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Emotional experiences of family caregivers of children with Dravet syndrome

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ABSTRACT

Background: Since the psychosocial implications of Dravet syndrome (DS) are much more serious and far-reaching than in other types of epilepsy, caring for a DS child seriously affects the entire family. This study describes the emotional experiences of family caregivers of DS children and evaluates the way caregiving affects their perceived quality of life.
Methods: An anonymous, self-administered online questionnaire was sent to family caregivers of DS children through the online patient advocacy organization the Association for People with Severe Refractory Epilepsy DRAVET.PL. It focussed on the psychosocial impact of caregiving for DS children, the perceived burden of caregiving, caregivers' emotional experiences and feelings related to caregiving, and the impact of DS on the perceived quality of life.
Results: Caregivers stressed that caring for a DS child is associated with a significant psychosocial and emotional burden that affects the entire family. Although most caregivers reported that it was the child's health problems and behavioral and psychological disorders that were the most challenging aspects of caregiving, they were also burdened by the lack of emotional support. As caregivers were profoundly engaged in caregiving, they experienced a variety of distressing emotions, including feelings of helplessness, anxiety and fear, anticipated grief, depression, and impulsivity. Many caregivers also reported that their children's disease disrupted their relationships with their spouses, family, and healthy children. As caregivers reported experiencing role overload, physical fatigue, and mental exhaustion, they stressed the extent to which caregiving for DS children impaired their quality of life, their social and professional life, and was a source of financial burden.
Conclusions: As this study identified specific burden domains affecting DS caregivers' well-being family carers often need special attention, support, and help. To alleviate the humanistic burden of DS carers a bio-psychosocial approach focusing on physical, mental, and psychosocial interventions should include both DS children and their caregivers.

1. Introduction

Dravet syndrome (DS), formerly known as severe myoclonic epilepsy of infancy (SMEI), is a life-long and life-threatening form of epilepsy that begins in the first year of life and evolves with increasing morbidity that significantly impacts individuals and their families [1]. While it was first reported and described in 1978 by French neurologist and psychiatrist Charlotte Dravet, in 1989 the International League Against Epilepsy named DS as a distinct syndrome [1,2].

Dravet syndrome usually manifests itself with focal or generalized convulsive seizures in otherwise healthy infants. Although the first seizure often strikes in conjunction with a fever, they are also provoked by changes in body temperature and infections. Other precipitating factors include warm weather, hot baths, flashing lights, visual patterns, listening to music, emotional stress and strong emotions, and overexertion [3–5]. While these initial seizures are usually tonic-clonic, temperature-sensitive/febrile, prolonged, and typically lateralized, they often occur on a weekly or daily basis. After 12 months of age, different types of seizure also begin to occur (clonic, tonic-clonic, motor and non-motor onset focal seizures, myoclonic) and a state of status epilepticus may occur frequently [5,6]. Because these seizures are frequently resistant to current anti-epilepsy drugs [7–9] up to 90% of DS children

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are unable to achieve freedom from persistent seizures [10]. Seizures in DS are consequently more severe than in other forms of epilepsy and they seriously affect children's development leading to cognitive, speech, and motor impairment and intellectual disability [10–12].

While the worldwide prevalence of DS ranges from 1 in 15,000 to 1 in 40,000 [13], its diagnosis is usually based on the recognition of seizure types, the clinical course of the condition, medical history, and electroencephalographic features. Since DS is a genetic condition, however, genetic testing is also used. Although DS may be inherited in an autosomal dominant pattern, in approximately 90% of cases the genetic mutation that causes DS occurs *de novo* [14,15]. Around 85% of cases of DS are caused by mutations in the gene SCN1A, which encodes the type I voltage-gated sodium channel (Nav1.1), a protein that subsequently alters how the brain functions leading to the development of seizures, behavioral changes including hyperactivity, social interaction deficits and cognitive impairment [16,17]. While not all SCN1A epileptic encephalopathies are Dravet syndrome [18], however, DS or DS-like phenotypes are also associated with other genetic changes, including PCDH19, SCN1A, SCN2A, SCN8A, SCN9A, SCN1B, GABRA1, GABRG2, GABRB3, STXBP1, HCN1, CHD2, and KCNA2 [17,19]. At the same time, even though pediatricians and neurologists are becoming increasingly aware of DS and genetic testing is ever more available, still, some DS patients remain undiagnosed or are faced with late diagnosis [20–22].

Although several specific medications for use in children with drug-resistant seizures due to DS have been approved (i.e. valproate and clobazam, levetiracetam, stiripentol, cannabidiol, and topiramate) [7,9,23,24], some children with DS could also benefit from the ketogenic diet [25]. Although some of these drugs may help to reduce the frequency of seizures and prevent status epilepticus, it is estimated that up to 20% of DS children die before they are 10 years old, mostly due to sudden unexpected death in epilepsy (SUDEP), which in DS patients is estimated to be 15-fold greater than other childhood-onset epilepsies [26,27].

While seizures are usually considered the most severe symptom of DS [3–5,12,28], DS patients often experience other comorbid conditions and symptoms that also seriously affect their quality of life [10,29]. Although, not every patient experiences all the comorbidities or symptoms and their severity may differ significantly from person to person, DS patients experience cognitive and developmental delay, speech impairment, behavioral and sensory integration disorders, motor system dysfunction, impaired sleep quality, cardiovascular conditions, autistic-like social interaction deficits, hyperactivity, eating problems that often worsen during adolescence [30,31]. Some studies suggest that, while comorbidities typical of DS result from damage caused by seizures, they may also be a consequence of the mutated gene, and that not only an epilepsy syndrome should be considered a disease but the whole phenotype [32].

Some special resources in relation to state entitlements, health services, and educational support are also available to DS families in Poland. Most importantly, in 2019 the *Personal assistant for persons with disabilities* program was introduced. This aims to combat the discrimination against and social exclusion of persons with disabilities by providing them with personal assistance services as a form of public support [33]. The *Respite Care Programme* offers family carers support in the form of 240 hours for daytime respite care, 14 days for respite care provided within a 24-hour stay, or up to 20 hours of specialist counseling (psychological or therapeutic) and support in the field of nursing, rehabilitation, and dietetics [34]. Parents of children with special education needs may also choose mainstream, integration, or special school for their child [35] Some of these measures exist only on paper since Poland still lacks the qualified personnel who might provide such specialist care. Another problem is that, except for parents who receive care-related benefits, most family caregivers are unregistered. Although informal carers are granted care allowance parents who receive this are disallowed to do any paid work.

What is also important is that after many years of delay in September 2021, the Polish government promulgated the *Plan for Rare Diseases*, which declares rare diseases (RDs) as a public health priority [36]. Although it may significantly improve access to diagnosis and treatment of all RDs, it is still in progress and a review has just begun. Dravet syndrome families consequently still struggle for support, relief, and mental health care. For example, while genetic testing for patients with suspected hereditary or genetic diseases is free of charge in Poland, due to the long waiting lists parents are often forced to pay for them themselves. Although most anti-epileptic drugs are relatively easily accessible, families are not reimbursed for all of them by the healthcare system. Due to long waiting lists, many parents are also forced to pay privately for specialist consultations and rehabilitation, which are extremely expensive. Although rehabilitation equipment may be financed by the state or from a variety of support programs, the complicated procedures mean that many carers are unable to receive such support within a reasonable time limit. Finally, both free psychiatric care for DS children and psychological support and ounselling for their parents are barely accessible.

For all these reasons a great deal of research stresses that the psychosocial implications of DS are much more serious and far-reaching than in other types of epilepsy and that caring for DS children has a serious impact on family caregivers [10,28,37–48]. While research often focuses on the clinical dimension of DS, less attention tends to be paid to informal carers of those with DS. On the other hand, although some studies describe the psychosocial experiences of DS carers from many European countries, including Germany [28,49,50], France [43,45], and Spain [46], as well as further afield in the United States [40,41,47] and Canada [37,51], still little is known about such caregivers in Poland. Research shows that it is often the family carers who need special attention, support, and help [10,28,39,42,44,45,48]. The aim of this study is therefore to understand the emotional experiences of family caregivers of children with Dravet syndrome. The specific aims were: 1. to recognize the emotional needs of DS caregivers, 2. to describe their perception of the caregiving role, and 3) to evaluate their quality of life.

2. Material and methods

2.1. Study design

The data were collected between 30th December 2022 and 28th February 2022 among caregivers of children with DS using an anonymous, self-administered, computer-assisted online questionnaire on the psychosocial impact of DS on family caregivers. Family caregivers involved in the care of children with DS (aged between 1 and 18 years) were targeted for recruitment.

The study was performed in line with the principles of the Declaration of Helsinki. The study was reviewed and approved by the Poznan University of Medical Sciences Bioethics Committee (KB – 833/22) and all survey participants provided informed consent.

2.2. Research tool

Since no specific tool for assessing the caregiving burden of caregivers of DS children has been developed, this survey was conducted using an original questionnaire that was constructed from themes based on a review of the literature [48,52] and the study aim.

The questionnaire was expanded in accordance with the guidelines of the European Statistical System [53]. Firstly, a group of research experts (a sociologist, a public health specialist, and a pediatrician) discussed the list of issues related to caring for a DS child. A standardiezd questionnaire was then developed. Finally, the questionnaire was pilot tested using five parents, which resulted in re-formulating six questions. The survey was revised based on the responses received.

The questionnaire consisted of four sections. The first asked questions concerning caregivers' demographic characteristics. The second section included questions regarding caregivers' feelings and emotional experiences related to the caregiving role. The third section was related to respondents' attitudes toward caregiving, their perception of the role of caregiving, and the perceived burden. The last section was related to caregivers' satisfaction with life.

2.3. Data collection

Eligible caregivers were contacted using the Polish support group of the Association for People with Severe Refractory Epilepsy DRAVET.PL on Facebook. A study coordinator contacted the caregivers to ascertain whether they were interested in participating in the study.

Since the topic of this study involved some sensitive issues that might have caused distress to study participants, caregivers were informed about the purpose of the study, the voluntary, anonymous, and confidential nature of the study, and the possibility of abandoning the survey at any given time and of refusing to reveal information regarding their personal circumstances. Once informed consent was obtained from all individuals who volunteered and were included in the study, a survey was posted on an online platform and electronically administered once for each caregiver. Two follow-up messages were sent to non-responders. The survey took approximately 15 minutes to complete.

2.4. Analysis

The questionnaire data was validated for accuracy, completeness, and consistency before being exported into the statistical program JASP (Version 0.17.1.0). Descriptive statistics are used to present the findings.

3. Results

A total of 75 caregivers completed the questionnaire (mean age: 39.7; range: 24–57), including 68 women (90.7%) and 7 men (9.3%), all of Polish origin (Table 1). Although the majority were caregivers for one DS child (94.7%), four parents provided care for two or more DS children (5.3%). Among DS children boys predominated (53.8% vs 46.2%, mean age: 9.7; range: 1–18). While the median time for diagnosis was 2.5 years (range 0.25–11 years) caregivers reported that on average they consulted 5.4 physicians before receiving a correct diagnosis (range 1–30). Most caregivers reported severe (18.7%) or very severe (68%) health problems in their children. 89.3% declared receiving care allowance and 80% used no type of extra-curricular help with their DS children.

While the majority of caregivers declared that it was their child's health problems that were the most challenging aspect of caregiving (86.7%), many were also burdened by changes in their child's behavior (69.3%), their psychological state (68%) and the lack of emotional support (61.3%) (Table 2). Parents consequently reported experiencing a range of upsetting emotions, including feelings of helplessness (72%), anxiety and fear (68%), impatience/irritation (58.7%), fear over their child's premature death (56%), sadness/depression (52%), and nervousness/impulsivity (50.7%). Although it was family that was indicated as the main source of emotional support (54.6%), more than one-third of respondents pointed out the Internet and support groups on Facebook (37.4%), while less than one quarter declared receiving support from doctors (22.7%).

Table 1
Socio-demographic characteristics of DS caregivers.

Characteristics	N (%)
Caregiver's sex	
female	68 (90.7)
Male	7 (9.3)
Caregiver's age	
Range	24–57
M(SD)	39.7 (6.5)
How many of your children experience DS?	
1	71 (94.7)
2 or more	4 (5.3)
Child's sex	
female	37 (46.2)
male	43 (53.8)
Child's age M(SD)	
range	1–18
M(SD)	9.7 (4.6)
How long did it take to obtain a diagnosis? (in years)	
range	0.25–11
M(SD)	2.5 (2.6)
How many physicians did you consult before receiving diagnosis?	
range	1–30
M(SD)	5.4 (4.7)
How would you rate you child's health problems	
very severe	51 (68)
severe	14 (18.7)
moderate	9 (12)
mild	1 (1.3)
none	0 (0)
How many hours per week do you use extra-curricular help with your DS child?	
1–6	7 (9.4)
7–15	4 (5.3)
<16	4 (5.3)
I use no extra help	60 (80)
Do you receive care allowance?	
yes	67 (89.3)
no	8 (10.7)
Professional activity	
unemployed	1 (1.3)
unemployed due to childcare	55 (73.3)
employed part-time	2 (2.7)
employed full-time	17 (22.7)

All respondents declared having been profoundly engaged in caregiving for their DS children (Table 3). While almost half of the caregivers reported that their child's disease had a detrimental impact on the relationship between parents (48%), many reported that it also had an unfavorable effect on their relationship with the family (38.7%) and healthy children (48%).

Even though caregivers felt a profound emotional connection with their DS children, respondents reported experiencing many harrowing or ambivalent feelings toward the caregiving role (Table 4). The majority were concerned that as the disease progressed their child might develop new symptoms (78.6%), others anticipated their child's death (46.7%) or worried over family finances (44%). Some were also concerned that their other children might develop DS (28.3%). While 46.7% of respondents saw no constructive impact of their child's disease on their lives, 44% declared that caregiving had made them stronger as a person.

For many respondents caregiving was a source of ambivalent or upsetting emotions: while 93.4% perceived their caregiving role as a duty, the majority reported physical fatigue (81.3%) and mental

Table 2
Caregiving burden in caregivers of children with DS.

	Never	Rarely	Sometimes	Often	Always
What aspects of your child's disease are the most challenging?					
the child's health problems	0 (0)	1 (1.3)	9 (12)	14 (18.7)	51 (68)
the child's emotional/psychological state	4 (5.3)	4 (5.3)	16 (21.4)	19 (25.3)	32 (42.7)
changes in behavior resulting from the disease	1 (1.3)	8 (10.7)	14 (18.7)	19 (25.3)	33 (44)
contacts with the healthcare system	0 (0)	8 (10.7)	31 (41.3)	25 (33.3)	11 (14.7)
problems with daily activities	1 (1.3)	9 (12)	30 (40)	22 (29.3)	13 (17.3)
financial issues	5 (6.7)	8 (10.7)	23 (30.7)	24 (32)	15 (20)
lack of emotional support	8 (10.7)	3 (4)	18 (24)	16 (21.3)	30 (40)
Does caring for a DS child make you experience any of the following emotional states?					
emotional lability	2 (2.7)	9 (12)	28 (37.3)	28 (37.3)	8 (10.7)
emotional control problem	3 (4)	12 (16)	30 (40)	24 (32)	6 (8)
impatience/irritation	2 (2.7)	7 (9.3)	22 (29.3)	37 (49.4)	7 (9.3)
nervousness/impulsivity	2 (2.7)	9 (12)	26 (34.7)	32 (42.7)	6 (8)
anger	5 (6.7)	16 (21.3)	30 (40)	20 (26.7)	4 (5.3)
anxiety/fear	2 (2.7)	5 (6.7)	17 (22.6)	29 (38.7)	22 (29.3)
helplessness	2 (2.7)	5 (6.7)	14 (18.6)	32 (42.7)	22 (29.3)
sadness/depression	3 (4)	6 (8)	27 (36)	32 (42.7)	7 (9.3)
lack of self-confidence	8 (10.7)	14 (18.7)	32 (42.7)	17 (22.7)	4 (5.3)
feelings of hopelessness	5 (6.7)	11 (14.7)	25 (33.3)	25(33.3)	9 (12)
feeling guilty	10 (13.3)	20 (26.7)	24 (32)	15(20)	6 (8)
sense of shame	32 (42.7)	24 (32)	13 (17.3)	5 (6.7)	1 (1.3)
loneliness	5 (6.7)	14 (18.7)	21 (28)	28 (37.3)	7 (9.3)
a desire to retreat from the environment	8 (10.7)	20 (26.6)	18 (24)	23 (30.7)	6 (8)
low self-esteem	12 (16)	19 (25.3)	23 (30.7)	15 (20)	6 (8)
anticipatory loss/fear of the child's premature death	3 (4)	9 (12)	21 (28)	18 (24)	24 (32)
Source of support for DS caregivers					
family	5 (6.7)	5 (6.7)	24 (32)	20 (26.6)	21 (28)
relatives/friends	12 (16)	30 (40)	18 (24)	11 (14.7)	4 (5.3)
association/foundation for people with DS	22 (29.3)	19 (25.4)	25 (33.3)	8 (10.7)	1 (1.3)
psychologist	39 (52)	16 (21.3)	10 (13.3)	8 (10.7)	2 (2.7)
local support group	48 (64)	14 (18.7)	11 (14.6)	2 (2.7)	0 (0)
Internet/Facebook support group	3 (4)	12 (16)	32 (42.7)	20 (26.7)	8 (10.7)
neighbors	36 (48)	18 (24)	16 (21.3)	5 (6.7)	0 (0)
doctor	15 (20)	25 (33.3)	18 (24)	15 (20)	2 (2.7)
other medical personnel	33 (44)	27 (36)	11 (14.6)	2 (2.7)	2 (2.7)
clergyman	58 (77.3)	8 (10.7)	6 (8)	3 (4)	0 (0)
others	43 (57.3)	14 (18.7)	13 (17.4)	4 (5.3)	1 (1.3)
religion/spirituality	36 (48)	11 (14.7)	20 (26.6)	6 (8)	2 (2.7)
leisure activity/hobby	16 (21.3)	11 (14.7)	31 (41.3)	15 (20)	2 (2.7)

exhaustion (80%). As 76% of caregivers declared that their entire life was subordinated to the role of caregiver, 66.6% reported that caregiving forced them to give up their passions, hobbies, and plans, and 53.3% experienced a caring overload. Many others felt they were not understood by others (62.7%), experienced conflict between their own needs and those of their DS child (50.7%), and 50.6% declared that caregiving impaired their ability to fulfill other social roles. Finally, caregivers reported experiencing sadness and depression (50.7%), an inability to cope with stress (46.6%), and solitude and isolation (41.4%).

Thirty-six percent of caregivers declared that caregiving for their DS child was a source of personal satisfaction (Table 5) and many were satisfied with various aspects of their lives, including their relationships with the family (72%), their financial situation (61.4%), their life situation (61.3%), their physical health (52%), and they enjoyed a sense of security (54.6%). While more than half of the respondents (50.7%) were dissatisfied with their caregiving role, many stressed the extent to which caring for their DS child impaired their quality of life (74.7%). In particular, respondents emphasized being overwhelmed by their caregiving role and they complained about the lack of time for their personal development (73.4%). Many stressed the way DS impinged on their relationships with friends (46.7%), their quality of sleep (46.7%), and their well-being (42.7%).

4. Discussion

While some approved therapies, including drugs, provide some benefits in managing seizures [7–9,23], this research shows that, since DS is a severe, developmental, and life-threatening form of epilepsy, it has a significant impact not only on the lives of children affected but also their family caregivers [28,29,38–40,42,45,49,50,54]. Numerous studies report that DS carers are under constant stress because of the diagnosis, persistent severe seizures, and associated comorbidities, which lead to their child's cognitive dysfunction, motor, behavioral, and communication impairments [5,10,12,28]. Nolan et al., for example, found that the uncertainty of the diagnosis, the time spent in the hospital, and the fear of prolonged seizures caused stress for DS parents from which they struggle to find respite or relief. They are often burdened by the disappointments of the healthcare system [51]. Camfield *et al.* likewise reported that DS carers suffer emotional exhaustion and anxiety related to "fear of the next seizure" that resist medication, and fear that each seizure could be "the seizure that kills my child" [37]. A growing body of research suggests that caring for a DS child seriously affects caregivers' physical and mental health, daily life, family relationships, professional and social life, leisure activities, and is a source of financial burden [10,40,43–45,48].

Consistent with these findings, this research shows that while Polish DS carers are deeply involved in care, their child's health problems and associated behavior, motor, cognitive and developmental delay are emotionally challenging. Most caregivers enrolled in the study reported a variety of distressing feelings toward their caregiving role and suggested that caregiving impaired their quality of life. Indeed, most respondents reported feelings of helplessness, sadness, depression, anxiety, and fear. While many caregivers felt they were not understood by others, the presence

Table 3
Psychosocial impact of caregiving for DS children.

	N (%)
How would you rate your emotional engagement in caregiving for your DS child?	
very big	63 (84)
big	12 (16)
average	0 (0)
little	0 (0)
negligible	0 (0)
Has your child's disease caused a disruption in the relationship with the other parent?	
the child's disease has not harmed the relationship	36 (48)
the child's disease has harmed the relationship with my partner but has not lead to its break-up	33 (44)
the child's disease has strengthened our relationship	1 (1.3)
the relationship broke up after the diagnosis was made	2 (2.7)
the relationship broke up as a result of challenges related to caring for DS child	1 (1.3)
other	2 (2.7)
How did your child's disease affect your relationship with your family?	
very positive	1 (1.3)
rather positive	25 (33.3)
it has not changed	18 (24)
rather negative	24 (32)
very negative	5 (6.7)
does not apply	2 (2.7)
How did your child's disease affect your relationship with your healthy child/children?	
very positive	4 (5.3)
rather positive	17 (22.7)
it has not changed	13 (17.3)
rather negative	25 (33.3)
very negative	11 (14.7)
does not apply	5 (6.7)
Are you a member of a support group for people caring for DS children?	
yes	65 (86.7)
no	10 (13.3)

of anticipated grief and general emotional stress among DS parents were identified in the survey study. They also complained about the lack of emotional support.

This study thus supports previous findings that reported that most DS carers experience a wide variety of distressing emotions, including anxiety, depression, helplessness, loneliness, anger, and frustration [28,29,38–40,45,49,55,56]. A multicentre study from Germany, for instance, showed that as DS carers constantly worry about their child's health, over 46% reported some symptoms of clinical depression (22% mild, 15% moderate, and 9% severe) [50]. A focus group study by Jensen *et al.* also demonstrated that over 54% of DS, parents reported sleep deprivation and the inability to 'turn off', which, in turn, resulted in compromised mental health, anxiety (57.4%), depression (55.3%), fatigue and physical exhaustion (57.9%). Many also experienced anger, guilt, helplessness, and lack of energy, as well as finding it difficult to make time for their self-care needs [38,39]. Another study found that 86% of DS parents experience grief regarding their child's condition, and 89% express the need for more support with stress management [57]. Villas *et al.* also demonstrated that, although 66% of DS caregivers had depressive symptoms, only 26% have received any form of therapy [29]. A German study showed that DS caregivers reported statistically more depressive symptoms than carers of children with other types of epilepsy, they experience higher social isolation and their quality of life is lower [28]. Finally, a recent literature review on the effects of DS on informal caregivers' mental health and their quality of life reported that DS caregivers had significantly higher levels of depression and anxiety than population norms and carers of other epilepsy suffers. It also showed that both depression and anxiety were associated with fatigue and impoverished quality of sleep in caregivers [52].

At the same time, although some studies highlight the positive aspects of caregiving and suggest that DS may bring a family closer [51,55], help to redefine the meaning of life, give the caregivers a feeling of mastery and make them more confident in themselves [38], this study shows that, although some respondents believed that caregiving made them stronger as a person, most Polish caregivers saw no positive impact on their lives as a result of their child's disease.

This study also shows that providing care for a DS child damages caregivers' relationships with other family members, including spouses, relatives, and healthy children. As the disease progresses, DS carers lack time for socializing, miss out on social relationships and experience increasing social isolation. This is in line with observations made by Nolan *et al.*, who demonstrated that 38% of family caregivers reported damage done by DS to relationships with family, 63% with friends, and 54% with spouses. Many also expressed concerns about the impact of DS on siblings [38,51,55]. Another study by Villas *et al.* showed that, as 74% of parents worried about the emotional impact of DS on patients' siblings, the impact of caring for a DS child on the family ranked among the top three major concerns below seizure control and behavioral and communication challenges [29]. A European survey showed that caring for a child with DS impedes parents' everyday life (91%), family relationships (70%), and social life (80%). 46% of caregivers also reported that their DS child's siblings missed out on some leisure opportunities [42].

This study confirms that caring for a DS child is a source of serious emotional stress and it impairs parents' quality of life. As most respondents experienced care overload and complained about the lack of time for themselves, they were concerned that their entire life was subordinated to the role of caregiver. While many respondents also reported sleep deprivation, deterioration of physical health and mental well-being, they also reported feeling lost and alone. This is in line with previous studies that demonstrated that DS carers experience fear, anxiety, grief, uncertainty, and sleep problems, which seriously lessen their quality of life, they also experience the encroaching of caregiving on relationships with friends, family, and spouses [42,50,56], but work and emotional stress were also identified [10,38,43,44,48,54]. While 33% of DS carers in Spain reported being unable to go on holiday, 51% said they had had less than one hour per week to themselves and 28% less than one hour per day [46]. In another study conducted in several European countries 77% of DS parents said they had less than one hour per day to themselves. While 64% received support from their partners and other family members or relatives (46%), social services were available for very few (19%), so 21% of caregivers had to use private sources [42].

This study confirms that apart from the humanistic burden caring for DS children results in serious financial strain. In fact, most parents stressed the extent to which caregiving affected their family finances. The available research confirms that caring for a DS child involves significant financial costs, which include hospital admission, rehabilitation, use of many antiepileptic drugs, ancillary treatment (speech therapy, occupational therapy, outpatient physiotherapy), and medical equipment (i.e., wheelchairs, special beds, and helmets). Apart from the many direct costs associated with the substantial use of the healthcare system research reports the high indirect costs and financial burden resulting from unemployment or early retirement, lost or impaired productivity, loss of income, lost leisure time, and time commitment [28,41,42,56,58,59]. While Strzelczyk et al., for example, demonstrated that the management of DS requires more resources than the management of other types of epilepsy, they evaluated a total annual direct health care costs of €20,000 related to in-patient stays, disability allowance, and medication expenditure), and €18,000 in indirect costs related to loss of

Table 4
Caregivers' emotional experiences and feelings related to caregiving.

	Never	Rarely	Sometimes	Often	Always
Feelings toward caregiving					
Do you feel emotionally disconnected from your DS child?	57 (76)	11 (14.7)	5 (6.7)	1 (1.3)	1 (1.3)
Do you worry that your other (or future) children might also develop DS?	24 (32)	18 (24)	11 (14.7)	13 (17.3)	9 (12)
Do you worry over family finances?	5 (6.7)	9 (12)	28 (37.3)	21 (28)	12 (16)
Do you feel supported by your family and relatives?	5 (6.7)	13 (17.3)	31 (41.3)	15 (20)	11 (14.7)
Do you feel uncomfortable when other people are in the presence of your DS child?	7 (9.3)	25 (33.3)	24 (32)	17 (22.7)	2 (2.7)
Are you worried by the progress of your child's disease and the emergence of new symptoms?	0 (0)	4 (5.3)	12 (16)	31 (41.3)	28 (37.3)
Are you bothered by the thoughts about your child's death?	4 (5.3)	15 (20)	21 (28)	27 (36)	8 (10.7)
Do you see any positive impact of your child's disease on your life?	16 (21.3)	19 (25.4)	28 (37.3)	8 (10.7)	4 (5.3)
Have you ever faced stigmatisation as a result of your child's disease?	26 (34.7)	21 (28)	23 (30.7)	4 (5.3)	1 (1.3)
Have you ever experienced discrimination as a result of your child's disease?	18 (24)	21 (28)	29 (38.7)	6 (8)	1 (1.3)
Is child's disease a source of social exclusion?	10 (13.3)	21 (28)	25 (33.3)	16 (21.3)	3 (4)
Is caregiving a source of satisfaction?	17 (22.7)	13 (17.3)	23 (30.7)	19 (25.3)	3 (4)
Has caregiving made you stronger as a person?	4 (5.3)	15 (20)	23 (30.7)	23 (30.7)	10 (13.3)
Feelings resulting from caregiving for your DS child					
Do you considered caregiving a duty?	1 (1.3)	1 (1.3)	3 (4)	11 (14.7)	59 (78.7)
Do you feel physical fatigue as a result of caregiving?	2 (2.7)	1 (1.3)	14 (18.7)	41 (54.6)	17 (26.7)
Do you suffer from mental exhaustion as a result of caregiving?	1 (1.3)	3 (4)	11 (14.7)	34 (45.3)	26 (34.7)
Do you feel uncomfortable when dealing with the hygiene of your DS child?	28 (37.3)	19 (25.4)	13 (17.3)	13 (17.3)	2 (2.7)
Is the role of caregiver a source of stress?	5 (6.7)	12 (16)	29 (38.6)	20 (26.7)	9 (12)
Do you have a feeling of care overload?	1 (1.3)	9 (12)	25 (33.4)	28 (37.3)	12 (16)
Do you have a feeling that the caregiving role is beyond you?	10 (13.3)	13 (17.3)	32 (42.7)	18 (24)	2 (2.7)
Do you have the feeling that you are not coping well with the stress?	1 (1.3)	14 (18.7)	25 (33.4)	31 (41.3)	4 (5.3)
Is caregiving a source of frustration or spite?	8 (10.7)	16 (21.3)	28 (37.3)	19 (25.3)	4 (5.3)
Do you have a feeling of solitude and isolation?	4 (5.3)	16 (21.3)	24 (32)	24 (32)	7 (9.4)
Do you experience sadness and depression?	0 (0)	10 (13.3)	27 (36)	33 (44)	5 (6.7)
Do you experience feelings of guilt and shame?	25 (33.3)	23 (30.7)	16 (21.3)	9 (12)	2 (2.7)
Do you have the feeling that your needs are unimportant to others?	4 (5.3)	13 (17.3)	26 (34.7)	24 (32)	8 (10.7)
Do you have the feeling that nobody knows or understands what you are going through?	0 (0)	4 (5.3)	24 (32)	33 (44)	14 (18.7)
Do you have a feeling that your entire life is subordinated to the role of caregiver?	1 (1.3)	3 (4)	14 (18.7)	24 (32)	33 (44)
Do you experience conflict between your own needs and those of your DS child?	3 (4)	14 (18.7)	20 (26.6)	33 (44)	5 (6.7)
Dose caregiving make it difficult to fulfil other roles, i.e. parent/spouse/employee	4 (5.3)	10 (13.3)	23 (30.7)	25 (33.3)	13 (17.3)
Has the role of caregiver forced you to give up your own passions, hobbies and plans?	0 (0)	6 (8)	19 (25.3)	36 (48)	14 (18.7)
Have you experienced feelings of hopelessness and a loss of meaning in what you do?	7 (9.3)	15 (20)	24 (32)	25 (33.4)	4 (5.3)

Table 5
Caregiving and the perceived quality of life.

How do you rate the following aspects of your quality of life?	Very bad	Rather bad	Neither good nor bad/I do not know	Rather good	Very good
Life situation	3 (4)	14 (18.7)	12 (16)	44 (58.6)	2 (2.7)
Satisfaction with life	8 (10.6)	21 (28)	14 (18.7)	29 (38.7)	3 (4)
Your health	5 (6.7)	20 (26.6)	11 (14.7)	36 (48)	3 (4)
Your well-being	9 (12)	23 (30.7)	14 (18.7)	28 (37.3)	1 (1.3)
Your sense of security	6 (8)	19 (25.3)	9 (12)	40 (53.3)	1 (1.3)
Your financial situation	4 (5.3)	10 (13.3)	15 (20)	41 (54.7)	5 (6.7)
Your relationship with your family	1 (1.3)	9 (12)	11 (14.7)	44 (58.7)	10 (13.3)
Your social life and relationships with friends	14 (18.7)	21 (28)	17 (22.7)	20 (26.6)	3 (4)
Your quality of sleep	9 (12)	26 (34.7)	7 (9.3)	29 (38.7)	4 (5.3)
Time to pursue your passions/hobbies	20 (26.7)	35 (46.7)	1 (1.3)	18 (24)	1 (1.3)
The impact of DS on your quality of life	0 (0)	16 (21.3)	3 (4)	35 (46.7)	21 (28)
Caregiving as a source of personal satisfaction	9 (12)	29 (38.7)	10 (13.3)	25 (33.3)	2 (2.7)
Your feelings of personal happiness	8 (10.7)	19 (25.3)	13 (17.3)	32 (42.7)	3 (4)

work, reduced working hours and missed days at work [50]. On the other hand, 80% of caregivers from the five European countries declared that caregiving for a DS child had compromised their professional careers. While 81% of caregivers who had lost their job declared that their unemployment resulted from caregiver responsibilities, 65% of those who were employed had missed a number of working days within the previous four weeks due to their child's disease, and 28% had missed over three days. Many also reported that it resulted in their salary being cut [42]. Among US carers 45% either resigned, took early retirement, or lost their jobs due to their caregiving responsibilities, and 18% changed jobs [40].

This study also supports others' observation that DS caregivers often struggle with prolonged or late diagnoses in their children [46]. 60% of caregivers enrolled in this study reported that the diagnostic journey lasted more than three years and Silvennoinen *et al.* showed that the median age at genetic diagnosis in DS patients was 44.5 years (range 28–52 years) [21]. Skluzacek *et al.* also found that almost 70% of DS patients reported consulting three or more neurologists before receiving an appropriate diagnosis, 50% received their diagnosis after three years from the initial seizure, 23% after five years, and 8% after 10 years. [57]. This is in line with previous studies that show that, as healthcare professionals possess no adequate knowledge regarding rare diseases [60,61], patients with rare diseases struggle with the diagnostic odyssey [62–65].

Our findings also confirm that there is a gender gap in caregiving. The mother tends to take on the role of the main caregiver, so it is the mother who experiences more strain from caregiving. This is important because previous studies showed the impact of caring for DS children is greater on mothers than fathers [10,38,42,51]. A recent study, for example, conducted in French reported that DS mothers had a poorer perception of their own general health than fathers. They declared that caregiving cost them more time and energy and encroached on their social and professional life and

50% of mothers had taken a break from work for more than six months, while only 7.1% of fathers did the same [44]. While 17.4% of German mothers had cut their working hours or given up work due to their child's disease, only 0.6% of fathers had done likewise [56]. Strzelczyk *et al.* also demonstrated that mothers were tenfold more affected by losses in productivity: 31% of mothers had given up work, while only 1% of fathers did so; 29% cut their working hours, while only 6% of fathers did; and 40% had missed days from work during the previous three months due to DS, but only 27% of fathers had [50]. All seven fathers enrolled in this study said that they worked full-time, but 74.6% of the mothers had given up work due to childcare.

4.1. Limitations

Although to the best of our knowledge, this is one of the few studies on the emotional experiences of family caregivers of children with DS in Poland, it also has its limitations, which should be considered when interpreting the findings. Firstly, since the survey was completed by only 75 DS caregivers, the results cannot be extrapolated for the entire population of DS carers in Poland. It should, however, be stressed that because to date there is no registry of DS (pediatric) patients in Poland the exact number of children suffering from DS is unknown. Moreover, not all members of the support group for people with DS on Facebook, which was used to recruit the participants of the study, are members of the Association for People with Severe Refractory Epilepsy DRAVET.PL and some are loosely related to DS (doctors or researchers interested in the condition, or distant relatives who do not provide care to DS children) neither it is possible to assess the exact number of family caregivers that were contacted and asked to participate, nor to assess the overall response rate. Secondly, while fathers/-male caregivers were also encouraged to participate in the study, the vast majority of participants were women, mainly mothers. It was therefore impossible to compare similarities and differences in emotional experiences and the impact on life based on gender. While previous studies reported the gender gap in caregiving, it was also suggested that the impact of DS on mothers is far greater than on fathers [i.e., 10,38,45,52,54]. Thirdly, since all participants were contacted via social media platforms, there is potential recruitment bias. It is likely that those caregivers who use no social media platforms or are not members of the Association for People with Severe Refractory Epilepsy DRAVET.PL was unaware of the study and was therefore unable to share their experiences. A fourth limitation results from the topic of this study. While on the one hand, it was focused on pediatric patients, it does not represent the experiences of caregivers of DS adults, on the other, it was focused on emotional experiences, so some parents who feel uncomfortable sharing their personal experiences might abandon the questionnaire. Finally, because some categories, such as depression or anxiety, were undefined, caregiver-reported responses are purely subjective assessments and may be unrepresentative of a well-defined medical assessment.

This research has some advantages that should also be acknowledged. Most importantly, as DS carers in Poland seem to be neglected by the healthcare system, this survey sheds light on a new insight into their emotional problems and needs. It may therefore stimulate further research into the situation of family caregivers of DS children. It seems that allowing caregivers to share their experiences had a therapeutic value.

5. Conclusions

While this study fills a gap in the literature on the caregivers of children with DS in Poland, it supports previous findings that DS is a multifaceted disease and that caring for a child with DS is associated with a significant psychosocial and emotional burden that affects the entire family. Caregivers enrolled in this study reported that it was the child's health problems followed by behavioral and psychic disorders that were the most challenging aspect of caregiving. They were also burdened by the lack of emotional support. As they were deeply involved in caregiving for their children, parents experienced feelings of helplessness, anxiety and fear, anticipated grief, depression, and impulsivity. Many caregivers reported that their child's disease encroached on their relationships with their spouses, family, and healthy children. As caregivers experienced care overload, suffered physical fatigue and mental exhaustion, they stressed the extent to which caregiving for DS impaired their quality of life, social and professional life, and was a source of financial burden.

All in all, as this study identified specific burden domains that affect DS caregivers' well-being, we believe that their empowerment is a huge project that requires the implementation of multilevel solutions. We, therefore, suggest that in order to alleviate the humanistic burden of caregiving for children with DS and address their emotional needs the following actions are necessary: (1) a bio-psychosocial approach to DS treatment, focusing on physical, mental, and psychosocial interventions, should include both DS children and their caregivers; (2) healthcare professionals should identify the specific domains of caregivers' lives that are affected by caring for DS children; (3) healthcare professionals should identify caregivers' emotional needs; (4) apart from identifying the factors that influence DS caregiving burden, healthcare professionals should encourage the optimization of caregivers' quality of life; and (5) as caring for a DS family requires a special and combined approach by multi-disciplinary teams consisting of various healthcare specialists, including doctors, nurses, physiotherapists, psychologists, and speech therapists to address the needs of DS children's families.

Authors' Contributions

JD and DW conceptualized the study and designed the research questionnaire. JD collected the data. DW performed the statistical analyses and prepared the tables. JD conducted the literature search and drafted the manuscript. JD and DW discussed the results, critically revised the article, read, and approved the submitted version. Both authors contributed equally to this paper.

Data availability statement

The datasets generated during the study are available from the corresponding author upon reasonable request.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethics Approval and Consent to Participate

This study was performed in line with the principles of the Declaration of Helsinki. Ethics approval and research governance approval were obtained from the PUMS Bioethics Committee (KB – 833/22). Because of the sensitive nature of the topic and potential disclosures of distress caused by the caregiving, the voluntary nature of the study was emphasized and participants were informed of the option to abandon the survey at any time and to refuse to reveal information regarding their personal circumstances. Informed consent was obtained from all individual participants in the study.

Consent for publication

Not applicable

Data availability statement

The datasets generated during the study are available from the corresponding author on reasonable request.

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References

[1] Dravet C. The core Dravet syndrome phenotype. Epilepsia 2011;52(Suppl 2):3–9.
[2] Brunklaus A, Zuberi SM. Dravet syndrome–from epileptic encephalopathy to channelopathy. Epilepsia 2014;55(7):979–84.
[3] Sanchez-Carpintero R, Patiño-Garcia A, Urrestarazu E. Musicogenic seizures in Dravet syndrome. Dev Med Child Neurol 2013;55(7):668–70.
[4] Verbeek NE, Wassenaar M, van Campen JS, Sonsma A, Gunning B, Knoers N, et al. Seizure precipitants in Dravet syndrome: What events and activities are specifically provocative compared with other epilepsies?. Epilepsy Behav 2015;47:39–44.
[5] Bjurulf B, Reilly C, Hallböök T. Caregiver reported seizure precipitants and measures to prevent seizures in children with Dravet syndrome. Seizure 2022;103:3–10.
[6] De Liso P, Pironi V, Mastrangelo M, Battaglia D, Craiu D, Trivisano M, et al. Fatal Status Epilepticus in Dravet Syndrome. Brain Sci 2020;10(11):889. https://doi.org/10.3390/brainsci10110889.
[7] Wirrell EC, Nabbout R. Recent Advances in the Drug Treatment of Dravet Syndrome. CNS Drugs 2019;33(9):867–81.
[8] Li W, Schneider AL, Scheffer IE. Defining Dravet syndrome: an essential prerequisite for precision medicine trials. Epilepsia 2021;62:2205–17.
[9] Strzelczyk A, Schubert-Bast S. A Practical Guide to the Treatment of Dravet Syndrome with Anti-Seizure Medication. CNS Drugs 2022;36(3):217–37.
[10] Lagae L, Brambilla I, Mingorance A, Gibson E, Battersby A. Quality of life and comorbidities associated with Dravet syndrome severity: a multinational cohort survey. Dev Med Child Neurol 2018;60(1):63–72.
[11] Dravet C, Oguni H. Dravet syndrome (severe myoclonic epilepsy in infancy). Handb Clin Neurol 2013;111:627–33.
[12] Strzelczyk A, Kurlemann G, Bast T, Bettendorf U, Kluger G, Mayer T, et al. Exploring the relationships between composite scores of disease severity, seizure-freedom and quality of life in Dravet syndrome. Neurol Res Pract 2022;4:22. https://doi.org/10.1186/s42466-022-00186-9.
[13] Brunklaus A, Ellis R, Reavey E, Forbes GH, Zuberi SM. Prognostic, clinical and demographic features in SCN1A mutationpositive Dravet syndrome. Brain 2012;135:2329–36.
[14] 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.
[15] Mei D, Cetica V, Marini C, Guerrini R. Dravet syndrome as part of the clinical and genetic spectrum of sodium channel epilepsies and encephalopathies. Epilepsia 2019;60:S2–7.
[16] Bender AC, Morse RP, Scott RC, Holmes GL, Lenck-Santini PP. SCN1A mutations in Dravet syndrome: impact of interneuron dysfunction on neural networks and cognitive outcome. Epilepsy Behav 2012;23(3):177–86.
[17] Steel D, Symonds J, Zuberi S, Brunklaus A. Dravet syndrome and its mimics: beyond SCN1A. Epilepsia 2017;58:1807–16.
[18] Sadleir LG, Mountier EI, Gill D, Davis S, Joshi C, DeVile C, et al. Not all SCN1A epileptic encephalopathies are Dravet syndrome: Early profound Thr226Met phenotype. Neurology 2017;89(10):1035–42.
[19] Wang JW, Shi XY, Kurahashi H, Hwang SK, Ishii A, Higurashi N, et al. Prevalence of SCN1A mutations in children with suspected Dravet syndrome and intractable childhood epilepsy. Epilepsy Res 2012;102:195–200.
[20] Bremer A, Lossius MI, Nakken KO. Dravet syndrome—considerable delay in making the diagnosis. Acta Neurol Scand 2012;125(5):359–62.
[21] Silvennoinen K, Puvirajasinghe C, Hudgell K, Sidhu MK, Martins Custodio Genomics England Research Consortium H, et al. Late diagnoses of Dravet syndrome: How many individuals are we missing?. Epilepsia Open 2021;6(4):770–6.
[22] Lo Barco T, Kuchenbuch M, Garcelon N, Neuraz A, Nabbout R. Improving early diagnosis of rare diseases using Natural Language Processing in unstructured medical records: an illustration from Dravet syndrome. Orphanet J Rare Dis 2021;16:309. https://doi.org/10.1186/s13023-021-01936-9.
[23] Strzelczyk A, Schubert-Bast S. Therapeutic advances in Dravet syndrome: a targeted literature review. Expert Rev Neurother 2020;20(10):1065–79.
[24] Samanta D. Changing landscape of Dravet Syndrome management: An overview. Neuropediatrics 2020;51(2):135–45.
[25] Wang YQ, Fang ZX, Zhang YW, Xie LL, Jiang L. Efficacy of the ketogenic diet in patients with Dravet syndrome: A meta-analysis. Seizure 2020;81:36–42.
[26] Kearney J. Sudden unexpected death in dravet syndrome. Epilepsy Curr 2013;13(6):264–5.
[27] Shmuely S, Sisodiya SM, Gunning WB, Sander JW, Thijs RD. Mortality in Dravet syndrome: A review. Epilepsy Behav 2016;64(Pt A):69–74.
[28] Strzelczyk A, Schubert-Bast S, Bast T, Bettendorf U, Fiedler B, Hamer HM, et al. A multicenter, matched case-control analysis comparing burden-of-illness in Dravet syndrome to refractory epilepsy and seizure remission in patients and caregivers in Germany. Epilepsia 2019;60(8):1697–710.
[29] Villas N, Meskis MA, Goodliffe S. Dravet syndrome: Characteristics, comorbidities, and caregiver concerns. Epilepsy Behav 2017;74:81–6.
[30] Brown A, Arpone M, Schneider AL, Micallef S, Anderson VA, Scheffer IE. Cognitive, behavioral, and social functioning in children and adults with Dravet syndrome. Epilepsy Behav 2020;112:. https://doi.org/10.1016/j.yebeh.2020.107319107319.
[31] Jansson JS, Hallböök T, Reilly C. Intellectual functioning and behavior in Dravet syndrome: A systematic review. Epilepsy Behav 2020;108:. https://doi.org/10.1016/j.yebeh.2020.107079107079.
[32] Gataullina S, Dulac O. Is epilepsy the cause of comorbidities in Dravet syndrome?. Dev Med Child Neurol 2018;60(1):8.
[33] Ministry of Family and Social Policy. What are the key facts about "Personal assistant for persons with disabilities"?; 2019. https://www.gov.pl/web/family/what-are-the-key-facts-about-personal-assistant-for-persons-with-disabilities.
[34] Ministry of Family and Social Policy. 80 million Polish zlotys for respite care. New programme for non-governmental organisations; 2020. https://www.gov.pl/web/family/80-million-polish-zlotys-for-respite-care-new-programme-for-non-governmental-organisations.
[35] Ministerstwo Edukacji. 2020. Rozporządzenie Ministra Edukacji Narodowej z dnia 24 lipca 2015 r. w sprawie warunków organizowania kształcenia, wychowania i opieki dla dzieci i młodzieży niepełnosprawnych, niedostosowanych społecznie i zagrożonych niedostosowaniem społecznym. https://isap.sejm.gov.pl/isap.nsf/DocDetails.xsp?id=wdu20150001113.
[36] Ministerstwo Zdrowia. 2021. Uchwała nr 110 Rady Ministrów z dnia 24 sierpnia 2021 r. w sprawie przyjęcia dokumentu Plan dla Chorób Rzadkich. https://isap.sejm.gov.pl/isap.nsf/DocDetails.xsp?id=WMP20210000883.
[37] Camfield P, Camfield C, Nolan K. Helping families cope with the severe stress of Dravet Syndrome. Can J Neurol Sci 2016;43(Suppl 3):S9–S12.
[38] 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.
[39] Jensen MP, Brunklaus A, Dorris L, Zuberi SM, Knupp KG, Galer BS, et al. The humanistic and economic burden of Dravet syndrome on caregivers and families: Implications for future research. Epilepsy Behav 2017;70(PtA):104–9.
[40] Campbell JD, Whittington MD, Kim CH, VanderVeen GR, Knupp KG, Gammaitoni A. Assessing the impact of caring for a child with Dravet syndrome: Results of a caregiver survey. Epilepsy Behav 2018;80:152–6.
[41] Whittington MD, Knupp KG, Vanderveen G, Kim C, Gammaitoni A, Campbell JD. The direct and indirect costs of Dravet Syndrome. Epilepsy Behav 2018;80:109–13.
[42] Lagae L, Irwin J, Gibson E, Battersby A. Caregiver impact and health service use in high and low severity Dravet syndrome: A multinational cohort study. Seizure 2019;65:72–9.
[43] Nabbout R, Auvin S, Chiron C, Irwin J, Mistry A, Bonner N, et al. Development and content validation of a preliminary core set of patient- and caregiver-relevant outcomes for inclusion in a potential composite endpoint for Dravet Syndrome. Epilepsy Behav 2018;78:232–42.
[44] Nabbout R, Auvin S, Chiron C, Thiele E, Cross H, Scheffer IE, et al. Zogenix and Adelphi Values study group. Perception of impact of Dravet syndrome on children and caregivers in multiple countries: looking beyond seizures. Dev Med Child Neurol 2019;61(10):1229–36.
[45] Nabbout R, Dirani M, Teng T, Bianic F, Martin M, Holland R, et al. Impact of childhood Dravet syndrome on care givers of patients with DS, a major impact on mothers. Epilepsy Behav 2020;108:. https://doi.org/10.1016/j.yebeh.2020.107094107094.
[46] Aledo-Serrano A, Mingorance A. Análisis del impacto familiar y necesidades del síndrome de Dravet en España. Rev Neurol 2020;70(3):75–83.

[47] Juandó-Prats C, James E, Bilder DA, McNair L, Kenneally N, Helfer J, et al. DRAVET ENGAGE. Parent caregivers of children with Dravet syndrome: Perspectives, needs, and opportunities for clinical research. Epilepsy Behav 2021;122(3):108198. https://doi.org/10.1016/j.yebeh.2021.108198.
[48] Sullivan J, Deighton AM, Vila MC, Szabo SM, Maru B, Gofshteyn JS, et al. The clinical, economic, and humanistic burden of Dravet syndrome - A systematic literature review. Epilepsy Behav 2022;130:. https://doi.org/10.1016/j.yebeh.2022.108661108661.
[49] Irwin J, Strzelczyk A, Kalski M, Bast T, Wiemer-Kruel A, Bettendorf U, et al. Socio-economic impact of Dravet syndrome in Germany: A real world study. Value Health 2018;21:S342. https://doi.org/10.1016/j.jval.2018.09.2044.
[50] Strzelczyk A, Kalski M, Bast T, Wiemer-Kruel A, Bettendorf U, Kay L, et al. Burden-of-illness and cost-driving factors in Dravet syndrome patients and carers: A prospective, multicenter study from Germany. Eur J Paediatr Neurol 2019;23(3):392–403.
[51] Nolan KJ, Camfield CS, Camfield PR. Coping with Dravet syndrome: parental experiences with a catastrophic epilepsy. Dev Med Child Neurol 2006;48 (9):761–5.
[52] Gonçalves C, Martins S, Fernandes L. Dravet syndrome: Effects on informal caregivers' mental health and quality of life - A systematic review. Epilepsy Behav 2021;122:. https://doi.org/10.1016/j.yebeh.2021.108206108206.
[53] Brancato G, Macchia S, Murgia M, Signore M, Simeoni G, Blanke K, et al. The Handbook of Recommended Practices for Questionnaire Development and Testing in the European Statistical System, 2005. https://unstats.un.org/unsd/EconStatKB/KnowledgebaseArticle10364.aspx.
[54] Postma A, Milota M, Jongmans MJ, Brilstra EH, Zinkstok JR. Challenging behavior in children and adolescents with Dravet syndrome: Exploring the lived experiences of parents. Epilepsy Behav 2023;138:. https://doi.org/10.1016/j.yebeh.2022.108978108978.
[55] Nolan K, Camfield CS, Camfield PR. Coping with a child with Dravet syndrome: insights from families. J Child Neurol 2008;23(6):690–4.
[56] Riechmann J, Strzelczyk A, Reese JP, Boor R, Stephani U, Langner C, et al. EpiPaed Study Group. Costs of epilepsy and cost-driving factors in children, adolescents, and their caregivers in Germany. Epilepsia 2015;56(9):1388–97.
[57] 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 (Suppl2):95–101. https://doi.org/10.1111/j.1528-1167.2011.03012.x.
[58] Strzelczyk A, Schubert-Bast S, Reese JP, Rosenow F, Stephani U, Boor R. Evaluation of health-care utilization in patients with Dravet syndrome and on adjunctive treatment with stiripentol and clobazam. Epilepsy Behav 2014;34:86–91.
[59] Elliott J, McCoy B, Clifford T, Wells GA, Coyle D. Economic Evaluation of Stiripentol for Dravet Syndrome: A Cost-Utility Analysis. Pharmacoeconomics 2018;36(10):1253–61.
[60] Walkowiak D, Domaradzki J. Are rare diseases overlooked by medical education? Awareness of rare diseases among physicians in Poland: an explanatory study. Orphanet J Rare Dis 2021;16:400. https://doi.org/10.1186/s13023-021-02023-9.
[61] Domaradzki J, Walkowiak D. Knowledge and attitudes of future healthcare professionals towards rare diseases. Front Genet 2021;12:. https://doi.org/10.3389/fgene.2021.639610639610.
[62] Anderson M, Elliott EJ, Zurynski YA. Australian families living with rare disease: experiences of diagnosis, health services use and needs for psychosocial support. Orphanet J Rare Dis 2013;8:22. https://doi.org/10.1186/1750-1172-8-22.
[63] Carmichael N, Tsipis J, Windmueller G, Mandel L, Estrella E. "Is it going to hurt?": the impact of the diagnostic odyssey on children and their families. J Genet Couns 2015;24(2):325–35.
[64] Domaradzki J. Family caregivers' experiences with healthcare services: a case of Huntington disease. Psychiatr Pol 2016;50(2):375–91.
[65] Llubes-Arrià L, Sanromà-Ortíz M, Torné-Ruiz A, Carillo-Álvarez E, García-Expósito J, Roca J. Emotional experience of the diagnostic process of a rare disease and the perception of support systems: A scoping review. J Clin Nurs 2022;31(1–2):20–31.