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Research Paper

Current challenges in focal epilepsy treatment: An Italian Delphi consensus

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ABSTRACT

Background: Epilepsy, a globally prevalent neurological condition, presents distinct challenges in management, particularly for focal-onset types. This study aimed at addressing the current challenges and perspectives in focal epilepsy management, with focus on the Italian reality.

Methods: Using the Delphi methodology, this research collected and analyzed the level of consensus of a panel of Italian epilepsy experts on key aspects of focal epilepsy care. Areas of focus included patient flow, treatment pathways, controlled versus uncontrolled epilepsy, follow-up protocols, and the relevance of patient-reported outcomes (PROs). This method allowed for a comprehensive assessment of consensus and divergences in clinical opinions and practices.

Results: The study achieved consensus on 23 out of 26 statements, with three items failing to reach a consensus. There was strong agreement on the importance of timely intervention, individualized treatment plans, regular follow-ups at Epilepsy Centers, and the role of PROs in clinical practice. In cases of uncontrolled focal epilepsy, there was a clear inclination to pursue alternative treatment options following the failure of two previous therapies. Divergent views were evident on the inclusion of epilepsy surgery in treatment for uncontrolled epilepsy and the routine necessity of EEG evaluations in follow-ups. Other key findings included concerns about the lack of pediatric-specific research limiting current therapeutic options in this patient population, insufficient attention to the transition from pediatric to adult care, and need for improved communication. The results highlighted the complexities in managing epilepsy, with broad consensus on patient care aspects, yet notable divergences in specific treatment and management approaches.

Conclusion: The study offered valuable insights into the current state and complexities of managing focal-onset epilepsy. It highlighted many deficiencies in the therapeutic pathway of focal-onset epilepsy in the Italian reality, while it also underscored the importance of patient-centric care, the necessity of early and appropriate intervention, and individualized treatment approaches. The findings also called for continued research, policy development, and healthcare system improvements to enhance epilepsy management, highlighting the ongoing need for tailored healthcare solutions in this evolving field.

1. Introduction

Epilepsies are complex neurological conditions affecting roughly 70 million people globally [1]. Incidence rates vary based on economic development: 40 to 60 cases per 100,000 population annually in developed regions, and 80 to 100 in less economically developed areas [2,3]. In Europe, epilepsy is estimated to be affecting at least 6 million individuals, among whom about 600,000 in Italy [4–6]. Epilepsy is the predisposition to recurrent unprovoked seizures, often accompanied by neurobiological and cognitive impairment, which may result in psychosocial repercussions [2,7,8]. Epidemiological data align with the understanding that most epilepsy diagnoses occur either in the pediatric

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phase or after the age of 60 [9,10]. The condition's heterogeneity arises from diverse etiological factors and a multifaceted genetic background [11–14]. Focal-onset epilepsies represent the most commonly diagnosed type [1,15].

Diagnosis and treatment are typically more challenging in case of focal epilepsy [16], and the presence of comorbidities often complicates the situation [17–19]. Although published evidence emphasizes the importance of early, differential diagnosis conducted by a specialized epileptologist, misdiagnosis rates are still alarmingly high [20,21]. Treatment choices for focal epilepsy are mostly symptomatic, and aim at achieving a seizure-free status with minimal side effects [22]. With a plethora of antiseizure medications (ASMs) available, it is putatively possible to tailor treatment with the aim to achieve the maximum benefit for specific patient populations [23–25]. Single-agent ASM-based approaches represent the most commonly prescribed therapeutic regimen due to the better efficacy/tolerability profile [26]. However, roughly 30–40 % of patients fail to attain seizure control with monotherapy [27]. Seizure control is a critical benchmark of epilepsy, which can be dichotomized into 'controlled' and 'uncontrolled'. Controlled epilepsy is defined by the complete cessation of seizures as a result of effective treatment. Conversely, uncontrolled epilepsy is characterized by the persistence of seizures despite treatment with one or more ASMs [28]. This distinction is crucial, as patient perceptions of control, often based on comparative seizure frequency reduction, may not align with clinical definitions, where any seizure occurrence, even as infrequent as annually, is considered indicative of uncontrolled epilepsy [29,30]. Drug-resistance phenomena concur to complicate the clinical management of focal epilepsies [31,32]. According to current criteria, drug resistance is defined as the failure of at least two well-tolerated, suitably selected antiepileptic drug regimens administered at the maximum tolerated dose, used either as monotherapies or in combination [28,31]. The concept of pharmacoresistance is constantly evolving in epilepsy research, with some authors proposing multiple definitions as clinical and preclinical evidence brings new insights on the matter [33,34]. Recent studies indicate that non-responsiveness to two specific treatments does not necessarily rule out a positive response to a subsequent therapy, although the likelihood of treatment failure with a newly introduced ASM increases with the number of previous pharmacological trials [33,35,36]. Moreover, pseudoresistance phenomena, originating from wrong diagnosis, inappropriate treatments (wrong drug or wrong dosing) or from insufficient compliance, can also be in play [37]. In this context, preclinical and translational studies may help indicating novel insights on synergism between drugs, or new underlying mechanisms of drug resistance, paving the way for targeted therapeutic strategies [38,39]. For the majority of patients who have not responded to two ASMs due to insufficient efficacy, the likelihood of achieving seizure freedom with additional pharmacological interventions has been demonstrated to be minimal [31,40]. In carefully selected patients, surgery may represent a viable option, especially if carried out early after diagnosis. The benefits may include increased chances of achieving seizure freedom while mitigating long-term medication risks [41–45].

Given the complexity of the scenario and its constant evolution, current guidelines highlight the importance of performing diagnoses at comprehensive Epilepsy Centers, where individuals can also be referred whenever possible for diagnostic re-evaluation and targeted management. The WHO has recently published a model for improving the care pathway, aiming to enhance treatment accessibility for individuals with neurological disorders, improving their Quality of Life (QoL) and that of their caregivers and families. Emphasizing brain health throughout one's lifespan, this approach integrates early diagnosis, tailored interventions, and holistic support to ensure enriched health outcomes and well-being [46]. It is becoming paramount to adopt a standardized care pathway for epilepsy, ensuring all patients receive the best possible care and adequate follow-up. Tailored strategies, both outside and within hospital settings, are essential to grant an acceptable QoL to patients and their caregivers. In this regard, specialized Centers can play a significant role in enhancing outcomes. Additionally, Patient-Reported Outcomes (PROs) have been shown as valuable tools in healthcare, providing direct insights from patients about their health and treatment experiences [47,48]. By capturing data on symptom severity, treatment side effects, and QoL, PROs help in designing more effective health policies and treatment strategies. This patient-centered information is key to tailoring healthcare services and interventions to better meet the specific needs of those living with focal epilepsy, aiming at reducing the psychosocial barriers such as stigma while indirectly lowering the associated costs [49,50].

In light of the described challenges and perspectives, the present study was designed to gauge consensus among Italian epileptologists on various domains concerning the clinical management of focal epilepsy. The ultimate aim was to identify existing gaps and explore future approaches for treating this condition.

2. Methods

2.1. Consensus determination through Delphi methodology

The level of consensus on a predetermined series of topics was measured by adopting the Delphi methodology [51,52]. For the purpose of the present research, multiple rounds of voting were allowed. Participants were able to express their agreement or dissent levels with regard to statements using a traditional 5-point Likert scale, where 1 signified "strongly disagree," 2 represented "disagree," 3 stood for "neutrality," 4 indicated "agree," and 5 meant "strongly agree." A consensus threshold was set at 75 %. Agreement was achieved when the combined scores of items 4 and 5 exceeded 75 %. Conversely, disagreement was established when the combined scores of items 1 and 2 surpassed 75 %. If the combined responses for either disagreement (items 1 and 2) or agreement (items 4 and 5) fell below 75 %, no consensus was determined.

2.2. Statements preparation

An Italian panel of experts, acknowledged in this paper as the Authors and recognized as the Steering Committee developed the statements on the basis of a series of unmet needs, particularly concerning the Italian scenario. The selection process for the Steering Committee was based on previous contributions to the field related to the study's subject matter and conducted systematically to ensure diversity, expertise, and representation within all relevant fields of the study. The Steering Committee comprised experts in the diagnosis and treatment of epilepsy and an expert in health economics to ensure diverse representation across disciplines and professional backgrounds, capturing a comprehensive spectrum of viewpoints and expertise. The formulation of the statements was discussed over a separate meeting and was performed according to a comprehensive literature review, coupled with insights extrapolated from challenges observed in clinical practice. Ultimately, a total of 26 statements distributed across five primary areas of interest have been identified (Table 1): patient flow (5 statements), treatment pathway (4 statements), controlled/uncontrolled epilepsy (5 statements), follow-up (4 statements), and PROs (8 statements). The statements, formulated in Italian, received approval after undergoing a validation process involving four external validators.

2.3. In-person expert panel

The statements were subsequently presented to an Expert Panel (EP) during an in-person event held in Rome on September 28–29, 2023. In order to ensure a meticulous selection of the Expert Panel, invitations were extended to the majority (n = 83) of Epilepsy Centers in Italy, of which 53 were accredited by the Italian League Against Epilepsy (LICE). The aim was to include representatives across Italy to account for potential regional differences arising from geographical heterogeneity.

Table 1
The statements discussed over the Delphi meeting.

Topic	Statement	
1. Patient Flow	1.1	The care of a person with the first epileptic seizure is always carried out by an epileptologist.
	1.2	The time span between the onset of focal epilepsy and its treatment by an Epilepsy Center affects the quality of life.
	1.3	The National Health Service (SSN) facilities have diagnostic-therapeutic algorithms for status epilepticus.
	1.4	Every Region requires the implementation of a PDTA (Diagnostic Therapeutic Assistance Pathway) for epilepsy.
	1.5	Awareness of the Centers for the diagnosis and treatment of epilepsy available nationwide is sufficient.
2. Treatment Pathway	2.1	The transition process from a pediatric facility to an adult facility is smooth.
	2.2	An individualized treatment path is necessary for each person affected by focal epilepsy.
	2.3	The National Health Service is able to promptly and adequately address the epileptic state.
	2.4	A drug proven effective for focal epilepsy in adults can also be used in children and adolescents from the age of 4.
3. Controlled Vs Uncontrolled Epilepsy	3.1	A "well-controlled" focal epilepsy condition is determined by clinical parameters and quality of life.
	3.2	Achieving seizure-free status is the primary goal in the treatment of focal epilepsy.
	3.3	The care path for "uncontrolled" focal epilepsy must always include an evaluation for epilepsy surgery.
	3.4	For individuals with drug-resistant focal epilepsy who are not candidates for surgery, pursuing additional drug treatments is not recommended.
	3.5	The side effects of drug treatments hold greater significance than the persistence of epileptic seizures.
4. Follow-up	4.1	The length of waiting lists does not hinder appropriate clinical follow-up.
	4.2	Regular follow-ups at an Epilepsy Center are crucial for optimal management of focal epilepsy.
	4.3	In focal epilepsies, it is advisable to not discontinue drug therapy even if the adult patient has achieved sustained seizure freedom.
	4.4	In the follow-up of a patient with focal epilepsy, an instrumental evaluation using EEG is always necessary.
5. Patient-Reported Outcomes (PROs)	5.1	Accurate measurement of patient-reported outcomes must necessarily complement the evaluation of efficacy and safety in the approval process for new drugs.
	5.2	Patient-reported outcomes are used in routine clinical practice.
	5.3	The primary barrier to collecting patient-reported outcomes in clinical practice is the lack of time and resources.
	5.4	The systematic use of patient-reported outcomes in clinical practice positively impacts the care pathway organization for individuals with focal epilepsy.
	5.5	The epileptologist is not always adequately prepared to handle doctor-patient communication.
	5.6	Evaluating patient-reported outcomes in focal epilepsy aids in the comparative analysis of different anti-seizure medications.
	5.7	Patient-reported outcomes from patients with focal epilepsy are essential in assessing the "indirect" effects of the condition, stemming from stigma and objective psychosocial limitations.
	5.8	Evaluating patient-reported outcomes allows for a more accurate estimation of the direct and indirect costs of the condition, taking into account the involvement of family members and caregivers.

Ultimately, 52 epileptologists, including 17 from Centers dedicated to childhood, convened to constitute the EP. It is noteworthy that a significant portion of EP members (40 out of 52) originated from LICE-associated Centers; the distribution by geographical region across the Country was as follows: 44.68 % from the North, 19.15 % from the Center, and 36.17 % from the South and Islands.

The members of the EP were required to express their opinions, anonymously and independently, on the statements proposed by the Delphi questionnaire. In case of a lack of consensus, participants were granted the opportunity to re-evaluate their positions by examining an aggregated compilation of all expert perspectives, aiming to possibly achieve convergence of opinions though pertinent discussion.

3. Results

Consensus was achieved for 23 out of the 26 statements. Three statements (2.4, 3.3, 3.5) did not attain consensus, indicating a need for additional discussion. Of the non-consensus items, two out of three were pertaining controlled/uncontrolled epilepsy (3.3, 3.5).

3.1. Patient flow

The initial topic discussed was patient flow, where consensus was reached with regards to all statements (Fig. 1). For statement 1.1, which reported that care for a first-time epileptic seizure is always provided by an epileptologist, there was a 90 % disagreement rate. Then, 90 % of the EP recognized the significant impact of the time between the onset of focal epilepsy and access to care at an Epilepsy Center (statement 1.2), with 4 % disagreeing. Regarding the National Health System (Sistema Sanitario Nazionale, SSN) facilities, 76 % of the EP disagreed about the availability of diagnostic and therapeutic algorithms for status epilepticus (statement 1.3). The panel concurred that every Region should implement a Diagnostic Therapeutic Pathway (Percorso Diagnostico-Terapeutico Assistenziale, PDTA) for epilepsy, with an 86 % consensus (statement 1.4). Lastly, after two total voting rounds, 79.6 % of the EP disagreed about the existence of sufficient awareness of nationwide Centers for epilepsy diagnosis and treatment (statement 1.5).

3.2. Treatment pathway

Consensus was achieved for 3 out of 4 statements (Fig. 2). Concerning the transition from pediatric to adult facilities, 94 % of the EP disagreed (statement 2.1). The panel agreed that an individualized treatment plan is essential for each person with focal epilepsy, with 86 % positive consensus (statement 2.2). The experts disagreed on SSN's capability to promptly and effectively address the status epilepticus, reaching 80 % negative consensus (statement 2.3). For statement 2.4, which discussed the use of a drug in children and adolescents from the age of 4 after being proven effective for focal epilepsy in adults, consensus was not reached: 43.8 % of the panelists agreed, 27.1 % remained neutral, and 29.2 % disagreed. Notably, this statement required three voting rounds.

3.3. Controlled/uncontrolled epilepsy

Consensus was reached for 3 out of 5 items (Fig. 3). The EP strongly agreed that both clinical parameters and QoL are factors in determining a well-controlled focal epilepsy condition, achieving a 91.9 % positive consensus (statement 3.1). Then, 77.1 % of the experts agreed that achieving a seizure-free status is the primary goal in treating focal epilepsy (statement 3.2). No consensus emerged for the inclusion of epilepsy surgery in the treatment pathway of uncontrolled epilepsy (statement 3.3), as 51 % agreed on its necessity, 44.9 % disagreed, and 4.1 % were neutral, after two voting sessions. For statement 3.4, a full negative consensus was recorded, with 100 % of the panelists opposing the idea that pursuing additional drug treatments is not recommended

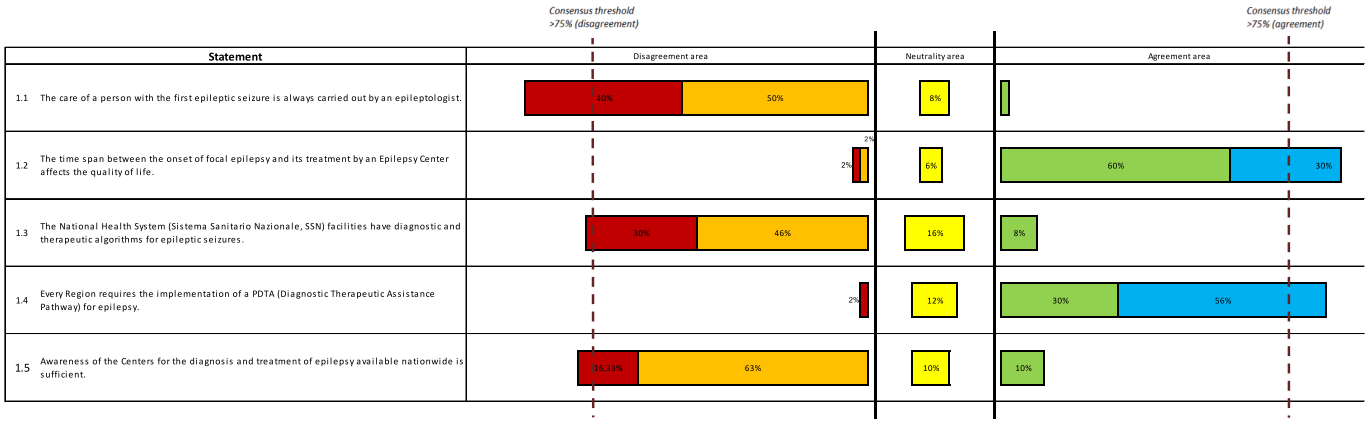

Fig. 1. Agreement or disagreement rate (%) by Likert scale score of the expert panel on each statement of the Delphi questionnaire for Topic # 1: "Patient Flow".

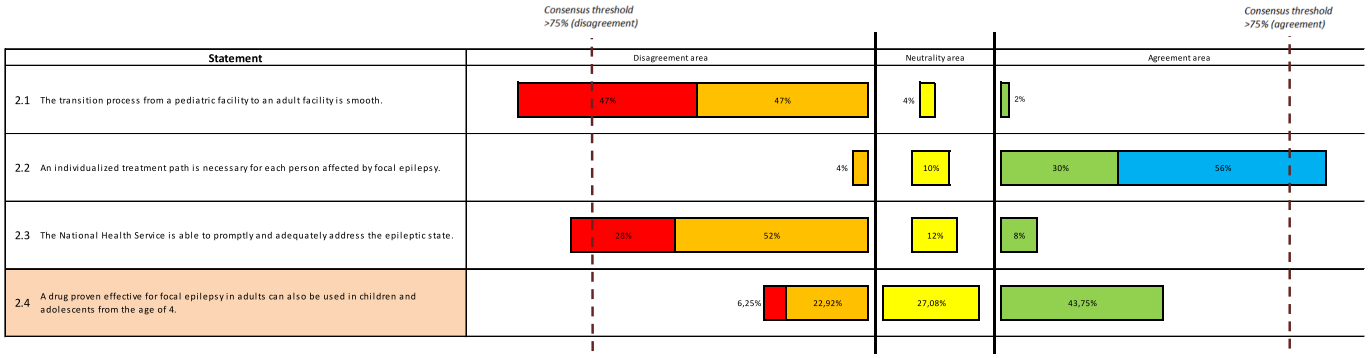

Fig. 2. Agreement or disagreement rate (%) by Likert scale score of the expert panel on each statement of the Delphi questionnaire for Topic # 2: "Treatment Pathway".

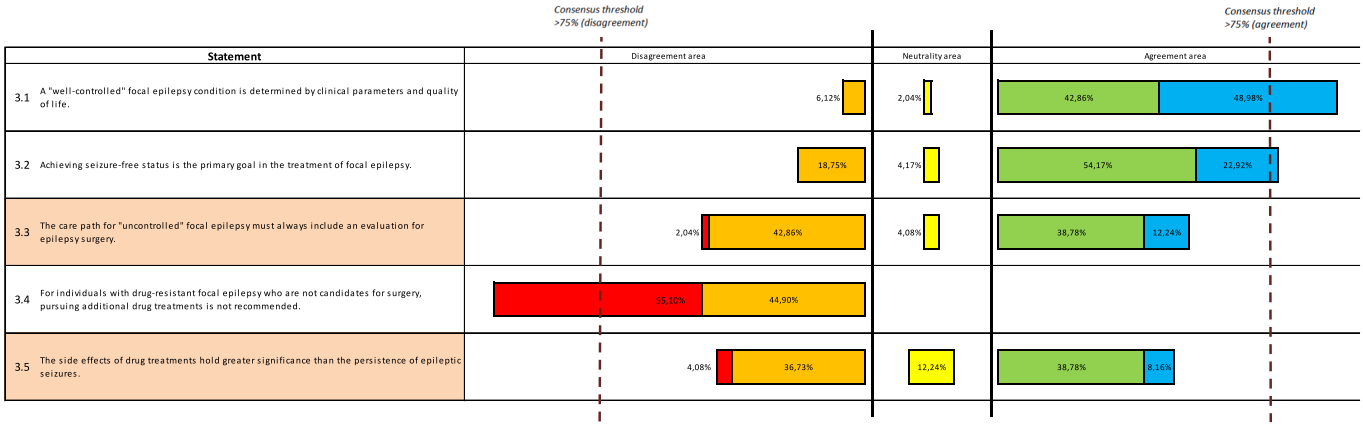

Fig. 3. Agreement or disagreement rate (%) by Likert scale score of the expert panel on each statement of the Delphi questionnaire for Topic # 3: "Controlled Vs Uncontrolled Epilepsy".

for individuals with drug-resistant focal epilepsy who are not surgery candidates. For statement 3.5, which discussed the importance of treatment tolerability versus the persistence of seizures, no consensus was reached despite 3 voting rounds, with 47.0 % of the panelists believing that the side effects of drug treatments are more significant than the persistence of seizures, 40.8 % disagreeing, and 12.2 % remaining neutral.

3.4. Follow-up

This topic consisted of 4 statements, and consensus was achieved for all (Fig. 4). The EP strongly disagreed with statement 4.1, which claimed that the length of waiting lists does not impede appropriate clinical follow-up, documenting an 83.7 % negative consensus. Moreover, 98 % of participants recognized the importance of regular follow-ups at an Epilepsy Center for optimal management of focal epilepsy, with only 2 % remaining neutral (statement 4.2). When discussing the possible discontinuation of drug therapy even if the adult patient has achieved sustained seizure freedom, 82 % of the panel disagreed, achieving a negative consensus after 2 total voting rounds (statement 4.3). For the final statement, which explored the role of the electroencephalogram (EEG) in patient follow-up, 87.5 % of panelists disagreed that an EEG

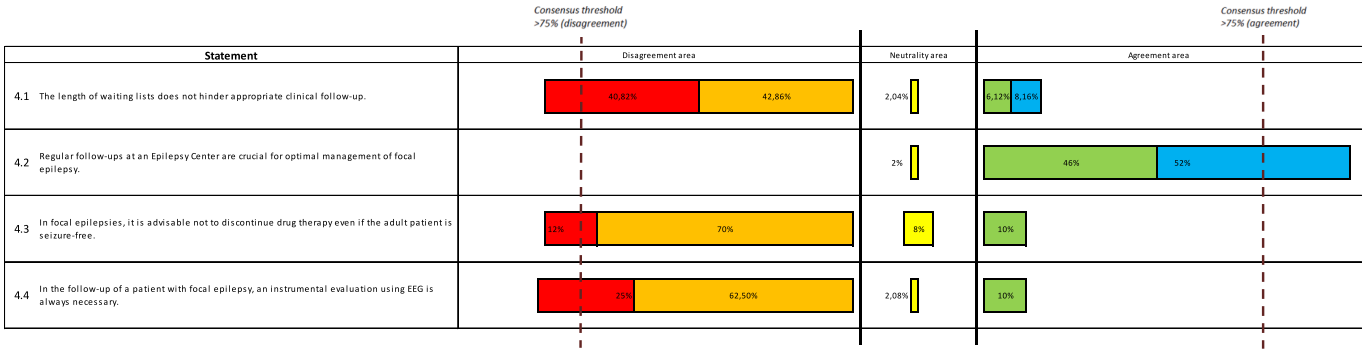

Fig. 4. Agreement or disagreement rate (%) by Likert scale score of the expert panel on each statement of the Delphi questionnaire for Topic # 4: "Follow-up".

evaluation is always necessary after 2 voting rounds (statement 4.4).

3.5. Patient-reported outcomes

The EP agreed, with an 82.2 % consensus, that accurate measurement of PROs is essential to complement evaluations of efficacy and safety in the drug approval process (statement 5.1) (Fig. 5). The experts also agreed that PROs are utilized in routine clinical practice, achieving a 77.8 % positive consensus (statement 5.2). The lack of time and resources represented the primary barrier to collecting PROs in clinical practice for 84.5 % of the experts (statement 5.3). Additionally, 91.1 % of the EP concurred on the positive impact of systematically using PROs in the care pathway organization for individuals with focal epilepsy (statement 5.4). After 3 total voting rounds, 76.1 % agreed that epileptologists are not always adequately prepared for doctor-patient communication (statement 5.5). The panel also recognized the value of evaluating PROs in focal epilepsy for comparing different ASMs, with an 89.4 % positive consensus (statement 5.6). An 88.6 % positive consensus was achieved regarding the importance of PROs in assessing the indirect effects of focal epilepsy, such as stigma and objective psychosocial limitations (statement 5.7). Lastly, 97.8 % concurred that PROs help to accurately estimate the direct and indirect costs of epilepsy, including family and caregiver involvement (statement 5.8).

4. Discussion

The results of this study provided a comprehensive overview of the consensus and divergences among Italian epileptologists regarding various aspects of focal epilepsy care and management.

Regarding Patient Flow, the high disagreement rate (90 %) among panelists on statement 1.1, which posits that care for a first-time seizure is always provided by an epileptologist, suggested that initial care may often be in the hands of general practitioners, emergency room physicians, or other healthcare professionals, rather than epilepsy specialists. A significant emphasis is placed on the timeliness of intervention, as evidenced by the 90 % positive consensus on the detrimental impact of the time elapsed between the onset of focal epilepsy and treatment initiation (statement 1.2). Furthermore, the panelists expressed concern about the lack of PDTAs, with a 76 % disagreement with the statement regarding the availability of diagnostic and therapeutic algorithms for status epilepticus in SSN facilities (statement 1.3). This result points to a perceived gap in standardized care protocols, leading to discussions about the need for more robust and accessible guidelines in epilepsy management within the SSN. Additionally, there was a strong consensus (86 %) on the necessity of every region to implement a PDTA for epilepsy (statement 1.4), suggesting a belief in the importance of standardized care pathways. In Italy, so far only four regions have implemented PDTAs for epilepsy, highlighting the challenges in

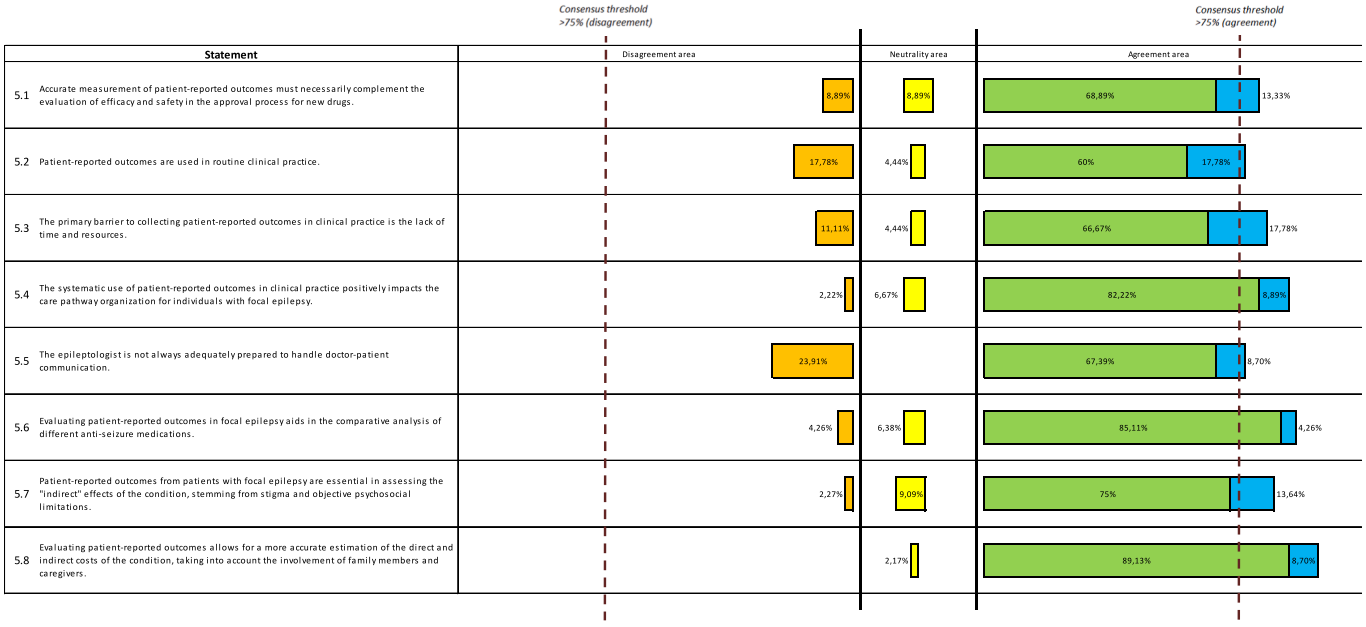

Fig. 5. Agreement or disagreement rate (%) by Likert scale score of the expert panel on each statement of the Delphi questionnaire for Topic # 5: "Patient-Reported Outcomes (PROs)".

implementing accreditation requirements and the need for institutional efforts [53]. In this sense, Epilepsy Centers play a crucial role in providing accurate diagnoses and tailored treatment plans. A disagreement rate (79.6 %) with the statement about the sufficiency of awareness of nationwide Centers for epilepsy diagnosis and treatment (statement 1.5) indicated a concern about the general awareness and accessibility of specialized epilepsy care, highlighting a significant gap in public knowledge. This issue gains particular significance given the uneven distribution of Epilepsy Centers in Italy and the difficulties in meeting PDTA requirements [54,55]. This finding suggests a need for institutional efforts to improve the availability of dedicated Centers, as well as educational campaigns and information dissemination strategies to increase the overall awareness. In turn, enhanced awareness can lead to more individuals seeking specialized care, which is crucial considering the psychosocial repercussions of epilepsy [56,57]. Public education can also play a role in reducing the stigma associated with epilepsy and correcting misconceptions about the condition [50,58].

Considering treatment pathway, the panel strongly agreed (86 %) on the importance of individualized treatment plans (statement 2.2). This result highlighted the need for personalized care strategies that consider the unique circumstances and needs of each patient and caregiver, including factors like age, sex, individual preferences, comorbidities, and lifestyle. In light of the heterogeneous etiological factors and genetic predispositions inherent in epilepsy, a "monolithic" therapeutic approach is inappropriate [59]. The individualization of treatment regimens according to specific patient needs can augment therapeutic efficacy while concurrently mitigating the incidence of side effects [38,60–62]. The almost full negative consensus (94 %) on the challenges in transitioning from pediatric to adult epilepsy care (statement 2.1) highlighted a critical gap in the continuum of care. This transition extends beyond mere logistical changes, necessitating a comprehensive adaptation of treatment plans and care strategies to align with the evolving needs of patients as they age [63–66]. A seamless integration of care approaches is therefore essential, requiring close collaboration between pediatricians and neurologists [67].

The lack of consensus on the appropriateness of using in children and adolescents as young as 4 years old those ASMs that have been proven effective in treating focal epilepsy in adults (statement 2.4), highlighted the complexities involved in translating adult epilepsy treatment protocols to younger demographics. Of note, the high rate of neutrality (27.1 %) documented with this statement further corroborated the high level of uncertainty on this topic. Epilepsy manifests differently across various age groups, and the pharmacokinetics and safety profiles of drugs can vary significantly between adults and children [68]. While existing studies suggest that the efficacy of many ASMs is generally consistent across adult and pediatric populations, the safety and pharmacokinetic adaptations for children as well as the potential long-term effects require careful consideration [69]. In addition, although pragmatic trials like the SANAD 2 study provided robust evidence for first- and second-line therapies for adults and children, newer ASMs were not included and only indirect comparative evidence exists [70,71]. Pediatric epileptologists are often reluctant to use adult-tested drugs in children, concerned about limited evidence and potential legal repercussions due to the reliance on extrapolated efficacy data [72,73].

In conditions like focal epilepsy, the significance of QoL is primarily correlated with achieving the seizure-free status, although many other factors are in play [74]. In the context of controlled/uncontrolled epilepsy, the strong positive consensus (91.9 %) documented with statement 3.1, which reported that both clinical parameters and QoL contribute to a "well-controlled" focal epilepsy condition, emphasized the importance of considering not just the clinical aspects, such as seizure frequency and intensity, but also the patient's mental health, social functioning, and overall well-being. Considering the complexity of epilepsy treatment, this result highlighted the need for strategies that address both the physical manifestations of the disorder and its broader implications on an individual's life. The agreement (77.1 %) about the seizure-free status as the primary goal in treating focal epilepsy (statement 3.2) reflects a common objective in focal epilepsy care. At the same time, the not negligible rates of disagreement (18.8 %) and neutrality (4.2 %) indicated that for some experts, the goal of achieving complete seizure freedom might be balanced with other considerations, such as treatment side effects or patient preferences. In line with available literature, while most clinicians seemed to prioritize a broader range of QoL factors, including treatment tolerability, patients tended to emphasize the importance of complete seizure control, even if at the expense of the disease burden [17,53].

The full negative consensus (100 %) achieved with statement 3.4, which opposed the idea of pursuing additional drug treatments for individuals with drug-resistant focal epilepsy who are not surgery candidates, underscored a commitment to exploring all potential treatment options. This perspective acknowledges that even in instances of drug-resistant epilepsy, there may be effective combinations of existing medications or new pharmaceuticals that could offer symptomatic relief [75–77]. The lack of consensus on statement 3.5, which discussed the importance of treatment tolerability versus the persistence of epileptic seizures, with 47 % viewing side effects as more significant and 40.8 % disagreeing, further corroborated the dilemma faced by both patients and clinicians in managing a chronic condition like focal epilepsy, where long-term treatment can raise significant tolerability issues [53]. Therapeutic possibilities may be represented by rational polytherapy, aiming at combining multiple medications to possibly exploit a synergistic effect allowing for reduced dosage, or overcoming drug resistance by elucidating and targeting novel molecular mechanisms [26,29,30,78–82]. Other therapeutic approaches for drug resistant focal epilepsy include surgery and neuromodulation [83].

The divided opinions on the inclusion of epilepsy surgery in the treatment pathway for "uncontrolled" focal epilepsy (statement 3.3), with 51 % agreeing and 44.9 % disagreeing, represented a non-consensus area and highlighted a significant debate. This split result reflected differing views on the appropriateness, timing, and criteria for considering surgery as a treatment option. It underscored the complexity of treatment decisions in cases of uncontrolled epilepsy and the importance of tailored patient evaluation. In selected individuals, epilepsy surgery is backed by substantial evidence as a therapeutic option, with applications for focal-onset forms [42,84,85]. The result aligns with published studies suggesting a potential educational gap regarding the inclusion of surgery, a factor that could significantly contribute to the underutilization of this treatment approach [86–88]. This phenomenon may be attributed to a tendency to overestimate the risks and complications associated with epilepsy surgery; the limited availability of Epilepsy Centers that can perform such procedures also plays a role [87]. Most EP members (83.7 %) disagreed that waiting list lengths do not affect epilepsy care follow-up (statement 4.1). This concern highlighted how long waits can delay patient care and treatment adjustments, stressing the need for better access to epilepsy care and timely follow-up. Additionally, there was near-unanimous agreement (98 %) on the importance of regular follow-up at specialized Epilepsy Centers, highlighting the value of specialized, continuous care in managing epilepsy (statement 4.2).

The panel suggested the need to re-evaluate ongoing medication for adults who have been seizure-free for a significant period (statement 4.3), indicating a willingness to consider medication tapering or discontinuation in some cases. The study results also indicated a notable negative consensus regarding the necessity of routine EEG evaluations in the follow-up of patients, particularly in cases of focal epilepsy (statement 4.4). While EEG is undeniably a crucial tool for the initial diagnosis of epilepsy and is particularly valuable in managing certain types, its utility in the routine follow-up of focal epilepsy appears to be more limited [15,16,89–93].

Over the past 15 years, PROs have been employed as a reliable tool by pharmaceutical companies to report the impact of new drugs on various aspects of a patient's life [47,94,95]. PROs are increasingly

pivotal in informing pharmacoeconomic policies, providing comprehensive insights into a patient's health status, QoL and indirectly aiding in cost evaluation [48]. There was a strong positive consensus on the value of PROs in the drug approval process (statement 5.1) and their routine use in clinical practice (statement 5.2). However, the panel acknowledged challenges in implementing PROs due to logistical constraints, mainly lack of time and resources (statement 5.3), suggesting a need for developing more efficient and feasible methods for incorporating them into routine care. The high positive consensus on systematically using PROs in organizing care pathways (statement 5.4) and evaluating their pharmacoeconomic impact (statement 5.8) reflected the belief that the use of these outcome measures may have broad implications in shaping treatment protocols and policies, as well as in improving the allocation of healthcare costs and resource. The panel also noted the need for improved doctor-patient communication skills (statement 5.5). The acknowledgment of the role of PROs in medication choice, allowing for a comparative analysis of the efficacy and tolerability of different ASMs (statement 5.6), and in assessing the direct and indirect effects of treatments on the disease condition, stigma, and objective psychosocial limitations (statement 5.7) further underscored the need to implement their use in clinical practice. These outcomes may also offer a valid source of information to improve pharmacoeconomic policies [96]. However, for these outcomes to be effectively integrated into policy-making, it is imperative that they are collected and reported in a standardized format, ensuring scientific rigor [97].

5. Conclusion

The results of this study provided valuable insights into the areas of consensus and divergence among experts in epilepsy care. The data underscored the importance of patient-centric care, early intervention, individualized treatment plans, and the need for systemic improvements in patient flow, treatment pathways, and follow-up processes. The areas of divergence, especially in the treatment pathway and management of uncontrolled epilepsy, highlighted the need for further research and discussion to develop evidence-based guidelines and best practices, policy developments, and healthcare system improvements.

6. Ethics approval and consent to participate

This Delphi study primarily aimed to collect opinions from panelists and did not involve the distribution of sensitive information. Therefore, the study did not require ethical approval. All experts who participated were fully informed about the study's objectives, including the possibility of publishing the results in a peer-reviewed journal. Participation was by invitation and entirely voluntary, with no compensation or incentives provided to the participants. The survey results have been maintained in anonymity and are presented collectively in aggregate form.

7. Strengths and limitations of this study

The results of the present study represent the Italian perspective. One strength point of the present study is represented by the inclusion of both adult and pediatric specialists in the EP. However, a few limitations of this study need to be acknowledged. Firstly, the participant pool, consisting of only 53 LICE Centers, was relatively small and not fully representative of the entire Italian landscape. This limitation restricted the generalizability of the study's findings across Italy. Additionally, the scope of the study was confined to the Italian context, which may not reflect the global picture of the subject matter. Another significant limitation was the format of the study. Conducted as an in-person meeting, it inadvertently excluded patient participation. Consequently, only clinical perspectives were obtained, leaving the crucial patient viewpoint unexplored. This gap highlighted an area for potential future research. Furthermore, there was a potential for bias stemming from the fact that all members of the EP were affiliated with LICE Centers. This could have influenced the study's findings, as the perspectives may have been more aligned with those of LICE Centers. The study's focus solely on focal epilepsy was a notable constraint. This narrow scope limited the study's applicability to other forms of epilepsy, which may have different dynamics and require separate considerations. Lastly, one study's limitation includes the inability to conduct sub-analyses on practice location or patient demographics for areas without consensus.

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Author contributions

All Authors conceived the project, discussed the results, and equally contributed to the final manuscript.

CRediT authorship contribution statement

Giancarlo Di Gennaro: Writing – review & editing, Validation, Supervision, Project administration, Methodology, Investigation, Conceptualization. **Simona Lattanzi:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Oriano Mecarelli:** Methodology, Investigation, Conceptualization, Project administration, Supervision, Validation, Writing – review & editing. **Francesco Saverio Mennini:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Investigation, Conceptualization. **Federico Vigevano:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Investigation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: GDG has participated in advisory boards and pharmaceutical industry-sponsored symposia for Angelini Pharma, Arvelle Pharmaceuticals, Eisai, Bial, Livanova, Lusofarmaco, UCB Pharma. SL has received speaker's or consultancy fees from Angelini Pharma, Eisai, GW Pharmaceuticals, Medscape, and UCB Pharma and has served on advisory boards for Angelini Pharma, Arvelle Therapeutics, BIAL, Eisai, GW Pharmaceuticals, and Rapport Therapeutics outside the submitted work. OM has participated in advisory boards and pharmaceutical industry-sponsored symposia for Angelini Pharma, Arvelle, Lusofarmaco, GW/Jazz Pharma, UCB Pharma. FSM has participated in advisory boards and pharmaceutical industry-sponsored symposia for Angelini Pharma, UCB Pharma, AstraZeneca, Gilead, Roche, Sanofi, J&J, Novartis, Edwards, Boston Scientific, Menarini, Takeda, Moderna, GSK, MSD, Merck, Galapagos, Daiichi, Novo Nordisk, Organon, Pfizer, Servier, Beigene, Janssen, Grunenthal, Abbott, Bayer, Astellas, Amarin, AAA, 3 M. FV has participated in advisory boards and pharmaceutical industry-sponsored symposia for Neuraxpharm, Angelini, UCB.

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