Industry report on global endovascular interventional instrument market

December 2022

Terms and abbreviations

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CAD	Coronary artery disease	**DES**	Drug-eluting stent
PAD	Peripheral artery disease	**DTS**	Dual therapy stent
PTCA	Percutaneous transluminal coronary angioplasty	**DEB**	Drug-eluting balloon
PCI	Percutaneous coronary intervention	**EPC**	Endothelial progenitor cell
PTA	Percutaneous transluminal angioplasty	**DAPT**	Dual antiplatelet therapy
NSTEMI	Non-ST segment elevation myocardial infarction	**MR**	Mitral regurgitation
STEMI	ST segment elevation myocardial infarction	**MS**	Mitral stenosis
CTO	Chronic total occlusion	**TR**	Tricuspid regurgitation
PMDA	Pharmaceuticals and Medical Devices Agency	**TS**	Tricuspid stenosis
NMPA	China Food and Drug Administration	**PR**	Pulmonary regurgitation
FDA	Food and Drug Administration	**PS**	Pulmonary stenosis
CE	Conformitè Europëenne	**AR**	Aortic regurgitation
OA	Orbital atherectomy	**AS**	Aortic stenosis
RA	Rotational atherectomy	**TMVr**	Transcatheter mitral valve repair
BMS	Bare metal stent	**TMVR**	Transcatheter mitral valve replacement

Terms and abbreviations

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TAVR	Transcatheter aortic valve replacement
SAVR	Surgery aortic valve replacement
TPVR	Transcatheter pulmonary valve replacement
SPVR	Surgical pulmonary valve replacement
NAS	Neuro artery stenting
CAGR	Compound annual growth rate
CEA	Carotid endarterectomy
RV	Right ventricular
LV	Left ventricular
CABG	Coronary artery bypass grafting
VHD	Valvular heart disease

Introduction, methodology and assumptions

Introduction, methodology and assumptions

China Insights Consultancy was commissioned to conduct research and analysis of, and to produce a report on global endovascular interventional instrument market at a fee of RMB1,070,000. The report commissioned has been prepared by China Insights Consultancy independent of the influence of the Company and other interested parties.

China Insights Consultancy is a consulting firm founded in Hong Kong and provides professional industry consulting services across multiple industries. China Insights Consultancy's services include industry consulting, commercial due diligence, strategic consulting, etc. Its consulting team has been tracking the latest market trends in industrial, energy, chemicals, healthcare, education, consumer goods, transportation, agriculture, internet, finance, etc., and has the most relevant and insightful market intelligence in the above industries.

China Insights Consultancy conducted both primary and secondary research using a variety of resources. Primary research involved interviewing key industry experts and leading industry participants. Secondary research involved analyzing data from various publicly available data sources, such as the National Bureau of Statistics, National Medical Products Administration, Food and Drug Association, National Health Commission of the People's Republic of China, the International Monetary Fund, World Health Organization, etc. The methodology of market size in terms revenue=population of the region*prevalence rate*surgery penetration*instruments used in surgery*ex-factory price

The assumptions adopted in the CIC Report in relation to the COVID-19 pandemic include (i) surgeries in different regions experienced an obvious but short-term drop in 2020 compared to in 2019 due to quarantine and temporarily shut down of hospitals pursuant to which all surgeries were suspended (ii) the volume of surgery will recover and increase in 2021 and therefore, as there was no material change in prevalence and prices of surgeries charged by the hospitals, which was based on the samples collected from hospitals and expert interview by China Insights Industry Consultancy Limited.

The market projections in the commissioned report are based on the following key assumptions: (i) the overall social, economic and political environment in the global economy is expected to remain stable during the forecast period; (ii) Relevant key drivers are likely to maintain a steady growth trend over the next decade; (iii) increasing number of procedures, increasing amount of R&D expenditures, increasing patient affordability, etc.; (iv) the negative impact caused by COVID-19 outbreak in 2020 on the industry is expected to be limited, taking into account the impact of the COVID-19 outbreak and estimating market growth for 2020 in a conservative manner based on the industry and economic recovery in China since the second quarter of 2020; and, (v) there is no extreme force majeure or industry regulation in which the market may be affected dramatically or fundamentally.

All statistics are reliable and based on information available as of the date of this report. Other sources of information, including from the government, industry associations, or market participants, may have provided some of the information on which the analysis or data is based.

All the information about the Company is sourced from the Company's audited report or management interviews. The information obtained from of the Company has not been independently verified by China Insights Consultancy.

List of important table and graph

Definition of different region involved in this report

A. The Industry Overview Section in the prospectus, industry report use the same market segmentation, including six regions:

i) Greater China, including Mainland China
ii) Japan
iii) Europe
iv) The United States
v) APAC, defined as all APEC member countries excluding Greater China, Japan, the The US and Russia
vi) Rest of World

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Growth drivers and future trends of global medical device market

- Global market device market is driven by several factors including aging population, improving affordability of customers and increasing R&D investment in innovative medical devices

Growth drivers and future trends of global medical device market

Growth drivers	Description
 **Aging population and increasing prevalence of chronic diseases**	• As of 2020, people aged 65 or above account for more than 13.0% of the total population in China. For the developed countries, the proportions of 65+ residents generally exceed 15.0% of their total population. The trend of aging population has been a common trend around the globe and is expected to continue in the coming decades. • The prevalence of chronic diseases such as cardiovascular diseases is expected to grow in the future as a result of aging population, which will also result in an increasing number of surgical procedures for these patients. The demand for surgical instruments is thus expected to increase continuously in the following decade.
 **Improving affordability and increasing awareness of health**	• Along with the global economic growth, the disposable income of residents in developed countries and developing countries are generally increasing, which improves the affordability of patients to pay for surgical procedures and preventative healthcare services, and thus increases the global demand for medical devices. • The growing awareness of healthcare as a result of growing income is another reason for the increasing demand for medical devices, which is reflected by the growing per capita healthcare expenditure around the globe. As people increasing their health consciousness, and willing to pay more for physical examination and surgical procedures is increasing, the penetration of medical procedures around the globe and demand for surgical or interventional instruments are expected to grow.
 **Increasing R&D investment of medical device manufacturers**	• The R&D investment of the leading companies in global medical device industry has been overall increasing in the past five years, and the proportion of R&D investment in the total revenue of the leading companies remains high, indicating a trend of increasing supply of innovative medical devices in the global market. • The innovation in medical devices is also expected to satisfy the existing unmet medical needs of patients around the globe, and thus expand the size of the overall medical device market.

Source: Annual reports of companies; China Insights Consultancy

Entry barriers of global medical device market

Entry barriers of global medical device market

Entry barriers	Description
 **Heavy R&D investment and high risks**	• Medical device industry is an undoubtedly high-tech industry that integrates materials, mechanical manufacturing, electronic engineering etc., where sophisticated technology is a must. Therefore, manufacturers should investment a lot in R&D • However, heavy investment may not achieve ideal success which means R&D of medical devices are ventures of high risk. What's more, despite extensive testing of products both ex vivo and in vivo, the chance of later failure of new products may cause serious medical problems for the individual and financial disaster for the producer.
 **Strict approval processes and regulatory issues**	• Medical devices, especially implantable devices which belong to Class III have strict requirements for getting to the market and are required to undergo premarket approval. Governments all almost use a slightly different classification system. For example, In the The US, this process is controlled by the FDA, a government agency. In Europe, the process is conducted by so-called Notified Bodies, which may be private companies or foundations. The FDA requires evidence of safety and efficacy from new devices, while premarket evaluation in Europe requires proof of safety. All these requirements make new manufacturers much more difficult to enter medical device industry.
 **Comprehensive product portfolio and solutions**	• Different procedures and symptoms require various types of specifications of medical devices. Even the same type of disease can have different therapies, and different medical devices are needed for coordinated treatment. A comprehensive product portfolio can eliminate compatibility concerns by providing one-stop and tailor-made treatment which will be welcomed by professionals. This consequently involves synergies for R&D, manufacturing and commercialization activities and growing economies of scale, with which new entrants are difficult to compete.
 **Customer stickiness and end-user recognition**	• Medical devices are mainly utilized by professional doctors in hospitals and clinics. Doctors have their own preferences for the use of medical devices. Some brands will cultivate their own user stickiness. Such process could take years of efforts for a brand to establish solid relationships with physicians and hospitals, especially with top-tier hospitals. And it could be difficult for a new entrant to break such stickiness and cultivate its own end-user recognition.

Source: China Insights Consultancy

I. Overview of global medical device market

II. Overview of global coronary artery disease interventional procedural instrument market

III.Overview of global peripheral artery disease interventional procedural instrument market

IV.Overview of global neuro artery disease interventional procedural instrument market

V. Overview of global structural heart disease interventional procedural instrument market

VI.Appendix

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Introduction to cardiovascular diseases

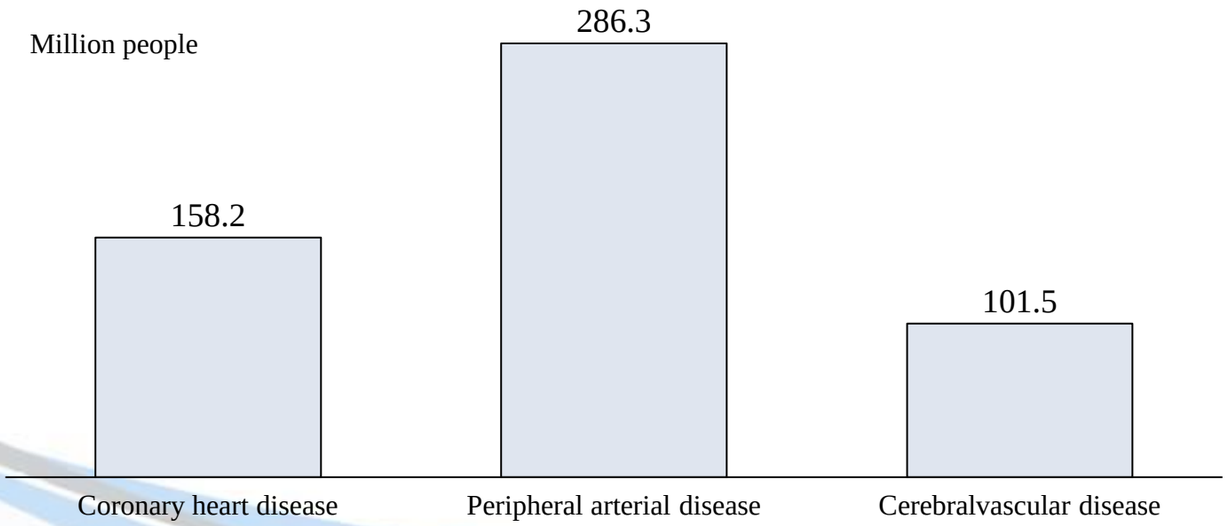
- Cardiovascular disease (CVD) is a general term for conditions affecting the heart or blood vessels

Introduction to cardiovascular diseases

Cardiovascular diseases (CVDs) are a group of disorders of the heart and blood vessels. They include:

- coronary heart disease – a disease of the blood vessels supplying the heart muscle;
- cerebrovascular disease – a disease of the blood vessels supplying the brain;
- peripheral arterial disease – a disease of blood vessels supplying the arms and legs;
- rheumatic heart disease – damage to the heart muscle and heart valves from rheumatic fever, caused by streptococcal bacteria;
- congenital heart disease – birth defects that affect the normal development and functioning of the heart caused by malformations of the heart structure from birth; and
- deep vein thrombosis and pulmonary embolism – blood clots in the leg veins, which can dislodge and move to the heart and lungs.

According to 2021 Heart Disease % Stroke Statistical Update Fact Sheet Global Burden of Disease, coronary heart disease, peripheral artery disease and cerebrovascular disease, accounted for approximately **28.8%, 52.0%, 18.5%.**



18.6 million death every year from CVD

33% of all global deaths

>75% of CVD deaths take place in low and middle-income countries

CVD	**18.6** million
Cancer	**10** million
Respiratory Diseases	**3.7** million
HIV	**1** million

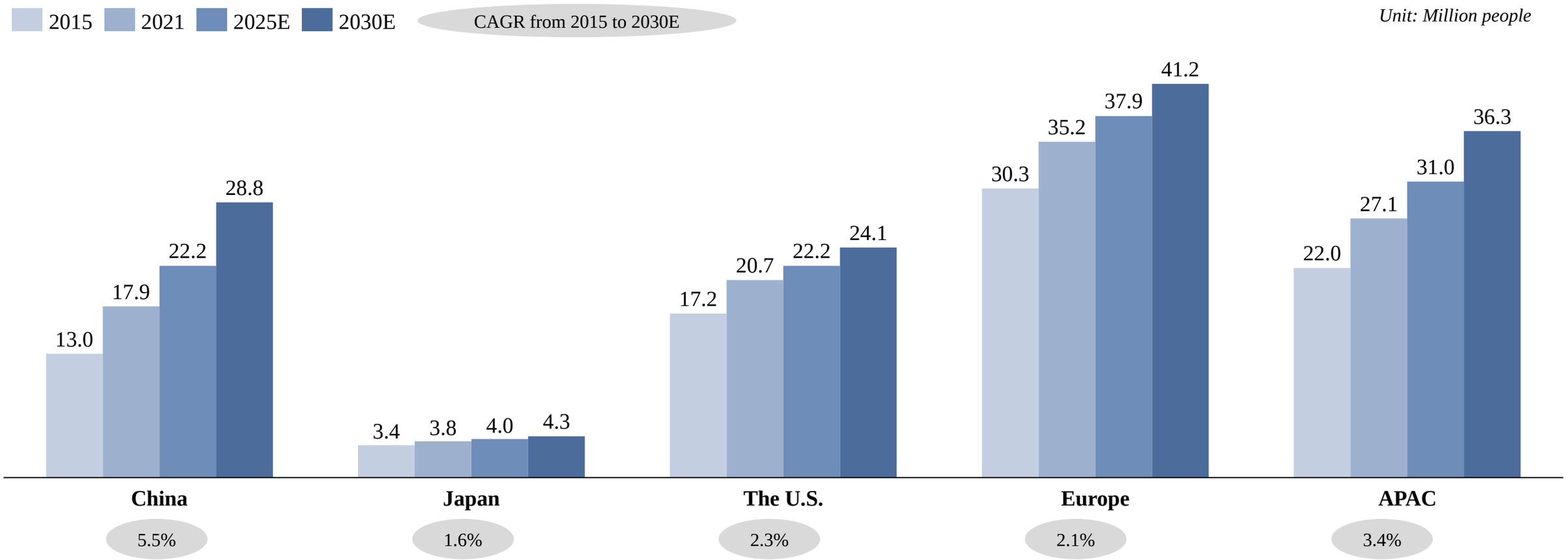
Risk factors for CVD

- High Blood Pressure
- Unhealthy Diet
- Overweight & Obesity
- Tobacco
- Air Pollution
- Harmful use of alcohol

Source: WHO; World Heart Federation; China Insights Consultancy

Global prevalence of CAD

Global prevalence of CAD, by region, 2015vs.2021vs.2025Evs.2030E



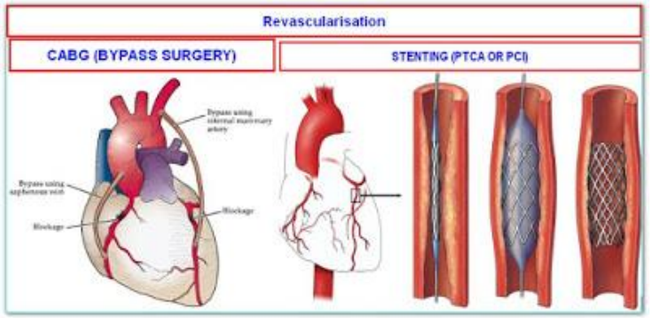
Source: China Insights Industry Consultancy Limited, American Heart Association, Journal of American College of Cardiology, Centers for Disease Control and Prevention, Census Bureau, European Society of Cardiology, Europe Association of PCI, Chinese Circulation Journal, National Healthcare Security Administration, World Heart Federation, Ministry of Health, Labour and Welfare (Japan) and other literature review and expert interviews

**APAC: APEC excluding China, Japan, The US and Russia*

Treatment guideline of CAD

- Treatment of CAD including medical therapy, percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG)

Treatment option of CAD



Definition of CAD:

Usually, coronary artery disease is due to

- **Coronary artery atherosclerosis**: is often irregularly distributed in different vessels but typically occurs at points of turbulence. As the atheromatous plaque grows, the arterial lumen progressively narrows, resulting in ischemia. The degree of stenosis required to cause ischemia varies with oxygen demand.

Less often, coronary artery disease is due to

- **Coronary artery spasm**: a transient, focal increase in vascular tone, markedly narrowing the lumen and reducing blood flow; symptomatic ischemia may result. Marked narrowing can trigger thrombus formation, causing infarction or life-threatening arrhythmia. Spasm can occur in arteries with or without atheroma.
- **Coronary artery dissection:** is a rare, non-traumatic tear in the coronary intima with creation of a false lumen. Blood flowing through the false lumen expands it, which restricts blood flow through the true lumen sometimes causing coronary ischemia or infarction. Dissection may occur in atherosclerotic or non-atherosclerotic coronary arteries.

1 *Medical therapy*

Medical management of patients with CAD depends on symptoms, cardiac function, and presence of other disorders. All patients with stable coronary artery disease require medical therapy to prevent disease progression and recurrent cardiovascular events or optimal medical treatment has failed but should be continued following PCI or CABG. Little evidence exists to guide therapy for patients with endothelial dysfunction. Treatment is generally similar to that for typical large-vessel atherosclerosis.	Recommended therapy includes antiplatelet drugs to prevent clot formation and statins to lower LDL cholesterol levels (improving short-term and long-term outcomes probably by improving atheromatous plaque stability and endothelial function). Beta-blockers are effective in reducing symptoms of angina (by reducing heart rate and contractility, decreasing myocardial oxygen demand) and reducing mortality post-infarction, especially in the presence of post-myocardial infarction (MI) LV dysfunction.

2 *Percutaneous coronary intervention (PCI)*

PCI is indicated for certain patients with acute coronary syndrome (ACS) or with stable ischemic heart disease who have angina despite optimal medical therapy. At first, PCI was done with balloon angioplasty alone. Now has evolved to the drug eluting stent and drug coated balloon. Future research on drugs such as antiplatelet drugs and anti-smooth muscle cell proliferation drugs will also be the direction of research, so as to form a more humanized segmented stent market.	Compared with CABG, PCI is a minimally invasive procedure using interventional instruments that requires no open-heart surgery, and is short in duration (only about one hour) and allows patients to get out of bed after an hour. Therefore, coronary intervention has the advantages of small trauma, quick recovery after operation, few complications, low risk and low cost, and the success rate of treatment is similar to that of surgical bypass grafting

3 *Coronary artery bypass grafting (CABG)*

CABG uses arteries whenever possible, and if necessary, sections of autologous veins to bypass diseased segments of the coronary arteries. At 1 year, about 85% of venous bypass grafts are patent, and after 5 years, one third or more are completely blocked. However, after 10 years, as many as 97% of internal mammary artery grafts are patent. Arteries also hypertrophy to accommodate increased flow. CABG is superior to PCI in patients with diabetes and in patients with multivessel disease amenable to grafting.	When the heart stopped; a bypass machine pumps and oxygenates blood. Risks of the procedure include stroke and MI. For patients with a normal-sized heart, no history of MI, good ventricular function, and no additional risk factors, risk is < 5% for perioperative MI, 1 to 2% for stroke, and ≤ 1% for mortality; risk increases with age, poor LV function, and presence of underlying disease. Operative mortality rate is 3 to 5 times higher for a second bypass than for the first.

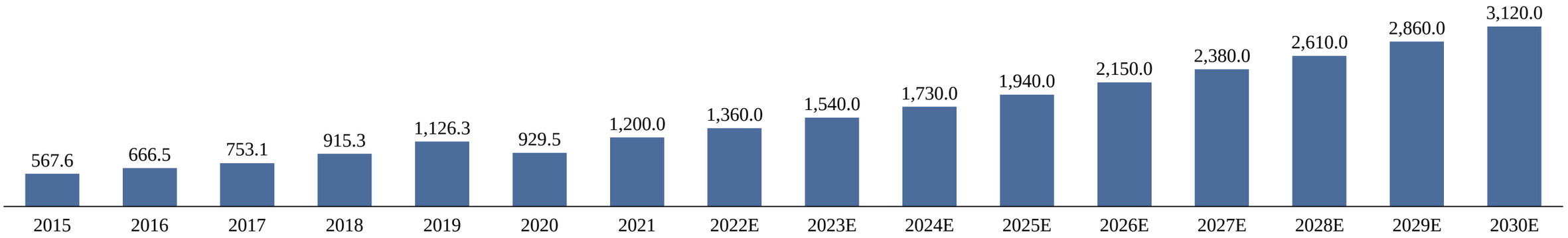
Source: MSD Manual China Insights Consultancy

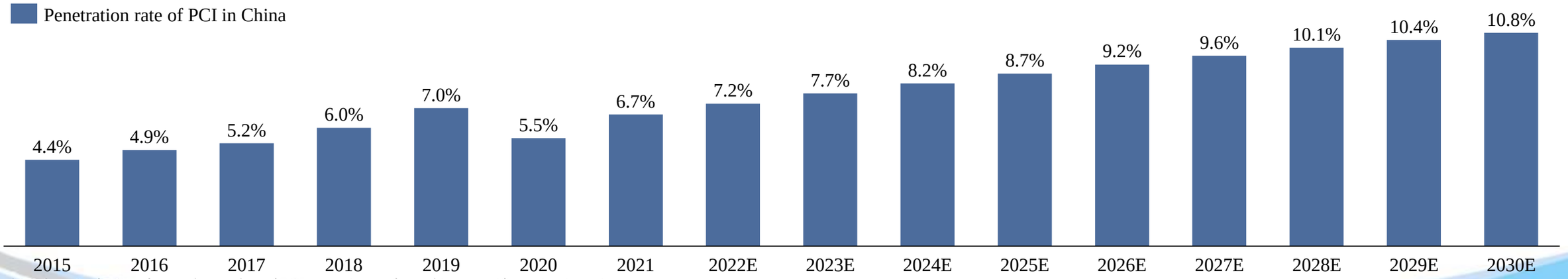
PCI Volume and penetration* rate in China

- The volume of PCI differs from country to country due to the different penetration rate of PCI procedure or local treatment guideline

PCI volume and penetration rate in China

CAGR	2015-2020	2021-2025E	2026E-2030E
China PCI volume	10.4%	12.8%	9.7%





**"Volume" of PCI refers to the number of PCI surgeries performed in a specific region in a given year, while the definition PCI penetration rate refers to percentage of patients that can be treated with PCI surgeries in a specific region at a specific time*

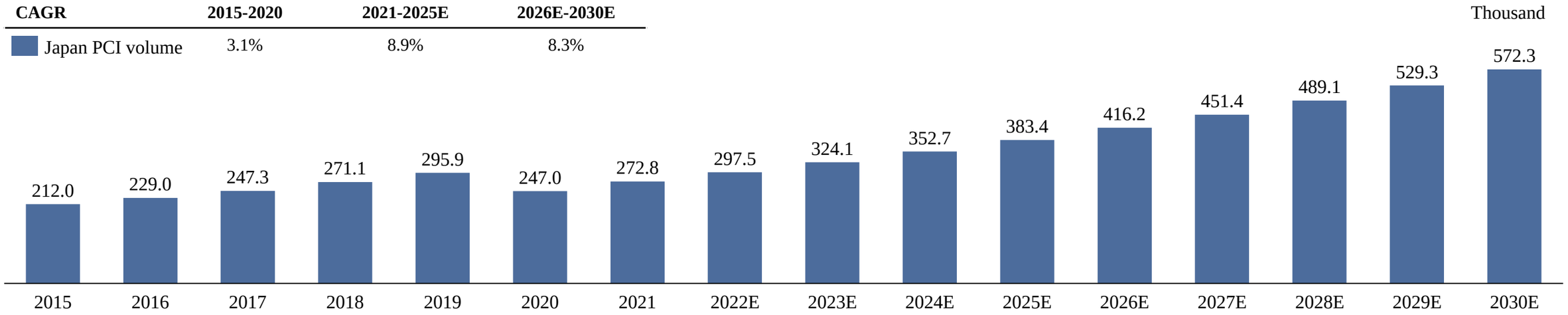
Source: China Insights Consultancy

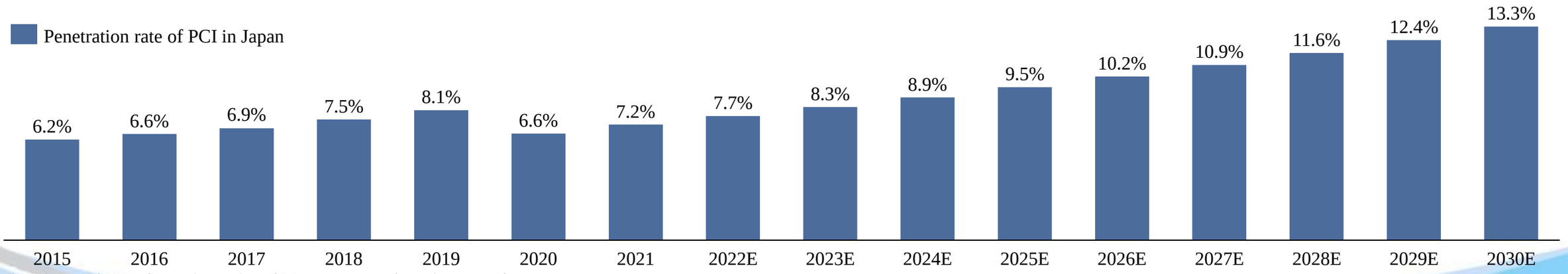
PCI Volume and penetration rate in Japan

- The volume of PCI differs from country to country due to the different penetration rate of PCI procedure or local treatment guideline

PCI volume and penetration rate in Japan

CAGR	2015-2020	2021-2025E	2026E-2030E
Japan PCI volume	3.1%	8.9%	8.3%





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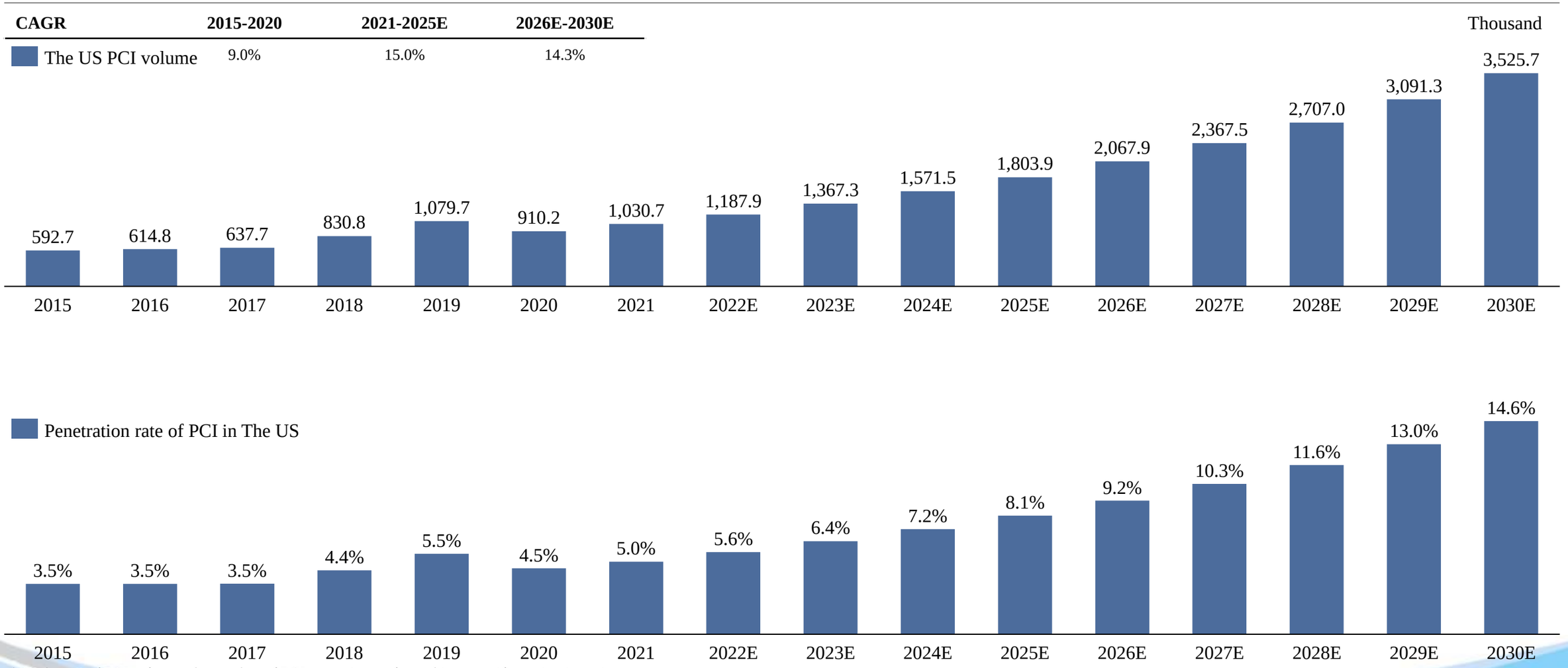
Source: China Insights Consultancy

PCI Volume and penetration rate in The US

- *The volume of PCI differs from country to country due to the different penetration rate of PCI procedure or local treatment guideline*

PCI volume and penetration rate in The US



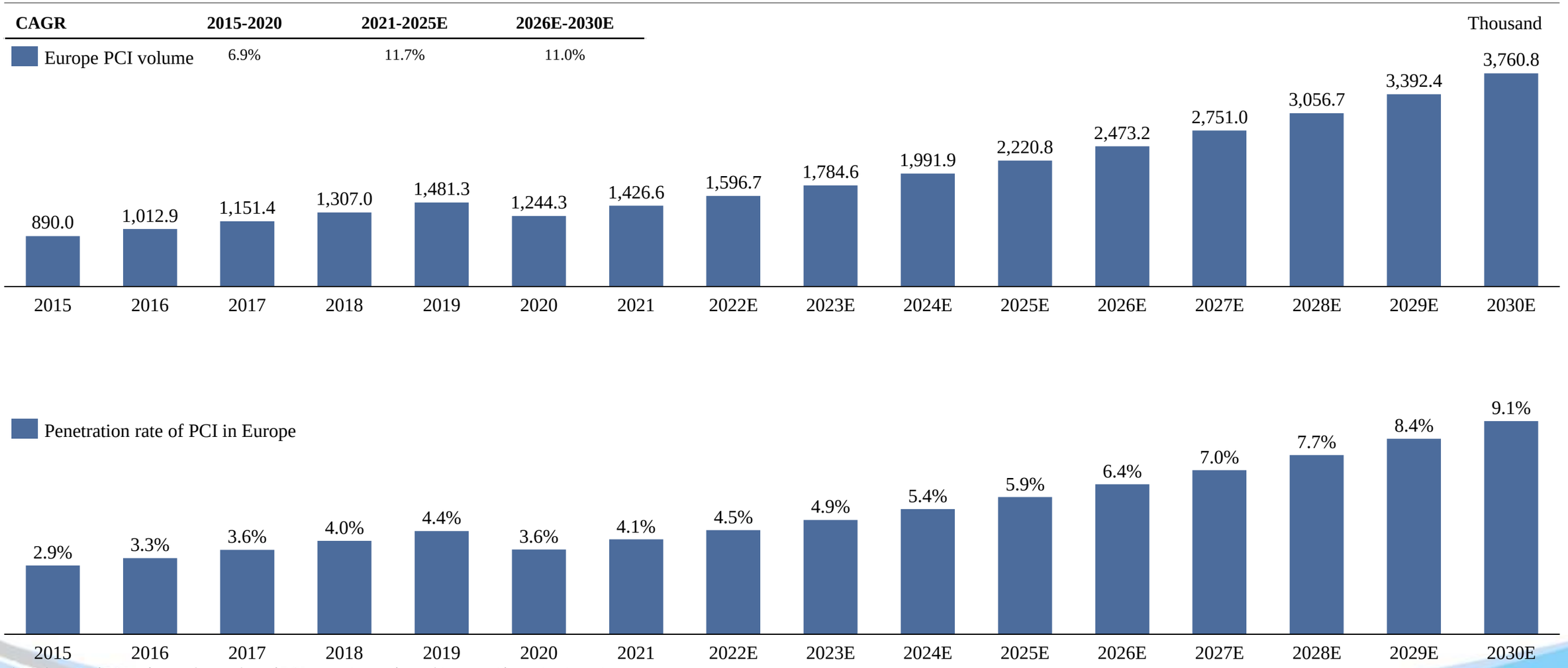
*"*Volume" of PCI refers to the number of PCI surgeries performed in a specific region in a given year, while the definition PCI penetration rate refers to percentage of patients that can be treated with PCI surgeries in a specific region at a specific time*

Source: China Insights Consultancy

PCI Volume and penetration rate in Europe

- *The volume of PCI differs from country to country due to the different penetration rate of PCI procedure or local treatment guideline*

PCI volume and penetration rate in Europe



**"Volume" of PCI refers to the number of PCI surgeries performed in a specific region in a given year, while the definition PCI penetration rate refers to percentage of patients that can be treated with PCI surgeries in a specific region at a specific time*

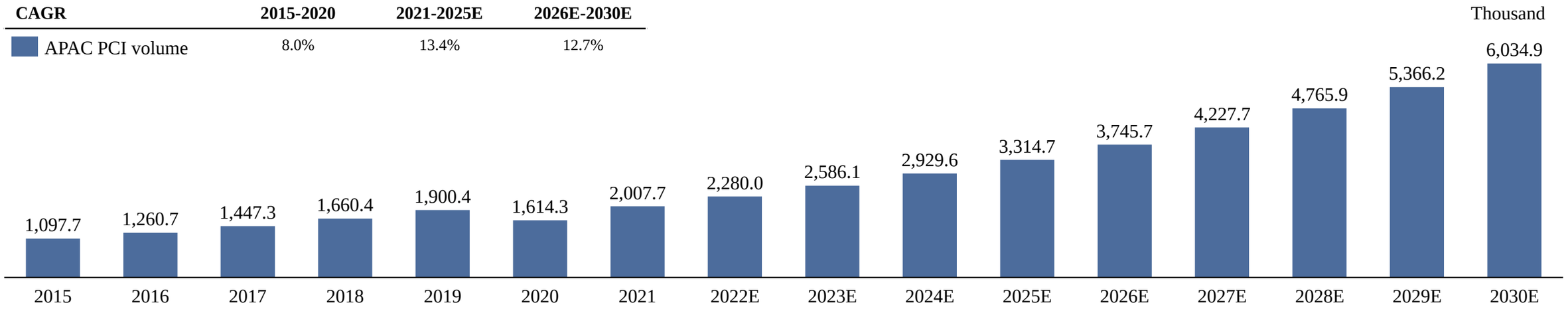
Source: China Insights Consultancy

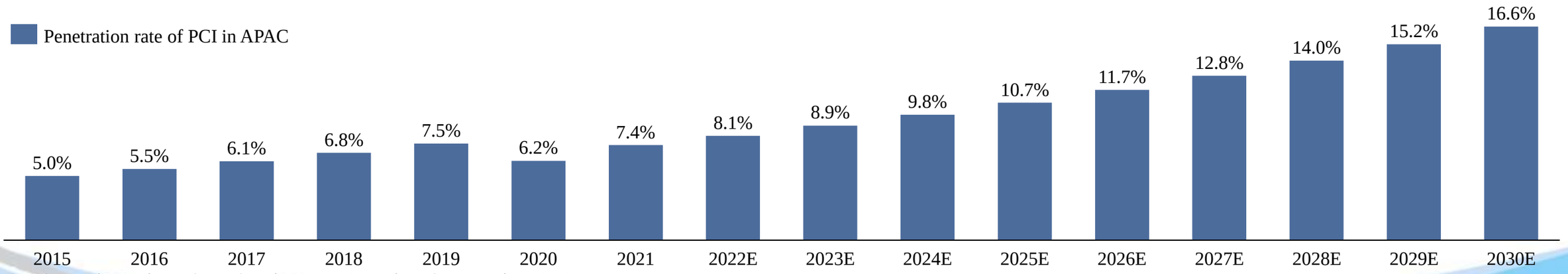
PCI Volume and penetration rate in APAC

- The volume of PCI differs from country to country due to the different penetration rate of PCI procedure or local treatment guideline

PCI volume and penetration rate in APAC

CAGR	2015-2020	2021-2025E	2026E-2030E
APAC PCI volume	8.0%	13.4%	12.7%



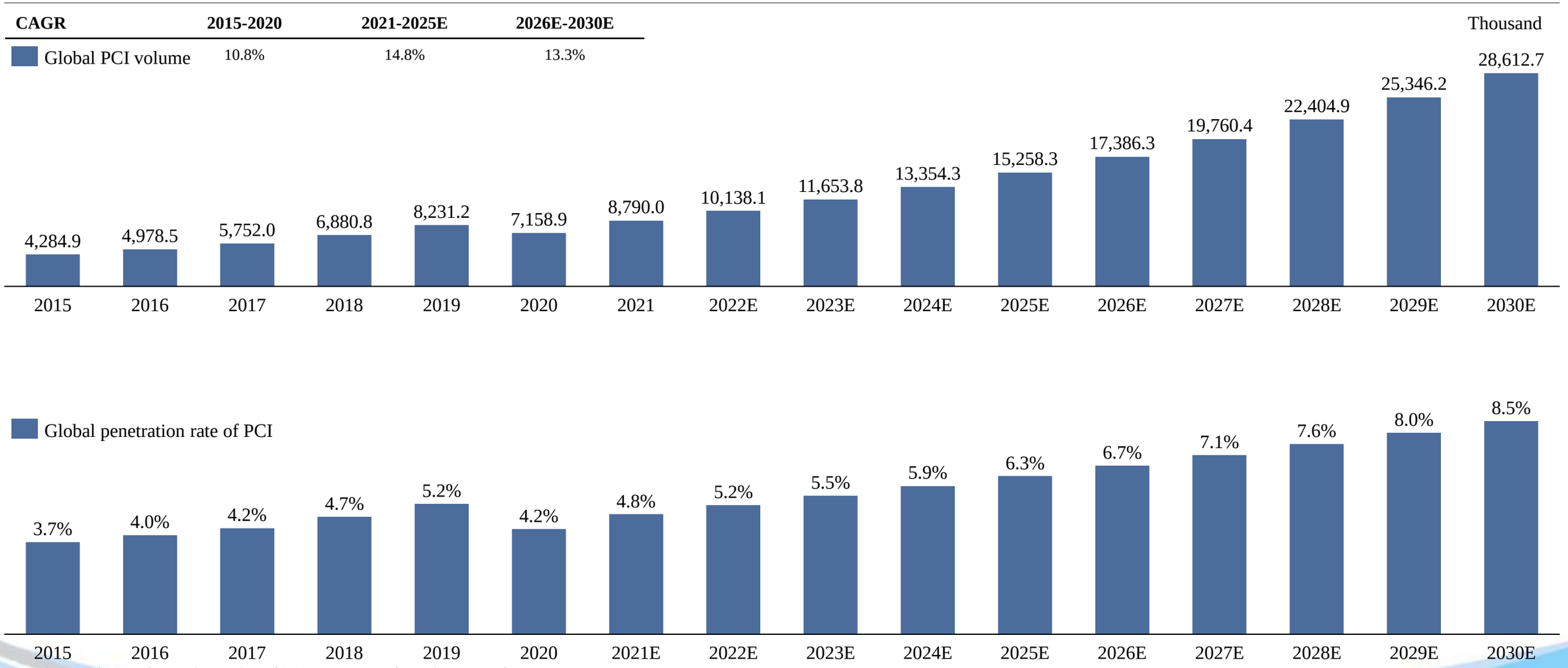


**"Volume" of PCI refers to the number of PCI surgeries performed in a specific region in a given year, while the definition PCI penetration rate refers to percentage of patients that can be treated with PCI surgeries in a specific region at a specific time*

Source: China Insights Consultancy

Global PCI Volume and penetration rate

Global PCI Volume and penetration rate



*"*Volume" of PCI refers to the number of PCI surgeries performed in a specific region in a given year, while the definition PCI penetration rate refers to percentage of patients that can be treated with PCI surgeries in a specific region at a specific time*

Source: China Insights Consultancy

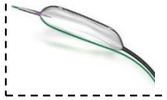
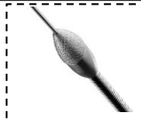
Overview of PCI Instruments

- Orbital atherectomy and rotational atherectomy are used in cases of moderate or severe calcification.

Overview of PCI instruments

Introduction to PCI instruments:

In a general PCI procedure, the doctor uses a semi-complaint balloon to pre-expand the vessel and to determine using a stent or drug-coated balloon in latter step (based on the remaining stenosis after the pre-dilation.) In some cases, which patient presents moderate or severe calcified lesion, atherectomy is performed for further crossing of balloons and stents.

Procedural step	Lesion Access	Lesion Preparation			Lesion Therapy	Lesion Optimization
Condition	Tight, total occlusion and challenging anatomy	De novo, routine cases	Fibrotic, Mild to moderate calcification	Heavy to severe calcification	DES/DCB	Post DES/ OAS
	 Guide catheter extension • Guide catheter extension provides pathway for balloon and/or stent delivery	 Semi-compliant Balloon • Semi-compliant balloon is used in pre-dilation to expand the lesion for further treatment	 Scoring Balloon • Scoring balloon consists of wires stick to the balloon. It is used to modify calcified lesions.	 Orbital Atherectomy • OA is used to break the lesion into smaller bricks with orbital movement of the orbital crown.	 Drug Coated Balloon • A balloon coated with anti-proliferative drug is used in post-dilatation without stent	 Scoring Balloon • Scoring balloon consists of wires stick to the balloon. It is used to modify calcified lesions.
	 CTO Balloon • CTO balloon is made to keep a low crossing profile to treat complex CTO stenosis		 Cutting Balloon • Cutting balloon consists of 3 or 4 scoring wires bonded longitudinally for creating incisions in targeted lesions.	 Rotational Atherectomy • RA use a rotating abrasive burr to advance and break the calcified lesions.	 Drug Eluting Stent • A metal stent coated with anti-proliferative drug is used in lesion therapy to keep lesion open after surgery	 Non-compliant Balloon • Non-compliant balloons are able to expand to a certain diameter and exert high pressure on lesions.
	 Microcatheter • Microcatheter is used in guidewire support, exchange and to access distal anatomy				 Dual Therapy Stent • An upgraded version of drug-eluting stent, which has another coating of CD34 antibody to help reendothelialization.	

Source: China Insights Consultancy

Introduction to chronic total occlusion (CTO)

- CTO is defined as the total occlusion of one or more coronary artery vessels. The prevalence of coronary artery disease differ in countries due to population and population risk factors

Introduction to CTO

CTO accounts for 16-20% of all CAD patients. CTO is defined as one or more coronary artery vessels being occluded for more than three months.

Symptoms of CTO

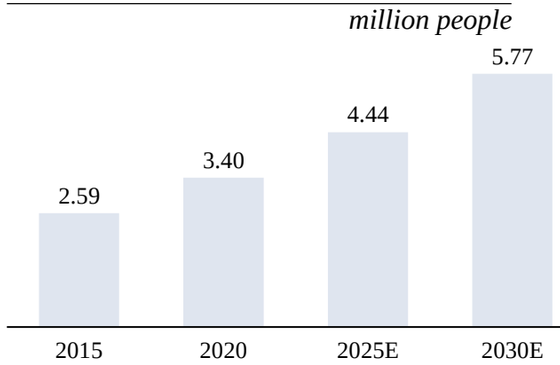
- Chest discomfort (pain, pressure and tightness)
- Pain in the upper body or arm
- Shortness of breath
- Dizziness or fatigue
- Rapid or irregular heartbeat

Risk factors of ischemic stroke

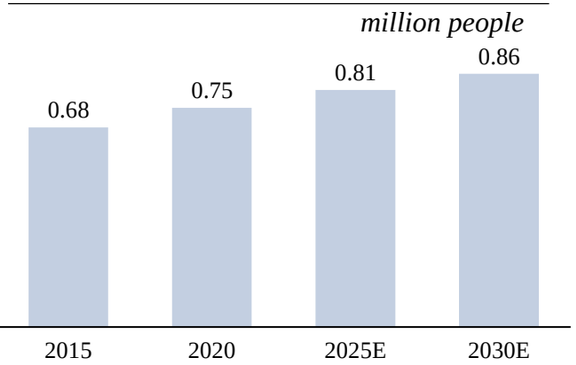
- High cholesterol:
  High cholesterol contributes to the likelihood of CTO occurrence
- Smoking:
  Smoking contributes to chances of getting CTO
- Obesity:
  Overweight people are more likely to get CTO
- Diabetes:
  People with diabetes are of higher risks
- Sedentary lifestyle:
  A lack a physical activity increases the risk
- Unhealthy diet:
  Excess consumption of saturated or trans fats increases the risk

Global CTO prevalence

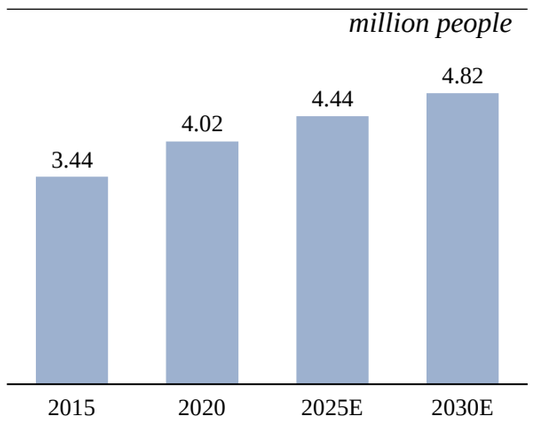
China CTO prevalence



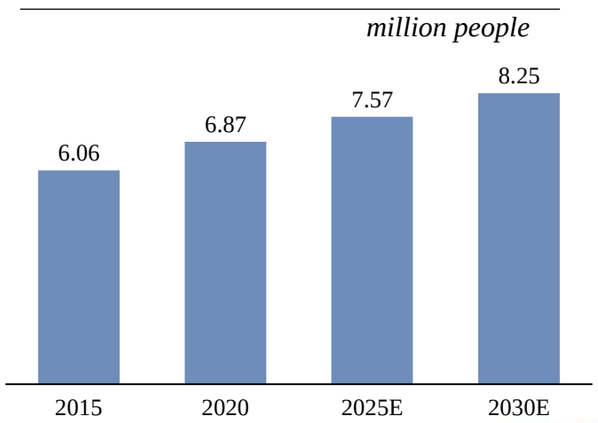
Japan CTO prevalence



US CTO prevalence



Europe CTO prevalence



Source: PMC; Michigan Medicine; China Insights Consultancy

Overview of CAD interventional procedural instruments

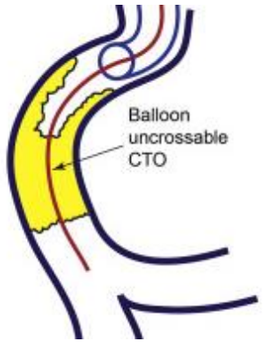
- Small CTO balloon is used in balloon uncrossable scenarios, which means when the catheter is able to cross the lesion while balloon is obstructed and cannot pass

CTO small balloon

Introduction

- CTO balloons are applied in balloon uncrossable lesions. Balloon uncrossable coronary lesions are lesions that cannot be crossed with a balloon after successful guidewire crossing, which happen in 6-9% of chronic total occlusions.
- The failure of a balloon to cross a lesion is often due to severe calcification or tortuosity proximal or at the lesion or both.
- Using a small balloon to modify lesion is the first option of solving balloon uncrossable lesions.

Application of small balloon in balloon uncrossable lesions



- **Small balloon technique**: When the traditional balloons can't pass the lesion, the first attempt is to use a small, single marker, non-compliant balloon with low crossing profile and long length and try crossing again.
- **Grenadoplasty**: A small balloon is advanced as far as possible into the lesion and inflated at high pressure until it ruptures The balloon rupture creates a contrast jet that often modifies the plaque, resulting in successful crossing with a new balloon.
- **Side branch anchor technique**: Advance a workhorse guidewire into a side branch, followed by a small balloon. The balloon is then inflated 6-8 atm to anchor the guide into the vessel and enhancing advancements of balloons or microcatheters.
- **"Inch-worming" technique**: When using guide catheter extension to increase support for crossing, "inch-worming" technique is often performed to advance guide extension to lesion proximal, which is to position a small balloon halfway in and out of the guide extension, and repeatedly inflate and deflate the balloon to advance the extension.

Comparison of leading small CTO balloon

	Balloon Diameter	Tip entry Profile	Crossing Profile
Alveo	0.75 mm	0.0156"	0.0203"
River	0.75 mm	0.0160"	N/A
Sapphire 3	0.85 mm	0.0159"	0.0208"
Nano	0.85 mm	0.0160"	0.0195"
Ikazuchi zero	1.0 mm	0.0167"	0.0229"
Ryurei	1.0 mm	0.0154"	0.0244"

Key Analysis

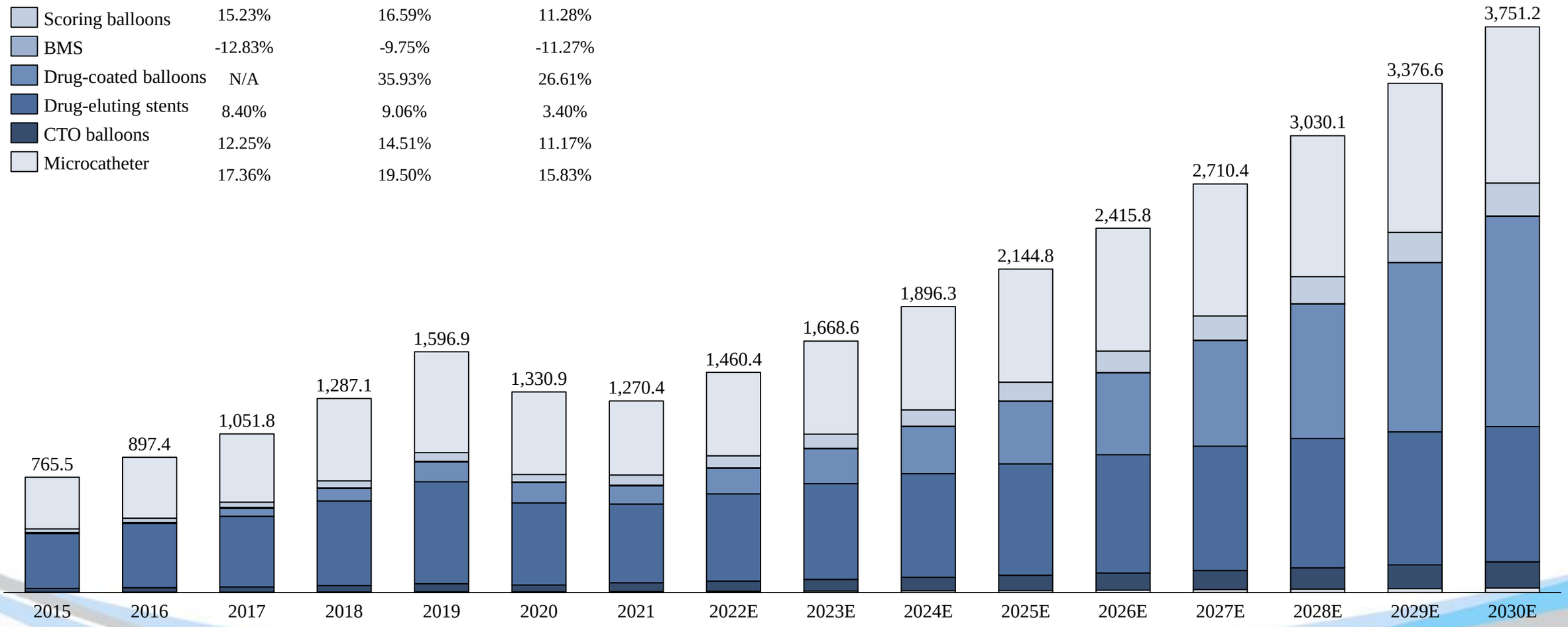
- The key to small balloon crossing is to have a very small tip entry profile, crossing profile and balloon diameter while maintaining sufficient expansion force.

Source: Catheterization & Cardiovascular Intervention; China Insights Consultancy

China market size of CAD interventional procedural instrument market, in terms of sales value

China market size of CAD interventional procedural instrument market, in terms of sales value*, 2015-2030E

CAGR	2015-2020	2021-2025E	2026E-2030E
Standard balloons	9.77%	11.15%	6.20%
Scoring balloons	15.23%	16.59%	11.28%
BMS	-12.83%	-9.75%	-11.27%
Drug-coated balloons	N/A	35.93%	26.61%
Drug-eluting stents	8.40%	9.06%	3.40%
CTO balloons	12.25%	14.51%	11.17%
Microcatheter	17.36%	19.50%	15.83%

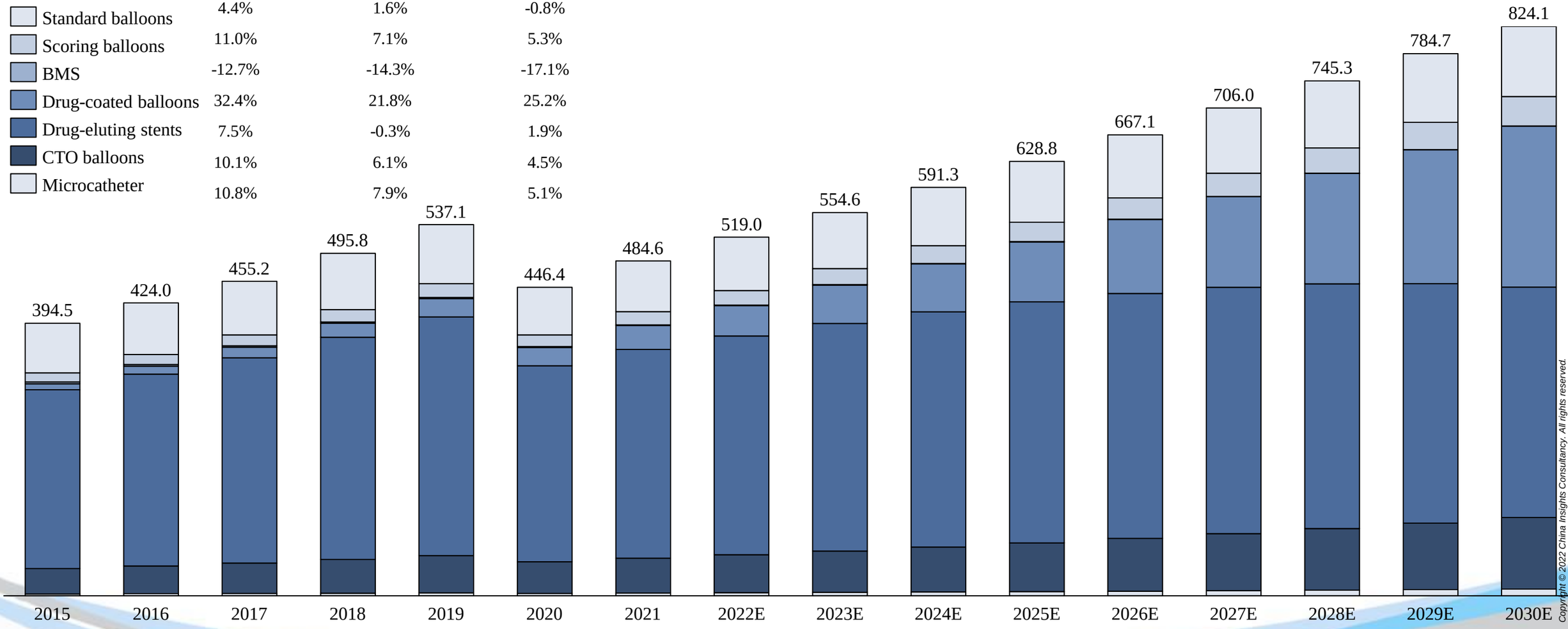


Source: China Insights Consultancy

Japan market size of CAD interventional procedural instrument market, in terms of sales value

Japan market size of CAD interventional procedural instrument market, in terms of sales value*, 2015-2030E

CAGR	2015-2020	2021-2025E	2026E-2030E
Standard balloons	4.4%	1.6%	-0.8%
Scoring balloons	11.0%	7.1%	5.3%
BMS	-12.7%	-14.3%	-17.1%
Drug-coated balloons	32.4%	21.8%	25.2%
Drug-eluting stents	7.5%	-0.3%	1.9%
CTO balloons	10.1%	6.1%	4.5%
Microcatheter	10.8%	7.9%	5.1%

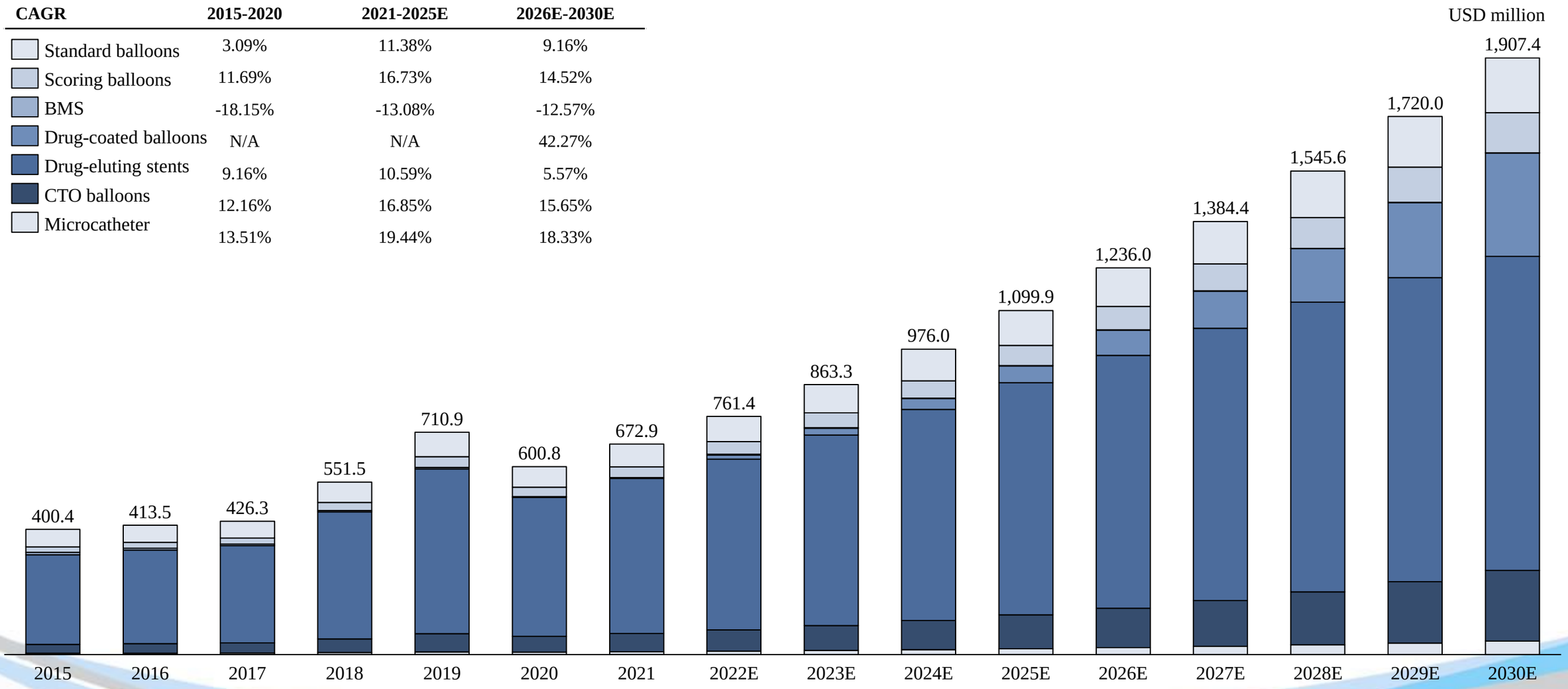


Source: China Insights Consultancy

The US market size of CAD interventional procedural instrument market, in terms of sales value

The US market size of CAD interventional procedural instrument market, in terms of sales value*, 2015-2030E

CAGR	2015-2020	2021-2025E	2026E-2030E
Standard balloons	3.09%	11.38%	9.16%
Scoring balloons	11.69%	16.73%	14.52%
BMS	-18.15%	-13.08%	-12.57%
Drug-coated balloons	N/A	N/A	42.27%
Drug-eluting stents	9.16%	10.59%	5.57%
CTO balloons	12.16%	16.85%	15.65%
Microcatheter	13.51%	19.44%	18.33%

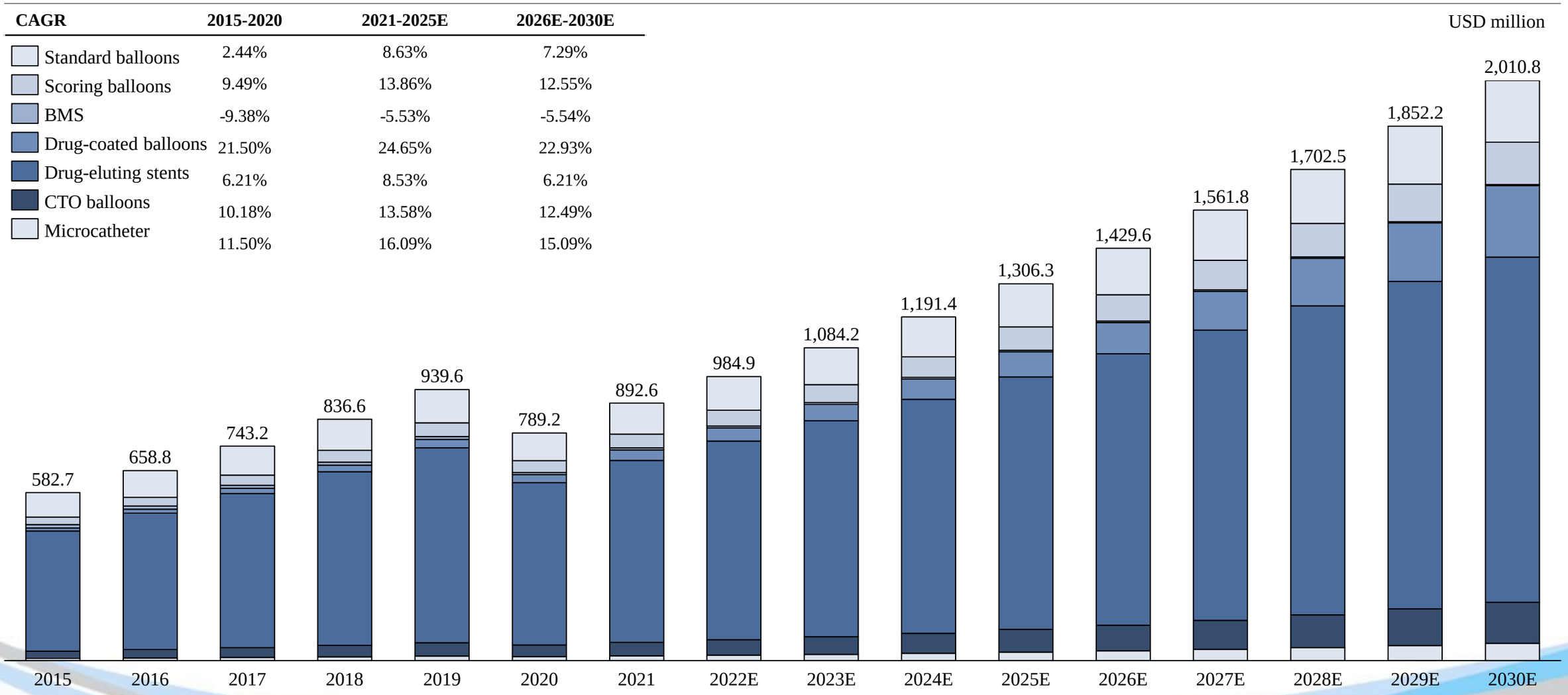


Source: China Insights Consultancy

Europe market size of CAD interventional procedural instrument market, in terms of sales value

Europe market size of CAD interventional procedural instrument market, in terms of sales value*, 2015-2030E

CAGR	2015-2020	2021-2025E	2026E-2030E
Standard balloons	2.44%	8.63%	7.29%
Scoring balloons	9.49%	13.86%	12.55%
BMS	-9.38%	-5.53%	-5.54%
Drug-coated balloons	21.50%	24.65%	22.93%
Drug-eluting stents	6.21%	8.53%	6.21%
CTO balloons	10.18%	13.58%	12.49%
Microcatheter	11.50%	16.09%	15.09%

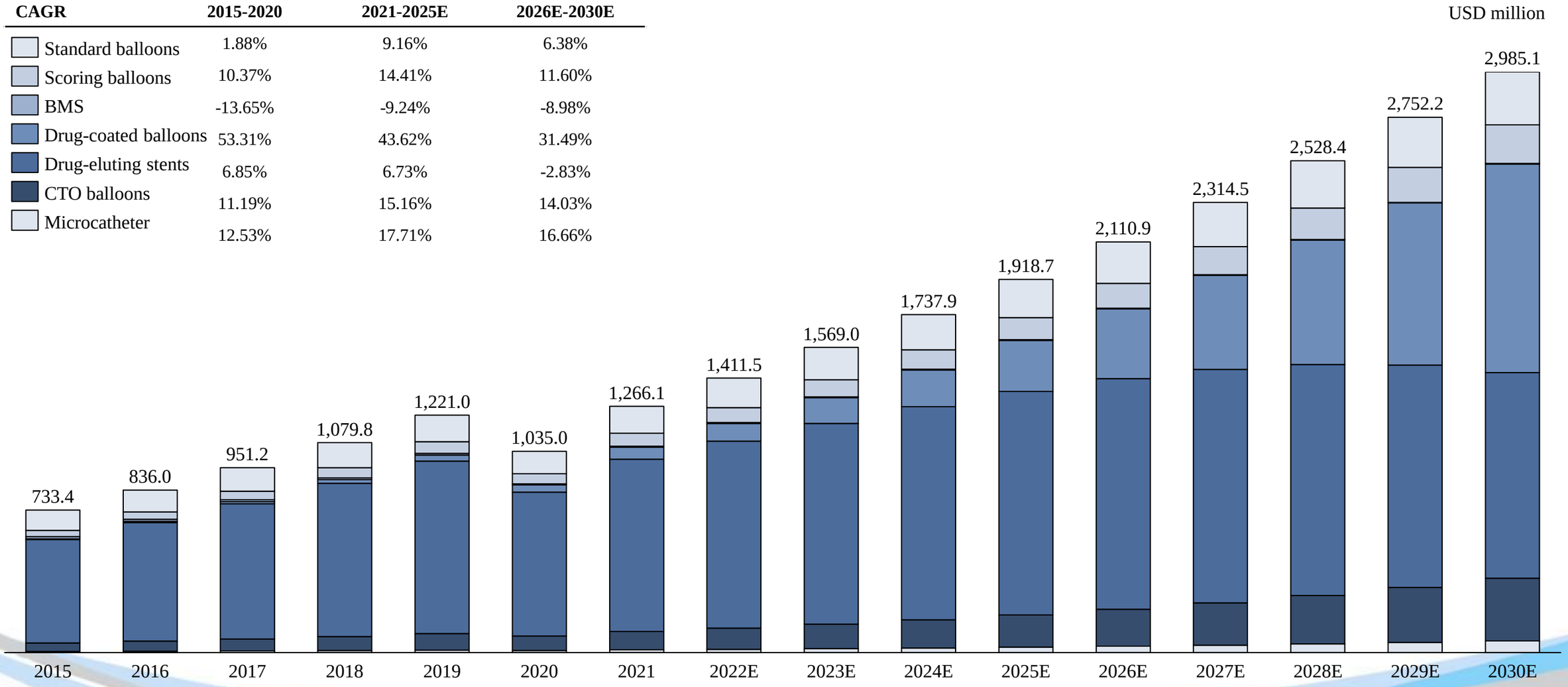


Source: China Insights Consultancy

APAC* market size of CAD interventional procedural instrument market, in terms of sales value

APAC market size of CAD interventional procedural instrument market, in terms of sales value*, 2015-2030E

CAGR	2015-2020	2021-2025E	2026E-2030E
Standard balloons	1.88%	9.16%	6.38%
Scoring balloons	10.37%	14.41%	11.60%
BMS	-13.65%	-9.24%	-8.98%
Drug-coated balloons	53.31%	43.62%	31.49%
Drug-eluting stents	6.85%	6.73%	-2.83%
CTO balloons	11.19%	15.16%	14.03%
Microcatheter	12.53%	17.71%	16.66%



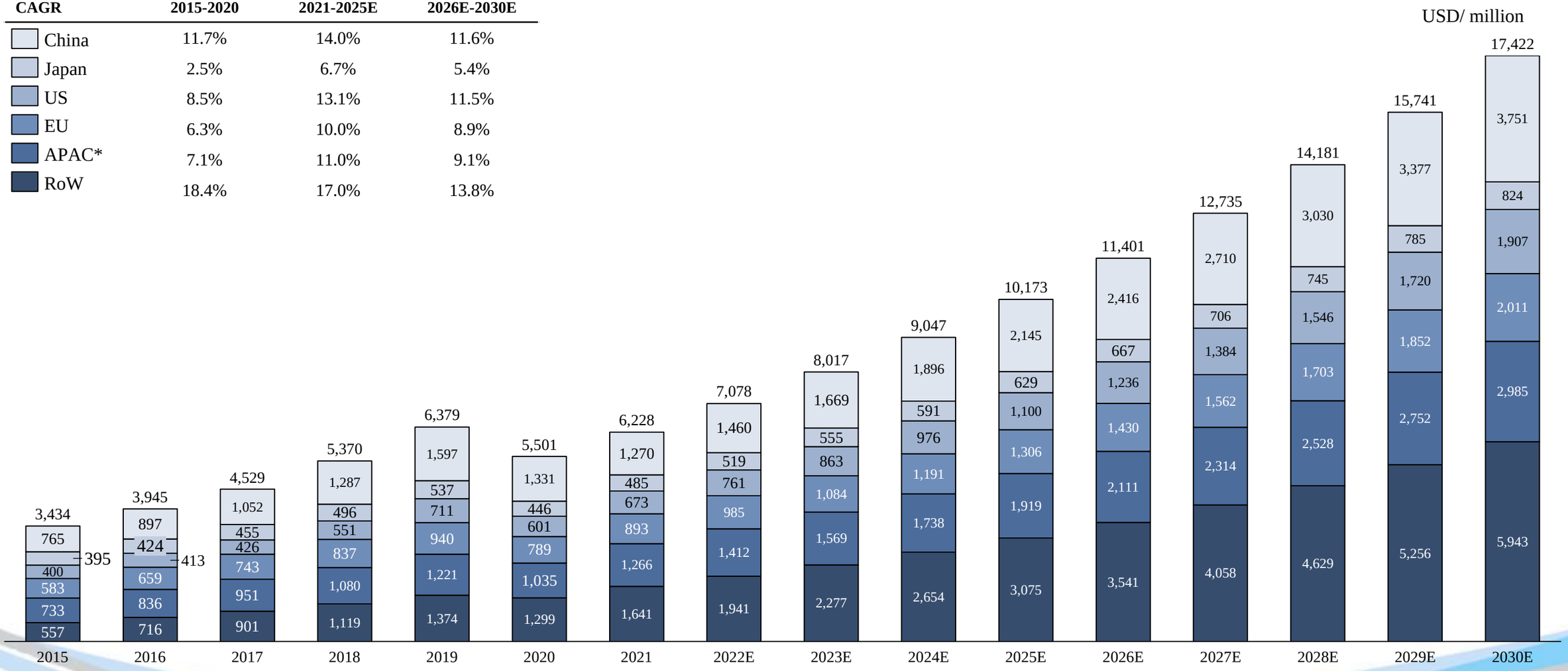
*APAC: APEC excluding China, Japan, U.S. and Russia

Source: China Insights Consultancy

Global PCI instrument market size by country, China, Japan, the U.S. and Europe are the main markets, accounted for 53% of market share in Global PCI instrument market in 2021

Global PCI instrument market size by country

CAGR	2015-2020	2021-2025E	2026E-2030E
China	11.7%	14.0%	11.6%
Japan	2.5%	6.7%	5.4%
US	8.5%	13.1%	11.5%
EU	6.3%	10.0%	8.9%
APAC*	7.1%	11.0%	9.1%
RoW	18.4%	17.0%	13.8%

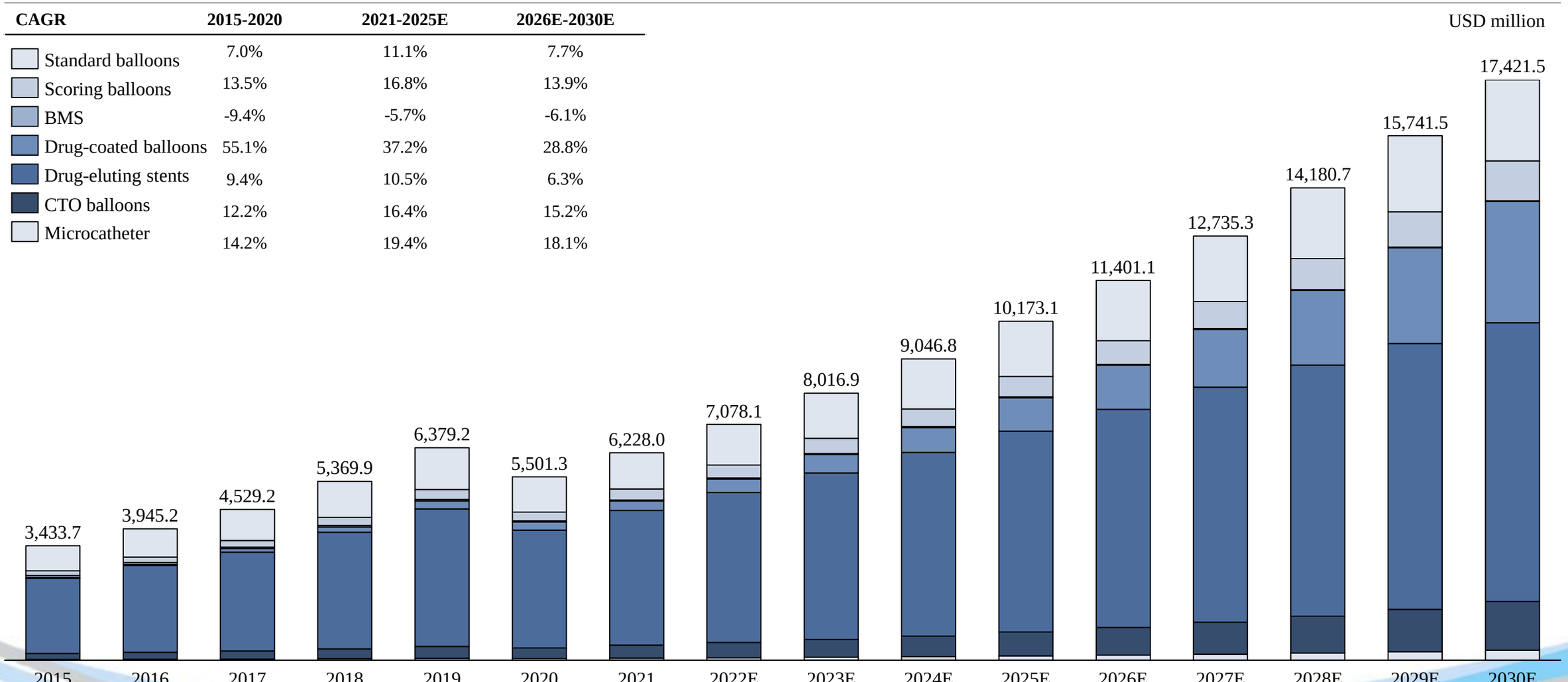


Source: China Insights Consultancy

Global market size of PCI procedural instrument market, in terms of sales value

Global market size of PCI procedural instrument market, in terms of sales value*, 2015-2030E

CAGR	2015-2020	2021-2025E	2026E-2030E
Standard balloons	7.0%	11.1%	7.7%
Scoring balloons	13.5%	16.8%	13.9%
BMS	-9.4%	-5.7%	-6.1%
Drug-coated balloons	55.1%	37.2%	28.8%
Drug-eluting stents	9.4%	10.5%	6.3%
CTO balloons	12.2%	16.4%	15.2%
Microcatheter	14.2%	19.4%	18.1%



Source: China Insights Industry Consultancy Limited, American Heart Association, Journal of American College of Cardiology, Centers for Disease Control and Prevention, Census Bureau, European Society of Cardiology, Europe Association of PCI, Chinese Circulation Journal, National Healthcare Security Administration, World Heart Federation, Ministry of Health, Labour and Welfare (Japan) and other literature review and expert interviews

Centralized procurement results of PCI stents

-Published results of centralized procurement of CAD drug-eluting stents, effective in Jan.1st 2021

Centralized procurement results of PCI stents

Device Name	Application Number	Company Name
药物涂层支架系统（雷帕霉素）	国械注准20173461407	Jw Medical Systems Limted
药物洗脱冠脉支架系统	国械注准20193131802	Essen Technology (Beijing) Co., Ltd.
冠脉雷帕霉素洗脱钴基合金支架系统	国械注准20163462305	Shanghai MicroPort Medical (Group) Co., Ltd.
钴基合金雷帕霉素洗脱支架系统	国械注准20173460564	Lepu Medical Technology (Beijing) Co., Ltd.
药物洗脱冠脉支架系统	国械注进20163460682	Medtronic Inc.
冠脉雷帕霉素洗脱钴基合金支架系统	国械注准20203130662	Shanghai MicroPort Medical (Group) Co., Ltd.
药物支架系统	国械注准20163461174	Kinhely Bio-Tech Co., Ltd.
铂铬合金依维莫司洗脱冠状动脉支架系统	国械注进20153130608	Boston Scientific Corporation
依维莫司洗脱冠状动脉支架系统	国械注进20173466661	Boston Scientific Corporation
冠状动脉钴铬合金可降解涂层雷帕霉素药物洗脱支架系统	国械注准20163460595	Medfavour (Beijing) Medical Co., Ltd.

Source: Healthcare Securitization Administration; China Insights Consultancy

Centralized procurement results of PCI pre-dilatation balloons

-Published results of centralized procurement of CAD pre-dilatation balloons in Guangdong province, effective in Feb.1st 2021

Centralized procurement results of PCI pre-dilatation balloons

Device Name	Application Number	Company Name	Purchase Volume
PTCA球囊导管	国械注准20153031321	Apt Medical Inc.	16751
PTCA球囊扩张导管	国械注准20153030384	Shanghai MicroPort Medical (Group) Co., Ltd.	13701
PTCA球囊扩张导管	国械注准20163772020	Lepu Medical Technology (Beijing) Co., Ltd.	11176
一次性使用冠状动脉球囊扩张导管	国械注准20153030676	Brosmed Medical Co., Ltd.	8251
冠状动脉球囊扩张导管 MINI TREK RX Coronary Dilatation Catheter	国械注进20153030390	Abbott Laboratories Trading (Shanghai) Co., Ltd.	7891
冠状动脉球囊扩张导管 TREK RX Coronary Dilatation Catheter	国械注进20153030391	Abbott Laboratories Trading (Shanghai) Co., Ltd.	6941
PTCA扩张导管	国械注进20173776638	BSC Int'l Medical Trade (Shanghai) Co., Ltd.	6478
PTCA球囊扩张导管Emerge PTCA Dilatation Catheter	国械注进20153032901	BSC Int'l Medical Trade (Shanghai) Co., Ltd.	5290
球囊扩张导管	国械注进20173771486	TERUMO MEDICAL(Shanghai) Co., Ltd.	5092
冠状动脉球囊扩张导管	国械注准20203030319	Neich Enterprise Co., Ltd.	5053
一次性使用冠状动脉球囊扩张导管	国械注准20173770784	Orbusneich Medical (Shenzhen) Co., Ltd.	4770
半顺应性PTCA球囊扩张导管	国械注准20183030557	Jiangsu Medoo Medical Equipment Technology. Co., Ltd.	3882
一次性使用无菌血管内导管：球囊扩张导管	国械注准20173770911	Scw Medicath Ltd.	1160
球囊扩张导管	国械注准20193030947	Shunmei Medical CO.,Ltd.	781
一次性使用无菌PTCA球囊扩张导管	国械注准20163771014	Beijing Demax Medical Technology Co., Ltd.	711
PTCA球囊扩张导管	国械注准20193030239	Shanghai Kindly Medical Instruments Co., Ltd.	507
PTCA球囊扩张导管	国械注准20183770054	Beijing Demax Medical Technology Co., Ltd.	292
一次性使用冠状动脉球囊扩张导管	国械注准20193030919	Nanjing MDP Medical Technology Co., Ltd	81
一次性使用冠状动脉球囊扩张导管	国械注准20183030523	Hengyi Medical Co., Ltd.	39

Source :Healthcare Security Administration of Guangdong Province; China Insights Consultancy

Centralized procurement results of PCI post-dilatation balloons

-Published results of centralized procurement of CAD post-dilatation balloons in Guangdong province, effective in Feb.1st 2021

Centralized procurement results of PCI post-dilatation balloons

Device Name	Application Number	Company Name	Purchase Volume
冠状动脉球囊扩张导管（商品名：NC TREK RX） NC TREK RX Coronary Dilatation Catheter	国械注进20173771561	Abbott Laboratories Trading (Shanghai) Co., Ltd.	10636
PTCA扩张导管PTCA Dilatation Catheter	国械注进20153033297	BSC Int'l Medical Trade (Shanghai) Co., Ltd.	10103
后扩张PTCA球囊导管	国械注准20183770045	Apt Medical Inc.	9789
快速交换球囊扩张导管（商品名：NC Sprinter）	国械注进20173770403	Medtronic Inc.	8018
一次性使用冠状动脉球囊扩张导管	国械注准20163030331	Brosmed Medical Co., Ltd.	5598
非顺应性PTCA球囊扩张导管	国械注准20153032227	Lepu Medical Technology (Beijing) Co., Ltd.	4347
冠状动脉球囊扩张导管	国械注准20193030599	Neich Enterprise Co., Ltd.	4181
非顺应性PTCA球囊扩张导管	国械注准20193031503	Sino Medical Sciences Technology Inc.	3732
一次性使用无菌非顺应性球囊扩张导管	国械注准20163771013	Beijing Demax Medical Technology Co., Ltd.	3468
球囊扩张导管	国械注进20173776796	TERUMO MEDICAL(Shanghai) Co., Ltd.	2073
一次性使用冠状动脉球囊扩张导管	国械注准20153030603	Orbusneich Medical (Shenzhen) Co., Ltd.	1941
非顺应性PTCA球囊扩张导管	国械注准20183770044	Beijing Demax Medical Technology Co., Ltd.	466
非顺应性冠状动脉球囊扩张导管	国械注准20193030800	Shunmei Medical CO.,Ltd.	202
非顺应性球囊扩张导管	国械注准20193030954	Kossel Medtech (Suzhou) Co., Ltd.	100
一次性使用非顺应性冠状动脉球囊扩张导管	国械注准20193030937	Nanjing MDP Medical Technology Co., Ltd	100
一次性使用冠状动脉高压球囊扩张导管	国械注准20193030114	Hengyi Medical Co., Ltd.	10

Source: Healthcare Security Administration of Guangdong Province; China Insights Consultancy

Centralized procurement results of PCI drug coated balloons

-Published results of centralized procurement of CAD drug coated balloons in Guangdong province, , effective in Feb.1st 2021

Centralized procurement results of PCI drug coated balloons

Device Name	Application Number	Company Name	Purchase Volume
紫杉醇释放冠脉球囊导管	国械注进20173771633	B.braun MEDICAL (SHANGHAI) International Trading Co., Ltd.	1336
紫杉醇释放冠脉球囊导管	国械注进20183030330	B.braun MEDICAL (SHANGHAI) International Trading Co., Ltd.	1087
药物涂层冠脉球囊导管	国械注准20203030561	Lepu Medical Technology (Beijing) Co., Ltd.	632
药物涂层冠脉球囊导管	国械注准20193031052	Shanghai Shenqi Medical Co., Ltd.	565
紫杉醇释放冠脉球囊扩张导管	国械注进20193030495	Cardionovum Medical Device (Wuhan) Co., Ltd.	243
药物洗脱球囊导管	国械注准20173771535	Yinyi(liaoning)Biotech CO.,LTD.	100

Source: Healthcare Security Administration of Guangdong Province; China Insights Consultancy

China's centralized purchasing leads to 90% drop in price of coronary stent

-10 varieties of coronary stents were successful following bidding from the results of the initial round of Chinese government's centralized procurement program, which were unveiled on Nov 5

Centralized procurement results of PCI instruments

Policy Unveiled date	**2020.11.05**
Price comparison	Coronary stents, once priced at more than **13,000 yuan (about $1,500)** each, are expected to become available in Chinese hospitals at roughly **700 yuan** for the treatment of corona3ry heart disease.
Decreasing rate	The average price for the same products from the same enterprises has decreased by **93 percent** from 2019. The average price reduction for domestically made products is **92 percent**, and it is **95 percent** for imported products.
Number of enterprises	The selected products are from eight of a total of **11 Chinese and foreign enterprises** that joined the bidding.
Number of institutions participated	More than **2,400 health institutions** across China participated in the centralized procurement, including those who usually purchase more than **500 coronary stents** a year.
Websites	http://www.gov.cn/xinwen/2021-07/14/content_5624766.htm http://www.gd.gov.cn/gdywdt/bmdt/content/post_3178389.html http://english.www.gov.cn/news/videos/202107/09/content_WS60e808f9c6d0df57f98dca8d.html http://english.www.gov.cn/news/topnews/202011/06/content_WS5fa4886ec6d0f7257693f2ff.html

Source: The state council; Healthcare Security Administration of Guangdong Province; China Insights Consultancy

Competitive landscape

Market share of PCI balloon in terms of sales volume by different regions, 2021

China		Japan		U.S.		Europe	
Company A (the U.S.)	~20%	Company C (Japan)	30%-35%	Company B (the U.S.)	~30%	Company A (the U.S.)	~30%
Company B (the U.S.)	15%~18%	**OrbusNeich (China)**	**20%**	Company D (the U.S.)	~28%	Company B (the U.S.)	~25%
Company C (Japan)	15%~18%	Company F (Japan)	~15%	Company A (the U.S.)	~22%	Company D (the U.S.)	~23%
Company D (the U.S.)	10%-15%	Company G (Japan)	~10%	Company J (the U.S.)	~10%	**OrbusNeich (China)**	**11%**
Company E (China)	~8%	Company B (the U.S.)	<5%	Company H (Europe)	<5%	Company H (Europe)	~10%
OrbusNeich (China)	**8%**	Company D (the U.S.)	<5%	**OrbusNeich (China)**	**3%**	Company J (the U.S.)	<5%

Other regions with significant market share, 2021

Hongkong	~52%	Pakistan	~59%	Russia	~26%
Singapore	~57%	Indonesia	~38%	Switzerland	~26%
Malaysia	~41%	Italy	~20%	Czech Republic	~33%
Taiwan	~40%	Slovakia	~40%	The Netherlands	~25%

Source: China Insights Industry Consultancy Limited, American Heart Association, Journal of American College of Cardiology, Centers for Disease Control and Prevention, Census Bureau, European Society of Cardiology, Europe Association of PCI, Chinese Circulation Journal, National Healthcare Security Administration, World Heart Federation, Ministry of Health, Labour and Welfare (Japan) and other literature review and expert interviews

Introduction to orbital atherectomy

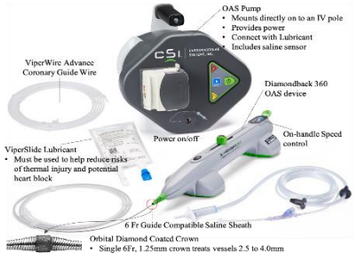
- Orbital atherectomy is performed with Diamondback 360º Orbital Atherectomy system and the crown can follow a forward and backward motion across the lesion for better plaque removal.

Introduction to Orbital Atherectomy(OA)

- **Orbital atherectomy(OA)** is an adjunctive therapy used for lesion preparation of calcified plaque before percutaneous coronary intervention (PCI) and peripheral percutaneous endovascular interventions. Its goal is to modify calcified plaque to enable balloon angioplasty and facilitate stent expansion.
- OA is performed with the **Diamondback 360° Orbital Atherectomy System**, a new atherectomy device utilizing an orbiting eccentric diamond-coated crown on the end of a drive shaft powered by a pneumatic drive console. The shaft and crown are advanced over a preplaced 0.014" proprietary guidewire, the ViperWire™. The orbital motion of the crown removes plaque from within a diseased arterial segment; as the crown orbits, the debulking area increases, and with increments in speed, the area increases further.
- About 2.21% of patients undergoing PCI will use atherectomy device, in which 34.5% of patients will use OA and about 60.15% will use RA.

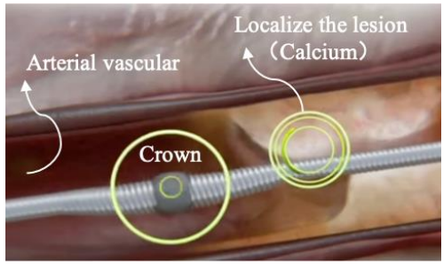
Procedure of Orbital Atherectomy

1 Prepare equipment



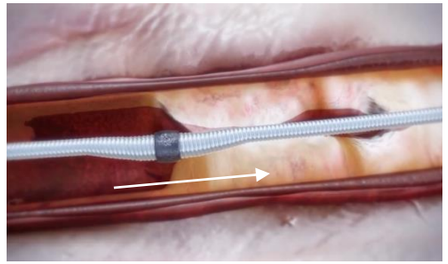
- Gather equipment (OAS, guide catheter, IV pole etc.)
- Set up the OAS pump
- Stiff coronary guidewire prepped for insertion

2 Access Arterial vascular Localize the target lesion



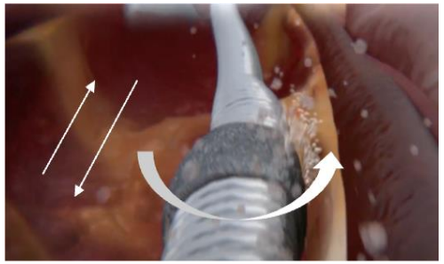
- Access arterial vascular using a 6 Fr sheath, access the lesion with a guide catheter
- Localize and evaluate the target lesion using angiography, IVUS, or OCT. Cross the lesion with coronary guidewire

3 Ensure appropriate crown advancement



- Prepare lubricant and ensure appropriate crown advancement via advancer knob and crown rotation using on/off button
- Advance the crown to about 10mm proximal to target lesion

4 Activate crown rotation



- Press down on the brake lever to engage the brake, press on/off button to activate crown rotation at low speed(80000rpm). Can consider high speed (120000 rpm) if no tortuosity is identified and vessel size is adequate.

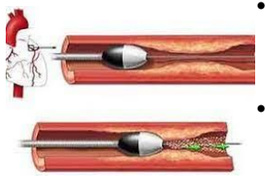
- **Maintain continuous movement**; Perform a series of intermittent treatment intervals **back and forth** across the lesion.
- Time limit: A maximum recommended treatment interval is **30 seconds**. The maximum treatment time per OAD is 5 minutes.

Source: NCBI ;ACC; Cath Lab Digest; China Insights Consultancy

Comparison between orbital atherectomy and rotational atherectomy

- Orbital atherectomy and rotational atherectomy are different in guide size, cutting direction and plaque debris released, and they are often used together for better calcified plaque modification.

Comparison between orbital atherectomy and rotational atherectomy



- **Rational atherectomy(RA)** is an atheroablative technology that enables percutaneous coronary intervention(PCI) for complex, calcified coronary lesions.
- RA is performed with a rotablator catheter consisting of a spring coil shaft with a burr at the tip. The front edge of the burr is the ablating portion, oval shaped and covered with diamond crystals.

Differences between OA and RA

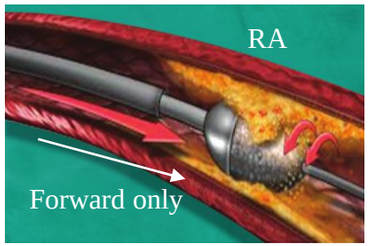
➢ **Guide size**

OA Crown

RA Burr

- OA: Treat all vessel diameters with a 6 Fr guiding catheter and don't need to upsize the guide catheter when using high-speed feature to treat larger diameter vessels.
- RA: Need to change the size of burr to fit the size of the vessel (Usually 6 Fr or larger can use a 1.25 mm burr with a 5F guide)

➢ **Cutting direction**

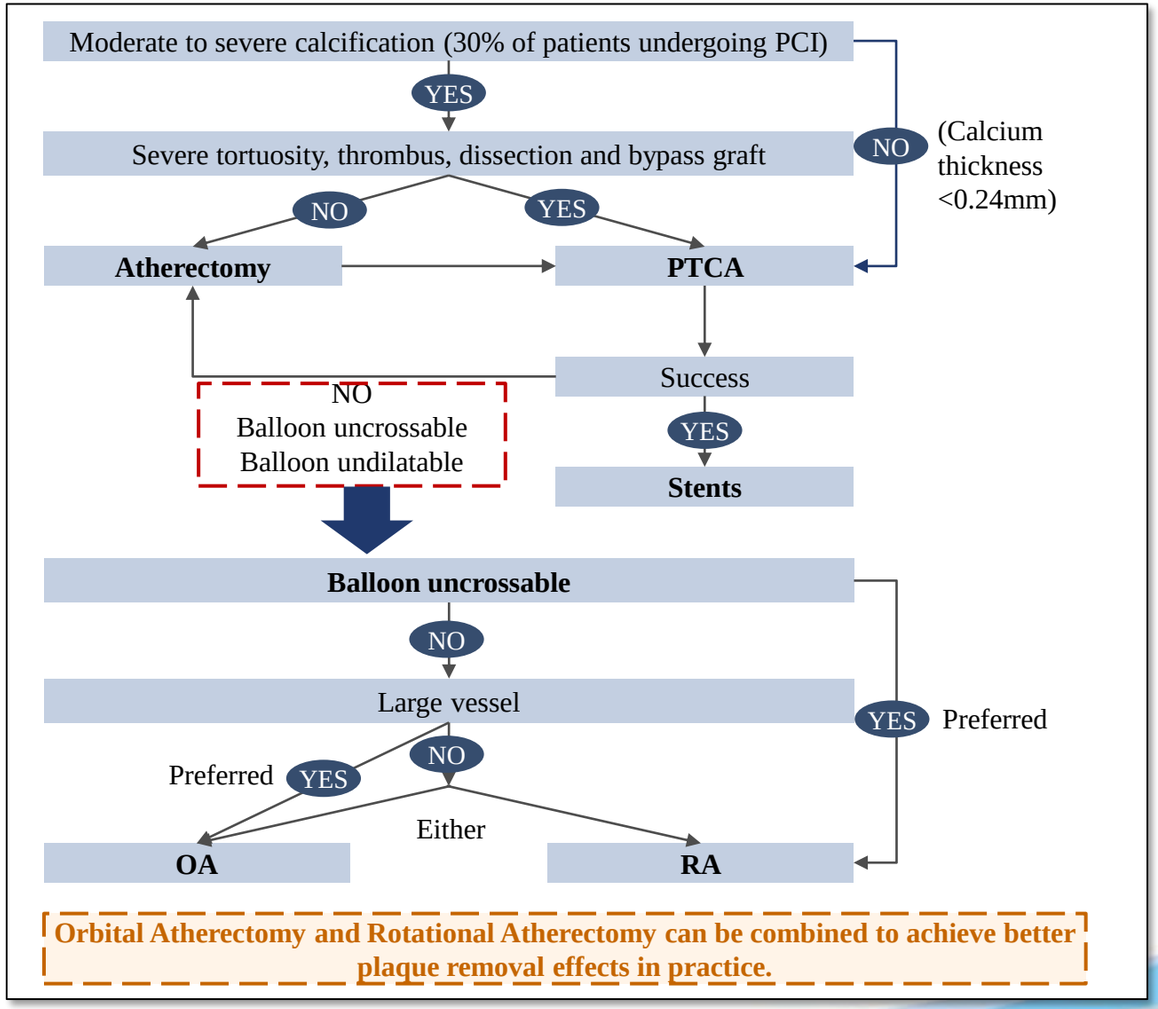


- OA: Forward and backward; Slow advancement
- RA: Forward only

➢ **plaque debris released**

- Smaller size released during OA (2 in OA vs. 5 to 10 mm in RA)

When to perform orbital atherectomy and rotational atherectomy



Source: NCBI; ICR; China Insights Consultancy

Growth drivers and future trends of global coronary artery interventional instrument market

Growth drivers and future trends of global coronary artery interventional instrument market

Growth drivers and future trends	Description
Increasing coronary artery disease prevalence	• Coronary artery disease is common among the elderly and with the rise in the geriatric population worldwide, the prevalence of CAD is increasing. What's more, people's unhealthy lifestyles such as smoking, alcohol consumption and increased stress are also key factors contributing to the rise in coronary artery disease among young people.
Continuous investment in the industry	• Coronary artery interventional instrument market is very important in treating CAD patients. Governments are paying increasing attention to coronary artery interventional instruments and have introduced several favorable policies. Manufacturers will invest continuously to do more research and innovate to keep their products up to date.
Rising demand for PCI	• Patients with coronary artery disease are more willing to choose percutaneous coronary intervention surgeries for treatment because of its advantages of small trauma, wide indications, safety and reliability compared with traditional treatment. Doctors also prefer to perform such surgeries because of less risks.
Continuous product development	• As development and innovation of medical devices accelerates, medical devices treating CAD are expected to increase in quality and prominence, and achieve better penetration in the global market. As such, the continuous development and innovation of medical devices also enhances room for market expansion.

Source: China Insights Consultancy

Growth drivers of coronary artery interventional instrument market in different markets

Growth drivers of coronary artery interventional instrument market in different markets

Countries and regions	Growth factors
China	• As domestic players increase their investment and gain more expertise in R&D and manufacturing, high quality and cost-effective domestic medical devices have gained increasing recognition and growing competitiveness against imported products in physicians and hospitals in China.
Japan	• Japan faces problem of increasingly elder population. In 2021, Japanese population has a median age of 48, the highest in the world. With more than 28.7% of the population over age of 65, the prevalence of age related diseases, such as coronary artery disease is high, creating a market with huge potential.
US	• The adaptation of sedentary lifestyle and high rates of obesity made US population vulnerable to coronary artery disease. According to CDC, approximately 36.9% of American adults age 20 or higher are obese, and obesity is an important risk factor of coronary artery disease. According to journal, over 80% of patients with CAD are overweight or obese.
Europe	• European countries tend to have well-established social securities systems and high social welfare. Medical expenditure per capita in Europe is largely higher than world average. Thus, creating a huge demand for medical devices. • European companies emphasize on the importance of medical innovations. In the past ten years, the number of patent applications in the field of medical devices has doubled and continues to grow.
APAC	• The APAC region (APAC) has more than 60% of the world's population for medical devices. Medical expenses in the APAC region are expected to be 7% per year growth, a growth rate surpassing that of the United States and Europe.

Source: China Insights Consultancy

Entry barriers of global coronary artery interventional instrument market

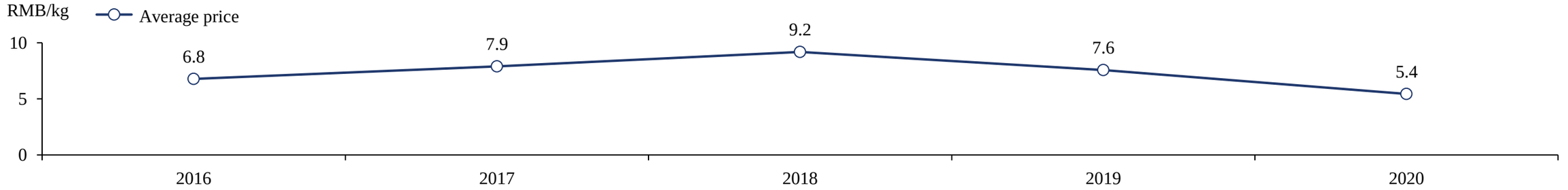
Entry barriers of global coronary artery interventional instrument market

Entry barriers	Description
Intensive technologies and continuous product innovation	• Multi-disciplinary expertise in material and mechanical engineering, product design and manufacturing are necessary in the development of coronary artery interventional instruments. And coronary artery is very important and complex which means related surgery instruments should be more sophisticated. New entrants may generally find it difficult to collect professionals and acquire the technologies in a short term.
Strict approval processes and regulatory issues	• Registration and regulation on Class III medical device are quite stringent in most of countries and regions that several government institutions take part in the separate parts of industry management and supervision. Strict access system and complex regulation make it tough for new entrants to keep compliance.
Manufacturing and quality management capabilities	• Medical device manufacturing is a complex process, especially for complicated devices. Experienced technicians with high productivity, advanced and highly automated facilities as well as the economies of scale contribute to the high entry barriers for the coronary artery interventional instrument industry. Meanwhile, a stringent quality control system is required to ensure product safety and efficacy. It is difficult for new entrants to establish such system due to lack of resources and experience.
Distribution channels	• Distributorship sales model is important for players in coronary artery interventional instrument market. Gaining recognition from target hospitals offering customized after-sales services and obtaining licenses and record-filing proof from regulatory authorities may all be important for sales. The entry barrier is formed due to the significant amount of time and funds needed to establish a network of qualified distributors.

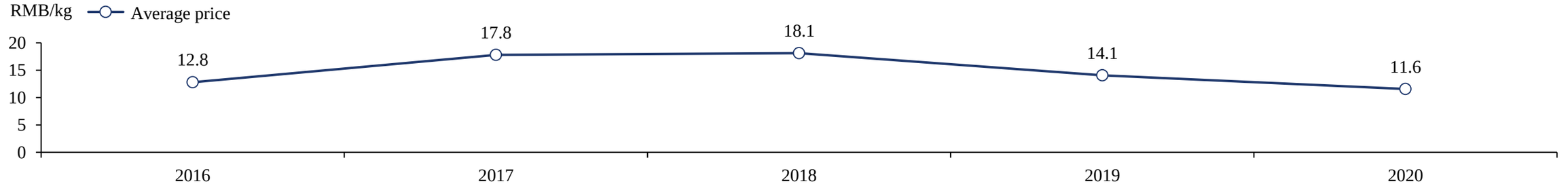
Source: China Insights Consultancy

Price of major raw materials used in producing balloon and stent

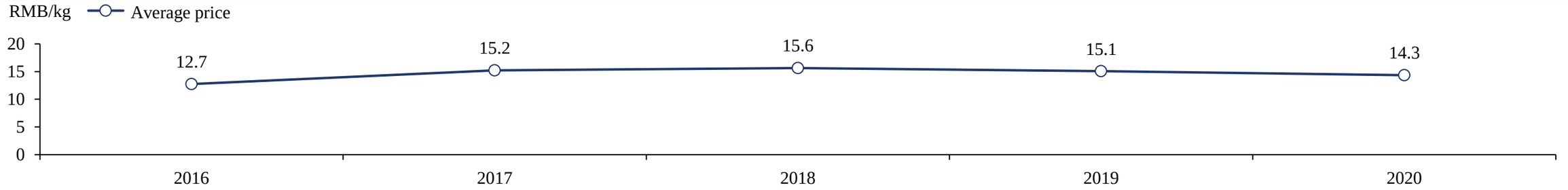
Annual average price of polyester in China, 2016-2020



Annual average price of nylon in China, 2016-2020



Annual average price of medical grade stainless steel in China, 2016-2020

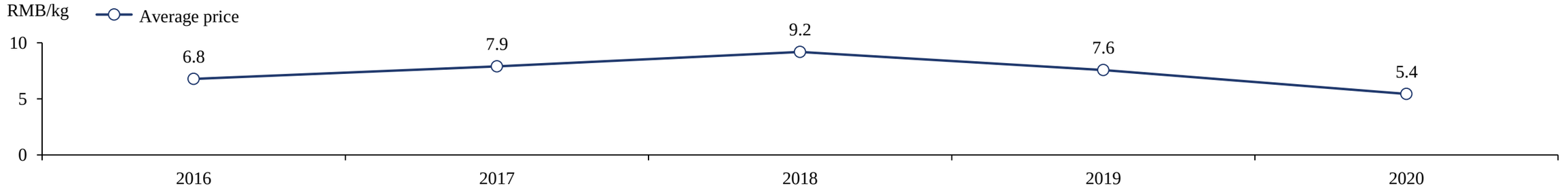


- Major raw materials used in producing balloons and stents include polyester, nylon and stainless steel. Fluctuations in prices of raw materials may affect the cost structure, product pricing and profitability of balloon and stent market players.

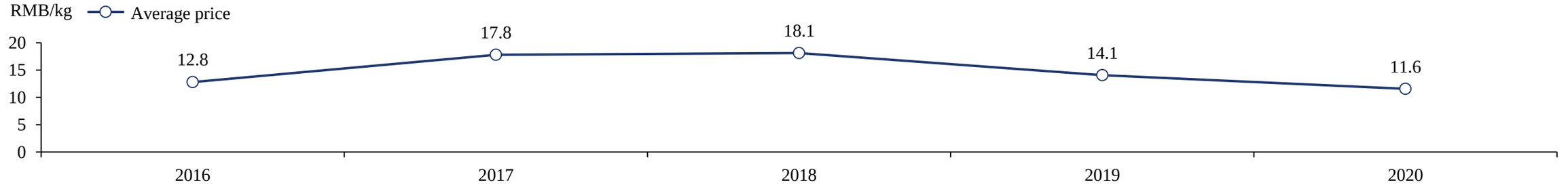
Source: iWind, China Insights Consultancy

Price of crude oil in comparison to raw materials used in producing balloon and stent

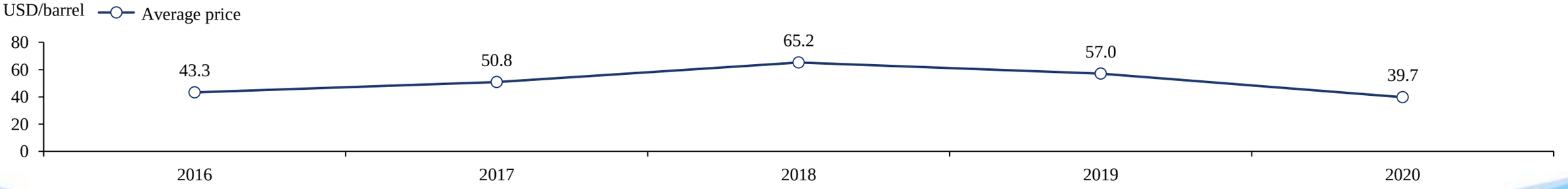
Annual average price of polyester in China, 2016-2020



Annual average price of nylon in China, 2016-2020



Annual closing price of crude oil, 2016-2020



Notes: Polyester is a manufactured synthetic fiber, it is a kind of plastic and is usually derived from petroleum. Like polyester, nylon is made from a non-renewable resource (oil) in an energy-intensive process. So the price fluctuations are similar.

Source: Yahoo finance, China Insights Consultancy

I. Overview of global medical device market
II. Overview of global coronary artery disease interventional procedural instrument market
III.Overview of global peripheral artery disease interventional procedural instrument market
IV.Overview of global neuro artery disease interventional procedural instrument market
V. Overview of global structural heart disease interventional procedural instrument market
VI.Appendix

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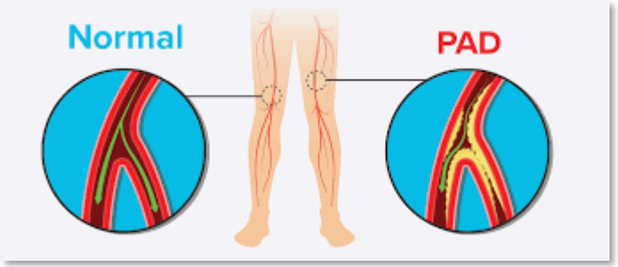
Introduction to peripheral artery disease

- Peripheral arterial disease that is common and is caused by a build-up of fatty deposits in the wall of leg arteries, and risk factors include high blood pressure, diabetes, smoking, high cholesterol, family history of heart disease, and old age

Introduction to and epidemiology of peripheral artery disease



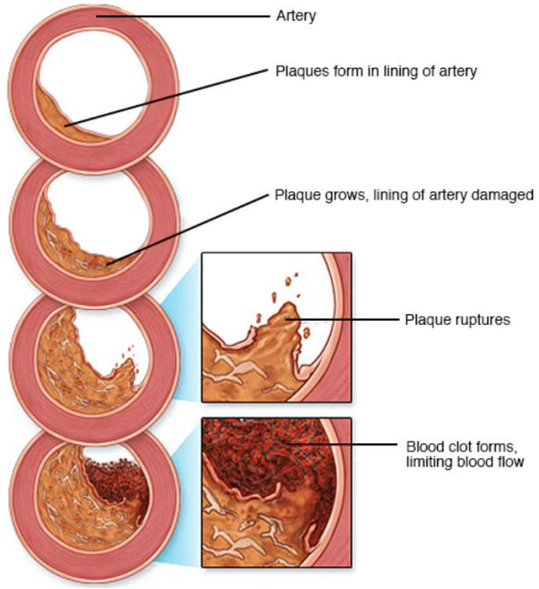
Introduction

- Peripheral artery disease (PAD) is usually caused by a build-up of fatty deposits in the walls of the leg arteries. The fatty deposits (atheroma) are made up of cholesterol and other waste substances. The build-up of fatty deposits on the walls of the arteries makes the arteries narrower and restricts blood flow to the legs. This process is called atherosclerosis. PAD affects the blood vessels causing them to narrow, therefore restricting the blood flow to the arms, kidneys, stomach, and most commonly, the legs.

Symptom

- The clinical spectrum of disease is wide and includes individuals who are asymptomatic as well as those with leg symptoms, notably intermittent claudication in which pain in the calf occurs on exercise and is relieved by rest. At the severest end of the clinical spectrum is critical limb ischaemia, which comprises rest pain, ulceration, and gangrene, and can lead to amputation.

Cause of peripheral arterial disease



Peripheral artery disease is often caused by atherosclerosis. Atherosclerosis is a process in which blood, fats such as cholesterol and other substances build up on artery walls.

Eventually, deposits called plaques may form. The deposits may narrow or block the arteries. These plaques can also rupture, causing a blood clot.

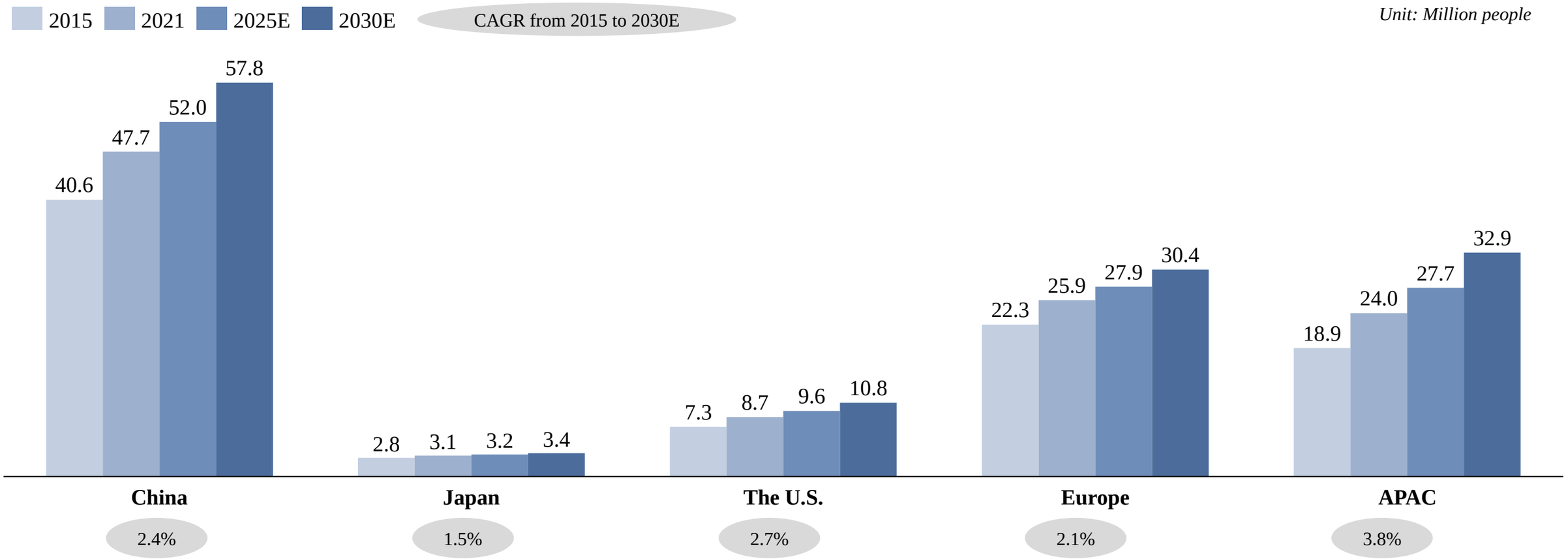
Risk factors

- People with high blood pressure
- People with diabetes
- Cigarette smoking
- People with family heart disease
- People with age over 50
- People with high cholesterol

Source: China Insights Consultancy

Global prevalence of PAD (lower limb)

Global prevalence of PAD (lower limb), by region, 2015vs.2022vs.2025Evs.2030E



**APAC: APEC excluding China, Japan, The US and Russia*

Source: China Insights Consultancy

Classification of lower extremity disease

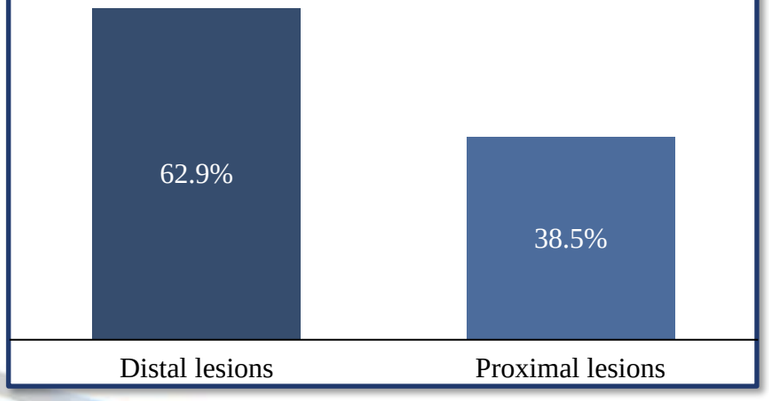
- Most of PAD patients have lower extremity arterial disease (LEAD), 62.9% LEAD patients have distal lesions, 38.5% LEAD patients have proximal lesions, and 13.4% LEAD patients have both distal and proximal lesions

Treatment path of peripheral arterial disease

Lesion location

- **Proximal lesions (above the knee)**—aortoiliac segments, including the distal abdominal aorta, right and left common iliac artery, right and left external iliac artery, and bifurcation of the right and left internal iliac artery;
- **Distal lesions (below the knee)**—femoropopliteal segments, including the right and left common femoral artery, bifurcation of the right and left deep femoral artery, the right and left superficial femoral artery, and right and left popliteal artery; and crural segments, including the right and left posterior tibial artery, right and left peroneal artery, and right and left anterior tibial artery;
- **Proximal and distal lesions**—including lesions or occlusions that presented at both proximal and distal locations.

In a cohort study, scientists enrolled 701 patients from two vascular surgery outpatient clinics with new-onset symptoms of peripheral arterial disease, most of them had lower extremity artery disease, approximately 13.4% of patients have both proximal and distal lesions.



- Lesions were proximal in 270, distal in 441, and proximal and distal in 94. Patients with proximal lesions were younger and less likely to be obese than those without proximal lesions. Older age, male sex, being without a partner, and lower anxiety scores were associated with distal lesions. Patients with both lesions were more likely to be single and less likely to be obese. Among 701 patients with peripheral arterial disease, approximately **88% have lower extremity disease**.

	With distal lesions	Without distal lesions	Total
With proximal lesions	**94 (13.4%)**	**176 (25.1%)**	270 (38.5%)
Without proximal lesions	**347 (49.5%)**	**84 (12.0%)**	431 (61.5%)
Total	441 (62.9%)	260 (37.1%)	701 (100%)

Source: ESC guidelines on the diagnosis and treatment of PAD; Journal of vascular surgery; China Insights Consultancy

Guidelines on the treatment of peripheral artery disease

- The treatment of peripheral arterial disease mainly includes three methods: medical treatment, surgical treatment and interventional treatment.

Guidelines on the treatment of peripheral arterial disease

Lesion	*Treatment type*	*Indication*	*Treatment method*	*Level of evidence*
Aorto-iliac occlusive lesions (above the knee)	**Interventional**	Patients with short (i.e. <5 cm) occlusive lesions	Endovascular therapy	I
	Surgical	Patients fit for surgery	Aorto-(bi)femoral bypass	IIa
	Interventional	Long and/or bilateral lesions in patients with severe comorbidities.	Endovascular therapy	IIa
	Surgical	Patients with an aortic occlusion extending up to the renal arteries	Open surgery	IIa
	Interventional and surgical	Patients with ilio-femoral occlusive lesions	Iliac stenting and femoral endarterectomy or bypass	IIa
	Surgical	Patients with no other alternatives for revascularization	Extra-anatomical bypass	IIb
Femoro-popliteal occlusive lesions (below the knee)	**Interventional**	Patients with short (i.e. <25 cm) lesions	Endovascular therapy	I
	Interventional	Patients with short (i.e. <25 cm) lesions	Primary stent implantation	IIa
	Interventional	Patients with short (i.e. <25 cm) lesions	Drug-eluting balloons	IIb
	Interventional	Patients with short (i.e. <25 cm) lesions	Drug-eluting stents	IIb
	Interventional	Patients with in-stent restenosis	Drug-eluting balloons	IIb

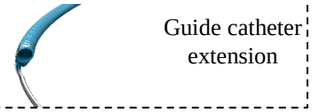
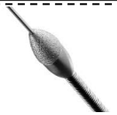
Source: ESC guidelines on the diagnosis and treatment of PAD; Journal of vascular surgery; China Insights Consultancy

Overview of PTA Instruments

Overview of PTA instruments

Introduction to PTA instruments:

In a general PCI procedure, the doctor uses a semi-complaint balloon to pre-expand the vessel and to determine using a stent or drug-coated balloon in latter step (based on the remaining stenosis after the pre-dilation.) In some cases, which patient presents moderate or severe calcified lesion, atherectomy is performed for further crossing of balloons and stents.

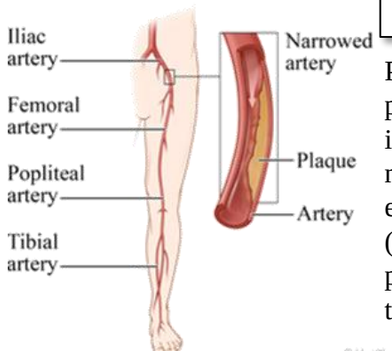
Procedural step	Lesion Access	Lesion Preparation		Lesion Therapy	Lesion Optimization
Condition	Tight, total occlusion and challenging anatomy	De novo, routine cases	Fibrotic, Mild to moderate calcification	Heavy to severe calcification	DES/DCB	Post DES/ OAS
	 Guide catheter extension • Guide catheter extension provides pathway for balloon and/or stent delivery	 Semi-compliant Balloon • Semi-compliant balloon is used in pre-dilation to expand the lesion for further treatment	 Scoring Balloon • Scoring balloon consists of wires stick to the balloon. It is used to modify calcified lesions.	 Orbital Atherectomy • OA is used to break the lesion into smaller bricks with orbital movement of the orbital crown.	 Drug Coated Balloon • A balloon coated with anti-proliferative drug is used in post-dilatation without stent	 Scoring Balloon • Scoring balloon consists of wires stick to the balloon. It is used to modify calcified lesions.
	 Microcatheter • Microcatheter is used in guidewire support, exchange and to access distal anatomy		 Cutting Balloon • Cutting balloon consists of 3 or 4 scoring wires bonded longitudinally for creating incisions in targeted lesions.	 Rotational Atherectomy • RA use a rotating abrasive burr to advance and break the calcified lesions.	 Drug Eluting Stent • A metal stent coated with anti-proliferative drug is used in lesion therapy to keep lesion open after surgery	 Non-compliant Balloon • Non-compliant balloons are able to expand to a certain diameter and exert high pressure on lesions.

Comparison between peripheral PTA and PTCA

- Except the difference of lesion positioning, the balloon used in PTA and PTCA are different in size parameter and the rate of burst pressure

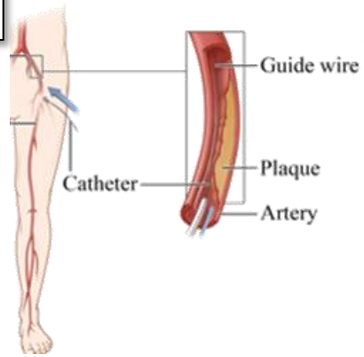
Comparison between peripheral PTA and PTCA

- Angioplasty is treatment designed to open blocked or narrowed arteries. An angioplasty is called a PTCA when used to treat a coronary artery obstruction and a PTA when treating other arteries, like carotid, subclavian, mesenteric, renal, and lower extremity artery. Generally, the differences between peripheral PTA and PTCA is the lesions location.



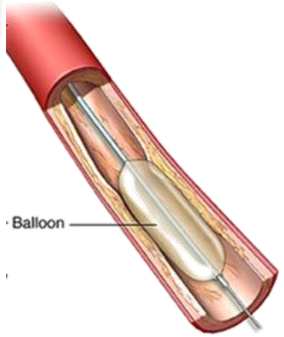
Lesion positioning

Peripheral artery plaque can occur in many areas, mainly in lower extremity artery (Iliac, femoral, popliteal, and tibial artery).



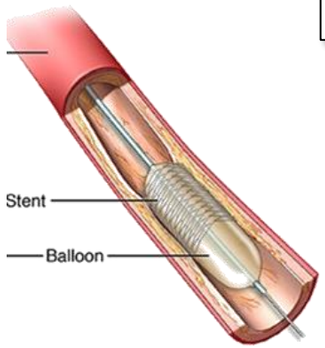
Catheter placing

Surgeon inserts a thin, flexible catheter through a femoral artery in the thigh. The catheter working length is **longer** than that used in coronary artery.



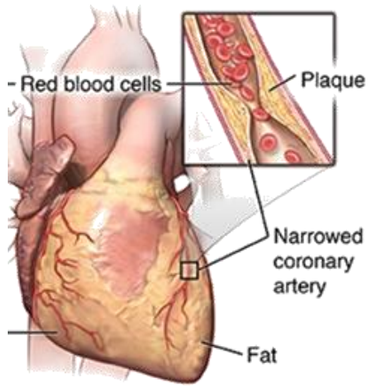
Pre-dilatation*

Surgeon uses a semi-compliant balloon to dilate the narrow artery before inserting the stent. The nominal pressure and rated burst pressure of peripheral semi-compliant balloon is **smaller**.



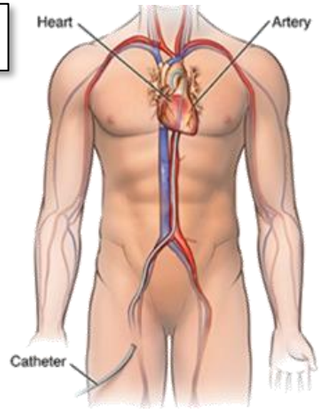
Post-dilatation

The non-compliant balloon is used in post-dilation. The peripheral balloon nominal pressure and rated burst pressure is **smaller** and the distal shaft diameter is **narrower**.



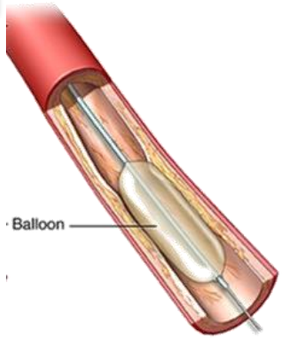
Lesion positioning

The coronary arteries wrap around the outside of the heart. Small branches dive into the heart muscle to bring it blood.



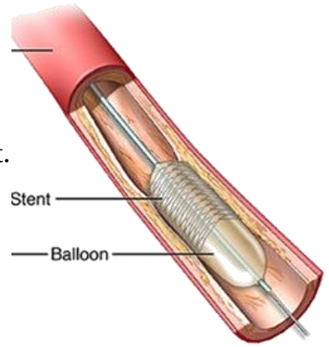
Catheter placing

Surgeon inserts a thin, flexible catheter in groin, neck or arm and threaded artery, through vessels to heart. The catheter working length is **shorter** than that used in peripheral artery.



Pre-dilatation*

Surgeon uses a semi-compliant balloon to dilate the narrow artery before inserting the stent. The nominal pressure and rated burst pressure of coronary semi-compliant balloon is **larger**.



Post-dilatation

The non-compliant balloon is used in post-dilation. The coronary balloon nominal pressure and rated burst pressure is **higher** and the distal shaft diameter is **wider**.

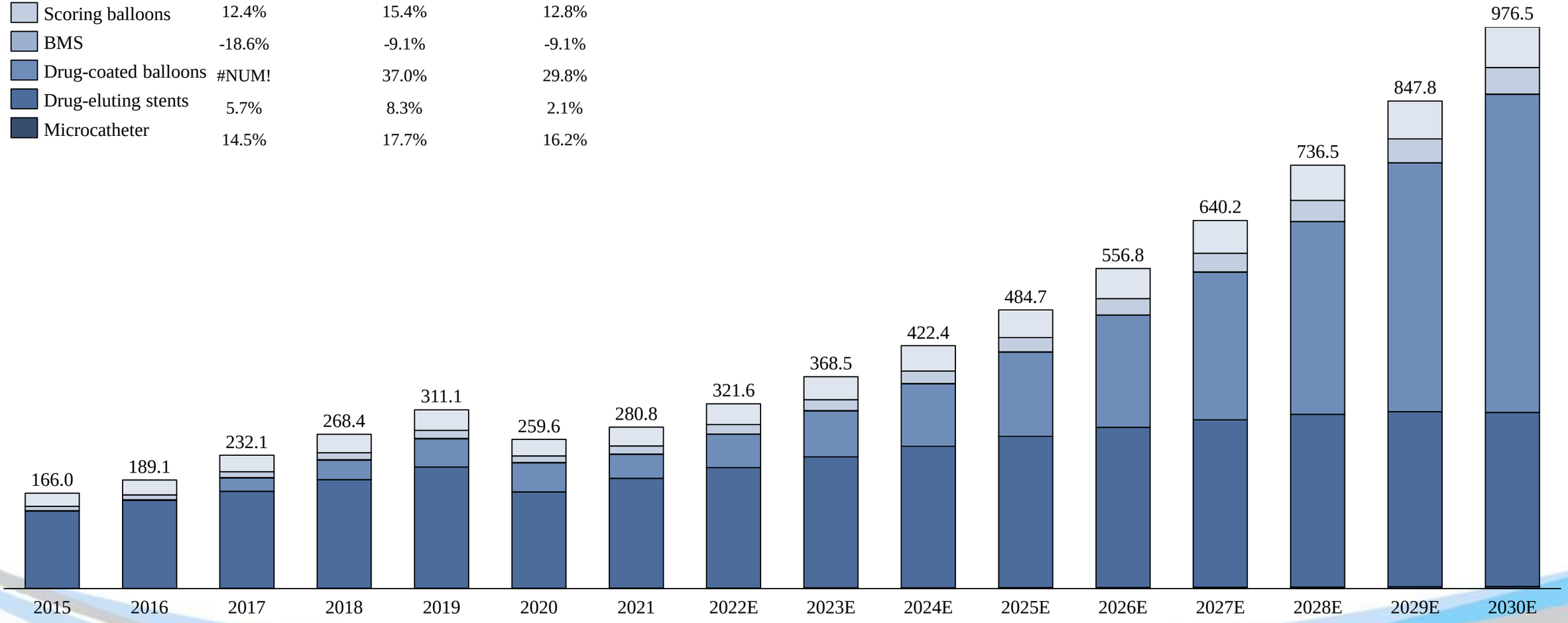
**Pre-dilatation: pre-dilatation could be used in peripheral PTA and PTCA but not always necessarily*

Source: China Insights Consultancy

China market size of PAD interventional procedural instrument market, in terms of sales value

China market size of PAD interventional procedural instrument market, in terms of sales value*, 2015-2030E

CAGR	2015-2020	2021-2025E	2026E-2030E
Standard balloons	4.5%	10.0%	7.7%
Scoring balloons	12.4%	15.4%	12.8%
BMS	-18.6%	-9.1%	-9.1%
Drug-coated balloons	#NUM!	37.0%	29.8%
Drug-eluting stents	5.7%	8.3%	2.1%
Microcatheter	14.5%	17.7%	16.2%

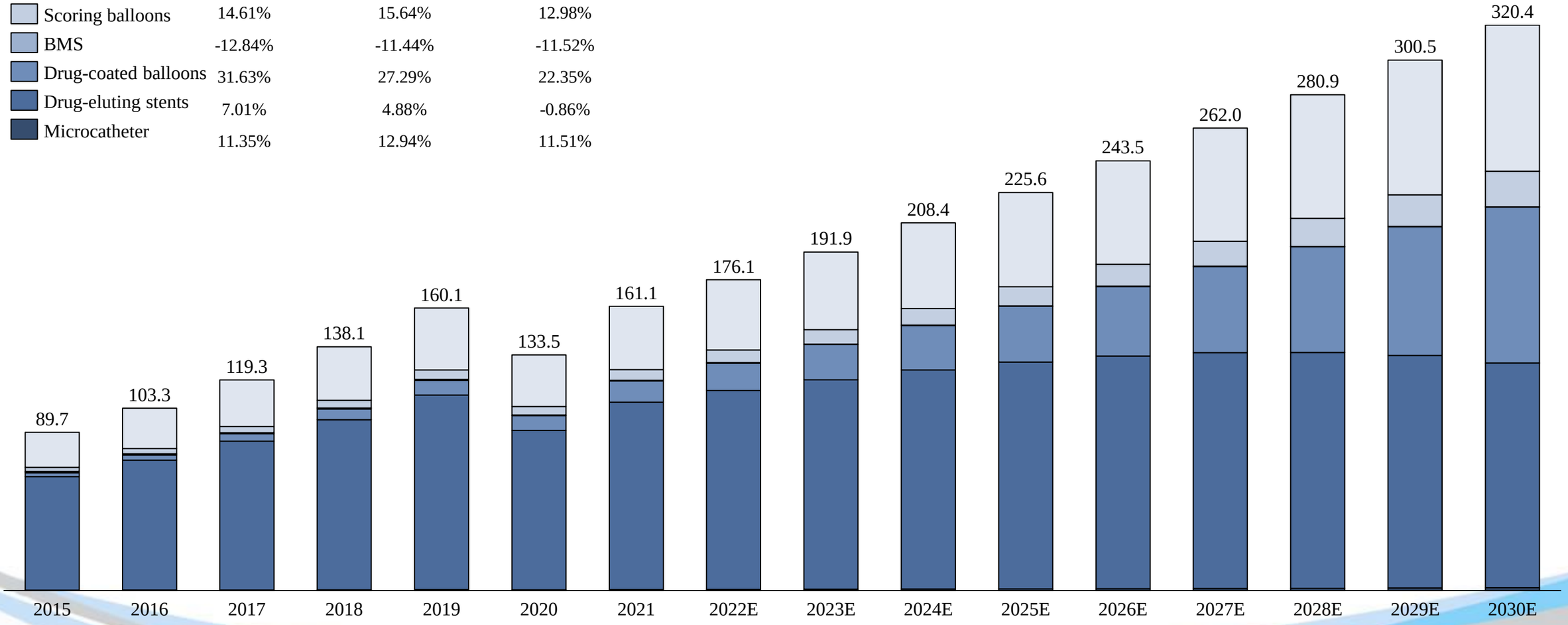


Source: China Insights Consultancy

Japan market size of PAD interventional procedural instrument market, in terms of sales value

Japan market size of PAD interventional procedural instrument market, in terms of sales value*, 2015-2030E

CAGR	2015-2020	2021-2025E	2026E-2030E
Standard balloons	8.05%	10.48%	9.00%
Scoring balloons	14.61%	15.64%	12.98%
BMS	-12.84%	-11.44%	-11.52%
Drug-coated balloons	31.63%	27.29%	22.35%
Drug-eluting stents	7.01%	4.88%	-0.86%
Microcatheter	11.35%	12.94%	11.51%

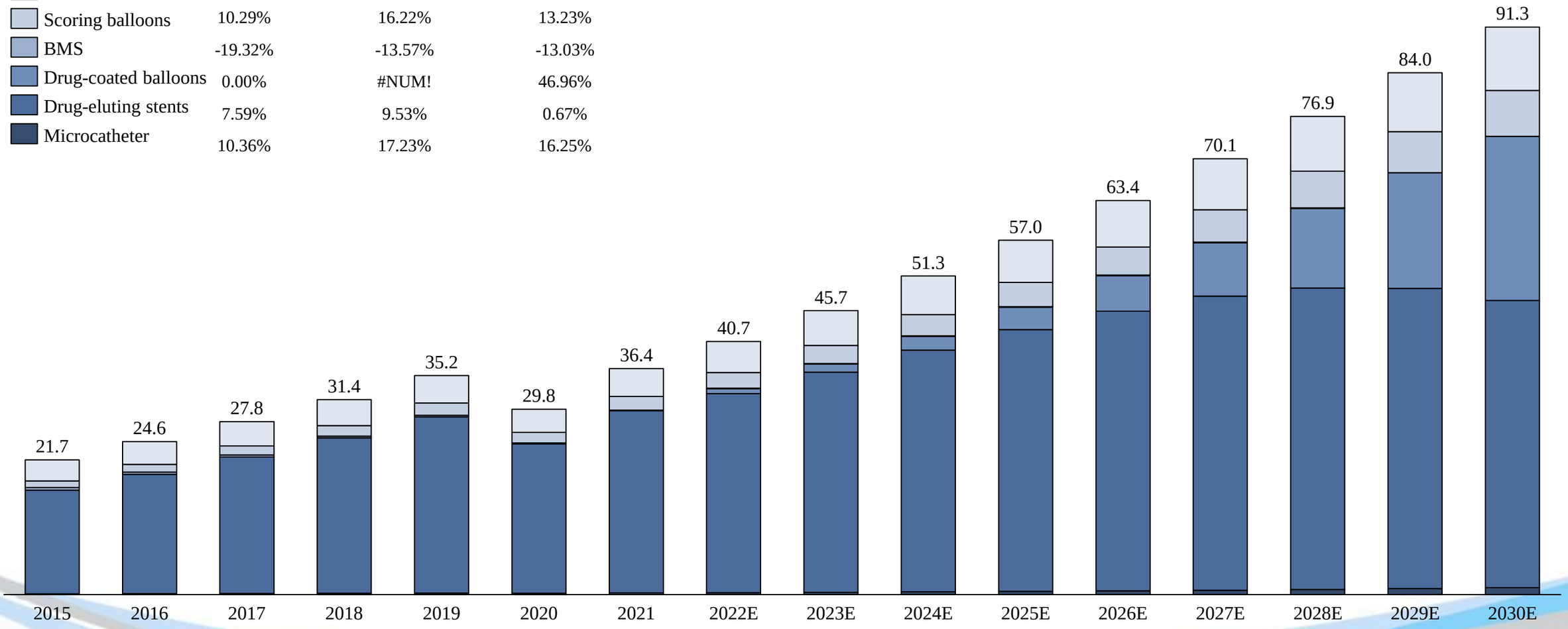


Source: China Insights Consultancy

The US market size of PAD interventional procedural instrument market, in terms of sales value

The US market size of PAD interventional procedural instrument market, in terms of sales value*, 2015-2030E

CAGR	2015-2020	2021-2025E	2026E-2030E
Standard balloons	1.79%	10.89%	7.93%
Scoring balloons	10.29%	16.22%	13.23%
BMS	-19.32%	-13.57%	-13.03%
Drug-coated balloons	0.00%	#NUM!	46.96%
Drug-eluting stents	7.59%	9.53%	0.67%
Microcatheter	10.36%	17.23%	16.25%

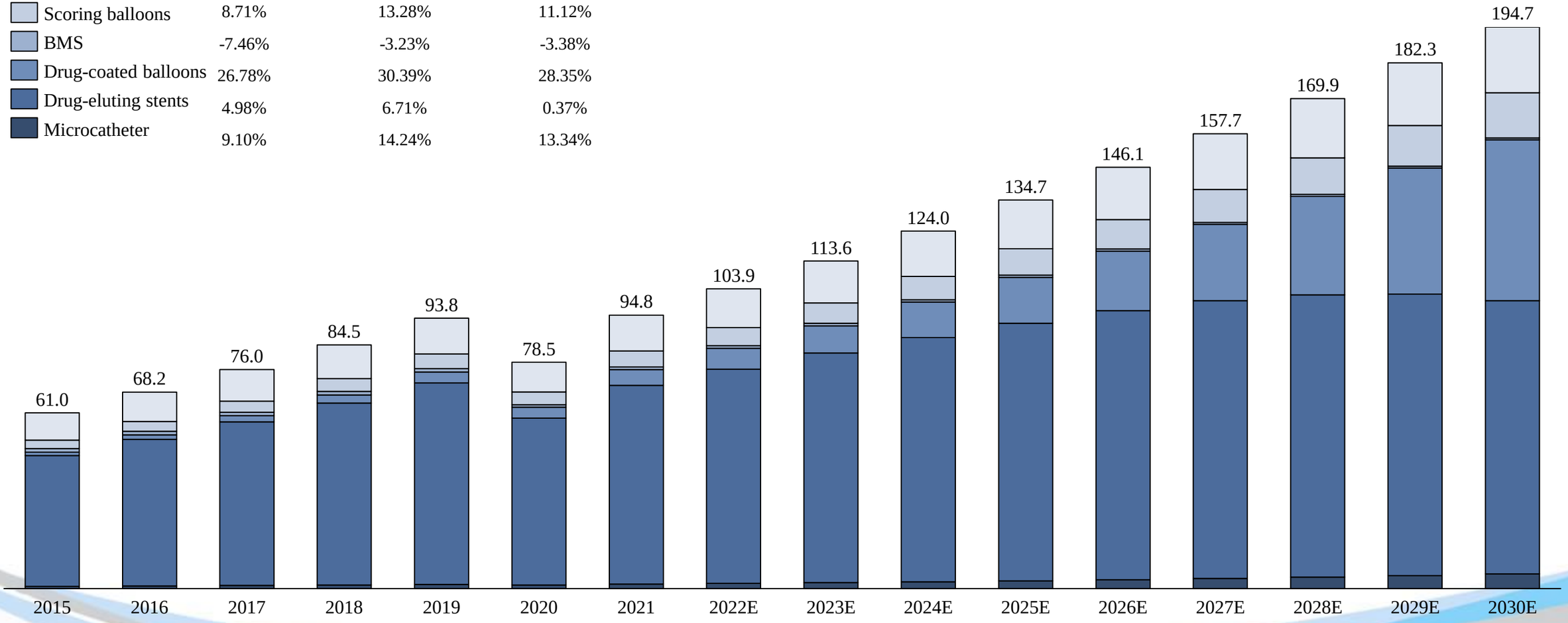


Source: China Insights Consultancy

Europe market size of PAD interventional procedural instrument market, in terms of sales value

Europe market size of PAD interventional procedural instrument market, in terms of sales value*, 2015-2030E

CAGR	2015-2020	2021-2025E	2026E-2030E
Standard balloons	1.71%	8.08%	5.92%
Scoring balloons	8.71%	13.28%	11.12%
BMS	-7.46%	-3.23%	-3.38%
Drug-coated balloons	26.78%	30.39%	28.35%
Drug-eluting stents	4.98%	6.71%	0.37%
Microcatheter	9.10%	14.24%	13.34%

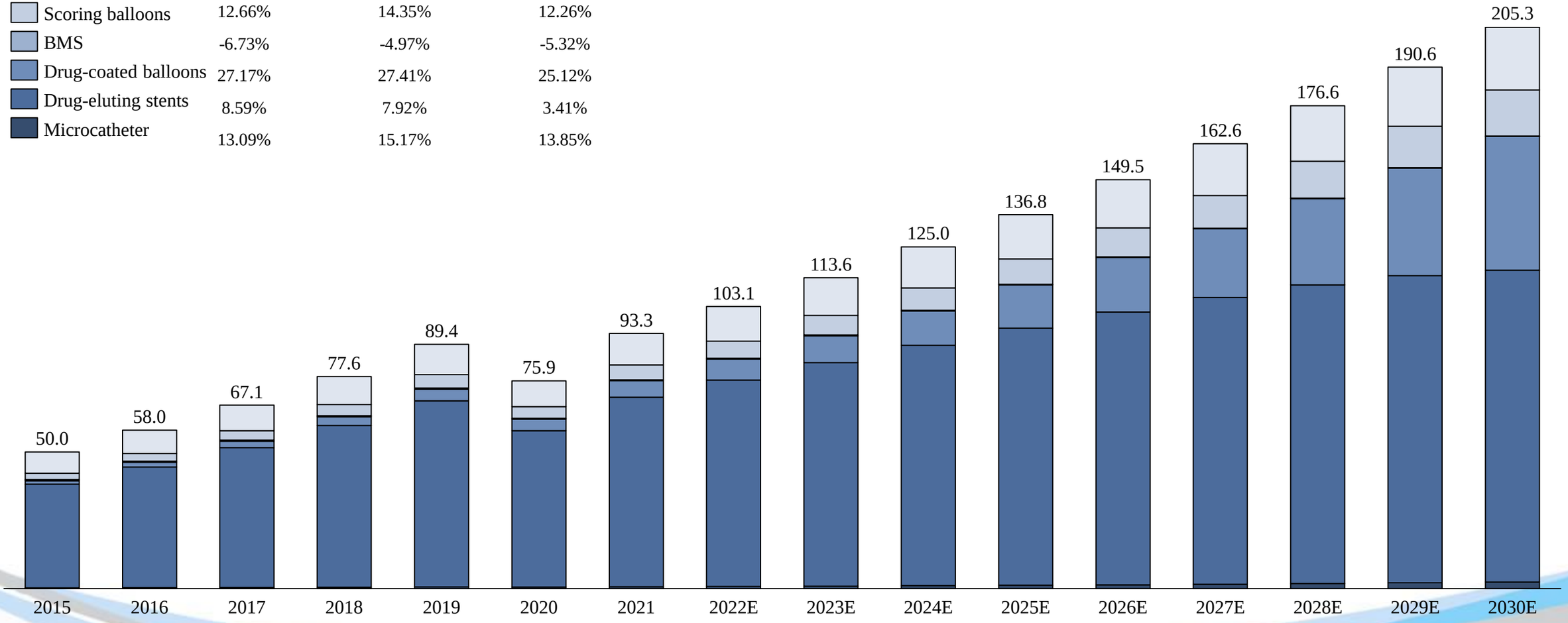


Source: China Insights Consultancy

APAC* market size of PAD interventional procedural instrument market, in terms of sales value

APAC market size of PAD interventional procedural instrument market, in terms of sales value*, 2015-2030E

CAGR	2015-2020	2021-2025E	2026E-2030E
Standard balloons	3.99%	9.11%	7.00%
Scoring balloons	12.66%	14.35%	12.26%
BMS	-6.73%	-4.97%	-5.32%
Drug-coated balloons	27.17%	27.41%	25.12%
Drug-eluting stents	8.59%	7.92%	3.41%
Microcatheter	13.09%	15.17%	13.85%



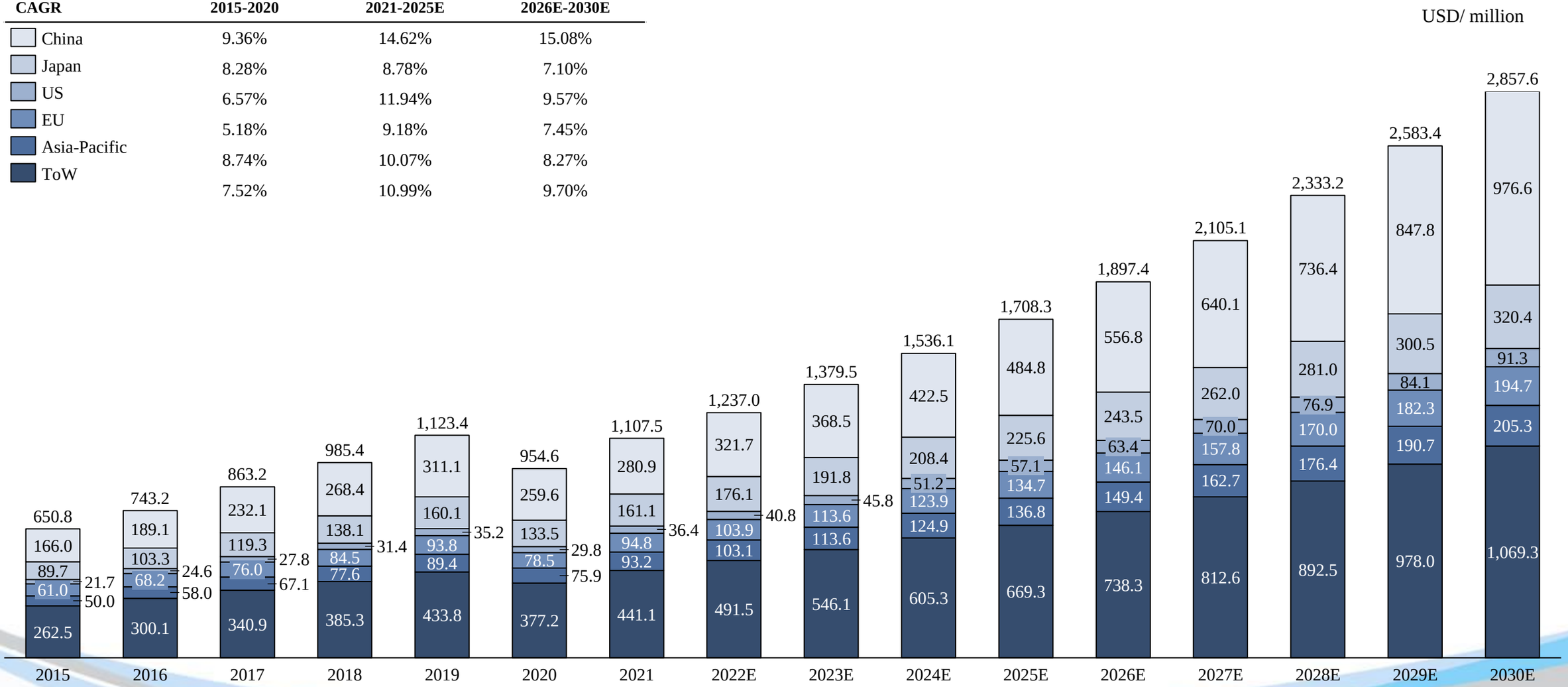
*APAC: APEC excluding China, Japan, U.S. and Russia

Source: China Insights Consultancy

Global PTA instrument market size by country

Global PTA instrument market size by country

CAGR	2015-2020	2021-2025E	2026E-2030E
China	9.36%	14.62%	15.08%
Japan	8.28%	8.78%	7.10%
US	6.57%	11.94%	9.57%
EU	5.18%	9.18%	7.45%
Asia-Pacific	8.74%	10.07%	8.27%
ToW	7.52%	10.99%	9.70%

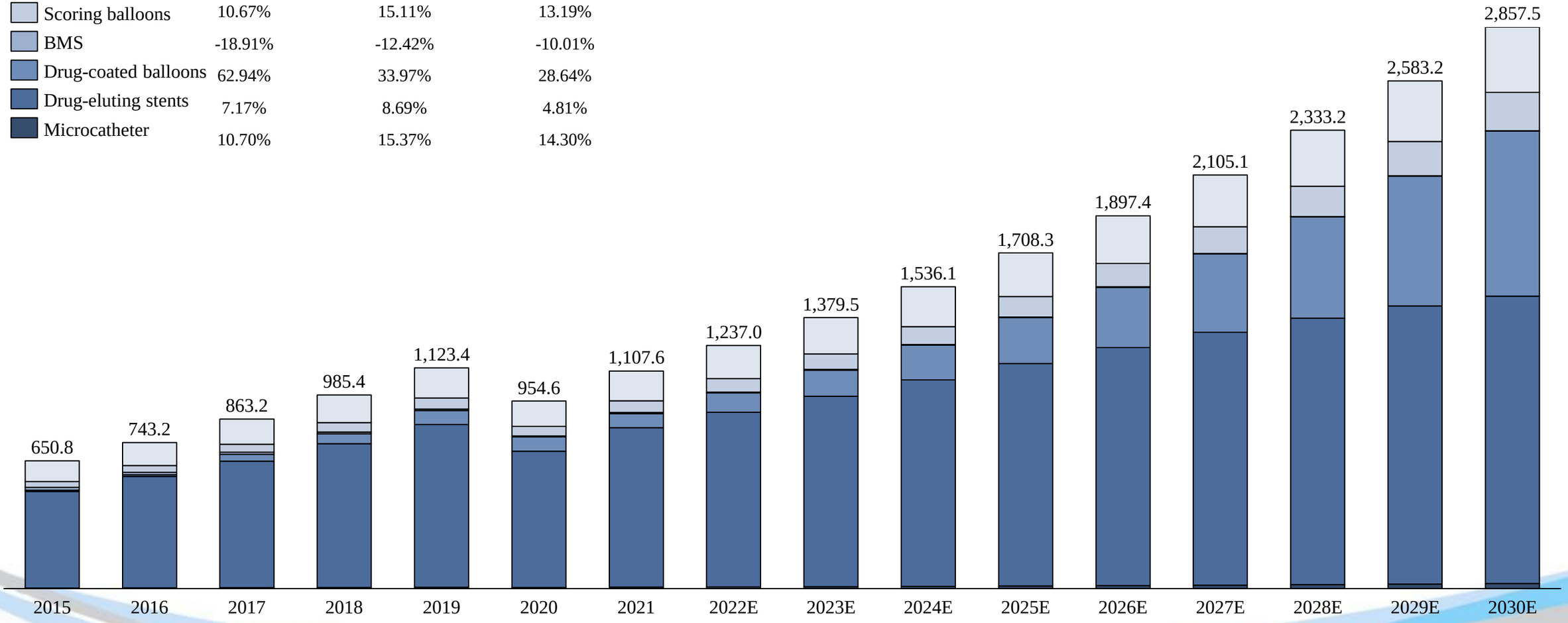


Source: China Insights Consultancy

Global market size of PAD interventional procedural instrument market, in terms of sales value

Global market size of PAD interventional procedural instrument market, in terms of sales value*, 2015-2030E

CAGR	2015-2020	2021-2025E	2026E-2030E
Standard balloons	3.95%	9.94%	8.20%
Scoring balloons	10.67%	15.11%	13.19%
BMS	-18.91%	-12.42%	-10.01%
Drug-coated balloons	62.94%	33.97%	28.64%
Drug-eluting stents	7.17%	8.69%	4.81%
Microcatheter	10.70%	15.37%	14.30%



Source: China Insights Consultancy

Competitive landscape

Market share of PTA balloon in terms of sales volume in 2021 by different regions

China		Japan		U.S.		Europe	
Company A (the U.S.)	~30%	Company C (Japan)	~30%	Company A (the U.S.)	~30%	Company A (the U.S.)	~30%
Company D (the U.S.)	~20%%	Company K (Japan)	~20%	Company J (the U.S.)	~15%	Company D (the U.S.)	~25%
Company I (the U.S.)	~16%	**OrbusNeich (China)**	**13%**	Company D (the U.S.)	~15%	Company B (the U.S.)	~20%
Company J (the U.S.)	~15%	Company D (the U.S.)	~10%	**OrbusNeich (China)**	**12%**	Company M (the U.S.)	~12%
Company N (China)	~13%	Company A (the U.S.)	~10%	Company L (Europe)	~8%	Company H (the U.S.)	<10%
						OrbusNeich (China)	**1% ranked 6-10**

Source: China Insights Industry Consultancy Limited

Growth drivers and future trends of global peripheral artery interventional instrument market

Growth drivers and future trends of global peripheral artery interventional instrument market

Growth drivers and future trends		Description
	**Increasing incidence of peripheral artery disease globally**	• The prevalence of peripheral artery disease is directly related to the increasing age and the prevalence of people over 40 years old will increase year by year. This is because, with age, genetic and lifestyle factors can lead to a buildup of plaque in the arteries. The global aging trend has caused the number of patients with PAD to grow rapidly.
	**Growing detection rate and per medical investment**	• In the context of progressively increasing medical resources and continuous improvement of clinicians‘ technical levels, the detection rate of peripheral vascular diseases will continue to improve especially in developing countries. Growth in healthcare scenario in Asian countries, coupled with growth in GDP and government initiatives are expected to boost growth of the peripheral arterial disease market.
	**Continuous product upgrades and innovation**	• Peripheral artery disease surgery related devices are typically high-tech products, representing technological advances, transforming the way of clinical care with innovation, for example, smaller incisions could reduce surgical trauma and shorten recovery time for patients. The emergence and iteration of peripheral artery disease medical devices will promote the development of global market.
	**Rise in demand for PTA**	• Patients with peripheral artery disease are willing to choose minimally invasive surgery owing to its shorter recovery time, lesser scaring, and lesser chances of post-surgery infections. Such rise in demand will drive the peripheral artery interventional instrument market to develop
	**Trend of import substitution**	• China’s peripheral artery interventional instrument market is mainly dominated by international brands such as Medtronic and Boston Scientific. At present, the market share of domestic brands in China is relatively low. In the future, as more domestic players increase their investment and launch new products, domestic devices of high quality and more affordable prices are expected to gain more recognition and competitiveness against the imported ones. • Moreover, the Measures for Management of Medical Consumables in Medical Institutions (Trial Implementation) issued in September 2019 requires medical institutions to take pricing as an important reference factor in the procurement process. Domestic players will have more opportunities in the domestic market.

Source: China Insights Consultancy

Entry barriers of global peripheral artery interventional instrument market

Entry barriers of global peripheral artery interventional instrument market

Entry barriers	Description
Strong R&D capabilities required	• Medical device industry is an undoubtedly high-tech industry that integrates materials, mechanical manufacturing, electronic engineering etc., which means a higher and more complicated technical content. Most of the proprietary technologies are hard to imitate, requiring a long time to research and accumulate. Therefore, a group of professionals and a long period of R&D are always necessary to overcome the technical obstacle. New entrants may generally find it difficult to collect professionals and acquire the technologies in a short term.
Strict registration and regulatory requirements	• Peripheral artery interventional instrument devices are Class III medical devices whose regulation process is the strictest in most of countries and regions. Rigorous registration standards on safety and efficacy are implemented to regulate the development and commercialization of these medical devices.
Heavy capital investment	• Cost of R&D on medical devices, enhancement of product quality and performance, payment to the professionals in the long term, brand promotion and marketing channel construction all need fund to a significant extent. If the players hope to survive and subsequently develop in this industry, financial pressure is an inevitable challenge for most of them in their initial years before they can break even. Attracting sufficient investments and arranging the funds effectively and efficiently are practically hard to fulfill, especially for new entrants.
Diverse product portfolio and solutions	• Peripheral artery diseases are very complex and there are more kinds of interventional products including stents, dilating balloon etc. to choose. Different procedures require various types and specifications of peripheral artery interventional instruments. A comprehensive product portfolio can eliminate compatibility concerns by providing one-stop and tailor-made solutions. This consequently involves synergies for R&D, manufacturing and commercialization activities and growing economies of scale, with which new entrants are difficult to compete.
End-user recognition	• Products that have been proven safe and effective are easier to gain trust from and be used more frequently by physicians and hospitals. However, it typically takes years of efforts for a brand to establish solid relationships with physicians and hospitals, especially with KOLs and top-tier hospitals.

Source: China Insights Consultancy

I. Overview of global medical device market
II. Overview of global coronary artery disease interventional procedural instrument market
III.Overview of global peripheral artery disease interventional procedural instrument market
IV.Overview of global neuro artery disease interventional procedural instrument market
V. Overview of global structural heart disease interventional procedural instrument market
VI.Appendix

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Introduction to the treatments for intracranial vascular diseases

- Neuro-interventional procedure is a quite advanced treatment method with typical advantages as a minimally invasive procedure, which allows it to have quicker development than intravenous thrombolysis and open surgery

Categorization of treatments for intracranial vascular diseases

Intravenous thrombolysis (IVT)

Definition:
Intravenous thrombolysis is a method using thrombolytic drugs to treat thrombosis. In the situation of ischemic stroke, this term specifically refers to degradation of fibrin, dissolving blood clots by activating plasminogen.

Categorization of thrombolytic drugs:
- Fibrin-specific thrombolytics, including alteplase, reteplase, and tenecteplase
- Nonfibrin-specific thrombolytics, including streptokinase or staphylokinase

Application scenarios:
- Onset of symptoms <3 hours (no more than 6 hours)
- The clot is not aged

Open surgery

Definition:
Open surgery for intracranial vascular diseases is the traditional type of surgery in which an incision is made using a scalpel. By opening the skull, surgeons can find the diseased vessels visually and do operations on them directly.

Categorization of open surgery:
- Craniotomy
  - Skull base surgery
  - Neurovascular surgery
  - Etc.

Application scenarios:
- Hemorrhagic stroke caused by vascular malformations and some aneurysms
- Some extreme situations like massive hemorrhage

Neuro-interventional procedures

Definition:
Neuro-interventional procedure is a minimally invasive procedure used to treat problems affecting the blood vessels with the help of radiology and advanced image-guidance technology. It is a cutting-edge method as a catheter based approach applied on intracranial vascular diseases

Categorization of neuro-interventional procedure:
- Thrombectomy
- Aneurysm embolization
- Balloon/stent angioplasty

Application scenarios:
- Ischemic stroke
- Intracranial stenosis
- Most aneurysms

➢ IVT is used firstly to treat ischemic stroke, while due to its limited effect, neuro-interventional procedure **will be applied sequentially in most cases.** However, when the **time widow** is not clear or exceeds the limit of IVT, neuro-interventional procedure will be conducted **without IVT**. And neuro-interventional procedure will also be used independent of **IVT** if patients have the conditions like huge aneurysm, history of intracranial hemorrhage, recent history of stroke and any other **exclusion criteria** for IVT that do not affect neuro-interventional procedure.

Comparison of the treatments for intracranial vascular diseases

Advantages of neuro-interventional procedure compared to IVT and open surgery	Compared to IVT	Longer time windows	• In the cases of ischemic stroke, IVT can only be used within 6 hours, while neuro-interventional procedure has a time widow up to 24 hours.
		Better drug effect	• Drug can be applied directly to the diseased vessels by neuro-interventional procedure, thus better effects are achieved by lower dosage.
	Compared to open surgery	Minimal damage	• Minimally invasive surgery means no large wound, thus not exposing the lesions to the air and reducing the risk of infection.
		Minimal recovery cycle	• Neuro-interventional procedure causes least damage to the body and avoids bleeding significantly, which allows the patient to recover sooner than open surgery.
		Minimal side effects	• Usage of drugs and operations are more concentrated on the diseased vessels, reducing the side effect of the treatment

➢ Treatments have been **matched with different application scenarios in practice.** Open surgery is most commonly used in cases doctors need to repair the problem **directly and visually** such as vascular malformations, while, neuro-interventional procedure is **much more effective and safer** in most aneurysms. Besides, open surgery is not recommended in the treatment for ischemic stroke.

Source: NCBI; Chinese Medical Association; China Insights Consultancy

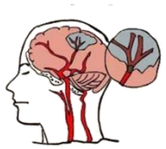
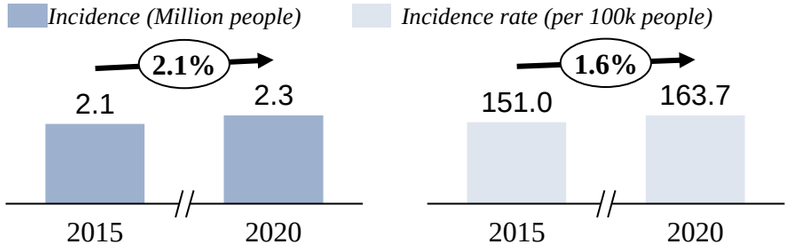
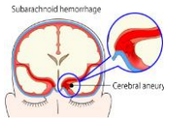
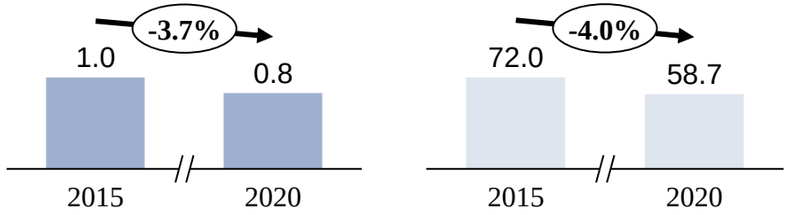
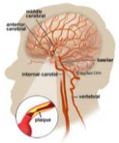
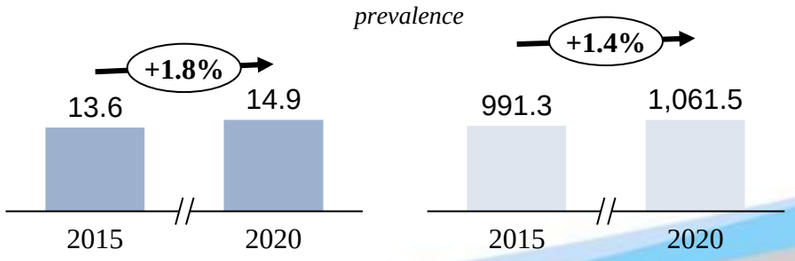
Introduction to and categorization of intracranial vascular diseases

- Intracranial vascular disease has a significantly high incidence in China, including ischemic stroke due to an obstructed blood vessel, hemorrhagic stroke due to bleeding, and intracranial stenosis caused by a narrowing of an artery

Introduction to and categorization of intracranial vascular diseases

Introduction to intracranial vascular disease:

- Intracranial vascular disease is the most common life-threatening neurological event, including all disorders in which an area of the brain is temporarily or permanently affected by ischemia or bleeding and one or more of the cerebral blood vessels are involved in the pathological process. Restrictions in blood flow may occur from vessel narrowing (stenosis), clot formation (thrombosis), blockage (embolism) or blood vessel rupture (hemorrhage).

		Definition	High-risk groups	Total addressable market, China, 2015 vs. 2020
1 **Ischemic stroke**		• Ischemic stroke occurs when a vessel supplying blood to the brain is obstructed. It is the most common stroke which accounts for approximately 73% of all strokes.	– People with high blood pressure – People over 55 years old – Heavy smokers – Overweight people – People with diabetes	
2 **Hemorrhagic stroke**		• A hemorrhagic stroke is bleeding that suddenly interferes with the brain's function. This bleeding can occur either within the brain or between the brain and the skull.	– People having excessive alcohol consumption – People with decreased low-density lipoprotein cholesterol – Old males	
3 **Intracranial stenosis**		• Intracranial stenosis is a narrowing of an artery inside the brain due to a buildup of plaque, which causes decreased blood flow that the affected vessels supply.	– People over 65 years old – Females with hypertension – People with diabetes – People with lipid disorder – People with coronary artery diseases	

Source: China Insights Consultancy

Introduction to and epidemiology of ischemic stroke

- Ischemic stroke accounts for approximately 73% of all stroke incidences, and its incidence as well as mortality keeps growing constantly in China along with the tendency of population ageing

Introduction to ischemic stroke

Ischemic stroke occurs when a vessel supplying blood to the brain is obstructed. It is the most common stroke which accounts for approximately 73% of all strokes.

Symptoms of ischemic stroke

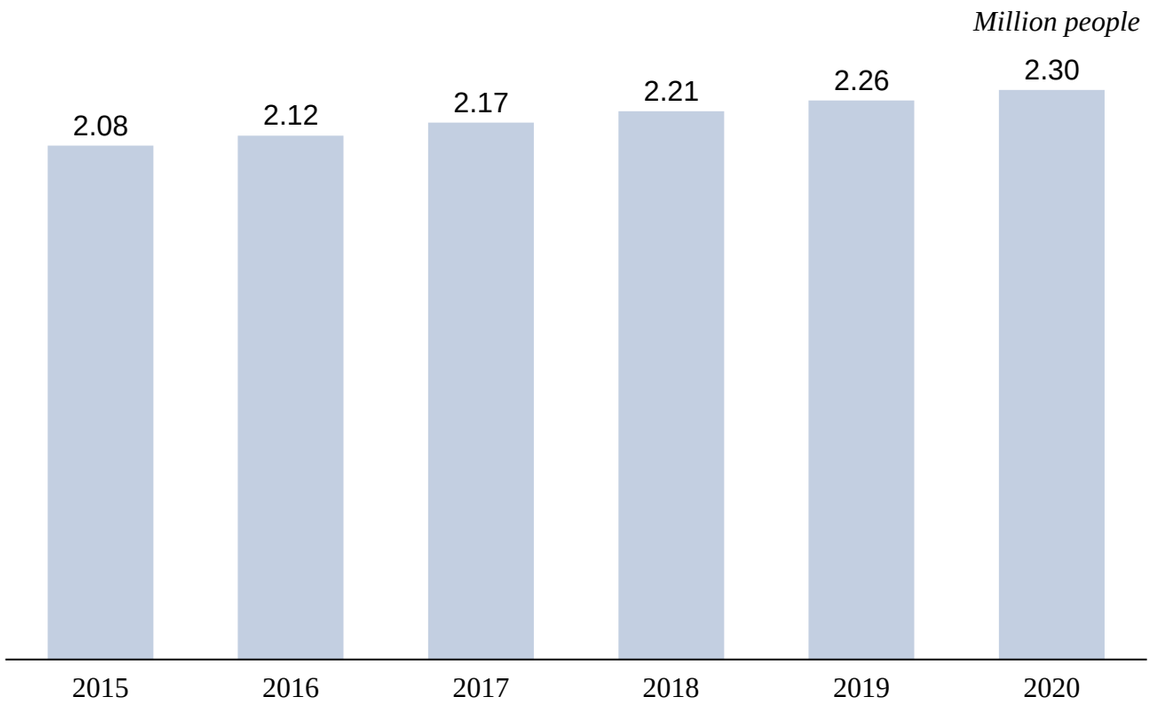
- Sudden numbness or weakness of the face, arm or leg, especially involving one side of the body
- Sudden confusion, trouble speaking or understanding
- Loss of vision in one or both eyes
- Walking problems, dizziness, loss of balance or coordination
- Sudden and severe headache with no known cause

Risk factors of ischemic stroke

- High blood pressure: High blood pressure is the primary cause
- Smoking: Smoking contributes to ischemic stroke
- Obesity: Overweight people are more likely to get ischemic stroke
- Diabetes: People with diabetes are of higher risks
- Ageing: People over 55 years old are of higher risks
- Sedentary lifestyle: A lack a physical activity increases the risk
- Unhealthy diet: Excess consumption of saturated or trans fats increases the risk
- Air pollution: An increased PM2.5 increases the risk

Epidemiology of ischemic stroke

Incidence and incidence rate, China, 2015-2020



Incidence rate (per 100k people)					
151.0	153.0	156.0	158.7	161.2	163.7

Source: The General Office of Stroke Prevention Project Committee; Brief Report on Stroke Prevention and Treatment in China, 2019; China Insights Consultancy

Surgical intervention for acute ischemic stroke

- Stent retrieving thrombectomy serves as the first-line neuro-interventional treatment for acute ischemic stroke, while aspiration thrombectomy is experiencing fast development in recent years with great efficacy

Categorization of surgeries for acute ischemic stroke

Procedure type	*Condition and procedure*		*Recommended level*	*Indication*
Stent retrieving thrombectomy (First-line treatment)	mRS is 0 or 1 before onset; cause is occlusion of internal carotid artery or middle cerebral artery M1; age≥18; NIHSS≥6; ASPECTS≥6; arterial puncture is conducted in 6 hours after onset		Level I recommendation, level A evidence	Acute ischemic stroke
	Occlusion of internal carotid artery or middle cerebral artery M1; mRS ＞1;ASPECTS＜6 or NIHSS＜6		Level II recommendation, level B evidence	
	Meeting the condition of both intravenous thrombolysis and arterial thrombectomy	Using bridging therapy	Level I recommendation, level A evidence	
		Waiting for the effect of intravenous thrombolysis	Level I recommendation, level B evidence	
	Occlusion of anterior cerebral artery, middle artery, basilar artery and middle cerebral artery M2		Level II recommendation, level B evidence	
	Within 6-16 hours after onset; occlusion of anterior circulation great vessels; meeting the criteria of DAWN or DEFUSE-3		Level I recommendation, level A evidence	
	Within 16-24 hours after onset; occlusion of anterior circulation great vessels; meeting the criteria of DAWN		Level II recommendation, level B evidence	
	Using the latest equipment according to the situation of individuals; strictly controlling the indications		Level II recommendation, level B evidence	
	Tandem lesions in intracranial and extracranial vessels		Level II recommendation, level C evidence	
Aspiration thrombectomy	Using aspiration thrombectomy alone or collaboration with other therapies		Level II recommendation, level C evidence	
Intravenous thrombolysis	Within 3 hours after onset; age≥18; according to the contraindications and relative contraindications (rt-PA 0.9mg/kg)		Level I recommendation, level A evidence	
	Within DNT 60min		Level I recommendation, level A evidence	
	Small dose of rt-PA(0.6mg/kg)		Level II recommendation, level A evidence	
	Within 6 hours after onset; 18＜age＜80(urokinase)		Level II recommendation, level B evidence	
	other thrombolytic drugs that are not recommended in clinical trials		Level II recommendation, level C evidence	
Angioplasty	Remedy for the failure of stent retrieving thrombectomy		Level III recommendation, level C evidence	Acute ischemic stroke and stenosis
	Severe carotid stenosis or dissection		Level III recommendation, level C evidence	

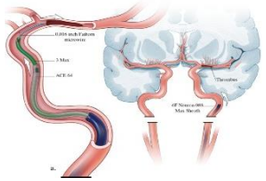
- The aim of surgical intervention is **recanalization** of the vessels related to acute ischemic stroke
- All the patients should be **strictly filtered** according to indications and contraindications

Source: Chinese Medical Association; China Insights Consultancy

Introduction to stent retrieving thrombectomy

- Stent retrieving thrombectomy is minimally-invasive and can be initiated within 24 hours of time last known well for patients with ischemic stroke by extracting the clot with a stent

Definition and procedure of stent retrieving thrombectomy

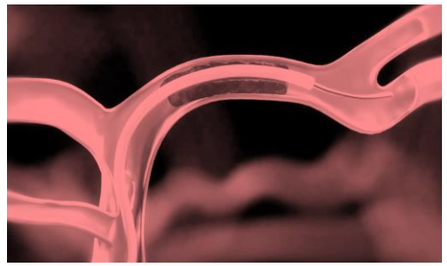


Definition:

- Stent retrieving thrombectomy is a type of **minimally invasive procedure** in which **specialized equipment** are required to remove a clot from a patient's artery. Using fluoroscopy or continuous x-ray, the doctor guides devices through the patient's arteries to the clot and then extracts the clot all at once.
- Stent retrieving thrombectomy is indicated for patients with acute ischemic stroke due to a **large artery occlusion** in the anterior circulation who can be treated **within 24 hours of time last known well**, performed independently or after intravenous thrombolysis.

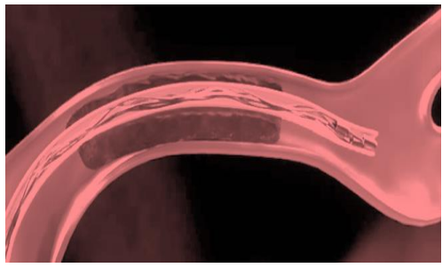
Procedure of thrombectomy

1 Position the clot



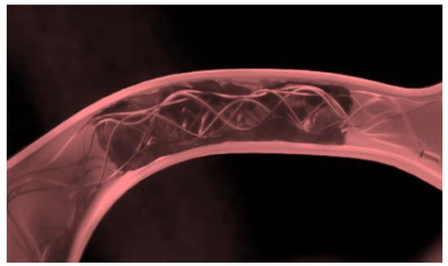
- Thread the micro guidewire and microcatheter to position the clot
- Follow the distal access catheter and prepare for delivering the stent

2 Deliver the stent retriever system



- Draw out the micro guidewire and microcatheter
- Insert the stent retriever by the push wire into the distal access catheter, and guide it to the blockage

3 Catch the clot



- Expand the stent retriever with the distal access catheter out
- Wait around 5 minutes until stent retriever fills up the artery and catches the whole clot

4 Extract the clot

- Pull the stent retriever to the incision site where the balloon guiding catheter is placed, the clot is thereupon extracted

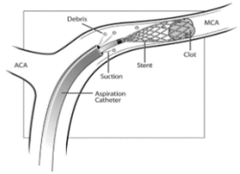
➢ *One point should be touched on that conducting thrombectomy **once is typically not enough** to resolve the problem of vessel embolism. It is possibly necessary for the patients to receive thrombectomy several times.*

Source: China Insights Consultancy

Introduction to aspiration thrombectomy

- Aspiration thrombectomy presents great outcomes independently or collaborated with stent retrieving thrombectomy, which has a promising development to treat ischemic strokes

Definition and procedure of aspiration thrombectomy

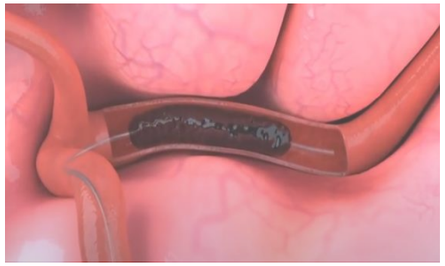


Definition:

- Aspiration thrombectomy is a kind of vessel interventional therapy adopting the principle of negative pressure to suck out the thrombus through an **aspiration catheter**. It is relatively a new approach to treat ischemic stroke which is still developing.
- Aspiration thrombectomy is proven to have **similar effects with stent retrieving thrombectomy**. Collaboration of the two types of thrombectomy is also frequently applied in real-world cases.

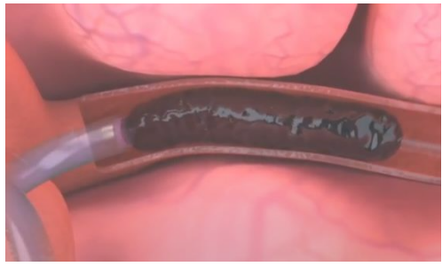
Procedure of thrombectomy

1 Position the clot



- Thread the micro guidewire and microcatheter to position the clot
- Follow the distal access catheter and prepare for delivering the aspiration catheter

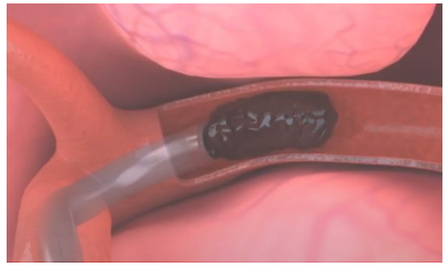
2 Deliver the aspiration catheter



- Insert the aspiration catheter and keep it parallel with the microcatheter
- Draw out the microcatheter

3 Suck out the clot

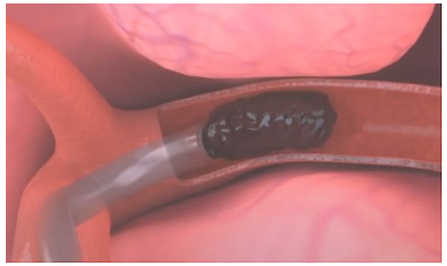
3a



Manual aspiration:

- Use the syringe to create a negative pressure to suck out the clot
- Push forward and withdraw the aspiration catheter slowly

3b



Mechanical aspiration:

- Use the aspiration pump to create a stable negative pressure, sucking the clot out (mainly applied when the vessels are of large diameter)

- *When conducting aspiration thrombectomy, it should begin **from the proximal to distal**, preventing shift of the clot.*
- *Aspiration is continued typically **for 1–2 min** to clear any intraluminal debris created during the thrombectomy*
- It utilizes widely used devices in endovascular surgeries but requires the navigation of fairly **large-diameter catheters**.

Source: China Insights Consultancy

Introduction to and epidemiology of hemorrhagic stroke

- Hemorrhagic stroke includes intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH)

Introduction to hemorrhagic stroke

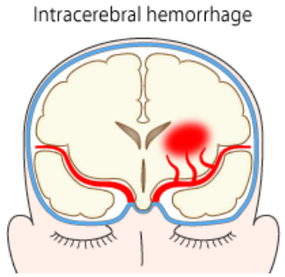
A hemorrhagic stroke is bleeding (hemorrhage) that suddenly interferes with the brain's function. This bleeding can occur either within the brain or between the brain and the skull.

Hemorrhagic strokes are divided into two categories depending on the site and cause of the bleeding.

Categorization of hemorrhagic stroke

1 Intracerebral hemorrhage (ICH)

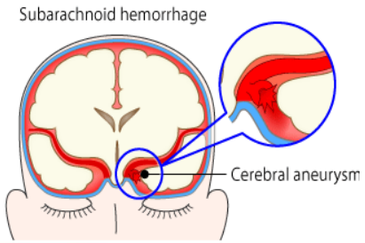
~75%



Definition	• As the most common type of hemorrhagic stroke, the bleeding occurs inside of the brain
Cause	• ICH is most commonly caused by hypertension, arteriovenous malformations, or head trauma

2 Subarachnoid hemorrhage (SAH)

~25%

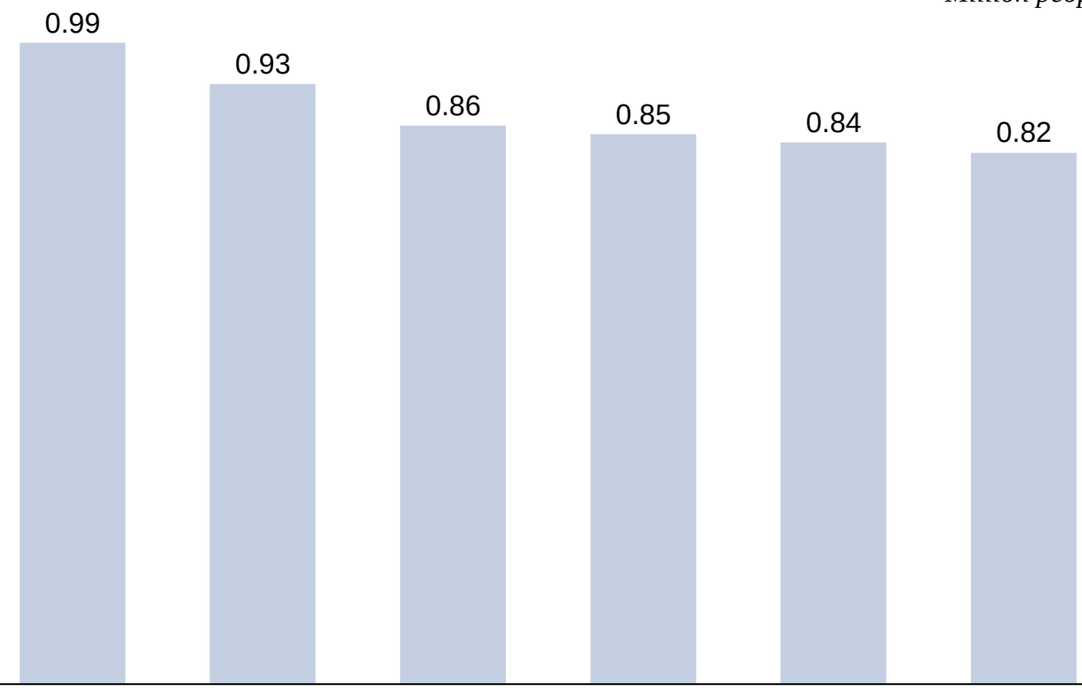


Definition	• The bleeding occurs between the brain and the membranes that cover it (subarachnoid space)
Cause	• SAH can be caused by a ruptured aneurysm, AVM, or head injury

Epidemiology of hemorrhagic stroke

Incidence and incidence rate, China, 2015-2020

Million people



Incidence rate (per 100k people)	2015	2016	2017	2018	2019	2020
	72.0	67.0	62.0	60.8	59.7	58.7

Source: The General Office of Stroke Prevention Project Committee; Brief Report on Stroke Prevention and Treatment in China, 2019; China Insights Consultancy

Introduction to intracranial aneurysm

- Formation, risk factors, symptoms, clinical presentation and its relations with SAH

Definition of intracranial aneurysm (IA)

- An abnormal dilatation on the arterial wall of the cerebral vessels, usually near a bifurcation point of a vessel segment.
- Most prevalent among people aged from 35 to 60. After age 40, female is 50% more likely to be affected.

Formation & risk factors

- Inflammation caused by hemodynamic insult is supposed to be the leading factor in the pathogenesis of intracranial aneurysm, and the main constituents of the inflammatory response are macrophages and smooth muscle cells (SMCs).
- Macrophages that infiltrate tissue will release proinflammatory cytokines and matrix metalloproteinases (MMPs), the former could result in more cells getting inflammatory and the later could digest arterial wall extracellular matrix.
- SMCs are the predominant matrix-synthesizing cells of the vascular wall. The endothelial injury due to inflammation will lead to proliferation and migration of SMCs, and these SMCs will under go phenotypic modulation from differentiated phenotype to dedifferentiated phenotype. As a result of the modulation, the SMCs are no longer tightly associated with each others and their ability to synthesize collagen is sharply weakened.
- There are several possible risk factors associated with IA formation or growth, such as smoking, alcohol abuse, female sex, older age and hypertension. In addition, genetics of IA is also an important contribution, and relevant studies suggest that people in from families with familial aneurysms have a prevalence rate from 4% to 9% depending on sample size, which is higher than that of general population.

Symptoms of unruptured IA:

- *Headache*
- *Cranial neuropathy*
- *Seizures*
- *Visual disturbances*
- *Pyramidal tract signs*
- *Facial pain*

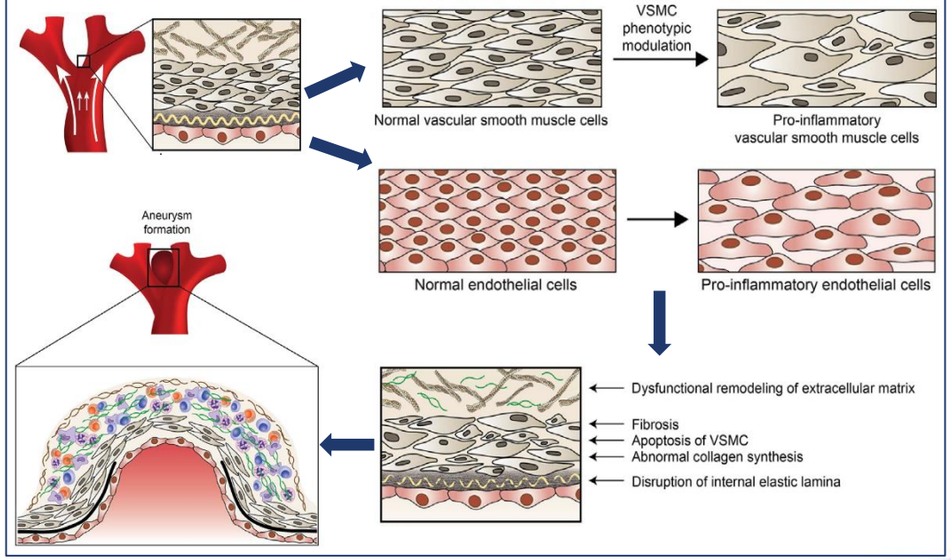
Clinical presentation of unruptured IA:

- *Hemorrhage of another aneurysm*
- *Headache*
- *Ischemic cerebrovascular disease*
- *Cranial nerve palsy*
- *Seizures*
- *Symptoms of mass effect*
- *Brain tumor*
- *Central nervous system degenerative disorders*
- *…*

Relations between IA and SAH

- The most terrible clinical presentation of IA is called Subarachnoid Hemorrhage (SAH) meaning that the aneurysm has ruptured and leaked, causing bleeding into the brain, which is usually fatal and requires prompt medical treatment, and more than 60% of the survivals suffer from permanent neurological deficit. However, the rupture of IA is a low-possibility event, there are only about 0.25% of aneurysms thought to end up in rupture, and approximately 3-5% of new strokes are due to SAH.

Formation of IA: figure



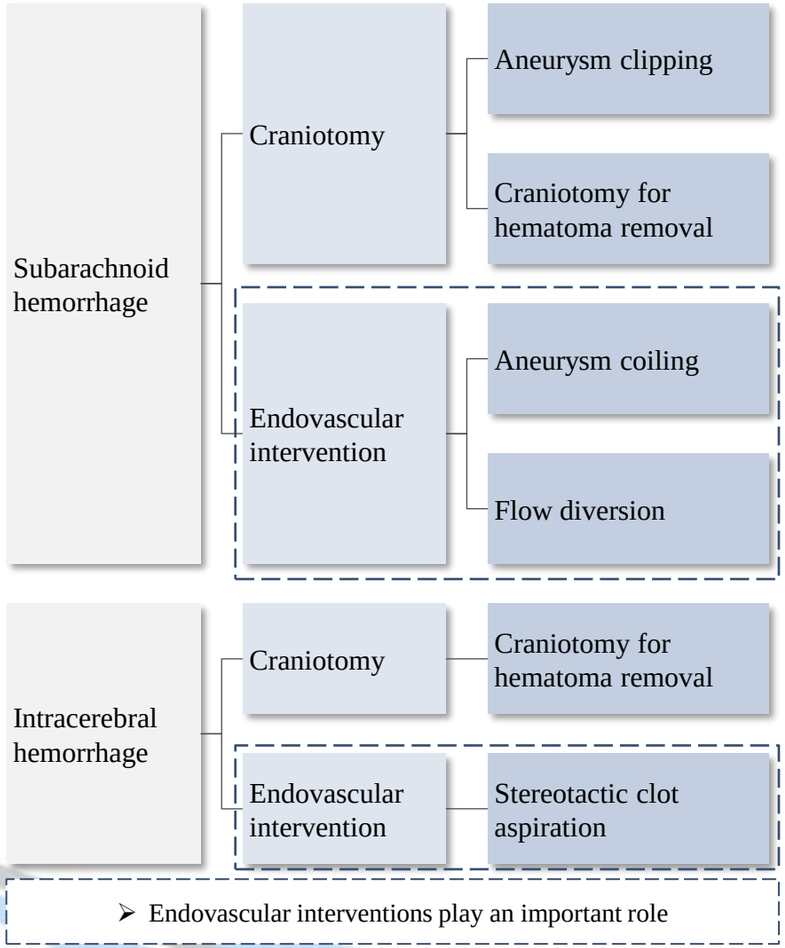
Source: Brain Aneurysm Foundation; NHS; Gabor Toth, Russell Cerejo.Intracranial aneurysms: Review of current science and management[J].CME Review Article: Core Curriculum in Vascular Medicine,2018,23:276-288.; Nohra Chalouhi, Brain L Hoh, David Hasan.Review of cerebral aneurysm formation, growth, and rupture.[D].US: Department of Neurosurgery Faculty Papers, Thomas Jefferson University,2013.

Source: China Insights Consultancy

Surgical interventions for hemorrhagic stroke

- Endovascular interventions represent the trends of procedure interventions for hemorrhagic stroke, widely applied and especially for patients with aneurysm

Overview of surgeries for hemorrhagic stroke



Procedure type	Condition		Recommendation
Aneurysm clipping	Younger age, hematoma with mass effect and aneurysm-related factors with (middle cerebral artery and pericardial aneurysm, aneurysm neck width, aneurysm body directly branching out, aneurysm and vascular morphology		Level II recommendation, level C evidence
Craniotomy for hematoma removal	Only when the hematoma is close to the surface of the brain or if it is associated with an arteriovenous malformation(AVM) or tumor that must also be removed	Patients with primary intracerebral hemorrhage	Level II recommendation, level B evidence
		Cerebellar hemorrhage with deterioration of nerve function or brainstem compression, regardless of whether there is ventricular obstruction caused by hydrocephalus	Level I recommendation, level B evidence
		Patients with cerebral lobe hemorrhage exceeding 30ml and within 1cm from the cortical surface	Level II recommendation, level B evidence
Aneurysm coiling	Age>70 years old, no hematoma with mass effect or aneurysm related factors (posterior circulation aneurysm, narrow neck aneurysm, unilobular aneurysm		Level II recommendation, level C evidence
Flow diversion	Flow diversion, or flow diversion, is an alternative method which is primarily applied to complicated aneurysm. Further experience still needs to be accumulated.		Level II recommendation, level B evidence
Stereotactic clot aspiration	Patients with cerebral lobe hemorrhage exceeding 30ml and within 1cm from the cortical surface		Level II recommendation, level B evidence
	Supratentorial hypertensive intracerebral hemorrhage with a hematoma volume of 20-40 ml and GCS≥9 within 72 hours of onset		Level II recommendation, level A evidence
	Severe intracerebral hemorrhage over 40ml with worsening of consciousness due to hematoma mess effect		Level II recommendation, level B evidence

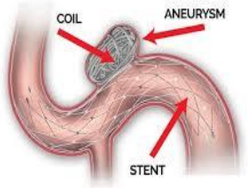
➢ All the patients should be strictly filtered according to indications and contraindications

Source: Chinese Medical Association; China Insights Consultancy

Introduction to aneurysm coiling

- Aneurysm coiling, compared to aneurysm clipping, is a relatively new method which prevents craniotomy and uses coils to fill up the aneurysm independently or with the assistance of stents or balloons

Definition and procedure of aneurysm coiling

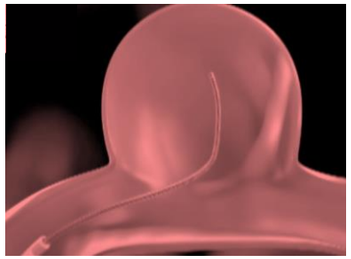


Definition:

- Coil embolization for aneurysm in hemorrhagic stroke is a minimally invasive procedure to treat an aneurysm by filling it with materials that **close off the sac to reduces the risk of bleeding.**
- The goal of endovascular coiling is to isolate an aneurysm from the normal circulation without blocking off any small arteries nearby or narrowing the main vessel. Coiling can treat most aneurysm cases.

Procedure of aneurysm coiling

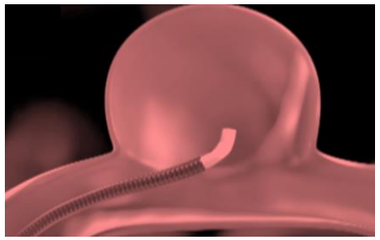
1 Position the aneurysm



- Thread the micro guidewire to position the aneurysm
- Follow the distal access catheter for device delivery

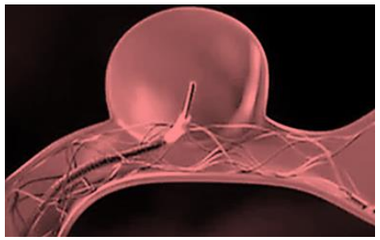
2 Prepare for inserting the coils

Independently → 2a



- Insert the microcatheter through the distal access catheter and guide it to the aneurysm

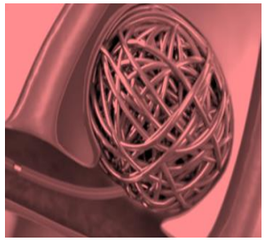
*Stent-assisted** → 2b



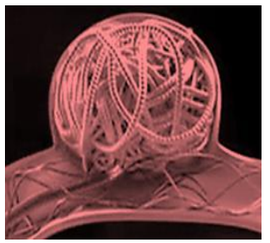
- Deliver the vascular reconstruction stent through the distal access catheter and place it in the neck of the aneurysm, so that the coils would not move to normal arteries

3 Insert the coils

3a



3b



- Advance the coils through the microcatheter until they emerge inside the aneurysm
- Insert the coils one after another until the aneurysm is packed
- Remove the catheters

- *The whole procedure of aneurysm coiling takes about **2 to 4 hours** generally.*
- *Pressure should be given to the groin area after removing the catheters **for 10-15 minutes** to prevent the artery from bleeding.*
- *Vascular reconstruction stent is applied when the aneurysm has **a wide neck or unusual shape**, to ensure that the coils stay in the aneurysm.*

Note: *Balloon may be used to assist aneurysm coiling in some cases, but generally the balloons could be replaced by stents.

Source: China Insights Consultancy

Introduction to flow diversion

- Flow diversion just starts to be applied in hemorrhagic strokes caused by aneurysm, principle of which is preventing blood from flowing into the aneurysm, and tend to have a better effect and broader applicability

Introduction to flow diversion

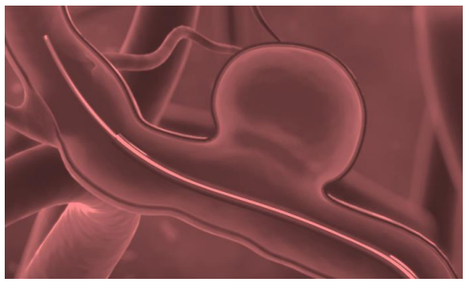
Definition of flow diversion

Definition:

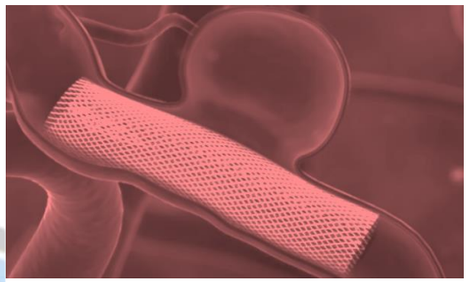
- Flow diversion is a minimally invasive way to treat aneurysm, which is theoretically **safer and more effective** than other methods.
- It uses an endovascular stent to **reinforce the wall** of the vessel next to the aneurysm, maintaining the **normal blood flow**.

Procedure of flow diversion

➢ The preparation steps that guide and position the aneurysm are generally similar with that of aneurysm coiling, while the catheters **do not enter the aneurysm**.

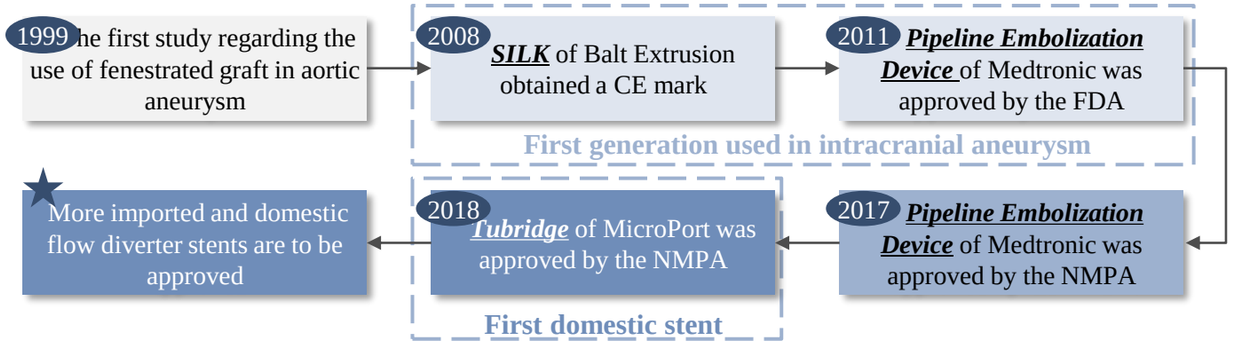


- The microcatheter and distal access catheter are placed in the vessel right next to the aneurysm, exceeding it a little bit to reserve space for flow diverter stent and make sure that the stent would cover the whole neck of the aneurysm.



- Then the flow diverter stent travels through the catheters and is released from the tip of the catheters.
- Once the stent is deployed, blood should travel through the lumen of it without entering the aneurysm, and the aneurysm will gradually shrink and disappear.

Development and features of flow diversion



- The use of flow diverter stent, which is also called **flow diverter**, in intracranial flow diversion is relatively **a new approach** which is applied in China in recent years. More experiments worldwide are taken to prove its superiority, and it is expected to have a promising prospect.
- The most significant advantage compared to aneurysm coiling is that flow diversion **reduces the risk of rupture** effectively as it avoids entering the aneurysm, and it is more suitable and effective **when the neck of aneurysm is wider**.

Penetration of flow diversion

➢ In light of the high requirements of the procedure and the freshness of this technique, the penetration of flow diversion has a large potential to grow in China.

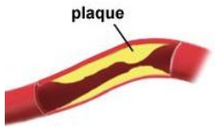
■ Number of doctors capable of performing flow diversion procedure in China	~200
■ Number of flow diversion surgeries taken in China in 2019	~4,300

Source: CE; FDA; NMPA; China Insights Consultancy

Introduction to intracranial stenosis

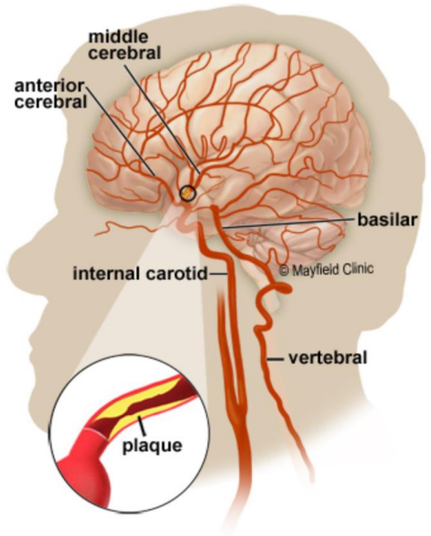
- Intracranial stenosis occurs when blood flow is restricted by narrowed arteries of plaque buildup, namely atherosclerosis, in the small twisting vessels deep within the brain, which may lead to strokes

Introduction to intracranial stenosis



- Intracranial stenosis is a narrowing of an artery inside the brain due to a buildup of plaque, which causes decreased blood flow to the area of the brain that the affected vessels supply.
- Without treatment, cerebral artery stenosis can greatly increase a person's chance of having transient ischemic attacks (TIAs).

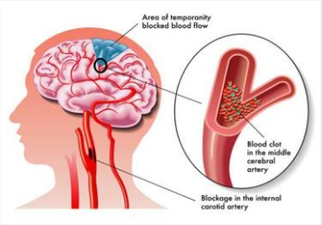
Blood supply of the brain



To understand Intracranial stenosis, it is helpful to know how blood circulates to the brain:

- Blood is pumped from the heart and carried to the brain by two paired arteries, namely the internal carotid arteries and the vertebral arteries .
- The internal carotid arteries supply the anterior (front) areas and the vertebral arteries supply the posterior (back) areas of the brain.
- After passing through the skull, the right and left vertebral arteries join together to form a single basilar artery.
- The basilar artery and the internal carotid arteries communicate with each other in a ring at the base of the brain called the Circle of Willis.
- The arteries most likely to be affected by stenosis are the internal carotid artery (ICA), the middle cerebral artery (MCA), the vertebral arteries, and the basilar artery.

Mechanism of intracranial stenosis causing stroke



Intracranial stenosis is a narrowing of the arteries inside the brain. Similar to carotid stenosis in the neck, it is caused by a buildup of plaque in the inner wall of the blood vessels. This narrowing of the blood vessels causes decreased blood flow to the area of the brain that the affected vessels supply. There are three ways in which intracranial artery stenosis can result in a stroke:

- Plaque can grow larger and larger, severely narrowing the artery and reducing blood flow to the brain. Plaque can eventually completely block (occlude) the artery.
- Plaque can roughen and deform the artery wall, causing blood clots to form and blocking blood flow to the brain.
- Plaque can rupture and break away, traveling downstream to lodge in a smaller artery and blocking blood flow to the brain.

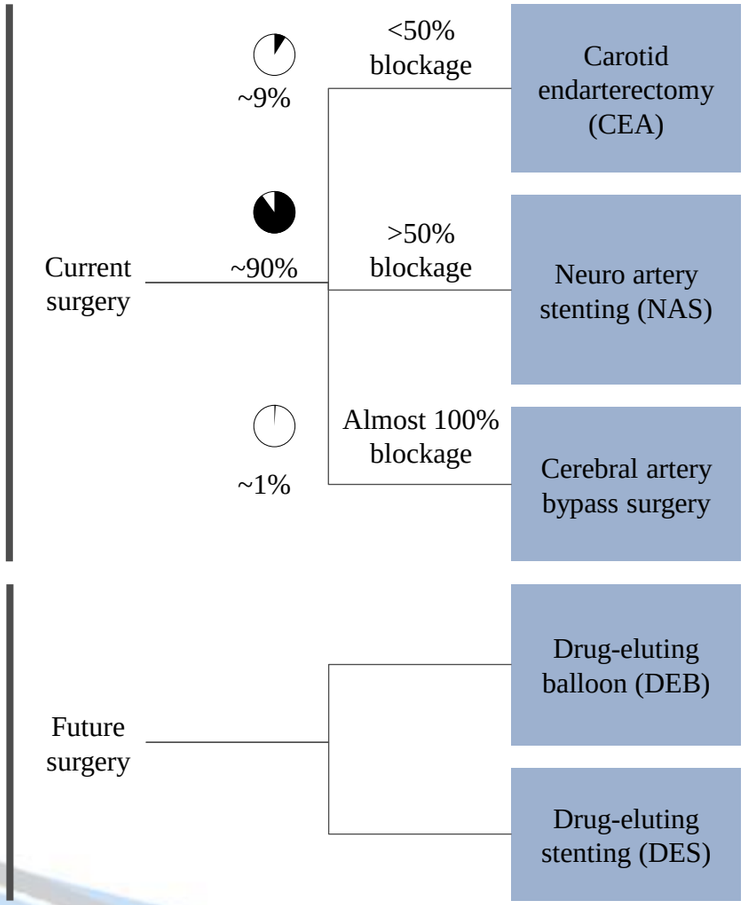
	Prevalence of intracranial stenosis	% Need surgical treatment	Penetration of endovascular surgeries
2020	14.9 million people	~15%	0.97%
2025E	16.2 million people	~15%	6.11%

Source: Mayfield; China Insights Consultancy

Surgical intervention for intracranial stenosis

- Neuro artery stenting serves as an important treatment for intracranial stenosis, and drug-eluting balloon as well as drug-eluting stenting are anticipated to experience fast development in the future

Categorization of surgeries for intracranial stenosis



Surgery type	*Condition and description*
Carotid endarterectomy (CEA)	• In carotid endarterectomy, the surgeon opens the artery and removes the plaque to reduce the risk of stroke. • The uses of CEA may have a better prognosis, especially when arterial anatomy is not conducive to the development of endovascular treatment.
Neuro artery stenting (NAS)	• Neuro artery stenting (NAS) is an endovascular surgery where a stent is deployed within the lumen of the carotid artery to treat narrowing of the carotid artery and decrease the risk of stroke. • NAS is used to treat narrowing of the carotid artery in high-risk patients, when carotid endarterectomy is considered too risky.
Cerebral artery bypass surgery	• Cerebral bypass surgery is performed to restore, or "revascularize," blood flow to the brain. • Bypass is typically recommended when the artery is 100% blocked and angioplasty is not possible.
Drug-eluting balloon (DEB)	• Drug-eluting balloon could maintain long-term vessel patency. • The effect of DEBs is based on the fast and homogenous transfer of antiproliferative drugs into the vessel wall during single balloon inflation by means of a lipophilic matrix without the use of permanent implants.
Drug-eluting stenting (DES)	• Drug-eluting stent (DES) is a peripheral or coronary stent (a scaffold) placed into narrowed, diseased peripheral or coronary arteries that slowly releases a drug to block cell proliferation.

Analysis

- Treatment options for intracranial stenosis vary according to the severity of the narrowing and whether the patient is experiencing stroke-like symptoms or not.
- Patients are first treated with medication and are encouraged to make lifestyle changes to reduce their risk of stroke. If medication fails, surgery is initiated to save the patients.
- The aim of surgery is to prevent stroke by removing or reducing the plaque buildup and enlarging the artery to allow more blood flow to the brain.

Source: China Insights Consultancy

Introduction and competitive analysis of different surgeries for intracranial stenosis

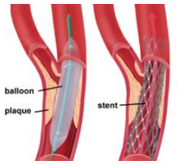
- Surgical treatments for intracranial stenosis include balloon/stent angioplasty, carotid endarterectomy and artery bypass, of which stenting accounts for approximately 90% of the cases

Introduction and competitive analysis of different surgeries for intracranial stenosis

Surgical treatment for intracranial stenosis:

- Surgical treatment for intracranial stenosis is to prevent stroke by **removing or reducing the plaque buildup and enlarging the artery lumen** to allow more blood flow to the brain.
- Surgical treatment is generally recommended for patients who have suffered one or more transient ischemic attacks (TIAs) or strokes and those with high grade of stenosis, especially when they **do not respond to medication**.

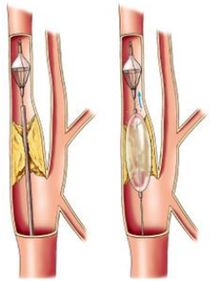
Introduction to balloon/stent angioplasty (NAS)



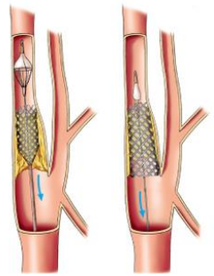
Definition:

- Balloon/stent angioplasty is a minimally invasive endovascular procedure that compresses the plaque and widens the lumen of the artery, using a balloon catheter or sometimes a stent.
- This procedure is also called angioplasty, which means rebuilding the vascular.

1 ➢ The first step is similar to other endovascular surgeries that general access devices are inserted from the groin to the artery with stenosis, building the path for the balloon catheter or the stent.



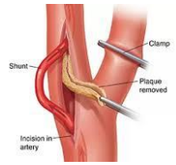
2 ➢ Insert a balloon catheter through the bloodstream to where the plaque-narrowed artery is located
➢ Inflate the balloon on the catheter to compress the plaque against the artery wall
➢ Deflate and remove the balloon catheter



3 ➢ Insert the vascular reconstruction stent through the distal access catheter to where the plaque-narrowed artery is located
➢ Expand the stent over the plaque, holding open the artery, and leave it in the vessel

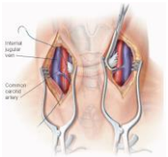
➢ The aim of NAS is to reduce the stenosis. A small increase of the vessel diameter leads to large increases of blood flow to the brain, thus preventing the ischemic stroke.

Introduction to carotid endarterectomy (CEA) and artery bypass



Carotid endarterectomy (CEA):

- CEA is an open surgery to remove the plaque that caused stenosis.
- An incision in the artery over the blocked area is made and the plaque is peeled out.



Carotid artery bypass:

- Carotid artery bypass is a surgery that reroutes the blood supply around the plaque-blocked area.
- A length of artery is harvested from somewhere else is connected above and below the blockage. (or connect the artery of the scalp to the artery of brain, replacing the blocked one)

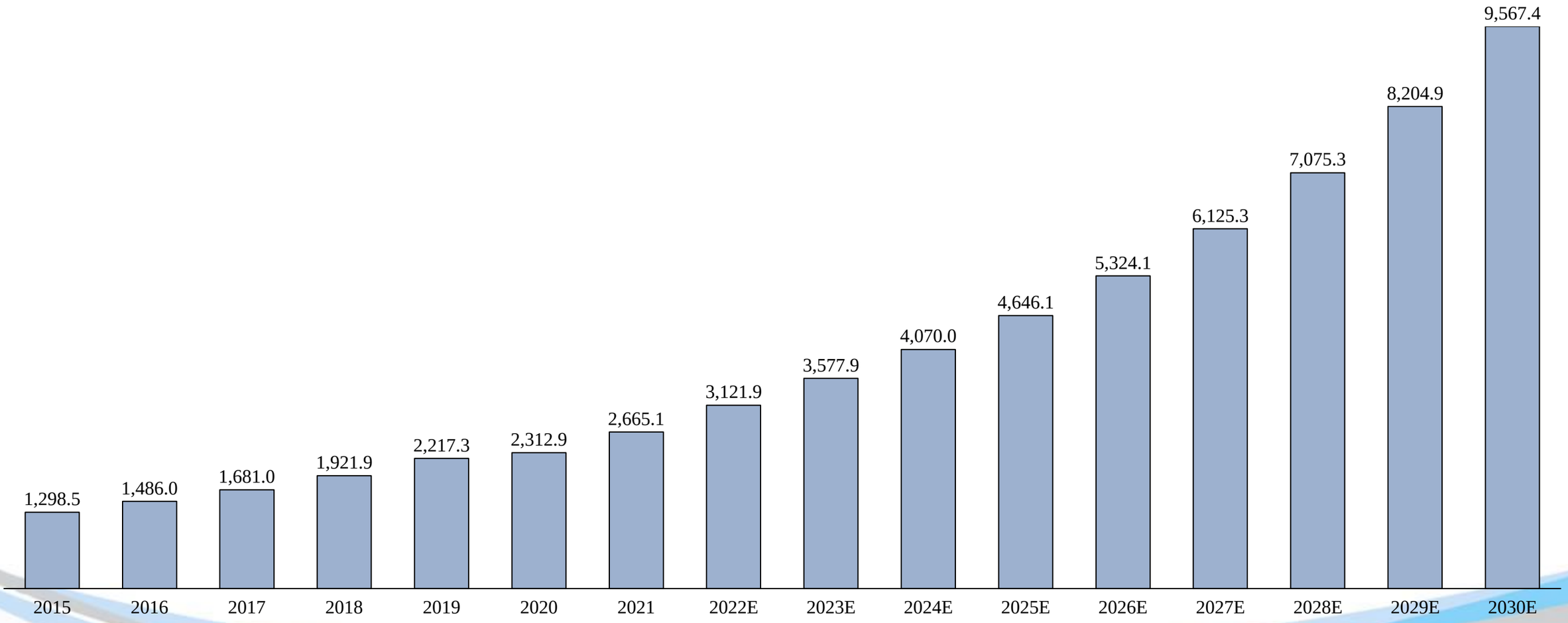
Key analysis

➢ Surgical treatments are recommended when stenosis is greater than 50%.	➢ CEA is more applied to patients over 70 years old.
➢ Artery bypass is less efficient and can only be used when artery is 100% blocked.	➢ **When patient is under 70 years old, NAS is considered better.**

Global market size of Neuro interventional instrument market, in terms of sales value

Global market size of Neuro interventional instrument market, in terms of sales value*, 2015-2030E

CAGR	2015-2020	2021-2025E	2026E-2030E
Global neuro-intervential procedure instrument market	12.2%	14.9%	15.8%



Source: China Insights Consultancy

Growth drivers and future trends of Global neuro-interventional device market

Growth drivers and future trends of Global neuro-interventional device market

	Growth drivers and future trends	Description
1	**Increasing prevalence of stroke**	• Stroke is an age-related disease with an increased prevalence for the elderly group. Considering the trend of population aging in (China and other countries), it is expected that an increasing number of patients will suffer from stroke in the future.
2	**Increasing number and penetration of neuro-interventional procedures**	• With more innovative neuro-interventional procedures developed for various indications, doctors and patients will have a wider range of choices, resulting in an increasing number of neurointerventional procedures. Despite the currently limited number of physicians capable of performing the procedures, more physicians will be trained to meet the large patient demand, allowing the neuro-interventional procedures to become a common clinical practice.
3	**Continuous product upgrades and innovation**	• Neuro-interventional procedure devices are typically high-end products, representing technological advances, transforming the way of clinical care with innovation, for example, smaller incisions could reduce surgical trauma and shorten recovery time for patients. The emergence and iteration of neuro-interventional medical devices will promote the development of China neuro-interventional medical device market.
4	**Advances in imaging techniques may improve access to vascular interventional therapy**	• In recent years, with the development of imaging technology and its increasing application in clinical practice, the intravascular environment can be better seen and the detection rate of vascular diseases (such as unruptured intracranial aneurysms, intermittent claudication, and threatening limb ischemia) can be improved. In addition, technological innovations such as ischemic penumbra have provided the basis for early stroke screening and prevention, resulting in the discovery of more eligible patients at high risk of stroke and the expansion of the patient population. As the use of AI algorithms increases, back-end automation of imaging systems and analytics software will accelerate in the coming years and help doctors achieve more efficient diagnoses

Source: China Insights Consultancy

Introduction and epidemiology of tricuspid regurgitation

- Tricuspid regurgitation (TR) is a very frequent manifestation of valvular heart disease, it may be due to the primary involvement of the valve or secondary to pulmonary hypertension or to the left-sided heart valve disease

Introduction and epidemiology of tricuspid regurgitation

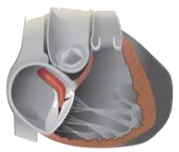
Introduction

- Tricuspid regurgitation (TR) is the backflow of blood through the tricuspid valve into the right atrium during ventricular systole
- The progression from a mild to significant degree of TR is influenced by age and gender.
  - Incidence for physiologically significant TR worldwide is < 1%.
  - 70% of normal adults will have a minimal degree of TR
  - Similar incidence rates in men and women
  - Regional variation in the prevalence of tricuspid regurgitation is apparent. Screening studies in populations of older individuals have demonstrated a prevalence of moderate or severe tricuspid regurgitation of 2.7% in the UK and 1.1% in China

Tricuspid regurgitation

Organic tricuspid regurgitation

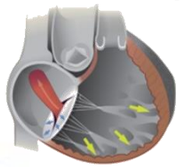
~15%



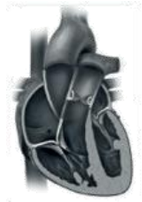
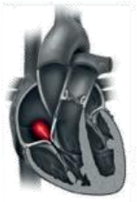
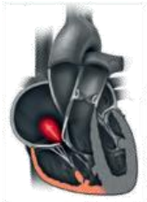
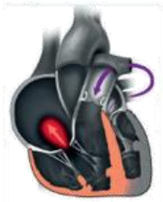
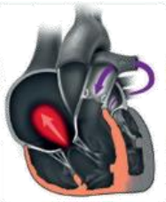
- Primary TR implies pathology of the tricuspid valve (TV) complex and may be of rheumatic, degenerative, congenital, infectious, traumatic or iatrogenic (usually secondary to pacemaker leads) origin.

Functional tricuspid regurgitation

~85%

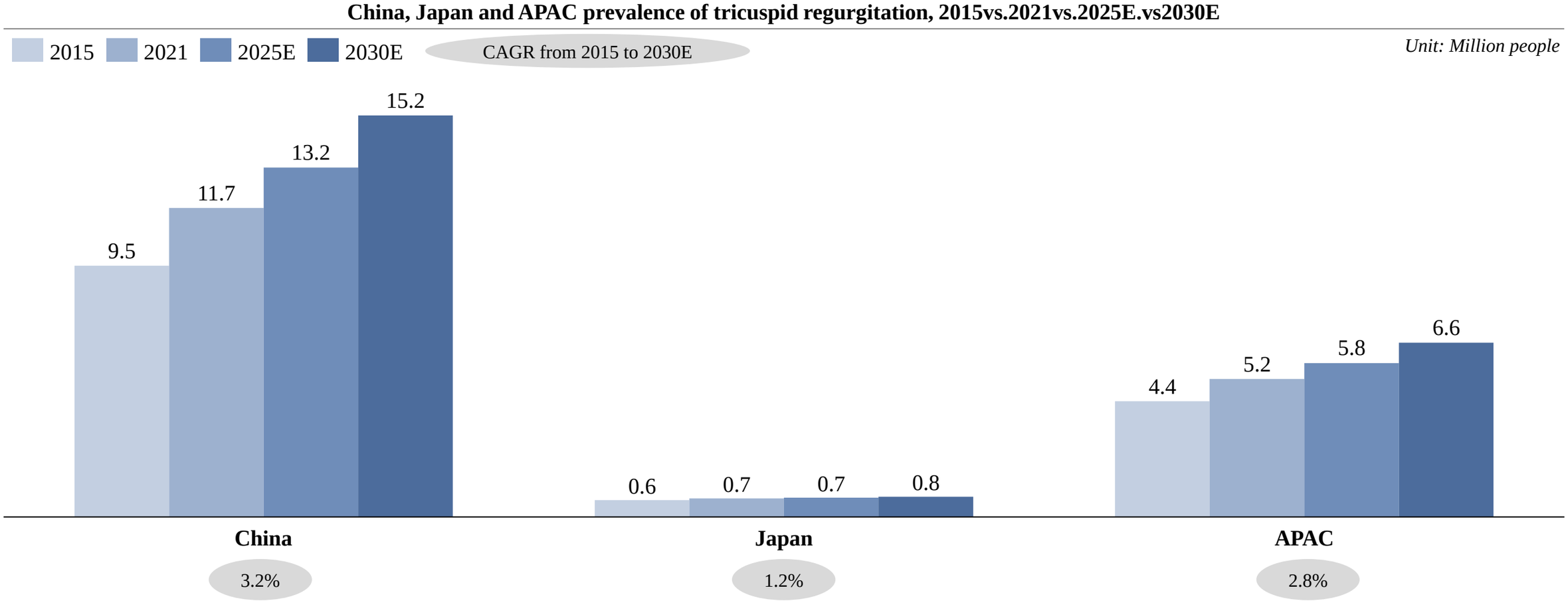


- Secondary TR related to right ventricular (RV) dilatation and/or dysfunction, annular dilatation and leaflet tethering, which are usually secondary to left-sided VHD, atrial fibrillation or pulmonary hypertension

Functional staging	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
					
Symptoms	• None	• None	• None-vague	• Current or previous episodes of RHF	• Overt RHF and/or end-organ damage due to chronic RV volume overload
TR grade	• Less than moderate	• >Moderate	• Severe	• Severe	• Torrential
Annular remodeling	• Normal	• Normal or mildly remodeled	• Present	• Moderate-severe	• Severe
Leaflet coaptation	• Normal	• Mildly abnormal	• Abnormal	• Coaptation gap	• Large coaptation gap
Tethering	• None	• None or mildly abnormal(<8 mm)	• Abnormal (usually <8 mm)	• Significantly abnormal with varying degree of tethering	• Significantly abnormal (usually >8 mm)
RV function and remodeling	• Normal	• Normal function Absent or mild remodeling	• Mild RV dysfunction and/or remodeling	• >Moderate dysfunction and remodeling	• Severe RV dysfunction and remodeling

Source: Lecturio; European Journal of Cardio-Thoracic Surgery; European Society of Cardiology; JACC; China Insights Consultancy

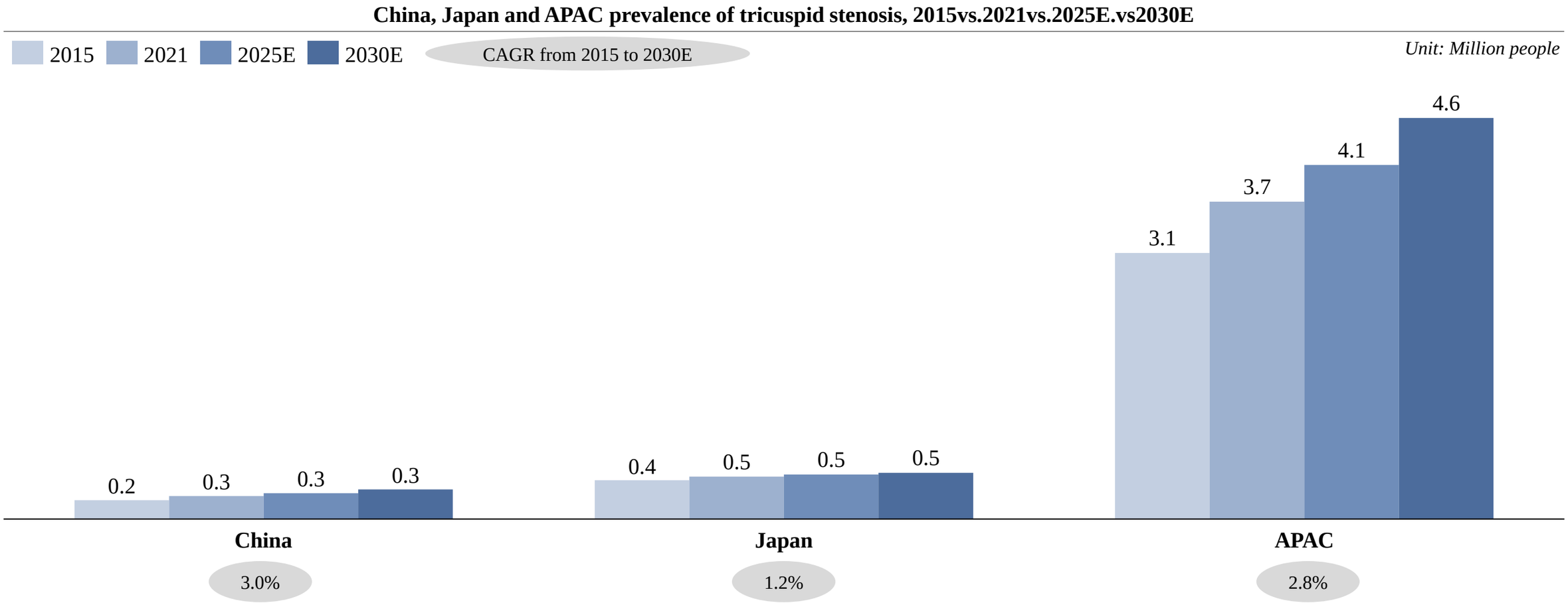
China, Japan and APAC prevalence of tricuspid regurgitation, 2015vs.2021vs.2025E.vs2030E



*APAC: APEC excluding China, Japan, The US and Russia

Source: China Insights Consultancy

China, Japan and APAC prevalence of tricuspid stenosis, 2015vs.2021vs.2025E.vs2030E



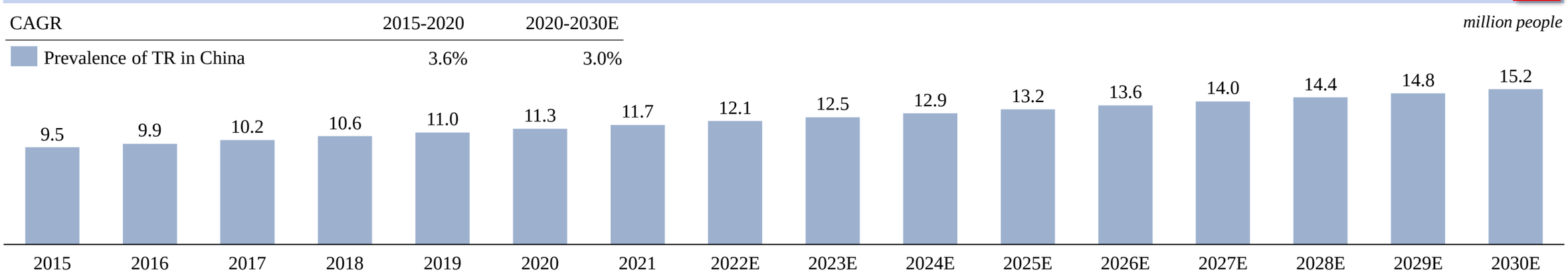
*APAC: APEC excluding China, Japan, The US and Russia

Source: China Insights Consultancy

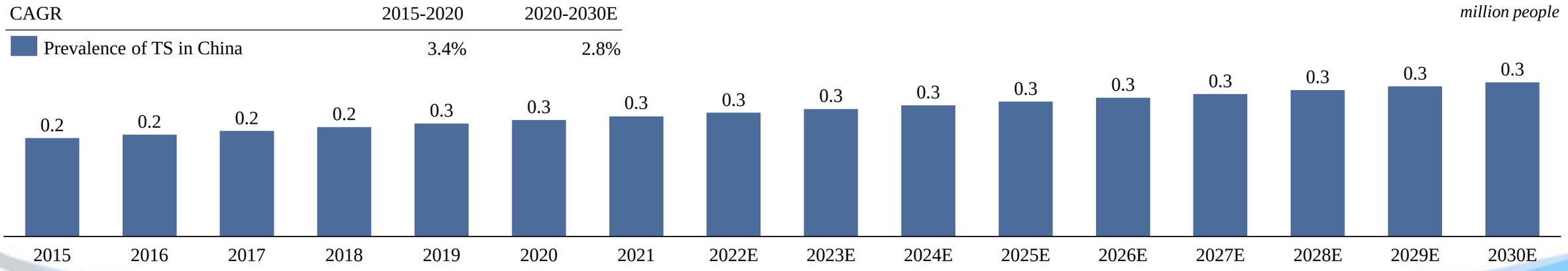
Prevalence of tricuspid regurgitation and tricuspid stenosis in China

Epidemiology of tricuspid regurgitation and stenosis

Prevalence tricuspid regurgitation in China, 2015-2030E



Prevalence of tricuspid stenosis in China, 2015-2030E

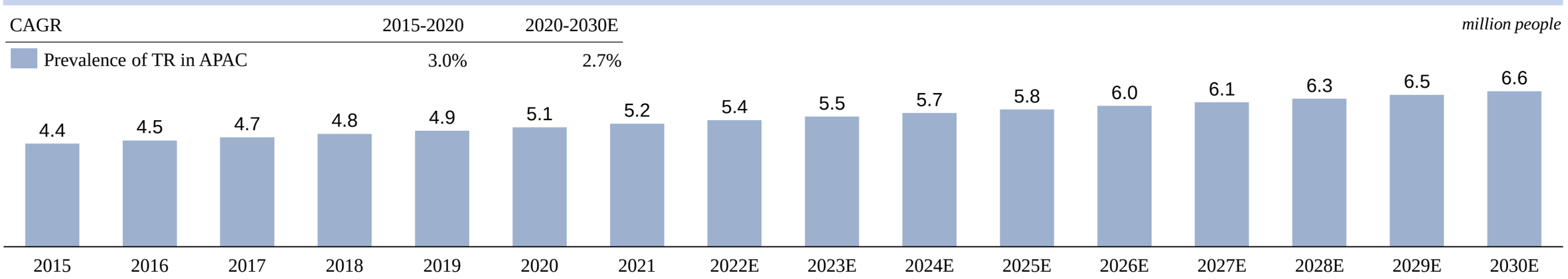


Source: Analyses for Prevalence and Outcome of Tricuspid Regurgitation in China; doi.org/10.1159/000496601; China Insights Consultancy

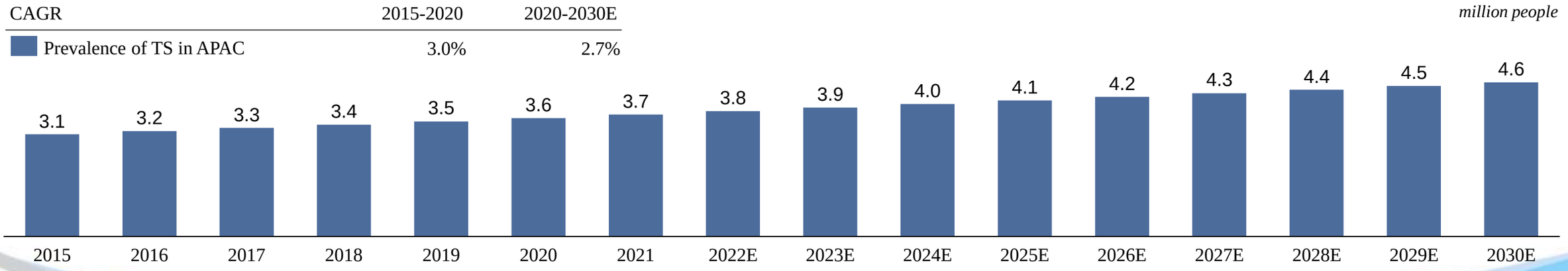
Prevalence of tricuspid regurgitation and tricuspid stenosis in APAC*

Epidemiology of tricuspid regurgitation and stenosis

Prevalence of tricuspid regurgitation in APAC, 2015-2030E



Prevalence of tricuspid stenosis in APAC, 2015-2030E

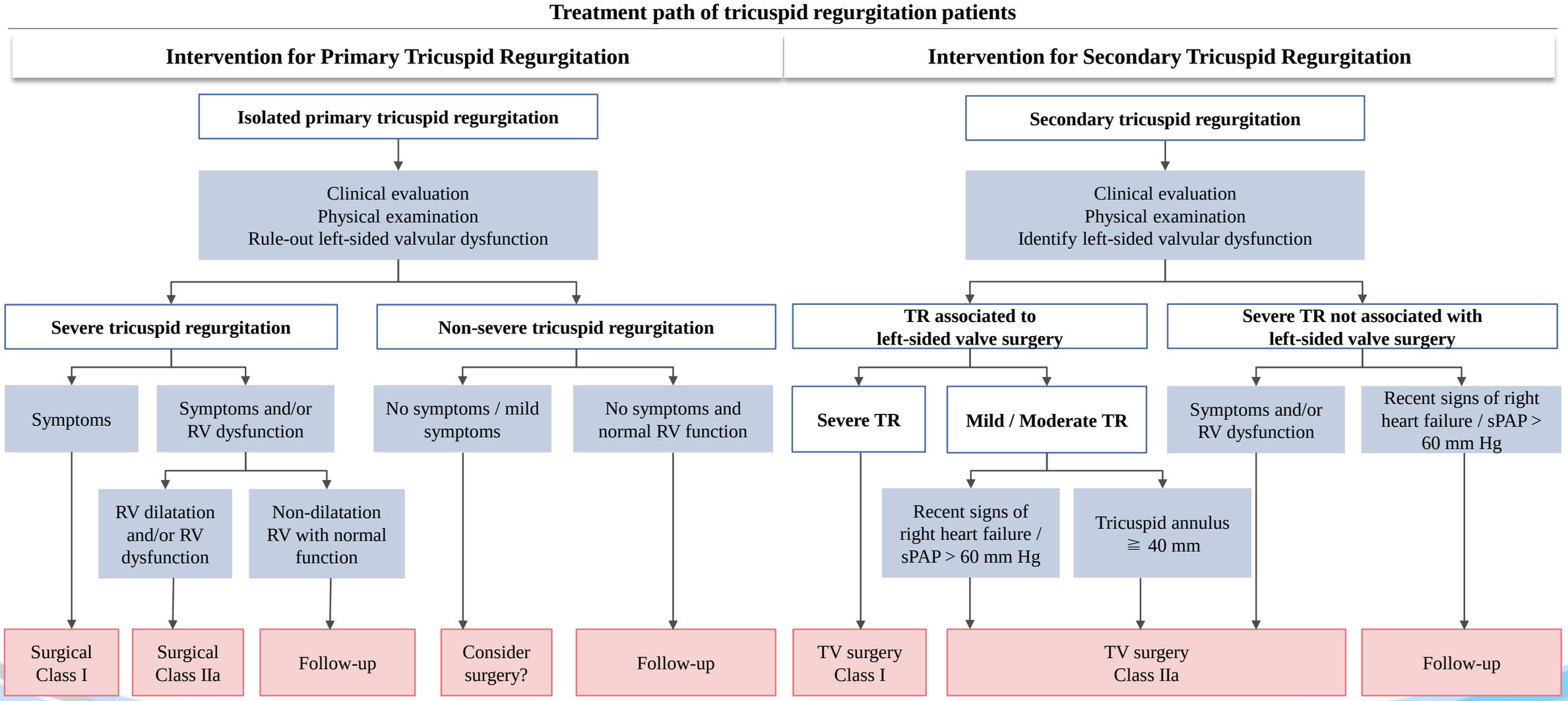


**APAC: APEC excluding China, Japan, The US and Russia*

Source: European Society of Cardiology; Tricuspid Regurgitation is a Public Health Crisis; China Insights Consultancy

Treatment path of tricuspid regurgitation patients

- A systematic multi-modality approach to diagnosis and assessment is essential based not only on TR severity but also on assessing annular size and RV function, due to the complex pathophysiology of TR



Notes: RV: right ventricular; sPAP: systolic pulmonary arterial pressure; TR: tricuspid regurgitation; TV: tricuspid valve.

Source: European Journal of Cardio-Thoracic Surgery; China Insights Consultancy

Overview of tricuspid regurgitation intervention

- TV surgery is recommended in patients with severe primary or secondary TR; For complex lesions, specific surgical repair techniques may be required and replacement may be superior to repair

Introduction of tricuspid regurgitation intervention

- Surgery including TR repair and TR replacement remains the first option in TR
  - TV repair: Tricuspid annuloplasty has great importance for treatment of FTR, even in initial stages of annular dilation (>40 mm) with TR less than severe; Ring annuloplasty produced better results than suture annuloplasty
  - TV replacement has great importance for treatment of primary TR with severe leaflet pathology; TV replacement should be considered when FTR occurs at end stage
- Medical therapy: Because the most important cause of heart failure hospitalization is pulmonary congestion, the first medical approach is diuretic therapy.
- Transcatheter TV interventions are emerging as an alternative for symptomatic patients who are deemed to be at high risk for conventional surgery by a multidisciplinary heart team.

	TR stage 1	TR stage 2	TR stage 3	TR stage 4	TR stage 5
Medication therapy	• No treatment but regular clinical and echo follow-up in patients with high likelihood of developing TR progression	• None or low-dose diuretics	• Diuretics	• Moderate to high-dose diuretics and/or requirement for IV diuretics	• Multiple admissions for RHF. Frequent need for IV diuretics and/or high-dose combination diuretics
Open-heart surgery	• No	• Consider TV surgery (preferably repair) at time of left-sided surgery	• TV surgery (preferably repair) at time of left-sided surgery. • Isolated TV surgery (preferably repair) in presence of symptoms or progressive RV remodeling and comorbidities	• Isolated TV surgery (repair or replacement) either isolated or at time of left-sided surgery in the absence of severe pulmonary hypertension and severe comorbidities • High risk of perioperative RV dysfunction	• Prohibitive intra- and peri-operative risk
Transcatheter intervention	• No	• Potential future target for percutaneous options as minimally invasive option could change natural history with minimal risk	• Potential candidates for isolated TR surgery who could be enrolled in upcoming IDE RCTs	• Current group of patients being treated in EFS if high-risk for surgery • May require combination of annuloplasty and leaflet device or TVR	• Prohibitive risk and potentially futile • Palliative procedures can be considered in highly selected patients

Notes: EFS=early feasibility studies; FTR=functional tricuspid regurgitation; IDE=investigational device exemption; IV=intravenous; RCT=randomized controlled trial; RHF=right heart failure; RV=right ventricular; TR=tricuspid regurgitation; TV=tricuspid valve; TVR=tricuspid valve replacement.

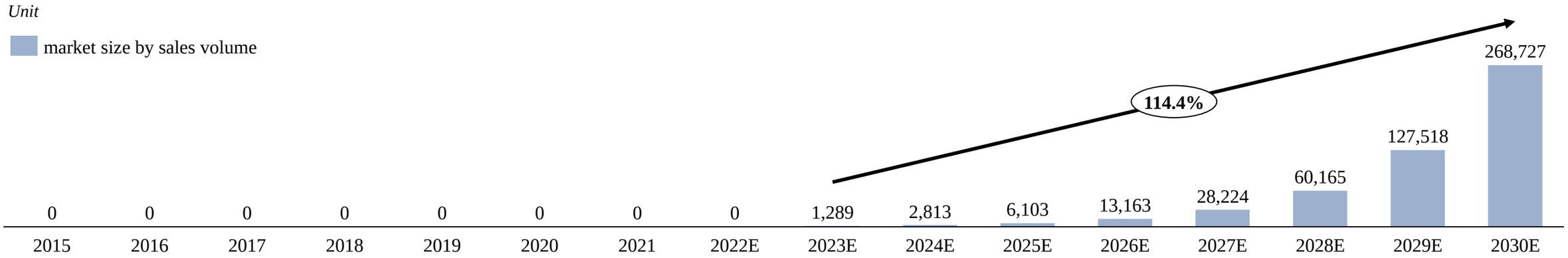
Source: JACC; China Insights Consultancy

China market size of transcatheter tricuspid valve replacement interventional surgical device

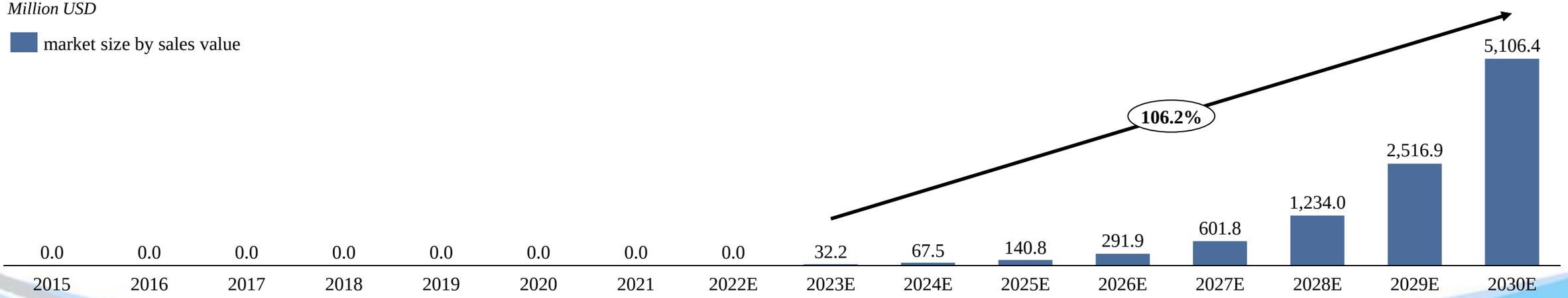
- It is expected that first TTVR device will be launched in 2023

China market size of transcatheter tricuspid valve replacement interventional surgical device

Market size by sales volume, China, 2015-2030E



Market size by sales value, China, 2015-2030E

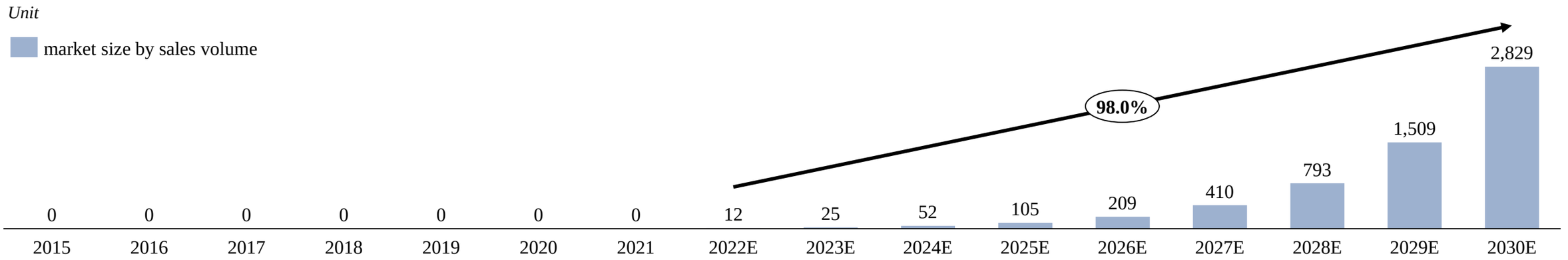


Source: China Insights Industry Consultancy Limited, expert interviews and public information

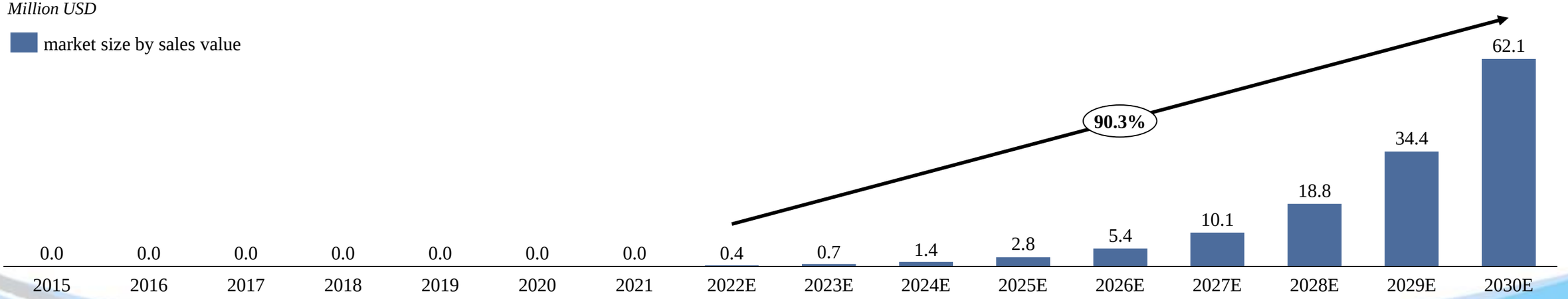
Japan market size of transcatheter tricuspid valve replacement interventional surgical device

Japan market size of transcatheter tricuspid valve replacement interventional surgical device

Market size by sales volume, Japan, 2015-2030E



Market size by sales value, Japan, 2015-2030E

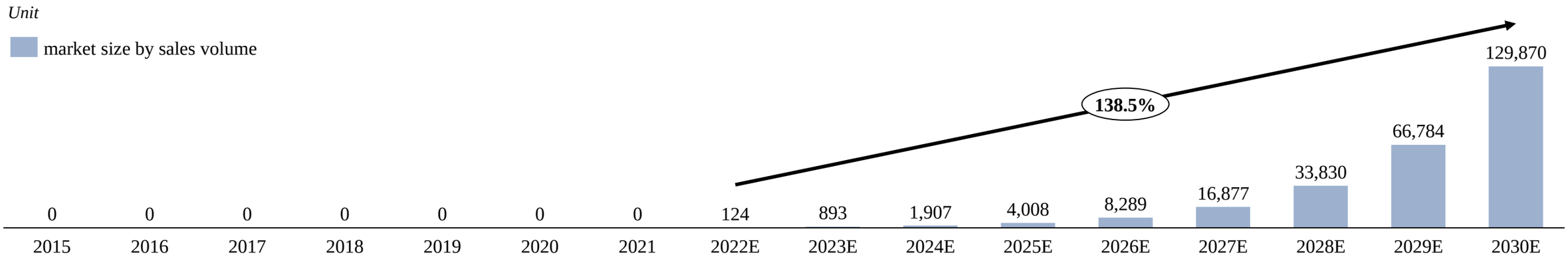


Source: China Insights Industry Consultancy Limited, expert interviews and public information

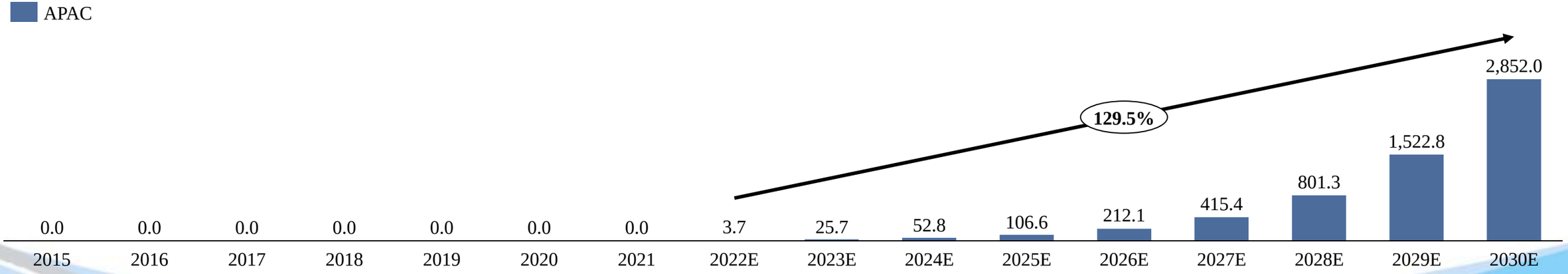
APAC* market size of transcatheter tricuspid valve replacement interventional surgical device

APAC market size of transcatheter tricuspid valve replacement interventional surgical device

Market size by sales volume, APAC, 2015-2030E



Market size by sales value, APAC, 2015-2030E



**APAC: APEC excluding China, Japan, The US and Russia*

Source: China Insights Industry Consultancy Limited, expert interviews and public information

Global tricuspid regurgitation interventional surgical device under research

- Multiple other repair techniques and devices are currently under investigation worldwide

Transcatheter tricuspid surgical device under research

Name	Company	Mechanism	Composition	Registered Trial Number	First posted date	Estimated Study Completion Date
Sapien XT	Edwards	Heterotopic	Balloon-expandable, cobalt-chromium frame, trileaflet bovine pericardial tissue valve, and polyethylene terephthalate (PET) fabric skirt	NCT02339974	2015/1/16	2022/1
TricValve	P &F	Heterotopic	Self-expanding pericardial tissue on nitinol stents	NCT03723239 NCT04141137	2018/10/29 2019/10/28	2026/7 2025/3
Cardiovalve	Boston Medical	Orthotopic	Nitinol Frame, bovine pericardial leaflets	NCT04100720	2019/9/24	2028/12
Evoque	Edwards	Orthotopic	Bovine pericardial leaflets	NCT04221490 NCT04482062	2020/1/9 2020/7/22	2025/12 2028/6
Intrepid	Medtronic	Orthotopic	Dual stent system with 29mm bovine pericardial valve	NCT04433065	2020/6/16	2026/11
Lux-Valve	Jenscare Biotechnology	Orthotopic	Self-expanding bovine pericardial tissue valve on nitinol stent covered by layer of polyethylene terephthalate	NCT04436653	2020/6/18	2026/6
Trisol Valve	Trisol Medical	Orthotopic	Self-expanding conical nitinol stent, porcine pericardium ventricular and polyester atrial skirts;	NCT04905017	2021/5/27	2027/7

Source:Clinicaltrials.gov; Frontiersin; China Insights Consultancy

Global tricuspid regurgitation interventional surgical device under research- introduction to TricValve

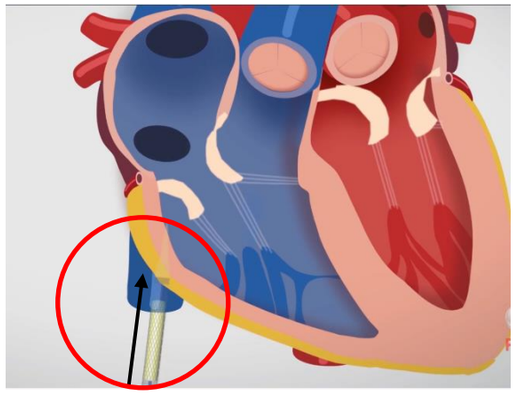
-TricValve® Transcatheter Bicaval Valves System is a method to address Tricuspid Regurgitation and caval reflux without disturbing the natural tricuspid valve

Introduction to TricValve transcatheter bicaval valves system

Introduction:

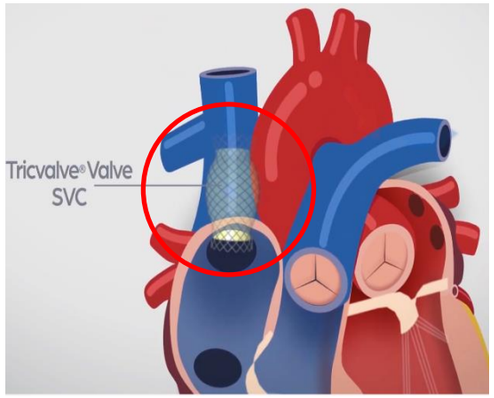
- TricValve® Transcatheter Bicaval Valves is a system of two self- expanding biological valves for the treatment of patients with hemodynamically relevant tricuspid insufficiency and caval reflux.
- The prostheses are implanted percutaneously into the inferior and superior vena cava without disturbing the native tricuspid valve.
- It is especially intended for use for patients at extreme risk or who are inoperable for open surgical therapy.
- TricValve® Transcatheter Bicaval Valves System is a method to address Tricuspid Regurgitation and caval reflux without disturbing the natural tricuspid valve.
- TricValve® Transcatheter Bicaval Valves System is the **only** CAVAL valve implantation available
- It has received CE mark approval.

Step 1



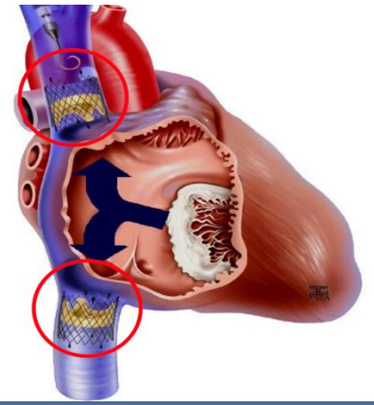
- Transfemoral access by delivery device to superior Vena Cave

Step 2



- Expand the balloon
- Implant the prostheses percutaneously into superior vena cava without disturbing the native tricuspid valve.

Step 3



- Repeat Step 1 and Step 2 but to the inferior vena cave
- Transfemoral access
- Expand the balloon
- Implant the prostheses percutaneously into inferior vena cava

Product name	Manufacturer	Clinical status	Mechanism	Approach	Access	Applicable Indication
TricValve	P&F Products & Features	Safety study underway	• Bicaval valve	• Heterotopic tricuspid valve replacement	• Transfemoral	• Primary and functional TR

Source: ICRjournal; Frontiersin; China Insights Consultancy

I. Overview of global medical device market
II. Overview of global coronary artery disease interventional procedural instrument market
III.Overview of global peripheral artery disease interventional procedural instrument market
IV.Overview of global neuro artery disease interventional procedural instrument market
V. Overview of global structural heart disease interventional procedural instrument market
VI.Appendix

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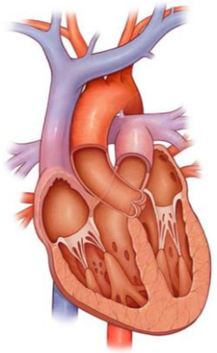
Overview of Structural heart disease

-Structural heart disease is caused by the abnormalities of the heart tissues and valves. It can be treated by medication, surgical options and transcatheter procedures according to its severity and patients' status

Introduction and treatment of structural heart disease



Introduction to structural heart disease	
Introduction	• Heart disease is a general term used to describe heart abnormalities such as coronary heart disease, structural heart disease, and arrhythmia. • Structural heart disease refers to the physical and physiological changes of heart disease caused by anatomical abnormalities of the heart tissues or valves. Many structural heart diseases are congenital, which means present at birth. Some structural heart disease will develop later in life.
Types	• **Valvular heart disease**: Stenosis or regurgitation of four valves(tricuspid valve, aortic valve, mitral valve, and pulmonary valve) • Congenital heart disease • Heart failure • Cardiomyopathy • Ventricular abnormalities

Treatment options of structural heart disease

Treatment options	Patient coverage	Features
Medication therapy	✓ Suitable for patients whose heart problem is very mild or for him or her the surgery is not an option.	• Increase the heart's pumping ability, control irregular heartbeats, relieve discomfort and prevent blood clots. • Possible medication class: ACE inhibitors and ARBs/Anti-arrhythmic medications/Antibiotics/Anticoagulants /Beta-blockers/Diuretics/Vasodilators.
Open-heart surgery	✓ Patients who have more advanced heart disease with severe symptoms ✓ Low risks for open-heart surgery	• Need to open chest • Patients will be placed on a heart and lung blood machine as the heart will be stopped during the surgery
Transcatheter intervention	✓ High-risk patients with heart valve disease or congenital heart defeats ✓ High risks for surgical options ✓ Minimally invasive procedures	• Transcatheter closure of congenital heart disease • Valvular heart disease: Transcatheter Aortic Valve Replacement(TAVR); Transcatheter mitral valve implantation(TMVI); Percutaneous pulmonary valve implantation(PPVI);Transcatheter edge-to-edge mitral valve repair(TEER) • Transcatheter left atrial appendage occlusion • Cardiomyopathy: Percutaneous transluminal septal myocardial ablation(PTSMA) or radiofrequency ablation for hypertrophic cardiomyopathy

Source: MedSci; AHA; China Insights Consultancy

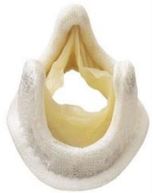
Introduction to artificial valve

- There are two types of artificial valves which are mechanical heart valve and biological heart valve. For biological heart valve, dry-storage is the cutting-edge technology with longer durability and better operability

Evolution and comparison of different kinds of artificial valve

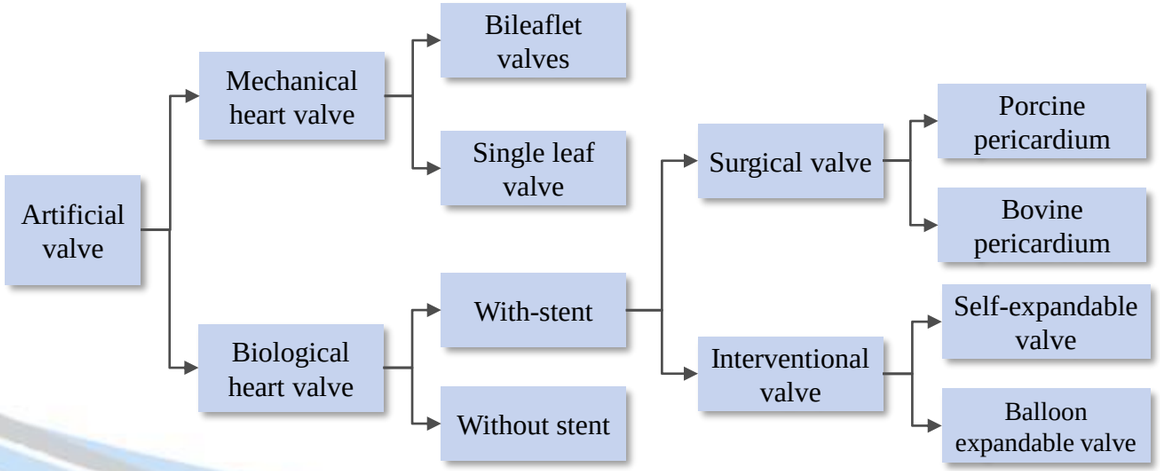
Mechanical heart valve

Mechanical heart valve was first invented and implanted in heart valve surgery. It is made of pyrolytic carbon-coated composite material and is durable to last for over 50 years which means more suitable for the young patients. Patients implanted mechanical heart valves necessitate lifelong anticoagulation therapy with a vitamin K antagonist and their blood coagulation function should be monitored regularly.



Tissue valve (Biological valve)

Tissue valves developed a little later than mechanical heart valve and mostly collected from animal valves which are most like human ones. The first generation of biological valves was substantially consisted of porcine valves and now there are two types now which are porcine and bovine pericardium valves. Biological valve can last for about 10 to 20 years and only need to take anticoagulation therapy for 3 to 6 months after surgery.



Introduction to Dry pericardium processing valve (Dry-storage)

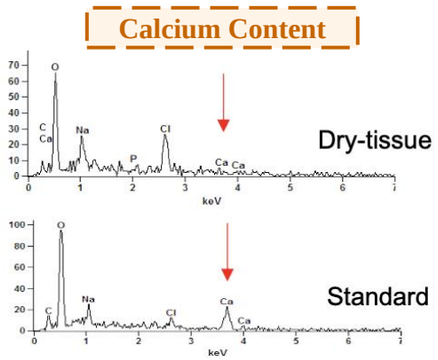
Introduction

- **Dry pericardium processing technology (Dry-storage), or pre-packaged/pre-mounted technology** is new in the development of biological valves. Compared with Wet Valve, Dry Valve permanently blocks free aldehyde groups within the tissue, which are known to lead to calcification and SVD. This also eliminates the need for glutaraldehyde preservation, enabling dry storage with no need for rinsing prior to use.

Technology

- **Reduce the thickness of leaflet:** Using innovative tissue technology, in addition to ordinary decellularization and decalcification, the thickness of the pericardium can be reduced to about 1/3 of similar products while retaining the content of structural protein.
- **Dehydrate during the installation process:** As 70% of the valve tissue is water, it is designed to be gradually dehydrated and will finally account for only 10% of the original tissue volume. And pre-install on the delivery system.

Advantages



- Less possibility of calcification and longer durability.
- Lower risks of operational mistakes during loading, because all process will be done during manufacturing process with adequate checking.
- Lower interventional time, because there is no need to wait for loading and checking while the patient is under intervention.
- Lower risks of contamination because valve manipulation is not necessary. Will have smaller team size.

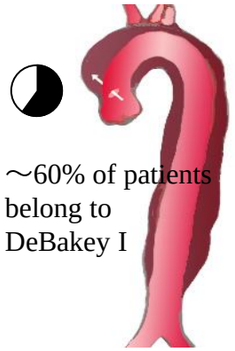
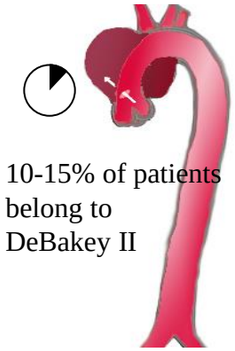
Source: NCBI; EuroIntervention; AHA; China Insights Consultancy

Overview of Aortic dissection

-Aortic dissection is a serious condition in which the inner layer of the aorta, the large blood vessel branching off the heart, tears. It can be divided into two types and can be treated by medication or surgery

Introduction and treatment of aortic dissection

- An aortic dissection is a tear in the inner layer of the aortic wall, which allows blood to enter into the wall of the aorta, creating a new passage for blood, known as the “false lumen.” Blood flow into the false lumen can cause several problems: It can rob crucial blood from the rest of the body, it can cause the dissection to spread and affect other arteries, and it can block blood flow in the true aortic channel (“true lumen”). These problems may cause decreased blood flow to vital organs. Aortic dissection also weakens the aortic wall and may lead to rupture, which may be fatal, or to formation of a balloon-like expansion of the aorta, known as an aneurysm.
- Aortic dissections can be divided into two groups which are type A and type B, depending on which part of the aorta is affected.

Images	Type	Description	Treatment
 ~60% of patients belong to DeBakey I  10-15% of patients belong to DeBakey II	**TYPE A (DeBakey I&II)**	• Type A involves the **ascending aorta** and/or **aortic arch**, and possibly the **descending aorta**. The tear can originate in the ascending aorta, the aortic arch, or more rarely, in the descending aorta. • Can be life-threatening	• Immediate surgery is indicated to repair or replace the first segment of the aorta (ascending aorta) where the tear started. • Dacron graft can be used to replace part of the aorta • On average, the risk of death from acute type A aortic dissection is approximately 20%.
 25-30% of patients belong to DeBakey III	**TYPE B (DeBakey III)**	• Type B involves the **descending aorta** or the **arch** (distal to the left subclavian artery), without the involvement of the ascending aorta.	• Take intravenous blood pressure medications to manage. At the same time, patients should be monitored closely and carefully. • If the dissection progresses rapidly, an interventional radiologist or surgeon may use a catheter-based procedure to improve vital organ arterial perfusion, or urgent aortic surgery may be required. • Endovascular stent grafting is now being tested as alternatives to surgery in certain patients with type B dissections

Source: AHA; China Insights Consultancy

Overview of Aortic dissection surgical devices

-Acute Type A Aortic dissection would be fatal if immediate treatment isn't performed. Patients could take a Bentall procedure surgery which needs to open chest or less-invasive surgery called Endovascular therapy depending on their own conditions

Overview of Aortic dissection surgical device

- Immediate surgery is required to treat patients with acute Type A aortic dissection(ATAAD). Patient may receive aortic root replacement surgery (also called Bentall Procedure)which is an open-chest surgery or interventional management where Endo Bentall procedure could be potential of endovascular therapy. And feasibility of Endo Bentall procedure has already been proved.
- Surgical management reduces mortality while 20% of the patients are deemed to be inoperable due to very high surgical risk and usually are left on medical treatment alone. Interventional management can be an alternative to surgery which has several advantages such as lower trauma, no need for cardiac arrest and extracorporeal circulation, less risky for elderly and comorbid patients, expected faster recovery. However, this type of therapy has its valid limitations: the complex anatomy of the aortic root, ascending aorta, and aortic arch with the challenge to preserve the patency of the aortic valve and blood flow of the brachiocephalic branches and coronary arteries.

Category	Definition	Patient coverage	Difference & Advantage	Risks
Surgical treatment (Bentall Procedure) 	• Bentall procedure is performed for the repair of ascending aortic root lesions. Typically, the native aortic root and aortic valve are replaced with a composite graft that comprises both ascending aortic and aortic valve grafts, to which the coronary arteries are anastomosed.	• Patients with Aortic regurgitation/Marfan's syndrome/Aortic dissection/Aortic aneurysm • Low risk to take open-chest surgery	• Still the first and long-term choice for patients with ATAAD • Need to open chest and the heart's activity is temporarily stopped; Performed under general anaesthesia.	• May have several complications like Arrhythmias/ Pneumonia/Septic shock etc.
Endovascular therapy (Endo Bentall procedure) 	• An endovascular valve-carrying conduit consisting of a proximal transcatheter aortic valve connected to a covered stent-graft would be close to a primary entry tear in the ascending aorta, ensure coronary perfusion, initiate true lumen expansion, treat malperfusion, treat aortic regurgitation, drain any pericardial effusion through a transapical approach, and possibly stabilize the distal aorta.	• An alternative option to medical treatment for high surgical risk patients.	• Minimally invasive • Lack of surgical trauma • No need for extracorporeal circulation • Less risky for elderly and comorbid patients • Expected faster recovery	• Lack of specific ascending aorta stent-grafts and hard to provide sufficient proximal landing zone for the implantation of existing stent-grafts • Missing sizes of stent-grafts and bare stents • Not suitable for patients with concomitant valve pathology

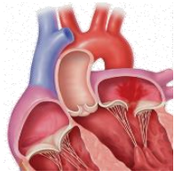
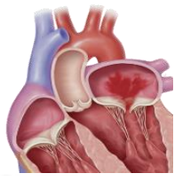
Source: Journal of Cardiology and Cardiovascular Sciences; NCBI; Sage Journal; China Insights Consultancy

Introduction and epidemiology of mitral regurgitation

- Mitral regurgitation (MR) is one of the most common structural cardiac disease and generally categorized into primary and secondary MR, with functional grades and quantitative severity standard to specifically illustrate

Introduction and classification of mitral regurgitation

Introduction	
Mitral valve	• The mitral valve is a complex structure, consisting of the annulus, leaflets, chordae tendinae, and papillary muscles; it interacts with the ventricular chamber to maintain its competency during systole. Abnormalities of any part of the mitral valve or ventricle can lead to incompetency, and frequently **more than one** component of the complex is affected.
Mitral regurgitation	• Mitral regurgitation (MR), also called mitral valve regurgitation, mitral insufficiency or mitral incompetence, is a condition in which your heart's mitral valve doesn't close tightly, allowing blood to flow backward in your heart. If the mitral valve regurgitation is significant, blood can't move through your heart or to the rest of your body as efficiently, making you feel tired or out of breath.

	Category	Prevalence	Mechanism	Associated diseases	Carpentier classification
	Primary mitral regurgitation				
	• Organic (or primary or degenerative) MR arises as a result of pathology affecting one or more components of the mitral valve (MV) apparatus.	• Lower	• Pathology of one or some of the components of the valve (leaflets, chordae tendinae, papillary muscles, annulus)	• Myxomatous valve – Barlow's disease, Fibroelastic deficiency disease • Rheumatic valvular disease • Endocarditis • Radiation therapy, connective tissues disease, drug induced, mitral annular calcification, cleft mitral valve	• Type 1 (leaflet perforation or cleft) • Type II (MV prolapse) • Type IIIa (rheumatic valve disease, drug induced MR, mitral annular calcification)
	Secondary mitral regurgitation				
	• Functional (or secondary) MR is a consequence of annular dilatation and geometrical distortion of sub-valvular apparatus secondary to left ventricular (LV) remodeling and dyssynchrony	• Majority of MR • Higher	• Left ventricular dysfunction with papillary muscle displacement, LV dyssynchrony, associated leaflet tethering and annular dilation. Normal (or nearly normal) mitral leaflet and chordae structure	• Dilated cardiomyopathy • Ischemic MR secondary to previous myocardial infarction • Hypertrophic cardiomyopathy	• Type I (atrial MR, non-ischemic cardiomyopathy) • Type IIIb (ischemic cardiopathy, LV dysfunction and systolic leaflet tethering)

Source: EHJ; Heartware; Abbott; Echopedia; Heart.org; BMJ; Mitralvlve.org; Lecturio; Frontiersin; China Insights Consultancy

Introduction and epidemiology of mitral stenosis

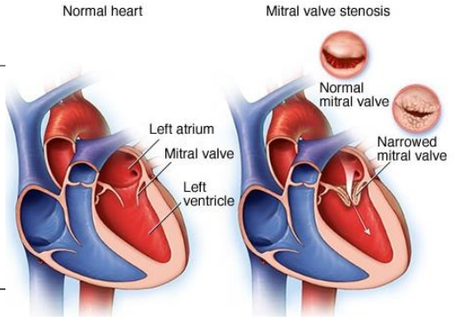
- Mitral Stenosis (MS) is a narrowing of the mitral valve and is mainly caused by rheumatic fever. It is usually asymptomatic and can be divided into four types according mitral valve area and diastolic pressure half-time

Introduction and classification of mitral stenosis

Introduction

Mitral Stenosis (MS)

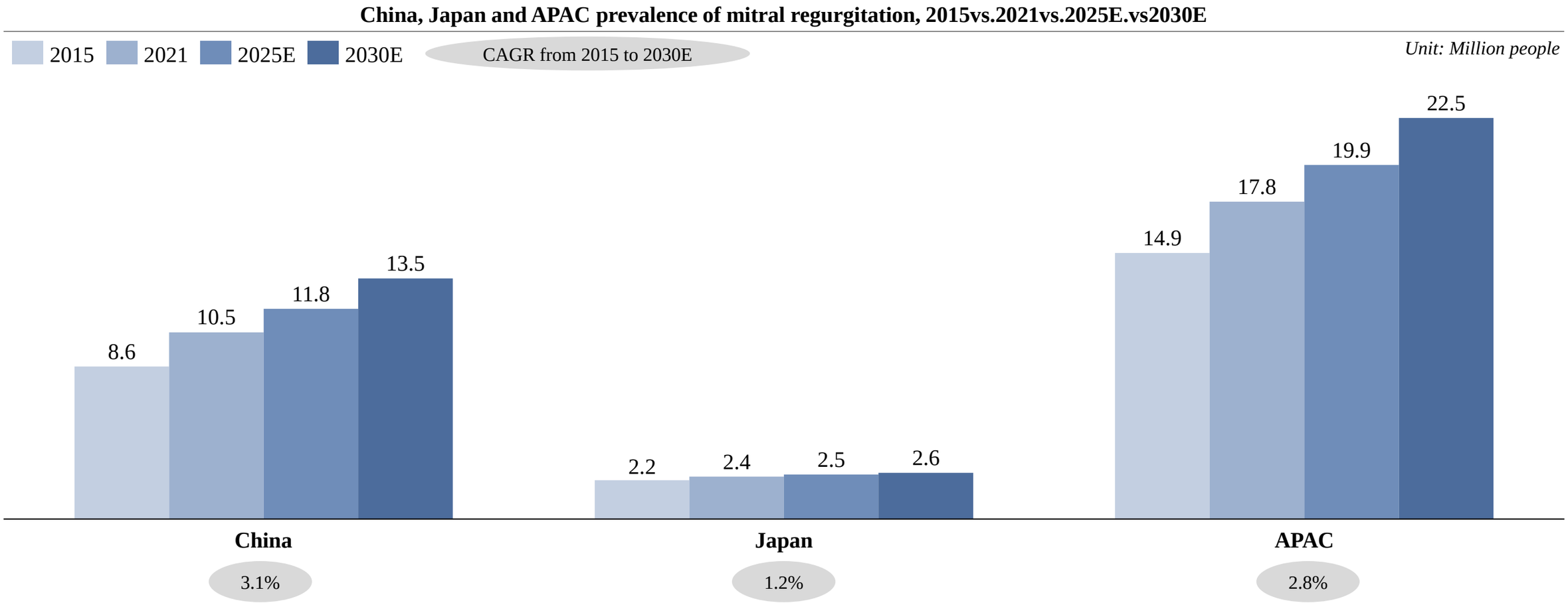
- Mitral valve stenosis (also called mitral stenosis) is a narrowing of the heart's mitral valve. This abnormal valve doesn't open properly, blocking blood flow into the main pumping chamber of your heart (left ventricle). Mitral valve stenosis can make you tired and short of breath, among other problems.
- Rheumatic valve disease is the primary cause of MS. Common complications are pulmonary hypertension, atrial fibrillation, and thromboembolism.



Category	Valve Anatomy	Valve Hemodynamics	Hemodynamic Consequences	Symptoms
At risk of MS	• Mild valve doming during diastole	• Normal transmitral flow velocity	• None	• None
Progressive MS	• Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets • Planimetered mitral valve area >1.5 cm^2	• Increased transmitral flow velocities • Mitral valve area > 1.5cm^2 • Diastolic pressure half-time<150 ms	• Mild to moderate left atrial enlargement • Normal pulmonary pressure at rest	• None
Asymptomatic MS	• Rheumatic valve changes with commissural fusion and diastolic doming of the mitral valve leaflets • Planimetered mitral valve area ≤1.5 cm^2	• Mitral valve area ≤ 1.5cm^2 • Diastolic pressure half-time ≥ 150 ms	• Severe left atrial enlargement • Elevated pulmonary artery systolic pressure >50mm Hg	• None
Symptomatic severe MS				• Decreased exercise tolerance • Exertional dyspnea

Source:NCBI;ACC; China Insights Consultancy

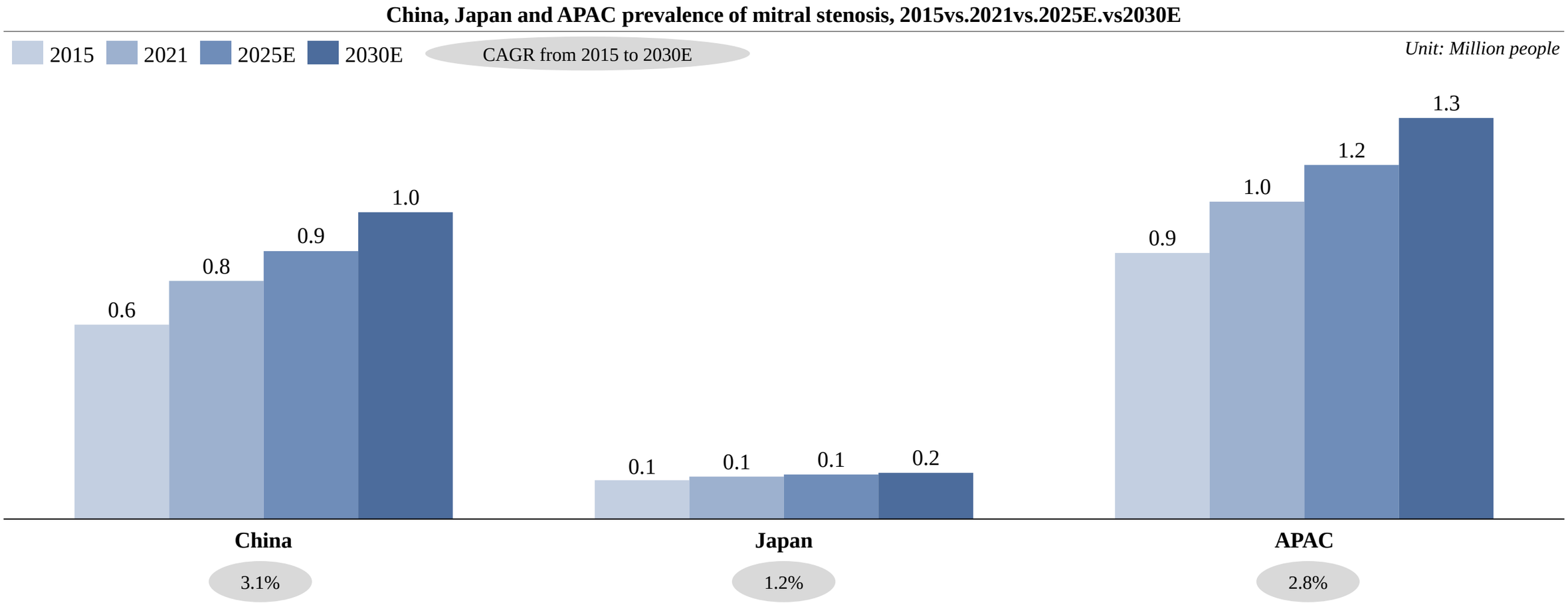
China, Japan and APAC prevalence of mitral regurgitation, 2015vs.2021vs.2025E.vs2030E



*APAC: APEC excluding China, Japan, The US and Russia

Source: China Insights Consultancy

China, Japan and APAC prevalence of mitral stenosis, 2015vs.2021vs.2025E.vs2030E



*APAC: APEC excluding China, Japan, The US and Russia

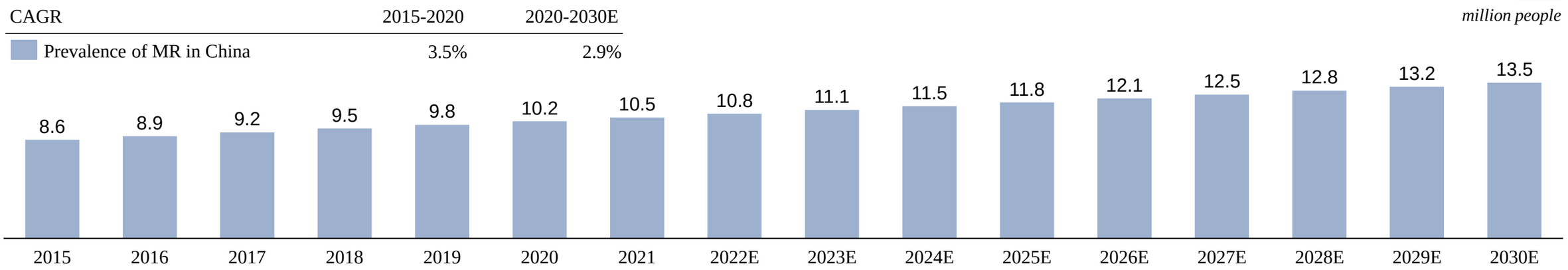
Source: China Insights Consultancy

Prevalence of mitral regurgitation and mitral stenosis in China

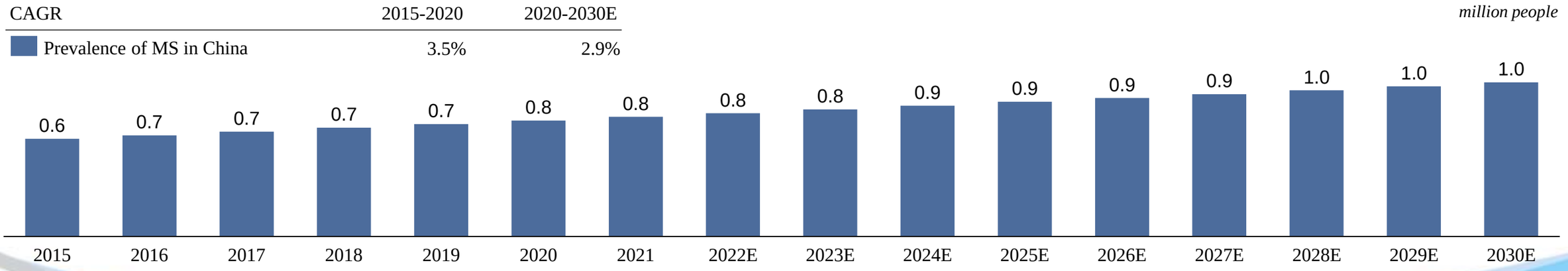
- Patients of mitral regurgitation account for considerable proportion among people suffering from valvular diseases, and meanwhile prevalence increases year over year

Epidemiology of mitral regurgitation and stenosis

Prevalence of mitral regurgitation in China, 2015-2030E



Prevalence of mitral stenosis in China, 2015-2030E

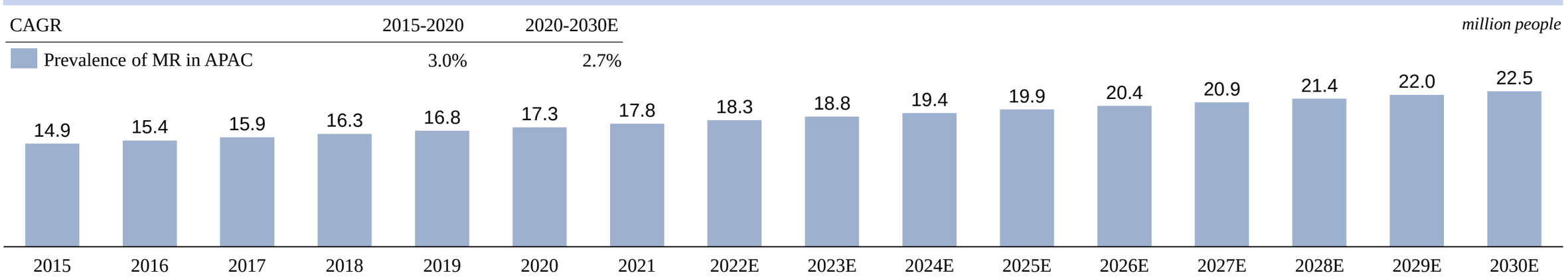


Source: Prevalence and Risk Factors of Mitral Regurgitation in the Population Aged ≥ 35 Years; Chinese Circulation Journal, May, 2017, Vol. 32 No.5（Serial No.227）; China Insights Consultancy

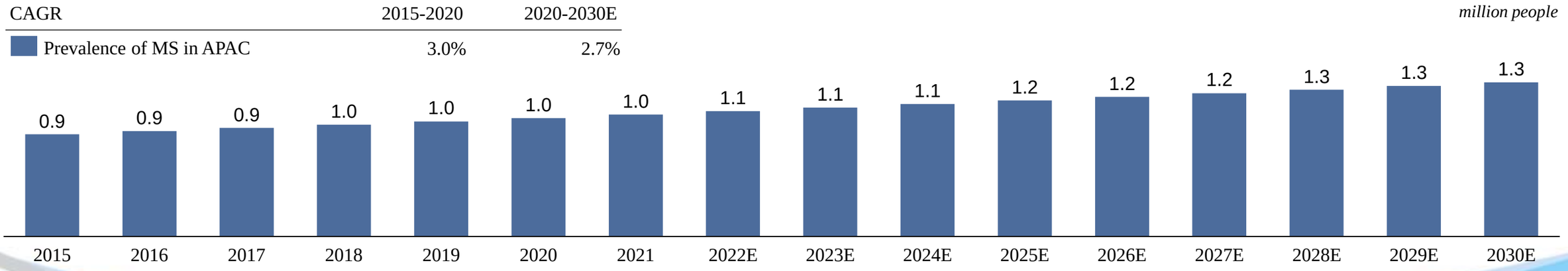
Prevalence of mitral regurgitation and mitral stenosis in APAC*

Epidemiology of mitral regurgitation and stenosis

Prevalence of mitral regurgitation in APAC, 2015-2030E



Prevalence of mitral stenosis in APAC, 2015-2030E



*APAC: APEC excluding China, Japan, The US and Russia

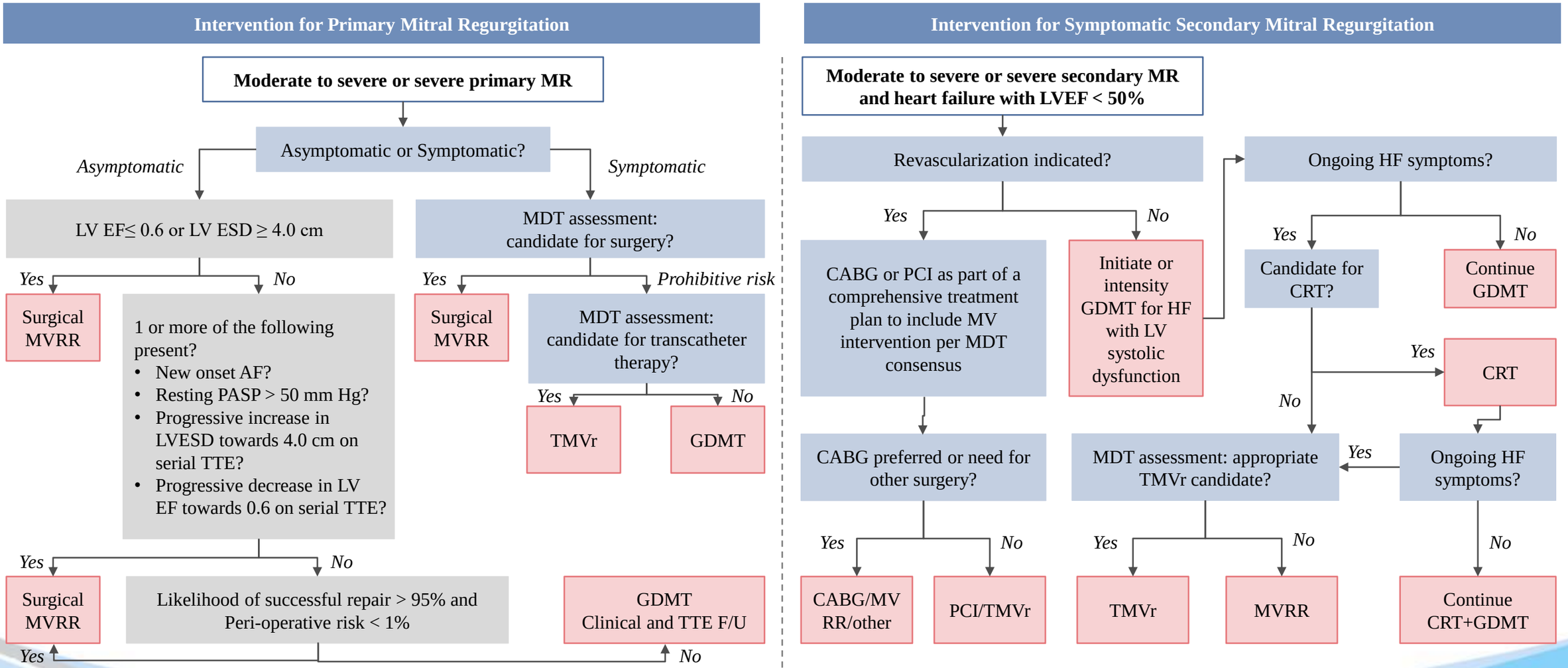
Source: Nature Reviews Cardiology; China Insights Consultancy

Treatment path of mitral regurgitation patients

- Management of mitral regurgitation can be divided into medical or surgical/percutaneous; The principal treatment modality for primary MR is surgical repair with some role for transcatheter interventions, where medical and device therapies are the first option for treatment of secondary MR

Treatment path of mitral regurgitation patients

Specific therapies



Notes: EF =ejection fraction; ESD =end-systolic dimension; F/U =follow-up; GDMT =guideline-directed management and therapy; LV =left ventricle; MDT =multidisciplinary team; MR =mitral regurgitation; MV =mitral valve; MVRR =mitral valve repair or replacement; PASP =pulmonary artery systolic pressure; SDM =shared decision-making; TMVr =transcatheter mitral valve repair; TTE =transthoracic echocardiography; AAD =antiarrhythmic drug; AF, atrial fibrillation; CABG =coronary artery bypass graft; CRT =cardiac resynchronization therapy; HF =heart failure; LVEF =left ventricular ejection fraction; PCI =percutaneous coronary intervention

Source: ACC; EHJ; AHA/ACC; China Insights Consultancy

Overview of transcatheter mitral valve repair (TMVr) and transcatheter mitral valve replacement (TMVR)

- During the last few years, two methods have been developed for percutaneous treatment of the mitral regurgitation, transcatheter mitral valve repair and transcatheter mitral valve replacement

Overview of TMVr and TMVR

- Open-heart surgery is the gold standard for the treatment of severe MR as excellent outcomes can be achieved in most patients, often adopting minimally invasive approaches. However, **in up to 50% of patients with severe MR surgical treatment is not performed owing to increased risk related to comorbidities.** Growing evidences support the ongoing development of **less invasive procedures which are better adapted to elderly patients with frequent comorbidities.**
- Transcatheter mitral interventions has been developed to address an unmet clinical need and may be an alternative therapeutic option to surgery with the intent to provide symptomatic and prognostic benefit. There are two percutaneous treatment of the MR, transcatheter mitral valve repair (TMVr) and transcatheter mitral valve replacement (TMVR). TMVR is sometimes also considered as transcatheter mitral valve implantation (TMVI)

Category	Definition	Patient coverage	Advantages	Challenges
Transcatheter mitral valve repair (TMVr)	• Patients keeps their own valve and multiple techniques like valvular plasty techniques are used to repair the valve so it functions normally again	• Potentially applicable to a greater proportion of patients	• Favorable safety profile • Conservation of the native anatomy • Low risk of thrombosis • No need for long-term anti-coagulation	• MR reduction is less predictable and MR may persist or reoccur • Possible need for combined therapies • Variability of disease/need for multiple devices
Transcatheter mitral valve replacement (TMVR)	• Patient’s valve is essentially cut out and a new valve (maybe a tissue or a mechanical valve) put in	• Less proportion of patient, maybe very high-risk patient, mainly with functional MR	• Simplicity, standardized strategy and short procedure duration • MR reduction is predictable • Versatility, potentially provide a concept of “One system fits all anatomies” • No further procedural need	• Dynamic mitral structure • Asymmetric anatomy • Complications may be more catastrophic and less forgiving • Deliverability (profile, rigidity) • Fixation (not relying on radial force) • Increased risk of left ventricular outflow tract (LVOT) obstruction • Near aorta and hard to replace

Source: European Heart Journal; AHA/ACC; China Insights Consultancy

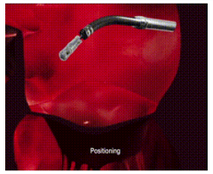
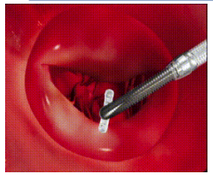
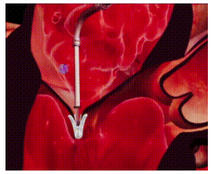
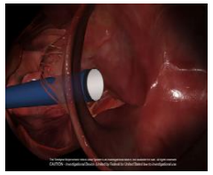
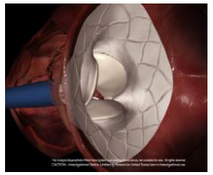
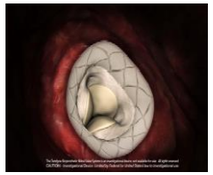
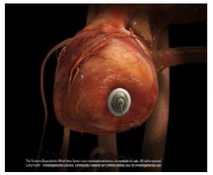
Overview of mitral regurgitation interventional surgical device

- From a surgical point of view, Percutaneous intervention can probably be divided into three categories: valvuloplasty, annuloplasty, and artificial chordae implantation; Mitral valve replacement involves removing much of the native mitral valve tissues and replacing it with an artificial valve consisting of animal and/or manufactured components

Introduction to procedure of mitral regurgitation interventional instrument

- Mitral valve repair: The main modalities of catheter access are through the peripheral vasculature and through small surgical incisions through the apex.
  - Percutaneous mitral valvuloplasty is based on the “edge-to-edge" technique used in traditional surgery. Not many patients can choose this therapy because of mitral valve condition.
  - Direct annuloplasty is performed by placing an adjustable prosthetic band at the annulus.
  - Indirect annuloplasty is performed by exerting force through a device deployed in the coronary sinus (CS)/great cardiac vein.
  - The use of artificial chordae to replace elongated or ruptured chordae responsible for mitral valve prolapse.

Mitral MR repair

	Step 1	Step 2	Step 3	Step 4
Valvuloplasty (Edge-to-edge repair)	 • Pass up through tube and into the left side of heart	 • Position over the leaky mitral valve and using the delivery system	 • With the arms opened, the system is passed down below mitral valve	 • After positioning the system pulled back upwards and mitral leaflets are grasped
Annuloplasty	 • Transseptal puncture: access via transseptal puncture	 • System insertion: insert into the position above mitral valve	 • Implant deployment: deploy implant via steerable catheter	 • Implant size adjustment: adjust and confirm real-time reduction of MR
Artificial chordae	 • Insert the device and move it through the heart through mitral valve	 • The device will be closed onto the leaky section of mitral valve	 • After the new heart strings are attached, the device will be removed	 • New heart strings will remain in the heart and keep mitral valve functioning
Mitral valve replacement	 • Transapical approach and Insert Catheter into LA	 • Intra-Annular Deployment	 • Ensure Valve Seating and Adjust Tether Tension	 • Secure Apical Pad

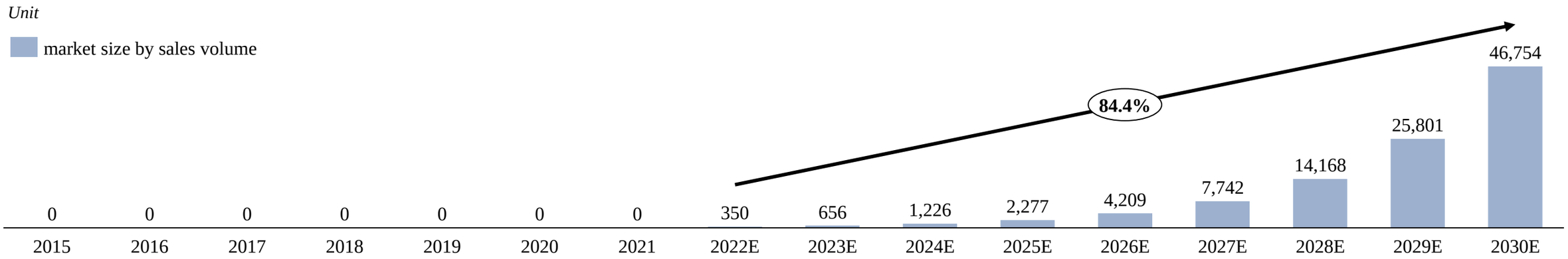
Source: Chinese Journal of CTCS; Myheart.net; EuroPCR; Neochord; Medstar Washington Hospital Center Medstar Washington Hospital Center; China Insights Consultancy

China market size of transcatheter mitral valve replacement interventional surgical device

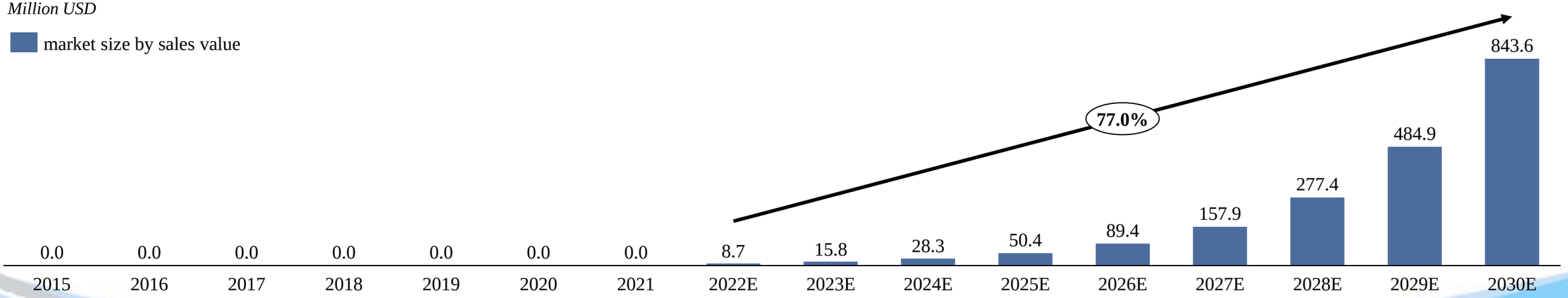
- It is expected that the first TMVR will be launched in 2022 in terms of sales value and sales volume

China market size of transcatheter mitral valve replacement interventional surgical device

Market size by sales volume, China, 2015-2030E



Market size by sales value, China, 2015-2030E

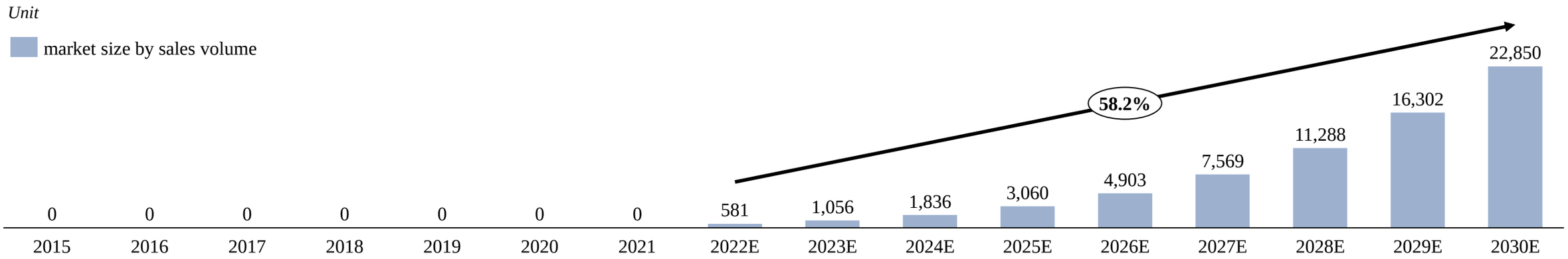


Source: China Insights Industry Consultancy Limited, expert interviews and public information

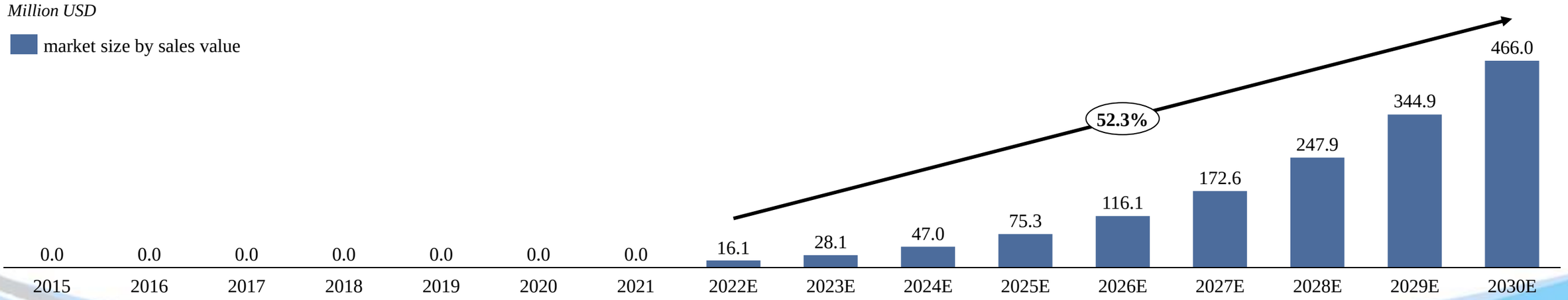
Japan market size of transcatheter mitral valve replacement interventional surgical device

Japan market size of transcatheter mitral valve replacement interventional surgical device

Market size by sales volume, Japan, 2015-2030E



Market size by sales value, Japan, 2015-2030E

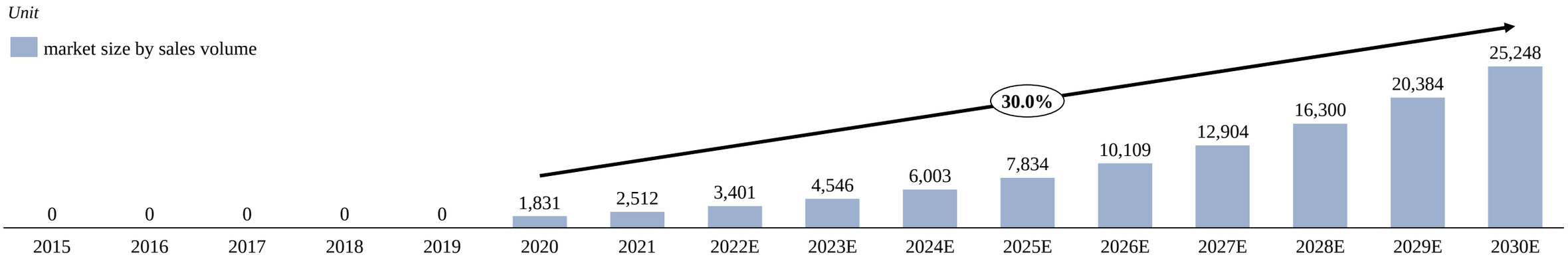


Source: China Insights Industry Consultancy Limited, expert interviews and public information

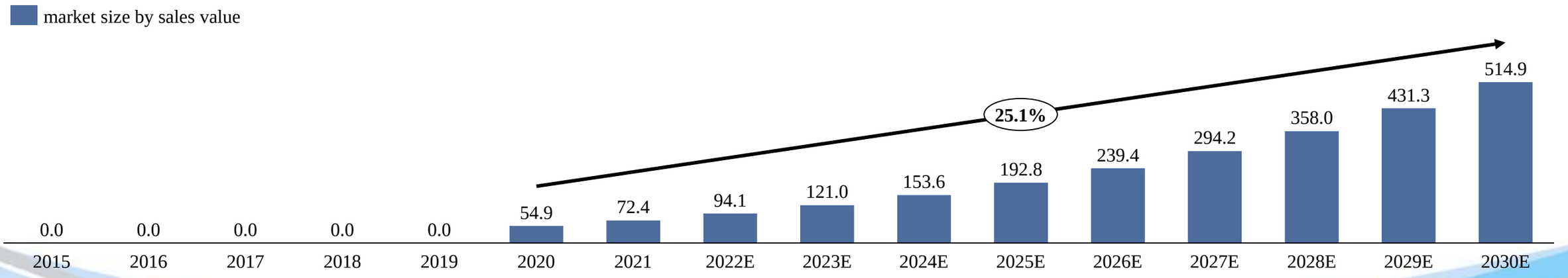
APAC* market size of transcatheter mitral valve replacement interventional surgical device

APAC market size of transcatheter mitral valve replacement interventional surgical device

Market size by sales volume, APAC*, 2015-2030E



Market size by sales value, APAC, 2015-2030E



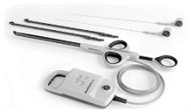
*APAC: APEC excluding China, Japan, The US and Russia

Source: China Insights Industry Consultancy Limited, expert interviews and public information

Globally approved mitral regurgitation interventional surgical device

- In the field of mitral valve disease, surgical treatment continues to play a predominant role, while transcatheter treatment is gaining increased significance for specific clinical scenarios and poses a viable treatment option for well-selected patients; there are currently eight interventional devices acquiring approval

Globally approved mitral regurgitation interventional surgical device

Product name	Image	Manufacturer	FDA Approval	NMPA Approval	CE mark Approval	Mechanism	Approach	Access	Applicable Indication
MitraClip		Abbott Vascular; IL	2013	2020	2008	• MV repair	• Percutaneous leaflet repair, edge-to-edge	• Transfemoral & Transseptal	• Symptomatic MR
Pascal		Edwards Lifesciences; CA	/	/	2019	• MV repair	• Percutaneous leaflet repair, edge-to-edge	• Transfemoral & Transseptal	• Symptomatic MR
Cardioband		Edwards Lifesciences; CA	/	/	2015	• MV repair	• Direct annuloplasty	• Transfemoral & Transseptal	• Secondary MR
MPAS		Mitralign, Inc.; US	/	/	2016	• MV repair	• Direct annuloplasty	• Transfemoral	• Secondary MR
Carillon		Cardiac Dimensions; WA	/	/	2009	• MV repair	• Indirect annuloplasty	• Right internal jugular vein	• Secondary MR
Neochord		Neochord Medical, US	/	/	2012	• MV repair	• Artificial chordae	• Transapical	• Secondary MR
Harpoon		Edwards Lifesciences; CA	/	/	2017	• MV repair	• Artificial chordae	• Transapical	• Severe primary MR
Tendyne		Abbott Vascular; CA	/	/	2020	• MV replacement	• Apical theter	• Transapical	• Symptomatic MR

Source: ACC; SMW; Chinese Journal of CTCS; China Insights Consultancy

A glance into the domestic development of mitral regurgitation interventional surgical device

- Currently there are several domestic market players within the investigation of MR interventional surgical device

Domestic development of mitral regurgitation interventional surgical device

Product name	Manufacturer	Clinical status	Mechanism	Approach	Access	Applicable Indication
Valve clamp	Hanyu Medical; CN	First-in-man study completed	• MV repair	• Leaflet repair, edge-to-edge	• Transapical	• Moderate-to-severe or severe MR
Amend *	MicroPort Cardioflow Medtech; CN	First-in-man study underway	• MV repair	• Direct annuloplasty	• Transapical	• Primary and secondary MR
Mitral stitch	Dejin Medical; CN	First-in-man study completed	• MV repair	• Artificial chordae and Leaflet repair	• Transapical	• Primary or secondary MR
SuperClip	Kokalife; CN	Preclinical study underway	• MV repair	• Artificial chordae and Leaflet repair	• Transapical	• Primary or secondary MR
Mi-thos	Newmed technology; CN	First-in-man study completed	• MV replacement	• Self-expanding frame with bovine pericardial tissue bioprosthesis	• Transapical	• Severe MR
AltaValve *	MicroPort Cardioflow Medtech; CN	Preclinical study underway	• MV replacement	• Self-expanding supra-annular device	• Transapical	• Severe MR
Corona *	MicroPort Cardioflow Medtech; CN	Preclinical study underway	• MV replacement	• Bioprosthesis	• Transapical	• Primary and secondary MR
AccuFit	Surgnova Medical; CN	Preclinical study underway	• MV replacement	• Nitinol self-expandable system	• Transapical	• /
TMVR device **	Peijia Medical; CN	Preclinical study underway	• MV replacement	• Self-expandable system	• Transapical	• /
Valve Mitral Venus	Venus Medtech; CN	Preclinical study underway	• MV replacement	• /	• /	• /
TMVR device **	MicroPort Cardioflow Medtech; CN	Preclinical study underway	• MV replacement	• /	• /	• /

Notes: Amend * and Corona * is the product under cooperation with Valcare; AltaValve * is the product under cooperation with 4C Medical; TMVR device** means self-innovative product without official name

Source: ACC; SMW; Chinese Journal of CTCS; EHJ; China Insights Consultancy

Global mitral regurgitation interventional surgical device under research (1/2)

- Multiple other repair techniques and devices are currently under investigation worldwide

Global mitral regurgitation interventional surgical device under research

Product name	Manufacturer	Clinical status	Mechanism	Approach	Access	Applicable Indication
Millipede Iris	Millipede, Inc.; US	International feasibility trial underway	• MV repair	• Direct annuloplasty	• Transfemoral & transseptal	• Secondary MR
AccuCinch	Ancora Heart; US	International feasibility trial underway	• MV repair	• Direct annuloplasty	• Transarterial	• Secondary MR
Amend	Valcare Medical, Israel	First-in-man study underway	• MV repair	• Direct annuloplasty	• Transapical	• Primary and secondary MR
Mitral cerclage	Transmural systems; US	Early feasibility study underway	• MV repair	• Indirect annuloplasty	• Transmural	• Secondary MR
ARTO	MVRx, Inc.; US	First-in-man study completed	• MV repair	• Indirect annuloplasty	• Two-vein access	• Secondary MR
V-Chordal	Valtech Cardio; Israel	First-in-man study completed	• MV repair	• Artificial chordae	• Transseptal	• Primary or secondary MR
Pipeline	Gore Medical; US	First-in-man study completed	• MV repair	• Artificial chordae	• Transfemoral & transseptal	• Secondary MR
ChordArt	CoreMedic; Germany	First-in-man study underway	• MV repair	• Artificial chordae	• Transfemoral & transseptal	• Primary or secondary MR
CardioMech	CardioMech AS; Norway	First-in-man study underway	• MV repair	• Artificial chordae	• Transfemoral & transseptal	• Symptomatic secondary MR
Mitral Butterfly	Angel Valve Vienna; Austria	Preclinical study completed	• MV repair	• Artificial chordae	• Transfemoral & transseptal	• Secondary MR

Source: ACC; SMW; Chinese Journal of CTCS; EHJ; China Insights Consultancy

Global mitral regurgitation interventional surgical device under research (2/2)

- Multiple other repair techniques and devices are currently under investigation worldwide

Global mitral regurgitation interventional surgical device under research

Product name	Manufacturer	Clinical status	Mechanism	Approach	Access	Applicable Indication
Cardiovalve	Cardiovalve; Israel	International feasibility trial underway	• MV replacement	• Dual nitinol frame	• Transfemoral & transseptal	• Primary and secondary MR
EVOQUE	Edwards Lifesciences; US	Early feasibility study underway	• MV replacement	• Mitral annulus clamping	• Transseptal	• Secondary MR
Intrepid	Medtronic; US	Early feasibility study underway	• MV replacement	• Radial force	• Transapical & transfemoral	• Severe MR
Caisson	Caisson Interventional; US	Early feasibility study underway	• MV replacement	• External anchor	• Transseptal	• Severe MR
HighLife	HighLife Medical, Inc.; US	Early feasibility study underway	• MV replacement	• External anchor	• Transapical	• Moderate-to-severe or severe MR
SAPIEN M3	Edwards Lifesciences; US	Early feasibility study underway	• MV replacement	• External anchor	• Transseptal	• Severe MR
Tiara	Neovasc Inc; Canada	Early feasibility study underway	• MV replacement	• Native leaflet engagement	• Transapical	• Moderate-to-severe or severe MR
CardiAQ	Edwards Lifesciences; US	First-in-man study completed	• MV replacement	• Apical tether	• Transseptal	• Native MR
MValve	Boston Scientific; US	First-in-man study completed	• MV replacement	• Valve docking system	• Transapical	• Severe MR
Navigate	NaviGate Cardiac; US	First-in-man study completed	• MV replacement	• Nitinol self-expandable system	• Transapical	• More in TR than MR
AltaValve	4C Medical Technologies; US	Preclinical study underway	• MV replacement	• Self-expanding supra-annular device	• Transapical	• Severe MR
Cephea	Cephea Valve Technologies	Preclinical study underway	• MV replacement	• Self-expanding double-disk	• Transseptal & transatrial	• Severe MR
Corona	Valcare Medical, Israel	Preclinical study underway	• MV replacement	• Bioprosthesis	• Transapical	• Primary and secondary MR

Source: ACC; SMW; Chinese Journal of CTCS; EHJ; Journal of the American Heart Association; China Insights Consultancy

Market drivers and development trends of mitral regurgitation interventional surgery

- The MR interventional surgery market is considerable because of the increasing disease prevalence and advanced techniques; Further developments are expected thanks to an understanding of the epidemiology and mechanisms of MR

Market drivers and development trends of mitral regurgitation interventional surgery

Market drivers		Restriction factors	
✓ Increasing ageing & high prevalence of cardiac disease	• Heart valve disease has a high mortality rate after the onset of heart valve disease, while the incidence of valve disease due to degenerative disease in the elderly is increasing in China.	☐ Insufficient medical resources	• Transcatheter intervention is a new team-based, complex technique, and there are Insufficient number of hospitals and physicians capable of performing transcatheter interventional procedures in China
✓ Improvement of bio-valve technology	• With the improvement of bio-valve technology and the strengthening of market education, bio-valve applications in China's valve devices market share gradually increased	☐ Evident competitiveness from MNCs	• At present, the heart valve device market is monopolized by foreign brands, the relatively high cost of treatment limits the demand of some patients, so some patients choose conservative medical treatment.
✓ Emerging interventional procedure	• Transcatheter interventional procedures are still in the early stages of use in China, and the market for heart valve devices will grow further as the technology matures.	☐ Poor medical education to patients	• China's hospitals and doctors to avoid doctor-patient disputes, clinical preference for mature surgical methods or imported products, new technologies and products take time to educate the market.

Future development trends

- Ongoing studies aim to show the benefit of transcatheter treatment compared to medical therapy, surgical treatment, or different devices.
- The future research focus of transcatheter interventional therapy is:
  - Expanding from aortic valve to mitral valve, tricuspid valve and pulmonary valve repair and replacement;
  - Breakthroughs in biological valve material and durability;
  - Expanding the indications to low-medium-risk and low-age patients

- Further evidence should be accumulated via randomized studies. Researches seek better understanding of the pathophysiology and disease progression will enable better patient selection and targeted therapy.
- The advent of interventional techniques in recent years has led to an increase in the number of patients referred for intervention, which is good.
- The future of transcatheter mitral valve interventions might therefore be a transseptal valve replacement in the vast majority of patients.

Source: Herz 2016; Frontiersin; China Insights Consultancy

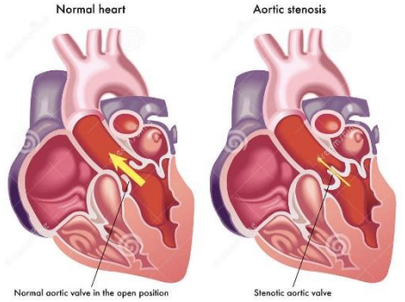
Introduction and classification of aortic stenosis

- Aortic Stenosis is a condition in which the aortic valve doesn't open fully, and it is common among the elder over 65 years old, usually have no symptoms in mild to moderate stage but can be fatal if no treatment is performed

Introduction and classification of Aortic Stenosis

Introduction

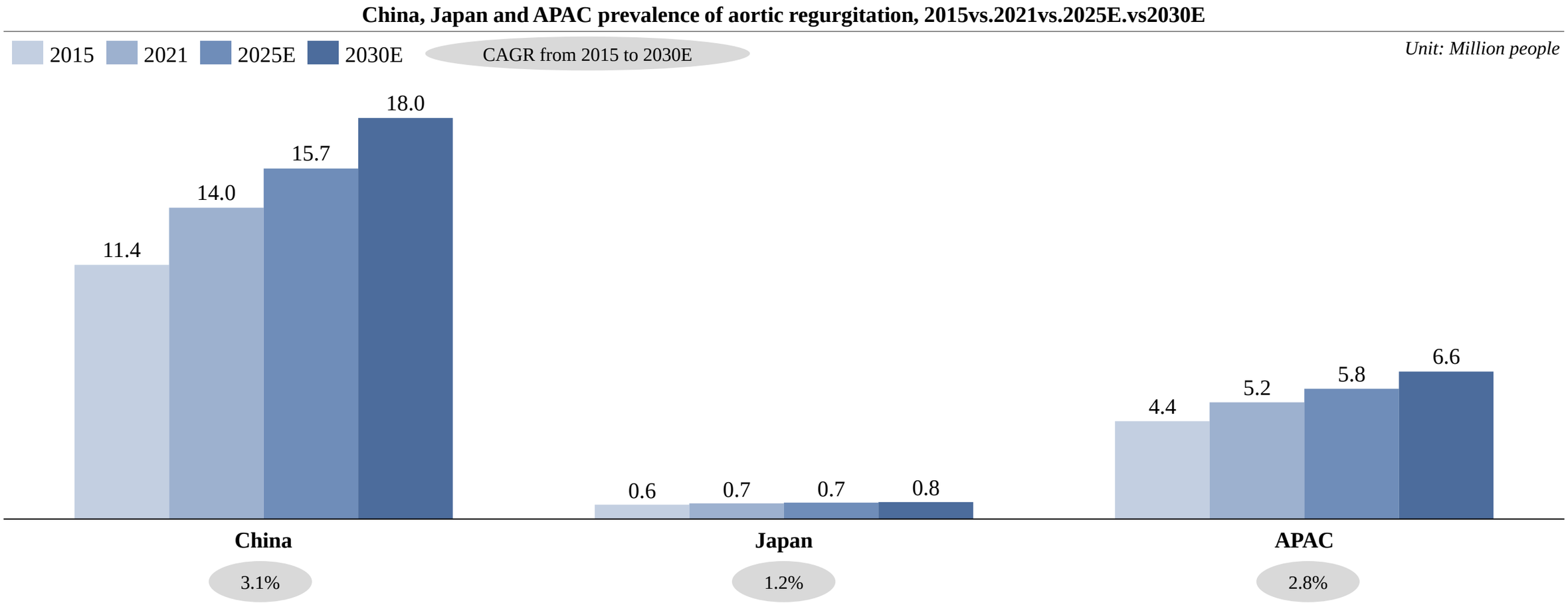
Aortic valve	• The aortic valve is a trileaflet structure and consists of three distinct layers, which are the fibrosa, spongiosa and ventricularis. It located at the junction between the left ventricular outflow tract and the aortic root. The aortic valve is covered on both the ventricular and aortic surfaces by endothelium in continuity with both the ventricular endocardium and the aortic endothelium.
Aortic Stenosis	• Aortic valve Stenosis (AS) is a condition in which the aortic valve become thickened and stiff, or they may fuse together which means it doesn't open fully, reducing or blocking blood flow from the heart into the aorta and the rest of the body. Chronic AS may weaken the heart over time and result in several life-threatening complications, including heart failure, abnormal heart rhythms and cardiac arrest.



Category	Prevalence	Mechanism	Aortic valve morphology	Symptom status	Determination criteria
Mild Aortic Stenosis	• Total prevalence of AS is 12.4% in Europe and the USA	• Physiological	• Normal	• Usually asymptomatic	• Peak aortic jet velocity is about 2.0-2.9 m/s • Mean pressure gradient < 20 mmHg • Aortic valve area >1.5 cm^2 • Indexed aortic valve area >0.85 cm^2/m^2
Moderate Aortic Stenosis	• 2% -7% among the elder over 65 years old have moderate to severe AS • 3.4% of the elder over 75 years old have severe AS	• Usually observed in patients with leaflet calcification/fibrosis of a bicuspid or trileaflet valve with some reduction in systolic motion	• Normal/abnormal	• Mild symptoms	• Peak aortic jet velocity is about 3.0-3.9 m/s • Mean pressure gradient ≤39 mmHg • Aortic valve area <1.5 cm^2 • Indexed aortic valve area <0.85 cm^2/m^2
Severe Aortic Stenosis		• Usually observed in patients with severe leaflet calcification/fibrosis or congenital stenosis	• Abnormal	• Asymptomatic or Significant symptoms: angina, syncope or presyncope	• Peak aortic jet velocity ≥4.0m/s • Mean pressure gradient ≥ 40 mmHg (very severe if ≥60) • Aortic valve area <1.0 cm^2 • Indexed aortic valve area <0. 6cm^2/m^2

Source: European Journal of Echocardiography; ESC; China Insights Consultancy

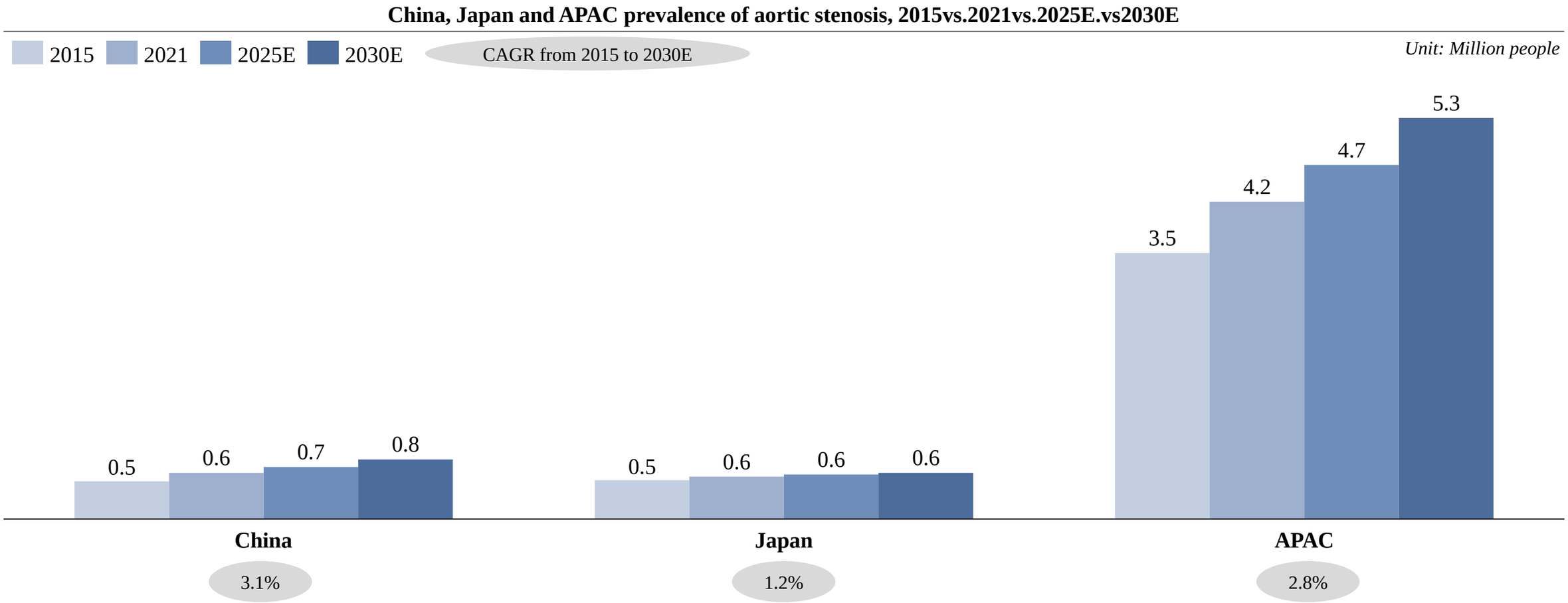
China, Japan and APAC prevalence of aortic regurgitation, 2015vs.2021vs.2025E.vs2030E



*APAC: APEC excluding China, Japan, The US and Russia

Source: China Insights Consultancy

China, Japan and APAC prevalence of aortic stenosis, 2015vs.2021vs.2025E.vs2030E



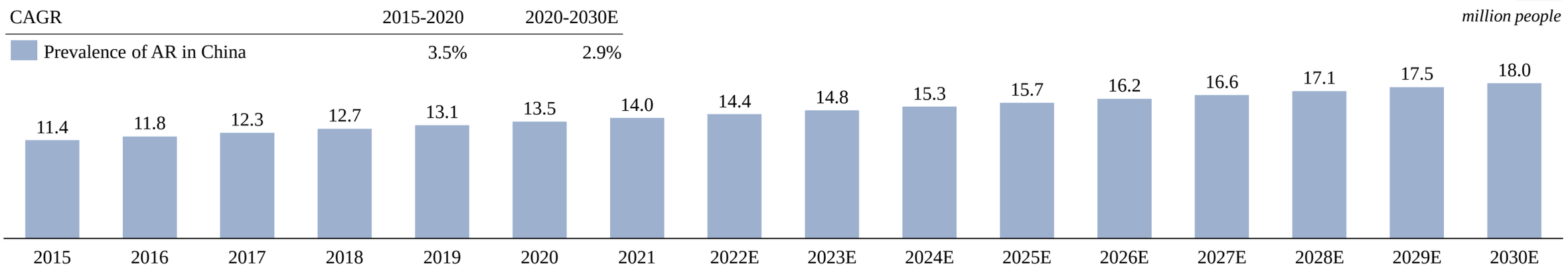
*APAC: APEC excluding China, Japan, The US and Russia

Source: China Insights Consultancy

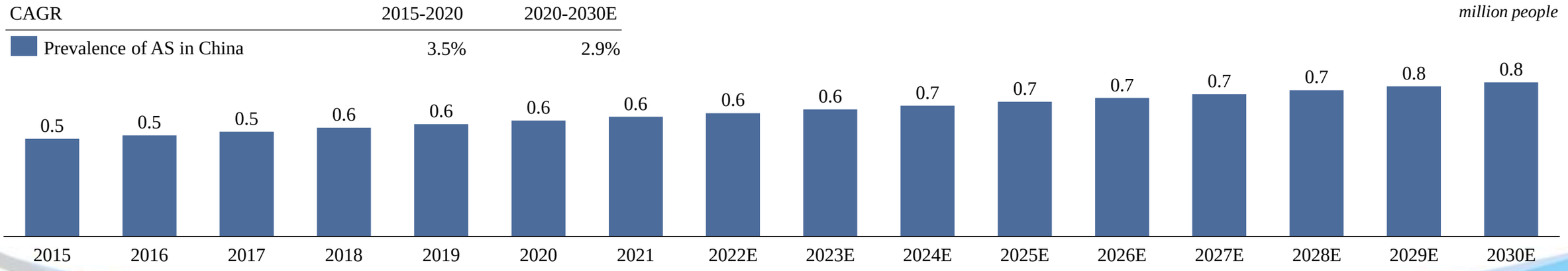
Prevalence of aortic regurgitation and aortic stenosis in China

Epidemiology of aortic regurgitation and stenosis

Prevalence of aortic regurgitation in China, 2015-2030E



Prevalence of aortic stenosis in China, 2015-2030E



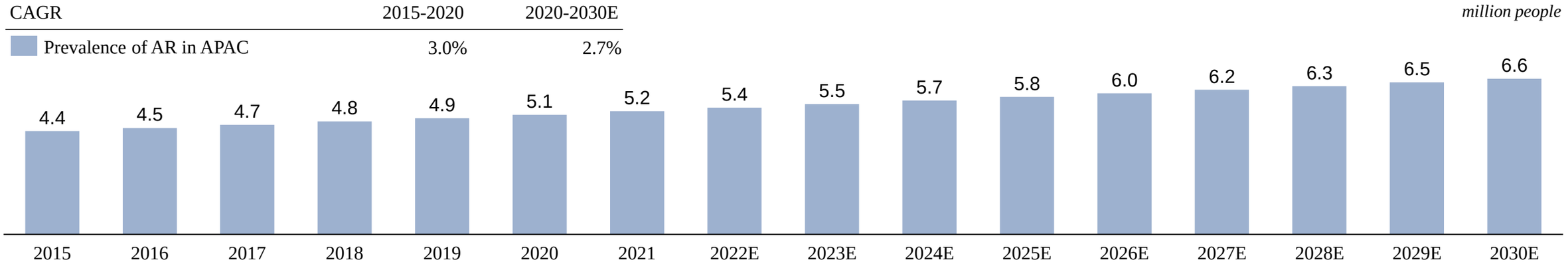
Source: Analyses for Prevalence and Outcome of Tricuspid Regurgitation in China; doi.org/10.1159/000496601; China Insights Consultancy

Prevalence of aortic regurgitation and aortic stenosis in APAC*

Epidemiology of aortic regurgitation and stenosis

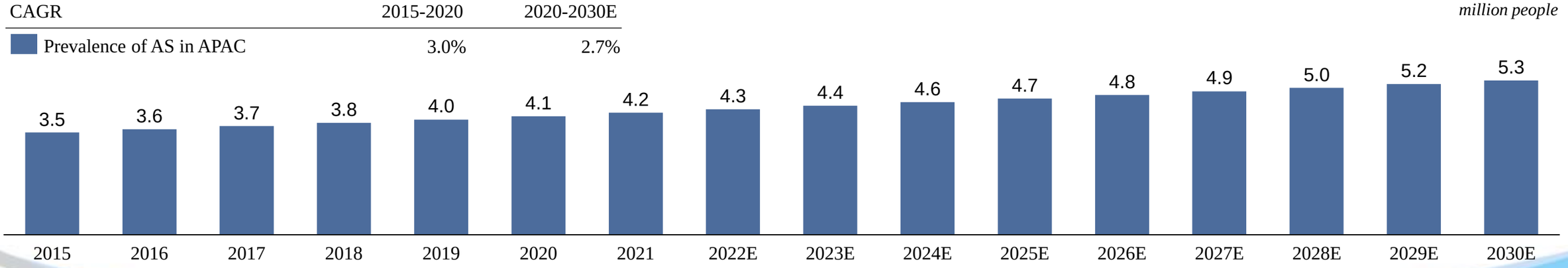
Prevalence of aortic regurgitation in APAC, 2015-2030E

CAGR	2015-2020	2020-2030E
Prevalence of AR in APAC	3.0%	2.7%



Prevalence of aortic stenosis in APAC, 2015-2030E

CAGR	2015-2020	2020-2030E
Prevalence of AS in APAC	3.0%	2.7%



*APAC: APEC excluding China, Japan, The US and Russia

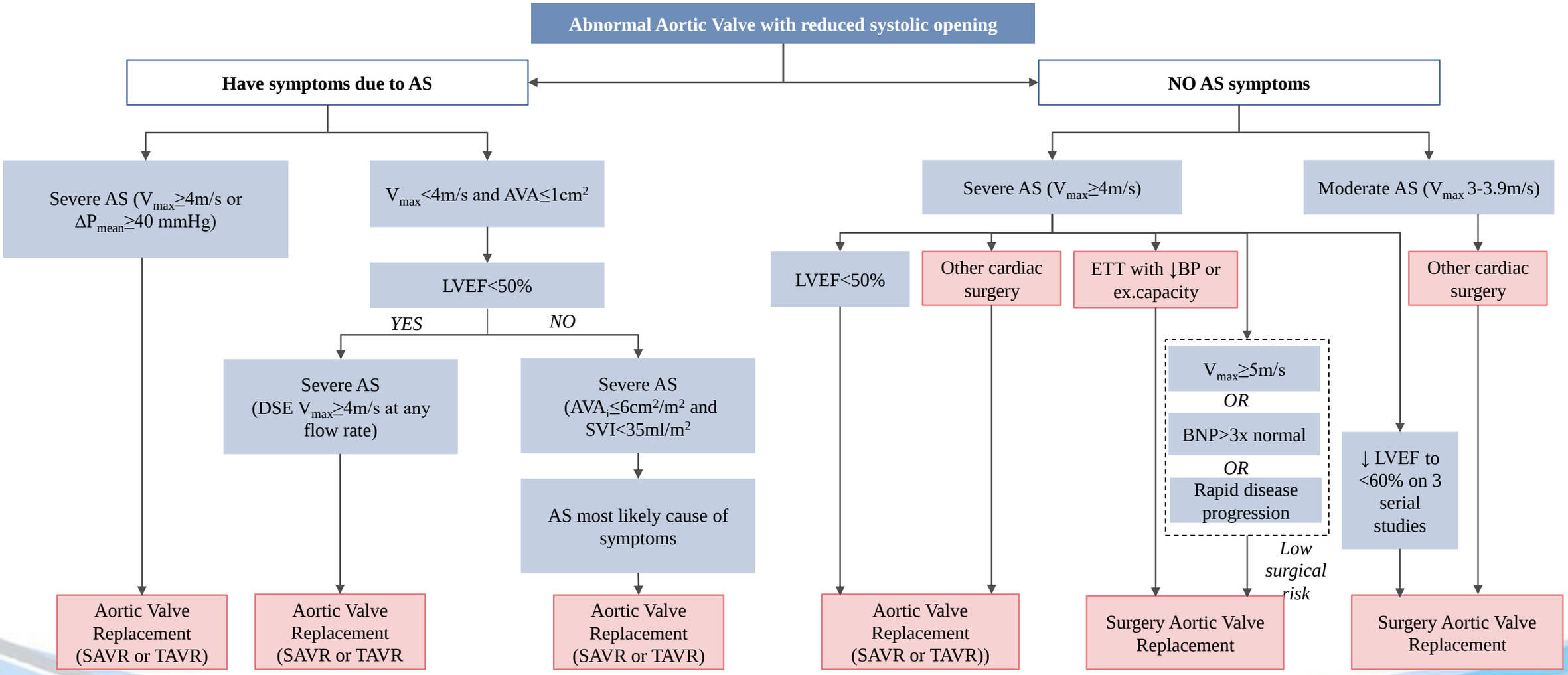
Source: Nature Reviews Cardiology; China Insights Consultancy

Treatment path of aortic stenosis patients

- Aortic Valve Replacement(AVR) including Transcatheter Aortic Valve Replacement(TAVR) and Surgery Aortic Valve Replacement(SAVR) is main treatment method for Aortic Stenosis.

Treatment path of aortic stenosis patients

Specific therapies



Source: ACC/AHA; China Insights Consultancy

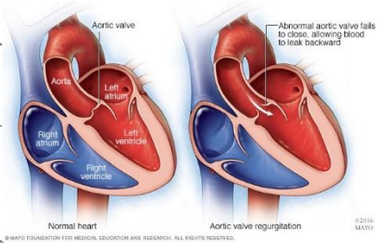
Introduction and classification of aortic regurgitation

-The aortic regurgitation is divided into four stages. A-at risk of getting AR, B-progressive AR; C-severe AR but no symptom present; D-severe AR with related symptoms caused by AR

Introduction and classification of aortic regurgitation

Introduction

Aortic valve	• The aortic valve connects the left ventricle and the aorta. The aortic valve consists of three leaflets, connecting the aorta and left ventricle. In 1-2% of populations congenitally has only two leaflets.
Aortic regurgitation	• In aortic valve regurgitation, the valve between the lower left heart chamber (left ventricle) and the main artery that leads to the body (aorta) doesn't close properly, which causes some blood to leak backward into the left ventricle. This forces the left ventricle to hold more blood, possibly causing it to enlarge and thicken.

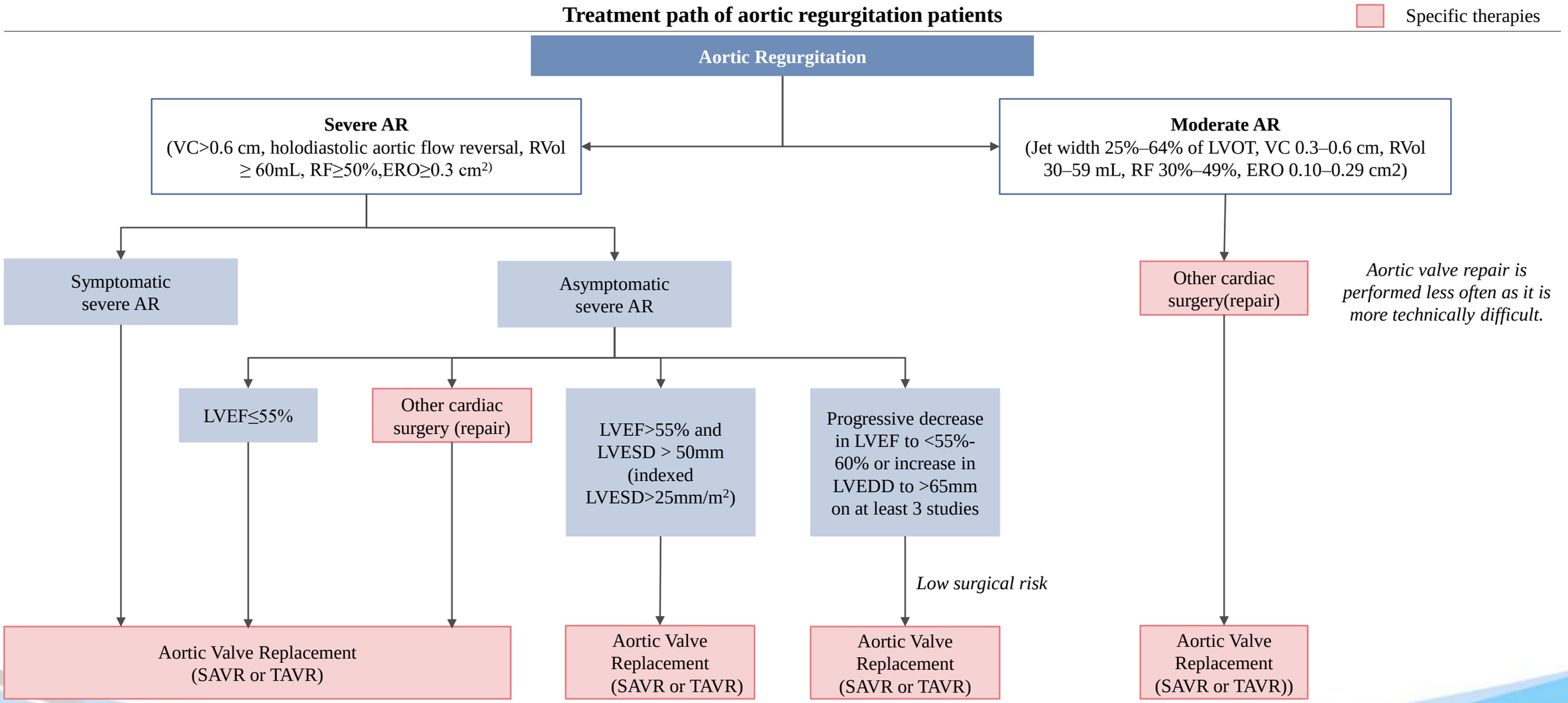


Stages	Symptoms	Valve hemodynamics	Valve anatomy
At risk of AR	• None	• AR severity: none or trace	• BAV (or other congenital valve anomaly) • Aortic valve sclerosis • Diseases of the aortic sinuses or ascending aorta • History of rheumatic fever or known rheumatic heart disease
Progressive AR	• None	• Mild AR: Jet width <25% of LVOT; Vena contracta <0.3 cm; Regurgitant volume <30 mL/beat; Regurgitant fraction <30%; ERO <0.10 cm2; Angiography grade 1 • Moderate AR: Jet width 25%–64% of LVOT; Vena contracta=0.3–0.6 cm; Regurgitant volume 30–59 mL/beat; Regurgitant fraction 30% to 49%; ERO 0.10–0.29 cm2; Angiography grade 2	• Mild to moderate calcification of a trileaflet valve BAV (or other congenital valve anomaly) • Dilated aortic sinuses • Rheumatic valve changes
Asymptomatic severe AR **Symptomatic severe AR**	• None; exercise testing is reasonable to confirm symptom status • Exertional dyspnea or angina or more severe HF symptoms	• Severe AR: Jet width ≥65% of LVOT; Vena contracta >0.6 cm; Holodiastolic flow reversal in the proximal abdominal aorta; Regurgitant volume ≥60 mL/beat; Regurgitant fraction ≥50%; ERO ≥0.3 cm2; Angiography grade 3 to 4 • In addition, diagnosis of chronic severe AR requires evidence of LV dilation	• Calcific aortic valve disease • Bicuspid valve (or other congenital abnormality) • Dilated aortic sinuses or ascending aorta • Rheumatic valve changes

Source: European Journal of Echocardiography; China Insights Consultancy

Treatment path of Aortic Regurgitation patients

- Aortic Valve Replacement(AVR) including Transcatheter Aortic Valve Replacement(TAVR) and Surgery Aortic Valve Replacement(SAVR) is main treatment method for Aortic Stenosis



Source: ACC/AHA; China Insights Consultancy

Overview of Aortic Valve Replacement (AVR)

- TAVR and SAVR are two main effective treatment for aortic stenosis or aortic regurgitation. TAVR is suitable for more vulnerable patients with symptoms and SAVR needs to open the chest and is suitable for asymptomatic patients

Overview and classification of Aortic Valve Replacement

- Once the aortic stenosis or aortic regurgitation become severe and patients start to have symptoms, treatment should be performed right away. Aortic Valve Replacement is the only effective way for treatment, and this can be done through transcatheter aortic valve replacement (TAVR) or open-heart surgery(SAVR). Balloon valvuloplasty (BAV) is the least effective method and it is used for palliation of those patients who cannot have aortic valve replacement because of serious comorbid conditions or as a bridge to definitive aortic valve replacement in patients with severe AS and hemodynamic instability.
- TAVR, also called TAVI, is a nonsurgical option which is less invasive without opening the chest. Open-heart surgery, also called SAVR, is an open-chest surgery which is generally indicated for patients who are at low risk for open-chest surgery, meaning the patient is well and strong enough to undergo this type of surgery and recovery.
- Aortic valve repair may be an option for patients who have bicuspid aortic valve disease or other aortic valve conditions that are associated with valve regurgitation (leaking valve). But it is performed less often and is more technically difficult. And about 20 to 25 percent of patients will require a valve replacement within ten years.

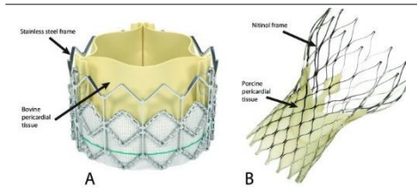
Category	Definition	Patient coverage	Difference & Advantage	Risks
Transcatheter aortic valve replacement (TAVR/TAVI)	• **Nonsurgical and less invasive:** performed by way of a catheter inserted into the leg, which then allows the replacement valve to be guided up to the aortic valve without opening the chest or heart.	• Have symptoms • Have SAVR in the past • Intermediate or high risk for open-chest surgery • Age ≥ 75 years	• The treatment will last for about 1to 2 hours. • The heart will continue to beat during the procedure • Patients must have a three-leaflet valve (tricuspid aortic valve) which means patients with a two-leaflet valve (bicuspid aortic valve) can't receive this therapy.	• More prone to vascular complications • Problems with the replacement valve, such as the valve slipping out of place or leaking • Heart rhythm problems (arrhythmias) and the need for pacemaker implantation
Surgical aortic valve replacement (SAVR)	• **Open-heart:** a type of open heart surgery that is performed to replace a diseased aortic valve.	• Asymptomatic patients at low risk for open-chest surgery • Age< 75 years	• The surgery will Last for about 4 hours. • The heart will be stopped and need to place the patient on a heart and lung blood machine. • The diseased valve will be removed.	• At risk for blood transfusion • Acute kidney injury • New onset of atrial fibrillation

Source: NHS; UpToDate; NCBI; ESC; AHA; China Insights Consultancy

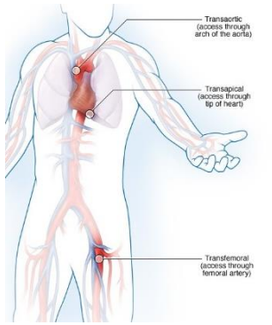
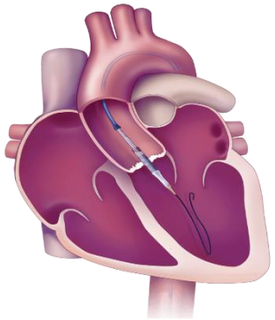
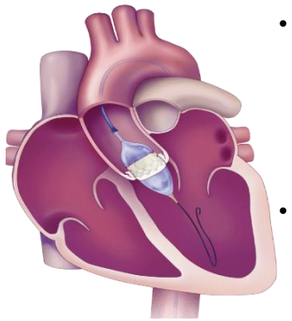
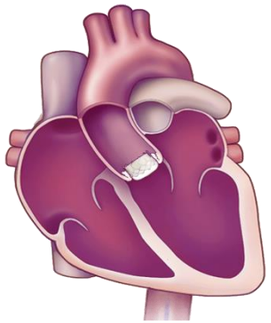
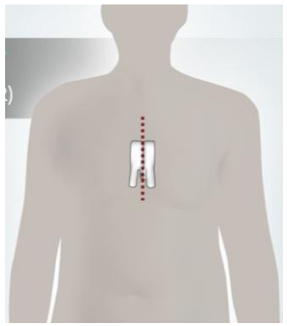
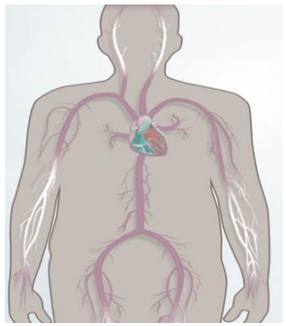
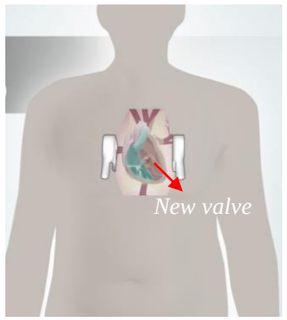
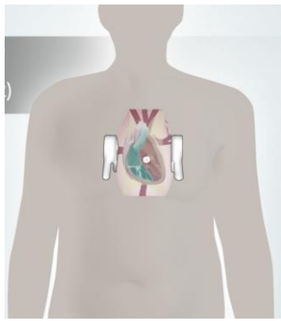
Procedure of transcatheter aortic valve replacement and surgery aortic valve replacement

-Replacement of the diseased aortic valve can be done either through open heart surgery or transcatheter. And mechanical or biological valve can be used depending on the doctor

Procedure of TAVR and SAVR



- Two ways of aortic valve replacement are transcatheter valve replacement and open-heart valve replacement: TAVR and SAVR
- Transcatheter valve replacement is the main choice of aortic valve replacement surgeries nowadays for its safeties and minimal-invasiveness.

	Step 1	Step 2	Step 3	Step 4
TAVR (transcatheter aortic valve replacement)	 • 3 places to make a small cut to guide a thin, flexible tube with the heart valve into the artery, and to the diseased valve.	 • Place a new valve on the delivery system or tube with a balloon on the end • The new valve is compressed on the balloon to make it fit through the sheath	 • Push up the delivery system to the aortic valve. Inflate balloon to expand the new valve into place • The new valve pushed aside the leaflets of the diseased valve. • Deflate and remove balloon	 • Make sure the new valve works properly • close the small incision
SAVR (surgery aortic valve replacement)	 • Make an incision across the full length of the breastbone or sternum	 • Connected to a heart lung machine which temporarily takes over the function of the heart and maintains blood circulation throughout your body	 • Completely remove the diseased aortic valve and insert a new valve. This can be either mechanical or biological valve	 • Use an ultrasound machine after the procedure to make sure the new valve is working properly • Close the small incision

Source: NMCTS; Uptodate; China Insights Consultancy

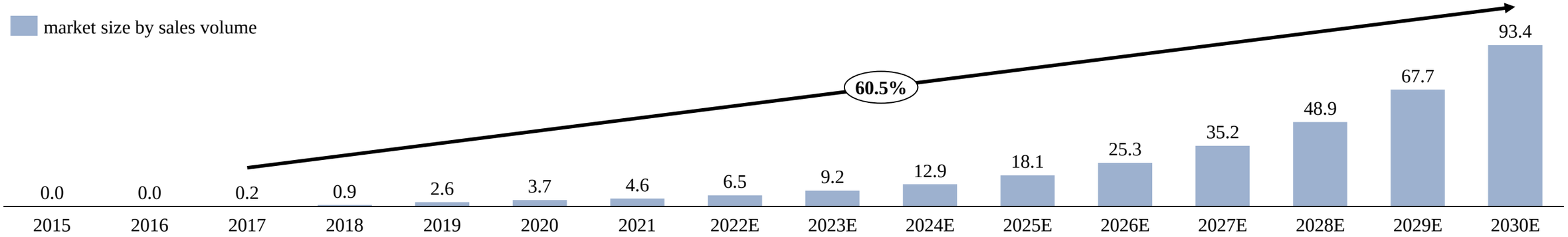
China market size of transcatheter aortic valve replacement interventional surgical device

- The market size of aortic replacement by sales volume and sales value

China market size of transcatheter aortic valve replacement interventional surgical device

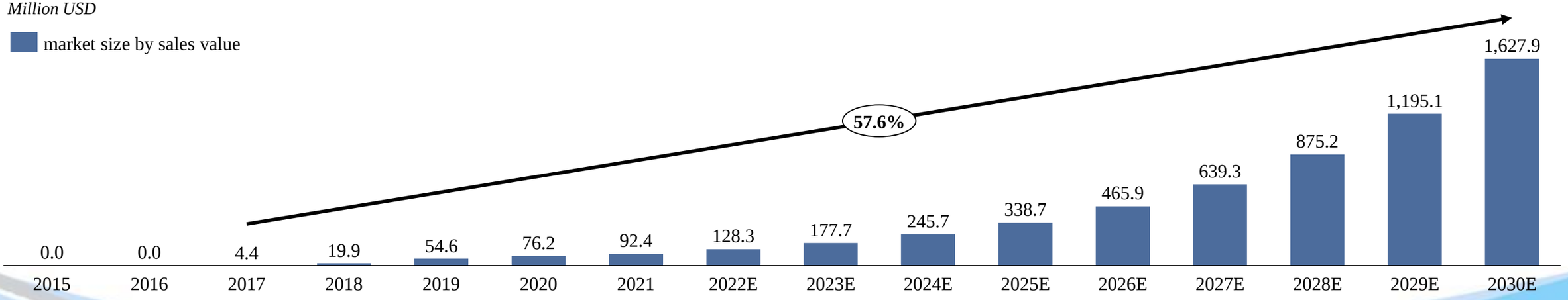
Market size by sales volume, China, 2015-2030E

Thousand unit



Market size by sales value, China, 2015-2030E

Million USD



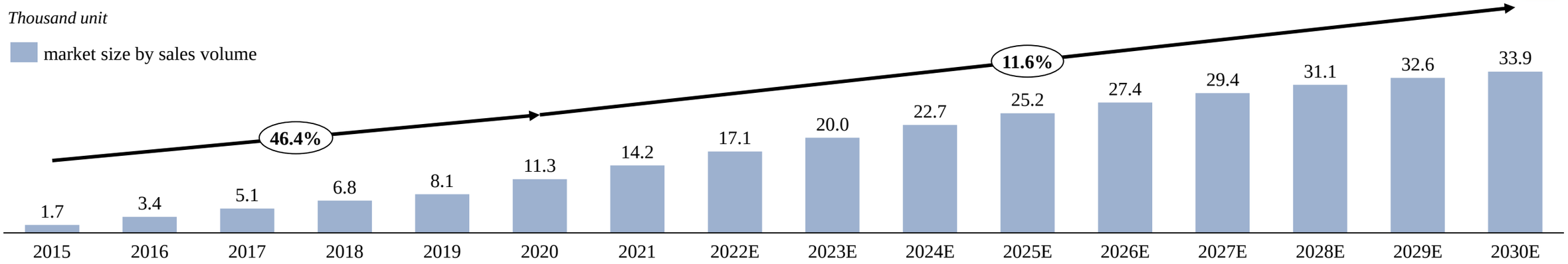
Source: China Insights Industry Consultancy Limited, expert interviews and public information

Japan market size of transcatheter aortic valve replacement interventional surgical device

Japan market size of transcatheter aortic valve replacement interventional surgical device

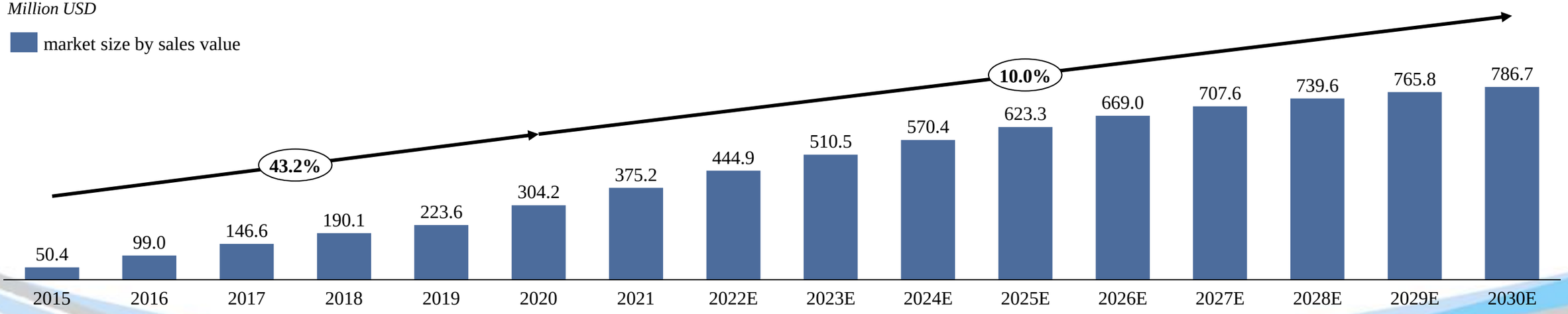
Market size by sales volume, Japan, 2015-2030E

Thousand unit



Market size by sales value, Japan, 2015-2030E

Million USD



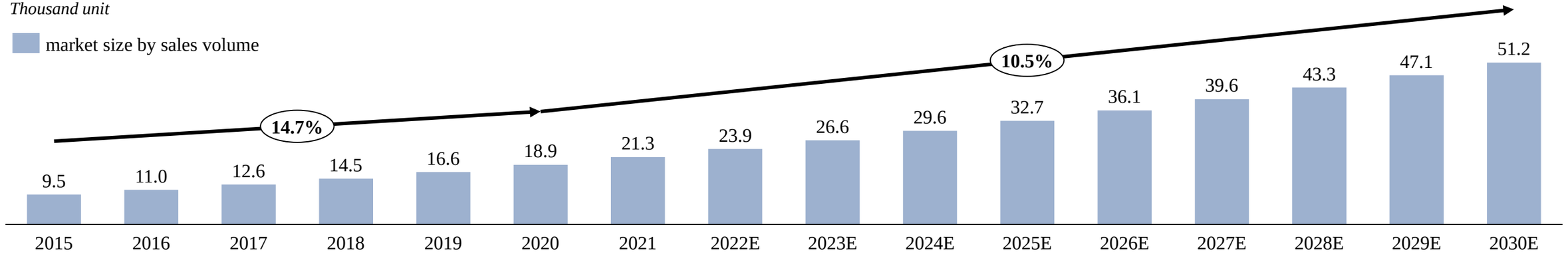
Source: China Insights Industry Consultancy Limited, expert interviews and public information

APAC* market size of transcatheter aortic valve replacement interventional surgical device

APAC market size of transcatheter aortic valve replacement interventional surgical device

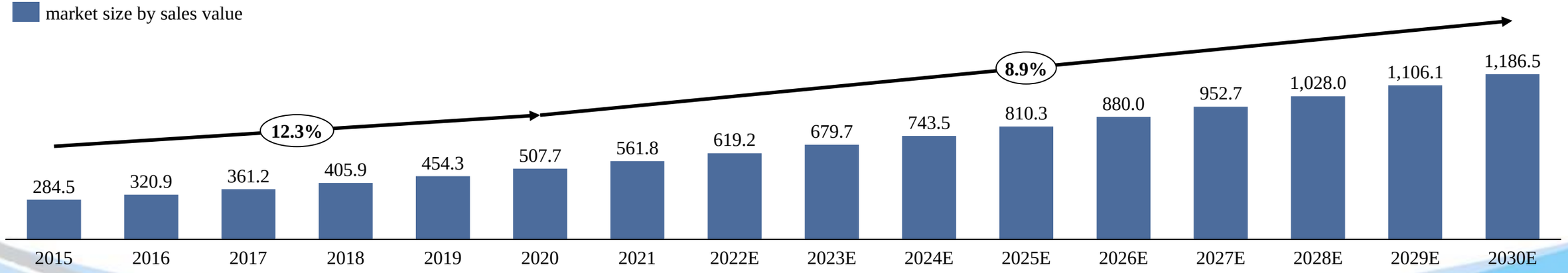
Market size by sales volume, APAC *, 2015-2030E

Thousand unit



Market size by sales value, APAC, 2015-2030E

Million USD

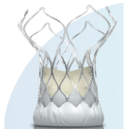
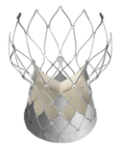


**APAC: APEC excluding China, Japan, The US and Russia*

Source: China Insights Industry Consultancy Limited, expert interviews and public information

NMPA approved transcatheter aortic valve replacement device

NMPA approved transcatheter aortic valve replacement device

Product name	Product Mechanism	Image	Company	Approval date	Registration number
VenusA-valve	Aortic valve replacement		Venus Meditech	2017/4/25	国械注准20173460680
J-Valve	Aortic valve replacement		Jiecheng Medical Tech	2017/4/28	国械注准20173460698
VitraFlow	Aortic valve replacement		Shanghai MicroPort Medical (Group) Co., Ltd.	2019/7/10	国械注准20193130494
Sapien 3	Aortic valve replacement		Edwards Lifescience	2020/6/5	国械注进20203130291
Taurus One	Aortic valve replacement		Peijia Medical Co., Ltd.	2021/4/19	国械注准20213130275

Source: NMPA; China Insights Consultancy

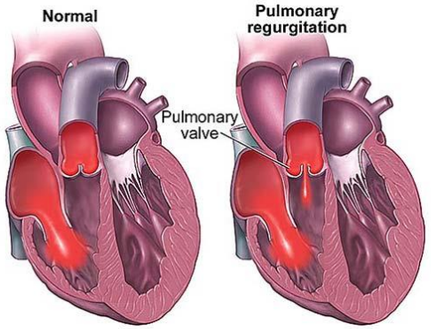
Introduction and classification of pulmonary regurgitation

- Pulmonary regurgitation(PR) is a condition in which the pulmonary valve can't close tightly, and it can be divided into three types according to the jet size and EROA value

Introduction and classification of pulmonary regurgitation

Introduction

Pulmonary valve	• The pulmonary valve consists of three leaflets of equal size, namely right, left and anterior cusps, located at the distal end of the right ventricular outflow tract at the junction of the pulmonary artery. The pulmonary valve is not attached to chordae tendinae or papillary muscles, and its opening and closing depend on the pressure gradient across the valve.
Pulmonary regurgitation	• Pulmonary valve regurgitation (PR) is a condition in which the pulmonary valve doesn't close tightly, allowing blood to flow backward into the right ventricle. Chronic PR can lead to right ventricular volume overload and right ventricular dilatation in long run, which will then cause the right ventricular heart failure, ventricular arrhythmia and sudden death. Severe pulmonary regurgitation is most commonly seen as the complication of the surgical repair of Tetralogy of Fallot.



Category	Prevalence	Mechanism	Pulmonic valve morphology	Symptom status	Determination criteria
Mild pulmonary regurgitation	• 40-78% of patients with normal pulmonary valves	• Physiological	• Normal	• Usually asymptomatic	• Small jet size (usually <10 mm in length with a narrow origin) in color flow Doppler imaging • Faint jet with slow deceleration in continuous-wave Doppler imaging • EROA value < 20 mm^2 by PISA method
Moderate pulmonary regurgitation	• Uncommon in contrast with mild cases	• Most common seen in patients with pulmonary hypertension with dilatation of the pulmonary artery	• Normal / abnormal	• Mild symptoms	• Intermediate jet size in color flow Doppler imaging • Dense jet with variable deceleration in continuous-wave Doppler imaging • EROA value ranging from 21 mm^2 to 115 mm^2 by PISA method
Severe pulmonary regurgitation	• Rare	• Usually observed in patients with congenitally anatomic abnormalities of the valve or after valvulotomy procedures.	• Abnormal	• Significant symptoms	• Large jet size (usually with a wide origin and may be brief in duration) in color flow Doppler imaging • Dense jet with steep deceleration and early termination of diastolic flow in continuous-wave Doppler imaging • EROA value > 115 mm^2 by PISA method

Source: European Journal of Echocardiography; China Insights Consultancy

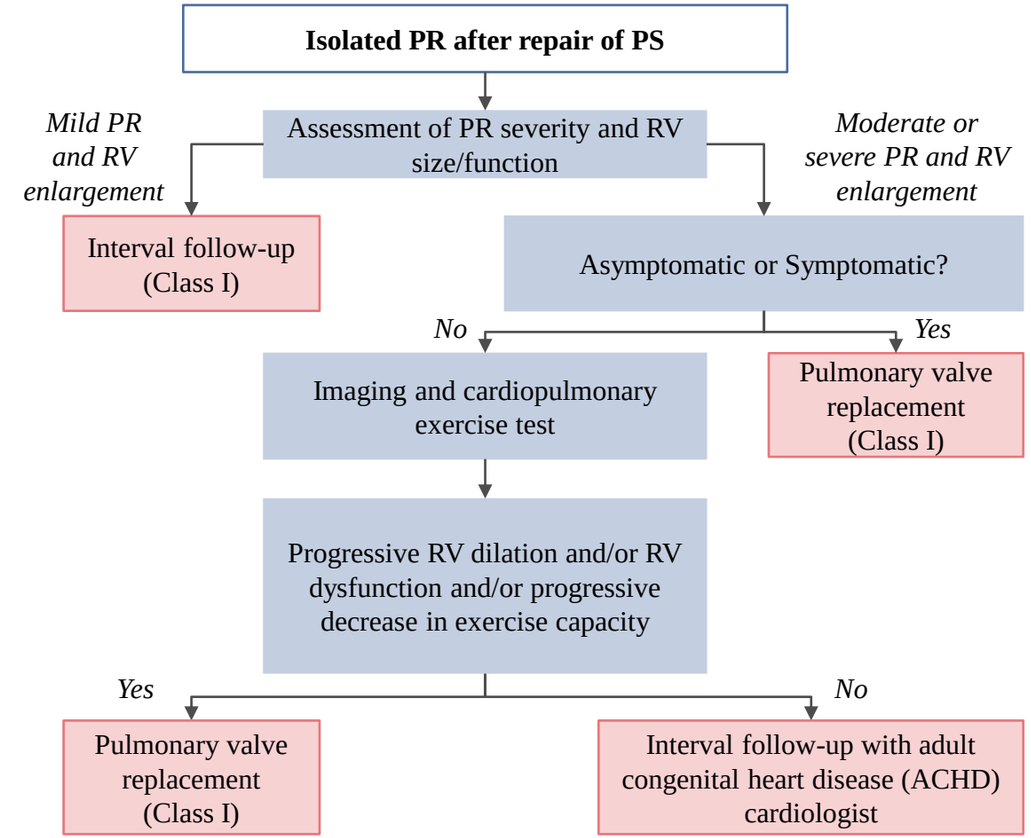
Treatment path of pulmonary regurgitation patients

- Mild PR patients can be treated with interval follow-up while moderate to severe patients could receive pulmonary valve replacement surgery according to patients' conditions

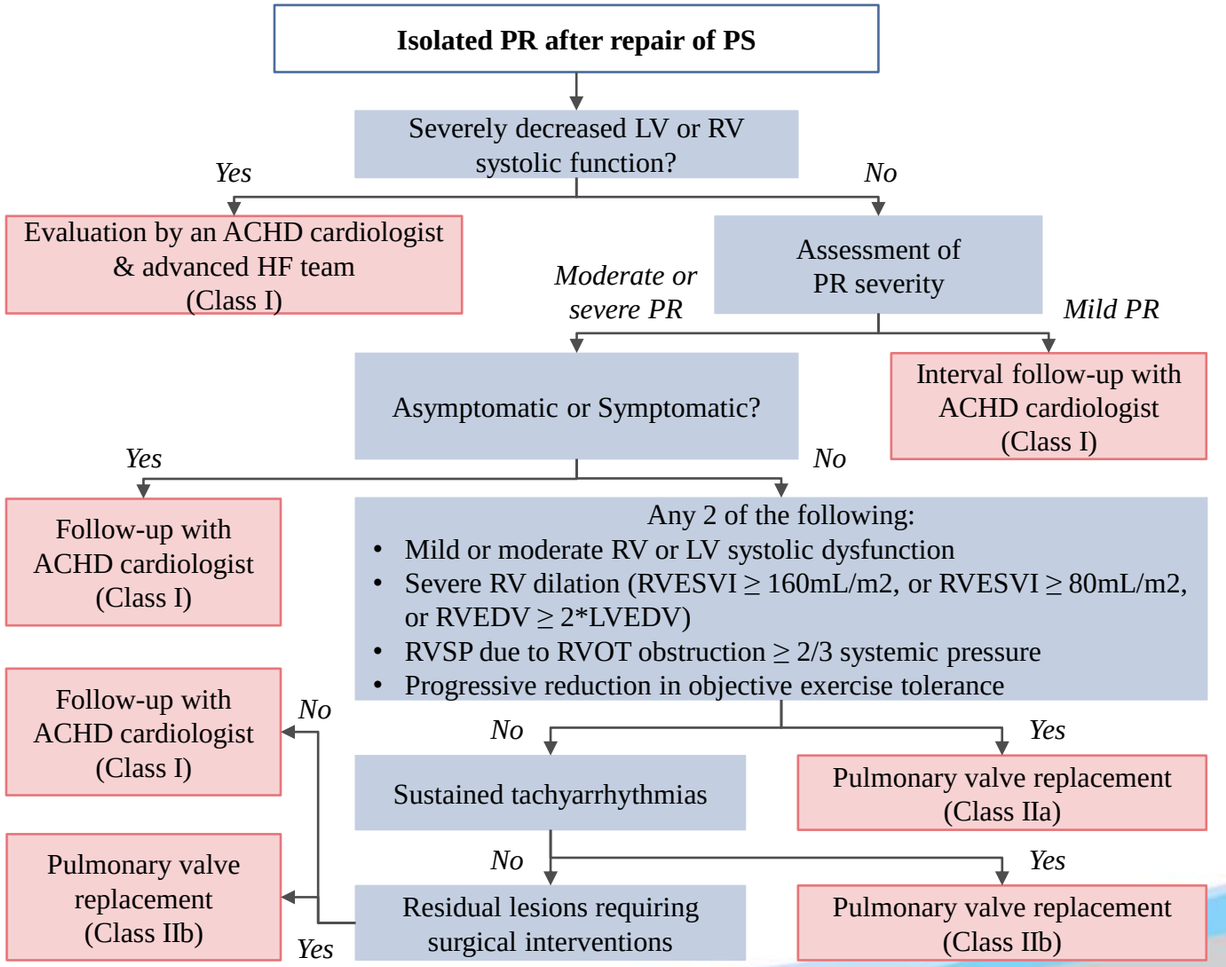
Treatment path of pulmonary regurgitation patients

Specific therapies

Intervention for isolated PR after repair of pulmonary stenosis (PS)



Intervention for PR with after repair of TOF



Source: ACC/AHA; China Insights Consultancy

Overview of transcatheter pulmonary valve replacement (TPVR)

- TPVR and SPVR are two main effective treatment for pulmonary regurgitation. TPVR is suitable a greater proportion of patients and SAVR needs to open the chest and is suitable for fewer patients

Overview and classification of pulmonary valve replacement

- Pulmonary valve replacement is the only treatment for severe pulmonary regurgitation which is usually identified as a post-surgery complication of repaired ToF or pulmonary stenosis patient, and it can be classified into transcatheter pulmonary valve replacement (TPVR) and surgical pulmonary valve replacement (SPVR) based on the way by which the artificial valve is delivered to and placed at the lesion site.
- TPVR, also called percutaneous pulmonary valve implementation (PPVI), is suitable for symptomatic patients with moderate or severe pulmonary regurgitation and right ventricular outflow tract dysfunction (RVOTD), according to the guideline in China. As of 2020, TPVR has almost substituted SPVR in developed countries because of its safeness and high patient compliance, but its feasibility is restricted by the condition of vessels by which the valve is delivered to the heart.

Category	Definition	Patient coverage	Advantages	Challenges
Transcatheter pulmonary valve replacement (TPVR)	• The artificial valve is placed on the balloon catheter and is delivered through the vein to the heart. The balloon will inflate at the diseased pulmonary valve to place the new valve	• Potentially applicable to a greater proportion of patients	• Smaller surgical incision and less pain • Less risky than SPVR with lower follow-up mortality • Only one procedure is required for each patient • Faster recovery	• High requirement for Intracardiac echocardiography specialists • Patients with severe pulmonary artery stenosis or pulmonary hypertension are not suitable for TPVR • Other anatomical limitations and potential complications
Surgical pulmonary valve replacement (SPVR)	• Patient's pulmonary valve is cut out in an open-heart surgery and an artificial valve is used to replace the diseased valve	• Less proportion of patient	• Traditional surgery with mature technology • No need for angiography • Suitable for cases of vascular stenosis which restricts the feasibility of TPVR	• Large surgical incision and painful for patients • Slow recovery and high risk • Repeated surgeries are usually required • Not feasible for patients that are not suitable for open-heart surgery

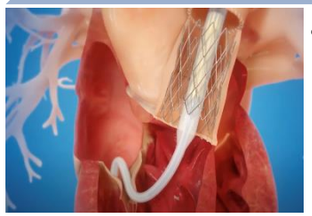
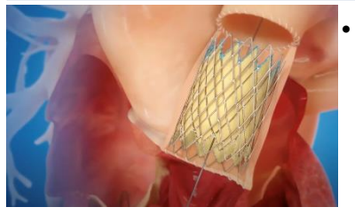
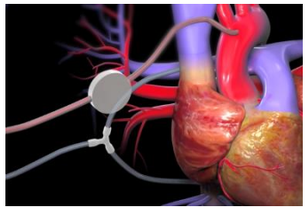
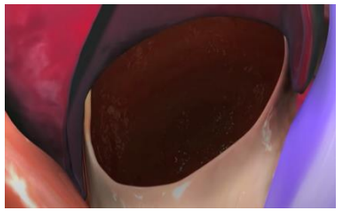
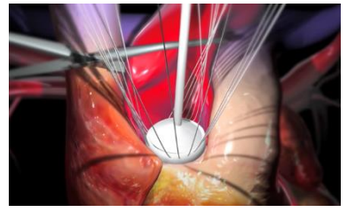
Source: BMJ journals; Uptodate; China Insights Consultancy

Overview of pulmonary valve replacement surgeries

- Replacement of pulmonary valve is the procedure of using a mechanical or tissue valve to replace the diseased pulmonary valve. It can be done either through open chest surgery or minimal invasive surgery

Introduction to procedure of pulmonary valve replacement surgeries

- Two ways of pulmonary valve replacement are transcatheter valve replacement and open-heart valve replacement.
- Transcatheter valve replacement is the main choice of pulmonary valve replacement surgeries nowadays for its safeties and minimal-invasiveness.

	Step 1	Step 2	Step 3	Step 4
• Transcatheter valve replacement	 • Incision on the leg and guidewire through Femoral vein	 • Insert balloon catheter to open the pulmonary valve	 • Insert delivery catheter and implant the replacement valve	 • Exit the catheters and monitor the valve efficacy
• Open chest valve replacement	 • Incision on the chest and separation of sternum	 • Connect to heart lung machine to take over the function of heart and lung	 • Surgical removal of the damaged valve	 • Sew the replacement valve into place, and close the incision

Comparison of tissue valve and mechanical valve

	Tissue Valve	• Made from pig heart valves or cow heart-sac tissue. • Last for about 15 years. • Does not require life-long anti-clotting drugs.
	Mechanical Valve	• Made from carbon, titanium or other materials. • Last for a life time. • Requires anti-clotting drugs.

Source: Harvard Health; Nucleus Medical Media; China Insights Consultancy

Approved transcatheter pulmonic heart valves

Approval list of transcatheter pulmonic heart valves

Product name	Manufacturer	FDA Approval	NMPA Approval	CE mark Approval	Mechanism	Approach	Access	Applicable Indication
Melody	Medtronic Inc.; US	2017	/	2006	• PV replacement	• Self-expanding bovine pericardial valve	• Transfemoral	• Pulmonary regurgitation and stenosis

Source: China Insights Consultancy

I. Overview of global medical device market
II. Overview of global coronary artery disease interventional procedural instrument market
III.Overview of global peripheral artery disease interventional procedural instrument market
IV.Overview of global neuro artery disease interventional procedural instrument market
V. Overview of global structural heart disease interventional procedural instrument market
VI.Appendix

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Approved bare-metal stents by FDA used in coronary artery disease

FDA bare metal stent approval list

Product name	Company	Approval date	Registration number
BIODIVYSIO AS PS (PHOSPHORYLCHOLINE)COATED STENT DELIVERY SYSTEM	Abbott vascular	2000/09/29	P000011
MULTI-LINK VISION/MINI/8 CORONARY STENT SYSTEMS	Abbott vascular	2003/07/16	P020047
MULTI-LINK ULTRA/ ZETA CORONARY STENT SYSTEMS	Abbott vascular	1997/10/02	P970020
RITHRON-XR CORONARY STENT SYSTEM	Biotronic Inc.	2005/04/29	P030037
PRO-KINETIC ENERGY COBALT CHROMIUM (CoCr) CORONARY STENT SYSTEM	Biotronic Inc.	2017/02/14	P160003
EXPRESS/EXPRESS 2 MR & OTW CORONARY STENT SYSTEMS	Boston Scientific Corporation	2002/09/11	P020009
VERIFLEX (LIBERTE) BARE-METAL CORONARY STENT SYSTEM	Boston Scientific Corporation	2005/04/12	P040016
REBEL PLATINUM CHROMIUM CORONARY STENT SYSTEM MONORAIL AND OVER THE WIRE	Boston Scientific Corporation	2014/06/27	P130030
SCIMED RADIUS CORONARY STENT WITH DELIVERY SYSTEM	Boston Scientific Corporation	1998/07/16	P970061
NIR ON TM RANGER TM PREMOUNTED STENT SYSTEM	Boston Scientific Corporation	1998/08/11	P980001
MAGIC WALLSTENT ENDOPROTHESIS	Boston Scientific Corporation	1998/09/29	P980009
COBRA PzF NanoCoated Coronary Stent System	Celonova Biosciences, Inc.	2017/02/21	P160014
GIANTURCO-ROUBIN CORONARY FLEX-STENT(TM)	Cook, Inc.	1993/02/08	P910030
PALMAZ-SCHATZ(TM) BALLOON EXPANDABLE STENT	Cordis Corporation	1994/08/02	P900043
NIRFLEX PREMOUNTED STENT	Medinol Ltd.	2003/10/24	P020040
PRESILLION PLUS COCR CORONARY STENT RX SYSTEM	Medinol Ltd.	2012/04/12	P110004
BESTENT 2 OVER-THE-WIRE (OTW)/RAPID EXCHANGE CORONARY STENT DELIVERY SYSTEM	Medtronic Inc.	2000/10/16	P000022
DRIVER OVER-THE-WIRE, RAPID EXCHANGE, AND MULTI-EXCHANGE CORONARY STENT SYSTEMS	Medtronic Inc.	2003/10/01	P030009
MEDTRONIC WIKTOR PRIME CORONARY STENT DELIVERY SYSTEM	Medtronic Inc.	1997/06/27	P960010

Source: China Insights Consultancy

Approved drug-eluting stent by FDA used in coronary artery disease

FDA drug-eluting stent approval list

Product name	Company	Approval date	Registration number
XIENCE AND PROMUS EVEROLIMUS ELUTING CORONARY STENT SYSTEMS	Abbott vascular	2008/07/02	P070015
XIENCE PRIME AND XIENCE PRIME LL EVEROLIMUS ELUTING CORONARY STENT SYSTEM	Abbott vascular	2011/11/01	P110019
ORSIRO Sirolimus Eluting Coronary Stent System	Biotronic Inc.	2019/02/22	P170030
TAXUS EXPRESS2 PACLITAXEL-ELUTING CORONARY STENT SYSTEM (MONORAIL AND OVER-THE-WIRE)	Boston Scientific Corporation	2004/03/04	P030025
TAXUS LIBERTE PACLITAXEL-ELUTING CORONARY STENT SYSTEM (MONORAIL AND OVER-THE-WIRE)	Boston Scientific Corporation	2008/10/10	P060008
ION PACLITAXEL- ELUTING CORONARY STENT SYSTEM (MONORAIL AND OVER-THE-WIRE SYSTEMS)	Boston Scientific Corporation	2011/04/22	P100023
PROMUS ELEMENT PLUS EVEROLIMUS-ELUTING PLATINUM CHROMIUM CORONARY STENT SYSTEM	Boston Scientific Corporation	2011/11/22	P110010
SYNERGY EVEROLIMUS-ELUTING PLATINUM CHROMIUM CORONARY STENT SYSTEM	Boston Scientific Corporation	2015/10/02	P150003
CYPHER SIROLIMUS-ELUTING CORONARY STENT ON THE RAPTOR OVER-THE-WIRE DELIVERY SYSTEM OR RAPTORRAIL RAPID EXCHANGE DELIVER	Cordis Corporation	2003/04/24	P020026
EluNIR™ Ridaforolimus Eluting Coronary Stent System	Medinol Ltd.	2017/11/28	P170008
ENDEAVOR ZOTAROLIMUS ELUTING CORONARY STENT SYSTEM	Medtronic Inc.	2008/02/01	P060033
RESOLUTE MICROTRAC/RESOLUTE INTEGRITY ZOTAROLIMUS-ELUTING CORONARY STENT SYSTEM	Medtronic Inc.	2012/02/17	P110013
RESOLUTE ONYX ZOTAROLIMUS-ELUTING CORONARY STENT SYSTEM	Medtronic Inc.	2017/04/28	P160043

Source: China Insights Consultancy

Approved bare-metal stents by FDA used in peripheral artery disease

FDA peripheral artery disease BMS approval list

Product name	Company	Approval date	Registration number
CORDIS PRECISE NITINOL STENT SYSTEM	CORDIS CORP.	2006/9/22	P030047
ACCULINK CAROTID STENT SYSTEM AND RX ACCULINK CAROTID STENT SYSTEM	ABBOTT VASCULAR	2004/8/30	P040012
XACT CAROTID STENT SYSTEM	ABBOTT VASCULAR INC.	2005/9/6	P040038
CAROTID WALLSTENT MONORAIL ENDOPROSTHESIS	Boston Scientific Corp.	2008/10/23	P050019
ENDOTEX NEXSTENT CAROTID STENT AND DELIVERY SYSTEM AND ENDOTEX CAROTID STENT AND MONORAIL DELIVERY SYSTEM	BOSTON SCIENTIFIC	2006/10/27	P050025
PROTEGE GPS AND PROTEGE RX CAROTID STENT SYSTEMS	MEDTRONIC VASCULAR INC	2007/1/24	P060001
EXPONENT SELF-EXPANDING CAROTID STENT SYSTEM WITH OVER-THE-WIRE OR RAPID-EXCHANGE DELIVERY SYSTEM	Medtronic Vascular	2007/10/23	P070012
ENROUTE TRANSCAROTID STENT SYSTEM	SILK ROAD MEDICAL, INC	2015/5/18	P140026
Gore Carotid Stent	W. L Gore & Associates, Inc	2018/11/1	P180010
MEDTRONIC AVE BRIDGE EXTRA SUPPORT OVER THE WIRE RENAL STENT SYSTEM	Medtronic Vascular	2002/12/18	P020007
BOSTON SCIENTIFIC EXPRESS SD RENAL MONORAIL PREMOUNTED STENT SYSTEM	Boston Scientific Corp.	2008/12/11	P060006
FORMULA BALLOON-EXPANDABLE RENAL STENT SYSTEM	COOK MEDICAL INCORPORATED	2011/1/14	P100028
RX HERCULINK ELITE RENAL STENT SYSTEM	ABBOTT VASCULAR	2011/7/20	P110001
PALMAZ BALLOON EXPANDABLE STENT	CORDIS CORP.	1991/9/27	P890017
S.M.A.R.T. AND S.M.A.R.T. CONTROL NITINOL STENT SYSTEM	CORDIS CORP.	2003/8/12	P020036
INTRASTENT DOUBLESTRUT STENT	MEDTRONIC VASCULAR INC	2004/6/8	P030045
ZILVER VASCULAR STENT	Cook Ireland, Ltd.	2006/6/26	P050017
INNOVA VASCULAR SELF-EXPANDING STENT WITH DELIVERY SYSTEM	BOSTON SCIENTIFIC CORPORATION	2015/7/21	P140028
GORE TIGRIS VASCULAR STENT	W. L. GORE & ASSOCIATES, INC.	2016/7/27	P160004

Source: China Insights Consultancy

Approved bare-metal stents by FDA used in peripheral artery disease

FDA peripheral artery disease BMS approval list

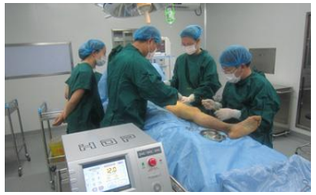
Product name	Company	Approval date	Registration number
BARD E-LUMINEXX VASCULAR STENT	BARD PERIPHERAL VASCULAR, INC.	2008/12/4	P080007
EXPRESS LD ILIAC PREMOUNTED STENT SYSTEM	BOSTON SCIENTIFIC CORPORATION	2010/3/5	P090003
COMPLETE SE VASCULAR STENT SYSTEM	Medtronic Vascular	2010/3/17	P090006
ASSURANT COBALT ILIAC BALLOON-EXPANDABLE STENT SYSTEM	MEDTRONIC IRELAND	2011/10/26	P110011
ABSOLUTE PRO VASCULAR SELF-EXPANDING STENT SYSTEM	ABBOTT VASCULAR INC.	2012/2/22	P110028
EPIC SELF-EXPANDING NITINOL STENT SYSTEM	Boston Scientific Corp.	2012/4/13	P110035
OMNILINK ELITE PERIPHERAL BALLOON-EXPANDABLE STENT SYSTEM	ABBOTT VASCULAR-CARDIAC THERAPIES	2012/7/31	P110043
ASTRON PERIPHERAL SELF-EXPANDING NITINOL STENT SYSTEM	BIOTRONIK, INC.	2015/12/17	P140030
WALLSTENT(R) ILIAC ENDOPROSTHESIS	BOSTON SCIENTIFIC SCIMED, INC.	1996/5/28	P940019
INTRA COIL SELF-EXPANDING PERIPHERAL STENT	MEDTRONIC VASCULAR INC	2002/4/3	P000033
VIABAHN ENDOPROSTHESIS	W.L. GORE & ASSOCIATES,INC	2005/6/14	P040037
LIFESTENT FLEXSTAR & FLEXSTAR XL VASCULAR STENT SYSTEM	BARD PERIPHERAL VASCULAR, INC.	2009/2/13	P070014
EVERFLEX SELF-EXPANDING PERIPHERAL STENT SYSTEM (EVERFLEX)	MEDTRONIC VASCULAR INC	2012/3/7	P110023
MEDTRONIC VASCULAR COMPLETE SE VASCULAR STENT SYSTEM	Medtronic Vascular	2013/9/19	P110040
SMA RT CONTROL AND SMART VASCULAR STENT SYSTEMS	CORDIS CORP.	2012/11/7	P120002
SUPERA PERIPHERAL STENT SYSTEM	ABBOTT VASCULAR (IDEF TECHNOLOGIES INC)	2014/3/28	P120020
MISAGO PERIPHERAL SELF-EXPANDING STENT SYSTEM	TERUMO MEDICAL CORPORATION	2015/5/22	P140002
ASTRON PULSAR STENT SYSTEM, PULSAR-18 STENT SYSTEM	BIOTRONIK, INC.	2017/3/23	P160025
BioMimics 3D Vascular Stent System	Veryan Medical Ltd.	2018/10/4	P180003

Source: China Insights Consultancy

Treatment path of peripheral arterial disease

- The treatment of peripheral arterial disease mainly includes three methods: medical treatment, surgical treatment and interventional treatment.

Treatment path of peripheral arterial disease



- The goals of peripheral arterial disease therapy depend on the severity of the disease. For all patients with symptomatic or asymptomatic, reducing the risk of cardiovascular morbidity and mortality is a primary concern. There are mainly three treatment paths that are medical, surgical and interventional.
- More advanced peripheral arterial diseases that are causing severe pain and limited mobility may require interventional or surgical treatment. Some of the same treatments that are used for heart disease are also used for treating peripheral arterial disease.

Lesion	*Treatment type*	*Indication*	*Treatment method*	*Level of evidence*
Carotid artery disease	**Interventional**	Patients with an asymptomatic carotid artery disease who deemed ‘high risk for carotid endarterectomy’	Carotid artery stenting	IIa
	Surgical	Patients with an asymptomatic carotid artery disease	Carotid endarterectomy	IIa
	Surgical	Patients have symptomatic carotid disease with 70–99% carotid stenoses	Carotid endarterectomy	I
	Surgical	Patients have symptomatic carotid disease with 50–69% carotid stenoses	Carotid endarterectomy	IIa
	Interventional	Patients have symptomatic carotid disease with 50–99% carotid stenoses who deemed ‘high risk for carotid endarterectomy’	Carotid artery stenting	IIa
	Medical	Revascularization is not recommended in patients with a < 50% carotid stenosis	Antiplatelet drugs; Statin, antihypertensive, anticoagulation agents, and etc.	I
Subclavian Artery disease	**Interventional**	Symptomatic patients with subclavian artery stenosis/occlusion	Revascularization	IIa
	Surgical	Patients with low operative risk or after endovascular therapy failure	Open surgery	IIa
	Medical	Symptomatic patients with contraindications for endovascular therapy or open surgery	Prostanoid infusion	IIa
Lower extremity artery disease	**Medical**	Patients with intermittent claudication	Using statins to prevention	I
	Interventional	When daily life activities are is severely compromised	Exercise and revascularization	IIa

Source: ESC guidelines on the diagnosis and treatment of PAD; China Insights Consultancy

Treatment path of peripheral arterial disease

- The treatment of peripheral arterial disease mainly includes three methods: medical treatment, surgical treatment and interventional treatment.

Treatment path of peripheral arterial disease

Lesion	Treatment type	Indication	Treatment method	Level of evidence
Mesenteric artery disease	Interventional	Patients with acute thrombotic occlusion of the superior mesenteric artery	Endovascular therapy	IIa
	Surgical	Patients with acute thrombotic occlusion of the superior mesenteric artery	Open surgery	IIa
	Interventional	Patients with chronic mesenteric ischemia	Interventional revascularization	I
	Surgical	Patients with chronic mesenteric ischemia but failed endovascular therapy	Open surgery revascularization	I
Renal artery disease	Medical	Hypertension associated with unilateral renal artery stenosis	ACEIs*, ARBs*, Calcium channel blockers, beta-blockers, and diuretics	I
	Interventional	Hypertension and/or signs of renal impairment related to renal arterial fibromuscular dysplasia	Balloon angioplasty with bailout stenting	IIa
	Surgical	Patients with complex anatomy of the renal arteries, after a failed endovascular procedure	Surgical revascularization	IIa
	Interventional	Renal artery stenosis patients and unexplained recurrent congestive heart failure or sudden pulmonary oedema	Balloon angioplasty, with or without stenting	IIb
	Interventional	Renal artery stenosis secondary to atherosclerosis	Routine revascularization	III
Acute limb ischaemia	Interventional	Neurological deficit	Revascularization	I
	Medical	Patients presenting with acute limb ischaemia	Heparin and analgesics	I
Chronic limb-threatening ischaemia	Interventional	Chronic limb threatening ischaemia and limb salvage	Infra-popliteal revascularization	I
	Surgical	Revascularization of infra-popliteal arteries	Bypass using the great saphenous vein	I
	Interventional	Revascularization of infra-popliteal arteries	Endovascular therapy	IIa

Note: Angiotensin-converting enzyme inhibitors (ACEIs), Angiotensin-receptors blockers (ARBs)*

Source: ESC guidelines on the diagnosis and treatment of PAD; China Insights Consultancy

Treatment path of peripheral arterial disease

- The treatment of peripheral arterial disease mainly includes three methods: medical treatment, surgical treatment and interventional treatment.

Treatment path of peripheral arterial disease

Lesion	Treatment type	Indication	Treatment method	Level of evidence
Patients with intermittent claudication and severe chronic limb ischaemia（aorto-iliac occlusive lesions）	**Interventional**	Patients with short (i.e. <5 cm) occlusive lesions	Endovascular therapy	I
	Surgical	Patients with aorto-iliac occlusions fit for surgery	Aorto-(bi)femoral bypass	IIa
	Interventional	Patients have long and/or bilateral lesions with severe comorbidities.	Endovascular therapy	IIa
	Surgical	Patients with an aortic occlusion extending up to the renal arteries	Open surgery	IIa
	Surgical	Patients with ilio-femoral occlusive lesions	Hybrid procedure combining iliac stenting and femoral endarterectomy or bypass	IIa
Patients with intermittent claudication and severe chronic limb ischaemia（femoro-popliteal occlusive lesions）	**Interventional**	Patients with short (i.e. <25 cm) occlusive lesions	Endovascular therapy	I
	Interventional	Patients with short (i.e. <25 cm) occlusive lesions	Primary stent implantation	IIa
	Interventional	Patients with short (i.e. <25 cm) occlusive lesions	Drug-eluting balloons / stents	IIb
	Surgical	Patients who are not at high risk for surgery	Bypass surgery	I
	Interventional	Patients with long (i.e. >25cm) femoro-popliteal lesions and unfit for surgery	Endovascular therapy	IIb

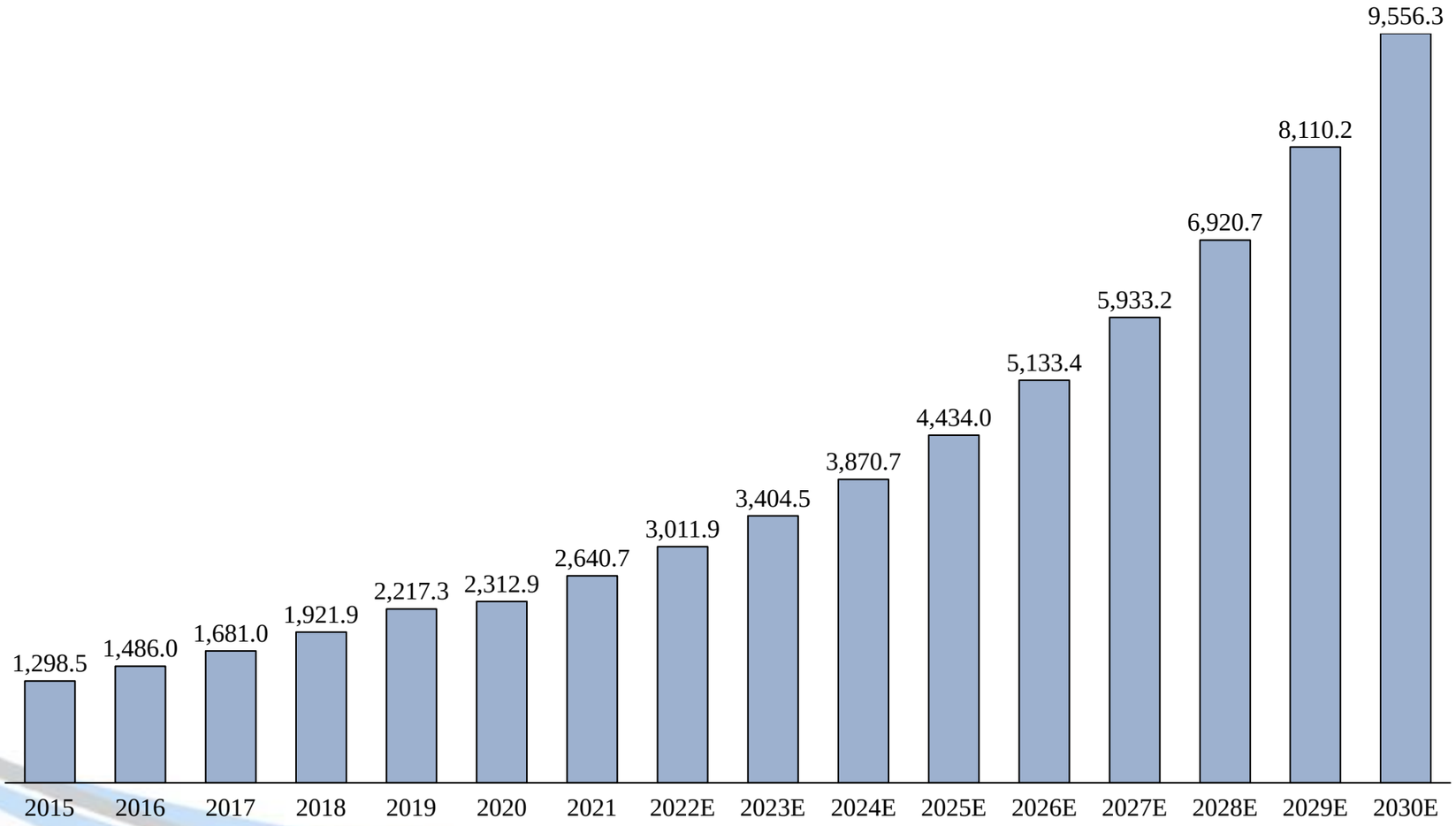
Source: ESC guidelines on the diagnosis and treatment of PAD; China Insights Consultancy

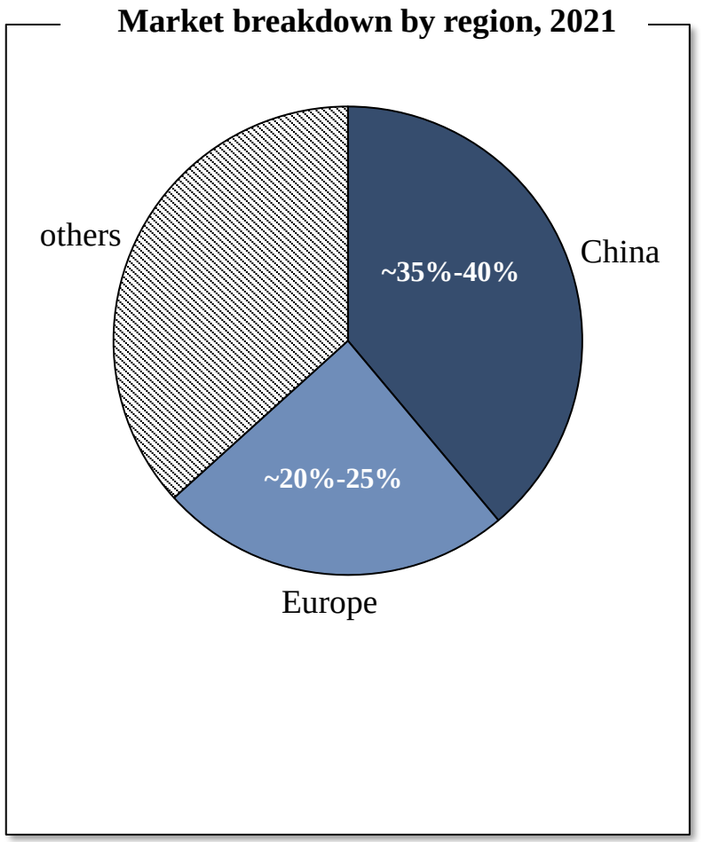
Global market size of Neuro interventional instrument market, in terms of sales value

Global market size of Neuro interventional instrument market, in terms of sales value*, 2015-2030E

CAGR	2015-2020	2021-2025E	2026E-2030E
Global neuro-intervential procedure instrument market	12.2%	13.8%	16.8%

USD million





Source: China Insights Consultancy

Threat, challenge and entry barriers of global coronary/peripheral artery interventional instrument market

Threat, challenge and entry barriers of global coronary/peripheral artery interventional instrument market

Threat and challenge	Description
Product upgrade and substitution	• The coronary/peripheral artery interventional instrument products continue to go through upgrades and substitutions. Companies would continuously research, innovate and develop new generations of products with better surgical results, and as a result, older generation products would gradually become obsolete. For example, after the development of drug eluting stents, the market share of bare metal stents shrunk drastically. The drug eluting stents also compete with dual therapy stents or absorbable stents. Therefore, the nature of the importance of continuous product upgrade and substitution poses can pose significant threat challenge on PCI/PTA instrument companies, and it is important for them to continuously upgrade their products.
COVID-19 pandemic	• The COVID-19 pandemic imposes negative effect on the whole medical health industry. Due to the pandemic, many hospitals enforce strict policies on hospital visits and limit the number of patients going to hospitals so that the resources being reallocated to treat COVID patients. Furthermore, the pandemic hit the global economy heavily, and the public's affordability of advanced medical services are impaired. Therefore, the pandemic heavily influences the global health expenditure, which as a result becomes a challenge for medical device companies to make a profit.
Government regulatory risk	• Strict approval regulations: Medical devices are required to go through stringent approval processes. Companies must obtain relative licenses and certificates to produce and sell medical devices and register again if they become invalid after expiry. Strict access systems and complex regulations are major challenges for medical device companies. • Government pricing-related policies: In many countries, government would control prices of medical devices through regulatory means in order to maintain costs of government medical insurances. The centralized procurement policies promulgated by the PRC government under which the purchases of the medical devices included in the centralized procurement scope by the public hospitals should be made through the public bidding or tender processes on the centralized procurement platform established by the respective local governments, often lead to a substantial decrease in the profitability of medical device products manufacturers. Other countries, such as Japan and the U.S., also have policies which would heavily influence the profit margin of medical device products.
Low public awareness	• The public awareness of peripheral artery diseases is generally lower than that of cerebral artery diseases or coronary artery diseases. The low public awareness results in low surgical penetration rate. For example, in 2020, the surgical penetration rate of PTA intervention is 0.5% in China, far lower than that of PCI intervention, which is 5.5%, although it is expected to grow by 1.2% in 2030 as a result of various factors including patients awareness of peripheral artery disease, the education from physician conferences or companies and government reimbursement policies. Increased awareness and education of the public about the seriousness of PAD diseases can overcome this challenge

Threat, challenge and entry barriers of global coronary/peripheral artery interventional instrument market

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Entry barriers	Description
Intensive technology and continuous product innovation	• Multi-disciplinary expertise in material and mechanical engineering, product design and manufacturing are necessary in the development of coronary/peripheral artery interventional instruments. In addition, coronary/peripheral artery is very important and complex, which implies a higher level of sophistication of means related to the surgical instruments. New entrants may generally find it difficult to recruit the necessary professionals and acquire the technologies in a short term. On the other hand, continuous product innovation is also important for medical device companies to maintain profitability. The key to success in the medical technology industry has been continuous innovation and a dedication to research and development. A key driver for this continuous innovation is the short lifecycles within the sector. Once a breakthrough technology has been established, improvements are made continuously. The value-based innovations of the medical device industry have proven to not only improve the lives of millions of patients, but also play an important role in making healthcare systems more efficient, which has become a priority for all governments. Also, the global PCI/PTA market players often challenge the intellectual property of their competitors. Therefore, robust intellectual property protection is important to survive, the building up of which may be costly and time consuming.
Commercialization capability	• It is important for medical device manufacturers to develop its global commercialization capabilities and utilize the distributorship sales model to access the global coronary/peripheral artery interventional instrument market. It requires market players to have the ability of mass production at a high quality standard that meets various regulatory bodies' requirements across the globe. In addition, establishing local sales offices with the relevant industry and cultural knowledge to manage direct sales anddistributors can be difficult. Identifying suitable distributors in the development of a strong distribution network can also be time consuming. Moreover, gaining brand reputation and awareness plays an important part in product commercialization, which partly means to acquire recognition from target stakeholders such as hospitals and physicians. However, it typically takes years of efforts for a brand to establish solid relationships with physicians and hospitals, especially with KOLs and top-tier hospitals.
Heavy capital investment	• Participation in the global PCI/PTA intervention instrument market requires heavy capital investment. Costs of research and development of coronary/peripheral artery interventional instrument products, enhancement of product quality and performance, payment to the professionals in the long term, brand promotion and marketing channel construction, establishing factories which enable mass production at a strict quality standard all require significant capital expenditure and investments. Particularly, a large amount of capital is necessary if the players hope to survive and continuously expand in this industry. Financial pressure is an inevitable challenge for most of the medical device startups in their initial years before they can break even, and it can take substantial time to achieve profitability. Attracting sufficient investments and utilizing the funds effectively and efficiently are practically hard to fulfill, presenting a huge barrier especially for new entrants in the market.

Source: China Insights Consultancy

Threat, challenge and entry barriers of global neuro interventional instrument market

Threat, challenge and entry barriers of global neuro interventional instrument market

Threat and challenge	Description
Uncertainties in macro-control	• In certain countries, such as the PRC, the government regards precision medical products as a key development area and considers it to be a national development strategy. For example, the Chinese government's policies in the medical field related to people's livelihood and health are very strong, which may have a great impact on the income and profit of the investors. It is not ruled out that the government will introduce restrictive policies for the industry due to economic factors, political factors, macro-control and other factors. If the government's policies and regulations on the management of medical institutions are strict and not biased, it will cause policy risks
Lack of core competitiveness	• Although the R&D investment of enterprises in neuro intervention industry is increasing year by year, the R&D investment of new enterprises is far less than that of large multinational corporations due to the limited operating income of the new enterprises. The low R&D investment may have negative impact on the quality of products and the core competitiveness of the new enterprise..
Entry barriers	
Product portfolio and solutions	• Different procedures require various types and specifications of neuro-interventional medical devices. New entrants may not be able to compete with other market players in terms of synergies for R&D, manufacturing and commercialization capabilities and economies of scale, and therefore cannot offer a comprehensive product portfolio to meet the various needs.
Registration and regulatory requirements	• In certain countries, such as China, Class III neuro-interventional medical devices generally require product registration testing and clinical trials if they are not exempted from clinical trials under the catalog published by the NMPA. Rigorous registration standards on safety and efficacy are implemented to regulate the development and commercialization of these medical devices. Further, the product development and registration process may take up to five years and neuro-interventional medical device manufacturers need to obtain manufacturing licenses and to maintain strict compliance with GMP requirements and other various regulations in China. As a result, registration and regulatory requirements in relevant jurisdictions would become entry barriers for new entrants in the market
Heavy capital investment	• Participation in the global neuro-intervention instrument market requires heavy capital investment. Costs of research and development of neuro-interventional instrument products, enhancement of product quality and performance, brand promotion and marketing channel construction, establishing factories which enable mass production at a strict quality standard all require significant capital expenditure and investments. Particularly, a large amount of capital is necessary if the players hope to survive and continuously expand in this industry. Financial pressure is an inevitable challenge for most of the medical device startups in their initial years before they can break even, and it can take substantial time to achieve profitability. Attracting sufficient investments and utilizing the funds effectively and efficiently are practically hard to fulfill, presenting a huge barrier especially for new entrants in the market.

Source: China Insights Consultancy

Threat, challenge and entry barriers of global structural heart disease device market

Threat, challenge and entry barriers of global structural heart disease device market

Threat and challenge	Description
Patient acceptance and pricing	• The risk awareness of structural heart disease is still in an early stages to the public, and it may be difficult for patients to accept even the world's leading technology products immediately. Then, the pricing of the commercialized heart valve products are expensive to most of the patient, how to adjust the price to a widely accepted range become a threat to the industry.
Lifetime, rejection reaction	• Patients who went through transcathter valve replacement surgeries usually would experience rejection reactions, and are required to take anti-rejection medications throughout lifetime. The improvement of valve designs and materials can reduce the rejection reactions. Thus, it is a challenge for companies to design and produce artificial valve products with reduced rejection reactions
Entry barriers	
Intensive technology and continuous product innovation	• Multi-disciplinary expertise in material and mechanical engineering, product design and manufacturing are highly demanded in structure heart interventional instrument industry. The complexity of heart and heart valve required highly sophisticated and precision interventional instruments. Difficulty to New entrants may generally find it difficult to hire professionals and acquire the technologies in a short term
Heavy capital investment	• Costs of R&D on structural heart interventional instrument are heavy, which are mainly for the enhancement of product quality and performance, payment to the professional developers and laboratory in the long term, brand promotion and marketing channel construction all need fund to a significant extent. If a manufacturer hopes to survive and subsequently expand in this industry, financial pressure is an inevitable challenge for most of them especially in the initial years before finally breaking even. Attracting sufficient investments and arranging the funds effectively and efficiently are practically hard to fulfill for new entrants

Source: China Insights Consultancy

Price of major raw materials used in producing balloon and stent and finished PCI balloon

Annual average price of polyester in China, 2016-2020

The key raw materials used in producing our balloon and stent products are medical grade stainless steel, polyester and nylon. Fluctuations in prices of these raw materials may be affected by the cost structure, product pricing and profitability of balloon and stent market players.

The average price of medical grade stainless steel in China was approximately RMB12.7 per kilogram, RMB15.2 per kilogram, RMB15.6 per kilogram, RMB15.1 per kilogram, RMB14.3 per kilogram and RMB14.9 per kilogram in 2016, 2017, 2018, 2019, 2020 and 2021, respectively. Over the past five years, the average price of medical grade stainless steel in China has been fluctuating, yet the price is demonstrating a growing trend overall.

The average price of medical grade stainless steel is expected to increase to RMB16.6 per kilogram in 2025.

The average price of polyester in China was approximately RMB6.8 per kilogram, RMB7.9 per kilogram, RMB9.2 per kilogram, RMB7.6 per kilogram, RMB5.4 per kilogram and RMB 5.6 per kilogram in 2016, 2017, 2018, 2019, 2020 and 2021, respectively. Over the past five years, the average price of polyester in China has been fluctuating, yet it demonstrates a gradual downward trend overall. The average price of polyester is expected to decrease to RMB4.2 per kilogram in 2025

The average price of nylon in China was approximately RMB12.8 per kilogram, RMB17.8 per kilogram, RMB18.1 per kilogram, RMB14.1 per kilogram, RMB11.6 per kilogram and RMB 13.1 per kilogram in 2016, 2017, 2018, 2019, 2020 and 2021, respectively. Over the past five years, the average price of nylon in China has been fluctuating, but exhibits a gradual downward trend. The average price of nylon is expected to decrease to RMB10.2 per kilogram in 2025.

PRICE TREND OF PCI BALLOONS ;

The average price of same model of standard PCI balloons is generally expected to decrease over time at approximately 2% per annum after its commercialization and product launch. In light of advances in technology and more medical device manufacturers entering into this market, the price of same model balloon will demonstrate a gradual downward trend in the future and new or more advanced generation of products will enjoy a higher average selling price.

For instance, there are local policies in Shanghai, Jiangsu, Zhejiang and Anhui with respect to a favorable reimbursement percentage by medical insurance for domestically-produced high-value medical consumables such as coronary interventional medical devices.

For instance, policies in Shenzhen such as the Shenzhen Dedicated Funds Support Policy on the Development of Strategic Emerging Industries (深圳市戰略性新興產業發展專項資金扶持政策) and the Shenzhen Technology Research and Development Funds Administration Measures (深圳市科技研發資金管理辦法) provide government grant to support of R&D investment.

After the issuance of the above reform plan, vascular interventional balloon products were gradually brought into the scope of the centralized procurement (also known as volume-based procurement and/or the centralized volume-based procurement, hereinafter referred to as “centralized procurement”) in Jiangsu, Hubei, Zhejiang, Sichuan, Shanxi, Liaoning, Jilin, Heilongjiang, Guangdong, Beijing, Tianjin, Hebei and other regions from the second half of 2019 to 2021 according to **their centralized procurement announcements** and were expected to be implemented across the PRC.

Source: China Insights Consultancy

The above policies influenced the PRC sales environment of the high-valued medical consumables in the scope of centralized procurement mainly in the following respects**: (i) the manufacturers (including the deemed manufacturer, such as the general agent of the imported products) or the holders of the medical device registration certificate are required to directly participate in the biding or tending process of the centralized procurement**, and (ii) the end prices of the high-value medical consumables within the scope of centralized procurement generally experienced downward changes caused by the pricing mechanism of the biding or tender process and the negotiation principle of high volume in exchange for high volume.

Sales of our products in the U.S. market, will depend, in part, on the extent to which our products are covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations.
Therefore, pricing of our products are predominately subject to market force.

Therefore, pricing of our products are predominately subject to market force.

In the PRC, the public medical institutions are required to, implement the centralized procurement for their purchase of the high-value medical consumables which are brought into the centralized procurement scope.

Sales of medical devices in the U.S. market, will depend, in part, on their coverage by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations.

The decrease in average selling price from 2020 to 2021 was mainly due to the decrease
in average selling price from 2020 to 2021 in the PRC market after our non-compliant balloons were brought into the scope of centralized procurement policies, and the decrease in average selling price in the Japan market as a result of **the decrease in reimbursement to hospitals for medical product**s also contributed to the overall decrease in pricing of our non-compliant balloons.

Such decrease was in line with the **overall decreasing price trend of interventional medical devices.**

	Number of Key Market Players*	Aggregate Market Shares of Key Market Players*	Our Market Share	Our Ranking
PCI Balloons				
Japan	4	88%	20%	No. 2
Europe	6	97%	11%	No. 4
PRC	9	[80]%	8%	No. 6
The U.S.	5	[95]%	3%	No. 6
PTA Balloons				
Japan	7	[83]%	13%	No. 3
The U.S.	7	[80]%	12%	No. 4
Europe	5	[97]%	1%	No. 6-10
PRC**	5	[94]%	/	/

End of report

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