

Epilepsy Centers  
of Excellence

DEPARTMENT OF VETERANS AFFAIRS

# THE CONSORTIUM CONNECTION

## ECoE Journal Highlights

## National VA Epilepsy Consortium Newsletter

### Articles Reviewed

- Effectiveness of AED combo therapy
- Epilepsy & TBI in OEF/OIF Vets Study
- Diagnosis of neuro-behavioral paroxysms in OEF/OIF Vets
- TBI and PNES in Vets
- Health Data Sharing Network Shows Improved Self-Management
- ECOE Study Protocol To Be Published
- Life after epilepsy surgery
- Patient Education
- Provider Education

### Effectiveness of antiepileptic drug combination therapy for partial onset seizures based on mechanisms of action

A health outcome research study that extracted recently diagnosed epilepsy patients taking an AED combination from a database of over 96 million Americans conducted by [Jose Enrique Cavazos, MD](#), PhD and colleagues has been published in [JAMA](#).

#### Abstract

**Importance:** The current study is the first to describe antiepileptic drug combination therapy patterns according to their mechanism of action in a real-world setting and to evaluate differences in outcomes comparing different mechanism of action combination therapy to same mechanism of action combination therapy for partial onset seizure patients.

**Objectives:** To compare treatment persistence and healthcare utilization with antiepileptic drug combinations categorized by mechanism of action in patients with partial onset seizures.

**Design:** Using the Truven Health MarketScan commercial claims database containing 94 million covered lives from 2005 through March 31, 2011, adults with concomitant use of two different antiepileptic drugs and a recent partial onset seizure diagnosis were selected. Antiepileptic drugs were categorized by mechanism of action: sodium channel blockers (SC), gamma-aminobutyric acid analogs (G), synaptic vesicle protein 2A binding (SV2), and multiple mechanisms (M). Patients were

assigned a combination category based on their concomitant antiepileptic drug use.

#### Main Outcome Measures:

Treatment persistence was measured from the start of antiepileptic drug combination therapy until the end of the combination. Healthcare resource utilization was measured during the combination treatment duration. Multivariate analyses evaluated antiepileptic drug discontinuation risk and healthcare utilization according to mechanism of action combinations.

**Findings:** Distribution of 8,615 selected patients by combination was 3.3% G+G, 7.5% G+SV2,

(continued on page 2)



U.S. Department  
of Veterans Affairs

### Prevalence of Epilepsy & TBI in OEF/OIF Vets Study Accepted for Publication

A study on the association of traumatic brain injury (TBI) and development of epilepsy in Veterans of Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) conducted by Mary Jo Pugh, PhD and colleagues has been accepted by *The Journal of Head Trauma Rehabilitation*. (Abstract follows.)

This is the first study to identify the risk of epilepsy in Veterans of OEF/OIF with TBI. "We can see not only is there an increased risk with more severe TBI including penetrating TBI but also for mild TBI," says Dr. Pugh. More studies of TBI in the OEF/OIF Veteran population are needed, according to Dr. Pugh. "Given that prior studies by Salinsky et al found that mild TBI and PTSD are associated with nonepileptic seizures, there is a lot of work that needs to be done to look at nonepileptic seizures in OEF/OIF population," says the lead author.

*The Journal of Head Trauma Rehabilitation*, the official journal of the Brain Injury Association of America (BIAA), is a peer-reviewed journal that provides information on clinical management and rehabilitation of persons with head injuries for the practicing professional. JHTR can be found online at [journals.lww.com/headtraumarehab](http://journals.lww.com/headtraumarehab).

#### Abstract

**The Prevalence of Epilepsy and Association with Traumatic Brain Injury in Veterans of the Afghanistan and Iraq Wars.** *Journal of Head Trauma Rehabilitation* (In Press).

**Objective:** Examine the association of epilepsy with traumatic brain injury in Afghanistan and Iraq (OEF/OIF) Veterans.

**Design:** Cross-sectional observational study.

**Participants:** 256,284 OEF/OIF Veterans who received inpatient and outpatient care in the Veterans Health Administration (VHA) in fiscal years 2009-2010.

**Main Outcome Measures:** The study used algorithms developed for use with ICD-9-CM codes to identify epilepsy, traumatic brain injury (TBI; penetrating TBI [pTBI]/other TBI) and other risk factors for epilepsy (e.g., stroke). TBI and other risk factors were identified prior to the index date (first date of seizure or October 1, 2009) for primary analyses.

**Results:** Epilepsy prevalence was 10.6 per thousand (N=2,719) in FY10; age-adjusted prevalence was 6.1. Of 37,718 individuals diagnosed with TBI, 29,297 Veterans were diagnosed with TBI prior to the index date. Statistically significant associations were found between epilepsy and prior TBI diagnosis (pTBI: adjusted odds ratio (AOR)

18.77 (95% CI 9.21-38.23); other TBI AOR 1.64 (1.43-1.89).

**Conclusions:** Among OEF/OIF Veterans, epilepsy was associated with previous TBI diagnosis, with pTBI having the strongest association. Because war-related epilepsy in Vietnam War Veterans with TBI continued 35 years postwar, a detailed, prospective study is needed to understand the relationship between epilepsy and TBI severity in OEF/OIF Veterans.

Mary Jo Pugh, Jean A. Orman, Carlos Jaramillo, Martin Salinsky, Blessen Eapen, Alan R. Towne, Megan E. Amuan, Shane D. McNamee, Thomas A. Kent, Katharine K. McMillan, Hamada Hamid, Gustavo Roman, Jordan H. Grafman.

## Effectiveness of antiepileptic drug combination therapy for partial onset seizures based on mechanisms of action (cont.)

8.6% G+M, 13.9% SC+SC, 19.0% G+SC, 21.5% SC+M, and 26.3% SC+SV2. Same mechanism of action (G+G and SC+SC) combinations had the shortest persistence (344±345 days; 513±530 days, respectively) and greater hazard of discontinuation compared to different mechanism of action combinations. Patients with different mechanism of action G combinations had significantly lower risk of inpatient admission (OR=0.716, p=0.021) compared to G+G combinations. Patients with different mechanism of action SC combinations had significantly lower risks of emergency room visits (OR=0.853, p=0.025) compared to SC+SC combinations.

**Conclusions:** Findings suggest antiepileptic drug combinations with different mechanisms of action have greater effectiveness as measured by treatment persistence, and lower risks of hospitalization and emergency visits. Further research is needed to more fully understand the role of the mechanism of action in achieving optimal outcomes.

JAMA Neurol. Published online June 09, 2014. doi:10.1001/jamaneurol.2014.808; Jay M. Margolis, PharmD1; Bong-Chul Chu, PhD2; Zhixiao J. Wang, PhD3; Ronda Copher, PhD4; Jose E. Cavazos, MD, PhD5,6

Dr. Cavazos and his colleagues have also collaborated on the following journal articles:

[“Validity of the Neurology Quality-of-Life \(Neuro-QoL\) measurement system in adult epilepsy”](#). *Epilepsy Behav.* 2014 Feb; 31:77-84. PMID: 24361767

The Neuro-QoL measurement initiative is an NINDS-funded system of patient-reported outcome measures for neurology clinical research, which was designed to provide a precise and standardized way to measure health related quality of life in epilepsy and other neurological disorders. In this study, empiric clinical validations in 121 adult patients with epilepsy were performed. The instrument is a freely available set of scales and is broader in scope than other

commercially available instruments such as QOLIE-31.

Victorson D, Cavazos JE, Holmes GL, Reder AT, Wojna V, Nowinski C, Miller D, Buono S, Mueller A, Moy C, Cella D.

[Responsive neurostimulation in epilepsy therapy: Some answers, lingering questions](#). *Epilepsy Behav.* 2014 May; 34:25-8. PMID: 24681381

An editorial and critical review of the RNS System (NeuroPace, Inc), a therapeutic medical device designed to sense focal electrographic seizures in selected brain regions and respond by delivering electrical stimulation to those regions aimed at terminating the seizures. The device was granted a pre-market approval by the FDA based on results of a randomized controlled trial. While the results showed that RNS System is clinically safe and effective, there are important questions about its use left unanswered. The study did not provide electrographic evidence that the device aborts seizures, which is the main

presumption underlying its operation and the basis for stimulation parameter adjustment. Also, the study did not provide dose-response data for efficacy or safety, or information about the most effective stimulation parameters. Choices for electrical stimulation parameters are important because a variety of neural responses can be evoked ranging from depolarization, long-term potentiation or depression, seizures, or cell death. RNS System data was reviewed and recommendations made aimed at expanding what is known of how the RNS device works, and at improving the FDA regulatory process of neurostimulation devices.

Lie OV, Cavazos JE.

[“Neurocysticercosis and Epilepsy”](#). *Epilepsy Curr.* 2014, Jan/Feb; 14(1 suppl):23-8.

A review of Neurocysticercosis and Epilepsy that was part of the annual course of the American Epilepsy Society.

Burneo JG, Cavazos JE.

## Diagnoses of neurobehavioral paroxysms in veterans of Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) – Experiences from A VA Epilepsy Center

### Abstract

**Summary:** We retrospectively reviewed the medical records of patients admitted for V-EEG monitoring at the Michael E. DeBakey VA Medical Center from January 2008 to May 2013. We identified a total of 78 OEF/OIF veterans admitted during this period. We excluded 14 patients who did not experience their typical habitual event of interest, which rendered them non-diagnostic. We also excluded 2 subjects who had mixed disorders of both epilepsy and psychogenic nonepileptic seizures (PNES). The remaining 63 subjects had V-EEG confirmed diagnosis of PNES (n=46), epileptic seizures (n=16) and physiologic nonepileptic seizures (n=1). In addition, we investigated V-EEG confirmed diagnosis in

subgroups with combat exposure and combat exposure + PTSD. We further investigated the positive predictive value, sensitivity and specificity of the following risk factors: psychiatrist confirmed PTSD, mild TBI (mTBI) acquired prior to the onset of the patient's habitual paroxysms, or the combination of both in predicting the diagnosis of PNES.

Among patients with a definitive diagnosis of PNES, 63% of the subjects had PTSD alone, 50% had mTBI alone, and 41.3% had a combination of both PTSD and mild TBI.

Among all patients with PTSD who received definitive V-EEG diagnoses, 90.6% had PNES. The sensitivity of PTSD in identifying patients with PNES

was 63%, while the specificity was 81.3%.

Among all patients with mild TBI who received definitive V-EEG diagnoses, 85.2% had PNES. The sensitivity of mild TBI in identifying patients with PNES was 50.0%, while the specificity was 75%.

Among all patients with both mild TBI and PTSD who received definitive V-EEG diagnoses, 90.5% had PNES. The sensitivity of having the combination of mTBI and PTSD in identifying patients with PNES was 41.3%, while the specificity was 87.5%. (ie. the highest specificity for PNES when a patient has both mild TBI and PTSD).

Shirish Satpute; Romay Franks; and, David K. Chen

## TBI and Psychogenic Seizures in Veterans

[Journal of Head Trauma Rehabilitation \(JHTR\)](#)

### Abstract

**Objective:** To evaluate a proposed seizure etiology of traumatic brain injury (TBI) as a risk factor for psychogenic nonepileptic seizures (PNES), the effect of reported TBI severity on the diagnosis of PNES vs. epileptic seizures (ES), and the potential moderating role of post-traumatic stress disorder (PTSD).

**Participants, Setting:** Veterans diagnosed with PNES or ES during inpatient epilepsy monitoring at the Portland Veterans Affairs Medical Center.

**Design:** Retrospective review of proposed seizure etiology, TBI severity, and PTSD diagnosis.

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## First Results Presented from Study of U.S. Veterans Using a Health Data Sharing Network Show Measurable Improvements in Epilepsy Self-Management

The U.S. Department of Veterans Affairs' Epilepsy Centers of Excellence (ECoE), biopharmaceutical company UCB, and health data sharing network PatientsLikeMe® presented the results of the Policy for Optimal Epilepsy Management (POEM) study at the 66th Annual Meeting of the American Academy of Neurology (AAN) in Philadelphia. This first-time, real-world study of an online health management platform demonstrated significant improvements in patient self-management and self-empowerment in U.S. Veterans who participated in the study, which used PatientsLikeMe®.

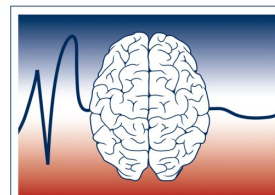
"The results of the POEM study reinforce the potential for an online data sharing network like PatientsLikeMe® to positively influence self-management and self-efficacy for Veterans with epilepsy. We're pleased to share these results with the scientific community at AAN and look forward to using what we've learned as a foundation for further research into how we can use digital health solutions to improve the care for the broader epilepsy community," said principal investigator and ECoE's John Hixson, M.D., Assistant Professor of Clinical Neurology and Deputy Associate Chief of Staff for

Clinical Informatics at the San Francisco VA Medical Center.

Epilepsy is a chronic neurological disorder affecting approximately 65 million people worldwide and more than 2 million people in the U.S. It is the fourth most common neurological disorder in the US after migraine, stroke and Alzheimer's disease. Anyone can develop epilepsy; it occurs across all ages, races and genders and is defined as two or more unprovoked seizures.

Read complete story [here](#).

## National VA Epilepsy Consortium Newsletter



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## ECOE Study Protocol To Be Published

*Implementation Science*, an open access peer-reviewed online journal, has accepted the study protocol describing research on the Epilepsy Centers of Excellence (ECOE) currently being conducted by Mary Jo Pugh, Ph.D., National Quality Assurance/ECOE.

"The importance of the study protocol is that it details methods that can be used to examine other kinds of care or epilepsy care in different

settings," says Dr. Pugh, adding, "These methods provide a means to systematically assess healthcare." The 4-year comparative case study, Restructuring Epilepsy Care: Organizational Dynamics and Quality: RECORD Quality (IIR-067-11-2), uses interviews, surveys, chart abstractions, and VA inpatient, outpatient, and pharmacy data to assess how the ECOE has affected epilepsy care.

"Implementation of the Epilepsy Center of Excellence to Improve Access to and Quality of Care—A Mixed Methods Study" will be posted online at [implementationscience.com](http://implementationscience.com).



Implementation  
Science

## Mood, anxiety, and incomplete seizure control affect quality of life after epilepsy surgery

### Abstract

**Objective:** We examined the complex relationship between depression, anxiety, and seizure control and quality of life (QOL) outcomes after epilepsy surgery.

**Methods:** Seven epilepsy centers enrolled 373 patients and completed a comprehensive diagnostic workup and psychiatric and follow-up QOL evaluation. Subjects were evaluated before surgery and then at 3, 6, 12, 24, 48, and 60 months after surgery. Standardized assessments included the Quality of Life in Epilepsy Inventory-89, Beck Depression Inventory (BDI), and Beck Anxiety Inventory (BAI). A mixed

-model repeated-measures analysis was used to analyze associations of depression, anxiety, seizure outcome, and seizure history with overall QOL score and QOL subscores (cognitive distress, physical health, mental health, epilepsy-targeted) prospectively.

**Results:** The groups with excellent and good seizure control showed a significant positive effect on the overall QOL compared to the groups with fair and poor seizure control. The BDI and BAI scores were both highly and negatively associated with overall QOL; increases in BDI and BAI scores were associated with decreased overall QOL score.

**Conclusions:** Depression and

anxiety are strongly and independently associated with worse QOL after epilepsy surgery. Interestingly, even partial seizure control, controlling for depression and anxiety levels, improved QOL. Management of mood and anxiety is a critical component to postsurgical care.

Hamada Hamid, Karen Blackmon, Xiangyu Cong, James Dziura, Lauren Y. Atlas, Barbara G. Vickrey, Anne T. Berg, Carl W. Bazil, John T. Langfitt, Thaddeus S. Walczak, Michael R. Sperling, Shlomo Shinnar, Orrin Devinsky

[Article | Neurology March 11, 2014 82:887-894; published ahead of print January 31, 2014.](#)

## TBI and Psychogenic Seizures in Veterans

Journal of Head Trauma Rehabilitation (JHTR) (cont.)

**Main outcomes and measures:** PNES and ES groups were compared for TBI history and severity, and prior diagnosis of PTSD.

**Results:** TBI was the proposed seizure etiology for 57% of 67 PNES patients vs. 35% of 54 ES patients ( $p < 0.05$ ). TBI was mild in 87% of PNES, and 37% of ES patients ( $p < 0.001$ ). PTSD increased the likelihood of diagnosing PNES vs. ES in Veterans with mild TBI as the proposed seizure etiology.

**Conclusions:** In Veterans with PNES, TBI was commonly cited as the cause for seizures. Mild TBI was strongly associated with PNES vs. ES. PTSD may moderate the development of PNES in Veterans with a history of mild TBI. These results may guide clinicians caring for Veterans with seizures to select patients for early diagnostic evaluation.

Martin Salinsky MD1,2, Daniel Storzbach PhD2, Elizabeth Goy PhD2, Collette Evrard FNP2

Portland Veterans Affairs Medical Center1, Oregon Health & Sciences University2; Portland, OR

# Brief group psychoeducation for psychogenic nonepileptic seizures: neurologist-initiated program in an epilepsy center

## Abstract

**Objective:** To evaluate therapeutic efficacy upon augmenting the initial communication to patients regarding the diagnosis of psychogenic nonepileptic seizures (PNES) with a novel, brief group psychoeducation administered by the same team that provided the video-electroencephalography (VEEG) confirmed diagnosis and within 4 weeks of the diagnosis.

**Methods:** Prior to discharge from the epilepsy monitoring unit (EMU), a standardized communication strategy was utilized to explain the diagnosis of PNES to all patients prior to enrollment. Enrolled patients were then randomized to either participation in three successive and monthly group psychoeducational sessions (intervention group), or routine seizure clinic follow-up visits (control group). Both groups completed questionnaires at time of enrollment, and then at approximately 3 months (follow-up 1) and 6 months (follow-up 2) after discharge, assessing for: (1) primary outcomes that include a measure of psychosocial functioning, as well as interval difference in seizure frequency/intensity; and (2) secondary outcomes that include interval seizure-related emergency room visits or hospitalizations, development of new and medically unexplained symptoms, and results of an internal measure of knowledge and perception outcomes.

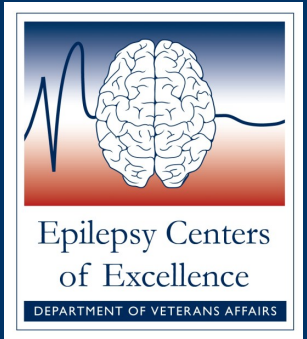
**Results:** The majority (73%) of patients from the intervention group commenced on therapy sessions within 4 weeks after learning of the diagnosis. Although we did not observe significant group difference in seizure frequency/intensity, patients from the intervention group showed significant improvement on the Work and Social Adjustment Scale (WSAS) scores at both follow-up 1 (p = 0.013) and follow-up 2 (p = 0.038) after discharge from the EMU. In addition, we observed a trend toward lesser likelihood for seizure-related emergency room visits or hospitalizations for the intervention group (p = 0.184), as well as meaningful insights from an internal measure of intervention outcomes.

**Significance:** These findings suggest that our cost/resource effective, brief group psychoeducational program, when administered early and by the same team who confirmed and communicated the diagnosis of PNES, may contribute to significant functional improvement among participating patients.

Chen DK1, Maheshwari A, Franks R, Trolley GC, Robinson JS, Hrachovy RA.

[Epilepsia. 2014 Jan;55\(1\):156-66. doi: 10.1111/epi.12481. Epub 2013 Dec 20.](#)

## National VA Epilepsy Consortium Newsletter



*Improving the health and well being of Veteran patients with epilepsy and other seizure disorders through the integration of clinical care, outreach, research and education.*

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[www.epilepsy.va.gov](http://www.epilepsy.va.gov)

## Patient and Caregiver Education

### Patient and Caregiver Education Audio Conferences

Sponsored by the Epilepsy Centers of Excellence & Employee Education System  
Patients, caregivers, and anyone interested in learning more about epilepsy and seizures are welcome to call in.

Dial-in: 1-855-767-1051 Access Code: 81024195  
1:00-2:00 PM Eastern Time  
10:00-11:00 AM Pacific Time

**August 7, 2014** – “Mental Health and Epilepsy”  
Collette Evrard, NP – Portland VAMC

## Educational Opportunities for Providers

### Healthcare Provider Education Audio Conferences

Sponsored by the Epilepsy Centers of Excellence & Employee Education System  
**Provider calls are CME accredited for Physicians and Nurses.**

Dial-in: 1-855-767-1051 Access Code: 81024195  
1:00-2:00 PM Eastern Time  
10:00-11:00 AM Pacific Time

**July 9, 2014** - “Driving and Epilepsy”  
Allan Krumholz, MD - Baltimore VAMC  
**September 10, 2014** – “Epilepsy and Imaging”  
Zulfi Haneef, MD – Houston VAMC

If you have any questions about patient and provider education, contact, Ryan Rieger, National Administrative Director, at 415-221-4810 x4119 or by email at [ryan.rieger@va.gov](mailto:ryan.rieger@va.gov).

### Helpful Links:

The Epilepsy Foundation  
[www.epilepsyfoundation.org](http://www.epilepsyfoundation.org)

American Epilepsy Society  
[www.aesnet.org](http://www.aesnet.org)

Citizens United for Research in Epilepsy  
[www.cureepilepsy.org](http://www.cureepilepsy.org)

The Anita Kaufmann Foundation  
[www.akfus.org](http://www.akfus.org)

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