

Willingness to Pay for Temporary Alleviation of Anemia Status in Transfusion-Dependent Beta-Thalassemia Patients in China

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Background

- Beta-thalassemia is a genetic blood disorder marked by ineffective erythropoiesis and anemia of varying severity. Transfusion-dependent B-thalassemia (TDT) includes B-thalassemia major, some B-thalassemia intermediate and severe HbE/B-thalassemia. It is characterized by chronic and progressive anemia and the thalassemia major has been categorized as a rare disease by the National Health Commission of the People's Republic of China in 2023 . TDT patients require lifelong blood transfusion and iron-chelation therapy, which imposes a substantial disease burden and significantly restricts their life expectancy and quality of life.
- At present, lifelong dependent red blood cell (RBC) transfusion with iron chelation is still the best supportive care for adult patients with TDT, allowing patients to temporarily get rid of the symptoms of anemia. However, it must be noted that RBC transfusion may cause infections, alloimmunization, damage from trace elements and other transfusion reactions, representing a major and unsustainable health burden.
- Furthermore, many TDT patients in China cannot receive adequate blood transfusions. A study conducted in Guangxi Province showed that only 26.7% of thalassemia major patients reported receiving transfusions on schedule, while 77% of patients believed that they did not have sufficient blood supply or were uncertain about it. In China, the cut-off value of Hb level is 7g/dl in two consecutive blood routine tests conducted with an interval of more than 2 weeks. However, due to insufficient blood supply, this cut-off value is often restricted to 60 g/L, resulting in only 32.1% of children receiving the necessary transfusions. Patients’ needs of RBC transfusion for temporarily alleviation of anemia status are not fully met.
- As a result, the monetary value of RBC for TDT patients may be underestimated, and assessment of the willingness to pay (WTP) of Chinese TDT patients for temporary remission of anemia status (by RBC transfusion) is warranted.
- This study aimed to assess the willingness to pay for temporary remission of anemia status among patients with TDT.

Methods

- “Anemia status” refers to the state in which patients exhibit noticeable anemia symptoms and require blood transfusions to sustain their lives.
- One unit of leukocyte-depleted suspended red blood cells was selected for WTP evaluation, which is endorsed by clinical experts. This WTP was then multiplied by the average number of units per transfusion to represent patients’ WTP for temporary alleviation of anemia status.
- The study includes a prestudy and a poststudy.
 - The significance of prestudy was to identify the bidding points and examine patients’ understanding of the questionnaire. The results of the prestudy showed that patients had a good understanding of the questionnaire.
 - In the poststudy, a double-bounded dichotomous choice contingent valuation method (CVM) was employed to estimate the WTP. Respondents were presented with a dichotomous choice to indicate whether they were willing to pay a provided amount for one unit of leukocyte-depleted suspended red blood cells. Subsequently, based on their responses, an additional amount was presented and corresponding choice was made.
- Online questionnaires were distributed to patients recruited from provinces with a high incidence of TDT, including Guangdong, Guangxi, Yunnan, and Guizhou Provinces in China.
- Interval regression analysis was performed to estimate WTP in two scenarios (consideration of economic restrictions / without considering economic constraints).

Sample

- The inclusion criteria were as follows:
 - Participants willing to participant in this study; ≥18 years old; diagnosed with TDT.
- The exclusion criteria included:
 - patients who were unable to complete the questionnaire independently due to health conditions; patients with cognitive impairments; patients receiving washed red blood cells.
- Sampling and data collection
 - The survey was conducted from March to August in 2023.
 - Patients were selected from hospitals in high-incidence provinces including Guangdong, Guangxi, Yunnan, and Guizhou in China using a cluster sampling method.
 - Patients who agreed to participate in the study completed online questionnaires on demographic information, health status, and transfusion burden with real-time WeChat communication assistance from researchers if necessary.
- Data quality control
 - Consistency and completeness checks were performed after the questionnaire was submitted. In case of any uncertainty in the questionnaire responses, clarification was sought from the patients to ensure accuracy.

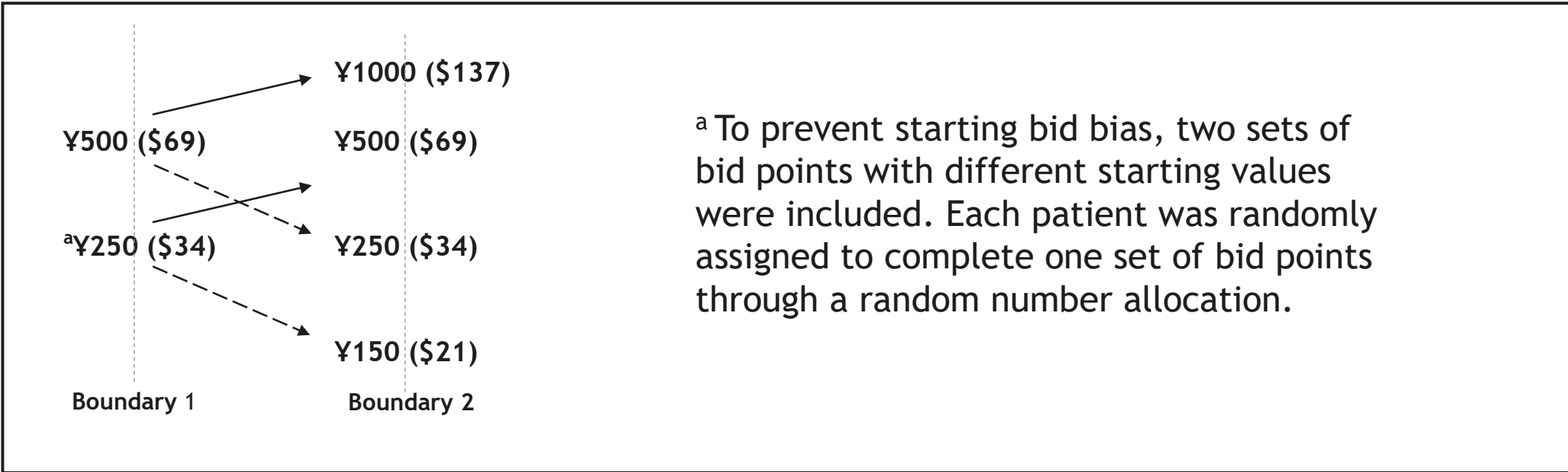
Questionnaire design

- The questionnaire consists of two parts.
 - The first part comprises questions focusing on patient demographics, socioeconomic conditions and information relevant to RBC transfusion treatment.
 - The second part of the questionnaire presents a willingness-to-pay section.
- In the given hypothetical market (blood transfusion for temporary relief from anemia, otherwise no temporary relief from anemia), each participant was asked whether to accept the first bid point of 1 unit of leukocyte-depleted suspended red blood cells. If respondents answered “yes”, the second bid point would be higher, otherwise it would be lower.
- The bid points were predetermined primarily based on the results of the prestudy including 20 patients, who responded in an open-ended manner in two scenarios (table 1).

Table 1. Patients’ WTP in prestudy

Statistic	Scenario1: Consideration of economic conditions	Scenario2: No consideration of economic conditions
average value	RMB 589 (SD=1123) [USD 81(SD=154)]	RMB 658 (SD=1111) [USD 90 (SD=152)]
1st percentile	RMB 40 (USD 5)	RMB 100 (USD 14)
25th percentile	RMB 100 (USD 14)	RMB 150(USD 21)
50th percentile	RMB 168 (USD 23)	RMB 235 (USD 32)
75th percentile	RMB 350 (USD 48)	RMB 500 (USD 69)
99th percentile	RMB 5000 (USD 686)	RMB 5000 (USD 686)

Figure 1. Tender point design



Data analysis

- Descriptive analysis was used to summaries the sociodemographic characteristics of the study participants.
- Interval regression analysis was performed to estimate the WTP mean using the following formula: $WTP_i(z_i, u_i) = \alpha_i \beta + u_i$
 - Where β is the coefficient value of covariates x_i , and u_i is the error term which is normally distributed. WTP_i indicates the interval outcome (y_{1i} , y_{2i}) determined by participants’ responses to the bid values, and its distribution will be $Pr(y_{1i} \leq y_i \leq y_{2i})$.
- A likelihood function was constructed to directly obtain estimates for β and u using maximum likelihood estimation.
- All analyses were done in Stata 15.0.

Results

- Formal study questionnaires were obtained from 149 TDT patients across four provinces with a high incidence of TDT, including Guangxi (75.2%), Guangdong (21.5%), Yunnan (2.0%), Hunan (0.7%) and Guizhou (0.7%).
- The average age of the patients was 26.2 years, and 31.5% of them were students. Regarding educational background, 71.8% of patients had education levels higher than junior high school. Their average monthly personal income was RMB 1446.9 (USD 198.5). A total of 46.3% of patients had no income, and 85.2% of patients reported a family monthly income per capita below RMB 5000 (USD 685.9) (China’s middle to low income levels).
- Regarding the current transfusion situation, an average of 3.7 units per single blood transfusion (SD=1.2) were needed, and an annual transfusion frequency is 15.4 times (SD=11.2).

Table 2. Sociodemographic characteristics of study participants

Items		
Gender, n (%)		
Man	82	(55.0%)
Woman	67	(45.0%)
Age (years), mean (SD)	26.2	(9.0)
Employment status, n (%)		
School students	47	(31.5%)
Unemployed	42	(28.2%)
Other conditions	60	(40.3%)
Educational background, n (%)		
Below junior high school	42	(28.2%)
Junior high school or above	107	(71.8%)
Degree, n (%)		
Bachelor degree or above	32	(21.5%)
below a bachelor's degree	117	(78.5%)
Account type, n (%)		
Rural	80	(53.7%)
Urban	69	(46.3%)
Personal monthly income, mean (SD)	¥1446.9 (1627.6)	\$198.5 (223.3)
No income, n (%)	69	(46.3%)
Have income, n (%)	80	(53.7%)
Monthly per capita family income, n (%) ^a		
RMB 3,000 and below	72	(48.3%)
RMB 3,001-5,000	55	(36.9%)
RMB 5,001-8,000	15	(10.1%)
More than RMB 8,001	7	(4.7%)
Self-evaluation household burden, n (%)		
Heavy burden	96	(64.4%)
Basic affordability	51	(34.2%)
Completely affordable.	2	(1.3%)

^a Contain patients with no personal income

The willingness to pay of TDT patients

- In scenario 1 (considering the economic level), TDT patients had an average WTP of ¥513.5 per unit of leukocyte-depleted suspended red blood cells (95% CI [¥452.0, ¥575.0]), equivalent to \$70.4 (95% CI [\$62.0, \$78.8]).
- In scenario 2 (without accounting for the economic level), patients had an average WTP of ¥1104.1 per unit of leukocyte-depleted suspended red blood cells (95% CI [¥931.5, ¥1267.7]), equivalent to \$151.5 (95% CI[\$127.7-\$175.0])
- Consequently, when considering the economic circumstances, the estimated WTP for temporary alleviation of anemia (per single transfusion) totaled at ¥1900 (\$260.6). When disregarding their own economic circumstances, patients exhibited an average WTP of ¥4085.2 (\$560.4) for temporary alleviation of anemia for a single transfusion.

Table 3. Estimates of WTP

	Coef.	Std. Err.	z	[95% CI]	Log likelihood	AIC	BIC
WTP-considering the economic level	¥513.5 (\$70.4)	31.4 (4.3)	16.4	¥452.0-¥575.0 (\$62.0-\$78.9)	-194.4	392.8	398.8
WTP-without accounting for economic level	¥1104.1 (\$151.5)	88.1 (12.1)	12.5	¥931.5-¥1276.7 (\$127.8-\$175.1)	-135.4	274.9	280.8

Factors associated with WTP

- To explore the determinants of WTP for 1 unit of leukocyte-depleted red blood cells, the basic model incorporated all possible factors. The expanded model (Wald chi2(9) =33.85, P = 0.0001) was employed.
- The analysis of influencing factors indicated that male patients, those with higher household income levels, and patients with education beyond junior high school had greater WTP. Additionally, patients with lower single-transfusion volumes and greater convenience of blood transfusion exhibited higher WTP (Table 4).

Table 4. Factors associated with WTP

	Beta	Coef.	Std. Err.	[95% Conf. Interval]
Age**		10.0	3.5	3.2 16.9
^a Gender**		157.5	58.4	43.0 272.0
^b Education**		149.8	68.7	15.2 284.4
Family income RMB3000-5000		-10.1	58.8	-125.3 105.1
Family income above RMB 5000***		359.4	94.0	175.1 543.7
^c Hemoglobin Level		-19.3	62.0	-140.8 102.3
^d Convenience transfusion**		-170.2	69.3	-306.0 -34.4
Units of transfusion***		-76.4	23.8	-123.0 -29.8
^e blood shortage		20.6	57.3	-91.7 132.8
constant term		334.2	157.0	26.6 641.9
WTP		522.2	28.2	466.9 577.4
Log likelihood				-176.2
AIC				374.4
BIC				407.5

***P<0.001; **P<0.05

^a 0= male, 1= female. ^b 0=without education level of junior high school, 1=with education level of junior high school; ^c 0=more than 9/dl, 1=less than 9/dl; ^d 0=No need for transfusion in another location or hospitalization procedures; ^e 0= no shortage or general shortage, 1= very shortage.

Conclusions

- This study is the first to investigate WTP for temporary relief from anemia among adult TDT patients in high-prevalence areas in China, serving as a reference for future pharmacoeconomic research on innovative TDT technologies.
- The results revealed that Chinese TDT patients exhibited a relatively high WTP for temporary relief from anemic conditions, reflecting a strong desire to sustain life, although more than half of the patients are in the poor group. Due to the long term shortage of blood resources, there exists unmet clinical demand for more innovative treatment solutions for TDT.
- The study pinpointed key determinants of WTP, notably age, gender, income, education, the convenience of blood transfusion and the number of units transfused in a single session.

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