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REVIEW

Effects of vitamin E incorporation in polyethylene on oxidative degradation, wear rates, immune response, and infections in total joint arthroplasty: a review of the current literature

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Abstract

Highly cross-linked ultrahigh molecular weight polyethylene (UHMWPE) was introduced to decrease wear debris and osteolysis. During cross-linking, free radicals are formed, making highly cross-linked polyethylene vulnerable to oxidative degradation. In order to reduce this process, anti-oxidant vitamin E can be incorporated in polyethylene. This review provides an overview of the effects of vitamin E incorporation on major complications in total joint arthroplasty: material failure due to oxidative degradation, wear debris and subsequent periprosthetic osteolysis, and prosthetic joint infections. Secondly, this review summarizes the first clinical results of total hip and knee arthroplasties with vitamin E incorporated highly cross-linked polyethylene. Based on in vitro studies, incorporation of vitamin E in polyethylene provides good oxidative protection and preserves low wear rates. Incorporation of vitamin E may have the beneficial effect of reduced inflammatory response to its wear particles. Some microorganisms showed reduced adherence to vitamin E–incorporated UHMWPE; however, clinical relevance is doubtful. Short-term clinical studies of total hip and knee arthroplasties with vitamin E–incorporated highly cross-linked UHMWPE reported good clinical results and wear rates similar to highly cross-linked UHMWPE without vitamin E.

Keywords Vitamin E · UHMWPE · Highly cross-linked polyethylene · Arthroplasty · Wear rates · Infection

Introduction

Ultrahigh molecular weight polyethylene (UHMWPE) has become the most frequently used material for acetabular components in total hip arthroplasty (THA) and tibial inserts in total knee arthroplasty (TKA) [1, 2]. As a result of polyethylene wear, intra-articular particle debris is formed. These particles can cause local immune system activation which leads to periprosthetic osteolysis and aseptic loosening [3].

In order to decrease the amount of wear, highly cross-linked UHMWPE was clinically introduced in the late 1990s. When UHMWPE is exposed to a high dose of ionizing radiation, free radicals are formed through C-bond scissoring. As soon as these free radicals are able to recombine with each other, the result will be cross-linking of the polyethylene.

Highly cross-linked UHMWPE has shown lower wear rates in vitro [4] and in vivo [5–7] compared to conventional (non-cross-linked) UHMWPE. However, a disadvantage of cross-linking is that not all free radicals are mobile enough to recombine, so some of them get trapped in the polyethylene [8]. If these residual free radicals react with oxygen, they cause oxidative degeneration, material embrittlement, and impairment of mechanical properties of the polyethylene [4, 9]. Thermal treatments of highly cross-linked UHMWPE like annealing or remelting were introduced, trying to reduce the amount of residual free radicals. Although these thermal treatments seem to improve the resistance against oxidative degeneration, [10, 11], they both have their limitations. Annealing highly cross-linked UHMWPE below its peak melting point reduces the amount of free radicals, yet, after terminally

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gamma sterilization, free radicals can still be measured [12, 13]. Studies of retrieved irradiated and annealed hip prosthesis have shown significant oxidation of the polyethylene [14–16]. Melting does eliminate the free radicals from highly cross-linked polyethylene. However, because of the formed crosslinks, recrystallization is hindered after melting and thereby the toughness and the fatigue strength are reduced [9, 17].

A more promising method to deal with this free radical issue seems to be the addition of vitamin E (alpha-tocopherol) to highly cross-linked UHMWPE. Vitamin E is a natural anti-oxidant which can bind to free radicals in polyethylene and thereby stop the oxidation cascade without reducing mechanical properties of the material [13, 18]. This could be especially useful for younger high demanding patients or arthroplasties more prone to PE wear such as dual mobility THAs [19, 20]. There are generally two methods of adding vitamin E to cross-linked UHMWPE. The first one is blending the vitamin E with UHMWPE resin powder before the irradiation and cross-linking process. Since vitamin E can also bind to free radicals during cross-linking, it reduces the cross-link formation. Therefore, the maximum amount of vitamin E blended into the UHMWPE without losing the desired decrease in wear rates is limited to 0.3 wt% [21–24]. Vitamin E containing UHMWPE produced by the second method is known as vitamin E–doped UHMWPE. Instead of adding the vitamin E before the cross-link formation, the polyethylene is first irradiated and afterwards doped in vitamin E. Since vitamin E is very hydrophobic, it diffuses into the cross-linked UHMWPE [25]. By doping the UHMWPE in vitamin E, a maximum concentration of approximately 0.7 wt% can be achieved due to the saturation limit of the cross-linked polyethylene [24]. The different UHMWPE stabilization methods are shown in Table 1.

Besides wear and material degradation, another major complication of total joint replacement is infection. The capability of microorganisms to attach to implanted material depends on several factors, such as the virulence of the involved microorganism, nutrient availability, the host immune system, and, moreover, the chemical surface characteristics of the implanted material [26, 27]. It has recently been suggested that the choice of bearing surface may affect the risk for prosthetic joint infections [28]. The addition of vitamin E to polyethylene could, besides improving oxidative resistance, influence these bearing surface characteristics and therefore play a role in the vulnerability of the implanted UHMWPE to infections.

In this study, we will point out the effects of adding vitamin E to UHMWPE on the major complications of total joint arthroplasty. Therefore, we will review the available literature on the influence of vitamin E on the mechanical properties, wear rates and subsequent aseptic loosening, and the risk of infections in total joint arthroplasties. Secondly, we will summarize the early clinical results of vitamin E–incorporated highly cross-linked UHMWPE in THA and TKA.

In vitro oxidation, mechanical behavior, and wear

Since oxidation leads to degeneration of polyethylene, and vitamin E increases the resistance of polyethylene against these oxidative processes by stabilizing the material, most in vitro studies used accelerating aging methods (i.e., exposure to high temperature, high pressure, and/or high oxygen concentrations) to simulate the natural oxidation process. Thereafter, oxidation and several mechanical properties are measured in order to test oxidative vulnerability.

Oxidation index

The oxidation index reflects the part of oxidized bonds on the surface of the material and can be used as a degree for oxidation in UHMWPE. Conventional UHMWPE with vitamin E showed significantly lower oxidation indexes after accelerated aging, compared to unstabilized conventional UHMWPE [29–31]. As for the non-cross-linked material, highly cross-

Table 1 Definitions used to describe studies with stabilized UHMWPE. These stabilization methods are used for free radical stabilization in highly cross-linked UHMWPE. However, for research purposes, a lot of studies described in this review used stabilization with vitamin E on conventional (non-cross-linked) UHMWPE as well

Free radicals stabilization	Method	Limitation
Unstabilized	None	No free radical stabilization
Annealing	Thermal treatment below melting point	Residual free radicals
Remelting	Thermal treatment above melting point	Decrease in fatigue strength
Vitamin E blended	Vitamin E mixed with UHMWPE resin powder before consolidation and irradiation	Decrease in cross-link formation, thereby limiting vitamin concentration to ± 0.3 wt%
Vitamin E doped	Consolidated UHMWPE infused with vitamin E after irradiation[a]	Vitamin E concentration limited to ± 0.7 wt% because of saturation limit

[a] Gamma sterilization (25–40 kGy) can be used to sterilize the final product, and therefore, it is done after vitamin E infusion in vitamin E–doped UHMWPE

linked UHMWPE incorporated with vitamin E showed lower oxidation indexes after accelerated aging, when compared to unstabilized conventional UHMWPE [32–37] and unstabilized highly cross-linked UHMWPE [23, 24, 32, 38]. Even when highly cross-linked vitamin E–blended UHMWPE was compared to highly cross-linked UHMWPE that had been stabilized by remelting, the vitamin E–incorporated material showed lower oxidation indexes after accelerated aging [10].

Both vitamin E–blended [10, 23, 29–32, 38] and vitamin E–doped [33–37] UHMWPE revealed excellent oxidative resistance in accelerated aging studies. When oxidation indexes of highly cross-linked vitamin E–blended UHMWPE and highly cross-linked vitamin E–doped UHMWPE were compared, the oxidation index of highly cross-linked vitamin E–blended samples showed a slight increase after ten months of real-time aging, whereas the oxidation indexes of vitamin E–doped samples did not increase throughout three years of real-time aging [24]. This can be explained by the higher antioxidant concentration of the vitamin E–doped samples and correlates with other studies, in which even low concentrations (i.e., 0.01 wt%) of vitamin E protected highly cross-linked UHMWPE against oxidation, notwithstanding the better oxidative protection provided by higher concentrations of vitamin E (i.e., 0.05–1 wt%) [32, 38].

Mechanical properties and fatigue strength

When conventional UHMWPE was exposed to accelerated aging, a severe decrease in mechanical strength, ultimate tensile strength, and elongation at break was seen afterwards, due to oxidative embrittlement of the material [29, 39]. On the contrary, when vitamin E was blended with conventional UHMWPE, these mechanical properties stayed nearly constant after accelerated aging [29]. The mechanical strength of unstabilized highly cross-linked UHMWPE decreased severely after accelerated aging, [23, 32]; however, when highly cross-linked UHMWPE was blended with [23, 32] or doped in [33, 34, 39] vitamin E, a significantly smaller decrease in mechanical properties was seen after accelerated aging. Kurtz et al. [32] have shown that blending just 0.0125 wt% vitamin E with highly cross-linked UHMWPE resulted in a smaller decrease of mechanical properties after accelerated aging; however, a higher concentration of 0.05 wt% ensured maintenance of mechanical properties for a longer period.

The fatigue strength or crack propagation is also affected by oxidative embrittlement. The fatigue strength of unstabilized conventional UHMWPE did significantly decrease after accelerated aging; addition of vitamin E prevented this decrease in fatigue strength [30, 31, 33, 34, 37]. Conventional UHMWPE blended with vitamin E showed less internal defect formation compared to unstabilized conventional UHMWPE, when tested in a knee simulator after accelerated aging [30, 31]. Before accelerated aging, the fatigue strength of highly cross-linked UHMWPE doped with vitamin E was lower compared to unstabilized conventional UHMWPE, at least similar to unstabilized highly cross-linked UHMWPE and higher compared to highly cross-linked remelted UHMWPE [36, 39]. This can be explained since cross-linking reduces the fatigue strength and remelting reduces it even more. Highly cross-linked UHMWPE doped in vitamin E maintained its original fatigue strength after accelerated aging [33, 34, 37] where, on the other hand, the fatigue strength of unstabilized conventional UHMWPE decreased till values below those of the highly cross-linked vitamin E–doped samples [34].

Wear rates

Highly cross-linked UHMWPE has proven lower wear rates than conventional UHMWPE [4–7], but its vulnerability to oxidation does not raise concerns just about mechanical properties; also, the increased wear of the material after oxidative embrittlement is an issue.

Highly cross-linked UHMWPE incorporated with vitamin E has shown lower wear rates compared to conventional UHMWPE when tested in a unidirectional wear tester [35], hip joint simulator [10, 39, 40], or knee joint simulator [33, 34], since cross-linking reduces wear rates. When the materials were exposed to accelerated aging, the wear rates of the conventional gamma-sterilized samples significantly increased, whereas the wear rates of the highly cross-linked vitamin E–incorporated samples remained constant [10, 33, 35, 36].

The incorporation of vitamin E seems to give an even better protection against oxidative embrittlement than remelting. When tested on a hip joint simulator, the wear rates of highly cross-linked vitamin E blends remained constant through six weeks of accelerated aging. The wear rates of highly cross-linked remelted UHMWPE remained constant for up to four weeks, but slightly increased after five weeks and showed a ten-fold increase after six weeks of accelerated aging [10].

Influence on the immune system

In order to analyze whether the incorporation of vitamin E could affect the immune response to UHMWPE wear particles, Bladen et al. [41] cultured human peripheral blood mononuclear cells (PBMNCs) with wear particles and measured the secreted inflammatory cytokines. PBMNCs cultured with wear particles from unstabilized conventional UHMWPE showed a significant increase in cytokines secretion compared to negative control PBMNCs. On the contrary, PBMNCs cultured with wear particles from the vitamin E blends secreted very low levels of cytokines, similar to

cytokines secretion of negative control PBMNCs. To confirm the ability of vitamin E to reduce the biological activity, the authors separately added vitamin E as a liquid to stimulate positive control PBMNCs, and a significant reduction in cytokine secretion was found compared to positive controls without the addition of vitamin E.

The in vitro immune response to highly cross-linked UHMWPE wear particles and highly cross-linked vitamin E–blended UHMWPE wear particles has also been studied [42]. PBMNCs cultured with particles from highly cross-linked vitamin E–blended UHMWPE secreted TNF-α levels similar to negative controls and significantly lower compared to PBMNCs cultured with unstabilized highly cross-linked wear particles. In accordance with this anti-inflammatory effect, two in vivo murine studies showed significantly less osteolysis after implantation of wear particles from highly cross-linked vitamin E–blended UHMWPE, compared to particles from highly cross-linked UHMWPE without vitamin E [43, 44].

On the contrary, Reno et al. [45] showed increased secretion of the inflammatory protease MMP-9 in response to vitamin E–blended conventional UHMWPE, compared to unstabilized conventional UHMWPE. The authors showed that this increased secretion might be actuated by vitamin E–dependent PP2A activation. In a second study, immunoglobulin G (IgG) adsorption was analyzed [46]. Since macrophages adhesion is known to be mediated by IgG, an increased IgG adsorption onto the surface could induce macrophages adhesion and activation. When conventional UHMWPE samples and vitamin E–blended conventional UHMWPE samples were placed in human plasma, the materials adsorbed similar amounts of plasma proteins; however, the vitamin E–blended samples adsorbed significantly less IgG and IgG fragments, compared to unstabilized samples. This suggests vitamin E–blended UHMWPE to have reduced macrophage adhesion and activation potential.

The immune response against wear particles is a very complex system including lots of different inflammatory cytokines and many different pathways. Therefore, different secretion of inflammatory mediators could be explained very well, and some of them might be influenced by vitamin E. In vivo response to wear particles is more complex, and the results of the few in vitro studies with vitamin E–blended wear particles may not be generalized.

Influence on bacterial adhesion and biofilm formation

The role of vitamin E on the physical and chemical properties of UHMWPE in regard to its vulnerability to prosthetic joint infections has been the subject of several studies. Gomes-Barrena et al. [47] compared adherence of *Staphylococcus aureus* and *S. epidermidis* strains on unstabilized conventional UHMWPE to vitamin E–blended and vitamin E–doped conventional UHMWPE after 90 minutes of incubation. When all the strains, per species, had been analyzed together, no significant difference in adherence was found between vitamin E–incorporated UHMWPE and unstabilized UHMWPE for both *S. aureus* and *S. epidermidis*. When the different strains were analyzed separately, high variation per stain was seen. Two strains were analyzed on vitamin E–doped UHMWPE. One *S. aureus* strain showed similar adhesion to conventional UHMWPE without vitamin E and vitamin E–doped UHMWPE; however, one *S. epidermidis* strain showed significant less adhesion to UHMWPE doped in vitamin E. Comparison between conventional vitamin E–blended UHMWPE and unstabilized conventional UHMWPE was done with 11 strains; two strains showed significant less adhesion and one strain showed significant more adhesion to vitamin E–blended UHMWPE compared to conventional UHMWPE without vitamin E. With regard to the physicochemical surface properties, the authors have found that doping samples in vitamin E resulted in an increased surface hydrophobicity and a lower total surface free energy. This might play a role in the lower bacterial adhesion seen on vitamin E–doped samples with one *S. epidermidis* strain. No difference in surface properties of vitamin E–blended samples was found compared to samples without vitamin E, and a direct antimicrobial effect of vitamin E was ruled out tested by vitamin E microdilution.

Banche et al. [48] have analyzed bacterial growth of three *S. epidermidis* strains after three, seven, 24, and 48 hours of incubation on conventional UHMWPE and vitamin E–blended conventional UHMWPE. After 24 and 48 hours, all strains showed significant less adhesion to vitamin E–blended samples. In a second study, they found significantly less bacteria after 48 hours of incubation on vitamin E–blended samples compared to conventional samples without vitamin E, with two *S. aureus* strains and two *Escherichia coli* strains [49]. A third study showed lower fungal adhesion to vitamin E–blended samples, with two *Candida albicans* strains at three, seven, 24, and 48 hours of incubation [50]. The beneficial effect of vitamin E blends on bacterial adhesion found in these studies could not be explained by different surface properties.

More recently, in their in vivo murine study, Chen et al. [44] found, besides less inflammatory cytokines secretion and less osteolysis, less *S. aureus* growth in the presence of wear particles from vitamin E–blended highly cross-linked UHMWPE compared to particles from highly cross-linked UHMWPE without vitamin E. This suggests the incorporation of vitamin E to affect the immune response to wear particles and thereby also to protect against infections.

Williams et al. [51] indicated that the statistically significant results found in the previously described bacterial adherence studies are not clinically relevant, since reductions in

bacterial adhesion of only 1 $\log^{10}$ CFUs/mL or less were found. They explained that such a small reduction will most likely not prevent a prosthetic joint infection. Therefore, they have used a more clinically relevant flow system to analyze adhesion of a *MRSA* strain to conventional UHMWPE, highly cross-linked UHMWPE without vitamin E, and highly cross-linked vitamin E–blended UHMWPE. After 48 h of incubation, no statistically different bacterial adhesion between the materials was seen. The authors concluded that highly cross-linked vitamin E–blended UHMWPE was not able to prevent prosthetic joint infection with the *MRSA* strain. In accordance, Kyomoto et al. [52] found no difference in *S. aureus* biofilm formation on highly cross-linked vitamin E–blended UHMWPE compared to highly cross-linked UHMWPE without vitamin E. They also found no effect of blending vitamin E on material surface properties.

Clinical data

Since vitamin E–incorporated UHMWPE was clinically introduced just a few years ago, only short-term follow-up studies are available yet. Recent clinical studies measured femoral head penetration (FHP) rates of vitamin E–incorporated acetabular liners with radiostereometric analysis in THA [53–60]. The results of these studies are summarized in Table 2. During the first years after implantation, no distinction between creep (material deformation without particle debris) and wear can be made. Two studies showed significantly lower FHP rates during the first year after implantation for highly cross-linked vitamin E–incorporated liners compared to highly cross-linked liners without vitamin E, suggesting that the vitamin E–doped liners were more creep resistant [55, 60].

Three RCTs compared FHP after more than two years between highly cross-linked vitamin E–incorporated acetabular liners and control liners without vitamin E [57, 59, 60]. They all found significantly lower FHP rates for the vitamin E–incorporated liners suggesting lower wear rates. However, control groups and vitamin E liner groups both had very low FHP rates, below the reported osteolytic threshold of 0.1 mm/year [61], and therefore, the measured statistically lower FHP is probably not clinically relevant. From the reported studies, we can conclude that both vitamin E–blended and vitamin E–doped highly cross-linked acetabular liners are well tolerated in vivo; all studies reported post-operative improved functional hip scores, and no aseptic loosening was reported.

Only one clinical study on TKA with vitamin E–doped tibial inserts was found [62]. One hundred sixty-three TKAs with a mean follow-up of 3.2 years showed good clinical results and no aseptic loosening. Three two-stage revisions were performed due to infection, and four revisions were performed for arthrofibrosis or instability.

Two case reports of early vitamin E–doped highly cross-linked polyethylene failure are reported, one acetabular liner fractured 46 weeks after implantation, and one tibial insert fractured 30 months after implantation without trauma [63, 64]. The reported infection rates do not directly support the hypothesis of reduced bacterial adherence in vitamin E–incorporated UHMWPE. Of 107 patients who received a highly cross-linked vitamin E–blended acetabular liner, two revisions were necessary due to infection [53]. Two studies with highly cross-linked vitamin E–doped acetabular liners together reported two revisions due to infection in 109 THAs [54, 55]. In comparison, just 0.6% revisions due to infection were reported in a large Scandinavian epidemiological study on THA [65].

Conclusions and future prospects

This review leads to the following conclusions:

1. Based on in vitro studies, incorporation of vitamin E to UHMWPE provides good oxidative protection, which prevents decrease in mechanical behavior and preserves low wear rates after exposure to oxidation.
2. Vitamin E–blended UHMWPE may have the beneficial effect of reduced inflammatory response to its wear particles; however, lack of clinical studies makes the evidence very weak.
3. Some bacterial strains showed reduced adherence to vitamin E–incorporated UHMWPE. However, the mechanism through which vitamin E might reduce bacterial adherence is unclear, and clinical relevance is doubtful. In vivo bacterial adhesion to vitamin E–incorporated UHMWPE is barely studied, and it is unknown if there is a combined effect of vitamin E incorporation on immune system response and vulnerability to infections.
4. Clinical studies of highly cross-linked vitamin E–incorporated acetabular liners, with a maximum of 5-year follow-up, reported good clinical results and femoral head penetration similar to highly cross-linked UHMWPE without vitamin E and no aseptic loosening.

Unfortunately, long-term clinical data on revision rates for vitamin E–incorporated UHMWPE are not available yet, and therefore, actual clinical influences on wear rates, oxidative material degradation, aseptic loosening, and infection cannot be evaluated. To assess the clinical influence of bearing type on revision rates, studies will require thousands of patients to be followed for several decades. Such data may soon become available from national joint registries, and their evaluation will shed a light on the net influence of bearing type and vitamin E incorporation on revision risk.

Table 2 clinical studies about femoral head penetration rates of vitamin E–incorporated acetabulum liners measured with radiostereometric analysis in THA

Study	Design	*N* (hips)	Material	Follow-up	Main outcome	Main result
Halma et al. (2014) [53]	Cohort study	107	Highly cross-linked vitamin E–blended acetabular liner (Vitamys, Mathys)	2 years	FHP at 1 and 2 years	1st year mean FHP 0.073 mm; 2nd year mean FHP 0.035 mm
Sillesen et al. (2015) [54]	2 centre cohort studies	84	Highly cross-linked vitamin E–doped acetabular liner (E1, Biomet)	3 years	FHP at 1 and 3 years	No significant increase in FHP between 1st and 3rd year. Median FHP after 1 year, 0.019 mm and 0.022 mm. Median FHP after 3 years, 0.028 mm and 0.043 mm
Salemyr et al. (2015) [55]	RCT	25 vitamin E liners, 26 HXLPE liners (control)	Highly cross-linked vitamin E–doped acetabular liner (E1, Biomet); control: highly cross-linked liners (Marathon-liner, Depuy Johnson&Johnson)	2 years	FHP at 6 weeks, 3, 6, 12, and 24 months	Significant lower FHP rates at 6 weeks and 3,6, and 12 months for vitamin E–doped liners. Vitamin E liner: 0.16 mm (6 weeks), 0.15 mm (3 months), 0.16 mm (6 months), 0.20 (12 months), and 0.23 mm (24 months); control: 0.22 mm (6 weeks), 0.24 mm (3 months), 0.26 mm (6 months), 0.31 mm (12 months), and 0.30 mm (24 months); $p < 0.05$
Shareghi et al. (2015) [56]	RCT	38 vitamin E liners, 32 HXLPE liners (control)	Study group: highly cross-linked vitamin E–doped acetabular liner (E-Poly, Biomet); control: highly cross-linked liners, stabilized by annealing (ArComXL, Biomet).	2 years	FHP at 3, 12 and 24 months	No significant differences between groups. Vitamin E liner: 0.04 mm (3 months), 0.05 mm (12 months), and 0.06 mm (24 months); control: 0.03 mm (3 months), 0.04 mm (12 months), and 0.10 mm (24 months)
Shareghi et al. (2017) [57]		37 vitamin E liners, 26 HXLPE liners (control)		5 years	FHP at 5 years	Significant lower FHP for vitamin E liner: 0.13 mm vs 0.2 mm ($p < 0.001$)
Nebergall et al. (2016) [58]	Cohort study	51	Highly cross-linked vitamin E–doped acetabular liner (E1, Biomet)	5 years	FHP at 0.5, 1, 2, 3, and 5 years	− 0.02 mm (0.5 years), 0.03 mm (1 year), 0.05 mm (2 years), 0.05 mm (3 years), 0.04 mm (5 years)
Nebergall et al. (2017) [59]	RCT	32 vitamin E liners, 35 HXLPE liners (control)	Study group: highly cross-linked vitamin E–doped acetabular liner (E1, Biomet); control: highly cross-linked liners, stabilized by annealing (ArComXL, Biomet)	5 years	FHP at 3 and 5 years	Significant lower FHP rates for vitamin E–doped liners. Vitamin E liner: − 0.04 mm (3 years), − 0.04 mm (5 years); control: 0.02 mm (3 years), 0.07 mm (5 years); $p = 0.029$ (3 years), $p = 0.019$ (5 years)
Scemama et al. (2017) [60]	RCT	50 vitamin E liners, 50 conventional liners (control)	Study group: highly cross-linked vitamin E –blended acetabular liner (Vitamys, Mathys); control: conventional gamma sterilized liners (RM pressfit, Mathys).	3 years	FHP at 3 years	Significant lower FHP rates for vitamin E–blended liners. Vitamin E liner: 0.072 mm; control: 0.318 mm; $p = 0.04$

FHP, femoral head penetration; *RCT*, randomized controlled trial; *HXLPE*, highly cross-linked polyethylene

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Compliance with ethical standards

Opinions and assertions contained herein are those of the authors and are not construed as necessarily representing views of their employer.

Conflict of interest The authors declare that they have no conflict of interest.

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