



# Rate of rehabilitative surgeries in patients with thyroid eye disease treated with intravenous steroids versus teprotumumab



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## INTRODUCTION

- Thyroid eye disease (TED) is an inflammatory disease that can be sight-threatening and disfiguring. Moderate/severe TED is treated medically in the active phase followed by surgery (orbital decompression, strabismus repair, eyelid surgery) in the chronic phase.
- Teprotumumab was the first FDA-approved treatment for TED in 2020 after showing significant improvement in proptosis, diplopia, clinical activity score and quality of life against placebo in RCTs of patients with moderate/severe, active TED<sup>1,2</sup>.
- Intravenous (IV) steroids were the standard of care for active moderate/severe TED prior to teprotumumab. Whether teprotumumab reduces rehabilitative surgery rates compared to IV steroids has not been studied.

## OBJECTIVE

This study aims to compare rehabilitative surgery rates within 18 months of treatment initiation in patients with TED treated with a course of teprotumumab versus IV steroids at our center as well as nationally.

## METHODS

- Retrospective cohort study of adults with Graves' and TED treated at Stanford University Medical Center from 2015-2023 with a complete course of IV steroids (12 weekly infusions) or teprotumumab (8 infusions) with 18 month follow-up after treatment initiation.
- The Atropos Health clinical informatics platform was used for patient identification, cohort building and analysis. ICD10 and CPT codes of de-identified electronic health records were used to identify patients:
  - Patients with Graves' and TED were identified using codes for thyrotoxicosis (E05.0, E05.8, and E05.9) combined with codes associated with TED symptoms.
  - Patients treated with teprotumumab were identified with teprotumumab-specific RxNorm codes (2619146 and 2274807).
  - Patients treated with IV steroids were identified with IV methylprednisolone medication codes after patients with common diagnoses associated with IV steroid therapy, such as other prevalent autoimmune diseases and cancer, were excluded. Patients with any history of teprotumumab treatment were also excluded.
- Logistic regression with inverse probability of treatment weighting was used to compare association between treatment and surgical rates. Inverse probability of treatment weighting (IPTW) was utilized to match propensity scores on pre-treatment characteristics including diagnoses, procedures, medications, and comorbidities.
- The study was replicated in the EVERSANA EHR national dataset. This is sourced from >2000 ambulatory health centers and >30 health systems and represents >130 million patients throughout the United States.

## RESULTS

Figure 1. Baseline patient characteristics at Stanford

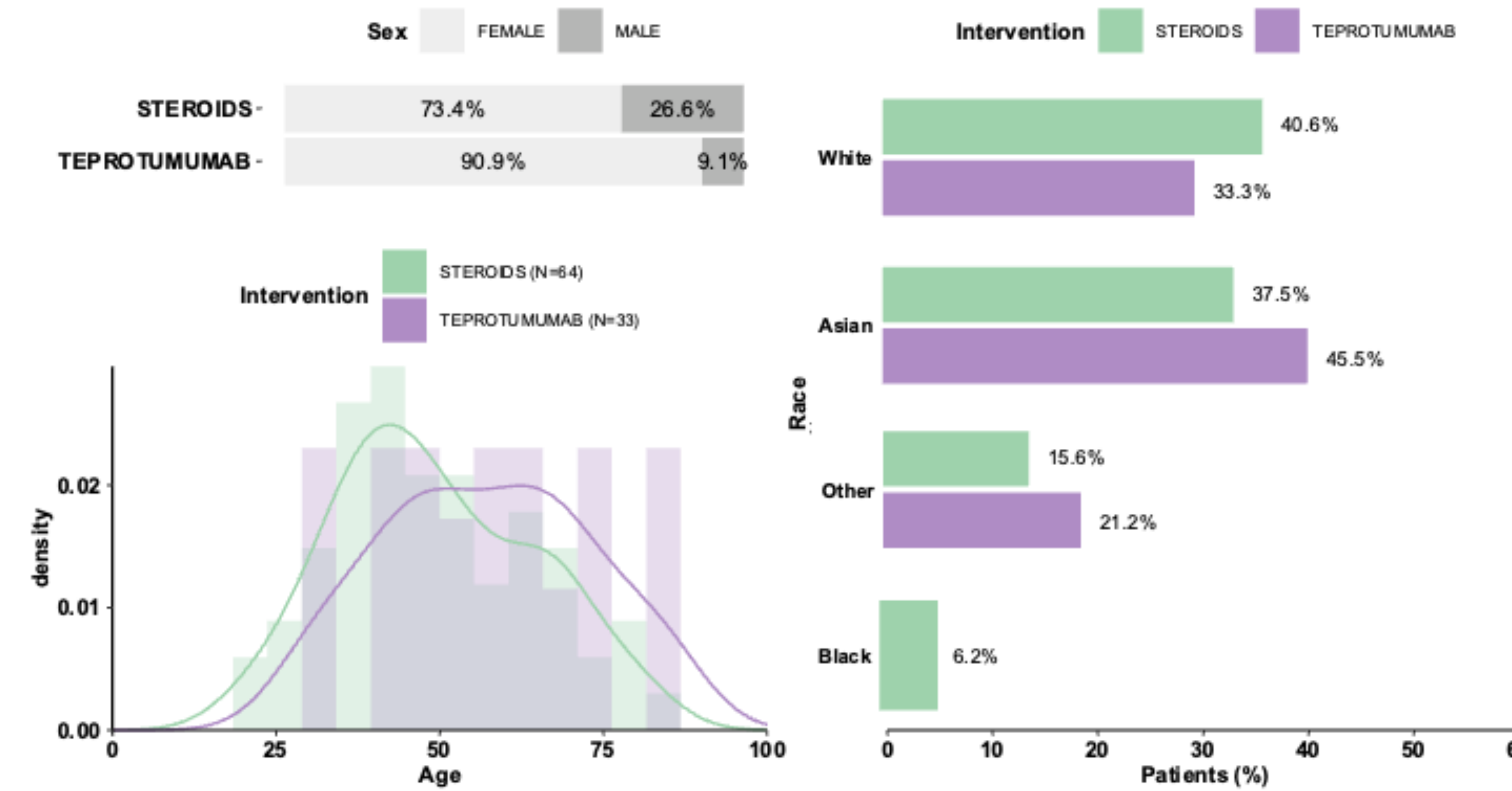
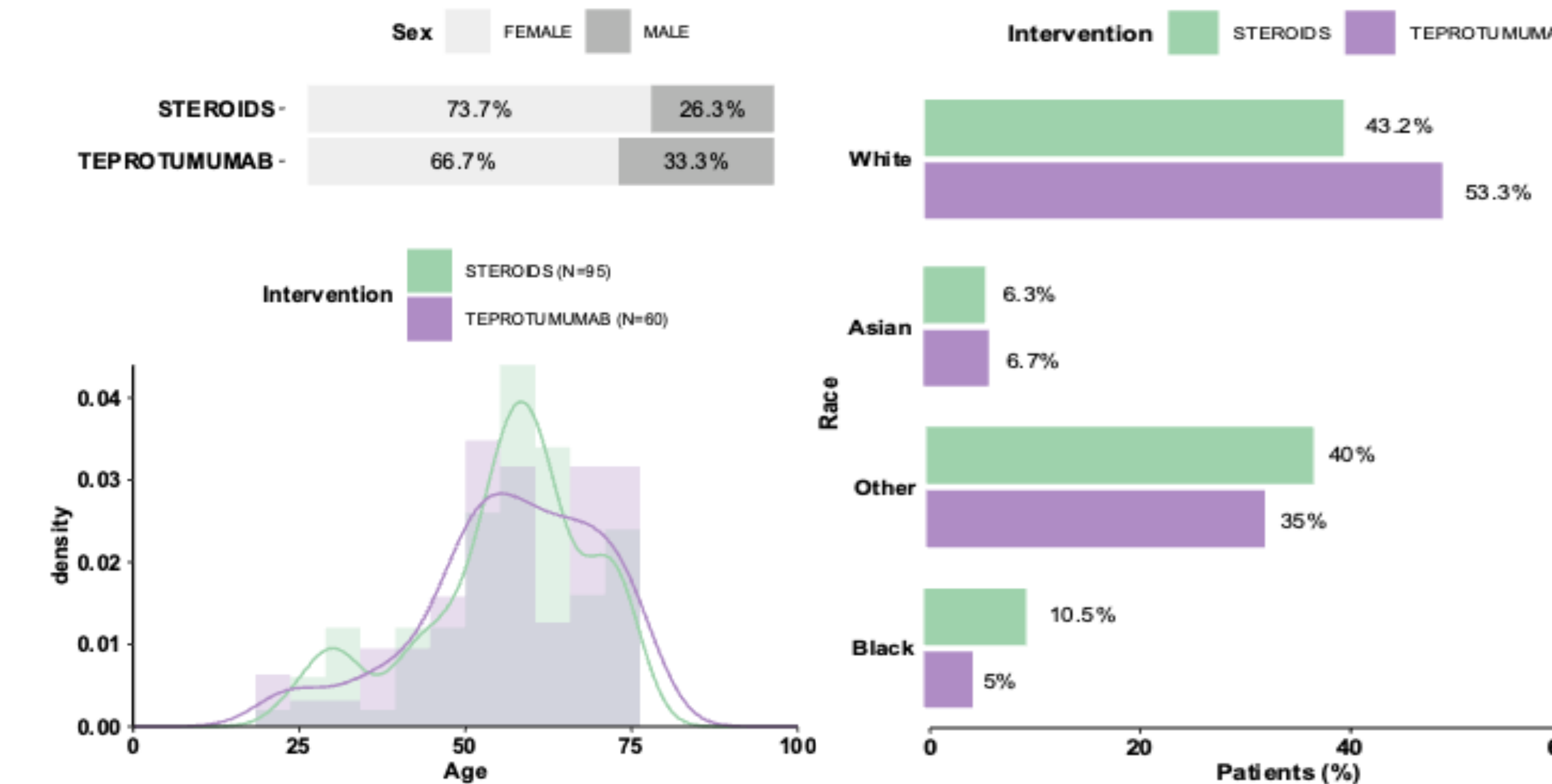


Figure 2. Baseline patient characteristics at the EVERSANA national dataset



- Demographics:** At Stanford, 64 patients completed a 12-week IV steroid course (mean age 49.4 years, 73.4% female) and 33 patients completed 8 teprotumumab doses (mean age 57.3 years, 90.9% female). In the national dataset, 95 patients completed IV steroids (mean age 55.9 years, 73.7% female) and 60 completed 8 teprotumumab doses (mean age 56.9 years, 66.7% female). The racial distribution of the subjects was different in the two datasets, with the Stanford population including a much higher proportion of Asian patients (37.5-45.5% vs 6.3-6.7%).
- Surgical rates:** In the Stanford data, 36.4% of the teprotumumab vs 59.4% of the IV steroid recipients had rehabilitative surgery within 18 months; however, after propensity score matching, OR was not statistically significant (0.37, 95% CI 0.11 – 1.22). Interestingly, retraction repair surgery was less likely with teprotumumab compared with IV steroids (OR 0.20, 0.04-0.94). In the national dataset, the overall surgical rates were lower than at Stanford: 26.7% of the teprotumumab group vs 9.5% of the IV steroid group had rehabilitative surgery. After propensity score matching, OR was not statistically significant (2.96, 95% CI 0.98 – 8.91).

## RESULTS

Table 1. Rates of orbital surgeries with teprotumumab vs IV steroids

Procedures N (%)	Stanford data (n=97)		EVERSANA national data	
	IV steroids (N=64)	Teprotumumab (N=33)	IV steroids (N=95)	Teprotumumab (N=60)
<b>Any orbital surgery</b>	38 (59.38%)	12 (36.36%)	9 (9.47%)	16 (26.67%)
<b>Blepharoplasty</b>	21 (32.81%)	3 (9.09%)	2 (2.11%)	3 (5%)
<b>Endoscopy</b>	2 (3.12%)	0 (0%)	0 (0%)	1 (1.67%)
<b>Orbitotomy</b>	32 (50%)	8 (24.24%)	5 (5.26%)	5 (8.33%)
<b>Retraction repair</b>	30 (46.88%)	5 (15.15%)	6 (6.32%)	6 (10%)
<b>Strabismus</b>	9 (14.06%)	5 (15.15%)	3 (3.16%)	6 (10%)

Table 2. Association between treatment with teprotumumab vs IV steroids and rates of rehabilitative surgery in patients with Graves' and TED. Reported as OR (95% CI). \*p<0.05

Procedures	Stanford data (n=97)		EVERSANA national data (n=155)	
	Unmatched	Propensity score matched	Unmatched	Propensity score matched
<b>Surgery within 18 months</b>	0.39 (0.16-0.93)*	0.37 (0.11-1.22)	3.47 (1.42-8.49)*	2.96 (0.98-8.91)
<b>Blepharoplasty</b>	0.21 (0.03-0.79)	0.22 (0.03-1.33)	2.43 (0.27-29.90)	1.62 (0.23-11.60)
<b>Orbitotomy</b>	0.55 (0.18-1.62)	0.29 (0.08-1.09)	1.63 (0.35-7.44)	1.55 (0.29-8.27)
<b>Retraction repair</b>	0.21 (0.05-0.63)*	0.20 (0.04-0.94)*	1.65 (0.51-5.37)	1.25 (0.29-5.40)
<b>Strabismus</b>	1.09 (0.26-4.05)	1.06 (0.20-5.62)	3.38 (0.69-21.70)	2.05 (0.36-10.90)

## CONCLUSIONS

- Teprotumumab recipients did not have significantly different rates of rehabilitative surgery in comparison to the IV steroid group within 18 months of therapy initiation after propensity score matching, but there was variation in the data obtained from our institution vs a national data set, likely due to differences in follow-up and heterogeneity of the national data.
- Further research is needed to assess the impact of teprotumumab on the rates of rehabilitative surgery in TED after long term follow-up, ideally in randomized controlled trials.

## REFERENCES

- Douglas RS et al. Teprotumumab for the Treatment of Active Thyroid Eye Disease. N Engl J Med. 2020; 382(4):341-352.
- Smith TJ et al. Teprotumumab for Thyroid-Associated Ophthalmopathy. N Engl J Med. 2017; 376(18):1748-1761.