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TREATMENT COST OF THERAPEUTIC PLASMA EXCHANGE VERSUS IMMUNOGLOBULINS IN AN OUTPATIENT SETTING

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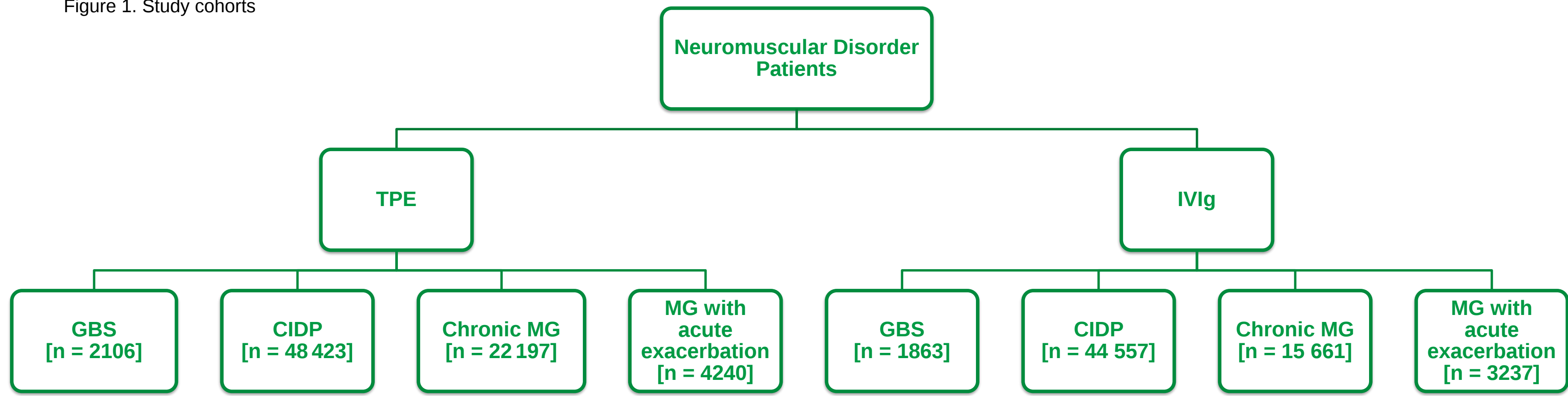
BACKGROUND

- Neuromuscular diseases are a broadly defined group of disorders that involve injury to or dysfunction of the peripheral nerves and/or neuromuscular junction with subsequent impairment of muscular function.¹⁻³
- Several of these disorders are immune-mediated, including myasthenia gravis (MG), chronic inflammatory demyelinating polyneuropathy (CIDP), and Guillain-Barré syndrome (GBS).¹⁻³
- Immune-modulating therapies, including therapeutic plasma exchange (TPE) and intravenous immunoglobulin (IVIg), have been found to be effective disease-stabilizing therapies for patients diagnosed with these immune-mediated neuromuscular diseases.⁴
 - IVIg is a biological product obtained through fractionation of blood in patients.
 - TPE is a blood separation technique to remove plasma that includes autoantibodies.
- To date, neither TPE nor IVIg has demonstrated clinical dominance for the treatment of immune-mediated neuropathies.
 - TPE and IVIg are considered to have equivalent efficacy for the selected immune-mediated neuropathies, and treatment selection is often based upon physician or patient preference, availability, underlying disease risk factors, or contraindications.

OBJECTIVE

- The objective of this study is to evaluate the treatment cost of therapeutic plasma exchange (TPE) and intravenous immunoglobulins (IVIg) for the rare diseases myasthenia gravis (MG), Guillain-Barré syndrome (GBS), and chronic inflammatory demyelinating polyneuropathy (CIDP) in outpatient settings [Figure 1].

Figure 1. Study cohorts



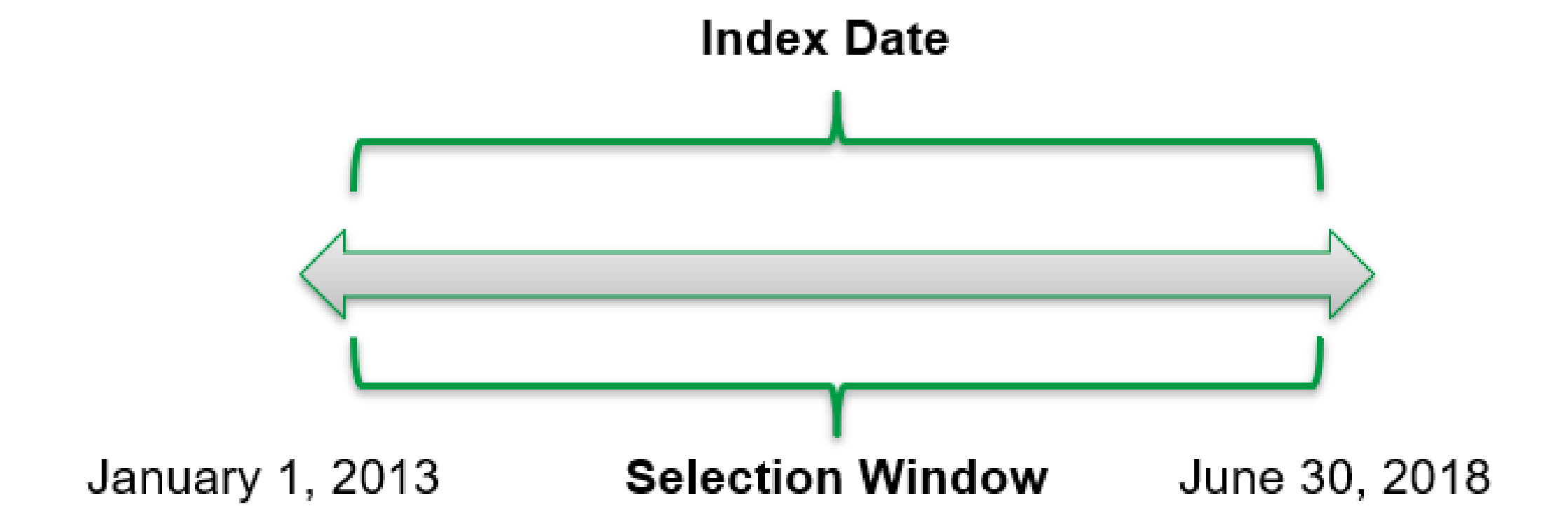
STUDY DESIGN AND DATA SOURCE

- A retrospective cohort study design utilizing hospital discharge records in the Premier Healthcare Database (PHD) was used to conduct this study.
 - At the time the study was conducted, PHD contained data from more than 900 million patient encounters that accounted for one in every four hospital discharges in the US.

POPULATION AND TIME PERIOD

- The study included adult patients with an outpatient encounter between January 1, 2013 and June 30, 2018 with a primary or secondary discharge diagnosis code of GBS, CIDP, or MG (with or without exacerbation) and at least one TPE or IVIg treatment during the encounter [Figure 2].

Figure 2. Study time period



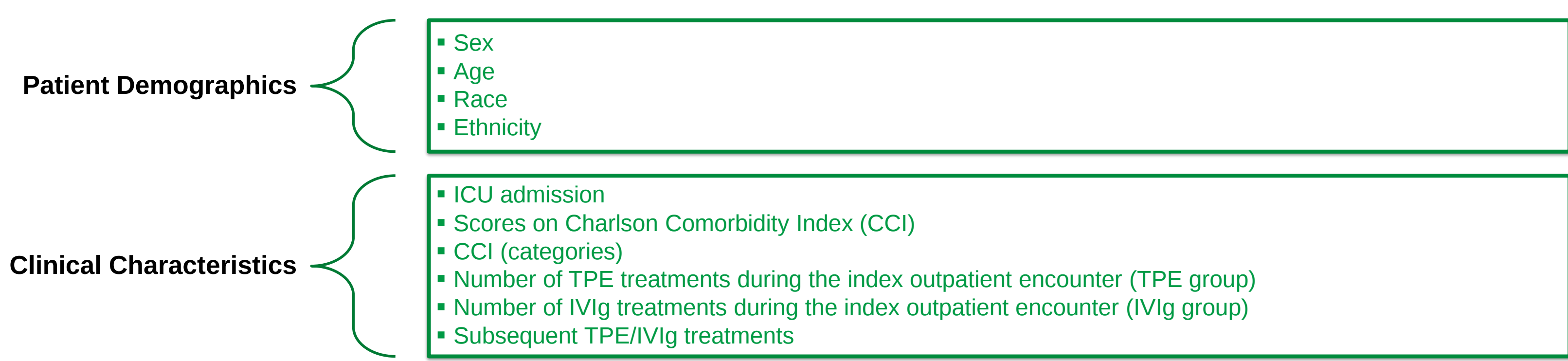
EXPOSURE AND OUTCOMES

- The study exposure included patients' receipt of either TPE or IVIg during an eligible outpatient encounter.
 - TPE or IVIg therapy was defined using a combination of either ICD-9/10 diagnosis or procedure codes, CPT codes, HCPCS codes, and charge master descriptions.
- The study outcomes included:
 - Total hospital costs during an index outpatient encounter
 - Total therapy costs during an index outpatient encounter

MEASURES

- Selected patient demographic and clinical characteristics variables were collected [Figure 3].

Figure 3. Study measures



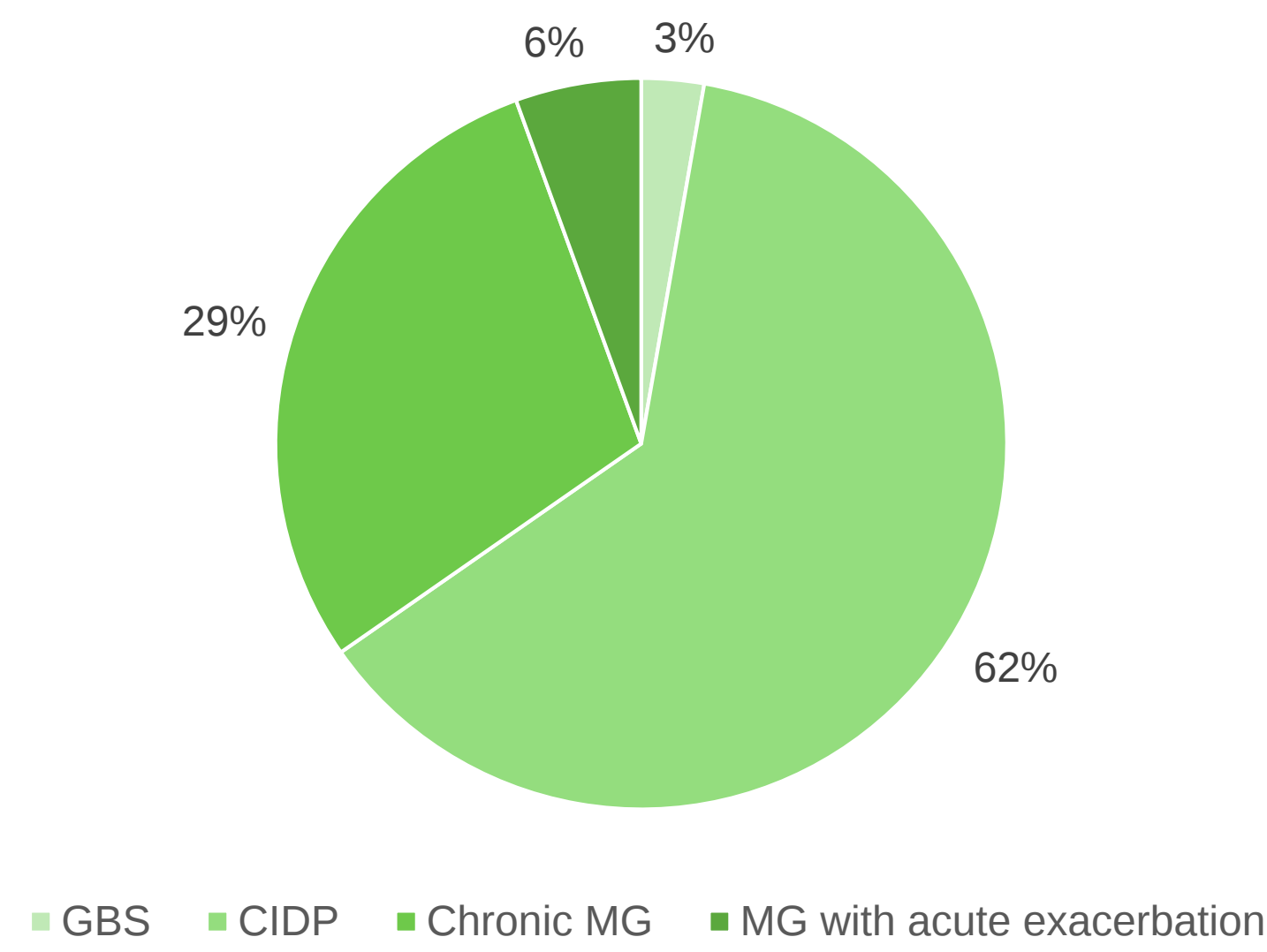
COST ANALYSIS

- Adjusted models were developed for the following outcomes:
 - Total cost of index outpatient encounters
 - Total cost of therapy during index outpatient encounters
- Generalized linear regression models with gamma link function were constructed to determine differences in the two cost-related outcomes between index outpatient encounters on TPE and IVIg therapy.
- Adjusted means with 95% CI were reported.
- Variables that were found to be significant in bivariate analyses were included for adjustment in the regression models.
 - All regression models were assessed for fitness and convergence of algorithm.
 - Regression diagnostics were conducted to assess multicollinearity between independent variables and did not warrant exclusion of any variables.
- Outliers for study outcomes, defined as being above the 99th percentile and below the 1st percentile were assessed and excluded from the regression models. $P < 0.05$ was used for making statistically significant inferences.
- All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

- Out of 76 966 outpatient encounters that were identified, CIDP accounted for the majority (62.9%), followed by MG (28.8%) and MG with acute exacerbation (5.5%) [Figure 4].

Figure 4. Outpatient encounters for selected neuromuscular disorders (n = 76 966).



- Most patients were treated with IVIg [Table 1].

Table 1. TPE/IVIg therapy in patients diagnosed with selected immune-mediated neuromuscular conditions (n = 76 966).

	Total	TPE		IVIg	
		n	%	n	%
GBS	2106	243	11.5%	1863	88.5%
CIDP	48 423	3866	8.0%	44 557	92.0%
MG	22 197	6536	29.4%	15 661	70.6%
MG with acute exacerbation	4 240	1003	23.7%	3237	76.3%

- In each of the evaluated clinical indications, the treatment cost for TPE was significantly lower than for IVIg ($P < 0.01$) [Table 2].
- Depending on the indication, savings up to 66% of treatment cost are possible when TPE is used instead of IVIg.

Table 2. Unadjusted and adjusted cost-related outcomes between outpatients diagnosed with selected neuromuscular conditions with receipt of TPE versus IVIg (n = 15,110).*

	Unadjusted Estimates			Adjusted Estimates		
	IVIg	TPE	P value	IVIg	TPE	P value
GBS	\$5487 (\$6814)	\$1405 (\$1491)	-	\$5718 (\$4076-8021)	\$1377 (\$876-2163)	<0.0001
CIDP	\$5962 (\$7625)	\$2132 (\$5493)		\$2505 (\$2264-2771)	\$788 (\$692-897)	<0.0001
MG	\$5939 (\$8821)	\$1521 (\$1968)		\$1430 (\$1293-1581)	\$362 (\$319-410)	<0.0001
MG with acute exacerbation	\$5948 (\$5598)	\$1759 (\$1645)		\$5903 (\$4735-7359)	\$1855 (\$1396-2466)	<0.0001

*GBS: Adjusted for age (in category), race, admission source, admission type, discharge status, ICU admission, myocardial infarction (MI), congestive heart failure (CHF), cerebrovascular disease, chronic obstructive pulmonary disease (COPD), ulcer, diabetes mellitus (DM), DM with chronic complications, hemiplegia, renal disease, CCI (in category), end stage renal disease (ESRD) at point of admission, sepsis at point of admission, invasive mechanical ventilation, hospital geographic region, number of beds, teaching status, and urbanicity.
CIDP: Adjusted for admission type, ICU admission, MI, renal disease, ESRD at point of admission, hospital geographic location, number of beds, and urbanicity.
MG: Adjusted for age (in category), admission source, admission type, cerebrovascular disease, COPD, ulcer, renal disease, hospital geographic location, number of beds, and teaching status.
MG with acute exacerbation: Adjusted for admission source, admission type, discharge status, ICU admission, CHF, peripheral vascular disease, DM, renal disease, ESRD at point of admission, sepsis at point of admission, invasive mechanical ventilation, hospital geographical region, number of beds, and teaching status.

LIMITATIONS

- Similar to all retrospective studies that utilize administrative claims data or hospital databases, this study has limitations that merit consideration:
 - Hospital-reported data was used to define the study variables and outcomes and was subject to potential reporting bias.
 - The Premier Health Database included follow-up only of patients who returned to the same facility (Premier member hospital), possibly resulting in underestimation of the readmissions.
 - Cost data has been assessed only at the hospital level and no attempt has been made to validate it at the patient level.
 - The assignment of immune-modulating therapy (TPE versus IVIg) to patients was not at random and might have been subject to selection bias.
 - Several covariates were adjusted in the models; however, a possibility of unmeasured or residual confounding cannot be ruled out.

CONCLUSIONS

- Hospitals providing TPE are likely to experience savings in their treatment costs.
- Reviewing data about outpatient encounters with a diagnosis of one of four selected neuromuscular conditions (GBS, CIDP, and MG without and with acute exacerbation) in the PHD, therapy costs with TPE were found to be significantly lower than those with IVIg.
- This has translated into similar cost patterns in total hospital/encounter-related costs, where significantly lower hospital/encounter-related costs were found among patients who received TPE compared to those who received IVIg.
- Future studies could be conducted to evaluate the comparative effectiveness of TPE and IVIg with clinical outcomes.

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