Cost-effectiveness of early rehabilitation after Traumatic brain injury

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SUMMARY

Traumatic brain injury (TBI) is a craniocerebral trauma which causes long-term physical, cognitive and emotional impairment and adds substantially to the healthcare burden. The cost of TBIs is believed to be huge in Norway. Moderate and severe TBIs require rehabilitation, which helps reduce disability and improves the quality of life of patients. It is important to determine the efficacy of early rehabilitation as a form of treatment after severe TBI both in terms of its costs and effectiveness. A project entitled “Rehabilitation after severe traumatic brain injury” was introduced at Oslo University Hospital, Ulleval (OUH_U) in 2005, and the results showed that patients who received early rehabilitation had a better functional outcome than those who received later rehabilitation. However, as there are limited beds for early rehabilitation at the Intensive Care Unit (ICU), Oslo University Hospital, Ulleval, an assessment of the cost-effectiveness of early rehabilitation versus later rehabilitation is needed to ensure the best use of health care resources. The main purpose of this study is to find an optimal choice in terms of the cost-effectiveness of different treatments with or without early rehabilitation and to estimate the total hospitalization costs of moderate-to-severe TBI in the Eastern part of Norway.

We developed a decision model to represent the two strategies after severe TBI and compared the incremental cost-effectiveness ratio (ICER) of early rehabilitation and later rehabilitation by measuring the costs and outcomes for both. The costs were estimated in diagnosis related group (DRG) prices, and the effect was estimated in the Glasgow Outcome Scale Extended (GOSE). The data source comes from the interviews, Patient Information System (Pasdoc) as well as NICEF.

The analyses mainly show that the total five-year expected cost per TBI patient for early rehabilitation was NOK 1,236,542 and for later rehabilitation NOK 1,274,302. The GOSE gain from 3 months to 5 years was 22% higher with the continuous chain of treatment (1.43) when compared to that of the broken chain of treatment (1.17). The continuous chain of treatment was dominant in both effect and cost calculations. The ICE scatterplot demonstrated that the probability that early rehabilitation is the optimal alternative was 61.6% in the model.

The findings indicate that early rehabilitation after TBI represents a dominant strategy in that it reduces costs and improves outcomes under reasonable assumptions.

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Jiajia Ye
Oslo, May 2013

DECLARATION

I have read and understood the paragraph above. I hereby declare that the thesis is written by me and:

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- It has not been used for another exam at another department, university, or university college in Norway or any other country.
- It does not refer to or quote works of others without stating it both in the text and in the reference list
- It does not refer to or quote previous writings of my own without stating it both in the text and in the reference list
- It mentions explicitly all sources of information in the reference list.

Title of thesis: Cost-effectiveness of early rehabilitation after Traumatic brain injury

Date and signature

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ACRONYMS

ABF	Activity-Based Financing
CBA	Cost-Benefit Analysis
CEA	Cost-Effectiveness Analysis
CEAC	Cost-Effectiveness Acceptability Curve
CUA	Cost-Utility Analysis
DRG	Diagnosis Related Group
DRS	Disability Rating Scale
GCS	Glasgow Coma Scale
GOSE	Glasgow Outcome Scale Extended
HRQoL	Health Related Quality of Life
HUI	Health Utilities Index
ICD-10	The 10th Revision of the International Statistical Classification of Diseases
ICER	Incremental Cost-effectiveness Ratio
ICU	Intensive Care Unit
NCSP	Nordic Classification of Surgical Procedures
NHB	Net Health Benefit
NICEF	Nirvaco Classification Engine (Frittstående)
NMB	Net Monetary Benefit
OUH_U	Oslo University Hospital, Ulleval
PSA	Probability Sensitivity Analysis
PTA	Post Traumatic Amnesia
QALY	Quality-adjusted life year
RCT	Randomized Controlled Trial
SG	Standard Gamble
TBI	Traumatic Brain Injury
TTO	Time Trade-Off
VAS	Visual Analogue Scale
WTP	Willingness-To-Pay

1. INTRODUCTION

Traumatic brain injury (TBI) is defined as damage to brain tissue caused by an external mechanical force as indicated by a medically documented loss of consciousness or post traumatic amnesia (PTA) due to brain trauma or by objective neurological findings that can be reasonably attributed to TBI by physical examination or mental status examination (National Data and Statistical Center, 2009). TBI changes the lives of otherwise healthy people, as a large proportion of patients with TBI sustain long-term physical, cognitive and emotional impairments (Andelic *et al.,* 2011). Severe TBI is the main cause of death among young adults and is considered to be a public health problem throughout the world. The direct and indirect costs of TBI in the US have been estimated to be $48.3 billion annually (Family Caregiver Alliance, 1998). Although there is no data about the exact costs of TBI in Norway, it is believed that TBI adds substantially to the healthcare burden. It is therefore important to know the cost of TBIs, including hospitalization costs, which are important indicators of the impact of TBI on healthcare resources. In addition to costs, it is important to know the effects of treatments, as health resources are scarce. A cost-effectiveness analysis (CEA) is therefore used in this study to compare different treatments following severe TBI.

Rehabilitation, which is defined as “a problem-solving educational process aimed at reducing disability and handicap experienced as a result of disease or injury” (Khan *et al.,* 2003), is the main treatment for the subacute and chronic stages of recovery from TBI (Office of Communications and Public Liaison, 2002). The goal of rehabilitation is to improve the functioning of TBI patients and to improve their quality of life. Early rehabilitation has been proven to result in better health outcomes after severe TBI in several countries, but there are some limitations of the study groups (Andelic, 2011; Sorbo *et al.,* 2005). It is usually believed that early rehabilitation is more costly, but from a long-term perspective, it may help reduce the lengths of hospital stays as well as the number of treatments required, which in turn may reduce the total costs associated with TBI. Therefore, conducting a CEA of early rehabilitation after severe TBI will make it easier to understand the pathways and compare the costs and effects.

In Norway, there was one short-term follow-up study about “Rehabilitation after severe TBI” (Andelic, 2011). The study analyzed the functional outcome of severe TBI in two patient groups

– one group was offered early rehabilitation at Oslo University Hospital, Ulleval (OUH_U) as part of a "continuous chain of treatment", while the other group was not offered early rehabilitation, but was transferred to a local hospital for further treatment while waiting for admittance to a rehabilitation institution ("broken chain of treatment"). The results showed that the first group, which was offered early rehabilitation, had a better functional outcome. However, there is no evidence whether the early rehabilitation has a lasting effect on functional outcome from a long-term perspective (5 years). The costs of these two rehabilitation groups are unknown as well. We want to study which chain of treatment is more cost-effective for severe TBI. There is a significant need to critically follow up with these two groups and do further analysis to determine which rehabilitation is more cost-effective in treating severe TBI with a long-term perspective.

This study aimed to estimate the total hospitalization costs of moderate-to-severe TBI in the Eastern part of Norway and to carry out a CEA by exploring the differences of costs and health-related consequences when comparing different rehabilitation trajectories after severe TBI, where one is a continuous chain of rehabilitation starting in the acute phase, and the other is a broken chain of rehabilitation starting in the subacute phase of TBI. The costs were estimated in diagnosis related group (DRG) prices, and the effect was estimated in Glasgow Outcome Scale Extended (GOSE).

A decision tree model is developed to analyze the CEA for two patient groups with or without early rehabilitation. The decision tree is most likely the simplest and most common form of decision model in an economic evaluation (Briggs *et al.,* 2011, p. 23; Drummond *et al.,* 2005, p. 291). It starts from individuals' possible prognoses, following some sort of intervention, by a series of pathways (Drummond *et al.,* 2005, p. 291).

This study consists of six sections. The second section explores some general knowledge about TBI and its treatments, and the third section introduces CEA and a literature review of CEA of TBI. The forth section builds a decision tree model for estimating the outcomes and costs of different treatments following TBI. In the fifth section, the results of the model are described, including the estimation of uncertainty. The sixth section focuses on the limitations of the study.

2. BACKGROUND ON TBI

2.1 Definition and classification

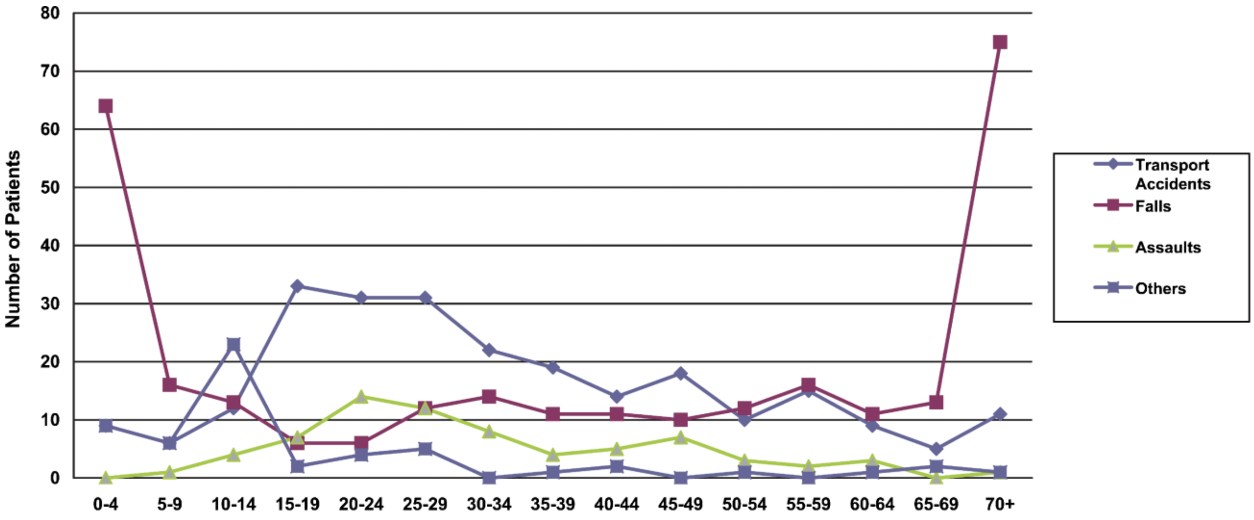
The definition of TBI varies among different studies (Andriessen *et al.,* 2011). The Centers for Disease Control and Prevention (CDC) define TBI as “craniocerebral trauma associated with neurological or neuropsychological abnormalities, skull fracture, intracranial lesions or death”. The effects of TBI range from a transient disturbance of consciousness to severe incapacity or death (McGregor *et al.,* 1997).

TBI is often classified by clinical indices of severity, pathoanatomic type or physical mechanism (Saatman *et al.,* 2008). TBI cases are usually characterized as mild, moderate and severe TBI on the basis of an assessment of impaired consciousness in the acute phase. In addition to consciousness at the injury scene, time required to return to consciousness is also an assessment of TBI severity (Andriessen *et al.*, 2011). Patients with mild TBI have a good recovery and are able to continue their previous activities; moderate TBI indicates that patients have moderate neurological deficiency with restricted activities, but they can perform functions independently; severe TBI indicates that patients have severe neurological deficiency and are often dependent on others for activities of daily life. The most used instruments to classify the severity TBI are the Glasgow Coma Scale (GCS), post-traumatic amnesia (PTA) and loss of consciousness (LOC). The GCS is most commonly used as a measurement for neurological injury severity criteria (Tomberg *et al.,* 2005). The GCS defines scores of 13-15, 9-12 and 3-8 as mild TBI, moderate TBI and severe TBI, respectively. Mild TBI usually accounts for 80-90 percent of all traumatic brain injuries while moderate and severe TBI account for the remaining 10-20 percent (Jennett, 1996).

2.2 Epidemiology

TBI can be caused in several ways: a) falls, which are the most common cause of TBI (Kayani *et al.,* 2009; Thompson *et al.,* 2006), especially among children under 14 years old and adults over 65 years old (CDC, 2010); b) motor vehicle traffic, including bicycles, motorcycles, cars, trucks and other vehicles (Kayani *et al.*, 2009), is the second leading cause of TBI and results in the largest proportion of TBI-related deaths (CDC, 2010); c) violence, including all types of firearms, is the leading cause of fatal TBI (Leon *et al.*, 2006). In Norway, falls comprise the most frequent causes of hospital-treated TBI among the elderly, and transport accidents are most frequent causes among teenagers (Figure 1).

Figure 1 Acute TBI patients by age and cause of injury from east Norway (n=663) (Sources from Borg et al., 2011)



TBI incidence is high in Europe, ranging from 100 per 100,000 to 800 per 100,000 (Berg, 2004). When classified by country, the yearly incidence of hospitalized TBI patients in Scandinavian countries is 365 per 100,000 in Sweden, 169 per 100,000 in Norway, 157 per 100,000 in Denmark and 100 per 100,000 in Finland. Among the countries of western and southern Europe, the yearly TBI incidence is 339 per 100,000 in Germany, 322 per 100,000 in UK, 250 per 100,000 in Italy and 227 per 100,000 in Spain (Berg *et al.*, 2005).

According to a more recent Scandinavian study on TBI (Borg *et al.*, 2011), the general trend of hospital-treated TBI patients has decreased in both Norway and Sweden. In the last 30 years, the incidence of TBI has declined from 236 per 100,000 to 83 per 100,000 in Norway. In Sweden, the incidence declined from 260 per 100,000 during 1998-2000 to 220 per 100,000 during 2007-2008. However, there is an increasing incidence of TBI in the elderly in Scandinavian countries (Borg *et al.*, 2011).

With regard to country, the mortality due to TBI in Europe is estimated as 9.7 per 100,000 per year, which is much lower than the US (30 per 100,000 per year), South Africa (81 per 100,000 per year) and Colombia (120 per 100,000 per year). However, the cost of TBI is high; the average income lost related to TBI mortality in Sweden was € 367m in 2001(Berg *et al.,* 2005).

2.3 Treatments

TBI may result in a complexity set of impairments that mix physical, cognitive, behavioral and emotional consequences (McGregor *et al.,* 1997). Health care services after TBI often include prevention, emergency, acute care, rehabilitation, vocational, educational, community support and long-term care (Andelic, 2010). Rehabilitation is required for moderate-to-severe TBI, which tends to be associated with worse outcomes compared to mild TBI (Donovan *et al.,* 2011). TBI rehabilitation is an interdisciplinary, team-based and goal-oriented service that aims to reduce disability and improve the quality of life of its patients (Andelic, 2010; Johnston, 2002). It may help patients return faster and more stably to society in terms of social participation and work. A multidisciplinary rehabilitation team usually constitutes of a number of professions such as doctors, nurses, occupational therapist (OT), physiotherapist (PT), speech therapist (ST), neuro-psychologists as well as social workers.

Several statistics about TBI patients at 1 year post-injury were reported in previous studies (Andelic *et al.,* 2011):

- 18% of patients died
- 35% of patients suffered isolated TBI while 65% had TBI combined with associated injuries
- Two-thirds of survivors suffered from severe TBI
- TBI patients face substantial disability and impaired overall health 1 year after injury (Andelic *et al.,* 2010), evidenced by the fact that 16.4% achieved good recovery levels (GOSE 7-8), 64 % had moderate disability (GOSE 5-6), 18% had severe disability (GOSE 3-4) and 1.6% were in a vegetative state (GOSE 2)

- Severe TBI patients who received the combination of early rehabilitation and a continuous chain of treatment had a better functional outcome as measured by GOSE and Disability Rating Scale (DRS) than those who delayed admission to rehabilitation

3. COST-EFFECTIVENESS ANALYSIS

3.1 Economic evaluation

Economic evaluation is important when health care resources are scarce, which enables the decision maker, clinician or individual patient to choose better health services. 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, p. 9). As there are various types of costs and measurements of consequences, a full economic evaluation often contains three separate analyses, the cost-effectiveness analysis (CEA), cost-utility analysis (CUA) and cost-benefit analysis (CBA). The main characteristics of these types of economic evaluation are described below (Table 1).

Table 1 Characteristics of the different types of economic evaluation

Type of study	**Measurement/ valuation of costs in both alternatives**	**Identification of consequences**	**Measurement/ valuation of consequences**
Cost-effectiveness analysis	Monetary units	Single effect of interest, common to both alternatives, but achieved to different degrees	Natural units (e.g., life years gained, disability days saved, points of blood pressure reduction, etc.)
Cost-utility analysis	Monetary units	Single or multiple effects, not necessarily common to both alternatives	Healthy years (typically measured as quality-adjusted life years)
Cost-benefit analysis	Monetary units	Single or multiple effects, not necessarily common to both alternatives	Monetary units

(Sources: Drummond *et al.*, Methods for the economic evaluation of healthcare programmes. 2005)

Of these methods, CEA is used in this study because it is of most use when two or more healthcare interventions are considered within a given budget. It measures costs in monetary units and consequences in natural units, such as life years gained, disability days saved and case correctly diagnosed, etc. The evaluation question of CEA is usually a comparison of interventions that have the same objective. CEA aims to provide information about costs and effects of alternatives options that serve the same goal (Polinder *et al.*, 2011). Drummond *et al.* (2005, p. 40) emphasized that the incremental costs are compared to the incremental health effect in a CEA evaluation, whose results can be expressed as an incremental cost-effectiveness ratio (ICER):

$$\mathrm{ICER} = \frac{\mathrm{C}_1 - \mathrm{C}_0}{\mathrm{E}_1 - \mathrm{E}_0} = \frac{\Delta\ \mathrm{C}}{\Delta\ \mathrm{E}} \qquad (1)$$

Where C_1 and E_1 are intervention costs and intervention effects, and C_0 and E_0 are comparator costs and comparator effects.

ICER can be represented visually in a cost-effectiveness plane, which is commonly used in CEA to illustrate the costs and consequences (Figure 2). In quadrants I and III, the choice depends on the maximum cost-effectiveness ratio one is willing to accept, or the ceiling cost-effectiveness. In quadrant II, the new treatment is more effective and less costly, thus dominating the alternative. In quadrant IV, the new treatment is dominated as it is less effective and more costly.

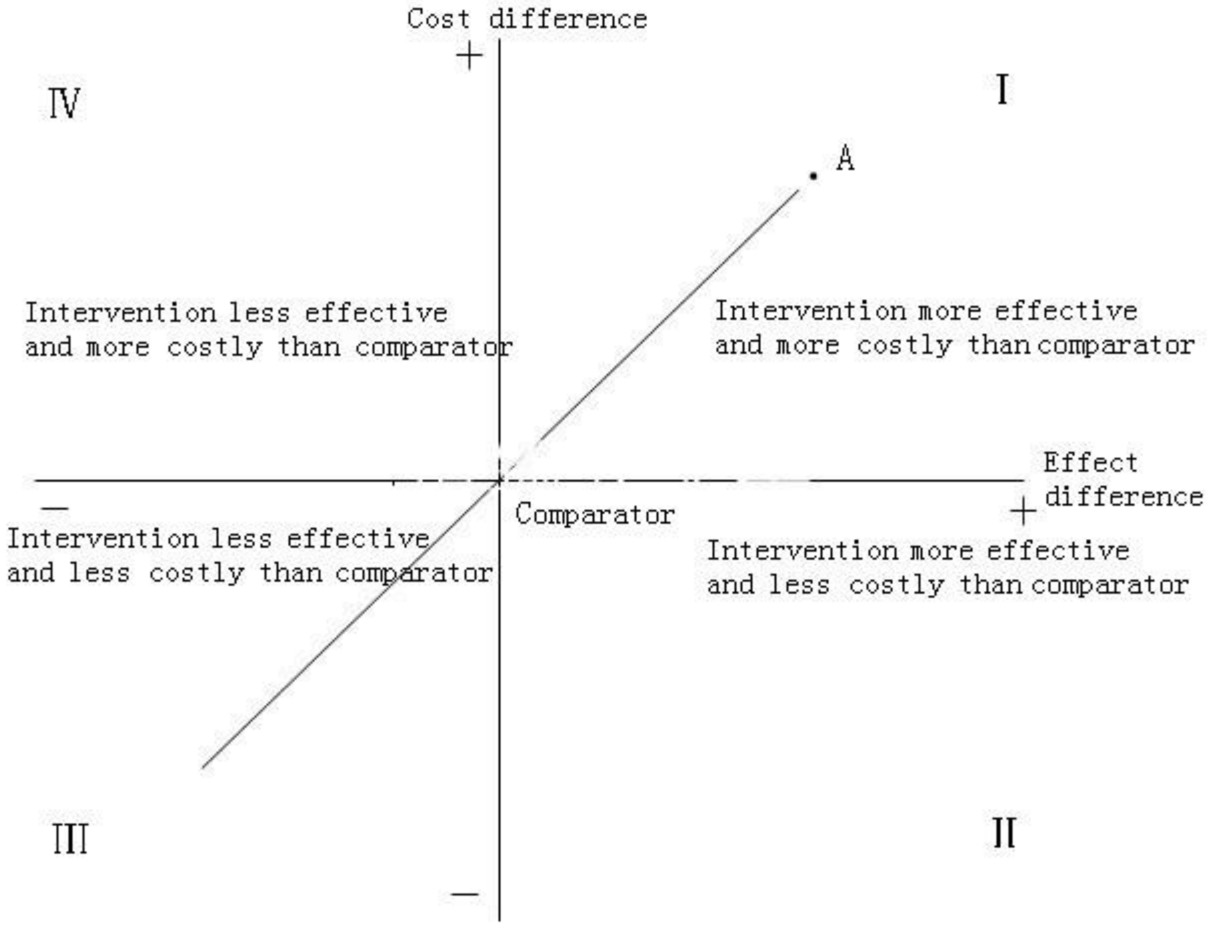


Figure 2 Cost-effectiveness plane

(Source: Drummond *et al.,* Methods for the economic evaluation of health care programmes. 2005)

The main drawback of the ICER is that the ratios of the same sign are not strictly comparable when they are from different quadrants. For example, although they are grouped together in any rank-ordering exercise, negative ICERs in the IV quadrant of the plane favors the initial treatment, while it favors the intervention treatment in the II quadrant (Briggs *et al.,* 2011, p. 128-129). Net-benefit can avoid this problem of conflating simulations of the same sign within opposite quadrants of the cost-effectiveness plane (Briggs *et al.,* 2011, p. 129). Net-benefit is a statistic to handle uncertainty in stochastic CEA, and it can sort out the 'acceptability' of an individual simulation trial when applied to Monte Carlo simulation data (Briggs *et al.,* 2011, p. 129). It can be presented on either a cost scale (net monetary benefit NMB) or effect scale (net health benefit

NHB) by rearranging the cost-effectiveness decision rule (Briggs *et al.,* 2011, p. 129; Drummond *et al.,* 2005, p. 131-132):

$$\mathrm{NMB} = \mathrm{R_T}\Delta\mathrm{E} - \Delta\mathrm{C} \qquad (2)$$

$$\mathrm{NHB} = \Delta\mathrm{E} - \frac{\Delta\mathrm{C}}{\mathrm{R_T}} \qquad (3)$$

Where Δ C and Δ E are increased costs and effects, and R_T is willingness-to-pay per unit of increased effectiveness. A program is deemed cost-effective if NMB > 0 (or NHB> 0), i.e., for NMB (or NHB) to be positive, $R_T\Delta$ E has to be greater than Δ C.

Due to imperfect information on the resources consumed and the effectiveness of intervention, both costs and effects of health interventions are associated with some degree of uncertainty (Fenwick *et al.,* 2006). Individual patients, for instance, differ from one another in terms of their characteristics and clinical experiences. Uncertainty in the model is also considered as it may imply the possibility of incorrect decision making, which imposes a cost in terms of forgone benefits (Briggs *et al.,* 2011, p. 82-83). There are two types of uncertainty in decision models for CEA, parameter uncertainty and decision uncertainty (Briggs *et al.,* 2011, p. 82). Parameter uncertainty relates to the imprecision of estimating an input parameter such as the probability of an event, a mean cost or a mean utility. It happens due to limited available information. Decision uncertainty refers to the assumptions imposed by the modelling framework. Any uncertainty in the model will be conditional on the structural assumptions, and it is important to know that different assumptions could result in different levels of uncertainty (Briggs *et al.,* 2011, p. 82-83).

Sensitivity analysis is used for dealing with parameter probability (Drummond *et al.,* 2005, p. 42-43). Probability sensitivity analysis (PSA) is a widely used form of sensitivity analysis in decision modeling. PSA defines input parameters as probability distributions to reflect uncertainty and simulates the model to propagate the uncertainty to reflect the combined parameter uncertainty (Drummond *et al.,* 2005, p. 302). For decision uncertainty, distribution can be used to indicate the probability that the right decision is made (Briggs *et al.,* 2011, p. 83). The cost-effectiveness acceptability curve (CEAC), which illustrates the uncertainty surrounding the estimate of cost-effectiveness (Fenwick *et al.,* 2005), is derived from the joint distribution of incremental costs and incremental effects, and it is constructed by plotting the proportion of the incremental cost-effectiveness pairs that are cost-effective for a range of willingness-to-pay values (Fenwick *et al.*, 2006).

3.2 Estimation of effects in health outcome

Effects can be measured as willingness-to-pay (WTP) in CBAs and quality-adjusted life years (QALYs) in CUAs. WTP refers to how much additional money people are willing to pay in order to obtain a better health state. For example, in order to introduce a program to an individual who gains from the program, we would determine the maximum amount that must be taken from the gainer to maintain them at the current level of utility. This is the maximum amount individuals would be willing to pay for the program (Drummond *et al.*, 2005, p. 223-224). Health Related Quality of Life (HRQoL) focuses on a multidimensional perspective of health as physical, psychological and social functioning and well-being (WHO, 1948). HRQoL evaluates the quality of life in managed health care plans and other health care applications. QALYs are arrived at in each case by adjusting the length of time affected by the health outcome by the utility value of the resulting level of health status, which is on a scale from 0 to 1 (Drummond *et al.,* 2005, p. 14). The amount of QALY gained usually consists of better quality of life and life extension. Today, many employ one of the generic preference-based health measures such as visual analogue scale (VAS), time trade-off (TTO), the standard gamble (SG), EQ-5D and the Health Utilities Index (HUI) (Hunink *et al.,* 2001). VAS is a scale from 0 to 100 with 0 representing death and 100 representing perfect health. Participants can indicate a position along a continuous line between these two end-points to specify a health care statement of their perception (Hunink *et al.,* 2001). TTO represents how many life years a patient would trade in order to be fully healthy or remain in ill health (Hunink *et al.,* 2001). In the standard gamble, respondents are asked to choose a medical intervention that has probability of either perfect health or death, or remain in ill health (Hunink *et al.,* 2001). Both EQ-5D and HUI use a questionnaire to classify patients into one of a pre-determined set of health states. The values of the health states can be measured from a scoring equation (EuroQol, 2013; Drummond *et al.,* 2005, p. 37).

Effectiveness measures used in CEAs can be expressed as final or intermediate outcomes (Drummond *et al.,* 2005, p. 104). Final outcomes such as ‘life years saved’ can be used in a CEA of cancer screening program. ‘Episode-free days’ is also a measure of final outcome in asthma.

Intermediate outcomes are appropriate, although care must be taken to link to a final health outcome (Drummond *et al.*, 2005, p. 104). Common examples of effectiveness measures are measuring blood pressure in treatment of hypertension, cases detected in diagnosis of deep vein thrombosis (DVT) as well as percentage serum cholesterol reduction in the treatment of hypercholesterolemia (Drummond *et al.*, 2005, p. 104). These measurements themselves have some value in providing relevant health gains for the desired objective. GOSE is usually used as the primary outcome to measure global functioning in terms of activities for TBI patients. The GOSE encompasses consciousness, self-sufficiency both in and outside the home, work, social and leisure activities, family and friends and time to return to normal activities. GOSE provides a global status description and captures changes and limitations to activities and participation that have occurred as a result of the injury (Andelic *et al.*, 2010). It is an intermediate outcome, and it is considered to be sufficient to measure the functional outcome of patients.

3.3 Estimation of costs in CEA

Perspective in economic evaluation consists of the societal perspective, the decision maker's perspective, the hospital perspective and the patient's perspective.

Identification, quantification and valuation of the costs are the underlying processes in an economic evaluation. Costs need to be identified when a health resource is consumed for a particular intervention. The costs of treatment following TBI include health sector costs, costs to the family, and social service costs as well as the costs related to loss of productivity (Drummond *et al.*, 2005, p. 17-20). Costs in the health sector include resource consumption such as the cost of drugs, equipment, hospitalization, nursing home and visits to a general practitioner and physiotherapist. Costs to family consist of out-of-pocket expenses such as travelling expenses to the hospital, copayments for drugs and examinations and expenditures in the home. Social service costs consist of resources such as homemaker services, voluntary sector, schooling and social workers. Productivity loss is mainly about the use of time, as both patient and family use time during the treatment and care of the patient, and it could be associated with productivity costs if patients lose time from work.

Quantification is the way we measure the consequences of an intervention. Quantification of costs usually uses the registered data during the treatment pathways. When registered data are not included or when there are some barriers to obtaining the cost information, questionnaires to participants, non-participants and control groups are useful to report costs. Relevant databases such as Pub-med, Medline or Cochrane can also be used to quantify the different cost components.

Valuation is the way we estimate the value of a resource used for an intervention. Opportunity cost is what health economists mean when they refer to cost. Opportunity cost is the benefit that would have resulted from the next best alternative use. Estimation of costs for intervention is how we value the costs of an intervention. Opportunity cost can be estimated by either a market method, such as fee-for-service, or the real cost of a specific intervention. Fee-for-service is a form of the payment where health services are paid separately.

Based on the level of accuracy, hospital costing can be divided into micro-costing, case-mix group, disease-specific per diem and average per diem from most precise estimates to least precise estimates (Drummond *et al.*, 2005, p. 71). Micro-costing usually estimates each component of resource use, for example, laboratory tests and drugs; case-mix group gives the costs for each category of case and takes account of length of stay; disease-specific per diem gives the average daily cost for treatments in each disease category, for example, orthopedic surgery; average per diem is based on average per diems or daily cost over all categories of patient expenses (Drummond *et al.*, 2005, p. 71). Activity-based costing, which belongs to the case-mix group, is becoming more and more popular in hospitals today for estimating costs.

To increase hospital efficiency and reduce waiting time in Norway, activity-based financing (ABF) was introduced in Norwegian hospitals from July 1, 1997. As a top-down method, it replaced a proportion of the block grant that funded Norwegian hospitals. Depending on the hospital treatment, 30% of the DRG-based costs were refunded by the state in 1997. This amount changed a bit in the following years; it was 60% in 2005 and was reduced to 40% from 2006.

ABF prices are calculated based on the DRG system (Mishra, 2004). DRG can be used to value the costs. Based on diagnosis codes, surgical procedure codes, gender, age and discharge status (Helsedirektoratet, 2007), patient treatment is classified into one DRG group within which patients are almost homogeneous in terms of resource consumption. There are approximately 900 DRGs in Norway, and each DRG has a specific cost weight based on the average costs of each patient group. There are two types of DRG in Norway: a surgical DRG group and medical DRG group. If a patient requires an operation during his/her hospital stay, he/she is assigned to a surgical DRG group. If no operation is performed during the hospital stay, he/she is assigned to a medical DRG group (Appendix 3; Table 5).

Hospital financing uses DRG as a primary measurement. Therefore, it is important to know what patient data are recorded and how they are registered. The most important data for DRG are diagnosis codes and procedure codes. In Norway, the DRG uses the ICD-10 diagnosis classification (the 10th revision of the International Statistical Classification of Diseases) and the NCSP classification of procedures (Nordic Classification of Surgical Procedures) (Helsedirektoratet, 2007). ICD-10 is used for the conversion of national diagnosis and procedure codes. It is a tool for the systematic classification and registration of diseases and other health problems. It is also part of the patient data information reported to the Norwegian Patient Register about hospital stays and outpatient contacts.

3.4 Literature on TBI, effects and costs

There are few studies exploring the cost-effectiveness of rehabilitation strategies after TBI, and there are only a limited number of studies discussing the outcome of TBI in a long-term perspective. The outcome of TBI varies in different studies. Hammond (2004) observed a high proportion of improvement in cognitive function following 292 TBI patients over 5 years, while Whitnall (2006) concluded that a high proportion of TBI patients had psychosocial disabilities after following 475 TBI patients over 5-7 years.

Rehabilitation has been proven to be effective for TBI (Kosar *et al.*, 2009). It may lead to fewer secondary complications, faster reintegration into society and reduction of the length of stay in the hospital, thus reducing hospital costs. Several studies have shown that patients receiving early rehabilitation had a better outcome than those who did not receive early rehabilitation (Sorbo *et al.*, 2005; Andelic *et al.*, 2011). However, these studies did not look at the cost-effectiveness perspective. Managed care payers increasingly question the value and cost-effectiveness of rehabilitation and constrain the delivery of clinical rehabilitation services (Johnston, 2002). The CEA should be conducted to show whether the improvement outcome from early rehabilitation increases overall costs. If yes, are these costs worthwhile compared to the functional improvement? The socioeconomic significance of these results is necessary to the work of prioritization of health services.

The costs of TBI can be huge due to TBI-related long term consequences, some of which are life-long. Most TBI patients cannot put a price on the emotional and physical suffering that they must endure as a result of their injury. Due to the lack of essential data on medical outpatient care, direct non-medical services and indirect costs (Berg *et al.,* 2005), there are only a few studies estimating the TBI costs in the US and some European countries. Acute-care costs of TBI ranged from about $8,200 for those with moderate injury severity to more than $33,500 for patients with critical injury in the United States between 1997 and 1999 (McGarry *et al.,* 2002). It is estimated today that annual TBI costs are $48.3 billion in the US. Within the price, $31.7 billion is due to hospitalization costs while the rest goes toward related fatalities and deaths (Brain and Spinal Cord, 2012). A TBI review in Europe found out that the average 1-year inpatient TBI costs in Germany, Spain and Sweden were approximately € 2,500, € 2,800 and € 3,000, respectively (Berg *et al.,* 2005). The average inpatient 1-year costs with severe TBI were € 6,600, € 6,000 and € 6,400 in Germany, Spain and Sweden (Berg *et al.,* 2005). According to the European Brain Council's Cost of Brain Disorders in Europe study (Gustavsson *et al.,* 2011), the total annual cost of TBI in Europe was €33,013,000,000, and, when specified by country, the highest total annual costs occurred in Germany, France and Italy, with value of €6,641,000,000, €4,307,000,000 and €3,652,000,000, respectively. The annual cost per person with TBI was €57,351 in Europe, and, when stratified by severity, the annual cost per person with moderate TBI was €23,551, and the annual cost per person with severe TBI was estimated to be €27,020. Estimating the costs can help us understand the potential burden of TBI and the amount of resources used, raise awareness of specific research needs, and provide insight in the decision-making process of resource allocation. Therefore, it is necessary to estimate the TBI costs in Norway related to patient hospitalization in acute hospitals and rehabilitation units and compare it with other international studies.

In addition to isolated TBI, many patients have multiple injuries. These are mainly caused by traffic accidents and often occur in younger adults (Erli *et al.*, 2000). The rehabilitation of patients with multiple injuries may take longer than those with isolated TBI. During the hospitalization, some patients may have complications such as pneumonia, sepsis and epilepsy, etc. Thus, dividing costs among isolated TBI, TBI with multiple injuries and TBI with complications is also a necessity.

In this study, costs of TBI are estimated as the hospitalization cost from the hospital perspective for both total cost and average cost. For the CEA, the average costs of the total hospitalization in different groups are calculated as inputs into the CEA model.

4. METHODS AND DATA

4.1 Decision Tree Model

A decision tree model is developed with TreeAge Pro 2012. The model starts with TBI patients admitted to hospital and has the following two strategies: 1) early rehabilitation and 2) later rehabilitation (Figure 3). Both strategies aim to reduce the injury severity, and they have different methods of treatment. Early rehabilitation after severe TBI offers treatment that focuses on reducing the extent of the brain injury, preventing complications and promoting functional recovery through multi-sensory stimulation performed by an interdisciplinary rehabilitation team integrated in the acute care. The other group receives specialized inpatient rehabilitation during the subacute phase of TBI consisting of reducing impairment, increasing functional independence, restoring social participation, and minimizing the distress of the patient as well as caretakers. There is a particular focus on the personal and domestic activities of daily life.

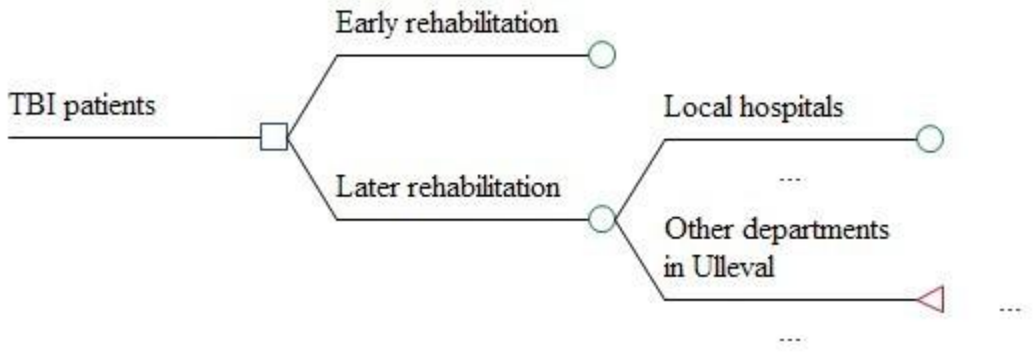


Figure 3 Decision tree for cost-effectiveness

The general features of a decision tree model are as follows (Briggs *et al.*, 2011, p. 24-27; Drummond *et al.*, 2005, p. 291): a) *Decision nodes*: a square box at the start of the tree that represents a decision point between alternative options; b) *Chance nodes*: circles coming out of the decision node that show a range of possible pathways; c) *Pathways*: the combination of different branches through the tree along which patients can pass. Clinical pathways refer to the treatments that patients receive during their hospitalization stays, such as vaccinations, drugs, operations, etc. They are mutually exclusive and exhaustive (a given patient must and can only follow one of the pathways). In some pathways, a patient may stay in a branch for a long time when he/she receives the same treatment several times; d) *Probabilities*: the likelihood of the event that patients may experience at that point in the tree. Moving from left to right, chance nodes show subsequent uncertain events. Subsequent probabilities are conditional as they only relate to those who have experienced a particular previous event. Multiplying probabilities along pathways estimates the pathway probability, which is a joint probability; e) *Pathway costs*: each pathway has costs associated with it. It represents the sum of the costs a patient experiences within a certain pathway; and f) *Expected values*: the probability of successful treatment can be seen as the relevant measure of effect.

The cost-effectiveness is estimated by jointly simulating the costs and effectiveness. For each strategy, the time perspective of the CEA is 5 years post-injury.

4.2 Patients

This study was part of a larger TBI project entitled "Rehabilitation after moderate and severe TBI", which was conducted at Oslo University Hospital, Ulleval from 2005 to 2009. OUH_U is the Trauma Referral Center for South-East of Norway and serves population of 2.8 million. The study included a cohort of 129 patients (Andelic et al., 2008; Andelic *et al.*, 2009; Andelic *et al.*, 2010; Andelic et al., 2011). The inclusion period was from May 15, 2005 to May 15, 2007, and the patients were followed for five years with a follow up at 1 year and 5 years post-injury. The inclusion criteria included patients who were (a) aged 16-55 years, (b) admitted to OUH_U with ICD-10 diagnoses of S06.0-S06.9 within 48 hours of an injury, (c) had GCS values between 3 and 12 and (d) resided in the south-east region of Norway. The exclusion criteria were patients (a) with severe abuse of intoxicants and psychiatric illnesses, (b) who had previous neurological injuries and illnesses, (c) who had spinal injuries and (d) who were criminals or without a permanent address.

The patient information includes sex, age, severity of TBI, chain of rehabilitation treatment (continuous versus discontinuous), length of stay, place of stay, diagnosis codes and treatment codes. Among these, the diagnosis classification ICD-10 and the classification of procedures

NCSP are the most important data for DRG grouping (Appendix 3). The ICD-10 diagnosis classification describes the main grounds of the patient's need for hospital care. Treatment is the procedure of observation, examination, treatment and care of a patient. The TBI diagnosis contains both isolated TBI diagnosis and diagnosis of TBI with multiple injuries.

There were two populations included in this study. All of the 129 moderate and severe TBI patients were included in the estimation of the costs. However, for the CEA, only the 59 severe TBI patients were included. This was a quasi-experimental study as it was untenable to randomize the patients (Andelic *et al.*, 2011). In general, the capacity (available bed principle) determined the assignment to whether the patients were received early rehabilitation or not. A flow chat of the inclusion in the CEA is presented in Figure 4, which was similar to the flow chart of the 1-year outcome study (Andelic *et al.,* 2011). In the 1-year post-injury study, 61 patients were included, but prior to the 5-year follow up, 2 patients died. Therefore, there were 59 patients included in this study.

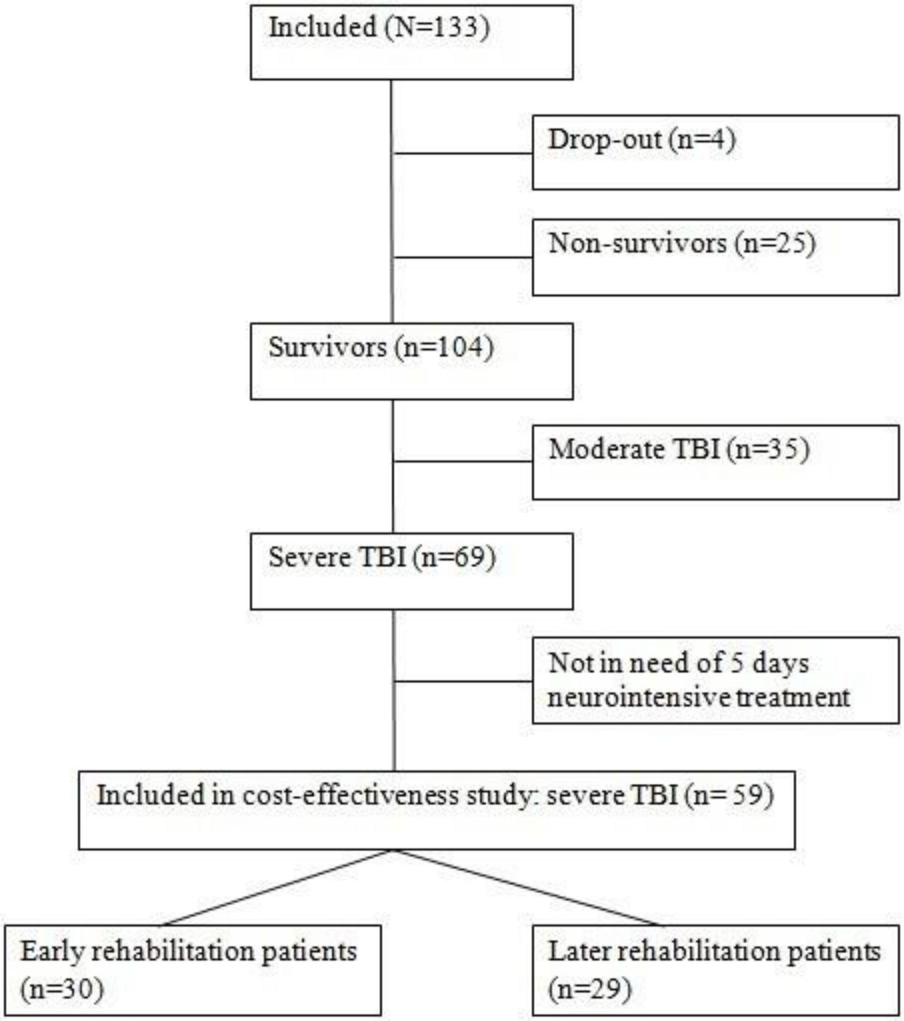


Figure 4 Flow data for patients included in the study

In this study of patients with severe TBI (n=59) in need of 5 days of neurointensive treatment, the patients were divided into two treatment groups, who were treated under the following treatment strategies: 1) early rehabilitation strategy; or 2) later rehabilitation strategy.

The early rehabilitation group received early comprehensive rehabilitation during acute TBI hospitalization at the Intensive Care Unit (ICU) at Oslo University Hospital, Ulleval. When the patients' medical conditions were sufficiently stable, they were transferred directly to Sunnaas Rehabilitation Hospital (eastern region) or to Rehabilitation Clinic in Kristiansand (southern region) for further subacute brain injury rehabilitation (*continuous chain of treatment).*

Patients in the later rehabilitation group did not receive early comprehensive rehabilitation, but they received inpatient brain injury rehabilitation in subacute rehabilitation departments after a waiting period at a local hospital (Vestre Viken Hospital, Innlandet Hospital, Akershus University Hospital, Ostfold Hospital, Lovisenberg Diakonale Hospital, Sorlandet Hospital), or they stayed in other departments in Oslo University Hospital, Ulleval while waiting for a place for early rehabilitation (*broken chain of treatment).*

4.3 Data

The data source comes from interviews, the Patient Information System (Pasdoc) as well as the NICEF. Some general information from these sources was constructed in SPSS 20 to estimate GOSE scores as well as costs for TBI patients. The data set in SPSS includes basic information of TBI patients such as age, gender, injury severity (severe/moderate) and rehabilitation groups (early/later). For each patient, all lengths of hospital stay were recorded, including the admission date and discharge date, as well as main diagnoses and procedures performed during each hospital stay. The data were collected at 3 months, 1 year and 5 years after the initial admittance to the hospital.

4.3.1 Outcomes

The health outcome is measured by GOSE for TBI patients. The GOSE can be divided into 8 groups: 1=dead, 2=vegetative state, 3=lower severe disability and complete dependence on others, 4=upper severe disability and some dependence on others, 5=lower moderate disability and working at a lower level of performance, 6=upper moderate disability and returning to previous work with some adjustments, 7=lower good recovery with minor physical or mental deficits and 8=upper good recovery. Alternatively, the GOSE can be divided into 3 groups: dead (1), unfavorable (2-5) and favorable (6-8) (Andelic *et al.*, 2010).

The differences between the 3 month and 5 year GOSE scores were used as measures of outcomes. The GOSE scores were collected from face-to-face interviews and examinations of each patient in the outpatient clinic or in the rehabilitation hospital, where they had been admitted for a clinical follow-up assessment. Two main parameters, mean and standard deviation, were used as inputs in the model (Table 2).

Table 2 Outcome parameters used in the model

	Mean difference of GOSE scores between 3 months and 5 years	**Standard deviation**
Sunnaas Rehabilitation	1.48	0.20
Kristiansand Rehabilitation	1.33	0.18
Vestre Viken Hospital	0.50	0.07
Innlandet Hospital	1.43	0.20
Akershus University Hospital	1.50	0.21
Ostfold Hospital	1.00	0.14
Lovisenberg Diakonale Hospital	1.00	0.14
Sorlandet Hospital	1.67	0.23
Ulleval Hospital	1.00	0.14

4.3.2 Transitions

The severe TBI patients were under conditional transitions. For patients in the early rehabilitation group, 70% of the patients were discharged to the Sunnaas Rehabilitation, and the rest were discharged to Rehabilitation Department in Kristiansand. For the later rehabilitation group, 69% of the patients were transferred to a local hospital and the rest remained in other departments in Ulleval while waiting for rehabilitation treatment (Table 3).

Table 3 Conditional transition of severe TBI patient

Early Rehabilitation	**N=30**		
Sunnaas	21 (0.70)		
Kristiansand	9 (0.30)		
Later Rehabilitation	**N=29**		**(N=20)**
Local hospitals	20 (0.69)	Vestre Viken Hospital	4 (0.20)
		Innlandet Hospital	7 (0.35)
		Akershus University Hospital	4 (0.20)
		Ostfold Hospital	1 (0.05)
		Lovisenberg Diakonale Hospital	1 (0.05)
		Sorlandet Hospital	3 (0.15)
Other departments in Ulleval	9 (0.31)		

4.3.3 Costs

Costs are different for different perspectives. In this study, we measure costs from the hospital perspective to estimate the hospitalization costs of TBI patients. The study is about the hospitalization costs, so the data used were inpatient but not outpatient data.

Costs estimates are based on the DRG system from Pasdoc as well as NICEF2011. Total hospitalization costs and average costs were estimated through the SPSS20 program. The average cost per patient for the severe TBI patients will become the input for the decision tree model for the CEA.

ICD-10 contains approximately 12,000 diagnoses. The following ICD codes were used for reviewing TBI medical records in Norway (Andelic *et al.*, 2008): S02.0 – S02.9 (skull and facial fractures), S06.0 – S06.9 (intracranial injuries), S07.0, S07.1, S07.8, S07.9 (crushing injury of head), S09.7 – S09.9 (other and unspecified injuries of head), and T04 (crushing injuries involving head with neck) and T06 (injuries of brain and cranial nerves) (Appendix 4).

NCSP covers approximately 5,000 operations and a number of procedures. The main procedures for TBI patients are TG601 (Respirator treatment), TP992 (Insertion of the arterial cannula), GBB00 (Tracheotomy) and AAA27 (Insertion of intracerebral pressure gauge) (Table 4).

All the DRG codes and procedure codes are included in the model to estimate the costs under the DRG system in this study. We found the 10 most commonly used DRG groups for TBI patients (Table 5). The top 10 DRG codes account for approximately 78% of the DRG groups, while the top 10 NCSP codes account for approximately 60% of the procedures. Among the top 10 DRG codes, tracheostomy excluding diseases of the face, mouth or throat, with cost weight 23.94, costs the most, NOK 840,940. Complex rehabilitation, with cost weight 0.15, costs much less at NOK 5,269.

Table 4 Top 10 procedures performed for TBI patients

NCSP	**Content**	**Percentage of diagnoses**	**Percentage of patients**
TG601	Mechanical ventilation	12.5%	57.4%
TP992	Insertion of the arterial cannula	8.4%	40.3%
GBB00	Tracheotomy	8.0%	44.2%
AAA27	Insertion of intracerebral pressure gauge	7.5%	37.2%
TPH20	Insertion of central venous catheter	6.4%	33.3%
TKC20	Bladder catheterization	4.4%	24.0%
UGC12	Flexible bronchoscopy	4.2%	20.9%
TJD00	Closure of the gastric tube	3.7%	20.2%
TAA03	Time-consuming EEG	2.5%	11.6%
JDB10	Percutaneous gastrostomy	2.0%	8.5%
Total	/	59.6%	/

Table 5 Top 10 DRG codes used (M: Medical DRG S: Surgical DRG)

DRG Code	Content	Percentage	Weight	Type	Cost (NOK)
027	Severe Traumatic Brain Injury	22.3%	1.41	M	49,529
483	Tracheostomy for excluding diseases of the face, mouth or throat	20.3%	23.94	S	840,940
487	Significant multi-trauma ITAD	9.9%	2.02	M	70,957
462A	Complex rehabilitation	7.1%	0.15	M	5,269
484	Craniotomy with significant multi-trauma	5.5%	14.34	S	503,721
002B	Other craniotomy in trauma	5.1%	2.08	S	73,064
002A	Surgery for chronic subdural hematoma	2.3%	4.94	S	173,527
486	Operations with significant multi-trauma ITAD	2.3%	6.50	S	228,326
467	Influences on health ITAD	1.6%	0.34	M	11,943
032	Concussion > 17 years u/bk	1.4%	0.29	M	10,187
Total	/	77.8%	/	/	/

The data source for the costs is the Patient Information system (Pasdoc). Costs data were estimated at the individual level. These data have been processed by the DRG-group program, which decides which DRG the data for the stay falls into. The DRG program is changed every year by the Norwegian Directorate of Health, according to their documents regulating DRG for the actual years from 2005 to 2008. This means that certain diagnoses and procedures may be emphasized more or less from one year to another year. Both Ulleval and Sunnaas rehabilitation data regarding cost weight were extracted from the Hospitals Discharge Registries. The data from local hospitals (Vestre Viken Hospital, Innlandet Hospital, Akershus University Hospital, etc.) as well as the rehabilitation hospital in Kristiansand were calculated by converting the patients' information from medical journals into costs through the NICEF 2011 software.

NICEF is a tool used in Norwegian hospitals for estimating cost weight as well as the DRG reimbursement cost. Reimbursement cost is equal to the hospital cost over a certain hospital stay. The hospital TBI costs are calculated by multiplying the cost weight by the average price of DRG reimbursement (price in the year 2009), as mentioned in Appendix 3. In NICEF, we chose the correct year for DRG price according to the patient's hospitalization data, put in some basic patient information like age, sex and length of stay on the top line, and added the main ICD-10 codes and NCSP codes in the main boxes. At the end, we obtained both cost weight and the hospital cost for the patient for a specific hospital stay. To avoid inflation, we set the price of DRG reimbursement of the year 2009 for calculating the costs, which was 35127 kroner. The cost data contain both uncorrected and corrected cost weight. The corrected cost weight tries to take into account the patients' length of stay while the uncorrected cost weight does not. Considering the importance of length of stay, we chose the corrected cost weights for all of the calculation processes.

4.4 Analysis

This study aimed to estimate the total hospitalization costs of moderate-to-severe TBI in the Eastern part of Norway and to carry out a CEA by exploring the differences of costs and health-related consequences. To estimate the total hospitalization costs, we used the 129 patient study population in the cost analysis, and we used the 59 severe TBI patients for the analysis to estimate the CEA.

4.4.1 Estimation of total hospitalization costs

In the analysis of total hospitalization costs, the costs were discounted 4% from 2006 on. According to Drummond *et al.* (2005, p. 98), the discount factor is $(1+r)^{-n}$, where r is 4% and n is 1, 2 and 3 per year from 2006 to 2008. The values of the discount factor in 2006, 2007 and 2008 using a rate of 4% are 0.9615, 0.9246 and 0.8890, respectively. Costs were discounted for each hospital stay for all the patients, and we estimated the total hospitalization cost across all patients (C_T) by summing the costs of each length of stay (C_i) (Equation 4). The average cost per patient ($\overline{C}_T$) was calculated by dividing the sum of the total hospitalization cost for each patient (C_{Ti}) by the number of patients (N) (Equation 5).

$$\mathrm{C_T} = \sum_{i=1}^{n} C_i \qquad (4)$$

$$\overline{\mathrm{C}}_\mathrm{T} = \frac{\sum_{i=1}^{n} \mathrm{C_{T(i)}}}{\mathrm{N}} \qquad (5)$$

To calculate the average hospitalization cost per patient per day, we first calculated the average cost per day for each patient and then the average cost per day ($\overline{\mathrm{C}}$) for all of the patients based on Equation 6

$$\overline{\mathrm{C}} = \frac{\sum_{i=1}^{n} \frac{\mathrm{C_{T(i)}}}{\mathrm{LOS_{T(i)}}}}{\mathrm{N}} \qquad (6)$$

Where N represents the total number of patients (n=129), $\mathrm{C_{T(i)}}$ is the total cost of each patient, and $\mathrm{LOS_{T(i)}}$ is total length of stay of each patient.

To estimate the total hospitalization costs (i.e., isolated TBI or TBI with multiple injuries as well as medical complications following TBI hospitalizations) of TBI patients in Norway, we calculated the average cost of all patients ($\overline{\mathrm{C}}_\mathrm{T}$) in the study trial and multiplied that average by the incidence number (N) of hospital-admitted moderate-to-severe TBI patients in the southern region of Norway (Equation 7).

$$\mathrm{TC} = \overline{\mathrm{C}}_\mathrm{T} * \mathrm{N} \qquad (7)$$

4.4.2 CEA analysis

For costs implemented in CEA, we took into account the different clinical pathways by using the average cost per patient under each group. For example, the average cost of patients who went to Sunnaas rehabilitation is equal to the average cost of those 22 patients.

$$\overline{\mathrm{C}}_\mathrm{CEA} = \frac{\sum_{i=1}^{n} \mathrm{C_{T(i)}}}{\mathrm{N}} \qquad (8)$$

Where N represents the total number of patients discharged to Sunnaas rehabilitation (n=22), and $C_{T(i)}$ is the total cost of each patient.

PSA is used to fully access parameters and reflect the model uncertainty, and it requires the simulation of a distribution of possible input values. A Monte Carlo simulation was used in this study to incorporate the effects, probability and costs parameters into the PSA. A Monte Carlo simulation is a probabilistic technique used to generate distributions of the mean effects and costs (Fenwick *et al.*, 2006). It has enabled the quantification of the uncertainty surrounding the estimation of effects and costs (Fenwick *et al.*, 2006). The effect parameters were defined as a normal distribution, and the probability parameters were defined as a beta distribution. The cost parameters in this study were defined as a gamma distribution. Due to the small data set, we assumed that standard error is equal to the standard deviation in both effect and cost parameters.

For effects, it is common to use lognormal or gamma distributions when the effects have infinity at the lower end and 1 at the upper end, representing the worst possible and perfect health state. In this study, however, intermediate outcome (GOSE) is used, whose scores are constrained on the interval 1-8 (GOSE level 1 represents dead). Therefore, the normal distribution might be a better method to sample the distribution of the mean. A histogram on SPSS regarding the GOSE differences from 3 months to 5 years also shows that they are generally normally distributed (Figure 5).

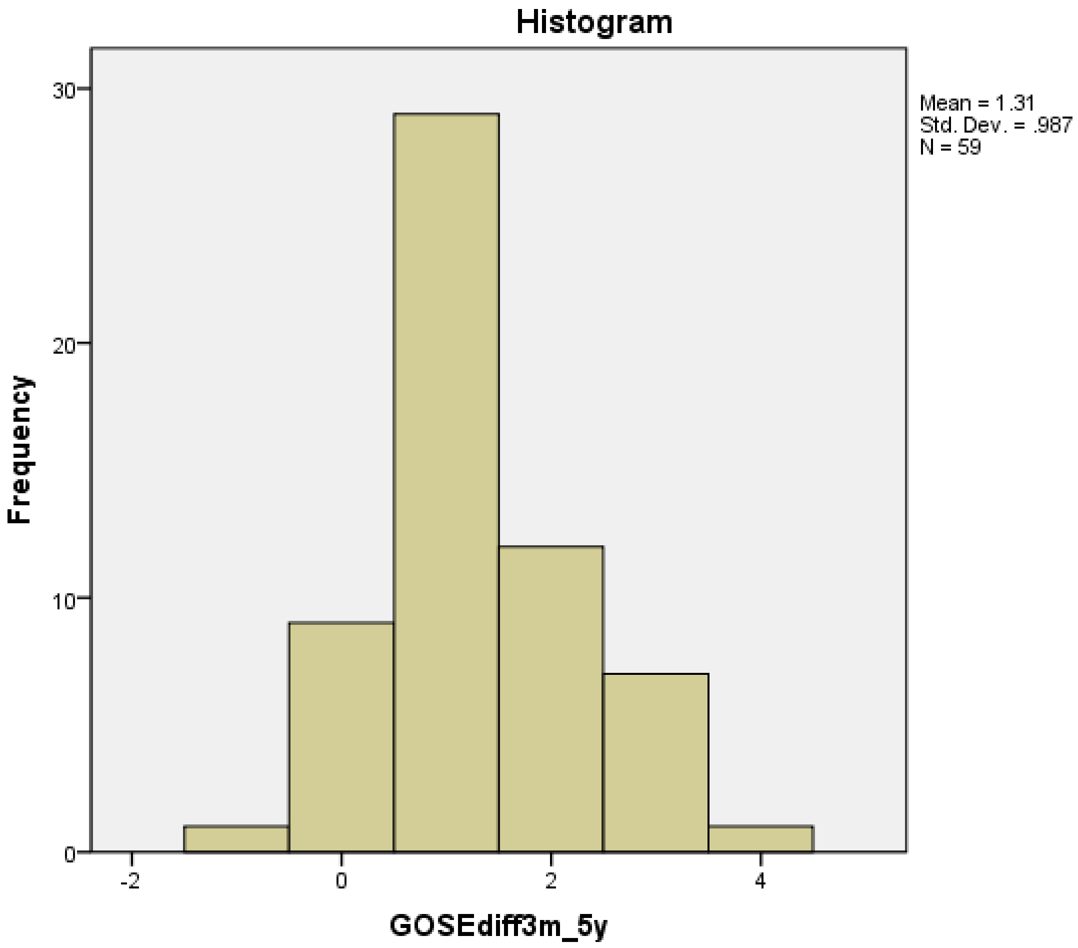


Figure 5 GOSE differences from 3 months to 5 years

A normal distribution has two parameters, μ and σ. μ is the mean of the distribution and σ is the standard deviation (Equation 9).

$$F(x) = \frac{1}{\sigma\sqrt{2\pi}} e^{-\frac{(x-\mu)^2}{2\sigma^2}} \qquad (9)$$

To estimate the standard error of effect for each end node, we first calculated the mean and standard error for the entire group. The mean GOSE increment between 3 months and 5 years were 1.43 and 1.21 for the continuous chain of treatment and the broken chain of treatment, respectively. Thus, the standard errors of the GOSE increment were 0.19 and 0.17 for the early rehabilitation and later rehabilitation group, respectively. Therefore, we obtained the ratios of mean and standard error (Ratio=Mean/SE), which were 7.55 and 7.21, respectively. By converting the ratio back to single end nodes in the model, we calculated standard errors for each end node. For example, $SE_{sunnaas}$= $Mean_{sunnaas}$ / Ratio (Appendix 5). These estimations are simplifications, as we have little data in the end nodes. Because some of the end nodes have only one patient, it is impossible to calculate a standard error, so we estimated by adding the ratio of mean and standard error.

The beta distribution is constrained over the interval 0-1 and is characterized by parameters α and β (Briggs *et al.,* 2011, p. 86-87). The beta distribution therefore is a natural choice to be used in uncertainty of probability parameters, and the probabilities of mutually exclusive events sum to one (Briggs *et al.,* 2011, p. 86-87). There are two forms of beta distribution, the integer form and real number form. The integer form is used when the data of occurrences (r) and population size (n) were available, while the real number form is used when mean and standard deviation can be estimated from the data. In this study, because we know the data on occurrence of TBI patients going to each branch, the integer form of beta distribution is used (Equation 10),

$$F(x) = \frac{(n-1)!}{(r-1)!\,(n-r-1)!} x^{r-1}(1-x)^{n-r-1} \qquad (10)$$

Where x is the probability, α= r and β = n-r. Therefore, under the beta distribution, when α is the number of patients going to one branch, β is the number of patients going to other branches.

The probability parameters were estimated on the basis of hospitalization data. Dis_P_Sun, for instance, represents the probability of patients going to Sunnaas Rehabilitation Hospital under the beta distribution, where α= 21 and β = 9. That is to say, 21 patients went to Sunnaas Rehabilitation Hospital while 9 patients went to Rehabilitation Clinic in Kristiansand (Appendix 1).

The gamma distribution, which is constrained over the interval from 0 to positive infinity, is usually used to represent uncertainty in cost parameters (Briggs *et al.*, 2011, p. 91). Parameters α and λ can be approximated from the mean and variance (s^2) of the distribution, and the gamma distribution can be shown by Equation 11,

$$F(x) = \lambda^{\alpha} \frac{1}{\Gamma(\alpha)} X^{\alpha-1} e^{-\lambda x} \qquad (11)$$

Where $x>0$, $\alpha = \text{mean}^2/s^2$ and $\lambda = s^2/\text{mean}$.

Similar to the effect parameters, to estimate the standard error of cost for each end node, we calculated the mean and standard error for the continuous chain of treatment (Mean=11,435, SE=691) and the broken chain of treatment (Mean=12,529, SE=3,060). The ratios were 16.56 and 4.09 for the continuous chain of treatment and the broken chain of treatment, respectively. We then estimated the standard errors for single end nodes by dividing their average costs into these ratios (Appendix 5).

5. RESULTS

Some demographic characteristics and the functional outcome of moderate and severe TBI patients were constructed in SPSS 20, and simple comparisons of patient groups between gender and injury severity and between age and injury severity were conducted using independent samples t-tests and chi-square tests (Table 6). The total length of stay in hospitals was 9802 days for moderate TBI patients, while over 8000 days were spent in hospitals by severe TBI patients. The average lengths of stay for severe TBI patients (n=91) are more than double of those of moderate TBI patients (n=38) (Table 6; Table 8).

Table 6 Demographic characteristics and functional outcome of moderate and severe TBI patients

Variables	**Moderate TBI patients (n=36)**	**Severe TBI patients (n=93)**	**Total TBI patients (n=129)**	**p**
Gender Male	27 (75.0%)	74 (79.6%)	101(78.3%)	0.57
Mean age (SD)	35.17(10.8)	30.95 (11.8)	32.12 (11.6)	0.13
Survivors	35 (97.2%)	71 (76.3%)	106 (82.2%)	0.00
Average GOSE score after 12 months (SD)	6.64 (1.2)	4.48(2.3)	5.09 (2.3)	0.00
Average GOSE 5 years post-injury(SD)	6.50 (1.6)	4.63 (2.5)	5.16 (2.5)	0.00
Average length of stay per patient (SD)	37.94 (43.41)	90.71 (86.05)	75.98 (80.01)	0.51

5.1 Outcomes

According to the decision tree model, the GOSE gain from 3 months to 5 years was 0.26 higher with the continuous chain of treatment (1.43) when compared to that of the broken chain of treatment (1.17) (Table 9).

Some statistical characteristics of severe TBI patients were constructed through Chi-square tests and t-tests in SPSS to compare GOSE scores at 3 months, 1 year, 5 years and to compare differences between 3 months and 5 years, 3 months to 1 year, etc. (Table 7).

Table 7 Statistical characteristics of severe TBI patients

Variables	**Early rehabilitation patients (n=30)**	**Later rehabilitation patients (n=29)**	**Total (n=59)**	**p**
Gender Male	23 (76.7%)	22 (75.9%)	45 (76.3%)	0.95
Mean age (SD)	26.73 (9.8)	31.21 (11.9)	28. 93 (11.0)	0.23
Average GOSE 3-month post-injury (SD)	4.63 (1.1)	4.24 (1.2)	4.44 (1.2)	0.21
Average GOSE 1-year post-injury (SD)	5.87 (1.3)	5.14 (1.3)	5.51 (1.3)	0.04
Average GOSE 5-year post-injury (SD)	6.07 (1.4)	5.41 (1.2)	5.75 (1.3)	0.08
Average GOSE change (3 months - 5 years) (SD, SE)	**1.43 (1.0; 0.2)**	**1.17 (0.9; 0.2)**	1.31 (1.0; 0.1)	0.00
Average GOSE change (1 year - 5 years) (SD)	0.2 (0.7)	0. 3 (0.7)	0.2 (0.7)	0.20

5.2 Costs

The expected total hospitalization costs of these 129 TBI patients varied from NOK 5,269 to NOK 3,107,522, and the amount of those 129 total costs reached NOK 99.7 million (Table 8). Among these costs, 86% (NOK 86 million) was spent on severe TBI. The total hospital lengths of stay for those 129 TBI patients ranged from 1 to 421 days. The sum of those 129 TBI patients was close to 10,000 bed days. The total costs per day differed from NOK 2,602 to NOK 185,119 among the patients. Based on Equation 6, we calculated that the average cost per patient was NOK 0.77 million at 5 years post-injury. The average cost per severe TBI patient reached NOK

0.92 million, which was more than twice of the price of the average cost per moderate TBI patient (NOK 0.39 million).

Table 8 Costs of TBI hospitalizations

	Number of patients (N)	**Total cost (Million NOK)**	**Average cost per patient (NOK) (SD;SE)**	**Lengths of stay (days)**	**Cost per day per patient (NOK) (SD)**
1-year post-injury	129	**92.2**	**714,000** (0.63m)	8,337	23,000 (28,200)
Severe TBI	93	79.7	857,000 (0.64m)	7,294	25,600 (31,100)
Moderate TBI	36	12.5	347,000 (0.46m)	1,043	16,100 (17,400)
5-year post-injury	129	99.7	773,000 (0.68m)	9,802	21,900 (28,300)
Severe TBI	93	85.7	922,000 (0.69m)	8,436	24,600 (31,100)
Moderate TBI	36	14.0	390,000 (0.48m)	1,366	14,800 (17,300)
Rehabilitations	82	31.9	389,000 (0.33m)	6,978	5,000 (2,800)
Severe TBI	64	26.5	414,000 (0.34m)	6,067	4,600 (2,400)
Moderate TBI	18	5.4	299,000 (0.31m)	911	6,300 (3,800)
Acute hospitalizations	129	67.8	526,000 (0.51m)	2,824	30,500 (30,100)
Severe TBI	93	59.2	637,000 (0.51m)	2,369	34,800 (31,200)
Moderate TBI	36	8.6	240,000 (0.37m)	455	19,700 (24,100)
CEA groups	59	72.3	1,255,000 (0.62m; 0.08m)	7338	13,000 (13,300)
Early rehabilitation	30	36.8	**1,237,000** (0.46m; 0.84m)	3378	12,800 (9,000)
Later rehabilitation	29	35.5	**1,274,000** (0.76m; 0.76m)	3960	13,300 (16,800)

In the same way, we calculated that the total costs of the first year following TBI were NOK 92 million, which accounted for 92% of the total costs after 5 years hospitalization. The average cost per patient at 1-year post-injury was NOK 715,000. When considering the severity of the injury, the average cost per moderate TBI increased by NOK 0.04 million from 1-year post-injury to 5-year post-injury, while the average cost per severe TBI increased NOK 0.06 million from 1-year post-injury to 5-year post-injury. The total length of stay was approximately 8,000 bed days in the first year stay of TBI patients, which accounts for 80% of the 5 years' bed days. The average cost per day per patient thus was calculated to be NOK 23,000, which was approximately NOK 1,000 higher than the 5 year average cost.

Total rehabilitation costs were NOK 31.9 million, which were approximately NOK 36 million lower than that of the acute hospitalizations. With regard to the cost per patient, the rehabilitation costs were NOK 0.4 million per patient, which were about NOK 0.2 million lower than the average cost per patient in the acute hospitalizations. The average cost of severe TBI in acute hospitalizations was NOK 0.2 million higher than rehabilitations, while the average cost of moderate TBI in acute hospitalizations was NOK0.1 million lower than rehabilitations. With regard to the cost per day per patient, the costs of acute hospitalizations were approximately 6 times higher than the costs of rehabilitations. For the severe TBI patients, the costs of rehabilitations were about NOK 30,000 lower than the costs of acute hospitalizations.

From Table 8, we can estimate the average costs per patient with moderate and severe TBI as NOK 0.71 million and 0.77 million at 1 year and 5 years post-injury. Average costs per severe TBI patient were 0.86 million at 1 year post-injury, and the average costs per moderate TBI patient were 0.35 million at 1-year post-injury. Andelic *et al.* (2008) estimated the incidence of hospitalized moderate TBI at 6.5 per 100,000, and the incidence of hospitalized severe TBI was 5.05 per 100,000 in 2005. The population of the south-east region of Norway was approximately 2,100,000; thus, the number of moderate TBI cases in 2005 was 136, and the number of severe TBI cases in 2005 was 106. Therefore, the number of hospitalized moderate and severe TBI patients was 242 in 2005. Based on Equation 7, we estimated that the total costs of moderate and severe TBI patients in south-east region of Norway were

$$TC_{\text{1st year}} = \bar{C}_T * N = 0.71 * 242 = 171.82 \text{ million}$$

$$TC_{\text{1st year\_severe}} = \bar{C}_T * N = 0.86 * 106 = 91.16 \text{ million}$$

$$TC_{\text{1st year\_moderate}} = \bar{C}_T * N = 0.35 * 136 = 47.6 \text{ million}$$

$$TC_{\text{5year}} = \bar{C}_T * N = 0.77 * 242 = 186.34 \text{ million}$$

5.3 Cost-effectiveness

The continuous chain of treatment with early rehabilitation had lower costs and better outcomes when compared to the broken chain of treatment without early rehabilitation (Table 9; Appendix 2). By replacing the broken chain of treatment with the continuous chain of treatment, NOK 37,760 could be saved and 0.26 GOSE scores could be gained. For the continuous chain of treatment, NOK 864,715 is needed for each unit GOSE score gained. For the broken chain of treatment, NOK 1,089,147 is needed for each unit GOSE score gained. In conclusion, the continuous chain of treatment was dominant in both effect and cost calculations.

The cost-effectiveness result was the same when the data were analyzed through SPSS (Table 7; Table 8), but with a larger uncertainty of the costs within the broken chain of treatment, whose standard deviation was 0.76 million. This standard deviation was 0.3 million higher than the standard deviation of the cost under the continuous chain of treatment.

Table 9 The incremental cost-effectiveness ratio (ICER) (NOK in 2009)

Strategy	C	E	C/E	∆ C	∆ E	ICER
Early rehabilitation	1,236,542	1.43	864,715	/	/	/
Later rehabilitation	1,274,302	1.17	1,089,147	-37,760	0.26	-154,231

*ICER refers to (1)

5.4 Uncertainty in cost-effectiveness

In the PSA, a scatter plot of simulated incremental cost and effect pairs on the incremental cost-effectiveness plane is used to represent the uncertainty by running a Monte Carlo simulation to propagate input parameters 10,000 times (Figure 6). The base case point estimate for the difference in effects and costs between the two strategies is 0.26 GOSE scores and NOK 37,760. The scatter plot also illustrates the uncertainty surrounding the expected incremental costs and effects associated with the continuous chain of treatment compared to the broken chain of treatment. With regard to effectiveness, the location and spread of the points indicate that there is uncertainty (GOSE scores from -0.82 to 0.82) regarding the benefit associated with the continuous chain of treatment versus the broken chain of treatment. With regard to the costs, the spread of the points in the vertical plane indicates that there is some uncertainty from NOK -35,000 to NOK 35,000.

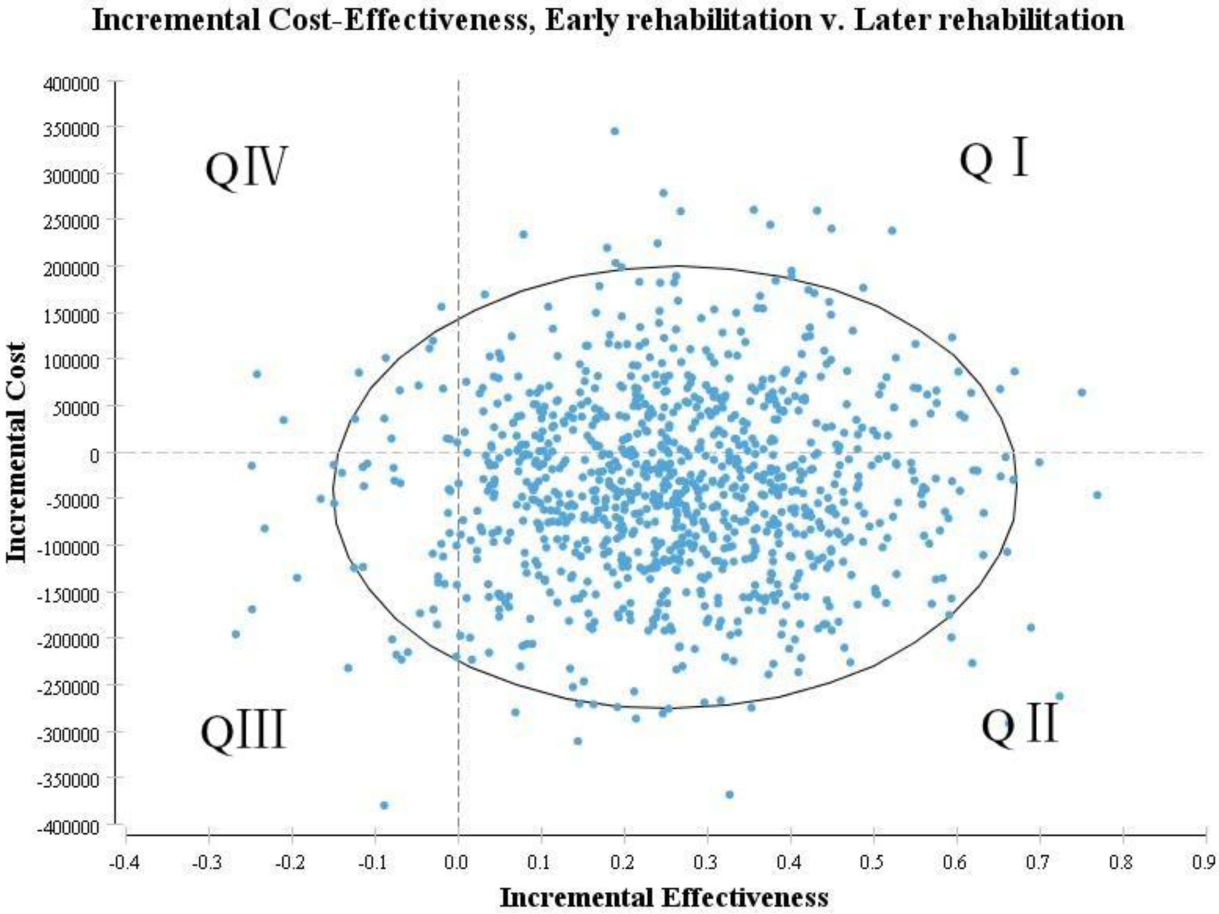


Figure 6 Scatterplot of cost-effectiveness of Early rehabilitation

The majority of incremental cost-effect pairs fall in quadrant II (61.45%) indicating that the continuous chain of treatment is less costly and more effective (Table 10). A small proportion (2.05%) of the points lies in quadrant IV, indicating that the continuous chain of treatment strategy is dominant, with a lower effect and higher cost. A total of 32.50% of pairs fall in quadrant I, and 4.00% pairs fall in quadrant III, indicating that there is uncertainty regarding the results of the continuous chain of treatment, either in terms of its higher effect and higher cost or lower effect and lower cost. This confirms that there is some uncertainty concerning whether and at what value the continuous chain of treatment strategy is cost-effective.

Table 10 The PSA results with the ICE Scatterplot (N=10,000 WTP=0)

Quadrant	**I**	**II**	**III**	**IV**	**Indifference**
Frequency (N)	32,495	61,451	4,000	2,054	0
Proportion (%)	0.32495	0.61451	0.04	0.02054	0

The CE acceptability curve (CEAC) shows that the continuous chain of treatment is cost-effective with a probability > 66% regardless of the value of willingness-to-pay (Figure 7). The CEAC summarizes the uncertainty of the incremental cost-effectiveness scatter plot, indicating that the probability that the ICER falls below the acceptable ratio is approximately 66% under the continuous chain of treatment when the willingness-to-pay is NOK 0, while the ratio increases to 73% when the willingness-to-pay increases to NOK 100,000.

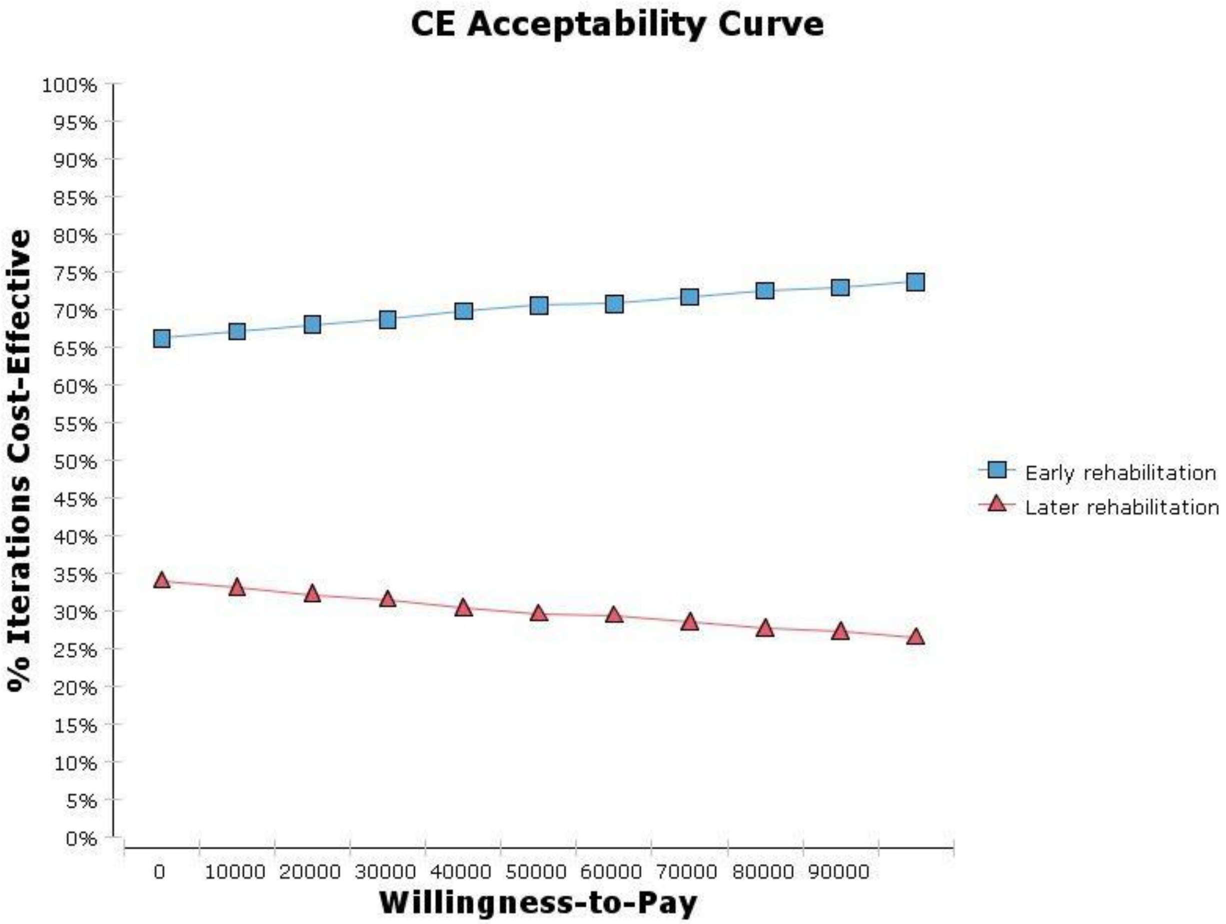


Figure 7 Cost-effectiveness acceptability curve *of the two strategies*

When we look at the cost-effectiveness scatterplot (Figure 8), it is clear to see that the continuous chain of treatment has higher effects. The GOSE increment with early rehabilitation is approximately 1.4 scores while the GOSE increment with later rehabilitation is approximately 1.2 scores. The two strategies overlap in a certain region where the effect is approximately 1.25 GOSE scores. From the overlap, the continuous chain of treatment goes towards better effects up to 1.95 GOSE scores. With regard to the broken chain of treatment, however, the scatterplot of the treatment extends towards lower effects of approximately 0.95 GOSE score.

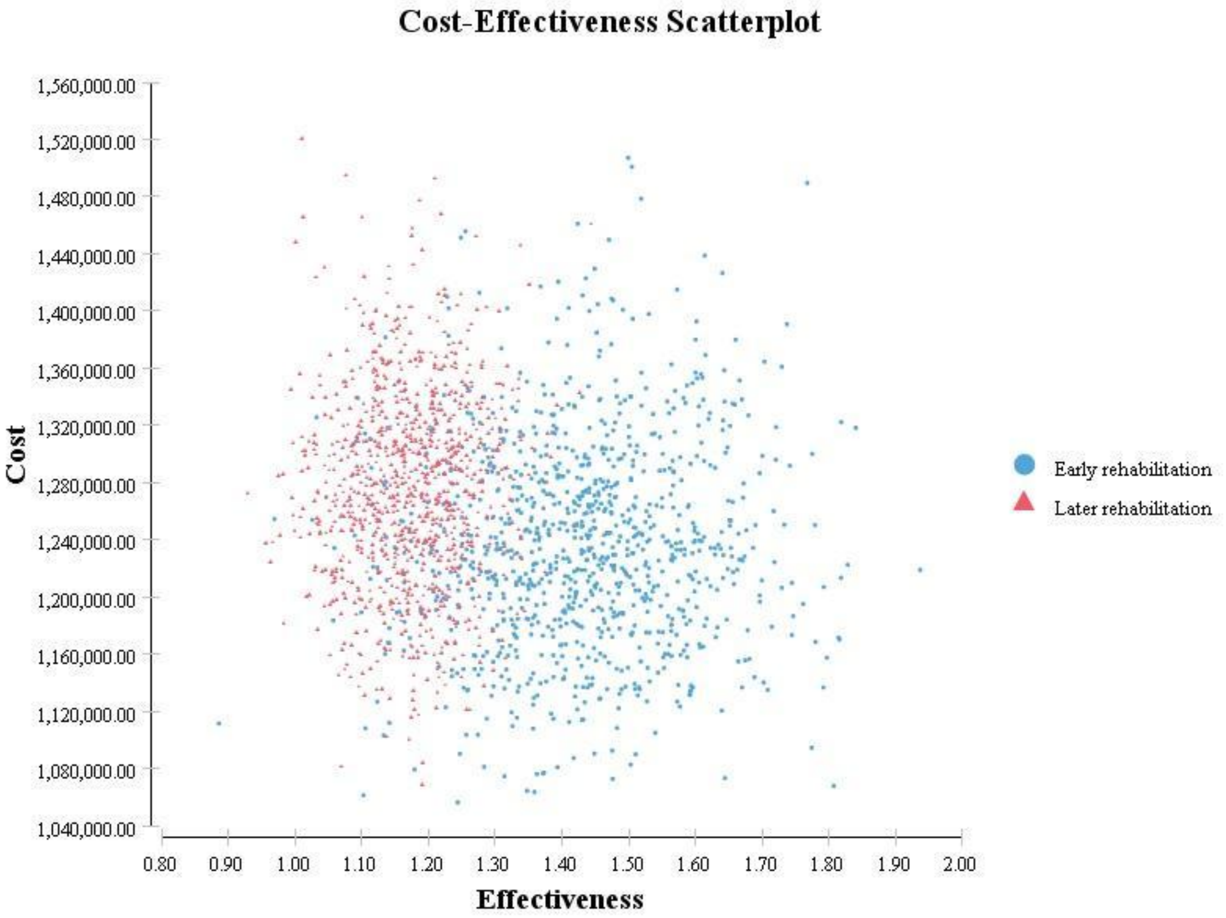


Figure 8 Cost-effectiveness scatterplot of the two strategies

In summary, although there is some uncertainty, there is a significant different between these two strategies. The continuous chain of treatment seems to be cost-effective with lower costs and higher effects compared to the broken chain of treatment.

6. DISCUSSION

The results of the study indicate the following: a) the continuous chain of treatment has lower costs and better outcomes than the broken chain of treatment over a long term period (5 years); and b) the total hospitalization costs of moderate-to-severe TBI are NOK 182 million in the first year and NOK 186 million 5 years post-injury in the Southeast part of Norway in 2005.

This study has some limitations. First, it might be difficult to generalize the study to other countries as the study is a quasi-experimental study based on "the available bed principle" instead of a randomized controlled trial (RCT). RCT specifies that the study objects are randomly allocated to receive the alternative treatments under study. In Norway, the ethical justification for randomizing patients seemed untenable for researching the acute care of patients with severe TBI. However, the inclusion criteria in this study helped the study patients more or less synonymously in terms of the acute and subacute care they received.

We did not estimate WTP while running the PSA. From Figure 8, 61.6% of the plots showed that early rehabilitation was cost-effective. Approximately 36.5% of the points fell in the quadrants I and III, showing a certain amount of uncertainty of the treatment. If we, for instance, used WTP = NOK 100,000, the cost-effective pairs increased to 74.4% (sum of points in section 1 to 3, where the comparator is chosen as an optimal alternative). When the WTP increased to NOK 500,000, the cost-effective pairs reached 90.7%, which means the early rehabilitation strategy was cost-effective in 90.7% of the simulations (Figure 9; Figure 10).

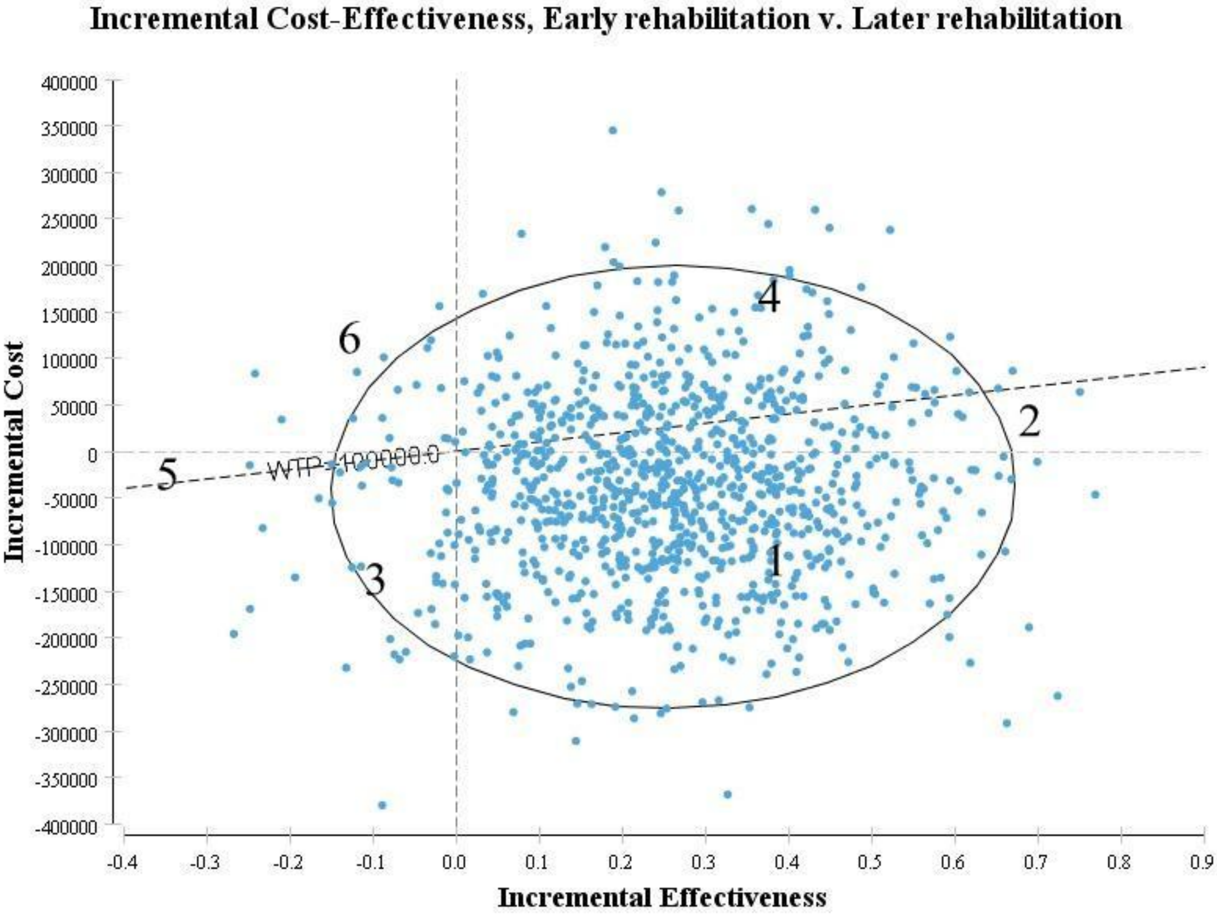


Figure 9 Scatterplot of cost-effectiveness of Early rehabilitation (WTP=NOK100,000)

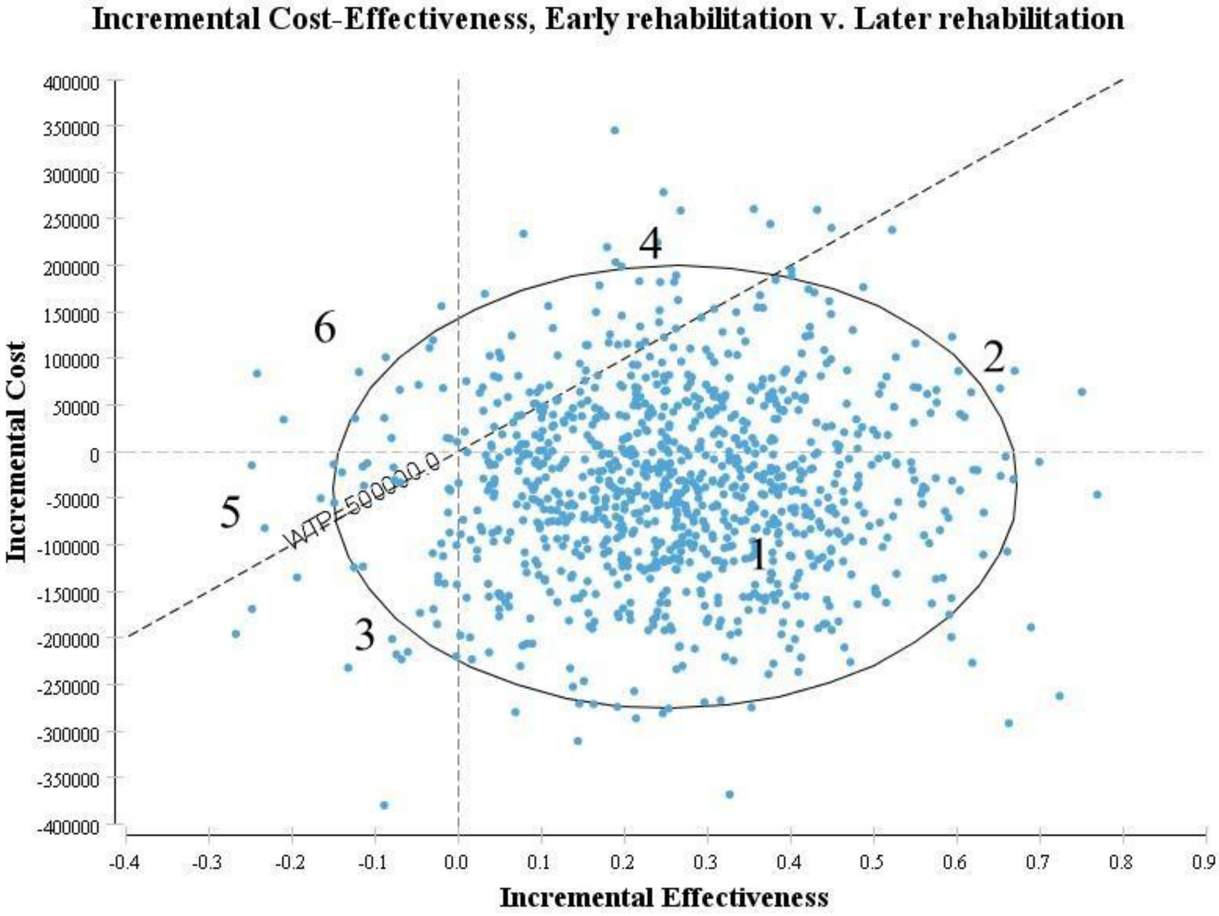


Figure 10 Scatterplot of cost-effectiveness of Early rehabilitation (WTP=NOK500,000)

Second, we did not translate the effect from GOSE scores to the QALYs. The use of QALYs will better show the utility of the model, as GOSE is not a final effect measurement. Here, the effect is more difficult to interpret because there is uncertainty about GOSE scores, and the increment from 2-3 and the increment from 7-8 actually varies significantly as well.

When estimating effects, we did not have the GOSE scores at 0 months, and the baseline used in the study was 3 months, which might be not yield precise results for the rehabilitation outcome output, which should have a higher GOSE effect if the difference from 0 month to 5 years was determined. However, the result of the CEA should not be affected because both groups were assessed by the same measurements.

In addition, the data of costs in this study are based on DRG pricing, obtained by simply multiplying DRG reimbursement by cost weight. It is relatively generalized and not accurate enough when compared with the bottom-up micro-costing method, which measures cost of every item in detail. However, the cost weight was calculated strictly for each patient according to their personal characteristics, which can still give us a general idea about the costs.

The study estimates inpatient hospitalization cost only, which is estimated from the hospital's point of view. The cost would have been higher if estimated from a patient or a societal perspective because these perspectives would be concerned with indirect costs such as time and productivity loss. The costs estimated in this study also exclude outpatient costs. If we include outpatient costs, the total costs of TBI patients in Norway will be higher. It would be interesting to include outpatient costs as well, given the broader view of costs. Therefore, further study about TBI costs from other perspectives and TBI outpatient costs are required.

The average inpatient cost for moderate and severe TBI in the first year after injury was NOK 0.71 million in this study, which is equivalent to € 94,000. When classified by severity, the average cost of inpatients with severe TBI in the first year was NOK 0.86 million, which is equivalent to € 114,000. The average cost of severe TBI was much higher than cost estimates in Europe in the review by Berg *et al.* (2005), which found that the average 1-year inpatient costs for severe TBI in Germany, Spain and Sweden were € 6,600, €6,000 and €6,400, respectively. These values may indicate that Norway has higher financial burden of TBI health care than Germany, Spain and Sweden. However, it is important to mention that our cost estimates included both the acute hospital care in Trauma Referral Centre, care in local hospitals and hospital-based rehabilitation costs. In addition, we included only patients who were survived at 5-year follow-up. According to McGarry *et al.* (2002), studies that include only survivors after TBI may tend to overstate average cost of care.

One strength of this study is the long time perspective (5 years) of the data that were collected and recorded. The findings of the study are practical for both hospital workers and government decision makers. Using the tool of decision model is a logical choice to handle all the data.

The results of this study indicate that treating TBI patients with early rehabilitation in a continuous chain of treatment is more cost-effective compared to the strategy of a broken chain of treatment with a waiting period for TBI rehabilitation. It should be noted, however, that there is a limit on the bed availability for early rehabilitation.

Even though the analysis shows that a continuous chain of treatment is cost-effective, there is a certain amount of uncertainty because of the small study group. While estimating uncertainty in end nodes for the model, simplifications were made because we have a small data set as was mentioned in section 4. Because the population of Norway is small and TBI is rare compared with other countries, it is difficult to obtain a large sample. Further research in the area should therefore focus on reducing uncertainty through Monte Carlo simulations.

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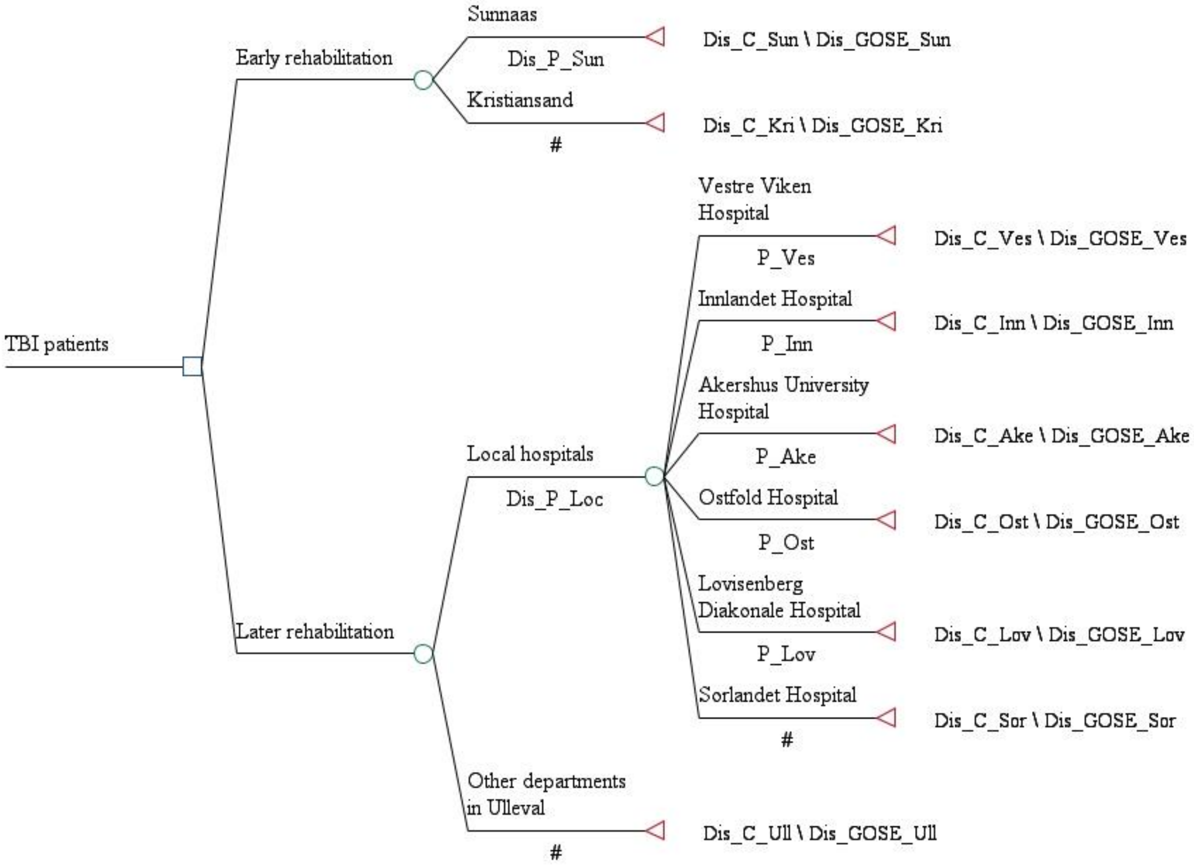
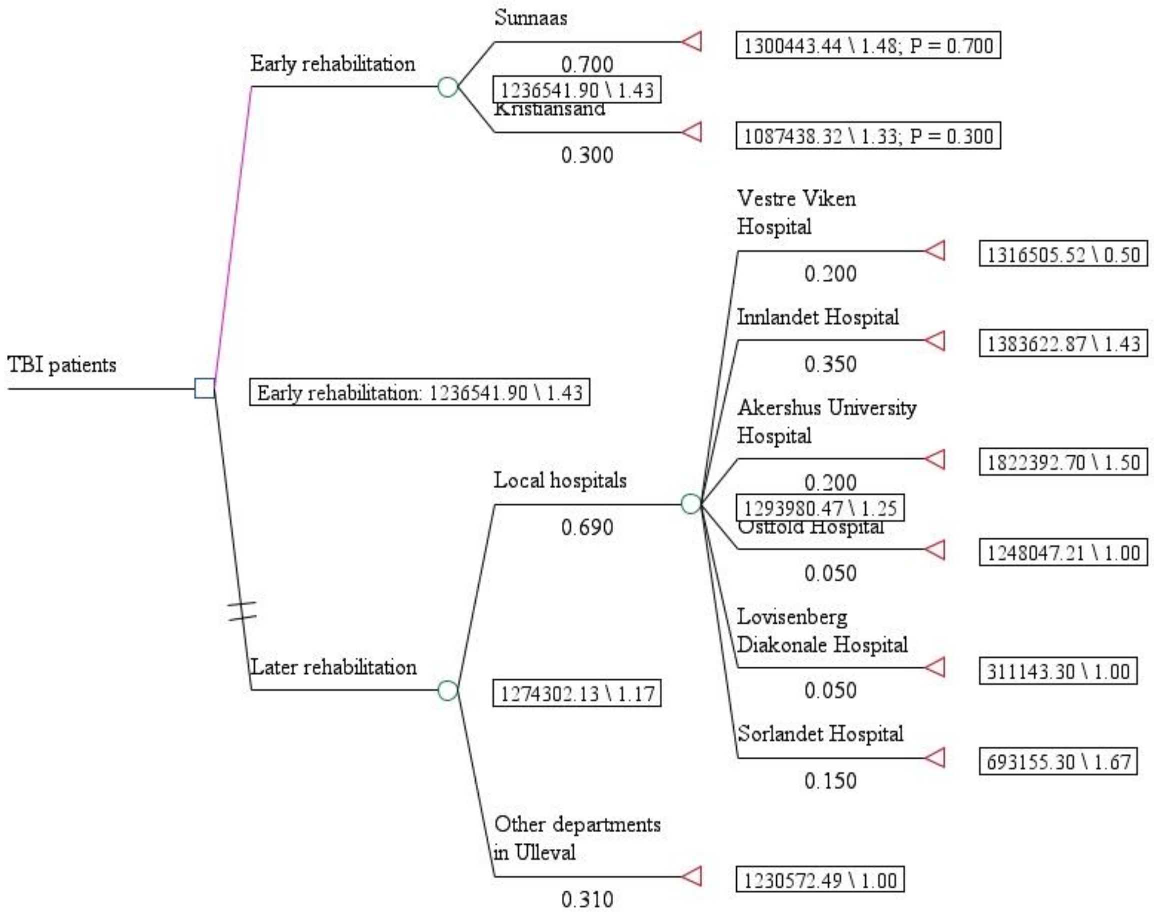
APPENDICES

Appendix I: Decision Tree Model for CEA



Appendix II: Result of Decision tree model



Appendix III: DRG system in Norway

The DRG system is based on two basic principles -- resource homogenous and medically meaningful. The DRG system is updated yearly in Norway with new diagnoses and new procedure codes. When treatment practices are changed or new methods are introduced, there is a need for changes to the grouping rules in the DRG system. According to the Norwegian Directorate of Health (Helsedirektoratet 2007), grouping rules are revised for mainly two reasons, either the DRG grouping is no longer medically appropriate, or groups are no longer homogeneous in terms of resource consumption.

Cost weights are the main measurement for hospital reimbursement in terms of ABF and are estimated from the cost and activity data from a range of hospitals. Cost weight is defined as the cost per patient in each DRG group. A DRG weight equal to one is defined as an average patient using an average amount of resources, and the relative use of resources is compared for all patients for this average patient cost. The DRG system thus estimates the mean cost of treatment for each group of patients based on the average patient (Skeie *et al.*, 2002).

The calculation for rehabilitation reimbursement is based on registered patient diagnoses and length of stay. The distinction between common and complex rehabilitation is the requirement for the multiple health care professions as in specialties. Complex rehabilitation, with DRG code Z5080, requires six health care professions to be involved in the treatment for individual treatment and collaboration with other agencies. There are some requirements for complex rehabilitation as well, including that the rehabilitation work is directed by a doctor who has special training in physical medicine and rehabilitation. The requirement for normal rehabilitation (with DRG code Z5089) is four health care professions involved for individual treatment and collaboration with other agencies.

Each patient’s stay has a corresponding cost weight. According to the ABF data from the directorate of health in Norway for 2009 (ISF 2008), the DRG reimbursement for one DRG weight was 35127 kroner. For TBI rehabilitation, if the cost weight was 1.21, the 100% DRG-derived revenue would amount to 35127*1.21= 42503.67 kroner accordingly.

Appendix IV: ICD-10 codes of TBI patients used in the study

Most of the ICD-10 codes used here regarding isolated TBI and TBI with multiple injuries were similar to a previous study (Andelic et al., 2008), and we estimated the percentage of diagnoses as well as the percentage of patients for the top 10 ICD codes used (Table 11; Table 12). The main diagnoses of isolated TBI are intracranial injuries (S06.0-S06.8), and TBI with multiple injuries includes skull and facial fractures (S02.0-S02.6) and some other fractures. In addition, we explored the ICD-10 codes of the TBI patients with complications, who are separated from isolated and multiple TBI (Table 13). Proportion of the top 10 diagnoses of isolated TBI, TBI patients with multiple injuries and TBI patients with complication account for the diagnoses are approximately 32.4%, 15.9% and 11.3%, respectively. Therefore, a total of 60% of the diagnoses are accounted for the diagnoses by summing their percentage.

Table 11 Top 10 diagnoses of isolated TBI patients

ICD-10 classification	**Disease**	**Percentage of diagnoses**	**Percentage of patients**
S06.2	Diffuse brain injury	7.3%	37.2%
S06.3	Focal brain injury	6.5%	39.5%
S06.5	Subdural hemorrhage	5.5%	31.8%
S06.6	Traumatic subarachnoidal hemorrhage	4.8%	30.2%
S06.1	Traumatic brain oedema	3.6%	25.6%
S06.4	Epidural hemorrhage	2.4%	12.4%
S06.0	Concussion	1.2%	10.1%
S09.9	Unspecified head injury	0.5%	4.7%
S06.8	Other intracranial injuries	0.4%	0.01%
S06.9	Intracranial injuries, unspecified	0.2%	2.3%
Total	/	32.4%	/

Table 12 Top 10 diagnoses of TBI patients with multiple injuries

ICD-10 classification	**Disease**	**Percentage of diagnoses**	**Percentage of patients**
S02.1	Skull base fracture	4.2%	26.4%
S02.0	Skull fracture	2.1%	14.0%
S27.3	Pulmonary injury	2.0%	16.3%
S02.4	Zygoma fracture	1.9%	14.0%
S27.0	Pneumothorax	1.2%	11.6%
S01.7	Open wounds in the head	1.1%	7.8%
S22.4	Rib fracture	1.0%	6.2%
S32.7	Fracture of lumbal spine and pelvis	0.9%	4.7%
T06.8	Injuries involving multiple regions	0.8%	4.7%
T02.8	Injuries involving specific combinations of body regions	0.7%	5.4%
Total	/	15.9%	/

Table 13 Top 10 diagnoses of TBI patients with complication

ICD-10 classification	**Disease**	**Percentage of diagnoses**	**Percentage of patients**
J13-15; J15.2; J15.5; J15.9; J18; J18.9; J69	Pneumonia	4.2%	27.1%
J96.0; J98.1	Respiratory failure	3.6%	26.4%
G40.9	Epilepsy	0.7%	5.4%
A40-40.9; A41	Sepsis	0.6%	3.1%
R56; R56.8	Seizures	0.4%	2.3%
B37; B37.3	Candidiasis	0.3%	0.8%
E87	Disorders of fluid and electrolyte balance	0.3%	2.3%
F10; F10.2; F10.9; F05.9	Conduct disorder	1.0%	7.8%
E23	Pituitary disorder	0.1%	0.8%
N30.9	Cystitis	0.1%	0.8%
Total	/	11.3%	/

Appendix V: Input parameters in Decision Tree

Distribution type	**Name**	**Description**	**Param 1**	**Param 2**
Beta (Param 1 = alpha; Param 2 = beta)	Dis_P_Sun	Probability of patients go to Sunnaas Rehabilitation	21	9
	Dis_P_Loc	Probability of patients go to Local Hospitals	20	9
	Dis_P_Ves	Probability of patients go to Vestre Viken Hospital	4	16
	Dis_P_Inn	Probability of patients go to Innlandet Hospital	7	13
	Dis_P_Ake	Probability of patients go to Akershus University Hospital	4	16
	Dis_P_Ost	Probability of patients go to Ostfold Hospital	1	19
	Dis_P_Lov	Probability of patients go to Lovisenberg Diakonale Hospital	1	19
Gamma (Param 1 = alpha; Param 2 = lambda)	Dis_C_Sun	Cost of patients in Sunnaas Hospital pathway	(10860^2)/(660^2)	10860/(660^2)
	Dis_C_Kri	Cost of patients in Kristiansand Rehabilitation pathway	(12780^2)/(770^2)	12780/(770^2)
	Dis_C_Ves	Cost of patients in Vestre Viken Hospital pathway	(8030^2)/(1960^2)	8030/(1960^2)
	Dis_C_Inn	Cost of patients in Innlandet Hospital pathway	(7770^2)/(1900^2)	7770/(1900^2)
	Dis_C_Ake	Cost of patients in Akershus University Hospital pathway	(7550^2)/(1840^2)	7550/(1840^2)
	Dis_C_Ost	Cost of patients in Ostfold Hospital pathway	(8270^2)/(2020^2)	8270/(2020^2)

	Dis_C_Lov	Cost of patients in Lovisenberg Diakonale Hospital pathway	(10040^2)/(2450^2)	10040/(2450^2)
	Dis_C_Sor	Cost of patients in Sorlandet Hospital pathway	(45180^2)/(11040^2)	45180/(11040^2)
	Dis_C_Ull	Cost of patients in Ulleval Hospital pathway	(10310^2)/(2520^2)	10310/(2520^2)
Normal (Param 1 = mean; Param 2 = stddev)	Dis_GOSE_Sun	GOSE scores of patients in Sunnaas Rehabilitation pathway	1.48	0.20
	Dis_GOSE_Kri	GOSE scores of patients in Kristiansand Rehabilitation pathway	1.33	0.18
	Dis_GOSE_Ves	GOSE scores of patients in Vestre Viken Hospital pathway	0.50	0.07
	Dis_GOSE_Inn	GOSE scores of patients in Innlandet Hospital pathway	1.43	0.20
	Dis_GOSE_Ake	GOSE scores of patients in Akershus University Hospital pathway	1.50	0.21
	Dis_GOSE_Ost	GOSE scores of patients in Ostfold Hospital pathway	1.00	0.14
	Dis_GOSE_Lov	GOSE scores of patients in Lovisenberg Diakonale Hospital pathway	1.00	0.14
	Dis_GOSE_Sor	GOSE scores of patients in Sorlandet Hospital pathway	1.67	0.23
	Dis_GOSE_Ull	GOSE scores of patients in Ulleval Hospital pathway	1.00	0.14