Patient-reported burden of transfusion-dependent ß-thalassemia in the USA and the UK measured using a digital app

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BACKGROUND

ß-thalassemia is a rare genetic disease, characterized by impaired production of the ß-globin chain of adult hemoglobin. In severe cases, this results in a deficiency of functional red blood cells, leading to chronic anemia, serious morbidity and a shortened lifespan compared with the general population.[1] Patients with the most severe form of the disease, thalassemia major, and some with the less severe thalassemia intermedia, are reliant on regular blood transfusions.[2] This is known as transfusion-dependent thalassemia (TDT).[1,2]

Individuals with TDT have been shown to have low health-related quality of life (HRQoL) compared with the general population, driven largely by disease-related complications and chelation-related toxicities.[3-6]

Until recently, there has been little research into the impact of TDT on patients' day-to-day lives. The collection of daily real-world data, direct from patients, may therefore provide valuable insights.

OBJECTIVES

The objectives of this analysis were to evaluate real-world management and symptom burden of TDT, as well as the quality of life of individuals with TDT in the USA and UK.

METHODS

Individuals with TDT were recruited to a 3-month study (rolling recruitment and 3-month participation during the period August 2018 to September 2019) to investigate the time and symptom burden of the disease and its impact on HRQoL. Adult participants or caregivers for individuals with TDT aged 12–17 years provided data via MyThalLog—a bespoke smartphone app.

Data collected via the app included the following:

- Blood transfusion dates
- Daily burden assessments:
  - Time burden questionnaire
  - Brief Fatigue Inventory (BFI) 'worst fatigue' question
  - Brief Pain Inventory Short Form (BPI-SF) 'worst pain' question
- Monthly burden assessments:
  - Complete BFI
  - Transfusion-dependent Quality of Life (TranQoL) questionnaire.

Minimal clinically important differences (MCIDs) were defined as >1 and >2 point changes in fatigue and pain scores, respectively, as per the literature.[7]

RESULTS

Key demographics

Demographics for the study population are presented in Table 1.

Table 1: Key demographics

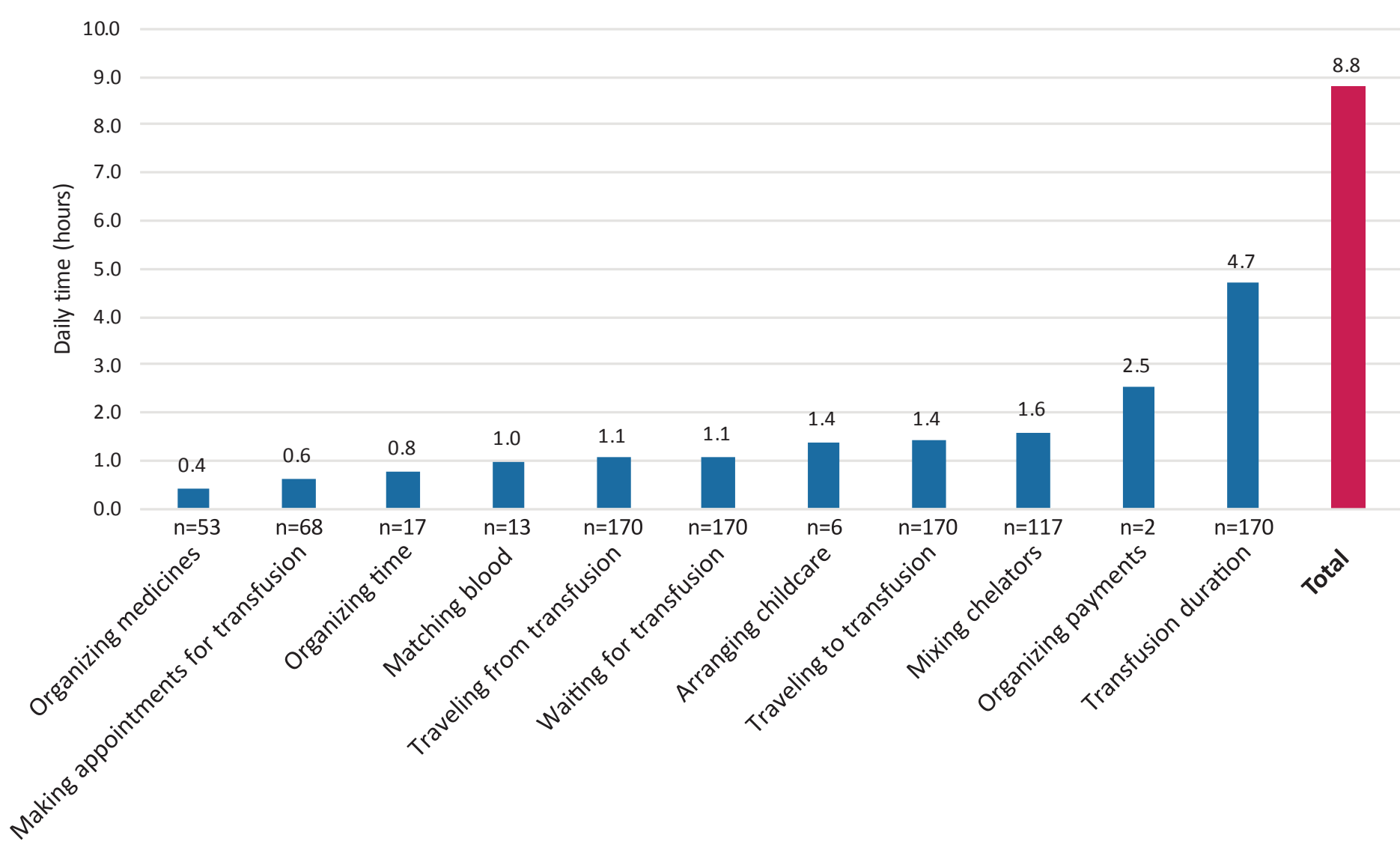
Parameter	Value
Country of residence (n,%)	
UK	43 (74)
US	15 (26)
Sex (n,%)	
Female	31 (53)
Male	26 (45)
Not Reported	1 (2)
Type of thalassemia	
Major	53 (91)
Intermedia	3 (5)
Don't know/haven't been tested	1 (2)
Not reported	1 (2)
Mean age	**36.45 (±10.77)**

Daily time burden, transfusion day

Mean daily time burden of transfusion and transfusion-related activities on a transfusion day is presented in Figure 1.

The time burden of TDT was substantial on transfusion days (mean: 8.8 hours, median: 8.2, Interquartile Range [IQR]: 3.4).

Figure 1: Mean daily hours spent on transfusion related activities on a transfusion day



Note: 178 transfusion day surveys, means are calculated amongst the individuals that reported ≥ 0 hours spent on these activities.

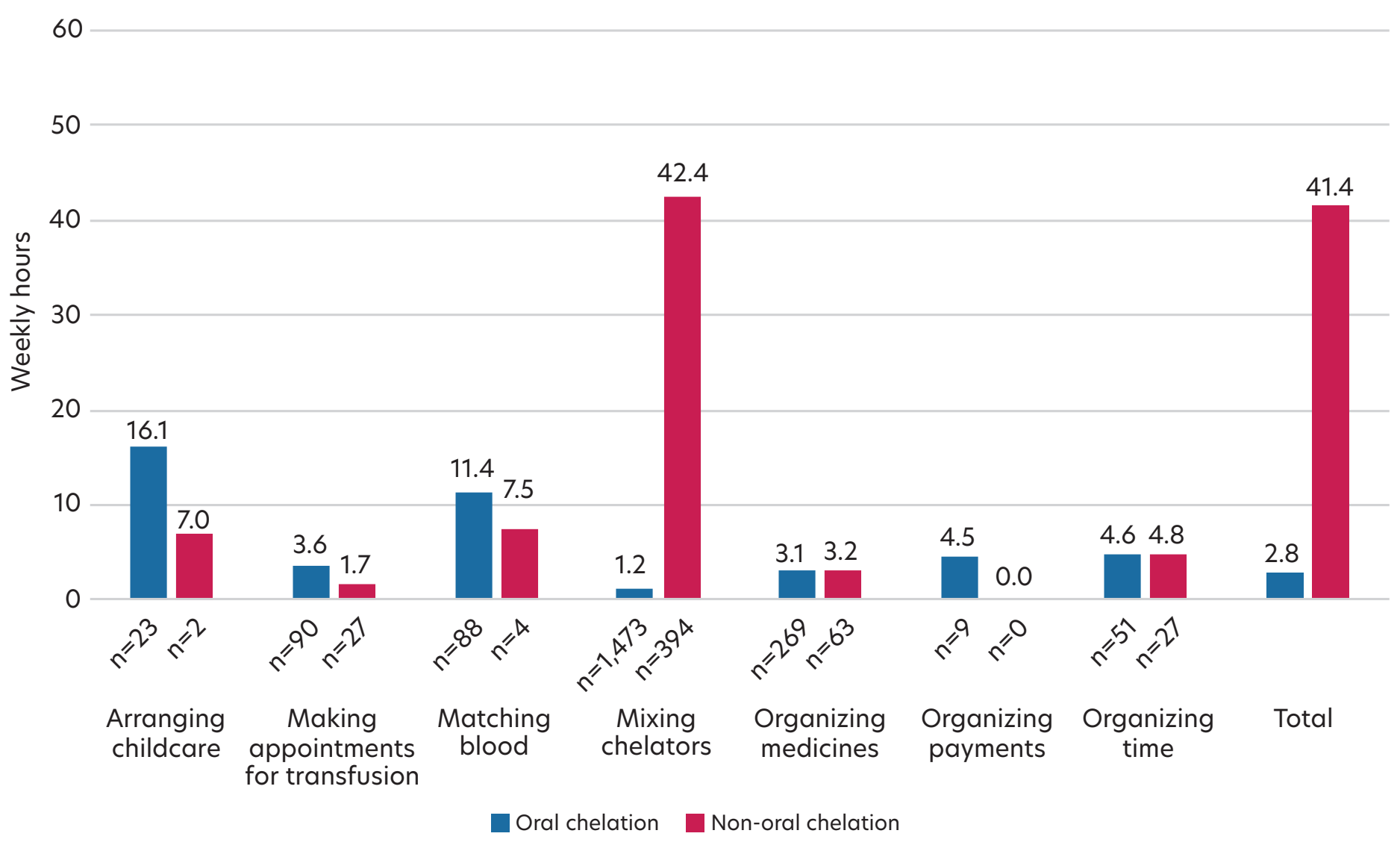
Weekly time burden, non-transfusion week

Mean weekly time burden of transfusion-related activities in a non-transfusion week (7 days, no transfusion) is presented in Figure 2.

The mean weekly time burden in non-transfusion weeks was as follows:

- 41.4 hours (median: 10.2, IQR: 87.5 - variation driven by time for chelation preparation) for participants on non-oral chelators
- 2.87 hours (median: 1.2, IQR: 1.2) for those on oral chelation only.

Figure 2: Mean weekly hours spent on transfusion related activities in non-transfusion weeks



Note: 1,613 oral chelator non-transfusion day surveys and 414 non-oral chelator non-transfusion day surveys.

Means are calculated amongst the individuals that reported ≥ 0 hours spent on these activities.

Daily health-related quality of life (worst pain and worst fatigue) around transfusion

Daily worst fatigue centred around transfusion timepoints is presented in Figure 3 and daily worst pain in Figure 4.

Mean worst fatigue and pain scores were higher in the five days pre-transfusion than in the five days post-transfusion (fatigue 5.6 vs 4.0; pain 4.8 vs 3.6; 10-point scale; 10 = worst symptoms).

The observed post-transfusion reduction in fatigue was clinically relevant (mean reductions versus transfusion day, over days one to three: 1.2, 1.4, 1.8 points, respectively; MCID: 1 point[8]), as seen in Figure 3.

The post-transfusion reduction in pain did not meet the MCID (mean reductions over days one to three: 0.9, 1.1, 1.4 points, respectively; MCID: 2 points), Figure 4.

Figure 3: Mean worst fatigue score, five days pre and post transfusion (day 0)

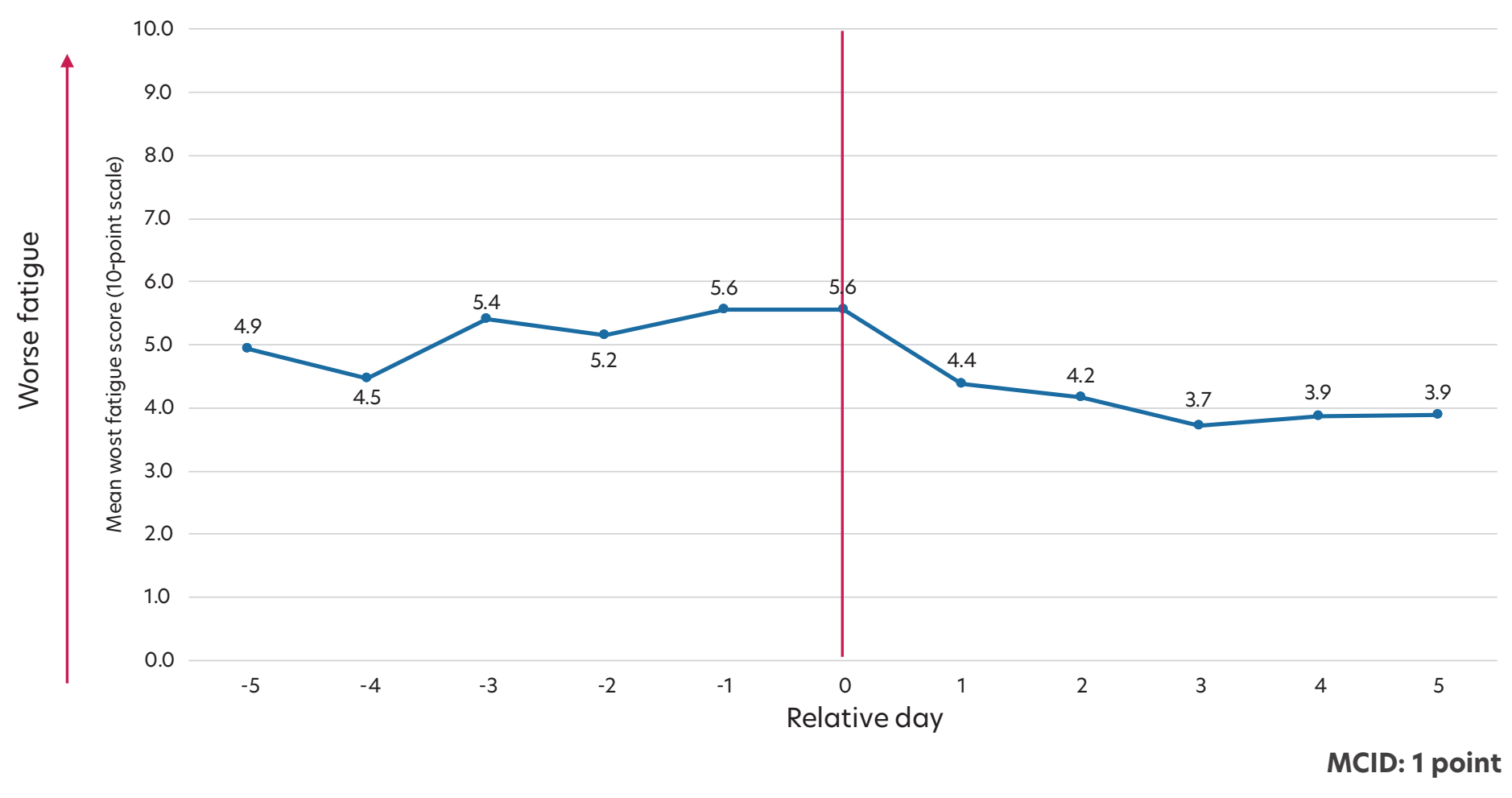
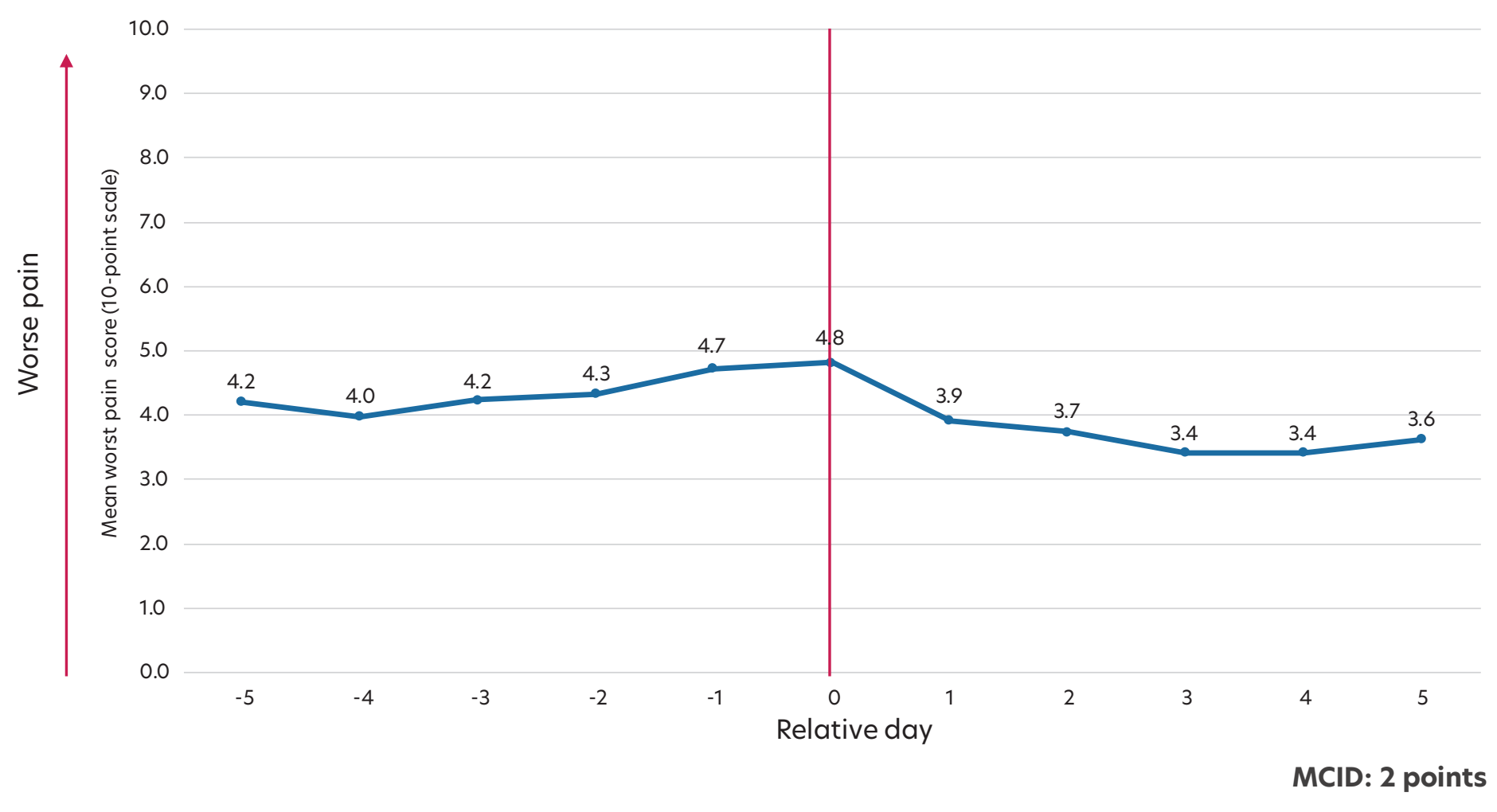


Figure 4: Mean worst pain score, five days pre and post transfusion (day 0)



Brief Fatigue Inventory

BFI global fatigue scores were as follows:

- Mean: 5.5
- Median: 6.2
- IQR: 4.0.

A higher global fatigue score is indicative of worse fatigue on a 10-point scale; 10=Worst Symptoms.

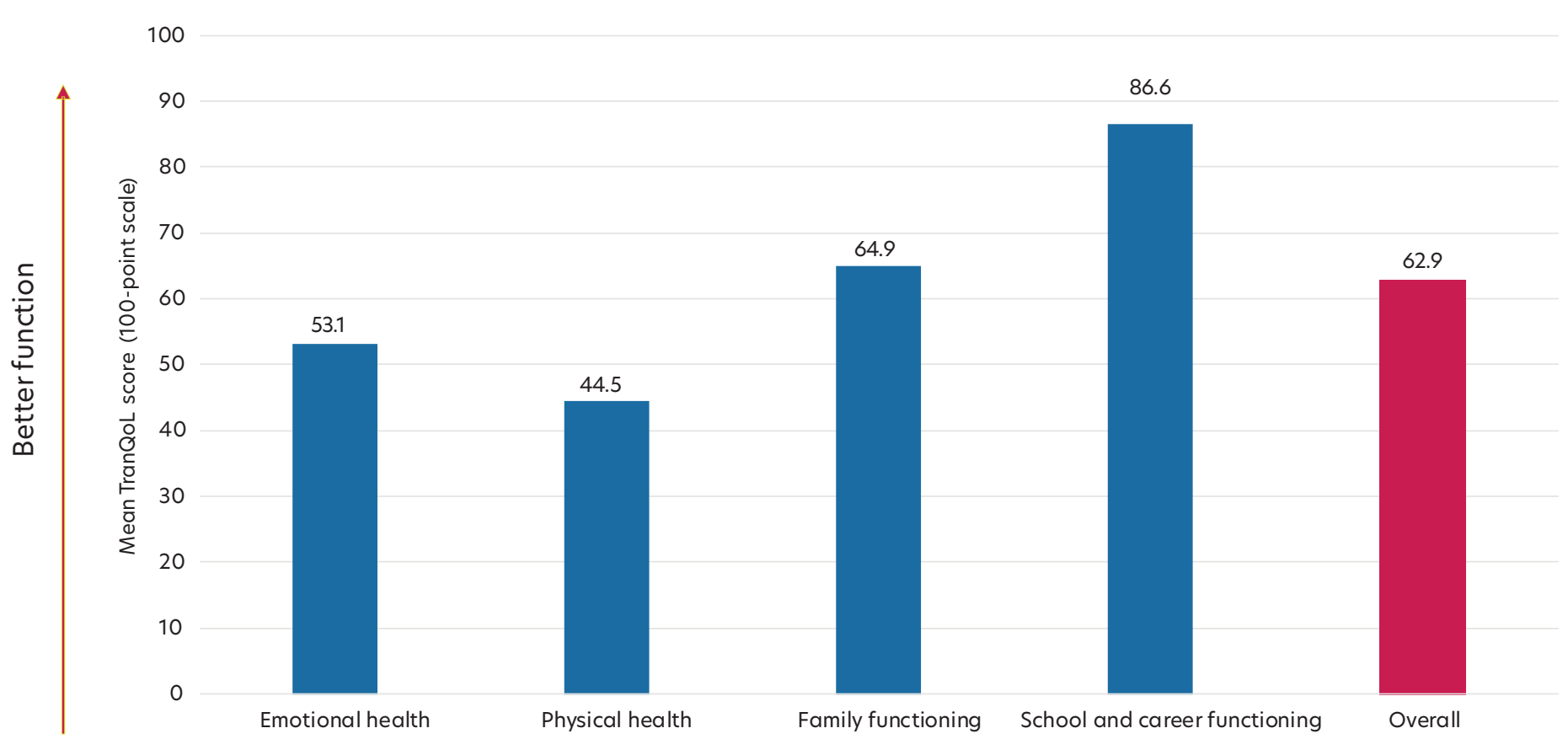
Transfusion-dependent Quality of Life questionnaire

Mean baseline (first survey entry) TranQoL overall and domain scores are presented in Figure 5. A higher domain score is indicative of higher functioning on a 100-point scale; 100 = best HRQoL.

Overall TranQoL scores were as follows:

- Mean: 62.9
- Median: 63.7
- IQR: 23.9.

Figure 5: Mean TranQoL scores, overall and by domain



DISCUSSION

The daily burden facing individuals with TDT is multifaceted; time spent managing aspects of the disease is high, as well as time spent on transfusion itself. Individuals on non-oral chelation mechanisms demonstrated the highest time burden for TDT-related activities in a non-transfusion week (7 days) versus those on oral chelation.

Daily pain and fatigue symptoms increased prior to transfusion; though fatigue symptoms showed relief in the days 2-5 post transfusion, pain remained at a consistent symptom level post transfusion.

TranQoL functioning scores for this real-world study were lower than reported previously in TDT populations from TranQoL validation studies in North America (i.e., Klassen et al) and higher (better) than Middle Eastern validation studies shown in Figure 6.[9-11] BFI global fatigue outcomes were consistent with outcomes published in other chronic diseases where time and disease burden are high. BFI scores were higher than some chronic disease populations and BFI validation studies shown in Figure 7.[8,13]

Figure 6: Comparison of published mean TranQoL overall scores

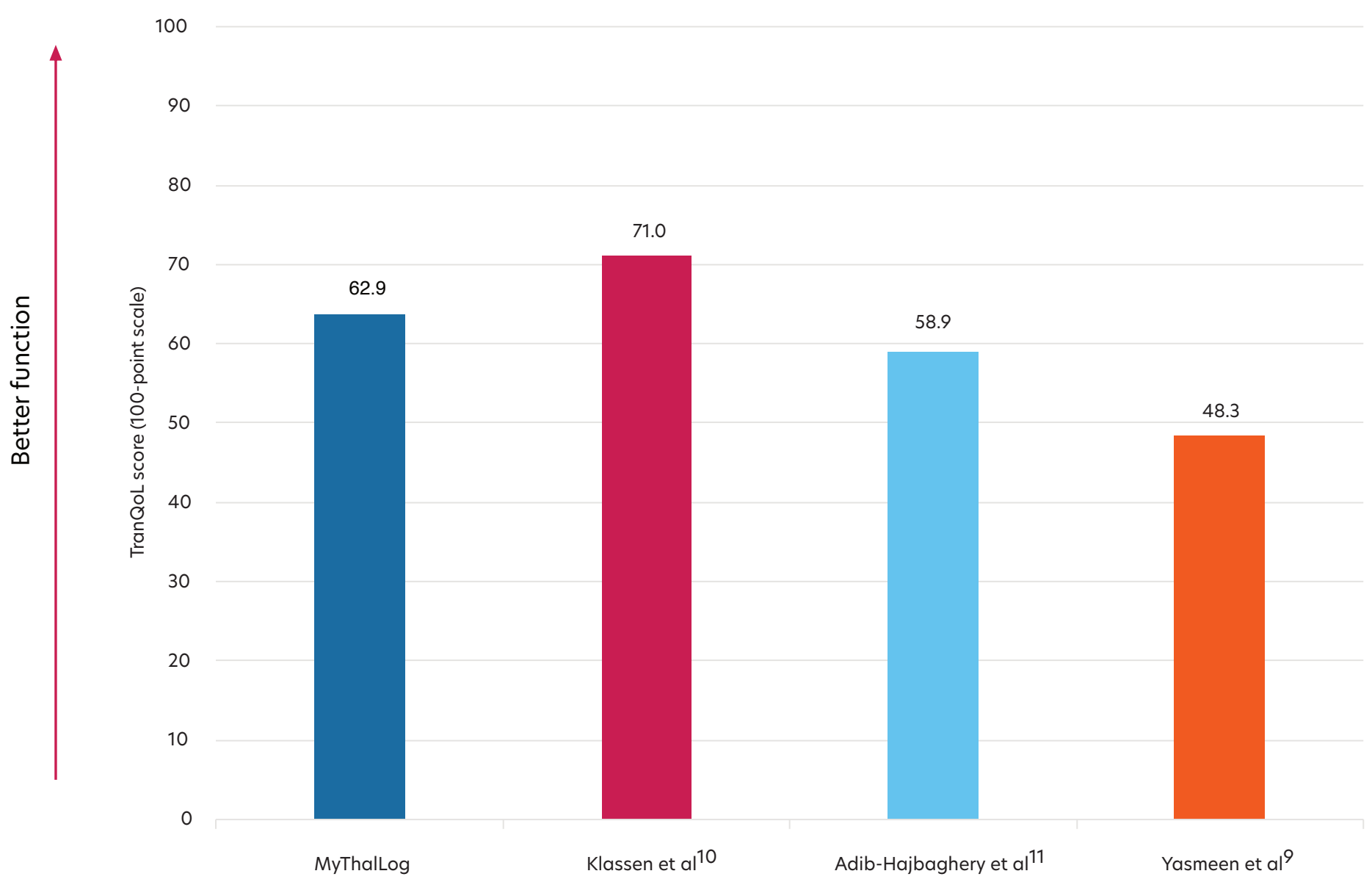
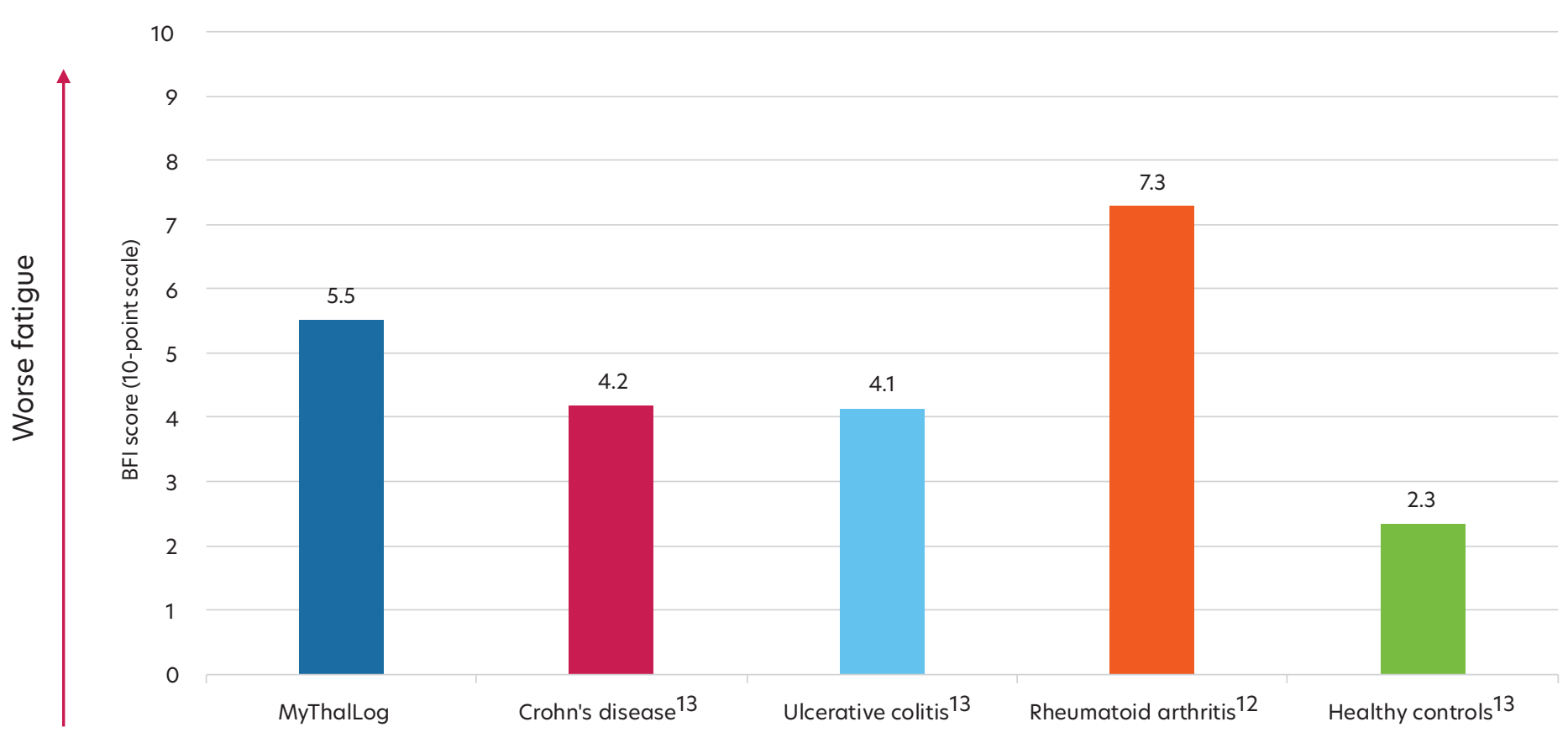


Figure 7: Comparison of published mean BFI global fatigue scores



CONCLUSIONS

The patient-reported burden of TDT in the real-world setting is high, driven by both time spent managing disease, and its impact on fatigue, pain, and HRQoL.

Despite the availability of current treatments, people with TDT continue to be burdened by the disease and may benefit from alternative therapeutic approaches.

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