US AND EUROPEAN MARKETS FOR JOINT ARTHROPLASTY PRODUCTS

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EXECUTIVE SUMMARY

The US and European joint arthroplasty product market includes implants for both large joints and extremities including hips, knees, shoulders, elbows, and ankles. Driven by aging populations, improvements in surgical and pain management techniques and moderate incremental innovations, the global market for joint arthroplasty implants was valued at over $15.4 billion in 2015.

The market for hip arthroplasty products in the US and Europe includes implants for primary total hip (cemented, cementless and hybrid hips), partial hip, hip resurfacing and revision hip arthroplasties. Over 570,000 hip arthroplasty procedures (including revision surgeries) were performed in the US in 2015. Recent advances in anesthesia, pain and nausea control are helping facilitate outpatient hip replacement surgeries in the US. The increased use of multi-modal pain control programs is playing a significant role in shifting total joint replacements to outpatient settings. The need for faster recovery, lesser post-operative pain and cost-effective procedures is driving the demand for minimally invasive hip replacements. There has been a moderate increase in the number of direct anterior approach hip arthroplasties in recent years. Market growth is being restrained by cost-cutting measures as well as the regulatory environment including the need for premarket approval as mandated by the US Food and Drug Administration (FDA) for sales of metal-on-metal hips. A shortage of orthopedic surgeons as well as a lack of significant expertise in certain procedures is further impeding market growth.

Over 834,000 knee arthroplasty procedures were conducted in the US in 2015. The aging population and increased incidence of osteoarthritis have been causing the number of joint arthroplasty procedures in the US to grow. In 2014, Medicare paid for more than 400,000 hip and knee replacements, at a cost of $7 billion to taxpayers for the hospitalizations alone. In late 2015, the Centers for Medicare & Medicaid Services announced its plans to commence a new program that would hold hospitals responsible for additional spending incurred during joint replacement procedures. The increasing awareness of overall accuracy and precision placement of implants in robotic knee replacements has been a key trend impacting the sales of knee implants in recent years. With robotic surgeries reducing the dependence of procedural outcomes on the expertise of surgeons, the long-term outcomes of knee...
replacements are likely to increase. However, the increased rates of revision knee procedures are likely to continue to augment the financial burden across the US and Europe. This has consequently given rise to a section of consumers demanding warranties on knee implants. Driven by the increased incidence of osteoarthritis within the aging population, the market for knee implants is expected to grow at a compound annual growth rate (CAGR) of 4.4% from 2015 to 2020.

Shoulder arthroplasty continues to be one of the fastest growing joint replacement procedures in the US and Europe. Over 56,000 shoulder arthroplasties were performed in Europe in 2015. Shoulder resurfacing procedures have benefitted from significant improvements in implant technologies over the years. New-generation implants have demonstrated improved clinical outcomes including reduced complication rates as well as reduced rates of revision due to implant loosening. In the coming years, higher awareness and the clinical benefits of stemless shoulders may help to increase shoulder arthroplasty volumes. The market for reverse shoulder arthroplasty is also being driven by the use of trabecular metal implants. While challenges such as high revision rates and the need for training remain, the global market for shoulder arthroplasty implants is likely to continue growing at a CAGR of 7.2% from 2015 to 2020.

Performed in selected incapacitating elbow diseases, elbow arthroplasty is a less common procedure as compared to other joint arthroplasties. About 21,000 elbow arthroplasties (including radial head arthroplasty) were performed in the US in 2015. Following clinical studies to establish better clinical outcomes between linked and unlinked elbow arthroplasty implants, a new generation of convertible or modern implants has been launched. With the introduction of next-generation semi-constrained linked, unlinked and convertible implants, the survival rate of different types of total elbow arthroplasty has improved. The market for elbow implants is also benefitting from the increased indications for the surgery. Despite permanent restrictions over strenuous activities, advancements in surgical techniques and prosthetic design have made the procedure suitable for younger patients. The market for elbow implants in Europe is expected to grow at a CAGR of 4.5% from 2015 to 2020.
Significant improvements in implant technology and the subsequent commercial launch of ankle implants are driving the market for ankle arthroplasties in the US and Europe. With increased adoption of three-part, mobile-bearing, uncemented ankle implants, the market for ankle arthroplasty products is likely to demonstrate significant growth opportunities. However two-part ankle implants are likely to lose market share. Apart from the introduction of three-part mobile-bearing third generation ankle implants, the market for ankle implants is likely to be benefitted by the acceptance of total ankle replacement in hemophilic ankle osteoarthritis. However, the high complication rates associated with total ankle arthroplasty and a limited center of excellence for the procedure are likely to impede short-term growth in procedural volume. The market for ankle arthroplasty products is likely to grow at a CAGR of 10.2% from 2015 to 2020 in the US.

### Methodology

Primary and secondary research methodologies were employed to understand the overall market dynamics, product segments and clinical applications of technologies and products discussed in the report. Multiple qualitative and quantitative techniques were used to develop the market segment forecasts for this report, allowing estimates to be cross-checked to ensure accuracy.

Secondary Research: Over 20 manufacturers of joint implants were analyzed to create the market analysis for the US and Europe. While several market participants in the joint arthroplasty market are private organizations, the data for the leading publicly listed firms were obtained by thoroughly analyzing Security and Exchange Commission filings, annual reports, websites, industry directories, industry magazines and catalogs, government sources and other public sources.

The procedural volume for various joint arthroplasties was derived based on data published by various national and regional joint arthroplasty registries. Numerous secondary sources for statistical and technological information were used in this report, including organizations such as the Centers for Disease Control and Prevention, the National Institutes of Health, the U.S. FDA, and publications in the scientific and trade literature.
The report was further fortified by utilizing content from leading proprietary medical technology/healthcare intelligence services. Informa Pharma Intelligence products: Meddevicetracker: [www.meddevicetracker.com](http://www.meddevicetracker.com)
Biomedtracker: [www.biomedtracker.com/](http://www.biomedtracker.com/)
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Medtrack: [www.medtrack.com/](http://www.medtrack.com/)
Strategic Transactions: [www.pharmamedtechbi.com/deals](http://www.pharmamedtechbi.com/deals)

Primary Research: Prices used in projections of market revenues are average prices paid by the end-user of the products and are derived via supplier and user quotations or estimates based on typical industry discounts from list prices. The average selling price of various implants gathered using hospital quotations and other secondary data sources were validated through interviews with hospital purchase departments and various stakeholders on the supply side including national product managers, sales managers, marketing managers etc. Data concerning unit shipments, market values, growth rates, and market share were incorporated into Meddevicetracker forecasting and market share analysis models, which were used to derive market estimates for future years.
1. BONE AND JOINT DISEASE OVERVIEW

1.1 Osteoporosis

Osteoporosis (OP) is a degenerative disease caused by decreased bone mass that leads to weak and fragile bones. As a consequence, most patients with osteoporosis have increased incidence of pathological fractures. Prior to full-fledged onset of OP, osteopenia could manifest. As a milder form of OP, bone density is typically lower in osteopenia as compared to normal peak density but not low enough to be classified as OP. While osteopenia can be a physiological issue that develops with advancing age, OP is always pathological. Caucasian and Asian women are observed to be at a greater risk of both these conditions.

Osteoporosis is common in postmenopausal women suggesting female sex hormones play a role in its genesis. Other etiological factors include cigarette smoking and alcohol consumption, sedentary lifestyle, and intake of anti-seizure and chemotherapeutic drugs. OP typically manifests in its late stages as chronic back pain due to prolapsed disc, stooped posture and increased incidence of pathological fractures. Osteoporotic fractures occur most commonly in the hip, wrist or spine. The gold standard test for the diagnosis of OP is a dual-energy X-ray absorptiometry scan, wherein the patient lies supine on a padded surface and a scanner passes over the entire body. The patient is diagnosed with OP when the bone mineral density is less than or equal to 2.5 standard deviation (National Institute of Arthritis and Musculoskeletal Diseases, 2014). Other tests include radiological tests such as X-ray, magnetic resonance imaging (MRI), computed tomography, and ultrasound. Presence of biomarkers such as enzyme cathepsin-K is also considered suggestive of OP.

Preventive measures include lifestyle modifications such as cessation of smoking, consumption of alcohol and bone loading exercises. Supplementation of the diet with vitamin D, vitamin K, and calcium has also been shown to be beneficial. Bisphosphonates are the most common medical therapies engaged for this condition.

In long standing and debilitating cases of OP wherein lifestyle modifications and medical therapy provide no relief, eventually leading to increased incidence of
fractures, joint arthroplasty is indicated. With joint reconstruction surgeries, pain relief, better mobility, and improved movement have been observed.

1.2 Osteoarthritis

Osteoarthritis (OA) is a degenerative disease that occurs when the cartilage or the cushion between the joints breaks down and is the most common form of arthritis. Purported to be more common in women over 45 years of age and in men aged below 45 years, OA reportedly represents over 2% of the years lived with disability (March, et al., 2014). The incidence of OA equalizes among both sexes with increasing age.

OA can be divided into two types: primary and secondary. While primary OA is typically attributed to aging, secondary OA occurs as a result of another underlying condition or disease. In primary OA, the water content of cartilage is known to increase, thereby degenerating its protein framework. With prolonged weight bearing and wear and tear of the joints, the cartilage degenerates, eventually leading to total loss of cushioning between the bones. This further leads to a reduced joint space and increased friction between the articular surfaces in contact.

While the exact causes of OA remain unknown, several factors play an important role in its development. In the case of genetic causes, the occurrence of the disease is attributed to a defect in the genes that leads to deficient formation of collagen, a protein that contributes to the formation of the articular cartilage. Several other genetic abruptions may lead to other defects such as misalignment of the bones in the joint capsule with the result that the cartilage wears faster than usual. Such patients present with the disease at a much earlier age. Obesity or higher body mass index (BMI) may also act as a triggering factor for the disease as it aids in faster destruction of the cartilage around the joints. Moreover, studies have shown that excess fat tissues produce cytokines that can damage the joints.

Injury and overuse of the joint may hasten the disease process causing repetitive trauma and increased wear and tear of the articular cartilage. Sometimes OA develops in joints that have been previously damaged by debilitating diseases such as rheumatoid arthritis and gout. Other causes include metabolic diseases such as hemochromatosis, diabetes and Wilson’s disease, as well as inflammatory diseases such as Lyme disease and Perthes disease.
OA presents itself as burning sensation and stiffness in the joints. Along with pain in the muscles and tendons, muscle spasms are also a common complaint. In chronic cases, muscle atrophy may also occur. Furthermore, in smaller joints such as fingers, patients may present with hard bony enlargements called Heberden’s nodes in distal interphalangeal joints and Bouchard’s nodes in the proximal ones.

OA is typically diagnosed with a physical examination of the symptoms presented. Diagnostic procedures and investigations required to confirm the disease typically include radiological investigations such as X-ray analysis of the joints. Typical findings include reduced joint space, osteophytes, spurs, subchondral sclerosis, and subchondral cyst formation. MRI has also been proven to be of significant value in diagnosing OA. In addition, joint aspiration—where the synovial fluid is withdrawn and examined for evidence of crystals or joint deterioration—may be performed.

Management options for OA include lifestyle, medical and surgical interventions. Under lifestyle modifications, physical activity is encouraged. Moderate exercises strengthen muscles around the joints and improve joint flexibility. This further reduces the burden, pain, and stiffness. Under medical interventions, acetaminophen is the first line of treatment for OA. In addition, joint injections of glucocorticoids such as hydrocortisone along with hyaluronic acid injections may also be advocated. Potent anti-inflammatory drugs such as corticosteroids may be prescribed either for oral or intra-articular use. When the pain is relatively tolerable, less potent nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen or paracetamol may be prescribed.

Surgical management of OA includes joint arthroplasty or joint replacement surgery. This treatment modality has been proven to provide clinical as well as monetary benefits. It is an orthopedic surgical procedure in which the articular surface of a musculoskeletal joint is replaced, remodeled, or realigned. In this process, the bones may be either resurfaced or an artificial joint called a prosthesis may also be used.

1.3 Rheumatoid Arthritis

Rheumatoid arthritis (RA) is an autoimmune disease where antibodies start acting against the body’s own cells and tissues, primarily the joints. Characterized by symmetrical joint swelling, it mostly affects the joints of the hands, feet, wrists, elbows, knees, and ankles. Typical symptoms of RA include warm, swollen and
painful joints owing to the inflammation of the joint capsule, further damaging the articular cartilage and the underlying bone. It is a systemic disease, so other organs such as the lungs and heart may also get impacted along with the joints. The disease mostly occurs between the ages of 30 and 60 years and has a slightly higher predisposition among females. However, above 60 years of age, the incidence of RA is found to rise among men.

With rheumatoid nodules being pathognomonic to the disease, RA is attributed to genetic, infectious, and environmental factors. Occurrence of RA is found to be five-fold higher in people with human leukocyte antigen alleles as genetic markers. Exposure to infectious agents such as Epstein-Barr virus, parvovirus, proteus and mycoplasma has been reported to increase the incidence of the disease. Female hormones such as estrogen and progesterone are associated with decreased risk. Consequently, a low incidence is observed among pregnant women and a higher incidence is seen in the post partum period.

Diagnosis of the disease most commonly includes blood tests to check inflammation levels and to identify the antibodies linked with RA such as rheumatoid factor and anti-cyclic citrullinated peptide. In the line of further investigations, detailed X-ray, ultrasound, and MRI scans are indicated.

Treatment includes:

- NSAIDs such as ibuprofen, ketoprofen, or celecoxib (beneficial to patients who are more prone to somach ulcers) which control inflammation
- disease suppression treatment in the form of corticosteroids like prednisone or prednisolone
- disease-modifying antirheumatic drugs such as methotrexate or sulfasalazine, and
- Januse kinase inhibitors or biologics.

In the case of long-standing disease where medical treatment fails to provide relief, joint arthroplasty may be indicated. Such surgeries provide relief from pain and restore function in joints badly damaged by the disease. After arthroplasty, the patient is required to stay in the hospital for a certain period; this is then followed by rehabilitation which may take weeks or months. Unlike surgeries undertaken for
other forms of arthritis - joint replacement surgeries in RA do not cure the disease - they only provide relief by reducing pain and the level of deformity caused by RA.

1.4 Perthes Disease

Marked by deficient blood supply to the head of the femur, Legg-Calvé-Perthes disease is a rare childhood disorder that impacts the hip. As a temporary phenomenon, the disease develops progressively over the years and eventually heals by itself. Although over a period of time, the blood supply is restored and the femoral head begins to grow back, the hip joint may gradually become weak due to initially compromised blood flow to the femoral head. This condition is commonly observed in young children age 5 to 10 years. Incidence of this rare condition may range from 0.4 per 100,000 to 29 per 100,000 children under 15 years of age (Loder RT., Skopelja EN, 2011).

Although the cause of the disease is unknown, synovitis leading to avascularization of the femoral head has been reported to be one of the predominant factors. Other risk factors include:

- age—more common in children aged 4—8 years
- gender—five times more common in boys than in girls
- race—common in Caucasians, and
- genetic factors—presence of a positive family history increases the chances of the child developing the disease.

The child typically presents with pain in the hip often radiating to the knee. In most cases knee pain is the first symptom. Along with wasting of the muscles in the upper thigh, the child may also present with shortening of the leg and stiffness of the hip, which may restrict movement and cause problems with gait. Upon radiological examination including X-ray, MRI, and ultrasound, hip joint space is observed to be wider due to progressive necrosis. In addition, a bone scan may also show decreased uptake by the femoral head.

Treatment of the disease aims to maintain the spherical structure of the femoral head. This may be achieved either by conservative methods, such as plaster or splint, or by surgical intervention. In a child under six years of age, conservative methods of treatment such as stretching, swimming and running have been reported
to provide excellent results. Traction and rest for pain relief, casts to keep the femoral head in position, and crutches to avoid weight bearing may also be recommended.

Surgical treatment includes contracture release, joint realignment, removal of excess bone or loose bodies and joint arthroplasty.

1.5 Developmental Dysplasia of the Hip

Developmental dysplasia of the hip (DDH) occurs before, during or shortly after birth and is six times more common in girls than in boys. Etiological factors involved in the development of DDH include hereditary predisposition to joint laxity, the influence of maternal ligament-relaxing hormone relaxin and mal-presentations during birth such as breech. The child typically presents with a peculiar gait, asymmetric groin creases and a clicking noise while walking. In a majority of children, the dislocated hip is brought to light only when the child starts walking.

Diagnosis of the abnormality is typically made with physical examination alone which includes tests such as the Barlow and Ortolani test. Radiological examination using detailed X-ray and ultrasound may also be performed.

A treatment plan for DDH entails reduction of the femoral head either manually which is then maintained through plasters and casts or using minor surgeries. In cases where reduction cannot be achieved, acetabular reconstruction procedures are undertaken. In children over 11 years old, total hip replacement is the only resort.

1.6 Rotator Cuff Tear

The rotator cuff is a sheath of tendons and ligaments that plays a pivotal role in maintaining stability of the shoulder joint. Comprised of the humeral head and glenoid cavity, only one-third of the glenoid cavity is in touch with the humeral head making the shoulder joint highly unstable. Thus the rotator cuff muscles—supraspinatus, infraspinatus, teres minor, and subscapularis—provide support to the joint making it sturdy. Rotator cuff tear (RCT) occurs as a result of trauma to one or more tendons involved in the formation of the rotator cuff. The tear of the supraspinatus is reported to be the most common.
Apart from trauma and progressive degeneration with age, the tendon muscles may be injured due to chronic irritation or over use. RCT is most commonly seen in physically active people. In the case of trauma, a fall on the outstretched arm could be a precipitating factor.

Patients typically present themselves with shoulder pain, limitation of movement, and an inability to perform day-to-day activities. Diagnosis of RCT is best made by MRI, which aids in differentiating complete tears from partial tears. An ultrasound and arthrogram may also be performed. Treatment modalities typically include both prevention and management. RCT can be prevented through regular shoulder exercises, abstaining from any physical work during episodes of shoulder pain and the application of ice packs on the painful shoulder joint. Treatment entails medical therapy which that aims to relieve pain through oral or topical NSAIDs, ice packs or in severe cases, subacromial corticosteroid injections. Surgical intervention such as joint arthroplasty may be deemed necessary especially in long standing cases where extensive arthritis has developed.

1.7 Traumatic Arthritis

When trauma in the form of fractures, cartilage injury, or meniscal tear leads to OA, the disease entity is termed traumatic arthritis. Traumatic arthritis occurs as a result of injury to the articular cartilage which leads to swelling, pain, and limitation of movement. The articular cartilage is a cartilaginous tissue that lines the surface of the bones involved in the formation of joints, preventing friction between the bones and assisting with movement. Since the blood supply to the articular cartilage is very scarce, any injury to the articular cartilage takes a much longer time to heal.

The causes of traumatic arthritis include sports injuries, fractures, car accidents, blunt force trauma, fall, or overuse. The patient presents with signs of inflammation such as swelling, pain, redness, and limitation of function. Diagnosis typically includes physical examination, and radiological examination such as X-ray, ultrasound, and MRI. Blood tests may also be indicated to confirm inflammatory mediators like cytokines. Lifestyle modifications including weight control and mild exercises are typically advocated and pain relief through NSAIDs or steroids may be administered. Surgical treatment includes joint reconstruction, joint replacement, or removal of the damaged cartilage.
1.8 Failed Previous Joint Replacement Surgery

A joint replacement surgery is said to have failed when the outcome does not match the expectations of either the patient or the doctor. Subsequent corrective surgery is termed as revision surgery. Since the prevalence of ailments that which require joint arthroplasties is on the rise, the frequency of failure following surgery has also increased.

The primary reasons that may lead to joint replacement failure include wear and tear, loosening of the implant, infection at the surgical site, fracture instability, and stiffness. Revision total knee replacement surgery is a complex surgical procedure that requires extensive pre-operative planning, specialized implants and tools, prolonged operation times and mastery of different surgical techniques. It includes three stages: the pre-operative stage, which includes assessment and patient preparation; the operative stage; and the post-operative stage, which includes monitoring the patient’s parameters and rehabilitation. Pain, fever, and limitation of movement are the most common warning signs suggestive of failed replacement surgery.

1.9 Epidemiology of Arthritis

Exhibit 1-1 presents the estimated prevalence of symptomatic knee OA in patients over 45 years for select countries for the years 2015–20; Exhibit 1-2 presents the estimated prevalence of symptomatic hip OA in patients over 45 years of age for select countries for the years 2015–20; Exhibit 1-3 presents the estimated prevalence of RA in patients over 45 years of age for select countries for the years 2015–2020.

1.10 Developments in Biomaterials for Joint Arthroplasty Implants

With both demand for orthopedic implants and long-term survival rates increasing, there have been continuous incremental technological advances in implant biomaterials. Broadly, efforts have been focused on developing novel bulk biomaterials and novel formulations of existing but sparsely used biomaterials. In addition, there is a growing focus on customizing the material properties of bioabsorbables and composite materials with fillers such as bioactive ceramics. A large proportion of the research on biomaterials also includes improvements to coatings in order to supplement the function of existing implants, with the goal of
## Exhibit 1-1: Estimated Prevalence of Symptomatic Knee Osteoarthritis in Patients Over 45 Years of Age, Select Countries, 2015–20

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>France</td>
<td>2,741</td>
<td>2,774</td>
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<td>2,847</td>
<td>2,886</td>
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<td>4,116</td>
<td>4,156</td>
<td>4,193</td>
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</tr>
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<td>5,613</td>
<td>5,679</td>
<td>5,742</td>
<td>5,803</td>
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</tr>
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<td>Spain</td>
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<td>3,880</td>
<td>3,953</td>
<td>4,032</td>
<td>4,116</td>
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</tr>
<tr>
<td>United Kingdom</td>
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<td>2,618</td>
<td>2,656</td>
<td>2,695</td>
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<td>2,774</td>
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<tr>
<td>United States</td>
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<td>22,684</td>
<td>23,115</td>
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<tr>
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<td><strong>41,261</strong></td>
<td><strong>41,937</strong></td>
<td><strong>42,624</strong></td>
<td><strong>43,314</strong></td>
<td><strong>44,010</strong></td>
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</tbody>
</table>

**Note:** Prevalent cases reported in thousands.
Exhibit 1-1: (Continued)

Source: Datamonitor Healthcare
### Exhibit 1-2: Estimated Prevalence of Symptomatic Hip Osteoarthritis in Patients Over 45 Years of Age, Select Countries, 2015–20

<table>
<thead>
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<tr>
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<td>1,204</td>
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<tr>
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<td>1,806</td>
<td>1,827</td>
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<td>1,696</td>
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</tr>
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<tr>
<td><strong>Total prevalence</strong></td>
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<td><strong>20,310</strong></td>
<td><strong>20,626</strong></td>
<td><strong>20,946</strong></td>
<td><strong>21,268</strong></td>
<td><strong>21,589</strong></td>
<td><strong>1.5%</strong></td>
</tr>
</tbody>
</table>

Note: Prevalent cases reported in thousands.

(Continued)
Exhibit 1-2: (Continued)

Source: Datamonitor Healthcare
### Exhibit 1-3: Estimated Prevalence of Rheumatoid Arthritis in Patients Over 45 Years of Age, Select Countries, 2015–20

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>159</td>
<td>161</td>
<td>163</td>
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<tr>
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<td>840</td>
<td>843</td>
<td>846</td>
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<tr>
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<td>207</td>
<td>209</td>
<td>210</td>
<td>212</td>
<td>214</td>
<td>0.8%</td>
</tr>
<tr>
<td>Spain</td>
<td>220</td>
<td>223</td>
<td>227</td>
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<tr>
<td>United Kingdom</td>
<td>542</td>
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<td>559</td>
<td>565</td>
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</tr>
<tr>
<td>United States</td>
<td>1,736</td>
<td>1,771</td>
<td>1,806</td>
<td>1,841</td>
<td>1,876</td>
<td>1,910</td>
<td>1.9%</td>
</tr>
<tr>
<td><strong>Total prevalence</strong></td>
<td><strong>3,693</strong></td>
<td><strong>3,746</strong></td>
<td><strong>3,799</strong></td>
<td><strong>3,848</strong></td>
<td><strong>3,899</strong></td>
<td><strong>3,948</strong></td>
<td><strong>1.3%</strong></td>
</tr>
</tbody>
</table>

Note: Prevalent cases reported in thousands.
Source: Datamonitor Healthcare
incorporating antimicrobial properties and improving the quality of the implants’ integration with the bones. Furthermore, with the increasing use of bone graft materials, the industry continues to put sustained effort into developing synthetic graft materials including bioactive glass, ceramic materials, and porous titanium particles.

**Carbon fiber-reinforced polyether ether ketone for orthopedic implants**

Polyaryletherketones (PAEKs) have been increasingly used as biomaterials for orthopedic implants since they were confirmed for biocompatibility in the 1980s. These are a family of high-temperature thermoplastic polymers incorporating an aromatic backbone molecular chain with interconnected ketone and ether functional groups. PAEKs have been preferred due to their strength, inertness, compatibility with reinforcing agents, and greater strength per mass than many metals. Furthermore, PAEKs can be customized to match a variety of materials such as cortical bone or titanium alloy by supplementing the bulk material with carbon fiber to create carbon fiber-reinforced (CFR) composites. Over the years, the family of PAEK polymers has grown to include polyether ether ketone (PEEK), polyether ketone ketone, and polyether ketone ether ketone, and so on.

The popularity of PEEK has increased over the years due to the need for replacing metal implant components with high-performance thermoplastic materials. CFR-PEEK is being extensively explored for application in femoral stems, bearing materials for hip and knee replacement, and hip resurfacing. Research on PEEK and PEEK composites continues for orthopedic applications. Williams et al., among others, have demonstrated the biocompatibility of these composites extensively in their research. However, there have been concerns around the inertness of PEEK as well as its limited fixation with bone, prompting research efforts around improving the bone-implant interface to increase fixation. This has been achieved by coating PEEK implants with titanium and hydroxyapatite (HA) and by creating porous PEEK networks for bone ingrowth. There have also been efforts to create bioactive PEEK composites by compounding PEEK with calcium phosphate biomaterials, such as β-tricalcium phosphate and HA. Clinical results continue to demonstrate high biocompatibility for CFR-PEEK as well as good biological interaction of PEEK. All mechanical tests showed CFR-PEEK implants to have similar or improved behavior compared to commercially used devices as well as generating a lower volume of wear particles. Nakahara et al. (2013) demonstrated the use of CFR-PEEK in an
ovine model for use as a material in cemented and cementless hip prostheses. The results suggested that both cementless and cemented CFR-PEEK stems with rough-textured surfaces and HA coatings may function well for fixation.

**Polycarbonate urethanes for hard-on-soft bearings**

Polyurethane biomaterials have demonstrated lower modulus values as compared to ultra-high-molecular-weight-polyethylene (UHMWPE), leading to reduced wear. Over the years, third-generation polyurethane biomaterials were developed. Known as segmented polycarbonate urethanes (PCUs), these materials have improved oxidative stability. Owing to their toughness, ductility, oxidation resistance and biostability, PCUs are being explored in the creation of bearing materials for use in total acetabular replacement.

Several attempts are underway to justify the appropriateness of PCUs as alternative materials for hard-on-soft bearings. Various research studies are being conducted to reconstruct damaged or eroded cartilage in the acetabulum with softer materials that better mimic the mechanical properties and lubrication of cartilage. A study by John et al. demonstrated the utility of PCUs in a hip joint simulator study. In the study, PCU cups showed at least 24% lower material loss as compared to cross-linked UHMWPE. Polycarbonate urethanes are also of immense interest as suitable candidates for bearing materials due to their high biocompatibility. *In vitro* studies by Smith et al. indicate that PCU particles cause less of an inflammatory response by macrophages than particles of UHMWPE. Currently, a majority of the bearing material for joint arthroplasties is made of UHMWPE. A shift from this to PCUs would involve significant efforts including incremental innovations such as the introduction of stabilizers to enhance implant durability.

**Silicon nitride for hard-on-hard hip bearings**

Silicones have been traditionally used and largely preferred for hand and foot joint implants primarily due to their biocompatibility and biodurability. Studies involving silicone metacarpophalangeal joint arthroplasty have continued to demonstrate positive long-term outcomes, with high survivorship. In the recent years, however, silicon nitride ($\text{Si}_3\text{N}_4$) has been under consideration as an important ceramic biomaterial for hard-on-hard hip bearings. Silicon nitride has higher strength characteristics than alumina, making it a suitable material for joint arthroplasty implants. While there are several advantages to its use, one of the key concerns...
with this material is the potential for superficial oxidation leading to increased third-body wear. It has also been observed that the biocompatibility of silicon nitride is largely dependent on the ceramic formulation. However, even as concerns remain, there is gradual commercial uptake of this material for orthopedic applications. Amedica commercializes silicon nitride ceramic formulation for ceramic-on-UHMWPE, ceramic-on-ceramic, and ceramic-on-metal hip bearing applications.

**Biocompatible ceramic and glass materials for improved acetabular fixation**
Glass Technology Services collaborated with various partners to receive a grant from the European Union’s Seventh Framework Programme for its project examining the use of biocompatible glass ceramic to improve hip prosthesis. Known as Monoblock Acetabular cup with Trabecular-like Coating (MATCH), the project was designed to improve wear rate, allow a wider range of prostheses sizes and reduce trauma during surgical implantation. Most hip replacement joints fit into acetabular cups that are housed in metal backs, leading to a high risk of wear and potential damage to the pelvis. The project aims to eliminate these innate limitations by incorporating biocompatible ceramic and glass materials to improve the interface between the implant’s acetabular cup and the patient’s pelvic bone, thereby extending implant life. The new cup is made of monolithic ceramic with a trabecular-like glass coating to promote integration with bone. It anchors to the bone through a bioactive trabecular coating. MATCH aims to develop prototypes which can accelerate osteointegration and prevent aseptic loosening due to wear, relative mobility, and bone damage. This is likely to improve the efficiency and longevity of hip arthroplasty procedures in coming years.

**Tantalum oxide nanotube array films for joint replacement implants**
With excellent biocompatibility and anticorrosion, tantalum has been an attractive material for joint implant fabrication. Its potential advantages in hip arthroplasty have included excellent bone and tissue ingrowth observed histologically and direct polyethylene intrusion into the metal substrate ensuring no backside wear in the monoblock cup. To improve its overall physicochemical properties, there have been increased global research efforts on tantalum surface modification.

One of the key areas of development is focused on tantalum oxide (Ta$_2$O$_5$) nanotube films. These films are about 1000 times thinner than human hair and can be produced on tantalum by controlling the conditions of anodization and annealing.
Hongyi et al. in their research published in ACS Applied Material & Interfaces suggest that these films can help tantalum joint replacements integrate better with existing bone. This study further suggests that tantalum oxide nanotube films can improve the anticorrosion, biocompatibility, and osteoinduction of pure tantalum, which—to a certain extent—provides the theoretical elaboration for the development of a tantalum endosseous implant or implant coating.

**Tantalum powder demonstrates potential for 3D printing of joint replacements**

A recent research study conducted by a UK-based firm, Metalysis, investigated the single-step process of producing metal powders directly from their oxides. In a partnership with research and technology organization TWI, the company published a study that demonstrates the effectiveness of selective laser melting, an additive manufacturing process for implants. The study utilized Metalysis’s tantalum powder to print lattice structures that hold significant potential in the development of customized hip replacements and spinal implants. The lattice structures produced in the study demonstrated the ability to replicate natural bone in terms of strength and stiffness, and to integrate with existing bone cells. The company anticipates that these implants can be produced at reduced cost compared to implants produced via traditional manufacturing methods.
2. HIP ARTHROPLASTY

Hip replacement or hip arthroplasty is a surgical procedure in which the femoral head and/or the acetabulum of the hip ball-and-socket joint are replaced by artificial prosthetic material. This surgical procedure may involve total replacement of the hip or part of it, that is to say only the femoral head. The damaged bone of the hip joint is removed and replaced with a prosthesis which may be composed of various materials including ceramic, plastic, metals, or combinations of any two. The prosthetic component may be attached to healthy bone with cement or without any such binding agent if the prosthesis is covered with a material like hydroxyapatite (HA) to mimic human bone. Total hip replacement (THR) is one of the most successful and cost-effective surgical procedures and remains the treatment of choice for long-term pain relief and restoration of function for patients with diseased or damaged hips. The procedure relieves symptomatic pain and offers the patient a good range of motion and stability.

Hip arthroplasty involves the use of a femoral stem, a femoral head, and an acetabular cup. While a modular femoral head attaches to the stem via a taper locking mechanism, a monoblock femoral head is attached to the stem as a one-piece unit. A modular acetabular cup consists of a shell that is fixed to the pelvic bone and an insert or liner that is fixed inside the shell. Conversely, a monoblock acetabular cup is a one-piece construct. The bearing surface of the artificial joint is composed of a metal or ceramic femoral head, with the inner surface of the cup typically comprising ceramic, metal, or polyethylene.

2.1 Indications for Hip Arthroplasty

The key indications for hip arthroplasty include conditions such as fractured neck of the femur in the elderly, rheumatoid arthritis, osteoarthritis, and osteoporosis in the elderly. When non-operative care, including weight reduction, activity modification, ambulatory aides, and non-steroidal anti-inflammatory drugs (NSAIDs) fail to relieve the pain and disability of end-stage osteoarthritis, total hip arthroplasty (THA) is recommended. Osteonecrosis with segmental collapse of the femoral head is another common indication for hip arthroplasty. Less frequent indications of hip arthroplasty include metastatic tumors of the hip joint and the residua of post-infectious arthritis.
2.2 **Types of Hip Arthroplasty**

Primary THA procedures are categorized as cemented, cementless, or hybrid hip replacement. In a cemented THR, the acetabular cup and prosthesis shaft are fixed to the skeleton with a self-curing bone cement, which completely fills the space between the skeleton and the surface of the prosthesis. Typical survival rates for conventional cemented, metal-on-polyethylene bearing joint replacement are greater than 90%, 85%, and 80% at 10, 15, and 20 years, respectively (Tamer TM, 2016).

2.2.1 **Cemented and Cementless Hip Arthroplasty**

In a cementless THR, the replacement components are press-fitted or blown directly into the space created by the surgeon in the skeleton and held in place by the elastic force generated in the bone tissue. The prosthesis typically used consists of a highly porous metal structure that aids in the promotion of bone and tissue fixation without the use of cement. The quality of the implant fixation to bone depends on the design of the stem and cup. Design options in cementless femoral fixation include anatomic proximal fixation, cylindrical distal fixation, and tapered fixation.

2.2.2 **Hybrid Hip Replacement**

A hybrid hip replacement procedure refers to hip surgery during which one of the two components (cup or stem) is inserted without cement, while the other is implanted with cement. In this procedure, the acetabulum is replaced either with a single-piece cup made from one material (polyethylene, ceramic, or metal) or a two-piece (modular) cup made from a metal outer shell and a polyethylene, ceramic, or metal liner. The head of the femur is replaced with either a single-piece metal stem and head, or a modular component consisting of a metal stem (which may consist of more than one piece) with a metal, ceramic, or ceramicized metal head.

2.2.3 **Hip Resurfacing**

Conventional hip replacements have been associated with the potential risks of bone loss, extending to the metaphyseal and diaphyseal femur, and gross migration of the femoral component. Consequently, hip resurfacing emerged as one of the alternative forms of hip arthroplasty that could help conserve proximal femoral bone. A key benefit for young patients, hip resurfacing also allows added hip stability from the larger diameter of the femoral prosthesis. In addition, this treatment option has also been observed to offer advantages such as higher accuracy in restoration of leg...
length, femoral offset, and femoral anteversion. Proponent surgeons of this procedure also advocate advantages such as a greater range of motion of hip joint post surgery, lower wear of prosthetic bearing, as well as a lower rate of dislocations. Most modern hip-resurfacing techniques incorporate the use of a non-cemented porous metal cup into the hip socket and a metal cap cemented onto the femoral head. The first generation of hip-resurfacing products was faced with innate limitations leading to femoral neck fractures caused by improper surgical technique, or osteolysis of the femoral neck from wear particles. A high failure rate in early follow-up periods led to the abandonment of this treatment option until improved techniques and implants were developed.

2.2.4 Revision Hip Surgeries
Revision hip surgeries are conducted to repair a hip prosthesis that has been damaged over a period of time due to various causes, including wear and tear of the implant or infection. Aseptic loosening, osteolysis, and instability are the most common indications for revision hip surgeries and the most common indications for revision surgery within five years of primary THA.

2.3 Clinical and Market Trends in Hip Arthroplasty

Outpatient hip arthroplasty gaining momentum due to innovative anesthesia approaches and pain-control mechanisms
Recent advances in anesthesia, pain, and nausea control are helping facilitate outpatient joint replacement surgeries. At the 2015 annual meeting of the American Academy of Orthopaedic Surgeons (AAOS), Doctor Henderson et al. reported significant increases in the number of arthroplasties performed in an outpatient setting from 2007 to 2011. Among the patient population from a large private insurer network, there was an increase of 17% in total knee arthroplasties, 37% in THAs, and an increase of approximately 66% in unicompartmental knee arthroplasties (AAOS, 2015). Consequently, various implant manufacturers are also looking to help make this transition seamless. At the AAOS 2015 annual meeting, Zimmer launched its Z-23 initiative to facilitate improved patient selection, enhanced patient experience, and efficient surgical procedures.

The increased use of multi-modal pain control programs is playing a significant role in the shift of total joint replacements to outpatient settings. These protocols include
the use of pre-emptive NSAIDs and other medications before the surgery, regional anesthesia and periarticular cocktails during the surgery, as well as aggressive physical therapy and/or cryotherapy post surgery. The pain control program also continues post discharge, where longer-acting analgesics, steroids, and newer drugs to reduce nerve pain are administered. Furthermore, use of non-opioid pain management solutions has helped joint replacement procedures reach outpatient settings.

The other key factor driving outpatient surgeries for joint replacement is the use of robotic techniques. Robotic assistance in total knee arthroplasty and, to an extent, THA is beneficial in optimal component alignment and fixation within the surgical exposure. Several clinical studies indicate that non-robotic replacements result in over 50% of joints being inaccurately placed (Brandon H, 2015). Given that these robotic techniques aim to improve overall accuracy and speed of recovery, their impact on outpatient joint replacement surgeries has been on the rise.

**Increasing acceptance of minimally invasive hip replacements**

The need for faster recovery, lesser post-operative pain, and cost-effective procedures is driving the demand for minimally invasive hip replacements. There has been a moderate increase in the number of direct anterior approach hip arthroplasties in recent years. This approach requires the creation of an incision of about 3–4 inches located at the front of the hips. Typically, the surgeons are not required to detach any of the muscles or tendons, in contrast to a traditional hip replacement where significant disruption to the connective tissues is caused. Furthermore, a high-tech operating table may be used in addition to the usage of intraoperative X-ray or computer navigation to confirm implant position and length. The direct anterior approach potentially helps to reduce blood loss, surgery time, and post-operative pain. The minimally invasive nature of the surgery may also lead to a reduced risk of hip dislocation post surgery. This technique also allows for potentially lesser restrictions, including the ability to freely bend the hips as well as to bear a patient’s full weight post surgery. While it is estimated that only around 20% of the members of the American Association of Hip and Knee Surgeons choose the anterior approach, its usage is likely to increase in coming years due to the overall clinical and economical benefits.
Metallosis continues to diminish surgeons’ trust in metal-on-metal implants

Metal-on-metal (MoM) bearings were reintroduced over the last two decades because of their lower volumetric wear rates in comparison to conventional metal-on-polyethylene bearings. With the potential to reduce wear-induced osteolysis and improve implant stability, their adoption rates have increased dramatically. While MoM implants have been proven to be successful in well-chosen patients and with meticulous implant positioning, there have been sufficient reports of severe early complications to suggest that great caution should be exercised when using this type of implant.

Various national joint registries including the UK’s National Joint Registry (NJR) and Australian Orthopaedic Association National Joint Replacement Registry have published findings that the failure rate of THAs with MoM bearings has been two- to three-fold higher than those using non-MoM bearings. There have been concerns around the complications that can result from the use of larger femoral head sizes and particular designs. Consequently, there have been various product recalls over the past few years. The ASR implants manufactured by DePuy Synthes were withdrawn following the publication of NJR statistics in 2010. The ADEPT 12/14 modular head used in MoM THA, manufactured by Finsbury Orthopaedics—acquired by DePuy Synthes—was withdrawn from the market as a result of significantly high revision rates of 12.1% at seven years, based on data from the NJR. In 2012, Smith & Nephew Orthopaedics initiated a market withdrawal for the metal liners of the R3 acetabular system due to a higher than expected number of revision surgeries associated with use of the device in THR outside the US. The recall was made after Stryker received post-marketing data that revealed the metal modular necks and stems of these devices are prone to corrosion and fretting that may release excessive metal debris into the body, damaging surrounding bone and tissue.

The increasing number of recalls and overall complication rates has resulted in negative revenue growth for most MoM implants. The decline in sales of such implants is likely to continue, with various regulatory authorities imposing strict vigilance. In October 2013, based on a study conducted by the UK’s National Institute for Health and Care Excellence (NICE), the National Health Service (NHS) drafted new rules to ban the use of all hip implants with a failure rate above 5%. In the US, the US Food and Drug Administration (FDA) continues to allow the usage of
MoM hip implants due to the distinct benefits they afford, such as high survivorship and a favorable risk-to-benefit ratio for most patients. However, growing concerns and speculations have led to moderately reduced confidence in MoM implants within patient populations across the US and Europe.

**Higher adoption of cementless hips despite high costs involved**
While there is significant momentum toward uptake of uncemented hip fixations, cemented fixation still has moderately higher survival rates. One of the largest observational studies published in the annual report of the NJR for England and Wales indicates that seven-year revision rates were the lowest for cemented (3.0%), hybrid (3.8%), and cementless prostheses (4.6%); however, it has been observed that revision for aseptic loosening is low with uncemented THR. This is particularly true for patients under 65 years of age, who are more likely to engage in more strenuous physical activities.

Commercially, the uptake of cementless hip implants has increased significantly over the past two decades in England, Wales, Sweden, Australia, and New Zealand and some countries, such as the US and Canada, have continued to predominantly use cementless implants for most hip replacement surgeries. Traditionally, cementless hip implants have been priced three to four times higher than cemented hip prostheses. In a scenario where the aging population is continuously imposing a significant strain on funding agencies, high cost implants are likely to add to the overall cost burden. In addition, the number of revision surgeries is likely to increase significantly in the coming years thus leading to a need for the balanced usage of economic resources, especially in aging societies. While the current cost implications are indeed a restraining factor for cementless implants, their long-term benefits may far exceed the immediate concerns. It is advocated that the usage of cementless implants may lead to a successful bonding of both the femoral and acetabular components to the bone. This is likely to cause future revision procedures (if any) to usually involve the exchange of articular surfaces only, thus allowing patients to recover rapidly while having a lower impact on overall health costs.

**Moderate uptake of cementless femoral implants**
While cementless acetabular implants are widely used across most regions and all age groups, the usage of cementless femoral implants is somewhat lower; hospital
registries across various European countries indicate a moderately higher preference for cemented femoral implants. This trend is also indicated by the increased adoption of hybrid THAs across most European countries and North America. A systematic review of the 2010 Cochrane Database indicates that cementing the femoral stem may provide a more stable fixation, thus reducing post-operative pain and providing better mobility as compared to a cementless prosthesis. A review of various other clinical studies published over the past decade indicates lower implant-related complications and reduced re-operation rates, especially for post-operative periprosthetic femoral fractures.

Currently, there are two variations of cemented femoral fixation: the composite beam and the polished, tapered wedge. The composite beam relies on rigid bonding to cement and is not intended to subside; this type of femoral fixation is largely preferred in the North American markets. The tapered wedge system converts radial compression into hoop stresses within the cement mantle and is intended to subside; this type of fixation is preferred in Europe.

Conversely to cemented femoral fixation, cementless stems generate fixation stability through bone ingrowth. A significant proportion of the cementless stems used globally are made of roughened titanium and, with the addition of HA, the stimulation of bony fixation has been improved while concerns over the production of ceramic particles have been reduced. Broadly, there are two major designs of cementless hip stem: proximal loading stems and fully coated stems. Proximal loading stems are typically designed to prevent the issue of stress shielding that has been observed with traditional distal fitting implants. In most cases, proximal loading implants are heavier in the proximal metaphyseal region for early resistance to subsidence and rotation. Fully coated stems, on the other hand, depend upon a graduated loading of the proximal femur. These stems allow bone apposition through their entire length and provide firmness to the implant by virtue of their wide, flat geometry.

**Improved survival rates of cemented stems**

There have been concerted efforts across the orthopedic industry to improve the cementing technique over the past two decades. This includes improvements in the preparation of the femoral canal as well as pressurization during the insertion of the cement. With these incremental advancements, enhanced cement-bone interfacing
and stable interlocking has been achieved. Consequently, the survival rates of cemented stems have improved. An analysis of records across various joint registries indicates that the cemented THR is likely to be a lifelong implant for patients above 62 years of age. Younger patients have a varying probability of undergoing revisions across their lifetime.

**Steady growth of hybrid hip replacements across Europe and the US**

An analysis of various joint replacement registries across Europe and the US indicates steady growth in hybrid hip replacement procedures. According to the NJR for England, Wales, and Northern Ireland, the adoption rate of hybrid hip replacements increased from 12.3% in 2003 to 20.2% in 2013. In addition, analysis of the registry data also indicates that 72.5% of UK surgeons had utilized hybrid THR. Furthermore, hybrid THR has been performed across 95.1% of surgical units in the region. Currently, about 13% of all primary THAs conducted in the US are of the hybrid type. The utilization of hybrid hip replacements is higher in certain parts of Europe, such as Germany, where over 17% of all primary THAs are hybrid.

**Increasing preference for reverse hybrid hip replacements**

Reverse hybrid hip replacement refers to the use of a cemented polyethylene cup with a cementless femoral stem and a modular head. As indicated by various large joint registries across regions such as Norway, Sweden, England, Wales, and Northern Ireland (among others), the adoption of reverse hybrid hip replacement is on the rise (Michael W, 2014). According to the NJR for the UK, hybrid THR demonstrated a steady adoption rate, rising from 0.6% in 2003 to 3.0% in 2013. A review of hip replacements included in the Norwegian Arthroplasty Register (NAR) indicates that uncemented femoral stems may have better long-term results than cemented ones in patients aged 60 years or younger. These findings further prompted the NAR to advocate the use of cemented cups in combination with uncemented stems for younger patients. Most proponents of reverse THR continue to advocate the use of this technique as it pre-empts the challenges related to femoral cementing and also saves operating time. Furthermore, the long-term outcomes of all-polyethylene cemented cups could provide longer survivorship over the mid to long term. With the introduction of moderately cross-linked polyethylene, the overall wear of cemented polyethylene cups is expected to reduce.
Reverse THR utilizes various components from different manufacturers. Consequently, concerns have been raised around the long-term results of the procedure since implants that are not designed to fit each other are used in conjunction. Despite such concerns, the uptake of reverse THR has been on the rise, especially in Europe.

**Hip resurfacing procedural growth is being driven by technological advancements**

Improved design modifications and surgical techniques are driving the adoption rates of hip resurfacing procedures globally. The complications related to periprosthetic bone loss in first-generation polyethylene acetabular resurfacing components has been reduced with the use of MoM bearings. There have also been significant improvements in implant designs leading to the development of polar bearing implants. These implants have been able to reduce surface asperity and provide better fluid film lubrication for the bearing surfaces. The development of thin acetabular shells has further allowed the removal of less acetabular bone. As a result, despite the complicated nature of the procedure, overall confidence in hip resurfacing and its outcomes have increased, leading to higher adoption rates in recent years.

**Increasing failure rates leading to reduced hip resurfacing procedure volume in Europe**

In recent years there has been a significant increase in the volume of hip resurfacing surgeries across Europe. The number of hip resurfacing procedures in Europe and Australia has traditionally been higher than that in the US. The increased acceptance of this procedure in Europe was largely attributable to the successful short- and medium-term results being achieved through design modifications and improvements in surgical techniques. In addition, the ease of conducting a revision hip resurfacing compared to correcting a failed THA provided more incentive to adopt the procedure.

However, in recent years, the number of hip resurfacing procedures has reduced significantly in Europe. According to the NJR for England, Wales, and Northern Ireland, the contribution of hip resurfacing procedures to overall hip replacement procedures has reduced from 9.8% in 2003 to around 1.0% in 2014. The number of hip resurfacing procedures in Germany too remains low as a result of the increasing
number of hip resurfacing failures in the country. Higher failure rates for hip resurfacing have been observed in women than males in Germany, which has prompted many surgeons to argue over the utility of this treatment option for women.

**Limited adoption of hip resurfacing in the US due to procedural complexity**
Following the FDA approval of MoM hip resurfacing devices, the complication rates in the US began to due to surgeons’ lack of experience with this new technique; hip resurfacing is considered more complex than THR and constitutes a substantial learning curve. The technique is considered difficult largely because the surgeon is required to prepare the acetabulum with the femoral head and neck still intact. Furthermore, the acetabular component must be positioned accurately. It is also of note that the femoral preparation is complicated and might not be a familiar procedure for most THR surgeons. Consequently, hip resurfacing requires rigorous training and experience (Edwin PS, 2012). With a limited number of surgeons in the US having been trained in this procedure, the adoption rates for hip resurfacing continues to be low in the country.

**High hip revision procedure rates across the US and various European countries**
Analysis of various national joint registries indicates a significant increase in the number of hip revision procedures across the US and certain European countries. It is further observed that patients undergoing hip revision usually suffer from several co-morbidities, technical difficulties, and complications requiring higher resource utilization as compared to THR. According to the American Joint Replacement Registry, the burden of revision hip replacements constituted around 10.0% of the overall hip replacements in 2014. Similar reviews of national joint registries across Italy, the UK, and Spain indicate revision rates of around 8.4%, 9.7%, and 8.5%, respectively. While this indicates a minor decrease over previous decades, the overall proportion of revision surgeries remains high. As per a study published in the *Journal of Arthroplasty* in 2016, primary and revision hip arthroplasties are often performed by surgeons without adult reconstruction fellowship training in their early practice (Eslam PA, 2016).

### 2.4 Procedure Volumes

During the forecast period covered by this report (2015–20), the total number of hip arthroplasty procedures performed in the US and the five major EU markets (France,
Germany, Italy, Spain, and the UK) is anticipated to expand at a compound annual growth rate (CAGR) of 2.6%, from approximately 1.2 million procedures in 2015 to an estimated 1.4 million procedures by 2020. Exhibit 2-1 presents the combined procedure volumes forecast for hip arthroplasty procedures across the US and EU5 for the years 2015 through 2020.

Exhibit 2-2 presents the hip arthroplasty procedure volumes forecast for the US for the years 2015 through 2020; Exhibit 2-3 presents the hip arthroplasty procedure volumes forecast for the UK for the years 2015 through 2020; Exhibit 2-4 presents the hip arthroplasty procedure volumes forecast for France for the years 2015 through 2020; Exhibit 2-5 presents the hip arthroplasty procedure volumes forecast for Germany for the years 2015 through 2020; Exhibit 2-6 presents the hip arthroplasty procedure volumes forecast for Italy for the years 2015 through 2020; Exhibit 2-7 presents the hip arthroplasty procedure volumes forecast for Spain for the years 2015 through 2020.

2.5 Industry Challenges for Hip Arthroplasty

Product recalls continue to hamper confidence of physicians as well as overall sales for OEMs

It is estimated that over 18% of the hip replacements in the US are revision surgeries that are necessary as a result of defective or failed devices. In the past 10 years, there have been over 1,300 recalls of various hip and knee components developed by the top six joint implant manufacturers. About 578 of these have been hip recalls. Approximately 231 hip recalls between 2002 and 2013 were attributed to Stryker products, while DePuy Synthes products counted for approximately 150 recalls.

While DePuy Synthes’ products continue to dominate sales in the hip arthroplasty implants market, it has been subjected to various product recalls. Between 2002 and 2013, the company had about 150 class II recalls. The majority of the recalled hip implants, components, and tools were due to labeling issues, design flaws, packaging issues, early failure, and manufacturing issues. Three of its key hip replacement designs—the Pinnacle Hip Replacement System, the ASR XL Acetabular System, and the ASR Hip Resurfacing System—have demonstrated significant failure rates. The faults with its products largely came from their MoM components; this was the cause of the two ASR systems’ recalls in 2010.
### Exhibit 2-1: Hip Arthroplasty, Combined Procedure Volumes Forecast, 2015–20

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<tr>
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</thead>
<tbody>
<tr>
<td>United States</td>
<td>575.0</td>
<td>601.1</td>
<td>630.2</td>
<td>662.3</td>
<td>696.4</td>
<td>732.5</td>
<td>5.0%</td>
</tr>
<tr>
<td>France</td>
<td>153.9</td>
<td>154.7</td>
<td>155.5</td>
<td>156.3</td>
<td>157.2</td>
<td>158.1</td>
<td>0.5%</td>
</tr>
<tr>
<td>Germany</td>
<td>231.8</td>
<td>231.9</td>
<td>232.1</td>
<td>232.3</td>
<td>232.5</td>
<td>232.6</td>
<td>0.1%</td>
</tr>
<tr>
<td>Italy</td>
<td>100.0</td>
<td>100.3</td>
<td>100.6</td>
<td>100.9</td>
<td>101.3</td>
<td>101.6</td>
<td>0.3%</td>
</tr>
<tr>
<td>Spain</td>
<td>49.4</td>
<td>49.5</td>
<td>49.6</td>
<td>49.6</td>
<td>49.7</td>
<td>49.9</td>
<td>0.2%</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>119.4</td>
<td>120.1</td>
<td>120.7</td>
<td>121.4</td>
<td>122.0</td>
<td>122.8</td>
<td>0.6%</td>
</tr>
<tr>
<td><strong>Total hip arthroplasty procedures</strong></td>
<td><strong>1,229.5</strong></td>
<td><strong>1,257.6</strong></td>
<td><strong>1,288.7</strong></td>
<td><strong>1,322.8</strong></td>
<td><strong>1,359.1</strong></td>
<td><strong>1,397.4</strong></td>
<td><strong>2.6%</strong></td>
</tr>
</tbody>
</table>

**Notes:** Total hip arthroplasty procedures include primary total hip arthroplasty, partial hip arthroplasty, hip resurfacing, and revision hip arthroplasty procedures. Procedure volumes are reported in thousands. Figures may not calculate due to rounding.

(Continued)
Note: Total hip arthroplasty procedures include primary total hip arthroplasty, partial hip arthroplasty, hip resurfacing, and revision hip arthroplasty procedures.

Sources: American Joint Replacement Registry; Catalan Arthroplasty Registry; Endo Prothesen Register Deutschland; Meddevicetracker; National Joint Registry of the United Kingdom; SoFCOT and Haute Autorité de Santé

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<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary THA</td>
<td>395.0</td>
<td>418.0</td>
<td>443.0</td>
<td>471.0</td>
<td>501.0</td>
<td>532.0</td>
<td>6.2%</td>
</tr>
<tr>
<td>Cemented</td>
<td>14.9</td>
<td>14.9</td>
<td>14.9</td>
<td>14.9</td>
<td>14.9</td>
<td>14.9</td>
<td>0.0%</td>
</tr>
<tr>
<td>Cementless</td>
<td>337.0</td>
<td>357.2</td>
<td>380.4</td>
<td>405.1</td>
<td>431.5</td>
<td>459.5</td>
<td>6.5%</td>
</tr>
<tr>
<td>Hybrid</td>
<td>43.1</td>
<td>45.9</td>
<td>47.7</td>
<td>51.0</td>
<td>54.6</td>
<td>57.6</td>
<td>5.9%</td>
</tr>
<tr>
<td>Partial Hip</td>
<td>127.0</td>
<td>129.0</td>
<td>132.0</td>
<td>134.0</td>
<td>137.0</td>
<td>140.0</td>
<td>2.1%</td>
</tr>
<tr>
<td>Hip Resurfacing</td>
<td>5.0</td>
<td>5.1</td>
<td>5.2</td>
<td>5.3</td>
<td>5.4</td>
<td>5.5</td>
<td>2.0%</td>
</tr>
<tr>
<td>Revision Hip Arthroplasty</td>
<td>48.0</td>
<td>49.0</td>
<td>50.0</td>
<td>52.0</td>
<td>53.0</td>
<td>55.0</td>
<td>2.9%</td>
</tr>
<tr>
<td><strong>Total hip arthroplasty procedures</strong></td>
<td><strong>575.0</strong></td>
<td><strong>601.1</strong></td>
<td><strong>630.2</strong></td>
<td><strong>662.3</strong></td>
<td><strong>696.4</strong></td>
<td><strong>732.5</strong></td>
<td><strong>5.0%</strong></td>
</tr>
</tbody>
</table>

**Notes:** THA = total hip arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

**Sources:** American Joint Replacement Registry; Meddevicetracker
### Exhibit 2-3: Hip Arthroplasty—United Kingdom, Procedure Volumes Forecast, 2015–20

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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary THA</td>
<td>85.0</td>
<td>85.4</td>
<td>85.7</td>
<td>86.1</td>
<td>86.4</td>
<td>86.8</td>
<td>0.4%</td>
</tr>
<tr>
<td>Cemented</td>
<td>25.0</td>
<td>24.6</td>
<td>24.2</td>
<td>23.8</td>
<td>23.5</td>
<td>23.1</td>
<td>-1.5%</td>
</tr>
<tr>
<td>Cementless</td>
<td>43.1</td>
<td>43.7</td>
<td>44.3</td>
<td>44.8</td>
<td>45.3</td>
<td>45.9</td>
<td>1.2%</td>
</tr>
<tr>
<td>Hybrid</td>
<td>16.9</td>
<td>17.1</td>
<td>17.3</td>
<td>17.5</td>
<td>17.6</td>
<td>17.8</td>
<td>1.0%</td>
</tr>
<tr>
<td>Partial Hip</td>
<td>23.1</td>
<td>23.3</td>
<td>23.6</td>
<td>23.8</td>
<td>24.1</td>
<td>24.3</td>
<td>1.0%</td>
</tr>
<tr>
<td>Hip Resurfacing</td>
<td>0.9</td>
<td>0.9</td>
<td>0.9</td>
<td>0.9</td>
<td>1.0</td>
<td>1.0</td>
<td>1.1%</td>
</tr>
<tr>
<td>Revision Hip Arthroplasty</td>
<td>10.3</td>
<td>10.4</td>
<td>10.5</td>
<td>10.5</td>
<td>10.6</td>
<td>10.6</td>
<td>0.5%</td>
</tr>
<tr>
<td><strong>Total hip arthroplasty procedures</strong></td>
<td><strong>119.4</strong></td>
<td><strong>120.1</strong></td>
<td><strong>120.7</strong></td>
<td><strong>121.4</strong></td>
<td><strong>122.0</strong></td>
<td><strong>122.8</strong></td>
<td><strong>0.6%</strong></td>
</tr>
</tbody>
</table>

Notes: THA = total hip arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

Sources: Meddevicetracker; National Joint Registry of the United Kingdom

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</tr>
</thead>
<tbody>
<tr>
<td>Primary THA</td>
<td>106.1</td>
<td>106.4</td>
<td>106.7</td>
<td>107.0</td>
<td>107.3</td>
<td>107.8</td>
<td>0.3%</td>
</tr>
<tr>
<td>Cemented</td>
<td>38.7</td>
<td>38.2</td>
<td>37.6</td>
<td>37.0</td>
<td>36.5</td>
<td>35.9</td>
<td>-1.5%</td>
</tr>
<tr>
<td>Cementless</td>
<td>52.9</td>
<td>54.0</td>
<td>55.1</td>
<td>56.2</td>
<td>57.3</td>
<td>58.5</td>
<td>2.0%</td>
</tr>
<tr>
<td>Hybrid</td>
<td>14.4</td>
<td>14.2</td>
<td>14.0</td>
<td>13.8</td>
<td>13.6</td>
<td>13.4</td>
<td>-1.5%</td>
</tr>
<tr>
<td>Partial Hip</td>
<td>28.3</td>
<td>28.6</td>
<td>28.8</td>
<td>29.1</td>
<td>29.5</td>
<td>29.7</td>
<td>1.0%</td>
</tr>
<tr>
<td>Hip Resurfacing</td>
<td>1.4</td>
<td>1.4</td>
<td>1.4</td>
<td>1.4</td>
<td>1.4</td>
<td>1.4</td>
<td>1.0%</td>
</tr>
<tr>
<td>Revision Hip Arthroplasty</td>
<td>18.1</td>
<td>18.3</td>
<td>18.5</td>
<td>18.7</td>
<td>19.0</td>
<td>19.2</td>
<td>1.1%</td>
</tr>
<tr>
<td><strong>Total hip arthroplasty procedures</strong></td>
<td><strong>153.9</strong></td>
<td><strong>154.7</strong></td>
<td><strong>155.5</strong></td>
<td><strong>156.3</strong></td>
<td><strong>157.2</strong></td>
<td><strong>158.1</strong></td>
<td><strong>0.5%</strong></td>
</tr>
</tbody>
</table>

**Notes:** THA = total hip arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

**Sources:** Meddevicetracker; SoFCOT and Haute Autorité de Santé
### Exhibit 2-5: Hip Arthroplasty—Germany, Procedure Volumes Forecast, 2015–20

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</tr>
</thead>
<tbody>
<tr>
<td>Primary THA</td>
<td>173.4</td>
<td>173.2</td>
<td>173.1</td>
<td>173.0</td>
<td>173.0</td>
<td>172.9</td>
<td>-0.1%</td>
</tr>
<tr>
<td>Cemented</td>
<td>54.9</td>
<td>54.1</td>
<td>53.3</td>
<td>52.6</td>
<td>51.9</td>
<td>51.1</td>
<td>-1.4%</td>
</tr>
<tr>
<td>Cementless</td>
<td>84.9</td>
<td>85.6</td>
<td>86.3</td>
<td>87.0</td>
<td>87.7</td>
<td>88.4</td>
<td>0.8%</td>
</tr>
<tr>
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<td>33.6</td>
<td>33.5</td>
<td>33.5</td>
<td>33.5</td>
<td>33.4</td>
<td>33.4</td>
<td>-0.1%</td>
</tr>
<tr>
<td>Partial Hip</td>
<td>30.2</td>
<td>30.5</td>
<td>30.7</td>
<td>30.9</td>
<td>31.1</td>
<td>31.3</td>
<td>0.6%</td>
</tr>
<tr>
<td>Hip Resurfacing</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Revision Hip Arthroplasty</td>
<td>26.2</td>
<td>26.2</td>
<td>26.3</td>
<td>26.3</td>
<td>26.4</td>
<td>26.4</td>
<td>0.2%</td>
</tr>
<tr>
<td><strong>Total hip arthroplasty procedures</strong></td>
<td><strong>231.8</strong></td>
<td><strong>231.9</strong></td>
<td><strong>232.1</strong></td>
<td><strong>232.3</strong></td>
<td><strong>232.5</strong></td>
<td><strong>232.6</strong></td>
<td><strong>0.1%</strong></td>
</tr>
</tbody>
</table>

**Notes:** THA = total hip arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

**Sources:** Endo Prothesen Register Deutschland; Meddevicetracker
### Exhibit 2-6: Hip Arthroplasty—Italy, Procedure Volumes Forecast, 2015–20

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</tr>
</thead>
<tbody>
<tr>
<td>Primary THA</td>
<td>63.6</td>
<td>63.7</td>
<td>63.9</td>
<td>64.0</td>
<td>64.1</td>
<td>64.3</td>
<td>0.2%</td>
</tr>
<tr>
<td>Cemented</td>
<td>8.9</td>
<td>8.8</td>
<td>8.6</td>
<td>8.4</td>
<td>8.3</td>
<td>8.1</td>
<td>-1.9%</td>
</tr>
<tr>
<td>Cementless</td>
<td>43.3</td>
<td>43.7</td>
<td>44.1</td>
<td>44.5</td>
<td>44.9</td>
<td>45.3</td>
<td>0.9%</td>
</tr>
<tr>
<td>Hybrid</td>
<td>11.4</td>
<td>11.3</td>
<td>11.2</td>
<td>11.1</td>
<td>11.0</td>
<td>10.9</td>
<td>0.9%</td>
</tr>
<tr>
<td>Partial Hip</td>
<td>25.3</td>
<td>25.4</td>
<td>25.5</td>
<td>25.6</td>
<td>25.6</td>
<td>25.7</td>
<td>0.3%</td>
</tr>
<tr>
<td>Hip Resurfacing</td>
<td>99.0</td>
<td>100.0</td>
<td>100.0</td>
<td>101.0</td>
<td>101.0</td>
<td>102.0</td>
<td>0.5%</td>
</tr>
<tr>
<td>Revision Hip Arthroplasty</td>
<td>11.0</td>
<td>11.1</td>
<td>11.2</td>
<td>11.3</td>
<td>11.4</td>
<td>11.5</td>
<td>1.0%</td>
</tr>
<tr>
<td><strong>Total Hip Arthroplasty Procedures</strong></td>
<td><strong>100.0</strong></td>
<td><strong>100.3</strong></td>
<td><strong>100.6</strong></td>
<td><strong>100.9</strong></td>
<td><strong>101.3</strong></td>
<td><strong>101.6</strong></td>
<td><strong>0.3%</strong></td>
</tr>
</tbody>
</table>

**Notes:** THA = total hip arthroplasty. Procedure volumes reported in thousands, with the exception of hip resurfacing procedures. Figures may not calculate due to rounding.

**Sources:** Italian Arthroplasty Registry (RIAP); Meddevicetracker
### Exhibit 2-7: Hip Arthroplasty—Spain, Procedure Volumes Forecast, 2015–20

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<tbody>
<tr>
<td>Primary THA</td>
<td>34.6</td>
<td>34.7</td>
<td>34.7</td>
<td>34.8</td>
<td>34.9</td>
<td>35.0</td>
<td>0.2%</td>
</tr>
<tr>
<td>Cemented</td>
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<td>4.6</td>
<td>4.5</td>
<td>4.4</td>
<td>4.3</td>
<td>4.3</td>
<td>-1.6%</td>
</tr>
<tr>
<td>Cementless</td>
<td>22.4</td>
<td>22.6</td>
<td>22.8</td>
<td>23.0</td>
<td>23.3</td>
<td>23.5</td>
<td>1.0%</td>
</tr>
<tr>
<td>Hybrid</td>
<td>7.6</td>
<td>7.5</td>
<td>7.4</td>
<td>7.4</td>
<td>7.3</td>
<td>7.2</td>
<td>-1.0%</td>
</tr>
<tr>
<td>Partial Hip</td>
<td>9.5</td>
<td>9.6</td>
<td>9.6</td>
<td>9.7</td>
<td>9.7</td>
<td>9.8</td>
<td>0.5%</td>
</tr>
<tr>
<td>Hip Resurfacing</td>
<td>81.0</td>
<td>81.0</td>
<td>82.0</td>
<td>83.0</td>
<td>83.0</td>
<td>84.0</td>
<td>0.8%</td>
</tr>
<tr>
<td>Revision Hip Arthroplasty</td>
<td>5.2</td>
<td>5.1</td>
<td>5.1</td>
<td>5.1</td>
<td>5.0</td>
<td>5.0</td>
<td>-0.7%</td>
</tr>
<tr>
<td><strong>Total Hip Arthroplasty Procedures</strong></td>
<td><strong>49.4</strong></td>
<td><strong>49.5</strong></td>
<td><strong>49.6</strong></td>
<td><strong>49.6</strong></td>
<td><strong>49.7</strong></td>
<td><strong>49.9</strong></td>
<td><strong>0.2%</strong></td>
</tr>
</tbody>
</table>

**Notes:** THA = total hip arthroplasty. Procedure volumes reported in thousands, with the exception of hip resurfacing procedures. Figures may not calculate due to rounding.

**Sources:** Catalan Arthroplasty Registry; Meddevicetracker
Zimmer, the market leader across various joint replacement implant markets, has also been prone to product failures. The company briefly recalled its Durom cup in 2008 to revise instructions and returned it to the market thereafter. The Durom cup is a hip socket made of metal and is currently the subject of various lawsuits against Zimmer. Biomet experienced around 25 recalls of hip devices between 2002 and 2013. In all, 24 of these recalls were class II, described by the FDA as “a situation in which use of or exposure to a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.”

Of all the hip implant manufacturers, Stryker has had the highest number of product recalls between 2002 and 2013. The company had around 178 class II recalls and 53 class III recalls during this period. In 2012, Stryker recalled the Rejuvenate and ABG II modular-neck hip stems. This came a few months after the company had issued an urgent field safety notice to surgeons about the potential risks linked with the two products. Both products have been associated with complications such as metallosis and loosening of the implants, leading to various lawsuits. The company’s Accolade TMZF model has also been subjected to multiple recalls in 2009, 2011, and 2013 due to packaging and manufacturing errors.

Certain implant components manufactured by Smith & Nephew have also been prone to failure. The company had approximately 40 hip product recalls between 2002 and 2013; most of them were class II recalls. The metal liner component of its R3 Acetabular System was recalled in 2012 after reports of pain, loosening, metal sensitivity, and dislocation. This has been attributed to the MoM design as the metal liner is composed of cobalt-chromium. The R3 device demonstrated a revision rate of >6% in four years, thereby surpassing the average of 2.89% for primary THRAs. Most recently, the company voluntarily recalled the smaller size femoral head components of its Birmingham Hip Resurfacing System after discovering that patients with these implants may be at higher risk of revision surgery.

**Emerging trend of replacing sales reps with in-house technicians may reduce revenue potential for implant manufacturers in the US**

In recent years, certain hospitals in the US have started training their operating room (OR) staff to help surgeons during joint arthroplasty procedures. This is being done with the long-term ambition of replacing key implant manufacturers’ sales representatives with in-house technicians within the OR. The sales reps traditionally
accompany the surgeon during a joint replacement procedure to help them decide on instruments, mostly influencing the product purchase decision. With hospitals training their technicians to take up the role formerly played by sales reps during joint arthroplasties, hospitals can procure implants at significant markdown prices. Losing the service component of the role of sales reps reduces the broad revenue potential for original equipment manufacturers (OEMs); this move is also likely to reduce the OEMs purchase influence by limiting the sales reps’ opportunities to up-sell costlier implants and instruments.

Need for PMA as mandated by the FDA may negatively impact MoM hip sales
In February 2016, the FDA announced that all current manufacturers of MoM hip implants would have to submit a premarket approval (PMA) application within three months. Unless this is submitted, manufacturers may be forced to recall their MoM brands from the market. The announcement has been made as the result of a series of concerns raised by surgeons and scientists around the world over the risk of adverse events related to such implants. MoM hips traditionally entered the US market through the 510(k) approval process until 2013, when the FDA implemented a PMA requirement for MoM implants. As sales of MoM hips are already declining, the PMA requirement may further curtail the sales prospects of these products.

Need for cost effectiveness may moderately impact uptake of computer-assisted techniques in hip arthroplasty
Despite the increased adoption of computer-assisted techniques and robotic surgeries, the need for cost effectiveness remains critical across US and European hospitals. With only a limited number of clinical studies indicating the overall cost benefit of using robotic techniques for hip and knee arthroplasties, hospitals may struggle to justify the initial cost of installation. Data presented at the 2015 AAOS annual meeting indicated that the clinical benefits of robotics do not outweigh the initial costs of using the systems, at least for unicompartmental knee arthroplasty. This is also true for hip replacements: Thakkar et al. noted that current studies have not shown any long-term functional and implant benefits with the use of robotics and advanced technologies. In a scientific exhibit at the 2015 AAOS annual meeting, Thakkar’s team indicated that this technology could add an additional cost of $430–$630 per case, not including the cost of purchasing, maintaining, and training for these systems. The increased pressure on hospitals to reduce costs on joint arthroplasties is likely to enforce moderate to low adoption rates for surgical robots in hip applications.
Use of untested hip implants may have long-term implications on the success of hip replacements in UK
Analysis of data from the NJR of indicates that almost a quarter of the prosthesis brands available to surgeons in these regions are not supported by clinical evidence. It is further estimated that these untested devices are used in about 8% of the overall hip replacement procedures in England and Wales (Irvin J, 2014). A study published by Kynaston-Pearson et al. of the University Hospitals of Birmingham indicates that there is a need for an improved and more rigorous approach to the regulation of devices to avoid those with no available evidence being used in a widespread and uncontrolled manner. With the increase in adverse events, implant failures, and the need for revisions, the overall rigor with which hip implants are tested is likely to increase in the coming years.

Shortage of orthopedic surgeons may impact procedure volumes in the coming years
There has been a gradual yet steady increase in the number of orthopedic surgeons in the US over the past two decades. Formulating reliable estimates for the number of ortho-surgeons needed in the country has been challenging since the demand for joint arthroplasties has fluctuated each year. In addition, as a function of changes in practice patterns, patient demographics, the availability of physician extenders, new technology, and new payment models, the overall demand for joint arthroplasties has been challenging to size. However, as per common consensus within the orthopedic industry in the US, there is currently a shortage of orthopedic surgeons. The shortage may assume a more acute form in the future when a large pool of the older surgeons retire. At present, many older surgeons have delayed their retirement plans and are awaiting an improvement in the US economy before making this decision. The general shortage of orthopedic surgeons is also likely to be felt in the future once a higher proportion of the US population gets insurance coverage through the Patient Protection and Affordable Care Act.

Flat-rate reimbursement for joint replacement surgeries may impede the growth of high-end implants in Germany
In order to contain costs, Germany has traditionally followed a flat-rate payment system based on German diagnosis related groups (G-DRGs) and this implementation of standardized reimbursement levels on a nationwide scale has been impacting the growth of high-end joint replacement implants. For instance, hip
replacement surgery anywhere across Germany would cost the same; however, the cost of the implant is the most important component behind the varying degree of profit levels of hospitals. Cemented hip implants are typically priced lower than uncemented ones, thus the distribution of cemented, uncemented, and partially cemented hip implants was observed to be uneven and hospital administrators across many hospitals have started opting for cheaper implants to raise profit margins. In many cases where patients do not pay out-of-pocket for hip implants, hospitals may settle for cheaper implants, thereby negatively impacting the sales of high-end products.

**Postcode lottery and rationing of essential clinical treatments by CCGs likely to restrict the procedural volume growth of hip replacement surgeries in UK**

In the UK, patient access to health and medical services may depend on the area or locale they live in. After the formal establishment of the NHS and clinical commissioning groups (CCGs), the new commissioners of a few CCGs have been observed to be rationing essential clinical treatments. Although 60% of patients suffering painful conditions of the hip joint are reported to exhibit sustained improvement over 12 months, hip replacement is a common surgical treatment (van der Waal et al., 2006). NICE and the Royal College of Surgeons (RCS) guidelines do not recommend thresholds such as pain “score” (among others) as a criterion for conducting the surgery. However, with the intention of limiting over-commissioning of hip replacement procedures, a few CCGs in the UK follow arbitrary referral criteria that limit patients undergoing the procedure. Of the 52 CCGs operating in the UK, 14 (29%) had no policy in place that governed or standardized referral practice. On the other hand, 23 CCGs (44%) had referral criteria, such as amount of pain score or body mass index before the surgery, which governed the number of patients receiving referral for a hip replacement procedure. For instance, the policies of the CCGs NHS Mid Essex and NHS Stoke on Trent mandate an assessed hip score of ≥20 for any hip replacement referrals to be accepted. The inclusion of such restricting criteria that differs from evidence-based guidelines such as NICE and RCS is likely to restrict commissioning policies and referrals, thereby impacting patient access to such procedures. While NHS Scotland has been able to reduce the postcode lottery for hip replacement surgeries, policies in some CCGs in England are yet to be overhauled.
Inequalities in the use of THA for hip fractures and a lack of skilled surgeons may hinder procedural growth in the UK

Based on a large, nationwide observational study conducted with hip fracture patients, an unexplained variation in the use of THA was observed. Between 1 July 2011 and 31 April 2015, the National Hip Fracture Database (NHFD) recorded a total of 248,013 patients with hip fractures. Although 21,193 patients satisfied the NICE criteria to undergo THA, only 11,683 within the NHFD actually underwent the surgery. Despite NICE recommendations around inclusion criteria for THA in patients with hip fracture, poor compliance to the guidelines is deemed to be the reason for this unexplained variation in the use of THA. Another probable barrier that may hinder the utilization of THA to its full potential is the lack of experienced hip surgeons in the UK. Owing to the high dislocation rate, need for revision surgery, post-operative complications, and mortality associated with THA when performed by low-volume surgeons, many orthopedic surgeons do not perform THA for hip fracture unless it is a part of their routine elective practice. The postcode lottery system and inconsistencies in compliance to NICE or other recommended guidelines on the part of CCGs may continue to impede the use of THA to its full potential in the UK.

Political corruption and corporate fraud around orthopedic implants in Spain likely to impact the market negatively

In 2015, news of the Sant Joan de Reus Hospital’s use of faulty and defective surgical implants as a result of pressure from city officials was released, creating a significant medical crisis in Spain. As part of the investigation, 1,700 cases were reviewed, 250 patients were called in, and about 20 cases were ordered for extraction and replacement with new implants. Faulty, defective, and expired hip, knee, and backbone implants manufactured by Traiber are speculated to have reached at least 6,000 patients in Spain, most in Catalonia, while many others live in the Valencia, Madrid, and Galicia regions. The Spanish Agency for Medicines and Health Product (Agencia Española de Medicamentos y Productos SanitariosAEMPS) further reported lack of CE marking conformity in Traiber products, which were reported to have been produced without official license.

For a market already faced with various product recalls, this incident is likely to further impact market growth negatively. Scrutiny over new product introduction and regulatory requirements are expected to heighten further, thereby increasing overall vigilance that may impact volume sales.
Owing to hip replacement scandal in France, the Medical Device Directive is likely to become stricter, impacting the arthroplasty market negatively

In 2013, over 650 patients in France were fitted with hip implants without a European safety certification (Henry S, 2013). Since the implant underwent slight modifications, the manufacturer did not find it necessary to go through the two-year approval process. Although physicians believed that the non-certified hip implants were unlikely to pose any health risk, around 1,000 artificial hips were confiscated by the French National Agency for the Safety of Medicines and Health Products (ANSM; Agence Nationale de Sécurité du Medicament et des Produits de Santé). With such fresh scandals in Spain and France, directives in the EU medical device regulatory framework are likely to become stricter before commercial and clinical use of the product.

Despite an aging population, growth of joint arthroplasty in Italy will be impeded by economic crisis and cuts on healthcare spends

Characterized by a low birth rate and rapidly aging population, Italy has the highest proportion of population (21%) in the age group of 65 years and above compared to the other four major EU markets. This has meant that the requirement for various joint arthroplasties has been burgeoning. At the same time, the age at which joint arthroplasties are indicated has been declining, further broadening the patient pool that requires arthroplasty.

However, a reduction in healthcare spending and the reimbursement rates of various implants have led to hospitals taking further cost-cutting measures. Furthermore, over 55% of the population aged over 55 years are women, for whom the prevalence of osteoarthritis and requirement for joint arthroplasty is reported to be higher. While the number of patients requiring arthroplasty is increasing, the economic burden on the Italian national health system has been mounting, leading to cost pressures and the utilization of cheaper implants in various hospitals.

2.6 Market Drivers for Hip Arthroplasty

Cost pressures in Germany leading to increased adoption of day surgeries for hip arthroplasty

There has been a significant increase in the number of hip arthroplasty procedures in Germany in recent years. The demand for this procedure, coupled with increased expenses including high implant and hospitalization costs, have led the German authorities to investigate cost-cutting measures. Over 230,000 hip replacements
(including revision surgeries) are conducted in Germany every year. The average reimbursement for these surgeries by statutory health insurance corresponds to about €7,626 (approximately $8,500), representing an overall spend of over €1.6 billion, or more than 2.5% of the total cost of inpatient hospital care in the country. Consequently, there is an increased focus on reducing the overall hospital stay as well as the time taken to conduct hip replacement surgeries in Germany. This is likely to promote the growth of hip arthroplasties in the outpatient setting. With high surgery volumes, surgeons are likely to have limited time for adequate training on new techniques for hip replacement; however, the need for cost-effective and time saving techniques (including positioning of implants and pain management) will continue to grow in hip arthroplasty procedures.

Value-added channel strategies aiding market growth

With the US and European markets demonstrating limited growth opportunities, hip implant manufacturers have been devising various strategies to improve sales. Providing value-added solutions and services to hospitals is one such strategy. In late 2014, Smith & Nephew announced a disruptive orthopedic supply chain model aimed at providing increased value and efficiency to hospitals performing hip and knee surgeries. Known as Syncera, the software platform helps to improve training time for surgeons and OR staff and reduce costs related to instrument sterilization. Smith & Nephew claims that by using Syncera, a hospital performing an average of 400 hip and knee arthroplasties over a three-year period can realize savings worth $4 million. Such innovative channel strategies are helping to create sticky relationships with major hospitals while providing additional value to the users of hip and knee implants.

Robot-assisted surgeries to aid growth of hip replacement procedures

In recent years, there has been a significant increase in the usage of computer-assisted robotic techniques in joint arthroplasty (Derar H. & Shahinpoor M., 2015). Already an existing modality in knee replacements, robotic surgeries are gradually gaining a foothold in hip arthroplasty surgeries too. These techniques utilize digital imaging systems to accurately map the position of surgical instruments in relation to anatomical landmarks, thus helping to obtain reproducible placements of the hip implants. Hip implant manufacturers are looking to tap this opportunity aggressively and are reaching out to an increasing number of surgeons with their robotic surgery offerings. In 2015, Stryker received a 510(k) clearance to use its Mako system for THR surgeries. As part of its long-term strategy, the company plans to make medical
robotics that will be adopted by hospitals due to the compatibility of the equipment with Stryker’s joint implants. With benefits such as the ability to perform hip arthroplasty with a muscle-sparing approach, the use of robotic techniques in hip arthroplasty is expected to increase in coming years.

**Upcoming disruptive innovations in hip replacement implants may aid procedural outcomes**

While hip implants have improved over the years in terms of their overall benefits and the biomaterials used, innovation has been largely incremental across various generations of implants. However, one of the upcoming innovations in hip implants is focusing on overhauling the hip implant design itself. The HIT Hip Replacement System (HRS) by Hip Innovation Technology is an upcoming development with a disruptive implant design. The HRS system is a conventional metal-on-polyethylene hip system with the usual components of a hip implant, including a femoral stem, an acetabular cup, and a cobalt-chrome ball within a polyethylene liner. However, the system differentiates itself with the unique placement of the ball on the acetabular cup instead of the femoral stem. During mechanical motion, the edge of the femoral cup interlocks within the space situated between the acetabular ball and the acetabular cup. This helps minimize the risk of dislocation at extended ranges of motion on all planes.

The HRS system is aimed at reducing some of the key complications related to THA. Central to this is the issue of dislocation of joints wherein the femoral head or ball dislodges from the acetabular cup. It is estimated that dislocation rates could be as high as 10% after primary surgeries and up to 25% after revision surgeries (Jens D, 2014). With its unique design, the HRS system aims to provide a greater range of motion across all planes, thereby increasing hip stability. This is expected to be advantageous compared to traditional methods, such as elevated rim liners, reorientation of implants, and abductor repair.

The HRS system also looks to address one of the key challenges associated with component positioning: by offering higher abduction angles and anteverted cups, it is expected to allow higher variability of component placement. The overall design would compensate for suboptimal positioning and help maintain range of motion and stability while reducing the likelihood of impingement. In addition to the other advantages of the HRS system, the optimal surface area contact between the acetabular ball and the femoral cup is likely to help eliminate edge loading.
Reduced waiting lines for elective surgeries in the UK to propel procedural volume of joint replacement surgeries

Waiting lines for hip and knee replacement surgeries in the UK have traditionally been high. The average waiting time for a patient requiring hip replacement may vary from 80–90 days and knee replacement times vary from 90–100 days (Luigi S et al., 2011). However, recent waiting lines for elective procedures such as hip and knee replacement have progressively reduced. Attributed to a range of policy initiatives—including higher spending, waiting-times target schemes, and incentive mechanisms—the NHS has been able to provide prompt services to many patients requiring joint replacement. Although discredited by many, a few hospitals in the UK have begun “self-pay” replacement surgeries with costs similar to private hospitals. While the NHS patients are prioritized, patients willing to pay for such a service could undergo the procedure within a week. Thus, similar schemes that ensure profits are reinvested in the hospitals’ infrastructures are likely to further reduce the waiting lines and any associated complications caused by the deteriorating health of patients.

Innovative implants and minimally invasive surgeries to pave way for growth in total hip replacement surgeries in Germany

With a prevalence of 287 surgeries per 100,000 population, Germany accounts for the second highest rates of hip replacement surgeries in Europe (OECD, 2014). Germany is traditionally known as an early adopter of new technology and minimally invasive hip replacement surgery has been gaining relevance. Associated with a reduced length of stay and better clinical outcomes, minimally invasive procedures currently account for one-third of the THRs performed in the country. Moreover, Germany provides a congenial environment for the innovation and introduction of new implants. These factors, coupled with the country’s experienced surgeons and technical improvements, have meant that hip replacement surgeries have been gaining impetus.

Growth of MAASH technique, coupled with relatively low cost of hip replacement, is likely to drive medical tourism in Spain

Traditionally, there are two main challenges associated with hip replacement surgery: dislocation of the joint and dissymmetry in the lower extremities. In order to eliminate the occurrence of dislocation, provide surgeons with a better opportunity to restore leg length, and optimize the acetabular cup position, a recently developed technique known as modified anterolateral approach for stable hip (MAASH) has
been gaining relevance. Developed by three doctors—Felipe G Delgado, Albert Broch, and Antoni Salvador at the Hospital de Sant Celoni in Spain—the MAASH technique is a modification of the classical Hardinge approach. MAASH incorporates a capsular incision that assures good exposure while maintaining adequate capsule integrity in closure. This soft tissue sparing technique preserves the function of the ligament and supports the speedy recovery of the patient. While the traditional technique takes six months for a full recovery, with the MAASH technique patients can resume work within two weeks. Courses are being disseminated by the developers on a global platform for other surgeons to propagate this technique further. The cost of hip and knee replacement in Spain is almost one-quarter that of the corresponding costs in the US; therefore, this technique, along with the cost advantage, is likely to boost medical tourism for hip replacement in Spain.

**Standardized implant database for product identification likely to facilitate further research in joint arthroplasty implants in Germany**

Although many countries have begun developing large, robust arthroplasty registries to gauge which implants have inferior performance, most countries follow paper-based models with codes affixed to a particular implant name used in an individual patient. While this scheme facilitates research around the failure of specific implants, failure in a design type may go unnoticed. Thus, to ensure speedy documentation and future analysis of implant components and designs, the German arthroplasty registry introduced an innovative standardized implant database system. Enabled by on-site barcode scanning of implant components using a detailed standardized classification describing arthroplasty components, this registry tool is likely to pave the way for future research and innovation in implant designs and biomaterials. The implant database is typically scrutinized based on completeness of components by algorithms and real-time data. With 38,000 items in the database, all classified by the manufacturers as per a pre-defined scheme and component description, this registry tool may set a trend for other countries to follow. Maintained by manufacturers, the registry allows classification of implant components based on a pre-defined algorithm that facilitates sophisticated analysis of implant design, features, material, and other characteristics regardless of brand or manufacturer.
2.7 Products

2.8 Market Forecast
The global hip arthroplasty implants market was valued at approximately $6.4 billion in 2015 and is expected to grow at a CAGR of 2.9%, reaching approximately $7.3 billion by 2020. Exhibit 2-8 presents the global combined market forecast for hip arthroplasty implants by country/region for the years 2015 through 2020. Exhibits 2-9 through 2-14 present the market forecasts for hip arthroplasty implants by individual countries for the years 2015 through 2020.

2.9 Competitors
In 2015, Zimmer was the market leader for hip implants in US with an estimated market share of 26%. Some of Zimmer’s most popular product brands in the region include the M/L Taper Hip Prosthesis, Taperloc Hip System, Arcos Modular System, Continuum Acetabular System, and G7 Acetabular System. The company’s overall sales volume increased in 2015 in comparison to the previous year as a result of the merger with Biomet. This merger is likely to bring tangible benefits to the company’s overall market shares in the hip and knee implant markets in coming years.

DePuy Synthes is the second largest competitor in the hip arthroplasty implant market, with an approximate US market share of 21%. Overall sales of DePuy Synthes’ hip implants have declined by 2.6% globally from the previous year (2014) due to negative currency impacts. Despite the setback, the company demonstrated operational growth driven by the sales of its hip primary stem platform in 2015.

In 2015, Stryker commanded an approximate US market share of 20%.
### Exhibit 2-8: Global Hip Arthroplasty Implant Sales by Country/Region, Combined Market Forecast, 2015–20

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>$3,150.0m</td>
<td>$3,231.6m</td>
<td>$3,315.4m</td>
<td>$3,398.8m</td>
<td>$3,481.9m</td>
<td>$3,562.8m</td>
<td>2.5%</td>
</tr>
<tr>
<td>Europe</td>
<td>1,271.1</td>
<td>1,276.9</td>
<td>1,282.4</td>
<td>1,288.1</td>
<td>1,293.3</td>
<td>1,298.2</td>
<td>0.4%</td>
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<tr>
<td>Rest of the World</td>
<td>1,928.9</td>
<td>2,021.5</td>
<td>2,120.5</td>
<td>2,226.5</td>
<td>2,337.9</td>
<td>2,457.1</td>
<td>5.0%</td>
</tr>
<tr>
<td>Total hip implant sales</td>
<td>$6,350.0m</td>
<td>$6,529.9m</td>
<td>$6,718.3m</td>
<td>$6,913.4m</td>
<td>$7,113.4m</td>
<td>$7,318.1m</td>
<td>2.9%</td>
</tr>
</tbody>
</table>

Notes: System sales for Europe include product sales in Germany, France, Italy, the United Kingdom, and Spain. The Rest of the World segment includes product sales from Africa, the Middle East, Asia-Pacific, Europe, and North and South America and excludes product sales for Germany, France, Italy, the United Kingdom, Spain, Japan, and the United States. Figures may not calculate due to rounding.
Notes: System sales for Europe include product sales in Germany, France, Italy, the United Kingdom, and Spain. The Rest of the World segment includes product sales from Africa and the Middle East, Asia-Pacific, Europe, and North and South America and excludes product sales for Germany, France, Italy, the United Kingdom, Spain, Japan, and the United States.

Sources: Company financials; Meddevicetracker
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</tr>
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<tbody>
<tr>
<td>Primary THA</td>
<td>$2,325.6m</td>
<td>$2,386.5m</td>
<td>$2,449.1m</td>
<td>$2,510.7m</td>
<td>$2,571.9m</td>
<td>$2,630.4m</td>
<td>2.5%</td>
</tr>
<tr>
<td>Cemented</td>
<td>66.8</td>
<td>66.7</td>
<td>66.7</td>
<td>66.6</td>
<td>66.5</td>
<td>66.5</td>
<td>-0.1%</td>
</tr>
<tr>
<td>Cementless</td>
<td>1,959.7</td>
<td>2,008.7</td>
<td>2,058.9</td>
<td>2,108.3</td>
<td>2,156.8</td>
<td>2,202.1</td>
<td>2.3%</td>
</tr>
<tr>
<td>Hybrid</td>
<td>299.1</td>
<td>311.1</td>
<td>323.5</td>
<td>335.8</td>
<td>348.6</td>
<td>361.8</td>
<td>3.8%</td>
</tr>
<tr>
<td>Partial Hip Arthroplasty</td>
<td>395.7</td>
<td>404.0</td>
<td>412.5</td>
<td>421.2</td>
<td>430.0</td>
<td>439.0</td>
<td>2.1%</td>
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<tr>
<td>Hip Resurfacing</td>
<td>49.5</td>
<td>50.5</td>
<td>51.5</td>
<td>52.5</td>
<td>53.6</td>
<td>54.7</td>
<td>2.0%</td>
</tr>
<tr>
<td>Revision Hip Arthroplasty</td>
<td>379.2</td>
<td>390.6</td>
<td>402.3</td>
<td>414.4</td>
<td>426.4</td>
<td>438.7</td>
<td>2.9%</td>
</tr>
<tr>
<td><strong>Total Hip Arthroplasty Sales</strong></td>
<td><strong>$3,150.0m</strong></td>
<td><strong>$3,231.6m</strong></td>
<td><strong>$3,315.4m</strong></td>
<td><strong>$3,398.8m</strong></td>
<td><strong>$3,481.9m</strong></td>
<td><strong>$3,562.8m</strong></td>
<td><strong>2.5%</strong></td>
</tr>
</tbody>
</table>

**Notes:** THA = total hip arthroplasty. Figures may not calculate due to rounding.

**Sources:** Company financials; Meddevicetracker
### Exhibit 2-10: Hip Arthroplasty—United Kingdom, Market Forecast, 2015–20

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary THA</td>
<td>$171.6m</td>
<td>$173.2m</td>
<td>$174.5m</td>
<td>$175.8m</td>
<td>$176.9m</td>
<td>$178.1m</td>
<td>0.7%</td>
</tr>
<tr>
<td>Cemented</td>
<td>26.4</td>
<td>26.0</td>
<td>25.6</td>
<td>25.2</td>
<td>24.8</td>
<td>24.5</td>
<td>-1.5%</td>
</tr>
<tr>
<td>Cementless</td>
<td>114.0</td>
<td>115.6</td>
<td>117.0</td>
<td>118.4</td>
<td>119.6</td>
<td>120.8</td>
<td>1.1%</td>
</tr>
<tr>
<td>Hybrid</td>
<td>31.3</td>
<td>31.6</td>
<td>31.9</td>
<td>32.2</td>
<td>32.5</td>
<td>32.9</td>
<td>1.0%</td>
</tr>
<tr>
<td>Partial Hip Arthroplasty</td>
<td>30.9</td>
<td>31.2</td>
<td>31.5</td>
<td>31.8</td>
<td>32.1</td>
<td>32.4</td>
<td>1.0%</td>
</tr>
<tr>
<td>Hip Resurfacing</td>
<td>1.1</td>
<td>1.1</td>
<td>1.1</td>
<td>1.1</td>
<td>1.1</td>
<td>1.2</td>
<td>1.1%</td>
</tr>
<tr>
<td>Revision Hip Arthroplasty</td>
<td>19.2</td>
<td>19.3</td>
<td>19.4</td>
<td>19.5</td>
<td>19.6</td>
<td>19.7</td>
<td>0.5%</td>
</tr>
<tr>
<td><strong>Total Hip Arthroplasty Sales</strong></td>
<td><strong>$222.8m</strong></td>
<td><strong>$224.7m</strong></td>
<td><strong>$226.5m</strong></td>
<td><strong>$228.2m</strong></td>
<td><strong>$229.8m</strong></td>
<td><strong>$231.4m</strong></td>
<td><strong>0.7%</strong></td>
</tr>
</tbody>
</table>

Notes: THA = total hip arthroplasty. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker

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</tr>
</thead>
<tbody>
<tr>
<td>Primary THA</td>
<td>$220.0m</td>
<td>$221.3m</td>
<td>$222.7m</td>
<td>$224.1m</td>
<td>$225.4m</td>
<td>$226.5m</td>
<td>0.6%</td>
</tr>
<tr>
<td>Cemented</td>
<td>64.5</td>
<td>63.5</td>
<td>62.6</td>
<td>61.6</td>
<td>60.6</td>
<td>59.5</td>
<td>-1.6%</td>
</tr>
<tr>
<td>Cementless</td>
<td>131.4</td>
<td>134.1</td>
<td>136.8</td>
<td>139.5</td>
<td>142.1</td>
<td>144.7</td>
<td>1.9%</td>
</tr>
<tr>
<td>Hybrid</td>
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<td>23.7</td>
<td>23.3</td>
<td>23.0</td>
<td>22.6</td>
<td>22.3</td>
<td>-1.5%</td>
</tr>
<tr>
<td>Partial Hip Arthroplasty</td>
<td>35.1</td>
<td>35.5</td>
<td>35.8</td>
<td>36.2</td>
<td>36.5</td>
<td>36.9</td>
<td>1.0%</td>
</tr>
<tr>
<td>Hip Resurfacing</td>
<td>1.6</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>1.0%</td>
</tr>
<tr>
<td>Revision Hip Arthroplasty</td>
<td>45.0</td>
<td>45.5</td>
<td>46.0</td>
<td>46.5</td>
<td>47.0</td>
<td>47.5</td>
<td>1.0%</td>
</tr>
<tr>
<td>Total Hip Arthroplasty Sales</td>
<td>$301.8m</td>
<td>$303.9m</td>
<td>$306.2m</td>
<td>$308.5m</td>
<td>$310.6m</td>
<td>$312.6m</td>
<td>0.7%</td>
</tr>
</tbody>
</table>

Notes: THA = total hip arthroplasty. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
### Exhibit 2-12: Hip Arthroplasty—Germany, Market Forecast, 2015–20

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary THA</td>
<td>$328.7m</td>
<td>$328.6m</td>
<td>$328.5m</td>
<td>$328.3m</td>
<td>$328.1m</td>
<td>$327.7m</td>
<td>-0.1%</td>
</tr>
<tr>
<td>Cemented</td>
<td>93.3</td>
<td>92.0</td>
<td>90.7</td>
<td>89.4</td>
<td>88.1</td>
<td>86.7</td>
<td>-1.5%</td>
</tr>
<tr>
<td>Cementless</td>
<td>178.3</td>
<td>180.1</td>
<td>181.7</td>
<td>183.4</td>
<td>185.0</td>
<td>186.5</td>
<td>0.9%</td>
</tr>
<tr>
<td>Hybrid</td>
<td>57.1</td>
<td>56.6</td>
<td>56.1</td>
<td>55.6</td>
<td>55.1</td>
<td>54.6</td>
<td>-0.9%</td>
</tr>
<tr>
<td>Partial Hip Arthroplasty</td>
<td>27.1</td>
<td>27.3</td>
<td>27.4</td>
<td>27.5</td>
<td>27.7</td>
<td>27.8</td>
<td>0.4%</td>
</tr>
<tr>
<td>Hip Resurfacing</td>
<td>2.2</td>
<td>2.2</td>
<td>2.2</td>
<td>2.2</td>
<td>2.3</td>
<td>2.3</td>
<td>0.5%</td>
</tr>
<tr>
<td>Revision Hip Arthroplasty</td>
<td>54.0</td>
<td>54.3</td>
<td>54.5</td>
<td>54.9</td>
<td>55.2</td>
<td>55.5</td>
<td>0.6%</td>
</tr>
<tr>
<td><strong>Total Hip Arthroplasty Sales</strong></td>
<td><strong>$412.0m</strong></td>
<td><strong>$412.4m</strong></td>
<td><strong>$412.6m</strong></td>
<td><strong>$413.0m</strong></td>
<td><strong>$413.2m</strong></td>
<td><strong>$413.3m</strong></td>
<td><strong>0.1%</strong></td>
</tr>
</tbody>
</table>

Notes: THA = total hip arthroplasty. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary THA</td>
<td>$138.7m</td>
<td>$139.3m</td>
<td>$139.9m</td>
<td>$140.6m</td>
<td>$141.2m</td>
<td>$141.9m</td>
<td>0.5%</td>
</tr>
<tr>
<td>Cemented</td>
<td>10.0</td>
<td>9.8</td>
<td>9.6</td>
<td>9.5</td>
<td>9.3</td>
<td>9.1</td>
<td>-1.9%</td>
</tr>
<tr>
<td>Cementless</td>
<td>108.7</td>
<td>109.7</td>
<td>110.6</td>
<td>111.6</td>
<td>112.6</td>
<td>113.7</td>
<td>0.9%</td>
</tr>
<tr>
<td>Hybrid</td>
<td>20.0</td>
<td>19.8</td>
<td>19.7</td>
<td>19.5</td>
<td>19.3</td>
<td>19.1</td>
<td>-0.9%</td>
</tr>
<tr>
<td>Partial Hip Arthroplasty</td>
<td>28.4</td>
<td>28.5</td>
<td>28.6</td>
<td>28.7</td>
<td>28.8</td>
<td>28.9</td>
<td>0.3%</td>
</tr>
<tr>
<td>Hip Resurfacing</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.5%</td>
</tr>
<tr>
<td>Revision Hip Arthroplasty</td>
<td>27.5</td>
<td>27.8</td>
<td>28.1</td>
<td>28.4</td>
<td>28.6</td>
<td>28.9</td>
<td>1.0%</td>
</tr>
<tr>
<td><strong>Total Hip Arthroplasty Sales</strong></td>
<td><strong>$194.8m</strong></td>
<td><strong>$195.8m</strong></td>
<td><strong>$196.7m</strong></td>
<td><strong>$197.7m</strong></td>
<td><strong>$198.8m</strong></td>
<td><strong>$199.8m</strong></td>
<td><strong>0.5%</strong></td>
</tr>
</tbody>
</table>

**Notes:** THA = total hip arthroplasty. Figures may not calculate due to rounding.

**Sources:** Company financials; Meddevicetracker
### Exhibit 2-14: Hip Arthroplasty—Spain, Market Forecast, 2015–20

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary THA</td>
<td>$106.4m</td>
<td>$106.8m</td>
<td>$107.1m</td>
<td>$107.4m</td>
<td>$107.7m</td>
<td>$108.1m</td>
<td>0.3%</td>
</tr>
<tr>
<td>Cemented</td>
<td>8.3</td>
<td>8.2</td>
<td>8.1</td>
<td>8.0</td>
<td>7.8</td>
<td>7.7</td>
<td>-1.7%</td>
</tr>
<tr>
<td>Cementless</td>
<td>71.5</td>
<td>72.3</td>
<td>73.0</td>
<td>73.7</td>
<td>74.4</td>
<td>75.2</td>
<td>1.0%</td>
</tr>
<tr>
<td>Hybrid</td>
<td>26.6</td>
<td>26.3</td>
<td>26.0</td>
<td>25.8</td>
<td>25.5</td>
<td>25.2</td>
<td>-1.1%</td>
</tr>
<tr>
<td>Partial Hip Arthroplasty</td>
<td>17.2</td>
<td>17.3</td>
<td>17.4</td>
<td>17.4</td>
<td>17.5</td>
<td>17.6</td>
<td>0.5%</td>
</tr>
<tr>
<td>Hip Resurfacing</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.8%</td>
</tr>
<tr>
<td>Revision Hip Arthroplasty</td>
<td>16.0</td>
<td>15.9</td>
<td>15.8</td>
<td>15.7</td>
<td>15.6</td>
<td>15.4</td>
<td>-0.8%</td>
</tr>
<tr>
<td><strong>Total Hip Arthroplasty Sales</strong></td>
<td><strong>$139.8m</strong></td>
<td><strong>$140.1m</strong></td>
<td><strong>$140.4m</strong></td>
<td><strong>$140.7m</strong></td>
<td><strong>$141.0m</strong></td>
<td><strong>$141.2m</strong></td>
<td><strong>0.2%</strong></td>
</tr>
</tbody>
</table>

Notes: THA = total hip arthroplasty. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
Smith & Nephew is the fourth largest supplier of hip arthroplasty implants to the US market with an estimated market share of 11% in 2015. Despite the launch of collared and valgus versions of its POLARSTEM Cementless Hip Stem System, the company’s overall sales of hip implants remained flat in 2015. Smith & Nephew voluntarily removed certain smaller sizes of its Birmingham Hip Resurfacing System in 2015.

Exhibit 2-15 presents estimated sales and market share data for the leading suppliers of hip arthroplasty implants for the US market in 2015.

The competitive landscape for the European hip arthroplasty implants market is similar to that of the US. Zimmer commands the largest portion of the market, with an estimated market share of 30% in 2015. DePuy Synthes is the second largest supplier in Europe, with an estimated market share of 22%. Stryker and Smith & Nephew are the third and fourth largest suppliers of hip arthroplasty implants, with estimated market shares of 19% and 12%, respectively.

Exhibit 2-16 presents estimated sales and market share data for the leading suppliers of hip arthroplasty implants for the European market in 2015.
Exhibit 2-15: 2015, United States Hip Arthroplasty Implants Market, Share by Supplier

<table>
<thead>
<tr>
<th>Company</th>
<th>Estimated Sales</th>
<th>Estimated Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zimmer/Zimmer Biomet</td>
<td>$820.0m</td>
<td>26.0%</td>
</tr>
<tr>
<td>DePuy Synthes/Johnson &amp; Johnson</td>
<td>660.0</td>
<td>21.0%</td>
</tr>
<tr>
<td>Stryker</td>
<td>630.0</td>
<td>20.0%</td>
</tr>
<tr>
<td>Smith &amp; Nephew</td>
<td>345.0</td>
<td>11.0%</td>
</tr>
<tr>
<td>Others</td>
<td>695.0</td>
<td>22.0%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$3,150.0m</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

Notes: The “Others” category includes B. Braun Melsungen, BioPro, DJO Global, Exactech, MicroPort Scientific, and Tornier, among others. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
**Exhibit 2-16: 2015, European Hip Arthroplasty Implants Market, Share by Supplier**

<table>
<thead>
<tr>
<th>Company</th>
<th>Estimated Sales</th>
<th>Estimated Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zimmer/Zimmer Biomet</td>
<td>$380.0m</td>
<td>30.0%</td>
</tr>
<tr>
<td>DePuy Synthes/Johnson &amp; Johnson</td>
<td>280.0</td>
<td>22.0%</td>
</tr>
<tr>
<td>Stryker</td>
<td>240.0</td>
<td>19.0%</td>
</tr>
<tr>
<td>Smith &amp; Nephew</td>
<td>150.0</td>
<td>12.0%</td>
</tr>
<tr>
<td>Others</td>
<td>221.0</td>
<td>17.0%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$1,271.1m</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

Notes: Estimated sales and market share data for Europe are for France, Germany, Italy, Spain, and the United Kingdom. The “Others” category includes includes Adler Ortho, B. Braun Melsungen, Corin, DJO Global, Evolutis, FH Orthopedics, Implants International, Implantcast, JRI Orthopedics, Lima Corporate, Medacta International, MicroPort Scientific, MatOrtho, Mathys, Tornier, and Waldemar Link, among others. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
3. **KNEE ARTHROPLASTY**

After hip, knee arthroplasty is the second most common arthroplasty performed worldwide. The procedure is conducted to replace the weight-bearing surfaces of the knee joint. Total knee replacement (TKR) involves several components, including: patellar and femoral prostheses, a cruciate-sparing tibial insert, and a tibial baseplate for resurfacing. Since cemented TKR reduces the risk of revision surgery, the outcome of the procedure may be influenced by the use of bone cement. Among other factors, the type of implant used depends on the damage and deformity sustained by the joint, age, and health status of the patient, anatomy of the joint, and condition of the ligaments.

3.1 **Indications for Knee Arthroplasty**

The human knee has three major compartments: the medial femorotibial, the lateral femorotibial, and the patellofemoral. Osteoarthritis (OA) or injury to one or all of the three compartments may have a damaging effect on the knee joints. While the associated pain can be treated using certain nonsurgical techniques, pain management may be difficult in other cases. Knee replacement/arthroplasty is performed in such cases to restore a pain-free, fully functional, and durable knee joint.

Some of the key symptoms that indicate the need for knee arthroplasty include knee pain that hinders normal activity, such as walking or climbing stairs, and pain that does not subside with rest. In addition, knee swelling that limits the bending or straightening of knees and an inability to cope with the side-effects of pain-relieving medications may also necessitate a knee arthroplasty. OA continues to be one of the key indications for knee arthroplasty, especially in people above 50 years of age. Other causes include rheumatoid arthritis, which can trigger the body’s immune system to attack the membranes in the knee and cause general damage and cartilage wear, and serious knee injury including fracture, ligament damage, and meniscus tear, which can lead to traumatic arthritis and result in the weakening of the joints. In teenagers and young adults, avascular necrosis may cause the knee bones to become soft, leading to the wearing of bone and cartilage. In addition, abnormal formation or alignment, also referred to as knock knees, may create high stress on the knee joint, causing abnormal wear.
3.2 Types of Knee Arthroplasty

Knee replacement is a surgical procedure to remove the patella (kneecap), damaged tissues, and cartilage from the knee joints, end of the femur, and tibia. The damaged parts are then replaced with an artificial knee implant.

Broadly, knee arthroplasty can be categorized as total knee, unicompartmental, and revision knee arthroplasty.

3.2.1 Total Knee Arthroplasty

A total knee arthroplasty (TKA) is required when all three compartments of the knee joint are damaged. In this procedure, a relatively large incision of about 8–12 inches is made to expose the knee joint. The bottom of the femur is then resurfaced and fitted with a prosthetic femoral head. Based on the condition of the bone the damaged part of the femur may have to be cut off. A small piece of the bone from the top of the tibia is then cut while a flat, weight-bearing metal piece is screwed to the tibial plate. A medical-grade flat plastic piece is then placed between the tibia and tibial plate to help absorb shock and allow smooth gliding of the knee. Finally, the back side of the patella facing the end of femur is resurfaced and fitted with a plastic button.

In certain specialized medical centers with state-of-the-art tools, minimally invasive TKAs are performed using an incision that is approximately 3–4 inches long. While this may lead to reduced blood loss and faster recovery, the probability of poor implant placement remains high. It is estimated that over 5% of the current population above 50 years in the US has undergone at least one replacement surgery (Losina E, 2012).

3.2.2 Unicompartmental Knee Arthroplasty

A partial or unicompartmental knee arthroplasty is performed when only one or two compartments of the knee are damaged. The surgeon attempts to spare a large majority of the healthy bones and tissues to help retain range of motion and reduce healing time. Partial knee arthroplasty may be categorized into unicompartmental, bicompartamental, or patellofemoral surgery. While the former two refer to replacement of one side and both sides of the knee respectively, the latter procedure involves replacing the end of the thigh bone with a metal implant and resurfacing the back of the kneecap.
The key advantages of unicondylar knee replacement include faster recovery, reduced post-operative pain, and lower blood loss. It is also reported that due to the retention of the healthy bone, cartilage, and ligaments, patients find the unicondylar knee replacement more natural than TKA. However, patients undergoing unicondylar knee replacement may be at risk of requiring a TKR in the future if arthritis develops in the other parts of the knee. The key complications of unicondylar knee arthroplasty include blood clots, poor joint mobility, altered leg lengths, and nerve damage.

### 3.2.3 Revision Knee Arthroplasty

Revision knee arthroplasty involves the removal of the primary implant that would have grown into the existing bone. Once the initial prosthesis is removed, it may result in reduced bone length. This can occasionally require a bone graft to be transplanted from a donor to support the new prosthesis. While a bone graft encourages new bone growth, it is a complicated procedure and requires specialized tools and advanced surgical skills.

Typically, the implants used in revision surgeries have thicker and longer stems to provide stability and to compensate for the weak ligaments and incremental bone loss caused. These implants are usually composed of four parts: the tibial component has two elements—a metal one attached directly to the bone and a plastic spacer that allows the thighbone to move over the tibia—and is used to replace the top of the tibia; the femoral component is used to replace the bottom of the femur and the groove in which the patella is located; the patellar component replaces the undersurface of the knee cap, which rubs against the thighbone; and the knee cap protects the joint while the resurfaced patellar component slides on the front of the joint.

Some of the key complications of a primary knee surgery that may warrant a revision include bone fracture, dislocation, joint pain, loosening of the implant, swelling of the joint, and a misaligned component. Osteolysis is another key contributor to the increasing number of revision knee surgeries. Wearing of the plastic component of the implant causes an attack on the body’s immune system, leading to osteolysis. With this condition, the bone in the area around the implant softens and makes it unstable.
3.3 Clinical and Market Trends in Knee Arthroplasty

Moderate to low uptake rates for gender-specific knee replacements due to lack of distinct clinical evidence

With a higher incidence of knee arthritis, women account for over two-thirds of all knee arthroplasty procedures in the US (US Department of Health and Human Services, 2005). It is also estimated that women are three times more likely to undergo knee arthroplasty than men. The growing number of knee surgeries needed in women has repeatedly prompted the orthopedic implants industry to devise innovations that cater to the customized needs of the female physiology. One such innovation is the gender-specific knee implant that aims to address the issues caused by the distinctive anterior condyle differences between the knees of men and women.

Zimmer's NexGen High-Flex knee implants are one such brand of gender-specific knee systems that cater to the specific needs of female knee arthroplasty. Even as the company advocates that the reduced anterior flange thickness leads to a more customized implant, reduced anterior knee pain, and higher success rates for women's knees, there continues to be resistance in a certain section of the industry. Proponents of a common knee implant for both genders believe that the polyethylene insert used by Zimmer may interact with the thinner condyle across a reduced contact area. This is likely to increase the corresponding contact stress. Supporters of gender-neutral knee implants also believe that the thickness of the anterior flange is not as critical a factor in the success of the procedure as is the geometry of the articular surface. It is further argued that the wider groove angle provided by gender-specific knee implants is a less important factor in promoting deep flexion than the groove itself. With limited studies and clinical evidence to create meaningful awareness, manufacturers of gender-specific knee implants will continue to face resistance from surgeons. Overall market adoption might also be negatively impacted due to the need for cost-effective solutions in the joint arthroplasty implants market.

CMS mandatory Comprehensive Care for Joint Replacement model to promote overall cost cutting

An aging population and increased incidence of OA have driven the growth of joint arthroplasty procedures in the US. In 2014, Medicare paid for more than 400,000 hip and knee replacements, at a cost of $7 billion to taxpayers for hospitalization fees alone (US Department of Health and Human Services, 2015). The average cost of
surgery, hospitalization, and recovery ranges from $16,500 to $33,000 across various regions within the US. The Centers for Medicare & Medicaid Services' (CMS’s) expenditures on total joint surgeries are expected to exceed $1.2 billion in 2016, and are anticipated to increase to $3 billion by 2020. This has prompted the CMS to impose periodic reimbursement cuts on hip and knee implant procedures. One of these reimbursement cuts was made from 2013 to 2014, where overall reimbursement rates for hip and knee procedures were reduced by 4% and 10%, respectively. However, more recently, the CMS has been looking at tighter control of long-term procedural costs for joint replacements.

In late 2015, the CMS announced its plans to commence a new program that would hold hospitals responsible for additional spending incurred during joint replacement procedures. Beginning in April 2016, the program is likely to put over 800 hospitals across 67 cities at financial risk for the cost and quality of each joint replacement procedure, including care provided outside the hospital for up to 90 days (Centers for Medicare & Medicaid Services, 2016). The program aims to plant a powerful incentive in hospitals to reduce unnecessary procedures, complications, hospital readmissions, and extended care provided in post-acute settings such as rehabilitation centers. With the CMS looking to cut costs by evaluating episodes of care rather than by curbing implant prices, overall procedural innovation may be boosted. This is also likely to ease some of the pricing pressure facing the orthopedic implant manufacturers over recent years.

**Bicruciate-retaining total knee arthroplasty to offer growth opportunities in future**

Traditional TKR implants have required the anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL) to be removed during the surgery. Bicruciate ligament retention in TKA has been evaluated over the last 50 years. It is widely acknowledged that retention of the ACL would help to improve knee kinematics, increase maximum flexion, and improve the overall function of the knee. It is further reported that a TKA that preserves the cruciate ligaments provides a stable, well-functioning knee with a low likelihood of revision at long-term follow up; however, retaining both cruciate ligaments while preserving their insertion on the tibial eminence makes the procedure more complicated and demanding. Consequently, there have been limited innovations in techniques and implants to consciously preserve cruciate ligaments.
Recently, bicruciate-retaining TKAs have presented a substantial opportunity for knee implant manufacturers, largely fueled by the limited satisfaction levels of people receiving TKA as compared with partial knee replacements. To cater to this opportunity, manufacturers have made several changes, especially in the biomaterials used. While the previous generation of bicruciates was faced with the issue of tibial tray fractures, the current generation has cobalt-chrome trays for added strength. The polyethylene used in the 1980s has been changed to vitamin E polyethylene. Biomet (now Zimmer Biomet) launched the Vanguard XP Total Knee System to help preserve the bicruciate ligaments during TKA. Blue Belt (recently acquired by Smith & Nephew) has also been developing a bicruciate-retaining system for TKAs to be launched in the next few years. Moreover, with gradual improvements in surgical techniques, it is likely that bicruciate-retaining TKAs will gain higher adoption in the coming years.

**Moderately high usage of unicondylar knee procedures despite high probability of revision**

Analysis of the various procedures recorded in the UK’s National Joint Registry (NJR), which collects information on all ankle, elbow, hip, knee, and shoulder replacement operations in England, Wales, Northern Ireland, and the Isle of Man, indicates sustained procedural volumes for unicondylar knee surgeries (NJR, 2015). Despite the high probability of revision surgeries, unicondylar knees have maintained about 8.7% of procedure volumes. It has been established that the 11-year revision rate for unicondylar replacements is higher than the revision rate of TKRs. Despite the associated risks, unicondylar replacements continue to account for the highest proportion of partial knee replacements. This is followed by patellofemoral unicompartmental knee replacements that account for 1% of the total knee replacement procedure volume in the UK. The increasing adoption of minimally invasive surgical techniques has helped to drive unicondylar knee procedures in the UK in recent years.

**Growing infection rates contributing to rise in knee revisions**

Infections at the site of a TKA can be classified into four types: type I (early post-operative), type II (late chronic), type III (acute hematogenous), and type IV (positive intraoperative cultures but clinically unapparent infection). In recent years, the rate of infection in TKA has been observed to increase. The current standard of care for late chronic infection is a two-stage revision arthroplasty. This involves the removal of
the implant and cement through debridement, the placement of an antibiotic-impregnated cement spacer, a course of intravenous antibiotics, and a delayed second-stage revision arthroplasty.

As per a study conducted by Kurtz et al. to quantify the current and historical incidence of periprosthetic infection associated with hip and knee arthroplasty in the US, the rate of infected knee arthroplasties was 0.92% (Kurtz SM, 2008). This is significantly greater than the rate of infected hip arthroplasties (0.88%). It is expected that the number of both primary and revision procedures will increase drastically in the next two decades. It is further estimated that the cost of infected revisions will be valued at $1.6 billion by 2020 (Kurtz SM, 2012). Consequently, techniques aimed at the prevention, early diagnosis, and treatment of infections in knee arthroplasty need to be continuously improved.

### 3.4 Procedure Volumes

During the forecast period covered by this report, the total number of knee arthroplasty procedures performed in the US and the five major EU markets (France, Germany, Italy, Spain, and the UK) are anticipated to expand at a compound annual growth rate (CAGR) of 4.7%, from approximately 1.4 million procedures in 2015 to an estimated 1.7 million procedures by 2020.

Exhibit 3-1 presents the combined procedure volumes forecast for knee arthroplasty procedures for the US and EU5 for the years 2015 through 2020.

Exhibit 3-2 presents the knee arthroplasty procedure volumes forecast for the US for the years 2015 through 2020; Exhibit 3-3 presents the knee arthroplasty procedure volumes forecast for the UK for the years 2015 through 2020; Exhibit 3-4 presents the knee arthroplasty procedure volumes forecast for France for the years 2015 through 2020; Exhibit 3-5 presents the knee arthroplasty procedure volumes forecast for Germany for the years 2015 through 2020; Exhibit 3-6 presents the knee arthroplasty procedure volumes forecast for Italy for the years 2015 through 2020; Exhibit 3-7 presents the knee arthroplasty procedure volumes forecast for Spain for the years 2015 through 2020.
### Exhibit 3-1: Knee Arthroplasty, Combined Procedure Volumes Forecast, 2015–20

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<tr>
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</thead>
<tbody>
<tr>
<td>United States</td>
<td>834.1</td>
<td>870.7</td>
<td>911.3</td>
<td>955.6</td>
<td>1,003.0</td>
<td>1,052.9</td>
<td>4.9%</td>
</tr>
<tr>
<td>France</td>
<td>103.8</td>
<td>108.4</td>
<td>113.1</td>
<td>118.0</td>
<td>123.1</td>
<td>128.5</td>
<td>4.3%</td>
</tr>
<tr>
<td>Germany</td>
<td>178.3</td>
<td>184.9</td>
<td>191.8</td>
<td>199.0</td>
<td>206.5</td>
<td>214.2</td>
<td>3.7%</td>
</tr>
<tr>
<td>Italy</td>
<td>70.6</td>
<td>74.0</td>
<td>77.5</td>
<td>81.2</td>
<td>85.0</td>
<td>89.1</td>
<td>4.8%</td>
</tr>
<tr>
<td>Spain</td>
<td>55.9</td>
<td>58.3</td>
<td>60.8</td>
<td>63.5</td>
<td>66.2</td>
<td>69.0</td>
<td>4.3%</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>112.1</td>
<td>118.6</td>
<td>125.4</td>
<td>132.6</td>
<td>140.3</td>
<td>148.4</td>
<td>5.8%</td>
</tr>
<tr>
<td><strong>Total knee arthroplasty procedures</strong></td>
<td><strong>1,354.8</strong></td>
<td><strong>1,414.9</strong></td>
<td><strong>1,479.9</strong></td>
<td><strong>1,549.9</strong></td>
<td><strong>1,624.1</strong></td>
<td><strong>1,702.1</strong></td>
<td><strong>4.7%</strong></td>
</tr>
</tbody>
</table>

Notes: Total knee arthroplasty procedures include primary total knee arthroplasty, unicompartmental knee arthroplasty, and revision knee arthroplasty. Procedure volumes are reported in thousands. Figures may not calculate due to rounding.
Exhibit 3-1: (Continued)

Note: Total knee arthroplasty procedures include primary total knee arthroplasty, unicondylar knee arthroplasty, and revision knee arthroplasty.

Sources: American Joint Replacement Registry; Catalan Arthroplasty Registry; Endo Prothesen Register Deutschland; Meddevicetracker; National Joint Registry of the United Kingdom; SoFCOT and Haute Autorité de Santé
## Exhibit 3-2: Knee Arthroplasty—United States, Procedure Volumes Forecast, 2015–20

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</thead>
<tbody>
<tr>
<td>Primary TKA</td>
<td>730.8</td>
<td>761.5</td>
<td>795.6</td>
<td>833.1</td>
<td>873.1</td>
<td>915.0</td>
<td>4.7%</td>
</tr>
<tr>
<td>Unicondylar Knee</td>
<td>27.3</td>
<td>28.8</td>
<td>30.4</td>
<td>32.1</td>
<td>33.9</td>
<td>35.9</td>
<td>5.7%</td>
</tr>
<tr>
<td>Revision Knee</td>
<td>76.0</td>
<td>80.4</td>
<td>85.2</td>
<td>90.4</td>
<td>96.0</td>
<td>102.0</td>
<td>6.1%</td>
</tr>
<tr>
<td><strong>Total knee arthroplasty procedures</strong></td>
<td><strong>834.1</strong></td>
<td><strong>870.7</strong></td>
<td><strong>911.3</strong></td>
<td><strong>955.6</strong></td>
<td><strong>1,003.0</strong></td>
<td><strong>1,052.9</strong></td>
<td><strong>4.9%</strong></td>
</tr>
</tbody>
</table>

Notes: TKA = total knee arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

Sources: American Joint Replacement Registry; Meddevicetracker
### Exhibit 3-3: Knee Arthroplasty—United Kingdom, Procedure Volumes Forecast, 2015–20

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</thead>
<tbody>
<tr>
<td>Primary TKA</td>
<td>97.0</td>
<td>102.8</td>
<td>109.0</td>
<td>115.5</td>
<td>122.5</td>
<td>129.8</td>
<td>6.0%</td>
</tr>
<tr>
<td>Unicondylar Knee</td>
<td>8.5</td>
<td>8.8</td>
<td>9.1</td>
<td>9.4</td>
<td>9.7</td>
<td>10.0</td>
<td>3.5%</td>
</tr>
<tr>
<td>Revision Knee</td>
<td>6.7</td>
<td>7.0</td>
<td>7.3</td>
<td>7.7</td>
<td>8.1</td>
<td>8.5</td>
<td>5.0%</td>
</tr>
<tr>
<td>Total knee arthroplasty procedures</td>
<td>112.1</td>
<td>118.6</td>
<td>125.4</td>
<td>132.6</td>
<td>140.3</td>
<td>148.4</td>
<td>5.8%</td>
</tr>
</tbody>
</table>

**Notes:** TKA = total knee arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

**Sources:** Meddevicetracker; National Joint Registry of the United Kingdom
## Exhibit 3-4: Knee Arthroplasty—France, Procedure Volumes Forecast, 2015–20

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</tr>
</thead>
<tbody>
<tr>
<td>Primary TKA</td>
<td>88.1</td>
<td>92.0</td>
<td>96.2</td>
<td>100.5</td>
<td>105.0</td>
<td>109.8</td>
<td>4.5%</td>
</tr>
<tr>
<td>Unicondylar Knee</td>
<td>8.3</td>
<td>8.6</td>
<td>8.8</td>
<td>9.1</td>
<td>9.4</td>
<td>9.6</td>
<td>3.0%</td>
</tr>
<tr>
<td>Revision Knee</td>
<td>7.5</td>
<td>7.8</td>
<td>8.1</td>
<td>9.4</td>
<td>8.7</td>
<td>9.1</td>
<td>4.0%</td>
</tr>
<tr>
<td><strong>Total knee arthroplasty procedures</strong></td>
<td><strong>103.8</strong></td>
<td><strong>108.4</strong></td>
<td><strong>113.1</strong></td>
<td><strong>118.0</strong></td>
<td><strong>123.1</strong></td>
<td><strong>128.5</strong></td>
<td><strong>4.3%</strong></td>
</tr>
</tbody>
</table>

Notes: TKA = total knee arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

Sources: Meddevicetracker; SoFCOT and Haute Autorité de Santé
### Exhibit 3-5: Knee Arthroplasty—Germany, Procedure Volumes Forecast, 2015–20

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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary TKA</td>
<td>134.1</td>
<td>139.5</td>
<td>145.1</td>
<td>150.9</td>
<td>156.9</td>
<td>163.2</td>
<td>4.0%</td>
</tr>
<tr>
<td>Unicondylar Knee</td>
<td>20.0</td>
<td>20.7</td>
<td>21.4</td>
<td>22.1</td>
<td>22.9</td>
<td>23.8</td>
<td>3.5%</td>
</tr>
<tr>
<td>Revision Knee</td>
<td>24.2</td>
<td>24.8</td>
<td>25.4</td>
<td>26.0</td>
<td>26.7</td>
<td>27.3</td>
<td>2.5%</td>
</tr>
<tr>
<td><strong>Total knee arthroplasty procedures</strong></td>
<td><strong>178.3</strong></td>
<td><strong>184.9</strong></td>
<td><strong>191.8</strong></td>
<td><strong>199.0</strong></td>
<td><strong>206.5</strong></td>
<td><strong>214.2</strong></td>
<td><strong>3.7%</strong></td>
</tr>
</tbody>
</table>

Notes: TKA = total knee arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

Sources: Endo Prothesen Register Deutschland; Meddevicetracker
### Exhibit 3-6: Knee Arthroplasty—Italy, Procedure Volumes Forecast, 2015–20

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</thead>
<tbody>
<tr>
<td>Primary TKA</td>
<td>58.6</td>
<td>61.5</td>
<td>64.6</td>
<td>67.8</td>
<td>71.2</td>
<td>74.8</td>
<td>5.0%</td>
</tr>
<tr>
<td>Unicondylar Knee</td>
<td>6.1</td>
<td>6.3</td>
<td>6.5</td>
<td>6.7</td>
<td>6.9</td>
<td>7.2</td>
<td>3.1%</td>
</tr>
<tr>
<td>Revision Knee</td>
<td>5.9</td>
<td>6.1</td>
<td>6.4</td>
<td>6.6</td>
<td>6.9</td>
<td>7.1</td>
<td>3.9%</td>
</tr>
<tr>
<td>Total knee arthroplasty procedures</td>
<td>70.6</td>
<td>74.0</td>
<td>77.5</td>
<td>81.2</td>
<td>85.0</td>
<td>89.1</td>
<td>4.8%</td>
</tr>
</tbody>
</table>

Notes: TKA = total knee arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

Sources: Italian Arthroplasty Registry (RIAP); Meddevicetracker
### Exhibit 3-7: Knee Arthroplasty—Spain, Procedure Volumes Forecast, 2015–20

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</tr>
</thead>
<tbody>
<tr>
<td>Primary TKA</td>
<td>48.3</td>
<td>50.4</td>
<td>52.7</td>
<td>55.1</td>
<td>57.6</td>
<td>60.2</td>
<td>4.5%</td>
</tr>
<tr>
<td>Unicondylar Knee</td>
<td>4.0</td>
<td>4.1</td>
<td>4.4</td>
<td>4.2</td>
<td>4.3</td>
<td>4.4</td>
<td>2.0%</td>
</tr>
<tr>
<td>Revision Knee</td>
<td>3.7</td>
<td>3.8</td>
<td>4.0</td>
<td>4.1</td>
<td>4.3</td>
<td>4.5</td>
<td>4.0%</td>
</tr>
<tr>
<td>Total knee arthroplasty procedures</td>
<td>55.9</td>
<td>58.3</td>
<td>60.8</td>
<td>63.5</td>
<td>66.2</td>
<td>69.0</td>
<td>4.3%</td>
</tr>
</tbody>
</table>

Notes: TKA = total knee arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

Sources: Catalan Arthroplasty Registry; Meddevicetracker
3.5 Industry Challenges for Knee Arthroplasty

Demand for warranties putting additional pressure on knee implant manufacturers

With an increasing number of product recalls and implant failures, there is a growing demand within patient communities for higher assurances of safety to be made by manufacturers. Furthermore, as the cost of revision procedures increases, higher transparency around product longevity is being sought. As a result, there has been a significant increase in the number of patients filing petitions seeking warranties from implant manufacturers. Proponents of warranties for large joint implants believe that since the US Food and Drug Administration (FDA) does not primarily rely on pre-market safety testing for these products, there is no standardized way to trace implant performance.

With only one manufacturer offering a warranty for its partial knee implant, there is added pressure on other original equipment manufacturers to address this issue. Certain hospitals such as Seattle's Virginia Mason Medical Center have started offering warranties to privately insured patients that cover avoidable complications stemming from total joint replacements. Unless the number of procedural complications and revision rates reduce, the demand for warranties may continue in countries such as the US before spreading to other regions.

Revision knee procedures leading to increased financial burden

Revision knee surgeries have been documented to have higher complication rates and poorer functional outcomes than primary knee arthroplasty. In addition to the increased cost of perioperative investigations, blood transfusions, surgical instrumentation, implants, and operating time, there is a well-documented increase in the length of stay for revision surgeries, which accounts for most of the actual costs associated with surgery (Lavernia C, 2006). Several clinical studies have reported that revision knee surgeries consume increased surgeon time and effort, and require a longer operating time and length of stay (Kallala RF, 2015). Despite innovations in knee implants, such as the personalized approach of implant selection and design, the inability to improve success rates beyond 90% remains a significant roadblock. Several studies also indicate that with declining surgical and hospital reimbursement rates for revision knee procedures, hospitals have failed to fully cover the costs associated with TKA revision. While the length of hospital stay for knee revision surgeries has been decreasing, the costs associated with the overall
surgery have been on the rise. This is likely to continue impeding the growth of knee arthroplasties, especially in the US and Europe.

**Increased number of knee implant recalls impeding safety assurances for patients**

It is estimated that over 4.5 million people in the US are currently living with knee implants (American Academy of Orthopedic Surgeons, 2012). Over 700,000 knee implant procedures are performed each year in the US. It is further estimated that over 500,000 adults currently living with knee implants have undergone revision surgeries. Even as the number of overall knee replacements and revision procedures increases, safety assurances to protect patients remain limited. It has been observed that between 2002 and 2013, around 709 product recalls were made by the top six knee implant manufacturers (Consumers Union Report, 2016). While almost all of these recalls were made voluntarily by the manufacturers, the FDA has exercised its recall authority three times over the past two decades.

Approximately 75 of the 709 knee recalls between 2002 and 2013 were attributed to Biomet implants, and all of the class II recalls were primarily due to sizing issues, improper assembly, and missing features. Smith & Nephew only had 11 recalls attributed to packaging and labeling issues, while Wright Medical Group had four class II recalls. Stryker made about 118 recalls in the same period. A majority of the recalled devices were implants rather than procedural devices. The key reasons for Stryker’s knee recalls included damaged components, disassociation, mislabeled components, component seizure, early wear, and delamination. Zimmer contributed 224 of the 709 knee recalls during this period. A majority of the recalls were attributed to faulty design, mislabeled components, manufacturing issues, missing components, implant loosening, and sterility issues. Of all the knee implant manufacturers, DePuy Synthes had the highest number of recalls between 2002 and 2013. The company recalled 477 devices or components, most of which were class II recalls. These implants were recalled primarily due to possible fracturing, sizing issues, metal debris, and assembly difficulties.

**Long length of stay associated with lower limb arthroplasty in the UK likely to impact the joint implants market negatively**

The optimal length of stay post-surgical intervention is important in driving patient care and clinical outcomes. However, in the UK the length of stay associated with lower limb arthroplasty is reported to be notably high. According to a recently
conducted study, most knee replacement patients remained in the hospital for a period of five to eight days without any identified morbidity (Elizabeth A et al., 2015). This inappropriate bed occupancy following lower limb arthroplasty is attributed to physiotherapy and occupational therapy. The longer hospital stay post-surgery is likely to result in an increase in the cost associated with the procedure. As a consequence, in order to control the overwhelming cost of healthcare, stringent criteria could be imposed on the referral of patients for knee replacement surgeries. This will further impact patient access to hip replacement surgeries, leading to a decline in the number of procedures performed each year. Moreover, in a bid to reach a majority of patients requiring surgery, the National Health Service may look to negotiate implant costs, impacting the market detrimentally.

**Innovation in subdermal implant in Italy to potentially limit TKR surgeries to patients in acute need**

An innovation in minimally invasive subdermal implants, known as the KineSpring Knee Implant System, may reduce the number of patients requiring TKR in the coming years. To be implanted directly on the bones of the knee, this device is expected to bring about natural knee movement, reduce leg load by up to 13 pounds, provide pain relief up to a threshold of 80%, and recover movement in approximately six weeks. With no damage to ligaments, cartilage, or adjacent bones, the device can be implanted in the subcutaneous tissue without altering the normal anatomy. Implantable in less than an hour, the KineSpring implant is expected to postpone the need for TKR in many patients. Having been successfully implanted in 750 patients, this system could be absorbed into routine practice as an option to be utilized after the failure of conservative management of OA of the knee. The commercial introduction of this device is likely to reduce the burgeoning cost burden associated with total joint arthroplasty and its associated revision surgeries (David AH, 2015).

### 3.6 Market Drivers for Knee Arthroplasty

**Robotic surgeries to continue driving sales of knee implants**

The increasing awareness of the overall accuracy and precision of implant placement in robotic knee replacements has been a key trend impacting the sales of knee implants in recent years. Several studies conducted across multiple centers indicate robotic surgery promotes higher accuracy in femoral rotational alignment compared to conventional surgery. It is also observed that surgeons using
robot-assisted techniques for knee replacements need not be highly experienced in these techniques to achieve superior results; the use of such technologies aids better surgical decisions by providing more data, thus making the process more predictable and repeatable. With robotic surgeries reducing the dependence of procedural outcomes on the expertise of surgeons, the long-term outcomes of knee replacements are likely to improve. Consequently, implant manufacturers have started focusing on making their implant offerings more comprehensive by adding robotic surgery capabilities to their portfolio.

In early 2016, Smith & Nephew announced the completion of its acquisition of Blue Belt Holdings, Inc. The company paid a significantly high premium for this acquisition, amounting to around $275 million. As a result of this deal, Smith & Nephew will have access to the Navio Surgical System, which currently provides robotic assistance in unicompartmental knee surgeries using CT-free navigation software and a hand-held robotic bone-shaping device. To strengthen its portfolio, the company is likely to invest in an R&D program to expand the Navio platform into total knee, bicondylar-retaining knee, and revision knee implants. As part of these plans, it is likely that a system for TKR will be launched in 2017 to augment sales of Smith & Nephew’s Journey II Total Knee Implant. Over a period of time, the company’s robotic-assistance systems are also likely to expand to total hip replacements. Stryker is another key market participant to have augmented its implants portfolio by acquiring Mako’s RIO system in 2013. In Q3 2015, Stryker announced its intentions to launch Mako’s system for TKRs in 2016. The launch has now been postponed to 2017 to address the need for detailed training protocols among other reasons. Johnson & Johnson’s subsidiary DePuy Synthes has also announced a collaboration with Brainlab AG to develop a knee navigation system to improve the procedural outcomes of knee replacement surgeries. With companies looking to aggressively target robotic surgery in knee arthroplasty, the overall market for knee implants is likely to benefit from the precision and distinct clinical benefits it promotes. Even though constraints such as bringing capital spending budgets into orthopedics remain, the delivery of consistent outcomes by robotic technologies will help to accelerate uptake of these systems in the future.

Need for personalized implants and approaches to drive knee replacements in long term
The increasing demand for tighter surgical fit has made manufacturers of knee implants acknowledge the need for patient-centric implant designs. In response to
such demands, various implant manufacturers have made small yet incremental moves to launch personalized implants. Zimmer introduced its Persona Knee System with the aim of supplying surgeons with varying sizes of implants to help them select the most precise implant size. An increasing number of manufacturers have also started providing cutting blocks that can be used during surgeries to guide the surgeon’s hands. New market entrants such as ConforMIS have also tapped this opportunity to develop personalized total and partial knee systems that follow the shape and contour of individual patients. This individualized approach is likely to help improve the overall satisfaction levels of patients who have undergone knee replacement.

**Increased demand among younger patients aiding procedural growth**

With the advent of new surgical technologies and improved implant materials, TKAs promise a better quality of life. An increasing number of young patients with knee pain perceive knee surgery to be a successful procedure resulting in improved mobility and reduced pain. Consequently, the number of knee replacement procedures in the US has increased from 250,000 in 2000 to over 700,000 in 2015 currently (AJRR, 2015). As per a study conducted by the American Academy of Orthopaedic Surgeons, the number of knee replacements in patients aged between 45 and 64 years increased by 205% between 2000 and 2012 (Centers for Disease Control and Prevention's National Center for Health Statistics). In contrast, the increase in people aged over 65 years was only 95% during the same period. Although various studies such as the one published by researchers at Virginia Commonwealth University in Richmond indicate that knee replacements are appropriate for only those whose arthritis in the knee is medically advanced, the adoption of knee surgeries in younger people continues to rise.

**Need for advanced technologies driving adoption rates in hospitals**

With the aim to attract an increasing number of patients for elective procedures such as knee implants, hospitals are looking to promote their technical superiority directly to patients. In recent years, an increasing number of hospitals have been looking to employ innovations such as medical robotics in their marketing campaigns to attract patients. It has been observed that various hospitals promote their robotic arms directly to consumers, using billboards and other methods. Certain hospital officials in the US believe that such marketing could draw enough new patients (at least 100 would be needed, generating an average of $8,900) to cover the nearly $1 million cost of the robotic systems (Pharma Intelligence, Informa, 2015). While hospitals are
typically hesitant to pay for incremental innovation in knee implants, they perceive
the high value of innovations such as medical robotics that may drive procedural
growth.

**Minimum volume standards for knee replacement procedures in Germany expected to drive better clinical outcomes**
In 2004, the German healthcare system introduced minimum volume standards in
hospitals for five procedures: complex esophageal and pancreatic interventions, and
liver, kidney, and stem cell transplantations (de Cruppé, W, 2007). In 2006, knee
replacement surgery was added to the list, mandating a minimum of 50 procedures
per year per hospital. In a bid to bring about the centralization of certain procedures
and drive higher clinical outcomes, this regulation was passed. A multivariate
analysis performed by Meyer et al. (2011) established that hospitals performing
fewer than 50 knee replacement surgeries in a year were more susceptible to higher
surgical site infection (SSI) rates. SSI rates at centers with higher surgical volume
was purported to be lower. However, after the promulgation of this directive, the
centralization of knee replacement surgeries has been indiscernible. In 2010, only
8.3% of hospitals in Germany did not comply with the minimum volume standards
directive, accounting for just 1.4% of the overall procedural volume that year (de
Cruppé W et al., 2015). Although the centralization of knee replacement centers is
not likely, high procedural volume at many hospitals is likely to drive better clinical
outcomes.

**Characterized by early adoption of new innovations by orthopedic surgeons, Germany will continue providing low entry barriers for new implant technologies**
Known to be the pioneers in reverse total shoulder replacement and joint resurfacing
techniques, German surgeons are deemed to be highly adaptable to new
technology. Apart from being early adopters, Germany's reimbursement system for
new medical products—Neue Untersuchungs und Behandlungsmethoden (NUB)—has been one of the key drivers for the introduction of new implants in the
country. The issue this reimbursement system addresses is that most manufacturers
are challenged by the unavailability of diagnosis related group (DRG) codes, leading
to resistance from hospitals to use the product. However, generating a new DRG
code requires the collection of data around procedure utilization. Thus, in most
cases, the presence of robust clinical data around utilization of the product is very
unlikely to justify the creation of a new DRG code. This makes the commercialization
of new entrants difficult. With an intention to reduce the gap between innovation and commercial usage, the German healthcare system began a short-term, intermediate reimbursement mechanism that reimburses hospitals with the required financial incentive to use a new device before it is officially reimbursed under the German-DRG system. Consequently, the faster introduction of newer implants in healthcare settings has further enhanced the skills of surgeons and their exposure to surgical techniques. More than two-thirds of German physicians believe that this innovation is one of the key reasons for the high standards of healthcare in Germany. Furthermore, around one-third of the medical sales revenue in Germany is accounted for by devices that are less than three years old. For instance, with more than 2,000 prostheses implanted, the EnduRo knee gained a 14% market share in Germany during its first year of availability according to Aesculap. Characterized as a highly innovative and dynamic market, Germany facilitates low entry barrier for new entrants, thereby making it easier for new implant designs to be used and approved in a relatively shorter turn-around time.

EndoCert certification system for medical facilities to drive better clinical outcomes and optimal treatment success in the German arthroplasty market

EndoCert is the first certification system in the world for medical facilities providing endoprosthetic care. It aims to drive high levels of quality, specialization, and competence in joint replacement surgery for patients. Designed by the German Society for Orthopedics and Orthopedic Surgery (DGOOC) along with the Society and Professional Association for Orthopedics and Trauma Surgery (DGOU and BVOU), the certification is conducted in accordance with nationally validated quality standards. As a permanent quality assurance system, endoprosthesis centers are required to comply with various quality indicators as warranted by the certification. Arthroplasty centers are audited at least once a year for compliance with criteria by certified external auditors, with further inspection by an expert commission and an accredited certification body. These standards are likely to improve outcomes and lower the cost of healthcare by reducing the need for a number of revisions.

Increasing prevalence of knee OA in France likely to drive the growth of knee replacement market

In 2007–2009, a two-phase, population-based survey was conducted in six regions of France. The standardized prevalence of hip and knee OA was 1.9% and 4.7% for men and 2.5% and 6.6% for women, respectively (Guillemin F et al., 2011). In comparison to the US, France observed a high prevalence of knee replacement per
100,000 in 2013. Owing to a higher inclination on the part of French surgeons to perform knee replacement surgeries with mobile-bearing knee implants and the ability to enjoy greater physical activity demanded by the French population, the knee replacement segment of the market is expected to experience the fastest growth. While fixed-bearing knee implants are used in elderly patients with low demand for physical activity, the knee replacement market in France will be driven by mobile-bearing knee implants.

3.7 Products

These companies offer a variety of knee implant systems including fixed-bearing implants, mobile-bearing implants, medial-pivotal implants, and gender-specific or customized implants.

3.7.1 Types of Knee Implants
Knee implants can be classified into fixed-bearing, mobile-bearing, medial-pivot implants, gender-specific knee implants, and patient-specific or customized implants.

3.7.1.1 Fixed-Bearing Implants
In fixed-bearing implants, the polyethylene cushion of the tibial component is fixed firmly to the metal implant beneath; the femoral component then rolls over this cushion. By providing a good range of motion and being moderately long lasting, fixed-bearing knee implants have traditionally represented a popular choice of knee replacement prosthesis. However, over the past decade, there has been increasing demand for mobile-bearing implants due to the need for a superior range of motion. The late failure of fixed-bearing implants has been associated with loosening and polyethylene wear. Fixed-bearing prostheses with a high degree of bearing-surface conformity are likely to provide low contact stress while producing high torque at the
bone–implant interface, predisposing them to component loosening. Conversely, prostheses with a low level of bearing-surface conformity are likely to produce less constraint force, decreasing component loosening while generating high contact stress that leads to the early failure of the polyethylene. In addition, the kinematic conflict between low-stress articulations and free rotation may never be solved by existing fixed-bearing knee implant designs.

### 3.7.1.2 Mobile-Bearing Implants

Also known as a rotating-platform implant, mobile-bearing implants comprise a polyethylene insert that can rotate short distances inside the metal tibial tray. This is designed to allow patients a few more degrees of rotation to the medial and lateral sides of their knee. These implants were developed in the late 1970s with the objective of reducing polyethylene wear and component loosening. The mobile-bearing design provides mobility and congruity in the tibiofemoral bearing surface. This helps to reduce contact stress and constraint force, improving wear resistance and minimizing loosening. Furthermore, this design also solves the kinematic conflict of fixed-bearing knees, since a high-conforming articular surface can co-exist with free rotation.

While mobile-bearing implants have theoretical advantages over fixed-bearing ones, both designs demonstrate high survival rates of up to 95% at the 10-year follow-up point (Huang CH, 2007). Even as certain proponents of mobile-bearing implants suggest that these implants lead to reduced wear, several studies published over the past two decades indicate that mobile-bearing implants may wear more than fixed-bearing implants. From a clinical viewpoint, there have been no major studies to biomechanically prove the implant longevity of mobile-bearing over fixed-bearing implants. However, the fixed-bearing design with its all-polyethylene tibial component may be suggested for relatively inactive, elderly people, while younger and active patients may benefit from the mobile-bearing design due to the potential for reduced polyethylene wear and more normal kinematic response after joint replacement.

### 3.7.1.3 Medial-Pivot Implants

Medial-pivot implants are designed to replicate the rotating, twisting, bending, flexion, and stability of a natural knee. The design takes into consideration the natural kinematics of the human knee. It features an asymmetrical tibial insert that
controls the anterior-posterior translation of the femur in the medial compartment, while allowing unrestricted movement of the femur in the lateral compartment. This helps the lateral condyle pivot around the medial condyle to create movement similar to that of the normal knee.

### 3.7.1.4 Gender-Specific Knee Implants

The anatomical differences between the knees of men and women have been widely noted over a period of time. One of the key differences between the knees of the two genders is the less pronounced nature of the female anterior condyle as compared to the male knee. While many researchers believe that women’s knees differ from those of men in size and shape, others believe that the size of the knee is linked with stature in general and has less to do with gender. Traditionally, most implant designs have been made using data on the average size of knee joints. However, manufacturers have developed gender-specific implants utilizing statistical measurements of men’s and women’s knees to design the implant.

Zimmer was the first manufacturer to design a gender-specific knee specially designed for women. These implants have a thinner profile, allow comparatively more natural movement of the kneecap, and have a design specifically contoured for women. Zimmer advocates that its gender-specific knee provides higher success rates for women by offering a decreased aspect ratio, thinner anterior flange, and lateralized trochlear groove. Since women have a distinctly higher Q angle compared to men, these implants help to replicate the natural Q angle by increasing the trochlear groove angle by about three degrees. The implants further avoid overstuffing that could occasionally occur while using a traditional implant in a woman’s knee, thus impeding the post-operative range of motion. However, there continue to be some observers in the industry who believe that these innovations are not absolutely necessary from a cost-benefit ratio viewpoint.

### 3.7.1.5 Customized Implants

The use of custom implants and instrumentation has been one of the key developments driving TKRs over the past decade. The adoption of this technology has not only helped patients by improving post-operative alignment and overall fitting, but has also allowed hospitals to improve operating room efficiency and reduce sterilization and inventory costs.
Custom implants were traditionally used in patients with unusual bone geometries or in revision surgeries where fixing standard implants would have been difficult due to bone erosion. In recent years, however, the use of custom implants and instrumentation has gained widespread acceptance. Broadly, computed tomography (CT) and/or magnetic resonance imaging (MRI) scan data are used to determine the implant size and shape characteristics, which are then converted using design engineering software through a process known as segmentation (John S, 2012). The segmentation of the entire joint surface leads to the creation of a point cloud over individual scanned slices to represent the outer surface of a real joint. Subsequently, the point cloud is imported into a traditional computer-aided design (CAD) program, which is then converted into a solid model to design the prosthesis. While MRI data are suited for soft tissue analysis, CT scan data are more suited for scanning hard tissue.

Currently, the customized implant market in the US and certain European countries encompasses unicompartmental, bicompartmental, patellofemoral, and TKR implants. The customized knee instrumentation market is comprised of primary placement jigs to set the initial femoral and tibial bone cuts. The majority of the market-leading implant manufacturers, as well as smaller competitors in the market, now produce customized implants and instrumentation for joint replacement.

### 3.8 Market Forecast

The global knee arthroplasty implants market was valued at approximately $7.6 billion in 2015 and is expected to grow at a CAGR of 4.4%, reaching approximately $9.4 billion by 2020.

Exhibit 3-8 presents the global combined market forecast for knee arthroplasty implants by country/region for the years 2015 through 2020.

Exhibits 3-9 through 3-14 present the market forecast for knee arthroplasty implants by individual countries for the years 2015 through 2020.

### 3.9 Competitors

In 2015, Zimmer was the US market leader in the knee implants segment with an estimated market share of 37%. The company has benefitted from its recent merger with Biomet, which has increased revenues from knee implant sales. The expanded
### Exhibit 3-8: Global Knee Arthroplasty Implant Sales by Country/Region, Combined Market Forecast, 2015–20

<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>$3,760.8m</td>
<td>$3,911.5m</td>
<td>$4,068.4m</td>
<td>$4,226.9m</td>
<td>$4,389.9m</td>
<td>$4,553.8m</td>
<td>3.9%</td>
</tr>
<tr>
<td>Europe</td>
<td>1,062.1</td>
<td>1,110.6</td>
<td>1,161.4</td>
<td>1,213.8</td>
<td>1,266.9</td>
<td>1,320.8</td>
<td>4.4%</td>
</tr>
<tr>
<td>Rest of the World</td>
<td>2,759.2</td>
<td>2,891.7</td>
<td>3,036.2</td>
<td>3,191.1</td>
<td>3,360.2</td>
<td>3,541.7</td>
<td>5.2%</td>
</tr>
<tr>
<td><strong>Total knee implant sales</strong></td>
<td><strong>$7,582.1m</strong></td>
<td><strong>$7,913.8m</strong></td>
<td><strong>$8,266.0m</strong></td>
<td><strong>$8,631.7m</strong></td>
<td><strong>$9,017.0m</strong></td>
<td><strong>$9,416.2m</strong></td>
<td><strong>4.4%</strong></td>
</tr>
</tbody>
</table>

Notes: System sales for Europe include product sales in Germany, France, Italy, the United Kingdom, and Spain. The Rest of the World segment includes product sales from Africa, the Middle East, Asia-Pacific, Europe, and North and South America and excludes product sales for Germany, France, Italy, the United Kingdom, Spain, Japan, and the United States. Figures may not calculate due to rounding.

(Continued)
Notes: System sales for Europe include product sales in Germany, France, Italy, the United Kingdom, and Spain. The Rest of the World segment includes product sales from Africa and the Middle East, Asia-Pacific, Europe, and North and South America and excludes product sales for Germany, France, Italy, the United Kingdom, Spain, Japan, and the United States.

Sources: Company financials; Meddevicetracker
## Exhibit 3-9: Knee Arthroplasty—United States, Market Forecast, 2015–20

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary TKA</td>
<td>$3,215.5m</td>
<td>$3,337.7m</td>
<td>$3,464.5m</td>
<td>$3,592.7m</td>
<td>$3,725.7m</td>
<td>$3,859.8m</td>
<td>3.7%</td>
</tr>
<tr>
<td>Unicondylar Knee Arthroplasty</td>
<td>112.0</td>
<td>117.6</td>
<td>123.5</td>
<td>129.3</td>
<td>135.1</td>
<td>141.1</td>
<td>4.6%</td>
</tr>
<tr>
<td>Revision Knee Arthroplasty</td>
<td>433.2</td>
<td>456.2</td>
<td>480.3</td>
<td>504.8</td>
<td>529.1</td>
<td>552.9</td>
<td>4.9%</td>
</tr>
<tr>
<td>Total knee implant sales</td>
<td>$3,760.8m</td>
<td>$3,911.5m</td>
<td>$4,068.4m</td>
<td>$4,226.9m</td>
<td>$4,389.9m</td>
<td>$4,553.8m</td>
<td>3.9%</td>
</tr>
</tbody>
</table>

Notes: TKA = total knee arthroplasty. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
### Exhibit 3-10: Knee Arthroplasty—United Kingdom, Market Forecast, 2015–20

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary TKA</td>
<td>$203.7m</td>
<td>$215.9m</td>
<td>$228.9m</td>
<td>$242.4m</td>
<td>$256.2m</td>
<td>$270.3m</td>
<td>5.8%</td>
</tr>
<tr>
<td>Unicondylar Knee Arthroplasty</td>
<td>9.8</td>
<td>10.1</td>
<td>10.5</td>
<td>10.8</td>
<td>11.2</td>
<td>11.5</td>
<td>3.3%</td>
</tr>
<tr>
<td>Revision Knee Arthroplasty</td>
<td>13.3</td>
<td>14.0</td>
<td>14.7</td>
<td>15.4</td>
<td>16.1</td>
<td>16.9</td>
<td>4.9%</td>
</tr>
<tr>
<td><strong>Total knee implant sales</strong></td>
<td>$226.8m</td>
<td>$240.0m</td>
<td>$254.0m</td>
<td>$268.6m</td>
<td>$283.5m</td>
<td>$298.7m</td>
<td>5.6%</td>
</tr>
</tbody>
</table>

**Notes:** TKA = total knee arthroplasty. Figures may not calculate due to rounding.

**Sources:** Company financials; Meddevicetracker
## Exhibit 3-11: Knee Arthroplasty—France, Market Forecast, 2015–20

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary TKA</td>
<td>$190.6m</td>
<td>$199.2m</td>
<td>$208.2m</td>
<td>$217.5m</td>
<td>$226.9m</td>
<td>$236.4m</td>
<td>4.4%</td>
</tr>
<tr>
<td>Unicondylar Knee Arthroplasty</td>
<td>9.9</td>
<td>10.2</td>
<td>10.5</td>
<td>10.8</td>
<td>11.1</td>
<td>11.4</td>
<td>2.9%</td>
</tr>
<tr>
<td>Revision Knee Arthroplasty</td>
<td>14.9</td>
<td>15.5</td>
<td>16.1</td>
<td>16.8</td>
<td>17.4</td>
<td>18.0</td>
<td>3.8%</td>
</tr>
<tr>
<td>Total knee implant sales</td>
<td>$215.5m</td>
<td>$224.9m</td>
<td>$234.8m</td>
<td>$245.1m</td>
<td>$255.4m</td>
<td>$265.9m</td>
<td>4.3%</td>
</tr>
</tbody>
</table>

Notes: TKA = total knee arthroplasty. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
### Exhibit 3-12: Knee Arthroplasty—Germany, Market Forecast, 2015–20

<table>
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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary TKA</td>
<td>$260.5m</td>
<td>$270.9m</td>
<td>$281.8m</td>
<td>$292.8m</td>
<td>$303.9m</td>
<td>$315.1m</td>
<td>3.8%</td>
</tr>
<tr>
<td>Unicondylar Knee Arthroplasty</td>
<td>21.3</td>
<td>22.1</td>
<td>22.9</td>
<td>23.7</td>
<td>24.5</td>
<td>25.3</td>
<td>3.4%</td>
</tr>
<tr>
<td>Revision Knee Arthroplasty</td>
<td>48.3</td>
<td>49.5</td>
<td>50.8</td>
<td>52.0</td>
<td>53.2</td>
<td>54.4</td>
<td>2.3%</td>
</tr>
<tr>
<td>Total knee implant sales</td>
<td>$330.2m</td>
<td>$342.6m</td>
<td>$355.4m</td>
<td>$368.4m</td>
<td>$381.6m</td>
<td>$394.8m</td>
<td>3.6%</td>
</tr>
</tbody>
</table>

Notes: TKA = total knee arthroplasty. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
## Exhibit 3-13: Knee Arthroplasty—Italy, Market Forecast, 2015–20

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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary TKA</td>
<td>$140.5m</td>
<td>$147.5m</td>
<td>$154.9m</td>
<td>$162.5m</td>
<td>$170.2m</td>
<td>$178.3m</td>
<td>4.8%</td>
</tr>
<tr>
<td>Unicondylar Knee Arthroplasty</td>
<td>6.8</td>
<td>7.0</td>
<td>7.2</td>
<td>7.4</td>
<td>7.6</td>
<td>7.8</td>
<td>2.9%</td>
</tr>
<tr>
<td>Revision Knee Arthroplasty</td>
<td>13.6</td>
<td>14.1</td>
<td>14.6</td>
<td>15.2</td>
<td>15.8</td>
<td>16.3</td>
<td>3.8%</td>
</tr>
<tr>
<td><strong>Total knee implant sales</strong></td>
<td><strong>$160.8m</strong></td>
<td><strong>$168.5m</strong></td>
<td><strong>$176.7m</strong></td>
<td><strong>$185.1m</strong></td>
<td><strong>$193.6m</strong></td>
<td><strong>$202.4m</strong></td>
<td><strong>4.7%</strong></td>
</tr>
</tbody>
</table>

**Notes:** TKA = total knee arthroplasty. Figures may not calculate due to rounding.

**Sources:** Company financials; Meddevicetracker
### Exhibit 3-14: Knee Arthroplasty—Spain, Market Forecast, 2015–20

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary TKA</td>
<td>$115.2m</td>
<td>$120.4m</td>
<td>$125.8m</td>
<td>$131.5m</td>
<td>$137.3m</td>
<td>$143.0m</td>
<td>4.4%</td>
</tr>
<tr>
<td>Unicondylar Knee Arthroplasty</td>
<td>5.2</td>
<td>5.3</td>
<td>5.4</td>
<td>5.6</td>
<td>5.7</td>
<td>5.7</td>
<td>1.9%</td>
</tr>
<tr>
<td>Revision Knee Arthroplasty</td>
<td>8.5</td>
<td>8.8</td>
<td>9.1</td>
<td>9.5</td>
<td>9.9</td>
<td>10.2</td>
<td>3.8%</td>
</tr>
<tr>
<td><strong>Total knee implant sales</strong></td>
<td>$128.9m</td>
<td>$134.5m</td>
<td>$140.4m</td>
<td>$146.5m</td>
<td>$152.8m</td>
<td>$159.0m</td>
<td>4.3%</td>
</tr>
</tbody>
</table>

**Notes:** TKA = total knee arthroplasty. Figures may not calculate due to rounding.

**Sources:** Company financials; Meddevicetracker
With an estimated US market share of 21%, DePuy Synthes was the second largest supplier of knee arthroplasty implants in 2015. The company’s growth in the US and European knee implants segment in 2015 is largely attributed to sales of its Attune Knee Systems.

Stryker had an estimated market share of 20.5% in the US knee arthroplasty implant market in 2015.

In the US, other suppliers of knee arthroplasty implants include Arthrex, BioPro, DJO Global, Exactech, and MicroPort Scientific, among others. For the European market, other suppliers of knee arthroplasty implants include Adler Ortho, Arthrex, Baumer, Corin, Evolutis, FH Orthopedics, Implants International, ImplantCast, JRI Orthopedics, Lima Corporate, MatOrtho, MicroPort Scientific, Medacta International, and Waldemar Link, among others.

Exhibit 3-15 presents estimated sales and market share data for the leading suppliers of knee arthroplasty implants for the US market in 2015.

In 2015, the European knee arthroplasty implants market was led by Zimmer with an estimated market share of 38%. DePuy Synthes was the second largest competitor in this market in 2015, with an estimated market share of 23%. Stryker and Smith & Nephew are the third and fourth largest suppliers of knee arthroplasty implant products in Europe, with estimated market shares of 19% and 11%, respectively.

Exhibit 3-16 presents estimated sales and market share data for the leading supplier of knee arthroplasty implants for the European market in 2015.
## Exhibit 3-15: 2015, United States Knee Arthroplasty Implants Market, Share by Supplier

<table>
<thead>
<tr>
<th>Company</th>
<th>Estimated Sales</th>
<th>Estimated Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zimmer/Zimmer Biomet</td>
<td>$1,391.0m</td>
<td>37.0%</td>
</tr>
<tr>
<td>DePuy Synthes/Johnson &amp; Johnson</td>
<td>789.6</td>
<td>21.0%</td>
</tr>
<tr>
<td>Stryker</td>
<td>770.8</td>
<td>20.5%</td>
</tr>
<tr>
<td>Smith &amp; Nephew</td>
<td>394.8</td>
<td>10.5%</td>
</tr>
<tr>
<td>Others</td>
<td>413.6</td>
<td>11.0%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$3,760.0m</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

Notes: The “Others” category includes Arthrex, BioPro, DJO Global, Exactech, and MicroPort Scientific, among others. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
### Exhibit 3-16: 2015, European Knee Arthroplasty Implants Market, Share by Supplier

<table>
<thead>
<tr>
<th>Company</th>
<th>Estimated Sales</th>
<th>Estimated Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zimmer/Zimmer Biomet</td>
<td>$403.0m</td>
<td>38.0%</td>
</tr>
<tr>
<td>DePuy Synthes/Johnson &amp; Johnson</td>
<td>244.0</td>
<td>23.0%</td>
</tr>
<tr>
<td>Stryker</td>
<td>202.0</td>
<td>19.0%</td>
</tr>
<tr>
<td>Smith &amp; Nephew</td>
<td>117.0</td>
<td>11.0%</td>
</tr>
<tr>
<td>Others</td>
<td>96.0</td>
<td>9.0%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$1,062.0m</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

**Notes:** Estimated sales and market share data for Europe are for France, Germany, Italy, Spain, and the United Kingdom. The “Others” category includes Adler Ortho, Arthrex, B. Braun Melsungen, Baumer, Corin, Evolutis, FH Orthopedics, Implants International, ImplantCast, JRI Orthopedics, Lima Corporate, MatOrtho, MicroPort Scientific, Medacta International, and Waldemar Link, among others. Figures may not calculate due to rounding.

**Sources:** Company financials; Meddevicetracker
4. SHOULDER ARTHROPLASTY

4.1 Indications for Shoulder Arthroplasty

The shoulder is essentially a ball and socket joint composed of three bones: the humerus or the upper arm bone, the scapula or the shoulder blade, and the clavicle or collarbone. The ball or head of the humerus fits into a shallow socket in the shoulder blade. The socket is also known as the glenoid.

Several conditions may lead to pain and disability of shoulders, eventually leading to shoulder arthroplasty. Some of the key indications for shoulder arthroplasty include: avascular necrosis, degenerative joint diseases (e.g., osteoarthritis [OA]), failure of primary shoulder arthroplasty, rheumatoid arthritis, post-traumatic arthritis, rotator cuff tear arthropathy, and severe fracture.

4.2 Types of Shoulder Arthroplasty

Shoulder arthroplasty was first performed in the US in the 1950s to treat severe shoulder fractures. Over the years, shoulder joint replacement has become an established surgery for restoring comfort and function to arthritic and damaged shoulders. In this procedure, the arthritic ball is replaced by a smooth metal ball fixed to the humerus by a stem that fits within it. The arthritic socket (glenoid) is resurfaced with a high-density polyethylene prosthesis. Depending on the amount of damage and the stage of the shoulder degeneration, various types of shoulder arthroplasties may be performed.

4.2.1 Total Shoulder Arthroplasty

A typical total shoulder replacement involves replacing the arthritic joint surfaces with a highly polished metal ball attached to a stem, and a plastic socket. The axis of the humeral neck is at an angle to the axis of the humeral body. The socket joint, also known as the glenoid fossa, is reamed with a hemispherical tool, and a metal cap with a polyethylene liner is inserted into the glenoid. There are risks and complications associated with shoulder arthroplasty/total shoulder arthroplasty (TSA), although these are no greater than the complications associated with other types of arthroplasty.
4.2.2 Shoulder Hemiarthroplasty

Shoulder hemiarthroplasty refers to a surgical procedure where the damaged humeral head is replaced with an artificial joint while the fractured bone is reconstructed around the artificial joint. The humeral head is replaced with a metal ball and stem and is known as stemmed hemiarthroplasty. Typically, a shoulder hemiarthroplasty is indicated when the humeral head is severely fractured while the socket is normal. Another key indication includes arthritis involving the head of the humerus with a glenoid that has a healthy and intact cartilage surface. A hemiarthroplasty may also be indicated for shoulders with severely weakened bone in the glenoid as well as for shoulders with severely torn rotator cuff tendons and arthritis.

4.2.3 Shoulder Resurfacing

Shoulder resurfacing is an alternative to TSA and is usually prescribed for younger patients with more active lifestyles. Instead of cutting and replacing the humerus and scapula in the joint, this procedure focuses on replacing the damaged top of the humeral head with a hemispheric metallic head. This helps provide a new surface to the ball of the joint while ensuring that most of the natural bone remains intact. Upon removal of the diseased or injured portion, the resurfacing implant is affixed to the bone.

The resurfacing procedure of the shoulder is a less traumatic surgery than TSA and offers various benefits. Resurfacing surgery is preferred in most cases as it preserves the humeral head and provides a stable, resurfaced shoulder capable of an excellent range of motion. It can be performed even if the bone is deformed and usually restores normal anatomy. The procedure poses no risk of fat embolus from surgery trauma or risk of fracture at the tip of the prosthesis. If required, a revision surgery is usually easier after a resurfacing compared to a TSA.

The key indications of shoulder resurfacing include OA, rheumatoid arthritis, avascular necrosis, rotator cuff disease or injury, and post-traumatic arthritis. Some of the important risks associated with the procedure include infection, injury to nerves and blood vessels, fracture, stiffness and instability of joints, dislocation, loosening of implants, pain, fracture of tendon or muscle attachment, and the need for revision.
4.2.4 Reverse Total Shoulder Arthroplasty

Originally designed in 1970s, reverse total shoulder arthroplasty (RTSA) was approved by the US Food and Drug Administration (FDA) for use in the US in 2004 (Boileau P, 2005). This surgery is typically indicated for patients with a completely torn rotator cuff that cannot be repaired or for patients with cuff tear arthroplasty, proximal humeral tumors, and proximal humeral fractures with anterosuperior escape. In RTSA, reversal of the physiological ball and socket configuration of the humerus and glenoid results in the medialization and distalization of the shoulder joint’s center of rotation. This helps to increase the moment arm of the deltoid muscle, thereby allowing recruitment of more deltoid fibers for elevation and abduction.

Implant designs for the treatment of rotator cuff tear have undergone several changes over the years. Constrained TSA was one of the earlier designs, whereby the humeral component was allowed to move within the glenoid component with the intent of providing a stable, fixed fulcrum through which the deltoid could move the humerus. This was eventually abandoned due to complication rates reportedly as high as 87.5%, caused primarily by excessive interface stresses due to the constrained design that caused rapid component loosening (Frederick A, 2008). Similarly, semi-constrained TSA implants have achieved limited clinical success in treating rotator cuff tear arthropathy. A retrospective review of publications analyzing the results of conventional TSA for the treatment of rotator cuff tear arthropathy indicates that there are high risks of edge loading and glenoid component failure. Consequently, conventional TSA is no longer considered an option for the treatment of rotator cuff tear arthropathy associated with an irreparable rotator cuff tear.

Reverse TSA has now been reintroduced to treat rotator cuff tear arthropathy. Over the years, implant designs have been modified to solve the dilemma of providing glenohumeral stability and improved shoulder biomechanics. Although modern day prostheses are not fully constrained, the congruent joint surfaces of the reverse ball-and-socket design are aimed at providing inherent stability while moving the joint center of rotation medially and distally to increase deltoid function and the range of motion.

One of the salient features of modern RTSA is the use of a large glenosphere component with no neck, which allows medialization of the center of rotation and reduced torque on the glenoid component. It also includes a humeral implant with a...
nonanatomic valgus angle, which moves the center of joint rotation distally, thus maximizing the length and tension of the deltoid to increase its ability to abduct the humerus, in addition to providing increased stability.

### 4.2.5 Revision Shoulder Arthroplasty

A revision shoulder surgery may be required when the primary shoulder implant fails due to aseptic loosening, progressive wear of the glenoid, and rotator cuff tears leading to abnormal biomechanics. The incidence of periprosthetic fracture during or after shoulder arthroplasty is 1–3% of all shoulder arthroplasties (Williams GR Jr, 2002). Periprosthetic fracture risk factors include osteopenia and avoidable technical factors such as overzealous reaming and impaction, excessive external rotation, and an overly large prosthesis stem. Revision shoulder arthroplasty represents a complex procedure for the surgeon with multiple potential complications. In the setting of a well-fixed humeral component, removal may lead to fractures and compromise the outcome of the revision.

### 4.3 Clinical and Market Trends in Shoulder Arthroplasty

**Total shoulder arthroplasty procedures restrained by a high incidence of glenoid component failure**

As per various clinical studies published over the past decade, glenoid component failure is the most common complication of TSA. Glenoid components fail mostly as a result of their inability to replicate essential properties of the normal glenoid articular surface in order to achieve durable fixation to the underlying bone, to withstand repeated eccentric loads and glenohumeral translation, and to resist wear and deformation. The failure of the glenoid component is typically characterized by pain, loss of function, and the presence of a clunking noise and sensation.

There have been continuous innovations in implant design year on year, especially in humeral components. Various studies published over the past 15 years have demonstrated that round-backed, all-polyethylene components with peg fixation perform better than flat-backed, metal-backed, or keeled components (Frederick A, 2008; De Wilde L, 2013). While many polyethylenes are available with varying amounts of cross-linking and different methods of component formation, there is no clear evidence supporting one over the other. A study by Anglin et al. concluded that glenoid components with a diameter of curvature greater than that of the
humeral head component are less at risk of loosening. Even though design innovations continue, there has been little progress in developing strategies that could reduce the risk of glenoid component failure in TSA.

**Increased indications of shoulder resurfacing in recent years**

The traditional indications of shoulder resurfacing only included active younger patients with OA and a concentric glenoid, patients with rheumatoid arthritis, and patients with avascular necrosis who had adequate supportive bone. However, in recent years, the overall indications for shoulder resurfacing have increased, allowing for significant procedural growth. These indications have now expanded to include instability arthritis with a concentric or resurfaced glenoid, arthritis associated with proximal humerus malunion, rotator cuff tear arthropathy with stable kinematics, arthroscopy, and dialysis arthropathy. While age is not a relevant inclusion or exclusion criterion, the quality of the proximal humerus is an important factor. It is also required that the subchondral surface should support at least 60% of the resurfacing implant (Joseph PI, 2013). As the number of indications increases, more surgeons are being trained on various arthroplasty procedures, thus leading to overall improvements in procedure numbers and outcomes.

**Consistent improvements in shoulder resurfacing implants over the years leading to reduced complication rates**

Shoulder resurfacing procedures have benefitted from significant improvements in implant technologies over the years. The first generation of humeral resurfacing arthroplasty implants depended on methylmethacrylate for fixation and lacked a central stem. With a deeper understanding of component fixation dynamics, the second-generation implants were developed. These implants incorporated a central stem and applied an ingrowth contact surface to improve intermediate and long-term component fixation. Over the years, as correlations between the humeral head height and the diameter of the humeral head were established, the third generation of shoulder resurfacing implants was developed. With their unique undersurface and cruciate stem designs, these implants achieve fixation at the time of implantation and provide immediate rotational stability. The long-term fixation of these implants has been improved in recent years with the addition of hydroxyapatite to the porous coating on the undersurface of the head and proximal portion of the stem, as well as by increasing the contact area with the apical flat surface on the undersurface. The new-generation implants have demonstrated improved clinical outcomes including...
reduced complication rates and reduced rates of revision due to implant loosening. With most new implants needing minimal bone stock removal to implant the device, the popularity of shoulder resurfacing procedures is likely to increase.

Gradual use of bone grafts aiding procedural outcomes in RTSA

It has been observed that the rate of bone graft incorporation is higher in RTSA than TSA. While approximately 15% of all primary shoulder reconstructions require bone grafting, the need for bone grafts is higher in revision surgeries (Riboh JC, 2012). When an RTSA is conducted without using cement on the glenoid side, surgeons are able to generate a construct that compresses the bone graft against the patient’s native glenoid and scapula. Although dependent on the experience of the surgeon, results of bone grafts are considered significantly positive and consistent. Surgeons using glenoid bone grafts in RTSA believe that it has allowed better alignment of the glenoid to its natural state in conjunction with the placement of glenoid base plate.

The use of bone graft is also increasing in revision RTSA and is reported to produce a better fit. Conducting a revision RTSA in a patient with glenoid bone loss is a challenging proposition for surgeons. Consequently, an increasing number of surgeons are looking to tackle this problem by reconstructing the glenoid with a bone graft. A study conducted by Wagner et al. (2015) concluded that although there were relatively high rates of glenoid loosening and re-operation at the mid-term follow-up, glenoid reconstruction with bone graft in the revision setting was able to relieve pain and restore shoulder function and stability. Various other studies including one by Boileau et al. have proposed the routine use of bone grafting to improve the outcomes of RTSA.

4.4 Procedure Volumes

During the forecast period covered by this report, the total number of shoulder arthroplasty procedures performed in the US and the EU5 (France, Germany, Italy, Spain, and the UK) is anticipated to expand at a compound annual growth rate (CAGR) of 6.2%, from approximately 179,900 procedures in 2015 to an estimated 242,700 procedures by 2020.

Exhibit 4-1 presents the combined procedure volumes forecast for shoulder arthroplasty procedures for the US and EU5 for the years 2015 through 2020.
**Exhibit 4-1: Shoulder Arthroplasty, Combined Procedure Volumes Forecast, 2015–20**

<table>
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</thead>
<tbody>
<tr>
<td>United States</td>
<td>123.9</td>
<td>131.5</td>
<td>139.6</td>
<td>148.3</td>
<td>157.6</td>
<td>167.5</td>
<td>6.2%</td>
</tr>
<tr>
<td>France</td>
<td>14.3</td>
<td>15.1</td>
<td>16.0</td>
<td>17.0</td>
<td>18.1</td>
<td>19.4</td>
<td>6.3%</td>
</tr>
<tr>
<td>Germany</td>
<td>26.5</td>
<td>27.9</td>
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<td>31.2</td>
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<td>5.9%</td>
</tr>
<tr>
<td>Italy</td>
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<td>8.1</td>
<td>8.3</td>
<td>8.7</td>
<td>9.1</td>
<td>9.6</td>
<td>4.2%</td>
</tr>
<tr>
<td>Spain</td>
<td>1.2</td>
<td>1.3</td>
<td>1.3</td>
<td>1.4</td>
<td>1.4</td>
<td>1.5</td>
<td>4.6%</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>6.3</td>
<td>6.8</td>
<td>7.3</td>
<td>7.9</td>
<td>8.6</td>
<td>9.4</td>
<td>8.3%</td>
</tr>
<tr>
<td><strong>Total shoulder arthroplasty procedures</strong></td>
<td><strong>179.9</strong></td>
<td><strong>190.6</strong></td>
<td><strong>202.1</strong></td>
<td><strong>214.5</strong></td>
<td><strong>228.0</strong></td>
<td><strong>242.7</strong></td>
<td><strong>6.2%</strong></td>
</tr>
</tbody>
</table>

Notes: Total shoulder arthroplasty procedures include primary total shoulder arthroplasty, reverse shoulder arthroplasty, hemiarthroplasty, shoulder resurfacing, and revision shoulder arthroplasty procedures. Procedure volumes are reported in thousands. Figures may not calculate due to rounding.

(Continued)
Notes: Total shoulder arthroplasty procedures include primary total shoulder arthroplasty, reverse shoulder arthroplasty, hemiarthroplasty, shoulder resurfacing, and revision shoulder arthroplasty procedures.

Sources: American Joint Replacement Registry; Catalan Arthroplasty Registry; Endo Prothesen Register Deutschland; Meddevicetracker; National Joint Registry of the United Kingdom; SoFCOT and Haute Autorité de Santé
Exhibit 4-2 presents the shoulder arthroplasty procedure volumes forecast for the US for the years 2015 through 2020; Exhibit 4-3 presents the shoulder arthroplasty procedure volumes forecast for the UK for the years 2015 through 2020; Exhibit 4-4 presents the shoulder arthroplasty procedure volumes forecast for France for the years 2015 through 2020; Exhibit 4-5 presents the shoulder arthroplasty procedure volumes forecast for Germany for the years 2015 through 2020; Exhibit 4-6 presents the shoulder arthroplasty procedure volumes forecast for Italy for the years 2015 through 2020; Exhibit 4-7 presents the shoulder arthroplasty procedure volumes forecast for Spain for the years 2015 through 2020.

4.5 Industry Challenges for Shoulder Arthroplasty

Need for dedicated surgical training and experience limiting procedure volumes of reverse total shoulder arthroplasty

The success of RTSA is heavily dependent on the level of training and overall experience of the surgeon. Most key opinion leaders in the joint arthroplasty industry believe that there is a steep learning curve associated with an RTSA procedure. This curve begins with proper selection of the patients requiring an RTSA and extends up to developing expertise in correct soft tissue management, capsule release, glenoid exposure, faceplate position, and screw position. Surgeons with experience in TSA could gain expertise in RTSA at a faster pace owing to the commonalities involved in the procedures and the tools used; a large proportion of the two procedures is similar, especially with regards to exposure of the humerus and the glenoid. With gradual understanding of the biomechanics and design features of RTSA, surgeons can extrapolate their skills with TSA and apply these to RTSA procedures. Recent years have been marked by an expansion in the number of indications for RTSA, which is prompting a larger number of joint replacement surgeons to improve their overall training and experience in the procedure. However, the current shortage of experienced shoulder arthroplasty surgeons is likely to continue impeding the widespread adoption of shoulder arthroplasty (Association of American Medical Colleges; AAMC Reporter, 2014).

High complication rates continue to plague reverse total shoulder arthroplasty procedures

Despite several improvements in implant design and surgical techniques, RTSA continues to be associated with high complication rates. As per some clinical
Exhibit 4-2: Shoulder Arthroplasty—United States, Procedure Volumes Forecast, 2015–20

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary TSA</td>
<td>49.2</td>
<td>52.4</td>
<td>55.8</td>
<td>59.4</td>
<td>63.2</td>
<td>67.4</td>
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<td>Reverse Shoulder Arthroplasty</td>
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<td>47.0</td>
<td>50.8</td>
<td>54.8</td>
<td>59.2</td>
<td>64.0</td>
<td>8.0%</td>
</tr>
<tr>
<td>Hemiarthroplasty</td>
<td>9.5</td>
<td>9.7</td>
<td>10.0</td>
<td>10.2</td>
<td>10.5</td>
<td>10.7</td>
<td>2.5%</td>
</tr>
<tr>
<td>Shoulder Resurfacing</td>
<td>10.3</td>
<td>10.7</td>
<td>11.0</td>
<td>11.4</td>
<td>11.8</td>
<td>12.2</td>
<td>3.5%</td>
</tr>
<tr>
<td>Revision Shoulder Arthroplasty</td>
<td>11.4</td>
<td>11.7</td>
<td>12.1</td>
<td>12.4</td>
<td>12.8</td>
<td>13.2</td>
<td>3.0%</td>
</tr>
<tr>
<td>Total shoulder arthroplasty</td>
<td>123.9</td>
<td>131.5</td>
<td>139.6</td>
<td>148.3</td>
<td>157.6</td>
<td>167.5</td>
<td>6.2%</td>
</tr>
</tbody>
</table>

Notes: TSA = total shoulder arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

Sources: American Joint Replacement Registry; Meddevicetracker
### Exhibit 4-3: Shoulder Arthroplasty—United Kingdom, Procedure Volumes Forecast, 2015–20

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<tbody>
<tr>
<td>Primary TSA</td>
<td>1.8</td>
<td>2.0</td>
<td>2.2</td>
<td>2.4</td>
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<tr>
<td>Reverse Shoulder Arthroplasty</td>
<td>2.3</td>
<td>2.6</td>
<td>2.9</td>
<td>3.3</td>
<td>3.7</td>
<td>4.2</td>
<td>12.5%</td>
</tr>
<tr>
<td>Hemiarthroplasty</td>
<td>1.3</td>
<td>1.3</td>
<td>1.3</td>
<td>1.2</td>
<td>1.2</td>
<td>1.2</td>
<td>-1.0%</td>
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<tr>
<td>Shoulder Resurfacing</td>
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<td>0.2</td>
<td>0.2</td>
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<tr>
<td>Revision Shoulder Arthroplasty</td>
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</tr>
<tr>
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<td>6.8</td>
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<td>7.9</td>
<td>8.6</td>
<td>9.4</td>
<td>8.3%</td>
</tr>
</tbody>
</table>

**Notes:** TSA = total shoulder arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

**Sources:** Meddevicetracker; National Joint Registry of the United Kingdom
### Exhibit 4-4: Shoulder Arthroplasty—France, Procedure Volumes Forecast, 2015–20

<table>
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<tr>
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</thead>
<tbody>
<tr>
<td>Primary TSA</td>
<td>5.4</td>
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<td>6.1</td>
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<td>7.0</td>
<td>7.5</td>
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</tr>
<tr>
<td>Reverse Shoulder Arthroplasty</td>
<td>4.7</td>
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<td>6.0</td>
<td>6.6</td>
<td>7.4</td>
<td>9.7%</td>
</tr>
<tr>
<td>Hemiarthroplasty</td>
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<td>2.8</td>
<td>2.8</td>
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<td>2.9</td>
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<td>1.0%</td>
</tr>
<tr>
<td>Shoulder Resurfacing</td>
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<td>0.2</td>
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</tr>
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<td>1.3</td>
<td>1.3</td>
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</tr>
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<td>Total shoulder arthroplasty procedures</td>
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<td>15.1</td>
<td>16.0</td>
<td>17.0</td>
<td>18.1</td>
<td>19.4</td>
<td>6.3%</td>
</tr>
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</table>

**Notes:** TSA = total shoulder arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

**Sources:** Meddevicetracker; SoFCOT and Haute Autorité de Santé
**Exhibit 4-5: Shoulder Arthroplasty—Germany, Procedure Volumes Forecast, 2015–20**

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<tr>
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<tr>
<td>Primary TSA</td>
<td>14.3</td>
<td>15.2</td>
<td>16.1</td>
<td>17.1</td>
<td>18.1</td>
<td>19.2</td>
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<tr>
<td>Reverse Shoulder Arthroplasty</td>
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<td>7.9</td>
<td>8.5</td>
<td>9.1</td>
<td>10.0</td>
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<td>8.5%</td>
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<td>2.2</td>
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<td>2.3</td>
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</tr>
<tr>
<td>Shoulder Resurfacing</td>
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<td>0.5</td>
<td>0.5</td>
<td>2.0%</td>
</tr>
<tr>
<td>Revision Shoulder Arthroplasty</td>
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<td>2.2</td>
<td>2.2</td>
<td>2.3</td>
<td>2.3</td>
<td>2.3</td>
<td>2.0%</td>
</tr>
<tr>
<td><strong>Total shoulder arthroplasty procedures</strong></td>
<td><strong>26.5</strong></td>
<td><strong>27.9</strong></td>
<td><strong>29.5</strong></td>
<td><strong>31.2</strong></td>
<td><strong>33.1</strong></td>
<td><strong>35.3</strong></td>
<td><strong>5.9%</strong></td>
</tr>
</tbody>
</table>

Notes: TSA = total shoulder arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

Sources: Endo Prothesen Register Deutschland; Meddevicetracker
### Exhibit 4-6: Shoulder Arthroplasty—Italy, Procedure Volumes Forecast, 2015–20

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<td>2.8</td>
<td>2.9</td>
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<td>5.7%</td>
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<tr>
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<td>3.1</td>
<td>3.2</td>
<td>3.4</td>
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<td>0.1</td>
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<td>0.5%</td>
</tr>
<tr>
<td>Revision Shoulder Arthroplasty</td>
<td>0.8</td>
<td>0.8</td>
<td>0.9</td>
<td>0.9</td>
<td>0.9</td>
<td>0.9</td>
<td>1.0%</td>
</tr>
<tr>
<td>Total shoulder arthroplasty procedures</td>
<td><strong>7.8</strong></td>
<td><strong>8.1</strong></td>
<td><strong>8.3</strong></td>
<td><strong>8.7</strong></td>
<td><strong>9.1</strong></td>
<td><strong>9.6</strong></td>
<td><strong>4.2%</strong></td>
</tr>
</tbody>
</table>

**Notes:** TSA = total shoulder arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

**Sources:** Italian Arthroplasty Registry (RIAP); Meddevicetracker
Exhibit 4-7:  Shoulder Arthroplasty—Spain, Procedure Volumes Forecast, 2015–20

<table>
<thead>
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</tr>
</thead>
<tbody>
<tr>
<td>Primary TSA</td>
<td>0.8</td>
<td>0.8</td>
<td>0.8</td>
<td>0.9</td>
<td>0.9</td>
<td>1.0</td>
<td>5.0%</td>
</tr>
<tr>
<td>Reverse Shoulder Arthroplasty</td>
<td>0.09</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>6.0%</td>
</tr>
<tr>
<td>Hemiarthroplasty</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.9%</td>
</tr>
<tr>
<td>Shoulder Resurfacing</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06</td>
<td>0.07</td>
<td>0.07</td>
<td>2.0%</td>
</tr>
<tr>
<td>Revision Shoulder Arthroplasty</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>3.2%</td>
</tr>
<tr>
<td>Total shoulder arthroplasty procedures</td>
<td>1.2</td>
<td>1.3</td>
<td>1.3</td>
<td>1.4</td>
<td>1.4</td>
<td>1.5</td>
<td>4.6%</td>
</tr>
</tbody>
</table>

Notes:  TSA = total shoulder arthroplasty. Procedure volumes reported in thousands. Figures may not calculate due to rounding.

Sources:  Catalan Arthroplasty Registry; Meddevicetracker
studies, the complication rates associated with RTSA can range from 5–28% depending on such factors as indication, the integrity of the patient’s subscapularis tendon, and surgeon experience (Farshad M, 2010). Some of the key complications identified in recent times include scapular notching, infection, instability, and acromial fractures. It is also estimated that infection rates could be two to three times higher with RTSA than with standard shoulder arthroplasty because of the geometry of the implant, which leaves a space beneath the shoulder on the acromion. In addition, limited implant longevity and a lack of long-term functional outcomes data continue to restrain the widespread adoption of this technique.

However, a significant proportion of the medical community continues to accept RTSA despite the high complication rates due to the enormous improvement in shoulder function and quality of life following implantation. With increasing surgical confidence and experience levels of surgeons, complication rates are expected to reduce in the coming years. Some clinical studies from the past decade indicate a moderate reduction in complication rates. In a retrospective study of patients undergoing RTSA between 1985 and 2003, Favard and colleagues showed 89% implant survivorship at 10 years. After adjusting for Constant-Murley scores lower than 30, 10-year survivorship decreased to 72%.

4.6 Market Drivers for Shoulder Arthroplasty

Growing incidence of shoulder arthritis likely to aid growth of shoulder arthroplasty

Shoulder OA is a growing cause of disability among the aging population. Although not as prevalent as OA of the hip and knee, OA of the shoulder is estimated to affect up to 32.8% of people in the US above sixty years (Chillemmi C, 2013). The prevalence of shoulder OA increases with age and women appear to be more susceptible than men. In the growing geriatric populations of Europe and the US, shoulder OA and rotator cuff diseases represent the two most common disorders of the shoulder, leading to pain, disability, and degeneration. While there was a moderate increase in the number of shoulder arthroplasties between 1990 and 2000, there has been an exponential rise in procedure volume since the FDA approval of RTSAs in 2004. With shoulder arthroplasty implants demonstrating long-term survival rates (over 15–20 years) of about 85%, there is increased impetus in the adoption of these procedures.
Increasing demand for shoulder arthroplasty in younger patients driving procedural growth

Shoulder arthritis in the young adult population represents a common disease management dilemma. With the younger population leading an active life, which can often include interest in sports involving the shoulder, there is an increased demand for treatments that bring pain relief and a long-lasting improvement in function. Even though patients with rotator cuff arthroplasty can be managed without surgery, the need for a higher quality of life continues to push patients towards opting for shoulder arthroplasty. Rehabilitation regimes, counseling, and education can help younger patients manage the non-intact cuff and live in moderate to low discomfort. However, with shoulder arthroplasty procedures demonstrating high success rates, an increasing number of patients with relevant indications are undergoing TSA. Bartelt et al. concluded in their 2011 study that there is intermediate- to long-term pain relief and improvement in motion with shoulder arthroplasty in young patients with OA. These results favor TSA in terms of pain relief, motion, and implant survival.

Total shoulder arthroplasty continues to demonstrate positive results in young patients with adequate glenoid bone stock and healthy soft tissue, such as a functioning rotator cuff to help prevent misalignment of the glenoid component implant. In carefully selected young patients, this procedure has been able to offer successful results often preferable in the long term to a hemiarthroplasty or partial replacement procedure. Furthermore, with improvements in implant designs, including the availability of ultrashort stem implants and bone-preserving glenoid components, these procedures can be performed in a less invasive manner compared to traditional techniques.

Higher awareness and clinical benefits of stemless shoulders likely to help increase shoulder arthroplasty volumes

Introduced in 2004, stemless shoulder implants are now becoming increasingly popular across US and European markets owing to the positive early clinical and radiographic results. Also referred to as canal-sparing implants, stemless shoulder implants are designed for metaphyseal fixation to minimize humeral bone removal, avoid intraoperative and post-operative humeral fracture complications, and decrease morbidity associated with revision operations. Some of the key shoulder implants available on the market include Arthrex’s Eclipse stemless shoulder
arthroplasty, the Total Evolutive Shoulder System (or TESS implant) from Biomet (now Zimmer Biomet), Mathys's Affinis implant, Simpliciti by Tornier, and Zimmer's Sidus System.

Since stem-free arthroplasty implants have been available to surgeons worldwide for only a relatively short amount of time, there are few published studies evaluating this technique. However, in recent years, an increasing number of clinical studies have demonstrated the distinct clinical benefits of stemless shoulders (Churchill RS, 2014). In 2010, Huguet et al. evaluated Biomet's TESS implants and determined that no subsidence or loosening of the corolla was evident. In addition, no evidence of osteolysis, stress shielding, or radiolucent lines surrounding the corolla were present in their most recent post-operative radiographs. In 2013, Berth and Pap reported their prospective, randomized, longitudinal study comparing the results of the Biomet TESS stemless implant with the Mathys Affinis stemmed prosthesis. As indicated in their publication, the use of the stemless shoulder prosthesis yielded acceptable results which, at a mid-term follow-up, were comparable with those provided by a standard anatomical shoulder prosthesis. Additionally, the lack of metal in the ultra-short stem designs reduces the risk of mid-shaft humerus fractures, which is a major concern in traditional shoulder implants. Given the increased satisfaction rates among young and active patients due to the preservation of native bones, reduced blood loss, and shorter procedure time, the demand for stemless arthroplasty is likely to increase at a rapid pace in the coming years.

Increasing applications of reverse shoulder arthroplasty in musculoskeletal oncology indications aiding growth in total procedure volumes

In recent years, there has been a significant increase in the number of indications for shoulder arthroplasty. Musculoskeletal oncology is one such emerging application for reverse shoulder arthroplasty, as the proximal humerus is the third most common site for the occurrence of bone tumors (Puri A, 2011). The incidence of soft tissue sarcomas and new bone and cartilage malignancies is approximately 1.8 in 100,000 for each, 15% of which occur within the shoulder (De Wilde L et al., 2011). A majority of the limb salvage procedures to manage such tumors are complicated and may require the sacrifice of the proximal humerus and the surrounding tissues to achieve tumor resection. This leads to loss of shoulder function post-surgery in most occasions. Reverse shoulder arthroplasty has been able to demonstrate improved results and success rates in short-term studies. In a study published in 2011, Lenarz et al. concluded that RTSA relieved pain and improved function in proximal humerus
fractures. Another study published in the same year by Boileau et al. concluded that RTSA is a reasonable option for tumors of the proximal humerus in medium-term follow up.

**Use of trabecular metal technology in reverse shoulder arthroplasty implants driving procedural growth**

The use of trabecular metal implants in reverse shoulder arthroplasty has been on the rise over the past five years. The increased adoption rate is largely attributed to the fact that these implants have been able to consistently provide the initial stability necessary to achieve biological ingrowth, thus enabling long-term fixation over a wide range of bone properties. In a study published in the *Journal of Shoulder and Elbow Surgery* in 2013, Bogle et al. concluded that cementless trabecular metal porous-coated implants for RTSA are associated with secure glenoid fixation and minimal radiographic evidence of humeral stem loosening or subsidence at short-term follow-up. Zimmer’s Trabecular Metal Reverse Shoulder System has continued to demonstrate sustained penetration across global markets, helping their extremities business grow by 5% in 2014 over the previous year, prior to the completion of the merger with Biomet (Zimmer Annual Report, 2014).

**Overall cost-effectiveness of the procedure aiding adoption rates for total shoulder arthroplasty**

With increasing instances of revision arthroplasty, there has been an increased focus across hospitals to look for cost-effective measures in joint arthroplasty procedures. Gunnarsson et al. reported in 2009 that arthritis costs the US around $185.5 billion in direct costs. Kotlarz et al. reported in 2010 that the cost of absenteeism due to OA was about $410.3 billion in the US. Re-admissions and additional hospital stays have also been adding to the overall burden. It is estimated that the cost of an extra day in hospital for a shoulder patient over 65 years of age is about $12,600 a day (Pfuntner A, 2013).

A 2013 study of the cost utility for reverse shoulder arthroplasty determined that the procedure was moderately to highly cost effective. In a study published in the *Journal of Shoulder and Elbow Surgery*, Chalmers et al. concluded that the treatment of complex fractures with a reverse arthroplasty technique had an equivalent overall cost to hemiarthroplasty and open reduction and plating. The higher cost of the RTSA surgery and implant was offset by reduced spending on
hospital visits and physiotherapy. Consequently, such cost drivers and the need to achieve overall cost efficiency is causing hospitals to increasingly adopt TSA procedures across US and Europe.

**High utilization of RTSA to drive growth of shoulder arthroplasty products in Italy and the UK**

Marred by limited clinical success, RTSA was not well received by joint arthroplasty surgeons after its introduction in the 1970s. Owing to its initial constrained design and lateralized glenohumeral center of rotation, the implant exerted excessive shear stress that led to the failure of the glenoid component. In acknowledgment of this design drawback, modern implants were designed to have a larger radius of curvature of the glenoid component and greater movement of the center of shoulder rotation, medially and distally. This helped in creating a more stable and efficient fulcrum that further reduced shear forces at the glenoid-bone interface. Post FDA approval in 2003, RTSA was utilized in wider indications beyond rotator cuff tear arthroplasty.

However, owing to high complication rates and the technically demanding nature of the procedure, successful outcomes with this procedure required experienced surgeons. With increasing exposure and better results, especially in the presence of rotator cuff deficiency, adoption of reverse shoulder arthroplasty has been increasing (Brian C, 2016). In 2014, RTSA accounted for 35% of the shoulder replacement procedures conducted in the UK, while standard total shoulder replacement accounted for 29% (NJR, 2015). The US has exhibited a similar trend, with RTSA accounting for 42% of all primary shoulder arthroplasty procedures in 2011. However, utilization of RTSA in Italy has been significantly high: at 55%, reverse prosthesis was the most frequently administered shoulder implant in 2014. Thus, with the growing acceptance of RTSA, higher clinical outcomes, and increasing confidence in the procedure, surgical volume for TSA, led by RTSA, is likely to gain momentum.

### 4.7 Products

Traditionally known for their hip and knee arthroplasty implants, companies such as DePuy Synthes, Exactech, Integra LifeSciences, Smith & Nephew, Stryker, Tornier, Wright Medical Group, and Zimmer have ventured into the shoulder arthroplasty...
market. Smaller participants in the shoulder arthroplasty products market include AAP Joints, Baumer, FH Orthopedics, Implants International, Implantcast, JRI Orthopaedics, Lima Corporate, and Mathys, among others.

### 4.8 Market Forecast

The global shoulder arthroplasty implants market was valued at approximately $1.4 billion in 2015 and is expected to grow at a CAGR of 7.2%, reaching approximately $1.9 billion by 2020.

Exhibit 4-8 presents the global combined market forecast for shoulder arthroplasty implants by country/region for the years 2015 through 2020.

Exhibits 4-9 through 4-14 present the market forecast for shoulder arthroplasty implants by individual countries for the years 2015 through 2020.

### 4.9 Competitors

In 2015, Zimmer was the overall market leader for shoulder arthroplasty implants. Shoulder implant sales were driven by the uptake of Zimmer’s Trabecular Metal Reverse Shoulder System and Comprehensive Total Shoulder System. The company’s estimated 2015 market shares were 38% and 33% for the US and European markets, respectively.

DePuy Synthes was the second largest supplier of shoulder arthroplasty implants in the US and European markets. The company’s broad portfolio of shoulder arthroplasty implants, which includes the GLOBAL series and DELTA XTEND Reverse Shoulder System, has contributed to its estimated 2015 market shares of 21% and 25% in the US and European markets, respectively.

Wright Medical Group was the third largest supplier of shoulder arthroplasty implants globally. In 2015, Wright Medical Group accounted for an estimated 20% and 25% of TSA implant sales in the US and European markets, respectively.

In the US, other suppliers of shoulder arthroplasty implants include Corin, DJO Global, Exactech, Smith & Nephew, and Stryker, among others. Other suppliers of shoulder arthroplasty implants to the European market include Baumer, Corin,
### Exhibit 4-8: Global Shoulder Arthroplasty Implant Sales by Country/Region, Combined Market Forecast, 2015–20

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>$667.7m</td>
<td>$712.5m</td>
<td>$760.6m</td>
<td>$811.8m</td>
<td>$865.4m</td>
<td>$922.4m</td>
<td>6.7%</td>
</tr>
<tr>
<td>Europe</td>
<td>130.2</td>
<td>139.9</td>
<td>148.6</td>
<td>158.2</td>
<td>168.6</td>
<td>180.2</td>
<td>6.7%</td>
</tr>
<tr>
<td>Rest of the World</td>
<td>572.1</td>
<td>615.0</td>
<td>662.3</td>
<td>715.3</td>
<td>773.3</td>
<td>836.7</td>
<td>7.9%</td>
</tr>
<tr>
<td>Total shoulder implant sales</td>
<td>$1,370.0m</td>
<td>$1,467.4m</td>
<td>$1,571.5m</td>
<td>$1,684.5m</td>
<td>$1,807.4m</td>
<td>$1,939.3m</td>
<td>7.2%</td>
</tr>
</tbody>
</table>

**Notes:** System sales for Europe include product sales in Germany, France, Italy, the United Kingdom, and Spain. The Rest of the World segment includes product sales from Africa, the Middle East, Asia-Pacific, Europe, and North and South America and excludes product sales for Germany, France, Italy, the United Kingdom, Spain, Japan, and the United States. Figures may not calculate due to rounding.
Notes: System sales for Europe include product sales in Germany, France, Italy, the United Kingdom, and Spain. The Rest of the World segment includes product sales from Africa and the Middle East, Asia-Pacific, Europe, and North and South America and excludes product sales for Germany, France, Italy, the United Kingdom, Spain, Japan, and the United States.

Sources: Company financials; Meddevicetracker
### Exhibit 4-9: Shoulder Arthroplasty—United States, Market Forecast, 2015–20

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</tr>
</thead>
<tbody>
<tr>
<td>Total Shoulder Arthroplasty</td>
<td>$196.7m</td>
<td>$209.3m</td>
<td>$222.6m</td>
<td>$236.7m</td>
<td>$251.3m</td>
<td>$266.7m</td>
<td>6.3%</td>
</tr>
<tr>
<td>RTSA</td>
<td>361.4</td>
<td>390.3</td>
<td>421.5</td>
<td>455.2</td>
<td>490.7</td>
<td>529.0</td>
<td>7.9%</td>
</tr>
<tr>
<td>Hemiarthroplasty</td>
<td>29.0</td>
<td>29.7</td>
<td>30.4</td>
<td>31.2</td>
<td>31.9</td>
<td>32.6</td>
<td>2.4%</td>
</tr>
<tr>
<td>Shoulder Resurfacing</td>
<td>33.0</td>
<td>34.1</td>
<td>35.3</td>
<td>36.5</td>
<td>37.7</td>
<td>38.9</td>
<td>3.3%</td>
</tr>
<tr>
<td>Revision Shoulder Arthroplasty</td>
<td>47.8</td>
<td>49.2</td>
<td>50.7</td>
<td>52.2</td>
<td>53.7</td>
<td>55.2</td>
<td>2.9%</td>
</tr>
<tr>
<td><strong>Total shoulder arthroplasty sales</strong></td>
<td><strong>$667.7m</strong></td>
<td><strong>$712.5m</strong></td>
<td><strong>$760.6m</strong></td>
<td><strong>$811.8m</strong></td>
<td><strong>$865.4m</strong></td>
<td><strong>$922.4m</strong></td>
<td><strong>6.7%</strong></td>
</tr>
</tbody>
</table>

Notes: RTSA = reverse total shoulder arthroplasty. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
Exhibit 4-10: Shoulder Arthroplasty—United Kingdom, Market Forecast, 2015–20

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</tr>
</thead>
<tbody>
<tr>
<td>Total Shoulder Arthroplasty</td>
<td>$3.5m</td>
<td>$3.9m</td>
<td>$4.2m</td>
<td>$4.7m</td>
<td>$5.1m</td>
<td>$5.6m</td>
<td>9.9%</td>
</tr>
<tr>
<td>RTSA</td>
<td>6.2</td>
<td>7.0</td>
<td>7.8</td>
<td>8.7</td>
<td>9.8</td>
<td>11.0</td>
<td>12.2%</td>
</tr>
<tr>
<td>Hemiarthroplasty</td>
<td>1.3</td>
<td>1.3</td>
<td>1.3</td>
<td>1.3</td>
<td>1.3</td>
<td>1.3</td>
<td>0.0%</td>
</tr>
<tr>
<td>Shoulder Resurfacing</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>2.9%</td>
</tr>
<tr>
<td>Revision Shoulder Arthroplasty</td>
<td>1.2</td>
<td>1.3</td>
<td>1.4</td>
<td>1.4</td>
<td>1.5</td>
<td>1.6</td>
<td>4.8%</td>
</tr>
<tr>
<td><strong>Total shoulder arthroplasty sales</strong></td>
<td><strong>$12.5m</strong></td>
<td><strong>$13.7m</strong></td>
<td><strong>$15.0m</strong></td>
<td><strong>$16.4m</strong></td>
<td><strong>$17.9m</strong></td>
<td><strong>$19.7m</strong></td>
<td><strong>9.5%</strong></td>
</tr>
</tbody>
</table>

Notes: RTSA = reverse total shoulder arthroplasty. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
## Exhibit 4-11: Shoulder Arthroplasty—France, Market Forecast, 2015–20

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<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Total Shoulder Arthroplasty</td>
<td>$10.9m</td>
<td>$11.6m</td>
<td>$12.4m</td>
<td>$13.3m</td>
<td>$14.2m</td>
<td>$15.1m</td>
<td>6.7%</td>
</tr>
<tr>
<td>RTSA</td>
<td>16.0</td>
<td>17.5</td>
<td>19.1</td>
<td>20.8</td>
<td>22.7</td>
<td>24.8</td>
<td>9.2%</td>
</tr>
<tr>
<td>Hemiarthroplasty</td>
<td>4.4</td>
<td>4.5</td>
<td>4.5</td>
<td>4.6</td>
<td>4.6</td>
<td>4.6</td>
<td>0.9%</td>
</tr>
<tr>
<td>Shoulder Resurfacing</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>3.3%</td>
</tr>
<tr>
<td>Revision Shoulder Arthroplasty</td>
<td>2.7</td>
<td>2.8</td>
<td>2.2</td>
<td>2.8</td>
<td>2.9</td>
<td>2.9</td>
<td>1.4%</td>
</tr>
<tr>
<td><strong>Total shoulder arthroplasty sales</strong></td>
<td><strong>$34.4m</strong></td>
<td><strong>$36.7m</strong></td>
<td><strong>$39.2m</strong></td>
<td><strong>$41.8m</strong></td>
<td><strong>$44.7m</strong></td>
<td><strong>$47.8m</strong></td>
<td><strong>6.8%</strong></td>
</tr>
</tbody>
</table>

**Notes:** RTSA = reverse total shoulder arthroplasty. Figures may not calculate due to rounding.

**Sources:** Company financials; Meddevicetracker
## Exhibit 4-12: Shoulder Arthroplasty—Germany, Market Forecast, 2015–20

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Total Shoulder Arthroplasty</td>
<td>$30.1m</td>
<td>$31.9m</td>
<td>$33.8m</td>
<td>$35.7m</td>
<td>$37.7m</td>
<td>$39.8m</td>
<td>5.7%</td>
</tr>
<tr>
<td>RTSA</td>
<td>26.2%</td>
<td>28.0%</td>
<td>30.0%</td>
<td>32.4%</td>
<td>35.1%</td>
<td>38.2%</td>
<td>7.8%</td>
</tr>
<tr>
<td>Hemiarthroplasty</td>
<td>3.5%</td>
<td>3.5%</td>
<td>3.6%</td>
<td>3.6%</td>
<td>3.7%</td>
<td>3.7%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Shoulder Resurfacing</td>
<td>0.8%</td>
<td>0.8%</td>
<td>0.8%</td>
<td>0.8%</td>
<td>0.8%</td>
<td>0.9%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Revision Shoulder Arthroplasty</td>
<td>4.8%</td>
<td>4.9%</td>
<td>5.0%</td>
<td>5.1%</td>
<td>5.2%</td>
<td>5.2%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Total shoulder arthroplasty sales</td>
<td>$65.3m</td>
<td>$69.1m</td>
<td>$73.1m</td>
<td>$77.7m</td>
<td>$82.5m</td>
<td>$87.8m</td>
<td>6.1%</td>
</tr>
</tbody>
</table>

Notes: RTSA = reverse total shoulder arthroplasty. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
### Exhibit 4-13: Shoulder Arthroplasty—Italy, Market Forecast, 2015–20

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Total Shoulder Arthroplasty</td>
<td>$4.1m</td>
<td>$4.2m</td>
<td>$4.4m</td>
<td>$4.6m</td>
<td>$4.9m</td>
<td>$5.2m</td>
<td>4.9%</td>
</tr>
<tr>
<td>RTSA</td>
<td>8.9</td>
<td>9.5</td>
<td>10.1</td>
<td>10.7</td>
<td>11.5</td>
<td>12.4</td>
<td>6.9%</td>
</tr>
<tr>
<td>Hemiarthroplasty</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>0.9%</td>
</tr>
<tr>
<td>Shoulder Resurfacing</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.5%</td>
</tr>
<tr>
<td>Revision Shoulder Arthroplasty</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.6</td>
<td>1.6</td>
<td>1.6</td>
<td>1.3%</td>
</tr>
<tr>
<td>Total shoulder arthroplasty sales</td>
<td>$16.3m</td>
<td>$17.1m</td>
<td>$17.9m</td>
<td>$18.8m</td>
<td>$19.8m</td>
<td>$21.1m</td>
<td>5.3%</td>
</tr>
</tbody>
</table>

**Notes:** RTSA = reverse total shoulder arthroplasty. Figures may not calculate due to rounding.

**Sources:** Company financials; Meddevicetracker
### Exhibit 4-14: Shoulder Arthroplasty—Spain, Market Forecast, 2015–20

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Shoulder Arthroplasty</td>
<td>$0.3m</td>
<td>$0.3m</td>
<td>$0.3m</td>
<td>$0.4m</td>
<td>$0.4m</td>
<td>$0.4m</td>
<td>5.0%</td>
</tr>
<tr>
<td>RTSA</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.5</td>
<td>6.0%</td>
</tr>
<tr>
<td>Hemiarthroplasty</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.1</td>
<td>0.9%</td>
</tr>
<tr>
<td>Shoulder Resurfacing</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.3</td>
<td>2.0%</td>
</tr>
<tr>
<td>Revision Shoulder Arthroplasty</td>
<td>2.2</td>
<td>2.3</td>
<td>2.3</td>
<td>2.4</td>
<td>2.5</td>
<td>2.6</td>
<td>3.4%</td>
</tr>
<tr>
<td>Total shoulder arthroplasty sales</td>
<td>$1.6m</td>
<td>$3.3m</td>
<td>$3.4m</td>
<td>$3.6m</td>
<td>$3.7m</td>
<td>$3.8m</td>
<td>3.6%</td>
</tr>
</tbody>
</table>

**Notes:** RTSA = reverse total shoulder arthroplasty. Figures may not calculate due to rounding.

**Sources:** Company financials; Meddevicetracker

Exhibit 4-15 presents estimated sales and market share data for the leading suppliers of shoulder arthroplasty implants for the US market in 2015.

Exhibit 4-16 presents estimated sales and market share data for the leading supplier of shoulder arthroplasty implants for the European market in 2015.
**Exhibit 4-15: 2015, United States Shoulder Arthroplasty Implants Market, Share by Supplier**

<table>
<thead>
<tr>
<th>Company</th>
<th>Estimated Sales</th>
<th>Estimated Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zimmer/Zimmer Biomet</td>
<td>$254.0m</td>
<td>38.0%</td>
</tr>
<tr>
<td>DePuy Synthes/Johnson &amp; Johnson</td>
<td>140.0</td>
<td>21.0%</td>
</tr>
<tr>
<td>Wright Medical Group</td>
<td>134.0</td>
<td>20.0%</td>
</tr>
<tr>
<td>Others</td>
<td>140.0</td>
<td>21.0%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$668.0m</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

Notes: The “Others” category includes Corin, DJO Global, Exactech, Smith & Nephew, and Stryker, among others. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
### Exhibit 4-16: 2015, European Shoulder Arthroplasty Implants Market, Share by Supplier

<table>
<thead>
<tr>
<th>Company</th>
<th>Estimated Sales</th>
<th>Estimated Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zimmer/Zimmer Biomet</td>
<td>$43.0m</td>
<td>33.0%</td>
</tr>
<tr>
<td>DePuy Synthes/Johnson &amp; Johnson</td>
<td>33.0</td>
<td>25.0%</td>
</tr>
<tr>
<td>Wright Medical Group</td>
<td>33.0</td>
<td>25.0%</td>
</tr>
<tr>
<td>Others</td>
<td>21.0</td>
<td>17.0%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$130.0m</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

**Notes:** Estimated sales and market share data for Europe are for France, Germany, Italy, Spain, and the United Kingdom. The “Others” category includes Baumer, Corin, Evolutis, FH Orthopedics, Implants International, Implantcast, JRI Orthopedics, Lima Corporate, Mathys, Smith & Nephew, and Stryker, among others. Figures may not calculate due to rounding.

**Sources:** Company financials; Meddevicetracker
5. **ELBOW ARTHROPLASTY**

The anatomy of the elbow joint facilitates a connection between the humerus bone in the upper arm and the ulna and radius in the forearm. Also known as elbow replacement, elbow arthroplasty refers to the removal and replacement of damaged parts of the ulna and humerus with artificial components.

### 5.1 Indications for Elbow Arthroplasty

Unlike other joint replacements such as hip, knee, and shoulder, elbow arthroplasty is most typically performed as a result of rheumatoid arthritis (RA), followed by post-traumatic arthritis, rather than degenerative osteoarthritis (OA). In 1997, RA was reported to be the main indication for total elbow arthroplasty (TEA) in New York, US. In 2006, however, trauma was considered to be one of the major indications for TEA (Gay DM et al, 2012). Other conditions include acute distal humerus fractures, hemophilia, juvenile RA, and tumors. Typically performed in aged patients with low functional demand, adoption of TEA has been evolving continuously.

Although TEA provides significantly high success rates for elderly patients with limited functional demand, it is associated with high complication rates. While complications such as loosening of the humeral component, infection, tricep weakness, and ulnar neuropathy are common, the most frequent cause of failure is excessive load placed on the implant by high-demand patients. Revision of a failed total elbow replacement is typically managed using a linked system.

### 5.2 Types of Elbow Arthroplasty

Accounting for only around 10% of overall elbow surgeries performed in the US in 2010, elbow arthroplasty can be classified into two main types: hemiarthroplasty and total elbow replacement (Ahmet K. et al, 2015).

#### 5.2.1 Hemiarthroplasty

As the name suggests, only a few components of the elbow joint may be replaced in hemiarthroplasty. Although the head of the radius, the distal humerus, or the proximal ulna (with a stemmed implant) can be replaced during this procedure, replacement of the humeral and ulnar components is rare owing to high failure rates. Thus, hemiarthroplasty effectively comprises replacement of the radial head with a
radial head implant. More recently, new techniques such as capitellar arthroplasty and radio-capitellar replacement are also being used to prevent OA and capitellar erosion in patients with a radial head prosthesis.

### 5.2.2 Total Elbow Replacement

In contrast to hemiarthroplasty, total elbow replacement comprises both ulnar and humeral components along with a plastic and metallic hinge. While in the past, terms such as constrained, unconstrained, hinged, and resurfacing were used, more recently total elbow replacement implants can be classified as linked and unlinked. Currently, based on the position of the implant, elbow arthroplasty implants can be classified as radial head prosthesis, unicompartmental lateral prosthesis, and total elbow prosthesis.

### 5.3 Clinical and Market Trends in Elbow Arthroplasty

**Evolution and improvement in surgical techniques and TEA implant designs**

Performed in selected incapacitating elbow diseases, elbow arthroplasty is a less common procedure in comparison to other joint arthroplasties. The elbow is a complex joint that amalgamates three bones, so mimicking the natural joint anatomically and physiologically has been considered challenging. Flawed by issues such as high loosening rate, joint dislocation, and limited functionality in addition to limited flexion and extension of the arm, adoption of this surgery has been gradual. However, owing to promising results demonstrated by a few early surgical experiments, a surge in the number of patients for elbow arthroplasties began in the 1970s. Despite innovations in various TEA models, overall post-operative complication rate was high at about 57% (Trancik T et al., 1987).

First-generation TEA models were constrained and linked, thereby imparting a high level of stress on the bone-implant interface that resulted in frequent loosening. In order to overcome this limitation, second-generation or semi-constrained linked implants were introduced. With sloppy hinges and a semi-constrained design, the implant allowed varus-valgus laxity and introduced less stress on the bone-implant interface. Unlinked implants that provided more flexibility were also introduced. In recent years, third-generation or convertible implants have also been introduced that allow the surgeon to make decisions around design type during the surgery.
Along with improvements in materials and models, corresponding surgical techniques have also been evolving. Two surgical approaches—triceps sparing and non-triceps sparing—have been documented. However, reports suggest that the triceps-sparing approach contributes to better tribology and reduced chances of infection. Therefore, although not very well utilized currently, the widespread usage of elbow arthroplasty is inevitable with the development of newer designs, materials, and surgical techniques.

**Wider clinical application driving procedural volume and outcomes**
Initially recommended for RA, elbow arthroplasty is gaining widespread adoption. Attributed to the availability of disease-modifying anti-rheumatic drugs, the key indication for elbow arthroplasty is steadily shifting from RA to trauma. As per a study by Gay et al. (2012), post-traumatic conditions accounted for 62% of elbow arthroplasty, while RA accounted for only about 25%.

Moreover, use of elbow arthroplasty for the primary management of comminuted elbow fractures is also rising. Techniques such as radial head replacement, unicompartmental replacement, and hemiarthroplasty for specific joints are also gaining relevance. In addition, adoption of TEA as the treatment of choice for most patients with post-operative resection of a neoplasm has been incremental. Characterized by limited bone stock, damage to the articular cartilage, joint contracture, and compromised bone viability, treatment of the distal humerus nonunion with internal fixation is particularly challenging. Elbow arthroplasty in such conditions has been reported to be useful and reliable. Despite permanent restrictions on strenuous activities, advancements in surgical techniques and prosthetic design have made the procedure suitable for younger patients as well. The introduction of linked semi-constrained prostheses and the continued publication of literature and research has further bolstered adoption of the procedure in a wider set of indications.

**Utilization of total elbow arthroplasty as an outpatient procedure could aid procedural growth in long-term future**
Characterized by severe post-operative pain, TEA requires hospitalization to provide a potent analgesic. Thus, the cost of the procedure and overall cost of the associated hospitalization is observed to be significantly high. With an intention to reduce the length of hospital stay and associated cost, a prospective investigation was conducted by Ilfeld et al. (2006) to evaluate the feasibility of converting TEA into
an outpatient or an ambulatory procedure, whereby a continuous infraclavicular nerve block as part of a multi-modal analgesic regimen was provided at home. The study suggested the conversion of TEA into an ambulatory process using this continuous infraclavicular nerve block in a subset of patients without any co-morbidities. Although far from being accepted into mainstream use, the conversion of TEA to an ambulatory procedure is likely to be investigated further.

Clinical studies to substantiate better outcomes of TEA over other fixation techniques in progress
With higher acceptance, TEA is now being used for wider clinical indications. As a viable treatment option for acute, displaced, and comminuted intra-articular fractures in the elderly, many studies are underway to substantiate and compare TEA’s clinical outcomes as compared to other fixation techniques. For example, studies are being conducted to compare primary TEA outcomes in the treatment of distal humerus intra-articular fractures in the elderly with open reduction and internal fixation (ORIF) surgery. At a 4.5-year follow-up, excellent results of 91% of the TEA patients compared to only 33% in the ORIF group was noted (Fajardo M and Kwon YW, 2013). Moreover, in a recent level-one incidence prospective randomized trial published in Orthopaedics & Traumatology: Surgery & Research, the Mayo elbow performance score and the disabilities of the arm, shoulder and hand (DASH) scores were reported to be better in the group of patients treated with TEA for their intra-articular distal humerus fractures.

Gradual fade-out in usage of constrained linked elbow joint implants in elbow arthroplasty
With distinct benefits, such as a significant reduction in pain as well as higher flexibility of the joint, TEA is gaining relevance worldwide. However, as a result of high complication rates and low utilization in comparison to other joint arthroplasties, improvements in design, biomaterials, and models are being sought. Traditionally, the majority of the elbow arthroplasty procedures utilized linked implants such as the Swanson and the Gschwend-Scheier-Bähler III (GSB III) prosthesis that provided robust joint stability. However, as the implants only allow motion on one plane, rotational and angular movements transmitted high levels of stress onto the cemented bone-implant interface, which further led to aseptic loosening and high rate of wear and tear. Thus, usage of linked constrained implants is nearly outdated. Semi-constrained linked implants such as the Coonrad-Morrey Total Elbow replacement and Discovery Elbow System are now gaining widespread popularity,
especially in patients with low bone stock, highly deformed bones, and ligament insufficiency. Preferred in patients with better ligamentous integrity, higher bone stock, and a requirement for higher flexibility, unlinked implants such as the Kudo, Norway, and Souter-Strathclyde have also been gaining prominence (Mark F, 2013; Kim JM, 2011).

Clinical studies pave the way for wider adoption of semi-constrained linked elbow implant prostheses
Multiple publications have reported the outcomes of various implant designs in isolation, but direct comparative studies between specific implant types are limited. In the few direct comparative studies conducted between unconstrained and semi-constrained elbow implants for the treatment of RA, the semi-constrained type of implant was reported to have better clinical outcomes and survivorship. Although both the implants were observed to have similar Mayo elbow performance and patient satisfaction, survivorship of semi-constrained implants, even after five years, was significantly high at 100%. In another study conducted by Little and colleagues in 2005, although all the implant types reported similar pain relief and flexibility, survivorship of the semi-constrained implant (Coonrad-Morrey) at five years was reported to be 90% as compared to 82% with the non-constrained implant. Moreover, owing to a wider application, even in patients with low bone stock and insufficient ligament integrity, utilization of the semi-constrained implant type has been increasing; they are currently deemed to be popular worldwide, especially in the US and Central Europe (Ante P, 2016; Kim JM, 2011).

Research underway on newer implant design to address patients with low bone stock and ligamentous structure
The usage of semi-constrained linked implants with sloppy hinges has been gaining acceptance worldwide. However, new-generation implants are also being developed with archetypal features that provide added advantages on one hand and the convenience to convert them to a linked or unlinked implant during the surgical procedure on the other. Also known as third-generation or modern implants, these prostheses are believed to allow more anatomic reconstruction with less contact pressure. Moreover, without revising the humeral stem, this system is purported to allow conversion of a distal humerus hemiarthroplasty to a TEA. Limited research has been carried out to establish the clinical benefits of the new-generation convertible implants. However, based on limited data, these implants were reported to reduce pain and improve motion significantly while causing minimal aseptic
loosening. Although yet to be absorbed in mainstream usage, convertible implants are likely to pave the way for further innovations aimed at addressing insufficient bone stock and ligaments, which is known to be a limiting factor in many cases. Recently, Japanese researchers in association with Kyocera Medical have been developing a new form of linked prosthesis initially to be used for relatively small bones (Nishida K et al., 2014). Yet to be considered for commercial use, the prosthesis known as PROSNAP could become an implant of choice in patients with small bony structures.

5.4 Procedure Volumes

During the forecast period covered by this report, the total number of elbow arthroplasty procedures performed in the US and the EU5 (France, Germany, Italy, Spain, and the UK) are anticipated to expand at a compound annual rate of 5.8%, from approximately 26.2 thousand procedures in 2015 to an estimated 34.8 thousand procedures by the year 2020.

Exhibit 5-1 presents the combined procedure volumes forecast for elbow arthroplasty procedures for the US and EU5 countries for the years 2015 through 2020.

5.5 Industry Challenges for Elbow Arthroplasty

Shortage of experienced orthopedic surgeons in Spain likely to impede growth of newer techniques and impact adoption of recently evolving extremity arthroplasty such as ankle and elbow

At the juncture of an acute doctor-shortage crisis, the Spanish government has been intensifying their efforts to rectify medical shortages. In 2009, Spain had a shortfall of over 3,000 medical professionals. Should the trend continue, by 2025 Spain is likely to reach a deficit of 25,000 seats (El Periódico De Aragón Society, 2016). Although the shortage is most pronounced in pediatrics and family medicine, anesthesiology and resuscitation, orthopedic surgery, and radiology are likely to be in imminent danger. In its last expansive phase in 2008, Spain had to make use of the services of physicians coming from Eastern Europe and Latin America. Although such fixes bridge the demand-supply gap temporarily, historically they have been observed to bring about professional and technical disharmony. Thus, recently evolved arthroplasty of the extremities, such as the ankle and elbow, that requires skilled
### Exhibit 5-1: Elbow Arthroplasty, Combined Procedure Volumes Forecast, 2015–20

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>21.6</td>
<td>22.8</td>
<td>24.2</td>
<td>25.6</td>
<td>27.2</td>
<td>29.1</td>
<td>6.1%</td>
</tr>
<tr>
<td>France</td>
<td>0.4</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.6</td>
<td>0.6</td>
<td>8.4%</td>
</tr>
<tr>
<td>Germany</td>
<td>2.6</td>
<td>2.7</td>
<td>2.8</td>
<td>3.0</td>
<td>3.1</td>
<td>3.3</td>
<td>4.9%</td>
</tr>
<tr>
<td>Italy</td>
<td>0.5</td>
<td>0.5</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>0.6</td>
<td>3.7%</td>
</tr>
<tr>
<td>Spain</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>2.9%</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>0.8</td>
<td>0.8</td>
<td>0.8</td>
<td>0.9</td>
<td>0.9</td>
<td>1.0</td>
<td>4.6%</td>
</tr>
<tr>
<td><strong>Total elbow arthroplasty procedures</strong></td>
<td><strong>26.2</strong></td>
<td><strong>27.6</strong></td>
<td><strong>29.1</strong></td>
<td><strong>30.8</strong></td>
<td><strong>32.6</strong></td>
<td><strong>24.8</strong></td>
<td><strong>5.8%</strong></td>
</tr>
</tbody>
</table>

**Notes:** Total elbow arthroplasty procedures include primary total elbow arthroplasty and radial head arthroplasty. Procedure volumes are reported in thousands. Figures may not calculate due to rounding.
Exhibit 5-1: (Continued)

Note: Total elbow arthroplasty procedures include primary total elbow arthroplasty and radial head arthroplasty.

Sources: American Joint Replacement Registry; Catalan Arthroplasty Registry; Endo Prothesen Register Deutschland; Meddevicetracker; National Joint Registry of the United Kingdom; SoFCOT and Haute Autorité de Santé
orthopedic surgeons for successful clinical outcomes are likely to be constrained. Owing to higher complication rates compared to hip and knee arthroplasty as well as a lack of knowledge regarding surgical techniques and approaches, widespread usage of elbow and ankle arthroplasty is likely to be negatively impacted.

**Significant anatomical challenges posed by elbow joint and difficulties in revision surgery likely to hinder widespread adoption of elbow arthroplasty**

In the past, functional improvement of fracture care was attributed to the patient's healing potential. However, owing to the emergence of arthroplasty procedures, complete functional recovery even in geriatric patients has become an important clinical expectation. Although arthroplasty provides better fracture stabilization and facilitates quick mobilization, adoption of elbow arthroplasty has been rather slow. Merely 10% of all elbow surgeries conducted in the US in the year 2006 were represented by arthroscopy and arthroplasty (Kinaci A et al., 2015). Attributed to common problems such as aseptic loosening rates that range from 15–49% over long-term follow-up, confidence in elbow arthroplasty implants has been bleak.

Challenges with fracture fixation in geriatric patients owing to brittle osteoporotic bones and lack of bone mass makes the procedure unfavorable in elderly patients. Furthermore, owing to the distinct anatomical challenges presented by the elbow joint, the chances of successful revision surgery are low. Thus, limited bone mass in the native joint and further bone loss post-fracture surgery make revision of elbow arthroplasty significantly challenging. Consequently, high complication rates as a result of slight biomechanical or soft tissue misalignment could affect the confidence of surgeons in performing elbow arthroplasty in the near future.

### 5.6 Market Drivers for Elbow Arthroplasty

**Improved survival rates in recent years providing impetus to total elbow arthroplasty**

Although introduced a few decades back, adoption of elbow arthroplasty has been rather slow when compared to hip and knee. Plagued by challenges such as intrinsic stability, high dislocation, and limited flexion and extension with old-generation implants, acceptance of this procedure for major indications impacting the elbow has been limited. However, in recent years, elbow implants have undergone various design and technological advancements. With the introduction of the new-generation
semi-constrained linked, unlinked, and convertible implants, the survival rate of different types of TEA has improved. With the survival rate reaching almost 90% in the last five years and the loosening rate using sloppy-hinged TEA remaining steady at about 5%, the confidence and expertise of those performing the surgery has been increasing (Ante P et al., 2016).

**Emerging elbow arthroplasty registries across various countries likely to substantiate clinical outcomes and aid further innovation**

Being a low-volume surgery, research papers with established clinical outcomes for elbow arthroplasty are limited. Due to improved management of RA with medical therapy, the need for surgical intervention such as elbow arthroplasty in RA has been declining. However, upcoming indications such as post-traumatic OA have triggered adoption of the procedure in many parts of the world; although registries for elbow joint replacement have been functional in the past, in recent years the procedure has been gaining significant importance. Beset by limited clinical research, outcomes, and survival data, elbow arthroplasty has always been under contention, largely as a result of its complication rate. However, with the recent change in perception and increased confidence in the procedure, many countries have begun formulating registries and conducting retrospective studies to evaluate associated costs, clinical outcomes, and patient satisfaction. The first arthroplasty register was established in Sweden in 1975. Since then, many countries such as Germany, the UK, and Canada have been trying to follow a fully fledged nationalized registry for all types of joint replacements. However, only a few countries such as the UK, Italy, Finland, and Norway, among others, have been able to establish a national registry for elbow replacement. With more emphasis now being laid on having a nationalized registry for elbow arthroplasty, the identification of poorly performing implants or operational procedures, the improvisation of surgical practice, and innovation in implant designs are all inevitable. Outcomes-related studies based on the Scottish Arthroplasty Project, Norwegian Arthroplasty Register, Finnish Arthroplasty Register, and others have been published, thus providing opportunities for further research and development.

**Encouraging outcomes in unicompartmental arthroplasty, such as radial head or radiocapitellar replacement, likely to drive market for elbow arthroplasty**

Indicated in comminuted fracture with inadequate reduction and unstable osteosynthesis, radial head replacement can be performed with unipolar or bipolar,
monoblock or modular, anatomical or non-anatomical, and cemented or press-fit prostheses. Owing to the absence of modularity that does not allow for the restoration of anatomy and radial head kinematics, unipolar monoblock radial head implants are becoming obsolete. Similarly, owing to a lack of duplicability of all the anatomical variants in the proximal radius and the need for meticulous surgical technique to avoid articular incongruity, adoption of anatomical modular implants has been limited. However, in recent times, bipolar modular prostheses have been gaining relevance as a result of their adaptability to myriad patient anatomies. The automatic placement of the radial head and neck with respect to opposite articular surfaces, along with decreased stress at the stem-bone and head-cartilage interfaces are likely to help reduce aseptic loosening and wear of the ulnar and humeral cartilage in this implant type.

As a new substitute to TEA, radiocapitellar replacement is gaining gradual prominence in the treatment of degenerative and inflammatory conditions of the elbow. As reported by various clinical studies, inflammatory as well degenerative conditions initially impact the radio-humeral joint. Thus, this clinical progression warrants arthroplasty that replaces only the lateral compartment of the joint. Owing to severe compartmental changes in diseases such as primary OA, RA, sequelae of lateral compartment fractures, complex elbow instability, and forearm longitudinal instability, arthroplasty continues to be the most effective therapy for pain relief. In the past, in the event of failure with procedures such as debridement, synovectomy, and capitellectomy, TEA was the only option. However, the limited usage of TEA in younger patients marked the emergence of unicompartmental arthroplasty. Currently available unicompartmental arthroplasty systems include UNI-Elbow Radio Capitellum System (from Small Bone Innovations) and the Lateral Resurfacing Elbow (from Biomet). Typically indicated in severe pain arising from degenerative and inflammatory conditions of the lateral component, unicompartmental arthroplasty preserves bone stock in cases where subsequent TEA could be required. Although unicompartmental arthroplasty or a lateral replacement elbow provides pain relief and functional recovery, mainstream usage is yet to be established owing to a lack of studies that validate implant survival. Moreover, limited biochemical analysis data show that currently available prostheses may not sufficiently emulate the radiocapitellar anatomy and could cause earlier failure due to progressive ulnohumeral erosion.
Elbow Arthroplasty procedures in the US driven by aging population and fracture of radial head

Elbow surgeries in the US are primarily aimed at addressing enthesopathies (such as tennis elbow), cubital tunnel syndrome, and trauma. It is estimated that more than three-quarters of the total elbow surgeries conducted in the US are for treating enthesopathy, cubital tunnel syndrome, or fracture (radial head in particular). Arthroscopy and arthroplasty typically account for approximately 10% of all elbow surgeries (Kinaci A et al., 2015). While sport-related surgeries for athletes form a small part of overall elbow procedures, trauma accounts for a substantial proportion. Fracture treatment is the second most common indication for elbow surgery in the US. It is estimated that the most common elbow fracture is that of the radial head; over 17,200 radial head arthroplasties were conducted in the US in 2015. Driven by falls among the expanding aging population that result in severe fractures of the olecranon and distal humerus, it is estimated that these procedures will grow at over 6% each year over the next five years in the US.

5.7 Products

Companies that offer elbow implant products for the US and European markets include Acumed, DePuy Synthes/Johnson & Johnson, DJO Global, Stryker, Wright Medical Group, and Zimmer-Biomet, among others.

5.7.1 Types of Elbow Arthroplasty Implants

Elbow arthroplasty implants can be classified as linked, unlinked, and modern or convertible elbow implants.

5.7.1.1 Linked Elbow Arthroplasty Implants

Marked by physical linking of the humeral and ulnar components at the time of surgery, previous-generation linked implants had constrained hinges that only allowed bending and extension of the arm. These implants had a significant failure rate owing to the high stress they transmitted to the implant-cement-bone interface and other design errors. Thus, recently launched semi-constrained linked implants with a loose-fitting hinge that allows some rotational and varus-valgus play are being widely accepted. However, their usage has traditionally shown better functional outcome in RA as compared to post-traumatic arthritis.
The advantages of linked elbow arthroplasty implants include: higher joint stability; a reduced chance of joint dislocation; utilization in patients with insufficient bone mass or ligament structure; and an expanded range of approved indications for use. The disadvantages of linked implants include: increased tension between the bone-implant interface, resulting in potential mechanical failure due to wear and/or loosening; linking mechanism failure; procedural complexity; and increased usage of canal space leading to procedural complications during revision surgery.

### 5.7.1.2 Unlinked/Uncoupled Elbow Arthroplasty Implants

Characterized by the absence of physical linkages between the humeral and ulnar component, unlinked TEA implants depend heavily on the surrounding musculature and soft tissues for joint stability. Apt for patients with reasonable bone stock, ligamentous integrity, and preserved surrounding tissues, unlinked TEA implants are believed to aid better motion between the bones and to transmit less pressure to the implant-bone interface. Although characterized by a higher rate of dislocation, potential risk of instability, and decreased elbow extension, unlinked TEA enjoys significant popularity in the US and Asia. While unlinked implants are favored in patients with well-preserved bone stock and ligaments, well-studied linked implants are preferred overall as they provide joint stability and are suitable for replacement in a broader gamut of indications.

The advantages of unlinked elbow arthroplasty implants include: reduced stress to the bone-implant interface, resulting in a lower risk of wear and loosening; reduced surgical invasiveness, limiting possible restrictions on revision surgery; and it allows the use of hemiarthroplasty-specific parts. The disadvantages of unlinked elbow implants include: increased risk of dislocation; dependence on surrounding musculature growth for proper positioning and joint attachment; the necessity for increased implant positioning; and incompatibility in patients with high bone loss and/or insufficient ligamentous network.

### 5.7.1.3 Convertible/Modern Implants

Following clinical studies to establish better clinical outcomes between linked and unlinked elbow arthroplasty implants, a new generation of convertible or modern implants has been launched. These implants allow the decision on linking or unlinking to be made during the surgery, depending on the surgeon's intraoperative
evaluation of stability. The Latitude prosthesis by Wright Medical Group and the Acclaim Total Elbow System by DePuy Synthes are completely modular and allow interchangeability between humeral and ulnar sizes, thereby providing better anatomical fit. Furthermore, these convertible implants are deemed to be particularly effective when the choice between linked or unlinked TEA is unclear owing to complications or other underlying conditions. In addition, with this type of system a distal humerus hemiarthroplasty can be converted to a TEA without any revision to the humeral stem. Despite predictable benefits, clinical literature on these implants is scarce; hence, they are likely to undergo a few outcomes-oriented clinical studies.

5.8 Market Forecast
The global elbow arthroplasty implants market was valued at approximately $66.4 million in 2015 and is expected to grow at a compound annual rate of 5.6%, reaching approximately $87.1 million by the year 2020.

Exhibit 5-2 presents the combined market forecast for elbow arthroplasty implants by country/region for the years 2015 through 2020.

Exhibit 5-3 presents the combined market forecast for elbow arthroplasty implants for the five major European markets for the years 2015 through 2020.

5.9 Competitors
Accounting for approximately 37% of the US elbow implant’s market revenues, Zimmer was the leader in the US elbow implants market in 2015. The company achieved significant growth in the elbow arthroplasty implants segment both internationally and in the US with sales of its Coonrad/Morrey Total Elbow implant. Outside of the US, Zimmer commanded an estimated 35% of total elbow implant sales for the five major European markets.

In 2015, Wright Medical Group accounted for an estimated 32% of total elbow implant revenues for the US market. The company offers its LATITUDE EV Total Elbow Arthroplasty System across major markets. In October 2015, Wright Medical Group and Tornier completed the planned merger between the two companies. The combined companies will continue to operate under the name Wright Medical Group. For the five major European markets, Wright Medical accounted for approximately 30% of total elbow implant sales in 2015.
### Exhibit 5-2: Global Elbow Arthroplasty Implant Sales by Country/Region, Combined Market Forecast, 2015–20

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>$41.6m</td>
<td>$43.9m</td>
<td>$46.5m</td>
<td>$49.3m</td>
<td>$52.3m</td>
<td>$55.6m</td>
<td>6.0%</td>
</tr>
<tr>
<td>Europe</td>
<td>9.0</td>
<td>9.4</td>
<td>9.8</td>
<td>10.2</td>
<td>10.7</td>
<td>11.2</td>
<td>4.5%</td>
</tr>
<tr>
<td>Rest of the World</td>
<td>15.8</td>
<td>16.6</td>
<td>17.4</td>
<td>18.3</td>
<td>19.3</td>
<td>20.4</td>
<td>5.2%</td>
</tr>
<tr>
<td>Total elbow implant sales</td>
<td>$66.4m</td>
<td>$69.9m</td>
<td>$73.7m</td>
<td>$77.8m</td>
<td>$82.8m</td>
<td>$87.1m</td>
<td>5.6%</td>
</tr>
</tbody>
</table>

Notes: System sales for Europe include product sales in Germany, France, Italy, the United Kingdom, and Spain. The Rest of the World segment includes product sales from Africa and the Middle East, Asia-Pacific, Europe, and North and South America and excludes product sales for Germany, France, Italy, the United Kingdom, Spain, Japan, and the United States. Figures may not calculate due to rounding.
Notes: System sales for Europe include product sales in Germany, France, Italy, the United Kingdom, and Spain. The Rest of the World segment includes product sales from Africa and the Middle East, Asia-Pacific, Europe, and North and South America and excludes product sales for Germany, France, Italy, the United Kingdom, Spain, Japan, and the United States.

Sources: Company financials; Meddevicetracker
### Exhibit 5-3: Elbow Arthroplasty—Major European Markets, Combined Market Forecast, 2015–20

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>$0.7m</td>
<td>$0.7m</td>
<td>$0.8m</td>
<td>$0.8m</td>
<td>$0.9m</td>
<td>$0.9m</td>
<td>5.2%</td>
</tr>
<tr>
<td>Germany</td>
<td>5.3</td>
<td>5.5</td>
<td>5.8</td>
<td>6.0</td>
<td>6.3</td>
<td>6.6</td>
<td>4.5%</td>
</tr>
<tr>
<td>Italy</td>
<td>1.0</td>
<td>1.0</td>
<td>1.1</td>
<td>1.1</td>
<td>1.1</td>
<td>1.2</td>
<td>3.7%</td>
</tr>
<tr>
<td>Spain</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.5</td>
<td>2.7%</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>1.6</td>
<td>1.7</td>
<td>1.7</td>
<td>1.8</td>
<td>1.9</td>
<td>2.9</td>
<td>4.6%</td>
</tr>
<tr>
<td><strong>Total elbow implant sales</strong></td>
<td><strong>$9.0m</strong></td>
<td><strong>$9.4m</strong></td>
<td><strong>$9.8m</strong></td>
<td><strong>$10.2m</strong></td>
<td><strong>$10.7m</strong></td>
<td><strong>$11.2m</strong></td>
<td><strong>4.5%</strong></td>
</tr>
</tbody>
</table>

**Note:** Figures may not calculate due to rounding.

**Sources:** Company financials; Meddevicetracker
Other suppliers of elbow arthroplasty implant products to the US market include Acumed, DJO Global, and Stryker, among others. Other suppliers of elbow arthroplasty implants to the European market include Implantcast, Stryker, and Waldemar Link, among others.

Exhibit 5-4 presents estimated sales and market share data for the leading suppliers of elbow arthroplasty implants for the US market in 2015.

Exhibit 5-5 presents estimated sales and market share data for the leading suppliers of elbow arthroplasty implants for the European market in 2015.
**Exhibit 5-4:** 2015, United States Elbow Arthroplasty Implants Market, Share by Supplier

<table>
<thead>
<tr>
<th>Company</th>
<th>Estimated Sales</th>
<th>Estimated Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zimmer/Zimmer Biomet</td>
<td>$15.4m</td>
<td>37.0%</td>
</tr>
<tr>
<td>Wright Medical Group</td>
<td>13.3</td>
<td>32.0%</td>
</tr>
<tr>
<td>Others</td>
<td>12.9</td>
<td>31.0%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$41.6m</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

Notes: The “Others” category includes Acumed, DJO Global, and Stryker, among others. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
Exhibit 5-5: 2015, European Elbow Arthroplasty Implants Market, Share by Supplier

<table>
<thead>
<tr>
<th>Company</th>
<th>Estimated Sales</th>
<th>Estimated Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zimmer/Zimmer Biomet</td>
<td>$3.2m</td>
<td>35.0%</td>
</tr>
<tr>
<td>Wright Medical Group</td>
<td>2.7</td>
<td>30.0%</td>
</tr>
<tr>
<td>Others</td>
<td>3.1</td>
<td>35.0%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$9.0m</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

Notes: The “Others” category includes Implantcast, Stryker, and Waldemar Link, among others. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
6. **ANKLE ARTHROPLASTY**

Ankle arthroplasty refers to the replacement of damaged articular surfaces and cartilage in the ankle joint with artificial prostheses. Although publicized as a promising treatment in the 1970s, procedural volume had declined progressively by the 1980s owing to high failure rates. Among extremity joint replacements, ankle joint replacement surgery continues to be one of the rarely performed procedures.

6.1 **Indications for Ankle Arthroplasty**

Total ankle arthroplasty (TAA) or total ankle replacement (TAR) is an alternative to ankle arthrodesis and is typically indicated in the treatment of end-stage ankle arthritis in select patients. More so than physiological condition, careful patient selection is particularly pertinent to successful clinical outcomes in this procedure. A limited number of patients qualify for the surgery owing to commonly cited contraindications. Patients more than 50 years of age, with low to normal body mass index (BMI) (non-obese), and modest physical demands are more likely to qualify. However, a few studies have stated similar outcomes between patients less than and above 50 years of age. While age is known to be a less determining factor, weight and activity levels are key considerations when recommending the procedure. Non-obese and less active patients are likely to exert less stress on the replaced ankle; hence, lower revision and failure rates are expected.

Research around TAR technique for arthrodesis and similar indications was triggered mainly as a result of dissatisfaction with the stagnation of developments in TAR compared to the improved clinical outcomes being achieved in other joint replacement surgeries. Moreover, stiffness caused by ankle fusion resulted in additional stress on other adjacent joints that further led to deterioration. Thus, the occurrence of degenerative alterations in other joints such as the subtalar, midtarsal, knee, hip, and contra-lateral ankle is likely to warrant a TAA.

Reported as another indication for TAR, bilateral end-stage ankle osteoarthritis (OA) may not be appropriately treated with ankle fusion. Significant detrimental effects on gait and the functional status of patients are limiting factors of an arthrodesis. Furthermore, in patients who have previously undergone a subtalar, triple, and/or midfoot fusion, the 2,3 tibiotalar fusion would completely stiffen the hindfoot, while
the TAR may preserve functional motion. It has been shown that the clinical outcomes of TAR when combined with hindfoot fusion is comparable to that of ankle replacement alone (Kim BS, 2010).

Consequently, an ideal candidate for TAR would be a young and middle-age adults with moderately less requirement of physical activity, minimal co-morbidities, normal or low BMI, sufficient bone stock, a well-aligned and firm hindfoot, good soft tissues conditions, and no neurovascular impairment of the lower extremity. TAR is contraindicated in patients with acute and chronic foot infections, an insensate foot, Charcot arthropathy, avascular necrosis of the talus, inadequate leg or foot musculature, paralysis, severe tibiotalar malposition, and lower limb deformities. Other contraindications for TAR may include younger age, a high demand for physical movement, high BMI, diabetes, and smoking.

Marred by complications such as loosening of components, infection, negative implant outcomes, and a high failure rate, ankle arthroplasty is now in the process of gaining momentum. Although minimal practice and exposure, newer implant designs and better surgical techniques are being researched. Although arthrodesis, or the fusion of bones, has traditionally been the treatment of choice in patients with ankle arthritis and severe disabling pain, ankle joint replacement has been gaining relevance due to better restoration of movement.

6.2 Clinical and Market Trends in Ankle Arthroplasty
Ankle replacement progressing towards becoming standard treatment for deteriorating ankle conditions such as ankle OA
Although known to be a conventional therapeutic measure for end-stage ankle OA and rheumatoid arthritis, ankle fusion is marked with complications, such as limited range of motion, diminished gait, and high re-operation rates. In ankle fusion, the worn-out part of the joint is disposed of and the bones are permanently locked together with screws and plates. Thus, loss of ankle joint motion could result in stress on other adjacent joints that are most often arthritic, leading to further degeneration in the long term. In various studies analyzing gait pattern, although slow, patients who underwent ankle replacement have exhibited better ankle motion, improved gait, and restored ground reaction force pattern. Moreover, with the launch of new and improved design options, implant survivorship has been increasing. In
one of the meta-analysis studies performed on the new-generation mobile-bearing implants, the five-year prosthesis survival rate was reported to be 90.6% (Gougoulias N et al., 2009). In a literature review of the two procedures, the revision and below-knee amputation rates with arthrodesis were reported to be 9% and 5%, respectively, as compared to 7% and 1% in TAR (Haddad SL et al., 2007). Consequently, with improved implant designs and a failure rate of 10–12% at around five years, TAR is increasingly gaining acceptance as the treatment of choice in many suitable patients.

**Biological ankle replacement could mark a new arena of customizable implants**

Despite recently established clinical outcomes, adoption of ankle replacement surgery has been rather slow. As a result of high complication rates, surgical site infection, and loosening, the usage of metal implants for ankles is contentious. Moreover, owing to the complicated technique involved, current metal ankle implants require a high level of clinical expertise, experience, and knowledge to ensure successful procedural outcomes. With the intention of closely mimicking the anatomy of the ankle and offering replacement without permanent metal implants, Dr DK Lee, the director of foot and ankle surgery at UC San Diego Medical Center, invented the non-metal biological ankle replacement system. Derived from human or animal collagen, the material has been used extensively for over a decade in abdominal and plastic surgery. In a two-hour long, minimally invasive surgical procedure, the damaged cartilage is removed and collagen is inserted. The collagen adapts and molds as per the contours of the patient’s ankle. Furthermore, to ensure complete blending of the material around the ankle joint, an external device is placed for a period of 4-6 weeks. Attached by small pins, the cylinder-shaped device serves as a shock system to keep the joint free from friction and movement until healing is complete. Apart from reducing the risk of rejection, the implant avoids fusion and provides flexibility.

### 6.3 Procedure Volumes

During the forecast period covered by this analysis, the total number of ankle arthroplasty procedures performed in the US and the EU5 (France, Germany, Italy, Spain, and the UK) is anticipated to expand at a compound annual growth rate (CAGR) of 9.5%, from approximately 20,900 procedures in 2015 to an estimated 32,900 procedures by 2020.
Exhibit 6-1 presents the combined procedure volumes forecast for ankle arthroplasty procedures for the US and EU5 countries for the years 2015 through 2020.

### 6.4 Industry Challenges for Ankle Arthroplasty

**High complication rates associated with total ankle arthroplasty and limited center of excellence for the procedure likely to impede short-term growth in procedural volume**

With the inception of three-component mobile-bearing ankle implants, acceptance of TAA as a routine procedure for ankle OA is imminent. However, at present the procedure is faced with high complication and revision rates arising from a lack of experienced surgeons in particular. In France, only 516 TAAs were performed in 2009, as compared to 1,331 ankle arthrodesis procedures (Pinar N et al., 2012). Additionally, in Germany each year only around 1,300 ankle arthroplasties are conducted currently, compared to at least three times as many ankle arthrodesis procedures. In the UK, although the number of ankle replacements conducted each year is increasing, at just above 500 ankle replacement procedures currently, the overall volume is substantially low. Owing to the advanced skill sets required and high difficulty levels involved with the procedure, the National Commission for the Evaluation of Medical Devices and Healthcare Technologies in France has suggested limiting the procedure to centers that have performed at least 10 TAAs per year for the past three years. Promulgation of such directives may only create pockets of excellence and hamper even distribution of the procedure. Thus, although on the verge of widespread adoption and acceptance, short-term growth is likely to be constrained (Jordan R et al., 2014; National Joint Registry UK, 2014; Pugely AJ et al., 2014; Kostuj T et al., 2014).

**Lack of surgeon experience in performing total ankle arthroplasty likely to limit faster adoption of the procedure**

With gradual improvements in success rates, TAA has gained sustained acceptance in the US and Europe. Although modern implants are associated with some risks and complications, failure and loosening rates have been significantly low and with the launch of third-generation mobile-bearing implants, design and biomechanics have been improving. However, despite improved implant design, issues around varying implantation techniques and the lack of a standard procedure make the success rate highly inconsistent. Thus, clinical success of the procedure depends
### Exhibit 6-1: Ankle Arthroplasty, Combined Procedure Volumes Forecast, 2015–20

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>17.4</td>
<td>19.0</td>
<td>20.9</td>
<td>23.0</td>
<td>25.3</td>
<td>28.1</td>
<td>10.1%</td>
</tr>
<tr>
<td>France</td>
<td>0.7</td>
<td>0.8</td>
<td>0.8</td>
<td>0.9</td>
<td>0.9</td>
<td>1.0</td>
<td>7.4%</td>
</tr>
<tr>
<td>Germany</td>
<td>1.6</td>
<td>1.8</td>
<td>1.9</td>
<td>2.0</td>
<td>2.2</td>
<td>2.4</td>
<td>8.4%</td>
</tr>
<tr>
<td>Italy</td>
<td>0.3</td>
<td>0.3</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>2.6%</td>
</tr>
<tr>
<td>Spain</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>2.7%</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>0.6</td>
<td>0.6</td>
<td>0.7</td>
<td>0.7</td>
<td>0.8</td>
<td>0.8</td>
<td>5.9%</td>
</tr>
<tr>
<td><strong>Total ankle arthroplasty procedures</strong></td>
<td><strong>20.9</strong></td>
<td><strong>22.7</strong></td>
<td><strong>24.8</strong></td>
<td><strong>27.2</strong></td>
<td><strong>29.8</strong></td>
<td><strong>32.9</strong></td>
<td><strong>9.5%</strong></td>
</tr>
</tbody>
</table>

**Notes:** Total ankle arthroplasty procedures include primary total ankle arthroplasty, partial ankle replacement, and revision surgery. Procedure volumes are reported in thousands. Figures may not calculate due to rounding.

(Continued)
Exhibit 6-1: (Continued)

Note: Total ankle arthroplasty procedures include primary total ankle arthroplasty, partial ankle replacement, and revision surgery.

Sources: American Joint Replacement Registry; Catalan Arthroplasty Registry; Endo Prothesen Register Deutschland; Meddevicetracker; National Joint Registry of the United Kingdom; SoFCOT and Haute Autorité de Santé
largely on the surgeon's experience and implantation technique; however, owing to
the procedure's limited exposure, only a few orthopedic surgeons have been able to
gain specialization. Moreover, as a result of the steep learning curve involved and
the absence of a standardized technique, adoption of TAA as a common procedure
is likely to be delayed (Daniels TR et al., 2012; Fevang B-TS et al., 2007).

6.5 Market Drivers for Ankle Arthroplasty

Acceptance of total ankle replacement in hemophilic ankle OA likely to drive
the procedural growth

Although a rare genetic condition, the prevalence of hemophilia worldwide is
reported to be increasing. According to 2013 statistics from the World Federation of
Hemophilia, the worldwide incidence of hemophilia is estimated at around 400,000
(World Federation of Hemophilia, 2013). In the US, hemophilia is estimated to occur
in one in every 5,000 male births. Moreover, age-adjusted incidence of acquired
hemophilia is reported to be between 1.3 and 1.5 per million per year (Tufano A,
2010). In 2010, more than 4,000 people in Germany and around 6,000 people in the
UK were diagnosed with hemophilia (German Hemophilia Registry, 2010; NHS,
2016). Fusion of the ankle joints was considered to be the standard treatment in
hemophilic patients with end-stage ankle OA; however, with the inception of three-
component, unconstrained ankle implants, studies are being conducted to evaluate
range of motion and gait patterns. While post-TAR patients are believed to have
similar gait patterns as healthy subjects, it was slightly diminished in patients with
hemophilia. However, when compared with ankle arthrodesis, gait pattern in
hemophilia patients was relatively superior. Since arthrodesis has been performed
for many more years than TAR, ankle fusion is currently deemed to be the standard
treatment. Despite limited studies due to the rarity of hemophilia, TAR remains the
recommended treatment option for hemophilia patients who present with a
preserved ankle range of motion. With this change in perception and growing
confidence in the procedure, indications for TAR are expected to broaden. The
growing prevalence of hemophilia in high-income countries is likely to further propel
expansion of TAR procedures.

Introduction of three-part, mobile-bearing, third-generation ankle implants to
drive adoption rates

Historically, TAR surgery was plagued by high failure and complication rates. First-
generation implants designed by Lord and Marotte were non-anatomical, restrictive,
and cemented. Composed of a long-stem tibial component coupled with a polyethylene talar component, the first-generation implant failed in almost 10 of the 25 surgeries conducted. First-generation constrained and cemented implant designs such as the Thompson Parkridge Richard ankle prosthesis and the Oregon ankle prosthesis impinged load on adjacent joints, thereby compromising joint mechanics and excessive loading. Consequently, the additional stress resulted in rapid aseptic loosening, which occurred in almost 90% of the implants (Alexej B et al., 2015).

Semi-constrained, two-component, second-generation implants such as DePuy Synthes’ Agility and the Buechel-Pappas' Total Ankle Replacement have succeeded the older generation. Although they mimicked the ankle’s anatomy and allowed lateral and limited rotational movement, implantation required significant bone removal. Moreover, mandatory fusion of the tibia and fibula during the procedure resulted in high complication rates. This led to the development of three-component, unconstrained, mobile-bearing implants. Designs such as the Salto Talaris Total Ankle Prosthesis by Integra LifeSciences and the STAR Ankle by Small Bone Innovations (acquired by Stryker in 2014) marked the beginning of wider acceptance, confidence, and usage of the procedure. The STAR Ankle implant eventually became the first TAA implant to complete a randomized, concurrently controlled, multicenter, US investigational device exemption (IDE) study against ankle fusion. In the study, STAR was proven to have statistical superiority and comparable safety to ankle fusion. As a result of the US Food and Drug Administration’s (FDA’s) approval of the three-part, mobile-bearing STAR device, uncemented ankle implants are likely to be the major contributors towards the future expansion and growth of the ankle implants market.

**Inclusion of three-component, mobile-bearing, third-generation total ankle replacement systems for reimbursement likely to boost the growth of ankle market**

Initially, Medicaid and Medicare in the US only covered two-component ankle implant systems. However, owing to high failure rates, the limited skill set required to perform the procedure, and an absence of evidence that suggested better clinical outcomes over ankle fusion, many insurers were hesitant to cover ankle replacement as a treatment for end-stage ankle OA. With completion of the STAR ankle replacement system’s randomized, multicenter, US IDE study against ankle fusion, perception towards three-component ankle replacement systems has improved remarkably. Moreover, with STAR being the first three-component ankle replacement system to receive FDA approval, insurers and surgeons have gained...
higher confidence in implant survival. In the coming years, they are likely to view three-component implants as a routine ingredient for ankle procedures in patients with high mobility requirement. The University of Pittsburgh Medical Center Health Plan (UPMC Health) has changed its coverage policy to exclusively reimburse TAR systems that have been approved by the FDA through premarket approval (PMA). This "PMA only" decision by UPMC Health limits its TAR coverage exclusively to Stryker's STAR ankle, thereby negatively impacting the usage of other implant systems in the US that have only 510(k) clearance. However, the success and overall market potential of STAR has prompted other major manufacturers such as Tornier, DePuy Synthes, and Wright Medical Group to develop similar innovative ankle offerings to be launched in the coming years (Medical Device and Diagnostic Industry, 2011).

6.6 Products

Some of the key companies offering ankle arthroplasty implants to the US and European markets include Corin, DePuy Synthes/Johnson & Johnson, Integra LifeSciences, Stryker, Smith & Nephew, Wright Medical Group, and Zimmer/Zimmer Biomet, among others.

6.6.1 Types of Ankle Arthroplasty Implants

Composed of the tibia, fibula, and talus, the ankle joint—along with tendons, ligaments, and the articular cartilage—facilitate plantar flexion (pointing the foot downward) and dorsiflexion (raising the foot upward). Based on progressive maturity of design, ankle arthroplasty can be trifurcated into first-, second-, and third-generation implants.

6.6.1.1 First-Generation Ankle Arthroplasty Implants

Designed in 1970, first-generation ankle implants were made of two components: a concave polyethylene tibial component and a convex metal (usually cobalt-chrome alloy) talar component. Over a period of time, constrained as well as unconstrained designs were introduced. However, both had disadvantages. While the constrained implants often resulted in failure due to their inability to reduce the rotational forces produced by continuous variation of rotational axis, the unconstrained design caused instability due to extreme stress imparted on neighboring tissues. Moreover, arthroplasties conducted using first-generation implants warranted large parts of
bone and tissue to be removed to allow cement fixation and component placement. Thus, owing to high component loosening rate, cement fixation, extensive stress, and high failure rates, first-generation implants became obsolete.

6.6.1.2 Second-Generation Ankle Arthroplasty Implants

With the advent of second-generation implants in the 1980s, the necessity for significant bone resection was deemed to be minimal. Equipped with a porous coating to encourage bone growth, cementless and semi-constrained second-generation prostheses gained credence.

The three main second-generation TAR designs—the Agility, Buechel-Pappas, and STAR prostheses—were reported to have encouraging clinical results. With good clinical outcomes, acceptable survivorship of prosthesis components, and reasonably low failure rates, second-generation TAR designs challenged ankle fusion’s position as the only therapy for end-stage OA.

Typically made of two metal components—a talus and a tibia fixed with polymethyl methacrylate cement—second-generation implants paved the way for further research into mobile-bearing, unconstrained, three-component prostheses.

6.6.1.3 Third-Generation Ankle Arthroplasty Implants

The introduction of third-generation prostheses with three-part, mobile-bearing systems further bolstered confidence in the TAR procedure. Mobile-bearing designs include a fixation element such as pegs, fins, or screws, a talar component, and components that resemble talar facets. Originally developed as a three-component, mobile-bearing implant system in Europe, the Salto prosthesis was also developed into a fixed-bearing design for use in the US, owing to FDA restrictions. STAR is the most widely used three-component, mobile-bearing ankle implant and has been gaining prominence owing to better survivorship and a low failure rate.

6.7 Market Forecast

The global ankle arthroplasty implants market was valued at approximately $107.4 million in 2015 and is expected to grow rapidly at a CAGR of 9.5%, reaching approximately $169.4 million by 2020.
Exhibit 6-2 presents the global combined market forecast for ankle arthroplasty implants by country/region for the years 2015 through 2020.

Exhibit 6-3 presents the combined market forecast for ankle arthroplasty implants for the five major European markets for the years 2015 through 2020.

### 6.8 Competitors

In 2015, the US market for ankle arthroplasty implants was led by Stryker with an estimated market share of 32%. Outside of the US market, the company accounted for approximately 31% of TAA implant sales for the five major European markets in 2015. The company entered the market in 2014 with the acquisition of Small Bone Innovations.

Wright Medical Group secured a close second behind Stryker in the US ankle arthroplasty products market, with an estimated market share of 31% in 2015. Across the five major European markets, Wright Medical Group accounted for approximately 22% of total sales in 2015. In October 2015, Wright Medical Group and Tornier completed the planned merger between the two companies; the combined companies will continue to operate under the name Wright Medical Group. The merger with Tornier strengthened Wright Medical Group’s already robust offerings in lower extremity implants; however, the company was required to divest Tornier’s ankle line to complete the merger, preventing the combined companies from completely dominating the ankle implants segment.

Integra LifeSciences is another key participant in the global ankle implants market. In 2015, Integra acquired the US distribution rights to Tornier’s Salto Talaris and Salto XT ankle replacement products, in addition to Tornier’s Futura Silastic toe replacement products. As a result of the acquisition, Integra LifeSciences now has access to the Salto product line, which accounted for over 15% of TAA implant sales prior to the Wright-Tornier merger. In the US, sales attributable to Integra LifeSciences accounted for approximately 23% of TAA product sales in 2015. For the five major European markets, Integra LifeSciences accounted for an estimated 15% of total ankle arthroplasty implant sales in 2015.
### Exhibit 6-2: Global Ankle Arthroplasty Implant Sales by Country/Region, Combined Market Forecast, 2015–20

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>$65.7m</td>
<td>$71.6m</td>
<td>$78.8m</td>
<td>$86.7m</td>
<td>$95.3m</td>
<td>$105.8m</td>
<td>10.0%</td>
</tr>
<tr>
<td>Europe</td>
<td>7.1</td>
<td>7.6</td>
<td>8.1</td>
<td>8.6</td>
<td>9.2</td>
<td>9.9</td>
<td>6.9%</td>
</tr>
<tr>
<td>Rest of the World</td>
<td>34.6</td>
<td>37.7</td>
<td>41.1</td>
<td>44.9</td>
<td>49.1</td>
<td>53.7</td>
<td>9.2%</td>
</tr>
<tr>
<td>Total ankle implant sales</td>
<td>$107.4m</td>
<td>$116.9m</td>
<td>$128.0m</td>
<td>$140.1m</td>
<td>$153.6m</td>
<td>$169.4m</td>
<td>9.5%</td>
</tr>
</tbody>
</table>

**Notes:** System sales for Europe include product sales in Germany, France, Italy, the United Kingdom, and Spain. The Rest of the World segment includes product sales from Africa, the Middle East, Asia-Pacific, Europe, and North and South America and excludes product sales for Germany, France, Italy, the United Kingdom, Spain, Japan, and the United States. Figures may not calculate due to rounding.

(Continued)
Notes: System sales for Europe include product sales in Germany, France, Italy, the United Kingdom, and Spain. The Rest of the World segment includes product sales from Africa and the Middle East, Asia-Pacific, Europe, and North and South America and excludes product sales for Germany, France, Italy, the United Kingdom, Spain, Japan, and the United States.

Sources: Company financials; Meddevicetracker
### Exhibit 6-3: Ankle Arthroplasty—Major European Markets, Combined Market Forecast, 2015–20

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>$1.5$m</td>
<td>$1.6$m</td>
<td>$1.7$m</td>
<td>$1.8$m</td>
<td>$2.0$m</td>
<td>$2.1$m</td>
<td>7.0%</td>
</tr>
<tr>
<td>Germany</td>
<td>3.2</td>
<td>3.5</td>
<td>3.7</td>
<td>4.0</td>
<td>4.4</td>
<td>4.8</td>
<td>8.4%</td>
</tr>
<tr>
<td>Italy</td>
<td>0.7</td>
<td>0.7</td>
<td>0.7</td>
<td>0.8</td>
<td>0.8</td>
<td>0.8</td>
<td>2.6%</td>
</tr>
<tr>
<td>Spain</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.5</td>
<td>2.7%</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>1.3</td>
<td>1.4</td>
<td>1.5</td>
<td>1.5</td>
<td>1.6</td>
<td>1.7</td>
<td>5.5%</td>
</tr>
<tr>
<td><strong>Total ankle implant sales</strong></td>
<td><strong>$7.1$m</strong></td>
<td><strong>$7.6$m</strong></td>
<td><strong>$8.1$m</strong></td>
<td><strong>$8.6$m</strong></td>
<td><strong>$9.2$m</strong></td>
<td><strong>$9.9$m</strong></td>
<td><strong>6.9%</strong></td>
</tr>
</tbody>
</table>

**Note:** Figures may not calculate due to rounding.

**Sources:** Company financials; Meddevicetracker
In the US, other suppliers of ankle arthroplasty implants include Corin, DePuy Synthes/Johnson & Johnson, and Zimmer/Zimmer Biomet, among others. For the European market, other suppliers of ankle arthroplasty implants include Corin, DePuy Synthes, Implantcast, MatOrtho, and Zimmer, among others.

Exhibit 6-4 presents estimated sales and market share data for the leading suppliers of ankle arthroplasty implants for the US market in 2015.

Exhibit 6-5 presents estimated sales and market share data for the leading suppliers of ankle arthroplasty implants for the European market in 2015.
**Exhibit 6-4: 2015, United States Ankle Arthroplasty Implants Market, Share by Supplier**

<table>
<thead>
<tr>
<th>Company</th>
<th>Estimated Sales</th>
<th>Estimated Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stryker</td>
<td>$21.0m</td>
<td>32.0%</td>
</tr>
<tr>
<td>Wright Medical Group</td>
<td>20.4</td>
<td>31.0%</td>
</tr>
<tr>
<td>Integra LifeSciences</td>
<td>15.1</td>
<td>23.0%</td>
</tr>
<tr>
<td>Others</td>
<td>9.2</td>
<td>14.0%</td>
</tr>
<tr>
<td>Total</td>
<td>$65.7m</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Notes: The “Others” category includes Corin, DePuy Synthes/Johnson & Johnson, and Zimmer/Zimmer Biomet, among others. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
### Exhibit 6-5: 2015, European Ankle Arthroplasty Implants Market, Share by Supplier

<table>
<thead>
<tr>
<th>Company</th>
<th>Estimated Sales</th>
<th>Estimated Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stryker</td>
<td>$2.2m</td>
<td>31.0%</td>
</tr>
<tr>
<td>Wright Medical Group</td>
<td>1.5</td>
<td>22.0</td>
</tr>
<tr>
<td>Integra LifeSciences</td>
<td>1.1</td>
<td>15.0</td>
</tr>
<tr>
<td>Others</td>
<td>2.3</td>
<td>32.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$7.1m</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

Notes: Estimated sales and market share data for Europe are for France, Germany, Italy, Spain, and the United Kingdom. The “Others” category includes Corin, DePuy Synthes/Johnson & Johnson, Implantcast, MatOrtho, and Zimmer/Zimmer Biomet. Figures may not calculate due to rounding.

Sources: Company financials; Meddevicetracker
COMPANY LISTING

Acumed
www.acumed.net

Adler Ortho
www.adlerortho.com

Arthrex
www.arthrex.com

B. Braun Melsungen
www.bbraid.com

Baumer
www.baumer.com

Biomet/
Zimmer Biomet
www.biomet.com

BioPro
www.bioproimplants.com

Corin
www.coringroup.com

DePuy Synthes/
Johnson & Johnson
www.depuy synthes.com

DJO Global
www.djoglobal.com

Evolutis
www.evolutisfrance.com

Exactech
www.exac.com

FH Orthopedics
www.fhorthopedics.com

Implantcast
www.implantcast.de

Implants International
www.implantsinternational.com

Integra LifeSciences
www.integralife.com

JRI Orthopedics
www.jri-ltd.com

Lima Corporate
www.limacorporate.com

MatOrtho
www.matortho.com

Mathys
www.mathysmedical.com

Medacta International
www.medacta.com

MicroPort Scientific
www.microport.com

Smith & Nephew
www.smith-nephew.com

Stryker
www.stryker.com

Tornier
www.tornier.com

Waldemar Link
www.linkorthopaedics.com

Wright Medical Group
www.wright.com

Zimmer/
Zimmer Biomet
www.zimmer.com
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Chapter 1


**Chapter 2**


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Stryker (2016) Direct Anterior Approach. Available from: 


Chapter 3:


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Chapter 4


**Chapter 5**


Chapter 6


