

AspireSR®

Empowers patients with seizure detection and automatic stimulation both night and day



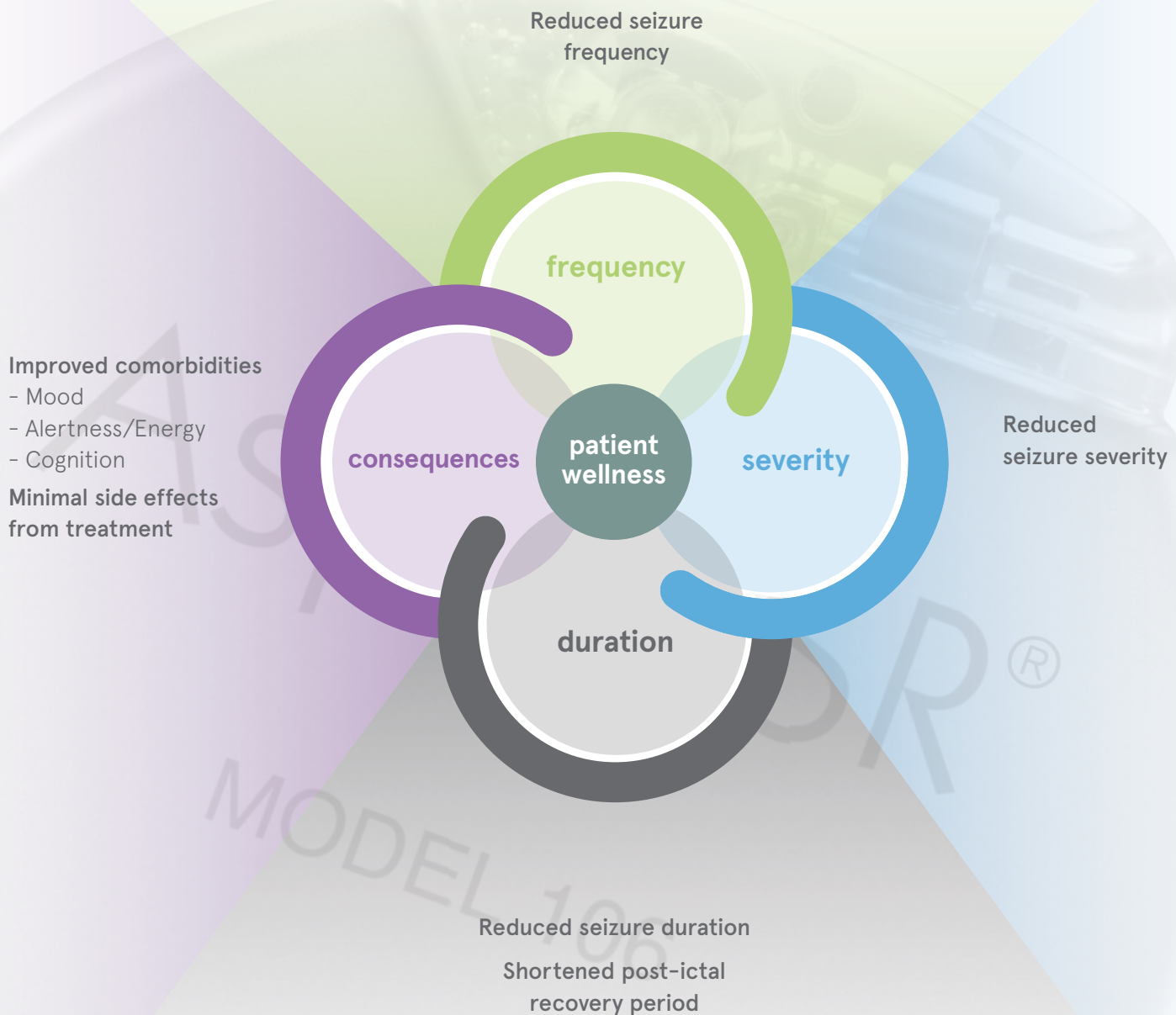
The first choice add-on
in drug-resistant epilepsy

Drug-Resistant Epilepsy:

A complex disease needs a comprehensive approach

VNS Therapy®:

- Can be used in combination with other approved treatments at any time
- Helps you to meet therapy goals and restore patient wellness





AspireSR detects and responds to seizures 24/7 to improve the lives of patients with epilepsy

AspireSR uses unique technology that detects seizures based on changes in heart rate and provides automatic stimulation to stop or shorten a seizure and improve postictal recovery



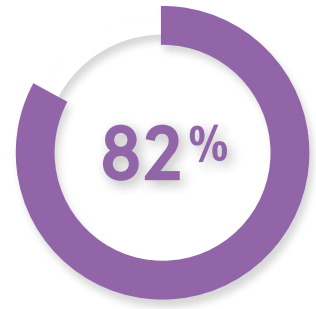
- **AspireSR** is proven in 2 clinical trials to reduce seizure frequency, severity, and duration, and improve quality of life outcomes.¹
- **AspireSR** advances the proven foundation of VNS Therapy[®] and offers a comprehensive approach for people living with drug-resistant epilepsy.
- **AspireSR** has demonstrated safety and tolerability comparable to currently available VNS Therapy.
- **AspireSR** provides 24/7 seizure detection and automatic stimulation. Patients can still use a handheld magnet for added control and confidence.





How **AspireSR** works

- Detects heart rate increases associated with seizures
- Delivers automatic stimulation
- Has customisable parameters to meet patients' needs
- Works in conjunction with normal and magnet mode



OF PATIENTS WITH EPILEPSY
HAVE SEIZURE-ASSOCIATED
TACHYCARDIA³



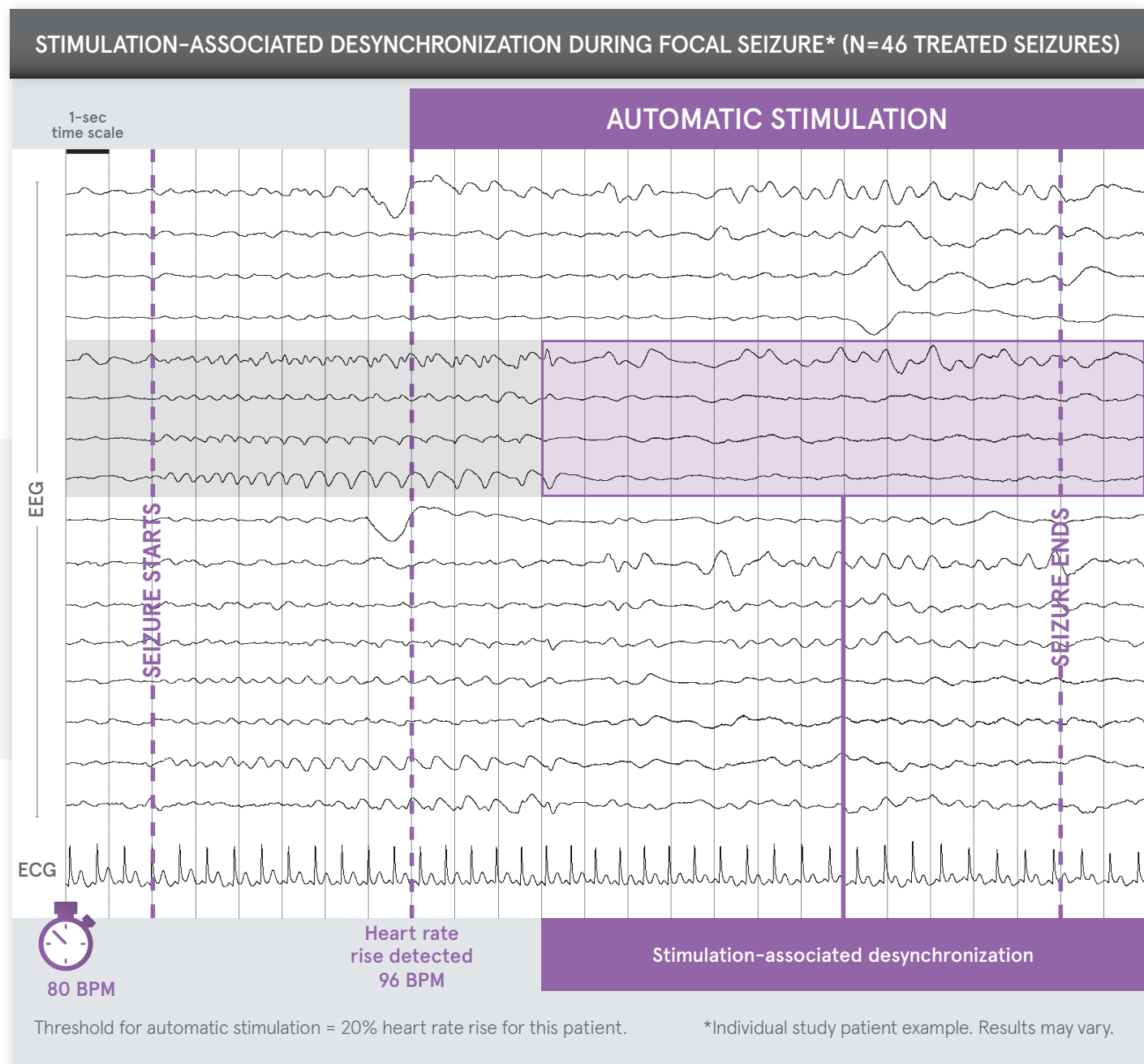
AspireSR[®]
MODEL 106



AspireSR provides 24/7 seizure detection and automatic stimulation

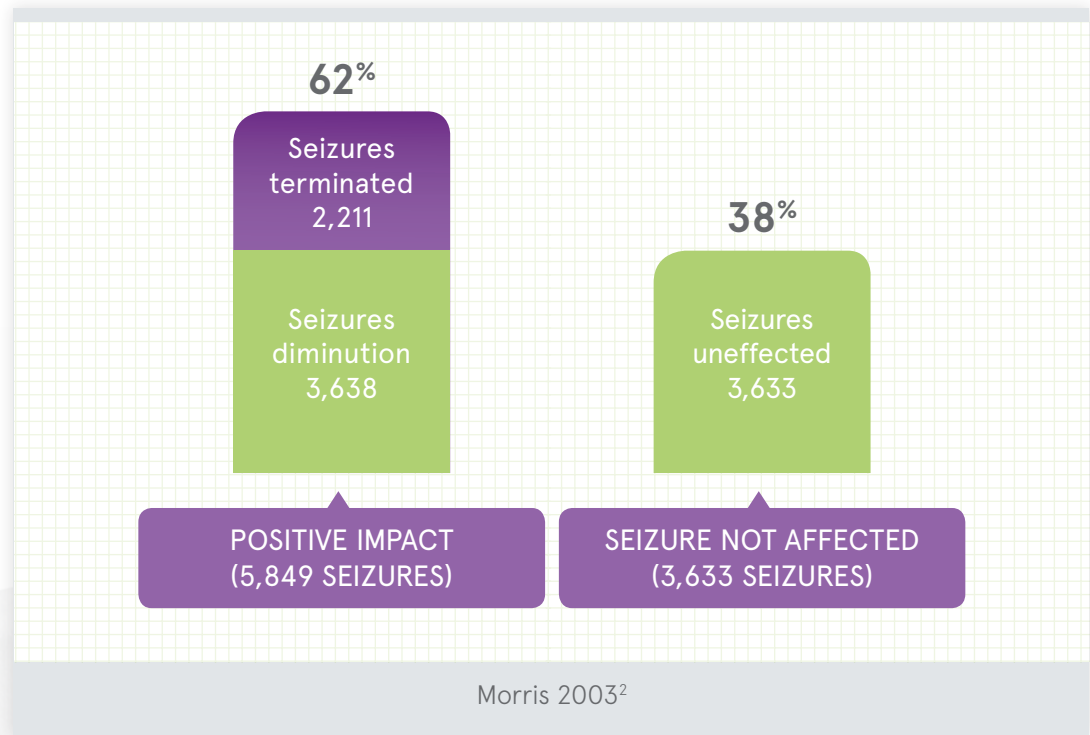
AspireSR may terminate seizures by delivering automatic stimulation when a seizure occurs¹

- **Over 60% of seizures treated (n=46) ended during automatic stimulation¹**
 - 48% of Complex Partial Seizures ended during automatic stimulation
- **For seizures that ended during stimulation (n=28), the closer stimulation was to seizure onset, the shorter the seizure duration¹**

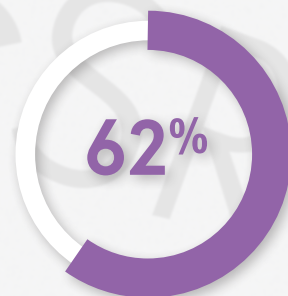


The handheld patient magnet helps empower patients to **stop or shorten seizures**²

Magnet use allows patients to stop or shorten a seizure, or decrease the intensity of the recovery period



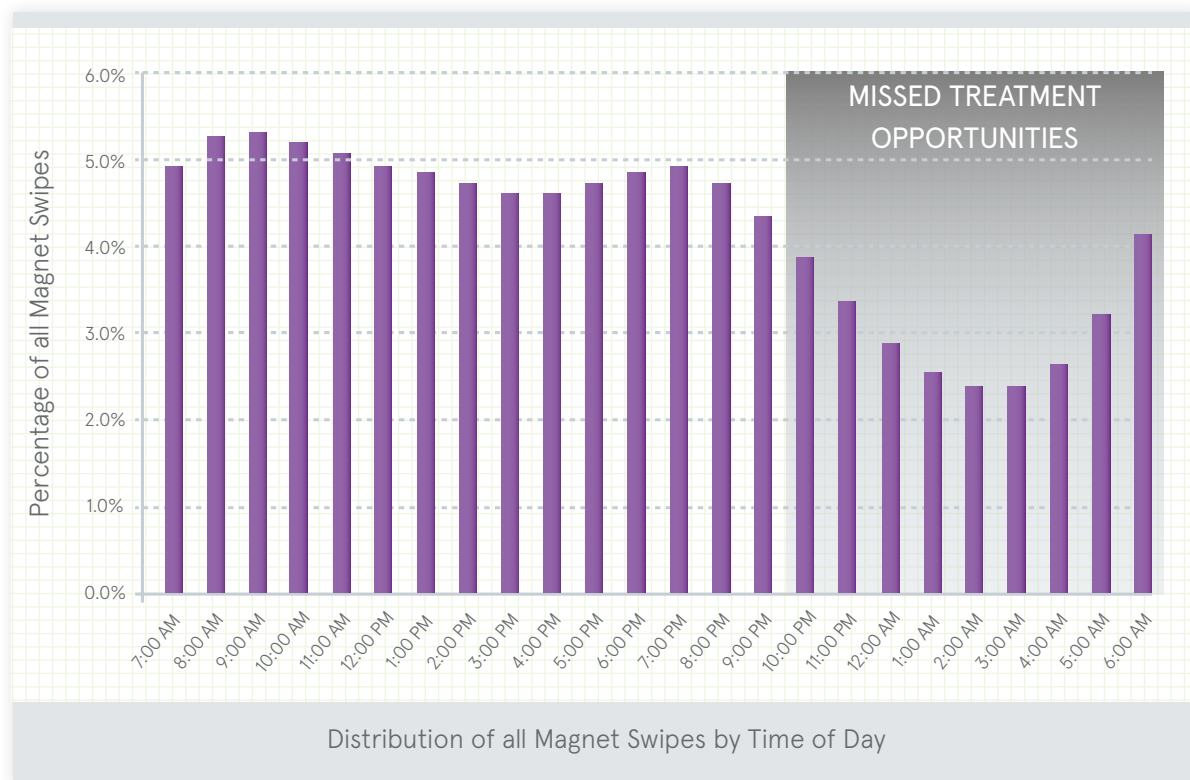
Robert on VNS Therapy since 2006



62% OF SEIZURES ARE TERMINATED OR DIMINISHED WHEN THE MAGNET IS USED²

Many seizures are missed during sleeping hours

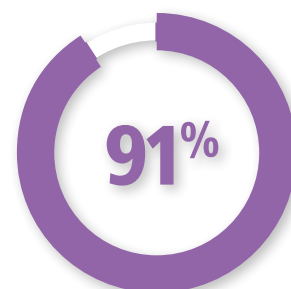
Records of over 10 million magnet activations since 1997 approval show that activations are far less common between midnight and 6 am¹



Handheld magnet activation is not always convenient¹

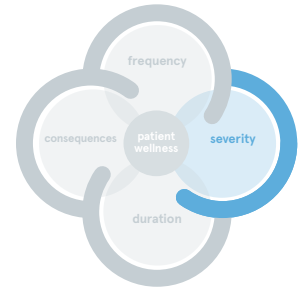
- Would not be able to perform manual magnet mode stimulation
- Do not have a magnet available when needed
- Do not apply magnet properly (at the wrong time or wrong device location)
- May not have enough time to apply the magnet once the seizure starts
- Do not experience auras
- Do not have a caregiver, or caregiver may not be near when patient is having a seizure
- Have a seizure during a period of sleep

OF PATIENTS SURVEYED
WOULD VALUE A DEVICE
THAT CAN AUTOMATICALLY
ACTIVATE STIMULATION¹



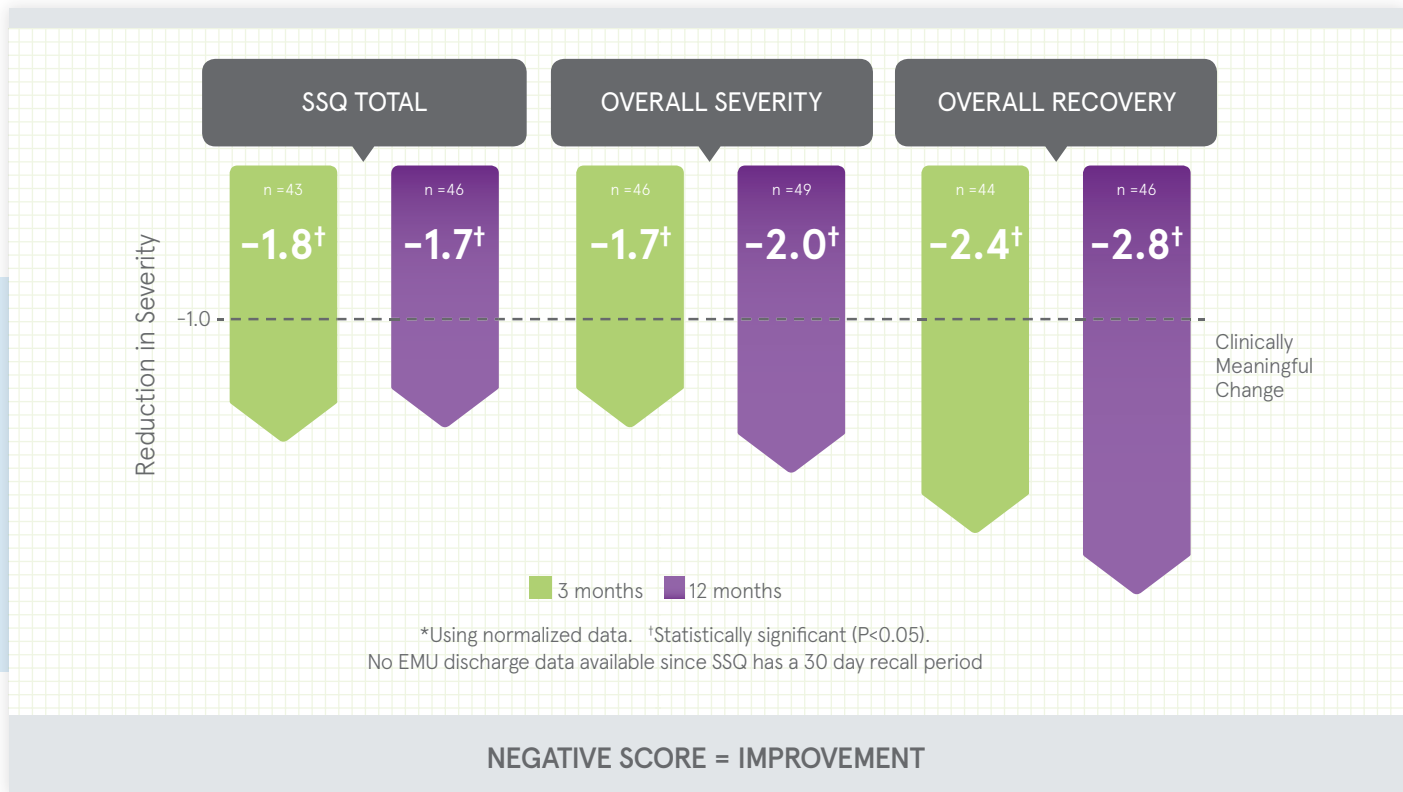
AspireSR is proven to reduce seizure severity^{1,4}

Sustained improvements in seizure severity were seen across multiple validated scales scored by patients and physicians:

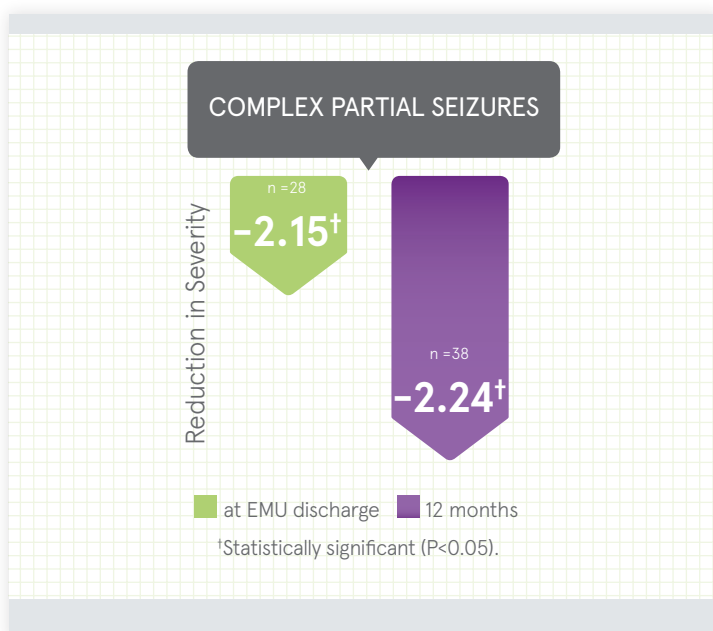


- Seizure Severity Questionnaire (SSQ) – Clinically meaningful and statistically significant change in overall seizure severity and recovery were seen at 3 and 12 months⁴

SSQ SCORE: MEAN CHANGE FROM BASELINE*



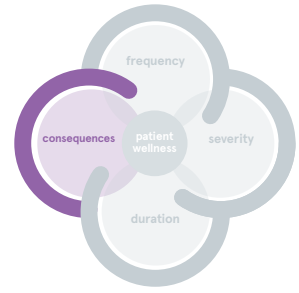
NHS3 SCORE : MEAN CHANGE FROM BASELINE



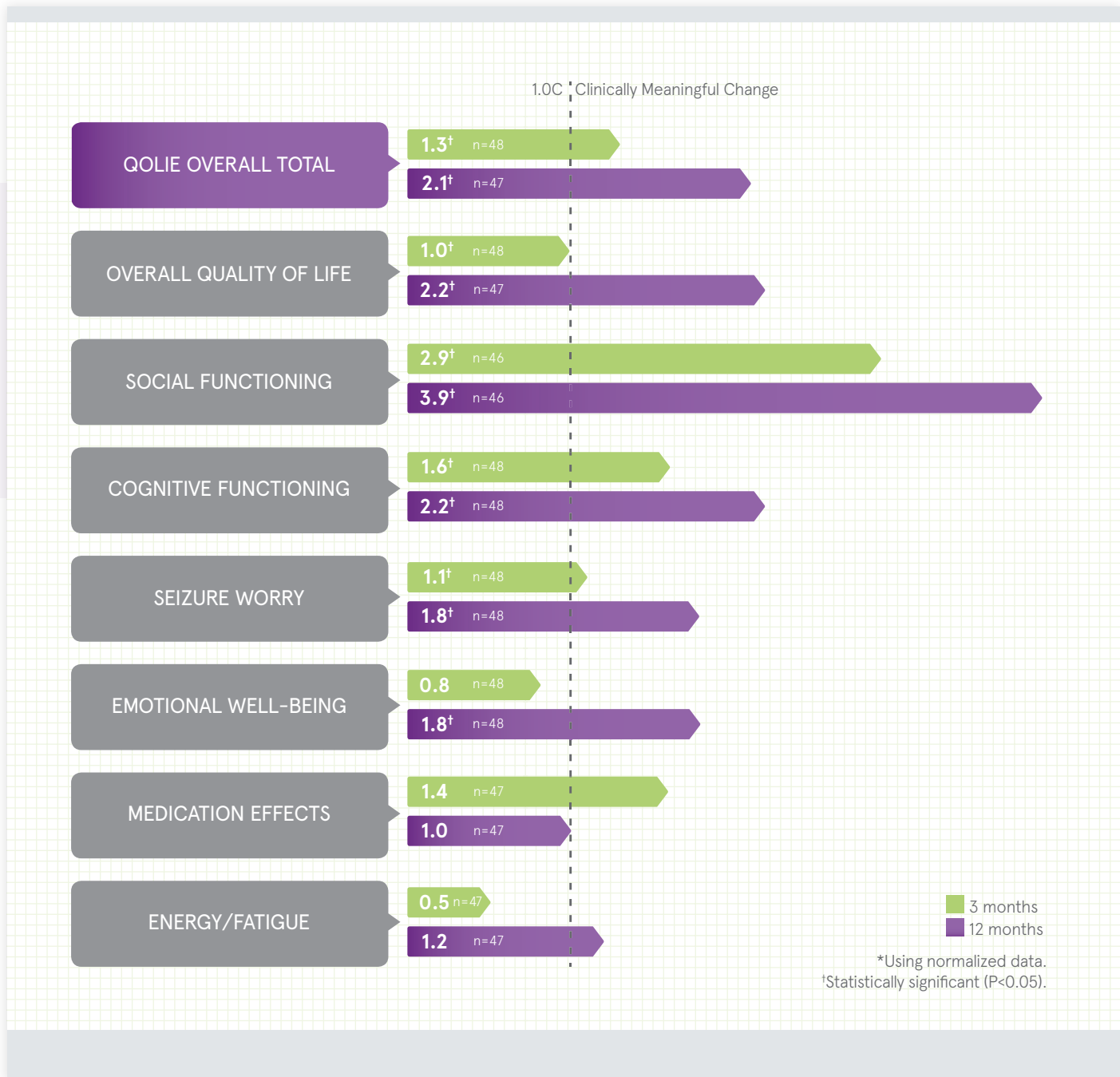
- National Hospital Seizure Severity Scale (NHS3) – Statistically significant reductions in seizure severity were observed after 3–5 days of only automatic stimulation in the EMU and at 12 months¹

AspireSR is proven to improve quality of life⁴

Clinically meaningful and statistically significant improvements in overall QOL were seen at 3 months and continued to improve over time.



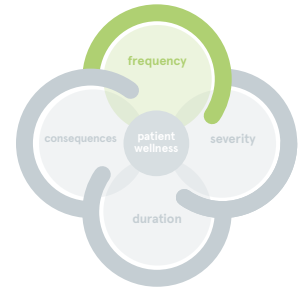
QUALITY OF LIFE (QOLIE-31-P) SCORE: MEAN CHANGE FROM BASELINE*



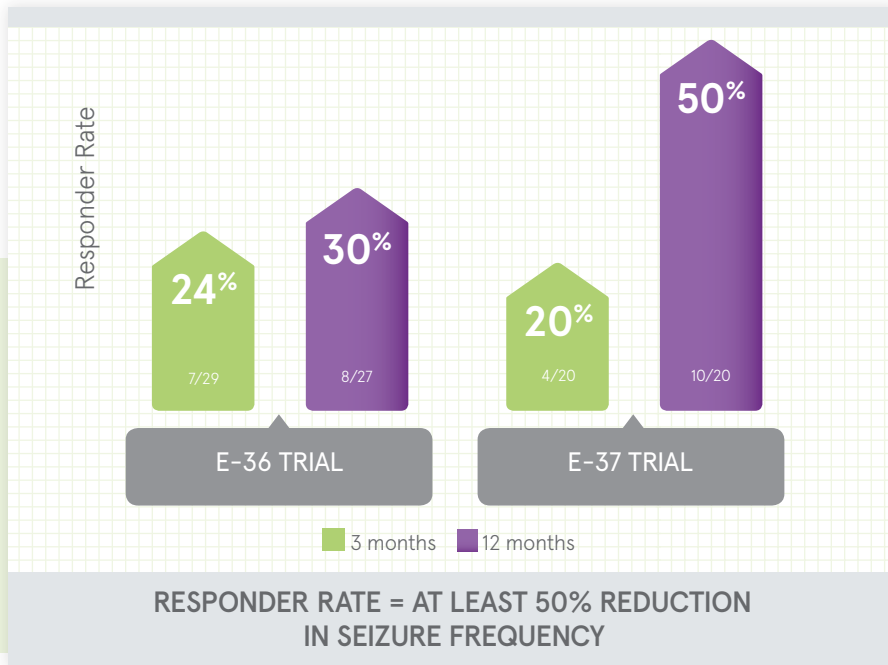
AspireSR provides seizure reduction that continues to improve over time¹

Of patients in AspireSR trials:

- 90% failed 4 or more anti-epileptic drugs
- Mean duration from diagnosis was 23 years
- Approximately 35% of patients had a prior resective surgery



SUMMARY OF RESPONDER RATE



E-36 Clinical Trial : Europe, N=31

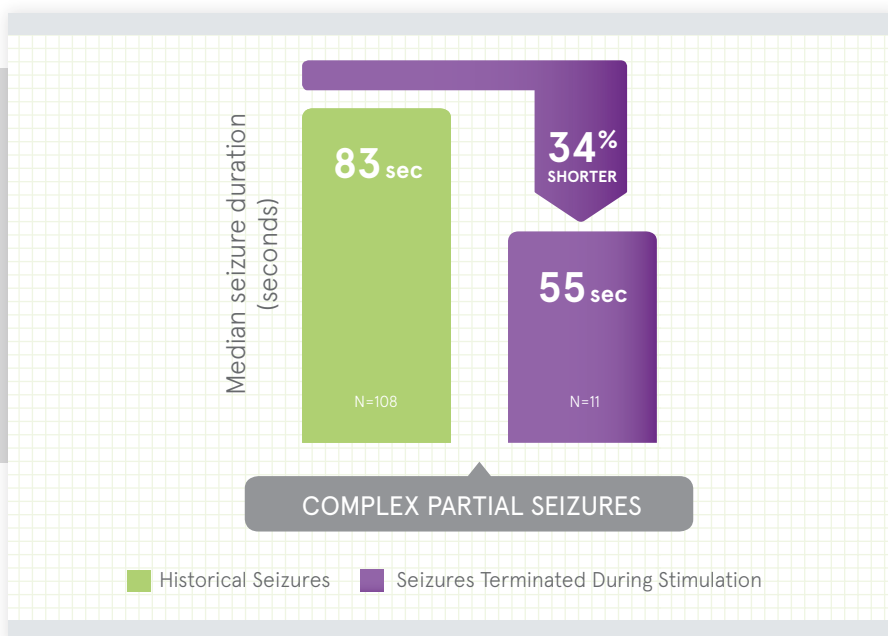
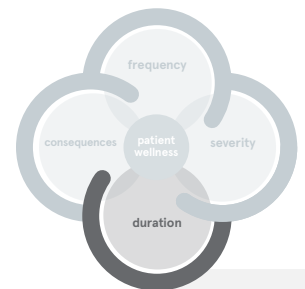
- During the EMU stay, patients were randomized to 3 different AutoStim threshold settings
- After the EMU stay, investigators adjusted the threshold for AutoStim using their discretion

E-37 Clinical Trial : US, N=20

- During the EMU stay, investigators set the threshold for AutoStim using their discretion
- Duty cycle held at 10% through 6 month follow-up to isolate the effect of the AutoStim feature.

AspireSR is proven to reduce seizure duration¹

Complex Partial Seizures that were treated with Automatic Stimulation were at least 34% shorter than historical seizures of the same type¹



Median duration of seizures by subgroup
n= number of seizures



AspiresR®
MODEL 106

 VNS Therapy®



AspireSR® Advancing the proven long-term efficacy and safety platform of VNS Therapy



VNS Therapy with AspireSR benefits:¹

- Provides the proven long-term efficacy and safety of VNS Therapy
- Uses a proprietary, customisable cardiac-based seizure detection algorithm to deliver stimulation when a seizure occurs
- May terminate seizures by delivering automatic stimulation when a seizure occurs
- Reduces seizure duration
- Reduces seizure severity
- Improves Quality of Life

AspireSR® is CE mark approved and commercial distribution may vary by country.

VNS THERAPY EUROPEAN INDICATION FOR USE

VNS Therapy is indicated for use as an adjunctive therapy in reducing the frequency of seizures in patients whose epileptic disorder is dominated by partial seizures (with or without secondary generalization) or generalized seizures that are refractory to seizure medications. The Model 106 AspireSR® (Seizure Response) features the Automatic Stimulation Mode, which is intended for patients who experience seizures that are associated with cardiac rhythm increases known as ictal tachycardia.

CONTRAINDICATIONS:

The VNS Therapy system cannot be used in patients after a bilateral or left cervical vagotomy. Do not use short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy on patients implanted with the VNS Therapy system. Diagnostic ultrasound is not included in this contraindication. Cardiac arrhythmia (Model 106 only)—The AutoStim Mode feature should not be used in patients with clinically meaningful arrhythmias or who are using treatments that interfere with normal intrinsic heart rate responses.

WARNINGS:

Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy Physician Manuals, including information that VNS Therapy may not be a cure for epilepsy. Since seizures may occur unexpectedly, patients should consult with a physician before engaging

References:

1. Data on file, Cyberonics Inc. Houston, TX
2. Morris GL, et al. Neurology. doi:10.1212/WNL.0b013e3182a393d1
3. Eggleston et al. 2014 Aug;23(7):496-505
4. Adapted from data on file, Cyberonics Inc. Houston, TX.

in unsupervised activities, such as driving, swimming, and bathing, or in strenuous sports that could harm them or others. A malfunction of the VNS Therapy system could cause painful or direct current stimulation, which could result in nerve damage. Removal or replacement of the VNS Therapy system requires an additional surgical procedure. Patients who have pre-existing swallowing, cardiac, or respiratory difficulties (including, but not limited to, obstructive sleep apnea and chronic pulmonary disease) should discuss with their physicians whether VNS Therapy is appropriate for them since there is the possibility that stimulation might worsen their condition. Postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. MRI can be safely performed; however, special equipment and procedures must be used.

ADVERSE EVENTS:

The most commonly reported side effects from stimulation include hoarseness (voice alteration), paresthesia (prickling feeling in the skin), dyspnea (shortness of breath), sore throat and increased coughing. The most commonly reported side effect from the implant procedure is infection.

*The information contained here represents partial excerpts of important prescribing information from the product labeling. Patients should discuss the risks and benefits of VNS Therapy with their healthcare provider. Visit www.VNSTherapy.com for more information.

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