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ORIGINAL ARTICLE

Redefining drug-resistant epilepsy: Insights from an Italian Delphi consensus study

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Abstract

Objective: Drug-resistant epilepsy (DRE) affects approximately one-third of people with epilepsy (PwE) despite advancements in anti-seizure medications and presents significant challenges in epilepsy care. This Delphi consensus study aimed to examine key aspects of DRE, including its definition, predictors, and therapeutic strategies.

Methods: A steering committee consisting of clinicians and researchers with expertise in epilepsy was responsible for formulating the statements. A total of 22 statements were developed across four thematic areas. Expert opinions from 99 Italian epileptologists were collected over two structured rounds of voting.

Results: The study highlighted a certain disagreement on the current International League Against Epilepsy definition of DRE, with experts advocating for a definition that better incorporates individual complexities. Strong agreement emerged on the importance of quality of life, psychiatric comorbidities, and multidimensional care in defining therapeutic success.

Significance: The findings of this study underscored the need for a patient-centered perspective of drug resistance and therapeutic success. Enhancing collaboration across specialties is critical for refining clinical practices and addressing unmet needs for PwE.

Plain Language Summary: About one in three people with epilepsy continues to have seizures despite trying several anti-seizure medications. This study asked Italian epilepsy experts for their opinions on how to define and manage drug-resistant epilepsy. The experts agreed that treatment success should not be measured by seizure control alone but also by improvements in quality of life. They also recommended more personalized care that considers each patient's unique condition.

KEYWORDS

Delphi consensus study, drug-resistant epilepsy (DRE), epilepsy management, uncontrolled epilepsy

1 | INTRODUCTION

Drug-resistant epilepsy (DRE) represents one of the most significant challenges in modern epilepsy care. The current definition of DRE, proposed by the International League Against Epilepsy (ILAE) in 2010, identifies the condition as the failure of at least two appropriately chosen and tolerated anti-seizure medications (ASMs) to achieve sustained seizure freedom.[1,2] While this definition has provided a pragmatic framework for identifying patients who may benefit from early presurgical evaluation, it has also been criticized for its binary nature, which may oversimplify the complex and heterogeneous presentation of DRE.[3–5]

The complexity of DRE extends beyond pharmacological resistance.[6,7] A growing body of evidence emphasizes that seizure control alone is insufficient as a therapeutic endpoint, particularly when addressing the broader impact of epilepsy on patient's quality of life.[4] Epilepsy is indeed often associated with a range of comorbidities, including psychiatric disorders such as anxiety and depression, cognitive impairments, as well as the burden of social stigma.[8–10]

Despite advancements in medical therapies, approximately 30% of people with epilepsy (PwE) fail to achieve seizure freedom.[6,11–14] For these individuals, alternative interventions, such as surgical options, and neuromodulation, become critical components of care.[15–20] However, the access to these interventions is often limited or delayed, and their use remains contentious due to variability in clinical outcomes and differences in expert opinions regarding patient selection criteria.[21]

To address these gaps, we conducted a Delphi consensus study involving Italian epilepsy experts. This study aimed to explore key aspects of DRE, including its definition, predictors of treatment response, and management strategies. By leveraging the structured and iterative Delphi methodology, we sought to identify areas of agreement and divergence among clinicians, thereby providing a framework for future clinical and research priorities. The results of this consensus process may offer critical insights into the evolving landscape of epilepsy care and highlight opportunities for advancing both clinical practice and patient outcomes.

Key points

- One-third of people with epilepsy continue to have seizures despite new anti-seizure medications.
- Experts challenge the current definition of drug-resistant epilepsy (DRE).
- Quality of life and psychiatric comorbidities are crucial in defining treatment success.
- Individualized definitions of DRE should reflect etiology, syndrome, and pharmacological history.
- A holistic, multidisciplinary approach is key to improving epilepsy care outcomes.

2 | METHODS

2.1 | Study design

This study utilized the Delphi methodology, an iterative and multistage group facilitation technique particularly useful in healthcare and social decision-making to transform opinions into group consensus.[22,23] The Delphi process included two structured rounds of voting conducted online between August and October 2024. The primary objective was to gather expert opinions on predefined statements and identify areas of agreement or divergence among Italian epilepsy experts (hereafter referred to as "experts" or "participants").

2.2 | Steering committee and statement development

A steering committee consisting of clinicians and researchers with expertise in epilepsy (the authors of the present manuscript) was responsible for formulating the statements. The process involved a comprehensive literature review, identification of unmet needs in clinical practice, and incorporation of perspectives from previous studies on epilepsy. A total of 22 statements were developed across four thematic areas: Redefinition of DRE; Definition of "Therapeutic Success" and "Control" in Epilepsy Care; Predictors of Treatment Response; Therapeutic Approaches, Management Strategies, and Care Objectives (Table 1).

2.3 | Participant selection

Initially, 103 experts were invited to ensure a comprehensive representation of the Italian epileptology landscape across the entire country. Of these, 99 experts participated in the first round, and 90 completed the second round, resulting in response rates of 96.1% and 90.9%, respectively. Participants were recruited to

TABLE 1 The statements presented over the Delphi project.

Area	Statement	
1. Redefinition of drug-resistant epilepsy	1.1	The current definition of drug resistance, introduced by the ILAE in 2010 and based on the failure of two appropriately selected and tolerated anti-seizure medications (ASMs), does not require revision.
	1.2	The definition of drug resistance should encompass individual complexities of epilepsy, including factors such as specific etiology and the number of previous treatments.
	1.3	To predict the likelihood of therapeutic success with a new ASM, it is essential to consider how many medications have been adequately trialed.
	1.4	The number of previously tested ASMs does not necessarily preclude the potential therapeutic success of a new treatment.
2. Definition of "therapeutic success" and "control" in epilepsy care	2.1	Seizure freedom is sufficient to achieve therapeutic success.
	2.2	Therapeutic success is a dichotomous concept, representing an "all or nothing" outcome.
	2.3	A person with epilepsy is considered to have their condition under control if seizures do not interfere with daily activities.
	2.4	The inclusion of comorbidities and their consequences is essential when assessing epilepsy control.
	2.5	Managing epilepsy based on a holistic definition of therapeutic success can improve the quality of life for people with epilepsy.
	2.6	The quality of life of the person with epilepsy should be considered an indicator of therapeutic success.
	2.7	A multidisciplinary assessment, incorporating the perspectives of the patient or caregiver, is necessary to define controlled epilepsy.
3. Predictors of treatment response	3.1	The individual neurobiological characteristics of a person with epilepsy are critical in predicting therapeutic success with ASM therapy.
	3.2	The number of previous pharmacological failures is an indicator of the likelihood of achieving seizure freedom with subsequent ASM therapy.
4. Therapeutic approaches, management strategies, and care objectives	4.1	Epilepsy surgery should not be considered for all individuals with drug-resistant epilepsy.
	4.2	The ketogenic diet represents an effective therapeutic option for reducing seizure frequency in certain cases of drug-resistant epilepsy.
	4.3	Early recognition and treatment of psychiatric comorbidities, such as depression and anxiety, are essential components of epilepsy management.
	4.4	Psychiatric comorbidities play a more significant role than seizures themselves in drug-resistant epilepsy.
	4.5	Including psychological support programs and support groups for patients and families helps reduce stigma and enhance resilience in epilepsy management.
	4.6	The involvement of the family or caregiver is crucial in managing drug-resistant epilepsy.
	4.7	A multidisciplinary community of clinicians, preclinical scientists, and patient representatives should be involved in defining therapeutic success.
	4.8	In pediatric focal structural epilepsies (e.g., focal cortical dysplasia-related epilepsy), the failure of the first appropriately chosen ASM already indicates drug resistance.
	4.9	The definition of control should also account for the potential impact of ASMs on the neuropsychological profile, particularly in pediatric epilepsy.

ensure national representation, with experts from all major regions of Italy. The number of centers participating in the Delphi survey was 76 in the first round and 71 in the second round. The panel of experts included both adult and pediatric epileptologists. In the first round, 48 participants (48.5%) focused on adult epilepsy, 28

(28.3%) on pediatric epilepsy, and 23 (23.2%) managed both adult and pediatric cases. In the second round, the distribution was similar, with 45 participants (50.0%) managing adult cases, 26 (28.9%) focused on pediatric cases, and 19 (21.1%) covering both populations.

Participants were highly experienced, with 41% having between 10 and 20 years of clinical and research expertise, 33% with 21–30 years, and 15% with over 30 years. Their professional roles included clinical directors (34%), department heads (32%), and senior specialists (26%), reflecting a high level of expertise and leadership in epilepsy management. The percentages mentioned refer to the distribution in the first round and did not change significantly in the second one.

2.4 | Voting procedure

The Delphi process employed a two-round voting system to determine the level of consensus. Statements were presented in Italian, and participants rated their agreement using a 5-point Likert scale, where 1 indicated "strongly disagree" and 5 indicated "strongly agree" and the midpoint of the scale (3) represented "neither agree nor disagree". A predefined threshold of 75% was used to define consensus: agreement was achieved if 75% or more participants selected "agree" or "strongly agree," while disagreement was established if 75% or more selected "disagree" or "strongly disagree." Statements that did not reach consensus in the first round were presented for re-voting in the second round, alongside supporting literature.

2.5 | Data analysis

The responses, collected anonymously, were aggregated, and consensus rates were calculated for each statement. First round results were shared via email with the panel of experts. Statements that did not reach consensus in the first round were resubmitted for voting. The results of the second round for those statements that again did not reach consensus were also analyzed according to the two professional subgroups—adult and pediatric specialists. Significant divergences between the aggregated results and those specific to adult versus pediatric specialists were highlighted in the results.

2.6 | Ethical considerations

This study did not involve patient data or interventions and was exempt from ethical approval. Participation was voluntary, and anonymity was maintained throughout the process.

3 | RESULTS

A total of 22 statements were evaluated across four thematic areas. After the first round of voting, 13 statements achieved consensus. Two additional statements reached consensus following the second round, resulting in a total of 15 out of 22 statements attaining consensus. Despite the iterative process, 7 statements did not meet the consensus threshold. Overall, responses from different professional subgroups (adult versus pediatric specialists or both) showed no substantial differences, except for Statements 2.1 and 4.8, where noteworthy discrepancies emerged.

3.1 | Area 1: Redefinition of drug-resistant epilepsy

Results from Area 1 (Redefinition of Drug-Resistant Epilepsy) are graphically represented in Figure 1. Statement 1.1 proposed that the current ILAE definition of drug resistance does not require revision. This statement failed to achieve consensus. In the first round, 23% of participants agreed or strongly agreed, while 46% strongly disagreed and 30% disagreed. The second round produced comparable results, with 18% agreeing or strongly agreeing and 68% disagreeing or strongly disagreeing.

Statement 1.2, suggesting that the definition of drug resistance should consider individual complexities of epilepsy, such as specific etiology and the number of prior treatments, achieved consensus in the first round. A total of 84% of participants agreed or strongly agreed, indicating strong alignment among experts.

Statement 1.3 emphasized the relevance of considering the number of adequately trialed ASMs in predicting the likelihood of therapeutic success with a new ASM. This statement also reached consensus in the first round, with 83% of participants agreeing or strongly agreeing, while disagreement was minimal (8%).

Statement 1.4, which posited that the number of previously tested ASMs does not necessarily preclude the potential success of a new treatment, failed to achieve consensus in both rounds. In the first round, 48% agreed or strongly agreed, while 31% strongly disagreed. The second round showed a similar division, with 49% agreeing or strongly agreeing and 42% disagreeing or strongly disagreeing, reflecting a continued lack of agreement.

3.2 | Area 2: Definition of "therapeutic success" and "control" in epilepsy care

Results from Area 2 (Definition of "Therapeutic Success" and "Control" in Epilepsy Care) are graphically reported

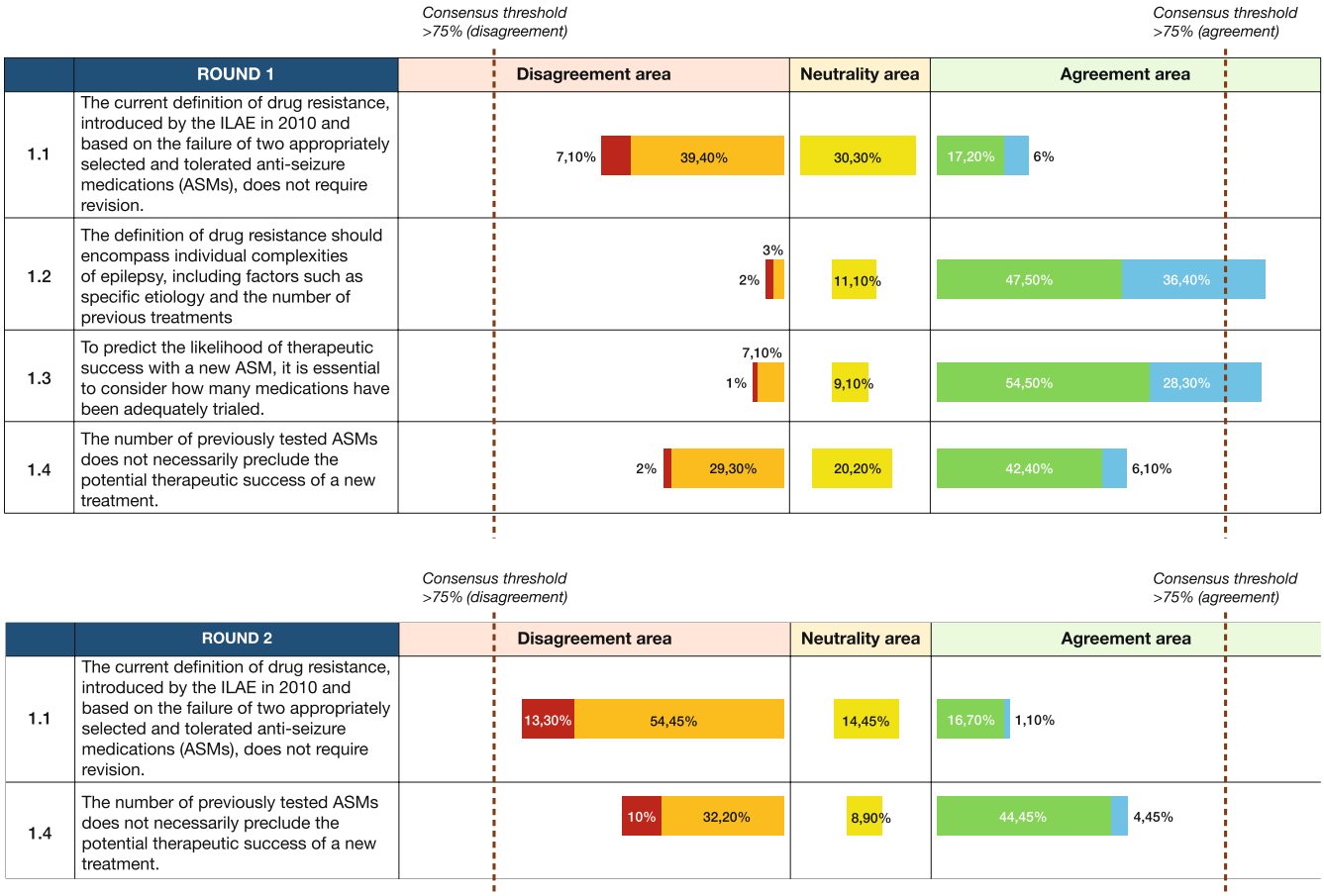

FIGURE 1 Graphical representation of Delphi results from Area 1.

in Figure 2. Statement, which suggested that seizure freedom alone is sufficient to define therapeutic success, failed to reach consensus. In the first round, 15% of participants agreed or strongly agreed, while 68% disagreed or strongly disagreed. The second round did not change this outcome significantly, with only 10% agreeing or strongly agreeing and 73% disagreeing or strongly disagreeing. When results were analyzed by professional subgroups, consensus was achieved in the disagreement area among pediatricians (77% versus 73% among experts of adult epilepsy).

Statement 2.2, which suggested that therapeutic success is a dichotomous concept representing an "all or nothing" outcome, achieved consensus in the disagreement area. In the first round, 78% of participants disagreed or strongly disagreed, with only 9% agreeing or strongly agreeing.

For Statement 2.3, which evaluated whether PwE could be considered under control if seizures do not interfere with daily activities, consensus was not reached. In the first round, 53% of participants agreed or strongly agreed, while 24% disagreed or strongly disagreed. After the second round, the division persisted, with 34% agreeing or strongly agreeing and 42% disagreeing or strongly disagreeing, showing an ongoing divergence of opinions.

In Statement 2.4, a strong consensus was achieved in the agreement area regarding the importance of including comorbidities and their consequences when assessing epilepsy control. In the first round, 97% of participants agreed or strongly agreed, demonstrating an overwhelming agreement.

Statement 2.5, which emphasized the role of managing epilepsy through a multidimensional definition of therapeutic success to improve quality of life, also reached a strong consensus in the first round, with 85% agreeing or strongly agreeing.

For Statement 2.6, there was widespread agreement that quality of life should be considered a key indicator of therapeutic success. In the first round, 98% of participants agreed or strongly agreed, reflecting near-full consensus.

Statement 2.7 highlighted the necessity of a multidisciplinary assessment incorporating the perspectives of the patient or caregiver to define controlled epilepsy. Strong consensus was achieved in the first round, with 84% of participants agreeing or strongly agreeing, emphasizing the value of integrating diverse perspectives in epilepsy care.

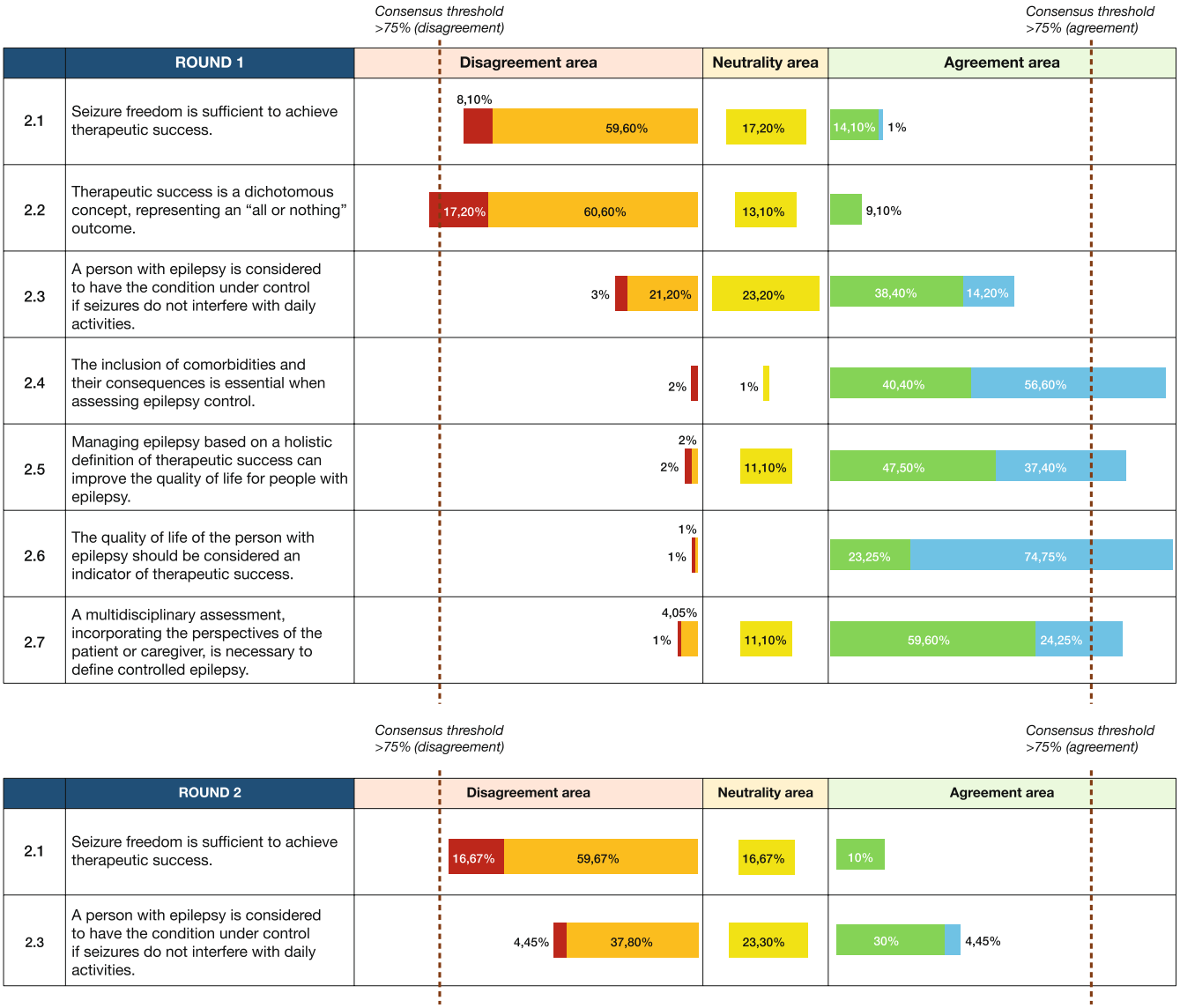

FIGURE 2 Graphical representation of Delphi results from Area 2.

3.3 | Area 3: Predictors of treatment response

Results from Area 3 (Predictors of Treatment Response) are graphically reported in Figure 3. Statement 3.1, asserting that the individual neurobiological characteristics of a PwE are critical in predicting therapeutic success with ASM-based therapy, reached consensus in the agreement area in the first round. A total of 76% of participants agreed or strongly agreed, while only 4% disagreed or strongly disagreed, and 20% remained neutral.

For Statement 3.2, experts voted on whether the number of previous pharmacological failures serves as an indicator of the likelihood of achieving seizure freedom with subsequent ASM therapy. In the first round, consensus was not achieved, with 72% of participants agreeing or strongly agreeing and 15% strongly disagreeing. After the second round, consensus was reached with 78% agreeing or strongly agreeing, while disagreement decreased to 12%.

3.4 | Area 4: Therapeutic approaches, management strategies, and care objectives

Results from Area 4 (Therapeutic Approaches, Management Strategies, and Care Objectives) are graphically reported in Figure 4. Statement 4.1, which proposed that epilepsy surgery should not be considered for all individuals with DRE, failed to achieve consensus. In the first round, 46% of participants agreed or strongly agreed, while 38% disagreed or strongly disagreed. The second

FIGURE 3 Graphical representation of Delphi results from Area 3.

round produced similar results, with 49% in the area of agreement and 43% in the disagreement area, reflecting a persistent division among experts.

Statement 4.2, suggesting that the ketogenic diet represents an effective therapeutic option for reducing seizure frequency in certain cases of DRE, achieved strong consensus in the first round. A total of 78% of participants were in the agreement area, with minimal disagreement (3%).

Statement 4.3, which emphasized the importance of early recognition and treatment of psychiatric comorbidities, such as depression and anxiety, in epilepsy management, achieved strong consensus in the first round. A total of 95% of participants were in the agreement area, with only 2% expressing disagreement.

Statement 4.4, suggesting that psychiatric comorbidities play a more significant role than seizures themselves in DRE, failed to achieve consensus. In the first round, 53% of participants were in the agreement area, while 13% strongly disagreed. The second round showed limited changes, with 56% agreeing or strongly agreeing and 11% strongly disagreeing.

Statement 4.5 addressed the inclusion of psychological support programs and support groups for patients and families to reduce stigma and enhance resilience. This statement achieved a strong consensus in the first round, with 98% of participants in the agreement area and negligible disagreement (1%).

Regarding statement 4.6, emphasizing the role of family or caregiver involvement in managing DRE, a strong consensus was achieved in the first round. A total of 95% of participants were in the area of agreement, with minimal disagreement (3%).

Statement 4.7, which highlighted the need for involving a multidisciplinary community—including clinicians, preclinical scientists, and patient representatives—in defining therapeutic success, failed to achieve consensus in the first round. In the second round, 80% of participants agreed or strongly agreed, while 4% strongly disagreed, reaching consensus in the agreement area.

Statement 4.8, suggesting that the failure of the first appropriately chosen ASM already indicates drug resistance in pediatric focal structural epilepsies (e.g., focal cortical dysplasia), failed to achieve consensus after two rounds. In the second round, 53% were in the area of agreement, while 36% disagreed or strongly disagreed, reflecting significant divergence of opinions. When responses were analyzed by professional subgroups, 58% of pediatric experts strongly disagreed or disagreed compared to 24% of adult specialists.

Statement 4.9, which emphasized that the definition of control should account for the potential impact of ASMs on the neuropsychological profile, particularly in pediatric epilepsy, achieved a strong consensus in the first round. A total of 97% of participants fell in the area of agreement, with only 2% expressing disagreement.

4 | DISCUSSION

The findings of the present Delphi study revealed both areas of broad agreement and persistent debate among Italian experts regarding the definition and management of DRE. One prominent source of contention is the current ILAE definition, which characterizes drug resistance as the failure of two properly chosen and tolerated

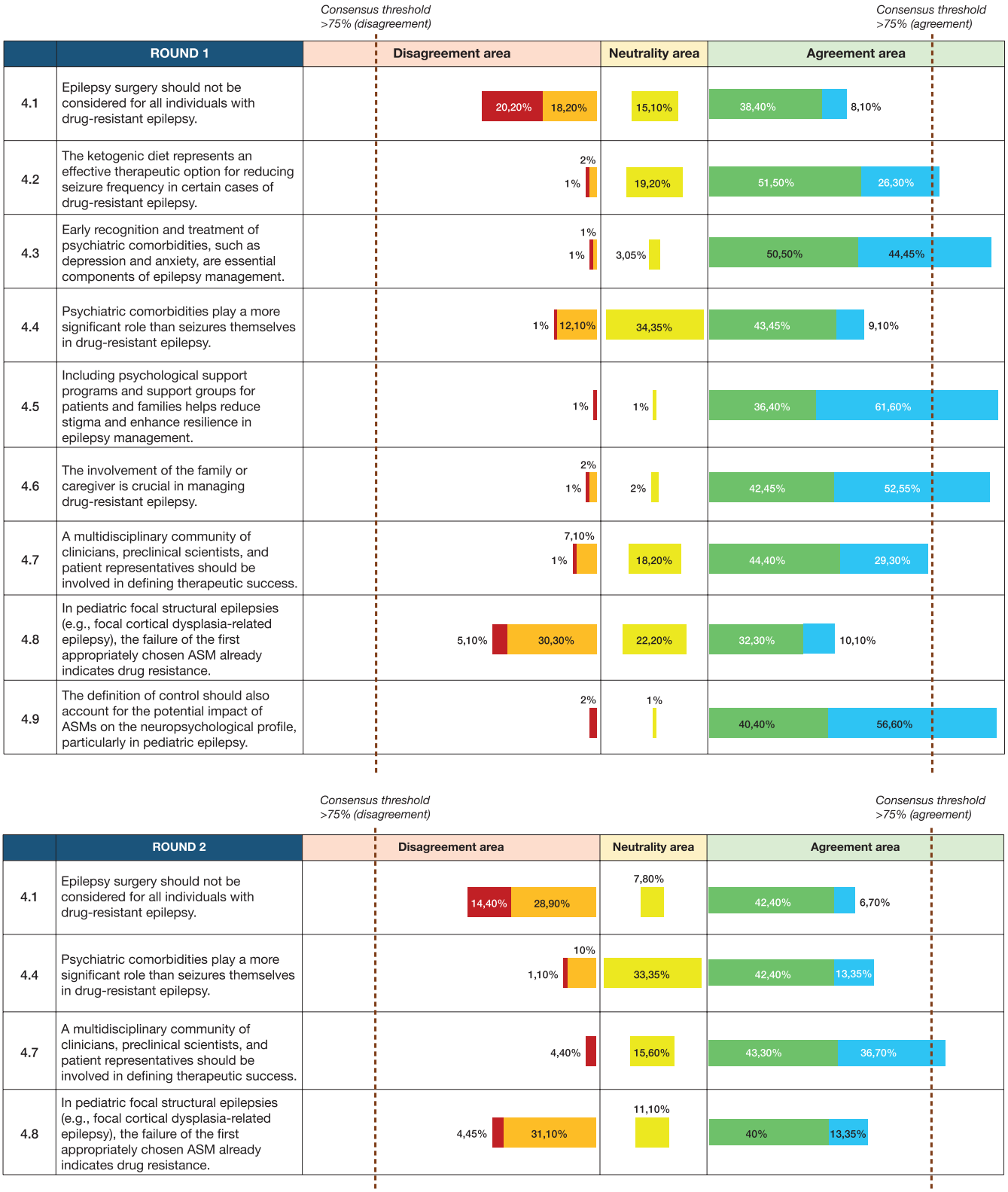

FIGURE 4 Graphical representation of Delphi results from Area 4.

ASMs.[1] Evidence showed that treatment likelihood declines with each prior failure and that failing two ASMs lowers, but does not eliminate, the chance of success with subsequent therapies.[4,11,24] Hence, such a definition has been questioned by the ILAE itself, highlighting the need for a reevaluation.[3] As highlighted by the results, the inability to achieve consensus on retaining it (Statement 1.1) and the trend to disagree on it suggest that such a

definitionmay not be adequate over the full spectrum of patient populations. This is particularly relevant given the recent introduction of new medications that have shifted the management paradigm, necessitating a redefinition of the concept.

A few recent retrospective studies have proposed that cenobamate, which has shown a high rate of seizure freedom in people with uncontrolled seizures,[14] might be considered when evaluating prior treatment failures in the context of defining epilepsy as drug resistant.[25,26] In this regard, however, it is worth noticing that similar considerations may apply to other clinical scenarios and treatment options. For example, in idiopathic generalized epilepsies, it has been suggested that drug resistance should not be declared unless patients have been adequately treated with valproic acid.[27] Pediatric epilepsy introduced another point of discussion. The failure to reach consensus on whether a single unsuccessful ASM trial indicates drug resistance in certain epilepsy subtypes, mainly epilepsy due to focal cortical dysplasia, highlights the difficulty of applying uniform criteria across different populations and perhaps a resistance to early neurosurgical treatment.[28,29]

Instead, there is strong support for incorporating a wider range of patient-specific factors—such as etiology, seizure type, epilepsy syndrome, and the number and nature of prior treatments—into the criteria that determine whether and when epilepsy can be truly defined as drug-resistant. The implicit assumption in the definition of DRE is that seizure freedom will not or is very unlikely to be attained with further manipulation of ASM therapy. Therefore, any definition should rely on the assessment of the likelihood of seizure remission after each drug failure. As highlighted by the Delphi study, this probability is highly individual and should encompass individual complexities of each specific epilepsy and patient, such as etiology, seizure type, and syndrome; in other words, "one size (two appropriately selected and tolerated ASMs) does not fill all". This approach reflects the evolving landscape of epilepsy care and the need for more nuanced and individualized definitions.

Another emerging theme is the complexity involved in defining therapeutic success, a concept that remains inadequately defined in epilepsy.[1] While some consider seizure freedom the ultimate goal, others emphasize the importance of achieving an acceptable quality of life, even in the presence of residual seizures.[30] While seizure freedom should still be considered as the ultimate goal of treatment, some experts favor a broader balance that includes reduced seizure burden, improved quality of life, better daily functioning, and the effective management of comorbid conditions.[30,31] These viewpoints illustrate a growing acknowledgment that seizure outcomes alone may not fully capture a patient's lived experience. Instead, success might manifest as fewer seizures that are less disruptive, improved psychological well-being, or enhanced social participation, depending on a tailored patient-centric approach. Therapeutic success could be thought of as a global measure to estimate how therapeutic interventions work in terms of favorable impact on the life of the PwE, and as such, it includes not only seizure frequency, seizure severity, and how much seizures are debilitating, but also incorporates the adverse events of therapeutic interventions, psychosocial outcomes, and level of patient satisfaction. How to measure (different scales have been developed to explore each of these dimensions) and weigh each of these domains should be the object of future joined efforts of a multidisciplinary community of clinicians and patient representatives.

The divergence of opinions concerning whether patients with residual seizures that do not significantly interfere with daily life can be considered "under control" demonstrates the fluidity and complexity of these definitions. This complexity reflects a departure from an overly rigid, dichotomous view of success and points toward a more personalized, context-dependent understanding of control and therapy outcome.[32,33] For Statement 2.7, the consensus on multidisciplinary assessment reflects a recognition of its importance but also highlights a need for clarity in terminology. Rather than a purely clinical focus on multidisciplinarity, a "multidimensional perspective" is more appropriate, emphasizing the inclusion of patient and caregiver perceptions. This approach aligns with the shift toward patient-centered care and resonates with previous studies that advocate for integrating patient-reported outcomes into the assessment of epilepsy control.[31]

The variability in opinions on epilepsy surgery highlights the need for clearer guidelines to identify appropriate candidates and probably also the current underutilization of this therapeutic approach. Statement 4.1, addressing the applicability of epilepsy surgery for all individuals with DRE, failed to achieve consensus, reflecting a crucial area of debate. The lack of agreement may stem from the statement's ambiguity, as surgery is recognized as a valuable intervention but not universally applicable. Reframing the statement to focus on "considering surgery for appropriate candidates" may have better captured the actual approach required in clinical practice. Surgical and neuromodulation interventions are indeed essential therapeutic options for epilepsy, particularly for patients with the most refractory cases who fail pharmacological treatments.[34–36] Such approaches require careful candidate selection through multidisciplinary approaches based on individual factors such as etiology, seizure characteristics,

and overall patient profile.[37–39] The study results align with these principles, highlighting the importance of tailoring surgical indications to patient-specific circumstances and ensuring decisions are informed by comprehensive, collaborative assessments.

Similarly, while the ketogenic diet was widely accepted as an effective approach for certain drug-resistant cases, and early recognition and treatment of psychiatric comorbidities were strongly endorsed, some debates persisted.[40,41] For instance, there was no unified stance on how much psychiatric conditions themselves might contribute to impaired life in patients with DRE. This suggests that although there is recognition of the importance of mental health management, determining its relative weight and impact remains challenging. Pediatricians, who often encounter developmental, cognitive, and behavioral challenges in their patients, may prioritize different considerations than the broader expert community. Such subgroup differences underscore again the need for more specialized guidance that accounts for distinct clinical scenarios and the perspectives of various professional roles.

5 | CONCLUSION

This Delphi consensus study highlighted the need to revisit the current ILAE definition of DRE to better capture the complexities of individual cases and align with evolving clinical priorities. The high responder rates of 96.1% in the first round and 90.9% in the second round underscore the robustness of the Delphi process and the representativeness of the results. These rates were in line with or exceeded those reported in other Delphi studies, further validating the reliability of the findings. Embracing a multidimensional framework for therapeutic success—one that integrates clinical outcomes, quality of life, and patient-reported experiences—emerges as a critical step forward. Clearer delineation of surgical indications and improved communication around patient suitability are also essential for optimizing treatment strategies. Furthermore, fostering collaboration between pediatric and adult specialties will ensure more comprehensive, age-appropriate care. By addressing these areas, this study provides a foundation for refining and advancing patient-centered epilepsy care.

AUTHOR CONTRIBUTIONS

Federico Vigevano: Conceptualization; methodology; data curation; project administration; supervision; writing—review and editing. **Irene Bagnasco**: Conceptualization; methodology; data curation; project administration; supervision; writing—review and editing. **Giancarlo Di Gennaro**: Conceptualization; methodology; data curation; project administration; supervision; writing—review and editing. **Oriano Mecarelli**: Conceptualization; methodology; data curation; project administration; supervision; writing—review and editing. **Simona Lattanzi**: Conceptualization; methodology; data curation; project administration; supervision; writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

FV has received speaker's or consultancy fees from UCB, Neuraxpharm, and Ethypharm. He has also served on advisory boards for Angelini, UCB, Neuraxpharm, and Ethypharm. GDG has received speaker's or consultancy fees from Angelini Pharma, Eisai, UCB Pharma, Lusofarmaco, GW pharmaceuticals. He has also served on advisory boards for Angelini Pharma, Arvelle Therapeutics, BIAL, Eisai, Neuraxpharma end UCB Pharma. OM has received speaker's or consultancy fees from Angelini Pharma, Jazz Pharmaceuticals, UCB Pharma, and Lusofarmaco. He has also served on advisory boards for Angelini Pharma. SL has received speaker's or consultancy fees from Angelini Pharma, Eisai, GW Pharmaceuticals, Medscape, and UCB Pharma. She has also served on advisory boards for Angelini Pharma, Arvelle Therapeutics, BIAL, Eisai, GW Pharmaceuticals, NewBridge Pharmaceuticals, Rapport Therapeutics, and UCB Pharma. IB and GDG declare no conflicts of interest. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

This study did not involve human subjects research requiring institutional ethics committee approval. No sensitive personal data were collected, and all responses were anonymized to maintain confidentiality and ensure impartiality throughout the analysis.

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