Substantial Productivity Impairment in Patients with Essential Tremor

Andrew Lee, PhD[1], presenting on behalf of:
Margaret E. Gerbasi[1], **Rodger J. Elble**[2], **Holly A. Shill**[3], **Eddie Jones**[4], **Alexander Gillespie**[4], **John Jarvis**[5], **Elizabeth Chertavian**[5], **Zachary Smith**[5], **Marie-Josee Martel**[1], **Mina Nejati**[6], **Ludy C. Shih**[7,8]

1. Sage Therapeutics, Inc., Cambridge, MA, USA; 2. Southern Illinois University School of Medicine, Springfield, IL, USA; 3. Barrow Neurological Institute, Phoenix, AZ, USA; 4. Adelphi Real World, Adelphi Mill, Bollington, United Kingdom; 5. Medicus Economics, Milton, MA, USA; 6. Biogen, Inc., Cambridge, MA, USA; 7. Boston University School of Medicine, Boston, MA, USA; 8. Boston Medical Center, Boston, MA, USA

PCR36

Introduction

- Essential tremor (ET) is among the most common movement disorders in the US, affecting an estimated 6.8 million US adults.[1,2] Primary manifestations of ET include kinetic and postural tremor.[3]
- Despite this high prevalence, the indirect burden of ET on patients is not well characterized.
- Given the misperception that ET manifests only in older adults, research examining the effect of ET on work productivity is limited.
  - Prevalence estimates reveal that a considerable number of ET patients are 69 years old or younger, making up roughly 50% of those living with ET[2] and about 40% of diagnosed cases[4]. This highlights the potential impact of ET on the working-age population and its implications for productivity.
- To assess the impact of ET on society and the potential for treatments of ET to enhance patient functioning, it is important to understand both the magnitude of indirect burden as well as its association with ET severity.

Objectives

1. Describe the activity impairment in patients with ET
2. Characterize the productivity impact of ET among employed patients
3. Evaluate the association between productivity and activity impairment and measures of ET tremor severity

Methods

- The study used real-world data collected in the US from March 2021 to August 2021 through an Adelphi ET Disease Specific Programme (DSP)™.
  - The DSP collects clinical information reported by treating physicians, information on physician/patient attitudes to treatment, and patient-reported outcomes.[5]
- The Adelphi ET dataset contains de-identified survey data from 1,003 patients diagnosed with ET; of these, 476 completed the patient-reported surveys. Patients with complete data were selected for inclusion in one or both of the following cohorts of interest:
  - Activity Assessment Cohort: Patients with ET who provided Work Productivity and Activity Impairment (WPAI)-based daily activity impairment information.
  - Employed Cohort: Patients with ET from the above cohort who provided WPAI-based complete work productivity information.
- Key measures included:
  - The Essential Tremor Rating Scale (TETRAS), a clinician-administered clinical rating scale composed of:
    - Performance subscale (PS) assessing tremor amplitude. Item 4 of the TETRAS Performance subscale (PS Item 4) measures upper limb tremor (3 maneuvers for each arm assessing postural and kinetic tremor).
    - Activities of Daily Living (ADL) subscale assessing the impact of tremor on speech, upper limb function, and social activities.[6]
  - Patient-reported Quality of Life in Essential Tremor Questionnaire (QUEST)[7]: measure items impacting quality of life, including ADLs that may be affected by ET.
  - Patient-reported employment status (full-time, part-time, retired, unemployed, student).
  - WPAI: Questionnaire measuring impairments in both paid work (absenteeism and presenteeism, e.g., reduced productivity while at work) and unpaid work and activity (i.e., such as household work, shopping, childcare, etc.) because of a health problem during the past seven days.[8]
  - Pearson correlations and regression models, adjusting for relevant covariates (age, employment status, household income, anxiety, and depression), were used to assess associations between productivity and activity impairment and tremor severity as measured by TETRAS ADL, TETRAS PS, and TETRAS PS Item 4.

Results

- **Table 1** presents the characteristics of the 2 cohorts analyzed in this study:
  1. In the Activity Assessment Cohort (N=420), patients were 64.4 years old on average (standard deviation [SD]=13.8), and 47% were female.
  2. In the Employed Cohort (N=165), patients were 55.0 years old on average [SD=10.1], and 41% were female. Most were employed full-time (n=133 [80.6%] vs part-time n=32 [19.4%]).
- The top comorbidities in both cohorts were hypertension, anxiety, hyperlipidemia, and depression.

TABLE 1. DEMOGRAPHICS AND CHARACTERISTICS OF BOTH COHORTS OF PATIENTS WITH ET

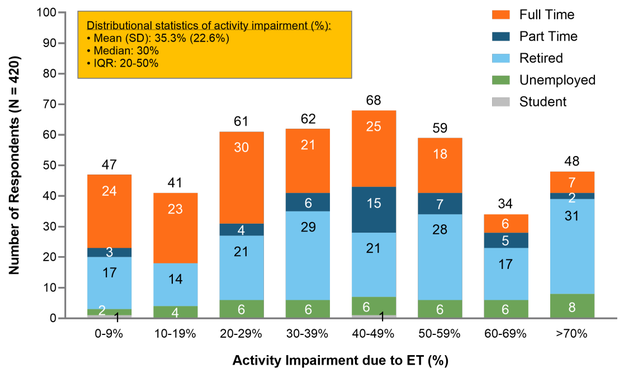
	Activity Assessment Cohort[a] (N=420)	Employed Cohort (N=165)[b]
Sex, n (%)[c]		
Female	198 (47%)	68 (41%)
Age (years), mean (SD)[c]	64.4 (13.8)	55.0 (10.1)
Age category (years), n (%)[c]		
≤18	1 (0.2%)	0 (0.0%)
19-64	191 (45.5%)	139 (84.2%)
≥65	228 (54.3%)	26 (15.8%)
Race / Ethnicity, n (%)		
White	335 (79.8%)	136 (82.4%)
African American	44 (10.5%)	19 (11.5%)
Hispanic	17 (4.0%)	4 (2.4%)
Asian	9 (2.1%)	1 (0.6%)
Other	15 (3.6%)	5 (3.0%)
Insurance coverage, % (n)		
Medicare	211 (50.2%)	18 (10.9%)
Commercial	183 (43.6%)	138 (83.6%)
Medicaid	13 (3.1%)	2 (1.2%)
Other	13 (3.1%)	7 (4.2%)
Employment status, n (%)[c]		
Full time	154 (36.7%)	133 (80.6%)
Part time	42 (10.0%)	32 (19.4%)
Retired	178 (42.4%)	N/A
Unemployed	44 (10.5%)	N/A
Student	2 (0.5%)	N/A
Education level achieved, n (%)		
Less than high school	22 (5.2%)	0 (0.0%)
High school	100 (23.8%)	14 (8.5%)
College degree (2-year bachelor)	155 (36.9%)	89 (53.9%)
College degree (4-year bachelor)	79 (18.8%)	36 (21.8%)
Graduate degree or higher	46 (11.0%)	20 (12.1%)
Other	18 (4.3%)	6 (3.6%)
BMI, mean (SD)	27.0 (4.7)	28.0 (4.9)
Charlson Comorbidity Index (CCI), mean (SD)[d]	0.7 (1.4)	0.4 (1.0)
TETRAS scores, mean (SD)		
TETRAS ADL score	17.4 (9.8)	15.2 (8.4)
TETRAS ADL Composite score[e]	8.6 (8.4)	6.2 (6.8)
TETRAS Performance score	22.7 (11.8)	20.2 (11.0)
TETRAS Performance Item 4 score	9.8 (4.8)	8.9 (4.3)
TETRAS total score	40.1 (20.8)	35.3 (18.7)

Notes:
[a]Table reports characteristics for patients who report activity impairment in the WPAI (Patient-reported, WPAI Q6).
[b]Table reports characteristics for patients who report complete work impairment information in the WPAI (Patient-reported, WPAI Q1, Q2, Q4 & Q5).
[c]In instances where responses differed between physician-reported and patient-reported surveys, responses from the patient-reported surveys were utilized.
[d]Calculated using standard CCI comorbidity weights; see Quan H et al. 2011.[9]
[e]TETRAS ADL Composite score calculated as the sum of scores from TETRAS ADL Items 1 through 11 and TETRAS Performance Item 6, with a range of 0 to 39 for each patient. All items were recoded as follows: 0 (Normal) = 0; 1 (Slight) = 0; 2 (Mild) = 1; 3 (Moderate) = 2; 4 (Severe) = 3.

Activity Impairment

- Most patients with ET (373/420; 88.8%) reported some activity impairment
  - In the Activity Assessment Cohort, the mean activity impairment was 35.3% (SD=22.6%) (**Figure 1**).
  - The Employed Cohort reported a similar pattern of activity impairment (mean activity impairment 29.0% [SD=22.5%]).

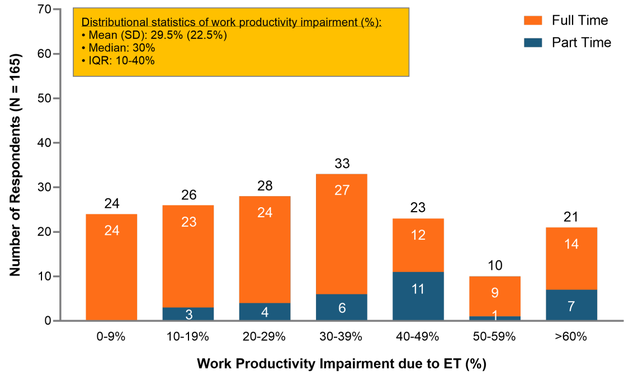
FIGURE 1. ACTIVITY IMPAIRMENT DUE TO ET IN THE ACTIVITY ASSESSMENT COHORT, STRATIFIED BY WORK STATUS



Work Impairment in the Employed Cohort

- Most patients (133/165; 80.6%) were employed full-time and had some level of work impairment (141/165; 85.5%) (**Figure 2**).
- Mean work productivity impairment (absenteeism and presenteeism) among patients was 29.5% (SD=22.5%), representing approximately 12 hours of work-loss per 40-hour workweek.
  - Among employed patients with ET reporting any work productivity impairment, over 90% of the work time lost was due to presenteeism versus absenteeism.

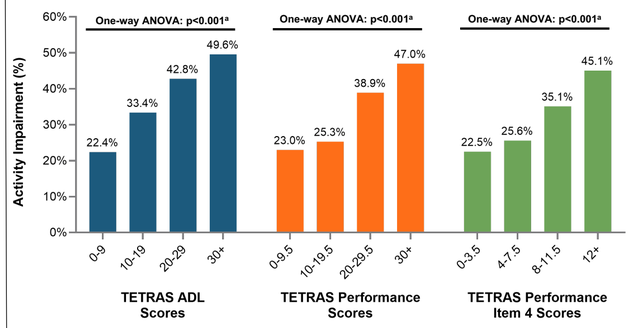
FIGURE 2. WORK PRODUCTIVITY IMPAIRMENT DUE TO ET IN THE EMPLOYED COHORT



Association between activity or work impairment and tremor severity

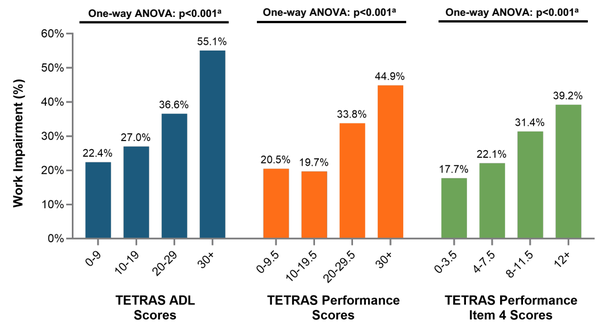
- Activity impairment in the Activity Assessment Cohort was significantly associated with worsening (increasing) TETRAS ADL scores, TETRAS PS, and TETRAS PS Item 4 scores (p<0.001 for trend; **Figure 3A**).
  - Higher patient activity impairment was moderately associated with greater tremor severity (rs=0.37-0.43).
- Work productivity impairment observed in the Employed Cohort was significantly associated with worsening (increasing) TETRAS ADL, TETRAS PS, and TETRAS PS Item 4 scores (p<0.001 for trend; **Figure 3B**).
- The QUEST provided more details to contextualize the impact of ET on working patients. Among those patients for whom QUEST responses were available:
  - 47% (n=64/135) of patients with ET working full-time and 88% (n=36/41) of those working part-time reported that tremor was interfering with work.
  - 61% (n=19/31) of patients with ET working part-time indicated that they were doing so due to tremor.
- Higher patient work productivity impairment was also moderately associated with greater tremor severity (rs=0.32-0.44).
- For both assessments, associations between impairment and TETRAS subscales were moderate and statistically significant in regression modeling.
  - The magnitude of relationships were not impacted by inclusion of covariates (age, full-time vs part-time, household income, depression, anxiety) in regression models.

FIGURE 3A. ACTIVITY IMPAIRMENT BY TETRAS SCORES IN THE ACTIVITY ASSESSMENT COHORT (N=420)



[a]*Statistical analyses tested a global null hypothesis that distributions are equal across the 4 subcategories within a given TETRAS measure. As such, p-values <0.05 indicate that the activity impairment percentage is not equal across the subgroups.*

FIGURE 3B: WORK PRODUCTIVITY IMPAIRMENT BY TETRAS SCORES IN THE EMPLOYED COHORT (N=165)



[a]*Statistical analyses tested a global null hypothesis that distributions are equal across the 4 subcategories within a given TETRAS measure. As such, p-values <0.05 indicate that the work impairment percentage is not equal across the subgroups.*

Limitations

- Given the sample recruitment method, the descriptive data may not be generalizable to all patients with ET.
  - Patients with more severe ET may make more frequent visits to their physician, and therefore may be more likely to be included in the study population.
- These analyses may not capture the full breadth of indirect impacts of ET, given the time horizon considered
  - Individuals who retired early or chose different career paths due to ET may not be represented in the work productivity impact reported here.
- Due to missing information for some questions of the QUEST, only a few questions could be used to provide context to our findings.

Conclusions

- This study showed that more than 4 out of 5 patients with ET have impairment in their daily activities and work, with a substantial portion of patients being younger and employed.
- The large contribution of presenteeism to overall work impairment highlights the risk to significantly underestimate the true impact of ET on indirect disease burden if only absenteeism is considered.
- The association between activity and productivity impairment and tremor severity substantiates the impact of ET on patient functioning and emphasizes the wide-ranging burden of ET.
- Overall, results of this study suggest that improvements in ET care and treatment may help mitigate the indirect burden of ET on patients and society.

Abbreviations

ADL, Activities of Daily Living; CCI, Charlson comorbidity index; DSP, Disease Specific Programme; ET, essential tremor; PS, performance subscale; PS Item 4, Performance Item 4; QUEST, Quality of Life in Essential Tremor Questionnaire; TETRAS, The Essential Tremor Rating Scale; WPAI, Work Productivity and Activity Impairment.

Acknowledgements

Study was funded by Sage Therapeutics, Inc. and Biogen, Inc. Logistical and editorial support was provided by Boston Strategic Partners, Inc. (funded by Sage Therapeutics, Inc. and Biogen, Inc.).

Ethics Approval

This study was approved by the Western Institutional Review Board (protocol number AG-8947).

References

1. Louis ED, McCreary M. *Tremor and Other Hyperkinetic Movements.* 2021; 11(1): 28,1–14.
2. Furtado J, et al. Poster presented at the International Conference on Pharmacoepidemiology & Therapeutic Risk Management; August 23-27, 2023; Halifax, Nova Scotia, Canada
3. Puschmann, A., & Wszolek, Z. K. Seminars in Neurology, 2011; 31(1), 65–77.
4. Saad, M. Markowitz, L. Gibbs, D. Fuller, W. Ni, R. Pahwa, K. Lyons, M. Baladi, J. Lin. Mov Disord. 2022; 37 (suppl 2).
5. P.M. Anderson, et al. *Curr. Med. Res. Opin.* 2008. 24: 3063–3072.
6. Elble RJ. *J Neurol Neuromedicine.* 2016;1:34-38.
7. Tröster et al. *Parkinsonism Relat Disord.* 2005;11(6):367-373.
8. Reilly MC, et al. *PharmacoEconomics* 1993; 4(5):353-65.
9. Quan, H et al. *American journal of epidemiology.* 2001: 173(6):676-682.

Disclosures: MG is an employee of Sage Therapeutics, Inc., and may hold stock and/or stock options. RJE has served as a consultant for Applied Therapeutics, Attune, Clexio, Encora, Fasikl, Jazz, Neurocrine, Praxis Precision Medicines, and Sage Therapeutics, Inc. HAS has received research support from Transposon, Parkinson Study Group/UCB, Parkinson's Foundation, NINDS, Supernus/US World Meds, MJFF, Jazz Pharmaceuticals, Barrow Neurological Foundation and Cerevel Therapeutics. HAS has served as a consultant for the Parkinson Study Group/Nq, Biogen, Abbvie, Sage/Biogen, Praxis, KeifeRx, Fasikl and Jazz Pharmaceuticals. EJ and AG are employees of Adelphi Real World and received no personal compensation for their involvement in this research. JJ, EC, and ZS are employed by Medicus Economics, which received consulting fees from Sage Therapeutics, Inc. and Biogen Inc. MJM is a consultant for Sage Therapeutics. MN is an employee of Biogen Inc. and may hold stock. LCS has received consulting fees from Medtronic, WCG MedAvante, and Encora Therapeutics.

Corresponding author: Margaret E. Gerbasi (Margaret.Gerbasi@sagerx.com)