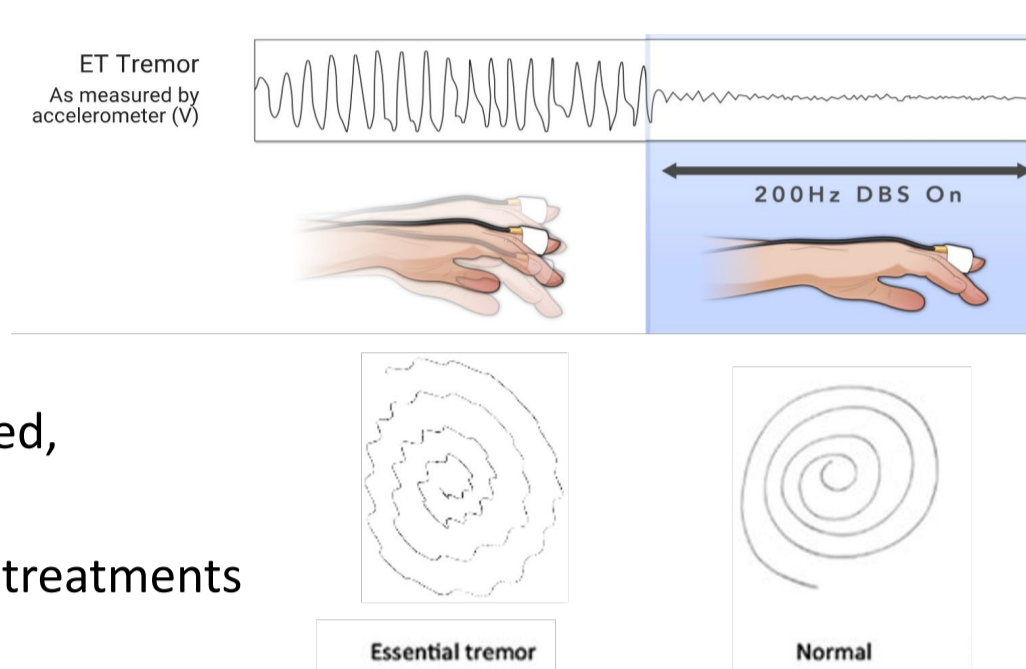


Background

- Essential tremor (ET) is the most common movement disorder and is typically marked by tremor in the upper limbs, but may also involve the head, voice, lower limbs, and trunk.¹⁻³
- In the US, ~7 million people have ET, representing more than 2% of the total population.^{4,5}
- Patients with ET are frequently undiagnosed, misdiagnosed, undertreated, or untreated.
- Importantly, the number of available ET pharmacological treatments remains limited, with only one FDA-approved option.⁶
- Pharmacological and surgical options have undesirable side effect profiles, high discontinuation rates, and limited and conflicting efficacy.¹
- There is a need for greater understanding of ET and its impact on patients in a real-world setting.
- The objective of this study was to describe the attributes of patients with ET, associated comorbidities, and ET treatments by evaluating a large US insurance claims database.



Methods

Data Source

- This retrospective observational study examined medical and prescription claims from the Compile database,⁷ which captures over 27 billion claims since 2015 for ~300 million unique patients.
- Data focused on disease burden and treatment experience were derived from a range of payer systems, including commercial plans, Medicare, Medicaid and Veteran's Affairs.
- ET diagnoses, comorbidities, and treatments used were assessed for 2019, and analysis of longitudinal patterns before and after ET diagnosis incorporated data from 2015-2019.

Patient Selection

Primary Study Cohort and Total Cohort

- The primary study cohort comprised patient data for the year 2019 (January 1 to December 31, 2019).
- The total cohort included unique patients with ET claims from 2015 to 2019 (2015-2016; 2017-2018; 2019) plus projected estimates for the period before 2015.
- For each cohort, total, possible, and confirmed ET cases were identified.
 - Possible ET** was identified by presence of at least 1 ICD-10 code of G25.0 (ET diagnosis), but not meeting criteria for confirmed cases
 - Confirmed ET** was defined based on presence of an ICD-10 code (G25.0) plus at least 2 relevant ET prescriptions, or 2 ICD-10 codes (G25.0 and R25.1 for unspecified tremor) at least 90 days apart.
 - Total ET** included all cases with at least 1 ICD-10 code (G25.0) and represented the sum of possible and confirmed ET.

Pre- and Post-diagnosis Cohorts

- Longitudinal data spanned from January 1, 2015, to December 31, 2019
- The pre-diagnosis cohort included patients with claims data for ≥46 months prior to the first ET diagnosis in the database.
- The post-diagnosis cohort included patients with claims data for ≥36 months after the first ET diagnosis.
- Eligible patients had a claim for a diagnosis, prescription, or procedure in ≥1 quarter of each year.
- In the pre-diagnosis cohort, data were collected for the presence of the following initial movement disorders before patients were diagnosed with ET (cerebral palsy, dystonia, other tremor, Parkinson's disease, and unspecified tremor).

Outcome Measures

- Patient demographics and comorbidity and treatment data are presented for the primary study cohort, and further for the pre- and post-diagnosis cohorts.
- Demographic data (age, sex, primary payer) were collected from the first ET diagnosis claim, while comorbidity and treatment data were collected in 6-month intervals for 46 months or 36 months, respectively.

Projection Analysis

- Based on an assumption that the claims database captures ~60% of the US population,⁷ projected estimates for possible and confirmed ET diagnoses were extrapolated to the total US population for the primary study cohort (2019) and for the longitudinal cohort (2015 through 2019).

ET Diagnoses

- A total of 353,822 patients with an ET diagnosis were identified for the year 2019 (Table 1).
 - Corresponding to a total projected US diagnosed estimate of 589,704 patients.
- A total of 1,336,183 patients with an ET diagnosis were identified between 2015 and 2019 (Table 1).
 - Corresponding to a total projected US diagnosed estimate of 2,226,971 patients.

Table 1. ET Diagnoses by Study Cohort and the US Population Projections

	Claims Database, N	Projected US Population Estimates, N
2019 Patients Diagnosed with ET	353,822	589,704
Possible ET	225,559	375,932
Confirmed ET	128,263	213,772
2015-2019 Patients Diagnosed with ET*	1,336,183	2,226,971
Possible ET	876,595	1,460,991
Confirmed ET	459,588	765,980

*Total includes unique patients with ET claims from 2015 through 2019, including projected pre-2015 patients

Demographics and Time to Diagnosis

- Patient demographics within the primary study cohort (2019) and the pre- and post-diagnosis cohorts (2015-2019) are presented in Table 2.
- Within the primary study cohort, a total of 128,263 patients had a confirmed ET diagnosis.
 - Of these, 25% received their first ET diagnosis that year, 75% were ≥65 years, and 57% were female.
- Analysis of pre- and post-diagnosis cohorts included 25,039 and 46,169 patients with ET, respectively.
 - Within both cohorts, ~75% of patients were ≥65 years, and ~60% were female.
- The median time to ET diagnosis was 477 days from initial diagnosis as other movement disorder, 441 days for other tremor, and 406 days for unspecified tremor.

Table 2. Demographic Characteristics of Patients with Essential Tremor by Study Cohort

Characteristic	Primary Study Cohort (2019)		Longitudinal Cohort (2015-2019)	
	Confirmed ET (N=128,263)	Pre-Diagnosis (N=25,039)	Pre-Diagnosis (N=25,039)	Post-Diagnosis (N=46,169)
Age group, n (%)				
<44	5,909 (5)	1,008 (4)	1,008 (4)	2,148 (5)
45-54	7,131 (6)	1,427 (6)	1,427 (6)	3,100 (7)
55-64	18,742 (15)	3,858 (15)	3,858 (15)	7,539 (16)
65-74	42,144 (33)	8,304 (33)	8,304 (33)	16,093 (35)
75-84	38,375 (30)	7,469 (30)	7,469 (30)	13,004 (28)
85+	15,962 (12)	2,973 (12)	2,973 (12)	4,285 (9)
Sex, n (%)				
Female	72,494 (57)	14,879 (59)	14,879 (59)	26,820 (58)
Male	55,769 (43)	10,160 (41)	10,160 (41)	19,349 (42)
Primary payer, n (%)				
Commercial	23,878 (19)	4,349 (17)	4,349 (17)	8,167 (18)
Medicaid	3,047 (2)	603 (2)	603 (2)	1,249 (3)
Medicare	100,134 (78)	19,503 (78)	19,503 (78)	33,396 (72)
Veteran's Affairs/others	1,151 (1)	262 (1)	262 (1)	622 (1)
Missing	53 (<0.01)	322 (1)	322 (1)	2,735 (6)

Comorbidities and Treatments

Comorbidities

- Primary study cohort: 123,263 (96%) patients had at least 1 comorbidity (Fig. 1).

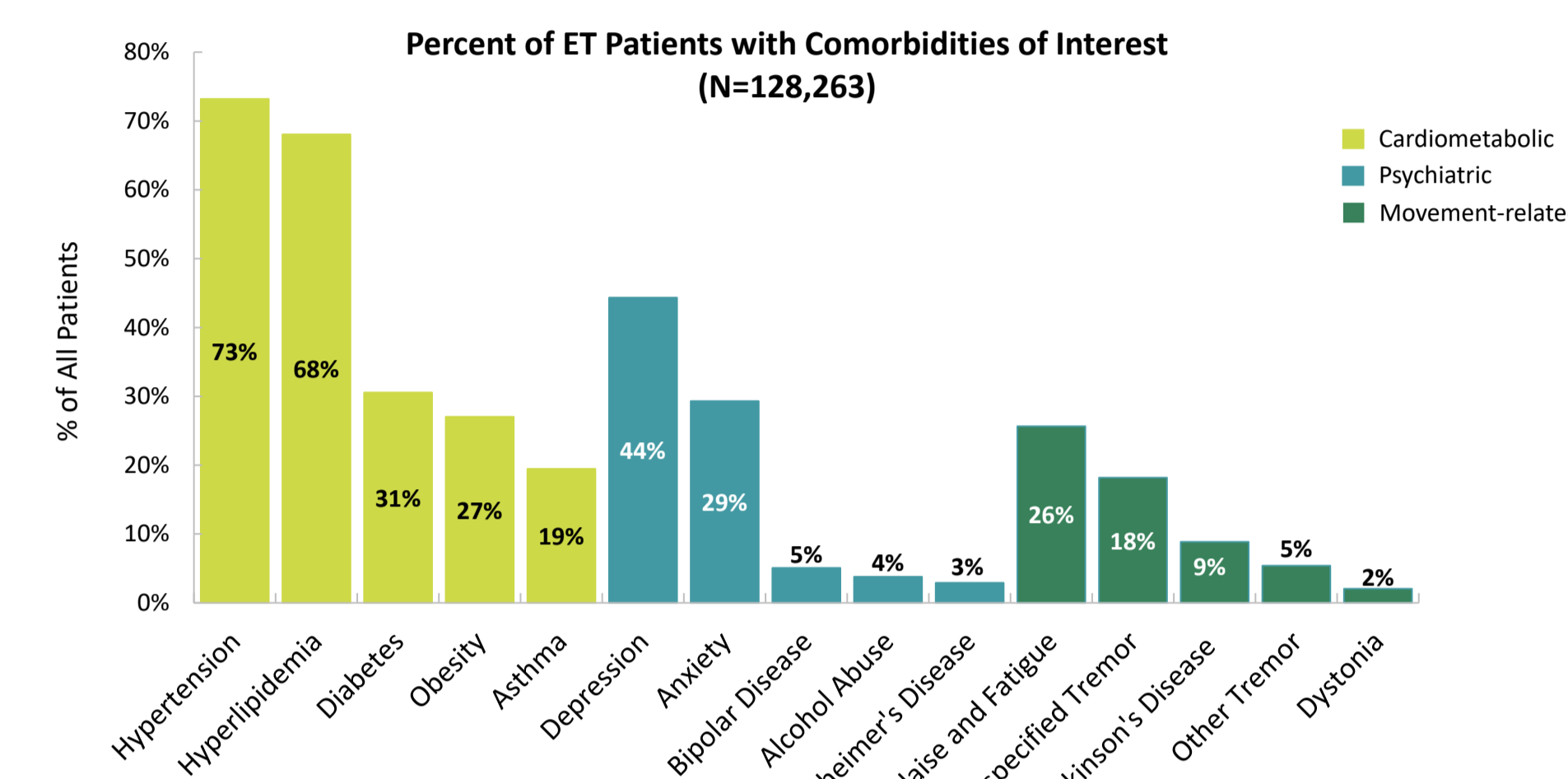


Figure 1. Comorbidities in Patients with Confirmed ET in Year 2019

- Pre-diagnosis cohort: claims for common cardiometabolic, psychiatric, and movement-related comorbidities continued to increase until ET diagnosis.
 - The percentage of patients with anxiety doubled (10-20%) at 48-42 months before diagnosis to within 6 months before diagnosis; depression rates increased from 31 to 42%.
- Post-diagnosis cohort: claims for common cardiometabolic, psychiatric, and movement-related comorbidities increased slightly 0-6 months post-diagnosis, becoming relatively stable up to 36 months post-diagnosis.

Pharmacological Treatments

- Primary study cohort: 82,323 (64%) patients received at least 1 pharmacological treatment (Fig. 2).

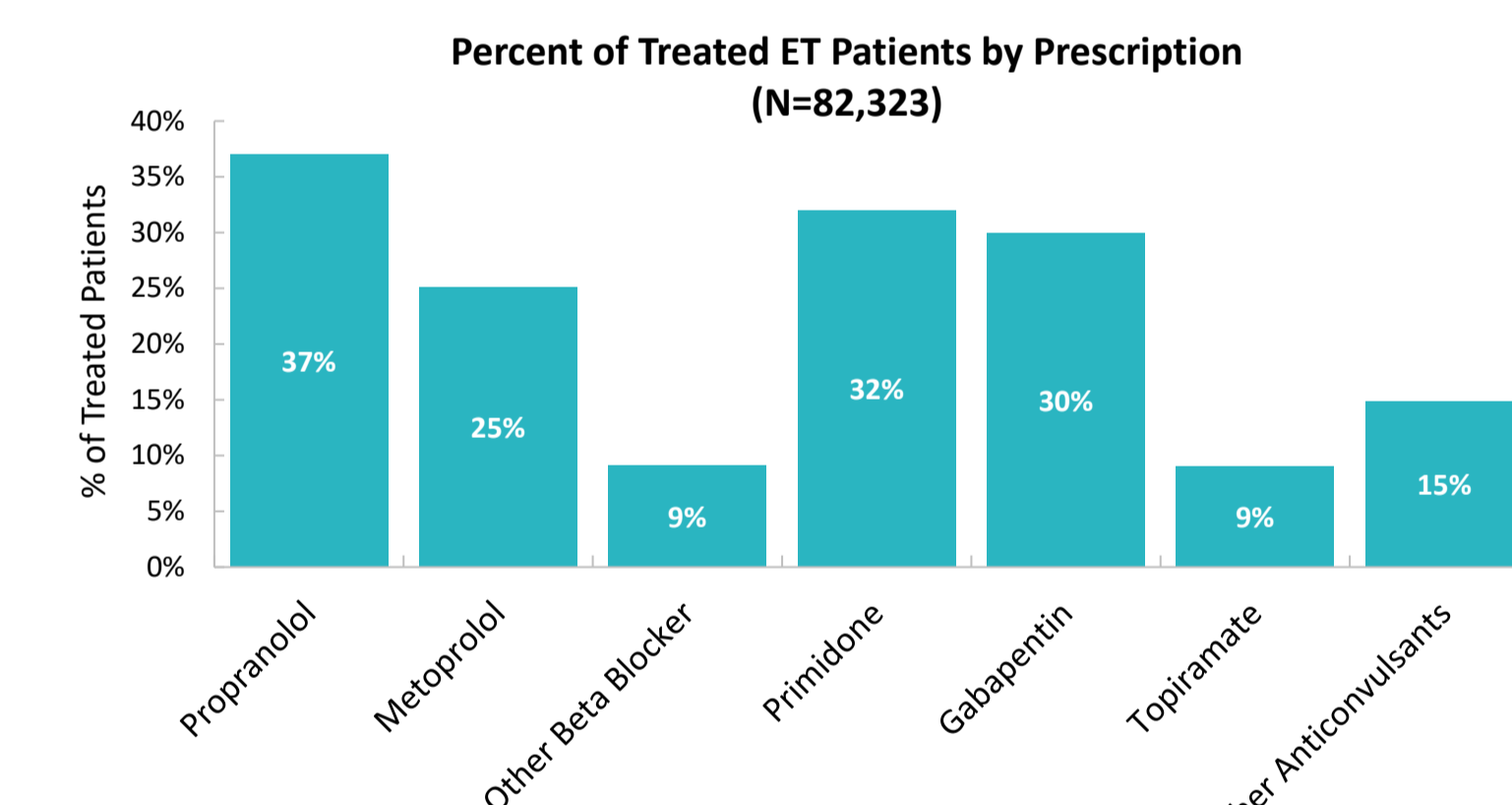


Figure 2. Treatments Prescribed to Patients with Confirmed ET in 2019

- In the pre-diagnosis cohort, 8-13% received propranolol and 6-10% received primidone from 48 months to within 6 months of ET diagnosis, with a slight increase in prescription utilization closer to ET diagnosis.
- In the post-diagnosis cohort, 17-20% received propranolol and 15-21% received primidone, with a slight decline in prescription utilization as the timeline progressed through 36 months post diagnosis.

Conclusions

- Claims-based analysis revealed ~1 million people were diagnosed and actively sought treatment for ET in the US from 2015-2019; however, projected population estimates of ~2 million diagnosed suggest a further 1 million remain untreated.
- While 2 in 3 patients receive pharmacological treatment for ET, primarily propranolol or primidone, discontinuation rates are high. Notably, prescribing patterns vary between neurologists and non-neurologists; the latter more likely to prescribe beta-blockers.
- Patient care in ET is complex, and complicated by a range of factors including delayed diagnoses, multiple comorbidities, as well as a lack of effective and tolerable therapies that can mitigate treatment adherence limitations.
- This complexity underscores the hidden impact on patients with ET and highlights the urgent unmet need for more efficient diagnosis and treatment options.

Prescription Patterns and Persistence

Prescribing Patterns

- Primary care providers (PCP), neurologists, and internal medicine (IM) specialists prescribed most ET treatments in 2019 (Fig. 3, right).
- Non-neurologists were more likely to prescribe propranolol and other beta-blockers, while neurologists were more likely to prescribe primidone (Fig. 3, bottom).

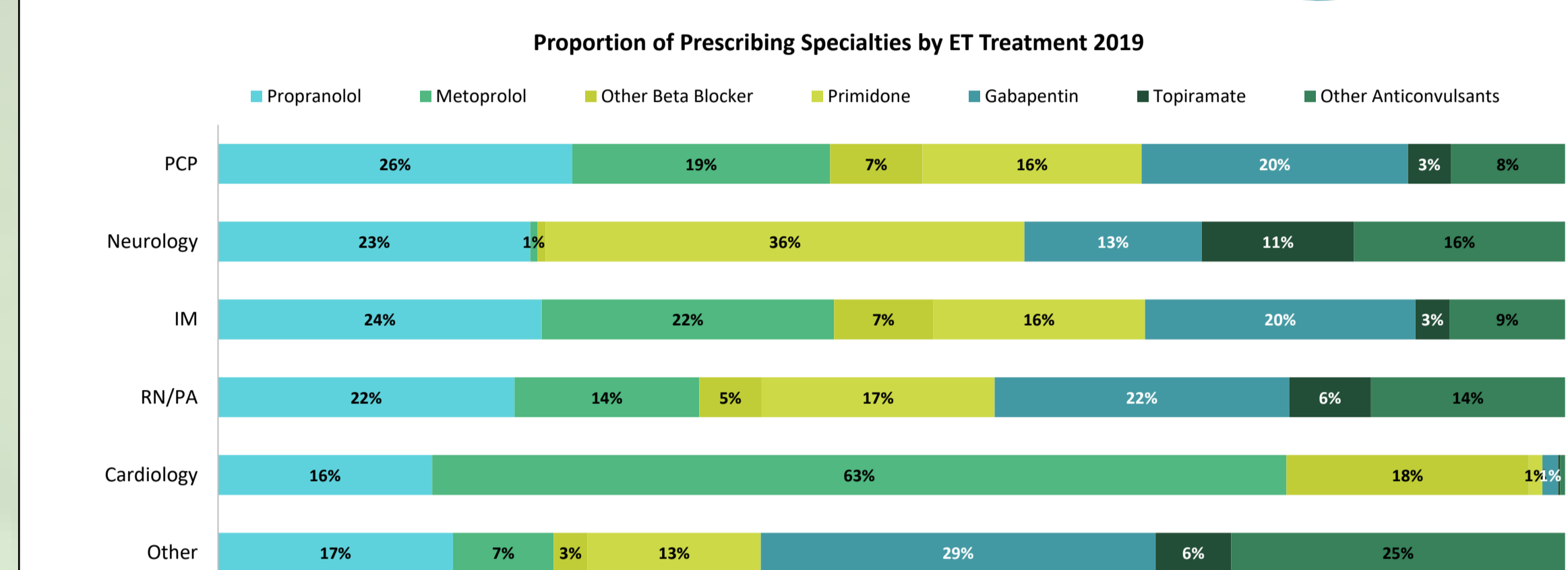
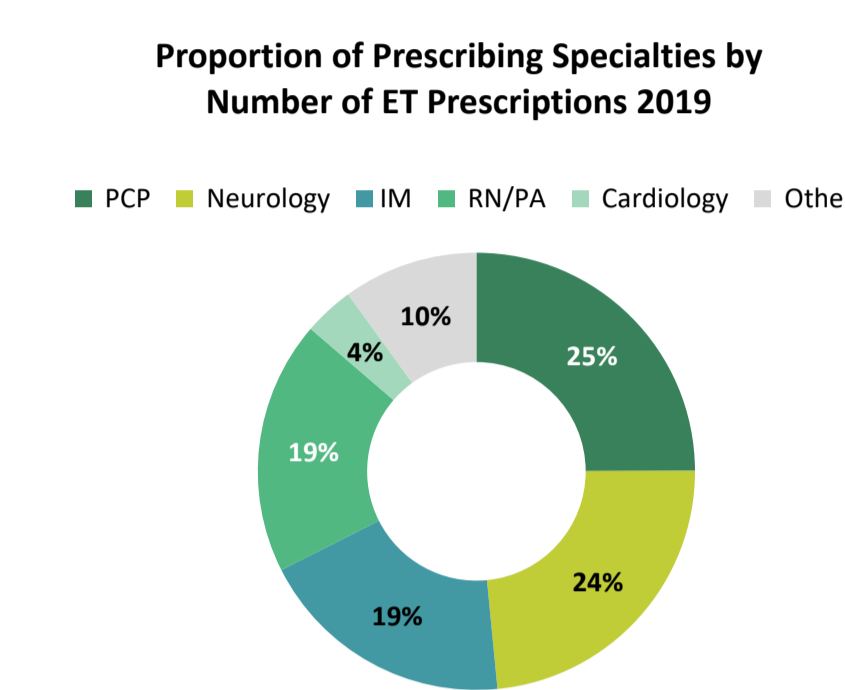


Figure 3. Prescription Patterns in Patients with Confirmed ET

PCP, primary care provider; IM, internal medicine; PA, physician assistant; RN, registered nurse.

Prescription Persistence

- Persistence analysis was applied to the use of the most frequently utilized prescriptions for ET starting within 0-6 months after ET diagnosis.
- The median prescription persistence was 27 months for primidone and 32 months for propranolol.
- By 2 years, the discontinuation rate was 40% for propranolol and 47% for primidone (Fig. 4).

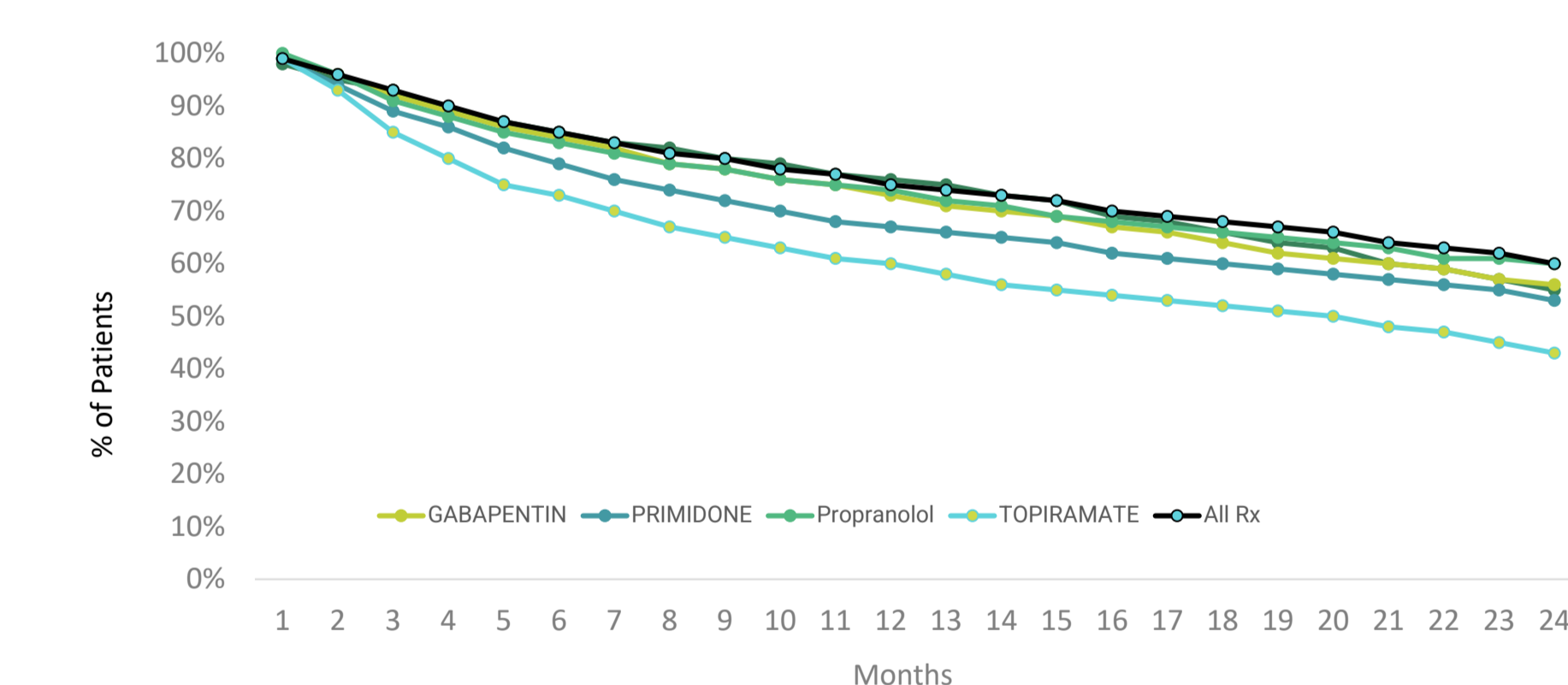


Figure 4. Prescription Persistence by Two Years of Treatment

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