Economic Evaluation of Iron Chelation Therapies for Thalassemia Patients in the West Bank- Palestine

تقييم اقتصادي لعلاجات ازالة الحديد من الجسم لمرضى الثلاسيميا في الضفة الغربية- فلسطين

Submitted by: Layali Hani Abdeen

Date of discussion: April 29th 2009

The committee: Dr. Awad Mataria
Dr. Muhammad Nasser
Dr. Rana Khatib

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Abbreviations:

CBA – Cost Benefit Analysis

CEA – Cost Effectiveness Analysis

CMA – Cost Minimization Analysis
CUA – Cost Utility Analysis

DFO – Deferioxamine/ Desferal

DFX – Deferasirox/ Exjade

FGD – Focus Group Discussion

GDP – Gross Domestic Product

ICER – Incremental Cost Effectiveness Ratio

ICUR – Incremental Cost Utility Ratio

L1 – Deferiprone / Ferriprox

MOH – Ministry of Health

NIS – New Israeli Shekel

QoL – Quality of Life

TPFA – Thalassemia Patients Friends Association

USD – Unites States Dollar

WTP – Willingness to Pay

Abstract:

Decreasing the amount of iron in the blood is crucial for thalassemia patients as they get regular blood transfusions for their treatment, and as a result iron accumulates in the body damaging vital organs such as the liver and heart, which ultimately leads to the death of the patient.

In Palestine, thalassemia patients undergo the difficult and painful infusion of a drug known as Deferoxamine (Desferal®/ DFO) that rids the body from excess iron. The drawback of such management strategy consists in its invasive character, where a needle, attached to a small battery-operated infusion pump, is worn under the skin overlying the stomach or legs, 5 to 7 times a week for up to 12 hours in each administration. Deferoxamine binds with iron in a process called "chelation", leading to the elimination of the excess iron from the body. This treatment is found cumbersome by many patients, implying low adherence from their side with the management regimen, thus limiting its effectiveness in real life settings.

Consequently, the oral iron chelators have been introduced to help patients get rid of excess iron in a convenient matter. The two 'Oral Iron Chelators' are:

1- Deferiprone: Ferriprox® / L1
2- Deferasirox: Exjade®/ DFX

However, these oral chelators have not yet been introduced in the Palestinian context. This paper will investigate **whether an introduction of the oral iron chelators will be more cost effective and whether they enhance Quality of Life (QoL) for patients in Palestine.**

Three analytical approaches were used to assess the costs and consequences associated with each of the treatment strategies. Firstly, a cost-effectiveness analysis was conducted. Here, the comparison between the different medications was in terms of incremental cost effectiveness ratio (ICER), and the effect that was considered is the intermediate outcome of reduced iron in the body, which was measured through serum ferritin levels. From the Ministry of Health perspective DFX had lower ICER of NIS 392,384.7 per percentage reduction in serum ferritin levels than L1 when compared to DFO. From the patient perspective however, oral chelators strongly dominated the Desferal, while from the society perspective DFX had also lower ICER than L1 when compared to DFO.

Along this a cost-utility analysis was used to incorporate the ‘Quality of Life’ of the patients under the different medications, where oral chelators strongly dominated over DFO in the age category of over 4 years old, while in the societal perspective the ICUR was NIS 153,370/ QALY gained for the age group below or equal to 4 years old, and NIS 151,832.1/ QALY gained for the age group above 4 years old.

The third approach which is cost benefit analysis was used in an attempt to measure the effectiveness gained from oral chelators monetarily through estimating directly and indirectly the willingness to pay for the oral chelators using a contingent valuation and a conjoint analysis respectively. The net social benefit was highly positive in both cases.

KEY WORDS: cost-effectiveness; cost utility; quality of life; conjoint analysis; thalassemia; oral chelators.

1. **Introduction**

1.1. Health Economics

Health economics is concerned with the connection between health and the resources which are consumed in promoting it (*Johansson and Jonson 1999*). Resources do not include only money, rather people, materials and time which could have been put to some other use (*Witter, 2000*).

Since resources are scarce, choices must and will be made concerning their deployment, thus allocating them to the most efficient programme or measure (*Drummond et al. 2005*). In order to measure the efficiency of such programs there are different methods. The most common is economic evaluation, where it provides important information to decision makers especially in the absence of effective markets. Economic evaluation is defined as the "comparative analysis of alternative courses of action in terms of both their costs and consequences" (*Drummond et al. 2005*). Therefore the basic task of any economic evaluation is to identify, measure, value and compare the costs and consequences of the alternatives being considered. There are different types of economic evaluation, depending on the outcome of each procedure; they are (*Drummond et al. 2005)*:

1- Cost minimization analysis (CMA).
2- Cost effectiveness analysis (CEA).
3- Cost benefits analysis (CBA).

4- Cost utility analysis (CUA)

The paper will attempt to use these techniques in assessing different management strategies of thalassemia patients in Palestine, and try to induce the most efficient strategy that enables to maximize the benefits to the patients and the society as a whole.

1.2. Thalassemia in Palestine

Thalassemia is the name of a group of genetic blood disorders, in which the production of normal hemoglobin is partly, or completely, suppressed due to defective synthesis of one or more of its component globin chains (*Gomber et al. 2004*). To elaborate, hemoglobin is the main constituent of human red blood cells, responsible for carrying, and delivering, oxygen molecules to aliment all body cells. It consists of several combinations of two different proteins, Alpha and Beta; in addition to an iron moiety located in the central part of the molecule. In the case of thalassemia, one or more of the globins are inadequately produced – or even not produced at all (*Thalassemia Organization 2006*). If the mal-production affects the alpha-chain, then the disorder is known as alpha-thalassemia. Similarly, if the defected component is the beta-chain, then the resulting condition is beta-thalassemia (*Gomber et al. 2004*).

In Palestine, beta thalassemia is the most common whether in its major, intermediate or minor form. There are 662 patients diagnosed with either major or intermediate beta thalassemia in 2007, 412 in the West Bank and 250 in Gaza. The annual increase in thalassemia between Palestinians was 20%-25% till 2000. This has led the Palestinian Government to take safety measurements such as applying the law that forces the couples to be examined for positive thalassemia before getting married and prohibiting any couple from getting married if proven so. Consequently, this has led to a decrease in the incidence of the disease between the Palestinians to reach 3.5% in the years to follow.

In Palestine thalassemia is mainly managed through regular blood transfusions to be done once or twice a month for a major thalassemic patient. In addition, patients are also subject to another management regimen aiming to reduce iron overload; i.e. excess iron accumulation, which results from frequent blood transfusions. In Palestine, thalassemia patients undergo the difficult and painful infusion of a drug known as Deferoxamine (Desferal®) that rids the body from excess iron (*Darwish 2006*). The drawback of such management strategy is represented by its invasive character, whereby a needle, attached to a small battery-operated infusion pump, is worn under the skin overlying the stomach or legs, 5 to 7 times a week for up to 12 hours in each administration (*Hidmi 2007*).

Deferoxamine (DFO) binds with iron in a process called “chelation”, leading to the elimination of the excess iron from the body (*Hershko 2005*). This treatment is found cumbersome by many patients, implying low adherence from their side with the management regimen (*Cappellini 2005*; *Porter 2005).*

The treatment regimen is financially supported by the Ministry of Health (MOH) in cooperation with the Thalassemia Patients Friends Association (TPFA). TPFA provides the blood through encouraging and providing blood donors, in addition to providing a program for blood transfusions, which enables the patients to have systematic blood transfusions. The TPFA also provides the following (*Nabulsi 2006)*:

- A nurse in each hospital.
- Register patients and their families in the health insurance which is provided freely by the MOH.
- Donating pumps necessary for the medicine injections and providing their maintenance which is only done outside the country in Jordan.
- Providing free periodical examinations for the hormones, heart, sight and hearing for the patients. Also they provide the quarterly, half yearly and yearly examinations needed by the patients through the corporation of several physicians who volunteer to supervise such examinations.
- TFPA has also established treatment centers in Hebron, Nablus and Tulkarem.
- In parallel the TFPA also provides a psychological program for the patients. This program supports the patients who feel isolated from the society through establishing educational programs in the society to identify the disease and limits its incidence by ensuring that the couples do adhere with the law of examining before marriage.

It must be noted that in Palestine there is another institution that works beside the TPFA known as The National Institution for Blood Diseases “Abiqrat”. This institution provides the patients with the opportunities to have bone marrow transplantations, which is considered the ultimate treatment regimen worldwide as it eliminates the disease and the patient can survive normally. However such a management is not affordable to all patients due to the following reasons:

- If the patients suffer from any side effects from thalassemia, such as enlargement of the spleen, this would lead to dangerous repercussions on the patients’ life, thus the success of this management regimen is very low in such cases.
- Patients under 10 years old have higher success probabilities than older patients.
- Such management also depends on the availability of bone marrow donors, on the compatibility between the donors’ body and the patients’ body, and the overall health of the donor.

The costs of such operations are high; however, Abiqrat provides such management for free. The institution has done 24 operations since 2003 for patients from the West Bank and Gaza Strip. Today, 22 cases revealed to be successful, whereas the other two suffered major complications leading to the death of one patient after two months from the operation.

1.3. Problem statement

As delineated, thalassemia patients in Palestine undergo the difficult and painful infusion of Deferrioxamine (Desferal®) that rids the body from excess iron. The drawback of such management strategy consists in its invasive character, where a needle, attached to a small battery-operated infusion pump, is worn under the skin overlying the stomach or legs, 5 to 7 times a week for up to 12 hours in each administration. This mechanism of chelation results in low compliance from patients thus affecting morbidity and mortality rates, in addition to its effects on the Quality of Life of the patients that results in increased costs on society.

The total cost of iron management strategy, when assessed from the perspective of the health care provider, is mainly driven by the cost of the Desferal needle that averages around NIS 15.3/ needle and patients usually need around 2 needles a day. The costs of infusion pumps and their maintenance cost (in the local context such a pump costs between USD1,000 and USD1,500, and remains functional for a period of 5-6 years) are high but they are not borne by the Ministry of Health since these pumps usually come as donations when acquiring the medication (*Hidmi 2007)*. However, it must be noted that in Palestine there are only 200 pumps available for an estimated number of 600 patients (*Abu Ghosh 2007*). Apart from the direct medical costs mainly borne by the health care providers, such treatment strategy has direct non-medical, indirect and intangible costs when assessed from the patients' perspective. This is due to the impact it has on patients' every day, remunerated and non-remunerated, activities and 'Quality of Life'. A recent graduate seminar paper, prepared by one of the Master in Economics students at Birzeit University, had already uncovered the high burden that the thalassemia condition and such its treatment strategies impose on Palestinian thalassemia patients, in terms of physical difficulties associated with the treatment procedure and the psychological burdens (*Nabulsi 2006*).

Desferal (DFO) has proved to be efficacious in preventing and managing iron overload, however, adherence with this treatment regimen is a major issue from the patients' perspective, thus limiting its effectiveness in real life settings (*Porter 2005*). Consequently, oral iron chelators have been introduced to help patients get rid of excess iron in a convenient matter (*Porter 2005*; *Hershko 2005*). Today, there are two available 'Oral Iron Chelators' and they are:

3- Deferiprone: Ferriprox®.
4- Deferasirox: Exjade®

Accordingly, and amongst the three available management strategies of iron overload in thalassemic patients subject to regular blood transfusions, a question repeatedly posed about which management strategy represents the most efficient strategy in terms of its cost effectiveness, cost utility and cost benefit, as related to Palestinian patients from the perspective of the patients, Ministry of Health and the society as a whole?

Such a problem is associated with a number of sub-problems that the thesis will aim to tackle, such as cost calculations, obtaining scores for quality of life for thalassemic patients and extracting willingness to pay for oral chelators.

Thus the analysis shall be conducted from the perspective of health care providers; and then challenged to assess the impact of incorporating a patients' perspective on the decision to be taken. Therefore the study will reflect the perspective of health care systems providers in the West Bank (MoH and TPFA) as well as the perspective of the patients.

It is worth mentioning that the conduct of such analysis is verified for two reasons:

1- the Palestinian MoH, with help from TPFA, is aiming to introduce one of the above mentioned Oral Iron Chelators, should their medical and economic values; e.g., cost-effectiveness and cost-utility, be ascertained.

2- There are costs, efficacy/effectiveness and utility repercussion differentials between the two oral chelators and when compared to the currently used parental therapy. This makes it difficult to pinpoint the most cost-effective medication without a systematic inquiry and profound scientific analysis of the benefits and burdens associated with each of the therapies.

This Master Thesis shall help inform the decision of adopting, or not, any of these two new ‘Oral Iron Chelators’ to replace the currently used parental Deferoxamine.

The research endeavor will pass by the following steps:

- A survey of the most popular databases such as: Medline and Hinari, will be carried out to extract relevant literature on the different clinical trials conducted to assess the consequences of the concerned management strategies.
- The costs of each medication will be estimated using information provided by: governmental and non-governmental bodies, any related organizations, the medical staff, and finally the patients themselves.
- In order to assess the current ‘Quality of Life’ of the thalassemia patients, a structured questionnaire will be administered on a selected sample of patients, using the one developed by *Ratip et al*, and recently tested in the Palestinian context by Nabulsi in 2006; the former has indeed been developed to assess the clinical and psychological burden of thalassemia (*Tefler et al. 2005*). However, the questionnaire will be validated in the local context through a focus group that will underlie the specificity of Palestine.
- To indirectly asses WTP for oral chelators, a questionnaire will be administered for the patients where several scenarios shall be proposed to

analyze the patients' stated preferences about how they would behave in a hypothetical situation. Such a technique is known as the conjoint analysis, where it is based on the premises that any good or service can be described by its characteristics (attributes) and that the extent to which an individual values a good or a service depends on the levels of these characteristics (*Ryan and Farrar 2000*).

- Cost-effectiveness, cost-utility and cost benefit analyses will be carried out, in order to help inform policies with regard to the most worthwhile strategy for Palestine.

2. Literature review

2.1. Economic Evaluation

There are four different full economic evaluations that distinguish from each other based on how the consequences of the programs being evaluated are measured and valued. These are:

1- Cost Minimization Analysis (CMA):

CMA is used when the consequences of the programs in consideration are exactly the same on all the dimensions of interest. Hence, the only difference between the different programs would be in the associated costs, leading the decision maker to choose the programmes with the least cost (*Durmmond 2005; Witter 2000*).

2- Cost Effectiveness Analysis(CEA):

CEA is applied on programmes that have the same outcome of interest but may have different success in achieving this outcome as well as different costs. The decision about which programme to choose is made based on the additional resources needed to achieve enhancements in health outcomes. The comparison between the programs could be in the form of incremental cost per incremental unit effect such as incremental cost per life year gained or effects per unit of cost such as life years gained per extra dollar spent (*Durmmond 2005; Donaldson and Shackley 1997a*). It is worth noting that life years gained are considered a final outcome of any medical intervention, however some clinical trials provide us with intermediate outcomes rather than a final outcome such as number of cases found or number of patients treated appropriately. These intermediate outcomes could be used in CEA as long as a link has been established between them and the final health output or in cases where the intermediate outcome is proven to have value *per se* (*Durmmond 2005*).

3- Cost Utility Analysis (CUA):

CUA is applied when researchers want to measure the outcome or value of any programme in utility terms. More importantly, CUA is used when valuation is done using ‘health state preferences’ through the use of utility. Utility refers to the preferences individuals or society may have for any particular set of health outcomes. CUA is viewed as a useful term because it allows for quality of life adjustments to a given set of treatment outcomes, while providing a generic outcome measure for the comparison of costs and outcomes in different programmes. The results of CUA are expressed in terms of incremental cost per healthy year gained or incremental cost per Quality Adjusted Life Year (QALY) gained by undertaking one programme over the other, where QALY takes both the quantity and quality of life due to health care intervention. A score of 1 usually represents a perfect health and 0 represents death (*Durmmond 2005*).

3.1. Measuring preferences:

There are various methods to measure preferences:

1- Rating scale and its variants is the simplest approach in measuring preferences, where respondents would be asked to rank health outcomes from most preferred to least preferred, and then place the outcomes on a scale with intervals between each outcome corresponding to differences in preferences. The scaling of such preferences has different variations where a rating scale refers to a scale of numbers (0-100), category rating consist of small number of categories (10 or 11) and subjects assume that they are equally spaced, and visual analogue scaling that consist of a line on a page with clearly defined end points.

2- Standard gamble, usually used to measure chronic conditions and the subject is offered 2 alternatives, the first one is a treatment with 2 possible outcomes either the patient returns to a perfect health and lives for an additional t years (with probability p) or dies immediately (with a probability 1-p). Alternative 2 however, would have a certain outcome of the chronic state under consideration for the rest of individuals' life. In this approach p is varied until the subject becomes indifferent between the two alternatives (*Klose 1999; Ryan et al 2003*).

3- Time trade off (TTO), was developed as a more easy technique compared to the standard gamble approach where a patient with chronic condition is given

2 alternatives: either state i for time t or healthy for a number of years x less than t followed then by death. The x is varied until the respondent is indifferent between the two alternatives (*Diener et al, 1998*).

4- <u>Pre scored multi attribute health status classification systems;</u> this approach is more favorable than the previous three that are very time consuming and involve complex tasks in calculations. There are many systems that could be used in this approach such as:

   a- Quality of Well Being (QWB).
   b- Health Utilities Index (HUI).
   c- EuroQol (EQ-5D).
   d- World Health Organization QoL (WHO-100)

The above measurements (a-d) are used to obtain quality of life (QoL) weights in order to obtain a measurement for the QALY.

In Palestine there have been several attempts to measure QoL for Palestinian patients through adapting international questionnaires and validating them in the local context. A study done by (*Giacman et al 2007*) has attempted to adapt the WHOQoL questionnaire and consequently has introduced new themes and aspects in measuring the QoL for the Palestinian population. A QoL score has also been estimated for post partum women in Palestine (*Hammoudeh, 2008*).

4.1. What is QoL?

According to the World Health Organization (WHO), QoL is defined as “*an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the persons’ physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment*.”

Thus and according to the above definition, a questionnaire for measuring the QoL was developed by the WHO and is known as the WHOQOL-100 which is constructed from 100 questions and has an abbreviated version called the WHOQOL-BREF. These two questionnaires have the following domains that help measure the QoL:

-Physical Health

-Psychological

-Level of independence

-Social relations

-Environment

-Spirituality/religion/personal beliefs

However, Thalassemia patients encounter different domains and determinants that affect their QoL that are not measured/ reflected in the generic WHO versions or any other versions for this matter that target the whole population rather than groups affected by specific diseases. Accordingly, Ratip et al. 1999 have developed another QoL questionnaire which is specific for thalassemia patients and measures the clinical and psychological burden of Thalassemia (*Tefler et al 2005*). It constitutes the following themes that are expected to affect the QoL of the patient:

-Impact of the diagnosis and treatment on family stability and family dynamics.

-Feeling different.

-Appearance.

-Treatment.

-Absent or delayed sexual development.

-Complications.

-Uncertainties about the future.

Ratip Questionnaire has been adapted in several countries to measure the psychosocial burden of the disease on thalassemic patients. Such studies were conducted in USA (*Sherman et al.1985; Woo et al. 1985*), UK (*Ratip and Modell 1996; Tsiantis et al. 1996*), Turkey (*Canatan et el. 2003*), Canada (*Klein et al. 1998*), Italy (*Di Palma et al. 1998; Politis et al. 1990; Tsiantis et al. 1996*), Greece (*Beratis 1993; Tsiantis 1990; Politis et al. 1990*) and Lebanon (*Der Kaloustian et al. 1987*). An attempt has also been made to use this questionnaire in Palestine by Nabulsi in 2006, however the questionnaire implemented was not the same as Ratips' and did not have the same layout rather it depended on the main themes outlined by Ratip et al.

4- Cost Benefit Analysis:

CBA is used in analyzing programmes that have multiple outcomes. In addition, any analyses that measure both costs and consequences in dollars terms is called cost – benefit analysis, consequently, outcomes are valued and not only measured in dollar terms. The results of such analysis might be stated either in the form of a ratio of dollar costs to dollar benefits or as a simple sum representing the net benefit (loss) of one programme over another, and the latter is usually more preferred than the former (*Durmmond 2005*).

In CBA there are several ways to measure and value health outcomes in monetary terms:

a- Human capital: this approach place monetary weights on healthy time using market wages rates (*Klose 1999; Koopmanschap 1995*) and the value of the programme is assessed in terms of the present value of future earnings. However such technique is accompanied with calculation difficulties due to imperfections in labor markets and also due to equity and welfare issues that are not considered in such an analysis (*Drummond, 2005*; *Mishan, 1971*).

b- Revealed preferences: this approach examines the relationship between particular health risks associated with each hazardous job and wage rates that individuals require to accept such a job (*Durmmond 2005*), this approach is based on individual preferences regarding the value of increased/decreased health risk as a trade off against increased/decreased income that represent all other goods and services the person may consume. However the weakness in such approach is in its high variations in valuations and estimations are very limited and job specific.

c- Stated preferences of willingness to pay: WTP measure could be computed in two ways, either directly or indirectly. This method attempts to measure directly the maximum willingness to pay for non-marketed goods (health care programmes) through surveys that present consumers/ patients with various hypothetical scenarios about the programme evaluated. Accordingly, Klose 1999 defines contingent valuation as "a survey based, hypothetical and direct method used for eliciting a monetary value of a health care intervention". This technique usually presents the health outcome as either improvements in health status or as attributes (*Donaldson and Schackley 1997*). The values revealed (consumer surplus) are then added across the individuals forming the basis for cost benefit calculus. The weakness in such technique comprises in the difficulties in measuring willingness to pay and the various debated and proposed methods in how to formulate the scenarios and questions to get a fairly "true" maximum willingness to pay figures.

When using the direct method to estimate WTP, there are several methods to elicit WTP measure, these vary from open ended questions, dichotomous approach (also known as take-it-or-leave-it (TIOLI), closed ended questions or referendum) and payment cards.

The ***Open Ended (OE***) approach present respondents with direct questions, where individuals will be asked to state their maximum willingness to pay for the product (*Klose, 1999*).

In the ***dichotomous approach*** individuals are asked whether they would pay a specified amount for a given commodity, and responses vary between “Yes” and “No”. the bid amount is varied across respondents and the information obtained is whether the individual maximum WTP is above or below the bid amount (*Ryan et al., 2004*).

The ***Payment card technique*** present the individuals with a range of bids and asks them to circle the amount that represents the most they would be willing to pay (*Ryan et al., 2004; Klose 1999; Donaldson et al., 1997*).

It is argued that the ***dichotomous approach*** and the ***payment card approach*** mimic real life settings (*Donaldson et al., 1997*) unlike the ***open ended (OE)*** questions approach. According to various studies *(Donaldson et al., 1997; Ryan et al., 2004; Klose, 1999; Arow et al., 1993; Johansson et al., 1991)* the concern with the OE approach is with its face validity as it does not reflect the way individuals behave in a real market. In addition to that the approach has proven to mislead respondents as when they answer such questions they do not reveal their maximum willingness to pay *(Donaldson et al., 1997; Ryan et al., 2004).* Another problem associated with this method is that it produces a large number of non-responses since respondents may find such open questions difficult to answer (*O'Brien et al., 1996; Klose, 1999).*

d- Indirect methods comprises of tradeoffs individuals make between the consequence of the health intervention and the monetary value of this intervention in what is known as conjoint analysis that measures marginal rate of substitution between various attributes of a health care intervention and when entering the cost of the intervention indirect WTP could be derived (*Ryan et al., 1999*).

The first attempts to use conjoint analysis to measure consumer preferences were in market (*Wardman 1988*) and environmental economics (*Swallow et al 1992; Opaluch et al 1993*). Conjoint analysis was then used extensively in health economics in the past 15 years (*Ryan and Gerard 2003*) to measure various issues such as the factors important to patients in the provision of health care systems (*Ryan 1999*).

2.2. Cost Analysis:

This thesis has reviewed how consequences of heath programmes could be measured but in order also to perform a full economic evaluation cost analysis should be performed for each health intervention. To an economist the costs do not only include mere expenditures and out of the pocket money, rather it also includes the consumption of resources not necessarily priced in the markets such as patients' leisure time, any volunteer work, donations, etc. Accordingly, the main costs that should be considered in any health economic evaluations are (*Durmmond 2005*):

a- Costs arising from the use of resources within the health sector, such as medications, hospitals, personals working in health sector…etc.

b- Costs arising from resources use by patients and their families such as time spent by the patient and family when using certain health programme, private monetary contributions to the health care system and any expenditures also on transportations.

c- Costs arising from resources use in other sectors.

The consideration of any cost resources should stem from the perspective of the study whether it was done from a patients' perspective, health care system perspective or societal perspective as each perspective may include one cost but not the other.

In costs analysis it must be noted than when comparing two programmes, any common costs between the 2 programmes need not be calculated since they will not affect the choice of any programme.

2.2.1. Calculating costs:

In order to calculate costs one must measure the quantities of resources used and then assign the unit cost/price for each unit. The costs of resources are usually taken as market prices for such resources rather than opportunity costs of the resources used unless serious justifications were given to do otherwise (*Durmmond 2005*).

As mentioned earlier, costs could include non priced resources such as patients leisure time or volunteer work. Volunteer work is usually valued using market wage rates. However leisure time lost could be valued either zero, average earnings or average overtime earnings and the most common approach is to value it at zero in the base case then analyze the impact of other estimates in a sensitivity analysis.

2.2.2. Time frame used:

The time frame the costs extends usually are not an arguable issue, however, the choice of follow up period when calculating a disease specific or therapy specific cost should not bias one intervention over the other as such costs could have a life time span even though the researcher could discount such future costs

2.3. Thalassemia

Thalassemia minor (also known as Thalassemia trait) occurs when a person inherits one thalassemia gene from one of the parents and a normal hemoglobin gene from the other parent. If one parent has thalassemia trait and the other parent has the normal type of hemoglobin there is a 50% chance with each pregnancy that the baby will be born with thalassemia trait. A person with thalassemia trait is usually healthy and might only have a mild anemia; consequently, most of those individuals are unaware that they have the disease (*University of Rochester Medical Centre 2006*).

Thalassemia Major, however, occurs when a person inherits two thalassemia genes, one from each parent. If both parents have thalassemia trait, there is a 25% chance with each pregnancy that the baby will have thalassemia major. The baby with thalassemia major appears normal at birth. At the end of the first year the following symptoms occur:1- appetite and energy diminish, 2- The skin becomes pale, 3- certain bones of the face may become prominent, and 4- growth is slower than normal (*University of Rochester Medical Centre 2006*).

Thalassemia intermedia, however, is somewhere between the minor state and the major state of thalassemia. Patients suffering from it could either be treated as major patients or as minor patients depending on the severity of the symptoms and it is most apparent between the siblings of the major patients (*Yaish, 2007*).

Thalassemia minor patients could survive with occasional or in certain cases, with no need for blood transfusion at all. However, patients suffering thalassemia major needs regular blood transfusions to guarantee regular replacement of non functional red blood cells (RBC) that are necessary to maintain vital metabolic activities, and hence, keeping the individual alive. Given that no natural mechanism is available to eliminate the excess iron resulting from repeated transfusions, the iron cumulates in different tissues of the human body resulting in a condition known as “ iron overload” (*Hershko 2005*). Iron excess is known to be toxic to several body tissues and organs, especially, the liver and the heart. Moreover, if left unmanaged, the iron overload would ultimately result in patients’ early death from organ failure (*Hershko 2005*).

2.4. Management of thalassemia

<u>Treating “iron overload”:</u>

Iron chelating therapy is the only method available for preventing early death caused mainly by myocardial and hepatic iron toxicity as results of iron overload (*Hershko 2002*). There are three medications for iron chelating and they are:

1- Desferrioxamine (DFO): Desferal®
2- Deferiprone (L1): Ferriprox®
3- Deferasirox (ICL 670/ DFX): Exjade®

Desferrioxamine:

DFO is a hexadentate chelator with a very high and selective affinity for iron. One molecule of desferrioxamine binds one atom of iron forming a stable complex that can be excreted via the bile or in the urine (*Hershko 2005*). It must be noted that DFO has been in widespread clinical use for more than 35 years. Many clinical trials established the efficacy of DFO in reducing morbidity and mortality related to iron toxicity in thalassemia patients (*Borgna, Pignati et al. 1998; Hershko et al. 2004; Olivieri et al. 1997; Olivieri et al 1994*). However the drawback of such management strategy consists of its invasive character, where a needle attached to a small battery- operated infusion pump, is worn under the skin overlying the stomach or legs 5 to 7 times a week for up to 12 hours in each administration (*Olivieri et al 1994*).

Deferoxamine is known to be efficacious in preventing and treating iron overload when applied in expert centers; however, adherence with the treatment from the side of the patients is a major issue and can significantly limit its effectiveness in real life setting (*Poter 2005*).

Therefore, the last two decades witnessed the introduction of new therapies worldwide in the form of ‘Oral Iron Chelators’. The latter are used to help patients get rid of excess iron in a more convenient manner (*Porter 2005* and *Hershko 2005*). Oral Iron Chelators are proven to limit further the mortality and morbidity associated with the thalassemia condition (*Piaga et al. 2003* and *Cohen et al. 2003*), due to a better adherence to the treatment strategy from the side of the patients (*Al Refaie et al. 1992* and *Neufeld 2006*). This shall also culminate in an enhanced 'Quality of Life' of the patients undergoing the treatment (*Abetz el al. 2006*).

Deferiprone:

Deferiprone (L1, 1, 2-dimethyl-3- hydroxypyrid-4-one) has been available for approximately 20 years and has been approved in some countries as a second line treatment for patients who are unable to receive DFO or whose response to DFO treatment is unsatisfactory. Deferiprone is a bidentate, orally active chelator. It has a high rate of intestinal absorption and all the chelated iron is excreted in the urine (*Hider et al. 1990*). It has less efficient binding profile than desferrioxamine, with 3 molecules of deferiprone required to bind one atom of iron (*Hershko 2005*).

A Meta analysis (*Addis et al 1999*) of the main deferiprone clinical trials conducted between 1989 and 1999 concluded that this drug, at a dose of at least 75 mg/kg/day, is clinically effective in inducing a negative iron balance and reducing the body iron burden in most patients with marked iron overload.

The most common reported side effects associated with the use of this drug are:

1- Agranulocytosis (less than a 1% occurrence).

2- A decrease in zinc levels.

3- Mild nausea.

4- Mild musculoskeletal symptoms (*Al Refaie et al. 1992*).

Deferasirox:

ICL 670 is a new oral iron chelator developed specifically for the treatment of chronic iron overload. It is an N- substituted bis- hydroxyphemyl- triazole (*Hershko 2005*). ICL 670 is a tridenate iron (FE +3) chelator, requiring two molecules to form a stable complex with each iron atom. The plasma half life of ICL 670 (11-19 hours) is suitable for one daily oral dosing (*Galanello et al. 2003*).

Early clinical studies indicate that ICL 670 effectively controls iron levels and that a dose of 20 mg/kg/day of it affords equivalent efficacy to DFO 40 mg/kg/day (*Galanello et al. 2003*). It must be noted that the first study in humans was conducted in Italy (*Galanello et al. 2003*) in 25 transfusion dependant thalassemic patients, receiving single oral doses of ICL 670, ranging from 2.5 to 80 mg/kg. A short term evaluation of this trial showed that the incidence of adverse events was low, even in the group of patients treated with the highest dose of drug (80 mg/kg). Its ability to mobilize and promote excretion of tissue iron and its good safety profile, as emerged from the first preclinical and clinical studies, make this drug the most attractive new iron chelating therapy (*Franchis 2004*), in terms of its effectiveness and impact on quality of life.

Below is a table summarizing the properties of each of the above mentioned iron chelating agents (*Hershko 2005*):

Table 1: Properties of iron chelators

Feature	**DFO**	**L1**	**DFX**
Iron binding efficiency (drug: iron)	1:1	3:1	2:1
Iron selectivity	Highly selective	Zinc deficiency	Highly selective
Regimen	Sc or iv infusion	Oral: 3x/day	Oral: 1x/day
Tolerability issues	Local reaction problematic	Joint problems	Skin rashes
Acceptable long term safety profile	Yes	Severe Neutropenia and Agranulocytosis	Unproven

It must be noted that aside from transfusions with iron chelation, there is bone marrow transplantation which has proved to be the ultimate treatment regimen worldwide as it eliminates the disease and the patient can survive free from it. However this management strategy has proven to be expensive and unaffordable to many patients. A study by Lucarelli et al have shown that patients who are adequately treated with iron chelation, do not have irreversible liver disease and have HLA identical related donor have a greater than 90% chance of survival with engraftment of the donor marrow three years after transplantation. However, less than 20% of patients with thalassemia meet this criterion (*Lucarelli et al. 1993*).

Efficiency of the various Iron chelators:

It must be noted that the liver is capable of storing large amount of iron reaching about 70% of total body iron stores (about 20 g). Any other extra iron in the body is deposited in the liver, or other tissues if the liver is full (*Eleftheriou 2003*). Consequently, iron stored in the liver or other tissues binds to the proteins ferritin and haemosiderin (in the same manner as the blood binds to the carrier protein transferring). A small amount of ferritin escapes from the liver into the blood stream, thus a measure of the level of ferritin in the blood is used to determine iron load.

Normal levels of ferritin in the blood (or serum ferritin) are up to 250µg/l for men, and between 10-120 µg/l for women. 1µg of ferritin in the blood is considered to correspond to 8 mg of iron in the body's stores. Patients with thalassemia major with considerably high levels of iron in the body are thus expected to have significantly higher ferritin levels (*Eleftheriou 2003*).

Although ferritin levels may be a reliable indicator of liver iron stores they are, however, less accurate in predicting iron load in other organs, such as the heart, or overall body iron load. In addition, other factors such as inflammation, viral or bacterial infections, chronic liver diseases, arthritis and vitamin C deficiency may affect serum ferritin levels, indicating higher or lower iron stores than are actually present (*Eleftheriou 2003; Olivieri et al. 1997*).

Nonetheless, serum ferritin levels are considered the most practical indicator of possible iron related complications, as it is the most accessible and inexpensive tool for long term monitoring of chelating efficiency (*Hershko 2002*), compared to other procedures such as liver biopsy, computed tomography or magnetic susceptibility (SQUID) (*Hershko 2002*).

Consequently, some studies have proved that where ferritin levels are consistently below 2500µg/l over many years, a patient risk of developing heart complications is low (*Eleftheriou 2003; Hershko 2002; Oliveiri et al. 1997)*, these studies have estimated a 91% cardiac disease free survival after 15 years compared with only less than 20% cardiac disease free survival after the same period otherwise. A recent study has also suggested that the combination of liver iron less than 7 mg/g dry weight and serum ferritin levels less than 1500µg/l is needed to predict for survival free of cardiac disease (*Hershko 2002).*

The aim should therefore be to keep serum ferritin levels between 1000-2000 µg/l, and to check levels at least every three months in order to establish whether the patient iron chelating regime needs any adjustments.

Compliance:

According to various studies on Deferoxamine the average compliance rates ranged between 77% and 64% (*Arboretti et al 2001*; *Boturao et al 2002*; *Beratis et al 1989*; *Richardson et al 1993*) and the lower rate is to be chosen since physicians tend to overestimate compliance rates among their patients (*Gabutti et al 1996*; *Delea et al 2007*).

Regarding L1 compliance rates, a study conducted in Italy have showed an increased compliance rate by 11.4% from baseline (i.e. from 88% to 98%) thus the compliance rate for L1 would be 71% (64%* 1.114) where 54 thalassemia patients using the three- times daily oral chelator (L1) and 51 thalassemia patients using deferoaxamine were observed for 24 months (*Fischer et al 2003*). The compliance with deferoxamine however has dropped by 4.3% from baseline (from 94% to 90%).

On the other hand, there was no published literature on the compliance rate of deferasirox since it’s a new medication, however, the compliance rate for this once daily oral chelator was calculated by Delea et al where they estimated that deferasirox would have an even greater compliance rate than L1 as it is a once daily oral chelators improving it by 16% (11.4% vs -4.3%) versus deferoxamine. Accordingly, compliance with deferasirox was estimated at 74% (64%* 1.16).

2.5. Economic Evaluation of iron chelating management

Up to our knowledge, there has been no attempt internationally to conduct a full economic evaluation of iron chelation therapies and management strategies, rather the studies were partial evaluation of the effectiveness of the medications in reducing iron overload in the body as has been shown previously.

3. **Methodology**

The study will be an exploratory, as well as, a descriptive and analytical one. Exploratory: since it represents the first attempt to be undertaken to evaluate the economic impact of different iron-chelation therapies in the specific context of the West Bank. Descriptive: since it will review and describe the characteristics of each of the different management strategies in terms of its cost and consequences (Efficacy, Effectiveness, and Quality of Life consequences). Predictive: since it will examine the cost-effectiveness, cost-utility and cost benefit of each of the management strategies to attain conclusions with regard to the most medically and economically efficient option to be adopted by the policy-makers in the area.

The study relies on cross-sectional data, to be compiled through structured and unstructured interviews and questionnaire administration throughout the Master Thesis work with both health system providers and patients.

3.1. Sampling

The study sample was selected from the thalassemia population in the West Bank that are registered in the Thalassemia Patients Friends Association and had 412 patients registered for 2007. The registered patients were minor, intermediate and major thalassemias along with sickle cell patients as they also need blood transfusion therefore requiring iron chelation therapies. The Patients were distributed among various West Bank localities; Ramallah, Jenin, Nablus, Hebron, Tulkarem, Qalqilya and Jericho. For our study, minor thalassemic patients were eliminated as they do not require iron chelation therapies. A proportional stratified sampling was carried out according to locality, sex and age. Such a sample method was used to better represent the stratum in the thalassemia population, as it is believed that patients in different age groups and different localities and gender would be affected differently and possess different characters that would affect the results of the study. The unit of analysis was the patient her/himself.

3.2. Theoretical framework

Three analytical approaches shall be used to assess the costs and consequences associated with each of the treatment strategies;

3.2.1. CEA

A cost effectiveness analysis will be conducted. Here, the comparison between the different medications will be in terms of incremental cost effectiveness ratio (ICER), and the effect to be considered is the intermediate outcome of reduced iron in the body, which will be measured through serum ferritin levels. As it was proved in the literature that reducing iron in the body is a life saver in thalassemia patients and contribute to the patients’ quality of life. This intermediate outcome will then be combined with the levels of compliance associated with each medication that have been proved in the literature as such compliance rates vary considerably among the three medications thus affecting the effectiveness of each.

In order to compute the ICER, the average costs of both oral chelators will be deducted from the average cost of DFO, and this incremental cost will be divided by the difference in the effectiveness of the oral chelators and DFO (incremental effectiveness). The ICER will be calculated for the three perspectives (MOH, patient and society) and the ratio will be compared with an international threshold adopted by various health ministries worldwide.

3.2.2. CUA

Such analysis will be used to incorporate the ‘Quality of Life’ of the patients under the different medications, to convert the descriptive quality of life information to a utility or a preference-based measure by mapping health states from a specific medication onto an established preference weighted classification. The QoL scores shall be obtained from Ratip et el questionnaire, where utility has to be measured for thalassemia patients in the current status as they are using Desferal and to measure the utility when using oral chelators. To perform this, quality of life (QoL) score is to be calculated to reflect the preferences of thalassemic patients for the various iron chelators.

However such questionnaire was developed in an international context and did not take into account some countries’ specificities such as occupation, oppression, religion or any other aspect that may affect the QoL of the thalassemia patient. Thus, and in order to validate this questionnaire into the Palestinian context, a focus group discussion (FGD) was administered to explore and identify any specificities that may affect the QoL for thalassemia patients in Palestine.

In order to compute the ICUR, the average costs of both oral chelators will be deducted from the average cost of DFO, and this incremental cost will be divided by the difference in the QALYs of the oral chelators and DFO (incremental utility), where the latter is calculated by multiplying the QoL scores obtained by the average life years a thalassemia patient lives and which averages around 15 years according to TPFA records and statistics. The ICUR will be calculated for the two perspectives (patient and society) and the ratio will be compared with an international threshold adopted by various health ministries worldwide.

The hypothesis to be tested regarding QoL measures would entail the following:

- Low QoL parameter for thalassemic patients in the Palestinian context.
- Females are expected to have lower QoL parameter than males.
- As both education and income levels increase, the QoL parameter would be enhanced.

A. Focus Group Discussion:

FGD is a form of group interview that explicitly uses individual interaction, and capitalizes on communication between research participants, in order to generate data (*Kitzinger et al. 1995*). It must be noted that FGD has proved to be efficacious in elaborating QoL instruments in various settings and contexts (*Giacaman et el. 2007*).

One FGD was completed in Ramallah, with 10 participants (7 females and 3 males), with ages ranging from 7 years to 28 years.

The participants covered different localities (Ramallah, Jenin and Tulkarem), as well as represented different socio economic backgrounds.

After representing in front of them the purpose of this FGD, they were asked to identify what does QoL means to them in general, then they were presented with the determinants of Ratip et al. questionnaire and were asked to identify any new determinants that they think determines their QoL as a thalassemia patient in Palestine (see appendix 1 for the FGD Script).

The qualitative data that was gathered was read repeatedly in order to reveal certain patterns and themes. The themes were then scheduled in a table and all the relative responses were clustered accordingly (*Giacaman et el. 2007; Krueger at el. 2000*).

B. QoL score calculation:

As mentioned above, Ratip et al. has developed a method for measuring the clinical and psychosocial burden of thalassemia. As Tefler explained the questionnaire process in his paper in 2005 "*The clinical instrument includes parameters of clinical burden (eg. Transfusion, cardiac problems…etc.) that are each scored on the basis of definitions of severity (0= unaffected, 1= mild, 2= moderate, 3= severe). Clinical parameters are weighted (eg. Cardiac scoring is multiplied by 4, transfusion and Desferal by 3 and growth deformities by 2) and can be assessed from patients' notes or in collaboration with the clinician in charge.*

It is worth mentioning that the weights were decided by 2 physicians Dr. Modell and Dr. Wonke (see appendix 4) who worked closely with thalassemia patients. This kind of scoring is considered reliable and it could be used in the local context as the physicians have the ability to assess these clinical burdens and their effects on mortality and weigh them accordingly (*Tefler et al*, *2005*).

The QoL scores were obtained from various questions that tackled the psychosocial aspects in patients' lives, these scores were then scaled from 0-3 were 0 represented normal life and 3 represented severe QoL. The same applied for the questions that were inserted from the FGD. The scores of each were then added (summed) together to give us a unique QoL score for each patient. This has been done by summing the parameters of QoL defined by Ratip et al questionnaire first, and then summing up the parameters obtained by the FGD.

In addition to that scores have been validated to account for the differences between medications, were the clinical burden varied between Desferal and the oral medications, in addition to that, certain side effects associated with Desferal were not accounted for when calculating the QoL scores for the oral medications. Thus we obtained 2 different kinds of QoL scores, one for Desferal and the other for the oral medications.

3.2.3. CBA

Cost benefit analysis (CBA) is usually favored among other valuation techniques as both the cost and the health outcomes take monetary terms.

To conduct such analysis both the direct and indirect methods are used to measure WTP. The WTP will be considered the Benefits from the patients' perspective, and a net social benefit would be calculated by deducting the Benefits (WTP estimated directly and indirectly) from the costs associated with the DFO and oral chelators. The hypothesis being tested would be:

- Patients would be willing to pay the highest amount in order to reduce iron levels in their bodies.
- As income increases patients willingness to pay will also increase.

1. Conjoint Analysis:

In this study we attempt to reflect patients' preferences to iron chelation therapies and whether a certain attribute of the medication is important relative to other attributes (i.e. if a patient would prefer practicing normal life to reducing iron!). In addition to that and since deferasirox or L1 (oral chelators) are not yet introduced in the Palestinian market we wanted to elicit patients' WTP indirectly for the oral medications thus acquiring the knowledge if patients would be willing to contribute in the cost of their medications since the MOH is refusing to acquire oral chelators due to their high costs.

1.1. How CA is conducted:

In a general conjoint analysis study respondents would be faced by various hypothetical scenarios, such that each involve different levels of attributes that have been identified as important and critical to that good or service being measured. Accordingly, the respondents are asked to rate, rank or make pair wise choices among the various scenarios.

Rating and ranking methods are largely used in market research, however, many researchers prefer to use the pair wise comparison method derived from the random utility theory that was developed in transport economics (*McFadden 1973; Ryan 1999).* It is argued that individuals are usually engaged in doing choices in their daily basis rather than carrying out ranking or rating methods to choose among various issues. Thus this study will use the choice approach depending on that argument.

The decision making process with the pair wise choices involves a comparison of indirect utility functions. Thus in the each scenario the individual is assumed to be choosing the alternative that leads to the higher level of utility. Thus a respondent will choose intervention B over A if:

$U\ (Ab, Y, Z^1) > U\ (Aa, Y, Z)$

U(.) represents the individuals' indirect utility function, Ab are the attributes of health care intervention B, Aa are the attributes of health care intervention A, Y is the individuals' income and Z represents the socioeconomic characteristics of the individual that influences their utility.

However, while the individual knows the nature of their utility function, the researcher has no such knowledge and thus this introduces the concept of random utility, were an error term is included in the utility function that reflects the unobservable factors in the individuals' utility function.

Consequently, the individual will choose B over A if:

$V\ (Ab, Y, Z) + \varepsilon b > V\ (Aa, Y, Z) + \varepsilon a.$

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[1] The attributes include the price of the commodity (price of the medication)

Where V (.) is the measurable component of utility estimated empirically, and εj (j= A, B) reflects the unobservable factors in the individuals' utility function.

1.1.1. Establishing attributes:

In our study 6 attributes were identified as significant predictors of utility for using iron chelation therapies and specifically for using infusion chelating therapy Deferoxamine or the oral chelators therapies L1 and Deferasirox. The attributes were: reducing iron, ease of administration, side effects from using the medications, costs per month, the ability to practice life normally and the existence of pain when the medications are taken (see table 2).

1.1.2. Levels of attributes:

In defining the levels of each attribute, the levels were sought to be realistic and that the individual would be willing and able to trade off between them (*Ryan, 1999*)

The cost of the medications represented the maximum and the minimum of medication prices in the market in 2007-2008. Table 2 summarizes the attributes and the levels of the medications.

Table 2: Attributes and levels included in the CA study

Attribute	Level
Reduces iron	Moderately, effectively
Ease of administration	Not easy/ easy
Side effects	Severe/ mild
Cost per month (NIS)	0, 1000, 1500, 2000, 2500
Ability to practice life normally	No, yes
Extent of pain while taking the medication	A lot of pain, mild pain, no pain

Each attribute had the following regression code:

Table 3: Regression codes for attributes and their levels

Attribute	Regression code	
Iron	0	reduce iron moderately
	1	reduce iron effectively
Admin	0	not easily administered
	1	easily administered
Comp	0	a lot of complications
	1	few complications
Life	0	cannot practice life normally
	1	could practice life normally
Pain	0	a lot of pain

	1 mild pain 2 no pain at all
Cost in NIS/ month	0 500 1000 1500 2000 2500

1.1.3. Generating the scenarios:

The attributes and levels presented above give rise to 280 possible scenarios (2^4 * 3^1 * 5^1). SPSS orthoplan procedure was used to reduce the number of scenarios whilst still being able to infer utilities for all possible scenarios (*Ryan 1999; SPSS ver.15).* The technique resulted in an orthogonal main effects design and gave 25 plus 4 holdout cases. From the 29 scenarios, 50% were selected randomly, giving us 18 scenarios, these were then split randomly to two groups each containing 9 scenarios. From these 9 scenarios, one was randomly selected and then all the other 8 were compared to it giving us 8 pair wise choices (see table 4 and Fig.1).

Figure One: Example of a pairwise choice experiment in CA questionnaire

Scenario One:

Characteristics	Medication A	Medication B
Reduces iron	Moderately	Moderately
Easily administered	Not easy	Easy
Side effects of the medication	Little/ mild	A lot/ severe
The costs per month (NIS)	2,000	1,000
The ability to have a normal life	Yes	Yes
Pain during administration	To a large extent	No pain

Which medication do you prefer?	**I prefer Med. A**	**I prefer Med. B**
(Tick the box)	☐	☐

Table 4: Differences between the choices: Medication B- Medication A

Choice	Reduces iron	Easily administered	complications	Cost	Ability to practice normal life	Pain Existence
1	0	1	-1	-1,000	0	2
2	1	1	-1	-2,000	-1	0
3[1]	1	0	0	-1,000	0	2
4	0	0	0	0	-1	2
5	0	0	0	-2,000	-1	1
6	0	0	0	-500	-1	1
7	0	1	-1	500	-1	1
8	1	0	-1	0	-1	1

[1] scenarios used to check for internal consistency.

1.1.4. Model used for Data Analysis:

The data obtained from these scenarios is to be analyzed using random effects probit model; a Random model was used since the data included a number of observations from the same individual (*Kennedy 2001*) and a probit model was used since the dependent variable was binary in form taking 1 and 0 values for choosing medication A and B respectively, thus using OLS (Ordinary Least Square regression) method would have resulted in heteroscedastic residuals yielding inefficient estimates (*Ramanathan*, *2002*).

The function to be estimated is:

$$\Delta V = \alpha c + \alpha 1 \text{ iron} + \alpha 2 \text{ admin} + \alpha 3 \text{ sideeffects} + \alpha 4 \text{ cost} + \alpha 5 \text{ life} + \alpha 6 \text{ pain} + e + u.$$

ΔV is the change in utility in moving from medication A to medication B, iron is the difference in iron reduced when moving from A to B, admin is the difference in the administration, side-effects is the difference between side effects, cost is the difference between costs, life is the difference of having a normal life and pain is the difference of pain during administration. The unobservable error terms are represented by e and u, where e is the error term due to differences amongst observations and u is the error term due to differences amongst respondents (*Ryan and Hughes 1997; Ryan 1999*), these error terms are present when using the random effects model.

The relative size of the coefficients for each attribute is interpreted as the propensity to choose a scenario with a specific attribute in it, the higher the positive coefficient, the more likely the individual will choose the scenario with the attribute in it (*Douglas et al 2005*). The ratio of the parameters represent the MRS with $\alpha j/\alpha 4$ (where j= 1, 2, 3, 4, 5, 6) being an estimate of WTP for levels of the individual attributes (*Ryan 1999*).

2. Contingent Valuation:

This paper has attempted to use OE questions sine we have used conjoint analysis to elicit WTP for thalassemia patients indirectly for oral chelators and thus our aim was to compare this measure with the indirect approach and we used OE questions for their ease of administration, and the little time required by the respondents to answer such questions so they would not feel boredom answering a long questionnaire as shown in the coming section.

In the questionnaire two open ended questions were asked:

1. Would you be willing to pay more to receive oral iron chelators?
2. How much would you be willing to pay per month?

A tobit model will be used to analyze the effects of socio economic variables on willingness to pay. This model is part of a limited dependent variable models. This model was used due to the nature of the dependent variable as it contained many zeros thus we have what is called censored data i.e. the dependent variable takes zero but the independent variables are known (*Kennedy, 2001*).

3.2.4. Cost analysis

The cost items for thalassemia patients were compiled through various interviews with the TPFA, physicians and medical labs. The cost items for the thalassemia major patients varies under the three different iron chelators due to differences in the medication costs and the requirement of certain examinations that must be done more periodically such as the liver function test and the kidney function test for the oral iron chelators. It is worth mentioning however that similar annual costs between the three medications were eliminated due the interest in incremental values between the three medications rather than the gross aggregated values for each medication.

Accordingly, the cost section will be divided to three parts:

1- Drug costs.
2- Administration costs.
3- Examinations needed to verify the effectiveness of the iron chelators in reducing body iron and their side effects.

The costs were calculated using three age categories since each age require different examinations and follow-ups:

1. Pediatric patients that are under 4 years old, where various heart tests, sexual and growth hormones examinations are not performed.
2. Pediatric patients between the ages of 4 and 12, as they start visiting a pediatric cardiologist every six months, and they need to perform the growth hormone examinations every year
3. Patients above 12 years old whom they need the various sexual hormones examination every six months.

In order to calculate the total costs of chelating therapies for the above three categories, the perspective of the cost must be specified, thus the paper aimed to calculate the costs from the perspective of the MOH, the Patient and the society as a whole and in the latter indirect costs shall be added such as the time spent by patient or family members of the patient to reach the labs and the working capital consumed in the process.

3.2.5. Questionnaire

The questionnaire consisted of 6 parts; the first was the patients' socio economic characteristics section as it consisted of name, sex, age, level of education, level of household income, residency and type of disease (intermediate, major and sickle cell). The second and the third part were Ratip et al questionnaire that were discussed earlier as he developed a method of measuring the clinical and psychosocial burden of thalassemias.

The fourth part contained the themes that were developed from the focus group that was administered on QoL. The questions included asked about social support, financial situation, occupation, mechanism of treatment in Palestine and personal believes and they were graded on a scale of 1-5 (1= never, 2= sometimes. 3= occasionally, 4= a lot, 5= always).

The fifth part consisted of 8 scenarios (see appendix 2), each scenario consisting of 2 choices of medications (A and B) and both having different attributes in order to elicit willingness to pay indirectly.

The last part consisted of a two direct willingness to pay questions; the first asked if they are willing to pay more to get an oral medication, and the second asked them to explicitly reveal how much they are willing to pay per month.

4. **Results**

4.1. Qualitative results

4.1.1. FGD

From the FGD it was found that the constituents of Ratip et al. were all agreed upon. For example when talking about the treatment mechanism many patients revealed their discomfort with the nightly subcutaneous infusions as patients expressed:

“I live a happy life, the needle is the only bad thing that I have to encounter, thus the most important thing is to get rid of the needle then I will feel more energetic, everything will be available to me and everything in my life will change”

“I wear the needle in the night; I can’t play in the school”

Another example on how Ratip et el components were agreed upon was on the dimension of feeling different:

“I am normal, I only remember that I’m ill when I go to get blood transfusions and the society makes me feel ill”

“Parents all the time tell me that you are ill, don’t tire yourself. This is a negative thing that affects my life.”

Regarding appearance, it was clear that females associated with this determinant more strongly than males and was considered the most important aspect that affects their QoL:

“My appearance is the most important thing in my life; I am always on the mirror. And thanks God that I don’t suffer from any facial deformities.”

“I care a lot for my appearance especially when my face gets yellowish, *my appearance affects my life and my daily follow ups of my normal life”*

“I don’t like my face getting darker in color; I love to be like my classmates who are white and beautiful”

However, when discussing the themes of Ratip et al. many other themes revealed that seemed specific for the Palestinian patient and that the international context did not cover. These were:

1- Support and Psychological assistance
2- Mechanism of treatment
3- Financial situation
4- Occupation
5- Lack of confidence in the medical body
6- Personal believes

Regarding the **Support and Psychological assistance** some patients reflected on how lack of support from their community affected them negatively and increased their feeling of isolation:

“People have to support the patient. I feel that I can accomplish anything in my life with a strong will”

“During work I had to get blood transfusion and the manager refused to let me go to the hospital. I saw this as a very negative thing that affected my life”

“Parents play a major role also in the patient’s life; they must explain to their child what to expect in the future so as not to get surprised. They must tell him/her about the nature of his/her life, about the iron accumulation and its side effects thus psychological preparation is very important”

“A female nurse (Shahinaz) relieved us from the needles pain”

“She (the nurse) encourages us to take the treatment; she explains it to us too”

“I want to thank my nurse Shahinaz, she talks to us more than our parents, she’s’ always telling us that we shouldn’t care that we are ill. She helps us not to feel different”

Many patients expressed their frustration with the **treatment mechanism** as Ratip et al has showed but what was different in the Palestinian context was not only the frequent visits to the hospitals or blood transfusions, rather many patients reported their worries on the blood quality they received and the long hours they had to wait for the blood transfusion to complete, also many expressed their fears from the side effects that they encounter from needles infusions:

"if they get us new blood I will feel more secure about myself, and I will be more encouraged to get Desferal"

"treatment would be okay for me, but the pain that is associated with taking the Desferal and the old blood that we receive is a concern to me, when we receive old blood we have to sit for 2 and a half hours getting the transfusion since it clots due to this fact. Thus we are getting old blood, iron and above all the Desferal needle. I believe that thalassemia patients must receive new blood."

"When receiving old blood I suffer from fast heartbeats. In addition to that, if the blood was old this means that I have to get blood transfusion every week, however we are aiming to get high blood concentrations but receiving old blood won't fulfill this target."

"I get bored when I receive blood"

Also many patients pointed out that the kind of needle that they use increases their pain:

‘’ the needle of blood transfusion won’t enter from the first time and this can affect my ability to write thus affecting my studying”

“I hate treatment I hate doctors and hospitals, everything related to the treatment I hate it.”

From the discussions it was showed that **occupation** had an effect on patients’ QoL as well as it had effects on the **financial status** of the patients’ families thus affecting more their QoL:

“The situation that we live in (the occupation) affects us negatively. The closures affect the person as he/she feels suffocated and that his/her life would end”

“The occupation affects my life, as I get blood transfusions in Ramallah and I am from Tulkarem, thus the sudden curfews could prohibit me from reaching the hospital, continuously affecting my life”

“Occupation affected my family resources due to closures; this in turn had affected my ability to get treatment”

“My father is a teacher, and when the political situation deteriorated and they went into strike our financial resources were affected and thus I couldn’t get my treatment.”

Interesting views were made concerning the **Palestinian medical body** as some patients expressed their frustrations from their physicians and hospital departments and others were impressed by the medical procedures concerning thalassemias outside Palestine:

“ there are many medical treatments that are not found in the West Bank but are available in Israel, I once suffered from internal bleeding inside my leg, in the West Bank they didn’t know what to do, but in Israel I made several tests and they treated me and stopped the bleeding”

“In Ramallah there is a big problem, even that we are a strategic location, but we don’t have units, it’s like we are living in the 90’s”

“when I was in Greece, I didn’t want to return, the needles the use don’t cause pain or irritations, the thalassemia department is fresh and they have special features for the kids that allows them to have fun”

“When I used to go to the pediatrics department no one took care of us”

From the discussions it was deducted that many patients relied on their personal believes to support them through any difficulties, many had built defense mechanism either through convincing themselves that they are normal and that all will be fine, or by resorting to God and that He is the one who could cure them.

Thus from the above discussion, each theme was tested for by a set of questions in the QoL questionnaire. These questions were placed after Ratip et al questions so as not to bias the instrument. The added questions took the label of PQOL (see appendix 2), and the following table outlines each theme and the corresponding questions for each:

Table 5: New themes and corresponding questions

Theme	Questions corresponding
Support and Psychological assistance	PQOL1, PQOL2, PQOL3
Mechanism of Treatment	PQOL4, PQOL16, PQOL 18, PQOL 19
Financial Situation	PQOL5, PQOL6 PQOL17
Occupation	PQOL7, PQOL8, PQOL9, PQOL10
Lack of confidence in the medical body	PQOL11, PQOL12, PQOL15
Personal believes	PQOL13, PQOL14

4.2. Quantitative results

4.2.1. Cost results

First: Drug Costs:

Table 6: Drug costs per patient per year in NIS

Main Cost Items	cost/daily use	Total Cost
DFO	31.2	11,232
L1	90	32,400
DFX	99	35,640

Source: Ministry of Health

Table 6 outlines the different iron chelation drug costs, and it can be seen that DFO is the cheapest among the 2 other drugs. It is worth mentioning that each drug daily cost has been calculated based on the average dosage required by the patients, and the total costs represent the average yearly cost per patient.

Second: Administration costs:

Table 7: Administration costs per patient per year in NIS

Main Cost Items	cost/daily use	Frequency of Use for DFO/year	DFO total cost/year	Frequency of use for L1/ year	L1 total cost/year	Frequency of use for DFX/year	DFX total cost/year
Butterfly needles	0.714	360	**257.04**	0	**0**	0	**0**
Plasters	2.04	360	**734.4**	0	**0**	0	**0**
PUMP	0	0	**0**	0	**0**	0	**0**
Canola and infusion set		0	**0**	0	**0**	0	**0**

syringe and needles	0.1416	360	**50.976**	0	**0**	0	**0**
TOTAL			**1,042.4**		**0**		**0**

Source: Ministry of Health

Table 7 summarizes the administration costs of the iron chelation therapies, such as needles and plasters etc. And as shown such costs are only true for the DFO due to its administration mechanism delineated previously, while the oral chelators have no such administration costs.

Third: Examinations required:

Table 8: examinations required per patient per year in NIS[2]

Main Cost Items	**cost/daily use**	**Freqency of Use for DFO/year**	**DFO total cost/year**	**Frequency of use for L1/ year**	**L1 total cost/year**	**Frequency of use for DFX/year**	**DFX total cost/year**
CBC	3	12	**36**	12	**36**	12	**36**
Urine	1.31	12	**15.72**	12	**15.72**	12	**15.72**
Ferritin levels	13.5	2	**27**	12	**162**	12	**162**
TSI	0.479	2	**0.958**	12	**5.748**	12	**5.748**
TIBC	1.765	2	**3.53**	12	**21.18**	12	**21.18**
GPT	0.479	2	**0.958**	12	**5.748**	12	**5.748**
GOT	0.479	2	**0.958**	12	**5.748**	12	**5.748**
Billiruben	0.27	2	**0.54**	12	**3.24**	12	**3.24**
BUN	0.479	2	**0.958**	12	**5.748**	12	**5.748**
Kreatinine	0.299	2	**0.598**	12	**3.588**	12	**3.588**
Alk.Phos.	1.617	2	**3.234**	2	**3.234**	2	**3.234**

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[2] It should be noted that any similar repeated costs were not included in the cost calculations in each perspective.

Electrolytes	6.767	2	**13.534**	2	**13.534**	2	**13.534**
LH	12.75	2	**25.5**	2	**25.5**	2	**25.5**
FSH	12.75	2	**25.5**	2	**25.5**	2	**25.5**
E2	10.375	2	**20.75**	2	**20.75**	2	**20.75**
Testosterone	22.875	2	**45.75**	2	**45.75**	2	**45.75**
progesterone	17.25	2	**34.5**	2	**34.5**	2	**34.5**
growth hormones*	60	2	**120**	2	**120**	2	**120**
GB checkup	20.5	4	**82**	4	**82**	4	**82**
pediatric and hematologists*	20.5	4	**82**	4	**82**	4	**82**
pediatric cardiologist*	150	4	**600**	4	**600**	4	**600**
ECHO*	150	2	**300**	2	**300**	2	**300**
Cardiologist*	150	2	**300**	2	**300**	2	**300**
ECG*	100	2	**200**	2	**200**	2	**200**
MRI*	500	2	**1000**	2	**1000**	2	**1000**
Eye check*	80	2	**160**	1	**80**	1	**80**
Hear check*	120	2	**240**	1	**120**	1	**120**

Source: Ministry of Health 2008,* Examinations that MOH don’t provide and thus patients pay them directly out of their pockets

Table 8 summarizes the medical examinations costs required by the patients on a monthly or yearly basis. Such examinations and their frequencies are what each thalassemic patient should have, although Palestinian thalassemic patients may not undertake such examinations. The frequency of examinations differ from one medication to the other pertaining to the severity of the side effects associated with such medications, especially the oral ones, which is reflected by the higher annual costs for these oral chelators when compared to the DFO.

Total Costs according to the various perspectives:

According to the above tables, the direct cost in the ***perspective of the MOH*** that include the direct costs associated with the drug costs, administration costs and examination costs (that are not paid directly by the patient) is as follows:

Table 9: treatment cost for one year per patient in NIS from MOH perspective

Age Category	**Total cost per year for DFO**	**Total cost per year for DFX**	**Total cost per year for L1**
Age<4 years	12,310	35,853	32,613
4=<age<12	12,310	35,853	32,613
Age>=12	12,310	35,853	32,613

As can be seen from the MOH perspective all age categories share the same level of costs for each oral chelators.

From the ***patient perspective*** the total direct costs would include only the out of the pocket money spent on any private examination (highlighted by the star in schedule 8) along with any transportation costs to reach a laboratory or a hospital which is averaged around NIS 7.00/visit for those who take public transportations and live in the major cities, however for those who live in rural areas the transportations costs would average around NIS 60/visit[3]. i.e. the patient perspective include both direct medical and direct non medical costs.

Table 10: treatment cost for one year per patient from patient perspective

Age Category	**Total cost per year for DFO**	**Total cost per year for DFX**	**Total cost per year for L1**
Age<4 years			
Rural	120	720	720
Urban	14	84	84
4<age<12			
Rural	2,720	3,120	3,120
Urban	2,614	2,484	2,484
Age>12			
Rural	2,840	1,920	1,920
Urban	2,734	2,604	2,604

However, when calculating the ***societal perspective*** indirect costs should be added that involve time lost and working capital used in the laboratories from water, electricity and rents that are realized by the labs that perform the tests and neither patients nor MOH pay for them, in addition to adding the costs associated with both the MOH and the patient perspectives. The following table represents total costs (direct and indirect) that the society encounters:

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[3] It is assumed the times required to visit the labs to do the associated examinations would be twice a year per DFO patient and 12 times a year per oral chelator patient.

Table 11: cost items from societal perspective

Main Cost Items	**cost/daily use**	**Frequency of Use for DFO/year**	**DFO total cost/year**	**Frequency of use for L1/ year**	**L1 total cost/year**	**Frequency of use for DFX/year**	**DFX total cost/year**
DFO	31.2	0	**11,232**	0	**0**	0	**0**
L1	90	0	**0**	0	**32,400**	0	**0**
DFX	99	0	**0**	0	**0**	0	**35,640**
Butterfly needles	1.428	360	**514.08**	0	**0**	0	**0**
Plasters	4.08	360	**1468.8**	0	**0**	0	**0**
PUMP	0	0	**0**	0	**0**	0	**0**
Canola and infusion set	0	0	**0**	0	**0**	0	**0**
syringe and needles	0.2832	360	**101.952**	0	**0**	0	**0**
CBC	6	12	**72**	12	**72**	12	**72**
Urine	2.62	12	**31.44**	12	**31.44**	12	**31.44**
Ferritin levels	27	2	**54**	12	**324**	12	**324**
TSI	0.958	2	**1.916**	12	**11.496**	12	**11.496**
TIBC	3.53	2	**7.06**	12	**42.36**	12	**42.36**
GPT	0.958	2	**1.916**	12	**11.496**	12	**11.496**
GOT	0.958	2	**1.916**	12	**11.496**	12	**11.496**

Billiruben	0.54	2	**1.08**	12	**6.48**	12	**6.48**
BUN	0.958	2	**1.916**	12	**11.496**	12	**11.496**
Kreatinine	0.598	2	**1.196**	12	**7.176**	12	**7.176**
HRS spent by patients	2.56 HRS/visit	990.72	**7925.76**	12	**245.76**	12	**245.76**

*Source: Nabulsi, 2006

Table 11 summarizes the cost items included from the societal perspective, were it has included direct and non direct medical costs in addition to direct non medical costs, mainly represented by the time spent by patients to reach a treatment centre, in addition to the time spent in the treatment centre itself. This has been differentiated for the 3 medications, where the total cost column for each medication indicate the total cost per year per patient for each of the needed medications, examinations and direct non medical costs.

And according to the age categories of patients the societal costs are as follows:

Table 12: treatment cost for one year per patient from societal perspective

Age Category	**Total cost per year for DFO**	**Total cost per year for DFX**	**Total cost per year for L1**
< 4 YRS			
rural	21,434	37,032	33,792
urban	21,328	36,396	32,156
4< Age<12			
rural	21,834	37,232	33,992
urban	21,768	36,596	33,356
>12 YRS			
rural	21,834	37,232	33,992
urban	21,768	36,596	33,356

4.2.2. Effectiveness results:

To establish the effectiveness of a patients' treatment regime, the amount of iron stored in the liver and other body tissues must be estimated.

<u>Efficiency estimates:</u>

If we were to calculate the percentage of serum ferritin levels reduced by the various medications, then the following simple arithmetic percentage could be used:

Change in serum ferritin level = {(New level- Old level)/ Old level}*100%

This would yield a reduction rate of -62.7% for the three medications when using the old level as 4,000 μg/l and the new level as 1,500 μg/l.

As delineated in the literature, the three medications have proved to be efficient in reducing iron to the required levels when compliance rates reach high levels (*Delea et al. 2007*) (Hershko 2002), which implies that our economic evaluation would be a cost minimization rather than a cost effectiveness one. However, since compliance is considered a crucial part in reducing iron levels, it could be incorporated in our effectiveness analysis, thus varying the results between the medications.

Effectiveness rate:

The following table shows the effectiveness of each medication in reducing serum ferritin levels, their compliance rates and the calculated effectiveness:

Table 13: Effectiveness rate calculations

	DFO	**DFX**	**L1**
Efficiency measured by amount of serum ferritin levels reduced	62.5%	62.5%	62.5%
Compliance rate	64%	74%	71%
Effectiveness rate	40%	46.3%	44.4%

It is worth mentioning that when computing the percentage by which each medication reduces the iron levels in the body, we took the 4,000 µg/l as the highest level of ferritin levels that would be reduced to an average of 1,500 µg/l.

4.2.3. Descriptive results

To carry out the proportional stratified sampling, 44.5% were selected from each locality, males and females represented 55.2% and 44.8% respectively in each locality whereas 30% from each locality sample represented the population less than 14 years old. Thus the sample size total was 182 patients across the various localities.

It is worth mentioning that when distributing the sample lists on the field workers whom were nurses working in the hospitals, it was found that many patients were either dead, out of the country, in jail or could not be reached as they stopped coming to regular examinations. To tackle this, new sample lists had to be made by replacing these patients with others under the same categories however the problem reoccurred and thus the nurses were forced to interview patients not listed in the sample schedule in order to reach the required sample number for each locality regardless of the categories of the patients.

Fifty five percent of the respondents were males and 44.8% were females. The respondents were relatively young as 14% were below the age of 6 years and 49.4% were under the age of 14 years, thus the mean age of the sample was 15.9 years. Continuously, the age group between 30 years and 63 years were only 6.4% of the sample population and this is relevant since most thalassemic patients in Palestine die in an early age (15-20 years) due to iron overload.

Illiteracy constituted 6.4% of the sample population excluding the 6 years and below age category (since they did not enroll in school), 44.9% had completed elementary level, 25% completed secondary level, followed by 17.3% who completed high school. Only 1.9% received a diploma and 4.5% completed their bachelors' degree.

The household income per month was relatively low in the thalassemic families as 14.4% received a monthly salary between 0-500 NIS and the majority of the sample (74.6%) received a salary between 500-2000 NIS, whereas only 0.6% received more than 4000 NIS per month. It must be noted that the average wage in the West Bank is 1,600 NIS per month.

The sample contained three forms of diseases of which 63% were major thalassemia and 28.2% were intermediate thalassemic patients and only 8.8% sickle cell patients. And the patients were distributed as follows: Hebron 21.6%, Jenin 21.5%, Jericho 3.3%, Nablus 19.9%, Qalqylia 11.1%, Ramallah 8.3% and Tulkarem 14.4%.

4.2.4. QOL results

Results of Ratip et al. questionnaire for measuring the QoL for thalassemic patients are presented in Table 14, which outlines the QoL parameters identified by Ratip et al, and the percentage of patients moderately to severely affected from thalassemia in each parameter:

Table 14: descriptive statistics for QoL parameters

Parameter	**% of patients scoring moderately to severe effect on QoL**
Education	69
Absenteeism	29
Sports	48
Social life	18
Self image	59
Feelings of difference	31
Social integration	56
Denial	5
Feeling healthy	34
Stigmatization	39
Social isolation	44
Family adjustments	7
Anxiety	69

Education was the most affected by thalassemia as 69% scored moderate and severe effects. Most patients revealed an affected social integration due to thalassemia and about near half of the sample had problems with self image indicating that more psychological help is needed for the patients in the Palestinian community. Also around 70% of the sample suffered from Anxiety from the disease.

However, only 7% of the sample population revealed moderate to severe effects on family adjustments from thalassemia and 5% of the patients scored moderate to severe effects on the denial parameter.

The QoL score:

The clinical burden and the social aspects measured were added together to form the QoL score that ranged from (7-87.5) where the lower limit represented patients with a high QoL whereas the upper limit represented the worse QoL score, due to the nature of the questionnaire coding, where 0 referred to unaffected, while 3 represented severely affected. The scores were transformed into a 0-100 scale so as 0 would represent the worst QoL score and the 100 would indicate a normal person, and the mean result was 64.76 out of 100.

However when adding the new questions obtained from the FGD the mean score became slightly lower giving a score of 61 out of 100, and indicating a worsening of the patients QoL. This means that the added questions managed to capture some aspects that affected the QoL of Palestinian thalassemic patients that the international one failed to pinpoint them.

Following is a table with the newly added themes, and the percentage of patients scoring moderate to severe effects on their QoL:

Table 15: FGD themes and the % of patients' scorings

Themes	**% of patients scoring moderate to severe affects on QoL**
Lack of Support	75%
Unstable financial situation	66%
Occupation	51%
Mechanism of treatment	61%
Lack of confidence in the medical body	59%

To review how patients responded to the FGD developed questions, 75% reported that they did not receive the support they needed; however, 64% indicated that they would feel happy if they received such support compared to 36% who would feel unhappy if receiving such a support.

On another hand, the results were mixed on whether thalassemic patients thought about their financial status, as 33.1% reported negatively while only

16% thought about their financial status frequently, which does contrast with the income results that we obtained from the patients indicating their unwillingness to reveal their true monthly income.

30% reported that occupation affected their ability to reach their medical centers moderately or severely and continuously, 70% felt anger/ frustration due to that fact. In addition to that 54.7% of the sample expressed moderate/severe worries of the unavailability of medications and 52% indicated that this made them feel insecure about their lives.

Only 29.8% felt unhappy going to the treatment centre while 70% reported that they are okay with that. Accordingly, 43.1% believed in the medical body in Palestine as they didn’t prefer to be thalasemic patients in any other country compared to 40% that preferred to be patients outside Palestine. However, 71% had no trust in their physicians and only 8.2% had complete trust in them.

Sixty seven percent had no trust in the treatment mechanism of Desferal compared to 11% who had complete trust and believe in the Desferal, in addition to that 34% reported that the Desferal mechanism affected their social life moderately or severely compared to 35% who believed that it did not have any kind of effect. Almost 96% had not enough financial resources to receive the treatment for chelating iron and 88% believed that the treatment mechanism should change compared to 7% who believed it should not change at all.

78% of the patients derived support from their personal believes especially in God and that all is in his hands, however 41% felt that their lives had no meaning and empty compared to only 19% that reported their content about their lives.

Socioeconomic characteristics and QoL scores:

When analyzing the effects of the socioeconomic characteristics of the patients on their QoL score it was found that the sex of the patient was insignificant and did not affect the QoL score. All other indicators; age, education, household income and kind of disease have impact on the QoL scores as the following table 16 shows:

Table 16: QOL affected by various variables

Coefficient		**S.E.**
Constant	53.549*	8.014
Age	0.643*	0.160
Sex	0.606**	2.598
Level of education	-3.242*	1.229
Household monthly income	-3.008*	0.962
Kind of disease	9.447*	2.321
R^2	0.256	
Adj-R^2	0.231	
F-statistic	10.33*	

*significant at the 1% level, **not significant

The coefficients with a positive sign indicate that as the parameter increases, the QoL score increases indicating a bad QoL condition and vice versa[4].

Accordingly it was found that as age increased the QoL for patients worsened while as patients became more educated their QoL improved

In addition to that major thalassemia patients had worse QoL scores than intermediate patients and this is realistic as intermediate patients have lower clinical burden thus lower psychosocial burden.

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[4] The regression analysis was done before transforming the scale to the 0-100 range.

To test the effects of the socioeconomic factors on the clinical burden of thalassemic patients, it was found that again sex was insignificant, while as age increased the clinical burden increased, and while the level of education increased the clinical burden decreased. This is partially mirrored into the QoL sums and could explain the relationship among the socioeconomic variables and the QoL scores.

Table 17: OLS on clinical effects and its relation with various variables

Coefficient		**S.E.**
Constant	5.936***	4.264
Age	0.370*	0.104
Level of education	-1.435**	0.805
Kind of disease	7.827*	1.526
R^2	0.199	
Adj-R^2	0.183	
F-statistic	12.953*	

*significant at the 1% level, **significant at the 10% level, ***not significant

QoL when using oral iron chelators:

In order to be able to compare QoL scores between infusion based iron chelators and oral chelators, it was attempted to recalculate the QoL score that we obtained by adjusting the questions that were relevant to the infusion based iron chelators which were questions PQOL19, PQOL18 and PQOL16 in the psychosocial section that asked directly whether patients wanted to change the current treatment mechanism and if they were satisfied or not with such a mechanism, and questions CL2 and CL7 in the clinical burden section that asked about the frequency of taking Desferal and the side effects associated with the medication(see appendix 2). The answers were modified to reflect the effects of the oral chelators instead thus they were given the values of 0 or 1, i.e. reflecting that under oral chelating regimen patients would have answered by none or mild effects to the questions discussed earlier.

Accordingly, the QoL score was enhanced as the mean QoL score after being transformed into a 0-100 scale was 74 out of 100 compared to 61 out of 100 indicating a significant improvement in the QoL for the patients when using oral iron chelators.

4.2.5. CA

From the 183 questionnaires sent 181 completed the conjoint analysis, respondents who did not answer scenario 3 correctly since it was the dominant one in the set were not included in the analysis since it indicated that they either did not understand the technique or did not take the questionnaire seriously and they were 38 respondents thus we were left with 143 questionnaires to analyze.

Using a random effects probit model Table 18 presents the main effects coefficients:

Table 18: Random effects probit model results

Attributes	Coefficients	Standard error
Iron reduction	0.8944*	0.1314
Administration	0.51653**	0.164
Complications	0.9975*	0.180
Practicing Life	0.6481*	0.0694
Extent of Pain	0.3099*	0.0428
Cost	-0.0001613*	0.0000479
rho	0.17159	
Log likelihood	-841.662	
n	145	
Chi2	170.71*	

*Significant at 1% level, ** significant at the 2% level

All attributes were significant at the 1% and 2% levels indicating that all attributes that were chosen affect the choice of medications by thalassemia patients and all attributes also had their expected signs depending on the regression codes, thus if the coefficient had a positive sign it indicates that the higher is the attribute in B compared to A the more likely patients would choose B, whereas if the coefficients had a negative signs it indicates that the lower the attribute in B relative to A the more likely patients to choose B. for example reducing iron had a positive sign meaning that if medication B reduced iron more compared to medication A then patients chose B, the same can be said about the easily administered medication and the ability to live normal life. However, the attributes pain and complication had also positive signs and this was due to the nature of the regression coding as 0 took the meaning of severe complications and 1 meant mild complication thus the positive sign means that patients chose B if medication B had mild complications compared to A and the same applies to pain. The cost attribute had a negative sign which means that the less the cost of medication B compared to A the more likely that patients chose B.

It must be noted that we had no dominant attribute; whereby most respondents would prefer one attribute over all the other presented attributes, thus choosing the medication that had the most preferred attribute. Thus even reducing iron was not a dominant attribute as shown in the following table:

Table 19: Non dominance for the reducing iron attribute

	Difference in reducing iron between medication B and A	**Prefer Medicine B**	**Prefer Medicine A**
Choice1	0	108	73
Choice2	1	87	94
Choice3	1	143	38
Choice4	0	64	116
Choice5	0	95	84
Choice6	0	92	89
Choice7	0	49	131
Choice8	1	63	117

As can be shown in table 19, even if medication B reduced iron more than Medication A, patients did not choose B over A, indicating that the existence of other attributes mattered to them.

Trade off between attributes:

According to the coefficients sizes, associated complication is the most important attribute in choosing the iron chelating medications compared to reducing iron, as patients prefer to have mild complications as a side effect from using iron chelating therapies compared to severe ones. i.e. they are willing to give up 1.12% (0.9975/0.8944)[5] of iron reduction to have mild rather than severe complications. Patients have shown also their willingness to suffer from pain as they consider pain temporary in order to be able to practice life normally and be able to easily administer the intake of the medication, thus patients are willing to give up 2% (0.6481/0.3099)of feeling pain in order to be able practice life normally more and they are willing to give up 1.7%(0.51653/0.3099) of feeling pain to have a medication that can be easily administered more. The cost attribute was the smallest in size.

Estimating WTP:

To estimate the indirect willingness to pay for the attributes, each attribute is to be divided by the cost attribute, and table 20 presents the WTP results:

Table 20: Indirect WTP values

Attribute	**Random effects probit model WTP (NIS/month)**
Reducing iron	5,544.9
To be easily administered	3,202.3
To have less complications	6,184.4
To practice normal life	4,018
To reduce pain	1,921.3

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[5] The ratio between attributes gives the marginal rate of substitution i.e. it indicates how much patients are willing to trade an attribute in order to get more of another attribute.

The table indicates that patients were willing to pay NIS 5,544.9/ month to reduce iron, whereas they were willing to pay NIS 6,184.4/ month to reduce complications. The least amount paid was for reducing pain which amounted to NIS 1,921.3/ month. If these were to be summed together, then patients were willing to pay NIS 20,870.9/ month to get a medication that reduced iron, could be easily administered, had less complications, allowed them to practice life normally and had less pain feelings when administered.

4.2.6. CV

The number of respondents to the open question; of whether they are willing to pay extra to get iron chelators were 180 with one missing value, compared to 179 to the open bid of how much they were willing to pay per month to get an oral chelators with 2 missing values. 56.7% indicated that they were willing to pay extra to get an oral chelators compared to 43.3% whom answered negatively. The amounts varied considerably as they took the amount of 5NIS/ month to 2,000NIS/ month. Around 24.6% were willing to pay between 100-200 NIS/month compared to 12.3% that were willing to pay between 300-500NIS/month while only 3.3% were willing to pay around 1,000-2,000 NIS/month. The mean value of the open question was 140.73

NIS/month for all respondents and 244NIS/month for respondents willing to pay for an oral chelator.

Table 21: descriptive statistics on direct WTP

	All respondents	**Only respondents WTP**
N	179	103
Mean **(S.D.)**	140.73 NIS/month (275.1)	244 NIS/month (326.2)
Minimum-Maximum	0 -2,000	5 – 2,000

In order to analyze the effects of socioeconomic variables on willingness to pay a tobit model was used which is part of a limited dependent variable models. This kind of model was used due to the nature of the dependent variable as it contained many zeros thus we have what is called censored data i.e. the dependent variable takes zero but the independent variables are known (*Kennedy, 2001*).

The full model which contained all socioeconomic variables; sex, age, education, income and kind of disease was significant with a chi square of 13.11 ($p>0.05$), however, both sex and income were insignificant in the model.

Table 22: tobit model results

Variables	**Coefficients**	**Standard error**	**Significance**
Constant	-260.53	151.9	0.088
Sex	-32.462	54.54	0.553
Age	-6.733	3.688	0.07
Education	63.12	25.676	0.015
Income	10.988	19.975	0.583
Kind of disease	113.596	47.83	0.019

LR chi-square (5) =13.11, p>chi-square=0.0224, loglikelihood=-688.24, pseudo R^2=0.0094

Thus we reduced the model by eliminating the non significant variables and the following model was produced:

Table 23: tobit model results 2

Variables	**Coefficients**	**Standard error**	**Significance**
Constant	-246.274	134.202	0.068
Age	-6.87	3.655	0.062
Education	65.004	25.598	0.012
Kind of disease	113.18	47.979	0.020

LR chi-square (3) =12.45, p>chi-square=0.0060, loglikelihood=-688.763, pseudo R^2=0.0090

It can be noticed that the significance improved for all coefficients and from the model it can be said that as patients get older they become less WTP for an oral chelator which could be due to the accommodation and the routine that the patients have established with the infusion based iron chelating therapy, however, it was interesting to note that as patients become more educated, they become more WTP for an oral chelators compared to less educated patients and major thalassemic patients are more WTP for an oral chelators compared to the intermediate thalassemic patients which is logical as major patients need more iron chelation than intermediate patients since they get more blood transfusions.

4.2.7. CEA

MOH Perspective:

Table 24: CEA using MOH perspective

OPTION	COST in NIS	EFFECT in %	INC.COST	INC. EFF.	ICER
DFO	12,309.92	0.4			
L1-DFO	32,613.00	0.44	20,303.08	0.04	507,577.1
DFX-DFO	35,853.00	0.46	23,543.08	0.06	392,384.7
DFX-L1	35,853.00	0.46	3,240.00	0.02	162,000

Patient Perspective:

Table 25: CEA using patient perspective for the age category below 4 years old

OPTION	COST in NIS	EFFECT in %	INC.COST	INC. Eff.	ICER
DFO					
Rural	**120**	**0.4**			
Urban	**14**	**0.4**			
L1-DFO					
Rural	**720**	**0.44**	**600**	**0.04**	**15,000**
Urban	**84**	**0.44**	**70**	**0.04**	**1,750**
DFX-DFO					
Rural	**720**	**0.46**	**600**	**0.06**	**10,000**
Urban	**84**	**0.46**	**70**	**0.06**	**1,167**

Table 26: CEA using patient perspective for age category above 4 years old

OPTION	COST in NIS	EFFECT in %	INC.COST	INC. Eff.	ICER
DFO					
Rural	**2,720**	**0.4**			
Urban	**2,614**	**0.4**			
L1-DFO					
Rural	**3,120**	**0.44**	**400**	**0.04**	**10,000**
Urban	**2,484**	**0.44**	**(130)**	**0.04**	**(3,250)**
DFX-DFO					
Rural	**3,120**	**0.46**	**400**	**0.06**	**6,667**
Urban	**2,484**	**0.46**	**(130)**	**0.06**	**(2,167)**

Societal Perspective:

Table 27: CEA using societal perspective for age category of less than 4 years old

OPTION	COST in NIS	EFFECT in %	INC.COST	INC. Eff.	ICER
DFO					
Rural	**21,434**	**0.4**			
Urban	**21,328**	**0.4**			
L1-DFO					
Rural	**33,792**	**0.44**	**12,358**	**0.04**	**308,954**
Urban	**33,156**	**0.44**	**11,828**	**0.04**	**295,704**
DFX-DFO					
Rural	**37,032**	**0.46**	**15,598**	**0.06**	**259,969**
Urban	**36,396**	**0.46**	**15,068**	**0.06**	**251,136**

Table 28: CEA using societal perspective for patients above 4 years old:

OPTION	COST in NIS	EFFECT in %	INC.COST	INC. Eff.	ICER
DFO					
Rural	**21,834**	**0.4**			
Urban	**21,728**	**0.4**			
L1-DFO					
Rural	**33,992**	**0.44**	**12,158**	**0.04**	**303,954**
Urban	**33,356**	**0.44**	**11,628**	**0.04**	**290,704**
DFX-DFO					
Rural	**37,232**	**0.46**	**15,398**	**0.06**	**256,636**
Urban	**36,596**	**0.46**	**14,868**	**0.06**	**247,803**

From the MOH perspective, the ICER for L1 when compared to DFO was NIS 507,577 in order to reduce 1% of the serum ferritin level in the body. While the DFX on another hand had an ICER of NIS 392,385 per 1% reduction of serum ferritin level when compared to DFO.

From the patient perspective, the age category below 4 years old had much higher costs than the age category above years old, and the patients residing in the urban areas had strong dominance for oral chelators over the DFO while rural patients ICER ranged from NIS 10,000- NIS 15,000 per percent reduction in serum ferritin levels, reflecting mainly the high transportation costs incurred by rural patients. The negative sign implies that the cost of both

L1 and DFX are lesser than DFO from the patient perspective while their efficiency is much more than DFO.

From the society perspective, there wasn’t a significant difference between age categories, and the DFX remained to be more cost effective than L1 when compared to DFO, while the rural patients incurred higher costs per percentage reduction in serum ferritin levels compared to urban patients.

4.2.8. CUA

Patient Perspective:

Table 29: CUA using patient perspective for age category less than 4 years

OPTION	COST in NIS	EFFECT in %	INC.COST	INC. Eff.	ICER
DFO					
Rural	**1,800**	**9.15**			
Urban	**210**	**9.15**			
Oral chelators					
Rural	**10,800**	**11.1**	**9,000**	**1.95**	**4,615**
Urban	**1,260**	**11.1**	**1,050**	**1.95**	**538**

Table 30: CUA using patient perspective for patients above 4 years old:

OPTION	COST in NIS	EFFECT in	INC.COST	INC. Eff.	ICER
DFO					
Rural	**7,800**	**9.15**			
Urban	**6,210**	**9.15**			
Oral chelators					
Rural	**13,800**	**11.1**	**6,000**	**1.95**	**3,077**
Urban	**4,260**	**11.1**	**(1,950)**	**1.95**	**(1,000)**

Societal Perspective:

Table 31: CUA using societal perspective for age category less than 4 years

OPTION	COST in NIS	EFFECT	INC.COST	INC. Eff.	ICER
DFO					
Rural	**321,504**	**9.15**			
Urban	**319,914**	**9.15**			
Oral chelators					
Rural	**531,176**	**11.1**	**209,673**	**1.95**	**107,524**
Urban	**521,636**	**11.1**	**201,723**	**1.95**	**103,448**

Table 32: CUA using societal perspective for patients above 4 years old:

OPTION	COST in NIS	EFFECT	INC.COST	INC. Eff.	ICER
DFO					
Rural	**327,504**	**9.15**			
Urban	**325,914**	**9.15**			
Oral chelators					
Rural	**534,176**	**11.1**	**206,673**	**1.95**	**105,986**
Urban	**524,636**	**11.1**	**198,723**	**1.95**	**101,909**

From the patient perspective, and for the age category less than 4 years old, the ICUR was 4,615/QALY for rural patients opposed to 538/QALY for urban patients. While for the age category of more than 4 years old the ICUR was 3,077/QALY for rural patients opposed to strong dominance over DFO for urban patients.

From the societal perspective, the ICUR yielded ranged from NIS 103,448 – NIS 107,524 for each additional QALY for the age category less than 4 years, whereas it ranged from NIS 101,909 – NIS 105,986 for the age category over 4 years old.

4.2.9. CBA

Patient Perspective:

Table 33: CBA using patient perspective for the oral chelators

Conjoint Analysis					**Contingent Valuation**	
Category	**Cost in NIS**	**Benefits in NIS**	**Net Benefits**		**Benefits in NIS**	**Net Benefits**
Age=<4						
Rural	**720**	**250,451**	**249,731**		**2,928**	**2,208**
Urban	**84**	**250,451**	**250,367**		**2,928**	**2,844**
Age>4						
Rural	**920**	**250,451**	**249,531**		**2,928**	**2,008**
Urban	**284**	**250,451**	**250,168**		**2,928**	**2,644**

When conducting the CBA, there were two outcomes for each category: the outcomes obtained from conjoint analysis and the ones obtained from contingent valuation.

Conjoint analysis results:

This approach had taken the indirect willingness to pay as the outcome to be compared with the programmes costs. In addition to that, such an outcome was analyzed by either summing up all the 6 attributes introduced earlier or by summing the most 2 important attributes to the patient. The net benefit using the conjoint analysis approach was positive for all categories and the values yielded were large, indicating the importance of the oral chelators to the patients.

Contingent valuation results:

This approach used the direct willingness to pay expressed by the patients as the benefits; this has also yielded positive net benefits although at lower values compared to the conjoint analysis.

5. Discussion

5.1. CEA

In the CEA, it was evident that DFX had lower ICER than L1 when compared to DFO for all age categories and in all the three perspectives. Whether the ICER for reducing 1% of ferritin level in the body is accepted or realistic is difficult to determine in the Palestinian context, since the MOH has no league tables for such thresholds, nor has the international health ministries any threshold values for reducing iron levels in the body.

However, the calculated ICER for reducing the serum ferritin levels in the Palestinian context may be considered too high and unacceptable to the MOH or the society, when taking into consideration the GDP levels. GDP /capita in the Palestinian territories range around USD 1,177 (NIS 4,708) (PCBS 2007), and when using the World Health Organization (WHO) threshold of 3*GDP/Capita= USD 3,531 (NIS 14,124), the cost of reducing 1% of serum ferritin levels would be considered high and very costly from the MOH and society perspective.

One of the major limitations that were faced when conducting CEA was the efficiency measure of the iron chelators. It was rigid and more comprehensive detailed indicator should be used in order to measure precisely such efficiency rate. For example in the Palestinian context, one could use the serum ferritin levels of the Palestinian patients for a specific time span, thus more reliable and realistic upper levels and lower levels of the serum ferritin would be obtained, providing the researcher with an accurate and measurable efficiency rate.

5.2. CUA

5.2.1. QoL

When comparing Ratip et al. QoL parameters obtained in Palestine within the international context, it was found that some parameters were worse than other countries while other parameters appeared to compare favorably to other countries.

The education parameter for an example did better in other developed countries than Palestine, where the percentage of patients scoring moderate to severe effects on education averaged 40% in US and UK, while in Turkey it reached 60%, similar to Palestine.

However regarding social life, denial and family adjustments Palestine has outpaced developed countries, and this could be explained by the strong social network that Palestine exhibit compared to other countries.

Regarding the QoL score obtained from Ratip et al. questionnaire, the result score indicated that thalassemic patients in Palestine while experiencing difficulties in education, social integration and anxiety, they still had a fairly good QoL which could be due to the nature of the Palestinian community where social networks secure the needed support, and religious believes help both patients and families to cope with the disease that they considered “qada’and qadar”.

Considering the socioeconomic characteristic and their effects on QoL score, it was surprising that sex was insignificant, as it was expected that females would have worse scores on the self image, social integration and social isolation indicators but this was proved wrong and that males or females experience the same hardships in this kind of disease.

Regarding the education parameter, it was found that as patients become more educated, their QoL was enhanced. This is due to the fact that well educated patients have the ability to better cope with the disease and better understand the nature of the disease, thus being able to take more care of themselves than others.

The analysis of QoL parameters and the socioeconomic impact on them mirrored the Palestinian context of the disease. Although the results were not anticipated regarding the high QoL scores given the factors influencing the patients from occupation, low financial capabilities and low treatment quality, but again, social networks and support has proved to be the ultimate factor contributing to the patients QoL. However, it can be said that these patients are in deep and urgent need for a psychological support in addition to financial support from their communities. And needless to say that the trust in the medical bodies is crucial for the these patients, and thus the Ministry of Health need to put more effort, in conjunction with civil institutions, to better enhance the medical services given to these patients.

The QoL score has improved significantly when using oral chelators, this is a direct result of higher compliance and an anticipated better satisfaction by patients if they used oral chelators. However such a score could have been more accurately calculated if direct questions regarding oral chelators were used, but the QoL questionnaire was designed to measure the current QoL for patients, where they used Desferal rather than oral chelators. It would be really interesting to examine directly the real changes in QoL for patients when they begin using the oral chelators, which have been in use since October 2008.

The ICUR varied substantially according to the life years survived by the patient. If we estimated that the healthy life years gained under oral chelators would be the same as DFO which is 15 YRS, then the ICUR would be NIS range between NIS 538- NIS 4,615 per QALY for the age under 4 years old from the patient perspective, which is considered acceptable using international thresholds levels as detailed in table 29 hereunder for UK, Australia, Sweden and Germany.

Table 29: International thresholds values

	Accepted
NICE (UK)	**< NIS 150,000**
PBAC (Australia)	**<NIS 115,000**
PHARMAC (New Zealand)	**< NIS 55,000**
SBU, LBF (Sweden)	**< NIS 175,000**
IQwiG (Germany)	**< NIS 100,000**
USA	**< NIS 200,000**

It is worth noting however that for the age category above 4 years old, urban patients had strong dominance for oral chelators when compared to DFO and this mainly reflect the transportation costs that are so low compared to rural patients.

From the societal perspective the ICUR ranged from NIS 101,909 to NIS 107,524 per QALY, which is also considered acceptable using international thresholds.

5.3. CBA

5.3.1. Conjoint Analysis

When CA was conducted, our hypothesis was that reducing iron would be the major and most important attribute to the patient; however, it came in the second place after reducing complication attribute. This was a clear sign that Palestinian patients had no clear information about the disease and the causes of complication. If they were more informed patients, they should have recognized that reducing iron would automatically reduce any severe complications that some patients may have experienced.

Another factor that needed attention was the cost attribute, which was significantly low compared to other attributes. This has indicated that patients have regarded the costs as unimportant item, and some patients didn’t even consider it when they chose the scenarios as most patients perceived that such costs would be accounted by the MOH rather than the patient her/himself. Such factor had distorted the results and affected our interpretation and is considered one of the major limitations of the paper. This could have been avoided by inserting a statement before the scenarios indicating that the costs would be paid directly by the patient. This in turn has caused the large values of the WTP when all attributes were divided by the cost attribute.

The WTP estimated from the conjoint analysis reflect the magnitude and importance of each attribute according to the patient, although it is impossible for patients to pay such huge amounts monthly for each attribute, such analysis is indicative of how important each attribute to the thalassemia patients, and that the MOH should not overlook such factors when considering any programme for thalassemia patients.

All in all thalassemia patients were willing to pay NIS 20,871 to get oral chelators.

Of course, the major limitation to such an outcome was the insensitivity and non clarity of the questionnaire regarding the cost attribute and that it was payable by patients rather than MOH as many patients had implicitly hypothesized, distorting the outcomes.

Another limitation was the length of the questionnaire that may have caused some respondents to feel bored and lose their concentration as they reached the CA questionnaire. If it were to be done again, a separate questionnaire should be designed for CA and all the proposed scenarios by the SPSS should be included in the questionnaire by splitting half of the scenarios and distributing them on 2 sets of questionnaires. Such a technique would provide more precise outcomes.

5.3.2. Contingent Valuation

As discussed earlier, CV was used to elicit willingness to pay directly from the patients. 43% were not willing to pay extra to get oral chelators and such negative/protest zero answers were expected to be around half the sample. The tobit model revealed that income and sex were insignificant regarding WTP. The insignificance of sex implied that whether a patient was male or female did not affect the patients' WTP. On another hand the insignificance of income revealed that the household income levels reported by the patients did not match the figures they revealed on how much they are willing to pay for an oral chelator per month. Some respondents who have identified their monthly household income level between NIS 0/month and NIS 1,000/ month were willing to pay more than 500 NIS/ month which is not logical since there are other expenditure items in the family indicating that patients did not reveal their true income levels.

This is considered from the major limitation of the paper, as the household income level question should have not been asked directly, as most respondents won't reveal such info. This should have been tackled by asking indirect questions such as asking about the monthly household expenditure levels.

The cost benefit analysis was conducted from the patient perspective, and the net benefit in both methods was positive and large indicating that oral chelators were highly beneficial from the patients' perspective. However, it is worth mentioning, that such outcome was also achieved due to the lower cost burdens on the patient as they are all insured and incur only transportation and private examinations costs.

6. Recommendations:

Although the results of economic evaluation that has been done in this paper could not be used specifically since they mirror some distortions and limitations, however, this paper has succeeded in identifying the major trends of the QoL for thalassemia patients in addition to pin pointing the relative importance of iron chelation therapy in their lives and its specific attributes. It is however, important to have effective awareness campaigns about thalassemia in the society in order to further decrease the incidence levels of thalassemia.

The following recommendations should be viewed with some seriousness from the MOH and the community as a whole to better enhance the QoL for thalassemia patients:

1- Oral chelators should be made available to thalassemia patients since it has been proved that they could better enhance QoL for patients, in addition to better compliance thus reducing side effects from accumulated iron and this has been proved by the cost effectiveness of oral chelators over DFO in the various perspectives and age categories

2- Educational sessions should be held for thalassemia patients and their families to be better able to handle and manage the disease and thus reducing the side effects associated with it. This was evident by the lack of support parameter which has severely affected the QoL for patients, in addition to the lack of knowledge about the disease by both patients and their families, and this was evident in the conjoint analysis exercise and how they weighted the importance of the attributes.

3- More support groups should be formed especially in schools to enhance self confidence and social confidence within the patients.

4- More nurses and medical staff, with enhanced capabilities, should be allocated to thalassemia patients, this could also expand to allocating special hospital departments for thalassemia or even special clinics distributed in various localities to be able to better manage thalassemia patients and assist them in their monthly blood intake, this would enhance the trust in the medical body thus improving complicate from the patients side.

5- Palestinian Labor Laws should be upgraded to include an enforcement law on employers to employ thalassemia patients and provide a suitable working environment for them.

6- More resources by the MOH should be allocated to the age category above 4 years old

7- Medical centers could be established on the outskirts of each locality rather in the centre of the locality, to decrease the financial burden on rural patients, and the productivity burden on the society as a whole.

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8. Appendix:

Appendix 1:

Focus Group Discussion:

Place: Thalassemia Patients Friends Association

Date: October 31, 2007

Number: 10 patients (3 males and 7 females)

Q1. What does QoL means to you?

Anwar: to live a normal life, I wish that my life could improve and develop; this is achievable to me when I take the pill and not the needle. This is because the place of the needle stains on my skin and it is very painful to insert the needle. Sometimes skin would come off when the needle is inserted. Also when we put the belt of the Desferal we cant practice any activities in the school such as sports, the muscles of my arm begins to hurt.

Ahmad: It means that everything others have should be available to me, such as medications and treatments.

Ayat: I feel that my life is normal, I don’t feel different.

Lubna: the society perceives us as weak people.

Dr Awad: QoL means to me how much I am satisfied with my life, is treatment the most important thing in your lives?

Lubna: what should the patient think of then? Future? No he thinks about treatment and about the availability of medication.

Dr Awad: your thoughts then are as patients only!

Anwar: we shouldn’t feel that we are sick.

Ayat: I am proud of my illness. Only the people around me make me feel that I’m ill. But I have to live a normal life.

Anwar: I live a happy life; the needle is the only bad thing in it.

Siham: I wear the needle in the night; I can’t play in the school.

Rasha: My motto in life is “no life with despair and no despair with life”. I don’t take things easily, even if I encountered something easy, I know for certain that another difficult issue will arise. I lived my childhood in its bitter and difficult moments. I admit that I didn’t live my childhood (didn’t enjoy it), but every moment I lived, I tried to perceive life from a positive perspective and I tried to develop my life. Taking the Desferal is suffering, but I don’t have any alternative, so I will continue using it to preserve and keep my life.

Dr. Awad: if there was an alternative, what would it be?

Anwar: the most important thing is to get rid of the needle.

Ayat: I will be more encouraged to take the medication and will be more committed if there was a pill.

Anwar: I will feel more energetic, everything will be available to me, and everything in my life will change.

Omar: I don’t feel that I am sick, everything is OK, like any human being. I shouldn’t think I’m sick always.

Lubna: To practice life normally, to go out and participate in society, to get rid of the thought of illness.

Anwar: Parents play a major role also in the patient’s life, they must explain to their child what to expect in the future so as not to get surprised. They must tell him about the nature of his life, about the iron and its side effects…etc. physiological preparation is very important.

Dr. Awad: do other people affect you QoL?

Anwar: Friends, they have to be considerate.

Layali: what are the negative or positive aspects in your life?

Ahmad: no negative aspects, all is positive. But people have to support the patient. I feel that I can accomplish anything in life with a strong will.

Rasha: when I was employed in the association, there was a law that all organizations must employ 5% from handicapped people. But in reality this is not applied, being a patient is an obstacle to me.

I also worked in the election campaign. In the interview I was very honest and told the interviewee that I had thalassemia and they were OK with it and hired me from a 4,000 applicant list. However, once and during work, I had to get blood transfusion and the manager refused to let me go to the hospital. I saw this as a very negative thing that affected my life.

Ayat: The situation that we live in (the occupation) affects us negatively. The closures affect the person as he feels suffocated and that his life would end. For me I don’t feel this, as in our country we have no closures.

Anwar: the occupation does affect my life, as I get blood transfusions in Ramallah and I am from Tulkarem, thus the sudden curfews could prohibit me from reaching the hospital, continuously affecting my life.

Rasha: the negative thing is that we can’t enter Jerusalem; we must have a permit.

Dr. Awad: Is there any medical treatments that are not found in the WB but are found in Israel?

Rasha: Many actually, I once suffered from internal bleeding inside my leg, in the WB they didn't know what to do! But in Israel I made several tests and they treated me and stopped the bleeding.

Anwar: I also get these bleedings occasionally, but I didn't know why! The doctors said to me not to play a lot.

Ahamd: the negative thing in my life is that I cannot travel because I need constant blood transfusions.

Q2. Do you think any of the following determinants affect you QoL?

A- Feeling different:

Anwar: I don't feel that I am different. I don't care.

Ayat: I'm normal. I only remember that I'm ill only when I go to get blood transfusions, and the society also makes me feel ill.

Anwar: I want to thank my nurse Shahinaz, she talks to us more than our parents, she's always telling us that we shouldn't care that we are ill. She helps us not to feel different.

Dr. Awad: Is feeling different something negative?

Anwar: I don't know, I just don't care. I am a normal person; the only difference is that I get blood transfusion.

Lubna: If parents gave us the support to fight this, it would have been something normal. But parents all the time tell me that you are ill, don't tire yourself. This is a negative thing that affects my life.

Ayat: My teacher also had a great role in my life, as he supports me and talks to me when I get tired, he tells me that everything is normal. For me I don't care.

Omar: no, it does not affect me.

Ahamd: relax

Ahamd T.: I don't feel anything.

B- Appearance:

Anawr: my appearance is the most important thing in my life, I am always on the mirror. People who suffer from deformities of the face bones may affect them negatively, for me thanks God, I don't suffer from this. The most important thing in my appearance is my face.

Rasha: I care a lot for my appearance especially when my face gets yellowish ,also my parents bother me in that matter ,but my appearance affects my life ,and my daily follow up of my normal life .

Ayat: I don't like my face getting darker ,because when iron increases in my body ,the darkness of my skin increases ,I love to be like my classmates who are white and beautiful.

Ahmad : I don’t care about my appearance as long as I’m with the company of my friends ,if somebody gave me the weird look ,I won’t go out ,if not ,then everything is Fine.

Omar: appearance is normal, it is not as important to me as females.

Anwaar : males are different than females ,they don’t care about their appearance as much .

C- Treatment:

Anwaar : treatment is normal only the pain that comes from the Desferal or associated with its use, and the old blood that we receive is a concern to me. When we receive old blood we have to sit for 2 and half hours getting the transfusion since it clots due to this fact. So we are getting old blood, iron and above all the Desferal needle, however treatment has only one negative side-effect to us stressing on the needle. Thus the negative aspect of the treatment to me is the needle of the Desferal and the old blood. I believe that all thalassemia patients must receive new blood.

Dr Awad: if treatment changed would this increase your lives satisfaction?

Anwaar: if they get us new blood, I’ll feel more secure about myself, and I’ll be encouraged to get Desferal .

Ayat : from the side effect I get from the old blood is fast heartbeats, and if the blood was old this means that I have to get blood transfusion every week .for us we are aiming to get high blood concentrations however receiving old blood wont fulfill that target .also my adherence to Desferal is low .

Ahmad: treatment is not encouraging; if there are people who encourage or care for me I will undergo the treatment.

Anwar asks Ahmad, when you get blood transfusion how do you feel ?

Ahmad : bored .

Rasha : in Ramallah there is a big problem ,even that we are a strategic location ,but we don't have Units it's like we are living in the 90's we have absent rights .I agree that you feel bored(you sit for 3 hours for the transfusion) and you put the Desferal daily at night ,however not all our patients love to read ,as some love to jog or watch Television ,there is pressure .

Ayaat: the needle of the blood transfusion won't enter from the first time and this can affect my ability to write thus affecting studying.

Ahmad (2): when I get blood transfusion I feel pain, it hurts my arm, I don't feel happy going to the hospital (I go to the hospital alone).

Mahdiya: treatment is a large part of my life, I don't receive Desferal because I'm allergic to it and this affects my health (but it became natural to me).

Lubna : I don’t also put Desferal ,I drink tea , with food as it breaks the iron , I used to feel very tired when I put Desferal ,and now thanks to God everything is normal .

Ayat: when I put the Desferal it hurts where the needle is placed, there are people who feel ashamed when they put that machine in front of people, I don’t. I want to be a nurse.

Anwaar: everything that we said refers to the nurse, when we were young we were attended by several nurses.

Lubna: Shahinaz relieved us from the needles pain.

Anwar: she encourages us to take the treatment, and she explains it to us.

Ahmad : if I was stressed I don’t get blood ,even if this would affect my life ,I don’t feel like receiving blood, this could be due to personal reasons or others .

Ayat: when I have my mid-terms I delay the blood transfusions date, I want also to add that when we used to go to the pediatrics department no one took care of us, and we faced problems, now at the Thalassemia department they care for us, at the Department people provide us with guidance and all the thanks for Shahinaz.

Omar :everything is normal ,treatment is not only blood and Desferal ,it is also spiritual ,we need a strong will ,the will that I don’t keep thinking I’m sick ,and not to feel that I cant get married because I have Thalassemia and such stuff .

Anwaar: the thing he is talking about goes back to feeling different ,if the girl wants to get married ,she will say I have Thalassemia and I don’t want to get married ,this is feeling different ,and I don’t want to think like this .

Ayat: I want to add that any bad thing that I encounter I don’t love for others to encounter or face.

Rahsa: also food is included within treatment, I shouldn’t eat food that contains Iron .

Siham: I feel normal, bored, the blood transfusion is so slow.

Anwaar: the food ! all the food has iron (I only eat milk dairies and tea).The Cola ,I love Cola I will die for it ,sometimes to drink it I pour in it tea but I’ve been avoiding it for four months .

Rasha: we don’t drink Cola due to Osteoporosis.

Ahmad:I hate treatment I hate doctors and hospitals ,everything related to the treatment I hate it ,I feel it is not good for me ,treatment doesn’t extend life ,treatment is something routine ,treatment doesn’t improve my life .

Anwaar: you aren't supposed to say these things, you will have spleen enlargement, Osteoporosis… etc leading to your death .

Ahmad: if they developed the treatment a person would think about the future more .I don't like treatment it's boring.

Siham :I don't like Desferal because it takes time and we have school so we have to remove it at 7:00 a.m. even if it was not completed ,I don't get upset but my mother get worried .

Ayat : I want you to know that when our weight increases we have to increase the Desferal thus the burn of the skin increases .

Rasha: we can evaluate how effective is the desferal through urine and the color of the face.

Layali: do you feel happy when Desferal is effective?

Anwar: absolutely every person wants the best for themselves.

Ahmad: no

Khitam: from the face appearance a person reveals if he/she has used Desferal or not.

D- Sexual development.

Lubna: I got affected when my period was late, it came to me when I was sixteen, then everything was normal.

Rasha: everybody who sees me knows how Rasha evolved ,I grew up fast, it wasn’t something easy. I used to talk to my mother and sister and ask my sister why is your weight more than mine, and this is this simplest matter that crosses the mind of a girl .

I used also to go and ask my friends why am I like this, why am I different!!

My father convinced me that what I have other don’t posses .my parents helped me a lot. parents play a major role.

Anwaar: I don’t think about this subject.

Siham: I don’t have fears ,but I think about it a lot .

Lubna: before, I used to think why my classmates had their period and I didn’t, it worried me.

Ahmad: I have a twin brother my brother works in the police force, he is as tall as the door, and he has all the male characteristics, I wish I can be like him.

Anwaar: because he is your twin you feel different more and more.

Omar: I feel normal; I’m like all the other guys.

Siham: I heard that if I don’t get the period, I wouldn’t have children, is that correct?

E- Side-effects.

Ayat: when I get blood infusion I get fast heartbeats thus I must return to the hospital, it hurts me deeply that I have to return to the hospital

Rasha: I used to develop allergies and used to return regularly to the hospital when I get blood transfusions, my relative who lives abroad is a professor and was visiting us when this occurred to me, and she examined me and subscribed to me a new medication, now I can’t take blood transfusion unless I take this medication, the problem is that this medicine makes me sleepy and has affected my life a great deal.

Anwaar : I get headaches .

Ayaat: the only thing is that when I get the blood transfusion I become normal, this gives me hope, to continue with the medication so that my blood would become more concentrated.

Anwar: the treatment has negative and positive aspects, for me I suffer from high pressure, fever and my joints occasionally hurt me .

Ahmad: I don’t have any side-effects only headaches.

Ahmad 2: headaches and pain in my legs, and that makes me upset.

F- Future uncertainties.

Ayat: I have ambitions, my classmates who are normal don’t have plans, for me I have plans and goals for my future. I want to be a nurse.

Lubna: I don’t think about the future and it does affect my life, I want to work because it stresses me to stay at home.

Ahmad: to me the future is a surprise, I don’t expect anything.

Lubna: not everyone gets what they plan.

Rasha: off course I have ambitions.

Siham: I think of Gaza all my relatives are there, I don’t have anybody here all our relatives are in Gaza, I want to return to Gaza.

Anwar: when I was young the days were good ,I used to run and play in the streets, when I grew up I began thinking about the advises my mother gave me ,by the way I’m a Television host ,and you know kids when I go back to school they all ask me about it ! and I answer them tomorrow you will see ,when the girls and the principle ask me what do you want to study I respond ,journalism ,and they answer back alas ,once a girl made fun of me and the principle told me that she is jealous ,I see myself as a television host and a journalist ,I am certain of my future inshala .

Omar: I’m like the rest of the world, off course every person thinks of the future, fate is in the hands of god, we do what we have to do.

Ahmad : sometimes I think about the future when I’m alone .when I’m taking the medication I don’t think about the future ,I’m not sure about the future .

Ahmad 2: I want to be a doctor.

G- Family stability.

Ahmad: there are some parents who care, and others who don’t, and this affects me; when they care I am encouraged, if not there will be negligence in every aspect.

Anwaar : the family shouldn’t distinguish between the patient and other siblings .they have to continue doing their activities. when the patient is aware he can go alone to the hospital ,without the need of anyone’s help. My family is a normal one.

Ayat : our parents try to engage us in the society that’s why they let us go alone to the hospital ,my parents put me in one hand and all the other family members are on the other hand ,I am considered a major part I occupy their thought a lot .my mother sacrifices here time by taking care of me and this makes me feel happy . I tell her not to stay with me and try to ease things on her, but I love her presence around me .

Lubna: off course my parents are beside me this makes me feel happy ,when I say Ahh my father becomes confused with thoughts and escorts me to the hospital ,I am happy .

Ayat : I feel my mother is more gentle with me than my father ,this makes me feel happy ,she abandons all here work to be with me .

Rasha: I am the concern of my family, my mother taught me to carry the responsibility ten years ago, I had benefited from my parents especially from my father, this made me feel happy but deep inside I felt that I consumed their time,if my mother was with me during my sickness I used to feel I'm a burden on her, as she used to spend enormous hours with me ,however this did not affect my family stability and our activities continued normally . I have lots of friends. at a certain point my grandfather and father became sick, thus tasks were delegated to other under this roof, it was a very difficult time, but I stayed the main and essential task among all.

Shahinaz: usually children above the age of 12 arrive alone to the hospital, other than that they come accompanied by their mothers.

Ayat :my parents have to come with me because I am a female and there are several army checkpoints ,and if I got sick in the hospital they would stay with me .once they denied me access on the checkpoint ,I started crying ,really got devastated this led me to the E.R.

Omar : no everything is normal I go alone to the hospital ,off course my mother sacrifices here time ,however parents shouldn’t give us advices left and right ,this makes me more sick .

Ahmad: everything is normal back home, I go to the hospital alone, when I was a child my parents used to escort me. I used to feel happy when my mother used to come with me.

Ahmad 2: I go alone to the hospital, I love going alone.

Q3. Determinants of QoL:

A- Age:

Anwar: I take everything normal, when the person is more aware he will know everything about himself, and now I am more aware about my disease. Children remain children, sometimes I get afraid, However, when I was a little girl I used to play and run and drink Cola, I wasn’t aware of my disease.

Lubna: when I used to take Desferal and blood I used to feel better, before when I was little, no I didn’t feel better or okay with that. I have a brother and a sister who died from that disease. I was devastated after their death. And Desferal destroyed me more, I don’t know why!

Ayat: whoever sees me doesn’t think I am a Tawjihi student. Things are different now as I became aware , before, I didn’t like to go to the hospital, but when I became a grown up, it became something normal, routine, I can’t abandon it, it makes me think about the future, makes me feel independent.

Omar: when I was a small boy I was short, but when I took the hormones I became taller.

Ahmad: I love to return to my childhood, because as I grow up I become more aware of my life and I know things. But when I was little things didn’t matter to me.

B- Sex:

Ayat: appearance affects me, I love being a Palestinian, because everybody is considerate in our case.

Because I am a female my parents don’t allow me to go out, that’s why I love school more than vacations.

Anwar: For me everything is normal, I have my freedom now more than before.

Lubna: yap it does affect me, when I want to go out they don’t allow me, I always feel suffocated.

Ahmad: In the night I want to go out but my parents begin to advise me that I shouldn’t be late, and that I shouldn’t go too far, I usually put the Desferal and go out.

Omar: for me its normal, it does not affect me.

Anwar: males are different than females, females are more restrained.

Ayat: males and females nowadays are the same; they all love to be cool and trendy.

C- Occupation:

Ayat: occupation affected my family resources due to closures; this in turn had affected my ability to get treatment.

Anwar: my father is a teacher, and when the political situation deteriorated and they went into strike our financial resources were affected and thus I couldn't get my treatment.

Q4. What do you think also determines your QoL?

Rasha: Having specialist physicians and having periodic checkups affect my life greatly.

Anwar and Ayat: The pre marital checkups affect our lives deeply, and also having a better department that could cater to our needs.

Q5. After your review of the Questionnaire do you think it needs any amendments or addition? Is it easy?

All: It is easy to read and we can understand.

Appendix 2:

جميع المعلومات في هذه الاستمارة هي لأغراض بحثية محضة و ليست لأي غرض أخر.			
هذه الاستمارة هي عبارة عن تتمة لرسالة ماجستير في الاقتصاد و تهدف الى قياس جودة حياة مرضى الثلاسيميا في الضفة الغربية، في البداية أود أن أسئلك بعض الاسئلة العامة عن نفسك:			
ID.1	الاسم		
ID.2	الجنس	1. ذكر 2. أنثى	☐
ID.3	ما هو عمرك بالسنوات الكاملة؟		
ID.4	ما هي أعلى شهادة أتممتها بنجاح؟	1. أمي 2. ابتدائي 3. اعدادي 4. ثانوي 5. دبلوم متوسط 6. بكالوريس 7. ماجستير	☐
ID.5	ما هو معدل الدخل الشهري للأسرة (بالشيقل)؟	1. 500-0 2. 1000-500 3. 1500-1000 4. 2000-1500 5. 2500-2000 6. 3000-2500 7. 3500-3000 8. 4000-3500 9. أكثر من 4000	☐
ID.6	أين تسكن (القرية/ المدينة)؟		
ID.7	ما هو نوع مرضك؟	1. ثلاسيميا متوسطة 2. ثلاسيميا عظمى 3. فقر الدم المنجلي	☐

الاسئلة التالية تتعلق بوضعك الصحي، الرجاء أن تجيب عن جميع الاسئلة و اذا كنت غير متأكد من الجواب الرجاء اختيار الجواب الأكثر تلاؤما.

CL.1	كم مرة تحتاج الى نقل دم؟	0. لا أحتاج 1. مرة أو مرتين في السنة 2. ثلاث أو أربع مرات في السنة 3. أكثر من أربع مرات في السنة	☐
CL.2	كم مرة تتلقى الديسفوال؟	0. لا أتلقى 1. مرة أو أقل من مرة في الاسبوع 2. مرتين أو 3 مرات في الاسبوع 3. أكثر من ثلاث مرات في الاسبوع	☐
CL.3	هل ظهرت لديك تقرحات في الأرجل؟	0. لا 1. نعم، مرة واحدة لمدة أقل من عام 2. نعم، مرتين أو مرة دامت ما بين سنة وسنتان 3. نعم، أكثر من مرتين/ أو مرة واحدة و دامت	☐

		أكثر من سنتين	
CL.4	هل عانيت من حصوة في المرارة؟	0. لا 1. نعم، أحيانا مع أعراض وألم 2. نعم، مع الام متكررة 3. نعم، تم إستئصال المرارة	☐
CL.5	هل يوجد لديك تضخم في الطحال؟	0. لا يوجد تضخم أو تضخم بدون تأثير على الدم 1. نعم، متضخم لكن تأثيره بسيط على الدم 2. نعم، متضخم مع تأثير واضح على الدم لكن ليس بالقدر الذي يتطلب إستئصال الطحال 3. نعم، تم إستئصال الطحال	☐
CL.6	هل لديك تشوهات في الوجه؟	0. لا 1. نعم، تشوه بسيط، يمكن رؤيته بالتدقيق 2. نعم، تشوه متوسط، واضح لكن ليس شديد 3. نعم، تشوه شديد أو يحتاج لعمليات تجميل	☐
CL.7	هل لديك ألام في العظام و المفاصل؟	0. لا 1. نعم، أحيانا وطفيفه، لا تؤثر على نشاطاتك اليومية 2. نعم، كثيرة ومتوسطة، تؤثر على نشاطاتك بشكل ملحوظ 3. نعم، مستمرة وشديدة، تؤثر على نشاطاتك بشكل كبير	☐
CL.8	هل عانيت من كسور؟	0. لا 1. نعم، كسر واحد 2. نعم، كسرين إثنين 3. نعم، ثلاثة كسور	☐
CL.9	هل لديك مشكلة في السمع؟	0. لا 1. نعم، في أذن واحدة وطفيف 2. نعم، في الأذنين وطفيف، أو أذن واحدة وشديد 3. نعم، في الأذنين وشديد	☐
CL.10	هل عانيت من عدوى/ التهابات؟	0. لا 1. نعم، ليست بتكرار لكن أكثر من باقي الناس 2. نعم، متكررة، أوتضطر لدخول المستشفى أحيانا بسبب الالتهابات 3. نعم، تضطر لدخول المستشفى كثيرا بسبب الالتهابات	☐
CL.11	هل لديك مشاكل في النمو؟	0. لا 1. نعم، الطول أقل من المعدل قليلا	

		2. نعم، الطول أقل من المعدل بالثلث 3. نعم، الطول أقل من المعدل بأكثر من الثلث	☐
اذا كنت أصغر من 13 عاما انتقل الى سؤال 13			
CL.12	هل تعاني من تأخر في التطور الجنسي؟	0. لا 1. نعم، عدم خصوبة لعام، أو تأخر في البلوغ لعام 2. نعم، عدم خصوبة لعام أو إثنين، أو تأخر في البلوغ لأكثر من عام، أو عجز بسيط (عدم القدرة على الانجاب) 3. نعم، عدم خصوبة لأكثر من عامين، أو عدم بلوغ، أو عجز	☐
CL.13	هل لديك مشكلة في الحركة و التنقل؟	0. لا 1. نعم، يوجد ضعف بسيط: تحتاج الى الراحة بشكل متواصل، تستطيع المشي أكثر من كيلو و تستطيع صعود 20 درجة 2. نعم، تأثرت الحركة بشكل واضح: تستطيع المشي بين نصف الكيلو و الكيلو أو صعود بين 10 – 15 درجة 3. نعم، تستطيع السير فقط لأقل من نصف ميل أو صعود أقل من 10 درجات	☐
CL.14	ما هو معدل دخولك للمستشفى في السنة الواحدة لغير حالات نقل الدم؟	0. و لا مرة 1. مرة واحدة 2. مرتان 3. ثلاث مرات	☐
CL.15	هل لديك مشكلة في الكبد؟	0. لا، لم يتأثر 1. نعم، أعاني من إلتهاب الكبد الوبائي Bأو C 2. نعم، أحتاج الى أخذ دواء (alpha interferon) 3. نعم، لدي تشمع كبد أو ورم في الكبد	☐
CL.16	هل لديك سكري؟	0. لا 1. نعم، تتبع حمية غذائية 2. نعم، تأخذ حبوب وتتبع حمية غذائية 3. نعم، تأخذ إبر انسولين وتتبع حمية أو لديك مشاكل في المسالك البولية أو العينين بسبب السكري	☐
CL.17	هل لديك مشاكل في القلب؟	0. لا، لم يتأثر 1. نعم، مشاكل طفيفة، و لا تؤثر على النشاطات اليومية 2. نعم، يوجد أعراض في القلب تحتاج إلى أدوية و تؤثر بشكل بسيط على النشاطات اليومية	☐

		3. نعم، لديك فشل في القلب يحتاج لعلاج مستمر بالأدوية و تضطر لملازمة البيت	
CL.18	هل لديك مشكلة في الغدة الدرقية أو الفوق درقية؟	0. لا 1. نعم، تأخذ حبوب لعلاج الغدة الدرقية أو الفوق درقية 2. نعم، تأخذ أدوية لعلاج الغدة الدرقية و الفوق درقية 3. نعم، تم إدخالك المستشفى بسبب نقص الكلس و وجود تشنجات تتطلب أدوية في الوريد	☐

الأسئلة التالية تخص جوانب حياتك اليومية:			
RT.1.A	ما هو/كان تقديرك في المدرسة؟	1. متدني 2. متوسط 3. متفوق	☐
RT.1.B	هل تعتقد أنه كان بامكانك ان تحصل على تقدير أفضل لو لم تكن تعاني من مرض الثلاسيميا؟	1. نعم 2. لا	☐
RT.2	هل تضطر/اضطررت الى الغياب عن بعض الأيام الدراسية؟	1. لا، ابدا 2. نعم، يوم أو أقل في الشهر 3. نعم، أسبوع أو أقل في الشهر 4. نعم، أكثر من أسبوع في الشهر	☐
RT.3.A	هل تؤثر الثلاسيميا على نشاطاتك الرياضية؟	1. لا، ابدا 2. نعم، قليلا 3. نعم، كثيرا	☐
RT.3.B	هل كان بامكانك تحقيق أفضل من ذلك لو لم يكن لديك ثلاسيميا؟	1. نعم 2. لا	☐
RT.4	هل تؤثر الثلاسيما على مشاركتك الإجتماعية؟ (الذهاب للنوادي/ الجامع...)	1. لا، أبدا 2. نعم، قليلا 3. نعم، كثيرا	☐
RT.5	هل تؤثر الثلاسيميا على علاقتك بأصدقائك؟	1. لا، أبدا 2. نعم، قليلا 3. نعم، كثيرا	☐
RT.6	هل مرض الثلاسيميا مصدر قلق لديك؟	1. لا، أبدا 2. نعم، قليلا 3. نعم، أحيانا 4. نعم، كثيرا 5. نعم، دائما	☐

RT.7	ما هو أكبر تخوف / قلق لديك؟		
RT.8	ما هي أهم آمالك للمستقبل؟	1. أن أكون سليم/طبيعي 2. أن أتمكن من الإنجاب 3. أن أعثر على شريك حياة 4. أن أكون جيدا في المدرسة/العمل 5. أن أشفى 6. أن يكون لدي أصدقاء أمور أخرى.................	☐
RT.9	ماذا يعني لك أن تكون مريض بالثلاسيميا؟	1. قلق دائم 2. لا تستطيع التأقلم 3. الشعور بعدم المقدرة 4. الشعور بالضعف 5. لست قلق أبدا أمور أخرى..................	☐
الرجاء الاجابة على الأسئلة التالية ب: **1 نعم 2 لا**			
RT.10	هل تشعر بأنك مختلف عن أصدقائك/عائلتك؟	☐	
RT.11	هل تعتقد أن الثلاسيميا تؤثر على علاقتك بأخيك/أختك؟	☐	
RT.12	هل تعتقد أن الثلاسيميا تؤثر على علاقتك بوالديك؟	☐	
RT.13	هل أنت متزوج ؟ اذا كانت الاجابة لا، حدد وضعك الاجتماعي	☐ اذا كانت اجابتك بنعم، انتقل الى سؤال RT.15 الوضع الاجتماعي هو -------------------	

RT.14	هل أنت قلق حول امكانيتك إنشاء عائلة في المستقبل؟		☐
RT.15	هل لديك وظيفة؟		☐
RT.16	هل سبق وكان لديك مشكلة في التوظيف؟		☐
RT.17	بمن تثق وتلجأ طالبا المساعدة بشكل أساسي؟	1. والديك 2. أخوتك 3. أقرباء 4. أصدقاء 5. طبيب 6. ممرضة 7. زوج/زوجة 8. رجل دين 9. مجتمع الثلاسيميا آخر......................	☐
RT.18	هل تتكلم حول مشاكلك و همومك؟	1. أبدا 2. قليلا 3. أحيانا 4. كثيرا	☐
الرجاء اجابة الاسئلة التالية ب: **1 نعم 2 لا**			
RT.19	هل تظن أنك بحاجة الى المزيد من الدعم المعنوي؟		☐
RT.20	هل قمت بالإنضمام الى مجموعات مساندة، مثل جمعية أصدقاء مرضى الثلاسيميا؟		☐
RT.21	هل قام أحد بتعليق مزعج حول مرضك؟		☐
RT.22	هل يعلم أصدقائك أو زملائك بأن لديك ثلاسيميا؟		☐
RT.23	هل يعلم مسؤولك/مدرسك بأن لديك ثلاسيميا؟		☐
RT.24	هل تشعر بأنك صحي؟		☐
الرجاء الاجابة عن الاسئلة التالية ب: **1 أبدا 2 قليلا 3 أحيانا 4 كثيرا 6 دائما**			

PQOL.1	هل تشعر أنك تتلقى الدعم المعنوي/ النفسي الذي تحتاجه من مجتمعك؟	☐
PQOL.2	هل تشعر بالسعادة عندما تتلقى الدعم؟	☐
PQOL.3	هل تشعر بأنك عبء على عائلتك ؟	☐
PQOL.4	هل تعاني من اضطرابات في النوم؟	☐
PQOL.5	هل تفكر في وضعك المادي؟	☐
PQOL.6	هل تشعر بعدم الأمان في حياتك؟	☐
PQOL.7	هل يعيق الاحتلال وصولك الى مركز العلاج بسبب الاغلاقات من الحواجز أو الجدار ؟	☐
PQOL.8	هل تشعر أنك مضطهد/ غاضب عندما لا تستطيع أن تصل الى مركز العلاج بسبب الاغلاقات من قبل الاحتلال؟	☐
PQOL.9	هل لديك قلق ان العلاج قد لا يتوفر في اي لحظة تحتاجه؟	☐
PQOL.10	هل تشعر بعدم الأمان لعلمك أن العلاج قد لا يتوفر بأي لحظة؟	☐
PQOL.11	هل تشعر بعدم السعادة لذهابك لمركز العلاج؟	☐
PQOL.12	هل تفضل ان تكون مريض ثلاسيميا في اي بلد اخر ؟	☐
PQOL.13	هل تشعر أن معتقداتك الشخصية تمدك بالدعم المعنوي؟ اذا كان الجواب نعم، لماذا؟	☐ ------------------------------
PQOL.14	هل تشعر بأن حياتك ذات معنى؟	☐
PQOL.15	هل لديك الثقة في أطبائك؟	☐
PQOL.16	هل تؤثر الية العلاج لازالة الحديد من الجسم عن طريق الديسفرال على حياتك الاجتماعية؟	☐
PQOL.17	هل لديك الموارد المالية الكافية لتلقي العلاج؟	☐
PQOL.18	هل لديك الثقة في علاجك؟	☐

PQOL.19	هل تشعر بان الية العلاج لازالة الحديد من الجسم عن طريق الديسفرال يجب ان تتغير؟	☐

لاستعمال الباحث الميداني فقط:

الرجاء تعبئة الجدول التالي استنادا لاختيارات المرضى للدواء أ أو الدواء ب في كل من السيناريوهات المقدمة لهم .

رقم السيناريو	الدواء أ	الدواء ب
السيناريو الأول		
السيناريو الثاني		
السيناريو الثالث		
السيناريو الرابع		
السيناريو الخامس		
السيناريو السادس		
السيناريو السابع		
السيناريو الثامن		

الرجاء الاجابة عن السؤالين التاليين:

DCA.1	هل أنت مستعد أن تدفع أي مبلغ من المال مقابل الحصول على دواء يؤخذ عن طريق الفم بدل من الابرة؟	1. نعم 2. لا	☐
DCA.2	اذا كان الجواب نعم، ما هو أكبر مبلغ من المال مستعد أن تدفعه مقابل هذا العلاج الجديد بالشهر؟	----------------------------- شيقل جديد	

Appendix 3:

السيناريو الأول:

الخصائص 1	الدواء أ
يقلل الحديد	بشكل متوسط
سهولة الية العلاج	غير سهلة
العوارض الجانبية	قليلة/خفيفة
تكاليف الدواء في الشهر (شيقل جديد)	2,000
القدرة على ممارسة الحياة اليومية بشكل طبيعي	نعم
وجود ألم عند تلقي العلاج	بشكل كبير

الخصائص 1	الدواء ب
يقلل الحديد	بشكل متوسط
سهولة الية العلاج	سهلة
العوارض الجانبية	كثيرة/شديدة
تكاليف الدواء في الشهر (شيقل جديد)	1,000
القدرة على ممارسة الحياة اليومية بشكل طبيعي	نعم
وجود ألم عند تلقي العلاج	لا يوجد

السيناريو الثاني

الخصائص 2	الدواء أ
يقلل الحديد	بشكل متوسط
سهولة الية العلاج	غير سهلة
العوارض الجانبية	قليلة/خفيفة
تكاليف الدواء في الشهر (شيقل جديد)	2,000
القدرة على ممارسة الحياة اليومية بشكل طبيعي	نعم
وجود ألم عند تلقي العلاج	بشكل كبير

الخصائص 2	الدواء ب
يقلل الحديد	بشكل فعال
سهولة الية العلاج	سهلة
العوارض الجانبية	كثيرة/شديدة
تكاليف الدواء في الشهر (شيقل جديد)	0
القدرة على ممارسة الحياة اليومية بشكل طبيعي	لا
وجود ألم عند تلقي العلاج	بشكل كبير

السيناريو الثالث

3 الخصائص	الدواء أ
يقلل الحديد	بشكل متوسط
سهولة الية العلاج	غير سهلة
العوارض الجانبية	قليلة/خفيفة
تكاليف الدواء في الشهر (شيقل جديد)	2,000
القدرة على ممارسة الحياة اليومية بشكل طبيعي	نعم
وجود ألم عند تلقي العلاج	بشكل كبير

3 الخصائص	الدواء ب
يقلل الحديد	بشكل فعال
سهولة الية العلاج	غير سهلة
العوارض الجانبية	قليلة/خفيفة
تكاليف الدواء في الشهر (شيقل جديد)	1,000
القدرة على ممارسة الحياة اليومية بشكل طبيعي	نعم
وجود ألم عند تلقي العلاج	لا يوجد

السيناريو الرابع

4 الخصائص	الدواء أ
يقلل الحديد	بشكل متوسط
سهولة الية العلاج	غير سهلة
العوارض الجانبية	قليلة/خفيفة
تكاليف الدواء في الشهر (شيقل جديد)	2,000
القدرة على ممارسة الحياة اليومية بشكل طبيعي	نعم
وجود ألم عند تلقي العلاج	بشكل كبير

4 الخصائص	الدواء ب
يقلل الحديد	بشكل متوسط
سهولة الية العلاج	غير سهلة
العوارض الجانبية	قليلة/خفيفة
تكاليف الدواء في الشهر (شيقل جديد)	2,000
القدرة على ممارسة الحياة اليومية بشكل طبيعي	لا
وجود ألم عند تلقي العلاج	لا يوجد

السيناريو الخامس

5 الخصائص	الدواء أ
يقلل الحديد	بشكل متوسط
سهولة الية العلاج	غير سهلة
العوارض الجانبية	قليلة/خفيفة
تكاليف الدواء في الشهر (شيقل جديد)	2,000
القدرة على ممارسة الحياة اليومية بشكل طبيعي	نعم
وجود ألم عند تلقي العلاج	بشكل كبير

5 الخصائص	الدواء ب
يقلل الحديد	بشكل متوسط
سهولة الية العلاج	غير سهلة
العوارض الجانبية	قليلة/خفيفة
تكاليف الدواء في الشهر (شيقل جديد)	1,000
القدرة على ممارسة الحياة اليومية بشكل طبيعي	لا
وجود ألم عند تلقي العلاج	بشكل طفيف

السيناريو السادس

6 الخصائص	الدواء أ
يقلل الحديد	بشكل متوسط
سهولة الية العلاج	غير سهلة
العوارض الجانبية	قليلة/خفيفة
تكاليف الدواء في الشهر (شيقل جديد)	2,000
القدرة على ممارسة الحياة اليومية بشكل طبيعي	نعم
وجود ألم عند تلقي العلاج	بشكل كبير

6 الخصائص	الدواء ب
يقلل الحديد	بشكل متوسط
سهولة الية العلاج	غير سهلة
العوارض الجانبية	قليلة/خفيفة
تكاليف الدواء في الشهر (شيقل جديد)	1,500
القدرة على ممارسة الحياة اليومية بشكل طبيعي	لا
وجود ألم عند تلقي العلاج	بشكل طفيف

السيناريو السابع

7 الخصائص	الدواء أ
يقلل الحديد	بشكل متوسط
سهولة الية العلاج	غير سهلة
العوارض الجانبية	قليلة/خفيفة
تكاليف الدواء في الشهر (شيقل جديد)	2,000
القدرة على ممارسة الحياة اليومية بشكل طبيعي	نعم
وجود ألم عند تلقي العلاج	بشكل كبير

7 الخصائص	الدواء ب
يقلل الحديد	بشكل متوسط
سهولة الية العلاج	سهلة
العوارض الجانبية	كثيرة/شديدة
تكاليف الدواء في الشهر (شيقل جديد)	2,500
القدرة على ممارسة الحياة اليومية بشكل طبيعي	لا
وجود ألم عند تلقي العلاج	بشكل طفيف

السيناريو الثامن

8 الخصائص	الدواء أ
يقلل الحديد	بشكل متوسط
سهولة الية العلاج	غير سهلة
العوارض الجانبية	قليلة/خفيفة
تكاليف الدواء في الشهر (شيقل جديد)	2,000
القدرة على ممارسة الحياة اليومية بشكل طبيعي	نعم
وجود ألم عند تلقي العلاج	بشكل كبير

8 الخصائص	الدواء ب
يقلل الحديد	بشكل فعال
سهولة الية العلاج	غير سهلة
العوارض الجانبية	كثيرة/شديدة
تكاليف الدواء في الشهر (شيقل جديد)	2,000
القدرة على ممارسة الحياة اليومية بشكل طبيعي	لا
وجود ألم عند تلقي العلاج	بشكل طفيف

Appendix 4:

Multipliers applied for the clinical features asked in the questionnaire under the clinical burden section.

Question Code	Clinical Feature	Multiplier to be applied
CL1	Transfusion	3
CL2	Desferal	3
CL5	Spleen	1
CL10	Infections	1
CL14	Hospital admissions	1
CL11	Growth	2
CL6	Facial deformity	2
CL12	Sexual dysfunction	3
CL7	Bone, Joint pain	1.5
CL8	Fractures	1
CL3	Leg Ulcers	2
CL13	Mobility	2
CL9	Deafness	1
CL4	Gallstones	1
CL18	Thyroid, parathyroid	1
CL17	Cardiac	4
CL15	Liver	1
CL16	Diabetes	1.5