

ANGIOEDEMA IN PATIENTS WITH CHRONIC SPONTANEOUS URTICARIA (CSU) HAS AN ADDITIONAL IMPACT ON QUALITY OF LIFE BUT IS REPORTED MORE OFTEN BY PATIENTS THAN PHYSICIANS

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INTRODUCTION

- The ASSURE-CSU study is the first international, multicentre study that assessed the burden of disease and history of angioedema in inadequately-controlled chronic spontaneous/idiopathic urticaria (CSU/CIU) patients¹
- Angioedema is defined as localized and self-limiting oedema of the subcutaneous and submucosal tissue, frequently occurring as part of urticaria²
- The initial analysis revealed a discrepancy in angioedema reported by physicians and patients³; with an underestimation of angioedema by the physicians

OBJECTIVE

- The aim of the current study is to analyse history of angioedema, as reported by physicians and patients, and assess the impact of angioedema on health related quality of life (HRQoL) of patients with inadequately controlled CSU

METHODS

Study design

- Observational study conducted in 7 countries (Canada, France, Germany, Italy, Netherlands, Spain, and the United Kingdom)³. The study included a 1-year retrospective medical record abstract, a cross-sectional patient survey and a 7-day prospective patient diary

Patient population

- Adult patients (≥18 years) with diagnosed CSU, with disease persisting for ≥12 months and symptomatic despite current treatment

Data sources

Data for the analyses came from the following sources:

- Medical charts: Patient demographics, history of angioedema as reported by the physicians
- Patient survey:
 - History and description of angioedema
 - Dermatology Life Quality Index (DLQI; recall period 1 week, score range 0–30, higher score indicating higher impairment) to assess the patients' dermatology specific quality of life
- Patient Diary
 - Twice-daily Urticaria Activity Score reported over 7 days (UAS7_{TD}; recall period 12 hours, score range 0–42) following the enrolment; and daily occurrence of angioedema

Group definitions

The following patient subgroups were defined:

- YES-ANGIO group: Both physicians (medical chart records) and patients (in the survey or diary) reported angioedema
- NO-ANGIO group: Neither physicians (medical chart records) nor patients (in the survey or diary) reported angioedema
- MISALIGNED group: Only one source (either the patient records or the medical chart records) reported angioedema

Outcomes for this analysis

- Frequency of angioedema, DLQI total and domain scores reported as per angioedema groups and DLQI analysis of covariance (ANCOVA)

Statistical analysis

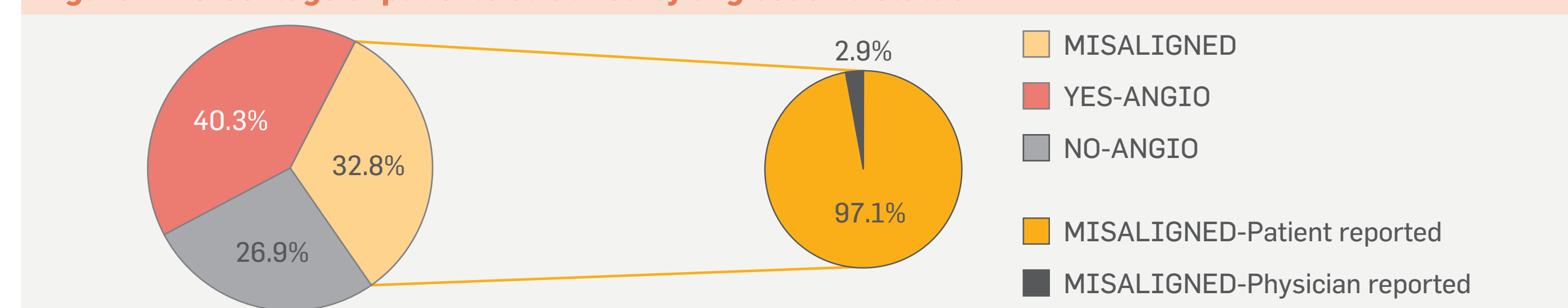
- Data were stratified by angioedema classification and analysed using descriptive statistics
- t-tests and Kruskal-Wallis tests were performed to compare the means and distributions for continuous variables, and chi-square tests were used to compare frequencies of categorical variables between the YES-ANGIO and NO-ANGIO groups
- An ANCOVA model was developed to assess the relationship between DLQI total score and angioedema controlling for covariates: UAS7_{TD}, age, sex, country, disease duration and comorbidities (hypersensitivity to nonsteroidal anti-inflammatory drugs, Hashimoto's, asthma), comparing "YES-ANGIO + MISALIGNED" vs. "NO-ANGIO" groups
- A sensitivity analysis was done removing "MISALIGNED" group, comparing only the mean DLQI scores between YES-ANGIO and the NO-ANGIO groups after covariate adjustment to confirm the results of the ANCOVA model

RESULTS

Patient demographics and characteristics

- A total of 673 patients from 64 centres were recruited and had medical records abstracted for patient demographics, history and presence of angioedema as reported by the physicians. Among these patients, 649 (96.4%) completed the patient survey and 614 (91.2%) completed the patient diary
- Mean age [SD] was 48.8 [15.47] years. Of the 673 patients, 90.4% were Caucasian and 72.7% female
- Among 643 patients with complete angioedema data, YES-ANGIO was reported in 259 cases (40.3%), NO-ANGIO in 173 cases (26.9%), and MISALIGNED in 211 cases (32.8%) (Figure 1)
- Among the "MISALIGNED" cases, 97.1% had angioedema being reported by patients and not the physicians (Figure 1)

Figure 1. Percentage of patients stratified by angioedema status



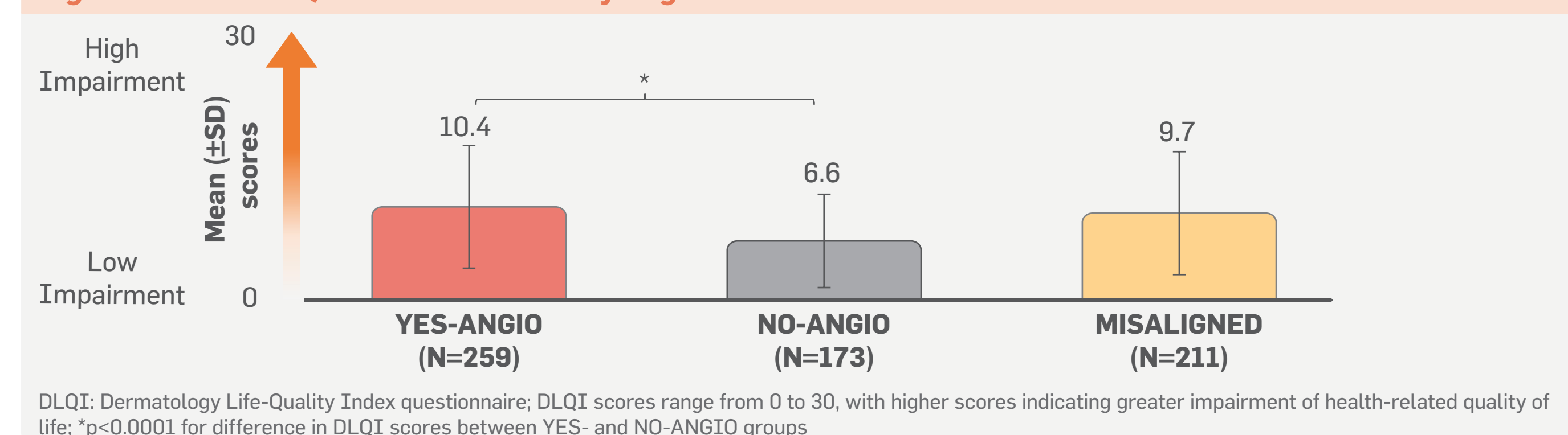
Demographic and disease characteristics stratified by angioedema

- There was no statistically significant difference in age, gender and comorbidities between YES- and NO-ANGIO groups except:
 - YES-ANGIO patients had longer disease duration from diagnosis to enrolment vs NO-ANGIO patients ($p < 0.05$); MISALIGNED patients followed similar pattern as angioedema patients
 - YES-ANGIO patients were more likely to have Hashimoto's disease at CSU diagnosis ($p < 0.05$)
- The YES-ANGIO and NO-ANGIO groups differed significantly with respect to CSU severity classification by the physician at the time of diagnosis ($p = 0.01$)

HRQoL impact assessed by DLQI

- The mean [SD] DLQI score was significantly higher in the YES-ANGIO (10.4 [6.85]) compared to the NO-ANGIO group (6.6 [5.21]), $p < 0.0001$ and was similar to "YES" in the "MISALIGNED" group (9.7 [6.87]) (Figure 2)

Figure 2. Mean DLQI scores stratified by angioedema



- There were significant differences in all domains of DLQI between patients with and without angioedema. 'Symptoms and feelings' and 'work and school' were the most affected domains (Figure 3)
- Significant difference was observed between YES-ANGIO and NO-ANGIO in the overall distribution of DLQI score bands ($p < 0.0001$) (Figure 4)

Figure 3. DLQI domain scores stratified by angioedema

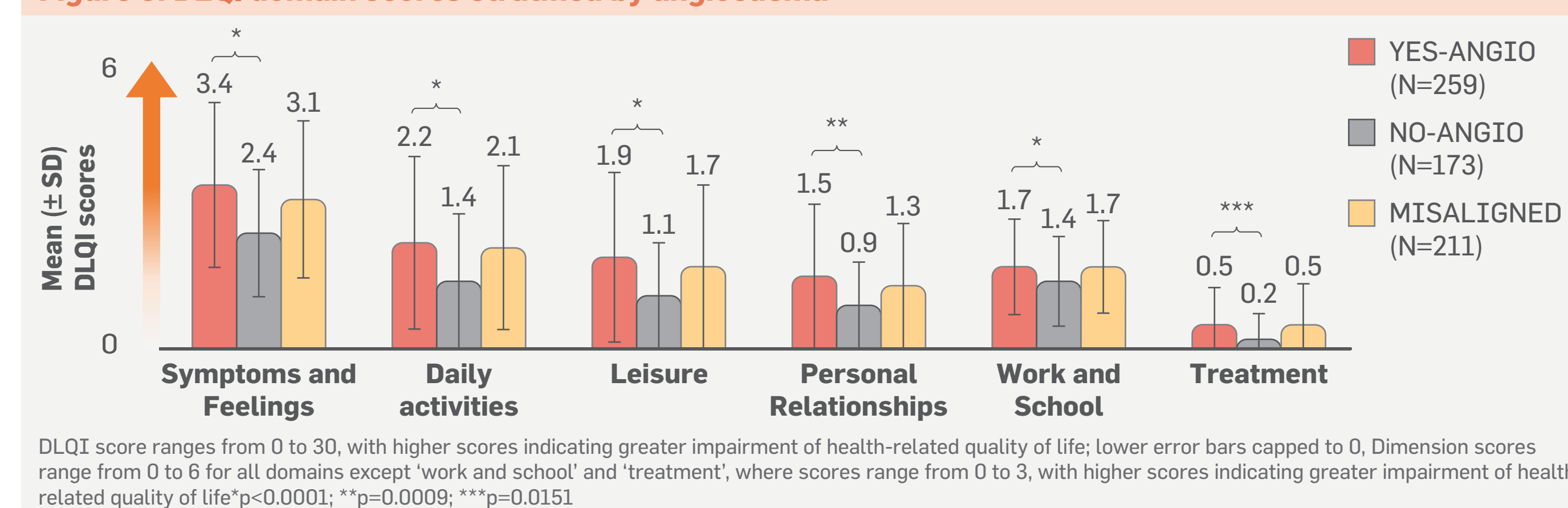
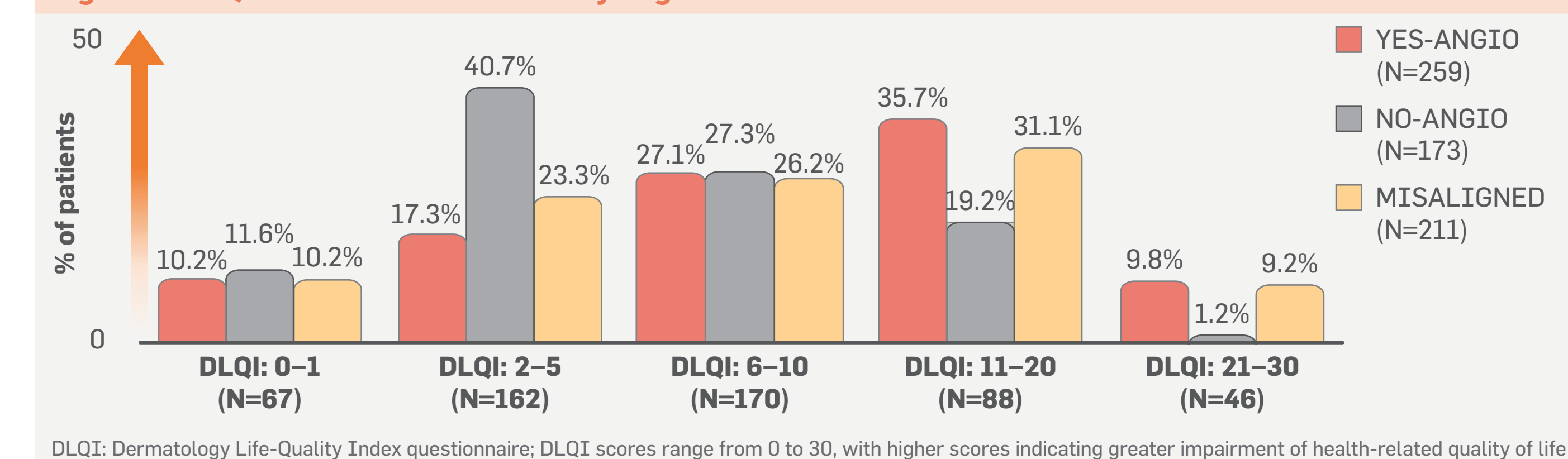


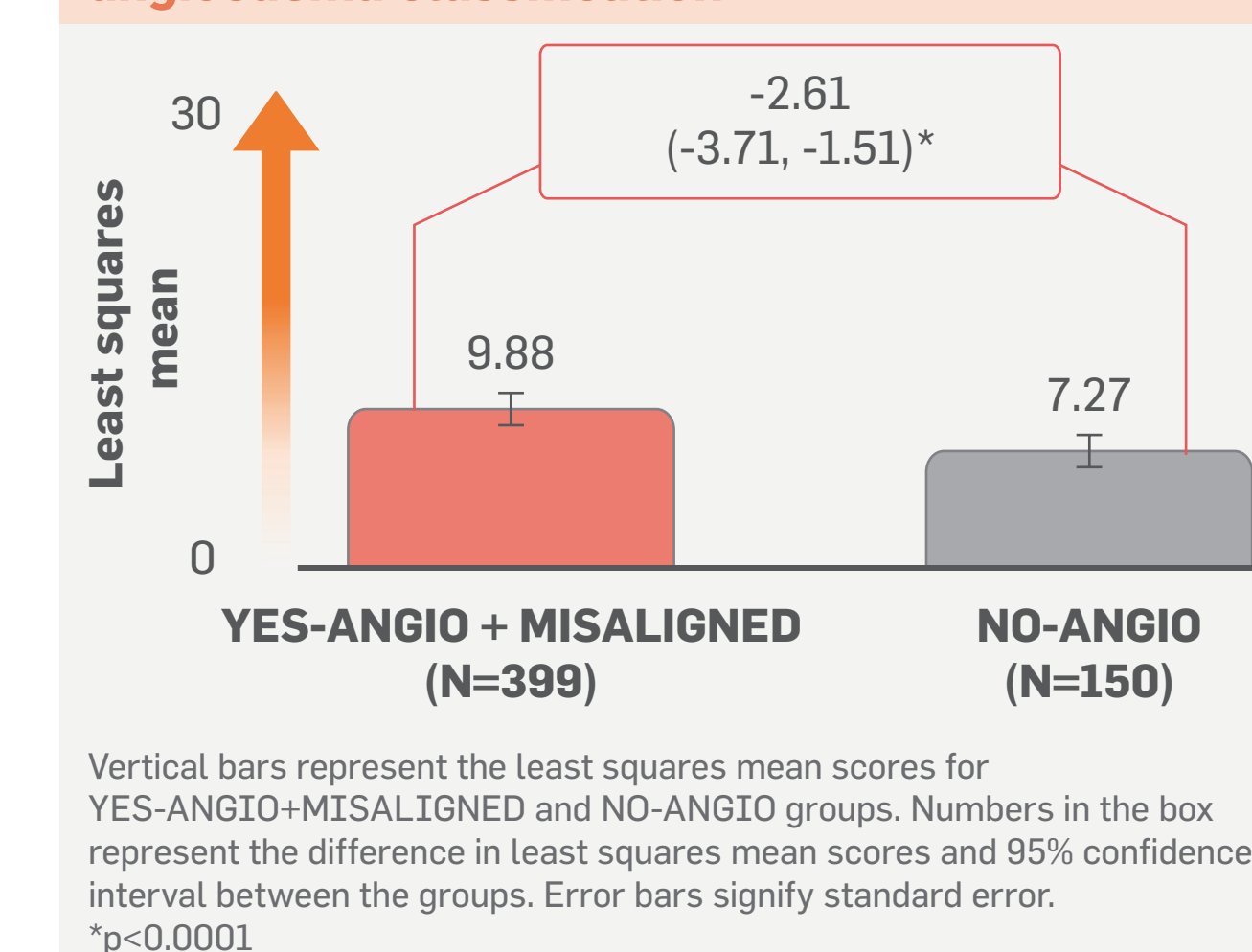
Figure 4. DLQI score bands stratified by angioedema



ANCOVA results

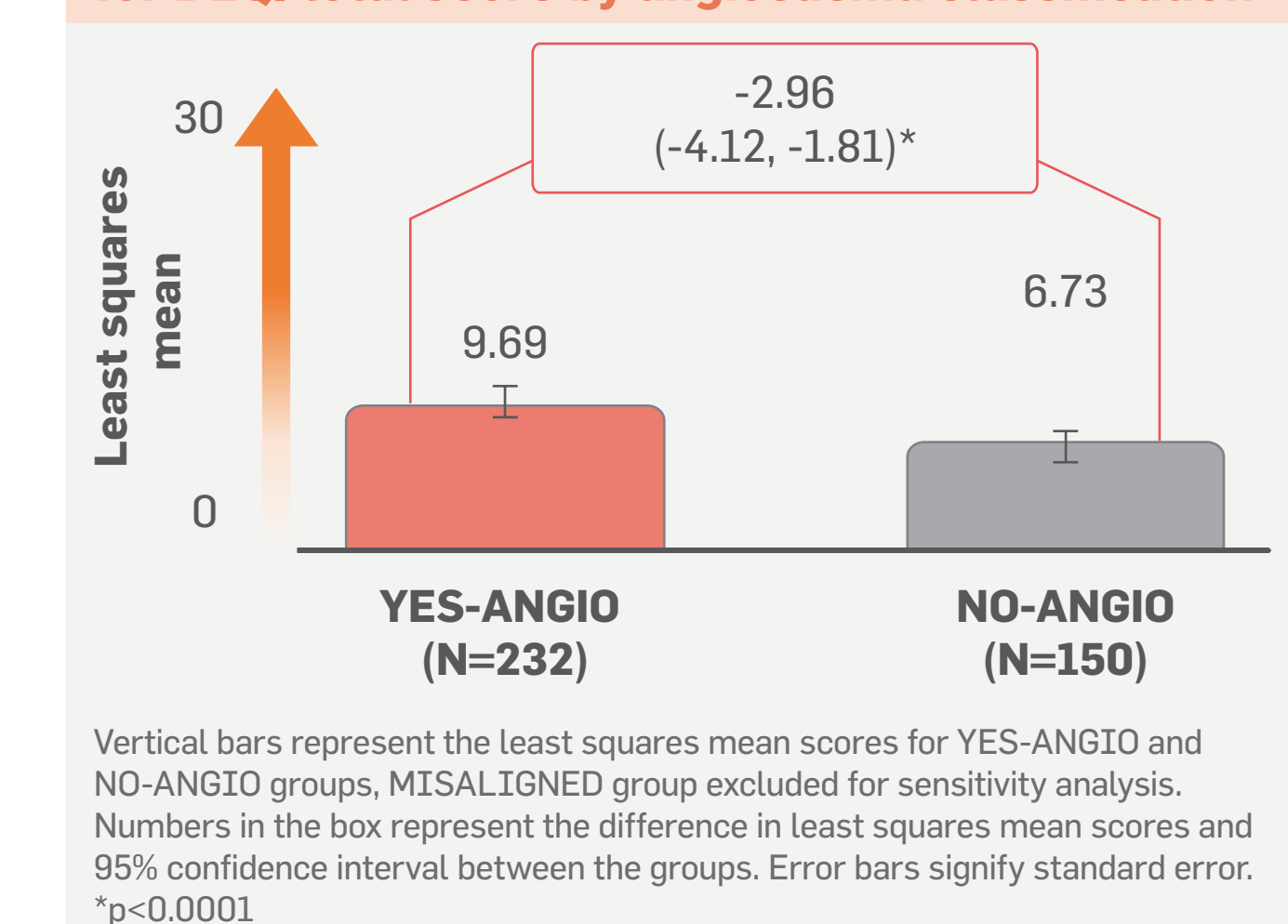
- The descriptive analysis revealed that patients in the MISALIGNED group appeared most similar to patients in the YES-ANGIO group, hence, two categorisations for angioedema were used in the regression analyses
- Analysis of covariance by DLQI total scores after covariate adjustment showed the mean DLQI to be significantly higher for "YES-ANGIO + MISALIGNED" than NO-ANGIO group (9.88 vs 7.27, $p < 0.0001$) (Figure 5)
- The sensitivity analysis excluding the MISALIGNED group confirmed the primary regression results, with significantly higher DLQI total scores for YES-ANGIO compared to NO-ANGIO group (9.69 vs 6.73, $p < 0.0001$) (Figure 6)

Figure 5. ANCOVA results for DLQI total score by angioedema classification



Vertical bars represent the least squares mean scores for YES-ANGIO+MISALIGNED and NO-ANGIO groups. Numbers in the box represent the difference in least squares mean scores and 95% confidence interval between the groups. Error bars signify standard error. * $p < 0.0001$

Figure 6. Sensitivity analysis for ANCOVA results for DLQI total score by angioedema classification



Vertical bars represent the least squares mean scores for YES-ANGIO and NO-ANGIO groups, MISALIGNED group excluded for sensitivity analysis. Numbers in the box represent the difference in least squares mean scores and 95% confidence interval between the groups. Error bars signify standard error. * $p < 0.0001$

CONCLUSION

- Among the inadequately-controlled symptomatic CSU patients in this study, nearly one-third of patients reported having angioedema, without documentation of angioedema in their medical records; this suggests that a higher proportion of these patients might experience angioedema than previously reported
- Patients who experienced angioedema had significantly worse HRQoL as assessed by DLQI scores, after adjusting for important covariates
- The findings suggest a misalignment between patients and physicians in reporting angioedema, and the need for improved education and physician-patient communication regarding angioedema in CSU

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CONFLICT OF INTEREST

Maria-Magdalena Balp is an employee of Novartis Pharma AG, Basel, Switzerland.