

1 **Solebo and Rahi response to Correspondents:**

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3 The suggestion by the correspondents that IoLunder2, one of the largest overall prospective
4 congenital cataract inception cohorts, is insufficiently powered to report on glaucoma in unilateral
5 cataract¹ is challenged by striking similarities to the Infant Aphakia Treatment Study (IATS) RCT.² This
6 lends credence to our finding of lack of protective effect of IoLs, as well as the overall robustness of
7 IoLunder2.

8 The correspondents' univariate re-analysis of our raw data on glaucoma outcome,^{1,3} without
9 adjusting for the undisputed key confounding factor – age at surgery - is simply inappropriate.

10 They cite a systematic review which was derived from largely retrospective studies,⁴ failed to analyse
11 separately bilateral and unilateral surgery outcomes, and was unable to adjust for the confounding
12 variable of ocular size: smaller eyes have a higher risk of glaucoma, and are less likely to undergo IoL
13 implantation. Its relevance is questionable.

14 A recent RCT cited as evidence of absence of association between IoLs and reoperation risk⁵ had
15 significantly higher complications overall in the IoL group versus the aphakic group: specifically
16 posterior synechiae in 28% of IoL children versus 8% aphakes. This structural inflammatory sequelae
17 is usually an uncommon event, and importantly is a key predictor of subsequent glaucoma.

18 The details sought about 'Intensive regimens' of topical steroids (at least 2 hourly for the first week)
19 were described within supplementary tables.⁶ We reiterate IoLs increase the risk of re-operation
20 *irrespective* of steroid use.

21 Correspondents also ask why we have corrected visual outcome by age at visual assessment: it
22 seems they misread that the variable of interest was age at surgery. Their unevidenced comment
23 that concordance with occlusion is easier to achieve in children with IoLs contradicts the evidence
24 from IATS.^{7,8}

25 The technique of optic capture implantation (suggested as holding promise of improved results) has
26 yet to be adopted by other groups and lacks evidence on reproducibility, 12 years since it was
27 described. In any case, our findings regarding IoL implantation as routinely practised hold true.
28 Finally, it is inappropriate to equate primary IoL implantation and subsequent reoperation with
29 initial aphakia and secondary implantation. Re-operation following primary IoLs causes repeated
30 exposure to general anaesthetic within a year of primary surgery, ie at a young age (under 3 years
31 old). It is this exposure which is the concern, not second surgery per se. This was entirely clear in our
32 paper.

33 A one-step solution is an attractive option in resource poor countries. Our findings and those of IATS
34 show children often require additional optical interventions following primary IoLs. We believe all
35 children should have care informed by robust evidence. In choosing to use IoLs in infants and young
36 children, ophthalmologists should be aware of the need for follow up and counsel parents
37 accordingly.

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- 39 1. Mataftsi et al correspondence to LCAH
- 40 2. Freedman SF, Lynn MJ, Beck AD, et al. Glaucoma-Related Adverse Events in the First 5 Years
41 After Unilateral Cataract Removal in the Infant Aphakia Treatment Study. *JAMA Ophthalmol.*
42 2015;133(8):907–914. doi:10.1001/jamaophthalmol.2015.1329
- 43 3. Hildebrand et al correspondence to LCAH
- 44 4. Mataftsi A, Haidich AB, Kokkali S et al. Postoperative glaucoma following infantile cataract
45 surgery. An individual patient data meta-analysis. *JAMA Ophthalmol* 2014; 132: 1059-1067
- 46 5. Vasavada AR, Vasavada V, Shah SK et al. Five-year postoperative outcomes of bilateral
47 aphakia and pseudophakia in children up to 2 years of age: A randomized clinical trial. *Am J*
48 *Ophthalmol* 2018; 193: 33-44
- 49 6. Solebo AL, Cumberland P, Rahi JS. 5-year outcomes after primary intraocular lens
50 implantation in children aged 2 years or younger with congenital or infantile cataract:

- 51 findings from the IoLunder2 prospective inception cohort study. *Lancet Child Adolesc Health*
52 2018; 2: 863–71
- 53 7. Celano M, Hartmann EE, Drews-Botsch C. Parenting stress in the infant aphakia treatment
54 study. *J Pediatr Psychol*. 2013 Jun;38(5):484-93
- 55 8. Drews-Botsch C, Cotsonis G, Celano M et al. Assessment of Adherence to Visual Correction
56 and Occlusion Therapy in the Infant Aphakia Treatment Study. *Contemp Clin Trials Commun*.
57 2016 Aug 15;3:158-166