

Quality of life of children and young adults with Down syndrome from caregivers' perspective: A systematic review and meta-analysis

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ABSTRACT

Introduction: Down syndrome (DS) negatively impacts the well-being of affected individuals. This study aimed to summarise the evidence on quality of life (QOL) of children and young adults with DS using quantitative measures from caregivers' perspective and identify factors that affected their QOL.

Method: Database search was conducted on PubMed, Embase, Web of Science and CINAHL on 24 April 2024. Meta-analysis using random effects model was conducted where feasible. All studies underwent qualitative synthesis. The study protocol was registered with PROSPERO (CRD42023413532).

Results: Seventeen studies involving 3038 children with DS using various QOL measures were included: Pediatric Quality of Life Inventory (PedsQL) (8 studies), KIDSCREEN (4 studies), KidsLife (2 studies), The Netherlands Organization for Applied Scientific Research Academic Medical Center Children's QOL (2 studies) and Personal Outcome Scale (1 study). Meta-analysis on PedsQL studies compared scores between children with DS and typically developing (TD) children. Total scale score was lower in children with DS (mean 70.28, 95% confidence interval [CI] 64.31–76.24) compared to TD children (mean 88.17, 95% CI 80.50–95.83). All subdomains of PedsQL were also lower in children with DS. Within the domain of psychosocial health, children with DS had statistically significant lower social functioning (standardised mean difference -1.40, 95% CI -2.27 to -0.53) and school functioning (standardised mean difference -1.09, 95% CI -1.55 to -0.62) scores, but similar emotional functioning scores. Qualitative synthesis revealed poorer subdomain QOL compared to TD children, especially in social functioning and cognitive functioning. QOL worsened during adolescent years. Family variables (parental education and occupation) did not affect parental perception of children's QOL. Children with DS who had higher intelligent quotient had better QOL.

Conclusion: Children with DS have lower caregiver-reported QOL than TD children, especially in social functioning and school functioning subdomains.

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Keywords: KidsLife-Down scale, KIDSCREEN, mental health, neonatology, paediatrics, parents, PedsQL, trisomy 21

CLINICAL IMPACT

What is New

- Children with Down syndrome (DS) have poorer overall caregiver-reported quality of life (QOL) compared to typically developing children, and experience poorer social and school functioning.
- Adolescents with Down syndrome are at risk of further deterioration of QOL.

Clinical Implications

- Clinical care of children with DS should include QOL assessment to identify gaps in service needs for targeted interventions.
- Targeted enhanced screening of QOL for adolescents with DS is recommended.

INTRODUCTION

Down syndrome (DS), with an incidence of about 1/1000 to 1/1100 live births¹ is the most common autosomal trisomy and genetic cause of intellectual disability. Individuals with DS may have multiple comorbidities including congenital cardiac and gastrointestinal anomalies, obesity, sleep disorders, and visual and hearing impairments.^{2,3} Despite the comorbidities, with advancements in care, survival of individuals with DS has significantly improved over the years.⁴ As the burden of disease at the population level has increased, service providers and researchers are paying more attention to quality of life (QOL) of individuals with DS.⁵

According to the World Health Organization, QOL measures one's position in life relating to culture, values, goals and standards.⁶ QOL provides insight into treatment and prognosis,⁷ and aids in holistic assessment of patients and

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their disease outcomes.⁸ Schalock et al. expanded the concept of QOL in persons with disability by proposing 8 core domains grouped into 3 higher order constructs: well-being (emotional well-being, physical well-being and material well-being), independence (personal development and self-determination), and social participation (interpersonal relations, social inclusion and rights).⁹ This broader and more inclusive definition of QOL can improve evaluation of healthcare and social welfare processes, and outcomes relevant to people with disabilities, including individuals with DS.

Systematic reviews on QOL of children and adolescents with DS are surprisingly limited. We identified only 2 scoping reviews. Lee et al. studied the relationship between family variables and QOL of children with DS, identified gaps in existing knowledge and concluded that “conducting systematic reviews including analyses of statistical significance will be salient”⁵ The second scoping review explored the self-reported QOL of adolescents with DS and included only 2 studies; the authors emphasised the need for more systematic investigations into the topic.¹⁰ In addition, there are conflicting reports on QOL of patients with DS. For example, Lee et al. reported moderate or favourable overall QOL score, with emotional well-being subdomain having the lowest score.¹¹ Conversely, Xanthopoulos et al.’s study in the US showed significantly lower overall QOL score in children with DS compared to those without DS, but emotional functioning did not differ between the 2 groups.¹²

Therefore, we undertook a systematic review of quantitative studies on QOL of children and young adults with DS. We included young adults with DS since they remain dependent on their family and continue to live with them.¹³ Our aims were to: (1) determine the QOL of children and young adults (≤ 21 years) from their caregivers’ perspectives; and (2) identify factors that improve or worsen their QOL. Subsequently in this manuscript, reference to children with DS includes young adults with DS as well.

METHOD

We performed the review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.¹⁴ The protocol was registered on PROSPERO on 12 April 2023 (CRD42023413532).

Search strategies

We conducted the search under the guidance of a medical librarian with expertise in systematic reviews. We searched 4 databases (PubMed, Embase, Web of Science and CINAHL) from their inception until 24 April 2024, for articles on QOL

of individuals with DS, using Medical Subject Headings (National Library of Medicine’s controlled vocabulary thesaurus used to index articles) or related search terms such as “quality of life”, “health related quality of life” and “trisomy 21”. We also searched grey literature (e.g. Google Scholar and OpenGrey) and the bibliography of the relevant articles. The full search strategy is presented in Supplementary Appendix S1.

Study selection

Peer-reviewed studies (cohort, case series and case-control) reporting QOL of caregivers of children and young adults with DS that used quantitative methodology and were written or translated into English were screened for inclusion. Articles which met the eligibility criteria were selected for full-text review. Discrepancies were resolved by consensus between 2 authors. We contacted authors for studies with incomplete information.

Data extraction

Two authors independently screened the articles and extracted the following data:

- (1) Study reference (author, year of publication, country, study design, aims and findings).
- (2) Demographics and characteristics of subjects (number, sex, age, disease severity and comorbidities).
- (3) Measurements and outcomes (QOL tools and variables).

Data synthesis and meta-analysis

We analysed extracted data, including subgroup analysis of the various QOL domains following the general principles set forth in the Cochrane Handbook.¹⁵ We performed meta-analysis using R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria) if data were available from 4 or more studies. In the meta-analysis, for 1 study¹⁶ that presented only the median and interquartile range, we estimated the mean and standard deviation (SD) using the method recommended by Hozo et al.¹⁷ In another study,¹⁸ where QOL scores were stratified by age groups, we combined the scores as described in the Cochrane Handbook.¹⁹

We chose random effect model due to the heterogeneity of studies. We evaluated I^2 statistics according to the Cochrane Handbook.¹⁵ The data from each study were pooled and used to calculate the mean scores with 95% confidence interval (CI). We calculated the standardised mean difference (SMD) using the means and SD of total QOL and subdomains scores for 4 studies which compared PedsQL 4.0 QOL scores between children with

DS and typically developing (TD) children. We performed qualitative synthesis of all studies according to the type of QOL instruments.

Quality assessment

Two authors independently evaluated the quality of included studies using the Newcastle-Ottawa Scale.²⁰ Any discrepancies were resolved through discussion with senior authors.

RESULTS

Literature search

We retrieved 2783 studies from our database search. After deduplication, and title and abstract screening, 21 studies met the inclusion criteria. After full-text review, 17 cross-sectional studies involving 3038 children with DS using the following QOL measures were included (Fig. 1): PedsQL (8 studies), KIDSCREEN (4 studies), KidsLife (2 studies), The Netherlands Organization for Applied Scientific Research Academic Medical Center (TNO-AZL) Children's QOL (2 studies), and Personal Outcome Scale (1 study). In our quantitative analysis, we excluded self-reported QOL data of 4

children from 1 study¹⁸ and parent-proxy QOL data of 41 young adults (>21 years old) from another study.²¹

Table 1 summarises the characteristics of included studies, and Supplementary Appendix S2 presents the extracted key information from qualitative synthesis of each study. Supplementary Appendix S3 summarises the tools used.

Quality of the studies

Inter-rater agreement between 2 reviewers was 94.1% (16 out of 17 studies). The quality of all the studies was satisfactory or better (≥ 5 ; maximum 10) as shown in Supplementary Appendix S4.

QOL measures using PedsQL

The PedsQL 4.0 is a 23-item, self-administered, child or parent-proxy report, multidimensional questionnaire validated for QOL measurement in children and adolescents.²² Eight studies involving 564 caregivers used PedsQL.^{12,16,18,23-27} Four studies^{12,16,23,27} included TD children as the control group. One study included children with autistic spectrum disorder (ASD),²³ and another included obese children without DS as the control group.¹²

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

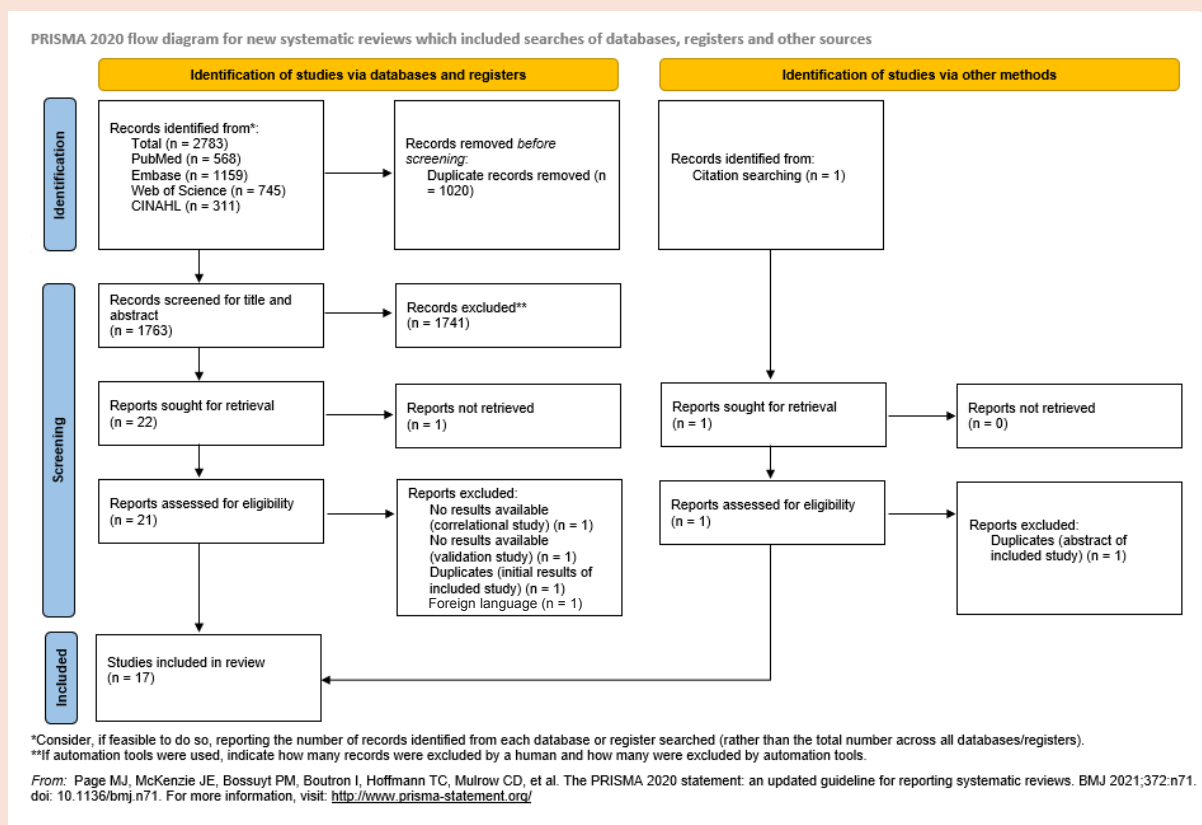


Table 1. Summary of included studies utilising the following quality of life measures: Pediatric Quality of Life Inventory (PedsQL) (8 studies), KIDSCREEN (4 studies), The Netherlands Organization for Applied Scientific Research Academic Medical Center (TNO-AZL) (2 studies), KidsLife (2 studies) and Personal Outcome Scale (1 study).

Author and publication date, study period, country, setting	Sample size, study design, instrument	Age of children with DS, mean ± SD/(SD) or median (IQR) or range in years	Age of caregivers, mean (SD) or median (IQR) and/or range in years; sex (F/M)	Comparison group	Main results		
					Better domain	Poorer domain	Unaffected domain
Studies utilising PedsQL							
Xanthopoulos 2017, ¹² US, Children’s Hospital of Philadelphia	209, secondary analysis from cross-sectional study, PedsQL	Mean ± SD: 14.6 ± 3.3	NA	Non-DS	NA	NA	NA
Katsiana 2020, ²³ Greece	206, cross-sectional, PedsQL	Mean (SD): 7.3 (1.51)	NA	Typically developing children, autism spectrum disorder	NA	All domains	NA
Rojnueangnit 2020, ¹⁸ Thailand, June 2016 to May 2017, Thammasat University Hospital	50, descriptive research, PedsQL	Mean (SD): 3.03 (2.9)	Mean (SD): 38.8 (7.5) Range: 25–56; M:F 7:32	NA	NA	NA	NA
Fucà 2022, ²⁴ Italy, December 2021 to April 2022, Child and Adolescent Neuropsychiatry Unit of the Bambino Gesù Children’s Hospital in Rome	73, retrospective cross-sectional, PedsQL	Mean ± SD: 8.97 ± 2.24	NA	NA	NA	NA	NA
Fernández Scotto 2023, ¹⁶ Argentina, 2020 to 2021, tertiary care teaching hospital	102, cross-sectional, PedsQL	Median (IQR): 3.9 (2.8–4.2)	NA	Non-DS	NA	Physical health, psychosocial health, social functioning, school functioning	Emotional functioning
Rozensztrauch ²⁵ 2023, Poland, January to December 2022	53, cross-sectional, PedsQL	Mean ± SD: 6.48 ± 4.56	NA	NA	NA	NA	NA

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Author and publication date, study period, country, setting	Sample size, study design, instrument	Age of children with DS, mean $\pm$ SD/(SD) or median (IQR) or range in years	Age of caregivers, mean (SD) or median (IQR) and/or range in years; sex (F/M)	Comparison group	Main results		
					Better domain	Poorer domain	Unaffected domain
Ciciora 2023, ²⁶ US, October to December 2020	113, cross-sectional, PedsQL	Mean (SD): 10.3 (3.7)	NA	NA	NA	NA	NA
Alqahtani 2023, ²⁷ Saudi Arabia, August to November 2021	67, cross-sectional, PedsQL	Median (IQR): 9.67 (8.58–11.17)	NA	TD	NA	All domains	NA
Rofail 2017, ²¹ multinational	90, longitudinal, non-intervention, KIDSCREEN-27	12–17 years old mean $\pm$ SD: 14.5 $\pm$ 1.6 18–30 years old mean $\pm$ SD: 22.7 $\pm$ 3.4	NA	KIDSCREEN-27 European normative group	Adolescents: School Environment	Adolescents: social support and peers	Physical well-being, psychological well-being, autonomy and parent relations
Shields 2018, ³³ Australia, October 2013 to May 2014 (Victoria)/ 2011 (Western Australia), podiatry clinic of university campus (Victoria)/ questionnaire (Western Australia)	75, cross-sectional, KIDSCREEN-27	Mean: 13 years 2 months (SD: 7 years 8 months)	NA	Non-DS (norm referenced data)	NA	Physical well-being, social support and peers	Psychological well-being, autonomy and parent relation, school environment
Alrayes 2023, ³⁴ Saudi Arabia	112, cross-sectional, KIDSCREEN-27	Female: 76.8%	NA	NA	NA	NA	NA
Jung 2017, ³² South Korea	36, KIDSCREEN-52	Mean: 6.8 $\pm$ 1.8	NA	Non-DS	NA	Overall QOL. Did not specify domains.	NA
Studies utilising TNO-AZL, TAPQOL and TACQOL-PF							
Van Gameren-Oosterom 2011, ³⁷ Netherlands, June 2000 to February 2003, Leiden University Medical Centre,	337 total, 70 DS, TNO-AZL	Mean (SD): 8.1 (0.15)	NA	General population	nil	Gross motor skills, autonomy, social functioning, cognitive	Physical complaints, positive emotions, negative emotions

Table 1. Summary of included studies utilising the following quality of life measures: Pediatric Quality of Life Inventory (PedsQL) (8 studies), KIDSCREEN (4 studies), The Netherlands Organization for Applied Scientific Research Academic Medical Center (TNO-AZL) (2 studies), KidsLife (2 studies) and Personal Outcome Scale (1 study). (Cont'd)

Author and publication date, study period, country, setting	Sample size, study design, instrument	Age of children with DS, mean $\pm$ SD/(SD) or median (IQR) or range in years	Age of caregivers, mean (SD) or median (IQR) and/or range in years; sex (F/M)	Comparison group	Main results		
					Better domain	Poorer domain	Unaffected domain
Alhaddad 2023, ³⁸ Saudi Arabia, June to August 2020, King Abdulaziz University Hospital	97, TNO-AZL, TAPQOL, TACQOL-PF	1–5 years old Mean $\pm$ SD: CHD: 2.7 ± 1.5 Non-CHD: 3 ± 1.2 6–15 years old Mean $\pm$ SD: CHD: 9.68 ± 2.6 Non-CHD: 9.67 ± 2.2	NA	NA	NA	NA	NA
Studies utilising KidsLife							
Lee 2021, ¹¹ multinational	211, cross-sectional, KidsLife	Mean (SD): 10.9 (4.9)	Mean (SD): 38.5 (7.1) Range: 27–63	NA	NA	NA	NA
Moran 2022, ²⁹ Spain	404, cross-sectional, KidsLife	Mean (SD): 12.1 (4.6)	Mean (SD): 45.3 (7) Female: 85%	NA	NA	NA	NA
Studies utilising Personal Outcome Scale							
Bermudez 2023, ³⁹ Brazil	1187, cross-sectional, Personal Outcome Scale	Range: 4 to ≥ 31	NA	NA	NA	NA	NA

CHD: congenital heart diseases; DS: Down syndrome; F: female; IQR: interquartile range; M: male; NA: not available or not applicable; QOL: quality of life; SD: standard deviation; TAPQOL: TNO-AZL Preschool Quality of Life; TACQOL-PF: TNO-AZL Child Quality of Life Parent Form

Superscript numbers: refer to REFERENCES

Quantitative analysis

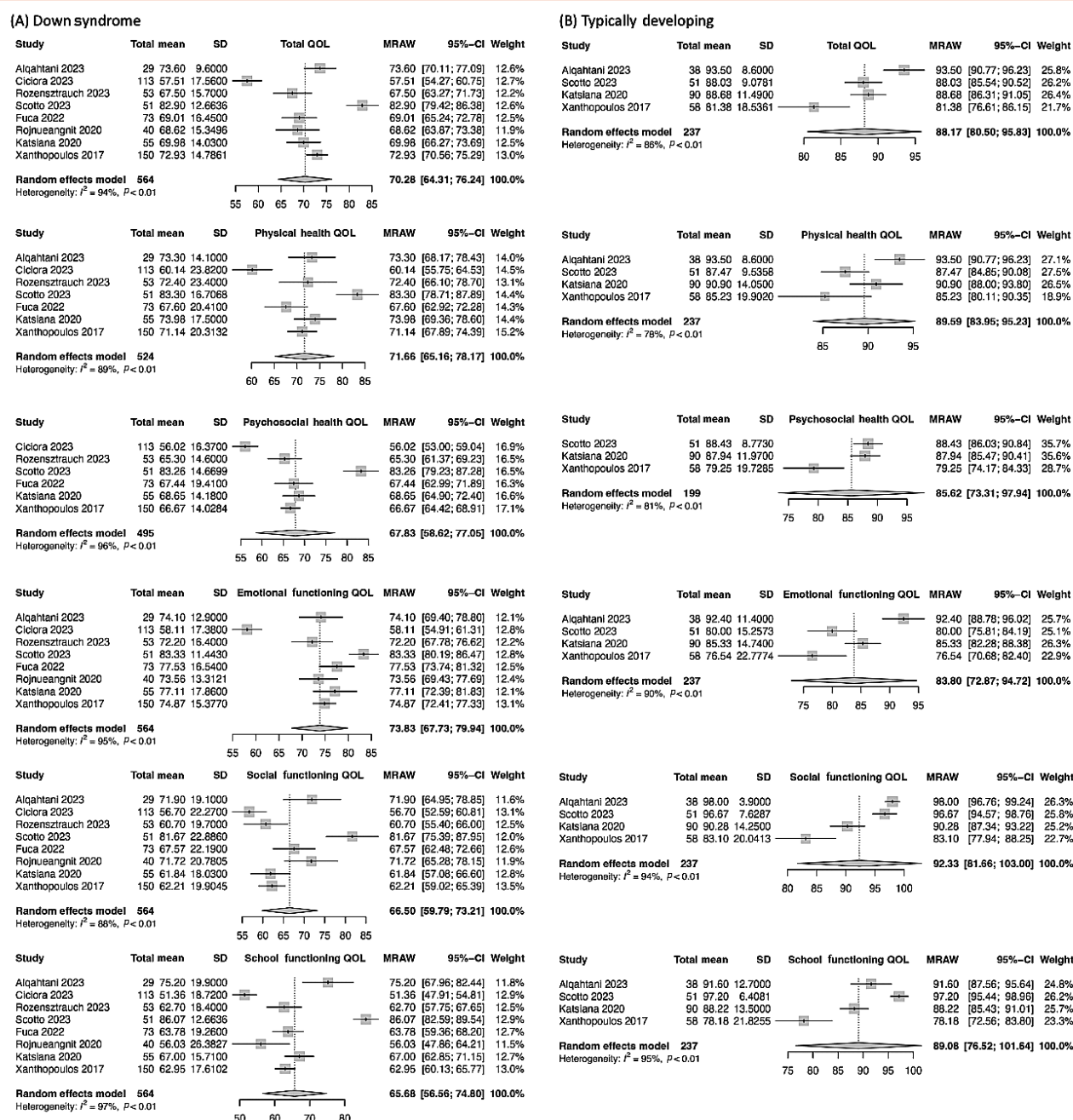
We performed meta-analysis on studies using PedsQL. Fig. 2 displays the forest plot of the summary and subdomain scores for children with DS and TD children.^{12,16,18,23-27}

Among children with DS, the pooled mean total scale score was 70.28 (95% CI 64.31–76.24; $I^2=94\%$, $P<0.01$). Physical health summary score was 71.66 (95% CI 65.16–78.17; $I^2=89\%$, $P<0.01$), and psychosocial health summary score (a composite score of emotional, social and school

functioning) was 67.83 (95% CI 58.62–77.05; $I^2=96\%$, $P<0.01$). For subdomain scores, emotional functioning scored the highest at 73.83 (95% CI 67.73–79.94; $I^2=95\%$, $P<0.01$). Caregivers reported children with DS to have poor scores in social functioning and school functioning subdomains: 66.50 (95% CI 59.79–73.21; $I^2=88\%$, $P<0.01$) and 65.68 (95% CI 56.56–74.80; $I^2=97\%$, $P<0.01$), respectively.

Fig. 3 presents pooled data from 4 case control studies,^{12,16,23,27} which compared children with DS

Fig. 2. Forest plot of the summary and subdomain PedsQL scores for (A) children with Down syndrome and (B) typically developing children.



CI: confidence interval; PedsQL: Pediatric Quality of Life Inventory; MRAW: raw mean; QOL: quality of life; SD: standard deviation

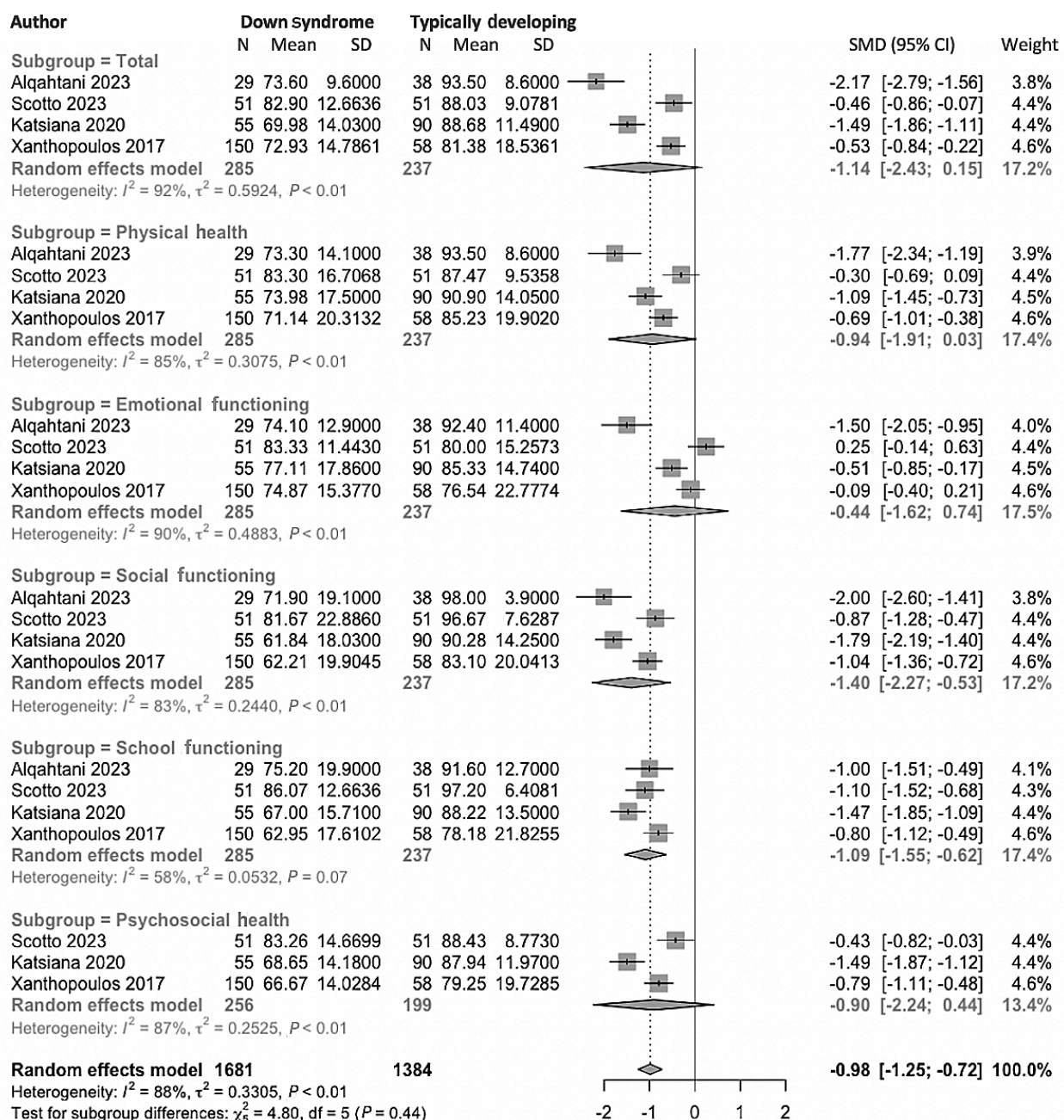
against TD children. Total QOL scores, physical health and psychosocial health between children with DS and TD children did not show statistical difference. However, within the psychosocial health domain, children with DS had poorer scores in social functioning (SMD -1.40; 95% CI -2.27 to -0.53) and school functioning (SMD -1.09; 95% CI -1.55 to -0.62), but equivalent scores in emotional functioning as compared to TD children.

A comprehensive analysis of these studies revealed several significant themes. First and

foremost, children with DS, when compared to their TD peers, have lower QOL scores as reported by caregivers. This is evident in all subdomains, where their scores are consistently lower. The subdomains of social and school functioning are the most adversely affected in children with DS. Children with DS with higher intelligent quotient have better QOL than those with lower intelligent quotient.²⁴

Qualitative synthesis of the articles revealed further findings. Younger children (2–4 years old) have better emotional functioning scores than

Fig. 3. Standardised mean difference (SMD) of PedsQL scores comparing children with Down syndrome and typically developing children.



CI: confidence interval; PedsQL: Pediatric Quality of Life Inventory; MRAW: raw mean; QOL: quality of life; SD: standard deviation

older children.¹⁶ Children with DS scored higher in emotional functioning than ASD children.²³ The presence of any comorbidity, whether physical (e.g. poor muscle tone)²⁵ or functional (e.g. irritable bowel syndrome)²⁶ triggers a domino effect on various subdomains of QOL in children with DS; whereas even a moderate level of physical activity has a positive effect on QOL.²⁷ Presence of obesity, a frequent comorbidity associated with DS, did not impact QOL among children with DS.¹² Self-reported scores from 4 children with DS were higher in emotional and school functioning, similar in physical health and lower in social functioning compared to parents' report, highlighting the importance of exploring self-reported QOL among suitable patients.¹⁸

QOL measures using KidsLife and KidsLife-Down

KidsLife was specifically developed to assess QOL of individuals with intellectual disabilities;⁹ whereas KidsLife-Down specifically assesses QOL of children and young people with DS.²⁸ Two studies used these instruments.^{11,29}

Lee et al. conducted a multinational study, with preponderance (77.7%) of children with DS from the US using KidsLife.¹¹ The authors reported moderate to favourable levels of QOL with the mean overall QOL score of 89.7 (SD 16.0; 70th to 71st percentile). Subdomains scores were at the following percentiles: social inclusion at 84th (highest), self-determination 75th, material well-being 63rd, physical well-being 50th, interpersonal relations 50th, personal development 50th, rights 50th and emotional well-being 37th. Morán et al. used KidsLife-Down in Spain and reported highest scores in the material well-being (43.35 ± 4.42), physical well-being (41.42 ± 5.25), and Rights (40.66 ± 5.33) subdomains.²⁹ Morán et al.²⁹ reported better scores in material well-being and physical well-being compared to Lee et al.,¹¹ which the authors attributed to wider availability of welfare programme for people with intellectual disability in Spain. On the other hand, self-determination and social inclusion were the 2 highest scoring subdomains reported by Lee et al., which is radically different from Moran et al.'s findings where these domains had the lowest scores. The plausible reasons include the use of KidsLife, rather than KidsLife-Down, by Lee et al. KidsLife was developed for people with significant intellectual disabilities who need extensive support. Thus, a ceiling effect may exist in some domains when high-functioning children with DS were surveyed.²⁹ Lee et al.'s cohort was also prone to self-selection bias as this was drawn from a support group with predominance of children with DS from

US. The unexpected finding of poorer emotional well-being among older children could be due to higher prevalence of psychopathology and internalising symptoms,³⁰ underscoring the need for continuing vigilance among this group.

QOL measures using KIDSCREEN

KIDSCREEN includes a child or parent-proxy report questionnaire validated for QOL assessment in individuals aged between 8–18 years.³¹ Four studies used KIDSCREEN.^{21,32–34}

Jung et al. determined improvement in function and activities, and participation section of International Classification of Functioning, Disability and Health – Children and Youth Version was significantly correlated with QOL ($R = -0.514$, $P < 0.05$), indicating importance of participation in physical activities among children with DS.³² A significant finding from Shields et al. was that adolescents with DS (aged 13–18 years) had clinically significantly lower scores (>5 points) in all QOL domains compared to younger children with DS (aged 5–12 years).³³ Rofael et al. reported significantly higher scores in school environment and poor scores in the social support and peers domains among adolescents compared to normative European counterparts.²¹ Alrayes et al. also reported higher scores in psychological well-being, autonomy, parental relation, and school and learning domains.³⁴ Plausible reasons for the unexpected high QOL results by Rofael et al. and Alrayes et al., as compared to Shields et al., include the use of KIDSCREEN-27,²¹ which lacks the sensitivity and accuracy to effectively measure QOL of DS patients. Another reason could be due to face-to-face interviews adopted in Rofael's study, which may have influenced reporting of QOL by the parents. Shields et al.'s³³ study highlights the importance of continuing physical well-being and social support for children with DS even in high-resource countries, and extra vigilance in adolescent for possible deterioration of QOL.

QOL measures using TACQOL and TAPQOL

The TNO-AZL Child Quality of Life Parent Form (TACQOL-PF) is a 56-item (7 domains), child-self report or parent-proxy report questionnaire for children aged 6–15 years.³⁵ The TNO-AZL Preschool Quality of Life (TAPQOL) is a 43-item (4 domains) parent-proxy report questionnaire for preschool children aged 1–5 years.³⁶ Two studies used these tools.^{37,38}

The study conducted by van Gameren-Oosterom stands as the earliest in this review and is unique in its national representation, encompassing nearly 50% of the Dutch population of children with

DS aged 8 years.³⁷ This study yielded significant findings, including a pronounced delay in development among children with DS, a higher prevalence of emotional and behavioral problems, and a less favourable QOL compared to TD children. A particularly noteworthy finding from Alhaddad's study, conducted in Saudi Arabia among children with DS with congenital heart disease, was the disparity in QOL between Saudi children who had ample social support and rehabilitation services, contrasted with non-Saudi children from lower-income families who lacked similar access.³⁸ This underscores the critical role of healthcare service accessibility for children with DS across all income groups.

QOL measures using Personal Outcome Scale

Bermudez et al.³⁹ studied 1187 patients with DS (including 151 patients >21 years old) from Brazil using Personal Outcome Scale, a specialised QOL tool for people with disability.^{9,40} Good QOL was associated with being female, higher parental education level, mosaicism, adequate prenatal care, first medical consult at earlier age and employed mother.³⁹ Bad QOL was associated with family history of alcohol abuse, psychiatric condition, and presence of comorbidities such as autism and epilepsy.³⁹

DISCUSSION

To our knowledge, this is the first systematic review and meta-analysis of the QOL of children, adolescents and young adults with DS from caregivers' perspectives.

Meta-analysis on included studies reporting PedsQL,^{12,16,18,23-27} found that the total scale QOL scores of children with DS was 70.28 (95% CI 64.31–76.24), with subdomain scores ranging from 65.68 (95% CI 56.56–74.80) for school functioning to 73.83 (95% CI 67.73–79.94) for emotional functioning. Among these studies, Fernández-Scotto et al.'s study that had the youngest cohort of children at 2–4 years old, reported higher QOL scores in all subdomains, indicating that parents with young children with DS perceive their children to have better QOL.¹⁶ Interestingly, parents of younger children with DS themselves self-reported poorer QOL.⁴¹

Using PedsQL, children with DS had significantly poorer scores in social functioning and school functioning compared to TD children.^{12,16,23,27} In contrast, using KIDSCREEN, studies reported children with DS to have comparable scores to TD children in specific QOL subdomains. With better social support and educational systems, Shields et al.³³ reported 3 dimensions (psychological

well-being, autonomy and parent relations, and school environment) in 13-year-old children with DS to be similar to normative data. In Rofail et al.'s study,²¹ parents of adolescents with DS reported high school environment domain scores compared to the European normative group dataset. With their intellectual disabilities, children with DS are dependent on opportunities presented by society to improve their personal physical, emotional and psychosocial outcomes. This highlights the importance of ensuring that children with significant disabilities participate meaningfully in community activities.⁴² Children with DS usually spend a lot more time than TD counterparts with their families, making familial support an integral part of social support, which can increase their QOL. Societal expectations about family responsibilities in caring for children with DS can vary greatly between Western and Eastern countries, depending on the support provided by each country.⁵ As children with DS become teenagers and adults, integration into community via work or hobbies may become the primary source of social support.

A stereotypical view of children with DS is their vivacious personality and cheerfulness, which can be expected to predict good scores in emotional subdomain of QOL.⁴³ Our findings of high emotional/psychological domain scores in meta-analysis of PedsQL studies supported this premise,^{18,24,33} and the scores were sometimes comparable to the TD population.¹² However, it is imperative to acknowledge that emotion is an inherently subjective experience of an individual. Therefore, caregivers' assessment of emotion is a surrogate of a child's emotional status, and self-reported QOL should be sought for whenever feasible.

QOL of children with DS deteriorate during adolescence. Adolescence and young adulthood are periods involving rapid change in biological and social factors. While a TD child may adjust to the changes by nurturing greater peer network, a child with DS may struggle to harness an adequate social and peer support network.³³ The decline in cognitive functioning and loss of previously achieved skills among adolescents is an area of emerging interest and concern.⁴⁴ Regression can happen unexpectedly, affecting cognitive and language functioning, ability to perform daily tasks, and cause alterations in personality and behaviour.⁴⁴ These abilities are closely linked to QOL measurements and may also explain the decline of QOL in an older child with DS. While there is a paucity of confirmed aetiologies, new evidence points towards immune dysfunction and stress from major life events and transitions as possible triggers

contributing to decline in QOL. Other causes may include psychiatric diseases like depression and anxiety, highlighting the importance of closer monitoring of adolescents with DS.^{44,45}

Early interventions and educational therapy are proven to be beneficial for young children with DS. These can begin shortly after birth and continue through the toddler years. Later on, services can be provided through school or specialised centres taking care of children with DS or other disabilities.² Other interventions can be explored as well. For example, Fujino reported 2 cases of young adults with DS with psychiatric symptoms and marked disruption in their daily lives whose maladaptive behaviours improved after participation in a Dohsa-hou treatment programme (a psychological rehabilitation method in Japan).⁴⁶

We would like to highlight several limitations of this review. The meta-analysis showed high heterogeneity with the lowest I^2 value of 89%. We postulate that the high heterogeneity is due to differences in age of the children with DS, study design, and country or regions of study. There are limited studies from non-Western countries. Caregivers were predominantly mothers, thus the views of other family caregivers were underrepresented. Finally, a minority of the informants were teachers and psychologists, and we could not separately analyse these data.

We identified several important research gaps. First, there were no longitudinal QOL studies as children with DS progress through developmental and biological stages. Second, only 1 study²⁹ used the DS specific KidsLife-Down that embraces the concept of individual QOL and includes a more comprehensive definition of QOL.

CONCLUSION

Based on our review, we recommend QOL measurements to be done every 6 months. During early childhood, this would allow healthcare providers to track caregivers' perception of their child's QOL as caregivers adapt to the child's diagnosis and medical conditions. We recommend the use of KidsLife-Down as it specifically assesses the QOL of children and young adults with DS. Due to the potential risk of QOL deterioration during adolescent and adult years, QOL during this period needs to be closely monitored. An unexpected change in QOL may suggest a change in clinical condition and therefore QOL may be used as a surrogate marker of the individual's health.

Declaration

No funding was received for this work. All authors have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

Supplementary materials

Supplementary Appendix S1. Search strategy.

Supplementary Appendix S2. Extracted key information from qualitative synthesis of studies.

Supplementary Appendix S3. Summary of quality of life (QOL) tools.

Supplementary Appendix S4. Quality of included studies using Newcastle-Ottawa scale.

REFERENCES

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