

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

Fergus Edward Cheok^{*1} MBBS, Natania Rae Tan Xiangqin^{*2}, Yu Yi Chan², Bryan Wong Wei Zhi¹ MBBS, Gwyneth Kong¹ MBBS, Zubair Amin^{3,4} MHPE, Yvonne Ng Peng Mei^{3,4} MRCP

ABSTRACT

Introduction: The aims of this systematic review and meta-analysis are to synthesise quality of life (QOL) of family caregivers of children and young adults with Down syndrome (DS) and determine factors affecting their QOL.

Method: This review was conducted as per Preferred Reporting Items for Systematic Reviews and Meta-Analyses guideline. Key search terms were "quality of life", "down syndrome" and "trisomy 21". Meta-analysis using random effect model was conducted where feasible. All studies underwent qualitative synthesis. The study protocol was registered with PROSPERO (CRD42023413532).

Results: Eighteen studies with 1956 caregivers were included. Of the 10 studies utilising the World Health Organization Quality of Life Instrument-Brief Version, 5 were included in the meta-analysis. Psychosocial domain had the highest score with mean (95% confidence interval [CI]) of 63.18 (39.10–87.25). Scores were poorer in physical, environmental and social domains: 59.36 (28.24–90.48), 59.82 (19.57–100.07) and 59.83 (44.24–75.41), respectively. Studies were heterogenous with I^2 values ranging from 99–100% ($P < 0.01$). The remaining 8 studies used 6 other instruments. Qualitative synthesis revealed that caregivers' QOL was adversely affected by child-related factors, such as level of functional independence, developmental delay, presence of multiple comorbidities, impaired activities of daily living and poor sleep quality. Environmental factors that adversely affected caregivers' QOL included number of children, housing and support from the family. Personal factors that affected caregivers' QOL included age, being a single mother, low education and low income.

Conclusions: QOL of caregivers of children with DS was lower than population reference data. Understanding the factors that influence family caregivers' QOL is an essential step towards improving the QOL of caregivers and their children with DS.

Ann Acad Med Singap 2024;53:490-501

Keywords: FIM, parents, PedsQL, trisomy 21, WHOQOL-BREF

CLINICAL IMPACT

What is New

- Quality of life (QOL) of caregivers of children with Down syndrome (DS) was found to be lower than population reference data.
- QOL of caregivers were affected by personal factors (e.g. age, education and marital status), child-related factors (e.g. level of independence and presence of comorbidities) and environmental factors (e.g. housing, number of children and support from families).

Clinical Implications

- The measurement of family caregivers' QOL is an important element for high-quality care of children with DS and should be incorporated into clinical practice.

INTRODUCTION

The family caregiver is "any relative, partner, friend or neighbor who has a significant personal relationship with, and provides a broad range of assistance for a person with a chronic or disabling condition."¹ Family caregivers for children with chronic illnesses are commonly parents, who fulfil their children's physical and emotional needs while attending to their developmental progress, education and changing health status.² These responsibilities may result in caregivers suffering from physical, psychosocial, emotional, social, and financial stress and burden.³

The World Health Organization (WHO) defines quality of life (QOL) as "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns."⁴ QOL, often used interchangeably with health-related quality of life

The Annals is an open access journal, allowing non-commercial use under CC BY-NC-SA 4.0.

¹ MOH Holdings, Singapore

² Yong Loo Lin School of Medicine, National University of Singapore, Singapore

³ Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

⁴ Department of Neonatology, Khoo Teck Puat-National University Children's Medical Institute, National University Hospital, Singapore

* Joint first authors

Correspondence: A/Prof Zubair Amin, Department of Neonatology, Khoo Teck Puat-National University Children's Medical Institute, National University Hospital, 5 Lower Kent Ridge Road, Singapore 119074.

Email: paeza@nus.edu.sg

This article was first published online on 19 August 2024 at annals.edu.sg.

or HRQOL,⁵ allows holistic and longitudinal assessment of outcomes related to overall health and well-being.⁶

Down syndrome (DS) is the most common genetic cause of intellectual disability.⁷ Due to associated comorbidities^{8,9} individuals with DS are typically dependent on family caregivers. Adolescents and young adults with DS are at risk of deteriorating emotional and social well-being,^{10,11} which in part contributes to continued care of individuals with DS by the family caregivers even in young adulthood.¹²

Qualitative studies reported family caregivers of children with DS to have emotional turmoil, high rates of depression, burnout and poorer overall mental health.^{13,14} Caregivers of children with DS face variable level of burden and many experience higher burden of care when their child has disabilities.¹³ Encouragingly, the majority of mothers adapt and gradually accept their child's condition,¹⁴ and caregivers of children with DS have better psychological well-being and coping skills than mothers of children with autism or fragile X syndrome.¹⁵

We conducted a systematic review and meta-analysis to synthesise QOL of caregivers of children and young adults with DS. We included young adults below 30 years old as they may continue to live with and depend on their family caregivers. Our overarching goal is to provide practitioners and policymakers with evidence to improve the QOL of caregivers by identifying determinants of better and poorer QOL. Henceforth, the term children is used to denote both children and young adults.

METHOD

We performed the review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).¹⁶ The protocol

was registered on PROSPERO on 12 April 2023 (CRD42023413532).

Search strategy

We conducted the search under the guidance of a medical librarian. We searched 4 databases (PubMed, Embase, Web of Science and CINAHL) from the inception of respective databases until 24 April 2024, using Medical Subject Headings (National Library of Medicine's controlled vocabulary thesaurus used to index articles) or related terms such as "down syndrome", "trisomy 21" and "quality of life". The term "caregiver" or "parent" was not included, as inclusion of these terms restricted the number of articles retrieved. We also searched grey literature (e.g. Google Scholar and OpenGrey) and bibliography of relevant articles. Supplementary Appendix S1 illustrates the search strategy.

Eligibility and selection criteria

Table 1 summarises inclusion and exclusion criteria. Two authors independently sieved all titles and abstracts for articles meeting eligibility criteria for full-text reviews. Any discrepancies were resolved after discussion with senior authors.

Data extraction

Two authors independently extracted the following data: study characteristics (e.g. year of study, country, study design and aims); participant demographics (e.g. sample size, sex/gender, age, race, education, employment and family income); and outcomes (e.g. QOL instruments and results).

Data analysis

We analysed extracted data including subgroup analysis following the Cochrane Handbook.¹⁷

Table 1. Eligibility criteria of studies.

	Inclusion criteria	Exclusion criteria
Population	Studies involving family caregivers of children and young adults (0–30 years old) with Down syndrome (DS)	Studies with DS patients >30 years old; studies that combined different age groups where data could not be extracted for family caregivers of DS patients <30 years old
Exposure	DS or trisomy 21 including mosaic, translocation and partial trisomy	Studies with other trisomy disorders, or intellectual disabilities without DS
Outcomes	Studies on quality of life (QOL) of family caregivers of children with DS from their own perspectives	Studies on QOL of formal caregivers such as healthcare professionals
Study design	Quantitative studies; cohort, case control and case series studies; mixed method studies where quantitative data are available	Qualitative studies, interventional trials, validation studies of instruments
Others	Peer reviewed, full-text articles, data available in English	Consensus statement, reviews, opinions, commentaries, abstracts

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. We chose random effect model due to the heterogeneity of the studies.¹⁷ For 1 study¹⁸ that presented only the median and interquartile range (IQR), we estimated the mean and standard deviation (SD) using the method recommended by Hozo et al.¹⁹ We performed qualitative synthesis of all studies according to the type of QOL instrument.

Quality assessment

Two authors independently assessed the quality of studies using the Newcastle-Ottawa Scale.²⁰ Any discrepancies were resolved through consensus.

RESULTS

We retrieved 2743 articles from literature search. After deduplication, and title and abstract screening, 18 studies with 1956 caregivers met inclusion criteria. We included 58 caregivers who participated in 2 different studies only once.^{21,22} Out of all the caregivers, the majority were mothers, accounting for 78.6% (n=1468). In contrast, 21.4% (n=400) were fathers; while a small fraction consisted of grandmothers (n=2). The sex/gender of the

remaining 86 caregivers was not specified. Fig. 1 presents the PRISMA flowchart and Supplementary Appendix S2 describes the instruments used. Ten studies used the World Health Organization Quality of Life Instrument-Brief Version (WHOQOL-BREF) while 8 studies used 6 other instruments. Table 2 and Table 3 summarise characteristics and key findings of the included studies using the WHOQOL-BREF and other instruments, respectively.

Quality of included studies

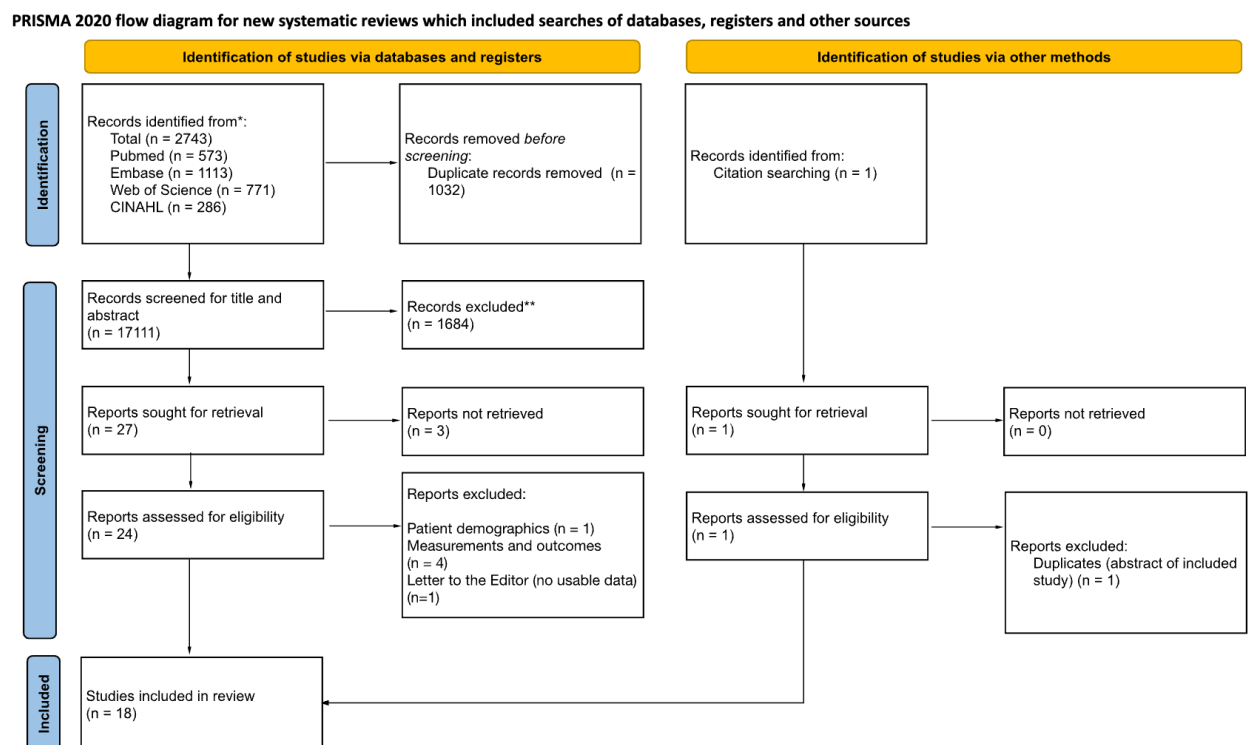
Supplementary Appendix S3 outlines the quality of included studies. The quality of all studies was satisfactory or better (≥ 5 ; maximum 10). Inter-rater agreement between 2 reviewers was 89% (16 out of 18 studies).

QOL measures using WHOQOL-BREF

The WHOQOL-BREF is an abbreviated version of the WHOQOL-100, which comprises 100 questions on the individual's perception of their health and well-being.²³

The 10 studies involved 970 family caregivers of children with DS.^{18,24-32} Two studies had parents/caregivers of typically developing (TD) children as the comparison group.^{18,24} Three studies^{24,25,27} used

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



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71 For more information, visit: <http://www.prisma-statement.org/>

Table 2. Summary of included studies using the World Health Organization Quality of Life Instrument-Brief Version (WHOQOL-BREF).

Author and publication date, country, setting, study period	Sample size, study design, instrument	Age of children with DS, mean $\pm$ SD and/or range	Caregivers' age, mean $\pm$ SD or mode (no., %) median and/or range in years; sex (F/M), no. %	Comparison group	Highest scoring domain OR biggest difference ^a (score)	Lowest scoring domain OR lowest difference ^a (score)	Total score	Key factors adversely affecting QOL scores
Geok 2013, ²⁵ Malaysia, 2009–2010	161, cross-sectional, WHOQOL-BREF	Mean $\pm$ SD: 9.3 $\pm$ 4.2 years	Mean: 43.67 SD: 8.49 F: 161, 100% M: 0, 0%	NA	Social (68.1)	Environment (58.1)	62.50	Rural household, low education, low income, being single and of older age
AlAhmari 2022, ²⁶ Saudi Arabia, 2018–2019	261, cross-sectional, WHOQOL-BREF	Range: 0–14 years	Mode: above 40 (164, 62.8%) F: 137, 52.5% M: 124, 47.5%	NA	Environment (105)	Social (41)	NA	Education level, number of children and average monthly income
Abbassi 2016, ²⁷ Iran, not specified	70, cross-sectional, WHOQOL-BREF	NA	Mean: 36.74 $\pm$ 7.5 F: 70, 100% M: 0, 0%	NA	Physical (61.88)	Environment (41.63)	46.30	Rental housing
Vadakedom 2017, ²⁸ India, 2016	31, cross-sectional, WHOQOL-BREF	Mean $\pm$ SD: 1.48 $\pm$ 0.51 years	Mean: 30.6 F: 31, 100% M: 0, 0%	NA	Social (61.32)	Environment (50.29)	52.82	Urban families, income level, mothers with spouses with higher education level
Buzatto 2008, ²⁹ Brazil, 2007	30, cross-sectional, WHOQOL-BREF	NA	Mean: 37 Range: 28–49 F: 24, 80% M: 6, 20%	NA	Social (80.72)	Psychological (60.28)	NA	
Oliveira 2011, ³⁰ Brazil, not specified	31, cross-sectional, WHOQOL-BREF	Mean: 8 years 5 months Range: 1–16 years	Mode: 40–49 (17, 55%) F: 24, 77% M: 7, 23%	NA	Social (69.92)	Environment (53.33)	NA	Education, socio-economic factors

Table 2. Summary of included studies using the World Health Organization Quality of Life Instrument-Brief Version (WHOQOL-BREF). (Cont'd)

Author and publication date, country, setting, study period	Sample size, study design, instrument	Age of children with DS, mean $\pm$ SD and/or range	Caregivers' age, mean $\pm$ SD or mode (no., %) median and/or range in years; sex (F/M), no. %	Comparison group	Highest scoring domain OR biggest difference ^a (score)	Lowest scoring domain OR lowest difference ^a (score)	Total score	Key factors adversely affecting QOL scores
Senses Dinc 2019, ¹⁸ Turkey, 2010–2011	75, cross-sectional, WHOQOL-BREF	Range: 0–3 years	Median: 31 Range: 18–55 F: 75, 100% M: 0, 0%	Parents/ caregivers of healthy children	^a Social (14.582)	Psychological (0.002)	NA	Comorbid disorders in the children, number of children in the household
Amaral 2020, ²⁴ Brazil, 2017–2018	82, cross-sectional, WHOQOL-BREF	Range: DS: 4–30 years TD: 4–8 years	Mean: 58.2 SD: 10.8 Range 23–78 F: 67, 81.7% M: 15, 18.3%	Caregivers of typically developing children	^a Environment (6.2)	Physical (0.6)	62.5	Family income, level of dependence on the child
Hussin 2022, ³¹ Malaysia, not specified–2020	151, cross-sectional, WHOQOL-BREF	Mean: 5 years Range: 1 month to 17 years	Mean: 43 Range: 28–61 F: 151, 100% M: 0, 0%	NA	Social (72.55) and environment (72.55)	Psychological (63.25)	NA	Older maternal age
Tekinarslan 2013, ³² Turkey, not specified	78, cross-sectional, WHOQOL-BREF	Range: 3–18 years	Median: 36–45 Range: <25 to >46 F: 78, 100%; M: 0, 0%	NA	Psychological (60.47)	Environment (57.01)	NA	

F: female; IQR: interquartile range; M: male; NA: Not applicable/not available; QOL: quality of life; SD: standard deviation

^aThe differences in individual QOL domain values between the control group and DS group of family caregivers (if applicable).

Table 3. Summary of included studies using instruments other than the World Health Organization Quality of Life Instrument-Brief Version.

Author and publication date, country, setting, study period	Sample size, study design, instrument	Age of children with DS, mean $\pm$ SD and/or range in years	Age of caregivers, mean $\pm$ SD or mode (no., %) or median $\pm$ SD and/or range in years; gender/sex (F/M), no. %	Comparison group	Highest domain OR biggest difference, ^a score (SD)	Lowest domain OR lowest difference, ^a score (SD)	Total score
Cetin 2017, ³⁵ Turkey, not specified	37, cross-sectional study, SF-36	Mean $\pm$ SD: 7.9 $\pm$ 3.5	Mean $\pm$ SD: 40.1 $\pm$ 6.1 F: 37, 100% M: 0, 0%	NA	Physical: 15.2	Mental: 12.5	130.5
Bourke 2008, ³⁶ Australia, 2004 to 2005	250, cross-sectional study, SF-12	Mean: 11.9	Mean: 44.4 F: 250, 100% M: 0, 0%	NA	Physical: 50.2	Mental: 45.2	NA
Darla 2020, ³⁸ India, not specified	102, cross-sectional study, PedsQL FIM	Range: 1–15	Mode: 35–39 (38, 37.25%) F: 51, 50% M: 51, 50%	NA	Cognitive function: 71.67	Worry: 57.33	NA
Rozensztrauch 2023, ³⁹ Poland, January 2022 to December 2022	53, cross-sectional study, PedsQL FIM	Mean $\pm$ SD: 6.48 $\pm$ 4.56 Range: 2–18	NA	NA	Cognitive function: 64.53 (24.42) Family relationship: 62.03 (24.49)	Worry: 41.98 (20.95) Daily activities: 44.97 (23.87)	57.51 (17.56)
Foley 2014, ⁴¹ Australia, 2009	289, cross-sectional study, BCFQOL	Range: 16–30	Range: 37–66 and older F: 150, 52% M: 139, 48%	NA	Physical/material well-being: 4.19	Emotional well-being: 3.49	NA
Brown 2006, ⁴² Canada, not specified	33, cross sectional study, FQOL	Range: 3–13	Mean (mothers): 38–40 Mean (fathers): 41–45	Typically developing children	^a Leisure and enjoyment of life (0.821)	Support from disability related services (0.300)	NA
Marchal 2013, ²¹ Netherlands, 1999 to 2001	98, cross sectional study, TAAQOL	Mean $\pm$ SD: 7.1 $\pm$ 0.6	Median $\pm$ SD: 41.3 $\pm$ 4.4 Range 32.4–51.9 F: 84, 86% M: 14, 14%	NA	Cognitive function (F=11.57)	Vitality (F=6.60)	NA
Marchal 2016, ²² Netherlands, 2012 to 2013	124, cross sectional study, TAAQOL	Range: 11–13	Mothers, mean $\pm$ SD: 45.9 $\pm$ 4.2 Fathers, mean $\pm$ SD: 47.8 $\pm$ 5.4 F: 80, 65.5% M: 44, 35.5%	NA	Fine motor function Mother 96.3 (9.2) Father 98.6 (7.7)	Vitality (57.2)	NA

BCFQOL: Beach Center Family Quality of Life; FQOL: Family Quality of Life; NA: Not applicable/not available; IQR: interquartile range; PedsQL FIM: Pediatric Quality of Life Inventory Family Impact Module; SD: standard deviation; SF-12: 12-Item Short Form Survey; SF 36: 36-Item Short Form Survey; TAAQOL: TNO-AZL Questionnaire for Adult's Health Related Quality of Life; TNO-AZL: The Netherlands Organization for Applied Scientific Research Academical Medical Center

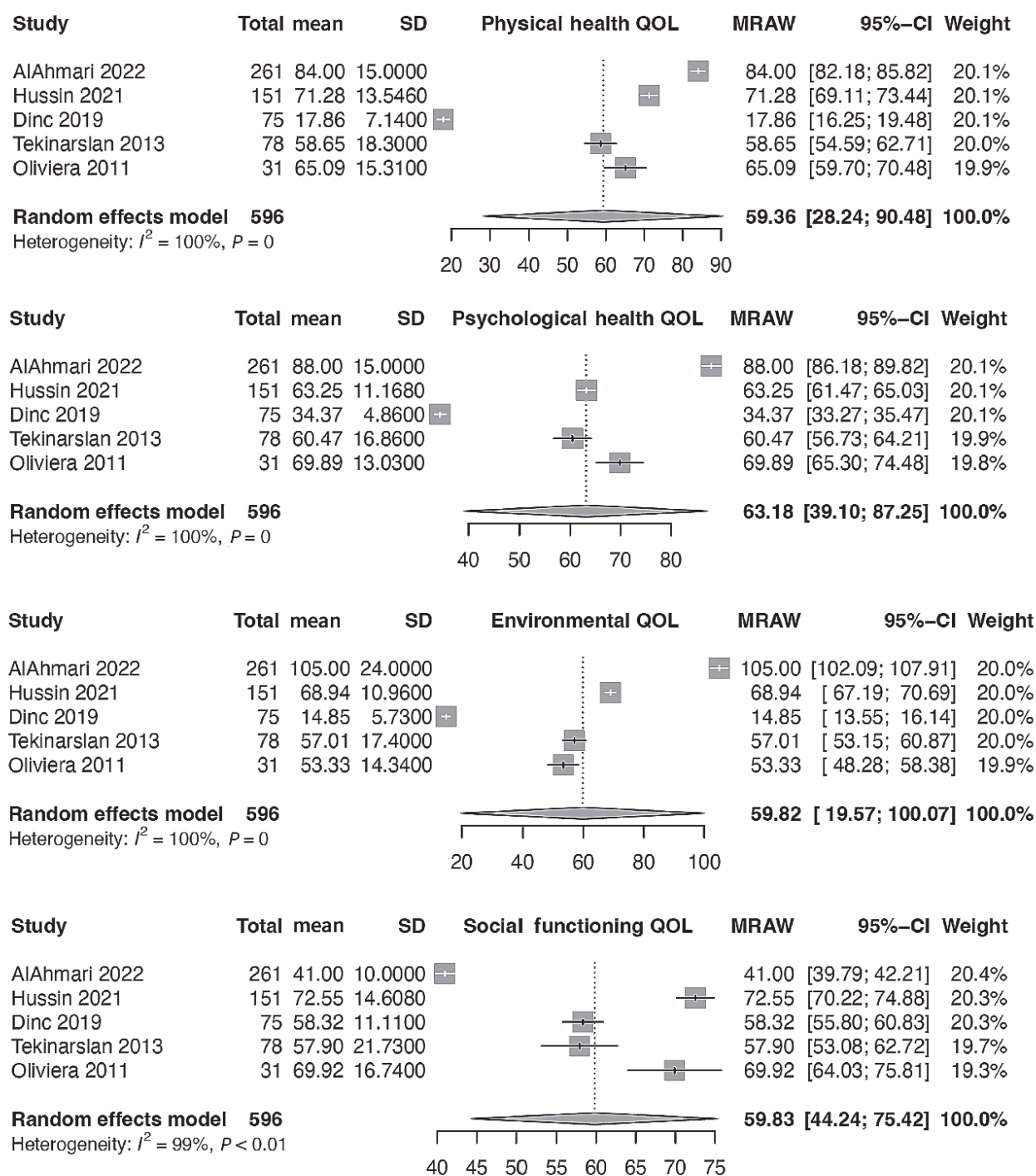
^a The differences in individual QOL domain values between the control group and DS group of family caregivers (if applicable).

the 0–20 scale for the WHOQOL-BREF, which we transformed to 0–100 to enable comparison, using the formula stated in Supplementary Appendix S2. Supplementary Appendix S4 presents the qualitative analysis of these 10 studies.

Quantitative analysis

We conducted a meta-analysis of WHOQOL-BREF scores on 5 of 10 studies^{18,26,30–32} with 596 participants. Five studies were excluded as standard deviation values were unavailable^{28,29} or not

Fig. 2. Forest plot of combined data of 5 studies using the World Health Organization Quality of Life Instrument-Brief Version.



CI: confidence interval; MRAW: raw mean; QOL: quality of life; SD: standard deviation

calculable from transformed scores.^{24,25,27} Fig. 2 shows the forest plot of compiled scores. Funnel plot was not constructed to measure publication bias due to the small number of studies.

Psychological health domain had the highest mean score (95% CI) of 63.18 (39.10–87.25). Scores were poorer in physical, environmental and social domains at 59.36 (28.24–90.48), 59.82 (19.57–100.07) and 59.83 (44.24–75.41), respectively. Studies were heterogenous with I^2 values ranging from 99–100% (all $P < 0.01$). High heterogeneity stemmed from the relatively small number of included studies and diversity in the population studied. For example, Senses Dinc et al.'s¹⁸ cohort stands out as an outlier with markedly poor physical, psychological and environmental health scores, which could be attributed to high prevalence (66%) of comorbidities, psychiatric symptoms and depressive disorders among mothers, high economic burden and caregiving for the youngest group of children with DS, aged 0 to 3 years. These factors may have exacerbated caregiving tasks for the caregivers and resulted in poorer QOL in multiple domains. AlAhmari et al.'s²⁶ study in Saudi Arabia reported much lower social functioning compared to other studies, where 64% of mothers had more than 4 children.

QOL measures using 36-Item Short Form Survey (SF-36) and 12-Item Short Form Survey (SF-12)

The SF-36 is a self-administered, standardised scale involving 8 domains of QOL studying limitations in various aspects in life.³³ The SF-12 is an abbreviated version of the SF-36.³⁴

Cetin et al. investigated the effects of functional independence and age of children with DS on the QOL of 37 mothers in Turkey using SF-36.³⁵ The children were classified into "need observation" and "independent" using the Functional Independence Measure. Mothers of "independent" children had significantly higher QOL compared to children "needing observation", particularly in total QOL and mental subdomain ($P = 0.036$ and $P = 0.018$, respectively); but no difference was found in physical subdomain ($P = 0.062$). The children's age did not have any effect on the mothers' QOL.

Bourke et al. explored the relationship of various characteristics of children with DS on their mothers' ($n = 250$) physical, mental and overall health in Australia.³⁶ The mothers experienced lower QOL in physical health domain if their child had current heart problems or higher body mass index ($P = 0.026$ and $P = 0.006$, respectively). Mothers of children with DS fared worse in mental health (mean [SD] 45.2 [10.6], $P < 0.0001$) than mothers of

children without DS. Higher scores on the child's Developmental Behavior Checklist, which indicates poorer behaviour, were significantly associated with lower maternal physical and mental health. The child's age and sex, number of siblings, and maternal factors (education, family income and partner status) did not affect maternal QOL.

QOL measures using Pediatric Quality of Life Inventory Family Impact Module (PedsQL FIM)

PedsQL FIM 4.0 is a 36-item, self-reported QOL instrument for parents of children with chronic health conditions.³⁷

Darla et al. studied 51 caregivers of children with DS in South India; majority were from upper-middle to upper class urban backgrounds.³⁸ Most of the caregivers experienced an average to good QOL (mean 68.98). They were most affected by worry (57.33%, z score = -1.91) and least affected in cognitive functioning (71.60%, z score = 1.22). Older caregivers (35–50 years) reported better QOL than younger caregivers (20–35 years). Upper-middle class caregivers reported better QOL compared to upper class caregivers (70.20 versus 59.92, respectively). Parents with children who had fewer comorbidities reported better QOL (73.78 for no comorbidities, 62.34 for 4 comorbidities). There was no correlation of QOL with the birth order and number of siblings.

Rozensztrauch et al. studied 53 Polish parents, and the relationship between child's QOL and parental QOL.³⁹ The total mean (SD) score was 57.51 (17.50), with worry and daily activities the worst affected domains. There was a positive association between the child's QOL and the QOL of their parents and family functioning, indicating that parental perception of better QOL in the child is positively correlated with parental QOL.

QOL measures using Beach Center Family Quality of Life Scale (BCFQOL)

BCFQOL is a self-report scale measuring quality of family life.⁴⁰

Foley et al. studied 150 families of young adults with DS in Australia. Family QOL was correlated with activities of daily living (ADL) and day occupations of young adults with DS.⁴¹ Families were most satisfied with their physical/material well-being (mean [SD] 4.19 [0.72]) and least satisfied in emotional well-being (mean [SD] 3.47 [1.00]). An open employment programme (mean [SD] 107.15 [13.63]), compared to sheltered employment (mean 94.91 [16.01]) or day recreation programmes (mean [SD] 93.24 [22.25]), improved family QOL moderately ($P < 0.001$). Family QOL

was higher in children with DS with higher ADL abilities. Factors that elevated family QOL included higher levels of familial support ($P<0.001$) and access to services that enhance ADL functions.

QOL measures using Family Quality of Life (FQOL)

FQOL is a self-report instrument that measures family's QOL in nine domains.⁴²

Brown et al. compared QOL of families in Canada who had children with DS ($n=33$), children with autism ($n=18$) and TD children ($n=18$, control group).⁴² The control group had higher satisfaction than families of children with disability (DS and autism) in 8 of the 9 domains (the domain of disability-related services is not relevant to TD children). Families with children with DS had statistically higher satisfaction scores than families with children with autism except for support for disability-related services domain. In spiritual and cultural belief, parents of children with DS reported lower scores than parents of autistic children ($P<0.001$). QOL of families with children with DS compared to the control group were statistically lower in the domains of health ($P<0.01$), financial well-being ($P<0.05$) and support from others ($P<0.001$).

QOL measures using The Netherlands Organization for Applied Scientific Research Academic Medical Center Questionnaire for Adult's Health-Related Quality of Life (TAAQOL)

TAAQOL has 45 items in 12 domains.²¹ Marchal et al. studied the effect of socio-demographic, child functioning and psychosocial factors on QOL of 98 parents of children with DS in Netherlands.²¹ Psychosocial variables (social support, quality of partner relations and time pressure) affected QOL domains of cognitive functioning, social functioning, daily activities and vitality. Socio-demographic factors (gender of child and parent, and parental educational level) had less effect on parental QOL. Cognitive function was most dampened by night sleeping hours of child ($P<0.01$) and parents giving up a hobby since birth of child ($P<0.01$). Social functioning was most predicted by quality of inter-partner relations ($P<0.001$). Daily activities QOL domain was best predicted by whether parents had time to care for ill friends or family ($P<0.01$), and vitality was best predicted by whether parents had sufficient personal time ($P<0.01$).

In another study, Marchal et al. studied QOL of 124 parents of 88 adolescents (11–13 years old) with DS compared to a control group, and QOL fluctuations when the children were aged between 6 to 8 years old.²² There were 58 parents with

children with DS who had participated in the preceding study by the same authors.²¹ Mothers of adolescents with DS compared to control group, reported lower score in the sexuality domain of QOL ($P=0.001$), while no QOL domain differed significantly in fathers. Fifty-eight parents of children with DS participated at 2 time points (children at age 6–8 years and 11–13 years).^{21,22} Parents of 11–13 years old reported improved trend in cognitive functioning (mean [SD] 65.9 [31.1] versus 74.4 [26.8]; $P=0.035$) and aggressiveness (mean [SD] 85.6 [17.0] versus 90.4 [15.9]; $P=0.041$), where a higher score in aggressiveness indicates better functioning over time. The other QOL subdomains did not differ between the 2 time points.

DISCUSSION

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

Our meta-analysis showed poorer scores among caregivers of children with DS compared to population norms of WHOQOL-BREF (who may or may not be involved in caregiving tasks) in high- and middle-income countries. Among caregivers of children with DS, the highest score was in psychological health with a mean of 63.18 (95% CI 39.18–87.28); all other domain scores were below 60. In comparison, population norms of Australian adults ages 20–79 years were: psychological health mean 70.6 (SD 14.0); physical health, mean 73.5 (SD 18.1); social relationship, mean 71.5 (SD 18.2) and environmental, mean 75.1 (SD 13.0).⁴³ Similarly, population norms in Brazilian adults aged 20–63 years were: psychological health, mean 65.9 (SD 10.8); physical health, mean 58.9 (SD 10.5); social mean 76.2 (SD 18.8) and environmental 59.9 (SD 14.9).⁴⁴ All 5 studies in the meta-analysis were from non-Western countries; therefore, generalisability could be limited to countries with similar socio-economic background. As QOL depends on personal and socio-cultural factors as well as individual values and expectations, interpretation of QOL data needs to consider these factors. Furthermore, 4 individual case-control studies generally reported lower QOL in caregivers of children with DS compared to TD children.^{18,22,24,42}

QOL of the caregivers is affected by various factors. Child-related factors included level of functional independence,^{24,35} poor development,³⁶ presence of multiple comorbidities,^{18,38} impaired ADL⁴¹ and poor sleep quality.²¹ Environmental factors included the number of children,²⁶ quality of housing²⁷ and support from family.⁴¹ Personal factors included age of the caregivers,³¹ being a single mother,²⁵ and having a low education and low

income among mothers.²⁵ Belief in organised religions had a positive impact of QOL.²⁸ Of note, the vast majority of individuals with DS, even in countries with good social support, continue to live with their family.⁴¹

Children and young adults with DS experience significant changes from infancy to young adulthood. During infancy, families grapple with the diagnosis (especially if it was not identified through antenatal screening) and cope with congenital conditions such as congenital heart diseases, feeding difficulties and gastrointestinal malformations.⁹ These challenges may contribute to the reported poor QOL among parental caregivers of younger children.¹⁸ As the child's congenital conditions are treated or improve, and the family adjusts to the diagnosis, coupled with the typical pleasant demeanour of children with DS,¹⁰ caregivers' QOL tends to improve during early childhood. However, during adolescence and young adulthood, individuals with DS face new challenges, including social adjustments, peer relationships, and a higher prevalence of anxiety and depression. The phenomenon known as idiopathic regression in DS, further impacts the well-being of individuals with DS.¹¹ As the QOL of family caregivers is closely related to QOL of the children with DS,³⁹ it is prudent to screen caregivers' QOL with higher frequency during infancy, late childhood and adolescent years.

Twelve out of 18 studies were from non-Western countries. Some studies included rural population, thereby increasing the diversity of the study population.^{25,28} As QOL is highly dependent on socio-cultural context, this global representation is a promising step towards broader understanding of QOL of family caregivers caring for children with DS from a diverse perspective.

We recommend using WHOQOL-BREF as a preferred tool to investigate QOL of caregivers caring for children with DS as this tool is more widely used, validated in many languages and free of cost. This would enable researchers to compare results across studies and aggregate data for future meta-analyses.

We would like to highlight several limitations. In the search strategy, we did not include intellectual disability, which could have broadened the search and plausibly retrieved more studies that included people with intellectual disabilities related to DS. We deviated slightly from the PROSPERO application where we specified an upper limit of age of 21 years, but we expanded the upper boundary of age to 30 years. Studies were heterogeneous as reflected in the I^2 values. We posit that one of the primary reasons for this heterogeneity is the wide

age range of children and young adults with DS (age range 1 month to 30 years) included in the studies. Across this wide age range, individuals with DS undergo significant changes in their developmental and medical needs, and emotional maturity resulting in varied caregiving tasks that can affect the QOL of caregivers. Most of participants in the studies were mothers, with underrepresentation of the fathers. In a few studies, a minority of the caregivers were not parents (e.g. maid, grandparents or sibling)²⁶ or not specified.²⁴ There was only 1 longitudinal follow-up study with a short follow-up duration (<5 years).²² As the life expectancy of individuals with DS continues to improve, there is a need to investigate QOL of young adults and older individuals with DS living in diverse socio-cultural settings.

CONCLUSION

In this comprehensive review, we have identified several critical areas for future research. First, there remains a significant gap in longitudinal cohort studies conducted over an extended period. Such studies are essential to understand how caregivers' QOL evolves as their children with DS experience changes in their developmental, psychosocial and medical needs. Second, existing research predominantly focuses on female caregivers, typically mothers. However, to gain a more holistic perspective, it is crucial to explore the views of male caregivers as well and consider the input of other extended family members, such as grandparents and siblings. Last, there is a pressing need to determine the barriers and challenges at the practice level to implement QOL measures directed to the patients and their family caregivers.

Our systematic review fills a void in our contemporary understanding of QOL in caregivers of children with DS. Periodic assessment of QOL of family caregivers is needed to identify caregivers at risk of poorer QOL and institute appropriate measures.

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. Summary of instruments.

Supplementary Appendix S3. Quality of included studies using Newcastle-Ottawa Scale.

Supplementary Appendix S4. Qualitative analysis of studies using the World Health Organization Quality of Life instrument-Brief Version (WHOQOL-BREF).

REFERENCES

1. Family Caregivers Alliance. Definitions: What do we mean by. <https://www.caregiver.org/resource/definitions-0/>. Accessed 6 July 2024.
2. Liu F, Shen Q, Huang M, et al. Factors associated with caregiver burden among family caregivers of children with cerebral palsy: a systematic review. *BMJ Open* 2023; 13:e065215.
3. Kasuya RT, Polgar-Bailey P, Takeuchi R. Caregiver burden and burnout. A guide for primary care physicians. *Postgrad Med* 2000;108:119-23.
4. World Health Organization. The World Health Organization Quality of Life (WHOQOL). <https://www.who.int/publications/i/item/WHO-HIS-HSI-Rev.2012.03>. Accessed 6 July 2024.
5. Karimi M, Brazier J. Health, Health-Related Quality of Life, and Quality of Life: What is the Difference? *Pharmacoeconomics* 2016;34:645-9.
6. Chow MYK, Morrow AM, Cooper Robbins SC, et al. Condition-specific quality of life questionnaires for caregivers of children with pediatric conditions: a systematic review. *Qual Life Res* 2013;22:2183-200.
7. United Nations. World Down Syndrome Day 21 March. <https://www.un.org/en/observances/down-syndrome-day#:~:text=The%20estimated%20incidence%20of%20Down>. Accessed 6 July 2024.
8. Raut P, Sriram B, Yeoh A, et al. High Prevalence of Hearing Loss in Down Syndrome at First Year of Life. *Ann Acad Med Singap* 2011;40:493-8.
9. Bull MJ, Trotter T, Santoro SL, et al. Health Supervision for Children and Adolescents With Down Syndrome. *Pediatrics* 2022;149:e2022057010.
10. Grieco J, Pulsifer M, Seligsohn K, et al. Down syndrome: Cognitive and behavioral functioning across the lifespan. *Am J Med Genet C Semin Med Genet* 2015;169:135-49.
11. Walpert M, Zaman S, Holland A. A Systematic Review of Unexplained Early Regression in Adolescents and Adults with Down Syndrome. *Brain Sci* 2021;11:1197.
12. Parish SL, Pomeranz A, Hemp R, et al. Family Support for Families of Persons with Developmental Disabilities in the U.S.: Status and Trends. <https://ici.umn.edu/products/prb/122/default.html>. Accessed 6 July 2024.
13. Barros ALO, Barros AO, Barros GL de M, et al. Burden of caregivers of children and adolescents with Down Syndrome. *Cien Saude Colet* 2017;22:3625-34.
14. AlShatti A, AlKandari D, AlMutairi H, et al. Caregivers' perceptions and experience of caring for persons with Down syndrome in Kuwait: a qualitative study. *Int J Dev Disabil* 2021;67:381-90.
15. Abbeduto L, Seltzer MM, Shattuck P, et al. Psychological well-being and coping in mothers of youths with autism, Down syndrome, or fragile X syndrome. *Am J Ment Retard* 2004;109:237-54.
16. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021:n71.
17. Higgins J, Thomas J, Chandler J, et al. *Cochrane Handbook for Systematic Reviews of Interventions* Version 6.4 (Updated August 2023). Cochrane; 2023. www.training.cochrane.org/handbook. Accessed 6 July 2024.
18. Senses Dinc G, Cop E, Tos T, et al. Mothers of 0-3-year-old children with Down syndrome: Effects on quality of life. *Pediatr Int* 2019;61:865-71.
19. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol* 2005;5:13.
20. Wells G, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed 6 July 2024.
21. Marchal JP, Maurice-Stam H, Hatzmann J, et al. Health related quality of life in parents of six to eight year old children with Down syndrome. *Res Dev Disabil* 2013;34:4239-47.
22. Marchal JP, Maurice-Stam H, Van Trotsenburg ASP, et al. Mothers and fathers of young Dutch adolescents with Down syndrome: Health related quality of life and family functioning. *Res Dev Disabil* 2016;59:359-69.
23. Vahedi S. World Health Organization Quality-of-Life Scale (WHOQOL-BREF): Analyses of Their Item Response Theory Properties Based on the Graded Responses Model. *Iran J Psychiatry* 2010;5:140-53.
24. Amaral MF, Carvalho KHTD, Aranega AM, et al. Evaluation of quality of life, depression, anxiety and stress among caregivers of people with or without Down Syndrome: a cross-sectional study. *Research, Society and Development* 2020;9:e813986193.
25. Geok CK, Abdullah KL, Kee LH. Quality of life among Malaysian mothers with a child with Down syndrome. *Int J Nurs Pract* 2013;19:381-9.
26. AlAhmari FS, Alageel AF, Aldosari MA, et al. The quality of life of parents of children with down syndrome in a tertiary care hospital: A qualitative research study at Saudi Arabia. *Ann Med Surg (Lond)* 2022;81:104428.
27. Abbasi S, Sajedi F, Hemmati S, et al. Evaluation of Quality of Life in Mothers of Children with Down Syndrome. *PCP* 2016;4:81-8.
28. Vadakedom SS, Mary Antony J, Krishnan Padma B, et al. Quality of Life of Mothers of Children with Down Syndrome. *JEMDS* 2017;6:2939-42.
29. Buzatto LL, Beresin R. Quality of life of parents with Down syndrome children. *Einstein* 2008;6:175-81.
30. Oliveira E de F, Limongi SCO. Quality of life of parents/caregivers of children and adolescents with Down syndrome. *J Soc Bras Fonoaudiol* 2011;23:321-7.
31. Hussin N, Ismail A, Ismail J, et al. The quality of life of mothers of down syndrome children with and without hearing impairment in Universiti Kebangsaan Malaysia medical center. *Indian J Otol* 2021;27:189.
32. Tekinarslan IC. A comparison study of depression and quality of life in Turkish mothers of children with Down syndrome, cerebral palsy, and autism spectrum disorder. *Psychol Rep* 2013;112:266-87.
33. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30:473-83.
34. Ware J, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34:220-33.
35. Cetin S, Calik B, Taspinar F, et al. The effect of functional independence level and age on the quality of life of mother's with down syndrome children. *Curr Pediatr Res* 2017; 21:652-7.

36. Bourke J, Ricciardo B, Bebbington A, et al. Physical and Mental Health in Mothers of Children with Down Syndrome. *Journal Pediatr* 2008;153:320-6.
37. Varni JW, Sherman SA, Burwinkle TM, et al. The PedsQL Family Impact Module: preliminary reliability and validity. *Health Qual Life Outcomes* 2004;2:55.
38. Darla S, Bhat D. Health-related quality of life and coping strategies among families with Down syndrome children in South India. *Med J Armed Forces India* 2021;77:187-93.
39. Rozensztrauch A, Wieczorek K, Twardak I, et al. Health-related quality of life and family functioning of primary caregivers of children with down syndrome. *Front Psychiatry* 2023; 14:1267583.
40. Hoffman L, Marquis J, Poston D, et al. Assessing Family Outcomes: Psychometric Evaluation of the Beach Center Family Quality of Life Scale. *J Marriage Fam* 2006; 68:1069-83.
41. Foley KR, Girdler S, Downs J, et al. Relationship between family quality of life and day occupations of young people with Down syndrome. *Soc Psychiatry Psychiatr Epidemiol* 2014;49:1455-65.
42. Brown RI, MacAdam-Crisp J, Wang M, et al. Family Quality of Life When There Is a Child With a Developmental Disability. *Policy Practice Intel Disabi* 2006;3:238-45.
43. Hawthorne G, Herrman H, Murphy B. Interpreting the WHOQOL-Brèf: Preliminary Population Norms and Effect Sizes. *Soc Indic Res* 2006;77:37-59.
44. Cruz LN, Polanczyk CA, Camey SA, et al. Quality of life in Brazil: normative values for the WHOQOL-bref in a southern general population sample. *Qual Life Res* 2011;20:1123-9.