

The Expanding Role of Patients and Advocacy Organizations in Advancing Research and Care

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Director of Research & Strategy, Contractor

LGS FOUNDATION
LENNOX-GASTAUT SYNDROME



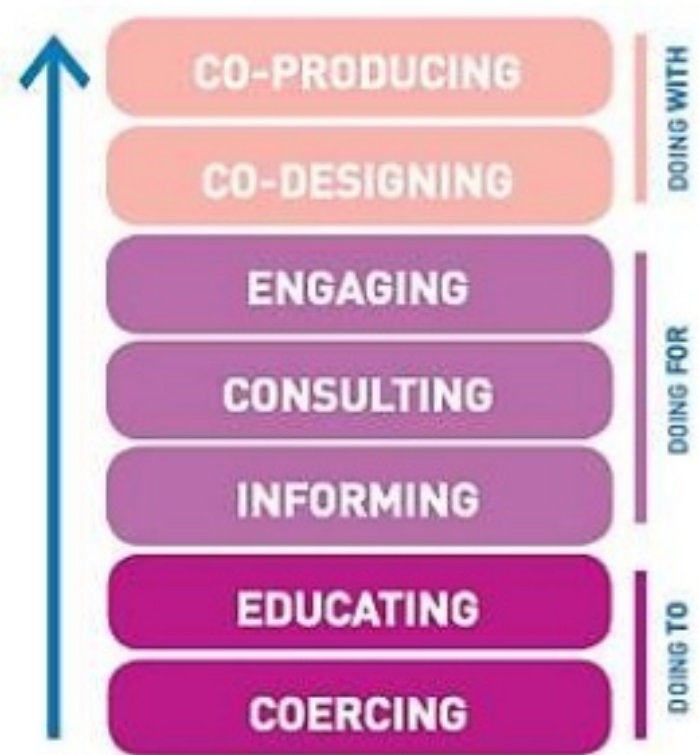
Expansion from Passive Patients to Patients as Full Partners

A Continuum of Co Production

Partnership

**Patient
Voice/influence**

Passive Patient



Source: new economics foundation

Savannah



Lennox Gastaut Syndrome

Age of onset – 1-7 years of age

Seizure types – tonic (mostly nocturnal), atonic, myoclonic, atypical absence, generalized tonic clonic, focal

Associated EEG patterns – generalized 1-2hz slow spike and wave, generalized slowing, paroxysmal fast activity (recruiting rhythm) during sleep (see figures)

Common etiologies – variety of etiologies, preceded by infantile spasms in 9-40% of cases

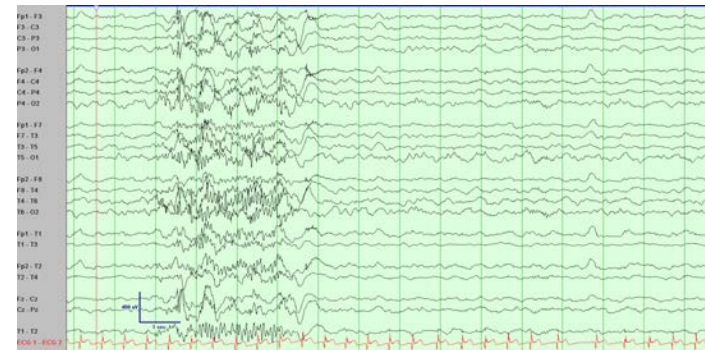
Treatment – felbamate, clobazam, rufinamide, topiramate, zonisamide, ketogenic diet, valproate, levetiracetam, VNS, corpus callosotomy, focal cortical resection (if there is a focus)

Prognosis – moderate to severe intellectual impairment, usually correlates with etiology and seizure control

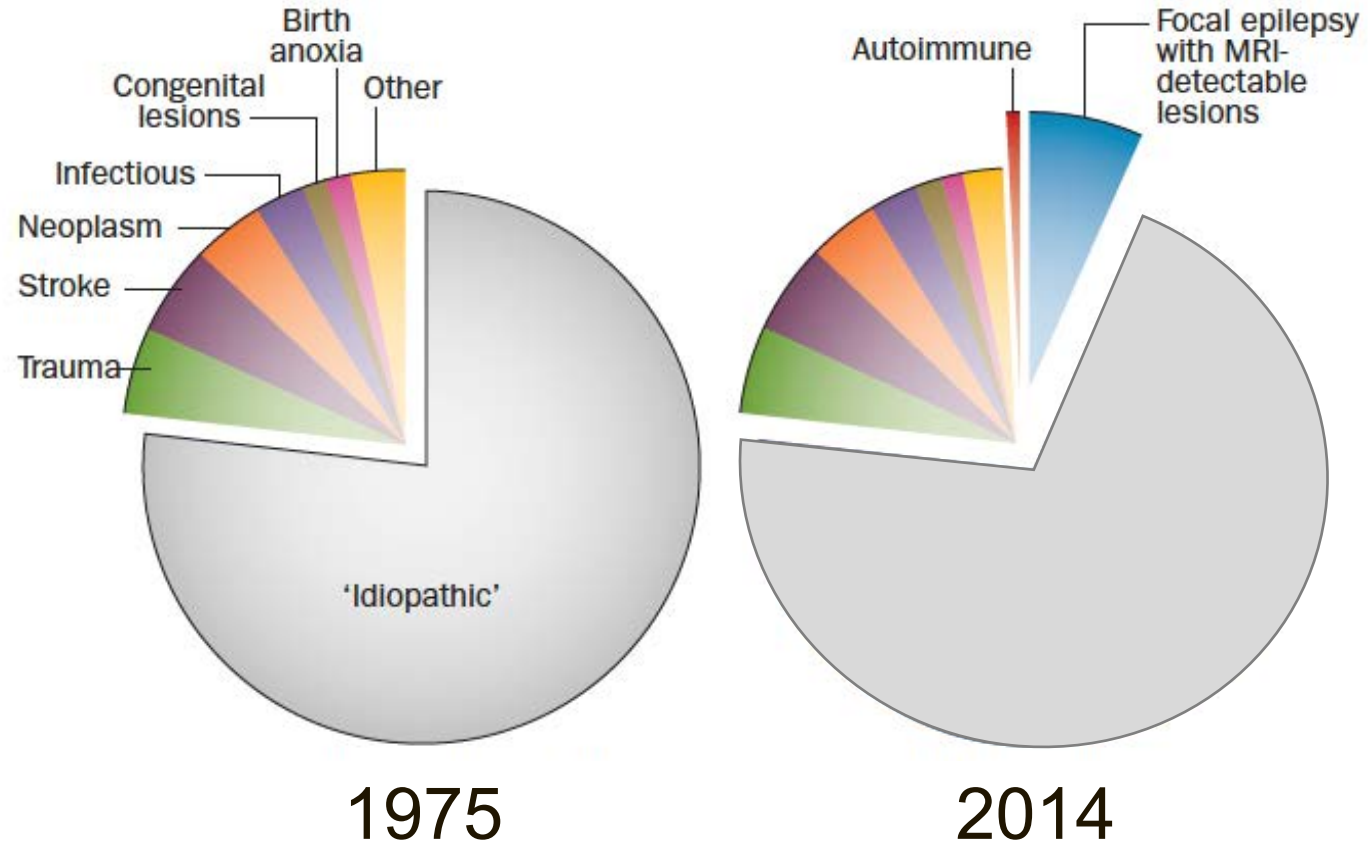
EEG: Slow Spike and Wave



EEG: Paroxysmal Fast Activity



Causes of Epilepsy

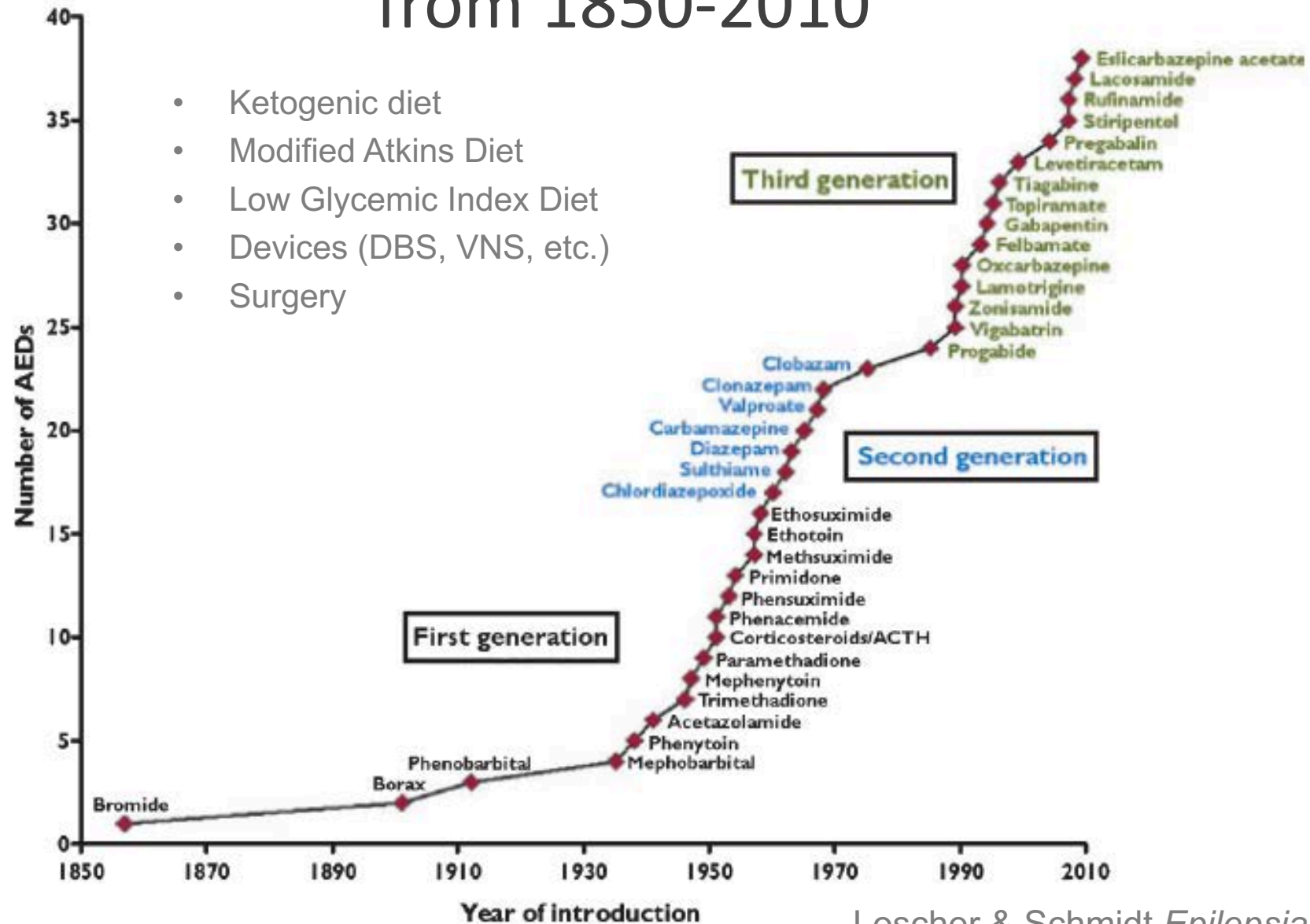


Hauser & Kurland 1975

Thomas & Berkovic 2014

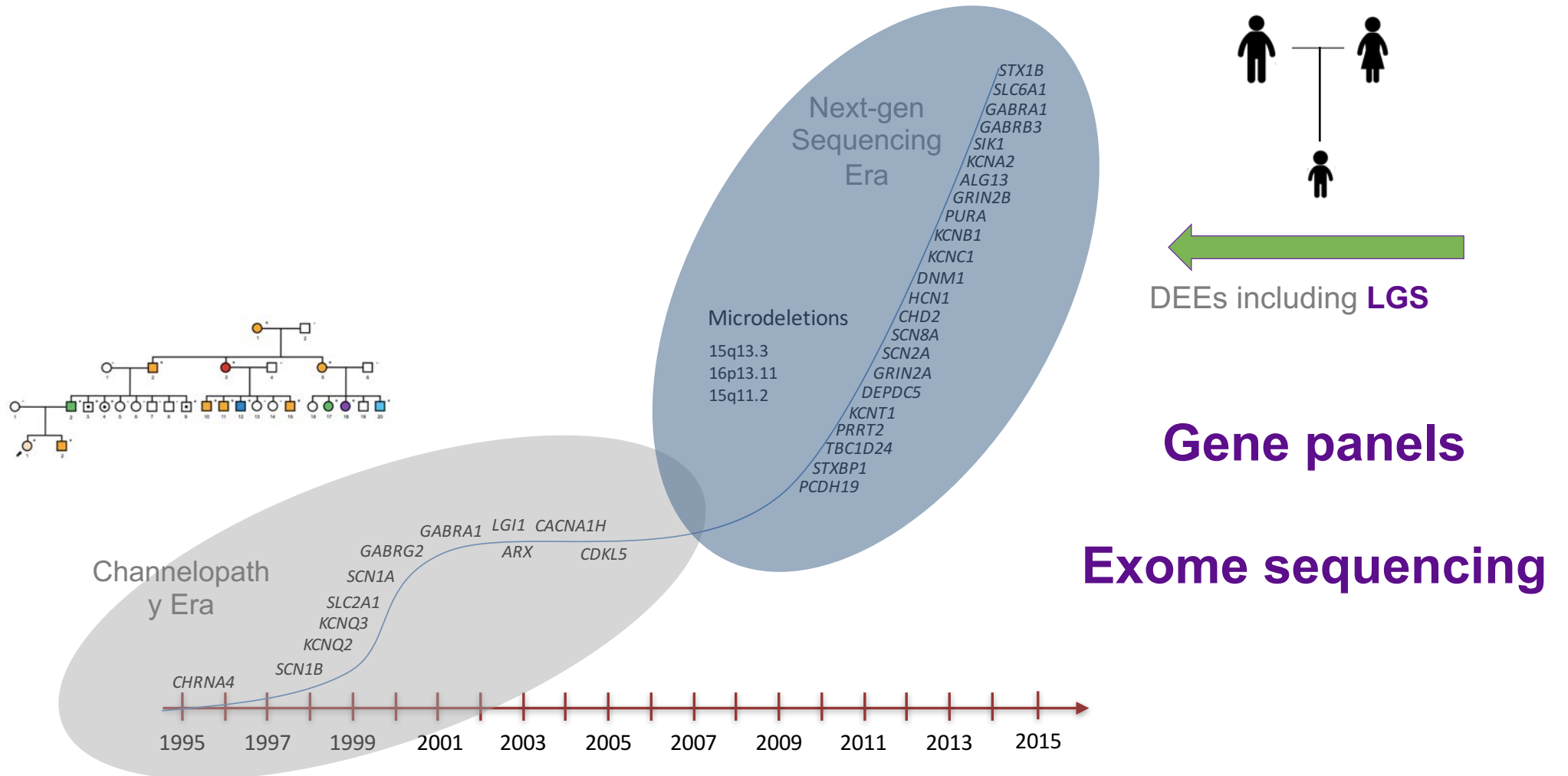
~40 approved epilepsy medications from 1850-2010

- Ketogenic diet
- Modified Atkins Diet
- Low Glycemic Index Diet
- Devices (DBS, VNS, etc.)
- Surgery

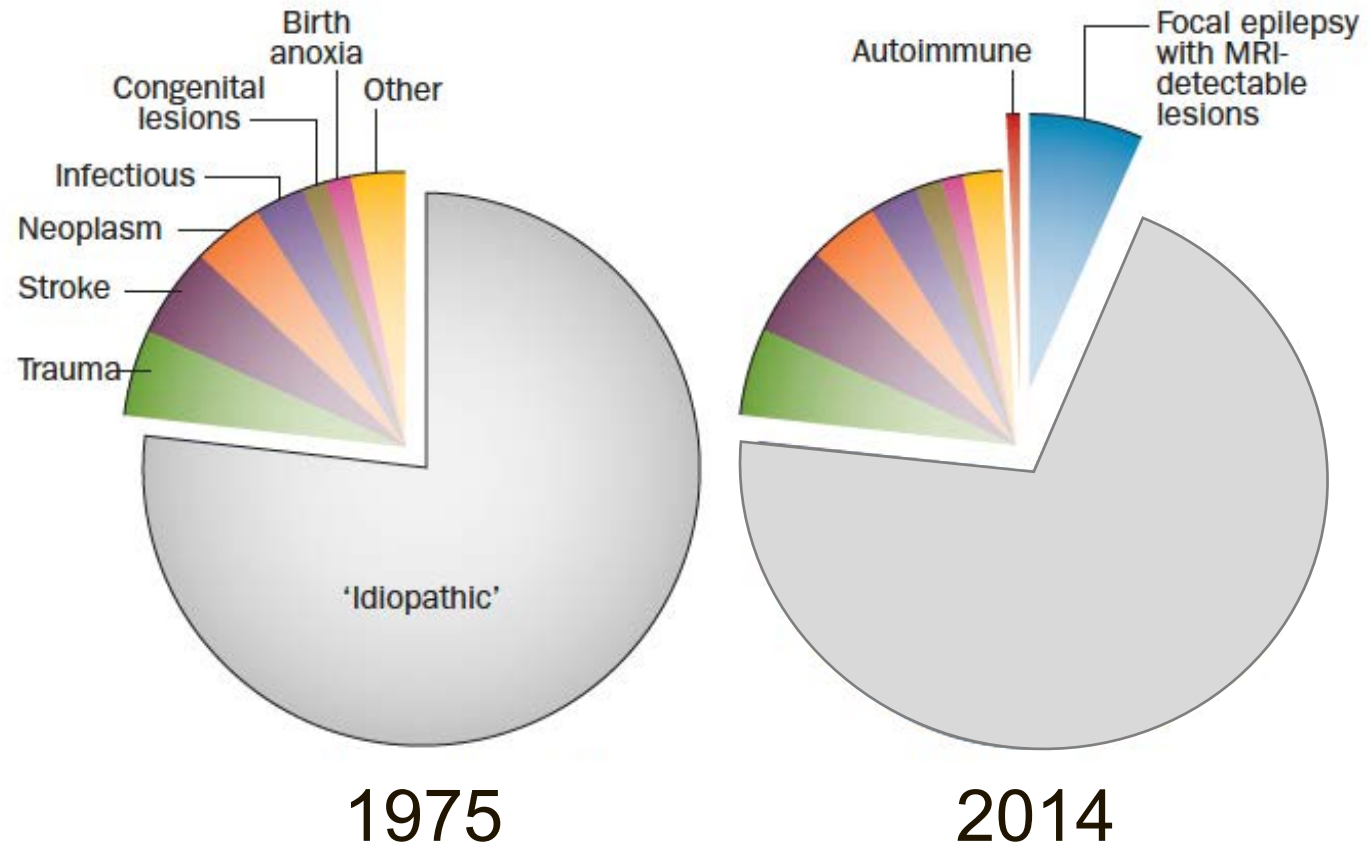




Gene discovery in epilepsy



Causes of Epilepsy



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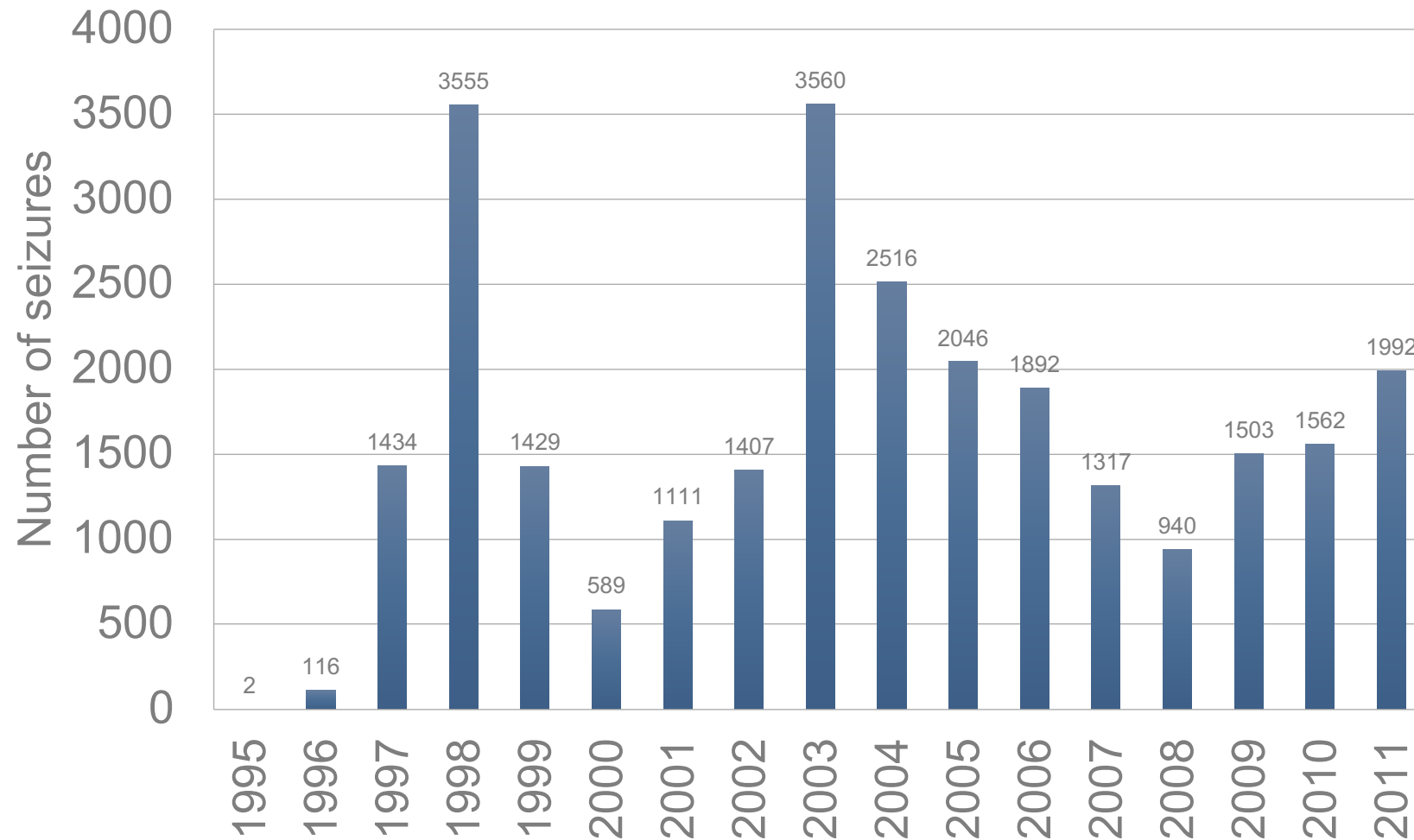
Savannah's Odyssey

1995-2011

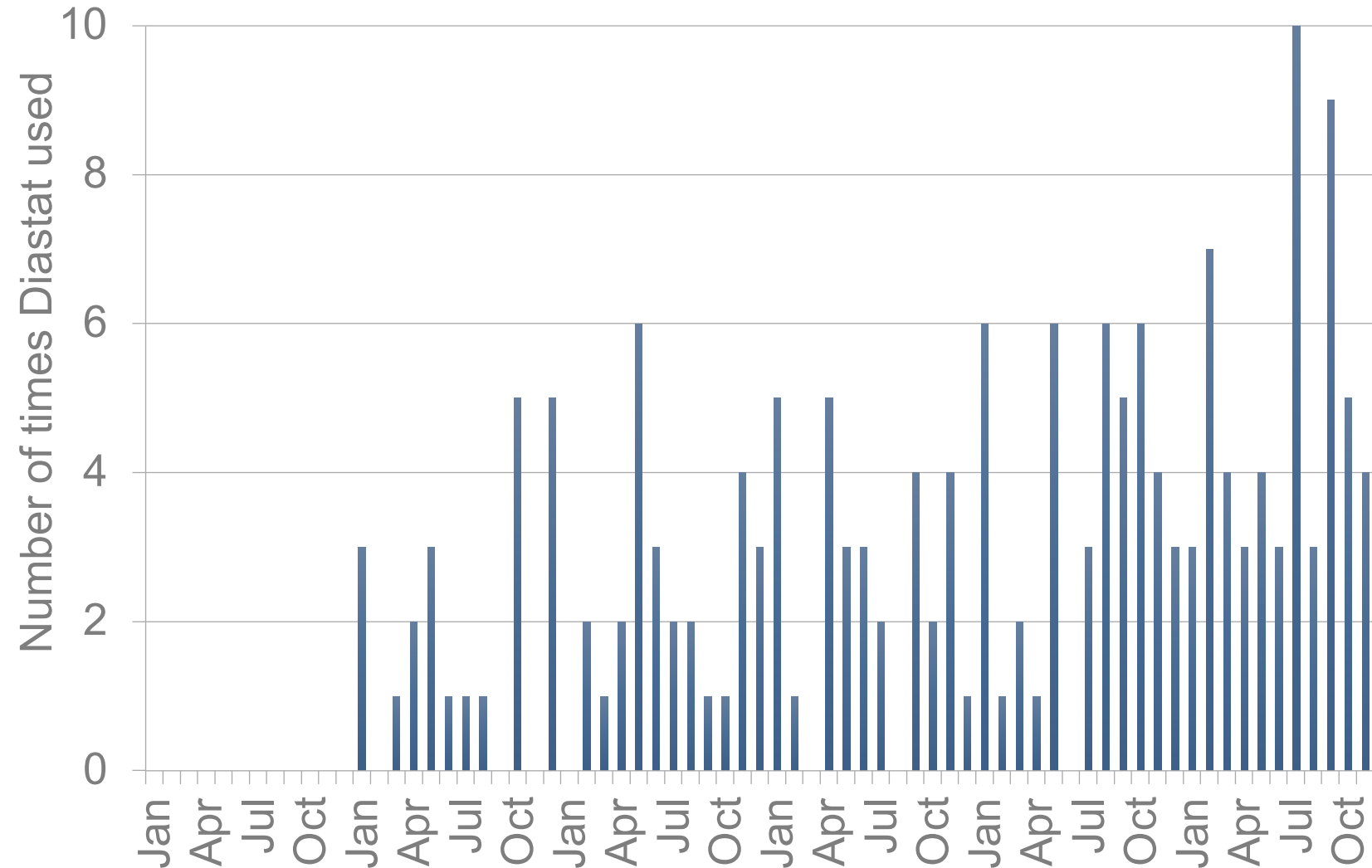
- # of Seizures: >40,000
- Diagnosis: 3 years
- # Neurologists: 7
- # Treatments: 26
- Cause: Unknown
- Hospitalizations: 15
- Surgeries: 5
- Monthly drug cost: \$1,640
- Diastat use: \$183 / dose
- Last stay: \$53,475



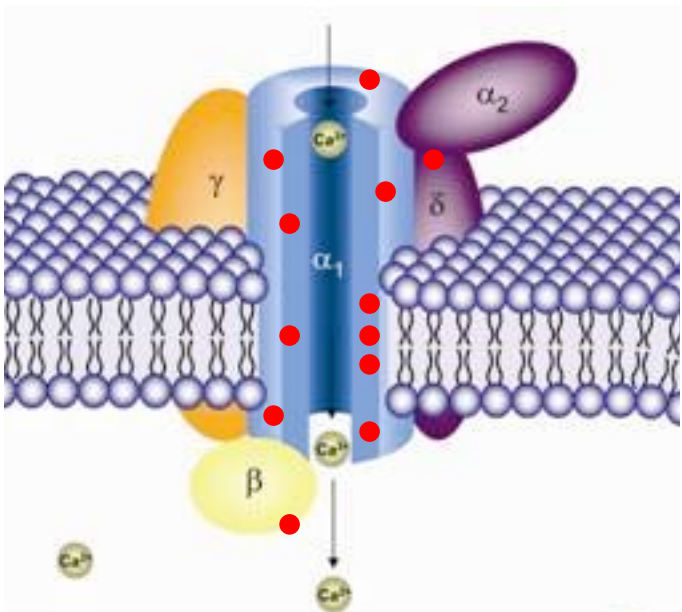
Number of seizures per year 1995 to 2011



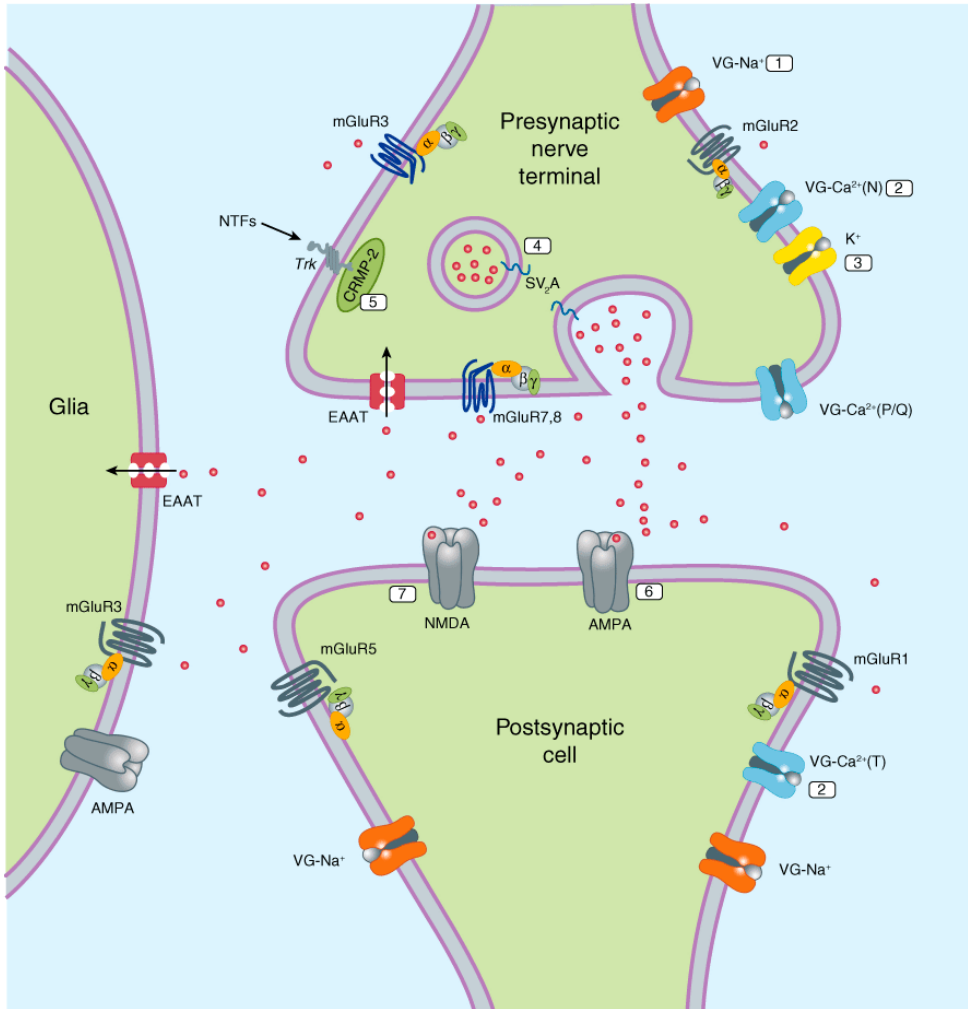
Monthly emergency medication use for non-stop seizures 2006 to 2011



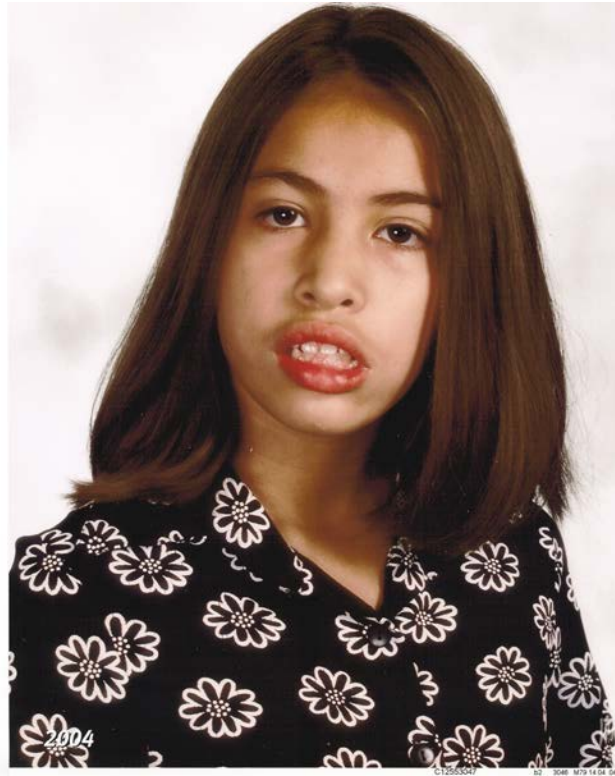
Exome identified numerous high impact variants in calcium channel subunits



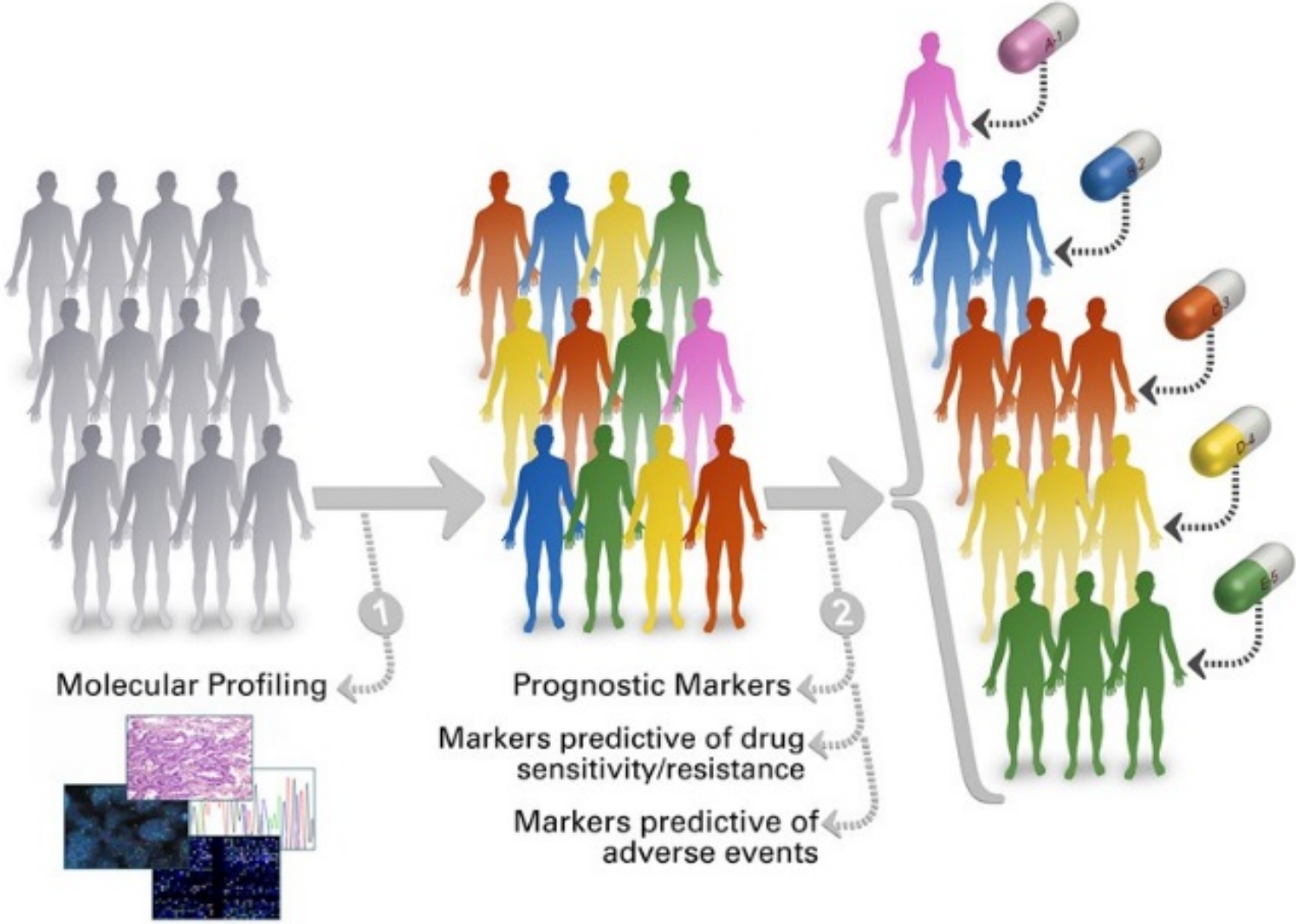
- Approximate variant location



Savannah Today



Stratify Patients by Etiology



Precision therapeutics – now

Gene	Syndrome	Change in Management	Other Clinical Implications
<i>SCN1A</i>	Dravet, Migrating epilepsy of infancy	Avoid sodium channel agents, Stiripentol	Monitor gait, Increased risk of premature death
<i>SLC2A1</i>	Glucose transporter deficiency (GLUT1)	Ketogenic diet	Monitor for movement disorder
<i>HLA-A, HLA-B</i>	Variants found in certain ethnic groups	Avoid Carbamazepine	-
<i>PRRT2</i>	Infantile convulsions	Consider Carbamazepine	Surveillance for other neurological issues
<i>TSC1, TSC2</i>	Tuberous sclerosis, Infantile spasms	Consider Vigabatrin, Rapamycin	Surveillance for tumors, non-neurological issues
<i>ALDH7A1, PNPO</i>	Severe early-onset epilepsy	Supplement with Pyridoxine (Vitamin B6)	-
<i>PCDH19</i>	Female epilepsy with intellectual disability	Avoid carbamazepine, consider Clobazam	-
<i>POLG1</i>	Mitochondrial epilepsy disorder	Fatal liver toxicity with Valproate	-

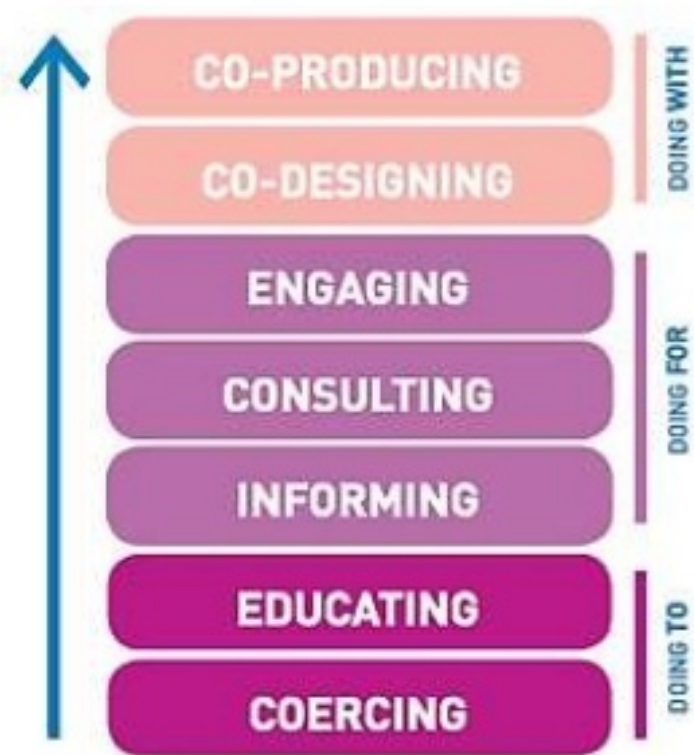
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**Patient
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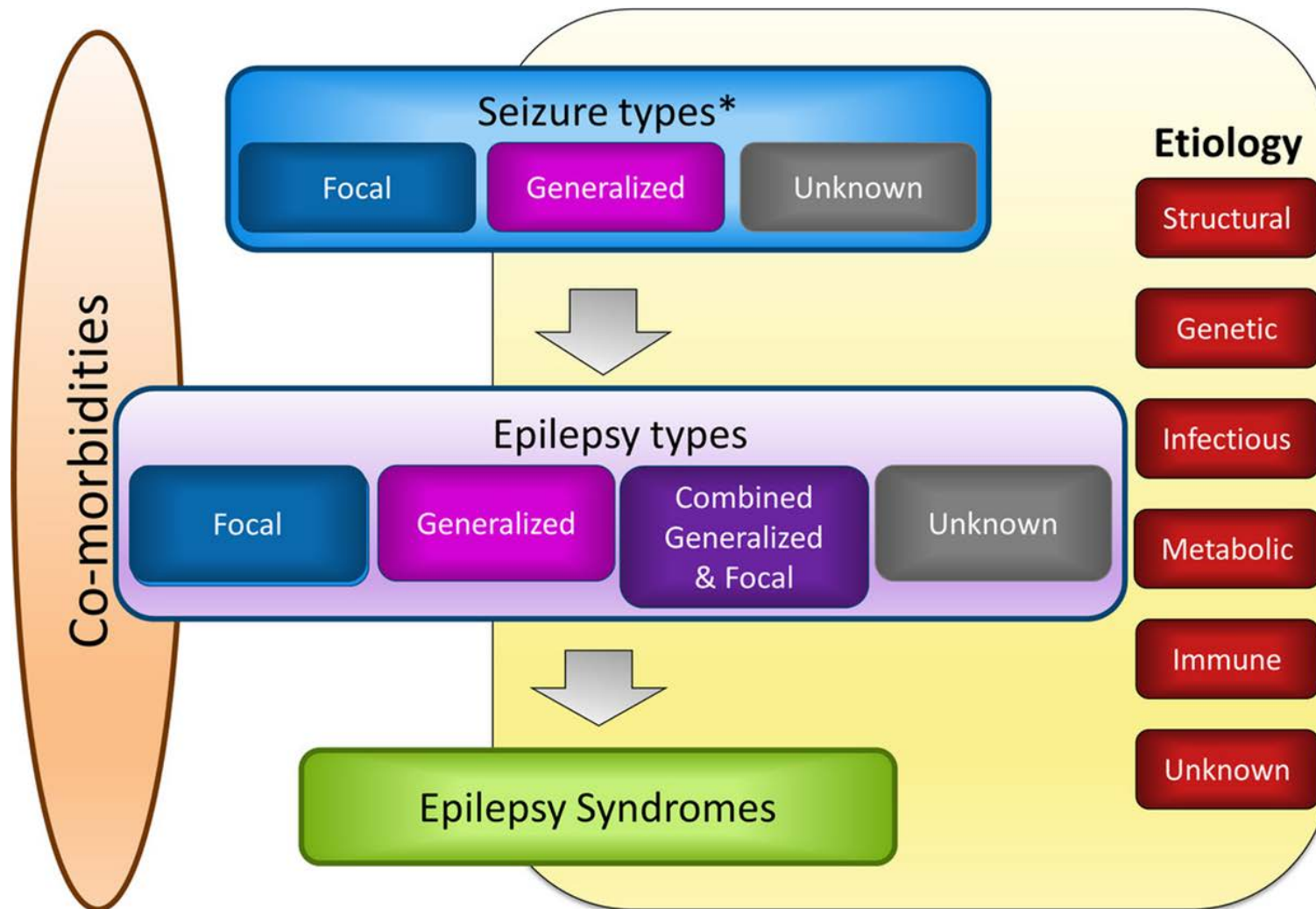


Source: new economics foundation

From Science to Patient Experience



ILAE Epilepsy Classification



Lennox Gastaut Syndrome

Age of onset – 1-7 years of age

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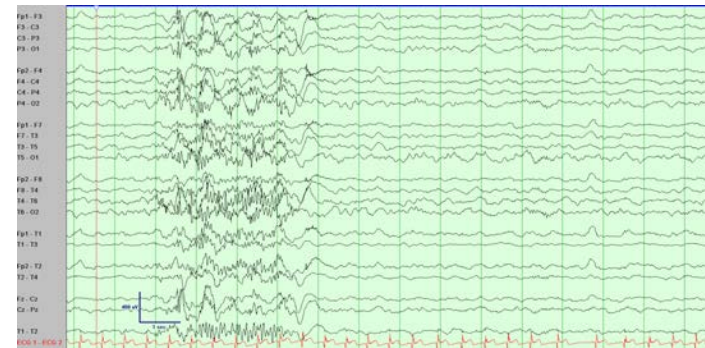
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EEG: Slow Spike and Wave



EEG: Paroxysmal Fast Activity



EVOLUTION OF LGS OVER TIME

40-50K cases of LGS in the US

- Structural**
- Congenital (17%)
 - Injury (33%)
- Genetic (15%)**
- Infectious (15%)**
- Metabolic (9%)**
- Immune (<1%)**
- Unknown (~10%)**

1st seizure → Epilepsy → Treatment resistant epilepsy (West, EIEE, etc.)

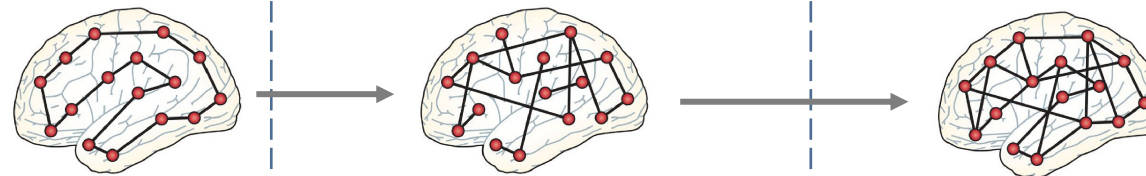
LGS Clinical Triad

- >1 seizure type
- SSW on EEG / PFA
- Cognitive impairment

Other seizure types emerge

Developmental delay emerges

- >90% seizures into adulthood
- >90% with tonic seizures in sleep
- >80% with cognitive impairment
- 14x↑ risk of death



ETIOLOGY

EVOLUTION

DISORDER OF THE NETWORK

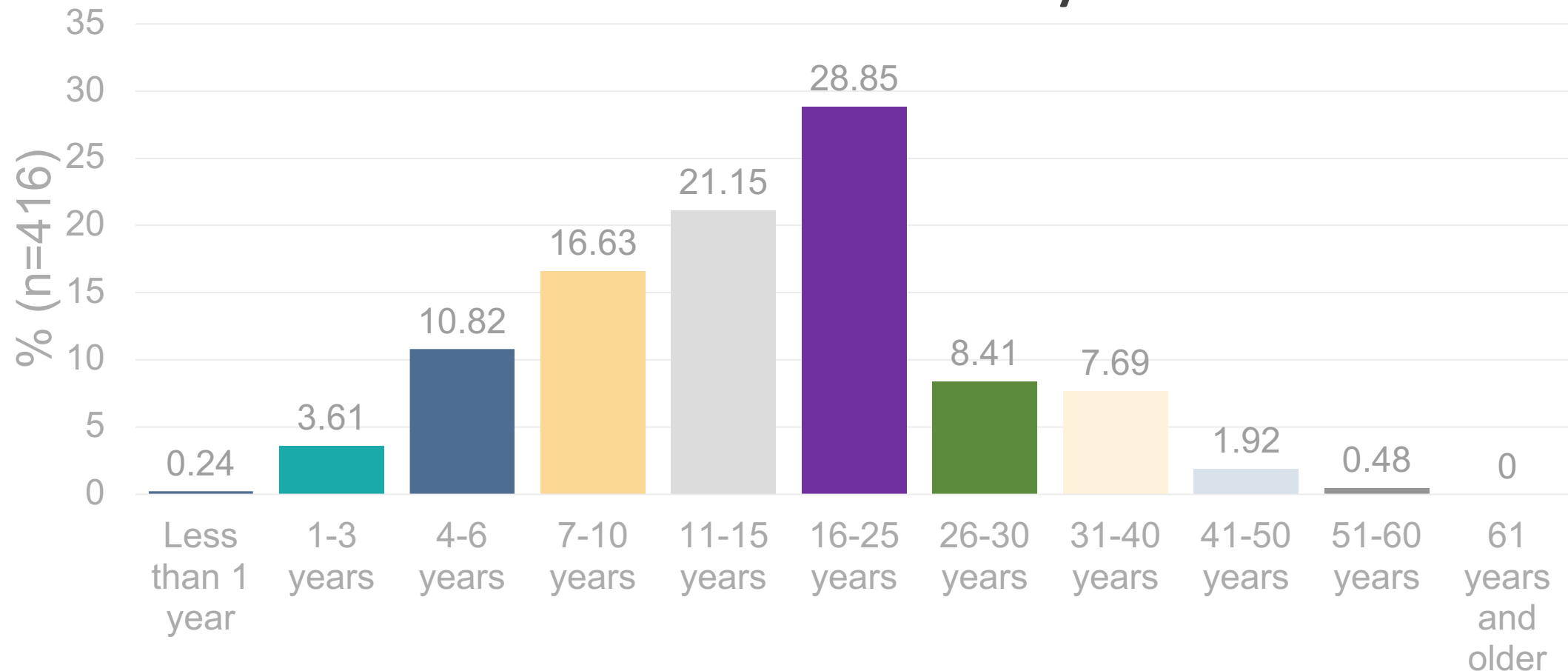
TIME

(For LGS onset <8 years, peak 3-5 years)

LGS CHARACTERISTICS & CAREGIVER CONCERNS

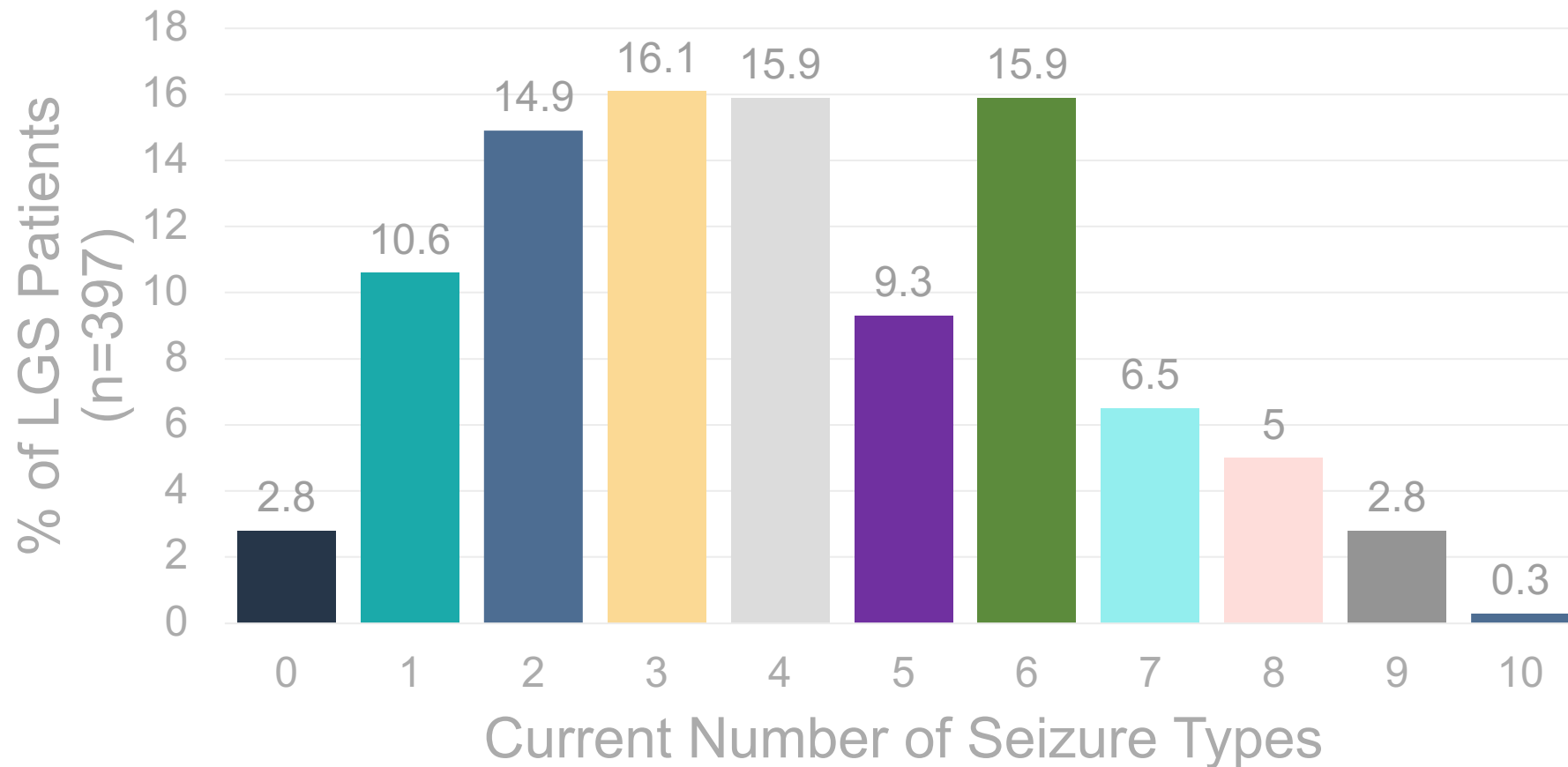
LGS Foundation Caregiver Survey

What is the current age of the person with LGS that you care for?



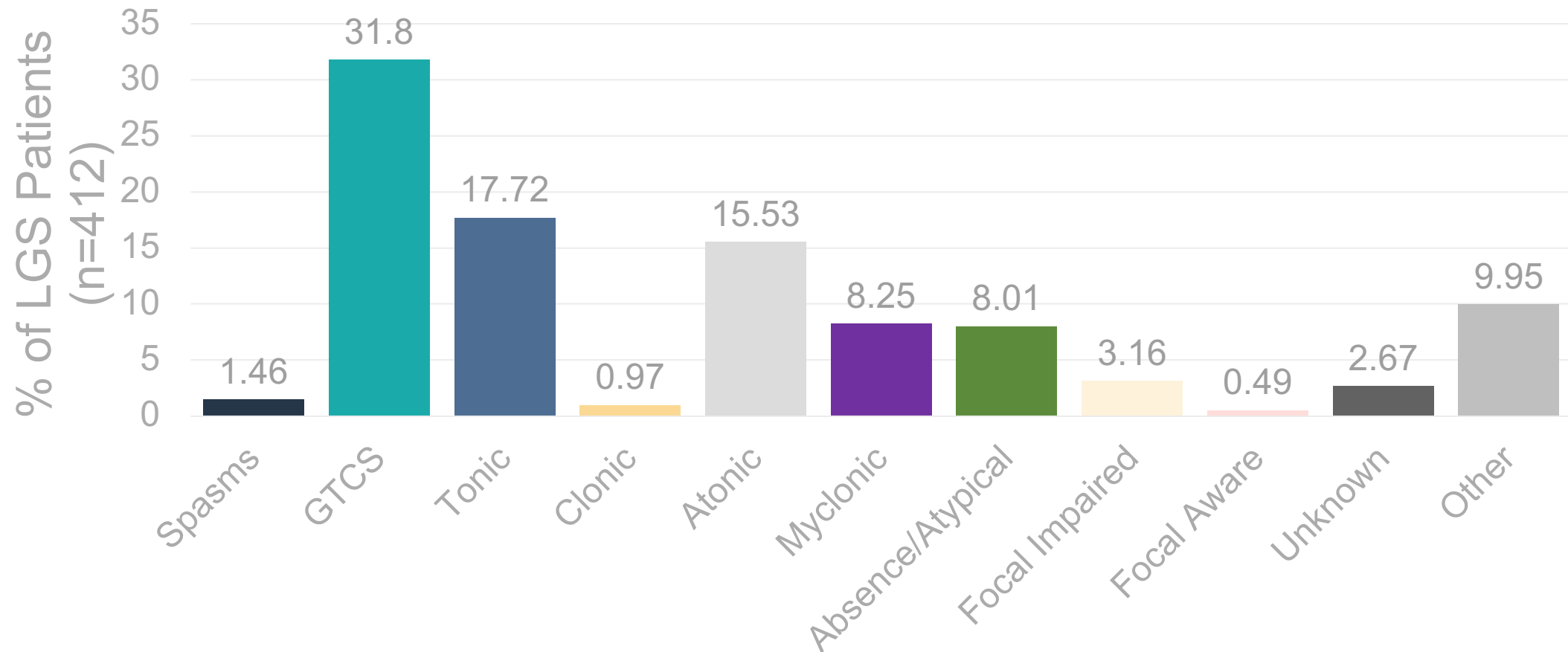
LGS CHARACTERISTICS & CAREGIVER CONCERNS

How many types of seizures is the person with LGS having AT THIS TIME?

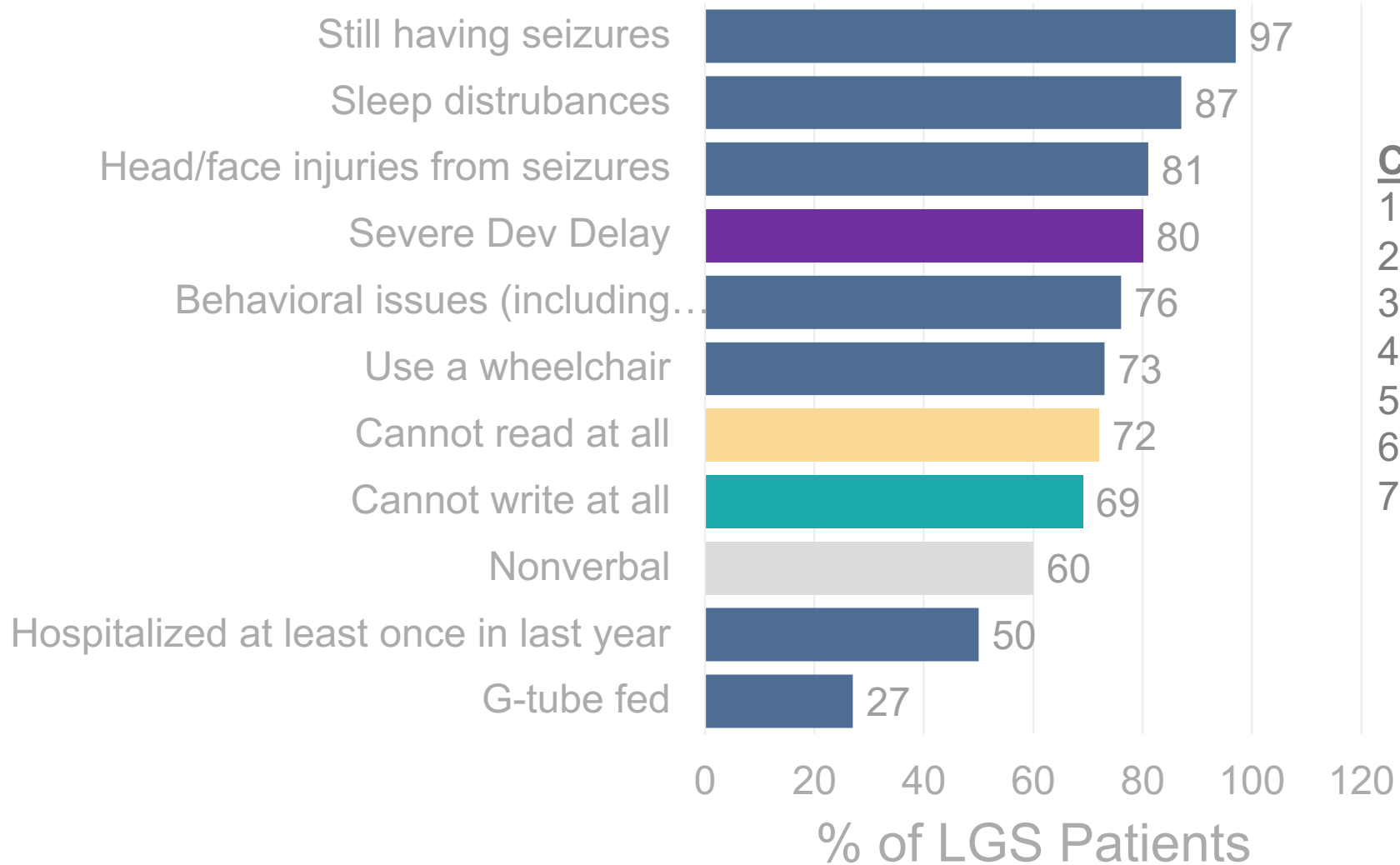


LGS CHARACTERISTICS & CAREGIVER CONCERNS

What is the most problematic seizure type they are dealing with AT THIS TIME?



MAJOR ISSUES IN LGS REPORTED BY CAREGIVERS



Caregiver Priorities:

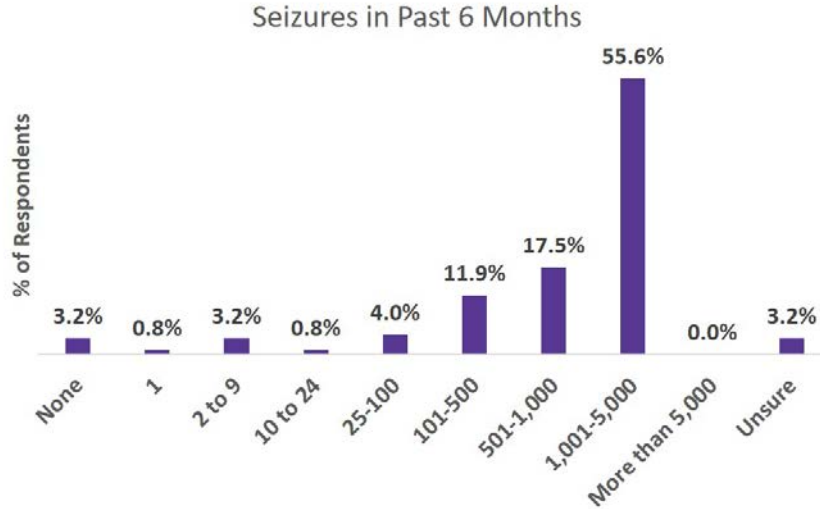
1. Seizures and safety
2. Delay/ID, especially communication
3. Behavior, especially aggression
4. Mobility and physical care issues
5. Sleep
6. Costs/Access to care
7. Social Isolation

LENNOX-GASTAUT MEDICAL HISTORY – REN SURVEY

Poor Seizure Control



A majority of respondents had observed over 1,000 seizures in the past 6 months



14% have never sat up without help

24% have never walked

43% have never spoken a 2 word sentence

Co-occurring Conditions?

- 33% have Autism
- 17% have ADD/ADHD
- 9% have Anxiety Disorder
- 5% have Depression

n=200

LENNOX-GASTAUT MEDICAL HISTORY – REN SURVEY

On average

10-11 Different Anti-Seizure Medications Tried



3 -4 Anti-Seizure Medications Currently Taking

Top 5 AEDs Currently Using

- Clobazam (58%)
- Rufinamide (35%)
- Valproic Acid (33%)
- Levetiracetam (27%)
- Felbamate (26%)

Top 6 Discontinued AEDs

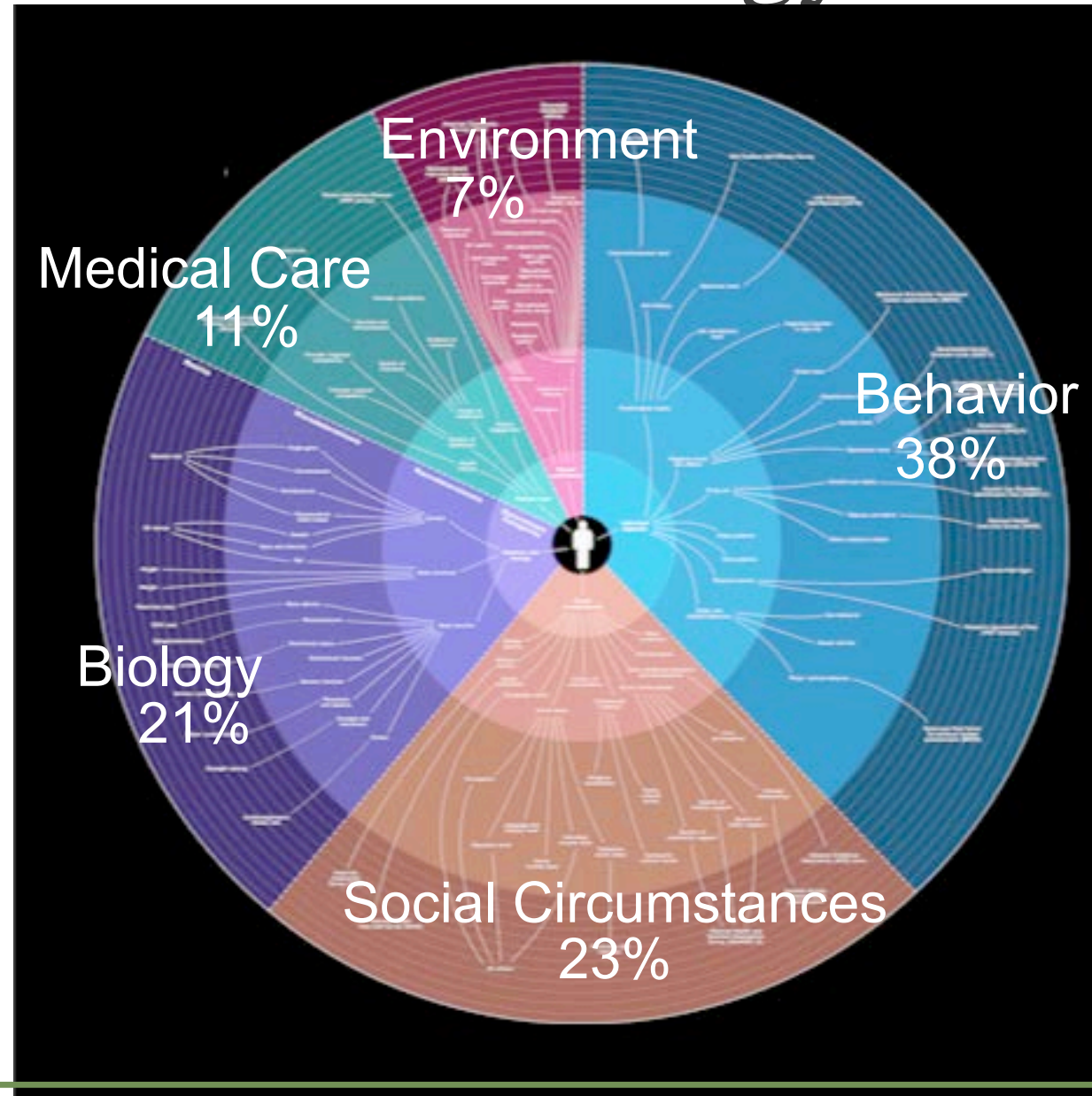
- Topiramate (67%)
- Levetiracetam (61%)
- Valproic Acid (60%)
- Lamotrigine (59%)
- Zonisamide (55%)
- Clonazepam (52%)

n=200

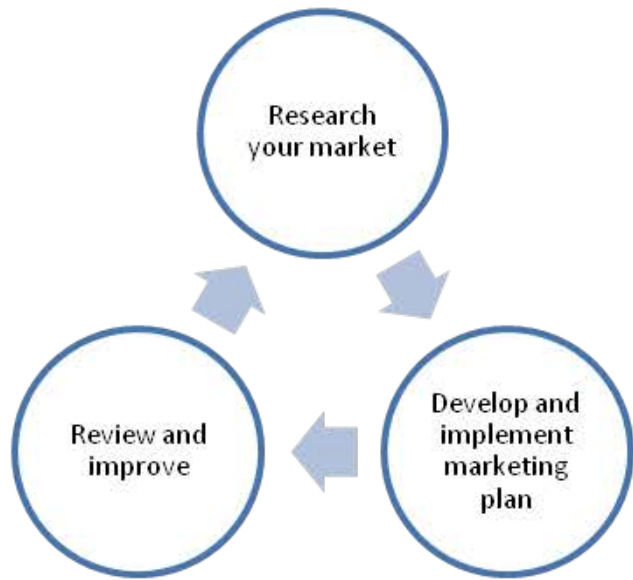
From Science to Patient Experience



Health is more than Biology & Medical Care

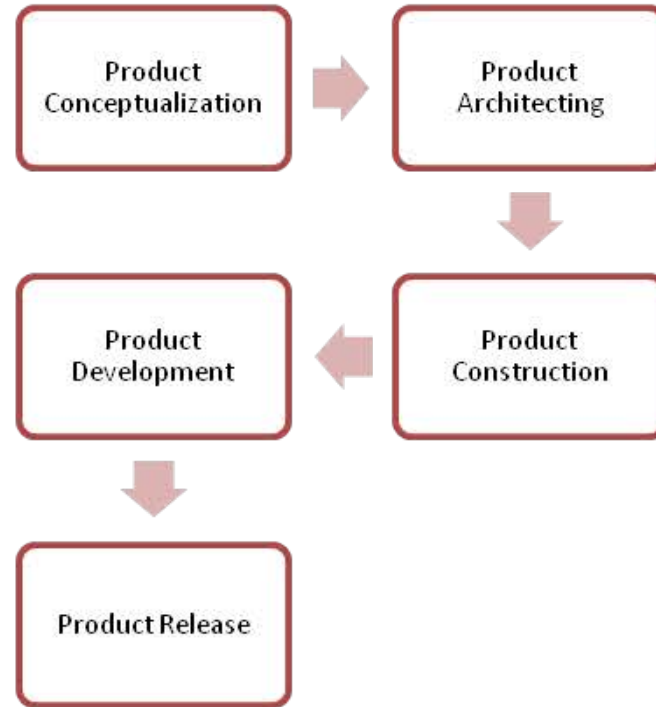


Change by Reframing Value



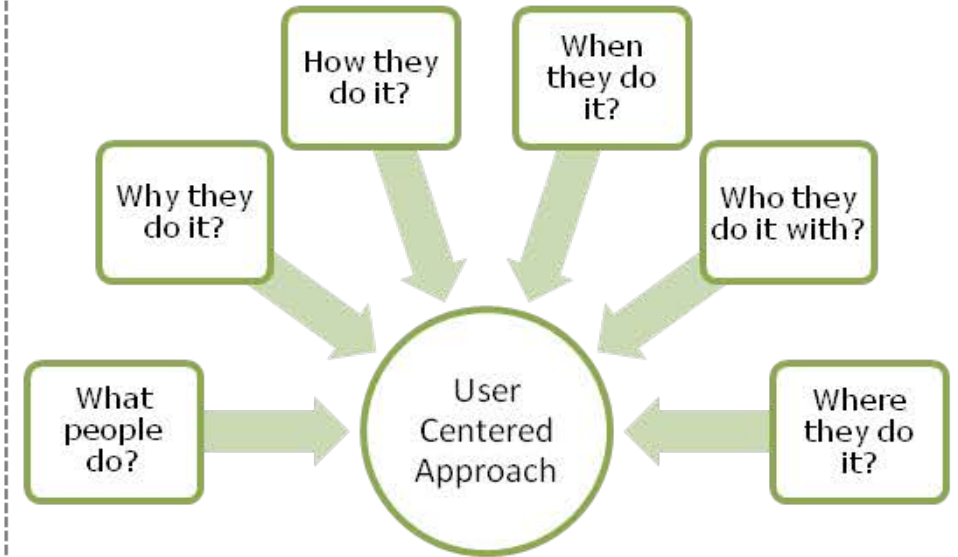
Consumer-led research

Marketing



Specific product development

Product Development



User Centered Design

Ethnographic Style Research

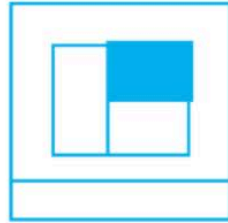
What do Patients Value?



Patient-Centered Outcomes





Patient & Family Costs

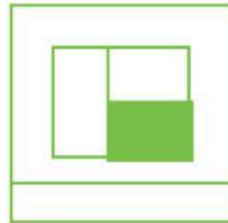
Quality & Applicability of Evidence



PATIENT-CENTERED OUTCOMES




What are the clinical, functional, and quality of life benefits/drawbacks of different healthcare options to the patient?

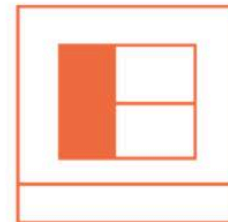
Quality of life 
Complexity of regimen 
Efficacy & effectiveness 
Safety: side effects/complications 



PATIENT & FAMILY COSTS




What are the overall costs of different healthcare options to the patient and family?

Medical out-of-pocket (OOP) costs 
Non-medical costs to the patient & family 
Future costs of care 

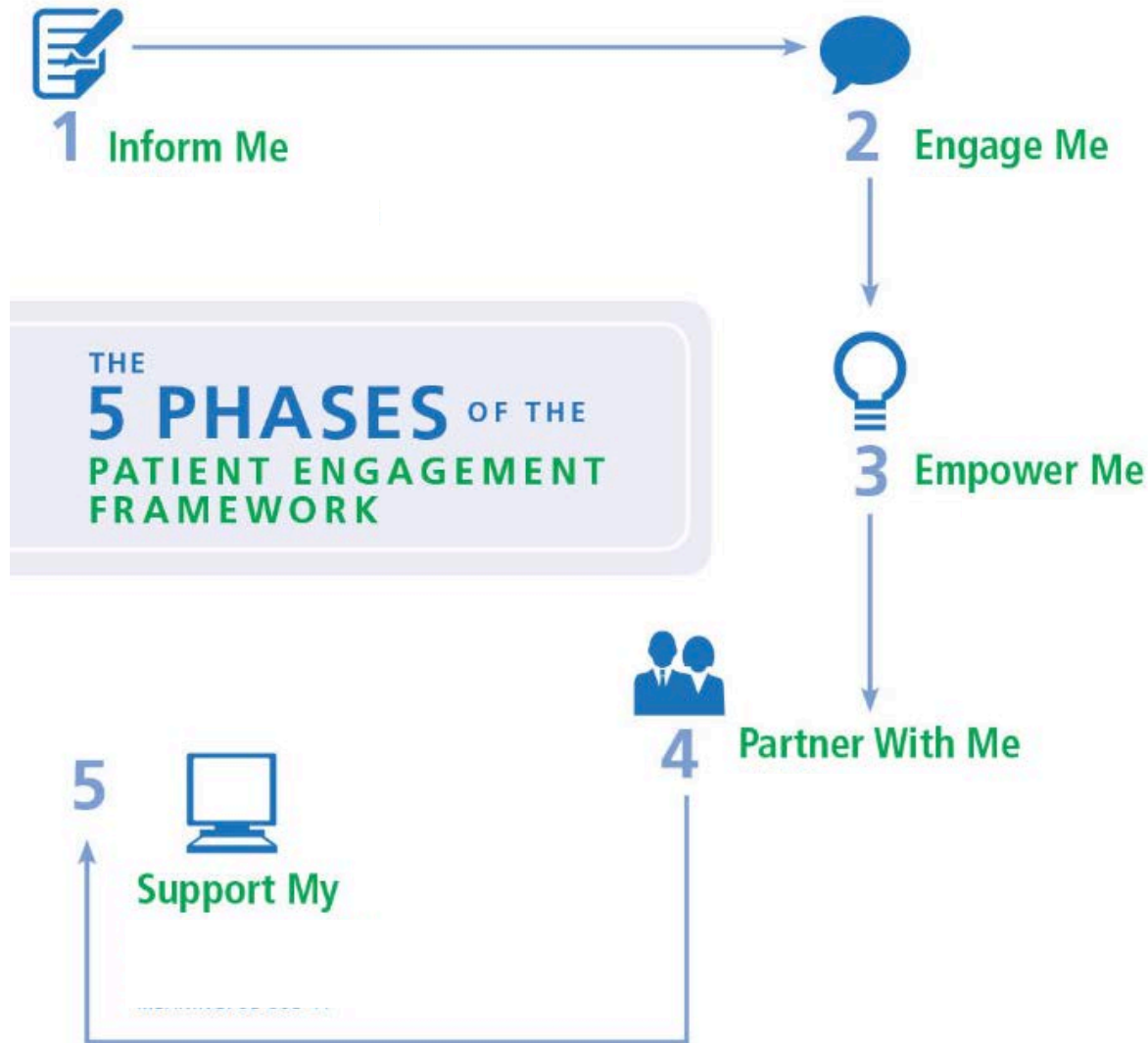


QUALITY & APPLICABILITY OF EVIDENCE

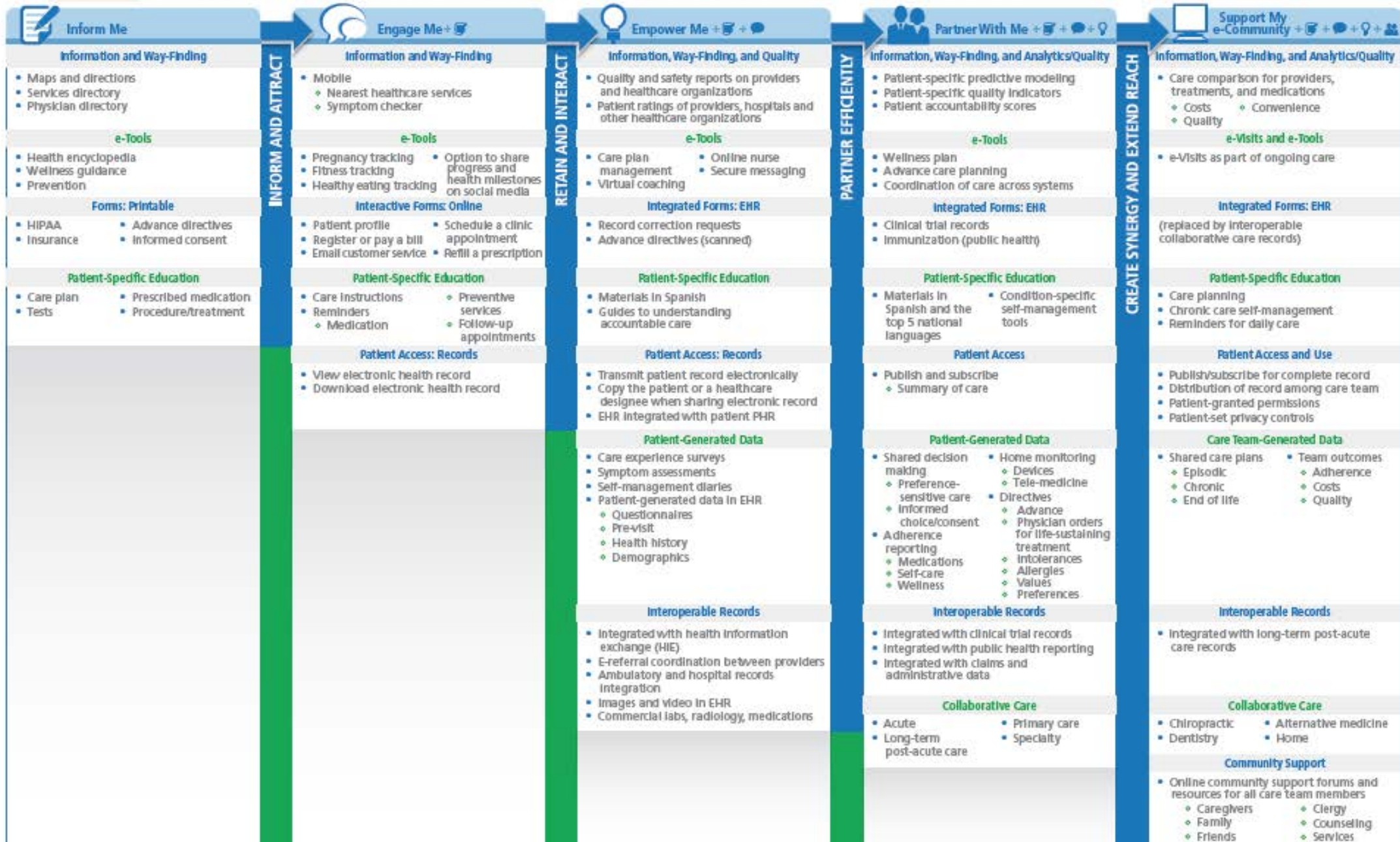
What level of confidence does the patient have that a healthcare option will have specific effects for them?

Quality of evidence 
Consistency of evidence 
Differences in treatment effects 

Change by Partnering with Patients & Caregivers

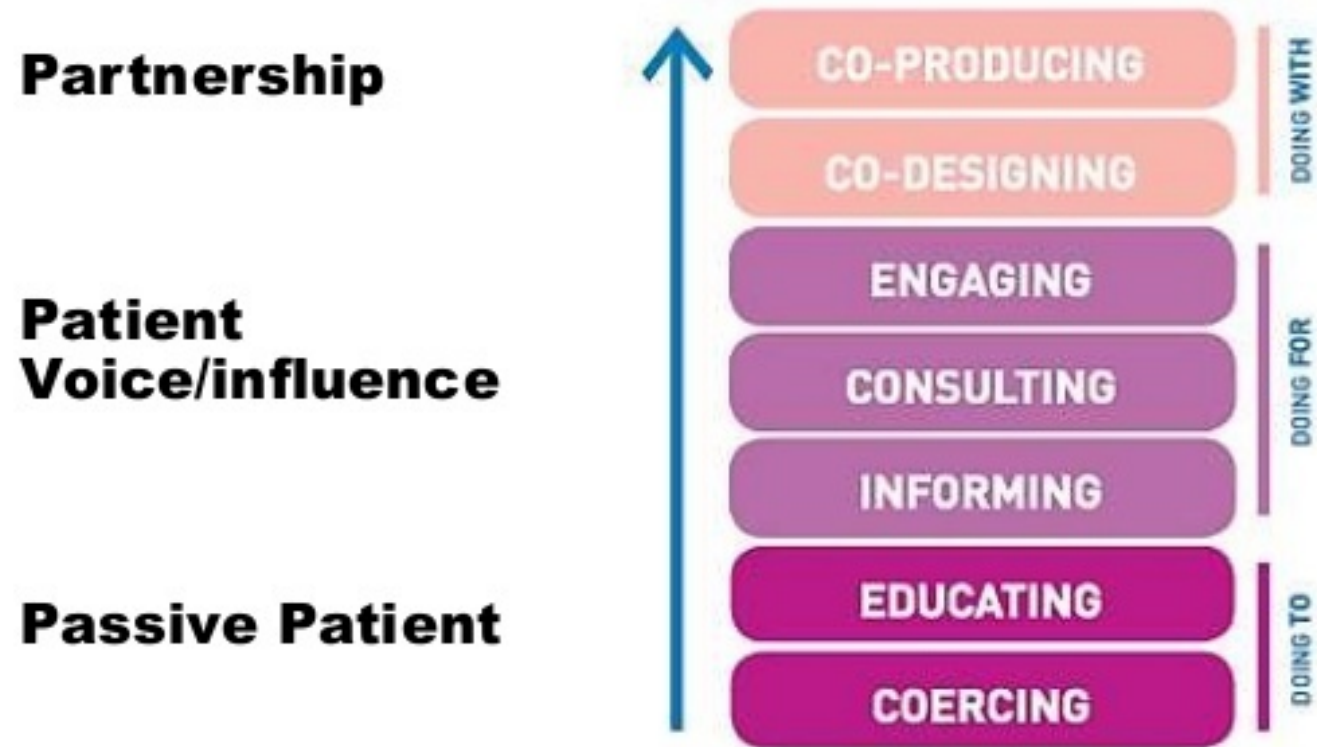


PATIENT ENGAGEMENT FRAMEWORK



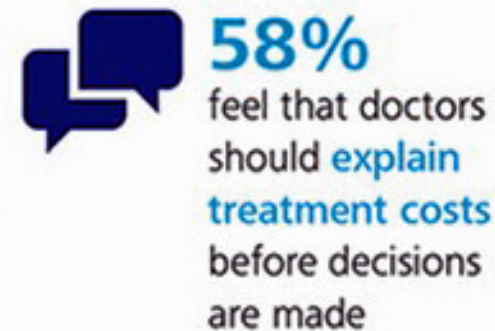
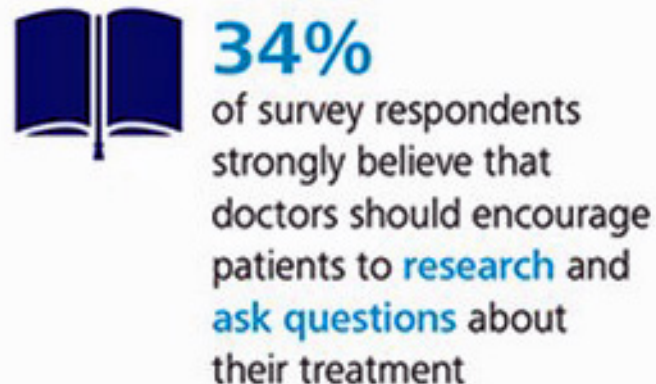
Change by Co-Production & Co-Design

A Continuum of Co Production



Source: new economics foundation

More Patients Report Wanting to Partner With Doctors



Shared Decision Making

PATERNALISTIC:

Information and recommendations



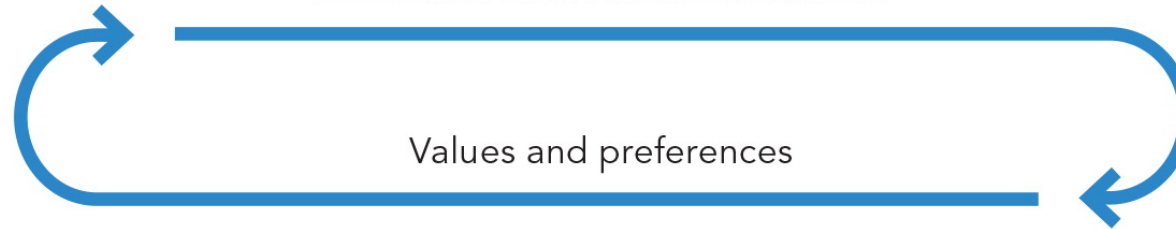
INFORMED MEDICAL DECISION MAKING:

Information



SHARED DECISION MAKING:

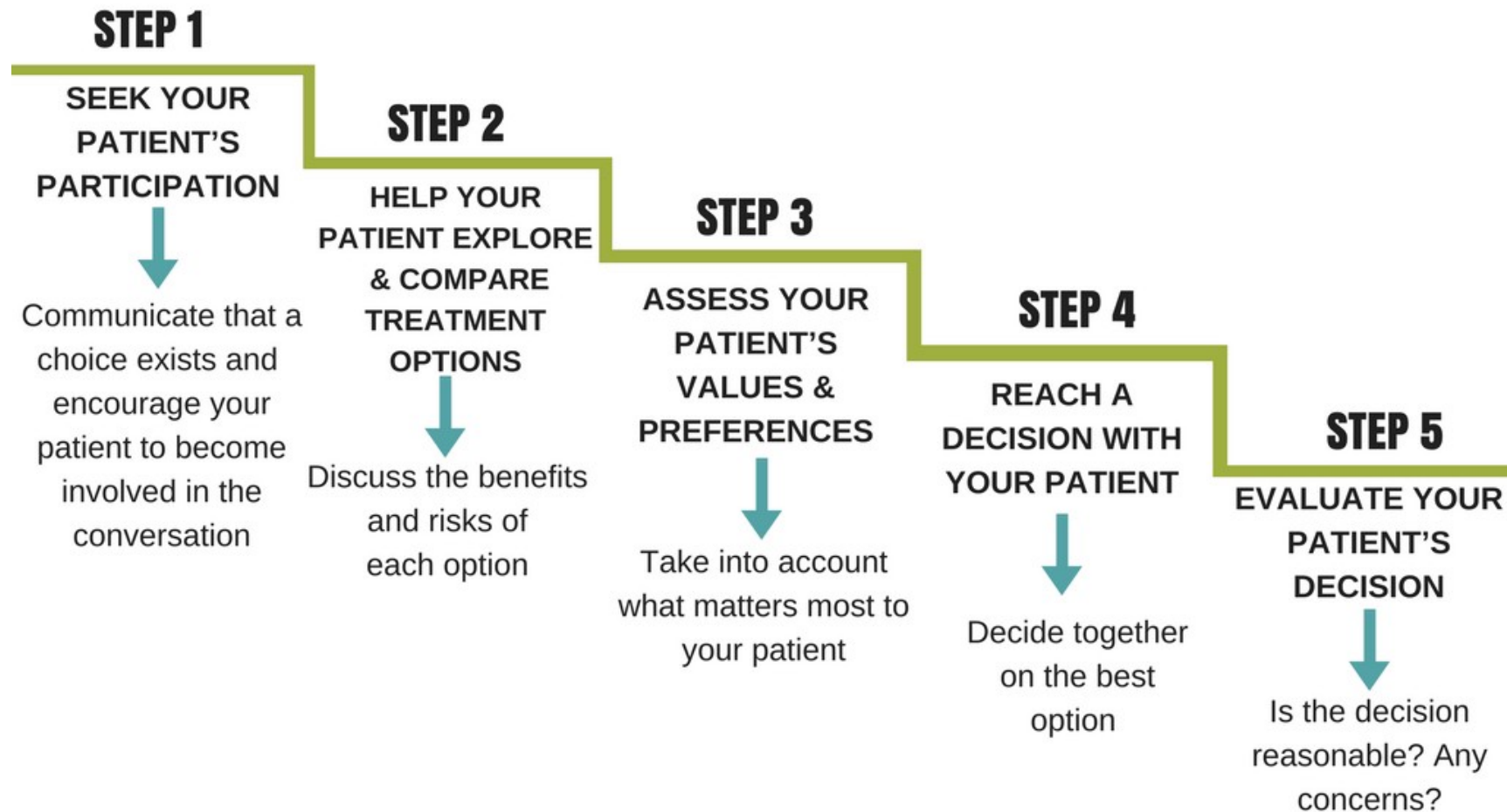
Information and recommendations



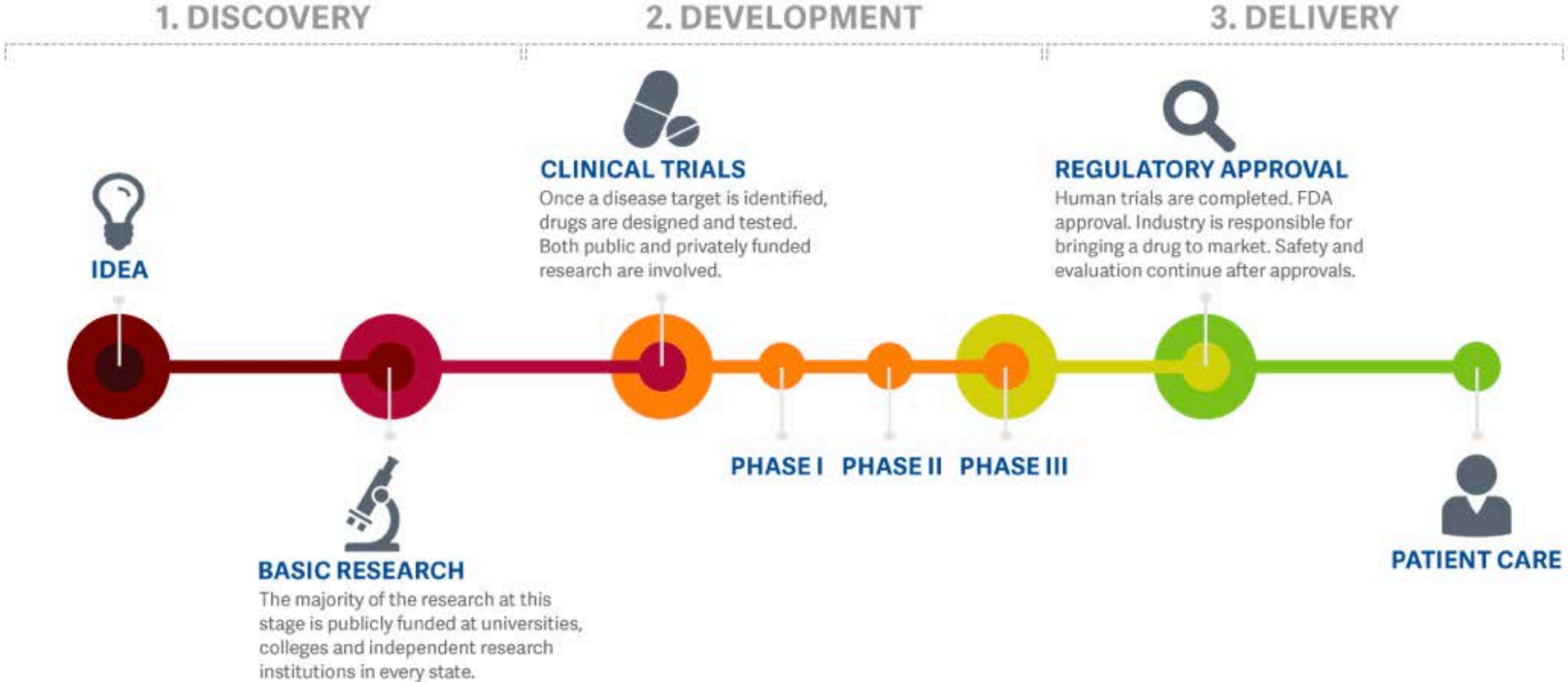
Values and preferences

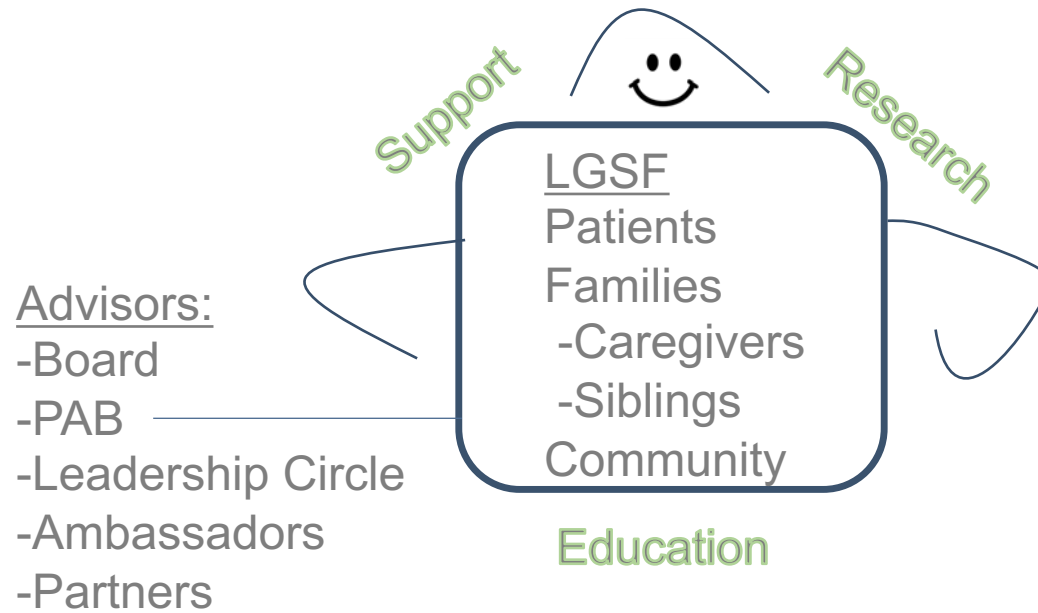


Essential Steps of Shared Decision Making



New Ways to Engage Patients & Caregivers





Causes

Malformations

Genes

Injury

Infections

Metabolic

Unknown

Symptoms

Seizures/Status

ID

CP

Behavior

Sleep

NPOs

'Rares'

RCSC, VLOG

CNF

TPAC, ISAN FSEP

Global Genes

RCSC, FC, Advisory

EF

REN, LHS, COE

CURE

LEEP

Faster Cures

HDB, PPVF

NORD

RDW, RDLA, ELF

AES/CNS/AAN

ELC, WS

Government

FDA

RRE, PFDD

NIH

iCARE, NPD

Congress

Ltrs, Visits

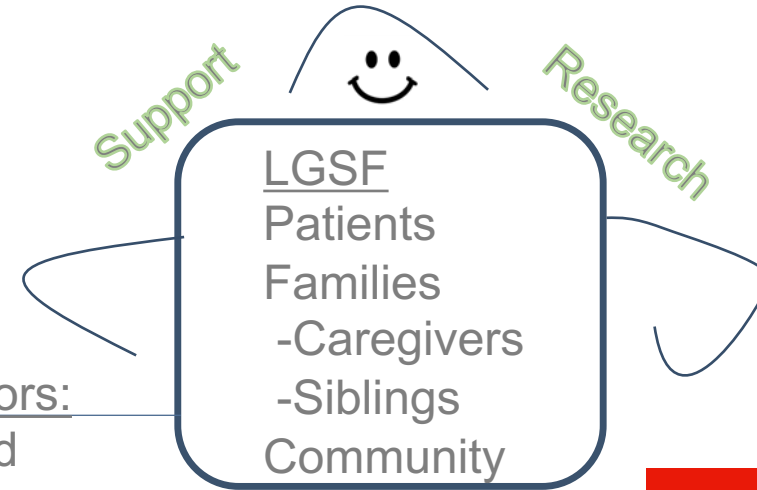
PCORI

LHS, REN

CDC

DOD

CDMRP, PRMRP



Advisors:

- Board
- PAB
- Leadership Circle
- Ambassadors
- Partners

Unmet need
Advisory/KOLs
Value added
Accelerate process

Partners

Researchers

Grants, Lab Visits, WPs, IW

HCPs

PERC, CME, Edu, GR, WP, SOC

Schools

Payors

Access, LOE, edu

Pharmacy

Access, LOE

Industry

Access, LOE, Toolkits, Unmet need

States

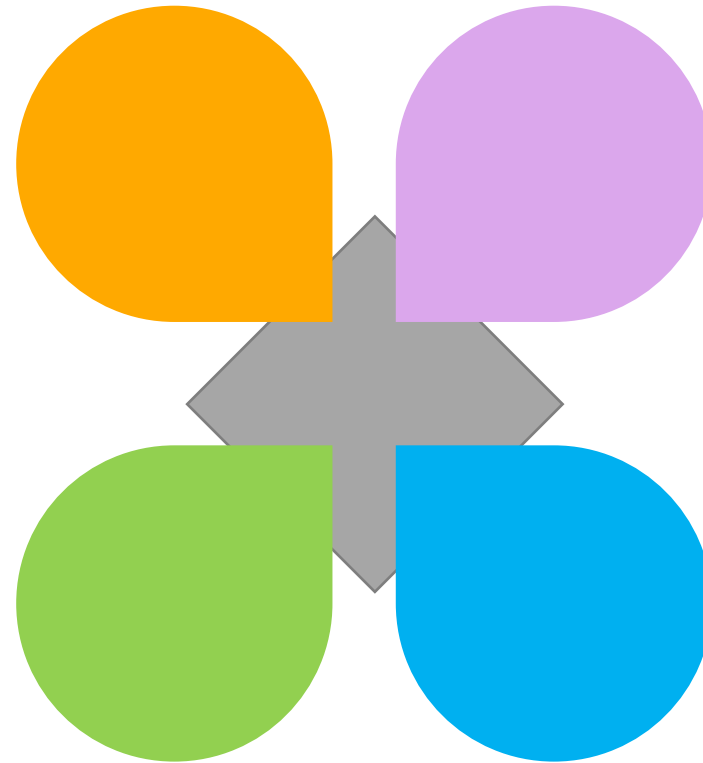
Services, Local

Media

SM PR, WS

LGS FOUNDATION

LENNOX-GASTAUT SYNDROME



Thank you

