vizient™

Heart valves, structural heart and endograft technologies

Technology Watch | 2017 Volume 1

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Introduction

The health care market is uncertain. The new administration has promised change, but we don't yet know what that change will look like or to what extent any new programs will affect the health care changes already underway. While we wait and speculate, there is information that we do know and we hope to provide a small bit to you in this report. We do know the hospital inpatient reimbursement schedule for 2017. We do know that suppliers continue to develop innovative technologies, create new markets and release evolutionary products. With each of these, price increases are expected.

Medical device suppliers continue to look for the next great medical device. Over the past two years several revolutionary medical devices have been introduced in the United States including leadless pacemakers, bioresorbable scaffolds, stented heart valves and the left atrial appendage closure device. Each introduction came with a significant increase in price to the devices that came before it. So what is the next big thing? Suppliers believe transcatheter mitral valves are one candidate. Based on the success and adoption rate of the transcatheter aortic valve, suppliers are investing billions in the mitral valve's development. Although development of both products started in the same year (2009) the transcatheter mitral valve has lagged.

Innovation drives the U.S. market and its health care sector. This year like never before, hospitals are under increasing price pressure. Administrators are requesting millions of dollars in savings from supply chain—and several are requesting hundreds of millions. This will be a very interesting year, and the only guarantee is that there will be uncertainty and change.

Disclaimer
Members of the Vizient™ cardiovascular staff attend clinical sessions at important cardiovascular meetings throughout the year. The staff meets with suppliers, reviews new technologies and monitors data from pertinent clinical trials. The information is consolidated into this overview of product and practice trends in the various cardiovascular segments. This document is intended to educate nonclinical hospital staff by offering them insights into new and innovative technologies. Vizient staff members have no personal financial connections with the suppliers and no conflicts of interest in the development of this document. The products presented are for educational purposes. Vizient does not endorse any of the products described in this document.

Market watch

The 12-month price trend and current average market pricing by product segment are shown in the tables that follow.

Pricing trends: change over last 12 months

Heart valves

Category	Change (%)
TAVR	↓ 0.1%
Surgical, tissue	↓ 0.8%
Surgical, mechanical	↑ 3.8%
Annuloplasty rings	↑ 0.5%

Occlusion devices

Category	Change (%)
Left atrial appendage	↓ 11.8%
Surgical, tissue	↑ 5.1%

Endografts

Category	Change (%)
AAA, body	↑ 0.6%
AAA, limbs/extensions	↑ 4.0%
TAA, body	↑ 7.1%

AAA = abdominal aortic aneurysm; TAA = thoracic aortic aneurysm; TAVR = transcatheter aortic valve replacement.

All prices in the tables that follow are the average prices for that category of products, not selling prices for specific products. Individual hospital pricing may vary given considerations such as rebates, quality and volumes that are not included in these estimates.

Heart valve average prices

Heart valve, aortic—tissue

Supplier	Average price
Abbott	$4,990
CryoLife	$12,500
Edwards Lifesciences	$5,750
LifeNet	$11,040
LivaNova	$4,800
Medtronic	$5,260

Heart valve, aortic—sutureless

Supplier	Average price
LivaNova	$9,240

Clip, mitral

Supplier	Average price
Abbott	$30,000

Heart valve, aortic—TAVI

Supplier	Average price
Edwards Lifesciences	$32,350
Medtronic	$30,030

Heart valve, mitral—tissue

Supplier	Average price
Abbott	$4,370
CryoLife	$11,630
Edwards Lifesciences	$5,900
LifeNet	$10,120
Medtronic	$5,000

Heart valve, pulmonary—TPVI

Supplier	Average price
Medtronic	$25,500

TAVI = transcatheter aortic valve intervention; TPVI = transcatheter pulmonary valve implantation

Heart valve, mechanical

Supplier	Average price
Abbott	$4,070
LivaNova	$4,690
ON-X Technologies	$4,540

Annuloplasty rings

Supplier	Average price
Abbott	$1,400
Edwards Lifesciences	$2,140
LivaNova	$1,710
Medtronic	$1,770

Aneurysm graft average prices

Aortic endografts (body)

Supplier	Average price
Cook Medical	$8,420
Endologix	$11,600
Medtronic	$9,500
WL Gore	$10,000

Aortic endografts (extensions)

Supplier	Average price
Cook Medical	$3,210
Endologix	$4,280
Medtronic	$5,100
WL Gore	$4,040

Thoracic endografts

Supplier	Average price
Cook Medical	$14,610
Medtronic	$17,170
WL Gore	$15,010

Heart occlusion device average prices

Septal occluders

Supplier	Average price
Abbott	$6,240
WL Gore	$6,980

Left atrial appendage occluders

Supplier	Average price
Atricure	$1,070
Boston Scientific	$15,620
SentreHeart	$6,930

All estimated selling pricing is the averaged pricing over a category of products. These are not selling prices for specific products. Your pricing may vary given considerations such as rebates, quality and volumes that are not included.

Reimbursement watch 2017

In support of our goal to help hospitals stay ahead of events, this section provides a glimpse into the fiscal year (FY) 2017 proposed Hospital Inpatient Prospective Payment System (IPPS) rulings affecting cardiovascular devices. Under the final rule, acute care hospitals must report quality data and be meaningful users of electronic health records (EHRs) to avoid reduction in 2017 rates. The final payment and policy changes are effective on Oct. 1, 2016. These changes will affect the hospital's cardiovascular department. In summary, the proposed changes include:

Overall impact

(Fed Regist. 2016;81(162):56772-56773)

Hospitals that participate in the Inpatient Quality Reporting (IQR) and Meaningful EHR programs will see an increase in their inpatient reimbursements.

Hospital Inpatient Prospective Payment System	Estimated percent change (FY 2017)
2017 annual impact	+0.95%

This new reimbursement rate includes a market-basket cut of 0.75 percent, as mandated by the Patient Protection and Affordable Care Act (ACA), and a 1.5 percent cut that would fulfill the requirement of the American Taxpayer Relief Act of 2012 and that the Centers for Medicare & Medicaid Services (CMS) claims is the effect of documentation and coding changes from FYs 2010 to 2012. The potential repeal of the ACA and other possible charges may increase inpatient reimbursements.

Cardiovascular impact

Reimbursement changes relative to specific cardiovascular procedures.

Key procedures	Estimated percent change (FY 2017)
Endovascular aortic valve replacement	-1%
Surgical heart valves	+2%
Left atrial appendage	+3%
Cardiac implantable cardioverter defibrillator/pacemaker implants	+1%
Coronary stents (drug eluting and bare metal)	+1%
Peripheral angioplasty/stenting	+2%

Two-Midnight Rule

(Fed Regist. 2016;81(162):57058-57060)

CMS is proposing to remove the −0.2 percent payment adjustment under the Two-Midnight rule. CMS initially imposed this cut because of an anticipated $220 million spending increase due to an expected increase in inpatient admissions. As a result of industry backlash and legal issues, CMS is permanently removing this adjustment and for FY 2017, hospitals will see an increase of approximately 0.8 percent to make up for the 0.2 percent reduction in payment rates from FY 2014 to 2016.

Hospital Readmissions Reduction Program

(Fed Regist. 2016;81(162):56979-56982)

The program mandated by the ACA will continue unless Congress acts to change its provisions. Beginning in FY 2017, hospitals that perform an index coronary artery bypass graft procedure will be added to this measured group. The index hospital will be penalized for unexpected 30-day readmissions, even if the patient is readmitted to a different hospital. The penalty will be 3 percent from the onset.

Hospital-Acquired Condition Reduction Program

(Fed Regist. 2016;81(162):57011-57013)

CMS made several changes to existing Hospital-Acquired Condition Reduction Program policies in the FY 2017 final rule, including changing the program scoring methodology from the current decile-based scoring to continuous scoring.

Data reporting requirement
(Fed Regist. 2016;81(162):56772-56773)

Hospitals that do not submit quality data would lose a fourth of the market-basket update (2.7 percent), and hospitals that are not meaningful users of EHRs will be subject to a three-fourths reduction of the market-basket update in fiscal 2017.

Value-based Purchasing Program
(Fed Regist. 2016;81(162):56772)

CMS added two condition-specific payment measures (for acute myocardial infarction and heart failure) beginning with the FY 2021 program year and a measure of 30-day mortality following coronary artery bypass graft surgery beginning with the FY 2022 program year. CMS states the condition-specific payment measures capture payments for all care, including readmissions and subsequent cardiac events, across multiple care settings, services and supplies during the 30-day episode of care.

Technology add-on payments
(Fed Regist. 2016;81(162):56880-56912)

The technology add-on payments in the table below are under proposal for FY 2017.

Device name	Company	Status	Maximum payment
CardioMEMS system	St. Jude Medical	3rd of 3 years	$8,875.00
Responsive neurostimulator	NeuroPace, Inc.	3rd of 3 years	$18,475.00
Lutonix drug-coated balloon[a]	Bard Vascular	2nd of 3 years	$1,035.72
In.Pact Admiral drug-coated balloon[a]	Medtronic	2nd of 3 years	$1,035.72
Gore Excluder iliac branch	WL Gore	FY 2017	$5,250.00
Magec spinal bracing	NuVasive	FY 2017	$15,750.00
Vistogard	BTG International	FY 2017	$37,500.00
Defitelio	Jazz Pharmaceutical	FY 2017	$75,900.00
Praxbind (darucizumab)	Boehringer Ingelheim	FY 2017	$1,750.00

[a] Technology add-on payment modified in 2017 to equalize payment for similar devices

MS-DRG coding changes
The following changes in Medicare severity diagnosis-related group (MS-DRG) coding are in place for FY 2017.

- Deleting MS-DRG 30 and modifying MS-DRG 228 and 229 for transcatheter mitral valve repair with implant procedures:
  - MS-DRG 228: Other cardiothoracic procedures with major complication and comorbidity (MCC)
  - MS-DRG 229: Other cardiothoracic procedures without MCC
- Revising MS-DRG logic behind assignments to MS-DRGs 242-243, 258-259 and 260-261 for certain pacemaker insertion and removal procedures
- Designating certain ICD-10-procedure coding system procedure codes describing implantation or revision of a loop recorder as O.R. procedures and assignment of those codes to MS-DRGs 40-42, 260-262, 579-581, 907-909 and 957-959

Supplier watch

Abbott Laboratories

Abbott Laboratories is rapidly becoming a leading supplier in the cardiovascular market. In January 2017, Abbott closed their acquisition of St. Jude Medical. The acquisition did not come as a surprise; rumors of an Abbott-St. Jude Medical deal was in the market for years. The acquisition strengthens Abbott's position as one of the leading cardiovascular suppliers. It wasn't until 2006 that Abbott became a significant cardiovascular supplier when they acquired the noncardiac rhythm management product lines line from Guidant. The recent acquisition is a good step for Abbott since St. Jude Medical had few products that competed. The largest product line affected was the vascular closure line. Abbott sold the St. Jude vascular closure product line, with the brands Angio-Seal vascular closure systems, FemoStop manual compression closure systems and Vado steerable sheaths, to Terumo Medical. The remaining products create a strong market portfolio for Abbott. The merged product lines will allow Abbott to enter cardiovascular markets it was not participating in.

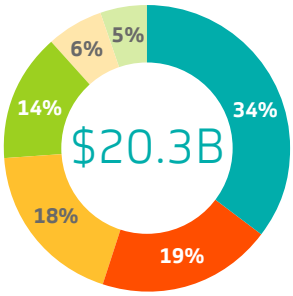
Post acquisition product portfolio and product types

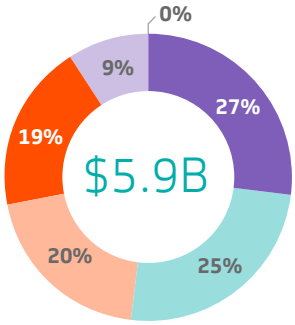
Heart failure	Atrial fibrillation	Neuromodulation	Cardiovascular	Cardiac rhythm
Cardiac resynchronization therapy	Atrial fibrillation systems	Spinal cord stimulation	Heart valves	Pacemakers
Ventricular assist	Left atrial appendage devices	Dorsal root ganglion stimulation	Percutaneous coronary intervention devices	Implantable cardioverter-defibrillators
Pulmonary artery pressure monitoring		Deep brain stimulation	Vascular closure	
		Radiofrequency ablation	Patent foramen ovale closure	
			Percutaneous heart pumps	

Company overview

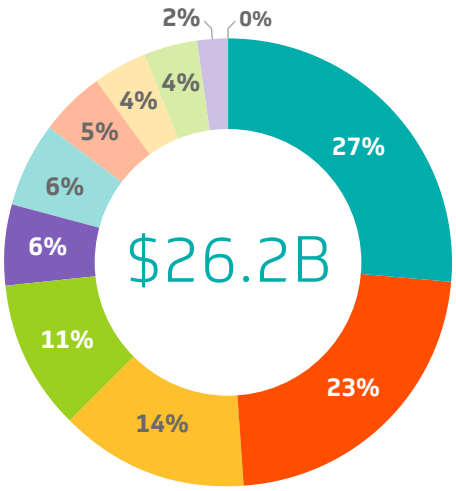
As mentioned above, the acquisition is complementary. The company will realize an additive impact from both companies' sales estimated at $26 billion. Market shares in key product categories will remain stable or grow. The increased diversity will sustain long-term growth and market leadership.

Pre-aquisition





Post-aquisition



Abbott

Nutritionals	34%
Atrial fibrillation	19%
Pharmaceuticals	18%
Vascular	14%
Diabetes care	6%
Vision	5%

St. Jude Medical

Cardiac rhythm	27%
Heart failure	25%
Cardiovascular	20%
Atrial fibrillation	19%
Neuromodulation	9%
Structural heart	0%

Abbott

Nutritionals	27%	Cardiovascular	5%
Atrial fibrillation	23%	Diabetes care	4%
Pharmaceuticals	14%	Vision	4%
Vascular	11%	Neuromodulation	2%
Cardiac rhythm	6%	Structural heart	0%
Heart failure	6%		

Product pipeline

The emerging Abbott has an innovative pipeline of cardiovascular products including:

HeartMate 3 left ventricular assist system: This system is the next-generation left ventricular assist device for use in patients with advanced heart failure. The system features the MagLev technology pump, which delivers up to 10 liters of blood per minute to support blood flow to the body.

Portico transcatheter aortic heart valve: The Portico valve is a low-profile (18 French scale [F]), repositionable transcatheter aortic heart valve. The valve is designed to address limitations in existing transcatheter valves by improving control and accuracy in positioning and placement of the valve, minimizing paravalvular leak and potentially reducing the need for the implantation of a permanent pacemaker after the procedure.

Amplatzer Amulet left atrial appendage occluder: The Amplatzer Amulet is a left atrial appendage occluder implant. The device is constructed of a double, self-expanding, nitinol mesh disc and lobe delivered via a transcatheter system. The implant is designed to completely occlude the left atrial appendage and block any blood clots, reducing the potential for stroke.

Nanostim leadless pacemaker: The Nanostim is a leadless pacemaker that is less than 10 percent of the size of a conventional pacemaker. The device is inserted through the femoral vein with the help of a steerable catheter and implanted directly into the right ventricle of the heart.

HeartMate PHP percutaneous heart pump: The HeartMate PHP system is a catheter-based heart pump designed to provide temporary hemodynamic left ventricular support. It will be a competitive alternative to the Abiomed Impella device. The device can be inserted into the femoral artery via an integrated 12F introducer sheath and facilitate four to five liters per minute of blood flow.

Infinity deep brain stimulator: The Infinity is the next generation in deep brain stimulators for patients suffering from Parkinson's disease, tremor and dystonia, a disorder that causes involuntary muscle contractions. The system is upgradable and uses Bluetooth® wireless technology to allow the device to communicate with an Apple® digital device. The system will provide enhanced patient therapy and a more intuitive patient experience.

Topera cardiac arrhythmia mapping system: Topera is an advanced electrophysiologic 3-D heart mapping system. The system has intraprocedural mapping and remapping capabilities. In addition, the system incorporates a color-imaging module to aid identification of "rotors," an electrophysiologic phenomenon previously shown to sustain atrial fibrillation. With the ability to visualize individual rotors, physicians can tailor treatment approaches for each patient.

Hospital impact

The immediate impact of Abbott's acquisition of St. Jude Medical on hospitals will be minimal. Changes in sales representation may occur, but availability of product and pricing will remain unchanged. The only exception will be the legacy St. Jude Medical product lines that are sold to Terumo Medical. For those vascular closure devices, including the Angio-Seal and Femoseal vascular closure products and Vado steerable sheaths, some price changes may occur as Terumo establishes their pricing strategy. For the legacy Abbott vascular closure products including Perclose ProGlide suture-mediated closure, StarClose SE vascular closure and Prostar XL percutaneous vascular surgical system, no price changes should be experienced. Abbott's sales approach to the market is anticipated to extend to the legacy St. Jude products over time. Over the longer period, it is anticipated that Abbott may leverage its market strength and product breadth, resulting in opportunities for committed hospitals to realize economic savings.

Heart valves

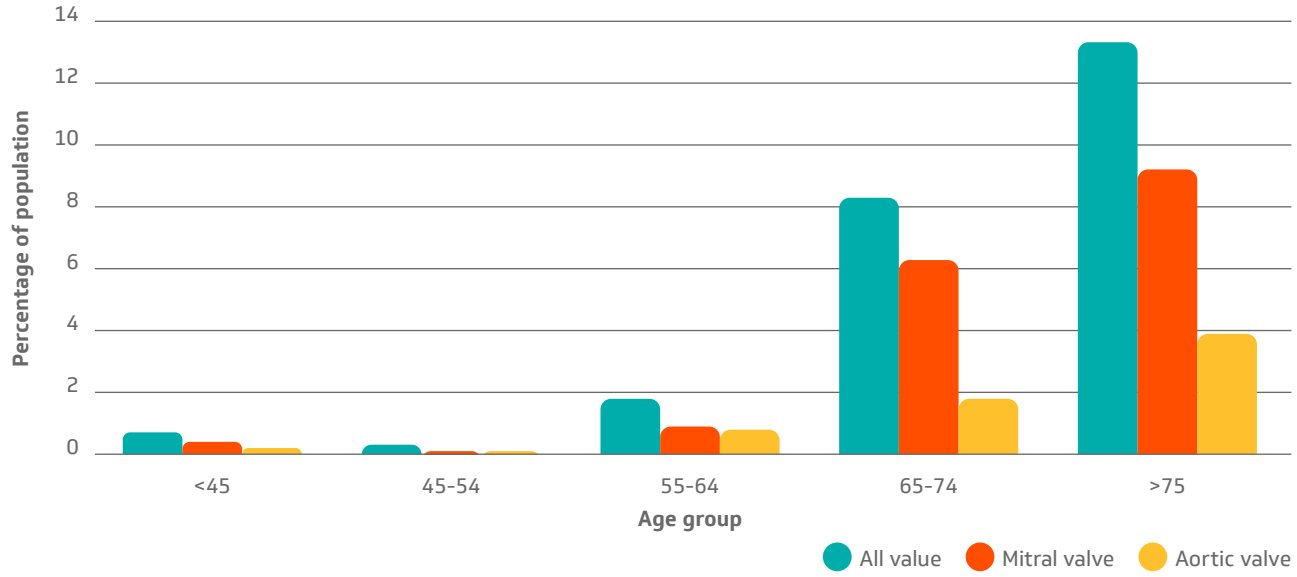
Transcatheter mitral valves

The U.S. market for transcatheter mitral valves does not exist, yet. The success experienced with the transcatheter aortic valves created significant interest and investment from all the important cardiovascular suppliers in the percutaneous mitral valve market. Over the past several years, billions of dollars have been invested in acquiring technologies and patents and in developing mitral repair valves. The chart below shows the key acquisition activities intended to strengthen the acquiring suppliers' percutaneous mitral valve development.

Supplier	Acquired company
Abbott Vascular	• St. Jude Medical • Tendyne Holdings, Inc. • Cephea Valve Technologies
Edwards Lifesciences	• Valtech Cardio • CardiAQ Valve Technologies
Medtronic	• Twelve, Inc. • HeartWare
Boston Scientific	• Neovasc, Inc. • MValve Technologies
LivaNova/Sorin	• Highlife SAS

So why are suppliers investing in this market segment? The driving factor is that in the United States, the prevalence of mitral valve disease is significantly greater than aortic valve disease (see following chart). Nkomo and colleagues showed that the prevalence of valve disease increases sharply with age and that mitral valve disease affects about 9 percent of the over-75 population, almost double the rate of aortic valve disease.[1] An estimated four million people suffer from moderate to severe mitral regurgitation and 250,000 new patients are diagnosed each year in the United States.[2] Only approximately 50,000 of these patients undergo surgery in the U.S. each year.[3] There are also an estimated 1.6 million patients suffering from tricuspid regurgitation.[4] Approximately 50 percent of patients with mitral regurgitation have moderate to severe tricuspid regurgitation.[5] The incidence of mitral valve and tricuspid regurgitation is expected to increase as the aging population grows. The existence of this large underserved population and the success of transcatheter aortic valves are driving development in this market. The statistics on mitral disease prevalence are dramatic for large suppliers looking to grow sales in an emerging market or to maintain their existing market positions.

Prevalence of valve disease



The emerging market in mitral valves is estimated to mirror the transcatheter aortic valve in both its developmental timelines and market impact. Due to the early stage of mitral valve device development, three attachment mechanisms appear to be emerging: hooking the valve, grasping the leaflets or docking the annulus. Below is a list of companies developing one or more of the percutaneous mitral valve technologies. Little clinical data has been collected to forecast which technology will provide the best patient outcomes.

Companies developing mitral valve repair devices

Vendor name	Device name	Device type	Therapy	Regulatory status
4Tech, Inc.	TriCinch	Annulus cinching	Valve remodeling	In development
Abbott Vascular	PMVR	Valve	Valve replacement	In development
Abbott Vascular	Tendyne Lutter	Valve	Valve replacement	In development
Caisson Interventional	Caisson TMR	Valve	Valve replacement	In development
Cardiac Dimensions Inc.	Carillon	Tethered nitinol stents	Indirect annuloplasty	CE mark approved
CardiAQ/Edwards Lifesciences	CardiAQ	Valve	Valve replacement	CE and FDA IDEs on hold
Cardiosolutions Inc.	Mitra-Spacer	Reversible anchor	Valve remodeling	In development
Cardiosolutions Inc.	Percu-Pro	Polymer buoy	Valve remodeling	In development
Cephea Valve Technologies/Abbott	Cephea	Valve	Valve replacement	In development
Direct Flow Medical	Direct Flow TMV	Valve	Valve replacement	In development
Edwards Lifesciences	Mobius	Suture	Valve remodeling	In development
Emory University	MitraPlug	Valve	Valve replacement	In development
Gorman Cardiovascular	Gorman TMV	Valve	Valve replacement	In development
Guided Delivery Systems	Accucinch	Subannular cinching	Direct annuloplasty	First-in-man trial ongoing
Harpoon Medical	Harpoon	ePTFE neochords	Valve remodeling	In development
Heart Repair Technologies	Mitral Bridge	Implantable anchoring system	Valve remodeling	In development
Highlife SAS/Sorin	Highlife	Valve	Valve replacement	In development
HT Consultant	Saturn TMVR	Valve	Valve replacement	In development
Mardil Medical	VenTouch	Inflatable silicone tension band	Valve remodeling	First-in-man trial ongoing
Medtentia International	CathHELIX	Helix ring	Valve remodeling	CE IDE ongoing
Medtronic, Inc.	TMVR	Valve	Valve replacement	In development
Micro Interventional Devices	Permavalve	Valve	Valve replacement	In development
Middle Peak Medical	TBD	Neo-leaflet implant	Valve remodeling	In development
MitraGen	MitraGen	Valve	Valve replacement	In development
Mitral Heal, Ltd.	Mitral Heal	Valve	Valve replacement	In development
Mitralign Inc.	MPAS	Transannular cinching	Direct annuloplasty	CE mark approved, FDA IDE ongoing

Vendor name	Device name	Device type	Therapy	Regulatory status
Mitralix	Maestro	Valve	Valve replacement	In development
MitrAssist Ltd.	MitrAssist	Valve in valve	Valve assist	In development
Mitricares	Mitricares	Valve	Valve replacement	In development
MValve Technologies	MValve	Valve docking system	Valve replacement	First-in-man trial ongoing
MVRx	Arto	Nitinol woven stabilizer and suture	Septal sinus shortening	CE IDE ongoing
NaviGate Cardiac Structures	Navi	Valve	Valve replacement	First-in-man trial ongoing
NeoChord Inc.	DS1000	Artificial chordate	Valve remodeling	CE mark approved, FDA IDE ongoing
Neovasc	Tiara	Valve	Valve replacement	CE IDE ongoing
Saturn Project	TBD	Valve	Valve replacement	In development
Sino Medical Science Technology	AccuFit	Valve	Valve replacement	In development
Tendyne Holdings/Abbott	Tendyne TMVR	Valve	Valve replacement	CE IDE ongoing
TransCardiac Therapeutics	MitraFlex	Artificial chordate	Valve remodeling	In development
Transcatheter Technologies	Tresillo	Valve	Valve replacement	In development
Twelve, Inc./Medtronic	TMVR	Valve	Valve replacement	In development
ValCare Inc.	Amend	Annuloplasty ring with anchors	Valve remodeling	First-in-man trial ongoing
ValCare Inc.	Trivid	Annuloplasty ring with anchors	Valve remodeling	In development
ValCare Inc.	Corona	Valve	Valve replacement	First-in-man trial ongoing
Valtech Cardio/Edwards Lifesciences	Cardiovalve	Valve	Valve replacement	In development
Valtech Cardio/Edwards Lifesciences	Cardioband	Annular fixation	Direct annuloplasty	CE mark approved
Valtech Cardio/Edwards Lifesciences	V-Chordal	Adjustable chordate	Valve remodeling	In development

CE = Conformité Européene; FDA = Food and Drug Administration; IDE = investigational device exemption

Potential new devices

Transcatheter mitral valve repair devices that appear to be leading in their development and to have a chance to enter the U.S. market include:

CardiAQ transcatheter mitral valve system
(Edwards Lifesciences)

The CardiAQ valve is a transcatheter mitral valve replacement that consists of a self-expanding nitinol frame and a bovine, three-leaflet tissue valve. The valve is built upon a proprietary method for anchoring the implant through leaflet engagement, chordal preservation and annular attachment, while offering greater durability, improved flow properties and a novel feature for the prevention of paravalvular leaks. Two sets of anchors grasp the mitral leaflets to secure the valve in place. In addition, foreshortening of the frame creates a clamping action that anchors the valve above and below the mitral annulus. The valve is designed so that it does not rely on radial force for fixation like the transcatheter aortic valves. The valve, which is placed through the femoral artery, can be repositioned before final deployment. In February 2017, the company paused enrollment in its clinical trial. Edwards anticipates a receiving a Conformité Européene (CE) mark for the valve in 2018. The valve is not available commercially or for distribution or sale in the U.S.

CardiAQ Transcatheter Mitral Valve Replacement (TMVR) Early Feasibility Study

Robert Guyton (United States, Emory University Hospital [Vizient member hospital]), co-principal investigator

Study size: 28 patients

Prospective, single-arm, nonrandomized, multicenter U.S. study

This U.S. multicenter study is designed to evaluate the safety and function of the Edwards Lifesciences CardiAQ transcatheter mitral valve. Six U.S. medical centers are participating. This is an early feasibility study of the valve and delivery system focused on the treatment of moderate to severe mitral regurgitation. No clinical data is available.

Tendyne transcatheter mitral valve replacement
(Tendyne Holdings, acquired by Abbott)

The Tendyne transcatheter mitral valve implant is a fully retrievable and repositionable system to treat degenerative mitral valve regurgitation. The valve is a three porcine pericardial bioprosthesis sewn onto a nitinol self-expanding stent frame. The valve is delivered transapically and is secured via a ventricular fixation system composed of tethering strings attached to the stent. The system is designed to give enhanced control to the physician during the procedure. The implants are not available commercially or for distribution or sale in the U.S.

Early Feasibility Study of the Tendyne Mitral Valve System

Tendyne Holdings lead

Study size: 110 patients

Prospective, randomized, multicenter U.S. study

This multicenter, randomized trial is designed to evaluate the safety and effectiveness of the Tendyne mitral valve for the treatment of mitral valve disease. The study includes adult patients with symptomatic mitral regurgitation who are not suitable candidates for conventional mitral valve repair or replacement. The study will include up to 110 subjects at up to 30 centers. Follow-up evaluations will be conducted through two years post-implantation. No data have been released.

Tiara transcatheter mitral valve system
(Neovasc, Inc.)

The Tiara mitral valve is a self-expanding mitral bioprosthesis specifically designed to treat mitral valve regurgitation by replacing the diseased valve. The bioprosthesis uses cross-linked bovine pericardial tissue leaflets mounted inside a metal alloy frame. The valve has a unique design: The atrial portion is designed specifically to fit the saddle-shaped mitral annulus. The D-shape is intended to match the natural shape of the mitral valve opening. Three anchoring structures create a three-point anchor that work to secure the prosthetic valve. The anchoring system does not rely significantly on the integrity of the native mitral leaflets and therefore may be suitable for certain patients with unstable or calcified leaflets. The valve is fully retrievable and repositionable until it is fully deployed. Implantation is performed transapically by means of a 32F delivery catheter. The company is currently involved in a patent lawsuit with Edwards Lifesciences. Edwards seeks to prevent Neovasc from further developing and commercializing the valve. The implants are not available commercially or for distribution or sale in the U.S.

TMVR mitral valve system
(Twelve, Inc, acquired by Medtronic)

Medtronic's TMVR is a tri-leaflet pericardial bioprosthesis to replace a diseased mitral valve and reduce leakage. The bioprosthesis brings together a valve technology featuring a large inflow atrial portion and a short outflow ventricular portion. It has a differentiated dual-stent fixation design with support arms that function to capture the mitral valve leaflets to secure the implant. The implant is also designed to use the mitral apparatus for axial fixation. The valve is designed to be fully retrievable and it should be possible to refold and withdraw the valve via a catheter. Implantation is performed transapically. The implants are not available commercially or for distribution or sale in the U.S.

Cardioband mitral reconstruction system
(Edwards Lifesciences)

The Cardioband mitral reconstruction system is a direct annuloplasty device that treats the valve's opening rather than its leaflets to reshape the valve opening. The implant is a polyester sleeve with radiopaque markers spaced 8 millimeters (mm) apart. A contraction wire built into the device enables the surgeon to shorten the implant. The implant is available in six lengths. The implant size is adjusted to the patient's unique needs. Stainless steel 6-mm anchors are used to fasten the implant to the heart, using 12 to 17 anchors to stabilize the implant. The anchors are fully repositionable and retrievable until fully deployed. The implant is large, requiring a 25F steerable sheath. It is implanted in the beating heart under fluoroscopic and transoesophageal echocardiographic guidance to reduce mitral valve leakage. The band is placed around the mitral valve opening with the help of a catheter and is sutureless, secured with small anchors and tightened using a wire until the valve's function is restored. The minimally invasive therapy does not require the use of a heart-lung machine, reducing the impact on the patient and lowering the risk. The implant is not available commercially or for distribution or sale in the U.S.

Companies with devices currently in clinical trials for FDA approval

The companies listed below have active U.S. clinical trials underway for the primary purpose of obtaining pre-market approval from the FDA.

Vendor name	Device name	FDA NCT no.	Study status
Neovasc Inc.	Tiara	NCT02276547 (TIARA-I)	Actively recruiting
Tendyne Holdings, LLC	Tendyne TMVR	NCT02321514	Actively recruiting
Henry Ford Hospital	Sapien 3	NCT02370511 (MITRAL)	Actively recruiting
Edwards Lifesciences	CardiAQ	NCT02718001	Actively recruiting
MValve Technologies	MValve	NCT02719912 (DOCK 1)	Active, not recruiting
Edwards Lifesciences	CardiAQ	NCT02722551	Actively recruiting
NeoChord	NeoChord	NCT02803957	Actively recruiting

Economic impact

The economic impact of transcatheter mitral valve technology will be significant. It is projected that FDA restrictions on facilities' ability to implant these devices will apply, similar to the restrictions imposed for aortic transcatheter valves. Based on the success of suppliers' pricing models for the aortic valve, it is anticipated that a similar pricing model will be used for mitral valves. The potential patient population will create increased demand on the hospital's infrastructure and increase supply chain costs.

Reimbursement

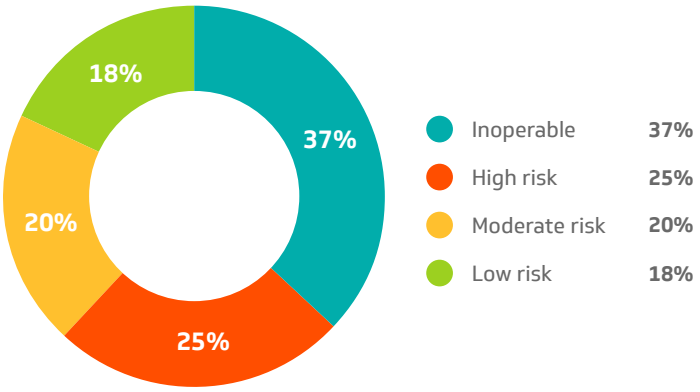
Reimbursement for a transcatheter mitral valve procedure should exist by the time of or shortly after the device's U.S. approval. Following the aortic experience, CMS should have reimbursement coverage in place, minimizing any negative net impact of this new technology on the hospital.

Transcatheter aortic valves

The U.S. market for transcatheter aortic valve intervention (TAVI) continues to expand. Just over five years ago, the Edwards Sapien transcatheter aortic heart valve was approved for use in the United States. The success of the technology created rapid change in how aortic valve repair is performed. Less than six months ago, the FDA approved the expanded use of the Sapien 3 transcatheter heart valve for the treatment of patients at intermediate risk for open-heart surgery. The use of transcatheter aortic valves continues to cannibalize surgical aortic valves at rate in the high single digits. We can look to Germany to get a glimpse into the future of TAVI in the United States. The rapid adoption of TAVI in Germany, shifting treatment of aortic valve stenosis in the elderly from surgery to a catheter-based approach, took less than 10 years. In 2013, the number of TAVI first surpassed surgical aortic valve replacement, and TAVI now exceeds surgical replacement by a factor of 1.3.[5]

The expansion of the indications for transcatheter aortic heart valves to include intermediate-risk patients continues to open options for patients. With the expansion, approximately 80 percent of patients suffering from aortic valve disease now have the option to choose TAVI.

Operative risk for severe, symptomatic aortic valve disease patients



Source: Bach et al., 2009; GlobalData, 2014

The 2016 U.S. market for transcatheter aortic valves is estimated at 68,000. It is estimated to reach approximately 100,000 by 2020.[6] For the next several years, product choice will remain limited and device pricing will remain high. Additional devices are forecast to become available in late 2018 or 2019. The chart below shows global suppliers developing transcatheter aortic valves.

Companies developing transcatheter aortic valves

Vendor name	Device name	Valve type	Structure	Approach	Regulatory status
Abbott	Portico	Bovine	Nitinol	Arterial	CE mark approved; FDA, IDE ongoing
Biotronik	BioValve	Porcine	Nitinol	Arterial	In development
Braile Biomedica	Inovare	Bovine	Cobalt chrome	Apical	In development
Boston Scientific	Lotus	Bovine	Nitinol	Arterial	CE mark approved; FDA, IDE ongoing
Colibri Heart/Venus Medtech	Colibri	Porcine	Stainless steel	Arterial	In development
Direct Flow Medical	Direct Flow	Bovine	Polymer	Arterial	CE mark approved; FDA, IDE ongoing
Edwards Lifesciences	Centera	Bovine	Nitinol	Arterial	CE, IDE ongoing
Hansen Medical	AorTx	Equine	Stainless steel	Both	In development
HLT Medical	Meridian	Porcine	Nitinol	Arterial	In development
JenaValve Technology	JenaValve	Porcine	Nitinol	Apical	CE mark approved; FDA, IDE ongoing
Medtronic	Engager	Bovine	Nitinol	Apical	CE mark approved
Medtronic	Evolut Pro	Bovine	Nitinol	Arterial	CE, IDE ongoing
Symetis	Acurate neo	Porcine	Nitinol	Arterial	CE mark approved
Symetis	Acurate TA	Porcine	Nitinol	Apical	CE mark approved

Vendor name	Device name	Valve type	Structure	Approach	Regulatory status
Thubrikar Aortic Valve, Inc.	Optimum TAV	Bovine	Nitinol	Both	In development
Transcatheter Technologies	Trinity	Bovine	Nitinol	Apical	CE, IDE ongoing
Venus MedTech (HangZhou) Inc.	Venus A	Tissue	Nitinol	Arterial	In development
University of Zurich	Zurich TEHV	Stem cell	TBD	TBD	In development

Potential new devices

Transcatheter aortic valve repair devices in clinical trials for U.S. pre-market approval include:

Lotus transcatheter aortic heart valve
(Boston Scientific)

The Lotus transcatheter aortic valve system is the first fully repositionable transcatheter valve. The value is a bovine tissue tri-leaflet implant supported by a self-expanding nitinol stent structure. It offers controlled mechanical expansion, which allows the valve to be fully deployed and assessed prior to being released. If necessary it can be retrieved and repositioned at any time prior to release of the aortic valve implant. The implants are not available commercially or for distribution or sale in the U.S.

Reprise III Clinical Trial

Ted Feldman (United States, NorthShore University Health [Vizient member hospital]), co-principal investigator

Study size: 2,092 patients

Perspective, Open-label U.S. trial

The clinical trial of the Lotus Transcatheter Aortic Valve is complete. A delay with the device's release mechanism resulted in a delay submitting to the FDA. The Reprise III trial is designed to study the safety and efficacy of the valve against an active comparator, the Medtronic CoreValve TAVR System. Recently released data from Europe on 250 patients demonstrated an extremely low rate of paravalvular leakage, plus a cardiovascular mortality rate of less than 2 percent at 30 days. This is the pivotal clinical trial for FDA device approval.

Portico transcatheter aortic heart valve
(Abbott)

The Portico device has the design advantages of both a low-profile delivery system (18F) and it can be repositioned at the implant site or retrieved before its final implantation. The valve is designed to address limitations in existing transcatheter valves by improving control and accuracy in positioning and placement of the valve, minimizing paravalvular leak and potentially reducing the need for the implantation of a permanent pacemaker after the procedure. The implants are not available commercially or for distribution or sale in the U.S.

Portico IDE Trial

Raj Makkar (United States, Cedars-Sinai Medical Center [Vizient member hospital]), co-principal investigator

Study size: 908 patients

Perspective, randomized, multicenter U.S. trial

The Portico clinical trial is a prospective, multicenter, randomized-controlled clinical study, designed to evaluate the safety and effectiveness of the Portico transcatheter heart valve and delivery systems via the transfemoral and transapical delivery methods, in high- and extreme-risk cohorts. The trial was temporarily halted in September 2014 when reports of reduced leaflet motion were observed in patients. The trial resumed enrolling patients in June 2015 after independent review found no excess rate of clinical events associated with the leaflet motion observation. The trial delay will delay the device's availability by nine to 12 months. This is the pivotal clinical trial for FDA device approval.

Direct Flow Medical Transcatheter Aortic Valve System
(Direct Flow Medical)

The Direct Flow Medical system combines several proven technology concepts into a single design—the polyester cuff and bovine pericardial leaflets of a surgical heart valve and the deployment attributes of noncompliant percutaneous coronary intervention technology. The device has no metal parts and can be deflated and repositioned or removed at any time during the procedure. A double-ring valve creates a tight and durable annular seal to prevent paravalvular leakage. When the valve is optimally placed, saline or contrast is easily exchanged via the positioning wires for a quick-curing polymer that forms the permanent structure. Rapid pacing of the heart is not required, reducing the stress put on the heart during the procedure. The delivery will be available in 23-, 25-, 27- and 29-mm sizes on an 18F delivery system. The implants are not available commercially or for distribution or sale in the U.S.

Direct Flow IDE Trial (SALUS)

Scott Lim (United States, University of Virginia [Vizient member hospital]), co-principal investigator

Study size: 878 patients

Perspective, Open-label, multicenter U.S. trial

Data on the device's safety and efficacy from the U.S. investigational device exemption (IDE) trial is unavailable. The U.S. IDE trial began in September 2014. Data recently reported from the 100-patient European study demonstrated an 80 percent survival rate at 24 months, continuing the positive trend showing 90 percent survival after one year and 99 percent after 30 days. All patients experienced mild or less post-procedural aortic regurgitation; 85 percent had no or only trace atrial regurgitation. This is the pivotal clinical trial for FDA device approval.

Centera transcatheter aortic heart valve
(Edwards Lifesciences)

The Centera transcatheter aortic valve is a deviation from the company's successful Sapien valve platform. The valve is self-expandable rather than balloon expandable. The implant is constructed with treated bovine pericardial tissue sewn onto a self-expanding nitinol frame and uses a motorized, low-profile delivery system. The valve is repositionable until fully deployed with a 14F profile. The company anticipates gaining the a CE mark in the second half of 2017. The implants are not available commercially or for distribution or sale in the U.S.

Companies with devices currently in clinical trials for FDA approval

The companies listed below have active U.S. clinical trials underway for the primary purpose of obtaining premarket approval from the FDA.

Vendor name	Device name	FDA NCT no.	Study status
Abbott Vascular	Portico	NCT02000115 (PORTICO IDE)	Actively recruiting
Boston Scientific	Lotus	NCT02329496 (REPRISE)	Active, not recruiting
Boston Scientific	Lotus Edge	NCT02202434 (REPRISE III)	Recruiting by invitation
Direct Flow Medical	Direct Flow	NCT01932099 (SALUS)	Actively recruiting
JenaValve Technology	JenaValve	NCT02732691	Not yet open
Medtronic	Evolut R	NCT02701283 (Low-risk patients)	Actively recruiting

Economic impact

The economic impact of transcatheter aortic valve technology will continue to be significant. As the growth in these valves continues, their use will eventually cannibalize the surgical valve market. The significant increase in procedural cost, primarily due to the implant cost, to the hospital resulting from the transition from surgical valve implantation to transcatheter valve implantation will erode hospital profitability. Based on the success of the current supplier pricing model, it is anticipated that marginal price reductions will occur as additional suppliers enter the U.S. market.

Reimbursement

Reimbursement for a transcatheter aortic valve procedure exists. It is anticipated that CMS will continue to reduce reimbursement payments to reflect the improving efficiencies hospitals are realizing. Transcatheter aortic valve procedures will remain neutral to unprofitable to the hospital for some time.

Sutureless aortic valves

An emerging segment within the surgical valve market is sutureless valves. These valves combine the proven performance of surgical tissue valves with the benefits of minimally invasive transcatheter valves. The benefits may include faster patient recovery and decreased procedural side effects. Two companies are selling this type of valve in the United States.

Intuity Elite aortic heart valve

(Edward Lifesciences)

The Intuity Elite valve system is a surgical aortic heart valve designed for rapid deployment. The valve is similar to the Perimount tissue valve platform and incorporates a stented skirt. The Intuity Elite valve system is designed to facilitate minimally invasive surgery and streamline complex aortic surgical valve replacements, thereby offering a cutting-edge treatment option for patients with aortic valve disease. The device received FDA pre-market approval in August 2016 and is commercially available for sale in the U.S.

Surgical Treatment of Aortic Stenosis With a Next-Generation, Rapid Deployment Surgical Aortic Valve (TRANSFORM)

Glenn Barnhart (United States, (Swedish Medical Center [Vizient member hospital]), co-principal investigator

Study size: 950 patients

Prospective, randomized, multicenter U.S. study

This multicenter, prospective, randomized controlled trial was designed to gain U.S FDA approval of an innovative heart valve. The clinical trial, which treated 839 patients in 29 centers in the U.S., demonstrated that at one year, the valve system is safe and effective and may reduce cross-clamp time and cardiopulmonary bypass time. This may provide patient benefits such as decreased mortality and morbidity, less time in an intensive care unit and reduced total hospital stay. Overall, the New York Heart Association (NYHA) Functional Classification, which categorizes patients into one of four groups based on their heart failure symptoms and physical limitations, improved in 73.1 percent of patients at one year.

Perceval aortic heart valve

(Sorin/LivaNova)

The Perceval aortic heart valve is a 100-percent sutureless heart valve for aortic valve replacement. The valve consists of a tissue component made from bovine pericardium and a self-expandable nitinol stent, which has the dual role of supporting and securing the valve. The tissue heart valve is supplied unmounted. Prior to implantation the valve diameter is reduced to a suitable size for loading it on the holder. The valve is then positioned and released in the aortic root, where the stent design and its ability to apply radial force to the annulus allow stable anchoring of the device. The platform is available in four sizes: small, medium, large and extra-large. The prosthesis is available in 31.0-, 33.0-, 35.5- and 37.5-mm sizes, respectively. The device received FDA pre-market approval in January 2016 and is commercially available for sale in the U.S.

PERSIST-AVR trial

Theodor Fischlein (Germany, Klinikum Nurnberg), co-principal investigator

Study size: 1,234 patients

International, prospective, post-market randomized multicenter trial

The PERSIST-AVR trial will be conducted at 60 sites worldwide where Perceval obtained regulatory clearance. It is expected to recruit patients with severe symptomatic aortic stenosis or steno-insufficiency who are candidates for surgical replacement of their native aortic valve. In the release of early data, the study found that the valve is safe, allowing surgeons to employ a minimally invasive approach during aortic valve replacement procedures. At follow-up at approximately 16 months, freedom from reoperation was 99 percent and patient survival was 91.3 percent. The valve has been implanted in more than 20,000 patients in 34 countries around the world.

Economic impact

It is too early to forecast the economic impact of sutureless heart valves. The potential benefits are demonstrated by the clinical trial data. The device's impact will be directly dependent on surgeons' willingness to change surgical technique. The device price is ranging $11,000 to $16,000 (U.S.).

Reimbursement

A unique reimbursement code for these valves does not exist. Using the existing surgical valve code significantly reduces hospital procedural profitability. It is anticipated that CMS may create a unique code if the device volume increases. Hospital profitability will decrease using this device.

Left atrial appendage closure devices

A left atrial appendage (LAA) is a muscular pouch connected to the left atrium of the heart. In patients with atrial fibrillation, blood clots may form from blood trapped in this pouch. Stroke is a common consequence of atrial fibrillation; approximately 15 percent of all strokes and as many as one-third of strokes in individuals aged 65 or older are caused by atrial fibrillation. The standard treatment is oral anticoagulation therapy, such as warfarin. Oral anticoagulants have a number of drawbacks, including excessive bleeding, dosage difficulties and frequent interactions with food and other drugs. For some patients—such as those with bleeding issues or who are pregnant or noncompliant with medication regimens—oral anticoagulants are not an option.

While device options were available earlier, the March 2015 FDA approval of the Boston Scientific's Watchman provided physicians with a clinically proven treatment option for their patients. Increasing numbers of patients are now receiving this implant. Slow adoption of the Watchman after its introduction was due to both lack of physician training and reimbursement constraints. Those constraints have been reduced, resulting in increased use of the device. Analysis forecasts use of these devices to grow at an average annual rate of 60 percent, increasing from 7,000 units to 30,000 units by early 2020.[8] With the success of the Watchman, other suppliers are entering the market. Johnson & Johnson's Biosense Webster acquired Coherex Medical and Abbott Vascular acquired St. Jude Medical, allowing them quicker access to the market. Left atrial appendage closure devices are expensive. Based on the suppliers in this market segment, do not expect price relief any time soon.

Companies developing left atrial appendage closure devices

Vendor name	Device name	Material	Regulatory status
Aegis Medical Innovations	Sentinel	Ligating loop	In development
Biosense Webster	WaveCrest	Nitinol	CE mark approved
Boston Scientific	Watchman FLX	Nitinol and polyester	CE mark approved
Cardia	Ultrasept LAA	Nitinol and polyester	In development
Custom Pediatric Medical Devices	Sideris	Frameless balloon covered with polyurethane	In development
Lifetech Scientific	LAmbre	Nitinol and polyester	CE mark approved
Occlutech	Occlutech	Nitinol mesh and nanomaterial cover	CE mark approved
Pfm Medical	Pfm	Nitinol mesh	In development
Abbott Vascular	Amplatzer Amulet	Nitinol mesh	CE mark approved; FDA, IDE ongoing

Potential new devices

Transcatheter aortic valve repair devices in clinical trials for FDA pre-market approval include:

Amplatzer Amulet left atrial appendage occluder
(Abbott Vascular)

The Amplatzer Amulet left atrial appendage occluder design is based on the Amplatzer occluder technology. The device is a double, self-expanding, nitinol mesh disc and lobe delivered via a transcatheter system. The two parts are connected by a central waist. Like other left atrial devices, this implant is designed to completely occlude the left atrial appendage at the ostium and block any blood clots. The end screw is flush with the disc to create a smooth surface within the left atrium. The device is offered in eight sizes (16 mm to 34 mm) to accommodate varying anatomies, with landing zone ranges from 11 to 31 mm in diameter. The implants are not available commercially or for distribution or sale in the U.S.

Amplatzer Amulet LAA Occluder Trial (Amulet IDE)

Dhanunjaya Lakkireddy (United States, University of Kansas), co-study chair

Study size: 1,600 patients

Prospective, randomized, multicenter active control worldwide trial

The Amulet device will be evaluated for safety and efficacy by demonstrating that its performance is noninferior to the commercially available Boston Scientific Watchman left atrial appendage closure device in patients with nonvalvular atrial fibrillation. Patients will be randomized in a 1:1 ratio between the Amulet LAA occlusion device (treatment) and the Watchman LAA closure device (control). The trial will be conducted at up to 150 sites worldwide. Patients will be followed for five years after device implant. The trial began enrolling U.S. patients in September 2016.

WaveCrest left atrial appendage occlusion system
(Biosense Webster)

The WaveCrest LAA occlusion system is a transcatheter self-expanding device constructed from a nitinol mesh and polyester patch. The mesh was selected for its unique ability to minimize undesired thrombus formation on the outside of the occluder and to demonstrate closure during the implant procedure. The device most closely resembles the Boston Scientific Watchman. The implants are not available commercially or for distribution or sale in the U.S.

LAmbre left atrial appendage occlusion system
(Lifetech Scientific)

The LAmbre LAA occlusion system combines the features of both the Watchman (Boston Scientific) and the Amplatzer Amulet (Abbott Vascular). The device has two connected parts: a cover and an umbrella. The titanium nitride-coated cover utilizes a mesh design with recessed hub to promote faster endothelialization and reduce delayed thrombus formation. The umbrella features eight frames, a polyethylene terephthalate (PET) membrane and eight hooks for multiple capture and repositioning points, and has three anchoring hooks. The double-membrane design seals the left appendage. The device only requires a small sheath (8F-10F), and will be available in sizes from 16 to 36 mm. The implants are not available commercially or for distribution or sale in the U.S.

Companies with devices currently in clinical trials for FDA approval

The companies listed below have active U.S. clinical trials underway for the primary purpose of obtaining pre-market approval from the FDA.

Vendor name	Device name	FDA NCT no.	Study status
Abbott Vascular	Amplatzer Amulet	NCT02879448 (AMULET IDE)	Actively recruiting
Aegis Medical Innovations	Sentinel	NCT02583178 (LASSO-AF)	Actively recruiting
Boston Scientific	Watchman FLX	NCT02702271 (PINNACLE FLX)	Active, not yet enrolling

Economic impact

The Watchman device comes in two parts: the implant and the access system. The U.S. list price for the system is $25,000. The average selling price is discounted and reimbursement will offset the majority of the device's cost. The economic impact of using the device will be increasingly significant for the hospital's cardiovascular budget.

Reimbursement

The CMS Technology Add-on Payment for fiscal 2016 was terminated and replaced in February 2016 with national coverage. For 2017, the Medicare reimbursement is:

DRG 273	Percutaneous intracardiac procedures with major complications or comorbidities	$ 21,495
DRG 274	Percutaneous intracardiac procedures without major complications or comorbidities	$ 15,089

The device cost consumes more than 70 percent of the reimbursement. Based on the current average selling price of the device, this procedure will be marginally profitable for hospitals after all procedural costs are included.

Heart failure devices

Many companies are developing innovative technologies to treat both acute and chronic heart failure. Some of these devices that have the potential to be approved for use in the United States and some interesting devices are presented below.

Revivent myocardial anchoring system
(BioVentrix)

The Revivent myocardial anchoring system is the second generation of the CE-marked device designed for the treatment of congestive heart failure. The anchoring system consists of two polyester fabric-covered anchor heads made of titanium. A flexible tether made of polyetheretherketone (PEEK) functions as a type of zip tie and is used to squeeze the anchors together and hold them in place. Increased ventricular wall tension is the underlying cause of left ventricular enlargement and causes worsening of heart failure symptoms. The implant reduces wall tension by directly reducing the left ventricular radius and preventing further left ventricular enlargement, thereby slowing the progression of the disease. The device is investigational and not for sale in the United States.

Clinical Study of the BioVentrix Revivent TC System for Treatment of Left Ventricular Aneurysms

Andrew S Wechsler (United States, Drexel University College of Medicine), principal investigator

Study size: 126 patients

Prospective, randomized, multicenter, dual-arm trial

The pivotal study of the Revivent TC System is designed as a 2:1 study versus active concurrent control group allocation ratio. This study will include 126 patients, of which 84 will be treated with the investigational device and 42 will be included in an active control group. The trial is designed to demonstrate the safety and effectiveness of the system. This is accomplished by implanting micro-anchoring pairs in the left ventricle to exclude scarred myocardium from the healthy tissue. The trial endpoints include positive effects on volume reduction, ejection fraction, quality of life, NYHA class, six-minute walk test and rehospitalization. The study began enrolling in mid-2016. No study results are available.

Harmony neuromodulation heart failure system
(Enopace Biomedical)

The Harmony neuromodulation system is designed to stimulate the aortic vagal afferents in the upper part of the descending aorta to restore the heart's autonomic balance and improve cardiac performance. The system is composed of two parts. The endovascular implant is a self-expandable nitinol stent housing both a receiving antenna and a four-electrode endostimulator. The patient control wirelessly powers the endovascular implant, manages the therapy and records treatment information. The implant is delivered via an arterial catheter. The system functions by simulating the nerve to alter the left ventricular mechanism and left ventricle-aorta coupling to reduce left ventricular pressure, serving as an indication of left ventricular unloading.

Endovascular Neuromodulation Treatment for Heart Failure Patients (ENDO-HF)

Daniel Weiss (Belgium, Enopace Biomedical)

Study size: 30 patients

Prospective, nonrandomized, multicenter, open-label trial

The purpose of the ENDO-HF study is to determine the safety and performance of the Harmony System for the treatment of heart failure. This is a first-in-man trial. No study results are currently available.

InterAtrial Shunt Device
(Corvia Medical)

The InterAtrial Shunt Device (IASD) is the first transcatheter device designed to treat heart failure with preserved ejection fraction. The "barrel" implant is a self-expanding nitinol star-shaped stent with a 19-mm outer diameter and 8-mm internal diameter. After a small opening is created in the atrial septum, the implant is deployed through a 14F delivery catheter, forming a passage between the left and right atria that enables the left atrium to decompress, with the aim of lowering left atrial pressure. The goals are to improve heart failure symptoms and quality of life, decrease heart failure hospitalization rates and reduce the overall cost burden of managing heart failure patients. The device is investigational and not for sale in the United States.

REDUCE LAP-HF Trial (REDUCE LAP-HF)

Jan Komtebedde (United States, Corvia Medical)

Study size: 100 patients

Prospective, randomized, multicenter trial

The REDUCE LAP-HF study is designed to evaluate the IASD System to reduce elevated left atrial pressure in patients with heart failure with preserved ejection fraction, also known as diastolic heart failure. The study will enroll patients at up to 20 sites in the United States and up to eight sites internationally. The results of the 64-patient CE-Mark study of the device showed that following device implantation, patients had significantly fewer heart failure symptoms and were able to exercise significantly longer. At six months post-implantation, median NYHA functional class improved from 3 to 2 ($P < .0001$), mean quality of life measurement (Minnesota Living with Heart Failure questionnaire) improved from 49 to 36 ($P < .0001$), mean six-minute walk distance improved from 313 meters to 345 meters ($P = .0023$) and mean exercise duration improved from 7.3 min to 8.2 min ($P = .0275$).

Parachute ventricular partitioning device
(CardioKinetix, Inc.)

The Parachute is designed to be a treatment for heart disease. The catheter-based partitioning device is deployed within the left ventricle for patients who develop

ischemic heart failure following a heart attack. The implant partitions the damaged muscle, isolating the nonfunctional muscle segment from the functional segment, decreasing the overall volume and restoring a more normal geometry and function in the left ventricle. The implant, composed of a fluoropolymer membrane stretched over a nitinol frame, is deployed into the apex of the left ventricle. The device will be available in 65-, 75-, 85- and 95-mm sizes. It is delivered through either a 14F or 16F system depending on size. The device is investigational and not for sale in the United States.

A Pivotal Trial to Establish the Efficacy and Long-term Safety of the Parachute Implant System (PARACHUTE IV)

William T Abraham (United States, The Ohio State University), co-principal investigator

Study size: 560 patients

Prospective, nonrandomized, multicenter, open-label trial

The Parachute IV clinical trial is a 1:1 randomized, multicenter trial designed to evaluate the PARACHUTE implant. The primary objective is to assess the safety and efficacy of the Parachute implant and delivery system in the partitioning of the left ventricle in patients with heart failure due to ischemic heart disease. The event-driven primary endpoint includes all-cause mortality and hospitalization for worsening heart failure. Other key endpoints include hemodynamic measures by echocardiography and imaging measures by computed tomography. The trial had more than half the required patients enrolled as of early 2016. No data is currently available. This is the U.S. IDE trial, being conducted at 78 U.S. sites.

Reducer coronary sinus stent

(Neovasc, Inc.)

The Reducer is a balloon-expandable hourglass-shaped metal stent. The stent is implanted in the coronary sinus, creating a narrowing to modulate flow and elevate pressure. Increasing the blood flow to the heart muscle reduces recurrent and severe heart pain (refractory angina). The implant provides relief of angina symptoms by altering blood flow in the heart's venous system, thereby increasing the perfusion of oxygenated blood to ischemic areas of the heart muscle. The implant is not available commercially or for distribution or sale in the U.S.

REDUCER-I: An Observational Study of the Neovasc Reducer System

Stefan Verheye (Belgium, ZNA Middelheim Hospital), principal investigator

Study size: 400 patients

Prospective, randomized, multicenter, multiarm European trial

This study is a multicenter, multicountry three-arm prospective and retrospective investigation in up to 400 subjects conducted at a maximum of 40 investigational centers. Arm 1 will include eligible prospective subjects. Arm 2 will include subjects who were previously enrolled and treated with the Reducer during the Coronary Sinus Reducer for Treatment of Refractory Angina study. Arm 3 will include subjects who received a Reducer under CE Mark.

TRVD transcatheter renal venous decongestion system

(Magenta Medical)

Magenta Medical developed a temporary venous catheter–based therapy for hospitalized patients with acute decompensated heart failure. The therapeutic principle is aimed at addressing a pathophysiological core element of acute heart failure—renal venous congestion and its deleterious effects on renal and cardiac function. The device is not available commercially or for distribution or sale in the U.S.

HeartMate PHP percutaneous heart pump

(Abbott)

The HeartMate PHP system is a catheter-based heart pump designed to provide hemodynamic left ventricular support. It will be a competitive alternative to the Abiomed Impella device. The device can be inserted into the femoral artery via an integrated 12F introducer sheath. The proprietary expandable catheter technology is advanced into the left ventricle, where the distal end of the catheter expands to 24F, allowing for enhanced blood flow. The system is designed to facilitate rapid insertion and four to five liters per minute of blood flow for support durations up to several days.

Shield II Trial

Maren Wagner (United States, St. Jude Medical), study coordinator

Study size: 425 patients

Prospective, 2:1 randomized, multicenter U.S. trial

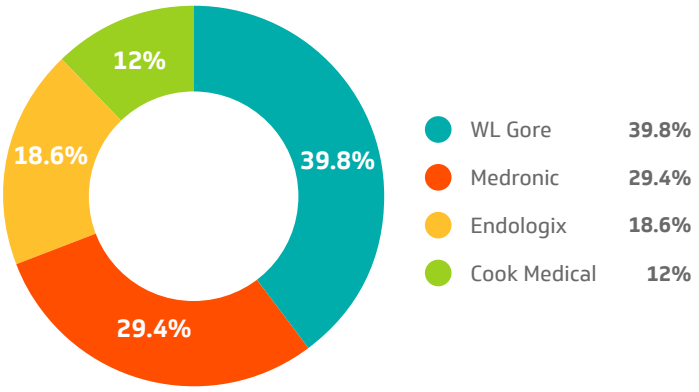
The Shield II U.S. clinical trial randomizes up to 425 patients at up to 60 sites against the Impella 2.5 at a 2:1 ratio. The primary objective of the trial is safety, efficacy and noninferiority at 90 days of follow-up. The trial was temporarily halted in February 2017 due to an issue with the catheter. No date to restart the trial has been provided.

Endografts

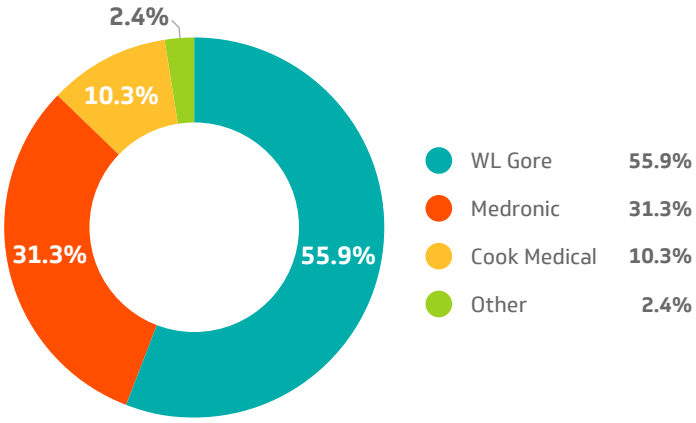
Endografts are medical implants used to treat aneurysms—ballooning of the vessel wall due to structural weakness. The pressure of blood traveling through the arteries can lead to this balloon-like bulge. An endograft comprises one of two types of stented grafts: abdominal aortic aneurysm (AAA) and thoracic aortic aneurysm (TAA). Both, as the names imply, are used to relieve pressure on the weakening wall of the ascending or descending aortic vessel. The endograft is a fabric-covered metallic stent that is inserted into an abdominal aortic aneurysm without need for a surgical approach and its resulting side effects. The endograft is placed via a transcatheter technique through the femoral artery. When the endograft is properly placed within the aortic aneurysm it reduces pressure on the vessel wall, protecting it from rupture. Abdominal endografts come in component form allowing the physician to customize implants to each patient's unique needs. This is in contrast to thoracic endograft, which is generally a one-piece implant.

According to Medtech Ventures, the global aortic endograft market was estimated at $1.8 billion in 2015, having grown by 6 percent. Abdominal aortic endografts generated $1.4 billion and accounted for 79 percent of the market and thoracic aortic endografts generated $300 million and accounted for 18 percent of the market.[9] Fenestrated, branched and flow-diverting aortic endografts generated $50 million and accounted for 3 percent of the market.[10] The abdominal endograft renal segment of the market is at maturity but is expected to continue growing in the low-single digit range through 2020.

Abdominal endograft market



Thoracic endograft market



Source: Millennium Research Group, 2016

Device development trends in this market are toward reduction of the implant profile. Once in the low 20F range, the delivery profiles have steadily decreased to a 14F delivery size today. As technology advances, even smaller-profile devices will become available, reducing complications. Fenestrated and branched endografts allow for endovascular treatment of aneurysms in close proximity to the renal arteries. Chimney and other procedural techniques are also improving patient care, reducing endoleaks and offering a greater range of options to treat an abdominal aneurysm. The high degree of difficulty associated with thoracic aortic surgery supports the adoption of transcatheter thoracic technique. Improving device designs and techniques will result in this segment of the market growing at a faster pace. W. L. Gore took the lead in the U.S. aortic stent graft market in 2016. The company now leads in both the U.S. AAA and TAA market segments.

Companies developing endograft devices

Vendor name	Device name	Device type	Regulatory status
Bolton Medical/Terumo Medical	TreoVance	AAA	CE mark approved; FDA, IDE trial ongoing
Bolton Medical/Terumo Medical	Relay Pro	TAA	In development
Cardiatis	Aortic MFM	TAA	CE mark approved
Cardiatis	Bifurcated MFM	AAA	Pending CE mark
Cook Medical	Zenith t-Branch	TAA	CE mark approved; FDA, IDE trial ongoing
Cook Medical	Zenith p-Branch	AAA	CE mark approved; FDA, IDE trial ongoing
Cordis	InCraft	AAA	CE mark approved; FDA, IDE ongoing
Endologix	Nellix	AAA	CE mark approved; FDA, IDE ongoing
Endologix	Nellix ChEVAS	AAA	CE IDE ongoing
Endologix	Ovation Alto	AAA	CE mark pending
Endospan	Horizon	AAA	CE mark approved
Endospan	Nexus	TAA	CE mark approved
Jotec	E-tegra	AAA	CE mark approved
Jotec	E-vita 3G	TAA	CE mark approved
Lombard Medical	Altura	AAA	CE mark approved
Medtronic	Valiant Mona LSA	TAA	CE and FDA IIDEs ongoing
Medtronic	Endurant Evo	AAA	CE and FDA IDEs ongoing
Medtronic	Fortevo	AAA	In development
Nano Endoluminal	Apolo	AAA	In development
Transcatheter Technologies	Tumbao	AAA	In development
Vascutek/Terumo Medical	Anaconda	AAA	CE mark approved, FDA IDE ongoing
WL Gore	Excluder Conformable	AAA	CE mark approved, FDA IDE ongoing

Potential new devices

Transcatheter mitral valve repair devices that appear to have potential to enter the U.S. market include:

Nellix AAA system

(Endologix, Inc.)

The Nellix AAA system is the first device in the class of endovascular aneurysm sealing (EVAS) systems. This means the device is designed to completely fill and seal the aortic aneurysm sac, with the aim of preventing device migration and endoleak. The device has two parts: a bilateral cobalt chromium stent that channels the blood past the aneurysm, and a polyurethane endobag that is inflated with a biostable polymer to seal the aneurysm sac. The implant is not available commercially or for distribution or sale in the U.S.

EVAS Forward IDE Trial

Jeffrey Carpenter (United States, Cooper Hospital), principal investigator

Study size: 279 patients

Prospective, nonrandomized, single-arm, open-label, multicenter U.S. trial

The objective of this study is to assess the safety and effectiveness of the Endologix endograft for the endovascular repair of infrarenal AAA. Patient enrollment is completed. Study results indicate 98 percent freedom from persistent endoleaks, no secondary interventions for Type II endoleaks, and 97 percent freedom from aneurysm-related mortality. Despite the positive clinical data, the FDA requested two-year patient follow-up data from the study. This

will delay the product release. The company expects these data to be available and submitted to the FDA in the second quarter of 2017. The supplier hopes the product will be available in the U.S. in second quarter of 2018.

Endurant EVO AAA endovascular stent graft system
(Medtronic)

The Endurant EVO AAA stent graft system is the next evolution of the Endurant family of endovascular stent graft systems. The device features a 3F reduction in profile, in situ sizing with a three-piece system and adjustable limb length, an enhanced delivery system that eliminates the tip-recapture step and incorporates an integrated flush port for contrast injection, smaller leg diameters and helical limb stents expanding options in tight distal aortas and tortuous iliac arteries, and multiple aortic body lengths with a larger range of limb lengths and diameters. The implants are not available commercially or for distribution or sale in the U.S.

Endurant Evo IDE Trial

Gilbert R. Upchurch (United States, University of Virginia Medical Center [Vizient member hospital]), co-principal investigator

Study size: 140 patients

Prospective, nonrandomized, open-label, multicenter U.S. trial

The purpose of this clinical trial is to demonstrate that the Endurant Evo AAA stent graft system is safe and effective for endovascular treatment of infrarenal abdominal aortic or aortoiliac aneurysms. The trial will enroll 140 patients at up to 30 sites in the United States and Europe. All study patients will be treated with the Endurant Evo AAA stent graft system. The trial began enrolling patients in April 2015. No current clinical trial data is available.

AortaFit System
(Aortica Corp)

The AortaFit System uses a proprietary system for the treatment of AAA. The system utilizes the patient's CT scan and employs a computer algorithm to create an accurate personalized 3-D printed template of the patient's diseased aorta. This enables a physician to precisely add fenestrations to an existing endograft. This process is intended to improve graft anchoring and minimize the potential of both endoleaks and graft migration. The implants are not available commercially or for distribution or sale in the U.S.

Companies with devices currently in clinical trials for FDA approval

The companies listed below have active U.S. clinical trials underway for the primary purpose of obtaining pre-market approval from the FDA.

Vendor name	Device name	FDA NCT no.	Study status
Bolton Medical	TreoVance	NCT02009644 (Treovance IDE)	Actively recruiting
Bolton Medical	Relay Pro	NCT03033043	Active, not yet recruiting
Cordis	InCraft	NCT01776450	Complete
Cook Medical	Zenith t-Branch	NCT02043691	Actively recruiting
Endologix	Nellix	NCT01726257 (EVAS IDE)	Actively recruiting
Medtronic	Valiant Mona LSA	NCT01839695 (Mona LSA)	Active, completed recruitment
Medtronic	Endurant Evo	NCT02393716 (Evo IDE)	Complete
Medtronic	Heli-FX EndoAnchor	NCT01534819 (Anchor)	Actively recruiting
Terumo Medical	Anaconda	NCT00612924 (Anaconda IDE)	Complete
WL Gore	Excluder Conformable	NCT02489539	Active, not yet recruiting

FDA = Food and Drug Administration; IDE = investigational device exemption; NCT = National Clinical Trial.

Economic impact

The economic impact of new devices for transcatheter aortic aneurysm repair will be marginal. The treatment modality is already the standard and reimbursement exists. Any impact will be from reimbursement decreasing sharply while suppliers continue to increase prices. Data from Millennium Research forecasts a 15 percent increase in procedures over the next 10 years,[11] with most of the growth coming from increased thoracic aortic aneurysm procedures and fenestrated abdominal endografts. Prices are forecast to increase at less than 1 percent annually.

Reimbursement

Reimbursement for endografts exists. It is anticipated that CMS will monitor reimbursement coverage and make annual adjustments to reflect improving procedural efficiencies and product pricing. This may also be a procedure CMS targets to become a bundled payment.

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