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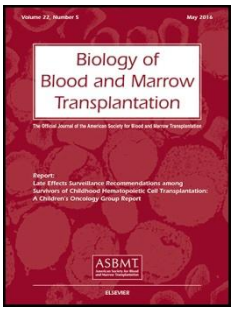

Title: Cost Effectiveness of Hematopoietic Stem Cell Transplantation Compared to Transfusion Chelation for Treatment of Thalassemia Major

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Cost Effectiveness of Hematopoietic Stem Cell Transplantation Compared to Transfusion Chelation for Treatment of Thalassemia Major

Running title: Cost Effectiveness of HSCT in Thalassaemia Major

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search, drafting the manuscript and proof reading. MJJ and SP would be the 'guarantor' with regard to the integrity of the work.

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Highlights

- HSCT for thalassaemia is a long-term value for money intervention in a developing country.
- The clinical and economic benefits of HSCT far outweigh Transfusion-Chelation.
- The ICER (QALY) with HSCT as compared to TC is ☐64,096 (US$ 986) in matched related donor transplant.
- The probability of HSCT to be cost-effective at the WTP threshold of Indian GDP per capita is 94 %.

Abstract:

Hematopoietic Stem Cell Transplant (HSCT) is the only cure for thalassaemia major (TM) which inflicts a significant one-time cost. Hence, it is important to explore the cost-effectiveness of HSCT versus lifelong regular transfusion chelation (TC) therapy. This study was undertaken to estimate incremental cost per quality adjusted life year (QALY) gained with the intervention group HSCT, and the comparator group TC, in TM patients. A combination of decision tree and Markov model was used for analysis. Hospital database, supplemented with review of published literature were used to derive input parameters for the model. A lifetime study horizon was used and future costs and consequences were discounted at 3%. Results are presented using societal perspective. Incremental cost per QALY gained

with use of HSCT as compared to TC was □64,096 (US$ 986) in case of matched related donor (MRD) and □1,67,657 (US$ 2579) in case of a matched unrelated donor (MUD) transplant. The probability of MRD transplant to be cost-effective at the willingness to pay threshold of Indian per capita gross domestic product is 94 %. HSCT is a long-term value for money intervention which is highly cost-effective and its long term clinical and economic benefits outweigh TC.

Key words: Cost effectiveness; thalassaemia; transfusion chelation; HSCT, transplant; India

1. Introduction:

Beta thalassemia is the commonest inherited hemoglobin disorder, which has an uneven distribution of 3.7 to 10% carrier state among different endogenous populations in India.[1] With an estimated 4.05% prevalence of beta thalassemia trait (BTT) in a population of 1.2 billion and a birth rate of 23 per 1000 live births, the estimated homozygous births using Hardy Weinberg (HW) equation is 11,376 per year. [2] With a thalassaemia prevalence of 3.96 % in Punjab [3] and using HW equation, it can be estimated that there would be 170 thalassaemia major (TM) births per year. Late presentation, low hemoglobin maintenance and growth failure are the major challenges in managing patients with thalassaemia in Punjab, India.[4]

Transfusion-Chelation (TC) is the conservative medical care which requires multidisciplinary care with dedicated and experienced units.[5] TM represents a significant economic burden from the global health care perspective. An Italian study from 7 different centers evaluating the survival of a cohort of 977 patients who were born since 1960s and continued on regular transfusion and chelation with deferrioxamine showed only 68% of patients were alive at the age of 35 years. The prevalence of complications was: heart failure 6.8%, arrhythmia 5.7%,

hypogonadism 54.7%, hypothyroidism 10.8%, diabetes 6.4%, HIV infection 1.7%, and thrombosis 1.1%.[6] Although, with better iron chelation techniques, safer blood transfusions and comprehensive care, the complications are expected to be reduced, a recent study from Lucknow, Uttar Pradesh (India) observed only 29/261 (11%) patients crossed the age of 20 years.[7]

TM has serious life-limiting and potentially life-threatening complications that cause significant disruption in education and social activities..[8] Leading a "normal life" is a challenge as their self-identity is compromised and they become increasingly dependent upon others.[9] Transplantation is a rescue from such a predicament.

Hematopoietic stem cell transplantation (HSCT) with a human leukocyte antigen (HLA) identical matched related donor (MRD) or matched unrelated donor (MUD) is the only curative option available for TM.[10] Recently, the Italian group published 30-year overall survival (OS) and thalassemia-free survival (TFS) across the age and risk groups to be 82.6±2.7% and 77.8±2.9% respectively.[11]

Nearly 71% of health spending in India is out of pocket (OOP).[12] This OOP spending poses barriers to accessing services, besides incurring catastrophic effects on those who utilize health care.[13–15] Cost constraints remain a major hurdle for patients to undergo HSCT for TM and many families continue to remain in TC therapy. Government initiatives like *Rashtriya Bal Swasthya Karyakram* (RBSK) focuses early identification and early intervention for children from birth to 18 years with thalassaemia where the blood transfusions and chelation therapy are covered.[16] Currently there are no state government funds offering HSCT. The annual treatment expenses of TC per patient have been reported to range from □ 41,515 (US$ 629) in <5 years age group to □ 1, 51,836 (US$ 2300) in >20 years age group.[7]

HSCT is an expensive treatment modality with economic consequences. There is a need for value-based assessment of HSCT using high-quality approaches to measure costs and outcomes to attain cost containment and make well informed decisions.[17]

A cost utility analysis from Thailand reported that reduced intensity HSCT is cost-effective as compared to blood transfusions combined with iron chelating therapy (BT-ICT).[18]. The present study intends to impress upon parents, analysts and the decision makers on the advantages and consequences of reallocating health care resources. We estimate the incremental cost per QALY gained (ICER- Incremental Cost Effectiveness Ratio) with HSCT (MRD and MUD) as compared to TC among TM patients India.

2. Materials and Methods

2.1 Model Overview:

A mathematical Markov model along with decision tree was parameterized on an MS Excel spreadsheet to estimate the incremental cost-effectiveness of HSCT as compared to TC for treatment of TM. Once patients are assigned to TC for treatment of thalassemia, decision tree was used to model their subsequent life course using a lifetime study horizon, in which a patient may develop iron overload complications (cardiac, liver and endocrine), transfusion transmitted infections (HBV, HCV and HIV) or die because of disease related complications or all-cause mortality (**Figure:1**). To model the life-course of patients assigned to HSCT, a Markov model with seven Markov transition states were considered; a) *1st year* post HSCT b) *2nd year post HSCT,* c) *Following years* post HSCT, d*) Chronic graft versus host disease* (cGVHD), e) *Transplant rejection* (returning to the TC arm). Apart from these health states, two absorbing states were also used; f) *death from Transplant related mortality* (TRM) and g) *death from natural causes*. The need for intensive health care services reduces from 1st to 2nd year following HSCT, with minimal follow-up services in the subsequent years. Similarly,

the consequences of HSCT were also different in 1st year, 2nd year and the subsequent years. **(Figure:2)**

Incremental costs and effects of HSCT were compared against the baseline scenario of TC. A life-time study horizon with cycle length of one year was used in the analysis. Future costs and consequences were discounted at 3% for time preferences of cost and utility. Consequences were valued in terms of life years and quality adjusted life years (QALYs) in both intervention (HSCT) and comparator (TC) scenarios. Clinical, cost and effectiveness parameters were used to model the lifetime costs and consequences for a hypothetical cohort of 1000 thalassemia patients, who could be treated by either of treatment regimens. Cost effectiveness was assessed by estimating incremental cost per life year gained and per QALY gained (ICER) with Intervention using HSCT as against TC. The analysis was done separately for MRD and MUD transplants, as the overall cost and resulting benefits are different for both. Uncertainties in parameters were assessed in a series of sensitivity analyses, including probabilistic sensitivity analysis, and results are presented using societal perspective.

2.2 Cost

For both HSCT and TC scenario, cost was estimated by the rates of a charitable private tertiary care center, in India. **(Table:1)** The cost estimation for the TC was based on the frequency of blood transfusions, outpatient department (OPD) visits, investigations, chelation therapy and supportive care given during the complications based on the charges and current practices as per the guidelines from both the tertiary care center. TC costs were estimated separately for five different age categories: 6 months to 2 years, 3 to 5 years, 6 to 10 years, 11 to 15 years and > 15 years. This stratification was done based on the difference in the intensity of transfusions, chelation and investigation requirements during different age intervals. All patients in this study were assumed to be started on transfusion from 6 months

of age and chelation with desferasirox was initiated orally from the age of 2 years. Although the Government of India is committed to provide the transfusions to TM patients at a subsidized cost, the actual cost of transfusion was included to reflect the true expenditure. Chelation cost was calculated based on the existing market rates of generic desferasirox for the median expected weight.

For the intervention group (HSCT), the accounts database of 57 TM patients aged between 1 and 18 years who underwent HSCT was used. Subgrouping of HSCT into MRD (n=43) and MUD (n=14) was done as there were differences in cost of transplant and complications between these groups. The pre-transplant work-up costs was not included in either group. Inpatient HSCT costs from admission to discharge during transplant were obtained from the institutional accounts department. The 1st and 2nd year costs included readmissions for the management of acute GVHD, infections or any other post- transplant complications. The outpatient costs were modelled based on the frequency of visits and the immunosuppressive and other supportive care drugs and immunization during the 1st and 2nd year following HSCT. Treatment costs related to chronic GVHD were calculated on the basis of projected costs for scheduled OPD visits, laboratory tests as per institutional protocols, immunosuppressant therapy and other supportive care medications. Indirect costs (transportation, accommodation, opportunity and productivity costs) were not taken into account in both the groups. Various cost parameters used in the model have been described in **Table:1**.

In this study, all costs are reported in Indian National Rupee (□) and US Dollars (US$) using the average conversion of 1 US$= □ 65 in 2017.[19]

2.3 Valuation of consequences

The efficacy of the two treatment options was assessed in terms of life years and quality adjusted life years (QALYs) lived in both the HSCT and TC scenarios. For the base case

analysis in HSCT group, the rejection rate used was 2.3% in MRD and 7% in MUD groups **(Table:1)**. Patients developing rejection were assumed to continue TC for the rest of their lives and their costs and consequences were modelled similar to a patient of TM on TC. The first year transplant related mortality rates in MRD group (12.4%) and MUD group (14.3%) used in the model was based on the study cohort with rejection predominantly occurring within the first year post HSCT.

Proportion of patients developing cGVHD was 14% and 43% in MRD and MUD groups respectively. The occurrence of cGVHD was limited to the first two years in this modelling. Mortality of patients entering third year post HSCT was assumed to be similar to all cause, age-wise probability of death as obtained from the Census of India Sample Registration System life tables.[20] Health related quality of life utility values were assigned to each of health states from published literature (0= death and 1= full health). In the absence of specific studies on the utility of TM patients undergoing HSCT, a value of 0.61 was assigned for first and second year.[21,22] The utility of HSCT patients from 3rd year onwards was assigned to be 0.93 based on the quality of life in patients who have undergone the hematopoietic stem cell transplantation for other diseases (Acute myeloid leukemia, non-Hodgkin lymphoma and Hodgkin lymphoma).[23] **Error! Bookmark not defined.**

A patient undergoing TC was modelled to develop iron overload complications (cardiac, liver and endocrine), transfusion transmitted infections (HBV, HCV and HIV) or die because of disease related complications or all-cause mortality. **(Table:1**) It was assumed that eventually every patient on TC group will develop a complication and continues with it for the rest of his/her life. On the basis of published literature, it was further assumed that the initiation and median age of developing iron overload complications was 3 years and 16 years respectively. It was also assumed that all the patients in TC group would develop iron overload by the age of 25 years, based on expert opinion. Once a patient has developed HBV, HCV or HIV, life

years and QALYs, were calculated by separate Markov models according to our previously reported study.[24] The age-wise probability of dying from all-cause was obtained from the Census of India Sample Registration System life tables.[20] Health related quality of life utility values were assigned to each of health states from published literature as referenced.

ICER was estimated as the ratio of difference in costs and the difference in effectiveness between HSCT and TC.

$$ICER\ (QALY) = \frac{Cost\ (HSCT) - Cost\ (TC)}{QALY\ (HSCT) - QALY\ (TC)}$$

2.4 Sensitivity Analysis

The effect of joint parameter uncertainty was analyzed by applying a probabilistic sensitivity analysis (PSA). Upper and lower bounds of ICER were estimated using the PSA, which was done using Monte Carlo method by simulating the results over 999 times. In order to do PSA, the cost parameters and health related quality of life utility values were varied 20% on either side of the base value. Discount rate was varied from 2% to 5%. The threshold cost of HSCT procedure below which the strategy remains cost-effective at a willingness–to-pay threshold was equal to the per capita gross domestic product. This was analyzed separately for MRD and MUD.

International society for pharmacoeconomics and outcomes research (ISPOR) task force, consolidated health economic evaluation reporting standards (CHEERS) statement was used to describe different aspects of methods used in the study.[25]

3. Results

3.1 Cost and Cost Effectiveness

Based on our model estimates, number of life years lived per thalassemia patient receiving TC, HSCT (MRD) and HSCT (MUD) are 21.8, 38.4 and 36.5 years respectively. Further, number of quality adjusted life years (QALYs) lived per thalassemia patient receiving TC, HSCT (MRD) and HSCT (MUD) are 18.2, 35.1 and 33.3 year respectively **(Table:2)**. Lifetime treatment cost incurred per TM patient was □ 12, 98,579 (US$ 19,978) for TC, □ 18, 32,461 (US$ 28,191) for HSCT (MRD) and □ 28,36,547 (US$ 43,649) for HSCT (MUD) groups. Accounting for comparative survival benefit, we estimated per life year costs incurred for TC, HSCT (MRD) and HSCT (MUD) to be □1,27,369 (US$ 1959), □89,080 (US$ 1370) and □145,663 (US$ 2240) respectively.

We found HSCT (MRD) incurs an additional cost of □59,560 (US$ 916) per life year gained (ICER) as compared to TC, which is less than half the per capita gross domestic product (GDP) of India (□ 1, 20,300, US$ 1861).[26] In case of MUD, this incremental cost is □1, 65,766 (US$ 2250) per life year gained.

With respect to cost per QALY gained, HSCT (MRD) and HSCT (MUD) incurred an additional cost of □ 64,096 and □ 1, 67,657 respectively as compared to TC. **(Table:2)**.

3.2 Sensitivity Analysis

In our probabilistic sensitivity analysis, we found HSCT (MRD) has a 94 % probability of being cost-effective at a willingness to pay threshold equal to per capita GDP of India. **(Figure:3)**. Threshold analysis suggests that if the initial cost of HSCT (MRD) is under □ 12, 00,000, it would be a dominant (less costly, more effective) strategy in TM patients as compared to TC **(Figure:4)**. It further suggests that HSCT continues to be cost- effective in comparison with TC, even up to a cost of procedure less than □24,00,000 (US$ 36,923) in case of MRD and □ 22,50,000 (US$ 34,615) in case of MUD **(Figure:5)**.

4. Discussion:

Our study compared the cost-effectiveness of HSCT vs TC and demonstrated HSCT to be highly cost-effective in the societal perspective. It was robust across all the sensitivity analyses and the cost-effectiveness acceptability curves suggested a 94% probability of HSCT (MRD) being cost-effective compared to TC using a willingness to pay threshold which equals to the GDP per capita. (**Figure: 3**)

Cost-effectiveness analysis (CEA) is a form of economic analysis that compares the relative costs and outcomes (effects) of different courses of action. With increasing costs in medical care, there is an imminent need to undertake economic evaluations, for policy makers to use these tools for rational allocation of resources. [27]

United Kingdom's NICE (National Institute for Clinical Excellence) appraises an intervention to be cost-effective on clinical (how well the treatment work) and economics (does it represent the value for money) with the implicit cost-effectiveness threshold ranging between £20,000 and £30,000 per quality adjusted life year (QALY) gained. In USA it is US$ 50,000/QALY gained and the difference is because of the different denominator used in its computation.[28]

The recommendations of the commission on Macroeconomics and Health of World Health Organization, suggests that health technologies with the ICER below the per capita GDP are considered very cost-effective, while those between one and three times per capita GDP being cost-effective, and ICER above three times per capita GDP indicate that a health technology is not cost-effective. .[18,29] More recently, however, use of 1-time GDP per capita threshold has been recommended as more appropriate than 3-times GDP per capita. [30,31] Even

at this lower threshold, HSCT (MRD) has a 94% probability to be cost-effective, given all the parameter uncertainties, which strengthens the conclusion about cost-effectiveness of the intervention. (**Figure:3**)

The discounted incremental cost-effectiveness of the HSCT (MRD) group was □59,560 (US$ 916) per life year gained and □ 64,096 (US$ 986) for every QALY gained which is only half of India's GDP per capita (□ 1,20,300, US$ 1861.5), suggesting this to be a "very cost-effective" approach. (**Table:2**)

A cost-utility analysis of HSCT among children aged 1 to 15 in Thailand showed that incremental cost-effectiveness ratio for MRD at different ages ranged between US$ 2373 to US$ 5382 per QALY gained as compared to TC. This was likely to be cost-effective for young children with severe thalassemia in Thailand at societal willingness to pay of US$ 2942. For patients undergoing MUD transplant, incremental cost per QALY gained ranged between US$ 6147 to US$ 28,029 as compared to TC.[32] Secondly, the Thai study reported that the ICERs of both MRD and MUD HSCT increase with patient age. This implies that HSCT given at an earlier age is likely to be more cost- effective. Undertaking such an analysis required more stratified data in terms of effects of HSCT, complications of patients receiving TC at different age intervals, and the quality of life of patients who undertake HSCT at different age. Since, such disaggregated country specific data is not available for India currently, it is recommended to generate such data and undertake a sub-group cost-effectiveness analysis in future in Indian context to generate evidence on cost-effectiveness of performing HSCT at different ages.

In another cost utility analysis study from Thailand among adolescent and young adults with thalassaemia, HSCT (MRD) showed an incremental cost per QALY gained to be US$ 3236 compared to transfusion and chelation. [18] In our study, the median age of transplant patients were 9 years ranging from 1 to 18 years and indirect medical costs were not included.

Although the utility assigned were similar in both the studies, and amount in dollars in India was much lower, direct comparison is not advisable as the expenditure pattern and GDP per capita are different in both the countries.

According to a study from India, the median cost of an allogeneic transplant in a cohort of predominantly TM patients (31.5%) at the time of initial discharge was □ 11,64,410 (US$ 17,914). This was a one-time cost incurred during the initial admission till first discharge.[33] In another study, the cost of allogeneic HSCT in India ranged between □ 9,75,000 to 13,00,000 (US$ 15,000 - 20,000).[34] These studies were done for varied indications and did not take re-admissions into account and were at different time frames.

In our study, the median cost incurred for MRD group for the first one year was □ 16,92,597 (US$ 26,039) which included repeat admissions for various indications including management of acute GVHD and estimated cost of OPD investigations and medications for one year. (**Table: 1**)

According to a study from Chennai, the cost of MUD transplant in India for TM has been approximately □ 25,00,000 (US$ 38,461) including procurement of the stem cells per child per HSCT.[27] In our study, the average cost incurred for MUD transplant was □ 27,17,977 (US$ 41,815) including the acquisition of cells (from either DKMS (German) or DATRI (Indian) donor registries), repeated admissions for infection and estimated OPD follow up for the first year. **(Table:1**)

The cost incurred in managing the patients in second year was higher in the MUD transplant group (□ 2,11,767, US$ 3257) as compared to the MRD transplant group (□ 1,45,915, US$ 2244) including admissions and estimated OPD visits and scheduled investigations. This is

attributed to the higher incidence of GVHD and infection among the MUD transplant group. **(Table:1)**

Conditioning regimen used in this cohort of patients were Thiotepa/Treosulfan/Fludarabine regimen which is much more expensive than busulfan/cyclophosphamide conditioning regimen as the drugs have to be imported and comprised 30-40% of the total transplant cost. With many Indian companies now manufacturing the generic drugs, the cost of TM transplant is bound to reduce further in the coming years.

We acknowledge certain limitations of our study. First, the survival data and transition probabilities for HSCT patients were obtained from a single institution database. Second, indirect costs (transportation, accommodation, opportunity and productivity costs) were not taken into account in both the groups. However, given the savings in indirect costs would have been much more in the HSCT arm; it would have made the HSCT procedure even further cost-effective and does not bias our conclusion. Third, utility values were assigned based on literature review and this may change in the social context in India. Fourth, the direct medical costs of HSCT were taken from only a single institution. However, the costs represent a societal perspective, and are rather on a higher side than what has been reported earlier. Lastly, in the TC group, the medical costs were modelled based on the accepted practices on the basis of recommended guidelines. However, the values matched with the recently published literature from India based on actual costs.[7]

The major deterrents for the patient's family to make the decision to undergo HSCT are high initial upfront costs and dilemma arising from the 10 -20% possibility of immediate mortality with HSCT in juxtaposition to deferred risk to life with TC. This predicament leads them to the classical cognitive "omission bias" and "loss aversion" where the "inaction" of continuing the TC seems morally more compelling than the "action" of HSCT. On the contrary

"commission bias" occurs by discounting the risks posed by the procedure and overestimating the likelihood of success and a poor outcome scenario can pave the way for 'regret and anguish' for the family.[35] Appropriate counselling with regard to significant improvement in outcome of stem cell transplantation and thalassaemia free survival between 77 - 95% across the different risk stratifications [36] with realistic expectations and providing adequate governmental and NGO funding will help mitigate this problem.

Adopting an explicit cost-effectiveness threshold facilitates consistency and transparency in the decision-making process and helps many patients to access transplant as a permanent cure especially in younger age group patients. CSR (Corporate social responsibility) project by Coal India Pvt limited in collaboration with Ministry of Health And Family Welfare "*Thalassaemia Bal Sewa Yojna*" is one such project which gives financial assistance of □ 10 lakhs per patient ages less than 10 years. Prime minister's relief fund also provides upto □3 lakhs which subsidizes transplant of thalassaemia patients. There are many other NGOs which support transplantation in such patients.

In our model, mean life years lived by a TM patient in the TC group was 21 years and in HSCT (MRD) was HSCT (MUD) groups it was 38 and 36 years which reflects HSCT doubles expected life span of the patient. (**Table:2**)

Universal health coverage is a major policy goal of the 12th Five Year Plan. The Government of India aspires to provide coverage for all essential services at a cost which the persons can afford. The Government of India has set up Health Technology Assessment Board (HTAB) to guide the Ministry of Health and Family Welfare on choosing cost-effective interventions for various programs.[37] Several state governments are also developing plans to enhance coverage of services. Against this background, there is a need to choose the interventions wisely so as to have best value for money.

With a definite long-term cost efficacy in HSCT and it being the only curative option for the patients with TM, it is time for the state governments to include this in health schemes like RBSK and extend the support for wider population. In the absence of infrastructure and expertise in the government medical colleges, collaborating with the private sector and fostering a partnership through Public Private Partnership (PPP) for providing services-subsidized transplant would be the way forward in reducing the societal burden and increasing the productivity of its citizens by extending the life spans. Various publicly financed insurance schemes should support HSCT for TM patients. In the long-term, capacity and infrastructure should be developed in the public sector to provide HSCT services.

Economic organization of a society, not merely in transactional terms, but as a moral issue, is inextricably linked to individual rights and dignity. HSCT remains the only curative option for patients with thalassaemia major which is highly cost-effective throughout the patient's lifetime. This study provides the necessary evidence for the policy makers to make a well informed decision for requisite resource allocation for HSCT which will enable a long-term value for money intervention for TM.

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Data statement*:* This study was a model based economic evaluation. We reviewed various literatures to draw parameter values. No primary data was collected as part of this study; hence no data is available for sharing. All parameters which were sourced from published literature is available in the manuscript.

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Figure title and legends

Figure 1: Decision tree used for modelling Transfusion Chelation arm of the model

Figure 2: Markov model used for Hematopoietic Stem Cell Transplant

Figure 3: Cost effectiveness acceptability curve at different levels of willingness to pay for HSCT (MRD)

Figure 4: Threshold analysis at different levels of HSCT (MRD) cost

Figure 5: Threshold analysis at different levels of HSCT (MUD) cost

560 **Table 1: Input parameters used in the base analysis of the model**

Input Parameters for HSCT Arm of Model		Reference
Proportion of patients developing rejection (MRD)	0.023	CMCL database
Proportion of patients developing rejection (MUD)	0.07	CMCL database
Proportion of patients having Transplant Related Mortality (MRD)	0.124	CMCL database
Proportion of patients having Transplant Related Mortality (MUD)	0.143	CMCL database
Proportion of patients developing Chronic GVHD (MRD)	0.14	CMCL database
Proportion of patients developing Chronic GVHD (MUD)	0.43	CMCL database
Utility score of a patient in the first year post-HSCT	0.61	[21]
Utility score of a patient in the second year post-HSCT	0.61	[22]
Utility score of a patient post-HSCT in the following years	0.93	[23]
Utility score of a patient in chronic GVHD	0.9	[37]
Cost incurred in first year after HSCT (MRD)	☐ 16,92,597.22	CMCL database
Cost incurred in second year after HSCT (MRD)	☐ 1,45,915.8	CMCL database
Cost incurred in first year after HSCT (MUD)	☐ 27,17,977.25	CMCL database
Cost incurred in Second year after HSCT (MUD)	☐ 2,11,767	CMCL database
Cost incurred in following years after HSCT	☐ 880	Modelled
Cost incurred in treating Chronic GVHD	☐ 1,09,070	Modelled
Input Parameters for Transfusion Chelation (TC) Arm of Model		
Proportion of patients having cardiac complications	0.091	[38]
Proportion of patients having liver complications	0.1	[39]
Proportion of patients having endocrine complications	0.5382	[40]
Proportion of patients having HBV	0.0104	[41]
Proportion of patients having HCV	0.25	[41]
Proportion of patients having HIV	0.0104	[41]
Utility score of a patient of Thalassemia having no complication	0.93	[21]
Utility score of a patient of Thalassemia having cardiac	0.8525	[42]

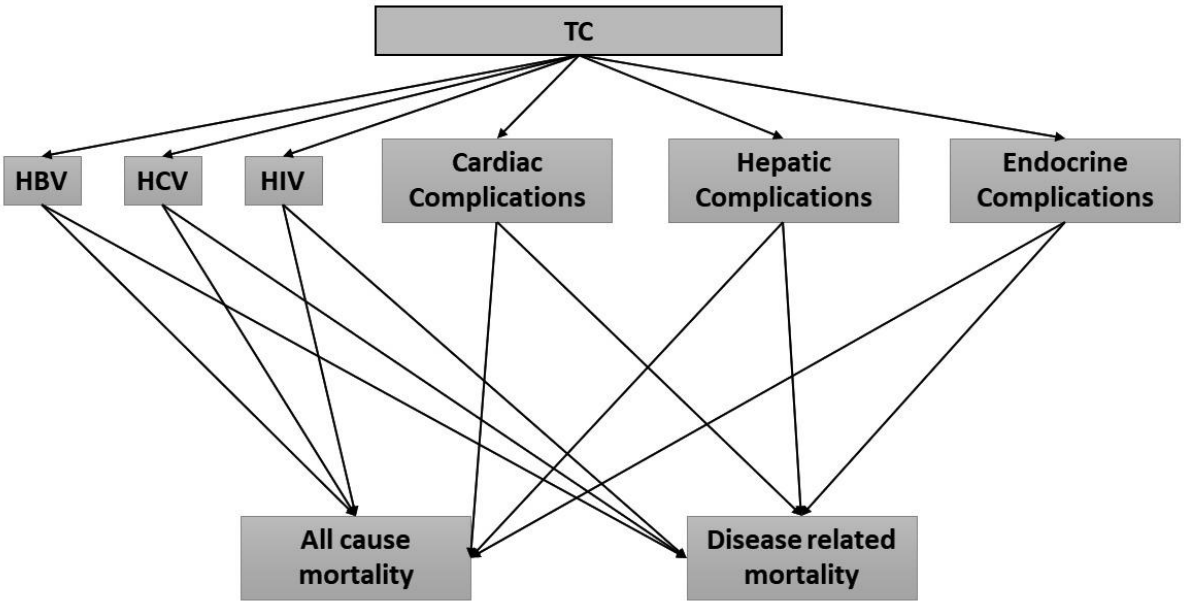
complications		
Utility score of a patient of Thalassemia having endocrine complications	0.8666	[42]
Cost of managing thalassemia patients having cardiac complications (In first year)	☐ 3,31,068.33	Modelled
Cost of managing thalassemia patients having cardiac complications (In following years)	☐ 3,01,668.33	Modelled
Cost of managing thalassemia patients having liver complications (In first year)	☐ 3,36,518.33	Modelled
Cost of managing thalassemia patients having liver complications (In following years)	☐ 2,96,778.33	Modelled
Cost of managing thalassemia patients having Endocrine complications (In first year and following years)	☐ 1,07,535.47	Modelled

Abbreviations: HSCT: Haematopoietic stem cell transplant, MRD: Matched Related Donor, MUD: Matched Unrelated Donor, GVHD: Graft versus host disease, CMCL: Christian Medical College, Ludhiana

Table 2: Outcomes and Cost- effectiveness of Haematopoietic Stem Cell Transplant as compared to Transfusion Chelation.

	TC	HSCT (MRD)	HSCT (MUD)
Life years lived by 1000 subjects	(Years)	(Years)	(Years)
Undiscounted	21,828.12	38,411.13	36,497.85
Discounted	10,195.41	20,570.86	19,473.31
Quality Adjusted Life Years	(Years)	(Years)	(Years)
Undiscounted	18,227.14	35,130.35	33,295.77
Discounted	8,363.81	18,568.78	17,537.11
Cost effectiveness of HSCT as compared to TC in Rupees (☐)			
		MRD	MUD
ICER per Life Year gained (Discounted)		☐ 59,559.59	☐ 1,65,766.35
ICER per QALY gained (Discounted)		☐ 64,096.12	☐ 1,67,656.58

Abbreviations: TC: Transfusion Chelation, HSCT: Hematopoietic Stem Cell Transplant, MRD: Matched Related Donor, MUD: Matched Unrelated Donor ICER: Incremental Cost Effectiveness Ratio, QALY: Quality Adjusted Life Year



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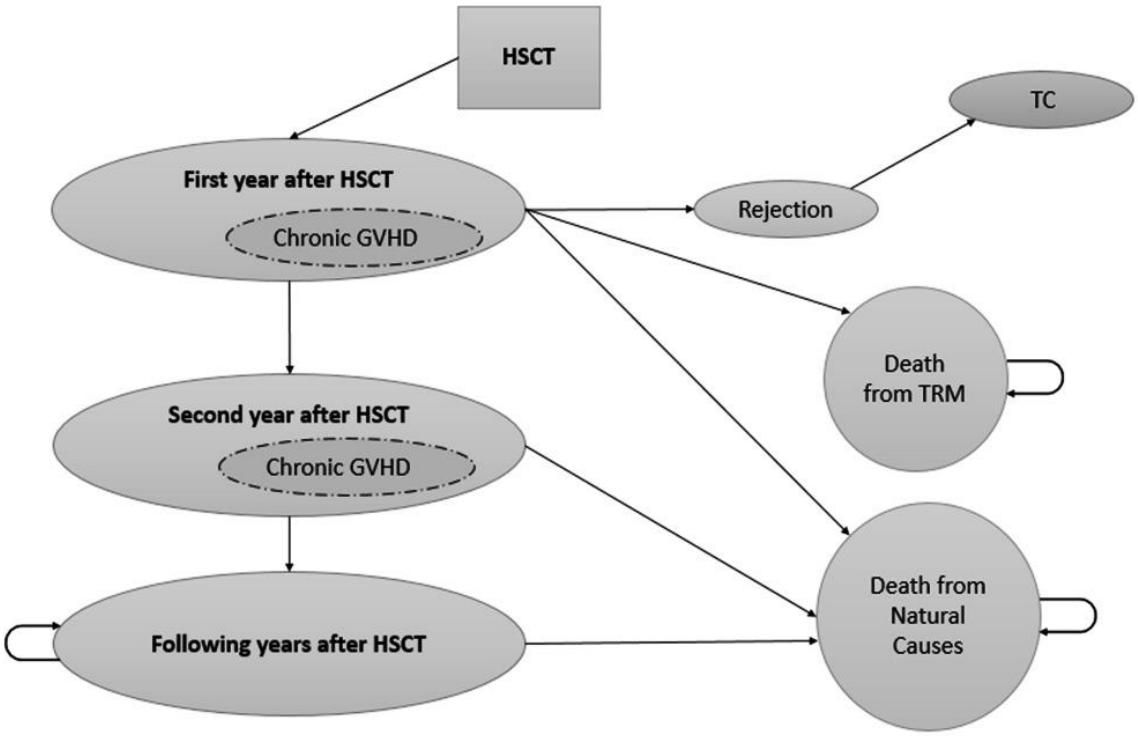

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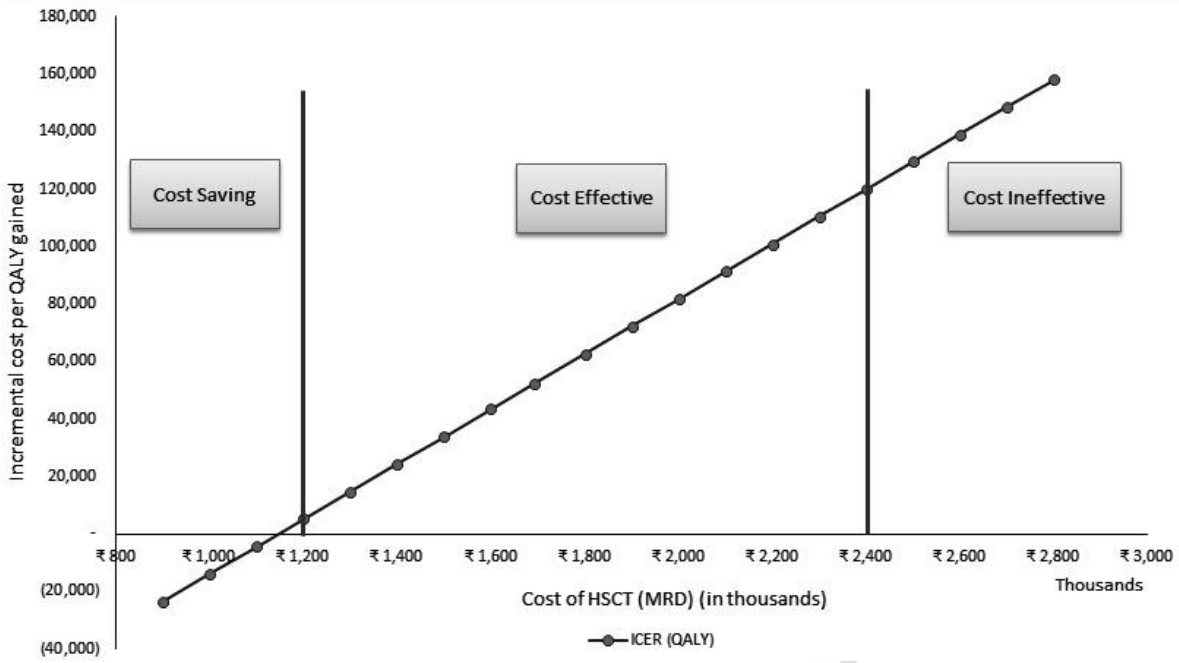

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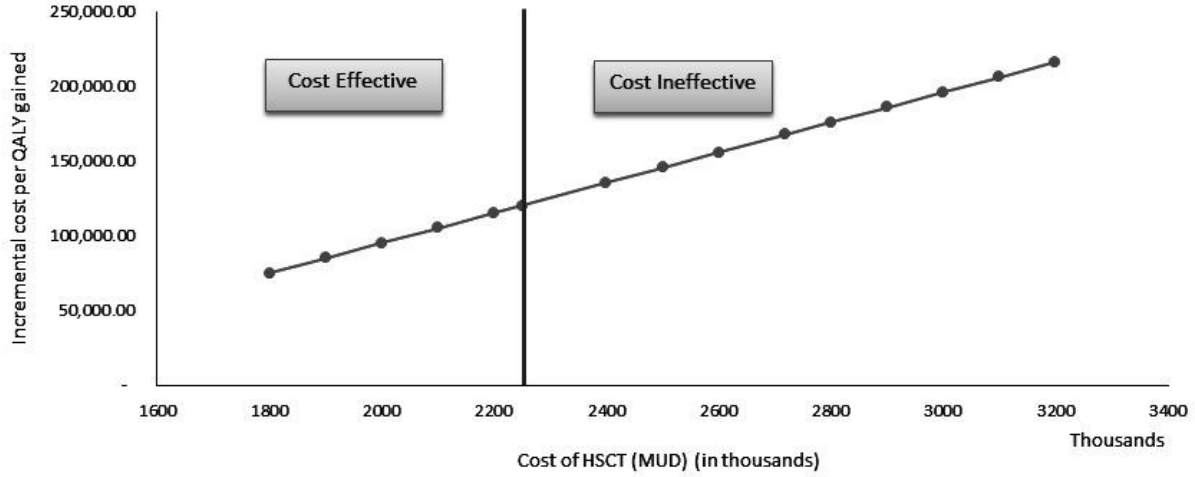

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