Received: 28 October 2025 | Revised: 30 December 2025 | Accepted: 17 January 2026

DOI: 10.1002/epi4.70226

Epilepsia Open® Open Access

ORIGINAL ARTICLE

Perspectives on the burden of drug-resistant epilepsy and treatment priorities: Findings from a multistakeholder survey

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Funding information
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Abstract

Objective: Drug-resistant epilepsy (DRE) imposes a significant burden on patients and their caregivers. This study aimed to explore the concerns and perceptions of healthcare providers (HCPs), patients, and caregivers regarding the burden of disease and quality of life (QoL) in patients with DRE.

Methods: This was a multinational, cross-sectional, online, survey-based study. Participants were HCPs managing at least 30–50 epilepsy patients per month, including ≥10 patients with DRE; patients aged ≥18 years with DRE; and caregivers aged ≥18 years supporting patients with DRE. Data collection was carried out between March and August 2024.

Results: In total, 213 stakeholders took part in the survey (146 HCPs, 42 patients, and 25 caregivers); 58% of the HCPs were neurologists and 42% were epileptologists. Caregivers were mainly parents (79%). Patients represented by caregivers were younger (84% vs. 29% aged 18–34 years) and had a higher incidence of seizures (20 vs. 5 seizures per month; $p < 0.05$) than patient participants. According to all stakeholders, DRE had a significant impact on multiple components of patient QoL, with work capability, psychological well-being, and daily management and logistics the most affected. Significantly fewer HCPs regarded "achieving complete seizure freedom" as of high importance for patients compared with patient participants ($p < 0.05$) and caregivers ($p < 0.05$). High satisfaction with current treatment was reported by only 35% of HCPs, 33% of patient participants, and 4% of caregivers. Most stakeholders reported insufficient time during consultations to investigate patients' concerns, and different topics for discussion were prioritized by HCPs and patients/caregivers.

Significance: This survey highlighted the continued and multifaceted burden of disease among patients with DRE. While seizure freedom is the ultimate goal

Social media and article promotion: New survey reveals the burden of drug-resistant epilepsy and different treatment priorities among patients, carers, and healthcare providers.

of treatment, disparities exist among key stakeholders regarding aims and outcomes of treatment as well as management of expectations.

Plain Language Summary: Patients with DRE have epileptic seizures despite receiving medicines to reduce their seizures. This survey shows that DRE places a heavy strain on patients and their carers. Satisfaction with current treatments is low, especially among carers. Patients and carers see stopping all seizures as very important, but doctors tend to rate this as less of a priority; patients and carers are also more open than doctors to using digital tools to improve communication with their doctor. Overall, the differences in expectations and approaches between patients, carers, and doctors may create barriers to improving seizure control.

KEYWORDS

burden of disease, drug-resistant epilepsy, quality of life

1 | INTRODUCTION

Epilepsy is a common chronic brain disorder affecting 50 million individuals worldwide.[1] Over one-third of patients have drug-resistant epilepsy (DRE),[2,3] which is defined by the International League Against Epilepsy (ILAE) as uncontrolled seizures despite treatment with at least two tolerated, appropriately chosen and used antiseizure medications (ASMs).[4] DRE imposes a substantial burden on patients and their families, with increased risks of injuries, comorbidities, treatment-related adverse events (AEs), and premature death, alongside psychological and social dysfunction, employment difficulties, and reduced quality of life (QoL).[5–10] Caregivers also report stress, financial distress, and limited time with other children as additional burdens.[7–12]

Systematic reviews of studies exploring the burden of DRE on patients and their families/caregivers suggest that a high seizure burden is associated with increased resource use, greater costs, and reduced health-related QoL for patients.[9,10] In Italy, a national consensus has emphasized the importance of personalized, multidisciplinary management of epilepsies characterized by a high seizure burden, highlighting the need for enhanced research to improve patient outcomes.[13] In this regard, stakeholder surveys are valuable for identifying, defining, and addressing the challenges faced by patients, caregivers, and healthcare providers (HCPs). In the United Kingdom, a cross-sectional survey reported a mismatch between the support requested by families of patients with epilepsy, especially regarding cognition and mental health, and the ability of HCPs to fulfill those needs.[14] In Spain, a National Healthcare System study identified poor HCP–patient communication as a barrier to excellent care at several stages of the patient journey, including drug treatment, follow-up, and referral.[15] Together, these findings underscore the importance of capturing diverse stakeholder perspectives to inform care strategies.

This study aimed to explore the perceptions of HCPs, patients, and caregivers across European countries regarding the burden of disease and QoL in individuals with DRE. Objectives included understanding the impact of epilepsy on QoL, evaluating satisfaction with current therapies, and assessing how treatment modifications affect patients. It also aimed to identify patient priorities when starting new treatments, highlight discussion needs during

Key points

- This survey highlights the continued and significant burden associated with drug-resistant epilepsy in patients and their caregivers.
- Stakeholders have low satisfaction with current treatment, and this is particularly acute among caregivers.
- Healthcare providers (HCPs) are less likely than patients/caregivers to see complete seizure freedom as of high importance for patients.
- Patients/caregivers are more receptive than HCPs to the use of digital tools to address gaps in HCP–patient communication.
- Differences in treatment expectations and management may hinder progress toward seizure freedom, potentially impacting patients' lives.

clinic visits, determine effective communication tools, and investigate logistical aspects of epilepsy management.

2 | METHODS

2.1 | Study design

This was a multinational, cross-sectional, online, survey-based study conducted between March 12 and August 6, 2024. The survey was conducted in accordance with applicable laws and regulations, including the European Pharmaceutical Marketing Research Association codes of conduct regarding anonymity and confidentiality in market research and laws related to protection of personal data.

2.2 | Participant selection and inclusion/exclusion criteria

For inclusion in the study, HCPs were required to be dedicating ≥25% of their time to epilepsy (20% in Portugal), have 3–35 years of experience, and be spending ≥70% of their time in direct patient care. Additionally, they needed to be managing or treating ≥75 patients across all conditions per month, including ≥50 epilepsy patients (≥30 in Portugal) and ≥10 patients with DRE. All participating HCPs were involved in managing adult patients.

Patient participants were included in the study if they were aged ≥18 years, had been diagnosed with epilepsy by a physician, and were under the care of a neurologist or epileptologist. They also had to be receiving current medication for epilepsy and to have previously received ≥2 ASMs and met the ILAE definition of DRE.

Caregivers were included if they were aged ≥18 years, were not nurses, and were caring for adult patients who met the same clinical criteria as the patient participants.

Patients and caregivers were recruited through patient organizations, including France Epilepsie, Federazione Italiana Epilessie, and Federación Española de Epilepsia. A web link to the survey was sent by the providers to the patient associations, who forwarded it directly to patients. Patients registered and answered questions anonymously, with no personal data collected.

Although the objective was to recruit a similar number of participants in each group, recruitment difficulties led to fewer patients and caregivers than HCPs.

2.3 | Data collection

A 20-min online survey was used to gather data from HCPs, patients, and caregivers regarding the burden of disease and QoL for patients with DRE. The questionnaire contained 28 items for HCPs and 36 items for patients and caregivers. Data were collected between March 12 and May 2, 2024 for HCPs and between May 23 and August 6, 2024 for patients and caregivers. Data collection was managed by IQVIA (Survey—Drug-resistant focal epilepsy, 2024).

2.4 | Definitions and endpoints

Endpoints adjudicated by impact, importance, and satisfaction were ranked on a Likert scale (1–10), where a mean score of 8–10 was considered to be "most impacted/important" or "highest satisfaction."

2.5 | Statistical analysis

Participant characteristics were reported using descriptive statistics. Numerical variables (including endpoints ranked using a Likert scale) were summarized using mean, minimum/maximum, standard deviation, and standard error of the mean; *T*-tests were used to assess significant differences between groups. Categorical variables were reported using frequency distribution; *Z*-tests were used to assess significant differences between groups.

Given the open recruitment and differential response rates, the sample was vulnerable to selection bias, including overrepresentation of HCPs and caregivers of younger and more severely affected individuals. Inferential statistics were conducted on available cases and were intended to be exploratory, given the small, heterogeneous, and unbalanced subgroups. Participants with missing values for a given variable were excluded from that specific analysis, and no imputation was applied. As subgroup sizes varied substantially, the resulting estimates should be interpreted cautiously.

3 | RESULTS

3.1 | Respondent profiles and patients' characteristics

The study included 146 HCPs, 42 patient participants, and 25 caregivers. Characteristics of HCPs, patient participants, caregivers, and patients attended by the caregivers are shown in Table 1. Out of 146 surveyed HCPs, 58% were neurologists and 42% were epileptologists. Overall, 90% of their time was dedicated to direct patient care, and 52% focused on epilepsy. The majority of HCPs (59%) worked in specialist, academic, or university hospitals, and none had direct or family ties to pharmaceutical companies (either

TABLE 1 Characteristics of the study participants. (A) Healthcare providers; (B) patient participants, caregivers, and patients supported by the caregivers.

A	Healthcare providers ($n = 146$)
Geographical location, *n* (%)	
France	30 (21)
Germany	31 (21)
Italy	30 (21)
Spain	30 (21)
Portugal	25 (17)
Role, *n* (%)	
Neurologist	85 (58)
Epileptologist	61 (42)
Proportion of time spent in epilepsy (%)	52
Experience in current specialty (years)	15
Proportion of time spent in direct patient care (%)	90
Workplace, *n* (%)	
Specialist/academic/university hospital	86 (59)
Community/regional/general hospital	44 (30)
Personal office/clinic	15 (10)
Other	1 (1)
Mean number of patients managed across all conditions per month	334
Mean number of epilepsy patients managed per month	136
Proportion of epilepsy patients with DRE[a], *n* (%)	56 (41)
Age of epilepsy patients in years, *n* (%)	
≤17	21 (14)
18–34	41 (28)
35–49	42 (29)
≥50	42 (29)
Age of DRE patients in years, *n* (%)	
≤17	23 (16)
18–34	44 (30)
35–49	41 (28)
≥50	38 (26)

B	Patient participants ($n = 42$)	Caregivers ($n = 25$)	Patients represented by caregivers ($n = 25$)
Geographical location, *n* (%)			
France	17 (41)	6 (24)	6 (24)
Germany	0	0	0
Italy	13 (31)	12 (48)	12 (48)
Spain	7 (17)	7 (28)	7 (28)
Portugal	5 (12)	0	0
Age in years, *n* (%)			
18–34	12 (29)	4 (16)	21 (84)
35–49	17 (40)	3 (12)	3 (12)
≥50	13 (31)	18 (72)	1 (4)
Gender, *n* (%)			
Female	29 (69)	18 (72)	13 (52)
Male	12 (29)	7 (28)	12 (48)
Prefer not to say	1 (2)	0	0

TABLE 1 (Continued)

B	Patient participants ($n=42$)	Caregivers ($n=25$)	Patients represented by caregivers ($n=25$)
Caregiver relationship to patient, *n* (%)			
Parent	–	19 (76)	–
Sibling	–	3 (12)	–
Spouse/partner	–	1 (4)	–
Other family member	–	1 (4)	–
Friend	–	1 (4)	–
Time since epilepsy onset in years, *n* (%)			
≤1	0 (0)	–	4 (16)
2–5	2 (5)	–	1 (4)
6–10	7 (17)	–	2 (8)
>10	33 (79)	–	18 (72)
Patient informed of epilepsy cause, *n* (%)	28 (67)	–	18 (72)
Factors in the brain	9 (32)	–	0
Genetic influence	5 (18)	–	13 (72)
Injury before birth	5 (18)	–	1 (6)
Infections	4 (14)	–	0
Head trauma	2 (7)	–	1 (6)
Developmental conditions	1 (4)	–	2 (11)
Stroke	1 (4)	–	0
Tumor	1 (4)	–	0
Autoimmune disease	0	–	1 (6)
Managing professional, *n* (%)			
Office-based neurologist	6 (14)	–	1 (4)
Hospital-based neurologist	16 (38)	–	7 (28)
Hospital-based epileptologist/epilepsy expert	20 (48)	–	17 (68)
Patient informed of DRE, *n* (%)	36 (86)	–	36 (100)
Number of prior ASMs, *n* (%)			
3	13 (31)	–	6 (24)
≥4	29 (69)	–	19 (76)

Abbreviations: ASM, antiseizure medication; DRE, drug-resistant epilepsy.

[a]Failure of adequate trials of two tolerated, appropriately chosen, and used ASM schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom.

as a consultant or researcher) other than participating in clinical trials. On average, HCPs managed 136 epilepsy patients per month, 41% of whom were classified as drug-resistant as per the ILAE criteria.

Among the 42 surveyed patient participants, 29% were aged 18–34 years, 40% were aged 35–49 years, and 31% were aged 50 or older; most (69%) were females (Table 1). The majority (79%) were diagnosed with epilepsy ≥10 years prior to the study. Most patients (67%) reported being told the cause of their epilepsy, and 86% had been informed that their epilepsy was drug-resistant. Regarding care, 48% were treated by a hospital epileptologist or epilepsy expert, and most (69%) had received ≥4 ASMs over their lifetime.

Patients supported by their caregivers were younger than the patient participants (84% vs. 29% were aged 18–34 years, respectively) and most (72%) were diagnosed more than 10 years prior to the study; 76% had received ≥4 ASMs in their lifetime.

Of the 25 surveyed caregivers, 72% were aged 50 or older, 72% were females, and 76% were parents of the patient under their care (Table 1). Most caregivers (72%) had been told the cause of the patient's epilepsy. HCP care for these patients was primarily provided by a hospital epileptologist or epilepsy expert (68% of cases).

The frequency of seizures was significantly higher in those patients described by the caregivers than in the patient participants (mean 20 vs. 5 seizures per month,

$p < 0.05$; Figure S1). Among patient participants, absence seizures were the most common seizure type experienced in the last 6 months (32% of patients), followed by focal aware seizures (30%; Figure S1).

The majority of patients represented in this study were not seizure-free. While HCPs stated that 59% of their DRE patients were non-seizure-free at the time of the interview, almost all patients surveyed in the study (90%) or described by caregivers (96%) were uncontrolled.

3.2 | Burden of disease and QoL

HCPs identified several significant challenges for patients in managing their condition, including identifying when to adjust their treatment regimen (24%), adhering to their prescribed ASM regimen (23%), accepting their epilepsy diagnosis (22%), and adapting to changes in their ASM regimen (16%). Additionally, 15% of HCPs noted that patients struggle to recognize when an unplanned visit to their HCP is necessary.

Predicting breakthrough seizures was considered the most challenging aspect of managing DRE for patients, with 68/146 HCPs (47%) ranking it as the top difficulty. Other identified challenges included determining the severity of a seizure as it begins (19%), deciding whether to use medication to reduce seizure severity (17%), estimating seizure duration (11%), and deciding whether to seek emergency care during a seizure (6%). Patients described by the caregivers were less likely than patient participants to be aware of warning signs of seizure onset (Figure S1).

DRE had a significant impact on multiple components of patient QoL, as assessed by all stakeholders (Figure 1A). Work capability, psychological well-being, and daily management/logistics were considered the QoL components most affected by DRE. HCPs and caregivers were in general agreement on the most affected QoL components, but patients were significantly less likely than HCPs and caregivers to report a high impact of DRE on QoL components. When asked to rate the impact of DRE on patients' QoL, HCPs reported at least a two-fold greater impact in those with ongoing versus controlled seizures (Figure 1B).

While 55% (23/42) of patient participants reported traveling independently, only 12% (3/25) of caregivers reported the same for patients under their care. A higher proportion of patient participants (26/42; 62%) reported being in work or education compared with patients reported by caregivers (9/25; 36%). A medium–high financial impact of epilepsy was reported by 60% (25/42) of patient participants and 72% (18/25) of caregivers.

3.3 | Treatment expectations

According to all stakeholder groups, "achieving complete seizure freedom" was ranked as the top priority for patients when considering a new ASM; other high priorities included effectiveness in reducing seizure frequency and improvement in overall well-being/QoL (Figure 2). Interestingly, a significantly lower proportion of HCPs (52%) than patient participants (88%; $p < 0.05$) and caregivers (88%; $p < 0.05$) rated seizure freedom as of high importance (i.e., score 8–10) to patients (Figure 3). This proportion was even lower (58%, 43%, and 43%) when HCPs were asked the same question specifically about those patients with 2, 3–5, or >5 previously failed ASMs, respectively. Both patients and caregivers were more likely to view seizure freedom as highly important to patients with 2 failed ASMs (100% for both groups) compared with those with >2 failed ASMs (83% and 84%, respectively).

Compared with HCPs, a significantly higher proportion of patients and caregivers considered no convulsive seizures (67% vs. 95% and 88%), no seizures with loss of awareness (65% vs. 98% and 88%), a reduction in seizure frequency (71% vs. 93% and 96%), a reduction in seizure severity (70% vs. 93% and 96%), and side effects that disappear/decrease with time (58% vs. 81% and 88%) as of high importance to patients when starting a new ASM ($p < 0.05$; Figure 4).

Regarding treatment goals, a significantly higher proportion of patients remained hopeful for full seizure control compared with caregivers (48% vs. 16%; $p < 0.05$). There was heterogeneity among the remaining 52% of patients, with 24% hoping for almost full seizure control with some sporadic seizures and 29% lacking any faith in achieving disease control.

3.4 | Treatment satisfaction

Treatment satisfaction for patients with DRE was low. Only one third of patient participants (33%) and HCPs (35%) reported high satisfaction (i.e., score 8–10) with current treatment, and this was significantly lower for caregivers (4%; $p < 0.05$ vs. both).

All stakeholders reported low satisfaction (mean scores <7) with most aspects of their current treatment, including effectiveness in reducing seizures, getting patients back to normal and promoting their overall well-being/

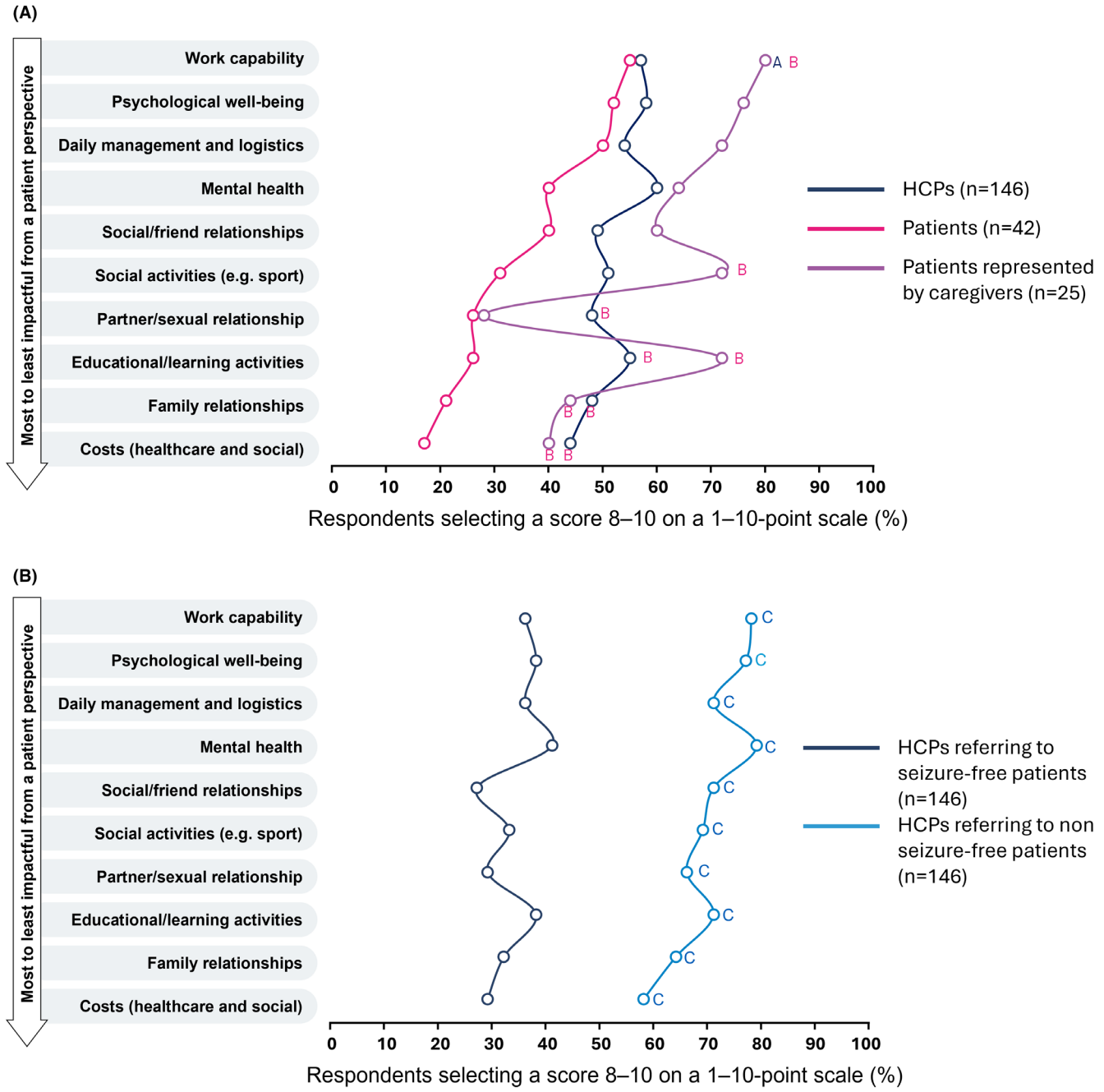

FIGURE 1 Impact of DRE on QoL components as assessed by (A) HCPs, patient participants and caregivers, and by (B) HCPs referring to their seizure-free and non-seizure-free patients. Mean scores for each QoL component are shown based on a Likert scale (1–10). (A) $p < 0.05$ versus HCPs; (B) $p < 0.05$ verssu patients; (C) $p < 0.05$ versus HCPs referring to seizure-free patients. DRE, drug-resistant epilepsy; HCPs, healthcare providers; QoL, quality of life.

QoL, tolerability, and the number of tablets/doses patients were taking or frequency of administration. Caregivers had significantly lower mean satisfaction scores across all measures compared with HCPs, and across several measures compared with patient participants (Figure 5; $p < 0.05$ for all). Patients had lower satisfaction scores for tolerability compared with HCPs ($p < 0.05$).

According to HCPs, 65% of their patients on average improve when starting a new ASM. When patient participants were asked, 52% reported an improvement, whereas fewer caregivers (28%) reported an improvement for the patients they care for ($p < 0.05$ vs. HCPs). Patients with DRE with higher seizure frequency (>4 seizures per month) were significantly less likely to report an improvement than patients experiencing ≤4 seizures per month ($p < 0.05$).

Refusal to take a new ASM was reported by HCPs in 30% of their patients, 12% of patient participants, and 24%

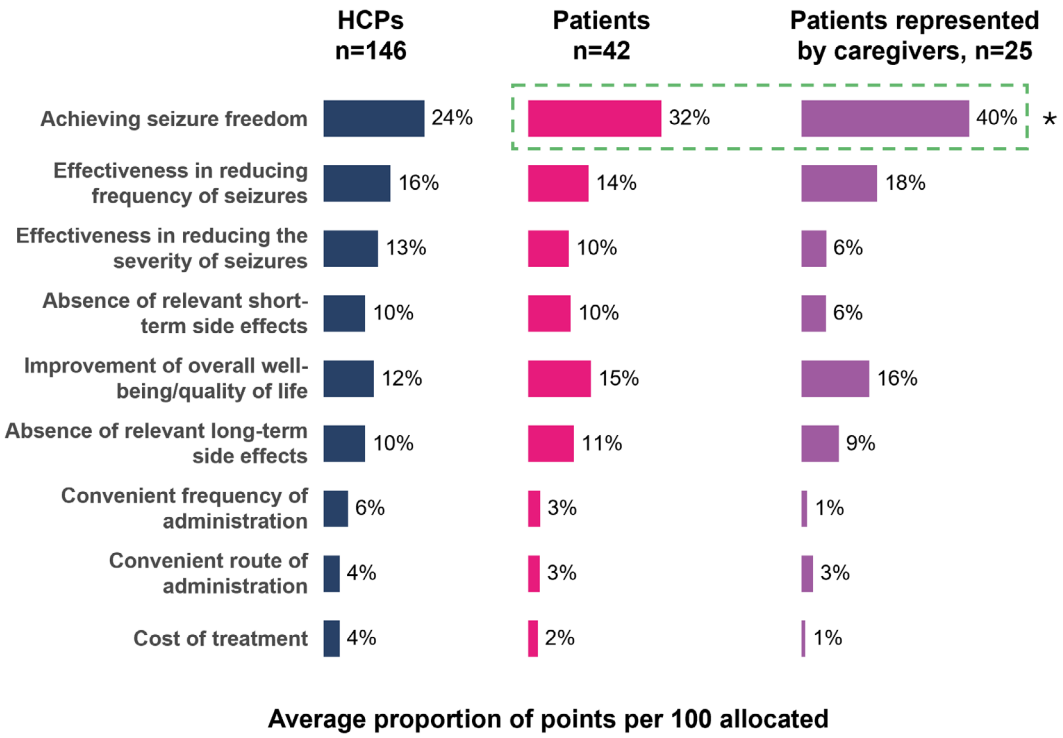

FIGURE 2 Relative importance of specific treatment objectives for patients with DRE when starting a new treatment, according to different stakeholders. Stakeholders were allocated 100 points to distribute across all treatment objectives. *Factors significantly more important for patients and patients represented by caregivers compared with other factors based on 95% confidence intervals. DRE, drug-resistant epilepsy; HCPs, healthcare providers.

of patients represented by their caregivers. According to HCPs, unwillingness to go through the uncertainty/adaptation phase (36%), lack of faith that a treatment could control their epilepsy (32%), and satisfaction with current treatment (31%) were the most popular reasons for patients' refusal to take a new ASM. Patients and caregivers reported fear of side effects (73%; particularly mental health and cognition), avoidance of polypharmacy (18%), and little hope of efficacy (9%) among the reasons for refusing a new ASM.

3.5 | Importance of support beyond ASMs

Only 25% of HCPs, in line with caregivers (28%), believed there is enough time (score >7) during visits to investigate any doubts, perplexities, or discomforts with treatment. In contrast, a higher percentage of patient participants (45%) considered that there was more than enough time during visits. HCPs were significantly less likely than patients to consider that there is sufficient time in this regard ($p < 0.05$).

While patients and caregivers were significantly more likely than HCPs to want to discuss ongoing research, the psychosocial impact, tools for psychosocial support, tolerability, and effectiveness of treatment ($p < 0.05$ for HCPs vs. patients or caregivers), HCPs were more likely than patients and caregivers to want to discuss pregnancy-related AEs ($p < 0.05$).

Patients and caregivers were also more likely than HCPs to place importance on HCP–patient communication tools, including support groups for people with epilepsy, patient-facing apps, wearable devices for seizure detection, and training courses dedicated to people with epilepsy and their caregivers (Figure S2).

Face-to-face dialog was considered important (mean score >8) by all stakeholders, but especially by caregivers (mean score 9.24).

4 | DISCUSSION

This multistakeholder survey emphasizes the continuing burden of DRE and uncontrolled seizures on patients and caregivers in five European countries, highlighting differences in assessment of the burden of DRE, treatment expectations, and treatment satisfaction between HCPs, patients, and caregivers.

There was general agreement among stakeholders that achieving complete seizure freedom was the top priority for patients when considering a new treatment. However, it is notable that 88% of patients and caregivers

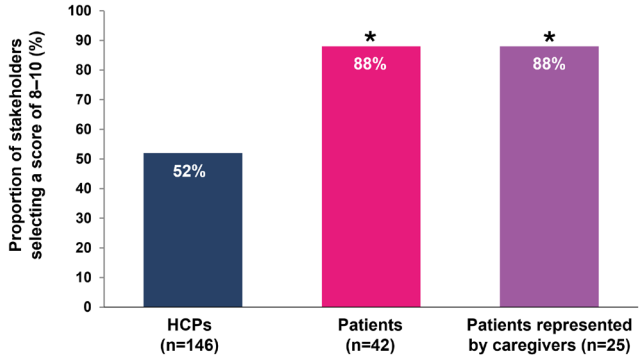

FIGURE 3 Importance of seizure freedom to patients when starting treatment, based on ranking by stakeholders. Bars show the proportion of stakeholders selecting a score of 8–10 (i.e., high importance) for each factor based on a 10-point scale. *$p < 0.05$ versus HCPs. HCPs, healthcare providers.

said they prioritized seizure freedom, whereas only 52% of HCPs reported this to be the case among their patients. While this disconnect may reflect HCPs' wider experience, it may also indicate greater focus among HCPs on reducing disease burden for uncontrolled patients rather than striving for complete seizure freedom. This approach could potentially impact patient outcomes, especially in those with uncontrolled seizures following multiple ASMs. In these cases, some HCPs may experience therapeutic/clinical inertia[16] and even nihilism,[17] in which they consider additional treatment to be futile,[17] despite the emergence of new treatments with efficacy in drug-resistant patients.[18,19] Therefore, HCPs need to be informed of all effective therapies and seizure freedom estimates to guide decision-making. Notably, additional ASMs up to the sixth line can increase seizure freedom rates,[2,20] and ASMs can also reduce SUDEP risk in refractory epilepsy.[21] Furthermore, newer agents with high efficacy in DRE and the potential to reduce concomitant ASM usage are now available,[18,22–25] though adoption into routine practice remains slow.[18,19] Given these complexities, machine-learning tools may aid treatment decision-making.[26]

Our observation that patients with DRE experiencing higher seizure frequencies were less likely to report improvement than those with four or fewer seizures per month underscores the need for personalized treatment. For ASM selection and dosing, the frequency, severity, and type of seizures should be considered. Furthermore, achieving seizure freedom as early as possible, particularly in the context of emerging therapeutic options, is key to improving outcomes.

Patients with epilepsy who achieve seizure freedom experience a significantly greater improvement in QoL than those who continue to experience seizures, even compared with those who have more than a 50% reduction in seizure frequency.[27] Persistent seizures have many physical, psychological, and socioeconomic impacts on patients, including affecting central nervous system structure and function. Seizures can lead to changes in neuronal hyperexcitability and axonal rewiring that result in a progressive decrease in the threshold for additional seizures[28–30]; in addition, they can induce structural changes in the brain that resemble premature aging and contribute to cognitive decline.[8,31] Seizures also increase the frequency of comorbidities,[32] increase the risk of premature death,[8] and lead to psychosocial, medical, and economic challenges.[8] In our survey, multiple components of QoL were found to be impacted by uncontrolled epilepsy, with work capability and psychological well-being/mental health considered by all stakeholders as the most affected. Persistent seizures adversely affected patients' ability to travel independently, work, and manage finances, consistent with other studies.[8,33,34] Notably, patients were significantly less likely than HCPs and caregivers to report a high impact of uncontrolled seizures on various aspects of QoL. This may suggest that while patient participants might be demonstrating resilience, the profound impacts of seizures on QoL may be more recognized by HCPs and caregivers. Additionally, patients may underreport their seizures or impacts on QoL for various reasons, such as employment pressures or the need to continue driving. Patient participants overall reported a lower seizure frequency compared with patients attended by caregivers, who are typically younger, have more severe disease and would be expected to have other comorbidities (e.g., learning disabilities). Therefore, impacts on QoL may simply reflect the burden of continuing seizures.

Similar findings have been reported in a self-administered online survey in which most patients and caregivers expressed seizure freedom as their primary goal of treatment. Those achieving this goal were 2.5-fold more likely to consider their health as "excellent" compared with those who had experienced a seizure in the previous 5 years. Furthermore, ongoing seizures were associated with limitations to education, employment, and activities of daily living, and had a significant impact on feelings of stigma and patients' overall lives.[35]

Low satisfaction with treatment was found across stakeholder groups. Low satisfaction was particularly pronounced among caregivers, with almost half reporting a loss of hope that the disease could be controlled. This could be attributed to the characteristics of patients receiving caregiver support, some of whom may have complex childhood conditions such as developmental and epileptic encephalopathies, which have a significant impact on the QoL of both patients and their caregivers.[12,36] In our study, patients supported by caregivers were younger, had a higher prevalence of genetic-related epilepsies, and were

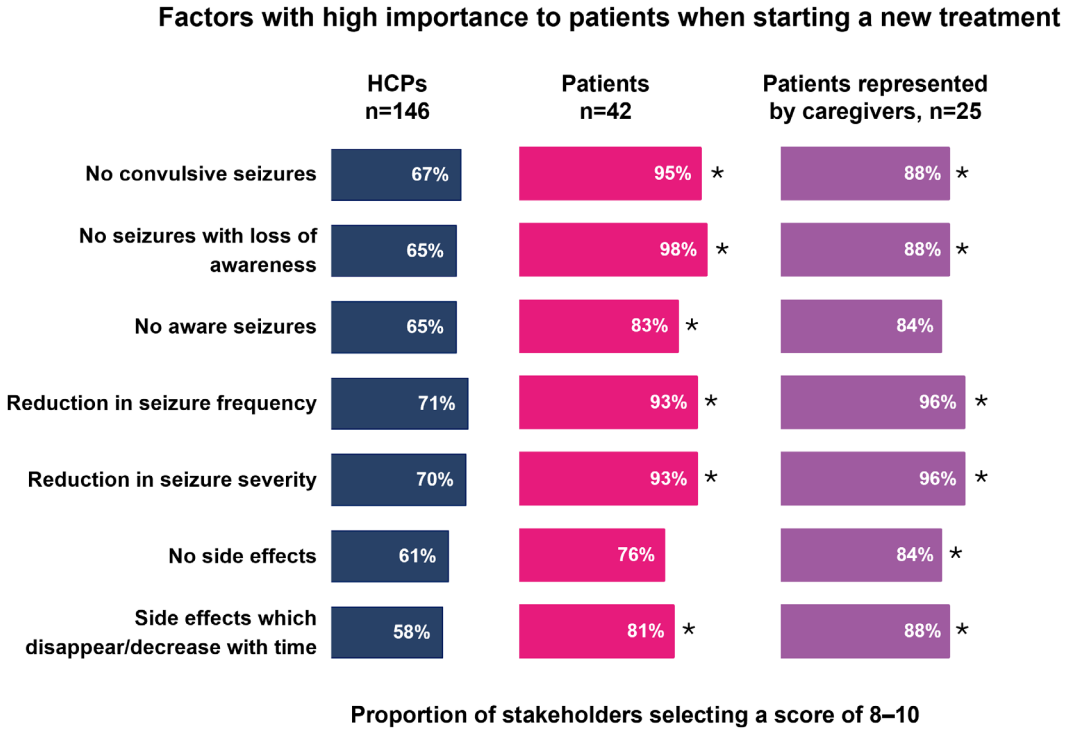

FIGURE 4 Factors with high importance to patients when starting treatment, based on ranking by stakeholders. Bars show the proportion of stakeholders selecting a score of 8–10 (i.e., high importance) for each factor based on a 10-point scale. *$p < 0.05$ versus HCPs. HCPs, healthcare providers.

more likely to be drug-resistant compared with the patient participants.

Our finding that satisfaction was low across multiple aspects of treatment suggests an unmet need for delivery of more effective and safer treatment options as quickly as possible, as described earlier. This is compounded by limited awareness of treatment options by all stakeholders.

Another burden reflected in low satisfaction scores among stakeholders was the excessive number of tablets/doses taken by patients and the frequency of administration. In this regard, simplifying treatment is known to provide a number of advantages for patients.[37] A higher number of ASMs and increased medication burden have been linked to a greater risk of AEs (e.g., cognitive effects), drug interactions, diminished QoL, and reduced compliance. Minimizing the ASM burden without compromising seizure control is crucial to mitigating these risks. Despite this, in clinical practice, HCPs may be reluctant to reduce ASM use due to concerns about seizure recurrence, particularly when additional medications have led to better seizure control.[37]

The finding that 29% of patients lacked confidence in achieving disease control indicates the potential for therapeutic nihilism among patients, particularly for those who may have experienced AEs with previous treatment. For patients, refusal to take new ASMs is an important barrier to favorable outcomes. While 12% of patients reported refusing new ASMs in our study, this proportion was much higher when reported by HCPs (30%), suggesting that patients may underestimate their willingness to try new treatments.

Patient awareness of treatment options, and their potential benefits with regard to efficacy and tolerability, is crucial in tackling this issue. This can be improved through better communication with HCPs and effective patient/caregiver education, including the use of online apps and patient support groups, all of which were acknowledged as important educational resources by patients/caregivers in our survey. Patients also cited difficulty predicting breakthrough seizures as a major challenge. These may occur when patients are particularly vulnerable and feel that life is on hold as they await seizure freedom.[26] Other significant challenges for patients include judging seizure severity at onset and deciding whether to use medication to reduce severity and/or seek emergency care. These insights emphasize the complexity of seizure management for patients and the importance of good educational support and shared treatment goals focused on seizure freedom.

Unsurprisingly, awareness of seizure warning signs in caregivers was lower than among patients, emphasizing the need for additional educational strategies to support caregivers. Indeed, empowerment-based education for

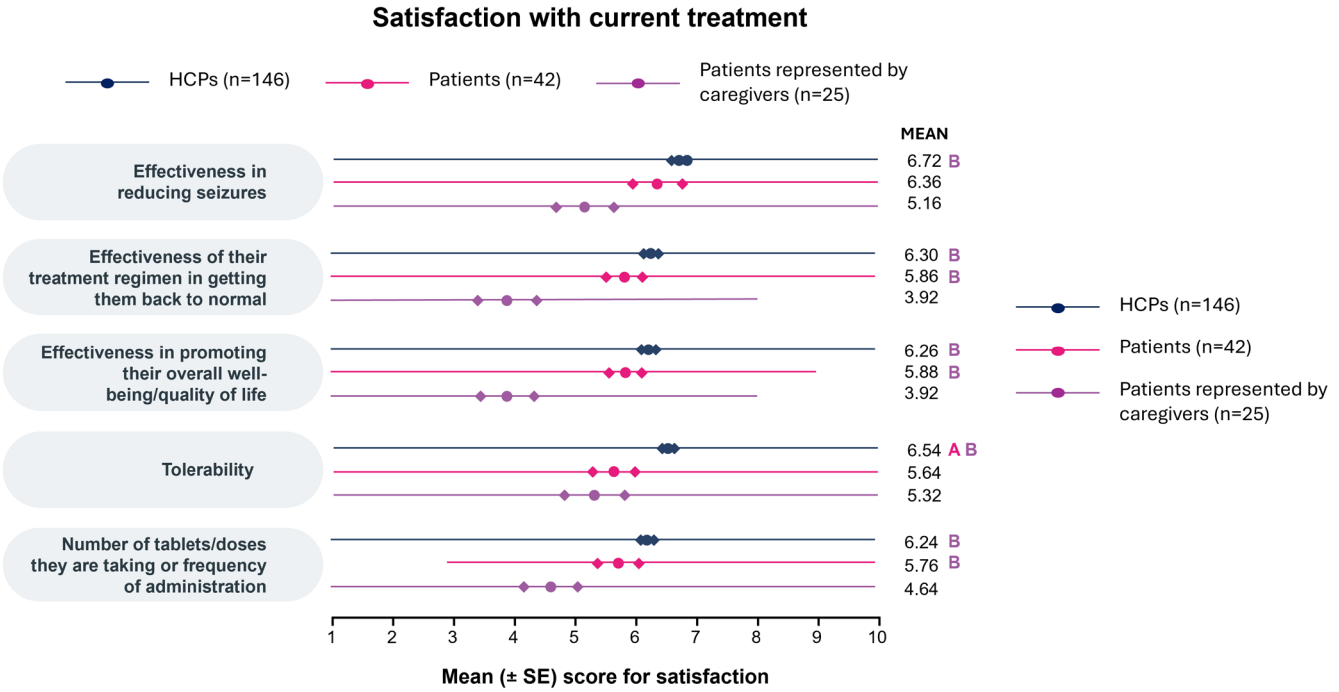

FIGURE 5 Satisfaction with current treatment according to different stakeholders. Mean (±SE) scores for satisfaction are shown based on a Likert scale (1–10). (A) $p < 0.05$ versus patients; (B) $p < 0.05$ versus patients represented by caregivers. HCPs, healthcare providers; SE, standard error.

caregivers has been shown to improve their ability to manage epilepsy for their patients.[38]

Our study revealed a significant gap between HCPs and patients/caregivers regarding the perceived value of technology to facilitate communication, including digital apps, wearable devices, online support groups, and training courses. Patients and caregivers were generally more receptive to these tools than HCPs, who may be discouraged by limited awareness or the lack of patient-focused evidence demonstrating their impact on patient outcomes. However, given the wide availability of supportive technologies for seizure detection/monitoring and the willingness of patients and caregivers to adopt them, there is an opportunity to expand their use and development in routine care,[39] thereby helping to bridge educational gaps among patients and caregivers.

Our study identified several other barriers to effective seizure control. Consistent with previous studies,[14] many stakeholders reported insufficient time during clinic visits to address patients' concerns; 55% of patients and 75% of HCPs felt there was inadequate time to explore doubts, uncertainties, or treatment-related discomforts. There is some debate on how long effective consultations should take. According to the Spanish Society of Neurology, initial consultations should last 45 min, with 20 min for follow-up consultations. In general settings, 18 min has been suggested as sufficient to undertake a shared decision, although time quality is also important.[40] The short consultation times emphasize the need for effective educational materials to support patient visits.

Disconnects between stakeholder groupings may also reflect different priorities. It is evident from our survey that different topics for discussion are prioritized by HCPs (e.g., adherence, pregnancy-related AEs) and patients/caregivers (e.g., psychosocial support, efficacy/tolerability). This may be a product of medicolegal concerns and professional pressures among HCPs, but may also relate to HCPs considering that there is a lack of evidence base or insufficient resources/service provision to warrant certain discussions.[14]

This study has a number of limitations. First, the sampling strategy resulted in relatively small and uneven groups, including an overrepresentation of HCPs and a tendency for patients in the caregiver group to be younger and more severely affected than those in the patient group. Therefore, we cannot exclude selection bias, and inferential findings should be considered with particular caution. In addition, the exclusion of participants with missing data may introduce additional bias and further limit the generalizability of subgroup comparisons. Second, the patient populations included multiple epilepsy diagnoses, and therefore seizure frequency, type, and severity would be expected to vary widely within groups. Third, we cannot exclude an element of response bias. For example, regional differences in access to epilepsy services may have affected responses, such as stakeholders based

in metropolitan versus rural areas. Finally, the study was conducted by online survey, which did not allow for clarification or follow-up of responses.

Several questions require further exploration. These include examining the heterogeneous burden of uncontrolled epilepsy and its impact on beliefs and behaviors. Additionally, it is essential to investigate whether HCPs perceive non-seizure-free patients as unlikely to pursue seizure freedom and whether a loss of hope among providers leads to fewer ASM modifications. Similarly, understanding whether a lack of hope discourages patients from accepting ASM modifications could offer valuable insights. It may also be beneficial to explore attitudes and beliefs around advanced epilepsy therapies, as clinical guidelines recommend that people with DRE should be considered for other treatments (e.g., surgery, neuromodulation, keto diet) in addition to more ASM trials. Finally, identifying preferred communication tools for patients and caregivers may help improve engagement and support.

5 | CONCLUSIONS

This survey highlighted the continued and multifaceted disease burden among patients with DRE and their caregivers and shows current unmet needs. While seizure freedom is considered the ultimate goal of treatment, disparities exist among key stakeholders regarding treatment expectations and management. This misalignment of expectations between stakeholders is a modifiable barrier to seizure freedom and to patient satisfaction with care.

AUTHOR CONTRIBUTIONS

Simona Lattanzi, Bettina Schmitz, Nuno Canas, John Paul Leach, Caroline Benoist, Daniela Pierucci, and Elena Álvarez-Barón contributed to the conception and design of the study, discussed the results, revised the first draft, and contributed to the final manuscript. All authors have read and approved the submitted version of the manuscript and accept responsibility for its content.

ACKNOWLEDGMENTS

Data collection and analysis was supported by Maria Bempelou, Francesco Capuzzi, Myriam Diard, and Izabel Freret at IQVIA. Medical writing support was provided by Ian Marshall at WriteMedical Ltd. and was funded by Angelini Pharma. Open access publishing facilitated by Universita Politecnica delle Marche, as part of the Wiley - CRUI-CARE agreement.

FUNDING INFORMATION

This research was funded by Angelini Pharma.

CONFLICT OF INTEREST STATEMENT

S.L. has received speaker's or consultancy fees from Angelini Pharma, Eisai, GW Pharmaceuticals, Medscape, NewBridge Pharmaceuticals, and UCB Pharma, and has served on advisory boards for Angelini Pharma, Arvelle Therapeutics, BIAL, Eisai, GW Pharmaceuticals, Rapport Therapeutics, and UCB Pharma. B.S. has received speaker's or consultancy fees from Angelini Pharma, Desitin, Eisai, Precisis, Sanofi, and UCB Pharma outside the submitted work. N.C. has no conflicts of interest to disclose. J.P.L., C.B., D.P., and E.A.B. are employees of Angelini Pharma. 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 original contributions generated for this study are included in the article or its Supplementary Materials. Further inquiries can be directed to the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Lattanzi S, Schmitz B, Canas N, Leach JP, Benoist C, Pierucci D, et al. Perspectives on the burden of drug-resistant epilepsy and treatment priorities: Findings from a multistakeholder survey. Epilepsia Open. 2026;11:787–800. https://doi.org/10.1002/epi4.70226