

DISEASE SEVERITY IS ASSOCIATED WITH POORER QUALITY OF LIFE OUTCOMES AND HIGHER COSTS IN THYROID EYE DISEASE (TED): EVIDENCE FROM SYSTEMATIC LITERATURE REVIEWS (SLRS)

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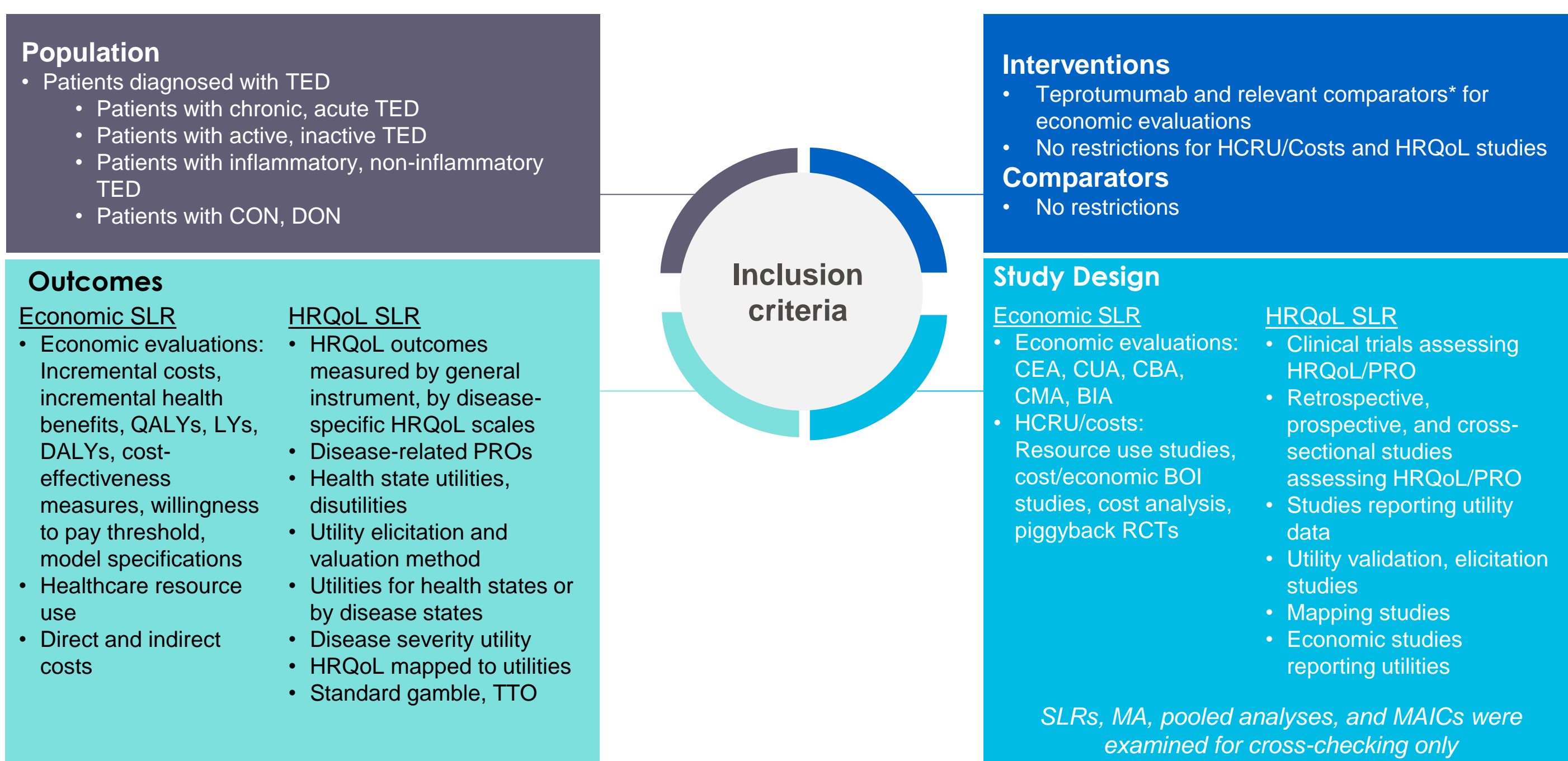
Background and Objectives

- TED is a rare autoimmune condition that manifests in approximately 30% to 40% of patients with Graves' disease.[†] Clinical presentation is heterogeneous, and symptoms can lead to pain, loss of vision, and change in appearance, impacting patients' well being and quality of life.
- The economic and humanistic burden associated with TED is not fully understood.
- Two SLRs were conducted to examine the costs, healthcare resource utilization (HCRU), economic evaluations, and health-related quality of life (HRQoL) associated with TED.

Methods

- Two SLRs examined evidence from databases without geographic limits. Both SLRs adhered to robust methodology by following NICE and PRISMA standards.
- The economic SLR conducted in May 2023 included five databases (Embase, MEDLINE, HTA, NHS EED, and Econlit) without time restriction, while the HRQoL SLR was conducted in June 2023 and included eight databases from the last ten years to prioritize the most recent and relevant data (Embase, MEDLINE, HTA, CDSR, DARE, CENTRAL, NHS EED, and Econlit).
- Database searches were supplemented with searches of four conference proceedings (AAO, AOS, ENDO, ESOPRS) from the last 3 years, 18 HTA databases, one economic registry, and bibliography searches from identified SLRs.
- Inclusion of studies followed pre-defined PICOS criteria (Figure 1).

Figure 1. PICOS criteria

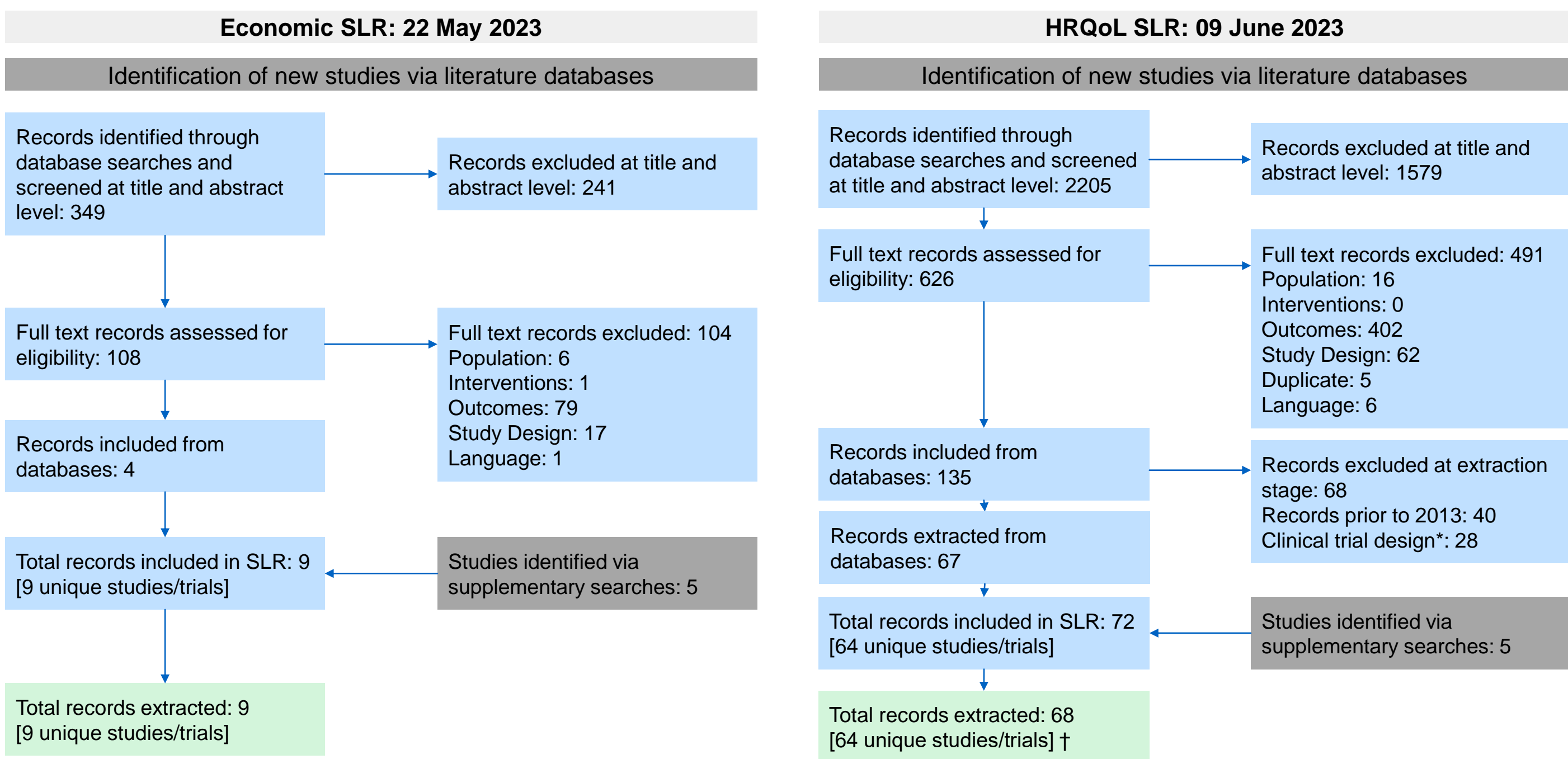


*Glucocorticoids, betamethasone, doxycycline, methylprednisone, mycophenolate, cyclosporin, azathioprine, orbital radiotherapy, orbital surgery [decompression, strabismus, eyelid surgery (blepharoplasty)], orbital surgery with pharmacological interventions, tolicizumab, rituximab, batoclimab, secukinumab, vunakizumab (SHR-1314), infliximab, adalimumab, VDRN-002, efgartigimod, VDRN-001, VB421, K1-70, atorvastatin, bimatoprost, sirolimus, selenium, antithymocyte globulin, ATX-GD-59, aflibercept, etanercept, linsitinib.

BIA, budget impact analysis; BOI, burden of illness; CBA, cost-benefit analysis; CEA, cost-effectiveness analysis; CMA, cost-minimization analysis; CON, compressive optic neuropathy; CUA, cost-utility analysis; DALYs, disability-adjusted life years; DON, dysthyroid optic neuropathy; HCRU, healthcare resource use; HRQoL, health-related quality of life; LYs, life-years; MA, meta-analysis; MAIC, matching-adjusted indirect comparison; PRO, patient-reported outcome; QALYs, quality-adjusted life years; RCTs, randomized clinical trials; SLR, systematic literature review; TED, thyroid eye disease; TTO, time trade-off.

Results

Figure 2. PRISMA diagrams



*RCTs and single-arm studies design were excluded except if the study reported utility values, or results from a scale that can be mapped to obtain utility values.

†Records with duplicated information were not extracted.

HRQoL, health-related quality of life; RCTs, randomized clinical trials; SLR, systematic literature review.

Economic SLR

- There was a paucity of data on economic burden in TED.
- Nine economic studies were identified reporting on costs only (n=4), HCRU + costs (n=3), HCRU only (n=1), and economic evaluation (n=1).
 - Geographic location included: Costs only (United States [US]: n=2, Denmark: n=1, Italy: n=1); HCRU + costs (US: n=2, Germany: n=1); HCRU only (US: n=1); economic evaluation (multinational: n=1).
- Six out of the nine studies were published as abstracts.

Total direct TED-associated costs

- Total direct disease-associated costs were observed to increase with TED disease severity.
- In a cross-sectional study examining TED costs between 2005 and 2009 at a multidisciplinary university orbital center in Germany, mean per patient yearly costs ranged from \$418 in mild TED to \$469 in moderate-to-severe TED to \$1,491 in sight-threatening TED.² Costs were converted from Euros to U.S. dollars using the exchange rate of 1.258 in 2012.

Indirect costs

- Indirect costs were greater in patients with all types of TED in comparison to autoimmune thyroid diseases, other autoimmune diseases, benign nodular goiters, and healthy patients (Figure 3).²
- Total indirect economic burden of TED was calculated at \$3,475,325,640. ² When adjusted for inflation since 2013, this figure rises to \$3,951,518,218 in 2021.³

HCRU in TED

- A retrospective study leveraging claims data in the US (2012-2018) estimated the mean number of annual outpatient visits at 27; comparatively higher than other chronic diseases (Figure 4).⁴
- In a cross-sectional study examining TED-associated resource use between 2005 and 2009 at a multidisciplinary university orbital center in Germany, ophthalmologist and endocrinologist appointments comprised the majority of outpatient resource use.²

Figure 3. Average Annual Indirect Costs Across TED and Comparator Groups²

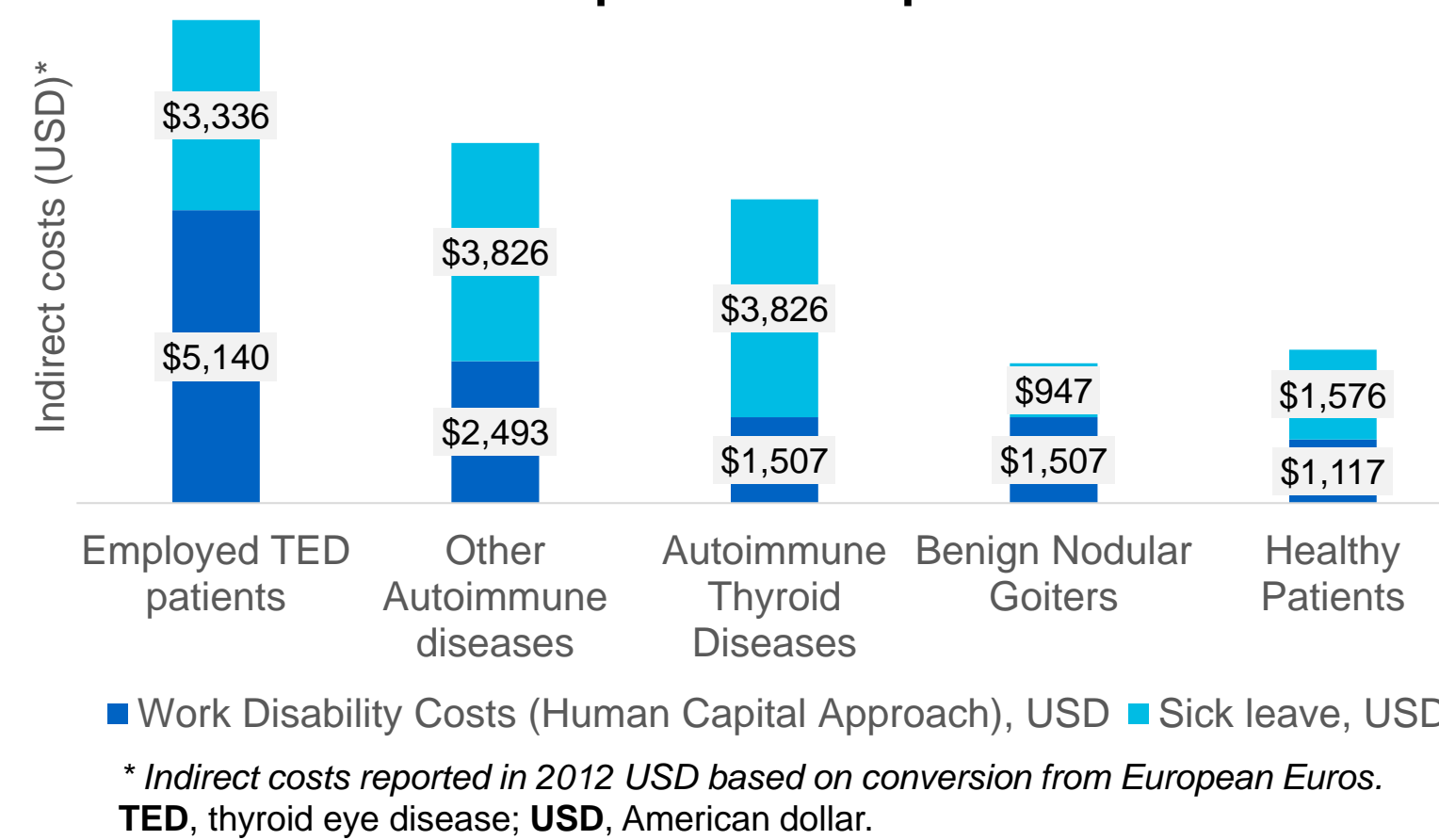
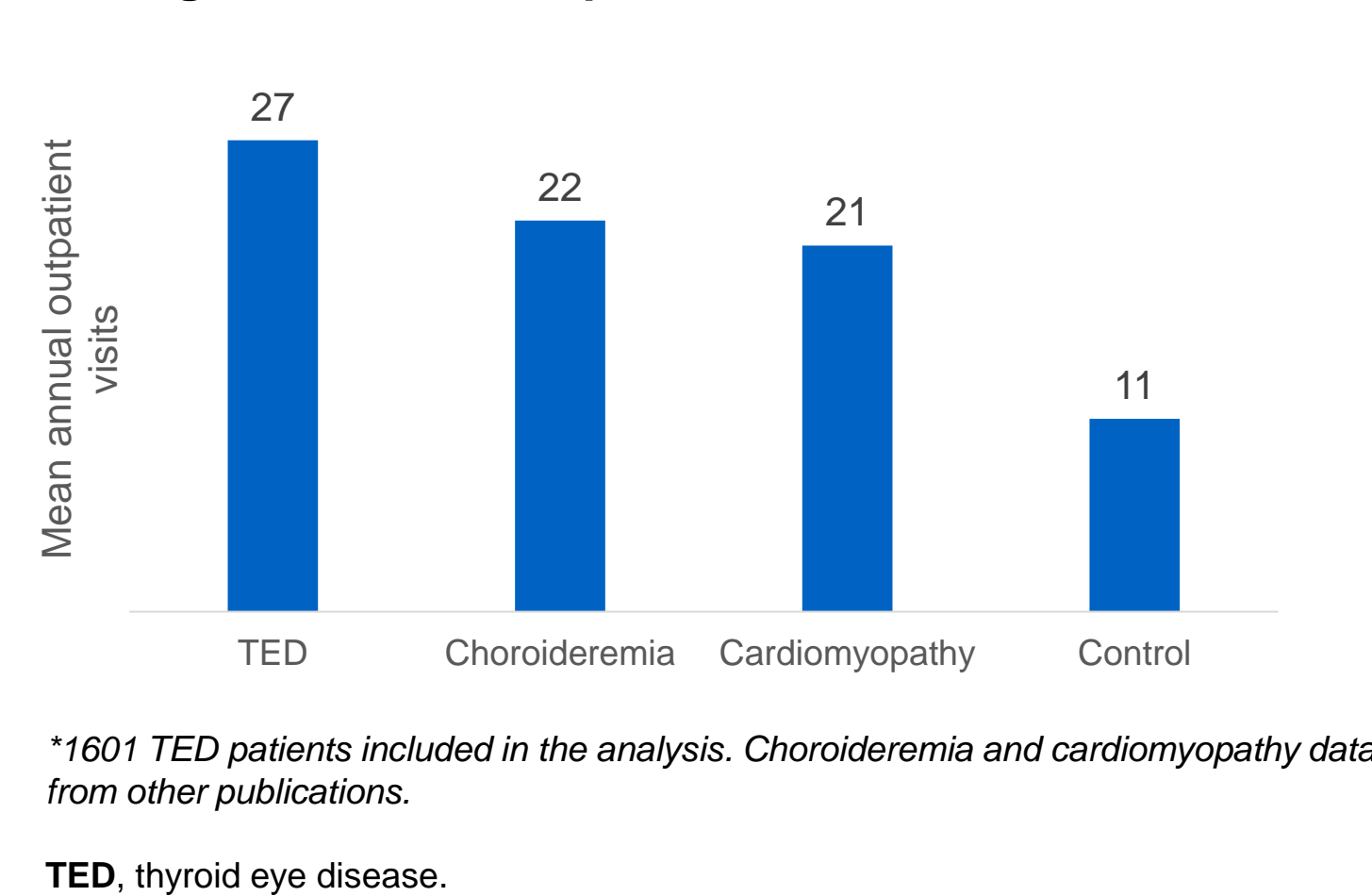


Figure 4. Mean Outpatient Visits Per Year⁴



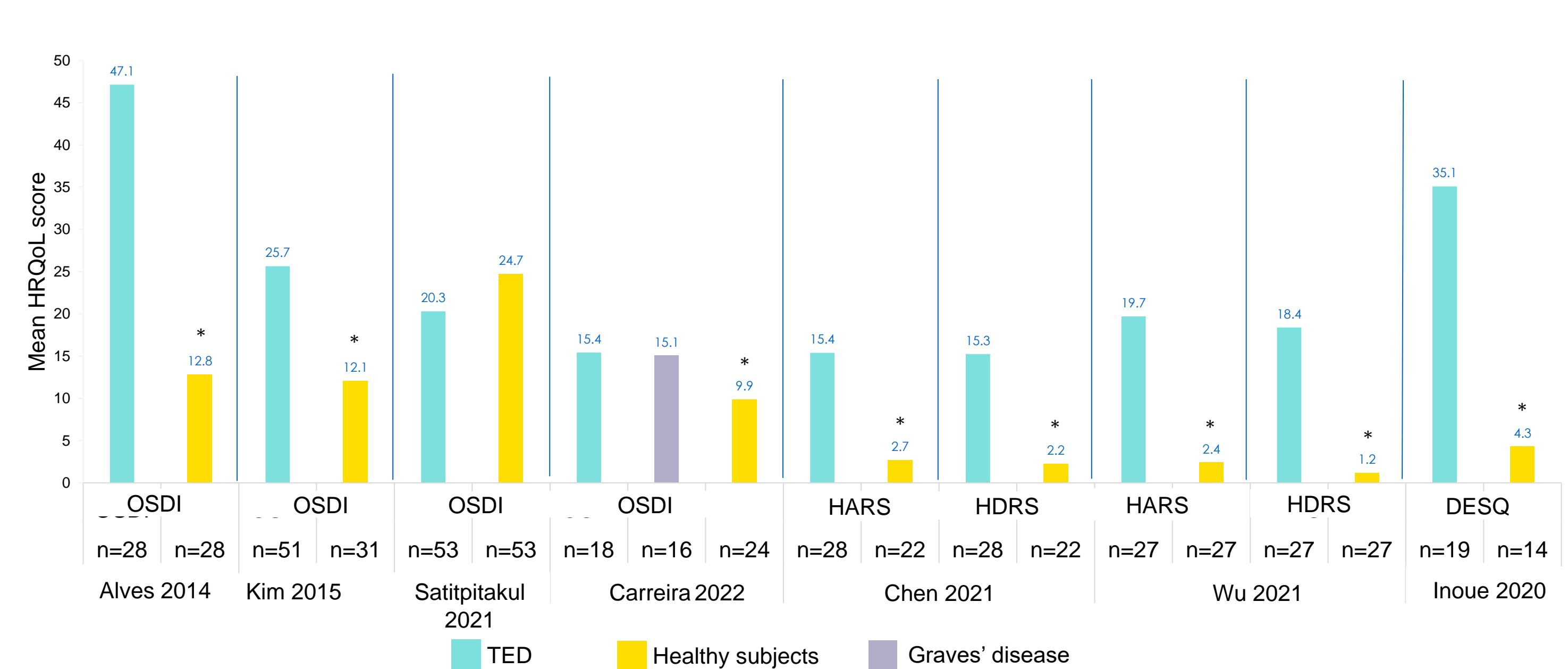
HRQoL SLR

- Humanistic burden in TED from RWE studies was mainly reported using disease-specific instruments.
- 64 humanistic studies were identified reporting on generic HRQoL instruments (n=4), disease-specific instruments (n=46), patient-related outcomes (n=20), and utilities (n=2) (Figure 2).
- 27 different instruments were used with the most common ones being OSDI, TAO-QOL, TED-QOL, SF-36 and GO-QOL. GO-QOL was assessed most often (n=40).

Humanistic burden in patients with TED

- HRQoL was lower among patients with TED compared to healthy populations or those with Grave's disease. Differences in QoL were statistically significant in 8/10 captured measures (Figure 5).

Figure 5. HRQoL Comparison Between Patients with TED and Control Population at Baseline⁵⁻¹¹



*Statistically significant difference compared to patients with TED; In OSDI, HARS, HDRS, and DESQ higher scores represent worse HRQoL.

DESQ, dry eye-related quality of life score; HARS, Hamilton anxiety rating scale; HDRS, Hamilton depression rating scale; HRQoL, health-related quality of life; OSDI, ocular surface disease index; TED, thyroid eye disease.

HRQoL SLR Continued

Humanistic burden by disease severity

- Among the studies reporting GO-QOL, where higher scores represent better HRQoL (0-100), higher median scores were noted in the visual function (VF) and appearance (AP) subscales among patients with lower disease severity (Table 1, Figure 6).

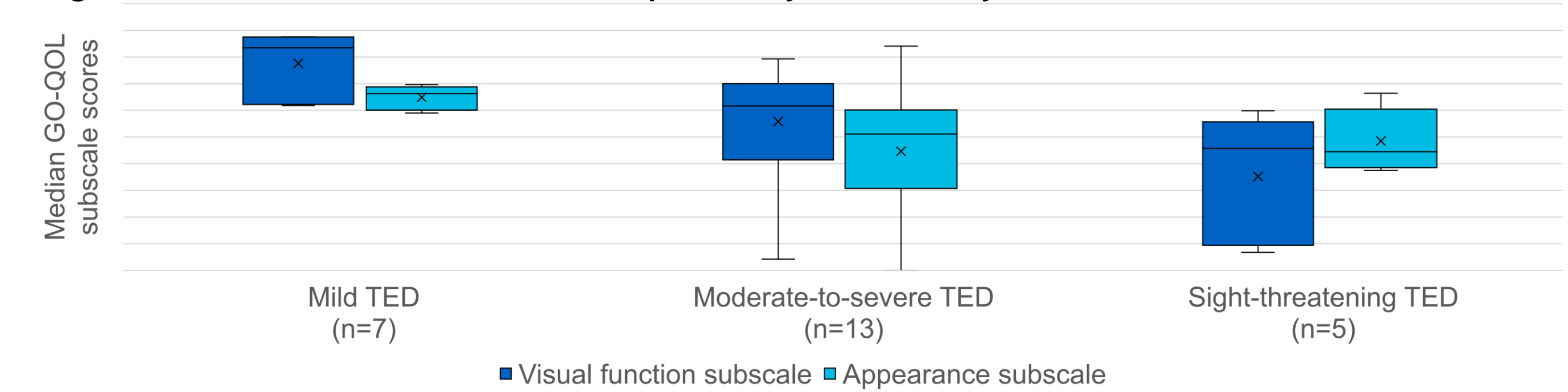
Table 1. Median GO-QOL Subscales and Significance by TED Severity

Median GO-QOL Subscale Score [Range]	Mild TED (n=7 studies)	Moderate-to-severe TED (n=13 studies)	Sight-threatening TED (n=5 studies)	Number of studies with significant differences, mild vs moderate-to-severe*	Number of studies with significant differences, moderate-to-severe vs sight-threatening*	Number of studies with significant differences, mild vs sight-threatening*
Visual Function	83.5 [61.8-87.6]	60.8 [4.2-79.3]	45.8 [6.8-59.8]	5/7	3/5	2/5
Appearance	66.3 [59.0-69.7]	50.1 [2.5-84.1]	44.4 [37.5-66.4]	4/7	2/5	NR

*In studies that included statistical evaluations.

GO-QOL, Graves' orbitopathy quality of life; NR, not reported; TED, thyroid eye disease.

Figure 6. Median GO-QOL Subscales Comparison by TED Severity



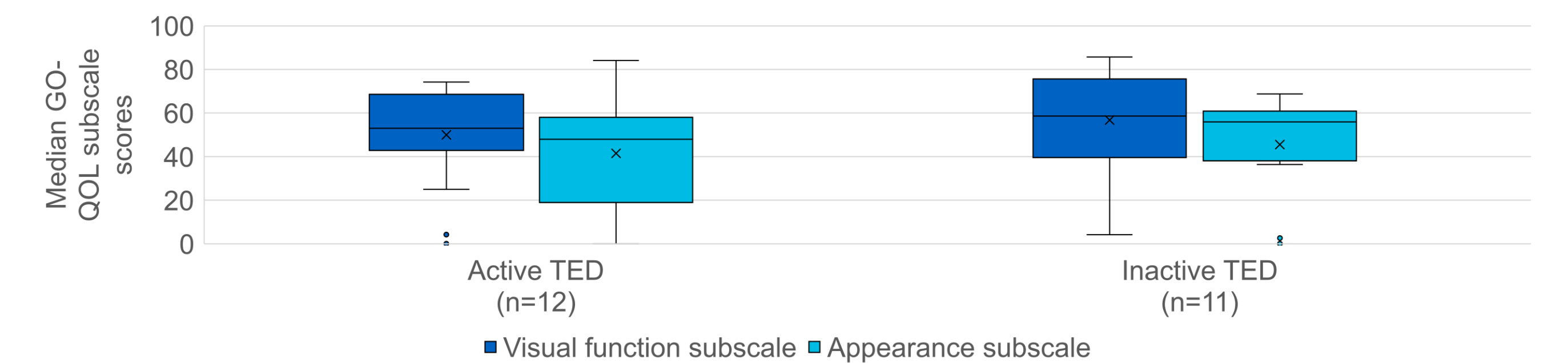
In GO-QOL higher scores represent better HRQoL; n = number of studies.

GO-QOL, Graves' orbitopathy quality of life; TED, thyroid eye disease.

Humanistic burden by disease activity

- Among studies reporting GO-QOL results, quality of life remained relatively low in patients with inactive TED, with similar median GO-QOL subscale scores among patients with active TED (Figure 7).
- VF:** Inactive TED (58.6 [4.2-85.7], n=11); Active TED (53.1 [4.2-74.2], n=12).
- AP:** Inactive TED (56.1 [2.7-69.0], n=11); Active TED (48.6 [2.5-84.1], n=12).

Figure 7. Median GO-QOL Subscales Comparison by TED Activity



In GO-QOL higher scores represent higher HRQoL; n = number of studies

GO-QOL, Graves' orbitopathy quality of life; TED, thyroid eye disease.

Conclusions

- There is a significant economic and humanistic burden associated with TED.
- Despite limited economic data, increased TED disease severity was associated with higher direct costs. Outpatient care was the key driver of HCRU in TED.
- Patients with TED had lower HRQoL compared to the general population, with higher disease severity associated with poorer HRQoL outcomes. HRQoL remains relatively low, irrespective of disease activity.
- The paucity of data concerning economic outcomes and the small sample sizes within subgroups reporting HRQoL data highlights the need for additional studies in these areas.

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- Abbreviations:** AAO, American academy of ophthalmology; AOS, American ophthalmological society; AP, appearance; CDSR, Cochrane Database of Systematic Reviews; CENTRAL, Cochrane central register of controlled trials; DARE, database of abstracts of reviews of effects; ENDO, annual meeting of the endocrine society; ESOPRS, European society of ophthalmic plastic and reconstruction surgery; GO-QOL, Graves' orbitopathy quality of life; HCRU, healthcare resource utilization; HRQoL, health-related quality of life; HTA, health technology assessment; NHS EED, National health Service economic evaluation database; NICE, national institute for health and care excellence; OSDI, ocular surface disease index; PICOS, population, intervention, comparator, outcomes, and study design; PRISMA, preferred reporting items for systematic reviews and meta-analyses; RWE, real-world evidence; SF-36, 36-item short form survey; SLRs, systematic literature reviews; TAO-QOL, thyroid-associated ophthalmopathy/orbitopathy quality of life; TED, thyroid eye disease; TED-QOL, thyroid eye disease quality of life; VF, visual function.

