ORIGINAL ARTICLE

Vision Screening in Preschool Children

Do the Data Support Universal Screening?

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SUMMARY

Background: Comprehensive, systematic reviews on the benefit of vision screening in preschool children were published in 2008 by major national organizations in both Germany and the United Kingdom. These reviews raised public interest in the topic.

Methods: This article contains a discussion of the sensitivity, specificity, efficacy, and cost-effectiveness of preschool vision screening, on the basis of the two national reports mentioned above as well as relevant literature retrieved by a selective PubMed search.

Results: All studies that have been published to date on the efficacy of preschool visual screening suffer from methodological flaws. The available data suggest a benefit from screening, though this has not been proven. Model calculations reveal that the positive predictive value of screening tests performed in isolation is inadequate. The authors of the two national reports applied different methods and arrived at similar, but not identical conclusions. Preschool vision screening may also be cost-effective; whether this is the case or not depends on the probability of a long-term benefit—specifically, on the probability of preventing bilateral loss of vision in adulthood. To prevent one such case, it is estimated that 13 cases of childhood amblyopia must be identified and successfully treated (number needed to treat [NNT] = 13).

Conclusion: The available data do not allow any firm conclusion about the efficacy and cost-effectiveness of preschool vision screening. Further clinical studies are needed to answer these questions.

To determine whether or not universal vision screening in preschool children is worthwhile, we must establish whether it reduces the prevalence of sight disorders and what the cost of testing is. These matters gained renewed public attention after the Joint Federal Committee commissioned the German Institute for Quality and Efficiency in Health Care (IQWiG) to compile a report on the subject, which was published in 2008 (1). A few months later, the UK's National Institute of Health Research published a work with a similar scope, in the form of a Health Technology Assessment (HTA) (2). This article aims to address the questions posed and summarize the current status of research. To do so, both the above-mentioned reports and the results of a selective PubMed literature search have been analyzed and evaluated.

The range of eye disorders in children

The *Table* shows how often various eye disorders occur in children, in relation to the number of children born in a given year. The sight-threatening disorders of the first few months of life include the following:

- Congenital cataracts
- Congenital glaucoma
- Retinoblastoma
- Retinopathy of prematurity.

Although these disorders are rare, they are often bilateral and lead to severe visual impairment if not swiftly treated. Retinopathy of prematurity is the only eye disorder for which there is selective ophthalmological screening in Germany if there is an increased risk of the disorder due to premature birth (3).

Amblyopia is one of the most common disorders in the first few years of life and is usually caused by ametropias (e.g. far-sightedness, astigmatism) or strabismus. Pathogenetically, amblyopia hinders the development of vision during the “sensitive phase” in the first few years of life, as a result of the following:

- Strabismus
- Ametropias
- Optical deprivation.

During this phase, amblyopia can be successfully treated by temporarily covering the better eye (occlusion therapy), prescribing glasses, or possibly operating (4).

Among other cases, screening is worthwhile when the disorder to be diagnosed is sufficiently common and successful treatment is guaranteed (5). Preschool visual screening therefore aims primarily to prevent

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amblyopia by identifying its main causes early on. At the same time, however, other, rarer but possibly more serious eye disorders might also be diagnosed, depending on the methods used. The figures in the literature for the prevalence of amblyopia range from 1% (6) to 5.3% (7). This variation can be explained by differences in the cohorts examined and the lack of a binding definition of amblyopia.

The current situation

German law establishes exploratory vision screening as part of routine childhood medical examinations. The statutory health insurance scheme allows for children to be screened if there is reason to suspect a vision disorder. It covers ophthalmological examination only if a disorder has been found. Remuneration for this is currently less than 20 euros per quarter. A pediatrician or family doctor may claim approximately 35 euros for all routine childhood examinations, but in return for this sum must provide a full somatic, neurological and developmental psychology report. Nine of the ten routine examinations include examination of the visual apparatus. For example, examination 5, which is carried out at six months, examines the following parameters:

- Fixation
- Ocular motility
- Eye position
- Pupil reactions
- Tear duct function
- Diameter of cornea
- Other eyeball abnormalities.

As the doctors carrying out examinations do not currently receive specific training for this, and as the remuneration for these measures is too low to cover the cost of the time required, we can conclude that the program is unable to provide what the law establishes.

The sensitivity of routine childhood medical examinations was ascertained as part of a study sponsored by the Bertelsmann Foundation. 665 preschool children aged 3.5 to 4.5 years underwent ophthalmological and orthoptic examination. 28% of the children displayed abnormalities. 70% of these were not classified as “disorders” in routine medical examinations (8). The German Pediatricians’ Association and Ophthalmologists’ Association have repeatedly pointed out flaws in the system.

The aim and purpose of screening programs

Screening is offered when a disorder cannot be identified by laypeople but can be revealed using sensitive, specific tests. These tests must be cost-effective and must not cause stress or harm to patients. Diagnosis of the disorder must lead to treatment and thereby be beneficial. The financial costs must not exceed the expected benefit (5, 9). Last but not least, the disorder must be common, as shown in the following specimen calculation.

Sensitivity is taken to be the probability that a test gives a positive result when a disorder is present. Specificity is the probability that a test gives a negative

result when the person tested is healthy. For screening, however, the positive predictive value is important. This is the probability that a disorder is present when the test gives a positive result (the number of people correctly diagnosed as positive divided by the total number of true positives and false positives). With an estimated prevalence of amblyopia of 3%, a population of 700 000 people born in the same year, test sensitivity 60% and test specificity 90%, the positive predictive value is 16%. This means that 16 of every 100 children are correctly referred to an ophthalmologist for further treatment, while this is considered unnecessary for the other 84. The value is therefore low, because the prevalence of amblyopia and the test sensitivity are low, although expressed realistically: the Vision in Preschoolers Study in 2004 showed that in 2588 four- to five-year-olds the sensitivities of individual tests (random dot stereo tests, the Lea Vision Test, autorefractor, non-cycloplegic skiascopy) with an assumed specificity of 90% were between 42% and 64% (10). The positive predictive value was thus between 11% and 17%. This means that screening using only one test cannot be recommended without reservation. Combinations of tests or multiple-stage examinations may be more beneficial.

Studies of screening tests

The selective literature search yielded 158 relevant hits. In accordance with the IQWiG report and the HTA, four studies were identified which matched the profile of a two-armed clinical trial and were therefore in line with the IQWiG report and the HTA. The trial with the strongest conclusions of the four is the Avon Longitudinal Study of Parents and Children, which tested 6081 seven-year-olds. The prevalence of amblyopia in children who were screened and treated as preschoolers was 1.1%, while the corresponding figure for non-screened children was 2% (11). The difference, which is slightly statistically significant, disappears when analysis takes into account children who were invited for screening but did not undergo it (intention-to-treat [ITT] analysis). The study also showed that the prevalence of amblyopia was correlated to membership of certain social strata. In the same cohort, 3490 children were randomized into two groups: one group was screened once, and the other group six times. In this latter group, the prevalence of amblyopia was stated as 0.6%, while it was 1.8% in those screened only once (12).

In Israel, 1580 eight-year-old children were tested for amblyopia. In children who had previously been screened and treated, the prevalence of amblyopia was 1%, while it was 2.6% in the others (13). This was a retrospective, non-blinded trial which did not use ITT. The prevalence of deep amblyopia with vision ≤ 0.32 was 0.1% vs. 1.7%.

In another Israeli study, dating from 2007, 292 255 sixteen-year-olds were tested for amblyopia. 89% had grown up in Israel and had been screened and treated as children. The other 11% had moved to Israel from the

USSR after the age of ten and had not been screened. The prevalence of amblyopia in those who had immigrated was 1.5%. In those born in Israel it was significantly lower, at 1% (14). This study was also retrospective and was affected by distorting factors, such as an unevenly distributed refraction between the two cohorts.

In summary, all studies published to date have methodological flaws, which means that the efficacy of screening in preventing amblyopia can be judged only conditionally. Despite these limitations, a positive effect of screening is consistently apparent. An absence of proof is no proof of absence of effect. A review published by the Cochrane Collaboration in 2009 (4) concludes that “Despite the large amount of literature available regarding vision screening no trials designed to compare the prevalence of amblyopia in screened versus unscreened populations were found.”

Comparison of the IQWiG report and the Health Technology Assessment

The IQWiG report concerns the effectiveness of vision screening in children up to the age of six. The British HTA examines the cost-effectiveness of screening programs for amblyopia and strabismus in children up to the age of four or five. The German report is 238 pages long and based on a draft report by external specialists, revised by the IQWiG. 28 882 scientific works were identified, and 36 studies were ultimately assessed on the basis of clearly-defined inclusion and exclusion criteria. In contrast to the British HTA, no clinical expert opinions were obtained while the report was being compiled. Experts were not consulted until after a preliminary report had been published. The British report is 214 pages long. It researched a total of 23 039 works, of which 90 publications were included in the analysis. This report does not define its inclusion and exclusion criteria clearly. The reports use differing methods. The IQWiG report covers three areas: screening, treatment, and diagnosis. Each area included a comparative benefit assessment of the following aspects:

- Universal vision screening versus no screening
- Screening strategies of varying intensiveness
- Varying treatment time frames.

The HTA focused on cost-effectiveness and used a mathematical decision-making model.

The authors of both reports conclude that the data are scarce and insufficient. They acknowledge some positive effects of screening, with this being emphasized more by the British authors than by the German authors. Both studies state clearly that it is difficult to provide a precise assessment because the literature gives neither a single definition of amblyopia nor a precise figure for its prevalence. Both the British and the German report hint that the current tests and procedures lack uniformity and that studies conducted to date have significant methodical weaknesses.

One critical question is the maximum age at which amblyopia can be successfully treated. The IQWiG authors come to the conclusion, criticized by many, that

TABLE

Prevalence and incidence of eye disorders in childhood

Disease	Prevalence (%)	Incidence (cases/year)
Ametropia	10	70 000
Strabismus	5	35 000
Amblyopia	3	21 000
Retinopathy of prematurity	0.3	2100
Glaucoma	0.06	420
Retinal dystrophy	0.04	310
Cataract	0.03	210
Retinoblastoma	0.007	49

the currently available data do not allow any optimum age to be identified and it is not impossible that treatment in adolescence may be as effective as treatment during childhood. In contrast, the British authors are convinced that early treatment is preferable to later treatment and should be provided before the age of seven. The IQWiG report emphasizes potential harm caused by screening. Although damage caused directly by screening is unlikely, according to the report, indirect damage is essentially unavoidable. The British report also mentions this point, but places greater emphasis on the potential harm caused by bullying of a child being treated for amblyopia with occlusion therapy and glasses.

The conclusions of the two reports are similar but not identical. The authors of the German report conclude that expansion of existing screening cannot be recommended, as there is little evidence of benefit and there are potentially harmful effects. In contrast, the British report comes to the conclusion that universal vision screening might reduce the prevalence of amblyopia. However, it also states that cost-effectiveness depends on long-term benefit, which in this case is low.

These diverging conclusions of the two reports, the authors of which had access to the same scientific database to address similar questions, raise the question of the extent to which such wide-ranging systematic reviews may come to an artificially critical or favorable conclusion. This is even truer for a subject on which the data are so weak. Until better-quality studies are published, the discrepancy in the evidence available can only be reinforced by practical clinical experience suggesting that treatment before children start school appears to be more effective.

Costs and benefits

The cost of preschool screening by orthoptists has been calculated at 13 euros (15) to 51 euros (8) per child. Multiplied by the current number of children born each year, this yields direct costs of 9 million to 35 million euros per year in Germany. When calculating the costs of amblyopia prevention, a distinction must be made

between diagnosis and treatment. Diagnosing one case of amblyopia costs an estimated 1000 euros (15, 16). The costs of treatment are estimated at around 2300 euros (16, 17). This means that one case of amblyopia (diagnosis plus treatment) costs approximately 3300 euros. The British HTA gives an estimate of around 5000 euros.

In assessing the benefits which offset these costs, a distinction must be made between short-term and long-term benefits. Short-term benefits focus on improved quality of life thanks to immediate gains in visual acuity.

In the Dunedin Longitudinal Study, 1037 people were interviewed using standardized questionnaires. In these studies, people with amblyopia felt no more restrictions on their sight-related quality of life than people without amblyopia (information given in person by G. Wilson, Rotterdam Amblyopia Meeting 2009). The Waterland Study, from the Netherlands, came to a somewhat different conclusion. In 135 amblyopia patients with an average age of 41 years, use of the time trade-off method yielded the conclusion that 70% of those surveyed would surrender an average of 11 months of life in exchange for a hypothetical cure of their amblyopia. On the basis of these data, a utility value of 0.96 was calculated (information given in person by E. van der Graaf, Rotterdam Amblyopia Meeting 2009). The same value was obtained by König and Barry (18). The utility value can be used to calculate quality-adjusted life years (QALYs). In 2002, Memreno et al. calculated a sum of 2300 euros/QALY for amblyopia treatment. At that time this value was equivalent to 2300 euros and must be considered cost-effective (19). For amblyopia diagnosis and treatment as a whole, the average estimated costs are relatively consistent at approximately 7500 euros/QALY (16, 18). However, the 90% confidence interval for this calculation ranges from 3452 to 72 637 euros (18), which reflects the uncertainty of the data. In the HTA, the costs were estimated at 18 800 euros/QALY (2). The UK's National Institute for Clinical Excellence (NICE) gave a cost-effectiveness threshold for a measure of 22 000 euros/QALY.

Long-term benefit revolves around the probability of bilateral visual impairment in later life. This risk is higher with amblyopia, because only one eye has normal visual acuity. In a subcohort of the Rotterdam Eye Study consisting of 5520 people, it was calculated that the lifetime risk of bilateral visual impairment (vision <0.5) was 10% for those without amblyopia and 18% for those with amblyopia (20). The 8% difference results in a reciprocally rounded-off number needed to treat of 13, to the nearest integer. In other words, 13 amblyopia patients must be diagnosed and successfully treated in order to prevent bilateral visual impairment in later life in one person. If this figure is multiplied by the cost of amblyopia diagnosis and treatment and compared with the annual costs of a visual impairment, a simplified calculation would show vision screening in childhood to cover its costs if this same person had a

remaining life expectancy of at least five years following the onset of bilateral visual impairment. This can be assumed.

Conclusion

The prevalence of amblyopia justifies screening. The results of clinical trials show that screening and treatment reduce prevalence. However, studies conducted to date suffer from methodological flaws and have ignored children who have not attended screening—a not unlikely scenario, particularly in lower social strata. Despite being readily accepted, it is doubtful whether the current system of routine childhood examination in Germany can meet expectations. Clinical experience and weak scientific evidence show that early treatment of amblyopia is preferable to later treatment. The immediate benefit may be low and must be weighed against the stress caused to children and their families by amblyopia treatment. There may be an additional long-term benefit, as early amblyopia treatment in childhood reduces the chance of later bilateral visual impairment due to a disease in the better eye. Despite the uncertainties, simplified estimates and analyses to date lead us to suspect that screening and amblyopia treatment are comparatively cost-effective. Future studies should address the following open questions:

- What is the precise prevalence of various severities of amblyopia?
- To what extent is quality of life reduced by amblyopia, and also by early amblyopia diagnosis and treatment?
- Do sensitive, specific, possibly multiple-stage tests allow cost-effective early diagnosis?

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Conflict of interest statement

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