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Increased Incidence of Mental Disorders in Children with Cataract: Findings from a Population-based Study



MOUG AL-BAKRI, ANNE METTE SKOVGAARD, DANIELLA BACH-HOLM, DORTE ANCHER LARSEN, VOLKERT SIERSMA, AND LINE KESSEL

- **PURPOSE:** To examine the incidence of mental disorders in children with cataract compared with children without cataract.
- **DESIGN:** Nationwide cohort study based on entries in comprehensive national databases.
- **METHODS:** The incidence of mental disorders in children born between 2000 and 2017 diagnosed with cataract before 10 years of age ($n = 485$) was compared with sex- and age-matched controls ($n = 4358$). Analyses were corrected to somatic disease in the child and parental socioeconomic status and psychiatric morbidity. The study was conducted at 2 university hospitals in Denmark managing children 6 years of age or younger with cataract.
- **RESULTS:** The incidence of mental disorders was nearly doubled in children with cataract compared with controls (odds ratio [OR], 1.83; 95% CI, 1.28–3.63). The risk of anxiety disorders was quadrupled (OR, 4.10; 95% CI, 1.90–8.84) and the risk of developmental delay was doubled (OR, 2.66; 95% CI, 1.45–4.90). The risk of mental disorders was significantly higher in children diagnosed with cataract in the first 3 years of life compared with controls (OR, 2.36; 95% CI, 1.53–3.64), whereas those diagnosed with cataract later in childhood did not have an increased risk (OR, 1.24; 95% CI, 0.66–2.30).
- **CONCLUSIONS:** The risk of mental disorders, in particular anxiety and neurodevelopmental delay, is markedly increased in children with cataract and even more so in those diagnosed within the first 3 years of life. Psychiatric screening instruments may be integrated in the management of these children. (Am J Ophthalmol 2022;236: 204–211. © 2021 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>))

CLINICAL AND RESEARCH EVIDENCE POINT TO AN increased risk of mental health problems and disorders in children and adolescents suffering from chronic diseases.^{1–4} Thus, attention deficit/hyperactivity disorders and autism spectrum disorders (ASD) are more frequent among children with cerebral palsy,⁵ and anxiety and depression have been found in 1 of 4 children with epilepsy.⁶ In children with diabetes type I, an increased risk of anxiety, mood disorders, and eating disorders have been shown in the years after disease onset.⁷

Childhood cataract is a significant cause of visual disability in infancy and early childhood, affecting approximately 200,000 children worldwide.⁸ It is a chronic condition requiring intensive management.⁹ Visually disturbing cataracts can be removed by surgery,¹⁰ but prolonged and intensive visual and optical rehabilitation is required.^{11,12} Childhood cataract can occur isolated or can be seen in combination with somatic comorbidities¹³ that may be associated with neurodevelopmental disorders.^{14–20} Most cases of childhood cataract occur in early childhood,²¹ which is also the period of onset of several childhood mental disorders, in particular neurodevelopmental disorders.²² Children with cataract are more likely to come from a socioeconomically disadvantaged background,²³ which may further increase the risk of pediatric child mental disorders.^{24,25}

Two questionnaire studies based on parental reporting found a higher risk of conduct problems, learning problems, psychosomatic problems, impulsiveness/hyperactivity, and anxiety problems in children with cataract compared with children with normal vision²⁶ and a lower level of psychosocial health in children with cataract, which was similar to the psychosocial health level of children with other severe somatic diseases like rheumatological disease and cancers.²⁷

The aim of the present study was to examine the risk of mental disorders in children with childhood cataract compared with children without cataract using Danish population registries and taking into account potential confounders such as parental socioeconomic status, family psychiatric load, and the children's somatic comorbidity.

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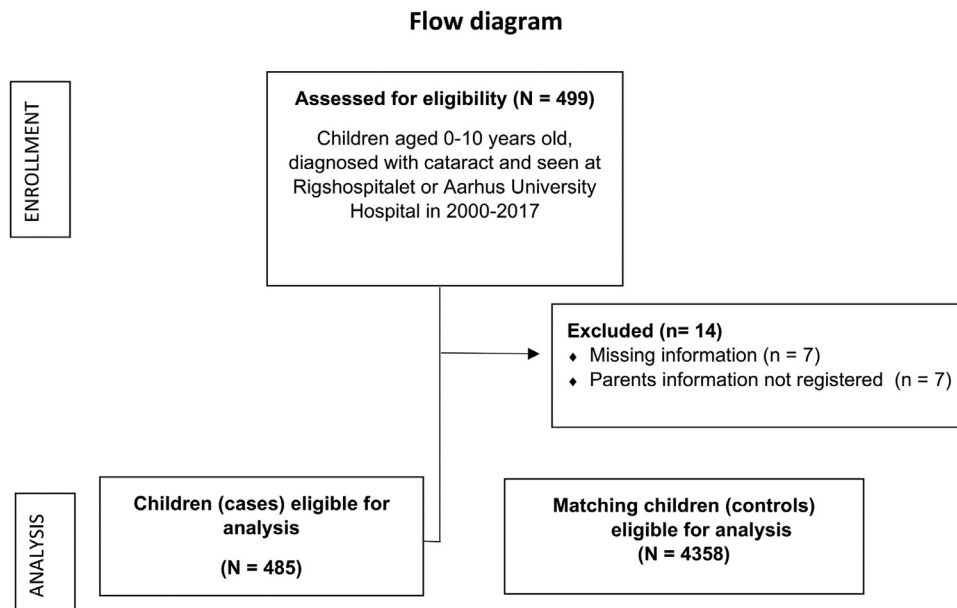


FIGURE 1. Flow chart showing inclusion and exclusion of the study population.

METHODS

- **STUDY POPULATION:** We included patients born from January 1, 2000, to December 31, 2017, who were diagnosed with cataract before age 10 years at 1 of the 2 hospitals that manage all children with cataract in Denmark: Rigshospitalet, Copenhagen, and Aarhus University Hospital, Aarhus (see Figure 1). In Denmark, each person has a unique identification number (CPR number). The CPR number is used in national administrative registries which makes it possible to link data from individuals accurately between registries. In addition, children are linked to their parents by the CPR number.

- **CONTROL POPULATION:** For each child with cataract, a sample of 10 children without cataract matched by age, sex, and municipality were sampled from the general Danish population by Statistics Denmark.²⁸

- **DATA FROM NATIONAL POPULATION REGISTRIES:** We used data from the following national registries: National Patient Registry (NPR), which contains information about diagnostic and procedural *International Classification of Diseases*, 10th edition (ICD-10) codes on all contacts to public hospitals, as in- or out-patient and including emergency settings. The Population Registry was used to access information about child sex, geographical birth origin, and parental socioeconomic status. Information regarding parental work status was extracted from the AKM registry (work classification module). Parental civil status was obtained from BEF registry (population registry) and information on parental

income was obtained from the income registry. In addition, we extracted information on parental mental disorders from the NPR (Supplementary Table 1). Any variables with fewer than 5 observations cannot be tabulated according to the policy of Statistics Denmark.

- **MENTAL DISORDERS:** The presence and type of mental disorders diagnosed during the first 10 years of life were assessed using the ICD-10 diagnostic codes (F00–F99 and R41.8, R62.0, R62.9) listed in the NPR. The latter codes for unspecific developmental delays are commonly used among Danish pediatricians and child psychiatrists to categorize unspecific developmental delay in younger children who often have more subtle and unspecific symptoms of developmental delays compared with older children.²⁹ In accordance with the latest version of the international classification schemes^{30,31} and recent research in the field,^{7,32} we grouped the mental disorders as neurodevelopmental and other mental disorders:

Neurodevelopmental disorders

Neurodevelopmental disorders included intellectual disability (F70–F79), specific developmental disorders (F80–F83), ASD (F84), unspecified developmental disorders (F88–F89), hyperkinetic disorder (F90), and unspecific developmental delay (R41.8, R62.0, R62.9).

Other mental disorders

Other mental disorders included psychoactive substance misuse (F10–F19), psychotic disorders (F20–F29), mood disorders (F30–F39), anxiety, dissociative, stress-related, and somatoform disorders (F40–F48), eating disorders

(F50), sleep disorders and medication abuse (F51–59), personality disorders (F60–F69), and other mental or behavioral disorders (F91–F99).

The term any mental disorders included all the above-mentioned diagnostic codes. Notably, a child could be diagnosed with 2 or more different mental disorders. However, each child could be counted only once in the analysis of overall incidence of any mental disorder. When exploring the risk of specific psychiatric disorders, each child could figure in more than 1 subgroup if they had more than 1 diagnosis, but only once in each category.

Somatic comorbidities

Because childhood cataract is often found in association with systemic disease or as part of a syndrome, we subgrouped the cataract population into (1) children with isolated cataract and (2) children with cataract and severe somatic comorbidities (Supplementary Table 2).

- **CONFOUNDERS:** Some somatic comorbidities were potential confounders (disease confounders) because either the disease itself or its treatment may increase the risk of cataract as well as mental disorders. This group included interstitial lung disease (J84.9 + J84.8 + J84.1) owing to treatment with high doses of prednisolone,^{33,34} congenital rubella syndrome (P35.0 + B06.0 + B06.8 + B06.9),^{15–17} congenital cytomegalovirus infection (B25.0 + B25.1 + B25.2 + B25.8 + B25.9 + P35.1),^{15,18} degenerative disease of the nervous system (G31 + G31.1 + G31.9)^{35,36} and cancer in the brain or meninges owing to radiation therapy (C70-72.9 + C76.0 + C69),^{37–39} microcephaly (Q02.9), megalencephaly (Q04.5), Smith-Lemli-Opitz' syndrome (Q87.11), trisomy 21 (Q90.0-90.2), Down's syndrome (Q90 + Q90.9), and autosomal trisomies (Q92-92.9). Severe somatic comorbidities in the cataract group are listed in Supplementary Table 2.

Children with cataract have previously been shown to be more likely to come from socioeconomically disadvantaged families²³ and many pediatric mental disorders are more prevalent in families of lower socioeconomic status.^{24,25} Hence, in addition to disease confounders, the statistical analyses were also adjusted for the geographical birth location of the child and parental socioeconomic status (income, employment, and civil status). Definition of these variables were described previously in detail²³ and are available in (Supplementary Table 3).

Because parental mental disorders may predispose to child mental disorder,⁴⁰ we adjusted for any mental disorders diagnosed at hospital (F00–F99) in 1 or both parents.

- **STATISTICAL METHODS:** The association between childhood cataract and mental disorders was assessed using odds ratios (OR) with 95% CIs in unadjusted analyses and in conditional logistic regression models, including age at onset of cataract, sex, and the confounders described else-

where in this article. Adjusted and unadjusted analyses were repeated separately in each of the 2 cataract onset age groups: 0 to 3 years and 4 to 10 years, a test for interaction was added. Statistical analyses were made using the R software package, V.3.4.1 (The R Foundation for Statistical Computing, <http://www.r-project.org>). The significance level was set at a *P* value of less than .05.

- **APPROVALS:** The study was approved by the Danish Data Protection Agency (RH-2016-336; I-Suite # 05070), and the Danish Patient Safety Authority (3-3013-1935/1/NAAN). According to the Committee on Health Research Ethics in the Capital Region of Denmark, ethical board review was not required (decision number: 16038234). The study followed the tenets of the Helsinki Declaration.

RESULTS

We included 485 children (243 boys and 242 girls) with childhood cataract and an age- and sex-matched control group (*n* = 4,358; 2,177 boys and 2,181 girls) drawn from the background population. Baseline characteristics of the study population are listed in Table 1. No difference in parental mental health was found between the 2 groups. The majority of the children in the cataract group had been operated (*n* = 282/485 [58.1%]).

The incidence of any mental disorder (21.8%), neurodevelopmental disorder (15.4%), and other mental disorder (9.0%) was significantly higher in children with cataract who had somatic comorbidities compared with children with isolated cataract (any mental disorders, 8.4%; neurodevelopmental disorders, 5.8%; and other mental disorders, 2.3%) (Table 2).

Children with cataract were twice as likely to have a mental disorder as children without cataract: 10.5% (*n* = 51/485) and 5.2% (*n* = 225/4358), respectively (OR, 1.83; 95% CI, 1.28–2.63; *P* = .0009) in analyses adjusted for geographical birth origin, somatic disease confounders, socioeconomic status, and parental mental disorders. A particularly high incidence of mental disorders was seen in children diagnosed with cataract during their first 3 years of life (*n* = 35/327 [10.7%]), compared with age-matched children without cataract (*n* = 118/2912 [4.1%]; OR, 2.36; 95% CI, 1.53–3.64; *P* = .0001), whereas we did not find a significantly increased risk in children diagnosed with cataract after 3 years of age compared with an age-matched cohort (Table 3). When we subgrouped the children with cataract and without cataract into those with and without severe somatic disease (isolated cataract), the risk of any mental disorder (adjusted OR, 1.72; 95% CI, 1.15–2.58; *P* = .009) and neurodevelopmental mental disorder (adjusted OR, 2.07; 95% CI, 1.31–3.26; *P* = .002) remained

TABLE 1. Characteristics of the Study Population.

	Children with Cataract (n = 485)	Children without Cataract (n = 4358)	P value ^a
Child's birth place, n (%)			.001 ^b
Denmark	428 (88.2)	4,030 (92.5)	
Outside Denmark	57 (11.8)	328 (7.5)	
Disease confounders ^c			<.00001 ^b
Yes	23 (4.7)	12 (0.3)	
No	462 (95.3)	4,346 (99.7)	
Parental civil status, ^d n (%)			.598
Single	52 (10.7)	519 (11.9)	
Not single	419 (86.4)	3,811 (87.4)	
Parental income ^{d,e} (DKK), mean (SD)	221,230 (101,047)	233,355 (160947)	.021 ^b
Parental work status, ^d n (%)			<.00001 ^b
Outside workforce	58 (12.0)	253 (5.8)	
One or both parent(s) at work	425 (87.6)	4,104 (94.2)	
Parental mental disorders			.192
None	398 (82.1)	3,467 (79.6)	
One or both parent(s)	87 (17.9)	891 (20.4)	

DKK = Danish Krone; SD = standard deviation.

^aP value: Likelihood ratio test in a conditional logistic regression.

^bSignificant p-value.

^cSevere somatic diseases: congenital syndrome: microcephaly, megalencephaly, Smith–Lemi–Opitz' syndrome, trisomy 21, Down's syndrome, partial autosomal trisomy, cytomegalovirus infection, interstitial lung disease, degenerative disease of the nervous system, congenital rubella infection, cancer in brain or meninges.

^dInformation on parental civil status was missing for 42 children, 28 children for parental income, and 3 for parental work status.

^eOne Danish Krone equals 0.13 Euro.

TABLE 2. Background Characteristics of Children with Cataract (n = 485).

	Isolated Cataract (n = 407)	Cataract and Severe Somatic Diseases (n = 78)	P value ^a
Sex, girls/boys, n (%)	197/210 (48.4/51.6)	45/33 (57.7/42.3)	.168
Age at cataract diagnosis (years), median (IQR)	1.4 (0.19–5.1)	0.6 (0.14–4.4)	.344
Age at surgery time (years), median (IQR)	2.1 (0.3–4.9)	0.6 (0.2–4.0)	.243
Number of operated/number of nonoperated (%)	232/175 (57.0/43.0)	50/28 (64.1/35.9)	.299
Unilateral/bilateral surgery (%)	131/101 (32.2/24.8)	12/38 (24.0/76.0)	.003 ^b
Children with any mental disorders ^c (%)	34 (8.4)	17 (21.8)	.0008 ^b
Children with neurodevelopmental disorder (%)	28 (5.8)	12 (15.4)	.023 ^b
Children with emotional/affective disorders (%)	11 (2.3)	7 (9.0)	.018 ^b

IQR = interquartile range.

^aP value: Pearson's χ^2 test for categorical variables, *t* test for continuous variables.

^bSignificant p-value.

^cEach child could be diagnosed with different mental disorders. The number of children with neurodevelopmental and other mental disorders, therefore, does not add up to the number of children with any mental disorders.

higher in those with isolated cataracts (Supplementary Table 4).

When we subgrouped the cataract children with and without cataract surgery, the risk of any mental disorder (adjusted OR, 2.26; 95% CI, 1.46–3.50; *P* = .0002), neurodevelopmental mental disorders (adjusted OR, 2.42; 95% CI,

1.46–3.99; *P* = .0006) and other mental disorders (adjusted OR, 2.34; 95% CI, 1.23–4.43; *P* = .0092), was significant higher among cataract children with surgery (Supplementary Table 5).

The risk of neurodevelopmental disorders was doubled in the cataract group (OR, 2.05; 95% CI, 1.35–3.11;

TABLE 3. Incidence of Mental Disorders among Children with and without Cataract.

	Children with Cataract	Children without Cataract	Unadjusted		Adjusted ^a	
	(n = 485)	(n = 4358)	OR (95% CI)	P value	OR (95% CI)	P value
Any mental disorders	51/485 (10.5)	225/4358 (5.2)	2.16 (1.57–2.78)	<.00001 ^b	1.83 (1.28–2.63)	.0009 ^b
0–3 years ^c	35/327 (10.7)	118/2912 (4.1)	2.84 (1.91–4.22)	<.00001 ^b	2.36 (1.53–3.64)	.0001 ^b
4–10 years ^c	16/158 (10.1)	107/1446 (7.4)	1.41 (0.81–2.45)	.224	1.24 (0.66–2.30)	.504
Neurodevelopmental disorders	40/485 (8.2)	148/4358 (3.4)	2.56 (1.78–3.67)	<.00001 ^b	2.05 (1.35–3.11)	.0007 ^b
0–3 years ^c	28/327 (8.6)	77/2912 (2.6)	3.45 (2.20–5.40)	<.00001 ^b	2.64 (1.59–4.4)	.0002 ^b
4–10 years ^c	12/158 (7.6)	71/1446 (4.9)	1.59 (0.84–3.00)	.152	1.37 (0.68–2.76)	.376
Other mental disorders	18/485 (3.7)	95/4358 (2.2)	1.73 (1.04–2.89)	.036 ^b	1.69 (1.0–2.87)	.052
0–3 years ^c	12/327 (3.7)	50/2912 (1.7)	2.18 (1.15–4.14)	.017 ^b	2.22 (1.18–4.18)	.014 ^b
4–10 years ^c	6/158 (3.8)	45/1446 (3.1)	1.23 (0.52–2.98)	.642	1.12 (0.40–2.85)	.814

OR = odds ratio.

Values are n/N (%).

^aAdjusted for parental socioeconomic status, family psychiatric load and the children's severe somatic comorbidity (congenital syndrome: microcephalia, megalencephaly, Smith–Lemi–Opitz syndrome, trisomy 21, downs syndrome, partial autosomal trisomy, cytomegalovirus infection, interstitial lung disease, degenerative disease of the nervous system, congenital rubella infection, cancer in brain or meninges)

^bSignificant p-value.

^cAge at cataract onset.

$P = .0007$) after adjustment for confounders (Table 3). The most frequent neurodevelopmental disorder was developmental delay ($n = 22/485$ [4.5%]) followed by ASD ($n = 11/485$ [2.3%]), and ADHD ($n = 6/485$ [1.2%]). The risk of developmental delay was higher in the cataract group than in the control group (OR, 2.66; 95% CI, 1.45–4.90; $P = .0017$), whereas we did not find a significantly increased risk of ASD (OR, 1.62; 95% CI, 0.78–3.39; $P = .192$) or attention deficit/hyperactivity disorders (OR, 1.31; 95% CI, 0.50–3.46; $P = .581$) in the children with cataract compared with children without cataract.

Children with cataract also had an overall higher risk of having a mental disorder of not primary neurodevelopmental origin in crude analyses (OR, 1.73; 95% CI, 1.04–2.89; $P = .036$), but became insignificant in analyses adjusting for several confounders (OR, 1.69; 95% CI, 1.0–2.87; $P = .052$). The risk of anxiety disorders was quadrupled in children with cataract ($n = 10/485$ [2.1%]; OR, 4.10; 95% CI, 1.90–8.84; $P = .0003$). In addition, an increased tendency of eating disorders was observed (OR, 4.19; 95% CI, 0.72–24.44; $P = .111$).

DISCUSSION

This study is the first to explore a broad range of mental disorders in children with cataract comparing the incidence in these children with the age- and sex-matched background population based on diagnoses made by medical doctors. We used nationwide population registries to account for the potential influences of a range of confounders, including somatic comorbidities, the socioeconomic status of the family,

and parental mental disorders. The risk of anxiety disorders was increased more than 4-fold, and the risk of neurodevelopmental delay was increased 2-fold in children with cataract. The risk was highest among children diagnosed with cataract before 3 years of age. In addition, the risk of mental disorders was highest in the group of children who had cataract in combination with systemic disease. Furthermore, mental disorders were increased for those cataract children who have undergone cataract surgery. However, it is difficult to distinguish whether the increased mental disorders is caused by the surgery itself, the visual impairment, or the pathology of the cataract.

Whereas the increased risk of neurodevelopmental disorders in children with cataract was expected, the 4-fold risk of anxiety disorders was a remarkable finding but in line with finding from studies of other chronic diseases in childhood, such as epilepsy⁶ and diabetes type I.⁷ Children with cataract are exposed to repeated examinations under anesthesia and hospital appointments and at-home patching therapy for amblyopia,^{11,41} and they may suffer from visual impairment associated with cataract, which influence social interactions, for example, response to facial expressions.^{8,42,43} It is already well-known that blind and visually impaired young people face an increased risk of depression and anxiety.^{44–46} Importantly, our incidence of anxiety disorders may be underestimated as anxiety often presents during adolescence²² and we only included children up to the age of 10 years.

For comparison, only a limited number of studies have been published in which mental health problems and disorders have been investigated in children with cataract. In a Chinese study of 119 children who were between 3 and 8 years of age, children with cataract used the Conners Par-

ent Rating Scale and found a doubling in the incidence of conduct problems, learning problems, psychosomatic, impulsiveness/hyperactivity, and anxiety problems compared with 143 children without cataract.²⁶ This study is consistent with our findings based on diagnoses made by medical doctors using the ICD-10 criteria. In a previously study of Danish children with cataract, we found that the subjective visual function related to academic achievements was rated as poor,⁴⁷ which is in line with the parental assessment of learning problems in the Chinese study. In contrast with the Chinese study, we did not find a statistically significant higher incidence of impulsiveness/hyperactivity-related diagnoses. Our study was based on mental disorders diagnosed in a hospital setting where only the most seriously affected children exceed the threshold for referral. A study of 41 British children aged 5 to 19 years with congenital cataracts found a lower psychosocial health level in these children compared with children with other systemic diseases,²⁷ which supports our findings.

Severe somatic disease may be directly linked to both development of cataract and presence of mental disease.^{14–20} We found a doubling of the risk of unspecific developmental delay disorder in children with cataract also in analyses adjusting for diseases with known neurodevelopmental comorbidity and diseases in which the treatment involves potential adverse neurodevelopmental exposures.^{33,34,37–39}

Our findings highlight the psychological burden on children living with chronic somatic disease. In some situations, the psychological load may influence treatment outcome, as shown in studies of children and adolescents with type I diabetes mellitus.^{32,48,49} The management of childhood cataract often includes patching of the better seeing eye to improve vision in the poorer seeing eye (amblyopia treatment).¹³ Compliance is essential for visual outcome in amblyopia treatment. The treatment of amblyopia can be associated with a high degree of distress, increased stigma, and logistical problems for children and parents.^{50–52} We were not able to discern whether amblyopia therapy contributed to the increased risk of anxiety in our cataract population, but attention should be paid to the mental vulnerability of the child and treatment adjusted based on a holistic perspective.

• **STRENGTHS AND LIMITATIONS:** The major strength of this population-based registry study is its nationwide character with no attrition bias. Mental disorders were diagnosed by medical doctors in hospital settings in accordance with ICD-10 diagnostic criteria. To ensure that the interaction of other confounders was minimized, we adjusted for relevant variables such as geographical birth origin, disease confounders, parental socioeconomic status, and parental mental disorders. Conversely, this study also has some limitations. There may be a risk of selection bias because children seen and treated by child psychiatrists working in private practice are not always reported into the NPR, which may result in an underestimated true incidence of mental

disorders. In addition, referral bias must be considered, because children with cataract are treated in hospital settings and therefore have a higher odds of being referred and diagnosed with a mental disorder. However, some families may also decline referral because they already have to deal with cataract, or they may interpret the child's behavior as related to the eye disease.

In this nationally representative sample, we found a markedly higher incidence of developmental disorders and anxiety among children with cataract compared with the background pediatric population. The associations between childhood cataract and mental disorders remained significant even after adjusting for relevant factors such as disease confounders and parental socioeconomic status and psychiatric disease. An increased awareness of the mental health burden associated with childhood cataract is important. Routine screening of mental health, for example, using the Strengths and Difficulties Questionnaire,⁵³ could guide the support to these children taking into account their mental health as well as overall quality of life, in the visual and optical rehabilitation.

All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.ajo.2021.09.034](https://doi.org/10.1016/j.ajo.2021.09.034).

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