International Scholars Journals

International Journal of Medical Sociology and Anthropology ISSN 2756-3820 Vol. 13 (8), pp. 001-009, August, 2024. Available online at www.internationalscholarsjournals.org © International Scholars Journals

Full Length Research Paper

The transition from pediatric to adult age in patients with Dravet Syndrome: A study on the current management pathways and the challenges ahead

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Received July 3, 2024; Accepted August 10, 2024 and Published September 06, 2024

Abstract

Dravet Syndrome (DS) is an infantile onset drug-resistant developmental and epileptic encephalopathy, often associated with comorbidities including intellectual disability, behavioral disorders and gait problems. Epileptic seizures usually begin in the first year of life and persist into adulthood, resistant to antiseizure medications. Within the complex care pathway faced by these patients and their families, the transition from pediatric care centers to adult centers represents a critical phase of the patient's journey. If not managed optimally, transition can have significant repercussions on the quality of care and patient management. We conducted a mixed-methods investigation, involving a quantitative survey of 54 neurologists and neuropsychiatrists from 28 national reference centers, and a qualitative survey with 5 specialists and 3 caregivers of patients with DS. The study aimed to investigate the transition of patients from child neurologist clinics to adult clinics exploring management methods, challenges, and unmet needs of patients and their caregivers. The results indicate that transitions to adult centers are currently heterogeneous and often unstructured, with significant implications in terms of the quality of care provided. Particularly, structured transition programs are available in only 70% of centers, and many patients remain in pediatric care beyond adulthood due to perceived better care quality and stability concerns. Additionally, around 19% of patients abandon adult care centers within a year of transition. In order to improve the quality of care and the quality of life for patients with this syndrome, it is essential to listen to the requests of their caregivers, including continuity in patient management, psychological support and planning for the future of their loved ones. The overall fragmented nature of transition strategies highlights the need for initiatives to provide greater structure and continuity in care pathways.

Keywords: Dravet Syndrome, transition, patient journey, rare disease, unmet needs, drug-resistant epilepsy.

1. INTRODUCTION

Dravet Syndrome (DS) is a rare developmental and epileptic encephalopathy associated with drug resistant, lifelong seizures. First described in 1978 by Charlotte Dravet (Dravet, 2011), it has recently been associated with a specific gene mutations (SCN1A) which affects the sodium channel (Mei at al., 2019; Brunklaus et al., 2022). These mutations account for more than 90% of DS cases (Dravet and Oguni, 2013), and they are usually *de novo*

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(Fukuma et al., 2004; Nabbout et al., 2003). The first epileptic seizure usually occurs during the first year of life in previously normal children. Typically, seizures are generalized tonic-clonic, triggered by fever (Connolly, 2016). They are associated with other comorbidities, such as intellectual disability, gait disorders, sleep disturbances and behavioral issues that persist into adulthood (Dravet, 2011; Mei et al., 2011; Dravet and Ogouni, 2013; Fukuma et al., 2004; Nabbout et al., 2003; Connolly, 2016). Prolonged seizures and convulsive or non-convulsive status epilepticus can be frequent. As patients age, they experience other types of seizures, such as myoclonic, atypical absences and focal seizures (Connolly, 2016; Dalla Bernardina et al, 1983; He et al, 2022; Scheffer, 2012), which can also occur without fever (He at al., 2022). Seizure frequency tends to reduce with age [6]. As the patients get older, they experience other neurological issues, such us gait problems, dysphagia, and behavioral comorbidities.

Diagnosis is based on the clinical features, as the identification of the-mutation alone is not sufficient to establish it (Wirrell et al., 2022; Li et al, 2021; Millichap et al., 2009). The treatment of DS is complex and involves the use of anti-seizure medications, some of which, such as valproate and benzodiazepines (especially clobazam), appear to be more effective in seizure control (Cross et al., 2019). Stiripentol therapy also showed promising results, becoming the first approved drug for DS treatment in Europe in 2013. Subsequently, Cannabidiol and Fenfluramine were approved in 2020 (Lagae et al., 2019; Lagae, 2021; Laux et al., 2019).

Despite significant advances in treatment, the long-term prognosis remains poor due to intellectual disability, persistence of drug resistant epileptic seizures and behavioral disorders. Moreover, DS is associated with a higher risk of sudden death compared to unaffected individuals of the same age, especially between the age of 2 and 4 years (Genton et al., 2011).

In the overall care pathway faced by these patients and their families, the transition from pediatric to adult care centers represents a critical phase of the patient's journey, both in terms of transitioning care from child neuropsychiatrists to neurologists and due to limited knowledge of clinical progression of the syndrome in adult patients (Andrade et al., 2021). Such crucial transition within the patient journey, if managed suboptimally, can cause significant repercussions on the quality of patient care and health.

Under these circumstances, the study aims to reconstruct the patient and family experience during the transition to adulthood, analyzing the quality of care provided, the prevalent pathways, and the overall impact on patients and caregivers. By examining the current transition practices in national reference centers and gathering insights from both healthcare professionals and caregivers, the study seeks to identify gaps and propose initiatives to enhance the structure, consistency, and continuity of the care pathway for DS patients.

Based on from the reported experiences of key players involved, gathered through a qualitative and quantitative survey, this study thus highlights the numerous gaps in the current healthcare provision, showcasing the fragmentation and heterogeneity of managing models, and the virtuous transition models that can be an example in order to promote a renovation of the approach and improve the overall care provided to these patients and their quality of life.

2. MATERIALS AND METHODS

A qualitative investigation on the patient journey of individuals with DS was conducted between April and May 2023, complemented by a quantitative survey mapping National Reference Centers involving some of the leading neurologists and child neuropsychiatrists, as well as caregivers of patients in transition age. The aim was to reconstruct the patient's and family's experience at the time of transitioning to adulthood, analyzing the type of care provided and the actual pathways prevalent.

Standardized interviews were administered using Computer-Assisted Web Interviewing (CAWI) and Computer-Assisted Telephone Interviewing (CATI) with a standard questionnaire lasting approximately 30 minutes to a sample of neurologists and child neuropsychiatrists comprising 54 respondents from 28 Centers (11 pediatric, 17 adult) for the quantitative phase. Meanwhile, the qualitative phase involved 5 specialists and 3 caregivers with in-depth interviews lasting approximately 60 minutes conducted remotely by social researchers.

Screening criteria

For clinicians, both in the qualitative and quantitative phases, the screening criteria were as follows:

- Specialization in neurology, pediatric neurology, or child neuropsychiatry.
- Minimum of 5 years of specialized practice.
- Currently treating at least 1 patient with Dravet Syndrome.

As for caregivers, the criteria for the qualitative phase were:

- Being the caregiver of an individual affected by Dravet Syndrome.
- Have been following the individual with DS for at least 1 year.
- Care for a patient aged 14 or older

Characteristics of the sample

The sample of pediatric and adult centers that participated in the survey is well distributed across the national territory, with 7 centers in the North, 11 in the Center (including Sardinia), and 10 centers in the South of Italy (including Sicily). Both in the pediatric and adult settings, a predominantly single specialist-based approach toward patients emerged, with the involvement of other professionals based on the single case in approximately 60% of the centers and a multidisciplinary approach in

approximately 40% of the centers. In the latter case, among the professionals predominantly composing the team, in the pediatric setting, we find child neuropsychiatrists, pediatricians, neurophysiologist, and psychologists, while in the adult setting, we find neurologists, neurosurgeons, psychologists, and cardiologists.

Looking at the profiles of the respondents, the sample is predominantly composed of adult neurologists (62%) with over 20 years of specialized practice, who hold the role of first- and second-level managers (65%). In the pediatric field, there is a more substantial proportion (51%) of highly specialized managers and complex facility managers. Regarding the pathology surveyed, there is a higher specific expertise among pediatric specialists and child neuropsychiatrists, where 42% of respondents hold the role of local/hospital representative and 25% regional representative, compared with 60% of clinicians in the adult field who report treating Dravet Syndrome without holding specific roles in this field.

Regarding the qualitative phase of caregiver interviews, the sample consisted of caregivers of individuals aged from 17 to 31 years, and with wide variability in terms of age at diagnosis (2 patients diagnosed at 17 years old, 3 patients within the first 3 years of life). At the time of the survey, 4 out of 5 patients were over the age of majority, and 3 out of 5 patients were still receiving treatment at the pediatric center.

Analysis Methodology

In reconstructing the patient journey, besides thematic, narrative, and phenomenological analysis, the ABCDE model of cognitive restructuring was applied as a framework for interpretation and analysis (Seligman and Csikszentmihalyi, 2000), as to explore in detail the mental processes influencing the emotions and behaviors of the actors involved. Specifically, this model emphasized the specific ways in which individuals interpret reality, helping to understand how beliefs, thoughts, and interpretations of events directly influence their emotional and behavioral responses.

In the ABCDE model, each letter of the acronym represents an element of analysis, where "A" denotes the activating event, "B" the beliefs that emerge in response to this event, "C" the emotional and behavioral consequences resulting from our interpretations, "D" the disputing phase of beliefs, and "E" the effect of the cognitive restructuring process. From this perspective, it was possible to explore the link between thoughts, emotions, and behaviors of healthcare professionals and caregivers throughout the various stages of the care journey for patients with DS, highlighting in particular the different perspectives at play during the critical junctures of this process and finally arriving at a deeper understanding of the dynamics at work. This model, developed by the renowned cognitive psychologist Albert Ellis, focuses on how our beliefs influence our emotional and behavioral reactions to events. This approach has made it possible to identify how the irrational beliefs of healthcare workers and caregivers can be modified through the process of disputation, leading to significant improvements in stress management and psychological well-being.

Limitations

This study has some limitations. The sample’s size and composition may not fully represent the broader population of DS patients and families, potentially affecting the generalizability of the findings. Additionally, as it is stated in the research itself, the extreme variability in transition programs across different centers could introduce biases and limit the generalizability of the results.

3. RESULTS

The reconstruction of the journey of patients with DS and the caregivers and physicians involved in their treatment (Figures 1 and 2) first allowed us to contextualize the time of the transition from pediatric to adult age, highlighting the functional, emotional, and social variables intertwined in the families' previous situation before reaching adulthood. These factors directly influence the choices and directions the subsequent journey will take.

Some elements emerged from the survey on the patient journey need to be highlighted to achieve better contextualization of the phenomena that will be reported subsequently. These elements refer both to critical management and healthcare-related issues and to the consequences of the impact of the condition on the patients' family history.

3.1 The search for stabilization

Based on the reports of physicians and caregivers regarding the early stages of the disease, analyzing the time factor becomes the key to understand subsequent therapeutic choices. Moreover, the survey revealed a diagnostic delay for DS in some cases significant, especially for two categories of subjects: individuals who do not fit the typical phenotype of DS and milder phenotypes. While the reported average time between the onset of first symptoms and the diagnostic suspicion is approximately 3-6 months, and although this delay has been considerably reduced in recent years, some patients currently are diagnosed only in late adolescence. It is assumed that an equal number, especially in older patients, are currently managed at home without ever having received a formal diagnosis of Dravet Syndrome.

Even patients who received an early diagnosis often report severe difficulties in finding an expert specialist and obtain both quality care in line with their expectations and a stable treatment. This is also due to the features of the disease

Fig. 1. Functional journey of patients with Dravet Syndrome.

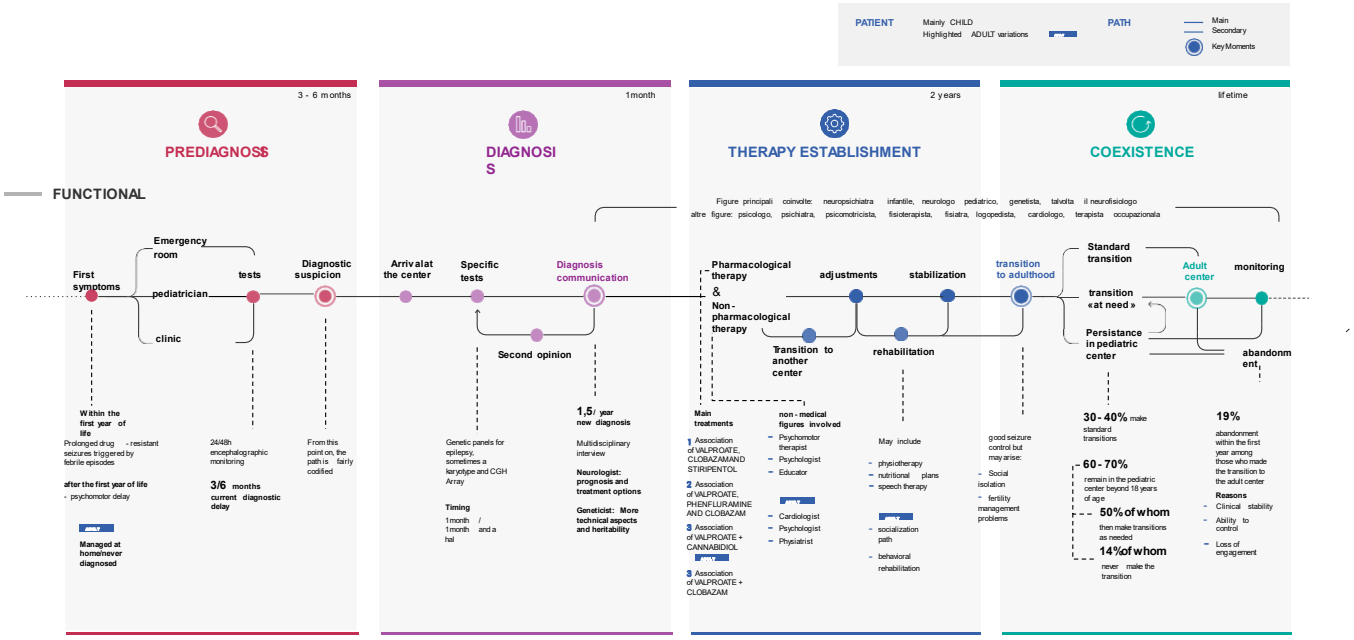
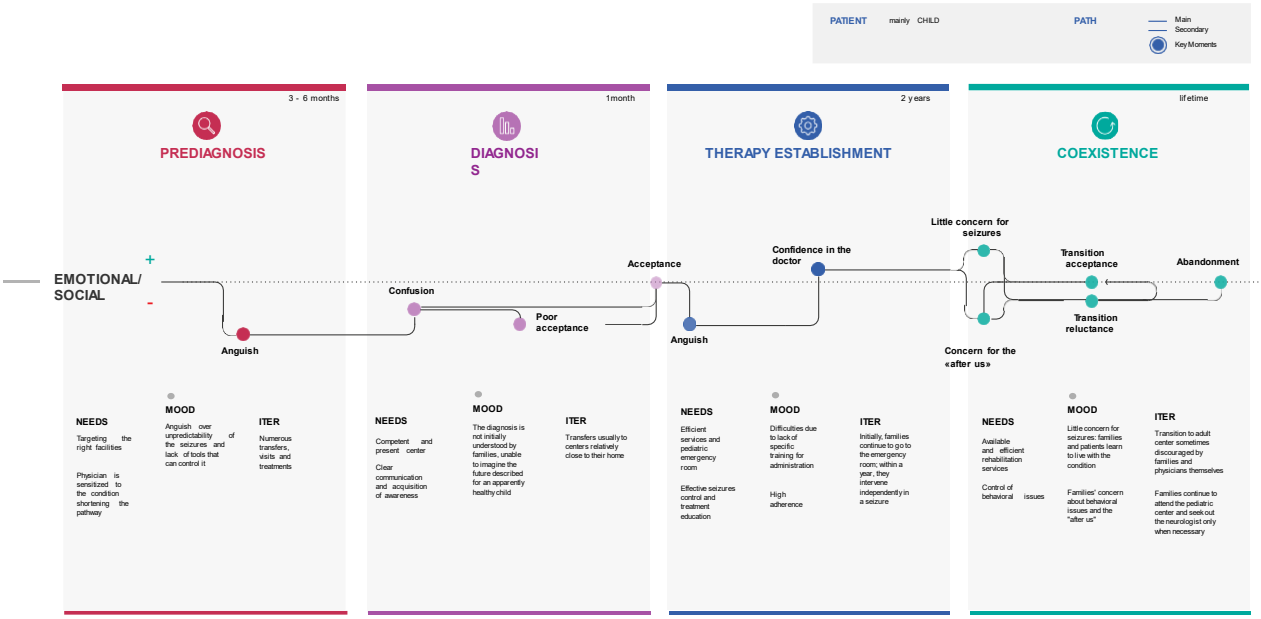


Fig.2. Emotional journey of patients with Dravet Syndrome.



and to the therapeutic options currently available. Obtaining a valid therapeutic option for the patient and simultaneously having a well-structured care pathway are both factors of significant importance in the overall analysis of the treatment of these patients. The challenge in obtaining a diagnosis or finding a therapy that adequately controls the seizures negatively affects the transition planning of these patients, as they are particularly reluctant to disrupt a clinical-caregiver balance that was achieved with difficulty.

Also, the onset of the disease and long-term coexistence with it can have a devastating impact on the psychological

health of family members and on the emotional relationships themselves. The discovery of the condition is usually followed by a long period of isolation and disruption of social, parental, and friendship relationships. In 3 out of 5 cases, mothers of individuals with Dravet Syndrome have had to leave their jobs. Additionally, children usually experience relational difficulties in the school setting, exacerbated by behavioral problems, and in many cases, they manage to build lasting emotional relationships only within cooperatives.

Another critical aspect is related to the impact of the condition on the family unit itself. Looking at the reports of caregivers, in 3 out of 5 families, the illness of their child played a decisive role in separations and divorces. It is important to highlight, therefore, that when talking about Dravet families, one often refers to single mothers who have to manage independently the needs of their affected children and any other children, often with little support from relatives and local health services.

Finally, a topic that is often overlooked when discussing rare and chronic diseases is the impact of the condition on siblings of the patients and who the most neglected social actors in the analysis of the journey are usually. They are usually the most neglected social actors in the analysis of the journey. The psychological and relational impact of the condition on siblings of affected children is remarkable and can lead to heavy long-term consequences, especially because no psychological support services are currently offered. As highlighted by the mapping, the latter, when available, are dedicated to the patient's parents.

3.2 Transitions period: prevalent scenarios

Moving on to the main subject of this study, the results show overall considerable heterogeneity in the transition programs from the pediatric to the adult setting for patients with DS, which differ based on the center, the clinical history, and the patient's condition. Several management patterns have emerged that can be traced to the following three scenarios.

SCENARIO 1: **Standard Transition**. In some centers, patients begin the transition process around the age of 16, following a defined pathway in terms of modality and timing. Generally, the transition to the new center is recommended by pediatric specialist or sometimes is required by families themselves who are facing new needs related to adulthood. This process usually involves a series of steps, which are not consistent across the different centers, and sometimes includes joint visits with both specialists (neurologist and child neuropsychiatrist) or the drafting of a clinical report that is handed over to the new referring specialist.

In general, the investigation has revealed that 70% of centers state that they provide structured transition programs for patients with DS, but it emerged at the same time how the existence of such programs on paper does not necessarily translate into a standardized transition with clearly defined procedures, methods and timelines. The different stages involved in transition programs are often incomplete and heterogeneous, and the existence of a pathway sometimes translates back to the simple compilation of a report for the new referring physician. Furthermore, this data reveals that, despite the need, many facilities (30%) have not yet implemented formal pathways to facilitate the transition of patients from pediatric to adult age.

SCENARIO 2: **Persistence in the Pediatric Center**. Many families and specialists choose to keep their patients in the pediatric center even after adulthood. In particular, this study has highlighted how 69% of patients remains in the pediatric center even after reaching adulthood, according to an average based on the integrated results of the qualitative-quantitative survey.

This persistence can be attributed to various reasons, notably:

- *Family Sphere*: Families often have the perception of a better quality of care in the center that they are currently attended and they are reluctant to switch to the adult center due to their fear of not receiving the same medical care. Furthermore, the qualitative investigation showed how caregivers' expectations for care in the adult center appear to be driven by previous experiences with pediatric specialists. Those who have had trouble finding a doctor capable of providing high-quality care for their loved one, and who have struggled to achieve stabilization, are usually skeptical about the possibility of finding the same level of expertise in the new center. This concern may delay the transition or lead some families to seek alternative ways for independent management of their loved one, which do not involve adult referral centers.

- *Specialist Sphere*: Not only families, but often specialists themselves postpone the beginning of a transition process. This is due to multiple factors, including awareness of the lack of equal care alternatives for patient’s treatment in the local/regional setting, the belief that the pediatric management model better suits the needs of these patients and the willingness and need to carry out certain research projects initiated within their own center.

SCENARIO 3: Transition "at need". This involves a consequential, but not mandatory, pathway compared to the previous scenario. In some facilities, patients are sent to the adult center only when treatment needs become too specific to adulthood. In this case, after a more or less prolonged period of persistence in the pediatric center beyond the age of majority, the patient is referred to the adult neurologist either on the recommendation of the previous specialist or by autonomous initiative of the families, who feel the need for a different type of care. In this scenario, there is no precise age of transition, and the transition typically occurs in an age range from 18 years to even beyond 25 years.

Fig 3. Caregivers attitude towards transition

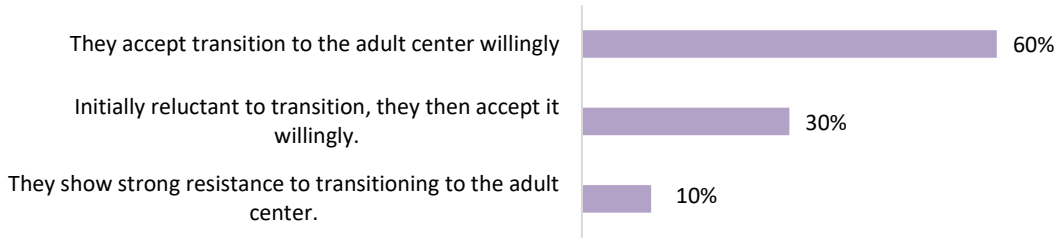


Table 1. Example of Cognitive Restructuring Using the ABCDE Model.

Activating Event (A)	*Beliefs (B)*	*Consequences (C)*	*Dispute (D)*	*Effect (E)*
Transition to the adult care center.	*Belief that the new center may not offer the same quality of care or that engagement is unnecessary.*	*Decreased interest in services, potential abandonment of the center, and increased isolation of patients and families*	*Challenge the belief by providing evidence that the adult center offers specialized care that can still meet the patient's needs and improve long-term outcomes.*	*By addressing these concerns, families may maintain their engagement with the adult care center, benefiting from continued support and care.*

3.3 Abandonment of centers

The abandonment of the referral center once the transition has been made is not uncommon. An alarming data concerns the abandonment rate of the adult center reported by the neurologist, which stands at around 19% within a year of referral. It is therefore crucial to understand the reasons why patients and families drop off the doctor's and center's radar during the transition to adulthood and any organizational and structural causes inherent in this phenomenon. This study highlighted three main reasons that lead to the abandonment of the adult center, namely:

1) CLINICAL STABILITY: Reaching adulthood typically coincides with clinical stability and a general reduction in the number of seizures. Patients tend to require less assistance from the epilepsy center and the neurologist and rather need therapies focused on behavioral, occupational, and social development to enhance autonomy and social skills.

2) CAREGIVERS EXPERTISE: After many years of experience and living with the condition, caregivers have often achieved good experience in management of patient's seizures.

3) LOSS OF ENGAGEMENT: With the transition to the adult center, some families may experience a loss of interest in center services, as they are deemed unsatisfactory or no longer necessary, and this can lead to a tendency toward isolation.

To address the challenge of abandonment and explore potential improvements, the ABCDE model of cognitive restructuring offers a valuable framework. By examining the beliefs and cognitive processes that influence patient and caregiver engagement, this model can provide insights into how these attitudes can be adjusted to enhance the overall care experience, allowing us to understand how changing beliefs about the quality of care and the need of ongoing engagement with adult centers can impact the likelihood of abandonment.

4. DISCUSSION

The transition from pediatric to adult care in individuals with Dravet Syndrome represents a critical phase in the

care pathway, revealing significant challenges for all parties involved, including care centers. Transition programs currently exhibit considerable variability, leading to a lack of standardized care that aligns with the needs of these patients and their caregivers.

The prevailing scenario is characterized by prolonged persistence in pediatric centers well beyond the age of adulthood. Many families and specialists opt to keep patients in pediatric care due to a perceived higher quality of care and fear of inadequate care in adult centers.

"The child neuropsychiatrist examines the child from every perspective, while the adult approach is purely pharmacological" (Federica, caregiver of a 17 years old DS patient). It is challenging because the adult neuropsychiatrist does not understand the disease and struggles to manage it. There isn't a proper transition, so the child neuropsychiatrist goes to the adult specialist to explain the situation. They don't give you advice on how to proceed; for them, it is enough to just provide the name of the doctor. They let you go, and you are on your own " (Emma, caregiver of a 21 yrs old DS patient)

Consequently, patients are often referred to adult neurologists only when their treatment needs become too complex for pediatric centers to manage, thus delaying the necessary transition and creating continuity issues in care. A careful assessment of patient needs, and adequate support are essential to facilitate a timely transition. Avoiding hasty procedures that fail to establish a solid foundation for quality care in adulthood is crucial, as evidenced by the concerning 19% abandonment rate in adult centers within the first year of care.

One of the main findings of this study is the significant impact that delays in therapeutic stabilization have on the overall clinical-care pathway for "Dravet families". This situation can result in diagnostic delays, especially for atypical phenotypes, and prolonged clinical and therapeutic instability, which affects transition planning and long-term patient management.

The study also highlights the consequences of the syndrome on the quality of life of patients' families. As highlighted in previous studies on the subject, caregivers of individuals with DS report higher social burden scores, with their physical and emotional health, as well as their social relationships, being negatively affected (Salom et al., 2023; Lagae at al., 2019; Nabbout et al., 2019). These families often face social isolation, job loss and, in some cases, separation or divorce due to the challenges of caregiving.

"I shut myself in the house with my daughter, but I didn't know how to navigate the situation or where to turn. I lost friends and family". (Arminda, caregiver of a 18 years old DS patient).

"The impact was difficult: schools, parents and teachers have always created a thousand problems for me. I was alone, and Giulia's father had left; today, he doesn't look for her, and she doesn't want to see or hear from him. Then she also felt abandoned by her brother when he started his own family. […] Psychological support could have helped us deal with the problem differently" (Lucia, caregiver of a 31 years old DS patient).

Recognizing the crucial role of caregivers, including siblings, in patient care is essential, and providing them with adequate psychological and social support to cope with the disease's associated difficulties is imperative (Nolan et al., 2006).

Moreover, as with many others rare diseases, the issue of the patient's therapeutic and care future beyond their caregivers (the "after us" situation) urgently arises in the case of Dravet Syndrome. Specialists currently demonstrate limited awareness of this issue. According to many respondents, the patient's future is often conjectured based on scenarios common to other rare and chronic diseases, lacking precise knowledge of the challenges adult patients face without family support. This is partly due to the limited number of patients over the age of 35 in referral centers, reducing opportunities for physicians to learn from the experiences of patients without caregivers and making it challenging to guide other families along defined care pathways. Conversely, families are acutely aware of the urgent concern regarding the patient's future, with most paths taken relying on the individual or collective initiatives of caregivers, who work towards increasing autonomy and, sometimes, the possibility of entering the workforce.

Long-term care planning is crucial for ensuring the ongoing well-being of these patients, especially those with serious cognitive impairments. Where centralized assistance is lacking in many areas, it is precisely the local network and associations that can provide real support to families and patients. This requires detailed coordination between healthcare professionals, caregivers, and local realities to create a sustainable care plan, with community support networks playing a vital role in this process, offering resources such as respite care, support groups, and social services that can alleviate the burden on family caregivers, or help them envision a future for their loved ones.

To address these challenges and enrich the discussion, it is essential to explore potential solutions and recommendations. First, implementing standardized and well-defined transition pathways across all centers is crucial. This includes joint consultations with pediatric and adult specialists and a thorough handover process to ensure continuity of care, as well as early transition planning, which should begin by age 14-16 to gradually prepare families and patients for the shift.

Additionally, supporting caregivers is equally important: educational programs can enhance their understanding and management of DS, while psychological support programs and support groups can alleviate their social and emotional burden. Also, recognizing the unique challenges faced by siblings as well and offering them support services can also mitigate long-term negative impacts.

CONCLUSIONS

The overall experience of individuals involved in the management of Dravet Syndrome, including physicians,

patients, caregivers and siblings, requires further commitment to investigate the current fragmented nature of transition strategies. This understanding is necessary to determine initiatives that can provide greater structure, consistency, and continuity to the overall care pathway, particularly during the delicate transition from pediatric to adult care.

In conclusion, the journey of patients with Dravet Syndrome, particularly the transition from pediatric to adult care, represents a complex challenge that requires a multidisciplinary approach and the improvement of existing models. Involving families and caregivers in the decision-making process and providing them with the necessary support to address the challenges associated with the disease is crucial. Furthermore, it is essential to enhance the structure of the overall care pathway and the transition phase to improve the quality of care and life for families dealing with Dravet Syndrome.

In addition to this, future efforts should prioritize the development of specialized training programs for both pediatric and adult care providers, focusing on the unique needs of DS patients, aimed at improving the overall management, not only by focusing on clinical aspects, but also on the social and relational context in which patient and their condition are situated, enhancing skills such as communication and empathy. Also collaboration between centers, including sharing best practices and outcomes, will be vital to creating a more cohesive and standardized approach to patient care.

Conflict of Interest

The authors declare that there is no conflict of interest.

REFERENCES

1. Andrade DM, Berg AT, Hood V, Knupp KG, Koh S, Laux L, Meskis MA, Miller I, Perry MS, Scheffer IE, Sullivan J, Villas N, Wirrell E (2021). Dravet syndrome: A quick transition guide for the adult neurologist. Epilepsy Res. 177:106743.

2. Brunklaus A, Brünger T, Feng T, Fons C, Lehikoinen A, Panagiotakaki E, Vintan MA, Symonds J, Andrew J, Arzimanoglou A, Delima S, Gallois J, Hanrahan D, Lesca G, MacLeod S, Marjanovic D, McTague A, Nuñez-Enamorado N, Perez-Palma E, Scott Perry M, Pysden K, Russ-Hall SJ, Scheffer IE, Sully K, Syrbe S, Vaher U, Velayutham M, Vogt J, Weiss S, Wirrell E, Zuberi SM, Lal D, Møller RS, Mantegazza M, Cestèle S (2022). The gain of function SCN1A disorder spectrum: novel epilepsy phenotypes and therapeutic implications. Brain. 21;145(11):3816-3831.

3. Connolly MB (2016). Dravet Syndrome: Diagnosis and Long-Term Course. Can J Neurol Sci. 43 Suppl 3:S3-8.

4. Cross JH, Caraballo RH, Nabbout R, Vigevano F, Guerrini R, Lagae L (2019). Dravet syndrome: Treatment options and management of prolonged seizures. Epilepsia. 60 Suppl 3:S39-S48.

5. Dalla Bernardina B, Colamaria V, Capovilla G, Bondavalli S (1983). Nosological classification of epilepsies in the first three years of life. Prog Clin Biol Res. 124:165–183

6. Dravet C, Oguni H (2013). Dravet syndrome (severe myoclonic epilepsy in infancy). Handb Clin Neurol. 111:627-33.

7. Dravet C. (2011). Dravet syndrome history. Dev Med Child Neurol. 53 Suppl 2:1-6.

8. Fukuma G, Oguni H, Shirasaka Y, Watanabe K, Miyajima T, Yasumoto S, Ohfu M, Inoue T, Watanachai A, Kira R, Matsuo M, Muranaka H, Sofue F, Zhang B, Kaneko S, Mitsudome A, Hirose S (2004). Mutations of neuronal voltage-gated Na+ channel alpha 1 subunit gene SCN1A in core severe myoclonic epilepsy in infancy (SMEI) and in borderline SMEI (SMEB). Epilepsia. 45(2):140-8.

9. Genton P, Velizarova R, Dravet C (2011). Dravet syndrome: the long-term outcome. Epilepsia. 52 Suppl 2:44-9.

10. He Z, Li Y, Zhao X, Li B (2022). Dravet syndrome: Advances in etiology, clinical presentation, and treatment. Epilepsy Res. 188:107041.

11. Lagae L, Sullivan J, Knupp K, Laux L, Polster T, Nikanorova M, Devinsky O, Cross JH, Guerrini R, Talwar D, Miller I, Farfel G, Galer BS, Gammaitoni A, Mistry A, Morrison G, Lock M, Agarwal A, Lai WW, Ceulemans B; FAiRE DS Study Group. (2019). Fenfluramine hydrochloride for the treatment of seizures in Dravet syndrome: a randomized, double-blind, placebo-controlled trial. Lancet. 21;394(10216):2243-2254.

12. Lagae L (2021). Dravet syndrome. Curr Opin Neurol. 1;34(2):213-218.

13. Lagae L, Irwin J, Gibson E, Battersby A. (2019). Caregiver impact and health service use in high and low severity Dravet syndrome: a multinational cohort study. Seizure. 65:72–79.

14. Laux LC, Bebin EM, Checketts D, Chez M, Flamini R, Marsh ED, Miller I, Nichol K, Park Y, Segal E, Seltzer L, Szaflarski JP, Thiele EA, Weinstock A (2019). CBD EAP study group. Long-term safety and efficacy of cannabidiol in children and adults with treatment resistant Lennox-Gastaut syndrome or Dravet syndrome: Expanded access program results. Epilepsy Res.154:13-20.

15. Li W, Schneider AL, Scheffer IE (2021). Defining Dravet syndrome: An essential pre-requisite for precision medicine trials. Epilepsia. 62(9):2205-2217.

16. Mei D, Cetica V, Marini C, Guerrini R (2019). Dravet syndrome as part of the clinical and genetic spectrum of sodium channel epilepsies and encephalopathies. Epilepsia. 60 Suppl 3:S2-S7.

17. Millichap JJ, Koh S, Laux LC, Nordli DR Jr (2009). Child Neurology: Dravet syndrome: when to suspect the diagnosis. Neurology. 29;73(13):e59-62.

18. Nabbout R, Gennaro E, Dalla Bernardina B, Dulac O, Madia F, Bertini E, Capovilla G, Chiron C, Cristofori G,

Elia M, Fontana E, Gaggero R, Granata T, Guerrini R, Loi M, La Selva L, Lispi ML, Matricardi A, Romeo A, Tzolas V, Valseriati D, Veggiotti P, Vigevano F, Vallée L, Dagna Bricarelli F, Bianchi A, Zara F (2003). Spectrum of SCN1A mutations in severe myoclonic epilepsy of infancy. Neurology. 24;60(12):1961-7.

19. Nabbout R, Auvin S, Chiron C, Thiele E, Cross H, Scheffer IE, Schneider AL, Guerrini R, Williamson N, Zogenix and Adelphi Values study group. (2019). Perception of impact of Dravet syndrome on children and caregivers in multiple countries: looking beyond seizures. Developmental Medicine and Child Neurology. 61(10):1229–1236

20. Nolan K, Camfield CS, Camfield PR. (2006) Coping with a child with Dravet syndrome: insights from families. Journal of Child Neurology. 23(6):690–694.

21. Salom R, Aras LM, Piñero J, Duñabeitia JA. (2023). The psychosocial impact of caring for children with Dravet Syndrome. Epilepsy Behav Rep. 24:100619.

22. Scheffer IE. (2012). Diagnosis and long-term course of Dravet syndrome. Eur J Paediatr Neurol. 16 Suppl 1: S5-8.

23. Seligman MEP, Csikszentmihalyi M (2000). Positive psychology: An introduction. American Psychologist. *55*(1), 5–14.

24. Wirrell EC, Hood V, Knupp KG, Meskis MA, Nabbout R, Scheffer IE, Wilmshurst J, Sullivan J (2022). International consensus on diagnosis and management of Dravet syndrome. Epilepsia. 63(7):1761-1777.