Cost-Utility Analysis of Orthoptic Screening in Kindergarten: A Markov Model Based on Data From Germany

Hans-Helmut König, MD, MPH*, and Jean-Cyriaque Barry, MD‡

ABSTRACT. Objective. To estimate the long-term cost-effectiveness of a hypothetical screening program for untreated amblyopia in 3-year-old children conducted by orthoptists in all German kindergartens in the year 2000.

Methods. A cost-utility analysis was performed for which a decision tree was combined with a Markov model. Incremental costs and effects during the children’s remaining lifetime were estimated. The model took into account the probability of treatment without screening, age-specific treatment success rates, costs of screening and treatment, as well as effects of unilateral and bilateral visual impairment caused by amblyopia and other eye diseases coming along later in life on quality of life (utility). Model parameter values were obtained from a field study of orthoptic screening in kindergarten, from the literature, and from expert interviews. Costs were estimated from a third-party payer perspective. Uncertainty was assessed by univariate and probabilistic sensitivity analysis (Monte Carlo simulation).

Results. The incremental cost-effectiveness ratio (ICER) of orthoptic screening was 7397 Euro (€) per quality-adjusted life year (QALY) when costs and effects were discounted at 5%. In univariate sensitivity analysis, the ICER was sensitive to the uncertainty regarding the utility of unilateral visual impairment and to the discount rate for effects; besides uncertainty regarding the prevalence of untreated amblyopia, the odds ratio of success of treatment when started late, and the probability of treatment without screening had a noticeable but much smaller effect. Monte Carlo simulation yielded a 90% uncertainty interval for the ICER of 3452 €/QALY to 72 637 €/QALY; the probability of an ICER <25 000 €/QALY was 84%.

Conclusions. The ICER of orthoptic screening seems to fall within a range that warrants careful consideration by decision-makers. Much of the uncertainty in results comes from the uncertainty regarding the effect of amblyopia on quality of life. To reduce this uncertainty, the impact of amblyopia on utility should be investigated.

Pediatrics 2004;113:e95–e108. URL: http://www.pediatrics.org/cgi/content/full/113/2/e95; amblyopia, vision screening, children, preschool, cost-effectiveness, decision modeling, Markov process.

ABBREVIATIONS. VA, visual acuity; QALY, quality-adjusted life year; ICER, incremental cost-effectiveness ratio; CI, confidence interval; OR, odds ratio; BMES, Australian Blue Mountain Eye Study.

Preschool vision screening mainly aims at preventing amblyopia by early detection and subsequent treatment of amblyogenic factors such as strabismus and certain refractive errors. Recently, there has been concern about the lack of scientific data on the effectiveness of preschool vision-screening programs4–6, and rigorous evaluation has been called for.2,5,7,8

Because of increasing health expenditure, there is a growing interest among decision-makers in the cost-effectiveness of medical interventions.9 Many argue that the cost-effectiveness of a service has to be demonstrated before it may be covered by social health insurance or national health service programs. However, little is known about the cost-effectiveness of childhood vision-screening programs.

In a recent field study, we analyzed the effectiveness and cost-effectiveness of vision screening performed by orthoptists in German kindergartens.10–12 Orthoptists are specialized medical aides with thorough training in infant and child vision assessment, ocular motility-disorder examinations, and amblyopia management. In this study, screening was performed at age 3 because, in Germany, children may attend kindergarten from age 3 onward and the fourth year of life was considered best for vision screening;13,14 From age 3 onward, in most children monocular visual acuity (VA) can be assessed reliably by simple screening methods,15 and there is evidence that treatment is most effective when administered as early as possible.16–18

In the field study, the clinical endpoint of analysis was the ophthalmologic diagnosis, with the number of newly detected cases of amblyopia being the measure of effects. However, diagnosis of amblyopia is only an intermediate endpoint, especially with respect to the cost-effectiveness of screening. A more comprehensive analysis should also take into account the costs and effects of subsequent treatment and the effect of a visual deficit on quality of life throughout the remaining lifetime. Such an analysis would require either many years of follow up or the use of economic modeling. Modeling allows one to combine different sources of evidence, to transfer study results to different contexts and extrapolate them to the longer term, and to analyze uncertainty of results in detail.19–21

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Building on the results of the field study, the purpose of this analysis was to model the long-term cost-effectiveness of a hypothetical orthoptic screening program for children at age 3 conducted in all German kindergartens in the year 2000. Incremental costs and effects that would occur during the children’s remaining lifetime were estimated. The uncertainty inherent in the model was analyzed in detail to assess the precision of results and to identify those variables with the greatest potential impact on cost-effectiveness.

METHODS

This section is organized as follows: First, the study design is described in general and then the decision-analytic model is explained in detail, followed by the description of the model parameters used.

Study Design

Based on a decision-analytic model, a cost-utility analysis was performed in which quality-adjusted life years (QALYs) were used as the measure of effects. QALYs are calculated by weighting the duration of health states by a preference-based score of health-related quality of life (utility), measured on a scale from 0 (dead) to 1 (perfect health).22

In the model, the strategy “orthoptic screening at age 3 in kindergarten” (“screening”) was compared with the strategy “usual care.” Although usual care involves no orthoptic screening in kindergarten, amblyopia still may be detected when children see an ophthalmologist with or without referral (eg, by their pediatrician). The main outcome measure was the incremental cost-effectiveness ratio (ICER), ie, the ratio of the difference in mean costs \( \Delta C \) and the difference in mean effects \( \Delta E \) between the screening and usual-care strategies:

\[
\text{ICER} = \frac{\Delta C}{\Delta E}
\]

Hence, for the comparison, a purely incremental approach was chosen, ie, only the differences in costs and QALYs between the 2 strategies were considered. This means that, when calculating QALYs, only health states were considered with utility losses set off by

- unilateral visual impairment caused by a not successfully treated target disease; or
- visual impairment caused by any other unilateral eye disease coming along later in life. In a proportion of patients already affected by unilateral visual impairment caused by a target disease, this would cause bilateral visual impairment; in all other persons, this would result in unilateral visual impairment.

Visual impairment caused by any bilateral eye disease was not considered in the model, because it would cause bilateral visual impairment in both patients with the target disease as well as persons without and hence would not set off differences in QALYs between the strategies compared.

For the model, a threshold for the presence of visual impairment had to be defined. In accordance with various therapeutic,16,17 epidemiologic,23,24 and disability studies,25 this threshold was set at a corrected VA of \(<0.5\) (20/40): Monocular visual impairment was defined as VA \(<0.5\) in the worse eye and \(\geq0.5\) in the better eye, and bilateral visual impairment was defined as VA \(<0.5\) in both eyes.

The target disease was defined as untreated unilateral amblyopia, which, without treatment, would cause a lasting visual impairment.

Decision-Analytic Model

A decision tree was combined with a Markov model. Analysis was performed by using the DATA software package (version 4.0, TreeAge Software, Inc, Williamstown, MA).

Decision Tree

The decision tree (Fig 1) has 1 decision node that distinguishes the strategies screening and usual care. In the screening strategy, the model takes into account, by respective chance nodes, that only a proportion of children attend kindergarten at age 3 (labeled

![Fig 1. Decision tree for comparison of screening strategy with usual-care strategy.](http://pediatrics.aappublications.org/)
"kindergarten +/−") and would be present and participate in screening on the scheduled examination day (participation +/−). It also takes into account that a proportion of participating children would not cooperate sufficiently with the screening examination (cooperation +/−). Children with a positive screening result as well as noncooperative children would be referred to an ophthalmologist. At this point, the model takes into account that a proportion of participating children would not cooperate sufficiently with the screening examination (cooperation +/−). Children in whom amblyopia was newly diagnosed by the ophthalmologist would be treated and, by a certain probability, successfully achieve VA ≥0.5 in the amblyopic eye. Therefore, at the end nodes of the screening strategy, 3 different health states can be reached:

1. “Healthy”: if a target disease was not present or was treated successfully.
2. “Unilateral visual impairment (amblyopia)”: if a target disease was detected by the screening but treatment was not successful.
3. “Untreated amblyopia”: if a target disease was not treated yet.

At the end nodes of the usual-care strategy, only the healthy (if no target disease was present) or untreated-amblyopia (if a target disease was present) health states can be reached.

**Markov Model**

At each end node of the decision tree, a Markov process starts, i.e., the end node of the decision tree corresponds to the initial health state of a Markov process. In a Markov process, the course of a disease is divided into distinct states, and transition probabilities are assigned for movement between them over a discrete time period called the Markov cycle.26 By attaching estimates of resource use and health effects to the states and transitions in the model and then running the model over a large number of cycles, long-term costs and effects can be estimated.

According to the 3 different initial health states, 3 Markov processes (A–C) were distinguished. Markov process A starts with the initial untreated-amblyopia health state (Fig 2), which corresponds, e.g., to the third end node from the top of the decision tree displayed in Fig 1. Besides, there are 5 additional health states defined in this Markov process. Transition to the healthy state takes place when the child is seen by an ophthalmologist and is treated successfully before age 11; transition to the unilateral-visual-impairment (amblyopia) health state occurs if the child is not treated successfully before age 11. From the healthy state, transition to the unilateral-visual-impairment health state takes place when a unilateral nonamblyopic eye disease comes along and causes unilateral visual impairment. From the unilateral-visual-impairment (amblyopia) health state, transition to the bilateral-visual-impairment (with amblyopia) health state occurs when the nonamblyopic eye of an amblyopic patient is affected by a unilateral eye disease, resulting in bilateral visual impairment. The state “death” can be reached from all other health states.

Markov processes B and C are subsets of Markov process A. Markov process B starts with the initial healthy state, and Markov process C starts with the initial unilateral-visual-impairment (amblyopia) health state. Possible transitions correspond to those described within Markov process A.

In the model presented here, the cycle length was 1 year. Simulation started in cycle 0, which corresponds to the 4th year of life (age 3), and was completed in cycle 86, which corresponds to the 90th year of life. To account for gender differences in mortality and incidence of visual impairment, all Markov processes were made gender specific.

**Fig 2.** Markov process A for course of disease with an initial untreated-amblyopia health state. Health states are represented by ovals, and possible transitions between those states are shown by arrows. Variable names adjacent to the arrows are the transition probabilities of the model (see Table 1). Variable names refer to men; for women, tp.mono.m, tp.vis.m, and tpDeathm are replaced by tp.mono.f, tp.vis.f, and tpDeathf, respectively. *, Initial health state of Markov process B (shaded in bright gray); **, initial health state of Markov process C (shaded in dark gray).
TABLE 1. Parameter Values for Decision Tree and Markov Model With Range for Univariate Sensitivity Analysis and Distribution of Monte Carlo Simulation

<table>
<thead>
<tr>
<th>Model Parameter</th>
<th>Source*</th>
<th>Name Used in Decision Tree or Markov Model</th>
<th>Parameter Value (Base Value)</th>
<th>Range Used for Univariate Sensitivity Analysis</th>
<th>Distribution Used in Monte Carlo Simulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening Population</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Proportion of 3-year-olds in kindergarten</td>
<td>L</td>
<td>p_kg3</td>
<td>0.563</td>
<td>(None)</td>
<td>(None)</td>
</tr>
<tr>
<td>Proportion male</td>
<td>L</td>
<td>p_male</td>
<td>0.513</td>
<td>(None)</td>
<td>(None)</td>
</tr>
<tr>
<td>Participation in screening program</td>
<td>L</td>
<td>p_screen</td>
<td>0.900</td>
<td>0.800–1.000</td>
<td>Beta (30.22; 3.36)†</td>
</tr>
<tr>
<td>Prevalence of target disease</td>
<td>F</td>
<td>p_ambly</td>
<td>0.022</td>
<td>0.010–0.050</td>
<td>Beta (27; 1159)†</td>
</tr>
<tr>
<td>Compliance with referral to ophthalmologist</td>
<td>F</td>
<td>comp_op1</td>
<td>0.972</td>
<td>0.935–0.990</td>
<td>Beta (107; 4)†</td>
</tr>
<tr>
<td>After positive screening</td>
<td>L</td>
<td>comp_op2</td>
<td>0.900</td>
<td>0.800–1.000</td>
<td>Uniform (0.8; 1.0)‡</td>
</tr>
<tr>
<td>Test Characteristics of Orthoptic Screening</td>
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<tr>
<td>Sensitivity</td>
<td>F</td>
<td>sens_ort</td>
<td>0.909</td>
<td>0.772–0.971</td>
<td>Beta (21; 3)†</td>
</tr>
<tr>
<td>Specificity</td>
<td>F</td>
<td>spec_ort</td>
<td>0.924</td>
<td>0.907–0.940</td>
<td>Beta (898; 75)†</td>
</tr>
<tr>
<td>Cooperation</td>
<td>F</td>
<td>p_co_o1</td>
<td>0.887</td>
<td>0.869–0.905</td>
<td>Beta (1048; 134)†</td>
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<tr>
<td>Effectiveness of Treatment</td>
<td></td>
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<tr>
<td>Probability of success of treatment started at age 3</td>
<td>L</td>
<td>p_eff</td>
<td>0.750</td>
<td>0.600–0.900</td>
<td>Beta (23.26; 7.75)‡</td>
</tr>
<tr>
<td>Utilities</td>
<td></td>
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</tr>
<tr>
<td>Healthy</td>
<td>L</td>
<td>u_health</td>
<td>1.000</td>
<td>(None)</td>
<td>(None)</td>
</tr>
<tr>
<td>Unilateral visual impairment</td>
<td>L</td>
<td>u_mono</td>
<td>0.960</td>
<td>0.920–1.000</td>
<td>Uniform (0.92; 1.00)‡</td>
</tr>
<tr>
<td>Bilateral visual impairment</td>
<td>L</td>
<td>u_impair</td>
<td>0.780</td>
<td>0.710–0.850</td>
<td>Beta (104.14; 29.38)†</td>
</tr>
<tr>
<td>Costs</td>
<td></td>
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<tr>
<td>Organization per screening examination, €</td>
<td>F</td>
<td>c_org</td>
<td>5.24</td>
<td>2.62–7.86</td>
<td>Normal (5.24 × 0.9/p_screen; 1.34 × 0.9/p_screen)§</td>
</tr>
<tr>
<td>Orthoptic screening examination excluding organization, €</td>
<td>F</td>
<td>c_fix</td>
<td>4.18</td>
<td>3.28–5.08</td>
<td>Normal (4.18 × 0.9/p_screen; 0.46 × [0.9/p_screen])§</td>
</tr>
<tr>
<td>Fixed costs, €</td>
<td>F</td>
<td>c_var</td>
<td>3.88</td>
<td>3.27–3.99</td>
<td>Normal (3.88; 0.16)§</td>
</tr>
<tr>
<td>Variable costs, €</td>
<td>F</td>
<td>c_op</td>
<td>36.40</td>
<td>27.30–45.50</td>
<td>Normal (36.40; 4.64)§</td>
</tr>
<tr>
<td>Ophthalmologic examination, €</td>
<td>E</td>
<td>c_b</td>
<td>665</td>
<td>232–1098</td>
<td>Student’s t (6; 665: 177)¶</td>
</tr>
<tr>
<td>Costs of treatment (€), by age at beginning of treatment</td>
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<tr>
<td>3 years</td>
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<td>4 years</td>
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<td>5 years</td>
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<td>6 years</td>
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<td>7 years</td>
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<td>8 years</td>
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<td>9 years</td>
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<td>10 years</td>
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<tr>
<td>Transition Probabilities</td>
<td></td>
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</tr>
<tr>
<td>Mortality for men</td>
<td>L</td>
<td>tpDeathm</td>
<td>#</td>
<td>(None)</td>
<td>(None)</td>
</tr>
<tr>
<td>Mortality for women</td>
<td>L</td>
<td>tpDeathf</td>
<td>**</td>
<td>(None)</td>
<td>(None)</td>
</tr>
<tr>
<td>Probability of visit to ophthalmologist per year, by age</td>
<td>L</td>
<td>op_visit</td>
<td></td>
<td>p_visit × op_visit, distribution of p_visit: Uniform [0.5; 1.5]¶</td>
<td></td>
</tr>
<tr>
<td>3 years</td>
<td></td>
<td></td>
<td>0.230</td>
<td>0.115–0.345</td>
<td></td>
</tr>
<tr>
<td>4 years</td>
<td></td>
<td></td>
<td>0.270</td>
<td>0.135–0.406</td>
<td></td>
</tr>
<tr>
<td>5 years</td>
<td></td>
<td></td>
<td>0.349</td>
<td>0.175–0.524</td>
<td></td>
</tr>
<tr>
<td>6 years</td>
<td></td>
<td></td>
<td>0.332</td>
<td>0.166–0.498</td>
<td></td>
</tr>
<tr>
<td>7 years</td>
<td></td>
<td></td>
<td>0.344</td>
<td>0.172–0.516</td>
<td></td>
</tr>
<tr>
<td>8 years</td>
<td></td>
<td></td>
<td>0.325</td>
<td>0.162–0.487</td>
<td></td>
</tr>
<tr>
<td>9 years</td>
<td></td>
<td></td>
<td>0.278</td>
<td>0.139–0.417</td>
<td></td>
</tr>
<tr>
<td>10 years</td>
<td></td>
<td></td>
<td>0.305</td>
<td>0.152–0.457</td>
<td></td>
</tr>
<tr>
<td>Probability of treatment success when started late:</td>
<td>L</td>
<td>eff_late</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>eff_late,k = [p_eff/(1 − p_eff) × OR_k]/[1 + p_eff/(1 − p_eff) × OR_k] with OR_k for treatment success, by age class (k)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 years</td>
<td></td>
<td></td>
<td>OR = 1.000</td>
<td>(None)</td>
<td>(None)</td>
</tr>
<tr>
<td>4–5 years</td>
<td></td>
<td></td>
<td>OR = 0.468</td>
<td>0.298–0.734</td>
<td>OR = 0.468; distribution of b: Normal (−0.76; 0.25)§</td>
</tr>
<tr>
<td>6–10 years</td>
<td></td>
<td></td>
<td>OR = 0.317</td>
<td>0.187–0.536</td>
<td>OR = 0.317; distribution of b: Normal (−1.15; 0.27)§</td>
</tr>
<tr>
<td>Model Parameter</td>
<td>Source*</td>
<td>Name Used in Decision Tree or Markov Model</td>
<td>Parameter Value (Base Value)</td>
<td>Range Used for Univariate Sensitivity Analysis</td>
<td>Distribution Used in Monte Carlo Simulation</td>
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<tr>
<td><strong>Transition probability per year from unilateral visual impairment (amblyopia) to bilateral visual impairment, by gender and age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td>L</td>
<td>tp_vis_m</td>
<td></td>
<td></td>
<td>(p_{trans} \times tp_vis_m), distribution of (p_{trans}): Uniform [0.5; 1.5]†</td>
</tr>
<tr>
<td>49–51 years</td>
<td></td>
<td>0.00166</td>
<td>0.00083–0.00248</td>
<td></td>
<td></td>
</tr>
<tr>
<td>52–59 years</td>
<td></td>
<td>0.00605</td>
<td>0.00303–0.00908</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60–69 years</td>
<td></td>
<td>0.00204</td>
<td>0.00102–0.00306</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70–79 years</td>
<td></td>
<td>0.00248</td>
<td>0.00124–0.00372</td>
<td></td>
<td></td>
</tr>
<tr>
<td>80–89 years</td>
<td></td>
<td>0.00729</td>
<td>0.00363–0.00488</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td>L</td>
<td>tp_vis_f</td>
<td></td>
<td></td>
<td>(p_{trans} \times tp_vis_f), distribution of (p_{trans}): Uniform [0.5; 1.5]†</td>
</tr>
<tr>
<td>49–51 years</td>
<td></td>
<td>0.00046</td>
<td>0.00023–0.00069</td>
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<td>52–59 years</td>
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<td>0.00026</td>
<td>0.00013–0.00039</td>
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<tr>
<td>60–69 years</td>
<td></td>
<td>0.00088</td>
<td>0.00044–0.00132</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70–79 years</td>
<td></td>
<td>0.00234</td>
<td>0.00162–0.00456</td>
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<tr>
<td>80–89 years</td>
<td></td>
<td>0.00201</td>
<td>0.00100–0.00301</td>
<td></td>
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</tr>
<tr>
<td><strong>Transition probability per year from healthy to unilateral visual impairment (no amblyopia), by gender and age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td>L</td>
<td>tp_mono_m</td>
<td></td>
<td></td>
<td>(p_{trans} \times tp_vis_f), distribution of (p_{trans}): Uniform [0.5; 1.5]†</td>
</tr>
<tr>
<td>49–51 years</td>
<td></td>
<td>0.00435</td>
<td>0.00217–0.00652</td>
<td></td>
<td></td>
</tr>
<tr>
<td>52–59 years</td>
<td></td>
<td>0.00012</td>
<td>0.00006–0.00018</td>
<td></td>
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</tr>
<tr>
<td>60–69 years</td>
<td></td>
<td>0.00541</td>
<td>0.00270–0.00811</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70–79 years</td>
<td></td>
<td>0.00629</td>
<td>0.00315–0.00944</td>
<td></td>
<td></td>
</tr>
<tr>
<td>80–89 years</td>
<td></td>
<td>0.00729</td>
<td>0.00365–0.01094</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td>L</td>
<td>tp_mono_f</td>
<td></td>
<td></td>
<td>(p_{trans} \times tp_vis_f), distribution of (p_{trans}): Uniform [0.5; 1.5]†</td>
</tr>
<tr>
<td>49–51 years</td>
<td></td>
<td>0.00121</td>
<td>0.00061–0.00182</td>
<td></td>
<td></td>
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<tr>
<td>52–59 years</td>
<td></td>
<td>0.00068</td>
<td>0.00034–0.00103</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60–69 years</td>
<td></td>
<td>0.00232</td>
<td>0.00116–0.00347</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70–79 years</td>
<td></td>
<td>0.00862</td>
<td>0.00431–0.01293</td>
<td></td>
<td></td>
</tr>
<tr>
<td>80–89 years</td>
<td></td>
<td>0.00431</td>
<td>0.00215–0.00646</td>
<td></td>
<td></td>
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<tr>
<td><strong>Discount Rate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discount rate for costs</td>
<td>L</td>
<td>cDR</td>
<td>0.050</td>
<td>0.000–0.050</td>
<td>(None)</td>
</tr>
<tr>
<td>Discount rate for effects</td>
<td>L</td>
<td>eDR</td>
<td>0.050</td>
<td>0.000–0.050</td>
<td>(None)</td>
</tr>
</tbody>
</table>

*Source of parameter value: L, literature; F, field study; E, expert opinion (see text for details).
† Beta distribution (α; β): values of α and β with decimal digits stand for fitted Beta distributions.
‡ Uniform distribution (minimum; maximum).
§ Normal distribution (mean; standard deviation).
¶ Discounted by 5% discount rate to year when treatment is started.
‖ Student's \(t\) distribution (degrees of freedom: mean; observed standard deviation).
# Mortality rate for men in Germany.
** Mortality rate for women in Germany.
Model Parameters

Model parameter values were obtained from a field study of orthoptic screening in kindergarten, from the literature, and from expert interviews (Table 1). For each parameter, a (mean) value, which was used for the base analysis, was defined as well as a possible value range, according to which parameter values were varied in 1-way sensitivity analysis. Furthermore, for parameters that, in principle, could be sampled, distributions were specified for probabilistic sensitivity analysis (Monte Carlo simulation) as follows: for proportions of the form \( \frac{a}{a + b} \), such as test characteristics and utilities, which are bound to a 0–1 interval, Beta distributions were specified [Beta (a, b) with \( a = a + 1 \) and \( b = b + 1 \)]. Normal or Student’s t distributions were specified for the mean of continuous parameter values. If there were only data on the mean and the likely range of the 95% confidence interval (CI) of a continuous parameter but not the variance, the standard error was estimated by the formula

\[
s = \frac{u - l}{2 \times 1.96},
\]

where \( u \) and \( l \) are the upper and lower limits of the range, respectively. If there was only information on the range but not on the mean of a parameter, then a uniform distribution was used.

Screening Population

In 2000, the number of children aged 3 in Germany was 814 700; 51.3% were male. Of these children, 458 700 (56.3%) were attending 1 of 43 728 kindergartens. Thus, the mean number of children aged 3 per kindergarten was 10.49. According to other field studies of vision screening in German kindergartens in which the participation rate ranged between 88% and 92%, the participation rate ranged between 88% and 92%, the participation rate was assumed to be 90%, which would yield a mean of 9.44 participating children per kindergarten. For univariate sensitivity analysis, the range of the participation rate was set at 80% to 100%. This range was assumed to represent the 95% CI, and the standard error was estimated according to formula 2. Based on the estimated mean and standard error, a Gamma distribution was fitted by using the method of moments estimation.

Prevalence of Target Disease and Test Characteristics of Orthoptic Screening

Data on the prevalence of untreated amblyopia, on the screening test characteristics (sensitivity, specificity, and proportion of inconclusive results), and on the compliance with ophthalmologic examinations were obtained from a field study in which 1180 3-year-old children were examined by orthoptists in 121 German kindergartens.

In the field study, the orthoptic screening examination consisted of static cover tests, examination of eye motility and head posture, and uncorrected monocular VA testing using the Lea single optotype test (required test distance 10 ft [3 m], Precision Vision, Villa Park, IL) with pass threshold set at \( \geq 0.8 \) (20/25) monocular VA in both eyes; or \( \geq 0.5 \) (20/40) in both eyes and \( \leq 1 \) line difference between the VA of the right and left eyes (L. Hvârinen, written communication, 1998). The ophthalmologic criteria for a target disease (positive gold standard) were: any newly administered patching therapy; or any newly administered spectacle therapy, if the corrected VA was \( \leq 0.4 \) (20/50) in either eye or if the difference of VA between the right and left eyes was \( \geq 2 \) lines.

For the base analysis it was assumed that, without treatment, children with a positive gold standard (2.2%) would be affected by a lasting unilateral visual impairment. For univariate sensitivity analysis, the range of prevalence was set at 1.0% to 5.0%, which includes the range of prevalence of amblyogenic factors stated in a recent review (2.7%–4.4%) and takes into account that more than half of all cases may already be detected at the time of screening. For the Monte Carlo simulation, a Beta distribution was defined based on the proportion of gold-standard-positive children found in the field study, \( a/(a + b) \), where \( a \) equals the number of children with positive gold standard, and \( b \) equals the number of children without positive gold standard.

For the test characteristics and compliance rates, values measured in the field study were used as baseline values. The limits of their 95% CIs were used for univariate sensitivity analysis, and Beta distributions were specified for the Monte Carlo simulation.

Because data on the compliance with direct referral to an ophthalmologist after inconclusive screening could not be obtained from the field study due to its design, this value had to be estimated based on other studies and was set at 90%. In univariate sensitivity analysis, this value was varied from 80% to 100%, and for Monte Carlo simulation a uniform distribution on this interval was used.

Success Rate of Treatment

In studies that used a VA \( \geq 0.5 \) as the threshold for treatment success for amblyopia, reported success rates range from 50% to 100%.

In a meta-analysis based on 23 studies with 689 patients included, Flynn et al found an overall success rate of 74.3%. The authors developed a multiple logistic regression model to analyze the effect of age at the beginning of treatment on the success rate, controlling for type of amblyopia and VA at beginning of treatment. In a second study, in which 589 patients were included and the overall success rate was 59.9%, Flynn et al validated the regression model and again found a significant influence of age on treatment success: Compared with age group 0 to 3, the odds ratio (OR) for the success of treatment started at age group 4 to 5 was 0.47, and at age group 6 to 10 it was 0.32.

They also reported the estimated regression coefficients \( b_k \) for the age groups \( k \) and their standard errors \( s_k \), from which the 95% CIs of OR\( \beta \) could be calculated by using the formula:

\[
\exp(b_k + 1.96 \times s_k),
\]

which yielded [0.30; 0.73] for age group 4 to 5 and [0.19; 0.54] for age group 6 to 10.

In the model, the mean treatment success rate at age 3 (p\( \text{eff} \)) was set at 75% with the range of 60% to 90% used for univariate sensitivity analysis. For the Monte Carlo simulation, a Beta distribution was fitted for (p\( \text{eff} \)), assuming that the mentioned range corresponds to the 95% CI and deriving the standard error according to formula 2.

Success rates of treatment started after age 3 (eff\( \text{late} \)) were calculated based on the mentioned OR\( \beta \) for older age groups \( k \) using the formula:

\[
\text{eff\( \text{late} \)} = \frac{p_{\text{eff}}}{1 + p_{\text{eff}}},
\]

Table 2 shows the resulting success rates of late treatment (eff\( \text{late} \)) for various success rates of treatment started at age 3. In univariate sensitivity analysis, OR\( \beta \) values were jointly varied according to their 95% CI, mentioned above. In the Monte Carlo simulation, OR\( \beta \) values were calculated by using the coefficients for age groups \( b_k \), which were estimated in the logistic regression model, in the formula:

\[
\text{OR} = \exp(b_k),
\]

assuming a normal distribution for \( b_k \), with the estimated \( b_k \) as the mean and the standard deviation \( s_k \). Thus, \( b_k \) was calculated according to the formula:

\[
b_k = b_k^* + z \times s_k,
\]

where \( z \) follows the standard normal distribution.

**TABLE 2.** Success Rate of Amblyopia Treatment Started After Age 3 by Success Rate of Amblyopia Treatment Started at Age 3

<table>
<thead>
<tr>
<th>Success Rate</th>
<th>Success Rate</th>
<th>Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 3, %</td>
<td>Ages 4–5, %</td>
<td>Ages 6–10, %</td>
</tr>
<tr>
<td>(p( \text{eff} ))</td>
<td>(OR = 0.47*)</td>
<td>(OR = 0.32*)</td>
</tr>
<tr>
<td>90</td>
<td>81</td>
<td>74</td>
</tr>
<tr>
<td>85</td>
<td>73</td>
<td>64</td>
</tr>
<tr>
<td>80</td>
<td>65</td>
<td>56</td>
</tr>
<tr>
<td>75</td>
<td>58</td>
<td>49</td>
</tr>
<tr>
<td>70</td>
<td>52</td>
<td>42</td>
</tr>
<tr>
<td>65</td>
<td>41</td>
<td>37</td>
</tr>
<tr>
<td>60</td>
<td>41</td>
<td>32</td>
</tr>
</tbody>
</table>

* OR for success rate of treatment started after age 3 (eff\( \text{late} \)) compared to success rate of treatment started at age 3; the success rate (eff\( \text{late} \)) is calculated according to the formula: eff\( \text{late} \) = \[ p_{\text{eff}}/(1 - p_{\text{eff}}) \times \text{OR}]/[1 + p_{\text{eff}}/(1 - p_{\text{eff}}) \times \text{OR}] .
Utilities

The utility of the bilateral-visual-impairment health state was derived from a recent study of a large series of patients with visual loss from various ocular diseases using the time trade-off method.\(^{36}\) In this study, a formula for converting VA of the better eye to a mean utility value was derived via regression analysis:

\[
U(\text{VA}) = 0.374 \times \text{VA} + 0.514. \tag{7}
\]

For the incremental approach, only the reduction of utility caused by visual impairment was relevant. Therefore, the utility of VA = 1.0 was set at \(U = 1.00\), ie, it was increased by 0.11 compared with the utility predicted by formula 7. For a conservative estimate of the utility of the bilateral-visual-impairment health state, the utility of VA = 0.4 was calculated by using formula 7 and then also increased by 0.11, resulting in \(U = 0.78\). For the health states without any visual impairment, the utility was constantly set at \(U = 1.00\). Thus, compared with no visual impairment, utility of bilateral visual impairment was reduced by 0.22. Based on utilities reported by the same working group,\(^{36}\) this reduction of utility was varied by \(\pm 1/3\), ie, from 0.15 to 0.29 for univariate sensitivity analysis, corresponding to utilities from 0.71 to 0.85. This interval was considered to reflect the 95% CI, and a Beta distribution was fitted for the Monte Carlo simulation.

The utility associated with unilateral visual impairment caused by amblyopia has not been investigated specifically thus far. In a recent study of the same working group, unilateral impairment (defined as VA \(\leq 0.5\) in the worse eye and VA \(>0.8\) in the better eye) from various ocular diseases was found to cause a mean reduction of utility of 0.08, using the time trade-off method.\(^{46}\) Because individuals with only 1 sound eye due to amblyopia since childhood may develop compensatory visual mechanisms,\(^{22}\) the reported utility reduction was considered a maximum. It thus was varied from 0.00 to 0.08 in univariate sensitivity analysis, ie, from no disutility at all to the disutility stated in the empirical study,\(^{46}\) which corresponds to utilities ranging from 0.92 to 1.00. Having no additional information, for the base analysis a utility of 0.96 was used, ie, the middle of the interval. For the Monte Carlo simulation, a uniform distribution on the interval [0.92,1.00] was used.

**Transition Probabilities of Markov Model**

**Probability of Successful Treatment Under Usual Care**

Data on the age-specific probability for an amblyopic child to receive treatment under usual care (ie, without orthoptic screening) were not available. It was assumed that untreated amblyopia was definitely detected and treated when an affected child was seen by an ophthalmologist (op.visit) was estimated based on a representative survey of ophthalmologic patients in Germany,\(^{41}\) from which the age-specific number of ophthalmologic patients in 1997 was estimated.\(^{42}\) The age-specific probability (op.visit) was derived by dividing the age-specific number of patients by the age-specific number of persons in the German population in 1997.\(^{43}\) For the model it was assumed that the age-specific probability (op.visit) was independent of former visits and of the presence of amblyopia. Table 1 shows the calculated probabilities. For example, without screening, at age 3, 23% of children with untreated amblyopia would be seen by an ophthalmologist and receive treatment; before age 8, a cumulated 94% would have received treatment, and 95% would have received treatment before age 11. In univariate sensitivity analysis, the age-specific probabilities were reduced and increased by the factors 0.5 and 1.5, respectively. For the Monte Carlo simulation, a uniform distribution on the interval [0.5;1.5] was used for this factor.

In Markov process A, before age 11 (cycles 0–7) the probability of transition from the untreated-amblyopia health state to the healthy state (ie, the probability of successful treatment under usual care) was obtained by multiplying the age-specific probability (op.visit) with the age-group-specific success rate of treatment started later (eff.late). From age 11 onward, the probability of this transition was assumed to be 0.

**Incidence of Unilateral Visual Impairment Other Than Amblyopia**

Because data on age- and gender-specific incidence of unilateral visual impairment were not available in the literature, incidence had to be derived from prevalence studies. Because such studies were not available for Germany, data from the Australian Blue Mountain Eye Study (BMES)\(^{36,44}\) were used, assuming Australian population and health care characteristics comparable to those in Germany. The BMES provides data on the prevalence of unilateral visual impairment by age group, gender, and severity as well as on the prevalence of amblyopia for a representative population sample aged \(\geq 49\) years. To estimate the prevalence of unilateral visual impairment not caused by amblyopia, age- and gender-specific prevalence data of unilateral visual impairment were reduced by prevalence data of amblyopia.\(^{44}\)

It was assumed that the reported age-group-specific prevalence is present in the middle of the age classes. Thus, new age classes were defined, the middle of the original age classes being the limits of the new age classes. Gender-specific transition probabilities \(q_{it}\) for the new age classes of the width \(t\) years and upper limit \(j\) years were derived by using the formula\(^{45}\)

\[
q_{ij} = p_{j} - p_{j-t},
\]

where \(p_{j}\) and \(p_{j-t}\) is the prevalence at the upper and lower limit of the new age class, respectively. One-year probabilities of the transition from the healthy state to the unilateral-visual-impairment (no amblyopia) health state \(q_{i}\) were derived by using the formula\(^{45}\)

\[
q_{i} = 1 - (1 - q_{ij})^{1/1},
\]

In the Markov model, this transition probability was labeled tp.mono.m for males and tp.mono.f for females.

**Incidence of Bilateral Visual Impairment Caused by Unilateral Eye Disease Affecting the Nonamblyopic Eye of Amblyopic Persons**

It was assumed that the prevalence of an eye being affected by unilateral, visually-impairing eye disease other than amblyopia is the same for amblyopic and nonamblyopic eyes. Thus, in persons with unilateral amblyopia, the prevalence of the nonamblyopic eye being affected, causing bilateral visual impairment, was estimated to be half of the prevalence of unilateral visual impairment in persons without amblyopia. Because VA in the amblyopic eye may improve when the other eye becomes visually impaired, the estimated prevalence was reduced by 23.6%, based on the results of a study of 144 amblyopic persons with visual impairment in the nonamblyopic eye, of whom 34 (23.6%) improved to VA \(\geq 0.5\) in the amblyopic eye.\(^{46}\) Based on these estimated prevalence data, age-group- and gender-specific incidence, ie, 1-year probability of transition from the unilateral-visual-impairment (amblyopia) health state to the bilateral-visual-impairment (with amblyopia) health state was derived as described above and labeled tp.vis.m for males and tp.vis.f for females.

In univariate sensitivity analysis, the transition probabilities tp.mono.m, tp.mono.f, tp.vis.m and tp.vis.f were jointly reduced and increased by the factors 0.5 and 1.5, respectively. For the Monte Carlo simulation, a uniform distribution on the interval [0.5;1.5] was used for this factor.

**Mortality**

Age- and gender-specific death rates were obtained from the most recent life table 1997/1999 of the German Federal Statistical Office.\(^{47}\)

**Costs**

Costs were calculated in Euro (€) from a third-party payer perspective, assuming no copayments by the patients, for the year 2000. In that year, the average Euro to US-dollar exchange rate was 0.92 per 1 €, and the average purchasing power adjusted conversion rate was 0.99 per 1 € (ie, close to parity).\(^{48}\)

**Costs of Orthoptic Screening Examination**

Data on costs of orthoptic screening examination were obtained from the field study mentioned above; the methodology of cost measurement performed in the field study has been described elsewhere.\(^{11}\) Costs of orthoptic screening were divided into costs for organizing the screening program (which were assumed to be fixed per kindergarten) and costs for conducting the screening examination in kindergarten, the latter being subdivided into fixed costs (eg, for traveling) and variable costs, which depended on the number of children examined per kindergarten (eg, labor...
Monte Carlo simulation. A normal distribution was likely to vary by region. This interval was considered to reflect the uncertainty of the expert with regard to the change in the average number of children examined per kindergarten, standard errors of the mean could be estimated in the study. Thus, these 2 cost categories were varied according to their 95% CI in univariate sensitivity analysis, and normal distribution was used for Monte Carlo simulation. With respect to organization, costs were varied by ±50% in univariate sensitivity analysis. This interval was considered to reflect the 95% CI, and for Monte Carlo simulation, a normal distribution was fitted by estimating the standard error according to formula 2. To account for changes in participation rates that would lead to changes in the average number of children examined per kindergarten, the mean and the standard error of fixed costs were adjusted accordingly.

**Costs of Diagnostic Ophthalmologic Examination**

Costs of a standard ophthalmologic examination of children referred from screening were based on the German social health insurance’s relative value scale for outpatient physician services, which defines individual physician services and states point volumes for them. For the conversion factor (point value), which varies by region, a German average of 0.041 €/point was used. For univariate sensitivity analysis, these costs were varied by ±25%, which corresponded to the range that the conversion factor was likely to vary by region. This interval was considered to reflect the 95% CI. For Monte Carlo simulation, a normal distribution was fitted by estimating the standard error according to formula 2.

**Treatment Costs**

Because there were no published data on the cost of amblyopia treatment, costs were estimated based on expert opinion. Seven experts of amblyopia treatment (4 ophthalmologists and 3 orthoptists) from different German treatment centers filled in a standardized questionnaire. In the questionnaire, medical services and items (eg, glasses, patches, etc) possibly used for amblyopia treatment were listed. Respondents were asked to estimate the mean costs and incremental effects were valued monetarily by using “administrative” prices paid by the German statutory health insurance. The methodology of estimating treatment costs has been described in detail elsewhere.49

It was assumed that treatment was completed before age 12. To estimate the costs of treatment started later than age 3, treatment costs were reduced by excluding the costs of years that would correspond to age >12.

Costs of treatment started at age 3 to 10 were calculated based on each expert’s estimate of resource utilization. From these figures, mean estimated costs $m_{ji}$ of treatment started at age $j$ were calculated (and used for the base analysis) as well as the standard errors $s_{ji}$ which reflect the uncertainty of the expert with regard to average costs (Table 3). In univariate sensitivity analysis, the treatment costs were jointly varied according to their 95% CIs. For the Monte Carlo simulation, age-specific treatment costs $k_{ji}$ were calculated by using the formula:

$$k_{ji} = m_{ji} + t \times s_{ji}, \quad (10)$$

where $t$ follows a standardized Student’s $t$ distribution with 6 degrees of freedom.

**Discounting**

Costs and effects were discounted at 5%. In sensitivity analysis, discount rates of 0% and 3% were also used.

**Sensitivity Analysis**

**One-Way Sensitivity Analysis**

To analyze the effect of uncertainty in single model parameters on the ICER, univariate sensitivity analysis was performed by varying single-parameter values according to the ranges described above and repeating the analytical solution of the model.

**Probabilistic Sensitivity Analysis (Monte Carlo Simulation)**

In the Monte Carlo simulation, values for all model parameters were sampled from their respective specified distributions, and the analytical solution of the model was repeated.27 This process of resampling from each of the distributions and recalculating the incremental costs and effects from the model was repeated 10 000 times to generate a distribution of the estimated ICER. Uncertainty intervals were estimated from the simulated data by taking the 2.5th and 97.5th percentile values to represent the endpoints for a 95% interval,27 and cost-effectiveness acceptability curves51–53 were constructed.

**RESULTS**

**Base Result**

The screening strategy was associated with incremental costs of 13.34 € per child and incremental effects of $1.803 \times 10^{-3}$ QALYs per child. Thus, for the total population of 814 700 3-year-old children, of whom 50.7% (90% × 56.3%) would participate in screening, incremental costs were 10.87 million €, and incremental effects were 1469 QALYs. The ICER was 7397 €/QALY.

**Univariate Sensitivity Analysis**

Figure 3 shows the effect of varying single-parameter values on the ICER. Uncertainty with respect to the utility of unilateral visual impairment had the strongest potential impact on the ICER. If this utility was 0.92, the ICER decreased to 3706 €/QALY; if it was 1.00 (ie, if only bilateral visual impairment but not unilateral visual impairment affected utility), the ICER increased to 1.904 million €/QALY. Figure 4 shows the association between the ICER and the utility of unilateral impairment for the range of 0.92 to 1.00: If the utility was >0.988, the ICER increased to >25 000 €/QALY; if it was >0.994, the ICER increased to >50 000 €/QALY.
Besides uncertainty with respect to the prevalence of the target disease, the OR of treatment success when started later and the probability for a child to be seen by an ophthalmologist (op. visit) had a marked, but much smaller impact on the ICER. All other parameters had only little impact, among those being the treatment costs. Almost no impact had the uncertainty with respect to the incidence of visual impairment caused by other eye disease and the utility of bilateral visual impairment.

If only costs but not effects (QALYs) were discounted, the ICER was 2219 €/QALY. If neither costs nor effects were discounted, the ICER was 2163 €/QALY. If costs and effects were both discounted at 3%, the ICER was 5138 €/QALY.

Monte Carlo Simulation

Uncertainty Intervals

Figure 5 shows the joint distribution of incremental costs and effects generated in 10 000 simulations.
on the cost-effectiveness plane. The 95% uncertainty interval for the incremental costs per child ranged from 10.14 to 18.63 €, and for incremental effects from $8.607 \times 10^{-5}$ to $5.005 \times 10^{-3}$ QALYs. For the total population of 814,700 3-year-old children, 95% of incremental costs lay between 8.26 million and 15.18 million €, and 95% of the effects lay between 70 and 4078 QALYs.

The 95% uncertainty interval of the ICER was 3138 to 148,228 €/QALY, which corresponds to the slope of the ICER on the cost-effectiveness plane.

![Fig 4. Effect of utility of unilateral visual impairment on ICER of the screening strategy (when base values are used for all other model parameters).](image)

![Fig 5. Joint distribution of incremental costs and effects of the screening strategy plotted on the cost-effectiveness plane. Results of 10,000 Monte Carlo simulations; lines represent 2.5th, 50th, and 97.5th percentiles of ICER.](image)
of the lines representing the interval endpoints in Fig 5. The 90% uncertainty interval was 3452 to 72 637 €/QALY. Without discounting effects, the 95% uncertainty interval was 903 to 30 053 €/QALY.

Cost-Effectiveness Acceptability Curves

When costs and effects were discounted at 5%, Monte Carlo simulation yielded an ICER <25 000 €/QALY in 84% and an ICER <50 000 €/QALY in 92%. Without discounting effects, an ICER <25 000 was yielded in 97%, and an ICER <50 000 in 99%. This is displayed by the cost-effectiveness acceptability curves in Fig 6, which give the proportion of observed simulation results lying below varying threshold values for the ICER.

Because much of the variability of the results was due to the uncertainty with respect to the utility of unilateral visual impairment, Monte Carlo simulations were also performed keeping this utility constant at different levels and varying all other parameters according to their distributions (Fig 7). If this utility was 0.92, 0.94, 0.96, 0.98, or 0.99, in 95% of the simulations the ICER was below 6375, 8491, 12 561, 25 296, and 50 789 €, respectively.

DISCUSSION

The Markov model aimed at estimating the life-long gain in health-related quality of life due to prevention of amblyopia through screening and subsequent treatment, as well as the associated costs. The model took into account that children with untreated amblyopia may be detected and successfully treated without screening.

The ICER of orthoptic screening at age 3 in German kindergarten was found to be ~7400 €/QALY when costs and effects were discounted at 5%. Thus, the ICER was more favorable than that of many routinely provided health care interventions and similar to the ICER found for diabetic retinopathy screening.

Because the analysis included effects occurring during the remaining lifetime of up to 86 years, discounting effects had substantial impact on the ICER. Without discounting, the ICER was just about one third of the base result. Discounting costs had only little impact on the ICER, because all considered costs occurred during the first 9 years after screening.

Univariate sensitivity analysis showed that uncertainty regarding the utility of unilateral visual impairment had great potential impact on the ICER. If unilateral visual impairment due to amblyopia was not associated with any loss in utility, then orthoptic screening would very likely not be cost-effective. In other words: Just the risk of developing bilateral visual impairment later in life would most likely not justify preschool vision screening. Yet, if unilateral visual impairment was associated with a utility loss of only 0.01, then the ICER fell below 30 000 €/QALY. ICERs obtained in Monte Carlo simulation showed a wide range but were mostly within limits likely to be acceptable to decision-makers. For example, the probability for the ICER being below 25 000 €/QALY was 84%.

Model Structure

For modeling, the course of disease had to be divided into distinct states, and hence thresholds for the presence or absence of visual impairment had to be defined. Because in reality no such thresholds

![Fig 6. Cost-effectiveness acceptability curves of the screening strategy for various discount rates](http://www.pediatrics.org/cgi/content/full/113/2/e95)
exist, this necessarily entails some simplification. Theoretically, more health states could have been defined, representing different degrees of visual impairment but also making the model more complicated. However, for this purpose, respective data were not available. Uncertainty with respect to the definition of thresholds was addressed by varying model parameters widely in sensitivity analyses.

The model did not distinguish between different causes of amblyopia. This simplification had to be made, because data on age-specific treatment success rates were not available in more detail. However, in 2 studies based on large patient samples, no significant effect of the cause of amblyopia on treatment success was identified after controlling for age and VA at the beginning of treatment, which both had a significant effect. Although the effect of age was explicitly modeled, the effect of VA on treatment success was accounted for by varying treatment success rate at age 3 widely in sensitivity analysis.

The model did not allow any return to preceding health states, eg, from unilateral visual impairment (without amblyopia) to healthy (eg, after treatment of other eye diseases) states. Although such a return may be possible in reality (eg, after treatment), the error introduced by this restriction is considered small because most transition probabilities were estimated from prevalence data. For improvement of unilateral visual impairment caused by amblyopia without treatment, no evidence was found in the literature.

The Markov process was restricted to 86 cycles. Thus, possible QALY gains accumulated from age 90 onward were not considered. When discounted, these QALY gains would be very small. Without discounting, however, they would make the ICER more favorable, as would a future increase in life expectancy.

In the model, only direct medical costs for detection and treatment of the target disease were considered from the perspective of a third-party payer. Thus, administrative prices (eg, fees) were used where applicable. Because these prices are likely to be comparable to opportunity costs, and no cost sharing by patients was assumed, the calculated costs are probably close to direct medical costs from the societal perspective. Direct nonmedical costs (eg, for traveling to an ophthalmologist) were not considered but probably were small. Direct costs caused by visual impairment coming along later in life were not considered either, but it would have had only little impact on the results due to discounting: If, eg, bilateral visual impairment caused direct costs of 10 000 € per year, the ICER would drop by only 2% to 7220 €/QALY. Indirect costs, caused by losses in productivity due to visual impairment, were not considered either. Including indirect costs would most likely make the ICER more favorable. However, according to the Panel on Cost-Effectiveness in Health and Medicine, effects of disease on productivity or income may already be reflected by the preference-based valuation of health-related quality of life (utility), and hence there would be no need to include indirect costs in cost-utility analysis.

Critical Model Parameter Values

Values for model parameters were obtained from a field study, the literature, and a survey of experts.
CONCLUSIONS

The ICER of orthoptic screening seems to fall within a range that warrants careful consideration by decision-makers. The presented uncertainty intervals and cost-effectiveness acceptability curves should enable decision-makers to appraise the results based on their own risk aversion. Much of the uncertainty in results comes from the uncertainty regarding the effect of amblyopia on health-related quality of life. To reduce this uncertainty, additional studies should investigate the impact of amblyopia on utility in more detail.

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