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Quality of Life Among U.S. Rare Disease Caregivers: Associations with Care Recipient Characteristics and Online Support Resources

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Abbreviations

QoL; caregiver quality of life; FB: Facebook; CarerQol: Care-related Quality of Life instrument; CarerQol-7D: CarerQol 7-dimension; CarerQol-VAS: CarerQol-Visual Analog Scale; SD: standard deviation; IQR: interquartile range; EFA: exploratory factor analysis; KMO: Kaiser–Meyer–Olkin; CrI: credible intervals

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Authors' contributions

CHL, MH, and TL developed the study concept. CHL, MS, and TL developed the methodology. CHL performed the formal analyses and prepared visualizations. CHL and TL wrote the original draft. All authors contributed to validation and investigation. MH and TL supervised the project, and MH acquired funding. All authors reviewed, critically revised the manuscript, and approved the final version.

Availability of data and materials

The survey data were collected from rare disease patients and are not provided publicly due to privacy concerns; the data are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

The study was approved by the Institutional Review Boards at Stanford University School of Medicine (IRB protocol no. 61783) and Tufts University (STUDY00004534).

Competing interests

The authors declare that they have no competing interests.

ABSTRACT (249/350)

Background and Objective

Informal caregivers of individuals with rare diseases face unique challenges impacting their health and well-being, yet systematic evidence of their quality of life (QoL) remains limited. This study evaluated QoL among U.S. caregivers across diverse rare diseases and examined associations with demographics and online support resources.

Methods

We conducted an online survey of U.S. informal caregivers recruited through rare disease–focused Facebook groups. We assessed caregiver QoL using the CarerQol-7D and the CarerQol Visual Analog Scale (VAS). The survey collected information on caregiver and care-recipient demographics and caregiver engagement with online support resources. We used exploratory factor analysis to identify underlying latent constructs of online support resources and beta regression to assess their association with CarerQoL-7D scores, adjusting for demographics.

Results

Among 207 U.S. caregivers of individuals with rare diseases, mean (SD) CarerQoL-7D and VAS scores were 73.6 (18.5) and 6.9 (1.8), respectively. We identified three online support resource factors: 1) information sharing on events, news, and opportunities; 2) information

sharing on rare disease experiences; and 3) peer support resources (connection and belonging). In adjusted analyses, online resource use was not significantly associated with CarerQol-7D scores. Caring for a disabled individual or someone with an ultra-rare condition was associated with 5.5- and 6.2-point decreases in CarerQol-7D, respectively.

Conclusions

Among informal caregivers of individuals with rare diseases, caring for individuals with a disability or an ultra-rare condition is significantly associated with lower CarerQol, whereas online resource engagement is not. This highlights the need for alternative support interventions.

KEY WORDS

Rare disease, quality of life, CarerQol, caregiver

INTRODUCTION

Rare diseases, although individually uncommon, collectively represent a major public health concern. More than 10,000 rare diseases have been identified worldwide, together affecting nearly 30 million individuals in the United States alone.(1,2) Despite their low individual prevalence, the cumulative impact of these conditions on individuals, families, and health systems is profound. A recent national analysis estimated that rare diseases account for nearly $1 trillion USD in annual economic burden.(3) Beyond their economic impact, individuals living with rare diseases experience lower health-related quality of life compared with those with common chronic conditions, reflecting prolonged diagnostic delays, fragmented care pathways, and limited access to effective therapies.(4,5)

Caregivers of individuals with rare diseases also face challenges. Because most rare diseases are lifelong conditions with childhood onset, parents frequently assume intensive and enduring caregiving roles. These caregivers are not only responsible for daily medical and emotional support but also for navigating multiple specialists, coordinating care, and advocating for their children. They report unmet informational, communication, and social-support needs(6) and typically receive limited financial support despite significant impact on caregiver employment opportunities and income.(7) These unmet needs are critical because research in non-rare disease conditions demonstrates a link between unmet needs and lower caregiver quality of life (QoL).(8–10) Caregivers of people with rare diseases also experience higher levels of psychological distress, social isolation, and occupational disruption than caregivers of people with more common chronic conditions.(11,12)

Despite growing recognition of these challenges, systematic evidence of caregiver QoL in rare diseases remains limited. A recent scoping review identified only 34 studies addressing caregiver QoL in any rare disease, highlighting the limited empirical evidence on the experiences of rare disease caregivers.(7) Filling this gap is important for providing caregivers with adequate support and developing evidence-based interventions that can target groups needing the most help. In addition, examining the relationship between resources addressing unmet needs and the QoL of rare disease caregivers can identify actionable areas for intervention.

To fill this gap, we sought to evaluate the QoL of informal caregivers (i.e., individuals providing unpaid, ongoing assistance to a person) of individuals with rare diseases and to examine how demographic, clinical, and social characteristics were associated with caregiver QoL. We also evaluated whether accessing online resources aimed at addressing caregivers' unmet needs was associated with QoL, hypothesizing that receipt of such resources would be significantly associated with higher caregiver QoL.

METHODS

Study design and participants

We conducted a cross-sectional online survey to characterize the QoL of individuals and caregivers of individuals with rare diseases between October and December 2021. The survey methods have been described in detail elsewhere.(5,13) Briefly, the study team first identified a systematic random sample of 1,200 rare diseases listed in the Orphanet database (https://www.orpha.net/) and then used targeted outreach through Facebook

(FB) groups to recruit participants.(13) Eligible respondents (1) were aged 18 years or older, (2) were able to read and write in English, and (3) self-identified as either an individual with a rare disease or a family member of individuals with a rare disease. The survey recruited individual with a rare disease and their caregivers globally. For this analysis, we included only U.S. caregivers who completed at least 80% of the survey. The Institutional Review Boards at Stanford University School of Medicine (IRB protocol no. 61783) and Tufts University (STUDY00004534) approved this study. All participants provided informed consent before beginning the survey.

Data collection

Participant characteristics

We asked respondents to report their sociodemographic characteristics, including their age, gender, race, ethnicity, household income, and whether their care recipient with a rare disease also had a disability, had undergone genetic testing, and had received a genetic diagnosis. We collapsed race into four categories (White, Asian, Black or African American, and Other) and ethnicity into two categories ((1) Hispanic, Latino, or Spanish origin or (2) Not of Hispanic, Latino, or Spanish origin). We derived disease prevalence using Orphanet prevalence categories (e.g., 1-9 in 100,000, 1-9 in 1,000,000) for the condition that was the focus of the FB group from which the respondent was recruited. Because Orphanet did not use the more commonly referenced threshold of 1 in 50,000 cases for ultra-rare disease,(14) we defined ultra-rare diseases as those with a prevalence of 1 to 9 cases per 1,000,000 individuals or lower, providing an approximate classification for our analysis.

158 Quality of life

159 The survey assessed caregivers' QoL using the validated Care-related Quality of Life
160 instrument (CarerQol), a caregiver-specific QoL instrument which includes the CarerQol 7-
161 dimension (CarerQol-7D) and the CarerQol-Visual Analog Scale (VAS).(15) The CarerQol-
162 7D measures subjective burden by assessing seven dimensions of caregiving, including (1)
163 fulfillment from caregiving, (2) relational problems, (3) mental health problems, (4)
164 problems combining care tasks with daily activities, (5) financial problems, (6) support with
165 carrying out care tasks, and (7) physical health problems. Dimensions are assessed on a
166 three-level scale: "a lot of," "some," and "no." Two dimensions, fulfillment and support,
167 represent positive domains where "a lot of" indicates better QoL. The remaining five
168 questions represent negative domains, where "no" indicates a better QoL. We used the US-
169 specific tariffs to calculate preference-weighted CarerQol-7D scores that range from 0
170 (worst informal care situation) to 100 (best informal care situation). The CarerQol-VAS rates
171 the caregiver's overall QoL on a scale from 0 (completely unhappy) to 10 (completely
172 happy).

173 Online support resources

174 We asked caregivers to report how they engage with various online support resources
175 provided in the specific FB group where the survey was posted, including the types of
176 resources accessed and their perceptions of FB group experiences. These survey
177 questions assessing engagement with online support resources are aligned with
178 established literature on the needs of individuals with rare diseases and their

caregivers.(16) Ten questions captured the frequency with which the respondent engaged with FB group support resources, specifically informational (e.g., prognosis) and practical (e.g., research opportunity) support on a scale from 0 (never) to 10 (very frequently) (Online Supplement Table 1). Three questions measured perceived social and emotional support.

Analysis

We summarized participant characteristics using descriptive statistics. We summarized the distribution of responses across the seven CarerQol-7D dimensions and computed the mean, standard deviation (SD), median, and interquartile range (IQR) of CarerQol-7D preference-weighted scores and CarerQol-VAS scores.

We conducted an exploratory factor analysis (EFA)(17) on the 13 ordinal variables of FB group support resources (Supplement Table 1) to identify and group related variables into underlying resource-related factors and to evaluate whether they reflected a smaller set of latent constructs. This grouping also simplified the subsequent analytical approach by using a smaller set of composite factors. We used the Kaiser–Meyer–Olkin (KMO) measure of sampling adequacy to assess whether the data were suitable for EFA, setting a KMO threshold of 0.5. We used parallel analysis to assess the appropriate number of factors (1-13) and compared the interpretability of various models to select the final number of factors. We retained variables in the factor analysis if they achieved a factor loading of ≥ 0.7. While best-practice recommendations consider loadings above 0.5 as “practically significant”, we used a threshold of 0.7 to ensure the reliability of each factor.(17,18) We re-ran the factor analysis after removing any variables that did not meet our loading criteria or

were not explainable by a single factor. This final step ensured that the original factor structure remained intact.

We used an ordered beta regression to examine associations between CarerQol-7D preference-weighted scores and caregiver characteristics, care recipient characteristics, and the resource-related factors identified from the factor analysis. Given that the CarerQol-7D scores are continuous and strictly bounded (0-100), traditional linear regression models were inappropriate. (19) Beta regression was chosen as the best modeling technique because it would allow predictors to directly influence the mean (μ) of the beta distribution and appropriately account for the bounded range of the CarerQol-7D scores.(20) We calculated the average marginal effects on the original bounded scale of CarerQol-7D scores (0–100) and reported 95% Bayesian credible intervals (CrI). We assessed model performance using posterior predictive plots to compare observed data against simulated data.

We used R version 4.5.1and the *psych*, *ordbetareg,* and *marginaleffects* packages to conduct the analysis.(21)

RESULTS

Caregiver characteristics

We included 207 US caregivers of individuals with rare diseases in our analytic sample after excluding 26 caregivers with more than 20% missing survey responses. Most caregivers

were younger than 40 years old, non-Hispanic, Latino, or Spanish origin, White, female, and reported an annual household income greater than $100,000 (Table 1). Fifty-eight percent (n = 119) of caregivers reported that their family member with a rare disease also had a disability. The sample included caregivers of individuals with rare diseases spanning a wide range of disease prevalence categories (Table 1).

Caregiver quality of life

Overall, the mean (SD) CarerQol-7D score was 73.6 (18.5), with a median (IQR) of 78.4 (62.3-86.9). The mean (SD) CarerQol-VAS score was 6.9 (1.8), with a median (IQR) of 7 (6-8) (Table 2). In the positive domains of CarerQol-7D, a plurality of caregivers had “a lot” of fulfillment from caregiving (n = 117, 57%) and “some” social support (n = 100, 48%) (Figure 1). In the negative domains of CarerQol-7D, a plurality of caregivers had “some” problems with combining daily activities (n = 91, 44%), “some” physical health problems (n = 97, 47%), “some” mental health problems (n = 123, 59%), “no” relational problems (n = 145, 70%), and “no” financial problems (n = 101, 49%) (Figure 1).

Factor analysis results

We derived a KMO value of 0.85, which exceeded the 0.5 threshold, indicating that the variables were adequate for EFA. Parallel analysis suggested a potential three or four factor structure (Supplement Figure 1.). We selected a three-factor structure due to better interpretability. We removed four variables because their factor loadings were below 0.7 or were explained by multiple factors (Supplement Table 2). Factor loadings for the retained variables ranged from 0.73 to 0.90 (Table 3). Factors were named based on their content:

Factor 1: information sharing on events, news, and opportunities, Factor 2: information sharing on rare disease experiences, and Factor 3: peer support resource (connection and belonging) (Table 3).

Regression results

The final model included the three factor variables, along with caregiver, care recipient, and disease characteristics. Posterior predictive plots show concordance between the observed and simulated data (Supplement Figure 2). We found significant associations between CarerQol-7D scores and care-recipient disability status, and disease prevalence (Table 4). Caregivers of individuals with a disability had, on average, a 5.5-point lower CarerQol-7D score (95% CrI −10.8 to −0.2). Caregivers of individuals with ultra-rare diseases (i.e., a prevalence of 1 to 9 cases per 1,000,000 individuals or lower) had, on average, a 6.2-point lower CarerQol-7D score (95% CrI –12.1 to −0.2). Online resource related factors, including having received rare disease information, peer support resource, and information sharing on events, news, and opportunities, showed no significant association with CarerQol-7D scores.

DISCUSSION

The results of this study indicated that caregivers of individuals with a wide range of rare diseases had a mean CarerQol-7D score of 73.6, and that caregivers of individuals with rare diseases whom they also identified as disabled, and those with ultra-rare conditions (i.e., a prevalence of 1 to 9 cases per 1,000,000 individuals or lower) reported significantly lower CarerQol-7D scores. In contrast, the receipt of online resources from social media

was not associated with CarerQol-7D scores. Our results contribute to improved understanding of the QoL of US caregivers of individuals with rare diseases and factors that influence their variation. The sample size is notable within the context of rare diseases, as is the diversity in disease prevalence and disability status, increasing the generalizability of our results.

Researchers have been examining caregiver QoL using the CarerQol-7D in US caregivers since the US tariffs were developed in 2017.(22) However, very few studies have used the CarerQol-7D in the US, and even fewer have done so in the context of rare diseases.(23) A study of caregivers from the US, UK, and Germany reported a median CarerQol-7D score of 67.7 for caregivers of individuals with progressive familial intrahepatic cholestasis, a rare genetic disease.(24) The lower value of this score compared to the estimate obtained in our study may be explained in part by the severity of this rare disease, in which only 50% of affected individuals survive up to the age of 10.(25) In contrast, a study of caregivers of children with cystic fibrosis in Ireland reported a mean CarerQol-7D score of 89 for fathers and 84 for mothers.(26) This higher score could be explained by the healthcare and social support systems in Ireland, or by the characteristics of cystic fibrosis which, though serious and life-threatening, has seen rapid advances in treatment over the last few decades.(27) Studies with US caregivers have reported mean CarerQol-7D scores of 77.6 for caregivers of people living with dementia (a non-rare condition)(28) and 64 for US caregivers of people with degenerative cervical myelopathy, a non-rare disease where most individuals retain lifelong disability. The proximity of our results (mean score of 73.6) suggests comparable caregiving burden across rare disease and dementia contexts.

Quantifying the impact of caregiving on QoL can contribute to discussions and policy frameworks that recognize family and caregiver outcomes as part of the broader impact of rare disease and help guide allocation of supportive resources. In addition, understanding factors that shape caregiver QoL in rare diseases has implications that extend beyond individual well-being. We found two important factors associated with caregivers' QoL: the disability status of care recipients and the rarity of the disease. First, caring for an individual with an ultra-rare disease is associated with lower CarerQol-7D scores compared to caring for individuals with more prevalent rare diseases. This finding aligns with previous research indicating that lower disease prevalence correlates with poorer caregiver QoL(5,29) and that caregivers of individuals with rarer conditions experience greater emotional, physical, and social burden.(30,31) Lower-prevalence diseases may entail disproportionate caregiver QoL loss in part due to diagnostic odysseys and the scarcity of informational and psychosocial support resources.(6,32)

Second, the mean CarerQol-7D was lower among caregivers of individuals with rare diseases who caregivers also identified as disabled. Prior studies across various disease areas similarly demonstrate that caregiving for individuals with greater functional impairment or disability is associated with poorer caregiver QoL and psychological health. For example, in a study of stroke survivors, the mean CarerQol-7D scores declined with increasing dependence of the individuals being cared for—57.1 in mild dependence, 56.6 in moderate, and 45.5 in severe.(33) A related review also found a higher level of stress and depression, as well as perceived caregiving difficulty, when caring for disabled

individuals.(34) Our results add to the literature and support this relationship in the context of rare disease.

Our results did not support the hypothesis that greater receipt of online resources and support to address unmet needs would improve the QoL of caregivers. This lack of association may suggest that the benefits of online support resources are offset by the inherent stressors of social media (i.e., FB), such as the emotional impacts of comparison, information overload, and witnessing negative outcomes from others.(35) Additionally, there is limited literature examining the benefit of online resources for caregivers of individuals with rare diseases. Evidence from other disease areas is mixed. For example, a study found that online educational and behavioral support can be as effective as in-person approaches for cardiovascular disease management.(36) Conversely, other research indicates that online support groups may not significantly improve caregiver psychological outcomes.(37) Future research should directly evaluate the impact of online support resources on improving caregiver QoL in rare disease contexts, where access to support and resources remains limited.(11)

The strengths of our study include being the first to use the CarerQol instrument with a specific focus on rare disease caregivers in the US. Additionally, our results contribute to the literature by identifying key drivers that influence QoL within the rare disease caregiver population. Moreover, we evaluated these outcomes using ordered beta regression, which allowed for a more robust analysis of the CarerQol-7D scores by explicitly modeling their bounded nature. However, some limitations are worth noting. First, respondents were recruited from FB groups. This recruitment method may result in a sample that is not

representative of the broader rare disease caregiver population, as individuals in online communities may have different characteristics, motivations, or health statuses. While social media recruitment can facilitate access to diverse voices and may enhance engagement, it can limit the generalizability of findings and could limit the observed range of certain variables we examined (e.g., receipt of online resources). Other sampling schemes could mitigate selection biases. Second, the survey did not incorporate caregiver unmet need assessment tools, such as the Carer Support Needs Assessment Tool,(38) which can identify specific domains of need. As specific subgroups may face distinct challenges, targeted resources tailored to these groups could be particularly beneficial; however, this aspect was not examined in our study. Given the complexity and variability of caregiver needs, tailoring the survey to account for unique circumstances may have been challenging. Therefore, we adopted a broader approach, focusing on resources for unmet needs most commonly reported in the literature. Future research could address this limitation by assessing how specific resources improve QoL among groups with the greatest need for the support those resources are designed to provide.

CONCLUSION

This is the first study to examine caregiver QoL using CarerQol across a variety of rare diseases in the US. These findings highlight the need for targeted support strategies that recognize the unique challenges faced by caregivers, particularly those of individuals with disability and ultra-rare conditions.

REFERENCES

1. Griggs RC, Batshaw M, Dunkle M, Gopal-Srivastava R, Kaye E, Krischer J, et al. Clinical research for rare disease: opportunities, challenges, and solutions. Mol Genet Metab. 2009 Jan;96(1):20–6. doi:10.1016/j.ymgme.2008.10.003 PubMed PMID: 19013090; PubMed Central PMCID: PMC3134795.

2. Haendel M, Vasilevsky N, Unni D, Bologa C, Harris N, Rehm H, et al. How many rare diseases are there? Nat Rev Drug Discov. 2020 Feb;19(2):77–8. doi:10.1038/d41573-019-00180-y PubMed PMID: 32020066; PubMed Central PMCID: PMC7771654.

3. Yang G, Cintina I, Pariser A, Oehrlein E, Sullivan J, Kennedy A. The national economic burden of rare disease in the United States in 2019. Orphanet J Rare Dis. 2022 Apr 12;17(1):163. doi:10.1186/s13023-022-02299-5

4. Bogart KR, Irvin VL. Health-related quality of life among adults with diverse rare disorders. Orphanet J Rare Dis. 2017 Dec 7;12(1):177. doi:10.1186/s13023-017-0730-1

5. Rao A, Yabumoto M, Ward-Lev E, Miller EG, Naik H, Halley MC. Health-related quality of life in patients with diverse rare diseases: An online survey. Genet Med Open. 2024;2:101889. doi:10.1016/j.gimo.2024.101889

6. Mcmullan J, Lohfeld L, McKnight AJ. Needs of informal caregivers of people with a rare disease: a rapid review of the literature. BMJ Open. 2022 Dec 12;12(12):e063263. doi:10.1136/bmjopen-2022-063263 PubMed PMID: 36523233; PubMed Central PMCID: PMC9748923.

7. Černe T, Kragelj LZ, Turk E, Pavlič DR. Experiences of quality of life and access to health services among rare disease caregivers: a scoping review. Orphanet J Rare Dis. 2024 Aug 31;19(1):319. doi:10.1186/s13023-024-03327-2

8. Kerpershoek L, De Vugt M, Wolfs C, Woods B, Jelley H, Orrell M, et al. Needs and quality of life of people with middle-stage dementia and their family carers from the European Actifcare study. When informal care alone may not suffice. Aging Ment Health. 2018 Jul 3;22(7):897–902. doi:10.1080/13607863.2017.1390732

9. Chong E, Crowe L, Mentor K, Pandanaboyana S, Sharp L. Systematic review of caregiver burden, unmet needs and quality-of-life among informal caregivers of patients with pancreatic cancer. Support Care Cancer. 2023;31(1):74. doi:10.1007/s00520-022-07468-7 PubMed PMID: 36544073; PubMed Central PMCID: PMC9771849.

10. Cochrane A, Woods S, Dunne S, Gallagher P. Unmet supportive care needs associated with quality of life for people with lung cancer: A systematic review of the evidence 2007–2020. Eur J Cancer Care (Engl). 2022;31(1):e13525. doi:10.1111/ecc.13525

11. Sandilands K, Williams A, Rylands AJ. Carer burden in rare inherited diseases: a literature review and conceptual model. Orphanet J Rare Dis. 2022 Dec 9;17(1):428. doi:10.1186/s13023-022-02561-w

12. Atkins JC, Padgett CR. Living with a Rare Disease: Psychosocial Impacts for Parents and Family Members – a Systematic Review. J Child Fam Stud. 2024 Feb;33(2):617–36. doi:10.1007/s10826-024-02790-6

13. Yabumoto M, Miller E, Rao A, Tabor HK, Ormond KE, Halley MC. Perspectives of Rare Disease Social Media Group Participants on Engaging With Genetic Counselors: Mixed Methods Study. J Med Internet Res. 2022 Dec 21;24(12):e42084. doi:10.2196/42084

14. Smith CIE, Bergman P, Hagey DW. Estimating the number of diseases - the concept of rare, ultra-rare, and hyper-rare. iScience. 2022 Aug 19;25(8):104698. doi:10.1016/j.isci.2022.104698 PubMed PMID: 35856030; PubMed Central PMCID: PMC9287598.

15. Hoefman RJ, Van Exel J, Brouwer WBF. Measuring Care-Related Quality of Life of Caregivers for Use in Economic Evaluations: CarerQol Tariffs for Australia, Germany, Sweden, UK, and US. PharmacoEconomics. 2017 Apr;35(4):469–78. doi:10.1007/s40273-016-0477-x

16. Long JC, Best S, Nic Giolla Easpaig B, Hatem S, Fehlberg Z, Christodoulou J, et al. Needs of people with rare diseases that can be supported by electronic resources: a scoping review. BMJ Open. 2022 Sep 1;12(9):e060394. doi:10.1136/bmjopen-2021-060394 PubMed PMID: 36581982; PubMed Central PMCID: PMC9438091.

17. Knekta E, Runyon C, Eddy S. One Size Doesn't Fit All: Using Factor Analysis to Gather Validity Evidence When Using Surveys in Your Research. Brickman P, editor. CBE—Life Sci Educ. 2019 Mar;18(1):rm1. doi:10.1187/cbe.18-04-0064

18. Chen MY, Lai LJ, Chen HC, Gaete J. Development and validation of the short-form adolescent health promotion scale.

19. Ferrari S, Cribari-Neto F. Beta Regression for Modelling Rates and Proportions. J Appl Stat. 2004 Aug;31(7):799–815. doi:10.1080/0266476042000214501

20. Kubinec R. Ordered Beta Regression: A Parsimonious, Well-Fitting Model for Continuous Data with Lower and Upper Bounds. Polit Anal. 2023 Oct;31(4):519–36. doi:10.1017/pan.2022.20

21. R: The R Project for Statistical Computing [Internet]. [cited 2025 Dec 8]. Available from: https://www.r-project.org/

22. Hoefman RJ, Van Exel J, Brouwer WBF. Measuring Care-Related Quality of Life of Caregivers for Use in Economic Evaluations: CarerQol Tariffs for Australia, Germany, Sweden, UK, and US. PharmacoEconomics. 2017 Apr;35(4):469–78. doi:10.1007/s40273-016-0477-x

23. Cejalvo E, Martí-Vilar M, Gisbert-Pérez J, Badenes-Ribera L. The CarerQol Instrument: A Systematic Review, Validity Analysis, and Generalization Reliability Study. J Clin Med. 2025 Mar 12;14(6):1916. doi:10.3390/jcm14061916

24. Mighiu C, O'Hara S, Ferri Grazzi E, Murray KF, Schattenberg JM, Ventura E, et al. Impact of progressive familial intrahepatic cholestasis on caregivers: caregiver-reported outcomes from the multinational PICTURE study. Orphanet J Rare Dis. 2022 Feb 2;17(1):32. doi:10.1186/s13023-022-02177-0 PubMed PMID: 35109890; PubMed Central PMCID: PMC8809495.

25. Jones-Hughes T, Campbell J, Crathorne L. Epidemiology and burden of progressive familial intrahepatic cholestasis: a systematic review. Orphanet J Rare Dis. 2021 Jun 3;16(1):255. doi:10.1186/s13023-021-01884-4 PubMed PMID: 34082807; PubMed Central PMCID: PMC8173883.

26. Fitzgerald C, George S, Somerville R, Linnane B, Fitzpatrick P. Caregiver burden of parents of young children with cystic fibrosis. J Cyst Fibros Off J Eur Cyst Fibros Soc. 2018 Jan;17(1):125–31. doi:10.1016/j.jcf.2017.08.016 PubMed PMID: 29150357.

27. Link SL, Nayak RP. Review of Rapid Advances in Cystic Fibrosis. Mo Med. 2020;117(6):548–54. PubMed PMID: 33311787; PubMed Central PMCID: PMC7721430.

28. Voormolen DC, Van Exel J, Brouwer W, Sköldunger A, Gonçalves-Pereira M, Irving K, et al. A validation study of the CarerQol instrument in informal caregivers of people with dementia from eight European countries. Qual Life Res. 2021 Feb;30(2):577–88. doi:10.1007/s11136-020-02657-5

29. Domaradzki J, Jabkowski P, Walkowiak D. Rare disease, common struggles: quality of life, caregiver burden and financial wellbeing of family caregivers in Poland. Sci Rep. 2025 Jul 2;15(1):22678. doi:10.1038/s41598-025-08866-7

30. Valcárcel-Nazco C, Ramallo-Fariña Y, Linertová R, Ramos-Goñi JM, García-Pérez L, Serrano-Aguilar P. Health-Related Quality of Life and Perceived Burden of Informal Caregivers of Patients with Rare Diseases in Selected European Countries. Int J Environ Res Public Health. 2022 Jul 5;19(13):8208. doi:10.3390/ijerph19138208

31. Johnson B, Gibson G, Baskerville D, Castellano G, de Courcy J, Iqbal H, et al. Health-related quality of life and productivity burden for non-professional caregivers of adults

with rare diseases: a real-world study. Orphanet J Rare Dis. 2025 Jun 6;20(1):282. doi:10.1186/s13023-025-03796-z PubMed PMID: 40481583; PubMed Central PMCID: PMC12142911.

32. Zurynski Y, Deverell M, Dalkeith T, Johnson S, Christodoulou J, Leonard H, et al. Australian children living with rare diseases: experiences of diagnosis and perceived consequences of diagnostic delays. Orphanet J Rare Dis. 2017 Apr 11;12(1):68. doi:10.1186/s13023-017-0622-4

33. Villa-García L, Salvat-Plana M, Slof J, Ossa NP de la, Abilleira S, Ribó M, et al. Care-related quality of life of informal caregivers of stroke survivors: Cross-sectional analysis of a randomized clinical trial. PLOS ONE. 2024 Oct 4;19(10):e0307930. doi:10.1371/journal.pone.0307930

34. Raina P, O'Donnell M, Schwellnus H, Rosenbaum P, King G, Brehaut J, et al. Caregiving process and caregiver burden: Conceptual models to guide research and practice. BMC Pediatr. 2004 Jan 14;4:1. doi:10.1186/1471-2431-4-1 PubMed PMID: 14723791; PubMed Central PMCID: PMC331415.

35. Davis C, Bogaert L, Powell J, Low K. Social Media Use Among Parents and Caregivers of Children With Rare Genetic Diseases: Scoping Review. J Med Internet Res. 2025 Nov 28;27:e77087. doi:10.2196/77087

36. Fatima SR, Alamgir Z, Anjum HS, Ch AS, Taif M, Azmatullah R. TELEMEDICINE VS. IN-PERSON CARE IN MANAGING CHRONIC DISEASES – A META-ANALYSIS OF TREATMENT OUTCOMES IN DIGITAL HEALTHCARE SETTINGS. Health Rehabil. 3(3).

37. Trail T, Friedman E, Rutter CM, Tanielian T. The Relationship Between Engagement in Online Support Groups and Social Isolation Among Military Caregivers: Longitudinal Questionnaire Study. J Med Internet Res. 2020 Apr 23;22(4):e16423. doi:10.2196/16423

38. Fisher V, Atkin K, Ewing G, Grande G, Fraser LK. Assessing the suitability of the Carer Support Needs Assessment Tool (CSNAT-Paediatric) for use with parents of children with a life-limiting condition: A qualitative secondary analysis. Palliat Med. 2024 Jan;38(1):100–9. doi:10.1177/02692163231214471 PubMed PMID: 38142279; PubMed Central PMCID: PMC10798015.

481 Table 1: Sample characteristics and mean CarerQol-7D scores (n = 207)

Characteristics of caregiver and care recipient	n (%)	Mean CarerQol-7D scores	p-value†
Age of caregiver	n = 206		
≤40 years old	92 (45%)	73.6	0.98
41-50 years old	69 (33%)	73.7	
>50 years old	45 (22%)	74.3	
Ethnicity of caregiver	n = 207		
Not of Hispanic, Latino, or Spanish origin	193 (93%)	74.3	0.08
Hispanic, Latino, or Spanish origin	14 (7%)	65.5	
Race of caregiver	n = 207		
White	185 (89%)	73.9	0.58
Asian	9 (4%)	68.6	
Black or African American	6 (3%)	80.4	
Other	7 (3%)	68.7	
Self-identified gender of caregiver	n = 205		
Female	191 (93%)	73.3	0.16
Male	14 (7%)	80.5	
Respondent's household income of caregiver	n = 207		
≤$50,000	26 (13%)	70.1	0.18
$50,001-$100,000	53 (26%)	70.6	
$100,001-$200,000	110 (53%)	76.3	
Prefer not to say or don't know	18 (9%)	71.8	
Care recipient has a disability	n = 206		
No	86 (42%)	78.6	**<0.05**
Yes	120 (58%)	70.3	
Care recipient had genetic testing	n = 207		
No	62 (30%)	77.7	**<0.05**
Yes	145 (70%)	72.0	

† We performed t-tests to compare differences in mean CarerQOL-7D scores between two groups and ANOVA to assess differences across three or more groups. Bolded p-values indicate significant results (i.e., p-values less than 0.05).

Care recipient received a genetic diagnosis	n = 204		
Yes, identified variant	68 (33%)	77.4	0.07
Yes, partial genetic diagnosis	15 (7%)	65.4	
Variants of unknown significance	5 (2%)	63.7	
No, or do not know	116 (57%)	73.1	
Disease prevalence	n = 207		
>1 / 1,000	6 (3%)	62.6	**<0.05**
1-9 / 10,000	52 (25%)	75.7	
1-9 / 100,000	60 (29%)	78.0	
1-9 / 1,000,000	48 (23%)	66.7	
<1 / 1,000,000	12 (6%)	73.3	
Unknown	29 (14%)	75.3	

Table 2: Summary of CarerQol-7D and CarerQol-VAS scores

	Mean (SD)	Median (IQR)
CarerQol-7D	73.6 (18.5)	78.4 (62.3-86.9)
CarerQol-VAS	6.9 (1.8)	7.0 (6.0-8.0)

Table 3: Factor analysis results

Survey questions	Factor loadings†			Factor
Members share or request information about *events, articles, news, or educational opportunities*	-0.09	**0.84**	0.07	Information sharing on events, news, and opportunities
Members share or request information about *research opportunities*	-0.01	**0.87**	-0.01	
Members discuss positive and negative *experiences with the healthcare system*	0.00	0.10	**0.73**	Information sharing on rare disease experiences
Members discuss *physical challenges* of living with the rare disease	0.02	-0.06	**0.84**	
Members discuss *financial concerns and healthcare costs*	-0.02	0.06	**0.81**	
I feel *connected* to other people in this Facebook group	**0.78**	0.10	-0.04	Peer support resource (connection and belonging)
I feel other Facebook group members understand *what our family goes through* every day.	**0.90**	-0.07	-0.05	
I can talk to people in this Facebook group *about my family's day-to-day problems* if I need to	**0.83**	-0.03	0.10	

† The pre-specified factor loading threshold was 0.7. Factor loadings above 0.7 are shaded in bold texts.

Table 4: Ordered beta regression of caregiver characteristics, care recipient characteristics, and resource factors, and their association with CarerQol-7D scores

Independent variable	Estimate[†]	l-95% CrI[‡]	u-95% CrI
(Intercept)	73.16	70.66	75.40
Factors related to informational and support resources			
Factor 1: Information sharing on events, news, and opportunities	-0.04	-0.53	0.45
Factor 2: Information sharing on rare disease experiences	-0.03	-0.54	0.51
Factor 3: Peer support resource (connection and belonging)	0.60	-0.52	1.74
Age of caregiver	-0.05	-0.25	0.16
Ethnicity of caregiver			
Not of Hispanic, Latino, or Spanish origin [Reference]			
Hispanic, Latino, or Spanish origin	-8.88	-19.79	1.22
Race of caregiver			
White [Reference]			
Asian	-1.58	-15.64	10.35
Black or African American	8.44	-3.34	17.83
Other	-0.10	-14.63	11.70
Self-identified gender of caregiver			
Female [Reference]			
Male	5.80	-2.64	12.64
Household income of caregiver			
≤$50,000 [Reference]			
$50,001-$100,000	-0.06	-8.61	8.25
$100,001-$200,000	0.86	-6.52	8.56
Prefer not to say or don’t know/not sure	-3.51	-14.44	6.64
Care recipient has a disability			

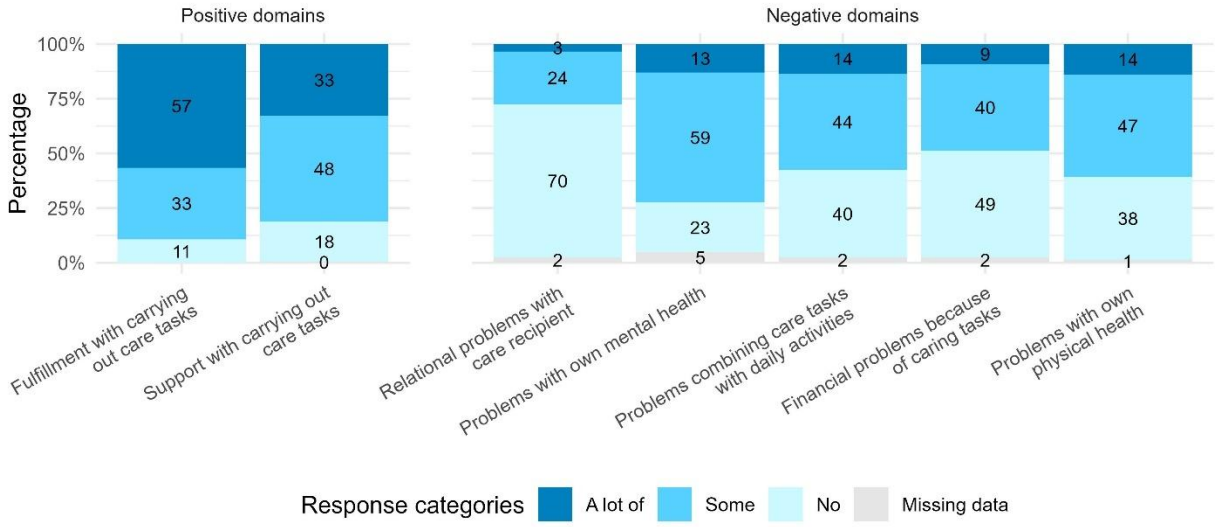
[†] We report average marginal effects on the CarerQoL-7D score scale (0–100).

[‡] l-95% CrI and u-95% CrI indicate the lower and upper bound of the 95% credible interval for each estimate

No [Reference]			
Yes	**-5.48**	**-10.80**	**-0.24**
Care recipient had genetic testing			
No [Reference]			
Yes	-2.56	-10.22	6.04
Care recipient received a genetic diagnosis			
Identified variant [Reference]			
Partial genetic diagnosis	-7.43	-19.63	4.31
Variants of unknown significance	-2.11	-20.32	13.54
No or do not know	0.19	-7.35	8.06
Prevalence			
Rare disease [Reference]			
Ultra rare disease[§]	**-6.15**	**-12.14**	**-0.22**
Unknown	2.46	-5.03	8.84

[§] A prevalence of 1 to 9 cases per 1,000,000 individuals or lower

Figure 1: Distribution of responses for each dimension of the CarerQol-7D, reported by caregivers of individuals with rare diseases



Supplementary Files

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- 20260811aSupplementCarerQolanalysis.docx