Published in final edited form as:
Ophthalmology. 2007 August ; 114(8): 1427–1432.

Factors Associated with Recurrence of Amblyopia on Cessation of Patching

Jonathan M. Holmes, B.M., B.Ch.[1], **Michele Melia, Sc.M.**[2], **Yasmin S. Bradfield, M.D.**[3], **Oscar A. Cruz, M.D.**[4], **Brian Forbes, M.D., Ph.D.**[5], and **Pediatric Eye Disease Investigator Group**

1*Department of Ophthalmology, Mayo Clinic College of Medicine, Rochester MN*

2*Jaeb Center for Health Research, Tampa, FL*

3*Department of Ophthalmology and Visual Sciences, University of Wisconsin, Madison, WI*

4*Department of Ophthalmology, Saint Louis University, St Louis MO*

5*Department of Ophthalmology, Children's Hospital of Philadelphia, and University of Pennsylvania School of Medicine, Philadelphia, PA*

Abstract

Purpose—In a prospective observational study, we previously reported that weaning (tapering or gradually reducing) treatment in children treated with 6 to 8 hours of daily patching for amblyopia resulted in a 4-fold reduction in odds of recurrence. We now report the association of additional factors with recurrence or regression of amblyopia in 30 this same cohort.

Design—Prospective, nonrandomized, observational study.

Participants—69 children aged less than 8 years, with successfully treated anisometropic or strabismic amblyopia (improved at least 3 logarithm of the minimum angle of resolution (logMAR) lines).

Methods—Patients were enrolled at the time they stopped patching for amblyopia. Patients were classified according to whether patching was stopped abruptly or weaned prior to cessation. They were followed off treatment for 52 weeks to assess recurrence of amblyopia.

Main outcome measure—Recurrence of amblyopia defined as a 2 or more logMAR level reduction of visual acuity from enrollment (cessation of patching), confirmed by a second examination. Recurrence was also considered to have occurred if treatment was restarted with a 2 or more logMAR level reduction of visual acuity even if it was not confirmed by a second examination.

Results—The risk of recurrence was higher with better visual acuity at the time of cessation of treatment (adjusted risk ratio (RR)=0.68 per line of worse visual acuity (VA), 95% confidence interval (CI)=0.51, 0.90), a greater number of lines improved during the previous treatment (adjusted RR=1.5 per line increase, 95% CI=1.1, 2.0), and a prior history of recurrence (adjusted RR=2.7, 95% CI=1.5, 4.9). Orthotropia or excellent stereoacuity at the time of patching cessation did not appear to have a protective effect on the risk of recurrence.

Conclusions—The higher risk of recurrence in the most successfully treated children with amblyopia and absence of protection from orthotropia and excellent randot dot stereoacuity suggests

Correspondence to: Dr. Jonathan M. Holmes, Ophthalmology E7, Mayo Clinic, Rochester, MN 55905. Phone: (507) 284-3760. Fax: (507) 284-8566. Email: holmes.jonathan@mayo.edu.

Précis Recurrence of amblyopia on cessation of patching was associated with more successful treatment and there appeared to be no protection from orthotropia or excellent randot dot stereoacuity, suggesting the need for careful and prolonged follow-up.

that careful and prolonged follow-up is needed for all children who have been previously treated for amblyopia.

In a prospective study of cessation of treatment in children aged 3 to <8 years with successfully treated amblyopia due to anisometropia, strabismus or both, we found the risk of amblyopia recurrence to be 24%.[1] We also found that patients treated with 6 to 8 hours of daily patching had a 4-fold greater odds of recurrence if patching was stopped abruptly rather than when it was reduced to 2 hours per day prior to cessation.[1] Although these analyses were adjusted to assess the effect of potential confounders on any weaning effect, we did not report on factors other than prior treatment that might be associated with recurrence. The present manuscript specifically addresses whether patient demographic and ocular factors such as initial amblyopic eye acuity, amblyopic eye acuity at the time of cessation of patching, tropia and stereoacuity at cessation of patching were associated with risk of recurrence.

Patients and Methods

The protocol has been described previously and is summarized below.[1] Eligibility criteria for the study included age less than 8 years at time of enrollment, history of treated amblyopia due to strabismus, anisometropia or both, continuous treatment of amblyopia for atleast the previous 3 months (within one week of enrollment) of at least 2 hours/day of patching (14 hours per week), acuity prior to treatment in the amblyopic eye of 20/40 or worse with at least 3 logMAR levels of inter-ocular acuity difference, and an improvement of amblyopia during the preceding period of continuous treatment of at least 3 logMAR levels. A cycloplegic refraction was required during the preceding 6 months. Visual acuity was measured using the Amblyopia Treatment Study (ATS) HOTV visual acuity testing protocol with the Electronic Visual Acuity tester.[2,3] The protocol and informed consent forms were approved by institutional review boards, and the parent or guardian of each study patient gave written informed consent.

Amblyopia treatment prior to enrollment (cessation of treatment) was not standardized. Some patients were enrolled directly after completing a previous Pediatric Eye Disease Investigator Group (PEDIG) amblyopia treatment study (N=21),[2–4] whereas others had been treated as part of usual practice (N=14), or had been PEDIG study patients but with an intervening period of non-standardized treatment (N=34) . Protocol-specified follow-up visits were conducted at 5±1 weeks, 13±2 weeks, 26±2 weeks, and 52±2 weeks.

Between May 2001 and November 2002, a total of 156 patients were enrolled at 30 sites. As weaning had already been found to be an important predictor of recurrence, we only included for the present analyses those patients (N=69) who could be completely categorized into one of 3 predefined treatment/weaning groups based on patching history. As described previously[1], three treatment/weaning groups were defined by both intensity of maximum treatment and intensity of treatment at the time of cessation; 1) maximum of 2 hours daily patching and 2 hours stopped at enrollment (21 patients); 2) maximum of 6–8 hours of daily patching and 2 hours stopped at enrollment (22 patients); and 3) maximum of 6–8 hours of daily patching and 6–8 hours stopped at enrollment (26 patients). These three groups could be considered to be 1) low intensity non-weaned, 2) moderate intensity weaned, and 3) moderate intensity non-weaned.

Recurrence of amblyopia was defined[1] as two consecutive visual acuity measurements in the amblyopic eye that were 2 or more logMAR levels worse than the enrollment acuity, in the absence of a reduction of acuity in the sound eye of 2 or more logMAR levels. The two measurements could be performed on the same or different days, but were required to occur within one month of each other. Recurrence was also considered to have occurred if treatment

was restarted due to a non-replicated 2 or more logMAR level reduction of visual acuity i.e. even if it was not confirmed by a second examination, in violation of the study protocol. For some patients the reduction in visual acuity might be better termed "regression," than "recurrence" as the amblyopic eye visual acuity might not have been within one logMAR line of the sound eye visual acuity at the time of cessation of treatment, but for simplicity the term "recurrence" is used throughout this manuscript.

Statistical Methods

For the current study, we evaluated the following factors for their association with recurrence; gender, race, age, duration of the immediately preceding period of treatment, visual acuity at diagnosis of amblyopia, interocular acuity difference at diagnosis of amblyopia, visual acuity at cessation of treatment, interocular acuity difference at cessation of treatment, improvement in amblyopic eye visual acuity during previous treatment (difference between amblyopic eye visual acuity at diagnosis and cessation of patching), previous recurrence, presence or absence of tropia, and presence or absence of any stereoacuity or fine stereoacuity (defined as 40 or 60 degrees of arc on the Preschool Randot Stereoacuity test). Our primary measure of effect was risk ratio, i.e. the risk of recurrence in one group (e.g. males) divided by the risk of recurrence in a second group (e.g. females).

For the primary analysis, risk ratios for recurrence and 95% confidence intervals were computed using Poisson regression with robust variance estimation[5] in an individual model for each factor that adjusted only for the treatment intensity/weaning group. As many of the factors were correlated to some degree, a composite model that included all factors that had relative risk greater than 2.0 or smaller than 0.5 was run to determine what factors were independently associated with risk of recurrence. Factors not meeting a statistical significance criterion of $p<0.05$ were eliminated from the composite model using backwards stepwise regression. The risk of recurrence for two of the treatment/weaning groups was similar at 14% (low-intensity nonweaned and moderate-intensity weaned), [1] so these groups were combined when adjusting for treatment/weaning group.

As several of the potential risk factors probably were influential in choice of treatment intensity and weaning, adjustment for treatment/weaning group had the potential to attenuate their estimated association with recurrence. Hence, a secondary analysis was performed to obtain a risk ratio that was unadjusted for treatment/weaning or any other factors, and both are reported in the results table.

For all analyses, a $p<0.05$ and a confidence interval that excluded 1 were considered evidence of an association with recurrence. With the number of covariates considered, it is likely that about one observed association occurred by chance. All analyses were conducted using SAS version 9.1. (SAS Institute Inc. Cary, NC).

Results

Recurrence of Amblyopia

In the cohort for the current analysis, the overall risk of recurrence was 25%, which is similar to the 24% previously reported for the full cohort[1]. Risk ratios obtained from the analyses that were unadjusted for treatment intensity and weaning were similar to those obtained from the analyses that adjusted for this factor.

Factors that were not associated with recurrence

There was no statistically significant increased risk of recurrence with being female versus male, being white versus non-white, or age at diagnosis (Table 1). There was no evidence of

association between recurrence and increased age at cessation of treatment or longer duration of treatment (Table 1). There were too few 7 to <8 year olds to interpret the finding that none of these 6 children had a recurrence.

The influence of depth of amblyopia at time of diagnosis was investigated by considering visual acuity as a continuous variable and also by categorizing severity as moderate (20/40 to 20/80) and severe (20/100 to 20/200). Although there was a suggestion that more severe amblyopia at the time of diagnosis was associated with a subsequently greater risk of recurrence, this was not statistically significant. These results were also similar to an analysis of interocular difference at the time of diagnosis (Table 2).

Unexpectedly, the risk of recurrence was very similar between those patients who were orthotropic, microtropic (1–8 pd deviation) and heterotropic (>8 pd deviation) (Table 3), and the risk of recurrence was very similar between those patients who had excellent stereopsis, moderate stereopsis, coarse stereopsis or no measurable stereopsis. Excellent stereopsis (40–60 sec arc) at the time of cessation of treatment did not appear to protect against subsequent recurrence (Table 3). Two of 6 patients with excellent stereopsis had recurrence of amblyopia.

Factors associated with recurrence

Visual acuity at the time of cessation of treatment—The risk of recurrence was higher with better amblyopic eye visual acuity at the time of cessation of patching (Table 2). An analogous effect of interocular difference was seen; the more severe the residual amblyopia the lower the risk of recurrence.

Improvement in visual acuity during previous treatment—The risk of recurrence was higher with greater improvement of amblyopic eye visual acuity during previous treatment (Table 2). This effect was related to the association of higher risk of recurrence with better visual acuity at the time of cessation of treatment described above.

Previous recurrence—Any previous recurrence of amblyopia was associated with subsequent recurrence (Table 3).

Composite Model

The following covariates with RR≤0.5 or ≥2.0 were included in the full composite model (composite model 1, Tables); age at enrollment (included as a continuous covariate), duration of preceding period of treatment (3 to <6, 6 to <9, and ≥9 months), interocular acuity difference at cessation of patching (continuous covariate), previous amblyopia recurrence (no versus yes), and lines improved from diagnosis to cessation of patching in the present study (continuous covariate). Although meeting the risk ratio criterion, amblyopic eye visual acuity at diagnosis and amblyopic eye visual acuity at cessation of patching were not included in the composite model as both were highly correlated with interocular acuity difference at cessation of patching and lines of improvement from diagnosis to cessation of patching, and the latter 2 factors were more strongly associated with recurrence. Treatment/intensity weaning category was included in the model regardless of statistical significance as a potential confounder.

In the full model, interocular acuity difference at cessation of patching and prior amblyopia recurrence were the only 2 covariates that met a statistical significance criterion of $p<0.05$. The risk ratio per additional line of interocular acuity difference was 0.51 (95% CI : 0.34, 0.77) and the risk ratio for prior recurrence (yes vs. no) was 2.6 (95% CI: 1.1, 6.5). Number of lines of improvement was marginally significant in this model (RR=1.3, 95% CI: 0.99, 1.6; $p=0.063$). 95% confidence limits on the risk ratio for the remaining factors, age and duration of preceding period of treatment, included 1 and p-values exceeded 0.2.

When covariates with statistical significance of p>0.05 or higher were eliminated from the model using backwards stepwise selection, the final reduced model (composite model 2, Table) contained prior amblyopia recurrence (RR=2.4 for no vs yes; 95% CI: 1.0, 5.8; p=0.042), interocular acuity difference at cessation of patching (RR=0.52 per additional line; 95% CI: 0.32, 0.82; p=0.005), and lines improved from diagnosis to cessation of patching (RR=1.3 per additional line; 95% CI: 1.1, 1.7; p=0.007). Treatment/weaning group was included in this model as a possible confounder, but did not meet criteria for statistical significance (p=0.17).

All of these covariates (prior recurrence, interocular acuity difference at cessation of patching, and lines of improvement) were related to treatment intensity/weaning to some degree. Seventy-five percent of children with prior recurrence were in the moderate treatment intensity/no weaning (i.e. high risk) group. Children whose interocular acuity difference was 1 line or less were more likely than children with larger interocular acuity difference to be in the moderate intensity/no weaning group. Children with large visual acuity improvement also were more likely to be in the moderate intensity/no weaning group. It is not possible to separate out whether risk of recurrence is due to the treatment/weaning group, or to the interocular acuity difference at cessation of patching, prior recurrence, and lines of improvement using our data.

Discussion

In this cohort of successfully treated children with anisometropic and strabismic amblyopia, we have previously reported[1] an amblyopia recurrence risk of 24%, a low risk of recurrence (14%) when treatment was low intensity (2 hours per day of patching), and a decreased risk of recurrence with weaning of treatment if the 6 to 8 hours of daily patching was chosen as the maximal regime. We now report the influence of other factors on the risk of recurrence. Our most striking findings were the association of recurrence with better visual acuity at the time of cessation of patching, with greater number of lines of amblyopic eye visual acuity improvement during previous treatment, with previous recurrence, and the lack of association with age, tropia status and excellent stereoacuity.

The lack of age effect in risk of recurrence in 3 to <8 year olds is noteworthy. It is commonly held that after a certain age, treatment for amblyopia can be discontinued with very little risk of recurrence, whereas at earlier ages the risk is higher.[6] Based on our data, the risk of recurrence between age 6 and 7 years (25%) is still clinically important. We had too few children age 7 to 8 years of age to draw definitive conclusions. This lack of age effect for recurrence of amblyopia was also reported by Levartovsky et al.[7] Ongoing susceptibility to recurrence of amblyopia appears to parallel our recent findings of very little influence of age on treatment effectiveness in children 12 years and under, and even into teenage years [2, 3, 8] Plasticity in the visual system appears to be a two-edged sword. Von Noorden and Campos comment in their textbook,[9] “amblyopia tends to recur until children have reached 8 to 10 years of age or even older because of the persistence of inhibitory effects from the fixating eye.” Further data on the recurrence risk of amblyopia in older children (7 to 17 year-olds) will be forthcoming from the follow-up phase of the recently completed PEDIG treatment trial in this age range. [8]

Other authors have reported an association of severity of amblyopia at the start of patching therapy with subsequent recurrence,[10, 11] where more severe initial amblyopia was associated with a greater risk of recurrence. We could not confirm this finding in our analysis of initial amblyopic eye acuity adjusting for treatment/weaning group. The composite model showed an association of recurrence with greater improvement of amblyopic eye acuity during previous treatment, and worse initial amblyopia is associated with greater improvement. However, the treatment/weaning group was so strongly associated with amblyopic eye acuity at diagnosis that our data are inadequate to evaluate this potential association.

We did find a related paradoxical relationship between visual acuity at cessation of treatment and risk of recurrence. Better visual acuity at cessation of treatment was associated with increased risk of recurrence. It might be thought that worse visual acuity i.e. less completely treated amblyopia would be associated with persistent amblyogenic factors which in turn might be associated with recurrence of amblyopia. This was not found to be the case. Scott and Dickey[6] reported findings contrary to ours, i.e. a higher recurrence rate in patients whose post-treatment acuity was 20/25 to 20/40 compared with those who were 20/20. It is possible that our findings might be explained by greater central plasticity in some patients, leading to greater improvement with amblyopia treatment, but also increased risk for recurrence once that treatment is stopped. It is also possible that part of the explanation of our finding is a "regression to the mean." This would occur if patients with better visual acuity on cessation of patching were more likely to have their visual acuity overestimated, for example a patient with a single measurement of 20/20 might have been felt more ready to have treatment stopped than a patient with 20/50, and that single measurement of 20/20 might have been better than their true visual acuity. In contrast, the patient with 20/50 would have been more likely to have been brought back several times before treatment was stopped. This raises the challenge of deciding how a single test of visual acuity relates to the true visual acuity of an individual. Our study design would have been improved if we had used multiple tests of visual acuity prior to cessation of patching to define a more accurate baseline. Even if this were performed in a clinical study, the same challenge exists for the clinician; caution needs to be exercised when making clinical decisions on a single measurement of visual acuity. Further work is needed in defining "stable visual acuity" and a combination of repeated measurements over a particular period of time.

Our results on the influence of ocular alignment and stereopsis are surprising. It would seem intuitive that in cases where the amblyogenic (amblyopiogenic) factors of strabismus and anisometropia are not present, as evidenced by no deviation, excellent stereopsis, and wearing spectacle correction based on a recent cycloplegic refraction, then recurrence of amblyopia should not occur. Levartovsky et al[11] reported an increased risk of recurrence with persistent strabismus combined with anisometropia, Sjostrand et al [12] reported an increased risk with persistent microstrabismus, and Kushner[13] described an increased risk of recurrence with a residual tropia of greater than 15 prism diopters. Our contrary finding, that excellent stereoacuity does not preclude recurrence of amblyopia, concurs with the report of Rutstein and Fuhr,[14] and might be explained in one of several ways. A single measurement of alignment or stereopsis might not represent the usual ocular status of the individual; there might be subtle strabismus that was not detected on a single examination, and suppression from such strabismus might cause recurrence. Alternatively, even if the eyes are straight and a single measurement of randot stereopsis demonstrates excellent stereoacuity, there may be residual central suppression mechanisms which continue beyond apparent successful treatment of the optotype visual acuity component of amblyopia. It is also possible that very small magnitude strabismus may go undetected by commonly used clinical tests. In addition, small angles of strabismus have been associated with excellent random dot stereopsis.[15] High anisometropia alone has been reported as a risk factor for recurrence of amblyopia, [13, 16] which would not be expected if the anisometropia were fully corrected and there was no manifest strabismus. Following the foregoing discussion, we speculate that some anisometropic patients may have a microstrabismus that may have eluded routine clinical detection, or there are persistent central suppression mechanisms. Further work is needed in this area.

Our study is not without limitations. Our sample size may not have been sufficient to detect small but real effects among the factors that we found were not associated with recurrence. Analyses of several factors were suggestive of an association, but the sample size was too small for definitive conclusions. Our study design allowed investigator discretion in prior treatment/weaning, and therefore, due to the association of some of our risk factors with that treatment/weaning choice, we are limited in our ability to independently assess the contributions of

associated factors, for example treatment/weaning and improvement of amblyopia eye visual acuity. It appears that some of our previously reported effect of weaning[1] was due to a parallel association with improved amblyopic eye visual acuity, but the odds ratio for recurrence in the moderate intensity non-weaned group remained numerically higher than the other groups (OR 2.5 95% CI 0.52, 12), even when adjusted for lines improved. In addition, there may have been other unconsidered factors that may have confounded our analyses.

In conclusion, recurrence of amblyopia after cessation of patching was associated with better visual acuity at the time of cessation, improvement of amblyopic eye visual acuity during treatment and previous recurrence. We did not find a protective effect of orthotropia or excellent stereopsis. Long term monitoring of visual acuity following cessation of treatment is needed in all children who complete a course of treatment for amblyopia to detect and treat potential recurrence.

Acknowledgements

Supported by the National Institutes of Health, Bethesda, MD, grants EY011751, (cooperative agreement from the National Eye Institute) and EY015799 (JMH)

References

1. Pediatric Eye Disease Investigator Group. Risk of amblyopia recurrence after cessation of treatment. J AAPOS 2004;8:420–428. [PubMed: 15492733]
2. Pediatric Eye Disease Investigator Group. A randomized trial of atropine vs. patching for treatment of moderate amblyopia in children. Arch Ophthalmol 2002;120:268–278. [PubMed: 11879129]
3. Pediatric Eye Disease Investigator Group. A randomized trial of patching regimens for treatment of moderate amblyopia in children. Arch Ophthalmol 2003;121:603–611. [PubMed: 12742836]
4. Pediatric Eye Disease Investigator Group. A randomized trial of prescribed patching regimens for treatment of severe amblyopia in children. Ophthalmology 2003;110:2075–2087. [PubMed: 14597512]
5. Zou G. A modified Poisson regression approach to prospective studies with binary data. Am J Epidemiol 2004;59:702–706. [PubMed: 15033648]
6. Scott WE, Dickey CF. Stability of visual acuity in amblyopic patients after visual maturity. Graefes Arch Clin Exp Ophthalmol 1988;226:154–157. [PubMed: 3360344]
7. Levartovsky S, Gottesman N, Shimshoni M, Oliver M. Factors affecting long-term results of successfully treated amblyopia: age at beginning of treatment and age at cessation of monitoring. J Pediatr Ophthalmol Strabismus 1992;29:219–223. [PubMed: 1512662]
8. Pediatric Eye Disease Investigator Group. Randomized trial of treatment of amblyopia in children aged 7 to 17 years. Arch Ophthalmol 2005:437–447. [PubMed: 15824215]
9. von Noorden, GK.; Campos, EC. Binocular Vision and Ocular Motility: Theory and Management of Strabismus. 6th ed.. St. Louis, MO: Mosby; 2002. p. 548
10. Ching FC, Park MM, Friendly DS. Practical management of amblyopia. J Pediatr Ophthalmol Strabismus 1986;23:12–16. [PubMed: 3950836]
11. Levartosky S, Oliver M, Gottesman N, Shimshoni M. Factors affecting long term results of successfully treated amblyopia: initial visual acuity and type of amblyopia. Br J Ophthalmol 1995;79:225–228. [PubMed: 7703198]
12. Sjostrand JB. Strabismus might be a risk factor for amblyopia recurrence. J AAPOS (forthcoming).
13. Kushner BJ. Functional amblyopia: a purely practical pediatric patching protocol. Ophthalmol Annu 1988;4:173–198.
14. Rutstein RP, Fuhr PS. Efficacy and stability of amblyopia therapy. Optom Vis Sci 1992;69:747–754. [PubMed: 1436994]
15. Leske DA, Holmes JM. Maximum angle of horizontal strabismus consistent with true stereopsis. J AAPOS 2004;8:28–34. [PubMed: 14970796]

16. Levartovsky S, Oliver M, Gottesman N, Shimshoni M. Long-term effect of hypermetropic anisometropia on the visual acuity of treated amblyopic eyes. Br J Ophthalmol 1998;82:55–58. [PubMed: 9536882]

Table 1

Risk ratios for each of potential predictive factors- demographic

Factor Gender	Total N	N (%) with recurrence	Unadjusted risk ratio (95% confidence interval)	Risk ratio adjusted for treatment intensity/ weaning (95% confidence interval)	Composite model 1 (Full model)*	Composite model 2 (Reduced model)**
Female	31	6 (19%)	Reference	Reference	--	--
Male	38	11 (29%)	1.5 (0.62, 3.6)	1.4 (0.62, 3.3)		
Race						
White	60	15 (25%)	Reference	Reference	--	--
Other	9	2 (22%)	0.89 (0.24, 3.3)	0.81 (0.22, 3.1)		
Age at diagnosis						
<3	5	1 (20%)	0.95 (0.72, 1.2)	0.94 (0.71, 1.2)	--	--
3 to <4	9	1 (11%)	per year	per year		
4 to <5	21	6 (29%)				
5 to <6	18	6 (33%)				
6 to <7	9	0 (0%)				
7 to <8	2	0 (0%)				
Unknown	5	3 (60%)				
Age at cessation of patching						
3 to <4	4	0 (0%)	0.84 (0.59, 1.2)	0.83 (0.59, 1.2)	0.90 (0.64, 1.3)	--
4 to <5	17	6 (35%)	per year	per year	per year	
5 to <6	22	6 (27%)				
6 to <7	20	5 (25%)				
7 to <8	6	0 (0%)				
Duration of preceding period of patching						
3 to <6 months	42	12 (29%)	Reference	Reference	Reference	--
6 to <9 months	16	1 (6%)	0.22 (0.03, 1.5)	0.18 (0.03, 1.2) 0.28 (0.04, 1.8)		
≥9 months	11	4 (36%)	1.3 (0.51, 3.2)	1.4 (0.62, 3.3)	0.80 (0.28, 2.2)	

*Includes factors with relative risk greater than 2.0 or less than 0.5 (age at cessation of patching, duration of preceding period of treatment, previous amblyopia recurrence, IOD at cessation of patching, and lines improved from diagnosis to enrollment). Amblyopic eye visual acuity at diagnosis and enrollment were not included as they are correlated with IOD at cessation of patching and lines of improvement and the latter are more strongly associated with recurrence. "—" "indicates that the factor did not meet the criteria for inclusion in the model.

**This model eliminates factors that are not statistically significant from the full model, and therefore includes only IOD at cessation of patching, lines of improvement and previous recurrence of amblyopia.

Table 2

Risk ratios for each of potential predictive factors- visual acuity

Factor	Total N	N (%) with recurrence	Unadjusted risk ratio (95% confidence interval)	Risk ratio adjusted for treatment intensity/ weaning (95% confidence interval)	Composite model 1 (Full model)	Composite model 2 (Reduced model)
Amblyopic eye visual acuity at diagnosis						
20/40 to 20/80	55	10 (18%)	1.3 (0.96, 1.6)	1.1 (0.87, 1.4)	--	--
20/100 to 20/200	14	7 (50%)	per line	per line		
Interocular acuity difference at diagnosis						
3	14	3 (21%)	1.2 (0.89, 1.6)	1.1 (0.82, 1.4)	--	--
4	25	4 (16%)	per line	per line		
5	16	5 (31%)				
6	9	4 (44%)				
7	3	0 (0%)				
8	2	1 (50%)				
Amblyopic eye visual acuity at cessation of patching						
20/16	2	1 (50%)	0.66 (0.46, 0.94)	0.68 (0.51, 0.90)	--	--
20/20	14	4 (29%)	per line	per line		
20/25	27	9 (33%)				
20/32	20	3 (15%)				
20/40	5	0 (0%)				
20/50	1	0 (0%)				
Interocular acuity difference at cessationof patching						
−1	4	2 (50%)	0.53 (0.34, 0.82)	0.57 (0.35, 0.91)	0.51 (0.34, 0.77)	0.52 (0.32, 0.82)
0	28	10 (36%)	per line	per line	per line	per line
1	21	4 (19%)				
2	13	1 (8%)				
3	3	0 (0%)				
Lines of improvement in visual acuity from diagnosis to cessation of patching						
2	1	0 (0%)	1.7 (1.3, 2.2)	1.5 (1.1, 2.0)	1.3 (0.99, 1.6)	1.3 (1.1, 1.7)
3	23	3 (13%)	per line	per line	per line	per line
4	22	2 (9%)				
5	12	6 (50%)				
6	7	3 (43%)				
7	4	3 (75%)				

Table 3

Risk ratios for each of potential predictive factors- previous recurrence, alignment, stereoacuity

Factor	Total N	N (%) with recurrence	Unadjusted risk ratio (95% confidence interval)	Risk ratio adjusted for treatment intensity/ weaning (95% confidence interval)	Composite model 1	Composite model 2
Previous amblyopia recurrence (at any time)						
No	61	12 (20%)	Reference	Reference	Reference	Reference
Yes	4	3 (75%)	3.8 (1.8, 8.2)	2.7 (1.5, 4.9)	2.6 (1.1, 6.5)	2.4 (1.0, 5.8)
Unknown	4	2 (50%)				
Ocular alignment at cessation of patching						
Ortho at distance and near	34	8 (24%)	Reference	Reference	--	--
Microtropia (1–8D) at distance or near	20	5 (25%)	1.1 (0.40, 2.8)	0.95 (0.38, 2.4)		
Heterotropia (>8D) at either distance or near	15	4 (27%)	1.1 (0.40, 3.2)	1.2 (0.45, 3.0)		
Randot preschool stereoacuity at cessation of patching						
40–60	6	2 (33%)	1.2 (0.35, 4.5)	1.0 (0.32, 3.2)	--	--
100–200	10	1 (10%)	0.38 (0.05, 2.6)	0.54 (0.09, 3.4)		
400–800	14	3 (21%)	0.80 (0.25, 2.6)	1.0 (0.32, 3.3)		
Nil	30	8 (27%)	Reference	Reference		
Failed pretest	7	3 (43%)				
Not done	2	0 (0%)				
40–60	6	2 (33%)	1.5 (0.44, 5.2)	1.1 (0.36, 3.2)	--	--
100–Nil	54	12 (22%)	Reference	Reference		