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## Background & Study Objective

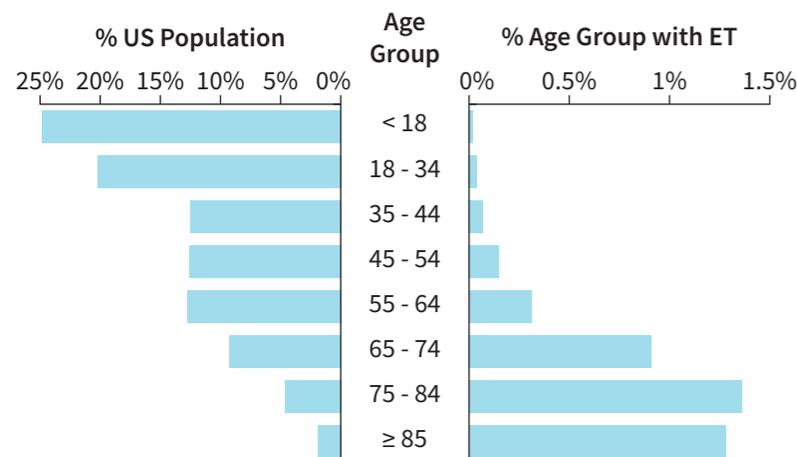
Essential tremor (ET) is the most common neurologic movement disorder. ET is associated with physical and cognitive impairments, avoidance of social settings, and related difficulties that negatively impact patients' lives.<sup>1,2</sup> Exploring comorbidities and all-cause resource utilization are needed to better evaluate the impact of ET on healthcare systems. **This study evaluated and compared mental health conditions and all-cause resource utilization in patients diagnosed with and without essential tremor, using claims data from Truven Health Analytics MarketScan database.**

## Methods

Using Truven Health Analytics MarketScan®, Commercial and Medicare Supplemental databases (1/1/2017-12/31/2018), adult patients with ET (> 22 years old) were identified. Newly diagnosed patients did not have a diagnosis for the 3 years prior to incident date. ET drug utilization in this population was used to identify type and frequency of initial prescription, as well as proportion of patients with ET who did not initiate treatment at diagnosis. The proportion of patients with mental health conditions was also identified and compared between cohorts of patients with and without ET in the commercial and Medicare Supplement setting.

## Population Demographics

In 2018, the total surveyed population constituted 327,167,439 lives (83.9% captured via Commercial databases). Population age distribution is pictured below (left). Estimates of ET prevalence by age group (below, right) indicate ET disproportionately affects seniors (age 65+ years).

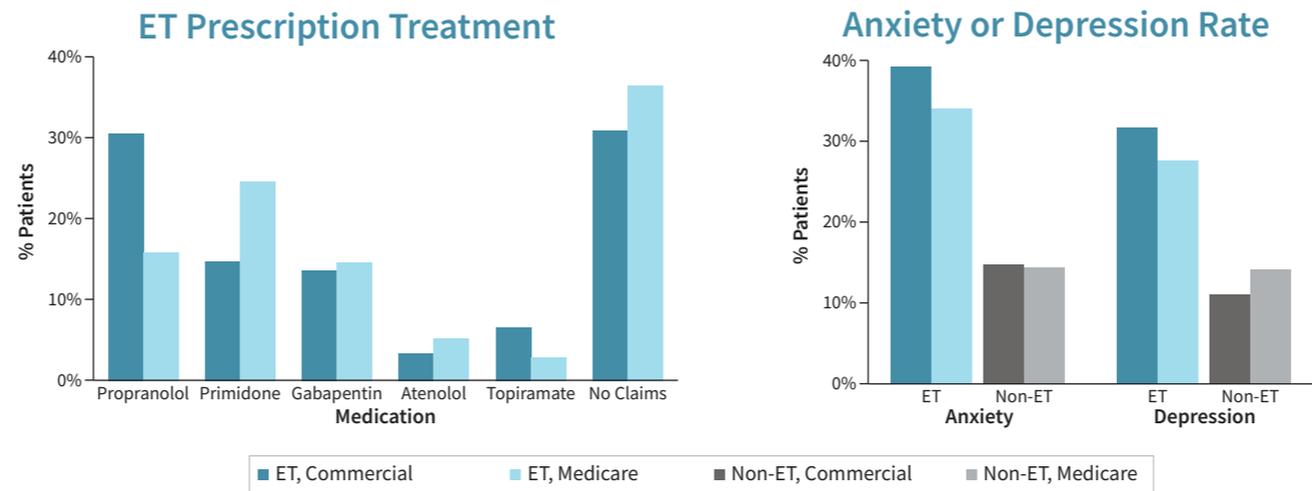


## All-Cause Cost of Essential Tremor Diagnosis and Care

All-cause cost was computed for ET and non-ET patients on Commercial and Medicare Supplemental insurance plans. For patients without ET, all-cause cost was measured over the entire study period (1/1/2017 - 12/31/2018). **The mean all cause cost at 24 months post-index is 2.3 (Commercial) and 1.6 (Medicare supplemental) times greater for ET patients than for those not diagnosed with ET.**

	ET Patients		Non ET-Patients	
	Commercial (N=379)	Medicare Supplemental (N=170)	Commercial (N=1,136,042)	Medicare Supplemental (N=61,054)
<b>Diagnosing physician, expenditures</b>				
% Patients with no neurologist visit on index date (N)	50.4% (191)	47.1% (80)	94.5% (1,073,249)	87.2% (53,222)
Mean all-cause 24-month post-index costs, USD (median)	\$28,831 (14,792)	\$67,291 (36,003)	\$14,669 (4,385)	\$42,378 (16,020)
% Patients with neurologist visit and ET diagnosis on index date (N)	49.3% (187)	52.9% (90)	5.5% (62,340)	12.8% (7,799)
Mean all-cause 24-month post-index costs, USD (median)	\$48,095 (19,848)	\$91,895 (48,376)	\$47,140 (19,953)	\$89,213 (41,597)
Mean all-cause 24-month post-index costs, USD	\$38,259.94	\$80,316.87	\$16,444.77	\$48,337.69

## Direct and Indirect Healthcare Costs of Essential Tremor



(Left) 68% of the newly diagnosed ET patients received 1 of the 5 drugs of interest (31% Propranolol, 15% Primidone, 14% Gabapentin). 31% of patients did not fill claims for any prescriptions within 24 months post-ET diagnosis.

(Right) 31.7% of ET patients with commercial coverage also received a diagnosis of depression during the 24 months post first ET claim, compared to 11.0% in the non ET cohort. (27.6% vs. 14.2% in a Medicare Supplement population). 39.3% of ET patients with commercial coverage received a diagnosis of anxiety in the same period, compared to 14.8% in the non-ET cohort. (34.1% vs. 14.4% in a Medicare Supplement population).

## Conclusions

The findings in this study highlight aspects of the healthcare burden of ET, including increased all-cause healthcare cost and increased rates of anxiety and depression. However, a considerable number of ET patients do not initiate any treatment up to 24 months following their first claim of ET. Future studies are required to identify key drivers of the cost difference.

## References:

- Yunusa et al. Prevalence, Disease Burden and Unmet Needs of Patients With Essential Tremor - A Systematic Review and Meta-Analysis (2018) *Value in Health*
- Louis et al. Defining the Treatment Gap: What Essential Tremor Patients Want That They Are Not Getting (2015) *Tremor & Other Hyperkinetic Movements*

**Disclosures:** AS, DK, SS, AR, and KR are employees of Cala Health.



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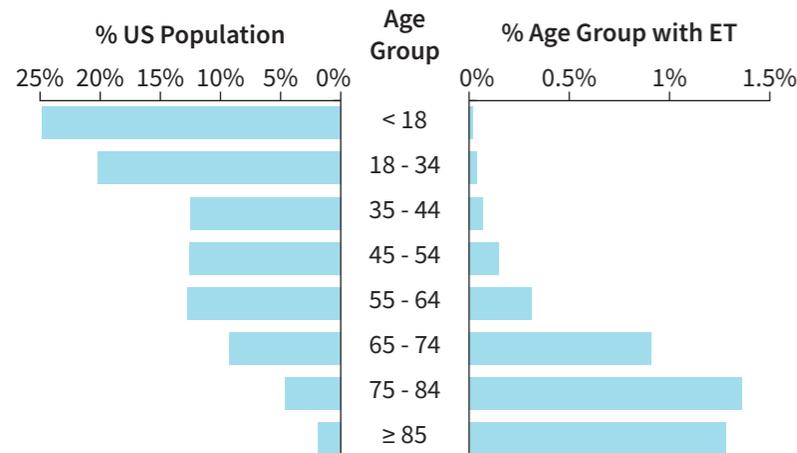
Essential Tremor (ET) is one of the most common neurologic movement disorders in adults. ET is associated with physical and cognitive impairments, avoidance of social settings, and other related difficulties that negatively impact patients' lives.<sup>1,2</sup> An up-to-date longitudinal prevalence rate of ET for Medicare and Commercial plans in the United States (US) will assist payers in understanding the impact of ET care on healthcare plans. **This study examined the longitudinal trend of essential tremor prevalence rates in 2010-2018 in individuals with Commercial and Medicare Supplemental insurance in the United States.**

## Methods

The longitudinal trend of ET prevalence was examined using Truven Health MarketScan® Commercial and Medicare Supplemental Databases, where patients can be followed over multiple years. ET prevalence rates were calculated as the total number of patients with ET divided by the total number of covered patients with medical and pharmacy benefit. In each calendar year, patients were considered if there was an ICD-10-CM diagnosis code for ET (ICD-10 Diagnosis G250 Essential tremor, or ICD-9 Diagnosis 333.1 Essential and other specified forms of tremor) in that year. Age was reported on the date of the ET claim during each calendar year.

## Population Demographics

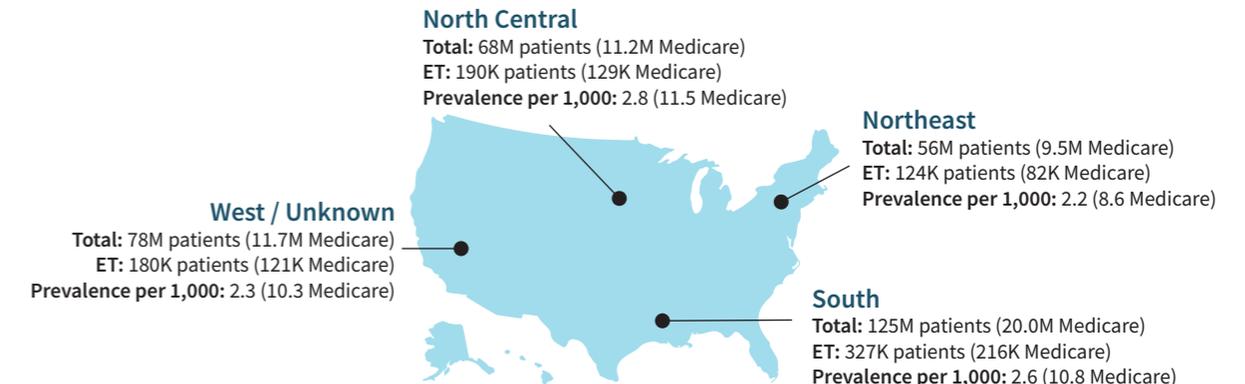
The market scan captured health insurance coverage and claims for the US population from 2009 - 2018. In 2018, the total surveyed population constituted 327,167,439 lives (83.9% captured via Commercial databases). Population age distribution is pictured below (left). Estimates of ET prevalence by age group (below, right) indicate ET disproportionately affects seniors (age 65+ years).



## ET Prevalence by Insurance Type & Region

A total of 819,661 patients with 1 or more claims for ET were identified in 2018. The median age of commercial plan members in 2017-2018 was 55 years, while the median age across Medicare patients during the same period was 74 years. Medicare insurance covered approximately twice as many ET patients as commercial insurers (542K vs 278K patients, respectively), consistent with the age distributions per subgroup. ET prevalence was approximately an order of magnitude higher in the Medicare Supplemental-covered patients compared to Commercial patients (10.311 vs 1.012 per 1,000 lives, respectively). The North Central had the highest prevalence of ET, while the South region had the absolute highest number of patients.

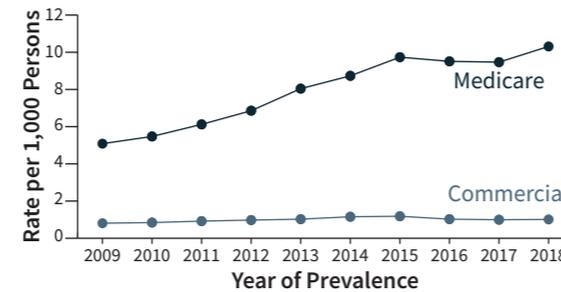
	Commercial	Medicare Supplemental
2018 Patient is continuously enrolled in calendar year (N)	274,632,469	52,548,288
Patient has 1 or more claims for ET (N, % subgroup)	277,846 (0.10%)	541,815 (1.03%)
Prevalence of ET per 1,000 persons	1.012	10.311



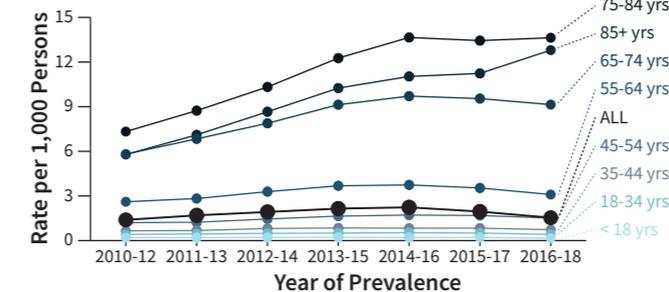
## Longitudinal Trends of ET Diagnoses and Prevalence

New ET diagnoses increased annually, primarily in the Medicare population. ET prevalence rates increased consistently from 2010 to 2018, increasing from 1.449 per 1,000 persons in 2010 to 2.505 per 1,000 persons in 2018 for all persons (6.27% annual growth); 5.473 to 10.311 per 1,000 persons for Medicare patients (7.29% annual growth); and 0.843 to 1.012 per 1,000 persons for Commercial patients (2.05% annual growth).

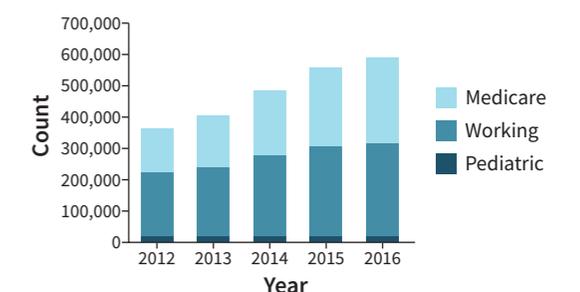
### 1-Year Prevalence Rates, by Insurance Type



### 3-Year Prevalence Rates, by Age Group



### New ET Diagnoses



## Conclusions

The prevalence rate of ET increased consistently from 2010 to 2018 in both populations under age 65 and above 65.

### References:

- Yunusa et al. Prevalence, Disease Burden and Unmet Needs of Patients With Essential Tremor - A Systematic Review and Meta-Analysis (2018) *Value in Health*
- Jankovic, J. Distinguishing Essential Tremor From Parkinson's Disease (2012) *Practical Neurology*

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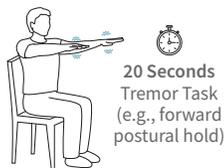
Essential tremor (ET) is one of the most common movement disorders in adults but has limited available treatment options. Transcutaneous afferent patterned stimulation (TAPS) is a wrist-worn, non-invasive neuromodulation therapy targeting the median and radial nerves with a bursting waveform individualized to each patient's tremor. TAPS has been shown to be a safe and effective symptomatic tremor relief therapy in single-session and extended-duration clinical studies<sup>1-3</sup>, but how these results translate from a closely monitored clinical trial into a real-world setting is unknown. **This early post-market analysis evaluated the real-world efficacy and safety of TAPS therapy for symptomatic tremor relief in 178 ET patients with non-supervised home use.**

## Device Design & Calibration

Stimulator & electrodes



Device Calibration



The device consisted of a stimulator and detachable band containing two working electrodes positioned over the median and radial nerves and a counter-electrode positioned on the dorsum of the wrist.

The patient's tremor frequency was captured from a 20 second postural hold. The peak tremor frequency was determined onboard the device and used to tune a patient-specific stimulation pattern.

## Therapy Prescription and Home Use

**Device prescription and setup.** Patients were prescribed a United States Food & Drug Administration-cleared TAPS therapeutic device (Cala Health, Burlingame, CA, USA) following evaluation by a neurologist. Patients were given written instruction for setting up and calibrating the therapeutic device, with phone support available as needed.

**Home use.** A therapy session consisted of 40 minutes of stimulation. Timing and frequency of device usage was at the discretion of each patient, though the therapy was labeled for symptomatic usage.

**Patient consent:** Patients provided informed consent for their data to be included in this analysis. All device and survey data was de-identified prior to analysis.

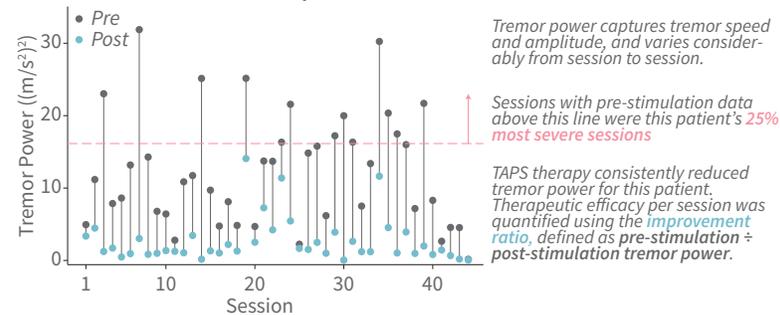
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## Tremor Motion Improvements

For the first 40 sessions and every 7<sup>th</sup> session thereafter, the device prompted patients to perform their tremor task before and immediately after stimulation. A triaxial accelerometer onboard the device measured tremor motion during this task. **Tremor severity was quantified using tremor power**, computed from the power spectral density of the accelerometer data.

### Sample Tremor Motion Remote Measurements

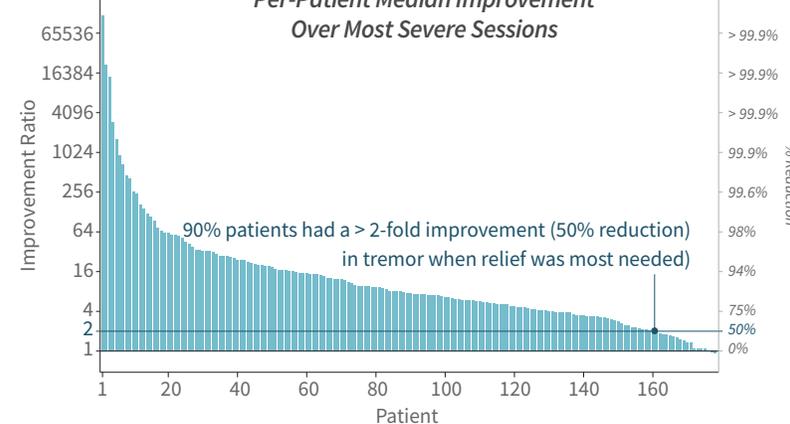
At-Home Sessions With Completed Pre- and Post-Stimulation Measurements



Sample pre-stimulation (grey) and corresponding post-stimulation (blue) tremor power measurements for a **representative patient**. Note, only sessions with completed pre- and post-stimulation measurements are illustrated; these sessions represent a subset of the total sessions completed by a patient over the patient's total home-use period.

### Symptomatic Tremor Improvement

Per-Patient Median Improvement Over Most Severe Sessions

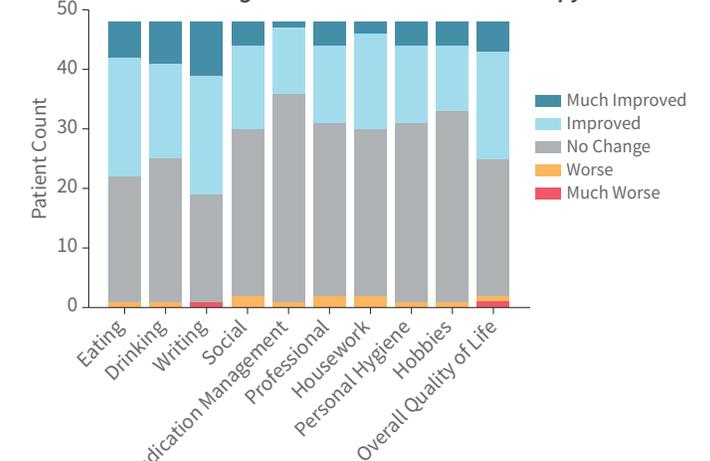


**Tremor reduction with therapy increased as a patient's tremor severity increased.** Tremor power measurements from 8,828 therapy sessions showed that **90% of patients (160 of 178) had a ≥2-fold improvement (i.e., 50% reduction) in tremor power during their most severe sessions (i.e., when tremor relief was most needed; above)**, and 57% of patients had ≥2-fold improvement in tremor power over all sessions (not shown). The median improvement ratio was 7.6-fold (87% reduction) for patients' 25% most severe sessions (distribution above), and 2.8-fold (56% reduction) for all sessions.

## Patient-Reported Outcomes

Patients were sent an opt-in post-market survey either at time of their prescription refill, or earlier if patients opted to discontinue therapy. The survey asked patients to rate their tremor burden, preference for TAPS therapy relative to existing treatment options, areas where they would most like therapy to improve tremor symptoms, and improvement in tasks and quality of life with TAPS therapy.

Self-Rated Change In Activities With TAPS Therapy



48 of the 178 patients completed the survey. Of these 48 patients, 54% reported having over 20 years of ET symptoms, and 94% reported having at least moderate tremor. Prior to trying TAPS, most (94%) patients had tried at least one medication for tremor control, and 77% had tried two or more medications for tremor relief. Patients overwhelmingly (92%) reported activities of daily living as the area of most important therapeutic need. With TAPS, **69% of patients reported improvement in at least one of eating/drinking/writing and 48% reported improvement in overall quality of life. Over half (56%) of patients preferred TAPS therapy to existing treatment options (medication or surgery).**

## Conclusions

This real-world evidence reinforces previous clinical trial findings on objective (kinematic) and patient-reported efficacy of TAPS<sup>3</sup>. Overall device-measured symptomatic benefit was comparable to standard-of-care medications, and benefit at time of most severe tremor was comparable to benefits observed with more invasive (e.g., deep brain stimulation) treatment options<sup>4</sup>. These objective data, along with self-reported patient preference data, suggest that TAPS may be an attractive symptomatic treatment option for ET patients.

### References:

- [1] Lin PT et al. Noninvasive neuromodulation in essential tremor demonstrates relief in a sham-controlled pilot trial. *Mov Disord* 2018.
- [2] Pahwa R et al. An Acute Randomized Controlled Trial of Noninvasive Peripheral Nerve Stimulation in Essential Tremor. *Neuromod* 2019.
- [3] Isaacson S et al. Prospective home-use study on non-invasive neuromodulation therapy for essential tremor. *Trem Hyperkin Mov* 2020.
- [4] Zesiewicz TS et al. Practice parameter: therapies for essential tremor: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2005