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Cost-Effectiveness Analysis of Descemet's Membrane Endothelial Keratoplasty Versus Descemet's Stripping Endothelial Keratoplasty in the United States

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Abstract

Purpose—To determine the cost-effectiveness of Descemet's membrane endothelial keratoplasty (DMEK) compared with Descemet's stripping automated endothelial keratoplasty (DSAEK) in the United States.

Design—Cost-effectiveness analysis in a surgical center in the United States.

Participants—Binocular adult patient undergoing endothelial keratoplasty.

Methods—A base case of a 70-year-old man undergoing his first endothelial keratoplasty for bilateral Fuchs endothelial dystrophy. The cost-effectiveness of DMEK was compared with DSAEK over a 15-year time horizon. The incidences and costs of complications were derived from PubMed English literature searches, Medicare reimbursements, and average wholesale prices. All costs were discounted 3% per annum and adjusted for inflation to 2018 U.S. dollars. Uncertainty was evaluated using deterministic and probabilistic sensitivity analyses.

Main Outcome Measures—Incremental cost-effectiveness ratios and incremental cost-utility ratios, measured in cost per quality-adjusted life-years (QALYs).

Results—Performing a DMEK instead of a DSAEK generated an extra 0.4 QALYs over a 15-year period. From a societal and third-party payer perspective, DMEK was cost-saving when compared with DSAEK in improving visual acuity in the base case. Probabilistic sensitivity analyses with variations in the costs and rebubble rates revealed that DMEK was cost-saving

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compared with DSAEK in 38% of iterations and was within a societal willingness-to-pay threshold of \$50 000 in 98% of models.

Conclusions—From the societal and third-party payer perspectives in the United States, DMEK generated greater utilities and was less costly than DSAEK. Therefore, DMEK was the dominant procedure and was cost-saving with respect to DSAEK. The economic model was robust based on sensitivity analyses.

In the last 20 years, posterior lamellar keratoplasties have replaced full-thickness penetrating keratoplasties as the treatment of choice in diseases with primarily endothelial disease.^{1–6} In 2005, only 1398 corneal tissues were used for endothelial transplants; in 2016, more than 28 000 endothelial grafts were used in the United States.⁷ Descemet's stripping automated endothelial keratoplasty (DSAEK) has become a popular procedure and involves transplantation of the Descemet's membrane with the endothelium and a thin portion of the posterior stroma.⁷

Descemet's membrane endothelial keratoplasty (DMEK) represents the next step in the evolution of endothelial surgery and consists of transplanting only the Descemet's membrane and the endothelium, without posterior stroma. Descemet's membrane endothelial keratoplasty is performed through a smaller incision, has a smaller impact on refraction, results in better visual acuity outcomes, and is associated with fewer rejection episodes than DSAEK or penetrating keratoplasty.⁵ However, there is a steep learning curve for the DMEK surgery, with less-experienced DMEK surgeons initially having higher rates of complications.⁸ Long-term data on the visual outcomes and rates of complications after DMEKs are now emerging.

The purpose of the study is to determine the cost-effectiveness of DMEK compared with DSAEK for the treatment of endothelial diseases in the United States.

Methods

The cost-effectiveness analyses followed the recommendations of the second panel on cost-effectiveness in health and medicine and the Consolidated Health Economic Evaluation Reporting Standards.^{9,10} A cost-effective decision-analytic model was created for patients undergoing DMEK or DSAEK transplantation (Fig 1) based on the average costs of the procedures, visual acuity outcomes, and rate and cost of postoperative complications (Table 1) derived from previously published literature, average wholesale prices (LexiComp Inc., Hudson, OH), and the 2018 physician and anesthesia fee schedules set forth by the Centers for Medicare and Medicaid Services (Appendices 1 and 2, available at www.aaojournal.org). All costs and utilities were discounted 3% per annum over 15 years and adjusted for inflation to 2018 U.S. dollars using the Consumer Price Index. The 15-year time horizon was selected because of average life expectancy at the mean age of intervention, because limited long-term data on DSAEK and DMEK outcomes are available, and the data were assumed to be valid similar to other published studies.^{11–13} Because this study does not involve human research, it does not fall under the oversight of the institutional review board of the University of Miami (Miami, FL). Calculations were performed on TreeAge Pro Version 2017 R2.1 (TreeAge Software Inc., Williamstown, MA).

An English literature search on PubMed was performed with no time restrictions, using the keywords *endothelial keratoplasty (EK)*, *DMEK*, *Descemet's membrane automated endothelial keratoplasty (DMAEK)*, *Descemet's stripping endothelial keratoplasty, DSAEK*, *posterior lamellar keratoplasty*, or *partial thickness corneal transplant*. Abstracts were evaluated, and the full articles of studies with possible relevance were reviewed (Appendix 3, available at www.aaojournal.org). Emphasis was placed on meta-analyses and systemic reviews, and the most recent, largest studies by the same authors were used in lieu of earlier, smaller studies. Preference was given to studies directly comparing the results of DMEK and DSAEK in the same article.^{5,6,8,14–22}

The costs were separated according to societal and third-party payer perspectives. Societal costs included all costs incurred, including direct medical costs, nonmedical costs, indirect costs such as loss of productivity, and informal healthcare sector costs such as patient time, caretaker time, and transportation costs. The third-party payer perspective included only direct medical costs such as physician services, medications, anesthesia fees, and facility fees.^{9,10} Societal perspectives are generally considered more important because they allow for cross-specialty comparisons and account for indirect medical costs, which can be as much as or more than the direct medical costs for the patient and society. Appendix 1 (available at www.aaojournal.org) provides detailed cost calculations for DMEK and DSAEK, separated according to societal and third-party payer costs.

A base case was evaluated from the societal and healthcare-sector perspective of a binocular 70-year-old patient with Fuchs endothelial dystrophy with 20/83 vision in both eyes, undergoing endothelial keratoplasty in his first eye, who experienced an improvement to 20/28 with DMEK and 20/36 with DSAEK.^{5,17,19,21,23–25} The patient demographics were based on the average age, corneal pathology, and visual acuity of the average patient undergoing endothelial keratoplasties in previously published articles.²⁶

Incremental cost-utility analyses were quantified in cost per quality-adjusted life-years (QALYs) gained, using previously published time trade-off vision utilities from the Center for Value-Based Medicine. A utility of 1 represented a perfect health state with permanent bilateral 20/20 vision, 0.26 no light perception bilaterally, and 0 death.²⁷ In the base case, a visual acuity of 20/83 equaled a time trade-off utility of 0.71, 20/26 equaled 0.86, and 20/35 equaled to 0.82.^{5,23–25,28} In the event of a repeat graft, the final visual acuities were reduced to 20/28 after DMEK (utility of 0.85) and 20/44 after DSAEK (utility of 0.79), as previously published.^{29–31} After endophthalmitis, only 43% of patients recovered vision of 20/40 or better (utility of 0.81), and the rest had vision worse than 20/200.³² In the event of a poor visual outcome after endophthalmitis, the other eye with 20/83 vision then became the better-seeing eye and was used in the analyses. Previous studies reported the uneventful resolution of most other postoperative complications with appropriate medical and surgical management, such as cystoid macular edema, and these complications were therefore assumed to resolve completely unless otherwise specified.^{5,14–16,19,22,26,33,34}

Uncertainty was evaluated with 1-way and 2-way deterministic sensitivity analyses and probabilistic sensitivity analyses using second-order Monte Carlo simulations repeated 10 000 times. The cost of the surgical technique, ambulatory surgery and hospital facility fees,

use of the tissue injectors, tissue costs, equipment, rebubble rate, incidences of postoperative complications, trabeculectomy and glaucoma drainage implant, and different cost of medications were varied from the highest and lowest reported rates in the literature in the sensitivity analyses. Societal willingness to pay (WTP) is traditionally assumed to be between \$50 000 and \$100 000/QALY in the United States.

Results

The base case was evaluated from a societal and healthcare sector perspective of a binocular 70-year-old male patient with Fuchs endothelial dystrophy, with 20/83 vision in both eyes, undergoing his first surgery. From a societal perspective, the average 15-year adjusted cost of uncomplicated DMEK surgery was \$14 553 (range, \$14 180–\$14 927) and \$14 511 (range, \$14 038–\$14 987) for uncomplicated DSAEK (Appendix 1, available at www.aaojournal.org). From a third-party payer perspective, the cost of DMEK was \$10 924 (range, \$10 540–\$11 310) and \$10 881 (range, \$10 393–\$11 371) for DSAEK.

In the base case, the adjusted incremental effectiveness gained from DMEK over DSAEK was negative 0.0408, which translated to 0.39 QALYs over a 15-year period. Descemet's membrane endothelial keratoplasty was the dominant intervention, meaning it was more efficient and less expensive than DSAEK. Because the incremental utility was negative in the dominant intervention, the incremental cost-utility ratios were reported as "Cost-Saving" as per the cost-effectiveness analyses reporting recommendations (Table 2).

The most frequent postoperative procedure was rebubbling or refloating the corneal graft by injecting air into the anterior chamber to reattach a partially dehisced graft; the average number of refloats based on previous studies was one. The injection of air can be performed in an office setting (at a cost of \$93.35) or in an operating room (at a cost of \$2305) from the societal perspective (Appendices 1–3, available at www.aaojournal.org). Regardless of the procedure setting, DMEK was still cost-saving compared with DSAEK from a societal and healthcare sector perspective (Table 2).

Sensitivity analyses varying the graft redetachment rates from 2.4% to 82% for DMEK and 0% to 14.5% for DSAEK (Table 1) resulted in incremental cost-utility ratios that went from cost-saving to \$6015/QALY (Table 2). In threshold analyses considering the societal perspective, with rebubbling performed in the operating room, DMEK remained within the \$50 000 WTP with rebubbling rates up to 76.1%. Descemet's membrane endothelial keratoplasty was the dominant model (cost-saving) when the rate of DMEK graft dislocation was below 21.6%; when DSAEK rebubble rate was set at 0%, this value decreased to 18%. If all the rebubbling procedures were done in the clinic setting, DMEK was still the dominant model when the rebubble rate was below 61.9%, which decreased to 59.6% if the DSAEK detachment rate was set at a theoretical 0%.

Sensitivity analyses that varied the use of surgeon-cut and pre-cut corneal tissue and other variables affecting the total cost of each case did not significantly affect the results (Fig 2). In 1-way and 2-way sensitivity analyses, there was no value with which DSAEK became cost-effective over DMEK.

In the probabilistic sensitivity analyses performed with costs from the societal perspective, DMEKs were cost-saving 37.6% of the time and were under \$50 000 WTP threshold 97.9% of the time (Fig 3). The probability of DSAEK refloat was between 0% and 14.5%, and the probability of DMEK refloat was between 2.4% and 82% to account for the wide range of reported refloat rates in the literature. The probability of late graft failure in DSAEK and DMEK was between 0% and 6%, and costs of the procedures were varied according to the data in the text and Appendices 1 to 3 (available at www.aaojournal.org).

Discussion

Both DMEK and DSAEK significantly improve visual acuity in patients with endothelial disease. Although DMEK had a slightly higher procedural cost in this study, it has been associated with higher rates of rebubbling, but better reported final visual acuity.^{19,21} In the cost-effectiveness analyses, the values most affecting the results were the rebubble rates. Refinements in the DMEK technique may decrease the rebubble rate over time, including using SF6 gas instead of air, creating larger descemetorhexis, and marking the graft to avoid incorrect orientation.⁵

In the current economic model, DMEK was cost-saving compared with DSAEK in the base case of a 70-year-old male patient with Fuchs endothelial dystrophy undergoing his first corneal transplantation in the United States. Differences in surgical techniques, such as surgeon-cut and precut corneal grafts, variations in rebubbling rates, and changes in visual acuity outcomes depending on the postoperative complication were evaluated; sensitivity analyses demonstrated the robustness of the model. The calculated adjusted incremental gain in QALY of DMEK over DSAEK was 0.39 over a 15-year time period. As a comparison, cataract surgery in the second eye is associated with a gain of 0.92 QALYs. Furthermore, the added benefit of performing a DMEK over DSAEK is similar to the cost-effectiveness of DSAEK over penetrating keratoplasty.^{11–13}

Study Limitations

The limitations of the current study include the theoretical nature of the model and assumptions made in the analyses. There was a wide range of complication rates, with more experienced DMEK surgeons having lower rates of rebubbling, especially when marking their tissue, and using SF6 gas instead of air.^{35,36} It was assumed that the visual acuity decreased only marginally after rebubble, commiserate with previously published data.³⁷ The impact of the more reliable refractive outcomes after DMEK was difficult to ascertain. Potential complications like endophthalmitis occur rarely after endothelial keratoplasty, and none have been reported in large case series, so the incidence was difficult to ascertain; however, the model did account for possible endophthalmitis. Furthermore, the models only applied to corneal transplants performed in the United States; the surgical costs and availability of corneal tissue may differ significantly in other countries. Finally, the current study uses utilities published by the Center for Value-Based Medicine (based on time trade-off); this does not allow for direct comparison with studies using utilities derived with other methods, so the reader should use caution when generalizing these results.

It is important to note that cost-effectiveness analysis is only one of several factors to consider when selecting the appropriate keratoplasty technique in an individual patient. The economic model was designed to evaluate cases that were equally amenable to both DMEK and DSAEK; however, some patients may not be appropriate surgical candidates for DMEK, such as those with aphakia and aniridia.³⁸ Furthermore, surgeon experience, patient preference, ocular comorbidities, systemic comorbidities, adherence to postoperative face-up positioning, and visual potential all play important roles in the decision-making process.^{16,17,39}

In conclusion, DMEK is a cost-saving procedure compared with DSAEK from a healthcare and societal perspective in the United States. Despite the wide variability in costs and complication rates, and the use of more unfavorable theoretical scenarios for DMEK, the majority of economic models revealed that DMEK was cost-effective over DSAEK.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations and Acronyms

DMEK	Descemet's membrane endothelial keratoplasty
DSAEK	Descemet's stripping automated endothelial keratoplasty
QALY	quality-adjusted life-year
WTP	willingness to pay

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Figure 1.

Decision-analytic model. A decision tree was used to determine clinical scenarios with endothelial keratoplasty. The branches from the Descemet's membrane endothelial keratoplasty (DMEK) model were the same as the Descemet's stripping automated endothelial keratoplasty (DSAEK) model. *Squares* represent decision nodes, *circles* represent chance nodes, and *triangles* represent terminal nodes. Under every chance node, the appropriate probability of an event was placed. The value to the right of the triangles represents both the cost and utility outcome for each node.

Figure 2.

Deterministic sensitivity analyses of incremental cost-effectiveness ratios of Descemet's stripping automated endothelial keratoplasty (DSAEK) vs. Descemet's membrane endothelial keratoplasty (DMEK). Surgical costs were varied to the maximum and minimum combinations, to account for varied costs of tissues and reflect changes in surgical technique. The probability of DSAEK refloat varied between 0% and 14.5%, with an average of 4.2%. The probability of DMEK refloat varied between 2.4% and 82%, with an average of 15.9%, to account for the wide range of reported refloat rates in the literature. The probability of DSAEK and DMEK late failure varied between 0% and 6%, with an average of 4.0% for DSAEK and 2.4% for DMEK. The costs of the procedures were varied according to the data in the text. The blue segments represent the effect of increasing the variable value, and the red segment represents the effect of decreasing the variable. The expected value (EV) line displays the EV at median cost; all variables that represented less than 1% risk in the model were excluded from the graph. The calculations were most sensitive to changes in the probability of DMEK refloat and cost of DSAEK (cumulative risk 65%–88%). There was no value in the on-way sensitivity analysis in which DSAEK became cost-effective. **Top.** One-way sensitivity analysis of the base case's incremental cost-effectiveness ratio from a societal perspective. **Bottom.** One-way sensitivity analysis of the incremental cost-

effectiveness ratio in the base case from a healthcare sector-based perspective. ICER = incremental cost-effectiveness ratio; WTP = willingness to pay.

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Figure 3.

Probabilistic sensitivity analyses. Probabilistic sensitivity analyses were performed with 10 000 second-order parameters from the societal perspective considering refloats done in the operating room. The ellipsoid enclosed the values within the 90% confidence interval. The diagonal willingness to pay (WTP) line is the limit, to which everything below is within the predefined \$50 000 mark. The horizontal line at “0” on the Y-axis is the line that marks cost-saving interventions found below. The models were cost-saving 37.6% of the time and under the \$50 000/QALY WTP threshold 97.8% of the time. QALY = quality-adjusted life-years.

Table 1.

Incidence of Most Common Postoperative Complications for DMEK and DSAEK

	Incidence Average (Range)		References
	DMEK	DSAEK	
Primary graft failure	1.9% (0%–12.5%)	5.0% (0%–29%)	5,6,8,14–22
Graft dislocation	15.9% (2.4%–82%)	4.2% (0%–14.5%)	5,6,8,14–22,30,31,40,41
Successful reattachments	90.9%	92.5%	
Failed repositioning	9.1%	7.5%	
Late graft failure	2.2% (0%–6%)	4.0% (0%–6%)	5,6,8,14–22
Graft rejection	1.9% (0%–5.9%)	10% (0%–15.2%)	5,6,8,14–22,41–44
Controlled medically	92.9%	93.3%	
Leading to graft failure	7.1%	6.7%	
Elevated intraocular pressure	7.6%	14.9%	5,6,8,14–22,41,45
Responding to topical treatment	99.6%	99.9%	
Requiring surgery	0.4%	0.1%	
Retinal detachment	0.2%	2% (0%–4%)	5,6,40,46
Cystoid macular edema	3.0% (0%–2.2%)	2.2%	5,6,8,14–22,40,45
Responding to topical treatment	97.2%	93.75%	
Requiring intravitreal triamcinolone	2.8%	6.3%	

DMEK = Descemet's membrane endothelial keratoplasty; DSAEK = Descemet's stripping automated endothelial keratoplasty.

The incidences of postoperative complications were obtained as reported on PubMed English literature searches.

Table 2.

Cost-Effectiveness Analyses and Cost-Utility Analyses of DMEK Compared with DSAEK of the Reference Case

Perspective	DMEK		DSAEK		DMEK vs. DSAEK		ICER	ICUR
	Cost (USD)	QALY	Cost (USD)	QALY	Incremental Cost (USD)	Incremental Effectiveness		
Refloat in the Office								
Healthcare Sector	\$11 702	0.8568	\$11 824	0.8160	\$122	−0.0408	Dominated	Dominated
Societal	\$15 695	0.8568	\$16 136	0.8160	\$441	−0.0408	Dominated	Dominated
Refloat in the Operating Room								
Healthcare Sector	\$11 788	0.8568	\$11 847	0.8160	\$59	−0.0408	Dominated	Dominated
Societal	\$16 047	0.8568	\$16 229	0.8160	\$182	−0.0408	Dominated	Dominated

DMEK = Descemet's membrane endothelial keratoplasty; DSAEK = Descemet's stripping automated endothelial keratoplasty; ICER = incremental cost-effectiveness ratio; ICUR = incremental cost-utility ratio; QALY = quality-adjusted life year.

The time horizon was lifetime, and all costs and health effects were discounted 3%. The incremental cost-effectiveness ratios and incremental cost-utility ratios were calculated for a variety of clinical scenario examples. A negative value reflected a dominant procedure resulting in a cost-saving scenario (more efficient and less costly) in favor of DMEK, this is displayed as "Dominated."