LITERATURE REVIEW ON PRESCHOOL VISION SCREENING

COOLS G., HOUTMAN A.C.*, SPILEERS W.*, VAN KERSCHAVER E.°, CASTEELS I.°*

SUMMARY

Amblyopia results from degradation of the retinal image during a sensitive period of visual development. Amblyopia is the most common cause of visual loss in children. Because of the failure in detection and in treatment, amblyopia is still an important cause of visual loss in adults. Results from recent randomised trials in amblyopia should change our approach to screening and treatment. Based on the current evidence, if a single screening session is used, screening at school entry could be the most efficient screening moment. Between researchers, however, there still exists a lot of controversy on the benefit of visual screening

KEYWORDS

Amblyopia, Preschool, Screening, Strabismus, Vision

* *Department of Ophthalmology University Hospitals Leuven, Kapucijnenvoer 33, 3000 Leuven.*

° *Scientific advisor, Chief medical officier Kind en Gezin (Child and Family), Hallepoortlaan 27, 1060 Brussel*

Submitted: 30-03-09
Accepted: 23-08-09

INTRODUCTION

The purpose of preschool vision screening for amblyopia and amblyogenic factors (strabismus, refractive abnormalities, organic diseases) is to treat amblyopia in an early stage or to prevent it from developing. Amblyopia can only develop during the visual maturation process; only during this period of plasticity of the brain the phenomenon can be reverted. At the age of 2 to 3 years old, young children are most susceptible to develop amblyopia. This susceptibility gradually diminishes towards the age of 6 to 7 years old. (1)

Firstly, screening may be aimed towards tracking congenital ocular abnormalities such as congenital cataract. However, congenital abnormalities are relatively rare and as such may not warrant an early screeningprogramme (2,3).
Secondly, screening is aimed at intercepting functional abnormalities of the visual system such as strabismus and amblyopia at an early stage. Early screening for strabismus is important because it is an important risk factor for amblyopia. Additionally, strabismus can be a symptom of underlying ocular or neurological diseases.
A third goal of screening is to trace refractive error (anisometropia and hypermetropia) that may cause strabismus and/or amblyopia.

The difficulty of screening young children is to define the ideal visual test set-up. The accuracy and thus the quality of the test depends greatly on the cooperation and the intellectual development of the young individual and therefore tests are not always reliable. (4,5,6)
In general, only from the age of 3 years old reliable visual acuity testing is possible.

New techniques such as photo- and videorefractive screening have been developed to counter these shortcomings when screening at preschool age. (7,8,9)

OBJECTIVE OF THIS PAPER

The objective of this paper is to present an overview of the controversy, recent research and opinions in preschool visual screening and treatment.

SEARCH STRATEGY

A search for the keywords "amblyopia" and "preschool vision screening" on PubMed was performed. We mainly selected recent publications, but we also considered older key articles. Furthermore, we have used information from renowned handbooks on amblyopia and strabismus. The review article of Stewart and Snowdon triggered many questions in the domain of preschool visual screening and has lead to recent research on the domain of amblyopia.

LIST OF ABBREVIATIONS

RCT: Randomised Controlled Trial
PPV: Positive Predictive Value
VOV: Vroegtijdige Onderkenning Visusstoornissen (Early Recognition of Visual Disorder)
PEDIG: Pediatric Eye Disease Investigator Group
ATS: Amblyopia Treatment Studies

AMBLYOPIA

Van Noorden described amblyopia as "a decrease of visual acuity in one eye when caused by abnormal binocular interaction or occurring in one or both eyes as a result of pattern vision deprivation during visual immaturity, for which no cause can be detected during the physical examination of the eye(s) and which in appropriate cases is reversible by therapeutic measures." (1)
There are several different types and causes of amblyopia. The three main types are strabismic amblyopia, deprivation amblyopia and refractive amblyopia. Each may require their particular type of treatment. Besides these three main types, idiopathic amblyopia, organic amblyopia and anisometropic amblyopia should be considered. A combination of the different types of amblyopia can occur. Remarkably, many studies about screening and treatment of amblyopia do not distinguish between the different forms of amblyopia and therefore, the final outcome within those studies is difficult to compare. Furthermore, the definition of amblyopia varies between studies.
Additionally, it turns out that the measure of visual acuity can differ significantly according to the visual test applied. The logarithmic and decimal scale are most commonly used in tables that represent visual test results. Ideally, visual acuity is expressed in LogMAR-units. Unfortunately, this is not always the case and this forms another obstacle to compare the results of different studies and evaluate the effectiveness of different types of amblyopia treatment.

AMBLYOPIA AND MORBIDITY

Potential morbidity of amblyopia has been investigated by assessing the risk of visual impairment attributable to loss of vision in the non-amblyopic eye. The projected lifetime risk of visual loss for an individual with amblyopia is at least 1,2 percent. (10) *Rahi and associates* (11) found that only 35 percent of 102 individuals in paid employment were able to continue work after newly acquired visual loss in their non-amblyopic eye,when the vision in the amblyopic eye was worse than 6/12.

HISTORY OF PRESCHOOL VISION SCREENING

Snowdon and Stewart-Brown published a review article in 1997 which provides a good insight on the versatile issue of "Preschool vision screening". (3) This article challenged the justification of preschool vision screening and the effectivity of amblyopia treatment; many studies on the subject have been published since. The authors list several criteria for a valid and efficient screening programme. First, the pre-

valence of the pathology should be significant and disabling. For children under age 7 years, the prevalence of amblyopia, refractive errors and strabismus is 2.4 - 6.1%, which is significant for justifying screening for these defects. Secondly, the condition should have a significant effect on the morbidity. According to Snowdon et al., no attempts have been made to assess the consequences of amblyopia on adults and children. A third criterium for justifying screening is the knowledge about the natural history of the condition. Lack of documentation of the natural history of the condition means that it is impossible to estimate the effect of treatment from studies which have no control group (children not receiving any treatment). Any improvement observed during the course of treatment might be occurring in spite of, rather than because of, the treatment. Randomized controlled trials (RCT) are difficult to justify from an ethical point of view, so knowledge about the natural history of amblyopia is very poor.

Effectiveness of treatment is a fourth criterium. According to Snowdon et al., there were no studies found designed to illustrate the effectiveness of the current treatment for amblyopia, refractive errors and strabismus. There is a strongly held clinical belief that treatment works. However, the evidence relating to the natural history of these conditions is inadequate and there do not appear to be any methodologically sound trials of the effect of treatment on any of the conditions on visual function. Current clinical practice appears to be based on theory and on observational studies of treatment. Although this may be considered sufficient as a basis for clinical practice, it is not sufficient for the establishment of a screening programme.

No studies were identified in which an attempt was made to assess any negative impact of orthoptic treatment on the child or the family. Studies on compliance with treatment suggest that orthoptic treatment is not without problems for families but the potential negative effects of treatment have not been explored.

A final important criterium for screening is to define a screening test with high sensitivity (= the proportion of people with a target condition who where correctly identified on screening) and specificity (= the proportion of individuals without a target condition who had a negative screening test result), resulting in a high positive predictive value (= the proportion of people with a positive test result who do have a target condition). The authors could identify only one relevant prospective study about screening. (12) This one study claims that orthoptic screening is effective to identify children with amblyopia.

No studies were found that aimed to measure the negative effects of screening, i.e. identifying the number of false positives and false negatives tests, resulting in respectively overtreatment and undertreatment. It is important to find out whether the negative effects of screening outweigh the advantages, in which case screening would be pointless.

The authors conclude that there is a lack of good quality research into the natural history of the target condition, the disabilities associated with them, and the efficacy of available treatments. An invitation to preschool vision screening carries with it the implicit assumption that screening is going to benefit the child. (13)

The conclusions and recommendations by Snowdon et al differ from those of other recent reviews, which judge that preschool vision screening is worthwhile. (14,15) The conclusions of these reviews are based on the literature that has been appraised in this review. This review differs in that a more rigorous approach to the evidence relating to disability and treatment has been taken. Snowdon et al. believe that this evidence is essential to support a screening programme for a non-fatal condition for which there have been no rigorously controlled trials. “In the case of screening, no evidence of effectiveness is sufficient evidence of no effectiveness”. (3) The controversy in this review article has triggered the attention of researchers and physicians, closely related to the topic. *Rahi and Dezateux (16)* claim that the review’s recommendations lack objectivity and suggest that the authors believe that preschool vision screening is not worthwhile, despite the lack of adequate data on which to base such a conclusion. *Lee J, Adams G en Sloper J* (17) state that in the everyday experience of those working with amblyopic children, the positive effect of amblyopia treatment is obvious. Against this background they do not believe it would be ethical to conduct any trial in which child-

ren were randomly allocated to a non-treatment group. They are not particularly surprised that there are no randomised clinical trials in the literature. In general the more effective a treatment the less likely it is to have been subjected to controlled trials. This review aims to find an equilibrated answer in the debate about the effectiveness of treatment and the importance of early detection of amblyopia.
We decided to focus on the recent literature *(Table 1)*, but we would like to emphazise that a lot of valuable review articles were published earlier. For further reading we refer to a review article of *Spiritus et al.* that was published in 1997 and gives a nice summary of precious work that has been done on this issue (18).

SCREENING OF AMBLYOPIA : PROGRAMS AND TESTS

Kvarnström et al report a comprehensive longitudinal and retrospective study on visual screening (19). The screening programme for eye disease and visual dysfunction in children has been in operation in Sweden for the last 20 years. Visual acuity screening at 4 years of age has been performed in a cohort (n= 3126) consisting of all children born in 1982 and who in 1993, were living in the municipalities of Huddinge, Lund and Linköping.
The aim of this study was to describe and analyse the various ophthalmological conditions in children that were detected in different phases of screening test in the period between 1982 and 1993.
Refractive errors and microtropias were mainly detected at the age of 4, when the first visual acuity test was performed, while manifest strabismus was detected in many cases before this age.
Screening and early treatment resulted in a significant reduction of prevalence of amblyopia (visual acuity $\leqslant$ 0.7) from 2,9-3,9% to 1-2,1%. The reduction of amblyopia after screening and treatment was most pronounced for the lower visual acuities (visual acuity $\leqslant$ 0.3). The number of children with amblyopia at 4 years age is much lower than would be expected from other studies of untreated amblyopia. The probable reason for it is that 55% of the strabismic children were referred and treated before the age of 4. The authors conclude that visual screening is effective in detecting visual and ocular disorders. Compared to an unscreened population, the prevalence of amblyopia is greatly reduced. A good distribution of the target population may explain the good results of this study.

The Rotterdam Amblyopia Screening Effectiveness Study (RAMSES,1996-2005) is a prospective cohort study about the effectiveness of screening for amblyopia in childcare. (20,21) The aim of the Ramses-research was to define whether the current method of screening is effective to detect children with amblyopia and start treatment at an early stage.
Stewart and Snowdon suggested that randomised clinical studies are required to evaluate the current screening programmes. But when screening is already applied at a broad-based level, it becomes difficult to organise a randomised controlled trial (RCT), meaning that there is a control group of children that will not undergo screening. Therefore, the researchers of the Ramses-study have opted for an observational study, which is less decisive than a randomised clinical study.
The screening programme in Rotterdam contains following parts:
VOV screening (Vroegtijdig Onderkennen van Visuele stoornissen), a screening test for early recognition of visual disorders and strabismus, carried out at the community childcare centre at the age of 9, 14 and 24 months old.
Children with abnormal results were referred to the general practitioner and from there to an ophthalmologic centre for further diagnosis and treatment.
All children, born in Rotterdam between September 1996 and May 1997 (n=4624), were included in the study and observed for a period of 7 years.
The prevalence and degree of amblyopia in the total cohort was evaluated by an independent orthoptist and ophthalmologist, at the end of the study period.
Whereas participation in the screening programme was relatively high, it appeared that the flow towards further specialised aid (“referral procedure”) failed. Only one third of the

Table 1

	Type of study	*Participants*	*Method of screening*	*Aim*	*Conclusion*
Kvärnström 2001	Longitudinal & retrospective study	Screening of all 4 years old children born in 1982 (n = 3126)	• General examination by a paediatrician or general practioner of the ocular media and ocular alignment at 6-12 weeks, 6 months, 18 months and 36 months • Visual acuity testing from the age of 4	To describe & analyse ophthalmological conditions in children detected by screening	• Visual screening is effective in detecting visual & ocular disorders • Reduction of the prevalence of amblyopia
Cobb 2002	Retrospective study	of 112 files of children with anisometropic amblyopia who had failed preschool or school screening	Information recorded from the notes: initial and first corrected visual acuity, presence and type of squint	To identify the effect of the age of detection of anisometropic amblyopia on the final visual outcome	The age of presentation has no significant effect on the final visual outcome
Clarke 2003	Pragmatic single masked RCT	of children referred to one of the 8 selcted UK children's eye clinics after two abnormal standard preschool screening tests	Assessment of vision at 24, 52, 54 and 78 weeks after inclusion in the study	To evaluate the efficacy of different treatments compared to no treatment and to define the extent to which effectiveness varies with initial visual acuity	• Children with moderate acuity loss ($\leqslant$ 6/18) have a clear cut response to treatment which justifies screening • children with mild acuity loss ($\geqslant$ 6/9) receive little benefit from treatment • The authors also support a relatively later screening
Williams 2002	Randomized controlled trial (longitudinal study)	Children born in Avon between 1 April 1991 and 31 December 1992	Orthoptic examination: cover test + vision testing. Failure of cover testing or vision testing led to referral to the hospital for full evaluation including cycloplegic refraction and funduscopy	To assess the effectiveness of early treatment for amblyopia in children	Early detection and treatment of amblyopia leads to a better outcome

	Type of study	*Participants*	*Method of screening*	*Aim*	*Conclusion*
Williams 2003	RCT (longitudinal study)	Children born in Avon between 1 April 1991 and 31 December 1992	An orthoptic preschool screening examination which includes a monocular vision test, a cover test and an assessment of binocularity	To compare the visual outcome at age $7^{1/2}$ for children who received preschool screening at 37 months with those who did not	Preschool screening for amblyopia leads to better acuity after treatment. But on population level the programme had little effect on the overall burden of amblyopia
RAMSES study 1996-2005	Prospective observational cohort study	Screening at the age of 9, 14, 24 months of all children who presented at the community childcare centre and who were born in Rotterdam between September 1996 and May 1997	The Rotterdam screening programme consists of: a screening test for strabismus at the age of 9, 14 and 24 months and a visual acuity test from the age of 36 months	To define whether the current method of screening is effective to detect children with amblyopia and start treatment at an early age	The researchers recommend to continue the early detection of amblyopia as screening contributes to the decrease in the number of children with remaining subnormal vision

Table II: *Amblyopia Treatment Study Group with Published Results*

	Study Design	*No. of Patients (Age at enrollment)*	*Follow-up Period*	*Result*
Occlusion versus pharmacologic therapy for moderate amblyopia (ATS 1)	RCT	419 (3 to <7 years)	6 months	• VA improved in both groups: 3.16 lines in patching group; 2.84 lines in atropine group • VA ⩾20/30 and/or improved by ⩾3 lines in 79% of patching group and 74% of atropine group
Occlusion versus pharmacologic therapy for moderate amblyopia (ATS 1)	RCT	419 (3 to <7 years)	2 years	• VA improved in both groups: 3.7 lines in patching group; 3.6 lines in atropine group • Atropine or patching for 6-month period produced a similar improvement in amblyopia 2 years after treatment
Randomised trial comparing part-time versus full-time patching for severe amblyopia (ATS 2A)	RCT	175 (3 to <7 years)	4 months	• VA improved in both groups: 4.8 lines in the 6 hours patching group; 4.7 lines in the full-time patching (all hours or all but 1 hour per day) group

	Study Design	*No. of Patients (Age at enrollment)*	*Follow-up Period*	*Result*
Randomised trial comparing part-time versus minimal-time patching for moderate amblyopia (ATS 2B)	RCT	189 (3 to <7 years)	4 months	• VA improvement in both groups was 2.40 lines • VA [00f2]›20/32 and/or [00f2]›3 lines in 62% of patients in both groups • VA improvement similar for 2 hours of daily patching and 6 hours of daily patching
Evaluation of treatment of amblyopia in 7 to <18 year olds (ATS 3)	RCT	507 (age 7 to 17 years)	6 months	• For moderate amblyopia in patients 7 to <13 years old, 36% achieved 20/25 or better with optical correction/patching/atropine use compared with 14% with optical correction alone • For moderate amblyopia in patients 13 to 17 years old, 14% achieved 20/25 or better with optical correction/patching compared with 11% with optical correction alone • For severe amblyopia in patients 13 to 17 years old, 14% achieved 20/40 or better with optical correction/patching compared with 0% with optical correction alone
Randomised trial comparing daily atropine versus weekend atropine for moderate amblyopia (ATS 4)	RCT	168 (3 to <7 years)	4 months	• VA improvement in both groups was 2.3 lines • 47% of daily group and 53% of the weekend group either had VA ⩾20/25 or greater than of equal to that of the nonamblyopic eye
Randomised trial to evaluate 2 hours of daily patching for amblyopia in children 3 to <7 years old (ATS 5 - eyeglasses phase)	Prospective multicenter noncomparative intervention	84 (3 to <7 years)	Up to 30 weeks	• Amblyopia improved with optical correction by ⩾2 lines in 77% • Amblyopia resolved with optical correction in 27%
Randomised trial to evaluate 2 hours of daily patching for amlyopia in children 3 to <7 years old (ATS 5 - randomization phase)	RCT	180 (3 to <7 years)	5 weeks	• After a period of treatment with eyeglasses until vision stopped improving, patients treated with 2 hours of daily patching combined with 1 hour of near visual tasks had an improvement in VA of 1.1 lines compared to 0.5 lines in the control group

ATS = Amblyopia Treatment Study; RCT = randomised clinical trial; VA = visual acuity

NOTE: In the ATS, mild to moderate amblyopia is defined as VA in the amblyopic eye of 20/80 or better; severe amblyopia is defined as VA in the amblyopic eye of 20/100 to 20/400

children with positive test results were further examined in an ophthalmologic centre, meaning that two third of children with a positive test result missed out on an early treatment of amblyopia.

This non-compliance with the referral procedure has an influence on the screening and there should be focused on the improvement of this part of the prevention programme.

The Positive Predictive Value (PPV) is the proportion of patients with positive test results who are correctly diagnosed. It reflects the probability that a positive test reflects the underlying condition being tested for. Its value does however depend on the prevalence of the disease, which may vary. From the PPV, the number of false positives can be derived (1-PPV).

The authors have compared the PPV of this study with data from simular studies about screening programmes with children and concluded the VOV screening method yields a low number of false positives.

The VOV screening turns out to have a positive PPV and thus considering the relatively high incidence, it has a relatively low number of false positives.

The basis cohort contained data about 4624 children in 1997. In 2004, only 2964 children could still be reached for the final evaluation.

This final evaluation at age 7 was carried out by orthoptists and consisted of the following examinations: a visual acuity test with Landolt-C card, orthoptic assessment, the TNO-randomdot stereo test, convergence testing and an external eye examination. If any abnormalities were detected during these examinations, the child was invited for further ophthalmologic examination in the Erasmushospital in Rotterdam. The final visual acuity to be registered was the best corrected visual acuity (BCVA) of the worse eye at the age of 7 years old. A distinction was made between (best possible corrected) visual acuity of < 0.5 of the worse eye (*bad eyesight*) and (best possible corrected) visual acuity of < 0.3 of the worse eye (*legal blindness*).

In the 10th Revision of the WHO International Statistical Classification of Diseases, Injuries and Causes of Death, subnormal vision is defined as visual acuity of less than 0.8.

Additional ophthalmologic examinations after referral revealed in the following numbers concerning visual acuity of the worse eye with the best possible correction:
63 children with visual acuity of < 0.8, 23 children with visual acuity of < 0.5, 9 children with visual acuity of < 0.3
Analyses showed that more frequent and earlier screening correlate with a better visual outcome.

As the authors concluded, the “referral procedure” needs improvement. The VOV screening test for amblyopia had a more favourable PPV than several other screening tests in the Dutch system. When early screening programmes are performed, the percentage of children with subnormal visual acuity (< 0.5) on one or both eyes is significantly lower than expected from the literature when no screening is done.
The sensitivity of this screening programme is about 70 tot 80%. Approximately one fifth of the cases of amblyopia (visual acuity of < 0.5 at the age of 7) stayed unnoticed.
Screening plays a major role in detecting refractive amblyopia; strabismic amblyopia is often detected outside the screening program.
Regular screening from early age on is more effective then a one-time screening.
There is also a significant difference between children with their first screening after the age of 3 years old and those signed in for the VOV-examination: 3.2% had a subnormal visual acuity (< 0.5), compared to 0.7%. This difference can possibly be assigned to a more unfavourable course of amblyopia, that is only detected with the decrease of visual acuity after the age of 3. The natural course of amblyopia is not enough described to determine how often the screening for amblyopia leads to overdiagnosis. But this is probably limited.
As the consequences of a false negative outcome are considerable, it is advisable to split up screening in different screening moments. However, it stays unclear whether screening for amblyopia is cost-effective, as the influence of an amblyopic eye on the quality of life in the short and long term, is not wel described.
The researchers of this study do recommend to continue the early detection of amblyopia, as screening contributes to the decrease in the number of children with remaining subnormal

vision. Furthermore, the sensitivity of the screening programme can still be increased by clear information sessions towards the parents about a possible unsatisfactory screening result, strict compliance with the guidelines of the "reference procedure" and a more active follow-up of children that have ever been referred for further examinations.

TREATMENT OF AMBLYOPIA: BENEFITS AND FAILURES

Snowdon and Stewart suggested a prospective randomized trial to prove the effectiveness of current treatment for amblyopia and to justify screening . This need was met by *'The Pediatric Eye Disease Investigator Group'*. The Amblyopia Treatment Studies consists of a series of randomized clinical trials designed to answer questions regarding the optimal management of amblyopia.
Table 2 summarizes the results of completed randomized controlled trials of amblyopia therapy (22-30).

EFFECTIVENESS OF TREATMENT AND IMPORTANCE OF EARLY DETECTION OF AMBLYOPIA

The retrospective study by *Cobb et al (2002)* was set up to identify whether the age of detection of anisometropic amblyopia has any effect on the final visual outcome. (31) Children with anisometropia, but no squint, have no external signs. Many of them are identified at a later age than strabismic children are. The files of 112 children with anisometropic amblyopia, who had failed preschool or school screening, were retrospectively studied. Anisometropia was defined as the difference in refractive error between the eyes of 2.0 dioptres or greater of sphere or cylinder. Amblyopia was defined as a difference in initial corrected visual acuity of two lines or greater when measured using a Snellen chart in the majority of cases, and in the younger children, the Sheridan-Gardiner test. All children underwent an orthoptic examination before cycloplegic refraction. Treatment consisted of a full spectacle correction followed by, if necessary, occlusion with patching. There was a strong inverse linear trend correlating refractive error (spherical equivalent) and degree of anisometropia with the final visual acuity. However, the age at presentation of a child with anisometropic amblyopia appeared to have no significant effect on the final visual acuity. Regression analysis showed that the degree of anisometropia, spherical equivalent, presence of strabismus and initial visual acuity did not vary significantly with age at presentation.

The authors state that the age at presentation could be of significant value in children with more severe eye abnormalities (and thus a greater risk of developing amblyopia) than in children with less severe eye problems.This study reports a correlation between refractive error / degree of anisometropia and final visual acuity. So, if children with more severe refractive error were detected earlier, they would be treated earlier and they could have a better visual outcome.
Mean visual acuity was significantly worse in strabismic versus non-strabismic children.
Two thirds of the strabismic patients had microdeviations. Patients with microdeviations and with pure anisometropia (without associated strabismus) are only likely to be identified with a screening programme. The investigators compared the analysis of purely anisometropic amblyopes and anisometropes with a microdeviation and they also report no association between age at presentation and final acuity in the amblyopic eye. This study concludes that active treatment is highly effective, independent of age at presentation. The fact that the age at presentation has no significant effect on the final visual outcome, suggests that the time at which screening is carried out may not be as critical for this group. The authors propose that screening for this common condition should ideally be carried out on one occasion, when the likelihood of the child attending is high, at an age when they can give reliable responses and if occlusion is necessary, this will not interfere with schooling.
An important remark on this study is that all children who have been analysed have had some

form of screening. So all children included were detected at a young age. It could be possible that without any form of screening these children wouldn't have been noticed in time.

The study of *Clarke et al.(2003)* aligns with the ideas of Stewart and Snowdon and supports a relatively later screening. (32) This study aims to evaluate the efficacy of different treatments (full treatment with glasses and patching, if required, and treatment with glasses only) compared to no treatment, and thereby defining the extent to which effectiveness varies with initial severity.
This study was a pragmatic, single masked, randomised controlled trial in eight UK children's eye clinics. Recruitment of participants was organized as follows. In all centres preschool vision testing had already been organized by community based orthoptists. Children were referred to dedicated recruitment clinics if, after two standard screening tests, they had 6/6 vision in one eye and 6/9 to 6/36 vision in the other. If the acuity findings were confirmed in the recruitment clinic, the child was eligible to join the trial. If the ophthalmologist found any other ocular abnormalities, the child was excluded from the trial. Once consent was obtained, the child was randomly allocated to a treatment group. After randomisation, all children were tested for refractive error with cycloplegic drops to eliminate artefact due to accommodation. Glasses were dispensed to children only in the full treatment and glasses groups, who were then seen after six weeks to verify the glasses prescription. Children in the full treatment group then started to wear a patch if their corrected acuity remained reduced. They were reviewed every six weeks and treated according to protocol. Children in the glasses group received no further treatment for 52 weeks. Children in the control group (no treatment) received no active treatment for 52 weeks. For those children receiving treatment, the researchers assessed compliance using weekly parental diaries for the first 12 weeks of glasses wear and with daily diaries for the duration of patching treatment. A research orthoptist, who remained masked throughout to the child's treatment group, assessed vision at 24, 52, 54 and 78 weeks. At six months, if a child in the no treatment and glasses treatment groups developed manifest squint or acuity below 6/36 they were offered full treatment. As children in the no treatment group did not receive glasses until after the 52 weeks follow- up, visual acuity testing was performed without glasses for all groups at 24 and 52 weeks. At 52 weeks follow-up, children in all groups were prescribed glasses. Children in the no treatment group were instructed to begin wearing glasses only the day before the 54 week follow up, when best corrected (that is without glasses) visual acuity was recorded. Six months later, at 78 weeks, all children were once more tested for their best corrected visual acuity.

Amblyopia and refractive error are common worldwide, and many countries have screening programmes to detect asymptomatic visual defects in children. Clarke et al. concluded that children with moderate acuity loss of 6/18 or worse showed a clear cut response to treatment, which itself justifies screening to identify and treat these children. In contrast, children with mild acuity loss, who represent over half those identified with unilateral acuity impairment at screening in this and other studies, received little benefit from either treatment. This level of impairment, though often excluded from studies, is still commonly treated in routine practice. The authors argue that children with 6/9 in only one eye should no longer constitute screen failures and do not justify treatment, even with glasses.
Nearly 40% of the children referred for treatment did not in fact have the target condition (amblyopia). This was despite two tests in the community and presumably reflects difficulties in testing preschool children. This, together with the good response seen in those whose treatment was deferred, support the use of relatively later screening, as recently suggested by Stewart and Snowdon.

The report spurred some criticism.
O' Brien remarked that children with an underlying ocular abnormality have been excluded from the study, whereas certain conditions of the eye also can be a cause for amblyopia and thus a valuable goal for screening (33).
Srinivas wrote that the effectiveness of occlusion depends on different variables such as the total length of the occlusion therapy, the de-

gree of amblyopia, the initial visual acuity, the cause of amblyopia and the compliance with the therapy. In the article of Clarke, no distinction is made between refractive and strabismic amblyopia. In the case of refractive amblyopia, treatment at a slightly older age can still be effective, whereas for strabismic amblyopia, more intensive treatment from a younger age may be required. Clarke et al do not specify the intensity of treatment and compliance (34).

Harrad remarked that Clarke et al suggest that a visual acuity of 6/9 in one eye and 6/12 in the other eye doesn't require any treatment. There are several reasons why there is no significant effect of treatment in this group. A visual acuity of 6/9 is a normal result for a crowded test within that age group, whereas for a single letter test, 6/9 would be a subnormal result. Additionaly, as there has not been a refractive test before randomisation and treatment, some of these children rather suffer from a simple uncorrected refractive error than from amblyopia. In fact, separate visual screening alone is not a good method to detect amblyopia. There are no data on binocular fusion or stereoscopic vision. These can improve significantly without improvement in visual acuity, thus meaning a valuable result of amblyopia treatment. Clark concludes that a correction on its own doesn't lead to good results, but he doesn't make a difference between children with or without central suppression. When suppression is present, a combination of correction and occlusion is the only workable therapy. So when the group consists of many children with suppression and where the treatment only consists of a correction, one wrongly concludes that this treatment is not effective (35).
Dutton challenges Clarke's recommendation of visual screening at older age because of the high percentage (40%) of false positive tests at young age. Instead, he could consider to improve the screening model. From the results from the authors, one concludes that it is not valuable to screen and treat children with a visual acuity of 6/9 up to 6/12. But the results could be approached alternatively by questioning the treatment protocol to end up with better results. The traditional occlusion model treats children less intensively as the visual acuity is better. But recent research has proven that children with a better visual acuity just need more intensive treatment to repair binocular fixation. (36)
The study officially ends 54 weeks after the first screening. From then on, all children receive the treatment they require. After 6 months, the children are screened again and from these results, the authors conclude that there is no significant difference between the 3 original groups, which is not surprising.
There is nothing mentioned about false negative screening results. One can also question whether it is ethically sound to deny a child the best possible treatment for the sake of a study. Unilateral visual impairment is not the same as amblyopia and this study thus draws conclusions from a mixed population. The group of the unilateral decrease in visual acuity also contains the myopic anisometropia, which is not amblyogenic, when manifested in a mild and mediocre form.

Williams et al. (2002) started a randomized controlled trial as a reaction on the systematic review of Snowdon et al. who emphasised the lack of evidence that treatment for amblyopia is better than placebo or that early treatment is more effective than later treatment (37,38). The objective of this study is to assess the effectiveness of early treatment for amblyopia in children.
Knowledge about the sensitive period for visual development suggests that the ideal age for screening is "as early as possible". Screening at school age (4-5 years of age) has a high sensitivity but there is the risk that treatment is not as effective any more compared to screening and treatment at younger age.
The original hypothesis tested was that a "de luxe" intensive early screening programme would detect and refer for treatment more children with amblyopia than would routine surveillance (the control programme) (37). The authors use follow-up results of outcomes of treatment for amblyopia in a randomised controlled trial comparing intensive orthoptic screening at 8, 12, 18, 25, 31 and 37 months (intensive group) with orthoptic screening at 37 months only (control group). The intensive screening protocol was associated with significant better acuity in the amblyopic eye and a significant lower

prevalence of amblyopia at 7 1/2 years of age, in comparison with screening at 37 months only. These data support the hypothesis that early treatment for amblyopia leads to a better outcome than later treatment.

An important question is whether feasible programmes could deliver the same benefits as the intensive programme without repeated testing, which would be extremely expensive. Further research need to investigate wether cost effective strategies can be designed that produce similar results.

In this study, all children received at least a screening at age 37 months, so the advantage from preschool vision screening compared to no screening cannot be deducted from this study.

Another study conducted by *Williams et al (2003)* compared the visual outcome at age 7 1/2 for children who received an existing, single sweep orthoptic screening programme at 37 months, with those who did not (38). All children in the study area were offered vision screening in the school reception class (4-5years). The prevalence of amblyopia (= VA < 0,3 logMAR) at the age 7 1/2 was approximately 45% lower in the children who received preschool screening at 37 months of age than in those who did not at 37 months of age. The mean acuity in the worse seeing eyes after patching treatment was significantly better for amblyopic children who received preschool screening than for those who did not. However, these effects did not persist in an intention to screen analysis. The difference between both groups remains no longer significant when children, who were offered screening but didn't comply, were included. These data support the hypothesis that preschool screening for amblyopia leads to better acuity after treatment. However, the improvement is clinically small and disappears when considering all children who were offered screening rather than only those who received it.

For screening programmes to be effective, the likelihood of screening the whole target population, the cost effectiveness of screening and treatment, and the individual and societal benefits to be expected from reducing the burden of amblyopia should be considered.

Coverage of the whole population at risk ideally requires a coordinated approach between different aspects of the child health and surveillance network (e.g. vaccinations). A study by *Memento* et al has shown that early detection and treatment of amblyopia are highly cost-effective when compared with other interventions in health care (39). But further research is still recommended here. The benefits to society of effective detection and treatment for amblyopia include preventing incapacitating visual impairment if an individual with unilateral amblyopia loses his better eye (40,41). But until today, it has not been proven that amblyopia is an impediment to education or career performance (42).
Williams et al. concluded that there is a small benefit in terms of final acuity after treatment for children who had amblyopia and were screened preschool, but on population level, this programme had little effect on the overal burden of amblyopia. The data suggest that on average, better results are obtained after earlier treatment for amblyopia. Therefore, more research is needed to explore whether photorefraction or other technologies could be sufficiently accurate to be useful on a pragmatic programme screening for amblyopia children aged 2-3 years, who would then be expected to benefit from age associated improvements in treatment

There may be an important improvement in outcome if children can be effectively screened earlier than was done here. Some forms of refractive screening may be more effective than acuity testing at detecting young children at the risk of amblyopia. The authors refer to more user-friendly devices such as autorefractors (such as Retinomax) and photo/videorefractors (such as Powerref). Recently published articles on photoscreening confirm that Powerref is a good screening device (43,44). However, photoscreening alone may miss a significant number of children with amblyopia/ amblyogenic risk factors (45). *Cordonnier et al.* conducted a lot of research on screening for amblyogenic factors in preschool children with the retinomax handheld refractor. The results of their research encourages early screening and treatment before visual acuity is measurable (46).

CONCLUSION

An article on amblyopia that was recently published in The Lancet by *Holmes* et al provides an excellent conclusion on the articles whe have discussed above (47).
A more uniform definition of amblyopia is the result of the recent increase of scientific research on amblyopia. A widely accepted definition of amblyopia based on visual acuity is 2 or more Snellen or LogMAR lines difference between eyes in best-corrected visual acuity. But in spite of this definition, it still remains difficult to compare results of different studies.
Amblyopia is the most common cause of monocular vision loss in children with an estimated prevalence of 1-5 % depending on population and study. Because of the failure of detection or treatment, amblyopia continues to be an important cause of vision loss in adults, with an estimated prevalence of 2-9 %. A study by the National Eye Institute in the USA, showed amblyopia to still be the leading cause of monocular visual loss in people aged between 20 and 70 years (28).
The diagnosis of unilateral amblyopia is made when reduced visual acuity is recorded in the presence of an amblyogenic factor, despite optimum refractive correction. Therefore a critical component of amblyopia diagnosis is the measurement of visual acuity. However, this is not always possible in young children.
One important feature of visual acuity testing to diagnose amblyopia is that there is a distribution or range of typical visual acuity in any population. This range changes with age because of neural maturational processes. For instance, with age-appropiate LogMAR tests in 4-year old children, the mean visual acuity is about 0.1 LogMAR. Thus the visual system is not fully developed at this age, and therefore doctors should not use failure to reach 6/6 as a criterion to diagnose and treat amblyopia.

Since measurement of best-corrected visual acuity is a critical part of amblyopia diagnosis, it might seem intuitive that screening for amblyopia would use a measurement of visual acuity next to other screening methods that rather rely on detection of amblyogenic factors (eg. refractive error using automated refractors, strabismus using photoscreening techniques).

The controversy of whether and when to screen remains and is based on beliefs regarding the sensitive period for the development and treatment of amblyopia. It is generally accepted that amblyopia should be treated before the age of 7 years and the earlier the treatment, the better. The philosophy to treat as early as possible has led to recommendations to screen for amblyopia as soons as a child can undertake a visual acuity measurement task. This approach is supported by data from a randomised trial of screening strategies by Williams et al. Nevertheless, further studies are needed to establish whether earlier screening strategies, or multiple screening strategies, would be best in decreasing the ultimate burden of amblyopia in a population.

Stewart and Snowdon have dared to raise the question whether treatment of amblyopia is really necessary because they think that the adverse effects of amblyopia are neglectable and the treatment causes a lot of psychological stress for the child and his family. Data for the natural history of untreated amblyopia are scarce, but they have indicated either no or minimum improvement. Little work has been done so far on the degree of disability associated with unilateral amblyopia and on the degree of disability associated with the resulting reduced stereoacuity.
Few data indicate that unilateral amblyopia greatly affects quality of life, as long as vision in the fellow eye remains good. Yet, Membreno and colleagues concluded that treatment of amblyopia in childhood resulted in a substantial lifetime gain in quality-of-life years. Permanent loss of acuity in the healthy eye will result in reduced quality of life. There are studies which proved that individuals with amblyopia are at increased risk of blindness. So, prevention of future disability is an important argument for the treatment of amblyopia in childhood.
The sensitive period for amblyopia treatment seems to vary depending on the cause of the disorder. Recent studies suggest that amblyopia can be treated beyond age 7 years. So, further investigation on maximum age of amblyopia treatment is needed.

The past few years have heralded a new era in evidence-based treatment for amblyopia and

there are a still a lot of ongoing studies who will give a clearer view on screening and treatment of amblyopia.

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Address of correspondance:
I. CASTEELS
Department of Ophthalmology
University Hospitals of Leuven
Kapucijnenvoer 33
3000 LEUVEN
tel.: +32 (0) 16 33 26 60
Fax: +32 (0) 16 33 23 67
ingele.casteels@uz.kuleuven.ac.be