

Milan, July 2022

*Focus Epilepsy*

# Headway

A new roadmap in Brain Health



## Report



- This Report arises from the initiative “Headway – A new roadmap in Brain Health: Focus Epilepsy”, realized by **The European House – Ambrosetti**<sup>1</sup> in collaboration with **Angelini Pharma**<sup>2</sup>. The information contained in this publication do not necessarily reflect the opinion or the position of the individuals and institutions referred to within the report. Decisions regarding the final analysis were ultimately made by The European House – Ambrosetti.
- The following report has been elaborated by The European House – Ambrosetti Team (Daniela Bianco – Partner and Head of Healthcare Area, The European House – Ambrosetti), Elisa Milani (“Headway” Project Coordinator and Consultant, The European House – Ambrosetti) and Irene Gianotto (Consultant, The European House – Ambrosetti).

<sup>1</sup>The European House - Ambrosetti is a professional Group, with 285 professionals, operating since 1965, which has grown significantly over the years, thanks also to the contributions of many of its Partners, developing numerous activities in Italy, Europe and the rest of the world. The European House – Ambrosetti was named — in the category Best Private Think Tanks — the no. 1 think tank in Italy, the no. 4 think tank in the European Union and among the most respected independents in the world out of 11,175 on a global level in the latest “Global Go To Think Tanks Report” of the University of Pennsylvania. The European House - Ambrosetti was recognized by Top Employers Institute as one of the 131 Top Employers 2022 in Italy. The European House - Ambrosetti has specific expertise in the healthcare sector with a dedicated professional practice, which for over 15 years has been developing different types of projects for all the players - both public and private - in the health ecosystem of health. For more information, please visit [www.ambrosetti.eu](http://www.ambrosetti.eu) and follow on [twitter.com/Ambrosetti](https://twitter.com/Ambrosetti).

<sup>2</sup>Angelini Pharma is the pharmaceutical division of Angelini Industries. The Group started almost 100 years ago as a small pharmaceutical laboratory, and over the years has grown into a leading international group in healthcare, present in Pharmaceuticals and Mass-Market. Angelini Pharma is a leader in healthcare, with particular strength and expertise in the fields of Central Nervous System (CNS) and Mental Health, including Pain, and Rare Diseases. The company is also a leading player in the Consumer Health segment, with highly successful OTC brands worldwide. The company operates directly in 25 countries employing more than 3.000 people. As part of its internationalization strategy, Angelini Pharma has also concentrated on development in countries with high growth potential. Current research focuses on Nervous System Diseases and Disorders, Pain and Inflammation and Rare Diseases, with a particular commitment to the research of new treatments for the pediatric population. The research embraces public-private partnerships with recognized academic institutions and centers of global importance. The Scientific Network and Partnerships both have an important role in creating innovation.

- The “Headway” initiative has been made possible through the **collaboration with experts of Epilepsy**. The European House - Ambrosetti acknowledges the time and expertise provided and would like to thank them for providing valuable insights, contributions and experiences to the elaboration of this Report. In particular (*in alphabetical order*):
  - **Helen Cross** – President, International League Against Epilepsy (ILAE);
  - **Reetta Kälviäinen** – Full Professor and Chair of Neurology, University of Eastern Finland; Director of the Kuopio Epilepsy Center, Kuopio University Hospital;
  - **Kristina Malmgren** – Professor in Neurology and Director, Sahlgrenska University Hospital Epilepsy Center;
  - **Thomas Porschen** – Vice Chair, European Executive Committee, IBE; Landerverband für Epilepsie Selbsthilfe Nordrhein-Westfalen E.V.;
  - **Torie Robinson** – CEO and Editor, Epilepsy Sparks;
  - **Philippe Ryvlin** – Full Professor of Neurology, UNIL; Head of the Department of Clinical Neurosciences, CHUV, Lausanne;
  - **Francesca Sofia** – President, International Bureau of Epilepsy (IBE).

- “**Headway – A new roadmap for Brain Health: Focus Epilepsy**” was conceived and launched at the beginning of 2022 by the Think Tank The European House - Ambrosetti in partnership with Angelini Pharma with the aim of **creating an expert panel for strategic reflection, analysis, dialogue and comparison** between various European experiences in the management of individuals with Epilepsy.
- The scope of the initiative is to share knowledge and know-how to prevent, diagnose, manage, and find solutions that reduce the **burden of Epilepsy not only in the healthcare sector**, but also in **workplaces, schools and society** in general.
- The initiative keeps the **trajectory and works in continuity and coherence with programs, activities and strategies of Governments and International Organizations** (such as the WHO) and **scientific societies / patient associations / advocacy groups** (among others, ILAE, IBE and Epilepsy Alliance Europe), as well as of European Institutions, with the objective of **contributing to reducing the burden of Epilepsy in Europe**.

## AIMS OF THE INITIATIVE



- To **increase knowledge and awareness** of the critical issues/specificities related to Epilepsy among policy makers, media and the general public, outlining the **current scenario in Europe** and **elaborate reflections on the impacts of Epilepsy** with a particular focus on health and quality of life



- Create **benchmarks** to compare **policies and action plans** developed and **implemented** across Europe



- Formulate **policy recommendations** to promote **good health for people with Epilepsy**



- Stimulate **debate among relevant stakeholders** (including policy makers, institutions, patient and caregiver associations, clinicians, health economists, etc.)



- Communicate and disseminate the **results of the initiative and its proposals for action** and **raise awareness** at European level

- Epilepsy is **one of the most widespread chronic neurological diseases** in the world, affecting approximately **50 million people of all ages worldwide**. This non communicable disease, that expresses itself in multiple forms that differ in age of onset, severity and treatment options, is characterized by abnormal electrical brain activity, causing **seizures that tend to recur for long periods of life or throughout life**. In addition, there is a series of other comorbidities related to the presence of the diseases.
- Even if **there is currently no cure for Epilepsy**, if properly diagnosed, it can be managed through appropriate treatments: it is estimated that **around 70% of cases can be treated**, allowing patients to live seizure-free and with a satisfactory quality of life. However, in the remaining 30% of cases there are currently no effective available treatments to control seizures. For these patients, Epilepsy proves to be **drug-resistant**, a condition that in the most severe cases may lead to **surgery**.
- Epilepsy poses a substantial **socio-economic burden for health systems and individuals and their families**. Although this is a common and relevant pathology, it is still misunderstood in many ways, probably also because of the unpredictability and often complex manifestation of seizures, the different reactions of patients, and the stigma that still accompanies the disease, all elements that worsen the quality of life of those who suffer from it and that require specific intervention.
- In the past decade, global health policy has recognized Epilepsy as a **leading cause of disability**. In 2009, the World Health Organization (WHO) defined it as a **social disease** with a high level of global disability and mortality burden, while in 2020 the 73<sup>rd</sup> World Health Assembly identified Epilepsy as one of the most common neurological disorders, adopting a resolution aimed to develop a **10-year intersectoral action plan** for people living with Epilepsy and other neurological disorders. First approved as a draft at the 150<sup>th</sup> session of the WHO Executive Board in January 2022, **in May 2022 the document has been unanimously approved by the WHO Member States**. The goal of the strategy is to **reduce the stigma, impact and burden** of these disabilities.



# Index

- **The epidemiological context of Epilepsy in Europe**
- The socio-economic impact of Epilepsy in Europe and the impacts of the COVID-19 pandemic
- The management of Epilepsy and the main critical points of the patient journey
- The management of Epilepsy in Europe
  - At healthcare level
  - In school settings
  - In workplaces
  - In society in general
- Research on Epilepsy in Europe
- Priority areas of intervention

# Neurological disorders, a global health challenge

- Neurological disorders are diseases of the **central and peripheral nervous system**, i.e. the brain, spinal cord, cranial and peripheral nerves, autonomic nervous system, nerve roots, neuromuscular plate and muscles. **More than 600 neurological diseases** are known worldwide.
- Neurological disorders account for a **large and increasing health burden worldwide**, being an important source of **premature mortality** and **transient or permanent disability** in survivors.
- According to the most recent estimates of the Global Burden of Disease, neurological diseases are responsible for about **2.2 million deaths per year** (about **3.9%** of total deaths), representing the **6<sup>th</sup> leading cause of death** worldwide, while being **the most prevalent treatment area** (about **2.6 billion** people worldwide) and the **5<sup>th</sup> largest** in terms of **years lived with disability** (66 million years). All three indicators (prevalence, mortality and years lived with disability) increased by **7.1%**, **75.9%** and **14%** respectively.
- The global health impact of neurological disorders, however, has been **underestimated over the years**. A growing awareness of the massive burden associated with neurological disorders has led to the recognition of the **scarcity of neurological services and resources**, the **unpreparedness of policy-makers and health-care providers** to cope with the predicted rise in the prevalence of neurological and other chronic disorders resulting from the extension of life expectancy and the **lack of policies and programmes** for their management.

## Global burden of neurological disorders (per 100.000 inhabitants), 1990 and 2019





# The burden of neurological disorders in Europe

## Top 10 non-communicable diseases in Europe, 2019



### DEATHS

1	Cardiovascular diseases
2	Neoplasms
3	Neurological disorders
4	Digestive diseases
5	Chronic respiratory diseases
6	Diabetes & CKD
7	Other non-communicable diseases
8	Musculoskeletal disorders
9	Skin diseases
10	Mental disorders

### YLD

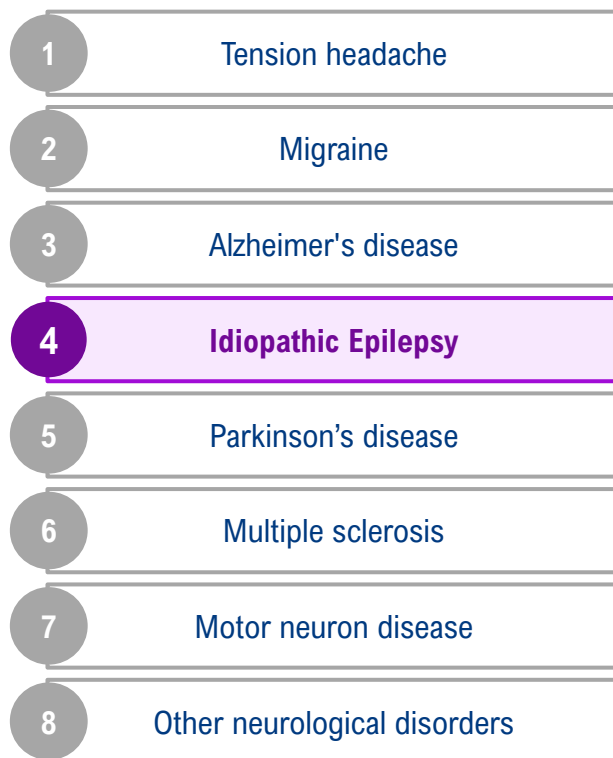
1	Musculoskeletal disorders
2	Mental disorders
3	Other non-communicable diseases
4	Neurological disorders
5	Sense organ diseases
6	Diabetes & CKD
7	Cardiovascular diseases
8	Skin diseases
9	Chronic respiratory diseases
10	Digestive diseases

- In Europe, neurological disorders are responsible for **6%** of all deaths positioning themselves as the **3<sup>rd</sup> leading cause of death** after cardiovascular diseases and neoplasms (neurological disorders ranked **5<sup>th</sup>** in 1990).
- Neurological disorders are also a **leading cause of disability**, responsible of over **10.4 million Years Lived with Disability (YLDs)** in 2019 (**8.5%** of the total).
- In terms of **Disability-Adjusted Life Years (DALYs)**, in 2019 neurological disorders ranked **6<sup>th</sup>** among all non-communicable diseases in Europe for a total of **17.2 million DALYs**.
- Given that the prevalence of most neurological disorders increases with age, **their burden is expected to rise** in countries with ageing populations, such as Europe.

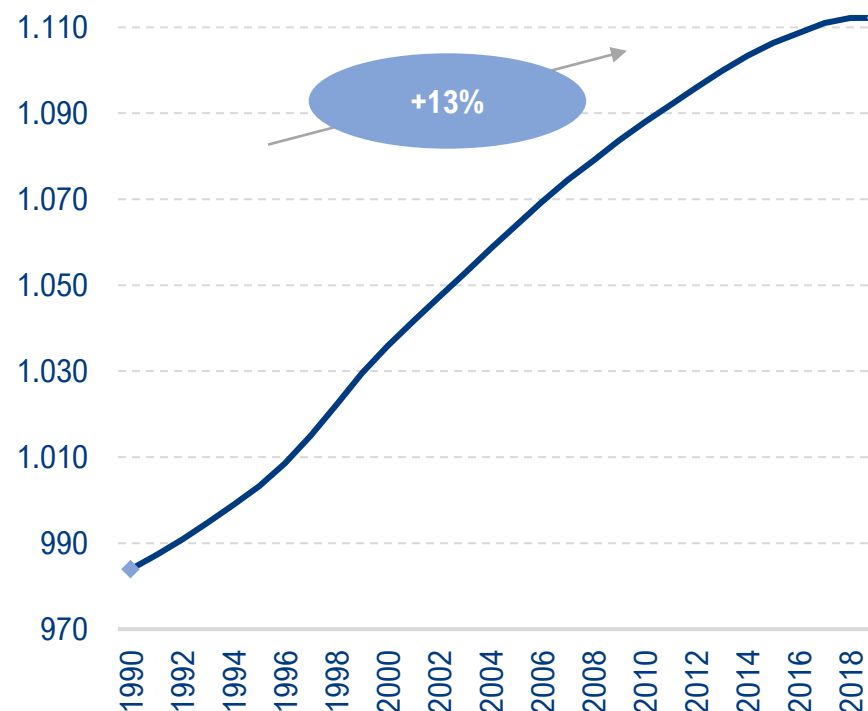
# Epilepsy is the 4<sup>th</sup> most common neurological disorder in Europe

- Among all neurological disorders, Epilepsy is the **4<sup>th</sup> most common** in Europe, causing **1.3 million DALYs** (0.46% of the total) and **941,000 YLDs** (0.73% of the total) in Europe. In both rankings, Epilepsy is preceded by **Migraine and Alzheimer's disease**.

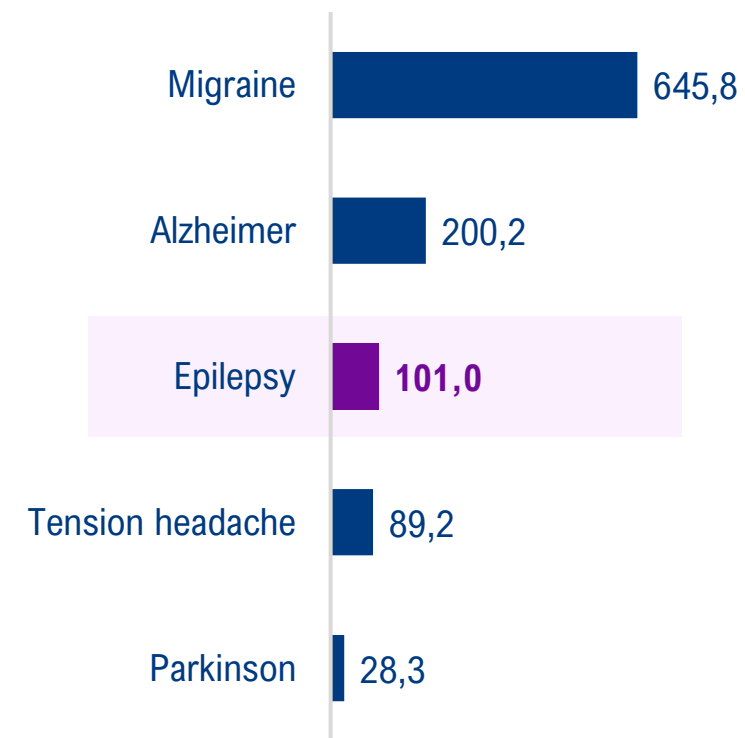
## Top neurological disorders in Europe by prevalence, 2019



## YLDs of neurological disorders (per 100.000 inhabitants), 1990-2019



## YLDs of the main neurological disorders in Europe (per 100.000 inhabitants), 2019



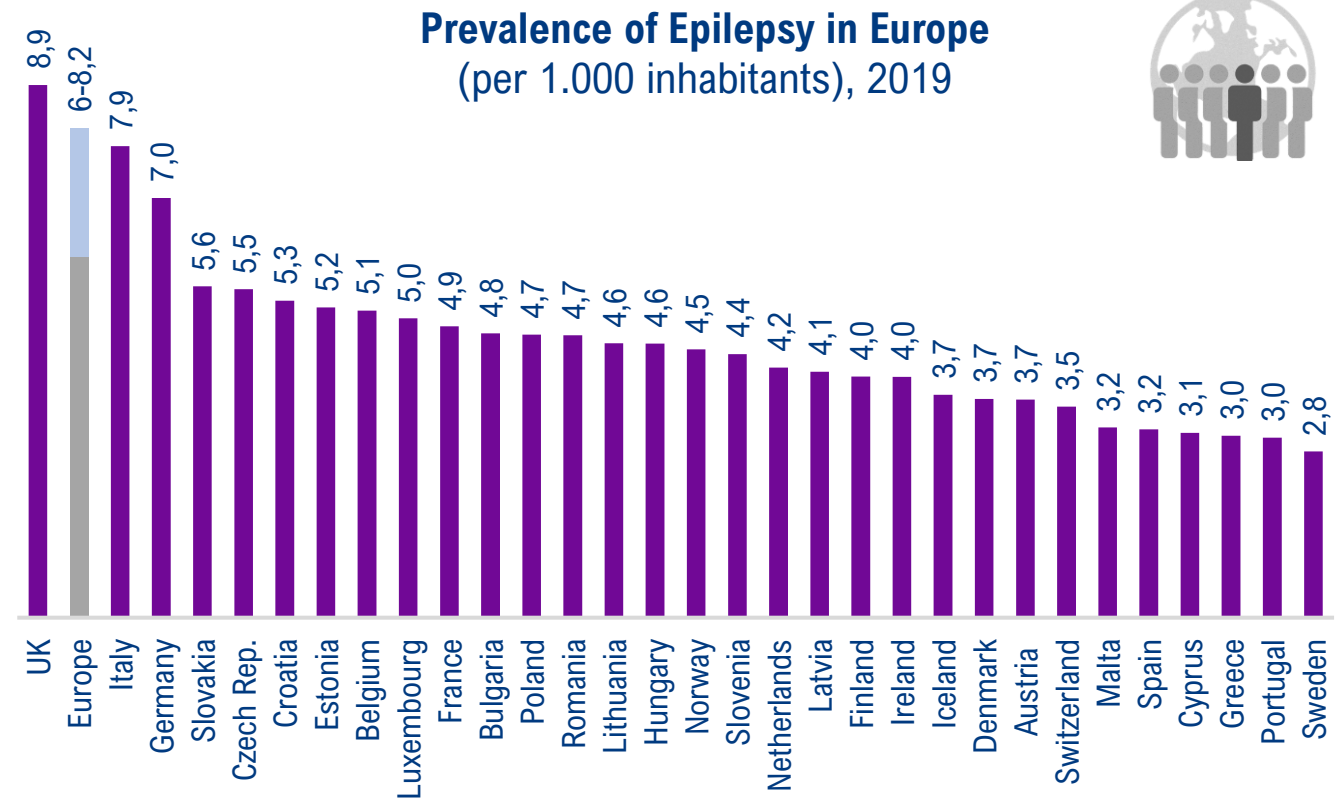
# The epidemiology of Epilepsy in Europe

- According to the EU Declaration on Epilepsy, **6 million people** have Epilepsy in Europe, with a prevalence around **6-8 per 1,000** individuals\*, while **15 million** citizens of all ages, race and social class have one seizure at some time in their lives.
- In the European population, the probability of developing Epilepsy is between **0.3-0.5%**, but increases to around **5% if one parent has idiopathic Epilepsy** (genetically determined) and reaches **10-12% if both parents** have Epilepsy.
- Nevertheless, in some countries of Europe, Epilepsy is not recognized as a brain disorder, and up to **40% of people** with this condition **may be untreated**.

There are  
**~400,000 new cases** in Europe  
each year



... **one**  
new case  
almost **every**  
**minute**



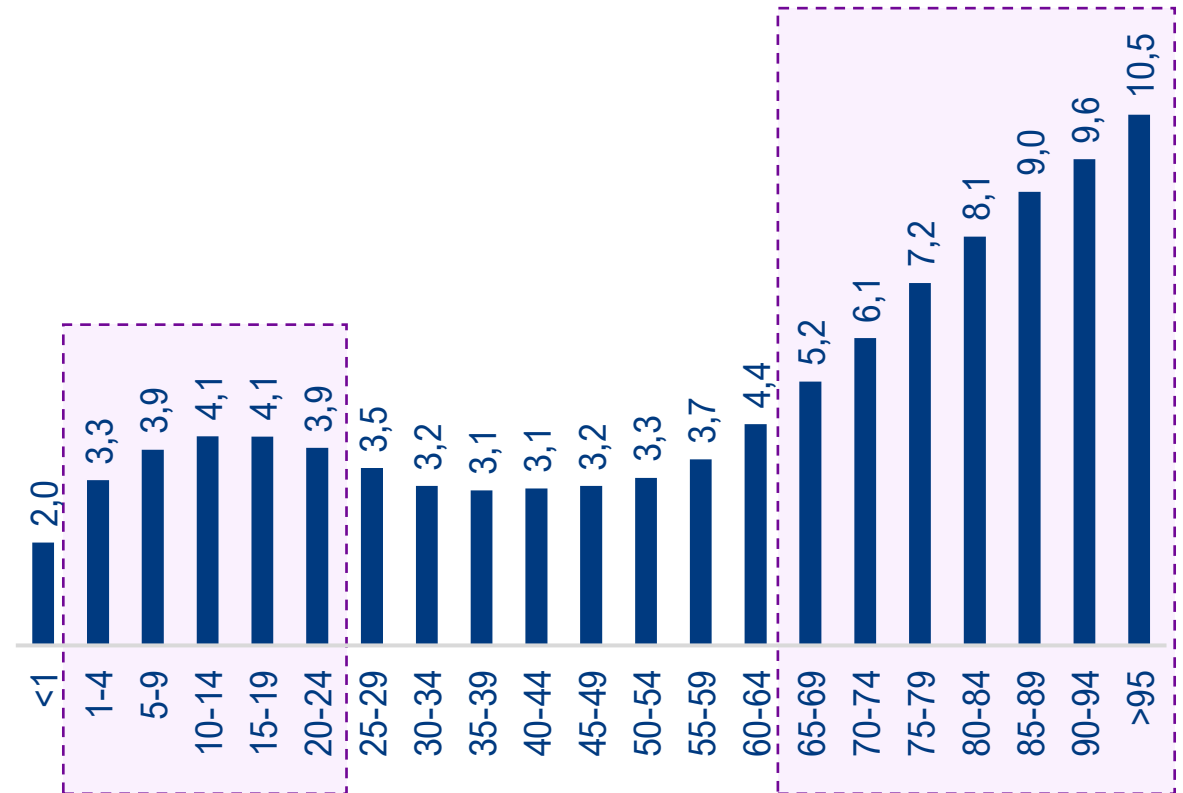
Due to the complexity of symptom manifestation and underlying causes, prevalence of **Epilepsy is often underestimated**. This is why many studies only consider Idiopathic Generalised Epilepsies (IGEs), defined by strict clinical and EEG features.

(\* ) According to an estimate considering persons with "current" Epilepsy across 53 countries comprising the European Region of the WHO, prevalence is equal to 8,23 per 1.000 persons.

# Prevalence of Epilepsy

- As mentioned before, the prevalence in Europe in the general population is estimated around **6-8‰**, with a median prevalence rate of **active Epilepsy\*** of **5.2** per 1.000.
  - In childhood and adolescence, prevalence is around **3.5-4‰**, **4‰** in adulthood and **7‰** after 65 years of age.
  - The prevalence of the disease tends to increase with age, with a **peak in people aged <25 years** and in **older individuals**.
- The difference between the **prevalence of active Epilepsy and lifetime prevalence** (between 2% and 5%) implies that for most non-epileptic individuals either the condition remits or the patient dies
- In general, most studies show that **Epilepsy is more common in males than females**, due to the fact that the former are more likely to be vulnerable to common risk factors (such as brain damage), but this **difference is rarely significant**. According to the Global Burden of Diseases study, the prevalence of Epilepsy among **women is equal to 4.4 per 1,000 inhabitants vs. 4.7 per 1,000 inhabitants in men**.

**Prevalence of Epilepsy by age group in Europe**  
(per 1.000 inhabitants), 2019

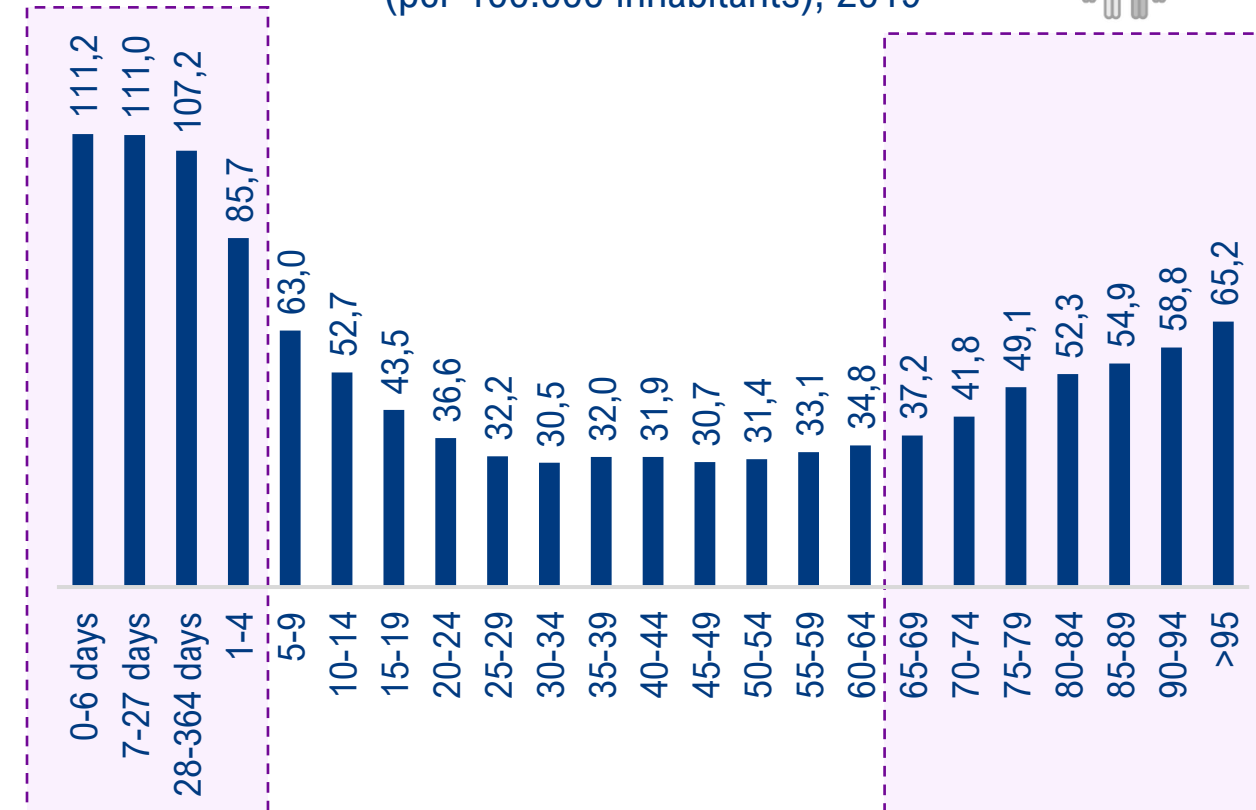


(\* ) Active Epilepsy is defined as individuals with doctor-diagnosed Epilepsy, either taking medication to control it or having one or more seizures in the last 12 years.

# Incidence of Epilepsy

- Even though Epilepsy is believed to be a disease that arises mainly during childhood, **Epilepsy and its seizures can develop in any person at any age.**
- Epilepsy, however, has **two peaks of incidence** during the course of life: the first during **childhood**, the second in the elderly population, **after the age of 65**. These peaks reflect the most common causes:
  - in the early years these are mainly linked to **genetic-metabolic causes**
  - in later life, these are due to not only **increased life expectancy**, but also to the higher incidence in the elderly of **cerebrovascular and neurodegenerative diseases**, to which the emerging group of immune-mediated **diseases of the central nervous system** has recently been added.
- According to the Child Neurology Foundation, among children with Epilepsy: **30-40%** have only the disease without provoked seizures, with normal intelligence, learning capability, and behavior; about **20%** also have an **intellectual disability**; between **20% to 50%** have normal intelligence but a **specific learning disability**.

Incidence of Epilepsy by age group in Europe  
(per 100.000 inhabitants), 2019



**One in every 4 people** who are newly diagnosed with Epilepsy is over the age of 65

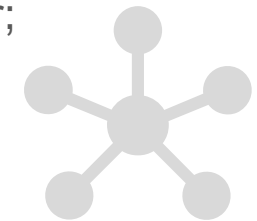
# Signs and symptoms of Epilepsy

- The **main symptom of Epilepsy is repeated seizures**, whose characteristics vary and depend on where in the brain the disturbance first starts, and how far it spreads. One seizure, in fact, does not signify Epilepsy (up to **10%** of people worldwide **have one seizure during their lifetime**): Epilepsy is defined as having **two or more** unprovoked seizures.
- Epileptic seizures\*, clinical events caused by **abnormal electrical discharges**, are classified into two main groups:
  - **Generalized seizures** which involve the entire cerebral cortex and can cause a complete loss of consciousness (tonic-clonic seizures) or rapid blinking or a few seconds of staring into space.
  - **Focal seizures** (also called partial and localized seizures), originating in a specific region of the cerebral cortex that possesses abnormal excitability, whose clinical manifestation depends on the area involved (e.g. a change in sensation such as a strange taste or smell, confusion or daze).
- Most seizures last from **30 seconds to 2 minutes**, while episodes that last more than 3-4 minutes are considered prolonged seizures. Seizures can become dangerous when they last between **5 and 10 minutes** or when a **second seizure** occurs immediately after the first one has ended.
- **Approximately 50% of the people with Epilepsy have coexisting physical or psychiatric conditions.** Physical and psychiatric comorbidities are associated with poorer health outcomes, increased health care needs, decreased quality of life and greater social exclusion:
  - Physical problems concern for example fractures and bruising from injuries related to seizures, while the most prevalent **psychiatric comorbidities** are **depression (23%)** and **anxiety (20%)**, and **intellectual disability** is the most common comorbidity in children with Epilepsy (**30-40%**). Epilepsy is also commonly associated with **neurodegenerative diseases**.



# Causes and risk factors (1/2)

- In about **50% of cases** globally the **cause of the disease is still unknown**. In the other half of cases, there are several factors that can cause the onset of the condition, including genetics (to date, over **500 genes** have been identified that are associated with Epilepsy). The causes of Epilepsy may differ depending on whether it is a partial or generalized form:
  - In focal Epilepsy, the most common cause is the presence of **structural lesions** such as ischemic or hemorrhagic areas (e.g. due to head injuries, strokes), tumors or even scars from previous trauma or surgery, and in this case, it is known as symptomatic Epilepsy. In other cases, even if there is clinical or instrumental evidence of the origin of crises from a specific cerebral area, **radiological examinations are not able to show any structural lesion** and, in this case, it is referred to cryptogenic focal Epilepsy.
  - In generalized Epilepsy there are idiopathic forms, in which it is believed that the patient, due to an **individual or sometimes hereditary predisposition**, has a reduced epileptogenic threshold so that his cerebral cortex can undergo an epileptic crisis even in the absence of specific causes or external stimuli. Seizures can also happen after an **infection**, such as meningitis or another illness.
- The **main known causes of Epilepsy** can be categorized in:
  - **Structural**: when there is a visible abnormality, and it may be acquired (e.g. from a stroke) or genetic (e.g. malformation);
  - **Genetic**: a known or presumed genetic mutation. Seizures are usually the core symptom of the disorder;
  - **Infectious**: a known infection in which seizures are the core symptom (e.g. meningitis or tuberculosis);
  - **Metabolic**: a known or presumed metabolic disorder in which seizures are the core symptom;
  - **Immune**: autoimmune disorders affect multiple organ systems, seizures are the core symptom.



## Causes and risk factors (2/2)

- Like many neurological conditions, it is estimated that **25% of the global burden of Epilepsy cases is preventable by acting on predisposing conditions**. Numerous determinants, including **environmental risk factors** and **protective factors**, in fact, are known to influence brain development in early life and brain health throughout life. The major modifiable risk factors for Epilepsy are perinatal insults, central nervous system infections, traumatic brain injury and stroke. The **most common risk factors** include:

- **Age:** the disease can show up at any age, but it is proven that the likelihood is higher among people younger than 25 or older than 65
- **Family history:** the risk of developing the disease in case of a family history is higher
- **History of head injuries:** seizures can manifest at any moment after a trauma (for example after road traffic injuries).
- **Seizures in childhood:** in case of seizures during childhood, the likelihood of having seizures in the future is higher
- **Birth factors:** being small at birth, oxygen deprived, or having abnormalities in the brain at birth are increasing risk of Epilepsy

- In addition to this, there are **triggering factors**, which include drug abuse, acute or chronic alcoholism, metabolic or electrolyte disorders, sleep deprivation, feeling stressed, low blood sugar, flashing lights or specific visual patterns, etc.

### SEIZURE TRIGGERS

- **Lack of sleep or disrupted sleep**
- **Stress**
- **Illness**
- **Alcohol or illegal drugs**
- **Flashing bright lights**
- **Stress**
- **Low blood sugar**
- **Visual patterns**
- Missed dose of **Anti-Epileptic-Drug**
- ...



# The mortality of Epilepsy

- The risk of **premature death** in people with Epilepsy is **up to 3 times higher** than for the general population, while **life expectancy** is reduced by **2-10 years**. The mortality risk associated with Epilepsy is closely dependent on the **type of Epilepsy and the degree of control achieved with current therapy**, this can also explain why mortality risk is highest in the early years following diagnosis.
- Gender, age, a previous episode of status epilepticus, frequency and severity of seizures and antiepileptic drug (AED) compliance, are all **factors of relevance**.
- The most common cause of death related to Epilepsy is **Sudden Unexplained Death in Epilepsy (SUDEP)**, the sudden, unexpected death of someone with Epilepsy, who was otherwise healthy. SUDEP has an incidence of about **1 in 1,000 cases** per year (about 50,000 per year worldwide) and its risk is greater in patients who are severely drug-resistant and have very intense and prolonged seizures.
  - Sudden death from Epilepsy, however, is an **often-underestimated phenomenon**. Moreover, in many cases **Epilepsy patients and their relatives are not informed** about SUDEP by their doctors. This is even more serious considering that, according to current scientific surveys, **70% of SUDEP cases are preventable** through risk-adapted behavior, precaution and timely first aid measures.
- Sometimes, however, the cause is merely **traumatic** and crisis-related, as in the case of a serious accident during a crisis (e.g. drowning, choking on food, head trauma from a sudden fall, etc.). In people with Epilepsy there is also an **increased risk of suicide**, which can be correlated with anxiety-depressive comorbidity and mood disorders. Studies have found a higher risk of death from suicide in people with Epilepsy, ranging from **2.6 to 5 times higher** than in the general population.

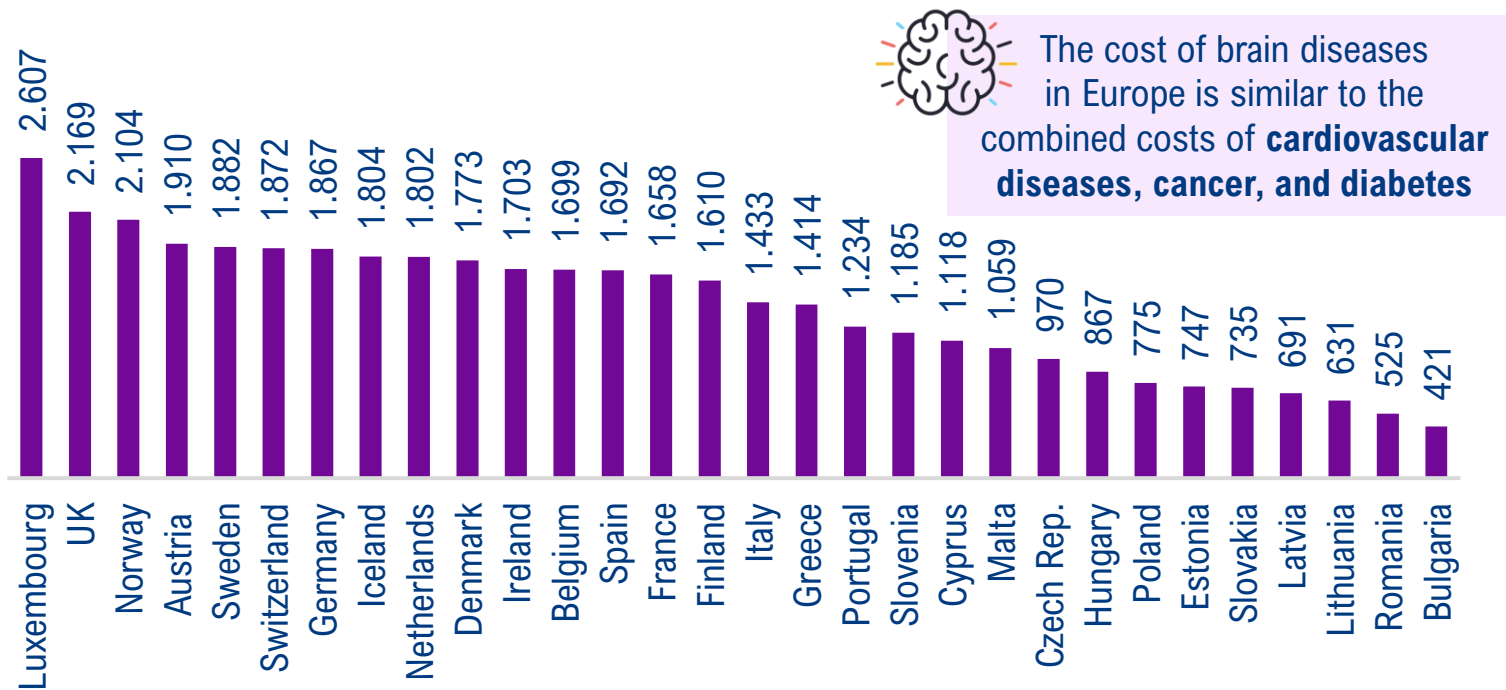
# Index

- The epidemiological context of Epilepsy in Europe
- **The socio-economic impact of Epilepsy in Europe and the impacts of the COVID-19 pandemic**
- The management of Epilepsy and the main critical points of the patient journey
- The management of Epilepsy in Europe
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  - In school settings
  - In workplaces
  - In society in general
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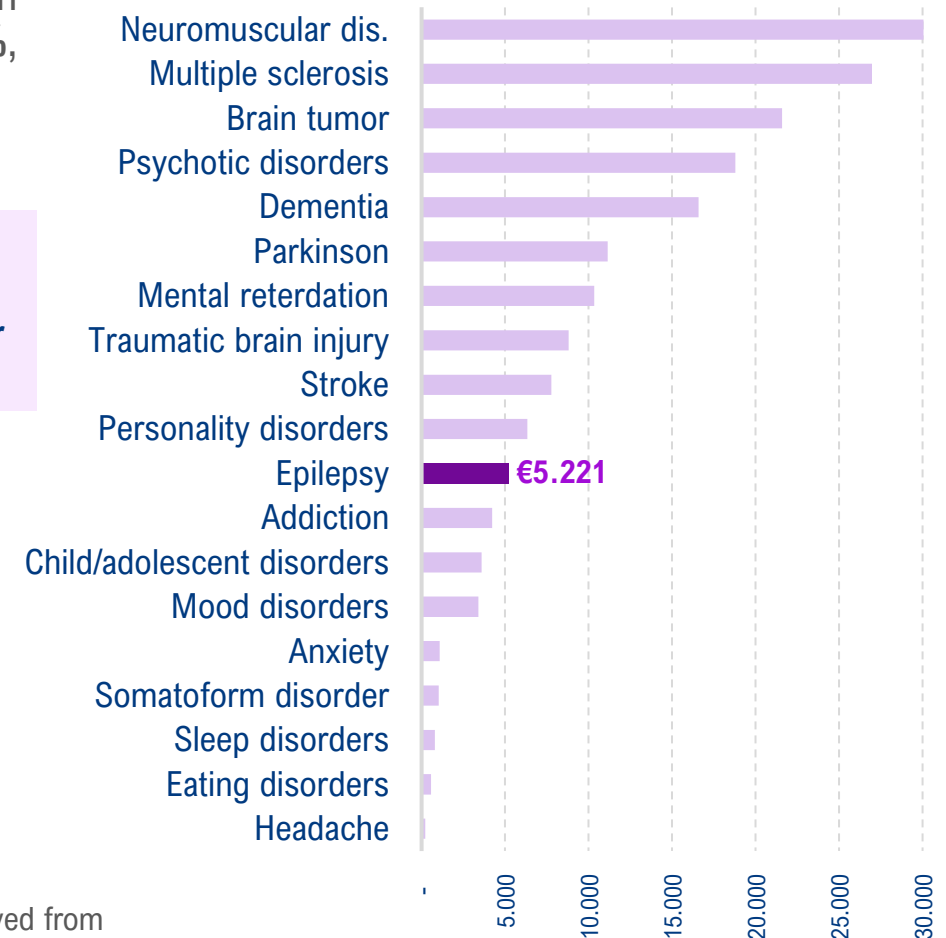
# The socio-economic impact of brain disorders

- Neurological disorders lead to increased costs for governments, communities, families and individuals, as well as to loss of productivity for economies. In 2010, **brain disorders\*** were estimated to cost **798 billion euro** in Europe alone, of which direct healthcare costs **37%**, direct non-medical costs (e.g. nursing homes) **23%**, and indirect costs (e.g. absenteeism from work, pensions) **40%**.

**Per capita cost of brain disorders\* in Europe by country (euro)**



**Per capita cost of specific disorders (euro)**



(\* ) The analysis refers to 19 major groups of mental and neurological disorders and is based on best estimates derived from systematic literature reviews by panels of experts in epidemiology and health economics.



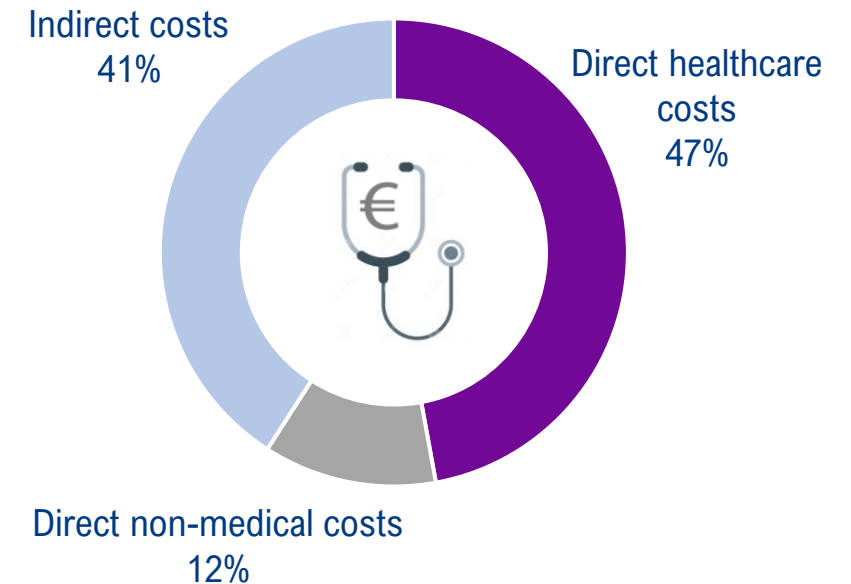
# The socio-economic impact of Epilepsy

- It has been estimated that the 6 million people with active Epilepsy in Europe have a **yearly cost** that ranges **between 13.8 billion euro and 20 billion euro**. Despite this, very few European countries have national plans for managing the disorder.
  - The **direct costs of Epilepsy** – which include payments for medical treatment and care (e.g. doctors, antiepileptic drugs and therapies) and for non-medical measures – are highly variable and significantly correlated with disease severity and response to treatment.
  - The main sources of expenditure are **hospital admissions** (due to first diagnosis or to the persistence of crises) and **drug therapies** (in particular the increasingly frequent use of new generation antiepileptic drugs). On the other side, non-healthcare items include **transportation costs** (for patients, their family and caregivers), **informal nursing** and **social services** provided in institutions or at home, and **unpaid care** or services provided by patients' relatives and caregiver.
  - To these costs must be added **indirect costs**, such as the loss of working hours and therefore of productivity, and the considerable impact that Epilepsy has on the quality of life of the patient himself and, often, on that of his/her family.

(\* ) Faught RE, Weiner JR, Guerin A, Cunnington MC, Duh MS, "Impact of nonadherence to antiepileptic drugs on health care utilization and costs: findings from the RANSOM study." (2009)

Source: The European House – Ambrosetti on J. Olesen et al., "The economic cost of brain disorders in Europe" (2012) and Cross, J. Helen. "Epilepsy in the WHO European region: fostering Epilepsy care in Europe" (2011) data, 2022

## Distribution of costs by type (% on total)



Adherence to antiepileptic drugs regimens can have a significant impact on costs. Nonadherence has been associated with a **+39%** increase in **hospitalization**, a **+76%** increase in **inpatient days**, and a **+19%** increase in **emergency department visits** compared with those who were **adherent.\***



## The burden of Epilepsy – Focus on stigma (1/2)

- **Social exclusion** and **stigma** largely contribute to the **global burden of Epilepsy**. Marginalization and stigma are, in fact, significant contributors to **poor physical and mental health** in people with Epilepsy. A multipronged strategy, which is culturally appropriate, multisectoral and collaborative, is needed.
- The causes of stigma depend on a variety of factors, such as:
  - **Low level of knowledge** as well as **misconceptions and poor understanding** of the nature of the disease. This includes the perception of Epilepsy as a form of insanity, ruining people’s lives, and being untreatable or contagious. Misconceptions and negative attitudes cause people with Epilepsy to feel shame and embarrassment.
  - The **lack of public awareness** on Epilepsy reflects on **low preparedness of educational institutions** to adequately accommodate students with Epilepsy and, in adulthood, **employers and co-workers**.
- Stigma can delay appropriate healthcare seeking, access to care, health financing and availability of treatment, whereas **institutional discrimination** in Epilepsy can affect employment, education, marriage and childbearing, as well as driving regulations.



In a study involving **>5,000 adults** from 15 European countries\*, **51%** felt **stigmatized** and **18%** felt **highly stigmatized** because of their Epilepsy



According to a survey performed in Germany with **high school students**:

- **1 in 5** thinks Epilepsy is **caused by emotional strain**
- **1 in 3** would **not tell** their class if they had Epilepsy
- **1 in 5** would **not date** a person suffering from Epilepsy

(\* ) Baker et al., Epilepsia Vol. 41, Issue 1, P. 98–104 (2000) (\*\* ) Jansen et al., “Knowledge and attitudes about Epilepsy: A survey of high school students in Germany” (2017)

## The burden of Epilepsy – Focus on stigma (2/2)

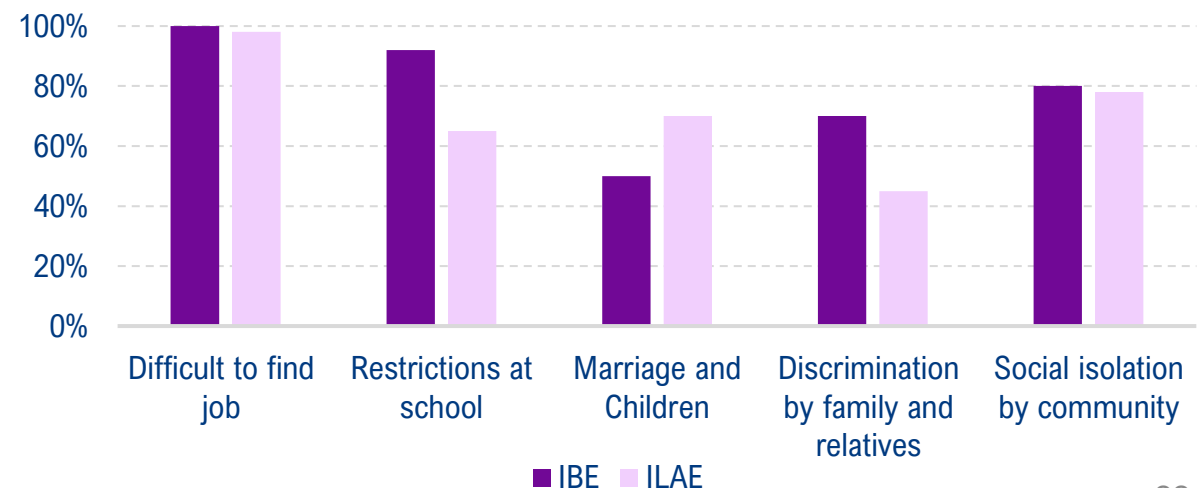
- In general, **two main types of stigma** can be distinguished:
  - Felt or internalized stigma** refers to the anguish and unhappiness felt due to misconceived notions about Epilepsy. It is **driven by internal conflicts and social anxiety**. This tends to be felt when people hide their condition, posing a barrier to help-seeking behavior. The lower the **public awareness** and the **negative stereotypes** promoted on media, which often depict seizure in an exaggerated way, the **higher the concealment of the condition and the felt stigma**.
  - Enacted or institutionalized stigma** refers to **legislations and regulations** limiting what individuals with Epilepsy can do (e.g. legislations restricting the issuance of driving licenses). Many of the restrictive laws have already been repealed; however, the latter left a mark in the way Epilepsy is perceived. For example, a ILAE/IBE survey reported that people with Epilepsy have difficulties **finding jobs, feel discriminated and isolated and encounter barriers** in school settings.

- There are **3 prevalent misconceptions** that can trigger stigma in Epilepsy:
  - “People with Epilepsy are **contagious, crazy and possessed by demons, bewitched** or punished by gods”



A higher prevalence of misconceptions has been found in **communities with low education and poor knowledge on Epilepsy**

Barriers for People with Epilepsy (% of total)



# The impact of the COVID-19 pandemic on patients with Epilepsy

- The **COVID-19 pandemic** has highlighted the **relevance of neurology** to global public health and its significance in broader global health dialogues. Disruption of services, difficult access to medicines, interrupted immunization programs and increased mental health issues have added to the **burden** of those with neurological disorders.
- The social impact is seen not only among individuals with Epilepsy, but also on **Epilepsy care facilities and services**, with consequences such as the **postponement of surgeries** and the switch from in-person outpatient services to **telemedicine solutions**, which may not always be appropriate. It is therefore fundamental to provide patients with Epilepsy more support and attention.

## MAIN IMPACTS OF THE COVID-19 PANDEMIC ON INDIVIDUALS WITH EPILEPSY



### DISEASE MANAGEMENT

Chronic conditions, such as Epilepsy, require **continuity of care** and linear **adherence patterns** to prevent breakthrough seizures. Limited access to healthcare facilities, lower social support and social isolation may reduce treatment adherence and **worsen seizure control**.

### RESTRICTION OF CLINICAL CARE

A survey of more than 200 Italian centres found a **75%** reduction in the **number of EEGs** during the crisis compared to the pre-COVID-19 baseline. Moreover, data on neurological disorders showed that **30% of patients suspended hospital treatments, physiotherapy or other support interventions**.



### PSYCHOLOGICAL IMPACT

Patients with Epilepsy are reportedly **more susceptible to psychological stress** from COVID-19 than the general population. As mental stress can increase **seizure frequency** and lead to **depression** and other mental health problems, the mental status of patients with Epilepsy needs to be actively assessed.\*



(\*) Nevertheless, reduced stress related to daily life activities may have had a positive impact on seizure development. In fact, according to some recent studies, no significant changes in seizures during COVID-19 lockdown has been reported.

Source: The European House – Ambrosetti on Assenza G. et al., “Electroencephalography at the time of Covid-19 pandemic in Italy” (2020), Kuroda N., “Epilepsy and COVID-19: Updated evidence and narrative review” (2021) and Grande, Eleonora, et al. “The impact of COVID-19 lockdown on people with epilepsy and vagal nerve stimulation” (2021), 2022

# Index

- The epidemiological context of Epilepsy in Europe
- The socio-economic impact of Epilepsy in Europe and the impacts of the COVID-19 pandemic
- **The management of Epilepsy and the main critical points of the patient journey**
- The management of Epilepsy in Europe
  - At healthcare level
  - In school settings
  - In workplaces
  - In society in general
- Priorities for Epilepsy research in Europe
- Key messages and priority areas of intervention

# World Health Assembly Resolutions on Epilepsy

- The Resolution WHA68.20 on Epilepsy approved on May 26<sup>th</sup>, 2015 by the 68<sup>th</sup> World Health Assembly emphasized the need for Governments to **formulate, strengthen and implement national policies** in order to promote and protect the rights of people with Epilepsy. The priorities were focused on 3 areas:
  - improving the **quality of care in Epilepsy**,
  - increasing **information about Epilepsy** in the population in order to **reduce prejudice and discrimination**,
  - **promoting research in Epilepsy** to improve the life prospects of people with Epilepsy
- In 2018, the **3<sup>rd</sup> high-level meeting on the prevention and control of noncommunicable diseases** highlighted the importance of mental health conditions, drawing the **attention of policy-makers to integrate Epilepsy** into action on NCDs and mental health
- In 2019, the first **official Epilepsy Side Event at the 72<sup>nd</sup> World Health Assembly** took place, which brought together policy makers, NGOs, patients, health care leaders and Member States to develop next steps for implementing the WHA68.20 Resolution
- In November 2020, the 73<sup>rd</sup> World Health Assembly adopted the Resolution 73.10 – Global Actions on Epilepsy and Other Neurological Disorders, which requested WHO Director-General to develop an **intersectoral global action plan on Epilepsy and other neurological disorders**. The WHO Secretariat prepared a draft of the Intersectoral Global Action Plan on Epilepsy and other Neurological Disorders (IGAP) that was submitted for review and approved at the **150<sup>th</sup> session of the Executive Board in January 2022**. The final version of the IGAP has been **unanimously approved by the World Health Assembly on 27 May 2022**.



**May 2015**  
*Publication of Resolution WHA68.20 on Epilepsy*



**September 2018**  
*3<sup>rd</sup> high-level Meeting on the prevention and control of NCDs*



**March 2019**  
*Side Event on Epilepsy at the 72<sup>nd</sup> World Health Assembly*



**November 2020**  
*Adoption of Resolution 73.10 – Global Actions on Epilepsy and Other Neurological Disorders*



**January 2022**  
*Draft Intersectoral global action plan on Epilepsy and other neurological disorders*



**May 2022**  
*Unanimous approval of the plan by WHO Member States*





# Intersectoral Global Action Plan on Epilepsy and Other Neurological Disorders 2022-2031

- On 27 May 2022, **World Health Organization Member States approved the Intersectoral Global Action Plan on Epilepsy and other Neurological Disorders (IGAP)** at the 75<sup>th</sup> World Health Assembly in Geneva, Switzerland. 116 Member States, together with ILAE, IBE, the World Federation of Neurology (WFN) and other international organizations, spoke in support of the plan, which **passed unanimously**.
- The objective of IGAP is to address the challenges and gaps for people living with Epilepsy and other neurological disorders by improving access to care and treatment, preventing new cases and promoting brain health and development across the life course. IGAP aims to ensure a **comprehensive, coordinated response across sectors**.
- It seeks to support the **recovery, well-being and participation of people living with neurological conditions**, while reducing associated mortality, morbidity and disability, promoting human rights, and addressing stigma and discrimination through interdisciplinary and intersectoral approaches.
- In particular, IGAP defines **2 global targets** specific to Epilepsy to be achieved by all Member States **by 2031**:

1

All countries will have **increased service coverage** for Epilepsy **by 50%** from the current coverage in 2021



2

**80%** of countries will have **developed or updated their legislation** with a view to promoting and protecting the **human rights of people with Epilepsy**



- By setting strategic goals and reachable targets, IGAP intends to encourage countries to **prioritize neurological diseases in their public health agendas**.



# Intersectoral Global Action Plan on Epilepsy and Other Neurological Disorders 2022-2031: Focus areas

- To meet the global targets, IGAP includes **proposed actions for Member States, the WHO Secretariat, and national and international partners** in mainly three areas:

## FOCUS 1

***Access to services for Epilepsy*** – Treatment gaps result from a combination of decreased capacity in health care systems (e.g., staff shortage), the inequitable distribution of resources (e.g., limited access to anti-seizure medicines, lack of knowledge and confidence of PHC workers in the management of Epilepsy) and the low priority assigned to Epilepsy care. With political will and a combination of innovative strategies, Epilepsy prevention, diagnosis and treatment can be integrated into primary health services in cost-effective ways, even in low-resource settings.

## FOCUS 2

***Engagement and support for people with Epilepsy*** – Introduction of innovative strategies to strengthen international efforts and national leadership to support policies and laws for people living with Epilepsy, while fully respecting their human rights. Patients and organizations that represent them should be empowered and involved in advocacy, policy, planning, legislation, service provision, monitoring and research in Epilepsy. It is fundamental to empower and amplify the patients' voice.

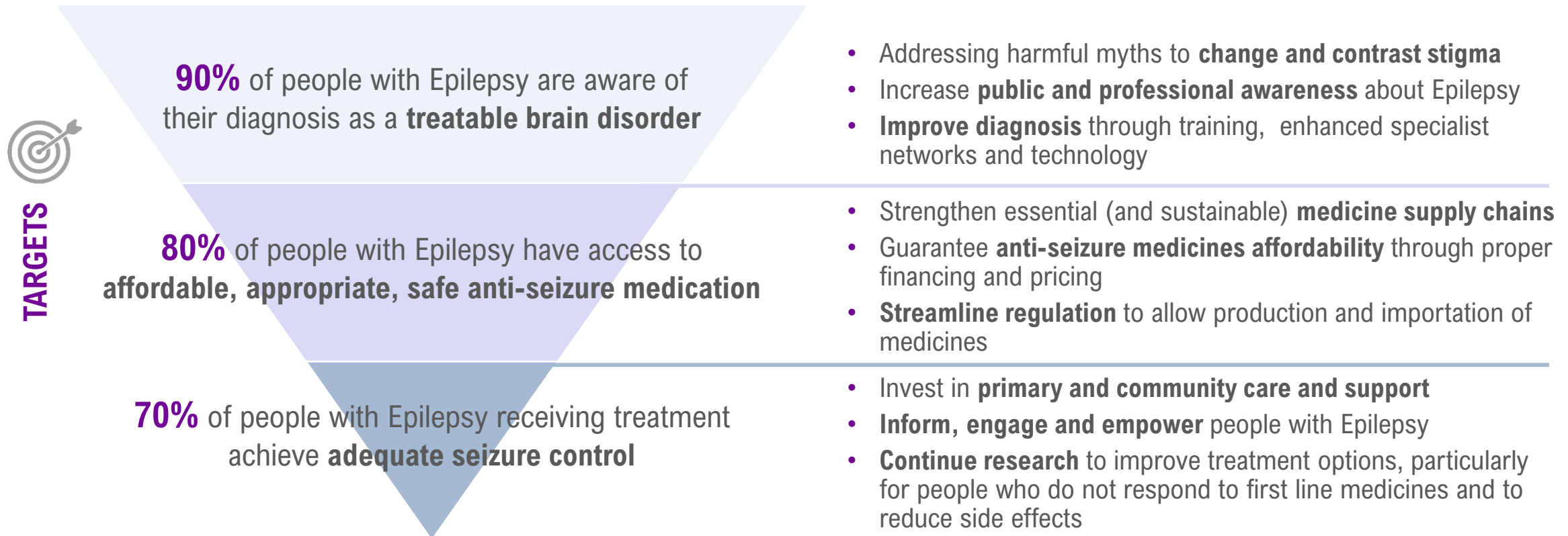
## FOCUS 3

***Epilepsy as an entry point for other neurological disorders*** – Epilepsy and a wide range of other neurological disorders share similar diagnostic and therapeutic technologies, as well as similar research, pharmacological and psychosocial approaches. For this reason, a well-functioning Epilepsy care service can present a good opportunity for strengthening the management of other neurological disorders.

- In this way, the IGAP aims to **strengthen the prevention, detection, care, treatment, and equal opportunities** for people with Epilepsy and other neurological disorders worldwide.

# The 90-80-70 cascade target for Epilepsy

- In coherence with the goals of the Intersectoral Global Action Plan, ILAE and IBE jointly developed a **90-80-70 cascade target\*** for Epilepsy, as part of the **roadmap to support the urgently needed expansion of health and care services** for people with Epilepsy.
- The **aims of the action cascade** are that **by 2031**:

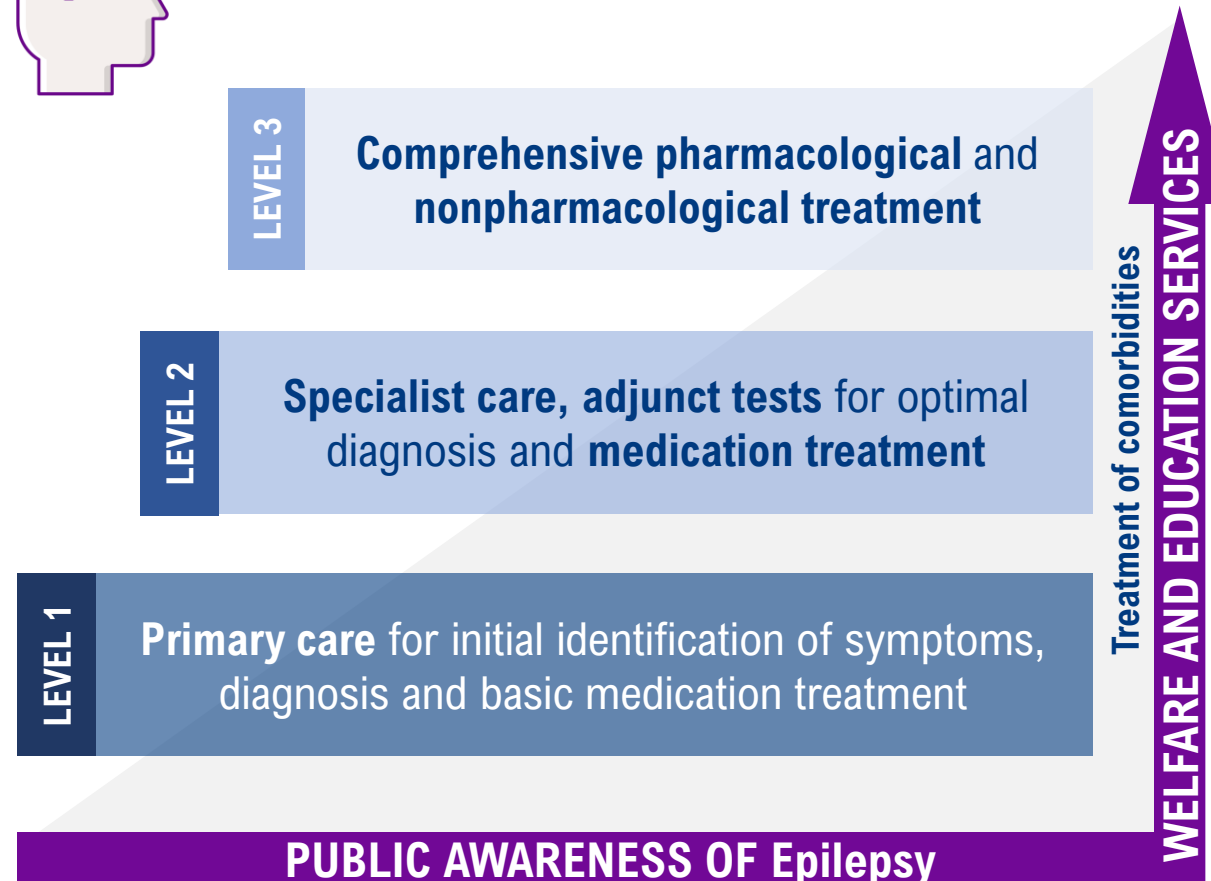


# Comprehensive healthcare response to Epilepsy

- According to the WHO, care for individuals with Epilepsy should involve the provision of health and social-care services aimed at decreasing “**morbidity, premature mortality and adverse psychosocial outcomes associated with the condition**”.
- Nevertheless, providing quality Epilepsy care is challenging due to the **condition’s complexity, chronicity and comorbidity**. As a consequence, the care needs to be **multifaceted**.
- In this scenario, the **management of comorbidities** should be an essential component at all levels of care through the involvement of **multidisciplinary healthcare teams** that emphasize person-centered care (e.g. physicians, nurses, pharmacists, therapists and social workers).
- **Community-based care** should be emphasized to increase access to all people in need of Epilepsy services. Social and educational services should provide individualized support to people with Epilepsy, throughout the levels of care and should continue, as needed, even when the person is no longer having seizures.



The needs of people with Epilepsy and their caregivers must be **distributed according to a stepped model**



# The Multidisciplinary Team (MDT) global trend

- In Epilepsy centers, an **MDT approach is usually implemented**, in which multiple professionals engage and collaborate to provide care to patients with complex situations and comorbidities.
  - **Members** of the teams usually include neurologists, neuropediatricians, clinical neurophysiologists, neurosurgeons, neuroradiologists, neuropsychologists, psychiatrists and Epilepsy nurses. Sometimes social workers, physiotherapist and speech therapists are involved as well.
  - A crucial role is played by the **Epilepsy Specialist Nurses** since they engage with physicians in providing care while also educating patients, families, schools, workplaces and the general public on Epilepsy.
- A significant issue in the management of individuals with Epilepsy is related to the **limited availability in the Epilepsy Centers where MDT approaches** are implemented.
- The remainder of patients are treated in the 2 lower levels: General Neurology and Primary Care. In these levels, education in Epilepsy is lacking among healthcare professionals. To contribute to this gap, the International League Against Epilepsy (ILAE) Educational Academy has introduced a **curriculum for epileptology promoting high-quality education among all levels of care.**

## THE CONTRIBUTION OF PHARMACISTS IN MDTs

An **integrated approach makes the combined effort of several individuals** necessary (including **pharmacists**). Here follows some European examples with pharmacists in MDTs:

- In the **Netherlands**, pharmacists can introduce risks assessments, which is a fundamental step preceding the definition of the treatment and play a critical role in home care treatment
- In **Belgium**, pharmacists have an important role in understanding the proper dosage of drugs, the effects of the drugs on people with Epilepsy and in monitoring adherence.
- In **Italy**, clinical pharmacists are fundamental because they help maximizing the pharmacotherapy effect, minimizing the risk of developing adverse reactions and reducing medication errors.
- In **France**, pharmacists perform therapeutic drug monitoring and check the appropriateness of the drug. They are crucial because they are often the point of contact between physicians and patients.

# Management and treatment: key facts and figures

## Prevention

The **major preventable risk factors** for Epilepsy (e.g. perinatal risk factors, stroke) account for **25%** of all cases.



One of the most frequent causes of Epilepsy and seizure disorders is a **traumatic brain injury**, for example due to **road traffic injuries**.

According to WHO estimates, **50 million** people are injured in **road crashes each year**.


## Diagnosis


**Diagnostic delay** is an increasingly recognized issue in Epilepsy: according to scientific literature it can range **from 2 to 7 years**.

**Misdiagnosis** also remains common, affecting around **20-30%** of patients.

Potential direct costs associated with delay in diagnosis and misdiagnosis include **recurrent emergency medical care, unnecessary non-emergent medical evaluations, inappropriate prescribing of antiepileptic drugs**.

## Treatment

Between **30** and **40%** of patients with Epilepsy continue to have seizures that are **not adequately controlled by pharmacotherapy**. 

When the first anti-seizure therapy fails, the chances of a **second therapy** eliminating the seizures are **14%** and only **2%** if a **third therapy** is adopted, when the second therapy also fails. 



**Surgical intervention** is associated with complete seizure control in **50-90%** of cases, depending on the type and site of the lesion.

## Follow-up

**Medication adherence** among epileptic patients ranges from **36%** to **70.8%**.

According to a recent study\*, the share of adherence with AED in patients with Epilepsy can be **lower than 50%** after **4 years of treatment**.

New options with cost-effective, **improved tolerability** and drugs with **fewer dosing intervals** may improve patient adherence towards therapy.

(\*). Asghar, M.A., Rehman, A.A., Raza, M.L. et al., "Analysis of treatment adherence and cost among patients with Epilepsy: a four-year retrospective cohort study in Pakistan" (2021).

# Prevention of Epilepsy (1/2)

- The high global burden of Epilepsy requires prevention where possible. The **major preventable risk factors for Epilepsy**, which account for **25% of all cases**, include:
  - **Perinatal risk factors** (such as gestational age at delivery, birth weight, maternal health conditions, presence and skills of birth attendants, method of delivery, perinatal infection, etc.)
  - **Central nervous system (CNS) infections** (bacterial meningitis, viral encephalitis and neurocysticercosis)
  - **Traumatic brain injury** (cause of Epilepsy in **5%** of cases in high-income countries; road traffic injuries, falls and violence are the most common causes)
  - **Stroke** (including ischemic and hemorrhagic types, representing **12%** of epilepsies in HIC. Seizures after stroke are associated with increased premature mortality, disability, and higher resource allocation and costs)
  - **Other factors** (such as alcohol and substance abuse use, may increase the development of Epilepsy)

- The **primary prevention of these causes has a substantial impact** on the development of epilepsies, whereas an understanding of the development of Epilepsy after a brain insult or parasitic infection is critical to the **development of secondary preventive strategies**.



## COMORBIDITIES

- The quality of life of people with Epilepsy is affected by **comorbid conditions** that include the **neurological, neuropsychiatric, and neurobehavioral disorders**
- Several diseases, including depression, anxiety, dementia, migraine, heart disease, peptic ulcers, and arthritis are **up to 8-times more common** in people with Epilepsy than in the general population
- Several mechanisms explain how Epilepsy and comorbidities are associated, including shared **risk factors and bidirectional relations**



## Prevention of Epilepsy (2/2)

- The prevention of Epilepsy is an **important subject**, but regrettably has not been deepened until recently. In fact, the identification of **preventable causes of Epilepsy is considered a fundamental step towards the development of primary preventive strategies.**
- On the other hand, secondary preventive strategies **require an understanding of epileptogenesis\*** after a brain injury (whether due to an infection, trauma or brain degeneration), but limited evidence is available until today.
- In general, the effective implementation of both primary and secondary Epilepsy prevention programs require the **involvement and collaboration of multidisciplinary stakeholders** (such as public policy-makers, public health officials, health researchers, healthcare providers, etc.).

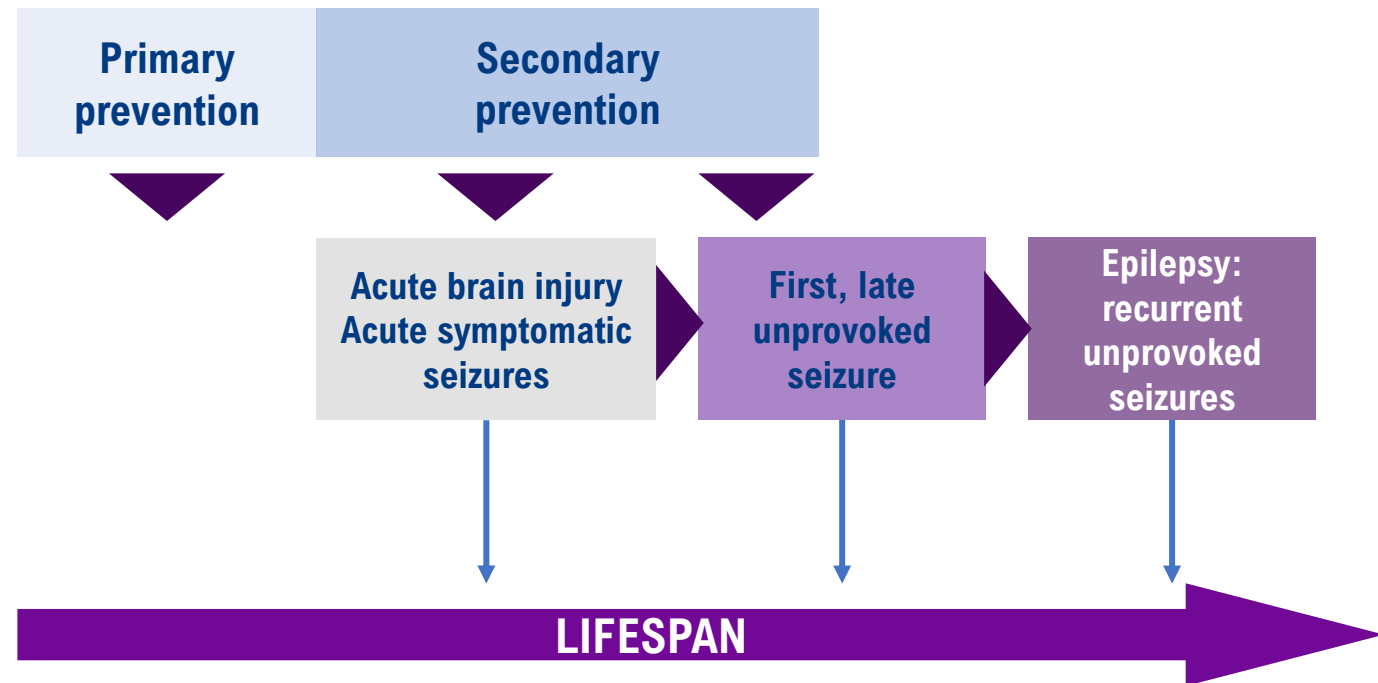
(\*) *Evolving process following brain insults by which the brain develops recurrent spontaneous seizures.*

### TIMELINE FOR PRIMARY AND SECONDARY EPILEPSY PREVENTION



*Preventing the **initial event** (insult, injury or disease) that affects the brain*

*Early therapies following an initial event **to limit the extent of brain injury** or otherwise **interrupt the process of epileptogenesis***



- **The diagnosis of Epilepsy is primarily clinical**, i.e. based on an accurate description of the critical episodes by the patient, when possible, or by people who observed the events. The most important diagnostic tests are **electroencephalogram (EEG)** and the **magnetic resonance imaging (MRI)** of the brain (or CT scan if not possible).
  - The EEG, recording the brain's electrical activity, can reveal specific abnormalities, called **epileptiform discharges**, at the base of an epileptic condition.
  - MRI, on the other hand, is fundamental in detecting or excluding a structural **brain pathology**, which must be taken into account when deciding on antiepileptic treatment.

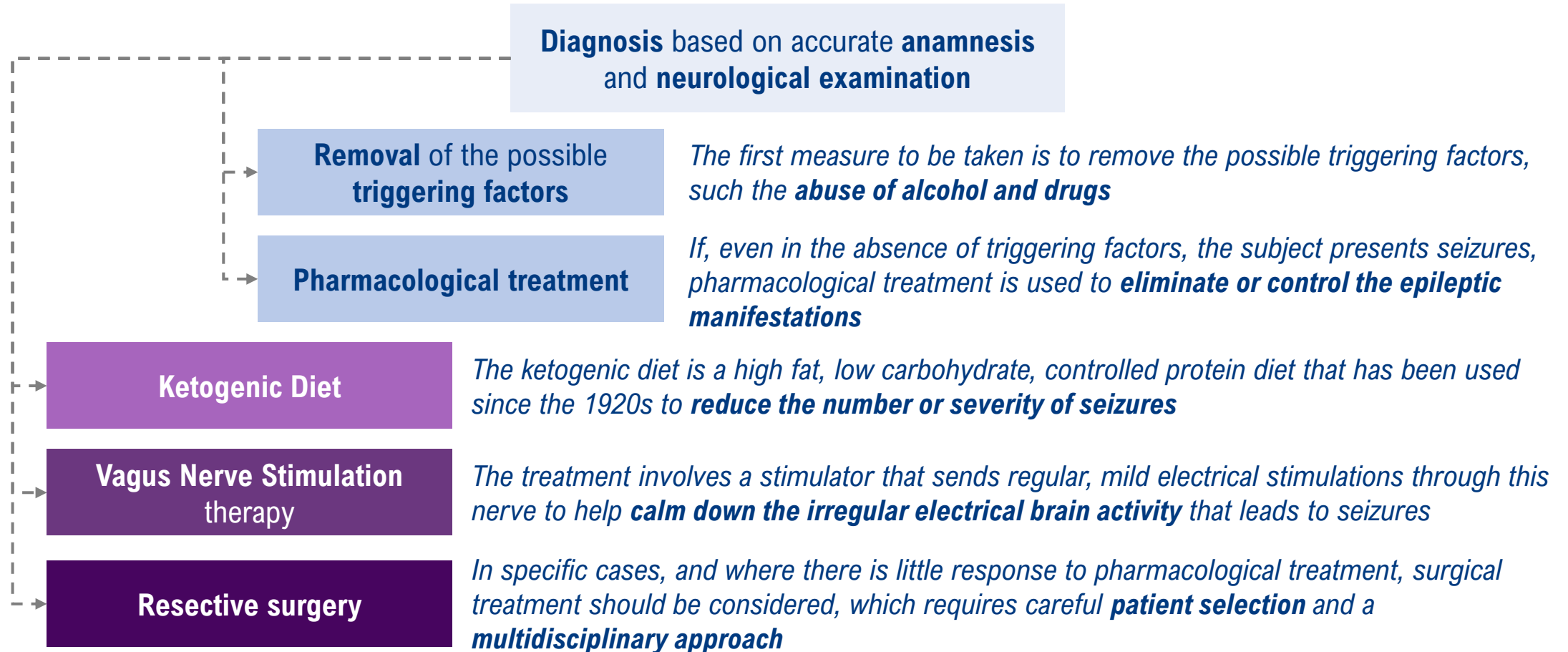
**EEG and brain MRI can however be completely negative** even in certain cases of Epilepsy, so the first diagnostic steps always represented by an **accurate anamnesis** and **neurological examination**.

- According to the definition given by the International League Against Epilepsy (ILAE), a person is considered to **have Epilepsy if they meet any of the following conditions**:
  - At least **2 unprovoked** (or reflex) **seizures** occurring greater than 24 hours apart
  - **1 unprovoked** (or reflex) **seizure** and a **probability of further seizures** similar to the general recurrence risk (at least **60%**) after 2 unprovoked seizures, occurring over the next 10 years
  - Diagnosis of an **Epilepsy syndrome**



# Management and treatment of Epilepsy

- While a single epileptic seizure should not be treated with drugs, except in very particular cases, Epilepsy (the tendency for seizures to recur) always requires treatment that must be prolonged at least **until the seizures are completely controlled**.

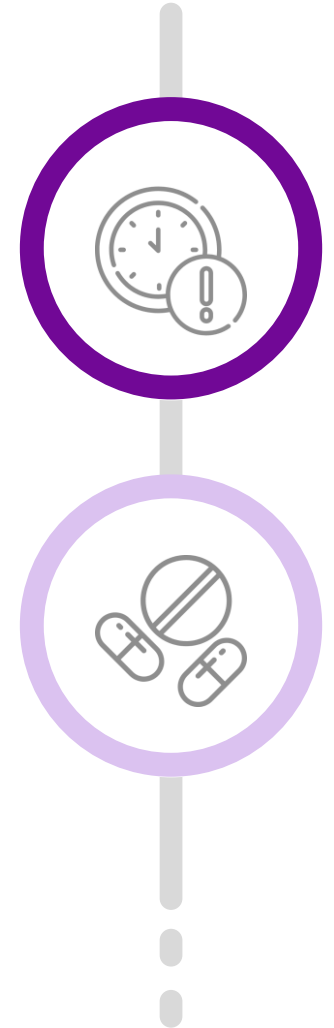


- Follow-up is an essential step in the management of Epilepsy in order to **keep seizures under control**. In this context, **adherence to medication** is crucial in preventing or minimizing seizures and their cumulative impact on everyday life. Non-adherence to antiepileptic drugs (AEDs), in fact, can result in breakthrough seizures many months or years after a previous episode and can have serious repercussions on an individual's perceived quality of life.
  - **Reasons for non-adherence are complex and multilayered:** patients can accidentally fail to adhere through forgetfulness, misunderstanding, or uncertainty about clinician's recommendations, or intentionally due to their own expectations of treatment, side-effects, and lifestyle choice.
  - There are various strategies suggested for managing patient adherence, starting from the **strengthening of the relationship between clinician and patient**, but these are highly dependent on the reasons why a patient has not followed clinician advice initially.
- Seizure control, however, is different from clinical remission. Epilepsy is **considered to be resolved** only for individuals:
  - who had an **age-dependent Epilepsy** syndrome but are now **past the applicable age**;
  - or those who have remained **seizure-free for the last 10 years**, with no seizure medicines for the last 5 years.



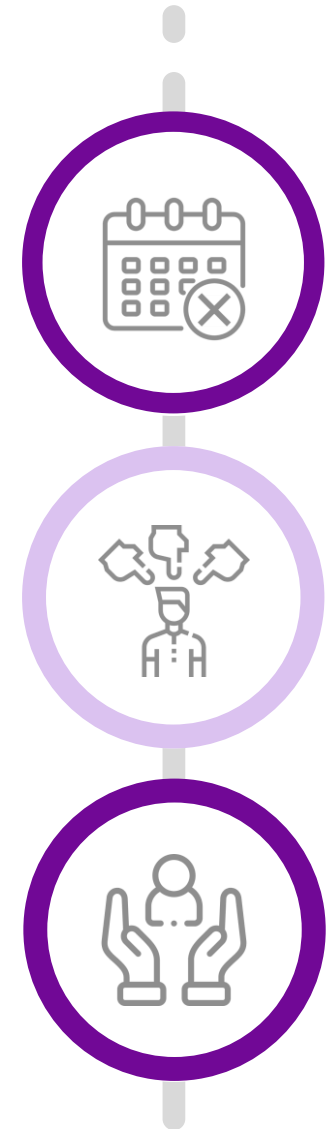
## Main critical points of the patient journey (1/2)

- **Diagnostic delay:** when entering the **emergency department**, it may happen that patients are examined by neurologists not specialized in Epilepsy, who are unlikely to be able to make a precise diagnosis. **A late or incorrect diagnosis**, especially if the patient is not referred to an **Epilepsy clinic** and/or a **referral center**, can lead to delayed treatment and potentially preventable morbidity and mortality. Given that the care networks dealing with the **elderly** do not always include a neurologist, the diagnostic delay has a significant impact on this population group.
- **Drug-resistant Epilepsy diagnosis:** patients may have to change **up to 20 drugs** before receiving a diagnosis of pharmaco-resistant Epilepsy. Instead, as soon as the second drug fails, if the conditions are right, the patient could be either sent for a **pre-surgical assessment** and if possible operated on, or if the patient is inoperable, he or she must have access to centers where therapy can be optimized and managed with **personalized and innovative drugs**. It is **crucial to intervene** right after the diagnosis:
  - the timely **determination is not sufficient if not followed by proper re-evaluation** of the condition and the treatment.



## Main critical points of the patient journey (2/2)

- **Poor adherence to treatment:** it has been estimated that **between 15% and 66% of epileptic patients do not take their medication as prescribed**. This may be due to a lack of motivation resulting from **perceptual barriers** (e.g. concerns about adverse effects, gaps in knowledge) or even practical obstacles, such as difficulties in obtaining the medication. Non-adherence to therapy is often **unreported by patients** and **unrecognized by professionals**, with the risk of exacerbating the impact of suboptimal therapies and leading to a higher risk of seizures (+21%).
- **Stigma and marginalization:** **misconceptions concerning Epilepsy** can act as a significant **barrier to inclusion in education and in the workplace**. For young people with Epilepsy, seizures, side effects of antiepileptic drugs and social stigma are all known to significantly disadvantage **academic progression** and achievement.
- **Lack of support to family/caregivers:** it is well established that Epilepsy impacts the **quality of life of patients**, starting from a loss of control and independence. In this context, families and caregivers need to be supported in **managing seizures** and all the **psychological and emotional consequences** of the disorder. Moreover, due to the heavy stress burden, families and caregivers (especially parents of epileptic children) can develop post-traumatic stress disorder.

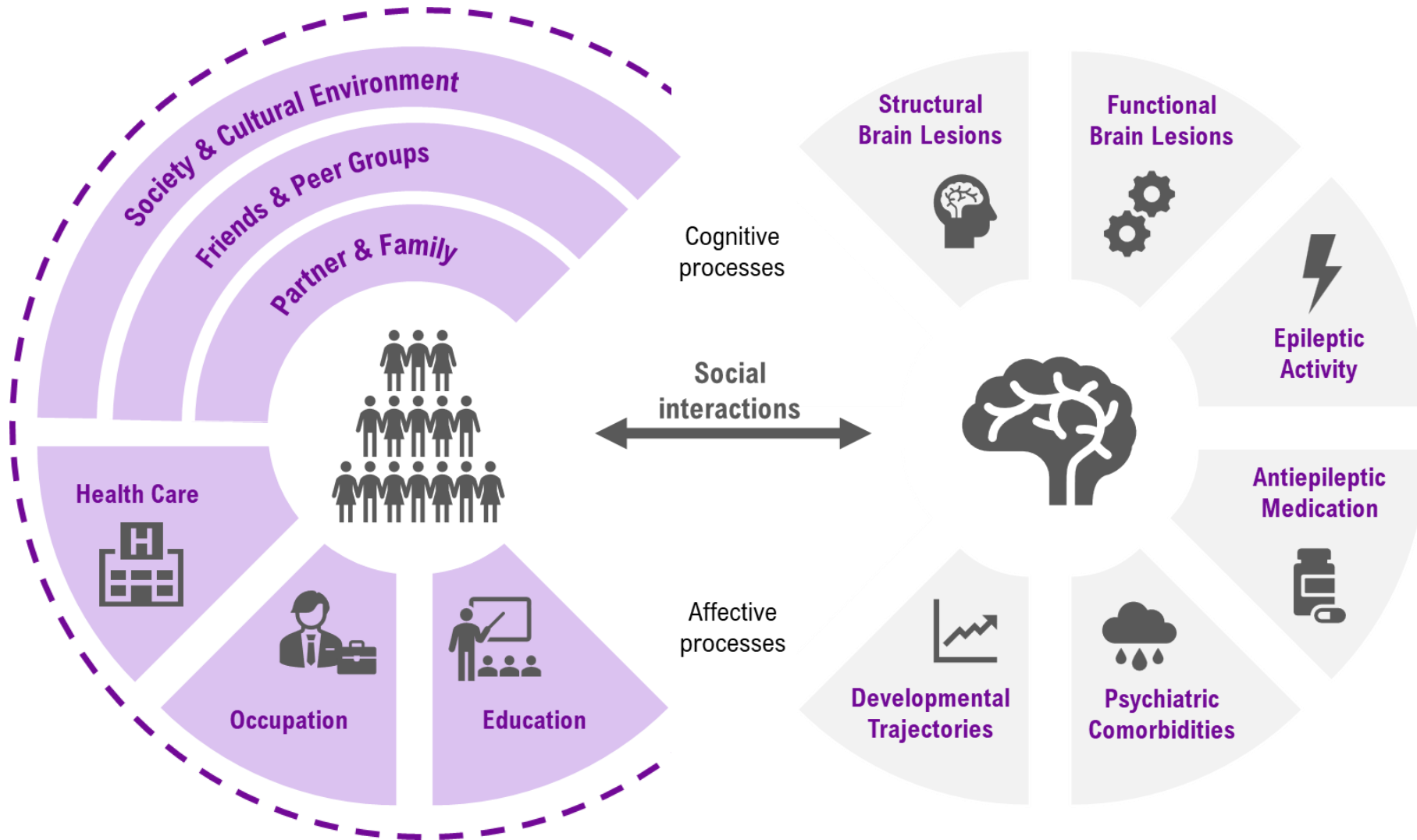




# Index

- The epidemiological context of Epilepsy in Europe
- The socio-economic impact of Epilepsy in Europe and the impacts of the COVID-19 pandemic
- The management of Epilepsy and the main critical points of the patient journey
- **The management of Epilepsy in Europe**
  - **At healthcare level**
  - **In school settings**
  - **In workplaces**
  - **In society in general**
- Research on Epilepsy in Europe
- Priority areas of intervention


# Individual and interpersonal determinants of social functioning in Epilepsy



- **Social Functioning** refers to the way an individual interacts with the environment and the ability to fulfill their role in society. Individuals with Epilepsy often experience **cognitive impairment** in social functioning
- There are many **underlying causes which are not only determined by medical conditions**. Specifically, stigma, role and experience restrictions, parental overprotectiveness, and fear of seizures are all to be considered **negative drivers affecting social competencies**.

# The management of Epilepsy at healthcare level in Europe (1/3)

- Epilepsy care has high rates of misdiagnosis and considerable variability in **organization and quality across European countries**, emphasizing the need for more cost-effective programs in Epilepsy care across Europe.
- As previously mentioned, at least **6 million people have Epilepsy** in Europe and **nearly one third fail to achieve a sustained seizure-free life**.
- Based on the latter figures, and considering that most European comprehensive Epilepsy centers manage between **2,000** and **4,000** patients, at least **one such center per a population of 1–2 million people should be accessible**:
  - These centers should have access to **high-resolution magnetic resonance imaging** and **in-patient video-electroencephalography** and a multidisciplinary team that should include neuropsychologists, and/or psychiatrists.
  - Genetic counselling should also be available. The possibility of recording from implanted electrodes and offering Epilepsy surgery should also be available in **comprehensive Epilepsy centers**.



The NICE guidelines recommend that all adult and children having a first seizure should be seen as soon as possible by a **specialist in the management of the epilepsies** to ensure **early diagnosis and treatment**



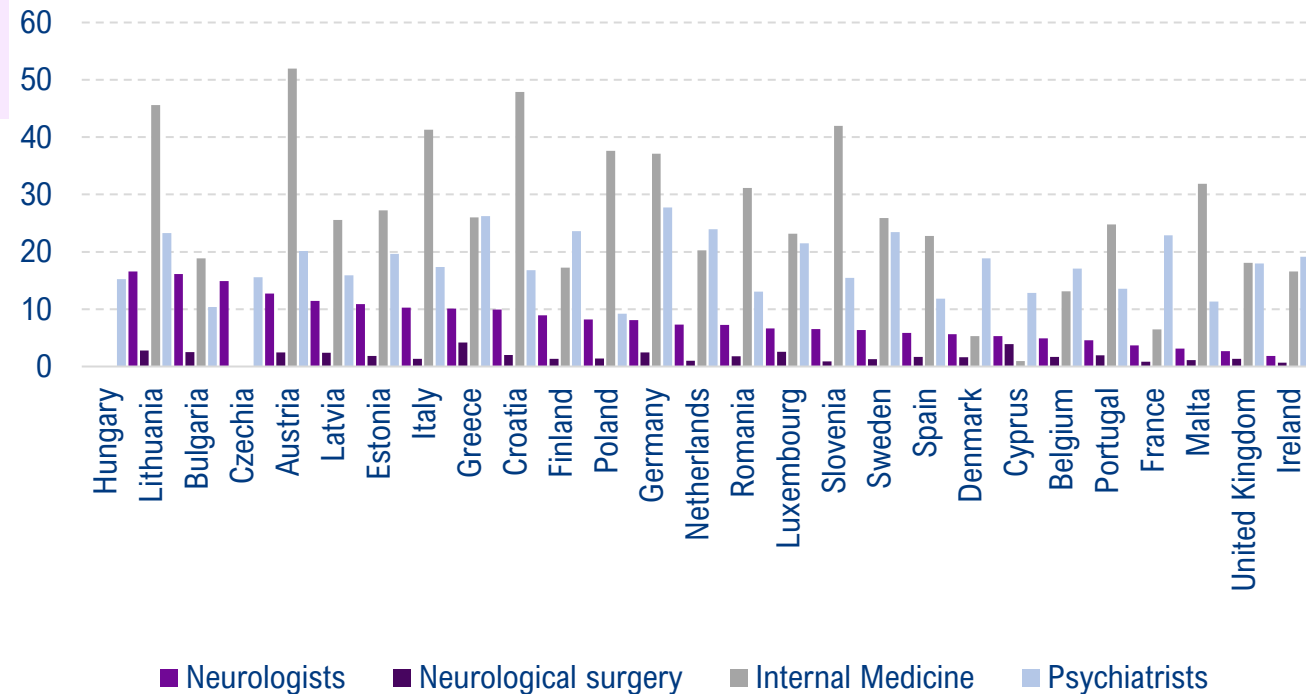
- up to **40%** of people with Epilepsy are untreated
- **6 million** people with active Epilepsy in Europe **cost over 20 billion euro** per year
- in some countries of Europe, Epilepsy is **not recognized as a brain disorder**
- very few European countries have **national plans for managing the disorder**

# The management of Epilepsy at healthcare level in Europe (2/3)

- In a paper published in 2019, the **provision of Epilepsy at European level** was analyzed: the number of healthcare professionals involved in the management of Epilepsy at healthcare level **varies significantly across the EU**. In general, responding countries were asked which **specialties most often provided basic Epilepsy care**:

- The **majority of adults with Epilepsy are reported to be generally treated by neurologists**. The number of neurologists varies between **1.8 neurologists per 100,000** inhabitants in Ireland to over **10.0 neurologists per 100,000 inhabitants** in countries such as Italy and Austria.
- The **presence of neurological surgeons** is significantly lower and diversified, with values ranging between **0.69** per 100,000 inhabitants in Ireland to **4.2** per 100,000 in Greece. Nevertheless, it is important to emphasize how the **lack or underuse of Epilepsy surgery** is reported as one of the main issues in many European countries.
- Children with Epilepsy are often treated by **pediatric neurologists**, but specific data on their presence are lacking.

## Healthcare professionals involved in the treatment of Epilepsy at European level (per 100,000 inhabitants), 2019 or last available data



Source: The European House – Ambrosetti on Zelano, Johan, et al. "The provision of Epilepsy care across Europe 2017: A 17-year follow-up survey" (2019) and Eurostat data, 2022

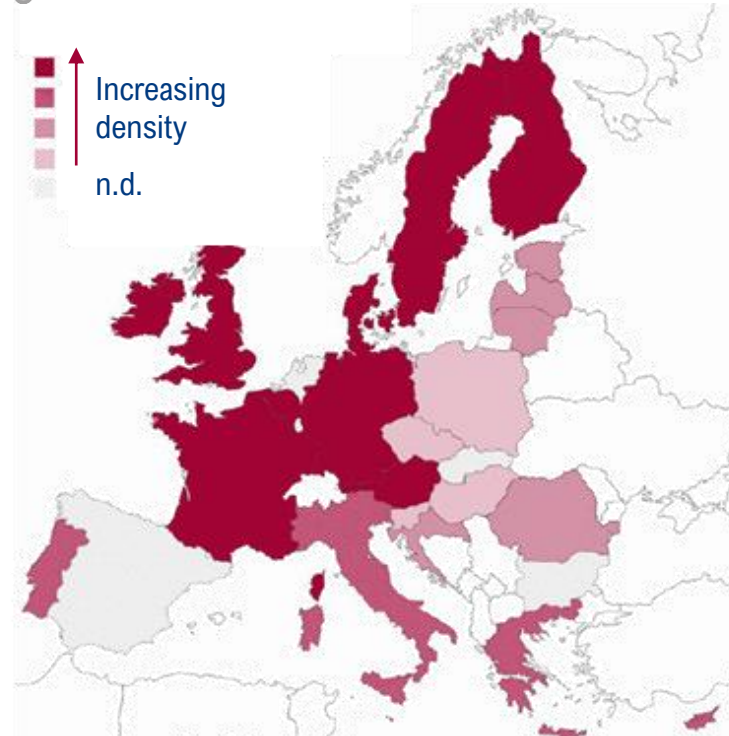


# The management of Epilepsy at healthcare level in Europe (3/3)

- Epilepsy management can be optimized thanks to the **presence of multidisciplinary teams (MDT)**. The expertise of MDTs involved in managing complex Epilepsy should include:
  - psychology, psychiatry, social work, occupational therapy, counselling, neuroradiology, internal medicine, nurse specialists, neurophysiology, neurology, neurosurgery and neuroanaesthesia.
- Some European countries report the **total absence of MDTs with or without a surgical program** (approx. **18%**), as shown in the images on the right. According to a paper published in 2017, the density of comprehensive MDTs with and without Epilepsy surgery programs **has not changed between 2002 and 2019**.
- The lack of such comprehensive teams suggests that people with Epilepsy might not obtain the **services needed to optimize treatment**, consider comorbidity, and give **necessary psychosocial support**.

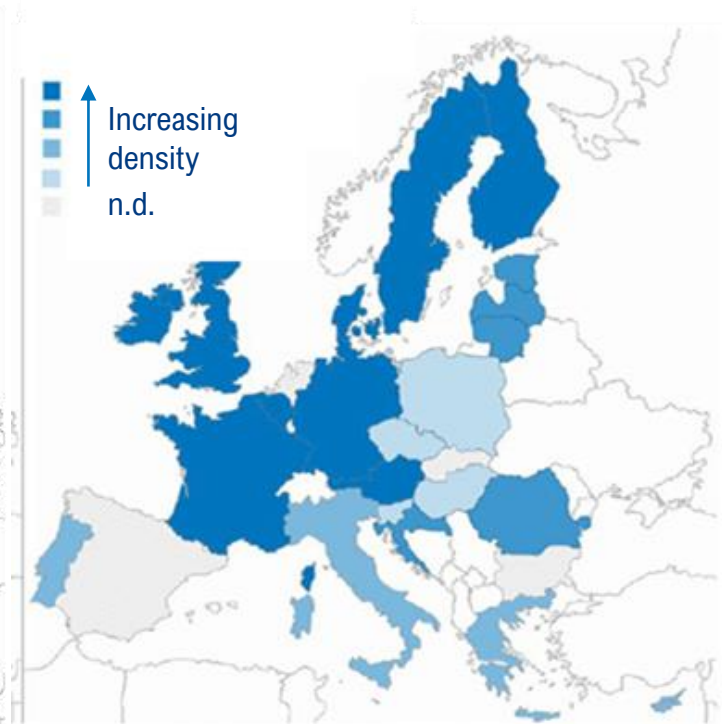


## Multidisciplinary teams in the EU without surgical programs



The **regional density of MDTs** without Epilepsy surgery programs is **1 per 3.94 million inhabitants**

## Multidisciplinary teams in the EU with surgical programs



The **regional density of MDTs** with Epilepsy surgery programs is **1 per 9 million inhabitants**

# Issues in the management of Epilepsy in Europe

- The burden of Epilepsy in Europe is significant, yet **access to quality care is lacking**. In fact, as highlighted in a recent report, even though **approximately 70%** of people with Epilepsy are likely to respond to treatment, **around 40% across the Europe** - and **up to 90%** in some areas - **are missing out** (treatment gap).
- Differences in access to treatment **between European countries** is not surprising, also given the **great variability in terms of national income, life expectancy, and healthcare systems organization**. However, **services also differ within countries**, based on the level of urbanization and socioeconomic factors.
- This **preoccupying situation emphasizes a serious underlying issue**, namely the poor awareness of Governments, communities and healthcare providers of the burden of Epilepsy, impacting also on the **experience of people with Epilepsy and their families**.
- In general, wide treatment gaps may result from a **combination of decreased capacity** in healthcare systems, inequitable distribution of resources and **low priority assigned to Epilepsy care**. Factors that widen this gap include staff shortage, limited access to anti-seizure medicines, lack of knowledge and confidence of workers across all relevant sectors (healthcare, welfare and education) in the management of Epilepsy, misconceptions and stigma.



- Most of those who do seek medical advice will initially be seen by **primary healthcare professionals** (with little experience of Epilepsy)



- **88%** of countries in Europe declare to have a **legislation in place for Epilepsy**
- **46%** of countries in Europe report Epilepsy in the **national annual reporting system**



- **~10%** of countries in Europe have **no Epilepsy specialists**



- **~50%** have **Epilepsy surgery programs** (i.e. many patients with refractory Epilepsy have no access to treatment that could greatly improve or even save their lives)



- **>30%** of countries have **no neuropsychological or rehabilitation services** for people with Epilepsy (with greater risks associated to behavioral issues, underachievement at school, underemployment, financial difficulties, mental disorders, etc.)



# Epilepsy in the school setting (1/2)

- Since **children spend a large part of their waking hours in school settings**, it is therefore crucial to **recognize Epilepsy and its effects in this setting**. Furthermore, it is well-known that Epilepsy is recurrent among individuals below 25 years; individuals in this age group are generally students and, consequently, exposed to the school settings dynamics. Given this aspect, it is not surprising to see the importance given to research on **how to better include and support children** and youth during their school years.



- Some **interesting studies carried out are:**

- A **Finnish** analysis which showed that students with Epilepsy tended to **drop out of school** at **higher rates during adolescence**;



- In two **Finnish provinces**, a population-based study showed a correlation between Epilepsy and disability; in addition, it documented the presence of **learning disabilities** in the **23%** of the 143 children aged 4-16 with Epilepsy. The most common difficulties were in **reading, writing and mathematics** (respectively **18.6%**, **17.6%** and **14.7%**).



- In the **Netherlands**, it was found that having Epilepsy **negatively impacts on education and achievement in later life**;



- A prevalence study in **Malta** showed that **53%** of children with Epilepsy attending mainstream schools were reviewed by educational psychological services because of **learning difficulties** (i.e. learning to read and write, alterations in memory processing, changes in sustained and focused attention, etc.)



- A **CDC Study**, found that **students aged 6-17 with Epilepsy** are more likely to miss **11 or more days of school, to have some difficulties, to use special education services, and have activity limitations** (e.g. less participations in sports or clubs, etc.)

## Epilepsy in the school setting (2/2)

- There is a complex interaction between **learning ability and Epilepsy**, which can result in a **greater risk of children with Epilepsy being misunderstood and excluded** and of **being denied equal opportunities** for learning and development of their full potential:



- It has been estimated that, excluding children with mental disability, between **25-50%** of children with Epilepsy have **some degree of educational difficulty**.



- In school settings, Epilepsy can have a **major impact on experience of children due to the impact** of both seizures and any medication.



- Within school settings, **psychological and social support** are of crucial importance, since (as previously mentioned) Epilepsy is often **associated with depression, poor effort in school, the possibility of isolation of adolescents**, anxiety about health and social standing and poor self-esteem.

- In **Austria**, with the goal of increasing high-school students' knowledge and awareness on Epilepsy, a **three-lesson teaching unit** was introduced. The impacts on students' attitudes were positive.
- In **Czechia**, school-aged children were exposed to **educational videos and drama** to raise awareness and improve knowledge on Epilepsy, hoping to reduced misconceptions.
- In **Canada**, the program **“Thinking about Epilepsy”** taught children aged 9-11 how to support a classmate with Epilepsy.

### MANAGING Epilepsy WHILE AT SCHOOL MAY INVOLVE:

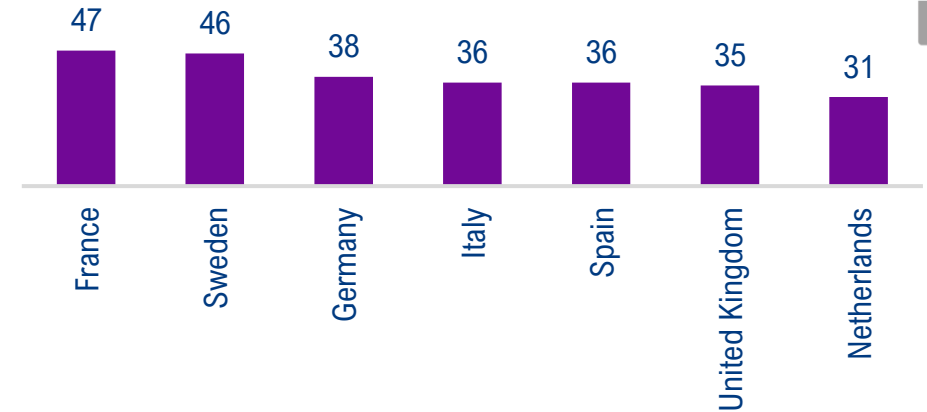
- Educating the school nurse, teachers, staff, and students about **Epilepsy and its treatment** and **possible stigma**
- Following the seizure action plan\* and administering first aid
- Understanding the **importance of medication adherence** and **supporting students** who take daily medications.
- Monitoring and addressing any **related medical conditions**, including mental health concerns such as depression

(\* ) contains essential information school staff may need to know in order to help a student who has seizures.

# Epilepsy in workplaces (1/2)

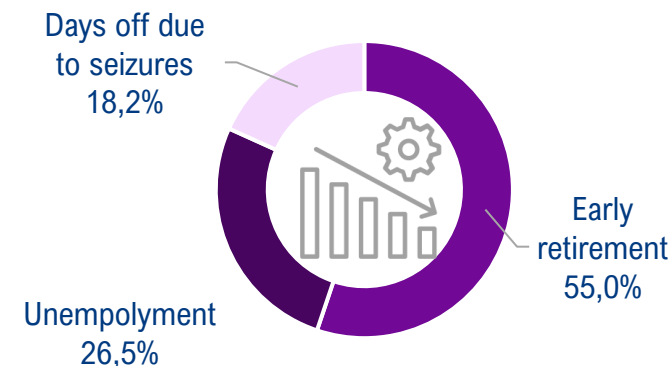
- Both **under- and unemployment** are more common in people with Epilepsy:
  - Studies have shown that people with Epilepsy have **significant difficulties in obtaining work**, perhaps in part due to educational underachievement;
  - Different studies have shown that, in Europe, **unemployment is twice to three times higher** among people with Epilepsy than in the general population.
  - Significantly **longer periods of unemployment** and **higher rates of early retirement** are also reported.
  - **Rates of underemployment** are reported to be higher for people with Epilepsy, but these rates are more difficult to quantify.
- Nevertheless, when Epilepsy is well controlled, it has been proven that it has much **less impact on employment rates and history**.
- **Loss of productivity** due to Epilepsy is difficult to estimate, but some studies indicate higher days off work and sick leave days of people with Epilepsy with respect to the general population. Data on **absenteeism do not indicate any markedly elevated rates** in people with Epilepsy and turnover rate has been reported as lower.

People with Epilepsy reporting how the diseases affected their ability to work (%)



Over **one-third of respondents** considered that Epilepsy affected their ability to work

Distribution of indirect costs by type (%)\*



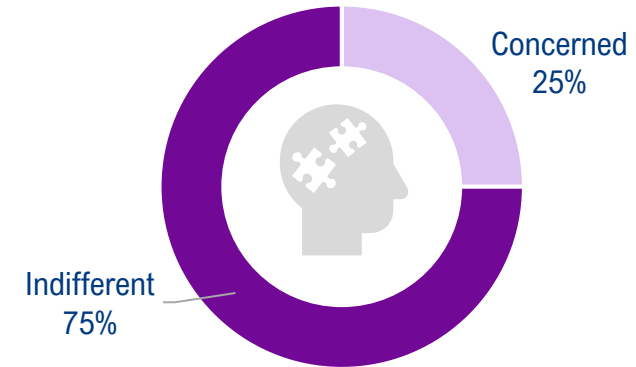
(\*). Willems, Laurent M., et al. "Trends in resource utilization and prescription of anticonvulsants for patients with active Epilepsy in Germany from 2003 to 2013—a ten-year overview" (2018)



## Epilepsy in workplaces (2/2)

- According to findings of Epilepsy Action, **people with disability encounter more difficulties in finding a job** partly because of the severity of their condition, which can hamper their ability to work. Among people with disabilities, individuals with **Epilepsy seem to have more difficulties with respect to any** other disabled people.
  - According to UK data, people with Epilepsy have **lower employment rates**; many individuals are unable to pursue a career, no matter their condition.
- Another alarming aspect is related to the **perception of colleagues**:
  - a quarter of those who responded to an Institute of Employment Studies stated that **they felt uncomfortable working with people with Epilepsy**. Furthermore, people with Epilepsy are often unaware of the legislations protecting their rights on the workplace and, indeed, **are reluctant to expose discriminatory behavior**.
- In addition to a low employment rate and a lack of understanding and acceptance, people with Epilepsy are also **paid, on average, 11.8% less** than non-disabled workers.

### Attitudes towards Colleagues with Epilepsy (%)



**1 individual out of 4** would be concerned **working with someone with Epilepsy**


### People with Epilepsy and Employment (%)



Only **34%** individuals with Epilepsy reported being employed

## Experience of good practices in Europe

- Individuals with Epilepsy and their families experience restrictions in many areas. As previously mentioned, these individuals may **experience issues in the school setting, at work and in society in general**. These are **non-medical issues** which, sometimes, are even worse than the medical ones, and contribute to a great burden for both patients and caregiver.
- **Some best practices exist at European level**, which try to contrast some of these issues experienced by individuals with Epilepsy.
  - In Germany, the **German Federal Government** implemented and funded, until December 2021, the **NEA Network «Epilepsy and Work»**. The idea of the project was to set up **special, regional Epilepsy counselling centers** to give support to those with Epilepsy and their families/caregivers. The centers are free of charge, and grant anonymity. Furthermore, they provide information, accompaniment, and support to everyone who is dealing with Epilepsy, personally or indirectly. The introduction of the program is moderate: 6 of the 16 federal states established regional centers. The aim is now to:
    - **expand** the program to the remaining Federal States;
    - call on the Epilepsy and Work Network in order to apply for **more implementation and assistance**;
    - provide **training** to specialists so that they can support employees with Epilepsy, employers and involved professionals in finding the right partners when clarifications on occupational issues with Epilepsy rise.

- 
- **“To tell or not to tell?”** is an interactive online self-test aid for employees with disabilities or other chronic condition
  - **Funded by the German Federal Government** and suited for school and work, it can be used for **social life in general**
  - It is used also, but not exclusively, for people with Epilepsy.



## Epilepsy in society in general (1/2)

- People with Epilepsy often **experiences social withdrawal and isolation**, which is frequently the result of anxiety about possible adverse reactions of others in case a seizure should occur in a public area.
- Studies indicate that the fear for their physical safety make many people with Epilepsy isolate themselves: more than **1 out of 5** individuals are afraid to go out because of the possibility of seizures occurring that might lead to accidents. It has been suggested that the latter might lead to **self-denial of opportunities**, which can in turn impact on other spheres of the social life.
- Issues in personal relationships are reflected in the **lower rates of marriage and fertility** among individuals with Epilepsy with respect to the general population:
  - For example, a comparison of Epilepsy and non-Epilepsy samples in the UK showed that **71% of the non-Epilepsy group** but only **42% of the Epilepsy group** were married (vs. 71% in general population).
- The evidence demonstrates that Epilepsy has a significant impact on **individual social and psychological well-being**.

	Plans for the future	Social Life	Standard of living	Relationship with friends	Relationship with family
France	56	49	41	36	33
Italy	52	40	44	36	31
Sweden	51	44	46	45	40
United Kingdom	50	44	34	44	25
Germany	48	43	35	23	21
Spain	40	34	32	40	24
Netherlands	37	32	30	32	17



Across European countries, **high percentages of respondents** reported that Epilepsy substantially affected their:

- **plans and ambitions** for the future, **feelings** about themselves and their social lives; conversely, **high percentages** considered
- relationships with **“significant others”** were unaffected





## Epilepsy in society in general (2/2)

- Under the **Discrimination law framework**, having an Epilepsy diagnosis is a form of disability
- Legislations based on internationally-accepted human rights standards can **prevent discrimination and the violation of certain rights**. However, people with Epilepsy, often experience limitations in their enjoyment of economic, social and cultural rights.
  - For example, restrictions on the **issuance of driving licenses** impose restrictions on social life and on choice of employment.
  - In addition, certain countries still have limitations on the **type of insurance available for people with Epilepsy**, limiting the protection from financial risks for the individuals and their family.
- One crucial problem is that laws are often **outdated and fail in promoting and protecting human rights**.



### DRIVING WITH EPILEPSY

- In seven European countries, the **share of people with Epilepsy with a driving license corresponds to 44% vs. 67%** of the general population.
- The restrictions on the issuance of licenses are developed on the belief that Epilepsy creates a risk for road traffic; however, it has been demonstrated that **there is not an overall difference in accident rates for people with Epilepsy**.
- Although high levels of variability across Member states exist, **all European countries have restrictions** for people with Epilepsy driving a power-driven vehicle.
- The current legislation in most countries allows people with Epilepsy who have controlled seizures to **obtain a driving license**. The risk is that the presence of bans lead to more people **with Epilepsy driving illegally because of the unfair regulation**.



# Index

- The epidemiological context of Epilepsy in Europe
- The socio-economic impact of Epilepsy in Europe and the impacts of the COVID-19 pandemic
- The management of Epilepsy and the main critical points of the patient journey
- The management of Epilepsy in Europe
  - At healthcare level
  - In school settings
  - In workplaces
  - In society in general
- **Research on Epilepsy in Europe**
- Priority areas of intervention

# Introduction to Epilepsy research and priorities areas

- Research related to Epilepsy is remarkably **broad and comprehensive**, as well as **particularly challenging** due to the complexity of the understanding of normal brain function and to the presence of many different types of Epilepsy, with unique causes and consequences.
- Clinical research related to Epilepsy concentrates on the **causes, diagnosis, co-morbidities** and **treatment** of the different forms of epileptic disorders, while entering a new era of **personalized Epilepsy management**.
- Research over the past two decades has resulted in more than **14 new anti-seizure medicines** being developed.
  - However, continued research is needed to expand further the **options available particularly for people who do not respond to first line medicines** and to **reduce side effects**.
- Non-medicinal therapies are also being investigated, including **new forms of brain surgery, wearable and implantable devices**, and methods of **electrical brain stimulation**.

Reducing the **life-compromising burden of seizures and Epilepsy**

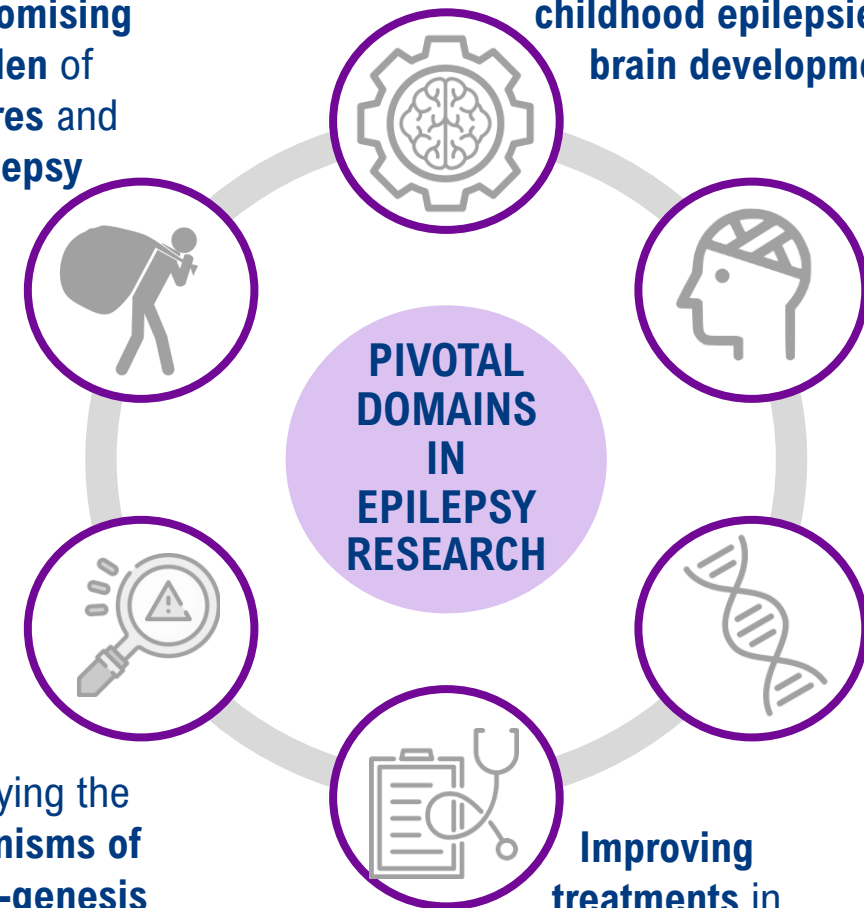
**Better understanding of childhood epilepsies and brain development**

**Preventing the development of Epilepsy after brain injury**

**Translating genetic knowledge to optimize the care of Epilepsy**

**Identifying the mechanisms of seizure-gensis**

**Improving treatments in Epilepsy**



## Relevant activities at European level (1/2)

- The **European Reference Networks (ERNs)** were launched in 2017 and now involve more than **900 highly specialized health care teams**, located **>300 hospitals** in **26 European countries**.
- Among them, **EpiCARE** is the ERN – co-funded by the EU - dedicated to **rare and complex epilepsies**. Its goals are to improve diagnostics accessibility, to develop treatment, improve awareness to protocols for physicians and patients, and to enhance educational activities and training opportunities. This has to be done **accounting for differences** between and within countries.

- **Epicluster** is part of the **European Brain Research Area (EBRA)**. Its primary objective is to establish a **collaborative framework** for the coordinated actions of Epilepsy research in Europe, based around **shared partnerships and research priorities**.
  - The Cluster's leadership team members have so far supervised **>250** doctoral and postdoctoral researchers, contributing to **over 2.500 publications** on the topic of mechanisms, treatment and biomarkers of Epilepsy.

### OBJECTIVES OF THE **EpiCARE NETWORK**

- **Accessibility** (*improve accessibility of detailed diagnostics to individuals of all ages with rare and complex epilepsies across Europe*)
- **Developing treatments** (*develop treatment protocols and monitor standardized outcomes of complex epilepsies*)
- **Awareness** (*improve awareness and accessibility to protocols for physicians and individuals with rare and complex epilepsies*)
- **Education** (*enhance educational activities and training opportunities*)
- **Collaborative research** (*enhance opportunities for registries, and collaborative research for the benefit of individuals with rare and complex epilepsies*)

### KEY OBJECTIVES ARE:

- **Maintaining cooperation** started under EpiXchange that brought together large-scale Epilepsy research projects and bring in new partnerships/projects and stakeholders
- Agree **shared priorities and work** toward addressing these including in the area of data sharing, preclinical studies and improving translation, access and sharing of research infrastructures and training.
- Develop and pursue funding of **joint research programs** of scale in Europe and beyond.

## Relevant activities at European level (2/2)

- **7 large EU-funded epilepsy-related research projects** joined forces in May 2018 in the **epiXchange conference**. During the latter conference, investigators from the projects DESIRE, EpimiRNA, EPISTOP, EpiTarget, EpiXchange, and EpiPGX as well as the European Reference Network EpiCARE, met up with key stakeholders **to share and review advances** made by each project in the previous years across 5.

### EPIXCHANGE CONFERENCE RECOMMENDATIONS

- The focus was on 5 **thematic areas**: biomarkers, genetics, therapeutics, comorbidities, and biobanks and resources.
- The achievements of the various programs showed the **advances made in the understanding of the pathogenesis, diagnosis, and treatment of Epilepsy**
- The recommendations define the most recent priorities in the Epilepsy agenda, driven towards **faster diagnosis, better treatment and end of stigma** in Epilepsy. The document displays a strategy based on **5 key points**:

BIG DATA

DIGITALIZATION

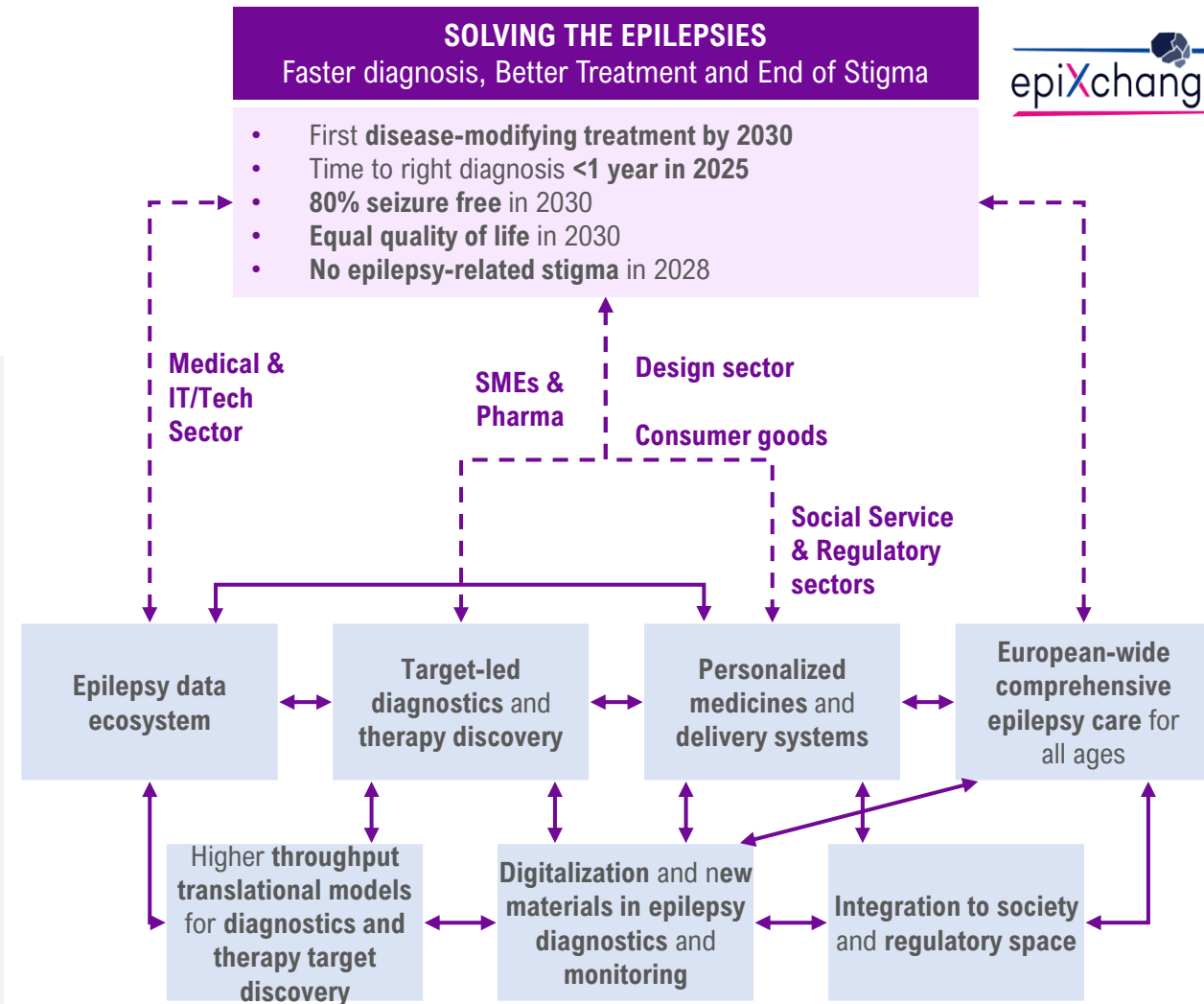
NEW VARIABLES  
EPILEPSY DATA

PERSONALIZED  
MEDICINE AND  
TREATMENT

EPILEPSY DATA  
ECOSYSTEM

### SOLVING THE EPILEPSIES Faster diagnosis, Better Treatment and End of Stigma

- First **disease-modifying treatment** by 2030
- Time to right diagnosis **<1 year in 2025**
- **80% seizure free** in 2030
- **Equal quality of life** in 2030
- **No epilepsy-related stigma** in 2028





# Key challenges of Epilepsy research in Europe

Although epilepsy can often be controlled, available treatments and management options are not cures. Epilepsy therefore is in need for more research in this field, but the **challenges encountered are significant, as reported below:**



## Clinical research/Trials

- **Complicated regulatory processes**
- **Lack of appreciation of differences** between trials and other research like epidemiology
- Need for more **clinician time**
- **Limited time** in health service provision
- Lack of **infrastructure and resources**
- Concerns on **reproducibility and transability of preclinical data**

## Reporting

- **Lack of consistent and updated epidemiological and economic data on Epilepsy**
- **Language barriers** (i.e. majority of research is done in English)
- **Publication biases in favor of novel/positive data** (on average, only **15%** of data are published with a bias against negative findings)
- Cost associated **with open access publication**

## Collaboration & Funding

- Existence **diverse procedures and methodologies** among Member states
- **High heterogeneity** across researchers, areas of research and technological expertise
- Presence of **intellectual property** due to **inadequate infrastructure** to promote collaboration
- **Insufficient funding** for Epilepsy, which has lagged that for other **common neurological conditions**

## Community & Societal

- Perception that **animal research**, despite providing findings, is **not transferrable into clinical discoveries**
- Epilepsy research is **not promoted** to the same degree across various EU Member states
- **Cultural stigma** across Epilepsy negatively impacts research activities



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# A new roadmap for Brain Health – Focus Epilepsy

Epilepsy care is the responsibility of Member States. Given the different nature of European healthcare systems, the implementation of Epilepsy policies has been uneven and **there appears to be a significant variability in the availability, accessibility and quality of services** provided. In this context it fundamental to:

## HEALTHCARE PROVIDERS, RESEARCHERS AND PATIENT ASSOCIATIONS

- Increase the **capacity to collect and monitor Epilepsy data** in order to evaluate Countries' **responsiveness to health and socio-economic needs**
- Formulate, pursue and advocate for **research priorities** in Epilepsy
- Develop **research tools and strategies**
- Stimulate studies of the **economic burden of epilepsy** to allow more effective use of limited resources
- Promote **collaboration and partnership between all actors** (both public and private)
- Create **training and mentoring opportunities** for stakeholders 

## POLICY MAKERS

- Enforce a “**holistic approach**” to **Epilepsy** aimed at **reducing stigma across all sectors**
- **Harmonize programs and European guidelines** to improve access to Epilepsy care
- **Promote** the inclusion of Epilepsy in **European and national public health agendas**
- **Enable policy changes** in response to outcomes and priorities
- Establish **new and innovative funding mechanism** for Epilepsy 

## GENERAL POPULATION

- **Engage representatives** in awareness activities
- **Increase public support** to improve treatments for Epilepsy and **better working, educational and social environments**
- **Engage general public** in **participatory action campaigns**
- Organize **educational campaigns on Epilepsy** for the media and the general population 



*Focus Epilepsy*

# Headway



A new roadmap in Brain Health