

Epidemiology and Treatment Patterns of Thyroid Eye Disease in Spain: Population-based Real-world Evidence

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BACKGROUND

Thyroid Eye Disease (TED) is an autoimmune condition characterized by orbital tissue inflammation; symptoms include proptosis, eyelid or periorbital swelling, diplopia and, in severe cases, vision loss¹.

Beyond clinical symptoms, TED imposes burden through frequent medical visits, treatment costs, and reduced productivity, severely impacting quality of life and causing psychosocial distress^{2,3}.

Based on severity, TED is classified as mild, moderate-to-severe, or sight-threatening, while based on clinical activity, TED is classified as active and inactive, in line with EUGOGO guidelines⁴. In more severe forms, TED imposes substantial clinical, psychological, and healthcare burden⁵.

Management varies by severity, from off-label use of corticosteroids and immunosuppressants to orbital radiotherapy and surgical interventions; off-label biologic use has also been observed⁶⁻⁹.

Improved understanding of TED epidemiology and treatment patterns may help optimize management and reduce its burden.

OBJECTIVE

To estimate the prevalence and incidence of diagnosed TED in Spain.

To investigate the patterns of treatments among a cohort of patients with moderate-to-severe TED.

METHODS

Study design: This was a retrospective observational study using the Spanish BIG-PAC electronic medical records database (1 January 2012–31 December 2024).

Study period: Patients were included between 1 January 2013 and 31 December 2023 to ensure ≥12 months baseline and follow-up (except in cases of death).

Patient identification: Clinically informed diagnostic algorithm was employed to identify adults with a TED-related eye manifestation combined with confirmed diagnosis of thyrotoxicosis within 12 months.

Disease classification: Patients were classified by disease activity using an expert-informed clinical activity score (CAS)-based algorithm incorporating ocular diagnoses and therapeutic interventions.

Consistent with EUGOGO guidance, patients were classified as active if CAS was ≥3 and inactive if CAS was <3. Inactive patients were further identified as those with CAS <3 plus ≥1 surgery and no dysthyroid/compressive optic neuropathy, or CAS <3 plus diagnoses of proptosis, diplopia, or orbital inflammation.

If a patient met both criteria within the same year, the last CAS determined cohort assignment.

Outcomes: Annual prevalence and incidence were estimated for 2013–2023 (per 100,000 patients/person-years [PY]) while treatment patterns were assessed among incident active and inactive moderate-to-severe TED cases from 2013–2024.

RESULTS

Study Cohort

From 2013–2023, 4,781 patients with TED were identified (mean age 58 years; 64% women); 2,948 individuals with mild TED, 808 with active moderate-to-severe and 1,025 individuals with inactive moderate-to-severe TED.

Active and inactive moderate-to-severe TED patients had significant functional and psychosocial burden at baseline, alongside ocular comorbidities that exacerbated visual impairment (Figure 1).

Prevalence

Overall TED prevalence changed modestly from 97.67 per 100,000 (2013) to 112.20 per 100,000 (2023), corresponding to 44,888 prevalent TED cases in Spain in 2023 (Figure 2).

Prevalence of active moderate-to-severe TED remained relatively stable (16.68–17.98 per 100,000 from 2013–2023), corresponding to 7,194 cases nationally in 2023 (Figure 2).

For inactive moderate-to-severe TED, prevalence moderately changed from 21.64 to 26.02 per 100,000, corresponding to 10,411 cases nationally in 2023 (Figure 2).

Prevalence was consistently ~3× higher in females than males. Rates increased gradually with age, particularly among individuals aged 30–39 years, indicating substantial disease burden during working-age years.

References

- Smith, T.J., et al., How patients experience thyroid eye disease. *Frontiers in Endocrinology*, 2023. 14: p. 1283374.
- Burch, H.B., et al., Management of Thyroid Eye Disease: A Consensus Statement by the American Thyroid Association and the European Thyroid Association. *Thyroid*, 2022. 32(12): p. 1439-1470.
- Leso, V., et al., The impact of thyroid diseases on the working life of patients: a systematic review. *International Journal of Environmental Research and Public Health*, 2020. 17(12): p. 4295.
- Bartalena L, et al. The 2021 EUGOGO clinical practice guidelines for the medical management of Graves' orbitopathy. *Eur J Endocrinol*. 2021;185(4):G43-G67.

KEY TAKEAWAYS

- Steady epidemiology over 11 years indicate a sustained and accumulating disease burden in Spain.
- Higher prevalence in women and notable impact in working-age adults suggests a disproportionate disease burden.
- Reliance on intensive off-label pharmacologic therapies and invasive procedures highlight an unmet need for approved, targeted treatments for moderate-to-severe TED.

RESULTS (CONT.)

Incidence

- Overall TED incidence was stable at approximately 9 per 100,000 person-years (PY) from 2013–2023, corresponding to 3,849 incident cases in Spain in 2023 (Figure 3).
- Incidence of active moderate-to-severe TED was steady at 1.62 to 1.01 per 100,000 PY, representing 404 incident cases nationally in 2023 (Figure 3).
- Incidence of inactive moderate-to-severe TED, too, was stable at 1.62 to 1.44 per 100,000 PY, corresponding to 577 incident cases nationally in 2023 (Figure 3).
- Incidence was consistently higher among women; lowest among individuals aged 18–29 years and highest among older age groups (60–79 years), with minor year-to-year fluctuations.

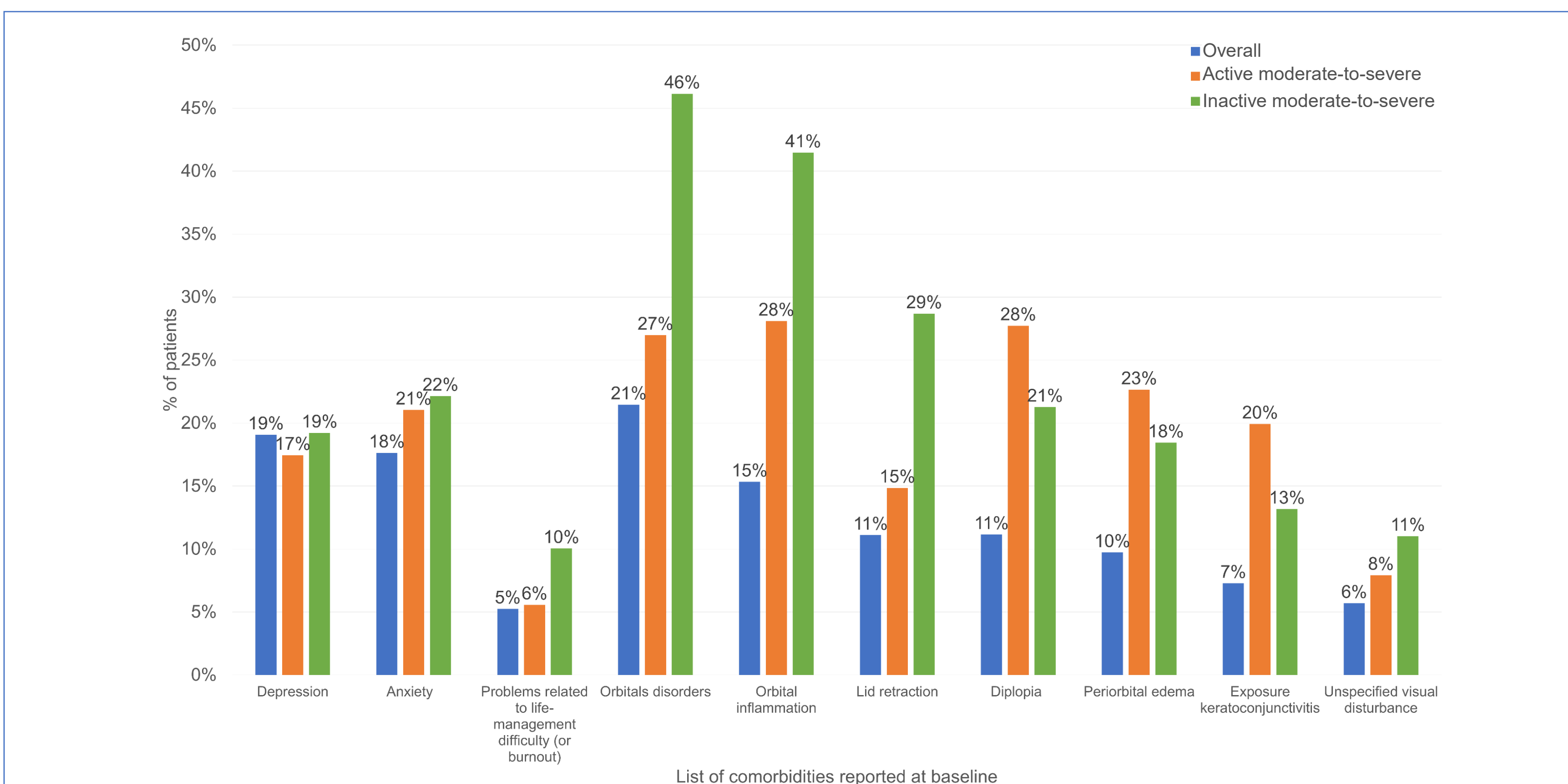


Figure 1. Top 10 comorbidities in the overall TED cohort and their burden in moderate-to-severe TED

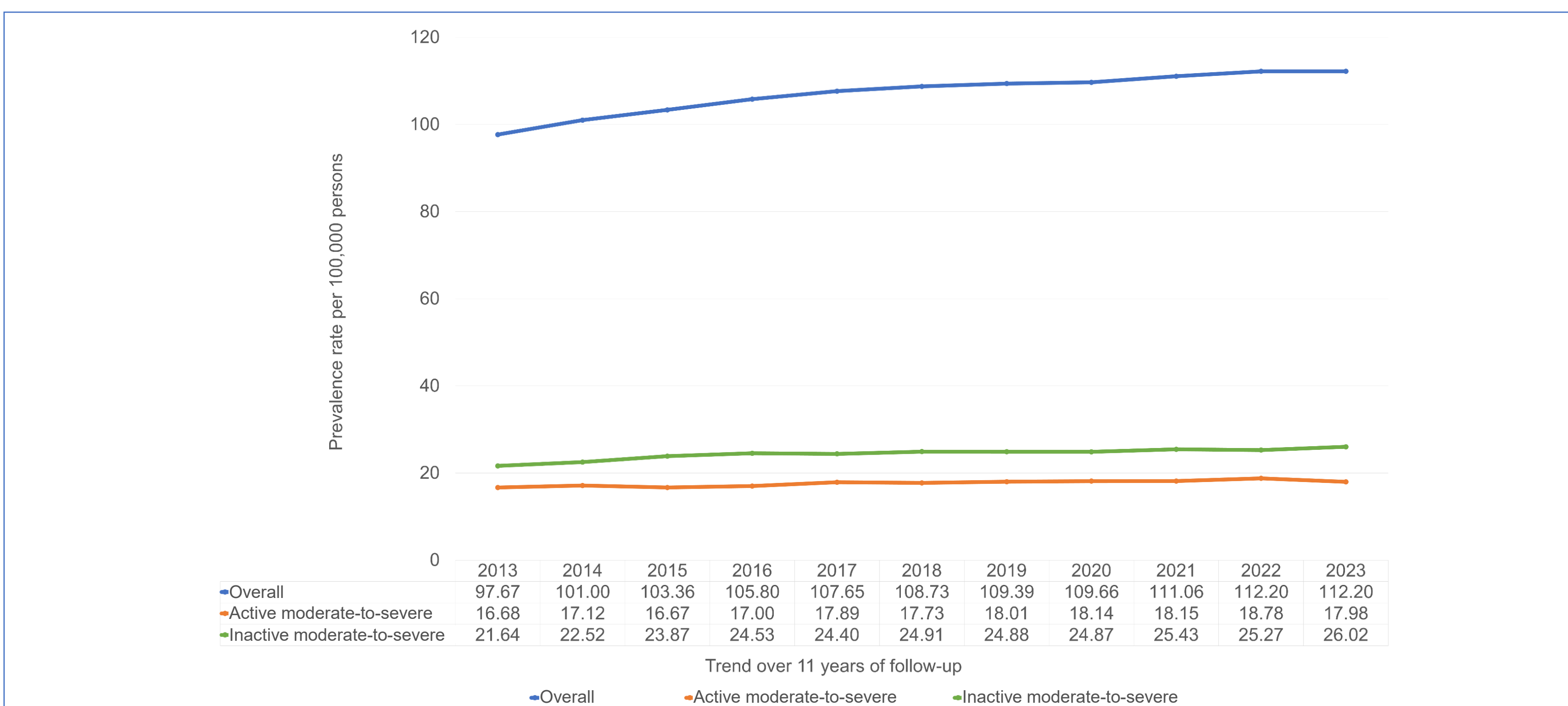


Figure 2. Prevalence of TED in the overall and moderate-to-severe cohorts; overall prevalence includes mild and moderate-to-severe TED

RESULTS (CONT.)

Treatment patterns

Treatment patterns were assessed among incident active (N = 185) and incident inactive (N = 241) moderate-to-severe TED patients (Figure 4).

Active patients were predominantly treated with pharmacologic therapies, whereas inactive patients more commonly underwent surgical interventions.

Common treatment for the active phase were off label drugs: intravenous corticosteroids (IV CS), mainly as monotherapy or in combination with immunosuppressants. Orbital radiotherapy, biologics, and oral CS were used less frequently while surgical procedures were rare.

For the inactive phase, pharmacologic treatment was rare; orbital decompression and eyelid surgery with blepharoplasty were most common surgical interventions.

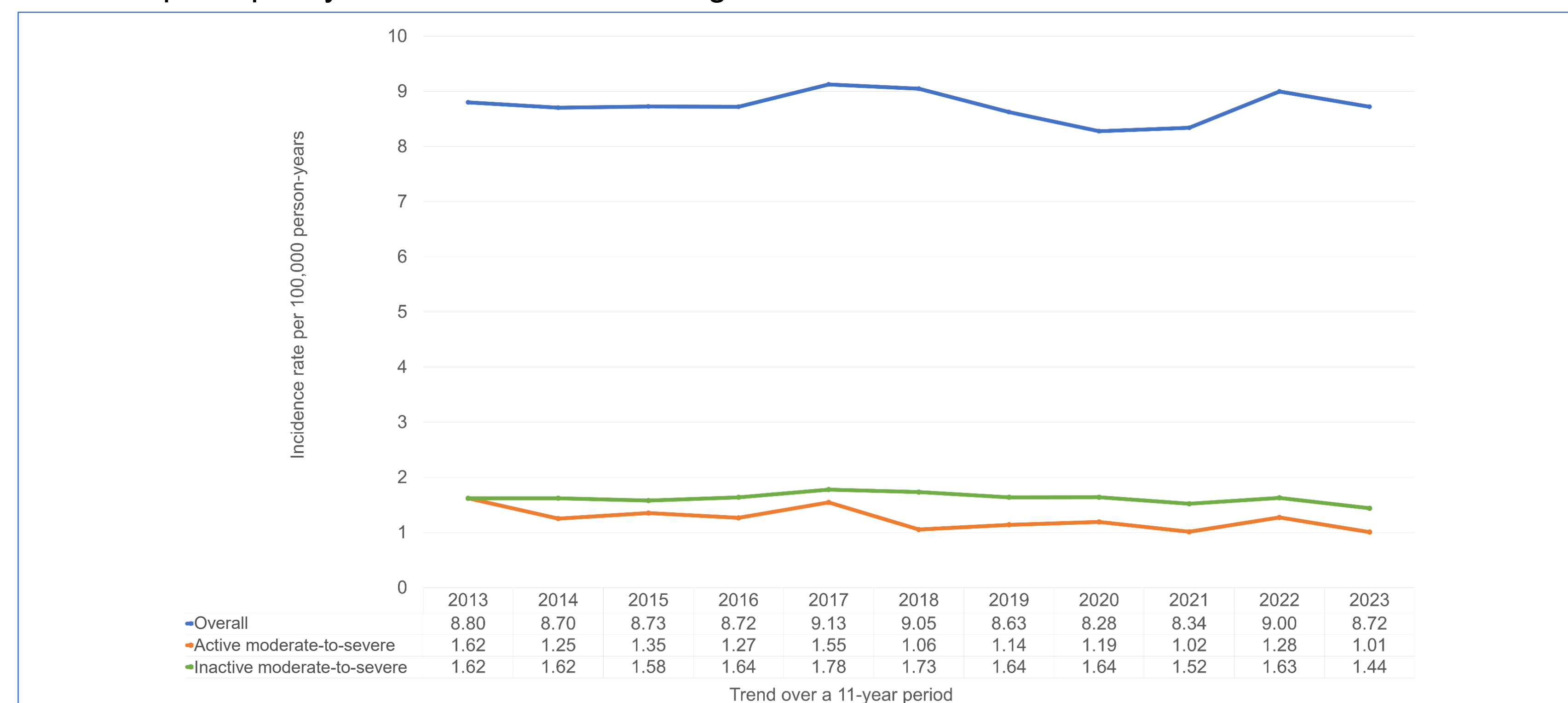


Figure 3. Incidence of TED in the overall and moderate-to-severe cohorts; overall incidence includes mild TED

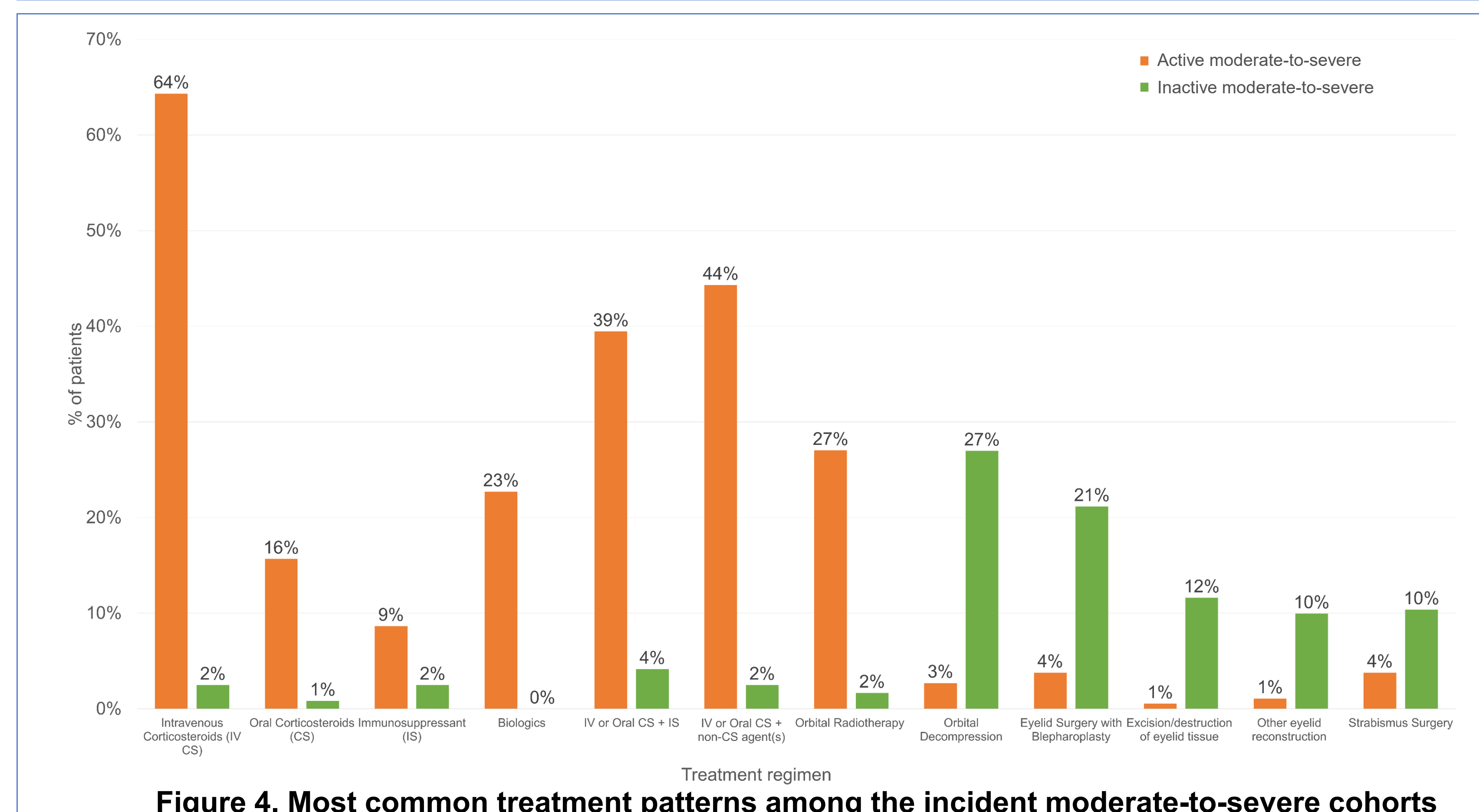


Figure 4. Most common treatment patterns among the incident moderate-to-severe cohorts

LIMITATIONS

Case identification used a clinically informed algorithm and may be subject to misclassification; exclusion of hypothyroid/euthyroid TED may underestimate burden.

Eyelid procedures were identified via administrative codes, which may not reflect clinically relevant categories (e.g., eyelid retraction repair); blepharoplasty codes should be interpreted with caution. Diagnoses of proptosis, diplopia, and orbital inflammation were identified using ICD-9/10 codes. Administrative codes and ICD-9/10 codes may be subject to coding errors.

DISCLOSURES

- This study was funded by Amgen, Inc.
- VS and SK are employees of Cytel, which was funded by Amgen (Europe) GmbH. IH is an employee of Atrys Health, contracted by Cytel.
- ICT, BJL, and CG are employees of Amgen and hold Amgen stocks.

