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## How are We Doing With the Treatment of Essential Tremor (ET)? Persistence of ET Patients on Medication: Data from 528 Patients in Three Settings

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### Abstract

**Background**—The pharmacological treatment of essential tremor (ET) is not optimal. There are only two first-line medications and troublesome side effects are common. It is not uncommon for patients to simply stop taking medication. Yet no published data substantiate or quantify this anecdotal impression.

**Objectives**—To determine, among ET patients who were prescribed medication for tremor, what proportion are still taking medication and what proportion have stopped?

**Methods**—528 ET patients from three distinct study settings (clinical, brain donors, population) were interviewed.

**Results**—A clear pattern that emerged across settings was that the proportion of ET patients who had stopped medication was sizable and consistently similar (nearly one-third): 31.4% (clinical), 24.3% (brain donors), 30.0% (population), 29.8% (overall). A similarly high proportion of cases with severe tremor had stopped their medication: 31.9% (clinical), 36.4% (brain donors). For the four most commonly-used medications (propranolol, primidone, diazepam, topiramate), one-half or more of the treated patients had stopped the medication; among the less commonly used medications, the proportion who stopped was even higher.

**Conclusions**—Nearly one of every three ET patients who had been prescribed medication for tremor had discontinued pharmacotherapy. Even more revealing was that a similar proportion of cases with severe tremor had stopped medication. These data make tangibly evident that there is a sizable population of ET patients who are untreated and disabled, and underscore the inadequacy of current pharmacotherapeutic options for this common neurological disease.

### Keywords

Essential tremor; clinical; treatment; medication

## Introduction

Pharmacological treatment of essential tremor (ET) is not optimal. There remain simply two first-line medications [1], a situation that has not changed in nearly 30 years. Medications are generally considered to be effective in only 50% of patients [2], rarely reduce tremor to asymptomatic levels, and are associated with unwanted side effects. Our impression is that there may be a sizable population of patients untreated, with impaired quality of life and disability. However, there are no published data to substantiate or begin to put a figure on this anecdotal clinical impression. To address this gap in the literature, we asked what proportion of ET patients who were prescribed medication for their tremor are still taking medication and what proportion have stopped? We addressed this question utilizing data available on ET patients from three distinct settings, a clinical sample, a population, and a brain repository, in order to sample a broad spectrum of cases across a variety of settings.

## Methods

528 ET cases from three studies were used, a clinical study in New York, a brain donor study, and a population-based study in northern Manhattan, New York; each study has been described in detail [3]. Cases were asked whether they had ever been prescribed any medication to treat their tremor and whether they were currently taking any medication to treat their tremor. Tremor severity was rated with a total tremor score (range 0 – 36) based on a videotaped neurological examination [3]. All cases signed written informed consent upon enrollment.

## Results

### Clinical sample in New York

82/261 (31.4%) 261 cases who had ever been prescribed medication for their tremor had had stopped medication (Table 1); these did not differ by age, gender, education, tremor duration, or tremor severity from the 179 who had continued medication. Among 69 patients with severe tremor (upper quartile of total tremor score [ $>24$ ]), 22 (31.9%) had stopped medication.

### Future brain bank donors

20/82 (24.3%) cases who had been prescribed tremor medication had stopped medication (Table 1); these did not differ from the 62 who had continued medication. Among 11 patients with severe tremor (upper quartile of total tremor score [ $>27$ ]), 22 (31.9%) had stopped medication. In this sample, data were available on the use of specific medications (Table 2). For the four most commonly-used medications (propranolol, primidone, diazepam, topiramate), one-half or more of the treated patients had stopped the medication; among the less commonly used medications, the proportion who stopped was even higher. Even among patients on newer medications, the proportion who had stopped was approximately 50% or higher.

### Population-based study

Three (30.0%) of 10 cases who had ever been prescribed medication for their tremor had had stopped medication (Table 1).

## Discussion

We examined data on more than 500 ET patients and a clear pattern that emerged across settings was that the proportion of ET patients who had stopped their medication was sizable; nearly one out of every three treatment-eligible ET patient is unmedicated, an indication of the limitations of our current pharmacotherapeutic options. Perhaps more revealing is that a

similarly high proportion of ET cases with severe tremor had stopped their medication, a further indictment of the inadequacy of current medical options. Combining the three samples (n = 528), nearly one-third of the 353 ET cases who had been prescribed medication for their tremor had stopped taking ET medication (105/353 = 29.8%).

In one of our samples, data were available on the use of specific medications. For the four most commonly-used medications (propranolol, primidone, diazepam, topiramate), one-half or more of the treated patients had stopped the medication; among the less commonly used medications, the proportion who stopped was even higher. Even among patients on newer medications, the proportion who had stopped was high.

How do these results compare to patients with other chronic conditions? Studies of other chronic conditions indicate that a sizable proportion of patients stop taking medication. A study of persistence on lipid lowering therapies after stroke found that 39% of patients had discontinued therapy one year after discharge [4]. Mild side effects were the most commonly supplied reason for discontinuation; lack of efficacy was not a reason [4]. In a study of patients with Type II diabetes mellitus, nonpersistence on medications was 37.0% at one year [5]. In a study of patients with hypertension [6], 14% reported that they had stopped taking their medication. Among this 14%, 46% has stopped medication because they believed that their blood pressure had normalized and that they were cured; however, none reported doing so due to lack of efficacy.

A limitation of this study is that we did not collect data on the reason for stopping medications; hence we are unable to elaborate on the reasons for discontinuing drugs. In general, the most likely reason for stopping medications is intolerable side effects; however, limited therapeutic efficacy is another likely reason in ET. Studies of medical adherence in patients with other conditions (e.g., hypertension), indicate that among the most common reasons for non-adherence are side effects ascribed to medication and general dislike of drugs [7] as well as perceived low medication efficacy [8].

This study had limitations. As noted above, we did not collect data on reason for medication discontinuation and hope that this study will stimulate future collection of such data. Also, our data were cross-sectional. Collection of prospective, longitudinal data would be of additional value as it would avoid problems with retrospective recall.

Nearly one out of every three treatment-eligible ET patient is unmedicated and one-third of cases with severe tremor were unmedicated. These data both make evident that current pharmacotherapeutic options for ET are severely limited, and they provide further impetus to advance the current state of treatment.

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**Table 1**

Data from three studies of essential tremor

	Clinical sample in New York	Future Brain Donors	Population-based study in New York
Number of ET cases	328	94	106
Age (years)	67.8 ± 15.0	74.1 ± 10.1	69.8 ± 18.4
Women	174 (53.0%)	57 (60.6%)	63 (59.4%)
Education (years)	15.0 ± 3.8	NA	NA
Education	NA		NA
High school graduate		92 (97.9%)	
Bachelor's degree		49 (52.1%)	
Total tremor score	19.8 ± 7.0	19.7 ± 6.6	16.4 ± 6.7
Tremor duration (years)	23.8 ± 18.9	40.0 ± 20.3	15.4 ± 18.8
Family history of ET or tremor**	213 (64.9%)	76 (88.3%)*	34 (32.1%)
Ever prescribed medication for tremor	261/328 (79.6%)	82/94 (87.2%)	10/106 (9.4%)
Currently taking medication for tremor	179/328 (54.6%)	62/94 (66.0%)	7/106 (6.6%)
Proportion of those ever prescribed medication who are currently taking medication for tremor	179/261 (68.6%)	62/82 (75.7%)	7/10 (70.0%)
Proportion of those ever prescribed medication who are no longer taking medication for tremor	82/261 (31.4%)	20/82 (24.3%)	3/10 (30.0%)

\* 86 of 94 cases knew their family history.

NA = data not available.

Values are mean ± SD or proportion (percentage).

\*\* ≥1 first-degree relative with ET or tremor.

**Table 2**

Use of specific medications among 82 future brain donors

Medication	Proportion of cases who had been prescribed the medication and remained on it	Proportion of cases who had been prescribed the medication and had stopped it
Propranolol	34/66 (51.5%)	32/66 (48.5%)
Primidone	19/45 (42.2%)	26/45 (57.8%)
Diazepam	3/30 (10.0%)	27/30 (90.0%)
Topiramate	7/13 (53.9%)	6/13 (46.1%)
Phenobarbital	0/8 (0%)	8/8 (100%)
Gabapentin	1/7 (14.3%)	6/7 (85.7%)
Clozapine	0/6 (0%)	6/6 (100%)
Mirtazapine	1/4 (25.0%)	3/4 (75.0%)
Acetazolamide	0/1 (0%)	1/1 (100%)

Some patients had used >1 medication.