

New Research Presented at AAN Demonstrates Burden Associated with Essential Tremor and the Unmet Patient Need

New analysis finds patients with Essential Tremor (ET) had a significantly higher number of comorbidities, including anxiety and depression, and higher healthcare costs compared to non-ET patients – demonstrating the need for effective treatment options

SAN MATEO, CA -- April 4, 2022 -- [Cala Health](#), the bioelectronic medicine leader setting a new standard of patient care for chronic disease, announces two research studies to be presented at the American Academy of Neurology's (AAN) Annual Meeting on April 2-7, 2022, in Seattle.

The retrospective real-world analysis, titled "Increased Healthcare Cost and Mental Health Burden Among Patients with Essential Tremor: A Retrospective Observational Study in a Large U.S. Commercially Insured and Medicare Advantage Population," sought to compare changes to comorbidities, psychiatric disorders, healthcare resource utilization (HCRU) and healthcare costs (HCCs) in patients with and without essential tremor (ET). Key findings include (for ET vs. non-ET patients):

- A higher mean of total healthcare costs (\$17,560 vs. \$13,237)
- A higher mean number of comorbidities (5.3 vs. 4.0)
- A higher prevalence of depression (25.6% vs. 15.3%), anxiety (27.7% vs. 15.5%) and total psychiatric disorders (45.9% vs 31.1%)

While ET has traditionally been regarded as a benign condition, this retrospective, observational study clearly demonstrated that ET is associated with a significant burden to patients and the healthcare system. Multiple comorbid conditions and psychiatric disorders are highly prevalent among patients with ET compared with non-ET patients. Additionally, ET patients use significantly greater HCRU and demonstrate increased HCCs compared to matched non-ET patients suggesting additional therapies are needed to address the unmet needs in this population of patients.

"Essential tremor patients – in addition to having to manage a debilitating condition – are shown to pay higher healthcare costs, have more chronic conditions, and suffer from more mental health challenges than patients without ET," said Ali Samiian, senior director of reimbursement at Cala and one of the researchers of the study. "This latest research further demonstrates the need for better therapeutic offerings for this population. We are dedicated to improving patients' quality of life and expanding access to our clinically proven treatment for ET, Cala TAPS therapy."

Another study presented at AAN, titled "Transcutaneous Afferent Patterned Stimulation Provides Upper Limb Motor Symptom Relief in Parkinson's Disease Patients," was designed to investigate the efficacy and safety of non-invasive transcutaneous afferent patterned stimulation (TAPS) to reduce postural and kinetic tremors in PD patients. TAPS is a neuromodulation therapy that uses surface electrodes for calibrating and delivering stimulation to peripheral nerves in the wrist resulting in tremor reduction. This investigational research in patients with PD found that:

- TAPS reduced postural tremor power by 66% from pre- to post-stimulation
- Bain and Findley Activities of Daily Living scores – which measure functions such as holding a cup or writing – improved by 0.5 ± 0.5 and 0.3 ± 0.4
- At study exit, clinicians observed symptom improvement in 83% of patients, and 81% of patients reported perceived symptom improvement
- Objective, clinician, and patient-rated outcomes demonstrate that TAPS improved upper limb action tremor symptoms in patients with PD

Cala TAPS therapy is not currently indicated for treating hand tremor in Parkinson's Disease patients. Cala was granted breakthrough device designation for TAPS therapy in Parkinson's disease patients, and these data will be submitted for U.S. FDA review.

About Cala Health

Cala is a bioelectronic medicine company transforming the standard of care for chronic disease. The company's wearable neuromodulation therapies merge innovations in neuroscience and technology to deliver individualized peripheral nerve stimulation, and its vertically integrated commercial model is reshaping the delivery of prescription therapies. Cala's lead product, Cala Trio™ therapy, is the only non-invasive prescription therapy for essential tremor. New therapies are under development in Parkinson's disease and other indications in neurology, as well as targets in psychiatry, cardiology, and autoimmune disorders. The company is headquartered in the San Francisco Bay Area and backed by leading investors in both healthcare and technology.

Indication: Cala Trio therapy is indicated to aid in the temporary relief of hand tremors in the treated hand following stimulation in adults with essential tremor.

Caution: Federal law restricts this device to sale by or on the order of a physician.

Prior to use, refer to the product labeling for complete product instructions for use, contraindications, warnings, and precautions at <https://calatrio.com/Safety>.

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Increased Healthcare Cost and Mental Health Burden among Patients with Essential Tremor: A Retrospective Observational Study in A Large US Commercially Insured and Medicare Advantage Population

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BACKGROUND & STUDY OBJECTIVES

Essential tremor (ET) is the most common movement disorder (1), affecting 7 million or 2.2% of individuals in the United States (2). ET is progressive in nature, and is characterized by tremor, most often of the hands or arms. It is associated with physical and cognitive impairments, avoidance of social settings, and has a negative impact on the performance of activities of daily living (ADLs) and mental health (1,3,4). There is an unmet need for a safe and effective treatment of patients with ET as existing pharmacologic and surgical options can be ineffective and associated with significant risk of side effects (1).

Limited data exists on the economic, mental health and comorbidity burden among ET patients within commercial and Medicare Advantage populations in the United States. The aims of this study were to assess comorbidities, psychiatric disorders, health care resource utilization (HCRU), and healthcare costs (HCCs) among patients with ET as compared to patients without ET (non-ET).

METHODS

This retrospective, observational study was conducted using an administrative claims database from a US healthcare payer with 15M covered lives. ET was identified using ICD-10-CM: G250 during the index period (7/1/2017 – 12/31/2019). The earliest claim date with evidence of ET was identified as the index date. A random index date was assigned to non-ET patients. Qualified patients had at least 6 months of enrollment before the index date, 12 months of enrollment after the index date and were ≥22 years of age. Patient demographics and comorbid conditions were assessed using all data within 6 months prior to and including the index date. Psychiatric disorders, HCRU and HCCs were examined using all data within 12 months after the index date. ET vs. non-ET patients were matched using 1:1 exact matching on age, gender, payer type, and first 3-digits ZIP-code. The outcomes were adjusted by comorbidities and household incomes using multivariable generalized linear models.

RESULTS & DISCUSSION

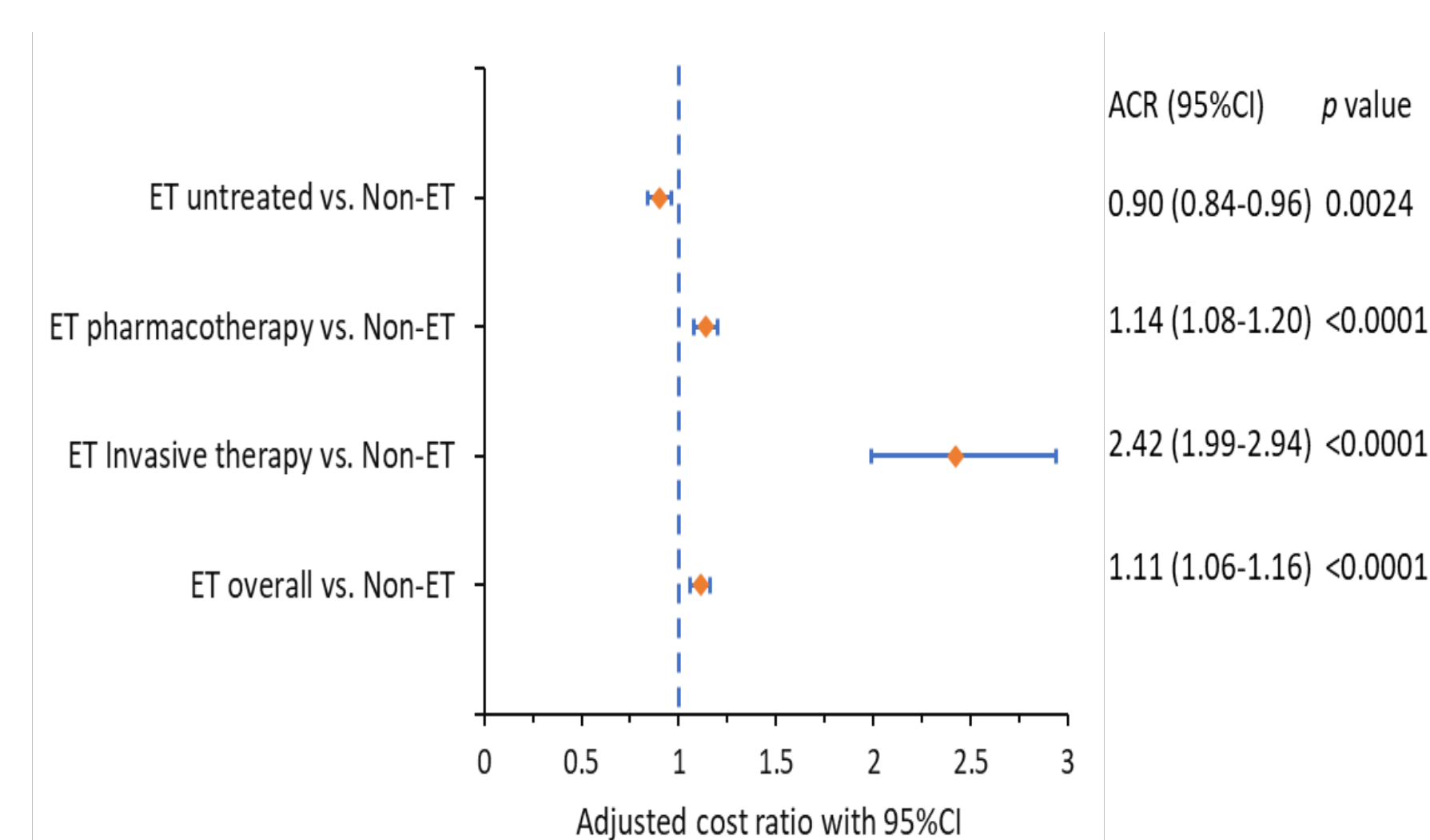
Of 5,244 patients in each of the ET and non-ET groups, the mean age was 70.8 years, 49.1% were female, 17.1% had commercial insurance coverage, and 82.9% were Medicare Advantage members. Demographics between the groups were similar, as planned for the comparison. ET patients had higher total HCCs with a mean (standard deviation) of \$17,560 (\$39,972) vs. non-ET patients \$13,237 (\$27,098). This aligns with the evaluation of the adjusted overall cost ratio. Adjusted overall cost ratio (95% CI) for ET vs. non-ET patients was 1.11(1.06-1.16) (Figure 1). There were a greater number of comorbidities in ET patients 5.3 (3.2) vs. non-ET 4.0 (3.3) (Figure 2 & 3). In addition, ET patients had a higher prevalence of psychiatric disorders than non-ET patients as follows (Figure 4):

- Depression: 25.6% vs. 15.3%, adjusted odds ratio (95% CI): 1.56(1.41-1.73)
- Anxiety: 27.7% vs. 15.5%, adjusted odds ratio: (95% CI): 1.78(1.61-1.96)
- Any psychiatric disorders (depression, anxiety, stress and adjustment disorders, dissociative and conversion disorders, somatoform disorders, substance use): 45.9% vs 31.1%, adjusted odds ratio: 1.57(1.44-1.70) (Figure 5).

The combination of increased comorbidities and higher prevalence of psychiatric disorders for ET patients likely leads to the increased HCCs and higher adjusted overall cost ratio.

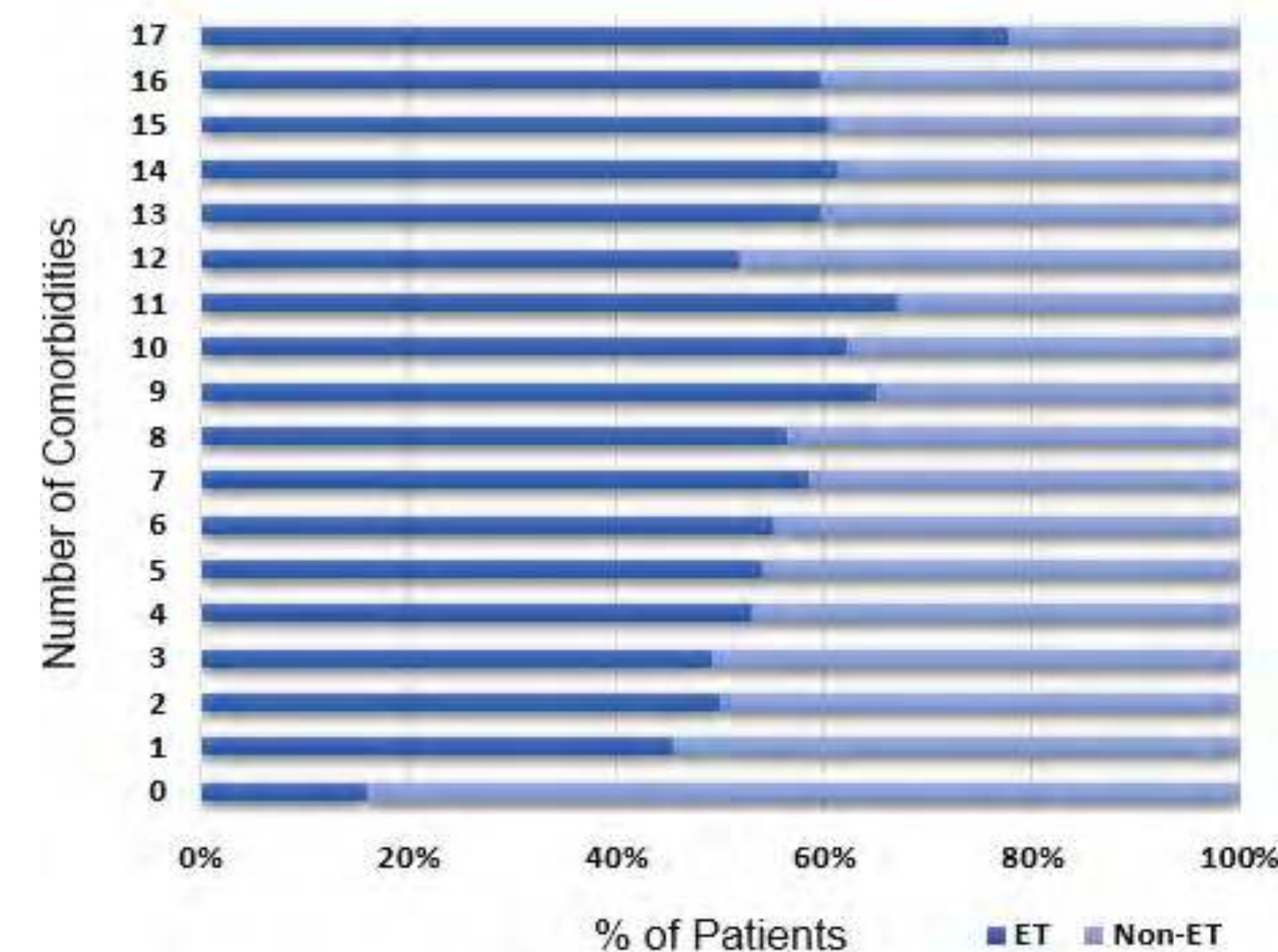
RESULTS (CONT'D)

FIGURE 1. FOREST PLOT OF TOTAL ALL CAUSE COSTS ACCRUED DURING THE 12-MONTHS FOLLOW-UP PERIOD, DISPLAYED AS COST RATIO (CR)*



*The vertical dashed blue line represents a CR of 1 as the reference line, which is associated with equal costs for both ET and Non-ET. ET is associated increased HCCs.

FIGURE 2. 100% STACKED BAR CHART OF PERCENT OF PATIENTS WITH SPECIFIC NUMBER OF COMORBID CONDITIONS AMONG PATIENTS WITH AND WITHOUT ET*



*ET patients have significantly higher number of comorbidities vs. non-ET patients

FIGURE 3. PREVALENCE OF THE TOP 12 MOST COMMON COMORBID CONDITIONS AMONG PATIENTS WITH AND WITHOUT ET AT BASELINE

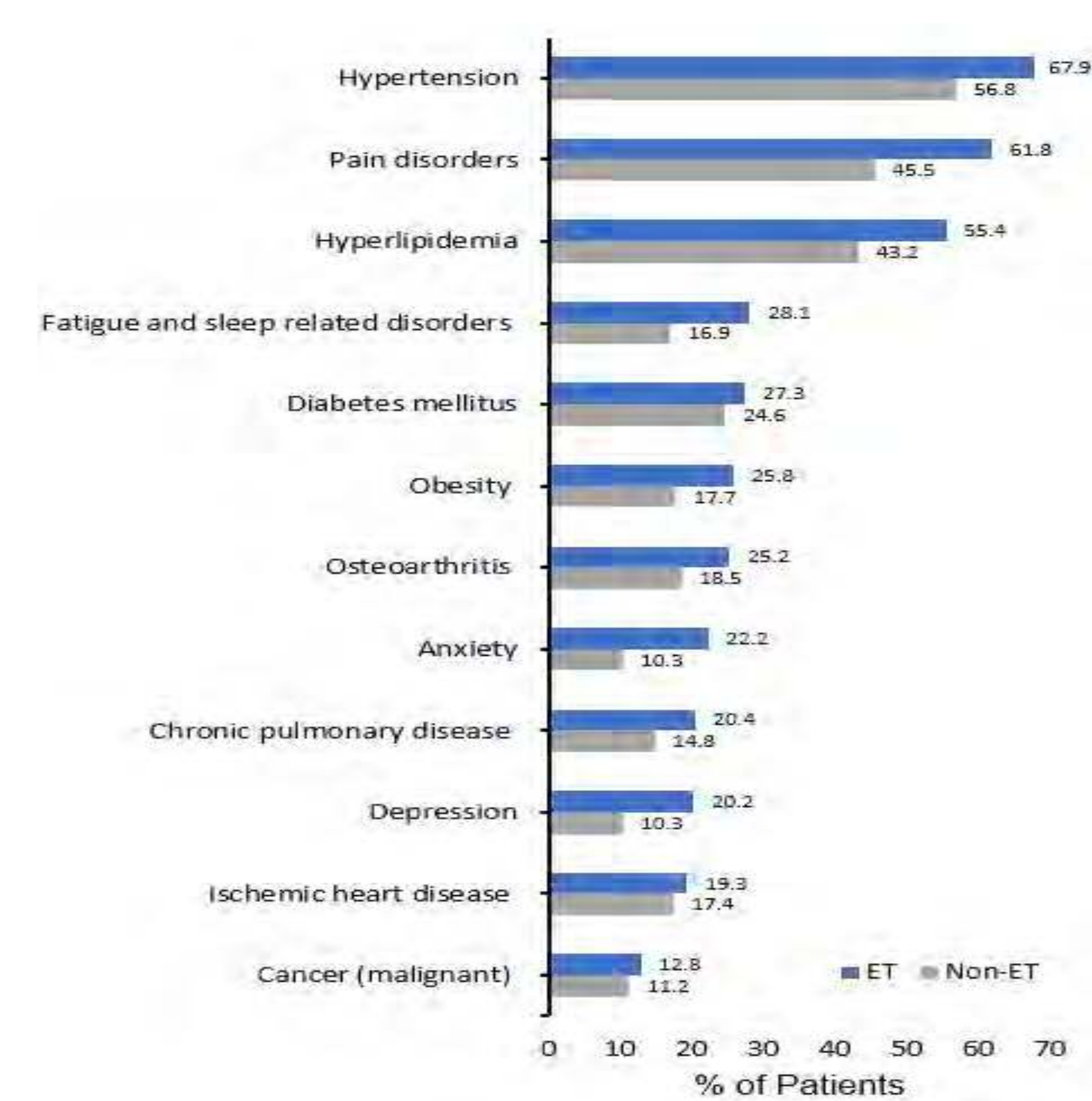


FIGURE 4. PREVALENCE OF PSYCHIATRIC DISORDERS AMONG PATIENTS WITH AND WITHOUT ET DURING THE 12-MONTHS FOLLOW-UP PERIOD

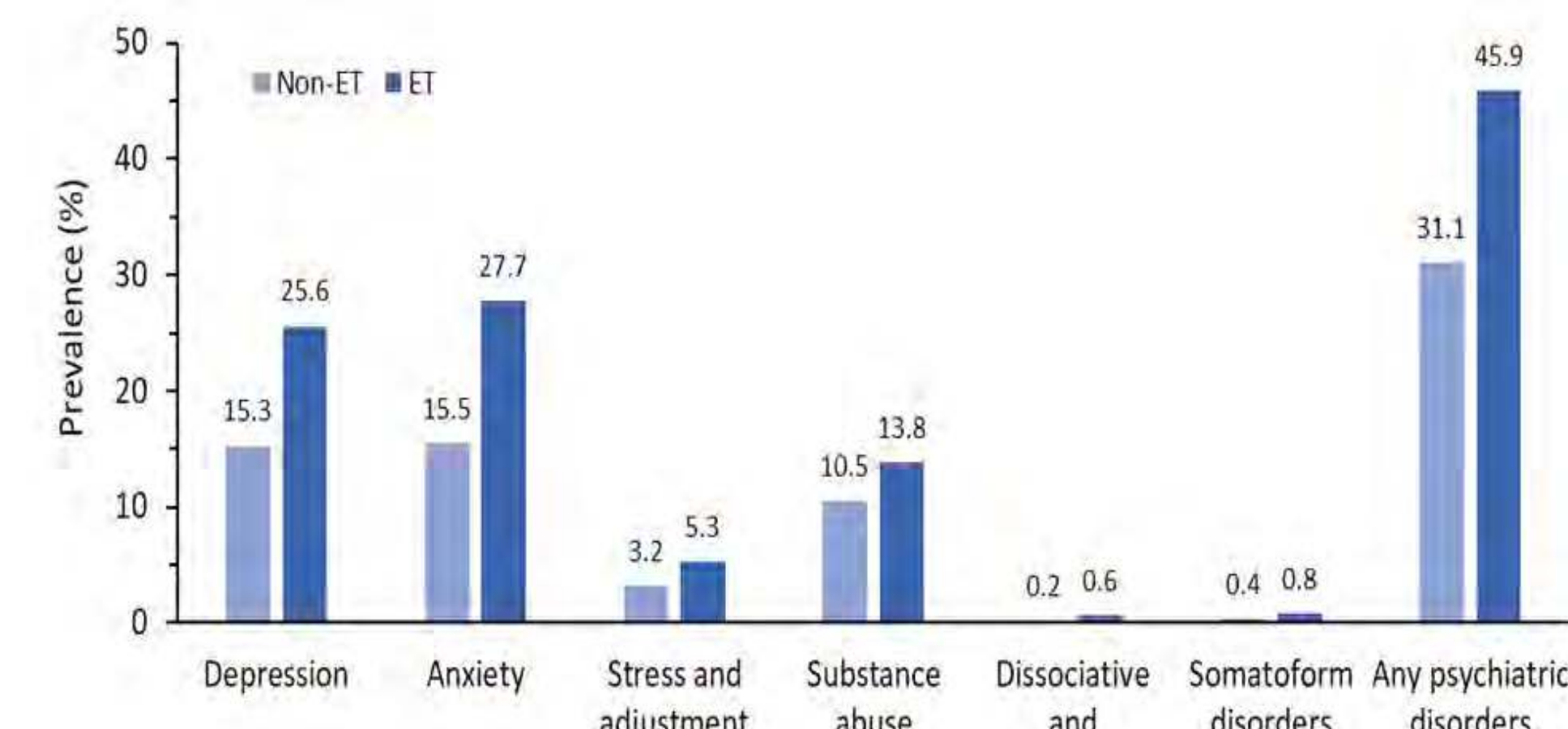
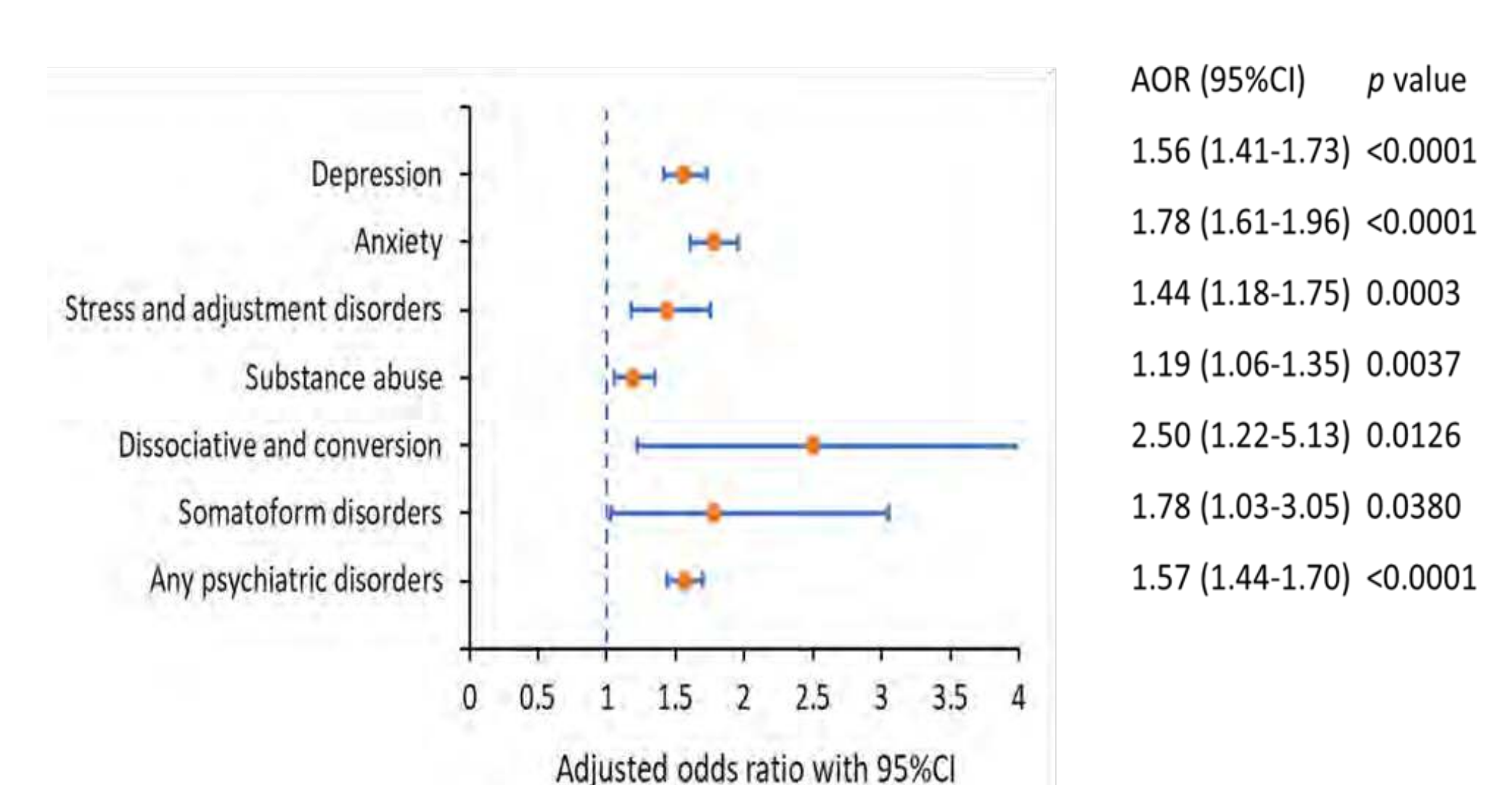


FIGURE 5. FOREST PLOT OF ADJUSTED ODDS RATIO (OR) OF PREVALENT PSYCHIATRIC DISORDERS DURING THE FOLLOW-UP PERIOD, ET VS. NON-ET*



*The vertical dashed blue line represents an OR of 1 as the reference line, which is associated with equal odds for both ET and Non-ET groups. For each OR displayed, the symbol orange dot depicts the OR, and the horizontal blue line represents the 95% CI. Lines which do not cross the dashed vertical blue line are statistically significant. ET is associated substantial mental health burden.

CONCLUSIONS

This retrospective, observational study in a large US commercially insured and Medicare Advantage population demonstrated that ET is associated with a significant burden to patients and the healthcare system. Multiple comorbid conditions and psychiatric disorders are highly prevalent among patients with ET compared with non-ET patients. Additionally, ET patients use significantly greater HCRU and demonstrate increased HCCs compared to matched non-ET patients. Future studies are needed to develop safe and cost-effective disease management strategies to improve outcomes and reduce healthcare expenditures in this complex population of patients.

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Objective:

To compare healthcare costs and prevalence of psychiatric disorders between patients with and without essential tremor (ET).

Background:

ET is one of the most common movement disorders in adults often impairing patients' quality of life. Real-world evidence on the economic and psychological burden on ET is limited.

Design/Methods:

This retrospective observational study was conducted using an administrative claims database from a large United States health care payer. Patients with ET (ICD-10-CM: G250) were identified during the study period (1/1/2017 – 12/31/2019). The earliest claim date with evidence of ET was identified as the index date. Patients age 22+ with 6 and 12 months of health plan enrollment before and after index date were included. Demographics and comorbidities were assessed within six months prior to the index date. Psychiatric disorders and costs were examined within 12 months after the index date. ET vs. Non-ET patients matching was determined using 1:1 exact matching on age, gender, payer type, first 3-digits ZIP-code. The outcomes were adjusted by comorbidities and household incomes using multivariable generalized linear models.

Results:

There were 5,244 patients in each of ET and Non-ET groups (mean age 70.8 years; 49.1% female). ET vs. Non-ET patients had higher total healthcare costs (mean (standard deviation)): \$17,560(\$39,972) vs. \$13,237(\$27,098), Adjusted cost ratio (95%CI): 1.11(1.06-1.16); higher number of comorbidities: 5.3(3.2) vs. 4.0(3.3); and higher prevalence of psychiatric disorders (depression: 25.6 vs. 15.3%, adjusted odds ratio (AOR) (95%CI): 1.56(1.41-1.73); anxiety: 27.7 vs. 15.5%, AOR: 1.78(1.61-1.96); any psychiatric disorders (depression, anxiety, stress and adjustment disorders, dissociative and conversion disorders, somatoform disorders, substance use): 45.9 vs 31.1%, AOR: 1.57(1.44-1.70)). All $p < 0.0001$.

Conclusions:

These data demonstrate increased healthcare costs and prevalence of psychiatric disorders among ET patients compared with matched non-ET patients and underscore the need for better therapeutic offerings for this complex population.