



# Eight-Year Outcomes of Bilateral Lateral Rectus Recessions versus Unilateral Recession-Resection in Childhood Basic-Type Intermittent Exotropia

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**Purpose:** To report 8-year outcomes from a randomized controlled trial (RCT) comparing bilateral lateral rectus muscle recession (BLRc) with unilateral recession-resection (R&R) for childhood intermittent exotropia (IXT).

**Design:** Eight-year follow-up of RCT cohort.

**Participants:** Of 197 randomized participants, 123 agreed to continue follow-up after the 3-year outcome visit (baseline age, 3–< 11 years; basic-type IXT, 15–40 prism diopters [ $\Delta$ ] by prism and alternate cover test [PACT]; baseline stereoacuity,  $\leq$  400 arcsec; no prior surgery).

**Methods:** After the RCT primary outcome at 3 years, annual follow-up from 4 through 8 years with treatment at investigator discretion.

**Main Outcome Measures:** Suboptimal surgical outcome by 8 years after randomization, defined as any of the following at any visit: exotropia of 10  $\Delta$  or more by simultaneous prism cover test (SPCT) at distance or near, constant esotropia (ET) of 6  $\Delta$  or more by SPCT at distance or near, loss of near stereoacuity by 0.6 log arcsec or more from baseline, or reoperation. Secondary outcomes included (1) reoperation by 8 years and (2) complete or near-complete resolution at 8 years, defined as exodeviation of less than 10  $\Delta$  by SPCT and PACT at distance and near and 10  $\Delta$  or more reduction from baseline by PACT at distance and near, ET of less than 6  $\Delta$  at distance and near, no decrease in stereoacuity by 0.6 log arcsec or more from baseline, and no reoperation or nonsurgical treatment for IXT.

**Results:** The Kaplan-Meier cumulative probability of suboptimal surgical outcome through 8 years was 68% (55 events among 101 at risk) for BLRc and 53% (42 events among 96 at risk) for R&R (difference, 15%; 95% confidence interval [CI], –2% to 32%;  $P = 0.08$ ). Complete or near-complete resolution at 8 years occurred in 15% (7/46) for BLRc and 37% (16/43) for R&R (difference, –22%; 95% CI, –44% to –0.1%;  $P = 0.049$ ). The cumulative probability of reoperation was 30% for BLRc and 11% for R&R (difference, 19%; 95% CI, 2%–36%;  $P = 0.049$ ).

**Conclusions:** Despite no significant difference for the primary outcome, the 95% CI did not exclude a moderate benefit of R&R, which together with secondary outcomes suggests that unilateral R&R followed by usual care may yield better long-term outcomes than BLRc followed by usual care for basic-type childhood IXT using these surgical doses.

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Intermittent exotropia (IXT) is a common form of childhood-onset strabismus<sup>1</sup> for which surgical correction often is performed.<sup>2–4</sup> One unresolved question is whether postoperative outcomes differ with bilateral lateral rectus recession (BLRc) versus unilateral lateral rectus muscle recession with medial rectus muscle resection, or recession-

resection (R&R). We previously reported the results of a randomized controlled trial (RCT)<sup>5</sup> comparing BLRc and R&R procedures for basic-type IXT in children 3 to younger than 11 years of age, in which we found no statistically significant difference in suboptimal outcome by 3 years after surgery (46% in BLRc and 37% in R&R;

difference, 9%; 95% confidence interval [CI], -6% to 23%).<sup>5</sup> We are aware of 3 other RCTs that have addressed this question. Both Kushner<sup>6</sup> and Somer et al<sup>7</sup> reported higher success rates at 1 year after surgery with R&R versus BLRc, whereas Zhang et al<sup>8</sup> reported that both groups showed similar success rates over the same period. Given the propensity of IXT to recur over time,<sup>9,10</sup> longer-term effectiveness of surgical approaches also should be evaluated. The purpose of the present study was to evaluate long-term outcomes 8 years after surgery in the Pediatric Eye Disease Investigator Group RCT for which 3-year outcomes previously were reported.<sup>5</sup>

## Methods

The study was funded by the National Eye Institute of the National Institutes of Health and was conducted according to the tenets of the Declaration of Helsinki by the Pediatric Eye Disease Investigator Group at 35 academic and community-based clinical sites (Jaeb Center for Health Research institutional review board). The protocol and Health Insurance Portability and Accountability Act-compliant informed consent forms were approved by institutional review boards for each site, and a parent or guardian of each study participant provided written informed consent. The study is listed on [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (identifier, NCT01032603)<sup>11</sup>; the full protocol is available at [www.pedig.net](http://www.pedig.net) (accessed February 6, 2023).

### Original 3-Year Randomized Controlled Trial

We enrolled 197 children 3 to younger than 11 years of age, with basic-type IXT by 15 to 40  $\Delta$  (largest deviation at near, distance, or remote distance) by prism and alternate cover test (PACT), and near stereoacuity of at least 400 arc-seconds using the Randot Preschool Stereoacuity test (Stereo Optical Co., Inc.). Participants were assigned randomly to 1 of 2 surgical procedures: BLRc or R&R. Follow-up visits occurred every 6 months after surgery for 3 years. Reoperation was permitted only after suboptimal surgical outcome criteria were met and confirmed by a retest. Additional details of the protocol and results have been published previously.<sup>5,12</sup>

### Four- to 8-Year Follow-up after Randomized Trial (Extension Study)

The extension study (4- to 8-year follow-up) was implemented in February 2015. The parent or guardian for each randomized participant was asked to consent again to extended follow-up, regardless of whether they were still active, had completed, or had withdrawn from the 3-year RCT. Participants whose parent or guardian consented to the extension study underwent follow-up visits at 4, 5, 6, 7, and 8 years ( $\pm 2$  months) from randomization. At each follow-up visit, an examiner masked to the participant's treatment group measured near stereoacuity using the Randot Preschool Stereoacuity test, exotropia control using the IXT Office Control Scale<sup>13,14</sup> (Table S1, available at [www.aojournal.org](http://www.aojournal.org); mean of 3 measurements [beginning, middle, and end of the masked examination]) at distance and near, cover-uncover test, simultaneous prism and cover test (SPCT), and PACT at distance and near. At the 8-year visit, the Intermittent Exotropia Questionnaire (IXTQ) was administered to the child and parent to measure IXT-related quality of life and the Diplopia Questionnaire<sup>15</sup> was administered to the child to assess the presence and frequency of diplopia in specific gaze positions.

## Statistical Methods

In parallel with the previously reported 3-year outcomes, the primary outcome for the current analysis was suboptimal surgical outcome by 8 years, defined as any of the following at any follow-up examination from 6 months to 8 years: (1) exotropia of 10  $\Delta$  or more measured by SPCT at distance or near, (2) constant esotropia of 6  $\Delta$  or more measured by SPCT, (3) loss of stereoacuity of 0.6 log arcsec or more compared with baseline, or (4) reoperation without meeting any other criteria. Suboptimal surgical outcome had to be confirmed by a retest during the 3-year RCT; however, retesting was not performed during the 4- to 8-year follow-up to streamline visits and to reduce participant testing burden.

For the primary analysis, the cumulative proportion of participants meeting criteria for suboptimal surgical outcome by 8 years was obtained using the Kaplan-Meier method and was compared between treatment groups using the  $z$  test. Assessment of suboptimal surgical outcome by 8 years included all participants originally enrolled in the RCT regardless of their participation in the extension study. Data for participants who did not meet suboptimal surgical outcome criteria were censored at the time of the last completed study visit.

Several secondary outcomes were analyzed. The cumulative proportion of reoperation by 8 years was compared between treatment groups using the same statistical methods used for the primary analysis. Additional secondary analyses were treatment group comparisons of outcomes at the 8-year visit (from participants who completed the 8-year visit within the analysis window of 7.5 to < 9 years from randomization). At 8 years, the proportions of participants with (1) suboptimal surgical outcome, (2) complete or near-complete resolution criteria, (3) spontaneous exotropia during the examination or average control score of 3 or more at distance or near, and (4) a decrease in Randot Preschool stereoacuity of 0.6 log arcsec or more from enrollment were compared between treatment groups using Barnard's unconditional exact test. Suboptimal surgical outcome at 8 years was defined as meeting any of the 3 suboptimal surgical outcome criteria at the 8-year follow-up visit (regardless of whether any criterion had been met at an earlier visit) or undergoing reoperation at any time before completing the 8-year visit. Complete or near-complete resolution at 8 years was defined as meeting all of the following at the 8-year visit: (1) exodeviation of less than 10  $\Delta$  (tropia or phoria) by both SPCT and PACT at distance and near and 10  $\Delta$  or more reduction in PACT magnitude from both the distance and near angles at enrollment if the exodeviation was 10  $\Delta$  or more at baseline (and reduction to 0 if the exodeviation was < 10  $\Delta$  at baseline), (2) esotropia of less than 6  $\Delta$  at distance and near by SPCT, (3) no decrease in Randot Preschool stereoacuity of 0.6 log arcsec or more from the enrollment stereoacuity or to nil, (4) no reoperation or treatment with botulinum toxin, and (5) no nonsurgical treatment for a recurrent or residual exodeviation. In addition, distance and near control, distance and near PACT, and Randot Preschool stereoacuity at the 8-year visit were compared between treatment groups using analysis of covariance, adjusting for the corresponding measurement at enrollment. In the analysis of covariance models, for the participants who underwent reoperation during the 8-year follow-up, their data at the last visit before reoperation were used for analyses. The type I error rate for all secondary outcomes was controlled using the adaptive false discovery rate<sup>16,17</sup> approach to account for multiplicity, with the false discovery rate controlled at the 5% probability level.

As exploratory analyses, we compared the mean Rasch-based health-related quality-of-life scores for the child IXTQ, each of the 3 parent IXTQ subscales, and the Diplopia Questionnaire scores<sup>15</sup> at 8 years between treatment groups using the Wilcoxon

rank-sum test and Hodges-Lehmann estimator without adjustment for multiplicity.

All treatment-group differences were calculated as the BLRc group minus the R&R group. Analyses were conducted using SAS software version 9.4 (SAS Institute, Inc.).

## Results

### Baseline Characteristics

In the original 3-year RCT, 197 children were enrolled at 34 clinical sites, with 101 assigned to the BLRc group and 96 assigned to the R&R group (Fig 1). One hundred twenty-three children (62%) elected to participate in the present extension study (64 from the BLRc group and 59 from the R&R group). In the BLRc and R&R groups, 46 participants (46% of 101 participants randomized; 72% of 64 participants enrolled in the extension) and 43 participants (45% of 96 participants randomized; 73% of 59 participants enrolled in the extension), respectively, completed the 8-year visit. No meaningful differences in demographic and clinical characteristics at baseline seemed to exist between those who completed the 8-year visit and those who did not (either did not participate in the extension or were dropped during the extension; Supplemental Table 1).

### Primary Outcome: Suboptimal Surgical Outcome by 8 Years

The Kaplan-Meier cumulative probability of suboptimal surgical outcome at any time point through 8 years was 68% (55 events among 101 participants at risk) in the BLRc group and 53% (42 events among 96 participants at risk) in the R&R group; the difference between BLRc and R&R was 15% (95% CI, -2% to 32%;  $P = 0.08$ ; Table 2; Fig 2). The most common reason for suboptimal surgical outcome was a residual or recurrent exotropia (34 of 55 participants [62%] in the BLRc group and 27 of 42 participants [64%] in the R&R group; Table 2).

### Secondary Outcomes

**Reoperation by 8 Years.** The cumulative probability of reoperation by 8 years was 30% (20 events among 101 participants at risk) with BLRc and 11% (7 events among 96 participants at risk) with R&R; the difference between BLRc and R&R was 19% (95% CI, 2%–36%;  $P = 0.049$ ; Fig 3). Among participants who met suboptimal surgical outcome criteria, reoperation was performed for 30% (16 of 51 participants) in the BLRc group and 14% (6 of 41 participants) in the R&R group. In the BLRc group, 18 of 20 reoperations (90%) were for residual-recurrent exotropia, 1 of 20 reoperations (5%) was for consecutive esotropia, and 1 of 20 reoperations (5%) was for oblique muscle dysfunction; in the R&R group, 4 of 7 reoperations (57%) were for residual or recurrent exotropia and 3 of 7 reoperations (43%) were for consecutive esotropia.

**Surgical Outcomes at the 8-Year Visit.** Suboptimal surgical outcome at the 8-year visit was more likely with BLRc (48% [22 of 46]) than R&R (23% [10 of 43]; difference, 25%; 95% CI, 0.2%–50%;  $P = 0.049$ ). Complete or near-complete resolution at the 8-year visit was less likely with BLRc (15% [7 of 46]) than with R&R (37% [16 of 43]; difference, -22%; 95% CI, -44% to -0.1%;  $P = 0.049$ ). Among participants completing the 8-year visit, reoperation was performed before 8 years in 14 of 46 participants (30%) in the BLRc group and 5 of 43 participants (12%) in the R&R group. Most participants who underwent reoperation before the 8-year visit (13 of 14 participants in the BLRc group and 4 of 5 participants in the R&R group) also did not meet at least 1

additional criterion for complete or near-complete resolution at 8 years.

**Change in Exotropia Control, Prism and Alternate Cover Test Magnitude, and Stereoacuity at 8 Years.** The mean  $\pm$  standard deviation distance exotropia control score at 8 years was  $1.6 \pm 1.8$  in the BLRc group and  $0.8 \pm 1.1$  in the R&R group (adjusted difference, 0.8; 95% CI, 0.0–1.5;  $P = 0.049$ ). No statistically significant differences were found in means between the BLRc and R&R groups for near exotropia control, distance or near PACT magnitude, and near stereoacuity at the 8-year visit (Table 3).

### Exploratory Outcomes: Intermittent Exotropia-Related Quality of Life and Diplopia at 8 Years

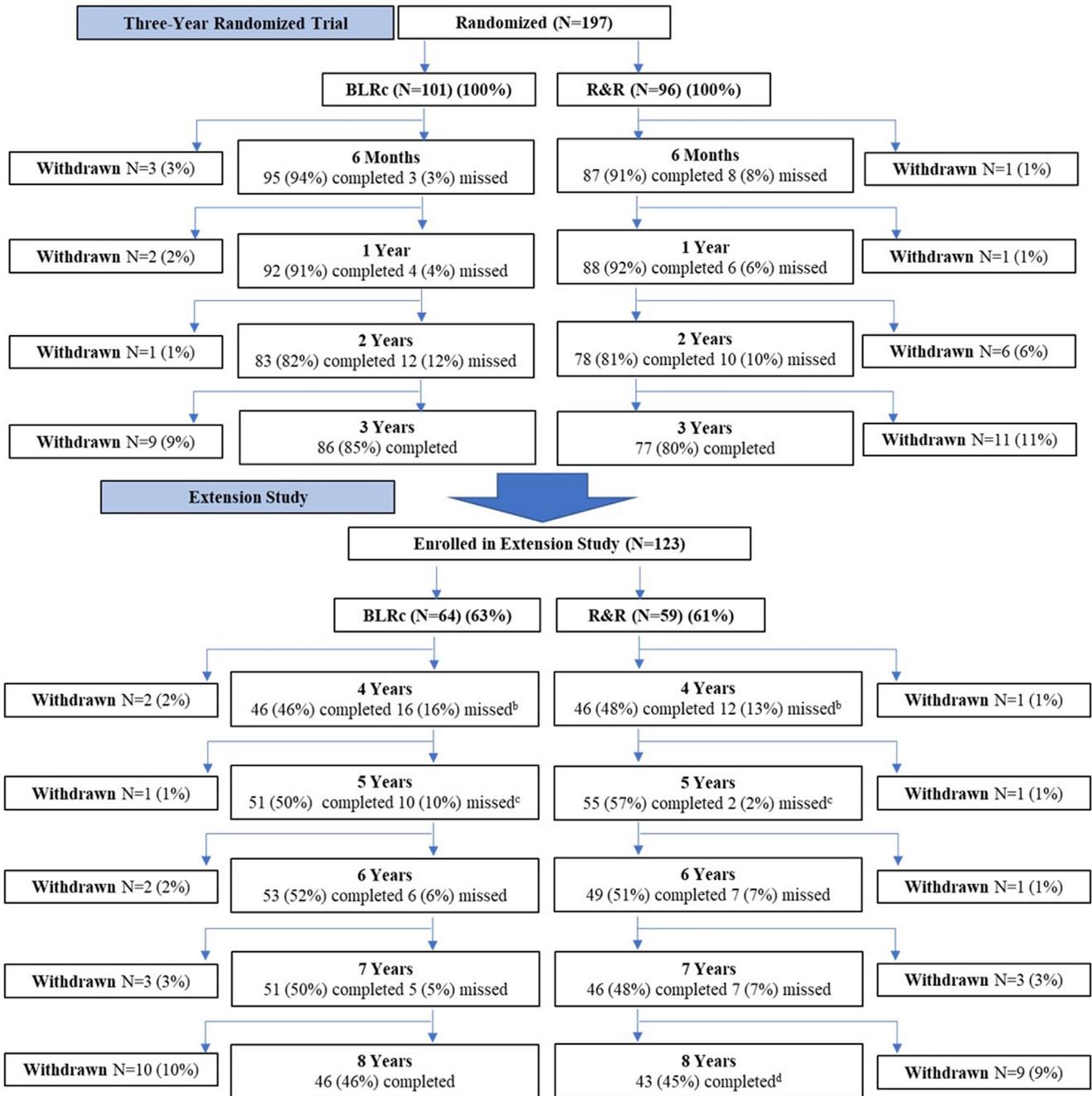
No substantial differences were found between the BLRc and R&R treatment groups in the distribution of the mean Rasch-based health-related quality-of-life scores for the child IXTQ and each of the 3 parent IXTQ domains (Table 4; Tables S5 and S6, available at [www.aaojournal.org](http://www.aaojournal.org)). On the Diplopia Questionnaire, diplopia in any direction in the past week was reported in 8 of 46 participants (17%) from the BLRc group and in 4 of 41 participants (10%) from the R&R group. For those 4 R&R participants who reported diplopia, 2 reported diplopia in side gaze, 1 reported diplopia in the direction of the nonoperated eye (in the field of action of the operated medial rectus muscle), and 1 reported diplopia in both the right and left gaze. Mean Diplopia Questionnaire scores at 8 years also did not differ substantially between treatment groups (Table 4; Table S7, available at [www.aaojournal.org](http://www.aaojournal.org)).

### Postoperative Nonsurgical Treatment

During 8 years of follow-up, postoperative nonsurgical treatment was prescribed in 26% of participants (26 of 101 participants) in the BLRc group and in 44% of participants (42 of 96 participants) in the R&R group (Table S8, available at [www.aaojournal.org](http://www.aaojournal.org)). Patching (alone or with other treatments) was prescribed for 4 participants (4%) and 26 participants (27%) in the BLRc and R&R groups, respectively. This difference primarily was the result of more patching for esotropia being prescribed in the R&R group early in the postoperative course, rather than patching for recurrent or residual exotropia. Orthoptic exercises (alone or with other treatments) were prescribed for 10 participants (10%) and 10 participants (10%) in the BLRc and R&R groups, respectively (Table S8).

## Discussion

This randomized controlled trial was designed to compare suboptimal surgical outcomes after BLRc versus R&R procedures followed by usual care for children with basic-type IXT. We now report that the cumulative incidence of suboptimal surgical outcome by 8 years was not significantly different between groups (68% in BLRc vs. 53% R&R; difference, 15%; 95% CI, -2% to 32%); however, the 95% CI of the estimated difference did not exclude a possible moderate benefit of R&R, but it did exclude a moderate benefit of BLRc. This result is consistent with our previous report<sup>5</sup> of this cohort after 3 years of follow-up, in which the cumulative incidence of suboptimal surgical outcome was not statistically different between the two groups (46% in BLRc vs. 37% in R&R; difference, 9%; 95% CI, -6% to 23%), and the 95% CI did not exclude a



**Figure 1.** Flowchart showing participants progress through the study. <sup>a</sup>All percentages were based on the number of participants initially enrolled in the 3-year randomized trial. <sup>b</sup>Eleven of the 16 participants in the BLRc group and 12 of the 12 participants in the R&R group were past the 4-year visit window when they were enrolled in the extension study. <sup>c</sup>Three of the 10 participants in the BLRc group and 1 of the 2 participants in the R&R group were past the 5-year visit window when they were enrolled in the extension study. <sup>d</sup>One participant in the R&R group completed the 8-year visit beyond 9 years from randomization and therefore was not included. BLRc = bilateral lateral rectus muscle recession; R&R = unilateral lateral rectus recession combined with medial rectus resection in the same eye.

possible moderate benefit of R&R, but did exclude a moderate benefit of BLRc. It is noteworthy that 4 of the secondary outcomes (reoperation by 8 years, complete or near-complete resolution, suboptimal surgical outcome at 8 years, and IXT distance control score at 8 years) also suggested a

statistically significant benefit of R&R over BLRc, consistent with the trend observed in the primary outcome.

We are unaware of any previous studies that compare long-term outcomes between BLRc and R&R procedures for childhood IXT. Nevertheless, our data, which suggest a

Table 2. Suboptimal Surgical Outcome at Follow-up Visits

| Variable                                                          | Randomized Trial Period (yrs) |     |       |     |       |     | Extension Study Period (yrs) |     |       |     |       |     | Total |     |       |     |      |     |
|-------------------------------------------------------------------|-------------------------------|-----|-------|-----|-------|-----|------------------------------|-----|-------|-----|-------|-----|-------|-----|-------|-----|------|-----|
|                                                                   | 0-1                           |     | > 1-2 |     | > 2-3 |     | > 3-4                        |     | > 4-5 |     | > 5-6 |     | > 6-7 |     | > 7-8 |     | BLRc | R&R |
|                                                                   | BLRc                          | R&R | BLRc  | R&R | BLRc  | R&R | BLRc                         | R&R | BLRc  | R&R | BLRc  | R&R | BLRc  | R&R | BLRc  | R&R |      |     |
| No. at risk                                                       | 101                           | 96  | 71    | 75  | 58    | 57  | 48                           | 50  | 31    | 39  | 25    | 37  | 22    | 29  | 21    | 25  | N/A  | N/A |
| No. with suboptimal surgical outcome                              | 26                            | 24  | 13    | 5   | 4     | 4   | 2                            | 1   | 6     | 6   | 1     | —   | 1     | 1   | 2     | 1   | 55   | 42  |
| Exotropia*                                                        | 17                            | 12  | 9     | 5   | 3     | 4   | 1                            | —   | 1     | 5   | —     | —   | 1     | 1   | 2     | —   | 34   | 27  |
| Constant esotropia <sup>†</sup>                                   | 1                             | 2   | —     | —   | —     | —   | —                            | —   | —     | —   | —     | —   | —     | —   | —     | —   | 1    | 2   |
| Stereo loss <sup>‡</sup>                                          | 4                             | 4   | 4     | —   | 1     | —   | —                            | 1   | 2     | 1   | 1     | —   | —     | —   | —     | 1   | 12   | 7   |
| Stereo loss and exotropia                                         | 1                             | —   | —     | —   | —     | —   | 1                            | —   | —     | —   | —     | —   | —     | —   | —     | —   | 2    | —   |
| Stereo loss and constant esotropia                                | 2                             | 5   | —     | —   | —     | —   | —                            | —   | —     | —   | —     | —   | —     | —   | —     | —   | 2    | 5   |
| Reoperated without meeting suboptimal surgical outcome            | 1                             | 1   | —     | —   | —     | —   | —                            | —   | 3     | —   | —     | —   | —     | —   | —     | —   | 4    | 1   |
| Cumulative probability of meeting suboptimal surgical outcome (%) | 27                            | 26  | 41    | 32  | 46    | 37  | 49                           | 39  | 60    | 49  | 62    | 49  | 64    | 51  | 68    | 53  | N/A  | N/A |

— = 0; BLRc = bilateral lateral rectus muscle recession; N/A = not applicable; R&R = recession-resection; SPCT = simultaneous prism cover test.

\*Exotropia of  $\geq 10 \Delta$  by SPCT at distance or near.

<sup>†</sup>Constant esotropia of  $\geq 6 \Delta$  by SPCT at distance or near.

<sup>‡</sup>Decrease in Preschool Randot near stereoacuity of  $\geq 0.6$  log arcsec from enrollment to or to nil.

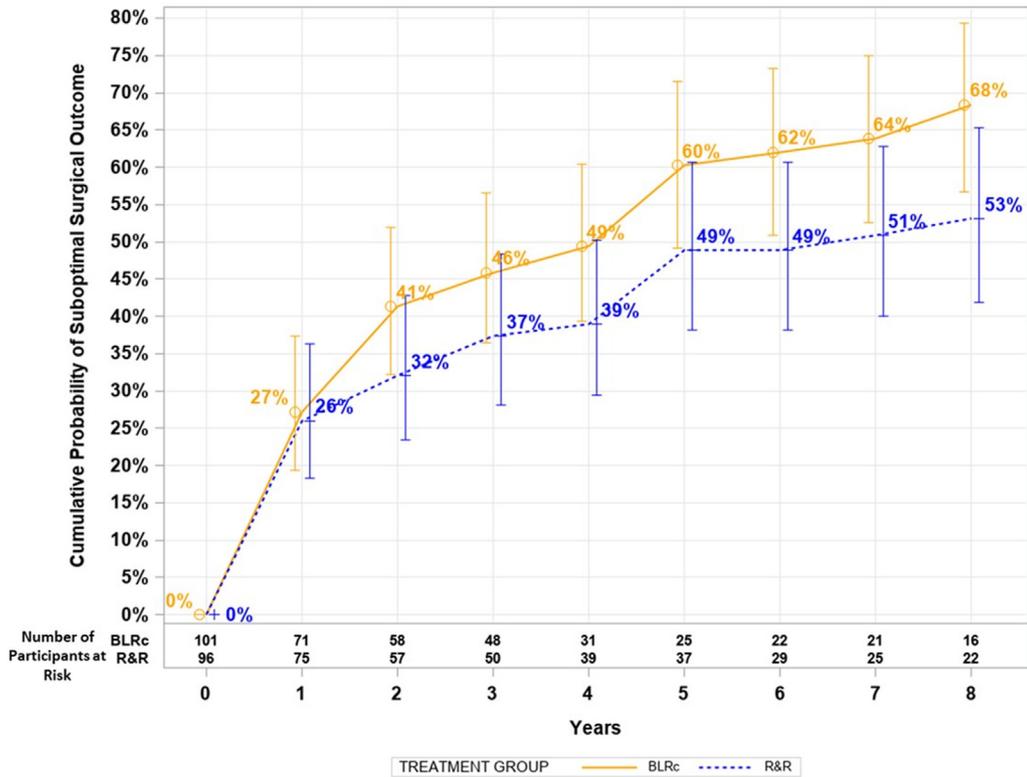


Figure 2. Kaplan-Meier analysis of suboptimal surgical outcome by 8 years showing cumulative probability (and 95% confidence interval). BLRc = bilateral lateral rectus muscle recession; R&R = unilateral lateral rectus muscle recession combined with medial rectus muscle resection in the same eye.

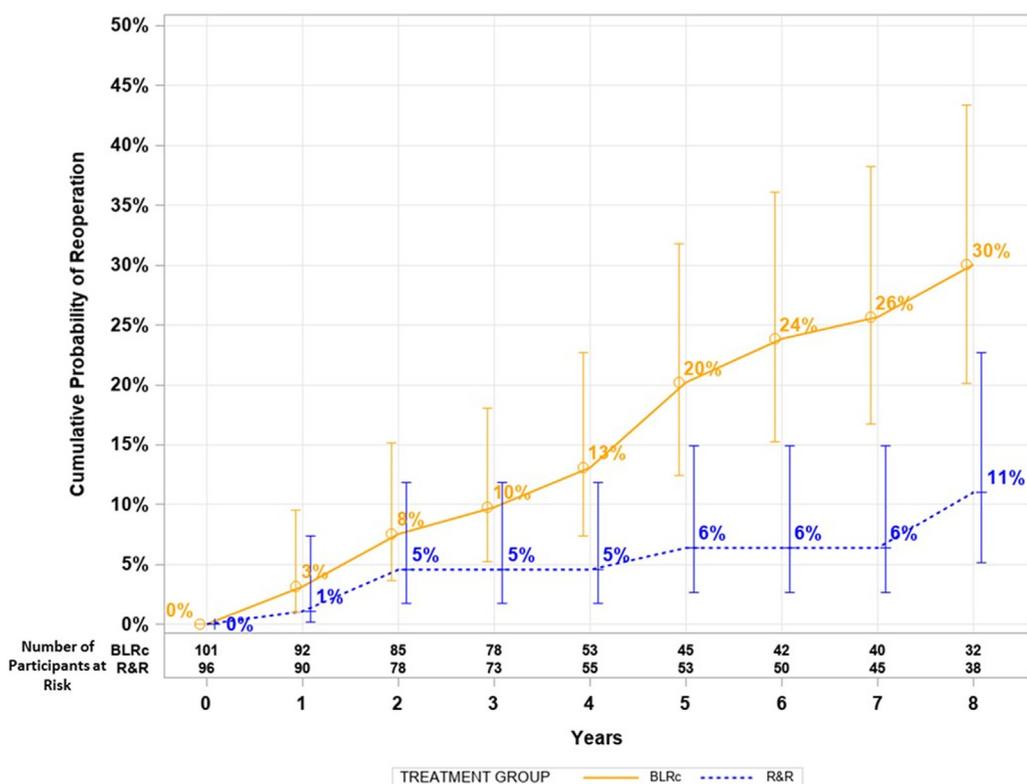
benefit of R&R over BLRc for IXT, are consistent with 2 previous RCTs reporting shorter-term outcomes. Kushner<sup>6</sup> found a benefit at 12 months of R&R versus BLRc for basic IXT (82% success for R&R vs. 52% for BLRc; n = 17 and n = 19, respectively). Kushner hypothesized that the restrictive effect created by the medial rectus resection tethers the eye in place, decreasing the tendency for an outward drift and recurrence. Kushner’s hypothesis is consistent with our finding that the primary reason for reoperation was residual or recurrent exodeviation, particularly when the initial surgery was BLRc, and that the reoperation rate over 8 years was significantly lower when the initial surgery was R&R. Similarly, Somer et al<sup>7</sup> reported 1-year success rates of 77% in 26 patients who underwent R&R and 48% in 21 patients who underwent BLRc. Conversely, Zhang et al<sup>8</sup> found no difference in 1-year success rates of 89% and 79% in patients who underwent R&R and BLRc, respectively (n = 58 in both groups), and the 3-year outcomes from the current RCT<sup>5</sup> did not indicate a statistically significant difference between R&R and BLRc in suboptimal surgical outcome by 3 years or reoperation by 3 years. Our report of 8-year surgical outcomes may be useful to patients, families, and clinicians by providing data regarding long-term alignment.

Another hypothesis consistent with the suggestion that BLRc results in worse long-term postoperative outcomes is that the dose tables used for the present study were insufficient for BLRc. It is noteworthy that while the original study protocol was in development, Lee et al<sup>18</sup> reported a

case series that suggested better results with augmented bilateral lateral rectus muscle recessions. It is possible that our study results might have differed from the current results had augmented surgery tables been used.

Although some might consider the rates of suboptimal surgical outcomes high, we suggest that our a priori definition of suboptimal surgical outcome was fairly liberal and our definition of complete or near-complete resolution was fairly strict. The severity of childhood intermittent exotropia often is judged by the parent and the provider as the level of control. Recent IXT treatment trials have used control as the primary outcome measure.<sup>19,20</sup> In the current RCT, if we consider an outcome measure that reflects control, it is noteworthy that at the final 8-year visit, 63% of the BLRc group and 72% of the R&R group did not demonstrate a spontaneous tropia during the examination or an average control score of 3 or more at distance or near. These data suggest that the overall impact of strabismus surgery for childhood IXT, followed by usual care, seems to be more favorable than when judged using the study’s primary outcome measure.

Our study has some limitations. First, we obtained 8-year outcome data in about half of the randomized cohort, and therefore we cannot rule out potential selection bias in our analysis. However, we found no appreciable differences in baseline characteristics between those who completed follow-up and those who did not. Second, reoperation was at investigator discretion after suboptimal surgical outcome for the first 3 years and at any time between 4 and 8 years. It is



**Figure 3.** Kaplan-Meier analysis of reoperation by 8 years showing cumulative probability (and 95% confidence interval). Among the reoperations that occurred during the 8-year follow-up in the BLRc and R&R groups, respectively, 90% (18 of 20 reoperations) and 57% (4 of 7 reoperations) were to correct residual or recurrent exotropia, 5% (1 of 20 reoperations) and 43% (3 of 7 reoperations) were to correct consecutive esotropia, and 5% (1 of 20 reoperations) and 0% (0 of 7 reoperations) were to correct inferior oblique overaction. BLRc = bilateral lateral rectus muscle recession; R&R = unilateral lateral rectus recession combined with medial rectus resection in the same eye.

**Table 3.** Exotropia Control, Prism and Alternate Cover Test Magnitude, and Near Stereoacuity Outcomes at 8 Years

| Variable                                                                                                           | Bilateral Lateral Rectus Muscle Recession (n = 46) | Recession-Resection (n = 43) | Treatment Group Difference (Bilateral Lateral Rectus Muscle Recession – Recession-Resection)* |                         |         |
|--------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|------------------------------|-----------------------------------------------------------------------------------------------|-------------------------|---------|
|                                                                                                                    |                                                    |                              | Difference                                                                                    | 95% Confidence Interval | P Value |
| Control (0–5)                                                                                                      |                                                    |                              |                                                                                               |                         |         |
| At distance                                                                                                        | 1.6 ± 1.8                                          | 0.8 ± 1.1                    | 0.8                                                                                           | 0.0–1.5                 | 0.049   |
| At near                                                                                                            | 1.1 ± 1.5                                          | 0.6 ± 1.1                    | 0.5                                                                                           | –0.2 to 1.1             | 0.21    |
| PACT (Δ)                                                                                                           |                                                    |                              |                                                                                               |                         |         |
| Distance                                                                                                           | 11.6 ± 8.7                                         | 9.3 ± 11.5                   | 2.3                                                                                           | –2.6 to 7.1             | 0.41    |
| Near                                                                                                               | 12.2 ± 10.5                                        | 8.5 ± 13.1                   | 3.6                                                                                           | –2.1 to 9.3             | 0.25    |
| Near stereoacuity (log arcsec)†                                                                                    | 2.0 ± 0.5                                          | 1.9 ± 0.4                    | 0.1                                                                                           | –0.1 to 0.3             | 0.44    |
| Participants with spontaneous exotropia during the examination or average control score of ≥ 3 at distance or near | 17 (37)                                            | 12 (28)                      | 9%                                                                                            | –13% to 32%             | 0.53    |
| Participants with decrease in near stereoacuity of ≥ 0.6 log arcsec from baseline‡                                 | 7 (15)                                             | 4 (9)                        | 6%                                                                                            | –10% to 22%             | 0.53    |

PACT = prism and alternate cover test.

Data are presented as no. (%) or mean ± standard deviation, unless otherwise indicated.

\*The confidence intervals and P values were adjusted using the adaptive false discovery rate approach to account for multiplicity, with the overall false discovery rate controlled at the 5% probability level. The analyses of control at distance, control at near, PACT at distance, PACT at near, and near stereoacuity were adjusted for corresponding measure at baseline.

†The near stereoacuity at 8 years was not available for 1 participant in the recession-resection group.

Table 4. Child Intermittent Exotropia Questionnaire, Parent Intermittent Exotropia Questionnaire, and Diplopia Questionnaire Scores at 8 Years

| Variable                      | Bilateral Lateral Rectus Muscle Recession |        |                     | Recession-Resection |        |                     | Treatment Group Difference (Bilateral Lateral Rectus Muscle Recession – Recession-Resection) |                         |                      |
|-------------------------------|-------------------------------------------|--------|---------------------|---------------------|--------|---------------------|----------------------------------------------------------------------------------------------|-------------------------|----------------------|
|                               | No.                                       | Median | Interquartile Range | No.                 | Median | Interquartile Range | Hodges-Lehmann Estimator*                                                                    | 95% Confidence Interval | P Value <sup>†</sup> |
| IXTQ domain scores            |                                           |        |                     |                     |        |                     |                                                                                              |                         |                      |
| Child                         | 46                                        | 86     | 77–95               | 41                  | 91     | 77–100              | 0.0                                                                                          | –9.1 to 4.6             | 0.54                 |
| Parent                        |                                           |        |                     |                     |        |                     |                                                                                              |                         |                      |
| Psychosocial                  | 42                                        | 97     | 86–100              | 40                  | 98     | 81–100              | 0.0                                                                                          | 0.0 to 3.1              | 0.86                 |
| Function                      | 42                                        | 88     | 78–94               | 40                  | 89     | 78–97               | 0.0                                                                                          | –5.6 to 2.8             | 0.67                 |
| Surgery                       | 42                                        | 92     | 69–100              | 40                  | 100    | 83–100              | 0.0                                                                                          | –8.4 to 0.0             | 0.45                 |
| Diplopia questionnaire scores | 46                                        | 0      | 0–0                 | 41                  | 0      | 0–0                 | 0.0                                                                                          | 0.0 to 0.0              | 0.26                 |

IXTQ = Intermittent Exotropia Questionnaire.

\*The median of all paired differences.

<sup>†</sup>Wilcoxon rank-sum test.

possible that the decision by the parent, child, and treating provider to reoperate might have been biased by the type of initial surgery.

In summary, we found that the cumulative incidence of a suboptimal surgical outcome by 8 years was not significantly different between BLRc and R&R followed by usual care for childhood basic-type IXT. Nevertheless, the 95% CI of the estimated difference did not exclude a possible moderate benefit of R&R, whereas it did exclude a

moderate benefit of BLRc. Taking this finding together with important secondary outcomes (including complete or near-complete resolution at 8 years and reoperation rate by 8 years) suggests that R&R may result in better long-term outcomes than BLRc using the surgical doses chosen for the present study. Overall, the results of surgery followed by usual care were somewhat disappointing, and therefore we need additional studies of alternative surgical and nonsurgical treatments.

## Footnotes and Disclosures

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**HUMAN SUBJECTS:** Human subjects were included in this study. The study was funded by the National Eye Institute of the National Institutes of Health and conducted according to the tenets of the Declaration of Helsinki by the Pediatric Eye Disease Investigator Group (PEDIG) at 35 academic and community-based clinical sites. The protocol and Health Insurance Portability and Accountability Act (HIPAA)-compliant informed consent forms were approved by institutional review boards for each site, and a parent or guardian of each study participant gave written informed consent.

No animal subjects were included in this study.

Author Contributions:

Conception and design: Donahue, Chandler, Kraker, Cotter, Holmes

Analysis and interpretation: Donahue, Chandler, Wu, Marsh, Law, Areaux, Ghasia, Li, Kraker, Cotter, Holmes

Data collection: Donahue, Chandler, Wu, Marsh, Law, Areaux, Ghasia, Li, Kraker, Cotter, Holmes

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Overall responsibility: Donahue, Chandler, Wu, Marsh, Law, Areaux, Ghasia, Li, Kraker, Cotter, Holmes

Abbreviations and Acronyms:

**BLRc** = bilateral lateral rectus muscle recession; **CI** = confidence interval; **Δ** = prism diopter; **IXT** = intermittent exotropia; **IXTQ** = Intermittent

Exotropia Questionnaire; **PACT** = prism and alternate cover test; **RCT** = randomized controlled trial; **R&R** = recession-resection; **SPCT** = simultaneous prism cover test.

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