



Zimmer®
Longevity®
Highly
Cross-linked
Polyethylene



Clinical Value Dossier

April 9, 2012

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List of Abbreviations

AHRQ	Agency for Healthcare Research and Quality
ASTM	American Society for Testing and Materials
BMI	Body mass index
CT	Computed tomography
CI	Confidence interval
HRQoL	Health-related quality of life
HXLPE	Highly cross-linked polyethylene
ISO	International Standards Organization
IT	Integrated Taper
LDH	Large Diameter Head
MCS	Mental Component Score
MC	Million cycles
NCHS	National Center for Health Statistics
NHDS	National Hospital Discharge Survey
NIDJD	Noninflammatory degenerative joint disease
NIS	Nationwide Inpatient Sample
OA	Osteoarthritis
PCS	Physical Component Score
PE	Polyethylene
QALYs	Quality Adjusted Life-Years
QoL	Quality of life
QWB	Quality of well-being
RSA	Radiostereometric analysis
SF-12	Short-Form 12-Item Health Survey
SF-36	Short-Form 36-Item Health Survey
THA	Total hip arthroplasty
UHMWPE	Ultra-high molecular weight polyethylene
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

Executive Summary

Key Findings

- Total hip arthroplasty (THA) is one of the most effective treatments for osteoarthritis of the hip joint¹² and the frequency of the procedure continues to increase in the US and in Australia, Canada, and many European countries.^{3, 4, 6}
- The number of THA procedures places a significant economic burden on hospitals and national health care systems.^{3, 6, 13, 16, 50}
- *Zimmer Longevity* Highly Cross-Linked Polyethylene (HXLPE) liners have a history of over 10-years of published clinical experience showing the long-term benefits of *Longevity* HXLPE. These studies report improvements in patient-reported outcomes, functional assessments, and quality-of-life measures in a broad population of hip replacement patients.^{20, 32, 38}
- *Zimmer Longevity* HXLPE exhibits a reduction in wear rates of up to 90% compared to conventional polyethylene (PE) in prospective, randomized clinical studies.^{25, 26}
- Rates of osteolysis are up to 92% less for *Longevity* HXLPE than conventional PE.³⁶
- Reduced wear rate of *Longevity* HXLPE is associated with reduction in revision rate as well as lower rates of osteolysis in clinical trials and potentially lower risk of revision surgery over the long term.^{30, 32, 36, 37}
- Nine-year follow-up data from the *Australian National Joint Replacement Registry* found that HXLPE liners are associated with a 25.4% reduced risk of revision surgery in THA patients compared with conventional PE liners.⁴
- Larger femoral heads improve stability, increase range of motion, and reduce the risk of neck-rim impingement in hip bearings; *Zimmer Longevity* HXLPE liners work well over a wide range of femoral head sizes⁴²⁻⁴⁵

Epidemiology

Total hip arthroplasty (THA) is one of the most common and successful types of joint replacement surgery. First introduced in the 1960s, THA is a cost-effective procedure that relieves pain and restores mobility in patients with a range of joint disorders.^{1, 2}

The number of THAs performed has grown substantially over the past two decades.

- Between 1993 and 2009, the annual THA rate in the U.S. increased by 68% to 436,011 procedures.³
- The rate of THA procedures is also increasing outside the U.S., including in Canada, Australia, and many European countries.⁴⁻⁶
- Based on market projections, the rate of primary THA procedures in the U.S. is expected to continue to rise by 3% to 4% annually.⁷
- The aging of the U.S. population will largely drive ongoing demand for THA, as it has been projected that the proportion of the U.S. population aged ≥ 65 years will increase by 36% between 2010 and 2020.^{8, 9}

Patients between the ages of 65 and 84 years make up the largest proportion of THA candidates.^{3, 10} In recent years, however, THA is increasingly performed in younger and more active patients.^{11, 12} This is due to the high success rate of the procedure, as well as improved surgical techniques and biomaterials that allow for improved implant durability.¹⁰

Primary THA accounts for the majority (~60%) of all U.S. reconstructive hip implant procedures; however, rates of revision procedures are also on the rise.⁷

- With increased life expectancy, many patients who undergo hip replacement will outlive the life span of their original prosthetic implant.⁷
- In 2010, revision THA accounted for ~13% of all U.S. reconstructive hip implant procedures.⁷
- The main reasons for THA revision are mechanical loosening due to osteolysis, joint instability/dislocation, and infection.^{12, 13}
- It has been projected that, between 2008 and 2014, the number of U.S. THA revision procedures will increase by ~36%.⁷

Clinical and Humanistic Burden

The clinical and societal burden associated with THA is substantial, and is caused not only by underlying conditions such as osteoarthritis (OA) and eventual surgical hip replacement, but also the need for revision surgery in some patients.

- Revision hip arthroplasty is associated with a higher complication rate and more negative outcomes than primary THA.¹⁴

- In addition, patient function and health-related quality of life (HRQoL) following revision surgery is lower than after primary hip surgery.^{9, 15}

The non-optimal clinical and health-related quality of life outcomes associated with revision procedures suggests strongly that purchasers and clinicians need prosthetic materials that:

- Reduce the risk of osteolysis.
- Reduce the likelihood of implant failure following the primary procedure.
- Ensure the greatest likelihood of revision success without complications.

Economic Burden

Available data indicate that THA, in particular revision THA, imposes a substantial economic burden.³

- In 2009, hospital costs associated with primary total hip replacement procedures were \$15,736, on average. The mean duration of hospitalization for primary THA was 3.5 days.³
- Mean hospital costs associated with revision hip surgery were \$21,390 in 2009, and the average hospital stay was 4.8 days.³
- Rising costs associated with THA have also substantially affected other national health systems outside of the US.^{6, 16}

However, in some circumstances, reimbursement rates for THA procedures have declined over time, particularly for revision arthroplasties. For example, after adjusting for inflation, total Medicare reimbursements for revision THA declined from \$319 million in 1997 to \$244 million in 2003.¹⁴

- It has been estimated that, if the hip revision burden in the U.S. could be reduced by even 1%, the potential national cost savings would range from \$42.5 to \$112.6 million.¹⁰

There is a clear need to lower the THA revision burden by increasing the effectiveness and durability of prosthetic implants used in THA procedures.¹⁵ Specifically, improvements in the manufacture of prosthetic components for THA, including the development of highly cross-linked polyethylene (HXLPE) acetabular components, have had a positive impact on prosthesis durability, and have been shown to reduce the need for revision procedures.^{4, 11}

Conventional Prosthetic Components for THA

THA replacement joints are typically manufactured from biocompatible metals, ceramics, and polyethylene (PE) components.

- The selection of an appropriate implant will vary based on the patient's specific needs and the treating physician's preference.
- When selecting a bearing option, wear and the impact that wear debris has on THA outcomes are primary concerns for orthopedic surgeons.
- In addition, improved patient durability and active lifestyles have led to increased physical demands being placed upon THA bearing surfaces.
- As a result, a great deal of effort and attention is focused on alternative bearing surfaces that may provide clinically meaningful solutions to address wear.¹⁷⁻¹⁹

The Development of Highly Cross-linked Polyethylene for Use in THA

By the late 1990s, the first HXLPE THA components became available. Initial *in vitro* testing provided evidence of substantial wear rate improvements versus conventional PE-based implants.²⁰

- By applying high-dose (5-10 Mrad) gamma or electron beam irradiation to ultra-high molecular weight polyethylene (UHMWPE), an extensively cross-linked material was produced that was more resistant to wear than conventional PE compounds.²¹
- HXLPE research also focused on the issue of oxidative stabilization. The free radicals created as a by-product of the cross-linking process cause implant material to degrade and become brittle over time. To address this, a thermal stabilization step was introduced to reduce free radicals.²¹
- Sterilization represented another challenge in the production of HXLPE bearings. There was a need for a terminal sterilization procedure that would not promote the formation of free radicals, as existing irradiation-based modalities were known to do.¹⁷

More than a decade later, a range of HXLPE bearings have been developed for use in hip arthroplasty. These products vary with regard to raw materials, irradiation type (gamma versus electron beam) and dose used for cross-linking, thermal stabilization process (annealing versus remelting), packaging environment, and terminal sterilization method.

Zimmer Longevity Highly Cross-linked Polyethylene

In 1999, Zimmer introduced *Longevity* HXLPE acetabular liners for use in THA. The manufacturing process employed for *Longevity* HXLPE includes a 10 Mrad electron beam radiation application, followed by thermal stabilization via remelting. This combination induces a high level of cross-linking in the PE molecules and minimizes free radicals, thereby creating a wear resistant liner material.

- Compared with the gamma irradiation approach utilized by manufacturers of other HXLPE products, the electron beam irradiation cross-linking process used for *Longevity* HXLPE is faster and more accurate, and allows for the delivery of a more controlled radiation dose. Electron beam irradiation also provides higher levels of cross-linking, leading to greater wear resistance.^{22, 23}
- *Longevity* HXLPE uses a unique remelting process for heat stabilization. The product is heated to 150°C; this causes unreacted free radicals that remain after cross-linking to recombine. Whereas annealing can leave measurable residual quantities of free radicals in HXLPE materials, the remelting process used for *Longevity* HXLPE reduces free radicals to nearly non-detectable levels. Certain annealed materials have been shown to oxidize *in vivo*.²⁴
- Some HXLPE products are terminally sterilized with gamma irradiation, which generates free radicals and increases oxidative degradation risk. *Longevity* HXLPE is sterilized with either gas plasma or ethylene oxide; these techniques do not create free radicals.
- *Longevity* HXLPE is compliant with American Society for Testing and Materials (ASTM) and International Standards Organization (ISO) standards.

In vitro testing has demonstrated up to a 90% reduction in wear rates with *Zimmer Longevity* HXLPE compared with conventional PE.^{25, 26}

- Improved wear rates with *Longevity* HXLPE have been observed through almost 30 million cycles (equivalent to 30 years of *in vivo* use) in hip simulator tests, and for femoral head sizes ranging from 22 to 46 mm in diameter.
- Third-body wear tests demonstrate that wear rate reductions with *Zimmer Longevity* HXLPE are retained in the presence of abrasive particles.
- *In vitro* data show that *Zimmer Longevity* HXLPE has an oxidation profile¹ superior to that of conventional PE.^{23, 25-29}

Compared with other HXLPE liners, *Longevity* liners have a long history of clinical use. Following more than 10 years of clinical experience, the long-term benefits of *Longevity* HXLPE have been established in a range of clinical trials covering a broad population of hip replacement patients.

- Clinical evidence obtained from prospective and retrospective trials shows that wear rates with *Longevity* liners are close to zero, resulting in a reduced risk of adverse events such as osteolysis, aseptic loosening, or revision surgery.^{20, 30-32}
- Studies with long-term follow-up (up to 10 years) show that femoral head penetration and wear rates increase progressively in patients with conventional PE liners, but remain stable over time in patients with *Zimmer Longevity* liners.^{33, 34}
- In a 10-year follow-up analysis of patients with *Longevity* HXLPE liners versus conventional PE, no radiographic signs of loosening, fracture, or evidence of osteolytic lesions were observed for patients with *Longevity* HXLPE liners, and no revisions had to be performed in the *Longevity* HXLPE group due to PE wear or liner fracture.³⁵
- Comparative studies demonstrate that *Longevity* HXLPE liners perform as well as or better than other HXLPE products with regard to implant wear rate and femoral head penetration.^{30, 32, 36, 37}
- *Zimmer Longevity* liners are also associated with clinically documented improvements in patient-reported outcomes, functional assessments, and quality-of-life measures.^{20, 32, 38}

The decreased acetabular liner wear rate with *Zimmer Longevity* HXLPE acetabular liners is associated with a reduced risk of osteolysis, or bone resorption. Osteolysis results from inflammation due to the response of the immune system to wear debris released from liners over time,³⁹ and is the primary complication seen in patients following hip arthroplasty.³⁹⁻⁴¹

- In a 7-year prospective, randomized clinical trial, 9% of the conventional PE group had wear rates exceeding the osteolytic threshold of 0.1 mm/year, while none of the *Zimmer Longevity* HXLPE patients had wear rates above this threshold value.³²
- In a retrospective study with a mean follow-up of 7.2 years, the use of *Zimmer Longevity* HXLPE was associated with a 92% reduction in the incidence of osteolysis. Osteolysis was identified in only 2% of the *Zimmer Longevity* HXLPE patient cohort, compared with 24% of patients with conventional PE.³⁶

Evidence indicates that HXLPE prosthetic components are associated with long-term reductions in revision THA rates.

- Nine-year follow-up data from the Australian National Joint Replacement Registry shows a revision rate of 5.9% with PE and 4.4% with HXLPE.⁴ This corresponds to a 25.4% reduced risk of revision surgery in THA patients who received HXLPE liners.

Another key consideration in implant selection is the effect of femoral head size on THA outcomes. Larger femoral heads improve stability, increase range of motion, and reduce the risk of neck-rim impingement in hip bearings.⁴²⁻⁴⁴ Available research indicates that *Zimmer Longevity* HXLPE liners work well over a range of femoral head sizes.

- In a 3-year study evaluating the effect of femoral head size on performance, no difference was reported in creep or wear rates for 28 mm versus 36 mm diameter heads in patients with *Zimmer Longevity* HXLPE liners.⁴⁵

2 Burden of Illness

2.1 Clinical Characteristics and Presentation

Key Findings

- Total hip arthroplasty (THA) is a successful and cost-effective intervention that relieves pain and restores mobility in patients with a range of joint disorders^{1,2}
- Published studies and registry analyses show 10- to 25-year THA implant survivorship rates are greater than 90%^{11,12}

THA is one of the most commonly performed types of joint replacement surgery. First performed in the 1960s, THA is a successful and cost-effective intervention that relieves pain and restores mobility in patients with a range of joint disorders.^{1,2} Long-term studies and registry analyses point to 10- to 25-year THA implant survivorship rates exceeding 90%. Based on this, THA is increasingly being performed in younger and more active patients.^{11,12}

THA is most frequently performed in patients with osteoarthritis (OA) of the hip (**Figure 1**).^{2,46} OA is the most common disease of the joints and can develop in any synovial joint; the condition is primarily characterized by degradation of cartilage in the joint due to biomechanical and biochemical changes, as well as chronic synovitis.⁴⁷ OA is associated with joint pain, functional limitation, and decreased quality of life.⁴⁸

Figure 1. Advanced osteoarthritis of the hip



Patients with OA usually present with a history of increasing pain and immobility. Pain is typically worse after exercise, and may impact a patient's ability to perform daily activities. Patients usually experience limitations in their range of movement, along with some fixed flexion deformity (i.e., the inability to fully straighten and/or bend the joint).² The incidence of OA increases with age, as well as in the presence of joint injuries and/or comorbidities.⁴⁸

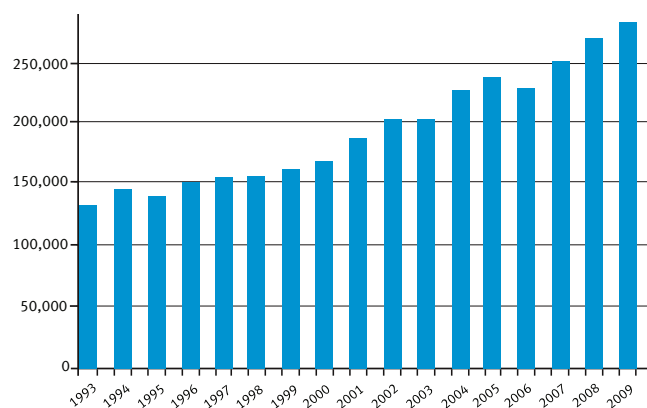
2.2 Epidemiology

Key Findings

- Over the past two decades (between 1993 and 2009), the number of hip arthroplasties performed in the U.S. has increased by 68%³
- THA frequency in the U.S. has been projected to grow by 174% between 2005 and 2030⁴⁹
- The rate of THA procedures is also increasing internationally in Australia, Canada, and many European countries⁴⁻⁶

The number of THAs performed in the U.S. has grown substantially over the past two decades. Based on data obtained from the Agency for Healthcare Research and Quality (AHRQ), 135,992 primary THA procedures were performed in 1993; by 2009, this annual figure had grown to 284,708, representing a 52% increase (**Figure 2**). When primary and revision procedures are both considered, the annual number of hip arthroplasties in the U.S. increased by 68% over the past 16 years.³

Figure 2. Total primary hip replacement procedures in the U.S.: 1993 to 2009³



The rate of THA procedures is also increasing internationally in Australia, Canada, and many European countries. Wells et al estimated that, between 1994 and 1998, the number of THA procedures in Australia grew by 26%.⁵⁰ More recent data indicates that annual Australian THA volume continued to rise between 2003 and 2009.⁴ In Canada, a 52% increase in all hip replacement surgeries was reported between 2002 and 2006.⁵ Last, current data suggest ongoing growth in the number of reconstructive hip implant procedures performed in France, Germany, Italy, and the United Kingdom.⁶

2.2.1 Patient Age and THA

Information retrieved from the National Center for Health Statistics (NCHS) annual survey between 1990 and 2002 shows that patients between 65 and 84 years of age make up the largest proportion of THA candidates. In 2009, this group represented nearly 63% of U.S. THA patients.^{3,10} Available data indicate that THA procedure rates continue to increase with age until patients reach their late 70s.^{7,10}

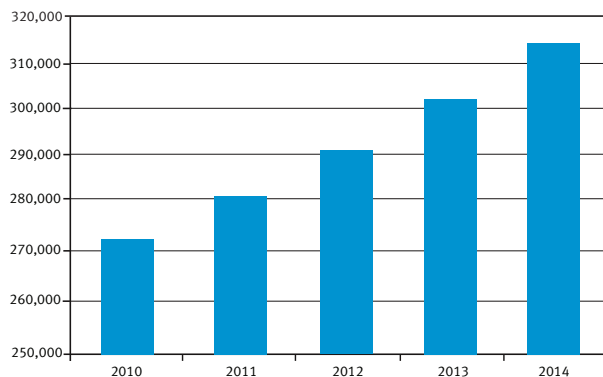
It has been projected that the overall proportion of the U.S. population aged ≥ 65 years will increase by 36% between 2010 and 2020 (from 40 million to 55 million).⁸ This trend will lead to a rise in the prevalence of arthritic disease and subsequent joint failure, which is expected to spur an ongoing, increased demand for arthroplasty.⁹

Younger patients are also increasingly likely to be candidates for joint replacement surgery. This is due to the high success rate of THA, and improved surgical techniques and biomaterials, which allow for improved implant durability.¹⁰ THA procedure survivorship rates in this population are high. Studies have shown that the survival rate of artificial joints in patients < 50 years of age is approximately 80% after ≥ 10 years.¹² Survivorship rates are also high for older individuals. Population-level data from a large, Finnish registry indicate that $> 90\%$ of patients ≥ 75 years of age who underwent THA had implant survivorship at 10 years.⁵¹

2.2.2 Primary THA

Primary THA accounts for the majority ($\sim 60\%$) of all reconstructive hip implant procedures performed in the U.S.⁷ During THA, the femoral head, proximal femur, and acetabulum are replaced with prosthetic implants.² In the U.S. and other countries, both the number and rate of primary hip arthroplasties have increased steadily over the past 20 years.^{5, 6, 10, 52} In the U.S., the number of primary THA procedures is expected to rise from 272,000 per year in 2010 to 314,900 per year in 2014 (Figure 3); this corresponds to a 3% to 4% annual increase.⁷

Figure 3. Projected total primary hip replacement procedures in the U.S.: 2010 to 2014⁷



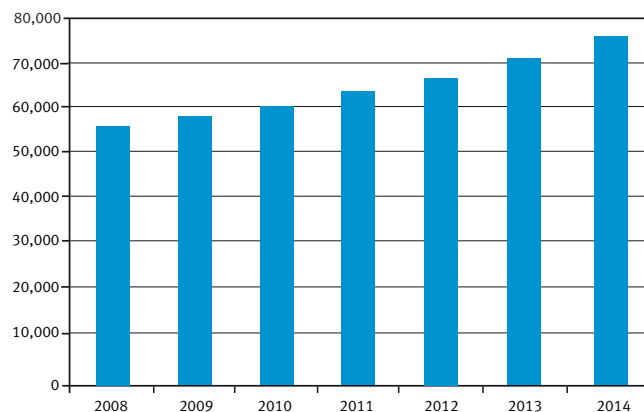
In addition, statistical projections based on historical data from the Nationwide Inpatient Sample (NIS) suggest that, by 2030, the number of primary THA procedures performed annually in the U.S. is likely to grow to 572,000.⁴⁹

2.2.3 Revision THA

With increased life expectancy, many patients who undergo hip replacement will outlive the life span of their original prosthetic implant. In 2010, revision THA accounted for $\sim 13\%$ of all reconstructive hip implant procedures performed in the U.S.⁷ International revision rates are similar to the U.S.; for example, revision rates in Australia, Canada, Finland, and Norway range from 13.1% to 18.3%.¹⁰ The primary reasons for THA revision are mechanical loosening due to osteolysis, joint instability/dislocation, and infection.^{12,13} As many as one-third of all implants may require early revision due to osteolysis associated with excessive wear (see Section 2.3 for more information on osteolysis and THA), while another third will need to be revised within 15 to 25 years due to normal wear.^{7,11}

Data from the National Hospital Discharge Survey (NHDS) indicate that, between 1990 and 2002 in the U.S., the rate of revision THA procedures grew by 79%. This represents a higher growth rate than primary THA, which increased by 62% over the same period.¹⁰ Ongoing U.S. growth in revision THA is expected, with the number of procedures projected to increase from 55,700 in 2008 to 76,000 in 2014 (Figure 4).⁷

Figure 4. Rates of revision THA in the U.S.: 2008 to 2009 (actual) and 2010 to 2014 (projected)⁷



2.3 Osteolysis – the Primary Limiting Factor in the Long-term Success of Total Hip Arthroplasty

Periprosthetic osteolysis is a process of progressive bone loss that takes place in the region surrounding prosthetic implants.⁴⁰ This disease process has emerged only within the last 50 years, since the advent of total joint replacement, and is considered a manmade condition.³⁹

Following joint arthroplasty, prosthetic wear occurs over time and leads to the shedding of small, biologically active foreign particles; this triggers an inflammatory response that ultimately results in resorption, or breakdown, of the periprosthetic bone. This type of resorption is distinct from the resorptive process that occurs during normal bone remodeling.⁴¹ (Figure 5) provides radiographic evidence of periprosthetic osteolysis, which is a particular risk with conventional PE implants.



Figure 5. Osteolysis risk is increased with conventional PE implants⁵³

The pathophysiology of periprosthetic osteolysis begins with the activation of phagocytes (white blood cells that aid in waste disposal and pathogen removal) in response to the presence of particulate wear debris. Once activated, these cells release cytokines and other inflammatory mediators, which stimulate the formation, maturation, and functioning of osteoclasts, the cells responsible for bone resorption. This process also leads to the suppression of osteoblasts, the cells responsible for bone formation. Thus, an increase in bone resorption activity combined with inhibition of bone formation results in progressive deterioration and loss of bone.^{40, 41, 54}

While osteolysis is not the only cause of bone loss following total joint replacement, it has historically been the primary complication seen in patients following hip arthroplasty.^{40, 41, 55} Calcar resorption is another wear-related condition in THA. Whereas osteolysis results in “punched-out” areas that are concave in shape, with a stiff, sclerotic border, calcar resorption leads to rounding of the calcar (the medial femoral neck), resulting in a convex shape.^{30, 56}

The bone resorption that occurs in response to the presence of particulate debris may also eventually lead to loosening of the implant, referred to as aseptic loosening.^{42, 55} Aseptic loosening, which can take place in either the acetabular or femoral regions, is the most common cause of revision hip surgery, and accounts for more than 50% of revision procedures.^{57, 58} The severity of aseptic loosening is likely to be correlated with the prosthetic wear rate.⁵⁹

Osteolysis may cause pain, but can also be asymptomatic and can therefore progress without diagnosis. Osteolysis is almost always progressive, however, and advanced osteolysis is a limiting factor to the success of THA surgery.⁵³ The pain associated with osteolysis is most commonly reported in the deep hip, groin, or buttocks, and it is most often of late onset (i.e., the pain is not present immediately following hip replacement surgery, but appears in the years following the procedure).⁶⁰

Periprosthetic osteolysis is most commonly triggered by particles of ultra-high molecular weight polyethylene (UHMWPE), commonly referred to as conventional PE.^{39, 61} It has been estimated that up to 17% of patients with conventional PE prosthetic components will develop osteolysis within 20 years of receiving a prosthetic hip.⁵³ The condition was first observed in the late 1960s, following the introduction of the Charnley technique for THA.⁶² Charnley’s procedure is still considered the gold standard for THA, and he was the first to use conventional PE as a prosthetic material.⁵³

The use of conventional PE in THA showed promising early results, including low wear and high durability.⁶¹ Because of the slow wear rate of conventional PE, however, complications resulting from osteolysis were not initially apparent. In 1968, Charnley and colleagues were the first to observe the effects of periprosthetic osteolysis. In a 4-year follow-up of patients with hip prostheses, investigators reported that bone atrophy was apparent in 4.7% of patients, with slight resorption evident in 37.2%.^{53, 63}

Subsequent research has shown that approximately 5 years of patient-level follow-up are necessary to detect the development of this complication.⁵⁵ Specifically, the risk of osteolysis rises as the wear rate increases; at wear rates <0.1 mm/year, osteolysis is rarely observed.⁵⁹ This rate has been defined as the osteolysis threshold.³²

The original condition leading to hip replacement has no bearing on the likelihood of osteolysis development. However, men and individuals <65 years of age are disproportionately affected by osteolysis.⁵³ The wear rate for any one patient will depend upon a variety of factors, including the type of prosthesis used, surgical technique applied, as well as patient-related factors, such as the amount and intensity of prosthesis use.^{39,41} In patients <50 years of age, increased activity coupled with a longer life expectancy are commonly associated with a need for revision surgery. Research shows that approximately 20% of hip replacements in younger patients require revision within only 10 years of the initial procedure.¹²

The seriousness of osteolytic complications has prompted extensive research into the development of wear-resistant prosthetic materials that will decrease the incidence of osteolysis and reduce the need for revision surgery. In the past decade, highly cross-linked polyethylene (HXLPE) has emerged as a leading prosthetic implant material with the properties necessary to meet these requirements.^{12,61}

2.4 Clinical Burden

Key Findings

- Both intraoperative and postoperative complication rates are low in primary THA, but when adverse events do occur, they can result in severe morbidity and mortality⁶⁴
- Revision hip arthroplasty is associated with more complications and negative outcomes than primary THA¹⁴
- Prostheses with lower failure rates may reduce the need for revision surgery, as well as reduce costs¹⁴

THA is a safe and effective procedure with a low associated mortality rate.³ In addition, many long-term studies have reported implant survivorship rates of 85% to 96% for up to 25 years following THA (Figure 6).¹¹

Figure 6. Charnley total hip arthroplasty with no detectable wear after 30 years of follow-up¹¹



Both intraoperative and postoperative complication rates are low in primary THA, but when adverse events do occur, they can result in severe morbidity and mortality.⁶⁴ Potential perioperative complications include infection, deep venous thrombosis, and pulmonary embolism.⁶⁵ Longer-term postoperative complications seen following THA include periprosthetic osteolysis (described in more detail in Section 2.3), aseptic loosening, periprosthetic fracture, and recurrent dislocation, all of which may require additional surgery.⁶⁴

Revision hip arthroplasty is associated with more complications and negative outcomes than primary THA.¹⁴ The most common cause of revision surgery is osteolysis leading to aseptic loosening; other causes for THA revision include infection, dislocation, and fracture.^{2,4} Patient function after revision surgery is lower than after primary hip surgery, and complications associated with revision surgery impose a burden on both caregivers and patients. However, prostheses with lower failure rates may reduce the need for revision surgery, as well as reduce costs.¹⁴

2.5 Humanistic Burden

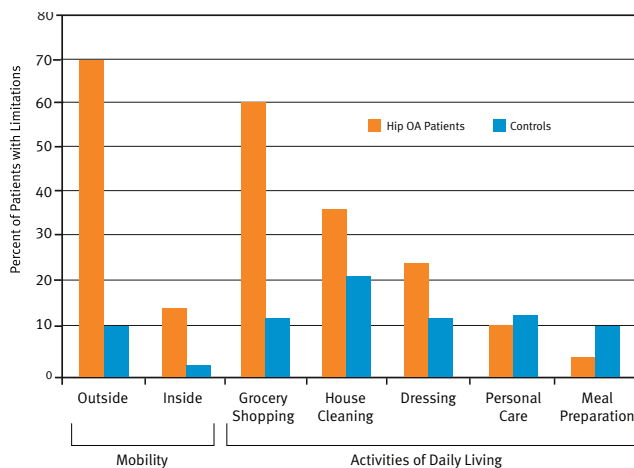
Key Findings

- As many as 90% of patients with osteoarthritis (OA) report functional limitations in their daily activities⁶⁶
- Following THA, patients report substantial improvement in terms of physical health and functioning, as well as pain reduction⁹

The clinical and societal burden associated with THA is substantial and is caused not only by the burden of OA and eventual surgical hip replacement, but also the need for revision surgery in some patients.

A survey of French physicians and their patients with OA found that > 80% of OA patients reported functional limitations in daily activities (Figure 7). For example, 70.1% of patients with OA of the hip experienced limitations in outdoor activities, 60.1% had difficulty grocery shopping, and 24.4% had trouble dressing. Among OA patients who were employed, 64.4% reported limitations in the workplace.⁶⁶

Figure 7. Self-reported functional limitations of patients with osteoarthritis of the hip⁶⁶



Shields et al assessed preoperative health-related quality of life (HRQoL) scores in 19 patients undergoing THA, as measured by the Medical Outcomes Study Short-Form 36-Item Health Survey (SF-36), and compared the scores to healthy population norms. (For more information on tools used to assess THA outcomes, such as the SF-36, see Section 2.6). Preoperatively, THA patients had significantly lower scores than the general population for the SF-36 scales related to physical functioning, ability to perform routine activities of daily living, and bodily pain. This highlights the significant impact of progressive joint disorders on patients' HRQoL.⁶⁷

However, multiple studies report that, after THA, patients report substantial improvement in terms of physical health and functioning, as well as reductions in pain. Ethgen et al, conducted a systematic literature review of relevant articles published over more than two decades (between January 1980 and June 2003). Twenty-six prospective cohort-designed THA studies that used at least one well-validated HRQoL instrument were identified. All studies found substantial improvements in physical health scores, such as for pain and physical functioning, following THA. The authors concluded that THA was highly effective at improving patient HRQoL.⁹

Although both primary and revision joint arthroplasty significantly improve HRQoL for patients, physical function and quality of life are often comparatively poorer following revision surgery.^{9, 15} In a study comparing 143 revision THA patients with 144 primary THA patients, Patil et al, reported that postoperative functional outcomes were significantly better in patients undergoing primary THA. The magnitude of QoL improvement was also greater for patients with primary compared with revision THA. In addition, following revision procedures, QoL gains took longer to realize.¹⁵

Improving clinical outcomes and HRQoL following THA revision procedures remains a substantial area of unmet need. The lower HRQoL outcomes associated with revision surgery suggest strongly that prosthetic materials that: a) reduce the likelihood of implant failure following the primary procedure; and, b) ensure the greatest likelihood of revision success without complications are critical for improving patient quality of life.

2.6 Economic Burden

Key Findings

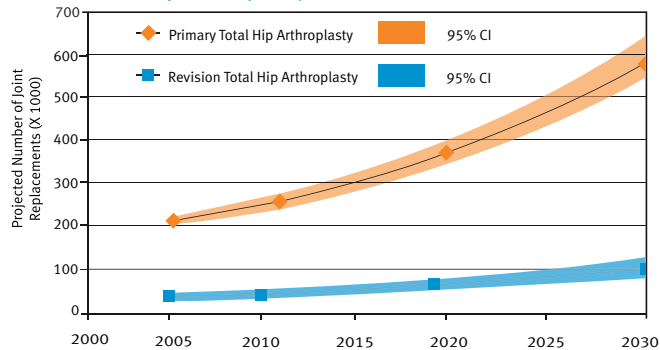
- The number of THA surgeries performed in the U.S. and other countries places a substantial burden on hospitals, as well as national health systems^{3, 6, 13, 16, 49}
- In the U.S., there is a growing discrepancy between charges and reimbursements in THA, particularly for revision procedures^{14, 49}
- Costs are higher and mean hospital stays are substantially longer for revision THA versus primary THA³
- Prostheses with increased durability may reduce the economic burden associated with THA revision surgery by reducing the revision rate.¹⁴
- Follow-up data from the Australian National Joint Replacement Registry shows a 9-year revision rate of 5.9% with PE and 4.4% with HXLPE.⁴ This corresponds to a 25.4% reduced risk of revision surgery in THA patients who received HXLPE liners.

Available data indicate that THA, in particular revision THA, imposes a substantial economic burden on U.S. hospitals.³ Rising costs associated with THA have also substantially affected other national health systems outside of the US.^{6, 16}

According to the U.S. AHRQ, the average hospital costs associated with a primary total hip replacement procedure in 2009 were \$15,736. The mean duration of hospitalization for primary THA was 3.5 days. During the same year, mean hospital costs associated with revision hip surgery were \$21,390, almost 30% higher than for primary THA. Revision surgery was associated with an average hospital stay of 4.8 days.³

Furthermore, the incidence of both THA procedure types is projected to increase. As noted previously, between 1990 and 2002, the rate of growth in revision surgeries exceeded that of primary THA procedures.¹⁰ Based on data from the U.S. Census Bureau and the NIS, it is projected that the number of primary and revision THA surgeries in the U.S. will grow by 174% between 2005 and 2030 (Figure 8).⁴⁹

Figure 8. Projected increase in U.S. numbers of primary and revision total hip arthroplasty: 2005 to 2030⁴⁹



However, in some circumstances, reimbursement rates for THA procedures have declined over time; this is particularly the case for revision arthroplasties. After adjusting for inflation, for example, Medicare reimbursement for revision THA declined from \$319 million in 1997 to \$244 million in 2003.¹⁴ Despite this, between 1997 and 2003, revision THA was estimated to have consumed 19% of Medicare hip replacement expenditures.⁴⁹

Clearly, there is a need to lower the THA revision burden by increasing the effectiveness and durability of prosthetic implants used in THA procedures.¹⁵ A 2002 analysis estimated that, if the hip revision burden in the U.S. could be reduced by even 1%, the potential national cost savings would range from \$42.5 to \$112.6 million.¹⁰

Improvements in the manufacture of prosthetic components for THA, including the development of HXLPE, have had a positive impact on prosthesis durability. Based on data from an Australian national registry,⁴ the use of HXLPE components reduces the need for revision procedures by 25.4% at 9 years.¹¹ This information suggests that it is feasible to achieve substantial, long-term savings in revision surgery costs when HXLPE is used in primary procedures; this will be discussed in more detail in Section 6 of this document.

2.7 Functional Status Measures Commonly Used to Assess Burden of Illness in Total Hip Arthroplasty

Evaluations of patient HRQoL and functional status can be used to characterize preoperative, baseline patient quality-of-life, as well as the degree of improvement achieved following primary or revision joint arthroplasty. A variety of generic and disease-specific instruments are available to measure HRQoL and functional status in THA patients. The following is a brief description of several of these instruments.

The Medical Outcomes Study Short-Form 36-Item Health Survey (SF-36) is a patient-administered questionnaire that measures the following 8 health concepts: physical functioning; role limitation (physical); bodily pain; general health; vitality; social functioning; role limitation (emotional); and mental health. In addition, two summary scores may be calculated.

- The Physical Component Score (PCS), comprised of the physical functioning, role limitation (physical), bodily pain, and general health subscales, provides a measure of the subject's perception of his/her physical health.
- The Mental Component Score (MCS), composed of the vitality, social functioning, role limitation (emotional), and mental health subscales, provides a measure of the patient's perception of his/her mental health.

The PCS and MCS were designed to reduce the SF-36 from an 8-scale assessment to two summary measures without a substantial loss of information. One of the strengths of these summary scores is their value in distinguishing physical outcomes from mental health outcomes.⁶⁸

The **Medical Outcomes Study Short-Form 12-Item Health Survey (SF-12)** reduces the SF-36 instrument to 12 items, but retains all eight domains and the two summary scores.⁶⁹

The **Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)** is a patient-administered, disease-specific instrument that evaluates clinically important and patient-relevant symptoms in the areas of pain, stiffness, and physical function in patients with OA of the hip and/or knee. The WOMAC is a valid, reliable, and responsive measure of patient-reported outcomes, and is used widely in the evaluation of hip and knee OA. The index comprises 24 questions and includes the following three subscales:

- The **WOMAC Pain subscale** contains five questions regarding the amount of pain experienced due to OA in the study joint in the past seven days. This subscale score ranges from 0 to 20, with higher scores indicating more pain.
- The **WOMAC Stiffness subscale** comprises two questions regarding the amount of stiffness experienced in the study joint in the past seven days. Stiffness is defined as a sensation of decreased ease when the subject moves the study joint. This subscale score ranges from 0 to 8, with higher scores indicating more stiffness.
- The **WOMAC Physical Function subscale** includes 17 questions regarding the degree of difficulty experienced (pain, stiffness, physical function) due to OA in the study joint in the past 7 days. This subscale score ranges from 0 to 68, with higher scores indicating worse physical function. Physical function refers to the subject's ability to move and perform usual activities of daily living.⁷⁰

The **Harris Hip Score** is a clinician-administered instrument that evaluates a patient's pre- and post-operative impression of the results of hip replacement. It also includes a physical exam to assess joint deformity and range of motion. This hip score has become widely used as a means of comparing results following intervention and includes 8 items that measure the following factors: pain (total score of 40); function including limp, use of a walking aid, and distance walked (total score of 47); and, functional activities including ability to climb stairs, put on shoes and socks, sit in a chair for some time, and ability to use public transportation (total score of 14). The physical exam portion includes range of motion (total score of 5) and absence of joint deformity (total score of 4) assessments. A total score is derived by summing each item score and is reported as 90-100 (excellent), 80-90 (good), 70-79 (fair), 60-69 (poor), and <60 (failed result).⁷¹

The **Oxford Hip Score** is a patient-completed questionnaire that assesses disability and function in patients undergoing THA. It contains 12 items that assess pain, daily activities, and function. The 12 items are summed to form a total score ranging from 0 (most severe symptoms) to 48 (least severe symptoms).⁷²

The **Quality of Well-being (QWB) Index** is a patient-completed questionnaire developed to provide a preference-weighted measurement of an individual's health status at a specific point in time. This instrument is generic and not specific to orthopedic procedures. The QWB combines 4 domains into a single score that ranges from 0 (death) to 1.0 (optimum functioning). The 4 domains include symptom/problem complex, mobility, physical activity, and social activity. The index measures an individual's actual performance on a particular day, in comparison to other people of the same age.⁶⁹

The **Revision Rate** describes the number of patients in a given study population who have undergone revision surgery. As a clinical study outcome, revision may be defined as the removal, exchange, or addition of any prosthetic component. The rate may be reported in various ways, depending on the study, including the cumulative revision rate (total percentage of the population over time), or the number of revision procedures per patient-years.^{4,73}

3 Conventional Treatments

3.1 Characteristics of Conventional Prosthetic Components for Total Hip Arthroplasty

Total hip arthroplasty (THA) is a common and safe surgical procedure, most often needed when a patient's existing joint becomes compromised by osteoarthritis (OA). Replacement joints are typically manufactured from biocompatible metals, ceramics, and polyethylene (PE) components. The selection of an appropriate implant will vary based on the patient's specific needs and the treating physician's preference.¹⁷

Patient durability and active lifestyles have led to an increase in the physical demands being placed upon THA bearing surfaces. As a result, implant manufacturers are searching for ways to improve bearing surface performance. When selecting a bearing option, wear and the impact that wear debris has on THA outcomes are primary concerns for orthopedic surgeons. As a result, a great deal of effort and attention is focused on alternative bearing surfaces, which may provide clinically meaningful solutions to address wear.¹⁷⁻¹⁹

This section provides brief information on currently available prosthetic components that are not constructed from highly cross-linked polyethylene (HXLPE).

3.2 Conventional Polyethylene

The 1962 introduction of ultra-high molecular weight polyethylene (UHMWPE) as an implant material for use in artificial joint bearings revolutionized THA. The high wear resistance of UHMWPE, commonly referred to as conventional PE, was an improvement over previously available products with poor wear performance, such as Teflon. Although there were initial concerns about the need for increased lubrication with conventional PE bearings, research revealed that the coefficient of friction of this new material was decreased under high stress. In addition, boundary lubrication of conventional PE in the presence of synovial fluid was found to further reduce friction levels.¹⁸ Registry data from as recently as 2006 reveal that metal-on-polyethylene bearings (all PE types) constitute approximately two-thirds of THA implants.²¹

3.3 Ceramic-on-ceramic Bearings

Ceramic bearings were introduced in the 1970s and have been used for THA since that time, with mixed results.⁷⁴ Among the surgical-grade ceramics available on the market today are bearings made from alumina, zirconia, and alumina matrix composite. Alumina was the first ceramic to be utilized as a bearing surface. The development of zirconia, with its increased fracture toughness relative to alumina, offered a reduced risk of fracture, allowing for smaller head sizes and longer neck lengths.⁷⁵ However, a widespread recall of certain types of zirconia heads in 2001 resulted in a marked reduction in the use of zirconia in THA implants.⁷⁶ Alumina matrix composite implants have demonstrated improved wear rates and fracture toughness compared with those made from alumina alone.⁷⁷

3.4 Metal-on-metal Bearings

Metal-on-metal bearing surfaces became popular for use in large diameter head applications to reduce the risk of dislocation.^{6,7} While some pure metals have excellent characteristics for implant use, the majority of metal implants are made from cobalt-chromium alloys, which are biocompatible, strong, wear-resistant, and corrosion-resistant.¹⁷ In recent years, metal-on-metal use has decreased.^{6,7}

4 Highly Cross-linked Polyethylene (HXLPE) in Total Hip Replacement

Key Findings

- HXLPE was created by applying high-dose (5-10 Mrad) gamma or electron beam irradiation to ultra-high molecular weight polyethylene to produce an extensively cross-linked material that was more resistant to wear than conventional polyethylene compounds used in joint arthroplasty.²¹
- Manufacturing HXLPE includes a thermal stabilization step to minimize free radicals, which may become oxidized in vivo and cause the implant material to degrade and become brittle over time.²¹
- The sterilization process must be optimized as well to reduce or eliminate the formation of free radicals. Various manufacturers utilize different sterilization techniques for liner materials including the use of gas plasma or ethylene oxide.²¹

4.1 Manufacturing Process

During the 1990s, researchers made significant strides toward the development of highly cross-linked polyethylene (HXLPE) bearings. By applying high-dose (5-10 Mrad) gamma or electron beam irradiation to ultra-high molecular weight polyethylene (UHMWPE), investigators produced an extensively cross-linked material that was more resistant to wear than conventional polyethylene (PE) compounds used in joint arthroplasty.²¹ This discovery represented an important milestone, since osteolysis and aseptic loosening were established clinical sequelae to excessive wear in patients with conventional PE-based implants (see Section 2.3).

In addition to optimizing wear resistance, HXLPE research efforts focused on the issue of oxidative stabilization. The free radicals created as a by-product of the cross-linking process necessitated some form of intervention, since free radical oxidation was known to cause implant material to degrade and become brittle over time. As such, a thermal stabilization step, involving either annealing (heating to below the melting point) or remelting (also referred to as melt-annealing), was introduced to reduce free radicals.²¹

Table 1. Currently available HXLPE implant products in the US*

Manufacturer	Zimmer	Zimmer	Zimmer	Biomet	DePuy	DePuy	Smith & Nephew	Stryker	Stryker	Wright
Product Name	<i>Longevity</i>	<i>Durasul</i> [®]	<i>Prolong</i> ^{**}	ArComXL	Marathon	AltrX	XLPE	Crossfire	X3	Lineage A Class
Launch date	1999	1999	2001	2005	1998	2007	2005	1999	2005	2005
Raw material	GUR 1050 molded sheet bar stock ^{24, 78}	GUR 1050 molded sheet preforms ²⁴	GUR 1050 molded bar stock ⁸⁰	GUR 1050 isostatic rod ⁸¹	GUR 1050 extruded rod ²⁴	GUR 1020 extruded rod ⁸⁵	GUR 1050 extruded rod ²⁴	GUR 1050 extruded rod ²⁴	GUR 1020 extruded rod ⁹¹	GUR 1020 extruded rod ⁹³
Cross-linking irradiation process (dose)	e-beam (10 Mrad) ^{24, 78}	e-beam (9.5 Mrad) ^{24, 79}	e-beam (6.5 Mrad) ⁸⁰	gamma (5 Mrad) ^{81, 82}	gamma (5 Mrad) ^{24, 83}	gamma (7.5 Mrad) ⁸⁵	gamma (10 Mrad) ^{24, 87}	gamma (7.5 Mrad) ^{24, 89}	gamma (9 Mrad total after sequence of three 3-Mrad doses) ⁸⁹	gamma (7.5 Mrad) ⁹³
Thermal stabilization process	remelting (150°C) ⁷⁸	remelting (150°C) ⁷⁹	remelting (150°C) ⁸⁰	annealing (130°C) ⁸¹	remelting (155°C) ⁸⁴	remelting (155°C) ⁸⁹	remelting (150°C) ⁸⁸	annealing (130°C) ⁹⁰	annealing (applied 3 times in sequence) ⁸⁹	remelting ⁹³
Additional steps				Heated bar is ram-extruded through a circular die, followed by stress relief via a second annealing step (130°C) ⁸¹						
Packaging environment	air	air	air	air	air	air	air	nitrogen ⁸⁹	air	air
Terminal sterilization method	gas plasma or ethylene oxide	ethylene oxide ^{89, 92}	gas plasma	gas plasma ^{81, 82}	gas plasma ^{24, 83}	gas plasma ⁸⁶	ethylene oxide ²⁴	gamma irradiation in nitrogen (3 Mrad) ^{24, 89}	gas plasma ^{89, 92}	ethylene oxide ⁹³

*Some of these products may not be available in other countries. Product names used are for identification purpose only and may be trademarks of their respective companies.

**Zimmer *Prolong*[®] HXLPE is a product used in total knee arthroplasty and is not discussed in this document.

Sterilization represented a third challenge in the production of HXLPE bearings. Specifically, there was a need to incorporate a terminal sterilization procedure that would not promote the formation of free radicals, as existing irradiation-based modalities were known to do. Different manufacturers have employed various sterilization techniques for liner materials; these include the use of gas plasma or ethylene oxide.²¹

4.1.1 Currently Available HXLPE Implants

By the late 1990s, the first HXLPE THA components became available, with *in vitro* testing providing evidence of substantial wear rate improvements versus conventional PE implants.²⁰ More than a decade later, a range of HXLPE bearings have been developed for use in hip arthroplasty. As shown in Table 1, these products vary with regard to raw materials, irradiation type (gamma versus electron beam) and dose used for cross-linking, thermal stabilization process (annealing versus remelting), packaging environment, and terminal sterilization method.^{17, 21, 40}

5 Product Information: Zimmer Longevity Highly Cross-linked Polyethylene

Key Findings

- *Zimmer Longevity* highly cross-linked polyethylene (HXLPE) is manufactured using a proprietary high-dose (10 Mrad) electron-beam irradiation cross-linking process that provides for higher levels of cross-linking for a given dose, leading to greater wear resistance.^{22, 23}
- Another distinguishing attribute of *Longevity* HXLPE is the remelting procedure utilized for heat stabilization which confers greater oxidative resistance and a lower risk of brittleness and degradation compared to the annealing procedure utilized by several other manufacturers.^{17, 24, 94-96}
- The terminal sterilization method utilized for *Longevity* HXLPE is another differentiating feature. *Longevity* HXLPE is sterilized using either gas plasma or ethylene oxide; these techniques do not create free radicals and thereby promote an environment that is more resistant to oxidation.¹⁷

5.1 Technology Description and Characteristics

In 1999, Zimmer introduced *Longevity* highly cross-linked polyethylene (HXLPE) liners for use in total hip arthroplasty (THA). Zimmer employs a proprietary high-dose (10 Mrad) electron beam irradiation cross-linking process. Compared with the gamma irradiation approach utilized by manufacturers of other HXLPE products, the electron-beam irradiation cross-linking process used for *Longevity* HXLPE is faster and more accurate, allowing for delivery of a more controlled dose of radiation (**Figure 9**). Most importantly, however, electron beam irradiation provides for higher levels of cross-linking for a given dose compared to gamma irradiation, leading to greater wear resistance.^{22, 23}

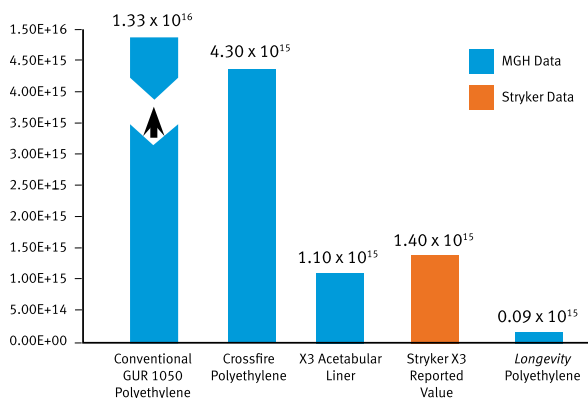
Figure 9. Comparison of gamma versus electron beam cross-linking processes

Gamma	E-Beam
<p>Slower process Less Control dose Lower levels of cross-linking than e-beam at the same dose</p>	<p>Faster process More Controlled dose Higher levels of cross-linking than gamma at the same dose</p>
<p>More cross-linking = Less Wear</p>	

Another distinguishing attribute of *Longevity* HXLPE is the remelting procedure utilized for heat stabilization. During remelting, the product is heated to 150°C, causing unreacted free radicals that remain after cross-linking to recombine. Compared with annealing, in which the HXLPE compound is heated to temperatures below the melting point, the remelting process is more effective in eliminating free radicals. Whereas annealing has been shown to leave measurable residual quantities of free radicals, remelting reduces free radicals to nearly non-detectable levels. Certain annealed materials have been shown to oxidize *in vivo*.²⁴ Compared with annealing, remelting confers greater oxidative resistance and a lower risk of brittleness and degradation.^{17, 24, 94-96}

Figure 10 provides a comparison of free radical measurements for *Longevity* HXLPE versus conventional polyethylene (PE) and 2 annealed competitor HXLPE liners.^{17, 35}

Figure 10. Free radical concentration (spins/gram) of *Zimmer Longevity* and other HXLPE liners¹⁷



While the mechanical properties of *Longevity* HXLPE are somewhat modified during the remelting process, evidence indicates that this effect has no clinical implications. *Longevity* HXLPE is compliant with American Society for Testing and Materials (ASTM) and International Standards Organization (ISO) standards. Its mechanical properties are stable over time (in comparison to conventional PE), making it highly resistant to aging.^{17, 24, 94-96} The advantages of remelting versus annealing are summarized in **Figure 11**.

Figure 11. Comparison of thermal stabilization with annealing versus remelting

Annealing	Remelting
<p>Leaves free radicals in material</p> <p>Free radicals, coupled with packaging in air could lead to oxidation</p> <p>Initially retains mechanical properties</p>	<p>Reduces free radicals to non-detectable levels</p> <p>Effectively eliminating free radicals = oxidative resistance</p> <p>Material properties remain stable over time</p> <p>Modest reduction in mechanical properties</p>
<p>Free radicals remaining in material after annealing could lead to oxidation, material degradation and revision</p>	

The terminal sterilization method used for *Longevity* HXLPE represents another differentiating feature. Some HXLPE products are terminally sterilized with gamma irradiation, which generates free radicals and increases the risk of oxidative degradation. By contrast, *Longevity* HXLPE is sterilized with either gas plasma or ethylene oxide; these techniques do not create free radicals and thereby promote an environment that is more resistant to oxidation.¹⁷

Table 2 shows a comparison of the attributes of *Zimmer Longevity* HXLPE with other currently available HXLPE liner materials, including wear rates, oxidative stability, and mechanical properties.

Table 2: Wear rates, oxidative stability, and mechanical properties of HXLPE products currently available in the US*

Manufacturer	Zimmer	Zimmer	Zimmer	Biomet	DePuy	DePuy	Smith & Nephew	Stryker	Stryker	Wright
Product Name	<i>Longevity</i>	<i>Durasul</i>	<i>Prolong**</i>	ArComXL	Marathon	AltrX	XLPE	Crossfire	X3	Lineage A Class
Launch date	1999	1999	2001	2005	1998	2007	2005	1999	2005	2005
Wear rate (in vitro)	Very low ^{24, 26, 78, 97, 98}	Very low ^{24, 100-103}	Very low	Low ^{81, 102}	Low ^{24, 26, 83, 84, 104, 106, 107}	Very low ^{86, 108, 109}	Very low ^{88, 111}	Very low ¹¹⁰	Very low ^{113, 114}	Very low ^{93, 115}
Free radicals	Below detection limit ^{78, 99}	Below detection limit ^{23, 99-101}	Below detection limit	Above detection limit ⁸¹	N/A	N/A	N/A	Above detection limit ^{26, 94, 111}	Above detection limit ^{22, 89, 99}	N/A
Risk of oxidation	Reduced compared to gamma-sterilized conventional PE ^{24, 26, 78}	Reduced compared to gamma-sterilized conventional PE ^{23, 24, 100, 101, 104}	Reduced compared to gamma-sterilized conventional PE	Reduced compared to gamma-sterilized conventional PE ^{24, 105}	Reduced compared to gamma-sterilized conventional PE ^{24, 26, 83, 106}	Reduced compared to gamma-sterilized conventional PE ¹⁰⁸	Reduced compared to gamma-sterilized conventional PE	No oxidative resistance ^{26, 105, 94, 112}	Reduced compared to gamma-sterilized conventional PE ^{91, 99, 113, 114}	Reduced compared to gamma-sterilized conventional PE ¹¹⁵
Mechanical properties	Retains necessary properties, uniform in all orientations ^{78, 98}	Retains necessary properties, uniform in all orientations ^{98, 100, 101}	Retains necessary properties	Vary with orientation ⁸¹	Less cross-linking results in smaller reduction of properties ^{83, 106}	Less cross-linking results in smaller reduction of properties ¹⁰⁸	N/A	More similar to conventional PE initially	More similar to conventional PE ^{91, 113, 114}	N/A
Mechanical properties stability	Stable over time ^{24, 98}	Stable over time ^{24, 100, 101}	Stable over time	No long-term data	N/A	N/A	N/A	Properties degrade with time ¹¹²	No long-term data	N/A

*Some of these products may not be available in other countries. Product names used are for identification purpose only and may be trademarks of their respective companies.

**Zimmer *Prolong*® HXLPE is a product used in total knee arthroplasty and is not discussed in this document.

6 Clinical Evidence for Zimmer Longevity Highly Cross-linked Polyethylene

6.1 Introduction

Evidence from both *in vitro* and *in vivo* studies have demonstrated the efficacy and safety of *Zimmer Longevity* highly cross-linked polyethylene (HXLPE) liners for use in patients undergoing total hip arthroplasty (THA). Introduced in 1999, *Longevity* HXLPE liners have a long history of clinical use and the longest-term, most robust clinical data set of all available HXLPE liners.

As described in this section, wear is significantly lower with *Longevity* HXLPE liners than with conventional polyethylene (PE) liners. In fact, while acetabular liners made with conventional PE continue to be subject to wear and femoral head penetration for as long as they are in place, *Longevity* HXLPE liners consistently exhibit wear rates close to zero, with little or no penetration after the bedding-in process is complete (see Section 6.3.1 for a discussion of bedding in).^{20, 30-32}

After more than 10 years of clinical experience with more than 1 million Zimmer HXLPE liners, comparative studies have demonstrated that *Longevity* HXLPE liners perform as well as or better than other highly cross-linked acetabular liners (discussed in Section 6.3) with regard to implant wear rate and femoral head penetration. The reduced wear with *Longevity* HXLPE liners is associated with lower rates of osteolysis in clinical trials (see Section 6.3.7) and a potentially lower risk of revision surgery over the long term.^{30, 32, 36, 37} In an Australian National Joint Replacement Registry report evaluating 2814 revision procedures in more than 102,000 patients,⁴ modified liners (including those made from HXLPE) were associated with a 25.4% reduction in revision rates at nine years compared with conventional PE liners. No difference in revision risk was observed for these patients based on prosthetic head size (i.e. ≤ 32 mm or > 32 mm).

Longevity HXLPE liners are also associated with clinical and functional improvements in patients, with increases in hip scores and quality of life (QoL) measures that persist over time.^{20, 32, 38}

6.2 Summary of Key *in vitro* Findings

Key Findings

- *Zimmer Longevity* HXLPE exhibits *in vitro* wear rate reductions of up to 90% versus conventional polyethylene (PE)^{25, 26}
- HXLPE demonstrates superior wear rates compared with conventional PE after almost 30 million cycles (equivalent to 30 years of *in vivo* use) in hip simulator tests, for femoral head diameters ranging from 22 to 46 mm^{23, 27-29}
- Wear rate reductions with HXLPE are retained in the presence of alumina and bone cement particles²⁵
- *In vitro* data have shown that *Zimmer Longevity* HXLPE has an oxidation profile superior to that of conventional PE.^{5, 23, 26}

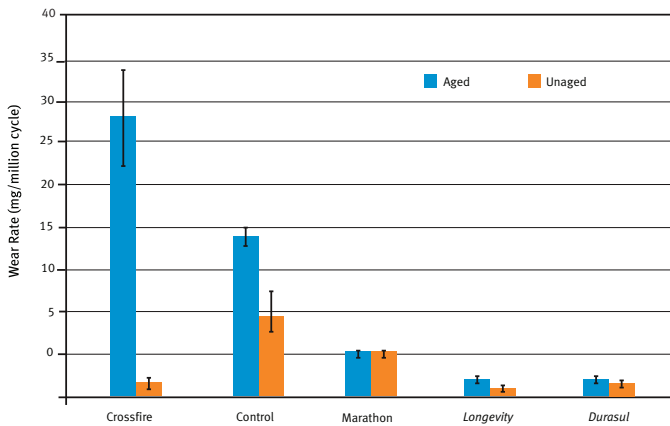
In vitro testing has demonstrated a reduction in wear rates of as much as 90% with *Zimmer Longevity* HXLPE compared with conventional PE; improved wear rates with HXLPE have been observed through almost 30 million cycles (equivalent to 30 years of *in vivo* use) in hip simulator tests, and for femoral head sizes ranging from 22 to 46 mm in diameter.^{23, 25-29} In addition, third-body wear tests have demonstrated that wear rate reductions with HXLPE are retained in the presence of abrasive particles.²⁵ *In vitro* data have also shown that *Zimmer Longevity* HXLPE has an oxidation profile⁵ superior to that of conventional PE.^{23, 26}

6.2.1 Pin-on-disc Tests

One study investigated the wear rates and oxidation indices of 4 HXLPE liner materials (*Zimmer Longevity*, *Zimmer Durasul*, DePuy Marathon, and Stryker Crossfire) compared with conventional PE as a designated control. Pin-on-disc wear testing was conducted for 2 to 5 million cycles (MC) for un-aged and aged samples of each material; the artificial aging process consisted of three weeks' exposure to 80°C in an air convection oven.²⁶

As shown below (Figure 12), un-aged wear rates were lowest (approximately 1.4 mg/MC) for *Zimmer Longevity*, *Zimmer Durasul*, and Stryker Crossfire Polyethylene, compared with 4.5 mg/MC for DePuy Marathon Polyethylene, and 9.4 mg/MC for conventional PE. While post-aging wear rates for *Zimmer Longevity*, *Zimmer Durasul*, and DePuy Marathon Polyethylene exhibited only minimal increases from un-aged values, after aging the wear rates of conventional PE and Stryker Crossfire Polyethylene were increased to approximately 14 and 28 mg/MC, respectively.²⁶

Figure 12. Pin-on-disc wear rate for aged and un-aged HXLPE products versus conventional PE control²⁶



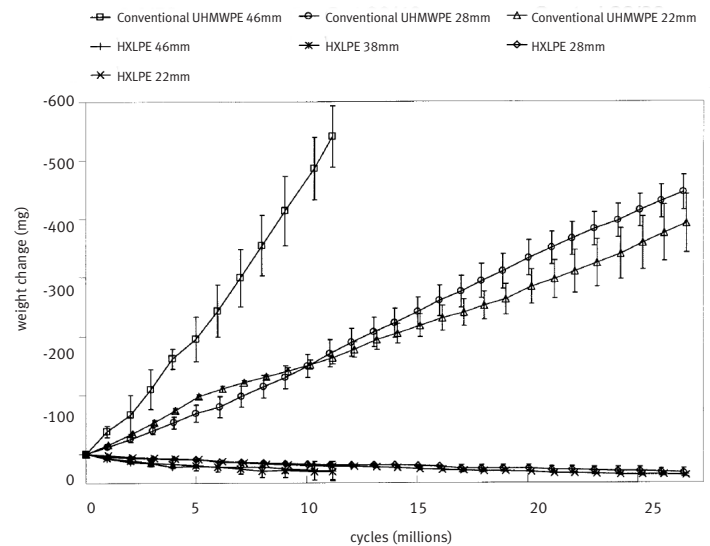
The oxidation profile findings for each of these materials were consistent with post-aging wear rate results. Three-week oxidation levels, assessed following completion of the aging process, but prior to wear testing, showed no oxidation for *Zimmer Longevity*, *Zimmer Durasul*, and DePuy Marathon Polyethylene, compared with an oxidation index of 0.4 for conventional PE and 1.7 for Stryker Crossfire Polyethylene.²⁶

6.2.2 Hip Simulator Tests

Hip simulator data have been utilized in a number of studies to analyze *in vitro* wear rates and the effects of femoral head size on wear with HXLPE versus conventional PE liners. In one investigation, Laurent et al reported significantly lower average total wear for 22 mm and 32 mm HXLPE liners versus conventional PE liners, with reductions of 89% after 5 MC (performed on 18 liners of each type, with half subjected to artificial aging) and 97% after 18 MC (performed on 6 liners of each type, all of which were artificially aged), respectively ($p < 0.0001$ for both).²⁷

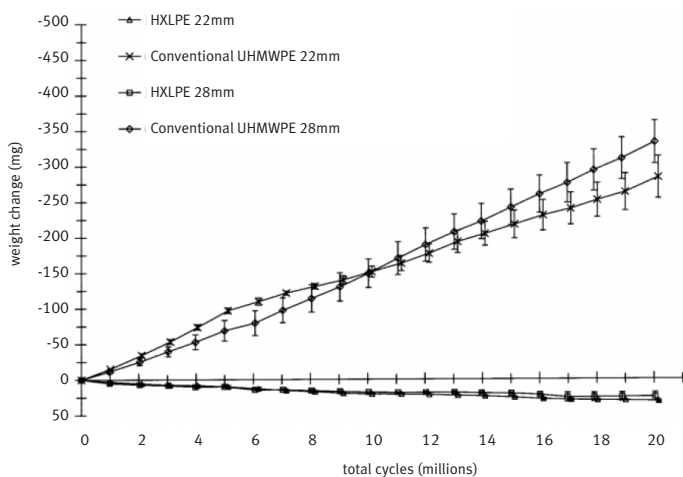
A study utilized hip simulator testing with gravimetric analysis of acetabular liner weight loss to assess the wear rate of HXLPE versus conventional PE liners with 22, 28, 38, and 46 mm diameter femoral heads. After 5 to 27 MC, while HXLPE liners exhibited no detectable wear for even the largest diameter head, conventional PE liners had an average wear rate of 13 to 48 mg/MC, with increases in the extent of wear as a function of head size (Figure 13).²⁸

Figure 13. Hip simulator weight change data for HXLPE and conventional PE with head sizes of 22, 38, and 46 mm²⁸



These findings were consistent with those reported in another study by Muratoglu and colleagues that compared HXLPE and conventional PE liner wear rates after 20 MC of hip simulator testing with 22 and 28 mm femoral heads. HXLPE liners showed no detectable wear based on measurements of acetabular liner weight loss (**Figure 14**); by contrast, wear rates were significantly higher for conventional PE liners, with values of 14 mg/MC for 22 mm heads ($P=0.002$) and 17 mg/MC for 28 mm heads ($P=0.001$).²³

Figure 14. Hip simulator (millions of cycles) weight change data for HXLPE and conventional PE with 22 and 28 mm heads²³

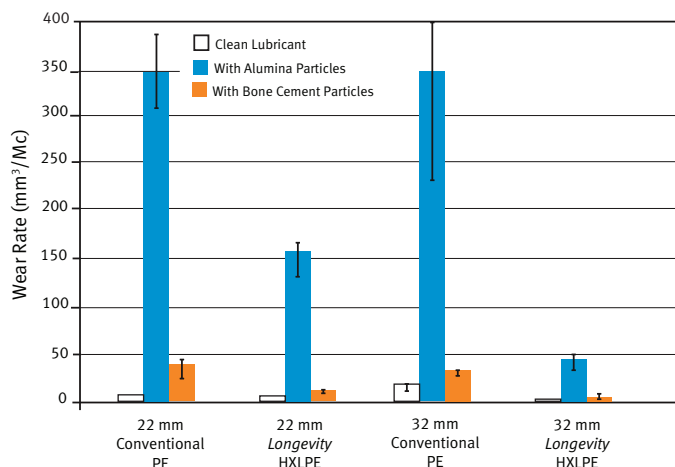


This study also included an analysis of the oxidation index for both HXLPE and conventional PE after 37 days of accelerated aging (80°C in a convection oven). Whereas HXLPE remained unoxidized, with a maximum oxidation index of <0.1, the maximum oxidation index of conventional PE was 1.5.²³

A hip simulator study by Laurent et al investigated the third-body wear rate⁶ of *Zimmer Longevity* HXLPE versus conventional PE liners after 5 MC with 22 mm and 32 mm diameter femoral heads. Prior to the introduction of abrasive particles, wear rates with *Zimmer Longevity* HXLPE were approximately 90% lower than with conventional PE for both head sizes tested; with abrasive particles added, wear rates remained significantly lower with *Zimmer Longevity* HXLPE ($p<0.0001$).²⁵

Specifically, in the presence of alumina grit, *Zimmer Longevity* HXLPE 22 mm liners exhibited a 69% decrease in wear rate relative to conventional PE; an 89% decrease was observed with 32 mm liners. When bone cement particles were added, the reduction in wear rates was 92% and 93% for the two head sizes, respectively (**Figure 15**). These data provide evidence that *Zimmer Longevity* HXLPE has a substantially lower average wear rate in the presence of bone cement debris compared with conventional PE liners with no abrasive particles present.²⁵

Figure 15. Third-body wear test with HXLPE versus conventional PE²⁵



6.3 *In vivo* Results

Key Findings

- *Longevity* HXLPE liners have significantly lower steady-state linear wear rates than conventional PE, with wear reductions of up to 100% versus conventional PE¹¹⁶
- *Longevity* liners exhibit little or no femoral head penetration after bedding-in is complete, while penetration continues with conventional PE^{32, 116}
- Rates of osteolysis with *Longevity* liners are up to 92% lower than those with conventional PE³⁶
- *Longevity* liners are associated with improvements in patient-reported outcomes and functional scores; these benefits persist over time^{20, 32, 38}
- Use of HXLPE liners has been shown to reduce the need for THA revision surgery⁴
- Published clinical data show reduced wear rates and femoral head penetration for *Zimmer Longevity* HXLPE compared to conventional PE in patients with up to 10-years of post-operative follow-up^{20, 30, 32-34, 37, 116, 120}

6.3.1 Wear Rate and Femoral Head Penetration

The majority of *in vivo* clinical studies of HXLPE in THA include the primary endpoints of wear rate and/or femoral head penetration. (For more information on wear rate assessment, see Section 6.3.2). During the first postoperative year after THA, the femoral head settles into the acetabular lining via a mechanical process known as “bedding in” or “creep.”¹¹⁷ This normal process occurs rapidly at first, but within 1-2 years becomes negligible. From that point forward, femoral head penetration results primarily from wear—that is, the femoral head articulates against the acetabular liner, wearing it away.^{34, 118}

The steady-state wear rate—or the rate of penetration measured after accounting for bedding in—is an important clinical outcome in THA, since wear is a primary factor contributing to adverse outcomes such as periprosthetic osteolysis, aseptic loosening, and the need for revision arthroplasty.³⁹ With conventional PE liners, the steady-state wear rate typically remains significantly above zero, meaning that the femoral head continues to penetrate the acetabular liner for as long as it is in place. In contrast, even after 7-10 years, *Zimmer Longevity* HXLPE consistently demonstrates minimal wear and little or no femoral head penetration once bedding in is complete. As such, HXLPE has the potential to reduce long-term adverse patient outcomes.⁴⁰

6.3.2 *In vivo* Hip Implant Wear Rate Assessment: Linear Versus Volumetric Wear

Hip implant wear rates may be reported in terms of 2-dimensional (occurring in the frontal plane) or 3-dimensional (in and out of the frontal plane) linear wear, or as volumetric wear, which measures the volume of material removed from a bearing surface.^{117, 118} Volumetric wear is calculated from either the 2-dimensional or 3-dimensional linear wear vectors; however, volumetric wear rates are not necessarily more accurate or informative than linear wear measurements.¹¹⁸ All studies of *Longevity* HXLPE liners presented in this document report linear wear data.

The preferred technique to assess HXLPE wear rates is radiostereometric analysis (RSA), which is a radiographic imaging technique that utilizes radiopaque markers to measure the direction and magnitude of femoral head penetration in 3 dimensions. RSA is considered an order of magnitude more accurate than 2-dimensional methods such as uniplanar radiographs.^{32, 118}

6.3.3 HXLPE versus Conventional Polyethylene Liners

Wear rates have been shown to be consistently lower with HXLPE liners than with conventional PE liners across a range of THA studies, from prospective, randomized, double-blind trials, to retrospective case control studies. In a meta-analysis of 10 clinical studies involving 852 THA procedures with a mean follow-up of 5.1 years, Kuzyk et al, found that HXLPE liners (including *Zimmer Longevity*, *Zimmer Durasul*, Stryker Crossfire, Stryker Duration, DePuy Marathon, and Kyocera Aeonian HXLPE Liners) outperformed conventional PE liners in terms of the radiological linear wear rate, with a significant difference of -0.07 mm/year (95% confidence interval [CI] -0.10 to -0.05; $p < 0.01$; $I^2 = 94\%$). Over this time period, the meta-analysis identified no significant differences in revision rate between HXLPE and conventional PE.¹¹⁹

6.3.4 Prospective Trials

Key Findings

- Prospective randomized double-blind studies have demonstrated wear rate reductions of up to 95% with HXLPE versus conventional PE in THA^{20, 33}
- In a randomized, double-blind, controlled study (N=54), the mean total linear femoral head penetration remained stable 7 years following primary THA in patients with *Zimmer Longevity* HXLPE liners (0.33 ± 0.10 mm); this measurement was significantly greater ($p=0.005$) in conventional PE patients (0.55 ± 0.10 mm)³²
- Mean total linear penetration from year 1 to year 7 post-THA was 0.04 ± 0.13 mm in *Longevity* HXLPE patients, demonstrating no significant change ($p>0.05$) versus year 1 measurements. Conventional PE patients had a mean total linear penetration of 0.23 ± 0.15 mm from year 1 to year 7, which was a significant increase ($p=0.01$) compared with year³²
 - Mean steady-state wear rates after 7 years were 87% lower with *Longevity* HXLPE (0.005 ± 0.015 mm/year) versus conventional PE (0.037 ± 0.019 mm/year)³²
 - In a blinded, controlled trial (N=100), the mean wear rate 5 years after primary THA was >95% lower in the *Zimmer Longevity* HXLPE group (0.003 ± 0.027 mm/year) compared with the conventional PE group (0.051 ± 0.022 mm/year)²⁰
- In a trial of 32 patients undergoing bilateral THA with *Zimmer Longevity* HXLPE liners implanted in one hip and conventional PE in the opposite hip, 5-year femoral head penetration rates were 0.016 mm/year with *Longevity* HXLPE versus 0.068 mm/year with conventional PE. Wear rates in this study were 99% to 100% lower with *Longevity* HXLPE than with conventional PE⁸

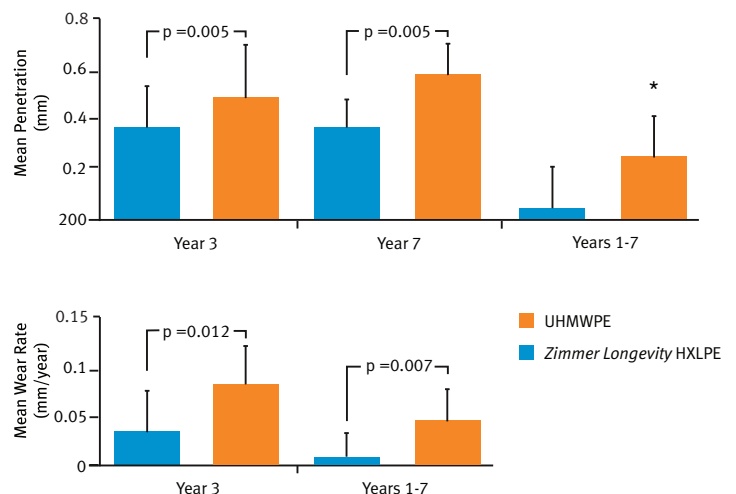
Prospective randomized double-blind studies have demonstrated an up to 95% reduction in wear rates with HXLPE versus conventional PE in THA.^{20, 33}

In a randomized, double-blind, controlled study performed by Glyn-Jones and colleagues, 54 patients received either *Zimmer Longevity* HXLPE or conventional PE liners in a primary THA procedure. Two-year outcomes showed that patients with *Zimmer Longevity* HXLPE liners experienced a 40% reduction in wear rate as assessed by RSA, as well as a significant reduction in the femoral head penetration rate: 0.06 ± 0.06 mm/year with

Longevity HXLPE versus 0.10 ± 0.07 mm/year with conventional PE ($p=0.04$). Both study groups exhibited similar improvements in Oxford Hip Scores (for more information on the Oxford Hip Score, see Section 2.6).³⁴

As shown in **Figure 16** (top graph), results at three years revealed a significantly lower mean femoral head penetration in the *Longevity* HXLPE group compared with the conventional PE group (0.35 ± 0.14 mm versus 0.45 ± 0.19 mm; $p=0.018$). In addition, as shown in the lower graph in **Figure 16**, after 3 years, the mean wear rate for patients remained significantly lower with *Longevity* HXLPE liners (0.03 ± 0.06 mm/year) than with conventional PE liners (0.07 ± 0.05 mm/year); this represented a 57% reduction in wear rate with *Longevity* HXLPE ($p=0.012$).³⁴

Figure 16. Mean penetration (top) and wear rate (bottom) in a prospective, double-blind, randomized study of *Zimmer Longevity* HXLPE versus conventional PE in THA³⁴

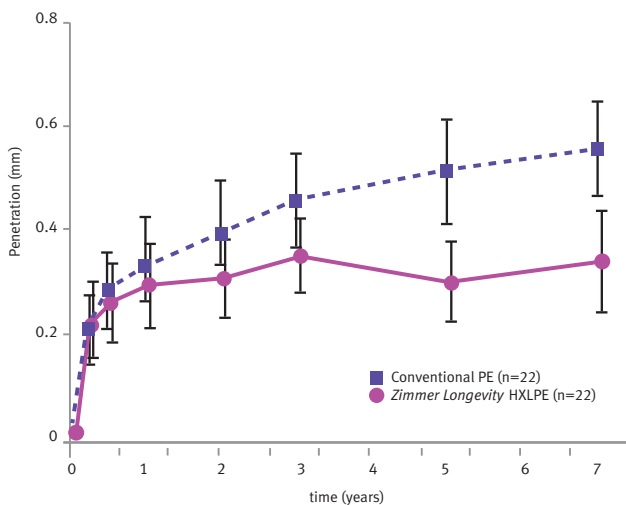


* $P=0.01$ versus penetration at one year in conventional PE group. Data for years 3 and 7 include changes due to creep. The contribution of creep has been eliminated in year 1-7 data

Study investigators also performed a seven-year follow-up analysis to determine outcomes with the effects of creep excluded. It was estimated that 95% of all creep occurred within six months of surgery, with nearly all creep occurring during the first year. No significant difference in the mean degree of creep was noted for the two liner types.³⁴

Figure 17 shows the mean total linear femoral head penetration over seven years for the *Zimmer Longevity* and conventional PE groups. At a minimum of seven post-operative years, the mean total linear penetration in the *Longevity* HXLPE group remained stable at 0.33 ± 0.10 mm, while it increased to 0.55 ± 0.10 mm in conventional PE patients ($p=0.005$). Excluding the contributions of creep (by assessing changes only between years 1 and 7), the mean total linear penetration was 0.04 ± 0.13 mm with *Longevity* HXLPE; this was not statistically significant compared with results at the end of year 1 ($p>0.05$). In contrast, mean total linear penetration between years 1 and 7 with conventional PE was significant (0.23 ± 0.15 mm; $p=0.01$).³²

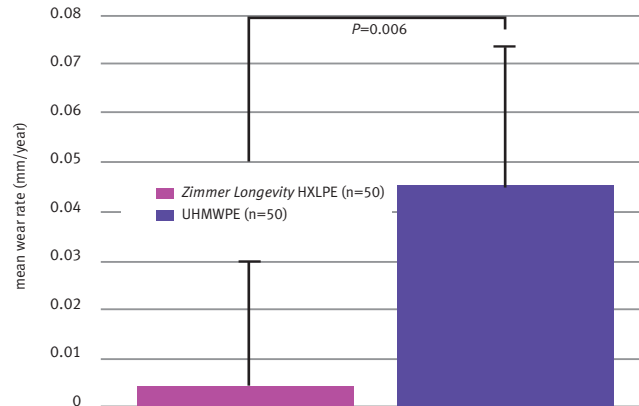
Figure 17.* Mean total linear femoral head penetration for *Zimmer Longevity* and conventional PE over 7 years in 44 patients who underwent primary THA³²



After the first year, both treatment groups exhibited a linear relationship between wear rates and time, with a mean steady-state wear rate (reflecting wear from year 1 to year 7) of 0.005 ± 0.015 mm/year for *Zimmer Longevity* HXLPE versus 0.037 ± 0.019 mm/year with conventional PE liners. As such, wear rate was reduced by 87% in patients who received *Longevity* HXLPE compared with the conventional PE group.³²

These study results are supported by five-year follow-up data from another blinded, controlled trial conducted by McCalden et al, in which 100 patients were randomized to receive either *Zimmer Longevity* HXLPE or conventional PE liners in a primary THA procedure. In this trial, the mean wear rate (defined as the femoral head penetration rate over years 1-5, and measured using an edge-detection method) was reduced by > 95% with *Longevity* HXLPE liners compared with conventional PE liners. As shown in **Figure 18**, wear rates were significantly lower in the *Longevity* HXLPE group than in the conventional PE group (0.003 ± 0.027 mm/year versus 0.051 ± 0.022 mm/year; $p=0.006$).²⁰

Figure 18. Steady-state wear rates over years 1-5 in 100 primary THA patients from a randomized, blinded, controlled clinical study²⁰



Curiously, among patients who received conventional PE liners, there was a significant difference in wear rates between men versus women ($p=0.014$). The femoral head penetration rate difference between women treated with either liner was not statistically significant ($p>0.05$). However, men in the conventional PE group experienced a significantly higher penetration rate (0.081 ± 0.065 mm/year) than either men (-0.013 ± 0.074 mm/year; $p<0.01$) or women (0.009 ± 0.028 mm/year; $p<0.05$) in the *Longevity* HXLPE group.^{7, 20}

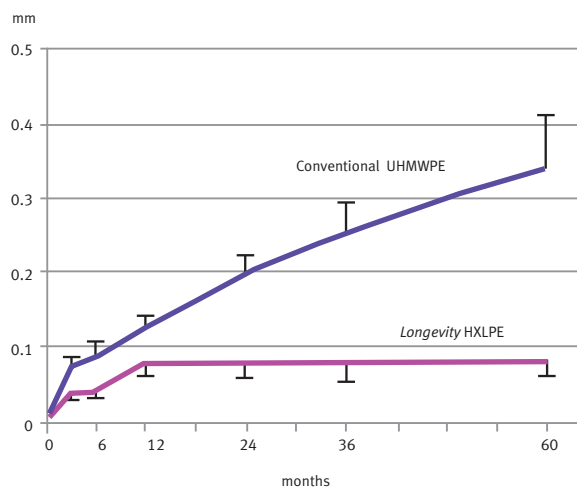
Similar differences in wear and penetration have been observed in another prospective five-year study. In this trial, 32 patients undergoing bilateral THA received *Zimmer Longevity* HXLPE liners in one hip joint and conventional PE liners on the opposite side; this study design facilitated a within-patient comparison between the two liner types.¹¹⁶

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As shown in **Figure 19**, femoral head penetration (measured with RSA) with *Longevity* HXLPE leveled off after the first year (measuring 0.079 mm at one year and 0.078 mm at five years), but continued to increase over time with the conventional PE liner. The penetration rate for *Longevity* HXLPE was 0.016 mm/year for the entire five-year study period (including the initial bedding in phase), compared with 0.068 mm/year for conventional PE.¹¹⁶

After the steady state had been reached (estimated at one year for Zimmer *Longevity* HXLPE and 6 months for conventional PE), no further penetration was detected with *Longevity* HXLPE, while the average penetration with conventional PE was 0.057 mm/year. Investigators concluded that wear rates were reduced by 99%-100% with *Longevity* HXLPE relative to conventional PE.¹¹⁶

Figure 19. Penetration of femoral head into the acetabular liner in patients with bilateral THA, *Zimmer Longevity* versus conventional PE¹¹⁷



*Penetration was measured in 19 patients from the study population for whom RSA data at 5 years were available

6.3.5 Retrospective Trials

Key Findings

- Retrospective analyses of THA patients have provided evidence of the benefits of HXLPE liners, demonstrating wear rate reductions of up to 95% with HXLPE versus conventional PE^{30, 33, 37, 120}
- In a 10-year comparative study of patients with *Zimmer Longevity* or *Durasul* HXLPE liners (n=224) versus patients with conventional PE liners (n=201), the HXLPE group exhibited no measurable wear, and had wear rates that were significantly lower than in the conventional PE group (p<0.0001)³³
- A 5-year study showed significantly lower total femoral head penetration with *Zimmer Longevity* HXLPE (0.496 mm) than with conventional PE (0.756 mm). Steady state wear rates were a significant 51% lower (p<0.001) in the *Longevity* HXLPE group (0.050 mm/year) versus the conventional PE group (0.101 mm/year)³⁷
- An investigation with a mean follow-up of 5.3 years found that total femoral head penetration and wear rates were significantly lower (p<0.001) in 34 *Zimmer Longevity* HXLPE patients (0.01 ± 0.34 mm and 0.002 ± 0.084 mm/year, respectively) than in 34 conventional PE patients (0.12 ± 0.073 mm and 0.12 ± 0.071 mm/year, respectively)³⁰
- In a study with a 2- to 4-year follow-up, the steady-state wear rate in 70 patients with *Zimmer Longevity* or *Durasul* HXLPE liners (0.007 ± 0.022 mm/year) was 95% lower than in 111 patients with conventional PE liners (0.174 ± 0.114 mm/year)¹²⁰

Retrospective analyses of THA patients have provided further evidence of the benefits of HXLPE liners, demonstrating reductions in wear rates of up to 95% with HXLPE versus conventional PE. In the longest comparative study conducted to date, Bragdon and colleagues investigated 10-year femoral head penetration and wear rates for *Zimmer Longevity* or *Zimmer Durasul*® HXLPE liners in 224 patients, representing 247 THA procedures, compared with a case-matched control set of conventional PE liners in 201 patients, representing 241 THA procedures. Steady-state penetration and wear rates were evaluated at each follow-up examination, relative to radiographic changes at one year.³³

As shown in **Figure 20**, femoral head penetration increased over time in the conventional PE group (top image); however, in the HXLPE group, penetration did not change after the first year (bottom image). In addition, wear rates with conventional PE were significantly greater than HXLPE wear rates ($p < 0.0001$); HXLPE liners exhibited no measurable wear.³³

Figure 20. Steady-state femoral head penetration (26 mm and 28 mm head sizes) assessed with follow-up radiographs: HXLPE (top) versus conventional PE (bottom)³³

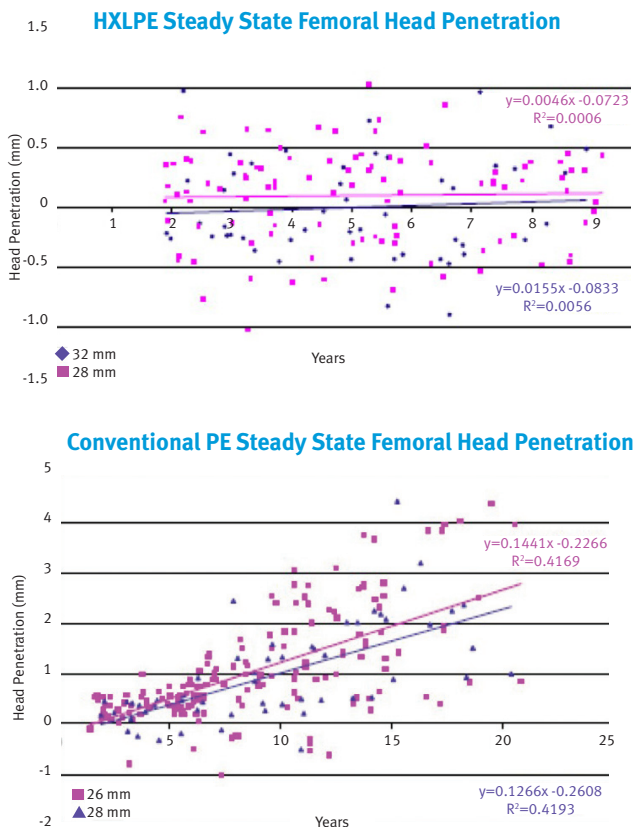


Table 3 shows the results from another retrospective study performed by Olyslaegers et al. This trial provided five years of follow-up data on femoral head penetration and steady-state wear rates in primary THA patients who received either *Zimmer Longevity* HXLPE (n=60) or conventional PE liners (n=20). Although femoral head penetration was similar in the two groups over the first year post-THA (0.297 mm versus 0.352 mm for *Longevity* HXLPE versus conventional PE), total penetration after five years was significantly greater in the conventional PE group (0.756 versus 0.496 mm, $p < 0.001$). Furthermore, *Longevity* HXLPE was associated with a significant 51% reduction in steady state wear compared with conventional PE (0.050 versus 0.101 mm/year, $p < 0.001$).³⁷

Table 3. Wear rates in retrospective study comparing the use of HXLPE to conventional PE in THA procedures

	HXLPE	Conventional PE	p value
Femoral head penetration at 1 year (mm)	0.297 ± 0.13	0.352 ± 0.12	$p > 0.05$
Femoral head penetration at 5 years (mm)	0.496 ± 0.14	0.756 ± 0.32	$p < 0.001$
Steady-state wear rate (mm/year)	0.050 ± 0.02	0.101 ± 0.07	$p < 0.001$

In another retrospective study with a mean follow-up of 5.3 years, Beksac and colleagues analyzed femoral head penetration and wear rates in 34 *Zimmer Longevity* HXLPE patients matched for age, gender, body mass index (BMI), and diagnosis, versus 34 conventional PE patients. All patients in the study underwent primary THA. Total penetration (0.01 ± 0.34 mm) and wear rates (0.002 ± 0.084 mm/year) were significantly lower with *Longevity* HXLPE than with conventional PE liners (0.12 ± 0.073 mm and 0.12 ± 0.071 mm/year, respectively; $p < 0.001$).³⁰

Even short-term results support the use of HXLPE over conventional PE. Manning et al conducted a study to retrospectively compare wear rates in primary THA patients who received *Zimmer Longevity* or *Zimmer Durasul* HXLPE liners (n=70) with patients who received conventional PE liners (n=111). Patients in the two groups were matched for age, sex, and BMI. The mean follow-up of HXLPE patients was 2.6 years (range: 24-44 months), compared with 2 to 4 years for the conventional PE group. The steady-state wear rate (assessed relative to two-year post-THA findings) in the HXLPE group was 95% lower than in the conventional PE group: 0.007 ± 0.022 mm/year versus 0.174 ± 0.114 mm/year, respectively ($p = 0.003$). Study investigators reported that the penetration rate in the HXLPE group was not affected by sex, age, activity, or BMI.¹²⁰

6.3.6 Retrieval Studies

Key Findings

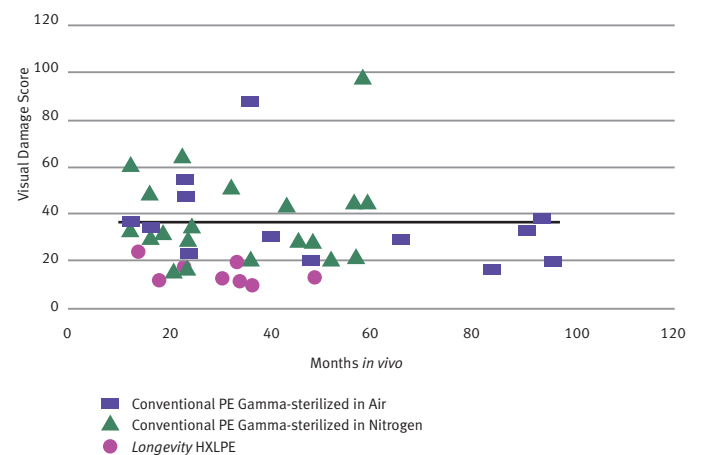
- In retrieval studies comparing *Zimmer Longevity* HXLPE with conventional PE liners, *Longevity* HXLPE liners have exhibited substantially less damage, including a reduction in cracking, pitting, scratching, burnishing, abrasion, impingement, and delamination of the liner surface³¹
- In one retrieval study of 46 acetabular components, the *Zimmer Longevity* HXLPE group (n=11) had an 80% reduction in wear, a 90% decrease in creep socket volume, and a 50% reduction in visual damage score compared with the conventional PE group (n=35)³¹
- Another retrieval study found that, compared with *Zimmer Longevity* and *Durasul* HXLPE liners (n=16), conventional PE liners (n=19) exhibited significantly greater signs of wear, including loss of machining marks and increased scratching and polishing. Remelt experiments showed that HXLPE liner wear was due to plastic deformation and not loss of material¹²¹

During retrieval studies, investigators assess changes in the condition of acetabular liners that are removed when patients undergo THA revision procedures. In two such studies comparing *Zimmer Longevity* HXLPE with conventional PE, *Longevity* HXLPE liners have exhibited substantially less damage, including a reduction in cracking, pitting, scratching, burnishing, abrasion, impingement, and delamination of the liner surface.³¹

In a retrieval study of 46 acetabular components performed by Salineros et al, wear and creep socket volume change were assessed at THA revision in patients who had received either *Zimmer Longevity* HXLPE liners (n=11) or conventional PE liners sterilized in air (n=12) or nitrogen (n=23). The most common reason for revision surgery in patients with conventional PE liners was implant loosening, while dislocation was the primary reason in the *Longevity* HXLPE group.³¹

Study findings revealed an 80% reduction in wear and a 90% decrease in creep socket volume in the *Longevity* HXLPE group compared with the conventional PE group. In addition, visual damage scores for *Longevity* HXLPE liners were 50% lower than those for conventional PE liners. As shown in **Figure 21**, the visual damage score did not correlate with length of *in vivo* implant time.³¹

Figure 21. Total visual damage score as a function of component time *in vivo*³¹



*Bold line indicates linear regression line, which demonstrates independence of component damage and time *in vivo*

Investigators found no evidence of delamination or cracking in any of the retrieved components. In addition, compared with conventional PE liners, *Longevity* HXLPE liners exhibited no notable damage due to impingement at the rim.³¹

In another retrieval study, the wear behavior of *Zimmer Longevity* or *Zimmer Durasul* HXLPE liners (n=16; *in vivo* duration 5 days to 18 months) versus conventional PE liners (n=19; *in vivo* duration 14 days to 10 months) in patients undergoing THA revision surgery due to sepsis, implant loosening, implant malpositioning, or recurrent dislocation was investigated.¹²¹

Compared with HXLPE liners, conventional PE liners exhibited significantly greater signs of wear, including loss of machining marks and increased scratching and polishing. Remelt experiments showed that wear signs in the HXLPE liners were the result of plastic deformation and not loss of material.¹²¹

6.3.7 Osteolysis

Key Findings

- Decreased acetabular liner wear rates are associated with a reduced risk of osteolysis
- The risk of osteolysis in THA patients rises as wear rate increases; osteolysis is rarely observed at wear rates <0.1 mm/year (defined as the osteolysis threshold)^{32, 59}
- A 7-year randomized, double-blind, controlled trial (N=54) showed that none of the patients with *Zimmer Longevity* HXLPE liners had wear rates exceeding the osteolysis threshold of 0.1 mm/year, while 9% of patients with conventional PE liners had wear rates above this threshold value³²
- In a retrospective study with a mean follow-up of 7.2 years, the incidence of osteolysis was 2% in the *Zimmer Longevity* HXLPE group (n=48) versus 24% in the conventional PE group (n=50), representing a 92% reduction in osteolysis risk with *Longevity* HXLPE³⁶
- An investigation with a mean follow-up of 5.3 years found that the average annual wear rate was significantly lower ($p<0.001$) in 34 *Zimmer Longevity* HXLPE patients (0.002 mm/year) than in 34 conventional PE patients (0.12 mm/year). Periprosthetic osteolysis was seen in 5.9% of hips implanted with *Longevity* HXLPE liners compared with 23.5% of those with conventional PE liners³⁰
- In a 5-year retrospective study, patients with *Zimmer Longevity* HXLPE liners (n=60) had a mean steady-state wear rate of 0.05 mm/year and an osteolysis incidence of 1.6%; corresponding values in patients with conventional PE liners (n=20) were 0.10 mm/year and 15%, respectively³⁷

Decreased acetabular liner wear rate is associated with a reduced risk of osteolysis, or bone resorption. Osteolysis results from inflammation due to the response of the immune system to wear debris released from liners over time, and is described in more detail in Section 2.3.³⁹ Investigations in THA patients have shown that the risk of osteolysis rises as the wear rate increases, and that at wear rates <0.1 mm/year, osteolysis is rarely observed.⁵⁹ By common convention, this rate has been defined as the osteolysis threshold.³²

In a seven-year randomized, double-blind, controlled trial (N=54) published by Thomas et al, osteolysis (identified by radiographic analysis) was found in 5% (n=1) of patients with *Zimmer Longevity* HXLPE liners patients versus 18% (n=4) with conventional PE liners. Although this difference was not

statistically significant ($p>0.05$), 9% of the conventional PE group had wear rates exceeding the osteolytic threshold of 0.1 mm/year, while none of the *Longevity* HXLPE patients had wear rates above this threshold value.³²

In a retrospective study with a mean follow-up of 7.2 years, Mall et al utilized computed tomography (CT) imaging to evaluate the incidence of osteolysis in 98 THA patients who had received either *Zimmer Longevity* HXLPE (n=48) or conventional PE liners (n=50). *Longevity* HXLPE was associated with a 92% reduction in the incidence of osteolysis, which was detected in only 2% of this patient cohort, compared with 24% of patients receiving conventional PE (statistical significance not reported). Although a statistical correlation between femoral head penetration and osteolysis could not be demonstrated, penetration was greater with conventional PE than *Longevity* HXLPE.³⁶

In another retrospective study, Beksac et al compared clinical outcomes with *Zimmer Longevity* HXLPE (n=34) versus conventional PE (n=34) liners in 68 THA patients over a mean follow-up of 5.3 years. *Longevity* HXLPE patients were found to have a significantly lower average annual wear rate (0.002 mm/year) than conventional PE patients (0.12 mm/year; $p<0.001$), as well as a reduced incidence of osteolysis and calcar resorption (rounding of the calcar with a convex shape and loss of contact between the prosthesis and microcollar bone). Periprosthetic osteolysis was found in 5.9% of hips implanted with *Longevity* HXLPE liners, compared with 23.5% of those with conventional PE liners, although this difference was not statistically significant ($p>0.05$). Approximately 9.8% of hips in the *Longevity* HXLPE group and 56.1% of hips in the conventional PE group had calcar resorption, which on average measured 2.5 mm (range, 2–3 mm) and 7.5 mm (range, 2–24 mm), respectively.³⁰

Finally, in a five-year retrospective study of 80 patients (n=60 *Longevity* HXLPE; n=20 conventional PE) detailed in Section 6.4.5, Olyslaegers et al documented osteolysis in 1.6% (n=1) of patients with a *Zimmer Longevity* liner. These patients had a mean steady-state wear rate of 0.05 mm/year. In contrast, 15% (n=3) of patients with a conventional PE liner had osteolysis. The wear rate in the conventional PE group was 0.10 mm/year.³⁷

Other studies investigating the risk of osteolysis with HXLPE versus conventional PE liners have reported no difference in osteolytic lesions with different liner types. In certain cases, the wear rates observed with both HXLPE and conventional PE liners were below the osteolysis threshold of 0.1 mm/year. In other instances, investigators have acknowledged that longer follow-up periods might be necessary to detect differences in osteolysis outcomes.^{20, 112} In addition, the majority of clinical trials comparing HXLPE with conventional PE liners have evaluated osteolysis based on radiographic analysis; however, radiographs may underestimate the incidence of osteolysis relative to other imaging modalities (eg, CT scans).^{36, 122, 123}

6.4 Other Clinical Considerations

6.4.1 Clinical Outcomes

Key Findings

- Clinical research has shown that the Harris and Oxford hip and WOMAC scores of patients with HXLPE liners are consistently improved over baseline values by one year post-THA^{20, 32, 38}
- A 5-year study showed significant postoperative improvements ($p < 0.01$) in Harris hip and WOMAC scores in 100 patients randomly assigned to receive either *Zimmer Longevity* HXLPE or conventional PE liners²⁰
- In an Australian registry with a follow-up of 9 years, the revision rate with HXLPE liners was 25.4% lower than with conventional PE liners⁴

Clinical outcomes following THA are typically evaluated using various disease-specific instruments, including the following:

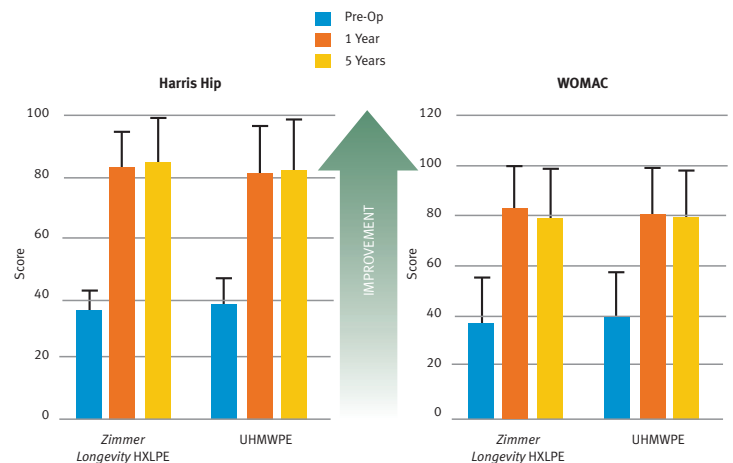
- The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), which consists of the WOMAC Pain subscale, the WOMAC Stiffness subscale, and the WOMAC Physical Function subscale
- The Harris Hip Score
- The Oxford Hip Score
- Revision Rate

In addition, general patient well-being may be evaluated using the Medical Outcomes Study Short-Form 36-Item Health Survey (SF-36) or the 12-item version (SF-12). All of these instruments are described in Section 2.6.

Clinical research has shown that the Harris and Oxford hip and WOMAC scores of patients with HXLPE liners are consistently improved over baseline values by one-year post-THA.^{20, 32, 38}

Figure 22 shows the results of a five-year study by McCalden et al, in which significant postoperative improvements ($p < 0.01$) in the Harris Hip Score and WOMAC score were observed in 100 patients randomly assigned to receive either *Zimmer Longevity* HXLPE or conventional PE liners.²⁰

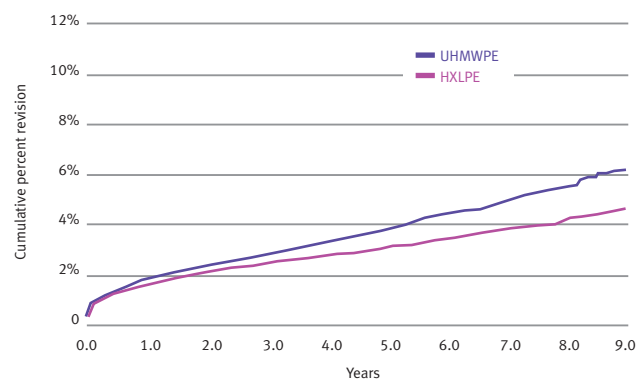
Figure 22. Harris Hip Scores and WOMAC over 5 years of follow-up in a double-blind, randomized, controlled trial of *Zimmer Longevity* versus conventional PE²⁰



*All changes from pre-operative status were significant ($p < 0.01$)

Based on existing studies with follow-up periods of ≤ 7 years, no prospective, randomized trials have demonstrated a difference between treatment groups in hip scores or other clinical outcomes (eg, revision rates, patient-reported outcomes) for HXLPE versus conventional PE liners.^{20, 32, 37, 119} However, as discussed in Section 6.1, a 25.4% lower revision rate with HXLPE versus conventional PE has been observed in a registry conducted in Australia with follow-up of up to nine years (**Figure 23**). These findings suggest that improved clinical outcomes might eventually be observed in longer-term prospective trials.⁴

Figure 23. Cumulative percent revision of primary total conventional hip replacement by type of polyethylene (primary diagnosis OA): data from the *Australian National Joint Replacement Registry*⁴



6.4.2 Femoral Head Size

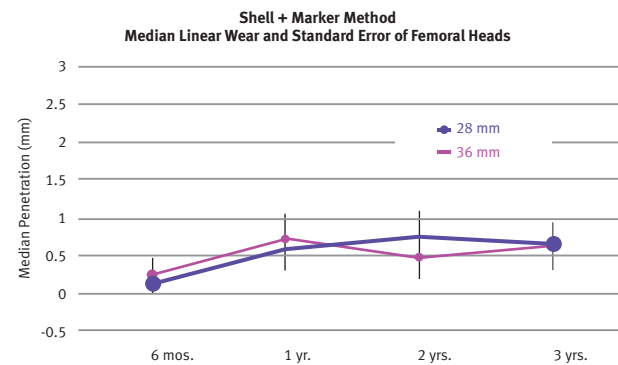
Key Findings

- Although some studies have shown an increase in volumetric wear rates with femoral head size, linear wear rates are generally independent of femoral head size¹²⁴⁻¹²⁶
- A 3-year study reported no difference in creep or wear rates for 28 mm (n=16) versus 36 mm (n=14) diameter heads in patients with *Zimmer Longevity* HXLPE liners⁴⁶
 - Median steady-state wear rates did not differ significantly ($p>0.05$) for 28 mm versus 36 mm head sizes (0.026 ± 0.024 mm/year and 0.000 ± 0.058 mm/year, respectively)
 - Total femoral head penetration did not differ significantly ($p>0.05$) for 28 mm versus 36 mm head sizes (0.062 ± 0.032 mm and 0.062 ± 0.063 mm, respectively)
 - No radiographic signs of osteolysis were detected
- A retrospective analysis with a minimum 10-year follow-up period showed no correlation between femoral head size and wear rates for 28 mm (n=25) and 32 mm (n=14) diameter heads with *Zimmer Longevity* or *Durasul* HXLPE liners^{35, 46}
 - Average steady-state wear rates were similar for the two head sizes (-0.015 mm/year for 28 mm and 0.045 mm/year for 32 mm)
 - No radiographic signs of osteolysis, loosening, or fracture were reported

Larger femoral heads are advantageous in that they improve stability, increase range of motion, and reduce the risk of neck-rim impingement in hip bearings.⁴²⁻⁴⁴ However, as femoral head size increases, acetabular liner thickness must be decreased due to physical space limitations.⁴⁴ Although some studies have shown that volumetric wear rates increase with femoral head size, linear wear rates are generally independent of head size.¹²⁴⁻¹²⁷ In one three-year study investigating the effect of femoral head size on performance, Bragdon et al reported no difference in creep or wear rates based on RSA of femoral head penetration for 28 mm (n=16) versus 36 mm (n=14) diameter heads in patients with *Zimmer Longevity* HXLPE liners. The median steady-state wear rate at three years (assessed relative to one-year post-THA findings) did not differ significantly between the two groups (0.026 ± 0.024 mm/year for 28 mm and 0.000 ± 0.058 mm/year for 36 mm diameter heads). As shown in [Figure 24](#), femoral head

penetration also did not differ significantly between groups or over time throughout the follow-up period. Total femoral-head penetration after three years was 0.062 ± 0.032 mm in the 28 mm and 0.062 ± 0.063 mm in the 36 mm groups ($p>0.05$). In addition, no radiographic signs of osteolysis or radiolucencies were detected.⁴⁵

Figure 24. Median superior femoral head penetration in patients with 28 and 36 mm diameter heads and *Zimmer Longevity* HXLPE liners⁴⁵



*Vertical lines represent standard deviations

In another study, conducted by investigators at Harris Orthopaedic Laboratory and based on a retrospective analysis with a minimum 10-year follow-up period, no correlation was found between femoral head size and wear rates for 28 mm (n=25) versus 32 mm (n=14) diameter heads in patients with *Zimmer Longevity* or *Durasul* HXLPE liners. The average steady-state wear rates, which were derived from linear femoral head penetration measurements at the latest follow-up (relative to 1-year post-THA findings) were similar for the two groups (-0.015 mm/year for 28 mm and 0.045 mm/year for 32 mm diameter heads). The negative value observed for patients with 28 mm heads indicates that wear rate values were below the resolution of the measurement device. No radiographic signs of peri-prosthetic osteolysis, loosening, or fracture were reported.^{35, 45}

These data are supported by findings from a case series study by Geller et al, in which larger femoral-head sizes were evaluated after 3.3 years of follow-up in 42 patients (45 hips) with *Zimmer Longevity* HXLPE (29 hips) or *Zimmer Durasul* HXLPE liners (16 hips). The average steady-state linear wear rate (assessed relative to 1-year post-THA findings) was 0.06 ± 0.41 mm/year for the overall population, and there was no significant difference in femoral head penetration rates for patients with 36, 38, or 40 mm diameter heads (-0.12 ± 0.22 mm/year, -0.08 ± 0.26 mm/year, and 0.11 ± 0.20 mm/year, respectively). When pooled, these data resulted in a wear rate approximating zero, suggesting no measurable wear in this population. Further, the investigators found no evidence of osteolysis, migration, aseptic loosening, or femoral component fracture in any of the patients.¹²⁴

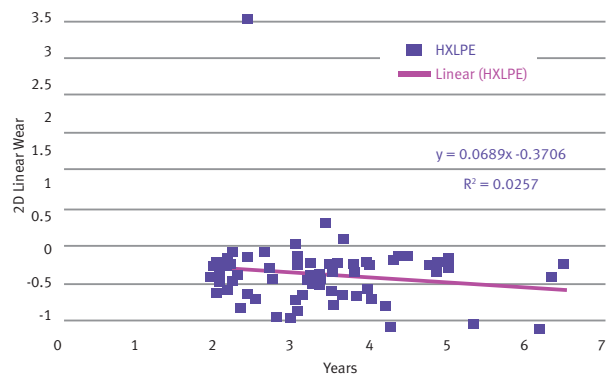
The potential for little or no wear and femoral head penetration over the long term may be of particular benefit for younger patients undergoing THA. In general, younger patients tend to be more active than elderly ones, which can lead to increased wear of hip implant material.¹²⁸ To date, three studies have examined the performance of HXLPE in patients <65 years of age.

In a two-year prospective, randomized study, Ayers et al compared the performance of *Zimmer Longevity* HXLPE (n=24) versus conventional PE (n=21) liners in THA patients ≤ 65 years of age (mean age 58 years). Mean total femoral head penetration was significantly lower with *Longevity* HXLPE than with conventional PE (0.07 mm versus 0.19 mm, respectively; $p < 0.05$), suggesting a 63% reduction in penetration and improved wear resistance. This difference was maintained even among obese patients (BMI > 30 kg/m²). All patients experienced improvements from baseline in functional and pain scores, with no significant differences between the two groups.³⁸

These findings are supported by a retrospective analysis performed by Mall et al in THA patients ≤ 55 years of age (mean age 43.2 [conventional PE group] and 46.5 [HXLPE group] years; N=98). After a mean follow-up of 7.2 years, CT imaging results revealed a 92% reduction in osteolysis incidence among patients with *Zimmer Longevity* HXLPE liners (n=48) compared with those with conventional PE liners (n=50).³⁶

In another retrospective study, Shia et al evaluated the performance of *Zimmer Longevity* HXLPE liners in 64 THA patients aged ≤ 50 years over an average follow-up of four years. As shown in **Figure 25**, the linear wear rate (assessed relative to 1-year post-THA findings) was -0.036 mm/year, representing an undetectable level of wear. There was no evidence of acetabular or femoral loss of fixation, subsidence, or loosening, and no incidents of catastrophic failure.³⁹

Figure 25. Linear wear of *Zimmer Longevity* HXLPE liners in patients ≤ 50 years of age, based on 2D radiographic analysis¹²⁸



6.4.3 Long-term Studies

Key Findings

- Since 1999, Zimmer HXLPE liners have been implanted in over 1 million patients, representing the most long-term, robust clinical dataset¹⁷
- *Zimmer Longevity* HXLPE liners consistently perform better than conventional PE in terms of wear rate, femoral head penetration, and osteolysis incidence in patients undergoing primary THA^{20, 32, 36, 122}
- In a 10-year follow-up study of 224 primary THA patients with *Zimmer Longevity* or *Durasul* HXLPE liners, steady-state femoral head penetration rates did not increase over time (after the first year) and were significantly lower than penetration rates observed with conventional PE ($p < 0.001$)^{33, 35}
 - The 10-year wear rate in HXLPE patients was -0.015 mm/year with 28 mm heads and 0.045 mm/year with 32 mm heads. Wear rates were significantly greater for conventional PE patients ($p < 0.001$), with values of 0.151 mm/year with 26 mm heads and 0.117 mm/year with 28 mm heads
 - There were no radiographic signs of loosening or fracture and no evidence of osteolytic lesions in the HXLPE group, and no revisions had to be performed due to wear or liner fracture
- A retrospective evaluation of 214 primary THA patients with 7 to 11 years of follow-up showed a significant reduction ($p < 0.01$) in femoral head penetration rates with HXLPE liners (0.0183 ± 0.065 mm/year) versus conventional PE liners (0.113 ± 0.131 mm/year)¹²⁷
 - No significant differences in penetration rates for 26 mm, 28 mm, and 32 mm diameter heads were reported in the HXLPE group
 - No radiographic evidence of osteolysis was observed

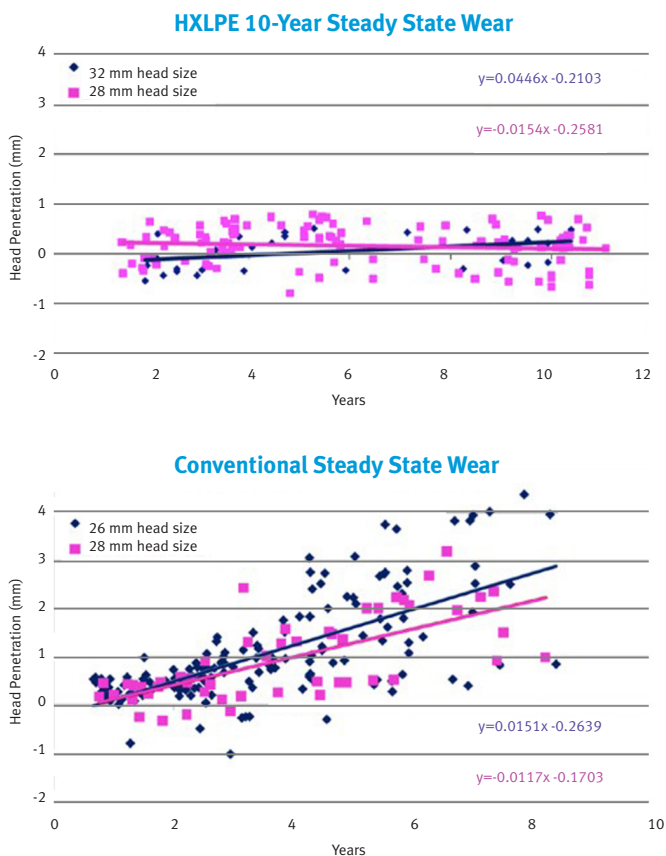
Since 1999, Zimmer HXLPE liners have been implanted in over 1 million patients, representing the most long-term, robust clinical dataset. In studies completed to date, *Longevity* HXLPE liners consistently perform better than conventional PE in terms of wear rate, femoral head penetration, and osteolysis incidence in patients undergoing primary THA.^{20, 32, 36, 122}

Ten-year follow-up data for patients receiving Zimmer HXLPE liners have recently been reported. As discussed earlier (see Section 6.3.5), in a 10-year follow-up study of 224 primary THA patients with *Zimmer Longevity* or *Zimmer Durasul* HXLPE liners, Bragdon et al found that steady-state femoral head penetration rates did not increase over time (after the first year) and were significantly less than rates observed with conventional PE ($p < 0.001$).³³

Among Zimmer HXLPE patients, the 10-year wear rate was -0.015 mm/year with 28 mm heads and 0.045 mm/year with 32 mm heads, with the negative wear rate indicating a level below the resolution of the detection equipment. In contrast, the conventional PE wear rate was 0.151 mm/year with 26 mm heads and 0.117 mm/year with 28 mm heads, with regression line slopes significantly greater than zero for both head sizes ($p < 0.001$).^{33, 35}

Figure 26 shows the steady-state wear rates based on femoral head penetration data for THA patients with Zimmer HXLPE (*Longevity* and *Durasul*) liners and conventional PE liners. The top graph shows results for 37 patients who had Zimmer HXLPE liners implanted for at least 10 years. The bottom graph shows results for 201 patients with conventional PE liners after a minimum follow-up of seven years. In the HXLPE patient group, there were no radiographic signs of loosening or fracture or evidence of osteolytic lesions, and no revisions had to be performed in this group due to wear or liner fracture.³⁵

Figure 26. Steady-state wear over at least 10 years in 37 patients receiving *Zimmer Longevity* or *Durasul* HXLPE liners (top) and at least 7 years in patients receiving conventional PE (bottom)³⁵



In another retrospective evaluation of 214 patients with 7 to 11 years of follow-up data, Jarrett et al provide further long-term evidence of the reduction in femoral head penetration rates with HXLPE liners (0.0183 ± 0.065 mm/year) versus conventional PE liners (0.113 ± 0.131 mm/year; $p < 0.01$) in primary THA, with no significant differences in penetration between head sizes with HXLPE (26 mm: 0.021 ± 0.035 mm/year, 28 mm: 0.0183 ± 0.065 mm/year, 32 mm: 0.007 ± 0.094 mm/year). No osteolysis was observed in radiographic assessment.¹²⁷

6.4.4 Quality of Life and Economic Value Outcomes

Key Findings

- Studies that measure patient quality of life (primarily using the 12- or 36-item Short Form [SF-12 or SF-36] questionnaire) have shown improvements over baseline values in patients with HXLPE liners^{20, 37}
- A blinded, randomized, controlled trial in 100 primary THA patients with *Zimmer Longevity* HXLPE or conventional PE liners showed that both treatment groups experienced significant improvements ($p < 0.01$) in SF-12 physical component scores at 1- and 5-year follow-up, compared with baseline. No significant differences were noted between the two groups ($p > 0.05$)²⁰
- In a 5-year retrospective study of patients with *Zimmer Longevity* HXLPE liners ($n=60$) and conventional PE liners ($n=20$), improvements in the SF-36 physical component score were observed, although there was no significant change in the SF-36 mental component subscores³⁷
- The observed 25.4% reduction in revision rate with HXLPE versus conventional PE liners in the Australian Registry is suggestive of an improved cost-benefit ratio for HXLPE liners⁴
- Since revision THA incurs substantially greater hospital charges than primary THA,³ an opportunity exists to reduce the long-term costs associated with additional revision THA procedures by using HXLPE prosthetic components

Studies that measure patient quality of life (primarily using the 12- or 36-item Short Form [SF-12 or SF-36] questionnaire, described in Section 2.6) have shown improvements (higher scores) over baseline values in patients receiving HXLPE, but have not demonstrated a significant difference versus conventional PE.^{20, 37} Table 4 shows one- and five-year results from a blinded, randomized, controlled trial conducted by McCalden et al involving 100 patients receiving either *Zimmer Longevity* HXLPE or conventional PE liners in a primary THA procedure. Both groups in this study experienced significant improvements in the SF-12 Physical Component Score (PCS) compared with pre-operative status ($p < 0.01$), but the between-group differences were not statistically significant ($p > 0.05$).²⁰

Table 4. Quality of life improvements in patients receiving *Zimmer Longevity* HXLPE or conventional PE liners²⁰

	Pre-operation	1 Year	5 Years
<i>Zimmer Longevity</i> HXLPE			
SF-12 MCS	53.38 ± 10.73	55.79 ± 7.38	55.24 ± 8.01
SF-12 PCS	25.70 ± 8.21	42.20 ± 11.37	37.24 ± 12.16
Conventional PE			
SF-12 MCS	54.40 ± 11.70	56.01 ± 8.55	53.36 ± 10.13
SF-12 PCS	26.10 ± 6.41	40.86 ± 11.11	40.00 ± 11.78

In a retrospective study with five years of follow-up conducted by Olyslaegers et al, no statistically significant differences were seen in the SF-36 mental component subscores among 60 patients who received *Zimmer Longevity* HXLPE liners and 20 patients with conventional PE liners (55.90 for HXLPE and 52.27, respectively), but there was improvement in the physical component score of the SF-36 (44.01 for *Longevity* HXLPE versus 37.34 for conventional PE).³⁷ It is likely that longer-term data will be needed to demonstrate quality of life improvements with *Longevity* HXLPE liners relative to conventional PE liners.

However, the 25.4% reduction in revision rate over 9 years that has been observed with HXLPE vs. conventional PE liners is suggestive of an improved cost-benefit ratio for HXLPE. Since revision THA incurs substantially greater hospital charges than primary THA,³ an opportunity exists to reduce the long-term costs associated with additional revision THA procedures by using HXLPE prosthetic components.

6.5 Summary

The benefits of *Longevity* HXLPE liners have been definitively established after 10 years of clinical experience—a longer duration of research-based follow-up than any other highly cross-linked acetabular liner. The unique manufacturing process used for *Longevity* HXLPE liners involves a high dose of proprietary e-beam radiation to induce polyethylene cross-linking, followed by remelting to reduce free radicals to nearly non-detectable levels. This process was specifically designed to minimize wear and increase long-term mechanical strength.

Longevity HXLPE liners provide the orthopedic surgeon with a highly advanced choice in bearing surfaces. Clinical evidence shows that *Longevity* HXLPE liners are highly wear-resistant and durable across a wide range of patient populations. *Longevity* HXLPE liners have also been studied in bearings with both small and large femoral heads, and exhibited no significant differences in linear wear rates as a function of femoral head size. These qualities translate to a reduced risk of osteolysis, a potentially reduced risk of revision surgery, and improvements in patient function and quality of life.

With an unparalleled body of clinical evidence demonstrating its efficacy and safety, *Longevity* HXLPE sets the standard for acetabular liners. As such, *Longevity* HXLPE liners are the ideal choice for a broad range of clinical situations.

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