Quality of Life Research (2022) 31:991–1011
https://doi.org/10.1007/s11136-021-02986-z

REVIEW

Quality of life of parents with children with congenital abnormalities: a systematic review with meta-analysis of assessment methods and levels of quality of life

Marisa Garcia Rodrigues[1,2] · Matilde Monteiro Soares[2,3] · José Daniel Rodrigues[2] · Luís Filipe Azevedo[2,3] · Pedro Pereira Rodrigues[2,3] · José Carlos Areias[4,5] · Maria Emília Areias[5,6]

Accepted: 26 August 2021 / Published online: 5 September 2021

Abstract

Purpose To quantify and understand how to assess the quality of life and health-related QoL of parents with children with congenital abnormalities.

Methods We conducted a systematic review with meta-analysis. The search was carried out in 5 bibliographic databases and in *ClinicalTrials.gov*. No restriction on language or date of publication was applied. This was complemented by references of the studies found and studies of evidence synthesis, manual search of abstracts of relevant congresses/scientific meetings and contact with experts.

We included primary studies (observational, quasi-experimental and experimental studies) on parents of children with CA reporting the outcome quality of life (primary outcome) of parents, independently of the intervention/exposure studied.

Results We included 75 studies (35 observational non-comparatives, 31 observational comparatives, 4 quasi-experimental and 5 experimental studies). We identified 27 different QoL instruments. The two most frequently used individual QoL instruments were WHOQOL-Bref and SF-36. Relatively to family QoL tools identified, we emphasized PedsQL FIM, IOFS and FQOL. Non-syndromic congenital heart defects were the CA most frequently studied. Through the analysis of comparative studies, we verified that parental and familial QoL were impaired in this population.

Conclusions This review highlights the relevance of assessing QoL in parents with children with CA and explores the diverse QoL assessment tools described in the literature. Additionally, results indicate a knowledge gap that can help to draw new paths to future research. It is essential to assess QoL as a routine in healthcare providing and to implement strategies that improve it.

Keywords Systematic review · Meta-analysis · Quality of life · Parents · Children · Congenital abnormalities

✉ Marisa Garcia Rodrigues
marisaigrodrigues@gmail.com

Matilde Monteiro Soares
matsoares@med.up.pt.com

José Daniel Rodrigues
jdmrodrigues@gmail.com

Luís Filipe Azevedo
lazevedo@med.up.pt

Pedro Pereira Rodrigues
pprodrigues@med.up.pt

José Carlos Areias
jcareias@med.up.pt

Maria Emília Areias
metega@sapo.pt

[1] Centro Hospitalar Universitário São João (CHUSJ), Porto, Portugal

[2] Centro de Investigação em Tecnologias e Serviços de Saúde (CINTESIS), Faculdade de Medicina da Universidade do Porto (FMUP), Porto, Portugal

[3] Departamento Medicina da Comunidade, Informação e Decisão em Saúde MEDCIDS, Faculdade de Medicina da Universidade do Porto (FMUP), Porto, Portugal

[4] Unidade de Investigação Cardiovascular da Faculdade de Medicina da Universidade do Porto (UnIC), Porto, Portugal

[5] Faculdade de Medicina da Universidade do Porto (FMUP), Porto, Portugal

[6] Instituto Universitário de Ciências da Saúde (IUCS), Unidade de Investigação Cardiovascular da Faculdade de Medicina da Universidade do Porto (UnIC), Porto, Portugal

Introduction

Congenital abnormalities (CA), also known as birth defects, congenital disorders or congenital malformations, are defined by the World Health Organization (WHO) as structural or functional anomalies that occur during intrauterine life [1]. They can be detected in the prenatal period, at birth, or sometimes only later [1].

CA does not affect only children; parents and the entire family are affected too [2, 3]. A CA's diagnosis comes unexpectedly to parents and challenges their expectations of the perfect and healthy newborn [4]. Parents face a double challenge: on one hand, transition to parenthood and, on the other, the news of pre or postnatal diagnosis of a CA with its medical, personal, social and economic consequences [4, 5]. In this context, it is understood that the birth of a child with a CA implies a reorganization of family roles and functions [5].

Literature reports that parents experience several mental health problems such as anxiety, depression and somatization [6, 7] and a reduction in quality of life (QoL) [3–5, 8–10]. This negative impact may persist over time with extensive emotional, familial and financial costs [3, 11].

Fewer psychosocial resources and less support are risk factors to higher psychological distress and lower QoL for both the parent and the child [3, 11].

The most common type of CA are congenital heart defects (CHD) [12]. They account for nearly one-third of all *major* CA [13]. The reported birth prevalence of CHD varies widely among studies worldwide. The estimate of 8 per 1000 live births is generally accepted as the best approximation [13].

The improvement of survival rates has directed attention to factors that affect the child's outcomes, both at short and long-term [10]. Most studies focus on CA's physical and psychosocial consequences for the child and pay little attention to the relationship between this condition and their parents' QoL [10]. However, a growing number of questionnaires developed to evaluate the QoL of parents/caregivers and families of children with chronic illness or disability shows the improved recognition of the importance of this subject [2]. Rempel and Harrison (2007) reported that parents' and families' factors might have a bigger impact on CHD child's outcomes than heart defect type or surgical palliation course [14]. The impairment of parental mental health was consistently related to the increased risk of child maltreatment and developmental differences achieved by the children [10].

The definition of *health* by the WHO, in 1946, as a "state of complete physical, mental and social well-being and not merely the absence of disease or infirmity", was an important mark in history [15]. WHO Quality of Life Group (WHOQOL Group) argues that the ideal health assessment should be multidimensional and measure physical health; physical, social and psychological functioning; and QoL [16].

The term *quality of life* (QoL) has gained prominence. The reduction of mortality, and the consequent increase in the average life expectancy as a result of the evolution of Medicine and Public Health, imposed a shift of the paradigm in the assessment of health outcomes [17]. In other words, measures of morbidity and mortality became insufficient to translate health outcomes [17]. Although health is an essential domain of QoL, other domains such as culture, values, and spirituality are key components of this concept and add complexity to its measurement [18].

The definition of QoL is far from being consensual [19]. However, there is a core concept that is common to most definitions. It is well summarized by WHOQOL definition as "an individual's perception of their position in life in the context of the culture and value systems in which they live and concerning their goals, expectations, standards and concerns" [20]. This definition points out three fundamental aspects of QoL: (A) that it is subjective; (B) includes both positive and negative facets of life; and (C) it is a multidimensional construct [21]. In this way, QoL allows a broad and holistic assessment of health outcomes in research and clinical settings [2, 6].

At the end of the twentieth century, a new concept of *health-related quality of life* (HRQOL) had emerged to encompass the aspects of QoL that influence health [22]. Centers for Diseases Control and Prevention (CDC) defined HRQOL like "an individual's or population's perceived physical and mental health over time" [23]. From the individual perspective, HRQOL includes physical and mental health perceptions and their correlates, including health risks and conditions, functional status, social support, and socioeconomic status [23]. The community perspective includes community-level resources, conditions, policies, and practices that influence a population's health perceptions and functional status [23].

Considering all the reasons mentioned, it is easy to understand that QoL assessment presents a real challenge.

Surprisingly, there is no systematic review exploring QoL or HRQOL of parents with children with CA, in the literature. The appropriate assessment of these outcomes of this vulnerable population is an essential part of planning, execution and evaluation of strategies to maximize outcomes of all family members [2, 10, 11]. This study's primary purpose was to identify the different assessment tools used to evaluate the QoL and HRQOL of parents with children with CA. A second aim is to analyze the quantitative assessments of QoL and HRQOL described in this population. This systematic review will allow us to establish informed recommendations to guide policy, clinical care, and research.

Methods

Search

The search was carried out in the bibliographic databases: MEDLINE (Pubmed), SCOPUS, Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL) and PsycINFO. To identify ongoing clinical trials, we also searched in *ClinicalTrials.gov*. The query search development was an iterative process in which controlled vocabulary, free text, synonyms, and related terms were used, connected by Boolean operators. We used three main concepts: parents, CA and QoL. The query search and respective adaptations to different databases are presented in online Appendix 1. Last search was done on 15th August 2020. No restriction on language or date of publication was applied.

The search was complemented by references of the studies found and studies of evidence synthesis. In addition, we conducted a manual search of abstracts of relevant congresses and scientific meetings held in the last five years (online Appendix 1). Lastly, experts in this field were also contacted as well as the authors of the articles found, in case of additional clarification was required.

Study selection

The inclusion criteria considered were (1) primary studies on parents of children with CA independently of the intervention/exposure studied; (2) reporting the outcome QoL or HRQOL of parents of children with CA; (3) observational, quasi-experimental or experimental studies. Other types of studies like qualitative studies, letters, systematic reviews, narrative reviews, and case-reports were excluded.

It is important to explain some operational aspects of inclusion criteria. First, we considered studies whose population was composed of children's caregivers when ≥80% were parents. Second, the age limit of Pediatrics is a controversial issue, and the literature discourages the establishment of an arbitrary age limit on pediatric care, especially in the case of children with special health care needs [24]. However, because we need to establish our study population, we adopted the definition of the *American Academy of Pediatrics*, published for the first time in 1988 and reaffirmed in the most recent recommendations, which consider the upper limit as 21 years old [25–27]. Third, in case of doubt, if the health condition studied should be considered a CA, we consulted the MeSH (Medical Subject Headings) terms database of the U.S. National Library of Medicine.

In the screening, we only analyzed the article's title and abstract. During the inclusion phase, all potential candidates were selected by reading their integral text. Both phases were carried out by two reviewers (MGR and MMS), blindly and independently. The reason for exclusion was recorded using an eligibility checklist – online Appendix 2. The method of resolution of disagreements was a third reviewer (JDR). The reproducibility of the selection process was evaluated using the proportion of agreement.

Data extraction

Data were collected through a specific form which was subjected to a pilot study. We extracted the following characteristics: general characteristics of the study (aim, study design, time frame, setting, sample size and sampling), sociodemographic characteristics of the sample (sex, age, marital status, and socioeconomic status), children clinical status characterization (type of CA, severity of disease and children's age), methods of assessment and results of parental outcomes QoL and HRQOL. Whenever possible, summary measures of the quantitative scores for different constructs and their respective estimates of precision were extracted (when necessary, the authors were contacted). As in the selection phase, the extraction was carried out by two reviewers (MGR and JDR), blindly and independently, and a third reviewer was used as a method for solving disagreements (MMS).

Risk of bias (quality) assessment

Considering that the review included several types of studies, we evaluated the studies' quality by adapting different recommendations. For observational studies, we selected five items from *STROBE Statement (STrengthening the Reporting of OBservational studies in Epidemiology)*: 3 from the methods section (6. Participants, 7. Variables and 8. Data sources/measurements) and 2 from the results section (13. Participants and 14. Outcome data). The *Cochrane Collaboration's tool for assessing risk of bias* was used for experimental studies assessment. The quality evaluation was performed by two reviewers (MGR and JDR), blindly and independently. Disagreements between the reviewers were solved by a third reviewer (MMS).

Strategy for data synthesis

The qualitative synthesis aimed to identify the instruments used to assess parents' QoL and HRQOL. In this analysis, studies were organized by type of study, CA, and outcome assessment method.

We can classify clinical studies as experimental, quasi-experimental and observational. We have considered observational studies when no controlled intervention was

applied. Observational studies can be mainly classified as cross-sectional when there only one contact with the participants, measuring both exposure and outcome variables simultaneously, or longitudinal, when the participants' follow-up after exposure is conducted. In experimental studies, participants are randomly allocated to receive or not a specific controlled intervention, while in quasi-experimental studies allocation is conducted without random procedures.

Relatively to the outcome, we consider the following division: the instruments that assessed individual QoL/HRQOL and the ones that measure the family QoL, in other words, the family impact of having a child with a CA. The QoL' tools were grouped as generic and disease-specific tools.

The quantitative data extracted from the primary studies were analyzed to decide whether it was suitable to perform quantitative synthesis through a meta-analysis. This quantitative analysis aimed to estimate the QoL/HRQOL in this population and, more importantly, assess, explore, and explain differences found across studies. When mothers and fathers' results were presented separately, we used mothers' results in the meta-analysis because, in more than half of all included studies, the samples had more than 50% of mothers (in 42.5% more than 80% of the participants were mothers).

However, we acknowledge that in most of the studies, when the two populations are analyzed separately, mothers had worse QoL when compared with fathers (online Appendix 3).

Whenever meta-analytical measures were presented, heterogeneity was evaluated using the Cochran Q test (significance level of 0.05), supplemented by the I2 statistic. For all meta-analysis we used the Random Effects Model. In case of severe heterogeneity (I2 > 40–50%), which impeded to obtain an aggregate measure of QoL, the exercise of an explanatory attempt of variability was carried out.

EndNote® software was used for reference management. Covidence® software was used in the selection phase and data extraction. With the help of Open Meta-Analyst® software, quantitative data were analyzed.

This study followed the orientations included in *Cochrane Handbook for Systematic Reviews of Interventions* and *PRISMA Statement*.

Results

Search

Figure 1 presents the flow chart of the selection process with mention of reasons for exclusion. We found 5616 records, 5604 from the bibliographic databases and 12 from other sources (references of the studies found and studies of evidence synthesis). From these, 1962 were identified as duplicates and removed. We screened 3654 records and excluded 3488 of them. The proportion of agreement for the screening phase was 0.95. In the inclusion phase, we reviewed the full-text of 166 papers and excluded 79. The proportion of agreement was 0.94. We identified 87 reports that met the inclusion criteria comprising 75 original primary studies (12 are companion reports of the same study [28–39]). Only in 51 of them, we were able to extract quantitative data.

Description of studies

Table 1 presents a summary of the included studies. A more detailed characterization is presented in the online Appendix 3. The included studies were published from 2002 through 2020. Considering the type of study, we included 35 (46.7%) observational non-comparatives studies [40–74], 31 (41.3%) observational comparatives studies [5, 75–104], 4 (5.3%) quasi-experimental studies [8, 105–107] and 5 (6.7%) experimental studies [108–112]. It is important to refer that 2 of the experimental studies are study protocols, so the results are not known yet.

The included studies were performed in 27 countries. Their distribution by continents is the following: Europe ($n = 32$), Asia ($n = 16$), North America ($n = 13$); South America ($n = 6$); Africa ($n = 6$) and Australia ($n = 2$).

A total of 9334 participants were assessed (range 15 to 1092 per study). In some studies, only part of the sample fulfilled the inclusion criteria of our systematic review (due to children's age range [58, 59, 61, 66, 73] or the health condition considered [8, 61, 78, 91, 97]).

Forty-one studies (56.2%) included fathers and mothers; sixteen studies (21.9%) included parents without other specification; fifteen studies (20.5%) included mothers solely; and one study (1.4%) did not provide information about the distribution of participants' family relationship with the child (caregivers).

We grouped the included studies by type of CA, considering the following categories: non-syndromic CHD ($n = 25$; 33.3%); Genetic Syndromes ($n = 16$; 21.3%); Craniofacial Malformations (CFM) ($n = 12$; 16.0%); Neural Tube Defects ($n = 7$; 9.3%); non-specific CA ($n = 6$; 8.0%); Urogenital Abnormalities ($n = 2$; 2.7%); and other CA, if they did not belong to any of the anterior categories ($n = 7$; 9.3%) – online Appendix 4. The severity of CA studied was very wide. Considering CHD's example, they could be as simple as asymptomatic CHD like Atrial Septal Defects to complex CHD as Hypoplastic Left Heart Syndrome.

In Table 2 we presented the different QoL assessment tools used in the included studies. We identified 27 different QoL instruments (online Appendix 5). Along with these instruments, two others were developed/adapted by authors.

The QoL assessment tools could be divided into individual QoL and family QoL assessment tools. Each one of these groups comprised generic and disease-specific instruments.

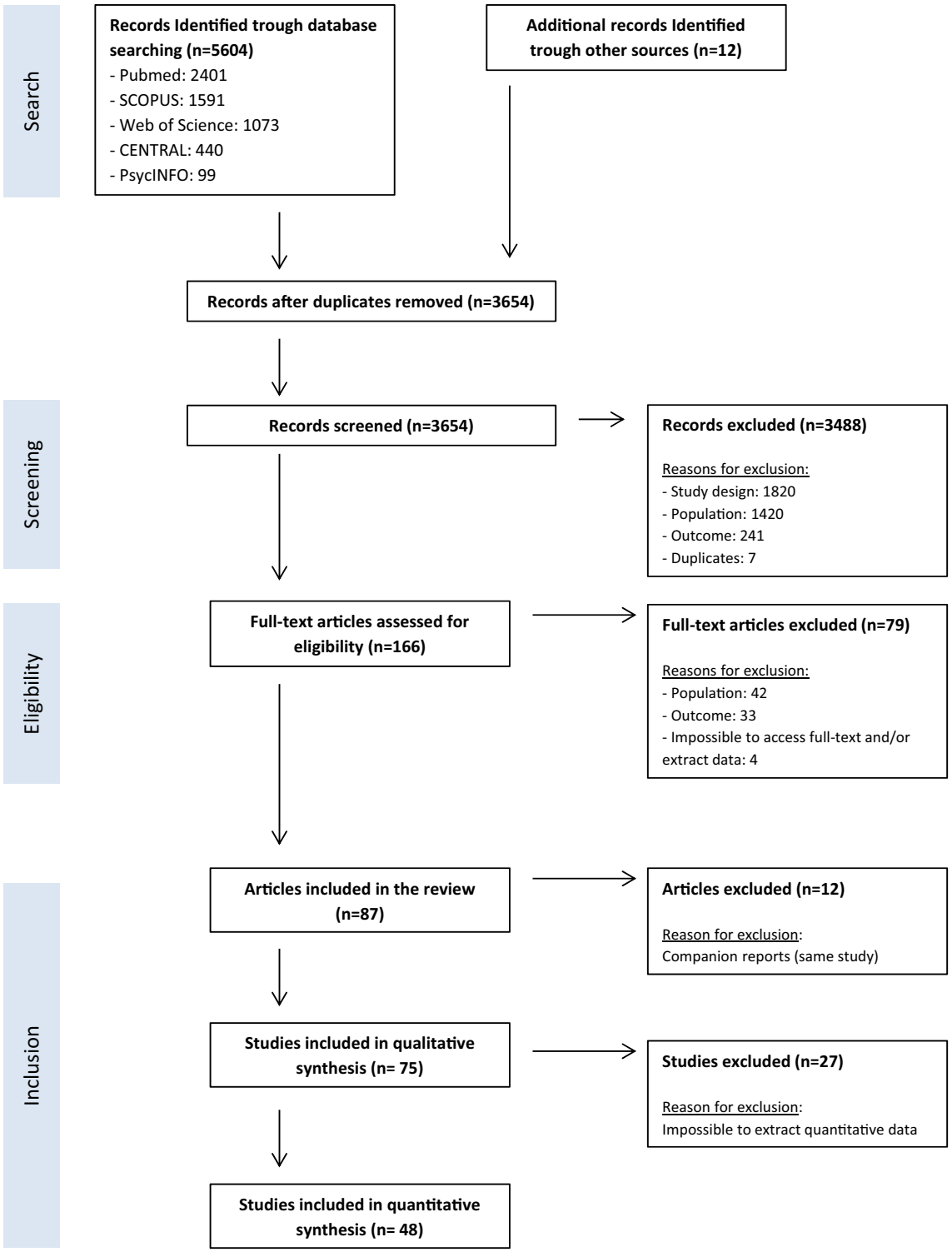

Fig. 1 Flow chart illustrating study selection process following PRISMA (Preferred reporting items for systematic reviews and meta-analyses) statement

The two most frequently used individual QoL instruments were WHOQOL-Bref and SF-36 (19 and 18 studies, respectively). The family QoL instruments identified most

Table 1 Description of included studies by country, study design, sample size, number of parents, congenital abnormalities, children's age range and parental QoL assessment tool

Study	Country	Design	Sample size	No. of parents, (% mothers)	Congenital abnormalities	Children's age range	QoL assessment tools	Observations
Observational non-comparative studies								
Albuquerque et al. (2012)[*1] [40]	Portugal	Cross-sectional	124	124 (50.0)	Congenital abnormalities	0 to 6 year	WHOQOL-Bref	
Albuquerque et al. (2013)[*1] [28]	Portugal	Cross-sectional	90	90 (50.0)	Congenital abnormalities	0 to 6 year	WHOQOL-Bref	
Alpern et al. (2017) [41]	USA	Cross-sectional	130	130 (68.5)	Disorders of sex development	0 to 6 year	QOL-DSD-Parent	
Awoyale et al. (2016) [52]	Nigeria	Cross-sectional Mixed-method	107	99 (92.6)	Orofacial clefts	1 month to 5 year	IOFS	
Azhar et al. (2016) [63]	Saudi Arabia	Cross-sectional	199	195 (90.3)	Congenital heart diseases	5 month to 16 year	Questionnaire adapted by the authors	180 families
Bektas et al. (2020) [68]	Turkey	Cross-sectional	124	114 (91.9)	Congenital heart diseases	1 to 18 year	WHOQOL-Bref	
Beluci et al. (2019) [69]	Brazil	Cross-sectional	77	74 (96.1)	Orofacial clefts	3 to 6 month	WHOQOL-Bref	77 family caregivers
Bevilacqua et al. (2013) [70]	Italy	Cross-sectional	76	76 (50.0)	Congenital heart diseases	0 to 3 month	SF-36	
Carter et al. (2013) [71]	USA	Cross-sectional	29	24 (86.2)	Potocki-Lupski Syndrome	–	PedsQL FIM	
Close et al. (2016) [72]	USA	Cross-sectional Mixed-method	40	33 (82.5)	Klinefelter Syndrome	0 to 26 year[a]	FQOL	
De Cuyper et al. (2019) [73]	Belgium	Cross-sectional study	45	45 (–)	Orofacial clefts	6 month to 6 year	IOFS FIS CarerQoL	A very extensive questionnaire that included the 3 validated instruments
Geok et al. (2013) [42]	Malaysia	Cross-sectional	161	161 (100)	Down Syndrome	0 to 18 year	WHOQOL-Bref	
Goldbeck et al. (2006)[*2] [43]	Germany	Cross-sectional	132	121 (94.2)	Congenital heart diseases	0 to 21 year	ULQIE	
Goldbeck et al. (2005)[*2] [29]	Germany	Cross-sectional	69	58 (84.1)	Congenital heart diseases	7 to 20 year	ULQIE	
Gregory (2019) [44]	USA	Cross-sectional	62	62(50)	Congenital heart diseases	under 6 year	PedsQL FIM	
Ihara et al. (2014) [45]	Japan	Cross-sectional	45	45 (100)	Prader-Willi Syndrome	6 to 19 year	WHOQOL-Bref	Study primarily designed to assess children
Kapoor et al. (2014) [46]	India	Cross-sectional	70	70 (–)	Down Syndrome	–	WHOQOL	
Kramer et al. (2007) [47]	Germany	Cross-sectional	260	260 (50.0)	Non-syndromic orofacial clefts	6 to 24 month	IOFS	130 families
Kumari et al. (2018) [48]	India	Cross-sectional	51	51 (100)	Esophageal atresia	up to 5 year	WHOQOL-Bref	

Table 1 (continued)

Study	Country	Design	Sample size	No. of parents, (% mothers)	Congenital abnormalities	Children's age range	QoL assessment tools	Observations
Levert et al. (2017) [49]	Netherlands	Cross-sectional	161	161 (47.2)	Congenital heart diseases	0 to 18 year	Linear Analog Scale	
Mao et al. (2019) [50]	China	Cross-sectional	32	28 (53.1)	Prader-Willi Syndrome	ranging from 6.1 to 71.2 month	WHOQOL-Bref	
Mazer et al. (2008) [51]	Netherlands	Longitudinal	147	147 (51.7)	Congenital abnormalities	6 wk. to 6 month	ICCAP SF-36	2 measurement moments
Molinas et al. (2008) [53]	France	Cross-sectional	292	292 (50.0)	Prader-Willi Syndrome	0 to 20 year	WHOQOL-Bref	146 families
Oliveira et al. (2011) [54]	Brazil	Cross-sectional	31	29 (75.9)	Down Syndrome	0 to 16 year	WHOQOL-Bref	
Ortiz-Quiroga et al. (2018) [55]	Colombia	Cross-sectional	51	50 (72.0)	Birth defects associated to disability	0 to 16 year	FQOL	40 families
Patjanasoontorn et al. (2010) [56]	Thailand	Cross-sectional	27	27 (–)	Orofacial clefts	–	THAICLEFT QoL questionnaire	27 families
Payakachat et al. (2011) [57]	USA	Cross-sectional	65	65 (98.5)	Craniofacial malformations	0 to 17 year	HUI3; SF-6D; QWB-SA; CarerQoL	
Sadhwani et al. (2019) [58]	USA	Cross-sectional	301	–	Angelman syndrome	Up to 60 year[a]	FQOL	301 caregivers
Sampogna et al. (2013) [59]	Italy	Cross-sectional	62	50 (100)	Recessive dystrophic epidermolysis bullosa	< 5 until > 35 year[a]	FDLQI	
Sawin et al. (2002) [60]	USA	Cross-sectional	60	60 (–)	Spina bifida	12 to 21 year	VA item: family's QoL	
Silva et al. (2020) [74]	Brazil	Cross-sectional	254	231 (90.9)	Congenital heart diseases	1 to 10 year	WHOQOL-Bref	
Steel et al. (2011) [61]	Belgium	Cross-sectional Mixed-method	25	25 (96.0)	Intellectual disability (includes families with Down Syndrome children)[b]	3 to 28 year[a]	FQOLS-2006	Only the families of Down Syndrome children (N = 9) fulfill the inclusion criteria
Stoffel et al. (2017) [62]	Switzerland	Longitudinal Mixed-method	15	15 (53.3)	Hypoplastic left heart syndrome or other types of univentricular malformations	*Neonates/Infants* (< 1 Year)	SF-36	4 measurement moments
Tonsello et al. (2017) [64]	France	Cross-sectional	33	33 (–)	Gastroschisis	*Newborns*(> 1 month)	SF-36	Study primarily designed to evaluate infants
Valença et al. (2012) [65]	Brazil	Cross-sectional	43	40 (95.0)	Meningomyelocele and neurogenic bladder	0 to 15 year	SF-36	

Table 1 (continued)

Study	Country	Design	Sample size	No. of parents, (% mothers)	Congenital abnormalities	Children's age range	QoL assessment tools	Observations
van't Veer et al. (2008) [66]	Kenya	Cross-sectional	40	40 (100)	Spina bifida	0 to 22 year[a]	Questionnaire designed by authors	
Warnakulasooriya et al. (2020) [67]	Sri Lanka	Cross-sectional	422	377(89)	Congenital heart diseases	–	WHOQOL-Bref	
Observational comparative studies								
Alkan et al. (2017) [75]	Turkey	Cross-sectional	80[c]	80 (100)	Congenital heart diseases	6 to 16 year	SF-36	
Allam et al. (2018) [86]	Egypt	Cross-sectional	60[c]	60 (–)	Congenital heart diseases	7 to 18 year	PCASEE QoL	
Arafa et al. (2008) [97]	Egypt	Cross-sectional	400[c]	400 (–)	Heart disease (congenital—CHD—and rheumatic heart diseases—RHD)[b]	–	SF-36	Only the parents of children with CHD (N = 270) fulfill the inclusion criteria[b]
Aslan et al. (2018) [99]	Turkey	Cross-sectional	148[c]	148 (50.0)	Non-syndromic orofacial clefts	0 to 18 year	WHOQOL-Bref	
Bannink et al. (2010) [100]	Netherlands	Cross-sectional	110[c]	110 (73.6)	Syndromic or complex craniosynostosis	2 to 18 year	SF-36	
Carrada et al. (2019) [101]	Brazil	Cross-sectional	144[c]	144 (50)	Down Syndrome	4 to 18 year	FIS	144 families
Choi et al. (2019) [102]	Korea	Cross-sectional	86[c]	86 (–)	Down Syndrome	4 to 18 year	WHOQOL-Bref	
Civilibal et al. (2014) [103]	Turkey	Cross-sectional	30[c]	30 (100)	Spina bifida with neurogenic bladder	–	SF-36	
Denniss et al. (2019) [104]	Australia	Cross-sectional	87[c]	87 (100)	Complex congenital heart disease	1 to 5 year	PedsQL FIM	
Dinc et al. (2019) [76]	Turkey	Cross-sectional	75[c]	75(100)	Down Syndrome	1 to 36 month	WHOQOL-Bref-TR	
Eagleson et al. (2013) [77]	Australia	Cross-sectional	57[c]	57 (94.0)	Complex congenital heart disease	2 to 18 year	PedsQL FIM	Study primarily designed to evaluate children 60 families
Fonseca et al. (2012)[*3] [5]	Portugal	Cross-sectional	84[c]	84 (50.0)	Congenital abnormalities	*Infants* (< 1 Year)	WHOQOL-Bref	
Fonseca et al. (2014)[*3] [32]	Portugal	Longitudinal	79[c]	79 (54.4)	Congenital abnormalities	From disclosure of diagnosis to 6 month	WHOQOL-Bref	2 measurement moments
Fonseca et al. (2016)[*3] [33]	Portugal	Longitudinal	72[c]	72 (50.0)	Congenital abnormalities	From disclosure of diagnosis to 6 month	EUROHIS-QOL-8	2 measurement moments
Hatzmann et al. (2008)[*4] [78]	Netherlands	Cross-sectional	533[c]	533 (85.0)	Several chronic illnesses, including Down Syndrome and Spina bifida[b]	1 to 19 year	TAAQoL	Only Down Syndrome and Spina Bifida (N = 121) fulfill the inclusion criteria[b]

Table 1 (continued)

Study	Country	Design	Sample size	No. of parents, (% mothers)	Congenital abnormalities	Children's age range	QoL assessment tools	Observations
Marchal et al. (2013)[*4] [34]	Netherlands	Cross-sectional non-comparative	98[c]	98 (85.7)	Down Syndrome	6 to 8 year	TAAQoL	
Marchal et al. (2016)[*4] [35]	Netherlands	Longitudinal	124[c]	124 (64.5)	Down Syndrome	11 to 13 year	TAAQoL	2 measurement moments
Kaugars et al. (2018) [79]	USA	Cross-sectional	54[c]	54 (–)	Congenital heart diseases	3 to 13 year	PedsQL FIM	54 families
Khoshhal et al. (2019) [80]	Saudi Arabia	Cross-sectional	120[c]	120 (56.7%)	Congenital heart diseases	1 to 10 year	WHOQOL-Bref	
Kubota et al. (2016) [81]	Japan	Cross-sectional	68[c]	68 (100)	Congenital diaphragmatic hernia Anorectal anomalies Esophageal atresia	6 to 17 year	WHOQOL-Bref	
Kun et al. (2013) [82]	China	Cross-sectional	143[c]	143 (–)	Orofacial clefts	–	GQOLI-74	
Landolt et al. (2011) [83]	Switzerland	Longitudinal	232[c]	232 (58.2)	Congenital heart diseases	0 to 16 year	SF-36	2 measurement moments
Lawoko et al. (2003) [84]	Sweden	Cross-sectional	1092[c]	1092 (61.2)	Congenital heart diseases	0 to 20 year	GQL	
Michel et al. (2013) [85]	France	Cross-sectional	32[c]	32 (–)	Congenital diaphragmatic hernia	2 to 14 year	SF-36	32 families
Poley et al. (2012) [87]	Netherlands	Cross-sectional	306[c]	306 (52.6)	Anorectal malformation Congenital diaphragmatic hernia	1 to 11 year	EQ-VAS EQ-5D	
Ridosh et al. (2016) [88]	USA	Cross-sectional (secondary analysis)	112[c]	112 (93.8)	Spina bifida	12 to 21 year	FQOL	
Sileshi et al. (2017) [89]	Ethiopia	Cross-sectional	135[c]	135 (100)	Congenital heart diseases	–	SF-36	
Suorsa et al. (2015)[*5] [90]	USA	Comparative Cross-sectional	51[c]	51 (52.4)	Disorders of sex development	0 to 2 year	SF-36	
Wolfe-Christensen et al. (2017)[*5] [36]	USA	Quasi-experimental	49	49 (55.1)	Disorders of sex development	6 to 23 month	SF-36	2 measurement moments
Ellens et al. (2017)[*5] [37]	USA	Quasi-experimental	45	45 (62.5)	Disorders of sex development	11 to 41 month	SF-36	3 measurement moments
Tekinarslan (2013) [91]	Turkey	Cross-sectional	252[c]	252(100)	Down Syndrome, Cerebral Palsy and Autism Spectrum Disorder[b]	3 to ≥ 18 year	WHOQOL-Bref	Only Down Syndrome (n = 38) fulfill the inclusion criteria[b]
Tilford et al. (2005) [92]	USA	Cross-sectional	98[c]	95 (99.0)	Spina bifida	0 to 17 year	QWB scale	

Table 1 (continued)

Study	Country	Design	Sample size	No. of parents, (% mothers)	Congenital abnormalities	Children's age range	QoL assessment tools	Observations
Weigl et al. (2005) [93]	Germany	Cross-sectional	50[c]	50 (100)	Orofacial clefts	1 to 10 year	SF-36	
Werner et al. (2019) [94]	Switzerland	Cross-sectional	126	126 (–)	Congenital heart diseases	3 to 18 year	SF-36	Only children with cardiac rhythm devices and structural CHD fulfill the inclusion criteria[b]
Witt et al. (2018) [95]	Germany	Cross-sectional	87	87(54.0)	Esophageal atresia	2 to 17 year	SF-8	49 families
Witvliet et al. (2016) [96]	Netherlands	Longitudinal	40[c]	40 (50.0)	Anorectal Malformation Hirschsprung Disease	0 to 18 year	WHOQOL-Bref	2 measurement moments
Witvliet et al. (2014)[*6] [38]	Netherlands	Cross-sectional	86[c]	86 (51,2)	Anorectal Malformation Hirschsprung Disease	0 to 13 year	WHOQOL-Bref	
Yanyan et al. (2015)[*6] [98]	China	Cross-sectional	115[c]	115 (–)	Orofacial clefts	–	GQOLI-74	
Quasi-experimental studies								
Emeka et al. (2017) [105]	Nigeria	Quasi-experimental	94	94 (–)	Orofacial clefts	1 to 48 month	IOFS	94 families 2 measurement moments
Macho et al. (2017) [106]	Slovakia	Quasi-experimental	40	40 (–)	Orofacial clefts	0 to 1 year	IOFS	40 families 2 measurement moments
Nanigian et al. (2008)[*7] [39]	USA	Observational comparative Cross-sectional	92[c]	92 (–)	Spina bifida[b]	4 to 16 year	FICQOL survey	
Ok et al. (2011)[*7] [107]	USA	Quasi-experimental	23	23 (–)	Spina bifida	–	FICQOL survey	2 measurement moments
West et al. (2009)[*8] [8]	Germany	Quasi-experimental	129	129 (58.9)	Chronic illnesses (includes Congenital heart diseases)[b]	–	ULQIE	Only the parents of children with CHD (N = 129) fulfill the inclusion criteria[b] 3 measurement moments
Goldbeck et al. (2011)[*8] [30]	Germany	Quasi-experimental	130	130 (–)	Chronic illnesses (includes Congenital heart diseases)[b]	4 to 17 year	ULQIE	Study primarily designed to evaluate children Only the parents of children with CHD (N = 130) fulfill the inclusion criteria[b] 3 measurement moments

Table 1 (continued)

Study	Country	Design	Sample size	No. of parents, (% mothers)	Congenital abnormalities	Children's age range	QoL assessment tools	Observations
Experimental studies								
Du et al. (2017) [108]	China	Randomized controlled trial	Target: 300	Target: 300 (–)	Congenital heart diseases	0 to 5 year	SF-36	*Study protocol* 4 measurement moments
Edraki et al. (2014) [109]	Iran	Randomized controlled trial	56	56 (100)	Congenital heart diseases	0 to 12 year	SF-36	3 measurement moments
Hancock et al. (2018) [110]	USA	Randomized controlled trial	38	38 (100)	Congenital heart diseases	*Fetus*	PedsQL FIM	2 measurement moments
van der Mheen et al. (2018)[*9] [31]	Netherlands	Randomized controlled trial	Target: 90	Target: 90 (–)	Congenital heart diseases	4 to 7 year	SF-36	*Study protocol* 2 measurement moments
van der Mheen et al. (2019)[*9] [111]	Netherlands	Randomized controlled trial	154	154 (52.6)	Congenital heart diseases	2 to 8 year	SF-36	93 families 2 measurement moments
Zou et al. (2020) [112]	China	Randomized controlled trial	Target: 190	Target: 190 (–)	Congenital ear malformation	0 to 3 d	SF-12	*Study protocol* 3 measurement moments

[*] *Companion reports (same study)*:

[a] Only a part of the sample, relative to pediatric age, would be included in our study

[b] Only a part of the sample, with congenital abnormalities, would be included in our study

[c] Sample size of study group

[*1]Albuquerque et al. (2012) [40], Albuquerque et al. (2013)[28]

[*2]Goldbeck et al. (2006) [43], Goldbeck et al. (2005)[29]

[*3]Fonseca et al. (2012) [5], Fonseca et al. (2014) [32], Fonseca et al. (2016)[33]

[*4]Hatzmann et al. (2008) [78], Marchal et al. (2013) [34], Marchal et al. (2016)[35]

[*5]Suorsa et al. (2015) [90], Wolfe-Christensen et al. (2017) [36], Ellens et al. (2017)[37]

[*6]Witvliet et al. (2014) [38], Yanyan et al. (2015)[98]

[*7]Ok et al. (2011) [107], Nanigian et al. (2008)[39]

[*8]West et al. (2009) [8], Goldbeck et al. (2011)[30]

[*9]van der Mheen et al. (2018) [31], van der Mheen et al. (2019)[111]

Table 2 QoL assessment tools used in the included studies

	CarerQoL	FIS	FQOL	GQOLI-74	IOFS	PedsQL FIM	QWS	SF-36	ULQIE	WHO-QOL-Bref	Others[a]
Observational non-comparative studies											
Albuquerque et al. (2012) [40][b]										✓	
Alpern et al. (2017) [41]											✓
Awoyale et al. (2016) [52]					✓						
Azhar et al. (2016) [63]											✓
Bektas et al. (2020) [68]										✓	
Beluci et al. (2019) [69]										✓	
Bevilacqua et al. (2013) [70]								✓			
Carter et al. (2013) [71]						✓					
Close et al. (2016) [72]			✓								
De Cuyper et al. (2019) [73]	✓	✓			✓						
Geok et al. (2013) [42]										✓	
Goldbeck et al. (2006) [43][c]									✓		
Gregory (2019) [44]						✓					
Ihara et al. (2014) [45]										✓	
Kapoor et al. (2014) [46]											✓
Kramer et al. (2007) [47]					✓						
Kumari et al. (2018) [48]										✓	
Levert et al. (2017) [49]											✓
Mao et al. (2019) [50]										✓	
Mazer et al. (2008) [51]								✓			✓
Molinas et al. (2008) [53]										✓	
Oliveira et al. (2011) [54]										✓	
Ortiz-Quiroga et al. (2018) [55]			✓								
Patjanasoontorn et al. (2010) [56]											✓
Payakachat et al. (2011) [57]	✓						✓				✓
Sadhwani et al. (2019) [58]			✓								
Sampogna et al. (2013) [59]											✓
Sawin et al. (2002) [60]											✓
Silva et al. (2020) [74]										✓	
Steel et al. (2011) [61]											✓
Stoffel et al. (2017) [62]								✓			
Tonsello et al. (2017) [64]								✓			
Valença et al. (2012) [65]								✓			
van't Veer et al. (2008) [66]											✓
Warnakulasooriya et al. (2020) [67]										✓	
Observational comparative studies											
Alkan et al. (2017) [75]								✓			
Allam et al. (2018) [86]											✓
Arafa et al. (2008) [97]								✓			
Aslan et al. (2018) [99]										✓	
Bannink et al. (2010) [100]								✓			
Carrada et al. (2019) [101]		✓									
Choi et al. (2019) [102]										✓	
Civilibal et al. (2014) [103]								✓			
Denniss et al. (2019) [104]						✓					
Dinc et al. (2019) [76]										✓	
Eagleson et al. (2013) [77]						✓					

Table 2 (continued)

	CarerQoL	FIS	FQOL	GQOLI-74	IOFS	PedsQL FIM	QWS	SF-36	ULQIE	WHO-QOL-Bref	Others[a]
Fonseca et al. (2012) [5][d]										✓	
Hatzmann et al. (2008) [78][e]											✓
Khoshhal et al. (2019) [80]										✓	
Kaugars et al. (2018) [79]						✓					
Kubota et al. (2016) [81]										✓	
Kun et al. (2013) [82]				✓							
Landolt et al. (2011) [83]								✓			
Lawoko et al. (2003) [84]											✓
Michel et al. (2013) [85]								✓			
Poley et al. (2012) [87]											✓
Ridosh et al. (2016) [88]			✓								
Sileshi et al. (2017) [89]								✓			
Suorsa et al. (2015) [90][f]								✓			
Tekinarslan (2013) [91]										✓	
Tilford et al. (2005) [92]							✓				
Weigl et al. (2005) [93]								✓			
Werner et al. (2019) [94]								✓			
Witt et al. (2018) [95]											✓
Tekinarslan (2013) [91][g]										✓	
Yanyan et al. (2015) [98]				✓							
Quasi-experimental studies											
Emeka et al. (2017) [105]					✓						
Macho et al. (2017) [106]					✓						
Ok et al. (2011) [107][h]											✓
West et al. (2009) [8][i]									✓		
Experimental studies											
Du et al. (2017) [108]								✓			
Edraki et al. (2014) [109]								✓			
Hancock et al. (2018) [110]						✓					
van der Mheen et al. (2018)[j] [31]								✓			
van der Mheen et al. (2019) [111]											✓
n total	2	2	4	2	5	6	2	18	2	19	18

Individual QoL

Family QoL

[a]*Instruments used only in one study*: EQ-5D; FDLQI; FICQOL; FQOLS-2006; GQL; HUI3; ICCAP; Linear Analog Scale; PCASEE QoL; QOL-DSD Parent; SF-6D; SF-8; SF-12; TAAQoL; THAICLEFT QoL; VA item – Family's QoL; WHOQOL; Questionnaire developed by authors

Companion reports (same study):

[b]Albuquerque et al. (2012) [40], Albuquerque et al. (2013) [28]

[c]Goldbeck et al. (2006) [43], Goldbeck et al. (2005) [29]

[d]Fonseca et al. (2012) [5], Fonseca et al. (2014) [32], Fonseca et al. (2016)[33]

[e]Hatzmann et al. (2008) [78], Marchal et al. (2013) [34], Marchal et al. (2016)[35]

[f]Suorsa et al. (2015) [90], Wolfe-Christensen et al. (2017) [36], Ellens et al. (2017)[37]

[g]Witvliet et al. (2014) [38], Yanyan et al. (2015) [98]

[h]Ok et al. (2011) [107], Nanigian et al. (2008) [39]

[i]West et al. (2009) [8], Goldbeck et al. (2011) [30]

[j]van der Mheen et al. (2018) [31], van der Mheen et al. (2019) [111]

frequently in included studies were PedsQL FIM, IOFS and FQOL (6, 5 and 4 studies, respectively).

In online Appendix 6 we explored the characteristics of the QoL instruments more used that we mentioned above, including their psychometric properties.

Risk of bias (quality) assessment

In online Appendix 7 we presented the results of the studies' quality evaluation. Twenty-one included studies (28.0%) had at least one parameter classified as *High risk*. Eighteen studies (24.0%) had two or more parameters classified as *Unclear*. Only eleven studies (14.7%) had all items scored as *Low risk*.

The item with the worse risk of bias assessment was outcome data, in the results section, which was classified as *High risk* in 14 studies.

Quantitative analysis

From de 75 studies included in the review, in 24 of them, we could not obtain QoL quantitative summary measures despite our efforts contacting the authors. Only 19 observational non-comparatives studies, 25 observational comparative studies, 4 quasi-experimental studies and 3 experimental studies could be considered in the quantitative analysis (online Appendix 8).

Because the outcome assessment instruments/tools were very heterogeneous, we decided to analyze only the two most frequently used: SF-36 ($n = 13$) and WHOQOL-Bref ($n = 12$) – online Appendix 9.

From the 13 that utilized SF-36, 7 of them studied CHD. The remaining 6 studies included the following CA: gastroschisis, congenital diaphragmatic hernia, disorders of sex development, syndromic craniosynostosis and neural tube defects with neurogenic bladder.

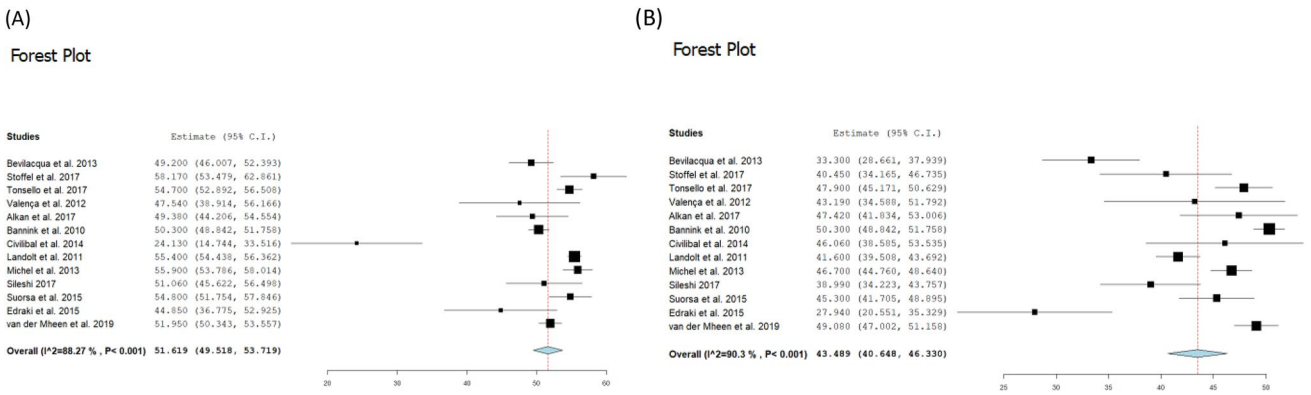

Fig. 2 Forest plots of SF-36 Physical Component Summary (**A**) and Mental Component Summary (**B**) scores of meta-analysis included studies. (Meta-analysis of SF-36 scores obtained by parents of children with congenital abnormalities (using random effects model). Physical Component Summary (PCS) and Mental Component Summary (MCS) scales are standardized and norm-based (mean of 50 and standard deviation of 10). Higher scores correspond to better QoL)

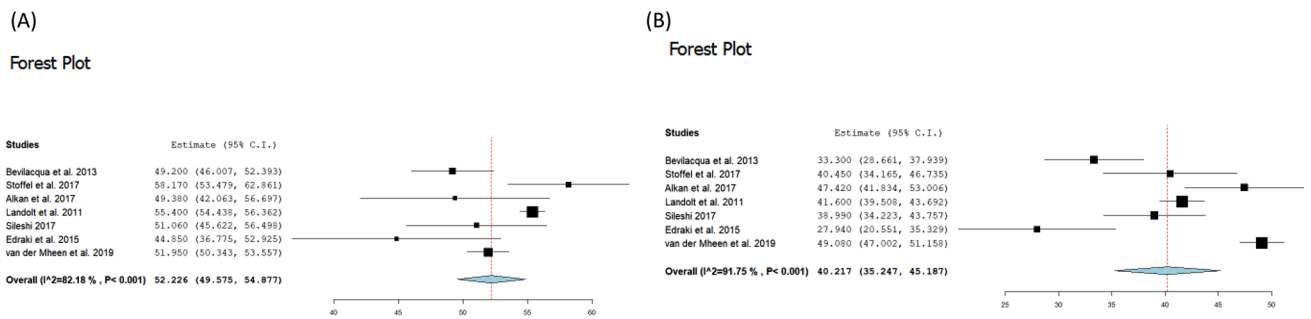

Fig. 3 Forest plots of SF-36 physical component summary (**A**) and mental component summary (**B**) of CHD subgroup of meta-analysis included studies. (Meta-analysis of SF-36 scores obtained by parents of children with CHD (using random effects model). Physical Component Summary (PCS) and Mental Component Summary (MCS) scales are standardized and norm-based (mean of 50 and standard deviation of 10). Higher scores correspond to better QoL)

Despite the severe heterogeneity observed, we presented the forest plots of the two SF-36 summary components (Fig. 2). The Physical Component Summary (PCS) score ranged from 14.74 to 62.86 and the Mental Component Summary (MCS) score from 20.55 to 53.54. We performed sensitivity analysis for studies of CHD subgroup (Fig. 3), but the heterogeneity remained high (I2 82.18% for PCS and 91.75% for MCS).

Six of the 12 studies that utilized WHOQOL-Bref were performed on parents with children with genetic syndromes (Down syndrome and Prader-Willi syndrome).

The forest plots of included studies that assessed QoL through WHOQOL-Bref were presented in Fig. 4. The physical domain ranged from 38.49 to 77.72; the psychological domain from 38.24 to 79.27; the social domain from 44.05 to 79.10 and the environment domain from 38.45 to 75.05. The sensitive analysis of the genetic syndromes' subgroup is shown in Fig. 5.

It is essential to point out that despite the severe heterogeneity observed, we presented the forest plots with a descriptive purpose only. The meta-analytic measures should be interpreted with extreme caution and may not be valid estimates.

To answer the research question if parental QoL/HRQOL was impaired or not by having a child with a CA, we analyzed the included comparative studies. We made three main subgroups based on the control group considered – see online Appendix 10 for more detailed information about the studies.

In the first subgroup, parents of children with CA were matched with parents of healthy children. In this subgroup, eleven studies found statistically significant differences between CA and controls, with better QoL/HRQOL in the control group [75, 76, 78, 84–86, 88, 92, 94, 99, 103].

In the second one, parents of children with CA were compared with parents of children with minor illnesses. This subgroup was formed by three studies where parents of children with CHD scored worse than controls, and this difference was statistically significant [80, 89, 97].

In the third and last subgroup, QoL/HRQOL of parents with children with CA were compared with population norms. In the seven studies were found statistically significantly scores, with better result in the control group than in the study group in six of them [82, 83, 87, 90, 95, 96, 100].

It is important to mention that in five studies, statistically significant differences between groups were not found [5, 79, 98, 101, 102].

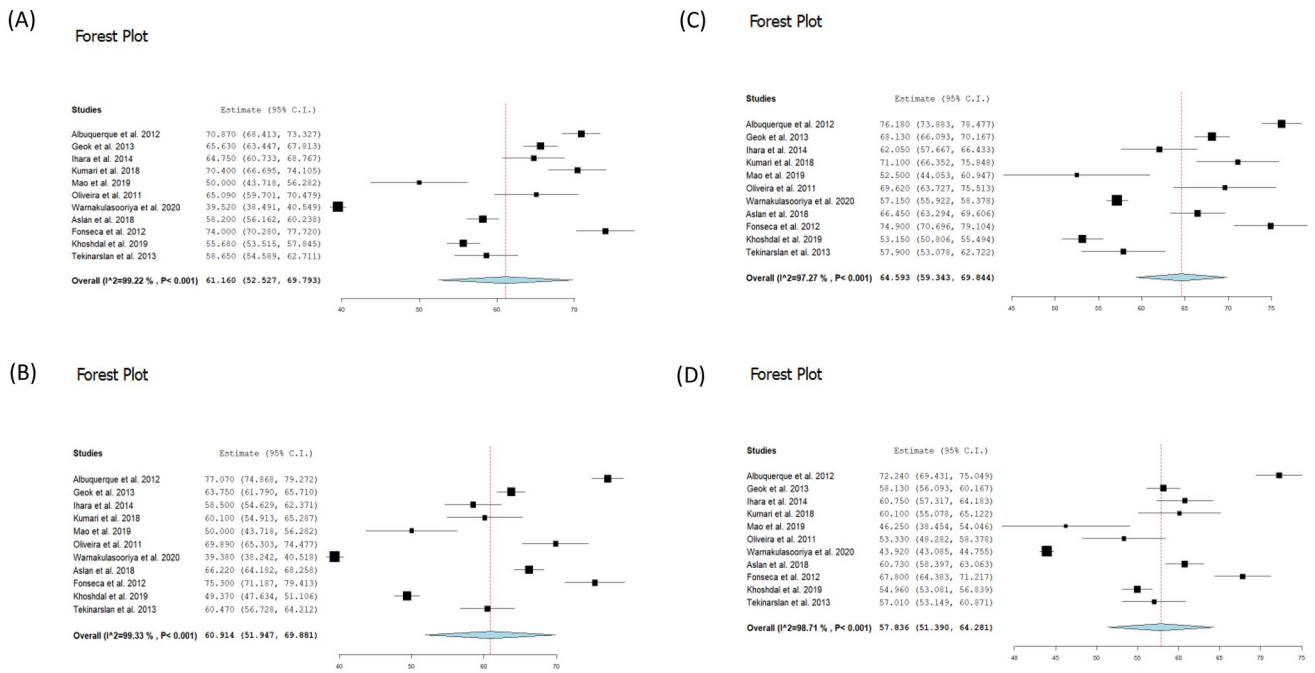

Fig. 4 Forest plots of the meta-analysis included studies that used WHOQOL-Bref presented by domains: **A** Physical; **B** Psychological; **C** Social; **D** Environment. (Meta-analysis of WHOQOL-Bref domains scores obtained by parents of children with CA (using random effects model). General norms for the WHOQOL-Bref domains: Physical 73.5(18.1); Psychological 70.6(14.0); Social 71.5(18.2) and Environment 75.1(13.0). Higher scores correspond to better QoL)

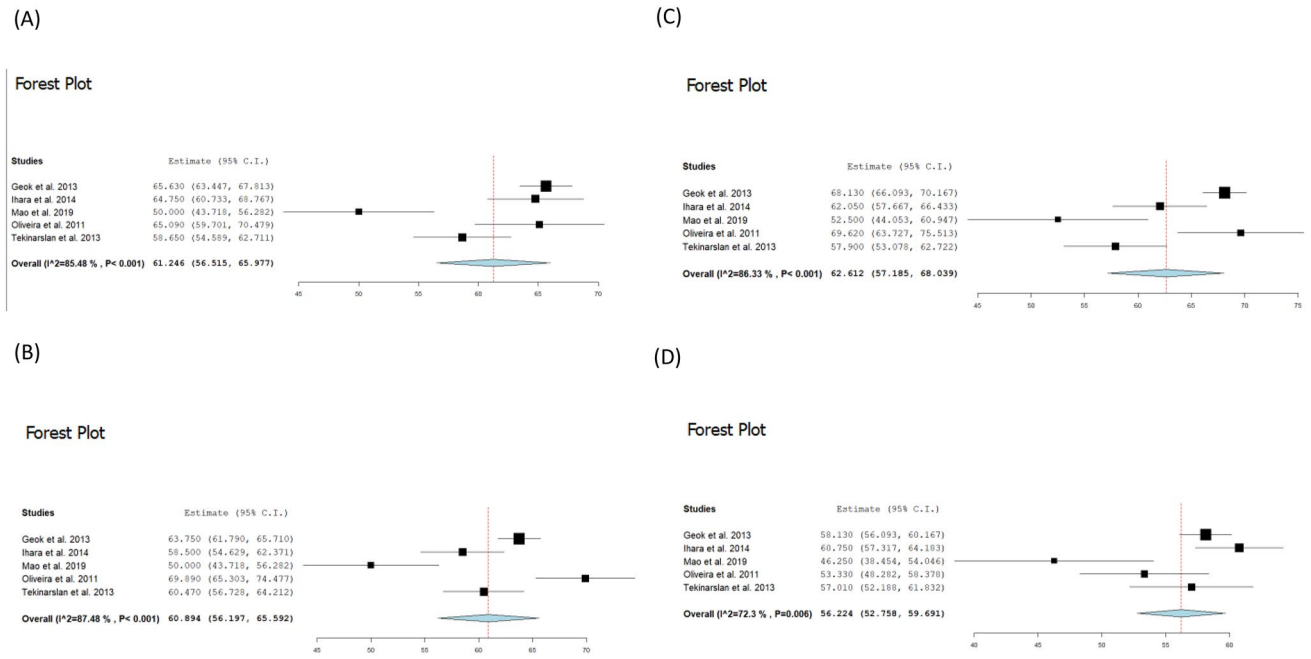

Fig. 5 Forest plots of WHOQOL-Bref domains: **A** Physical; **B** Psychological; **C** Social; **D** Environment of genetic syndromes subgroup of meta-analysis included studies. (Meta-analysis of WHOQOL-Bref domains scores obtained by parents of children with genetic syndromes (using random effects model). General norms for the WHOQOL-Bref domains: Physical 73.5(18.1); Psychological 70.6(14.0); Social 71.5(18.2) and Environment 75.1(13.0). Higher scores correspond to better QoL)

Conclusions

A clear conceptual definition of the clinical outcomes and the selection of measures that capture these concepts is an essential part of the process that enables the evaluation of health interventions effectiveness [19].

Inherent to the difficulty of establishing a unique and universal definition of QoL, the existence of several assessment tools found in this study was not surprising. However, it is essential to reflect on QoL assessment tools described in the literature and their adequacy to measure QoL's impact in this population.

In this review, we identified 27 different tools used to assess QoL/HRQOL. In this pool of instruments, it is essential to distinguish the ones that evaluate the individual perspective of QoL/HRQOL from the ones that capture the perception of family QoL/HRQOL. In the first group, we have the most frequently used, like SF-36 and WHOQOL-Bref, that are globally used and have already demonstrated being psychometric robust. From the second group of instruments, that assessed family QoL, we highlighted the IOFS, the PedsQL FIM and the FQOL. Inside the previous groups we had generic and disease-specific measures.

The several tools that had been developed are proof of the increased engagement of research to answer the needs of this new growing population, the families with children with CA.

Manyfold studies found an impairment of QoL/HRQOL of this population. Considering that having a child with a CA has profound consequences that are not limited to parents as individuals but affects all the family, a holistic approach seems to be the best option to capture this life event's reality and their repercussions in all dimensions. A comprehensive evaluation should engage both types of instruments, individual and familial, in a complementary way.

Beyond the concept definition and the operationalization of QoL's concept through an instrument able to capture the defined outcome, other aspects must be considered in the interpretation of the results of this review.

In the first place, the scope of our review was extensive. We included all the CA (with different degrees of severity) in the pediatric age (0 to 21 years old). Both factors significantly influence the parental adaptation process and, consequently, the QoL/HRQOL scores reported.

Secondly, the small sample size and the different cultural and socioeconomic contexts are variables that could help to explain the variance found.

The gender distribution of parents is a source of bias too, resulting from the overrepresentation of mothers compared to fathers in the included studies.

The severe heterogeneity found in the included studies, namely in the study population (age, type of CA, the severity of CA, the context), control groups, and the instruments used, limited the presentation and interpretation of

an aggregate meta-analytical QoL/HRQOL measure. However, this study highlights the importance of this subject, the assessment of QoL of parents and families of children with CA.

Nevertheless, we considered that this approach was necessary to obtain a *big picture* of assessing the multidimensional concept of QoL/HRQOL described in the literature so far.

Although with all these limitations, we found that QoL/HRQOL of parents and families with children with CA was impaired. In comparative studies, QoL/HRQOL in parents and families of children with CA was statistically significantly worse than in parents and families of healthy children, children with minor illnesses, and population norms.

Considering that parents and family are one of the vectors that mediate children's outcomes, interventions that address parents QoL's improvement will have repercussions in children and all family members, thinking in a micro-environment, and in the society in general, considering a macro perspective. So, it is of main importance to assess QoL and to implement interventions that enhanced adaptation, coping strategies and resilience. This approach decreases the burden associated with care of a child with a CA and should be an integral part of adequate healthcare provision.

The present study highlights the importance of this subject, the assessment of QoL of parents and families of children with CA. We hope that future research will clarify this subject, that is basilar in a society with emergent new treatments and health interventions that compete for limited resources. It is important to investigate the factors that influence parental perception of QoL in order to implement effective strategies that improve it. The impact on different QoL dimensions should be explored, as well as different intervention strategies should be tested. For example, encouraging of social support to decrease caregiver's burden; providing information about the impact of CA of individual health and family life and to promote coping strategies that improve the adaptation. Psychosocial support, including professional counseling and meeting with other parents in similar situation, to share experiences, to provide a group identity and to decrease isolation seem to be valid approach. In an era where the patient and the family's paradigm as the central piece of all the health care process is assuming a bigger relevance, the conceptualization and measurement of QoL should be priority topic of research.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11136-021-02986-z.

Acknowledgements Marisa Gacia Rodrigues was funded by Fundação para a Ciência e a Tecnologia (FCT), Portugal; Grant number: SFRH/BD/123908/2016. The protocol of this review was registered in PROSPERO, International prospective register of systematic reviews, with the number *CRD42017062271*.

Funding This study is part of one of the authors PhD studies, which is funded by Fundação para a Ciência e a Tecnologia, Portugal.

Data availability All data are provided either in the manuscript or appendixes.

Code availability Not applicable.

Declarations

Conflict of Interest All authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

Consent to participate Not applicable.

Consent for publication Not applicable.

References

1. World Health Organization, Congenital anomalies. (2016). https://www.who.int/news-room/fact-sheets/detail/c. https://doi.org/10.1046/j.1525-1594.2002.06876.x.
2. Chow, M. Y. K., Morrow, A. M., Robbins, S. C. C., & Leask, J. (2013). Condition-specific quality of life questionnaires for caregivers of children with pediatric conditions: A systematic review. *Quality of Life Research, 22*, 2183–2200. https://doi.org/10.1007/s11136-012-0343-z
3. Jackson, A. C., Frydenberg, E., Liang, R. P. T., Higgins, R. O., & Murphy, B. M. (2015). Familial Impact and Coping with Child Heart Disease: A Systematic Review. *Pediatric Cardiology, 36*, 695–712. https://doi.org/10.1007/s00246-015-1121-9
4. Albuquerque, S., Fonseca, A., Pereira, M., Nazaré, B., & Canavarro, M. (2011). Estudos psicométricos da versão Portuguesa da Escala de Impacto Familiar (EIF). *Laboratório Psicol, 9*, 173–187. https://doi.org/10.14417/lp.632.
5. Fonseca, A., Nazaré, B., & Canavarro, M. C. (2012). Parental psychological distress and quality of life after a prenatal or postnatal diagnosis of congenital anomaly: A controlled comparison study with parents of healthy infants. *Disability and Health Journal, 5*, 67–74. https://doi.org/10.1016/j.dhjo.2011.11.001
6. Kolaitis, G. A., Meentken, M. G., & Utens, E. M. W. J. (2017). Mental health problems in parents of children with congenital heart disease. *Frontiers in Pediatrics, 5*, 1–7. https://doi.org/10.3389/fped.2017.00102
7. Wei, H., Roscigno, C. I., Hanson, C. C., & Swanson, K. M. (2015). Families of children with congenital heart disease: A literature review. *Heart Lung Journal of Acute Critical Care, 44*, 494–511. https://doi.org/10.1016/j.hrtlng.2015.08.005
8. West, C. A., Besier, T., Borth-Bruhns, T., & Goldbeck, L. (2009). Effectiveness of a family-oriented rehabilitation program on the quality of life of parents of chronically ill children. *Klinische Padiatrie, 221*, 241–246. https://doi.org/10.1055/s-0029-1216364
9. Lawoko, S. (2007). Factors influencing satisfaction and well-being among parents of congenital heart disease children: Development of a conceptual model based on the literature review. *Scandinavian Journal of Caring Sciences, 21*, 106–117. https://doi.org/10.1111/j.1471-6712.2007.00444.x

10. Gregory, M. R. B., Prouhet, P. M., Russell, C. L., & Pfannenstiel, B. R. (2018). Quality of life for parents of children with congenital heart defect: A systematic review. *Journal of Cardiovascular Nursing, 33*, 363–371. https://doi.org/10.1097/JCN.0000000000000466
11. Woolf-King, S. E., Anger, A., Arnold, E. A., Weiss, S. J., & Teitel, D. (2017). Mental health among parents of children with critical congenital heart defects: A systematic review. *Journal of the American Heart Association, 6*, 1–14. https://doi.org/10.1161/JAHA.116.004862
12. Dolk, H., Loane, M., & Garne, E. (2011). Congenital heart defects in Europe: Prevalence and perinatal mortality, 2000 to 2005. *Circulation, 123*, 841–849. https://doi.org/10.1161/CIRCULATIONAHA.110.958405
13. van der Linde, D., Konings, E. E. M., Slager, M. A., Witsenburg, M., Helbing, W. A., Takkenberg, J. J. M., & Roos-Hesselink, J. W. (2011). Birth prevalence of congenital heart disease worldwide: A systematic review and meta-analysis. *Journal of the American College of Cardiology, 58*, 2241–2247. https://doi.org/10.1016/j.jacc.2011.08.025
14. Rempel, G. R., & Harrison, M. J. (2007). Safeguarding precarious survival: Parenting children who have life-threatening heart disease. *Qualitative Health Research, 17*, 824–837. https://doi.org/10.1177/1049732307303164
15. W. health Organization. (1946). United States Treaties and International Agreement. https://www.loc.gov/law/help/us-treaties/bevans/m-ust000004-0119.pdf.
16. Power, M., & Kuyken, W. (1998). World Health Organization Quality of Life Assessment (WHOQOL): Development and general psychometric properties. *Social Science and Medicine, 46*, 1569–1585. https://doi.org/10.1016/S0277-9536(98)00009-4
17. Centers for Disease Control and Prevention, HRQOL Concepts, HRQOL Concepts. (2018). http://www.cdc.gov/hrqol/concept.htm. http://www.cdc.gov/hrqol/concept.htm. Accessed 21 Oct 2020.
18. Campbell, J. D., Brooks, M., Hosokawa, P., Robinson, J., Song, L., & Krieger, J. (2015). Community health worker home visits for medicaid-enrolled children with asthma: Effects on asthma outcomes and costs. *American Journal of Public Health, 105*, 2366–2372. https://doi.org/10.2105/AJPH.2015.302685
19. Anderson, K. L., & Burckhardt, C. S. (1999). Conceptualization and measurement of quality of life as an outcome variable for health care intervention and research. *Journal of Advanced Nursing, 29*, 298–306. https://doi.org/10.1046/j.1365-2648.1999.00889.x
20. T.W. Group. (1998). Development of the World Health Organization WHOQOL-BREF quality of life assessment. *Psychological Medical, 28*, 551–558.
21. T.W. Group. (1995). The World Health Organization Quality of Life Assessment (WHOQOL): Position paper from the World Health Organization. *Social Science and Medicine, 41*, 1403–1409.
22. Centers for Disease Control and Prevention. (2016). HRQOL Concepts, Centers Disease of Control Prevention, 4–7. http://www.cdc.gov/hrqol/concept.htm. Accessed 23 Aug 2018.
23. Centers for Disease Control and Prevention. (2000). Measuring healthy days: Population assessment of health-related quality of life. http://www.cdc.gov/nccdphp/brfss/.
24. A.C.O.P.A.A.M., Hardin, A. P., Hackell, J. M. (2017). Age limit of paediatrics. *Pediatrics, 140*, e20172151. https://doi.org/10.1542/peds.2017-2151.
25. C. on C. and A. Health. (1988). Age limits of paediatrics. *Pediatrics, 81*, 736. https://doi.org/10.1007/bf02734309.
26. A.A. of Pediatrics. (2017). Brigth futures: Guidelines for the health supervision of infants, children, and adolescents, 4th ed, American Academy of Pediatrics.
27. U.S.D. of H. and H.S.F. and D.A.& C. for D. and R. Health. (2003). Guidance for Industry and FDA Staff: Pediatric Expertise for Advisory Panels. Food and Drug Administration. http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm082188.pdf.
28. Albuquerque, S., Pereira, M., Fonseca, A., & Canavarro, M. C. (2013). Qualidade de vida e sintomatologia psicopatológica em pais de crianças com diagnóstico de deficiência/anomalia congénita: A importância das características de resiliência. *Analise Psicologica, 31*, 171–184. https://doi.org/10.14417/ap.589.
29. Goldbeck, L., & Melches, J. (2005). Quality of life in families of children with congenital heart disease. *Quality of Life Research, 14*, 1915–1924.
30. Goldbeck, L., Hölling, I., Schlack, R., West, C., & Besier, T. (2011). The impact of an inpatient family-oriented rehabilitation program on parent-reported psychological symptoms of chronically ill children. *Klinische Padiatrie, 223*, 79–84. https://doi.org/10.1055/s-0030-1262831
31. van der Mheen, M., van Beynum, I. M., Dulfer, K., van der Ende, J., van Galen, E, Duvekot, J., Rots, L. E., van den Adel, T. P. L., Bogers, A. J. J. C., McCusker, C. G., Casey, F. A., Helbing, W. A., & Utens, E. M. W. J. (2018). The CHIP-Family study to improve the psychosocial wellbeing of young children with congenital heart disease and their families: design of a randomized controlled trial. *BMC Pediatrics, 18*
32. Fonseca, A., Nazaré, B., & Canavarro, M. C. (2014). Parenting an infant with a congenital anomaly: An exploratory study on patterns of adjustment from diagnosis to six months post birth. *Journal of Child Health Care, 18*, 111–122. https://doi.org/10.1177/1367493512473856
33. Fonseca, A., Nazaré, B., & Canavarro, M. C. (2016). Medical information concerning an infant's congenital anomaly: Successful communication to support parental adjustment and transition. *Disability and Health Journal, 9*, 150–156. https://doi.org/10.1016/j.dhjo.2015.08.005
34. Marchal, J. P., Maurice-Stam, H., Hatzmann, J., van Trotsenburg, A. S. P., & Grootenhuis, M. A. (2013). Health related quality of life in parents of six to eight year old children with Down syndrome. *Research in Developmental Disabilities, 34*, 4239–4247. https://doi.org/10.1016/j.ridd.2013.09.011
35. Marchal, J. P., Maurice-Stam, H., van Trotsenburg, A. S. P., & Grootenhuis, M. A. (2016). Mothers and fathers of young Dutch adolescents with Down syndrome: Health related quality of life and family functioning. *Research in Developmental Disabilities, 59*, 359–369. https://doi.org/10.1016/j.ridd.2016.09.014
36. Wolfe-Christensen, C., Wisniewski, A. B., Mullins, A. J., Reyes, K. J., Austin, P., Baskin, L., Bernabé, K., Cheng, E., Fried, A., Frimberger, D., Galan, D., Gonzalez, L., Greenfield, S., Kolon, T., Kropp, B., Lakshmanan, Y., Meyer, S., Meyer, T., Nokoff, N. J., … Mullins, L. L. (2017). Changes in levels of parental distress after their child with atypical genitalia undergoes genitoplasty. *Journal of Pediatric Urology, 13*(32), e1-32.e6. https://doi.org/10.1016/j.jpurol.2016.10.024
37. Ellens, R. E. H., Bakula, D. M., Mullins, A. J., Scott Reyes, K. J., Austin, P., Baskin, L., Bernabé, K., Cheng, E. Y., Fried, A., Frimberger, D., Galan, D., Gonzalez, L., Greenfield, S., Kolon, T., Kropp, B., Lakshmanan, Y., Meyer, S., Meyer, T., Mullins, L. L., Nokoff, N. J., Palmer, B., Poppas, D., Paradis, A., Yerkes, E., Wisniewski, A. B., & Wolfe-Christensen, C. (2017). Psychological adjustment of parents of children born with atypical genitalia 1 year after genitoplasty. *Journal of Urology, 198,* 914–920. https://doi.org/10.1016/j.juro.2017.05.035.
38. Witvliet, M., Sleeboom, C., de Jong, J., van Dijk, A., Zwaveling, S., & van der Steeg, A. (2014). Anxiety and Quality of Life of Parents with Children Diagnosed with an Anorectal

Malformation or Hirschsprung Disease. *European Journal of Pediatric Surgery, 24*, 70–74.
39. Nanigian, D. K., Nguyen, T., Tanaka, S. T., Cambio, A., DiGrande, A., & Kurzrock, E. A. (2008). Development and validation of the fecal incontinence and constipation quality of life measure in children with spina bifida. *Journal of Urology, 180*, 1770–1773. https://doi.org/10.1016/j.juro.2008.03.103
40. Albuquerque, S., Pereira, M., Fonseca, A., & Canavarro, M. C. (2012). Impacto familiar e ajustamento de pais de crianças com diagnóstico de anomalia congênita: Influência dos determinantes da criança. *Rev. Psiquiatr. Clin., 39*, 136–141. https://doi.org/10.1590/S0101-60832012000400004
41. Alpern, A. N., Gardner, M., Kogan, B., Sandberg, D. E., & Quittner, A. L. (2017). Development of health-related quality of life instruments for young children with Disorders of Sex Development (DSD) and their parents. *Journal of Pediatric Psychology, 42*, 544–558. https://doi.org/10.1093/jpepsy/jsw022
42. Geok, C. K., Abdullah, K. L., & Kee, L. H. (2013). Quality of life among Malaysian mothers with a child with Down syndrome. *International Journal of Nursing Practice, 19*, 381–389. https://doi.org/10.1111/ijn.12083
43. Goldbeck, L., & Melches, J. (2006). The impact of the severity of disease and social disadvantage on quality of life in families with congenital cardiac disease. *Cardiology in the Young, 16*, 67–75. https://doi.org/10.1017/S1047951105002118
44. Gregory, M. (2019). A descriptive, cross-sectional, correlational exploration of perceived stress, quality of life, and family functioning in parents of a child with congenital heart disease: the pinched study, Faculty of the University of Missouri-Kansas City.
45. Ihara, H., Ogata, H., Sayama, M., Kato, A., Gito, M., Murakami, N., Kido, Y., & Nagai, T. (2014). QOL in caregivers of Japanese patients with Prader-Willi syndrome with reference to age and genotype. *American Journal of Medical Genetics, 164*, 2226–2231. https://doi.org/10.1002/ajmg.a.36634
46. Kapoor, S., Bhayana, S., Singh, A., & Kishore, J. (2014). Comorbidities leading to mortality or hospitalization in children with down syndrome and its effect on the quality of life of their parents. *Indian Journal of Pediatrics, 81*, 1302–1306. https://doi.org/10.1007/s12098-014-1389-4
47. Kramer, F. J., Baethge, C., Sinikovic, B., & Schliephake, H. (2007). An analysis of quality of life in 130 families having small children with cleft lip/palate using the impact on family scale. *International Journal of Oral and Maxillofacial Surgery, 36*, 1146–1152. https://doi.org/10.1016/j.ijom.2007.06.009
48. Kumari, V., Joshi, P., Dhua, A. K., Sapra, S., Srinivas, M., Agarwala, S., & Bhatnagar, V. (2019). Developmental status of children operated for esophageal atresia with or without tracheoesophageal fistula along with maternal stress, their quality of life, and coping abilities at AIIMS, New Delhi. *European Journal of Pediatric Surgery, 29*, 125–131. https://doi.org/10.1055/s-0038-1676825
49. Levert, E. M., Helbing, W. A., Dulfer, K., Van Domburg, R. T., & Utens, E. M. W. J. (2017). Psychosocial needs of children undergoing an invasive procedure for a CHD and their parents. *Cardiology in the Young, 27*, 243–254. https://doi.org/10.1017/S1047951116000391
50. Mao, S. J., Shen, J., Xu, F., & Zou, C. C. (2019). Quality of life in caregivers of young children with Prader-Willi syndrome. *World J. Pediatr., 15*, 506–510. https://doi.org/10.1007/s12519-019-00311-w
51. Mazer, P., Gischler, S. J., Koot, H. M., Tibboel, D., van Dijk, M., & Duivenvoorden, H. J. (2008). Impact of a child with congenital anomalies on parents (ICCAP) questionnaire; a psychometric analysis. *Health and Quality of Life Outcomes, 6*, 1–10. https://doi.org/10.1186/1477-7525-6-102
52. Awoyale, T., Onajole, A. T., Ogunnowo, B. E., Adeyemo, W. L., Wanyonyi, K. L., & Butali, A. (2016). Quality of life of family caregivers of children with orofacial clefts in Nigeria: A mixed-method study. *Oral Diseases, 22*, 116–122. https://doi.org/10.1111/odi.12379
53. Molinas, C., Cazals, L., Diene, G., Glattard, M., Arnaud, C., Tauber, M., Lorenzini, F., Jésuran-Pérelroizen, F., Nègre-Pagès, L., Thuilleaux, D., Jauregui, J., Demeer, G., Copet, P., Barat, P., Boulard, S., Colle, M., Puel, O., Lacombe, D., Dalla Vale, F., Jeandel, C., Garnier, P., Grandjean, H., Lienhardt, A., Mas, J. C., Wagner, K., Simonin, G., Moncla, A., Voelckel, M. A., & Nicolino, M. (2008). French database of children and adolescents with Prader-Willi syndrome. *BMC Medical Genetics*. https://doi.org/10.1186/1471-2350-9-89.
54. Oliveira, E. D. F., & Limongi, S. C. O. (2011). Quality of life of parents/caregivers of children and adolescents with Down syndrome. *Revista da Sociedade Brasileira de Fonoaudiologia, 23*, 321–327. https://doi.org/10.1590/S2179-64912011000400006.
55. Ortiz-Quiroga, D. M., Ariza, Y., Pachajoa, H. (2018). Calidad de vida de familias de niños y adolescentes con discapacidad asociada a defectos congénitos. *University of Psychology, 17*, 1–10. https://doi.org/10.11144/Javeriana.upsy17-1.cvfn.
56. Patjanasoontorn, N., Pradubwong, S., Mongkoltawornchai, S., Phetcharat, T., & Chowchuen, B. (2010). Development and reliability of the THAICLEFT quality of life questionnaire for children with Cleft Lip/Palate and families. *J. Med. Assoc. Thail., 93*, S16-18.
57. Payakachat, N., Tilford, J. M., Brouwer, W. B. F., Van Exel, N. J., & Grosse, S. D. (2011). Measuring health and well-being effects in family caregivers of children with craniofacial malformations. *Quality of Life Research, 20*, 1487–1495. https://doi.org/10.1007/s11136-011-9870-2
58. Sadhwani, A., Willen, J. M., LaVallee, N., Stepanians, M., Miller, H., Peters, S. U., Barbieri-Welge, R. L., Horowitz, L. T., Noll, L. M., Hundley, R. J., Bird, L. M., & Tan, W. H. (2019). Maladaptive behaviors in individuals with Angelman syndrome. *American Journal of Medical Genetics, 179*, 983–992. https://doi.org/10.1002/ajmg.a.61140
59. Sampogna, F., Tabolli, S., Di Pietro, C., Castiglia, D., Zambruno, G., & Abeni, D. (2013). The evaluation of family impact of recessive dystrophic epidermolysis bullosa using the Italian version of the Family Dermatology Life Quality Index. *J. Eur. Acad. Dermatology Venereol., 27*, 1151–1155. https://doi.org/10.1111/j.1468-3083.2012.04682.x
60. Sawin, K. J., Brei, T. J., Buran, C. F., & Fastenau, P. S. (2002). Factors associated with quality of life in adolescents with Spina Bifida. *Journal of Holistic Nursing, 20*, 279–304. https://doi.org/10.1177/089801010202000307
61. Steel, R., Poppe, L., Vandevelde, S., Van Hove, G., & Claes, C. (2011). Family quality of life in 25 Belgian families: Quantitative and qualitative exploration of social and professional support domains. *Journal of Intellectual Disability Research, 55*, 1123–1135. https://doi.org/10.1111/j.1365-2788.2011.01433.x
62. Stoffel, G., Spirig, R., Stiasny, B., Bernet, V., Dave, H., & Knirsch, W. (2017). Psychosocial impact on families with an infant with a hypoplastic left heart syndrome during and after the interstage monitoring period – a prospective mixed-method study. *Journal of Clinical Nursing, 26*, 3363–3370. https://doi.org/10.1111/jocn.13694
63. Azhar, A. S., Al Shammasi, Z. H., & Higgi, R. E. (2016). The impact of congenital heart diseases on the quality of life of patients and their families in Saudi Arabia: Biological, psychological, and social dimensions. *Saudi Medical Journal, 37*, 392–402. https://doi.org/10.15537/smj.2016.4.13626.
64. Tosello, B., Zahed, M., Guimond, F., Baumstarck, K., Faure, A., Michel, F., Claris, O., Massardier, J., Gire, C., & Merrot, T.

(2017). Neurodevelopment and health-related quality of life in infants born with gastroschisis: A 6-year retrospective French Study. *European Journal of Pediatric Surgery, 27*, 352–360. https://doi.org/10.1055/s-0036-1597268
65. Valença, M. P., De Menezes, T. A., Calado, A. A., De Aguiar Cavalcanti, G. (2012). Burden and quality of life among caregivers of children and adolescents with meningomyelocele: Measuring the relationship to anxiety and depression. *Spinal Cord, 50*, 553–557. https://doi.org/10.1038/sc.2012.10.
66. van't Veer, T., Meester, H., Poenaru, D., Kogei, A., Augenstein, K., & Bransford, R. (2008). Quality of life for families with spina bifida in Kenya. *Tropical Doctor, 38*, 160–162. https://doi.org/10.1258/td.2007.070053.
67. Warnakulasooriya, P. H., & Kasturiaratchi, K. (2020). Quality of life of caregivers with children having congenital heart disease awaiting cardiac surgery at the Lady Ridgeway Hospital for Children, Colombo, Sri Lanka. *Sri Lanka J. Child Heal., 49*, 17–22. https://doi.org/10.4038/sljch.v49i1.8892
68. da Silva, G. V., de Moraes, D. E. B., Konstantyner, T., & Leite, H. P. (2020). Social support and quality of life of families with children with congenital heart disease. *Cienc. e Saude Coletiva., 25*, 3153–3162. https://doi.org/10.1590/1413-812320202502581840218
69. Bektas, İ, Kır, M., Yıldız, K., Genç, Z., Bektas, M., & Ünal, N. (2020). Symptom frequency in children with congenital heart disease and parental care burden in predicting the quality of life of parents in Turkey. *Journal of Pediatric Nursing, 53*, e211–e216. https://doi.org/10.1016/j.pedn.2020.04.012
70. Beluci, M. L., da Silva Demoro Mondini, C. C., dos Santos Trettene, A., & Spadoti Dantas, R. A. (2019) Correlation between quality of life and burden of family caregivers of infants with cleft lip and palate. *Revista da Escola de Enfermagem da USP, 53,* 1–6. https://doi.org/10.1590/S1980-220X2017047603432.
71. Bevilacqua, F., Palatta, S., Mirante, N., Cuttini, M., Seganti, G., Dotta, A., & Piersigilli, F. (2013). Birth of a child with congenital heart disease: Emotional reactions of mothers and fathers according to time of diagnosis. *J. Matern. Neonatal Med., 26*, 1249–1253. https://doi.org/10.3109/14767058.2013.776536
72. Carter, R. D., Raia, M., Ewing-Cobbs, L., Gambello, M., Hashmi, S. S., Peterson, S. K., Robbins-Furman, P., & Potocki, L. (2013). Stress and well-being among parents of children with potocki-lupski syndrome. *Journal of Genetic Counseling, 22*, 633–642. https://doi.org/10.1007/s10897-013-9602-6
73. Close, S., Sadler, L., & Grey, M. (2016). In the Dark: challenges of caring for Sons with Klinefelter syndrome. *Journal of Pediatric Nursing, 31*, 11–20. https://doi.org/10.1016/j.pedn.2015.05.002
74. De Cuyper, E., Dochy, F., De Leenheer, E., & Van Hoecke, H. (2019). The impact of cleft lip and/or palate on parental quality of life: A pilot study. *International Journal of Pediatric Otorhinolaryngology, 126*, 109598. https://doi.org/10.1016/j.ijporl.2019.109598
75. Alkan, F., Sertcelik, T., Yalln Sapmaz, S., Eser, E., & Coskun, S. (2017). Responses of mothers of children with CHD: Quality of life, anxiety and depression, parental attitudes, family functionality. *Cardiology in the Young, 27*, 1748–1754. https://doi.org/10.1017/S1047951117001184.
76. Senses Dinc, G., Cop, E., Tos, T., Sari, E., & Senel, S. (2019). Mothers of 0–3-year-old children with Down syndrome: Effects on quality of life. *Pediatrics International, 61*, 865–871. https://doi.org/10.1111/ped.13936.
77. Eagleson, K. J., Justo, R. N., Ware, R. S., Johnson, S. G., & Boyle, F. M. (2013). Health-related quality of life and congenital heart disease in Australia. *Journal of Paediatrics and Child Health, 49*, 856–864. https://doi.org/10.1111/jpc.12296
78. Hatzmann, J., Heymans, H. S. A., Ferrer-i-Carbonell, A., Van Praag, B. M. S., & Grootenhuis, M. A. (2008). Hidden consequences of success in pediatrics: Parental health-related quality of life-results from the care project. *Pediatrics, 122*, e1030–e1038. https://doi.org/10.1542/peds.2008-0582
79. Kaugars, A., Shields, C., & Brosig, C. (2018). Stress and quality of life among parents of children with congenital heart disease referred for psychological services. *Congenital Heart Disease, 13*, 72–78. https://doi.org/10.1111/chd.12547
80. Khoshhal, S., Al-Harbi, K., Al-Mozainy, I., Al-Ghamdi, S., Aselan, A., Allugmani, M., Salem, S., El-Agamy, D., & Abo-Haded, H. (2019). Assessment of quality of life among parents of children with congenital heart disease using WHOQOL-BREF: A cross-sectional study from Northwest Saudi Arabia. *Health and Quality of Life Outcomes, 17*, 1–8. https://doi.org/10.1186/s12955-019-1249-z
81. Kubota, A., Yamakawa, S., Yamamoto, E., Kosugi, M., Hirano, S., Shiraishi, J., Kitajima, H., Yoneda, A., Taduke, Y., Mitani, Y., Watanabe, T., Takifuji, K., & Yamaue, H. (2016). Major neonatal surgery: Psychosocial consequence of the patient and mothers. *Journal of Pediatric Surgery, 51*, 364–367. https://doi.org/10.1016/j.jpedsurg.2015.09.017
82. Kun, Z., Xiong, Y., Yan-Hua, X., Zhongwei, Z., Jian, M., Jinfang, Z., Yirui, W., & Yongqing, H. (2013). Study on life quality and influence factors in cleft lip and palate parents. *West China J. Stomatol., 31*, 279–282.
83. Landolt, M. A., Buechel, E. V., & Latal, B. (2011). Predictors of parental quality of life after child open heart surgery: A 6-month prospective study. *Journal of Pediatrics, 158*, 37–43. https://doi.org/10.1016/j.jpeds.2010.06.037
84. Lawoko, S., & Soares, J. (2003). Quality of life among parents of children with congenital heart disease, parents of children with other diseases and parents of healthy children Author(s): S. Lawoko and J. J. F. Soares. *Source : Quality of Life Research, 12*(6), 655–666.
85. Michel, F., Baumstarck, K., Gosselin, A., Le Coz, P., Merrot, T., Hassid, S., Chaumoître, K., Berbis, J., Martin, C., & Auquier, P. (2013). Health-related quality of life and its determinants in children with a congenital diaphragmatic hernia. *Orphanet Journal of Rare Diseases, 8*. https://doi.org/10.1186/1750-1172-8-89.
86. Allam, L. E., Nabih, M. A. E., & El-Missiry, M. A. (2018). The psychological impact of permanent cardiac pacemakers on pediatric patients and their parents: A case control study. *Indian Heart Journal, 70*, 872–878. https://doi.org/10.1016/j.ihj.2018.02.007
87. Poley, M. J., Brouwer, W. B. F., Van Exel, N. J. A., & Tibboel, D. (2012). Assessing health-related quality-of-life changes in informal caregivers: An evaluation in parents of children with major congenital anomalies. *Quality of Life Research, 21*, 849–861. https://doi.org/10.1007/s11136-011-9991-7
88. Ridosh, M. M., Sawin, K. J., Schiffman, R. F., & Klein-Tasman, B. P. (2016). Factors associated with parent depressive symptoms and family quality of life in parents of adolescents and young adults with and without Spina Bifida. *Journal of Pediatric Rehabilitation Medicine, 9*, 287–302. https://doi.org/10.3233/PRM-160399
89. Sileshi, L., & Tefera, E. (2017). Health-related quality of life of mothers of children with congenital heart disease in a sub-Saharan setting: Cross-sectional comparative study. *BMC Research Notes*. https://doi.org/10.1186/s13104-017-2856-6.
90. Suorsa, K. I., Mullins, A. J., Tackett, A. P., Scott Reyes, K. J., Austin, P., Baskin, L., Bernabé, K., Cheng, E., Fried, A., Frimberger, D., Galan, D., Gonzalez, L., Greenfield, S., Kropp, B., Meyer, S., Meyer, T., Nokoff, N., Palmer, B., Poppas, D., Paradis, A., Yerkes, E., Wisniewski, A. B., & Mullins, L. L. (2015). Characterizing early psychosocial functioning of parents of children

with moderate to severe genital ambiguity due to disorders of sex development. *Journal of Urology, 194*, 1737–1742. https://doi.org/10.1016/j.juro.2015.06.104.
91. Tekinarslan, I. L. C. (2013). A comparison study of depression and quality of life in Turkish mothers of children with Down syndrome, cerebral palsy, and Autism Spectrum Disorder. *Psychological Reports, 112*, 266–287. https://doi.org/10.2466/21.02.15.PR0.112.1.266-287.
92. Tilford, J. M., Grosse, S. D., Robbins, J. M., Pyne, J. M., Cleves, M. A., & Hobbs, C. A. (2005). Health state preference scores of children with spina bifida and their caregivers. *Quality of Life Research, 14*, 1087–1098.
93. Weigl, V., Rudolph, M., Eysholdt, U., & Rosanowski, F. (2005). Anxiety, depression, and quality of life in mothers of children with cleft lip/palate. *Folia Phoniatrica et Logopedica, 57*, 20–27. https://doi.org/10.1159/000081958
94. Werner, H., Balmer, C., & Lehmann, P. (2019). Posttraumatic stress and health-related quality of life in parents of children with cardiac rhythm devices. *Quality of Life Research, 28*, 2471–2480. https://doi.org/10.1007/s11136-019-02202-z
95. Witt, S., Dellenmark-Blom, M., Dingemann, J., Dingemann, C., Ure, B. M., Gomez, B., Bullinger, M., & Quitmann, J. (2018). Quality of life in parents of children born with esophageal atresia. *European Journal of Pediatric Surgery, 29*, 371–377. https://doi.org/10.1055/s-0038-1660867
96. Witvliet, M. J., Bakx, R., Zwaveling, S., Van Dijk, T. H., & Van Der Steeg, A. F. W. (2016). Quality of life and anxiety in parents of children with an anorectal malformation or hirschsprung disease: The first year after diagnosis. *European Journal of Pediatric Surgery, 26*, 2–6. https://doi.org/10.1055/s-0035-1559885
97. Arafa, M. A., Zaher, S. R., El-Dowaty, A. A., & Moneeb, D. E. (2008). Quality of life among parents of children with heart disease. Health and Quality of Life Outcomes. https://doi.org/10.1186/1477-7525-6-91.
98. Yanyan, Z., Caixia, G., Hong, W., Ying, C., Xiaolin, Z., Yuye, L., Pin, H., Bing, S., Lip, C., & Surgery, P. (2015). Analysis of quality of life of 115 parents with cleft lip and/or palate children. 33, 169–173.
99. Aslan, B. I., Gulsen, A., Tirank, S. B., Findikcioglu, K., Uzuner, F. D., Tutar, H., & Ucuncu, N. (2018). Family functions and life quality of parents of children with cleft lip and palate. *The Journal of Craniofacial Surgery, 29*, 1614–1618. https://doi.org/10.1097/SCS.0000000000004611
100. Bannink, N., Maliepaard, M., Raat, H., Joosten, K. F. M., & Mathijssen, I. M. J. (2010). Health-related quality of life in children and adolescents with syndromic craniosynostosis. *J. Plast. Reconstr. Aesthetic Surg., 63*, 1972–1981. https://doi.org/10.1016/j.bjps.2010.01.036
101. Carrada, C. F., Scalioni, F. A. R., Abreu, L. G., Ribeiro, R. A., & Paiva, S. M. (2020). Impact of oral conditions of children/adolescents with Down syndrome on their families' quality of life. *Spec. Care Dent., 40*, 175–183. https://doi.org/10.1111/scd.12444
102. Choi, E. K., Lee, Y. J., Lee, H., & Jung, E. (2019). Bladder and bowel dysfunction in korean children with down syndrome and parental quality of life. *Journal of Pediatric Nursing, 49*, e74–e80. https://doi.org/10.1016/j.pedn.2019.09.016
103. Civilibal, M., Suman, M., Elevli, M., & Duru, N. S. (2014). The quality of life of mothers of children with spina bifida. *J. Pediatr. Orthop. Part B., 23*, 319–321. https://doi.org/10.1097/BPB.0000000000000063
104. Denniss, D. L., Sholler, G. F., Costa, D. S. J., Winlaw, D. S., & Kasparian, N. A. (2019). Need for routine screening of health-related quality of life in families of young children with complex congenital heart disease. *Journal of Pediatrics, 205*, 21-28.e2. https://doi.org/10.1016/j.jpeds.2018.09.037
105. Emeka, C. I., Adeyemo, W. L., Ladeinde, A. L., & Butali, A. (2017). A comparative study of quality of life of families with children born with cleft lip and/or palate before and after surgical treatment. *Journal of the Korean Association of Oral and Maxillofacial Surgeons, 43*, 247–255. https://doi.org/10.5125/jkaoms.2017.43.4.247
106. Macho, P., Bohac, M., Fedeles, J. J., Fekiacova, D., & Fedeles Sr, J. (2017). Impact of cleft lip and/or palate in children on family quality of life before and after reconstructive surgery. *Bratisl Med J., 118*, 370–373.
107. Ok, J. H., & Kurzrock, E. A. (2011). Objective measurement of quality of life changes after ACE Malone using the FICQOL survey. *Journal of Pediatric Urology, 7*, 389–393. https://doi.org/10.1016/j.jpurol.2011.02.012
108. Du, Q., Salem, Y., L, H. H Liu, Zhou, X., Chen, S., Chen, N., Yang, X., Liang, J., & Sun, K. (2017). A home-based exercise program for children with congenital heart disease following interventional cardiac catheterization: Study protocol for a randomized controlled trial. *Trials*. https://doi.org/10.1186/s13063-016-1773-7.
109. Edraki, M., Kamali, M., Beheshtipour, N., Amoozgar, H., Zare, N., & Montaseri, S. (2014). The effect of educational program on the quality of life and self-efficacy of the mothers of the infants with congenital heart disease: A randomized controlled trial. *IJCBNM., 2*, 51–59.
110. Hancock, H. S., Pituch, K., Uzark, K., Bhat, P., Fifer, C., Silveira, M., Yu, S., Welch, S., Donohue, J., Lowery, R., & Aiyagari, R. (2018). A randomised trial of early palliative care for maternal stress in infants prenatally diagnosed with single-ventricle heart disease. *Cardiology in the Young, 28*, 561–570. https://doi.org/10.1017/S1047951117002761
111. van der Mheen, M., Meentken, M. G., Van Beynum, I. M., Van Der Ende, J., Van Galen, E., Zirar, A., Aendekerk, E. W. C., Van Den Adel, T. P. L., Bogers, A. J. J. C., McCusker, C. G., Hillegers, M. H. J., Helbing, W. A., & Utens, E. M. W. J. (2019). CHIP-Family intervention to improve the psychosocial well-being of young children with congenital heart disease and their families: Results of a randomised controlled trial. *Cardiology in the Young, 29*, 1172–1182. https://doi.org/10.1017/S1047951119001732
112. Zou, K., Fan, Y., Jiang, L., Huang, J., Miao, Y., Yang, C., Yang, M., & Zhao, L. (2020). Ear mold for congenital ear malformation: A randomized controlled trial. *Medicine (Baltimore), 99*, e21313. https://doi.org/10.1097/MD.0000000000021313