



## Introducing Vagus Nerve Stimulation for Epilepsy



**The Most Proven Neuromodulation Therapy  
For Drug-Resistant Epilepsy Patients**

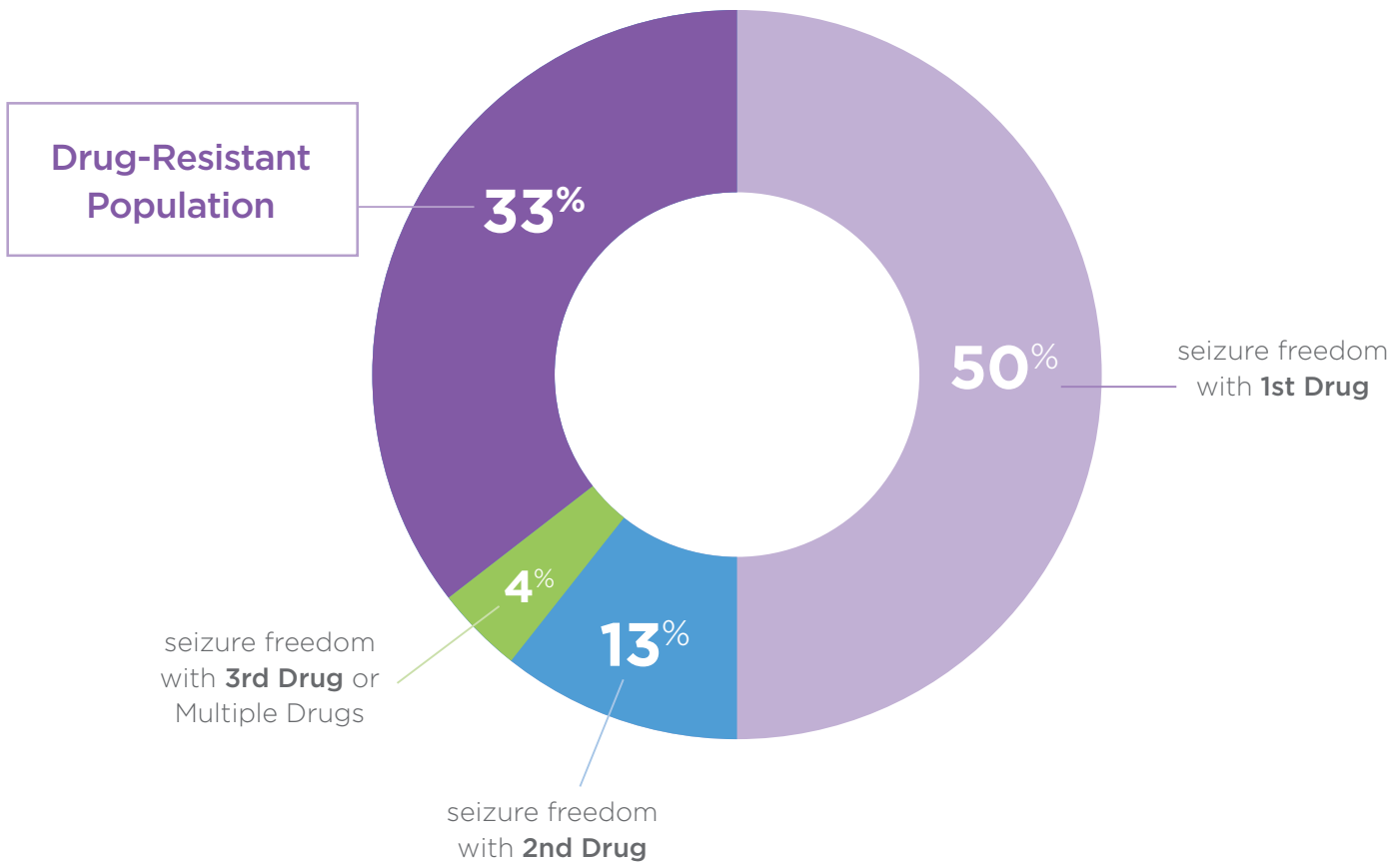


# Drug-Resistant Epilepsy

A complex disease needs a comprehensive approach

**1 in 3 of your patients** will not respond adequately to anti-epileptic drugs (AEDs)<sup>1</sup>

Epilepsy population (seizure freedom rates)<sup>1</sup>



The rate of Drug-Resistant Epilepsy (DRE) has not been significantly reduced over the last 20 years despite the entry of new AEDs with unique mechanisms of action (MOAs)<sup>1</sup>

DRE: The failure of two appropriately chosen and tolerated AEDs (whether as monotherapy or in combination)<sup>2</sup>

# Consequences of Drug-Resistant Epilepsy

extend **beyond seizures**<sup>3,4,7</sup>



- Seizure-related injuries
- Increased hospital stays
- Increased mortality & morbidity including SUDEP

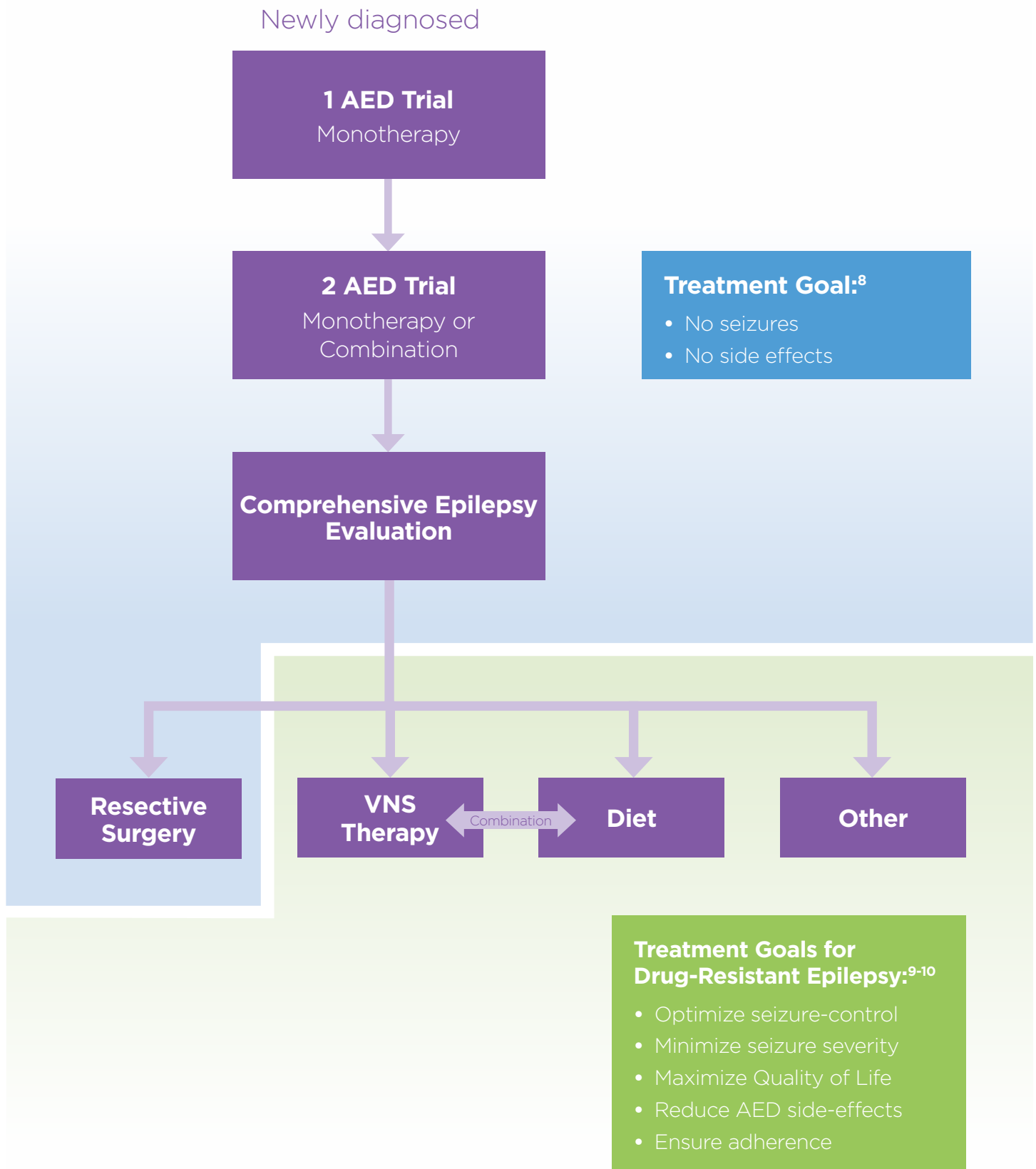


- Depression, anxiety & sleep disturbance
- Cognitive & memory impairment
- Adverse effects with long-term AED use

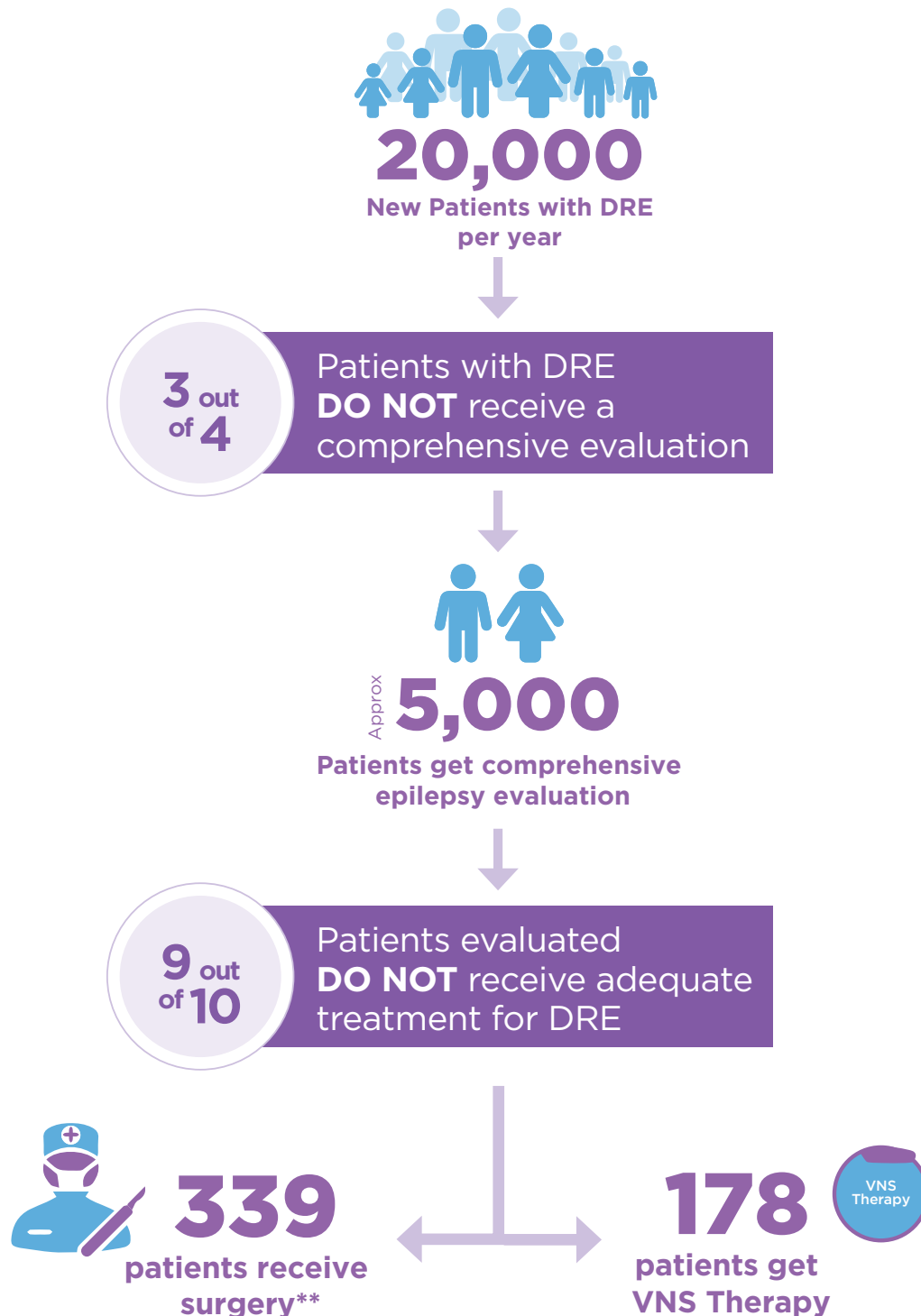


- Impaired ability to:**
- Obtain education
  - Work
  - Develop and maintain social relations

# Treatment options and treatment goals<sup>2,5,6</sup>



# A treatment gap exists for Drug-Resistant Epilepsy patients\*

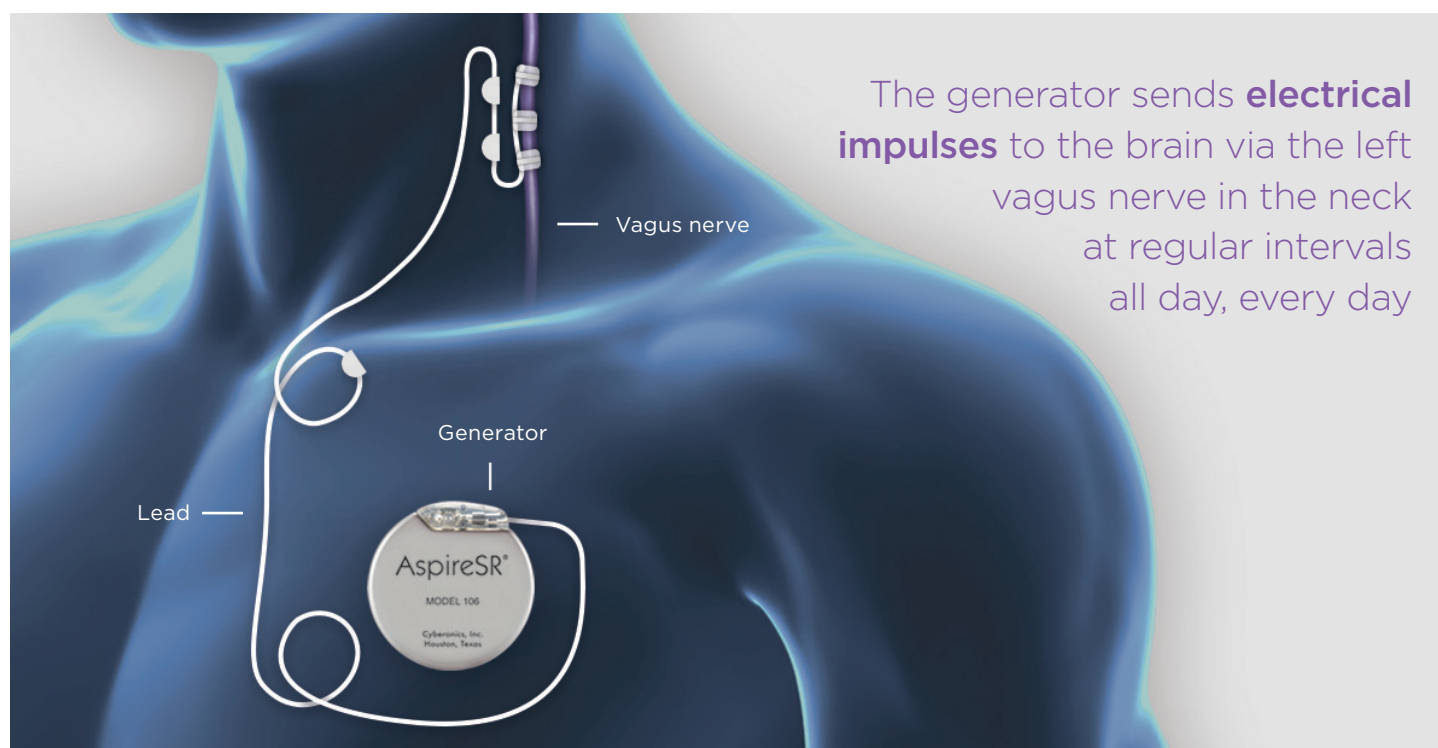


**New strategies** are needed to improve patient wellbeing

\* Data on file: longitudinal cohort study using data from the German statutory health insurance system, 2010

\*\* All epilepsy surgeries

# VNS Therapy: clinically proven treatment that is easy to use<sup>11</sup>



VNS Therapy Physician's Manual. Houston, TX: LivaNova

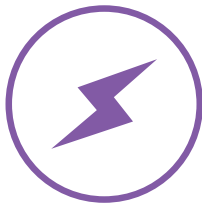
**The stimulation has** an anti-convulsive effect via several pathways

- **Desynchronises** ictal EEG patterns<sup>12</sup>
- **Alters neurotransmitter expression and release**<sup>13-14</sup>  
(↑ Norepinephrin, ↑ GABA, ↑ Serotonin, ↓ Aspartate)
- **Increases Cerebral Blood Flow** in the Thalamus and in the Cortex<sup>15</sup>

## Easy to use treatment

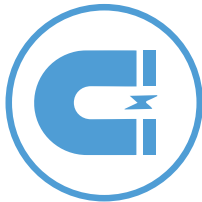
- **Short procedure**, typically 1-2 hours
- Can be safely used in **combination with any approved therapy at any time**
- **Built-in compliance**
- **No drug interactions**

# VNS Therapy is customisable to patient needs<sup>11</sup>



## Standard Mode

**Ongoing delivery of mild pulses** to the vagus nerve. Treatment is delivered at regular intervals.



## Magnet Mode

**Manual delivery of an extra dose** of therapy as needed. Magnet Mode may be used during Standard Mode and Detect & Respond Mode.



## Detect & Respond Mode\*

**Responsive automatic delivery** of an extra dose of therapy when a rapid increase in heart rate is detected that may be associated with seizures.



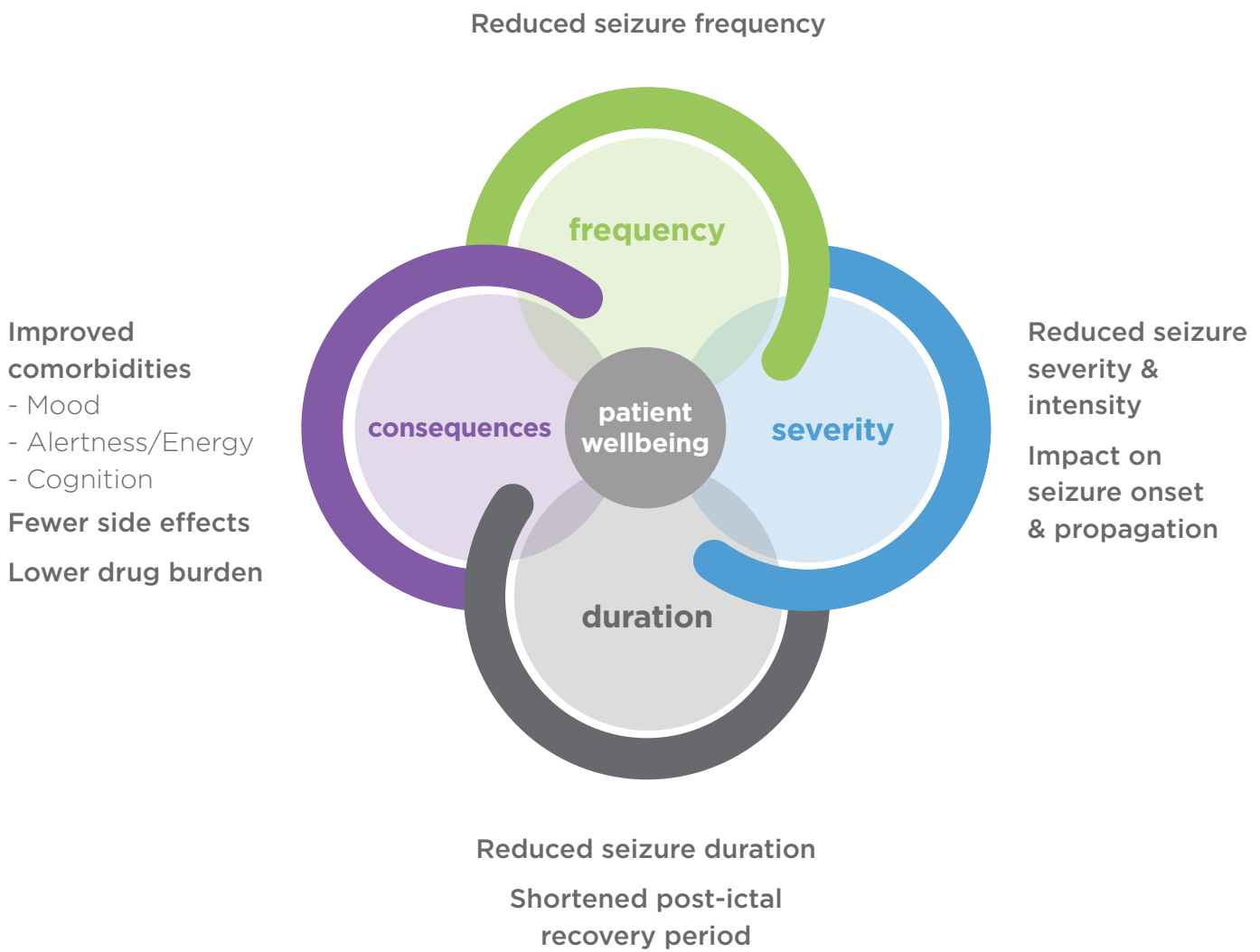
Generator shown is actual size

### VNS Therapy is indicated for use as:

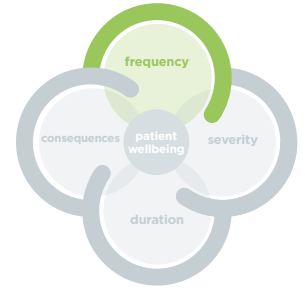
an **adjunctive therapy** in reducing the frequency of seizures in patients whose epileptic disorder is dominated by **partial seizures** (with or without secondary generalization) or **generalized seizures** that are **refractory to seizure medications**.

\*Also known as Auto Stimulation Mode/Available for AspireSR® only

# Optimising treatment outcomes with VNS Therapy

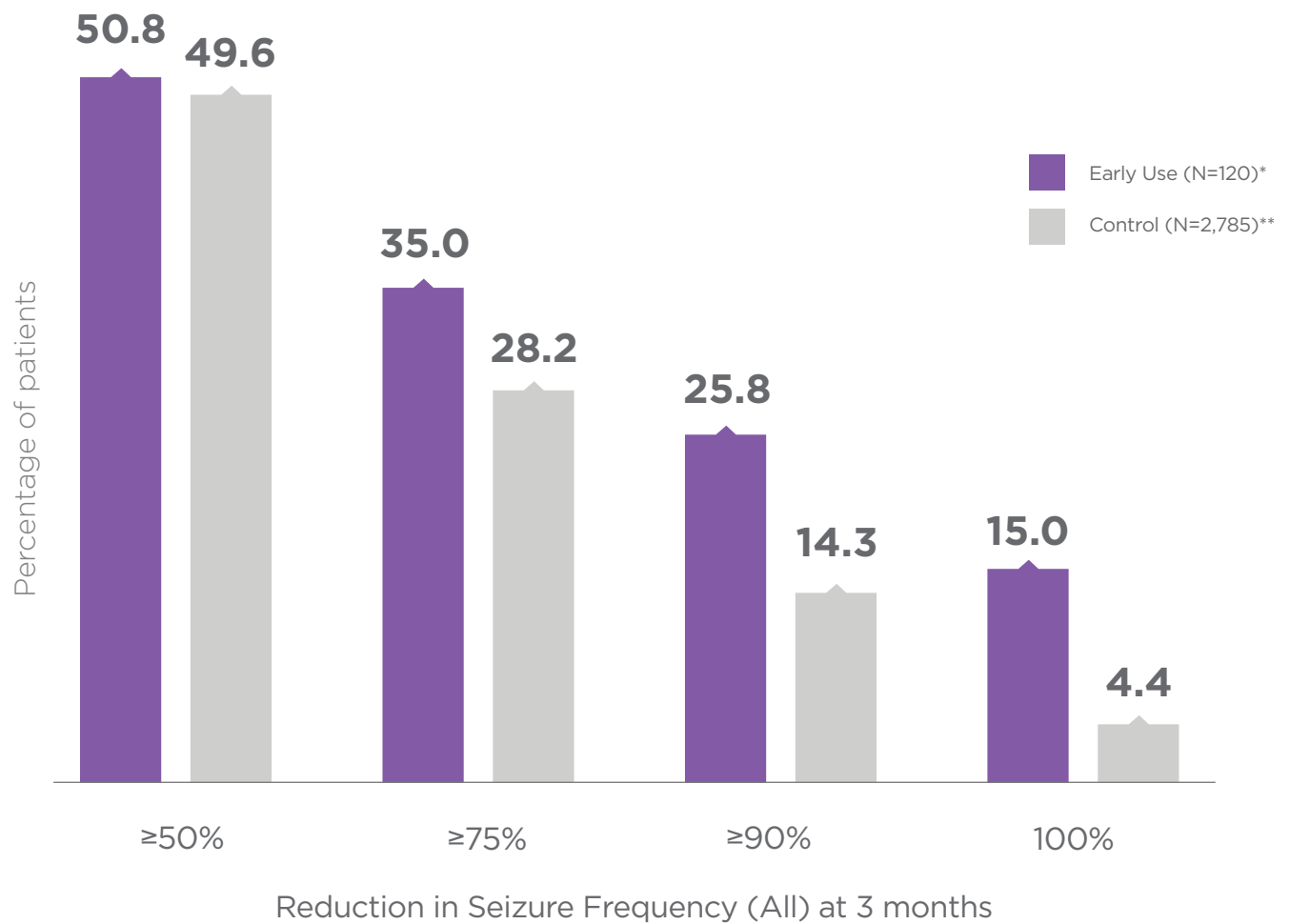






# Why wait for wellbeing?

**Earlier use** is proven to enhance seizure control<sup>16</sup>

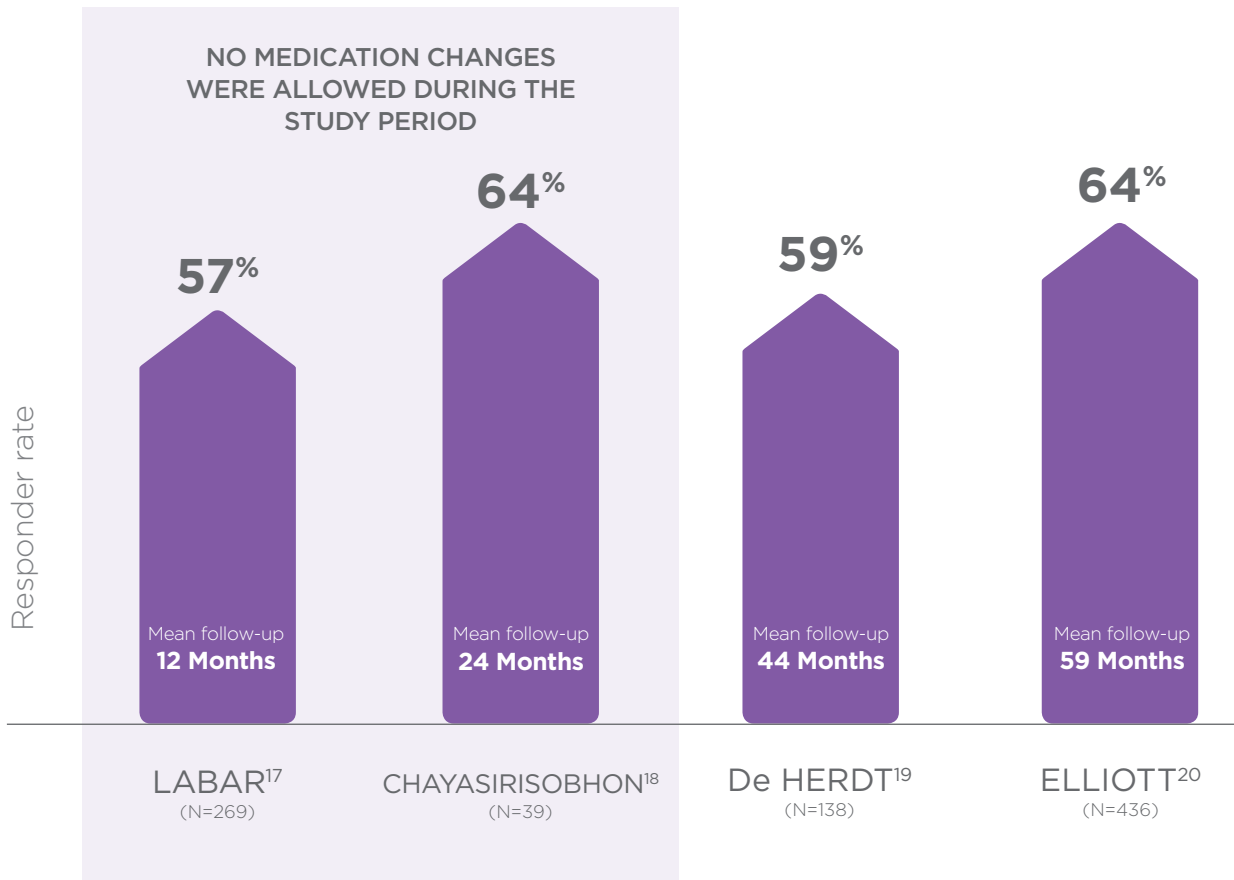


\* VNS Therapy within 5 years of epilepsy onset  
 \*\* VNS Therapy after 5 years of epilepsy onset, mean 21 years



# Long-term efficacy of VNS Therapy

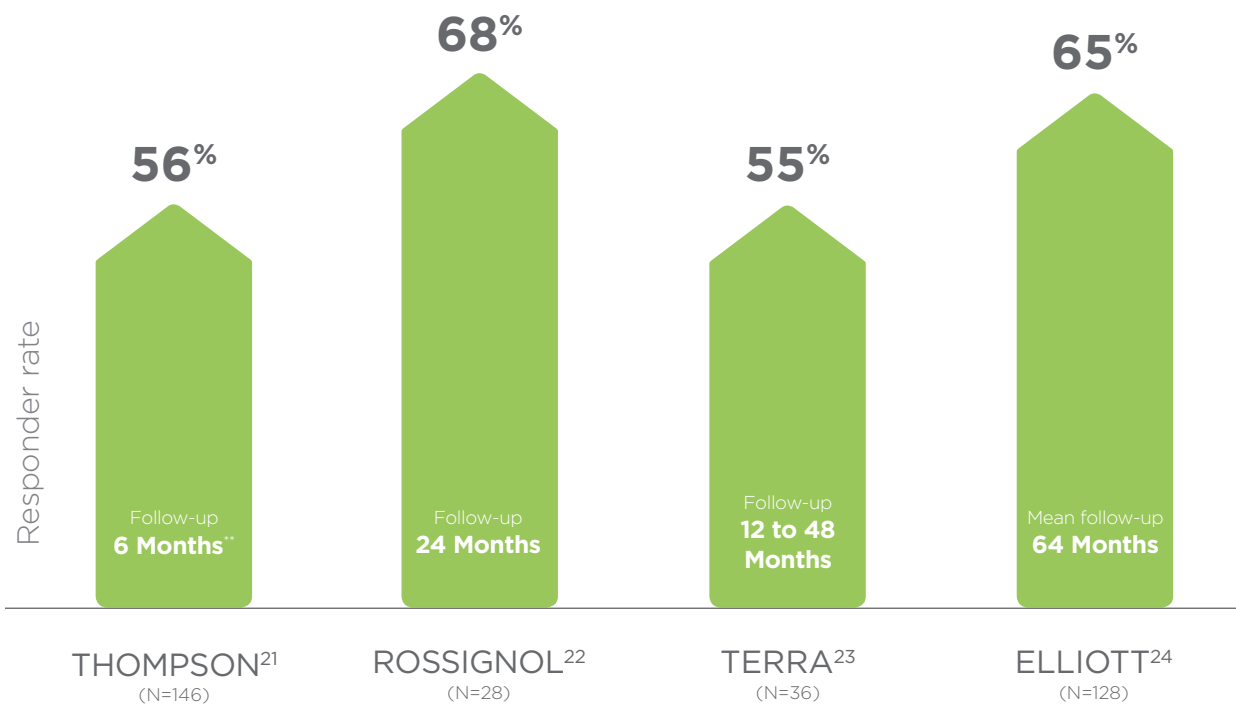
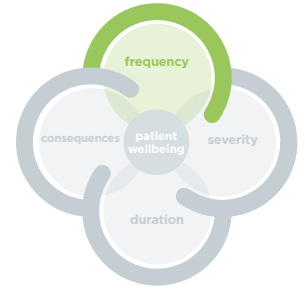
## Adult Patients



PERCENTAGE OF PATIENTS  $\geq 50\%$  SEIZURE FREQUENCY REDUCTION

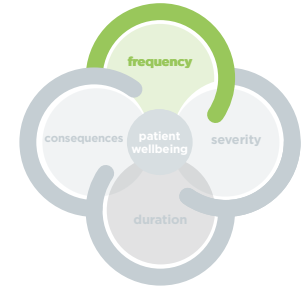
# Long-term efficacy of VNS Therapy

## Paediatric Patients



### PERCENTAGE OF CHILDREN WITH ≥50% SEIZURE FREQUENCY REDUCTION

\*\*Maintained at mean follow-up of 41 months



## Early reductions in seizure frequency that continued to improve over time

Improvements in seizure frequency were seen in a highly intractable patient population<sup>25</sup>

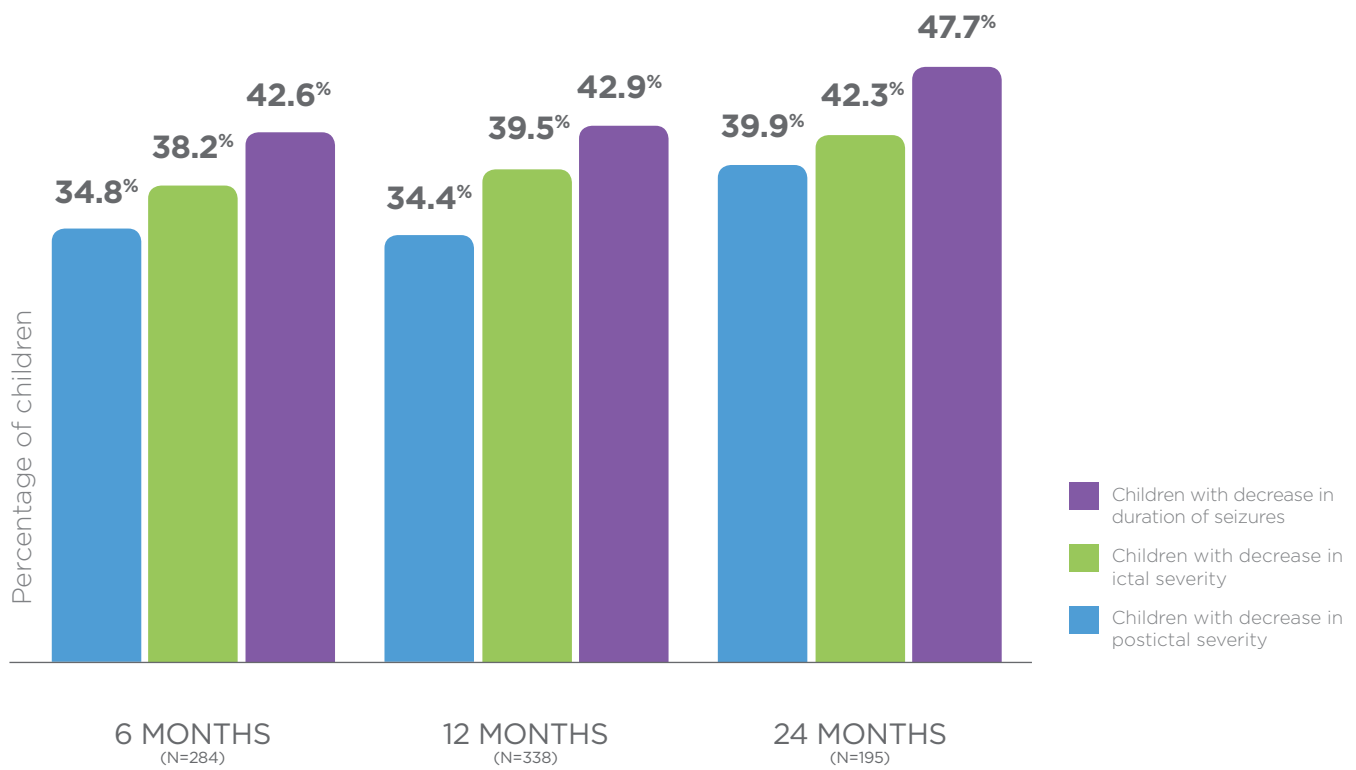
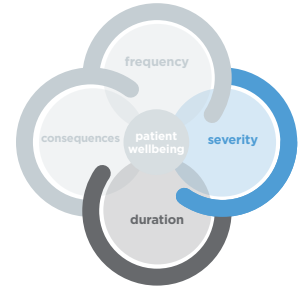
- 2.8 AEDs at baseline (median)
- 6 AEDs failed (mean)
- 20 years mean duration of epilepsy
- 31% prior brain or epilepsy surgery



MEAN % SEIZURE REDUCTION N=65



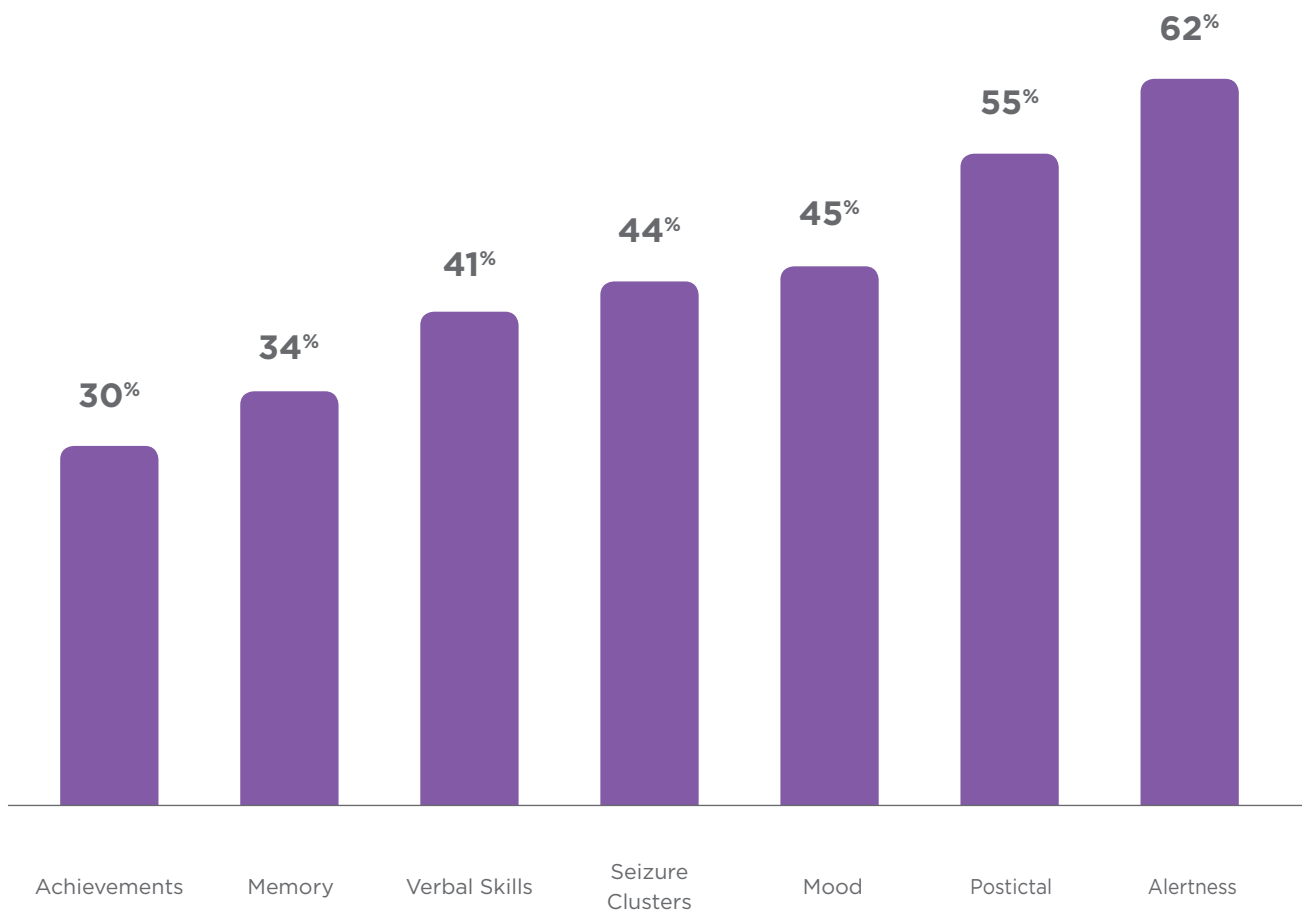
# Reductions in **seizure severity** and duration



## CHANGES IN SEIZURE SEVERITY OF PREDOMINANT SEIZURE TYPE<sup>26</sup>

# Significant improvements in quality of life

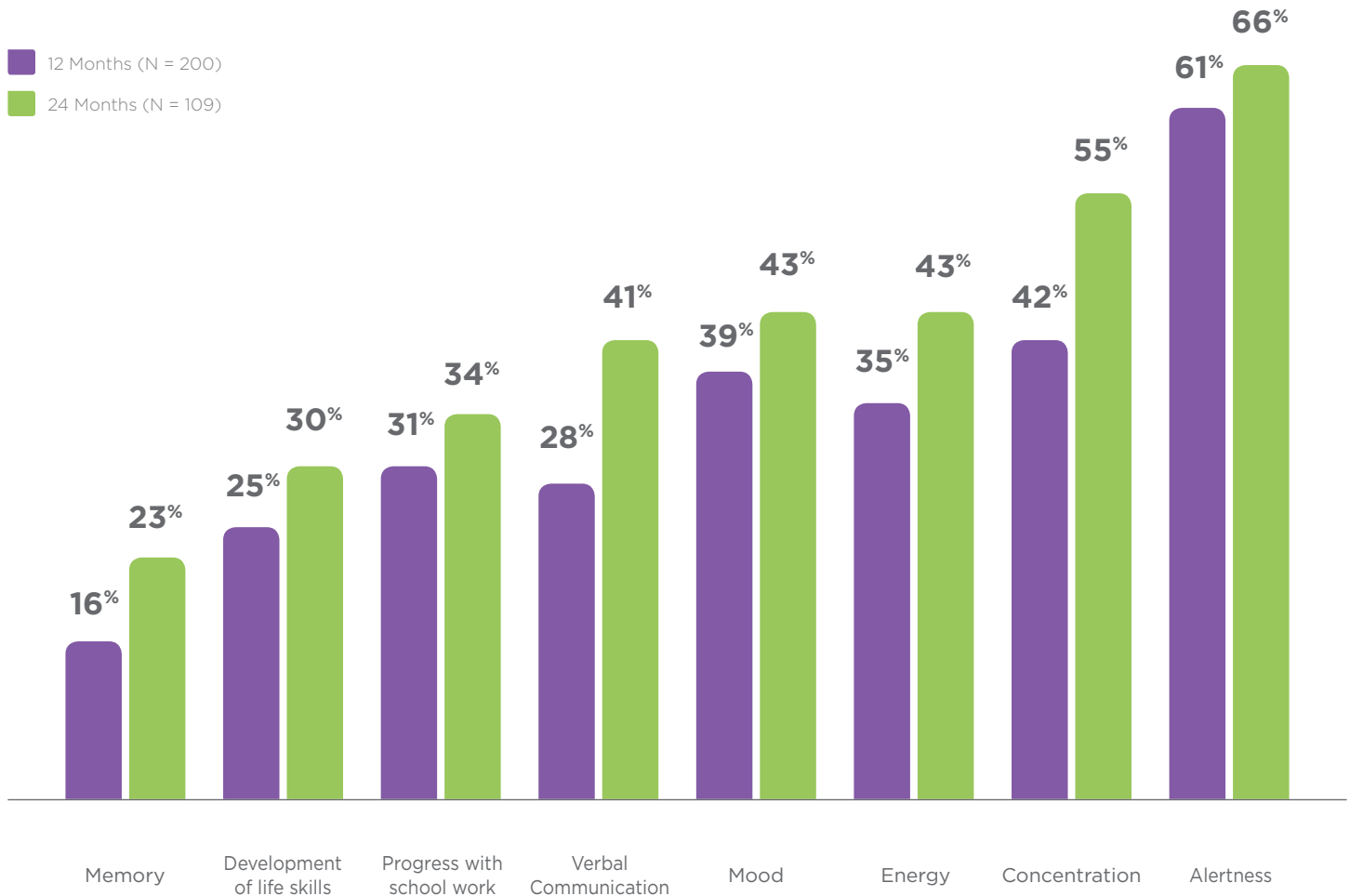
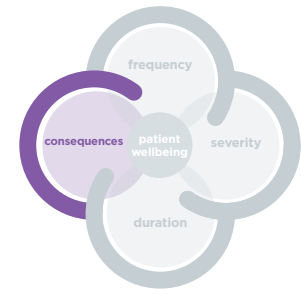
## Adult Patients



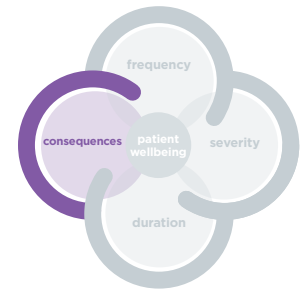
**IMPROVEMENT WAS DEFINED AS PATIENT BEING "BETTER" OR "MUCH BETTER"  
AT 12 MONTHS (N=2,229)<sup>30</sup>**

# Significant improvements in quality of life

## Paediatric Patients



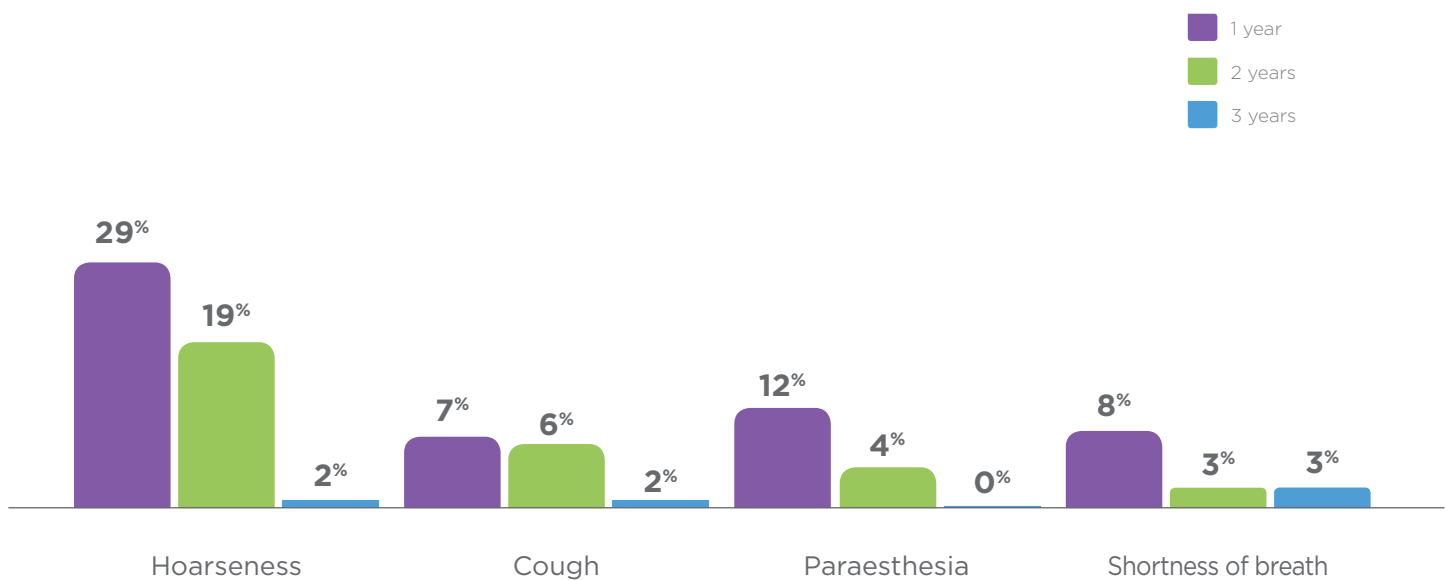
**IMPROVEMENT WAS DEFINED AS PATIENT BEING "BETTER" OR "MUCH BETTER"  
AT 12 & 24 MONTHS (N=109)<sup>26</sup>**



# Proven safety and tolerability

## Non-pharmacological side effect profile

- Occur **only during stimulation** and generally **diminish over time** <sup>27,28</sup>
- May be diminished or eliminated by the adjustment of parameter settings <sup>27,29</sup>



**MOST COMMON VNS THERAPY SIDE EFFECTS**  
(ADULTS AND CHILDREN, N=440) <sup>28</sup>

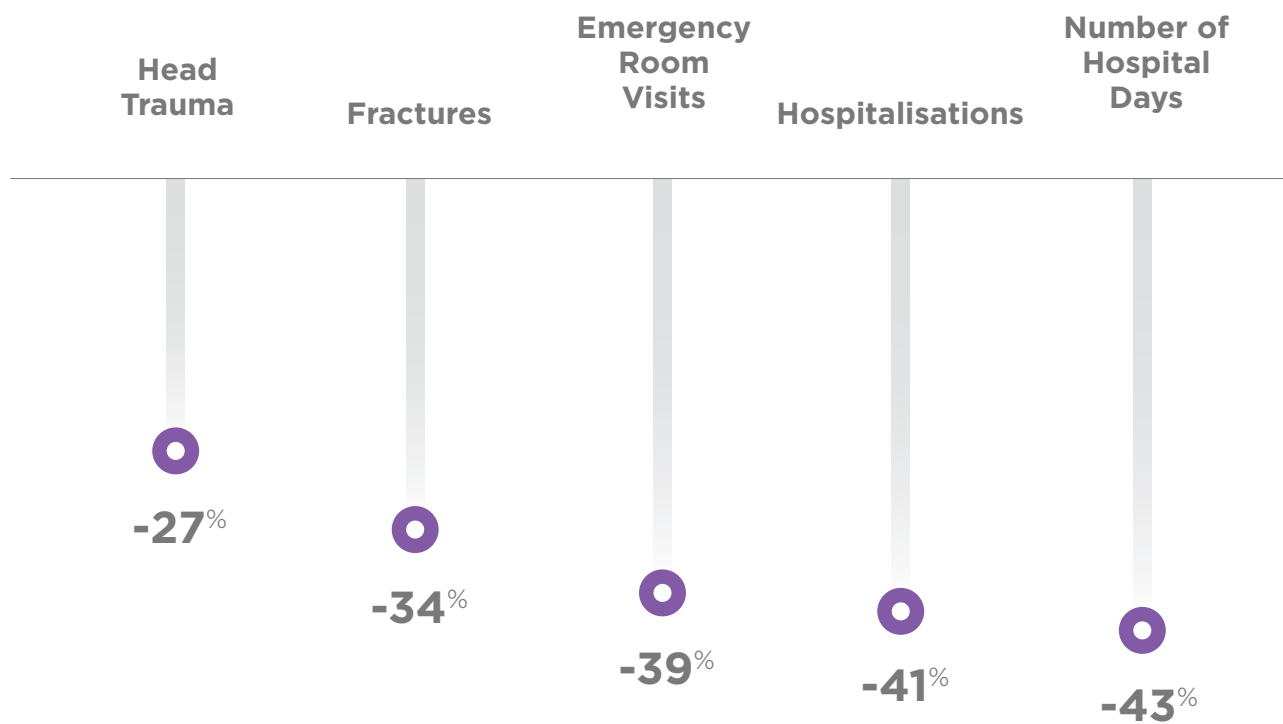
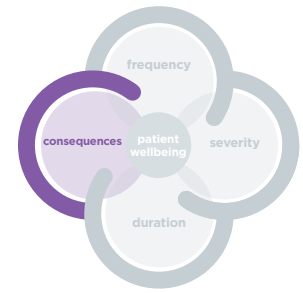
- Incidence of adverse events following stimulation (>5%) were dysphonia, convulsion, headache, oropharyngeal pain, depression, dysphagia, dyspnea, dyspnea exertional, stress, and vomiting.







# VNS Therapy reduces hospitalisations and health-related events

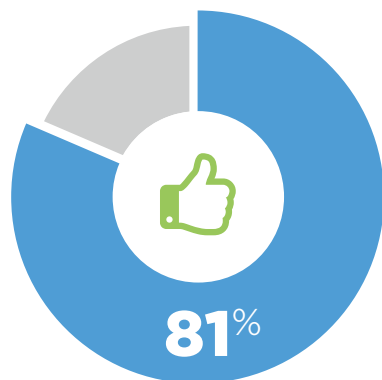
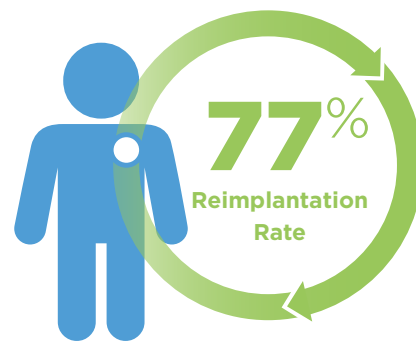


POST-VNS THERAPY REDUCTIONS IN HOSPITALISATIONS AND HEALTH-RELATED EVENTS N=1,655 AVERAGE FOLLOW-UP 30.4 MONTHS<sup>7</sup>



# The most proven neuromodulation therapy in use for Drug-Resistant Epilepsy patients<sup>30</sup>

**85,000**  
Patients treated



report VNS Therapy to be worthwhile, irrespective of seizure response and psychosocial outcomes<sup>31</sup>

(N=21)

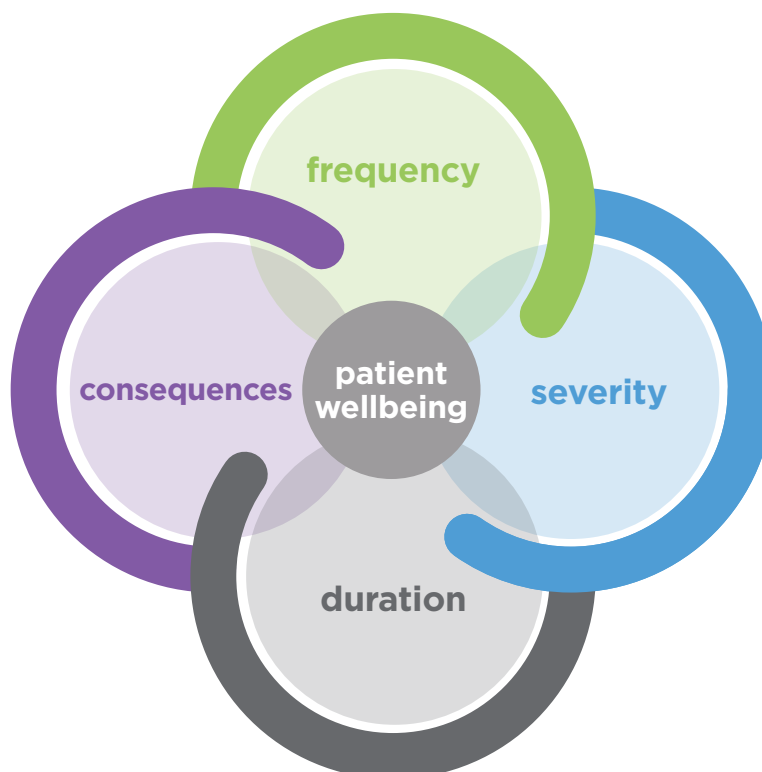
**1000**  
Peer-reviewed publications



## Why wait for patient wellbeing?



- **Seizure reduction** that continues to **improve over time**
- **Decreased seizure severity** and **duration**
- **Improves quality of life**
- **Decreased hospitalisation**
- **Non-pharmacological side effects** that typically **diminish over time**
- **Easy to use** treatment





#### 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 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](http://www.VNSTherapy.com) for more information.

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

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