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Assessing the impact of caring for a child with Dravet syndrome: Results of a caregiver survey

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ABSTRACT

Objective: The objective of this study was to describe and quantify the impact of caring for a child with Dravet syndrome (DS) on caregivers.
Methods: We surveyed DS caregivers at a single institution with a large population of patient with DS. Survey domains included time spent/difficulty performing caregiving tasks (Oberst Caregiving Burden Scale, OCBS); caregiver health-related quality of life (EuroQoL 5D-5L, EQ-5D); and work/activity impairment (Work Productivity and Activity Impairment questionnaire, WPAI). Modified National Health Interview Survey (NHIS) questions were included to assess logistical challenges associated with coordinating medical care.
Results: Thirty-four primary caregivers responded, and 30/34 respondents completed the survey. From OCBS, providing transportation, personal care, and additional household tasks required the greatest caregiver time commitment; arranging for child care, communication, and managing behavioral problems presented the greatest difficulty. EuroQoL 5D-5L domains with the greatest impact on caregivers (0 = none, 5 = unable/extreme) were anxiety/depression (70% of respondents ≥ slight problems, 34% ≥ moderate) and discomfort/pain (57% of respondents ≥ slight problems, 23% ≥ moderate). The mean EQ-5D general health visual analogue scale (VAS) score (0 = death; 100 = perfect health) was 67 (range, 11–94). Respondents who scored <65 were two- to fourfold more likely to report ≥moderate time spent and difficulty managing child behavior problems and assisting with walking, suggesting that children with DS with high degrees of motor or neurodevelopmental problems have an especially high impact on caregiver health. On the WPAI, 26% of caregivers missed >1 day of work in the previous week, with 43% reporting substantial impact (≥6, scale = 1–10) on work productivity; 65% reported switching jobs, quitting jobs, or losing a job due to caregiving responsibilities. National Health Interview Survey responses indicated logistical burdens beyond the home; 50% of caregivers made ≥10 outpatient visits in the past year with their child with DS.
Conclusions: Caring for patients with DS exerts physical, emotional, and time burdens on caregivers. Supportive services for DS families are identified to highlight an unmet need for DS treatments.
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1. Introduction

Dravet Syndrome (DS) is a rare, devastating, genetic epilepsy that begins in the first year of life and is marked over the course of the disease by frequent seizures and multiple seizure types, including status epilepticus [1]. Dravet Syndrome is usually determined by clinical diagnosis and is often associated with an *SCN1A* gene mutation, which may be a loss-of-function mutation. More than 80% of people with DS are found to have a mutation in *SCN1A* [2], the gene that encodes the pore-forming subunit of the type I voltage-gated sodium channel (NaV 1.1), found in the brain and the heart [3–5]. No drug is currently approved in the United States (US) for DS. It is a highly pharmacotherapy-resistant and refractory

Abbreviations: DS, Dravet syndrome; EQ-5D, EuroQoL 5D-5L quality-of-life survey; IQR, interquartile range; NHIS, National Health Interview Survey; OCBS, Oberst Caregiving Burden Scale; QoL, quality of life; SD, standard deviation; US, United States; VAS, visual analogue scale; WPAI, Work Productivity and Activity Impairment questionnaire.

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epilepsy syndrome. Attaining substantial seizure reduction (i.e., ≥75% reduction) or seizure-freedom in affected children, even with combination therapy, is rare, thereby placing a heavy impact of disease on children with DS and on the caregivers they are dependent upon. Contributing to this impact is the lack of medical literature regarding treatment of the associated characteristics of DS, such as concomitant developmental and behavioral issues. While much focus in the literature has been understandably placed on finding new treatments for these patients, only recently has the literature begun to highlight the broader impact of DS on caregivers and the family as a whole.

In a cohort of Canadian caregivers, Nolan et al. found that persistent severe seizures in patients with DS, along with cognitive, developmental, behavioral, and sleep issues, resulted in high stress for caregivers and little ability to find relief [6]. Stress was characterized in this parental cohort by deterioration of relationships with others (including spouses), as well as fear, uncertainty, and sleep problems [6]. Skluzacek et al. identified grief as an additional stressor on parents and emphasized the need for support in managing the stress of caring for a child with DS [7]. More recent studies have identified additional stress factors on caregivers, including sleep deprivation, reduced mental health, deterioration of social relationships, financial burden [8], and a substantial incidence of depression, in addition to family-related factors such as concern regarding the emotional impact of having a child with DS may be having on siblings [9].

To further identify and quantify the factors impacting the well-being of caregivers of children with DS, we conducted a prospective, single-center survey study within Children's Hospital Colorado, a hospital with a large population of patients with DS.

2. Methods

We assessed the burden of DS on a cohort of caregivers of patients with DS actively being seen at Children's Hospital Colorado. An electronic survey (Appendix) was administered to caregivers, who were eligible if they provided care for a friend or a family member with DS. The survey was administered through REDCap (https://www.project-redcap.org/), a metadata-driven methodology and workflow process for providing translational research informatics support [10]. The study design was reviewed and approved by the Colorado Multiple Institutional Review Board, and all survey participants provided informed consent.

An e-mail inviting DS caregivers to participate in the survey was sent if an e-mail address was available in the patient's electronic health record. Fifteen eligible participants did not have an e-mail on file; a coordinator contacted the caregivers by telephone to see if they were interested in participating and providing their e-mail. Eight agreed; of the remaining 7, 4 could not be reached, 2 were not English-speaking, and 1 declined. Consent was obtained before participants could begin the survey questions. The survey was administered one time for each caregiver and asked for information pertaining to the previous year. Survey areas of assessment included time spent and difficulty performing caregiver tasks, caregiver health-related quality of life (QoL), and caregiver work-related productivity/activity impairment.

To understand the time spent and difficulty performing tasks associated with caregiving, we modified a version of the Oberst Caregiving Burden Scale (OCBS) [11,12], a 15-item instrument that rates caregiving tasks based on time spent (1 = none, 4.5 = a large amount) and difficulty of task (1 = not difficult, 4.5 = very difficult).

Caregiver QoL was assessed using the EuroQoL 5D-5L (EQ-5D) health-related QoL survey [13]. The EQ-5D survey is a standardized measure of health status and assesses 5 different domains on a 5-point scale (0 = no problems, 4 = unable; or 0 = none, 4 = extreme). An EQoL Index was computed using responses across all 5 domains, adjusted by population-based preference weights [14]. A general health assessment was also measured on a visual analogue scale (VAS; 0–100 scale where 0 = death and 100 = perfect health). Visual analogue scale scores were used to stratify OCBS and Work Productivity and Activity Impairment questionnaire (WPAI) results to assess if there were differences in these measures for VAS scores <65 or ≥65.

Caregiver productivity and activity impairment was assessed using a subset of the WPAI questionnaire [15], which was tailored to focus on the impact of DS caregiving on employment. Work Productivity and Activity Impairment items generate percentages (0%–100%) that quantify absenteeism (percentage of time missed from work), presenteeism (percentage of restriction while at work), overall work restriction (percentage of total restriction due to either absenteeism or presenteeism), and overall activity limitation (percentage of limitation in daily activities) due to caregiving responsibilities, with higher values indicating greater limitation. Only caregivers currently employed (full-time, part-time, or self-employed) were asked to respond about work productivity, but all caregivers were asked about activity limitation.

Finally, to assess logistical challenges required of the caregiver to coordinate healthcare visits of the patient with DS selected and modified questions from the National Health Interview Survey (NHIS) were included in the survey [16]. Items included questions such as "During the past 12 months, how many times has your child gone to a hospital emergency room? (This includes emergency room visits that resulted in a hospital admission)"; see Appendix.

Survey responses for the different OCBS, EQ-5D, WPAI, and NHIS subdomains were totaled and presented as percentages, means (±SD), medians, and ranges as appropriate.

3. Results

The survey was open for 3 weeks, from November 30, 2016 to December 20, 2016; it was e-mailed to 60 primary caregivers of patients with DS routinely seen at the Children's Hospital Colorado who were asked to participate; 34 (57%) agreed. Of those who participated, 30 (88%) fully completed the survey. The 34 participants were primary caregivers for 34 patients with DS; 91.2% of the patients had confirmed sodium channel α-subunit gene mutation in *SCN1A*. Patients ranged in age from 2 to 22 years (mean ± SD, 11.7 ± 5.8 years). Additional demographic information on caregivers or patients with DS was not collected.

Responses to the OCBS are provided in Fig. 1 and show that a substantial number of caregiver domains were impacted from both a difficulty and time perspective. The top five domains in terms of proportion of caregivers reporting moderate or greater time burden were: providing transportation (93% of respondents), personal [patient with DS] care (87%), additional household tasks (83%), communication (80%), and symptom observation (77%). The top five domains with regard to proportion of caregivers reporting moderate or greater difficulty included: arranging for care (73%), communication (70%), coordinating resources (67%), managing behavior problems (67%), and personal [patient with DS] care (63%).

From the EQ-5D, the domains with the greatest impact on caregivers were anxiety/depression (70% of respondents ≥ slight problems, 33% ≥ moderate) and discomfort/pain (57% of respondents ≥ slight problems, 23% ≥ moderate). The EQoL Index score, a summary measure of the five EQ-5D health domains adjusted by population-based preference weights, was 0.78 ± 0.17, suggesting an overall reduction in QoL as compared with perfect health (1 = perfect health). The EQ-5D general health assessment mean VAS score of 67 (range 11–94; Table 1) also provided evidence of substantial reduction from what would be expected in a normative population, where 63% of respondents scored between 80 and 100, and 71 was the mean score reported for those with one major health condition [17]. Forty percent of respondents scored <65 on the VAS scale of general health, where 0 = death and 100 = perfect health, as compared with 22% in a normative population [17].

Work Productivity and Activity Impairment responses (Table 2) indicated a substantial effect of DS on caregivers' missed work and

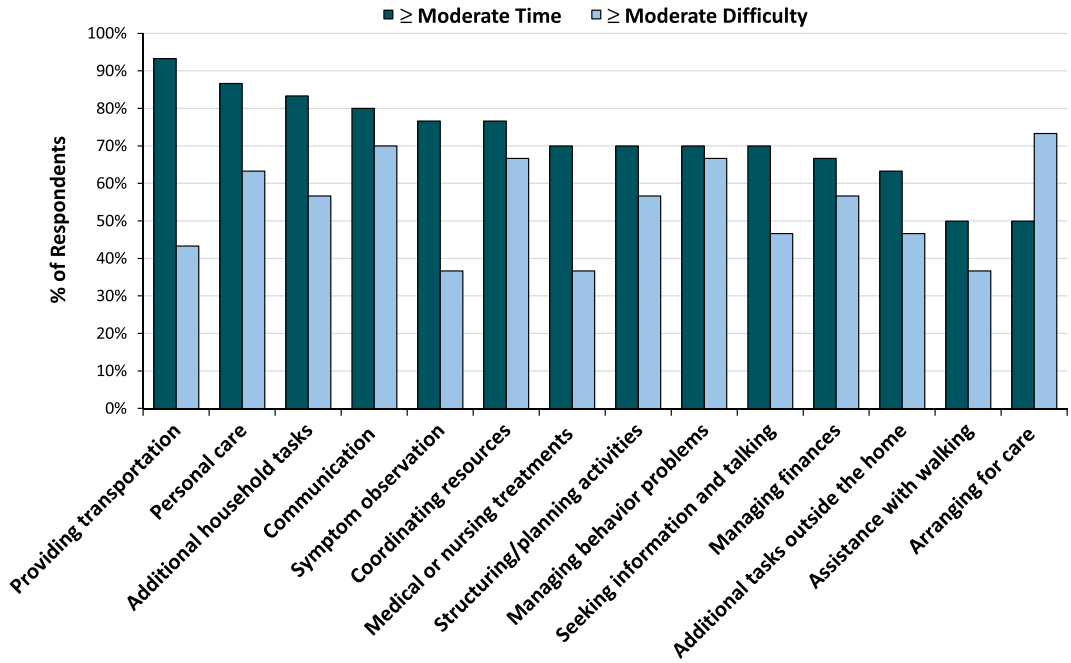

Fig. 1. OCBS results: percent of DS caregiver respondents experiencing moderate to severe time and difficulty limitations when performing routine caregiving tasks. DS, Dravet syndrome; OCBS, Oberst Caregiving Burden Scale.

leisure time, work productivity, and regular activities. Forty-five percent (15/33) either quit, retired early, or lost their jobs, and 18% (6/33) found it necessary to switch jobs. Of those caregivers who were not employed (n = 9), a majority of respondents (7/9, 78%) felt that caregiving was an impediment to employment.

National Health Interview Survey responses showed that the majority of caregivers were faced with coordinating hospital/ER (67% of caregivers) and outpatient visits (97% of caregivers) (Fig. 2) for their patients with DS annually, with some having the added burden of coordinating in-home visits and other services that were, overall, minimally used. Outpatient visits were an intensely utilized medical service, with 50% of DS caregivers making ≥10 outpatient visits yearly, while 23% made ≥20 outpatient visits yearly with their child with DS. There was minimal ambulance use, flight-for-life use, overnight stays, ICU admissions, and medical marijuana prescriptions. The majority of patients with DS utilized no in-home visits (n = 20), although 4 patients had 100+ visits.

Table 1
Impact of DS Caregiving on EQ-5D tasks.

Survey variable	n	Min	Max	Score = 0	Score ≥ slight	Score ≥ moderate
Mobility/walking about (0–4)[a]	30	0	3	80%	20%	13%
Self-care/washing & dressing self (0–4)[a]	30	0	1	93%	7%	0%
Usual activities (0–4)[a]	30	0	4	73%	27%	13%
Pain/discomfort/(0–4)[b]	30	0	4	43%	57%	23%
Anxiety/depression (0–4)[c]	30	0	4	30%	70%	33%
				Mean	±SD	
EQoL Index[d]	30	0.31	1	0.78	0.17	
General Health (0–100; VAS)[e]	30	11	94	67	21	

DS, Dravet syndrome; EQ-5D, EuroQoL 5D-5L health-related quality-of-life survey; EQoL, EQ-5D summary index; VAS, visual analogue scale.

[a] Scores: 0 = I have no problems; 1 = I have a slight problem; 2 = I have a moderate problem; 3 = I have severe problems; 4 = I am unable.

[b] 0 = I have no pain; 1 = I have slight pain; 2 = I have moderate pain; 3 = I have severe pain; 4 = I have extreme pain.

[c] 0 = I am not anxious or depressed; 1 = I am slightly anxious or depressed; 2 = I am moderately anxious or depressed; 3 = I am severely anxious or depressed; 4 = I am extremely anxious or depressed.

[d] US time-trade-off mapping using the EQ-5D-3 L crosswalk (0 = death; 1 = perfect health).

[e] 0 = death; 100 = perfect health.

3.1. Stratifications of survey results by VAS score

An EQ-5D general health VAS score < 65 was used to stratify results from other survey domains. On average, caregivers reporting a VAS < 65 vs those reporting a VAS ≥ 65 had nearly 27 mean hours fewer per week for leisure activities (31.0 vs 57.8), reported a nearly twofold higher impact on mean work productivity (39.1 vs 76.9), and a 1.5-fold greater impact on leisure activities (55.1 vs 82.6) (Table 2). Approximately twofold more caregivers reported moderate or greater difficulty with watching and reporting symptoms, providing transportation, household tasks, managing behavior, and seeking information (Table 3). A two- to fourfold greater proportion of caregivers in this group reported moderate or greater time and difficulty dealing with assistance with walking.

These observations suggest that certain patient characteristics such as greater behavioral problems or decreased motor ability added stress to caregivers' lives and may be contributing to an even greater negative impact on caregivers as measured by EQ-5D general health VAS.

4. Discussion

In this single-center cohort, caring for patients with DS exerted substantial physical, emotional, and time impact on caregivers. These data corroborate recent findings reported in the literature and further add to our knowledge about the direct impact of DS on caregivers' emotional, and financial well-being. Our methodological approach enabled us to provide some degree of quantitation for this burden. This assessment found that caring for a child with DS increased the difficulty of performing relatively simple tasks while also increasing levels of anxiety and depression and decreasing a caregiver's quality of life.

A growing body of literature suggests that caregivers of patients with DS are under considerable stress and would benefit from the attention of the medical community. Caregivers, often the parents, suffer

Table 2
Influence of DS caregiving on WPAI work productivity and leisure time, by EQ-5D VAS category.

	EQ-5D VAS ≥ 65 (n = 18)		EQ-5D VAS < 65 (n = 12)	
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)
Weekly time missed from work (hours)	7.4 (15.2)	0.5 (0.0, 2.8)	6.9 (12.3)	0 (0.0, 8.0)
Weekly time missed from leisure (hours)	31.0 (53.9)	7.0 (1.8, 23.0)	57.8 (59.2)	40.0 (7.3, 84.0)
Effect caregiving had on work productivity[a]	39.1 (25.6)	52.0 (13.8, 58.0)	76.9 (19.8)	75.0 (68.0, 90.0)
Effect caregiving had on leisure time[a]	55.1 (24.0)	55.5 (39.5, 69.3)	82.6 (12.4)	81 (77.3, 91.8)

DS, Dravet syndrome; EQ-SD, EuroQoL 5D-5L health-related quality-of-life survey; IQR, interquartile range; SD, standard deviation; VAS, visual analogue scale; WPAI, Work Productivity and Activity Impairment questionnaire.
[a] Data are scores; scale: 0 = no impact to 100 = completely prevented productivity or leisure time.

emotional exhaustion and anxiety related to "fear of the next seizure" and whether each seizure will be "the seizure that kills my child." Due to the severity of this condition, it is hard to find additional caregivers, which often results in one or both parents having to quit their jobs or careers to care for their child with DS. A study by Nolan et al. identified the challenges faced by parents caring for children with DS [6]. They found that the combination of persistent severe seizures, along with developmental, cognitive, behavioral, and sleep issues, result in a high stress load with little ability for caregivers to find respite or relief [6]. The psychiatric and neurodevelopmental comorbidities that can occur in up to 50% of young patients with epilepsy [18], and a likely even higher percentage of patients with DS, further exacerbate the impact of DS on caregivers.

A recent study by Jensen et al. [8] identified stress factors that impacted caregivers of patients with epilepsy, the majority of whom (12/16, 63%) were patients with DS. These investigators identified sleep deprivation (with attendant physical exhaustion), reduced mental health (brought about by feelings of anxiety, guilt, and helplessness), deterioration of social relationships (including spouse, friends, and extended family), and financial burden (including difficulty with employment and the financial burden of patient care) as significant factors in the lives of most caregivers. Such distortions in caregiver's daily life made social interaction, employment, and care of one's own physical health difficult.

In another recent study, Villas et al. [9] found that caregivers of children with DS reported a substantial incidence of depression (66%) as well as concern about the emotional impact of a patient with DS may be having on siblings (74%). Caregivers in this study ranked their top 4 concerns, aside from seizure control, as speech and communication challenges, the impact of the patient with DS on siblings, cognitive/developmental delay, and behavioral issues including violence and autistic traits. Thus, prior and recent studies have begun to quantify the emotional and physical state of well-being of caregivers, and in doing so have identified areas of unmet need where additional support services are required in order to ease the challenges of caring for patients with DS in the hope of improving caregivers physical and financial well-being.

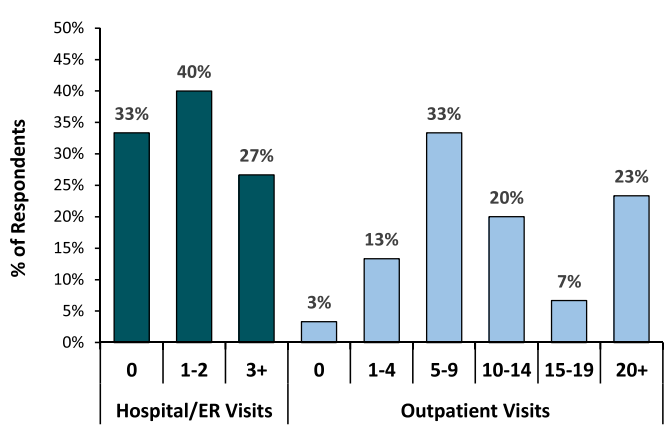

Fig. 2. NHIS results: yearly hospital/ER/outpatient visits coordinated by caregivers for children with DS.
DS, Dravet syndrome; ER, emergency room; NHIS, National Health Interview Survey.

4.1. Study limitations

The sample size we evaluated (34 participants) is small and therefore may not be representative of the DS caregiver population as a whole. This was a single-center study, which may also limit the generalizability of our data. However, given the relatively high response rate (57%), the likelihood is high that the findings are representative of the Children's Colorado DS caregiver population. Finally, our primary data depend heavily on the impressions and recollections of survey participants, thus making our data subject to various response and recall biases. However, the consistency of our findings with observations from recently-published studies by Villas et al. [9] and Jensen et al. [8] support the external validity of our results to the larger population of DS caregivers.

4.2. Significance

To our knowledge, this is the first study to attempt to provide a more quantitative basis for the degree of impact of caring for a child with DS on the well-being of the caregiver. Nolan et al. [6] and Skluzacek et al. [7] used qualitative methods to identify specific stressors that impacted parent caregivers' QoL, such as grief, fear, relationship difficulty, uncertainty, and sleep problems. These stressors were identified in the larger context of the parent caregiver's description of their child's DS symptoms and disease progression; in other words, how DS affected their child. Similarly, Villas et al. [9] and Jensen et al. [8] provided descriptive narrative to characterize the impact of caring for a DS child with little quantitative description of the impact.

Our study attempted to identify those factors in caring for a child with DS that specifically impacted the caregiver and to provide some measurement of this effect with quantitative data. Our findings are

Table 3
Influence of DS caregiving on OCBS domains, by EQ-5D VAS category[a].

	EQ-5D VAS ≥ 65 (n = 18)	EQ-5D VAS < 65 (n = 12)
Moderate or more time spent		
Assistance with walking	33.3%	75.0%
Moderate or more difficulty		
Assistance with walking	16.7%	66.7%
Watching/reporting symptoms	27.8%	50.0%
Providing transportation	27.8%	66.7%
Household tasks	38.9%	83.3%
Managing behavior	44.4%	100.0%
Seeking information	33.3%	66.7%

DS, Dravet syndrome; EQ-SD, EuroQoL 5D-5L health-related quality-of-life survey; OCBS, Oberst Caregiving Burden Scale; VAS, visual analogue scale.
[a] Table shows OCBS domains with an approximately twofold or greater difference between VAS groups.

congruent with those of Villas et al. [9] and Jensen et al. [8] in identifying depression and anxiety, communication challenges, and the emotional and physical challenges attendant with caring for a child with DS as contributing to the overall level of stress in DS caregivers.

We have expanded the contributors of stress on caregivers to include quantitation of the effects on caregivers' employment and the frequency of hospital and outpatient visits. These findings highlight the unmet need for better, more comprehensive treatments for DS as well as potential areas for which supportive services would be helpful in reducing the overall impact on caregivers.

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Disclosure

JDC, MDW, and KGK received research support from Zogenix. CHK and GRV have no conflicts to report. AG is an employee of Zogenix and has stock ownership in Zogenix.

Appendix A. Survey questions

Supplementary data to this article can be found online at https://doi.org/10.1016/j.yebeh.2018.01.003.

References

[1] Dravet C, Bureau M, Oguni H, Fukuyama Y, Cokar O. Severe myoclonic epilepsy in infancy: Dravet syndrome. Adv Neurol 2005;95:71–102.
[2] Ohmori I, Ouchida M, Ohtsuka Y, Oka E, Shimizu K. Significant correlation of the SCN1A mutations and severe myoclonic epilepsy in infancy. Biochem Biophys Res Commun 2002;295:17–23.
[3] Claes L, Del-Favero J, Ceulemans B, Lagae L, Van Broeckhoven C, De Jonghe P. De novo mutations in the sodium-channel gene SCN1A cause severe myoclonic epilepsy of infancy. Am J Hum Genet 2001;68:1327–32.
[4] Fujiwara T. Clinical spectrum of mutations in SCN1A gene: severe myoclonic epilepsy in infancy and related epilepsies. Epilepsy Res 2006;70(Suppl. 1):S223–30.
[5] Mulley JC, Scheffer IE, Petrou S, Dibbens LM, Berkovic SF, Harkin LA. SCN1A mutations and epilepsy. Hum Mutat 2005;25:535–42.
[6] Nolan KJ, Camfield CS, Camfield PR. Coping with Dravet syndrome: parental experiences with a catastrophic epilepsy. Dev Med Child Neurol 2006;48:761–5.
[7] Skluzacek JV, Watts KP, Parsy O, Wical B, Camfield P. Dravet syndrome and parent associations: the IDEA League experience with comorbid conditions, mortality, management, adaptation, and grief. Epilepsia 2011;52(Suppl. 2):95–101.
[8] Jensen MP, Liljenquist KS, Bocell F, Gammaitoni AR, Aron CR, Galer BS, et al. Life impact of caregiving for severe childhood epilepsy: results of expert panels and caregiver focus groups. Epilepsy Behav 2017;74:135–43.
[9] Villas N, Meskis MA, Goodliffe S. Dravet syndrome: characteristics, comorbidities, and caregiver concerns. Epilepsy Behav 2017;74:81–6.
[10] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81.
[11] Bakas T, Austin JK, Jessup SL, Williams LS, Oberst MT. Time and difficulty of tasks provided by family caregivers of stroke survivors. J Neurosci Nurs 2004;36:95–106.
[12] Carey PJ, Oberst MT, McCubbin MA, Hughes SH. Appraisal and caregiving burden in family members caring for patients receiving chemotherapy. Oncol Nurs Forum 1991;18:1341–8.
[13] EuroQol Group. EQ-5D-5L User's Guide. https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/; 2015, Access date: 15 November 2017.
[14] Shaw JW, Johnson JA, Coons SJ. US valuation of the EQ-5D health states: development and testing of the D1 valuation model. Med Care 2005;43:203–20.
[15] Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. Pharmacoeconomics 1993;4:353–65.
[16] Centers for Disease Control and Prevention. National Health Interview Survey. https://www.cdc.gov/nchs/nhis/nhis_questionnaires.htm; 2017, Access date: 15 November 2017.
[17] Stewart ST, Cutler DM, Rosen AB. Comparison of trends in US health-related quality of life over the 2000s using the SF-6D, HALex, EQ-5D, and EQ-5D visual analog scale versus a broader set of symptoms and impairments. Med Care 2014;52:1010–6.
[18] Wagner JL, Berg AT. Direct health care charges for new-onset pediatric epilepsy: how much does it cost? Neurology 2015;85:486–7.