CHAPTER 3

RESEARCH METHODOLOGY

3.1 Research Design

The design of this Analytic study was based on a retrospective design. Considering the Bone Marrow Transplant as an intervention, the experimental group is the patients who received the Bone Marrow Transplant under Social Security Scheme in Thailand, while the control group is the patients who did not received the Bone Marrow transplant under Social Security Scheme in Thailand. Cost data was collected retrospectively from payer and patient perspectives, while cost of provider was calculated from a secondary data of cost analysis of patients' service at King Chulalongkorn Memorial Hospital: Diagnosis related groups. Effectiveness data was reviewed and collected retrospectively from medical record and survival analysis. The time dimension of this study starts when the patients were approved to entering into Bone Marrow Transplant during 1997 to 2001 and ends on February 1, 2004 upon effectiveness evaluation. The based referring year is 2001 with 3% discount rate.

3.2 Population

1.   Target population and sampling population: employees in Social Security Scheme who suffer illness with 7 hematological diseases during 1997 to 2001.

2.   Inclusion criteria: the patients with 7 diseases who had Bone Marrow Transplant and Conventional Therapy, Conventional Therapy including Chemotherapy, Interferon and Spontaneous Remission. The patients required an approvement from the medical committee of Social Security Office before undertaking the Bone Marrow Transplant.

3.   Exclusion criteria: the patients who died or recover the condition before entering the program by medical committee's approvement.

4.   Sample size: 103 cases of Bone Marrow Transplant and Conventional Therapy who meet the inclusion criteria of the study. Nevertheless, 7 cases were removed from the Social Security Scheme. So, their statuses were recorded on the date they left the scheme and considered as a loss follow up case. And the patient of retied 7 cases, their cost was calculated from the means cost of each year.

3.3 In Perspective of Provider, Patient and Payer

- Provider refers to 5 university hospitals; King Chulalongkorn Memorial Hospital, Ramatibhodi Hospital, Siriraj Hospital, King Pramongkutkloa Hospital and Songklanakarin Hospital.
- Patients refer to formal employees in Social Security Scheme before sickness of 7 diseases with Bone Marrow Transplant and Conventional Therapy.
- Payer refers to Social Security Office who pays additional for Bone Marrow Transplant and Conventional Therapy.

3.4 Data Collection

The calculation of the cost of provider is based on the report of cost analysis of DRG at King Chulalongkorn Memorial Hospital. The payer cost is a secondary data collected from hospital and Social Security Office during 1997 to 2001, while the costs of patients are collecting from telephone interview regarding the cost that occurred during 1997 to 2001. The effectiveness is collecting from medical record, survival analysis and interviewing quality of life from each patient. The complete of the data collection is on February1, 2004.

3.5 Cost Method

    3.5.1 Cost identification of Bone Marrow Transplant and Conventional Therapy is divided in three different perspectives.

- Provider

Though 5 university hospitals are the discussion in this study, but the information of cost analysis is available only in King Chulalongkorn Memorial Hospital. Thus, this study assumed the cost of King Chulalongkorn Hospital in place of other four hospitals due to their similarities as teaching hospitals in medical student level, residency level as well as the fellowships. The five university hospitals are also tertiary care hospitals, contracted hospital, and referred hospitals in supra-contractor of other hospitals in Social Security Scheme. The cost of Bone Marrow Transplant and Conventional Therapy are reference from Cost Analysis of Patients Services in King Chulalongkorn Memorial Hospital: Diagnosis Related Groups. The total cost and unit cost of out-patient department (OPD), in-patient department (IPD) services in each patient ward, and cost of each Diagnosis Related Groups (DRG) were collected within 6 month, during October1, 2000 to March 31, 2001. The hospital departments were grouped into major 3 groups: the Non-revenue Producing Cost Centers (NRPCCs), the Revenue Producing Cost Centers (RPCCs) and the Patient Service Areas (PS). The costs of treating 425 DRGs costs were based on 19,191 patients and were calculated from the unit cost of wards and operation rooms.

- Patient

The cost of patients mainly consists of direct medical cost, direct non-medical cost and indirect cost. Direct medical cost refers to all medical expense that patients have to pay for the treatment, including lab charge, drug cost, secondary opinion, and etc. Direct non-medical cost refers to various categories of transportation, for example travelling expenses, supplemental food, media expenses, supplies and materials associated with Bone Marrow Transplant and Conventional Therapy, and etc. Indirect cost comes from the

donors of Bone Marrow Transplant and care taker of programs as well as transportation cost, travel expenses, salary, wages, fringe benefit, and etc. However, there are 7 patients who were retrenched from Social Security Scheme, where 1 patient from Bone Marrow Transplant and 6 patients from Conventional Therapy. Then, the cost of retrenched patient was estimated from means cost of patient in each particular year in order to complete the calculation.

- Payer

The cost from payer perspective is an additional payment for 5 university hospitals. In Bone Marrow Transplant, the Social Security Office allows payment for the procedure of Bone Marrow Transplant for 3 times and HLA-typing until patient can be matched with related-HLA donor. In Conventional Therapy, Social Security Office allows additional payment once a year for Chemotherapy, but allows fee for service with Interferon and payment based on capitation with registered hospital including these 5 university hospitals.

3.5.2 Cost calculation of Bone Marrow Transplant and Conventional Therapy in each perspective

Discount Rate

In this study, it used 3% of discount rate which traditionally there have been 2 competing theories regarding the proper measure for the discount rate for public projects (the social discount rate)

a) The real rate of return (to society) forgone in the private sector (known as the social opportunity cost approach). This can be estimated empirically, although not without controversy;

b) The social rate time preference, use the social rate of time preference to discount cost and benefits, once they have been transformed. The stream of program costs is transformed into the corresponding stream of consumption gains.

From Oxford Medical Publication, Methods for the Economic Evaluation of Health Care Program, There is suggested in practice analysis has followed one of two conventions in choosing a discount rate. First, in jurisdictions (like the United Kingdom); where the government announces a common discount rate for all public sector projects, the advised rate is used. Alternatively, where there is no announced rate, the convention has been to use a rate consistent with the existing literature. In Thailand, there was not the government announces a common discount rate for all public sector projects so the alternative has been to use a rate consistent with the existing literature. The US Public Health Service Panel on Cost-Effectiveness in Health and Medicine (Drummond et al. quote in Gold et al. 1996) has recently revisited the issue of discount rate for health programs. They argue that costs and consequences should be discounted at a rate consistent with the shadow-price-of-capital approach to evaluating public investments. Currently they estimate that 3% would be the most appropriate real (riskless) discount rate for economic evaluations.

- Provider

a) Separate each part of King Chulalongkorn Memorial Hospital into 30 NRPCC, 26 RPCC and 89PS.
b) Cost consists of labor cost, material cost, capital cost, direct cost, indirect cost into Routine Service cost, and Medical Care cost.
c) From allocating RPCC and NRPCC to PS, there are 67 allocating criteria in the study of cost analysis in King Chulalongkorn Memorial Hospital.

d) Unit cost of routine service cost comes from labor cost, material cost, capital cost and indirect cost which allocated from RPCC and NRPCC. These will be concluded as routine service cost.

e) Routine service cost is divided by number of service for OPD and by length of stay for IPD. These will be concluded as a unit cost of routine service.

f) Unit cost comes from Lab cost, Radiology cost, Pharmacy and Supplies cost. These will be calculated as a Medical care cost

g) Medical care cost plus Routine service cost is considered as a Full cost.

h) Full cost is divided by number of service for OPD and by length of stay for IPD. These will be concluded as Unit cost for each ward (PS).

Table 3.1 The Criteria of Allocation in King Chulalongkorn Memorial Hospital

Code	Units	Allocation criteria
101	Equipment	No. of set
102	Milk mixer	No. of patient
103	House keeper	No. of cloths
104	Nurse administration	No. of nursing personal
105	Dorm	No. of personal
106	Dead body	No. of dead body
107	Help taker	No. of services
108	Development of health	No. of OPD
109	General administration	No. of personal
110	Package	No. of material
111	Building	Unit of area
112	Fixing	No. of items
113	Vehicles	No. of paper request
114	Supplies	No. of supplies
115	Guard	Unit of area

116	Secretary	No. of personal
117	Personal	No. of personal
118	Media	No. of OPD
119	Telephone	Cost of telephone bill
120	Work sheet	No. of times
121	Vice administration	No. of personal
122	Publication	No. of publication
123	Finance and accountant	No. of personal, No. of OPD
124	Social welfare	No. of consult cases, No. of IPD
125	Statistic	No. of IPD
126	Nutrition	No. of personal, No. of IPD
127	OPD	No. of OPD
128	Card	No. of OPD
129	Admit	No. of IPD
130	Health promotion	No. of OPD
131	Computer	No. of computer
134	Anatomy	% of physician work
135	Biochemistry	% of physician work
136	Anesthesia	% of physician work
137	Medicine	% of physician work
138	Surgery	% of physician work
139	OB-GYN	% of physician work
140	Pediatric	% of physician work
141	Eye	% of physician work
142	Orthopedics	% of physician work
143	ENT	% of physician work
144	Psychology	% of physician work
145	Community medicine	% of physician work

201	Cardio-Cath	No. of operation
202	OR of specific Surgery	No. of operation
203	OR of general Surgery	No. of operation
204	OR of NS	No. of operation
205	OR of ENT, Eye	No. of operation
206	OR of Emergency	No. of operation
207	OR of Orthos	No. of operation
208	OR of OB-GYN	No. of operation
209	OR of Pediatrics	No. of operation
210	OR of CVT	No. of operation
211	Delivery room	No. of operation
212	Hemodialysis	No. of operation
213	Rehabilitation	No. of patients
215	X-ray	No. of patients
222	Dental care	No. of patients
223	Cardio-center	No. of patients
224	Medical supplies	Cost of supplies
225	Pharmacy	Cost of pharmacy
226	Blood bank	No. of services
368	S-ICU	No. of patients
374	CVT-ICU	No. of patients
373	P-ICU	No. of patients

i) Disease related group (DRG) is calculated from medical record from October, 2000 to March, 2001 by method of transforming HN into computer data using program Converse HN. Then categorizing the disease by ICD-10 and ICD-9CM and transforming into DRG with Visual FoxPro6 and Thai DRG Grouper Version programs.

j) Analyzing DRG data links with HN data and separated into individual ward. Summation length of stay in the same DRG, then multiplying with Unit cost in each ward. These are concluded as a Person full cost for each DRG.

k) Person full cost is divided by number of patient as Unit cost of DRG with out operation room (OR).

l) If DRG with OR means a disease, the study will calculate it differently.

m) Regarding, before calculating Full cost, there will need to select patient with operation and then assume number of hours in operation by anesthetic physician. These will be concluded as OR-Hr.

n) Taking the previous Unit cost of ward to cut off cost of operation to allocate to ward. These will be calculated to be Unit cost without OR.

o) Taking the OR-Hr multiplied by number of patients will share the same operation in the same DRG and then sum up them. These will be calculated to be Proc OR-Hr.

p) Unit cost without OR multiplied with length of stay of IPD in the same DRG. These will be calculated to be a Full cost without OR.

q) Full cost without OR plus Sum of OR-Hr and then divided by number of patient in the same DRG. These are calculated to be Unit cost of DRG with OR.

r) Calculating the future value for each year based on DRG in year 2001, in order to produce the future value of cost in Bone Marrow Transplant and Conventional Therapy.

The cost of provider perspective is calculated as the following

1. Chronic Myeloid Leukemia (CML) in chronic phase, with BMT and dead*642,686.98, with BMT and alive*519,279.36, without BMT and dead*218,641.53, without BMT and alive*66,708.11.

2. Acute Non-Lymphocytic Leukemia (ANLL) in first complete remission phase, with BMT and dead*642,686.98, with BMT and

alive*519,279.36, without BMT and dead*121,035.98, without BMT and alive*66,708.11.

3. Acute Lymphocytic Leukemia (ALL) with high risk in first complete remission and Acute Lymphocytic Leukemia (ALL) with normal risk maybe allowed in secondary complete remission, with BMT and dead*642,686.98. with BMT and alive*519,279.36, without BMT and dead*121,035.98, without BMT and alive*66,708.11.

4. Malignant Lymphoma with relapse or refractory period from first line chemotherapy or Non-Hodgkin's lymphoma (NHL), with BMT dead*642,686.98 and alive*519,279.36, without BMT and dead*218,641.53, without BMT and alive*66,708.11.

5. Multiple Myeloma (MM), there was no cases of MM available in this study.

6. Severe Aplastic Anemia (SAA), with BMT and dead*332,038, with BMT and alive*381,340.75, without BMT and dead*111,011.08, without BMT and alive*111,011.08

7. Breast Cancer with lymph node metastasis > 10 nodes, there was no cases of MM available in this study.

■ Patients

The cost from patients calculated from patients. care taker. donors, and family members both in Bone Marrow Transplant and Conventional Therapy. Due to 7 patients retrenched from the Social Security Scheme, their cost estimation was calculated from a mean cost in each year upon the year that they were approved to enter the Bone Marrow Transplant and Conventional Therapy.

The cost was collected from patients and used the present value formula to produce based year in 2001 with 3% discount rate. Indirect costs of patient (loss wages)

to patients were not calculated both in Bone Marrow Transplant and Conventional Therapy because patients were assumed to be too ill to return to work while they still receiving the treatment during 1997 to 2001.

■ Payer

The costs of payer were calculated from Social Security Office data and produced a future value based on year 2001 with discount rate. In the first one and a half year, the Social Security Office allowed 600,000 baht per case reimbursement for Bone Marrow Transplant without Tissue examination additional payment. But nowadays the payment for Bone Marrow Transplant has gone up to 750,000 baht per case with 3 times allowance, while the Tissue examination is only 7,000 baht per each time with out limitation.

Payment in capitation is 30,000 per case per year for Chemotherapy and fee for service for Interferon. The payment of Bone Marrow Transplant maybe comes from the previous study of Cost Analysis of Bone Marrow Transplantation in Hematological Disorders at Chulalongkorn Hospital, Thailand. The direct provider cost per case treated was averaged as 645,535 baht, cost per patient with intermediate effectiveness was 821,590 baht and cost per patient with full effectiveness was 1,063,234 baht in 1997's price. Intermediate effectiveness means the patients who survived more than 6 months after Bone Marrow Transplant but less than 1 year. Full effectiveness means more than 1 year survival after Transplantation.

3.6 Effectiveness Method

3.6.1 Effectiveness Identification of Bone Marrow Transplant and Conventional Therapy

■ Number of life saved

Refers to a status of patients in Bone Marrow Transplant and Conventional Therapy, during 1997 to 2001, who survived through these programs. The study applied the survival rate from the result of Bone Marrow Transplant and Conventional Therapy to estimate the number of life saved together with the status of patients that recorded including some patients who lost follow up from the Social Security Scheme.

■ Number of year of life saved

Refers to a number of years extended after Bone Marrow Transplant and Conventional Therapy, and calculated from long-term survival rate of Bone Marrow Transplant and Conventional Therapy. Due to unavailable result on the survival rate in Bone Marrow Transplant and Conventional Therapy of the same stage of 7 Hematological diseases in literature review, this study intended to use the survival rate of Bone Marrow Transplant and Conventional Therapy even though the result has not yet reach the 5-year-survival-disease-free. Other previous results in many studies come from variety of Bone Marrow Transplant and Conventional Therapy such as Autologous Bone Marrow Transplant, HLA-Compatible unrelated donor, Interferon, and other medical method that differently performed in Thailand.

The study also deployed the life expectancy of general population in Thailand to estimate the year of life extended with survival rate existing between Bone Marrow Transplant and Conventional Therapy.

■ Quality of life

Due to the limitation of this study which tool is not affordable to test for validity and reliability of questionnaire, by that reason, this tool will provide to illustrate quality of life of

patients after received the treatments. There are only 7 patients left in the Social Security Scheme: 1 patient left out from Bone Marrow Transplant and 6 patients left from Conventional Therapy. So, the quality of life was done in descriptive study as only 43 living patients after received the Bone Marrow Transplant and Conventional Therapy, 27 patients of Bone Marrow Transplant and 16 patients of Conventional Therapy. Then, 6 months later is considered as acute period, 12 months later as intermediate period and more that 12 months until death or until complete of data collection on February1, 2004 considered as a long - term quality of life. Though the following points were used for the Functional Class in general medical condition, but not as an entire estimation for Functional Class criteria. More questions to be answered such as mobility, self-care, usual activities, depression, anxiety, pain, discomfort and other complaints of specific patient of Bone Marrow Transplant and Conventional Therapy.

From Health Decision Strategies provided programs which developed from concern about the rising cost of health care, new and innovative approaches to cost-effective, quality health care must be found. EQ-5D is a measure of health status for use in evaluating health and healthcare. It provides a simple descriptive profile and generates a single index value for heath status on which full health is assigned a value of 1 and death a value of 0.

One of the components of the EQ-5D is the self-classifier which describes health status according to 5 dimensions. Each dimension is divided into 3 levels. By combining different levels from each dimension, EQ-5D defines a total of 243 health states. These may be converted to a score using "sets of values" derived from general population samples. But this program is used for the demonstration only that calculated scores are for illustration and not based on official algorithms. Even though from that reason, this information will be given to help the descriptive data more clearly picture of quality of life.

Quality of life for the rest of the patients' life, it will be calculated from the expert opinion, 6 Hematologist in 5 university hospital of Bone Marrow Transplant under Social Security Scheme, they will give the opinion in term of quality of life of patient in both program to realize the well-being of the rest of patients' life.

Definition of terms in health condition

1. Mobility: ability of walking, go up the stairs, go down stairs, how long the patient can walk and in what condition, for example 50 meter in one trip, confided in bed or in the room or in the house, etc.

2. Uncomfortable or Pain: ability in sense a pain, a little pain, sharp pain, tolerated pain, in tolerated pain, have to take a pain killer and after pill what condition of pain, can sleep at night, ever wake up with pain, uncomfortable of other parts of the body, how the degree of uncomfortable, none or slightly or moderate or severe, etc.

3. Anxiety or Depression: ability of mood, the behavior of eating, sleeping, memorizing, and represent of mood and emotional. The pattern of the speech and content of the speech, knowing reality condition, feeling degree of anxiety or depressed in term of none, slightly, seldom, sometimes, moderated, severe, etc.

4. Self-care: ability to dress up by themselves, glooming, change the cloths, take a bath, wash the hair, combing, washing, take the make up for the women, caring themselves hygiene, etc.

5. Usual activity: ability to work or study as much as before received the treatment, can do hobby as usual such as sporting, gardening, shopping, reading, etc.

3.6.2 Effectiveness Calculation of Bone Marrow Transplant and
Conventional Therapy

- Number of life saved

Divided patients into 2 groups; Bone Marrow Transplant group and Conventional
Therapy group. And then calculated the number of survival patients in each group with
survival analysis. There are an accumulating number of lives saved for each program.

Life saved = Total number of patients in each treatment * Survival rate

- Number of year of life saved

The extended year of life saved in Bone Marrow Transplant and Conventional
Therapy was calculated from the patients with survival rate in order to predict the number
of year of life saved in Bone Marrow Transplant and Conventional Therapy, in comparison
with the mean age in the Social Security Scheme. The life expectancy for general
population is 71.45 year old where mean age of the study was calculated from the basis
data of Bone Marrow Transplant and Conventional Therapy. The study also estimated a
long term survival by assuming that longevity of patients who survive for 3 year (2001 to
2004) is equivalent to the general population.

Number of year of Life Saved = Total patients * Survival rate * Expected year
*Expected year = Life expectancy of general population – mean age in this study

- Quality of life

The quality of life was described by patients who remain living after Bone Marrow
transplant and Conventional Therapy and to make a descriptive comparison on the

problems of both programs. Also life after treatment in which way can return the better result in term of quality of life.

$$QALY = Utility * Life\ Expectancy$$

3.6.3 Survival Analysis of Bone Marrow Transplant and Conventional Therapy

Survival Analysis

The clinical studies of medical or surgical interventions for hematological disorder will be used in this study, for example, success usually is measured in terms of the length of time that some desirable outcome (such as survival or remission of disease) is maintained. An analysis of the time-related patterns of survival commonly involves using life tables and techniques that were developed in the insurance field, and survival analysis requires that the dependent (outcome) variable be dichotomous (e.g., survival/death, success/failure, or presence/absence of improvement). The reporting of the proportion of patients who are alive at the termination of a study's observation period is obviously inadequate, because it does not account for how long the individual patients were observed, nor does it consider when they died or how many were lost to follow-up. The statistical techniques use to control for these problems are person-time methods and life table analysis using the actuarial method or the Kaplan Meier method.

3.7 Cost-Effectiveness Analysis

Cost-Effectiveness Analysis is not uniformly applied in the healthcare system. Decision makers often adopt new treatments without knowing if they are cost-effective. Even when cost-effectiveness has been studied, decision makers may not be able to interpret the data, or they may not agree with result. Despite this limitation, cost-effectiveness is increasingly used to support healthcare decision makers.

Cost-Effectiveness Analysis is a tool used to assist decisions about which medical care should be offer. It is a method of comparing the cost and effectiveness of two or more alternatives. Such comparisons are useful when Conventional therapy considered is a standard care, as this allows the decision maker to consider the Bone Marrow Transplant is better than the status quo.

Furthermore, knowledge of the incremental cost-effectiveness of interventions that have been approved can be helpful. The criteria for assessing cost-effectiveness are various among dissimilar healthcare systems and in different countries.

The conclusion methodology of this study as following

1. Statistical data collection comes from Social Security Office, other health care agencies, and patients about the Bone Marrow Transplant and Conventional Therapy during 1997-2001.

2. Data analysis for the patients who pass all criteria's and going to perform the bone marrow transplant, patients who don't receive Bone Marrow Transplant and be HLA-identical donor is the equivalent patients treat with conventional therapy. Patients with HLA-identical donors and received the Bone Marrow Transplant considered as the Bone Marrow Transplant group.

3. Results comparison of patients who were treated with bone marrow transplant and patients who were treated with conventional therapy.

4. Use the Cost-Effectiveness method to measure the Bone Marrow Transplant program and analysis the Cost-Effectiveness ratio comparing between Bone Marrow Transplant and Conventional Therapy.

5. Use the results from the Cost-Effectiveness Analysis to evaluate the Bone Marrow Transplant program in perspective of provider, payer and patient compare with effectiveness consist of life saved, years of life saved and quality of life.

6. Incremental Cost-Effectiveness Analysis to evaluate the Bone Marrow Transplant program in perspective of provider, payer and patient compare with effectiveness consists of life saved, years of life saved and quality of life.

7. Timeframe covers 1997 – 2001, where the priced year is 2001 with 3% of discount rate.

8. Data collection of effectiveness in term of life saved, number year of life saved and quality of life is completed on Febuary1, 2004.

9. Sample size is 103 patients under Social Security Scheme, Thailand.

3.8 Sensitivity Analysis

There should be undertaken to evaluate the effect of different discount rate among, 3% discount rate of provider, patient and payer, Consumer Price Index (CPI) of all 3 perspective and different discount rate in each perspective; Marginal Loan Rate (MLR) of provider, CPI of patient and Interest Rate (IR) of payer. These will be affected or not in on the cost.

Because of life expectancy for patients in 7 Hematological diseases after received Bone Marrow Transplant and Conventional Therapy with 3-year-disease-free that is very difficult to estimate for life expectancy in each group of treatment so there should be done to estimate the effect of different life expectancy; 10 years, 20 years, 30 years and 40 years.