Cardiovascular disease and effective treatments: The SYNERGY™ coronary stent system

1. **Cardiovascular disease (CVD) –** leading cause of mortality worldwide
   - CVDs are the leading cause of death globally. In 2012, an estimated 17.5 million people died from CVDs, representing about 31% of all global deaths.[1]
   - More people die each year from CVDs than from other causes such as different types of cancer (8.2 million), respiratory diseases (4 million), or diabetes (1.5 million).[2]
   - It is expected that the number of people who die from CVDs, mainly from heart disease and stroke, will reach up to 22.2 million by 2030[3], remaining the single leading cause of death worldwide.
   - Early symptoms of heart disease may include fatigue, pain, and dizziness. Symptoms may be similar to those associated with angina: a squeezing, suffocating or burning feeling in the chest that may extend to the arm, neck, back, throat, or jaw. Women are more likely to experience atypical symptoms such as vague chest discomfort.[4]

2. **Coronary artery disease (CAD) –** obstruction of coronary artery and restriction of blood flow to the heart
   - Coronary artery disease (CAD), also known as ischemic heart disease (IHD), is the most common form of CVD. Of all deaths caused by CVDs, an estimated 7.4 million are due to CAD.[1]
   - CAD affects the blood vessels supplying the heart muscle and is caused by atherosclerosis, the narrowing (stenosis) and/or blockage of the blood vessels that supply the heart. It is the leading cause of heart attack and angina.[5]
   - Risk factors of heart disease include unhealthy diet, physical inactivity, tobacco use and alcohol abuse. The negative effects of these lifestyle-associated risk factors may show up in individuals as high blood pressure, raised blood glucose levels, increased blood lipids, overweight and obesity.[1]
   - People with diabetes are twice as likely to have heart disease or a stroke, which typically occurs at a younger age than in patients who do not have diabetes. In addition, myocardial infarction in people with diabetes is more likely to be fatal. Furthermore, persistent elevated blood glucose can result in an increase in fatty deposits that may affect blood flow, thereby increasing the risk of developing atherosclerosis and thus CAD.[6]

3. **Coronary intervention –** stent treatment for blocked vessels
   - Most cardiovascular diseases can be prevented by addressing the risk factors mentioned above and treating high blood pressure, diabetes, or dyslipidaemia. When preventive measures fail and are insufficient to treat existing disease, CVDs may require treatments such as medications or surgery.
   - One main interventional method is coronary artery stenting, which involves the use of stents. Sometimes it is also referred to as balloon angioplasty.
   - During this procedure, a catheter is inserted into a blood vessel and threaded into the narrowed coronary artery of the heart. Once in place, a balloon tip attached to a stent is inflated.

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- The balloon compresses the plaque and expands the stent. Once the plaque is compressed and the stent is in place, the balloon is deflated and withdrawn. The stent remains in the artery, holding it open.

4. **Drug-eluting stents –** devices improving clinical outcomes for people with CAD and many other heart diseases
   - By keeping the artery open, stents restore normal blood flow to narrowed or blocked arteries. Over time, the artery wall heals around the stent but excess healing tissue can narrow the vessel once again, in a process called restenosis.[7]
   - Drug-eluting stents (DES) were designed to limit the growth of healing tissue, thus reducing the likelihood of stent restenosis. It was shown that the elution of drugs from a stent can result in high local concentrations of the drug, directly at the target lesion – annular or arciform areas of pathological or traumatic discontinuity of tissue or its partial function loss, with minimal systemic side effects.[8]
   - DES are metal stents coated with a drug/polymer mix in which the drug is temporarily held in place by a polymer that has been 'painted' onto the stent. The drug is then delivered directly into the surrounding tissues.
   - Recent developments in DES technology are improving on the deliverability, strength, and fracture resistance of current stents, while novel DES have the additional potential to reduce the impact of polymer exposure and thereby potentially improve clinical outcomes for patients with CAD and other forms of heart diseases.

5. **SYNERGY™ –** designed for treating complex patients and lesions
   - The SYNERGY™ everolimus-eluting coronary stent system is a DES featuring the ultrathin Synchrony™ bioabsorbable polymer/drug coating, which is applied to the abluminal (outer) surface of the stent. It is designed to absorb and elute in a synchronised manner over the course of about three months.[9,10]
   - SYNERGY™ is indicated for improving coronary luminal diameter in patients with symptomatic ischemic heart disease, including patients with acute myocardial infarction and patients with concomitant diabetes mellitus due to discrete de novo native coronary artery lesions. In addition, it is also indicated for treatment of patients presenting with acute coronary syndrome, bifurcation lesions, chronic total occlusion, in-stent restenosis, left main stenting, multi-vessel disease, ostial lesion stenting, renal failure, saphenous vein grafts, and unstable angina.
   - The specific attributes of the SYNERGY™ stent synergistically work together to promote optimal healing within the vessel:[9] Its polymer dissipates when it is no longer needed, shortly after the drug is completely eluted at three months. This provides the potential to optimise early vessel healing while also eliminating long-term polymer exposure[9,10], a possible cause of late adverse events including stent thrombosis.
   - SYNERGY™ also features an evolved platinum chromium (PtCr) alloy stent design, which demonstrates exceptional strength and deliverability while maintaining visibility and flexibility to naturally conform to the vessel wall, with exceptional fracture resistance.

6. **SYNERGY™ stent clinical programme –** addressing cardiovascular disease complexity
    - Boston Scientific established a robust clinical trial programme and is supporting investigator-sponsored research (ISR)[11] studying the SYNERGY™ stent system in different patient populations.
    - The SYNERGY™ stent clinical trial programme involves multiple trials designed for regulatory approval, label expansion and includes a broad range of patient populations including diabetes mellitus:
        - **EVOLVE**: the first human use, prospective, randomised, single-blind study evaluating the non-inferiority of the SYNERGY™ stent versus Boston Scientific's PROMUS Element™ Plus DES system which utilises a durable polymer coating applied to the entire stent (inner and outer) surface. EVOLVE is the first in a continuing cadence of clinical trials evaluating the performance of the SYNERGY™ stent in a range of patients.
        - **EVOLVE II**: a global, multi-centre, randomised, single-blind, non-inferiority pivotal IDE (Pre-market **I**nvestigational **D**evice **E**xemption) trial designed to evaluate the performance of the SYNERGY™ stent system versus the PROMUS Element™ Plus DES System with regard to one-year rate of target lesion failure (TLF) as the chosen primary endpoint in patients showing both clinical and angiographic complexity. The trial also includes a non-randomised, single-arm diabetes study (EVOLVE II Diabetes Substudy). It pooled patients with diabetes randomised to the SYNERGY™ arm in the EVOLVE II pivotal trial with patients enrolled in the non-randomised single-arm diabetes study as pre-specified in the study protocol.

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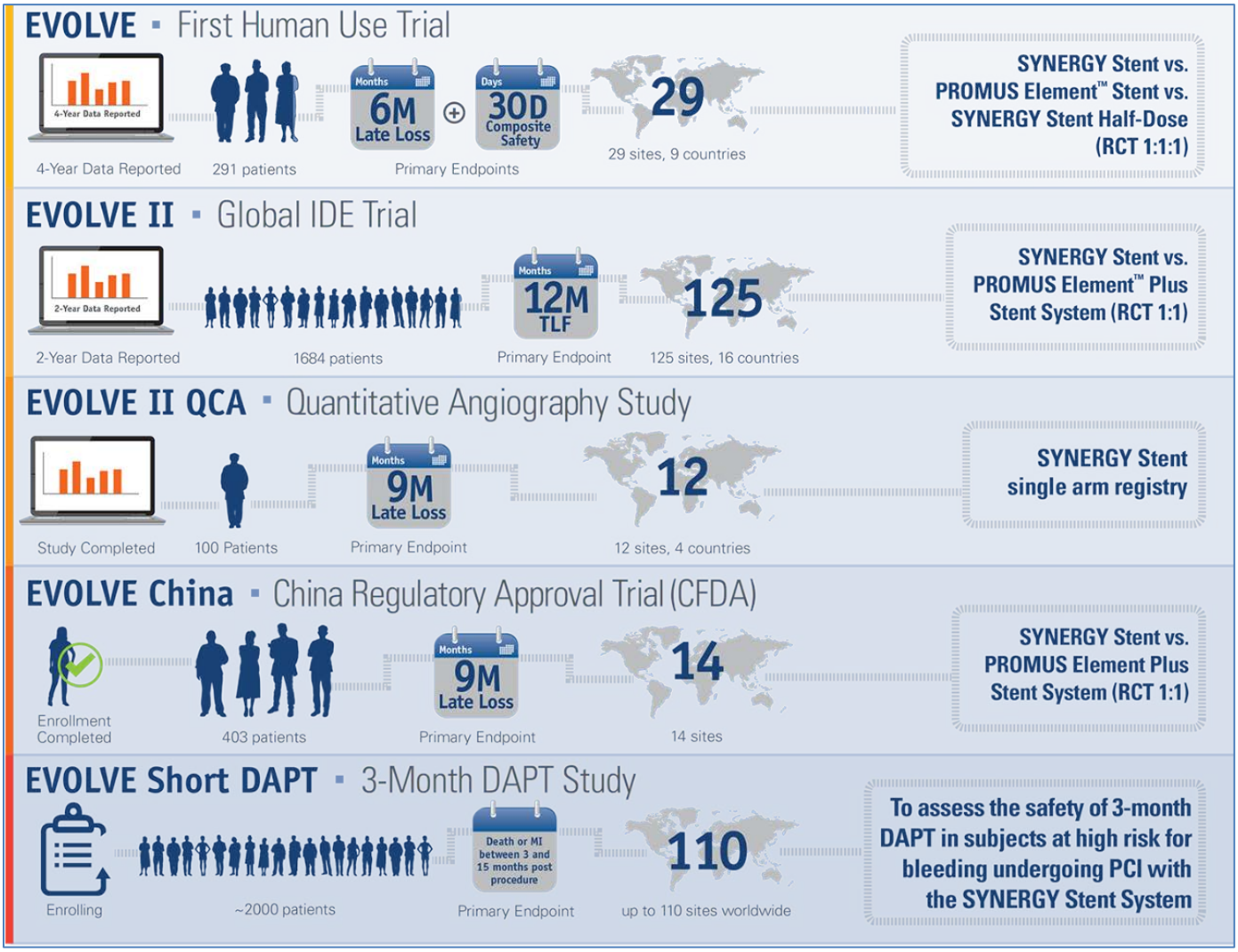
Figure 1: SYNERGY™ stent clinical programme at a glance



For more information about SYNERGY™, coronary artery disease or Boston Scientific in cardiology, please visit our newsroom.

About Boston Scientific

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References

[1] World Health Organisation (WHO). Cardiovascular diseases. Fact sheet N 317. Updated January 2015. http://www.who.int/mediacentre/factsheets/fs317/en Last accessed May 8, 2016.
[2] World Health Organisation (WHO). Noncommunicable disease fact sheet. Updated January 2015. http://www.who.int/mediacentre/factsheets/fs355/en Last accessed May 8, 2016.
[3] World Health Organisation (WHO). Global status report on noncommunicable diseases 2014. Geneva. http://apps.who.int/iris/bitstream/10665/148114/1/9789241564854_eng.pdf?ua=1 Last accessed May 8, 2016.
[4] Heart and Stroke Foundation, http://www.heartandstroke.com/site/c.ikIQLcMWJtE/b.3484067/k.6657/Heart_disease__What_is_coronary_artery_disease.htm#symptoms Last accessed May 8, 2016.
[5] World Heart Federation (WHF). Different Heart Diseases. http://www.world-heart-federation.org/cardiovascular-health/heart-disease/different-heart-diseases Last accessed May 8, 2016.
[6] National Diabetes Information Clearinghouse (NDIC). A service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH). http://diabetes.niddk.nih.gov/dm/pubs/stroke/#connection Last accessed May 8, 2016.
[7] Grech ED. ABC of Interventional Cardiology: Percutaneous Coronary Intervention II: the Procedure. BMJ 2003;326–73.
[8] Regar E, Sianos G and Serruys PW. Stent development and local drug delivery. Br Med Bull 2001;59(1):227-248.
[9] Eppihimer M. Impact of polymer type and location on stent thrombogenicity and endothelial cell coverage. EuroIntervention, EuroPCR 2013, Abstract 341. http://www.pcronline.com/eurointervention/Abstracts2013_issue/europcr-abstracts-2013/341/impact-of-polymer-type-and-location-on-stent-thrombogenicity-and-endothelial-cell-coverage.html Last accessed May 8, 2016.
[10] Chen Y-L, Foss A, Eppihimer M, et al. Characterisation of in vivo poly(DL-lactic-co-glycolic acid) bioabsorption from a drug-eluting stent. EuroIntervention 2012;8(Suppl N):N043.
[11] Boston Scientific is not responsible for the collection, analysis or reporting of the investigator-sponsored research output which is the sole responsibility of the investigators. Boston Scientific's involvement in investigator-sponsored research is limited to providing financial support for research that advances medical and scientific knowledge about our products.