TITLE: Boston Keratoprosthesis for the Treatment of Corneal Blindness: Clinical Effectiveness and Cost-Effectiveness

DATE: 22 April 2016

CONTEXT AND POLICY ISSUES

Corneal disease is the third most common cause of recoverable blindness in Canada, and the most common cause of visual handicap in Canadians under 30 years of age. In 2013, 2,000 to 3,000 Canadians were on wait lists for corneal transplants. In some instances, wait times were as long as three years.

Penetrating keratoplasty (PK), a corneal transplantation procedure to treat corneal blindness, is subject to complications such as infection, development of glaucoma, loss of visual acuity, and graft failure despite delivering positive visual outcomes.

Keratoprosthesis, an artificial cornea, was developed to treat patients whose corneas are at high risk for immunological rejection after PK, or corneas with factors that might predispose them to graft failure after a failed PK. Implantation is performed by corneal surgeons, and visual acuity is assessed at baseline and at various time points postoperatively. Following the operation, eye is treated with a bandage soft contact lens, which is changed on a monthly basis. Daily antibiotics are initiated and continued indefinitely.

Boston keratoprosthesis, a new design of artificial cornea available in type 1 and type 2 configurations (with type 1 being the most common, and type 2 reserved for end-stage ocular surface disease desiccation), has resulted in positive clinical outcomes in the treatment of corneal blindness. It is also subject to complications, such as the development of retros prosthetic membrane, glaucoma and infectious endophthalmitis.

This Rapid Response report aims to review the clinical and cost-effectiveness of Boston Type 1 (KPro) keratoprosthesis for the treatment of corneal blindness.
RESEARCH QUESTIONS

1. What is the clinical effectiveness of the Boston type 1 Keratoprosthesis for the treatment of corneal blindness?

2. What is the cost-effectiveness of the Boston type 1 Keratoprosthesis for the treatment of corneal blindness?

KEY FINDINGS

The evidence suggests that Boston keratoprosthesis (KPro) implantation has favourable visual acuity and graft retention, and lower complication rates. There was significant improvement in vision-related quality of life. In patients with advanced ocular surface conditions, (KPro) implantation, despite offering the potential for an efficient rehabilitation tool, can lead to postoperative infections that may compromise device retention and reduce visual outcomes. No evidence on the cost-effectiveness of the KPro for the treatment of corneal blindness was found.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2011 and March 23, 2016.

Selection Criteria and Methods

Table 1: Selection Criteria

One reviewer screened the titles and abstracts of the retrieved publications and examined the full-text publications for the final article selection. Selection criteria are outlined in Table 1.

<table>
<thead>
<tr>
<th>Table 1: Selection Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
</tr>
<tr>
<td>Patients with a history of corneal graft failure (e.g., standard penetrating keratoplasty [PK])</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
</tr>
<tr>
<td>Boston Type 1 Keratoprotheses (KPro)</td>
</tr>
<tr>
<td><strong>Comparator</strong></td>
</tr>
<tr>
<td>Penetrating PK corneal transplantation, no comparator</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
</tr>
<tr>
<td>Q1: Clinical effectiveness, safety (e.g., adverse events and complications including glaucoma, infection, graft failure, loss of vision)</td>
</tr>
<tr>
<td>Q2: Cost-effectiveness</td>
</tr>
<tr>
<td><strong>Study Designs</strong></td>
</tr>
<tr>
<td>Health technology assessments (HTAs), systematic reviews (SRs), meta-analyses (MAs), randomized controlled trials (RCTs), non-randomized studies (NRS), and economic evaluations.</td>
</tr>
</tbody>
</table>
Exclusion Criteria

Articles were excluded if they did not meet the selection criteria in Table 1, if they were published prior to January 2011, if they were duplicate publications of the same study, or if they were referenced in a selected systematic review.

Critical Appraisal of Individual Studies

The quality of the included systematic review and clinical trials was assessed using the AMSTAR\textsuperscript{15} and Downs & Black\textsuperscript{16} checklists, respectively. Numeric scores were not calculated. Instead, the strengths and limitations of the study are summarized and presented.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 371 citations. After screening of abstracts from the literature search and from other sources, nine potentially relevant studies were selected for full-text review. Seven studies were included in the review.\textsuperscript{17-23} The PRISMA flowchart in Appendix 1 details the process of the study selection.

Summary of Study Characteristics

A detailed summary of the included SR and clinical studies is provided in Appendices 2 and 3, respectively.

Study design, setting, length of follow-up, year of publication

One SR review and MA\textsuperscript{17} and six clinical studies, including three pre and post prospective cohort studies\textsuperscript{19,21,22} and three retrospective chart reviews\textsuperscript{18,20,23} were included.

The SR\textsuperscript{17} included 26 primary studies with various settings which were published between 1990 and 2014 and enrolled a total of 29,855 eyes. The clinical studies, published between 2013 to 2016, were conducted in tertiary care centres with sample sizes that ranged from 24 to 300 eyes, and had a follow-up period between six and 32 months.\textsuperscript{18-23}

Population

The SR included studies of participants with corneal opacity who had at least one failed PK.\textsuperscript{17} One study also included patients with failed PKs.\textsuperscript{18} The remaining clinical studies reported patients with various eye conditions eligible to KPro implantation.\textsuperscript{19-23} The clinical studies included patients with a mean age ranging from 53.5 to 65.3 years old with various gender ratios. Comorbidities were not reported in any of the clinical studies.\textsuperscript{18-23}

Interventions and comparators

The intervention was KPro procedure.\textsuperscript{17-23} In the SR, the comparator was PK.\textsuperscript{17} The remaining studies reported pre and post implantation outcomes or retrospective chart reviews.

Outcomes
The SR\textsuperscript{17} and five clinical studies reported visual acuity, graft retention and complication rates.\textsuperscript{17-20,22,23} One study reported patient-reported vision-related quality of life, using the National Eye Institute Visual Function Questionnaire (NEI VFQ-25).\textsuperscript{21}

**Summary of Critical Appraisal**

Details of the strengths and limitations of the included studies are summarized in Appendix 4.

The included SR provided an a priori design, performed a comprehensive literature search, and had independent studies selection and data extraction procedure in place.\textsuperscript{17} The review, however, compared meta-analysis results (PK) to a retrospective case series (KPro). It included NRS, such as prospective and retrospective cohort studies, and case series. The review did not provide a list of included or excluded studies or describe the study characteristics and quality assessment of included studies. There was diversity across the studies in the underlying diagnosis for the intervention cohort (KPro), and no assessment of publication bias was performed.

The included pre and post and retrospective clinical studies described their hypothesis, selection method from the source population, patient characteristics, interventions, outcomes measured, main study results, estimates of random variability, and probability values provided losses to follow-up.\textsuperscript{18-23} As the studies were non-randomized, there were potential selection or recall biases and confounding issues that may have affected the internal validity of the results. It is also not sure if they had sufficient power to detect a clinically important effect.

**Summary of Findings**

Main findings of included studies are summarized in detail in Appendix 5.

1. **What is the clinical effectiveness of the Boston type 1 Keratoprosthesis for the treatment of corneal blindness?**

The SR evaluated KPro in patients with corneal opacity who had failed PKs.\textsuperscript{17} Pooled estimates from 26 studies on PK were compared to results from one retrospective review of case series on KPro. Visual acuity had improved with KPro compared to repeat PK. The same trend was found in graft retention with KPro performing better than repeat PK. Fewer patients developed glaucoma at three years with repeat PK than with KPro. After 47 months follow-up, the proportion of patients with repeat PK who developed infectious keratitis was 18%. After five years follow-up, the proportion of patients with KPro who developed infectious keratitis was 2.9%, and infectious endophthalmitis was 10.3%. The authors concluded that KPro had favorable outcomes compared to repeat PK.

A retrospective chart review evaluated the outcomes of KPro in 24 eyes with failed PK.\textsuperscript{18} At a mean 28.9 months follow-up, post-operative best corrected 20/200 visual acuity as measured by the patient’s best corrected visual acuity improved in 70.9% of eyes, remained unchanged in 12.5% of eyes, and was worse in 16.7% of eyes. KPro graft retention was retained in 91.7% of eyes. At least one serious complication occurred in 33.3% of eyes. The authors concluded that KPro is associated with satisfactory visual improvement and excellent prognosis for prosthesis retention in eyes with previous failed PKs.
A pre and post prospective study examined the visual acuity in 300 eyes with advanced ocular surface diseases. Visual acuity improved for 84.7% of eyes after an average of 17 months post-operation, and this improvement was retained for an average of 47.8 months. The authors concluded that KPro was an effective device for rehabilitation in advanced ocular surface disease.

A retrospective chart review evaluated the complication rates of KPro in 52 eyes with advanced ocular surface conditions. After a mean 37.7 months follow-up, post-operative infections occurred in 25.0% of eyes. Approximately 10.7% of procedures led to infectious keratitis, and 9.3% led to infectious endophthalmitis. Treatment of the infected eyes required prosthesis removal in 53.8% of eyes, and reduced pre-infection visual acuity in 53.8% of eyes. The authors concluded that postoperative infections were a serious issue that compromised device retention and visual outcomes after KPro implantation.

A pre and post prospective study determined the impact of KPro on patient-reported vision-related quality of life in 24 patients with various eye conditions undergoing KPro implantation. Using the NEI VFQ-25, there were significant improvements in general vision, near and distance activities, social functioning, mental health, role difficulties, dependency, color vision, and peripheral vision compared with baseline values after a mean 16-month follow-up. The authors concluded that KPro significantly improved patients’ quality of life.

A pre and post prospective study evaluated visual acuity, graft retention rates, and complication rates following KPro implantation in 30 eyes with various advanced eye conditions in Brazil. After a mean 32 months follow-up, post-operative visual acuity improved in 80% of eyes. KPro was retained in 93.3% of eyes. Three eyes developed glaucoma, two eyes had retinal detachment, and one eye developed infectious keratitis. The authors concluded that KPro implantation was a viable option after failed PK or for conditions with poor prognosis for PK in a developing country.

A retrospective chart review determined the visual outcomes and complications of KPro in 41 eyes with various advanced eye conditions. Visual acuity was improved after a mean 22 months follow-up, and was maintained or improved in 82.92% of eyes. In terms of complications, the formation of retroprosthetic membrane occurred in 53.65% of eyes. Moreover, 4.87% of eyes had infectious keratitis, and 12.19% had infectious endophthalmitis. The authors concluded that KPro was an effective alternative in patients with ocular pathology and imminent risk of rejection of a new PK.

The results from pre and post clinical studies and retroprospective chart reviews showed that KPro implantation had favorable visual acuity outcomes, graft retention and complication rates, such as the formation of glaucoma, retroprosthetic membrane and infections in patients with failed PKs. The study findings also suggested a significant improvement in vision-related quality of life, such as near and distance activities, social functioning, and mental health. In patients with advanced ocular surface conditions, KPro implantation, despite offering the potential of an efficient rehabilitation tool, may lead to postoperative infections that may compromise device retention and reduce visual outcomes.
2. **What is the cost-effectiveness of the Boston type 1 Keratoprosthesis for the treatment of corneal blindness?**

There was no evidence found on the cost-effectiveness of the KPro for the treatment of corneal blindness.

**Limitations**

The quality of the included studies is limited by the nature of their pre and post and chart review designs. One Canadian study was included in the review, so the generalizability of the findings of the remaining studies to the Canadian setting should be interpreted with caution. There was no evidence found on the cost-effectiveness of the KPro for the treatment of corneal blindness.

**CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING**

Results from the studies in this review indicate that KPro implantation had favorable visual acuity outcomes, graft retention and complication rates such as the formation of glaucoma, retroprosthetic membrane and infections in patients with failed PKs. The study findings suggested a significant improvement in vision-related quality of life such as near and distance activities, social functioning, and mental health. In patients with advanced ocular surface conditions, KPro implantation, despite offering the potential of an efficient rehabilitation tool, can lead to postoperative infections that may compromise device retention and reduce visual outcomes.

Evidence on the clinical effectiveness and safety of KPro must be interpreted with caution since the quality of the included studies is limited by the nature of their non-randomized study designs with potential biases and confounding factors affecting the internal validity of the results such as selection and recall biases. There was no evidence found on the cost-effectiveness of the KPro for the treatment of corneal blindness.

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REFERENCES


Appendix 1: Selection of Included Studies

371 citations identified from electronic literature search and screened

9 potentially relevant articles retrieved for scrutiny (full text, if available)

0 relevant reports retrieved from other sources (grey literature, hand search)

9 potentially relevant reports

2 reports excluded (irrelevant population, interventions or outcomes)

7 reports included in review
Appendix 2: Characteristics of Included Systematic Reviews

<table>
<thead>
<tr>
<th>First Author, Year, Country</th>
<th>Literature Search Strategy</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
<th>Studies Included</th>
<th>Main Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmad, 2016, US, Saudi Arabia</td>
<td>&quot;Articles with data regarding repeat PK published between 1990 and 2014 were identified in PubMed, EMBASE, the Latin American and Caribbean Health Sciences Literature Database, and the Cochrane Central Register of Controlled Trials and were reviewed. Results were compared with a retrospective review of consecutive, nonrandomized, longitudinal case series of KPro implantations performed at 5 tertiary care centers in the United States&quot; (p 165)</td>
<td>&quot;We planned to include nonrandomized control trials, prospective and retrospective cohort studies, and interventional case series that were published between 1990 and 2014&quot; (p 166)</td>
<td>&quot;Studies that reported on fewer than 20 patients or cases were excluded&quot; (p 166)</td>
<td>26 studies (21 case series and 5 cohort studies) for PK</td>
<td>1 retrospective review of case series for KPro Visual acuity at 2 years (likelihood of attaining 20/200 or better) Graft retention at 5 years Glaucoma rate at 3 years Infection rate at 5 years</td>
</tr>
</tbody>
</table>

KPro: Boston type 1 keratoprosthesis; PK: penetrating keratoplasty.
## Appendix 3: Characteristics of Included Clinical Studies

<table>
<thead>
<tr>
<th>First Author, Year, Country</th>
<th>Study Objectives, design, setting, length of follow-up</th>
<th>Interventions/Comparators</th>
<th>Patients</th>
<th>Main Study Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hager, 2016, US</td>
<td>&quot;The purpose of this study was to evaluate the outcomes of the Boston type 1 keratoprosthesis (Kpro-1) in eyes with failed keratoplasty&quot; (p 73)</td>
<td>KPro, PK</td>
<td>24 eyes</td>
<td>Visual acuity (BCVA)</td>
</tr>
<tr>
<td></td>
<td>Retrospective chart review</td>
<td></td>
<td></td>
<td>Graft retention (in situ maintenance of the initial prosthesis)</td>
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<tr>
<td></td>
<td>Tertiary care centre</td>
<td></td>
<td></td>
<td>Complications (i.e., infectious keratitis, wound dehiscence)</td>
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<tr>
<td></td>
<td>Mean 28.9 months follow-up</td>
<td></td>
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<tr>
<td>Rudnisky, 2016, Canada, US</td>
<td>To report improvement of visual outcomes of KPro</td>
<td>KPro</td>
<td>300 eyes</td>
<td>Visual acuity (20/200 acuity)</td>
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<tr>
<td></td>
<td>Pre and post prospective study</td>
<td></td>
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<tr>
<td></td>
<td>Tertiary care centre</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Mean 17 months follow-up</td>
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<tr>
<td>Wagoner, 2016, US</td>
<td>&quot;To determine the incidence, ocular surface disease associations, microbiological profile, and clinical course of postoperative infections after implantation of the Boston type 1 keratoprosthesis (KPro-1)&quot; (p 486)</td>
<td>KPro</td>
<td>52 eyes</td>
<td>Post-operative infections (i.e., infectious keratitis, endophthalmitis)</td>
</tr>
<tr>
<td></td>
<td>Retrospective chart review</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Tertiary care centre</td>
<td></td>
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<tr>
<td></td>
<td>Mean 37.7 months follow-up</td>
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<tr>
<td>Cortina, 2015, US</td>
<td>&quot;The aim of this study was to determine the impact of Boston keratoprosthesis (KPro) implantation on patient-reported visual function using the National Eye Institute Visual Function Questionnaire 25 (NEI VFQ-25)&quot; (p 160)</td>
<td>KPro</td>
<td>24 patients</td>
<td>Vision-related quality of life (using the National Eye Institute Visual Function Questionnaire 25)</td>
</tr>
<tr>
<td></td>
<td>Pre and post prospective study</td>
<td></td>
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<tr>
<td></td>
<td>Tertiary care centre</td>
<td></td>
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<tr>
<td></td>
<td>Mean 16 months follow-up</td>
<td></td>
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<tr>
<td>de Oliveira, 2014, Brazil</td>
<td>&quot;To report the experience of the Federal University of São Paulo, Brazil, in performing Boston keratoprosthesis type 1&quot;</td>
<td>KPro</td>
<td>30 eyes</td>
<td>Visual acuity (BCVA)</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td>Graft retention (in situ maintenance of the initial prosthesis)</td>
</tr>
</tbody>
</table>
Table A2: Characteristics of Included clinical studies

<table>
<thead>
<tr>
<th>First Author, Year, Country</th>
<th>Study Objectives, design, setting, length of follow-up</th>
<th>Interventions/Comparators</th>
<th>Patients</th>
<th>Main Study Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muñoz-Gutierrez, 2013, Spain</td>
<td><em>To describe the visual outcome of patients who underwent Boston type 1 keratoprosthesis (KPro1) implantation, and describe serious sight-threatening post-operative complications</em> (p 56)</td>
<td>KPro</td>
<td>41 eyes</td>
<td>Visual acuity (BVCA) Complications (i.e., infectious keratitis, retroprosthetic membrane)</td>
</tr>
<tr>
<td></td>
<td>Implantation in the developing world&quot; (p 351)</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Pre and post prospective study</td>
<td></td>
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<tr>
<td></td>
<td>Tertiary care centre</td>
<td></td>
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<tr>
<td></td>
<td>Mean 22.17 months follow-up</td>
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<tr>
<td></td>
<td>Retrospective chart review</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tertiary care centre</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean 22.17 months follow-up</td>
<td></td>
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</tr>
</tbody>
</table>

BVCA: best corrected visual acuity, KPro, KPro-1 or PPPro1: Boston type 1 keratoprosthesis; NEI VFQ-25: National Eye Institute Visual Function Questionnaire 25; PK: penetrating keratoplasty.
### Appendix 4: Summary of Critical Appraisal of Included Studies

#### Table A3: Summary of Critical Appraisal of Included Studies

<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Critical appraisal of included systematic review (AMSTAR)</strong></td>
<td></td>
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</tbody>
</table>
| Ahmad, 2016                   | - a priori design provided  
- independent studies selection and data extraction procedure in place  
- comprehensive literature search performed  
- conflict of interest stated | - comparing meta-analysis results (penetrating keratoplasty) to a retrospective case series (KPro)  
- the meta-analysis included studies that are randomized controlled trials, prospective and retrospective cohort studies, and case series  
- list of included studies and studies characteristics not provided  
- list of excluded studies not provided  
- quality assessment of included studies not provided and not used in formulating conclusions  
- diversity in the underlying diagnosis for the intervention cohort (KPro)  
- no assessment of publication bias performed |

| **Critical appraisal of included clinical studies (Blacks & Down)** |
| Hager, 2016                   | - hypothesis described  
- method of selection from source population and representation described  
- main outcomes, interventions, patient characteristics, and main findings described  
- estimates of random variability and actual probability values provided losses to follow-up described | - retrospective chart review with potential recall bias and confounding factors  
- not sure if study had sufficient power to detect a clinically important effect |
| Rudinsky, 2016                | - hypothesis described  
- method of selection from source population and representation described  
- main outcomes, interventions, patient characteristics, and main findings clearly described  
- estimates of random variability and actual probability values provided losses to follow-up described | - pre and post prospective cohort study with potential selection bias and confounding factors  
- not sure if study had sufficient power to detect a clinically important effect |
| Wagoner, 2016                 | - hypothesis described  
- method of selection from source population and representation described  
- main outcomes, interventions, patient characteristics, and main findings described  
- estimates of random variability and actual probability values provided losses to follow-up described | - retrospective chart review with potential recall bias and confounding factors  
- not sure if study had sufficient power to detect a clinically important effect |
| Cortina, 2015                 | - hypothesis described  
- method of selection from source population and representation described | - pre and post prospective cohort study with potential selection bias and confounding factors  
- not sure if study had sufficient power to detect a clinically important effect |
## Table A3: Summary of Critical Appraisal of Included Studies

<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
</table>
|                               | • main outcomes, interventions, patient characteristics, and main findings described  
• estimates of random variability and actual probability values provided  
• losses to follow-up described | detect a clinically important effect |
| de Oliveira, 2014              | • hypothesis described  
• method of selection from source population and representation described  
• main outcomes, interventions, patient characteristics, and main findings described  
• estimates of random variability and actual probability values provided  
• losses to follow-up described | • pre and post prospective cohort study with potential selection bias and confounding factors  
• unclear if study had sufficient power to detect a clinically important effect |
| Muñoz-Gutierrez, 2013          | • hypothesis described  
• method of selection from source population and representation described  
• main outcomes, interventions, patient characteristics, and main findings described  
• estimates of random variability and actual probability values provided  
• losses to follow-up described | • retrospective chart review with potential recall bias and confounding factors  
• not sure if study had sufficient power to detect a clinically important effect |
## Appendix 5: Main Study Findings and Authors’ Conclusions

<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Main Study Findings</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Research question 1 (clinical effectiveness of the Boston Keratoprosthesis (KPro) for the treatment of corneal blindness)</strong></td>
<td></td>
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</tr>
</tbody>
</table>
| Ahmad, 2016 | **Visual acuity** (likelihood of maintaining 20/200 visual acuity or better at 2 years)  
Repeat PK: 42% (95% CI, 30% - 56%)  
KPro: 80% (95% CI, 68% - 88%)  
**Graft retention** (probability of maintaining a clear graft at 5 years)  
Repeat PK: 47% (95% CI, 40% - 54%)  
KPro: 75% (95% CI, 64% - 84%) | “These results demonstrate favorable outcomes of KPro surgery for donor corneal graft failure with a greater likelihood of maintaining visual improvement without higher risk of postoperative glaucoma compared with repeat donor PK” (p 165) |
| **Complications** | | |
| Glaucoma (proportion of patients at 3 years)  
Repeat PK: 25% (95% CI, 10% - 44%)  
KPro: 30% (CI not reported) | | |
| Infection  
Repeat PK: (proportion of patients at 47 months follow-up)  
Infectious keratitis: 18% (95% CI, 9% - 30%)  
KPro: (proportion of patients after 5 years follow-up)  
Infectious keratitis: 2.9% (CI not reported)  
Infectious endophthalmitis: 10.3% (CI not reported) | | |
| Hager, 2016 | **Visual acuity** (BCVA improvement; mean 28.9 months follow-up)  
Post-operative BCVA improved in 17 (70.9%) eyes, unchanged in 3 (12.5%) eyes, worse in 4 (16.7%) eyes | “The Boston Kpro-1 is associated with an excellent prognosis for prosthesis retention and satisfactory visual improvement in eyes with previous failed keratoplasty” (p 73) |
| **Graft retention** (mean 28.9 months follow-up)  
KPro was retained in 22 (91.7%) eyes | | |
| **Complications** (mean 28.9 months follow-up)  
One or more serious complications occurred in 8 (33.3%) eyes (among 1 case of wound dehiscence, 1 case of fungal keratitis, 4 cases of endophthalmitis, and 5 retinal detachments) | | |
| Rudnisky, 2016 | **Visual acuity** improved (P < 0.0001) for 254 (84.7%) eyes (after mean 17 months post-op). This improvement was retained for an average 47.8 months.  
The median time to achieve 20/200 visual acuity was 1 month | “The Boston keratoprosthesis type 1 is an effective device for rehabilitation in advanced ocular surface disease, resulting in a significant improvement in visual acuity” (p 89) |
| Wagener, 2016 | Procedures were performed in 52 eyes (mean 37.7 months follow-up)  
8 cases (10.7%) developed infectious keratitis (fungal in 5 cases, bacterial in 3 cases)  
7 cases developed infectious endophthalmitis (fungal in 2 cases, bacterial in 5 cases)  
Mean interval from surgery to infection was 11 months (range 1 to 60 months)  
Treatment of the infected eyes required prosthesis removal in 7 eyes (53.8%), and reduced pre-infection visual acuity in 7 eyes (53.8%) | “Postoperative infections are a serious issue that compromises device retention and visual outcomes after keratoprosthesis implantation” (p 486) |

*Boston Keratoprosthesis for the Treatment of Corneal Blindness*
<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Main Study Findings</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortina, 2015</td>
<td>Using the NEI VFQ-25:</td>
<td>“The quality of life of patients who underwent KPro significantly improved postoperatively compared with their preoperative status” (p 160)</td>
</tr>
<tr>
<td></td>
<td>Compared to baseline (pre implantation) values, significant improvement in general vision, near and distance activities, social functioning, mental health, role difficulties, dependency, color vision, and peripheral vision ($P &lt; 0.05$) (mean 16 months follow-up; range 2-36 months).</td>
<td></td>
</tr>
<tr>
<td></td>
<td>VFQ overall score: baseline 44.6; KPro 72.2 ($P &lt; 0.0001$)</td>
<td></td>
</tr>
<tr>
<td>de Oliveira, 2014</td>
<td>Visual acuity (BCVA improvement; mean 32 months follow-up)</td>
<td>“Performing Boston type 1 keratoprosthesis in a developing country is a viable option after multiple keratoplasty failures and conditions with a poor prognosis for keratoplasty” (p 351)</td>
</tr>
<tr>
<td></td>
<td>Post-operative BCVA improved in 24 (80%) eyes</td>
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<td></td>
<td>Graft retention (mean 32 months follow-up)</td>
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<td></td>
<td>KPro was retained in in 93.3%</td>
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<td></td>
<td>Complications (mean 32 months follow-up)</td>
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<td></td>
<td>3 eyes developed glaucoma</td>
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<tr>
<td></td>
<td>2 eyes had retinal detachment</td>
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<tr>
<td></td>
<td>1 eye developed infectious keratitis</td>
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<tr>
<td>Muñoz-Gutierrez, 2013</td>
<td>Visual acuity (BCVA improvement; mean 22.17 months follow-up)</td>
<td>“We consider KPro as an effective alternative in patients with multiple ocular pathology and imminent risk of rejection of a new KP” (p 56)</td>
</tr>
<tr>
<td></td>
<td>Mean BVCA (converted to log): 2.05 (range 1.10 to 2.52) before surgery; 1.16 (range 0.08 – 2.70) after surgery</td>
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<tr>
<td></td>
<td>BVCA was maintained or improved in 34 (82.92%) of patients</td>
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<td>Complications (mean 22.17 months follow-up)</td>
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<td>Formation of retroprosthetic membrane in 22 (53.65%) eyes</td>
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<td>2 (4.87%) eyes had infectious keratitis</td>
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<td></td>
<td>5 (12.19%) had infectious endophthalmitis</td>
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</tr>
</tbody>
</table>

**Research question 2 (cost-effectiveness of the Boston Keratoprosthesis (KPro) for the treatment of corneal blindness)**

There was no evidence found on the cost-effectiveness of the Boston Keratoprosthesis (KPro) for the treatment of corneal blindness.

**Notes:** BCVA: best corrected visual acuity; CI: confidence interval; KPro: Boston type 1 keratoplasty; NEI VFQ-25: National Eye Institute Visual Function Questionnaire; PK: penetrating keratoplasty.