Original article

Estimating the cost of thalassaemia care across the world:

A Thalassaemia International Federation model

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Conflict of Interest: None

Abstract

Background: Estimating the cost of thalassaemia care is important for the optimization of care planning and resource allocation and the empowerment of patient advocacy. Available evidence is however heterogeneous, reflecting diverse healthcare systems and cost estimation methods. We sought to build a globally applicable cost model for thalassaemia care.

Study Design and Methods: We followed a three-step approach including (i) a targeted literature review to identify previous cost-of-illness studies on thalassaemia; (ii) a generic model development based on the main determinants of cost in different countries emerged from literature review and validated by a team of medical experts; (iii) a piloting of the model using data from two diverse countries.

Results: Literature review revealed studies focusing on the total costs of thalassaemia care or the cost or cost-effectiveness of specific treatment or prevention modalities in high- and low-prevalence countries across the world. The resulting evidence was used to build a model that calculates total annual therapy cost based on entry of country-level and patient-level data and data on healthcare modalities, indirect costs and prevention. Testing the model using published data from the United Kingdom (UK) and the Islamic Republic of Iran revealed an annual cost of 81,796 GBP for UK and 18,777 IRR (equal to 9,951.20 GBP) for Iran, both estimations being consistent with existing evidence.

Conclusions: A globally applicable model that calculates total annual cost of thalassaemia care was built based on existing evidence. The model successfully predicted the annual cost of thalassaemia care in UK and Iran.

Keywords: thalassaemia; healthcare; cost; blood transfusions; iron chelation; multidisciplinary care**.**

Introduction

Haemoglobinopathies, including thalassaemia and sickle cell disease, are genetically determined disorders of haemoglobin synthesis that lead to chronic haemolytic anaemia. They constitute the most common monogenic disorders in humans and although once confined to certain geographical areas, they now have a global distribution owing to the migration of populations from high-prevalence areas to Europe and other parts of the world [1,2]. In thalassaemia, particularly beta thalassaemia major, anaemia is often severe and requires life-long treatment with repetitive blood transfusions coupled with iron chelation therapy to prevent or reduce transfusional iron overload. As a result, thalassaemia poses a huge financial burden to health funders, including governments and social insurance funds and companies, as well as to patients, who may often need to pay out-of-pocket money for their care. Besides life-long blood transfusions and iron chelation, the cost also derives from frequent laboratory and other diagnostic tests, multidisciplinary medical consultations, hospitalizations and treatment of side effects or complications [3]. Indirect costs, such as loss of productive days and travel expenses should also be taken into account [4]. This huge cost is expected to increase further with the introduction of novel therapeutic approaches such as drugs targeting erythropoiesis and gene- and cell-based therapies. In addition, therapeutic advances over the past decades have given rise to a new era of prolonged survival, which tends to reach that of the normal population for patients with access to modern therapy [5]. The ageing of thalassaemia populations prolongs on one hand the need for life-long treatment and follow-up and leads, on the other, to a new spectrum of age-related conditions that create, in turn, new healthcare needs, thus resulting in increasing costs.

Estimating the cost of thalassaemia therapy is crucial for the better planning of care and the optimized allocation of resource, while it may further empower advocacy of patients. However, this is not an easy task as the organization of general and disease-specific care is quite diverse among different countries and particularly between high- and low-income ones. In addition, the available published

literature remains limited and quite heterogeneous as it is derived by studies reflecting diverse healthcare systems and with different methods of cost estimation.

Thalassaemia International Federation (TIF) is a global patient-driven organization aiming at ensuring equal access to quality care for all patients with thalassaemia across the world by promoting education, research and advocacy for services that satisfy real patient needs. Through this study, TIF sought to build a cost model that could be applied globally to estimate the cost of thalassaemia care.

Methods

To elaborate a cost model for thalassaemia, we engaged a highly qualified team of health economists from the University of Barcelona and BCN Health, a small-sized enterprise based in Barcelona, Spain and a team of medical experts on thalassaemia from Cyprus and Greece. The project consisted of three distinct stages, (i) a targeted literature review; (ii) development of a generic cost-of-illness model; (iii) a pilot application of the model. The targeted literature review aimed at identifying previous cost-of-illness studies on thalassaemia, the countries where these studies were performed and the components that have been taken into consideration for the estimation of treatments costs. Search was performed in PubMed database, using the following terms: “thalassaemia” or “thalassemia”, “therapy”, “treatment”, “prevention”, “blood transfusions”, “iron chelation”, “haematopoietic stem cell transplantation”, “gene therapy”, “screening”, “cost”, “direct cost”, “indirect cost”, “cost-effectiveness” and “healthcare expenditure”.

A generic cost model was subsequently built to be applicable to all settings, whether local or national. To build the model, we identified determinants of cost in the studies derived by the literature review. The most common parameters found for the different countries were included in the model, grouped and categorised to render the model user friendly, and then validated by the team of medical experts. Piloting aimed at verifying whether the model was comprehensive and useful for end users, including patient advocates, healthcare professionals, care payers and health authorities. To test the model, we

applied data from two diverse countries, one of the Western World and one of the Eastern World.

Results

Targeted Literature Review

Cost analyses have focused either on the total cost of thalassaemia care or on the cost and, more often, the cost-effectiveness of specific treatment or prevention modalities, such as iron chelation, haematopoietic stem cell transplantation (HSCT) or prenatal screening. Cost studies were identified in both high- and low-prevalence countries of either the Western or the Eastern world including Australia, China, India, Iran, Israel, France, Sri Lanka, Thailand, United Kingdom and United States. Specific cost studies addressed the expenditure resulting from treatments including blood transfusions, iron chelation, gene therapy and HSCT, screening programs including premarital and prenatal diagnosis, laboratory testing, medical consultation, management of complications, usage of disposables as well as productivity loss (Supplementary Table S1).

Generic cost-of-illness model

The model consists of seven tabs with different colours to differentiate which need to be completed by the users. Tabs in grey are informative; tabs in green and blue need data input from the user; the tab in red automatically calculates results and the last tab provides in grey provides a space to note down data sources and other reference documents. The initial page allows the user to select the country through a drop-down menu, the level of data, whether local, regional or national and the year of reference (Supplementary Figure S1). The next page is the How-to-Use tab that provides key information on the model's content and the type of data needed to complete it (Supplementary Figure S1). In the next tab, entitled "1. Affected Population", the user needs to introduce the number of transfusion- or non-transfusion-dependent thalassaemia patients taken into account for the estimation of costs; the model uses the sum of the two values entered for calculation purposes (Supplementary Figure S2). In the next tab, under "2. Treatment-related Costs", the user needs to fill in two different

columns, one dedicated to costs (per unit, visit, package, etc.) and one dedicated to quantities used in a year. All data entered in the second column needs to be annual. To calculate the total cost per year per parameter, the model multiplies the cost per unit (column 1) with the corresponding quantities (column 2). There is no need to fill in all parameters, as different parameters apply in each country. The model lists all parameters that need to be present for the provision of optimal health care services to patients (Supplementary Figure S2). In the next tab, under "Other Costs", the user needs to enter data not directly related to treatment, such as any state-provided benefits or allowances (Supplementary Figure S2). Data on productivity loss needs to be entered under "4. Indirect Costs" (Supplementary Figure S2). To calculate productivity loss, the user needs to introduce under "Cost per Unit" the cost of a day of work and under "No of Units Used (per Annum)", the mean number of days that a patient with thalassaemia is absent from work. To calculate the total costs linked to productivity loss, the number of patients is multiplied by the number of days missed and then by the cost of a day of work. The model may also estimate the cost of prevention, under "5. Prevention Costs" (Supplementary Figure S2). This amount is not, however, considered part of the cost of treatment calculations. The results are automatically calculated under "6. Summary of Results" (Supplementary Figure S3). Besides the totals for each parameter of costs, the user may also view an estimation of the annual cost of treatment per patient. A last tab ("7. References) has been created to enter any reference documents or other details useful to the user or justifying the data used (Supplementary Figure S3).

Piloting

To verify that the model is functional, the team entered published data found in literature for the United Kingdom and the Islamic Republic of Iran. The two countries were selected based on geography and the amount of published data available. In the United Kingdom, the annual cost of thalassaemia care amounts to 81,796 GBP, while in Iran, this is estimated at 18,777 IRR (equal to 9,951.20 GBP; Figure 1).

Discussion

Estimating the cost of thalassaemia care would allow the better planning, allocation of resources and reduction of waste in healthcare and would further empower patient and professional advocacy. A cost analysis for thalassaemia therapy bears, however, several limitations. These include the diverse structure and organization of healthcare systems and social security services in high-prevalent and other countries across the world, the variable level, components and intensity of provided services, the different degree of healthcare coverage and the difficulty to estimate the amount of out-of-pocket contribution that many patients and families have to pay in several countries. In addition, evidence in the literature remains limited and is based on diverse methods of cost calculation, a fact that renders comparisons among studies and countries problematic. For example, in the United States, a retrospective cost analysis using payer claims estimated an average total annual cost per transfused patient of 128,062 USD [3], while in the Islamic Republic of Iran, a cost analysis from a social services perspective estimated an average annual cost per patient of 8322 USD, including direct and indirect costs, plus another 1361 USD due to the distress caused by the disease [4]. Similarly, the total cost for treating one thalassaemia patient for 50 years was estimated at 1,971,380 USD in Israel versus 720,201 USD (at 2013-2014 prices) in the United Kingdom [6,7]. The estimated cost-effectiveness of prevention programs such as premarital screening and prenatal diagnosis programmes also varies widely. Screening programmes were estimated to save 7,825,000 USD in 10 years in Iran, 76 million USD in 10 years in Israel and 356,499 USD in one year (2016) in China [6,8,9]. Estimating the cost of individual therapies and particularly blood transfusions may further be challenging as there are several implicated processes. In Australia, the total cost per packed red cell unit, covering every step of the transfusion pathway for thalassaemia patients, was estimated at 695.59 USD from a healthcare provider perspective [10].

TIF proceeded to the development of a generic cost-of-illness model for thalassaemia to quantify the burden of thalassaemia on health systems and allow decision makers to translate the adverse effects of

thalassaemia into monetary terms. TIF anticipates that these estimates will be helpful to (i) define the magnitude of the disease in financial terms in different settings; (ii) justify intervention programmes; (iii) assist in the allocation of funding and resources on thalassaemia management; (iv) provide a basis for policy and planning with regard to prevention and control; and (v) provide an economic framework for the evaluation of existing thalassaemia control and management programmes [11].

Such a model, simple in inception but powerful in execution, may be used to help affected countries include thalassaemia in policy planning and address the imminent research gap on this specific topic. It may also be used by health authorities, health partnerships and consortia both nationally and transnationally to identify needs and address them. Moreover, it is a powerful advocacy tool for the implementation of prevention strategies and the reduction of new affected births.

In comparative studies, it is important to take into account a set of parameters that may affect the cost of the disease, including labour costs, equipment and supplies costs and the availability thereof. The comparison between the United Kingdom and Islamic Republic of Iran may help a policy expert identify what works well and what not in each setting and what corrective measures need to be taken.

Over the past few years, novel therapeutic advances in thalassaemia management have emerged, including drugs targeting erythropoiesis and curative treatments such as gene therapy [12,13]. These therapies provide impressive outcomes but are also followed by considerable costs. For example, the average cost for HSCT and gene therapy in France was estimated at 215,571 and 608,086 euros, respectively [14]. Given these advances, TIF's model may also be of added value in any discussion on the introduction of new medicines or therapies into national essential or advanced medicines' lists and formularies. An estimation of the annual cost for the treatment of thalassaemia per patient is expected to allow governments to determine each product's or therapy's return in investment and thus the provision of access to such products or therapies would be informed and evidence-based, for the benefit of the patient.

Statement

The manuscript has not been published elsewhere and has not been submitted simultaneously for publication elsewhere.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article. There were no sources of funding.

References

1. Modell B. Global epidemiology of haemoglobin disorders and derived service indicators. Bull World Health Organ. 2008;2008:480–487.

2. Angastiniotis M, Vives Corrons J-L, Soteriades ES, Eleftheriou A. The impact of migrations on the health services for rare diseases in Europe: the example of haemoglobin disorders. ScientificWorldJournal. 2013;2013:727905.

3. Weiss M, Parisi Jun M, Sheth S. Clinical and economic burden of regularly transfused adult patients with β-thalassemia in the United States: A retrospective cohort study using payer claims. Am J Hematol. 2019;94:E129–E132.

4. Esmaeilzadeh F, Azarkeivan A, Emamgholipour S, *et al*. Economic Burden of Thalassemia Major in Iran, 2015. J Res Health Sci. 2016;16:111–115.

5. Farmakis D, Giakoumis A, Angastiniotis M, Eleftheriou A. The changing epidemiology of the ageing thalassaemia populations: A position statement of the Thalassaemia International Federation. Eur J Haematol. 2020;105:16–23.

6. Koren A, Profeta L, Zalman L, *et al*. Prevention of β Thalassemia in Northern Israel - a Cost-Benefit Analysis. Mediterr J Hematol Infect Dis. 2014;6:e2014012.

7. Weidlich D, Kefalas P, Guest JF. Healthcare costs and outcomes of managing β-thalassemia major over 50 years in the United Kingdom. Transfusion. 2016;56:1038–1045.

8. Ahmadnezhad E, Sepehrvand N, Jahani FF, *et al*. Evaluation and cost analysis of national health policy of thalassaemia screening in west-azerbaijan province of iran. Int J Prev Med. 2012;3:687–692.

9. Yang Y, Li D-Z, He P. A Program on Noninvasive Prenatal Diagnosis of α-Thalassemia in Mainland China: A Cost-Benefit Analysis. Hemoglobin. 2016;40:247–249.

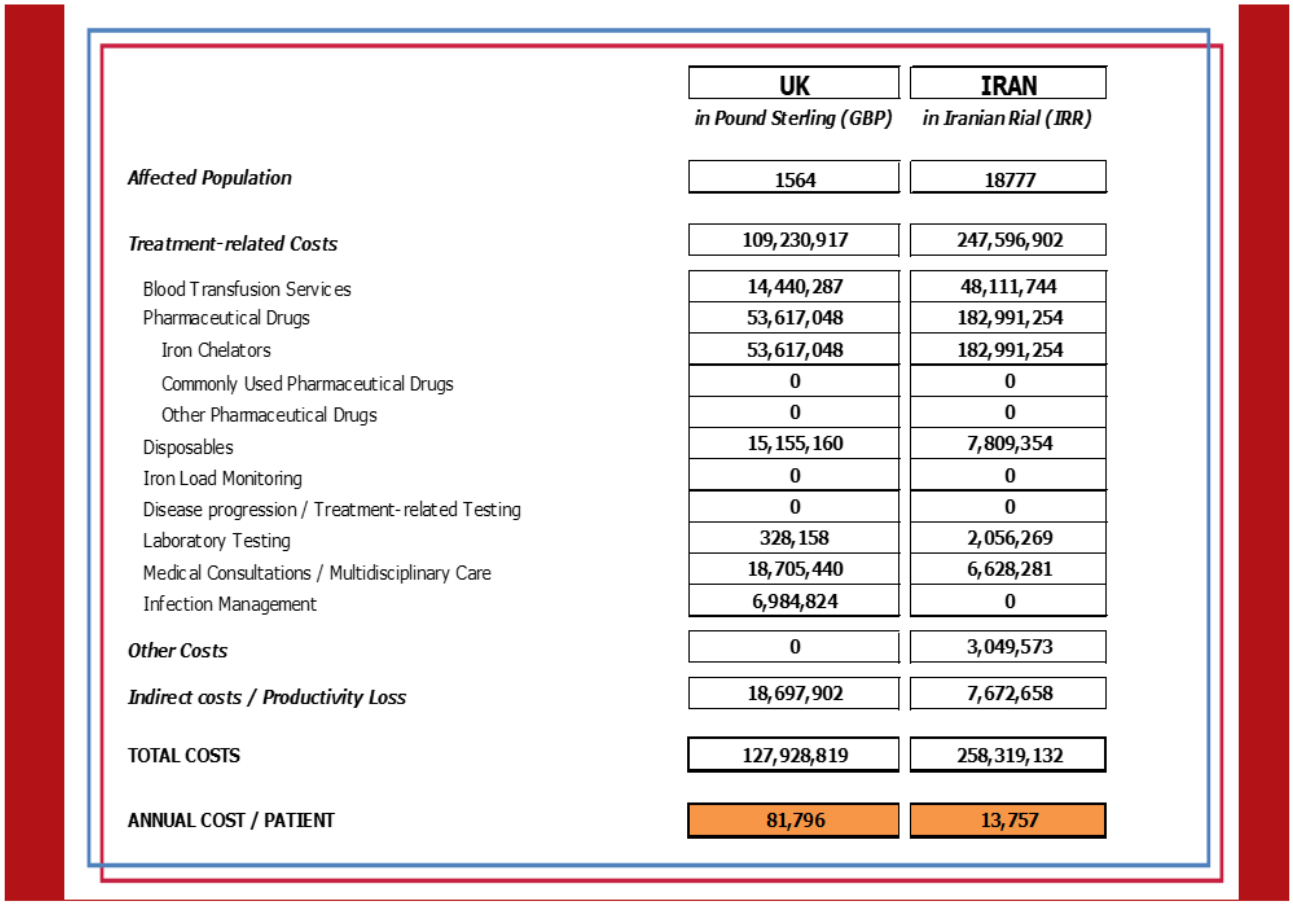
10. McQuilten ZK, Higgins AM, Burns K, *et al*. The cost of blood: a study of the total cost of red blood cell transfusion in patients with β-thalassemia using time-driven activity-based costing. Transfusion. 2019;59:3386–3395.

11. Rice DP. Cost of illness studies: what is good about them? Inj Prev J Int Soc Child Adolesc Inj Prev. 2000;6:177–179.

12. Cappellini MD, Viprakasit V, Taher AT, *et al*. A Phase 3 Trial of luspatercept in patients with transfusion-dependent β-thalassemia. N Engl J Med. 2020;382:1219–1231.

13. Thompson AA, Walters MC, Kwiatkowski J, *et al*. Gene therapy in patients with transfusion-dependent β-thalassemia. N Engl J Med. 2018;378:1479–1493.

14. Coquerelle S, Ghardallou M, Rais S, *et al*. Innovative curative treatment of beta thalassemia: Cost-efficacy analysis of gene therapy versus allogenic hematopoietic stem-cell transplantation. Hum Gene Ther. 2019;30:753–761.



	UK *in Pound Sterling (GBP)*	IRAN *in Iranian Rial (IRR)*
Affected Population	1564	18777
Treatment-related Costs	109,230,917	247,596,902
Blood Transfusion Services	14,440,287	48,111,744
Pharmaceutical Drugs	53,617,048	182,991,254
Iron Chelators	53,617,048	182,991,254
Commonly Used Pharmaceutical Drugs	0	0
Other Pharmaceutical Drugs	0	0
Disposables	15,155,160	7,809,354
Iron Load Monitoring	0	0
Disease progression / Treatment-related Testing	0	0
Laboratory Testing	328,158	2,056,269
Medical Consultations / Multidisciplinary Care	18,705,440	6,628,281
Infection Management	6,984,824	0
Other Costs	0	3,049,573
Indirect costs / Productivity Loss	18,697,902	7,672,658
TOTAL COSTS	127,928,819	258,319,132
ANNUAL COST / PATIENT	81,796	13,757

Figure 1: Estimated annual costs of thalassaemia care in the United Kingdom and the Islamic Republic of Iran derived by the model.

Supplementary material

Supplementary Table S1: Parameters concerning general treatment costs and costs of specific therapeutic modalities as identified in the literature.

Article	Country	Parameters
General cost		

Weiss M, et al. 2019	USA	- Medication
		- Medical
		  - Outpatient
		  - Inpatient
		  - ED
		  - Other medical

Weidlich D, et al. 2016	United Kingdom	- RBC transfusion - ICTs - Routine monitoring tests and regular visits to haematologists - Managing complications
Moirangthem A, et al.	India	- Hospital admission and BT - Travel related - Medications

		- Lab investigations - Mean annual income
Reed-Embleton H, et al. 2020	Sri Lanka	Blood transfusion - Number of transfusions - Staff Drug therapy - ICT - Concomitant medication Overheads - Indirect costs Household costs - Transport and foods
Esmaeilzadeh F, et al. 2016	Iran (Islamic Rep. of)	- Total costs per patient - Direct medical costs - Direct non-medical costs - Indirect costs
Blood Transfusion		
McQuilten ZK, et al. 2019	Australia	- number of RBC units transfused - staff costs - consumables costs - transfusion process costs - RBC procurement costs
Burns KE, et al. 2019	Australia	- Red blood cell (RBC) unit cost - Costs associated with clinical transfusion processes - Costs of laboratory transfusion (pathology) processes - Costs of full blood count and ferritin assays performed - Costs of clinical transfusion processes - Costs for management of iron overload - Medical therapy unit expenses and overheads
Ravangard R, et al. 2018	Iran (Islamic Rep. of)	*Direct medical costs* - Medicine - Blood transfusion - Visit - Laboratory - Diagnostic and treatment services - Hospitalization *Direct non-medical costs* - Transportation - Accommodation and food *Indirect costs* - Potential production lost due to the absence from work to receive medical care
Iron Chelation		
Saiyarsarai P, et al. 2020	Iran (Islamic Rep. of)	- Direct medical cost: included the cost of medicine and laboratory - Cost of medical equipment and infusion pump - Annual cost of cardiac complication Indirect costs: transfusion time cost, cost of productivity loss
Li J, et al. 2020	China	- Chelator costs - DFO administration cost - Monitoring cost

		Complications therapy cost
Pepe A, et al. 2017	Italy	- Drug costs - DFO administrations costs Monitoring tests
Vekeman F, et al. 2016	USA	- inpatient stays - emergency room (ER) visits - outpatient visits - all-cause healthcare costs disease-related healthcare costs
Bentley A, et al. 2013	United Kingdom	- Drug costs - Administration costs (DFO and combination therapy) - Monitoring tests Managing treatment-related adverse events
Keshtkaran A, et al. 2013	Iran (Islamic Rep. of)	- Direct costs: drug, pump, transfusion kit cost and treatment of adverse events - Indirect costs: transfusion time cost
Ho WL, et al. 2013	Taiwan (China)	- Drug costs - Administration costs - Adverse events costs
Karnon J, et al. 2012	United Kingdom	- Chelation drug - Administration - Monitoring - Adverse events - Complications
Luangasanatip N, et al. 2011	Thailand	- Direct medical care *DFO costs: drug cost, cost of medical visit, cost of infusion pump and cost of injection set *DFP costs: drug cost, cost of medical visit, cost of complete blood count (CBC) monitoring and cost of neutropenia treatment - DSX: drug cost and cost of medical visit - Direct non-medical care Indirect costs
Zhang B, et al. 2011	USA	Treatment with DFO
Delea TE, et al. 2007	USA	- Drug costs - Administration costs - Complications
Lee TA, et al. 2014	Worldwide	Drug costs
Li J, et al. 2019	Worldwide	Literature review that provides all the costs included in each study

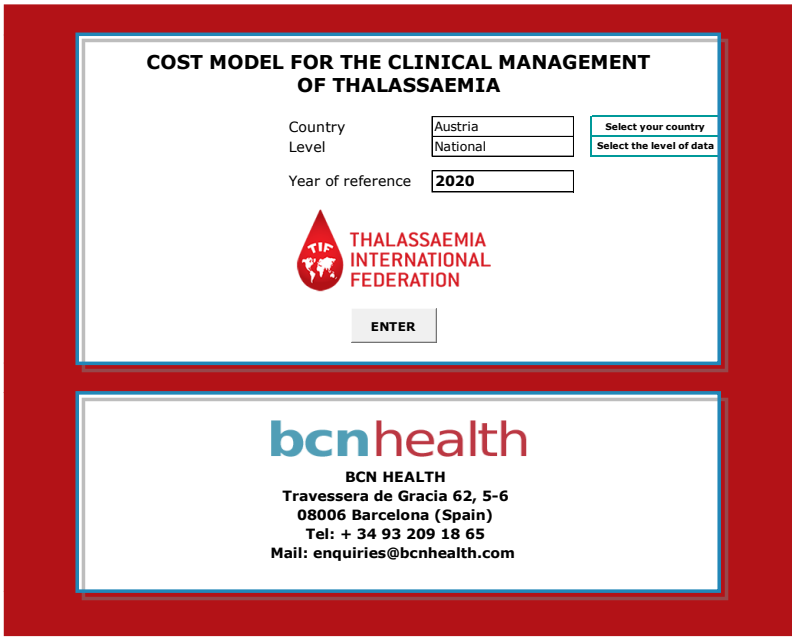
Curative Therapies		
John MJ, et al. 2018	India	*Hematopoietic Stem Cell Transplantation* - Cost incurred after HSCT(MRD) - Cost incurred after HSCT(MUD) - Cost incurred in treating cGVHD *Transfusion Chelation* - Cost of managing cardiac complications - Cost of managing liver complications Cost of managing endocrine complications
Coquerelle S, et al. 2019	France	*Hospital professionals* - Laboratory technician for production - Laboratory quality control technician - Nurse (FDI) - Laboratory engineer - Laboratory quality assurance manager (pharmacist) - Doctor - Laboratory director - Ambulatory medical consultations *Tests performed* - Haematological analysis - Genetic chimerism *Treatments* - Cyclosporine Mycophenolate mofetil (Cellcept)
Sruamsiri R, et al. 2013	Thailand	- Direct Medical Cost - Direct Non-Medical Cost Indirect Cost
Disease progression and complications		

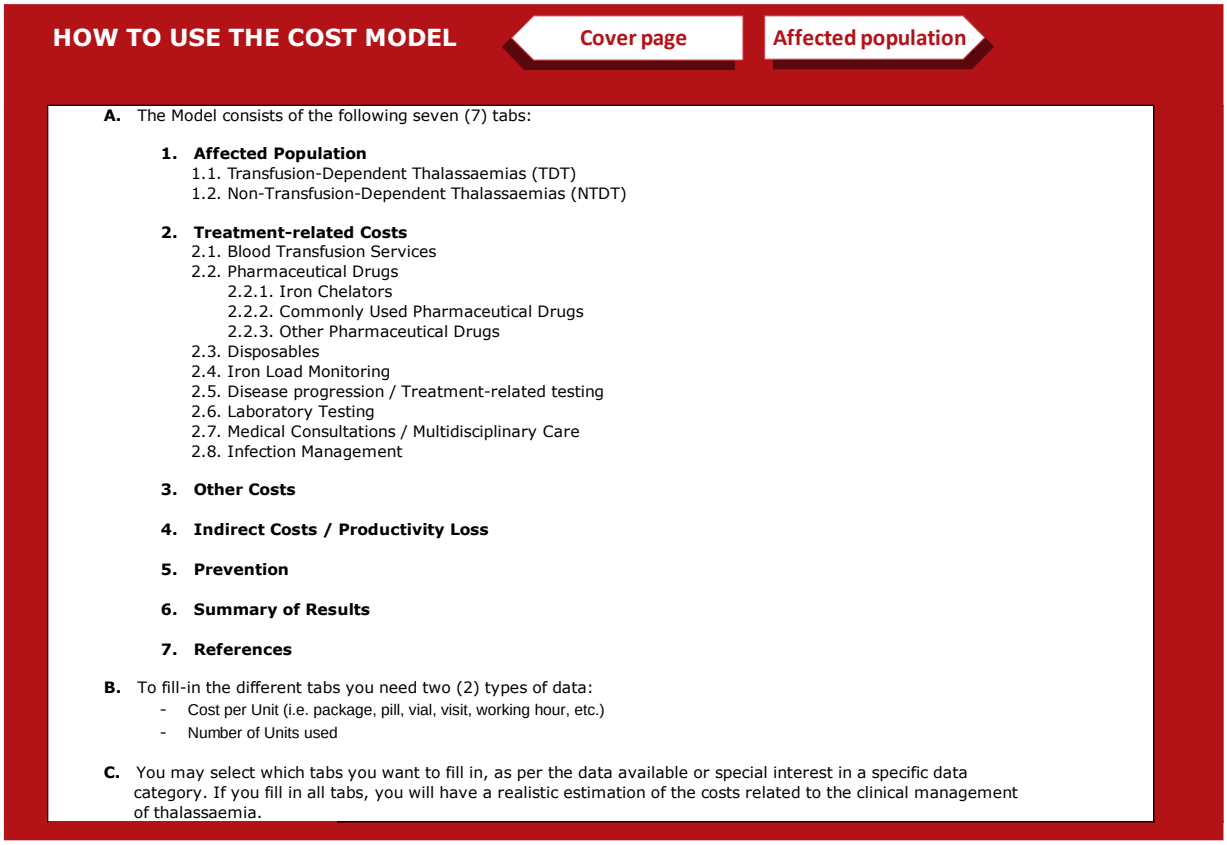
Farmakis D, et al. 2020	Worldwide	- Cardiovascular disorders Atherosclerotic cardiovascular disease Atrial fibrillation Aortic stenosis Heart failure with preserved left ventricular ejection fraction Supraventricular arrhythmias Diastolic left ventricular dysfunction - Hepatic disorders Hepatocellular carcinoma Hepatitis C infection Hepatic epithelioid hemangioendothelioma (related to iron overload)
Demosthenous C, et al. 2019	Worldwide	- Epidemiology of renal complications Renal manifestations - Tubular dysfunction - Glomerular dysfunction - Haematuria - Nephrolithiasis
Sinakos E, et al. 2017	Greece	- Chronic liver diseases, namely liver cirrhosis and hepatocellular carcinoma, are currently the main causes of death in patients with b-TM. - CHC along with iron overload are the main reasons for the progression of liver disease in this population. - SVR could also lead to prolongation of life expectancy in b-TM patients.
Ozturk Z, et al. 2017	Turkey	- Hypozincaemia - Copper deficiency and toxicity - Deficiency of selenium - Hypomagnesaemia Calcium
Karimi M, et al 2018	Worldwide	- Osteoporosis (21.6%) - Hypogonadism (12.6%) - Central hypothyroidism (8.3%) - Non-insulin-dependent diabetes mellitus (7.8%) - Primary hypothyroidism (5.5%) - Insulin-dependent diabetes mellitus (4.2%) - Hypoparathyroidism (2.2%) - Growth hormone deficiency (1.1%) - Adrenal mass (1%) Thyroid cancer (0.5%)
Fung EB, et al. 2016		- Low bone mass: 60-85% of adults - Growth deficiency Diabetes

Finianos A, et al. 2018		- Incidence of HCC: 1.02% - Risk factors for the development of HCC: iron overload and viral hepatitis with or without cirrhosis. - Recommendation of screening patients with: - Liver iron concentration (LIC) measurement by means of magnetic resonance imaging (MRI) - Liver ultrasound - HCC in thalassemia risk factors: hepatitis B, cirrhosis and iron overload. - Nontransferrin-bound free iron (NTBFI) and ferritin are associated with impaired immunity by impairing lymphocyte proliferation and tumoricidal activity of macrophages. There have been no randomized trials looking at HCC management interventions in thalassaemic patients.
Pepe A, et al. 2019	Italy	- Cardiac complications: 13.1% of the patients (heart failure, arrhythmias, pulmonary hypertension, myocardial infarction, angina, myo/pericarditis, peripheral vascular disease)
Yang G, et al. 2014	China	- Myocardial iron overload: 33.8% - Severe myocardial iron overload: 12.6% Left Ventricle Ejection Fraction (LVEF): 64%
de Sanctis V, et al. 2019	Worldwide	- Central hypothyroidism: 4.8% (adults) 0.5 (children and adolescents) - Thyroid cancer: 0.44% (adults) - Latent hypocortisolism: 1.3% (adults) 4.4% (children and adolescents) GH deficiency: 3.2%(adults) 4.5% (children and adolescents)
Farmakis D, et al. 20 1749	Worldwide	- Chronic haemolysis - Left ventricular dysfunction - Vascular disease - Myocardial ischaemia - Myocarditis - Pulmonary hypertension - Right ventricular dysfunction - Angina - Arrhythmias Valvular abnormalities
Tartaglione I, et al. 2020	Italy	- Headache: 38.2% - No more common or severe than in the general population.
Mettananda S, et al. 2020	Sri Lanka	- Abnormal emotional: 18% - Conduct: 17% - Hyperactivity: 9% Peer relationship symptom: 14%
Screening and prevention		
Ahmadnezhad E, et al. 2012	Iran (Islamic Rep. of)	- Cost of providing optimum care - Prevention costs - Cases prevented in 10 years Savings

Bryan S, et al. 2011	United Kingdom	- Carrier test (woman) - Carrier test (father) - Carrier status counselling (woman only) - Carrier status counselling (couple) - PND - TOP counselling TOP procedure
Leung KY, et al. 2004	China	- Screening - Follow-up - Total screening programme Savings
Yang Y, et al. 2016	China	- Non-invasive PND program - Invasive programme Savings
Ginsberg G, et al. 1998	Israel	- Lifetime healthcare costs - Lost earnings - Premature mortality - Prevention program Savings
Koren A, et al. 2014	Israel	- Cost of preventing one affected new-born Treatment of a patient during 50 years
Productivity Loss		-
Wong JHY, et al. 2019	Malaysia	- Lifetime healthcare cost - Lifetime patient and family healthcare expenditure - Total lifetime transfusion dependent thalassaemia cost
Shah F, et al. 2019	United Kingdom	- EQ-5D-3L utility scores - EQ-5D-3L VAS scores - WPAI (%) - TranQoL - TranQoL domain scores

Supplementary Figure S1: The model's cover page (upper panel) and how-to-use page (lower panel).





Supplementary Figure S2: The model's data entry pages, including (1) selection of population category (transfusion-dependent or not), (2) cost and frequency of specific treatment modalities, (3) other costs, (4) indirect costs, (5) prevention costs

1. AFFECTED POPULATION

How to use | Treatment-related costs

Please complete, as appropriate.
Kindly note that the sum will be used to calculate the annual cost of treatment per patient.

1.1. Patients with Transfusion-Dependent Thalassaemia (TDT)	
1.2. Patients with Non-Transfusion-Dependent Thalassaemia (NTDT)	

2. TREATMENT-RELATED COSTS

Affected population | Other costs

Please complete all highlighted /coloured cells, as appropriate.

NB:
- To calculate personnel costs, please insert a **median salary / wage** (monthly or annual) under "Cost per Unit".
- Please use information that is available and reliable in your setting.

2.1. Blood Transfusion Services	**Cost per Unit**	**No of Units Used (per Annum)**	**Total Cost**
2.1.1. ABO, Rh compatibility kits			**0**
2.1.2. Cross-matching donor/recipient			**0**
2.1.3. Red cell transfusion - Component separation			**0**
2.1.4. Pre-storage filtration			**0**
2.1.5. Bedside filtration			**0**
2.1.6. Washed red blood cells (e.g. cost of saline)			**0**
2.1.7. Test for TTIs (HCV, HBV, HIV, syphilis et al) - Serological (blood donor)			**0**
2.1.8. Test for TTIs (HCV, HBV, HIV, syphilis et al) - NAT testing (blood donor)			**0**
2.1.9. Transportation			**0**
2.1.10. Test for other TTIs (e.g. malaria, etc)			**0**
2.1.11. Storage (Addition of nutrients and additive solutions)			**0**
2.1.12. Personnel costs			**0**
2.1.13. Other [...]			**0**
2.1.14. Other [...]			**0**
TOTAL			**0**

2.2. Pharmaceutical Drugs	**Cost per Package**	**No of Packages Used (Per Annum)**	**Total Cost**
2.2.1. Iron Chelators			
2.2.1.1. Deferoxamine			
Deferoxamine (Desferal®) 500 mg			**0**
Deferoxamine (Desferal®) 2 g			**0**
Deferoxamine (generic) 500 mg			**0**
Deferoxamine (generic) 2 g			**0**
2.2.1.2. Deferiprone			
Deferiprone (Ferriprox®) 500 mg			**0**
Deferiprone (Ferriprox®) 1000 mg			**0**
Deferiprone (Ferriprox®) Oral Solution 100 mg/mL			**0**
Deferiprone (generic) 500 mg			**0**
Deferiprone (generic) 1000 mg			**0**
2.2.1.3. Deferasirox			
Deferasirox (Exjade® / Asunra®) 125 mg			**0**
Deferasirox (Exjade® / Asunra®) 250 mg			**0**
Deferasirox (Exjade® / Asunra®) 500 mg			**0**
Deferasirox New Formulation (EMA / Jadenu® FDA) 90 mg			**0**
Deferasirox New Formulation (EMA / Jadenu® FDA) 180			**0**
Deferasirox New Formulation (EMA / Jadenu® FDA) 360			**0**
Deferasirox (generic - e.g. Mylan, Accord)			**0**
Other [...]			**0**
Other [...]			**0**
TOTAL			**0**

2.2.2. Commonly Used Pharmaceutical Drugs			
Insulin			0
Folic acid			0
Hormone replacement therapy (HRT)			0
Calcium / Vitamin D			0
Other [...]			0
Other [...]			0
TOTAL			0

2.2.3. Other Pharmaceutical Drugs (e.g. Management of Complications)			
Other [...]			0
Other [...]			0
Other [...]			0
Other [...]			0
TOTAL			0

2.3. Disposables	Cost per Unit	No of Units Used (Per Annum)	Total Cost
Infusion pump - Mechanical (deferoxamine-related)			0
Infusion pump - Balloon (deferoxamine-related) *Ongoing Costs			0
Infusion pump - Electronic (deferoxamine-related)			0
Injection kit (e.g. thalasets)			0
Other [...]			0
Other [...]			0
TOTAL			0

2.4. Iron Load Monitoring	Cost per Test	No of Tests Permormed (Per Annum)	Total Cost
MRI (Heart Measurements)			0
MRI (Liver Measurements)			0
Serum ferritin			0
Other [...]			0
Other [...]			0
TOTAL			0

2.5. Disease progression / Treatment-related testing	Cost per Unit	No of Tests Done	Total Cost
DEXA			0
Abdominal Ultrasound			0
Fibroscan			0
Echocardiogram			0
Other [...]			0
Other [...]			0
TOTAL			0

2.6. Laboratory Testing	Cost per Test	No of Tests Performed (Per Annum)	Total Cost
Complete Blood Count			0
Liver Function Tests (LFT)			0
Renal Function Tests (RFT)			0
T3, free T4, TSH			0
Parathyroid Hormone (PTH)			0
Calcium, ionized calcium			0
Fasting glucose			0
Glucose tolerance test			0
IGF-1, IGF BP-3			0
LH-ICMA			0
FSH			0
Estradiol			0
Vitamin D			0
Zinc test			0
Test for TTIs (HCV, HBV, HIV, syphilis et al) - Serological (Patients)			0
Test for TTIs (HCV, HBV, HIV, syphilis et al) - NAT testing (Patients)			0
Other [...]			0
Other [...]			0
TOTAL			0

2.7. Medical Consultations / Multidisciplinary Care	Cost per Visit	No of Visits (Per Annum)	Total Cost
Cardiologist			0
Opthalmologist			0
ENT (Audiometry)			0
Endocrinologist			0
Hepatologist			0
Other [...]			0
TOTAL			0

2.8. Infection Management	Cost per Pill or Package	No of Pills or Packages Used (Per Annum)	Total Cost
Prophylactic antibiotics (e.g. penicillin)			0
Vaccine (Streptococcus pneumoniae)			0
Vaccine (Haemophilus influenzae type B)			0
Vaccine (Neisseria meningitides)			0
Vaccine (Influenza virus)			0
Other [...]			0
Other [...]			0
TOTAL			**0**

TOTAL TREATMENT-RELATED COSTS	0

3. OTHER COSTS

Treatment-related costs | Indirect costs

Please complete all highlighted /coloured cells, as appropriate.

3. Other Costs	Cost per Person	No of Beneficiaries (Per Annum)	Total Cost
Transportation Allowance			0
Subsistence Allowance (Accommodation & Food)			0
Disability Benefit			0
Unemployment Benefit			0
Other [...]			0
TOTAL			**0**

4. INDIRECT COSTS

Other costs | Prevention costs

Please complete all highlighted /coloured cells, as appropriate.

NB:
- Please insert a median salary / wage (**per day**) under "Cost per Unit".
- Please insert the **median number of work days that a patient loses in a year** under "No of Units Used".

4. Indirect Costs	Cost per Unit	No of Units Used (Per Annum)	Total Cost
Productivity Loss			0
Other [...]			0
TOTAL			**0**

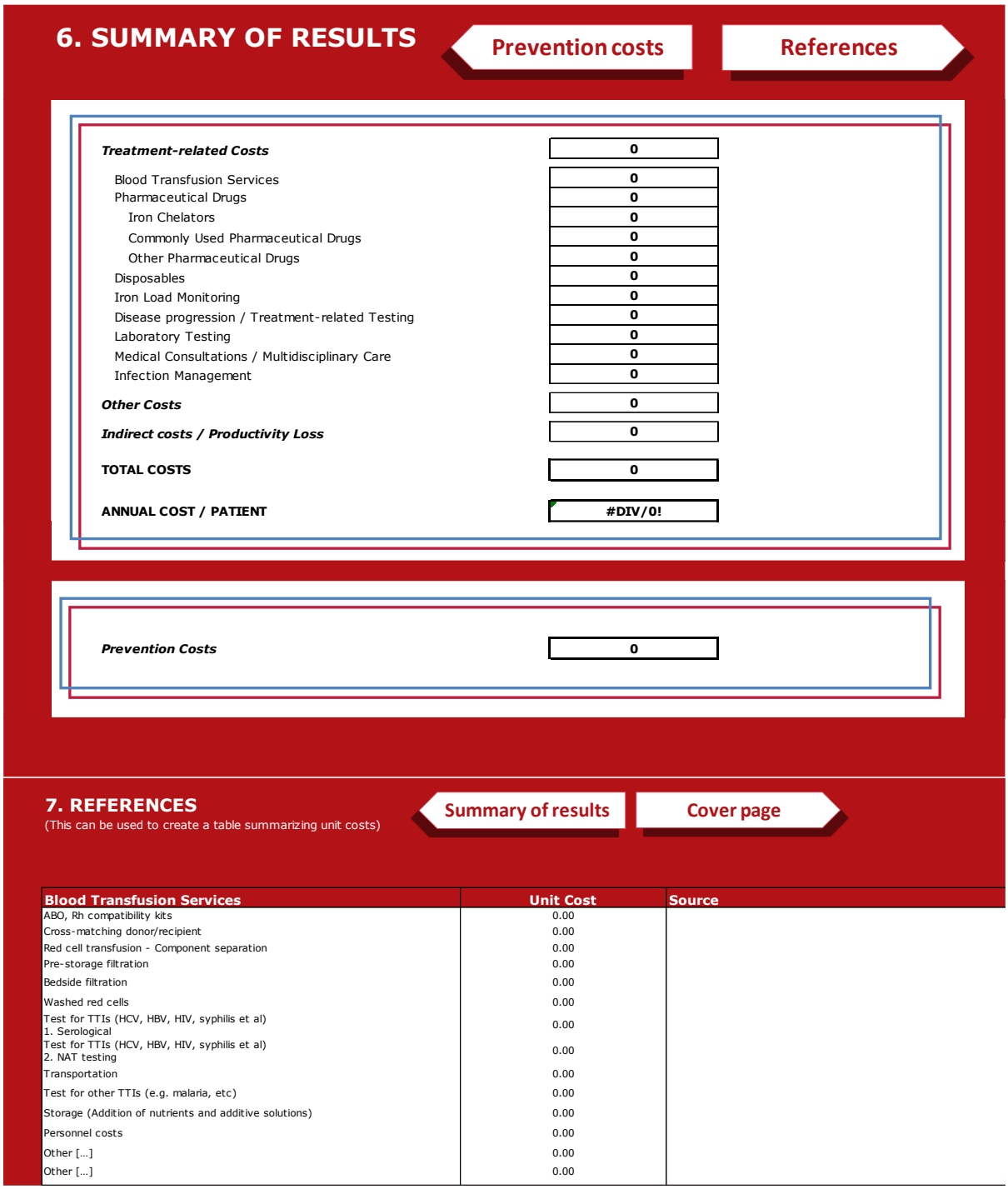
5. PREVENTION COSTS

Indirect costs | Summary of results

Please complete all highlighted/coloured cells, as appropriate.

5. Prevention	Cost per Unit	No of Units Used (Per Annum)	Total Cost
Carrier test			0
Genetic Counselling			0
Prenatal diagnosis			0
Termination of pregnancy procedure			0
Awareness-raising activities			0
Screening and prevention programme			0
TOTAL			**0**

Supplementary Figure S3: Summary of results based on data entry and references



6. SUMMARY OF RESULTS

Prevention costs | References

Treatment-related Costs	**0**
Blood Transfusion Services	**0**
Pharmaceutical Drugs	**0**
Iron Chelators	**0**
Commonly Used Pharmaceutical Drugs	**0**
Other Pharmaceutical Drugs	**0**
Disposables	**0**
Iron Load Monitoring	**0**
Disease progression / Treatment-related Testing	**0**
Laboratory Testing	**0**
Medical Consultations / Multidisciplinary Care	**0**
Infection Management	**0**
Other Costs	**0**
Indirect costs / Productivity Loss	**0**
TOTAL COSTS	**0**
ANNUAL COST / PATIENT	**#DIV/0!**

Prevention Costs	**0**

7. REFERENCES

(This can be used to create a table summarizing unit costs)

Summary of results | Cover page

Blood Transfusion Services	Unit Cost	Source
ABO, Rh compatibility kits	0.00	
Cross-matching donor/recipient	0.00	
Red cell transfusion - Component separation	0.00	
Pre-storage filtration	0.00	
Bedside filtration	0.00	
Washed red cells	0.00	
Test for TTIs (HCV, HBV, HIV, syphilis et al) 1. Serological	0.00	
Test for TTIs (HCV, HBV, HIV, syphilis et al) 2. NAT testing	0.00	
Transportation	0.00	
Test for other TTIs (e.g. malaria, etc)	0.00	
Storage (Addition of nutrients and additive solutions)	0.00	
Personnel costs	0.00	
Other [...]	0.00	
Other [...]	0.00	