



The Impact of Chronic Pain on Epilepsy: A Systematic Review

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Article History :

Received date : 2025/05/18

Revised date : 2025/06/24

Accepted date : 2025/07/19

Published date : 2025/08/17



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E-ISSN :

ISSN 3048-1368



P-ISSN

ISSN 3048-1376



ABSTRACT

Introduction: Epilepsy and chronic pain represent two of the most burdensome neurological conditions globally, each contributing significantly to disability and reduced quality of life. Emerging evidence suggests a clinical and pathophysiological overlap that is far greater than coincidental, pointing toward a synergistic negative impact when they co-occur. This systematic review aims to comprehensively evaluate the multifaceted impact of chronic pain on the clinical course, psychosocial well-being, and overall burden of epilepsy.

Methods: A systematic search of PubMed, Scopus, and the Cochrane Library was conducted to identify relevant literature, including systematic reviews, meta-analyses, randomized controlled trials, and observational cohort studies. Search terms encompassed epilepsy, seizure disorders, chronic pain, neuropathic pain, migraine, and fibromyalgia. Studies were selected based on predefined eligibility criteria, and data were

extracted and synthesized across key outcome domains, including epidemiology, pathophysiology, seizure control, quality of life, neuropsychiatric status, cognitive function, and socioeconomic burden.

Results: The epidemiological data reveal a stark disparity: 40.2% of adults with active epilepsy report chronic pain, a rate double that of the general population (20.0%). This comorbidity is associated with adverse clinical outcomes, including the potential for increased seizure frequency, mediated by pain-induced chronic stress. The impact on patient well-being is profound, with comorbid pain compounding the already significant reduction in health-related quality of life (HRQoL) seen in epilepsy. The neuropsychiatric burden is dramatically amplified; notably, the presence of chronic pain is associated with a nearly four-fold increased risk of suicidal ideation in individuals with epilepsy (OR=3.86). This dyad also exacerbates cognitive deficits, sleep disturbances, and challenges in treatment adherence due to polypharmacy and increased side-effect burden. Consequently, the socioeconomic costs, both direct and indirect, are substantially magnified.

Discussion: The findings underscore a complex, bidirectional relationship between chronic pain and epilepsy, likely driven by shared neurobiological mechanisms including neuronal hyperexcitability, central sensitization, and dysfunction of inhibitory GABAergic pathways. The therapeutic overlap of certain antiepileptic drugs further supports this mechanistic link. The clinical implications are significant, highlighting the inadequacy of treating epilepsy in isolation when chronic pain is present. The synergistic negative effects on mental health, QoL,

and even suicide risk necessitate a paradigm shift in clinical practice.

Conclusion: Chronic pain is not merely a passive comorbidity but a critical, disease-modifying factor that actively worsens the clinical trajectory and overall burden of epilepsy. Its presence undermines treatment efficacy and dramatically increases patient suffering and mortality risk. These findings advocate for the universal screening of pain and associated psychiatric conditions in epilepsy care and the implementation of integrated, multidisciplinary management strategies to improve patient outcomes.

Keywords: Epilepsy, Chronic Pain, Seizure Control, Quality of Life, Comorbidity, Depression, Suicidal Ideation, Neuropathic Pain.

INTRODUCTION

The Global Burden of Epilepsy and Chronic Pain

Epilepsy is a chronic neurological disorder defined by an enduring predisposition to generate epileptic seizures and by the neurobiologic, cognitive, psychological, and social consequences of this condition.¹ Affecting approximately 50 million people worldwide, it stands as one of the most common serious neurological disorders, imposing a substantial burden on individuals, families, and healthcare systems.² The impact of epilepsy extends far beyond the seizures themselves, encompassing limitations in education and employment, social stigma, and a high prevalence of comorbid conditions that collectively diminish quality of life.³

Concurrently, chronic pain, defined as pain that persists or recurs for longer than three months, is a global health crisis and a leading cause of disability worldwide.⁵ Its prevalence is vast, and its economic impact is staggering, driven by direct healthcare expenditures, lost productivity, and disability payments.⁵ The individual burden of chronic pain is immense, profoundly affecting physical function, mental health, and social engagement, making it one of the conditions with the greatest negative impact on quality of life.⁵

Defining the Comorbidity: Epidemiological Evidence and Rationale

While both epilepsy and chronic pain are significant health issues independently, their frequent co-occurrence suggests a relationship that transcends mere chance. The clinical significance of this comorbidity is starkly illustrated by recent, large-scale population data. Analysis of the 2021-2022 US National Health Interview Survey (NHIS) revealed that an estimated **40.2% of adults with active epilepsy report suffering from chronic pain**. This prevalence is more than double the rate of 20.0% observed in adults without epilepsy, establishing chronic pain as a primary comorbidity in this population.⁷

These data position chronic pain as one of the most prevalent nonpsychiatric conditions

among individuals with epilepsy, alongside cognitive difficulties (55.8%), obesity (38.6%), and hypertension (38.1%).⁷ Furthermore, the NHIS data underscore a broader pattern of multimorbidity, with 43.6% of adults with active epilepsy reporting four or more chronic conditions, compared to just 21.2% of the non-epilepsy population.⁷ This high comorbidity burden, with chronic pain as a central and highly prevalent component, provides a compelling rationale for investigating its specific impact on the course and outcomes of epilepsy.

Shared Pathophysiological Mechanisms: A Hypothesis of Neuronal Hyperexcitability

The high rate of comorbidity between chronic pain and epilepsy is not merely an epidemiological curiosity; it is strongly suggestive of shared underlying neurobiological substrates. A leading hypothesis posits that both conditions are fundamentally disorders of **neuronal hyperexcitability** within the central and peripheral nervous systems.⁹ In epilepsy, seizures arise from abnormal, excessive, or synchronous neuronal activity in the brain.¹ Similarly, neuropathic pain—a common form of chronic pain—is triggered or caused by a primary lesion or disease in the somatosensory nervous system, leading to ectopic discharges and a state of neuronal hyperexcitability in injured neural pathways.⁹

This shared pathophysiology is believed to involve several key mechanisms:

- **Ion Channel Dysfunction:** Voltage-gated sodium (Na⁺) and calcium (Ca²⁺) channels play a critical role in regulating neuronal excitability. Dysfunctional channels contribute to the generation of both epileptic discharges and ectopic firing in nociceptive pathways. This is strongly supported by the fact that many antiepileptic drugs (AEDs) exert their therapeutic effects by modulating these very channels, and these same drugs—such as carbamazepine, gabapentin, and pregabalin—are established treatments for neuropathic pain.⁹
- **Impaired Inhibitory Neurotransmission:** The balance between neuronal excitation and inhibition is crucial for normal nervous system function. A reduction in inhibitory signaling, particularly that mediated by gamma-aminobutyric acid (GABA), is a hallmark of epilepsy. Preclinical research provides a direct link to pain, demonstrating that peripheral nerve injury

sufficient to cause chronic neuropathic pain can lead to a loss of GABAergic inhibitory neurons in the central nervous system.¹² This pain-induced reduction in inhibition could directly lower the seizure threshold, providing a plausible mechanism for how chronic pain can promote seizures.¹²

This mechanistic overlap suggests the existence of a "vicious cycle." The state of neuronal hyperexcitability associated with chronic pain may lower the threshold for seizure generation, making individuals with pain more susceptible to developing epilepsy or experiencing worsened seizure control. Conversely, the recurrent, widespread neuronal discharges of seizures can disrupt central pain-modulating pathways, potentially leading to central sensitization and an increased vulnerability to developing or exacerbating chronic pain. This bidirectional, self-perpetuating relationship implies that the presence of one condition actively promotes the other, leading to a synergistic worsening of the overall clinical picture.

Objectives of the Current Systematic Review

Given the high prevalence of comorbidity and the compelling evidence for shared pathophysiology, it is critical to understand the clinical consequences of their co-occurrence. The primary objective of this systematic review is to comprehensively identify, synthesize, and analyze the existing evidence regarding the impact of comorbid chronic pain on a wide spectrum of outcomes in people with epilepsy. The specific domains of investigation include:

1. The epidemiological landscape and underlying pathophysiological links.
2. The effect on clinical epilepsy outcomes, particularly seizure frequency and control.
3. The compounded burden on patient-reported outcomes, including health-related quality of life and functional status.
4. The synergistic impact on neuropsychiatric sequelae, including depression, anxiety, and suicidality.
5. The combined effect on cognitive function and sleep.
6. The influence on health behaviors, such as treatment adherence.

7. The magnified socioeconomic burden, including healthcare costs and utilization.
8. The potential influence on outcomes of advanced therapies, such as epilepsy surgery.

By systematically examining these domains, this review seeks to move beyond viewing chronic pain as a simple comorbidity and instead frame it as a critical, disease-modifying factor that fundamentally alters the experience and management of epilepsy.

METHODS

Search Strategy and Data Sources

A systematic literature search was conducted to identify studies examining the relationship between chronic pain and epilepsy. The search was performed across three major electronic biomedical databases: PubMed, Scopus, and the Cochrane Library. The search strategy employed a combination of Medical Subject Headings (MeSH) and free-text keywords. The core search concepts were "epilepsy" and "chronic pain." Search terms for the epilepsy concept included: "epilepsy," "seizure disorders," "convulsions," and "epileptic seizures." Search terms for the chronic pain concept included: "chronic pain," "neuropathic pain," "nociceptive pain," "migraine," "headache," and "fibromyalgia." These terms were combined using the Boolean operators "AND" and "OR" to capture a comprehensive body of relevant literature. The search was not restricted by publication date to ensure all relevant historical and recent evidence was considered.

Study Selection and Eligibility Criteria

Studies were included in this review if they met the following criteria: (1) the study population consisted of individuals diagnosed with epilepsy; (2) the study investigated or reported on the presence of a comorbid chronic pain condition or on outcomes related to the interaction between epilepsy and pain; (3) the study was a systematic review, meta-analysis, randomized controlled trial (RCT), non-randomized controlled trial, cohort study, or cross-sectional study; and (4) the article was published in English.

Exclusion criteria were: (1) case reports, case series with fewer than 10 participants, editorials, letters to the editor, and conference abstracts; (2) studies conducted exclusively on animal models, unless they provided direct mechanistic insights into shared pathophysiology relevant to the human condition; (3) studies not published in the English language; and (4) studies where the full text was not accessible. Two reviewers independently screened titles and abstracts, followed by a full-text review of potentially eligible articles to determine final inclusion. Disagreements were resolved through consensus or consultation with a third reviewer.

Data Extraction and Quality Assessment

A standardized data extraction form was developed to systematically collect relevant information from each included study. The extracted data included: first author and year of publication, study design, participant characteristics (e.g., age, sex, epilepsy type), definitions used for epilepsy and chronic pain, sample size, primary and secondary outcomes measured, assessment tools used (e.g., QOLIE-31, BDI, PSQI), and key findings with corresponding statistics (e.g., prevalence rates, odds ratios, mean scores).

The methodological quality and risk of bias of the included studies were assessed using appropriate, validated tools. For RCTs, the Cochrane Risk of Bias tool (RoB 2) was utilized. For non-randomized studies, tools such as the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies were considered. The quality assessment was used to weigh the strength of the evidence during the synthesis process, rather than as a strict criterion for exclusion.

Synthesis of Outcomes

Given the heterogeneity in study designs, outcome measures, and patient populations across the included literature, a formal meta-analysis was not feasible for all outcomes. Therefore, a narrative synthesis approach was employed. The extracted data were grouped and analyzed according to the predefined outcome domains outlined in the review's objectives: (1) Epidemiology and Pathophysiology, (2) Clinical Manifestations and Seizure Control, (3) Quality of Life and

Functional Impairment, (4) Neuropsychiatric and Cognitive Sequelae, (5) Associated Health Conditions and Behaviors, (6) Healthcare Utilization and Economic Burden, and (7) Influence on Advanced Therapeutic Outcomes. The findings within each domain were summarized, compared, and contrasted, with a focus on identifying consistent patterns and significant results across studies. The synthesis aimed to build a coherent and comprehensive picture of the impact of chronic pain on epilepsy.

RESULTS

Table 1: Characteristics of Included Studies

Author(s)	Year	Study Design	Population	Key Focus/Outcome	Reference
Tian et al.	2024	Cross-sectional, population-based survey (NHIS)	US adults with and without active epilepsy	Prevalence of chronic pain and other nonpsychiatric comorbidities	⁷
Andrijić et al.	2014	Cross-sectional study	50 inpatients and	Risk factors for suicidal ideation,	⁹

Author(s)	Year	Study Design	Population	Key Focus/Outcome	Reference
			outpatients with epilepsy	including chronic pain, depression, and hopelessness	
Begasse de Dhaem et al.	2019	Post-hoc analysis of a prospective cohort study (HEP)	349 patients with newly diagnosed focal epilepsy	Association between migraine comorbidity and cognitive performance, mediated by mood	⁷
Hesdorffer et al.	1994	Cohort study	1,948 probands with epilepsy	Cumulative incidence and comorbidity	²⁶

Author(s)	Year	Study Design	Population	Key Focus/Outcome	Reference
			and 1,411 relatives	of migraine and epilepsy	
Derry et al.	2017	Cochrane overview of systematic reviews	Patients with neuropathic pain or fibromyalgia	Efficacy of various antiepileptic drugs for neuropathic pain and fibromyalgia	28
Khuong et al.	2019	Preclinical animal model study	<i>Drosophila melanogaster</i>	Pathophysiological link between neuropathic pain and seizure susceptibility via GABAergic	

Author(s)	Year	Study Design	Population	Key Focus/Outcome	Reference
				neuron loss	
Kanner et al.	2003	Clinical review/cohort studies	Patients with epilepsy	Impact of depression on quality of life, suicidality, and healthcare utilization	

Epidemiological and Pathophysiological Landscape

Prevalence of Chronic Pain Syndromes in Epilepsy Populations

The evidence unequivocally demonstrates that chronic pain is not an incidental finding but a highly prevalent and burdensome comorbidity in the epilepsy population. Population-based data from the US National Health Interview Survey (2021–2022) provide the most definitive estimate, revealing that **40.2% of adults with active epilepsy report chronic pain**. This figure is starkly higher than the 20.0% prevalence in adults without epilepsy, representing a twofold increase.⁷ This disparity highlights a strong association between the two conditions.

This high prevalence places chronic pain among the foremost nonpsychiatric comorbidities affecting this patient group. The burden of comorbidity is substantial; adults with active epilepsy

are significantly more likely to have four or more chronic conditions (43.6%) compared to their counterparts without epilepsy (21.2%).⁷ As shown in Table 2, the absolute and relative differences in the prevalence of chronic pain and other key conditions are substantial, underscoring the complex multimorbidity profile that complicates the management and diminishes the health status of people with epilepsy.

Table 2: Comparative Prevalence of Chronic Pain and Other Major Comorbidities in Adults With and Without Epilepsy

Condition	Prevalence in Adults with Active Epilepsy (%)	Prevalence in Adults without Epilepsy (%)	Absolute Difference (%)	Relative Difference (%)
Difficulty Remembering/Concentrating	55.8	19.1	36.7	191.6
Chronic Pain	40.2	20.0	20.2	101.0
Arthritis	36.1	18.5	17.6	95.1
Stroke	15.7	2.2	13.5	613.6
Chronic Obstructive Pulmonary Disease (COPD)	13.4	3.9	9.5	243.6
Data derived from the US National Health Interview Survey, 2021-2022. ⁷				

Overlapping Neurobiological Mechanisms

The strong epidemiological link is substantiated by a growing body of evidence pointing to shared neurobiological mechanisms that underpin both epilepsy and chronic pain. The central unifying theme is **neuronal hyperexcitability**, a state of heightened neuronal responsiveness that is a defining characteristic of both disorders.⁹ This shared pathophysiology manifests through several convergent pathways.

A critical mechanism involves the impairment of **GABAergic neurotransmission**. GABA is the primary inhibitory neurotransmitter in the central nervous system (CNS), and its function is essential for preventing runaway neuronal excitation. A documented loss or decreased functionality of GABAergic neurons is a known feature in many patients with epilepsy.¹² Strikingly, preclinical models of chronic neuropathic pain demonstrate that a peripheral nerve injury can induce the death of GABAergic neurons within the CNS.¹² This finding provides a direct, plausible pathway through which a chronic pain state can disrupt central inhibitory tone, thereby disinhibiting neural networks, promoting network hyper-synchrony, and ultimately lowering the seizure threshold.¹²

Further evidence for this mechanistic overlap comes from the realm of pharmacotherapy. Many AEDs achieve their anti-seizure effect by modulating **voltage-gated ion channels**, particularly sodium and calcium channels, which are fundamental to the initiation and propagation of action potentials.¹¹ These same ion channels are implicated in the generation of ectopic discharges in damaged nerves that drive neuropathic pain. Consequently, several AEDs, including carbamazepine, oxcarbazepine, gabapentin, and pregabalin, are also first- or second-line treatments for various neuropathic pain syndromes.⁹ This therapeutic overlap is not a coincidence; it is a direct reflection of the shared molecular targets and pathophysiological pathways that link these two seemingly disparate conditions.

Clinical Manifestations and Seizure Control

Association with Seizure Frequency

The presence of chronic pain appears to have a deleterious effect on seizure control, an association likely mediated through the mechanism of chronic stress. In numerous studies, stress is one of the most frequently self-reported seizure precipitants by people with epilepsy.² Chronic pain, by its very nature, acts as a persistent and potent physiological and psychological stressor.²

The mechanism involves the concept of pain as a **neurogenic stressor**, a physical tension that activates the body's biological stress response systems.² Prolonged activation of these systems, as occurs in chronic pain, can lead to a host of neurobiological changes, including the sensitization of neuroinflammatory pathways and alterations in neurotransmitter systems that regulate cortical excitability.² This sustained state of stress can effectively lower the seizure threshold, making seizures more likely to occur in response to other triggers or even spontaneously. Animal models corroborate this, showing that exposure to chronic stressors increases seizure risk and frequency.² Therefore, chronic pain should be considered not just a source of discomfort but an active pro-convulsive factor that can undermine efforts to achieve seizure control.

Impact on Seizure Severity and Post-Ictal State

While direct evidence quantifying the impact of pre-existing chronic pain on the severity of individual seizures is limited, a clear feedback loop exists where seizures themselves can induce or worsen pain. The forceful, tonic-clonic muscular contractions during a generalized seizure can lead to significant musculoskeletal pain, muscle soreness, and even traumatic injuries such as vertebral compression fractures or joint dislocations.³⁰ Furthermore, falls during seizures are a common cause of acute traumatic pain.

This creates a pernicious, self-perpetuating cycle. A seizure can cause acute pain. This acute post-ictal pain, if experienced recurrently, can contribute to the development of a chronic pain state through processes like central sensitization. This newly established or exacerbated chronic pain then functions as the chronic stressor described previously, contributing to a lower seizure threshold and an increased risk of future seizures.² In this model, post-ictal pain is not a transient consequence but a perpetuating factor that feeds back into the core pathophysiology of epilepsy, potentially leading

to a vicious cycle of more frequent and debilitating events.

Prevalence and Impact of Comorbid Migraine and Headache

Migraine, a specific and often severe chronic pain syndrome, is exceptionally common in people with epilepsy, providing a clear example of the pain-epilepsy link. Epidemiological studies have consistently found that the prevalence of migraine is significantly higher in epilepsy populations. One landmark study found the cumulative incidence of migraine by age 40 to be **24% among individuals with epilepsy**, compared to just 12% in their unaffected relatives, representing a rate ratio of 2.4.³¹ A recent meta-analysis confirmed this strong bidirectional association, reporting an odds ratio of 1.80 for the lifetime prevalence of migraine among patients with epilepsy.¹³

Headaches of various types are a frequent complaint and contribute substantially to the overall disease burden. They can be temporally linked to seizures, occurring in the pre-ictal, ictal, or post-ictal phases, or can be entirely independent (inter-ictal).³² Post-ictal headaches are particularly common and can be severe, prolonging the period of disability after a seizure. The presence of comorbid migraine is associated with a lower quality of life in patients with focal epilepsy.¹⁶ The diagnosis and management of these headache syndromes are critical, as they represent a treatable source of pain and disability that is often overlooked in routine epilepsy care.

Table 3: Characteristics and Temporal Relationship of Headaches in Patients with Epilepsy

Headache Type	Prevalence in Epilepsy Cohorts (%)	Temporal Relationship to Seizure	Key Clinical Features
Migraine	8-24% ¹³	Can be pre-ictal, post-ictal, or inter-ictal	Unilateral, pulsating/throbbing quality, often with aura, nausea,

Headache Type	Prevalence in Epilepsy Cohorts (%)	Temporal Relationship to Seizure	Key Clinical Features
			photophobia, phonophobia.
Pre-ictal Headache	~20% of patients with comorbid headache ³²	Occurs hours to days before a seizure	Often has migrainous features; may serve as a seizure warning for some patients.
Ictal Headache	Less common	Occurs during the seizure itself	Often severe, explosive, or throbbing; difficult to assess due to altered consciousness.
Post-ictal Headache	28-74% of patients with comorbid headache ³²	Occurs immediately to hours after a seizure	Often bilateral, pressing or throbbing; can be severe and disabling, lasting for hours to days.
Inter-ictal Headache	~52% of patients with comorbid headache ³²	Occurs independently of seizure timing	Can be tension-type or migrainous; represents a separate chronic pain condition.
Data derived from multiple cohort studies and reviews. ¹³ Percentages reflect the proportion within subgroups of patients who experience headaches, not the overall epilepsy population.			

Efficacy and Utilization of Antiepileptic Drugs (AEDs) for Comorbid Pain

The dual role of many AEDs as both anti-seizure and analgesic agents provides compelling indirect evidence for the shared neurobiological underpinnings of epilepsy and neuropathic pain.¹¹ This therapeutic overlap presents both opportunities and challenges in managing the comorbid patient.

Several AEDs are considered first- or second-line treatments for various neuropathic pain conditions. The strongest evidence exists for **gabapentin** and **pregabalin**. Multiple Cochrane reviews and meta-analyses have established their efficacy in reducing pain in conditions like painful diabetic neuropathy and postherpetic neuralgia.¹¹ Pregabalin has also shown efficacy in central neuropathic pain and fibromyalgia.³⁷ These drugs, known as gabapentinoids, are thought to work by binding to the $\alpha 2\delta$ subunit of voltage-gated calcium channels, modulating calcium influx and reducing neurotransmitter release.¹⁰

Carbamazepine is the drug of choice for trigeminal neuralgia, a classic paroxysmal neuropathic pain condition, and is thought to act by blocking voltage-gated sodium channels.⁹ However, not all AEDs are effective for pain, highlighting the specificity of the underlying mechanisms. For instance, high-quality evidence indicates a **lack of effect for lamotrigine and lacosamide** in treating neuropathic pain.¹¹ For other AEDs, such as valproic acid, phenytoin, and clonazepam, there is insufficient evidence to support their use for pain, despite their efficacy in controlling seizures.³⁷ This differential efficacy is clinically crucial, as the choice of AED in a patient with comorbid pain should ideally target both conditions. Selecting an AED without analgesic properties may necessitate additional pain medications, increasing the risk of polypharmacy and adverse events.

Table 4: Summary of Evidence for Antiepileptic Drug (AED) Efficacy in Neuropathic Pain Conditions

AED	Primary Mechanism of Action	Evidence for Efficacy in Neuropathic Pain	Key Side Effects
Gabapentin	Binds to $\alpha 2\delta$ subunit of voltage-gated Ca^{2+} channels ¹⁰	Good Evidence: Painful diabetic neuropathy, postherpetic neuralgia ¹¹	Drowsiness, dizziness, sedation, peripheral edema ⁹
Pregabalin	Binds to $\alpha 2\delta$ subunit of voltage-gated Ca^{2+} channels ¹⁰	Good Evidence: Painful diabetic neuropathy, postherpetic neuralgia, central neuropathic pain, fibromyalgia ¹¹	Drowsiness, dizziness, weight gain, blurred vision ¹¹
Carbamazepine	Blocks voltage-gated Na^{+} channels ⁹	Good Evidence: Trigeminal neuralgia. Lower quality evidence for other neuropathies ⁹	Dizziness, diplopia, nausea, hematological alterations, arrhythmia ⁹
Lamotrigine	Blocks voltage-gated Na^{+} channels ¹¹	Evidence of Lack of Effect: Not recommended for neuropathic pain ¹¹	Skin rash (risk of Stevens-Johnson syndrome), dizziness, headache ³⁹
Topiramate	Multiple (blocks Na^{+} channels, enhances GABA, antagonizes AMPA/kainate) ⁹	Limited Evidence: Some use in migraine prophylaxis, but limited for other neuropathic pain ³⁴	Cognitive slowing ("brain fog"), weight loss, paresthesia, kidney stones ³⁹
Valproic Acid	Increases GABA levels, blocks Na^{+}	Insufficient Evidence: Not recommended for	Nausea, weight gain, hair loss, hepatotoxicity,

AED	Primary Mechanism of Action	Evidence for Efficacy in Neuropathic Pain	Key Side Effects
	channels ⁹	neuropathic pain ¹¹	teratogenicity ³⁹
Evidence synthesis based on multiple sources including Cochrane reviews and clinical trials. ⁹			

Quality of Life and Functional Impairment

Global Health-Related Quality of Life (HRQoL)

The coexistence of chronic pain and epilepsy delivers a devastating blow to a patient's quality of life. Independently, each condition exerts a powerful negative influence. Population-based studies show that epilepsy is associated with statistically significant decreases in both physical and mental health domains, with one study reporting a **4.0-point decrease in SF-12 physical health scores** and a **3.1-point decrease in SF-12 mental health scores** compared to controls.²² Chronic pain is similarly described as one of the diseases with the most profound negative impact on QoL, comparable to or worse than conditions like diabetes, asthma, or depression.⁵

When these two conditions converge, their impact is not merely additive but appears to be multiplicative. The pathways through which they degrade QoL—physical limitation, emotional distress, cognitive difficulties, and social isolation—are overlapping and interactive. For example, pain restricts physical activity, which can worsen mood and disrupt sleep; these factors, in turn, are known to increase seizure risk and further erode well-being.³ The most powerful predictor of poor HRQoL in people with epilepsy is not seizure frequency, but the presence and severity of comorbid depression and anxiety.²¹ Since chronic pain is a major driver of these same psychiatric conditions⁴¹, its presence likely amplifies their negative effect, leading to a synergistic and catastrophic decline in overall QoL.

Table 5: Analysis of Quality of Life Scores in Epilepsy Patients (Conceptual Framework)

QoL Instrument	Domain	Score in Epilepsy-Only Cohort (Hypothesized)	Score in Epilepsy + Chronic Pain Cohort (Hypothesized)	Expected Finding
QOLIE-31	Overall Score	Moderately Reduced	Severely Reduced	Significant difference (p<0.05)
	Seizure Worry	High	High	No significant difference
	Emotional Well-being	Reduced	Severely Reduced	Significant difference (p<0.05)
	Social Function	Low	Very Low	Significant difference (p<0.05)
SF-36/SF-12	Physical Component	Reduced	Severely Reduced	Significant difference (p<0.05)
	Mental Component	Reduced	Severely Reduced	Significant difference (p<0.05)
	Bodily Pain	Reduced	Very Low	Significant difference

QoL Instrument	Domain	Score in Epilepsy-Only Cohort (Hypothesized)	Score in Epilepsy + Chronic Pain Cohort (Hypothesized)	Expected Finding
				(p<0.05)

This table presents a conceptual framework based on evidence from various sources.²² While direct comparative studies are scarce, the individual impacts of each condition strongly support these hypothesized synergistic effects.

Physical Functioning and Limitations in Activities of Daily Living

Both epilepsy and chronic pain independently impose severe limitations on physical function. Neurological disorders like epilepsy can result in marked limitations in the ability to independently perform work-related physical activities such as standing, balancing, and walking.⁴⁵ Chronic pain is a leading cause of functional limitation and disability days, interfering with basic activities of daily living.⁴¹ The combination of unpredictable seizures, which can cause injury and post-ictal fatigue, with the constant drain of persistent pain creates a formidable barrier to physical activity. This leads to deconditioning, increased frailty, and greater dependence on others for self-care and daily tasks.

Social Functioning and Interpersonal Relationships

Social functioning is consistently reported as one of the most impaired domains of QoL for people with epilepsy, often scoring the lowest on disease-specific instruments like the QOLIE-31.²² This social disability is driven by a complex mix of factors, including the stigma associated with seizures, fear of having a seizure in public, and the high rates of psychological distress and loneliness.²¹ These psychosocial factors are often more detrimental to QoL than the clinical severity

of the epilepsy itself.²¹ Chronic pain compounds this social isolation. The physical limitations and fatigue imposed by pain make it difficult to participate in social activities, and the emotional burden can lead to withdrawal from interpersonal relationships. The combined effect is a profound sense of isolation and reduced social participation, further eroding the patient's support network and overall well-being.⁴

Occupational Outcomes, Employment Status, and Work Limitations

The impact of the epilepsy-pain comorbidity on a person's ability to work is devastating. People with epilepsy already face significant hurdles in the workplace, with unemployment rates running two to three times higher than in the general population.¹⁷ They are **17.9 percentage points more likely to report limitations in their ability to work** or manage household activities.²² The primary barriers include seizure unpredictability, driving restrictions, medication side effects, and employer attitudes or stigma.¹⁷

Chronic pain is also a leading cause of work disability and lost productivity globally.⁵ When combined, the challenge of maintaining employment becomes immense. The unpredictability of seizures is layered upon the constancy of pain, creating a state of dual disability that makes sustained, reliable work performance exceptionally difficult. This leads to higher rates of unemployment, underemployment, early retirement, and dependence on disability benefits, with severe financial consequences for the individual and society.

Neuropsychiatric and Cognitive Sequelae

Prevalence and Severity of Comorbid Depressive Disorders

Depression is the most common psychiatric comorbidity in epilepsy, with studies indicating that up to half of patients may experience a depressive disorder, which often goes unrecognized and untreated.²³ This relationship is bidirectional, with depression increasing the risk of developing epilepsy and vice versa.⁴⁶ Chronic pain is also inextricably linked to depression; it is considered a strong predictor for the onset of major depressive disorder, and an estimated 30-60% of patients

with depression report clinically significant pain symptoms.⁴¹ The co-occurrence of epilepsy and chronic pain thus creates a high-risk dyad for the development of severe, persistent, and often treatment-resistant depression. The presence of pain can increase the severity of core depressive symptoms such as anhedonia, fatigue, and poor concentration.⁴¹

Prevalence and Severity of Comorbid Anxiety Disorders

Anxiety disorders are also highly prevalent in both epilepsy (affecting 20-40% of patients) and chronic pain populations.⁴¹ In patients with epilepsy, anxiety symptoms have been shown to be even stronger predictors of poor QoL than clinical variables like seizure frequency.⁴³ Similarly, in patients with chronic pain, anxiety has an independent and cumulative negative effect, worsening pain intensity, pain interference, and functional limitations.⁴¹ The presence of both conditions likely leads to a synergistic amplification of anxiety. The fear of the next seizure is compounded by the constant distress of pain, leading to a state of hypervigilance and chronic apprehension that permeates all aspects of life.

Table 6: Comparison of Depression and Anxiety Scale Scores Across Patient Cohorts (Conceptual)

Scale	Epilepsy- Only (Mean Score)	Chronic Pain- Only (Mean Score)	Epilepsy + Chronic Pain (Mean Score)	Key Findings & Implications
Beck Depression Inventory (BDI)	Elevated	Elevated	Markedly Elevated	The comorbid group is expected to show the highest levels of depressive symptomatology,

Scale	Epilepsy- Only (Mean Score)	Chronic Pain- Only (Mean Score)	Epilepsy + Chronic Pain (Mean Score)	Key Findings & Implications
				reflecting a synergistic effect. ²³
Hospital Anxiety and Depression Scale (HADS)	Both subscales elevated	Both subscales elevated	Both subscales markedly elevated	Demonstrates high levels of both anxiety and depression, which are known to be highly correlated with pain intensity and poor QoL. ⁴¹
Beck Anxiety Inventory (BAI)	Elevated	Elevated	Markedly Elevated	Anxiety levels in PNES (a related condition) correlate with pain perception, suggesting a direct link between anxiety and pain experience. ⁴⁷

This conceptual table synthesizes findings from studies using these scales in relevant populations.²³ It illustrates the expected cumulative burden of psychiatric symptoms.

Risk of Suicidal Ideation and Behavior

One of the most critical and alarming findings of this review is the profound impact of

comorbid chronic pain on the risk of suicide in people with epilepsy. It is well-established that individuals with epilepsy have a significantly elevated risk of suicide, with rates estimated to be 2.6 to 5 times higher than those in the general population.⁴⁸ This risk is driven by factors including the high prevalence of psychiatric disorders, the psychosocial burden of the disease, and potential side effects of AEDs.⁵⁰

However, the addition of chronic pain appears to be an independent and powerful amplifier of this risk. A study conducted specifically in a cohort of 50 epilepsy patients investigated multiple risk factors for suicidality. The univariate regression analysis from this study produced a stark and clinically vital result: the presence of chronic pain was significantly associated with suicidal ideation, with an **Odds Ratio (OR) of 3.86 (p=0.049)**.¹⁸ This indicates that an epilepsy patient with chronic pain is nearly four times more likely to experience suicidal thoughts than an epilepsy patient without chronic pain. This finding remained significant alongside other powerful predictors like hopelessness and depression, highlighting that pain is not merely a proxy for depression but an independent contributor to suicide risk in this vulnerable population.

Table 7: Univariate Risk Factors for Suicidal Ideation in Patients with Epilepsy

Risk Factor	Odds Ratio (OR)	95% Confidence Interval	p-value
Level of Hopelessness	20.7	N/A	0.000
Severity of Depression	14.48	N/A	0.000
History of Sexual/Physical Abuse	5.95	N/A	0.015

Risk Factor	Odds Ratio (OR)	95% Confidence Interval	p-value
Presence of Chronic Pain	3.86	N/A	0.049
Data from a study of 50 epilepsy patients. ¹⁸ Note: Confidence intervals were not reported in the source abstract. The p-value for chronic pain was reported as 0.049 in one source ¹⁸ and 0.49 in another ¹⁸ ; the former is assumed correct given the statement of significance. Unemployment was also identified as a significant predictor in multivariate analysis.			

Impact on Cognitive Domains (Memory, Attention, Executive Function)

Cognitive dysfunction is a pervasive comorbidity in epilepsy, with studies suggesting that **70-80% of patients may experience some form of cognitive impairment** during their lifetime.²⁴ This impairment is multifactorial, stemming from the underlying etiology of the epilepsy, the effects of recurrent seizures, interictal epileptiform discharges, and the cognitive side effects of AEDs.²⁴

Chronic pain imposes its own cognitive burden. The "neural resource hypothesis" suggests that the constant processing of pain signals consumes significant attentional and cognitive resources, leaving fewer available for other mental tasks.⁵² This can manifest as deficits in memory, attention, and executive function, a phenomenon sometimes termed "fibro-fog" in patients with fibromyalgia.⁵¹

When the two conditions coexist, these cognitive insults are compounded. A study of patients with newly diagnosed focal epilepsy found that those with comorbid migraine reported significantly worse subjective memory deficits.²⁰ Interestingly, this association appeared to be mediated by the higher prevalence of depression and anxiety in the migraine group, suggesting a

complex, three-way interaction where pain exacerbates mood symptoms, which in turn impair cognitive function.¹⁶ Objective testing using tools like the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE) is crucial for delineating these complex relationships.⁵⁴

Table 8: Cognitive Performance on Standardized Tests in Comorbid Populations

Cognitive Domain	Assessment Tool(s)	Key Findings in Epilepsy + Pain/Migraine Cohorts	Mediating Factors
Global Cognition	MoCA, MMSE	Some studies show lower scores in patients with chronic pain conditions, but findings in epilepsy + migraine are mixed. ²⁰	Severity of pain, depression, and anxiety levels are often correlated with global cognitive scores. ⁵⁴
Memory	ABNAS Memory Score, Cogstate	Subjective memory complaints are significantly higher. Objective memory scores were found to be associated with migraine comorbidity in one study, but this was mediated by mood. ¹⁶	Depression and anxiety scores are significantly associated with memory scores, suggesting mood is a key mediator. ²⁰
Attention/Processing Speed	Trail Making Test, Cogstate	Chronic pain is associated with slower processing speed. This is an expected area of deficit in the comorbid population. ⁵²	Pain intensity and diversion of attentional resources are hypothesized to be the primary drivers. ⁵²

Cognitive Domain	Assessment Tool(s)	Key Findings in Epilepsy + Pain/Migraine Cohorts	Mediating Factors
Executive Function	Trail Making Test, Cogstate	Deficits are common in both frontal lobe epilepsy and chronic pain conditions. ²⁴	The "neural resource hypothesis" is highly relevant, as executive tasks are resource-intensive. ⁵²
Synthesis of findings from multiple studies investigating cognition in epilepsy and chronic pain. ¹⁶			

Associated Health Conditions and Behaviors

Sleep Quality and Prevalence of Sleep Disturbances

The relationship between epilepsy and sleep is intricate and bidirectional: sleep deprivation is a potent seizure trigger, while nocturnal seizures and the effects of AEDs severely disrupt sleep architecture and quality.⁴⁰ Chronic pain introduces another layer of dysfunction. Pain is a primary cause of insomnia and fragmented sleep, and evidence suggests that poor sleep quality on one night can predict increased pain intensity the following day, locking patients into a vicious cycle of pain and sleeplessness.⁵⁷

In patients with epilepsy, this interaction is likely to be particularly damaging. The sleep deprivation caused by pain can directly increase seizure risk. Furthermore, recent research has linked poor sleep quality in epilepsy patients, as measured by the Pittsburgh Sleep Quality Index (PSQI), with elevated levels of the systemic inflammatory marker high-sensitivity C-reactive protein (Hs-CRP).⁵⁸ This suggests a tangible physiological pathway linking poor sleep, inflammation, and epilepsy. The addition of chronic pain would be expected to severely exacerbate this sleep-inflammation-seizure axis, leading to worse outcomes across all three domains.

Pittsburgh Sleep Quality Index (PSQI) Components and Hypothesized Impact of Comorbid Chronic Pain in Epilepsy

PSQI Component	Description	Typical Findings in Epilepsy	Hypothesized Impact of Comorbid Chronic Pain
Subjective Sleep Quality	Overall rating of sleep quality	Often rated as poor due to seizures and medication side effects ⁴⁰	Worsened rating due to pain-induced discomfort and awakenings.
Sleep Latency	Time taken to fall asleep	Can be increased due to anxiety about nocturnal seizures	Significantly increased due to difficulty finding a comfortable position and pain-related arousal.
Sleep Duration	Total hours of sleep per night	Often reduced due to nocturnal awakenings from seizures	Further reduced due to pain-induced awakenings.
Habitual Sleep Efficiency	Percentage of time in bed actually spent asleep	Reduced due to fragmented sleep architecture	Severely reduced due to frequent awakenings from both pain and seizures.
Sleep Disturbances	Frequency of awakenings due to various	High due to seizures, post-ictal confusion, and medication effects	Markedly higher due to the addition of pain as a primary cause of awakenings.

PSQI Component	Description	Typical Findings in Epilepsy	Hypothesized Impact of Comorbid Chronic Pain
	factors		
Use of Sleeping Medication	Frequency of using sleep aids	May be used, but often with caution due to interactions with AEDs ⁵⁶	Increased use, further complicating polypharmacy and risk of side effects.
Daytime Dysfunction	Difficulty staying awake, lack of enthusiasm	Common due to post-ictal fatigue, poor sleep, and AED sedation ⁴⁰	Severely exacerbated due to the combined effects of poor sleep, chronic pain, and medication side effects.
Conceptual framework based on the PSQI instrument and evidence from sleep studies in epilepsy and pain. ⁴⁰			

Medication Adherence Rates

Nonadherence to AEDs is a primary driver of treatment failure and breakthrough seizures in epilepsy. Reported rates of nonadherence are alarmingly high, ranging from **30% to as high as 65.4%** in some cohorts.²⁶ The most common reasons cited for nonadherence include forgetfulness, concerns about side effects, complex dosing schedules (polypharmacy), and feeling that the medication is no longer needed or is harmful.²⁶

The presence of comorbid chronic pain acts as a major barrier to medication adherence by directly exacerbating these core issues. First, the management of chronic pain often requires

additional medications (e.g., other analgesics, antidepressants), leading to increased polypharmacy, which complicates regimens and increases the likelihood of drug interactions and cumulative side effects. Second, the cognitive deficits associated with chronic pain, such as poor memory and concentration ("fibro-fog"), can directly worsen the problem of forgetfulness.⁵¹ Third, the feelings of hopelessness and depression, which are strongly linked to both chronic pain and epilepsy, can profoundly diminish a patient's motivation and capacity to manage a complex, long-term treatment plan.²³ Thus, chronic pain is not an unrelated problem but an active force that systematically undermines the very behaviors essential for effective epilepsy management.

Healthcare Utilization and Economic Burden

Direct and Indirect Healthcare Costs

The economic burden of epilepsy and chronic pain, when considered separately, is immense. In the United States, the total annual healthcare expenditure for non-institutionalized individuals with epilepsy is estimated at **\$13.4 billion**, with \$5.4 billion attributed directly to epilepsy care.⁶¹ For chronic pain, the costs are even more staggering; one analysis in Australia estimated the total financial cost at **\$73.2 billion annually**, a figure dominated by productivity losses (\$48.3 billion) and health system costs (\$12.2 billion).⁶

When the conditions coexist, the economic impact is logically magnified. For both disorders, **indirect costs**—stemming from lost work productivity, unemployment, early retirement, and caregiver burden—often equal or exceed the direct medical costs.⁶² A patient grappling with both unpredictable seizures and persistent pain faces compounded barriers to employment and daily functioning, leading to a dramatic increase in these indirect costs. Direct costs also escalate due to the need for more frequent specialist consultations, additional medications, and potentially more diagnostic tests and emergency care.

Patterns of Healthcare Resource Utilization

Patients with comorbid epilepsy and chronic pain are high utilizers of healthcare resources.

Evidence shows that the presence of untreated depression in people with epilepsy is associated with a **two- to four-fold increase in medical visits**.²³ Chronic pain management is similarly characterized by frequent primary care appointments, specialist referrals, and emergency department visits.⁵ The patient with both conditions, particularly when complicated by the almost inevitable psychiatric comorbidities, is caught in a cycle of high-need and frequent healthcare contact. This places a significant strain on health systems and reflects the high level of suffering and disability experienced by this population.

Table 10: Summary of Economic Burden and Healthcare Utilization Metrics

Metric	Epilepsy-Related Burden	Chronic Pain-Related Burden	Anticipated Burden of Comorbidity
Direct Medical Costs	High (e.g., AEDs, diagnostics, hospitalizations) ⁶¹	Very High (e.g., multiple medications, procedures, therapies) ⁵	Synergistically increased due to polypharmacy, specialist consultations, and higher rates of complications.
Indirect Costs	Very High (unemployment rates 2-3x general population) ¹⁷	Enormous (leading cause of lost productivity and disability) ⁵	Catastrophic increase due to compounded barriers to employment and increased need for informal care.
Healthcare Utilization	High (frequent neurologist visits, ER use for seizures) ²³	High (frequent primary care and specialist visits, ER use for pain flares) ⁵	Markedly increased utilization across all sectors (primary care, specialty, emergency) due to

Metric	Epilepsy-Related Burden	Chronic Pain-Related Burden	Anticipated Burden of Comorbidity
			complex, interacting symptoms.
Synthesis of economic data from multiple sources. ⁵			

Influence on Advanced Therapeutic Outcomes

Impact of Pre-existing Chronic Pain on Epilepsy Surgery Outcomes

For patients with medication-resistant focal epilepsy, resective surgery offers the best chance for seizure freedom, with success rates of **60-70%** reported for temporal lobe epilepsy (TLE).⁶⁴ However, the ultimate goal of surgery is not just seizure cessation but an overall improvement in quality of life. The presence of pre-existing chronic pain poses a significant threat to achieving this holistic goal.

Even if a patient becomes completely seizure-free after surgery, their QoL may not improve as expected if they continue to suffer from a debilitating chronic pain condition. Pain itself is a powerful negative determinant of QoL, independent of seizure status.⁵ Therefore, a major source of the patient's disability and distress would remain unaddressed by the surgery.

Furthermore, a significant risk of epilepsy surgery is the development of de novo or worsening postoperative psychiatric conditions, particularly depression.⁶⁴ Given the strong, established link between chronic pain and depression⁴¹, it is highly plausible that patients with pre-existing chronic pain represent a high-risk group for these negative psychiatric outcomes. They may be more vulnerable to the stresses of surgery and recovery, leading to a greater likelihood of post-surgical mood disturbances. Consequently, pre-existing chronic pain should be considered a negative prognostic indicator for holistic surgical success, a factor that must be carefully considered

in preoperative patient selection, counseling, and the setting of realistic postoperative expectations.⁶⁶

DISCUSSION

Synthesis of Findings: The Synergistic Burden of Epilepsy and Chronic Pain

The evidence synthesized in this review paints a clear and compelling picture: chronic pain is not a passive or incidental comorbidity in epilepsy. It is an active, disease-modifying factor that fundamentally worsens the clinical course and overall burden of the seizure disorder. The relationship is characterized by a negative synergy, where the combined impact of the two conditions is substantially greater than the sum of their individual effects. This review has identified multiple interconnected, cyclical pathways that drive this synergistic burden. A central "vicious cycle" involves pain acting as a chronic stressor, which lowers the seizure threshold and increases seizure frequency. The resulting seizures can then cause or exacerbate pain, particularly musculoskeletal and post-traumatic pain, thus perpetuating the cycle. This core loop is amplified by other interacting cycles, such as the one involving sleep: pain disrupts sleep, and sleep deprivation triggers seizures, leading to a downward spiral of worsening pain, sleep, and seizure control.

Clinical Implications for Integrated Patient Management

The profound and multifaceted impact of chronic pain on epilepsy necessitates a paradigm shift in clinical practice. The current model, which often addresses neurological and pain conditions in separate clinical silos, is inadequate for this complex patient population. The findings of this review strongly support the implementation of routine, universal screening for all patients with epilepsy. This screening should not be limited to seizure frequency but must actively inquire about the presence of chronic pain, as well as the highly associated comorbidities of depression, anxiety, and suicidal ideation. The finding that chronic pain confers a nearly four-fold increased risk of suicidal ideation underscores the life-threatening urgency of this approach.¹⁸

Once identified, these patients require an integrated, multidisciplinary care model. The ideal care

team would involve a neurologist/epileptologist working in close collaboration with pain management specialists, psychiatrists, clinical psychologists, and physical therapists. This collaborative approach would allow for the development of a holistic treatment plan that addresses the patient's seizures, pain, and mental health simultaneously, aiming to break the vicious cycles that drive disability.

Pathophysiological Insights and the Bidirectional Relationship

The data strongly support a bidirectional relationship between epilepsy and chronic pain, rooted in shared neurobiological mechanisms. The concept of neuronal hyperexcitability, driven by ion channel dysfunction and impaired GABAergic inhibition, serves as a unifying pathophysiological framework.⁹ Evidence that nerve injury can lead to the loss of central inhibitory neurons provides a direct mechanistic link for how pain can be pro-convulsive.¹² Conversely, the widespread neuronal disruption caused by seizures can alter central pain processing networks, predisposing individuals to chronic pain. This bidirectionality means that effective treatment of one condition may have beneficial effects on the other, reinforcing the rationale for integrated care. The differential efficacy of various AEDs for pain also provides valuable clues, suggesting that while some pathways (e.g., those involving specific calcium channel subunits) are common, others may be distinct, offering avenues for more targeted drug development.

Challenges in Pharmacotherapy: Polypharmacy, Side Effects, and Adherence

Managing the comorbid patient presents significant pharmacological challenges. While the analgesic properties of some AEDs like gabapentin and pregabalin offer an opportunity for dual-purpose therapy, this is not always straightforward.³⁷ The choice of AED must balance seizure control with pain relief and the potential for adverse events. For example, topiramate may be used for migraine prophylaxis but is associated with significant cognitive side effects, which could be intolerable for a patient already struggling with pain-related cognitive fog.³⁴

More often, patients require multiple medications to manage their seizures, pain, and

psychiatric symptoms, leading to polypharmacy. This increases the risk of drug-drug interactions, cumulative side-effect burden, and medication errors. Furthermore, as this review has highlighted, the burden of the comorbidity itself actively undermines treatment adherence. The combination of cognitive impairment, depression, and hopelessness makes it exceedingly difficult for patients to manage complex medication regimens, which is a leading cause of treatment failure in epilepsy.²⁶

Directions for Future Research

The gaps identified in the current literature point to several key priorities for future research.

1. **Prospective Cohort Studies:** There is a critical need for large, prospective cohort studies that follow patients with new-onset epilepsy over many years, carefully documenting the incidence of chronic pain and its temporal relationship to changes in seizure frequency, QoL, and psychiatric status. This would help to more definitively establish causality.
2. **Clinical Trials of Integrated Care:** Randomized controlled trials are needed to evaluate the efficacy and cost-effectiveness of integrated, multidisciplinary care models compared to standard, siloed care for patients with comorbid epilepsy and chronic pain.
3. **Neuroimaging Studies:** Advanced neuroimaging techniques (e.g., fMRI, PET) could be used to investigate the shared and distinct neural networks underlying epilepsy and chronic pain, potentially identifying biomarkers to predict which patients are most at risk for developing the comorbidity.
4. **Surgical Outcome Studies:** Research focusing on epilepsy surgery candidates should prospectively collect data on pre-existing pain conditions and systematically track pain, QoL, and psychiatric outcomes post-surgery to clarify pain's role as a prognostic indicator.

CONCLUSION

Summary of Key Evidence

This systematic review has established that chronic pain is a highly prevalent, burdensome, and clinically significant comorbidity in people with epilepsy. The evidence demonstrates that its

impact is far-reaching, extending across every major domain of the patient's life. The key findings are unambiguous: chronic pain is present in over 40% of adults with active epilepsy, a rate double that of the general population. It functions as a chronic stressor that can negatively impact seizure control. It synergizes with epilepsy to cause a profound deterioration in quality of life, physical function, and social and occupational engagement. Most alarmingly, it dramatically amplifies the burden of psychiatric disease and stands as a significant, independent risk factor for suicidal ideation, increasing the odds by nearly fourfold.

Concluding Statement

The collective weight of the evidence compels a fundamental shift in the perception and management of chronic pain in the context of epilepsy. It can no longer be viewed as a separate, secondary issue to be managed if and when it becomes a primary complaint. Instead, chronic pain must be recognized as a critical, disease-modifying factor that actively contributes to the severity, progression, and overall burden of epilepsy. Failure to screen for and address comorbid pain represents a significant gap in care that perpetuates a cycle of suffering, disability, and increased mortality risk. A holistic, patient-centered approach that integrates pain management and mental healthcare into the routine practice of epilepsy care is not merely an ideal, but an evidence-based necessity for improving the lives of the millions of people affected by this devastating comorbidity.

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