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Perspective

Ethical considerations in the surgical and neuromodulatory treatment of epilepsy

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ABSTRACT

Surgical resection and neuromodulation are well-established treatments for those with medically refractory epilepsy. These treatments entail important ethical considerations beyond those which extend to the treatment of epilepsy generally. In this paper, the authors explore these unique considerations through a framework that relates foundational principles of bioethics to features of resective epilepsy surgery and neuromodulation. The authors conducted a literature review to identify ethical considerations for a variety of epilepsy surgery procedures and to examine how foundational principles in bioethics may inform treatment decisions. Healthcare providers should be cognizant of how an increased prevalence of somatic and psychiatric comorbidities, the dynamic nature of symptom burden over time, the individual and systemic barriers to treatment, and variable sociocultural contexts constitute important ethical considerations regarding the use of surgery or neuromodulation for the treatment of epilepsy. Moreover, careful attention should be paid to how resective epilepsy surgery and neuromodulation relate to notions of patient autonomy, safety and privacy, and the shared responsibility for device management and maintenance. A three-tiered approach—(1) gathering information and assessing the risks and benefits of different treatment options, (2) clear communication with patient or proxy with awareness of patient values and barriers to treatment, and (3) long-term decision maintenance through continued identification of gaps in understanding and provision of information—allows for optimal treatment of the individual person with epilepsy while minimizing disparities in epilepsy care.

1. Introduction

Epilepsy is among the most common neurological disorders worldwide, affecting greater than 70 million people and with an overall incidence of 50.4 per 100,000 individuals annually [1,2]. For people with epilepsy (PWE) with seizures poorly controlled by medication, different surgical procedures may be indicated [3]. Today, many different surgical procedures, including ablative procedures such as resection or laser interstitial thermal therapy (LITT), and palliative neuromodulatory device (ND) procedures such as implantation of systems for vagus nerve stimulation (VNS), deep-brain stimulation (DBS), or responsive neurostimulation (RNS), are employed for the management of epilepsy, and these treatments continue to be advanced and refined [4,5]. In this narrative review-based opinion piece, we explore important considerations in the surgical and neuromodulatory treatment of epilepsy and employ a bioethics-laden framework to highlight key elements of a comprehensive approach (Table 1).

2. Methodology

This manuscript is a narrative review-based opinion piece with ethical analysis based on the viewpoints of the authors. The prescriptive and proscriptive statements made in this manuscript reflect the views of the authors considering relevant empirical evidence when present. We emphasize that this is an opinion piece, rather than an authoritative piece or consensus statement.

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Table 1
Summary of considerations relating to epilepsy treatment and associated **ethical issues**.

Domain	Consideration	Summary
Epilepsy treatment	Progression of therapy	Epilepsy treated with resection/ablation or neuromodulation if refractory to antiseizure medications
	Comorbidities	People with epilepsy have many comorbidities, most notably cognitive impairment and psychiatric disorders
	Barriers to surgical treatment	Barriers are access to care, limited knowledge, misconceptions, negative perceptions, stigma, difficulty navigating healthcare system, poor self-management
	Cultural considerations	Levels of knowledge and conceptions of epilepsy vary among cultures
Surgical treatment of epilepsy	Decision-making capacity and informed consent	Stepwise process that requires neurosurgeons to take appropriate measures to best inform patients
	Beneficence and nonmaleficence	Essential in determining the appropriate treatment option for an individual
	Justice, access to care, and resource allocation	Guides prioritization of treatments for people with epilepsy and of people with epilepsy for a given treatment
Specific to neuromodulatory devices in epilepsy	Autonomy	Anticipation problem, desperation problem, intraoperative revocation of consent, and brainjacking
	Privacy, confidentiality, and safety	Data may be accessed inappropriately or used for purposes other than patient care or research
	Responsibility for device management and maintenance	People are responsible for knowing how to use their device and what to do when it is not functioning properly
Additional aspects	Status epilepticus	Substitutes for informed consent may be necessary due to urgent nature
	Multidisciplinary care teams	Allow weighting of ethical principles while considering appropriate progression of therapy, comorbidities, barriers, cultural considerations, and treatment maintenance

3. Epilepsy treatment considerations

3.1. Progression of therapy

The International League Against Epilepsy (ILAE) recommends antiseizure medicines (ASM) as the initial therapy for epilepsy [6,7]. Though most PWE respond well to pharmacological treatment, approximately seizures of 30% of PWE are medically refractory [8], defined as a failure of 2 ASMs at appropriate doses [9]. Surgery is a well-established and efficacious treatment for medication-resistant epilepsy, if the seizure focus can be localized and removed/ablated without causing unacceptable neurologic effects [10-16]. Many different types of epilepsy surgery exist, including resective approaches such as anteromedial temporal lobectomy and focal neocortical resection, stereotactic ablative procedures such as LITT, and disconnective approaches such as corpus callosotomy and multiple subpial transections [10,17,18]. Neuromodulation is a promising alternative for those with epilepsy not amenable to resection/ablation [19,20]. Neuromodulatory techniques, including VNS, DBS, and RNS, lack undesired systemic effects of ASMs and offer reversible alternatives to surgical resection. However, seizure freedom rates for neuromodulation are far lower than for resection [19]. Although approved for focal epilepsy and some associated targets, VNS, RNS, and DBS may be used for generalized epilepsy, off-label targets, or as part of clinical trials [21,22]. Treatment progression may not be linear. Physicians may experience uncertainty regarding optimal or feasible treatment approaches based on factors such as epileptogenic zone, underlying pathology, age, PWE or proxy values, and resource or technical limitations.

3.2. Multidisciplinary care teams

Multidisciplinary care teams are often involved in managing PWE. Many surgical centers have multidisciplinary patient management conferences, in which neurologists, neuroradiologists, neuropsychologists, neurosurgeons, and psychiatrists discuss patients and develop treatment strategies [23,24]. These teams may optimize treatment selection by weighing core ethical principles while considering appropriate progression of therapy, comorbidities, barriers, cultural considerations, and treatment maintenance.

3.3. Comorbidities

Compared to the general population, PWE are up to eight times more likely to have comorbidities including heart disease, peptic ulcers, arthritis, migraine, depression, and anxiety relative to the general population [25-27]. The increased burden of comorbidities accounts for much of the economic costs associated with epilepsy. Among PWE who are privately insured in the US, approximately 80% of healthcare expenditures are related to comorbid conditions, rather than direct costs of epilepsy [28].

Two particularly relevant categories of comorbidities for the management of epilepsy are cognitive impairment and psychiatric disorders [27,29,30]. The association between cognitive impairment and epilepsy is well-documented, occurring in 25% of people with temporal lobe epilepsy, and signs of impairment may precede the diagnosis of epilepsy [31]. Significant memory impairment may also be a consequence of surgery [32,33]. The manifestations of cognitive impairment in epilepsy are heterogeneous, depending on both the location of epileptogenic area(s), the duration of disease, frequency of seizures, and the underlying pathology [34]. Of note, the presence of any neurological comorbidity has been associated with a greater than four-fold increase in mortality from epilepsy [35]. Additionally, failure to treat psychiatric comorbidities may entail a heightened risk of suicide [36,37] and diminished quality of life [38]. Given the interplay between the treatment strategies of epilepsy and psychiatric disorders, early recognition of risk factors for psychiatric comorbidities is essential [39].

3.4. Barriers to surgical treatment

Perhaps the most studied barrier to epilepsy surgery is lack of access to specialized neurology and neurosurgical care. Approximately 80% of people globally with epilepsy live in low- and middle-income countries (LMICs) [1,40] and 75% of these individuals receive no or inadequate care for their epilepsy [41,42]. The proportion of PWE in LMICs who are candidates for and receive epilepsy surgery is low, though existing studies suffer from methodological weaknesses [43,44]. These gaps extend to high-income countries, where < 1% of people with drug-resistant epilepsy are evaluated at a specialized epilepsy center due to underreferral and delays in referral [45-47]. A total of 36.7% of people with newly diagnosed epilepsy in the United States remained untreated up to 3 years after diagnosis [48]. A lack of awareness of the seriousness of the diagnosis, trained providers, facilities, and funding may be responsible [49]. Additionally, many PWE report having limited knowledge about their condition [50]. Overestimation of risks is common: 51% of PWE would not consider surgical treatment even if guaranteed to stop seizures without deficits [51-54]. Negative perceptions of procedures, stigma [55,56], difficulty navigating the healthcare system [50], and poor self-management also occur [50]. In LMICs, systemic barriers, including the magnitude of the epilepsy burden, poverty, few epilepsy specialists, inadequate healthcare infrastructure and resources, inability to travel to an epilepsy center, limited knowledge about epilepsy, and social stigma, are common [55,57,58]. Up to 80% of countries do not have an epilepsy surgery program [59]. Individual barriers often interact synergistically [45].

3.5. Cultural considerations

Culture remains an important consideration in the diagnosis and treatment of epilepsy. Conceptualizations of the etiology of epilepsy vary among cultures, often involving biological, sociospiritual, or biospiritual factors. A common belief is that epilepsy is a communicable and contagious disease [60-63]. Other explanations for the cause of epilepsy include possession by an evil spirit, a form of dementia, a type of mental disorder, a blood disorder, or solely a psychiatric disease [63-70]. Cultural variations extend to treatment practices. Some individuals may believe that epilepsy cannot be cured or controlled [62], while other PWE may be sent to traditional healers or religious clerics [71-74]. These cultural beliefs, along with stigma, present further challenges to surgical treatment.

4. Ethical considerations for surgical treatment of epilepsy

4.1. Decision-making capacity and informed consent

Informed consent involves substantive communication between doctors and PWE to ensure PWE have been provided with requisite knowledge to make decisions about their medical care (Fig. 1) [75,76]. The first step of informed consent between doctors and PWE involves determination of decision-making capacity (Fig. 1) [77,78]. People with temporal lobe epilepsy and generalized epilepsy may have deficits in decision-making [79]. Similarly, PWE with significant cognitive impairment or other comorbidities may not have decision-making capacity [80-82]. Baseline neurocognitive assessment is a routine component of a presurgical evaluation and helps in ascertaining this. If an individual is judged not to have decision-making capacity, this responsibility transfers to a legal representative, who may be family, a pre-appointed proxy, or a party determined by a court [83].

Once determination of decision-making capacity has occurred, PWE or proxies must be given enough information so that they may make an informed decision about treatment [77]. This does not require that PWE or proxies retain all information conveyed to them, but rather that information is conveyed in a comprehensive and comprehensible manner [77]. Baseline recall among PWE after informed consent discussions may be low [84], and the complexities of epilepsy treatment may be challenging to understand. Interventions used during informed consent discussions, such as a

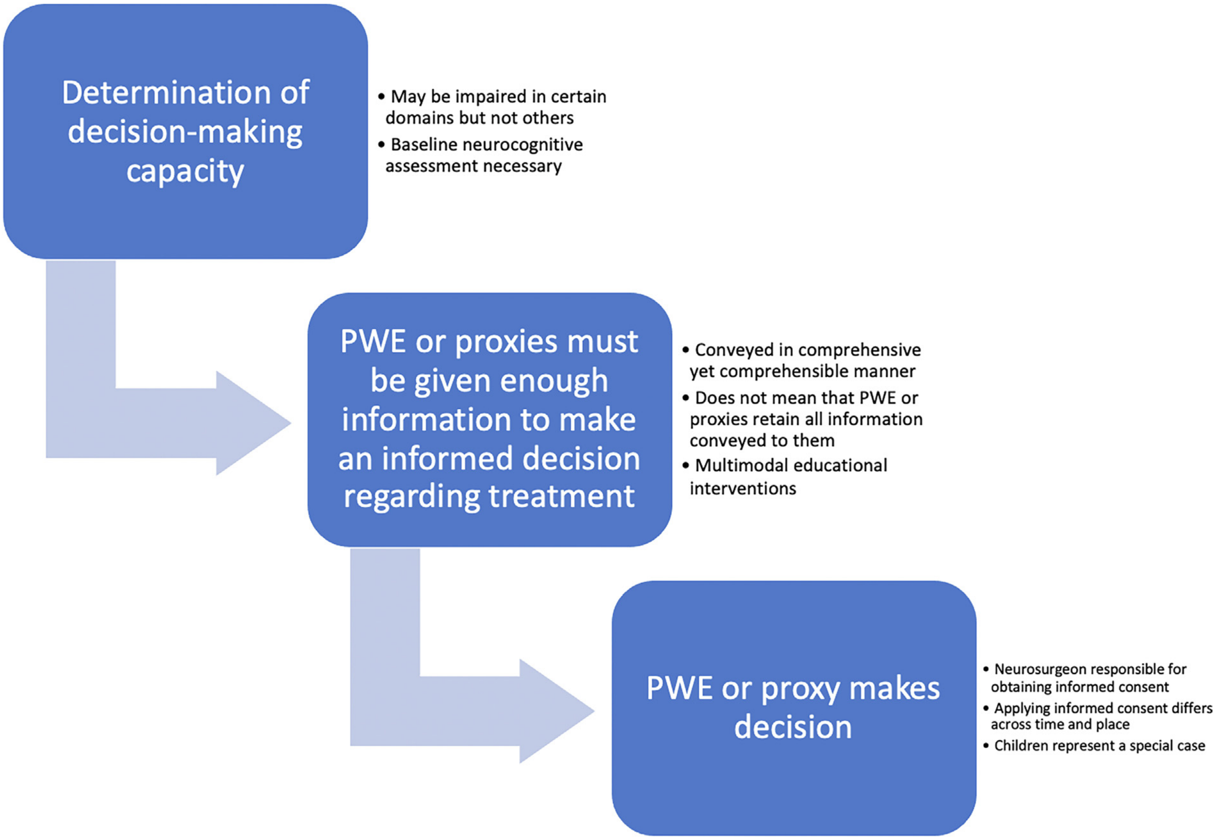

Fig. 1. The steps in the process of informed consent for people with epilepsy (PWE): 1) determination of decision-making capacity, 2) information provision to enable informed consent, and 3) patient or proxy selection of a decision regarding medical care.

specialized consent form, interactive websites, question prompt lists, and illustrations, must be appropriately designed based on the informational needs and preferences of PWE or their proxies and anticipated baseline levels of health literacy [77,85,86]. Similarly, clear communication, including avoidance of jargon, must be utilized. These tools and practices may help bridge gaps in clinical understanding between healthcare personnel and PWE or proxies. Assessment of PWE or proxy understanding of the consent discussion is also necessary [77]. Providers should answer questions in appropriate detail, correct misunderstandings and misconceptions, and convey additional detail where appropriate.

There are caveats in the informed consenting process. First, the question of who is responsible for obtaining informed consent commonly arises. It is important to distinguish the act of obtaining informed consent, involving a discussion with PWE or proxies to communicate relevant knowledge, from the act of documenting informed consent for liability purposes. Per the legal ruling in *Shinal v. Toms*, the attending neurosurgeon cannot delegate the informed consent discussion given their role as the individual performing the surgery [77,87]. Of equal importance are informed discussions between PWE and neurologists responsible for programming the ND because of their role in the long-term management. Auxiliary staff may document informed consent given that this involves completing paperwork to maintain compliance with legal standards, but documentation of informed consent by the treating physician is optimal. Second, applying informed consent to clinical practice differs across time and place [77]. Conceptualization of informed consent as a continual process is useful [88]. Physicians must iteratively assess decision-making capacity and inform PWE or proxies regarding the condition and treatment developments throughout the duration of treatment [77]. This is particularly relevant to PWE due to the propensity for memory decay and changes in decision-making capacity after epilepsy surgery [79,84]. Third, it is important to consider the case of children with epilepsy. Children under age 18 are generally considered to not have decision-making capacity and are therefore unable to provide informed consent [89]. In these situations, healthcare providers should promote a shared decision-making approach wherein informed consent is provided by the parents with the assent of the PWE [90]. To protect the best interests of the PWE, assent should include helping them to achieve a developmentally appropriate awareness of their condition, conveying what to expect with treatment or diagnostic tests, assessing the understanding of the situation, and soliciting an expression of their desire to participate in any proposed treatment [90]. Taking a comprehensive approach to informed consent for epilepsy surgery and neuromodulation will allow for greater patient-centered care.

4.2. Beneficence and nonmaleficence

Beneficence requires optimization of the short- and long-term effectiveness of treatment [91]. Nonmaleficence involves minimization of risks and possible adverse effects resulting from treatment [91]. Determining the optimal treatment option inherently involves maximizing both principles to the extent possible based on the individual context [92]. Consideration of subsidiarity, defined as selecting the least burdensome alternative, and proportionality, ensuring comparable risks and benefits, provides a conceptual structure for leveraging beneficence and non-maleficence [91].

First, treatment strategies must be initially considered in order of highest benefit-to-risk ratio [21]. Often, PWE are candidates for multiple procedures. Resective epilepsy surgery is traditionally utilized prior to neuromodulation, when possible, if it has a higher chance of seizure freedom. As an example, although temporal lobectomy carries greater risk than implantation of a VNS system for mesial temporal sclerosis, lobectomy may be more effective as the initial surgical option. However, modern advances such as minimally invasive LITT may thread the needle between risk and benefit in cases such as these. In many cases, however, uncertainty may limit the ability of a single physician to determine the most feasible, effective, and safe treatment. Factors such as off-label use of NDs or qualification for clinical trials may complicate treatment decisions further.

Second, decision-making for the individual patient must consider group-level patient-reported outcomes in addition to common clinical parameters [21]. Traditionally, seizure freedom and neurological deficits have been utilized as the primary outcomes for determining whether surgery is useful. However, patient-reported outcomes must also be considered. Epilepsy surgery is often associated with improvement in quality of life, but factors such as preoperative psychological function, postoperative seizure freedom, antiepileptic drug adverse effects, and employment status, largely mediate this relationship [93-97]. The potential for improved quality of life must be considered relative to preoperative quality of life to avoid cases in which surgery is offered to a PWE with low probability of improvement in quality of life or cases in which surgery is not recommended for PWE with a low baseline quality of life when there may be substantial improvements [92].

Third, an individual's values and preferences must be incorporated into decision making [98]. Improvement in seizure freedom may entail experiencing expected sensorimotor deficits or long recovery times and is not always sufficient to improve quality of life alone [99]. For example, while LITT may be less effective than resection based on short-term data for mesial temporal sclerosis [100-102], many PWE readily accept this in exchange for a shorter recovery time and lower probability of complications.

Fourth, considerations of subsidiarity and proportionality change over time. Consideration of alternative treatment is necessary when the current treatment option is no longer the least burdensome alternative or when the risks outweigh the benefits. When PWE who experience limited reduction in seizure frequency after resection, they may be transitioned to neuromodulation given neuromodulation allow them to attain symptomatic relief. Continued appraisal of these ethical principles is required.

Lastly, it is important to remain cognizant that statistical improvements in clinical parameters do not necessarily correlate with meaningful improvements with quality of life for the individual, necessitating individualized weighing of risks and benefits when making treatment decisions.

4.3. Justice, access to care, and resource allocation

Justice mandates appropriate distribution of risks and benefits [91]. This principle guides the prioritization of treatments for patients and of patients for a given treatment. People with epilepsy who stand to attain the greatest benefit from surgery should be prioritized if necessary. Similarly, the treatment with greatest utility for the individual based on risk to benefit ratio, quality of life, and values and preferences should be prioritized for the individual. Two salient practical issues relating to justice are access to intervention and resource allocation.

Access to surgery continues to be a considerable limitation for PWE worldwide. Lack of access to care occurs on two levels. First, PWE may not have access to the baseline epilepsy care that would help determine candidacy for surgery [1,40-42]. Second, PWE may not have access to specialized surgical intervention [43-47]. These factors interact in a synergistic fashion to lead to profound disparities in epilepsy surgery locally and globally. This is more profound for access to neuromodulation surgery for epilepsy, given the cost of NDs, long-term maintenance and the need for revisions over time, and the essential nature of expertise in programming/managing. Moreover, making epilepsy surgery available geographically may cause differences in the quality of care. Centers with greater volumes of epilepsy surgery have lower complication rates [103-106]. The National Association of Epilepsy Centers' designation of centers as level 1 through level 4 reflects the availability of services at different institutions. Certain surgical procedures such as RNS are typically performed only in level 4 centers due to the multidisciplinary expertise at these institutions, and these centers may then become quite experienced with these procedures. Balancing the concentration of expertise at certain locations for patient safety while increasing access to care is paramount.

Comprehensive approaches are necessary to improve access to epilepsy surgery [45]. People with epilepsy and family-level measures involve increasing availability of information about surgical options, location of epilepsy centers and managing comorbidities [45]. Physician and health system measures include increasing the referral of appropriate patients for surgery, training multidisciplinary teams to address cultural and personal barriers, and creation and promulgation of surgical referral guidelines [45]. Partnerships with outside epilepsy centers of lower levels have also been shown to improve access to epilepsy surgery [107]. Society-level steps include reducing stigma regarding epilepsy and epilepsy surgery, empowering community advocacy groups, and creating financial mechanisms to mitigate the financial costs of epilepsy surgery [45]. Protection of vulnerable PWE and the pursuit of equity must pervade these initiatives in order to optimally promote justice [108]. Additional educational and resource support may be provided to low-volume centers to enable access to care while maintaining patient safety.

The related principle of resource allocation is particularly important for NDs. Factors such as number of devices, cost, return on investment, reimbursement, sufficient healthcare personnel, and sufficient neurosurgeon time affect how NDs are allocated. Moreover, specialists must weigh the expected costs of NDs against those of ASMs, which have been implicated as the main contributor to direct costs associated with the treatment of epilepsy [109]. The degree to which resource allocation considerations are relevant may be divided into three possible scenarios [110]. In the first scenario, provision of NDs to PWE is restricted by substantial issues such as a limited number of devices, high costs, and a paucity of specialists to implant the devices and manage preoperative and postoperative care [110]. Prioritization of some PWE is the norm, and maximizing benefits relative to risks guides allocation in these situations. In the second scenario, resource limitations are moderate [110], due to quotas on NDs, prohibitive costs for some, reimbursement, adequate neurosurgical staff, or ability of neurosurgeons to devote time to ND implantation. In these contexts, some PWE are prioritized over others. In the third scenario, there are no resource-limiting factors [110]. Neuromodulatory devices are readily available and accessible, reimbursement is available and adequate, and time and staff are adequate for neurosurgeons to perform these procedures. Here, prioritization of certain PWE over others is unnecessary. However, there are associated challenges in practice. The "return on investment" is increasingly utilized as initiatives to expand access to care while decreasing cost continue to arise [21], though the definition of "return" is controversial. Although the quality-adjusted life year (QALY) is often used to define "return," there is inherent subjectivity in adjudicating the acceptable threshold for provision of treatment, and this threshold likely varies based on context [21]. Similarly, the triumvirate of increasing costs with increasing sophistication of NDs, inability to afford care for some PWE, and undervaluing of these procedures in reimbursement structures adds complexity. These challenges necessitate three corresponding solutions to ensure justice. First, methods to appraise which scenario is applicable are necessary to guide resource allocation initiatives. Second, development of context-specific strategies for financing and resource allocation is required to ensure PWE who may benefit from NDs are able to access them [21]. Third, these strategies must adapt as innovative treatment options are developed [21]. Opportunities for remote device programming and uploading of device data to cloud-based servers for remote analysis may improve the access to specialized care for people who live far from a managing center for epilepsy NDs.

5. Ethical considerations specific to neuromodulatory devices in epilepsy

5.1. Autonomy

Autonomy considerations particularly relevant to ND implantation include the anticipation problem, the desperation problem, intraoperative revocation of consent, and brainjacking (Table 2) [21]. First, the anticipation problem describes the inability to predict identity, attitudes, or satisfaction after treatment [111]. After ND implantation, PWE may feel a change in identity due to altered mood, interest, beliefs, values, or activities [111-113]. While individuals may understand the possibility of identity change when deciding to undergo ND implantation [111-113], there may be a discrepancy between this understanding in theory and in practice as PWE cannot reasonably understand how they will interpret having an implanted brain device until this actually occurs [111-113]. It is important to underscore the possibility of perceived identity change and associated challenges during informed consent discussions with PWE [111]. Additionally, a PWE may be dissatisfied with the treatment due to exaggerated hopes for clinical improvement or the discrepancy between the objective medical view and subjective perspectives of PWE [111,112]. Although this may occur for resective epilepsy surgery, the likelihood or extent of this issue is greatest for NDs due to their technologically advanced nature, media focus, and associated potential for sensationalized accounts of the effects of these devices [114,115]. Moreover, expectation setting is of specific importance for NDs because the rate of seizure freedom is lower than with some types of resective/ablative surgery and there is limited possibility of "cure" [116,117]. Strategies focused on providing comprehensive information to PWE epilepsy regarding the effects and limitations of NDs, correcting misconceptions, and tempering expectations enables the alignment of PWE and provider expectations and result in improved patient-reported outcomes [111,118,119].

Second, the desperation problem occurs when patients disregard realistic information provided to them during informed consent discussions due to the belief that they must receive the ND [111]. People with medically intractable epilepsy who are not candidates for traditional epilepsy surgery or whose seizures failed to experience clinical improvement or improved quality of life following resective/ablative surgery experience considerable distress and may wish to receive ND implantation regardless of potential risks or other advice [120,121]. At times this takes the form of an attitude that "something has got to be done." The decision-making capacity of the PWE should be validated before implantation of the ND through an assessment of cognitive status [122]. Additionally, repeated assessment of decision-making capacity, understanding of expectations, and continued counseling over time are useful to honor patient autonomy due to changes in hopes and opinions over time and to assess any changes in cognitive status that may have occurred as a consequence of prior procedures [21,123].

Third, PWE may revoke consent in the middle of any awake surgery, whether resection or ND implant, requiring that providers

Table 2
Considerations regarding autonomy in implantation of neuromodulatory devices.

Term	Definition
Anticipation problem	People with epilepsy are unable to predict identity, attitudes, or satisfaction after treatment
Desperation problem	People with epilepsy disregard realistic information provided to them during informed consent discussions due to the belief that they must receive the neuromodulatory device
Intraoperative revocation of consent	Patients may decide that they no longer wish to receive surgery during the procedure
Brainjacking	Hackers gain access to and exert malicious control over neuromodulatory devices

balance the current wishes of PWE with expected therapeutic effects in a case-by-case manner [124-126]. Cognitive and psychological testing batteries prior to ND implantation or cognitive testing in the operating room may reduce this possibility but may result in financial burden [21].

Fourth, autonomy may be compromised if a third party manipulates the stimulation parameters in clinic or remotely [111]. Blind or targeted "brainjacking" occurs when hackers exert malicious control over NDs, particularly DBS devices [127,128]. Although the true effect of brainjacking on autonomy depends on the third party and effects of the attack, autonomy is nonetheless compromised [129]. This possibility renders ethical considerations of autonomy in ND implantation particularly complex [129]. The likelihood of brainjacking can be reduced by mandating that parameters of NDs are altered only after obtaining consent by designated providers and adding further advanced security features to protect against hacking [21]. It is important to note that concerns regarding "brainjacking" remain hypothetical given that no cases of malicious third-party manipulation have been reported.

5.2. Privacy, confidentiality, and safety

Given the large amount of data collected and stored, privacy, safety, and confidentiality concerns exist when using NDs for epilepsy [130]. Collection of data may allow others to infer the thoughts or emotions of a PWE and associated misuse of thoughts and emotions in non-medical settings including employment, insurance, or the legal system [113,127]. Similarly, confidentiality may be compromised if these data are accessed without just cause of consent, court order, continued treatment, compliance with the law, or to communicate a threat [131]. Violations of privacy and confidentiality may endanger the safety and security of the individual [132]. Storage of large quantities of data including demographics, clinical scales, surgical data, device parameters, outcomes, EEG tracings, brain imaging, and complications in registries exacerbates these risks due to the potential for detailed data to be compromised on a large scale [113,127]. To address these concerns, data must be used solely for treatment of epilepsy, individuals who will have access to data must be trained in how to handle and secure data, and appropriate security measures such as encryption and partitioning must be instituted to ensure that individuals not involved in care are unable to access the data [21]. Additionally, some companies store patient data from surgical sites on their corporate servers for internal research, and provide treating physicians with limited web-based access to that data. People with epilepsy must be made aware of this practice. In conjunction, these tenets will promote privacy, safety, and confidentiality.

5.3. Responsibility for device management and maintenance

Neuromodulation is a distinct surgical treatment modality for epilepsy relative to traditional surgery because management and maintenance are required for continued efficacy and safety (Table 3). First, PWE and families must understand what daily life with an ND involves to the greatest extent possible. Although it is impossible to know exactly what life with an ND will involve for an individual person until the ND is implanted, providers should make sure to illustrate how the life of the PWE may change after ND implantation, particularly using relatable examples. People with epilepsy may be informed of programs that certain companies offer in which PWE with implanted NDs serve as ambassadors to convey what life is like with a ND, provided a conflict of interest does not exist. Second, PWE and families must have realistic expectations of NDs. This is particularly important given that unrealistic expectations may lead to a poor perception of outcomes even when implantation is technically successful and clinical parameters improve [133]. Conveying the purpose of the device, limitations, and associated activity restrictions to PWE is particularly important to promote realistic perspectives of the potential effects of NDs [21]. Third, the uncertainty and anxiety over living with an implanted device that PWE commonly experience should be mitigated [110]. For example, PWE may be unsure if they can travel in airplanes or participate in certain activities, feel required to continually monitor the ND, excessively adjust device settings, have difficulty adapting to life with an ND, or experience associated distress [110]. In addition to informed provision, providers must assess the capacity of PWE and caregivers to undertake the psychosocial burden of NDs in addition to the psychosocial burden of epilepsy itself when determining candidacy for ND implantation [21]. Fourth, PWE and families must be able to control and monitor the device [110]. People with epilepsy and caregivers must demonstrate knowledge regarding how to turn their device on or off, change settings if necessary, and maintain auxiliary equipment such as remote controls and chargers and upload data as needed [21]. Increasingly, NDs allow PWE and caregivers greater control of their devices. In order for these features to be useful, PWE must understand these features and avoid losing or breaking auxiliary equipment [21]. Providers must assess the utility of these features and adjust their approach as necessary based on the capabilities of the PWE and sources of social support [21]. People with epilepsy and caregivers must also demonstrate an understanding of how to assess the effects of a device and associated side effects [21]. Fifth, PWE must also demonstrate knowledge regarding factors contributing to ND failure, action steps required if seizure frequency increases or quality of life decreases, and what routine maintenance and long-term management with NDs entail [21,110]. This consideration is important for rechargeable models due to the necessity of recharging, greater maintenance needs, and adverse events, and perhaps more important for RNS, which requires daily interrogations by the PWE to download data [134-136]. All five aforementioned considerations necessitate greater patient-centered care to empower PWE and families [21].

6. Ethical framework

6.1. Framework

Treatment of epilepsy with resection/ablation/disconnection or ND implant requires a layered approach. Based on the aforementioned considerations and our opinions, we propose a tiered model to surgical treatment of epilepsy (Fig. 2). The first tier consists of a decision regarding the appropriate treatment for the PWE on based on the clinical judgement of the multidisciplinary epilepsy team.

Table 3
Components of use of neuromodulatory devices (NDs).

Domain	Explanation
Perceptions	Understanding what daily life with a ND involves
Expectations	Realistic expectations of NDs
Unknowns	Mitigation of uncertainty and anxiety over living with an ND
Daily use	Controlling and monitoring device
Maintenance	Knowledge regarding ND failure and properly taking care of ND

Abbreviations: neuromodulatory device (ND).

This involves a sequential process. First, using relevant imaging, diagnostic testing, and clinical data, all treatment options are identified to ensure that all treatment options are considered [21]. The use of a multidisciplinary patient management conference is a key component in this process, particularly given neurologists care for patients with epilepsy for long periods of time prior to surgery. Second, risks and benefits of each treatment are listed based on the type of epilepsy, etiology, previous treatments, comorbidities, and other characteristics of individual PWE. Third, risks and benefits are compared to determine the optimal treatment [21]. This involves consideration of potential clinical and patient-reported outcomes in addition to known cultural conceptions, values, and barriers.

The second tier involves communication with the PWE or proxy. Neurosurgeons should utilize clear communication strategies coupled with multimodal educational interventions to convey all information, including treatment options, risks, benefits, and alternatives, to PWE or proxies that is required to make a decision regarding care [77]. In this process, neurosurgeons must specify the relative efficacy and safety each treatment option and convey the rationale for their preferred treatment approach, including both clinical knowledge and their understanding of PWE conceptualizations, values, and barriers. Neurosurgeons must also convey if PWE qualify for a clinical trial and provide a reasoned recommendation for or against participation in the trial. People with epilepsy should be allowed ample time to clarify their conceptualizations, values, and barriers to neurosurgeons and ask questions. Neurosurgeons should assess understanding of these discussions through strategies such as teach backs, while correcting gaps in understanding of PWE and their families/proxies, and provide additional information and resources as appropriate [85,86]. Neurosurgeons and multidisciplinary teams may modify their judgment of the optimal treatment approach, if necessary, based on additional information conveyed by the PWE or viewed on imaging workup.

The third tier involves decision maintenance [21]. This tier incorporates two aspects. One is between the neurosurgeon and neurologist, involving continued communication regarding the symptomatology of the patient and potential changes to treatment plans. The other is between the neurosurgeon and patients or families. This is a longitudinal process necessitating the continued identification of gaps in understanding, provision of information, and correction of misconceptions across the duration of care [77]. Importantly, to extend the process for the individual PWE to the societal level, these steps must be considered on the axis of access to care and resource allocation. Expansion of access to epilepsy care and specialized surgical intervention worldwide, particularly in LMICs, through initiatives to scale up training, appropriate facilities, and funding is necessary to alleviate the substantial epilepsy treatment gap [1,40-47]. Similarly, determination of the appropriate treatment for the individual must consider the resource status of the local setting when a ND may be indicated to ensure optimal use of these devices [110]. The protection of vulnerable people is a particular imperative throughout this process [108].

6.2. Future directions

Fortunately, the landscape of treatment of epilepsy continues to advance in the service of improved PWE outcomes. These include more refined surgical techniques and NDs, medications, gene therapy, and stem-cell-based therapy [137,138]. As with all new treat-

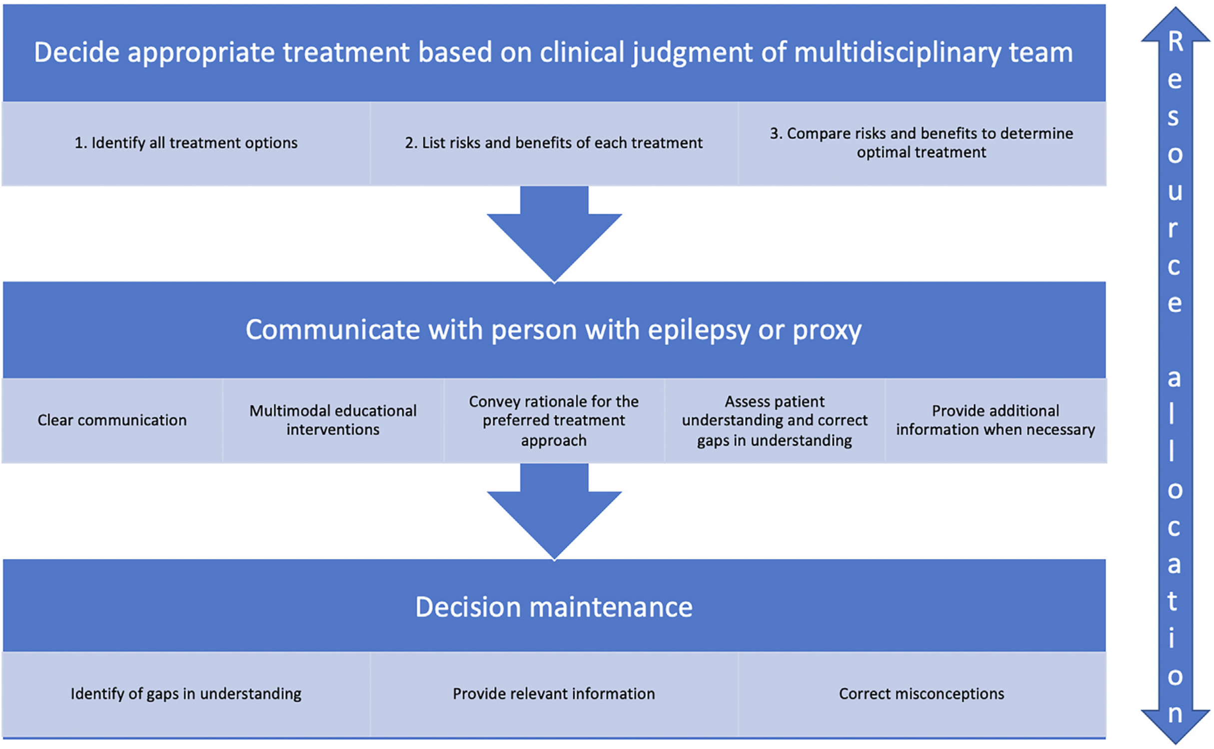

Fig. 2. Ethical framework for the resective surgical and neuromodulatory treatment of people with epilepsy (PWE): 1) decide appropriate treatment based on clinical judgment, 2) communicate with the PWE or proxy, and 3) provide information so that the PWE or proxy remains informed.

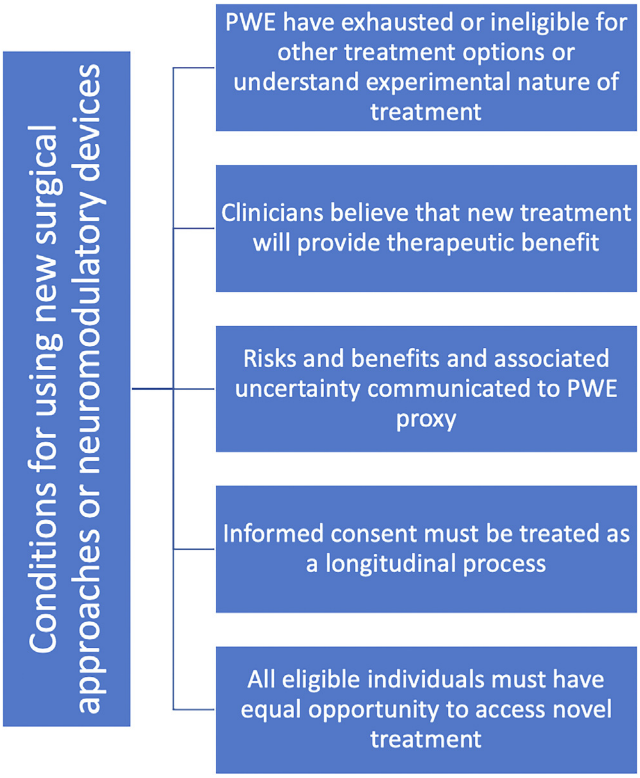

Fig. 3. This figure illustrates the requirements for using novel surgical approaches or neuromodulatory devices for people with epilepsy (PWE). It is important to consider these factors in the context of the individual PWE.

ments, the safety and efficacy of new surgical approaches and NDs must be validated in well-designed studies considering clinical and patient-reported outcomes [21]. Until this occurs, we believe that new surgical approaches or NDs may be utilized under certain additional conditions (Fig. 3). First, the PWE must have exhausted or be ineligible for other medical, surgical, and neuromodulatory treatment options [21] or demonstrate understanding of the experimental nature of and subsequent willingness to pursue the intervention. Second, clinicians must believe that the new treatment approach will provide therapeutic benefit based on a risk–benefit assessment of PWE characteristics, clinical factors, and specifics of the treatment approach [21]. Third, immediate, short-term, and long-term risks and benefits and associated uncertainty must be clearly communicated to the PWE or proxy [21]. Fourth, the concept of informed consent as a longitudinal process must be continually recognized through provision of emerging information to PWE and proxies in a timely manner [21]. Fifth, the principle of justice must be maintained in terms of providing all eligible individuals with equal opportunity to access a novel surgical or neuromodulatory treatment. Additionally, with the rise of artificial intelligence, machine learning algorithms may be translated to clinical use for tasks such as outcome prediction [139]. It is particularly important to safeguard the aforementioned ethical principles given potential for abuse [140]. Machine learning may also improve ethical calculations due to the potential for refined risk stratification, patient selection, and clinical decision making. Finally, data-driven approaches will assist in validating the ethical framework we have detailed across the scope of PWE who undergo surgery or implantation of a ND.

7. Conclusion

In this narrative review-based opinion piece, we indicate that the surgical treatment of epilepsy requires numerous considerations, including progression of therapy, comorbidities, barriers, and culture. Principles of informed consent, beneficence and non-maleficence, and justice are essential. Additional considerations regarding autonomy, privacy and confidentiality, and device maintenance arise when NDs are utilized for treatment. Consideration of these ethical principles in a tiered approach consisting of the care of the individual PWE on an axis of societal considerations will allow for optimal treatment of the individual person with epilepsy while minimizing disparities in epilepsy care.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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