

# CLINICAL BENEFIT, COMPLICATION PATTERNS AND COST EFFECTIVENESS OF LASER IN SITU KERATOMILEUSIS (LASIK) IN MODERATE MYOPIA: RESULTS OF INDEPENDENT META ANALYSES ON CLINICAL OUTCOME AND POSTOPERATIVE COMPLICATION PROFILES\*

J. Lamparter<sup>1</sup>, H. B. Dick<sup>2</sup>, F. Krummenauer<sup>1</sup>

<sup>1</sup>Clinical Epidemiology and Health Economy Unit, Dresden University of Technology Dresden / Germany  
(Head of the unit: Prof. Dr. F. Krummenauer)

<sup>2</sup>Department of Ophthalmology, University of Mainz, Mainz / Germany (Head of the department: Prof. Dr. N. Pfeiffer)

## Abstract

**Purpose:** Laser in situ keratomileusis (LASIK) means a patient investment of 2426 € per eye, which usually cannot be funded by European health care insurers. In the context of recent resource allocation discussions, however, the cost effectiveness of LASIK could become an important indication of allocation decisions. Therefore an evidence based estimation of its incremental cost effectiveness was intended.

**Methods:** Three independent meta analyses were implemented to estimate the refractive gain [dpt] due to conventional LASIK procedures as well as the predictability of the latter [%] (fraction of eyes achieving a postoperative refraction with maximum deviation of  $\pm 0.5$  dpt from the target refraction). Study reports of 1995 – 2004 (English or German language) were screened for appropriate key words. Meta effects in refractive gain and predictability were estimated by means and standard deviations of reported effect measures. Cost data were estimated by German DRG rates and individual clinical pathway calculations; cost effectiveness was then computed in terms of the incremental cost effectiveness ratio (ICER) for both clinical benefit endpoints. A sensitivity analysis comprised cost variations of  $\pm 10$  % and utility variations alongside the meta effects' 95% confidence intervals.

**Results:** Total direct costs from the patients' perspective were estimated at 2426 € per eye, associated with a refractive meta benefit of 5.93 dpt (95% meta confidence interval 5.32 – 6.54 dpt) and a meta predictability of 67% (43% – 91%). In terms of incremental costs, the unilateral LASIK implied a patient investment of 409 € (sensitivity range 351 – 473 €) per gained refractive unit or 36 € (27 – 56 €) per gained percentage point in predictability. When LASIK associated complication patterns were considered, the total direct costs amounted up to 3075 €, resulting in incremental

costs of 519 € / dpt (sensitivity range 445 – 600 € / dpt) or 46 € / % (34 – 72 € / %). Most frequently reported LASIK complications were "central islands / over- / undercorrection / regression" (meta incidence estimate 24%) and "haze" (15%), which were identified by means of an independent meta analysis.

**Conclusion:** Bearing incremental costs of 519 € per gained refractive unit in mind, the conventional LASIK procedures showed an encouraging cost effectiveness range; the latter estimate may serve as a rationale for future allocation discussions in ophthalmology.

**Key words:** Laser in situ keratomileusis (LASIK), cost effectiveness, incremental costs

## 1. INTRODUCTION

Within the last years laser in situ keratomileusis (LASIK) has become a common surgical method for correcting moderate myopia. The principle concept of LASIK procedures consists in lowering an eye's corneal refraction by surgical reduction of the corneal thickness. A microkeratome is used to cut off a small flap of the cornea, which enables to laser off a small segment of corneal tissue by means of an excimer laser. The flap is then re-directed onto the remaining corneal surface [30]. This strategy is already established for the correction of moderate myopia (down to -8 dpt) and gradual hyperopia (up to +2 dpt). The acceptance of this laser-based procedure becomes evident by consideration of the increasing demand for LASIK [7-9; 33]. Despite its acceptance in correcting myopia, however, the complication pattern of LASIK procedures is an important point of discussion, since the principle violation of corneal tissue as well as the fact of inevitably tearing the Brownian membrane apart cannot be ensured to be free of long-time complications; note, that the latter can hardly be identified at the time being, for recent LASIK procedures being yet in use for less than 10 years.

Nevertheless, the risk benefit ratio of LASIK is discussed in an encouraging matter: A large number of trials and publications already dealt with the refractive

\*The content of this paper is part of the doctoral thesis of Ms Julia Lamparter (Dresden University of Technology).

**Financial Interests:** The authors have no commercial or political interests in the methodological or medical aspects presented in this paper.

outcome of LASIK on the one hand and its short-time complication profile on the other hand. Furthermore, the discussions on LASIK increasingly involve an additional dimension, which is related to the fact, that most European health care insurers refuse to reimburse this intervention disregarding putative socio-economic benefits and social circumstances of patients attending the intervention. The corresponding underlying health economic aspects of LASIK, however, are hardly covered in literature. Since myopia can be conservatively corrected by seeing aids and the LASIK surgery therefore cannot be considered as a “necessary” intervention, its cost effectiveness is of great importance for both patients and ophthalmologists [6, 24]. Only few studies consider the cost effectiveness of LASIK, but demonstrate a remarkably positive performance and encouraging results [5; 22] from the patient’s perspective. According to these findings, the patient investment for LASIK procedures is complimented with an overly positive clinical outcome. These early studies, however, only involve rather few patients and restrict to a quite short follow-up period of the latter [5; 22]. Cost effectiveness considerations therefore hardly consider the entire complication profile of LASIK and might thereby have ended up in overly liberal cost effectiveness estimates: Note that LASIK associated complications often afford surgical or at least conservative re-treatment, which means both additional costs for patients and health care insurers as well as sometimes a remarkable reduction in subjective and, in particular, ophthalmological well-being. The consideration of LASIK complication profiles will therefore correct the existing cost effectiveness estimates for the clinical and economical effects of re-treatment requirements, i.e. the cost effectiveness will become more realistic, but maybe also more pessimistic. Allocation discussions in ophthalmology, however, crucially call for such realistic estimates. Further investigations on the costs and benefits of LASIK are therefore necessary. To become able to also consider the maximum available information on complication patterns, an evidence based analysis of the LASIK cost effectiveness seems appropriate.

In summary this evidence based investigation was made in order to evaluate the incremental cost effectiveness of LASIK in moderate myopia, which means estimation of the costs per benefit unit as gained by the LASIK intervention from the health care service’s perspective. The latter perspective was chosen to derive a cost effectiveness estimate as a rationale for recent allocation decisions in ophthalmology, i.e. to enable health care insurers to simulate expectable costs and related patient benefits of a LASIK funding scenario.

Three independent meta analyses were implemented for this purpose to enroll the literature published between 1995 and 2004. The first and second meta analyses were to estimate the clinical benefit due to the LASIK interventions, the third one was to evaluate the corresponding expectable complication profile. Costs for the primary intervention and for the correction of complications were then related to the clinical benefit, where cost estimates were thoroughly based on rates of German official health care insurers (complication re-treatment).

## 2. MATERIAL AND METHODS

### 2.1 STUDY DESIGN, CLINICAL AND ECONOMICAL ENDPOINTS

This investigation intended to relate the direct costs of the conventional LASIK procedure to its clinical benefit in terms of a cost effectiveness ratio [23]. The clinical benefit was to be estimated by means of a meta analysis, i.e. an evidence-based cost effectiveness evaluation was intended.

The primary clinical endpoints of this study were the refractive gain [dpt] due to conventional LASIK procedures as well as the LASIK predictability [%], which means the relative frequency of eyes, which attained a post operative refraction with deviation of less than  $\pm 0.5$  dpt from the target refraction. The economical endpoint were the total direct costs caused by the LASIK treatment, corrected for putative additional costs for re-treatment of complications. The target parameter of the cost effectiveness evaluation is then the ratio of the primary economical and clinical endpoints (ICER, **I**ncr**E**mental **C**ost **E**ffectiveness **R**atio), where the LASIK treatment is contrasted to the alternative of its omission. In the present scenario the latter can be estimated as follows [23]:

$$\begin{aligned} \text{ICER} &= (\text{LASIK costs} - \text{costs of no treatment}) / \\ &\quad (\text{LASIK benefit} - \text{benefit of no treatment}) \\ &= \text{LASIK costs} / \text{LASIK benefit}, \end{aligned}$$

which means that the incremental costs of LASIK (when contrasted to the alternative “treatment” of its omission) coincide with its marginal costs. Note that this alternative “treatment” might, for example, consist in the supplementation of patients with seeing aids, which are usually not or hardly funded by European health care insurers and statutory health care services. Furthermore the supplementation with seeing aids does not change the patient’s refraction, i.e. both the refractive gain becomes 0 dpt and the alternative treatment’s predictability is 0% (as none of the patients profit from any refractive correction). The alternative “treatment” of supplementation with seeing aids therefore imposes costs of 0 € for a clinical benefit of 0 dpt or 0 % predictability, respectively. Summarizing the above formula for incremental cost estimation reduces to the direct LASIK cost / benefit ratio.

### 2.2 IMPLEMENTATION, INCLUSION CRITERIA AND STATISTICAL EVALUATION OF META ANALYSES

Three independent meta analyses concerning the refractive gain, the postoperative complication patterns and the predictability of LASIK were implemented by means of the German and English speaking literature published between 1995 and 2004. Via pre-specified keywords (such as “LASIK refraction”, “complications”, “predictability”, “visual gain” and their respective combinations) relevant journal articles were identified by means of the internet database MedLine.

In general studies were included into the respective meta analysis, when the number of treated eyes was designed by an appropriate statistical sample size cal-

ulation (i.e. the study showed a sufficient statistical power), and when the study patients' preoperative refraction and astigmatism did not exceed -14.0 dpt and  $\pm 4.0$  dpt respectively, such as recommended by the FDA [36]. Furthermore, only publications were included, which covered a follow-up period of at least 6 months. In disaccordance to standard meta analysis recommendations, the inclusion of non-randomised trials was allowed (which was necessary for the complication endpoint).

Since the aim of the meta analysis on the refractive gain was to determine the mean change in refraction attained by LASIK, this meta analysis additionally demanded the availability of estimates on the mean pre- and postoperative refraction or the mean intraindividual change of the latter. Accordingly, the meta analyses on LASIK complications and predictability required the reporting of a complication incidence or a predictability estimate. Furthermore studies were only included, if effective sample sizes (on which the reported refractive gain, complication incidence and predictability estimates were based) could be identified precisely; the latter enabled the computation of study-specific confidence intervals, if not already provided by the authors.

The study reports' estimates on mean refractive gains were then averaged to derive a "meta estimate" for the LASIK's refractive benefit; accordingly, the study reports' estimates for predictability and complications incidences were averaged to derive a "meta predictability" and "meta incidences" for the identified LASIK complications. Appropriate empirical 95% confidence intervals were estimated for each study report (if not already provided by the authors); the empirical 95% confidence intervals for the meta mean estimates were derived accordingly. Funnel plots were used to simultaneously display the studies' reported effect estimates and the resulting meta effect.

### 2.3 COST DATA

The direct cost evaluation was based on the treatment cost profiles reported from the Mainz University Eye Hospital for both the primary LASIK treatment as well as for complication associated re-treatments. Direct costs of 2426.46 € per eye were then imputed for the primary LASIK procedure. For both clinically and economically relevant complications (i.e. complications, which afford clinical treatment and thereby cause treatment costs) as identified by the meta analysis on LASIK complications, standard clinical pathways for re-treatment as established in the Mainz University Eye Hospital were assumed. Treatment costs were simulated alongside these pathways according to worst cost scenarios (i.e. the most cost-intensive method for re-treatment was considered, which could be reimbursed by statutory health care insurers). The resulting costs for individual re-treatment were then used to correct the total costs for the primary treatment: If the meta analysis on complications identified a LASIK complication with incidence, for example, 0.5% and costs for the re-treatment due to this complication were simulated as 100 €, the total cost correction due to this complication amounted to  $0.5\% \times 100 \text{ €} = 0.50$

€ (i.e. a complication's re-treatment costs were averaged over the expectable frequency of this complication such as indicated by its meta incidence).

### 2.4 SENSITIVITY ANALYSIS

To evaluate the impact of the above input parameters on the ICER estimate, a sensitivity analysis comprised a deterministic cost variation of  $\pm 10\%$  and a stochastic benefit variation alongside the respective meta effect's 95% confidence intervals. Furthermore, a sensitivity analysis for the meta effect of the meta analysis on the LASIK predictability was performed, which varied the predictability cutpoint  $\pm 0.5$  (strong predictability) to  $\pm 1.0$  (weak predictability). The latter means a maximum deviation of  $\pm 1.0$  instead of  $\pm 0.5$  between intended and achieved refraction after LASIK, and thereby will result in a more optimistic cost / benefit relation due to the weaker benefit requirement.

## 3. RESULTS

A total of 18 study reports complied with the inclusion criteria for the meta analysis on the refractive benefit of LASIK [4; 10-12; 14; 16; 20; 25-27; 29; 33-35; 37; 38; 42; 43]. Since two of these studies reported the stratified results for several treatment groups, a total number of 21 trial arms could be evaluated. The meta analysis on the LASIK predictability could include 15 study reports [4; 10-12; 14; 16; 20; 25-27; 34; 35; 38; 42; 43] and evaluate 16 trial arms, the meta analysis on LASIK complications comprised a total of 30 trial reports [1-4; 10-14; 16; 20; 21; 25-27; 29-35; 37-44].

### CLINICAL BENEFIT

The meta analysis on refractive gains due to LASIK showed a mean preoperative refraction of -6.31 dpt (95%-confidence-intervall -6.52 dpt to -6.1 dpt) and a mean postoperative value of -0.38 dpt (-0.46 dpt to -0.3 dpt), suggesting a mean meta refractive gain of 5.93 dpt (5.32 to 6.54 dpt) as demonstrated in Figure 1.

Figure 2 shows the results emerged from the meta analysis concerning the "strong" predictability: If a maximum deviation of  $\pm 0.5$  is demanded between intended and achieved refraction, only a predictability estimate of 67% is obtained with a 95% confidence interval ranging from 43 – 91% (note the remarkable heterogeneity among the underlying trials). In terms of a sensitivity analysis for the predictability cutpoint, Figure 3 presents the results for a "weak" predictability requirement (maximum deviation of  $\pm 1.0$ ); the corresponding meta predictability was estimated at 85% with a somewhat less heterogeneous distribution among the study reports.

### COMPLICATIONS

Table 1 shows the LASIK-associated complications with the corresponding meta incidences, which resulted from the meta analysis on complications. Further-

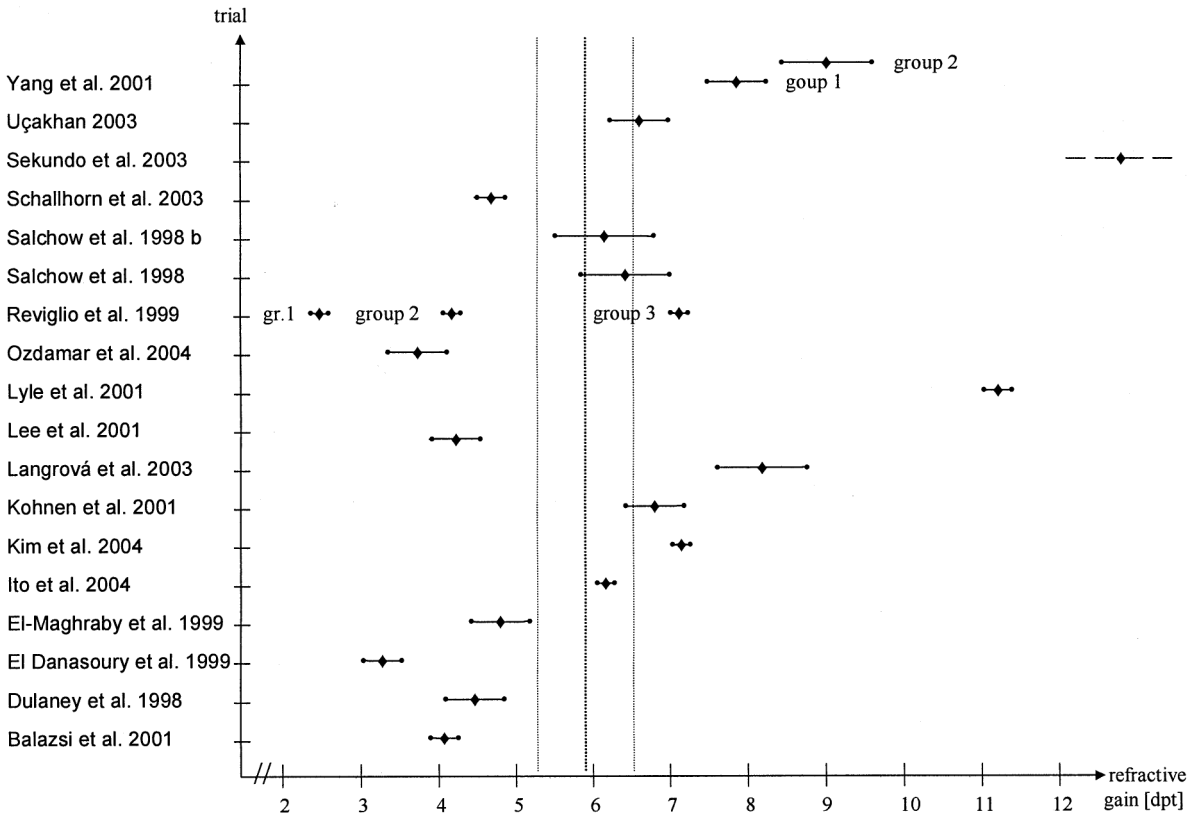


Fig. 1. Study effects on refractive gain [dpt] included into the meta analysis on LASIK refractive benefit. Verticals display the corresponding meta gain with 95%-confidence interval, horizontal extensions indicate reported or re-calculated 95%-confidence intervals of single trials.

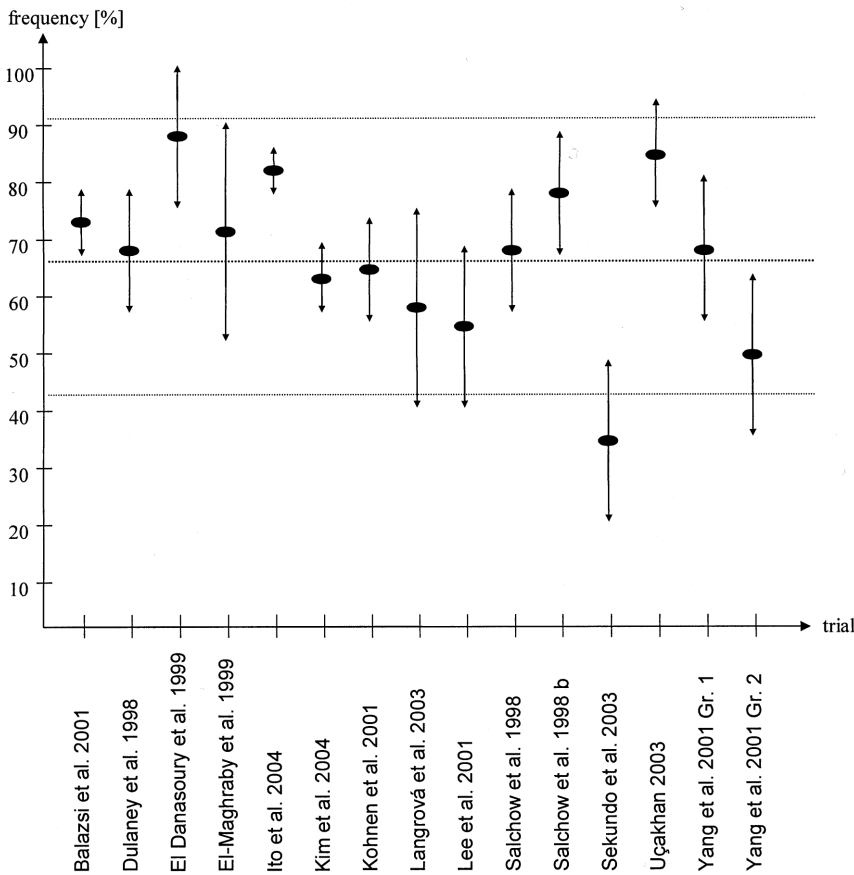


Fig. 2. Study effects on predictability [%] included into the meta analysis on "strong LASIK predictability" (relative frequency of eyes with attained refractions of less than  $\pm 0.5$  dpt deviation from the target refraction). Horizontals display the corresponding meta gain with 95%-confidence intervals, vertical extensions indicate reported or re-calculated 95%-confidence intervals of single trials.

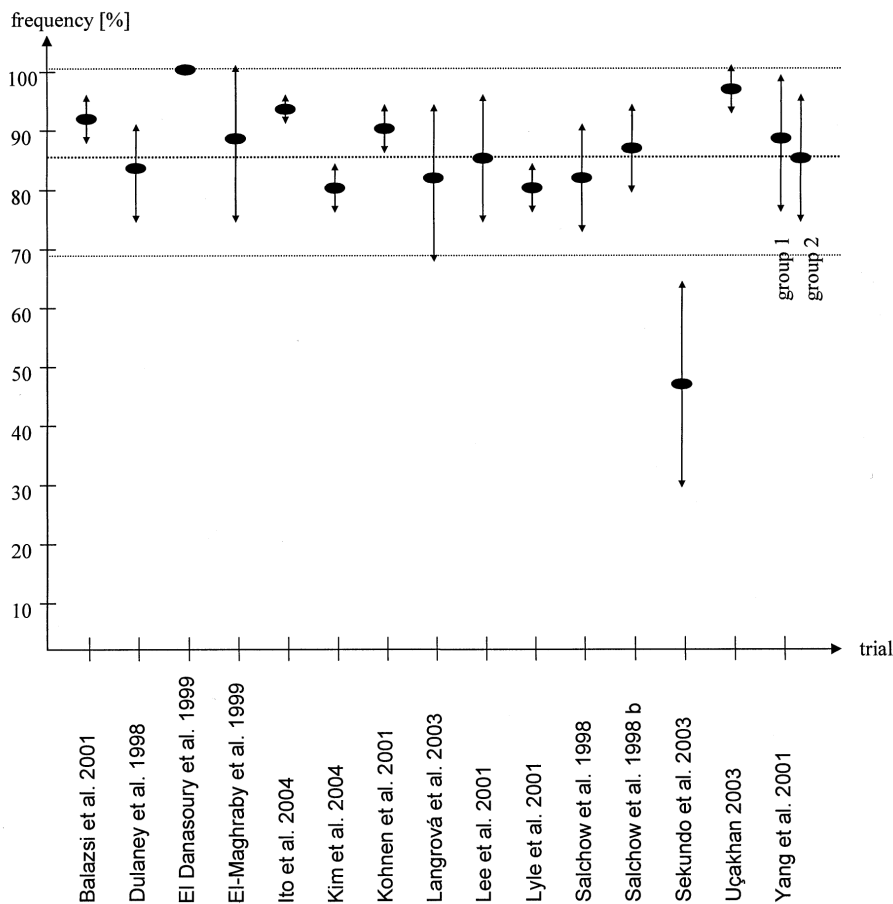


Fig. 3. Study effects on predictability [%] included into the meta analysis on “weak LASIK predictability” (relative frequency of eyes with attained refractions of less than  $\pm 1.0$  dpt deviation form the target refraction). Horizontals display the corresponding meta gain with 95%-confidence intervals, vertical extensions indicate reported or re-calculated 95%-confidence intervals of single trials.

Table 1. LASIK associated complications identified by the meta analysis with estimated mean meta incidence rates and simulated costs for complication treatment (simulation based on clinical pathways).

complication	meta incidence	simulated costs for treatment	expectable additional costs
central islands, overcorrection, undercorrection, regression	24%	1870.46 €	448.91 €
haze	14.5%	50.09 €	7.26 €
buttonhole, free flap, thin / thick / irregular flap, incomplete / irregular cut, decentration	11.1%	568.62 €	63.12 €
foreign body in the interface	9%	2439.00 €	54.88 €
dry eyes	7.1%	121.50 €	8.63 €
inflammation	6.5%	14.44 €	0.94 €
striae	2.5%	2112.30 €	52.81 €
erosio corneae	1.3%	36.14 €	0.47 €
keratectasia	0.1%	8600.15 €	8.60 €
retinal detachment	0.1%	2682.79 €	2.68 €

more, it presents the cost simulation results for these complications, when corrections are performed according to the standard clinical pathways implemented at the University Eye Hospital of Mainz. Since most of the cost-intensive complications are rather rare, they will hardly change the overall cost sum. Table 1 therefore also demonstrates the expectable total cost increase due to each complication after accounting for its incidence.

Whereas the total direct costs for the primary LASIK intervention were estimated – according to the reported rate at the University Eye Hospital of Mainz – at 2426.46 € per eye, the cost correction due to LASIK associated complications as indicated in Table 1 revealed expectable total costs of 3074.76 €. The latter means an expectable increase in direct costs of 27% or 648.30 € due to clinically and economically relevant complications.

#### COST EFFECTIVENESS

The expectable cost investment of 3074.76 € is complemented with a refractive gain of 5.93 dpt and a strong predictability of 67%. The LASIK procedure therefore implied expectable costs of 518.51 € per gained refractive benefit unit (sensitivity range 444.90 € / dpt – 599.69 € / dpt). The corresponding expectable costs for the strong LASIK predictability requirement amounted to 45.89 € per percentage point (sensitivity range 33.79 € / % – 71.51 € / %).

#### 4. DISCUSSION

The primary aim of this investigation was to estimate the cost effectiveness of laser in situ keratomileusis (LASIK) under accountance for its re-treatment cost requirements as caused by complications. The mean refractive benefit of LASIK, its complication profile and predictability were estimated by means of three independent meta analyses on literature published between 1995 to 2004. As a main result this investigation revealed complication-corrected costs of 518.51 € per gained refractive unit (dpt), where a mean refractive benefit of -5.93 dpt is achieved by the total cost investment of 3074,76 €. The latter contains an economically relevant cost fraction of 648.30 € due to LASIK-associated postoperative complications, despite the fact, that severe adverse events after the primary surgery were rather rare as indicated in Table 1.

The results on predictability suggested 85% of eyes within a maximum deviation of  $\pm 1.0$  dpt from the intended correction and 67% of eyes within  $\pm 0.5$  dpt; these findings are confirmed by comparison with independent international studies [17-19; 28]. Both results can be regarded as an indication of both an encouraging clinical and economical LASIK performance. Note that the above cost effectiveness estimate of 519 € per gained refractive benefit unit can be regarded quite similarly optimistic as the “native” estimate of 334 – 415 € per dpt [22], which was not corrected for LASIK complications. From a health economic point of view, these estimates are quite comparable [23, 24] and would imply the same allocation decision, when taken into account by statutory health service insurers.

Therefore the above estimates on the conventional LASIK's cost effectiveness may serve as a rationale for such recent discussions in Western Europe.

#### PRECISION OF REFERENCE EVALUATION

A manual search for articles was performed according to the recommendations of the Cochrane Collaboration in order to quantify the precision and thereby the validity of the MedLine-based meta analyses in the LASIK setting. For this purpose two specialist journals, the Journal of Cataract and Refractive Surgery (edition 2003) and the Journal of Refractive Surgery (edition 2002 / 2003) were searched for relevant articles, which would serve the purpose of at least one of the above meta analysis. Each article in these journal volumes was carefully examined in its full-text version according to the searching and inclusion criteria. It turned out that all the relevant articles identified by manual search had already been included by means of the electronical search based on MedLine; i.e. this validation study suggested an accuracy of 100% concerning the detection of relevant articles for each of the three meta analyses.

#### VALIDITY OF INPUT DATA

In order to estimate cost and benefit input data for the cost effectiveness evaluation it proved to be necessary to apply approximations and model assumptions. In either cases, however, these factors were used as carefully and rarely as ever possible; nevertheless, it is important to consider their potential biasing impact on the above results. One major problem of the meta analyses was the rather heterogeneous documentation and the sometimes even – from a methodological point of view – wrong analysis and presentation of the study reports' effect estimates. The heterogeneity of input data became apparent in the meta analysis concerning refraction, for example in the partially different number of patients or in the drastically varying range of underlying follow-up periods. In addition to this, we found a wide variety of applied lasers and microceratomes, which are definitely associated with the clinical outcome and the incidence of complications after LASIK [15].

Patient sample sizes varied as well among studies, so that a sample size re-calculation was performed for each included study in order to ensure, that its results are due to a sufficient statistical power. To enforce comparability of the included studies' effect measures, 95% confidence intervals were estimated for each endpoint. However, due to sometimes lacking documentation quality in study reports, computation of these intervals often afforded statistical approximations [23]. This became overly difficult, as soon as the trial publication did not provide sufficient information (for example, on the preoperative refraction or on its standard deviation). This lacking documentation quality of study reports may to some extent explain the rather limited number of publications included in the meta analyses described here (even though the inclusion criteria allowed the consideration of non-randomized trials).

Simplifications were made concerning classification of complications: for example, specific complications such as “small fiber in the interface”, “interface debris” or “interface epithelial cells” were reported in terms of one combined incidence estimate for the complication “foreign body in the interface”. Similarly it was rarely possible to weight complications according to their severity level because of lacking information in the underlying study report; mild and severe stages of the same complication type were aggregated in one overall incidence estimate disregarding the stage-dependence of clinical and economical consequences of the actual complication’s stage.

Note that also the cost data might be biased due to an intrinsic model assumption of the above analyses and estimations procedures: Most cost data and the underlying clinical pathways were derived from the standards and experiences of the refractive surgery unit at the Mainz University Eye Hospital. However, the latter may crucially differ from the corresponding cost and treatment data of other ophthalmological departments in Germany and will vary even more over Europe. The same holds for the “worst complication case” and thereby “most expensive re-treatment strategy” scenario as applied to derive an upper bound for the expectable complication-associated cost profile. Therefore a cost sensitivity analysis introduced a cost variation of  $\pm 10\%$  of the cost factors derived from the department in Mainz. The lower range of the resulting cost effectiveness variation (444 € per gained dpt) merely coincides with the estimate derived in [22] based on individual patient data. Therefore the cost effectiveness estimates obtained in this meta analysis (i.e. evidence) based investigation can be considered rather robust against model assumptions in the cost input data.

In summary, the presented estimates on clinical outcome, complications and cost effectiveness were derived by taking several approximations and thereby maybe biases into account. On the other hand, the obtained estimates were found robust in sensitivity analyses and can be considered evidence based by covering the maximum available reference information at the time of the investigation.

## 5. CONCLUSION

In order to account for the expectable complication pattern and the resulting costs for re-treatment, an evidence (meta analysis) based estimation of the cost effectiveness of the conventional laser in situ keratomileusis (LASIK) was implemented. Bearing total direct costs of 519 € per gained refractive unit in mind, the LASIK shows an encouraging investment from both the patient’s and the health insurer’s perspective; the latter estimate may serve as a rationale for future allocation discussions in ophthalmology. The results of this investigation indicate that the LASIK is a highly cost-effective procedure in the correction of myopia.

### REFERENCES’ ALLOCATION TO META ANALYSES

References for meta analysis concerning “LASIK clinical outcome, refraction”:  
4; 10-12; 14; 16; 20; 25-27; 29; 33-35; 37; 38; 42; 43

References for meta analysis concerning “LASIK complications”:

1-4; 10-14; 16; 20; 21; 25-27; 29-35; 37-44

References for meta analysis concerning “LASIK clinical outcome, predictability”:

4; 10-12; 14; 16; 20; 25-27; 34; 35; 38; 42; 43

*Acknowledgement:* The authors are grateful to Ms Karen Faulkner (medical student) for a native speaker revision of this manuscript.

## REFERENCES

1. Albiets JM, Lenton LM, McLennan SG (2004). Chronic dry eye and regression after laser in situ keratomileusis for myopia. *J Cataract Refract Surg* 30:675-684
2. Arevalo JF, Ramirez E, Suarez E, Cortez R, Ramirez G, Yopez JB (2002). Retinal detachment in myopic eyes after laser in situ keratomileusis. *J Refract Surg* 18:708-714
3. Arevalo JF, Ramirez E, Suarez E, Cortez R, Antzoulatos G, Morales-Stopello J, Ramirez G, Torres F, Gonzalez-Vivas R (2001). Rhegmatogenous retinal detachment in myopic eyes after laser in situ keratomileusis. *J Cataract Refract Surg* 27:674-680
4. Balazsi G, Mullie M, Lasswell L, Lee PA, Duh Y-J (2001). Laser in situ keratomileusis with a scanning excimer laser for the correction of low to moderate myopia with and without astigmatism. *J Cataract Refract Surg* 27:1942-1951
5. Berdeaux G, Alió JL, Martinez J-M, Magaz S, Badia X (2002). Socioeconomic aspects of laser in situ keratomileusis, eyeglasses and contact lenses in mild to moderate myopia. *J Cataract Refract Surg* 28:1914-1923
6. Busbee BG, Brown GC, Brown MM (2003). Cost-effectiveness of ocular interventions. *Curr Opin Ophthalmol* 14:132-138
7. Duffey RJ, Leaming D (2004). Trends in refractive surgery in the United States. *J Cataract Refract Surg* 30:1781-1785
8. Duffey RJ, Leaming D (2003). US trends in refractive surgery: 2002 ISRS survey. *J Refract Surg* 19:357-363
9. Duffey RJ, Leaming D (2002). U.S. trends in refractive surgery: 2001 international society of refractive surgery survey. *J Refract Surg* 18:185-188
10. Dulaney DD, Barnet RW, Perkins SA, Kezirian GM (1998). Laser in situ keratomileusis for myopia and astigmatism: 6 month results. *J Cataract Refract Surg* 24:758-764
11. El Danasoury MA, El Maghraby A, Klyce SD, Mehrez K (1999). Comparison of photorefractive keratectomy with excimer laser in situ keratomileusis in correcting low myopia (from -2.00 to -5.50 Diopters). *Ophthalmology* 106:411-420
12. El-Maghraby A, Salah T, Waring GO, Klyce S, Ibrahim O (1999). Randomized bilateral comparison of excimer laser in situ keratomileusis and photorefractive keratectomy for 2.50 to 8.00 diopters of myopia. *Ophthalmology* 106:447-457
13. Gimbel HV, Anderson Penno EE, van Westenbrugge JA, Ferensowicz M, Furlong MT (1998). Incidence and management of intraoperative and early postoperative complications in 1000 consecutive laser in situ keratomileusis cases. *Ophthalmology* 105:1839-1847
14. Ito M, Hori-Komai Y, Toda I, Tsubota K (2004). Risk factors and retreatment results of intraoperative flap complications in LASIK. *J Cataract Refract Surg* 30:1240-1247

15. Jacobs JM, Taravella MJ (2002). Incidence of intraoperative flap complications in laser in situ keratomileusis. *J Cataract Refract Surg* 28:23-28
16. Kim JK, Kim SS, Lee HK, Lee IS, Seong GJ, Kim EK, Sueng HH (2004). Laser in situ keratomileusis versus laser-assisted subepithelial keratectomy for the correction of high myopia. *J Cataract Refract Surg* 30:1405-1411
17. Knorz MC, Wiesinger B, Liermann A, Seiberth V, Liesenhoff H (1998)a. Laser in situ keratomileusis for moderate and high myopia and myopic astigmatism. *Ophthalmology* 105:932-940
18. Knorz MC, Jendritza B, Liermann A, Hugger P, Liesenhoff H (1998)b. LASIK zur Myopiekorrektur. *Ophthalmologie* 95:494-498
19. Knorz MC, Liermann A, Wiesinger B, Seiberth V, Liesenhoff H (1997). Laser-in-situ-Keratomileusis (LASIK) zur Myopiekorrektur. *Ophthalmologie* 94:775-779
20. Kohnen T, Steinkamp GWK, Schnitzler E-M, Baumeister M, Wellermann G, Bühren J, Brieden M, Herting S, Mirshahi A, Ohrloff C (2001). LASIK mit superiorem Hinge und Scanning-Spot-Excimerlaserablation zur Korrektur von Myopie und myopem Astigmatismus. *Ophthalmologie* 98:1044-1054
21. Kramann C, Tehrani M, Dick HB (2004). Laser-in-situ-Keratomileusis mit einem Flying-Spot-Excimerlaser und dem Mikrokeratom nach Carriazo-Barraquer – Ergebnisse nach 6 Monaten. *Klin Monatsbl Augenheilkd* 221:35-39
22. Krummenauer F, Roden M, Knorz MC, Dick HB (2003). Refraktiver Nutzen und inkrementelle Kosten der LASIK: Ergebnisse einer Kosten-Nutzen-Studie an zwei universitären LASIK-Zentren. *Klin Monatsbl Augenheilkd* 220:320-325
23. Krummenauer F, Landwehr I (2005): Incremental cost effectiveness evaluation in clinical research. *Eur J Med Res* 10:18–25
24. Landwehr I, Tehrani M, Dick HB, Krummenauer F, (2003). Kosteneffektivitätsanalyse der Versorgung von Kataraktpatienten mit monofokalen Intraokularlinsen aus Sicht der Leistungserstatter. *Klin Monatsbl Augenheilkd* 220:532-539
25. Langrová H, Derse M, Hejzmanová D, Feuermannová A, Rozsival P, Hejzmanová M (2003). Effect of photorefractive keratectomy and laser in situ keratomileusis in high myopia on logMAR visual acuity an contrast sensitivity. *Acta medica* 46:15-8
26. Lee JB, Kim JS, Choe C-M, Seong GJ, Kim EK (2001). Comparison of two procedures: photorefractive keratectomy versus laser in situ keratomileusis for low to moderate myopia. *Jap J Ophthalmol* 45:487-491
27. Lyle WA, Jin GJC (2001). Laser in situ keratomileusis with the VISX Star laser for myopia over -10.0 diopters. *J Cataract Refract Surg* 27:1812-1822
28. McDonald MB, Carr JD, Frantz JM, Kozarsky AM, Maguen E, Nesburn AB, Rabinowitz YS, Salz JJ, Stulting RD, Thompson KP, Waring GO (2001). Laser in situ keratomileusis for myopia up to -11 diopters with up to -5 diopters of astigmatism with the Summit Autonomous LADAR Vision excimer laser system. *Ophthalmology* 108:309-316
29. Ozdamar A, Küçüksümer Y, Aras C, Akova N, Ustundag C (2004). Visual field changes after laser in situ keratomileusis in myopic eyes. *J Cataract Refract Surg* 30: 1020-1023
30. Pallikaris IG, Katsanevaki VJ, Panagopoulou SI (2002). Laser in situ keratomileusis intraoperative complications using one type of microkeratome. *Ophthalmology* 109: 57-63
31. Randleman JB, Russel B, Ward MA, Thompson KP, Stulting D (2003). Risk factors and prognosis for corneal ectasia after LASIK. *Ophthalmology* 110:267-275
32. Recep ÖF, Cagil N, Hasiripi H (2000). Outcome of flap subluxation after laser in situ keratomileusis: Results of 6 month follow-up. *J Cataract Refract Surg* 26:1158-1162
33. Reviglio VE, Luna JD, Rodríguez ML, García FE, Juárez CP (1999). Laser in situ keratomileusis using the Laser-Sight 200 laser: Results of 950 consecutive cases. *J Cataract Refract Surg* 25:1062-1068
34. Salchow DJ, Zirm ME, Stieldorf C, Parisi A (1998)a. Laser in situ keratomileusis for myopia and myopic astigmatism. *J Cataract Refract Surg* 24:175-182
35. Salchow DJ, Zirm ME, Stieldorf C, Parisi A (1998)b. Laser-in-situ-Keratomileusis (LASIK) zur Myopie- und Astigmatismuskorrektur. *Ophthalmologie* 95:142-147
36. Sanders DR, Doney K, Poco M (ITM Study Group) (2004). United States Food and Drug Administration clinical trial of the implantable collamer lens (ICL) for moderate to high myopia. *Ophthalmology* 111:1683-1692
37. Schallhorn SC, Kaupp SE, Tanzer DJ, Tidwell J, Laurent J, Bourque LB (2003). Pupil size and quality of vision after LASIK. *Ophthalmology* 110:1606-1614
38. Sekundo W, Bönicke K, Mattausch P, Wiegand W (2003). Six-year follow-up of laser in situ keratomileusis for moderate and extreme myopia using a first-generation excimer laser and microkeratome. *J Cataract Refract Surg* 29:1152-1158
39. Stulting RD, Carr JD, Thompson KP, Waring GO, Wiley WM, Walker JG (1999). Complications of laser in situ keratomileusis for the correction of myopia. *Ophthalmology* 106:13-20
40. Suarez E, Torres F, Vieira JC, Ramirez E, Arevalo JF (2002). Anterior uveitis after laser in situ keratomileusis. *J Cataract Refract Surg* 28:1793-1798
41. Toda I, Asano-Kato N, Hori-Komai Y, Tsubota K (2002). Laser-assisted in situ keratomileusis for patients with dry eye. *Arch Ophthalmol* 120:1024-1028
42. Uçakhan Ö (2003). Laser in situ keratomileusis for compound myopic astigmatism using the Meditec MEL 70 G-Scan excimer laser. *J Refract Surg* 19:124-130
43. Yang C-N, Shen EP, Hu F-R (2001). Laser in situ keratomileusis for the correction of myopia and myopic astigmatism. *J Cataract Refract Surg* 27:1952-1960
44. Yeo H-E, Song B-J (2002). Clinical feature of unintended thin corneal flap in LASIK: 1-year follow-up. *Korean J Ophthalmol* 16:63-69

*Received: June 29, 2005 / Accepted: August 18, 2005*

*Address for correspondence:*

Prof. Dr. Frank Krummenauer  
 Clinical Epidemiology and Health Economy Unit  
 Dresden University of Technology, Medical Faculty  
 Fetscherstr. 74; Haus 29  
 D-01307 Dresden (Germany)  
 Phone: +49-351-458 3747  
 Fax: +49-351-458 4344  
 Email: Frank.Krummenauer@uniklinikum-dresden.de