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REVIEW ARTICLE

Cost-effectiveness of the ADVISE trial: An intraoperative OCT protocol in DMEK surgery

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Abstract

The *intraoperative optical coherence tomography* (iOCT) is recently introduced in Descemet membrane endothelial keratoplasty (DMEK) surgery, which aims to increase clinical performance and surgery safety. However, the acquisition of this modality is a substantial investment. The objective of this paper is to report on the cost-effectiveness of an iOCT-protocol in DMEK surgery with the *Advanced Visualization in Corneal Surgery Evaluation* (ADVISE) trial. This cost-effectiveness analysis uses data 6 months postoperatively from the multicentre prospective randomized clinical ADVISE trial. Sixty-five patients were randomized to usual care ($n=33$) or the iOCT-protocol ($n=32$). Quality-Adjusted Life Years (EQ-5D-5L), Vision-related Quality of Life (NEI-VFQ-25) and self-administered resources questionnaires were administered. Main outcome is the incremental cost-effectiveness ratio (ICER) and sensitivity analyses. The iOCT protocol reports no statistical difference in ICER. For the usual care group compared with the iOCT protocol, respectively, the mean societal costs are €5027 compared with €4920 (Δ€107). The sensitivity analyses report the highest variability on time variables. This economic evaluation learned that there is no added value in quality of life or cost-effectiveness in using the iOCT protocol in DMEK surgery. The variability of cost variables depends on the characteristics of an eye clinic. The added value of iOCT could gain incrementally by increasing surgical efficiency, and aiding in surgical decision-making.

KEYWORDS

corneal transplantation, cost-effectiveness, Descemet membrane endothelial keratoplasty, intraoperative OCT, quality-adjusted life years, vision-related quality of life

1 | INTRODUCTION

In the past decades, novel surgery methods enabled selective transplantation of diseased corneal layers (Dunker et al., 2020; Godinho & Mian, 2019; Singh et al., 2019; Stuart et al., 2016; Tan et al., 2012). In particular, posterior lamellar keratoplasty techniques improved recovery, visual outcomes and quality of vision (Dunker, Dickman, et al., 2021; Dunker, Veldman, et al., 2021; Gellert et al., 2022). Current standard of care for endothelial diseases is *Descemet membrane endothelial keratoplasty* (DMEK), in which only the Descemet membrane and endothelial cell layers are transplanted (~30 μm) (Melles et al., 2006). To achieve better results, new equipment and surgery protocols are developed as well. An example of new equipment is the *intraoperative optical coherence tomography* (iOCT), a non-invasive imaging technology to obtain real-time images of the eye during surgery (Geerling, 2005). Utilization of iOCT in corneal surgery aims to increase clinical performance and safety of DMEK surgery (Steven et al., 2013).

In general, OCT revolutionized the field of ophthalmology. It benefits clinical decision-making and aids in advancing practice patterns (e.g. De Benito-Llopis

et al., 2014; Siebelmann et al., 2015). However, the acquisition of this new diagnostic modality is a substantial investment for most eye clinics which calls for judicious deployment and assessment of the cost-effectiveness (Juergens et al., 2021; Katkar et al., 2018). With rising healthcare costs, policymakers urgently demand economic assessments to justify their scarce resources spent (WHO, 2019).

To elaborate on the question whether an investment in iOCT can be justified, we conduct an economic evaluation of the prospective multicentre randomized clinical *Advanced Visualization in Corneal Surgery Evaluation* (ADVISE) trial, an international noninferior single-blinded randomized clinical trial (RCT). The researchers primarily investigated the use of iOCT in terms of efficacy and safety in DMEK surgery, and additionally collected data on costs and health- and vision-related quality of life. The aim of this paper is to evaluate the cost-effectiveness of an iOCT protocol in DMEK surgery with the ADVISE trial.

2 | MATERIALS AND METHODS

This economic evaluation of the ADVISE trial was performed from a societal perspective over a time horizon of 6 months, meaning costs are not limited to a hospitals' perspective. Participants were recruited between December 2018 and April 2021 at the University Medical Center Utrecht (UMCU), University Hospital Leuven (UZL) and Maastricht University Medical Center+ (MUMC+). This study was conducted in accordance with the Declaration of Helsinki, local and national laws regarding research, European directives with respect to privacy and 2010 CONSORT standards for reporting RCTs (Schulz et al., 2010). The study was approved by the Medical Ethics Committee Utrecht no. 18–487 for both the UMCU and MUMC+, and Ethical Committee Leuven no. S61527, and registered at clinicaltrials.gov (NCT03763721).

2.1 | Study procedures

The study procedures of the ADVISE trial have been reported in detail (Muijzer et al., 2023). In summary, patients needing DMEK surgery due to irreversible corneal endothelial dysfunction resulting from Fuchs endothelial corneal dystrophy were recruited. Patients were randomized to two groups of different DMEK surgery protocols. In the control group ($n = 33$), the intraocular pressure was raised above physiological limits (i.e. overpressure) for 8 min at the end of surgery and iOCT was not available during the surgery. In the intervention group ($n = 32$), the anterior chamber was briefly pressurized to adhere the graft and the iOCT was used to check for complete adherence of the graft without prolonged overpressurizing the eye. In addition, the iOCT was available during the surgery for all study participants at the surgeon's discretion due to ethical considerations.

Each participant underwent a comprehensive ophthalmic examination preoperatively and 1 day, 1 week, 1 month, 3 months and 6 months after surgery. Preoperatively, 3 and 6 months after surgery questionnaires on health-related and vision-related Quality of Life (EQ-5D-5L, NEI-VFQ-25) and productivity/absenteeism questionnaires were administered. All surgical procedures were performed by experienced corneal surgeons, following a standardized procedure. All patients were pseudophakic. The grafts were cultured and provided prepeeled by ETB-Bislife (Beverwijk, the Netherlands). In case of graft detachment larger than 30% of the graft area or affecting visual acuity, a rebubbling procedure was performed. If graft failure occurred, a regraft procedure was performed.

2.2 | Costing procedures

Prices used in this evaluation are reported in accordance with Dutch national guidelines on costing and expressed in Euros (€). Unit prices are multiplied by resource volumes to determine costs. Costs are converted to 2022 Euros in accordance with the Consumer Price Index (CPI) (voor de Statistiek, 2022). Standardized prices are provided by the abovementioned national guideline for cost analyses. Prescribed medication is valued using 2022 reimbursement prices (Zorginstituut Nederland, 2022). Resource data were obtained through the ADVISE trial database and administered questionnaires.

The trial database provided data on hospital admissions, outpatient visits, personnel costs, home care, productivity costs, family costs, informal caregiver costs, general practitioner (GP) consultations and home care. The number of posterior lamellar transplantations performed per year in the UMCU is based on national quality registration data. Costs per minute of the operating theatre are calculated by taking the average of the UMCU, provided by the business controller. Costs of the MUMC+ are provided by earlier literature (Simons et al., 2019). Costs of the UZL are not directly compared with the UMCU and MUMC+ because of the difficulty to compare different healthcare systems within one analysis (the Netherlands and Belgium). UZL units are calculated to reflect Dutch societal prices. The average price of the UMCU and MUMC+ is in line with the mean costs of other regions and hospitals in Europe, the UK and the USA, according to present literature (Abbott et al., 2011; Childers & Maggard-Gibbons, 2018; Christou et al., 2022; Macario, 2010). Surgery times are derived from the ADVISE trial database. The average add-on price of the iOCT system was determined by the manufacturer (RESCAN 700, Carl Zeiss Meditec GmbH, Oberkochen, Germany) at €100.000 and exploitation costs of 5%, depreciated in 10 years. Prices of the donor tissues are provided by the tissue bank ETB-Bislife. Some patients required secondary procedures. Regrafts are calculated by adding the surgical cost per minute for the additional regraft performed, costs for an extra cornea donor, medication during surgery and an extra day care submission. For rebubblings, reimbursement rates from 2021 are used since procedure times are unknown.

2.3 | Effectiveness procedure

The main outcome is the incremental cost-effectiveness ratio (ICER), which often used as a way to directly compare different healthcare interventions in terms of costs and effects of a patients' quality of life. Here, the effects of this ratio are measured in costs per Health-Related Quality of Life (HRQL). Secondary outcomes are Vision-Related Quality of Life (VRQL), and corrected distance visual acuity (CDVA) expressed in logarithm of minimum angle of resolution (LogMAR). All data are collected at three points in time: the preoperative visit, at 3 months and at 6 months after surgery.

HRQL is measured with the EQ-5D-5L questionnaire, developed by the EuroQol Study Group (Balestroni & Bertolotti, 2015; Rabin & De Charro, 2001). This is a standardized nondisease-specific instrument for describing and valuing HRQL. It evaluates the generic quality of life in five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each answer distinguishes five different levels and provides 243 unique health statuses. The EQ-5D-5L also includes a visual analogue scale, on which participants respond their perceived health between 0 (worst possible status) and 100 (best possible health status). Combined, this can be converted to utility scores between 0 (death) and 1 (perfect health).

VRQL is measured with the NEI-VFQ-25 questionnaire (Mangione et al., 2001). The National Eye Institute Visual Function Questionnaire is a vision-specific quality-of-life instrument used in a large number of ophthalmological diseases and interventions (Hirneiß et al., 2010; Mangione, 1998; Mangione et al., 2001). Responses are scored on a scale of 0 (lowest value) to 100 (best value) on which subset scores are calculated for, for example vision-related difficulties in overall health, near and distance vision, limitations in social functioning and dependency on others and mental health symptoms. These scores can be averaged to obtain a composite score. Composite scores ≥10-point improvement were considered significant (Mangione, 2000). Lastly, the CDVA is measured using the chart of the Early Treatment of Diabetic Retinopathy Study at a 4-metre distance, measured in logMAR units by multiplying the number of letters read by −0.02 log units and adding 1.7 log units (Beck et al., 2003).

2.4 | Cost-effectiveness analyses

Cost-effectiveness is calculated over 6-month follow-up. ICER thresholds are used to assess ceiling ratios for health policymakers, since new interventions were often not cost-effective (Cherla et al., 2020; Hakkaart-van Roijen et al., 2016). The ICER represents the additional (or saved) costs for the surgery protocol for every additional unit of effect, here HRQL. It is calculated by dividing the difference in cost (new–old) by the difference in HRQL (new–old). To assess the ICER uncertainty, the outcomes are nonparametric bootstrapped with 1000 replications and expressed in a cost-effectiveness plane, comparing difference in Quality-Adjusted Life Years (QALY) to difference in costs.

2.5 | Sensitivity analyses

As eye clinics are diverse, their cost characteristics of their clinics differ as well. For example, a clinic might perform more surgeries per year or have a lower costs per minute compared with another clinic. Therefore, cost variables are expected to have a high variability. To interpret the robustness of these variables, sensitivity analyses are performed. These analyses are conducted on all variables that considerably influenced the surgery costs. This is done by defining variables for a base case situation and calculate at what point in time costs equal savings, after which variables used for the base case situation are changed to estimate different scenarios, that is different eye clinics. Variables used for this valuation are surgery costs per minute, surgeries performed per year, mean saved minutes per DMEK surgery and the investment costs of the iOCT depreciated in 10 years, including exploitation.

2.6 | Statistical analyses

The analyses are performed according to the intention-to-treat principle. Missing observations for the questionnaires and CDVA are considered missing at random and are imputed using multiple imputation (van Buuren & Groothuis-Oudshoorn, 2011). Missing measurements of subjects that developed a graft failure were considered missing not at random since they were excluded from the trial and are therefore not imputed. The baseline variables concerned were used as predictors for imputing. The number of imputations was equal to the maximum percentage of missing data plus one. Correction for multiple comparisons was performed using the Bonferroni correction. A two-sided p-value <0.05 was considered statistically significant. All statistical analyses were performed using R statistical software version 4.1.3 (Comprehensive R Archive Network, Vienna, Austria).

3 | RESULTS

A total of 65 eyes of 65 patients were included for analysis. Seven subjects were lost to follow-up as a result of graft failure ($n=3$) and reduction in care following the COVID-19 pandemic ($n=4$). In one of 65 patients, the gross surgical time was missing which was imputed. Fifty-four of 390 (14%) of questionnaires contained missing values, which were imputed. No significant differences regarding the incidence of adverse events were found between the treatment arms. A complete overview of the study participant flow was previously reported in more detail in the ADVISE trial. After the characteristics, the results report on costs of the intervention and afterwards on the effects. The costs and effects are then combined to the ICER, that is the cost per QALY.

3.1 | Characteristics and costs

In the usual care and iOCT-protocol group, respectively, the mean age is 72.4 (SD±6.6) and 73.3 (SD±6.4) years, mean baseline CDVA was 0.42 (SD±0.25) and 0.41 (SD±0.26) LogMAR, and included 51.5% and 53.1% females. Table 1 reports on resources used and related costs. The mean net surgical time (i.e. the skin-to-skin time) difference is in favour of the iOCT protocol of ~5 min, including refraining from overpressuring the corneal graft (−13%; SD±2.51), as reported before in the ADVISE trial. The mean graft unfolding time is 1.7 min less in the iOCT group (−26.8%; SD±0.85), reported before as well. Total costs differ €107 in favour of the iOCT: €4920 in the iOCT protocol compared with €5027 in the usual care control group.

3.2 | Effects

The health-related quality of life, vision-related quality of life and visual acuity outcomes are reported in Table 2. All outcomes increase 3 months after surgery and remain stable at 6 months. No statistical difference is found between both groups.

3.3 | Cost per QALY

As reported in Table 2, where usual care is compared WITH the iOCT protocol, the difference in QALY between T = 0 and T = 6 is nonsignificant ($p = 0.596$) and the ICER is fluctuating. Therefore, reporting mean ICERs is not meaningful. The ICER uncertainty is better reflected graphically as a distribution of ICERs (Figure 1). Every dot on the graph represents an individual bootstrapped estimate of the ICER. The four quadrants of the graph represent whether the iOCT protocol has, in comparison with usual care, incremental effect and incremental costs (northeast part of the graph), incremental effect and less costs (southeast), less effect and less costs (southwest), or less effect and incremental costs (northwest). Every datapoint represents a bootstrapped estimate of the ICER. All ICERs are fluctuating and evenly divided over every quadrant, showing contradictory results whether the iOCT protocol adds value in terms of ICER, that is cost-per-QALY compared with the usual care group. As the QALYs are nonfluctuating, this is due to the fluctuation of costs.

3.4 | Sensitivity analyses of fluctuating costs

The sensitivity analyses asses the fluctuation of costs. The iOCT protocol reported an absolute difference in total cost compared with usual care (Δ€107). To interpret the robustness of this cost difference, the variance of impactful variables is assessed individually by calculating a base case scenario and changing every variable individually in a best- and worst-case scenario when other variables remain constant (ceteris paribus). Variables that have a substantial effect on the cost of DMEK surgery are described in Figure 2. Variables that have the substantial impact on the variance of cost are the price per minute of surgery, length of the surgery and the number of surgeries performed per year.

TABLE 1 DMEK surgery resource use and costs in 2022 € from a societal care perspective.

		Usual care ($n = 33$)	iOCT protocol ($n = 32$)		Usual care ($n = 33$)	iOCT protocol ($n = 32$)	
	Unit, €	**Resources, *n* (%)**		***p*-Values**	Costs, mean € (SD)		***p*-Values**
Cornea	1706/unit	33 (100)	32 (100)	NA	1706 (0)	1706 (0)	NA
Rebubbling	365/unit	6 (18.2)	11 (34.4)	0.23	67 (145)	136 (769)	0.14
Regrafts	Variable	2 (6.1)	1 (3.1)	1.00	264 (1056)	202 (582)	0.58
Day care	315/day	33 (100)	32 (100)	NA	315 (0)	315 (0)	NA
Medication	252/DMEK	33 (100)	32 (100)	NA	252 (0)	252 (0)	NA
	Unit, €	**Resources, mean (SD)**		***p***	**Costs, mean € (SD)**		***p***
Ophthalmologist visit	186/visit	5.4 (1.0)	5.7 (1.1)	0.31	1013 (187)	1063 (210)	0.31
Home care	57/h	0.0 (0.0)	0.4 (2.3)	0.31	0 (0)	23 (131)	0.31
ER visits	295/visit	0.1 (0.3)	0.0 (0.0)	0.33	18 (103)	0 (0)	0.33
Travel	0.19/km[a]	35.6 (25.5)	33.9 (16.1)	0.74	10 (5)	9 (3)	0.74
Productivity	40/h	2.2 (10.0)	3.2 (12.1)	0.71	87 (401)	128 (483)	0.71
Time unfolding (min)		6.3 (8.1)	4.6 (5.4)	0.33			NA
Net OR time (min)		37.5 (10.0)	32.7 (11.0)	0.05			NA
Gross OR time	27.72/min	43.8 (11.8)	38.9 (13.1)	0.12	1213 (326)	1079 (363)	0.12
Total costs				NA	5027 (1463)	4920 (1134)	0.75

Note: Net surgery time is the surgical skin-to-skin time, the actual time of a surgery. Net OR time is the skin-to-skin time, gross OR time includes preparation of the patient. Of all cases, three regrafts and 17 rebubblings were performed.

Abbreviations: DMEK, Descemet membrane endothelial keratoplasty; GP, general practitioner; OR, operating room; SD, standard deviation.

[a]Plus €3 parking fee.

4 | DISCUSSION

To justify a substantial investment in new diagnostic modalities, such as an iOCT, an eye clinic needs to interpret the variability on their expected variable costs. The aim of this post hoc economic evaluation of the prospective ADVISE trial is to report on the cost-effectiveness of the iOCT protocol of DMEK surgery. The iOCT protocol reports no statistical difference in QALYs and no superiority of cost-effectiveness in ICERs compared with usual care. Results show a marginal difference in total costs per DMEK of €107 in favour of the iOCT protocol. The sensitivity analyses report the highest variability on cost prices for the time difference, that is the length of a surgery and the costs per minute.

The point where costs equal savings is dependent on many effects which is not accounted for in this paper, such as potential cost variables after 6 months. However, the sensitivity analyses give insight by highlighting contributions that might look small on first hand but could have a larger impact than expected. It underlines that the added value of an iOCT is dependent on the characteristics of the eye clinic, as the variability fluctuates.

Time saving is a substantial variable in the sensitivity analysis. The total time saving of the iOCT-optimized protocol—including refraining from overpressuring—results in a shorter mean net surgical time of 4.9 min (−13%; SD ± 2.51) and the mean graft unfolding time is 1.7 min less in the iOCT group (−26.8%; SD ± 0.85). Though the independent effect of iOCT use cannot be reliably estimated, this suggests that both surgical efficiency and refraining from overpressurizing play a role in decreased surgical time. Additionally, in the previous ADVISE trial we mentioned that the iOCT-optimized protocol assisted in surgical decision-making in 40% of cases for graft unfolding, positioning and orientation.

The sensitivity analyses are calculated for the number of surgeries performed in corneal transplantations. In a broader perspective, the iOCT is widely known to be used in other ophthalmological subspecialisms as well, such as vitroretinal, glaucoma and strabismus (Ang et al., 2020; Shah & Pihlblad, 2021; Siebelmann et al., 2016; Ung & Miller, 2019). Furthermore, the clinical added value of the iOCT differs on a case by case basis. The added value is considered less in straightforward surgery, but increases when difficult anterior chamber conditions exist, such as a shallow anterior

TABLE 2 Effectiveness in quality of life and quality of vision at baseline.

	Usual care ($n=33$)	iOCT protocol ($n=32$)	p-Value
QALY, mean (SD)			
T = 0	0.80 (0.22)	0.84 (0.14)	0.431
T = 3	0.90 (0.16)	0.90 (0.15)	0.930
T = 6	0.90 (0.18)	0.91 (0.13)	0.792
Δ (T0–T6)	0.10 (0.24)	0.07 (0.13)	0.596
NEI-VFQ-25, mean (SD)			
T = 0	74.55 (20.51)	72.85 (16.27)	0.714
T = 3	78.07 (16.35)	78.97(17.07)	0.829
T = 6	83.32 (13.94)	79.54 (16.63)	0.324
Δ (T0–T6)	8.77 (13.49)	6.69 (12.70)	0.524
CDVA in LogMAR, mean (SD)			
T = 0	0.42 (0.25)	0.41 (0.26)	0.882
T = 3	0.14 (0.13)	0.18 (0.19)	0.342
T = 6	0.13 (0.14)	0.22 (0.29)	0.373

Note: T is time for baseline, 3 months and 6 months after surgery.

Abbreviations: CDVA, corrected distance visual acuity; QALY, quality-adjusted life years; T, time in months after surgery; VFQ, visual functioning questionnaire.

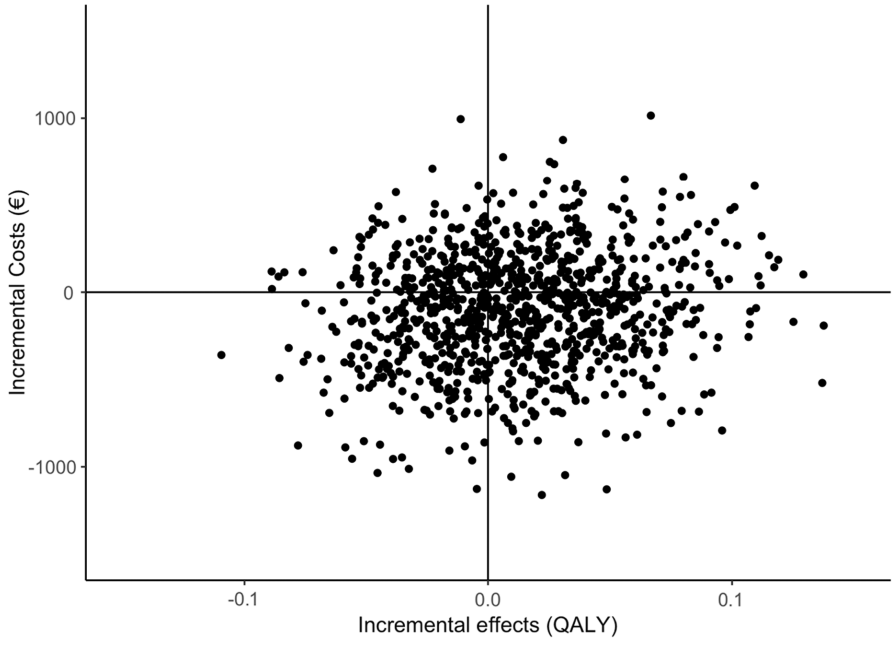

FIGURE 1 Cost per QALY. This graph presents the ICER plane for usual DMEK surgery compared with the iOCT protocol. Each datapoint represents a bootstrapped estimate of the ICER. The incremental costs (y-axis) and the incremental QALY's are compared with usual care on a societal perspective after 6 months. ICER, incremental cost-effectiveness ratio; DMEK, Descemet membrane endothelial keratoplasty; iOCT, intraoperative optical coherence tomography; QALY, quality-adjusted life year.

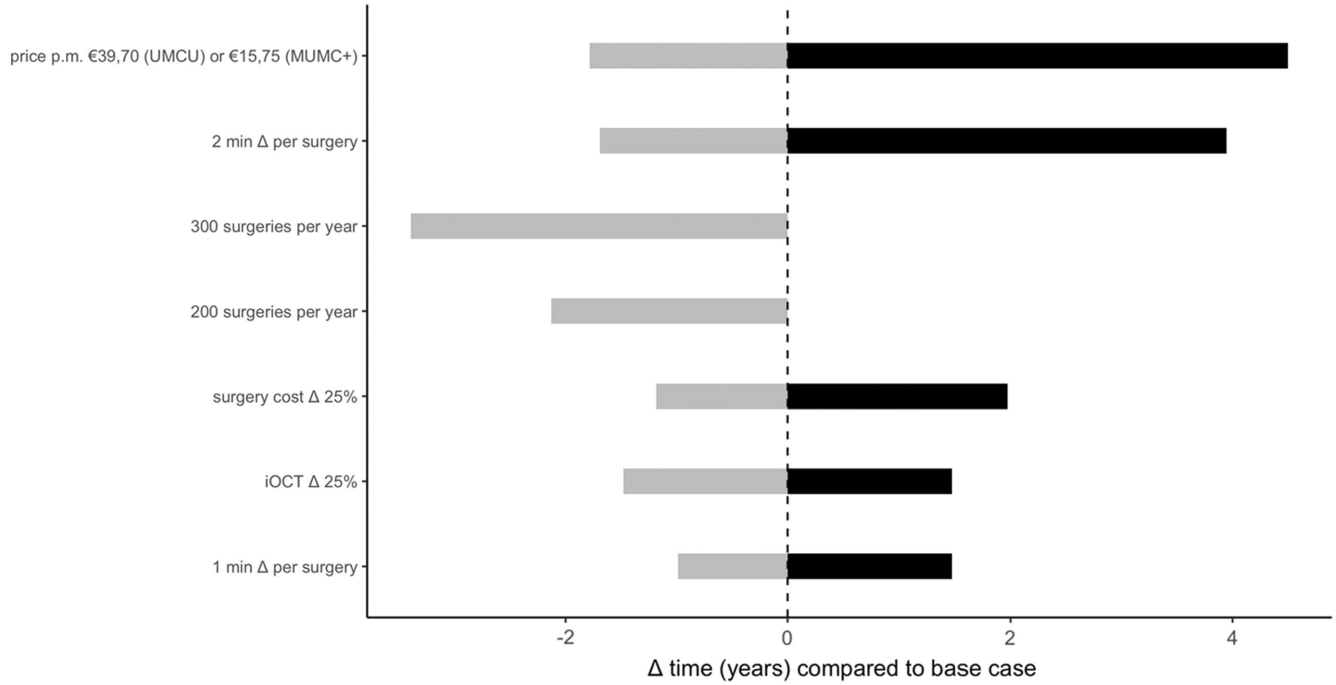

FIGURE 2 Sensitivity analyses of fluctuating costs. This tornado plot reports on the sensitivity analyses when costs equal savings in years compared a base case scenario. When one variable is changed, we assume ceteris paribus. The base case presumes 128 surgeries per year in one academical centre where the iOCT is used for DMEK surgery only, 5 min saved per surgery, operating costs per minute of €27,72, and an investment in the iOCT of €105.000 including exploitation depreciated in 10 years. p.m., per minute; iOCT, intraoperative optical coherence tomography; DMEK, Descemet membrane endothelial keratoplasty; UMCU, University Medical Center Utrecht; MUMC+, Maastricht University Medical Center+.

chamber, synechiae or reduced vision due to corneal oedema. A vast amount of case reports for complex and difficult cases in which iOCT proved decisive and improved surgical decision-making show the value of iOCT (Coppola et al., 2018; Gonzalez-Cortes et al., 2018; Hartmann et al., 2020; Lim et al., 2022; Lytvynchuk et al., 2017; Muijzer, Schellekens, et al., 2022). Lastly, promising innovations are being developed which are dependent on the availability of iOCT (e.g. placement of stents in the suprachoroidal space during glaucoma surgery) that may improve quality of care and thus the added value of iOCT. Therefore, if multiple subspecialisms simultaneously urge to use the iOCT, the added value could increase incrementally by potentially shortening surgery time, increasing surgical efficiency and aiding in surgical decision-making, expanding the iOCT's added value. It must be noted, though, that the iOCT used in this study is an add-on option in the microscope, meaning an eye clinic cannot buy the iOCT isolated. Stand-alone devices are on the market, though research has shown these devices are less effective during surgery (Branchini et al., 2016; Knecht et al., 2010; Muijzer, Kroes, et al., 2022).

This paper has several strengths. First, cost analyses are based on a societal perspective instead of a hospital perspective, meaning that the costing scope is much wider than the hospital alone. Second, this paper included data in the database for prices that are usually difficulty to identify, such as transplant cost directly from the tissue bank and surgery cost per minute direct from two academical hospitals. Usually, these prices are identified using literature and therefore more difficult to interpret.

Third, the database provides data on vision-related quality of life besides HRQL, which is considered an important parameter in the visual impaired patient in addition to HRQL. Fourth, the sensitivity analyses allow readers to put the robustness and variability of cost variables of this iOCT protocol in perspective for eye clinics with different characteristics, for example when surgeries are shorter, cheaper or more often performed.

Likewise, the paper is prone to several limitations. First, the ADVISE trial is powered for postoperative adverse events as a primary outcome, not for a cost-effectiveness analysis or other relevant clinical outcomes, for example detachment or rebubbling rates. This means variability in outcomes could potentially be less if a different setup was used. Second, the time horizon is 6 months postoperatively, which means long-term effects cannot be directly measured, although previous RCTs and real-world studies show little to no difference in graft survival between 6 and 12 months (Chamberlain et al., 2019; Dunker et al., 2020; Schlögl et al., 2016). For the cost variability, we report on the robustness present at 6 months using sensitivity analyses but expected costs after 6 months are not included. A long-term perspective using cost-effectiveness modelling could be interesting as the iOCT is depreciated for about 10 years. Another limitation is the limited number of surgeries performed in each group. Moreover, this study is conducted in the Dutch healthcare system. Outcomes on prices may differ in other healthcare systems as care pathways (the care patients receive) might differ in other countries. Also, for fair comparison, the base case analyses are performed with characteristics specific for the UMC Utrecht (e.g. number of surgeries). These variables differ widely from

clinic to clinic, which introduces bias when results are extrapolated.

Previously, we have observed that the utilization of iOCT in corneal surgery could increase clinical performance, increase the safety of DMEK surgery and aid in surgical decision-making (Carlà et al., 2022; Cost et al., 2015; Dunker, Dickman, et al., 2021; Dunker, Veldman, et al., 2021; Pasricha et al., 2015; Sharma et al., 2020). Also, corneal transplantations are known to be cost-effective, increase health utility and different transplantation techniques are compared before in cost-effectiveness analyses (Beauchemin et al., 2010; Bose et al., 2013; Prabhu et al., 2013; Shah et al., 2021; Simons et al., 2019, 2022; van den Biggelaar et al., 2012). Likewise, we have seen that optimizing the surgical protocol using iOCT leads to a significant reduction in surgery time (Muijzer et al., 2020). Whether the iOCT impacts the cost-effectiveness remained unclear and is mentioned as one of the primary barriers to the adoption of iOCT (Juergens et al., 2021; Katkar et al., 2018; Price, 2021; Sharma et al., 2020). This is the first paper that contributes to that literature gap and is therefore a contribution to the scientifical discussion whether the iOCT adds value.

In conclusion, this clinical trial learned that there is no added value in quality of life and cost-effectiveness in using the iOCT protocol in DMEK surgery specifically, but there is benefit in decreased surgery times and marginal lower costs of €107 per DMEK of the iOCT protocol. The robustness of these cost variables depends on the characteristics of an individual eye clinic. The added value of iOCT could increase incrementally by shortening surgery time, increasing surgical efficiency and aiding in surgical decision-making, for example in difficult surgical conditions.

For future perspectives, additional long-term studies with larger study groups powered specifically for cost-effectiveness are required to better inform policymakers regarding the added value of an iOCT specifically. Also, the potential impact of an iOCT protocol could be increased by evaluating other ophthalmological subspecialisms as well, where this study is only focused on corneal transplantation. Last, although challenging, it might be favourable to power the study on other relevant clinical outcome measurements, as a primary study outcome (i.e. graft detachments and rebubbling rates or difficulty during surgery).

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CONFLICT OF INTEREST STATEMENT

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