Quality of Life and Comorbidities Associated With Essential Tremor: A Systematic Review

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Introduction

- Essential tremor (ET), primarily characterised by action tremor of the upper limbs, is among the most common movement disorders[1-3]
- ET is progressive and often disabling, leading to negative impacts on patients' functional ability, work productivity, and overall quality of life (QoL)[4]
- Despite the disabling nature of the disease, little has been published on the humanistic burden of ET

Objective

- To summarise the disease burden (including QoL and comorbidities) associated with ET through a systematic review (SR) of the literature

Methods

- Electronic databases (Embase, MEDLINE, Evidence-Based Medicine Reviews, International Network of Agencies for Health Technology Assessment, EconLit) from 2000 to 2022 were used to identify potentially relevant real-world publications; additional handsearching included interrogation of reference lists of eligible studies, conference proceedings, and movement disorder-related databases and websites
- Real-world publications included cohort studies, database analyses, registries, naturalistic studies, cost-of-illness studies, and treatment guidelines
- Individual citations were excluded if: 1) nonpharmacological treatments were solely discussed, 2) neurologic movement disorders other than ET were solely discussed, 3) a study was not conducted in a real-world setting or was very limited (ie, reviews, editorials, controlled clinical studies, case reports, or animal/*in vitro* studies), 4) a citation was a duplicate or linked publication
- Citations were screened by 2 independent reviewers, and discrepancies were resolved by consensus

References: 1. Song P, et al. *J Glob Health*. 2021;11:04028. **2.** Louis ED, McCreary M. *Tremor Other Hyperkinet Mov (N Y)*. 2021;11:28. **3.** Bhatia KP, et al. *Mov Disord*. 2018;33(1):75-87. **4.** Agarwal S, Biagioni MC. *StatPearls*. Treasure Island (FL): StatPearls Publishing Copyright © 2022, StatPearls Publishing LLC.; 2022. **5.** Kovacs M, et al. *Ideggyogy Sz*. 2017;70(5-6): 193-202.

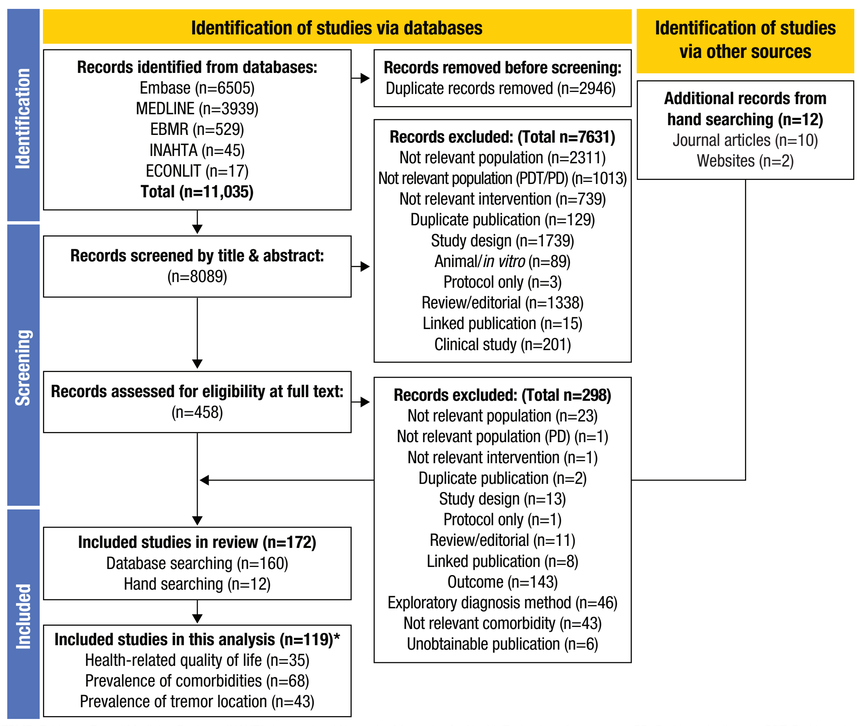
Support and Acknowledgements: This study was supported by Jazz Pharmaceuticals. Under the direction of the authors, Kelly Birch, MPH, and LeeAnn Braun, MPH, MEd, of Peloton Advantage, LLC, an OPEN Health company, provided medical writing and editorial support for this poster, which was funded by Jazz Pharmaceuticals.

Disclosures: SA Mitchell and **G Redhead** are full-time employees of Mtech Access Ltd. **H Viswanathan, D Girfoglio,** and **J Lin** are full-time employees of Jazz Pharmaceuticals who, in the course of this employment, have received stock options exercisable for, and other stock awards of, ordinary shares of Jazz Pharmaceuticals, plc.

Results

Study Selection

Figure 1. PRISMA Diagram – Study Identification and Selection

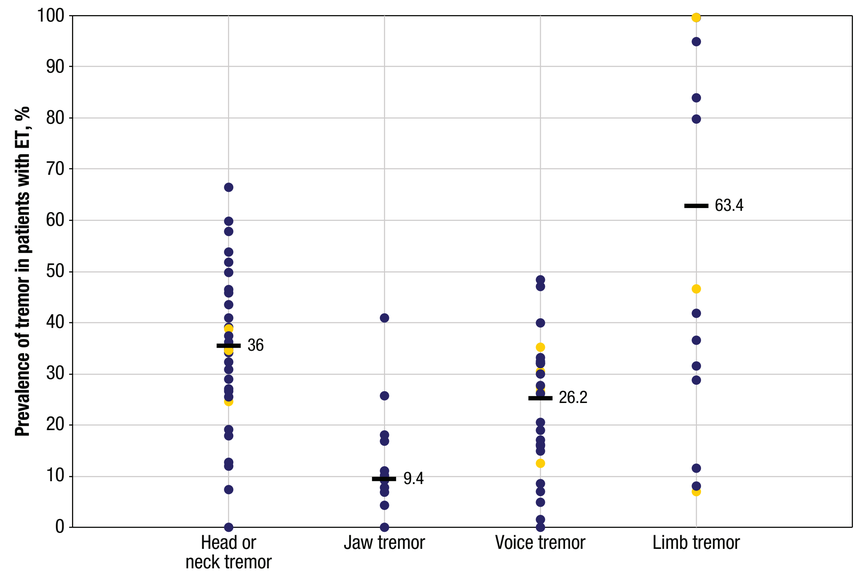


EBMR, Evidence-Based Medicine Reviews; INAHTA, International Network of Agencies for Health Technology Assessment; PD, Parkinson's disease; PDT, Parkinson's disease tremor; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.
*Studies on each topic do not add to the total of n=119 due to overlap in content of the publications.

- Of a total 11,035 publications, 172 were included in this SR after screening, and 119 reported health-related quality of life (n=35), prevalence of comorbidities (n=68) and prevalence of tremor location (n=43) in patients with ET

Prevalence of Tremor Locations

Figure 2. Prevalence of Tremor Locations in Patients With ET, Median

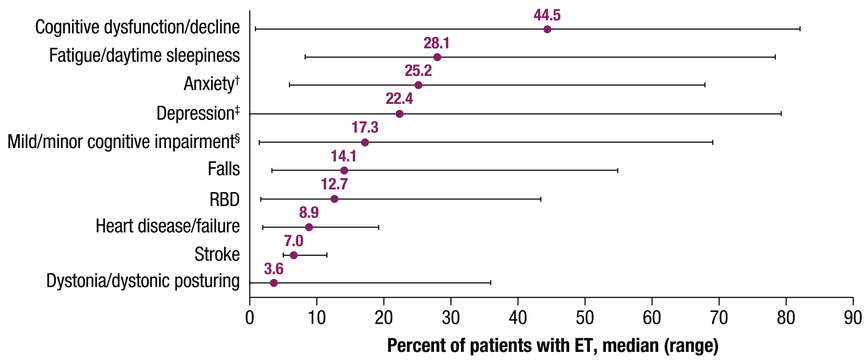


The median prevalence value for each location of tremor was calculated and is indicated by a horizontal bar. The prevalence values reported by the 5 publications with the largest population sizes are indicated by yellow dots for those outcomes with ≥15 data points. Population sizes for studies indicated by the yellow dots range from 135 (Sun 2020) to 884 (Chen 2017).
ET, essential tremor.

- The prevalence of various tremor locations in patients with ET was reported in 43 publications (covering 36 unique studies)
- The most common tremor locations were limb (median prevalence: 63.4%), head/neck (36.0%), voice (26.2%), and jaw (9.4%)
- However, given variability in study design and patient populations, there was substantial heterogeneity in the reported prevalence rates of tremor locations

Prevalence of Comorbidities

Figure 3. Prevalence of Comorbidities in Patients With ET, Median (Range)

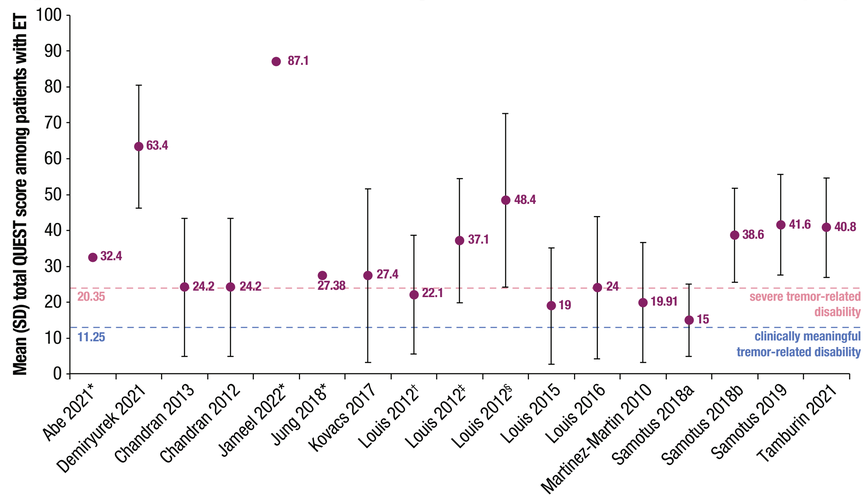


†Includes mild, moderate, and severe anxiety. ‡Includes demoralisation and mild, moderate, or severe depression. §Includes diagnosis of mild cognitive impairment (MCI).
ET, essential tremor; RBD, rapid eye movement sleep behaviour disorder.

- The prevalence of various medical comorbidities in patients with ET was reported in 68 publications (covering 55 unique studies)
- Common comorbidities included cognitive dysfunction (median prevalence: 44.5% [decline/impairment] to 17.3% [mild/minor]), fatigue/daytime sleepiness (28.1%), anxiety (25.2%), depression (22.4%), rapid eye movement sleep behavior disorder (12.7%), heart disease/failure (8.9%), and stroke (7.0%)
- However, substantial heterogeneity in the reported prevalence of comorbidities was observed, potentially due to variability in study designs and patient populations

Quality of Life: Tremor-Specific Measurement

Figure 4. Total QUEST Scores Reported Across Studies, Mean (SD)

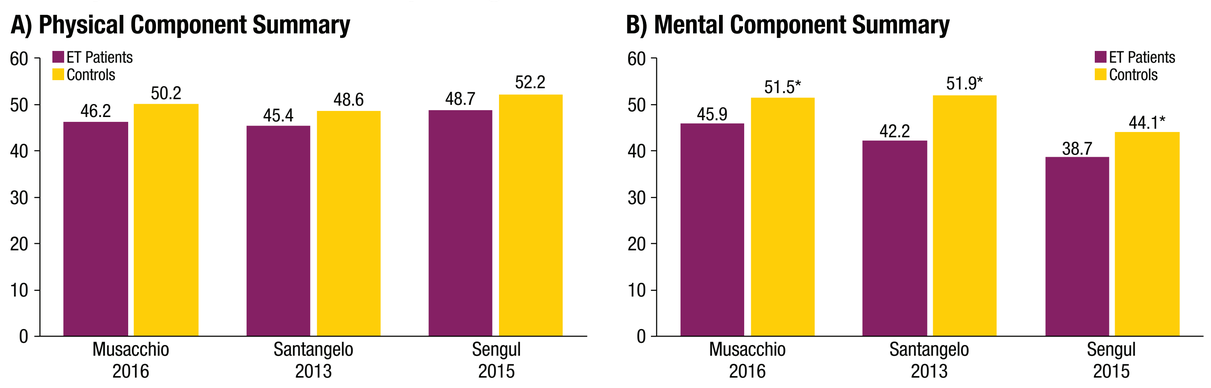


*Study did not report standard deviation. †Subset of patients in Louis 2012 including patients with mild depression. ‡Subset of patients in Louis 2012 including patients with moderate depression. §Subset of patients in Louis 2012 including patients with severe depression.
Kovacs et al (2017) suggest that mean total QUEST score values above 11.25 indicate the presence of clinically meaningful tremor-related disability, and mean scores above 20.35 suggest severe tremor-related disability.
ET, essential tremor; QUEST, Quality of Life in Essential Tremor; SD, standard deviation.

- All studies found that mean total QUEST scores (for ET patients) were consistent with clinically meaningful tremor-related disability (mean score ≥11.25),[5] and all but 3 studies found mean scores consistent with severe tremor-related disability (mean score ≥20.35)
- There was considerable variability in the reported tremor-specific QoL outcomes, likely due to heterogeneity in study designs and populations

Quality of Life: General Measurement

Figure 5. Mean Physical and Mental Component Summary Scores for ET Patients versus Healthy Controls in Studies Reporting SF-36 Results



*Signifies statistically significant differences between patients with ET and controls, as reported by study authors.
Note: Nguyen 2007 and Shalash 2019 also used the SF-36 in patients with ET and healthy controls, but mean scores for physical and mental component summaries were not reported.
ET, essential tremor; SF-36, 36-Item Short Form Health Survey.

- The most commonly used generic QoL measure was the 36-item Short Form Health Survey (SF-36), and the most commonly used disease-specific measure was the Quality of Life in Essential Tremor (QUEST) Questionnaire (**Figures 4 and 5**)
- Patients with ET consistently scored lower (worse QoL) than unaffected controls on both the physical component summary and mental component summary of the SF-12 and SF-36
- Some variability in generic QoL outcomes was observed across studies, likely due to heterogeneity in study designs and populations

Conclusions

- Patients with ET experience disease-related disability, reduced QoL, and substantial medical and mental health-related comorbidities
- The humanistic burden of ET elucidated by this SR underscores the need for improved patient care, including early diagnosis and effective treatment strategies
- This review identifies substantial inter-study heterogeneity related to study design, patient characteristics, and diagnostic criteria among the published research, thereby indicating gaps in generalizable real-world evidence using robust methods and appropriate study cohorts

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Presented at ISPOR EUROPE 2023; 12–15 November 2023; Copenhagen, Denmark