Postoperative Glaucoma Following Infantile Cataract Surgery
An Individual Patient Data Meta-analysis

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IMPORANCE Infantile cataract surgery bears a significant risk for postoperative glaucoma, 
and no consensus exists on factors that may reduce this risk.

OBJECTIVE To assess the effect of primary intraocular lens implantation and timing of surgery 
on the incidence of postoperative glaucoma.

DATA SOURCES We searched multiple databases to July 14, 2013, to identify studies with 
eligible patients, including PubMed, MEDLINE, EMBASE, ISI Web of Science, Scopus, Central, 
Google Scholar, Intute, and Tripdata. We also searched abstracts of ophthalmology society 
meetings.

STUDY SELECTION We included studies reporting on postoperative glaucoma in infants 
undergoing cataract surgery with regular follow-up for at least 1 year. Infants with concurrent 
ocular anomalies were excluded.

DATA EXTRACTION AND SYNTHESIS Authors of eligible studies were invited to contribute 
individual patient data on infants who met the inclusion criteria. We also performed an 
aggregate data meta-analysis of published studies that did not contribute to the individual 
patient data. Data were pooled using a random-effects model.

MAIN OUTCOME MEASURES Time to glaucoma with the effect of primary implantation, 
additional postoperative intraocular procedures, and age at surgery.

RESULTS Seven centers contributed individual patient data on 470 infants with a median age 
at surgery of 3.0 months and median follow-up of 6.0 years. Eighty patients (17.0%) 
developed glaucoma at a median follow-up of 4.3 years. Only 2 of these patients had a 
pseudophakic eye. The risk for postoperative glaucoma appeared to be lower after primary 
implantation (hazard ratio [HR], 0.10 [95% CI, 0.01-0.70]; \( P = .02; I^2 = 34\% \)), higher after 
surgery at 4 weeks or younger (HR, 2.10 [95% CI, 1.14-3.84]; \( P = .02; I^2 = 0\% \)), and higher 
after additional procedures (HR, 2.52 [95% CI, 1.11-5.72]; \( P = .03; I^2 = 32\% \)). In multivariable 
analysis, additional procedures independently increased the risk for glaucoma (HR, 2.25 
[95% CI, 1.20-4.21]; \( P = .01 \)), and primary implantation independently reduced it (HR, 0.10 
[95% CI, 0.01-0.76]; \( P = .03 \)). Results were similar in the aggregate data meta-analysis that 
included data from 10 published articles.

CONCLUSIONS AND RELEVANCE Although confounding factors such as size of the eye and 
surgeon experience are not accounted for in this meta-analysis, the risk for postoperative 
glaucoma after infantile cataract surgery appears to be influenced by the timing of surgery, 
primary implantation, and additional intraocular surgery.
A systematic review of the literature reveals that cataract surgery during the first year of life bears a significant risk for postoperative glaucoma. Some studies suggest that primary implantation of an intraocular lens (IOL) may reduce this risk, whereas other reports do not find this association. In addition, some studies suggest that surgery during the first week of life may involve a higher risk for postoperative glaucoma, whereas others contradict this suggestion. Contradictory results may be owing to differences in glaucoma definition, length of follow-up, subcategorization of age at surgery, inclusion of eyes with other anomalies (eg, microcornea and persistent fetal vasculature [PFV]), type of surgical technique, and statistical method. However, because the eyes at highest risk for glaucoma are those most likely to be left aphakic, it is difficult to distinguish the effect of each of the 2 factors, that is, surgery in younger vs older patients and aphakia vs primary pseudophakia. Thus, no consensus exists on the optimal timing or surgical technique, and surgeons have to make decisions with significant consequences without having solid evidence on which to base them.

An ongoing prospective randomized clinical trial, the Infant Aphakia Treatment Study (IATS), has published 1-year follow-up results reporting greater odds of developing glaucoma for patients with PFV and for younger patients undergoing surgery. Although no statistically significant difference was found in the incidence of glaucoma between the aphakic and pseudophakic arms of the study at 12 months, results of a longer follow-up are expected to elucidate the aforementioned questions. These results may take several years, because postoperative glaucoma can have a delayed onset. The aim of this individual patient data meta-analysis was to review the existing literature systematically and synthesize the results to assess the effect of the timing of surgery and of primary IOL implantation during cataract extraction among infants on the incidence of postoperative glaucoma.

Methods

We searched PubMed, MEDLINE, EMBASE, ISI Web of Science, Scopus, Central, Google Scholar, Intute, Tripdata, and abstracts from 2010 major ophthalmology society meetings for the titles and abstracts of articles published under the following search criteria: cataract surgery OR cataract operation OR lens extraction OR cataract extraction OR lens aspiration AND infantile cataract OR infant cataract OR congenital cataract AND glaucoma. The last search date was July 14, 2013. All studies including infants (age, ≤12 months) undergoing surgery for congenital cataract by a contemporary surgical technique and regular follow-up for at least 1 year underwent assessment. Exclusion criteria included ocular anomalies or factors known to predispose to glaucoma (ie, microcornea, microphthalmia, PFV, congenital glaucoma, trauma, and Lowe syndrome), the use of polymethyl methacrylate lens or sulcus implantation, the presence of intraoperative complications, or intraoperative additional procedures in the same eye. Additional studies were found from the reference lists of reviewed publications. No language or time of publication exclusions applied. The identified records were screened independently by 2 of us (A.M. and S.K.), and in case of disagreement consensus was met by a third researcher (A.-B.H.). The protocol methods are published on PROSPERO (registration number CRD42012002058; http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42012002058#.U0JO9PmSxNA). Ethical approval was granted by the Bioethics Committee of Aristotle University of Thessaloniki.

An individual patient data meta-analysis was conducted to acquire the raw data of includable cases because in most publications, our inclusion and exclusion criteria could not be consistent. The initial search revealed 4258 records, of which 703 were screened and 120 full-text articles were assessed for eligibility (Figure 1). These articles correspond to 40 authors, who were invited by e-mail and post to contribute raw data. Investigators from 7 centers provided information for a total of 470
patients. Contributed data did not necessarily reflect the reported data in the original publication because the former were updated. Clarification and confirmation were sought from each center for discrepancies. Raw data were contributed after institutional review board approval from the respective institutes.

Some centers were willing to participate but could not do so for reasons such as lack of resources to achieve raw data extraction or lack of institutional review board approval to share the originally collected data. The relatively low participation rate (9 studies) prompted us to examine any differences between studies that provided individual patient data and studies that did not by conducting an additional aggregate data meta-analysis. Ten studies were eligible for this purpose and contributed 204 more patients, because only data on patients meeting our inclusion criteria were used. The total number of studies included in this meta-analysis was 19.

Primary outcome was time to glaucoma, which was measured from initial surgery to glaucoma diagnosis and from initial surgery to last follow-up for those who did not experience an event. We performed a sensitivity analysis that included also suspected glaucoma as glaucoma. Whenever both eyes were eligible for the analysis, 1 eye was selected randomly using the statistical program’s random sampling method. The effect of the following factors on the risk for glaucoma was investigated: IOL implantation, age at surgery, additional procedure(s) before the glaucoma diagnosis (if any), and type of cataract (bilateral or unilateral). Additional procedures were defined as any reported intraocular surgery subsequent to cataract surgery and before glaucoma diagnosis or last follow-up (eg, visual axis opacification removal or secondary IOL implantation). Patients from Saudi Arabia were classed as Asian.

We used Kaplan-Meier curves to display the time to glaucoma, and each risk factor was analyzed using the log-rank test stratified by study. Cox proportional hazards regression was performed with models stratified by study where the hazard ratios (HRs) and corresponding 95% CIs were reported (in addition to 99% CIs in the eTable in the Supplement). We used the following 2-step process for meta-analysis: an HR was estimated for each trial, and then HRs were pooled in a meta-analysis with the random-effects model. Heterogeneity was assessed with the inconsistency index I², and published guidelines were used to define low (I² = 25%-49%), moderate (I² = 50%-74%), and high (I² ≥ 75%) heterogeneity. 18

We conducted secondary analyses to assess the results’ robustness by including aggregate data from other studies that did not provide their individual patient data. 19, 20 When related data were not available directly from the studies, we calculated the corresponding HR and its 95% CI using the method described by Tierney et al. 21 In a sensitivity analysis, we tested methods of handling studies of zero and rare events, such as the treatment arm continuity correction and the empirical continuity correction. 22 In this analysis, the fixed-effect Mantel-Haenszel method was used with odds ratios as an approximation of HRs, because the inverse variance weighted method has been shown to perform poorly with respect to bias when continuity corrections are applied. We performed an influence analysis by omitting 1 study at a time and recalculating the estimates of the meta-analysis. We also examined the possibility that larger studies showed systematically different effects from those of smaller studies by visually inspecting the counter-enhanced funnel plots for asymmetry when 10 or more studies were included in the analysis. 23, 24 The publication bias was assessed with the test developed by Egger et al. 25 All P values were 2 tailed. Analysis was performed with commercially available software (SPSS, version 20.0 [IBM]; STATA, version 11.2 [StataCorp]; and Review manager, version 5.2 [The Cochrane Collaboration]).

Results

Seven medical centers (3 from the United States, 1 from Canada, 1 from the United Kingdom, 1 from Saudi Arabia, and 1 from Australia) contributed data on 470 infants (659 eyes) undergoing infantile cataract surgery, with follow-up of 3380 person-years (Table 1). The surgery was performed at a median age of 3.0 months, and the median postoperative follow-up was 6.0 years. Eighty infants (17.0%) underwent surgery at no older than 4 weeks. In 106 infants, the assessed eye was pseudophakic (22.6%), and in 364 infants it was aphakic (77.4%) (Table 2). One hundred eleven infants (24.2%) had an additional postoperative procedure.

The median age at surgery was higher in patients for whom the assessed eye was pseudophakic (3.7 [interquartile range, 1.9-7.6] months) than in those in whom it was aphakic (2.78 [1.07-4.93] months) (P < .001). A lower percentage of infants undergoing surgery at 4 weeks or younger had primary IOL implantation (5 of 80 [6.3%]) than infants undergoing surgery at older than 4 weeks (101 of 390 [25.9%]) (P < .001). Eighty patients (17.0%) developed glaucoma at a median postoperative interval of 4.3 years (interquartile range, 1.2-6.3). Only 2 of these 80 infants had pseudophakic eyes: one underwent surgery at 2 months of age and developed glaucoma 1 month later, and the other underwent surgery at 3 weeks of age and developed glaucoma 2 months later. With inclusion of suspected glaucoma as glaucoma, the entire database consisted of 102 patients with glaucoma (21.7%) who developed postoperative glaucoma at a median age of 5.0 (interquartile range, 2.0-7.8) years. Nevertheless, only 2 infants had pseudophakic eyes as described above. Nineteen of 80 patients (23.8%) with glaucoma had undergone cataract surgery when 4 weeks or younger, whereas 18 patients (22.5%) had an additional postoperative procedure before the glaucoma event. A difference in the risk for glaucoma between unilateral and bilateral cases, corrected for age, was not identified (HR, 0.93 [95% CI, 0.53-1.61]; P = .78).

Four centers (392 patients) provided data on infants with aphakic and pseudophakic eyes and a secondary meta-analysis of this smaller data set showed that patients who underwent primary implantation appeared to have a lower risk of developing glaucoma (HR, 0.10 [95% CI, 0.01-0.70]; P = .02; F = 34%) (Figure 2A). We truncated the survival curves after 10 years because no pseudophakic cases had follow-up longer than that period. Infants who were no older than 4 weeks at surgery appeared to have an increased risk for glaucoma (HR, 2.10 [95% CI, 1.14-3.84]; P = .02; F = 0%) (Figure 2B). Six centers (435 patients) had eligible data for this analysis. Infants who had an additional procedure postoperatively appeared to have an increased risk for glaucoma (HR, 2.52 [95% CI, 1.11-
5.72); \( P = .03; F = .32\% \) (Figure 2C). Four centers (385 patients) had eligible data for this analysis.

In multivariable analysis, both primary implantation (HR, 0.10 [95% CI, 0.01-0.76]; \( P = .02 \)) and an additional procedure (HR, 2.25 [95% CI, 1.20-4.21]; \( P = .01 \)) were shown to be independent risk factors for glaucoma, the first by reducing and the second by increasing this risk, whereas no effect could any longer be shown for age at surgery (HR, 1.39 [95% CI, 0.70-2.77]; \( P = .35 \)). When suspected glaucoma was considered to be glaucoma, the results were similar for the effect of IOL implantation (HR, 0.09 [95% CI, 0.01-0.66]; \( P = .02; F = 37\% \), age at surgery (HR, 1.71 [95% CI, 1.02-2.85]; \( P = .04; F = 0\% \), and the additional procedure (HR, 2.35 [95% CI, 1.15-4.79]; \( P = .02; F = 37\% \)) on the risk for glaucoma. Similarly, in multivariable analysis, both primary implantation (HR, 0.09 [95% CI, 0.01-0.68]; \( P = .02 \)) and an additional procedure (HR, 1.87 [95% CI, 1.10-3.18]; \( P = .02 \)) were independently associated with the risk for glaucoma, whereas no effect could any longer be shown for age at surgery (HR, 1.49 [95% CI, 0.91-2.44]; \( P = .12 \)).

Another 10 studies with aggregate data were available for the meta-analysis (Table 3 and Table 4). Including these data showed results similar to those of the individual patient data alone. Primary implantation appeared to have a protective effect against developing glaucoma (HR, 0.27 [95% CI, 0.12-0.61]; \( P = .002; F = 0\% \) (Figure 3)); infants who were 4 weeks or younger at surgery appeared to have an increased risk for glaucoma (HR, 2.28 [95% CI, 1.34-3.89]; \( P = .002; F = 0\% \) (Figure 4), as did infants who had an additional procedure (HR, 2.68 [95% CI, 1.44-5.00]; \( P = .002; F = 0\% \) (Figure 5).

For publication bias, the association of age with glaucoma risk included more than 10 studies, with no funnel-plot asymmetry and no bias (\( P = .22 \)) (eFigure 1 in the Supplement).
When the treatment arm and empirical continuity corrections were applied, the results did not change. For the association of primary implantation with glaucoma risk, the pooled odds ratio (OR) estimate with the empirical continuity correction was 0.26 (95% CI, 0.09-0.73; \( P = .01 \); \( F = 0% \)); with the treatment arm continuity correction, the OR estimate was 0.29 (95% CI, 0.10-0.80; \( P = .02 \); \( F = 0% \)). For the association of age at surgery with glaucoma risk, the respective OR estimates were 1.93 (95% CI, 1.09-3.43; \( P = .02 \); \( F = 0% \)) and 1.94 (95% CI, 1.09-3.45; \( P = .03 \); \( F = 0% \)). Similarly, for the association of an additional procedure with glaucoma risk, the respective OR estimates were 2.90 (95% CI, 1.46-5.75; \( P = .002 \); \( F = 0% \)) and 3.01 (95% CI, 1.50-6.06; \( P = .002 \); \( F = 0% \)).

**Discussion**

Contribution of raw data on 470 infants from 7 medical centers across the world permitted this individual patient data meta-analysis. The meta-analysis provides evidence that infants with nontraumatic infantile cataract appear to run a higher risk for postoperative glaucoma when surgery is undertaken during the first 4 weeks of life and when a postoperative additional intraocular procedure takes place, whereas the risk appears to be reduced when a primary IOL is used. The results were similar when studies with aggregate data were included. When cases of suspected glaucoma were grouped under glaucoma, these associations remained the same, whereas in multivariable analysis, the following 2 factors were shown to be independent risk factors: primary implantation appears to have a protective effect, and an additional procedure appears to infer a higher risk for postoperative glaucoma.

The effect of primary implantation and the optimal age at surgery to minimize the risk for postoperative glaucoma have been major controversies among pediatric cataract surgeons and remain unresolved issues, because a high level of evidence is still scarce. In most of the existing studies, a large range of ages and different conditions are grouped, and a large heterogeneity exists in the definition of outcomes and length of follow-up.

In the 2 population-based cohorts that address risk factors for postoperative glaucoma, one finds that being 9 months or younger at surgery is the only important factor, whereas the other finds younger age at detection of cataract, and not age at surgery, to be the only independently associated factor. Age at detection may be related to type of cataract, because some types of cataract may not be detected until they become sufficiently large and/or dense and thus undergo later surgery. It is plausible that age at surgery of 4 weeks or younger may be a proxy for type of cataract, because many of these children have dense fetal nuclear cataracts at birth, whereas those who have surgery after 4 weeks of age may have posterior lentiglobus or cortical or posterior subcapsular cataracts.
genital unilateral cataracts are reported to be associated with mild microphthalmia and mild PFV (eg, plaque). However, in our meta-analysis, unilateral and bilateral cases appeared to run a similar risk for postoperative glaucoma.

Availability bias, a known threat for individual patient data meta-analysis that is often neglected, was investigated by assessing the potential impact of studies lacking individual participant data, and we showed that the results were similar with the addition of these studies. Moreover, our assessment found no publication bias for the association of age at surgery and glaucoma risk, with at least 10 studies available for the analysis. No heterogeneity between studies was present in any of the meta-analyses.

The association between primary implantation and glaucoma risk needs to be interpreted with caution, given that only 2 patients with pseudophakic eyes developed glaucoma. This finding is in agreement with the large retrospective multicenter study of Asrani et al, who report only 1 case of glaucoma among pseudophakic eyes, although their series included many patients who underwent surgery when older than 1 year. Our meta-analysis cannot exclude the possibility that being older at the time of cataract surgery rather than having pseudophakia offers these children “protection.” However, the multivariable analysis indicates that a primary IOL implantation is an independent risk factor with a protective effect. An effort was made to handle zero and rare events by applying different continuity corrections, which demonstrated that this effect remained.

The attending clinician’s decision to treat was the definition of glaucoma chosen, which may have underestimated the actual rate of glaucoma. Although conservative, this definition was judged to be the most appropriate for classifying patients from retrospective data, when documentation of disc changes, significant myopic shift, and corneal size and clarity may be insufficient.

Given the increased likelihood of the need for an additional procedure in pseudophakic vs aphakic eyes and the increased risk for postoperative glaucoma when an additional procedure is undertaken in this meta-analysis, one would expect to find a higher risk for glaucoma in pseudophakic eyes. However, the contrary association was found. Confounding factors for postoperative glaucoma risk, such as size of eye, size

<table>
<thead>
<tr>
<th>Source</th>
<th>Country</th>
<th>Study Period</th>
<th>No. of Patients</th>
<th>Age at Surgery, mo</th>
<th>Follow-up, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plager et al, 2002</td>
<td>United States</td>
<td>Not reported</td>
<td>21</td>
<td>2.5 (1.6-3.9)</td>
<td>≥1</td>
</tr>
<tr>
<td>Lundvall and Kugelberg, 2002</td>
<td>Sweden</td>
<td>1991-1996</td>
<td>24</td>
<td>1.2 (0.4-3.0)</td>
<td>7.0 (5.1-8.0)</td>
</tr>
<tr>
<td>Tuncer et al, 2005</td>
<td>Turkey</td>
<td>1996-2002</td>
<td>6</td>
<td>5.0 (3.8-7.3)</td>
<td>3.8 (2.1-5.0)</td>
</tr>
<tr>
<td>Lundvall and Zetterström, 2006</td>
<td>Sweden</td>
<td>1999-2004</td>
<td>10</td>
<td>2.7 (0.4-6.4)</td>
<td>2.9 (1.9-3.2)</td>
</tr>
<tr>
<td>Michaelides et al, 2007</td>
<td>United Kingdom</td>
<td>1994-2000</td>
<td>23</td>
<td>&lt;12 mo</td>
<td>&gt;5 y</td>
</tr>
<tr>
<td>Hussin and Markham, 2009</td>
<td>United Kingdom</td>
<td>1988-1999</td>
<td>10</td>
<td>6.1 (2.5-9.0)</td>
<td>5.6 (5.1-5.9)</td>
</tr>
<tr>
<td>Lu et al, 2010</td>
<td>China</td>
<td>2002-2007</td>
<td>16</td>
<td>9.0 (7.0-10.0)</td>
<td>3.8 (2.9-4.9)</td>
</tr>
<tr>
<td>Tatham et al, 2010</td>
<td>United Kingdom</td>
<td>1998-2009</td>
<td>5</td>
<td>0.7 (0.4-1.2)</td>
<td>4.9 (1.0-14.0)</td>
</tr>
<tr>
<td>Kirwan et al, 2010</td>
<td>Ireland</td>
<td>1984-2007</td>
<td>89</td>
<td>3.0 (0.5-12.0)</td>
<td>7.1 (0.4-21.2)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>204</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Unless otherwise indicated, data are expressed as median (interquartile range).  
Reported as mean (range).
Glaucoma After Infantile Cataract Surgery

Original Investigation Research

Figure 3. Risk for Glaucoma by Intraocular Lens (IOL) Implantation in Aggregate Data (AD) and Individual Patient Data (IPD) Meta-analysis

<table>
<thead>
<tr>
<th>IOL Implantation Study or Subgroup</th>
<th>Log (HR) SE</th>
<th>Total No. Pseudophakic</th>
<th>Total No. Aphakic</th>
<th>Weight, %</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KKESH, Saudi Arabia, 2003</td>
<td>-3.30</td>
<td>2.20</td>
<td>24</td>
<td>114</td>
<td>1.7</td>
</tr>
<tr>
<td>EUSM, United States, 2011</td>
<td>0.94</td>
<td>2.90</td>
<td>2</td>
<td>24</td>
<td>2.1</td>
</tr>
<tr>
<td>GOSH, United Kingdom, 2011</td>
<td>-3.49</td>
<td>3.01</td>
<td>31</td>
<td>70</td>
<td>2.0</td>
</tr>
<tr>
<td>RFS, United States, 2011</td>
<td>-3.10</td>
<td>5.27</td>
<td>9</td>
<td>118</td>
<td>0.6</td>
</tr>
<tr>
<td>Subtotal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>66</td>
<td>326</td>
<td>8.5</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Heterogeneity: τ² = 2.81; χ² = 4.56 (P = .21), I² = 34%
Test for overall effect: z score = 2.31 (P = .02)

AD

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Log (HR) SE</th>
<th>Total No. Aged ≤4 wk</th>
<th>Total No. Aged &gt;4 wk</th>
<th>Weight, %</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lundvall and Kugelberg, 2002</td>
<td>-3.08</td>
<td>11.51</td>
<td>1</td>
<td>23</td>
<td>0.1</td>
</tr>
<tr>
<td>Plager et al, 2002</td>
<td>-3.37</td>
<td>2.55</td>
<td>4</td>
<td>17</td>
<td>2.8</td>
</tr>
<tr>
<td>Kirwan et al, 2010</td>
<td>-1.17</td>
<td>0.45</td>
<td>46</td>
<td>43</td>
<td>88.6</td>
</tr>
<tr>
<td>Subtotal</td>
<td></td>
<td>51</td>
<td>83</td>
<td>91.5</td>
<td>0.29</td>
</tr>
</tbody>
</table>

Heterogeneity: τ² = 0.00; χ² = 0.75 (P = .60), I² = 0%
Test for overall effect: z score = 2.80 (P = .005)

Total

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Log (HR) SE</th>
<th>Total No.</th>
<th>Total No.</th>
<th>Weight, %</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heterogeneity: τ² = 0.00; χ² = 2.83 (P = .83), I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: z score = 3.13 (P = .002)</td>
<td></td>
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</tr>
<tr>
<td>Test for subgroup differences: χ² = 0.45 (P = .50), I² = 0%</td>
<td></td>
<td></td>
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</tbody>
</table>

Eyes were stratified as pseuophakic vs aphakic. Vertical line indicates no difference between the 2 groups. The size of each square denotes the proportion of information provided by each study; diamonds indicate the pooled estimates. Pooled hazard ratios (HRs) were calculated from random-effects models with the inverse variance method. EUSM indicates Emory University School of Medicine; GOSH, Great Ormond Street Hospital; KKESH, King Khaled Eye Specialist Hospital; and RFS, Retinal Foundation of the Southwest.

Figure 4. Risk for Glaucoma by Age at Surgery in Aggregate Data (AD) and Individual Patient Data (IPD) Meta-analysis

<table>
<thead>
<tr>
<th>Age at Surgery</th>
<th>Log (HR) SE</th>
<th>Total No. Aged ≤4 wk</th>
<th>Total No. Aged &gt;4 wk</th>
<th>Weight, %</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UMSM, United States, 2001</td>
<td>1.299</td>
<td>0.77</td>
<td>8</td>
<td>30</td>
<td>12.6</td>
</tr>
<tr>
<td>KKESH, Saudi Arabia, 2003</td>
<td>0.188</td>
<td>1.02</td>
<td>3</td>
<td>135</td>
<td>7.2</td>
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<td>SEH, Australia, 2010</td>
<td>-3.346</td>
<td>10.75</td>
<td>1</td>
<td>4</td>
<td>0.1</td>
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<td>GOSH, United Kingdom, 2011</td>
<td>0.602</td>
<td>0.57</td>
<td>24</td>
<td>37</td>
<td>22.8</td>
</tr>
<tr>
<td>RFS, United States, 2011</td>
<td>1.193</td>
<td>0.56</td>
<td>35</td>
<td>91</td>
<td>23.5</td>
</tr>
<tr>
<td>EUSM, United States, 2011</td>
<td>-0.154</td>
<td>0.80</td>
<td>7</td>
<td>19</td>
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<td>Subtotal</td>
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<td>79</td>
<td>356</td>
<td>77.6</td>
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</tbody>
</table>

Heterogeneity: τ² = 0.00; χ² = 2.91 (P = .71), I² = 0%
Test for overall effect: z score = 2.39 (P = .02)

AD

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Log (HR) SE</th>
<th>Total No. Aged ≤4 wk</th>
<th>Total No. Aged &gt;4 wk</th>
<th>Weight, %</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lundvall and Kugelberg, 2002</td>
<td>-3.833</td>
<td>8.45</td>
<td>4</td>
<td>6</td>
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<td>Lundvall and Zetterström, 2006</td>
<td>0.868</td>
<td>1.23</td>
<td>11</td>
<td>13</td>
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<tr>
<td>Michaelides et al, 2007</td>
<td>1.32</td>
<td>0.7</td>
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<td>12</td>
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<td>Hussin and Markham, 2009</td>
<td>0.5236</td>
<td>2.85</td>
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<td>Tatham et al, 2010</td>
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<td>3</td>
<td>2</td>
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<tr>
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<td>30</td>
<td>42</td>
<td>22.4</td>
<td>3.05</td>
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Heterogeneity: τ² = 0.00; χ² = 0.58 (P = .97), I² = 0%
Test for overall effect: z score = 1.94 (P = .05)

Total

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Log (HR) SE</th>
<th>Total No.</th>
<th>Total No.</th>
<th>Weight, %</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heterogeneity: τ² = 0.00; χ² = 3.82 (P = .95), I² = 0%</td>
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<td>Test for overall effect: z score = 3.03 (P = .002)</td>
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<tr>
<td>Test for subgroup differences: χ² = 0.33 (P = .56), I² = 0%</td>
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</table>

Ages were stratified as 4 weeks or younger vs older than 4 weeks. Vertical line indicates no difference between the 2 groups. The size of each square denotes the proportion of information provided by each study; diamonds indicate the pooled estimates. Pooled hazard ratios (HRs) were calculated from random-effects models with the inverse variance method. EUSM indicates Emory University School of Medicine; GOSH, Great Ormond Street Hospital; KKESH, King Khaled Eye Specialist Hospital; and RFS, Retinal Foundation of the Southwest; SEH, Sydney Eye Hospital; and UMSM, University of Minnesota School of Medicine.
Glaucoma After Infantile Cataract Surgery

Figure 5. Risk for Glaucoma by Additional Postoperative Procedures (AP) in Aggregate Data (AD) and Individual Patient Data (IPD) Meta-analysis

Additional postoperative procedures were stratified as present (yes) vs absent (no). Vertical line indicates no difference between the 2 groups. The size of each square denotes the proportion of information provided by each study; diamonds indicate the pooled estimates. Pooled hazard ratios (HRs) were calculated from random-effects models with the inverse variance method. EUSM indicates Emory University School of Medicine; GOSH, Great Ormond Street Hospital; KKESH, King Khaled Eye Specialist Hospital; and RFS, Retinal Foundation of the Southwest.

Conclusions
With this individual patient data meta-analysis of infantile cataract, we provide a high level of evidence that postoperative glaucoma risk appears to be associated not only with surgery within the first month of life vs surgery later, but also with additional intraocular surgical procedures subsequent to the cataract surgery and before glaucoma diagnosis or last follow-up. Our evidence suggests that pseudophakic eyes appear to have a reduced risk for early-to-intermediate-onset glaucoma.

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Advances in the management of congenital and paediatric cataract surgery: a 20-year retrospective study.


