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CHAPTER 2

LITERATURE REVIEW

There are many aspects relevant to this study. There is no exact definition of catastrophic illness and thus there are uncertainties concerning in both financing and reimbursement for insured persons. Severe hematologic disorders constitute one group of catastrophic illness as with a common treatment , bone marrow transplantation is the choice treatment for severe hematologic disorders, it is a highly technical and complicated procedure, and is very expensive. No patient is able to work independently after discharge, so they have to lose their income for quite a long period of time and this absolutely affects their economic status. As well as the high expenditure for treatment, another aspect is the effectiveness of bone marrow transplantation when compared to its costs.

In 1990, The World Bank and the World Health Organization studied about the impact in loss of healthy life from about 100 diseases and injuries. The global burden of diseases (GBD) combined the loss of life from premature death in 1990 with the loss of healthy life from disability. The GBD was measured in units of disability- adjusted life years (DALYs) The criterion for selecting the diseases and injuries studied was the expected magnitude of the burden within a specific age group. The selected diseases and injuries accounted for more than 90% of premature deaths and probably for a similar proportion of the burden attributable to disability. The results found are :

1.The burden of disease in Female by cause in worldwide level (In hundred of thousand of DALYs lost) of Lymphoma was 11.4, Leukemia was 18.0, and Anemia was 83.0. For Males, the burden of disease by Lymphoma is 20.3, Leukemia is 23.3 , and Anemia is 57.2

2.The Deaths by cause In worldwide level (in thousand of deaths) of Lymphoma was 218 , Leukemia was 219 , and Anemia was 163 (World Development Report, 1993)

From the results above , there were a lot of people died because of hematologic disorders like lymphoma , leukemia , and anemia In one year so the productivity loss occurred in a large amount all over the world.

As hematologic disorder is Catastrophic illness so it is wondering that whether it is worthwhile to spend a lot of money for its treatment , Bone marrow transplantation to save life. Because BMT is only one choice of treatment to cure this severe illness therefore there is another one aspect to be considered which is the effectiveness of BMT in hematologic disorder.

2.I Catastrophic Illness.

Catastrophic Illness (CI) is illness that has very high expenditure for treatment by the patients and their families because it is a big burden for the household to be responsible for. (Khongsil , 1997) They often have to sell producing factors such as : land , cows , buffaloes , or they have to take a loan from external sources, especially it seeking treatment at private hospitals. After being admitted to private hospitals for some time , normally , the patients would be referred to government hospitals, so involving the problem of referral between the sending hospital and the accepting hospital. Moreover , if the patients cannot pay for the health services at the government hospitals , there would be a big burden to the government which would then incur most of the costs for the operations, so it has to get compensation from other resources for example ; from the Civil Servant Medical scheme or general hospital revenue. The main problems of the high expenditure for the catastrophic illness are : the patients who cannot pay for the full charges, and have no low income scheme , the loan from the social network of the patients , and sell their assets and producing factors leading decreased the financial resources of households.

Catastrophic Illness is a major hazard, because it causes productivity loss to the patient. Example of catastrophic illness are Trauma , spinal cord Injury , cancer , aplastic anemia , mental problems and a senility. If one of these illness occurred to anyone or any family , there will absolutely affect their financial status.

Catastrophic Insurance should be considered in relation to cost - effectiveness. Besides the present treatment in Thailand now that can lead to long term recovery with a high quality of life , the treatment and the financial implications can usefully be compared with , for example , the treatment of acute pediatric leukemia and breasts cancer or coronary bypass surgery. It seems that the type of treatment and the difficulties of treatment affect the goals of the investment, as to whether there would be any good result for life and health. As for the very high expenditure in treatment, for example , liver cancer or spleen cancer have a low effectiveness of treatment , but a similar high cost. (Khongsil , 1997)

Many countries have established the relevant health insurance schemes. For example , in the Netherlands , the government established the National Health Insurance for Catastrophic Risks (AWBZ) to regulate everyone who has income in order to cover the premium to the health expenditure fund for people in case of :

A) chronic illnesses which require treatment more than 1 year.

B) mental or physical handicapped that they have to be admitted to hospitals.

C) geriatric nursing care

In Singapore , the government has established the Medishield fund by deducting from the Medisave fund of everyone who has income except those who does not want to join this scheme. Medishield will be responsible for 80% of the excess expenditure that they cannot afford. (excess 20 % of annual

income). These two examples can illustrate the different definitions of catastrophic illness and indicate the different ways to manage this class of illness in each country.

2.2 Health Service System and Catastrophic Illness in Thailand .

The most important point in suggestions for the health service system and catastrophic illness in Thailand is " accessibility" or a chance for anyone to get health care service, especially the poor people. There are lots of difficulties to enter the health care service from the government sector :

A) Occupancy rate : because there are lots of patients in every government hospital so some patients have to firstly consume services from the private sector even though the charges are very expensive before being referred to the government hospital. If they still have some money at this stage , they would have paid some to the government hospital until the last reserve was gone. If they cannot be referred to the government hospital , they have to accept the catastrophe as untreatable, they have no alternative.

B) Some consumers do not believe in health care services from the government sector so they prefer to consume services from the private sector but finally , as the limited money is consumed they would get into a catastrophic situation.

There are alternatives to cope with the above problems :

- Improving the health care services in both quantity and quality : in quantity ,the hospital should be able to serve more patients and in quality , the hospital should separate the patients in each department into intensive care beds and normal care beds. For example , patients who are admitted for rehabititation , the non - responsive patients who have to get parenteral nutrition, and the chronic

diseased patients who do not need intensive care. This is a way to decrease the number of occupied beds to make way for the acute phase patients.

- Service charge / price control in private sector so that the patients can get quality care at reasonable price.

Thai health care system is also one part of the general Economic system. There are both government and private sectors but the people as consumers still have not enough information about the health care services. There are 3 classes of the consumers :

I.) Low income people or poor people : this group will get the healthcare services from the government sector at health centers , district hospitals , general hospitals , and regional hospitals.

II.) Middle class people which are contributors to insured groups like the Health card scheme , Social Security scheme , Civil Servant Medical scheme , and Workmen Compensation scheme. They can choose whether to get the services from the government or the private sector.

III.) Rich people who may have private Insurance or can afford to pay out - off - pocket for the high charge of the private sector. They also can choose to get services from efficient and high quality government hospitals as they have ability to pay.

2.3 Criteria and Rate of Reimbursement in the Social Security Scheme in Thailand

As the SSO has just approved the bone marrow transplantation to be included in the criteria of reimbursement for high health expenditure so there are many criteria for the insured people which they have to know. According to the Proclamation of the Social Security Organization , the Third Proclamation : Criteria and rate of reimbursement in case of injury or illness not caused by working , 1996, It stated that the SSO would be responsible for the expenditure of organ

transplantation (include BMT) which is equal to Bt.600,000 per case. In such a case, the hospitals must be approved by the medical committee in order to be the contractor providers. The insured person would have this right if he/she was included in the following criteria :

A. Insured person must be ill by these diseases :

1) Chronic myeloid leukemia in chronic phase.
2) Acute nonlymphocytic leukemia in the first complete remission.
3) Acute lymphocytic leukemia in the first complete remission for the high risked patient and in the second complete remission for the normal risked patient.
4) Relapse or refractory malignant lymphoma to the first line chemotherapy .
5) Multiple myeloma.
6) Breast cancer in which cancer cells spread to exceed 10 lymph nodes.

B. Insured person must not get the above illness before he being insured with the SSO.

C. The medical committee will advice SSO. in order to permit the insured person to have BMT.

In the case that the insured person who gets BMT permission from SSO. is injured or sick from other diseases , he must contact the contractor provider during the period of treatment. (The Third Proclamation : Criteria and rate of reimbursement in case of injure or sick that not caused by the working , SSO. , 1996)

2.4 Indications for Bone Marrow Transplantation.

In 1994 , The Children's Hospital , Philadelphia assessed the indications for bone marrow transplantation and found that BMT is used to treat a number of cancers , blood diseases and immune disorders for which BMT has been shown to be effective or has the potential to be effective. This table shows the selected uses for BMT. (Table 2.1)

Table 2.1 Indications for Bone Marrow Transplantation

Malignant Diseases
Leukemia
Acute and chronic myelogenous leukemias
Acute lymphocytic leukemia
Preleukemia
Myelodysplastic syndromes
Lymphoma
Hodgin 's Disease
Non-Hodgkin ' s lymphoma
Solid tumors
Marrow failure disorder
Acquired disorders
Aplastic anemia
Paroxysmal nocturnal hemoglobinuria
Myelodysplastic syndromes
Immunodeficiency disorders
Severe combined immunodeficiency syndrome (SCIDS)
Congenital neutropenia
Chediak - Higashi syndrome
Wiskott - Aldrich syndrome
Hematopoietic defects
Thalassemia
Fanconi 's anemia
Chronic granulomatous disease
Osteopetrosis
Storage Diseases
Mucopolysacchridoses

Source : The Children 's Hospital of Philadelphia , 1994

2.5 Marrow Donation

In 1997, William Peters studied about the marrow donation in BMT and found that the chance of a bone marrow match between two unrelated people ranged from 1 in 100 to 1 in 2 million , depending on the genetic code of the patient. Matches are easier to find among siblings. About 30 % of patients have a brother or sister who is able to donate marrow. The chances of a match between two unrelated persons varies according to their Human Leukocyte Antigen (HLA) typing or genetic code , the more common a patient's antigen , the better the chances of finding a matching donor. Usually , a patient's HLA among members of their own ethnic group - for example ,it is easier for an African American to find a matching donor among other African American.(Peters , 1997)

2.6 Long Term Result of Allogeneic Bone Marrow Transplant.

Dr.Imad A. Tabbara indicated about the long term results of allogeneic BMT for several blood diseases as following :

In acute myelogenous leukemia , allogeneic BMT in young adults with HLA - matched donors in first complete remission (CR) is associated with long term , disease - free survival (DFS) rates of 40% to 70%. DFS in patients receiving transplants at the time of early first relapse is around 30%. Patients who have a refractory disease or have transplants in second or subsequent remission have a DFS rate between 10% and 40% .

In adults with acute lymphoblastic leukemia , allogeneic BMT is recommended in second remission. The DFS rate is comparable in patients with low - risk acute lymphblastic leukemia whether they have transplants in first or second remission. However, in patients with high-risk disease, such as those with Philadelphia chromosome - positive acute lymphoblastic leukemia , allogeneic BMT may be indicated in first

remission. In chronic myelogenous leukemia , allogenic BMT within a year of diagnosis and while the diseases is in chronic phase is associated with a DFS rate of approximately 70%. The use of hydroxyurea rather than bisulfan as initial treatment for these patients appears to be associated with a better prognosis.

Allogeneic BMT is considered to be the treatment of choice in young patients with myelodysplastic syndrome who have an HLA - matched sibling donor. Limited data suggest a 30% to 40% long term DFS rate. Allogeneic BMT in patients with multiple myeloma is associated with a CR rate of approximately 40% and 20% DFS on follow up at 2 years. The overall relapse - free survival rate of patients who achieve CR after BMT is 35% at 6 years. The transplant - related mortality rate is approximately 50% , with infections , interstitial pneumonitis , and acute and chronic GVHD accounting for the majority of causes of death. Favorable pretransplant prognostic factors include female sex , stage I disease at diagnosis , one line of previous treatment , and being in CR before allogeneic BMT. The most important postransplant prognostic factor is the achievement of CR.

In patients with intermediate or high - grade non Hodgkin 's lymphoma , DFS with allogeneic BMT at 2 to 3 years of follow up is superior to that seen with autologous BMT , most likely due to a graft-versus-lymphoma effect. However , prospective , randomized trials are needed to confirm these results and to assess the long term outcome of these patients. Good prognostic factors include transplantation early in the course of the disease , sensitivity of the disease to conventional chemotherapy , good performance status of the patient , and absence of bulky disease. In Aplastic anemia , previous transfusion therapy has a significant negative impact on transplant outcome. In these patient , allogeneic BMT is superior to other immunosuppressive therapy in producing a complete hematologic remission. However , in older patients and in patients with milder disease , an initial trial of immonosuppressive therapy may be indicated.

Allogeneic BMT has been shown to be highly effective in patients with thalassemia major. The most important negative prognostic factor appears to be the presence of hepatic cirrhosis. Allogeneic BMT has been used to a limited extent in sickle cell disease. In the United States , five patients received HLA - matched , sibling donor marrow grafts. with a median follow up of 16 months (range , 8 months to 9.3 years) , all five patients were alive , with donor engraftment as well as the donor's hemoglobin electrophoretic pattern. In Europe , 41 patients with sickle cell disease have had allogeneic BMT from sibling donors. At a follow up of 2 to 74 months , all patients were alive , and 38 patients (92%) had the donor 's hemoglobin electrophoretic pattern and were free of symptoms.(Imad , 1996) These limited experimental data indicated that allogeneic BMT may cure sickle cell disease in selected patients.

2.7 Costs for the Transplantation.

In 1994 , Aplastic anemia Foundation of America studied about the costs for transplantation and found that the cost of any surgery varies significantly between surgeons , medical facilities , and regions of the country. Patients who are younger , sicker , or need more extensive surgery will require more intensive and expensive treatment. The approximate cost for a bone marrow transplantation varies from $ 190,000 to $ 410,000 depending on the cross - matching between the recipient and the donor (for example ; allogeneic related , autologous , and allogeneic unrelated). Surgery charges can be separated into five parts :

1.surgeon ' s fee : variable

2.anesthesiologist ' s fee : averages $ 350 to $ 400 per hour.

3.hospital charges : basic rate averages $ 1,500 to $ 1,800 per day (more for the intensive care unit or ICU or private room)

4.medication charges : $ 200 to $ 400.

5.additional charges : assisting surgeon , treatment of complications , diagnostic procedures , medical supplies , and equipment use.

Insurance coverage for surgery expenses depends on many factors and should be explored for each individual instance. (Aplastic Anemia Foundation of America , 1994)

Anna T. Meadows et. al. also studied about the cost of BMT and found that the BMT procedures require up to 6 months of hospitalization and extensive care that can cost $100,000 to $250,000 or more. While health insurance usually covers most of these expenses , the family may still be responsible for a considerable amount. (Meadows et al , 1994)

In 1995, Intragumtornchai et al studied about costs for BMT at Chulalongkorn Hoapital, Thailand and found that the average total cost In allogeneic BMT accounted for Bt.977,300 , In allogeneic PBSTC was Bt.908,000 , and in autologous PBSTC was Bt.847,000 which they estimated these costs from the charge price only, not in term of real economics cost .(Intragumtornchai et al , 1995)

From the studies above , there are lots of differences between cost of BMT which depends on each organization. Anyway , BMT is a very high cost of treatment.

2.8 Cost Effectiveness of Bone Marrow Transplantation.

In 1989 , Welch H.G. and Larson E.B. identified the cost effectiveness of bone marrow transplantation compared to the conventional chemotherapy , they evaluated the resources used in the care of adult patients with acute nonlymphocytic leukemia who were enrolled in a prospectively trial and received induction chemotherapy at a single university hospital and found that the total costs over five were estimated at $193,000 per patient for transplantation and $136,000 per patient for chemotherapy (P = 0.02) At five years , the costs per year of saved (life-year) were nearly equal ($62,500 per life-year for transplantation VS. $64,000 per life-year

for chemotherapy) because of the better rate of disease - free survival in patients who underwent bone marrow transplantation. They concluded that the cost - effectiveness of bone marrow transplantation to treat acute nonlymphocytic leukemia compares favorably that of chemotherapy and could be further enhanced if intensive care resources were used more selectively. (Welch and Larson, 1989)

2.9 Economic Evaluation of Allogeneic Bone Marrow Transplantation.

In 1996 , the American Society of Clinical Oncology , by Ronald B. et al. Identified the Economic Evaluation of Allogeneic Bone Marrow Transplantation : a Rudimentary Model to Generate Estimates for the Timely Formulation of Clinical Policy. The purpose of this study is to provide an evidence - based approach to the formulation of clinical policy with respect to allogeneic bone marrow transplantation that involves perceived trade off between two major factors : costs and consequences. For the sample and methods are adults with acute myelo leukemia (AML) in second complete remission (2CR) and those with acute lymphoblastic leukemia (ALL) in first complete remission (1CR) were assigned to BMT or control group solely on the availability of a suitable donor and they found that the incremental cost (in 1992 Canadian dollars) per life-year gained by BMT (cost-effectiveness) for AML(2CR) was $ 29,200 ; and for ALL(1CR) was minus $29,200. For AML (2CR), allogeneic BMT creates better outcomes than standard treatment , but is more costly. For ALL (1CR) , both the costs and outcomes are similar for BMT and standard therapy. Quality adjustment made to life-years gained did not change these conclusions. (Ronald et al , 1996)

2.10 Effectiveness of Bone Marrow Transplantation.

In a study published in the Feb. 1, 1998 issue of Blood , Memorial Sloan-Ketting researchers reported that 77% of adult AML patients who received a transplant of T-cell depleted bone marrow from a donor were cancer free as long as six years later. Less than 4% of patients suffered a relapse. (Memorial Sloan-Ketting Cancer Center , 1998) This is especially significant because the majority of patients with AML are at high risk for cancer recurrence even if chemotherapy can successfully produce remission.

In 1997 , Hillard M. L. sought to clearify whether older patients fare as well as younger after high dose chemotherapy and autologous blood and bone marrow transplantation and found that although initially autologous transplantation is used in young patients (less than 45 of age), now it is regularly used in persons over 50 years of age and increasingly in persons older than 60 years of age. However , high dose chemotherapy , as used in autotransplantation, is associated with substantial risks of infection and toxicity to heart, lungs, liver, kidney, and other organs. Older age may increase susceptibility to such toxic effects.(University of Pennsylvania Cancer Center , 1997)

In 1996, The Autologous Blood and Marrow Transplant Registry of North America (ABMTR) studied 3,744 patients receiving autotransplants for NHL to determine whether outcome differed among patients in four age ranges : 30-39, 40-49, 50-59, and 60-69 years of age by one hundred-day mortality rates and two-year survival rates were compared and found that there was little difference between the outcomes of autologous transplants in younger and older patients and the older patients can tolerate and benefit from more intensive cancer therapies. (University of Pennsylvania Cancer Center , 1997)