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INTRODUCTION

- Transfusion-dependent β -thalassemia (TDT) is a genetic blood disorder requiring regular, lifelong red blood cell transfusions (RBCTs) and iron chelation therapy; RBCTs are associated with iron overload that can then lead to end-organ damage and reduced life expectancy¹
- It is well known that individuals with TDT have high rates of healthcare resource utilization driven by frequent RBCTs, which can lead to high healthcare costs²
- In the United States, there is evidence to suggest that individuals with TDT also experience substantial indirect impacts due to out-of-pocket (OOP) costs and productivity loss³
- To date, little is known about the indirect costs incurred by individuals with TDT in Europe

OBJECTIVE

- This analysis used data collected from a quantitative survey of individuals with TDT to quantify indirect economic impacts of living with this disease in Europe

METHODS

Survey Study Design and Inclusion Criteria

- The overall mixed-methods study consisted of qualitative interviews and a longitudinal online quantitative survey administered at 3 timepoints (Month 0 [Baseline, M0], Month 3 [M3], and Month 6 [M6]) in the United States, France, Germany, Italy, and the United Kingdom
- Indirect economic impact results presented here are from the quantitative M3 survey among participants living in Europe (France, Germany, Italy, and the United Kingdom)
- Key inclusion criteria:
 - Aged \geq 18 years
 - Self-reported TDT diagnosis
 - Received \geq 8 RBCTs/year in each of the last 2 years

Survey Design and Administration

- Survey questions were designed based on information gathered from interviews with individuals living with TDT in the United States and United Kingdom and a scientific advisory team for the study consisting of clinicians, patient advocates, and outcomes researchers
- The baseline survey at M0 included items assessing demographic, clinical, and socioeconomic characteristics:
 - Demographics included age, gender, race, and marital status
 - Clinical characteristics included the number of RBCTs in the past 12 months
 - Socioeconomic characteristics included geographic region of residence, educational attainment, employment status, annual household income, and primary health insurance coverage (if any)
- The survey administered at M3 included questions to assess the time required to manage TDT and indirect medical costs related to the management of TDT
- At M3, the Work Productivity and Activity Impairment (WPAI) questionnaire was included to quantify employment and impairments in paid work

Measures and Calculations Used to Quantify Monthly and Annual Indirect Costs

- Annual OOP costs were calculated by totaling the estimated monthly cost of individual TDT-related expenses and then multiplying the total by 12 months
 - Country-specific currencies were converted to United States dollars (USD) using the following purchasing power parity ratios, as reported by the Organisation for Economic Co-operation and Development (OECD) year-to-date data 2022: France = 0.725, Germany = 0.741, Italy = 0.654, and United Kingdom = 0.693⁴
- The calculation for annual health-related activity costs was guided by the Human Capital Approach wherein the estimated monthly time spent performing individual activities was totaled, multiplied by 12 months, and then multiplied by the mean hourly wage (24 USD in France, Germany, Italy, and the United Kingdom, as reported by the OECD, 2021)⁴
- Costs associated with absenteeism (days missed from work), presenteeism (reduced productivity while at work), and work productivity loss (overall work impairment) were calculated by multiplying composite scores measured by the WPAI by the mean annual salary across the 4 countries (49,025 USD, as reported by the OECD, 2021)⁴

Statistical Analysis

- Descriptive statistics were conducted for participant characteristics, OOP costs, health-related activities, and WPAI composite scores for absenteeism, presenteeism, and work productivity loss
 - Frequency (n) and proportion (%) were reported for categorical variables, and mean and standard deviation (SD) were reported for continuous variables

RESULTS

Demographic and Clinical Characteristics

- Sixty-one adults with TDT living in Europe participated in the survey (**Table 1**)
- Most participants were female (n = 38 [62.3%]), and participants' mean age was 40.6 years (SD: 10.7) (**Table 1**)
- Participants received a mean of 17.8 (SD: 5.9) RBCT events in the year prior to study entry (**Table 1**)

Table 1. Demographic and Clinical Characteristics

Adults With TDT (N = 61)	
Age, years, mean (SD)	40.6 (10.7)
Gender, n (%)	
Female	38 (62.3)
Male	22 (36.1)
Non-binary	1 (1.6)
Marital status, n (%)	
Single	28 (45.9)
Married/domestic partner	20 (32.8)
Separated/divorced	8 (13.1)
In a committed relationship	4 (6.6)
Prefer not to say	1 (1.6)
RBCT events in the past 12 months, mean (SD)	17.8 (5.9)

RBCT, red blood cell transfusion; SD, standard deviation; TDT, transfusion-dependent β -thalassemia.

Socioeconomic Characteristics

- Among participants, 29% held a bachelor's degree, 4.9% held a master's degree, and 29.5% held a high school diploma as their highest level of educational attainment (**Table 2**)
- Approximately 25% of participants were unemployed and 29.5% worked full-time (**Table 2**)
- Of the 39 participants who reported an annual household income, 79.4% earned 50,000 USD or less, with 17.9% earning less than 10,000 USD (**Table 2**)

Table 2. Socioeconomic Characteristics

Adults With TDT (N = 61)	
Characteristic, n (%)	
Geographic region of residence	
Large city	24 (39.3)
City or town ^a	20 (32.8)
Suburb near a large city	9 (14.8)
Small city or town ^{a,b}	6 (9.8)
Rural area/other	2 (3.2)
Highest level of education achieved	
Did not complete high school	3 (4.9)
High school diploma	18 (29.5)
Some college credit, no degree	3 (4.9)
Trade or technical school	5 (8.2)
Bachelor's degree	18 (29.5)
Master's degree	3 (4.9)
Other/prefer not to say	11 (18.0)
Employment status	
Full-time	18 (29.5)
Unemployed	15 (24.6)
Part-time	8 (13.1)
On-leave or waiting for approval for leave	8 (13.1)
Retired	4 (6.6)
Other ^c	8 (13.1)
Annual household income (USD) ^{d,e}	
<10,000	7 (17.9)
10,000 to 25,000	10 (25.6)
25,000 to 50,000	14 (35.9)
50,000 to 75,000	3 (7.7)
75,000 to 100,000	0
100,000 to 200,000	4 (10.3)
\geq 200,000	1 (2.6)
Primary health insurance ^f	
NHS ^g /universal/public healthcare	41 (91.1)
No insurance/do not know	4 (8.8)

NHS, National Health Service; SD, standard deviation; TDT, transfusion-dependent β -thalassemia; USD, United States dollars.
^aNot a suburb of a large city; ^b<25K population; ^cOther, homemaker/caregiver, student, or prefer not to say; ^dBefore taxes from all sources; ^en = 39; ^fn = 45.

OOP Costs

- Costs associated with medical appointments (e.g., transportation, childcare) (47 USD [SD: 72]) and attending medical appointments related to TDT (35 USD [SD: 61]) were the highest reported monthly OOP expenses for participants (**Table 3**)
- Average OOP costs for all items totaled 222 USD per month (SD: 266) (**Table 3**)
- Participants reported spending a mean of 2,670 USD on OOP costs annually (**Table 3**)

Table 3. OOP Costs

Adults With TDT (N = 61)	
Category, Mean (SD)	
Monthly costs, USD	
Transportation, parking, and other costs associated with attending medical appointments and hospitalizations (e.g., childcare)	47 (72)
Medical appointments related to TDT	35 (61)
Holistic care (e.g., massage, acupuncture)	30 (76)
Paid caregivers or support services (e.g., personal care, housework)	29 (78)
Prescription medications	24 (48)
Vitamins or nutritional supplements	22 (34)
OTC medications	18 (32)
Physical therapy and rehabilitation	8 (35)
Mental health services	8 (50)
Other	0 (4)
Total costs, USD	222 (266)
Annual costs, USD	2,670

OOP, out-of-pocket; OTC, over-the-counter; SD, standard deviation; TDT, transfusion-dependent β -thalassemia; USD, United States dollars.

Health-Related Activities

- The health-related activities in which participants spent the most time (mean [SD]) engaging every month were attending medical appointments (8.8 hours [4.7]) and traveling to medical appointments (4.2 hours [4.4]) (**Table 4**)
- The average time participants spent engaging in all health-related activities per month was 22.0 hours (SD: 14.2), which translates to 529 USD in unpaid labor managing the disease (**Table 4**)
- Participants reported spending an average of 264.4 hours on health-related activities annually, which translates to 6,345 USD in unpaid labor managing the disease (**Table 4**)

Table 4. Health-Related Activities

Outcome	Adults With TDT (N = 61)	
	Time, Hours, Mean (SD)	Cost, USD
Monthly time and costs		
Time at medical appointments	8.8 (4.7)	210
Traveling to medical appointments	4.2 (4.4)	102
Scheduling medical appointments	2.6 (3.9)	62
Preparing and administering treatments at home	1.9 (2.6)	45
Arranging time off from work and school to receive treatment	1.7 (3.2)	41
Arranging refills and picking up medications	1.6 (1.3)	39
Arranging childcare due to healthcare needs	0.8 (1.6)	18
Organizing payments from health insurance	0.6 (1.3)	15
Total	22.0 (14.2)	529
Annual time and costs		
Total	296.4	6,345

SD, standard deviation; TDT, transfusion-dependent β -thalassemia; USD, United States dollars.

WPAI

- Thirty-one (50.8%) participants were employed (working for pay) and thus included in the analysis of the WPAI (**Table 5**)
- Employed participants reported substantial absenteeism (28.5%) and presenteeism (43.5%) (**Table 5**)
- Average lost annual wages due to absenteeism and presenteeism were 13,972 USD and 21,326 USD, respectively (**Table 5**)

Table 5. WPAI, Composite Scores

Category ^a	Employed Adults With TDT Living in Europe, Mean (SD), % n = 31	Corresponding Indirect Cost of TDT, USD
Absenteeism	28.5	13,972
Presenteeism	43.5	21,326
Work productivity loss	58.1	28,484

SD, standard deviation; TDT, transfusion-dependent β -thalassemia; USD, United States dollars; WPAI, Work Productivity and Activity Impairment.
^aActivity impairment for employed adults with TDT (n = 31) was 51.1% (SD: 29.6). Activity impairment was not coded.

LIMITATIONS

- The calculation for mean annual OOP and health-related activities costs assumes these costs are consistent from month-to-month for a duration of 1 year
- Indirect impacts for individuals with SCD who were unemployed were not captured using the WPAI; potential additional indirect impacts of lack of employment were not fully captured in this analysis
- Study participants were self-selected, which may impact the generalizability of the results
- All data were self-reported; data eligibility and accuracy were not directly verified with medical records
- Individuals who did not have Internet and email access required to complete the survey were excluded

CONCLUSIONS

- Patients with TDT incur substantial indirect costs due to OOP costs, health-related activities, and work productivity
- Half of the participants were employed, and these participants reported substantial absenteeism and presenteeism due to TDT
- The substantial indirect costs for individuals living with TDT, as well as for society, highlight the unmet needs of this underserved patient population
- Further analyses of indirect costs for caregivers of individuals living with TDT are needed to understand the total burden of disease-related indirect impacts

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