Published in final edited form as:

Arch Ophthalmol. 2012 December 1; 130(12): 1525–1533. doi:10.1001/archophthalmol.2012.2853.

A Randomized Trial Comparing the Cost-Effectiveness of 2 Approaches for Treating Unilateral Nasolacrimal Duct Obstruction

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Abstract

Objective—To compare the cost-effectiveness of two approaches for treating unilateral nasolacrimal duct obstruction (NLDO)

Methods—163 infants 6 to <10 months old with unilateral NLDO were randomly assigned to immediate office-based nasolacrimal duct probing (N=82) or to six months of observation/non-surgical management (N=81) followed by facility-based probing for persistent symptoms.

Main Outcome Measures—Treatment success was defined as the absence of clinical signs of NLDO (epiphora, increased tear lake, mucous discharge) upon masked examination at 18 months of age. Cost of treatment between randomization and 18 months of age included costs for all surgeries and medications.

Results—In the observation/deferred facility probing group, NLDO resolved within 6 months without surgery in 44 of the 67 patients (66%, 95% confidence interval (CI)=54% to 76%) who completed the 6-month visit. Twenty-two (27%) of the 81 patients in the observation/deferred facility probing group underwent surgery, 4 of whom were operated within the initial 6 months. At 18 months of age, 69 (92%) of 75 immediate office probing group patients were treatment

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This article contains online-only material: eTable1

Meeting Presentation: Content from this manuscript was presented at the annual AAPOS meeting in March 2012 in San Antonio, TX.

Conflict of Interest: No conflicting relationships exist for any author.

successes, compared with 58 (82%) of 71 observation/deferred facility probing group patients (difference=10%, 95%CI=-1% to 21%). The average cost of treatment was \$562 in the immediate office probing group compared with \$701 in the observation/deferred facility probing group (difference=-\$139, 95%CI=-\$377 to \$94). The immediate office probing group had 3.0 fewer months of symptoms (95%CI=-1.8 to -4.0).

Conclusions—The immediate office probing approach is likely more cost effective than observation followed by deferred facility probing if needed. Adoption of the immediate office probing approach would result in probing about two-thirds of infants who would have resolved with 6 months of non-surgical management, but would largely avoid the need for probing under general anesthesia.

Application to Clinical Practice—Although unilateral NLDO often resolves without surgery, immediate office probing is an effective and potentially cost-saving treatment option.

The study is listed on www.clinicaltrials.gov (NCT00780741).

Congenital nasolacrimal duct obstruction (NLDO) is estimated to occur in 1.2% to 20% of infants¹⁻⁴ and often resolves without surgery.³⁻⁹ For children less than 6 months of age, surgery is usually deferred. After 6 months of age, the preferred clinical approach for treating NLDO is controversial. One approach is to probe the nasolacrimal duct to clear the blockage with the infant awake in the office using topical anesthesia and restraint. The alternative approach is to continue observation, and prescribe massage of the lacrimal sac and/or topical antibiotics, as many cases will resolve. If signs of obstruction remain after several months, a probing of the nasolacrimal duct is performed under general anesthesia in a surgical facility since by then the child is too strong to be sufficiently restrained in order for the procedure to be performed safely in the office. Because the costs of a probing in the office are about \$1000 to \$1600 less than the costs in a surgical facility,¹⁰ understanding the comparative cost effectiveness of the two approaches is important. Is it more cost effective to perform a probing procedure at an earlier age in the office on more patients or to defer surgery allowing many to resolve, recognizing that the procedure will need to be performed under general anesthesia in a surgical facility if the obstruction does not resolve? To address this question, we conducted a prospective randomized trial comparing the cost effectiveness of immediate office probing with that of deferral and probing in a surgical facility for unresolved cases.

Methods

The study was supported through a cooperative agreement with the National Eye Institute of the National Institutes of Health, and was conducted by the Pediatric Eye Disease Investigator Group (PEDIG) at academic and community-based ophthalmology practices. The study was conducted according to the tenets of the Declaration of Helsinki. The protocol and Health Insurance Portability and Accountability Act (HIPAA) -compliant informed consent forms were approved by institutional review boards, and a parent or guardian of each study patient gave written informed consent. An independent data and safety monitoring committee provided study oversight. The study is listed on www.clinicaltrials.gov (NCT00780741, accessed 9/27/11). The protocol is available on the PEDIG website (www.pedig.net, accessed 9/27/11), and is summarized below.

Patient Selection

Major eligibility criteria included age 6 to <10 months; onset of NLDO symptoms before 6 months of age; presence of at least one clinical sign of NLDO (epiphora, increased tear lake, and mucous discharge) in the absence of an upper respiratory infection or ocular surface

irritation; no prior nasolacrimal duct surgery; and at least one patent punctum in the study eye. The study excluded children with Down syndrome or craniofacial anomalies.

Randomization

Clinic personnel entered data on the PEDIG web site to randomly assign each patient (using a permuted block design stratified by site) with equal probability to one of two treatment groups: (1) immediate office probing or (2) observation/deferred facility probing for unresolved cases.

Follow-up

Both groups were contacted by phone 3 months (± 2 weeks) after randomization and had visits 6 months (± 2 weeks) after randomization and at 18 months of age (± 4 weeks). At both visits, presence or absence of each of 3 clinical signs of NLDO (epiphora, increased tear lake, and mucous discharge) was assessed. At the primary outcome visit at 18 months of age, this assessment was made by an examiner who was masked to the patient's treatment group.

Treatment

Patients in the immediate office probing group underwent a nasolacrimal duct probing in the office on the day of randomization or within 2 weeks. Office probings were performed using topical conjunctival anesthesia and infant restraint.

Patients in the observation/deferred facility probing group were prescribed 6 months of observation, lacrimal sac massage and topical antibiotics as indicated. Lacrimal sac massage was to be performed twice daily when discharge was present and antibiotic eye drops supplied at randomization (investigator choice of tobramycin sulfate 0.3% or moxifloxacin 0.5%), were to be used 1 drop up to 4 times a day when the discharge was purulent. Patients in the observation/deferred facility probing group who had one or more clinical sign of NLDO present at the 6-month post-randomization visit were to have a probing procedure within 4 weeks, performed under general anesthesia in a surgical facility.

Patency following probing was confirmed with metal on metal touch beneath the inferior turbinate, visualization of probe beneath the inferior turbinate, irrigation with saline in the office inciting a swallow reflex, or irrigation and recovery of fluorescein-colored saline from the nose when performed in a surgical facility. Antibiotic/steroid eye drops (tobramycin/dexamethasone 0.3%/0.1%) were used for one week postoperatively. Antibiotic eye drops could be prescribed at investigator discretion for persistent symptoms (investigator choice of tobramycin sulfate 0.3% or moxifloxacin 0.5%).

After the initial treatment approach of immediate office probing or 6 months of observation followed by deferred probing, further treatment (including reoperation) was at investigator discretion. The only stipulation was that reoperations could not occur within the first 6 weeks after an initial surgery or within one month before the 18 months of age visit.

Costs of Treatment

Estimates of treatment costs were obtained primarily from the 2011 Medicare Fee Schedules¹⁰⁻¹³ (eTable 1). The costs are for direct medical care and do not include costs of missed wages, child care or travel. The total cost of treatment for each patient included the cost of an initial office consultation and all surgeries received (i.e. initial surgeries and reoperations) and medications prescribed for NLDO between randomization and the 18 months of age visit. The cost of a probing surgery was \$174 in the office setting, \$1148 in an ambulatory surgery center, and \$1750 in a hospital outpatient department.¹⁰ Costs for

other surgeries depended on procedure type and site of service. Medication costs reflected the drug prescribed and the number of prescriptions. Costs of follow-up visits were not included because practice patterns vary and the two study visits were study-specific and not necessarily reflective of general clinical practice.

Clinical Outcomes

The primary efficacy outcome was treatment success, defined as the absence of clinical signs of NLDO assessed by a masked examiner at the 18 months of age visit. A secondary outcome was months of NLDO symptoms between randomization and 18 months of age. When resolution of NLDO occurred without surgery, the time of resolution was estimated as the midpoint between randomization and the first time point at which symptoms/signs were reported as absent (i.e. 3-month phone call, 6-month visit, or 18 months of age visit) without a subsequent report of symptoms/signs. For patients who underwent successful surgery, months of symptoms was estimated as months between randomization and the surgery. Patients who had clinical signs present at the 18 month of age visit were considered to have had symptoms present since randomization.

Statistical Methods

We expected the proportion of patients with treatment approach success at age 18 months to be similar with both treatment approaches after accounting for potential resolution without surgery in the observation/deferred group and for surgery(ies) in both treatment groups; therefore the sample size was based on precision for the proportion of observation/deferred facility probing patients whose NLDO resolves within 6 months without surgery, a primary determinant of the relative cost effectiveness of the two treatment approaches.¹⁴ The study planned to enroll 220 patients in order to have 110 patients assigned to observation/deferred facility probing, which after accounting for up to 10% loss to follow-up would yield a 95% confidence interval (CI) on the six-month rate of resolution without surgery that is no wider than $\pm 10\%$. During development of the statistical analysis plan, we decided not to combine patients with unilateral and bilateral NLDO in the same analysis because the cost-effectiveness profile might differ. Specifically, bilateral NLDO patients would have higher costs as they would require surgery even if the NLDO resolved in one eye without surgery. With 163 unilateral NLDO patients enrolled overall, the 95% CI for the proportion of observation/deferred facility probing group with six-month resolution without surgery would be no wider than $\pm 12\%$.

The primary analysis followed the intent to treat principle. The primary outcome was cost-effectiveness based on treatment success. Treatment group differences in average total cost and in the proportion of patients with treatment success were directly calculated. The bootstrap method sampling with replacement¹⁵ was used to calculate 95% CIs on the treatment group differences in success and total cost. The differences in cost and success from the bootstrap samples (N=10,000) were plotted on a scatter plot to describe the distribution of incremental costs and effect.

A secondary outcome, cost-effectiveness based on months of symptoms experienced between randomization and 18 months of age, was evaluated using the same methods as for the primary analysis. As all of the bootstrap estimates indicated the immediate office approach had fewer months of symptoms, we estimated the upper limit of the 95% CI on the ratio of difference in cost to difference in months of symptoms (i.e., the incremental cost-effectiveness ratio) by calculating the slope of the line below which 97.5% of bootstrap samples fell.

For both treatment success and months of symptoms outcomes, the bootstrap samples were also used to evaluate cost-effectiveness varying 1) the six-month rate of resolution without surgery in the observation/deferred facility probing group to the upper and lower limits of its 95% CI, and 2) site of deferred surgery in the observation/deferred facility probing group from 100% occurring in an ambulatory surgery center to 100% occurring in a hospital outpatient department.

All analyses were conducted using SAS version 9.1. (SAS Institute Inc. Cary, NC).

Results

Between November 2008 and September 2010, 163 patients with unilateral NLDO were enrolled at 22 clinical centers with 82 assigned to the immediate office probing group and 81 assigned to the observation/deferred facility probing group (Figures 1a and 1b). The patients were an average of 7.7 (± 1.2) months of age, 74 (45%) were female, and 134 (82%) were white (Table 1).

Visit Completion

The 3-month phone call was completed by 81 (99%) of the 82 patients in the immediate office probing group, and by 80 (99%) of the 81 patients in the observation/deferred probing group. The 6-month visit was completed by 73 (89%) of patients in the immediate probing group, 68 (93%) of whom completed the visit within the protocol-specified time window of 22 to 28 weeks, and by 67 (83%) of patients in the observation/deferred probing group, 63 (94%) of whom completed the visit within the protocol-specified time window of 22 to 28 weeks.

The 18 months of age primary outcome examination was completed by 75 (91%) of the 82 patients in the immediate probing group, 69 (92%) of whom completed the visit within the protocol-specified time window of 17 to 19 months of age, and by 71 (88%) of the 81 patients in the observation/deferred facility probing group, 64 (90%) of whom completed the visit within the protocol-specified time window of 17 to 19 months of age. The primary outcome was assessed by a masked examiner in all but one case.

Treatment

In the immediate office probing group, 81 (99%) of the 82 patients had an office probing within two weeks of randomization. The other patient's NLDO resolved before the scheduled surgery. A reoperation was performed in 7 (9%) cases of persistent NLDO; all were performed in a surgical facility under general anesthesia. No complications were reported for any surgery.

In the observation/deferred facility probing group, clinical signs of NLDO had resolved without surgery in 44 (66%; 95% CI = 54% to 76%) of the 67 patients who completed the 6-month visit. Twenty two patients (27%) underwent surgery, 4 of whom were operated before the end of the 6-month deferral period. Of the 4 early surgeries, 1 patient underwent a facility nasolacrimal intubation because cellulitis developed, and 3 patients underwent surgery at parental request due to continued or worsening symptoms (2 were office probings and 1 was a balloon catheter dilation in a surgical facility). Five patients who had clinical signs of NLDO at 6 months did not have surgery because the NLDO either subsequently resolved or was not severe enough to warrant surgery. A reoperation was performed for 1 case, in a surgical facility under general anesthesia. No complications were reported for any surgery.

The mean antibiotic eye drop prescriptions were 0.3 in the immediate office probing group and 1.1 in the observation/deferred facility probing group, with 61% of prescriptions in both groups for moxifloxacin 0.5%. The mean post-operative antibiotic/steroid eye drop prescriptions were 0.9 and 0.4 in the immediate office probing and observation/deferred facility probing groups, respectively.

Cost Effectiveness at 18 Months of Age

In the immediate office probing group, 69 (92%) of 75 patients completing the 18 months of age primary outcome examination had no clinical signs present (meeting success definition) compared with 58 (82%) of 71 patients in the observation/deferred facility probing group (difference in success = 10%, 95% CI = -1% to 21%) (Table 2).

The average cost of treatment was \$562 in the 75 patients in the immediate office probing group overall--\$141 for the single patient who had no surgery, \$383 for the 67 patients who had one surgery, and \$2330 for the 7 patients who had two surgeries. The average cost of treatment was \$701 in the 71 patients in the observation/deferred facility probing group overall--\$209 for the 50 patients who had no surgery, \$1826 for the 20 patients who had one surgery, and \$2794 for the single patient who had two surgeries. Overall, using our observed data the average cost of treatment was \$139 less in the immediate office probing group compared with the observation/deferred facility probing group (95% CI = office probing is \$377 less to \$94 more). The immediate office probing approach largely dominates when performing a cost-effectiveness analysis for the clinical success outcome—it is more successful and less costly in 86% of the bootstrap estimates for incremental cost effectiveness (Figure 2a). Results were similar when the analysis was repeated including 7 patients (3 in immediate office probing group and 4 in observation/deferred probing group) who did not complete the 18 months of age visit but had outcome information obtained from the parents.

The immediate office probing group had an average of 3.0 fewer months of symptoms (95% CI = 1.8 to 4.0 fewer) than the observation/deferred facility probing group (1.8 vs. 4.8) and cost \$139 less. Ninety-seven point five percent of the incremental cost-effectiveness ratios were below \$40, indicating that the immediate office approach is statistically unlikely to cost more than \$40 per month of symptoms avoided. The immediate office probing approach has fewer months of symptoms and is less costly in 88% of the bootstrap estimates for incremental cost effectiveness (Figure 2b).

Varying the six-month rate of resolution without surgery for the observation/deferred facility probing group between 54% to 77% (the two limits of the 95% CI using data derived from bootstrap estimates) showed that immediate office probing would be 13% to 7% more successful, have 3.4 to 2.4 fewer months of symptoms, and would be \$263 to \$34 less expensive (Table 3). Within this range of rates for six-month resolution without surgery, immediate office probing would cost \$375 to \$80 less if all deferred probings were performed in the hospital outpatient department, but would cost \$131 less to \$67 more if all procedures were performed in an ambulatory surgery center.

Under our observed data, if the less costly (\$23) tobramycin sulfate was prescribed for all antibiotic prescriptions instead of the more costly moxifloxacin (\$96) being prescribed 61% of the time in both treatment groups, the average cost of treatment would be \$551 in the immediate office probing group and the \$652 in the observation/deferred facility probing group.

Discussion

We performed a prospective randomized clinical trial comparing the cost-effectiveness of immediate office probing versus observation and deferred facility probing when needed for unilateral nasolacrimal duct obstruction in infants presenting at 6 to <10 months of age. Despite the substantial difference in the cost between performing a probing in an office setting vs. a surgical facility, the difference between the cost of the immediate office probing approach vs. the observation/deferred facility probing approach was small from a population perspective, primarily because only 27% of patients assigned to the latter approach underwent the more costly surgery in a facility. Although not statistically significant, our results suggest that the immediate office probing approach is likely to be at least as successful as the observation/deferred facility probing approach and slightly less costly. However, the immediate approach does subject about two-thirds of the population to a surgery they could avoid with 6 months of non-surgical treatment.

As in our published model¹⁴ of cost-effectiveness of NLDO treatments, the current study demonstrates that relative cost effectiveness of the two approaches is sensitive to certain factors. The cost of the observation/deferred facility probing approach is highly dependent on the rate of resolution without surgery. The higher the rate of resolution without surgery, the fewer patients require more expensive facility probing, and the less cost-effective office probing becomes. Use of ambulatory surgical centers also impacts cost-effectiveness because the cost of the observation/deferred facility probing approach decreases when more deferred probings are performed in ambulatory surgery centers instead of hospital outpatient surgery departments. In addition, exclusive use of the less costly of the two antibiotics would result in this approach costing an average of \$101 dollars more than the immediate office probing approach, instead of \$139 more. Thus, costs were influenced by both regional availability of ambulatory surgical centers and physician choice of antibiotic.

We are not aware of any studies with which to compare our results. Previous attempts to compare the cost effectiveness of these two treatment approaches have been limited to hypothetical models based on data from non-randomized studies.^{14, 16}

Several factors should be considered when interpreting our results. First, our conclusion would be more definitive with a larger sample size, allowing for greater precision in the estimates used for the analysis. Second, some misclassification may have occurred given that outcome was assessed at a single encounter. Third, because of wide variation in cost by region and payer, we based the costs in our analysis on the 2011 Medicare physician and outpatient prospective payment fee schedules as opposed to the actual costs incurred. Fourth, we did not include the costs of any follow up visits because the study visits were study specific and practice patterns vary; however, we would expect that including costs of follow up would increase the cost difference in favor of immediate office probing because in usual practice patients prescribed the deferred approach would likely have one or more visits before surgery. Fifth, our analysis is based on the perspective of the health care insurer. Lastly, our results are not generalizable to patients with bilateral obstructions.

Aside from cost-effectiveness, several other factors could influence choice of treatment approach. Early office probing provides faster resolution of symptoms and is convenient, often able to be performed on the same day as the initial office visit. Alternatively, because the observation/deferred facility probing approach avoids surgery entirely in a majority of infants, some parents and clinicians may view immediate office probing as unnecessary. Risks are another consideration and appear to be minimal with both treatment approaches. The current study detected no surgical complications and data from a previous larger prospective study showed that complications were rare.¹⁷ This earlier study found no

complications among 239 office probings and 2 (0.3%) minor complications among 661 facility probings: one episode of laryngospasm managed without sequelae and one case of mild bleeding from a lacrimal punctum¹⁷. Other complications which could potentially occur with probing in any setting include damage to the punctum and very rarely, aspiration. Aside from the risks of the probing procedure itself, general anesthesia carries a very slight risk of morbidity. Controversy also exists about whether general anesthesia exposure in young children could potentially have negative developmental effects, although most of the data supporting this hypothesis come from animal studies involving prolonged exposure.¹⁸⁻²¹ Parents who would prefer to avoid the risks of general anesthesia and the discomfort associated with airway management might prefer early office probing: patients in the observation/deferred treatment group were about two and a half times more likely to require a procedure under general anesthesia. Conversely, because office probing utilizes restraint and may cause the child some discomfort despite the use of topical anesthetic, parents may be concerned about its potential negative psychological effects.

For treatment of unilateral NLDO, the immediate office probing approach is likely more cost effective than observation followed by deferred facility probing for unresolved cases. Adoption of the immediate office probing approach would result in probing about two-thirds of infants who would have resolved with 6 months of non-surgical management, but would largely avoid the need for probing under general anesthesia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Alcon Laboratories, Inc. (Fort Worth, Texas) provided antibiotic eye drops and antibiotic/steroid eye drops at no cost to the study. The sole purpose was to standardize the drugs used in study; no comparisons were made between drugs. The company did not have any input into the study design, analyses, or manuscript preparation.

Financial Support: Supported by National Eye Institute of National Institutes of Health, Department of Health and Human Services EY011751 and EY018810. The funding organization had no role in the design or conduct of this research.

APPENDIX

Clinical Sites that Participated in this Protocol

Sites are listed in order by number of subjects enrolled into the study. Personnel are listed as (I) for Investigator, (C) for Coordinator, and (E) for Examiner.

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Lancaster PA - Family Eye Group

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Tomball TX - Houston Eye Associates

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Albuquerque NM - Family & Children's Eye Center of New Mexico

Todd A. Goldblum, (I); Angela Alfaro, (C)

Springfield MO - St. John's Clinic - Eye Specialists

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Arnold MD - Ophthalmology Associates of Greater Annapolis

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*Center received support utilized for this project from an unrestricted grant from Research to Prevent Blindness Inc., New York, New York.

**Center received support utilized for this project from an unrestricted grant support from the Ohio Lions Eye Research Foundation, Bellville, Ohio.

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Figure 1a. Data for Immediate Office Probing Group Patients (N=82)^a

Prob of path = Probability of following specified pathway.

Avg mos of sx = Average months of symptoms.

Avg cost = Average cost of treatment between randomization and 18 months of age.

^aNote that Ns decrease over time due to 7 patients being lost to follow-up.

^bAll initial surgeries were office nasolacrimal duct probings.

^cAll seven reoperations occurred in a facility (ASC or HOPD)—one was a probing and six were intubations.

Figure 1b. Data for Observation/Deferred Facility Probing Group Patients (N=81)^a

Prob of path = Probability of following specified pathway.

Avg mos of sx = Average months of symptoms.

Avg cost = Average cost of treatment between randomization and 18 months of age.

^aNote that Ns decrease over time due to 10 patients being lost to follow up.

^bOf the four surgeries performed within the first 6 months after randomization, 2 were office probing, 1 was facility intubation, and one was facility balloon catheter dilation.

^cOne patient appeared resolved at the 6 month visit but underwent intubation before 18 months of age.

^dOne deferred surgery was an office probing and one was balloon catheter dilation.

^eThe reoperation was a balloon catheter dilation.

^fFive patients in the observation/deferred facility probing group had clinical signs of NLDO at the 6-month visit but did not receive surgery (symptoms resolved before the scheduled surgery or the surgeon and/or parents felt surgery was not warranted).

Difference in Cost versus Difference in Probability of Success at 18 Months of Age

Figure 2a. Cost-Effectiveness for Treatment Success at 18 Months of Age

The scatter plot indicates the extent of uncertainty in the observed cost effectiveness estimate. Each point represents the incremental cost effectiveness derived using one of the 10,000 bootstrap samples. The white 'X' indicates the observed incremental cost effectiveness for the treatment success outcome (the immediate office probing approach is 10% more successful and costs \$139 less than the observation/deferred facility approach).

Difference in Cost versus Difference in Months of Symptoms

Figure 2b. Cost-Effectiveness for Months of NLDO Symptoms between Randomization and 18 Months of Age

The scatter plot indicates the extent of uncertainty in the observed cost effectiveness estimate. Each point represents the incremental cost effectiveness derived using one of the 10,000 bootstrap samples. The white 'X' indicates the observed incremental cost effectiveness for the months of symptoms outcome (the immediate office probing approach has 3.0 fewer months of symptoms and costs \$139 less than the observation/deferred facility approach).

Table 1
Baseline Characteristics of Study Cohort

	Immediate Office Probing Group (N = 82)	Observation/ Deferred Facility Probing Group (N = 81)
Female gender, n (%)	32 (39)	42 (52)
Race/ethnicity, n (%)		
White	68 (83)	66 (81)
Hispanic	10 (12)	7 (9)
African American	3 (4)	6 (7)
Asian	1 (1)	1 (1)
Age at enrollment, n (%)		
6 to <7 months	25 (30)	27 (33)
7 to <8 months	28 (34)	20 (25)
8 to <9 months	15 (18)	13 (16)
9 to <10 months	14 (17)	21 (26)
Mean (SD) months	7.6 (1.2)	7.8 (1.3)
Previous treatment, n (%)		
Lacrimal massage and topical antibiotics	36 (45)	39 (48)
Lacrimal massage only	15 (19)	18 (22)
Topical antibiotics only	14 (18)	10 (12)
None	15 (19)	15 (18)
Epiphora present, n (%)	70 (86)	63 (77)
Increased tear film present, n (%)	81 (100)	79 (96)
Mucous discharge present, n (%)	63 (78)	60 (73)

Table 2
Outcomes at 18 Months of Age Primary Outcome Visit

Outcome at 18 Months of Age Visit	Immediate Office Probing Group (N=75)	Observation/Deferred Facility Probing Group (N=71)
Clinical outcome and number of surgeries at 18 months of age, n (%)		
Success	69 (92)	58 (82)
No surgery	1	43
Initial surgery	62	15
Reoperation	6	0
Failure	6 (8)	13 (18)
No surgery	0	7
Initial surgery	5	5
Reoperation	1	1
Months of symptoms between randomization and 18 months of age, n (%)		
<1	58 (77)	0 (0)
1 to <3	1 (1)	27 (38)
3 to <6	3 (4)	18 (25)
6 to <9	5 (7)	17 (24)
9 to 12	8 (11)	9 (13)
Mean	1.8	4.8
Median	0.0	4.5
Range	0.0 to 12.0	1.5 to 12.0
Total estimated costs for surgical procedures and medications between randomization and 18 months of age, n (%)		
\$101 to \$250	1 (1)	46 (65)
\$251 to \$500	67 (89)	5 (7)
\$501 to \$1000	0 (0)	1 (1)
\$1001 to \$1500	0 (0)	4 (6)
\$1501 to \$2000	1 (1)	2 (3)
\$2001 to \$2500	5 (7)	11 (15)
\$2501 to \$3000	1 (1)	2 (3)
Mean	\$562	\$701
Median	\$385	\$237
Range	\$141 to \$2597	\$141 to \$2794

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Table 3
Cost-effectiveness at 18 Months of Age According to Six-Month Resolution without Surgery and Site of Service for Deferred Probing in Observation/Deferred Facility Probing Group^a

	Clinical Success at 18 Months of Age		Average Months of Symptoms Between Randomization and 18 Months of Age ^b				Average Total Cost ^c	
	Immediate Office Probing Group N=75	Observation/Deferred Facility Probing Group N=71	Immediate Office Probing Group N=75	Observation/Deferred Facility Probing Group N=71	Immediate Office Probing Group N=75	Observation/Deferred Facility Probing Group N=71	Immediate Office Probing Group N=75	Observation/Deferred Facility Probing Group N=71
Observation/Deferred Probing Group Six-Month Rate of Resolution without Surgery and Site of Service for Deferred Probing								
54% (lower limit of 95% CI)	92%	80%	1.8	5.2	\$560	\$823		
All in ambulatory surgery center						\$691		
All in hospital outpatient department						\$935		
66% (observed)	92%	82%	1.8	4.8	\$562	\$701		
All in ambulatory surgery center						\$584		
All in hospital outpatient department						\$775		
77% (upper limit of 95% CI)	91%	84%	1.9	4.3	\$556	\$590		
All in ambulatory surgery center						\$489		
All in hospital outpatient department						\$636		

^a Bolded row represents observed data. Other rows represent data obtained from bootstrap estimates for both treatment groups; because each of these rows represents a separate set of bootstrap estimates, very slight changes in the data are possible for the immediate probing group.

^b Months of symptoms experienced between randomization and 18 months of age visit. The surgery date was considered the date of resolution if the surgery was successful. Months of symptoms for patients who resolved without surgery were assumed to be uniformly distributed between randomization and the first study contact at which NLDO was reported resolved.

^c Costs include all medications prescribed and surgeries received in the study. Costs based on Medicare reimbursement rates and retail prices from [drugstore.com](https://www.drugstore.com), not actual costs.