

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 cataract<sup>1</sup> is challenged by striking similarities to the Infant Aphakia Treatment Study (IATS) RCT.<sup>2</sup> 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,<sup>1,3</sup> 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,<sup>4</sup> 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 risk<sup>5</sup> 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.<sup>6</sup> 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.<sup>7,8</sup>

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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