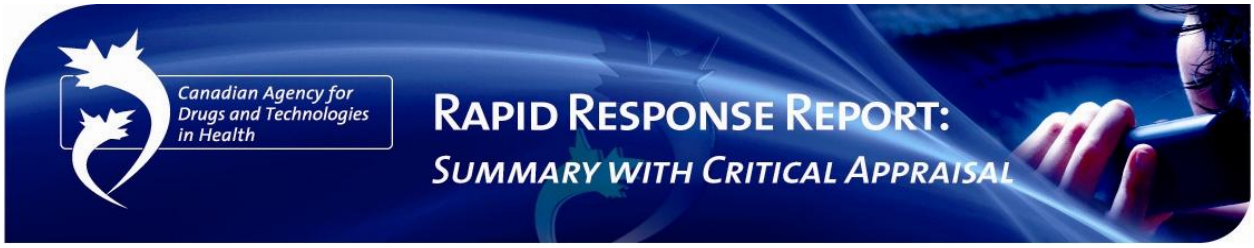

TITLE: Vitamin E Infused Polyethylene Liners, Conventional Polyethylene Liners, and Cross-Linked Polyethylene Liners for Knee Articular Resurfacing in Adults: A Review of Clinical and Cost-Effectiveness

DATE: 21 November 2012

CONTEXT AND POLICY ISSUES

Total knee arthroplasty (TKA) or total knee replacement (TKR) consists of resectioning the diseased knee articular surfaces, followed by resurfacing with metal and/or polyethylene prosthetic components.[1] In 2009-2010, the Canadian Joint Replacement Registry reported 22,545 knee replacements occurred in Canada.[2] For the properly selected patient, it is believed the procedure results in significant pain relief, improved function and quality of life.[1] The knee articular surface consists of articular cartilage that touches three bone surfaces of the knee: lower femur, upper tibia surface, and the back surface of the patella.[3] The tibial component is typically a flat metal platform with a cushion of strong, durable polyethylene in between the bones.[3]

There are numerous types of polyethylene prosthetic components, which could be used during knee articular resurfacing or total knee arthroplasty (or replacement) to restore the "cushion" between the bones. The options include conventional polyethylene (CPE) liners/implants, highly cross-linked polyethylene (HXPE) liners/implants and vitamin E infused polyethylene liners/implants. CPE liners differ from HXPE liners in terms of their properties and composition. HXPE implants are sterilized and thermally stabilized with more gamma radiation than the CPE implants.[4] Gamma radiation sterilization causes crosslinking of polymer. It is believed the process of crosslinking may reduce fracture strength or toughness and fatigue resistance.[4,5] It has been suggested these factors could make individuals uneasy when selecting highly cross-linked polyethylene in TKA.[4] However, some sources suggest cross-linking increases wear resistance of polyethylene knee bearing by as much as 100 fold.[5]

The addition of vitamin E to the polyethylene "cushion" component of knee resurfacing could be a promising approach to increase the wear resistance of polyethylene.[6] This approach involves vitamin E blended into the resin homogenously through the insert component.[6] The proposed benefits may occur because vitamin E forms a protective lining for our cells. This approach aims to alleviate the key issues limiting the longevity and durability of polyethylene joint replacements: polyethylene wear particles, wear particle mediated aspect loosening and

oxidation.[7] It is believed vitamin E may reduce the rate of revision surgery (or failure).[7] In addition, there are claims vitamin E may improve tensile strength while preventing polyethylene degeneration by oxidation.[6]

The purpose of the current review is to examine the comparative clinical effectiveness and cost-effectiveness of vitamin E infused polyethylene liners, cross-linked polyethylene liners and conventional polyethylene liners for knee articular resurfacing.

RESEARCH QUESTIONS

1. What is the comparative clinical effectiveness of vitamin E infused polyethylene liners, cross-linked polyethylene liners, and conventional polyethylene for knee articular resurfacing in adults?

2. What is the cost-effectiveness of vitamin E infused polyethylene liners, cross-linked polyethylene liners, and conventional polyethylene liners for knee articular resurfacing in adults?

KEY FINDINGS

There is no evidence to suggest highly cross-linked polyethylene liners and conventional polyethylene liners differ on failures, revisions and reasons for failure for adults undergoing knee articular resurfacing. There is no literature available comparing vitamin E infused polyethylene liners to highly cross-linked liners or conventional polyethylene liners. No literature was available on the cost-effectiveness of vitamin E infused polyethylene liners, highly cross-linked polyethylene liners, and conventional polyethylene liners.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including Ovid Medline, PubMed, The Cochrane Library (2012, Issue 10), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI (Health Devices Gold), Canadian and major international health technology agencies, as well as a focused Internet search. No methodological filters were applied to limit retrieval by publication type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2007 and October 25, 2012.

Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications and evaluated the full-text publications for final article selection (Table 1).

Table 1: Selection Criteria

Population	Adults undergoing knee articular resurfacing
Intervention	**THREE COMPARISONS** 1. Vitamin E infused polyethylene liners versus cross-linked polyethylene liners 2. Vitamin E infused polyethylene liners versus conventional polyethylene liners 3. Cross-linked polyethylene liners versus conventional polyethylene liners
Comparator	
Outcomes	Failure rates, reasons for failure, costs, cost-effectiveness
Study Designs	Health technology assessments, systematic reviews meta-analyses, randomized controlled trials, non-randomized studies and economic evaluations

Exclusion Criteria

Studies were excluded if they did not meet the selection criteria, were duplicate publications or included in a selected systematic review, or were published prior to 2007.

Critical Appraisal of Individual Studies

Randomized controlled trial (RCT) and non-randomized study quality was evaluated using the Downs and Black instrument.[8] A numeric score was not calculated for each study. Instead, strengths and weaknesses of each study were summarized and described.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 341 citations. From these, 15 articles were selected for further examination. From the 15 articles, two non-randomized (retrospective cohort) studies were identified. No relevant health technology assessments, systematic reviews, meta-analyses, randomized controlled trials and economic evaluations were identified. The study selection process is outlined in a PRISMA flowchart (Appendix 1).

Additional references of potential interest are provided in Appendix 5.

Summary of Study Characteristics

A detailed summary of study characteristics, critical appraisal and findings can be found in Appendices 2, 3, and 4.

Study Design
Two non-randomized, retrospective cohort studies were included in the review.[4,9] Minoda et al. (2009)[9] included patients who were followed-up for at least two years. Hodrick et al. (2008) included patients who were followed up for at least 69 months.

Country of Origin
One study was conducted in the USA[4] and one was conducted in Japan.[9]

Patient Population
Both studies were composed of samples of patients who all had undergone TKA, and were on average $\geq$ 67 years of age. One study had equal proportions of females and males.[4] while the other study had a substantially greater proportion of females compared to males.[9]

Intervention and Comparators
None of the included studies had a comparison of vitamin E infused polyethylene liners to highly cross-linked polyethylene liners or vitamin E infused polyethylene liners to conventional polyethylene liners. Both included studies compared highly cross-linked polyethylene to conventional polyethylene liners.[4,9]

Outcomes
The study conducted in the USA[4] included the following outcomes: time to revision for wear (primary outcome), number of reoperations/revisions, range of motion, tibial revisions. The study conducted in Japan included the following outcomes: range of motion, knee society score, number of revisions, radiolucent time, osteolysis, loosening of knees.[9]

Summary of Critical Appraisal

Two non-randomized studies retrospective cohort studies were included. One of the strengths of the included studies were in each case the study was conducted by the same surgeon[4] or the same surgical team.[9] This design aspect helps minimize performance bias due to different surgical care, however learning curve effects were not accounted for. No adjustments were made to the analysis to account for differences in baseline patient characteristics, which may have affected the outcomes (e.g. range of motion). The length of follow-up in the Japanese study[9] (2 years) may have been too short to observe failures; as a result, the findings of the study may have limited external validity.[9] In the American study, the outcomes were not clearly defined a priori in the methods section.[4] In the same study, a large proportion of patients were lost to follow up in both treatment groups (17 to 18%). This could limit the generalizability of study findings. Another limitation of this study was the lack of reporting of the time frame when the surgeries were performed. It possible that there is limited overlap in the time frame when the surgeries were performed. If the majority of patients who received one type of liner had their surgeries before patients who received the other type of liner factors such as the surgeon's experience and improvements in the other components involved in the knee replacement surgery could affect the outcomes. In both included studies, the setting where these surgeries were performed was not reported.

Summary of Findings

What is the comparative clinical effectiveness of vitamin E infused polyethylene liners, cross-linked polyethylene liners, and conventional polyethylene liners for knee articular resurfacing in adults?

As noted in the summary of study characteristics, none of the included studies compared the effectiveness of vitamin E infused polyethylene liners to highly cross-linked polyethylene liners or conventional polyethylene liners. Two retrospective cohort studies compared the effectiveness of highly cross-linked polyethylene liners to conventional polyethylene liners for knee articular resurfacing.

The study conducted in the USA[4] compared 100 patients treated with highly cross-linked polyethylene liners/implants to conventional polyethylene liners/implants. They reported no significant differences in revision rates for loose tibial components between the highly cross-linked polyethylene group and the standard or conventional polyethylene group (log rank test, P = 1.00; Fisher exact test, P = 0.25). There were no differences reported between the highly cross-linked polyethylene group and conventional group for postoperative range of motion in the knee.

The study conducted in Japan[9] comparing 89 patients with highly cross-linked polyethylene liners to 113 patients treated with conventional polyethylene liners reported there were no patients in either group who required knee revision surgery.

What is the cost-effectiveness of vitamin E infused polyethylene liners, cross-linked polyethylene liners, and conventional polyethylene liners for knee articular resurfacing in adults?

No studies were identified that addressed the cost-effectiveness of vitamin E infused polyethylene liners, cross-linked polyethylene liners and conventional polyethylene liners for knee articular resurfacing.

Limitations

There are numerous limitations in the included studies. These studies have the potential for selection bias because patients are not randomized to treatments. None of the included studies reported measures of patient activity, which may be a factor in component wear. Furthermore, in both studies patients were lost to follow-up; however, no data on these patients was reported. Both included studies had small sample sizes (n≈200), which may limit the generalizability of the study findings. In addition, there were few failures or revision in both studies (three combined), which may make it difficult to interpret study findings because the studies may be underpowered to detect an effect. The study conducted in the USA was designed with time to revision for wear as the primary outcome.[9] The primary outcome was not specified in the Japanese study.[4] No justification was provided for the selection of length of follow-up in either study. It is possible that the length of follow-up may have been too short to observe typical proportions of failures observed over a long-term period in the real world; as a result, the findings of the studies may have limited external validity. In addition, because none of the included studies were conducted in Canada, it is unclear if the surgical techniques used in the studies are generalizable to Canadian setting.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

There was no evidence to suggest a difference in revision surgery/failure between highly cross-linked polyethylene implants and conventional polyethylene implants. There was no evidence available comparing vitamin E infused polyethylene liners/implants to either highly cross-linked polyethylene liners/implants or conventional polyethylene liners/implants. Numerous factors might be considered when selecting the type of polyethylene implant for knee articular

resurfacing including patient activity, implant variability and surgical technique.[4] It remains unclear if the addition of vitamin E to polyethylene liners provides any benefit for implant failures compared to highly cross-linked polyethylene liners or conventional polyethylene liners. More studies are needed, which directly compare vitamin E infused polyethylene liners to highly cross-linked polyethylene liners or conventional polyethylene liners.

The current review concludes there is no significant difference between the highly cross-linked polyethylene liners compared to conventional polyethylene liners for revisions and failures. In addition, there was no literature examining the cost-effectiveness of vitamin E infused polyethylene liners, highly cross-linked polyethylene liners and conventional polyethylene liners.

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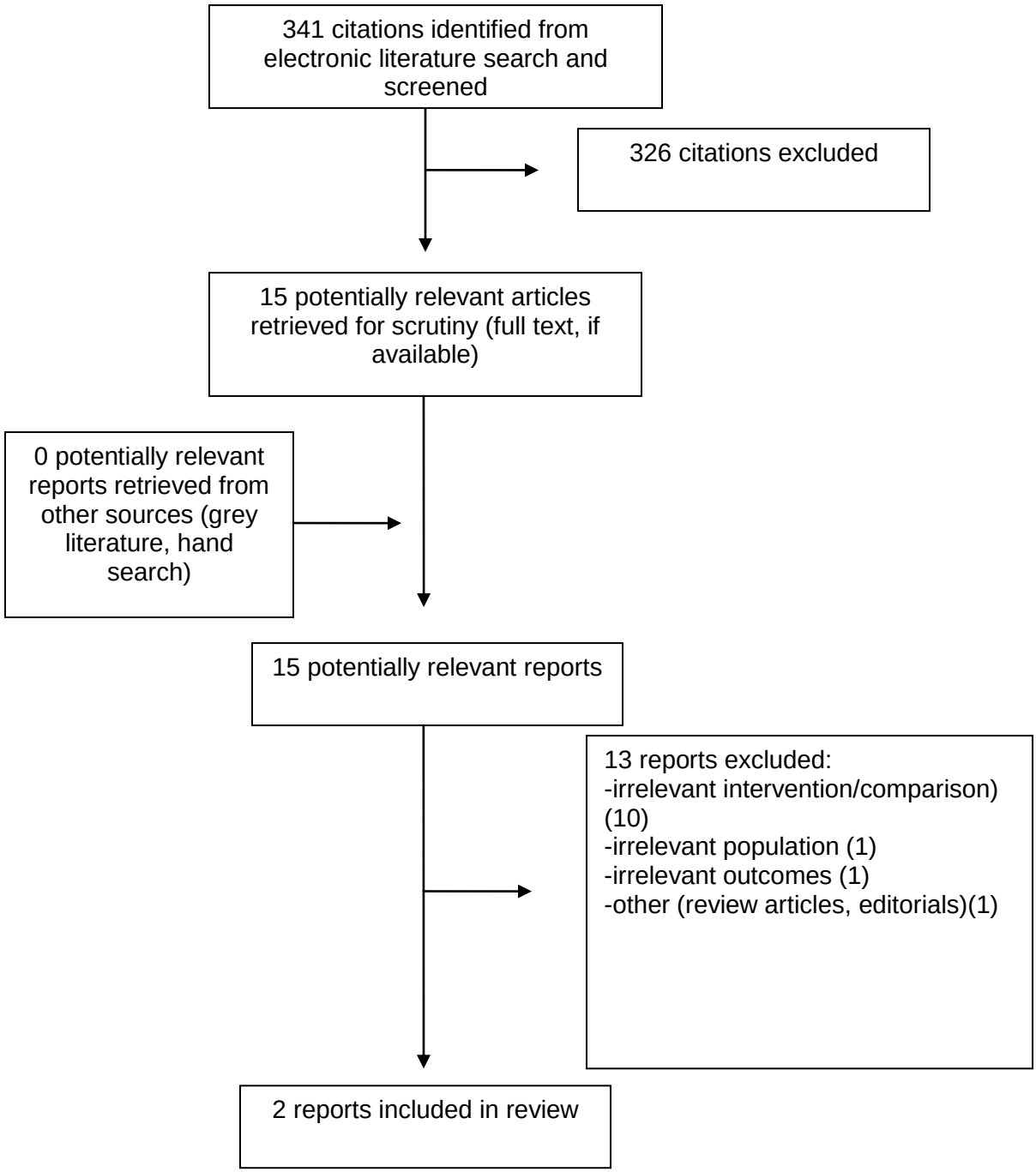
APPENDIX 1: Selection of Included Studies



APPENDIX 2: Characteristics of Included Clinical Studies

First Author, Publication Year, Country	Study Design and Length	Patient Characteristics	Intervention	Comparator	Clinical Outcomes Measured
Minoda et al. (2009),[9] Japan	Retrospective Cohort study At least two years follow-up from time of procedure	All patients undergoing total knee arthroplasty N= 207 knees/187 patients **Conventional polyethylene implants group** (n=113 knees/ 99 patents): **High Cross-linked polyethylene implants group** (n=89 knees/83 patients) Five patients were lost to follow up (2 with conventional polyethylene implants and 3 with cross-linked polyethylene implants)	Highly cross-linked polyethylene implants (Durasul, for Natural Knee System)	Conventional polyethylene implants	Range of motion, knee society score, number of revisions, radiolucent time, osteolysis, loosening of knees
Hodrick et al. (2008),[4] USA	Retrospective Cohort Study Minimum of 69 months follow-up from the time of the procedure	All patients have undergone TKA **Conventional polyethylene implants group** (n=100): 40% male; mean age= 70 years; 14 patients dead; 17 patients lost to follow up; 34 cemented , and 66 cementless **Highly cross-linked polyethylene implants group (n=100):** 42% male; mean age= 67 years; 10 patients dead; 18 patients lost to follow up; 30 cemented, 70 cementless	High cross-linked polyethylene Implants (NexGen Cruiciate Retaining Implant)	Conventional polyethylene implants (NexGen Cruciate Retaining Implant)	Number of Reoperation/revisions, range of motion, number of patients with radiolucencies, Difference between groups for tibial revisions, time to revision for wear

TKA=Total knee arthroplasty;

APPENDIX 3: Summary of Critical Appraisal

First Author, Publication Year	Strengths	Limitations
Minoda et al. (2009)[9]	• Identical surgical procedure in both groups • Similar prosthesis design • Included consecutive patients • Included the number of knees operated on • All surgeries performed by the same surgical team	• Preoperative differences between the 2 groups, which may confound the relationship (cross-linked significantly better knee score and functional score) • No adjustment for differences in potentially clinically relevant baseline characteristics • Small sample size without power calculations • Short duration of follow-up (2 years) • No information provided on patients lost to follow up • No measures of patient activity
Hodrick et al. (2008)[4]	• There no differences between the two groups for demographic and baseline characteristics • Sample size and power calculations are reported • All surgeries were performed by the same surgeon	• Large percentage of patients were lost to follow-up • No characteristics reported on patients lost to follow-up • No measures of patients activity included • The main outcomes were not described a priori

APPENDIX 4: Summary of Findings

First Author, Publication Year	Main Study Findings	Authors' Conclusions
Minoda et al. (2009) [9]	• No patients required knee revision surgery	" The present study showed that differences in the postoperative clinical scores, range of motion, and radiographic results of CR TKA between highly cross-linked and conventional polyethylene with the same design were not significant. Our results showed there was no early failure due to use of the new material." (p.349)
Hodrick et al. (2008)[4]	• There were no significant differences in revision rates for loose tibial components between the conventional polyethylene group and the highly cross-linked polyethylene group (log rank test, p= 1.00; Fisher exact test, p= 0.25) • Five patients in the highly cross-linked polyethylene group underwent reoperation/ revision (one open reduction and internal fixation of periprosthetic femur fracture, one infection, one laxity, one loose body, and one open synovectomy for arthrofibrosis) • Nine patients in the conventional polyethylene group underwent reoperation/revision (three patients for loose tibial components, two for treatment of infection, two for instability, one for patellar revision and one for an arterial popliteal thrombus treated with revascularization)	• "The data suggest highly crosslinked polyethylene in TKA should be considered a viable option. The data suggest highly-cross-linked polyethylene when used in the setting of TKA is as safe as standard polyethylene at early to mid-term follow up and provide an impetus for further long-term investigation." (p.2810)

APPENDIX 5: Additional Information

Irrelevant Outcomes

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