

1 **Title: Quality of Life and Functional Vision in children with glaucoma.**

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3 **Running head: Quality of Life in children with glaucoma**

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5 Authors

6 Annegret Dahlmann-Noor<sup>1,4</sup> MD PhD

7 Vijay Tailor<sup>1</sup> MSc

8 Catey Bunce<sup>1,2,3</sup> DSc

9 Yassir Abou-Rayyah<sup>1,5</sup> MD PhD

10 Gillian Adams<sup>1,4</sup> MD FRCS

11 John Brookes<sup>1,6</sup> MD FRCOphth

12 Peng T. Khaw<sup>1,6</sup> MD PhD

13 Maria Papadopoulos<sup>1,6</sup> MD, FRCOphth

14

15 Authors' addresses:

16 1. National Institute of Health Research Biomedical Research Centre for

17 Ophthalmology, University College London Institute of Ophthalmology

18 and Moorfields Eye Hospital, London, United Kingdom

19 2. London School of Hygiene & Tropical Medicine, Keppel Street, London

20 3.  Primary Care & Public Health Sciences, King's College London, London

21 4. Paediatric Service, Moorfields Eye Hospital, London, United Kingdom

22 5. Adnexal Service, Moorfields Eye Hospital, London, United Kingdom

23 6. Glaucoma Service, Moorfields Eye Hospital, London, United Kingdom

24

25 Corresponding author:

26 Annegret Dahlmann-Noor

27 NIHR Biomedical Research Centre at Moorfields Eye Hospital and UCL Institute of Ophthalmology

28 162 City Road, London EC1V 2PD, UK

29 [annegret.dahlmann-noor@moorfields.nhs.uk](mailto:annegret.dahlmann-noor@moorfields.nhs.uk)

30

31 Contribution of authors: ADN and MP developed the study protocol. VT enrolled participants, collected data and  
32 entered data onto the electronic database which ADN had developed. ADN and CB conducted data analysis. All  
33 authors reviewed and discussed and interpreted the data acquired. ADN drafted the manuscript, which was  
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35

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41 Functional vision, Childhood glaucoma

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45

46 **Abstract**

47 **Objective:** To evaluate the effect of glaucoma on functional vision and vision and health-related quality of life in  
48 children up to the age of 16 years.

49 **Design:** Cross-sectional observational study

50 **Participants:** 119 children aged 2 to 16 years (mean 9.4, SD 4.56) with glaucoma and their parents.

51 **Methods/Interventions:** Completion of three validated instruments for children to assess (i) functional visual ability  
52 (FVA) with the Cardiff Visual Ability Questionnaire for Children (CVAQC), (ii) vision -related quality of life (VR-QoL)  
53 with the Impact of Vision Impairment for Children (IVI-C) and (iii) health-related quality of life (HR-QoL) with the  
54 PedsQL™ V 4.0.

55 **Main Outcome Measures:** Cardiff Visual Ability Questionnaire for Children, Impact of Vision Impairment for Children  
56 and PedsQL™ scores.

57 **Results:** Scores for FVA, VR- and HR-QoL are reduced in children with glaucoma: median CVAQC score -1.24  
58 (interquartile range IQR -2.2 to -0.11, range: -3.00 higher visual ability to +2.80 lower visual ability), mean IVI-C score  
59 67.3 (SD 14.4) (normal VR-QoL = 96), median PedsQL™ self-report 78.8 (IQR 67.4-90.2), parent report 71.2 (IQR  
60 55.7-85.8) and family impact score 74.3 (IQR 56.9-88.5) (normal HR-QoL = 100). Psychosocial PedsQL™ subscores  
61 are lower than physical subscores. Older children report less impairment on CVAQC, IVI-C and PedsQL™ than  
62 younger children. Parents state greater impact on their child's HR-QoL than children themselves.

63 **Conclusions:** Glaucoma and its management have a marked impact on a child's functional visual ability and quality  
64 of life. Children with glaucoma report HR-QoL scores similar to those described by children with severe congenital  
65 cardiac defects, liver transplants or acute lymphoblastic leukemia.

66

67 **Precis (35 words)**

68 Childhood glaucoma not only impacts a child's vision, but also severely affects their quality of life and that of the  
69 family.

70 **Introduction**

71  
72 Childhood glaucoma (CG) is a rare, but significant and potentially sight-threatening condition associated with  
73 elevated intraocular pressure (IOP).<sup>1 2</sup> Common causes of childhood glaucoma are primary developmental  
74 defects of the aqueous drainage pathways leading to primary congenital glaucoma (PCG), and more extensive  
75 ocular maldevelopment and/or systemic disease such as Axenfeld-Rieger anomaly, aniridia, phakomatoses along  
76 with acquired glaucoma after lensectomy for congenital cataract. CG poses significant management challenges  
77 and visual outcomes may be disappointing.<sup>3 4 5</sup> Primary treatment for PCG is surgical but secondary glaucomas  
78 often also require surgical intervention to control intraocular pressure (IOP) should topical medications fail.<sup>6</sup>  
79 Surgical success is often compromised by aggressive postoperative inflammation and scarring, potentially  
80 leading to multiple surgical interventions.<sup>6</sup> Children often require topical medication to control IOP prior to and  
81 after surgery, which may cause discomfort and be a burden to families. Correction of ametropia and amblyopia  
82 in young children require additional monitoring and treatment. Furthermore, examinations under anesthesia  
83 (EUA) may be necessary in infants and young children for accurate assessment.

84  
85 The diagnosis of glaucoma in a child can be very stressful for the child and for the parents/caregivers  
86 (henceforth referred to as “parents”), siblings and extended family members for many reasons. Glaucoma is a  
87 chronic, sight threatening condition with an uncertain prognosis which requires lifelong treatment and follow  
88 up. Associated visual impairment may have a significant impact on the child’s development, education, social  
89 integration and independence. Treatment may involve multiple operations often when the patient is a neonate  
90 or infant. A decision to proceed to incisional or laser surgery may be made during an EUA, so children and  
91 parents face the anxiety of not knowing whether the child will wake up in discomfort or pain. The challenges  
92 associated with assessing and controlling glaucoma in children also result in numerous hospital appointments  
93 requiring parents to take time off work and absences from school as the child grows older, affecting education.

94 Secondary glaucoma may be associated with systemic disease requiring treatment, which may further  
95 compound these absences. Furthermore, buphthalmos, a physical manifestation of glaucoma in infancy, may  
96 further highlight a child's difference from their peers especially if unilateral, as may a port wine stain. Lastly, the  
97 potential financial burden on the family should not be underestimated. In some countries, medical expenses  
98 may have to be paid for by the family. Loss of earnings due to hospital visits affects parents everywhere.

99  
100 Published data on the impact of glaucoma on children and their families is scarce partly due to a paucity of  
101 suitable instruments in children to measure functional visual ability (FVA) (i.e. an individual's use of their given  
102 vision in activities of daily living) and quality of life (QoL) (i.e. an individual's subjective impression of various  
103 aspects of their life such as physical, emotional, social and schooling), as it relates to their vision (VR-QoL) and  
104 health (HR-QoL). Three previous studies have used validated tools to explore QoL in children with glaucoma and  
105 their parents. Children with glaucoma report lower VR-QoL scores than healthy children <sup>7</sup> and better visual  
106 acuity is associated with higher VR-QoL. <sup>8</sup> Glaucoma surgery in children is associated with an improvement in the  
107 quality of life of their parents. <sup>9</sup> No study has assessed HR-QoL or FVA in children with glaucoma. Our main  
108 objective was therefore to explore FVA, VR-QoL and HR-QoL in children with glaucoma and their parents.

109

## 110 **Methods**

111 This work presents an analysis of children with glaucoma who took part in a larger cross-sectional  
112 observational study of quality of life in children with developmental eye defects, approved by the National  
113 Research Ethics Committee South Central – Oxford A (14/SC/1052). It adhered to the tenets of the  
114 Declaration of Helsinki.

115 Between 25 June 2014 and 03 June 2015 we enrolled children age 2-16 years with primary or secondary  
116 glaucoma who attended clinics at Moorfields Eye Hospital, London, UK. Exclusion criteria were: inability to  
117 communicate in English, surgical intervention (incisional or laser) within one month of date of completing

118 questionnaires (before or after). We screened the notes of all children attending our pediatric glaucoma  
119 clinics in advance to identify those who met the inclusion criteria. These children were then approached  
120 consecutively for inclusion in the study. For those who did not wish to take part, we noted the reasons given.  
121 Age-appropriate written information material was provided; we addressed any questions before obtaining  
122 written consent and assent.

123 We recorded age at study participation, gender and ethnic background. From the medical notes, we  
124 recorded ocular and systemic diagnoses, age at diagnosis of the eye condition (primary glaucoma, or eye  
125 defect causing secondary glaucoma), and best corrected visual acuity (BCVA) with both eyes open in logMAR  
126 on the day of study participation. Where visual acuity was recorded as “counting fingers”, we noted a BCVA  
127 of 2.1 logMAR, for “hand movements only” we noted 2.4 logMAR, for “perception of light” 2.7 logMAR, and  
128 for “no perception of light” or “ocular prosthesis/artificial eye”, 3 logMAR.<sup>10</sup> Details of previous and current  
129 treatment were recorded. The number of previous glaucoma-related surgical interventions performed in  
130 the operating room only were noted, as these were considered more significant than clinic procedures due  
131 to factors such as the potential traumatic experience of hospital admission, anesthesia and postoperative  
132 pain. The sum of interventions to the right and left eye including incisional surgery (angle surgery,  
133 trabeculectomy and glaucoma drainage device surgery), laser treatment, bleb needling, and removal of  
134 sutures and/or subconjunctival injections performed under EUA. The number of general anesthetics for  
135 both surgical procedures and examinations under anesthesia, and the number of current topical medications  
136 (sum of eyedrop applications per day right and left eye) were also noted.

137

### 138 **Main outcome measures**

139 To evaluate functional vision, children from the age of 5 years completed the Cardiff visual ability questionnaire  
140 for children (CVAQC).<sup>11</sup> The CVAQC was developed to assess the difficulty in performing activities in children’s  
141 daily lives in the developed world following extensive work with focus groups of children with and without sight

142 impairment to determine the relevant questions. The tool was validated in children with visual impairment. It is  
143 self-report tool consisting of 25 questions with answers selected on a four-point scale (“very easy” to “very  
144 difficult”) which cover the areas of education, near and distance vision, getting around, social interaction,  
145 entertainment and sports.<sup>11</sup> For example, children were asked “Because of your eyesight and with your glasses  
146 and low vision aids if you use them, how difficult do you find it to walk in a crowded place ?” or “Because of your  
147 eyesight and with your glasses and low vision aids if you use them, how difficult do you find it to watch  
148 television ?”. Using a Rasch conversion calculator provided by the developers of the CVAQC tool, we  
149 transformed the raw CVAQC scores into logarithmic scores. The resulting scores range from -3.00 (higher visual  
150 ability) to +2.80 (lower visual ability).

151  
152 To assess VR QoL, a subgroup of children aged 8 years and older enrolled after 01 August 2014, when required  
153 agreements and permissions were granted, completed the Impact of Vision Impairment for Children (IVI-C) tool.  
154 <sup>12</sup> The IVI-C tool was validated in visually impaired and normally sighted children. It entails 24 questions with 5  
155 possible answers plus an additional option of “no, for other reasons”. We scored the IVI-C responses using the  
156 relevant scoring sheet which allocates values between 0 and 4 to the responses from “never” to “always” to  
157 questions covering areas of school (aspects of school life and classroom activity), mobility (travel and access to  
158 the environment), interaction (with non vision impaired peer group and people in broader community) and  
159 emotion (the emotional impact of visual impairment on day-to-day life). For example children were instructed  
160 to give an answer which best described what they did and felt most of the time in response to a questions such  
161 as “Do you find it difficult to go down stairs or to step off the footpath ?”, “Are you confident in places you don’t  
162 know ?” and “Can you find your friends in the playground at lunch and play time?”. We did not allocate a score  
163 when the response “no, for other reasons” was selected. As the tool comprises 24 items, the resulting raw  
164 scores range from 0 to 96, with the highest score indicating normal VR-QoL. No Rasch conversion table is  
165 available for this tool as yet, and we did not carry out a Rasch transformation on our data, as the sample size

166 was small.

167

168 For HR QoL, age-specific versions of the PedsQL™ Inventory ([www.pedsq.org](http://www.pedsq.org)) enable children aged 5-18  
169 years to express their views on different aspects of their physical and emotional state and their social and  
170 school life.<sup>13 14</sup> Parents completed two questionnaires, one about the child (“parental report”) and another  
171 about the impact on the family (“family report”). The parental report is specific to the age of the child and  
172 usually consists of 23 questions covering children aged 2-4 years (21 questions), 5-7 years, 8-12 years and  
173 13-18 years. The family report contains 36 questions. Children from the age of 5 up to 16 self-administered  
174 the questionnaire (PedsQL™ administration guidelines) and gave answers on a 5-point Likert scale from 0  
175 (“never a problem”) to 4 (“always a problem”) to questions such as “It is hard to keep up when I play with  
176 other kids” or “I worry what will happen to me”.

177

178 We calculated the PedsQL™ scores as detailed in the scoring instructions. If items were left blank, we  
179 adjusted the denominator, using the number of completed items instead of the number of total items. It is  
180 recommended to remove questionnaires from the analysis if 50% or more of the items have been left blank;  
181 this did not occur in our sample. PedsQL™ scores range from 0 to 100 providing physical functioning,  
182 psychosocial (school, social, emotional) functioning and summary total scores with a score of 100 indicating  
183 normal HR-QoL.

184

185 All questionnaires were completed on the same day, during a regular clinic appointment. When children  
186 needed help completing the questionnaires, they were assisted by a member of the research team or play  
187 leaders, but not by family members.

188

189



190 **Statistics**

191 We aimed for a sample size of 100 children to allow for a limits of agreement comparison (Bland-Altman plot) of  
192 parent and child scores for the PedsQL™ questionnaire. Demographic and clinical data, CVAQC, IVI-C scores and  
193 PedsQL™ scores were transferred to a dedicated database in Microsoft Office Excel by a member of the research  
194 team. Calculation of scores and data transfer were double-checked by a second member of the team.

195 Where data were missing for individual items in the PedsQL™ and IVI-C, we adjusted the denominator accordingly.  
196 For the CVAQC, a Rasch-analysis based calculator transforms raw data into standardized scores, and this takes into  
197 account missing data.

198 Analysis was carried out in SPSS v23 (IBM) and Stata (V14). Where data were missing, datasets were excluded from  
199 the relevant analyses. We applied descriptive statistics throughout, reporting means and standard deviations for  
200 normally distributed data or median and interquartile range (IQR) for data not normally distributed. We assessed  
201 relationships between age at participation, age at diagnosis, unilateral / bilateral disease, BCVA in better eye, sum of  
202 surgical interventions, sum of eyedrops, sum of general anaesthetics and CVAQC, IVI-C and Peds QL™ scores using  
203 Spearman rank correlation and assessed whether differences observed between groups were statistically significant  
204 using the Rank Sum test or independent t-test. Agreement between adult and child PedsQL™ scores was assessed  
205 using Bland-Altman techniques. Statistical significance was set at the 5% level and all tests conducted were two-  
206 tailed.

207

208 **Enrollment**

209 We approached 158 consecutive children with glaucoma and their families who met the inclusion criteria; 30  
210 declined because of a perceived lack of time to complete the questionnaires. We enrolled 128 children (Fig  
211 1). We removed six children who had undergone incisional surgery or laser treatment within four weeks of  
212 study participation. One child who developed glaucoma after extensive trauma related injury and surgery  
213 along with another child with multiple non-glaucoma surgical interventions had significant visual loss

214 unrelated to secondary glaucoma and so were excluded on the basis that their complex ophthalmic history  
215 prior to glaucoma management may have influenced their responses leading to a different impact on our  
216 main outcome measures. We also excluded one dataset, as neither parents nor child completed the  
217 questionnaires after having given consent. The statistical analysis was carried out on the remaining 119  
218 datasets (Fig 1).

219

## 220 **Missing data**

221 The proportion of missing data was low. No data were missing for age, gender, diagnoses, laterality, BCVA  
222 and number of daily eye drops. Ethnicity was unknown in 14 participants (11.76%). Age at diagnosis of the  
223 eye condition could not be determined exactly in 2 children (1.7%). Five children had previous surgical  
224 interventions at other centers, and information about previous number of operations and general  
225 anesthetics was incomplete (4.2%). For all questionnaires administered, response and completion rates were  
226 high (Supplementary Material).

227 CVAQC and IVI-C response rates were 85.87% and 90.91%, respectively. CVAQC and IVI-C scores both contain a  
228 “for other reasons” category; selection of this category is taken into account during calculation of the scores.  
229 The response rate for the PedsQL™ self-report was 96.74%, parent report 97.48% and the family report was  
230 98.32%. The proportions of fully completed questionnaires were 94.38%, 92.24% and 94.02%, respectively.

231

## 232 **Results**

### 233 **Participants**

234 The mean age (SD) of participants was 9.40 (4.56) years (Table 1). Fifty-seven participants (47.9%) were  
235 female. Seventy percent of participants were White, 4.2% Asian or Asian British, 5.9% Black or Black British,  
236 0.84% mixed, 7.56% other; ethnicity was unknown in 11.76%.

237

238 **Clinical details**

239 Fifty-two participants (43.7%) had PCG, most commonly diagnosed before the age of two years. Glaucoma  
240 following lensectomy for infantile cataract (n=32, 26.9%) was the commonest cause of secondary glaucoma  
241 (Table 1). Glaucoma was bilateral in 89 cases (74.79%), and the mean age (SD) at diagnosis was 1.56 years  
242 (2.94). Further clinical data are summarized in Table 1.

243

244 **Functional visual ability**

245 Seventy-nine children age 5-16 years completed the CVAQC. The median of the Rasch transformed scores  
246 was -1.24 (IQR -2.2 to -0.11) indicating moderate impairment of FVA (-3.00 higher visual ability to +2.80  
247 lower visual ability) (Table 2). Median scores were better in older children than in the younger age groups  
248 (Fig. 2). There was evidence of an association between CVAQC score with age, BCVA and bilateral glaucoma  
249 (Table 3).

250

251 **Vision-related quality of life**

252 Thirty children age 8-16 years completed the IVI-C. The mean score was 67.3 (SD 14.4) with 96 indicating normal VR-  
253 QoL (Table 2). The mean score was higher in older than younger children (Fig 2). There was evidence of an  
254 association between IVI-C score with age and BCVA (Table 3). Bilateral glaucoma was not associated with worse VR-  
255 QoL, but the sample size for this analysis was small (unilateral glaucoma n=10 with bilateral glaucoma n=20).

256

257 **Health-related quality of life**

258 The PedsQL™ self report was completed by 89 children, with a median score of 78.8 (IQR 67.4-90.2) with 100  
259 indicating normal HR QoL (Table 2). Self-report scores were higher in the older age groups than the younger  
260 ones but there was variability and overlap in score distribution (Fig 2). There was an association between self-  
261 report scores and BCVA but no association with laterality (Table 3) nor the number of daily eye drops,

262 operations and anesthetics ( $p$  value > 0.05, data not presented). The PedsQL™ parent report (n=116) median  
263 score was 71.2 (IQR 55.7-85.8) and family impact report (n= 117) median score was 74.3 (IQR 56.9-87.5) (Table  
264 2). Parental HR-QoL scores were lower than child self-report scores, with a mean difference of -7.901  
265 (confidence interval CI -11 to -4.8) (Fig.3).

266  
267 The median “psychosocial wellbeing” subscores were lower than the “physical wellbeing” scores. Parent report  
268 scores were lower than self-report scores, with a mean difference of -8.24 (CI -12.4 to -4.1) for physical and -  
269 8.21 (CI -11.35 to -5.1) for psychosocial subscores (Table 2).

270

## 271 **Discussion**

272 The main aim of this study was to explore the effects of childhood glaucoma (CG) on functional visual ability, vision  
273 related QoL and health related QoL, as perceived by children and their parents. A strength of our approach is that  
274 we included both children and parents, and used multiple instruments to address these questions.

275

276 Our study demonstrates that most children with glaucoma have to apply numerous eyedrops and have undergone  
277 several surgical procedures and additional general anesthetics. Children with glaucoma report a significant reduction  
278 in their VR-QoL and HR-QoL compared to normal-sighted individuals, and decreased functional visual ability.

279 Psychosocial HR-QoL is affected to a greater degree than physical HR-QoL. Although our study was not powered to  
280 detect associations, older children reported less impairment than younger children and better BCVA was associated  
281 with higher functional visual ability, VR- and HR-QoL (even when unilateral cases which may have skewed BCVA to  
282 better visual acuity were excluded). Bilateral glaucoma was associated with worse functional visual ability only.

283 With regards HR-QoL, there was no association between the number of eye drops, surgical interventions or general  
284 anesthetics and PedsQL™ self-report scores, however our sample size is likely to have limited our ability to find  
285 associations had they existed.

286 The reduction in HR-QoL in children with CG we report here is comparable to levels reported by children  
287 with severe congenital heart defects, liver transplants and acute lymphoblastic leukemia.<sup>15 16 17</sup> A previous  
288 study exploring HR-QoL in children with congenital cataract and their parents reported similarly reduced  
289 levels<sup>18</sup>. The reporting of children with glaucoma stratified by age results in the novel finding which suggests  
290 that perceived HR-QoL is higher in older children than in younger children. Possibly child and family adjust  
291 over time, and children develop a better understanding of their condition and a greater range of coping  
292 strategies to deal with their condition and visual disability.

293  
294 We found that parents report a greater impact of glaucoma on their child's HR-QoL than children themselves. A  
295 similar observation has been made in parents of children with cataract and other conditions.<sup>18,19</sup> This may be  
296 explained by parents having different expectations, and children themselves having a different benchmark for  
297 "normality".

298  
299 Our study design is prone to some bias. Firstly, enrolling children attending a single site may induce selection  
300 bias. We reduced this as far as possible by approaching consecutive patients eligible for inclusion, of which  
301 19% of families declined to take part citing time constraints. Some families may have stopped attending  
302 clinics due to dissatisfaction with the services, or unwillingness or inability to comply with intense treatment  
303 regimes. However, from clinical experience consider the overwhelming majority of parents to be eager to  
304 provide the best possible healthcare for their child. We limited inclusion to families able to communicate in  
305 English, which may induce selection bias. Lack of a control group of normally sighted children stratified by  
306 age may be considered a limitation as it may have helped determine whether the effect of age on the  
307 CVAQC and IVI-C was due to a better understanding of the questionnaire by older children. Although this is  
308 possible, these tools were completed by children within the age range for which they were developed and  
309 validated. In addition, all tools we used have either been specifically developed for children with sight

310 impairment leading to an expected ceiling effect if used in healthy children (CVAQC), or normative data are  
311 available from healthy children (IVI-C, PedsQL™). Whilst logMAR visual acuity is a well established measure  
312 of visual function, it is not always possible to use logMAR methods in children with sight impairment, and  
313 “hand movements” or “counting fingers” at a specified testing distance are still occasionally used. Complete  
314 blindness, “no perception of light”, or “artificial eye/ocular prosthesis” can also not be expressed in logMAR.  
315 In order to allow a quantitative analysis, we used logMAR values of 2.1 to 3 in these cases.<sup>10</sup> This may have  
316 led to an underestimation of logMAR acuity, however this was only necessary in 3 children.

317  
318 Within the limits of the study design, such as selection bias which may have led to inclusion of a higher  
319 proportion of more treatment-adherent families and the limitation of enrolling participants at a single site in  
320 a highly developed country, our findings can be generalized to other children with glaucoma who receive  
321 care in similar settings. But, it is possible that our study over- or underestimates the impact of glaucoma on  
322 children and their families due to the number of participants studied. Whilst treatment for glaucoma in  
323 adults is mainly medical and often successful at preserving vision, childhood glaucoma requires intensive  
324 management and frequent surgical interventions with dramatic impact on the life of affected children and  
325 also their families. It is important to highlight this multifaceted impact, and encourage its assessment to be  
326 part of the management of childhood glaucoma. More research is needed into childhood glaucoma specific  
327 instruments to better identify and measure the effect of glaucoma and its management on the quality of life  
328 on both children and their families. Along with clinical outcomes such as IOP control and visual acuity, the  
329 quality-of-life of children with glaucoma should be considered as a crucial outcome when evaluating  
330 treatment success and when comparing established with new interventions.

331

332

333

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393 **Figure legends**

394 **Fig. 1.** Enrollment, intervention and analysis flowchart (modified from CONSORT, [www.consort-statement.org](http://www.consort-statement.org) ).

395 **Fig. 2.** Box plots of median and interquartile range (IQR) Cardiff Visual Ability for Children (left), Impact of Vision  
396 Impairment for Children (center) and PedsQL™ self-report scores (right) of children with glaucoma. Overall,  
397 there is a trend towards self-reported less impairment with increasing age, however there is considerable  
398 variation in scores within age groups.

399 **Fig. 3.** Bland Altman plot showing agreement between parental and child self-report PedsQL scores. The fact so  
400 many of the points lie below the  $y = 0$  line highlights the point that parents tend to rate the impact on HR- QoL  
401 greater than the children themselves.

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408 **Table legends**

409 **Table 1.** Age at study participation and at diagnosis and clinical characteristics (top); detailed diagnostic  
410 categories of study participants and laterality of glaucoma (bottom).

411 **Table 2.** Scores for functional visual ability (FVA), vision- and health-related quality of life (VR-QoL, HR-QoL)  
412 reported by children and parents according to age and laterality. Possible CVAQC scores (FVA) extend from -3.00  
413 (higher FVA) to +2.80 (lower FVA). IVI-C scores range from 0 to 96 (severe reduction to normal VR-QoL);  
414 participants reported markedly reduced VR-QoL. PedsQL™ scores range from 0 to 100 (severe reduction to  
415 normal HR-QoL); scores were significantly reduced in all versions and subscales of the instrument (parent report,  
416 family report, self report, physical and psychosocial subscores).

417 **Table 3.** Statistical significance and strengths of associations. Younger age is significantly associated with  
418 reduced functional visual ability (CVAQC) and vision-related quality of life (IVI-C). Lower visual acuity is  
419 significantly associated with all outcome measures. Bilateral glaucoma is significantly associated with lower  
420 functional visual ability (CVAQC) and parent-reported and family health-related quality of life (PedsQL™).

421 **Supplementary Material:**

422 Table “Response and Completion Rates”. Parents were asked to complete two questionnaires, and children from  
423 the age of 5 years were asked to complete two or three questionnaires. Response and completion rates were  
424 high.

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