

## PD142 Implantable Neurostimulation Devices For The Treatment Of Drug-Resistant Pediatric Epilepsy

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**Introduction:** Epilepsy affects approximately 10.5 million individuals under the age of 15 years worldwide. In Spain, 3.7 per 1,000 inhabitants aged 6 to 14 years have epilepsy, making it the third most common neurological emergency. Drug resistance is observed in eight to 33 percent of cases. Responsive neurostimulation (RNS) systems could improve seizure control in pediatric patients who are not eligible for brain surgery.

**Methods:** We systematically searched for articles published up to September 2022 in the following bibliographic databases: MEDLINE, Embase, Web of Science, and CINAHL. We included primary experimental and observational studies as well as case series studies addressing the safety, efficacy, and cost effectiveness of RNS in the treatment of drug-resistant pediatric epilepsy.

**Results:** Two systematic reviews of prospective and retrospective case series studies and four primary experimental studies were identified. The case series studies found that a large proportion of pediatric patients responded to RNS, with a reduction of between 50 and 75 percent in the frequency of seizures. The intensity and duration of seizures also decreased after using RNS. Adverse effects of the RNS implantation process were related to infections, erythema, and hematomas. Only one study (n=17) reported moderate adverse effects related to stimulation (dysesthetic pain in the upper and lower right limb), but there were no serious reactions leading to RNS discontinuation.

**Conclusions:** Randomized controlled trials in pediatric drug-resistant populations ineligible for brain surgery with adequate sample sizes are needed to determine the effectiveness of RNS in terms of seizure frequency, duration, and intensity. No cost-effectiveness studies have been conducted on RNS in this cohort.

## PD144 Uncertainty In Precision Medicine: The Value Of Research To Support The Value Of Personalized Intervention Policies

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**Introduction:** One-size-fits-all policies are not always optimal. Stratified decision-making is only possible when the characteristics used to define subgroups can be identified for stratum-specific predictions of outcomes. Conditioning decisions on characteristics that are not readily known may require information (diagnostic, prognostic, predictive) to be derived, the value of which needs to be assessed to support personalized strategies.

**Methods:** A general framework was developed to show how personalized policies can be accountably informed by characterizing uncertainty, heterogeneity, and bias in evidence. In the framework, observed heterogeneity was disentangled from random variability by conditioning the value of the model input parameters on a set of prognostic or predictive variables, while unobserved heterogeneity was quantified as the systematic variability that cannot be explained given current information. Value of information analysis was used to quantify the value of additional information for resolving decision uncertainty in model input parameters and to identify individual- or subgroup-level attributes that contribute to the degree of heterogeneity.

**Results:** Decision-making based on average cost effectiveness fails to account for the role that sources of outcome variability play in guiding nuanced decision-making. Conditioning on a set of known covariates to reflect observable heterogeneity may be extended to conditioning on the latent random variable for unobservable covariates to quantify unobservable heterogeneity. Quantifying the potential value of research to inform subgroup- or individual-level attributes may be used to direct further research toward the attributes expected to be of most interest because they drive the value of individualized decisions—the expected value of sample information for attributes.

**Conclusions:** Two distinct, but interrelated concepts for assessing the value of stratified decision-making are important: (i) the value of heterogeneity; and (ii) the value of further research to inform both heterogeneous factors and to reduce decision uncertainty in precision medicine. Assessing the value of unexplained heterogeneity and bias can be central to supporting the value of personalized intervention strategies in health technology assessment.