Attune®
Knee System

Confidence in the ATTUNE® Knee is Driven by Real World Scientific Evidence: Response to Bonutti, et al. Article[1]

Dear Clinician, June 14, 2017

On June 7, 2017, The Journal of Knee Surgery published an article titled, "Unusually High Rate of Early Failure of Tibial Component in ATTUNE Total Knee Arthroplasty System at Implant–Cement Interface," raising questions regarding the performance of the ATTUNE® Knee Tibial Base.[1]

At DePuy Synthes our primary goal is to provide surgeons and patients with products that meet the safety and efficacy requirements of the relevant health authorities as well as our own internal requirements. For that reason, we remain vigilant in detecting any safety and performance signals related to our products. We take the conclusions of this article very seriously. We recognize that published and peer reviewed scientific literature is necessary for the growth of orthopaedic science. However, this literature should be scrutinized for accuracy and reliability and evaluated in relation to all available data. It is only when the information in its entirety is analyzed that a scientifically sound conclusion can be derived.

This response includes our assessment of statements in the article, as well as provides a summary of the broader published clinical and registry data supporting the performance of the ATTUNE Knee System. Contact information for our medical affairs team is included at the end and we welcome any comments or questions.

Article Assessment

In our assessment, there are several aspects of the Bonutti, et al. article that we believe are inaccurate. There are also some limitations:

- The title of the article is misleading as it suggests there is a failure "rate" included in the article. However, a rate calculation is not provided. Although the number of revisions in the article is stated as 15 (numerator), there is no information regarding the number of ATTUNE Knee implants performed in total (denominator), thus a rate cannot be determined.
- The authors state that aseptic loosening is a rare presentation for early total knee revision. An abundance of literature demonstrates that infection is the most common cause of revision, followed by aseptic loosening as the second most common cause of revision in the first two years post-operatively.[13,19] After two years, aseptic loosening becomes the most frequent cause of revision for the rest of the implant life and is the most common cause overall.[10]
- The authors note that when the implant was extracted there was no bone cement attached to the tibial base at the time of revision surgery. This has been previously observed and reported for some other tibial base plates in other studies.[5,7,9] Some published studies have indicated that fixation strength as determined by pull off force has been shown to be independent of and not correlated to whether the fixation fails at the bone/cement or cement/interface junction.[15]
- The mean BMI reported in the article is 35 kg/m^2 (range 21-54). In the class of TKA, increased BMI over 35 has been associated with early aseptic loosening of the tibial component.[2,14] A mean BMI of 35 in this article would indicate that about half of the 15 patients had a BMI greater than 35 and consequently would have increased risk for revision.
- The article is a retrospective study with no control. There are multiple confounding factors that were not accounted for including, but not limited to, the type of cement, surgical technique, post-operative protocol.
- The article indicates that radiographs of the 15 patients were examined and that two had signs of tibial loosening. There is no description of radiographic technique or positioning included. Routine x-rays are not inherently

accurate in diagnosing aseptic tibial loosening as it is dependent on the variability of radiographic technique.[16]

- Included in the article are inaccuracies related to the mechanical hypothesis for the observation of cement debonding from the implant. It is unclear which of the SIGMA® Knee components the authors are using as a comparator, however the information regarding surface roughness is inaccurate.
  - o There is a technical inaccuracy in the article regarding the relationship between grit blast and surface roughness. It should be clarified that the higher the grit number, the smoother the surface.
  - o The SIGMA Knee Fixed Bearing Tibial Base has a 220-glass bead blasted finish, which is the smoothest in the SIGMA Knee portfolio.
  - o The SIGMA MBT Tibial Base is a 20 grit blast and the ATTUNE Knee is 60 grit blasted.
  - o The measured R_A Range (a scientifically determined measurement of average roughness) between 20 and 60 grit blast overlap significantly.
- The authors quote the MAUDE database information in the article. This use of the MAUDE database conflicts with the intent of the database and FDA guidance. The FDA's guidance is that, "MDR data alone cannot be used to establish rates of events, evaluate a change in event rates over time or compare event rates between devices. The number of reports cannot be interpreted or used in isolation to reach conclusions about the existence, severity, or frequency of problems associated with devices."[6]
- The information contained in MAUDE database is self-reported by manufacturers and each manufacturer may use a different reporting criteria. For reportable incidents, DePuy Synthes Companies submits MDRs to cover each component. For example, for one revision, DePuy Synthes Companies may submit five MDRs because a separate MDR is submitted for each associated component – femoral, tibial, insert, patella and cement.
- A rate determination requires both a numerator and a denominator. The MAUDE database reports the number of events observed, the numerator, but does not report on the number of opportunities for the event to occur, the denominator. The rate of an event's occurrence cannot be determined in the MAUDE database.
- The authors note that these incidences might be underreported, as representatives from other companies cannot report to the MAUDE database. This premise is incorrect as anyone can submit reports to the MAUDE database: manufacturers, importers, device users, facilities and voluntary reporters such as healthcare professionals, patients and consumers.
- DePuy Synthes has self-reported all of the cases presently in the MAUDE database for the ATTUNE Knee, and these cases have been previously reviewed during Post Market Surveillance and Safety activities. No safety signals have been detected from these reviews.

ATTUNE® Knee Clinical and Registry Evidence

The data and evidence on the ATTUNE Knee indicates the following:

- An Implant Summary Report, which is an independent anaysis obtained by DePuy Synthes from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man (NJR) of 10,605 ATTUNE Knee implantations, showed that the cumulative revision rate for the ATTUNE Knee is 1.3% at four years (98.7% implant survivorship at four years), comparing favorably to the 1.9% cumulative revision rate (98.1% implant survivorship at four years) for the overall class of total knee replacement.[11] Of the 10,605 ATTUNE Knees included in the same analysis, 46 required revision.[10,11] Based on a separate analysis within the same Implant Summary Report, it was concluded that 63 ATTUNE Knee revisions would be expected at four years – a difference that was statistically significant ($p<0.05$).[11] The expected number of ATTUNE Knee revisions was calculated by the NJR based on duration of implantation, age group, gender and indications.
- Per the 2016 AOANJRR, in which 4,831 ATTUNE Knees are being tracked (N=3199 CR, N=1632 PS), the ATTUNE Knee estimated cumulative percent revision was 0.5% (ATTUNE Cruciate Retaining Knee), 0.4% (ATTUNE Posterior Stabilized Knee) at one year.[4] This compares favorably to the overall class of cemented total knee arthroplasty (TKA) at one year, which has an estimated cumulative percent revision of 1.0%.[4]
- One year results from two worldwide studies showed improved patient reported outcomes with the ATTUNE Knee compared to other leading knee systems examined in those studies.[17]

- This week at the Canadian Orthopedic Association Annual Meeting, Radiostereometric Analysis (RSA) data was presented by the Canadian RSA Network that showed the ATTUNE Knee tibial base migrated an average of 0.02 mm in the superior-inferior (up and down) direction over 24 months, with an average maximum total point motion of 0.21 mm.[3] This study's 2-year RSA results showed that the ATTUNE Knee tibial base achieved stable fixation by demonstrating average micromotion of 0.17 mm between one and two years.[3] This is consistent with implants that have acceptable revision rates due to aseptic loosening.[12,18]

- A recent poster presentation at the European Federation of National Associations of Orthopedic and Traumatology (EFORT) meeting in Vienna showed biomechanical pull off testing for the ATTUNE Knee, and some predicate and comparative devices. This data indicated that the dry pull off strength of the ATTUNE Knee was consistent to that of the other test devices. This indicates that the mechanical bonding of cement, in distraction for the ATTUNE Knee, is not significantly different than the predicate and comparative devices that were examined under the study test conditions.[8]

The first clinical implantation of the ATTUNE Knee was in November 2011 and to date more than 470,000 patients have been implanted with the ATTUNE Knee. DePuy Synthes, part of the Johnson & Johnson Family of Companies, continues to be vigilant in its post market surveillance of the performance of our implants. The ATTUNE Knee was evaluated prior to commercial introduction through both clinical and pre-clinical analysis and is evaluated on an ongoing basis. The Medical Safety organization continues to review all the information available to the company on the ATTUNE Knee and has determined that currently, there is no safety signal with respect to the ATTUNE Knee Tibial Base.

The comprehensive evidence on the performance of the ATTUNE Knee is available at www.ATTUNEevidence.com (US link) and www.provingthepromise.com (EMEA link), and includes data from registries and clinical studies. For further information please contact the following:

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Table KT9 Cumulative Percent Revision of Primary Total Knee Replacement with Cemented Fixation

Femoral Component	Tibial Component	N Revised	N Total	1 Yr	3 Yrs	5 Yrs	7 Yrs	10 Yrs	15 Yrs
Attune CR	Attune	17	3199	0.5 (0.3, 0.9)					
Attune PS	Attune	7	1632	0.4 (0.2, 0.9)					
Genesis II CR	Genesis II	421	13019	0.9 (0.8, 1.1)	2.4 (2.2, 2.7)	3.1 (2.8, 3.5)	4.0 (3.6, 4.4)	4.3 (3.9, 4.7)	5.6 (4.7, 6.7)
Genesis II PS	Genesis II	518	14812	1.2 (1.1, 1.4)	2.8 (2.6, 3.1)	3.7 (3.4, 4.1)	4.3 (3.9, 4.7)	5.0 (4.5, 5.5)	
Journey Oxinium	Journey	220	3032	1.4 (1.0, 1.9)	4.5 (3.8, 5.3)	6.4 (5.5, 7.4)	8.8 (7.6, 10.0)		
Nexgen CR Flex	Nexgen	254	16286	0.7 (0.6, 0.8)	1.5 (1.3, 1.7)	2.0 (1.8, 2.3)	2.3 (2.0, 2.6)	2.7 (2.2, 3.2)	
Nexgen LPS Flex	Nexgen	838	27014	0.9 (0.8, 1.0)	2.3 (2.1, 2.5)	3.2 (3.0, 3.4)	3.9 (3.6, 4.2)	5.0 (4.7, 5.5)	
PFC Sigma CR	PFC Sigma	277	11461	0.8 (0.7, 1.0)	1.9 (1.6, 2.2)	2.4 (2.1, 2.7)	2.9 (2.5, 3.3)	3.4 (3.0, 3.9)	
PFC Sigma PS	PFC Sigma	241	7167	1.2 (1.0, 1.5)	2.6 (2.2, 3.0)	3.2 (2.7, 3.6)	3.5 (3.1, 4.0)	4.5 (3.9, 5.3)	
Triathlon CR	Triathlon	497	25632	0.8 (0.7, 0.9)	2.1 (1.9, 2.3)	2.6 (2.4, 2.8)	3.0 (2.7, 3.4)	3.8 (3.2, 4.5)	
Triathlon PS	Triathlon	185	5886	1.5 (1.2, 1.8)	3.2 (2.7, 3.7)	4.0 (3.4, 4.6)	4.6 (3.9, 5.3)		
Vanguard CR	Maxim	133	6778	0.6 (0.4, 0.8)	2.2 (1.8, 2.7)	2.8 (2.4, 3.4)	3.3 (2.7, 4.0)		
Vanguard PS	Maxim	166	3500	1.9 (1.5, 2.4)	4.6 (3.9, 5.4)	5.7 (4.9, 6.7)	6.8 (5.7, 8.0)		

Table KT22 Cumulative Percent Revision of Primary Total Knee Replacement by Fixation (Primary Diagnosis OA)

Fixation	N Revised	N Total	1 Yr	3 Yrs	5 Yrs	7 Yrs	10 Yrs	15 Yrs
Cemented	8439	258789	1.0 (0.9, 1.0)	2.6 (2.5, 2.6)	3.4 (3.4, 3.5)	4.2 (4.1, 4.3)	5.1 (5.0, 5.3)	7.3 (6.9, 7.7)
Cementless	4612	103903	1.2 (1.1, 1.3)	3.2 (3.1, 3.3)	4.3 (4.2, 4.4)	5.0 (4.9, 5.2)	6.1 (5.9, 6.3)	8.1 (7.7, 8.6)
Hybrid	3964	119262	0.9 (0.9, 1.0)	2.5 (2.4, 2.6)	3.3 (3.2, 3.5)	3.9 (3.8, 4.1)	4.8 (4.7, 5.0)	6.6 (6.2, 7.0)
TOTAL	17015	481954						

Note: Excluding cementless Genesis Oxinium and Profix Oxinium femoral prostheses

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