January 2013

Predicting the Clinical Outcome in Patients with Traumatic Brain Injury using Clinical Pathway Scores

Jennifer Lorena Mendoza Alonzo
University of South Florida, jennifermend@mail.usf.edu

Predicting the Clinical Outcome in Patients with Traumatic Brain Injury Using Clinical Pathway Scores

by

Jennifer L. Mendoza Alonzo

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science in Industrial Engineering
Department of Industrial and Management Systems Engineering
College of Engineering
University of South Florida

Co-Major Professor: Jose Zayas-Castro, Ph.D.
Co-Major Professor: Peter Fabri, M.D., Ph.D.
Patricia Zarate, Ph.D.

Date of Approval:
March 18, 2013

Keywords: Functional Independence Measures, Support Vector Regression, Polytrauma/TBI Rehabilitation Center, Veterans Affairs Hospital, Percentage of Potential Recovery

DEDICATION

I dedicate this work to my family.

ACKNOWLEDGMENTS

I would like to express my gratitude and thanks to my advisors Dr. Jose Zayas-Castro and Dr. Peter J. Fabri for their patience and guidance throughout my research.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF EQUATIONS

ABSTRACT

The Polytrauma/TBI Rehabilitation Center (PRC) of the Veterans Affairs Hospital (VAH) treats patients with Traumatic Brain Injury (TBI). These patients have major motor and cognitive disabilities. Most of the patients stay in the hospital for many months without major improvements. This suggests that patients, family and the VAH could benefit if healthcare provider had a way to better assess or "predict" patients' progression. The individual progress of patients over time is assessed using a pre-defined multi-component performance measure Functional Independence Measures (FIM) at admission and discharge, and a semi-quantitative documentation parameter Clinical Pathway (CP) at weekly intervals. This work uses already de-identified and transformed data to explore developing a clinical outcome predictive model for patients with TBI, as early as possible. The clinical outcome is measured as percentage of recovery using CP scores. The results of this research will allow healthcare providers to improve the current resource management (e.g. staff, equipment, space) through setting goals for each patient, as well as to provide the family more accurate and timely information about the status and needs of the patient.

CHAPTER I:

INTRODUCTION

The James A. Haley Veterans Affairs Hospital (JAHVAH) receives soldiers from the Operation Enduring Freedom (OEF) in Afghanistan and in the Operation Iraqi Freedom (OIF) in Iraq. They present Traumatic Brain Injuries (TBI) caused by exposure to explosion on the field of combat. Veterans Affairs Hospital (VAH) operates a designated Polytrauma Rehabilitation Center (PRC) caring for wounded servicemen with complex injuries. Patients are admitted at distinct functional levels and have variable degrees of recovery. Many require total care, which includes comprehensive rehabilitative therapies over multiple stages, leading to high utilization of resources.

This work main objective is to explore the development of a predictive model to forecast the patient's clinical outcome as early as possible. The effort is deemed necessary due to the following: a) the complexity of rehabilitating these patients: b) the families' need of accurate information and proper preparation for the discharge/transfer event; and c) the hospital's need of an effective and efficient utilization of resources.

The model is based on one of the functional metric utilized in the PRC to measure motor and cognitive disabilities: "Clinical Pathway" (CP). This metric is comprised by 18 different components, each one measured in a scale from 1 to 7.

The two models propose in this work use as output variable a percentage of potential recovery, which is a transformation of the regularly used delta score, i.e. the difference between discharge score and admission score. It is hypothesize that the use of this new variable will improve the accuracy of the prediction and be more meaningful than the "regularly variable delta".

The limitation of this work, however, lies in the sample size, which is49 patients. This amount of patients does not allow validating the metric "Clinical Pathway" as a tool to measure clinical outcomes, nor allows having training and testing sets.

An effective predictive model should help in: deciding when to discharge transfer patients, a better utilize staff and equipment, provide more accurate and early information to the families about the rehabilitative status of the patients, and a better prepare the families for the discharge or transfer instance.

This work is divided in four chapters. Chapter II explains the context and foundations that have motivated to develop this study. Chapter III explains the methodology used to achieve the objective

stated before, basically this work is based on applying the initial four data mining steps: data extraction, data cleaning, data transformation, and model building. Chapter IV analyzes the proposed models considering the contributions and limitations of each one. Finally, Chapter V summarizes the main conclusions of this research and lays out possible future work.

CHAPTER II:

CONTEXT

Chapter II is divided into three sections. The first section addresses TBI and its relationship with the "Wounded Warriors" that come from the OEF and the OIF. The second section explains the relationship between the TBI and the Polytrauma/TBI System of Care (PSC) of the VAH. The third section shows the impacts and needs of the families in the rehabilitation process of the patients with TBI.

Traumatic Brain Injury

On December 31st 2011, 152,000 active military personnel were deployed in the OEF in Afghanistan and in the OIF in Iraq, as consequence of the Global War on Terror (GWOT) (Belasco, 2009; Department of Defense, 2012). In the OEF, 18,191 soldiers were wounded between October 2001 and December 2012 (Department of Defense, 2013a), and in the OIF, 31,926 soldiers were wounded between March 2003 and December 2012 (Department of Defense, 2013b).

Blast injury has been the main war wound in action in the GWOT (Mernoff & Correia, 2010; Owens et al., 2008; Sayer et al., 2008). This is a damage caused by a "*violent explosion*" or by the "*wave of pressure from such an explosion*" (Department of Veterans Affairs, 2011b). The most substantial sources that produce this wound are rocket-propelled grenades *(*RPGs*)*, improvised explosive devices (IEDs), explosively formed projectiles (EFP), mines, and booby traps (Belanger, Uomoto, & Vanderploeg, 2009; Veterans Health Initiative, 2010). Technological advances in equipment have allowed that more soldiers survive to blast injuries than in previous conflicts (Gawande, 2004; Mernoff & Correia, 2010; Peake, 2005; Sayer et al., 2008). Among blast injuries occurred in GWOT, 60% result in Traumatic Brain Injury (TBI) (Gawande, 2004; Ling, Bandak, Armonda, Grant, & Ecklund, 2009; Okie, 2005; DL Warden et al., 2005).

According to the (Department of Veterans Affairs, 2011b), TBI is defined as *"[…] the result of a severe or moderate force to the head, where physical portions of the brain are damaged and functioning is impaired […]".* The severity of the TBI depends on the brain region that was impacted, the nature and the strength of the force, and the physical and genetic characteristics of the victim (Kimberly Meyer, Kathy Helmick, Selina Doncevic, & Rachel Park, 2011). It can vary from mild (brief change in consciousness) to severe (long period of

unconsciousness). The most frequent diagnosis is mild TBI (mTBI) (Belanger et al., 2009). Only an 8% of the OEF and OIF veterans are diagnosed with severe TBI (Kimberly Meyer et al., 2011).

The symptoms after a head injury are called Post-Concussion Syndrome (PCS), and depending on the severity of the injury, they can persist for months or years (Department of Veterans Affairs & Department of Defense, 2010). In the case of moderate or severe TBI, they can even be considered as permanent sequelae (Veterans Health Initiative, 2010). These symptoms are physical (e.g. headaches, dizziness, vision changes), cognitive (e.g. concentration problems, memory problems, abstract thinking problems), and emotional (e.g. irritability, anxiety, aggression) (Veterans Health Initiative, 2010). The previous conditions can make the diagnosis difficult because many of the patients may not show visible signals of injury (Mental Illness Research Education and Clinical Centers, 2009).

The majority of the patients who are screened as positive for TBI are also diagnosed with a mental problem; the most frequent mental problem is Post-Traumatic Stress Disorder (PTSD) (Taylor et al., 2012). In turn, patients with moderate to severe TBI increase the risk of Post-Traumatic Epilepsy (PTE) (Masel & DeWitt, 2010), which can be showed up in a range of years from the moment that the head injury occurs (Aarabi, Taghipour, Haghnegahdar, Farokhi, & Mobley, 2000).

The prevalence of soldiers with TBI has labeled this injury is considered as the "signature wound" of this war (Okie, 2006; D. Warden, 2006). Likewise, the VA, which is defined as *"[…] the most comprehensive system of assistance for veterans in the world […]"* (Department of Veterans Affairs, 2012a) has taken into account TBI as a priority in healthcare service (Belanger et al., 2009; Veterans Health Initiative, 2010).

Polytrauma/TBI System of Care

In 2005, the VA created a specialized care system for individuals with TBI and multiple injuries or polytrauma, which is known as Polytrauma/TBI System of Care (PSC) (Sigford, 2008). The mission of the PSC is: *"[…] provides comprehensive, high-quality, and inter-disciplinary care to patients. Teams of physicians from every relevant field plan and administer an individually tailored rehabilitation plan to help the patient recover as much as possible […]"* (Department of Veterans Affairs, 2012c).

Even though VA provides health care services for veterans, collaborative agreements with the Department of Defense (DoD) have allowed that active duty Service Members (SMs) also can receive care in PSC (Uomoto, 2012; Veterans Health Initiative, 2010). From October 2001 until the fiscal year (FY) 2012, 804,704 SMs that left

active duty in OEF and OIF (including Operation New Dawn (OND)) have obtained care in the VA Health Care System, of which 7% have been inpatients (Department of Veterans Affairs, 2012). Between the FY 2003 and FY 2011, PSC received 2,160 inpatients with TBI (Cifu, 2012), thus, it is estimated that over 2,600 patients with TBI have been treated in the PSC from the beginning of the GWOT.

PSC is composed of four modules of care: 5 PRCs which are located in Richmond, VA, Tampa, FL, Minneapolis, MN, Palo Alto, CA, and San Antonio, TX; 23 Polytrauma Network Sites (PNS); 87 Polytrauma Support Clinic Teams (PSCT); and 38 Polytrauma Point of Contact (PPOC) (Department of Veterans Affairs, 2012d).

The OEF and OIF militaries who enter the VA health care system may receive an initial TBI screen (Mernoff & Correia, 2010; Uomoto, 2012; Veterans Health Initiative, 2010). The screen consists of determining any injury in the brain that *"has made an effect in the consciousness"* through a 5 minutes survey with questions related to the "*current health*" and "*combat experiences*", as first step (Department of Veterans Affairs, 2012b; Veterans Health Initiative, 2010). The diagnosis is ratified using severity ratings (such as Glasgow Coma Scale (GCS)), computed tomography (CT) and magnetic resonance imaging (MRI), if the patient's condition allows (Veterans Health Initiative, 2010).

The patients diagnosed with TBI are referred to an adequate unit of care depending on the severity of the damage. All of those that return with a deeper level of unconsciousness or in coma are sent to acute rehabilitation programs such as Emerging Consciousness Program or Brain Injury Rehabilitation in one of the five PRCs (Department of Veterans Affairs, 2011a; Uomoto, 2012). In these programs, patients may emerge from the coma and then they start the rehabilitation process.

The rehabilitation process consists of cognitive, physical and emotional treatments such as: improving the communication skills, dealing with changes in behavior, treatment for dizziness and pain, and supporting in adjustment and coping (Department of Veterans Affairs, 2011a). In this stage of recovery, two Activities of Daily Living (ADL) assessment tools play an important role in the PSCs: Functional Independence Measure (FIM) and Clinical Pathway (CP) scores, which evaluate the progress of patients in terms of cognitive and motor functions.

FIM measures the functions of the patients routinely at admission and at discharge from the rehabilitation unit, and consists of 18 components: 13 of them measure motor tasks, and the 5 remainder, measure cognitive tasks (Uniform Data System for Medical Rehabilitation, 2013). CP measures similar functions weekly and also

comprises 18 components: 11 refer to motor functions and 7 to cognitive functions (Table 1).

Table 1 Motor and cognitive FIM and CP components

Functional Independence Measure FIM	**Clinical Pathway CP**
Motor	*Motor*
Eating	Eating
Grooming	Grooming
Bathing/showering	Bathing
Dressing upper body	Dressing - Upper Body
Dressing lower body	Dressing - Lower Body
Toileting	Toileting
Bladder management	Bladder Management
Bowel management	Bowel Management
Transfers: bed/chair/wheelchair	Bed Mobility
Transfer s: Toilet	Locomotion
Transfers: bathtub/shower	Transfer
Locomotion: walk/wheelchair	*Cognitive*
Locomotion: stairs	Language Comprehension
Cognitive	Expression
Comprehension	Attention
Expression	Memory
Social interaction	Social Language
Problem solving	Problem Solving
Memory	Safety

Source: VA Hospital Data Set

FIM score has been used to measure the progress of rehabilitation in a number of different condition such as: stroke, spinal cord injury, brain injury, multiple sclerosis, orthopedic conditions, and geriatrics (Uniform Data System for Medical Rehabilitation, 2013). It has been the most widely used assessment tool used to measure clinical outcomes in the United States (Cournan, 2011).

(Black, 2012) states measuring the clinical outcome can help in: providing feedback to the team to improve the services/programs and

to monitor the resources utilization; facilitating the communication among the stakeholders (clinicians, family members, patients), through a *"meaningful"* and *"readily available"* information flow; establishing individual goals for each patient; and assisting in decision-making about the discharge time.

Similarly, (Poon, Zhu, Ng, & Wong, 2005) established that predicting clinical outcomes of patients with TBI has a positive effect in the *"priority-setting of the limited resources"*, as well as, an impact in the family members since it provides *"essential information for counseling of the family"*. This last effect is very important due to the leading role of the family in the rehabilitation process, and at discharge, since the usual discharge destination is "home" with 67% of the patients treated in the PRCs VAH (Cifu, 2012).

Impacts on and Needs of the Family System

A war has great consequences life of a family and many studies refer to the effects caused by the war on family members (Kelley & Jouriles, 2011; Lester et al., 2010; Paris, DeVoe, Ross, & Acker, 2010). The characteristics of the service member's family before the injury, named as pre-TBI, are important in determining the way that the family members will deal with the *"psychological adjustment"* and

the *"quality of life"* once the injured soldier returns (Dausch & Saliman, 2009; McFarlane, 2009).

Relocation and employment problems, changes in the family roles, concern for the deployed family member, economic problems, and family conflicts are some of the pre-TBI problems that the families of the SMs have to face (Makin-Byrd, Gifford, McCutcheon, & Glynn, 2011; McFarlane, 2009). (Mansfield et al., 2010) concluded that the length of deployment in Iraq and Afghanistan has a mental health effect on the wives of the SMs: depressive disorder, anxiety, and acute stress reaction or adjustment disorder are the most common diagnoses. In addition, the previous causes can contribute to an increase in the rate of maltreatment (e.g. neglect, physical abuse, emotional abuse, and sexual abuse) in children of the families with active duty SMs (Gibbs, Martin, Kupper, & Johnson, 2007).

On the other hand, the different family reactions post-TBI associated with the stage of rehabilitation of the patients were established by (Lezak, 1986) and adapted by VA (Veterans Health Initiative, 2010), which range from depression, shock, and denial, to complete reorganization of the family. The work of (Verhaeghe, Defloor, & Grypdonck, 2005) states that spouses have a greater psychological impact than parents in caring for individuals that have

TBI and, at the same time, the negative effects on the caregivers increase when there are children living at home.

To reduce the negative psychological consequences for the family during the rehabilitation process, (Bond, Draeger, Mandleco, & Donnelly, 2003) established four needs of the families of the patients with TBI: *"need for involvement"* (contribution of the family in the care of patient), *"need for consistent information"* (the condition of the patient must be reported to the family beyond doubts or contradictions by health care personnel), *"need to make sense of the experience"* (understandable and comprehensive information about the procedures performed to the patient), and *"need to know"* (family members prefer to know the truth about the patient's condition whatever the outcome may be). This last need is directly related to the clinical outcome.

On the other hand, an early study (Mintz, Van Horn, & Levine, 1995) stated that family welfare indices improve when treatment is given in an outpatient program, as opposed to when the care is provided in the center of rehabilitation. In turn, the necessities of both, the patient and the family are different when the patient stays in the hospital as inpatient, from those required when patients receive outside assistance (Griffin, Friedemann-Sánchez, Hall, Phelan, & van Ryn, 2009). The information and the support that the caregivers can receive at discharge is important since they not only deal with helping

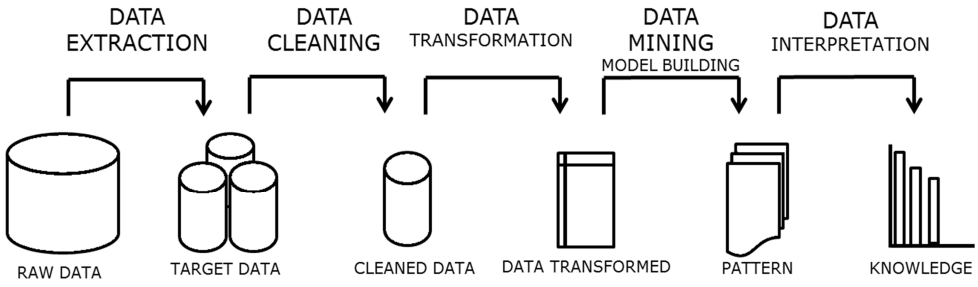
the family members in ADLs, but also with appointments, devices, and management of emotions and pain (Griffin et al., 2012).

Based on the benefits for both healthcare providers and the families, to estimate in advance the possible clinical outcomes in patients with TBI, this work shows an approach to predict the potential recovery using the CP scores. The use of CP for this analysis provides a new metric, using serial, weekly measure which has not previously been published.

CHAPTER III:

METHODOLOGY

This chapter describes the methodology used to achieve the objective of predicting clinical outcome in patients with TBI using clinical pathway score. The work is based on the five steps depicted in the Figure 1. This chapter has been divided in the four first stages of the data mining process: data extraction, data cleaning, data transformation, and data mining or model building.



Source: Own creation

Figure 1 Data mining steps

Data Extraction

The data used in this study corresponds to a dataset of 49 patients, which was extracted from the VA electronic medical records. Important note, the data was appropriately pre-processed by

authorized people before being analyzed in this work, to de-identify the patients, with conversion of dates to hospital day number. This action generated the following two "sub-datasets":

Sub-dataset 1: False patient ID, FIM scores per component at admission and at discharge (Table 2).

Table 2 Example of data collection for FIM score

Component	False Patient ID					
	1	**2**	**3**	**4**	**5**	**6**
Eating	1	1	2	2	2	…
Grooming	1	1	2	2	…	…
Bathing	1	1	1	…	…	…
Dressing – U	1	1	…	…	…	…
…	2	…	…	…	…	…

Sub-dataset 2: False patient ID, weekly score of the 18 CP components. Measurement numbering begins with 0 (Table 3).

Table 3 Example of data collection for CP score (record of one patient)

False ID	Measurement	Eating	Grooming	Bathing	Dressing - Upper Body	
1	0	3	2	4	3	…
	1	3	2	4	2	…
	2	3	2	4	…	…
	3	3	2	…	…	…
	4	2	…	…	…	…
	5	…	…	…	…	…

Data Cleaning

Cleaning sub-dataset 2 basically consists of dealing with CP missing values including missing rows related to US federal holidays. The data set has a total of 72 missing rows and, additionally, around 100 missing values.

Missing values can be classified in four categories: (1) first measurement (or measurement 0) with missing values/row, (2) missing values/rows in the middle, (3) last measurement with missing values/row, and (4) a segment of missing values (i.e. more than two consecutive missing values in a column).

The criteria used to fill the missing values are explained below:

First Measurement with Missing Values/Row

To deal with *missing values* in the first row the cross-multiplication technique is used considering the tendency shown by the patient in the scores of the other components, from the first to the second measurement. Table 4 shows an example**.**

Table 4 Example of a missing value in the first row

ID	Measurement	Eating	Grooming	Bathing	…	Safety
1	0	■	**?**	■	■	■
	1	▲	●	▲	▲	▲
	2				…	…
	3			…	…	…

The missing value of the "Grooming" in the first row, is calculated by the ratio between the summation of the squares (first row) and the summation of the triangles (second row), the result is multiplied by the circle.

On the other hand, if there is a missing row in the measurement 0 and all the values in the measurement 1 are equal to 7 (Table 5), the missing row is replaced by the score 7. Otherwise, the row is deleted and all the measurements are moved one week up, i.e. measurement 1 becomes measurement 0, due to the uncertainty of the extrapolation process in a complete row and the importance of the admission scores for the prediction model.

Table 5 Example of a missing row in the first row

ID	Measurement	CP1	CP2	CP3	...	CP18
1	0	**?**	**?**	**?**	**...**	**?**
	1	7	7	7	…	7
	2				…	…
	3			…	…	…

Middle Missing Values/Rows

The criterion for replacing a *missing value in the middle* is the same as a *middle missing row*. If the empty cell falls between two different numbers that are two units apart (e.g. 4 and 2) it is replaced by the mean (e.g. 3). If the mean is a decimal value, i.e. the missing number falls between two different values that are consecutive (e.g. 4

and 3), the number is rounded to the nearest integer (e.g. 3.5 ≈ 4). If there are more than a two unit distance (e.g. 7 and 2 or 6 and 2) the two previous criteria are used depending on if the mean is decimal or integer, respectively. The use of the mean is based on the assumption of progressive in the recovery.

Last Measurement Missing Value/Row

A *missing row in the last* measurement is deleted and the prior is considered the last record as the discharge measurement. A *missing value in the last row* is replaced using cross-multiplication, as in the example described in Table 4.

Segment of Missing Values

If there are two or more consecutive *missing values in a column* in the middle of the dataset, all the missing values are replaced by the previous measurement, assuming that the patient has kept the same condition during that time. Cross-multiplication is used if the patient does not have data in a specific segment, which includes a *missing value in the admission row* or in *the discharge row*.

On the other hand, since the FIM scores do not present missing values no replacement rule has been used.

Data Transformation

In this section the transformation of the data to create the input and the output variable for setting the model is explained. In the first section the response variable and, in the second section the selection of the explanatory variables is explained.

Response Variables

The response variables should measure the clinical outcome. Based on the purpose of the clinical outcome presented before, the variable should measure the progress achieved during the inpatient rehabilitation. The data collection related to the FIM and the CP scores is used to create a continuous variable in terms of the improvements in the motor and cognitive skills of the patients.

FIM and CP are metrics that represent the level of independence of the patient. Table 6 and Appendix B show the scoring criteria for FIM and CP, respectively. The metrics are rated from 1 to 7 and they are considered as ordinal Likert-scales (Nanna & Sawilowsky, 1998) because it is uncertain if the values are equally spaced.

Although some literature suggests that the use of parametric methods in Likert-type scales accomplishes acceptable conclusions (Norman, 2010), in this work the individual components will be analyzed as ordinal scales. However, the sum of the scores for FIM and

CP metrics will be considered as interval scale, as it was suggested by (Kidd et al., 1995) in an early study developed for the FIM scores.

Table 6 FIM scoring criteria

Score	Description
1	Total assistance (patient can perform less than 25% of the task or requires more than one person to assist
2	Maximal assistance (patient can perform 25% to 49% of tasks)
3	Moderate assistance (patient can perform 50% to 74% of task)
4	Minimal contact assistance (patient can perform 75% or more of task)
5	Supervision or Setup
6	Modified independence (patient requires use of a device, but no physical assistance)
7	Complete independence

Source: (Uniform Data System for Medical Rehabilitation, 2013)

Based on the previous statement, the total "FIM Admission/Discharge" and the total "CP Admission/Discharge" is the result of dealing with all the components in each metric, as a group. Consequently, the total "FIM Admission" is calculated based on the score when the patient is admitted, and total "FIM Discharge" is computed by considering the last score registered as an inpatient. In the FIM scale, 1 indicates total dependence of the patient, and 7 means complete independence, thus, the possible total FIM score ranges from 18 to 126, where a higher score implies more independence of the patients.

The same analysis can be performed for CP, in which it is also possible to calculate the total weekly progress achieved by the patient between admission and discharge. The meaning of the CP scale is opposite to the FIM scale: 1 indicates that the patient is totally independent and 7 means the patient is completely dependent. In turn, the possible total CP score can vary from 126 to 18with 126 indicating complete dependence in the motor and cognitive functions.

Table 7 displays the descriptive statistics of the total "FIM Admission/Discharge" and total "CP Admission/Discharge" of the sample.

Table 7 Descriptive statistics of FIM and CP at admission and discharge

	FIM Admission	**FIM Discharge**	**CP Admission**	**CP Discharge**
Mean	52.65	88.22	84.20	56.04
Median	46	108	95	37
Mode	18	18	126	126
Trimmed Mean (10%)	50.28	92.62	85.74	51.62
Standard Deviation	31.61	39.61	36.20	40.05
Minimum	18	18	23	18
Maximum	122	126	126	126

* *The range for FIM score is [18, 126], and the range for CP score [126, 18].*

The difference between the "FIM/CP Discharge" and the "FIM/CP Admission" is called "gain", "delta", or "maximum improvement achieved". It refers to the progress in motor and cognitive skills accomplished by the patient during the rehabilitation time. Many

studies utilize the "delta" as the outcome in predicting/analyzing functional improvement (Ng, Stein, Ning, & Black-Schaffer, 2007; Poon et al., 2005; Ring, Feder, Schwartz, & Samuels, 1997; Sayer et al., 2008).

In this study we propose the use of a new variable, "delta transformed", as outcome variable. In this variable, the delta between discharge and admission achieved during the length of stay in the hospital are converted to a proportion based on the maximum delta possible at the time of admission, resulting in two possible response variables: Delta FIM Transformed or DFT (Eq. 1), and Delta CP Transformed or DPT (Eq. 2). DFT and DPT are computed by dividing the delta (or "maximum improvement achieved") by the maximum potential recovery of the specific patient at the time of admission. These variables indicate what percentage of the total possible recovery of the patient is accomplished at the end of the rehabilitation.

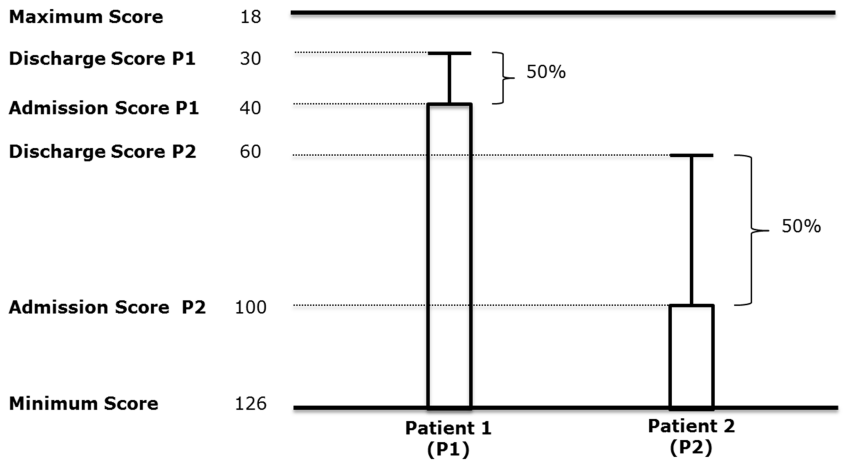
$$DFT = \frac{\text{FIM Discharge - FIM Admission}}{\text{126 - FIM Admission}} \qquad \text{Equation 1}$$

$$DPT = \frac{\text{CP Discharge - CP Admission}}{\text{18 - CP Admission}} \qquad \text{Equation 2}$$

The use of the DFT or DPT allows equaling two patients who have different initial conditions and different deltas, at the end of rehabilitation. The base on this postulate lies on the conclusion

established by (Sayer et al., 2008) for this type of patients: at low levels of motor and cognitive functions the patients "*make considerable progress over the course of the hospitalization"* and, conversely, at high levels of functioning the patients "*do not exhibit much functional gain over the course of the treatment".*

Figure 2 depicts an example where two patients have the same percentage of recovery (DPT) at discharge time, the admission score is different and the delta of patient 2 is higher than the delta of patient 1.



Source: Own creation

Figure 2 Example of two patients with similar percentage of recovery (DPT) at the end of the rehabilitation

On the other hand, note that the Eq. 1 is defined as long as *FIM Admission* is different from 126, and the Eq. 2 is defined if *CP Admission* is different than 18. Insofar as the FIM/CP Admission scores are equal to the maximum scores possible indicates that the patient is

completely independent and consecutively, he/she does not require care in the PRC.

DFT and DPT can take values equal to or close to 0, which means that the patient's state is the same (no or minimal recovery). In the same way, DFT or DPT close to 1 means that the patient showed significant progress relative to his/her potential. In turn, according to the Eq. 1 and 2, DFT and DPT can also be negative values i.e. the patient can worsen during rehabilitation. Even though this latter case is not expected, it is possible. A negative DFT or DPT may be the result of factors independent of the treatment. Nevertheless, the expected result is that the clinical outcome of the patient shows a recovery or at least the patient keeps his/her initial motor and cognitive conditions, i.e. DFT and DPT are constrained to a range between 0 and 1.

The summary statistics of the DFT and DPT of the sample are shown in Table 8; both variables are skewed to the left, and their means are less than the medians. The trimmed means for DFT and DPT are very close to the untrimmed means, indicating the absence of instance(s) far from the rest of the data. The standard deviation is similar between DFT and DPT.

The sample shows values between 0 and 1 for DFT. On the other hand, the values of the sample for DPT, are ranged between -0.02 and

1 (the negative value corresponds to a single patient). It is possible to keep the patient's record or to consider the value as an outlier, and then, delete the patient. In this case, since the value corresponds to a single instance and it is close to 0, it is not expected that it significantly affects the model, thus, the first option is used.

Table 8 Descriptive statistics of DFT and DPT

Descriptive Statistic	DFT	DPT
Mean	0.57	0.52
Median	0.65	0.62
Mode	0	0
Trimmed Mean (10%)	0.59	0.54
Standard Deviation	0.35	0.34
Minimum	0	-0.02
Maximum	1	1

On the other hand, the values obtained for DFT and DPT seem to be associated according to the scatterplot in Figure 3. The Pearson's Correlation Coefficient r between DFT and DPT is 0.93, with a p-value <0.001, which suggests that the correlation is statistically significant.

The association between these two variables indicates the use of either of them as response variable for the prospective model. The CP seems to be the best choice, since it is a weekly metric for the entire segment of care and provides more evidence about the progress of the patients in comparison to the FIM score, which is only at admission

and discharge. To be consistent with the metric selected, "DPT" is used as the response variable.

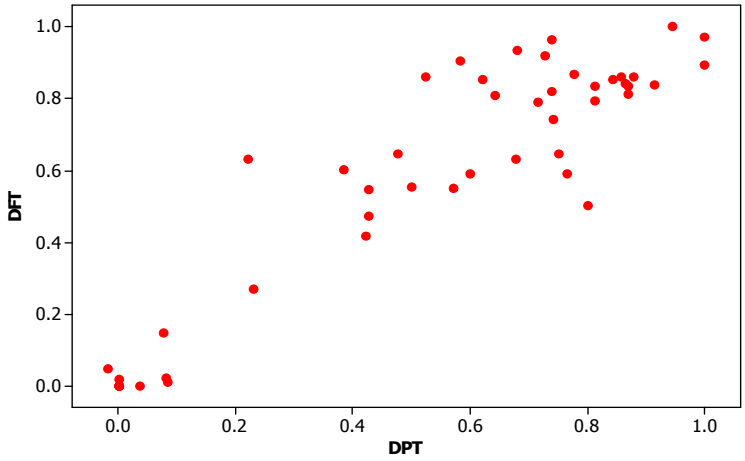
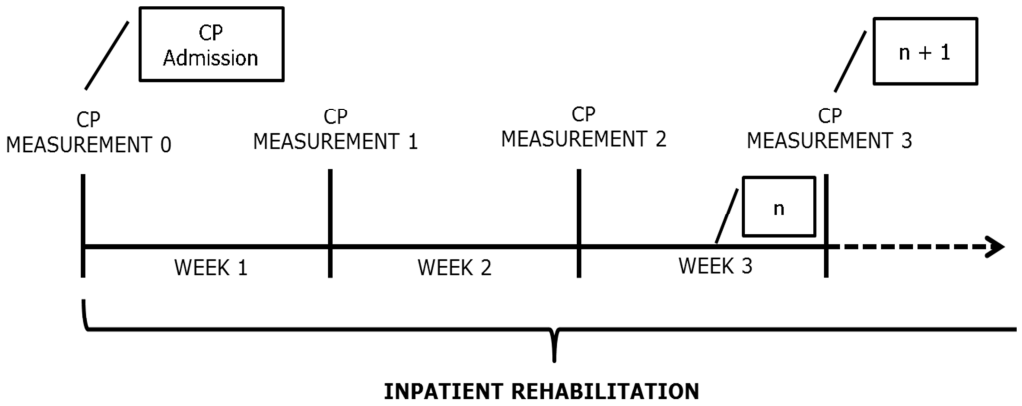


Figure 3 Relationship between DFT and DPT

Explanatory Variables

Since CP is a metric with weekly measurements, each week is a potential explanatory variable for the predictive model. To create appropriate input variables it is assumed that the motor and cognitive disabilities of the patient are evaluated n + 1 times, where n is the amount of weeks of treatment. This means that once the patient is admitted into the PRC the staff initially measures the 18 components, and based on the results they schedule the first week of treatment. After the first week, the 18 components are evaluated again to schedule the treatment of the subsequent week, and so on (Figure 4).



n: length of stay in the PRC in weeks
Source: Own creation

Figure 4 Measurement and length of stay

The selection of number of weeks being analyzed as early predictors is based on the number of inpatients per week, and then, the correlation of the input variables with the response variable, DPT. Figure 5 shows the percentage of patients by duration of inpatient segment of care. The curve decreases as weeks accrue and the patients are discharged.

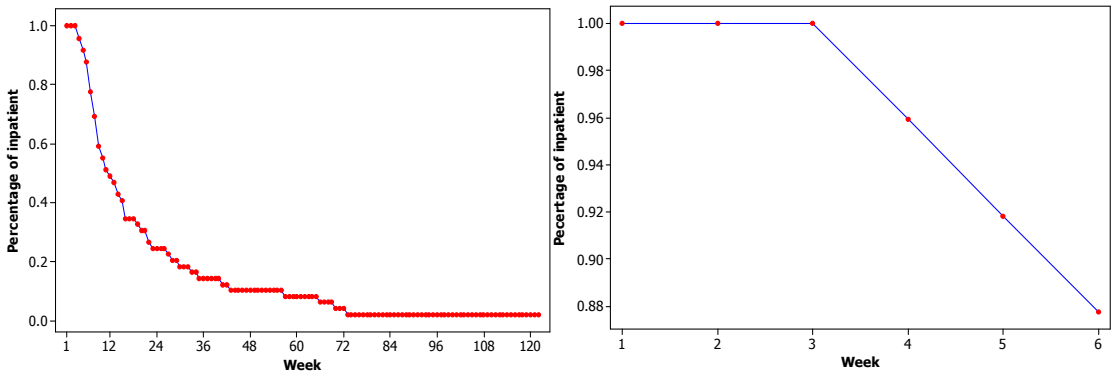


Figure 5 Percentage of patients by duration of inpatient segment of care, 122 weeks (left) and 6 first weeks (right)

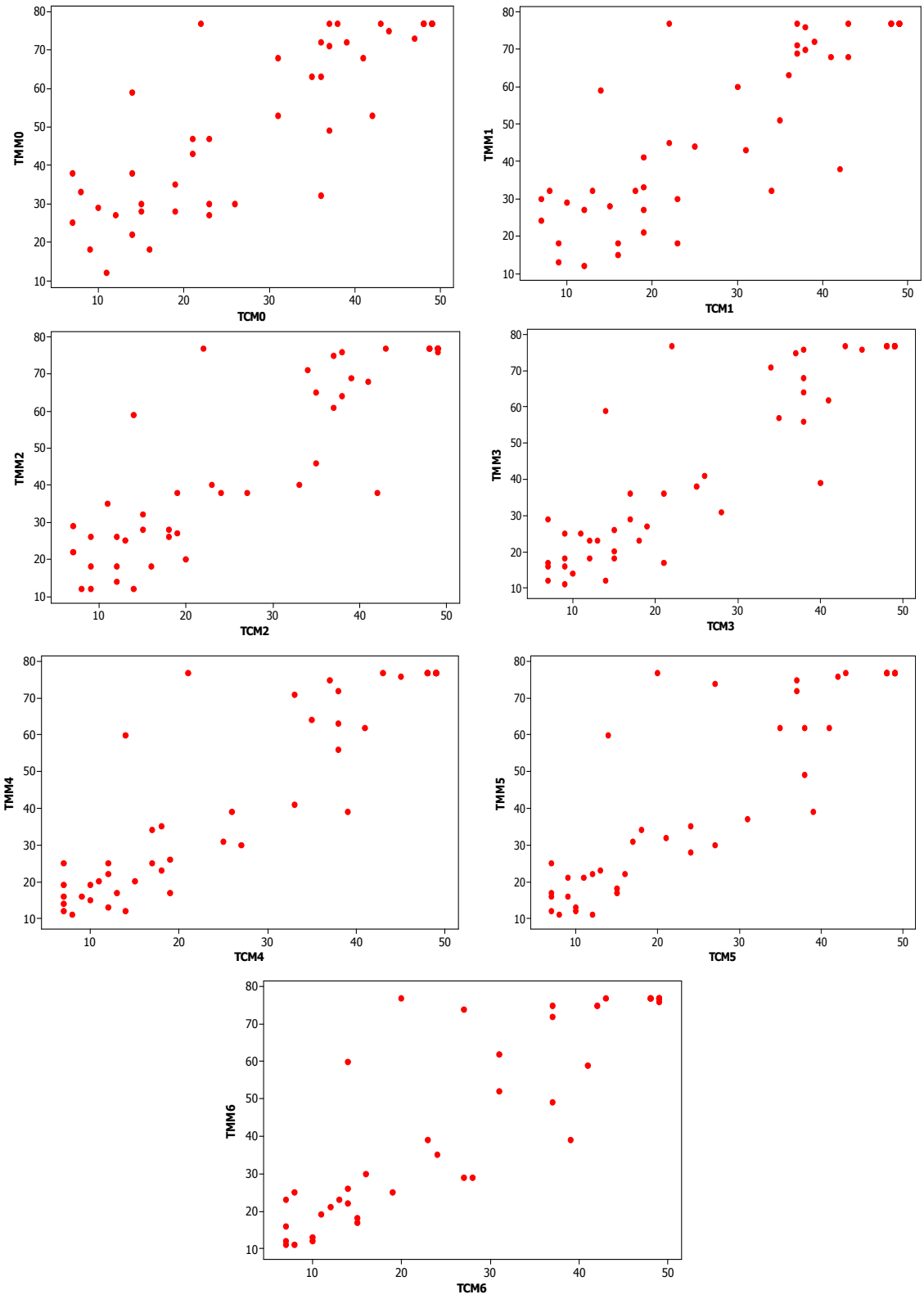
Figure 5 shows that over 80% of the inpatients stay in the hospital for 6 weeks. The percentage of inpatients falls to 78% in week 7 and 69% in week 8. The sample has a mean of length of stay of 21 weeks, with a minimum of 3 weeks, and a maximum of 122 weeks. Each of these 6 first weeks will be considered in the analysis of explanatory variables. The 6 weeks is involving 7 measurements: admission score (or measurement 0), and the measurement from week 1 to 6.

The correlation between Total Motor Measurement m or TMM_m (sum of the 11 motor CP components), and Total Cognitive Measurement m or TCM_m (sum of the 7 cognitive CP components), showS a strong positive linear association in the 7 measurements with a p-value <0.001 according to the Pearson Correlation Coefficient r in Table 9 and the scatterplots in Figure 6.

Table 9 Pearson Correlation Coefficient between TMM_m and TCM_m

	TMM_0	**TMM_1**	**TMM_2**	**TMM_3**	**TMM_4**	**TMM_5**	**TMM_6**
TCM_0	0.860						
TCM_1		0.861					
TCM_2			0.891				
TCM_3				0.907			
TCM_4					0.906		
TCM_5						0.890	
TCM_6							0.884
P-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

TMM_m = Total Motor Measurement m
TCM_m = Total Cognitive Measurement m



Source: Own creation

Figure 6 Scatterplots of the TMM_m and TCM_m

We conclude from the previous exploration of the 7 measurements that it is possible to use the summation of the 18 components as a single input variable each week instead of using the TMM_m and TCM_m as two different weekly potential inputs to the model. Note that since motor and cognitive functions are pre-defined groups, it is implied that the components that shape both groups are related to each other.

The input variables considered in the analysis are two different types: the "CP Admission" (Eq. 3) and the "Delta Pathway Transformed Measurement m ($DPTM_m$)", where m is the week number of the measurement (Eq. 4).

$$\text{CP Admission} = \sum_{i=1}^{18} (\text{CP components } 1^{st} \text{ week})_i \qquad \text{Equation 3}$$

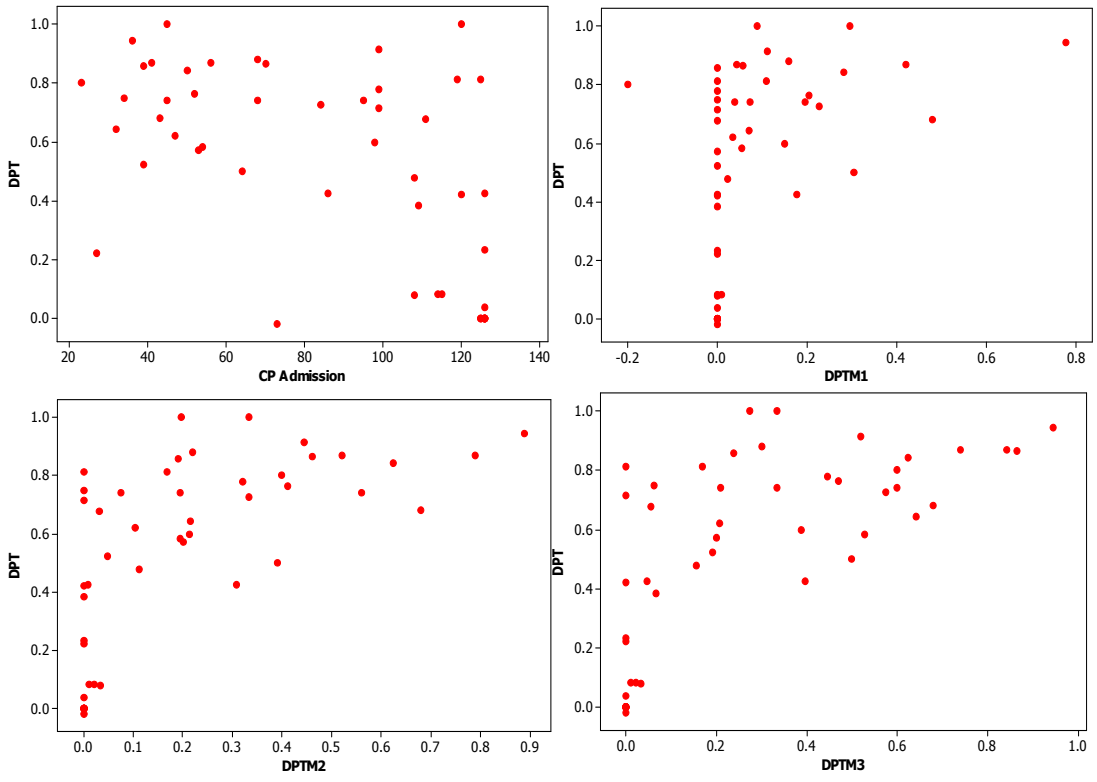
$$DPTM_m = \frac{\text{CP Measurement m - CP Admission}}{\text{18 - CP Admission}} \qquad \text{Equation 4}$$

CP Admission corresponds to the summation of the 18 components once the patient is admitted in the PRC and represents the motor and cognitive skills of the patient in a specific instance since it is not compared with any previous time. The domain of the variable is between 18 and 126.

On the other hand, the $DPTM_m$ is a variable that takes into consideration the treatment received for the patient previous to the

m^{th} measurement. It evaluates the progress of the patient in percentage of recovery achieved every week using as reference the CP Admission. The variable $DPTM_m$ is based on the same foundations of the DPT, explained previously. The domain of $DPTM_m$ is between -1 and 1, with expected values between 0 and 1.

Figure 7 depicts the scatterplots between each potential explanatory variable and the response variable, DPT. The non-parametric Spearman Correlation Coefficient (r_s) is used to determine the existence of a monotonic association between the variables, since they do not seem to follow a linear relationship.



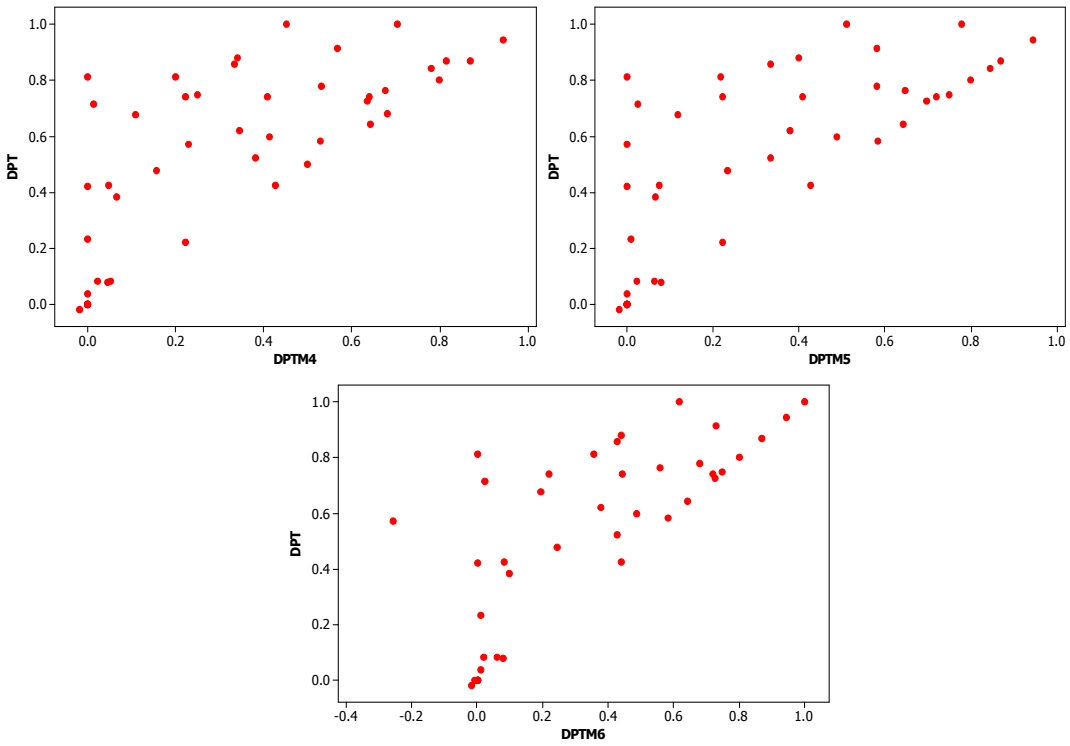


Figure 7 Scatterplot input/output

Table 10 displays the r_s per measurement. The results point out a negative correlation between CP Admission and DPT since the variables have opposite direction. In turn, the correlations of $DPTM_1$/DPT and $DPTM_2$/DPT can be considered as moderate. The correlations from the third measurement on are stronger.

The measurements for the first six weeks are analyzed in the next section as input variables to determine a model for predicting percentage of recovery of the patient with TBI since the CP Admission and $DPTM_m$ with m=1,…,6 seem to be related to the output variable DPT.

Table 10 Spearman Correlation Coefficients between the inputs and the output variables

	CP Admission	$DPTM_1$	$DPTM_2$	$DPTM_3$	$DPTM_4$	$DPTM_5$	$DPTM_6$
DPT	-0.612						
DPT		0.536					
DPT			0.688				
DPT				0.716			
DPT					0.799		
DPT						0.796	
DPT							0.813

Model Building

Support Vector Regression (SVR) is utilized to determine a good relationship between the input and the output variables. SVR is a machine learning technique, which lies in predicting the DPT given a new input value after observing the behavior of the training set.

The selection of SVR is based on its two main characteristics: generalizability and robustness. The generalizability characteristic helps avoid over-fitting because it searches for the simplest model through the use of specific margin-limiting data points to define the function, which are called Support Vectors (SVs) (Nalbantov, Groenen, & Bioch). On the other hand, the robustness characteristic decreases the effect of outliers in the model, since SVR works with the absolute value of the errors (Nalbantov et al.).

SVR is approximated through Eq. 5. w determines the orientation of the hyperplane in the space and b defines the distance of the hyperplane from the origin, both are the parameters of the model.

x is the input space, and ø(x) is a function that allows transforming the input space into a higher dimensional feature space for mapping.

$$f(x) = w \cdot \boldsymbol{\phi(x)} + b \qquad \text{Equation 5}$$

This work uses linear and non-linear functions to create a model. To obtain a linear function, the input space ø(x) is replaced by Eq. 6, where v_i are the SVs.

$$K(v_i, x) = \mathbf{v_i^T} \cdot x \qquad \text{Equation 6}$$

To estimate a non-linear function, the Radial Basis Function (RBF) is often used since it works well for small samples (Zhang, Tang, Zhu, & Wang). In addition, the RBF models are less complex than the models developed with others kernels since the extra hyperparameter required is only one (Hsu, Chang, & Lin, 2003). To obtain a RBF, ø(x) is substituted by Eq. 7**,** where v_i are the SVs, and Γ is a pre-defined parameter which is greater than zero.

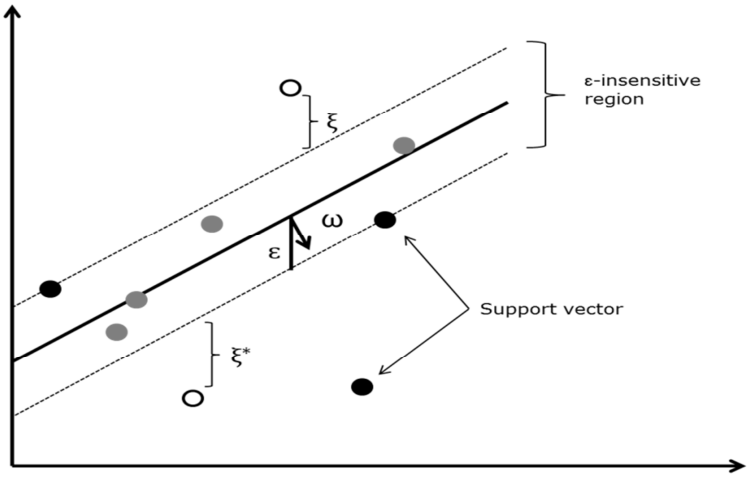
$$K(v_i, x) = e^{(-\Gamma \|\mathbf{v_i} - x\|^2)} \qquad \text{Equation 7}$$

To estimate the parameters w and b in Eq. 5, the convex optimization problem depicted in Eq. 8 must be solved.

$$\begin{aligned} \text{Minimize} \quad & \tfrac{1}{2}\|w\|^2 + C\sum_{i=1}^{l}(\xi_i + \xi_i^*) \\ \text{Subject to} \quad & y_i - (w\cdot\emptyset(x) + b) \le \varepsilon + \xi_i \\ & (w\cdot\emptyset(x) + b) - y_i \le \varepsilon + \xi_i^* \\ & \xi_i, \xi_i^* \ge 0 \\ & \text{for } i = 1,2,\ldots, l \end{aligned} \qquad \text{Equation 8}$$

The objective function in Eq. 8 shows a trade-off between the flatness of the solution through the *regularization term* $\frac{1}{2}\|w\|^2$, and the amount of training errors through the *empirical risk* represented by $C\sum_{i=1}^{l}(\xi_i + \xi_i^*)$. In turn, the data points that fall inside of the ε-insensitive region are considered with an error equal to 0 (i.e. $\xi_i=0$ and $\xi_i^*=0$), thus, they are not penalized. In the same way, if the error is greater than ε (i.e. the data point falls outside of the ε-insensitive region), a penalty C is assigned. The data points that fall in the border or outside of the ε-insensitive region are SVs which define the function (Figure 8).

Eq. 8 can be transformed into a dual problem after applying the Lagrange Multiplier method (LMM). The use of the LMM is due to its quadratic objective function and linear constraints. After solving the dual problem the parameters w and b for the linear and the RBF kernels can be determined.



Source: Own creation

Figure 8 Support Vector Regression (SVR)

The SVR approximation function, thus, can be re-written as shown in Eq. 9, where $\alpha_i^* \geq 0$ and $\alpha_i \geq 0$ are Lagrange Multipliers, and v_i are the SVs.

$$f(x) = \sum_{i=1}^{l} (\alpha_i^* - \alpha_i) K(v_i, x) + b \qquad \text{Equation 9}$$

The flatness and the training errors of the solution are directly associated with the hyperparameters ε *(ε-insensitive loss function)* and C (*cost*). They must be specified in advance for the linear and the RBF kernels, as well as the hyperparameter Γ, which is specific for the RBF kernel.

The hyperparameters C, Γ and ε are determined using the Grid Search Method, which is performed using the function tune() of the package e1071 in R (Team, 2008). Grid Search Method performs

exhaustive analysis of the possible combinations of the hyperparameters values. The selection of the values of the hyperparameters, and therefore, the selection of the model(s) is based on the Mean Square Error (MSE) after 10-fold cross validation.

To analyze the effect of different sizes of the ε-insensitive region over the MSE, three values of the parameter ε are preliminarily utilized: 1, 0.1, and 0.01. These values are used for both, linear and RBF kernels. Once the hyperparameters C and Γ are defined, they are fixed to tune the hyperparameter ε.

To find the appropriate hyperparameter C for the linear kernel, two ranges were analyzed per each input/output combination totaling 2000 trials: [0.001, 1] increasing by 0.001, and [1, 1000] increasing by 1. Two more iterations were performed for the second range to obtain a more accurate value. The second iteration has 11 trials that were performed using a range of ±0.5 over the best values in the first iteration. The third iteration has 11 trials from the best value in the second iteration in a range of ±0.05. Table 11 summarizes the ranges of iteration for the linear kernel.

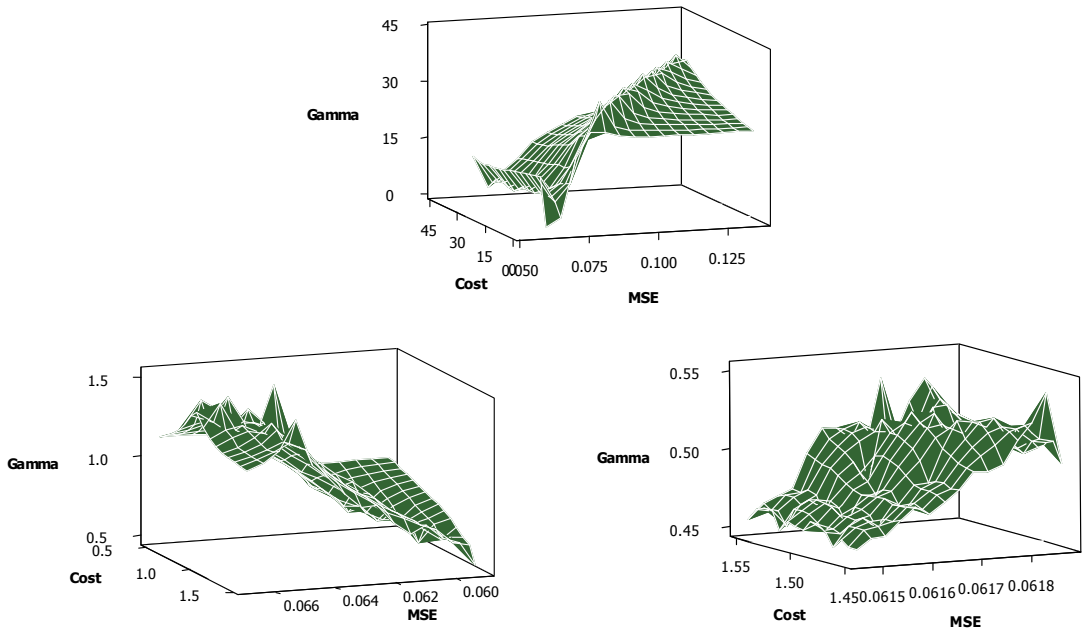
The first iteration for the RBF kernel has the same range for both hyperparameters: C and Γ: from 1 to 40 increasing by 1, totaling 1600 trials. The second iteration has a range of ±0.5 from the best value in the first iteration. The third iteration has a total of 121 trials in a range

of ±0.05 from the best value in the second iteration. Figure 9 shows an example of one of the combination with three iterations for the RBF kernel.

Table 11 Grid Search method: ranges for the linear kernel

LINEAR				
Range 1	**Hyperparameter**	**Iteration 1**		
	C	(0.001,1)		
	ε	1 0.1 0.01		
Range 2	**Hyperparameter**	**Iteration1**	**Iteration2**	**Iteration3**
	C	(1,1000)	Cost1 ±0.5	Cost2 ±0.05
	ε	1 0.1 0.01	1 0.1 0.01	1 0.1 0.01

Cost 1: Best cost obtained in the iteration 1
Cost 2: Best cost obtained in the iteration 2



Source: Own creation

Figure 9 Example of relationship among Γ, C and MSE of a RBF. First iteration with 1600 trials (up) second iteration with 121 trials (left) third iteration with 121 trials (right).

A second range is analyzed for the RBF kernel from 0.001 to 1 increasing by 0.001 for the hyperparameter C, and from 0.1 to 1 increasing by 0.1 for the hyperparameter Γ. To obtain a more accurate value of Γ two more iterations are performed, where the hyperparameter C is fixed according to the value obtained in the first iteration, Γ ranges ±0.05 over the best value in the first iteration. The third iteration is performed over the best value of the second iteration in a range of ±0.005. The summary of the ranges used for the RBF kernel are shown in Table 12.

Table 12 Grid Search method: ranges for the RBF kernel

RADIAL				
Range 1	**Hyperparameter**	**Iteration1**	**Iteration2**	**Iteration3**
	C	(1,40)	Cost1±0.5	Cost2±0.05
	ε	1 0.1 0.01	1 0.1 0.01	1 0.1 0.01
	Γ	(1,40)	Gamma1±0.05	Gamma2±0.05
Range 2	**Hyperparameter**	**Iteration1**	**Iteration2**	**Iteration3**
	C	(0.001,1)	Best Cost	Best Cost
	ε	1 0.1 0.01	1 0.1 0.01	1 0.1 0.01
	Γ	(0.1,1)	Gamma1±0.05	Gamma2±0.005

Cost 1: Best cost obtained in the iteration 1
Cost 2: Best cost obtained in the iteration 2
Gamma 1: Best gamma obtained in the iteration 1
Gamma 2: Best gamma obtained in the iteration 2

The results of the Grid Search Method (Appendix C) show that the MSEs are similar when comparing the values for C less than 1 and C greater than 1. On the other hand, the iterative process fails to

improve the MSE in any of the input/output combinations. Basically, the iterations do not find a better value for the parameter *C* and Γ that considerably decreases the MSE.

According to the MSE criterion the best model for the linear kernel corresponds to the percentage of recovery measured after the 4th week of treatment, i.e. the $DPTM_4$ (Table C2). This model corresponds to a ε-insensitive loss function equal to 1, the number of SVs is 6, and the value of the hyperparameter C is equal to 0.94. The MSE after 10-fold cross validation is 0.052.

If the parameter C is fixed at 0.94, and ε is tuned in the range [0.5, 1] increasing by 0.001, the MSE decreases slightly to 0.051 at ε equal to 0.99. Since the MSE does not have a significant improvement, and the value of C is virtually unchanged, the hyperparameter ε is set at 1 to find w and b.

The linear model is obtained by replacing the linear Eq. 6 in Eq. 5, as shown in Eq. 10.

$$f(x)= \sum_{i=1}^{l} (\boldsymbol{\alpha_i^*} - \boldsymbol{\alpha_i})\ \mathbf{v_i^T}\ x_j + b \qquad \text{Equation 10}$$

The parameter w is defined for the linear kernel, as the summation of the multiplication between the Lagrange Multipliers and their SVs. Table 13 shows the Lagrange Multipliers for the 6 SVs of the linear case.

Table 13 Patient ID, Lagrange Multipliers, and Support Vectors of the best linear model

Patient ID	Lagrange Multiplier	Support Vector
6	0.94	-1.05
9	0.94	-1.02
23	0.36	0.46
37	-0.94	-1.05
38	-0.94	-1.12
45	-0.36	-1.05

SVR gives better results standardizing the variables to mean zero and to unit variance as this procedure equalize the data variability and the ranges and avoids calculation problems related to range variability (Bao & Liu, 2006; Hsu et al., 2003). The input variable $DPTM_4$ is Z-score scaled according to Eq. 11, where 0.313 is the mean of the input variable, and 0.297 is the standard deviation. The SVR approximation for the linear kernel with $\varepsilon = 0.1$ and $C = 0.94$ is shown in Eq. 12, where 0.638 is w and -0.139 is b.

$$DPTM4' = \frac{DPTM4 - 0.313}{0.297} \qquad \text{Equation 11}$$

$$DPT_F' = 0.638 * DPTM4' - 0.13 \qquad \text{Equation 12}$$

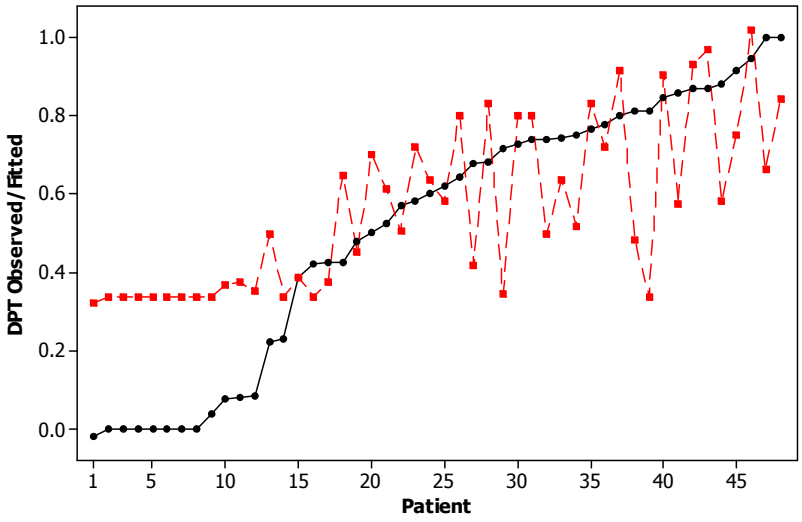
Note that the fitted values obtained using Eq. 12 are scaled due to the standardization of the variables before solving the optimization problem. In turn, the parameters w and b are also affected by the standardization of the variables. Therefore, it is necessary to scale back the fitted values calculated through SVR (Eq. 12). The scale back

formula for the fitted values is shown in Eq. 13**,** where 0.036 is the mean of DPT variable (observed values) and 0.517 is its standard deviation.

$$DPT_F = DPT_F' * 0.337 + 0.517 \qquad \text{Equation 13}$$

The final linear model is obtained by re-writing the Eq. 12 using the scale back formula Eq. 13 and replaced the $DPTM_4'$ by Eq. 11. Eq. 14 illustrates the final linear model and Figure 10 depicts the observed and fitted values using the linear model.

$$DPT_F = 0.724 * DPTM4 + 0.337 \qquad \text{Equation 14}$$



Black instances: observed values
Red instances: fitted values
Source: Own creation

Figure 10 Linear model with the lower MSE: DPT observed/DPT fitted of each patient

On the other hand, the values of the RBF parameters (Appendix C) point out that ε = 0.1 and ε = 0.01 have the smaller MSE (0.045). In both scenarios the $DPTM_3$ is considered as the best input variable. In this case the model that has fewest numbers of SVs has been chosen

The hyperparameter C and Γ are fixed to the values 1.25 and 15.74, respectively and ε is tuned in the range [0.05, 0.5] increasing by 0.001. For an ε equal to 0.483, slight improvement can be obtained (0.043 MSE) by cross validation. For simplicity we will continue using the value of ε = 0.1 for the analysis of the RBF model.

The equation for the best RBF is obtained by replacing Eq. 7 in Eq. 5 as shown in Eq. 15. Eq. 16 shows the RBF model with the lower MSE, where 0.450 is the parameter b and 15.74 is the parameter Γ.

$$f(x) = \sum_{i=1}^{l} (\boldsymbol{\alpha_i^* - \alpha_i}) e^{(-\Gamma \|\mathbf{v_i} - x\|^2)} + b \qquad \text{Equation 15}$$

$$DPT_f' = \sum_{i=1}^{l} (\alpha_i^* - \alpha_i) e^{(-15.74 * \|v_i - DPTM3'\|^2)} + 0.450 \qquad \text{Equation 16}$$

The input variable $DPTM_3$ is also scaled according to Eq. 17, where 0.271 is the mean of the input variable and 0.282 is its standard deviation.

$$DPTM3' = \frac{DPTM3 - 0.271}{0.282} \qquad \text{Equation 17}$$

In this case is not possible to calculate the parameter w explicitly since the SVs must be handled in the RBF kernel before multiplying them by the Lagrange Multipliers α_i^* and α_i. Table 14 shows the 40 Lagrange Multipliers and the SVs for the RBF model.

Table 14 Lagrange Multipliers and Support Vectors for the best model of RBF kernel

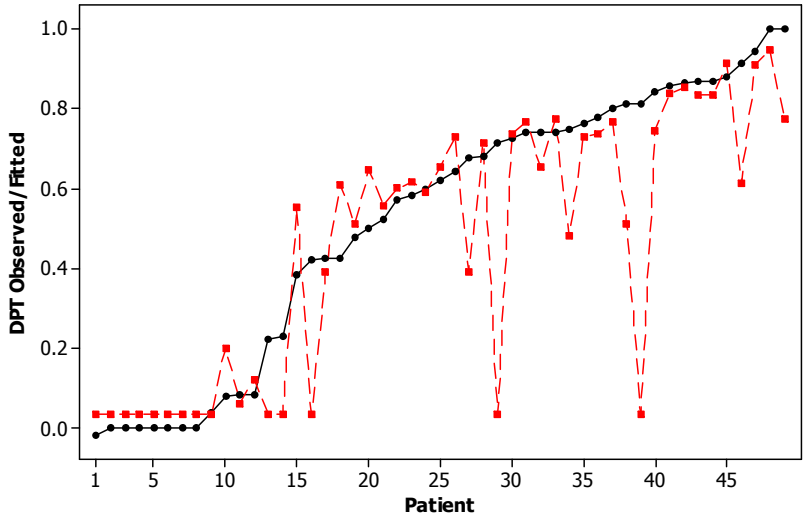
Patient ID	Lagrange Multiplier	Support Vector	Patient ID	Lagrange Multiplier	Support Vector
3	-1.250	-0.853	29	1.250	-0.959
4	1.250	-0.782	30	-0.695	0.210
5	-1.250	-0.711	31	0.270	1.166
6	1.250	-0.959	32	1.250	-0.747
9	1.250	-0.959	33	-1.250	-0.959
10	1.250	0.883	34	-1.250	0.812
11	1.250	0.599	35	1.250	0.210
12	0.308	2.016	36	-1.250	-0.959
13	-1.250	1.308	37	-1.250	-0.959
15	-1.250	-0.888	38	-1.250	-0.959
16	0.519	1.662	39	0.274	0.706
17	-1.166	-0.215	40	1.250	1.272
18	-1.028	-0.286	41	0.652	2.371
19	0.716	-0.782	43	-1.031	-0.393
21	-0.604	0.103	44	-0.069	1.449
23	1.250	-0.003	45	1.250	-0.215
24	-0.858	0.918	46	-0.294	-0.959
25	-0.743	-0.959	47	1.250	-0.959
26	-1.250	-0.959	48	1.250	-0.959
28	1.250	-0.357	49	-1.250	0.458

Since Eq. 15 gives a fitted value scaled, it must be scaled back according to Eq. 17, where 0.524 is the standard deviation and 0.337 is the mean of the DPT variable. Eq. 15 can be re-written as shown in

Eq. 18. The observed and fitted values for the sample are depicted in Figure 11.

$$DPT_F = DPT'_F * 0.337 + 0.524 \qquad \text{Equation 18}$$

$$DPT_F = 0.337 * [\sum_{i=1}^{l} (\boldsymbol{\alpha_i^* - \alpha_i}) e^{(-15.74 * \left\| \mathbf{v_i} - \left(\frac{DPTM3 - 0.271}{0.282}\right) \right\|^2)}] + 0.676 \qquad \text{Equation 19}$$



Black instances: observed values
Red instances: fitted values
Source: Own creation

Figure 11 RBF model with the lower MSE: DPT observed/DPT fitted of each patient

CHAPTER IV:

RESULTS AND DISCUSSION

Results

The analysis developed in the previous chapter indicates that after applying the SVR approach, the models based on $DPTM_4$ and $DPTM_3$ have the lower MSE after 10-fold cross validation for linear and RBF models, respectively.

Below are some general considerations of both the linear and the RBF models. Also there are specific considerations for each model.

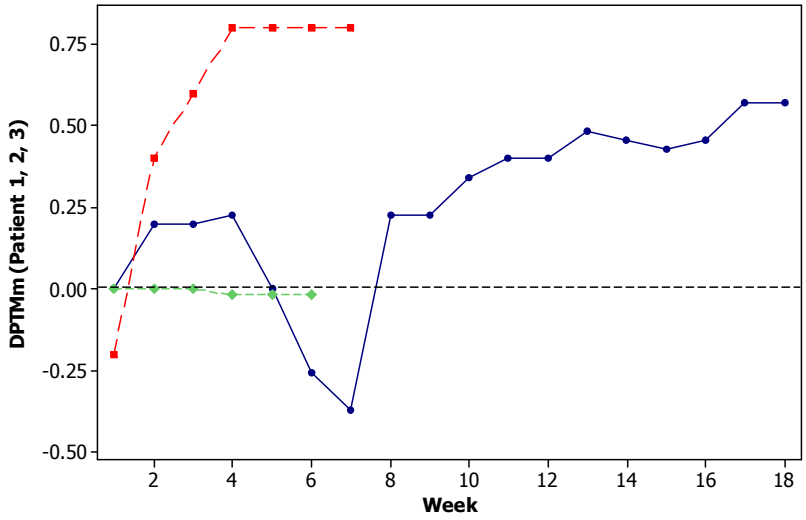
General Considerations of the Models

The RBF model is optimum using as the input variable week 3 ($DPTM_3$), whereas the linear model uses week 4 ($DPTM_4$). Since it is desirable to predict the expected recovery (DPT), as early as possible, the RBF model could be more advantageous.

The RBF model, on the other hand, is a more complicated calculation since it requires handling the SVs and the Lagrange multipliers each time that a new input data point is considered. The linear model is simpler than the RBF model, since the form resembles

a simple linear regression. However, both SVR models have the disadvantage that the parameters do not have a direct and intuitive interpretation.

Negative input variables or negative output results are possible, but unexpected. Figure 12 shows three patients who present negative values at different points in their rehabilitation: the squares represent a patient who had a negative value after the first week of treatment, the circles a patient with a negative value in the middle of the rehabilitation, and the diamonds a patient that had a negative value at the end.



Source: Own creation

Figure 12 Examples of trajectories of the patients with negatives values

The negative values may be due to the effect of some factors external to the treatment received. These factors can be caused by adverse reactions to medication; the genetic, physical, and cognitive

characteristics of the patient; or by the evaluator, e.g. error in the application of the metrics, an error in recording information in the database, or an error in collecting the data.

Considerations for the Linear Model

According to the linear model, the fitted values DPT_F is -0.39 when $DPTM_4$=-1 and 1.06 when $DPTM_4$=1. Therefore, a potential output range is $-0.39 \leq DPT_F \leq 1.06$, note however, that the upper limit exceeds the allowed value 1. On the other hand, the linear model fits better in the interval $-0.02 \leq DPTM_4 \leq 0.94$ since this is the input range of the dataset. In turn, the range of fitted values according to the previous input range is $0.32 \leq DPT \leq 1.02$, which also exceeds the upper limit allowed (Table 15).

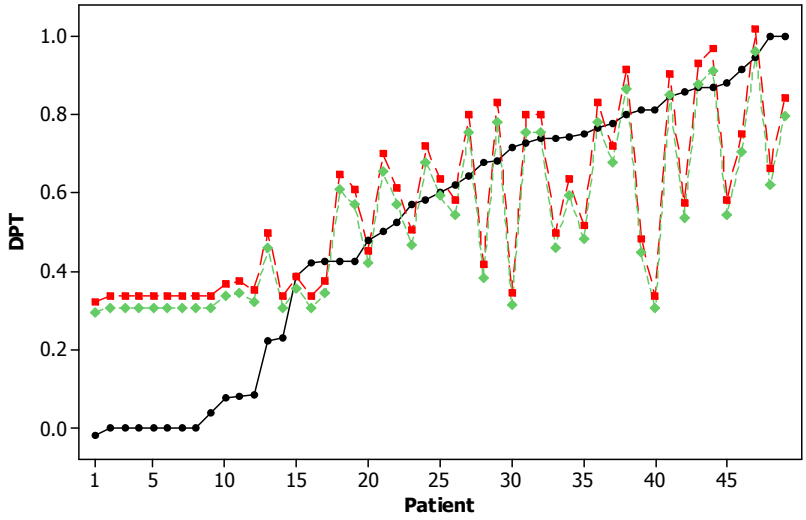
Table 15 Output ranges for the linear model

	Input Range	**Output Range**
Potential input range	$-1 \leq DPTM_4 \leq 1$	$-0.39 \leq DPT_F \leq 1.06$
Input range of the sample	$-0.02 \leq DPTM_4 \leq 0.94$	$0.32 \leq DPT \leq 1.02$

As it has been shown previously, the linear model presents an "inconvenience" with the upper limit since the measurement of the input and the output variables is a "percentage", and thus the

predicted values should not be more than 1. On the other hand, the linear SVR model can predict values in the interval -∞, +∞.

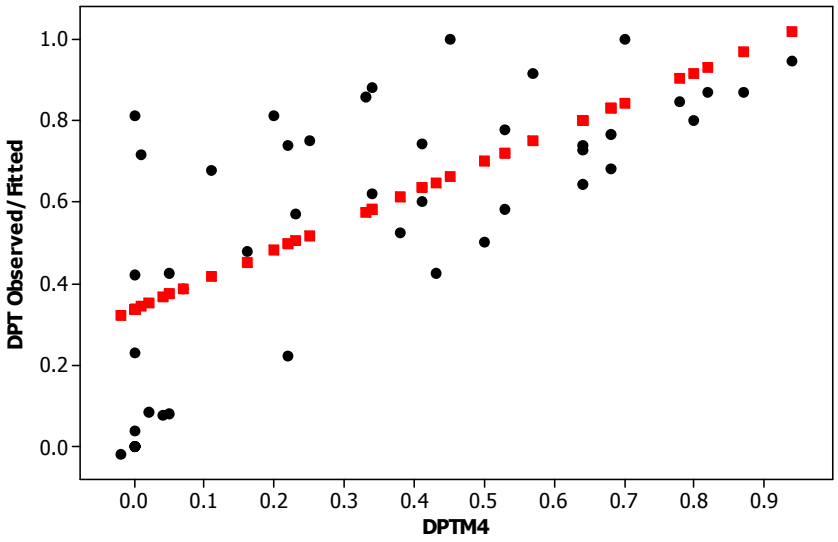
There are some alternatives to deal with this situation. These include rescaling the DPT_F to a proper interval (e.g. [-0.39, 1] for the potential input range or [0.32, 1] for the input range of the sample) or truncate the data at 1, i.e. fitted values over 1 are considered as 1. The first option is problematic since modifying the upper value implies a change in all the values of the interval as shown Figure 13. The second option is considered more appropriate for this situation since the values that go beyond the upper limit are close to 1, and there are just a few cases.



Circles: Observed values
Squares: Fitted values
Diamonds: Fitted values scaled
Source: Own creation

Figure 13 Rescale the data in the interval [-0.39, 1]

A linear model better fits the premise that the expected result after treatment is that the patient improves. However, the linear SVR model does not predict if a patient with a lower probability of recovery at week 4 maintains the same condition nor if he/she will have a significant improvement at discharge. This situation could mean an under-fitted linear model (Figure 14). Unfortunately, it is possible to confirm or reject this postulate only if there is a validation dataset for testing. As mentioned before, since the sample used is small, it was not feasible to separate the data into training and test sets and cross validation was employed. This will assess repeatability but does not fully evaluate systematic error in the model.



Circles instances: Observed values
Squares instances: Fitted values
Source: Own creation

Figure 14 Scatterplot $DPTM_4$ vs. DPT observed and DPT fitted

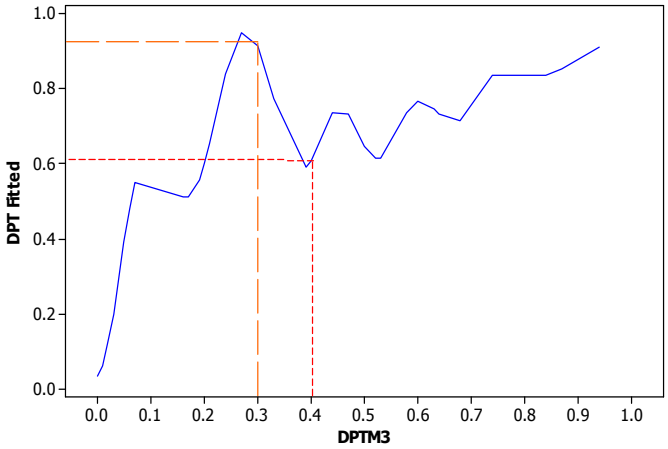
Considerations for the RBF Model

The fitted value DPT_F, according to the RBF model is 0.68 for $DPTM_3$=-1, and 0.78 for $DPTM_3$=1. However, the RBF model works better for the range of input data points: $0 \leq DPTM_3 \leq 0.94$, since it corresponds to the input range of the sample analyzed. The output fitted values, DPT_F, for this input interval is 0.03 for $DPTM_3$=0 and 0.95 for $DPTM_3$=0.94 (Table 16).

Table 16 Output ranges for the RBF model

	Input Range	**Output Range**
Potential input range	$-1 \leq DPTM_3 \leq 1$	$DPT_F(-1)=0.68$ $DPT_F(1)=0.78$
Input range of the sample	$0 \leq DPTM_3 \leq 0.94$	$DPT_F(-1)=0.03$ $DPT_F(1)=0.95$

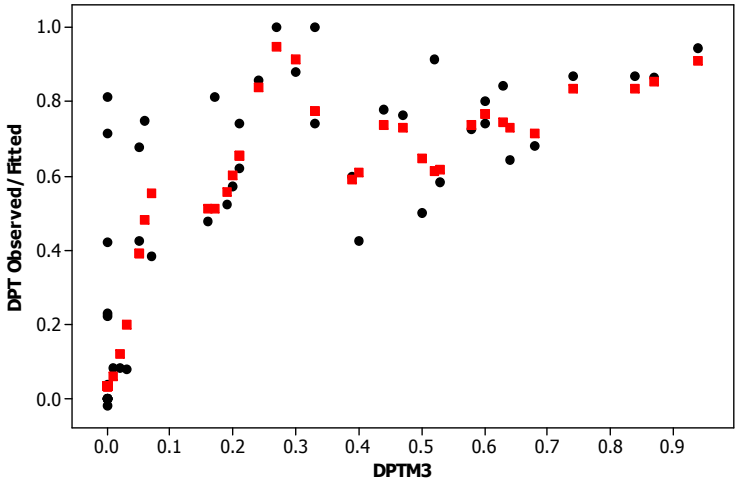
The results establish that the output interval $0.68 \leq DPT_F \leq 0.78$ cannot be considered as the wider output range of the RBF model since there are other input values (e.g. $DPTM_3$=0) in the range $-1 \leq DPTM_3 \leq 1$ that estimate lower final percentages of recovery (e.g. $DPT_F(0)= 0.03$). In this sense, the fitted values computed using the RBF model may not be "as expected" due to the radial curves of the model. As shown Figure 15, the RBF model predicts improvement in over 90% of patients in whom the percentage of recovery in week 3 is close to 30%, while the DPT_F is about 60% for a patient close to 40% of recovery in week 3.



Source: Own creation

Figure 15 RBF model

The DPT_F estimated could point out a possible problem of over-fitting in the RBF model, which means that the RBF model adjusts the instances of the sample fairly well but could not fit properly a new data point (Figure 16). Since the sample used is too small to create a testing set, it is not possible to confirm or reject this postulate.



Square instances: Observed values
Circle instances: Fitted values
Source: Own creation

Figure 16 Scatterplot $DPTM_3$ vs. DPT observed and DPT fitted

Comparison of Delta Transformed and Not-Transformed

After defining the best input variables to predict DPT using a linear and a RBF model, it is analyzed if the transformation of the delta generates significant improvement than a delta no transformed in term of MSE. Thus, a new linear and RBF models were created considering the Delta Pathway Not-transformed (DP) as output variable and the Delta Pathway Not-transformed Measurement 4 (DPM_4) and Delta Pathway Not-transformed Measurement 3 (DPM_3) as input variables for the linear and RBF model, respectively.

The parameters ϵ and C for the linear model and the parameters ϵ, C and Γ for the RBF model are determined using the Grid Search method considering the same ranges used for the delta transformed (Table 11 and Table 12). The parameters that define the linear model with the lower MSE is shown in Table 17, and the parameters that define the lower MSE for the RBF model is shown in Table 18**.**

Table 17 Comparison between linear model using Delta No-Transformed (DP and DPM_4) and Delta Transformed (DPT and $DPTM_4$)

	LINEAR Delta Transformed	**LINEAR** Delta No-Transformed
Input	$DPTM_4$	DPM_4
Output	DPT	DP
Epsilon	1	0.1
Cost	0.94	881.45
Min Observed Value	-0.018	102
Max Observed Value	1	-1
MSE	0.052	509
NRMSE	0.22	0.21

Table 18 Comparison between RBF model using Delta No-Transformed (DP and DPM3) and Delta Transformed (DPT and $DPTM_3$)

	RBF Delta Transformed	**RBF** Delta No-Transformed
Input	$DPTM_3$	DPM_3
Output	DPT	DP
Epsilon	0.1	1
Gamma	15.74	0.1
Cost	1.25	0.573
Min Observed Value	-0.018	102
Max Observed Value	1	-1
MSE	0.045	523
NRMSE	0.21	0.22

Since the MSE of the Deltas Transformed and Deltas Not Transformed have different units, the comparison cannot be done directly between the MSEs, it is necessary to normalize them before making a conclusion. In this case the Normalized Root Mean Square Error (NRMSE) technique was used (Eq. 20).

According to Table 17 and 18, the values of the NRMSE are the same in variables transformed and variables not-transformed. This indicates that for this sample the use of a delta transformed does not improve the accuracy of the prediction. Again, a larger sample could provide more information if the transformation of the variables has a significant effect over the prediction.

$$NRMSE = \frac{\sqrt{MSE}}{Y_{obs,\,max} - Y_{obs,\,min}} \qquad \text{Equation 20}$$

Discussion

Predicting accurate clinical outcomes in patients with TBI is a challenge, particularly in patients returning from the OEF or OIF with multiple, sever injuries (polytrauma), since the rehabilitation process is complex and slow. Although it is true that the data used are not sufficient to say that a model is robust, this work has shown that it is possible to find patterns in this type of patients, despite the different ranges in the rate of the progress of each one.

Since a metric used to measure outcome requires validation in terms of responsiveness, reliability and validity, it could indicate that there is an additional "task" related to the CP which seems to have not been "quantified" previously. The literature is devoid of studies validating the use of CP as a tool to measure outcomes. The CP metric was not validated in the work presented above because it requires a much larger sample size to reflect the use of the metric by different personnel and at different times. It was assumed that the CP is an appropriate metric to assess outcomes, as a result of the similarity between CP and FIM, where the latter has been widely studied. Thus, although face validity can be reasonably accepted, responsiveness and reliability of CP must be studied further.

On the other hand CP has an advantage over FIM, since it is measured weekly. A weekly metric provides a larger input set to

choose the possible input variables. Assessing data from points other than admission (first measurement) allows incorporating the effect that the treatment has had for the patient.

On the other hand, even though a model that uses DPT as outcome presents similar NRMSE to a model that uses Delta as output, the use of DPT as a measure of the clinical outcome better communicates the significance of the patient's progress to all involved. Consequently, interested parties, such as the family, do not need a working knowledge of the CP metric. In turn, the clarity and simplicity in the information that the families may receive address two of their needs: the need to make sense of the experience and the need to know. Furthermore, the variable used as "clinical outcome" is based on the individual potential recovery, which will help in better determining the necessary resources and staff when setting personalized objectives for a patient.

On the other hand, it is possible that the models created using SVR are influenced by confounding variables since the data do not come from a controlled experiment. Other variables, such as age, marital status, damage area of the brain, psychological problems (e.g. PTSD), physical and genetic conditions, among others, can also affect the recovery of the patient. Ideally these could be controlled in a randomized experiment. However, such an experiment is not realistic

when it involves people in circumstances where the effect of the "natural recovery" is unclear (Paolucci et al., 2000; Roth & Harvey, 2000).

The models proposed in this study should be validated using a testing set to make a better decision about which model is more appropriate and to further explore the possibility of over or under fitting the models. This requires a larger sample of patients who completed their rehabilitation in the PRCs. The present study suggests that recording of CP has to be emphasized in the first, third, fourth and last week of rehabilitation since the models ware optimum at based on those 4 weeks.

Lastly, this study is retroactive and it is the first one that uses CP as a predictor of clinical outcomes. It sets a precedent for future research related to this metric given the advantage of the CP over FIM, the assessment of continuous improvement and the accountability of the processes that are carried out.

CHAPTER V:

CONLUSIONS AND FUTURE WORK

Conclusions

The use of the CP as a tool to measure the clinical outcome in rehabilitation has positive effects for prediction since the metric is weekly. This allows having a wider range of alternatives as potential model inputs. In turn, the selection of a measurement other than to the admission (first measurement), but at the same time close to this first measurement, allows for the inclusion of the progress of the patient before predicting the possible clinical outcome.

The output used to measure the clinical outcome, DPT (Delta Pathway Transformed), is the potential recovery achieved by the patient, and it is based on the fact that a patient with lower functionality makes considerable progress over the rehabilitation time as opposed to the patients that arrive to the PRCs with higher functionality. However, for the sample analyzed, DPT fails in improving the accuracy of the model in comparison with the widely used output "delta". The use of either of them is a good outcome variable since they have the same NRMSE. Though, the variable DPT, conceptually, is

meaningful and easier to understand which contributes to a better communication with the stakeholders, especially the family. A bigger sample can address better the advantage of a transformation in terms of accuracy of the prediction.

The input variables analyzed $DPTM_m$ are based on the same foundations as DPT. The correlation of the first 7 measurements studied shows that all of them are related to the output variable, DPT. However, the correlation is stronger from measurement 3.

The machine learning technique, SVR (Support Vector Regression) has been used to determine both a linear and a non-linear model and has intrinsic properties of robustness and generalizability. For the non-linear case, the RBF (Radial Basic Function) kernel was used because of the good results in small samples. In turn, the parameters ϵ, C, and Γ for the linear and RBF cases were defined using the Grid Search Method, which is the most widely used method to optimize the parameters.

The linear model has a MSE around 4.5% when $DPTM_4$ is the input variable. The RBF model, on the other hand, has a lower MSE when the input variable is the measurement done after the 3^{rd} week of treatment ($DPTM_3$). More data to validate the models are required.

The rehabilitation process for individuals with TBI that have been exposed to blast injury in OIF and OEF is prolonged and complex. The

recovery of the patients is influenced by additional unmeasured factors such as: support of the family in the rehabilitation process; genetic, physical and psychological conditions; and the severity and location of the injury. These factors, although critically important in assessing patient rehabilitation, are very difficult to measure and incorporate in a predictive model.

Finally, the necessity of clear information to support decision making, communication with the family and preparation for discharge, highlights the importance of determining outcomes as early as possible. This approach is the first study that uses the weekly metric CP in an attempt to predict the clinical outcome of patients with TBI.

Future Work

Increase the sample data: Additional data should be collected from the 5 PRCs over a larger range of years (e.g. 2001 – 2013 These data will allow validating the CP metric and the models.

Validation of the CP metric: CP metric must be validated as a tool to measure clinical outcomes. The validation will measure the ability of the metric in detecting changes, the ability in quantifying motor and cognitive progress, and the consistency of the metric when it is used by different evaluators and in repeated measures.

Validation of the linear and RBF models: The linear and the RBF models should be validated using the CP scores of the new patients incorporated. The methodology used in this work could then be applied to a larger sample.

Resources required: once a model is validated, it will assist in determining the resources required to achieve the maximum improvement of each patient. These resources refer to the amount and type of procedures that the facility should emphasize for the efficient and effective provision of treatments.

Create cooperative links with other rehabilitation centers: extending the use of CP scores to other centers of rehabilitation (private) will help to more fully analyze the methodology used in this study in other type of patients and diseases, collecting more data, more quickly since the patients in the private sector, with less complex injuries/illnesses, typically have more rapid progress.

LIST OF REFERENCES

Aarabi, B., Taghipour, M., Haghnegahdar, A., Farokhi, M., & Mobley, L. (2000). Prognostic factors in the occurrence of posttraumatic epilepsy after penetrating head injury suffered during military service. *Neurosurgical focus, 8*(1), 1-6.

Bao, Y., & Liu, Z. (2006). A fast grid search method in support vector regression forecasting time series. *Intelligent Data Engineering and Automated Learning–IDEAL 2006*, 504-511.

Belanger, H. G., Uomoto, J. M., & Vanderploeg, R. D. (2009). The Veterans Health Administration system of care for mild traumatic brain injury: Costs, benefits, and controversies. *The Journal of head trauma rehabilitation, 24*(1), 4-13.

Belasco, A. (2009). *Cost of Iraq, Afghanistan, and Other Global War on Terror Operations Since 9/11*: DIANE Publishing.

Black, T. (2012). Outcomes: What's All the Fuss About? *Rehabilitation Nursing, 24*(5), 188-191.

Bond, A. E., Draeger, C. R. L., Mandleco, B., & Donnelly, M. (2003). Needs of Family Members of Patients With Severe Traumatic Brain Injury Implications for Evidence-Based Practice. *Critical Care Nurse, 23*(4), 63-72.

Cifu, D. X. (2012). Rehabilitation Care of Combat-related TBI: Experience of the Departments of Defense and Veterans Affairs.

Cournan, M. (2011). Use of the Functional Independence Measure for Outcomes Measurement in Acute Inpatient Rehabilitation. *Rehabilitation Nursing, 36*(3), 111-117.

Dausch, B. M., & Saliman, S. (2009). Use of family focused therapy in rehabilitation for veterans with traumatic brain injury. *Rehabilitation Psychology; Rehabilitation Psychology, 54*(3), 279.

Department of Defense. (2012). Active duty military personnel strengths by regional area and by country (309a); December 31, 2011.

Department of Defense. (2013a). Defense Casualty Analysis System, U.S. Military Casualties - Operation Enduring Freedom (OEF) Casualty Summary by Month.

Department of Defense. (2013b). Defense Casualty Analysis System, U.S. Military Casualties - Operation Iraqi Freedom (OIF) Casualty Summary by Month.

Department of Veterans Affairs. (2012a). History - VA History.

Department of Veterans Affairs. (2012b). Polytrauma/TBI System of Care. Understanding Traumatic Brain Injury. TBI Symptoms & Screening.

Department of Veterans Affairs. (2012c). Polytrauma/TBI System of Care. VA Polytrauma System of Care

Department of Veterans Affairs. (2012d). Polytrauma/TBI System of Care. VA Polytrauma System of Care. Care Facilities.

Department of Veterans Affairs. (2011a). Polytrauma/TBI System of Care. Understanding Traumatic Brain Injury. Recovery & Rehabilitation.

Department of Veterans Affairs. (2011b). Terminology & Definitions.

Department of Veterans Affairs. (2012). Analysis of VA Health Care Utilization among Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) Veterans: Cumulative from 1st Qtr FY 2002 through 1st Qtr FY 2012 (October 1, 2001 – December 31, 2011).

Department of Veterans Affairs, & Department of Defense. (2010). Mild Traumatic Brain Injury - Concussion. Pocket guide for clinicians.

Gawande, A. (2004). Casualties of war—military care for the wounded from Iraq and Afghanistan. *New England Journal of Medicine, 351*(24), 2471-2475.

Gibbs, D. A., Martin, S. L., Kupper, L. L., & Johnson, R. E. (2007). Child maltreatment in enlisted soldiers' families during combat-related deployments. *JAMA: The Journal of the American Medical Association, 298*(5), 528-535.

Griffin, J. M., Friedemann-Sánchez, G., Hall, C., Phelan, S., & van Ryn, M. (2009). Families of patients with polytrauma: Understanding the evidence and charting a new research agenda. *Journal of Rehabilitation Research and Development, 46*(6), 879-891.

Griffin, J. M., Friedemann-Sánchez, G., Jensen, A. C., Taylor, B. C., Gravely, A., Clothier, B., . . . Thors, C. (2012). The Invisible side of war: families caring for US service members with traumatic brain injuries and polytrauma. *The Journal of head trauma rehabilitation, 27*(1), 3.

Hsu, C.-W., Chang, C.-C., & Lin, C.-J. (2003). A practical guide to support vector classification.

Kelley, M. L., & Jouriles, E. N. (2011). An introduction to the special section on US Military operations: Effects on military members' partners and children. *Journal of Family Psychology, 25*(4), 459.

Kidd, D., Stewart, G., Baldry, J., Johnson, J., Rossiter, D., Petruckevitch, A., & Thompson, A. (1995). The Functional Independence Measure: a comparative validity and reliability study. *Disability & Rehabilitation, 17*(1), 10-14.

Kimberly Meyer, M., Kathy Helmick, M., Selina Doncevic, M., & Rachel Park, B. (2011). Severe and Penetrating Traumatic Brain Injury in the Context of War. *Heart Failure*.

Lester, P., Peterson, K., Reeves, J., Knauss, L., Glover, D., Mogil, C., . . . Wilt, K. (2010). The long war and parental combat deployment: effects on military children and at-home spouses. *Journal of the American Academy of Child & Adolescent Psychiatry, 49*(4), 310-320.

Lezak, M. D. (1986). Psychological implications of traumatic brain damage for the patient's family. *Rehabilitation Psychology, 31*(4), 241.

Ling, G., Bandak, F., Armonda, R., Grant, G., & Ecklund, J. (2009). Explosive blast neurotrauma. *Journal of neurotrauma, 26*(6), 815-825.

Makin-Byrd, K., Gifford, E., McCutcheon, S., & Glynn, S. (2011). Family and couples treatment for newly returning veterans. *Professional Psychology: Research and Practice, 42*(1), 47.

Mansfield, A. J., Kaufman, J. S., Marshall, S. W., Gaynes, B. N., Morrissey, J. P., & Engel, C. C. (2010). Deployment and the use of mental health services among US Army wives. *New England Journal of Medicine, 362*(2), 101-109.

Masel, B. E., & DeWitt, D. S. (2010). Traumatic brain injury: a disease process, not an event. *Journal of neurotrauma, 27*(8), 1529-1540.

McFarlane, A. C. (2009). Military deployment: the impact on children and family adjustment and the need for care. *Current Opinion in Psychiatry, 22*(4), 369-373.

Mental Illness Research Education and Clinical Centers, M. (2009). Traumatic Brain Injury: A guide for patients.

Mernoff, S. T., & Correia, S. (2010). Military blast injury in Iraq and Afghanistan: the Veterans Health Administration's polytrauma system of care: DTIC Document.

Mintz, M., Van Horn, K., & Levine, M. J. (1995). Developmental models of social cognition in assessing the role of family stress in relatives' predictions following traumatic brain injury. *Brain Injury, 9*(2), 173-186.

Nalbantov, G., Groenen, P. J., & Bioch, J. C. Support Vector Regression Basics.

Nanna, M. J., & Sawilowsky, S. S. (1998). Analysis of Likert scale data in disability and medical rehabilitation research. *Psychological Methods, 3*(1), 55.

Ng, Y. S., Stein, J., Ning, M., & Black-Schaffer, R. M. (2007). Comparison of clinical characteristics and functional outcomes of ischemic stroke in different vascular territories. *Stroke, 38*(8), 2309-2314.

Norman, G. (2010). Likert scales, levels of measurement and the "laws" of statistics. *Advances in health sciences education, 15*(5), 625-632.

Okie, S. (2005). Traumatic brain injury in the war zone. *New England Journal of Medicine, 352*(20), 2043-2047.

Okie, S. (2006). Reconstructing lives—a tale of two soldiers. *New England Journal of Medicine, 355*(25), 2609-2615.

Owens, B. D., Kragh Jr, J. F., Wenke, J. C., Macaitis, J., Wade, C. E., & Holcomb, J. B. (2008). Combat wounds in operation Iraqi Freedom and operation Enduring Freedom. *The Journal of trauma, 64*(2), 295.

Paolucci, S., Antonucci, G., Grasso, M. G., Morelli, D., Troisi, E., Coiro, P., & Bragoni, M. (2000). Early versus delayed inpatient stroke rehabilitation: a matched comparison conducted in Italy. *Archives of physical medicine and rehabilitation, 81*(6), 695-700.

Paris, R., DeVoe, E. R., Ross, A. M., & Acker, M. L. (2010). When a parent goes to war: Effects of parental deployment on very young children and implications for intervention. *American Journal of Orthopsychiatry, 80*(4), 610-618.

Peake, J. B. (2005). Beyond the purple heart—continuity of care for the wounded in Iraq. *New England Journal of Medicine, 352*(3), 219-222.

Poon, W., Zhu, X., Ng, S., & Wong, G. (2005). Predicting one year clinical outcome in traumatic brain injury (TBI) at the beginning of rehabilitation. *Re-Engineering of the Damaged Brain and Spinal Cord*, 207-208.

Ring, H., Feder, M., Schwartz, J., & Samuels, G. (1997). Functional measures of first-stroke rehabilitation inpatients: usefulness of the Functional Independence Measure total score with a clinical rationale. *Archives of physical medicine and rehabilitation, 78*(6), 630-635.

Roth, E., & Harvey, R. (2000). Rehabilitation of stroke syndromes. *Physical medicine and rehabilitation. 2nd ed. Philadelphia: WB Saunders*, 1117-1160.

Sayer, N. A., Chiros, C. E., Sigford, B., Scott, S., Clothier, B., Pickett, T., & Lew, H. L. (2008). Characteristics and rehabilitation outcomes among patients with blast and other injuries sustained during the Global War on Terror. *Archives of physical medicine and rehabilitation, 89*(1), 163-170.

Sigford, B. J. (2008). " To care for him who shall have borne the battle and for his widow and his orphan"(Abraham Lincoln): the Department of Veterans Affairs polytrauma system of care. *Archives of physical medicine and rehabilitation, 89*(1), 160.

Taylor, B. C., Hagel, E. M., Carlson, K. F., Cifu, D. X., Cutting, A., Bidelspach, D. E., & Sayer, N. A. (2012). Prevalence and costs of co-occurring traumatic brain injury with and without psychiatric disturbance and pain among Afghanistan and Iraq War Veteran VA users. *Medical Care, 50*(4), 342.

Team, R. C. (2008). R: A language and environment for statistical computing. *R Foundation Statistical Computing*.

Uniform Data System for Medical Rehabilitation. (2013). Rehab Measures: Functional Independence Measure.

Uomoto, J. M. (2012). Best Practices in Veteran Traumatic Brain Injury Care. *The Journal of head trauma rehabilitation, 27*(4), 241-243.

Verhaeghe, S., Defloor, T., & Grypdonck, M. (2005). Stress and coping among families of patients with traumatic brain injury: a review of the literature. *Journal of Clinical Nursing, 14*(8), 1004-1012.

Veterans Health Initiative. (2010). Traumatic Brain Injury.

Warden, D. (2006). Military TBI during the Iraq and Afghanistan wars. *The Journal of head trauma rehabilitation, 21*(5), 398-402.

Warden, D., Ryan, L., Helmick, K., Schwab, K., French, L., Lu, W., . . . Ling, G. (2005). War neurotrauma: The defense and veterans brain injury center (DVBIC) experience at Walter Reed Army Medical Center (WRAMC). *J Neurotrauma, 22*(10), 1178.

Zhang, W., Tang, S.-Y., Zhu, Y.-F., & Wang, W.-P. Comparative Studies of Support Vector Regression between Reproducing Kernel and Gaussian Kernel.

APPENDICES

Appendix A: Nomenclature

ADL: Activities of Daily Living
CP: Clinical Pathways
CT: Computed Tomography
DFT: Delta FIM Transformed
DoD: Department of Defense
DP: Delta Pathway
DPM_m: Delta Pathway Measurement m
DPT: Delta CP Transformed
$DPTM_m$: Delta Pathway Measurement m
FIM: Functional Independence Measure
FY: Fiscal Year
GCS: Glasgow Coma Scle
GWOT: Global War on Terror
JAHVAH: James A. Haley Veterans' Hospital
MRI: Magnetic Resonance Imaging
MSE: Mean Square Error
mTBI: mild TBI (mTBI)
NRMSE: Normalized Root Mean Square Error
OEF: Operation Enduring Freedom
OIF: Operation Iraqi Freedom
OND: Operation New Dawn
PCS: Post-Concussion Syndrome
PNS: Polytrauma Network Sites
PPOC: Polytrauma Point of Contact
PRC: Polytrauma Rehabilitation Center
PSC: Polytrauma/TBI System of Care
PSCT: Polytrauma Support Clinic Teams
PTE: Post-Traumatic Epilepsy
PTSD: Post-Traumatic Stress Disorder
RBF: Radial Basic Function
SM(s): Service Member(s)
SV(s): Support Vector (s)
SVR: Support Vector Regression
TBI: Traumatic Brain Injury
TCM_m: Total Cognitive Measurement m
TMM_m: Total Motor Measurement m
VA: Department of Veterans Affairs
VAH: Veteran Affair Hospital

Appendix B: Pathway Components Scale

Table B1 Pathway component "eating"

Scale	Description
1	Independent.
2	Feeds self with extra time safety, or needs assistive device, wears dentures, or needs modified food consistency
3	Needs supervision for safety or to help cut food, open containers, pour liquids, butter bread or apply orthosis
4	Needs occasional help to scoop food or place utensil in hand
5	Feeds self about half the time but needs help to complete meals.
6	Feeds self-less than half the time or less than half the meals.
7	Unable to feed self, needs helper to hold utensil, bring food/liquid to mouth or needs total assistance with tube feeding

Table B2 Pathway component "grooming"

Scale	Description
1	No issues / needs related to grooming, grooming problems or needs
2	Grooming requires and assistive device, takes more than reasonable time, or there are safety considerations
3	Requires no more help than standby assistance, verbal cueing, or coaxing, without physical contact, or helper sets up needed items or applies orthosis.
4	Expends 75% or more the effort and requires no more than touching or hands-on assistance.
5	Expends 50% to 74% of the effort and requires more help than touching assistance. The assistance of only one person is required
6	Expends 25% to 49% of the effort. The assistance of only one person is required. Is able to direct another person to perform the task.
7	Expends less than 25% of the effort. Can require assistance of one or more persons or in the clinician's judgment, the subject would be put at risk for injury if the task was performed

Table B3 Pathway component "bathing"

Scale	Description
1	Complete independence
2	Modified independence. Requires adaptive or assistive device, or extra time.
3	Supervision or setup
4	Minimal contact assistance. Performs 75% or more of tasks
5	Moderate assistance. Performs 50% to 74% of tasks
6	Maximal assistance. Performs 25% to 49% of tasks
7	Total assistance. Performs less than 25% of tasks, or is not bathed

Appendix B (continued)

Table B4 Pathway component "dressing - upper body"

Scale	Description
1	Complete independence
2	Modified independence. Requires adaptive or assistive device, or extra time
3	Supervision or setup
4	Minimal contact assistance. Performs 75% or more of tasks
5	Moderate assistance. Performs 50% to 74% of tasks
6	Maximal assistance. Performs 25% to 49% of tasks.
7	Total assistance. Performs less than 25% of tasks, or is not dressed

Table B5 Pathway component "dressing - lower body"

Scale	Description
1	Complete independence
2	Modified independence. Requires adaptive or assistive device, or extra time
3	Supervision or setup
4	Minimal contact assistance. Performs 75% or more of tasks
5	Moderate assistance. Performs 50% to 74% of tasks
6	Maximal assistance. Performs 25% to 49% of tasks.
7	Total assistance. Performs less than 25% of tasks, or is not dressed

Table B6 Pathway component "toileting"

Scale	Description
1	Complete independence
2	Modified independence. Requires equipment or extra time, or there are safety considerations.
3	Supervision or setup
4	Minimal contact assistance. Performs 75% or more of toileting tasks
5	Moderate assistance. Performs 50% to 74% of toileting tasks
6	Maximal assistance. Performs 25% to 49% of toileting tasks.
7	Total assistance. Performs less than 25% of toileting tasks

Appendix B (continued)

Table B7 Pathway component "bladder management"

Scale	Description
1	Complete independence. Controls bladder completely and intentionally and is never incontinent
2	Modified independence. Requires a device or medication for control; device is used independently. No accidents.
3	Supervision or setup to maintain voiding pattern or external device. Has accidents less often than every two weeks.
4	Minimal contact assistance. Has accidents less often than weekly
5	Moderate Assistance. Has accidents less often than daily
6	Maximal assistance. Wet almost on a daily basis, needs diaper or other device.
7	Total assistance. Wet on a daily basis, needs diaper or other device.

Table B8 Pathway component "bowel management**"**

Scale	Description
1	Complete Independence. Controls bowel completely and intentionally and is never incontinent
2	Modified independence. Requires a device or medication for control. Device is used independently. No accidents
3	Supervision or setup. To maintain bowel pattern or external device. Has accidents less often than every two weeks.
4	Minimal contact assistance. Has accidents less often than weekly.
5	Moderate assistance. Has accidents less often than daily.
6	Maximal assistance. Incontinent almost on a daily basis, needs diaper or other device
7	Total assistance. Incontinent or a daily basis, needs diaper or other device.

Table B9 Pathway component "bed mobility"

Scale	Description
1	Can be left alone to perform the activity safety and within a reasonable length of time
2	Uses equipment or needs extra time
3	Cannot be left alone to perform the activity safely. May require set-up, cueing or stand-by assist
4	Perform 75% or more of the task. May require hands-on or "contact" guard
5	Performs 50% to 74% of the task. Only one person is required for physical assistance.
6	Performs 25% to 49% of the task. Only one person is required for physical assistance.
7	Total assistance. Performs less than 25% of the task. One or more persons may be required.

Appendix B (continued)

Table B10 Pathway component "locomotion"

Scale	Description
1	Walks 150 feet + (50 meters) without devices. Does not use a wheelchair. Performs safety
2	Walks 150 feet + (50 meters) but uses a device, needs extra time or there are safety considerations
3	Requires standby supervision, cueing, or coaxing to walk 150 feet + (50 meters). Or requires standby supervision, cue, or coax to go a minimum of 150 feet (50 meters) in wheelchair.
4	Performs most of locomotion effort to go a minimum of 150 feet (50 meters)
5	Performs approximately half of locomotion effort to go a minimum of 15o feet (50 meters)
6	Provides lees than half of locomotion effort to go a minimum of 50 feet (17 meters). Requires assistance to one.
7	Makes little effort, or needs assistance of two people, or does not walk or wheel a minimum of 50 feet (17 M)

Table B11 Pathway component "transfer**"**

Scale	Description
1	Complete independence
2	Requires device, takes more than reasonable time or there are safety considerations
3	Requires supervision (e.g. standing by, cueing, or coaxing) or set-up
4	Performs 75% or more of transferring tasks
5	Performs 50% to 74% of transferring tasks
6	Performs 25% to 49% of transferring tasks
7	Performs less than 25% of transferring tasks

Table B12 Pathway component "language comprehension"

Scale	Description
1	Participation in activities is not limited by spoken language comprehension
2	Understands complex messages. Rarely requires minimal cueing
3	Understands structured conversations. Occasionally requires cueing for complex messages.
4	Occasionally understands simple directions and conversations about routine daily activities without cues.
5	Answers simple yes/no questions and follows simple directions with moderate cues.
6	Follows simple directions and answers simple yes/no questions with maxima cues.
7	Alert, but does not follow simple direction or responds to yes/no questions , even with cues.

Appendix B (continued)

Table B13 Pathway component "expression"

Scale	Description
1	Independent participation in activities is no limited by expressive language/speech skills
2	Rarely requires minimal cueing to produce complex sentences
3	Communicates successfully in structured conversations. Occasionally requires cueing for complex sentences.
4	Communicates in simple conversations in routine daily activities with familiar communication patterns.
5	Produces words and phrases that are appropriate and meaningful in context with moderate cues
6	Occasionally produces automatic or imitative words/phrases, rarely meaningful
7	The individual attempts to speak, but verbalizations are not meaningful at any time

Table B14 Pathway component "attention"

Scale	Description
1	Independent functioning but may occasionally include the use if compensatory strategies
2	Maintains attention within complex activities and attends simultaneously to multiple demands with rare minimal cues
3	Maintains attention within simple living activities with occasional minimal cues within distracting environments
4	Maintains attention during simple living task with consistent minimal cueing
5	Maintain attention to complete simple living tasks of short duration with consistent moderate cueing.
6	Can attend with consistent maximal stimulation, but not long enough to complete even simple living tasks
7	Attention is nonfunctional. The individual is generally unresponsive to most stimuli.

Appendix B (continued)

Table B15 Pathway component "memory"

Scale	Description
1	Independent in recalling or using strategies for complex information and planning future events in all activities
2	Recalls or uses strategies for complex information and planning events most of the time or with rare minimal cues.
3	Consistently requires minimal cues to recall or use strategies for complex/novel information
4	Requires minimal cues to use aids for simple information. Requires maximal cues to use aids for complex information
5	Occasionally requires maximum cues to recall or use external aids for simple routine and personal information
6	Consistently requires maximal verbal cues or uses external aids to recall personal information
7	The individual is unable to recall any information regardless of cueing

Table B16 Pathway component "social language"

Scale	Description
1	Consistently and independently able to modify behaviors in response to feedback from the environment
2	Socially appropriate in most settings or situations with occasional minimal cues. Responds to subtle feedback
3	Socially appropriate in unfamiliar settings and with unfamiliar partners with consistent minimal cueing
4	Adheres to simple rules of social communication is structured settings, but needs maximum cues in unfamiliar situations
5	Rarely uses common and simple social communication without cues even in structured settings
6	Pragmatics are functional in familiar and structured settings with familiar people and maximum cueing
7	Cannot initiate appropriate responses and is unaware of the need and feedback of the communication partner

Appendix B (continued)

Table B17 Pathway component "problem solving"

Scale	Description
1	Initiates and completes complex tasks. Acknowledges deficits and need to use compensation as appropriate
2	Initiates and completes complex tasks with occasional prompting. Repair errors with minimal cues.
3	Initiates complex tasks with prompting and consistently completes certain multi-step tasks. Responds impulsively
4	Initiates routine tasks; requires repeated prompts to complete multi-step tasks. Recognize errors when pointed out.
5	Requires prompt to initiate tasks, but completes them with no prompting. May trouble with perseveration or switching.
6	Requires prompt to initiate simple tasks, but may be able to complete some of them without constant prompting
7	Initiates only with physical prompting; requires repeated prompts. Is automatic, reflexive, or perseverative.

Table B18 Pathway component "safety"

Scale	Description
1	Can be left alone indefinitely and/or can pursue all normal activities alone
2	Can be left alone for an entire day but may need supervision with new or complex activities
3	Needs daily supervision and/or some help in the community. Can be left alone for short periods
4	Independent only within the hospital. Could not be left alone, due to safety considerations.
5	May go to therapies, but must to be supervised in all other areas. Client could not be left alone.
6	Needs supervision in all settings. Off the ward only when accompanied by staff or trained family
7	Requires close supervision (poseyed or one on one supervision)

Appendix C: SVR Parameters

The results of Grid Search for linear kernel and for RBF kernel include the SVs, the best hyperparameter *C*, the best hyperparameter Γ (for RBF kernel), and the MSE after a 10-fold cross validation for the three iterations of the combination DPT/M1 and DPT/$DPTM_m$ (m=1,…,6).

Table C1 Linear kernel-range 1: C (1,1000)

INPUT **OUTPUT**	**M_0** **DPT**	**$DPTM_1$** **DPT**	**$DPTM_2$** **DPT**	**$DPTM_3$** **DPT**	**$DPTM_4$** **DPT**	**$DPTM_5$** **DPT**	**$DPTM_6$** **DPT**
Epsilon	**1**	**1**	**1**	**1**	**1**	**1**	**1**
SVs	14	20	9	12	6	6	9
Cost	307	1	1	630	6	4	5
MSE	0.081	0.099	0.067	0.069	0.052	0.055	0.057
SVs	16	0.5	9	12	6	5	9
Cost	306.6	20	0.9	630	5.5	4.5	4.5
MSE	0.085	0.099	0.065	0.069	0.052	0.054	0.062
SVs	16	20	9	11	6	5	9
Cost	306.6	0.45	0.86	630.04	5.55	4.55	4.45
MSE	0.082	0.099	0.067	0.069	0.052	0.054	0.058
Epsilon	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**
SVs	47	47	43	44	42	42	40
Cost	7	203	866	3	968	2	1
MSE	0.085	0.110	0.075	0.069	0.066	0.062	0.068
SVs	47	47	43	44	42	42	38
Cost	6.7	202.5	866.3	2.7	967.5	1.7	0.5
MSE	0.093	0.103	0.075	0.070	0.067	0.068	0.061
SVs	47	47	43	44	42	42	38
Cost	6.75	202.55	866.31	2.68	967.48	1.75	0.45
MSE	0.102	0.106	0.074	0.066	0.068	0.069	0.077
Epsilon	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**
SVs	49	49	49	48	46	45	43
Cost	449	1	4	250	2	1	1
MSE	0.088	0.109	0.072	0.070	0.066	0.065	0.071
SVs	49	49	49	48	46	45	43
Cost	993.5	1.4	4.4	249.8	2.5	1	0.6
MSE	0.103	0.106	0.071	0.073	0.065	0.068	0.062
SVs	49	49	49	48	46	45	43
Cost	993.53	1.38	4.43	249.83	2.51	0.45	0.57
MSE	0.102	0.106	0.073	0.068	0.070	0.074	0.078

Appendix C (continued)

Table C2 Linear kernel-range 2: C (0.001, 1)

INPUT OUTPUT	M_0 DPT	$DPTM_1$ DPT	$DPTM_2$ DPT	$DPTM_3$ DPT	$DPTM_4$ DPT	$DPTM_5$ DPT	$DPTM_6$ DPT
Epsilon	**1**	**1**	**1**	**1**	**1**	**1**	**1**
SVs	14	20	10	12	**6**	6	8
Cost	0.829	0.247	0.319	0.264	**0.94**	0.746	0.782
MSE	0.083	0.097	0.066	0.062	**0.052**	0.055	0.058
Epsilon	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**
SVs	49	49	49	47	47	44	43
Cost	0.064	0.624	0.658	0.093	0.096	0.124	0.058
MSE	0.083	0.109	0.072	0.068	0.057	0.059	0.065
Epsilon	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**
SVs	47	47	43	42	41	39	38
Cost	0.117	0.081	0.545	0.103	0.158	0.14	0.078
MSE	0.083	0.109	0.074	0.070	0.057	0.057	0.065

Table C3 RBF kernel-range 1: C (1.40), Γ (1,40)

INPUT OUTPUT	M_0 DPT	$DPTM_1$ DPT	$DPTM_2$ DPT	$DPTM_3$ DPT	$DPTM_4$ DPT	$DPTM_5$ DPT	$DPTM_6$ DPT
Epsilon	**1**	**1**	**1**	**1**	**1**	**1**	**1**
SVs	13	16	9	8	9	7	8
Cost	27	21	30	3	9	4	4
Gamma	5	2	1	1	1	1	1
MSE	0.075	0.075	0.063	0.062	0.059	0.063	0.062
SVs	11	16	10	9	8	8	7
Cost	27.3	20.8	29.7	3.2	8.7	4.2	4.5
Gamma	5.5	1.6	0.5	0.5	0.5	0.7	0.5
MSE	0.074	0.076	0.058	0.058	0.057	0.062	0.066
SVs	11	16	10	9	8	7	7
Cost	27.26	20.8	29.67	3.17	8.67	4.23	4.55
Gamma	5.45	1.64	0.46	0.45	0.45	0.65	0.53
MSE	0.080	0.073	0.062	0.057	0.057	0.060	0.063
Epsilon	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**
SVs	45	46	45	40	38	38	35
Cost	2	1	1	1	4	40	1
Gamma	1	3	1	16	0.1	1	3
MSE	0.082	0.077	0.055	0.047	0.049	0.060	0.044
SVs	45	44	46	40	38	37	33
Cost	2.5	0.6	0.6	1.2	4.3	39.8	1.2
Gamma	0.5	2.8	1.3	15.7	1	0.9	3.2
MSE	0.083	0.079	0.061	0.046	0.049	0.056	0.048
SVs	45	45	45	**40**	39	37	33
Cost	2.55	0.65	0.65	**1.25**	4.35	39.77	1.15
Gamma	0.55	2.85	1.34	**15.74**	0.99	0.91	3.24
MSE	0.082	0.072	0.059	**0.045**	0.047	0.062	0.049
Epsilon	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**
SVs	49	48	49	49	46	43	42
Cost	2	2	1	1	1	1	1

Appendix C (continued)

Table C3 (Continued) RBF kernel-range 1: C (1.40), Γ (1,40)

Gamma	1	1	1	19	1	1	3
MSE	0.085	0.075	0.055	0.047	0.050	0.061	0.046
SVs	48	49	47	48	47	45	43
Cost	2.4	0.5	0.9	0.6	1.5	1.5	0.5
Gamma	0.7	1.9	0.6	19.5	0.6	0.5	2.5
MSE	0.086	0.076	0.059	0.046	0.051	0.059	0.052
SVs	49	49	48	48	47	45	43
Cost	2.39	0.55	0.95	0.65	1.55	1.46	0.55
Gamma	0.65	1.95	0.61	19.54	0.65	0.45	2.55
MSE	0.083	0.072	0.055	0.045	0.046	0.061	0.055

Table C 4 RBF kernel-range 2: C (0.001,1), Γ (0.1,1)

INPUT OUTPUT	**M_0 DPT**	**$DPTM_1$ DPT**	**$DPTM_2$ DPT**	**$DPTM_3$ DPT**	**$DPTM_4$ DPT**	**$DPTM_5$ DPT**	**$DPTM_6$ DPT**
Epsilon	**1**	**1**	**1**	**1**	**1**	**1**	**1**
SVs	13	20	10	11	6	6	6
Cost	0.857	1	1	0.833	1	1	0.914
Gamma	0.3	1	0.9	0.3	0.3	0.2	0.2
MSE	0.082	0.083	0.063	0.061	0.058	0.061	0.062
SVs	12	20	10	11	6	6	6
Cost	0.857	1	1	0.833	1	1	0.914
Gamma	0.25	1.05	0.9	0.35	0.25	0.22	0.2
MSE	0.088	0.082	0.061	0.060	0.056	0.062	0.063
SVs	12	20	10	11	6	6	6
Cost	0.857	1	1	0.833	1	1	0.914
Gamma	0.253	1.055	0.85	0.345	0.255	0.217	0.205
MSE	0.086	0.080	0.064	0.061	0.057	0.060	0.061
Epsilon	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**	**0.1**
SVs	44	44	44	44	40	39	39
Cost	0.489	0.765	0.668	0.464	0.93	0.274	0.547
Gamma	0.5	1	0.9	1	0.6	0.5	1
MSE	0.075	0.080	0.055	0.046	0.048	0.053	0.049
SVs	44	43	44	44	40	40	39
Cost	0.489	0.765	0.668	0.464	0.93	0.274	0.547
Gamma	0.53	1.04	0.95	0.99	0.6	0.55	1.05
MSE	0.080	0.080	0.062	0.053	0.052	0.057	0.050
SVs	44	43	44	44	44	40	39
Cost	0.489	0.765	0.668	0.464	0.93	0.274	0.547
Gamma	0.535	1.045	0.954	0.995	0.605	0.55	1.055
MSE	0.088	0.077	0.060	0.052	0.050	0.060	0.057
Epsilon	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**	**0.01**
SVs	48	47	48	49	48	45	43
Cost	0.35	0.59	0.656	0.382	0.235	0.228	0.322
Gamma	0.9	1	0.9	0.9	1	1	0.9
MSE	0.073	0.078	0.053	0.045	0.047	0.052	0.049
SVs	48	47	48	49	47	45	43

Appendix C (continued)

Table C4 (Continued) RBF kernel-range 2: C (0.001,1), Γ (0.1,1)

Cost	0.35	0.59	0.656	0.382	0.235	0.228	0.322
Gamma	0.94	1.05	0.88	0.85	1.05	0.95	0.85
MSE	0.078	0.078	0.059	0.053	0.053	0.054	0.052
SVs	48	48	48	49	47	45	43
Cost	0.35	0.59	0.656	0.382	0.235	0.228	0.322
Gamma	0.935	1.055	0.876	0.845	1.055	0.955	0.855
MSE	0.082	0.078	0.056	0.048	0.052	0.059	0.061