THE ATTUNE PRIMARY TOTAL KNEE REPLACEMENT SYSTEM VALUE DOSSIER
1 The Burden of Total Knee Arthroplasty ............................................................... 19
  1.1 Osteoarthritis of the Knee ............................................................................. 21
      1.1.1 Definition and Etiology of Osteoarthritis ................................................... 21
      1.1.2 Diagnosis of Osteoarthritis ....................................................................... 21
      1.1.3 Disease Progression of Osteoarthritis ....................................................... 21
      1.1.4 Epidemiology of Osteoarthritis ................................................................. 23
      1.1.5 Humanistic Burden of Osteoarthritis ......................................................... 23
      1.1.6 Economic Burden of Osteoarthritis ............................................................ 24
    1.2 Epidemiology of Total Knee Arthroplasty .................................................... 25
    1.3 Clinical Burden of Total Knee Arthroplasty .................................................. 35
      1.3.1 Clinical Issues .......................................................................................... 35
      1.3.2 Patient Outcomes ..................................................................................... 39
      1.3.3 Room for Improvement Following Total Knee Arthroplasty ...................... 41
    1.4 Economic Burden of Total Knee Arthroplasty .............................................. 49
  2 Unmet Treatment Need ................................................................................. 52
<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Overview</td>
<td>55</td>
</tr>
<tr>
<td>4</td>
<td>The ATTUNE Primary Total Knee System Value</td>
<td>59</td>
</tr>
<tr>
<td>4.1</td>
<td>Motion and Stability</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>The ATTUNE Primary Total Knee System is designed to deliver a high level of motion and stability.</td>
<td>61</td>
</tr>
<tr>
<td>4.2</td>
<td>Individualized Fit and Improved Function</td>
<td>69</td>
</tr>
<tr>
<td></td>
<td>The ATTUNE Primary Total Knee System provides a broad range of sizes for matching patients in today's global population.</td>
<td>70</td>
</tr>
<tr>
<td>4.3</td>
<td>Patellofemoral Tracking</td>
<td>73</td>
</tr>
<tr>
<td></td>
<td>The ATTUNE Primary Total Knee System is designed to deliver a high level of patellofemoral function.</td>
<td>73</td>
</tr>
<tr>
<td>4.4</td>
<td>Durability</td>
<td>77</td>
</tr>
<tr>
<td>4.4.1</td>
<td>Design</td>
<td>77</td>
</tr>
<tr>
<td>4.4.2</td>
<td>Polyethylene Performance</td>
<td>77</td>
</tr>
<tr>
<td></td>
<td>The ATTUNE Primary Total Knee System is designed to increase durability.</td>
<td>78</td>
</tr>
<tr>
<td>4.4.3</td>
<td>The AOX™ Advantage</td>
<td>78</td>
</tr>
<tr>
<td>4.4.4</td>
<td>Wear Testing</td>
<td>80</td>
</tr>
<tr>
<td>4.5</td>
<td>Efficiency of Care</td>
<td>83</td>
</tr>
<tr>
<td></td>
<td>The ATTUNE Primary Total Knee System is designed to enable efficiency in the operating room.</td>
<td>83</td>
</tr>
<tr>
<td>5</td>
<td>Overview of the ATTUNE Clinical Evidence Development Program</td>
<td>89</td>
</tr>
<tr>
<td>5.1</td>
<td>Clinical Development Studies</td>
<td>89</td>
</tr>
<tr>
<td>5.2</td>
<td>Patient's Knee Implant Performance Scale</td>
<td>91</td>
</tr>
<tr>
<td>6</td>
<td>References</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>Appendix A: Fundamentals of Total Knee Arthroplasty</td>
<td>A-1</td>
</tr>
<tr>
<td></td>
<td>Appendix B: Product Description</td>
<td>B-1</td>
</tr>
</tbody>
</table>
ACKNOWLEDGMENTS

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The Value Dossier features work conducted by DePuy Synthes Joint Reconstruction staff. It also reflects substantial input from the ATTUNE Knee System product development team and those supporting the product in the field.
LIST OF TABLES

Table 1. Compound Annual Growth Rates of Total Knee Arthroplasty ............................................25
Table 2. Age-standardized Incidence Rates for Total Hip and Knee Arthroplasties in 2007 ......................28
Table 3. Number of Primary Total Knee Arthroplasties in the Younger Patient Population (Aged < 65 Years) in 2006 ...........................................................................................................29
Table 4. Distribution of Reasons for Total Knee Arthroplasty Failure/Revision ..............................35
Table 5. Mortality Within 5 Years and Length of Hospital Stay for Patients Who Received a Primary Knee Arthroplasty, April 2003 - December 2009 ..................................................40
Table 6. Oxford Scores Following Total Hip Arthroplasty and Total Knee Arthroplasty .............42
Table 7. Oxford Pain and Function Items for Total Hip Arthroplasty and Total Knee Arthroplasty Patients .................................................................................................................................42
Table 8. Economic Burden of Total Knee Arthroplasty Performed in the United States ..................49
Table 9. Distribution of Cost (Australian dollars) Associated With Total Knee Arthroplasty ........50
Table 10. In Vivo Study Plans for the ATTUNE System ......................................................................90
LIST OF FIGURES

Figure 1. Healthy Joint (A) and Joint Affected by Osteoarthritis (B)................................. 22
Figure 2. Arthroplasty by Type in the United States, 2004 .................................................. 26
Figure 3. Total Knee Arthroplasty Procedures in the United States, 1991 to 2004............. 26
Figure 4. Changes in Age of Knee Arthroplasty Recipients Between 1997 and 2004 in the United States ......................................................................................... 29
Figure 5. The Projected Relative Proportion of the Younger Patient Population (Aged < 65 Years) for Primary and Revision Total Joint Arthroplasty in the United States, 2010 to 2030 .................................................................. 30
Figure 6. Changes in Total Knee Arthroplasty Utilization by Age Group, 1999 to 2008 .............................................................................................................. 30
Figure 7. Projected Number of Primary Total Knee Arthroplasies in the United States, 2005 to 2030 ......................................................................................... 32
Figure 8. Proportion of Knees With Femoral Component Overhang of 3 mm or More in at Least 1 of 10 Areas ............................................................................... 36
Figure 9. Distribution of Reasons for Revision in the United States, England and Wales, Australia, and Sweden .................................................................................. 37
Figure 10. Articular Oxidation Rates Vary Among Highly Crosslinked Materials ............ 38
Figure 11. Proportion of Patients With Poor Outcomes in Each Volume Category 2 Years After Total Knee Arthroplasty ................................................................. 40
Figure 12. SF-36 Scores for Hip Arthroplasty, Knee Arthroplasty, and Population Norms by Age Group ............................................................................................... 43
Figure 13. Mean Forgotten Joint Scores for Total Hip Arthroplasty and Total Knee Arthroplasty .......................................................................................................... 44
Figure 14. Total Knee Arthroplasty Patients Limited in Activities of Daily Living .......... 45
Figure 15. Knee Patients Limited in Activities 1 Year Following Total Knee Arthroplasty .... 45
Figure 16. Percentage of Total Knee Arthroplasty Patients and Control Subjects Reporting Significant Difficulty While Doing Various Activities .............................................. 46
Figure 17. Percentage of Total Knee Arthroplasty Patients’ Preoperative Expectations That Were Met or Exceeded at 6 and 12 Months After Surgery ................................ 47
Figure 18. Projected Number of Primary Total Knee Arthroplasties in the United States, 2005 to 2015 ......................................................................................... 50
Figure 19. Single-Radius J Curve .......................................................................................... 62
Figure 20. Multiradius J Curve .............................................................................................. 62
Figure 21. The ATTUNE System Radius: ATTUNE GRADIUS™ Curve ......................... 62
Figure 22. Implant Stability and Rotation: ATTUNE System Cruciate Retaining ............... 64
Figure 23. ATTUNE System Cruciate Retaining Femoral-Insert Conformity ....................... 64
Figure 24. Implant Stability and Rotation: Zimmer NexGen® Cruciate Retaining ............... 65
Figure 25. Implant Stability and Rotation: Stryker Triathlon® Cruciate Retaining ............... 65
Figure 26. Posterior Condyles for Cruciate Retaining and Posterior Stabilized Components .................................................................................................................. 66
Figure 27. Post-cam Engagement Velocity .............................................................................. 67
Figure 28. Femoral Low Point Anterior-Posterior Contact Position on the Medial and Lateral Condyle for Each Implant .................................................. 67
Figure 30. The ATTUNE System Sizing Is Indicated for 2 Sizes Up or 2 Sizes Down ............... 68
Figure 29. The ATTUNE System Insert Thickness ................................................................ 68
Figure 31. Consistent 3-mm Anterior-Posterior Increments Between Femoral Sizing .......... 69
Figure 32. The ATTUNE System Tibial Base Components .................................................. 70
Figure 33. Development of the ATTUNE System Femoral Component Sizes ...................... 71
Figure 34. The ATTUNE System Medialized Dome ......................................................... 74
Figure 35. Quadricep Angle ................................................................................................. 75
Figure 36. The ATTUNE System Posterior Stabilized Proportional Box/Spine ..................... 76
Figure 37. Posterior Stabilized Articulation Surface ....................................................... 77
Figure 38. Polyethylene Performance Requires a Balance of Wear Resistance, Oxidative Stability, and Mechanical Integrity .................................................... 78
Figure 39. The Relationship Between Increasing Irradiation Dose and Cross Linking ........ 78
Figure 40. Wear for the SIGMA® XLK Knee System and ATTUNE AOX Knee Systems .......... 81
Figure 41. Comparison of Peak Linear Wear Rate for Different Designs, for Different Activities of Daily Living Alternatives ................................................. 81
Figure 42. The ATTUNE System Exhibits Lower Micromotion ........................................ 82
Figure 43. The ATTUNE System Instruments Are Designed for Visual Clarity ................... 84
Figure 44. Efficient Path Through Polymer Shimming ........................................................ 84
Figure 45. The ATTUNE System Includes Multipurpose Instruments ................................ 85
Figure 46. Precise Control for Intraoperative Flexibility .................................................. 85
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAOS</td>
<td>American Academy of Orthopaedic Surgeons</td>
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<td>AARP</td>
<td>Association of American Retired Persons</td>
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<td>ADL</td>
<td>activities of daily living</td>
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<td>AOANJRR</td>
<td>Australian Orthopaedic Association National Joint Replacement Registry</td>
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<td>AOX</td>
<td>Antioxidant</td>
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<td>A-P</td>
<td>anterior-posterior</td>
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<td>ASIR</td>
<td>age-standardized incidence rate</td>
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<td>ASIS</td>
<td>anterior superior iliac spine</td>
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<td>ASTM</td>
<td>American Society for Testing and Materials</td>
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<td>BMI</td>
<td>body mass index</td>
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<td>CE</td>
<td>Conformité Européenne</td>
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<td>CI</td>
<td>confidence interval</td>
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<td>CPT</td>
<td>Current Procedural Terminology</td>
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<td>CR</td>
<td>Cruciate Retaining</td>
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<td>CT</td>
<td>computed tomography</td>
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<td>DRG</td>
<td>diagnosis-related group</td>
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<td>EQ-SD</td>
<td>EuroQol 5 Dimensions questionnaire</td>
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<td>EU</td>
<td>European Union</td>
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<td>FDA</td>
<td>Food and Drug Administration</td>
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<td>FJS</td>
<td>Forgotten Joint Score</td>
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<td>FJS-12</td>
<td>Forgotten Joint Score, 12-item version</td>
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<tr>
<td>HCUP</td>
<td>Healthcare Cost and Utilization Project</td>
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<td>HRQOL</td>
<td>health-related quality of life</td>
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<td>ICER</td>
<td>incremental cost-effectiveness ratio</td>
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<td>I-E</td>
<td>interior-exterior</td>
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<td>IIS</td>
<td>Investigator Initiated Study</td>
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<td>KOOS</td>
<td>Knee Injury and Osteoarthritis Outcome Score</td>
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<td>MCL</td>
<td>medial collateral ligament</td>
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<td>mCPI</td>
<td>medical Consumer Price Index</td>
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<td>MET</td>
<td>metabolic equivalent of task</td>
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<td>M-L</td>
<td>medial-lateral</td>
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<td>MRI</td>
<td>magnetic resonance imaging</td>
</tr>
<tr>
<td>N/A</td>
<td>not applicable</td>
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<td>NHS</td>
<td>National Health Service of England and Wales</td>
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<td>NICE</td>
<td>National Institute for Health and Clinical Excellence</td>
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<td>NIS</td>
<td>Nationwide Inpatient Sample</td>
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<td>NJR</td>
<td>National Joint Registry of England and Wales</td>
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<td>OA</td>
<td>osteoarthritis</td>
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<td>OHS</td>
<td>Oxford Hip Score</td>
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<td>OKS</td>
<td>Oxford Knee Score</td>
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<td>OR</td>
<td>operating room</td>
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<td>PCL</td>
<td>posterior cruciate ligament</td>
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<td>PKIP</td>
<td>Patient’s Knee Implant Performance</td>
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<td>PRO</td>
<td>patient-reported outcome</td>
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<td>PS</td>
<td>Posterior Stabilized</td>
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<td>QALY</td>
<td>quality-adjusted life-year</td>
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<td>Q-angle</td>
<td>quadriceps angle</td>
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<td>QOL</td>
<td>Quality of life</td>
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<td>SD</td>
<td>standard deviation</td>
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<td>SF-36</td>
<td>SF-36 Health Survey</td>
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<td>SOc</td>
<td>standard of care</td>
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<td>THA</td>
<td>total hip arthroplasty</td>
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<td>TJA</td>
<td>total joint arthroplasty</td>
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<td>TKA</td>
<td>total knee arthroplasty</td>
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<td>UHMWPE</td>
<td>ultra-high-molecular-weight polyethylene</td>
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<td>UK</td>
<td>United Kingdom</td>
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<td>US</td>
<td>United States</td>
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<td>WHO</td>
<td>World Health Organization</td>
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<td>WOMAC</td>
<td>Western Ontario and McMaster Universities Osteoarthritis Index</td>
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<td>WPAI</td>
<td>Work Productivity and Activity Impairment</td>
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EXECUTIVE SUMMARY

The Burden of Total Knee Arthroplasty

Osteoarthritis (OA), a degenerative chronic condition characterized by the breakdown of the joint’s cartilage, is worldwide the most common form of arthritis (Arthritis Foundation, 2011). Osteoarthritis most often presents as localized joint pain (Hunter et al., 2008). Other symptoms include reduced function, joint stiffness, joint instability, reduced range of motion, and crepitus (either as a crackling, crunching, or creaking noise or a grinding sensation in the joints) (Hunter et al., 2008). A total knee arthroplasty (TKA) procedure involves replacement of the damaged ends of the bones and cartilage in an arthritic knee with a prosthesis that is shaped to restore knee movement and function (American Academy of Orthopaedic Surgeons [AAOS], 2007).

With the increase in osteoarthritis, the prevalence of degenerative conditions of the knee will rise and contribute to the proliferation of total knee arthroplasty.

Total knee arthroplasty is currently used for treating degenerative and rheumatologic knee joint disease, when conservative treatment is no longer an option. With an increase in the prevalence of OA, there has been a further increase in the number of TKAs performed globally each year. Among persons older than 50 years, TKA has become considerably more prevalent than rheumatoid arthritis or congestive heart failure (AAOS, 2012). The prevalence of OA and TKA is increasing globally. In the United States (US), the National Arthritis Data Workgroup estimates that the national prevalence of OA was 26.9 million (12.1% of the adult population) in 2005, and had risen nearly 30% over the course of the preceding 10 years (Altman, 2010; Bitton, 2009). In other countries, the rates of primary TKA have increased; England and Wales reported an increase of 5.7% in 2010 compared with 2009 (National Joint Registry of England and Wales [NJR], 2011), whereas in Australia, 9.6% more procedures were reported in 2010 compared with 2009 (Australian Orthopaedic Association National Joint Replacement Registry [AOANJRR], 2011). In Sweden, the number of TKAs has more than doubled since 1998 (Swedish Knee Arthroplasty Register, 2011), and in Taiwan, the prevalence rate of TKR increased 140.38% from 1996 to 2004 (Tien et al., 2009).

The incidence of total knee arthroplasty is significantly increasing in those younger than 65 years.

In Finland, the annual cumulative incidences of TKA rose rapidly over a 27-year period (1980-2006) among 30- to 59-year-olds, with the greatest increase occurring in patients aged 50 to 59 years. Similar projections have been reported in the US and other Western countries (Wells et al., 2002; Jain et al., 2005; Kim et al., 2008).

In the US, one of the factors currently contributing to the anticipated increase in future demand for joint arthroplasty surgery is the aging of the “baby boom” generation. By 2016, more than 50% of patients undergoing TKA will be younger than 65 years. By 2030, it is expected that up to 62% of patients undergoing primary or revision TKAs will be younger than 65 years (Kurtz et al., 2009). It is projected that future demand for primary TKA will grow the fastest among those aged 45 to 54 years; an estimated 59,077 individuals in this age group underwent primary TKA in 2006, and it is anticipated that 994,104 individuals in this age group will undergo this procedure in 2030 (Kurtz et al., 2009).
Implant performance expectations have greatly increased because of factors such as obesity, younger patients undergoing total knee arthroplasty, and increasing patient demand for maintenance of activity and lifestyle.

Although TKA has been successful in relieving pain, correcting deformity, and providing mobility in the joint, patients are now seeking earlier interventions and expecting better outcomes compared with 20 years ago. Moreover, the demographics of a patient undergoing TKA are changing; patients are now younger and more likely to be obese, or live a more active lifestyle (Ranawat, 2010; Hedley et al., 2004; Fehring et al., 2007). Obese individuals place higher demands on the implants used for TKA. Younger patients have higher expectations in terms of activity level after their TKA. Finally, in increasingly multicultural societies, range of motion is no longer a regional requirement but rather a global demand.

Clinical Burden of Total Knee Arthroplasty

Clinical Issues

Surgical issues such as implant overhang, wear, malalignment, imprecise sizing, and loosening can result in pain, stiffness, impaired range of motion, and instability for patients.

Primary TKA can be a successful operation associated with pain reduction and restoration of patient function; however, challenges after TKA persist. These challenges include impaired range of motion and instability, imprecise sizing, patellofemoral kinematic issues, wear, and loosening.

Based on numerous studies characterizing in vivo knee motion after TKA over the past 2 decades, it has been concluded that knee motion after TKA does not generally replicate normal knee motion (Banks and Hodge, 2004). Furthermore, instability can occur after a mechanical complication following TKA. There are two types of instability: extension and flexion. During implantation, the surgeon must “balance” the knee by a combination of implant sizing, implant positioning, implant alignment and ligament tensioning to ensure stability; this is usually established at only 0° and 90° flexion. However, there may sometimes be an imbalance observed between those angles, where the ligaments are more slack, leading to “mid-range instability” (Stoddard et al., 2012). In addition, implant design, size offerings, and surgical issues can lead to imprecise sizing. Overhang can occur if an implant is incorrectly sized and, as a result, extends beyond the side of the bone, causing irritation of the surrounding soft tissue. In a study of a single design of TKA implant (Scorpio NRG posterior stabilized total knee system; Stryker Orthopaedics, Mahwah, NJ), 76% of all patients had overhang of more than 0 mm in at least one area (Mahoney and Kinsey, 2010).

Patellofemoral kinematic issues, such as patellar “maltracking” (the patella is not following a normal, stable path of movement within the femoral trochlear groove when the knee is flexing/extending) can result in stiffness after TKA. Patellar maltracking can be a disabling problem after TKA and is associated with both pain and diminished function. Internal rotational malalignment of components has been implicated as a cause of pain after TKA. In addition, overstuffing of a joint occurs during TKA if insufficient flexion, extension, or patellofemoral space is generated for the thickness of the inserted implant. Overstuffing can lead to increased component wear, pain, and increased force and stress on the patella, and may result in extensor mechanism tightness and subsequent reduction in postoperative knee flexion (Ghosh et al., 2009; Mihalko et al., 2008; Bengs and Scott, 2006).
Primary TKA can be a successful operation associated with improvements in pain and restoration of function for the patient. However, failures of TKA may occur for a variety of reasons, including wear, loosening, infections, instability, fracture, and mechanical failure (Sharkey et al., 2002). This failure can cause pain, instability, and loss of function. To relieve pain and restore function, revision TKAs are performed.

Wear and loosening are the major reasons for revision TKAs in the US, England and Wales, Australia, and Sweden. Australia had the highest distribution of revisions due to loosening (34.9%), followed by England and Wales (33.0%) and Sweden (25.0%) (AOANJRR, 2011; NJR, 2011; Swedish Knee Arthroplasty Register, 2011). England and Wales had the highest distribution of revisions due to wear (11.0%), followed by Sweden (6.0%) and the US (4.9%) (AOANJRR, 2011; NJR, 2011; Swedish Knee Arthroplasty Register, 2011; Bozic et al., 2010).

Patient Outcomes

Surgical process and patient outcomes from total knee arthroplasty can vary among institutions, surgeons, and surgical staffs.

Variation in surgical process across institutions, surgeons, and surgical staffs may lead to corresponding variations in outcomes such as surgical complications, patient functional status, mortality, length of stay, and rate of revision. For example, patients who undergo a range of surgical procedures in centers with higher procedural volume experience fewer perioperative deaths and complications and improved functional status compared with patients undergoing these procedures in lower-volume centers (Katz et al., 2007). Total knee arthroplasties performed in centers and/or by surgeons with lower procedure volume are associated with higher risks of mortality, longer lengths of stay, and increased complications following TKA (NJR, 2011; Tomek et al., 2012). Longer operating time also has been associated with a longer length of stay. Operating times trend lower with higher surgeon case loads (Tomek et al., 2012).

Room for Improvement Following Total Knee Arthroplasty

Recovery and outcomes following total knee arthroplasty are not the same as recovery and outcomes following total hip arthroplasty.

The goal of both TKA and total hip arthroplasty (THA) is the same: to reduce joint pain, increase range of motion, and improve function (Halket et al., 2010). However, evidence shows that patients with TKA actually experience significantly smaller improvements in postoperative pain and function compared with patients undergoing THA (O’Brien et al., 2009; Bourne et al., 2010; March et al., 1999).

Unlike hip replacement and the concept of the “forgotten hip,” there is no “forgotten knee.”

Both patients and clinicians increasingly identify that the objective of TKA is to closely approximate with a prosthesis the feel and function of a healthy knee that has never undergone surgery (Morra et al., 2008; Behrend et al., 2011). As such, another important aspect of the discrepancy in THA and TKA outcomes is that THA patients can “forget” about their prosthesis following surgery, whereas TKA patients are much more likely to be aware of the prosthesis (Behrend et al., 2011).

One year following total knee arthroplasty, limitations in function remain for some patients.

Up to 1 year following TKA, patients continue to report problems with kneeling, persistent pain, pain on walking, and pain when shopping (Baker et al., 2007). Noble et al. (2005) and
Tippett et al. (2010a) found that although TKA restores a patient’s ability to perform many routine activities, a substantial deficit remains in meeting the challenges of many functional tasks that are important to the patient, especially tasks involving kneeling or squatting. Despite high expectations of patients undergoing primary TKA, statistically and clinically significant differences between actual and expected activity were observed at 12 months, suggesting that patients’ expectations may not have been fulfilled.

**Economic Burden of Total Knee Arthroplasty**

The economic burden of total knee arthroplasty is significant. The demand for joint arthroplasties and increase in hospital costs are causing a significant economic burden to society. The national US bill for primary joint arthroplasties has increased dramatically because of the increasing number of joint arthroplasty procedures performed and the increasing hospital charges (Kim et al., 2008). By the year 2015, the annual number of primary knee arthroplasties in the US will be greater than 1.3 million, and the national bill for hospital charges will be $49 billion (Kim et al., 2008).

There are opportunities to increase efficiency of care in total knee arthroplasty. Total knee arthroplasty procedures are complex and can be inefficient because of the number, weight, and cost of surgical instruments used. Typically, TKA requires multiple heavy instrument cases. This can make instrument handling and the surgical procedure less intuitive, which, in turn, can lead to longer operating room (OR) times and higher costs. Instrument-processing errors can potentially cost a surgical facility $48,000 annually (Swanson, 2008). In addition, new TKA technology, just-in-time TKA instrument inventory management, and added demands for faster and less-invasive surgeries have increased the complexity of sterile processing.

**The ATTUNE™ Primary Total Knee System Value**

The ATTUNE Primary Total Knee System (ATTUNE System) was designed with the goal of addressing the clinical needs of patients, surgeons, and hospital providers around the world. Extensive research and science have gone into the design to help improve functional outcomes for patients, performance for surgeons, and efficiency for providers.

The ATTUNE System represents an innovative, comprehensive, integrated knee system. DePuy Synthes Joint Reconstruction has recently applied for extensive patent protection in countries throughout the world for the ATTUNE System implants, instruments, and surgical methods. In the US alone, as of this writing, there are already seven patents granted for key inventions related to the ATTUNE System implants. After extensive research and understanding of clinically proven designs, the system was developed to synergize implant design with native soft tissues. In addition, the system offers new innovative instrumentation to work in harmony with the implants. A host of expertly engineered advancements elevate instrument performance. The ATTUNE System includes both Cruciate Retaining (CR) and Posterior Stabilized (PS) femoral components. The ATTUNE System is designed to achieve optimal articulation between component interfaces. The ATTUNE System patented fixed-bearing LOGICLOCK™ Tibial Base allows independent femoral and tibial sizing to achieve optimal tibiofemoral articulation. The ATTUNE System is only available with DePuy Synthes Joint Reconstruction’ most advanced AOX™ Polyethylene Material, which was designed to provide a balance of the performance of the material while ensuring wear resistance, oxidative stability, and mechanical integrity. The ATTUNE System design has been extensively tested in vitro, and early clinical performance is being comprehensively reviewed.
Motion and Stability

The ATTUNE Primary Total Knee System is designed to deliver a high level of motion and stability.

The ATTUNE System is a new integrated knee system with technology unique to the industry. The patented ATTUNE GRADIUS™ Curve is designed with a series of gradually reducing radii and infinite centers of rotation. The shape of the ATTUNE GRADIUS Curve is designed to help maintain high stability of the knee by minimizing unnatural sliding of the femur on the tibia as it articulates on the polyethylene surface (Clary et al., 2012a).

The ATTUNE System also combines the carefully controlled gradual reduction in femoral curvature with a finely tuned tibial insert curvature. In the ATTUNE System, the higher conformity ratios required for stability through mid-flexion gradually give way to the lower values that provide the desired rotational freedom in deeper flexion.

The ATTUNE System fixed-bearing tibial component has been designed with a patented central locking mechanism (LOGICLOCK) to provide a secure attachment between the tibial base and the polymer insert. In addition, the universal nature of the central features in the design enables multiple sizes of polyethylene inserts to attach to a single-size tibial base. This enables one-to-one matching of the femoral and polyethylene insert sizes to achieve tibiofemoral articulation without compromising kinematic function. In addition, size-matched articulations enable fully proportional features, enabling key features to be properly sized for the patient.

Individualized Fit and Improved Function

The ATTUNE Primary Total Knee System provides a broad range of sizes for matching patients in today’s global population.

DePuy Synthes Joint Reconstruction conducted extensive anthropometric research based on a global database in order to arrive at the unique size offering for the ATTUNE System (Courtis et al., 2012; University College Dublin; Fitzpatrick, 2012 [data on file]). There are 10 standard sizes of femoral and tibial components and 4 narrow femoral component sizes. With the full complement of standard and narrow sizing, the ATTUNE System offers a comprehensive size range to allow the surgeon to meet the specific needs of virtually all patients and minimize implant overhang or underhang (Courtis et al., 2012). The number of sizes and the consistent 3mm anterior-posterior (A-P) increment between sizes allows the surgeon to choose a size that is the best fit for an individual patient. In addition, the instrumentation system is designed to work in harmony with the implant design to optimize positioning of the implant through multiple referencing options and half-size position adjustments.

Patellofemoral Tracking

The ATTUNE Primary Total Knee System is designed to deliver a high level of patellofemoral function.

Patellar tracking is defined as the motion of the patella relative to the femur or femoral groove during knee flexion and extension (Katchburian et al., 2003). The ATTUNE System was designed specifically with patellofemoral function in mind to provide controlled motion and stability (Clary et al., 2012b; Shalhoub et al., 2012; Cyr et al., 2012). The ATTUNE GLIDERIGHT™ Articulation strikes a balance between accommodating the natural soft tissues and also providing the appropriate amount of stability in the implant. For patellar resurfacing, the ATTUNE System offers two designs: a Medialized Dome patellar component and a
Medialized Anatomic patellar component. The ATTUNE System includes a femoral component design that permits treatment with an unresurfaced patella.

With many current systems, patellar implants are designed as a symmetrical dome that does not reflect the shape of the natural patella. This creates the need to manually offset the implant on the bone during implantation. Offsetting the symmetrical dome leaves exposed bone and can cause soft-tissue disruption.

The ATTUNE System Medialized Dome patellar component is designed with an offset dome. The offset is designed to reflect the natural patella shape and enhance patellofemoral function. This allows for more opportunities to use a larger-size patellar component and therefore increase bone coverage. The small and consistent increments between component sizes give surgeons flexibility to avoid overstuffing the patellar joint, which can result in reduced range of motion.

Finally, the shape of the patellar groove on the ATTUNE System femoral component is designed to reflect the patient's natural anatomy. Based on the human study (University College Dublin; Fitzpatrick, 2012 [data on file]), the angle of the ATTUNE System patellar groove is designed to match patients of different statures. The ATTUNE System patellar component tracks differently relative to each implant size and relative to the stature of typical patients.

Durability

The ATTUNE Primary Total Knee System is designed to increase durability.

Product design (geometry of implants and component interaction) and polyethylene performance are the major drivers in durability of TKA devices.

Design

The ATTUNE System is designed to achieve precise articulation between component interfaces. The system offers both fixed-bearing and rotating-platform configurations. For the fixed-bearing configuration, the ATTUNE System patented LOGICLOCK Tibial Base allows matched fits between the femoral and polyethylene insert surfaces independent of the tibial tray size to achieve precise tibiofemoral articulation without compromising fit with the bone. The long history of matched femoral/poly bearing articulations in the rotating-platform knee design has previously demonstrated this benefit.

The shape and design of the femoral component are critical factors in the survivorship of a knee implant (Whiteside and Nakamura, 2003). Specifically, the ATTUNE System PS component is designed to maintain a low contact position between the cam and spine during deep flexion, reducing the forces on the locking mechanism and tibial fixation. In the ATTUNE System PS design, after initial contact, the cam moves low on the spine and stays low, transferring forces down through the center of the insert and delivering controlled and stable cam-and-spine interaction during flexion. This results in controlled motion and reduced force transmission between implant and bone fixation (Insall et al., 1982).

Polyethylene Performance: The AOX Advantage

The ATTUNE System is only available with the most advanced AOX polyethylene technology from DePuy Synthes Joint Reconstruction. The fourth-generation material with proprietary synthetic antioxidant COVERNOX™ provides a balance of wear resistance, mechanical integrity, and oxidative stability. These material properties have been tested throughout development, and the biocompatibility, extraction, and distribution of COVERNOX have been evaluated (King et al., 2012a).
Wear Testing

The articular geometry of the ATTUNE System is designed to be highly wear resistant during high demand activities such as going up and down stairs. The stability provided by the articular geometry of the ATTUNE System is designed to reduce sliding and cross shear, leading to increased wear in other less stable implants (Strickland and Taylor, 2012).

Efficiency of Care

The ATTUNE Primary Total Knee System is designed to enable efficiency in the operating room.

The development process for the ATTUNE System included a dedicated team to research and understand the role of instrumentation in TKA. This research led to a new appreciation of the effect of instrumentation on patient outcomes.

The ATTUNE INTUITION™ Instrumentation is unique in its ability to combine the surgical process with implant options to allow the surgeon to balance the soft tissue and precisely control the implant position and fit for each patient. The instruments are intuitive to use and reduce steps throughout the surgical process, providing efficiency to the entire OR team.

Design features including red actuators, high-contrast markings, and quick set/release functions make ATTUNE INTUITION Instruments clear and easy to use. The instrument designs incorporate advanced composite materials, which reduce weight and therefore minimize the number of cases in the OR, while maintaining instrument durability.
PART A
THE PROBLEM
THE BURDEN OF TOTAL KNEE ARTHROPLASTY
KEY TAKEAWAYS

• As the population ages and obesity increases, the prevalence of osteoarthritis will increase.

• Osteoarthritis of the knee significantly impacts patients’ quality of life.

• The economic burden of osteoarthritis is significant.

• With the increase in osteoarthritis, the prevalence of degenerative conditions of the knee will rise and contribute to the proliferation of total knee arthroplasty.

• The incidence of total knee arthroplasty is significantly increasing in those younger than 65 years.

• Implant performance expectations have greatly increased because of factors such as obesity, younger patients undergoing total knee arthroplasty, and increasing patient demand for maintenance of activity and lifestyle.

• The global supply of orthopaedic surgeons is not expected to be able to meet the expected increase in demand for joint arthroplasty procedures.

• Surgical issues such as implant overhang, wear, malalignment, imprecise sizing, and loosening can result in pain, stiffness, impaired range of motion, and instability for total knee arthroplasty patients.

• Surgical process and patient outcomes from total knee arthroplasty can vary among institutions, surgeons, and surgical staffs.

• Recovery and outcomes following total knee arthroplasty are not the same as recovery and outcomes following total hip arthroplasty.

• Unlike hip replacement and the concept of the “forgotten hip,” there is no “forgotten knee.”

• One year following total knee arthroplasty, limitations in function remain for some patients.

• The economic burden of total knee arthroplasty is significant.

• Total knee arthroplasty failure represents a substantial clinical challenge and economic burden on the health system.

• There are opportunities to increase efficiency of care in total knee arthroplasty.
1.1 Osteoarthritis of the Knee

1.1.1 Definition and Etiology of Osteoarthritis

Osteoarthritis (OA), a degenerative chronic condition characterized by the breakdown of the joint’s cartilage, is worldwide the most common form of arthritis (Arthritis Foundation, 2011). The breakdown of cartilage causes the bones to rub against one another, resulting in stiffness, pain, and loss of movement in the joint. The most frequently affected joints are those of the hands, knees, hips, and spine (Goldring and Goldring, 2006).

Osteoarthritis most often presents as localized joint pain (Hunter et al., 2008). Other symptoms include reduced function, joint stiffness, joint instability, reduced range of motion, and crepitus (either as a crackling, crunching, or creaking noise or a grinding sensation in the joints) (Hunter et al., 2008).

1.1.2 Diagnosis of Osteoarthritis

The main goal of diagnostic criteria is to clearly demonstrate the presence of OA, or to rule it out. The major elements of the diagnostic evaluation are a medical history, physical examination, and radiographic imaging (Michael, 2010). A distinction is made between clinical diagnosis (based on physical examination and laboratory results) and radiographic diagnosis of OA or a combination of both.

1.1.3 Disease Progression of Osteoarthritis

The signature pathological feature of OA is the loss of hyaline articular cartilage (Felson, 2009). Along with hyaline cartilage loss, bone remodeling and bone loss occur relatively early in the disease process (Felson, 2009). Although OA once was considered a disease of just the cartilage, the pathology of OA is broadening to one of the whole joint, involving the synovium (or joint lining), bone, and cartilage.

- Osteoarthritis evolves slowly over time and is characterized by several stages (Arthritis Foundation, 2011):
  - Cartilage loses elasticity and is more easily damaged by injury or use.
  - Wear of cartilage causes changes to underlying bone. The bone thickens, and cysts may occur under the cartilage. Bone spurs or osteophytes develop near the end of the bone at the affected joint, causing pain.
  - Pieces of bone or cartilage float loosely in the joint space and cause additional pain and deterioration.
  - The synovium becomes inflamed because of cartilage breakdown; this inflammation causes cytokines (inflammation proteins) and enzymes that further damage cartilage.
  - The inflammation present in the synovium triggers changes in the peripheral nervous system, leading to abnormalities in the processing of nociceptive signals from the joint and surrounding tissues (Felson, 2009). These processing abnormalities lead to the sensation of pain associated with OA.

In normal anatomy, the cartilage between bones produces loading that is distributed evenly across the joint during movement. When cartilage becomes damaged, this loading becomes unevenly distributed, and the excess loading on areas of the joint leads to further damage and malalignment within the joint during movement. This malalignment within the joint exposes the cartilage to excess focal loading, resulting in progressive damage to the joint (Felson, 2009). Inflammation within the joint may cause further nervous system and muscle changes, leading to further deterioration and pain (Felson, 2009).
Figure 1 shows a healthy joint in comparison with a joint affected by severe OA.

**Figure 1. Healthy Joint (A) and Joint Affected by Osteoarthritis (B)**

(A) (B)

In the absence of proven disease-modifying agents for OA, current treatment of OA focuses on the management of the symptoms of OA, seeking to reduce pain and stiffness and to improve physical function. The management of OA includes several modalities, including nonpharmacological management (e.g., weight loss, exercise, physical therapy, and activity modification), pharmacological management, and surgery.

Surgery may be an option if a patient experiences joint damage, pain, or limited motion as a result of OA. There are several different types of joint surgery. The most common surgeries for people with OA are arthroscopic surgery, osteotomy, and joint replacement surgery, or arthroplasty. In arthroscopic surgeries, the surgeon inserts a very thin tube with a camera at the end into the joint through a small incision. The procedure is performed to take tissue samples, remove loose cartilage, repair tears, smooth a rough surface, or remove diseased synovial tissue. Arthroscopic surgery is most commonly performed on the knee and shoulder; however, there is a lack of evidence showing a significant benefit (Arthritis Foundation, 2010; Rönn et al., 2011). Osteotomy is used to increase stability by redistributing the weight on the joint. This procedure is useful in people with unilateral hip or knee OA (involvement in only one joint) and who may be too young for a total joint arthroplasty (TJA) (Arthritis Foundation, 2010). Compared with joint arthroplasty surgery, osteotomy is considered a demanding procedure with an unpredictable outcome and is associated with significant complications (Rönn et al., 2011). Total joint arthroplasty surgery is considered if other treatment options do not relieve the pain and disability caused by OA (American Academy of Orthopaedic Surgeons [AAOS], 2007). In TJA, the arthritic joint is removed and replaced with an artificial joint. A total knee arthroplasty (TKA) procedure involves replacement of the damaged ends of the bones and cartilage in an arthritic knee with a prosthesis that is shaped to restore knee movement and function (AAOS, 2007).
1.1.4 Epidemiology of Osteoarthritis

As the population ages and obesity increases, the prevalence of osteoarthritis will increase.

The National Arthritis Data Workgroup estimates that the prevalence of OA in the United States (US) in 2005 was 26.9 million, or 12.1% of the adult population, and had risen nearly 30% over the course of the preceding 10 years (Altman, 2010; Bitton, 2009). This increase in prevalence is likely due to the aging US population, to increases in other related factors such as obesity, and to the methods of OA detection (Moskowitz, 2009). In Australia, the prevalence of arthritis is approximately 3 million people, representing 15% of the population (March and Bagg, 2004). The United Kingdom (UK)–based organization Arthritis Care published the report OANation 2012, which estimates that there are 8.5 million people in the UK with OA (Arthritis Care, 2012). The prevalence of symptomatic OA of the hip in the UK has been found to range from 0.7% to 4.4% (Arden and Nevitt, 2006). In addition, worldwide estimates are that 9.6% of men and 18.0% of women older than 60 years have symptomatic OA (World Health Organization [WHO], 2011), and that approximately 10% of the world’s population aged 60 years and older has symptomatic problems that can be attributed to OA (Symmons et al., 2012). Incidence data from a large US health maintenance organization database showed that for every 100,000 person-years, the incidence of knee OA occurred 240 times, compared with 100 times for hand OA and 88 for hip OA (Moskowitz, 2009).

Osteoarthritis is a complex disorder with multiple risk factors that may vary across different joint sites and in their contribution to the initiation and progression of OA. A number of factors, both systemic and biomechanical, contribute to the risk of developing OA (Garstang and Stitik, 2006). In terms of systemic risk factors, OA is more likely to occur in women, those older than 40 years, those born with malformed joints or defective cartilage, and those with certain conditions including gout, rheumatoid arthritis, Paget’s disease of the bone, and septic arthritis (Mayo Clinic, 2009). In terms of biomechanical risk factors, those with joint injuries from sports or an accident, obese individuals, and those with occupations involving repetitive stress on the joints are more likely to develop OA (Mayo Clinic, 2009). Risk factors for the progression of knee OA are malalignment and generalized OA, in addition to low vitamin D and vitamin C intake.

1.1.5 Humanistic Burden of Osteoarthritis

Osteoarthritis of the knee significantly impacts patients’ quality of life.

A substantial humanistic burden, in terms of reduced function and the experience of pain, is associated with OA. Patients with symptomatic OA commonly suffer reduced quality of life, which is more pronounced in patients with more advanced disease (Moskowitz, 2009). Based on various surveys, databases, disease registers, and epidemiological studies, OA was found to be the seventh leading cause of disability in women and the twelfth leading cause in men (Moskowitz, 2009). Among people aged 65 to 74 years, OA was found to be the fifth leading cause of disability—over dementia, diabetes, prostate cancer, and breast cancer (Moskowitz, 2009).

Disability caused by knee OA is an interplay of pain and comorbid, pathophysiological, sociodemographic, psychological, and social factors (Kauppila et al., 2009). Pain is one of the main symptoms of knee OA, and several studies have established the association between knee pain and disability (Kauppila et al., 2009). A recent systematic review (Vissers et al., 2012) found that in follow-ups shorter than 1 year, there was strong evidence that
patients with catastrophizing knee pain reported more pain postoperatively. In long-term follow-up, 1 year after TKA, there was strong evidence that lower preoperative mental health was associated with lower scores on function and pain (Vissers et al., 2012). Psychosocial and social factors may play an important role in the development of pain and pain experience and can be considered as moderators and mediators of pain and functional impairment. Further, the pathological function of a large lower extremity joint could be one of the major determinants of an individual’s physical functional status.

Patients with OA report higher absenteeism from work than the general population (Rossignol, 2004) and lower health-related quality of life (HRQOL) than the general population (Desmeules et al., 2009; Glazebrook et al., 2008). Depression and poor mental health are associated with OA and have a considerable impact on overall HRQOL in OA patients (Axford et al., 2008; Glazebrook et al., 2008; Sale et al., 2008).

1.1.6 Economic Burden of Osteoarthritis

The economic burden of osteoarthritis is significant.

1.1.6.1 Osteoarthritis

The direct and indirect economic costs attributable to OA are substantial. Across countries, the majority of direct health expenditures associated with OA are due to hospital services to treat OA, costs associated with the management of complications related to treating OA (e.g., gastrointestinal effects) and personal out-of-pocket expenditures, such as medications, nonprescription medications, and special equipment (Bitton, 2009). Currently, there is a lack of effective preventative or early-stage treatments known to reduce OA disability (Dawson et al., 2012). However, indirect costs have been recognized as an important component in evaluating the economic impact of OA (Bitton, 2009). Indirect costs, also known as productivity costs, are those associated with lost or impaired ability to work or to engage in usual activities due to morbidity or mortality, such as sick leave, permanent disability, and premature death. Osteoarthritis can lead to substantial productivity losses and early retirement (Bitton, 2009). A 1997 analysis of the economic costs of musculoskeletal disorders in five industrialized countries (Australia, Canada, France, UK, and US), in which OA was the most common of these disorders, found a rising trend of costs between 1% and 2.5% of the gross national product of the countries (Bitton, 2009). In 2000, the estimated economic cost of OA in the US was $60 billion; it is expected to increase to $100 billion by 2020 (Mehrotra et al., 2005). Osteoarthritis also has a significant negative impact on the UK economy. In 1999-2000, 36 million working days were lost due to OA alone, at an estimated cost of £3.2 billion in lost production. Moreover, two-thirds of individuals with OA reported an increase in their own costs, such as travel and treatment, totaling an average of £480 per patient with OA each year (Arthritis Care, 2012).
1.2 Epidemiology of Total Knee Arthroplasty

With the increase in osteoarthritis, the prevalence of degenerative conditions of the knee will rise and contribute to the proliferation of total knee arthroplasty.

Total knee arthroplasty is used for treating degenerative and rheumatologic knee joint disease, when conservative treatment is no longer an option. (Appendix A presents an overview of the TKA procedure.) Table 1 presents the compound annual growth in the incidence of TKA, based on results of an international survey. The compound annual growth in the number of TKA procedures ranged by country, from 5.3% in France to 17.0% in Portugal (Kurtz et al., 2011).

Table 1. Compound Annual Growth Rates of Total Knee Arthroplasty

<table>
<thead>
<tr>
<th>Country</th>
<th>Years of Available TKA Data</th>
<th>Annualized Growth in TKA Procedures</th>
<th>Annualized Growth in Procedure Rate per 100,000 Persons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>2003-2008</td>
<td>6.7%</td>
<td>5.0%</td>
</tr>
<tr>
<td>Canada</td>
<td>2002-2008</td>
<td>10.3%</td>
<td>9.1%</td>
</tr>
<tr>
<td>Finland</td>
<td>1997-2009</td>
<td>7.2%</td>
<td>6.9%</td>
</tr>
<tr>
<td>France</td>
<td>2002-2007</td>
<td>5.3%</td>
<td>3.6%</td>
</tr>
<tr>
<td>Germany</td>
<td>2005-2008</td>
<td>6.9%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Italy</td>
<td>1999-2008</td>
<td>12.8%</td>
<td>12.2%</td>
</tr>
<tr>
<td>Netherlands</td>
<td>1997-2007</td>
<td>9.4%</td>
<td>8.8%</td>
</tr>
<tr>
<td>Portugal</td>
<td>1997-2008</td>
<td>17.0%</td>
<td>16.6%</td>
</tr>
<tr>
<td>Spain</td>
<td>1997-2008</td>
<td>11.5%</td>
<td>10.1%</td>
</tr>
<tr>
<td>Switzerland</td>
<td>1998-2008</td>
<td>14.7%</td>
<td>14.0%</td>
</tr>
<tr>
<td>United States</td>
<td>1997-2008</td>
<td>7.9%</td>
<td>6.8%</td>
</tr>
</tbody>
</table>

TKA = total knee arthroplasty.

Note: Source of information were national inpatient administrative databases, registries, and census data. Source: Kurtz et al., 2011.

The prevalence of OA in the US is increasing and will continue to rise as the population increases and ages, as obesity becomes more common, and as life expectancy increases (see Section 1.1.4). In 1995, an estimated 40 million Americans (15% of the population) reported symptoms related to arthritis (Iorio et al., 2008). By the year 2020, it is estimated that 59.4 million Americans (18.2% of the population) will be affected by arthritis (Iorio et al., 2008). The demand for orthopaedic services in the US is expected to increase by 23% between 2000 and 2020 (Iorio et al., 2008).

The volume of arthroplasties is projected to increase as the demand for TJA grows. Total joint arthroplasty is treatment for advanced and symptomatic joint destruction. Arthroplasty procedures have been developed for several joints, including the hips, knees, shoulders, ankles, elbows, wrists, and smaller joints of the hand and foot. However, the most frequently replaced joints are the knee and hip. In 2004, knee and hip arthroplasties, accounted for 95% of the 1.07 million arthroplasty procedures performed in the US (Figure 2) (Burden of Musculoskeletal Diseases in the United States, 2008). Females undergo 62% of all TJA procedures and approximately twice as many TKAs procedures as males (Burden of Musculoskeletal Diseases in the United States, 2008).
With an increase in the prevalence of OA, there has been a further increase in the number of TKAs performed in the US each year. Among persons older than 50 years, TKA has become considerably more prevalent than rheumatoid arthritis or congestive heart failure (AAOS, 2012). Approximately 97% of TKAs are performed almost exclusively because of an underlying diagnosis of OA (Burden of Musculoskeletal Diseases in the United States, 2008).

From 1991 to 2004, the annual number of TKAs increased almost threefold in the US (Figure 3).

**Figure 2. Arthroplasty by Type in the United States, 2004**

**Figure 3. Total Knee Arthroplasty Procedures in the United States, 1991 to 2004**
In 2004, approximately 431,485 primary knee arthroplasties were performed in the US, a 53% increase from the year 2000 (281,534 TKAs) (Kim et al., 2008). In 2008, 615,050 TKAs were performed in the US, a 134% change from 1999 (262,601 TKAs) (Losina et al., 2012). The prevalence of TKA also is increasing globally:

- In the UK, TKA rates increased between 1991 and 2006. Among women, TKA rates per 100,000 person-years increased from 42.5 (95% confidence interval [CI], 37.0-48.0) in 1991 to 138.7 (95% CI, 132.3-145.0) in 2006; among men, TKA rates per 100,000 person-years increased from 28.7 (95% CI, 23.9-33.6) in 1991 to 99.4 (95% CI, 93.9-104.8) in 2006 (Culliford et al., 2010).
- In English National Health Service (NHS) hospitals, the number of primary TKAs performed rose from 9,068 in 1989-1990 to 23,846 in 1995-1996 (Dawson et al., 2012).
- In England and Wales, the number of knee arthroplasty procedures recorded on the National Joint Registry of England and Wales (NJR) during 2010 was 81,979, an increase of 5.7% compared with 2009 (NJR, 2011). Of the 81,979 procedures submitted, 76,870 were primary procedures, an increase of 5% compared with 2009, and 5,109 were revision procedures, an increase of 11% compared with 2009 (NJR, 2011).
- In Australia, primary TKAs are increasing steadily; there were 9.6% more procedures in 2010 compared with 2009, and 72.3% more than in 2003 (Australian Orthopaedic Association National Joint Replacement Registry [AOANJRR], 2011). There were a total of 11,335 first revision procedures in 2010—an additional 2,047 procedures compared with 2009.
- In Sweden, the number of TKAs has more than doubled since 1998 (Swedish Knee Arthroplasty Register, 2011). During 2000-2009, 2,542 revisions were performed after TKA for OA (Swedish Knee Arthroplasty Register, 2011).
- Knee replacement surgery is an increasingly common procedure: more than 650,000 TKAs were performed in the US in 2008, more than 77,500 TKAs were performed in the UK in 2009, and 103,601 TKAs were performed in South Korea between 2002 and 2005 (Carr et al., 2012; Kim et al., 2008).
- In Taiwan, the prevalence rate of TKA was 22.86 per 100,000 persons in 1996 and gradually increased to 54.95 per 100,000 persons in 2004, representing an increase rate of 140.38% (Tien et al., 2009).

De Pina et al. (2011) analyzed the worldwide geographic distribution of incidence rates of TKA. Data on knee arthroplasty procedures (number of inpatient cases in 2007) from 28 countries were included in the study; 1,198,148 individuals had undergone TKA, corresponding to a crude rate of 104.3 per 100,000 person-years. Table 2 presents age-standardized incidence rates (ASIRs) for TKA. Strong geographic disparities were observed across the countries. The highest ASIR per 100,000 inhabitants was in the US (221.5 [95% CI, 222.0-222.6]), and the lowest was in Brazil (4.3 [95% CI, 4.4-4.5]).
### Table 2. Age-standardized Incidence Rates for Total Hip and Knee Arthroplasties in 2007

<table>
<thead>
<tr>
<th>Country</th>
<th>TKAs per 100,000 PersonYears</th>
<th>ASIR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>171.3 (173.2-175.2)</td>
<td></td>
</tr>
<tr>
<td>Austria</td>
<td>183.6 (186.5-189.5)</td>
<td></td>
</tr>
<tr>
<td>Belgium</td>
<td>149.2 (151.5-153.8)</td>
<td></td>
</tr>
<tr>
<td>Canada</td>
<td>144.3 (145.6-146.9)</td>
<td></td>
</tr>
<tr>
<td>Czech Republic</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Denmark</td>
<td>104.8 (107.6-110.4)</td>
<td></td>
</tr>
<tr>
<td>Finland</td>
<td>157.0 (160.3-163.7)</td>
<td></td>
</tr>
<tr>
<td>France</td>
<td>108.0 (108.8-109.6)</td>
<td></td>
</tr>
<tr>
<td>Germany</td>
<td>165.5 (166.3-167.1)</td>
<td></td>
</tr>
<tr>
<td>Greece</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Hungary</td>
<td>39.4 (40.6-41.9)</td>
<td></td>
</tr>
<tr>
<td>Iceland</td>
<td>124.5 (139.0-154.8)</td>
<td></td>
</tr>
<tr>
<td>Ireland</td>
<td>57.6 (60.3-63.0)</td>
<td></td>
</tr>
<tr>
<td>Italy</td>
<td>75.8 (76.4-77.1)</td>
<td></td>
</tr>
<tr>
<td>South Korea</td>
<td>98.3 (99.3-100.3)</td>
<td></td>
</tr>
<tr>
<td>Luxembourg</td>
<td>160.6 (172.8-185.6)</td>
<td></td>
</tr>
<tr>
<td>Mexico</td>
<td>7.8 (8.0-8.3)</td>
<td></td>
</tr>
<tr>
<td>Netherlands</td>
<td>123.1 (124.8-126.6)</td>
<td></td>
</tr>
<tr>
<td>New Zealand</td>
<td>113.7 (117.3-121.0)</td>
<td></td>
</tr>
<tr>
<td>Norway</td>
<td>86.2 (88.9-91.8)</td>
<td></td>
</tr>
<tr>
<td>Poland</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Portugal</td>
<td>42.7 (43.9-45.2)</td>
<td></td>
</tr>
<tr>
<td>Slovenia</td>
<td>56.3 (53.1-59.7)</td>
<td></td>
</tr>
<tr>
<td>Slovak Republic</td>
<td>28.5 (30.1-31.7)</td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td>101.3 (102.2-103.1)</td>
<td></td>
</tr>
<tr>
<td>Sweden</td>
<td>101.1 (103.1-105.2)</td>
<td></td>
</tr>
<tr>
<td>Switzerland</td>
<td>173.6 (176.5-179.5)</td>
<td></td>
</tr>
<tr>
<td>UK</td>
<td>137.1 (138.0-139.0)</td>
<td></td>
</tr>
<tr>
<td>US</td>
<td>221.5 (222.0-222.6)</td>
<td></td>
</tr>
<tr>
<td>Brazil</td>
<td>4.3 (4.4-4.5)</td>
<td></td>
</tr>
<tr>
<td>Romania</td>
<td>5.3 (5.6-5.9)</td>
<td></td>
</tr>
</tbody>
</table>

ASIR = age-standardized incidence rate; CI = confidence interval; UK = United Kingdom; US = United States.

a Last available year 2006.
b Last available year 2005.
c Last available year 1999.
Source: de Pina et al., 2011.

The incidence of total knee arthroplasty is significantly increasing in those younger than 65 years.

In Finland, the annual cumulative incidences of TKA rose rapidly over a 27-year period (1980-2006) among 30- to 59-year-olds, with the greatest increase occurring in patients aged 50 to 59 years. There was a 130-fold increase in the incidence of TKAs over the whole study period: the incidence increased from 0.5 to 65 operations per 100,000 individuals, with the most rapid increase occurring from 2001 to 2006 (18 to 65 operations per 100,000) (Leskinnen et al., 2012). In the last 10 years of the study, the incidence of total knee replacements was 1.6- to 2.4-fold higher in women than in men (Leskinnen et al., 2012). The
incidence of TKA increased very rapidly in patients younger than 60 years with primary knee OA in Finland during 1980 to 2006.

Similar projections have been reported in the US and other Western countries. Wells et al. (2002) reported an increase in the incidence of TKA in younger patients (aged 45-64 years) with primary OA in Australia between 1988 and 1998. In the US, Jain et al. (2005) reported that the incidence of TKA had increased 54% in those aged 50 to 59 years and 95% in those aged 40 to 49 years between 1990-1993 and 1998-2000. Between 1997 and 2004, knee arthroplasties in the US increased by 83% (from 12 to 22 per 10,000 people) among individuals aged 45 to 64 years (Figure 4) (Kim et al., 2008).

**Figure 4. Changes in Age of Knee Arthroplasty Recipients Between 1997 and 2004 in the United States**

![Figure 4](image-url)

In the US, one of the factors currently contributing to the anticipated increase in future demand for joint arthroplasty surgery is the aging of the “baby boom” generation. As the number of total knee arthroplasties increases, there is a need for orthopaedic surgeons and hospitals to provide efficient care. The incidence of TJA has increased not only in older patients (aged ≥ 65 years) but also in younger patients (aged < 65 years) over the past decade (Kurtz et al., 2009). According to the Nationwide Inpatient Sample (NIS) dataset, the relative percentage of the younger patient population grew between 1993 and 2006, especially for TKA. In 1993, 25% of primary TKAs were performed in patients younger than 65 years (Kurtz et al., 2009). In 2006, this percentage increased to 41% (Table 3) (Kurtz et al., 2009).

**Table 3. Number of Primary Total Knee Arthroplasties in the Younger Patient Population (Aged < 65 Years) in 2006**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>&lt; 45 Years</th>
<th>45 to 54 Years</th>
<th>55 to 64 Years</th>
<th>Total</th>
<th>Percentage &lt; 65 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary TKA</td>
<td>9,900</td>
<td>59,100</td>
<td>147,000</td>
<td>524,600</td>
<td>41%</td>
</tr>
</tbody>
</table>

TKA = total knee arthroplasty.
Source: Kurtz et al., 2009.

By 2016, more than 50% of patients undergoing TKA will be younger than 65 years. By 2030, it is expected that up to 62% of patients undergoing primary or revision TKAs will be younger than 65 years (Kurtz et al., 2009). It is projected that future demand for primary
TKA will grow at the fastest rate among those aged 45 to 54 years; an estimated 59,077 individuals in this age group underwent primary TKA in 2006, and it is anticipated that 994,104 individuals in this age group (or approximately 17 times more people) will undergo this procedure in 2030 (Figure 5) (Kurtz et al., 2009).

Figure 5. The Projected Relative Proportion of the Younger Patient Population (Aged < 65 Years) for Primary and Revision Total Joint Arthroplasty in the United States, 2010 to 2030

TKA = total knee arthroplasty.
Source: Kurtz et al., 2009.

Total knee arthroplasty utilization in the US more than doubled in the period from 1999 to 2008 (Losina et al., 2012). Using data from the NIS, TKA utilization increased in all age groups; however, increases were largest among people aged 45 to 64 years, for whom TKA utilization more than tripled. The number of TKAs performed from 1999 through 2008 increased 119% in those aged 18 to 44 years, 218% in those aged 45 to 64 years, and 97% in those aged 65 years or older (Figure 6).

Figure 6. Changes in Total Knee Arthroplasty Utilization by Age Group, 1999 to 2008

Source: Losina et al., 2012.
Implant performance expectations have greatly increased because of factors such as obesity, younger patients undergoing total knee arthroplasty, and increasing patient demand for maintenance of activity and lifestyle.

As the baby boomers age, the evolving Western cultures demand more of TJA (Leskinen et al., 2012). The baby boom generation comprises individuals born between 1946 and 1964, and in 2008 included approximately 78 million Americans (26% of the US population) (Iorio et al., 2008). This population will have longer life spans than earlier generations (thus requiring health care services for increased lengths of time), and more will have multiple chronic medical conditions that require medical care (Guralnik et al., 1989). By 2030, 60% of this generation will have more than one chronic condition, 50% will be affected by arthritis, and more than 33% will be obese (Iorio et al., 2008). Moreover, as the baby boomers age, their expectations and wealth are expected to drive an increasing demand for health care and the maintenance of activity and lifestyle, which will increase the demand for reconstructive musculoskeletal services dramatically.

Although TKA has been successful in relieving pain, correcting deformity, and providing mobility in the joint, patients are now seeking earlier interventions and expecting better outcomes compared with 20 years ago. Moreover, the demographics of a patient undergoing TKA are changing; patients are now younger and more likely to be obese, or live a more active lifestyle (Ranawat, 2010; Hedley et al., 2004; Fehring et al., 2007).

The relationship between obesity and an increased risk of knee OA has been well documented in the literature. A large, prospective, population-based cohort study conducted by Lohmander et al. (2009) demonstrated that body mass index (BMI), weight, and waist circumference were major risk factors for knee arthroplasty or osteotomy to treat OA. Among adults (aged ≥ 20 years) in the US between 1999 and 2002, 65.1% were overweight or obese (BMI ≥ 25 kg/m²), 30.4% were obese (BMI ≥ 30 kg/m²), and 4.9% were extremely obese (BMI ≥ 40 kg/m²) (Hedley et al., 2004). In a study by Losina et al. (2012), the overall US adult obese population grew 24% during a 10-year period (1999-2008). Severely obese patients (mean BMI ≥ 30 kg/m²) have worse outcomes (measured by the Knee Society Scores and radiography) and a higher level of revisions after undergoing TKA (Núñez et al., 2009). Thus, obese individuals place higher demands on the implants used for TKA. A study conducted by Reijman et al. (2007) investigated the relationship between BMI and the incidence and progression of radiological knee OA and concluded that BMI, particularly a high BMI (> 27 kg/m²), is associated with the incidence and progression of knee OA in The Netherlands. In addition, a study conducted by Grotle et al. (2008) investigated the impact of obesity on incident OA of the knee in a general population over 10 years and found that a high BMI (> 30 kg/m²) was significantly associated with knee OA (Grotle et al., 2008).

Based on future projections, the demand for TKA in adults aged 45 to 54 years is anticipated to grow 17-fold by 2030 (Kurtz et al., 2009; Leskinen et al., 2012). Because patients in their late 40s and early 50s are undergoing TKA, the demand placed on implant performance has increased. These younger patients will require their implants to function several decades longer and with increased durability than would be required for the average older patient (Ranawat, 2010).

A study by Losina et al. (2012) showed that the increase in utilization of TKA cannot be fully explained by the growth in population size and the obesity epidemic. The recent increase is likely related to a multitude of factors such as a growing prevalence of sports-related knee injuries, expanded indications for TKA, and patients who wish to maintain or resume higher levels of physical activity. In the past, a good surgical outcome for patients who underwent TKA would be if patients could walk 5 to 10 blocks and achieve 95° to 110° of motion.
with good pain relief (Mulholland and Wyss, 2011). Today, that expectation has expanded to include an increased range of motion of approximately 120° to 125° and the ability to participate in recreational sporting activities (Ranawat, 2010). In certain situations, such as gardening, sitting on the floor, reading a line for golf putting, other activities that require a squatting position, and special cultural activities (particularly in Asia), deep knee bending is required (Kurosaka et al., 2002). Moreover, patients whose activities of daily living (ADL) involve sitting cross-legged, kneeling, and squatting require motion of more than 125° without pain (Mulholland and Wyss, 2011).

- Kapoor et al. (2008) found that with a cross-legged sitting posture, the flexion at the knee can range from 126° to 142° (mean of 135°).
- Muslims have been shown to routinely flex the knee between 150° and 165° during prayer (Acker et al., 2011)
- Hemmerich et al. (2006) found that a mean maximum flexion of 157° at the knee joint was required for squatting with heels up.

In increasingly multicultural societies, range of motion is no longer a regional requirement but rather a global demand.

**The global supply of orthopaedic surgeons is not expected to be able to meet the expected increase in demand for joint arthroplasty procedures.**

The demand for health care services, particularly musculoskeletal care, is expected to increase substantially in the US because of the growing and aging population, increasing patient expectations, economic growth, investment in health care interventions, and improvements in diagnosis and treatment. It is projected that by 2030, the annual number of TKA procedures will be approximately 3.5 million (Kurtz et al., 2007a; Iorio et al., 2008; Burden of Musculoskeletal Diseases in the United States, 2008) (Figure 7).

**Figure 7.** Projected Number of Primary Total Knee Arthroplasties in the United States, 2005 to 2030

![Projected Number of Primary Total Knee Arthroplasties in the United States, 2005 to 2030](image)

Source: Kurtz et al., 2007a.

It is not expected that the future supply of orthopaedic surgeons will be sufficient to meet the increasing demand for musculoskeletal care. Between 2000 and 2020, the demand for orthopaedic services in the US will increase by 23%, whereas the number of orthopaedic
surgeons will increase by only 2% (Iorio et al., 2008). By 2020, the federal government predicts an overall shortage of approximately 12,000 to 15,600 orthopaedic surgeons in the US (Iorio et al., 2008). The inadequate supply of joint arthroplasty surgeons in the US may not meet the increasing demand for joint arthroplasty.

The number of orthopaedic surgeons is limited because more surgeons are selecting specialty areas other than adult knee and hip reconstructions, the number of fellowship programs is decreasing, orthopaedic fellowship positions are not consistently being filled, and US immigration policies limit the number of physicians entering the country (Iorio et al., 2008). In a US postresidency fellowship program, only 6% of orthopaedic surgeons cited adult knee and adult hip reconstructions as a specialty area, in contrast to the more popular specialty areas of sports medicine (27%) and hand surgery (21%) (Iorio et al., 2008). Moreover, as of 2008, there were approximately 64 adult reconstruction fellowship programs, and 10 programs had been discontinued over the previous 5 years because of the inability to attract fellowship candidates (Iorio et al., 2008). This amounted to a 14% decrease in the number of available programs. During the 2006-2007 academic year, only 77% of available fellowship positions were filled; during the 2007-2008 academic year, only 62% were filled (Iorio et al., 2008). Of the filled fellowship positions, only 20% in the 2006-2007 academic year and 27% in the 2007-2008 academic year were occupied by international medical graduates, owing to the limited number of physicians that can enter the US according to immigration policies (Iorio et al., 2008).
1.3 Clinical Burden of Total Knee Arthroplasty

1.3.1 Clinical Issues

Surgical issues such as implant overhang, wear, malalignment, imprecise sizing, and loosening can result in pain, stiffness, impaired range of motion, and instability for total knee arthroplasty patients.

Primary TKA can be a successful operation associated with pain relief and restoration of patient function; however, some challenges with TKA persist.

1.3.1.1 Impaired Range of Motion and Instability

Knee implant motions have a direct influence on patient function and implant longevity. Based on numerous studies characterizing the in vivo motions of knee arthroplasties during the past 2 decades, it has been concluded that motions after knee arthroplasties generally do not replicate normal knee motions (Banks and Hodge, 2004).

Another effect that can occur following TKA is instability. Tibiofemoral stability is dependent on multiple factors including: surgical technique factors, implant design factors, and patient factors. Tibiofemoral instability can be observed in extension, flexion, and mid-flexion. Symmetric extension instability can occur when the thickness of the components is less than the extension gap between the bone ends. Asymmetric extension instability can occur when the bone cuts are made without regard to the ligament asymmetry of a knee and the arthroplasty is unstable on one side. Flexion instability can occur when the knee is stable in extension but not in flexion because the flexion space is relatively too large for the thickness of the tibial components (Insall and Scott, 2006). During implantation, the surgeon must “balance” the knee by a combination of implant sizing, implant positioning, implant alignment, and ligament tensioning to ensure stability; this is usually established at only 0° and 90° flexion. However, there may sometimes be an intermediate arc of flexion where the ligaments are more slack, leading to “mid-range instability” (Stoddard et al., 2012). This instability may occur with both posterior cruciate ligament (PCL)–retaining and PCL-sacrificing designs. Table 4 presents the distribution of reasons for TKA failure/revision identified in the literature. The main causes of failure and revision were loosening, instability, and wear. Based on selected articles, instability was reported as a reason for 21.2% to 30.3% of failures/revision (Mulhall et al., 2006).

Table 4. Distribution of Reasons for Total Knee Arthroplasty Failure/Revision

<table>
<thead>
<tr>
<th>Article</th>
<th>Sample Size</th>
<th>Reason for Failure/Revision</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Loosening</td>
</tr>
<tr>
<td>Fehring et al., 2001</td>
<td>279a</td>
<td>37b (13%)</td>
</tr>
<tr>
<td>Sharkey et al., 2002</td>
<td>212</td>
<td>51 (24%)</td>
</tr>
<tr>
<td>Mulhall et al., 2006</td>
<td>318</td>
<td>141 (41%)</td>
</tr>
</tbody>
</table>

a Publication focused on early failures
b Cementless implants
Source: Mulhall et al., 2006.

1.3.1.2 Imprecise Sizing and Decline in Function

Overhang can occur if an implant is incorrectly sized and, as a result, overhangs the side of the bones, causing irritation of the surrounding soft tissue. The presence of an overhang of 3 mm or more in at least one area of the femoral component is associated with a
90% increase in the patient reporting clinically important knee pain 2 years after surgery (Mahoney and Kinsey, 2010). In a study of a single design of TKA implant (Scorpio NRG posterior stabilized total knee system; Stryker Orthopaedics, Mahwah, NJ), 76% of all patients had overhang of more than 0 mm in at least one area (Mahoney and Kinsey, 2010). The observed prevalence of femoral component overhang of 3 mm or more was high; overhang affected approximately 40% of men and 68% of women (Mahoney and Kinsey, 2010). The prevalence of overhang increased with larger femoral component sizes among both men and women (Mahoney and Kinsey, 2010). Figure 8 shows the proportion of knees that had femoral component overhang of 3 mm or more in at least 1 of 10 areas among men and women managed with each femoral component size.

**Figure 8.** Proportion of Knees With Femoral Component Overhang of 3 mm or More in at Least 1 of 10 Areas

* A bar is not shown when the denominator is 10 or less.


1.3.1.3 Patellofemoral Kinematics

Patellar tracking is defined as the motion of the patella relative to the femur or femoral groove during knee flexion and extension (Katchburian et al., 2003). The patellofemoral joint is incongruent, and the patella is a small bone that moves a large amount during knee flexion-extension and is acted upon by powerful muscles that converge from different directions (Amis et al., 2006). Patellar “maltracking” implies that the patella is not following a normal, stable path of movement within the femoral trochlear groove when the knee is flexing and extending. Clinically, this might relate to a lateral translation or tilt of the patella, which causes the medial facet to lift off the trochlea. The relationship between patellofemoral joint stability and maltracking is unclear, but presumably they are related; if the patella is stable in the trochlear groove, then it is difficult to move the patella away from this position. (Amis et al., 2006). There is general agreement that the natural patella translates medially in early knee flexion and then translates laterally (Katchburian et al., 2003).

Stiffness, a disabling problem that occurs following TKA, is associated with both pain and diminished functional capacity. Nelson et al. (2005) estimated the prevalence of knee stiffness—defined as one having a flexion contracture of 15° and/or less than 75° of flexion—after primary TKA. The prevalence of stiffness in a series of 1,000 primary knee arthroplasties was 1.3% an average of 32 months postoperatively (Nelson et al., 2005).
Patients with a stiff knee had significantly less preoperative extension and flexion than did those without a stiff knee.

Overstuffing of a joint occurs during TKA if an insufficient flexion, extension, or patellofemoral space is generated for the thickness of the implants inserted. Overstuffing the patellofemoral component can lead to increased component wear, pain, and force and stress on the patella (Ghosh et al., 2009; Mihalko et al., 2006; Bengs and Scott, 2006). In addition, overstuffing may result in extensor mechanism tightness and subsequent reduction in postoperative knee flexion (Mihalko et al., 2008).

### 1.3.1.4 Durability

Primary TKA can be a successful operation associated with improvements in pain and restoration of function for the patient. However, failures of TKA may occur for a variety of reasons, including wear, loosening, infections, instability, fracture, and mechanical failure (Sharkey et al., 2002). This failure can cause pain, instability, and loss of function. To relieve pain and restore function, revision TKAs are performed.

Several studies have reported the distribution of reasons cited for revision TKAs within a particular country, although direct comparison of these distributions across countries is difficult because of methodological differences among the studies (e.g., the definition of concepts such as loosening, wear, or infection; differences in data collection; reporting more than one reason for revision). It is important to note that the distribution of reasons for revision is not the same as the incidence of revision for a particular diagnosis. However, noting these differences, the major reasons for revision TKAs in the US, England and Wales, Australia, and Sweden were loosening and wear (Figure 9). Australia had the highest distribution of revisions due to loosening (34.9%), followed by England and Wales (33.0%) and Sweden (25.0%) (AOANJRR, 2011; NJR, 2011; Swedish Knee Arthroplasty Register, 2011). England and Wales had the highest distribution of revisions due to wear (11.0%), followed by Sweden (6.0%) and the US (4.9%) (AOANJRR, 2011; NJR, 2011; Swedish Knee Arthroplasty Register, 2011; Bozic et al., 2010).

**Figure 9.** Distribution of Reasons for Revision in the United States, England and Wales, Australia, and Sweden

![Distribution of Reasons for Revision in the United States, England and Wales, Australia, and Sweden](image_url)

Source: Bozic et al., 2010; NJR, 2011; AOANJRR, 2011; Swedish Knee Arthroplasty Register, 2011.
Oxidation of polyethylene impacts durability of the implant. Gamma-air sterilization was an industry standard until the mid-1990s, when the process was shown to result in oxidative embrittlement of the ultra-high-molecular-weight polyethylene (UHMWPE) bearings. Thermal processing protocols have been used to stabilize highly crosslinked materials against oxidative degradation either by annealing below melt temperature (e.g., Crossfire and X3) or remelting above melt temperature (e.g., Durasul, Longevity, Marathon, Prolong, XLK, XLPE). Because conflicting findings have been reported in the literature on the oxidative stability of highly crosslinked UHMWPE, Currier et al. (2012) studied a large cohort of retrieved highly crosslinked tibial inserts. They evaluated 1) the environment in which oxidation could occur (in vivo or postexplant) and 2) the effect of fabrication variables and thermal processing after irradiation (annealing or remelting) on oxidation resistance. They hypothesized that annealed highly crosslinked UHMWPE oxidized at a comparatively higher rate in vivo than remelted highly crosslinked UHMWPE. Three materials were compared: Prolong (Zimmer, Warsaw, IN), X3 (Stryker Orthopaedics, Mahwah, NJ), and XLK (DePuy Synthes Joint Reconstruction, Warsaw, IN).

The three highly crosslinked materials each had a significantly different range of calculated articular oxidation rates (Figure 10). The three materials were compared in pairs. Of the remelted highly crosslinked inserts (Prolong and XLK), Prolong showed a significantly higher articular oxidation rate ($P = 0.001$). X3 compared with either Prolong or XLK showed a significantly higher articular oxidation rate ($P < 0.001$) (Currier et al., 2012).

**Figure 10. Articular Oxidation Rates Vary Among Highly Crosslinked Materials**

Oxidation of highly cross-linked material can occur in vivo (Curier et al., 2012). When postretrieval shelf time was minimized, the different fabrication methods used to produce highly crosslinked tibial inserts were seen to cause differences in oxidation potential.

Crosslinking irradiation dose and postirradiation thermal treatment (remelting vs. annealing) significantly impacted the oxidation potential of highly crosslinked materials. Edge oxidation was present only in annealed materials.
1.3.2 Patient Outcomes

Surgical process and patient outcomes from total knee arthroplasty can vary among institutions, surgeons, and surgical staffs.

Depending on the institution, surgeon, and surgical staff performing a TKA, surgical process and outcomes such as functional status, mortality and length of stay, infection, and revision can vary by patient. The following subsections present studies focusing on the difference in these surgical processes and patient outcomes among different providers.

1.3.2.1 Functional Status

Patients who undergo a range of surgical procedures in centers with higher procedure volume experience fewer perioperative deaths and complications than patients undergoing these procedures in lower-volume centers (Katz et al., 2007). The annual volume of TKAs performed by the hospital and the surgeon is inversely associated with perioperative mortality and select complications (Katz et al., 2007). Katz et al. (2007) studied the association between procedure volume and functional status 2 years following TKA:

- In univariate analysis, the proportion of patients with Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) functional status scores less than 60 (100 representing the best possible status) increased from 12% in hospitals with volumes exceeding 200 Medicare TKA cases per year to 19% in hospitals with 1 to 10 cases per year.
- Similarly, the proportion of patients with WOMAC functional status scores less than 60 increased from 10% among surgeons who performed more than 50 TKA procedures per year in the medicare population to 20% among surgeons who performed 12 per year.

The associations between volume and functional outcomes (WOMAC functional status score < 60, inability to flex the knee 90°, inability to extend knee fully, dissatisfaction) were highly statistically significant, ranging from P < 0.0001 to 0.004. Patients who underwent TKA procedures in high-volume hospitals by high-volume surgeons had the lowest rates of worse functional outcomes, whereas patients who underwent TKA procedures in lower-volume centers by lower-volume surgeons had the highest rates of these poor functional outcomes. Total knee arthroplasties performed in centers and/or by surgeons with lower procedure volume are associated with higher risks of mortality and select complications following TKA.
1.3.2.2 Mortality and Length of Stay

Bozic et al. (2010) identified revision TKA procedures performed in the US and assessed average length of stay by US Census region using the NIS. Average length of stay and total charges differed by US Census region. The shortest average length of stay (4.8 days) was reported in the Midwest and the West, whereas the longest average length of stay (5.8 days) was reported in the Northeast (Bozic et al., 2010).

The 8th Annual Report of the NJr for England and Wales (NJR, 2011) reported mortality and length of stay by type of provider and country in patients who received a primary knee arthroplasty (Table 5). Within 5 years after receiving a primary knee arthroplasty, mortality was lower in patients who were treated in an independent hospital (6.3%) or independent sector treatment center (3.8%) compared with being treated in a NHS hospital (9.8%) or NHS treatment center (9.1%) (NJR, 2011). The average length of stay of patients treated in independent hospital (4.9 days) or independent sector treatment center (4.4 days) were shorter than those treated in an NHS hospital (6.9 days) or NHS treatment center (5.9 days) (NJR, 2011).

Table 5. Mortality Within 5 Years and Length of Hospital Stay for Patients Who Received a Primary Knee Arthroplasty, April 2003-December 2009

<table>
<thead>
<tr>
<th>Category</th>
<th>Number of Patients</th>
<th>Mortality Rates(^a) (95% CI)</th>
<th>Average Length of Stay, Days (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of provider</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NHS hospital</td>
<td>195,923</td>
<td>9.8% (9.6%-10.0%)</td>
<td>6.9 (6.97.0)</td>
</tr>
<tr>
<td>NHS treatment center</td>
<td>16,039</td>
<td>9.1% (8.2%-10.0%)</td>
<td>5.9 (5.96.0)</td>
</tr>
<tr>
<td>Independent hospital</td>
<td>16,049</td>
<td>6.3% (5.7%-7.1%)</td>
<td>4.9 (4.95.0)</td>
</tr>
<tr>
<td>Independent sector treatment center</td>
<td>10,719</td>
<td>3.8% (2.7%-5.3%)</td>
<td>4.4 (4.34.5)</td>
</tr>
<tr>
<td>Country</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>England</td>
<td>223,745</td>
<td>9.5% (9.3%-9.7%)</td>
<td>6.5 (6.56.6)</td>
</tr>
<tr>
<td>Wales</td>
<td>14,986</td>
<td>9.1% (8.3%-10.1%)</td>
<td>7.9 (7.88.0)</td>
</tr>
</tbody>
</table>

CI = confidence interval; NHS = National Health Service.
\(^a\) Calculated using the Kaplan-Meier survival analysis method.
Source: NJR, 2011.
Patients treated in England had a higher mortality (9.5%) than patients treated in Wales (9.1%) (P = 0.01) (NJR, 2011); however, patients treated in England had a shorter length of stay (6.5 days) in hospital than those treated in Wales (7.9 days) (P < 0.001).

In a recent analysis of the Taiwan National Health Insurance database, Cheng et al. (2011) confirmed a correlation between TKA surgical volume and mortality rates. The authors found that mortality rates decrease as the TKA volume increases. Further, they demonstrated that surgeons and hospitals with higher TKA volumes exhibit better operation quality and lower postoperative complication rates. The authors also found significant differences in infection and mortality rates between large medical centers and district hospitals (local teaching hospitals and local hospitals) (Cheng et al., 2011).

In 2010, the High Value Healthcare Collaborative in the US initiated a collective study of the characteristics of TKA delivery in six member health care systems (Tomek et al., 2012). Unadjusted hospital lengths of stay varied by health care system, individual surgeons’ total number of knee replacements performed, and day of the week on which the surgery occurred. Across organizations, patients whose surgeons had performed more TKAs generally had shorter lengths of stay. Generally, if the surgery occurred later in the week, lengths of stay were longer and complication rates were higher. Overall, longer operating time was associated with longer length of stay, and operating time trended lower with high surgeon case loads.

1.3.2.3 Infection

Deep infection is an infrequent but catastrophic complication of TKA. It has been projected that the number of primary and revision procedures will increase dramatically over the next 25 years, as will the infection burden for patients, clinicians, and society. Between 1990 and 2004, a nearly twofold increase was observed in the incidence of infection for knee arthroplasties in the US. The highest infection burden was seen in the northeast region of the US, urban nonteaching hospitals, and small hospitals (Kurtz et al., 2008).

1.3.2.4 Revision

In the US, total knee arthroplasty procedures that were performed due to revisions were most commonly reported in urban nonteaching hospitals (48.8%), compared with 41.2% in urban teaching hospitals, and only 9.9% in rural hospitals. The highest percentage of TKA procedures due to revisions was seen in large hospitals (61.3%), whereas 13.7% of TKA procedures due to revisions were reported in small hospitals. Geographically, the highest percentage of TKA procedures due to revisions was reported in the South (37.5%) and the lowest percentage of TKA procedures due to revisions was reported in the Northeast (16.3%) (Bozic et al., 2010).

1.3.3 Room for Improvement Following Total Knee Arthroplasty

Recovery and outcomes following total knee arthroplasty are not the same as recovery and outcomes following total hip arthroplasty.

The goal of both TKA and total hip arthroplasty (THA) is the same: to reduce joint pain, increase range of motion, and improve function (Halket et al., 2010). Clinicians and patients generally have the misconception that THA and TKA have similar recovery patterns (O’Brien et al., 2009). However, evidence shows that patients with TKA actually experience significantly smaller improvements in postoperative pain and function compared with patients undergoing THA (O’Brien et al., 2009; Bourne et al., 2010; March et al., 1999; Behrend et al., 2012).
A comparison of early and intermediate outcomes among 337 THA patients and 256 TKA patients whose procedures were performed by the same surgeon illustrates this difference in outcomes, which were assessed with the Oxford Knee Score (OKS) and Oxford Hip Score (OHS). Oxford Knee and Hip scores were measured at three consecutive time points (preoperative, 6 weeks [THA] or 3 months [TKA] postoperative, and 1 year [THA and TKA] postoperative) (O’Brien et al., 2009) (Table 6). Although preoperative Oxford scores were significantly higher (worse) in THA patients, at both postoperative time points (6 weeks or 3 months and 1 year), Oxford scores were significantly lower (better) among THA patients compared with TKA patients, indicating greater improvements in patients undergoing THA. Both groups of patients showed significant improvements in outcomes as evidenced by reductions in Oxford scores; however, the improvements were greater in the THA group. Further, pain and functional outcomes were generally better in THA patients compared with TKA patients (O’Brien et al., 2009) (Table 7).

### Table 6. Oxford Scores Following Total Hip Arthroplasty and Total Knee Arthroplasty

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Mean Oxford Score (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>THA</td>
</tr>
<tr>
<td>Preoperative</td>
<td>49.2 (5.5)</td>
</tr>
<tr>
<td>6 weeks (THA) or 3 months (TKA) postoperative</td>
<td>25.1 (8.3)</td>
</tr>
<tr>
<td>1 year postoperative</td>
<td>21.1 (8.9)</td>
</tr>
</tbody>
</table>

THA = total hip arthroplasty; TKA = total knee arthroplasty; SD = standard deviation.
Source: O’Brien et al., 2009.

### Table 7. Oxford Pain and Function Items for Total Hip Arthroplasty and Total Knee Arthroplasty Patients

<table>
<thead>
<tr>
<th>Oxford Score Item</th>
<th>% of Patients (at First Review Time Point)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>THA</td>
</tr>
<tr>
<td>Pain (moderate or severe)</td>
<td>9.8</td>
</tr>
<tr>
<td>Pain (severe)</td>
<td>1.2</td>
</tr>
<tr>
<td>Daily ablution (extremely difficult/impossible)</td>
<td>5.0</td>
</tr>
<tr>
<td>Transport (extremely difficult/impossible)</td>
<td>3.0</td>
</tr>
<tr>
<td>Shopping (extremely difficult/impossible)</td>
<td>24.6</td>
</tr>
<tr>
<td>Walking ability (household/nonambulant)</td>
<td>6.5</td>
</tr>
<tr>
<td>Stair climbing (extremely difficult/impossible)</td>
<td>5.6</td>
</tr>
<tr>
<td>Pain on standing (very painful/unbearable)</td>
<td>2.4</td>
</tr>
<tr>
<td>Limping (most of the time/all of the time)</td>
<td>15.1</td>
</tr>
<tr>
<td>Interfered with work or housework (greatly/total)</td>
<td>9.5</td>
</tr>
<tr>
<td>Night pain (most nights/every night)</td>
<td>7.7</td>
</tr>
</tbody>
</table>

THA = total hip arthroplasty; TKA = total knee arthroplasty.
Source: O’Brien et al., 2009.
Other reports indicate that a larger proportion of TKA patients (11%) are classified as having “moderate to severe problems” versus THA patients (6.1%) according to OKS and OHS scores (NJR, 2005).

A prospective cohort study compared TKA or THA patients’ HRQOL before and after surgery with age-related population norms (general population without OA) (March et al., 1999). A total of 50 patients undergoing THA and 92 patients undergoing TKA completed the SF-36 Health Survey (SF-36) before surgery and 12 months after surgery. Scores were calculated for patients in the following age groups: 55-64 years, 65-74 years, and ≥ 75 years. Results showed that although both procedures significantly improved patients’ HRQOL and well-being 12 months after surgery, there was room for improvement among the TKA patients. For example, among the group aged 55-64 years undergoing TKA, SF-36 scores 1 year following TKA for physical function, role physical, bodily pain, and vitality remained significantly lower than the population norms, whereas THA patients’ scores returned to population norms (Figure 12). Scott et al. (2010) noted that “the limitations of TKA in restoring premorbid function and feeling like a natural knee should be emphasized.”

Figure 12. SF-36 Scores for Hip Arthroplasty, Knee Arthroplasty, and Population Norms by Age Group

The SF-36 is the most commonly used health profile. It includes 36 questions, organized into multi-item scales to measure health status across eight dimensions: Physical Functioning, Role Limitations due to Physical Health Problems, Bodily Pain, Social Functioning, General Mental Health, Role Limitations due to Emotional Problems, Vitality, and General Health Perceptions. Higher scores indicate better health.

SF-36 = SF-36 Health Survey.
Source: March et al., 1999.
Unlike hip replacement and the concept of the “forgotten hip,” there is no “forgotten knee.”

Both patients and clinicians increasingly identify that the objective of TKA is to closely approximate with a prosthesis the feel and function of a healthy knee that has never undergone surgery (Morra et al., 2008). As such, another important aspect of the discrepancy in THA and TKA outcomes is that THA patients can “forget” about their prosthesis following surgery, whereas TKA patients are aware of the prosthesis. A new questionnaire, the Forgotten Joint Score (FJS), assesses the patient’s ability to forget an artificial joint in everyday life (Behrend et al., 2011; Behrend et al., 2012). This 12 item questionnaire (FJS-12) was completed by 243 patients (157 THA patients and 86 TKA patients) as part of a validation study for the instrument. Results showed that THA patients scored significantly higher on the FJS-12 than TKA patients (59.8 vs. 50.0, respectively, P = 0.017; (Figure 13), demonstrating THA patients’ greater ability to forget their implant.

**Figure 13. Mean Forgotten Joint Scores for Total Hip Arthroplasty and Total Knee Arthroplasty**

Note: Higher scores indicate greater ability for a patient to forget their artificial joint in everyday life (P = 0.017).
Source: Behrend et al., 2011.

One year following total knee arthroplasty, limitations in function remain for some patients.

Limitations in the ability to perform certain activities following joint replacement likely contribute to the discrepancy in outcomes and satisfaction between THA and TKA patients. Specifically, many TKA patients remain limited, to some degree, in their ADL following surgery (Figure 14).
Other ongoing pain and functional limitations following TKA can have a strong impact on patient satisfaction, with patients who experience more pain and functional impairment being less likely to be satisfied with their surgery. TKA patients continue to report problems with kneeling, persistent pain, pain on walking, and pain when shopping up to 1 year following TKA (Figure 15) (Baker et al., 2007).

Figure 14. Total Knee Arthroplasty Patients Limited in Activities of Daily Living


Figure 15. Knee Patients Limited in Activities 1 Year Following Total Knee Arthroplasty

Source: Baker et al., 2007.
Noble et al. (2005) investigated whether TKA restores normal knee function. Responses were collected from 243 patients at least 1 year after they had undergone TKA and 257 individuals who had no previous history of knee disorders who completed the Total Knee Function Questionnaire. Respondents who had undergone TKA were recruited from Veterans Affairs clinics, orthopaedic department affiliations, public and private hospital clinics, and Association of American Retired Persons (AARP) meetings throughout Houston, Texas. There were large differences between the group of patients who had undergone TKA and the age- and gender-matched control group. The TKA and control groups had similar knee function with activities such as swimming, golfing, and stationary biking. However, the control group exceeded the function scores of the TKA group in activities such as kneeling, squatting, carrying loads, and stretching. Overall, compared with patients who had undergone TKA, approximately one-third more control subjects were able to kneel (63% vs. 42%) or squat (59% vs. 35%). Two to three times as many patients who had undergone TKA experienced difficulties doing most other activities attributable to impaired knee function (Figure 16). As the activities became more demanding, the gap between the two populations widened; approximately four times as many control subjects reported symptom-free function compared with patients who had undergone TKA when squatting (52% vs. 14%) or kneeling (54% vs. 13%).

Figure 16. Percentage of Total Knee Arthroplasty Patients and Control Subjects Reporting Significant Difficulty While Doing Various Activities

TKA = total knee arthroplasty.
Source: Noble et al., 2005

Noble et al. (2005) found that a TKA does not restore normal knee function. Although TKA restores patients’ ability to perform many routine activities, a substantial deficit remains in meeting the challenges of many functional tasks that are important to the patient, especially tasks involving kneeling or squatting.
Nilsdotter et al. (2009) analyzed the relationship between preoperative expectations and postoperative satisfaction and self-reported outcomes among 102 patients undergoing TKA. Expectations and outcomes were assessed using the Knee Injury and Osteoarthritis Outcome Score (KOOS), the SF-36, and the questions regarding the relevance of improvement on the following KOOS subscales: expectations, satisfaction, and patient characteristics. Results showed that, at the 5-year follow-up, patients’ expectations of walking ability were better fulfilled than expectations of leisure activities. Preoperatively, 39% of patients reported expectations to have unlimited walking ability on even ground following their surgery. At 12 months postoperatively, 28% of patients had unlimited walking ability on even ground and at 5 years postoperatively, 21% of patients had unlimited walking ability on even ground. However, patients’ expectations regarding their leisure activities were generally much higher than the results seen at 1 and 5 years (Figure 17). For example, whereas 41% of patients expected to be able to go dancing and golfing, only 24% of patients were able to do so 12 months after surgery. Preoperatively, 96% of patients expected to have major improvements in their ability to perform ADL; at 12 months, 90% reported better or much better ADL function; this percentage dropped to 61% at 5 years. Similarly, 98% of patients expected to have major improvements in pain; at 12 months, 93% reported less or much less pain; this percentage dropped to 63% at 5 years.

Tippett et al. (2010a; 2010b) compared preoperative expectations and postoperative satisfaction among patients undergoing TKA. Results of this randomized, multicenter trial showed that, 6 months after surgery, preoperative expectations and postoperative satisfaction did not match in more than 60% of patients who were asked about their ability to kneel, squat, get in/out of a car, ascend/descend stairs, rise from a chair, get on/off the toilet, or bend to retrieve an object from the floor (Tippett et al., 2010b).

**Figure 17.** Percentage of Total Knee Arthroplasty Patients’ Preoperative Expectations That Were Met or Exceeded at 6 and 12 Months After Surgery

Jones et al. (2012) conducted a prospective cohort study to determine the type, frequency, intensity, and duration of actual versus expected leisure activity among a cohort of patients,
45 years and older, who were undergoing primary TKA. Patients were recruited before surgery from two community hospitals and one academic medical center in the US. Data on actual and expected participation in 36 leisure activities were collected preoperatively and at 12 months in patients with knee OA. At baseline, 83 patients reported a median ± interquartile range of 2.2 ± 12.4 metabolic equivalent of task (MET)–hours of total leisure activity per week, with expectations of performing significantly more activity (23.3 ± 41.1 MET-hours) by 12 months after surgery (P = 0.005). At 12 months, the cohort reported performing significantly more leisure activity than at baseline (10.8 ± 2.8 vs. 2.2 ± 12.4 median MET-hours, P < 0.0005); however, the actual amount of activity at 12 months was significantly less than expected (23.3 ± 41.1 vs. 10.8 ± 2.8 median MET-hours, P = 0.001). Despite high expectations, there were statistically and clinically significant differences between actual and expected activity at 12 months, suggesting that patients’ expectations may not have been fulfilled.
1.4 Economic Burden of Total Knee Arthroplasty

The economic burden of total knee arthroplasty is significant. Joint arthroplasties have become a popular treatment option and have received widespread acceptance because they provide improved physical function and pain relief to patients. The demand for joint arthroplasties and increase in hospital costs is causing a significant economic burden to society.

The national US bill for primary joint arthroplasties has increased dramatically because of the increasing number of joint arthroplasty procedures performed and the increasing hospital charges (Kim, 2008) (Table 8). Median hospital charges for primary TKAs increased from $19,309 in 1997 to $29,509 in 2004 (1.53 times). In 2004, approximately $14.6 billion (95% CI, $13.2 billion-$15.9 billion) was charged by hospitals for primary knee arthroplasties.

Table 8. Economic Burden of Total Knee Arthroplasty Performed in the United States

<table>
<thead>
<tr>
<th>Year</th>
<th>Frequency (95% CI)</th>
<th>Median Hospital Charges</th>
<th>National Bill of Hospital Charges in Millions of Dollars (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>264,331 (245,611-283,051)</td>
<td>$19,309</td>
<td>$5,618 ($5,202-$6,034)</td>
</tr>
<tr>
<td>1998</td>
<td>251,309 (233,138-269,480)</td>
<td>$18,946</td>
<td>$5,325 ($4,930-$5,721)</td>
</tr>
<tr>
<td>1999</td>
<td>262,687 (241,201-284,173)</td>
<td>$19,700</td>
<td>$5,847 ($5,324-$6,370)</td>
</tr>
<tr>
<td>2000</td>
<td>281,534 (260,476-302,592)</td>
<td>$21,067</td>
<td>$6,612 ($6,062-$7,162)</td>
</tr>
<tr>
<td>2001</td>
<td>313,618 (289,151-338,085)</td>
<td>$22,570</td>
<td>$7,994 ($7,332-$8,656)</td>
</tr>
<tr>
<td>2002</td>
<td>350,122 (323,803-376,441)</td>
<td>$24,705</td>
<td>$9,831 ($9,072-$10,590)</td>
</tr>
<tr>
<td>2003</td>
<td>379,719 (353,194-406,244)</td>
<td>$26,800</td>
<td>$11,867 ($10,958-$12,775)</td>
</tr>
</tbody>
</table>

CI = confidence interval.
Source: Kim, 2008.
By the year 2015, the annual number of primary knee arthroplasties in the US will be greater than 1.3 million, and the national bill for hospital charges will be $49 billion (Kim, 2008) (Figure 18).

**Figure 18.** Projected Number of Primary Total Knee Arthroplasties in the United States, 2005 to 2015

Dowsey et al. (2011) conducted a cost-identification study in a cohort of 530 patients who underwent TKA between 2006 and 2007 at a university-affiliated tertiary referral center in Melbourne, Australia. The mean cost per episode of care was $16,454 (standard deviation [SD], $8,474). Table 9 summarizes the distribution of costs. The highest percentages of total cost were attributable to operating room (OR) costs (41.5%) and nursing costs (40.8%). Dowsey et al. (2011) also compared the hospital inpatient costs between nonobese and obese patients and found that obesity was associated with higher inpatient surgery costs and episode of care costs.

**Table 9.** Distribution of Cost (Australian dollars) Associated With Total Knee Arthroplasty

<table>
<thead>
<tr>
<th>Cost Category</th>
<th>Mean ± SD</th>
<th>Percentage of Total Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical (surgical)</td>
<td>1,231.79 ± 794.25</td>
<td>7.5</td>
</tr>
<tr>
<td>Medical (nonsurgical)</td>
<td>149.27 ± 106.99</td>
<td>0.9</td>
</tr>
<tr>
<td>Nursing</td>
<td>6,706.29 ± 4,974.56</td>
<td>40.8</td>
</tr>
<tr>
<td>Allied health</td>
<td>664.13 ± 427.17</td>
<td>4.0</td>
</tr>
<tr>
<td>Imaging</td>
<td>172.19 ± 265.17</td>
<td>1.1</td>
</tr>
<tr>
<td>Pathology</td>
<td>110.17 ± 154.93</td>
<td>0.7</td>
</tr>
<tr>
<td>Pharmacy</td>
<td>531.36 ± 663.41</td>
<td>3.2</td>
</tr>
<tr>
<td>Operating room*</td>
<td>6,821.74 ± 2,598.31</td>
<td>41.5</td>
</tr>
</tbody>
</table>

*SD = standard deviation.
*a includes implant costs.
Source: Dowsey et al., 2011.
Total knee arthroplasty failure represents a substantial clinical challenge and economic burden on the health system.

The number of revision TKA procedures is increasing globally (see Section 1.2). Revision TKA procedures are more expensive than primary TKA procedures owing to the longer operations, extended hospital stay, and increased complication rates. The cost of a revision knee surgery is conservatively estimated to be approximately $22,000 (Riaz and Umar, 2006). In 1999, 22,000 knee revisions operations were performed in the US, costing approximately $262 million (Riaz and Umar, 2006).

In the US between 2005 and 2015, it is projected that annual hospital charges will increase by 450%, to $40.8 billion, for primary TKA, and that corresponding surgical charges will increase by 250%, to $5.06 billion (Kurtz et al., 2007b). For revision TKA, it is projected that hospital charges will increase by 450%, to $4.1 billion, and that surgical charges will increase 160%, to $0.34 billion. In 2005, the estimated overall charges for primary TKAs were $8.85 billion, and in 2015, it is projected that they will be $45.84 billion (Kurtz et al., 2007b).

There are opportunities to increase efficiency of care in total knee arthroplasty.

Total knee arthroplasty procedures are complex and can be inefficient compared with other joint arthroplasty procedures owing to the number, weight, and cost of surgical instruments used. Currently, TKA requires multiple heavy instrument cases, making it difficult to handle the instruments. A requirement of 6 to 10 trays for a patient’s first knee replacement is not uncommon (Swanson, 2008). In addition, multiple trays and cases can make the surgical procedure less intuitive, which results in longer OR time and higher costs.

New TKA technology, equipment arriving just in time for a TKA procedure, and added demands for faster and less-invasive surgeries have increased the complexity of sterile processing (Swanson, 2008). At present, the estimated cost of 20 instrument-processing errors that create delays in the OR is $4,000. If a similar rate of instrument-processing errors causing delays were to occur monthly in a facility, the annual cost to the facility would be $48,000 (Swanson, 2008). Resterilization costs of instruments also can be a significant burden on the hospital and health care system.

There are both fixed (e.g., rent and personnel) and variable (e.g., supplies and implants) costs associated with the OR when performing a TKA. In addition, there is a cost for the time in the OR, which can be approximately $350 to $1,500 every 15 minutes. Instrument processing can cost approximately $80 to $100 per tray, totaling approximately $500 per knee set. Other processing costs include those for disposing waste, which can amount to $12,000 annually ($0.52/lb for the 25.75 lbs of waste that a TKA procedure generates), and disposing of instruments that are approximately an additional 2 lbs with a $1.04 additional cost per case.
Total knee arthroplasty does not have the same recovery and outcomes as THA. Studies and reports have shown that THA patients had lower Oxford scores (indicating greater improvements in outcomes), fewer problems following surgery, and higher SF-36 scores than TKA patients.

The ability to forget an artificial joint in everyday life can be regarded as the ultimate goal in joint arthroplasty, resulting in the greatest possible patient satisfaction. Unlike hip replacement and the concept of the “forgotten hip,” there is no “forgotten knee.” Both patients and clinicians increasingly identify that the objective of TKA is to closely approximate with a prosthesis the feel and function of a healthy knee that has never undergone surgery (Morra et al., 2008).

Limitations in the ability to perform certain activities following joint replacement likely contribute to the discrepancy in outcomes and satisfaction between THA and TKA patients. Specifically, many TKA patients remain limited, to some degree, in their ADL following surgery, particularly with kneeling and squatting (DePuy Synthes Joint Reconstruction, AARP Survey, 2007 [data on file]). Other ongoing pain and functional limitations following TKA can have a strong impact on patient satisfaction, with patients who experience more pain and functional impairment being less likely to be satisfied with their surgery.

Compared with THA, there is room for greater improvements in recovery, outcomes, and the ability to perform certain activities in TKA. More importantly, there is room to improve expectations and satisfaction of TKA patients following surgery.

Total knee arthroplasty procedures are complex and can be inefficient compared with other joint arthroplasty procedures owing to the number, weight, and cost of surgical instruments used in the OR. In addition, there is concern that the current supply of joint arthroplasty surgeons will not be sufficient to meet the increasing demand for total knee arthroplasty. There is an unmet treatment need for hospitals to adequately meet the care of patients with knee OA.
Each year, TKA relieves pain and restores function and mobility for patients with arthritis pain. It is widely recognized as one of the most performed and most successful surgical procedures. However, following TKA, some patients are limited, to some degree, in their ADL (see Part A). For example, research shows that 38% of patients are “limited a lot” when squatting after knee arthroplasty (Baker et al., 2007).

The ATTUNE Primary Total Knee System (ATTUNE System) was designed with the goal of addressing the clinical needs of patients, surgeons, and hospital providers around the world. Extensive research and science have gone into the design to help improve functional outcomes for patients, performance for surgeons, and efficiency for providers.

The ATTUNE System represents an innovative, comprehensive, integrated knee system. DePuy Synthes Joint Reconstruction has recently applied for extensive patent protection in countries throughout the world for the ATTUNE System implants, instruments, and surgical methods. In the US alone, as of this writing, there are already seven patents granted for key inventions related to the ATTUNE System implants. After extensive research and understanding of clinically proven designs, the system was developed to synergize implant design with native soft tissues. In addition, the system offers new innovative instrumentation to work in harmony with the implants. A host of expertly engineered advancements elevates instrument performance.

The ATTUNE System includes both Cruciate Retaining (CR) and Posterior Stabilized (PS) femoral components with ATTUNE GRADIUS™ Curve technology. The ATTUNE System is designed to achieve optimal articulation between component interfaces. The ATTUNE System patented fixedbearing LOGICLOCK™ Tibial Base design allows independent femoral and tibial sizing to achieve optimal tibiofemoral articulation. The ATTUNE System is only available with the most advanced AOX polyethylene technology from DePuy Synthes Joint Reconstruction, which was designed to provide a balance of the performance of the material while providing wear resistance, oxidative stability, and mechanical integrity.

The ATTUNE System design has been extensively tested in vitro, and these results are presented in Section 4. Plans for additional extensive clinical evidence development of early clinical performance of the ATTUNE System are discussed in Section 5. Additional product information is presented in Appendix B.
THE ATTUNE PRIMARY TOTAL KNEE SYSTEM VALUE
KEY TAKEAWAYS

• The ATTUNE Primary Total Knee System is designed to deliver a high level of motion and stability.

• The ATTUNE Primary Total Knee System provides a broad range of sizes for matching patients in today’s global population.

• The ATTUNE Primary Total Knee System is designed to deliver a high level of patellofemoral function.

• The ATTUNE Primary Total Knee System is designed to increase durability.

• The ATTUNE Primary Total Knee System is designed to enable efficiency in the operating room.
4.1 Motion and Stability

The ATTUNE System represents an innovative, comprehensive, integrated knee system. After extensive kinematic research and understanding of clinically proven designs, the system was developed to synergize implant design with native soft tissues. The result is an advanced implant featuring unique tibiofemoral articulation and advanced patellofemoral kinematics that enable more natural rollback and rotation with reduced anterior slide.

The ATTUNE Primary Total Knee System is designed to deliver a high level of motion and stability.

Tibiofemoral kinematics are a function of both the femoral component shape and design of the insert articulation surface. Instability of the knee in patients who have undergone TKA has been reported during high-demand activities both through clinical observations and during fluoroscopic evaluation (Dennis et al., 2004; Leszko et al., 2010; Dennis et al., 2003a). In vivo kinematic evaluations have cited implant-design factors as determinants of knee instability (Ploegmakers et al., 2010).

For patients to have a greater sensation of stability in high-demand activities such as ascending and descending stairs and rising from a chair, the implant must be stable. In the natural knee, balanced compartment tension in flexion and extension ensures good contact pressure and bearing stability throughout the arc of motion (Buechel, 2002). The restoration of normal knee function through surgical reconstruction is highly dependent on load sharing among the implant, surrounding ligaments, and other supporting soft-tissue structures. Excision, surgical release, and progressive pathological weakening of ligamentous structures result in an increased dependency on the implant system for stability. Intrinsic stability, achieved in nonhinged TKA through geometric variation of the condylar surfaces, is influenced by the relationship to the active and passive soft-tissue structures. Stability in this regard is the capacity of the implant to work with the remaining soft-tissue structures to control rotational, anterior-posterior (A-P), and medial-lateral (M-L) displacements to within normal physiologic ranges (Greenwald, 2002).

The goal of knee implant systems is to provide stability while not sacrificing rotational freedom to allow natural knee rotation at maximum flexion. Motion and stability are enhanced when sudden changes in radii of femoral curvatures (i.e., discontinuity in motion) are avoided, conformity of insert is maximized, and abrupt post-and-cam engagement is eliminated. Currently, available systems fall short of this ideal (Fitzpatrick et al., 2012a).

The ATTUNE System is a new, integrated knee system designed to deliver a high level of stability throughout the entire range of motion. The ATTUNE System femoral technology is unique in the industry. Historically, singleradius and multiradius designs (Figure 19 and Figure 20) have resulted in suboptimal kinematic function. In contrast, the ATTUNE GRADIUS Curve (radius of curvature of the femoral condyles) is designed with a series of gradually reducing radii and infinite centers of rotation. This creates a smooth transition with no abrupt changes from axis center to axis center during 5° to 65° of flexion. This smooth transition enables the ATTUNE System to
deliver a high level of motion and stability. The shape of the ATTUNE GRADIUS Curve (Figure 21) is designed to help produce high stability of the knee by minimizing unnatural sliding of the femur on the tibia as it articulates on the polyethylene surface (Clary et al., 2012a).

**Figure 19. Single-Radius J Curve**

Allows rollback to mimic a hinge-like device which does not allow for natural femoral rotation

One center of axis

Creates no transition. Similar to a hinged knee

**Figure 20. Multiradius J Curve**

Allows abrupt femoral rotation and potential for anterior slide or irregular motion during femoral rollback

A series of axis points

Creates a transition with abrupt changes from axis center to axis center

**Figure 21. The ATTUNE System Radius: ATTUNE GRADIUS Curve**

Allows smooth rotation of the femoral axis and controlled femoral rollback motion

A gradually reducing femoral radius

Creates movement in smooth transition with no abrupt or radical changes from axis center to axis center
In vitro experimental and computational simulations are critical preclinical tools in the evaluation of new implant designs. Advanced analytical and experimental methodologies were used to isolate the cause of anterior motion as an abrupt change in the radius of the sagittal condylar curvature (Clary et al., 2012a). The curvature of the ATTUNE System was specifically designed to attenuate abrupt anterior sliding during knee flexion. The ATTUNE System CR femoral component has a gradually reducing radius through 65° of flexion to deliver stability and then transitions to a slightly larger “brake radius.” The subtle transition to a slightly larger radius prevents anterior slide of the femur on the inserts to deliver knee stability and encourages femoral rollback (Clary et al., 2012a).

The ATTUNE System also combines the carefully controlled gradual reduction in femoral curvature with a finely tuned tibial insert curvature. The resulting conformity (defined as the ratio of femoral radius to polyethylene insert radius) is compared with the conformity of other knee systems. In the ATTUNE System, the higher conformity ratios required for stability through mid-flexion gradually give way to the lower values that provide the desired rotational freedom in deeper flexion (Figure 22-Figure 25).

To determine the relative impact on stability and mobility, Fitzpatrick et al. (2012a) assessed the influence of implant geometry on the inherent stability, motion, and contact mechanics of the knee joint. Specifically, A-P and internal-external (I-E) motions of the knee for four current TKA implant designs (Triathlon® [Stryker Orthopaedics, Mahwah, NJ], NexGen® [Zimmer, Warsaw, IN], ATTUNE Primary Total Knee System [DePuy Synthes Joint Reconstruction, Warsaw, IN], and SIGMA® Knee System [DePuy Synthes Joint Reconstruction, Warsaw, IN]) were compared. Each design was assessed for A-P stability during a step-down (high A-P shear) and rotational stability/freedom during stance-phase gait (high I-E torque). The simulation was carried out for the four components, including current CR and PS designs. The results were compared with data typical of the native knee. The ATTUNE System provides a greater degree of A-P stability than do the least constrained designs while avoiding excessive rotational constraint. The result is a balanced level of stability and freedom that more closely matches that found in the native knee (Sathasivan and Walker, 1999).
Figure 22. Implant Stability and Rotation: ATTUNE System Cruciate Retaining

Source: Fitzpatrick et al., 2012a.

Figure 23. ATTUNE System Cruciate Retaining Femoral-Insert Conformity
The tibiofemoral conformity ratio also has a significant impact on the resulting contact pressures between the tibia and femur. Damage to polyethylene is related to increased stresses within the material, which are in turn related to increased contact pressures. The contact pressures for the ATTUNE System are significantly lower than those for less-conforming designs.
The curvature and thickness of the posterior condyles also have been carefully designed to maintain appropriate contact stresses in the polymer tibial component in deeper flexion while simultaneously minimizing bone resection. In addition, the geometry is designed to work in harmony with the soft tissues to maintain proper ligament tension in deep flexion. The thickness and length of the posterior condyles are different for the CR and the PS components (Figure 26). The thickness of the posterior condyles on the PS component has been pushed outward by 1 mm relative to the CR design to compensate for the increase in flexion space that often accompanies loss of the PCL during PS surgery with a measured resection technique.

Figure 26. Posterior Condyles for Cruciate Retaining and Posterior Stabilized Components

CR = Cruciate Retaining; PS = Posterior Stabilized.

The ATTUNE System PS femoral component is designed to maintain a low contact position between the cam and spine during flexion, reducing the forces on the locking mechanism and tibial fixation. The proprietary s-curve of the ATTUNE SOFCAM™ Contact technology is designed so that, after initial contact, the cam moves low on the spine and stays low, transferring forces down through the center of the insert and delivering controlled and stable cam/spine interaction during flexion (Fitzpatrick et al., 2012b). From deep knee bend activity, the velocity of the cam at engagement correlates with the distance from the center of the condylar radius of curvature at engagement to the point of first contact on the cam (Figure 27). The TKA with the largest distance (NexGen® LPS-Flex) had the highest cam velocity (Figure 27), resulting in an abrupt change in low-point kinematics after engagement (Figure 28). Conversely, the TKAs with the smallest distance (ATTUNE System PS and Triathlon® PS) had the slowest cam velocity and a more gradual rollback of the femoral condyles after engagement.
**Figure 27. Post-cam Engagement Velocity**

Source: Fitzpatrick et al., 2012b.

<table>
<thead>
<tr>
<th></th>
<th>DePuy Synthes Joint Reconstruction ATTUNE System PS</th>
<th>Zimmer NexGen LPS-Flex</th>
<th>Stryker Triathlon PS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flexion at engagement (°)</td>
<td>87</td>
<td>90</td>
<td>53</td>
</tr>
<tr>
<td>Distance (mm)</td>
<td>4.8</td>
<td>15.1</td>
<td>5.2</td>
</tr>
<tr>
<td>Contact velocity (mm/°)</td>
<td>0.10</td>
<td>0.22</td>
<td>0.08</td>
</tr>
</tbody>
</table>

**Figure 28. Femoral Low Point Anterior-Posterior Contact Position on the Medial and Lateral Condyle for Each Implant**

Source: Fitzpatrick et al., 2012b.
The interaction among the PS cam and spine, the articular surface geometry, and the collateral ligaments is both complex and essential to the function of the PS knee in deep flexion. A computational model of the knee was developed to predict ligament interaction with implant geometry (i.e., ligament strain patterns) (Clary et al., 2012c). The model was used to assess several prototype femoral implant designs and optimize the strain pattern of the medial collateral ligament (MCL). The results of the modeling were confirmed through a cadaveric evaluation by a team of surgeons. The shape of the ATTUNE System PS posterior condyles worked with the knee’s soft tissue, whether using a “balanced gap” or “measured resection technique.” As a result of this experiment, the ATTUNE System has a geometry that maintains a consistent MCL length across the entire attachment site into deep flexion.

Knee arthroplasty is a soft-tissue procedure (Dennis et al., 2010; Heesterbeek, 2011). Balancing the flexion and extension gaps is extremely important in achieving optimal motion and stability. The ATTUNE System provides a comprehensive insert offering. With the ATTUNE System, insert thicknesses of 1mm increments in the core range provide surgeons with interoperative flexibility to match flexion and extension gaps and balance the knee (Figure 29).

**Figure 29. The ATTUNE System Insert Thickness**

The ATTUNE System fixed-bearing tibial component has been designed with a patented central locking mechanism (LOGICLOCK Tibial Base) to provide a secure attachment between the tibial base and the polymer insert.

In addition, the universal nature of the central features in the design enables multiple sizes of polyethylene inserts to attach to a single-size tibial base. This enables one-to-one matching of the femoral and polyethylene insert sizes to achieve ideal tibiofemoral articulation without compromising kinematic function. It also enables key features such as the PS SOFCAM and box to be fully proportional to minimize bone loss. The ATTUNE System is indicated for 2 sizes up or 2 sizes down when sizing the tibia to the polyethylene insert ( ).

The highly engineered locking mechanism greatly reduces micromotion between the polyethylene insert and the tibial base in comparison with other fixed-bearing systems available in the market (Leisinger et al., 2011). When combined with highly polished superior side surfaces, backside wear between the polyethylene insert and tibial base is greatly reduced.
4.2 Individualized Fit and Improved Function

To accommodate a very broad range of patient demographics, the sizing of the ATTUNE System was determined by conducting extensive anthropometric research with a diverse population (multiracial and multigender) of 353 patients worldwide (University College Dublin; Fitzpatrick, 2012 [data on file]). This research helped determine the implant size range. In order to evaluate and refine the ATTUNE System implant sizes, the design surgeons performed intraoperative size templating of femurs and tibias.

The ATTUNE System offers 14 femoral sizing options: 10 standard options in 3mm A-P increments and 4 narrow sizes.

Femoral component overhang has been associated with soft-tissue irritation and pain (Mahoney et al., 2010). The ATTUNE System femoral size range corresponds to the 30th percentile of the anthropometric database (University College Dublin; Fitzpatrick, 2012 [data on file]), where most current systems reside. This enables the core sizing line to avoid femoral component overhang in a majority of patients. A narrow femoral sizing line consisting of 4 additional sizes was created to avoid femoral overhang in patients with narrow femurs. With the full complement of standard and narrow sizing, the ATTUNE System offers a comprehensive size range to allow the surgeon to meet the specific needs of virtually all patients (Courtis et al., 2012).

Consistent size increments have been incorporated to aid in implant placement and fit:

- There are 3mm A-P increments between femoral component sizes. When a patient is between sizes, the surgeon's options for component fit are never more than a 1.5mm adjustment from the next larger or smaller size (Figure 31).
- Narrow femorals are 3.5 mm narrower (ML) than standard femorals.
- There are 3mm ML increments between tibial base sizes (Figure 31).

The A-P cutting blocks provide the ability to shift the position of the implant 1.5 mm anterior or posterior (Figure 31). The tibial inserts are available in 1mm increments (up to 8-mm thickness) to aid in flexion and extension gap balancing. Thus, the consistent 3-mm A-P increments between femoral sizes, the cutting blocks' ability to shift the position of the implant, and the 1-mm insert thicknesses allow the implants and the instruments to work together to provide the surgeon opportunities to offer patients the best possible implant fit.

Figure 31. Consistent 3-mm Anterior-Posterior Increments Between Femoral Sizing

A/P = anterior-posterior.
The ATTUNE System offers the surgeon the ability to independently size the tibial and femoral components. The ATTUNE System patented fixed-bearing LOGICLOCK Tibial Base allows independent femoral and tibial sizing to achieve optimal tibiofemoral articulation. The ATTUNE System allows for 2-up and 2-down sizing between femur and tibia.

The size and shape of the tibial base component have been designed for proper placement, surgical preparation, and the conservation of healthy bone stock (Figure 32). The design creates a small profile of the stem and keel to conserve bone, aid in placement, and deliver good fixation and stability. The small profile accommodates surgeons who prefer smaller incisions.

Figure 32. The ATTUNE System Tibial Base Components

FB = fixed-bearing.

The ATTUNE Primary Total Knee System provides a broad range of sizes for matching patients in today's global population.

Studies of distal femoral geometry have improved implant sizing, reducing postoperative problems and extending implant survival rates (Siu et al., 1996). These studies have obtained knee measurement data using a variety of methods including cadaveric, intraoperative, and, more recently, computed tomography (CT)/magnetic resonance imaging (MRI)–based analyses (University College Dublin; Fitzpatrick, 2012 [data on file]). These studies typically use data primarily from one geographic region and are not globally representative. Given the variability of the data sources forming the basis of current implant geometry, significant population variance is possible, as is inadequate femoral implant fit for some patients with today's implants. Overhang and underhang of metal beyond the bone cut edge (i.e., exposed bone) results from inadequate femoral implant fit in TKA. Excess overhang has been linked to poor patient prognoses including soft-tissue irritation and reduced joint mobility (Mahoney et al., 2010).

An analytical model of the shape of the human knee was developed, upon which a virtual implantation of femoral implants was performed to assess the fit of the implant to the bone (Courtis et al., 2012). Using recent advances in the application of probability through statistical shape modeling, the fit of the implant was based on 1,000 different probable femoral bone shapes generated from an initial population of 76 Caucasian and Japanese subjects. The outer profile of the ATTUNE System implant, in particular the anterior flange and the intercondylar notch, was designed to reduce femoral overhang for the best fit to the patients' anatomy. The improved fit was accomplished by reducing the profile of the anterior flange and utilizing a proportional intercondylar notch across implant sizes.

To minimize overhang and underhang, DePuy Synthes Joint Reconstruction conducted extensive anthropometric research based on a global database with 353 subjects in order to arrive at the unique size offering for the ATTUNE System (Courtis et al., 2012; University
There are 10 standard sizes of femoral and tibial components and 4 narrow femoral component sizes. With the full complement of standard and narrow sizing, the ATTUNE System offers a comprehensive size range to allow the surgeon to meet the specific needs of virtually all patients (Courtis et al., 2012). The number of sizes and the consistent 3mm A-P increment between sizes allows the surgeon to choose a size that is the best fit for an individual patient (Figure 33).

The broad range of ATTUNE System implant sizes offers the surgeon the potential for optimal positioning to match most patients’ natural anatomy. As a result of the ATTUNE System implant shape, the surgeon does not have to compromise on component size, allowing more flexibility with soft-tissue balancing during surgery. The extensive femoral and tibial sizes paired with 1-mm increment insert offering delivers 4,554 potential sizing combinations (DePuy Synthes Joint Reconstruction, data on file).

**Figure 33. Development of the ATTUNE System Femoral Component Sizes**

AP = anterior-posterior; ML = medial-lateral.
Source: University College Dublin; Fitzpatrick, 2012 (data on file).
4.3 Patellofemoral Tracking

Patellar tracking is defined as the motion of the patella relative to the femur or femoral groove during knee flexion and extension (Katchburian et al., 2003). The patellofemoral joint is incongruent, and the patella, a small bone that moves a large amount during knee flexion-extension, is acted upon by powerful muscles that converge from different directions (Amis et al., 2006). Patellar “maltracking” implies that the patella is not following a normal stable path of movement within the femoral trochlear groove when the knee is flexing and extending. Clinically, this might relate to a lateral translation or tilt of the patella, which causes the medial facet to lift off of the trochlea. The relationship between patellofemoral joint stability and maltracking is unclear, but presumably they are related; if the patella is stable in the trochlear groove, then it is difficult to move the patella away from this position (Amis et al., 2006).

The patellofemoral interaction is one of the most studied and challenging aspects of TKA (Amis et al., 2006; Rand, 2004). Research has demonstrated that the best surgical placement of the patella is in a medial aspect relative to the patellar groove (Anglin et al., 2008). Medialization of the patellar articular surface relative to the bony resection has been shown to be consistent with the natural anatomy (Baldwin and House, 2005) and beneficial in reducing patellar complications (Lachiewicz and Soileau, 2006).

Patellar tracking is greatly influenced by the interaction between the articular geometry of the groove and patella (Takahashi et al., 2011). Shalhoub et al. (2012) measured the patellofemoral kinematics during a squat for natural, unresurfaced, and two different patellar implant geometries: a dome and an anatomic shape. Results showed that the anatomical kinematics were similar to the unresurfaced and natural patella, suggesting that resurfacing the patella after TKA with an anatomic implant would result in more similar patellar tracking to the natural patella (Shalhoub et al., 2012). The shape of the ATTUNE System femoral trochlear groove is designed to accommodate both unresurfaced and resurfaced patellae.

The ATTUNE Primary Total Knee System is designed to deliver a high level of patellofemoral function.

The ATTUNE System was designed specifically with patellofemoral function in mind to provide controlled motion and stability (Clary et al., 2012b; Shalhoub et al., 2012; Cyr et al., 2012). The ATTUNE GLIDERIGHT™ Articulation strikes a balance between accommodating the natural soft tissues and also providing the appropriate amount of stability in the implant. For resurfacing, the ATTUNE System offers two designs: a Medialized Dome patellar component and a Medialized Anatomic patellar component.

The ATTUNE System Medialized Dome patellar component is designed with a 3mm medialized dome to ensure tracking without sacrificing coverage (Figure 34). This design enables the apex of the patellar implant to be medialized in alignment with the native
anatomy without creating exposed lateral patella bone, which can painfully impinge on the femoral component. As a result of this medialization and subsequent bone coverage, there is a better chance that the implant will go through full range of motion with good articulation and tracking while reducing anterior knee pain due to impingement.

**Figure 34. The ATTUNE System Medialized Dome**

Recent research indicates that patellar component medialization potentially reduces strain in the lateral patellofemoral ligament, improving patellar tracking and reducing the risk of lateral release (Anglin et al., 2008; Clary et al., 2012c). Clary et al. (2012b) demonstrated in a cadaveric study that the medialized apex of the ATTUNE System patellar component improves patellar tracking while maintaining good bone coverage (Clary et al., 2012b).

Patellofemoral complications, such as patellar maltracking, subluxation, dislocation, and implant failure, have been linked to femoral and patellar component alignment. Fitzpatrick et al. (2011) assessed how sensitive three patellar component designs were to patient and surgical alignment parameters. The medialized dome yielded substantially reduced patellar ML contact force when compared with a standard dome. The medialized dome component provides a robust solution for consistent patellar tracking despite patient and surgical variability, whereas the anatomic patellar component provides more natural patellofemoral kinematics and reduced patellofemoral contact pressures (Fitzpatrick et al., 2011).

The ATTUNE System femoral component accommodates the quadriceps-angle (Q-angle) to promote patellar tracking. The Q-angle is formed in the frontal plane by two line segments: one from the tibial tubercle to the middle of the patella and the other from the middle of the patella to the anterior superior iliac spine (ASIS) (Figure 35). The Q-angle of the patient combined with proper tracking of the patellar implant along the patellar groove correlates with the patient’s natural stature (Bellemans et al., 2010; Blaha et al., 2009; Merchant et al., 2008). For example, a 5’-4” female with a templated size 4 native knee will have a 12.5°
groove angle, and a 6’4” female with templated size 8 native knee will have an 11° angle. The ATTUNE System was designed with a size-specific trochlear angle for each different component size based on patient stature and the appropriate Q-angle for each size femoral component (Figure 35).

**Figure 35. Quadriceps Angle**

![Quadriceps Angle Diagram](image)

ASIS = anterior superior iliac spine; Q-angle = quadriceps angle.

Based on the anthropometric study (Fitzpatrick et al., 2012a), the ATTUNE System patellar groove was designed to match the angle of the patellar groove to the Q-angle of patients for 10 different statures. The ATTUNE System patellar component tracks relative to each implant size and relative to the stature of 10 typical patients. The ATTUNE System femoral component is designed to articulate with the natural patella, as well as with a resurfaced patella. The medialized dome and medialized anatomic patellar components are designed to provide proper resected bone coverage and encourage proper tracking. DePuy Synthes Joint Reconstruction studied the shape of the natural patella to create the medialized dome and anatomic implant geometry (i.e., how much medialization and the coronal cross-section). Because the implant emulates the shape of the natural patella, the trochlea could be designed to articulate with both unresurfaced and resurfaced patellae.

The angled anatomic groove on the femoral component has less prominent medial and lateral shoulders, providing less strain on the parapatellar and capsular tissues. The femoral trochlear groove, from 0° to 45°, acts as a funnel to aid in a smooth transition from extension to flexion and control lateral tracking. This funneling effect aids in early flexion stability. In addition, the shape of the anterior flange is designed to reduce the incidence of soft-tissue impingement (DePuy Synthes Joint Reconstruction, EN-075 [data on file]).

The shape of the ATTUNE System femoral component is designed to complement the patient’s natural anatomy. These shapes are designed to reduce patient soft-tissue discomfort. The ATTUNE System femoral components utilize proportional intercondylar spacing and posterior condyle height for optimal bone coverage and improved articulation in high flexion.

Computational modelling was performed simulating a deep knee bend to assess the influence of the femoral shape on the contact mechanics of the patellofemoral joint (i.e., kinematics, contact pressure, and contact area). The shape of the ATTUNE System trochlear geometry was designed to articulate with the unresurfaced patella based on the clinically successful lineage.
of the LCS implant system (DePuy Synthes Joint Reconstruction, Warsaw, IN). The shape of the ATTUNE System trochlear geometry results in lower contact pressure and higher contact area between the femoral component and unresurfaced patella than previous designs (Deacy et al., 2012). Implant design does influence unresurfaced patellofemoral mechanics in early and mid-flexion; however, the soft-hard bearing surface increases patellar contact pressures compared with the natural knee, even with perfectly anatomic geometry (Deacy et al., 2012).

In the ATTUNE System PS component, the box and spine width changes proportionally per implant size to allow for conservation of good bone (Figure 36). By reducing the width of the intracondylar box, blending trochlea edge, and extending the length of the trochlear groove, factors that could lead to patellar clunk have been reduced (Figure 36).

**Figure 36.** The ATTUNE System Posterior Stabilized Proportional Box/Spine

A.

Blend trochlea edge

B.

Extend trochlea

C.

Proportional box / spine
4.4 Durability

Product design (geometry of implants and component interaction) and polyethylene performance are the major drivers in durability of TKA devices.

4.4.1 Design

The ATTUNE System is designed to achieve optimal articulation between component interfaces. The ATTUNE System patented fixed-bearing LOGICLOCK Tibial Base allows independent femoral and tibial sizing to achieve optimal tibiofemoral articulation.

The shape and design of the femoral component are critical factors in the survivorship of a knee implant (Whiteside and Nakamura, 2003). Specifically, the ATTUNE System PS component is designed to maintain a low contact position between the cam and spine during deep flexion, reducing the forces on the locking mechanism and tibial fixation. In the ATTUNE System PS design, after initial contact, the cam moves low on the spine and stays low, transferring forces down through the center of the insert and delivering controlled and stable cam-and-spine interaction during flexion (Figure 37) (Fitzpatrick et al., 2012b). This results in controlled motion and reduced force transmission between implant and bone fixation (Insall et al., 1982).

Figure 37. Posterior Stabilized Articulation Surface

Fixation is critical in knee arthroplasty, and the ATTUNE System incorporates new research to help achieve better initial fixation (DePuy Synthes Joint Reconstruction, WR090235 [data on file]). On the femoral implant, the cement pockets on the posterior condyles are angled to provide additional pressurization of the bone cement to aid in better bone cement interdigitation and a tighter bond.

Additional fixation design is built into the femoral lugs. Although relatively simple in concept, the shape and length of the femoral lugs are designed to increase initial fixation. Femoral lugs add a level of fixation and early stability, but all lugs are not alike. DePuy Synthes Joint Reconstruction tested nearly a dozen different shapes and sizes to determine the best possible design for the ATTUNE System.

To address aseptic loosening, a leading cause of failure in TKA (Aglietti et al., 2005; Callaghan et al., 2004), the underside of the base plate was designed with a surface finish to accommodate better fixation of initial bone cement to the tibial base (DePuy Synthes Joint Reconstruction, WR090235 [data on file]). Changing the surface finish, combined with new technology to treat the underside of the implant, increases the force required to pull out the base plate.

4.4.2 Polyethylene Performance

Polyethylene performance in TKA is generally measured by wear resistance, oxidative stability, and mechanical integrity (Figure 38). Wear resistance is very important, as improved wear properties can lead to improved survivorship of the implant. Oxidative stability refers to the ability of a material to resist oxidation. If oxygen has the opportunity to react with
free radicals (which can be present in polyethylene sterilized with gamma irradiation), the material will degrade (Currier et al., 2012). Finally, mechanical integrity is important, as mechanical strength and toughness have a direct impact on the durability of the material.

The manufacturing process used to make polyethylene implants has a dramatic effect on the characteristics of the resulting material. A change in the manufacturing process typically has an effect on more than one of the properties described above.

**Figure 38. Polyethylene Performance Requires a Balance of Wear Resistance, Oxidative Stability, and Mechanical Integrity**

The ATTUNE Primary Total Knee System is designed to increase durability.

**4.4.3 The AOX Advantage**

It is well accepted within the orthopaedic community that gamma irradiation of polyethylene has additional benefits aside from sterilization. Irradiation breaks the molecular bonds, which then promotes cross-linking. Cross-linking dramatically improves the wear resistance of polyethylene by improving its resistance to surface orientation (see the purple line in Figure 39). This is especially important in fixed-bearing knees given the multidirectional motion that occurs on the articulation surface of the insert.

**Figure 39. The Relationship Between Increasing Irradiation Dose and Cross Linking**
However, although an increased gamma irradiation dose increases the wear resistance of the material, it also decreases the mechanical integrity (see the green line in Figure 39). The optimal irradiation dose is one that strikes the perfect balance of providing good wear resistance with minimal impact to mechanical properties.

In addition, gamma irradiation creates free radicals that, if unaddressed, can lead to oxidation and degradation of the polyethylene and a subsequent decrease in survivorship of the implant. There are many manufacturing processes to address free radicals generated by gamma irradiation. Common practices include the following:

- **Barrier packaging** was designed to prevent oxygen from entering the package, allowing the material to maintain oxidative stability while on the shelf. During this time, recombination and/or cross-linking of the broken molecular bonds is encouraged due to the lack of oxygen. However, once the package is opened, any remaining free radicals are exposed and may combine with oxygen throughout the life of the implant.

- **Remelting** is a heat treatment that brings the material above its crystalline melting temperature. This process has been found to eliminate all free radicals by providing them with enough energy to mobilize, recombine, and/or cross-link. However, there is a small loss of mechanical integrity associated with this process. The majority of manufacturers utilize this process because the resulting mechanical properties are well above American Society for Testing and Materials (ASTM) standards. Because the free radicals are eliminated, oxidation is less likely to occur, providing the confidence that mechanical integrity will remain constant over the life of the implant.

- **Annealing** is a heat treatment that brings the material to a temperature just under its melting temperature. The annealing process provides increased thermal energy resulting in increased molecular motion. The increased motion of the polymer chains helps promote additional reactions between free radicals. However, because the crystalline regions have not melted, the polymer chains do not have unrestricted mobility, and, thus, all of the free radicals are not eliminated. Because the material is not subjected to its crystalline melting temperature, their effect on the material’s mechanical integrity is minimized. However, because free radicals still exist within the material, oxidation may occur over time, which results in a decrease of mechanical integrity (Currier et al., 2012).

- **Doping agents** are now considered the fourth generation of polyethylene materials. The evolution of this next generation is driven by the need to retain the crystalline properties while preserving the oxidative stability of the molecular chains upon irradiation. The doping agent used to date is antioxidants, which neutralize the free radicals created during gamma irradiation without the need for a heat treatment (annealing or remelting). The elimination of a heat treatment reduces the decrease in mechanical properties as seen with both remelting and annealing.

The ATTUNE System is only available with the most advanced AOX polyethylene technology from DePuy Synthes Joint Reconstruction. The fourth-generation material with proprietary synthetic antioxidant COVERNOX™ provides a balance of wear resistance, mechanical integrity, and oxidative stability. These material properties have been tested throughout development, and the biocompatibility, extraction, and distribution of COVERNOX have been evaluated (King et al., 2012a; King et al., 2012b).

AOX polyethylene has high oxidative stability. AOX polyethylene utilizes fourth-generation polyethylene material and the antioxidant doping agent COVERNOX, which is a proprietary synthetic antioxidant material. COVERNOX material is solid at room and body temperature, which permits the dispersion of the antioxidant into GUR 1020 polyethylene powder; this ensures the antioxidant is universally blended throughout the material. COVERNOX stabilizes the free radicals created during gamma irradiation.
A two-part study was conducted to evaluate the effects of antioxidant content, radiation dose, accelerated aging, and physical form on biocompatibility of polyethylene (King et al., 2012a). The screening biocompatibility tests showed that the combination of COVERNOX (fourfold excess) and gamma irradiation (up to 100 Kgy) does not induce any adverse biological response. The screening biocompatibility tests also showed that accelerated-aged AOX does not induce any adverse biological response, nor does irradiated AOX powder (to simulate wear debris) induce any adverse biological response. The comprehensive biocompatibility study of AOX polyethylene demonstrated no evidence of any adverse effects when used as an implant material in various preclinical settings (King et al., 2012a).

Testing was done to characterize the physical and mechanical properties as well as the oxidative stability of AOX polyethylene. AOX polyethylene demonstrated long-term oxidative stability and improved mechanical properties and fatigue resistance relative to remelted polyethylene (King et al., 2012b).

Spectroscopic analysis was conducted to verify the concentration and uniformity of distribution of COVERNOX, both in powder and molded forms. COVERNOX material was uniformly distributed throughout AOX polyethylene both in powder and compression molded sheet form (Senyurt et al., 2012).

Aggressive extraction conditions were employed to confirm the low extractability of COVERNOX from AOX. AOX demonstrated long-term migration/elution resistance of the antioxidant COVERNOX (King et al., 2012c).

4.4.4 Wear Testing

Total knee arthroplasty wear testing, using experimental and computational methods, is a key stage in the preclinical analysis of new implant designs. Wear simulator testing was conducted and compared between implant designs.

In vitro wear testing of the ATTUNE System CR fixed-bearing design with AOX polyethylene and the SIGMA CR fixed-bearing system with XLK polyethylene was conducted under specific laboratory conditions. The ATTUNE System wore 50% less than the clinically successful SIGMA knee system. As such, the wear rate for the ATTUNE System provides further improvement upon clinical standards of modern fixed-bearing designs and materials. This significantly reduced wear rate is primarily the effect of design, as the different sagittal curvatures create distinctly different contact kinematics. Also, AOX polyethylene was developed to have wear properties similar to those of XLK.
Computational simulations of high-demand wear tests also were developed to assess the relevant metrics of implant design and resulting kinematics, which contribute to the implant’s overall wear rate. The articular geometry of the ATTUNE System is designed to be resistant to wear mechanisms during high-demand activities such as going up and down stairs. The stability provided by the articular geometry of the ATTUNE System is designed to reduce sliding and cross shear, relative to other design geometries (Strickland and Taylor, 2012) (Figure 41).
A major concern in the use of modular knee implants has been particle generation from the backside of the UHMWPE tibial insert. Motion of the tibial insert against the proximal tibial base, commonly referred to as micromotion, can generate microscopic particles that with time can propagate throughout the joint and lead to osteolysis, a condition that can promote bone resorption and, finally, implant loosening. The ATTUNE System fixed-bearing locking mechanism features a LOGICLOCK Tibial Base that resists motion of the insert regardless of the direction of the forces. It further reduces backside motion and wear compared with existing DePuy Synthes Joint Reconstruction and competitive designs (Figure 42) (Leisinger et al., 2011).

**Figure 42. The ATTUNE System Exhibits Lower Micromotion**

\[ R = (AP^2 + ML^2)^{0.5} \]

Source: Leisinger et al., 2011 (ISTA).
4.5 Efficiency of Care

Total knee arthroplasty procedures are complex and can be inefficient compared with other joint arthroplasty procedures given the complexity, number, weight, and cost of surgical instruments used. Currently, the multiple trays and heavy instrument cases that are required for a TKA surgery can make the procedure complicated and can increase the time required to learn appropriate use and handling of the instruments. This “learning curve” can result in longer OR times and higher costs. Instruments that reduce surgical steps, reduce the physical burden on the OR team, and reduce the overall cost of a total knee procedure are necessary in the current surgical environment.

The ATTUNE Primary Total Knee System is designed to enable efficiency in the operating room.

The development process for the ATTUNE System included a dedicated team to research and understand the role of instrumentation in TKA. This research led to a new appreciation of the effect of instrumentation on patient outcomes. Surgeons use TKA instruments as tools to position the implant. Implant positioning may affect outcomes such as stability, range of motion, and, ultimately, patient satisfaction. Moreover, hospital systems are facing pressure to increase efficiency and reduce costs. These factors create challenges and opportunities for advancement in TKA instrumentation.

DePuy Synthes Joint Reconstruction set out to create a new set of innovative tools based on these unmet needs, which required a new way of thinking about instrument design. A team of external partners and orthopaedic surgeons was assembled to provide perspective on the design and usability of the instruments. The team approached the development process first by describing the value the instruments should provide and then creating design criteria based on accuracy, robustness, and usability. Hundreds of design iterations were manufactured for use in cadavers by surgeons on and external to the design team. In addition, the instruments were tested and validated in their ability to meet the design criteria. Ease of manufacture, packaging, delivery cases, storage, and sterilization also were addressed.

The ATTUNE INTUITION™ Instrumentation combines the surgical process with intuitive and efficient instruments to allow the surgeon to balance the soft tissue and precisely control the implant position and fit for each patient.

The ATTUNE inTuiTion™ instrumentation is unique in its ability to combine the surgical process with implant options to allow the surgeon to balance the soft tissue and precisely control the implant position and fit for each patient. The instruments are designed to be intuitive to use and to reduce steps throughout the surgical process, providing efficiency to the entire OR team.

In order to allow the OR team to remain focused on the patient, orthopaedic instruments should provide clear and accurate information to reduce confusion and shorten the learning curve. Design features including red actuators, high-contrast markings, and quick set/release functions make ATTUNE inTuiTion instruments clear and easy to use from the moment the user picks them up. An intuitive, highly visible, color-coded identification system has been used to improve visual clarity (Figure 43). The ergonomics of the instruments have been
developed to deliver better surgeon satisfaction (the instruments “feel good” and are well balanced in the surgeon’s hand). Surgeon touch points are color-coded and easy to see, removing much of the complexity currently experienced with traditional instruments.

**Figure 43. The ATTUNE System Instruments Are Designed for Visual Clarity**

The instrument designs incorporate advanced composite materials, which reduce weight and therefore minimize number of cases in the OR, while maintaining instrument durability (Figure 44). With the inclusion of advanced glass-filled, highly engineered polymers, the INTUITION Instrument weight was reduced by 49% as compared with current instrumentation. This reduction was designed to help hospitals comply with safety requirements around manual handling of heavy objects (Innovia Technology, 2010). By minimizing the number of instruments and instrument trays, the effort and cost associated with the management of instruments are reduced (Health and Safety Executive, 2011).

INTUITION Instruments combine intuitive designs that are easy to learn and reduce steps, contributing to a more efficient procedure. An intuitive user interface provides ease-of-use, a reduced learning curve, and improved OR team experience (Figure 43). Single-layer instrument cases, light weight, and fewer instruments are just a few efficiencies that reduce the hospital team’s effort from start to finish. The ATTUNE System includes multipurpose instruments, allowing for more efficient use through reduction in the number of single-purpose instruments (Figure 45). The total number of instruments required to carry out all of the common surgical steps has been reduced. Further, the instruments have been designed to be easy to clean in an effort to reduce the risk of contaminated instruments.

**Figure 44. Efficient Path Through Polymer Shimming**
Figure 45. The ATTUNE System Includes Multipurpose Instruments

Figure 46. Precise Control for Intraoperative Flexibility

Ability to shift femoral component 1.5mm anterior or posterior
OVERVIEW OF THE ATTUNE CLINICAL EVIDENCE DEVELOPMENT PROGRAM

The ATTUNE System has met all US and European Union (EU) regulatory requirements for marketing. Specifically, the ATTUNE System has been extensively tested in vitro (Section 4). In vitro testing forms the basis of the US Food and Drug Administration (FDA) regulatory clearance for the ATTUNE System (Appendix B). DePuy Synthes Joint Reconstruction has recently applied for extensive patent protection in countries throughout the world for the ATTUNE System implants, instruments, and surgical methods. In the US alone, as of this writing, there are already seven patents granted for key inventions related to the ATTUNE System implants.

The ATTUNE System was designed with input from 35 design surgeons around the globe. These varied perspectives during design were essential in ensuring that the ATTUNE System would be designed for the needs of all patients regardless of age, gender, ethnicity, or geographic region.

DePuy Synthes Joint Reconstruction is closely monitoring the initial experience with the ATTUNE System. Specifically, early implant performance data are being collected on 1,200 implants (300 for each of the four configurations: CR fixed bearing, CR rotating platform, PS fixed bearing, PS rotating platform). The early performance data focus on patient safety. This early performance assessment also assesses surgeons’ learning curve associated with the ATTUNE System and its instruments. Through careful evaluation of these data, DePuy Synthes Joint Reconstruction can better educate investigators and surgeons and provide any other clarifications required during commercial launch.

5.1 Clinical Development Studies

In vitro experimental and computational simulations are critical preclinical tools in the evaluation of new implant designs. The ATTUNE System has undergone extensive in vitro evaluations for the following:

- Tibiofemoral kinematics
- Patellofemoral kinematics
- Oxidation and wear studies
- Durability (fixation surface)
- Anatomical variation (improved sizing)

Findings from these studies are presented in Section 4.

In addition to the in vitro and computational simulation evidence, the ATTUNE System will be extensively studied in more than 2,300 knees in several in vivo studies, as outlined in Table 10. Further experience with the ATTUNE System will be captured in the national joint replacement registries for countries such as Australia, Sweden, and the UK.

In addition to collecting information on the ATTUNE Knee System performance, DePuy Synthes Joint Reconstruction was interested in learning about patient’s experiences with the ATTUNE System. Qualitative in-depth telephone interviews were conducted with 20 patients who recently had undergone TKA surgery with an ATTUNE System knee implant.
(i.e., CR knee and PS knee). Patients were recruited through six surgeons who were part of the ATTUNE System design team; these surgeons provided a flyer about the study to ATTUNE patients at their 6-week follow-up visit. Interested patients elected to contact an independent health care consulting firm (The Dominion Group) to schedule their interview. Patients were required to complete a consent form prior to participation in the interviews. Interviews were conducted by The Dominion Group and were 30-45 minutes in duration.

Based on the interviews, pain and function were the issues of greatest concern to these TKA patients. The decision to move forward with knee arthroplasty was primarily driven by pain; patients often reported that they were looking forward to surgery to achieve pain relief. Postsurgery, the focus shifted to returning to “normal” activities. Patients reported being highly satisfied with their ATTUNE System knee. Patients reported fast pain resolution and fast return to function. In addition, among those who had previous TKA (n = 9), following TKA with the ATTUNE System, patients reported that experiences with the ATTUNE System included faster pain resolution and less need for pain medications, as well as faster recovery and faster return to function and work.

While the information collected in this market research activity is qualitative in nature and limited to a small number of respondents, the data suggest that the patented technology and advanced materials of the ATTUNE System provided patient benefit to this group of patients.

### Table 10. In Vivo Study Plans for the ATTUNE System

<table>
<thead>
<tr>
<th>Evidence</th>
<th>Study</th>
<th>Objective</th>
<th>Anticipated Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Functional</td>
<td>10004: PROs on ATTUNE System knees</td>
<td>Primary TKA functional performance: a prospective, single-arm, stratified, longitudinal, multicenter worldwide investigation</td>
<td></td>
</tr>
<tr>
<td>Durability</td>
<td>10008: Primary long term survivorship (15 years)</td>
<td>Primary TKA survivorship of the ATTUNE System</td>
<td></td>
</tr>
</tbody>
</table>

CR = Cruciate Retaining; PRO = patient-reported outcome; PS = Posterior Stabilized; TKA = total knee arthroplasty.

In addition to the studies described previously, DePuy Synthes Joint Reconstruction has an Investigator Initiated Study (IIS) Program. This program is intended to complement the company-initiated studies. The IIS studies will be identified via an active pathway and a passive pathway. The active approach will utilize a Request for Proposal approach, which will allow DePuy Synthes Joint Reconstruction to competitively assess proposals that are consistent with defined evidence needs. This active approach is intended to be the preferred mechanism for IIS identification. The passive approach is one where investigators submit unsolicited ideas for funding consideration. All IIS proposals are reviewed by a cross-functional team for scientific merit, business need, resource requirements, timing of evidence delivery, and health care compliance.
5.2 Patient's Knee Implant Performance Scale

The goal of TKA, like the goal of THA, is to reduce joint pain, increase range of motion, and improve function (Halket et al., 2010). Clinicians and patients generally have the misconception that THA and TKA have similar recovery patterns (O’Brien et al., 2009). However, evidence shows that patients undergoing TKA actually experience significantly smaller improvements in postoperative pain and function compared with patients undergoing THA (O’Brien et al., 2009; Bourne et al., 2010; March et al., 1999).

Both patients and clinicians increasingly identify that the objective of TKA is to closely approximate with a prosthesis the feel and function of a healthy knee that has never undergone surgery (Morra et al., 2008). As such, another important aspect of the discrepancy in THA and TKA outcomes is that THA patients can “forget” about their prosthesis following surgery, whereas TKA patients are aware of the prosthesis (Behrend et al., 2012).

Postsurgical knee motion is typically assessed via gait analysis and/or kinematic studies (Fantozzi et al., 2003). Key learnings from biomechanical analyses highlight that the knee motion of the three main implant components (femoral component, tibial component, and patellar component) do not routinely follow patterns similar to normal knees and also exhibit increased variability (Leszko et al., 2010; Dennis et al., 2003a; Dennis et al., 2003b; Dennis et al., 2004). The altered biomechanics after TKA, particularly with higher knee flexion activities such as deep knee bends and stair ascent/descent, are thought to contribute to why knee patients are not as satisfied with their implanted joints compared with hip patients and also compared with their nonimplanted knee. Further, the observed suboptimal biomechanics pose greater challenges, as knee patients have their surgery at younger ages (AAOS, 2012) and have high functional expectations. Although these biomechanical analyses are sensitive and quantitative measurement tools, they are typically done on small sample sizes, and the actual results are very technical and may not resonate with all stakeholders, particularly patients.

Currently, no patient-reported measure is available to assess patients’ perception of their biomechanics. Although a variety of knee-specific instruments currently exist (e.g., WOMAC, KOOS, OKS), no PRO measure correlates function with improved stability, motion, satisfaction, and confidence. Lewis et al. (2012) developed a conceptual model linking the impact of clinical mechanics to hypothesized functional outcomes following a literature review of available assessment tools. Focus groups with patients who had undergone a TKA within the past 10 to 18 months indicated that the concepts of confidence, stability, and satisfaction in their replacement knee when performing activities requiring certain motions were felt to be distinct from one another and important in the patients’ assessment of their TKA. Subsequent in-depth interviews with patients resulted in the development of an assessment for the Patient’s Knee Implant Performance (PKIP). The PKIP items assess the broader concepts of stability, confidence, and satisfaction in association with activities.

The PKIP is included in the large prospective 2-year study of all four configurations of ATTUNE System implants.
REFERENCES


Fitzpatrick CK, Clary CW, Rullkoetter PJ. Post-cam engagement during dynamic activity with current posterior stabilized TKR. Presented at the European Society of Biomechanics 18th Congress; July 1-4, 2012b. Lisbon, Portugal.


Insall JN, Lachiewicz PF, Burstein AH. The posterior stabilized condylar prosthesis, a modification of the total condylar design. J Bone Joint Surg Am. 1982;64(9):1317-23.


Sathasivam S, Walker PS. The conflicting requirements of laxity and conformity in total knee replacement, J Biomechanics;1999;32:239-47.

Rossignol M. Primary osteoarthritis and occupation in the Quebec national health and social survey. Occup Environ Med. 2004 Sep;61(9):729-35.


Swanson SC. Shifting the sterile processing department paradigm: A mandate for change. AORN J 2008;88:241-7.


APPENDIX A:
FUNDAMENTALS OF TOTAL KNEE ARTHROPLASTY

The knee is the largest and strongest joint in the body. The knee joint is where the lower end of the femur meets the upper end of the tibia. The patella sits in front of the joint, and is vital in the flexor mechanism (transmitting force around a corner [i.e., pulley] and creating mechanical advantage [i.e., lever]). When the knee is healthy, the lower leg can flex and extend and rotate slightly in flexion (see Figure A-1). Ligaments and cartilage stabilize and support the joint and musculature.

Figure A-1. Knee (A) in Extension and (B) in Flexion

The knee is often referred to as a “hinge” joint because of its ability to bend and straighten, but its mechanisms are much more complex than a hinge because the bone surfaces roll, glide, and rotate as the knee bends. Newer implant designs now more closely mimic the motion of a normal knee (American Academy of Orthopaedic Surgeons [AAOS], 2011).

During knee arthroplasty, an orthopaedic surgeon replaces the damaged knee with an artificial device (implant). Implants may be made of metal alloys, ceramic materials, and medical grade plastics. Implants can be attached to the bone by acrylic bone cement or biologic fixation, where new bone itself secures the implant in place.

Knee Implant Components

In total knee arthroplasty (TKA), up to three bone surfaces may be replaced (Figure A-2 and Figure A-3):

- The lower end of the femur. The metal femoral component curves around the end of the femur and is grooved so that the patella can move up and down smoothly against the implant as the knee flexes and extends.
- The upper surface of the tibia. The tibial component typically has a metal base plate with a modular bearing called a tibial insert made of a strong, durable, medical-grade plastic such as ultra-high-molecular-weight polyethylene (UHMWPE).
- The back surface of the patella. The patellar component also is made of medical grade polyethylene and is designed to replace the articular surface of the patella and track along the corresponding groove of the femoral component.
Components are designed so that the femoral and tibial components have contact with the polyethylene to provide smooth movement and minimize wear.

**Figure A-2. Mediolateral Fit of the Femur**

![Mediolateral Fit of the Femur](image)


**Figure A-3. Anteroposterior Fit of the Femur**

![Anteroposterior Fit of the Femur](image)


### Knee Implant Materials

The parts of a knee implant are typically made of titanium or cobalt-chromium-based alloys and UHMWPE.

**Material Criteria**

The materials used in an implant must meet several criteria:
• They must be biocompatible; that is, they can be placed in the body without creating an adverse immune response.
• They must be strong enough to support weightbearing loads, flexible enough to bear stress without breaking under repeated loading, and able to move smoothly against other components of the implant as required.
• They must be able to retain their strength and shape for a long time.
• They must be able to be formed into appropriate shapes to take the place of the bone that is removed during TKA.
• They must be available in range of sizes to meet the spectrum of patients’ anatomies.
• For metallic components, all surfaces that contact polyethylene should be highly polished to reduce wear (DePuy Synthes Joint Reconstruction, Rotating Platform value dossier, 2011 [data on file]).
• Polyethylene components need to have good wear resistance, toughness, and resistance to long-term degradation (oxidation) in the body (Collier et al., 2005; Leisinger et al., 2008).

Cemented and Cementless Implants
Two types of fixation methods are used in TKA:
• Cemented fixation uses a fast-curing bone cement (polymethylmethacrylate).
• In cementless implants, the surface that is adjacent to the bone is typically textured or covered with a porous metallic coating to provide initial primary fixation, into which new bone grows to provide long-term secondary fixation.

Cruciate Retaining Designs
This implant design retains the posterior cruciate ligament (PCL) to stabilize the knee during flexion. Cruciate Retaining (CR) implants do not have the center post-and-cam design. This implant may be appropriate for a patient whose PCL is sufficiently healthy to continue stabilizing the knee joint.

Posterior Stabilized Designs
In Posterior Stabilized (PS) designs, the PCL is excised and its function is replaced by a post-and-cam mechanism to stabilize the knee during flexion.

Appendix A References
APPENDIX B: PRODUCT DESCRIPTION

Classification and Clearance/Approval

Table B-1 presents the US and Conformité Européenne (CE) approval dates for the various configurations of the ATTUNE System and instrumentation.

Table B-1. ATTUNE System Regulatory Approval Dates

<table>
<thead>
<tr>
<th>Configuration</th>
<th>US Clearance Date</th>
<th>CE Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fixed Bearing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cruciate Retaining</td>
<td>December 10, 2010</td>
<td>September 28, 2011</td>
</tr>
<tr>
<td>Posterior Stabilized</td>
<td>August 30, 2011</td>
<td>September 28, 2011</td>
</tr>
</tbody>
</table>

CE = Conformité Européenne; US = United States.

Indication

The ATTUNE System is intended for cemented use as a total knee replacement system. Candidates for TKA include patients with a severely painful and/or severely disabled joint resulting from osteoarthritis (OA), posttraumatic arthritis, rheumatoid arthritis, or a failed previous implant.