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Systematic Review of Instruments for the Assessment of Patient-Reported Outcomes and Quality of Life in Patients with Childhood Glaucoma

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Topic: To identify patient-reported outcome measures (PROMs) that have been used in children and adolescents with glaucoma and to evaluate their methodologic quality.

Clinical relevance: Childhood glaucoma impairs vision and quality of life (QoL) throughout all stages of life. Thus, a PROM needs to cover many different age groups and topics. Various instruments have been used to evaluate patient-reported outcomes (PROs) in patients with childhood glaucoma, however, it is unclear which PROM has the highest methodologic quality and complies best with the needs of patients with childhood glaucoma.

Methods: A systematic literature review was performed searching MEDLINE (PubMed), the Cochrane Library, Web of Science, and PsycINFO (EBSCO). We included peer-reviewed full-text articles of the past 10 years in English, German, or Spanish language that reported PROMs in children with glaucoma. The study selection and methodologic quality assessment of the identified PROMs was performed by 2 independent reviewers using a 7-point checklist. The content was mapped onto the World Health Organization International Classification of Functioning, Disability and Health. The systematic review was prospectively registered in PROSPERO (ID CRD42022353936).

Results: The search strategy retrieved 3295 matches. A total of 2901 studies were screened, and 11 relevant articles were identified using 10 different instruments. The instruments addressed functional visual ability, vision-related QoL, health-related QoL, and life satisfaction. Six instruments were applicable for the use in children. Seven of the questionnaires received the highest number of positive ratings (5/7). None of the instruments considered the views of patients with childhood glaucoma during their development.

Conclusion: This systematic review provides a descriptive catalog of vision-specific and generic health PRO instruments that have been used in childhood glaucoma cohorts. An instrument specifically developed for childhood glaucoma is lacking which might result in missing important factors, such as permanent treatment with eye drops, repeated surgeries, and heritability of the disease, when investigating the QoL in children with glaucoma.

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Patient-reported outcome measures (PROMs) reflect patients' perceptions of their health and are useful to evaluate effectiveness of interventions. They quantify treatment benefit and harm beyond survival, morbidity, and biomarkers and are of highest relevance for patients and their environment.[1] Patient-reported outcome measures are usually represented in the form of questionnaires that may target different constructs. Quality of life (QoL) refers to physical, social, and emotional well-being and can be evaluated in relation to general health (health-related quality of life [HRQoL]) or vision (vision-related quality of life [VRQoL]). Functional status measures a patient's ability to accomplish activities of daily life[2]; in ophthalmology, visual function is a common construct used for patients who are visually impaired. Other constructs concern symptom burden or life satisfaction.

Glaucoma is the second leading cause for blindness worldwide and affects 1.4% to 2.0% of the adult population in European countries.[3] Several PROMs have been developed to measure patient-reported outcomes (PROs) in adults with glaucoma.[4–8] They have been applied in randomized controlled trials comparing treatment

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strategies[9–12] with the aim to measure their influence on patients' QoL. A lower QoL is associated with a lower probability of treatment adherence, thus, QoL potentially influences the treatment success.[13]

In contrast to adult types of glaucoma, childhood glaucoma is a rare disease with an incidence of 10 to 30 in 10 000 in European countries.[14,15] Apart from the small numbers of patients, there are challenges to use a PROM in children, e.g., childhood comprises different developmental stages and age-specific needs that must be covered by such an instrument. It is accepted that children are able to answer PROMs from the age of 5 years, but reliable and valid answers are usually not obtained before the age of 8 years.[16] Before the age of 5 years, a proxy measure is necessary.

Childhood glaucoma usually requires a surgery to prevent the child from blindness, followed by regular intraocular pressure monitoring, amblyopia prophylaxis, and potentially further surgeries or adjuvant topical antiglaucomatous therapy. It affects not only the children's visual ability and QoL,[17,18] but has also impact on their families.[19–21] Only a few studies investigated PROs in children with glaucoma. The aim of this systematic review was to identify PROMs that have been used in children and adolescents with glaucoma and to evaluate their methodologic quality.

Methods

The protocol to this systematic review was prospectively registered in PROSPERO (ID CRD42022353936). The study was deemed exempt from human subjects research by the Institutional Review Board. The study adhered to the Declaration of Helsinki.

Eligibility Criteria for Considering Studies for This Review

Included were studies investigating PROs, such as QoL or functional visual ability (FVA). Only peer-reviewed, published full-text articles in English, Spanish, and German language were included in this review. Further inclusion criterion was a study sample containing at least 50% children or adolescents (age $<$ 18 years) with glaucoma (childhood or juvenile onset, either primary or secondary). Because of the small number of matches, the age restriction was dissolved after the first title and abstract screening; thus, studies reporting on adults with childhood or juvenile onset of glaucoma were subsequently permitted. Included were further studies that were as follows: (1) developing or evaluating a PROM, or (2) reporting PROs in the abovementioned population. The PROM could be answered by the child or the caregivers.

Search Methods for Identifying Studies

The search strategy was developed by a medical librarian (L.C.O.) in consultation with topic experts (J.V.S, E.M.H, and A.A.B.) following the COSMIN recommendations.[22] A combination of MeSH and free text terms for glaucoma, children, and PROMs were used. Four databases were searched on November 4, 2022: MEDLINE (PubMed), PyscINFO (EBSCOhost), Cochrane Library, and Web of Science. The search was limited to publications from 2012 to 2022 because of the advances of health care and PROMS development in the recent years.[23] All languages were included in the search results, non-English, non-Spanish, or non-German language results were removed during the review process. For the MEDLINE (PubMed) search, a comprehensive PROM filter developed by the Patient-Reported Outcomes Measurement Group, University of Oxford,[24] a filter to identify pediatric studies[25] and an exclusion filter to remove irrelevant records, such as case reports and animal studies,[24] from the search were used. These filters were adapted to the different databases, except for the pediatric studies filter, where it was decided to use a specific search block developed by the Dutch Medical Information Specialist[26] for each database. The search strategies for all databases are available in Material S1 (available at www.ophthalmologyglaucoma.org).

Study Selection

After the references were imported in EndNote 20.0.1, duplicates were removed by the librarian (L.C.O.) following the Bramer Method.[27] Afterward, 2 independent authors (J.V.S. and E.M.H.) screened the titles and abstracts for eligibility using Covidence. The full texts were then independently assessed by the 2 authors. If different articles were selected for inclusion, the disagreement was discussed between the 2 authors and, if necessary, a third author (A.A.B.) was asked to finally decide about eligibility.

A data extraction sheet was developed according to the quality-assessment following the strategy published by previous authors.[28] For each instrument used in the identified studies, 2 independent authors (J.V.S. and E.M.H.) extracted the data from the corresponding PRO development studies. In case of disagreement, the 2 authors discussed the item and if not resolved, a third author was involved to decide (A.A.B.).

Data Collection and Quality Assessment

Two authors conducted the quality-assessment of the corresponding PRO development studies to the identified instruments using a published tool.[29] The tool is presented in Table 1. In brief, 5 criteria assess the quality of the instruments' development; 1 criterion addresses the proportion of subjects with glaucoma during the item identification process. This was adjusted to the needs of this review and patients with glaucoma were replaced by patients with childhood glaucoma. Another criterion rated English translations and validations in English speaking populations.

The assessment was graded into positive rating (✔✔), minimal acceptable rating (✔), negative rating (✖), not reported (NR), or not applicable (NA). A higher number of positive ratings resulted in a higher quality valuation. This tool tried to capture COSMIN criteria[30,31] to assess the quality of PROMs using a pragmatic approach.[28,29]

If data relevant to the abovementioned criteria were NR in the development studies, the authors of the relevant publications were contacted and asked for completion of the missing data.

Data Synthesis and Analysis

Baseline characteristics of the PROMs comprising construct, target population, mode of administration, year of publication, original language, and available translations were compiled. The instruments were categorized into either vision-specific or generic health, and child-specific or adult-targeted measures. Furthermore, each item was classified using the World Health Organization International Classification of Functioning, Disability and Health (WHO ICF).[32] The framework addresses human functioning and restrictions and contextual components. Items were classified into the following categories: body structure or function ("B"), activity ("A"), participation ("P"); as an additional category, satisfaction ("S") was added. Instruments were then classified as *vision or health impairment* measure if they only contained body structures/

Table 1. Tool for Quality Assessment[28,29]

Quality Criteria	Definition	Rating
Prestudy hypothesis	The prestudy specification of the aim of the instrument and the intended population	✔✔ A clear description is provided of the aim of the instrument and the intended population ✔ Only one of the above ✖ Neither reported
Intended population	The extent to which the instrument has been studied in the intended population	✔✔ Intended population studied ✔ Partly studied only or sample size was small (< 50 patients) ✖ Not studied in the intended population, only generic
Actual content area	The extent to which the content meets the prestudy hypothesis specifications	✔✔ Content as intended, and is relevant to the intended population ✔Some of the intended content areas missing ✖ Content area not relevant to intended population
Item identification	Selection of the items relevant to the target population for inclusion in the pilot instrument	✔✔ Comprehensive consulting with patients (focus groups or in-depth interviews) and a literature review ✔ Minimal consultation with patients and experts opinion and literature review ✖ No consultation with patients
Item selection	Determining the items included in the final instrument	✔✔ A pilot instrument was developed and tested with Rasch or factor analysis and statistical justification provided for removing items, plus items with floor and ceiling effects removed and the amount of missing data considered ✔ Only some of above techniques were used ✖ No pilot instrument OR no statistical justification of items included in the final instrument
Views of patients with childhood glaucoma considered	The percentage of patients with childhood glaucoma involved in item identification during the development of PRO instrument	✔✔ At least 50% of patients with childhood glaucoma were involved in the consultation with patients in the item identification ✔ Less than 50% patients with childhood glaucoma were involved in the consultation with patients in the item identification ✖ No patients with childhood glaucoma were involved in the consultation with patients in the item identification
Instrument translated and validated in English speaking population	The extent to which the instrument has been translated and validated in English speaking population	✔✔ Instrument translated to English and validated in English speaking population ✔ Instrument translated to English but not validated in English speaking population ✖ Instrument has not been translated to English nor validated in English speaking population

PRO = patient-reported outcome.

function. If body structures/functions, activity and participation were covered, the instrument was classified as *vision or health status* measure. When the instruments only addressed activity and participation components, they were classified as *vision or health disability* measure. Instruments containing only satisfaction components were classified as *satisfaction* measures.

Results

Study Selection

The literature research retrieved 3295 matches (Fig 1). After removing duplicates (n = 394) and excluding studies in the title and abstract screening (n = 2877), 24 studies were assessed for eligibility. Thirteen studies were excluded after full-text screening: 4 studies investigated outcomes other than PROs ("not relevant outcome"), 4 studies investigated patient populations other than children/adolescents with glaucoma or adults with childhood glaucoma ("different patient population"), no full-text was available for 3 references, and 2 references referred to qualitative studies aiming at developing a PROM. In total, 11 studies using 10 different PROMs were identified and the 10 PROMs were included in this review.[17,18,33–41]

Description of PROMs

Among the 10 reviewed PROMs, 6 were vision-specific and 4 were generic health instruments. Four of the vision-specific instruments were developed for children and/or adolescents and 2 for adult patients. Two of the generic health instruments were intended for the use in children and/or adolescents and 2 for the use in adults. Details are provided in Table 2.[42–57]

Vision-Specific Instruments for Children/Adolescents (n = 4)

Identified vision-specific instruments for children/adolescents were the Impact of Vision Impairment on Children (IVI_C),[42,43] the Cardiff Visual Ability Questionnaire for Children (CVAQC),[44] the Children's Visual Function Questionnaire (CVFQ)[45,46] and the L.V. Prasad-Functional Vision Questionnaire II (LVP-FVQ-II).[47] Two PROMs measure the VRQoL (IVI_C and CVFQ), and 2 measure functional visual ability (CVAQC and

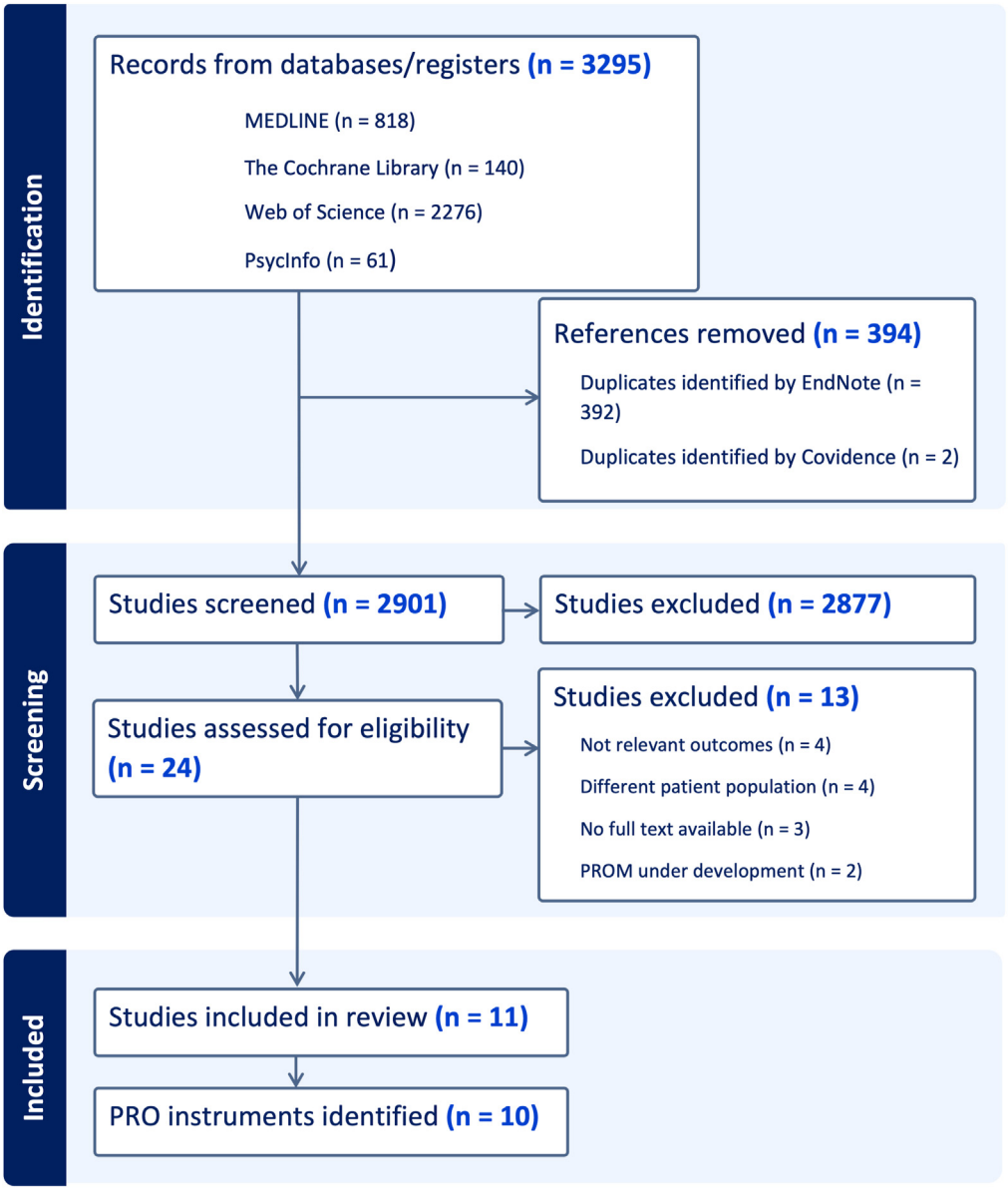

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram presenting the selection process. PRO = patient-reported outcome; PROM = patient-reported outcome measures.

LVP-FVQ-II). All of them cover body, activity, and participation content according to the WHO ICF Framework. One PROM was intended for children in developed countries (CVAQC),[44] another for children in developing countries (LVP-FVQ-II).[47] Three PROMS used a self-administered mode (IVI_C, CVAQC and LVP-FVQ-II), 1 a proxy-administered mode (CVFQ). The CVFQ further differed from the other PROMs by addressing children aged $\leq$ 7 years; 2 versions are available covering both children aged $<$ 3 years and of $\geq$ 3 years.

Vision-Specific Instruments for Adults (n = 2)

Two vision-specific instruments developed in adult populations were identified, the 25-Item National Eye Institute Visual Function Questionnaire (NEI VFQ-25)[48] and the Glaucoma Quality of Life-15 (GQL-15).[5] Both PROMs measure VRQoL and contain body, activity, and participation content according to the WHO ICF Framework. The GQL-15 is a glaucoma-specific measure. The NEI VFQ-25 is available in both self-administered and interview-based modes, the GQL-15 uses a self-administered approach. The NEI VFQ-25 has been translated into 95 languages.

Generic Health Instruments for Children/Adolescents (n = 2)

Two generic health instruments for children and/or adolescents were identified, the Pediatric Quality of Life Inventory Version 4.0 (PedsQL 4.0),[50] and the KIDSCREEN-27.[52] Pediatric Quality of Life Inventory Version 4.0 measures activity and participation content, KIDSCREEN-27 is related to body, activity, participation, and satisfaction content. For both instruments, the construct to be investigated is health-related QoL, PedsQL 4.0 has an additional

Table 2. Details on the Identified Patient-Reported Outcome Measures

PROM	Construct	Target Population	Therapeutic Area/ Indication	Mode Of Administration	Year Of Publication	Original Language	Available Translations	Strengths	WHO ICF Content
IVI_C[42,43]	VRQoL	Children (8 −18 yrs)	Eye diseases/ vision disorders	Self-report	2010	English	2 translations*	Positive item phrasing	B, A, P
CVAQC[44]	FVA	Children and young people (5 −18 yrs) in developed countries	Eye diseases/ vision disorders	Self-report	2010	English	7 translations*		B, A, P
CVFQ[45,46]	VRQoL	Children ≤ 7 yrs	Eye diseases/ vision disorders	Proxy-report	2007	English	3 translations*	Two instruments: (a) < 3 yrs (b) ≥ 3 yrs	B, A, P
LVP-FVQ-II[47]	FVA	Children (8 −17 yrs) in developing countries	Eye diseases/ vision disorders	Self-report	2012	Indian English	2 translations[47]	Specific for developing countries	B, A, P
NEI VFQ-25[48]	VRQoL	Adults	Eye diseases/ vision disorders	Self-report, interview-based	2001	English	95 translations*		B, A, P
GQL-15[5,49]	VRQoL	Adults	Glaucoma	Self-report	2003	English	6 translations*	Glaucoma-specific	B, A, P
PedsQL 4.0[50,51]	HRQoL, role functioning	Children and adolescents (2−18 yrs)	Generic	Self-report, proxy-report	2001	English	See www.pedsql.org	6 versions: toddlers (2−4 yrs), young child (5−7 yrs), child (8−12 yrs), adolescent (13−18 yrs), young adult (18 −25 yrs), and adults (≥ 26 yrs)	A, P
Kidscreen-27[52−54]	HRQoL	Children and adolescents	Generic	Self-report, proxy-report	2001	Czech, Dutch, English, French, German, Greek, Hungarian, Polish, Spanish, Swedish	50 translations*	Developed simultaneously in 13 European countries	B, A, P, S

(*Continued*)

Table 2. (Continued.)

PROM	Construct	Target Population	Therapeutic Area/ Indication	Mode Of Administration	Year Of Publication	Original Language	Available Translations	Strengths	WHO ICF Content
WHOQOL-BREF[55,56]	HRQoL	Adults	Generic	Self-report	1998	Croatian, Dutch, English, French, Hebrew, Japanese, Russian, Spanish, Thai	78 translations*	Developed simultaneously in several countries	B, A, P, S
SWLS[57]	Life satisfaction	Adults	Generic/ lifestyle	Self-report	1985	English	37 translations*	Short and universal	S

The references refer to the PROM development studies.
A = activity; B = body structure and/or function; CVAQC = Cardiff Visual Ability Questionnaire for Children; CVFQ = Children's Visual Function Questionnaire; FVA = functional visual ability; GQL-15 = Glaucoma Quality of Life-15; HRQoL = health-related quality of life; ICF = International Classification of Functioning, Disability and Health; IVI_C = Impact of Vision Impairment on Children; LVP-FVQ-II = L.V. Prasad-Functional Vision Questionnaire II; NEI VFQ-25 = 25-Item National Eye Institute Visual Function Questionnaire; P = participation; PedsQL 4.0 = Pediatric Quality of Life Inventory Version 4.0; PROM = patient-reported outcome measures; S = satisfaction; SWLS = Satisfaction with Life Scale; VRQoL = vision-related quality of life; WHOQOL-BREF = World Health Organization Quality of Life-BREF.
*Source of translation numbers: https://eprovide.mapi-trust.org (accessed June 19th, 2023).

focus on role functioning. Both are available in self-report and proxy-report modes. The PedsQL 4.0 instrument exists in 6 different age-specific versions. A strength of KIDSCREEN-27 is the simultaneous development in 13 European countries.

Generic Health Instruments for Adults (n = 2)

There were 2 generic health instruments for adults identified, the brief version of World Health Organization Quality of Life (WHOQOL-BREF)[55] and the Satisfaction with Life Scale (SWLS).[57] World Health Organization Quality of Life-BREF covers body, activity, participation, and satisfaction subjects targeting the construct of HRQoL. It was simultaneously developed in 15 international field centers. Satisfaction with Life Scale is a brief instrument consisting of 5 short questions regarding life satisfaction that universally fit for every country, age, and time.

WHO ICF Framework Classification

Six instruments were classified vision status measures (IVI_C, CVAQC, CVFQ, LVP-FVQ-II, NEI VFQ-25, and GQL-15). Two instruments were classified health status measures with satisfaction components (KIDSCREEN-27 and WHOQOL-BREF). One instrument was classified a health disability measure (PedsQL 4.0), another was categorized as satisfaction measure (SWLS).

Quality

The results of the quality assessment of the identified instruments are presented in Table 3. Altogether, none of the instruments' development studies reported whether the view of children with glaucoma was considered. The participants involved in the development studies of the vision-specific instruments for children/adolescents were closest to the target population, namely visually impaired and aged > 18 years; however, the diseases were only roughly classified and the proportions of children with glaucoma remain unclear. The authors of the development studies were contacted for more information, however, the eye conditions were not precisely recorded or the authors did not respond. Similarly, the generic instruments for children were developed in both healthy and children who were chronically ill, but the proportion of visually impaired children or children with glaucoma was not specified. The adults' questionnaires were developed in adults, thus children with glaucoma were not considered.

All PROMs were developed and validated in English language, so the translation criterion was NA (not applicable).

In the group of vision-specific instruments for children/adolescents, IVI_C, CVAQC, and LVP-FVQ-II performed well. Children's Visual Function Questionnaire was inferiorly rated because of the item identification and selection process. Pediatric Quality of Life Inventory Version 4.0 and KIDSCREEN-27, as generic health instruments for children/adolescents, were also rated well in all categories except the childhood glaucoma patients' view and the language category. In the group of vision-specific instruments for adults, only the NEI VFQ-25 was rated well; the GQL-15 was rated with one tick in categories 1 to 5, because of incomplete description of the prestudy hypothesis, small sample size, missing content areas, minimal consultation with patients during the item identification, and inferior methods for item selection. Regarding the generic health instruments for adults, the SWLS was rated worse than the WHOQOL-BREF, which reached

Table 3. Quality Assessment of the Content Validity of Included Instruments

PRO Instrument	Prestudy Hypothesis	Intended Population	Actual Content Area	Item Identification	Item Selection	Views of CG Patients Considered	Translated and Validated in English Speaking Population
IVI_C	✔✔	✔✔	✔✔	✔✔	✔✔	NR	NA
CVAQC	✔✔	✔✔	✔✔	✔✔	✔✔	NR	NA
CVFQ	✔✔	✔✔	✔✔	✔	✔	NR	NA
LVP-FVQ-II	✔✔	✔✔	✔✔	✔✔	✔✔	NR	NA
PEDQL	✔✔	✔✔	✔✔	✔✔	✔✔	NR	NA
KIDSCREEN-27	✔✔	✔✔	✔✔	✔✔	✔✔	NR	NA
NEI VFQ-25	✔✔	✔✔	✔✔	✔✔	✔✔	NR	NA
GQL-15	✔	✔	✔	✔	✔	NR	NA
SWLS	✔✔	✔	✔✔	x	✔	NR	NA
WHOQOL-BREF	✔✔	✔✔	✔✔	✔✔	✔✔	NR	NA

CG = childhood glaucoma; CVAQC = Cardiff Visual Ability Questionnaire for Children; CVFQ = Children's Visual Function Questionnaire; GQL-15 = Glaucoma Quality of Life-15; IVI_C = Impact of Vision Impairment on Children; LVP-FVQ-II = L.V. Prasad-Functional Vision Questionnaire II; NA = not applicable; NEI VFQ-25 = 25-Item National Eye Institute Visual Function Questionnaire; NR = not reported; PedsQL 4.0 = Pediatric Quality of Life Inventory Version 4.0; SWLS = Satisfaction with Life Scale; WHOQOL-BREF = World Health Organization Quality of Life-BREF.

5 of 7 good ratings, because the questionnaire was only validated in undergraduates and elderly people; because the target population was not involved in the item identification process; and because of limited use of techniques for item selection.

Discussion

This systematic review identified 10 different PROMs that have been used in cohorts of children and adolescents with glaucoma. Four of them were developed to measure vision-specific constructs in children and adolescents and 2 in adults. Two PROMs were generic health instruments for children and adolescents, 2 were generic health instruments for adults. None of the instruments was specifically developed for use in children or adolescents and none of them reported that the view of patients with childhood glaucoma was considered during the development process. To ensure content validity, the population, which the PROM was developed in and for, should correspond to the intended population.[29,31] Although this criterion was rated as "not reported" for the included PROMs, it can be assumed that only an insignificant number of children contributed to the development studies. Thus, none of the identified questionnaires can be unreservedly recommended for evaluation of QoL in children or adolescents with glaucoma.

Seven out of 10 identified PROMs received the highest number of positive ratings (5/7). In the group of vision-specific instruments for children/adolescents, these were the IVI_C,[42,43] the CVAQC,[44] and the LVP-FVQ-II.[47] The PedsQL 4.0[50,51] and the KIDSCREEN-27[52,53] both received 5 of 7 positive ratings in the group of generic health instruments for children/adolescents, and so did the NEI VFQ-25[48] in the group of vision-specific instruments for adults, and the WHOQOL-BREF[55,56] in the group of generic health instruments for adults.

The IVI_C is the children-specific version of the former IVI.[58] However, it is not a derived version, as the IVI_C newly developed using focus groups, which included visually impaired children, parents, and class teachers of visually impaired children, and specialist instructors.[42] It has been used to evaluate the vision-related QoL in childhood glaucoma cohorts from Saudi Arabia,[33] United Kingdom,[18,35] United States of America,[36] and India.[17] The IVI_C score ranges from 0 to 96, a lower score indicating a higher VRQoL. In the childhood glaucoma populations, mean scores of moderate to good scores were achieved.[33,36] Gothwal et al[17] found that the VRQoL measured with the IVI_C was significantly higher in children with better visual acuity (VA) and with primary than with secondary glaucoma.

The CVAQC was also developed using focus groups, which comprised both visually impaired and normally sighted children and adolescents.[44] The items target FVA in daily activities, such as education, social interaction, sports, getting around, but also near and distance vision. The Rasch-transformed scale ranges from − 3.0 (higher FVA) to + 2.8 (lower FVA). The visual ability of children or adolescents with childhood glaucoma using the CVAQC was evaluated in the United Kingdom[18,35] and Saudi Arabia.[33] The studies found a moderate impairment of FVA ranging from − 0.68[33] in the Saudi Arabian cohort and − 1.24[18] in the UK cohort, to − 1.42[35] in another UK cohort, in which primary aim was to investigate the FVA in children with cataracts; thus, the proportion of childhood glaucoma was only 51%, which might be partly responsible for the better FVA results. Functional visual ability was associated with lower VA, greater number of eye drops and surgeries, and bilaterality of disease.[18,33]

The LVP-FVQ-II was developed for children in developing countries. It assesses the self-reported difficulties in performing daily tasks, i.e., the FVA, of visually impaired school-going children.[47] The content was identified from both focus groups and already existing questionnaires (LVP-FVQ-II, IVI_C, and CVAQC). One study from India reported that higher VA in the better eye, primary congenital glaucoma compared with secondary childhood glaucoma and unilateral disease compared with bilateral disease were independently associated with a higher FVA. Furthermore, children with > 1 glaucoma surgery reported worse FVA.[17]

The PedsQL 4.0 is a generic health score for children measuring HRQoL in the domains physical, emotional, social, and school functioning. The instrument was derived from former versions of PedsQL, for which the content identification was performed using focus groups and cognitive interviews.[50,51] The PROM has been used in 2 UK cohorts, 1 comprising children with glaucoma,[18] and 1 both children with cataract and glaucoma.[35] The scores were comparable with 78.8 in the glaucoma and 76.1 in the cataract and glaucoma cohort (score ranging from 0−100, 100 indicating a normal HRQoL). The scores were positively associated with higher VA and the psychosocial HRQoL is affected to a higher degree than physical HRQoL. The scores were comparable with scores measured in children with severe congenital heart defects, with occurred liver transplants or even with acute lymphoblastic leukemia.[18,35]

The KIDSCREEN-27 is derived from the longer 52-item version, assessing HRQoL across the 5 dimensions physical well-being, psychological well-being, autonomy and parent relation, peers and social support, and school environment. The 52-item version was developed using focus groups across 13 European countries.[52−54] Gothwal et al[39] investigated the HRQoL in children with primary congenital glaucoma after glaucoma surgery[39] and the agreement on HRQoL with their parents.[41] They found that older children had a better HRQoL than younger children; laterality, duration since surgery and VA were not associated.[39] The parent−child agreement was low, parents both overestimating and underestimating their children's reports.[41]

The NEI VFQ-25 is a reduced version of the vision-specific 51-item for adults. It covers 12 subscales: general health, general vision, near vision, distance vision, driving, peripheral vision, color vision, ocular pain, role limitations, dependency, social function, and mental health.[48] It was applied to cohorts of childhood glaucoma from Iran[37] and Spain.[38] The results of the subscales differed between the studies, which might be explained by the high number of subscales and low case numbers. Miraftabi et al[37] found a decrease of general and peripheral vision, general health, and social functioning scores, and Moreno et al[38] of near and distance vision, social functioning, dependency, and peripheral vision scores with increasing visual field mean deviation.

The WHOQOL-BREF instrument is also a shortened version of the former 100-item WHOQOL questionnaire. It is a generic instrument measuring HRQoL in adults and covers the 4 domains physical health, psychological health, social relationships, and environment.[55] The instrument was applied to an Indian childhood glaucoma cohort and found that patients living in rural regions and with longer education had a better HRQoL score. Other variables, that have been associated with QoL using other instruments, such as visual field, surgeries, or medications, did not influence the HRQoL measured by WHOQOL-BREF.[40]

The selection of a PROM to measure QoL in children with glaucoma must be made carefully. Some generic health instruments seem to be less responsive to discriminate between the levels of glaucoma severity, which results in the detection of more general influencing factors, such as age, education, or living environment[39,40] instead of mean deviation of visual field, number of surgeries and eye drops or laterality and severity of disease, which are associated with vision-specific instruments.[17,18,33,35,36] Because no instrument has been developed for the specific purpose of patients with childhood glaucoma yet, we cannot exclude that there might be factors we have not considered yet that possibly influence the QoL in these patients. Knight et al[19] conducted the qualitative interview studies with children with glaucoma, adults with glaucoma and caregivers of childhood glaucoma patients to identify content for a childhood glaucoma-specific PROM.[59,60] They reported that children and adults with childhood glaucoma worry about their future and particularly about occupational career. Further, inconveniences of appointments with their ophthalmologists, anxieties about more surgeries and about the family planning were frequently addressed topics in the studies. They are insufficiently covered by the PROMs identified with this systematic review and pose possible influencing factors of QoL in patients with childhood glaucoma.

A limitation of this systematic review was the restriction to English, German, and Spanish language. Studies in other languages might have used a PROM, which was not included to this review. Furthermore, the literature search was restricted to the past 10 years due to new developments in childhood glaucoma therapy, such as microcatheter-illuminated circumferential trabeculotomy, and due to the change of requirements for children in the digital age. However, using this approach older, more childhood glaucoma-specific PROMs might have been missed.

Conclusion

To date, there is no instrument that has been developed for measurement of QoL or other PROs in children or adolescents with glaucoma. Most of the instruments that already have been used in childhood glaucoma cohorts received good ratings regarding their quality and development for their intended populations; however, generic health instruments might be less responsive to disease specific factors than vision-specific instruments. A childhood glaucoma-specific instrument might possibly complement to the identification of QoL-impairing factors and help to improve the treatment and care of patients with childhood glaucoma.

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Abbreviations and Acronyms:
CVAQC = Cardiff Visual Ability Questionnaire for Children; **CVFQ** = Children's Visual Function Questionnaire; **FVA** = functional visual ability; **GQL-15** = Glaucoma Quality of Life-15; **HRQoL** = health-related quality of life; **IVI_C** = Impact of Vision Impairment on Children; **LVP-FVQ-II** = L.V. Prasad-Functional Vision Questionnaire II; **NEI VFQ-25** = 25-Item National Eye Institute Visual Function Questionnaire; **PedsQL 4.0** = Pediatric Quality of Life Inventory Version 4.0; **PRO** = patient-reported outcome; **PROM** = patient-reported outcomes measure; **QoL** = quality of life; **SWLS** = Satisfaction with Life Scale; **VA** = visual acuity; **VRQoL** = vision-related quality of life; **WHO ICF** = World Health Organization International Classification of Functioning, Disability and Health; **WHOQOL-BREF** = World Health Organization Quality of Life-BREF.

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