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Sustained Humanistic Burden and Work Impact in Adults With Transfusion-Dependent β-Thalassemia: Results From a Global Longitudinal Survey

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INTRODUCTION

- Transfusion-dependent β-thalassemia (TDT) is a genetic blood disorder and severe form of β-thalassemia that requires frequent, lifelong red blood cell transfusions (RBCTs) and iron chelation therapy (ICT)[1]
  - RBCTs are associated with iron overload and may lead to end-organ damage and reduced life expectancy
- The health-related quality of life (HRQoL) of those living with TDT is impacted by many factors, including iron overload–related morbidity, the experience and management of fatigue and pain, the substantial time required to manage the disease, and disease-related work and activity impairments[1-3]
- Fatigue is a major concern for patients with TDT, but limited data using patient-reported outcome (PRO) measures exists to benchmark the severity and enable comparisons with other patient populations, especially among adults with TDT
- There is little evidence on disease impacts, such as work productivity impairment and financial concerns, in this patient population, and few studies have investigated HRQoL using PRO measures
- Therefore, we aimed to assess disease impacts, as well as HRQoL longitudinally, among adults with TDT receiving current treatments

OBJECTIVES

- To better understand the humanistic burden associated with living with TDT in individuals receiving standard-of-care treatments, as well as the following:
  - To further describe the key symptom of fatigue using PRO measures
  - To assess the impact of TDT on work productivity and personal finances and the time required to manage the disease
- To evaluate the impact of TDT on HRQoL and assess HRQoL longitudinally

METHODS

Study Design

- An online longitudinal survey was administered at 3 timepoints (Month 0 [baseline], Month 3, and Month 6) to participants in the United States and Europe (the United Kingdom, France, Germany, and Italy)
- The results presented here focus on the findings from Month 3 and the changes in PRO measure scores since Month 0

Key Inclusion Criteria

- Self-reported TDT diagnosis
- Received ⩾8 RBCTs per year in each of the last 2 years
- Aged ⩾18 years

Statistical Analysis

- Descriptive analyses were conducted for participant characteristics and PRO measures based on survey findings among those completing surveys at Months 0 and 3
- Minimal clinically important differences (MCIDs) and US general population data are provided for context, as available

Survey Design and Administration

- Questions were informed by qualitative interviews with individuals living with TDT in the United States and United Kingdom and the scientific advisory team consisting of clinicians, patient advocates, and outcomes researchers
- The Month 3 survey included assessments of symptoms and comorbidities, as well as bespoke questions related to other impacts, such as financial concerns, financial distress, and the time required to manage TDT

Survey Design and Administration (Continued)

- Survey invitations at Month 3 were sent to Month 0 participants, who were first informed about the study via multichannel outreach by patient advocacy groups
- PRO measures were included to assess the impact of TDT on HRQoL, fatigue, and work productivity and activity impairment (**Table 1**)

Table 1. Longitudinal Survey: PRO Measures

PRO Measure	Description
Functional Assessment of Cancer Therapy - Bone Marrow Transplantation (FACT-BMT)[4]	General measure of HRQoL (FACT-General [FACT-G]) and treatment-specific concerns of bone marrow transplantation (BMT subscale; data not shown)
EuroQol 5 Dimensions 5 Levels (EQ-5D-5L) and Visual Analog Scale (VAS)[5]	General measure of health status and self-rated health
Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-Fatigue)[6]	Measures the severity and impact of fatigue, including the social, physical, functional, and emotional consequences
Work Productivity and Activity Impairment (WPAI)[7]	Quantifies impairments in paid work and unpaid activity due to a condition

HRQoL, health-related quality of life; PRO, patient-reported outcome.

RESULTS

Demographics

- The survey was completed at Months 0 and 3 by 121 adults with TDT living in the United States (n = 60) and Europe (United Kingdom, Germany, Italy, and France; n = 61) (**Table 2**)
- The mean age of participants was 38.5 years (standard deviation [SD]: 10.5), and 70.0% of participants were female (**Table 2**)
- Only 33.9% of participants had full-time employment (⩾32 hours/week), and 32.2% were unemployed or unable to work due to TDT (**Table 2**)

Table 2. Baseline Demographics

	Adults With TDT (N = 121)
Age (years), mean (SD)	38.5 (10.4)
Geography, n (%)	
Europe (United Kingdom, Germany, Italy, and France)	61 (50.4)
United States	60 (49.6)
Gender, n (%)	
Female	84 (69.4)
Male	36 (29.8)
Non-binary	1 (0.8)
Employment, n (%)	
Full-time (⩾32 hours/week)	41 (33.9)
Unemployed	26 (21.5)
Homemaker/caregiver	9 (7.4)
Part-time (<32 hours/week)	20 (16.5)
Receiving/awaiting disability payments or on leave due to TDT	13 (10.7)
Other[a]	12 (9.9)

SD, standard deviation; TDT, transfusion-dependent ß-thalassemia.
Reporting data for participants who completed both Month 0 and 3 surveys.
[a]Response options included retired, prefer not to say, student, and other.

Clinical Characteristics

- Participants received a mean of 18.2 (SD: 7.9) RBCTs annually (assessed at Month 0), equivalent to a mean of 1 RBCT every 2.9 weeks (**Table 3**)
- Among Month 3 participants, 96.7% were prescribed ICT and 59.5% had taken prescription or over-the-counter pain medicine in the past 3 months (**Table 3**)

Table 3. Clinical Characteristics

	Adults With TDT (N = 121)
Frequency of transfusions in the past 12 months[a] at Month 0	
Mean (SD)	18.2 (7.9)
Median (IQR)	17 (12–20)
Transfusion-related complications in the past 3 months at Month 0, n (%)	
Transfusion reaction	65 (53.7)
Transfusion-related infection	30 (24.8)
Alloimmunity	24 (19.8)
Other	20 (16.5)
Current treatments in the past month at Month 3, n (%)	
ICT	117 (96.7)
Over-the-counter pain medicine	46 (38.0)
Prescription pain medicine	26 (21.5)
Estrogen replacement therapy	22 (18.2)
Luspatercept	13 (10.7)
Testosterone replacement therapy	12 (9.9)
Bisphosphonates	9 (7.4)
None	1 (0.8)

ICT, iron chelation therapy; IQR, interquartile range; SD, standard deviation; TDT, transfusion-dependent ß-thalassemia.
Reporting data for participants who completed both Month 0 and 3 surveys.
[a]April 2021 to 2022.

FACT-G: Month 3

- Participants reported lower HRQoL based on the FACT-G total score at Month 3 (69.3) compared with the US general population score (80.1). This difference was driven by reduced scores in the physical, emotional, and functional wellbeing domains (**Table 4**)
- The FACT-G total score changed by an average of –0.8 points from Month 0 to 3, below the MCID range of 3 to 7 points.[8,9] This PRO measure suggests that, on average, HRQoL impacts were sustained over time (**Figure 1A**)

Table 4. FACT-G Results

FACT-G Domain, Mean Score (SD)	Score Range[a]	Adults With TDT at Month 3 (N = 121)	US Adults[10]
Physical wellbeing	0–28	17.8 (6.7)	22.7 (5.4)
Social and family wellbeing	0–28	19.6 (6.0)	19.1 (6.8)
Emotional wellbeing	0–24	15.3 (5.2)	19.9 (4.8)
Functional wellbeing	0–28	16.6 (6.2)	18.5 (6.8)
FACT-G total	0–108	69.3 (19.8)	80.1 (18.1)

FACT-G, Functional Assessment of Cancer Therapy - General; HRQoL, health-related quality of life; MCID, minimal clinically important difference; SD, standard deviation; TDT, transfusion-dependent ß-thalassemia.
The FACT-G MCID range is 3 to 7 points (based on publications in other hematological conditions).[8,9]
[a]Higher scores indicate better HRQoL.

EQ-5D-5L VAS: Month 3

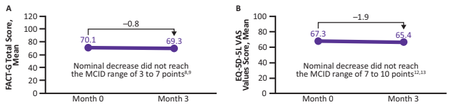
- Participants reported lower self-reported health (mean score) on the EQ-5D-5L VAS at Month 3 (65.4) compared with the US general population (80.4)[11] (**Table 5**)
- VAS scores from Month 0 to 3 changed slightly (–1.9 points) among participants with TDT; however, the scores did not reach the MCID of the measure (7 to 10 points),[12,13] suggesting that, on average, participants did not have consistently low HRQoL, as measured by the EQ-5D-5L VAS, when on standard-of-care treatments (**Figure 1B**)

Table 5. EQ-5D-5L VAS Results

	Score Range	Adults With TDT at Month 3 (N = 121)	US Adults[11] (n = 60)
VAS score, mean (SD)	0–100	65.4 (19.2)	80.4 (15.6)

EQ-5D-5L, EuroQol 5 Dimensions 5 Levels; SD, standard deviation; TDT, transfusion-dependent ß-thalassemia; VAS, Visual Analog Scale.

Figure 1. Sustained HRQoL Impact of TDT Over Time as Measured by A) FACT-G and B) EQ-5D-5L VAS



EQ-5D-5L, EuroQol 5 Dimensions 5 Levels; FACT-G, Functional Assessment of Cancer Therapy - General; HRQoL, health-related quality of life; MCID, minimal clinically important difference; SD, standard deviation; TDT, transfusion-dependent ß-thalassemia; VAS, Visual Analog Scale.

FACIT-Fatigue: Month 3

- The average fatigue score was 27.9, which is substantially lower than that of the US general population (43.6)[14,15] (**Table 6**)
- The average fatigue score of participants with TDT was comparable to that of patients with cancer and anemia (23.9)[15] (**Table 6**)

Table 6. FACIT-Fatigue Results

	Score Range	Adults With TDT (n = 91)	US General Population[14,15]	Patients With Cancer and Anemia[15]
FACIT-Fatigue score, mean (SD)[a]	0–52	27.9 (13.7)	43.6 (9.4)	23.9 (12.6)

FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy - Fatigue; SD, standard deviation; TDT, transfusion-dependent ß-thalassemia.
[a]Lower numbers indicate higher fatigue.[11]

WPAI: Month 3

- Employed participants missed an average of 5.9 hours of work in the past week, corresponding to an average absenteeism of 17.8% (**Table 7**)
- Participants' work productivity in the past week was reduced by 43.5% (**Table 7**)
- Among participants, 45.0% reported daily activity impairment (data not shown) and, overall, there was a 45.0% mean reduction in daily activities in the past week (**Table 7**)

Table 7. WPAI Results

WPAI Domain	Mean (SD)
Work missed in the last 7 days, hours	5.9 (10.4)
Absenteeism: Work time missed due to TDT, %[a]	17.8 (28.3)
Presenteeism: Reduced effectiveness/impairment, %[a]	34.2 (28.7)
Work productivity loss: Overall work impairment, %[a]	43.5 (32.4)
Activity impairment, %[b]	45.0 (28.6)

SD, standard deviation; TDT, transfusion-dependent ß-thalassemia; WPAI, Work Productivity and Activity Impairment.
Higher WPAI percentages represent increased impairment.
[a]n = 64 (participants indicating employment); [b]n = 54.

Time Burden Associated With Managing TDT: Month 3

- On average, participants spent a mean of 23.0 hours in the last month managing their disease, equivalent to an average of 5.3 hours per week (**Table 8**)
- The 2 most time-consuming tasks were time spent traveling to medical appointments and time spent at medical appointments (inclusive of time spent receiving transfusions) (**Table 8**)

Table 8. Time Per Month Spent Managing TDT by Task

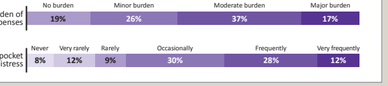
Task, Mean (SD)	Time Per Month (Hours) (N = 121)
Time at medical appointments	9.8 (5.2)
Travelling to medical appointments	3.9 (3.9)
Scheduling medical appointments	2.2 (3.1)
Preparing and administering treatments at home	2.0 (3.9)
Arranging time off from work, college, or school to receive treatment	1.8 (3.7)
Arranging refills and picking up medications	1.6 (1.6)
Organizing payments from health insurance	1.1 (1.6)
Arranging childcare due to healthcare needs	0.8 (1.7)
Mean total time by participant spent managing TDT	**23.0 (15.3)**

SD, standard deviation; TDT, transfusion-dependent ß-thalassemia.

Financial Burden and Distress: Month 3

- Among adults with TDT, 39.2% reported that they did not have sufficient money to cover the costs associated with managing their disease and estimated that they would need an additional median of $290 per month (interquartile range: $150–$500) to fully manage it
- Out-of-pocket expenses were reported to be a moderate-to-major burden for 54% of participants (**Figure 2**)
- Financial distress was reported to be experienced frequently or very frequently by 40% of participants (**Figure 2**)

Figure 2. Financial Burden and Distress



LIMITATIONS

- Study participants were self-selected and needed access to the Internet and email, which may impact the generalizability of these results
- All data were self-reported, and eligibility and accuracy were not directly verified by a clinician

CONCLUSIONS

- Despite receiving current treatments, adults with TDT experienced significant and sustained negative impacts on their HRQoL, as measured by the FACT-G, EQ-5D-5L, and WPAI
- Adults with TDT spent considerable time managing their disease (an average of 5.3 hours each week), which represents a large humanistic burden in this patient population
- On average, participants with TDT reported severe fatigue, with scores similar to those of patients with cancer and anemia, as measured by the FACIT-Fatigue
- A sizable proportion of participants reported that they had insufficient money to cover the costs associated with managing TDT (39.2%), that out-of-pocket expenses were a moderate-to-major burden (54%), and that they frequently or very frequently experienced financial distress (40%)
- Taken together, these results demonstrate the substantial humanistic burden among those living with TDT and significant unmet needs in this patient population

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AUTHOR DISCLOSURES

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