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Proceedings from ERN EpiCARE "BEYOND SEIZURES" meeting, Aalesund, Norway, May the 27th. Advancing holistic care for rare and complex epilepsies in adults

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1. Introduction

This proceedings document presents the results of the European Reference Network for Rare and Complex Epilepsies (ERN EpiCARE) "Beyond Seizures" meeting held in Ålesund, Norway, on May 26th and 27th, 2025. Organized by Working Group 18, this meeting gathered experts in the field to explore the multifaceted nature of epilepsy and its wide-ranging implications beyond seizure control. Participants shared their latest findings and engaged in discussions centered around the complex interplay between epilepsy, cognitive function, psychological and social comorbidities, and the advancements in treatment modalities.

Epilepsy is a complex neurological disorder characterized not only by its hallmark seizure activity but also by a wide array of cognitive, psychological, and social comorbidities. Advances in research methodologies and treatment interventions have afforded us novel insights into how these multifaceted issues interplay in the lives of individuals with epilepsy. This paper brings together findings from multiple studies that examine the nuances of epilepsy beyond the mere control of seizures, offering a comprehensive perspective on the challenges patients face and the advancements in treatment approaches.

Research in animal models has significantly broadened our understanding of epilepsy. While most studies have traditionally utilized rodent models, zebrafish have recently emerged as a promising alternative for exploring neurobehavioral consequences associated with epilepsy. With a genetic similarity of approximately 70% to humans and advanced genetic tools available for manipulation, zebrafish models enable the examination of cognitive and psychological dimensions of epilepsy with greater precision. The bidirectional relationship between epilepsy and its comorbidities becomes apparent as these models elucidate potential mechanisms through which cognitive deficits may arise before or as a result of seizure activity.

In the realm of neuropsychology, the focus has shifted alongside the

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changing demographics and clinical presentations of epilepsy patients. A study conducted over two decades revealed a significant increase in the age of onset for mesial temporal lobe epilepsy (mTLE) and a decline in early-onset cases associated with hippocampal sclerosis. This evolving landscape has implications on cognitive performance, necessitating standardized neuropsychological phenotyping systems to tailor assessments and treatments to patients' unique profiles. Collaboration and flexible assessment tools are projected to become crucial components of epilepsy management, especially with the increasing complexity of patient needs.

The landscape of antiseizure medications (ASMs) has also undergone transformative changes. A growing emphasis on precision medicine has led to the development of targeted treatments for rare and severe epileptic conditions, including developmental and epileptic encephalopathies (DEEs). Strategies such as drug repurposing and molecular modifications are being employed to create more effective therapies tailored to specific genetic profiles. The promising results from clinical trials have highlighted the importance of individualized treatment paradigms, potentially improving outcomes for patients with genetic epilepsies.

Epilepsy surgery remains a vital intervention for treatment-refractory patients, but its cognitive implications are substantial. Numerous studies indicate positive effects on cognitive functions following seizure freedom, especially when anti-seizure medications can be reduced or discontinued. However, ongoing research is necessary to understand the long-term cognitive and behavioral effects of surgical interventions, as factors such as age and surgery type play a crucial role in outcomes.

Furthermore, social cognition—comprising skills such as emotion recognition and theory of mind—is essential for maintaining interpersonal relationships and overall quality of life in individuals with epilepsy. While surgery may alleviate seizures, cognitive functioning relating to social situations may decline over time, particularly in patients with more complex epilepsy histories.

Additional challenges arise in the context of drug-resistant epilepsy, where neurostimulation therapies, such as Vagus Nerve Stimulation (VNS) and Deep Brain Stimulation (DBS), are increasingly being utilized. Although initial findings indicate some cognitive improvement with these interventions, ongoing assessment and further studies are needed to comprehensively evaluate their cognitive effects.

Psychosocial dimensions, particularly stigma, also significantly affect the quality of life for those living with epilepsy. Stigma can lead to social isolation and diminished treatment adherence, necessitating systemic changes to address and mitigate the damaging repercussions of societal misconceptions about epilepsy.

Lastly, ensuring optimal patient care requires a shift toward needs-based follow-up models, which utilize digital Patient-Reported Outcome Measures (PROMs) to enhance personalized care and improve satisfaction levels in patients. Initial findings suggest that such models can foster greater involvement and tailored approaches that resonate with individual patient needs.

In light of these multifaceted aspects of epilepsy, this paper aims to integrate theoretical and practical insights across various domains, including animal research, pharmacological advancements, surgical outcomes, social factors, and patient perspectives. By doing so, we hope to provide a cross-sectional understanding of epilepsy that not only emphasizes seizure management but also promotes holistic, individualized care designed to improve the quality of life for those affected by this complex disorder.

2. What can we learn from animal models in beyond seizures issues in epilepsy

2.1. Sverre Myren

Most studies have been performed in rodent models, the zebrafish is now a rising model for exploring neurobehavioral consequences of epilepsy. Relationships between epilepsy and its cognitive, psychological and social comorbidities are assumed to be bidirectional [1]. Animal models offer an experimental control over confounding factors including cause and severity of seizures, that is more difficult to obtain in clinical studies. Models of acquired epilepsies may elucidate whether comorbidities occurred before the onset of epilepsy. Insights from rodent models of neurobehavioral comorbidities of epilepsy was covered in a recent review [1]. Two decades after it was introduced, zebrafish is now well-established as an epilepsy model [2,3]. The zebrafish shares ca. 70% of genes with humans and has an advanced experimental genetic toolbox available. Brain activity can be monitored and perturbed in neural and glial networks across the entire brain using calcium imaging and opto-/chemogenetics [2,4]. Novel CRISPR-Cas9 genome editing techniques allow cost-effective and rapid generation of zebrafish mutants to model human epilepsy conditions [2]. In a recent study, among $>$ 2,200 candidate epilepsy-genes, 48 were developed into stable loss-of-function mutants [5]. The functional consequences of the mutations were comprehensively assessed combining behavior, electrophysiology, imaging and cellular biology. Such studies demonstrate zebrafish as a powerful model to study both seizures, neurobiological and neurobehavioral effects of epilepsy. A myriad of experimental paradigms are established for dissecting behavioral signatures suggested to represent depression/anxiety, learning and memory, social behavior and sleep [6]. The snc1lab Dravet's syndrome model (homologous to SCN1A human gene) is likely the most extensively studied epilepsy model in zebrafish [7]. Behavioral studies have revealed night-time hyperactivity (suggesting disrupted sleep behaviors), diurnal locomotor activity deficit and 'wall-hugging' behavior (considered as a sign of increased anxiety). Specific drugs (clemizole and diazepam) reduced the nighttime hyperactivity and decrease the anxiety-like wall hugging-behavior. Importantly, it is an inherent challenge to extrapolate what a specific behavior in an animal represents. Attribution of human characteristics to animal data (anthropomorphizing) should be avoided [8]. The Research Domain Criteria (RDoC) classification and terminology system may assist translation of behavioral data.

3. Temporal trends in beyond seizures issues and challenges for neuropsychology in adults with epilepsy

3.1. Christoph Helmstaedter

Mainly driven by epilepsy surgery and pharmacological treatment related research neuropsychology in epilepsy has gained a central role in the diagnostics monitoring and outcome control in epilepsy and common rules on indications and expectations have been established [9]. However, over the past few decades the field of neuropsychology in epileptology has undergone substantial transformation, driven by shifts in patient demographics, disease presentation, and clinical priorities. For many years an increasing number of surgeries was noted the mayor target group being patients with temporal lobe and mesial temporal lobe epilepsy in particular [10]. In this regard one of the most significant developments is the decreasing number and profile of mesial temporal lobe epilepsy (mTLE) which has been noted in Europe and the USA as well [10–14]. A preliminary analysis of own monocentric data comprising about 1000 patients with mTLE between 1997 and 2017/18 reveals a clear temporal trend [15]: the age at epilepsy onset has increased markedly, early-onset mTLE associated with hippocampal sclerosis, once the dominant subtype, is now less frequently encountered, while late-onset mTLE—often suspected to be related to limbic encephalitis (LE)—has seen a significant rise. Additionally, bilateral MRI pathologies in mTLE patients have become more common. These evolving etiologies are mirrored in changing neuropsychological profiles. Over time cognition has appeared less impaired overall and the classic distinction of verbal versus figural memory impairment in left respectively right mTLE has become less pronounced, suggesting a

blurring of neuropsychological phenotypes. These phenotypic patterns may reflect not only the lateralization of epilepsy but also its etiology, age at onset, and associated neuropathology. Supporting these findings, a recent retrospective review of the Bonn Neuropsychological Database (1986–2024) further documents the evolution of clinical neuropsychology [16]. Among about 14.000 first-time assessments, the average assessments in individuals aged over 50 grew from 2% (1986–1990) to 39% (2020–2024). At the same time, surgery-related assessments dramatically declined from 90% to just 9%. In place of comprehensive evaluations, modular and screening-based tools, such as EpiTrack [17 18], have become increasingly utilized—rising from 1% to 26% between 2018 and 2023. This shift reflects both the decreased prevalence of surgically remediable epilepsy and the increasing diversity and complexity of cognitive concerns among patients.

One of the field's responses to these changes has been the development of neuropsychological phenotyping systems aimed at standardizing cognitive profiles across diverse patient populations. The utility of the IC-CoDE model, for example, was evaluated in a pooled analysis again of about 14.000 patients and tested against an alternative code developed for members of the European EpiCare network [19]. For both models patients performances were categorized based on impairments in attention/executive function, verbal/figural memory, language, and visuoconstruction (IC-CoDE = 0,1,2,>2 domains impaired vs. EpiCare Code 0–4 step ratings of the 5 individual domains). Less than on third of all assessments covered all five core cognitive domains needed for the IC-CODE. Depending on domain coverage, extremes in impairment ranged from 10 to 58%. While IC-CoDE showed high correlation with the alternative code suggested for the EpiCare network the codes relation to clinical data were poor to moderate. While the IC-CoDE was mainly predicted by IQ/education, age, and number of seizures, the EpiCare code was related to IQ/education, temporal/extratemporal location, age, bilateral epilepsy, temporal/extratemporal location, behavioral problems, and drug/load. The IC-Code requires time and staff consuming assessment of 5 domains and some critics noted that dementia screening tools might provide comparable insights with less effort [20]. Overall, there appeared to be better arguments for using the EpiCare code. Nonetheless, both models reveal some meaningful phenotypic differences associated with age at onset, education, hippocampal sclerosis, and gender. In light of these findings, there is growing consensus around the need for more flexible, collaborative, and scalable neuropsychological assessment methods. A recent proposal within the EpiCare European Reference Network emphasizes the importance of international cooperation, shared data infrastructures, and innovative tools such as online neuropsychological toolboxes and mobile or wearable-based behavioral assessments. Standardized retrospective coding systems and prospective data integration platforms are being explored as means of harmonizing cross-center evaluations.

Particular attention must be being paid to late-onset epilepsies (LOE), a rapidly growing segment of the epilepsy population, especially in aging societies [21]. LOE is frequently linked to cerebrovascular events or neurodegenerative changes, and cognitive impairments in these cases often precede the first clinical seizure. As such, both seizures and cognitive decline may represent early manifestations of the same underlying disease process. Differentiating between effects of the disease, medication, and active epilepsy is complex but essential. Importantly, dementia is rare in patients whose seizures are the initial symptom, provided that cognitive or psychiatric features do not develop progressively. Neuropsychologists must therefore take detailed clinical histories, employ sensitive screening tools, and prioritize longitudinal monitoring—regardless of seizure control [21]. This complexity is especially evident in patients with limbic encephalitis, where cognitive and behavioral impairments are often dynamic and can precede radiological findings or immune markers [22]. LE typically results in episodic long-term memory dysfunction (including accelerated forgetting and autobiographical memory loss), executive deficits, and affective disorders. Psychiatric symptoms may also occur, sometimes severely. Neuropsychological assessments are essential not only for diagnosis but also for monitoring disease progression and treatment efficacy. Ideally, evaluations should be conducted before treatment begins and repeated at clinically relevant junctures, such as changes in anti-seizure or immunomodulatory therapy. Importantly, cognitive and behavioral outcomes may diverge from seizure activity or MRI findings, reinforcing the independent clinical value of neuropsychological monitoring. In sum, neuropsychology in epilepsy has entered a new era characterized by an aging patient base, changing etiologies, and a greater demand for individualized, scalable, longitudinal, and dynamic approaches to assessment. Emerging technologies and international collaborations such as EpiCare are paving the way for this transformation. However, adapting effectively to these changes will require not only new tools but also a broader reconceptualization of how we evaluate and understand cognitive function in the diverse spectrum of epilepsy.

4. How does the new ASM treatment of adults with DEEs influence Non-Seizure Outcomes?

4.1. *Adam Strzelczyk*

Developmental and epileptic encephalopathies (DEEs) represent a complex group of severe epilepsies that begin early in life, typically associated with developmental delays, intellectual disability, refractory seizures, and emotional and behavioral difficulties. While antiseizure medications (ASMs) remain the cornerstone of treatment, seizure freedom is rarely achieved, especially in adults with long-standing DEEs such as Lennox-Gastaut syndrome (LGS). As individuals age, comorbidities become more prominent, and the influence of ASMs on non-seizure outcomes grows increasingly relevant. The burden of illness on patients and their caregivers far exceeds that observed in patients with refractory focal epilepsies or those in seizure remission [23,24]. In addition, caregiver stress, sleep disruption, and emotional distress are markedly higher, reflecting the continuous and intensive care needs required for individuals with DEEs [24–27].

With the introduction of novel ASMs and a better understanding of disease trajectories, attention has shifted toward broader outcomes beyond seizures including cognitive, behavioral, psychiatric, sleep, and caregiver-related impacts. This manuscript explores how the recently introduced ASMs, such as cannabidiol (CBD), fenfluramine (FFA) and cenobamate (CNB) influence these non-seizure outcomes in adults with DEEs. Treatment of adults might be challenging as they frequently exhibit worsening behavioral disturbances, reduced mobility, and increasing dependency, while ASMs may lose efficacy, tolerability diminishes with age, and side effects can compound existing deficits [1,28].

CBD was recently approved as an adjunctive therapy for seizures associated with DS, LGS—in combination with clobazam (CLB) in the EU—and tuberous sclerosis complex (TSC). CBD exerts its effects through multiple mechanisms, including modulation of intracellular calcium via G protein-coupled receptor 55 (GPR55), regulation of extracellular calcium influx through transient receptor potential vanilloid type 1 (TRPV1) channels, and inhibition of adenosine cellular uptake. While CBD is generally well tolerated, gastrointestinal symptoms and sedation are among the most common adverse events. Sedation is particularly frequent in patients also receiving CLB due to a pharmacokinetic interaction that increases norclobazam plasma levels; therefore, CLB dose reductions are advised if somnolence occurs. Beyond seizure control, emerging evidence suggests that CBD may contribute to improvements or stabilization in non-seizure outcomes such as sleep, cognition, and behavior. In particular, recent real-world studies have underscored the potential of CBD to positively impact quality of life domains. The BECOME study showed that caregivers observed meaningful gains in sleep quality, alertness, and overall responsiveness in adults with DEEs receiving CBD [29], while a recent real-world analysis highlighted reductions in caregiver-reported behavioral disturbances

and overall impact on disease burden [30].

FFA is approved in both the EU and US as an adjunctive treatment for seizures associated with LGS and DS. Its mechanism of action includes agonistic activity at multiple serotonin receptors and positive modulation of sigma-1 receptors. This dual action is thought to restore the disrupted balance between inhibitory GABAergic and excitatory glutamatergic signaling, contributing to its antiseizure efficacy. FFA has been shown to be generally well tolerated, though echocardiographic monitoring is required prior to initiation and at regular intervals—every 6 months for the first two years, followed by annual assessments—to ensure cardiac safety. Beyond seizure control, recent studies have highlighted potential benefits on non-seizure outcomes, particularly in cognition and executive functioning. Long-term observational data suggest that patients receiving FFA may exhibit improvements in attention, alertness, and daily functioning, especially in the context of DS [31,32]. In addition, caregiver-reported outcomes and neuropsychological assessments have shown positive changes in behavioral regulation and social engagement, suggesting that FFA may impact domains essential for quality of life [33,34], while sleep appears to remain largely unaffected by FFA [32].

Although CNB is currently licensed for the treatment of focal-onset seizures in adults, emerging data suggest potential benefits for the treatment of DEEs. A recent real-world analysis of CNB in 41 children and adults showed that CNB may offer meaningful seizure reduction and favorable tolerability, especially in those with LGS or TSC, where its use appears particularly promising and merits broader clinical consideration [35]. However, evidence in DS remains limited and controversial, with concerns regarding safety and inconsistent efficacy outcomes reported in early observations [36,37]. Further targeted studies are warranted to delineate cenobamate's role across the DEE spectrum, while data from adult patients with focal epilepsy shows a good tolerability and safety profile, especially regarding mood and cognition [38,39].

Current evidence for CBD, FFA and CNB suggests that all three ASMs may offer broader clinical benefits beyond seizure reduction, especially in adults, the goal of ASM therapy must encompass optimization of daily function, reduction in caregiver burden, and mitigation of behavioral disruptions.

5. Towards precision medicine in developmental and epileptic encephalopathies and refractory epilepsy

5.1. Cecilie Johannessen Landmark

During the last years numerous new antiseizure medications (ASMs) have been developed and went through clinical studies for approval. It has been a shift towards focus on drugs with orphan indications to be used in rare and severe developmental and epileptic encephalopathies (DEEs). Various strategies have been employed for the development of new ASMs and approaches towards precision drugs [40–42]. By phenotypic screening of newly synthesied drugs, diverse mechanisms of action have been revealed and tested as broad-spectrum antiseizure medications (ASMs). An example is cenobamate with effects both on voltage-gated sodium channels and $GABA_A$-receptors [41,43]. Structural modification of existing drugs is another strategy to develop drugs with more specific mechanisms of action e.g. bexicaserin from fenfluramin [40]. With a target-based design towards one mechanism of action both new and well known targets are in focus, e.g. soticlestat as a cholesterol-24-hydroxylase inhibitor to decrease excitability or XEN-1101 (azetukalner), a new generation of potassium channel openers following retigabine [40,44,45]. Repurposing of existing drugs has become more useful and rational in drug development, such as fenfluramine as a serotonergic but effective treatment in Dravet syndrome [41,46]. Furthermore, everolimus is considered a precision drug as a specific mTOR inhibitor with potentially antiepileptogenic and immune modulationg properties used in epilepsy related to tuberous sclerosis complex, recently evaluated in a clinical setting [47]. Finally, herbal remedy based development such as cannabidiol is an example where a drug with pure cannabidiol has been approved and used for a few years in Dravet and Lennox Gastaut syndrome and tuberous sclerosis complex [41,48,49]. These strategies have mainly been focused on severe and rare epilepsies like developmental and epileptic encephalopathies (DEEs). Dravet syndrome is considered as a model disease where a known genetic deficiency is the cause in the large majority of patients, animal models have been developed, specific drugs tested, and fenfluramine was the first in a series of repurposed drugs with serotonergic action [42,46].

Clinical experience of efficacy and tolerability of everolimus in epilepsy related to tuberous sclerosis was recently evaluated in a study of Danish and Norwegian patients (n = 59), where about one third were responders (>50% seizure reduction), various treatment challenges as changes in comedications and interactions were identified, and almost all experienced adverse effects as stomatitis or infections [47](Cockerell et al 2023). In a new TDM-study with cannabidiol in 53 patients with Dravet or Lennox Gastaut syndrome, extensive pharmacokinetic variability was observed of cannabidiol itself and its active metabolite 7-OH-CBD. A potential of various interactions with concomitant drugs, where the most pronounced was with clobazam was quantified [49]. More data on clinical experience in a real-world setting is awaited. Fenfluramine was effective (>50% seizure reduction in convulsive seizures in > 70% of patients with Dravet syndrome in a Danish cohort with follow-up time of up to six years. The number of concomitant drugs as stiripentol could be tapered, and hospital or specialist meetings were significantly reduced [50]. Cenobamate is used as add-on treatment in focal seizures but has shown to be specifically effective in subgroups of patients with genetic epilepsies, as four patients with Dravet syndrome in Germany, and in 12 patients with SCN8A-mutations in Denmark [51,52].

Other new ASMs in the pipeline include bexicaserin, a superagonist to 5-HT2a-receptors similar to fenfluramin, the new potassium channel opener XEN1101 or azetukalner [44], perhaps soticlestat, and the mRNA-based (antisense oligonucleotide, ASO) therapy STK-001, which is currently undergoing clinical trials [40]. Thus, new ASMs are directed towards precision treatment of the most severe and genetic epilepsies. New drugs also give rise to new challenges when it comes to pharmacological properties, pharmacokinetics and drug interactions. By the use of the precision-TDM concept, tailored therapy may be offered by following the individual serum concentrations of the drugs in use, active metabolites, and biochemical markers of toxicity [49,53]. The levels of precision medicine for most drugs are still aiming at lower levels where we have evidence of efficacy in epilepsies with specific seizure types or genetic mutations. Future directions will lead towards precision and disease-modifying effects by e.g. ASO or gene therapy.

6. Positive effects of ASM withdrawal in adults and children with epilepsy

6.1. Morten Lossius

Among epilepsy patients who have been free of seizures for some time, determining who should stop taking anti-seizure medication (ASM) and when, is challenging. There are very few solid studies in epileptology that can be used to guide clinicians in deciding to whom, and at what point, discontinuation of ASM use should be recommended. Instead, a proper understanding of an individual patient's epilepsy is necessary, and advantages and disadvantages must be carefully weighed.

Two randomized controlled studies (RCTs) on ASM withdrawal in patients with epilepsy have been conducted [54,55], one of which was double blinded [55]. In both studies, the risk of relapse was doubled in the withdrawal group. A *meta*-analysis of ASM withdrawal studies including 7082 patients showed a cumulative seizure recurrence rate of 34% within 3–4 years after withdrawal [56].

Patients' fear of long-term negative effects or unpleasant side effects

are the main reasons for stopping ASM. According to Perucca et al. [57] around 90% of patients who use ASMs experience at least one side effect. In addition, many patients believe that regular taking of medications sustains their patient role; many patients feel cured or free from epilepsy once ASMs are no longer needed [58].

Cognitive functions may be negatively impacted by both new and old ASMs [59]. These adverse cognitive and behavioral side effects associated with ASM are among those that are least tolerated [60]. As dosage and number of ASMs increase, the likelihood of negative cognitive side effects rises [61–64]. Chronic ASM exposure at important phases of brain development can have a deleterious impact on academic achievement and side effects of ASM treatment in children may disrupt normal brain development [65–67].

Some side effects may be reversible after discontinuation. Significant exceptions include adverse effects that impact the cognitive development of children with epilepsy and potentially irreversible outcomes following *in utero* exposure [65].

In two trials, ASM decrease or withdrawal in children after successful epilepsy surgery was linked to IQ improvement [68,69]. In addition, a lower dosage of ASM can enhance executive functions and improve IQ test results in children after epilepsy surgery [68]. A study on cognitive outcomes more than 5 years after temporal lobe epilepsy surgery by Helmstaedter and co– workers also indicate that ASM can have a suppressive effect on cognition and lowering dose alone can have positive effects in adults [70].

In a double-blind RCT in adults, the authors reported significant improvements in cognition, especially in psychomotor tempo, in patients who were randomized to ASM withdrawal [55]. Significant positive change was also found in heart rate variability, lipid profiles, thyroid function, and sex-hormones were also found in the withdrawal group [71–74].

The postoperative ASM tapering policy after successful epilepsy surgery has been modified over time. This issue was addressed in a global electronic survey of 446 doctors (pediatricians and neurologists) in 53 countries [75]. The authors reported that pediatricians discontinued ASM treatment after a shorter seizure-free interval (1 year or less) following temporal lobe resection than neurologists treating adults.

The decision to stop ASM treatment in epilepsy patients who are seizure free should be made on an individual basis, taking into consideration the patient's epilepsy, the drug's tolerability, and their personal preferences. This question should be addressed when adults have been seizure-free for two to five years, and earlier in children, but for both children and adults should be considered following successful epilepsy surgery, with a thorough risk–benefit analysis being conducted before the decision is made.

7. Cognitive and behavioral long term consequences of epilepsy surgery

7.1. Eli B. Kyte

Epilepsy surgery has proved efficient in alleviating seizures among patients with treatment refractory epilepsy. Seizure reduction or cessation is the clinical goal of surgery, and pre surgery questions about “chance of success” are often answered with “chance of seizure freedom”. Patients, however, often hope for broader improvements in quality of life. Thus, knowledge of effects on cognition and behavior is important, including knowledge about long term consequences. Given their needs for adaptions in school and social settings to support development and the large societal and personal costs of not meeting such need, knowledge of long term effects of surgery in children are of utmost importance. Several studies have shown positive effects on intellectual development and social functioning after epilepsy surgery in childhood. Seizure free children have been found to improve in IQ scores in the years after surgery, particularly if anti seizure medication (ASM) can be discontinued. Further, behavior and psychosocial function has been found to improve if seizure freedom is achieved [69,76]. Research on long term effects of epilepsy surgery in adults has largely been limited to research on temporal lobe epilepsy patients. Knowledge about extratemporal epilepsies is still limited. Some studies have been done on frontal lobe surgery patients. As a rule, most of these patients show cognitive stability following surgery [77]. One study found improvement for most patients in psychiatric symptoms after surgery [78]. Of note, most studies have few included patients and relatively short follow-up periods (often as little as two years). Generally, the extratemporal epilepsies have lower likelihood of post surgery seizure freedom, and patients who do not become seizure free have poorer cognitive and behavioral outcomes [79].

Up until recently, about 80% of epilepsy surgeries were temporal lobe resections (TLR) [80]. Temporal lobe epilepsy (TLE) patients often have memory problems prior to surgery. One year follow-up studies typically show a further memory loss. 11 studies have measured long term cognitive outcomes [81]. Results have varied, but it is now generally agreed upon that with seizure freedom no further loss is expected in the following years, even when follow-up periods are ten years or more [70,82]. For some patients, particularly if ASMs can be reduced, a recovery of verbal memory may be seen. Regarding figural memory, age has been found to be a predictor for outcome, as younger age is associated with better outcomes [70]. Many patients hope for the effects of TLE surgery to go beyond seizure reduction/cessation, and enable them to start or maintain education and employment. They also hope for greater personal freedom, less loneliness and reduced feelings of being different from others [83]. For postoperative employment, seizure freedom and being employed prior to surgery have been found to be the best predictors [84]. However, our work shows that maintaining employment many years after surgery can be hard, particularly if patients struggle with memory [83]. It is known that the prevalence of anxiety and depression is increased among TLE patients, few studies have been done on long term post surgery effects on these measures. One study [85] found decreased levels of both in the long run, anxiety reduction depending on time since surgery and depression reduction depending on improved seizure control. An association has been found between lower levels of depression at long term follow-up and improved quality of life [86].

Long-term follow-up studies are difficult to conduct due to costs, logistic challenges and problems with tracking former patients. Often, patients are recruited from outpatient settings leading to a bias as the best functioning patients (those who are seizure and ASM free and no longer in need of medical follow-up) are not included. It is a future challenge to include this group. Currently, a long term population based follow-up study is being conducted at the National Centre for Epilepsy, Oslo University Hospital. We hope that our study will aid in providing new insights into the needs of present and former patients. Further, research is needed to explore long term consequences of other types of epilepsy surgery than TLR.

8. Social cognition and the effect of surgery

Petr Marusic.

Social cognition encompasses the mental processes involved in perceiving, interpreting, and responding to social stimuli [87]. It includes a range of functions, from basic abilities like recognizing emotions through facial expressions (facial emotion recognition) to complex behaviour such as being able to infer other people’s thoughts, feelings, and intentions (Theory of Mind, ToM) [88]. These processes are connected and their integration is crucial for effective interpersonal communication. In social environments, individuals rely on intact social cognition to lead harmonious lives and maintain a satisfactory quality of life [89]. The biological basis for these processes is viewed as a set of interconnected neural networks, with their main hubs situated in the temporal and frontal lobes – specifically amygdala, anterior insula and ventrolateral prefrontal cortex for facial emotion recognition, and

ventromedial prefrontal cortex with temporoparietal junction for ToM, and superior temporal sulcus and fusiform gyrus for both [90,91]. In people with epilepsy, social cognition deficits significantly influence QoL even when seizure freedom is achieved [89]. TLE patients show a high rate of pharmacoresistance and therefore are often referred as candidates of epilepsy surgery. Surgical removal of an epileptogenic tissue offers the potential for full remission or at least for significant seizure reduction. While seizure control is the primary goal, the effects of surgery on cognitive and psychosocial outcomes warrant closer examination. Standard neuropsychological domains, such as memory, executive function, and attention, are typically assessed one year after surgery. Our previous study extended this research to include assessments of ToM and facial emotion recognition before and 12 months after the surgery [92]. Neither significant improvements nor deterioration was found in social cognition at the group level, but several factors were related to poorer neuropsychological outcomes including longer epilepsy duration, earlier disease onset, and lower IQ [92]. To evaluate a potential long-term impact of temporal lobectomy we conducted a longitudinal follow-up study of the same patients for up to 15 years (11.6 ± 2.2 years) to examine long-term post-surgical changes in social cognition [93]. As in the previous study, we used Faux-pas test (FPT) to measure ToM, and Emotion recognition test (ERT) to measure facial emotion recognition. Our findings indicate that on a group level, ERT remained stable over time whereas FPT performance decreased gradually after surgery in a linear fashion. Overall later age of epilepsy onset predicted higher baseline performance, but also a faster rate of decline. Furthermore, higher FSIQ scores were associated with better baseline performance on both tests. Importantly, neither ERT nor FPT were significantly influenced by sex, epilepsy duration, side of epilepsy, or depressive symptoms at baseline or in terms of change in scores over time. The presence of both notable improvements and declines among individual patients suggests that the small sample size may have masked more subtle effects, rendering them statistically non-significant. Alternatively, it is possible that additional factors such as social integration or other unmeasured variables, may be influencing the outcomes.

9. Cognitive and behavioral effects of neurostimulation in Drug-Resistant epilepsy

Jukka Peltola.

Cognitive deficits are a major comorbidity in chronic epilepsies, affecting up to 70–80% of patients. The most commonly reported impairments involve attention, executive functions, and memory [94]. For patients with drug-resistant epilepsy (DRE), neurostimulation therapies—alongside resective surgery—aim to reduce or eliminate seizures by targeting specific brain regions. In Europe, vagus nerve stimulation (VNS) and deep brain stimulation (DBS) are approved for clinical use. In the United States, responsive neurostimulation (RNS) has also received FDA approval. Preliminary studies have also explored the potential of repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (tDCS), and external trigeminal nerve stimulation (eTNS). While interest in the cognitive effects of neurostimulation is growing, particularly for VNS, overall knowledge remains limited.

Vagus Nerve Stimulation (VNS).

The cognitive effects of VNS are believed to involve the vagus nerve's connection to the locus coeruleus, which regulates noradrenaline production. Research has primarily focused on memory, with more recent studies examining attention and executive functions. While short-term memory improvements have been observed, robust evidence for long-term cognitive benefits is still lacking. Meta-analyses and reviews conclude that current data are insufficient to establish a consensus. However, VNS does not appear to impair cognition, and some studies suggest it may enhance specific functions. [95]. For example, a recent Finnish study reported clinically meaningful improvements in attention and executive functioning over a two-year follow-up in patients with initially severe impairments [96].

Deep Brain Stimulation (DBS).

DBS targets the anterior nucleus of the thalamus in DRE treatment. As a more recently approved therapy, the literature on its cognitive effects is less extensive than for VNS. High-quality randomized controlled trials (RCTs) are scarce due to the complexity of patient populations and the invasive nature of the procedure. The SANTE study reported improvements in attention, executive function, and visual memory over seven years [97](Salanova et al, 2015), while a Norwegian RCT found no significant cognitive changes after one year [98]. Other non-RCT studies have shown mixed results, ranging from modest improvements in executive and language functions to no observable changes. Although some patients report subjective memory decline, objective assessments generally do not support this, and the consensus is that DBS does not negatively affect cognition [95].

Emerging research suggests that pre-treatment cognitive profiles—particularly executive functions—may predict DBS treatment outcomes. Another Finnish study indicated a potential link between baseline cognitive performance and therapeutic response, though further investigation is needed to confirm this relationship and understand the underlying mechanisms [99].

Other Neurostimulation Methods.

For less commonly used or experimental methods, cognitive data are limited. RNS studies generally report no significant cognitive changes, though one RCT suggested seizure focus–specific improvements [95] (Chan et al, 2018). Navigated transcranial magnetic stimulation (nTMS) is used clinically for language mapping, and one RCT found that rTMS may enhance inhibitory control and reaction time without impairing cognition. Studies on tDCS and eTNS have not demonstrated significant cognitive effects.

10. Conclusion

Current evidence suggests that neurostimulation therapies do not impair cognitive functioning and may offer a possibility for improvements in specific domains. However, subjective reports of cognitive decline—particularly in DBS—raise questions about the sensitivity of standard neuropsychological assessments and the influence of secondary factors. Future research should incorporate comprehensive cognitive evaluations within high-quality longitudinal designs, while also considering patients' subjective experiences and broader neurological and psychosocial variables that may shape cognitive outcomes [100].

11. Beyond seizures challenges in young adults with epilepsy without ID. Population- vs. Hospital-based data

Kristin Å. Alfstad.

Youth or young adulthood is a period in life characterized by many changes and may be particularly challenging for youth with epilepsy (YWE). The transition into adulthood and independence and the important relationship with peers may be influenced by both epilepsy and comorbid conditions. The idiopathic generalized epilepsies have in many cases debut during these years, as well as many psychiatric disorders [101,102]. Cognitive impairment has been noted even at seizure debut and the early course of epilepsy and deficits in executive function has been particularly studied in juvenile myoclonic epilepsy (JME) [103].. It has been discussed if this impairment may contribute to an unwanted social outcome. Psychopathology and social outcome was studied in a population-based cohort of JME and 1/3 was treated with antidepressants and 31% were unemployed although almost 90% had graduated from high school. An unfortunate social outcome was found in 3/4, among them unwanted pregnancies [104]. Risk taking behavior has also been linked to executive dysfunction and JME [105].

The comorbid conditions can be a result of common etiology where the underlying cause of epilepsy also gives rise to the comorbid disorder. There may also be common pathophysiological or genetic mechanisms and psychosocial consequences of epilepsy and seizures [106]. The

treatment with anti-seizure medication (ASM) can influence both psychiatric and cognitive function and having a psychiatric disorder can increase the risk of experiencing adverse events of ASMs [106]. ASMs with a negative impact on cognition can reduce the ability to complete education.

The prevalence of beyond seizure challenges differ according to the population studied and methodology. Hospital based cohorts often consist of a larger proportion of participants with refractory epilepsy and generally have higher prevalence rates of psychiatric comorbidity and cognitive challenges than population based studies. Seizure variables are of importance although several studies find psychopathology and unwanted social outcomes even when seizures are controlled [107,108].

Psychopathology may in some studies be defined by a pathological score on a patient reported outcome measure (PROM) and thus not fulfilling the criteria of a psychiatric diagnosis. Other studies use a clinical consultation that often include the use of validated questionnaires like the Beck Depression Inventory (BDI) or The Neurological Disorders Depression Inventory-Epilepsy (NDDI-E) which even has a version for Youth (NDDI-E-Y). A structured diagnostic interview is time consuming and is the basis of a psychiatric diagnosis. These different methodological approaches influence prevalence rates. In a study using the Strengths and Difficulties Questionnaire (SDQ) in a hospital based cohort of children and youth with epilepsy, a pathological score on the screening questionnaire was found in 46,5% of participants and a psychiatric diagnosis was confirmed in 93,6% in a following diagnostic interview [109]. Population based studies using health register data often combine an epilepsy diagnosis with a psychiatric diagnosis. In a cohort of over 7 mill. individuals the lifetime prevalence of a psychiatric diagnosis was 44% in people with epilepsy [110]. A Danish population based study examined psychiatric comorbidity in YWE who had epilepsy onset in childhood. By the age of 30 at least one psychiatric diagnosis was fund in 17, 0% of those with epilepsy compared to 11, 5% in healthy youth. A stronger association between epilepsy and psychiatric disorders was found with later onset of epilepsy [111].

Cognitive function influence outcome of epilepsy with debut in childhood and adolescence. Cognitive impairment increases the risk of a reduced educational level, unemployment, and social difficulties. A long-term community-based US study of young adults with childhood onset epilepsy found different social outcomes when comparing complicated and uncomplicated epilepsy and healthy sibling controls [112]. Complicated epilepsy was defined by an abnormal neurologic exam findings, an abnormal brain imaging or intellectual disability. A high risk of not completing high school, of unemployment, having no driver license and not living independently was found. Social outcome in those seizure free ≥ 5 years was comparable to healthy siblings, whereas those having uncomplicated epilepsy but were < 5 years seizure free had an intermediate outcome.

Comorbid conditions have a negative effect on health related quality of life (HRQOL). A study of 281 YWE recruited from a neurology outpatient, inpatient or epilepsy monitoring unit collected data on epilepsy characteristics and used several questionnaires to assess mood/anxiety, behavioral symptoms, adverse events of ASM, cognitive function and HRQOL [113]. The strongest predictive factor of worse HRQOL was found to be mental and behavioral problems.

Adolescence and early adulthood constitute formative years and comorbid conditions affect outcome and many aspects of life in YWE. Comprehensive care is resource demanding and the use of screening tools and PROMs can assist in detecting comorbidities [114,115]. Psychiatric, cognitive and other comorbidities must be addressed in addition to seizure outcome to improve quality of life for people with epilepsy.

12. Is depression in epilepsy dependent on aetiology?

Marco Mula.

The pathophysiological mechanisms contributing to the association between depression and epilepsy are complex and multifactorial, involving neurobiological, psychological, social, and pharmacological components. One crucial yet under-explored question is whether the aetiology of epilepsy plays a determinative role in the development of depression.

Depression is the most frequent psychiatric comorbidity in people with epilepsy, with prevalence estimates ranging from 20% to 55%, depending on diagnostic criteria and population studied [116]. It is notably more common in people with drug-resistant epilepsy, as shown in studies involving people undergoing epilepsy surgery evaluation.

However, the relationship between epilepsy and depression is not necessarily unidirectional, and depression seems to be associated with an increased risk of developing epilepsy, suggesting shared aetiological and pathophysiological mechanisms [117].

There is no doubt that temporal lobe epilepsy and dysfunction in brain networks involving mesolimbic structures play a role in depression, but other factors are also likely to contribute significantly to the association.

Antiseizure medications (ASMs), psychosocial stressors (e.g., stigma, social isolation, unemployment, and lack of autonomy), genetic and epigenetic factors (e.g., a personal or family history of depression), other conditions implicating neurotransmitter imbalance, inflammation, and neuroplasticity alterations, seizure burden, and treatment resistance [118].

The clinical presentation of psychiatric comorbidities has itself been a matter of debate. Patients with epilepsy can develop psychiatric disorders clinically identical to those of individuals without epilepsy, but it is also established that some develop psychiatric syndromes characterised by unusual features not adequately captured by classificatory systems such as DSM and ICD [119]. Psychiatric presentations can be atypical and sometimes challenging in people with intellectual disabilities [120], where the pattern of psychiatric side effects of antiepileptic drugs can also be different. This is further complicated by the fact that depression can also sometimes be experienced as a symptom occurring before or after a seizure (*peri*-ictal depression), and the pathophysiology of these symptoms is still unknown [121].

However, depression is not just reported in focal epilepsies and generalised epilepsy syndromes, such as juvenile myoclonic epilepsy, seem to have elevated risks of depression and anxiety [122], albeit potentially to a lesser extent than in temporal lobe epilepsy. One possible explanation lies in dysfunction within fronto-limbic-thalamic circuits. However, independent of the potential cause, the presence of depression has a substantial clinical value and represents an important prognostic indicator. People with psychiatric disorders are associated with reduced seizure control, poorer medication adherence, lower quality of life, and increased mortality, particularly due to suicide [118]. Still, depression as well as any psychiatric comorbidity increases the global burden of epilepsy from a public health perspective, with increased health costs. People with epilepsy and psychiatric disorders have high health resource utilisation, including increased emergency department admissions and outpatient visits [123].

13. Epilepsy and sleep disorder interactions: How does they influence cognition and prognosis in refractory epilepsy

Guido Rubboli.

Epileptic seizures and sleep are interconnected through a complex bidirectional relationship. Sleep, sleep deprivation, and sleep disorders can influence epilepsy by increasing the likelihood of seizures, while seizures—especially those occurring during sleep—along with medications and interictal epileptic activity, can fragment sleep and impair its restorative and neuroplastic functions. Seizures originating from various brain networks tend to follow specific daily patterns, with some types, predominantly occurring during sleep or shortly after waking [124]. These specific epilepsy syndromes, collectively called sleep-related epilepsies (SREs), often have a high incidence of comorbid sleep disorders,

which can negatively impact seizure control and overall quality of life [125,126].

Sleep plays an essential role in early development: a wealth of evidences demonstrate the importance of REM sleep for neuroplasticity and memory consolidation, while non-REM sleep supports declarative memory through processes like active system consolidation and synaptic homeostasis [127,128]. Studies show that interictal epileptic discharges (IEDs) and seizures are more frequent during drowsiness and non-REM sleep, where IEDs tend to be more diffuse, whereas during REM sleep, they become more localized. Nocturnal IED and seizures can impact sleep-dependent functions and daytime performance either directly or indirectly through sleep disruption. Indeed, sleep fragmentation often results in daytime drowsiness and impaired psychomotor skills. Additionally, the presence of nocturnal IEDs may directly affect cognitive processes, by interfering with the delicate oscillatory patterns essential for sleep-related plasticity processes associated with cognition. Typically, nocturnal seizures are regarded as less disabling than those occurring during the day, especially concerning driving and work activities. Similarly, IEDs during sleep are also considered less impactful and often do not warrant specific treatment. Nonetheless, some data suggest that addressing nocturnal epileptic activity may improve sleep-related complaints and cognitive functions. Conversely, unstable sleep patterns can exacerbate nocturnal epileptic activity, as seen in disorders with high sleep fragmentation, such as obstructive sleep apnea. Ideally, epilepsy patients with sleep issues should undergo polysomnography (PSG) that includes sleep architecture assessments, complete EEG monitoring for epilepsy, and video recording. In drug-refractory epilepsy patients, intracranial EEG registrations can demonstrate that unexplained significant sleep fragmentation might be related to IEDs that may not be visible on scalp EEG [129].

In individuals with developmental epileptic encephalopathies (DEE), comorbidities such as sleep disorders together with intellectual disability, attention deficits, and movement disorders further complicate their condition. In children with drug-resistant epilepsy and DEE, a reduction of REM sleep has been observed, potentially impacting neuronal development. Conversely, REM sleep has been found to suppress IEDs and seizures in certain epileptic syndromes such as self-limited epilepsy with centrotemporal spikes (SELECTS) and in other childhood conditions with extreme potentiation of epileptic discharges during sleep [130]. Although sleep disturbances and disrupted sleep architecture are common in DEE, contributing to decreased quality of life and possibly exacerbating cognitive impairments and regression independently from the effects of uncontrolled epileptic seizures, very few studies have addressed this issue.

In Dravet syndrome, sleep-related disorders – including difficulty falling asleep, sleep-wake transition disorders, breathing problems, oxygen desaturation, and increased heart rate—have been reported in up to 75% of children, underscoring the need for routine sleep evaluations and targeted interventions [131] Similarly, a recent study found that over 80% of individuals with *SCN8A*-related DEE experience sleep disturbances, particularly difficulties initiating or maintaining sleep and breathing abnormalities, which are more severe in those with persistent seizures. Polysomnographic recordings suggest that *SCN8A* variants might directly disrupt sleep networks, resulting in sleep instability, independently from the occurrence of sleep-related seizures [132].

Encephalopathy related to Status Epilepticus during Sleep (ESES), now included in the group of DEE with Spike Wave Activation during Sleep (DEE-SWAS) is a distinct condition characterized by a striking enhancement of epileptic discharges during non-REM sleep, whose appearance is associated with cognitive, behavioral, and motor disturbances, that can persist also after the resolution with age of the epileptic activity. Neurophysiological research indicates that epileptic spikes during sleep interfere with normal synaptic homeostasis – an essential process for brain development – by disrupting sleep slow-wave activity (SWA). This interference during critical developmental periods can impair cortical connectivity and neuroplasticity, contributing to the neuropsychological deficits typical of ESES [133].

Anti-seizure medications (ASMs) may also play a role in the relationships between epilepsy and sleep, with some drugs that have been shown to negatively affect sleep architecture, while others, such as corticosteroids, have been observed to improve sleep patterns in certain epileptic encephalopathies [134].

In conclusion, current evidences indicate that investigating sleep features should become part of the diagnostic work-up of drug-resistant epilepsies, either in childhood and adulthood. The effects of treating sleep disorders on epilepsy management are still largely unclear and warrant further studies, however since sleep disturbances can be treatable, improving sleep quality, particularly in the developmental age, holds promise for enhancing cognitive outcomes and seizure control.

14. Stigma in adults with refractory epilepsy without intellectual Disability: A Hidden burden

Reetta Kälviäinen.

While the clinical management of refractory epilepsy continues to evolve, the psychosocial dimensions—particularly stigma—remain inadequately addressed. This presentation focuses on a distinct yet often overlooked subgroup: adults with drug-resistant epilepsy who do not have intellectual disability. Despite preserved cognitive function, these individuals frequently experience stigma that impacts their quality of life, treatment adherence, and psychosocial well-being.

Historically, epilepsy has been associated with superstition, discrimination, and exclusion, with remnants of these attitudes persisting into the 21st century [135]. People with epilepsy continue to face various forms of social stigma, including infantilization, stereotyping, social isolation, employment discrimination, and microaggressions [136]. These challenges are compounded by misconceptions about the causes of epilepsy and the invisibility of the condition.

Drawing on recent qualitative interviews and validated stigma scales, this presentation explores how stigma in this population is shaped not only by seizure frequency and visibility but also by societal misconceptions and the invisibility of their cognitive intactness [136]. Unlike individuals with comorbid intellectual disability, this group often internalizes stigma more acutely, leading to concealment of diagnosis, social withdrawal, and underutilization of support services [137],

In recent Finnish socio-legal study based on only a few existing court cases, the problems faced by people with epilepsy in Finland seem to be similar to those faced by other groups of people with disabilities. According to a survey results from Finland, people with epilepsy experience inequalities in many different spheres of life, the most typical of which was healthcare [138].

Efforts to reduce stigma have included educational campaigns, advocacy, and the promotion of inclusive language and media representation. However, the lack of robust tools to measure stigma and the limited reach of current interventions suggest that progress remains superficial. The presentation emphasizes the need for systemic change through education, accessibility, inclusive employment practices, and the empowerment of individuals and communities affected by epilepsy [139]. There are also new emerging interventions, including psychoeducation, peer-led support, and clinician-mediated disclosure strategies [140,141].

This talk aimed to equip epileptologists with a deeper understanding of the nuanced stigma landscape in this population and to advocate for integrated care models that address both seizure control and psychosocial resilience.

15. Patients perspective, adherence and other challenges

Oliver Henning.

Adherence to drug treatment in epilepsy populations Adherence is defined as “the extent to which a person takes the medicines in accordance with what is prescribed by a health care provider” [142]. Non-

adherence is defined as any deviation from the recommendations regarding both timing and dosage of a prescribed regime [143]. Non-adherence to anti-seizure drug treatment can result in seizure relapse [144], status epilepticus [145,146], hospital admission [147], and increased healthcare costs [148,149]. Non-adherence is also suspected of being involved in SUDEP [150,151]. Studies have shown a considerable variation in estimates of poor adherence to treatment in epilepsy populations. A recent review reported non-adherence in 26–79% of patients [143]. Different study populations, different definitions of adherence, and different methods of measuring non-adherence may account for this wide variability. Measuring the degree of adherence is difficult. Recall bias can occur when patients are interviewed or when using questionnaires to measure adherence [151–153]. Objective measures include electronic medication-monitoring systems, which are expensive and impractical on a larger scale [154]. The medication possession ratio has also been utilized, i.e., the day's supply of medication delivered divided by the days from when it was dispensed to the end of the follow-up period [155]. Non-adherence may be unintentional — for example, the patient forgets to take a dose or accidentally takes an incorrect dosage. Moreover, there may be misunderstandings between the physician and patient regarding the agreed dosage or medication, as demonstrated in one of our previous studies [156]. Non-adherence may also be intentional; i.e. for various reasons the patient makes a conscious decision not to follow the agreed treatment plan. A changed dosing regimen may result in lower or higher serum concentrations of the drug. We performed two studies looking at intentional and unintentional non-adherence in two patient cohorts; in one study 40% of the participants were seizure-free, and in the other study all participants had refractory epilepsy. In the group with refractory epilepsy, about 22% admitted that they sometimes or often forgot to take their drugs as scheduled, while 19% reported that they intentionally did not follow the treatment plan agreed upon with their physician [157]. In the less refractory cohort, about 40% reported that they sometimes or often forgot to take their drugs as prescribed, and about 30% reported that they consciously chose not to follow the treatment plan [158]. Other studies have disclosed that depression [155,159], anxiety, hippocampal sclerosis [153], being young, using older anti-seizure drugs [160], having side effects, and polytherapy are all linked to not sticking with prescribed drug treatment. It's not clear whether this is done on purpose or not. In children with epilepsy, the caregiver's socioeconomic factors, especially their level of education, annual income, and marital status, had a significant impact on the outcome and adherence [161]. Factors associated with good adherence to drug treatment are refractory epilepsy [158,162], high socio-economic status, perceived adverse events [154], employment, "medication reminders" [152], learning disability, location of residence, use of newer drugs, use of brand vs. generic drugs [163], a comorbid chronic disease, having a driving license, and having had a seizure after a missed dose [164]. We found that feeling depressed, being male, having experienced stigmatization, and being young (< 36 years) were significantly associated with intentional non-adherence [157,158]. Identification of both satisfactory adherence and non-adherence is important and should be part of comprehensive epilepsy care. Better adherence to the treatment may reduce morbidity and mortality among the patients. A trusting relationship between doctor and patient is of great importance. Aids to improve adherence cover different factors; adequate financing and availability, education, prompting and reminders [152], a simplified drug dosing regimen [165], increased frequency of follow-up by both physicians or other health personnel, like an epilepsy nurse [166]. Finally, digital tools, some of them quite cheap and with broad usage like mobile medical apps, and some pricier and limited to selected groups like smart pill bottles or smart pill dispensers, will in the future play an increasing role to maintain adherence.

16. Needs-based epilepsy follow-up: Seizure Control, treatment Adherence, patient care and patient satisfaction

Eline Dahl-Hansen.

Epilepsy impacts between 0.5% and 1% of people globally and necessitates continuous, long-term follow-up to ensure effective disease control and treatment outcomes [167]. Regular contact with a specialist is regarded as a key component of high-quality epilepsy management [168]. Traditionally, such follow-up has been structured through fixed, pre-arranged appointments. However, many outpatient clinics face capacity limitations that hinder their ability to offer timely consultations to all patients. In many cases, individuals with stable epilepsy may not need regular appointments, making routine visits a potentially inefficient use of time and healthcare resources. Conversely, seizures and complications may develop between scheduled visits and escalate into emergencies.

To improve efficiency and tailor care to individual needs, we introduce a new follow-up model based on patient-reported data. This approach allows patients to complete the PRO-EPI, a digital patient-reported outcome measure (PROM), twice a year from home. Based on the patient's responses, further contact with healthcare professionals is initiated only when necessary. The model focuses on enhancing individualized care, encouraging active patient engagement, and allocating healthcare resources more precisely. Since its introduction in 2019, this needs-based system has been adopted by several Norwegian hospitals.

Comparable strategies have been explored in other countries, notably in Denmark, where PROM-based follow-up models were implemented for a variety of chronic conditions—including epilepsy—as early as 2015. Clinicians and patients alike reported high satisfaction levels, and the system was found to be both practical and effective in guiding outpatient care [169].

In line with this, a recent systematic review and *meta*-analysis evaluated the impact of electronic patient-reported outcome measures (ePROMs) for managing outpatient scheduling. The findings supported the integration of ePROMs into follow-up procedures, highlighting their feasibility and acceptability for triaging adult patients across various medical conditions [170].

In conclusion we suggest the use of a digitalized needs-based epilepsy follow-up outcome assessment and beyond seizure issues monitoring. The evaluation of the user satisfaction and experience with the digital needs-based questionnaire in comparison to traditional standard-of-care follow-up is work in progress at present at three hospitals in Norway.

CRediT authorship contribution statement

C. Helmstaedter: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Conceptualization. **KA. Alfstad:** Writing – review & editing, Writing – original draft, Conceptualization. **E. Dahl-Hansen:** Writing – review & editing, Writing – original draft, Conceptualization. **O. Henning:** Writing – review & editing, Writing – original draft, Conceptualization. **C.Johannessen Landmark:** . **R. Kälviäinen:** Writing – review & editing, Writing – original draft, Conceptualization. **EB. Kyte:** Writing – review & editing, Writing – original draft, Conceptualization. **P. Marusic:** Writing – review & editing, Writing – original draft, Conceptualization. **M. Mula:** Writing – review & editing, Writing – original draft. **S. Myren:** Writing – review & editing, Writing – original draft, Project administration, Conceptualization. **J. Peltola:** Writing – review & editing, Writing – original draft, Conceptualization. **G. Rubboli:** Writing – review & editing, Writing – original draft, Project administration, Conceptualization. **A. Strzelczyk:** Writing – review & editing, Writing – original draft, Conceptualization. **S. Jozwiak:** . **MI. Lossius:**

Writing – review & editing, Writing – original draft, Project administration, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Given his role as Editor-in-Chief, Marco Mula had no involvement in the peer review of this article and had no access to informaiton about it. Ful responsibility for the editorial process for this article was delegated to another journal editor.

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