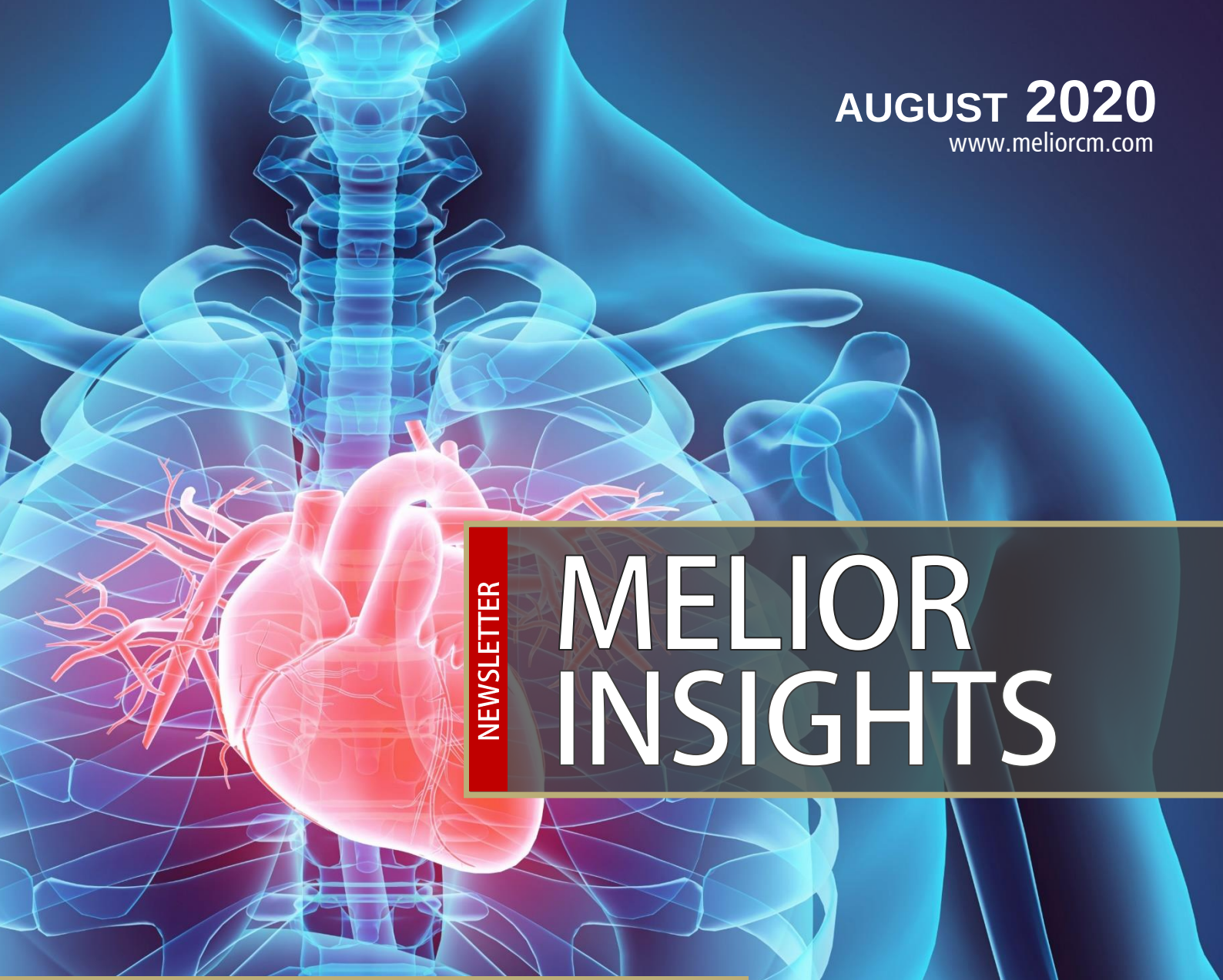

AUGUST 2020

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NEWSLETTER

MELIOR INSIGHTS

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This newsletter is for education purposes only and addresses past events. This newsletter is not an offer nor an invitation to subscribe.

Melior
CAPITAL MANAGEMENT

Introduction to Melior Capital Management

MELIOR

/me'ljor/
(from Latin)

BETTER, SOUNDER, SUPERIOR

Melior Capital Management is a Swiss domiciled company introducer and advisory firm focused exclusively on the global life science sector.

We specialise in finding funding for medtech, biotech and pharmaceutical companies by applying institutional quality service and process to raise capital.

Our investment approach is to find qualified innovative projects, with proven management teams, promising data, robust IP, strong corporate governance and a likely opportunity for significant commercial upside in a three to five-year horizon.

In the current environment, many existing companies seeking capital for medical trials have encountered a diminishing supply of funding from governments, private equity firms, investment banks and research foundations in favour of start-ups. At Melior, we combine the global reputation of our scientific, management and advisory members to select best in class investment opportunities with credible upside potential.

Our value proposition is attributable to our world class team and their proven track record in the life-science sector, plus the strong emphasis that we place upon due diligence and first-hand experience. Our goal is to offer attractive and diverse investments to both high net worth private clients and larger corporates through their professional advisers. For our business to be truly successful, we consider the needs of all parties, including our investees, investors and professional advisers at introduction and throughout the life of the investment. Our financial success depends on funds raised and the financial return of our investees as we share a common goal.

In this edition of our newsletter – the Melior Insights, we look at the Cardiovascular system, what makes it so important, its weaknesses, the market of cardiovascular conditions, with a focus on the cardiovascular device market. This market is a great case study of the overall life science space, which is bustling with activity of research and development, innovation, as well as mergers and acquisitions.

Melior does not accept enquiries from members of the general public, but we welcome enquiries from professional intermediaries.

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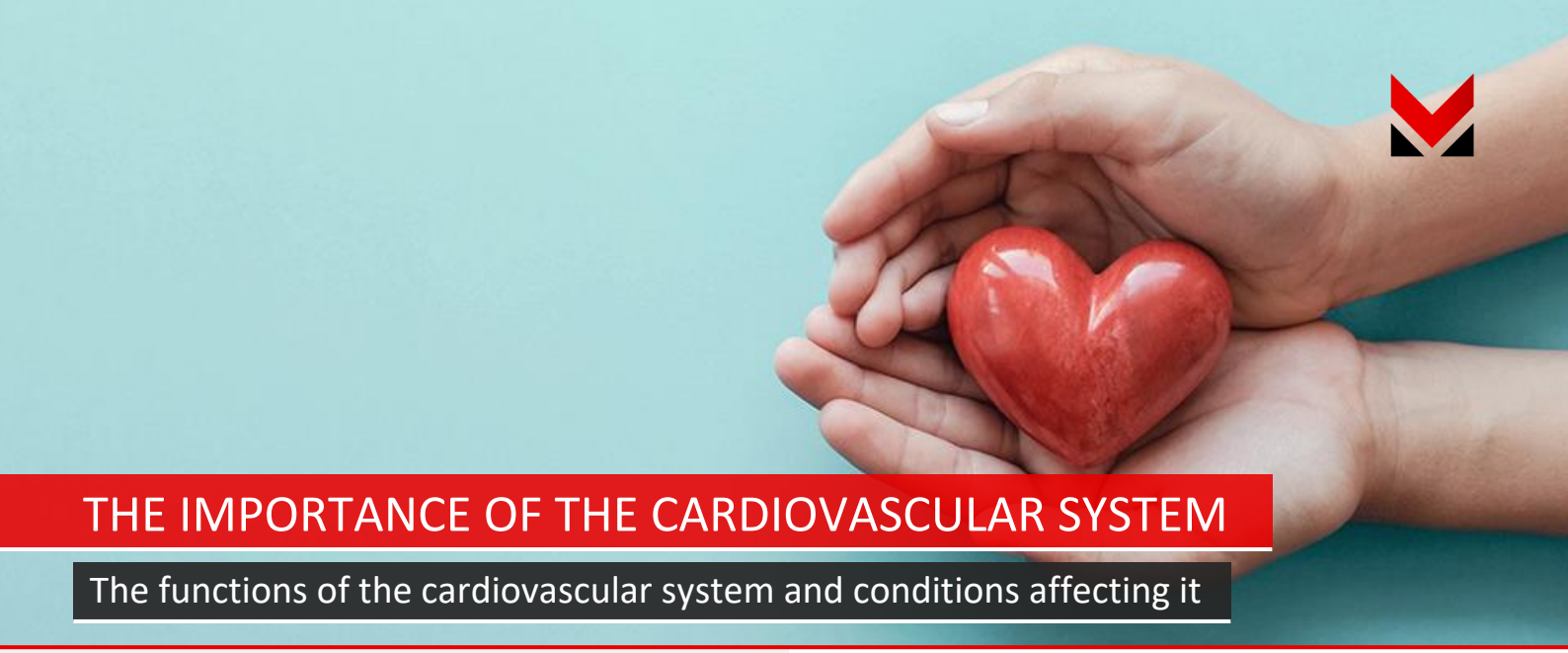


THE IMPORTANCE OF THE CARDIOVASCULAR SYSTEM

The functions of the cardiovascular system and conditions affecting it

The cardiovascular system, also called circulatory system, is **one of the key organ systems of the human body** and its functions are to permit the circulation of blood and transportation of nutrients, oxygen, carbon dioxide, hormones and blood cells to and from tissues. In addition to providing essential nutrients, the **circulatory system is critical in fighting diseases** and it regulates the temperature and pH of the body.

At the core of the circulatory system is the heart – the "engine" that continuously pumps blood through our bodies. It is the first functional organ to develop and starts beating at around the third week of development of the human embryo. In addition to the heart, the cardiovascular system is composed of a myriad of blood vessels (arteries, veins and capillaries), a number of organs with functions to enrich and cleanse the blood (lungs, liver and kidneys), with blood being delivered to the tissues of our bodies.

Any deviation from the normal functioning of the cardiovascular system can result in significant problems, resulting in a myriad of diseases and disorders:

- CORONARY ARTERY AND VASCULAR DISEASES
- HEART RHYTHM DISORDERS
- STRUCTURAL HEART DISEASES
- HEART FAILURE

Coronary artery and vascular diseases

Just like each and every organ of the human body, the cells of the heart also need nutrients and oxygen; these are supplied via the coronary artery. Coronary artery disease (CAD) is the most common kind of heart disease, also called ischemic heart disease, it occurs when the artery hardens and narrows (atherosclerosis) and can result in heart attacks (myocardial infarction) and/or chest pain (angina). Vascular diseases occur when blood vessels are affected and are no longer capable of ensuring circulation of blood through the body. Some of the most common vascular diseases include peripheral arterial diseases (disease of blood vessels that supply blood to the arms and legs) and cerebrovascular disease (disease of blood vessels that supply blood to the brain, including stroke).

Heart rhythm disorders

The heart is a muscular pump that operates continuously and at a regular pace. However, there are hundreds of millions of people around the world, whose hearts either beat too slowly, too quickly or in a disorganised fashion. These rhythm disorders are also called arrhythmias. These are very dangerous as they can severely affect the health of the heart and the blood vessels and result in heart failure and other health issues.

Structural heart diseases

Abnormalities of the structure of the heart, including its valves, walls, muscles or the blood vessels near the heart are included in this group of conditions. These diseases can be present at birth (congenital) or acquired after birth

through wear and tear, infection (caused by bacteria, viruses or parasites) or other factors. It is often the case that people with such conditions need ongoing medical care and even repeated surgical procedures.

Heart failure

Heart failure is a serious condition that occurs when the heart becomes damaged or weakened; the two most common causes of this being high blood pressure and heart attacks. There is no cure for it, but early diagnosis, lifestyle changes and medication can help people live longer, lead an active life and stay out of hospital.

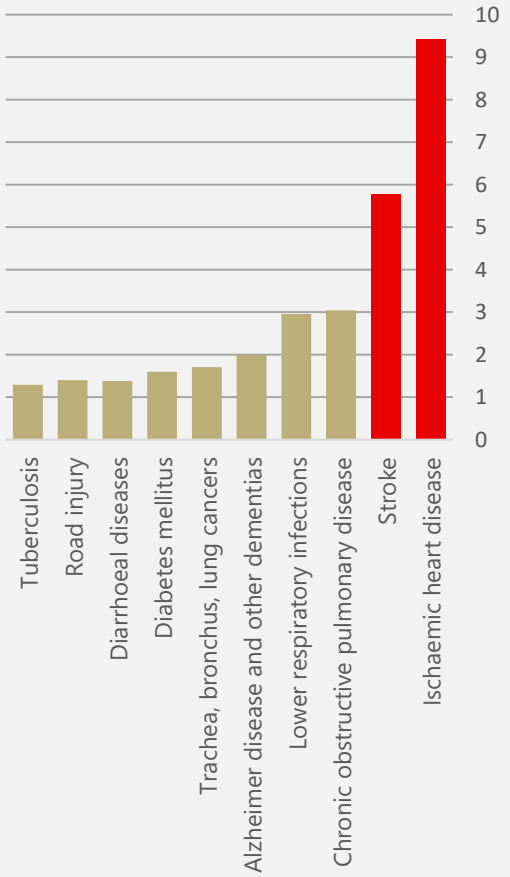
PREVALENCE OF CARDIOVASCULAR DISEASES

According to the WHO, cardiovascular diseases (CVD) are the number one cause of global death, with an estimated 17.9 million people or 31% dying from this cause in 2016. These diseases have remained the leading causes of death globally for the last 15 years.

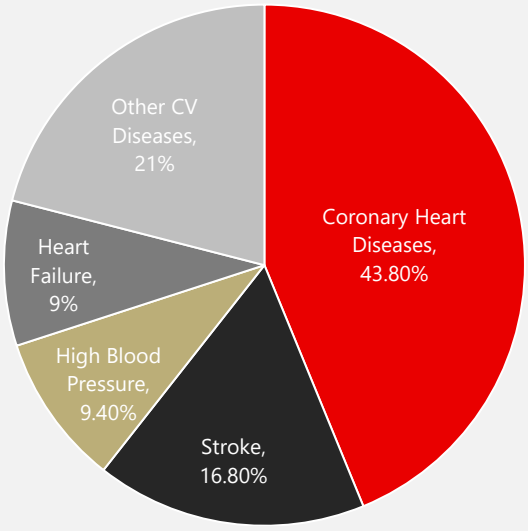
In the United States, the situation is very similar – **CVD is the leading cause of death** of men, women and people across most racial and ethnic groups:

- One person dies every 36 seconds from CVD
- One heart attack occurs every 40 seconds
- 655 thousand deaths happen yearly, or 1 in 4 deaths are attributable to CVD
- Approximately 1 in 5 heart attacks are silent – damage is done, but the person is not aware of it
- The yearly costs of CVD (cost of health care services, medicines and lost productivity) reach $219 billion
- 18.2 million adults, or 6.7% of the population that is older than 20, have CAD

LEADING CAUSES OF DEATH GLOBALLY (MILLIONS)



THE PERCENTAGE OF DEATHS ACCORDING TO CVD IN THE UNITED STATES IN 2018



CAUSES OF CARDIOVASCULAR DISEASES

There are a number of **causes that increase the chances of CVDs:**

MEDICAL CONDITIONS

- high blood pressure
- high cholesterol levels
- diabetes
- sleep apnoea

LIFESTYLE RISK FACTORS

- unhealthy diet
- insufficient physical activity
- unhealthy weight
- smoking
- alcohol abuse
- stress
- recreational drug use

OTHER RISK FACTORS

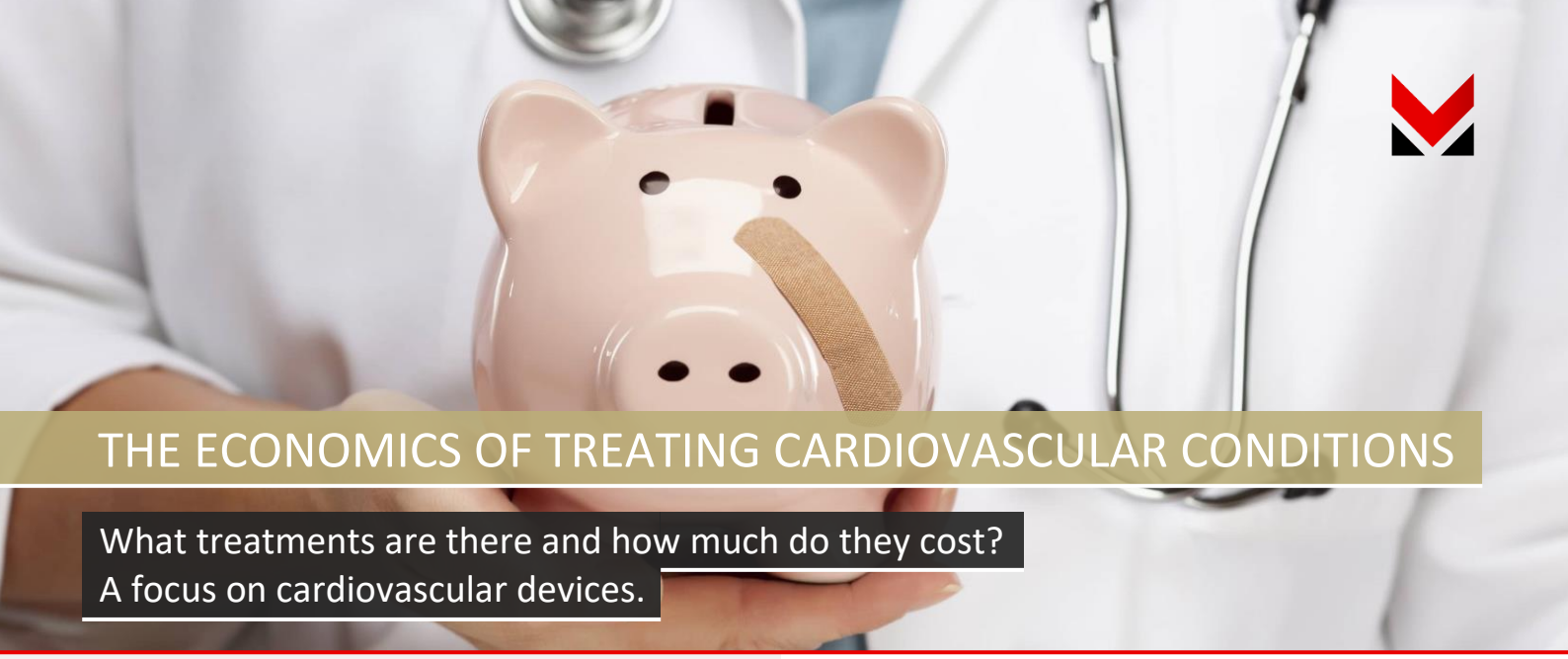
- age – the risk of heart disease increases in time
- family and medical history
- lack of access to healthy food, safe drinking water, health services and social services

PREVENTION OF CARDIOVASCULAR CONDITIONS

There are a number of **actions that can significantly reduce the risk of CVDs**:

- Smoking cessation
- Physical activity
- Monitoring blood pressure
- Eating a healthy diet that is lower in fat, especially saturated and trans fats
- Achieving and maintaining a healthy weight
- Dietary control of diabetes when present
- Limiting alcohol use
- Reducing stress
- Visiting the doctor regularly and following their advice
- Practicing good hygiene in order to reduce the chance of infections

Sources: *The WHO, Mayo Clinic, Heart and Stroke Foundation of Canada, MedicineNet, and the Melior Insights Team*



THE ECONOMICS OF TREATING CARDIOVASCULAR CONDITIONS

What treatments are there and how much do they cost? A focus on cardiovascular devices.

Cardiovascular conditions are not only the **leading cause of death**, but are also **widely spread across different age and ethnic groups with varying levels of severity**. There are specialised treatments for each condition and the specific circumstances of each patient.

However, broadly speaking, **treatments** for CVDs can be divided into three categories:

LIFESTYLE CHANGES	MEDICATION	MEDICAL PROCEDURES OR SURGERY

Lifestyle changes

These measures are especially effective for the prevention and treatment of early-stage cardiovascular conditions. Diet, exercise, smoking cessation and limiting alcohol consumption can all improve the health of the circulatory system.

Medication

For cases where lifestyle changes are not sufficient to alleviate symptoms, drugs may be prescribed to treat or control heart disease. CVD drugs are divided into classes:

- **Antihypertensives** – drug that treat hypertension
- **Antihyperlipidemics** – drugs that reduce the level of cholesterol in the blood
- **Anticoagulants** – drugs that reduce blood clotting
- **Antiplatelets** – drugs that prevent platelets in the blood from sticking together and forming a blood clot
- **Others**

The cardiovascular drugs market is valued at USD 80.5 billion in 2020 and is **estimated to grow to USD 92.3 billion in 2026**, at a CAGR of around 2.3%.

Medical procedures or surgery

In many cases the only viable solution to patient's condition is surgery, such as the installation of an artificial cardiac pacemaker to ensure a regular heartbeat or inserting a stent to enable proper blood circulation. The usage of medical devices in these cases usually leads to sustainable lives with little or no surgical intervention. In addition, medical devices are used to properly diagnose the condition and to monitor the situation of the patient, both prior and after the surgical procedure. A more detailed overview of the cardiovascular device market follows.

THE CARDIOVASCULAR DEVICE MARKET

The cardiovascular device market can be partitioned in a number of ways, but the two most popular ways are by:

A. **Device Type**

1. Diagnostic and Monitoring Devices
   - i. Electrocardiogram (ECG)
   - ii. Remote cardiac monitoring
   - iii. Other diagnostic and monitoring devices
2. Therapeutic and surgical devices
   - i. Cardiac assist devices
   - ii. Cardiac rhythm management devices (pacemakers)
   - iii. Catheters
   - iv. Grafts

v. Heart valves
vi. Stents
vii. Other therapeutic and surgical devices

B. Application

1. Coronary artery disease (CAD)
2. Cardiac arrhythmia
3. Heart failure
4. Others

In 2019, diagnostic and monitoring tools dominated the global cardiovascular device market with a 57.89% share. Holter monitors, ECG, event monitors, echocardiograms, implantable loop recorders, PET scans, cardiac CT, MRI and doppler foetal monitors are some of the most common cardiovascular diagnostic and monitoring devices.

The cardiovascular device market is currently witnessing considerable demand across the globe as a result of **3 main factors**:

1. **Increased awareness** of the various cardiovascular diseases
2. **Increasing geriatric population** across the world
3. **Increasing affordability** for cardiovascular procedures driven by both the increase in purchase power of the patients leading to lower prices and more efficient procedures.

The cardiovascular device market is valued at USD 46.3 billion in 2020 and is expected to slightly decrease in 2020/2021 due to the COVID-19 pandemic as a consequence of a drop in the number of cardiac surgeries conducted during this period (government and health authorities' restrictions and re-scheduling/cancellations, as well as no-shows by patients). However, the market is set to recover and grow steadily through 2027, reaching USD 71.1 billion, growing at 6.5% CAGR. From a geographical point of view, North America is the most dominant region accounting for 42.35% of the 2019 market.

CARDIOVASCULAR DEVICE MARKET KEY PLAYERS

This market is made up of both long-standing leaders as well as new and disrupting entrants. The established players of the cardiovascular device market tend to hold their positions well through R&D and acquisitions of leading start-ups.

TERUMO

Country: Japan
Founded: 1921
Type: Public. Listed on Tokyo Stock Exchange and a Nikkei 225 component
Revenue: $3.1 billion (Cardiovascular products, 2018. 54.9% of total revenue)

SIEMENS Healthineers

Country: Germany
Founded: 1847 (as Siemens & Halske)
Type: Public. Listed on Frankfurt Stock Exchange
Revenue: $34.2 billion revenue (total, 2019)

B BRAUN

Country: Germany
Founded: 1839
Type: Private
Revenue: $8.2 billion (total, 2018)

Johnson & Johnson

Country: US
Founded: 1886
Type: Public. Listed on NYSE and a S&P 100 Component
Revenue: $82.1 billion (total, 2019)

Medtronic

Country: US
Founded: 1949
Type: Public. Listed on NYSE and a S&P 100 Component
Revenue: $30.6 billion (total, 2019)

CardinalHealth

Country: US
Founded: 1971
Type: Public. Listed on NYSE and a S&P 500 Component
Revenue: $152.9 billion (total, 2020)

LivaNova

Country: UK
Founded: 1956 (as Sorin Biomedica)
Type: Public. Listed on NASDAQ and a S&P 400 Component
Revenue: $0.8 billion (Cardiovascular products, 2019. 74.6% of total)

GE Healthcare

Country: US
Founded: 1893
Type: Public (as GE). Listed on NYSE and a S&P 100 Component
Revenue: $19.8 billion (total, 2018)

Edwards

Country: US
Founded: 1958
Type: Public. Listed on NYSE and a S&P 500 Component
Revenue: $4.3 billion (total, 2019)

Boston Scientific

Country: US
Founded: 1979
Type: Public. Listed on NYSE and a S&P 500 Component
Revenue: $10.8 billion (total, 2019)

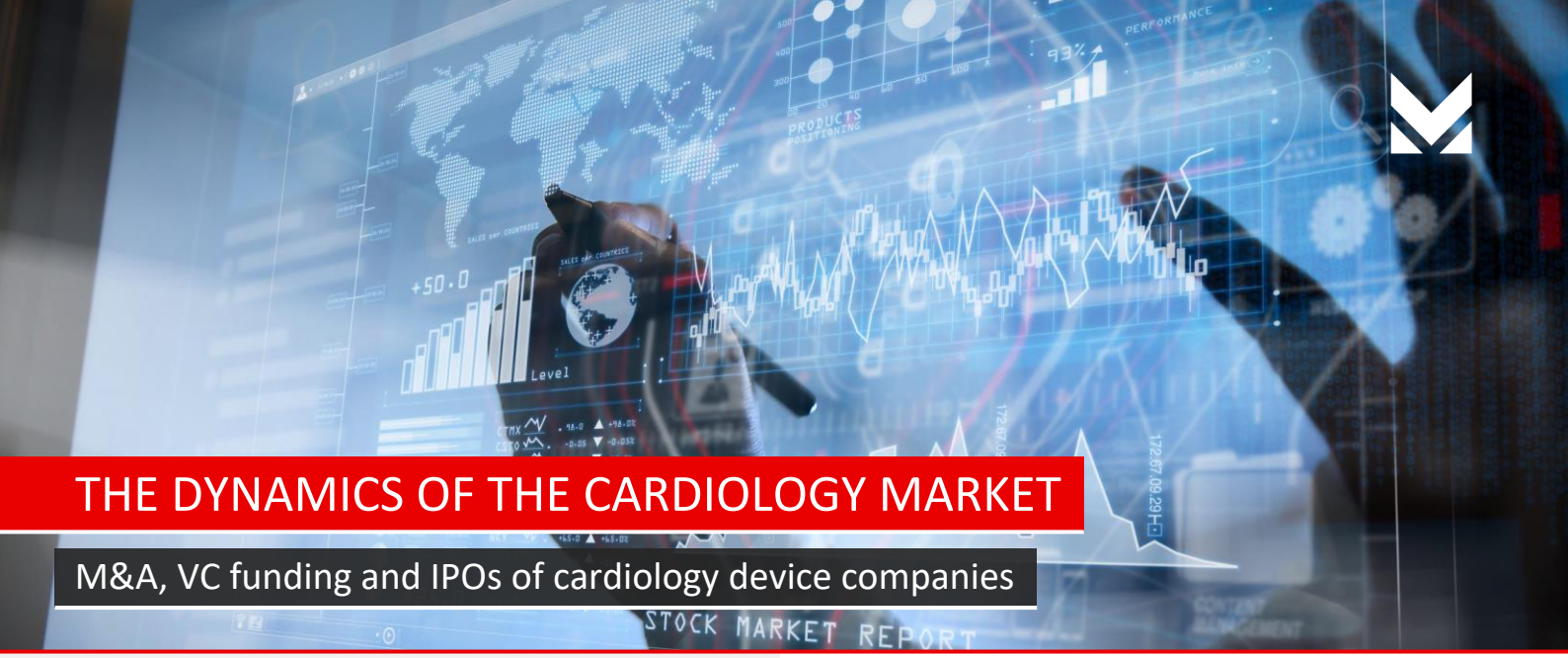
BD

Country: US
Founded: 1897 (as Becton & Dickinson)
Type: Public. Listed on NYSE and a S&P 500 Component
Revenue: $17.3 billion (total, 2019)

Abbott

Country: US
Founded: 1888
Type: Public. Listed on NYSE and a S&P 100 Component
Revenue: $31.9 billion (total, 2019)

Sources: *Mayo Clinic, The Insight Partners, The Business Research Company and the Melior Insights Team*



THE DYNAMICS OF THE CARDIOLOGY MARKET

M&A, VC funding and IPOs of cardiology device companies

The market for cardiovascular devices is a **very active space with many exciting new start-ups**, encouraging innovation and the consolidation of established companies. Product innovations, collaborations, joint ventures, partnerships as well as merger & acquisitions persist in this market. Below, a selection of the most important transactions conducted in recently are outlined. Both the number and the volumes have been affected by the COVID-19 pandemic but are still very encouraging.

Mergers and acquisitions

Miami Instruments | **$17 million** | **JUNE 2019** | LivaNova

Miami Instruments, a company founded in 2007, developing and selling minimally invasive cardiac surgery instruments was sold to LivaNova for $17 million. The transaction included all the patents and assets of the company including its minimally invasive aortic valve and mitral repair technology. Miami Instruments raised $3 million in its 2011 Angel round.

Corindus Vascular Robotics | **$1.1 billion** | **AUG 2019** | SIEMENS Healthineers

Corindus Vascular Robotics, a company founded in 2002, developing and producing a minimally invasive platform for coronary, peripheral and neurovascular procedures was acquired by Siemens Healthineers for $1.1 billion, after raising $25 million in March 2018. Corindus reported earnings of $4.6 million in Q2 2019, which was a +175% growth compared to Q2 2018. Corindus developed the first medical device and software cleared by the FDA to bring robotic precision to percutaneous coronary and vascular procedures.

SentreHeart | **$300 million** | **AUG 2019** | AtriCure

AtriCure, a leading company in the treatment of atrial fibrillation (Afib) and left atrial appendage, acquired SentreHeart, a private company founded in 2005. SentreHeart raised four rounds of VC funding totalling $69 million and is developing a technology for treating persistent and longstanding Afib. The shareholders received $40 million in cash and AtriCure stock, and are entitled to $140 million based on clinical trial results, as well as $120 million based on sales. As of Q2 of 2019, 3,743 left atrial appendage devices were implanted in France, Germany, Italy, Spain and UK – 47.9% being Abbott's Amplatzer Amulet, 42.8% Boston Scientific's Watchman/Watchman Flex and 4.8% being the SentreHeart device, AtriCure's devices having less than 1.7% of the market share.

biovotion | **$ Undisclosed** | **NOV 2019** | biofourmis

Biovotion, developer of a clinical-grade wearable biosensor platform, was acquired by BioFourmis, the financial terms

not being disclosed. Biovotion raised $14.3 million in 2017, and its assets include more than 60 global patents and devices to help monitor the vital indicators of patients with complex chronic conditions such as coronary artery disease and chronic obstructive pulmonary disease (COPD). The company's leading device is capable of measuring 22 parameters in real-time, including heart rate, inter-beat interval, respiratory rate, blood oxygenation, skin temperature, actigraphy, blood pulse wave, motion, energy expenditure, sleep quality and heart rate variability. These devices will allow BioFourmis to leverage its artificial intelligence platform, which has already been clinically validated and approved by the FDA.

MEDlight | $ Undisclosed | AUG 2020 | Rakuten Medical

Medlight, a Swiss producer of catheters and diffusers for optical light delivery, was acquired by the global biotech firm Rakuten Medical, the financial terms were not disclosed. Medlight's technology is used for treating cardiovascular, dermatologic and dental diseases. Medlight served as a contract manufacturer for Rakuten Medical in Germany prior to the acquisition. The company also has a number of cell-targeting investigational therapies in preclinical studies for the treatment of cancer.

Private Equity funding

viz.ai | $50 million | OCT 2019 | Series B

Viz.ai, a company founded in 2016, raised $50 million in its Series B round. The company is developing proprietary artificial intelligence-powered healthcare software and is planning to use the funds to expand its synchronised stroke care. The company's product received FDA De Novo clearance in 2018. More than 300 hospitals across the US use this technology, which applies deep learning algorithms to detect suspected large vessel occlusion in CT scans, which allows specialists to prevent and treat stroke before it occurs. The company raised $10 million in its Seed stage and $21 million in its Series A round in July 2018.

Nightingale | $94.7 million | NOV 2019 | Unknown

Nightingale Health, founded in 2013, a Finish-based blood testing company has announced the opening of a fundraise of $94.7 million, in order to grow its international presence. The company has recently obtained European regulatory approval. Their proprietary technology detects factors not routinely analysed such as inflammation, omega-3 and omega-6 fatty acids and insulin sensitivity, with predictions of disease incidence up to ten years in advance. The blood test results are available on a smartphone app also developed by the company. In January 2019, Nightingale obtained a $23.7 million from the European Investment Bank to accelerate its R&D for chronic disease prevention.

ANACONDA BRAIN | $22.2 million | DEC 2019 | Series B

Anaconda Biomed, a medtech company founded in 2015, develop thrombectomy systems for the treatment of

ischemic stroke, raised $22.2 million in its Series B funding round. This funding will be used for clinical studies, regulatory submissions, product development and scale-up of manufacturing. The company raised another $17 million in 2017 and is continuously working to improve its Advanced Thrombectomy System, consisting of a delivery catheter, a funnel-shaped aspiration catheter and a stent retriever.

IMPULSE DYNAMICS | $80.3 million | DEC 2019 | Series D

Impulse Dynamics, developer of the Optimiser Smart System for delivering Cardiac contractility modulation (CCM) therapy, raised $80.3 million in its Series D financing, the funds will be used to accelerate commercialisation of the company's devices. The technology of the company has already been approved by the FDA and is intended to treat chronic heart failure; it has already been proven that it acts to strengthen the heart.

Emboline | $5 million | JAN 2020 | Series C

Emboline, a company that was started in 2011 with a $60 thousand Series A fund and a subsequent $10 million series B fund raised in 2018, has successfully raised another $5 million in its January 2020 Series C round. The company is planning to use the funds to obtain the CE Mark for its Emboliner embolic protection catheter, to prepare for its commercial launch in Europe and to start a pivotal trial in the US. The devices are designed to be used during transcatheter aortic valve replacement (TAVR) surgeries collecting debris resulting from the procedure. Debris left over from TAVR procedures can cause a range of neurological outcomes, resulting in major stroke (6% chance), overall stroke (22% chance) and cerebral lesions (94% chance). The Emboline device has proven to be five times more efficient than the competition during clinical trials.

Cardiologs | $15 million | JAN 2020 | Series A

Cariologs, a medical technology company founded in 2014, raised its Series A of $15 million. This financing round was led by the VC firm Alven and increased the cumulative amount of funds raised to $25 million in total. The company is planning to use the proceeds to grow its market share in North America and Europe, as well as to extend its applications and to integrate its technology platform. Its artificial intelligence-based platform is designed to analyse more than 100 different cardiac abnormalities by interpreting data from a range of cardiac monitoring devices, and generating a report within minutes. The technology has been approved both in the EU and the US.

JENAVALVE | $50 million | FEB 2020 | Series D

JenaValve, a company founded in 2006, developing and manufacturing a proprietary Pericardial Transcatheter Aortic Valve Replacement (TAVR) System treating aortic valve disease, raised $50 million from a series of equity financing led by Bain Capital Life Sciences. The company raised $4.5 million in October 2006 (Series A), $22.5 million in June 2010 (Series B), split its Series C across 3 fundraises in July 2013 ($62.5 million), April 2014 ($10 million) and August 2015 ($26.5 million), and in August 2016 the company raised another $10 million, while in February 2018 it raised $4.9 million in debt financing. JenaValve has submitted applications for FDA Premarket Approval and the CE mark for the conditions of aortic stenosis and aortic regurgitation.

Heartbeat | $8.2 million | MAR 2020 | Series A

Heartbeat Health, a company founded in 2017, developing a digital cardiology platform has raised $8.2 million in its

Series A round. Heartbeat is using digital tools to aggregate heart data and provide care management to patients. The funds will be used to expand the use of the app beyond New York. The company is competing with tech giants like Apple, with its Apple Watch, as well as Fitbit and Withings.

ARTIRIA Neurovascular solutions

$3.3 million

JULY 2020

Series A

ARTIRIA Medical, a company founded in 2019, aiming to improve stroke treatments raised $3.3 million in its Series A round. There are 13 million people every year that suffer a stroke, which often also results in severe disabilities and even death. The company have developed a guidewire that facilitates micromotion interventions deep in the brain arteries towards cerebral lesions and offers a superior stroke treatment. The funds will be used to advance clinical trials and its regulatory work.

Initial Public Offerings

ACUTUS™ MEDICAL

$158.8 million

AUG 2020

NASDAQ: AFIB

Acutus Medical, a company founded in 2011, developing heart mapping technology for treating arrhythmia, launched its IPO raising $158.8 million at a valuation of $469.9 million. The funds will be used to expand its commercial efforts and complete clinical testing of its heart-mapping catheters. The company has raised over $235 million in equity funding and $72.5 million in debt financing since inception:

- **Aug 2011** – Seed - $1 million
- **Sep 2011** – Series A – $5.5 million
- **Aug 2012** – Debt – $2.5 million
- **Aug 2013** – Series B – $54.2 million
- **Mar 2016** – Series C - $75 million
- **Jun 2019** – Debt - $70 million
- **Jun 2019** – Series D - $100 million

The company recently received FDA clearance for its real-time, 3D heart-mapping algorithm, intended to help electrophysiologists diagnose and treat both constant and transient arrhythmias.

Sources: *Fierce Biotech, AtriCure, Rakuten Medical, Medical Device Network, Miami Instruments, BusinessWire, Cardiology 2.0, Mass Device, Cardiologs, Anaconda Biomed, Impulse Dynamics, Nightingale Health, Viz.ai, StartUpTicker, Acutus Medical and the Melior Insights Team*

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PIONEERING LIFE SCIENCE INVESTMENT

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