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THE LIFE WITH DRAVET SYNDROME: SOCIOECONOMIC IMPACT OF THE DISEASE ON PATIENTS AND THEIR CAREGIVERS IN THE CZECH REPUBLIC

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Background

Dravet syndrome (DS) is a rare, treatment-resistant, lifelong, developmental and epileptic encephalopathy characterized by multiple seizure types and high seizure burden. (1) DS is a severe form of epilepsy with an annual incidence estimated at around 1 in 15,700 to 1 in 33,000 births, affecting approximately 125 patients over the age of 2 in Czechia. (2–4)

From early childhood, patients with DS experience multiple types of seizures, including generalized clonic or hemiclonic seizures. The severity of the disease in DS patients is usually assessed by the type and frequency of seizures, along with the presence of comorbid neurological and cognitive disorders, such as motor and speech disorders, learning difficulties, autism, or attention deficit hyperactivity disorder (ADHD). (2,5,6)

Higher seizure frequency is associated with poorer long-term prognosis, an increased incidence of comorbidities and lower overall quality of life (QoL). (7–10) The premature mortality rate in DS patients is high, with the main causes of death being status epilepticus and sudden unexpected death in epilepsy (SUDEP), a condition whose severity is associated with higher seizure frequency and poor seizure control, with frequent generalised tonic-clonic seizures at night generally considered to be the main risk factor. SUDEP can affect people of any age, but it most commom in patients ranging from young children to young adults (ages 2-20). (11–14)

Objectives

The objective of this study was to collect local data on the socioeconomic burden of Dravet syndrome on patients, their caregivers, as well as on society, the healthcare system, and the social system, thereby describing the burden of DS in Czechia.

Methods

A cross-sectional questionnaire survey was conducted to collect local Czech data on the socioeconomic impact of DS on patients and their caregivers. Data were collected between 03-Oct-2022 and 09-Oct-2022 in cooperation with the patient association Epicana.

We collected demographic and clinical data for both patients and caregivers, as well as data on healthcare resource use, out-of-pocket costs, social transfer costs, and caregiver responses to validated questionnaires: WPAI (Work Productivity and Activity Impairment), EQ-5D-5L, and the Zarit Scale of Caregiver Burden (ZBI). Work productivity costs were assessed using a human capital approach and discounted by 3%. For the EQ-5D-5L questionnaires, the UK tariff tables (value set) were used to evaluate utility values. (15,16) The productivity loss costs of caregivers were assessed using a human capital approach and discounted by 3%, with an average retirement age of 64 years.

The gross wage used for calculating costs is based on the Wages and Labour Costs statistics published by the Czech Statistical Office (CZSO) for Q2/2022, which were the most recent statistics available. (17) The average gross wage was equal to CZK40,086 (€1,634) per month, with employer contributions amounting to 33.8% (9.0% for health insurance and 24.8% for social insurance). As a result, the average total cost per employee, including all contributions, amounted to CZK53,635 (€2,186) per month. The 'super-gross' wage reflects the total cost of the employee from the perspective of the employer and the state, including all taxes paid to the state and the net wage. (18)

For the WPAI questionnaire, the relevant parameter for our purposes was work impairment (WI). In the case of caregiver productivity loss, we conservatively assumed that the caregiver would experience fixed productivity loss until retirement. For caregivers on maternity or parental leave, productivity loss for the first 4 years was calculated as that of an unemployed caregiver, and thereafter, until retirement, as that of a working caregiver. Productivity loss costs were calculated for the entire cohort of caregivers based on their mean age, wage, and work productivity loss. These values were then proportionally averaged per caregiver.

The unemployment rate among caregivers in the study was much higher than that of the general population in Czechia (38% vs. 2.4% in Q2/2022). Therefore, we assume that there is additional work productivity loss due to the excessive caregiving demands for patients with DS.

All costs were converted from Czech crowns (CZK) to euros (€) using the exchange rate from October 2022, which was 24.532 CZK/€. (19)

Results

In total, 21 caregivers completed the questionnaires, and 20 of them also completed questionnaires for their underage patients. The mean age of the patient was 7 years with the oldest being 16 years old, and the mean age at diagnosis was 2 years (**Table 1**). At the time of data collection, the average patient was taking 3.65 anti-seizure medications. The most severe epileptic convulsive (grand mal) seizures in these patients occurred an average of 9 times per month and lasted an average of 8.4 minutes per seizure. Additionally, 100% of the patients experienced other types of seizures, most commonly absence and myoclonic seizures.

The mean age of primary caregivers was 41 years, all of them were female, and all but one were the mother of the patient they were caring for and none suffered from DS themselves (**Table 2**).

Caregivers reported that in the 6 months prior to data collection, on average they had seen their GP 4 times outside of scheduled check-ups and specialist once. 30% (n=6) of the patients had used ambulance services for transport to a health facility due to a DS-related emergency in the last 6 months, 4 out of 6 (66.7%) reported using the ambulance service repeatedly. 45% (n=9) of the patients had been hospitalized in the last 6 months, with 4 out of 9 (44.4%) being hospitalized more than once. The average number of hospitalizations for these 9 patients over the last 6 months was 1.6, with an average length of 34.7 days.

In relation to their DS patient, all caregivers (100%, n=21) used their own car for transportation to medical appointments, with mean monthly transportation costs of €127.79. 19% (n=4) of caregivers also used other means of transport (train, bus, etc.), with an average monthly cost of €14.27. Caregivers spent an average of €97.38 per month on prescribed and over-the-counter medicines, vitamins, supplements, and medical supplies. Monthly costs for therapies and services, such as physiotherapy or a personal assistant, were €112.71. Some patients also utilized spa stays, with the average monthly out-of-pocket cost for spa treatments being €18.87. Total out-of-pocket costs per caregiver (n=21) related to their DS patient were €357/month (22% of the average gross wage in Czechia) (**Table 3**).

Care allowance is received by 86% (n=18) of the caregivers on behalf of their patients. One caregiver stated that they had not even applied for this benefit, and in two cases, the benefit was not granted to the patient. The most common level of dependency for determining the amount of care allowance was level 4 (6 patients), followed by level 3 (5 patients). Level 2 was assigned to 3 patients, and level 1 to 4 patients. 19 % (n=4) of caregivers also reported receiving a child allowance on behalf of their patients, which averaged €198.96 per month, and 62% (n=13) reported receiving a mobility allowance, which averaged €22.62 per month (**Table 4**).

The quality of life (QoL) of caregivers of patients with DS was assessed using the EQ-5D-5L questionnaire. The mean reported quality of life in the caregiver cohort (n=21) was 0.733 (**Table 2**). The mean EQ-5D-5L Visual Analogue Scale (VAS) score in the cohort was 69. The mean QoL of caregivers of patients with DS (0.733) is much lower than the QoL of the general population in the 30–39 age group (0.879) and still lower than that of the 40–49 age group (0.837), according to the Catalogue of EQ-5D scores by Sullivan et al. (2011). (20)

The study also assessed caregiver burden using the Zarit burden interview (ZBI) questionnaire. The mean ZBI score for the caregiver cohort (n=21) was 49.2, which is in the moderate to heavy burden range. For caregivers of patients with advanced cancer, this score is equal to 23.3 points (21), highlighting that caring for patients with DS imposes a very high burden on caregivers.

The overall proportion of working caregivers was 48% (n=10), with a mean age of 40.7 years and their overall productivity loss was 41.08% (16.4 hours/week). Absenteeism (time away from work) was equivalent to 8.93%. Presenteeism (reduction in productivity while working) was 36.25%. There was a 68.10% reduction in normal daily activities, indicating significant activity impairment (**Table 5**). **Table 6** shows the mean productivity loss costs of caregivers of patients with DS. The total lifetime discounted productivity loss costs for the entire estimated Czech caregiver cohort (n=100), it was assumed that each underage patient has one caregiver, were €25,113,821 (€251,138 per caregiver), with undiscounted costs for the entire cohort amounting to €34,480,061.

Additionally, 38% (n=8) were unemployed (mean age 44.1 years), and 14% (n=3) were on maternity or parental leave (mean age 34.0 years) (**Table 6**). 100% (n=21) of the caregivers who were unemployed or worked part-time stated that they were unable to work full-time due to the time demands of caring for their patient. Moreover, 90% (n=19) of caregivers reported that other family members were also involved in the patient's care in addition to themselves.

Table 1. Baseline characteristics of DS patients

Demographic characteristics (N=20)	
Mean age (Min-Max)	7 years (2.5-16)
Mean age at diagnosis (Min-Max)	2 years (0.5-8)
Gender (number; % female)	14 (70%)
Clinical information (N=20)	
Average number of convulsive seizures per month (Min-Max)	9 (0-60)
Average length of convulsive seizure (Min-Max)	8.4 minutes (1-90)

Table 2. Baseline characteristics of caregivers of DS patients

Demographic characteristics (N=21)	
Mean age (Min-Max)	41 years (28-58)
Gender (number; % female)	21 (100 %)
Employment status (N=21)	% (N)
Full-time	14% (3)
Part-time	19% (4)
Freelance contract	5% (1)
Casual contract	10% (2)
Maternity or parental leave	14% (3)
Unemployed due to patient care	38% (8)
Unemployed	0% (0)
Disability pension	0% (0)
Pension	0% (0)
Quality of Life (N=21)	
EQ-5D-5L (Min-Max)	0.733 (0.338-1)
VAS (Min-Max)	65 (5-99)

Conclusions

The results of this study confirmed that Dravet syndrome imposes a significant societal burden and is associated with numerous challenges. It causes substantial limitations for both patients and their caregivers, impacting all aspects of their daily and social activities. The caregivers' quality of life, ability to work, and capacity to perform routine daily tasks are severely affected.

The high burden that Dravet syndrome imposes on the healthcare system is significant, not only financially but also in terms of personnel, as patients often require the assistance of multidisciplinary medical teams to manage the numerous complications associated with this disease.

To conclude, DS brings a significant socioeconomic burden to patients, caregivers, families, healthcare system, social system, employers as well as to the whole society. With high unmet need, there is potential to reduce this burden in the future with new innovative anti-seizure therapies. Our study may prove useful in preparing future economic analyses related to DS.

Table 3. Direct monthly costs per DS patient

Transportation costs (N=21)	Mean costs per month
Transport using own car	€127.79
Transport other than by car – train, bus, taxi	€14.27
Drugs costs (N=21)	
Prescription drugs/over-the-counter drugs/ supplements/vitamins	€97.38
Other costs (N=21)	
Therapies and services (physiotherapy, personal assistant etc.)	€112.71
Spa treatments	€18.87
Total direct monthly costs of DS/month	€356.76

Table 4. Social security costs of DS patients

Care allowance (N=18)	N (%)
1st level of dependency	4 (22%)
2nd level of dependency	3 (17%)
3rd level of dependency	5 (28%)
4th level of dependency	6 (33%)
Child allowance (N=4)	Mean costs per month
Child allowance	€198.96
Mobility allowance (N=13)	
Mobility allowance	€22.62

Table 5. WPAI in caregivers of DS patients

WPAI in caregivers	%
Absenteeism (N=8)*	8,93%
Presenteeism (N=8)*	36,25%
Work impairment (N=8)*	41,08%
Activity impairment (N=21)	68,10%

*Two working carers did not complete the full WPAI questionnaire

Table 6. Productivity loss costs of the whole caregiver cohort of DS patients in Czechia

	Proportion of caregivers in the study (n=21)	Number of caregivers in Czech cohort (n=100)	Productivity loss costs per caregiver	Productivity loss costs per cohort
Employed	48%	48	€182,527	€8,761,287
Maternity or parental leave	14%	14	€175,497	€2,456,964
Unemployment	38%	38	€365,673	€13,895,570
Total per the whole cohort	**100%**	**100**	**–**	**€ 25,113,821**
Total costs per one patient	**–**	**–**	**–**	**€ 251,138**

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Disclosure

Chlad R, Berezna J, Miczova L, Hazlingerova M, Fiserova D, Krsek P, Blazkova T, Dolezal H and Dolezal T are employed by Value Outcomes which was contracted by UCB to perform the work presented here. Mlcoch T was employee of Value Outcomes at the time of the study was conducted and is now employee of Merck Sharp and Dohme (MSD) Czech Republic. Hazlingerova M and Fiserova D are employees of UCB and holds restricted shares/stock options. Krsek P and Miczova L did not report any conflicts of interest.

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