Acronyms

AS	aortic stenosis
BP	blood pressure
HF	heart failure
RCT	randomized clinical trial
SDM	shared decision making
TAVR	transcatheter aortic valve replacement
VHD	valvular heart disease

VHD are driven primarily by clinicians and often fail to answer the questions of most importance to patients.

Patient-centered research is characterized both by its orientation and the process by which that research is formulated and executed. While acknowledging that basic science research involving cells and animals is relevant to patients, as the long-term goal of those avenues of investigation is often to prevent or slow VHD progression, patient-centered research involves and studies patients either prospectively or retrospectively. Every bit as important, though, patient-centered research ought to involve patients at each stage of the research process, from identifying research questions to prioritizing outcome measures to implementation into clinical practice. Although researchers and patients will agree on many questions and outcomes, patients often identify other issues that may not have been considered.

RATIONALE AND WORKING GROUP GOALS

The National Heart, Lung, and Blood Institute convened a Working Group on Patient-Centered Research in Valvular Heart Disease in July 2019 to identify gaps in patient-centered VHD research, develop a list of important patient-centered research questions, and consider any barriers that discourage investigators from pursuing these questions. Predictably, there are areas of overlap and distinctiveness with respect to these issues for patients with VHD versus other forms of cardiovascular disease. Because considerable attention has recently focused on devices and procedures, we concentrated less on important questions surrounding device performance and procedural optimization (acknowledging that these are patient-centered lines of investigation) and more on knowledge gaps regarding preprocedural and postprocedural management, decision making, and the opportunity to consider other end points for device trials. We also recognize that there is overlap between patient-centered care, patient-centered research, and patient-centered policy—the focus of this Working Group is the "research" piece, recognizing that an ultimate goal of this research is to inform healthcare delivery and policy.To meet the objectives for this Working Group, we included representatives from VHD-related patient organizations, clinicians with expertise in VHD, and researchers with active studies on VHD, while recognizing that many other areas of expertise are included in a Heart Valve Team and in caring for patients with VHD. We chose to frame our discussion in terms of the "patient journey" from diagnosis to long-term management (Figure 1). The specific aims of this Working Group were to: (1) identify knowledge gaps and generate a list of patient-centered VHD research questions spanning the patient journey from the initial diagnosis to long-term outcomes; (2) identify gaps in patient-oriented information about VHD and effective decision aids and implementation strategies for shared decision making; (3) identify barriers to patient-centered VHD research; and (4) disseminate an open access summary to researchers, clinicians, policymakers, the general public, and patient interest groups.

ACCESS TO CARE

Access to care for patients with VHD is not equitable with, for example, documented racial disparities in diagnosis and treatment of black patients with severe aortic stenosis (AS) (Table 1).[4–7] Black patients with severe AS are more likely to decline AVR when recommended, raising questions about trust, historical discrimination, and delivery of care.[6,8] Understanding the role that access to care has in the mechanisms of these outcome differences is difficult, since black patients also have a higher prevalence of risk factors for VHD than white patients, including hypertension, diabetes mellitus, and chronic renal insufficiency. Importantly, black patients are not the only racial minorities affected, with emerging data of undertreatment of valve disease among Latino populations and Native Americans.

Sex disparities in care are also seen in patients with VHD. Women have higher mortality than men after mitral surgery and present with higher case complexity, possibly because of less guideline-directed surveillance.[9,10] For patients with AS, the relative mortality benefit of transcatheter aortic valve replacement (TAVR) versus surgical aortic valve replacement appears to be greater for women compared with men.[11]

Innovation in care delivery is being studied, although there are few links to reduction in disparities. Electronic consults have been shown to be amenable to clinical questions about valve disease with cardiologists reviewing electronic data and images (eg, echocardiogram) in a shared electronic medical record and then providing detailed clinical recommendations in the electronic medical record to the referring clinician

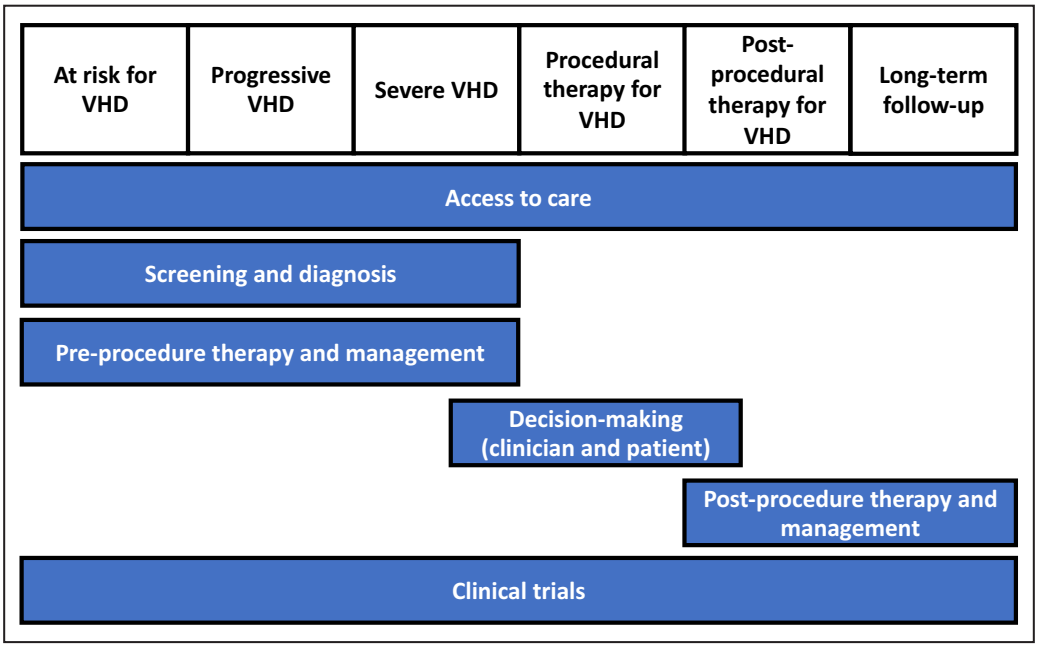

Figure 1. Context for patient-centered research in valvular heart disease (VHD)—the patient journey.
This figure outlines the patient journey and puts the sections of our report in context of this journey.

without an office visit.[12,13] Cardiology electronic consults are cost-saving relative to traditional care[14] and associated with fewer emergency department visits in a cluster-randomized trial.[14] Overall, evidence suggests that cardiology electronic consults improve access to outpatient cardiology care.[15] As such, electronic consults and other alternatives to office-based visits may improve access to care for patients with VHD. However, differences in valve-specific end points in electronic consults are unknown.

Table 1. Access to Care—Patient-Centered Research Questions in VHD

Disparities in care delivery • What factors underlie disparities in care delivery (eg, echocardiographic surveillance according to guidelines and performance of valve repair/replacement at the appropriate time) for women, minorities, low-income, and rural patients? How can those factors best be addressed and corrected? • How do referral rates differ among various subgroups and why? • Why is there a higher refusal rate for valve intervention among blacks? • What alert systems (eg, echo parameter alert) would promote equitable, timely identification, and appropriate monitoring and treatment of VHD? • How are Medicare coverage and reimbursement policies impacting access to available valve interventions, in general and among subgroups? • Do current health insurance systems limit access?
Telemedicine • How might telemedicine be employed to address challenges in the diagnosis and delivery of care for patients with significant VHD?
Heart valve centers • What are the pros and cons, benefits, and costs of having valve care delivered via heart valve centers (concentrated expertise and procedures) vs a more disseminated model? • Do heart valve centers have better clinical outcomes after adjustment for risk? • How do patients weigh differences in outcomes between centers and the burden of travel to centers further from home? How aware are patients of the options available to them regarding where to receive care?

VHD indicates valvular heart disease.

Specialized comprehensive valve centers are recommended in guidelines for patients with asymptomatic severe VHD, patients who may benefit from repair versus replacement, and patients with multimorbid disease.[1,16] This recommendation is based on a known surgical volumes-outcomes relationship as well as high rates of mitral repair for mitral valve prolapse at some centers.[17,18] In addition, more recent data suggest that mortality following transfemoral TAVR is higher and more variable at lower-volume centers.[19] Lower-volume centers treat greater proportions of rural patients, black patients, and Hispanic patients.[19]

The implications of concentrating VHD care at high-volume comprehensive valve centers are unclear. For coronary artery disease, centers of excellence do not appear to have better outcomes.[20] Adding nuance, the focus of high-volume comprehensive valve centers is on the procedural aspect of care for patients with VHD. However, there may be value to patients with VHD being followed in more specialized heart valve clinics during the progressive stage of disease and after a valve procedure.[21–23] How this specialized longitudinal care would be integrated into a system of care that might concentrate expertise and procedures in certain centers (that may be less practical to access for

patients longitudinally) is unclear. Optimizing and integrating care for patients with VHD along the continuum of disease before and potentially after an intervention is fraught with challenges and uncertainties, particularly in a healthcare environment of increasingly restricted lines of referral mandated by insurance providers or other forces.[16] The cost implications of various models are also uncertain but inevitably intersect with considerations of quality and access to care. These issues are clearly not unique to patients with VHD, but there are some particular ways in which these system-of-care issues may specifically affect them. Diverse stakeholders need to engage Centers for Medicare & Medicaid Services (CMS) and other policy makers to ensure that policies are developed that are evidence based and in the best interests of our patients.

SCREENING AND DIAGNOSIS

A comprehensive understanding of risk factors for VHD will allow for a more targeted approach to screening and diagnosis as well as prevention (Table 2). Current screening of VHD primarily relies on patient symptoms and physical examination, despite wide variation in clinical practice and lack of accuracy for diagnosis of VHD, leading to variations in treatment.[24] In a study comparing auscultation by primary care clinicians and cardiologists against echocardiography, both groups had poor sensitivity for detecting mild or significant VHD (22–32%) with suboptimal specificity ranging from 67% to 83%.[25] Accordingly, tools other than auscultation are needed to effectively screen for VHD. Notably, undiagnosed VHD appears to be more common in lower socioeconomic groups, but the reasons for this are not fully understood.

Screening for VHD using echocardiography and advanced imaging approaches has not been well studied. Among individuals 65 years and older without a prior diagnosis of VHD, systematic echocardiography identified 51% with mild or more left-sided VHD or moderate or severe right-sided VHD, including 6.4% with significant (moderate or more) VHD.[26] The increasing availability of handheld ultrasound machines and application of artificial intelligence algorithms is likely to lower costs. Research is needed to determine optimal screening algorithms, including the scope of these efforts, cost-effectiveness, tools utilized, how to leverage new technologies, and how these efforts may need to be adapted based on geography, clinical setting, and available resources. Important areas for study are determining which patient populations will benefit from screening (eg, relatives of those with VHD and age-based or risk-based [based on genetics, biomarkers, or comorbidities] subgroups) and how detection of VHD early in the pathophysiological process (eg, mild in severity) impacts costs and patient outcomes and how this may differ depending on the type of VHD. Whether screening should be focused on identifying only more significant (eg, moderate to severe) VHD versus mild disease needs to be considered and will likely depend on the specific VHD and whether interventions are available to prevent or slow progression of earlier-stage disease. Finally, there is wide variation among practitioners with respect to monitoring for progression of diagnosed VHD.[27] Patients who are women, black, or on Medicaid are less likely to be screened for progression of VHD at appropriate intervals.[10] Further studies are needed to clarify optimal monitoring timeframes and the factors underlying variations in surveillance for progression of VHD. The role of multimodality imaging in the diagnosis and assessment of severity of VHD requires additional research.[28–31]

Table 2. Screening and Diagnosis—Patient-Centered Research Questions in VHD

Risk factors for VHD • What risk factors are associated with the development of each type of valve disease and how could knowledge of these factors inform screening and prevention efforts?
Tools to screen for VHD • What is the effectiveness of potential tools to screen for VHD? Examples include patient questionnaires, cardiac auscultation, serum biomarkers, point-of-care cardiac ultrasound, machine learning image analysis, and standard echocardiography • How often should testing be repeated for patients with and without a prior diagnosis of VHD?
Scope of screening for VHD • What are the pros and cons, benefits, and costs of screening efforts focused on specific patient groups or broadly applied to entire populations? • If screening efforts are focused, which prescreening or enrichment criteria for patients "at risk" are best?
Integrated screening for VHD • Which combination of screening tools and approaches will identify the most patients with significant valve disease for the least costs/resources? • Which approaches will ensure appropriate and consistent screening of all patients without bias related to age, sex, ethnicity, finances, and insurance?
Consequences of screening for VHD • What are the consequences of improved screening for VHD in terms of costs, patient anxiety/well-being/satisfaction, procedural volumes, survival, and quality of life?
Accurate diagnosis of significant VHD • How can adjunctive imaging tools (eg, cardiac magnetic resonance or computed tomography), circulating biomarkers, or other tools be employed to improve the accuracy of diagnosis of significant/severe VHD?

VHD indicates valvular heart disease.

PREPROCEDURE THERAPY AND MANAGEMENT

Valve lesions, such as AS and mitral regurgitation, are commonly viewed as mechanical problems requiring a mechanical solution with a transcatheter or surgical

Table 3. Preprocedure Therapy and Management—Patient-Centered Research Questions in VHD

Prevent/slow/reverse VHD with medical therapy • What factors are associated with the development and progression of VHD? • What medical therapies (currently available or targeting new pathways) are effective at slowing or reversing established VHD?
Prevent/slow/reverse maladaptive ventricular remodeling and dysfunction with medical therapy • What factors/pathways are associated with the development and progression of maladaptive ventricular remodeling and dysfunction in the setting of pressure or volume overload? • Despite potentially progressive valve disease, are there medical therapies that could prevent, slow, or reverse adverse consequences to the ventricle resulting from pressure or volume overload? If so, what is the optimal timing for those therapies to be utilized? • What differences exist between the right and left ventricles with respect to pathophysiology and targets for and timing and efficacy of intervention with medical therapy?
"Prehabilitation" in frail patients • In patients with impaired physical function needing a valve procedure, does a rehabilitation strategy before intervention improve periprocedural and short-term outcomes? • What types of prehabilitation are feasible and which components (eg, resistance exercise, aerobic exercise, reducing sedentary behavior, and nutrition) are most important? • What patient-centered delivery strategies are best suited to optimize the impact of prehabilitation programs?
Blood pressure targets in patients with VHD • What are the optimal blood pressure targets in patients with VHD? Should they differ from the general population? • How do age, type of valve disease, severity of valve disease, and comorbidities influence optimal targets for blood pressure?
Activity recommendations and restrictions in patients with VHD before a procedure • What activities and exercises promote the progression or increased risk of adverse events for specific types of VHD? • What activity recommendations should be made to patients with VHD? How can this evidence be best conveyed?

VHD indicates valvular heart disease.

procedure (Table 3). This is attributable to the fact that there have been no medical therapies proven to prevent, slow, or reverse primary VHD to date.[1,32] There was enthusiasm that statins might play such a role for patients with aortic sclerosis or AS based on preclinical studies, but several clinical trials demonstrated a lack of clinical benefit.[33,34] Progress is being made in elucidating underlying mechanisms of valve disease, but these discoveries have yet to be translated into effective therapies.[32,35,36] In some cases, promising targets and therapies exist, but they have not been tested in patients with VHD. For example, elevated Lipoprotein(a) is associated with incident and progressive AS and emerging data indicate a potential role for PCSK9 in valve calcification. Therapies targeting these molecules are available, but they have not been tested as potential medical therapies to prevent or slow progression of AS.[37,38]

The morbidity and mortality of valve disease often stems from how pressure or volume overload affects the ventricle. The sequelae of VHD overlap significantly with heart failure (HF) with preserved ejection fraction and HF with reduced ejection fraction both in terms of ventricular remodeling and dysfunction as well as clinical manifestations and symptoms. Most patients with VHD develop manifestations and symptoms of HF before an intervention on their valve and many have residual HF after a valve procedure. Even if the primary valve abnormality progresses, perhaps medical therapy targeting the maladaptive ways in which the ventricle responds to pressure or volume overload could delay the onset of HF symptoms or leave the heart in a healthier structural and functional place after a valve procedure is performed to mitigate HF after a procedure. For example, in patients with AS, excessive hypertrophy and the presence and extent of myocardial fibrosis are associated with increased HF, worse left ventricular function, and increased mortality.[39,40] Accordingly, medical therapy targeting maladaptive hypertrophy or fibrosis may promote ventricular health and improve survival even if the AS progresses and valve replacement is still needed. Although the mechanism for the potential benefit is unclear, there are retrospective studies suggesting that renin-angiotensin system blockade may be associated with improved survival and a lower risk of cardiovascular events.[41]

Several tools will be needed to elucidate pathobiology in the valve and the ventricle and to test medical therapies directed at promising targets. Phenotyping should include circulating biomarkers (including -omic approaches), multimodality and molecular imaging, tissue analyses (eg, myocardium, valve), studies done under resting and stress (eg, exercise) conditions, and invasive hemodynamics.

Beyond medical therapy targeting the valve and ventricle, there are other knowledge gaps pertinent to the stage of progressive valve disease related to the blood pressure (BP) and physical activity goals and guidelines. With respect to BP goals, the VHD guidelines defer to BP guidelines for the general population and offer no specific targets for patients with VHD.[1] However, for AS, while hypertension is a risk factor for incident AS and faster progression, a post hoc analysis of SEAS (Simvastatin Ezetimibe in Aortic Stenosis Study) showed that event rates were higher for those with a systolic BP <120 mm Hg or diastolic BP <70 mm Hg.[42–44]

Guidelines on physical activity and restrictions for patients with progressive VHD are generally based on expert consensus, but further research could refine and improve those recommendations.[45] At the other end of the spectrum, given the increased procedural risk and postoperative events associated with impaired physical function and frailty, it is unclear whether "prehabilitation" (rehabilitation before an intervention) before a valve procedure may reduce risk and improve outcomes.

DECISION MAKING WHEN A PROCEDURE IS CONTEMPLATED (CLINICIAN PERSPECTIVE)

There are a number of factors a clinician must consider in order to determine whether to recommend a valve procedure or surgery to a patient: appropriateness, timing, feasibility, and approach, and whether the recommendation is reflective of the patient's goals and preferences. Each of these areas has potential for important research questions (Table 4). Particularly among younger patients, considering the longitudinal patient journey and the potential need for multiple interventions over the patient's life, consideration needs to be given to and research directed at clarifying the optimal treatment path when multiple procedures over a lifetime can be predicted.

A critical step in the decision-making process for clinicians is to determine whether the procedure is *appropriate*. Determining the appropriateness of a procedure centers on assessing whether the anticipated benefits of the procedure are likely to outweigh the risks, which is inextricably linked to understanding the patient's goals and preferences and determining whether the procedure has a reasonable likelihood of achieving these goals. Notably, the research suggests that clinicians often make a "preference misdiagnosis," and thus tools and skill sets to clarify patient values are needed.[46] There are generally 2 broad categories of inappropriate (or ineffective) procedures: (1) futility of a valve procedure because of comorbidities and frailty—even if the procedure is technically successful, the patient will die soon or experience an ongoing decline in health status; or (2) nonresponder to a valve procedure—even if the procedure is technically successful, it does not improve health status, survival, or other goals of the patient. The first scenario is easier to conceptualize; an example of the second from another cardiovascular specialty would be the lack of clinical response to cardiac resynchronization therapy among patients with a nonleft bundle block QRS morphology.[47] While we are gaining more insight into patients for whom TAVR may be futile, much work remains to be done to clarify which patients will not benefit from mitral or tricuspid procedures.

Timing of the procedure is also an important step in decision making: Does the patient meet criteria for treatment of the valve? Our current indications for treatment with transcatheter therapies reflect practice patterns when surgery is the only option. With less invasive treatments and increasing options for repeat procedures, the optimal timing of intervention should be questioned. With the introduction of TAVR and the opportunity for valve-in-valve TAVR in the treatment of AS, strategy trials are important to better understand whether TAVR may be beneficial earlier in the disease, ie, before symptoms (eg, EARLY TAVR [Evaluation of Transcatheter Aortic Valve Replacement Compared to Surveillance for Patients With Asymptomatic Severe Aortic Stenosis] NCT 03042104], or in symptomatic moderate disease (eg, TAVR UNLOAD [Transcatheter Aortic Valve Replacement to Unload the Left Ventricle in Patients With Advanced Heart Failure: A Randomized Trial] NCT 02661451). Similar questions about timing exist for the treatment of mitral and tricuspid valve disease. The technology, however, is at an earlier stage in defining the efficacy of approaches and devices.

An additional step in the decision process is to determine the best *approach* to treating the valve. The best approach might depend on technical feasibility (eg, is the left ventricular outflow tract too large or small, are the mitral [or tricuspid] leaflets amenable to clipping, how much mitral annular calcification is too much) but also consider other issues. The choice of a transcatheter versus surgical versus hybrid approach, optimal choice of valve, simultaneous versus sequential procedures for multiple valve disorders, and whether concurrent cardiac conditions (eg, coronary disease) need to be addressed depend on the patients' medical condition, procedural risk, age, and cardiac function, as well as patient preferences and values.

To improve decision making from the clinician perspective, the emphasis should be on identifying factors and developing and validating risk models that will inform, influence, and guide clinical decisions and actions regarding: (1) timing of a procedure (perform it now versus later); (2) whether to recommend a procedure when futility is anticipated (either because of frailty and impaired physical function or a predicted lack of clinical response to the intervention); or (3) whether a specific adjunctive intervention should be employed in a subgroup of patients alongside a procedure to optimize outcomes. For example, a risk prediction tool for poor outcome after TAVR identified 8.4% of patients with a ≥70% predicted risk of a poor 1-year outcome; of those very high-risk patients, 60.3% were dead and an additional 16.9% had poor quality of life or quality of life decline by 1 year after TAVR.[48] Given that average 1-year mortality in patients with symptomatic severe AS not getting TAVR is ≈50%, knowing that a patient is in this very high-risk subgroup may inform shared decision-making conversations regarding whether to perform TAVR.[49] Similarly, a risk score for outcomes after TAVR that includes a frailty component is useful not so much because it improves discrimination of mortality (eg, improved c-statistic), but because it identifies patients at very high risk for death or disability at 1 year for whom TAVR may be futile and also identifies patients for whom an aggressive rehabilitation plan is particularly important as an adjunct to TAVR for outcomes to be optimized.[50]

Table 4. Decision Making (Clinician and Patient Perspectives) When a Procedure is Contemplated—Patient-Centered Research Questions in VHD

Clinician Perspective
Optimal timing of a valve procedure • What is the optimal timing of a valve procedure for patients with asymptomatic severe valve disease or symptomatic moderate valve disease? Do cut points for "severe" valve disease need to be re-evaluated and refined? Do recommendations for valve intervention need to more explicitly integrate the severity of the valvular lesion with the ventricular response to it? Examples include clarifying the optimal timing of valve replacement for patients with severe asymptomatic AS, moderate AS with left ventricular dysfunction or symptoms of HF, and severe asymptomatic aortic regurgitation with evidence of left ventricular dilation or subclinical dysfunction. • For these patient groups, if all patients do not benefit from earlier intervention, which subgroups (as identified by imaging, biomarkers, or other factors) may benefit from earlier intervention?
Nonresponders to a valve procedure • What are the reasons that some patients do not experience an improvement in survival, quality of life, or functional status after a valve procedure? • What are the reasons for a lack of reverse ventricular remodeling or improvement in ventricular function in some patients after a valve procedure? • How can we predict who will be a nonresponder to a valve procedure and how can that inform our recommendations and SDM with the patient? Areas of particular interest include patients with significant secondary mitral regurgitation or tricuspid regurgitation. • Which patients with secondary mitral regurgitation (eg, based on age, left ventricular size or function, severity of mitral regurgitation, biomarkers, and comorbidities) will benefit from a mitral procedure (eg, transcatheter valve repair or replacement or surgery) vs left ventricular assist device /transplant vs guideline-directed medical therapy alone? • Which patients with secondary tricuspid regurgitation (eg, based on right ventricular size/function, associated pulmonary vascular disease, biomarkers, and severity of tricuspid regurgitation) will benefit from a tricuspid procedure? • How best can we understand patient goals and preferences and determine whether the selected therapy is likely to meet patient goals?
Futility of a valve procedure caused by comorbidities and frailty • Can we accurately predict when, caused by comorbidities and/or frailty, a valve procedure will not substantively improve the health status of patient even if the procedure is successful? • Can current or future risk scores be efficiently and effectively utilized in practice to improve patient counseling and SDM? • What role might palliative care consultation play in these scenarios in particular?
Clarifying the relationship between valve disease and symptoms and anticipated benefit of a procedure • When is valve disease significant enough such that treating it with a valve intervention is likely to benefit the patient? • How do we determine whether symptoms are caused by valve disease or other cardiac or noncardiac comorbidities?
Health status assessment • Are currently HF-specific health status measures appropriate for monitoring patients with valve disease and their response to therapy? • What role might alternative or adjunctive assessments tailored to patients with valve disease have in evaluating and monitoring the well-being of patients with valve disease longitudinally, including before and after a procedure?
Approach to valve procedures • Based on patient and anatomical factors, when are surgical vs transcatheter vs hybrid approaches preferred? • What are the pros and cons, benefits, and risks of valve choices in various clinical settings (eg, mechanical vs bioprosthetic at a younger age and surgical vs transcatheter valve or type of transcatheter valve when a bicuspid valve is present)? • What type and severity of coronary disease ought to be fixed before transcatheter valve repair or replacement and what can be deferred? • For multivalve disease, when is a concomitant procedure preferred and when is a staged approach preferred?
Patient Perspective
Patient goals and preferences and integration into VHD trials • What do patients with VHD understand about their disease process? What early educational interventions are most effective so patients are prepared to participate in SDM? How does this differ among a diverse patient population (ie, age, frailty, comorbidities, race, sex, language, health literacy)? • What outcomes are most important to patients with VHD? How do they vary across diverse patients, including geography (ie rural vs urban locations)? How may this inform the operationalization of advanced heart valve centers? • Can a patient-reported outcome measure based on patients' goals for therapy perform with reliability and validity to evaluate new treatment options within clinical trials? • How would such a goal-attainment patient-reported outcome measure correlate with other outcomes, including health status measures, rehospitalization, and mortality? • How can a goal-attainment patient-reported outcome measure be implemented successfully into clinical practice? What are the measures of success?
Selection of outcomes for SDM trials in VHD • Which outcomes most accurately reflect the patient experience as defined by patient stakeholder groups (eg, trust, knowledge, and anxiety)? • How do patients prioritize outcomes in the treatment of VHD? • Which additional outcomes might also be evaluated to assess the value of SDM (eg, choice of therapy and costs)? • How is SDM most accurately measured in cardiovascular care settings? How does the quality of decision making change? How is this different from other clinical scenarios when a heart team is involved in decision making?
Strategies to support an SDM process • How is SDM most effectively delivered? • Where and when in the care process are SDM interventions most effective (eg, at home, before and/or after clinic)? Who is the most effective at delivering SDM interventions? What is the effect of limited diversity among VHD clinicians on measured outcomes of SDM? Can the interventions be divided up among team members effectively? • How might technology be leveraged to aid in SDM (ie, telehealth, electronic health record, smart phones)? • What is the comparative effectiveness of an electronic health record–embedded vs paper decision aids for patients with VHD? • How does the method of delivery of SDM interventions influence clinician SDM skill sets and attitudes and sustained use?

(*Continued*)

Table 4. Continued

Patient Perspective
Impact of policy on delivery of care to patients with VHD • Following Medicare mandates for SDM, how does care delivery change? • Are changes associated with improved outcomes? • What are the unintended consequences of policy mandates for decision aid use or documentation of SDM?

AS indicates aortic stenosis; HF, heart failure; SDM, shared decision making; and VHD, valvular heart disease.

DECISION MAKING WHEN A PROCEDURE IS CONTEMPLATED (PATIENT PERSPECTIVE)

The expansion of treatment options for VHD and the increase in the number of older adults with multiple competing comorbid conditions make shared decision making (SDM) increasingly relevant (Table 4).[51] SDM is a process in which clinicians and patients deliberate reasonable treatment alternatives and collaborate on a final treatment plan, with the final choice informed by patients' goals and preferences.[52] An SDM process is most applicable for preference-sensitive decisions, defined as those in which more than one reasonable option exists; there remains uncertainty in the evidence; or patient preferences vary between patients or compared with clinicians. In these types of medical decisions, patients' values and preferences play a significant role in identifying which treatment may be best for them.[53]

SDM is distinct from patient education, which is a 1-way stream of information from clinician to patient. SDM involves listening to the values and preferences of informed patients incorporating this into decision making.[54] There is consistent evidence that clinicians do not elicit patient values and preferences, nor adjust care to preferences.[55,56]

SDM research, pioneered and rigorously evaluated in fields including oncology and orthopedics over the past 3 decades, includes the study of strategies to improve patient-clinician communication when making medical decisions.[57–60] Numerous randomized trials on the effectiveness of decision aids to promote an SDM process have demonstrated improvement in patient-centered outcomes including knowledge, satisfaction, and decisions consistent with patients' values.[57] Decision aids, which may include paper handouts, videos, websites, or tools embedded in the electronic health record, raise awareness there is a choice to be made, provide information on risks and benefits, and may also assist in values clarification.[61,62] However, large-scale implementation projects identify that while decision aids are helpful, clinician skill sets in SDM—combined with positive clinician and leadership attitudes towards meaningful change in healthcare delivery—are critical for effective SDM.[54] An SDM approach is consistently advocated across multiple disease conditions in cardiology by professional society guidelines, yet there remains a lack of recommendations regarding best practices or most effective tools for implementation.[16]

It is essential that validated frameworks and measures are used in study conceptualization, design, deployment, evaluation, and implementation of SDM interventions, such as patient decision aids.[61–64] Study designs often include cluster randomized trials, quasi-experimental designs with pre-post testing, or repeated observations over time.[65] While a review of all measures of the quality of decision making is outside the scope of this review, examples include independent, third-party review of audiotaped clinical encounters, patient surveys, or simply noting that a decision aid was used in the visit.[66]

Because some of the research in SDM is striving to describe natural phenomena, including clinician and patient attitudes, beliefs, and behaviors, qualitative research is also utilized. These studies may employ nominal group technique, semistructured interviews leading to framework-guided qualitative analysis, or more traditional focus groups.[56,67,68] The National Quality Forum provides additional best practices to help guide implementation efforts of evidence-based tools, such as decision aids.[53] SDM is the "science of allocating time for care," and time will remain a significant barrier until SDM is no longer seen as "a 'nice-to-have' extra for which new time needs to be found."[69] This requires an investment in research into healthcare delivery innovations that embed the process of SDM into our existing structures, valuing the outcomes that reflect high-quality decisions so that patient engagement returns to its rightful place as intrinsic to our actions as clinicians.

POSTPROCEDURE THERAPY AND MANAGEMENT

Continuity of care and seamless management of the complexity of VHD after an intervention are central to ensuring patients derive their expected benefits of treatment (Table 5). For example, the 3M TAVR (Multimodality, Multidisciplinary, But Minimalist TAVR) study recently demonstrated the safety and reproducibility of a clinical pathway inclusive of minimalist periprocedure approach, a standardized

Table 5. Postprocedure Therapy and Management—Patient-Centered Research Questions in VHD

Supporting a Safe Recovery
Getting home safely—improving transitions of care • Which postprocedure care pathway(s) yield the best patient outcomes? • Do different patient groups have different early recovery requirements? • What clinician and patient factors are associated with early readmissions and what are the most effective interventions to reduce readmissions in risk-stratified groups? • How do we improve self-care among patients discharged after a valve procedure? How should patients be monitored upon discharge after a valve procedure (including components and delivery of monitoring)? • How can mobile health and technology be leveraged to optimize these processes?
Getting better after a heart valve procedure—rehabilitation and improving physical functioning • What factors are associated with improvement in physical function? • How can frailty be treated after a heart valve procedure? • What interventions (eg, aerobic exercise, resistance exercise, nutrition, medications, mindfulness, and coaching) are most effective to optimize physical function? • What are the most effective, translatable, and generalizable ways to implement these interventions? • How can interventions in the home and those that leverage technology and mobile health facilitate these objectives?
Managing complications and the long-term sequelae of valve procedures • How should conduction disturbances and potential need for a pacemaker be monitored after transcatheter aortic valve replacement? • What is the long-term impact of conduction disturbances and pacemakers after valve procedures? • How do patients report their experience of needing a new pacemaker after a valve procedure? • What are the implications of leaving the inter-atrial septum open or closing it after a left-sided valve procedure? • What are the implications for cognitive function of small particle emboli to the brain?
Managing Heart Disease Related to VHD
Treating HF and abnormal ventricular structure and function after a valve procedure • What is the relationship between changes in ventricular structure and function after a valve procedure and subsequent clinical outcomes? • What factors/pathways underlie these changes and could they be targeted with existing or novel medical therapies? For example, greater regression of left ventricular mass after aortic valve replacement has been associated with improved clinical outcomes. What medical therapies may augment left ventricular mass regression after valve replacement and would such a strategy improve clinical outcomes? • Residual pulmonary hypertension and increased systemic vascular load are associated with worse outcomes after valve procedures. What medical therapies might target this pathophysiology and improve clinical outcomes?
Blood pressure targets in patients with VHD • What are the optimal blood pressure targets in patients with VHD after a valve procedure? Should they differ from the general population? • How do age, type of valve disease, type of intervention, and comorbidities influence optimal targets for blood pressure?
Anticoagulation and antiplatelet therapy after valve procedures • After specific types of valve procedures, what anticoagulation and/or antiplatelet regimens are best, including which agent(s) and timing of initiation and length of administration? • What are the benefits and risks of various treatment options? How do certain comorbidities (eg, afibrillation or coronary disease postpercutaneous coronary intervention) affect these decisions? • To reduce stroke risk in patients with VHD and a concomitant atrial arrhythmia, which patients may benefit from left atrial appendage closure devices vs anticoagulation?
Device Surveillance and Durability
Valve durability and surveillance • What is the average lifespan of normal function for various surgical and transcatheter valves? • What factors are associated with degeneration and which of those may be modified? • What is the optimal cardiac imaging (eg, echocardiography and cardiac computed tomography) monitoring regimen after a valve procedure and how might the type of valve disease and valve procedure performed influence that? • How should the interval development of a high transvalvular gradient during follow-up be managed?

HF indicates heart failure; and VHD, valvular heart disease.

postprocedure protocol of rapid mobilization and reconditioning, and criteria-driven discharge to achieve safe next-day discharge.[70] These findings reflect the experience of single-center observational studies that prioritize a bundle of care that promotes the mitigation of postprocedure risks in the mostly elderly patient population with VHD.[71] The development and evaluation of health service delivery interventions is complex because of the multiple interacting components, the number and difficulty of behaviors required by those delivering or receiving the interventions, the number of organizational levels targeted by the intervention, and the measurement of outcomes that must be reflective of and responsive to the intervention.[72]

The CMS, Joint Commission, and the Institute of Medicine have consistently highlighted that the failure of ensuring appropriate transition of care—the movement of patients between healthcare practitioners, settings, and home as their condition and care needs change—can have devastating effects on patients.[73,74] We currently lack evidence to guide and risk-stratify the use of postprocedure pathways, determine the optimal length of stay, and support patient-centered discharge planning in an increasingly heterogenous VHD

population. There is a pressing need to focus research on strategies to address patients' vulnerabilities in the early recovery period and optimize care transitions in healthcare systems to improve outcomes. Given the high prevalence of frailty in patients with VHD and its association with poor outcomes after valve procedures, effective strategies to improve postprocedural physical function are sorely needed. However, enrollment in center-based cardiac rehabilitation programs is low and there are numerous barriers to participation.[75] Novel approaches that leverage technology and can be implemented entirely or partially at home may be more effective.[76] More research is also needed regarding the consequences of and how to monitor for complications of valve procedures.

Many patients continue to have a poor quality of life and adverse outcomes after intervention for VHD. Maladaptive left ventricular remodeling and dysfunction in response to pressure or volume overload does not always reverse toward normal after the valve is fixed, which is associated with worse outcomes.[39,40,77,78] Research to elucidate mechanisms of persistent maladaptive ventricular remodeling and dysfunction after a valve procedure may identify novel targets for medical therapy to improve outcomes as an adjunct to a procedure.[49,79–81] Optimal BP targets after a valve procedure may differ than those for the general population, but further work is needed to clarify these relationships and appropriate goals.[82,83]

It is also critical to identify best practices for antiplatelet and anticoagulant medications after different

Table 6. Barriers to Effective Patient-Centered Research on VHD

Barrier	Impact
Lack of recognition of VHD as a specific area of expertise	• No specific training pathway and lack of training opportunities for VHD experts. • Inadequate numbers of noninterventional VHD physician and advance practice provider experts. • Inadequate focus on VHD research at scientific meetings as specified pathway.
Limited funding and lack of recognition of need for VHD research	• Industry funding is focused on device-related questions, which limits innovative research on many nondevice-related VHD research questions. • Pharmaceutical companies often exclude patients with VHD from clinical trials on medical therapy and are reluctant to perform medical therapy studies that target VHD populations. • VHD grant applications to the National Institutes of Health assigned to reviewers with limited expertise in VHD.
Lack of patient involvement in VHD research priorities, study design, and implementation	• Research fails to consider important patient-based questions. • Challenge to change the culture of research and implementation science. • Reduces patient engagement in shared decision making if tool development does not include the patient perspective.
Lack of diversity in VHD researchers	• Lack of diversity among researchers reduces the range of research questions. • Lack of diversity in VHD researchers reduces recruitment of diverse patient groups in clinical trials.
Lack of inclusion of patients with VHD in clinical trials of HF, hypertension, arrhythmias, and other cardiac conditions	• Medical therapies that may benefit patients with VHD have not been studied. • Clinical trials of hypertension treatment in patients with VHD are not available. • Effect of medical therapy on HF with preserved ejection fraction in patients with VHD has not been studied.
Lack of validated VHD-specific patient-reported outcome measures	• Patient-reported outcome measures developed for other cardiac conditions may not capture all aspects of VHD or the diversity of patient perspectives.
Few measures of effectiveness of approaches to improving outcomes in patients with VHD	• Standardized measures of effectiveness would allow more rigorous research on approaches to shared decision making, heart team approaches, and heart valve centers.
Traditional views on diagnosis and treatment of VHD	• Reluctance to consider that screening with a stethoscope by primary providers might not be the optimal approach to screening for VHD. • Reluctance to treat patients with VHD with medications known to be effective for hypertension and HF.
Healthcare system inertia in the approach to provision of care to patients with VHD	• Lack of implementation science studies of pathways of care to improve outcomes in patients with VHD.
Silos based on type of physician and type of medical center	• Particularly in settings without integration of transcatheter therapy options, care for patients with VHD is often siloed between cardiologists (pretreatment and posttreatment care) and surgeons (procedural care). • Communication and care handoffs between smaller community or rural facilities and large medical centers are often poor, leading to suboptimal care for patients with VHD. • Procedure-focused programs vs comprehensive VHD centers that provide continuity of care, access to multiple modalities of treatment, and seamless communication with primary care providers.
Lack of diversity in the clinical VHD workforce	• Poor recognition of barriers to care in specific populations, including poor communication, geography, and access to care. • Lack of trust and engagement by patients with backgrounds different from clinicians.
Difficulty in publishing patient-centered research in cardiology journals	• Educating editors about patient-centered research, patient-centered outcomes, and standards for qualitative research would increase acceptance by major medical journals.

HF indicates heart failure; and VHD, valvular heart disease.

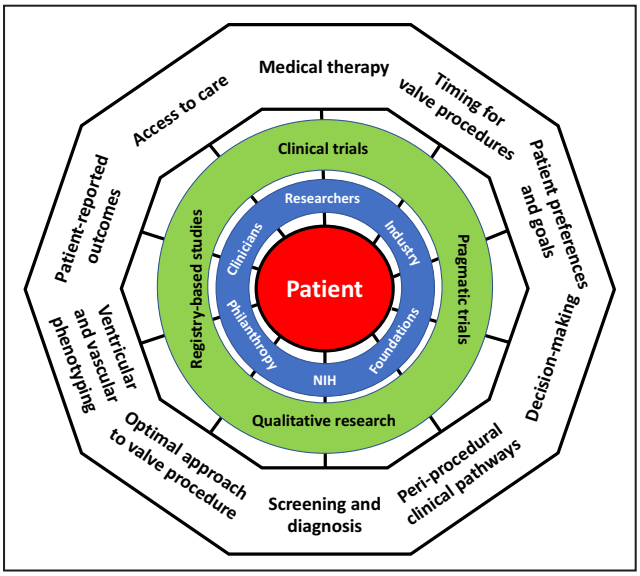

Figure 2. Patient-centered research in valvular heart disease (VHD).
This figure shows the multifaceted aspects of what we define and characterize as patient-centered research in VHD. The patient (red) is a participant in and focus of the research. The outer ring represents some of the many research questions and knowledge gaps in the field. The most common research tools and methodologies to address those knowledge gaps are shown in the next inner circle (green). Those doing and funding the research are shown in the final inner circle (blue).

valve procedures. While valve thrombosis does occur after TAVR and may influence valve durability, indiscriminate treatment with anticoagulation is associated with harm.[84] The rapid increase in the number and types of devices to treat VHD also emphasizes the need for research to rigorously assess device durability, identify best practices for surveillance of device performance, and determine the clinical significance and appropriate treatment of abnormalities identified.

CLINICAL TRIALS IN VHD—CHALLENGES AND OPPORTUNITIES

With the introduction of transcatheter options to treat VHD as an alternative to surgery, a rapid succession of numerous well-designed RCTs have been completed, providing a robust evidence base particularly for the role of TAVR in the treatment of AS (Table S1). Most trials in VHD over the past decade are device-focused. While there is an ongoing need for more device and procedure-related trials, there is also an urgent need for RCTs to address many nondevice research questions in VHD along the full spectrum of the patient's journey from screening to long-term post-procedure management. Indeed, many of the questions included herein could be optimally addressed by RCTs. Yet, there are several challenges to performing clinical trials, particularly those addressing questions not related to a device. Leveraging existing registries (eg, TVT [Transcatheter Valve Therapy] and STS [Society of Thoracic Surgeons]) to perform pragmatic trials could be a good starting point. These registries capture an extensive number of data but they are designed for tracking quality and outcomes and less as a vehicle for prospective research. Incorporating use of their data into prospective studies is currently onerous and expensive.

BARRIERS TO PATIENT-CENTERED RESEARCH IN VHD

There are many barriers to patient-centered research in VHD as summarized in Table 6. Until recently, VHD was not recognized as a common and important clinical condition and there are no defined training pathways for clinical expertise in VHD. Research on VHD tends to be spread across different specialty scientific meetings and medical journals, which are organized by the type of research rather than the patient with VHD (eg, the disease not the method). Similarly, the concept that patients should be involved in clinical research is relatively new and has yet to gain wide acceptance, although some medical journals now require a statement about patient involvement.[64] Some patient-centered research questions and outcomes seem "soft" compared with the traditional "hard" end points of clinical trials; researchers and reviewers are often unfamiliar and uncomfortable with standards for performing and reporting qualitative data.[63] Investigator-initiated funding for VHD research is difficult to obtain given this lack of expertise and priority by funding agencies. Many of these barriers can be reduced or eliminated by promotion of training and research in VHD; education of researchers, reviewers, and journal editors about patient-centered research; increased funding opportunities for VHD research; and closer collaboration between researchers, clinicians, and patients with VHD.

CONCLUSIONS

Over the past decade, an explosion of research in VHD has centered on new opportunities to perform valve procedures less invasively utilizing transcatheter approaches. There is little doubt that, on the whole, this is good for patients. Numerous opportunities exist to build on these advances and improve outcomes for patients with VHD. Herein, we have outlined knowledge gaps and research priorities for patient-centered research in VHD, recognizing that the patient ought to be the center of our attention and not simply a valve or device (Figure 2). There are a number of barriers that impede progress, but also numerous opportunities for

collaboration and progress among diverse stakeholders who can be united with a common purpose (Table S2). Ultimately, patient-centered research needs to intersect with, promote, and provide evidence for patient-centered care and policy to yield the greatest benefits for those who have the most at stake: our patients.

ARTICLE INFORMATION

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Supplementary Materials

Tables S1–S2

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Supplemental Material

Table S1. Clinical Trials in VHD – Challenges and Opportunities.

• How should the "patient voice" be incorporated into trial design and endpoints selected and prioritized in way that aligns with FDA and other policies? What are the best ways to analyze these endpoints?
• Most trials in the valve space are device-based trials sponsored by industry and there is a lack of medical therapy trials. Heart failure trials tend to exclude patients with significant valve disease or those who have recently had a procedure. Pharmaceutical companies seem to view patients with valve disease as a small/niche population despite the epidemiology studies which clearly show the large size of this population of patients. Accordingly, there is a lack of data on the effects of medications for heart failure on patients with valve disease and it is often challenging to convince the relevant stakeholders of the importance of these studies.
• What is the most effective way to study imaging-based studies with imaging efficacy endpoints in the context of their expense?
• How can people of color, women, rural, and less resourced patients be appropriately represented in clinical trials?
• What is the appropriate "control arm" for device studies (e.g. GDMT, surgery, or another transcatheter therapy)? How do they affect trial enrollment?
• How do the heterogeneity of patients with secondary MR and TR (e.g. spectrum of valve and ventricular anatomy and function, differences in patient characteristics, sensitivity to loading conditions, etc.) impact identification and enrollment of appropriate patient groups? What are strategies to overcome resulting challenges?
• How can registries (e.g. TVT, STS, etc.) be leveraged effectively to answer patient-centered research questions and run pragmatic clinical trials?

FDA, Food and Drug Administration; GDMT, guideline directed medical therapy; MR, mitral regurgitation; STS, Society of Thoracic Surgeons; TR, tricuspid regurgitation; TVT, Transcatheter Valve Therapies.

Table S2. Resources for Patient-Centered Research in Valvular Heart Disease.

Heart Valve Voice US https://www.heartvalvevoice-us.org	Heart Valve Voice US is the only patient advocacy organization in the U.S. solely focused on heart valve disease (HVD). The organization works to increase public awareness and understanding of HVD, provides patient and care giver education, and advocates for increased HVD research and access to all valve disease treatments.
Heart Valve Voice UK https://heartvalvevoice.com	The six objectives that drive all of the work we do: (1) raise awareness of the symptoms and severity of heart valve disease in the UK in order to save lives and improve the quality of life; (2) increase the awareness of symptoms of heart valve disease; (3) work towards ensuring there is a clear and effective treatment pathway among care providers to ensure more effective management of the disease; (4) effectively campaign for early diagnosis and treatment of heart valve disease across the UK; (5) provide credible, independent and practical advice and information about heart valve disease; and (6) represent the UK's heart valve disease patients to help ensure that they receive the best treatment at the right time, improving quality of life and overall outcome for each individual.
Heart Valve Society https://heartvalvesociety.org	The mission of the Heart Valve Society is to promote awareness, advance knowledge, and innovate to reduce the burden of heart valve disease with a global and multidisciplinary approach.
Alliance for Aging Research https://www.agingresearch.org/	The Alliance for Aging Research (AAR) is the leading nonprofit organization dedicated to accelerating the pace of scientific discoveries and their application to vastly improve the universal human experience of aging and health. AAR provides education on heart valve disease and leads activities every February for National Heart Valve Disease Awareness Day.
Mended Hearts https://mendedhearts.org/	Mended Hearts (MH) is the largest patient-to-patient heart disease support network in the world. MH provides education, support and hope to patients with all types of heart disease and activates its extensive network of patient volunteers to visit patients in more than 460 hospitals nationwide.
National Heart Valve Disease Awareness Day www.valvediseaseday.org	The goal of National Heart Valve Disease Awareness Day on February 22 is to increase recognition of the specific risks and symptoms of heart valve disease, improve detection and treatment, and ultimately save lives. While heart valve disease can be disabling and deadly, available treatments can save lives,

	making education and awareness particularly important. On this day and throughout the year, the campaign partners—60+ non-profits, advocacy organizations, professional societies, and hospitals and heart centers—are helping to spread the word about valve disease.
Association of Black Cardiologists www.abcardio.org/	Mission: To promote the prevention and treatment of cardiovascular disease, including stroke, in Blacks and other minorities and to achieve health equity for all through the elimination of disparities.
NHLBI site on VHD https://www.nhlbi.nih.gov/health-topics/heart-valve-disease	
European Society of Cardiology Council on Valvular Heart Disease https://www.escardio.org/Councils/Council-on-Valvular-Heart-Disease/About	The ESC Council on Valvular Heart Disease aims to be a multidisciplinary forum for the Heart Valve Team, to encourage research, knowledge exchange, teaching and other educational activities in valvular heart disease.
HeartValveSurgery heartvalvesurgery.com	Robust online patient community
Living with Valve Disease livingwithvalvedisease.org	
WomenHeart womenheart.org	The National Coalition for Women with Heart Disease was founded in 1999 by three women who had heart attacks while in their 40s and faced many obstacles, including misdiagnosis, inadequate treatment, and social isolation.
Patient-Centered Outcomes Research Institute (PCORI) www.pcori.org	PCORI funds studies that can help patients and those who care for them make better-informed healthcare choices. PCORI funded a project on aortic stenosis: valveadvice.org
Society for Cardiovascular Angiography and Interventions (SCAI) http://www.scai.org SCAI Patient Site http://secondscount.org http://www.secondscount.org/treatments/treatments-detail-2/transcatheter-aortic-valve-replacement-tavr-2#.XW6ONflKi2w	
The Society of Thoracic Surgeons https://www.sts.org/	
American College of Cardiology https://www.acc.org ACC Patient Site **Cardio Smart** https://www.cardiosmart.org/TAVRDecisionAids	
American Heart Association https://www.heart.org/	
MAGIC Project https://app.magicapp.org/app#/guideline/1308	TAVI versus SAVR for patients with severe symptomatic aortic stenosis at low to intermediate perioperative risk

Sharedcardiology: A resource for clinical cardiologists and their patients sharedcardiology.org	A website updated by a practicing cardiologist, collating decision aids for cardiology clinicians; includes links to relevant policy documents (e.g. National Coverage Determinations).

JAMA Cardiology | Original Investigation

Characteristics of Clinical Trial Sites for Novel Transcatheter Mitral and Tricuspid Valvular Therapies

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IMPORTANCE Racial and ethnic minority and socioeconomically disadvantaged patients have been underrepresented in randomized clinical trials. Efforts have focused on enhancing inclusion of minority groups at sites participating at clinical trials; however, there may be differences in the patient populations of the sites that participate in clinical trials.

OBJECTIVE To identify any differences in the racial, ethnic, and socioeconomic composition of patient populations among candidate sites in the US that did vs did not participate in trials for novel transcatheter therapies.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional analysis used Medicare Provider Claims from 2019 for patients admitted to hospitals in the US. All clinical trials for transcatheter mitral and tricuspid valve therapies and the hospitals participating in each of the trials were identified using ClinicalTrials.gov. Hospitals with active cardiac surgical programs that did not participate in the trials were also identified. Data analysis was performed between July 2021 and July 2022.

EXPOSURES Multivariable linear regression models were used to identify differences in racial, ethnic, and socioeconomic characteristics among patients undergoing cardiac surgery or transcatheter aortic valve replacement at trial vs nontrial hospitals.

MAIN OUTCOME AND MEASURES The main outcome of the study was participation in a clinical trial for novel transcatheter mitral or tricuspid valve therapies.

RESULTS A total of 1050 hospitals with cardiac surgery programs were identified, of which 121 (11.5%) participated in trials for transcatheter mitral or tricuspid therapies. Patients treated in trial hospitals had a higher median zip code–based household income (difference of $5261; 95% CI, $2986-$7537), a lower Distressed Communities Index score (difference of 5.37; 95% CI, 2.59-8.15), and no significant difference in the proportion of patients dual eligible for Medicaid (difference of 0.86; 95% CI, −2.38 to 0.66). After adjusting for each of the socioeconomic indicators separately, there was less than 1% difference in the proportion of Black and Hispanic patients cared for at hospitals participating vs not participating in clinical trials.

CONCLUSIONS AND RELEVANCE In this cohort study among candidate hospitals for clinical trials for transcatheter mitral or tricuspid valve therapies, trial hospitals took care of a more socioeconomically advantaged population than nontrial hospitals, with a similar proportion of Black and Hispanic patients. These data suggest that site selection efforts may improve enrollment of socioeconomically disadvantaged patients but may not improve the enrollment of Black and Hispanic patients.

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Supplemental content

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Racial and ethnic minority and socioeconomically disadvantaged patients have been underrepresented in randomized clinical trials.[1,2] Underrepresentation limits clinicians' ability to apply the findings of major clinical trials to these patients and may contribute to limiting their access to novel, experimental therapies after their ultimate regulatory approval.[3-5] To address inequities in trial enrollment, the National Institutes of Health (NIH) Revitalization Act of 1993 mandated appropriate inclusion of racial and ethnic minority groups; however, representativeness remains a problem for clinical trials, including both industry-funded and NIH-funded trials enrolling patients with cardiovascular conditions.[6-10] In 1 review of 143 clinical trials conducted between 2008 and 2017 to evaluate 35 novel cardiometabolic drugs, just 2.1% of enrollees were Black and 2.1% were Hispanic.[11]

Efforts from the NIH and the US Food and Drug Administration have focused on enhancing inclusion of minority groups at sites participating at clinical trials; however, another factor that may limit representation of racial and ethnic minority groups and socioeconomically disadvantaged patients in clinical trials is the characteristics of the hospitals that most often participate as clinical trial sites and enroll patients.[12] If hospitals that participate in clinical trials take care of relatively few patients from racial and ethnic minority groups and/or socioeconomically disadvantaged patients, this would represent a systemic barrier to trial access for these populations.

Transcatheter therapies to treat mitral and tricuspid valve disease are not yet standard of care in most circumstances but are an area of rapid development with multiple ongoing industry-sponsored clinical trials. In this study, we sought to identify the characteristics of sites that participate in clinical trials for novel transcatheter tricuspid and mitral valvular therapies among candidate hospitals with active cardiac surgery programs. We specifically aimed to identify any differences in the racial, ethnic, and socioeconomic composition of patient populations among candidate sites in the US that did and did not participate in these trials.

Key Points

Question What are the racial, ethnic, and socioeconomic characteristics of patients treated at sites that participate in clinical trials for novel transcatheter valve therapies compared with candidate sites that do not participate in these trials?

Findings In this cohort study of 1050 hospitals, patients treated in trial hospitals were more socioeconomically advantaged than patients treated at nontrial hospitals. There was no meaningful difference in the proportion of Black and Hispanic patients at trial vs nontrial hospitals.

Meaning Site selection may improve socioeconomic diversity in clinical trials for transcatheter valves but may not improve racial and ethnic diversity.

Methods

Study Cohort

This study was deemed to be exempt by the institutional review board at the University of Pennsylvania due to the use of deidentified data, and informed consent was waived due to institutional policy for deidentified administrative data. The Medicare Provider Analysis and Review data files and the Master Beneficiary Summary data files were used to identify Medicare fee-for-service beneficiaries aged 66 years or older who were admitted to hospitals with existing cardiac surgery programs between January 1, 2019, and December 31, 2019. To identify representative patients undergoing cardiovascular and cardiac surgical procedures at these hospitals, Medicare beneficiaries undergoing cardiac surgery procedures or transcatheter aortic valve replacement (TAVR) during this period were identified using *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* procedure codes. We used an age cutoff of 66 years to ensure a minimum 12-month preoperative period to assess comorbidities. Hospitals were considered to have an active cardiac surgery program if they coded for 10 or more major cardiac surgery procedures in 2019. We chose 10 procedures to minimize the effect of administrative coding errors at the hospital level (eFigure in the Supplement).

Trial hospitals for transcatheter tricuspid and mitral valvular therapies were identified using ClinicalTrials.gov. ClinicalTrials.gov was queried on September 30, 2021, for the terms *transcatheter tricuspid valve repair*, *transcatheter tricuspid valve replacement*, *transcatheter mitral valve repair*, and *transcatheter mitral valve replacement*. Trial hospitals were identified, and the Centers for Medicare & Medicaid Services certification number obtained from the Medicare Inpatient Hospital Look-up Tool from 2018.[13]

The terms *transcatheter aortic valve replacement* and *transcatheter aortic valve repair* were not queried given the establishment of transcatheter aortic valve replacement as the treatment modality of choice for the majority patients with aortic stenosis. We did not investigate *transcatheter pulmonary valve replacement* and *transcatheter pulmonary valve repair* because these therapies are predominantly used among pediatric and adolescent patients rather than the older adult population.

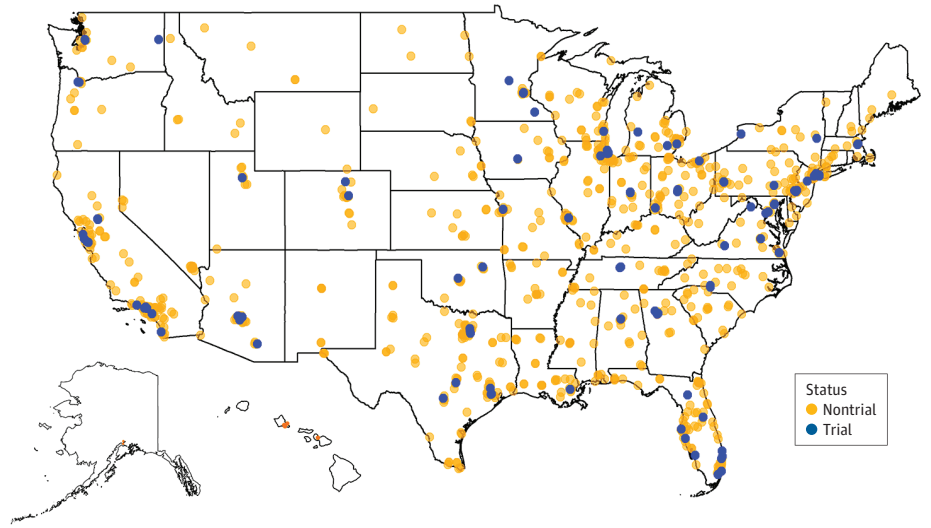
Geographic Identification

Patient and hospital zip code information was obtained from the Hospital Data Claims and Demographic Data files. Patients and hospitals were assigned to Core-Based Statistical Areas using zip code information from US Department of Housing crosswalk files using 2010 Census geographies, as described previously.[14] The US Office of Management and Budget defines metropolitan areas as urban clusters of at least 50 000 people and micropolitan areas as urban clusters of between 10 000 and 50 000 people. Zip codes that were not linked to metropolitan or micropolitan Core-Based Statistical Areas were defined as rural.

Race, Ethnicity, and Socioeconomic Identification

Race and ethnicity were defined as per the Master Beneficiary Summary data files. Existing categories were Asian, Black,

Figure. US Trial and Nontrial Cardiology Hospitals



Geographic map of hospitals with cardiac surgery programs that did or did not participate in clinical trials for transcatheter mitral and tricuspid valve therapies between January 1, 2019, and December 31, 2019.

Hispanic, White, other, and unknown. For the purposes of this analysis, since the categories were mutually exclusive, we will use *Black* to refer to non-Hispanic Black individuals and *White* to refer to non-Hispanic White individuals throughout.

Socioeconomic status of Medicare fee-for-service patients was defined using 3 measures, as described previously.[14] Median household income for each patient was assessed using patient zip code data cross-linked with the Dartmouth Atlas.[15] Dual-eligibility status for Medicaid for each patient was assessed using Medicare Denominator files.[16] The Distressed Communities Index (DCI) score for each patient was obtained using patient zip code data and crosswalk files for DCI data between 2012 and 2016.[17] The DCI combines 7 economic indicators (percentage of population with high school diploma, housing vacancy rate, percentage of adults not working, poverty rate, median income ratio, change in employment, and change in business establishments) to generate a single index score, with a range from 0 (least distressed) to 100 (most distressed).

Statistical Analysis

Characteristics of hospitals with cardiac surgery programs that participated in transcatheter tricuspid and mitral valvular trials were compared with hospitals that did not participate in trials using the *t* test to compare means and χ^2 analysis to compare proportions, as appropriate. Similarly, baseline clinical, demographic, and socioeconomic characteristics of patients who underwent cardiac surgery or TAVR between 2016 and 2019 at hospitals that participated in transcatheter valvular trials were compared with those of patients treated in hospitals that did not participate in trials using the *t* test to compare means and χ^2 analysis to compare proportions, as appropriate.

To estimate the associations between participation in clinical trials among cardiac surgery hospitals and hospital location (metropolitan, micropolitan, rural), proportion of Black or Hispanic patients treated at each hospital, and the socioeconomic characteristics of patients undergoing cardiac surgery or TAVR at each hospital, 3 separate multivariable linear regression models were generated, with hospital characteristic variables and patient characteristics aggregated at the hospital level. Each model included only 1 socioeconomic indicator (median household income, proportion of dual eligibility for Medicaid, mean DCI score) to avoid collinearity.

As secondary analyses, we determined the clinical and demographic characteristics of all Medicare beneficiaries at the studied hospitals and repeated the above analyses. Statistical analyses were performed using SAS, version 9.4 (SAS Institute) and R Studio, version 1.3.959 (R Foundation). All statistical testing was 2-tailed, with *P* values less than .05 designated statistically significant.

Results

We identified 1050 active cardiac surgical programs between January 1, 2019, and December 31, 2019. There were 32 unique clinical trials for transcatheter mitral and tricuspid valve therapies (10 transcatheter mitral valve repair, 10 transcatheter mitral valve replacement, 6 transcatheter tricuspid valve repair, 6 transcatheter tricuspid valve replacement). Only 4 of the 32 trials had demographic data of trial participants available on ClinicalTrials.gov. Among those 4 trials, proportions of Black trial participants ranged from 0% to 16.7%, and proportions of Hispanic trial participants ranged from 3.3% to 6.9%. A list of all included trials is provided in eTable 1 in the Supplement. Of the 1050 hospitals with cardiac surgery programs, 121 (11.5%) participated in 1 or more trial of transcatheter mitral or tricuspid therapies. Among the 121 trial hospitals, the median (IQR) hospital participated in 3 (2-5) trials. Details on mitral and tricuspid valve procedures performed at trial and nontrial hospitals during the study period are provided in eTable 2 in the Supplement. Geographical maps of sites that participated in clinical trials for percutaneous mitral or tricuspid valve therapies were generated (**Figure**).

Table 1. Characteristics of Hospitals With Cardiac Surgery Programs That Did and Did Not Participate in Clinical Trials for Transcatheter Mitral and Tricuspid Valve Therapies

Variable	No. (%)		*P* value
	Nontrial hospitals (n = 929)	Trial hospitals (n = 121)	
Bed size			
<100 Beds	23 (2.5)	2 (1.7)	<.001
100-399 Beds	624 (67.2)	23 (19.0)	
≥400 Beds	282 (30.4)	96 (79.3)	
Teaching hospital	154 (16.6)	74 (61.2)	<.001
Profit status			
For-profit	181 (19.5)	16 (13.2)	.19
Nonprofit	651 (70.1)	94 (77.7)	
Government	97 (10.4)	11 (9.1)	
Region			
Midwest	249 (26.8)	25 (20.7)	.11
Northeast	115 (12.4)	24 (19.8)	
South	363 (39.1)	47 (38.8)	
West	202 (21.7)	25 (20.7)	
Area			
Metropolitan	881 (94.8)	120 (99.2)	.03
Nonmetropolitan	48 (5.2)	1 (0.8)	

Trial hospitals for percutaneous mitral or tricuspid valve therapies were larger (79.3% vs 30.4% with greater than 400 beds; $P < .001$) and were more likely to be academic centers (61.2% vs 16.6%; $P < .001$) (**Table 1**). Trial hospitals were more likely to be in metropolitan areas (99.2% vs 94.8%; $P = .03$). Further, patients undergoing cardiac surgery or TAVR at trial hospitals tended to have higher rates of clinical comorbidities than patients undergoing cardiac surgery or TAVR at nontrial hospitals (**Table 2**).

In unadjusted models, compared with patients undergoing cardiac surgery or TAVR for at nontrial hospitals, patients undergoing cardiac surgery or TAVR at trial hospitals resided in zip codes with higher median (IQR) income ($57 966 [$44 034-$79 215] vs $50 498 [$40 142-$65 422]; $P < .001$) and lower levels of community distress (median [IQR] DCI score, 31.1 [13.6-58.7 vs 44.3 [20.4-70.8]; $P < .001$) and were less often dual eligible for Medicaid (5.6% vs 6.2%; $P < .001$) (Table 2). We found similar results when studying the socioeconomic characteristics of all Medicare beneficiaries at trial vs nontrial hospitals, although trial hospitals treated a higher proportion of Black patients among total beneficiaries compared with nontrial hospitals (9.7% vs 8.0%; $P < .001$) (**Table 3**).

Differences in the racial, ethnic, and socioeconomic characteristics of patients undergoing cardiac surgery or TAVR in trial and nontrial hospitals are summarized in **Table 4**. After adjusting for hospital and patient clinical characteristics, patients undergoing cardiac surgery or TAVR at trial hospitals had higher median zip code–based household income than patients treated in nontrial hospitals (difference of $5261; 95% CI, $2986-$7537; $P < .001$). Patients at trial hospitals also lived in less distressed communities (difference in mean DCI score of 5.37; 95% CI, 2.59-8.15; $P < .001$). However, there was no significant difference in the proportion of patients dual eligible for Medicaid between trial and nontrial hospitals (difference of 0.86; 95% CI, −2.38 to 0.66; $P = .27$).

In both unadjusted and adjusted models, there was less than 1% difference in the proportion of Black and Hispanic patients cared for at hospitals participating and not participating in clinical trials (Table 4). Similar findings were seen when studying all Medicare beneficiaries at trial vs nontrial hospitals (eTable 3 in the Supplement).

Discussion

In this cohort study, we sought to identify whether site selection may be associated with inequities in randomized clinical trial participation by race, ethnicity, and socioeconomic status by describing differences in the racial, ethnic, and socioeconomic composition of the patient populations of hospitals that participated in clinical trials for transcatheter valvular therapies vs candidate hospitals that did not. We found that hospitals that participated in trials for transcatheter mitral and tricuspid valve therapies cared for a patient population that was socioeconomically more advantaged than the patient population of hospitals that did not participate in trials. However, they also cared for a population that had similar proportions of Black and Hispanic patients. These data would suggest that broader inclusion of potential clinical trial sites may improve access to clinical trials among socioeconomically disadvantaged patients, but may not improve the enrollment of Black and Hispanic patients. Given the inequities that have been well documented in cardiovascular clinical trials, these data would suggest that hospitals currently participating in clinical trials for structural heart disease need to actively engage Black and Hispanic communities to improve enrollment in clinical trials.

Table 2. Characteristics of Patients Undergoing Cardiac Surgery or TAVR at Hospitals That Did and Did Not Participate in Clinical Trials for Transcatheter Mitral and Tricuspid Valve Therapies

Variable	No. (%)		*P* value
	Patients treated in nontrial hospitals (n = 334 453)	Patients treated in trial hospitals (n = 154 369)	
Age, mean (SD), y	74.9 (6.6)	76.1 (7.2)	<.001
Sex			
Female	113 458 (33.9)	56 984 (36.9)	<.001
Male	220 995 (66.1)	97 385 (63.1)	
Race and ethnicity			
Asian	5413 (1.6)	3072 (2.0)	<.001
Black	14 294 (4.3)	6889 (4.5)	
Hispanic	14 481 (4.3)	6.028 (3.9)	
White	291 577 (87.2)	134 282 (87.0)	
Other[a]	4125 (1.2)	1745 (1.1)	
Unknown	4563 (1.4)	2353 (1.5)	
Region			
Midwest	84 186 (25.2)	32 793 (21.2)	<.001
Northeast	56 752 (17.0)	39 390 (25.5)	
South	135 123 (40.4)	57 966 (37.6)	
West	58 392 (17.5)	24 220 (15.7)	
Patient residence			
Metropolitan	259 243 (77.5)	129 468 (83.9)	<.001
Nonmetropolitan	75 210 (22.5)	24 901 (16.1)	
Median household income, median (IQR), $	50 498 (40 142-65 422)	57 966 (44 034-79 215)	<.001
DCI score, median (IQR)	44.3 (20.4-70.8)	31.1 (13.6-58.7)	<.001
Dual eligibility for Medicaid	20 632 (6.2)	8657 (5.6)	<.001
Elixhauser Comorbidity Score, mean (SD)	6.2 (3.2)	6.6 (3.2)	<.001
Comorbidities			
Heart failure	175 917 (52.6)	96 580 (62.6)	<.001
Hypertension	314 071 (93.9)	144 684 (93.7)	.02
Diabetes	152 870 (45.7)	65 177 (42.2)	<.001
Stroke	16 227 (4.9)	7860 (5.1)	<.001
Peripheral vascular disease	92 251 (27.6)	47 220 (30.6)	<.001
Kidney disease	111 504 (33.3)	55 070 (35.7)	<.001
Liver disease	15 389 (4.6)	8067 (5.2)	<.001

Abbreviations: DCI, Distressed Communities Index; TAVR, transcatheter aortic valve replacement.

[a] "Other" is used per the Centers for Medicare & Medicaid Services data files.

Surgical treatment has been the standard of care for patients with mitral and tricuspid pathology who require intervention. However, the surgical treatment of valvular heart disease is invasive and may not be an option for patients who have clinical comorbidities that put them at high risk or prohibitive risk for adverse events around the time of surgery. Advances in percutaneous therapies for mitral and tricuspid repair and replacement are less invasive and may provide treatment options for those patients who may otherwise die of their valvular heart disease.[18-20]

We have previously shown that the initial growth in the availability of novel commercial therapies may not be equally afforded to all segments of the population.[4,21] With TAVR, a transformative device therapy for the treatment of patients with severe symptomatic aortic stenosis, we found that sites that adopted this technology after US Food and Drug Administration approval were predominantly in metropolitan areas that took care of socioeconomically more advantaged patients.[14] Further, within metropolitan areas with several centers performing TAVR, we found that areas with higher proportions of Black, Hispanic, and socioeconomically disadvantaged patients had lower age-adjusted rates of TAVR, suggesting the presence of inequities in access to this procedure.[5]

The current study aimed to build on these prior findings by examining potential inequities in access to novel and experimental valvular heart disease therapies that are still in the clinical trial phase. While still investigational, these therapies may address unmet clinical needs and provide potentially lifesaving treatments to patients who otherwise may have only high-risk options or no options at all. Often, hospitals that

Table 3. Patient Characteristics Among All Medicare Beneficiaries Admitted to Sites Between 2016 and 2019 That Did or Did Not Participate in Clinical Trials for Transcatheter Mitral and Tricuspid Valve Therapies

Variable	No. (%)		*P* value
	Patients admitted to nontrial hospitals (n = 7 798 324)	Patients admitted to trial hospitals (n = 1 845 297)	
Age, mean (SD), y	77.4 (8.2)	76.8 (8.1)	<.001
Sex			
Female	4 197 226 (53.8)	958 450 (51.9)	<.001
Male	3 601 098 (46.2)	886 847 (48.1)	
Race and ethnicity			
Asian	162 151 (2.1)	46 451 (2.5)	<.001
Black	621 308 (8.0)	178 291 (9.7)	
Hispanic	393 700 (5.0)	93 194 (5.1)	
White	6 452 666 (82.7)	1 479 903 (80.2)	
Other[a]	93 325 (1.2)	20 723 (1.1)	
Unknown	75 174 (1.0)	26 735 (1.4)	
Region			
Midwest	2 046 133 (26.2)	404 531 (21.9)	<.001
Northeast	1 093 522 (14.0)	466 924 (25.3)	
South	3 229 663 (41.4)	703 778 (38.1)	
West	1 429 006 (18.3)	270 064 (14.6)	
Patient residence			
Metropolitan	6 479 885 (83.1)	1 622 535 (87.9)	<.001
Nonmetropolitan	1 318 439 (16.9)	222 762 (12.1)	
Median household income, median (IQR), $	50 917 (40 111-66 062)	57 725 (43 189-78 568)	<.001
Distressed Communities Index score, mean (SD)	45.8 (29.0)	37.6 (27.8)	<.001
Dual eligibility for Medicaid	984 458 (12.6)	201 927 (10.9)	<.001
Elixhauser Comorbidity Score, mean (SD)	12.22 (13.09)	12.26 (13.34)	<.001
Comorbidities			
Heart failure	2 274 190 (29.2)	523 807 (28.4)	<.001
Hypertension	6 493 140 (83.3)	1 506 613 (81.6)	<.001
Diabetes	2 646 785 (33.9)	585 275 (31.7)	<.001
Stroke	323 191 (4.1)	60 003 (3.3)	<.001
Peripheral vascular disease	1 113 069 (14.3)	270 164 (14.6)	<.001
Kidney disease	2 078 343 (26.7)	465 948 (25.3)	<.001
Liver disease	375 208 (4.8)	96 636 (5.2)	<.001

[a] "Other" is used per the Centers for Medicare & Medicaid Services data files.

participate in clinical trials for novel therapies will have early access to the procedure when it becomes commercially available.[22] Despite the various benefits to hospitals and patients of participating in clinical trials, inequities in clinical trials persist.

Historically, efforts to improve equity in clinical trials have focused on the sociocultural dynamics among patients, physicians, and communities. Setting racially stratified recruitment targets prior to recruitment was associated with greater diversity among recruited participants.[23] A similar community-focused approach was found to be largely successful in a hypertension trial that recruited and randomized Black male participants via Black barbershops in the Los Angeles metro area.[24] Comparably fewer efforts have focused on changes in the selection of sites based on patient populations to improve equity in access to novel technologies in trials. Typically, site-selection practices favor the same large sites that routinely conduct trials to meet recruitment goals and project timelines. However, these sites generally do not serve disadvantaged populations and fail to adequately engage community-based clinicians, who serve as key liaisons in connecting low-income, racial and ethnic minority patient populations with clinical trials.[25] Moreover, while many clinical trial sites are within short driving distances for patients living in densely populated areas, some clinical trial sites are not and remain largely inaccessible to patients living in rural areas. Thus, there may be disparities in access to trial participation even among established clinical trial sites.

We found that hospitals with the capability to participate in clinical trials for novel transcatheter mitral and tricuspid valve therapies, but did not, took care of a more socioeconomically disadvantaged patient population compared with hospitals that did participate in trials. Patients at hospitals that did participate in clinical trials had a median household in-

Table 4. Differences in Racial, Ethnic, and Socioeconomic Status Among Patients Undergoing Cardiac Surgery or TAVR in Trial vs Nontrial Hospitals Adjusted for Hospital, Demographic, and Clinical Characteristics

Variable	Difference between trial and nontrial hospitals (95% CI)	*P* value
Median household income, $	5261 (2986 to 7537)	<.001
Proportion Black patients, %	0.09 (−0.01 to 0.18)	.06
Proportion Hispanic patients, %	0.02 (−0.03 to 0.09)	.36
Mean DCI score	−5.37 (−8.41 to −2.59)	<.001
Proportion Black patients, %	0.12 (0.01 to 0.23)	.03
Proportion Hispanic patients, %	0.03 (−0.04 to 0.10)	.47
Proportion dual eligible for Medicaid, %	−0.86 (−2.38 to 0.66)	.26
Proportion Black patients, %	0.38 (0.34 to 0.43)	<.001
Proportion Hispanic patients, %	0.39 (0.34 to 0.43)	<.001

Abbreviations: DCI, Distressed Communities Index; TAVR, transcatheter aortic valve replacement.

come that was $5000 higher than that for patients treated in candidate hospitals that did not participate in trials. They also were from areas with less community distress. Though on unadjusted analyses there were fewer patients in trial hospitals who were dual eligible for Medicaid services, this was not statistically significant in multivariable analysis after adjusting for race and ethnicity.

To participate in clinical trials, hospitals need to have considerable investment in necessary infrastructure, including institutional review boards, clinical research coordinators, physicians with the interest and training to serve as principal investigators, and attorneys to handle an often complicated contracting process. These barriers are exacerbated by low enrollment rates in clinical trials (<1 patient per site per month in some trials) due to narrow inclusion criteria, substantial participant burden, and contracting practices that pay sites per patient enrolled.[26,27] Though larger hospitals with robust clinical research operations can break even (or make money) under this system using economies of scale, start-up costs may be prohibitive for hospitals that care for poorer patients and may have smaller revenue margins. Efforts to increase participation of sites caring for socioeconomically disadvantaged patients should focus on reducing participant burden to increase enrollment rates and on reducing the site-level financial and administrative burdens required for clinical trial participation. Alternatively, companies sponsoring clinical trials could be incentivized to include sites caring for more socioeconomically disadvantaged patients.

In contrast, we found that the proportion of Black and Hispanic patients undergoing cardiac surgery or TAVR at trial hospitals was similar to the proportion at nontrial hospitals. Differences were less than 1% and were either not different or significantly greater at trial hospitals adjusting for each marker of socioeconomic status. However, the proportion of patients undergoing cardiac surgery or TAVR who were Black or Hispanic were lower than the overall Medicare population at studied hospitals. Given the well-documented racial and ethnic inequities in trial enrollment, these data would suggest that inequities in trial enrollment of Black and Hispanic patients are not caused by the selection of sites with few racial and ethnic minority patients, but instead are due to issues with enrollment among existing sites.[8,9]

Black and Hispanic patients may face structural barriers limiting their enrollment in trials. In particular, the health care system has failed to earn and maintain trust from minoritized racial and ethnic groups due to historical mistreatment in scientific research and clinical care, as well as structural racism and implicit biases among treating clinicians.[28-33] It is also possible that racial and ethnic enrollment disparities in mitral and tricuspid valve therapy trials may, in part, stem from upstream disparities in referrals to structural heart programs and diagnosis of underlying valvular heart disease. Rather than trying to recruit sites that care for more racial and ethnic minority groups, efforts to improve the representation of Black and Hispanic patients could focus on enriching the enrollment of these patients at existing sites. Specifically, increasing diversity among clinical trial leadership, liaising partnerships between site-level principal investigators and community stakeholders, and addressing unconscious biases in all stages trial recruitment and enrollment may be potentially effective strategies to increase representation of minoritized racial and ethnic groups.[34-37]

Limitations

There are several limitations to this study. First, the use of administrative claims data precludes us from the granularity necessary to identify eligible patients at each of these hospitals for the studied trials with severe mitral or tricuspid valve disease meeting trial eligibility criteria. Instead, we used the population of patients undergoing cardiac surgery or TAVR, which we felt would be reflective of the pool of patients potentially eligible for trial participation for percutaneous valve therapy. We included patients who underwent their operation in 2019, which we felt would be representative of the patients undergoing cardiac surgery and TAVR at these hospitals. Second, we limited our analysis to transcatheter mitral and tricuspid valve therapies. This represents just one area of technological advancement in medicine. These results may not be generalizable to other clinical trials for other conditions. Third, we limited our analysis to fee-for-service beneficiaries and did not have access to Medicare Advantage beneficiaries. However, taken together, this represents a unique analysis of the basis of inequities in clinical trials for transcatheter therapies for mitral and tricuspid valve disease, and clinical trials overall.

Conclusions

In this cohort study among candidate hospitals for clinical trials for transcatheter mitral or tricuspid valve therapies, trial hospitals took care of more socioeconomically advantaged patients and similar numbers of Black and Hispanic patients compared with nontrial hospitals. These data suggest that site selection efforts may improve enrollment of socioeconomically disadvantaged patients but may not improve the enrollment of Black and Hispanic patients.

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Editor's Note

Equity in Clinical Trial Participation Requires Equity in Identification and Treatment of Valvular Heart Disease

Ann Marie Navar, MD, PhD

There are numerous potential benefits to clinical trial participation, including early access to novel therapies. Accordingly, ensuring equal access to clinical trials is paramount to achieving justice in both clinical research and clinical care. Unfortunately, disparities in enrollment in cardiovascular clinical trials are well documented, including in surgical and interventional trials, which have historically disproportionately underenrolled Black and Hispanic persons.[1] Reasons for this are numerous and include potential differential access to sites that participate in clinical trials.[2] If clinical trials are conducted at sites that care for disproportionately fewer Black and Hispanic persons, one potential solution to improving diversity in clinical trials is through diversification of clinical trial sites.

Related article page 120

Nathan et al[3] sought to shine light on the degree to which the characteristics of patients undergoing transcatheter mitral and tricuspid valve surgery differ between hospitals that do and do not participate in clinical trials of transcatheter mitral and tricuspid valve procedures. The researchers found that the racial and ethnic makeup of patients undergoing cardiac surgery in hospitals that participated in clinical trials vs those that did not was similar. Among Medicare beneficiaries, trial hospitals actually treated higher proportions of Black patients than nontrial hospitals. This suggests that site selection for these trials is unlikely to be driving racial and ethnic disparities in enrollment. Improving racial and ethnic diversity in clinical trials will require multifactorial interventions within participating sites to ensure that patients are being equitably identified and offered clinical trials, remove barriers to trial participation, and improve outreach and build trust in research among Black and Hispanic individuals.

Considerations of equity in access to clinical trials should go beyond demographic characteristics and consider other areas of health care inequality. Unfortunately, disparities in the socioeconomic status of persons participating in large cardiovascular outcomes trials are harder to quantify, as socioeconomic indicators are not routinely collected. In contrast to what was seen for race and ethnicity, Nathan et al[3] found that hospitals that did not participate in clinical trials did care for more socioeconomically disadvantaged patients. This highlights the need to improve support for clinical trials in health systems that care for a greater number of socioeconomically disadvantaged persons.

The findings in Nathan et al[3] highlight an even more important barrier to diversity in clinical trial participation in patients with valvular disease: disparities in identification and referral for valve intervention in the first place. In the present analysis, Black and Hispanic patients represented fewer than 5% of patients undergoing cardiac surgery or transcatheter aortic valve replacement at both trial and nontrial hospitals, a dramatically lower proportion than would be expected based on the demographic characteristics of persons in the US. Other registries have shown similar underrepresentation of Black and Hispanic persons in patients undergoing transcatheter aortic

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Original Investigation | Diversity, Equity, and Inclusion

Racial and Ethnic Disparities in Access to Minimally Invasive Mitral Valve Surgery

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Abstract

IMPORTANCE Whether people from racial and ethnic minority groups experience disparities in access to minimally invasive mitral valve surgery (MIMVS) is not known.

OBJECTIVE To investigate racial and ethnic disparities in the utilization of MIMVS.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional study used data from the Society of Thoracic Surgeons Database for patients who underwent mitral valve surgery between 2014 and 2019. Statistical analysis was performed from January 24 to August 11, 2022.

EXPOSURES Patients were categorized as non-Hispanic White, non-Hispanic Black, and Hispanic individuals.

MAIN OUTCOMES AND MEASURES The association between MIMVS (vs full sternotomy) and race and ethnicity were evaluated using logistic regression.

RESULTS Among the 103 753 patients undergoing mitral valve surgery (mean [SD] age, 62 [13] years; 47 886 female individuals [46.2%]), 10 404 (10.0%) were non-Hispanic Black individuals, 89 013 (85.8%) were non-Hispanic White individuals, and 4336 (4.2%) were Hispanic individuals. Non-Hispanic Black individuals were more likely to have Medicaid insurance (odds ratio [OR], 2.21; 95% CI, 1.64-2.98; $P < .001$) and to receive care from a low-volume surgeon (OR, 4.45; 95% CI, 4.01-4.93; $P < .001$) compared with non-Hispanic White individuals. Non-Hispanic Black individuals were less likely to undergo MIMVS (OR, 0.65; 95% CI, 0.58-0.73; $P < .001$), whereas Hispanic individuals were not less likely to undergo MIMVS compared with non-Hispanic White individuals (OR, 1.08; 95% CI, 0.67-1.75; $P = .74$). Patients with commercial insurance had 2.35-fold higher odds of undergoing MIMVS (OR, 2.35; 95% CI, 2.06-2.68; $P < .001$) than those with Medicaid insurance. Patients operated by very-high volume surgeons (300 or more cases) had 20.7-fold higher odds (OR, 20.70; 95% CI, 12.7-33.9; $P < .001$) of undergoing MIMVS compared with patients treated by low-volume surgeons (less than 20 cases). After adjusting for patient risk, non-Hispanic Black individuals were still less likely to undergo MIMVS (adjusted OR [aOR], 0.88; 95% CI, 0.78-0.99; $P = .04$) and were more likely to die or experience a major complication (aOR, 1.25; 95% CI, 1.16-1.35; $P < .001$) compared with non-Hispanic White individuals.

CONCLUSIONS AND RELEVANCE In this cross-sectional study, non-Hispanic Black patients were less likely to undergo MIMVS and more likely to die or experience a major complication than non-Hispanic White patients. These findings suggest that efforts to reduce inequity in cardiovascular medicine may need to include increasing access to private insurance and high-volume surgeons.

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Key Points

Question Do non-Hispanic Black and Hispanic individuals experience disparities in access to minimally invasive mitral valve surgery?

Findings In this cross-sectional study of 103 753 patients, non-Hispanic Black individuals were less likely to undergo minimally invasive mitral valve surgery, whereas Hispanic individuals had similar rates of minimally invasive surgery compared with non-Hispanic White individuals. Non-Hispanic Black individuals were more likely than non-Hispanic White individuals to have Medicaid insurance and to be treated by low-volume surgeons, both factors being associated with lower rates of minimally invasive surgery.

Meaning These findings suggest that efforts to improve equity in cardiovascular medicine may need to include expanding access to commercial insurance and high-volume surgeons.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Introduction

Race-based disparity may be the most common cause of death among Black men and women under age 65 years of age.[1,2] Cardiovascular disease accounts for more than one-third of the mortality difference between Black and White individuals in the US[3] and remains the number 1 cause of death in the US.[4] Cardiovascular procedures are the most common inpatient surgical procedures in adults aged 45 to 64 years and 75 years and older in the US.[5] Despite the effectiveness of cardiovascular interventions, adults from racial and ethnic minority groups and those with low incomes are less likely to receive these interventions and are more likely to have poorer outcomes after undergoing these therapies. For example, Black patients with coronary heart disease are less likely than White patients to undergo cardiac catheterization, percutaneous coronary intervention, or surgical revascularization.[6-10] Black patients with severe aortic stenosis are less likely than White patients to undergo aortic valve replacement.[11] Adults from racial and ethnic minority groups and with low incomes who do undergo surgical revascularization or heart valve surgery are more likely to receive care from lower quality, lower volume hospitals and surgeons, and have higher periprocedural mortality.[8,12-20]

One potential mechanism underlying these differences in outcomes could be related to the surgical approach. For many noncardiac surgical procedures, minimally invasive approaches are associated with less pain, decreased morbidity, and a faster recovery, and are increasingly considered the standard of surgical care.[21-25] For cardiac surgery, in particular, the use of minimally invasive approaches to mitral valve disease is increasing.[26,27] Minimally invasive mitral valve surgery may be associated with a lower risk of surgical site complications and mortality, a similar need for reoperation, faster recovery, better functional outcomes, and higher patient satisfaction rates than conventional sternotomy.[28-32]

However, although racial disparities in the use of minimally invasive surgery have been reported for noncardiac surgery,[33] disparities in utilization of and outcomes after minimally invasive approaches for mitral valve surgery have not been examined. Our primary goal was to examine racial and ethnic disparities in the utilization and outcomes of minimally invasive mitral valve surgery. We also sought to determine whether people from racial and ethnic minority groups were more likely to undergo mitral valve surgery with low-volume surgeons because, for many surgical procedures, there is a well-described association between higher case volumes and better outcomes.[34,35]

Methods

Study Approval

The University of Rochester research study review board reviewed this study and determined that it met federal and university criteria for exemption because it consisted of secondary research on existing data. Therefore, informed consent was not required. This study was approved by the Society of Thoracic Surgeons (STS) Research Center and followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.[36]

Data Source

This retrospective cross-sectional study was conducted using preexisting patient-level data from the STS National Adult Cardiac Surgery Database (ACSD). The data for this research were provided by the STS National Database Participant User File Research Program. Data analysis was performed at the University of Rochester. The ACSD contains more than 7.4 million patient records from 2903 surgeons and has been used for public and nonpublic performance assessment, quality improvement, and comparative effectiveness research.[37] These data have been used in many prior studies.[18,19,38] The database includes information on patient demographics (age, sex, race, ethnicity, height, and weight), payer status (Medicaid, self-paid, Medicare, health maintenance organization [HMO], commercial), urgency (elective, urgent, emergent, salvage), severity-of-disease (ejection

fraction, heart failure, prior myocardial infarction, valvular heart disease, mechanism of mitral regurgitation), comorbidities (stroke, kidney function, lung disease, atrial fibrillation), surgical approach (sternotomy, less invasive), encrypted surgeon and hospital identifiers, and outcomes (mortality, complications). Race and ethnicity are self-reported by the patient or by the family.

Study Population

We identified 121 709 patients undergoing planned isolated mitral valve repair or replacement (MVRR) between 2014 and 2019. We excluded patients on extracorporeal membrane oxygenation or with mechanical circulatory support before surgery (n = 277), percutaneous approaches (n = 1216), operative approach missing (n = 235), other operative approach (n = 239), race not Black or White (n = 7942), race missing (n = 2701), Hispanic ethnicity missing (n = 4101), and payer missing (n = 962). The full list of exclusions is shown in the flow diagram (eFigure 1 in Supplement 1). The final data set consisted of 103 753 cases by 2690 surgeons at 1085 hospitals.

Statistical Analysis

Utilization of Minimally Invasive Surgery

We used multivariable logistic regression to estimate the association between race and ethnicity and the use of a minimally invasive approach for isolated mitral valve repair or replacement (MVRR). The dependent variable was the surgical approach: minimally invasive vs full sternotomy. We defined the minimally invasive approach when the operative approach was coded as either a thoracotomy, partial sternotomy, parasternal incision, or sub-xyphoid approach. In this intention-to-treat analysis, procedures converted from a minimally invasive to a standard approach were considered minimally invasive. The exposure was race and ethnicity categorized as follows: (1) Hispanic, (2) non-Hispanic Black, and (3) non-Hispanic White. We treated the findings from the unconditional analyses (in which we did not adjust for patient risk factors) as the main findings. Non-Hispanic Black and Hispanic patients may present for surgery with more advanced disease and greater comorbidity burden because of the impact of social determinants of health and structural racism. Hence, adjusting for patient disease may underestimate the magnitude of disparities.[39]

We estimated a nonparsimonious model in which race and ethnicity was the exposure variable, and in which we controlled for age; sex; body mass index (BMI, calculated as weight in kilograms divided by height in meters squared) (underweight [BMI: <18.5], normal weight [BMI: 18.5-24.9], overweight [BMI: 25.0-29.9], obese [BMI: 30.0-39.9], morbid obesity [BMI: ≥40.0]); surgical urgency (elective, urgent, emergent), prior myocardial infarction (less than 24 hours, 1 to 7 days, 8 to 21 days, more than 21 days), aortic insufficiency (trivial, mild, moderate, severe), chronic kidney disease (mildly decreased [stage 2: glomerular filtration rate [GFR], 60-89 mL/min], mildly to moderately decreased [stage 3A: GFR, 45-59], moderately to severely decreased [stage 3B: GFR, 30-44 mL/min], severely decreased [stage 4: GFR, 15-29 mL/min], kidney failure [stage 5: GFR, <15 mL/min]); lung disease (mild, moderate, severe), pneumonia (remote [more than 1 month prior to procedure], recent [within 1 month of procedure]); stroke (remote [more than 1 month prior to procedure], recent [within 1 month of procedure]); liver disease; atrial fibrillation; mechanism for mitral insufficiency (myxomatous, rheumatic, functional, infectious endocarditis); prior cardiac surgery (prior coronary artery bypass graft, prior valve surgery, prior coronary artery bypass graft and valve surgery); preoperative intraaortic balloon pump, and year of surgery. We then estimated sequential models (eTable 2 in Supplement 1) to examine the extent to which controlling for payer status, the hospital proportion of non-Hispanic Black patients undergoing mitral valve surgery, and surgeon case volume would attenuate the association between race and ethnicity and the use of a minimally invasive approach: (1) model 2: baseline model plus payer status (Medicaid, self-paid, Medicare, HMO, commercial, other); (2) model 3: baseline model plus payer status plus hospital proportion of non-Hispanic Black patients (less than 5%, 5.0% to 9.9%, 10.0% to 19.9%, 20.0% to 29.9%, 30.0% or more) plus surgeon case volume. We chose to characterize high-minority hospitals using the proportion of non-Hispanic Black patients undergoing mitral valve surgery because racial

and ethnic disparities in the use of minimally invasive surgery were much more pronounced for non-Hispanic Black patients than for Hispanic patients. For the purpose of our analyses, we specified patients with both Medicare and Medicaid coverage (ie, dual-eligible) as having Medicaid coverage.

Outcomes After Minimally Invasive Surgery

We also examined the association between the composite outcome of inpatient and 30-day mortality and major morbidity as defined by the STS (stroke, kidney failure, cardiac reoperation, deep sternal wound infection, prolonged ventilation) and race and ethnicity. We also performed additional analyses in which we interacted race and ethnicity with payer status to determine whether the association between the use of minimally invasive surgery was different by race and ethnicity within each of the payer groups (eg, commercial insurance). We then examined the interaction between race and ethnicity and (1) hospital proportion of non-Hispanic Black patients and (2) surgeon case volume. We also examined the interaction of race and ethnicity and surgeon case volume for the composite outcome.

Finally, we used logistic regression analysis to examine the association between patient race and ethnicity and (1) payer status, (2) hospitalization in a Black-serving hospital, and (3) treatment by a high-volume surgeon. These analyses were unadjusted except for payer status, where we adjusted for patient age.

We used multivariate multiple imputation (mi impute chained) with chained equations (MICE) to impute missing data. We specified multinomial logistic regression models for categorical variables and logistic regression models for binary variables.

All statistical analyses were performed using STATA/MP version 17.0 (StataCorp LLC) from January 24 to August 11, 2022. We used cluster robust variance estimators to account for the clustering of observations within hospitals. We estimated adjusted rates and outcomes using average marginal effects. The threshold for statistical significance was a 2-sided $P < .05$.

Results

Patient Population

The study was based on data from 103 753 surgical procedures (**Table 1**; eFigure 2 in Supplement 1). Among these patients, 47 886 (46.2%) were women; 4336 (4.2%) were Hispanic individuals; 10 404 (10.0%) were non-Hispanic Black individuals; 89 013 (85.8%) were non-Hispanic White individuals; and the mean (SD) age was 62.4 (13.0) years (Table 1). Non-Hispanic White individuals were more likely to have commercial insurance (32.8% [n = 29 167]) compared with non-Hispanic Black (24.2% [n = 2517]) and Hispanic individuals (23.0% [n = 997]). Non-Hispanic White individuals were less likely to have Medicaid insurance (6.3% [n = 5609]) compared with non-Hispanic Black (22.5% [n = 2340]) and Hispanic individuals (20.3% [n = 878]), and less likely to be self-paid (2.5% [n = 2199]) compared with non-Hispanic Black (5.8% [n = 602]) and Hispanic (5.5% [n = 240]) individuals. Non-Hispanic White individuals were less likely to have obesity (23.2% [n = 20 665]) and morbid obesity (3.8% [n = 3369]) compared with non-Hispanic Black (obesity: 30.6% [n = 3180]; morbid obesity: 9.5% [n = 990]) and Hispanic (obesity: 29.6% [n = 1283]; morbid obesity: 5.0% [n = 217]) individuals. Non-Hispanic White individuals were less likely to have a history of congestive heart failure (54.2% [n = 48 220]) compared with non-Hispanic Black (69.7% [n = 7257]) and Hispanic (59.7% [n = 2859]) individuals, and less likely to have kidney failure (1.6% [n = 1433]) compared with non-Hispanic Black (10.4% [n = 1086]) and Hispanic (5.3% [n = 229]) individuals.

Non-Hispanic Black patients were more likely to be seen at high-minority hospitals and to receive care from low-volume surgeons (eTable 1 in Supplement 1). Non-Hispanic Black individuals had 31-fold higher odds (OR, 30.6; 95% CI, 25.49-36.72; $P < .001$) of being treated in a hospital with a very high proportion of non-Hispanic Black individuals (30% or higher) compared with hospitals with a low proportion of non-Hispanic Black individuals (less than 5%) (eFigure 2 in Supplement 1). Non-Hispanic Black individuals had 2-fold higher odds of being treated by a low-volume surgeon (OR,

Table 1. Patient Characteristics

Characteristic	Patients, No. (%)				*P* value
	All	Non-Hispanic White	Non-Hispanic Black	Hispanic	
No.	103 753	89 013 (85.8)	10 404 (10)	4336 (4.2)	
Payer					
Medicaid	8827 (8.5)	5609 (6.3)	2340 (22.5)	878 (20.3)	<.001
Self-paid	3041 (2.9)	2199 (2.5)	602 (5.8)	240 (5.5)	
Medicare	40 983 (39.5)	36 882 (41.4)	2938 (28.2)	1163 (26.8)	
HMO	13 456 (13)	11 330 (12.7)	1301 (12.5)	825 (19)	
Other	4765 (4.6)	3826 (4.3)	706 (6.8)	233 (5.4)	
Commercial	32 681 (31.5)	29 167 (32.8)	2517 (24.2)	997 (23.0)	
Age, y					
<40	6664 (6.4)	4847 (5.5)	1408 (13.5)	409 (9.4)	<.001
41-50	10 515 (10.1)	7985 (9)	1950 (18.7)	580 (13.4)	
51-60	24 450 (23.6)	20 270 (22.8)	3129 (30.1)	1051 (24.2)	
61-70	32 150 (31)	28 395 (31.9)	2614 (25.1)	1141 (26.3)	
71-80	23 920 (23.1)	21 861 (24.6)	1126 (10.8)	933 (21.5)	
≥81	6054 (5.8)	5655 (6.4)	177 (1.7)	222 (5.1)	
Sex					
Male	55 867 (53.9)	49 380 (55.5)	4408 (42.4)	2079 (48)	<.001
Female	47 886 (46.2)	39 633 (44.5)	5996 (57.6)	2257 (52.1)	
BMI					
<18.5	2534 (2.4)	2157 (2.4)	309 (3)	68 (1.6)	<.001
18.5-24.9	35 028 (33.8)	31 090 (34.9)	2764 (26.6)	1174 (27.1)	
25-25.9	36 487 (35.2)	31 732 (35.7)	3161 (30.4)	1594 (36.8)	
30-39.9	25 128 (24.2)	20 665 (23.2)	3180 (30.6)	1283 (29.6)	
≥40	4576 (4.4)	3369 (3.8)	990 (9.5)	217 (5.0)	
Surgical urgency					
Elective	80 396 (77.5)	70 683 (79.4)	6677 (64.2)	3036 (70)	<.001
Urgent	22 065 (21.3)	17 263 (19.4)	3555 (34.2)	1247 (28.8)	
Emergent	1198 (1.2)	984 (1.1)	166 (1.6)	48 (1.1)	
Salvage	94 (0.1)	83 (0.1)	6 (0.1)	5 (0.1)	
Transfer from other hospital					
None	92 874 (89.5)	79 949 (89.8)	9101 (87.5)	3824 (88.2)	<.001
Transfer	9039 (8.7)	7290 (8.2)	1265 (12.2)	484 (11.2)	
Missing	1840 (1.8)	1774 (2)	38 (0.4)	28 (0.7)	
Shock	381 (0.37)	306 (0.34)	55 (0.53)	20 (0.46)	.007
Ejection fraction					
≥60%	54 974 (53)	48 485 (54.5)	4439 (42.7)	2050 (47.3)	<.001
50%-59.9%	31 402 (30.3)	27 126 (30.5)	2923 (28.1)	1353 (31.2)	
40%-49.9%	8758 (8.4)	7014 (7.9)	1307 (12.6)	437 (10.1)	
30%-39.9%	4516 (4.4)	3223 (3.6)	1009 (9.7)	284 (6.6)	
20%-29.9%	1824 (1.8)	1263 (1.4)	453 (4.4)	108 (2.5)	
<20%	250 (0.2)	169 (0.2)	66 (0.6)	15 (0.4)	
Missing	2029 (2)	1733 (2)	207 (2)	89 (2.1)	
Prior myocardial infarction					
None	93 885 (90.5)	80 898 (90.9)	9130 (87.8)	3857 (89)	<.001
>21 d	8234 (7.9)	6831 (7.7)	1009 (9.7)	394 (9.1)	
8-21 d	708 (0.7)	530 (0.6)	137 (1.3)	41 (1)	
1-7 d	763 (0.7)	614 (0.7)	112 (1.1)	37 (0.9)	
<24 h	163 (0.2)	140 (0.2)	16 (0.2)	7 (0.2)	

(continued)

Table 1. Patient Characteristics (continued)

Characteristic	Patients, No. (%)				*P* value
	All	Non-Hispanic White	Non-Hispanic Black	Hispanic	
CHF					
None	45 687 (44)	40 793 (45.8)	3147 (30.3)	1747 (40.3)	<.001
>2 wk	37 953 (36.6)	31 440 (35.3)	4820 (46.3)	1693 (39.1)	
≤2 wk	20 113 (19.4)	16 780 (18.9)	2437 (23.4)	896 (20.7)	
Aortic insufficiency					
None	60 410 (58.2)	51 515 (57.9)	6418 (61.7)	2477 (57.1)	<.001
Trivial	19 753 (19)	17 332 (19.5)	1672 (16.1)	749 (17.3)	
Mild	14 974 (14.4)	12 957 (14.6)	1297 (12.5)	720 (16.6)	
Moderate	3168 (3.1)	2675 (3)	339 (3.3)	154 (3.6)	
Severe	161 (0.2)	120 (0.1)	30 (0.3)	11 (0.3)	
Missing	5287 (5.1)	4414 (5)	648 (6.2)	225 (5.2)	
Glomerular filtration rate					
Normal, (≥90 mL/min)	20 462 (19.7)	16 340 (18.4)	3101 (29.8)	1021 (23.6)	<.001
Mildly decreased (60-89 mL/min)	54 459 (52.5)	48 436 (54.4)	4061 (39)	1962 (45.3)	
Mildly to moderately decreased (45-59 mL/min)	16 784 (16.2)	14 868 (16.7)	1259 (12.1)	657 (15.2)	
Moderately to severely decreased (30-44 mL/min)	7316 (7.1)	6322 (7.1)	640 (6.2)	354 (8.2)	
Severely decreased (15-29 mL/min)	1770 (1.7)	1433 (1.6)	241 (2.3)	96 (2.2)	
Kidney failure (<15 mL/min)	2748 (2.7)	1433 (1.6)	1086 (10.4)	229 (5.3)	
Missing	214 (0.2)	181 (0.2)	16 (0.2)	17 (0.4)	
Lung disease					
None	77 874 (75.1)	67 766 (76.1)	6807 (65.4)	3301 (76.1)	<.001
Mild	10 301 (9.9)	8586 (9.7)	1340 (12.9)	375 (8.7)	
Moderate	4644 (4.5)	3786 (4.3)	660 (6.3)	198 (4.6)	
Severe	4293 (4.1)	3472 (3.9)	649 (6.2)	172 (4)	
Severity unknown	5028 (4.9)	4114 (4.6)	720 (6.9)	194 (4.5)	
Missing	1613 (1.6)	1289 (1.5)	228 (2.2)	96 (2.2)	
Home oxygen					
None	99 108 (95.5)	85 011 (95.5)	9953 (95.7)	4144 (95.6)	<.001
Partial	1632 (1.6)	1408 (1.6)	158 (1.5)	66 (1.5)	
Oxygen-dependent	1565 (1.5)	1304 (1.5)	204 (2)	57 (1.3)	
Missing	1448 (1.4)	1290 (1.5)	89 (0.9)	69 (1.6)	
Pneumonia					
None	88 106 (84.9)	75 736 (85.1)	8702 (83.6)	3668 (84.6)	<.001
Remote	8144 (7.9)	7002 (7.9)	843 (8.1)	299 (6.9)	
Recent	4820 (4.7)	3847 (4.3)	693 (6.7)	280 (6.5)	
Missing	2683 (2.6)	2428 (2.7)	166 (1.6)	89 (2.1)	
Stroke					
None	93 767 (90.4)	81 094 (91.1)	8834 (84.9)	3839 (88.5)	<.001
>30 d	7207 (7)	5715 (6.4)	1128 (10.8)	364 (8.4)	
≤30 d	2199 (2.1)	1728 (1.9)	357 (3.4)	114 (2.6)	
Missing	580 (0.6)	476 (0.5)	85 (0.8)	19 (0.4)	
Liver disease					
No liver disease	98 560 (95)	84 852 (95.3)	9649 (92.7)	4059 (93.6)	<.001
Present	4545 (4.4)	3610 (4.1)	699 (6.7)	236 (5.4)	
Missing	648 (0.6)	551 (0.6)	56 (0.5)	41 (1)	

(continued)

Table 1. Patient Characteristics (continued)

Characteristic	Patients, No. (%)				*P* value
	All	Non-Hispanic White	Non-Hispanic Black	Hispanic	
Atrial fibrillation					
None	72 627 (70)	61 599 (69.2)	8013 (77)	3015 (69.5)	<.001
Present	30 913 (29.8)	27 240 (30.6)	2357 (22.7)	1316 (30.4)	
Missing	213 (0.2)	174 (0.2)	34 (0.3)	5 (0.1)	
Mediastinal radiation					
None	101 099 (97.4)	86 625 (97.3)	10 225 (98.3)	4249 (98)	<.001
Yes	1710 (1.7)	1541 (1.7)	124 (1.2)	45 (1)	
Missing	944 (0.9)	847 (1)	55 (0.5)	42 (1)	
Peripheral vascular disease					
None	97 774 (94.2)	84 088 (94.5)	9641 (92.7)	4045 (93.3)	<.001
Present	5734 (5.5)	4735 (5.3)	731 (7)	268 (6.2)	
Missing	245 (0.2)	190 (0.2)	32 (0.3)	23 (0.5)	
Mechanism for MR					
Myxomatous degenerative	46 720 (45)	42 284 (47.5)	2962 (28.5)	1474 (34)	<.001
Rheumatic	8467 (8.2)	6284 (7.1)	1462 (14.1)	721 (16.6)	
Functional	2852 (2.8)	2101 (2.4)	610 (5.9)	141 (3.3)	
Infectious endocarditis	12 248 (11.8)	9909 (11.1)	1731 (16.6)	608 (14)	
Other	16 624 (16)	13 891 (15.6)	1938 (18.6)	795 (18.3)	
Missing	16 842 (16.2)	14 544 (16.3)	1701 (16.4)	597 (13.8)	
Prior cardiac surgery					
None	89 462 (86.2)	77 060 (86.6)	8797 (84.6)	3605 (83.1)	<.001
Prior CABG	2486 (2.4)	2210 (2.5)	163 (1.6)	113 (2.6)	
Prior valve surgery	9749 (9.4)	7936 (8.9)	1282 (12.3)	531 (12.3)	
Prior CABG and valve surgery	2056 (2)	1807 (2)	162 (1.6)	87 (2)	
Prior PCI					
None	95 600 (92.1)	82 009 (92.1)	9627 (92.5)	3964 (91.4)	.004
PCI, not acute	7620 (7.3)	6569 (7.4)	715 (6.9)	336 (7.8)	
PCI, acute	533 (0.5)	435 (0.5)	62 (0.6)	36 (0.8)	
IABP					
None	102 149 (98.5)	87 689 (98.5)	10 184 (97.9)	4276 (98.6)	<.001
Present	1604 (1.6)	1324 (1.5)	220 (2.1)	60 (1.4)	
Hospital proportion of non-Hispanic Black patients, %					
<5	46 116 (44.5)	43 257 (48.6)	1158 (11.1)	1701 (39.2)	<.001
5-9.9	25 686 (24.8)	22 129 (24.9)	2146 (20.6)	1411 (32.5)	
10-19.9	19 940 (19.2)	15 996 (18)	3150 (30.3)	794 (18.3)	
29-29.9	7393 (7.1)	5171 (5.8)	1935 (18.6)	287 (6.6)	
≥30	4618 (4.5)	2460 (2.8)	2015 (19.4)	143 (3.3)	
Surgeon case volume					
<20	8410 (8.1)	6688 (7.5)	1230 (11.8)	492 (11.4)	<.001
20-49	18 219 (17.6)	15 220 (17.1)	2095 (20.1)	904 (20.9)	
50-99	23 363 (22.5)	19 886 (22.3)	2530 (24.3)	947 (21.8)	
100-199	23 569 (22.7)	20 524 (23.1)	2204 (21.2)	841 (19.4)	
200-299	12 144 (11.7)	10 887 (12.2)	1030 (9.9)	227 (5.2)	
≥300	18 048 (17.4)	15 808 (17.8)	1315 (12.6)	925 (21.3)	
Outcomes					
Minimally invasive surgery	29 596 (28.5)	26 045 (29.3)	2208 (21.2)	1343 (31)	<.001
30-d or in-hospital mortality or morbidity	14 621 (14.1)	11 844 (13.3)	2074 (19.9)	703 (16.2)	<.001

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CABG, coronary artery bypass graft; CHF, congestive heart failure; HMO, health maintenance organization; IABP, intraaortic balloon pump; MR, mitral regurgitation; PCI, percutaneous coronary intervention.

2.21; 95% CI, 1.64-2.98; *P* < .001) than a very-high volume surgeon compared with non-Hispanic White individuals (eFigure 2 in Supplement 1).

Utilization of Minimally Invasive Surgery

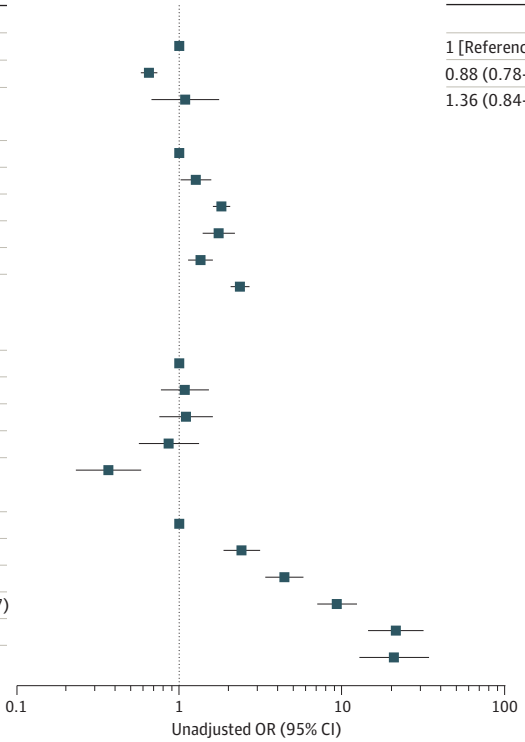
Non-Hispanic Black individuals were less likely to undergo minimally invasive surgery (OR, 0.65; 95% CI, 0.58-0.73; *P* < .001) compared with non-Hispanic White individuals (**Figure 1**). Hispanic individuals were not less likely to undergo minimally invasive surgery (OR, 1.08; 95% CI, 0.67-1.75; *P* = .74) compared with non-Hispanic White individuals.

Several other patient, hospital, and surgeon characteristics were associated with the use of minimally invasive surgery. Patients with commercial insurance had 2.35-fold higher odds of undergoing minimally invasive surgery (OR, 2.35; 95% CI, 2.06-2.68; *P* < .001) than those with Medicaid insurance. Patients in high-minority hospitals had 63% lower odds of undergoing minimally invasive surgery (OR, 0.37; 95% CI, 0.23-0.58; *P* < .001) compared with patients in low-minority hospitals (Figure 1). Patients operated by a high-volume (200 to 299 cases) and very-high volume (300 or more cases) surgeon had 21.2-fold (95% CI; 14.4-31.4; *P* < .001) and 20.7-fold (95% CI, 12.7-33.9; *P* < .001) higher odds of undergoing a minimally invasive procedure compared with patients treated by low-volume surgeons (less than 20 cases) (Figure 1).

Even in patients with commercial insurance, non-Hispanic Black individuals were still less likely to undergo a minimally invasive approach compared with non-Hispanic White individuals (26.1% [95% CI, 22.2%-29.9%] vs 34.4% [95% CI, 30.9%-37.8%]; *P* < .001) (**Figure 2**A). Non-Hispanic Black individuals were less likely to undergo minimally invasive surgery in high-minority hospitals than

Figure 1. Disparities in the Utilization of Minimally Invasive Approach for Mitral Valve Surgery

Characteristic	Unadjusted OR (95% CI)	Adjusted OR (95% CI)			Rate, %
		Model 1	Model 2	Model 3	
Race and ethnicity					
Non-Hispanic White	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	29.3
Non-Hispanic Black	0.65 (0.58-0.73)	0.88 (0.78-0.99)	0.93 (0.82-1.04)	0.99 (0.9-1.09)	21.2
Hispanic	1.08 (0.67-1.75)	1.36 (0.84-2.19)	1.43 (0.89-2.3)	1.59 (1.11-2.29)	31.0
Payer status					
Medicaid	1 [Reference]		1 [Reference]	1 [Reference]	17.8
Self-paid	1.26 (1.02-1.57)		1.23 (0.99-1.53)	1.25 (1.02-1.55)	21.5
Medicare	1.81 (1.6-2.05)		1.4 (1.22-1.59)	1.18 (1.05-1.34)	28.2
HMO	1.74 (1.39-2.19)		1.29 (1.02-1.62)	0.95 (0.77-1.16)	27.4
Other	1.35 (1.13-1.6)		1.11 (0.93-1.32)	1.04 (0.88-1.24)	22.6
Commercial	2.35 (2.06-2.68)		1.53 (1.37-1.71)	1.23 (1.09-1.38)	33.8
Proportion of Non-Hispanic Black individuals, %					
<5	1 [Reference]			1 [Reference]	28.7
5-9.9	1.08 (0.77-1.52)			0.98 (0.68-1.39)	30.3
10-19.9	1.1 (0.75-1.61)			1.21 (0.81-1.8)	30.6
20-29.9	0.86 (0.56-1.32)			1.03 (0.68-1.57)	25.7
≥30.0	0.37 (0.23-0.58)			0.59 (0.29-1.22)	12.8
Surgeon volume					
<20	1 [Reference]			1 [Reference]	4.79
20-49	2.41 (1.86-3.13)			2.25 (1.73-2.92)	10.8
50-99	4.41 (3.36-5.77)			3.94 (3-5.19)	18.1
100-199	9.26 (6.99-12.27)			7.86 (5.91-10.5)	31.8
200-299	21.2 (14.4-31.4)			18.2 (12.2-27.3)	51.7
≥300	20.7 (12.7-33.9)			16.2 (9.8-26.7)	51.1

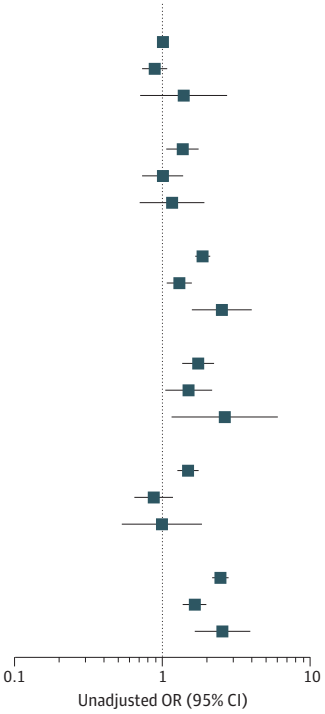


Odds ratio (ORs) were adjusted in model 1 for patient risk (patient demographics, surgical urgency, prior myocardial infarction, aortic insufficiency, chronic kidney disease, lung disease, pneumonia, stroke, liver disease, atrial fibrillation, infectious endocarditis, prior cardiac surgery, preoperative intraaortic balloon pump, and year of surgery); in model 2 for patient risk and payer status; and in model 3 for patient risk, payer status, hospital proportion of non-Hispanic Black patients, and surgeon case volume. The rates are based on average marginal estimates using bivariate logistic regression. HMO indicates health maintenance organization.

Figure 2. Disparities in the Utilization of Minimally Invasive Approach for Mitral Valve Surgery Within Payers and Hospitals

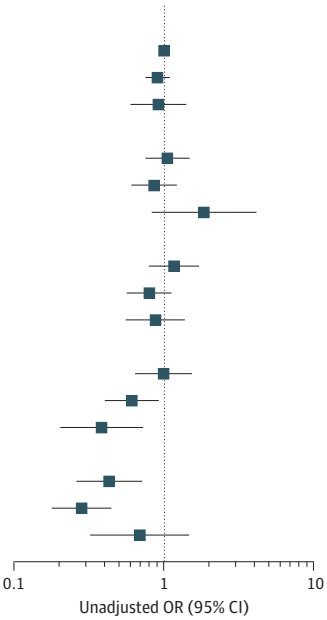
A Payer

Payer	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Rate, %	*P* value
Medicaid				
Non-Hispanic White	1 [Reference]	1 [Reference]	17.78	NA
Non-Hispanic Black	0.88 (0.73-1.07)	1 (0.82-1.22)	16.03	.21
Hispanic	1.38 (0.71-2.69)	1.48 (0.76-2.9)	23.01	.34
Self-paid				
Non-Hispanic White	1.36 (1.06-1.74)	1.33 (1.04-1.72)	22.7	NA
Non-Hispanic Black	1 (0.73-1.37)	1.1 (0.8-1.52)	17.77	.06
Hispanic	1.16 (0.7-1.9)	1.17 (0.7-1.97)	20	.52
Medicare				
Non-Hispanic White	1.85 (1.64-2.07)	1.43 (1.25-1.63)	28.5	NA
Non-Hispanic Black	1.29 (1.06-1.57)	1.31 (1.07-1.6)	21.8	<.001
Hispanic	2.48 (1.57-3.93)	2.29 (1.49-3.52)	34.9	.19
HMO				
Non-Hispanic White	1.73 (1.35-2.21)	1.28 (1-1.63)	27.2	NA
Non-Hispanic Black	1.49 (1.04-2.1)	1.41 (0.99-2.01)	24.4	.22
Hispanic	2.59 (1.15-5.8)	2.34 (1.07-5.1)	35.9	.31
Other payer				
Non-Hispanic White	1.47 (1.25-1.74)	1.19 (1.01-1.42)	24.2	NA
Non-Hispanic Black	0.87 (0.65-1.17)	0.89 (0.66-1.2)	15.9	<.001
Hispanic	0.99 (0.53-1.83)	0.96 (0.51-1.82)	17.6	.19
Commercial				
Non-Hispanic White	2.42 (2.13-2.75)	1.58 (1.4-1.79)	34.4	NA
Non-Hispanic Black	1.63 (1.36-1.95)	1.38 (1.15-1.67)	26.1	<.001
Hispanic	2.5 (1.64-3.82)	1.98 (1.31-3)	35.1	.88



B Percentage of Non-Hispanic Black individuals

Percentage of non-Hispanic Black Individuals	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Rate, %	*P* value
<5%				
Non-Hispanic White	1 [Reference]	1 [Reference]	28.77	NA
Non-Hispanic Black	0.91 (0.75-1.09)	1.16 (0.95-1.42)	26.77	.30
Hispanic	0.92 (0.59-1.42)	1.16 (0.74-1.81)	27.04	.70
5-9.9%				
Non-Hispanic White	1.06 (0.75-1.49)	1.08 (0.76-1.55)	29.9	NA
Non-Hispanic Black	0.86 (0.6-1.22)	1.14 (0.79-1.65)	25.68	.01
Hispanic	1.87 (0.82-4.24)	2.38 (1.04-5.45)	43	.15
10-19.9%				
Non-Hispanic White	1.17 (0.79-1.74)	1.33 (0.89-1.99)	32.1	NA
Non-Hispanic Black	0.79 (0.56-1.13)	1.14 (0.79-1.65)	24.3	<.001
Hispanic	0.87 (0.55-1.38)	1.22 (0.75-1.96)	26.1	.15
20-29.9%				
Non-Hispanic White	0.99 (0.64-1.55)	1.12 (0.73-1.74)	28.6	NA
Non-Hispanic Black	0.61 (0.4-0.92)	0.87 (0.56-1.35)	19.6	<.001
Hispanic	0.38 (0.2-0.72)	0.5 (0.26-0.96)	13.2	.001
≥30.0%				
Non-Hispanic White	0.42 (0.25-0.71)	0.47 (0.27-0.82)	14.6	NA
Non-Hispanic Black	0.28 (0.17-0.44)	0.41 (0.25-0.66)	10.0	.02
Hispanic	0.69 (0.32-1.49)	1.01 (0.43-2.35)	21.7	.21



Odds ratios (ORs) were adjusted for patient demographics, surgical urgency, prior myocardial infarction, aortic insufficiency, chronic kidney disease, lung disease, pneumonia, stroke, liver disease, atrial fibrillation, infectious endocarditis, prior cardiac surgery, preoperative intraaortic balloon pump, and year of surgery. The adjusted rates are based on average marginal estimates based on the unadjusted logistic regression model. A, Disparities within payers; *P* values are for comparisons with non-Hispanic White individuals within the same payer strata (unadjusted). B, Disparities within hospitals; *P* values are for comparisons with non-Hispanic White individuals within the same hospital strata (unadjusted). HMO indicates health maintenance organization. NA indicates not applicable.

non-Hispanic White individuals (10.0% [95% CI, 6.10%-14.0%] vs 14.6% [95% CI, 8.59%-20.7%]; *P* = .02) (Figure 2B). Non-Hispanic Black individuals were also less likely to undergo minimally invasive surgery if they were treated by high-volume (44.9% [95% CI, 35.2%-54.5%] vs 52.5% [95% CI, 44.1%-60.9%]; *P* = .03) compared with non-Hispanic White individuals (**Figure 3**).

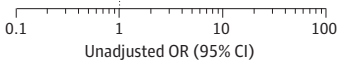
After adjusting for age, sex, BMI, surgical urgency, aortic insufficiency, comorbidities, prior surgery, and intraaortic balloon pump, non-Hispanic Black individuals were still less likely to undergo minimally invasive surgery (adjusted OR [aOR], 0.88; 95% CI, 0.78-0.99; *P* = .04) compared with non-Hispanic White individuals, although the effect size was smaller than in the unadjusted analyses (Figure 1). After controlling for these factors and adjusting for payer status, there was no significant association between non-Hispanic Black individuals and minimally invasive surgery (aOR, 0.93; 95% CI, 0.82-1.04; *P* = .21) (Figure 1). Further adjusting for the hospital proportion of non-Hispanic Black individuals and surgeon case volume resulted in further attenuation of this association: aOR, 0.99; 95% CI, 0.90-1.09; *P* = .81) (Figure 1).

Outcomes After Minimally Invasive Surgery

Compared with White individuals, non-Hispanic Black individuals had 62% higher odds (OR, 1.62; 95% CI, 1.51-1.74; *P* < .001) of death or major morbidity and Hispanic individuals had 26% higher odds (OR, 1.26; 95% CI, 1.09-1.45; *P* < .001) (**Table 2**). After adjusting for patient risk factors, non-Hispanic Black individuals had 25% (aOR, 1.25; 95% CI, 1.16-1.35; *P* < .001) higher odds of death or major morbidity. Hispanic individuals did not have a statistically significant greater risk of death or major morbidity (OR, 1.08; 95% CI, 0.95-1.22; *P* = .25) compared with non-Hispanic White individuals. The odds of death or complications in non-Hispanic Black individuals were unchanged after adjusting for the use of a minimally invasive approach (aOR, 1.25; 95% CI, 1.16-1.34; *P* < .001) or after adjusting for both the use of a minimally invasive approach and payer status (aOR, 1.22; 95% CI, 1.14-1.32; *P* < .001) compared with non-Hispanic White individuals. Further adjusting for the hospital proportion of

Figure 3. Disparities in the Utilization of Minimally Invasive Approach for Mitral Valve Surgery Within Surgeons

Cases, No.	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Rate, %	*P* value
<20 Cases				
Non-Hispanic White	1 [Reference]	1 [Reference]	4.67	NA
Non-Hispanic Black	0.99 (0.68-1.46)	1.18 (0.8-1.74)	4.63	.97
Hispanic	1.52 (0.56-4.08)	1.66 (0.63-4.35)	6.91	.41
20-49 Cases				
Non-Hispanic White	2.58 (1.99-3.34)	2.43 (1.87-3.16)	11.2	NA
Non-Hispanic Black	1.82 (1.29-2.55)	2.04 (1.45-2.88)	8.16	.006
Hispanic	2.4 (1.54-3.74)	2.56 (1.63-4.01)	10.5	.72
50-99 Cases				
Non-Hispanic White	4.74 (3.62-6.2)	4.31 (3.28-5.66)	18.8	NA
Non-Hispanic Black	3.17 (2.27-4.43)	3.54 (2.52-4.98)	13.4	.001
Hispanic	4.03 (2.45-6.64)	4.37 (2.61-7.34)	16.5	.47
100-199 Cases				
Non-Hispanic White	9.6 (7.26-12.71)	8.34 (6.27-11.09)	32.0	NA
Non-Hispanic Black	7.96 (5.72-11.1)	8.57 (6.13-11.97)	28.0	.06
Hispanic	12.2 (6.95-21.6)	12.9 (7.14-23.4)	37.5	.36
200-299 Cases				
Non-Hispanic White	22.6 (15.3-33.4)	19.7 (13.2-29.5)	52.5	NA
Non-Hispanic Black	16.6 (10.7-25.8)	18.8 (11.7-30.1)	44.9	.03
Hispanic	15.2 (8.3-28)	15.9 (8.52-29.8)	42.7	.11
≥300 Cases				
Non-Hispanic White	21 (12.9-34)	16.8 (10.2-27.7)	50.7	NA
Non-Hispanic Black	15.2 (7.75-29.6)	15.8 (7.99-31.3)	42.6	.12
Hispanic	47.3 (19.3-115.8)	47.2 (18.5-120.6)	69.8	.04



Odds ratios (ORs) were adjusted for patient demographics, surgical urgency, prior myocardial infarction, aortic insufficiency, chronic kidney disease, lung disease, pneumonia, stroke, liver disease, atrial fibrillation, infectious endocarditis, prior cardiac surgery, preoperative intraaortic balloon pump, and year of surgery. The adjusted rates are based on average marginal estimates based on the unadjusted logistic regression model. *P* values are for comparisons with non-Hispanic White individuals within the same surgeon strata (unadjusted). NA indicates not applicable.

non-Hispanic Black patients (aOR, 1.14; 95% CI, 1.06-1.23; *P* < .001) was associated with a slight reduction in the odds of death or major complications. Further adjusting for surgeon case volume was not associated with a decrease in the odds of mortality or major complications (aOR, 1.14; 95% CI, 1.06-1.23; *P* < .001).

Surgeon case volume was associated with death or major complications. Patients treated by high-volume surgeons had 57% lower odds of death or major complications (aOR, 0.43; 95% CI, 0.37-0.51; *P* < .001) compared with patients treated by low-volume surgeons, after adjusting for patient risk, payer status, the use of a minimally invasive approach, and the hospital proportion of non-Hispanic Black individuals (Table 2). When treated by high-volume surgeons, non-Hispanic Black individuals were more likely to die or have a major complication (aOR, 0.57; 95% CI, 0.44-0.73) than

Table 2. Thirty-Day Mortality or Morbidity

	Unadjusted		Patient-level		Patient-level + minimally invasive surgery		Patient-level + minimally invasive surgery + payer		Patient-level + minimally invasive surgery + payer + Black serving		Patient-level + minimally invasive surgery + payer + Black serving + surgeon volume	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Race and ethnicity												
Non-Hispanic White	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA	1 [Reference]	NA
Non-Hispanic Black	1.62 (1.51-1.74)	<.001	1.25 (1.16-1.35)	<.001	1.25 (1.16-1.34)	<.001	1.22 (1.14-1.31)	<.001	1.14 (1.06-1.23)	.001	1.14 (1.06-1.23)	<.001
Hispanic	1.26 (1.09-1.45)	<.001	1.08 (0.95-1.22)	.246	1.09 (0.96-1.23)	.171	1.08 (0.96-1.21)	.227	1.07 (0.95-1.21)	.257	1.06 (0.95-1.18)	.325
Minimally invasive	NA	NA	NA	NA	0.85 (0.78-0.92)	<.001	0.86 (0.79-0.93)	<.001	0.86 (0.79-0.93)	<.001	1.01 (0.94-1.09)	.735
Payer												
Medicaid	NA	NA	NA	NA	NA	NA	1 [Reference]		1 [Reference]		1 [Reference]	
Self-paid	NA	NA	NA	NA	NA	NA	0.89 (0.78-1.02)	.107	0.88 (0.77-1.01)	.060	0.88 (0.77-1.01)	.074
Medicare	NA	NA	NA	NA	NA	NA	0.95 (0.87-1.04)	.303	0.95 (0.87-1.04)	.294	0.98 (0.9-1.07)	.727
HMO	NA	NA	NA	NA	NA	NA	0.85 (0.77-0.94)	.002	0.85 (0.77-0.94)	.002	0.91 (0.82-1.01)	.067
Other	NA	NA	NA	NA	NA	NA	0.94 (0.83-1.06)	.341	0.94 (0.83-1.06)	.313	0.95 (0.84-1.07)	.396
Commercial	NA	NA	NA	NA	NA	NA	0.8 (0.73-0.87)	<.001	0.8 (0.73-0.87)	<.001	0.84 (0.77-0.91)	<.001
Proportion of non-Hispanic Black, %												
<5	NA	NA	NA	NA	NA	NA	NA	NA	1 [Reference]		1 [Reference]	
5.0-9.9	NA	NA	NA	NA	NA	NA	NA	NA	1.06 (0.98-1.15)	.147	1.1 (1.02-1.19)	.019
10.0-19.9	NA	NA	NA	NA	NA	NA	NA	NA	1.02 (0.92-1.13)	.707	1.05 (0.96-1.14)	.287
20.0-20.9	NA	NA	NA	NA	NA	NA	NA	NA	1.22 (1.08-1.38)	.002	1.23 (1.11-1.38)	<.001
≥30.0	NA	NA	NA	NA	NA	NA	NA	NA	1.32 (1.13-1.54)	<.001	1.25 (1.09-1.44)	.001
Surgeon volume	NA	NA	NA	NA	NA	NA	NA	NA	NA			
<20	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	1 [Reference]	
20-49	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.81 (0.74-0.89)	<.001
50-99	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.69 (0.63-0.76)	<.001
100-199	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.61 (0.55-0.67)	<.001
200-299	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.55 (0.47-0.63)	<.001
≥300	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.43 (0.37-0.51)	<.001

Abbreviations: HMO, health maintenance organization; NA, not applicable; OR, odds ratio.

non-Hispanic White individuals (aOR, 0.42; 95% CI, 0.36-0.50) compared with non-Hispanic White patients treated by low-volume surgeons (P = .02 for comparison of non-Hispanic Black with non-Hispanic White within same surgeon volume strata) (eTable 3 in Supplement 1).

Discussion

Using national all-payer data on 103 753 patients undergoing mitral valve surgery at 1085 hospitals, we found that non-Hispanic Black individuals had 35% lower odds of undergoing a minimally invasive approach than non-Hispanic White individuals. This gap was no longer significant after adjusting for patient risk factors, payer status, and access to high-volume surgeons. Hispanic individuals were not less likely to receive a minimally invasive approach compared with non-Hispanic White individuals. Non-Hispanic Black individuals were also 62% more likely to die or experience a major complication than non-Hispanic White individuals, whereas Hispanic individuals were 26% more likely to experience death or a major complication than non-Hispanic White individuals.

Our findings demonstrate the extent of differential access to minimally invasive mitral valve surgery. These findings are unfortunately not surprising in light of the extensive evidence of racial and ethnic disparities in cardiovascular medicine.[3] The American Heart Association recently endorsed the need to address structural racism by addressing uneven access to health insurance and quality medical care.[39] Our findings have possible policy implications for promoting equity in cardiovascular care. We noted a number of patterns that may suggest potential mechanisms by which these inequities occur, and therefore suggest ways they might be addressed. We found that Black patients were much less likely to have private insurance than White patients, and that patients with private insurance were more likely to undergo minimally invasive surgery than patients with Medicaid or without insurance. Thus, reducing the number of uninsured individuals via Medicaid expansion alone may not reduce disparities in access to minimally invasive cardiac procedures. Instead, efforts to increase access to commercial insurance or expand Medicare coverage—as opposed to Medicaid expansion alone—may be more successful in promoting racial equity. Lowering the age of eligibility or creating a Medicare buy-in may reduce disparities.[40] Of note, even among patients with commercial or Medicare insurance, non-Hispanic Black individuals were still less likely to undergo minimally invasive surgery than non-Hispanic White individuals. However, any policy solutions implied by our results should be considered hypothesis-generating; testing programmatic changes can best be evaluated using a randomized clinical trial as was done for Medicaid expansion in the Oregon experiment,[41] and for bundled payments in the Comprehensive Care for Joint Replacement.[42,43] While most policies are not evaluated in this manner, this degree of rigor may be necessary to ensure policies are optimally improving equity.

Second, the segregation of non-Hispanic Black individuals in high-minority hospitals likely contributes to disparities in the use of minimally invasive surgery. High-minority hospitals have fewer resources than hospitals that serve a lower proportion of individuals from racial and ethnic minority groups,[44] and are more often penalized by CMS value-based purchasing programs.[45] Although recent policy changes have attempted to mitigate these disproportionate penalties,[46] efforts to improve racial equity may require CMS to shift resources toward hospitals that care for greater numbers of disadvantaged individuals, or to explicitly incentivize and reward providing access to care for patients who have been historically marginalized due to structural and systemic racism. Groups such as US News and World Report and the Lown Group have recently published hospital equity performance measures that begin to examine these areas,[47,48] but more work is needed to create, validate, and apply better measures of equitable access to important procedures and technologies.

Finally, given the striking volume-outcome association for mitral valve surgery, increasing access to high-volume operators is essential. This may be more challenging in rural areas, particularly rural areas that are disproportionately communities of racial and ethnic minority groups. However, a systems approach to health care, which prioritizes regionalizing care in areas where the volume-outcome association is particularly strong, might help improve these patterns. Patient education is

also crucial, so that patients can make more informed decisions and advocate for themselves in terms of seeking care that is as optimal as possible.

Limitations

Our study has several limitations. First, we chose to present the results of our unadjusted analyses as our main findings because health disparities begin long before surgery. Black individuals have worse cardiovascular health overall compared with non-Hispanic White individuals.[3] Individuals from racial and ethnic minority groups face social and structural barriers to preventive health resources, and excessive activation of the stress response caused by safety, socioeconomic concerns, and racial discrimination, which lead to worsening health over time—sometimes described as "weathering."[3,39] Controlling for preexisting health conditions caused partly by structural and interpersonal racism may unintentionally minimize the magnitude of disparities. Nonetheless, because it is also essential to understand the impact of the health care system on disparities, we also report our findings after controlling for a wide range of patient factors, payer status, and surgeon case volume. This approach allowed us to consider changes in health policy that may help promote greater equity.

Second, our analysis does not consider patient preferences for minimally invasive surgery. Non-Hispanic Black individuals may be less willing to undergo surgery using a relatively new minimally invasive approach if they trust their physician less than non-Hispanic White individuals. In particular, Black individuals may distrust the health care system because of historical traumas (ie, Tuskegee) and, perhaps more importantly, because of everyday challenges of navigating a health care system that treats Black and White individuals differently.[49-51] However, our finding that both non-Hispanic Black and non-Hispanic White individuals had greater than 15-fold higher use of the minimally invasive approach when treated by high and very-high volume surgeons suggests that lack of physician trust may not be the dominant factor influencing the choice of a minimally invasive approach, and that access is a primary consideration.

Finally, our study focused on one very innovative change in cardiovascular care, and does not include other recent advances, such as the use of minimally invasive approaches for aortic valve surgery, aortic surgery, and percutaneous approaches to aortic and mitral valve surgery. It will be important to examine disparities in these areas before drawing more definitive conclusions on differential access to some of the most innovative approaches in cardiovascular medicine.

Conclusions

In this cross-sectional national study, we found that non-Hispanic Black patients are less likely to undergo minimally invasive mitral valve surgery and are more likely to die or experience major complications after mitral valve surgery than non-Hispanic White patients. Hispanic patients had similar rates of minimally invasive surgery as non-Hispanic White patients. Non-Hispanic Black patients were also more likely to have Medicaid, receive treatment from low-volume surgeons, and be hospitalized in high-minority hospitals compared with non-Hispanic White patients—all factors associated with less use of a minimally invasive approach. Efforts to reduce inequity in cardiovascular medicine may need to focus on expanding insurance coverage beyond Medicaid expansion and increasing access to high-volume surgeons.

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SUPPLEMENT 1.

eFigure 1. Flow Diagram Describing Selection of Cases in the Analytic Cohort
eFigure 2. Disparities in the Utilization of Minimally Invasive Surgery in Non-Hispanic Black Individuals
eTable 1. Hospital and Surgeon Characteristics
eTable 2. Utilization of Minimally Invasive Approach
eTable 3. 30-Day Mortality and Morbidity

SUPPLEMENT 2.

Data Sharing Statement

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Cardiovascular Revascularization Medicine

Racial Disparities in the Utilization and Outcomes of Transcatheter Mitral Valve Repair: Insights From a National Database

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ABSTRACT

Background: There is paucity of data on racial disparities in the utilization and outcomes of transcatheter mitral valve repair (TMVR).
Methods: We queried the National inpatient Sample database (2012–2016) for TMVR hospitalizations among Caucasian and African American patients. We conducted a propensity score matching analysis to compare outcomes of Caucasians versus African Americans. The main study outcome was in-hospital mortality.
Results: Among 7940 TMVR procedures performed, 680 (8.6%) were performed in African Americans. TMVR was increasingly performed for both Caucasians and African Americans ($P_{trend} = 0.01$), although the proportion of African Americans did not change significantly over time ($P_{trend} = 0.45$). Compared to African Americans, Caucasians undergoing TMVR were significantly older (77.7 ± 10.8 vs. 67.2 ± 14.28, $p < .001$) and less likely to be women (45.3% vs.60.3%, $p < .001$). Caucasians undergoing TMVR had a higher in-hospital mortality compared with African Americans before matching (2.5% vs. 1.5%, odds ratio [OR] 1.75; 95% confidence interval [CI] 1.17:2.63, $p = .01$) as well as after matching (4.7% vs. 1.6%, OR 3.10; 95% CI 1.61:5.97, $p < .001$). Caucasians had higher in-hospital cardiac arrest and pacemaker insertion and shorter median length of stay. There was no difference in the incidence of other in-hospital outcomes between Caucasians and African Americans.
Conclusion: This nationwide observational analysis showed a steady increase in number of TMVRs among Caucasians and African Americans. TMVR was performed in a select cohort of African Americans who were significantly younger and more likely to be women compared with Caucasians. Caucasians undergoing TMVR had higher in-hospital mortality compared with African Americans. Further research is needed to explore the reasons behind the racial disparities in the utilization and outcomes of TMVR.

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1. Introduction

Mitral valve surgery is considered the gold standard for symptomatic severe primary mitral regurgitation (MR) [1]. Transcatheter mitral valve repair (TMVR) with MitraClip (Abbott Structural, Menlo Park, CA) is an effective therapy for mitral regurgitation (MR) reduction, and is currently approved for use in patients with degenerative valve disease and prohibitive risk for surgery, as well as those with secondary moderate-to-severe or severe MR who develop heart failure symptoms despite being treated with optimal medical therapy [2,3]. In light of expanding indications of TMVR, it is important to identify higher risk patient subsets, to improve procedural selection and outcomes. There is paucity of data on the impact of race on the outcomes of transcatheter mitral valve repair (TMVR). Racial disparity in percutaneous cardiac procedures has been suggested, including outcomes of percutaneous coronary intervention and transcatheter aortic valve replacement [4,5]. More specifically, racial disparities have been demonstrated in the uptake and outcome of mitral valve surgeries, with African Americans associated with higher procedural complications [6,7]. Therefore, we conducted this analysis to explore the disparities in the

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uptake and outcomes of TMVR among Caucasians versus African Americans using a large national database.

2. Methods

2.1. Data source

The data source for this analysis was the National Inpatient Sample (NIS) database. The NIS is the largest publicly available inpatient database in the United States. It is developed through a Federal-State-Industry partnership sponsored by the Agency for Healthcare Research and Quality (AHRQ). Unweighted, it contains data from >7 million hospital stays each year. Weighted, it contains >35 million hospitalizations annually. The NIS has been used to describe national estimates of health care utilization, access, charges, quality, and outcomes [8,9]. The NIS covers all patients, including individuals covered by Medicare, Medicaid, private insurance and the uninsured. For Medicare, the NIS includes Medicare Advantage patients, a population that is often missing from Medicare claims data but comprises as much as 30% of Medicare beneficiaries [10]. The NIS reports data using the International Classification of Diseases, Ninth Edition (ICD-9) until September 2015, while data from October 2015 through 2016 are reported using ICD-10 codes. This study was exempt from the institutional review board at the University of Texas Medical Branch, since data are de-identified and publicly available.

2.2. Study population and outcome measures

We queried the NIS database (2012–2016) to identify patient hospitalizations with ICD-9 and ICD-10 procedural codes for TMVR among those with Caucasian or African American race. We excluded hospitalizations with missing data on mortality or baseline characteristics. We reported the temporal changes in the uptake of TMVR in Caucasians and African Americans during the study period. The main study outcome was comparative in-hospital mortality for TMVR among Caucasians versus African Americans. Secondary outcomes included cardiac arrest, cardiogenic shock, use of mechanical circulatory support devices (MCS), acute kidney injury (AKI), hemodialysis for AKI, acute myocardial infarction (MI), acute stroke, postoperative bleeding, blood transfusion, cardiac tamponade, complete heart block, permanent pacemaker implantation, respiratory complications, discharge to nursing facilities, and length of hospital stay. Procedures, clinical characteristics and inpatient outcomes were abstracted and reported using ICD-9 and ICD-10 codes, Clinical Classifications Software (CCS) codes and Elixhauser comorbidities as reported by the Healthcare Cost and Utilization Project (HCUP) (Supplemental Table 1).

2.3. Statistical analysis

We used a propensity score model to match hospitalizations for TMVR among Caucasians to African Americans using a 1:1 ratio. The matching was performed using MatchIt R package (R software) [11]. Each case was matched to a control that is closest in terms of calculated propensity score, using nearest neighbor technique, with a caliper width of 0.2. The propensity score was calculated from the following 25 matching variables: age, sex, diabetes mellitus, hypertension, obesity, history of heart failure, chronic lung disease, peripheral arterial disease, pulmonary circulation disorders, chronic liver disease, chronic kidney disease (CKD), chronic anemia, fluids/electrolytes disturbance, coagulopathy, hypothyroidism, history of smoking, carotid artery disease, history of implantable cardiac defibrillator, history of cardiac pacemaker, carotid artery disease, prior stroke, prior percutaneous coronary intervention (PCI), hospital bed-size, hospital region, and hospital teaching status. Pre-specified subgroup analyses were conducted for in-hospital mortality among Caucasians and African Americans undergoing TMVR based on age, sex, CKD and prior CABG status. To maintain the baseline balance between both the TMVR in Caucasians and African Americans groups, only the corresponding matched pairs in a subgroup were selected.

All analyses were conducted using the complex sample feature of SPSS and appropriate weighting samples to account for hospital clustering, weights and stratification in accordance with HCUP regulations. Trend analysis was conducted using linear regression analysis. We compared categorical variables using the chi-square test, while continuous variables were compared using the student *t*-test if normally distributed or Mann-Whitney *U* test if not normally distributed. We reported categorical variables as numbers and percentages, and continuous variables as mean±standard deviation or median and interquartile range (IQR) depending on the skewness of their distribution. For the subgroup analyses, Breslow-Day test was used to measure the homogeneity of the odds ratio. Associations were considered significant if the *p*-value was ≤.05. We used the SPSS software (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp. Released 2016) for all statistical analyses.

3. Results

The analysis initially yielded 7945 hospitalizations for TMVR in Caucasians and African Americans from 2012 to 2016. After excluding cases with missing data ($n = 5$), final analysis included 7940 hospitalizations; 7260 (91.4%) were Caucasians, and 680 (8.4%) were African Americans. After propensity score matching, there were 640 hospitalizations in each group (Fig. 1). During the study period, there was an increase in the number of TMVR procedures for both Caucasians (350 in 2012 versus 3275 in 2016, $P_{trend} = 0.01$) and African Americans (10 in 2012 versus 350 in 2016, $P_{trend} = 0.01$), with a non-significant trend in the proportion of TMVR procedures for African Americans (2.8% in 2012 vs. 9.7% in 2016, $P_{trend} = 0.45$). (Fig. 2).

The baseline characteristics of both groups are outlined in Table 1. Before matching, Caucasians undergoing TMVR were significantly older (77.7 ± 10.8 vs. 67.2 ± 14.3 years, $p < .001$) and less likely to be women (45.3% vs.60.3%, $p < .001$). Caucasians had higher incidence of prior pacemaker insertion or prior CABG status, while African Americans had higher incidence of diabetes, CKD, chronic lung disease, chronic anemia and prior ICD (Table 1). After matching, standardized mean differences were <10% between both groups, suggesting minimal differences. (Supplemental Fig. 1).

Caucasians undergoing TMVR were associated with higher in-hospital mortality compared with African Americans before matching (2.5% vs. 1.5%, odds ratio [OR] 1.75; 95% confidence interval [CI] 1.17:2.63, $p = .01$) as well as after matching (4.7% vs. 1.6%, OR 3.10; 95%CI 1.61:5.97, $p < .001$). Subgroup analyses within the matched cohort for in-hospital mortality showed no significant interaction based on age > 80 ($P_{interaction} = 0.51$), sex ($P_{interaction} = 0.30$), chronic kidney disease ($P_{interaction} = 0.25$), or prior CABG status ($P_{interaction} = 0.38$).

In addition, Caucasians undergoing TMVR were associated with higher in-hospital cardiac arrest (3.1% vs. 0.8%, $p < .001$) and pacemaker insertion (0.8% vs. 0%, $p < .001$) while they were associated with shorter median length of stay (3 (4) vs. 3.5 (7) days, $p < .001$). There was no difference in the incidence of other in-hospital outcomes including: cardiogenic shock (2.3% vs. 3.9%, $p = .34$), use of MCS (3.1% vs. 5.5%, $p = .30$), AKI (21.1% vs. 19.5%, $p = .71$), hemodialysis (2.3% vs. 2.3%, $p = 1.00$), acute stroke (0.8% vs. 2.3%, $p = .29$), acute myocardial infarction (3.1% vs. 1.6%, $p = .41$), postoperative bleeding (13.3% vs. 18.7%, $p = .16$), blood transfusion (11.7% vs. 8.6%, $p = .35$), cardiac tamponade (0.8% vs. 0.0%, $p = .32$), complete heart block (1.6% vs. 1.6%, $p = 1.00$), respiratory complications (1.6% vs. 3.1%, $p = .37$) and discharge to nursing facility (10.9% vs. 11.7%, $p = .83$) between Caucasians and African Americans. Conversion to surgical mitral valve intervention was similar in both groups as well (0.8% vs. 1.6%, $p = .57$) (Fig. 3) (Table 2).

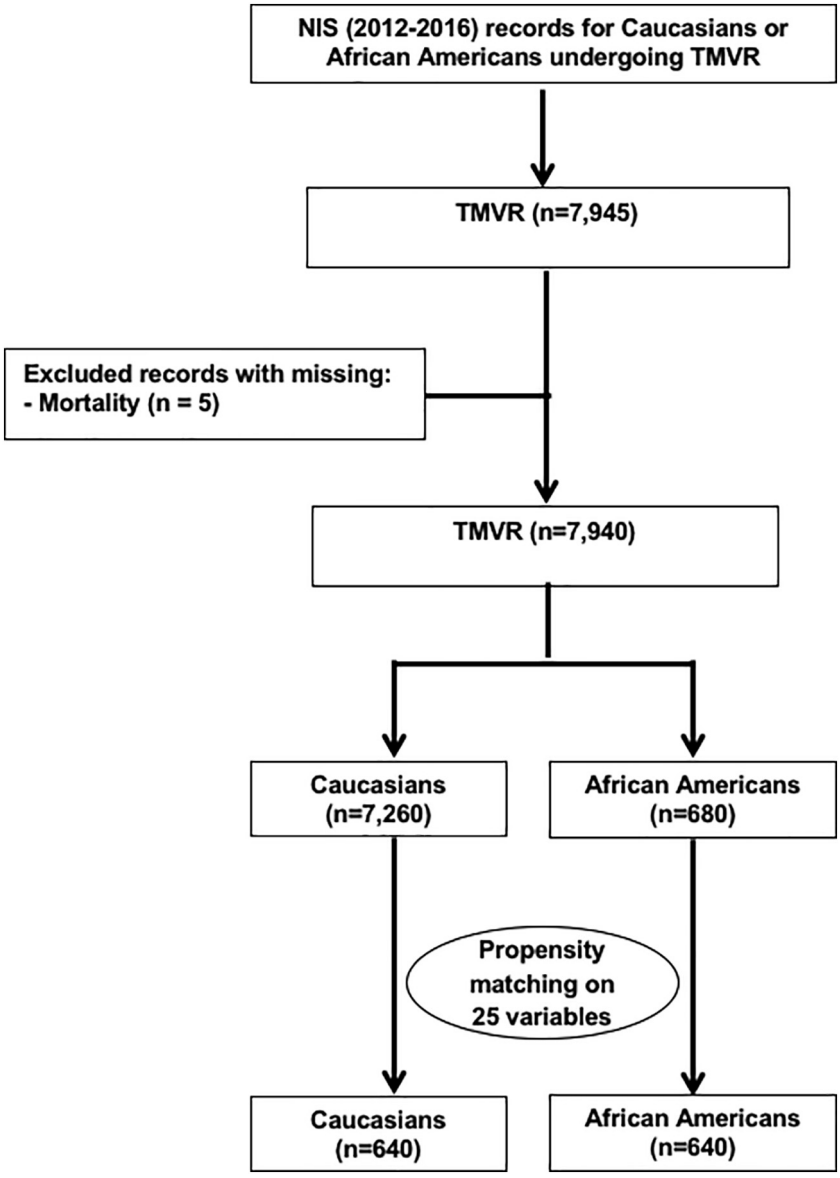

Fig. 1. Study flow sheet.

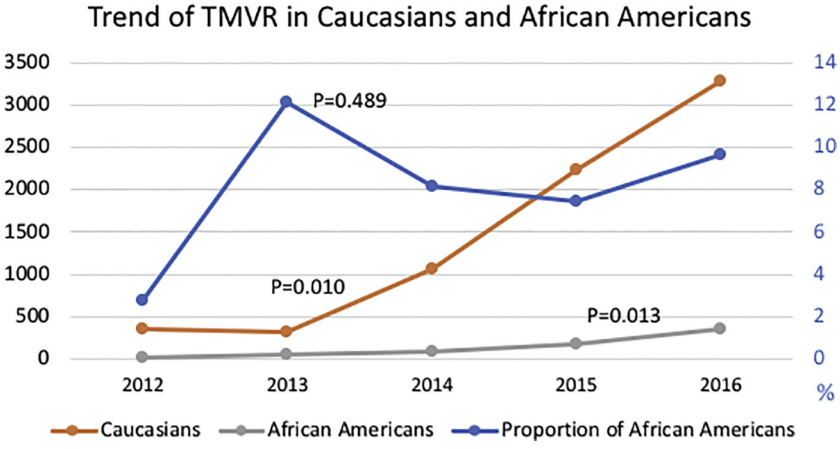

Fig. 2. Temporal trend in the number and proportion of TMVR procedures in Caucasians and African Americans.

Table 1
Baseline characteristics for Caucasian versus African American undergoing TMVR.

Characteristic	Unmatched cohort				SMD %	Matched cohort				SMD %	Percent reduction in SMD
	Caucasians (n = 7260)		African Americans (n = 680)			Caucasians (n = 640)		African Americans (n = 640)			
Age	77.73 + 10.77		67.21 + 14.28		83	71.93 + 13.81		68.20 + 13.31		0.9	99
Female sex	3290	45.3%	410	60.3%	30.3	380	59.4%	375	58.6%	4.7	84
Coagulopathy	915	12.6%	65	9.6%	9.7	55	8.6%	65	10.2%	5	48
Obesity	620	8.5%	115	16.9%	25.3	70	10.9%	105	16.4%	4	84
Fluid and electrolyte disorders	1445	19.9%	160	23.5%	8.8	140	21.9%	150	23.4%	3.6	59
Hypertension	4935	68.0%	485	71.3%	7.3	465	72.7%	460	71.9%	5.2	29
Hypothyroidism	1380	19.0%	85	12.5%	17.9	85	13.3%	85	13.3%	2.3	87
Chronic kidney disease	2515	34.6%	360	52.9%	37.5	305	47.7%	325	50.8%	3.1	92
Chronic liver disease	150	2.1%	35	5.1%	16.6	30	4.7%	30	4.7%	5	70
Chronic lung disease	2080	28.7%	250	36.8%	17.4	245	38.3%	240	37.5%	4.9	72
Diabetes mellitus	1615	22.2%	245	36.0%	30.7	245	38.3%	229	34.4%	1.6	95
Anemia	1670	23.0%	245	36.0%	28.9	185	28.9%	215	33.6%	1.6	94
Prior ICD	705	9.7%	120	17.6%	23.3	115	18.0%	100	15.6%	8.4	64
Prior cardiac pacemaker	935	12.9%	45	6.6%	21.2	75	11.7%	45	7.0%	7	67
CAD	4565	62.9%	400	58.8%	8.3	415	64.8%	370	57.8%	7.8	6
Prior PCI	1225	16.9%	110	16.2%	1.9	140	21.9%	100	15.6%	1.5	21
Prior CABG	1810	24.9%	95	14.0%	28	115	18.0%	95	14.8%	8	71
Prior stroke	960	13.2%	60	8.8%	14.1	75	11.7%	60	9.4%	8.5	40
Tobacco abuse	1485	20.5%	145	21.3%	2.1	170	26.6%	145	22.7%	1.9	10
Carotid Artery disease	75	1.0%	NR	NR	14.4	NR	NR	NR	NR	0.1	99
History of heart failure	105	1.4%	NR	NR	0.2	NR	NR	NR	NR	0.1	50
Pulmonary circulation disease	45	0.6%	NR	NR	8.4	NR	NR	NR	NR	0.1	99
Peripheral vascular disease	1045	14.4%	80	11.8%	7.8	65	10.2%	65	10.2%	5	36
Hospital bed-size											
Small sized	390	5.4%	40	5.9%	7.9	40	6.2%	35	5.5%	7.3	8
Medium sized	1390	19.1%	110	16.2%		85	13.3%	110	17.2%		
Large sized	5480	75.5%	530	77.9%		515	80.5%	495	77.3%		
Hospital region											
Northeast	1275	17.6%	115	16.9%	33.3	80	12.5%	110	17.2%	5.6	83
Midwest or North Central	1510	20.8%	120	17.6%		115	18.0%	120	18.7%		
South	2705	37.3%	315	46.3%		305	47.7%	295	46.1%		
West	1770	24.4%	130	19.1%		80	21.9%	110	18.0%		
Hospital teaching status											
Rural	15	0.2%	NR	NR	19.5	NR	NR	NR	NR	8	59
Urban non-teaching	715	9.8%	15	2.2%		40	6.2%	15	2.3%		
Urban teaching	6530	89.9%	665	97.8%		595	93.0%	625	97.7%		

ICD = implantable cardiac defibrillator; CAD = coronary artery disease; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting. NR = not reportable. Per HCUP regulations, frequencies fewer than 11 should not be reported.

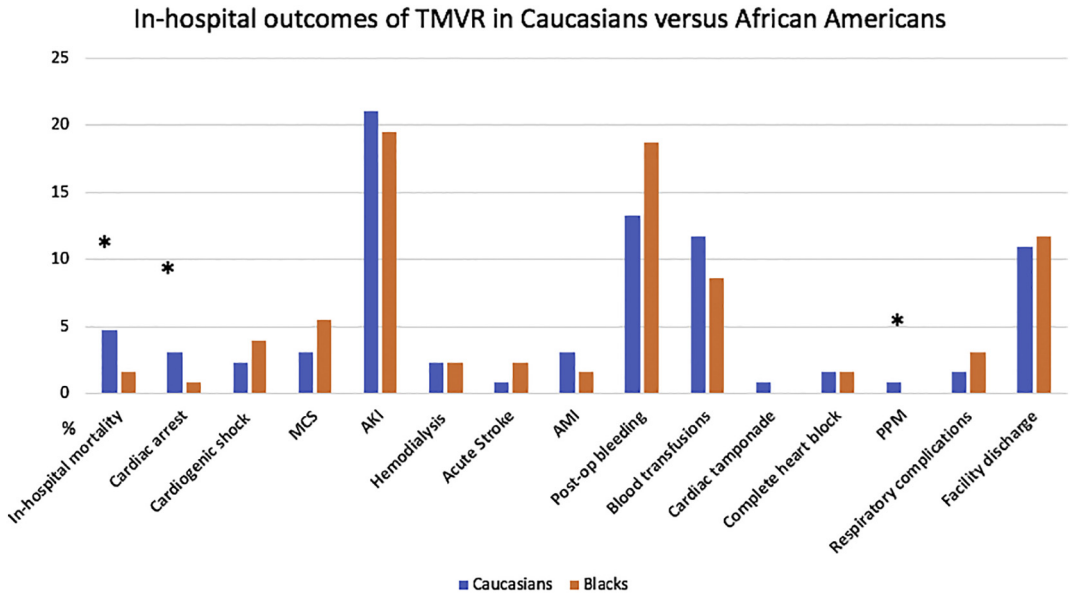

Fig. 3. Forrest plot for in-hospital outcomes of TMVR in Caucasians versus African Americans.

Table 2
Comparative outcomes of TMVR in the matched cohort of Whites versus Blacks.

Outcome	Caucasians (n = 640)		African Americans (n = 640)		OR	95% CI		p-Value
In-hospital mortality	30	4.7%	NR	1.6%	3.098	1.610	5.965	.000
Cardiac arrest	20	3.1%	NR	0.8%	4.097	1.934	8.678	.000
Cardiogenic shock	15	2.3%	25	3.9%	0.590	0.195	1.792	.344
MCS	20	3.1%	35	5.5%	0.558	0.181	1.713	.299
AKI	135	21.1%	125	19.5%	1.101	0.657	1.848	.712
Hemodialysis	15	2.3%	15	2.3%	1.000	0.266	3.766	1.000
Acute Stroke	NR	NR	15	2.3%	0.328	0.036	2.954	.293
AMI	20	3.1%	NR	1.6%	2.032	0.358	11.537	.411
Post-op bleeding	85	13.3%	120	18.7%	0.664	0.374	1.177	.157
Blood transfusions	75	11.7%	55	8.6%	1.412	0.678	2.942	.352
Cardiac tamponade	NR	0.8%	NR	0%	.	.	.	.315
Complete heart block	NR	1.6%	NR	1.6%	1.000	0.168	5.943	1.000
PPM	NR	0.8%	NR	0%	.	.	.	<0.001
Respiratory complications	NR	1.6%	20	3.1%	0.492	0.099	2.437	.372
Facility discharge	70	10.9%	75	11.7%	0.925	0.461	1.855	.825
Length of stay, median (IQR)	3 (4)		3.5 (7)					<.001

NR = not reportable. Per HCUP regulations, frequencies fewer than 11 should not be reported.
MCS = mechanical circulatory support; AKI = acute kidney injury; AMI = acute myocardial infarction; PPM = permanent pacemaker implantation.

Discussion

In this observational analysis inclusive of 7945 hospitalizations with TMVR, we examined the disparities in the trend and outcomes of TMVR among Caucasians versus African Americans. The main study findings were: 1 — TMVR was increasingly performed in both Caucasians and African Americans, with the proportion of African Americans largely unchanged (overall 8.4%); 2 — African Americans undergoing TMVR represented a select cohort, who were significantly younger (~10 years mean difference) and more likely to be women compared with Caucasians; 3 — Caucasians undergoing TMVR had higher in-hospital mortality compared with African Americans (Fig. 4).

In our analysis, TMVR was increasingly performed in both Caucasians and African Americans at similar rates. However, significant differences in patient profiles were demonstrated. Caucasians were significantly older and less likely to be women compared with African Americans. Data on surgical mitral valve interventions come in line with our results. Taylor et al. conducted a large analysis using the Society of Thoracic Surgeons (STS) database to evaluate the impact of race on valve surgeries. In their analysis inclusive of almost 50,000 patient, Taylor et al. found that Caucasians undergoing isolated SMVR were older (63.8 vs. 52.9 years) and less likely to be women compared with African Americans [7]. Similar results were reported by Vassileva et al. in their report on racial differences in 35,074 patients undergoing mitral valve surgeries [6]. Vassileva et al. found Caucasian referred for surgical mitral valve interventions to have older age and less likely to be women compared with non-Caucasians [6]. In their analysis, Digiorgi et al. evaluated 1425 Caucasians and African Americans presenting for isolated mitral valve repair or replacement. Similar to our analysis, African Americans represented 8.6% of that study population, and Caucasians were significantly older and less likely to be women. Collectively, those findings suggest that African Americans might have accelerated mitral valve disease process, and require intervention at younger ages. A finding that is probably related to difference in risk profile compared with Caucasians. In our analysis as well as others, African Americans had higher incidence of CKD, which has been associated with progression of degenerative mitral valve disease in previous reports [7,12].

Our analysis demonstrated that Caucasians were significantly associated with higher in-hospital mortality before and after propensity matching. In addition, Caucasians had higher in-hospital cardiac arrest and pacemaker insertion. Racial disparities in outcomes after other transcatheter cardiac procedures have been demonstrated previously [13]. Similarly, studies on surgical mitral valve intervention have demonstrated racial disparities in risk profile and procedural complications.

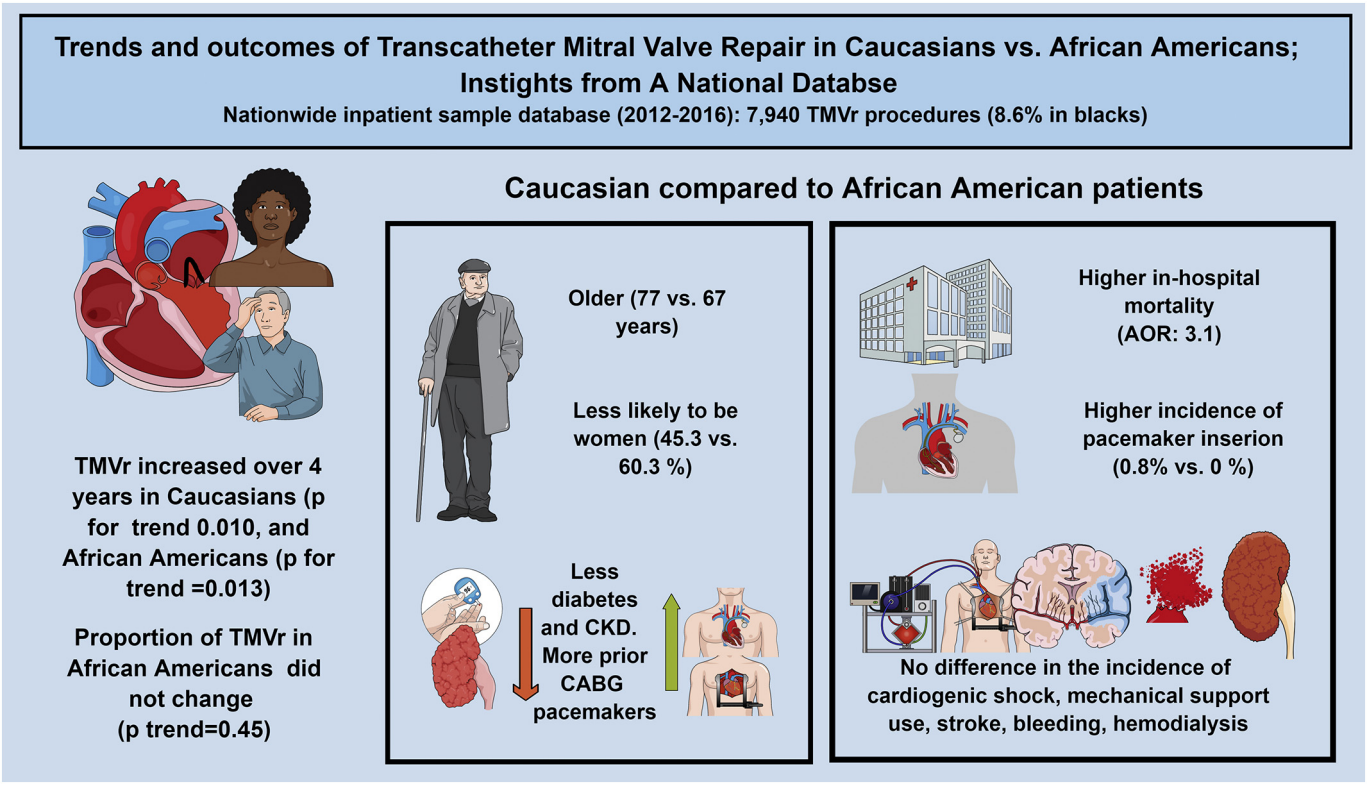

Fig. 4. Comparative outcomes in the uptake and outcomes of TMVR in Caucasians versus African Americans.

In their analysis, Digiorgi et al. reported a numerically higher in-hospital mortality among Caucasians undergoing SMVR compared with African Americans (5.1% vs. 2.4%). The reasons for the higher in-hospital mortality among Caucasians in our study are unclear. While our results do not imply causality, they highlight important associations, that could be hypothesis generating. It is possible that African Americans are more carefully selected for TMVR, and despite our adjusted analysis, they still represented a more select cohort that had better in-hospital outcomes. Signals for such selective approach are highlighted by the significant discrepancy in age and sex between Caucasians and African Americans. In addition, there might be other procedural risk factors that were not captured through this analysis that might have impacted outcomes independent of racial difference. Such factors include etiology of MR (functional versus degenerative) and baseline echocardiographic and other imaging data.

Our analysis showed that African Americans had a longer length of hospital stay, In line with our results, Taylor et al. and Vassieleva et al. showed that African Americans were associated with longer length of stay after SMVRs [7]. Such finding has important implication on cost of stay and warrant further evaluation in future research. Since TMVR is an emerging procedure, characterization of patients subgroups who might be at higher risk to undergo TMVR is important, in order to improve patient selection and outcomes of TMVR. In our subgroup, analysis we did not identify any subgroup interaction according to age, sex, CKD or prior CABG status.

The background for the demonstrated racial disparities in outcomes of TMVR might be multifactorial. Studies have suggested racial variation in natural history and presentation of MV diseases. Among patients with significant MV disease referred to surgical intervention, Caucasians were more likely to have degenerative mitral valve disease compared with African Americans (84.8% vs. 62.5%), in the study by Digiorgi et al. [14] Such finding might also explain our study findings with higher rates of pacemaker insertion in Caucasians compared with African Americans after TMVR. Differences in risk profile among Caucasians and African Americans with significant mitral valve disease have been suggested as well [6,14]. Socioeconomic factors and insurance coverage might play a role in disparities of outcomes and length of stay between Caucasians and African American. Reports from the United States Census Bureau highlighted higher rates of non-insured individuals among African Americans (10.5%) compared with Caucasians (6.3%) [5]. The lack of access to preventive health care facilities might also explain the observed racial disparity in comorbidities burden.

The strength of our analysis comes from the national representation and large sample size. Our results highlight the need for future research to better characterize the underlying reasons for the observed racial disparities in our study. In addition, studies exploring the long-term racial disparities in outcomes of TMVR are still needed. The current has certain limitations. Being an administrative dataset, the NIS is liable to coding and documentation errors. Nevertheless, the NIS has been internally and externally validated via annual reports and quality assessments [15,16]. The dataset is time discrete, with only available data for in-hospital outcomes, with no available longer-term outcomes. Many important variables were irretrievable for our analysis, including etiology of MR, echocardiographic data for MR, laboratory and medication data. Being an observational analysis, there is a potential for selection bias. Despite conducting propensity matching analysis with residual standardized mean differences <10% in all baseline characters, there is still possibility for unmeasured confounders affecting the study results.

5. Conclusion

In this observational nationwide analysis, TMVR was increasingly performed in both Caucasians and African Americans at similar rates. TMVR was performed in a select cohort of African Americans, who were significantly younger and more likely to be women compared with Caucasians. Caucasians undergoing TMVR were associated with higher in-hospital mortality compared with African Americans. Further research is needed to explore the reasons behind the racial disparities in the selection and outcomes of patients undergoing TMVR.

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Author credit statement

All authors meet the criteria for authorship. Ayman Elbadawi, Karim Mahmoud, Islam Y. Elgendy, Mohammed Elzeneini, Mohmed Omer and Michael Megaly were mainly responsible for study conception and design. Ayman Elbadawi, Karim Mahmoud, Gbolahan O. Ogunbayo, Michelle Albert, Samir Kapadia, and Hani Jneid performed data collection, acquisition, analysis, and interpretation. All authors shared in drafting the manuscript. Hani Jneid was responsible for the initial critical revision of the manuscript. All authors contributed to final critical revision of the manuscript for important intellectual content and the final approval of the version to be published.

All authors have no conflict of interest to declare.

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