# OUTCOME AND STATE TRANSITION MODELING FOR ADAPTIVE INTERDISCIPLINARY PAIN MANAGEMENT

by

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Abstract

OUTCOME AND STATE TRANSITION MODELING FOR ADAPTIVE INTERDISCIPLINARY PAIN MANAGEMENT

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Pain management is a major global health problem. The World Health Organization estimates that, globally, 1 in 5 adults suffer from chronic pain and in the United States alone, chronic pain affects nearly 100 million adults resulting in an estimated annual cost of $560 to $635 billion. The University of Texas at Arlington and the Eugene McDermott Center for Pain Management at the University of Texas Southwestern Medical Center at Dallas (The Center) are collaborating to seek adaptive treatment strategies for interdisciplinary pain management in a two-stage program. Interdisciplinary pain management combines multiple disciplines of professionals to understand the biological and psychosocial factors causing a patient's pain and to determine the best treatments among many to administer. To improve current and future pain outcomes, our adaptive interdisciplinary pain management framework employs approximate dynamic programming with state transition and outcome models estimated from actual patient data. The sequential treatment structure of the data leads to a form of endogeneity. This research develops a process based on the inverse probability of treatment weighted method to address the endogeneity while estimating state transition and outcome models. First, a method is developed for independent treatments then a

general method is developed for correlated treatments. Results are presented using data from the Center.

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# Chapter 1

## Introduction

### 1.1 Background

Pain management is a major global health problem. The World Health Organization estimates that, globally, 1 in 5 adults suffer from chronic pain (Schatman et al. 2007) and the International Association for the Study of Pain estimates that 1 in 10 adults are newly diagnosed with chronic pain annually. According to the Medical Expenditure Panel Survey in 2008, in the United States alone, chronic pain affects nearly 100 million adults resulting in an estimated annual cost of $560 to $635 (in 2010 dollars) mainly due to incrementally increasing healthcare costs, rehabilitation, and lost productivity (Gaskin 2012).

Typically, pain is classified into two types, acute and chronic pain, according to its duration. For example, pain is considered acute if its duration is less than 3 months whereas pain is considered chronic if the patient is under persistent pain for equal to or greater than 3 months (Gatchel 2005, D'Arcy 2007, Schatman et al. 2007, and Gould et al. 2007).

The goal of a pain management program is to help individuals suffering from chronic pain to take back their quality of life. In the past, this was met with little success as pain management focused mainly on the physical side and patients were treated by only analgesic (pain killing) medications. Improvements were made as theories eventually evolved from single-cause to multi-cause explanations. For example, the "gate control model", first introduced by Melzack and Wall (1965), stated that pain experiences should consider both physical and psychosocial factors. As a result, adjuvant therapies (additional treatments to the primary analgesic treatment), which were designed for other medical conditions, were introduced to treat pain.

Currently, multidisciplinary and interdisciplinary pain management practices are now being developed widely (Main et al. 2000, Gatchel 2005, Schatman et al. 2007, Gould 2007, and Gatchel et al. 2007). This has led to the use of cognitive-behavioral or non-pharmacological treatments which are prescribed when a medication cannot manage pain or provide a desired level of pain relief (Schatman et al. 2007, Gould et al. 2007, Gatchel 2005, D'Arcy 2007, and Gatchel et al. 2006). With a growing number of treatment options and new medications, formulating an evidence-based, individually-tailored treatment plan has become increasingly complex. Rather than incorporating evidence-based practices, these judgments can be subjective and are dependent on patients' information and physicians' experiences (Schaefer et al. 2004). Given this treatment environment, a fundamental question arises: how can physicians determine the most clinically effective pain management plan for individual patients?

Relatively new research on adaptive treatment strategies have been developed on similar issues in other areas besides pain management (Murphy et al. 2007, Collins et al. 2007, and Pineau et al. 2007) but for cases with only a few treatment options, often only binary. For example, an adaptive treatment strategy (or regime), as seen in Figure 1.1, has been used which is a set of decision rules which identifies the best treatment level and type based on a patients' covariates such as medical history and past and present pain outcomes.

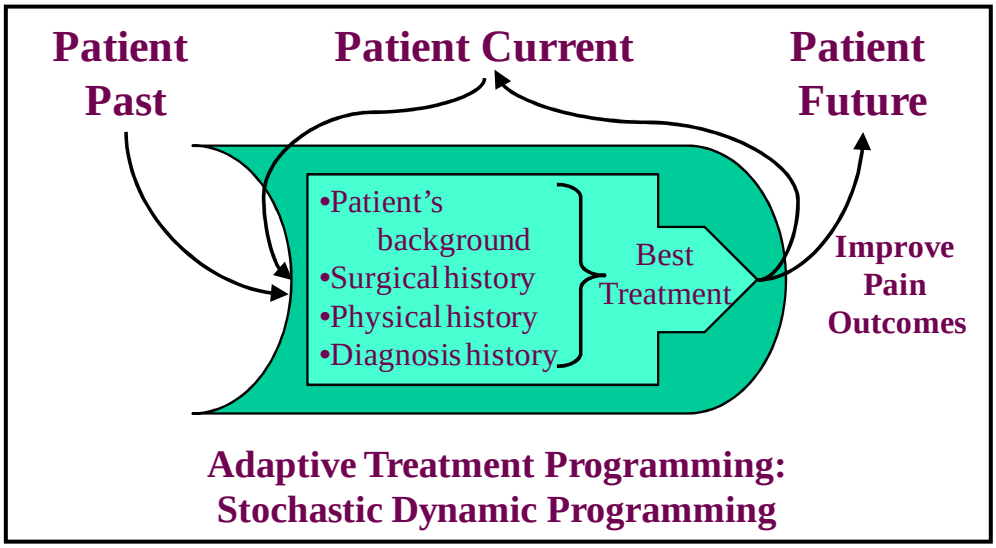



Figure 1.1 Adaptive Treatment Strategy

The first attempt at developing adaptive treatment strategies using a reinforcement learning adaptive dynamic programming approach (see Barto et al. 2004, Werbos 1992, Werbos 1974, Kaelbling et al. 1996, Sutton et al. 1998, Lee et al. 2004, and Werbos 2007) was published by Murphy (2003). Murphy and colleagues focused on sequential randomized clinical trials, which yielded ideal data for optimizing adaptive treatment strategies (e.g., Murphy et al. 2007, Collins et al. 2007, Pineau et al. 2007, Guez et al. 2008, Murphy et al. 2009, and Shortreed et al. 2011). By contrast, pain management data is not randomized but is observational data in sequential treatment which are not ideal for adaptive treatment strategy optimization because of the complex relationship between the time-dependent treatments and related variables, such as patient characteristics. In the adaptive treatment scenario, the patient variables at one stage are influenced by the treatments at the previous stage, and they themselves will influence the treatments at the following stage. Such mutual interactions will lead to bias in estimating the true effect of treatments on the outcomes. This problem is commonly referred to as endogeneity or time-dependent confounding in literature (Robins 1999,

Little et al. 2000, and Moodie et al. 2009). The general definition of endogeneity is that in a regression model the problem of endogeneity occurs when the independent variable is correlated with the error term. This means that the regression coefficient in an Ordinary Least Squares regression is biased (Heckman 1978). Throughout this research, the version of endogeneity that affects adaptive treatments will simply be referred to as endogeneity.

Adaptive treatment strategies were first applied to pain management by Lin (Lin 2010, Lin et al. 2013, and LeBoulluec et al. 2013), who developed a framework for adaptive pain management based on the adaptive treatment strategy concept. Regression modeling that uses patients' past and current information was employed to estimate the outcomes and transitions in the pain management system. However, Lin's framework did not address the inherent endogeneity in the data. Hence, in this dissertation, the regression modeling approach is modified to address the endogeneity, by developing new procedures for the Inverse Probability Treatment Weighted (IPTW) method that handles the complexity of the interdisciplinary pain management data set.

Data used for this research is from The Eugene McDermott Center for Pain Management at the University of Texas Southwestern Medical Center at Dallas (referred to as the Center from here on). Two sets of pain management data are used in this research. The smaller data set was collected from August 1998 to May 2001 containing 89 patients and is a subset of a larger data set collected from January 1998 to June 2007 consisting of 294 patients. The smaller data set was specifically part of a study by Robbins et al. (2003), for which additional measures were collected. The larger data set was derived from data the Center regularly collects while administering an interdisciplinary pain treatment via a two-stage program, as shown in Figure 1.2. This research will utilize this two-stage interdisciplinary pain management program.

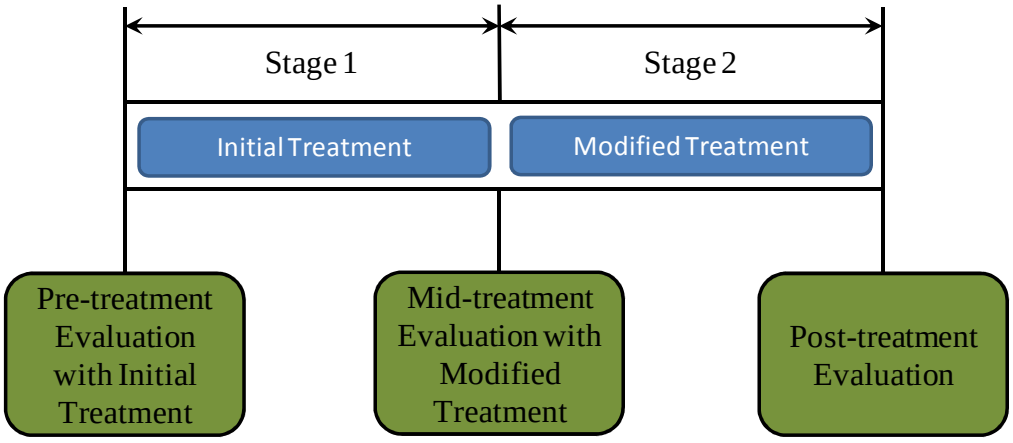



Figure 1.2 Two-Stage Interdisciplinary Pain Management Program

This program was developed by the Center to enable an adaptive treatment of pain by implementing multiple stages and usage of a variety of treatment options. In this program, a Center physician evaluates a patient at four different times: pre-treatment, mid-treatment, post-treatment evaluation, and one year following the post-treatment evaluation. Officially, patients complete the program after the post-evaluation thus the last evaluation is not considered in this research. During the evaluations, the patient's pain characteristics, related health parameters, and pain levels are monitored and reviewed against previously set targets. At each evaluation after the pre-treatment evaluation, the physician can alter the choice of treatment based on the patient's latest pain and health readings (Robbins et al. 2003).

The pre-treatment evaluation at the beginning of Stage 1 consists of a patient's background and characteristics including a detailed review of their medical records, and physical examination. A three-phase pain treatment plan is then custom-made and implemented for the patient by the Center physicians. The duration of Stage 1 varies for different patients, from 1 to 6 months. The mid-treatment evaluation is conducted at the beginning of Stage 2 to establish how the patient is responding to the treatment plan. The

physician can alter the choice of treatment based on the patient's current pain and health readings. The duration of Stage 2 varies from 1 to 6 months and at the completion of Stage 2, a post-treatment evaluation is conducted. The physician then gives the patient pain management recommendations and an additional evaluation is conducted one year after completion of the program.

## 1.2 Research Methodology Overview

The focus of this research is to develop an approach to provide adaptive treatment strategies for interdisciplinary pain management. The approach taken is to develop outcome and state transition modeling (OSTM) as part of a dynamic programming (DP) framework. While DP is an appropriate choice for handling adaptive treatment strategies, the outcome and state transition functions are unknown for pain management. This complicates the implementation of DP. Reinforcement learning (as was mentioned earlier) does not require known outcome and state transition functions, but does assume there is some way to "realize" outcomes and state transitions, typically via a simulation model. Since such a simulation model does not exist for pain management, the selected DP solution method is the design and analysis of computer experiments (DACE) based approach (Foufoula-Georgiou et al. 1988, Johnson et al. 1993, and Chen et al. 1999). For this approach, outcome and state transition models can be developed using available data (Lin 2010, Lin et. al. 2013, and LeBoulluec et al. 2013).

For multi-stage problems, stochastic dynamic programming (SDP) has been applied as an optimization approach for solving problems in a variety of systems such as manufacturing systems, finance, environmental engineering and others (White 1985, 1988, Brandeau et al. 2004, and Yang et al. 2009). The adaptive treatment strategy for interdisciplinary pain management uses a two-stage dynamic programming model, as

illustrated in Figure 1.2. The goal is to minimize treatment cost and a penalty cost on outcome measures of patients suffering from chronic pain.

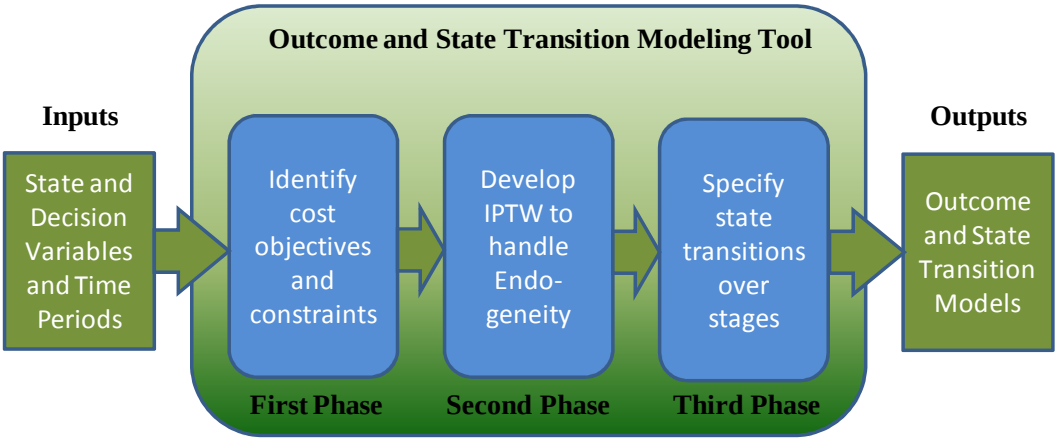



Figure 1.3 Outcome and State Transition Modeling Tool

The inputs into the OSTM tool are the state and decision variables and time periods. State variables include the patients' relevant medical background, such as age, gender, surgical and physical histories, and past diagnoses. Decision variables consist of 21 pharmaceutical treatments and 22 procedural treatments for a total of 43 types of treatment options. Based on the 2-stage interdisciplinary pain management program (see Figure 1.2), the pre-evaluation information is used as the Stage 1 state variables. For the Stage 2 state variables, the pre- and mid-evaluation information from the first treatment plan are utilized. The timing of the pre-, mid-, and post-evaluations, as set by the Center, give the time periods.

The OSTM tool that will be developed in this research will include 3 phases as shown in Figure 1.3. The first phase will be to identify cost objectives and constraints by focusing on a penalty cost function for pain outcomes only. Two outcome measures of pain levels are monitored. The first measure is the Oswestry Pain Disability Questionnaire (OSW), which is a measure of perceived functional disabilities caused by

pain. The second measure is the Pain Drawing Analogue (PDA), which is a measurement in which patients mark their level of pain along a 10 cm visual analog scale. Although there are several other outcome measures, all of them have too many missing values. Therefore, in this research we are using only 2 outcome measures which are collected at the pre-, mid-, and post-evaluations. Constraints used in this research are the limitations on dosage of medication and treatment options (Robbins et al. 2003).

The second phase in the OSTM tool is dealing with the endogeneity presence in pain management data. In section 1.1 we mentioned that pain management data is observational data in sequential treatment which is imbedded with endogeneity. IPTW has been successful in past research in dealing with endogeneity on a limited basis, thus we adapt the IPTW method for the endogeneity problem. The endogeneity problem is a very challenging issue in pain management data. To adapt the IPTW method for endogeneity in this research, several special issues are addressed. For example, the data set has high dimensionality; there are different types of treatments such as binary, polychotomuos, and continuous treatments; there are multiple treatment options.

The third phase in the OSTM tool is specification of state transitions over time periods (stages). Pain management is a complex application that requires estimation of state transitions and depends on the real data set. Figure 1.4 illustrates how this research formulates outcome and state transition models from Stage 1 to 2 in pain management. In Stage 1, patient information is used as state variables. Decision variables for Stage 1 include treatments. Outcome measures are predicted by using the state and decision variables.

As shown in Figure 1-4, all Stage 1 variables and outcome measures are added to Stage 2 state variables. Decision variables at Stage 2 are the treatments given during Stage 2. Stage 2 outcome measures are then predicted from the Stage 2 state and

decision variables. To estimate these predicted outcome measures and state transitions for the objective functions, a stepwise regression model is built.

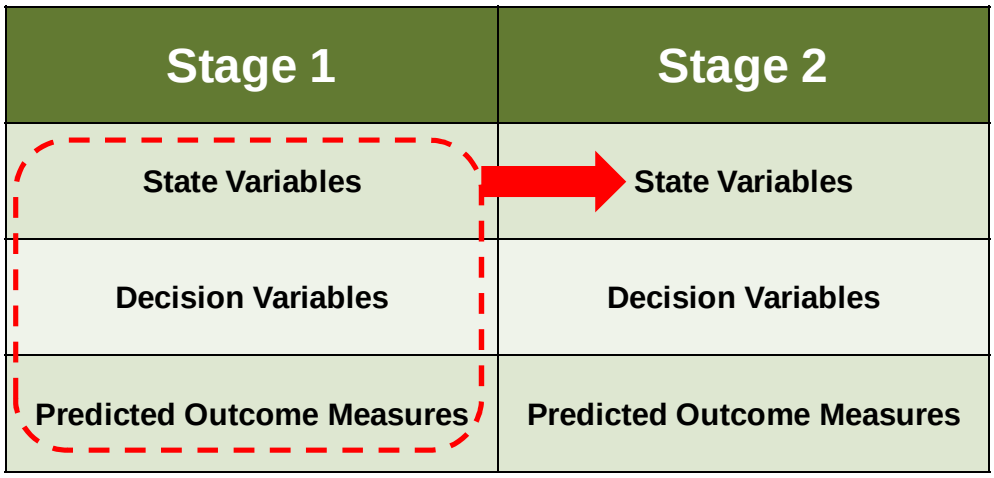



Figure 1.4 Outcome and State Transitions from Stage 1 to 2

Once all the modeling is completed then an optimization routine is used to solve the SDP problem via the Bellman backward recursion (Bellman 1957). Specifically, an approximate SDP solution method based on a statistical perspective can be employed (Chen et al. 1999). In this research, we focus on estimation of the state transitions whereas optimizing an SDP solution will be the future work.

The remainder of this dissertation is organized as follows. Chapter 2 provides the literature review on pain management as well as on adaptive treatment strategies including SDP, endogeneity, and IPTW. Chapter 3 explains how the OSTM tool functions by reviewing data processing techniques. The methodology of how endogeneity is managed is then broken up into two chapters. Chapter 4 discusses the IPTW method applied to treatments that are independent and reviews a case study to prove this. Chapter 5 reviews the general IPTW method applied to treatments that are independent and/or dependent with a case study. The general method is also called IPTW with

Correlated Treatments. Chapter 6 discusses the overall results and future work. Finally, references are given and supporting material if found in the appendix.

# Chapter 2

# Literature Review

## 2.1 Pain Management

Compared to major illnesses such as heart disease, cancer and diabetes, chronic pain affects more people and is more costly. According to the Medical Expenditure Panel Survey (MEPS) which is cosponsored by the Agency for Healthcare Research and Quality and the National Center for Health Statistics, approximately 100 million adults, 18 years or older, in the United States suffer from chronic pain, including arthritis. Pain affects about 4 times more people than heart disease and diabetes and about 9 times more than cancer. The annual cost of pain is estimated to be $560 to $635 billion in 2010 dollars which is more than the annual cost of heart disease ($309 billion), cancer ($243 billion), or diabetes ($188 billion) (Gaskin 2012). The average patient with chronic pain has been suffering for 7 years, has had three major surgeries, and has incurred medical bills of $50,000 to $100,000 (D-Arcy 2007). Given the scope of the chronic pain issue, pain management is a very important endeavor to improve the health and wellbeing of the world's population.

Pain management's goal is to achieve a targeted amount of pain outcome reduction to improve the quality of life of patients suffering from chronic pain. Due to the complexities of pain, an interdisciplinary team of professionals are assembled to create individualized pain management programs. These programs offer broad forms of treatment and utilize multiple disciplinary components depending on the type of pain and a patient's response to the treatment. These include pharmacologic measures (medications), medical interventions, physical therapy and exercise, and psychological treatments. To gain an understanding of the challenges faced in pain management, the anatomy of pain will be briefly discussed followed by the types of pain.

*2.1.1 Anatomy of Pain*

Prior to 1965, our theory on pain was based on Descartes' belief that the body works like a machine where pain results from peripheral injuries which travel as pain impulses through a spinal pathway and into a pain center in the brain. Pain was most often treated with analgesic medications which either block pain signals going to the brain or interfere with these signals. In cases of severe chronic pain, this physical interpretation of pain even lead doctors to attempt a variety of neurosurgical created lesions as treatment which was usually unsuccessful (Melzack 1993). However, in 1965, Melzack and Wall proposed the Gate Control Theory of Pain which introduced a dynamic spinal gate mechanism and highlighted the central nervous system as an essential component in the pain process (Melzack 1965).

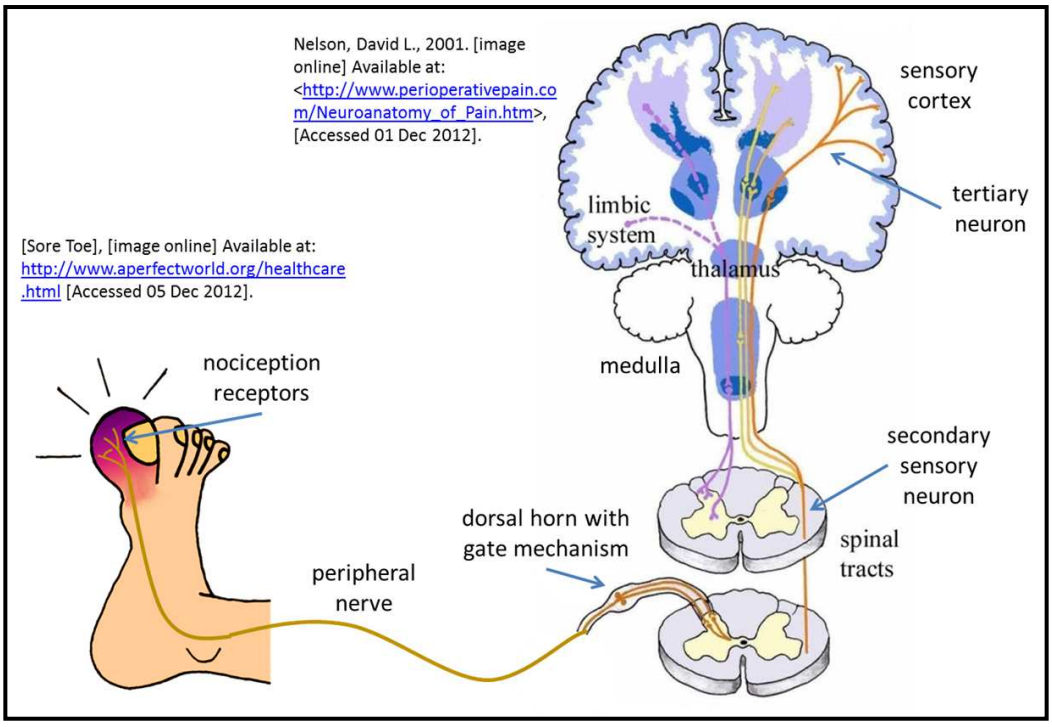



Figure 2.1 Pathway of Pain

This theory, as illustrated in Figure 2.1, has changed the theories on pain from a single caused physical model to multiple caused explanations.

The basic process for pain is illustrated in Figure 2.1 above. Pain is first detected by nociception peripheral receptors found in the skin and viscera or internal organs which respond to strong noxious stimuli (chemical, mechanical, or thermal) that may cause tissue damage. The pain signal travels in a primary sensory neuron or peripheral nerve to the dorsal horn of the spinal cord where there is a gating or switch mechanism. The pain signal may be transmitted to the secondary sensory neuron and into the brain or central nervous system depending on the relative activity and type of incident signals at the gate. In the brain, the second sensory neuron terminates in the thalamus which then transmits the pain signal into third order neurons to the sensory cortex. The thalamus is a junction of the sensory system and the limbic system which is involved in emotion. It is thought that the interaction in the thalamus causes a relationship between pain and emotion. The brain then regulates the pain accordingly through a feedback mechanism (Silverthorn 2010).

The most common sources for chronic pain in America are as noted in Figure 2.2 (American Research 2003). These are based on responses to a survey conducted by American Research in 2003. Most chronic pain originates from back pain, specifically, lower back pain. Due to the natural aging process, spinal discs in the lower back begin to loose vascularity by the age of 20. Disc desiccation begins at 30 years old which is a degenerative process where there is a loss of cushion between the vertebrae or bones of the spinal column. It is estimated that 95% of the population will experience the start of degenerative disc disease by the age of 50 (D'Arcy 2009) which can cause chronic pain.

The second most common source of chronic pain is arthritis at 19%, followed by headaches and migraines at 17%, knee pain at 17%, and shoulder pain at 7%.

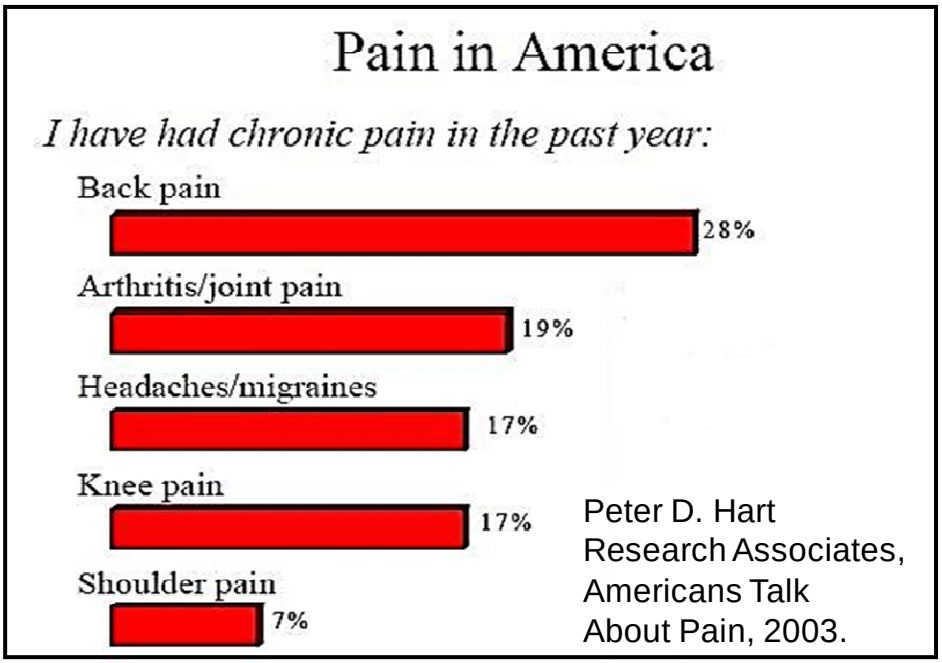



Figure 2.2 Sources of Pain

*2.1.2 Types of Pain*

Pain is commonly divided up into acute and chronic pain. Acute pain occurs at the time of an injury or disease process and may persist through the healing process. Acute pain normally last less than 3 months but can also be recurring as when moving joints with arthritis. Chronic pain persists beyond the healing phase and has a duration normally greater than 3 months. Chronicity is characterized by changes in mobility and major psychological impairment including the occurrence of abnormal behaviors or thoughts. Patients with chronic pain are more distressed rather than in pain. Acute and chronic pain can be further broken down into 4 subgroups known as nocigenic, behavioral, neurogenic, and psychogenic pain (Hardy 1997).

Nocigenic pain is characterized by the classical pain pathways originating in the peripheral pathways (see Figure 2.1). Most pain related to injury or disease is nocigenic

in the initial stages and can be treated by pharmacologic measures such as analgesics and nerve blocks.

Behavioral pain may begin during or after the nocigenic phase in which patients exhibit changes in behavior. Some changes are overt in which the new or modified behavior is associated with the pain which results in a continuation of the pain after the nocigenic phase. Other changes can be covert where the behavioral change appears to be a result of the pain however there is no basis for the change.

Neurogenic pain is caused by damage to the nervous system, either peripherally or centrally. Peripheral damage progresses from nocigenic components to neurogenic in an interval of 36 months. Patients with neurogenic pain normally suffer from sensory disturbances such as absence or increased sensation, and changes in duration to a perceived sensation. This pain is often persistent and causes significant depression in patients.

Psychogenic pain occurs as a form of mental illness of process. For example, a patient may be inflicted with hysterical or delusional pain in the brain or other parts of the body. Diagnosis must be made with positive indicators of psychiatric illness (Hardy 1997).

*2.1.3 Pain Management Programs*

The traditional approach to pain management was to treat the pain as nocigenic pain and eliminate the pain by addressing the physical original with the application of pharmacologic treatments, mainly analgesics, which affect the peripheral nervous system. Physicians would prescribe individualized medical treatments to patients based on the diagnosis and their own clinical experiences. It was expected that the patient's physical signs and symptoms would be alleviated after taking the prescribed medications (Spanswick & Main 2000, D'Arcy et al. 2007, and Schatman & Champbell 2007).

The failures of the traditional approach and the introduction of the Gate Control Theory lead to the idea of multi-disciplinary and interdisciplinary pain management to treat chronic pain cases which did not respond to the standard pharmacological treatment. Both the multi-disciplinary and interdisciplinary pain management methods use a biopsychosocial model for pain management, meaning that the model addresses the dependence of human health on biological, psychological, and social behaviors. The difference between these two methods is in their goals. Multi-disciplinary pain management involves a variety of specialists with independent goals. For interdisciplinary pain management, these specialists all work together to set one goal (Schatman & Champbell 2007).

*2.1.4 Interdisciplinary / Multidisciplinary Pain Management*

Today, our understanding of chronic pain has improved to where we understand that pain is not just a result of an injury or diseased tissue or organ. Pain can also be caused by behavioral changes, or be the result of damage to the central or peripheral nervous system, or is a form of mental illness. This indicates that the pain a patient perceives can be produced by the patient's mind which is not something that can be treated with prescribed medication. Thus, application of Interdisciplinary and Multidisciplinary Pain Management has introduced novel approaches such as cognitive behavioral treatment and other non-pharmacological treatments for cases where medication does not alleviate the pain to a desired level of pain relief. Cognitive–behavioral approaches emphasize how thoughts and beliefs can influence patients' pain outcomes and functional status to mediate their behavioral changes. In addition, some medications have been discovered to provide better pain relief than analgesics (Schatman & Champbell 2007, and Gould 2007).

Applying approaches from the psychological and emotional side is more patient driven than in the past. The pain management team needs more commitment and responsibility from patients. Feedback is also needed to adjust the duration of treatments based on each patient's progress. The pain management treatment team usually consists of a physician, psychologist or psychiatrist, occupational therapist (vocational counselor), registered nurses, biofeedback therapist, social workers and various specialized physical therapists. Patients can choose where they want to complete treatment tasks, at home or in a clinic. Treatment tasks vary due to the type and location of pain and the patient's response. Tasks include relaxation, meditation techniques, stretching, aerobics, aquatic exercises, massage, and individual physical therapy (Spanswick & Main 2000, D'Arcy et al. 2007, and Schatman & Champbell 2007).

There are a growing number of studies that indicate that the integration of interdisciplinary/multidisciplinary pain management programs has promising effectiveness on pain management. For example, Flor et al. (1992) reviewed the result of sixty-five studies which supports the efficacy of multidisciplinary pain management centers. In a more specific study, Kames et al. (1988) gave evidence that the application of an interdisciplinary pain management program provided noticeable chronic pelvic pain reduction. A study by Olason (2004) applied an interdisciplinary pain management program to focus more on increasing a patient's functioning and eliminating analgesics in a rehabilitation clinic. Applying physiotherapies within a cognitive behavioral framework was shown to be successful by Eccleston & Eccleston in 2004. The cases implementing cognitive–behavioral treatments opposed to only pharmacological treatments are increasing, resulting in more evidence that patients experience reductions in pain, anxiety and depression using an interdisciplinary pain management program.

The goal of this research is to analyze the effects of various treatments on relevant outcome measures. The pain management database utilized was created by the Eugene McDermott Center for Pain Management at the University of Texas Southwestern Medical Center at Dallas. This database is composed of 294 patients in the time period from January 1988 to June 2007.

The interdisciplinary pain management program used at the Center uses a two-stage treatment program which each lasts for a duration of several weeks to 6 months. Treatments are given at the beginning of Stage 1 (initial treatment), and the beginning of Stage 2 (mid-treatment), and after the end of Stage 2 (post-treatment). Evaluations of patients are made pre-treatment (pre) of Stage 1, midpoint (mid) between Stage 1 and Stage 2, post-treatment (post) after the treatment at Stage 2 and one year following the completion of the program (see Figure 1.2). However, the one year follow up is not included in this research. Outcome data was obtained over the pre, mid, and post treatment periods.

*2.1.5 Treatment Guidelines and Standards*

Due to the various and growing forms of treatment, many health organizations have attempted to define best practices and create standards and guidelines for pain management. The first of these efforts is from the Agency for Health Care Policy and Research (AHCPR) in 1992. Based on a panel of experts on pain treatment, it provided guidelines for acute pain, cancer pain, and low back pain. Eventually, the AHCPR gave the work of guideline development for pain management to the American Pain Society (APS). The APS set many guidelines for specific pain and treatment such as Low Back Pain Guidelines and Principles of Analgesic use in the Treatment of Acute pain and Cancer Pain. Over time, many national specialty organizations such as the American Geriatrics Society for the elderly, the American Pediatric Society for children, and NCCN

for cancer patients developed their own pain management guidelines for their specific patients' population. One of the strongest national guidelines used today is the Joint Commission on Accreditation of Healthcare Organizations (JCAHO). These guidelines direct the practice of pain management in all hospitals that the regulatory body surveys (D'Arcy et al. 2007).

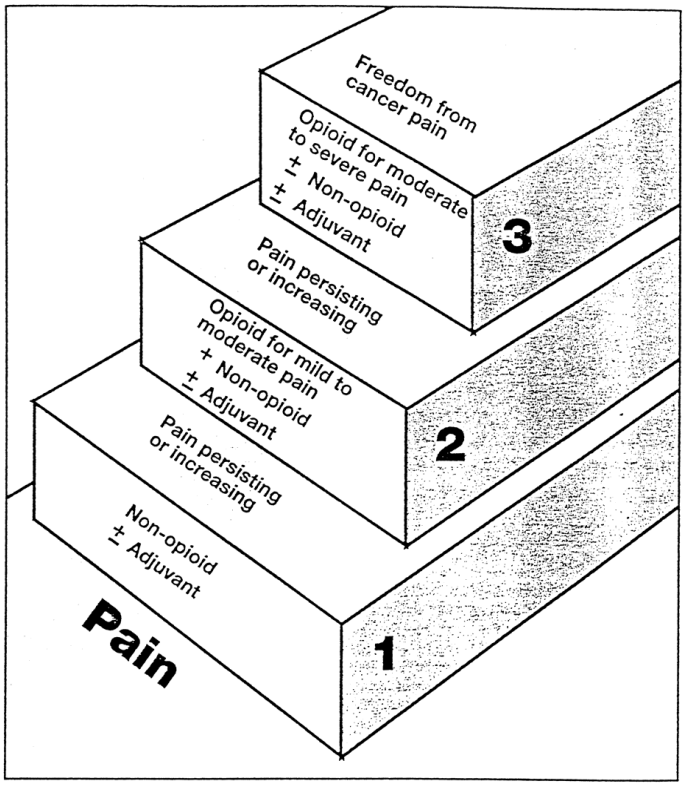



Figure 2.3 The World Health Organization's Analgesic Ladder Approach for Relief of Cancer Pain. (Dalton and Youngblood 2000).

Another guideline which is very popular today is the analgesic ladder shown in Figure 2.3 for the use of pharmacologic treatments for pain management. This was first recommended in 1986 by the World Health Organization (WHO) to give clear guidelines

on pain relief for cancer, but it has now been adopted for all types of pain models in pain management (Dunn et al. 2010).

The first level of the analgesic ladder can treat patients with mild pain in which non-steroidal anti-inflammatory drugs (NSAID) are given such as acetaminophen (aspirin) and ibuprofen which affect the peripheral nervous system. If pain levels persist or increase, then second level medications are prescribed which are mild forms of opioids, such as hydrocodone and codeine, in combination with NSAID. Opioids are derived from opium poppy and caution must be taken to avoid substance abuse, misuse, and addiction. If pain levels do not subside, level three medications are given which include morphine and other strong opioids which affect both the central nervous system and peripheral nervous system mainly with the gating mechanism in the dorsal horn. The specific level three medication chosen depends on the type of pain.

With a deeper understanding of the physiology of pain, the use of adjuvant medications as alternatives to using analgesics alone is growing. The analgesic ladder reflects this by noting the possible use of adjuvant medications at each of the three levels. Some of the benefits of prescribing adjuvants are to help alleviate pain and depression, calm fears and anxiety, relax muscles, and increase the effects of opioids (Dalton and Youngblood 2000).

*2.1.6 Treatment Options*

In addition to analgesics and adjuvant medications as discussed in the analgesic ladder above, non-pharmacological adjuvant therapies are now considered for pain management especially when medications cannot manage the pain (Gould 2007, and D'Arcy et al. 2007). These include medical interventions, physical relaxation strategies, and psychological strategies. Treatments are carefully selected since some may be detrimental for pain management. For example, in covert cases of behavioral pain,

prescription of analgesics and nerve blocks can be dangerous since they can reinforce the abnormal response. For neurogenic pain, classical analgesics normally do not offer relief from this pain. Instead, antidepressants can be given and psychological and physical relaxation strategies are followed. It is also important that duration, intensity, and follow-up of treatment plans are varied according to a patient's response.

Most options of pain treatment are listed below (Warncke et al. 1994, Zaza et al. 1999, Dalton and Youngblood 2000, Davies McVicar 2000, and Gould 2007).

Table 2.1 Pain Treatment Options

| Pharmacological Therapies | |
|---|---|
| Analgesic Therapies | • Non-opioids<br>  o Nonsteroidal anti-inflammatory drugs (NSAIDs, e.g., acetaminophen, aspirin, ibuprofen)<br>  o Paracetamol<br>  o Corticosteroids (e.g., dexamethasone) |
| | • Weak opioid (e.g., codeine, hydrocodone, dihydrocodeine, propoxyphene, tramado,) |
| | • Strong opiod (e.g., fentanyl, hydromorphone, levorphanol, methadone, morphine, oxycodone, pentazocine, meperidine, buprenorphine, pentazocine, nalbuphine) |
| Adjuvant Therapies | • Alcohol<br>• Anticonvulsants (e.g., cabamazepine, diazepam, phenytoin, valproic acid)<br>• Antidepressants (e.g., amitriptyline, imipramine, trazadone)<br>• Anxiolytics<br>• Coricosteroids<br>• Muscle Relaxers (e.g., soma, flexeril, norflex)<br>• Neuroleptics (e.g., chlorpromazine, levomepromazine or methotrimeprazine)<br>• Benzodiazepines ( e.g., sedatives: valium, ativan, versed)<br>• Local Anesthetics (e.g., local, topical, systemic)<br>• Eutectic Mixture of Local Anesthetics (EMLA)<br>• Lidoderm Patch<br>• Subcutaneous Continuous Infusion |
| Non-Pharmacological Adjuvant Therapies | |
| Physical Relaxation Strategies | • Autogenic training<br>• Biofeedback<br>• Cognitive behavioral therapy<br>• Hypnosis<br>• Individual psychotherapy |

Table 2.1—*Continued*

| | |
|---|---|
| | • Meditation<br>• Music or art therapy<br>• Operant conditioning<br>• Progressive muscle relaxation<br>• Regular exercise<br>• Support groups<br>• Visualization or imagery |
| Medical Interventions | • Anesthetic blocks<br>• Epidural steroid injections<br>• Neuromodulation<br>• Radiotherapy / radiation<br>• Surgery<br>• Transcutaneous electrical nerve stimulation (TENS) |

*2.1.7 Outcome Measurements / Pain Assessments*

Pain measurement and assessment can be classified as single dimensional/one-dimensional or multidimensional measurements. The traditional measures of pain intensity, which are still the most common used to evaluate patients' pain in clinics, are one dimensional pain scales. Of the many one dimensional pain scales, the visual analog scale (VAS), verbal descriptor scale (VDS) and numerical pain scales (NPS) are most often used. A drawback to these scales is that they cannot detect motivational-affective dimensions of pain. Thus, multidimensional measurements were proposed (Raj 2003, D'Arcy 2007, and Turk & Melzack 2001).

In the multidimensional measurements, 6 dimensions are commonly used which are sensory, affective, cognitive, physiologic, behavioral and sociocultural (McGuire 1992, and Cady 2001). The first three were introduced by Melzack and Wall (1965, 1982, and 1988); the last three were proposed by Ahles et al. (1983) and McGuire (1987). The most frequently used multidimensional measurements are the brief pain inventory (BPI) and short form McGill pain questionnaire (SF-MPQ). The outcome measurements of pain are listed below:

Table 2.2 Outcome Measurements

| Unidimensional Measurements | Authors |
|---|---|
| Visual analog scale (VAS) | Raj 2003, D'Arcy 2007 |
| Verbal descriptor scale (VDS) | Raj 2003, D'Arcy 2007 |
| Numerical pain scales (NPS) | Raj 2003, D'Arcy 2007 |
| 11-point box scale | Raj 2003 |
| 101-pint numerical rating scale | Raj 2003 |
| 4-point and 5-point verbal rating scale | Raj 2003 |
| Graphic Rating Scale (GRS) | Huskisson 1974, Heft and Parker 1984 |
| Color Scale | Dalton and McNaull 1998 |
| Verbal Descriptor Scale | Melzack and Torgerson 1971, Scott and Huskisson 1976, Dalton et al. 1988 |
| Multidimensional measurements | Authors |
| Brief pain inventory(BPI) | Raj 2003, D'Arcy 2007 |
| McGill pain questionnaire (MPQ): | |
| Short form (SF-MPQ) | Raj 2003 |
| Long form (LF-MPQ) | Melzack 1975 |
| Pain disability index | Raj 2003 |
| Neck disability index | Raj 2003 |
| Dallas pain questionnaire | Raj 2003 |
| West Haven-Yale multidimensional pain inventory | Raj 2003 |
| Descriptor differential scale | Raj 2003 |
| Wisconsin brief pain questionnaire | Raj 2003 |
| Sickness impact profile | Raj 2003 |
| Abu-Saad pediatric pain assessment | Raj 2003 |
| Pain Assessment Tool and Flow Sheet | McMillan et al. 1988 |
| Body Chart | Twycross and Lack 1983 |
| Memorial Pain Assessment Card | Fishman et al. 1987 |
| Pain/Comfort Journal | Keating and Kelman 1988 |
| Chronic Pain Experience Instrument | Davis 1989 |

## 2.2 Adaptive Treatment Strategies

To prescribe a treatment to a patient requires not only an evaluation at the current state but also analyzing their changing state by understanding their past history regarding response to previous treatments. An adaptive treatment strategy (ATS) is a framework for adapting a treatment according to a patient's changing state (Lavori et al., 2000, and Murphy 2005). To prescribe treatments, ATS uses patient information such as a patient's risk factors, response, irregularity to following the treatment plan, and outcomes as inputs to decision rules. The treatment level and type is repeatedly modified by the decision rules according to the patient's needs. Medical professionals utilize many methods today for various purposes such as clinical experience, trial and error, behavioral, and psychosocial and biological theories. These methods can be utilized to create decision rules for ATS. "Adaptive treatment strategies" is also known as dynamic treatment regimes, adaptive interventions, or tailored communications (Murphy 2003, and Murphy et al. 2007).

Research on adaptive treatment strategies has been increasing. For example, Two different adaptive treatment strategies, baseline and adaptive randomization, were implemented by Dawson & Lavori (2003) for a major depressive disorder. In 2006, a comparison of two dynamic treatment regimes to acquired immunodeficiency syndrome (AIDS)-free survival in a study of human immunodeficiency virus (HIV)-infected patient was analyzed by Hernάn et al. (2006). In 2007, several engineering control principles to improve the design of adaptive interventions in the chronic treatment of substance abuse were proposed by Rivera et al. (2007).

In health care research, ATS has successfully employed different algorithms. These algorithms can be divided into two categories: randomized experimentation and Markov decision process. Randomized experimentation includes the multiphase

optimization strategy (Collins et al. 2007) and sequential multiple assignment randomized trials (Murphy 2005). The multiphase optimization strategy (MOST) and sequential multiple assignment randomized trials (SMART) are similar in that they attain valid inferences by implementing randomized experimentations. In MOST, important components are efficiently defined by using factorial analysis of variance (Collins et al. 2007). In SMART, decision rules are developed by experimental trials (Murphy 2005).

In this research, Markov decision processes (MDP) are discussed in section 2.2.1 and section 2.3 discusses Stochastic Dynamic Programming (SDP).

*2.2.1 Markov Decision Process*

To determine the best treatments for patients, a physician must consider the current and changing state of a patient as well as the treatment options available. Due to time constraints and other reasons, physicians often make spontaneous, subjective decisions which are complex due to many uncertainties, yielding inaccurate treatments (Morris 2000, and Tversky et al. 1982). Markov decision processes (MDPs) are appropriate mathematical decision models that can improve the accuracy of sequential and stochastic decision problems however, are underutilized. The goal of MDPs is to find a decision strategy to optimize a particular criterion such as maximizing a total discounted reward. To acquire good results from MDPs, quality medical data must be obtained which is expensive because it is normally done manually. Today, with the increasing use of electronic medical records, large amounts of quality medical data are obtained for researchers (Tierney et al. 1995).

Four basic types of MDPs are: Finite-horizon MDPs, Infinite-horizon MDPs, Partially observed MDPs, Semi-Markov decision processes. When there is a finite number of time period, Finite-horizon MDPs are used. If the quantity of time periods is undetermined, Infinite-horizon MDPs are utilized. When enough information is known

about a true state, partially observed state is replaced. Researchers use SMDPs when the time between decisions varies probabilistically. Overall, the MDP is advantageous and flexible since it allows the choice of different actions across multiple time periods according to the patient's state.

## 2.3 Stochastic Dynamic Programming

In deterministic dynamic programming, parameters are known such as the next state, given a state and a decision. In Stochastic Dynamic Programming (SDP), the next state parameters are estimated based on their probability function since these are unknown. SDP has been used in systems such as manufacturing systems, finance, environmental engineering, economics, and others (White 1985, 1988, Brandeau et al. 2004, and Yang 2004) as an optimization approach for multi-stage problems changing over time. SDP can also be used to solve MDPs. There are three main parameters utilized in SDP. The state of system at each stage is defined by state variables. Decision variables can be controlled to minimize expected current and future costs. State changes from the current stage to the next stage are identified by transition functions. The optimal solution can be solved via a backward recursion algorithm. At each stage of the system, the optimal expected current and future costs are calculated over all possible current states and stored as the future (or optimal) value function. This can be computationally complex and time consuming since the state space is very large. In particular, continuous-state DP has infinite state spaces; hence, interpolation over a discretized state space has been used to approximate the continuity of the system (Chen 1999).

*2.3.1 Continuous-State Dynamic Programming*

State and decision variables are all continuous in continuous-state SDP. An example of this is in the case of ozone pollution (Yang 2004, and Lin 2010). A continuous-state, finite-horizon SDP model is described as follows (Chen et al. 1999):

$$\begin{aligned} &\min E\left\{\sum_{t=1}^{T} c_t\left(x_t, u_t, \varepsilon_t\right)\right\} \\ &s.t.\ x_{t+1} = f_t\left(x_t, u_t, \varepsilon_t\right),\ \text{for } t = 1,...,T-1 \\ &\left(x_t, u_t\right) \in \Gamma_t,\ \text{for } t = 1,...,T-1 \end{aligned} \tag{2.1}$$

In equation 2.1, the minimum expected value, $\min E$, is equal to the sum of the cost function over the total number of stages, $T$. The cost function, $c_t(\cdot)$, for period $t$ is a function of the state vectors, $x_t$, decision vectors, $u_t$, and the random vector, $\varepsilon_t$. This is subject to the transition function, $x_{t+1}$, which is equal to the transition function, $f_t(\cdot)$, from stage $t$ to $t+1$. The transition function is also a function of the state and decision vectors and the random vector. Furthermore, $x_t \in R^n$ and describes the state of system; $u_t \in R^m$ and is the only vector which can be controlled to minimize the current plus future cost; $c_t(\cdot): R^{(n+m+1)} \to R^1$; $\varepsilon_t \to R^1$; $\Gamma_t$ is the set of constraints where $\Gamma_t \subset R^{n+m}$.

A future value function, $F_t\left(x_t\right)$, at stage $t$ can be defined as equation 2.2; a recursive future value function at stage $t$ is defined as equation 2.3 (under those same constraints:

$$F_t(x_t) = \min_{u_t \ldots u_t} E\left\{\sum_{\tau=t}^{T} c_\tau(x_\tau, u_\tau, \varepsilon_\tau)\right\}$$
$$s.\,t.\; x_{\tau+1} = f_\tau(x_\tau, u_\tau, \varepsilon_\tau), \text{ for } \tau = t,\ldots,T-1 \quad (2.2)$$
$$(x_\tau, u_\tau) \in \Gamma_\tau, \text{ for } \tau = t,\ldots,T$$

$$F_t(x_t) = \min_{u_t} E\left\{c_\tau(x_\tau, u_\tau, \varepsilon_\tau) + F_{t+1}(x_{t+1})\right\}, \text{ for } t = 1,\ldots,T \quad (2.3)$$

The traditional way for solving continuous-state SDP is to discretize the state space, solve for the optimal solution at each discretization point, then provide a continuous approximation of the future value function using interpolation or some functional approximation scheme (Foufoula-Georgiou et al. 1988, Johnson et al. 1993, and Chen et al. 1999).

In traditional methods of discretization, as used by Foufoula-Georgiou et al. (1988) and Johnson et al. (1993), the number of data points increases exponentially as the number of variables grows linearly which causes computational limitations due to dimensionality. This exponential growth in computational effort has been mitigated by Chen et al. (1999) by applying statistical experimental design and statistical modeling.

This research builds state transition modeling for SDP. However, optimization of pain management is future work.

### 2.4 Endogeneity in Adaptive Treatment Strategies

The field of study of adaptive treatment strategies has been pioneered by Robins (1986, 1994, and 1997). The first attempt at developing a method for adaptive treatment strategies was developed by Murphy (2003) and followed up by Robins et al. (2004). The method developed uses a reinforcement learning adaptive dynamic programming approach (Barto 2004, and Werbos 1920) focused on sequential randomized clinical trials, which yields ideal data for optimizing adaptive treatment strategies (Murphy, Collins

et al. 2007, and Pineau et al. 2007). By contrast, observational data in sequential treatment are not ideal.

*2.4.1 Definition of Endogeneity*

The general definition of endogeneity is given in equation 2.4 below.

$$y = f(X) + \varepsilon \tag{2.4}$$

The independent variable $X$ in a regression model is called endogenous if it is correlated with the error term. An example of endogeneity is shown in Figure 2.4 below which is an adaptive treatment study in epidemiology.

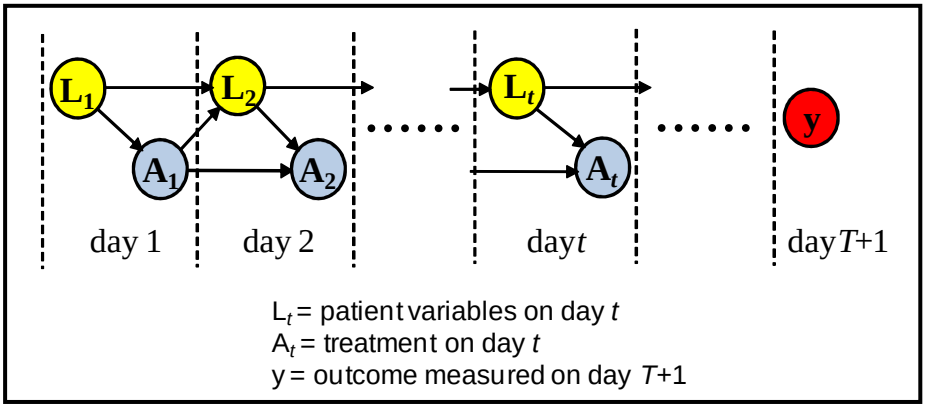



Figure 2.4 Definition in Adaptive Treatment Studies in Epidemiology (Robins 1999)

The time-dependent treatment $A_t$ is called endogenous if its probability depends on the history of time-dependent patient variables $\{L_1, L_2, \ldots L_t\}$ conditional on the treatment history prior to $t$. This can be expressed mathematically in equation 2.5

$$Corr\left(A_t, \bar{L}_T \middle| A_{t-1}\right) \neq 0, \tag{2.5}$$

where $Corr\left(A, B \middle| C\right)$ denotes the correlation of $A$ and $B$ given $C$, the patient variables on day $t$ are denoted by $\bar{L}_t = \{L_1, L_2, \ldots L_t\}$, and the treatment on day $t$ are

denoted by $\bar{A}_{t-1} = \{A_1, A_2, \ldots A_{t-1}\}$. Equation 2.5 states that treatment on each day depends on the history of both treatment and patient variables.

The definition given in Robins' paper (Robins 1999) is about exogenous, the opposite of endogenous. Robins states that, "A process is "statistically exogenous" does not imply it is "causally exogenous", because there may be unmeasured confounders that predict the probability of treatment $A_t$ at time $t$ given past treatment history. We can test from the data whether $A_t$ is statistically exogenous but are unable to test whether a statistically exogenous process is causally exogenous. We warn the reader that there is no agreed upon definition of "causally exogenous" or "statistically exogenous" in the literature. I find my definition quite useful and appropriate, but there are other definitions. In particular, the definitions I have given here do not agree with the definition of exogeneity found in the econometric time series literature (Eficcsson et al. 1998)."

*2.4.2 Problem Caused by Endogeneity in Parameter Estimation*

In the presence of endogeneity, the estimation of the treatment effect will be biased. More specifically, the main concern in epidemiology studies is the causal effect of the treatment on an outcome of interest. Here a causal effect means a direct effect from the treatment to the outcome, not from any other variable, or through any other variable. Correspondingly, the bias caused by endogeneity is with respect to the true causal effect. In other words, with endogeneity, we cannot obtain an unbiased estimate of the causal effect of treatment on the outcome.

This does not mean that the estimate of the treatment effect in a hypothesized model is biased. For example, in the following model (equation 2.6):

$$y = \gamma_1 + \gamma_2 \cdot cum\left(\bar{A}_T\right) + \gamma_3 \cdot \bar{L}_T + \varepsilon$$
$$cum\left(\bar{A}_T\right) = \sum_{t=1}^{T} A_t \tag{2.6}$$

is the subject's cumulative treatment. The estimate of $\gamma_2$ using conventional methods, e.g., least squares estimation, will be unbiased for this model, but biased as the causal effect of treatment. This is because the correlation of treatment and patient variables is very complex: in the time-dependent setting, patient variables at a stage will affect the following treatments and themselves are affected by the previous treatments. In this case, not only $\gamma_2$ does not represent the causal effect of treatment, but it generally does not have a causal interpretation (Robins 1999, and Robins et al. 2000). The essential purpose of statistical modeling in epidemiology research is identifying the causal effect of treatment on outcomes, so the development of methods.

## 2.5 Inverse Probability of Treatment Weighted (IPTW) Method

The endogeneity problem is very challenging for which the conventional methods for confounder adjustment, such as stratification, matching and propensity score methods (Weitzen et al. 2004, D'Agostino 2007, and Klungel et al. 2004) do not work. A standard approach to this problem is the instrumental variable methods (Hogan et al. 2004) which obtain unbiased estimation of the treatment effect by making use of some instruments or additional information. However, the reliance on the availability of instruments limits the applicability of these methods. Recently, a class of methods known as inverse probability of treatment weighed (IPTW) estimators has been developed and gained popularity in epidemiology research for its convenience in use and good properties (Robins et al. 2000, Hernán et al. 2001, Joffe et al. 2004, Bodnar et al. 2004, Fewell et al. 2004, Cole et al. 2008, Garcia-Aymerich et al. 2008, and VanderWeele 2009).

### *2.5.1 Approaches to Adjusting for Confounding Variables (Selection Bias)*

#### 2.5.1.1 The Problem

One main focus in research fields such as epidemiology, economics, clinical medicine and public health is to identify the causal effect of treatment on outcomes. However, in general, there are always some confounding variables (e.g., patient variables), the effect of which needs to be adjusted to obtain an unbiased or consistent estimate of the causal effect of treatment. This problem is also commonly referred to as 'adjusting for treatment selection bias', which is a key limitation of observational studies compared to randomized trials.

#### 2.5.1.2 Approaches in Different Fields

Popular approaches to adjust for selection bias are different in different fields: in public health and epidemiology, methods like propensity matching, stratification, regression adjustment, and standardization are often used. By contrast, in economics and social sciences, instrumental variable (IV) methods prevail. The main reason for this difference is that normally all confounders are observed in epidemiology studies as the collection of possible confounders. This is an integral part of the design of the study. While there is at least one and possibly several unmeasured confounders in the data set in economical and social science studies, they are not designed for a specific research agenda. These data sets are typically collected or maintained by government agencies or survey organizations (Hogan et al. 2004).

#### 2.5.1.3 Regression Methods for Selection Bias Adjustment with Known Confounders

There are three cases of regression methods for selection bias adjustment with confounders that are known as follows:

Case I--Intermediate confounding: When confounding variables are intermediate variables, that is, they are caused by the treatment and they cause the

outcome, no adjustment is needed. In this case, the coefficient in the outcome model, i.e., Outcome= $f$ (Treatment), represents the total effect of treatment, though not causal, or direct, effect. This is shown in Figure 2.5.

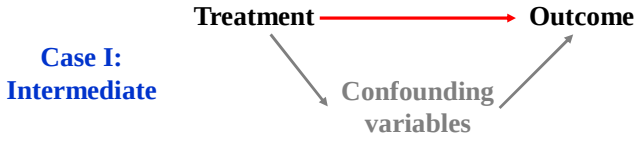



Figure 2.5 Case I: Intermediate

Case II--Common cause: When confounding variables are common causes for both treatment and outcome, the causal effect of treatment can be obtained by regression adjustment, i.e., including confounders in the outcome model as shown in Figure 2.6. That is, the outcome model will be (equation 2.7):

$$\text{Outcome} = f\left(\text{Treatment, Confounders}\right). \tag{2.7}$$

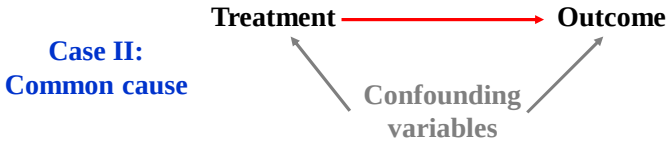



Figure 2.6 Case II: Common Cause

Case III--Time-dependent treatment with endogeneity: When confounders are both intermediate and common causes, the causal effect of treatment cannot be obtained by merely including confounders in the outcome model as regressors (Figure 2.7). Instead, they should be adjusted for by using the weighted regression methods, i.e., the IPTW method.

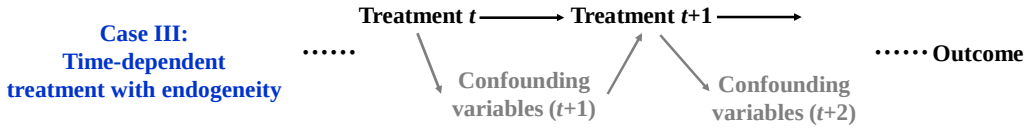



Figure 2.7 Case III: Time-Dependent Treatment with Endogeneity

*2.5.2 Why is the IPTW Method Used in Epidemiology Studies?*

In epidemiology papers, the inverse probability weighted method is often used to adjust for patient variables instead of regression adjustment. The reason is that in epidemiology studies, the main concern is the causal effect of treatment on the entire source population, and the effect of patient variables is not of interest. In other words, the model they want to build is weighted $y = \gamma_1 + \gamma_2 \cdot A_1 + \varepsilon$ in which $\gamma_2$ should also represent the causal effect of treatment.

Essentially, what they want to find is $E\left(y|\mathrm{A}_1\right)$ not $E\left(y|\mathrm{A}_1, L_1\right)$. Robins (1999) mentioned that, "I regard the subjects as randomly drawn from a near-infinite hypothetical superpopulation of subjects about whom we wish to make inference. Expectations refer to averages in the superpopulation and probability statements to proportions in the superpopulation".

That is why the IPTW method is also popular in the point-treatment scenario in addition to the adaptive treatment scenario in epidemiology studies. As put in (Joffe et al. 2004), "In standard regression modeling, controlling for confounding by a variable requires including it in the structural part of a statistical model. This is unfortunate, because these variables may be mere nuisance variables of little wider interest. A new class of causal models, the marginal structural models, and their associated weighted estimation allow separation of model selection from confounder control, so permitting one to keep variables of little intrinsic interest out of the structural part of the model while still controlling for confounding by those variables".

# Chapter 3

## Outcome and State Transition Modeling for Adaptive Interdisciplinary Pain Management

In this research, we seek adaptive treatment strategies for interdisciplinary pain management using data from the Center. An adaptive dynamic programming approach is formulated to improve current and future pain outcomes. The Pain Management data are observational data in sequential treatment which will lead to bias in estimating the true effect of treatments on the outcomes. This problem is referred to as endogeneity. Our outcome and state transition modeling (OSTM) handles the problem of endogeneity via an IPTW approach. The purpose of applying IPTW is to eliminate the bias due to patient characteristics. However, existing methods focus on the simplistic case of a single binary treatment variable (i.e., 1 = received treatment, 0 = did not receive treatment). In this dissertation, two IPTW methods are developed for OSTM to handle a mix of multiple treatment variables in binary and multinomial forms. One method assumes independent treatments to deal with endogeneity while the other method accommodates correlated treatments. The former is called IPTW with Independent Treatments and the latter is IPTW with Correlated Treatments.

The goal of adaptive strategies for pain management is to minimize treatment cost and patients' pain outcomes via OSTM. As stated in section 1.2, there are three phases for OSTM which achieve these goals. The first phase is identifies cost objectives and constraints by focusing on a penalty cost function pertaining to pain outcomes only. The second phase is implements IPTW to handle the presence of endogeneity in pain management data. The third phase of the OSTM tool is specification of state transitions over the stages in which the state transitions and outcome measures for objective functions are modeled with a stepwise regression model. This chapter covers data preparation which includes the basic components of stochastic dynamic programming

(SDP), stages, state variables, decision variables, categorical variables and outcome measures. Moreover, it also talks about imputation of missing values, and some issues on handling the raw data set.

## 3.1 Data Preparation

Two data sets were used for this research. At the beginning of this research, the raw data set was provided by the University of Texas Southwestern Medical Center at Dallas (The Center) and included data collected from August 1998 to May 2001 on 127 patients with over 200 variables (Robbins et al. 2003). This data set was used by Lin (2010) to conduct adaptive treatment research in pain management, and it is used to illustrate the IPTW Method with Independent Treatments (Chapter 4). Later, the Center released a larger data set, which was used to create a more general methodology, referred to as the IPTW Method with Correlated Treatments (Chapter 5). The Robbins et al. data is part of the larger data set.

The larger raw data set includes data from patients who were in an interdisciplinary pain management program at various treatment points and patients who would be entering the program during the time frame from January 1998 to June 2007. Patients that had just entered the program but were not participating for at least one year were excluded. In total, 3,586 patients were entered into the database of which 619 variables were observed by the Eugene McDermott Center for Pain Management at the University of Texas Southwestern Medical Center at Dallas (The Center). It was found that the database is complex since it contained many variables and often had many missing or invalid values among the observations. In this application, the data is modeled by dividing it into two stages. In each stage there are state variables and decision variables. State variables include age, gender, surgical and physical histories,

past diagnosis, and past treatment. Decision variables include pharmaceutical and procedural treatments.

The following sub-sections detail the data preparation, pre-evaluation information, treatment options, and outcome measures.

When all observations with missing data were dropped, there would be 227 observations for modeling. However, to preserve the use of as much data as possible, many missing and invalid values were imputed via regression models. To accommodate the different types of treatments, they were grouped based on similarity of function, so that there were no zero counts for any group. The final cleaned data set contained 294 patients with 88 variables, 25 treatments and 2 outcome measures.

*3.1.1 Data Preparation Process*

The database was found to contain questionable values possibly due to human error on data entry as well as many missing values. To detect and help correct most of these problems, a Perl Script was developed (Miller, 2012). Most of the problems can be classified and resolved as noted below.

1) A common error detected was a set of consecutive variables with invalid values. The invalid values were identified by noting relationships between the variables. For example, the data set contains many pairs of binary variables and multinomial/ordinal variables. One binary variable may indicate that a patient was not prescribed a drug (‘0’ for no drug prescribed, ‘1’ for drug prescribed), yet a multinomial variable may indicate the level of dosage (low, medium, or high) applied of that prescribed drug. Once these discrepancies were identified, people at the Center familiar with the data entry procedure were consulted. It was determined that some data entry

personnel inadvertently entered data in incorrect columns, often in adjacent columns. Some remedies were simply to shift the values one column over.

2) Some variables were found to be missing most of their observations (patients). To ensure a meaningful statistical analysis, variables representing drugs, procedural, and surgical history were grouped based on similarity of function. Other variables such as a patient's characteristics were not grouped. This process is described in section 3.1.3. After grouping, grouped and other variables remaining that had less than 4 observations were eliminated.

3) Some missing values that were known to be missing were entered as specific entries but had differing notations. For example, some missing values were reported with a value of 9999 and others as 6666. The Perl Script identified these values and replaced them with a single standard notation.

4) A duration variable was created which is the difference between two date formatted variables, 'doa' and 'doa2'. These represent the date of arrival of a patient into the interdisciplinary pain management program ('doa') and the departure of the patient from the interdisciplinary pain management program ('doa2'). A Perl Script was made to parse the dates and calculate the duration between 'doa' and 'doa2'.

5) While the variables mentioned above were checked for validity, there are many other variables in the set that likely contain errors. The Center provided a SPSS (Statistical Product and Service Solutions) data file which contains a dictionary that lists accepted values for each variable. This dictionary was used to check against the actual data to find errors. The invalid data entries that were found by this method were handled on a case

by case basis. Some were eliminated and some corrected after consultation with the Center.

*3.1.2 Observation Counts of Drug, Procedural, and Surgical Variables*

The counts of variables representing drugs, procedural, and surgical history are shown in the three tables below. Tables 3.1, 3.2, and 3.3 show the counts at the pre-, mid-, and post-evaluation points, respectively. It is shown that there are many variables with few to zero counts. This gives motivation to group the data.

Table 3.1 Counts at Pre-evaluation Surgical and Treatment Variables

| Variables | Cnts | Variables | Cnts | Variables | Cnts | Variables | Cnts |
|---|---|---|---|---|---|---|---|
| proced1 | 52 | surghx1 | 17 | surghx23 | 0 | dosran1 | 58 |
| proced2 | 65 | surghx2 | 0 | surghx24 | 1 | dosran2 | 134 |
| proced3 | 22 | surghx3 | 0 | surghx25 | 0 | dosran3 | 79 |
| proced4 | 41 | surghx4 | 1 | surghx26 | 0 | dosran4 | 42 |
| proced5 | 13 | surghx5 | 27 | surghx27 | 1 | dosran5 | 94 |
| proced6 | 2 | surghx6 | 5 | surghx28 | 0 | dosran6 | 33 |
| proced7 | 1 | surghx7 | 2 | surghx29 | 2 | dosran7 | 44 |
| proced8 | 5 | surghx8 | 3 | surghx30 | 1 | dosran8 | 6 |
| proced9 | 9 | surghx9 | 3 | surghx31 | 3 | dosran9 | 15 |
| proced10 | 5 | surghx10 | 1 | surghx32 | 1 | dosran10 | 1 |
| proced11 | 60 | surghx11 | 1 | surghx33 | 2 | dosran11 | 51 |
| proced12 | 22 | surghx12 | 0 | surghx34 | 0 | dosran12 | 2 |
| proced13 | 36 | surghx13 | 1 | surghx35 | 1 | dosran13 | 5 |
| proced14 | 52 | surghx14 | 5 | surghx36 | 0 | dosran14 | 1 |
| proced15 | 7 | surghx15 | 10 | surgh37a | 46 | dosran15 | 42 |
| proced16 | 13 | surghx16 | 5 | surgh37b | 32 | dosran16 | 5 |
| proced17 | 10 | surghx17 | 0 | | | dosran17 | 8 |
| proced18 | 27 | surghx18 | 0 | | | dosran18 | 3 |
| proced19 | 122 | surghx19 | 0 | | | dosran19 | 0 |
| proced20 | 33 | surghx20 | 2 | | | dosran20 | 2 |
| proced21 | 1 | surghx21 | 0 | | | dosran21 | 12 |

Table 3.1—*Continued*

| Variables | Cnts | Variables | Cnts | Variables | Cnts | Variables | Cnts |
|---|---|---|---|---|---|---|---|
| proced22 | 47 | surghx22 | 1 | | | | |

Table 3.2 Counts at Mid-evaluation Treatment Variables

| Variables | Cnts | Variables | Cnts |
|---|---|---|---|
| proc2.1 | 16 | dsran2.1 | 45 |
| proc2.2 | 32 | dsran2.2 | 103 |
| proc2.3 | 11 | dsran2.3 | 66 |
| proc2.4 | 16 | dsran2.4 | 38 |
| proc2.5 | 16 | dsran2.5 | 90 |
| proc2.6 | 1 | dsran2.6 | 43 |
| proc2.7 | 0 | dsran2.7 | 43 |
| proc2.8 | 0 | dsran2.8 | 7 |
| proc2.9 | 3 | dsran2.9 | 23 |
| proc2.10 | 3 | dsra2.10 | 0 |
| proc2.11 | 8 | dsra2.11 | 43 |
| proc2.12 | 8 | dsra2.12 | 1 |
| proc2.13 | 1 | dsra2.13 | 0 |
| proc2.14 | 1 | dsra2.14 | 1 |
| proc2.15 | 0 | dsra2.15 | 33 |
| proc2.16 | 0 | dsra2.16 | 0 |
| proc2.17 | 2 | dsra2.17 | 4 |
| proc2.18 | 242 | dsra2.18 | 1 |
| proc2.19 | 228 | dsra2.19 | 1 |
| proc2.20 | 4 | dsra2.20 | 0 |
| proc2.21 | 6 | dsra2.21 | 11 |
| proc2.22 | 28 | | |

Table 3.3 Counts at Post-evaluation Treatment Variables

| Variables | Cnts | Variables | Cnts |
|---|---|---|---|
| proc3.1 | 15 | dsran3.1 | 45 |
| proc3.2 | 26 | dsran3.2 | 89 |

Table 3.3—*Continued*

| Variables | Cnts | Variables | Cnts |
|---|---|---|---|
| proc3.3 | 11 | dsran3.3 | 54 |
| proc3.4 | 12 | dsran3.4 | 28 |
| proc3.5 | 13 | dsran3.5 | 83 |
| proc3.6 | 1 | dsran3.6 | 40 |
| proc3.7 | 0 | dsran3.7 | 33 |
| proc3.8 | 2 | dsran3.8 | 3 |
| proc3.9 | 3 | dsran3.9 | 24 |
| proc3.10 | 1 | dsra3.10 | 0 |
| proc3.11 | 12 | dsra3.11 | 37 |
| proc3.12 | 2 | dsra3.12 | 2 |
| proc3.13 | 1 | dsra3.13 | 3 |
| proc3.14 | 1 | dsra3.14 | 2 |
| proc3.15 | 1 | dsra3.15 | 28 |
| proc3.16 | 0 | dsra3.16 | 5 |
| proc3.17 | 1 | dsra3.17 | 5 |
| proc3.18 | 189 | dsra3.18 | 0 |
| proc3.19 | 173 | dsra3.19 | 0 |
| proc3.20 | 0 | dsra3.20 | 1 |
| proc3.21 | 14 | dsra3.21 | 6 |
| proc3.22 | 20 | | |

### *3.1.3 Grouping Variables*

The grouping process is done according to Lin, 2010. Considering the tables 3.1, 3.2, and 3.3 of variable counts above, there are many values that are zero which indicate that treatments were never administered. A statistical analysis cannot give meaningful results with zero-count treatments. To perform an improved analysis without eliminating treatment outcomes and surgical history, the variables representing surgical history, procedural treatments, and pharmaceutical treatments are placed in groups due to their similarity, which yields non-zero group variables. The grouped variables are

shown in Tables 3.4, 3.5, and 3.6 for surgical history, procedural treatments, and pharmaceutical treatments, respectively.

In Table 3.4, the variables of surgical history are reduced from 36 to 11. An example of a grouping is combining variables surghx15, 16, 17, 18, 19, and 20 into group SGhxGr6 since these variables are all a type of neural decompression.

Table 3.5 shows that the number of variables is reduced from 21 to 8 after grouping. Dsran_3 and 4 is placed into RxGr3 because they are all narcotic. Drsran_6, 7, 8 and 9 are grouped together as RxGr5 since they are all antidepressant. Drsran_10, 11, 12, 13 are all grouped together as RxGr6 since they are different kinds of tranquilizers. Drsran_15, 16, and 17 are in the group of RxGr7 because they are all sleeping pills. Drsran_14, 18, 19, 20, and 21 is placed into the group of others, RxGr8.

Moreover, in Table 3.6, the procedural treatment variables are reduced from 22 to 11 after the grouping. The first group, ProcGr1, has variables of proced_1, 2, 3, 4, and 5 because they are all types of injection. ProcGr2 has proced_6, 7, 8, and 9 because they are all related to pain block. In the fourth group, ProcGr4, procede_11, 12, and 21 is placed together because they are all types of stimulation. In ProcGr7, it has procede_15, 16, and 20 variables because they are auxiliaries. It should be noted here that procede_20 and 21 are not in the number order as grouped.

After the groupings were made, any variables, including the grouped variables, that have counts less than 4 were eliminated.

Table 3.4 Grouping Variables of Surgical History

| Variables | Description | Group | Counts | Total |
|---|---|---|---|---|
| surghx1 | Unspecified discectomy | SGhxGr1 | 17 | 17 |
| surghx2 | Microdiscectomy | | 0 | |
| surghx3 | Percutaneous discectomy | | 0 | |
| surghx4 | Chemonucleolysis | SGhxGr2 | 1 | 1 |

Table 3.4—*Continued*

| Variables | Description | Group | Counts | Total |
|---|---|---|---|---|
| surghx5 | Unspecified fusion | SGhxGr3 | 27 | 40 |
| surghx6 | Anterior fusion | | 5 | |
| surghx7 | Posterior interbody fusion | | 2 | |
| surghx8 | Posterior lateral fusion | | 3 | |
| surghx9 | 360 (anterior/posterior) fusion | | 3 | |
| surghx10 | Pseudoarthrosis repair | SGhxGr4 | 1 | 3 |
| surghx11 | Hardware removal | | 1 | |
| surghx12 | Bone stimulator removal | | 0 | |
| surghx13 | Discectomy + fusion | | 1 | |
| surghx14 | Decompression + fusion | SGhxGr5 | 5 | 5 |
| surghx15 | Neural decompression, spinal (foraminal/central) | SGhxGr6 | 10 | 17 |
| surghx16 | Neural decompression, carpal tunnel | | 5 | |
| surghx17 | Neural decompression, cubital tunnel | | 0 | |
| surghx18 | Neural decompression, thoracic outlet or brachial plexus | | 0 | |
| surghx19 | Neural decompression, sympathectomy | | 0 | |
| surghx20 | Neural decompression, other | | 2 | |
| surghx21 | Fracture-dislocation: closed reduction | SGhxGr7 | 0 | 1 |
| surghx22 | Fracture-dislocation, open reduction | | 1 | |
| surghx23 | Pseudoarthrosis repair (same with surghx10) | SGhxGr8 | 0 | 1 |
| surghx24 | Hardware Removal | | 1 | |
| surghx25 | Amputation | | 0 | |
| surghx26 | Repair nerve laceration | | 0 | |
| surghx27 | Repair tendon tear | SGhxGr9 | 1 | 1 |
| surghx28 | Repair ligament tear | | 0 | |
| surghx29 | DJD: unspecified procedure | SGhxGr10 | 2 | 3 |
| surghx30 | DJD: arthroscopic joint decompression or chondroplasty, unspecified | | 1 | |
| surghx31 | soft tissue procedure, unspecified | | 3 | |
| surghx32 | /DJD: open arthroplasty | | 1 | |
| surghx33 | /joint replacement | SGhxGr11 | 2 | 7 |
| surghx34 | /Joint denervation (ex-facet rhizotomy) | | 0 | |
| surghx35 | /Neurostimulator | | 1 | |
| surghx36 | /Medication Pump | | 0 | |

Table 3.5 Grouping Variables of Pharmaceutical Treatments

| Mid-point | Description | * # of Counts (mid) | Total Counts | Group |
|---|---|---|---|---|
| dsran_1 | Tramadol | 45 | 45 | RxGr1 |
| dsran_2 | *NSAIDs | 103 | 103 | RxGr2 |
| dsran_3 | Schedule III Narcotic | 66 | 98 | RxGr3 Narcotic |
| dsran_4 | Schedule II Narcotic | 38 | | |
| dsran_5 | Muscle Relaxant | 90 | 90 | RxGr4 |
| dsran_6 | Antidepressant-Tricyclic | 43 | 98 | RxGr5 Antidepressant |
| dsran_7 | Antidepressant-SRI | 43 | | |
| dsran_8 | Antidepressant-NE | 7 | | |
| dsran_9 | Antidepressant-Multireceptor | 23 | | |
| dsran_10 | Lithium | 0 | 44 | RxGr6 Tranquilizer |
| dsran_11 | Anticonvulsant | 43 | | |
| dsran_12 | Neuroleptic | 1 | | |
| dsran_13 | 5HT Agonist | 0 | | |
| dsran_15 | Benzodiazepine | 33 | 36 | RxGr7 Sleeping Pills |
| dsran_16 | Non Benzodiazepine Anxiolytic | 0 | | |
| dsran_17 | Non Benzodiazepine Sedative | 4 | | |
| dsran_14 | Topical Cream | 1 | 12 | RxGr8 Others |
| dsran_18 | Beta Blocker | 1 | | |
| dsran_19 | Alpha Adrenergic Agonist | 1 | | |
| dsran_20 | Calcium Channel Blocker | 0 | | |
| dsran_21 | Others | 11 | | |

* NSAIDs (Non-steroidal anti-inflammatory drugs)
* # of Count (mid): Grouping of Prescriptions (counts at midpoint)

Table 3.6 Grouping Variables of Procedural Treatments

| Variables | Description | # of Counts (mid) | Total Counts | Group |
|---|---|---|---|---|
| Proced_1 | Procedures for pain/Trigger Point Injections | 16 | 76 | ProcGr1 Injection |
| proced_2 | Procedures for pain/Lumbar Epidural Steroid Injections | 32 | | |

Table 3.6—*Continued*

| Variables | Description | # of Counts (mid) | Total Counts | Group |
|---|---|---|---|---|
| proced_3 | Procedures for pain/Cervical Epidural Joint Injection | 11 | | |
| proced_4 | Procedures for pain/Facet Joint Injection | 16 | | |
| proced_5 | Procedures for pain/Major Joint Injection | 16 | | |
| proced_6 | Procedures for pain/Stellate Ganglion Block | 1 | 4 | ProcGr2 Block Procedure |
| proced_7 | Procedures for pain/Bier's Block | 0 | | |
| proced_8 | Procedures for pain/Ilroinguinal Nerve Block | 0 | | |
| proced_9 | Procedures for pain/Somatic Nerve Block | 3 | | |
| proced_10 | Procedures for pain/Spinal Cord Implant | 3 | 3 | ProcGr3 |
| proced_11 | Procedures for pain / TENS (Transcutaneous Electrical Nerve Stimulation) | 8 | 21 | ProcGr4 Stimulation Procedure |
| proced_12 | Procedures for pain/Muscle Stimulator | 8 | | |
| proced_21 | PENS (Percutaneous Electrical Nerve Stimulation) | 6 | | |
| proced_13 | Acupuncture | 1 | 1 | ProcGr5 |
| proced_14 | Chiropractic | 1 | 1 | ProcGr6 |
| proced_15 | Splints | 0 | 4 | ProcGr7 Auxiliaries |
| proced_16 | Braces | 0 | | |
| proced_20 | Bedrest | 4 | | |
| proced_17 | Traction | 2 | 2 | ProcGr8 |
| proced_18 | Psychotherapy | 242 | 242 | ProcGr9 |
| proced_19 | Physical Therapy | 228 | 228 | ProcGr10 |
| proced_22 | Number of Additional Procedures | 28 | 28 | ProcGr11 |

*# of Count (mid): Grouping of procedures (counts at midpoint)

*3.1.4 Imputation of Missing Values*

In this research, 10 different variables are imputed. The process for imputation is described by taking the example of the litigation (litigat) variable that has 6 missing values. The steps are as follows.

First, locate every patient that has a missing value for litigat. Of these 6 patients, eliminate every column (variable) that has at least one missing value. Also, eliminate variables that should have no impact on litigat.

Then take the remaining patients that have a litgat value and eliminate those that don't have a value for every column left over from the previous step. A multiple linear regression model is then built with these patients with litigat as the dependent variable and every other variable as an explanatory variable.

Significant variables are identified with a stepwise procedure and the missing values of litigat are imputed. However, if too many values are missing, the imputed value is not meaningful.

## 3.2 Variables in Pain Management

### *3.2.1 Variables for Patient's Background*

A patient's background is recorded when a patient first enters the PM program. These include 33 types of physical histories as shown in Table 3.7, 38 types of patients' surgical histories shown in Table 3.8, 34 types of patients' diagnoses shown in Table 3.9, and 156 types of other variables shown in Table 3.10. These tables include the variable names and descriptions.

Table 3.7 Patients' Physical Histories, 33 Types

| Variables | Description |
|---|---|
| phydx1 | Facial 784.0 |
| phydx2 | TMJ 524.62 |
| phydx3 | Headache 784.0 |
| phydx4 | Cervical723.1 |
| phydx5 | Thoracic724.1 |
| phydx6 | Lumbar724.2 |
| phydx7 | Myofascial-Fibromyalgia 729.1 |
| phydx8 | Abdominal789.0 |
| phydx9 | Pelvic (Female) 625.9 |
| phydx10 | Pelvic (Male) 789.0 |
| phydx11 | Upper Extremity 729.5 |
| phydx12 | Low Extremity 729.5 |

Table 3.7—*Continued*

| Variables | Description |
|---|---|
| phydx13 | Cancer |
| phydx14 | Osteoarthritis716.9 |
| phydx15 | Sacro-illitis 724.6 |
| phydx16 | Reflex Sympathetic Dystrophy, Unspecified 337.20 |
| phydx17 | Reflex Sympathetic Dystrophy, of the Upper Limb 337.21 |
| phydx18 | Reflex Sympathetic Dystrophy, of the Lower Limb 337.22 |
| phydx19 | Reflex Sympathetic Dystrophy, of Other specified Site 337.29 |
| phydx20 | Neuralgia, Neuritis, Unspecified |
| phydx21 | Trigeminal Neuralgia 350.1 |
| phydx22 | Atypical Face Pain 350.2 |
| phydx23 | Phantom Limb Syndrome 353.6 |
| phydx24 | Herpes Zoster with Unspecified Nervous System Complication 053.10 |
| phydx25 | Polyneuropathy in Diabetes 357.2 |
| phydx26 | Physical Dx26/Facet Arthropathy |
| phydx27 | Physical Dx27/Muscle Spasm |
| phydx28 | Physical Dx28/Post Laminectomy Syndrome |
| phydx29 | Physical Dx29/Myalgia, Myositis, Unspecified |
| phydx30 | Physical Dx30/Lumbosacral Spondylosis w/o myelopathy |
| phydx31 | Physical Dx/Cervical Spondylosis W/O Myelopathy (721.0) |
| phydxcd1 | Physical Dx Other1 ICD Code |
| phydxcd2 | Physical Dx Other2 ICD Code |

Table 3.8 Patients' Surgical Histories, 38 Types

| Variables | Description | Variables | Description |
|---|---|---|---|
| surghx1 | Unspecified discectomy | surghx20 | Neural decompression, other |
| surghx2 | Microdiscectomy | surghx21 | Fracture-dislocation: closed reduction |
| surghx3 | Percutaneous discectomy | surghx22 | Fracture-dislocation, open reduction |
| surghx4 | Chemonucleolysis | surghx23 | Pseudoarthrosis repair (same with surghx10) |
| surghx5 | Unspecified fusion | surghx24 | Hardware Removal |
| surghx6 | Anterior fusion | surghx25 | Amputation |
| surghx7 | Posterior interbody fusion | surghx26 | Repair nerve laceration |

Table 3.8—*Continued*

| Variables | Description | Variables | Description |
|---|---|---|---|
| surghx8 | Posterior lateral fusion | surghx27 | Repair tendon tear |
| surghx9 | 360 (anterior/posterior) fusion | surghx28 | Repair ligament tear |
| surghx10 | Pseudoarthrosis repair | surghx29 | DJD: unspecified procedure |
| surghx11 | Hardware removal | surghx30 | DJD: arthroscopic joint decompression or chondroplasty, unspecified |
| surghx12 | Bone stimulator removal | surghx31 | soft tissue procedure, unspecified |
| surghx13 | Discectomy + fusion | surghx32 | DJD: open arthroplasty |
| surghx14 | Decompression + fusion | surghx33 | Joint replacement |
| surghx15 | Neural decompression, spinal (foraminal/central) | surghx34 | Joint denervation (ex-facet rhizotomy) |
| surghx16 | Neural decompression, carpal tunnel | surghx35 | Neurostimulator |
| surghx17 | Neural decompression, cubital tunnel | surghx36 | Medication Pump |
| surghx18 | Neural decompression, thoracic outlet or brachial plexus | surgh37a | # of additional surgeries related to condition |
| surghx19 | Neural decompression, sympathectomy | surgh37b | # of additional surgeries not related to condition |

Table 3.9 Patient's Diagnoses, 34 Types

| Variables | Description |
|---|---|
| Pastdx1 | Facial 784.0 |
| Pastdx2 | TMJ 524.62 |
| Pastdx3 | Headache 784.0 |
| Pastdx4 | Cervical 723.1 |
| Pastdx5 | Thoracic 724.1 |
| Pastdx6 | Lumbar 724.2 |
| Pastdx7 | Myofascial-Fibromyalgia 729.1 |
| Pastdx8 | Abdominal 789.0 |
| Pastdx9 | Pelvic (Female) 625.9 |
| Pastdx10 | Pelvic (Male) 789.0 |
| Pastdx11 | Upper Extremity 729.5 |
| Pastdx12 | Low Extremity 729.5 |
| Pastdx13 | Cancer |
| Pastdx14 | Osteoarthritis 716.9 |

Table 3.9—*Continued*

| Variables | Description |
|---|---|
| Pastdx15 | Sacro-illitis 724.6 |
| Pastdx16 | Reflex SymPathetic Dystrophy, Unspecified 337.20 |
| Pastdx17 | Reflex SymPathetic Dystrophy, of the Upper Limb 337.21 |
| Pastdx18 | Reflex SymPathetic Dystrophy, of the Lower Limb 337.22 |
| Pastdx19 | Reflex SymPathetic Dystrophy, of Other specified Site 337.29 |
| Pastdx20 | Neuralgia, Neuritis, Unspecified |
| Pastdx21 | Trigeminal Neuralgia 350.1 |
| Pastdx22 | Atypical Face Pain 350.2 |
| Pastdx23 | Phantom Limb Syndrome 353.6 |
| Pastdx24 | Herpes Zoster with Unspecified Nervous System Complication 053.10 |
| Pastdx25 | PolyneuroPathy in Diabetes 357.2 |
| pastdx26 | Physical Dx26/Facet Arthropathy |
| pastdx27 | Physical Dx27/Muscle Spasm |
| pastdx28 | Physical Dx28/Post Laminectomy Syndrome |
| pastdx29 | Physical Dx29/Myalgia, Myositis, Unspecified |
| pastdx30 | Physical Dx30/Lumbosacral Spondylosis w/o myelopathy |
| pastdx31 | Physical Dx31Cervical Spondylosis |
| pastdx32 | Past Dx/Number of Additional Diagnoses |
| pastdxcd1 | Physical Dx Other1 ICD Code |
| pastdxcd2 | Physical Dx Other2 ICD Code |

Table 3.10 Other Variables, 156 Types

| Variables | Description | Variables | Description |
|---|---|---|---|
| Duration age | Patient's Age | mpi11 | MPI scale 11 activities away from home |
| gender | Patient's gender | mpi12 | MPI scale 12 social activity |
| race | Race of Patient | mpi13 | MPI scale 13 general activity level |
| insurance | Primary Insurance Type | mpistyle | MPI Coping style |
| disab.$ | Disability Payments? | aerobic | Aerobic Exercise Scale - physical therapy |
| litigat | Pending litigation related to pain? | romscale | ROM scale |
| status | Status of Condition | strength | Strength Scale |

Table 3.10—*Continued*

| Variables | Description | Variables | Description |
|---|---|---|---|
| onset | Time (in months) since the first onset of pain | adlscale | ADL Scale |
| sf36hp | SF36/Health Perception | fear | Fear of Exercise Scale |
| sf36pf | SF-36 Physical functioning | ptsessio | Number of PT Sessions |
| sf36rp | SF-36 Role limitations/physical | ptcout | PT Carve-Out |
| sf36re | SF-36 Role limitations/emotional | ptelse | PT elsewhere |
| sf36sf | SF-36 Social functioning | othtreat | Other treatment modality |
| sf36mh | SF-36 Mental health | psysess | Number of Psychologist Sessions |
| sf36bp | SF-36 Bodily pain | psycout | Psychology Carve-Out |
| sf36ef | SF-36 Energy/fatigue | psyelse | Psychology elsewhere |
| sf36pcs | SF36/Physical Component Scale | groupses | Number of Group Sessions |
| sf36mcs | sf36/Mental Component Scale | psychtry | Physician sessions |
| mmpil | MMPI-2 L Scale  Lie Scale | famgroup | Family Group |
| mmpif | MMPI-2 F Scale | dsmax1a | DSM-IV Axis I diagnosis |
| mmpik | MMPI-2 K Scale K Corrected | dsmax1b | DSM-IV Axis I diagnosis |
| mmpi1 | MMPI-2 Scale 1 Hypochondriasis | dsmaxis2 | DSM-IV Axis II diagnoses |
| mmpi2 | MMPI-2 Scale 2 Depression | vocstat | Vocational Status |
| mmpi3 | MMPI-2 Scale 3 Hysteria | sec.gain | Secondary gain issues |
| mmpi4 | MMPI-2 Scale 4- Psychpathic Deviate | secgain2 | Secondary gain issues |
| mmpi5 | MMPI-2 Scale 5 Masculine Feminine | pschostr | Psychosocial stressors |
| mmpi6 | MMPI-2 Scale 6 Paranoia | visithc | Number of healthcare visits in last 6 months |
| mmpi7 | MMPI-2 Scale 7 Psychastenia | visiter | Number of ER visits in the last 6 months |
| mmpi8 | MMPI-2 Scale 8 Schizophrenia | comments | |
| mmpi9 | MMPI-2 Scale 9 Hypomania | marital | Marital Status of Patient |
| mmpi0 | MMPI-2 Scale 0 Social Introversion | children | Patient's number of children |
| mmpi.es | MMPI-2/Ego Strength | smoker | Smoker |
| mmpi.mac | MMPI-2/MAC-R | pmq1 | PMQ Item #1 |
| mmpi.aps | MMPI-2/APS | pmq2 | PMQ Item #2 |
| mmpi.aas | MMPI-2/AAS | pmq3 | PMQ Item #3 |

Table 3.10—*Continued*

| Variables | Description | Variables | Description |
|---|---|---|---|
| mmpi.dp4 | MMPI-2/DEP4 Suicidal Ideation | pmq4 | PMQ Item #4 |
| csqtotal | CSQ Total Score - Pre | pmq5 | PMQ Item #5 |
| csqcatas | CSQ Catastrophizing - Pre | pmq6 | PMQ Item #6 |
| hamd | HAMILTON-D | pmq7 | PMQ Item #7 |
| mbmdaa | MBMD - Anxiety Tension | pmq8 | PMQ Item #8 |
| mbmdbb | MBMD - Depression | pmq9 | PMQ Item #9 |
| mbmdcc | MBMD - Cognitive Dysfx | pmq10 | PMQ Item #10 |
| mbmddd | MBMD - Emotional Lability | pmq11 | PMQ Item #11 |
| mbmdee | MBMD - Guardedness | pmq12 | PMQ Item #12 |
| mbmd1 | MBMD - Introversive | pmq13 | PMQ Item #13 |
| mbmd2a | MBMD - Inhibited | pmq14 | PMQ Item #14 |
| mbmd2b | MBMD - Dejected | pmq15 | PMQ Item #15 |
| mbmd3 | MBMD - Cooperative | pmq16 | PMQ Item #16 |
| mbmd4 | MBMD - Sociable | pmq17 | PMQ Item #17 |
| mbmd5 | MBMD - Confident | pmq18 | PMQ Item #18 |
| mbmd6a | MBMD - Nonconforming | pmq19 | PMQ Item #19 |
| mbmd6b | MBMD - Forceful | pmq20 | PMQ Item #20 |
| mbmd7 | MBMD - Respectful | pmq21 | PMQ Item #21 |
| mbmd8a | MBMD - Oppositional | pmq22 | PMQ Item #22 |
| mbmd8b | MBMD - Denigrated | pmq23 | PMQ Item #23 |
| mbmda | MBMD - Illness Apprehension | pmq24 | PMQ Item #24 |
| mbmdb | MBMD - Functional Deficits | pmq25 | PMQ Item #25 |
| mbmdc | MBMD - Pain Sensitivity | pmq26 | PMQ Item #26 |
| mbmdd | MBMD - Social Isolation | pmqtot | PMQ Total |
| mbmde | MBMD - Future Pessimism | RiskMed-MIS | At Risk for Medication Misuse |
| mbmdf | MBMD - Spiritual Absence | asah | Acknowledgment of Sub. Abuse Hx |
| mbmdg | MBMD - Interventional Fragility | cage1 | CAGE #1 |
| mbmdh | MBMD - Medication Abuse | cage2 | CAGE #2 |
| mbmdi | MBMD - Information Discomfort | cage3 | CAGE #3 |
| mbmdj | MBMD - Utilization Excess | cage4 | CAGE #4 |
| mbmdk | MBMD - Problematic Compliance | cagetot | Cage Total |

Table 3.10—*Continued*

| Variables | Description | Variables | Description |
|---|---|---|---|
| mbmdl | MBMD - Adjustment Difficulties | hxdrug | Hx Drug Abuse |
| mbmdm | MBMD - Psych Referral | hxalc | Hx Alcohol Abuse |
| mpi1 | MPI Scale 1 Pain severity | opdetox | Hx Opioid Detox |
| mpi2 | MPI Scale 2 Pain interference | rehab | Hx Rehab/Drugs & Alc |
| mpi3 | MPI Scale 3 Life control | finance | Current Financial Strain |
| mpi4 | MPI Scale 4 Affective Distress | hxjail | Hx Jail or Prison |
| mpi5 | MPI Scale 5 Social support | hxsexab | Hx Sexual Abuse |
| mpi6 | MPI Scale 6 Punishing responses | hxphysab | Hx Physical Abuse |
| mpi7 | MPI Scale 7 Solicitous Response | hxsxassa | Hx Adult Sexual Assault |
| mpi8 | MPI scale 8 Distracting responses | hxphassa | Hx Adult Physical Abuse |
| mpi9 | MPI scale 9 household chores | hxemoab | Hx Emotional Abuse |
| mpi10 | MPI scale 10 outdoor work | medrsn | Reason for med-only status |

*3.2.2 Variables for Treatment Options*

Treatment options are prescribed for patients at the pre-evaluation, mid-evaluation and post-evaluation points. At each evaluation point, there are 43 treatment options for pain which are used by the Center, including 21 pharmaceutical treatments and 22 procedurals. The treatment variables are listed in the Tables 3.11 and 3.12 which show the variable names and descriptions.

Table 3.11 Pharmaceutical Treatments, 21 Types

| Variables | Description | Variables | Description |
|---|---|---|---|
| dosran1 | Tramadol | dosran12 | Neuroleptic |
| dosran2 | NSAIDs | dosran13 | 5HT Agonist |
| dosran3 | Schedule III Narcotic | dosran14 | Topical Cream |
| dosran4 | Schedule II Narcotic | dosran15 | Benzodiazepine |
| dosran5 | Muscle Relaxant | dosran16 | Non Benzodiazepine Anxiolytic |
| dosran6 | Antidepressant-Tricyclic | dosran17 | Non Benzodiazepine Sedative |
| dosran7 | Antidepressant-SRI | dosran18 | Beta Blocker |
| dosran8 | Antidepressant-NE | dosran19 | Alpha Adrenergic Agonist |

Table 3.11—*Continued*

| Variables | Description | Variables | Description |
|---|---|---|---|
| dosran9 | Antidepressant-Multireceptor | dosran20 | Calcium Channel Blocker |
| dosran10 | Lithium | dosran21 | Other |
| dosran11 | Anticonvulsant | | |

Table 3.12 Procedural Treatments, 22 Types

| Variables | Description | Variables | Description |
|---|---|---|---|
| proced1 | Trigger Point Injections | proced12 | Muscle Stimulator |
| proced2 | Lumbar Epidural Steroid Injections | proced13 | Acupuncture |
| proced3 | Cervical Epidural Joint Injection | proced14 | Chiropractic |
| proced4 | Facet Joint Injection | proced15 | Splints |
| proced5 | Major Joint Injection | proced16 | Braces |
| proced6 | Stellate Ganglion Block | proced17 | Traction |
| proced7 | Bier's Block | proced18 | Psychotherapy |
| proced8 | Ilroinguinal Nerve Block | proced19 | Physical Therapy |
| proced9 | Somatic Nerve Block | proced20 | Bedrest |
| proced10 | Spinal Cord Implant | proced21 | PENS |
| proced11 | TENS | proced22 | Additional procedures |

*3.2.3 Other Variables Observed Only at Mid-evaluation and Post-evaluation*

Variables that are found only in the mid-evaluation point are shown in Table 3.13. These variables are used as state variables in Stage 1 of the SDP. Variables that are found only in the post-evaluation point are shown in Table 3.14. These variables are used as state variables in Stage 2 of the SDP. However, many of the variables in both the mid- and post-evaluation points had to be eliminated because they had too many missing values that could not be successfully imputed.

Table 3.13 Variables at Mid-evaluation

| Variables | Description | Variables | Description |
|---|---|---|---|
| sf36hp | SF36/Health Perception | mpmq1 | PMQ Question #1 |
| sf36pf | SF-36 Physical functioning | mpmq2 | PMQ Question #2 |

Table 3.13—*Continued*

| Variables | Description | Variables | Description |
|---|---|---|---|
| sf36rp | SF-36 Role limitations/physical | mpmq3 | PMQ Question #3 |
| sf36re | SF-36 Role limitations/emotional | mpmq4 | PMQ Question #4 |
| sf36sf | SF-36 Social functioning | mpmq5 | PMQ Question #5 |
| sf36mh | SF-36 Mental health | mpmq6 | PMQ Question #6 |
| sf36bp | SF-36 Bodily pain | mpmq7 | PMQ Question #7 |
| sf36ef | SF-36 Energy/fatigue | mpmq8 | PMQ Question #8 |
| sf36pcs | SF36/Physical Component Scale | mpmq9 | PMQ Question #9 |
| sf36mcs | sf36/Mental Component Scale | mpmq10 | PMQ Question #10 |
| fsc2 | Functional Status Component | mpmq11 | PMQ Question #11 |
| pc2 | Psychosocial Component | mpmq12 | PMQ Question #12 |
| aerobic2 | Aerobic Exercise Scale - physical therapy | mpmq13 | PMQ Question #13 |
| romscal2 | ROM scale | mpmq14 | PMQ Question #14 |
| strngth2 | Strength Scale | mpmq15 | PMQ Question #15 |
| adlscal2 | ADL Scale | mpmq16 | PMQ Question #16 |
| fear2 | Fear of Exercise Scale | mpmq17 | PMQ Question #17 |
| md2.in | Number of physician sessions within clinic | mpmq18 | PMQ Question #18 |
| md2.out | Number physician visit outside of clinic | mpmq19 | PMQ Question #19 |
| numpsyc2 | number of psychological sessions | mpmq20 | PMQ Question #20 |
| num.grp2 | Number of group sessions | mpmq21 | PMQ Question #1 |
| num.pt2 | Number of physical therapy sessions | mpmq22 | PMQ Question #2 |
| family | Family Group | mpmq23 | PMQ Question #3 |
| comments | Comments | mpmq24 | PMQ Question #4 |
| | (no description) | mpmq25 | PMQ Question #5 |
| | (no description) | mpmq26 | PMQ Question #6 |
| | (no description) | mpmqtot | PMQ Total - MID |

Table 3.14 Variables at Post-evaluation

| Variables | Description | Variables | Description |
|---|---|---|---|
| sf36hp | SF36/Health Perception | numpsy3 | Number of psychological sessions |
| sf36pf | SF-36 Physical functioning | num.pt.3 | Number of PT sessions |
| sf36rp | SF-36 Role limitations/physical | md2.in | Number of physician sessions within clinic |

Table 3.14—*Continued*

| Variables | Description | Variables | Description |
|---|---|---|---|
| sf36re | SF-36 Role limitations/emotional | md2.out | Number physician visit outside of clinic |
| sf36sf | SF-36 Social functioning | num.grp3 | Number of group sessions |
| sf36mc | SF-36 Mental health | grp.post | Group/Post treatment score |
| sf36bp | SF-36 Bodily pain | tx.compl | Completed treatment as prescribed |
| sf36ef | SF-36 Energy/fatigue | dpmq1 | PMQ Question #1 |
| sf36pcs3 | SF36/Physical Component Scale | dpmq2 | PMQ Question #2 |
| sf36mcs3 | sf36/Mental Component Scale | dpmq3 | PMQ Question #3 |
| mpi1.3 | MPI Scale 1 Pain severity | dpmq4 | PMQ Question #4 |
| mpi2.3 | MPI Scale 2 Pain interference | dpmq5 | PMQ Question #5 |
| mpi3.3 | MPI Scale 3 Life control | dpmq6 | PMQ Question #6 |
| mpi4.3 | MPI Scale 4 Affective Distress | dpmq7 | PMQ Question #7 |
| mpi5.3 | MPI Scale 5 Social support | dpmq8 | PMQ Question #8 |
| mpi6.3 | MPI Scale 6 Punishing responses | dpmq9 | PMQ Question #9 |
| mpi7.3 | MPI Scale 7 Solicitous Response | dpmq10 | PMQ Question #10 |
| mpi8.3 | MPI scale 8 Distratcting responses | dpmq11 | PMQ Question #11 |
| mpi9.3 | MPI scale 9 household chores | dpmq12 | PMQ Question #12 |
| mpi10.3 | MPI scale 10 outdoor work | dpmq13 | PMQ Question #13 |
| mpi11.3 | MPI scale 11 activities away from home | dpmq14 | PMQ Question #14 |
| mpi12.3 | MPI scale 12 social activity | dpmq15 | PMQ Question #15 |
| mpi13.3 | MPI scale 13 general activity level | dpmq16 | PMQ Question #16 |
| mpistyl3 | MPI Coping style | dpmq17 | PMQ Question #17 |
| pdq3tot | PDQ total score | dpmq18 | PMQ Question #18 |
| pdq3fsc | PDQ FSC | dpmq19 | PMQ Question #19 |
| pdq3pc | PDQ PC | dpmq20 | PMQ Question #20 |
| aerobic3 | Aerobic Exercise Scale - physical therapy | dpmq21 | PMQ Question #1 |
| romscal3 | ROM scale | dpmq22 | PMQ Question #2 |
| strngth3 | Strength Scale | dpmq23 | PMQ Question #3 |
| adlscal3 | ADL Scale | dpmq24 | PMQ Question #4 |

Table 3.14—*Continued*

| Variables | Description | Variables | Description |
|---|---|---|---|
| fear3 | Fear of Exercise Scale | dpmq25 | PMQ Question #5 |
| vocaton3 | Present vocational status | dpmq26 | PMQ Question #6 |
| secgain3 | Secondary gain issues | dpmqtot | PMQ Total - D/C |
| secgn3.2 | Secondary gain issues | | |

*3.2.4 Time Periods, State Variables, and Decision Variables*

The PM program has two time periods which are Stage 1 and Stage 2. Stage 1 starts at the pre-evaluation point and Stage 2 starts at the mid-evaluation point. State variables are the variables storing a patient's health parameters. This includes a patient's personal information, surgical history (surghx), review of the medical record (pastdx), physical examination (phydx) and 43 prior treatments (treatments at pre-evaluation). A patient's personal information includes gender, age, status of condition, time (in months) since the first onset of pain, marital status, the number of children, and pending litigation related to pain. Decision variables are a patient's treatment options at each stage in which there are 43 decision variables in each stage.

*3.2.5 Final Database Variables*

The final data set was a result of eliminating observations and variables with missing data, grouping similar treatment and surgical history variables, imputing possible values, and creating the duration variable. This yielded 294 observations with 88 variables. The variables consisted of the following groups:

- 56 variables of patients' information,
- 14 treatment variables for the 1st Stage (6 groups of procedure treatments, 8 groups of dosage treatments),
- 13 treatment variables for the 2nd Stage (5 groups of procedure treatments, 8 groups of dosage treatments),
- 2 variables of mid-evaluation, and

- 2 variables of post-evaluation.

Furthermore, we count variables for state, decision, and outcome variables as follow:

- State variables (total = 56):
- Outcomes: preOSW, prePDA =2
- Patient's background = 12
- Physical and Surgical histories = 13 + 5=18
- Past diagnoses = 12
- Treatment variables (e.g. ProcGr1_0, RxGr1_0)= 6+8 =14
- Decision variables (total =27):

  Stage 1 decision variables = 14

  Stage 2 decision variables = 13

- Outcomes (total =4):

  midOSW, midPDA, postOSW, postPDA = 4.

Table 3.15 lists and re-specifies all the variables, descriptions, and values which were used in the models. In the treatment variables, the underscored numbers (i.e. _1) represent the stage of that variable. The stages are illustrated in Figure 1.2.

Table 3.15 Variables in the Final Data Set

| 56 Patients' State Variables | Descriptions | Values |
|---|---|---|
| age | Patient's Age | Continuous |
| children | Children | Continuous |
| onset | Time (in months) since the first onset of pain | Continuous |
| duration | Duration | Continuous |
| status | Status of Condition | {{1: acute (< 3 months), 2:acute (< 6 months), 3:acute (< 9 months)} |
| race | Race of Patient | {1:caucasian, 2: African American, 3: Hispanic, 4: Asian/Pacific, 5:Other} |

Table 3.15—*Continued*

| 56 Patients' State Variables | Descriptions | Values |
|---|---|---|
| litigat | Pending litigation related to pain? | {0:no, 1:yes} |
| gender | Patient's gender | {1:male, 2:female} |
| phydx1 | Physical Dx1/Facial 784.0 | {0:no, 1:yes} |
| phydx3 | Physical Dx3/Headache 784.0 | {0:no, 1:yes} |
| phydx4 | Physical Dx4/Cervical 723.1 | {0:no, 1:yes} |
| phydx5 | Physical Dx5/Thoracic 724.1 | {0:no, 1:yes} |
| phydx6 | Physical Dx6/Lumbar 724.2 | {0:no, 1:yes} |
| phydx7 | Physical Dx7/Myofascial-Fibromyalgia 729.1 | {0:no, 1:yes} |
| phydx8 | Physical Dx8/Abdominal 789.0 | {0:no, 1:yes} |
| phydx11 | Physical Dx11/Upper Extremity 729.5 | {0:no, 1:yes} |
| phydx12 | Physical Dx12/Low Extremity 729.5 | {0:no, 1:yes} |
| phydx14 | Physical Dx14/Osteoarthritis 716.9 | {0:no, 1:yes} |
| phydx15 | Physical Dx15/Sacro-illitis 724.6 | {0:no, 1:yes} |
| phydx20 | Physical Dx20/Neuralgia, Neuritis, Unspecified | {0:no, 1:yes} |
| phydx31 | Physical Dx/Cervical Spondylosis W/O Myelopathy (721.0) | {0:no, 1:yes} |
| ProcGr1_0 | Injection in stage 0 | {0:no, 1:yes} |
| ProcGr2_0 | Block Procedure in stage 0 | {0:no, 1:yes} |
| ProcGr4_0 | Stimulation Procedure in stage 0 | {0:no, 1:yes} |
| ProcGr9_0 | Psychotherapy in stage 0 | {0:no, 1:yes} |
| ProcGr10_0 | Physical Therapy in stage 0 | {0:no, 1:yes} |
| ProcGr11_0 | Number of Additional Procedures in stage 0 | {0:no, 1:yes} |
| pastdx3 | Past Dx3/Headache 784.0 | {0:no, 1:yes} |
| pastdx4 | Past Dx4/Cervical 723.1 | {0:no, 1:yes} |
| pastdx5 | Past Dx5/Thoracic 724.1 | {0:no, 1:yes} |
| pastdx6 | Past Dx6/Lumbar 724.2 | {0:no, 1:yes} |
| pastdx7 | Past Dx7/Myofascial-Fibromyalgia 729.1 | {0:no, 1:yes} |
| pastdx8 | Past Dx8/Abdominal 789.0 | {0:no, 1:yes} |

Table 3.15—*Continued*

| 56 Patients' State Variables | Descriptions | Values |
|---|---|---|
| pastdx11 | Past Dx11/Upper Extremity 729.5 | {0:no, 1:yes} |
| pastdx12 | Past Dx12/Low Extremity 729.5 | {0:no, 1:yes} |
| pastdx14 | Past Dx14/Osteoarthritis 716.9 | {0:no, 1:yes} |
| pastdx15 | Past Dx15/Sacro-illitis 724.6 | {0:no, 1:yes} |
| pastdx20 | Past Dx20/Neuralgia, Neuritis, Unspecified | {0:no, 1:yes} |
| pastdx32 | Past Dx/Number of Additional Diagnoses | {0:no, 1:yes} |
| SghxGr1 | Surgical History/Unspecified discectomy | {0:no, 1:yes} |
| SghxGr3 | Surgical History/Percutaneous discectomy | {0:no, 1:yes} |
| SghxGr5 | Surgical History/Unspecified fusion | {0:no, 1:yes} |
| SghxGr6 | Surgical History/Anterior fusion | {0:no, 1:yes} |
| SghxGr11 | Surgical History/Hardware removal | {0:no, 1:yes} |
| RxGr1_0 | Tramadol in stage 0 | {0:no, 1, 2,3} |
| RxGr2_0 | NSAIDs in stage 0 | {0:no, 1, 2, 3} |
| RxGr3_0 | Narcotic in stage 0 | {0:no, 1, 2, 3} |
| RxGr4_0 | Muscle Relaxant in stage 0 | {0:no, 1, 2, 3} |
| RxGr5_0 | Antidepressant in stage 0 | {0:no, 1, 2, 3} |
| RxGr6_0 | Tranquilizer in stage 0 | {0:no, 1, 2, 3} |
| RxGr7_0 | Sleeping Pills in stage 0 | {0:no, 1, 2,3} |
| RxGr8_0 | Others in stage 0 | {0:no, 1, 2,3} |
| marital_1 | Marital Status of Patient | {0:no, 1:single} |
| marital_2 | Marital Status of Patient | {0:no, 1:married} |
| marital_3 | Marital Status of Patient | {0:no, 1:divorced} |
| marital_4 | Marital Status of Patient | {0:no, 1:widow} |
| 27 Treatment Decision Variables | Descriptions | Values |
| ProcGr1_1 | Injection in stage 1 | {0:no, 1:yes} |
| ProcGr2_1 | Block Procedure in stage 1 | {0:no, 1:yes} |
| ProcGr4_1 | Stimulation Procedure in stage 1 | {0:no, 1:yes} |

Table 3.15—*Continued*

| 56 Patients' State Variables | Descriptions | Values |
|---|---|---|
| ProcGr9_1 | Psychotherapy in stage 1 | {0:no, 1:yes} |
| ProcGr10_1 | Physical Therapy in stage 1 | {0:no, 1:yes} |
| ProcGr11_1 | Number of Additional Procedures in stage 1 | {0:no, 1:yes} |
| RxGr1_1 | Tramadol in stage 1 | {0:no, 1, 2} |
| RxGr2_1 | NSAIDs in stage 1 | {0:no, 1, 2, 3} |
| RxGr3_1 | Narcotic in stage 1 | {0:no, 1, 2, 3} |
| RxGr4_1 | Muscle Relaxant in stage 1 | {0:no, 1, 2, 3} |
| RxGr5_1 | Antidepressant in stage 1 | {0:no, 1, 2, 3} |
| RxGr6_1 | Tranquilizer in stage 1 | {0:no, 1, 2, 3} |
| RxGr7_1 | Sleeping Pills in stage 1 | {0:no, 1, 2} |
| RxGr8_1 | Others in stage 1 | {0:no, 1, 2} |
| ProcGr1_2 | Injection in stage 2 | {0:no, 1:yes} |
| ProcGr2_2 | Block Procedure in stage 2 | {0:no, 1:yes} |
| ProcGr4_2 | Stimulation Procedure in stage 2 | {0:no, 1:yes} |
| ProcGr9_2 | Psychotherapy in stage 2 | {0:no, 1:yes} |
| ProcGr10_2 | Physical Therapy in stage 2 | {0:no, 1:yes} |
| RxGr1_2 | Tramadol in stage 2 | {0:no, 1, 2, 3} |
| RxGr2_2 | NSAIDs in stage 2 | {0:no, 1, 2, 3} |
| RxGr3_2 | Narcotic in stage 2 | {0:no, 1, 2, 3} |
| RxGr4_2 | Muscle Relaxant in stage 2 | {0:no, 1, 2, 3} |
| RxGr5_2 | Antidepressant in stage 2 | {0:no, 1, 2, 3} |
| RxGr6_2 | Tranquilizer in stage 2 | {0:no, 1, 2, 3} |
| RxGr7_2 | Sleeping Pills in stage 2 | {0:no, 1, 2} |
| RxGr8_2 | Others in stage 2 | {0:no, 1, 2, 3} |
| 6 Evaluation variables | Descriptions | Values |
| pre_PDA | Pain Drawing Analogue at pre-evaluation point | Continuous |
| pre_OSW | Oswestry at pre-evaluation point | Continuous |
| mid_PDA | Pain Drawing Analogue at mid-evaluation point | Continuous |
| mid_OSW | Oswestry at mid-evaluation point | Continuous |

Table 3.15—*Continued*

| 56 Patients' State Variables | Descriptions | Values |
|---|---|---|
| post_PDA | Pain Drawing Analogue at post-evaluation point | Continuous |
| post_OSW | Oswestry at post-evaluation point | Continuous |

## 3.3 Outcome Measurements

There are many different outcomes possible including depression, pain, health status, behavior, etc. To measure these, the Center used 23 different outcome measures which were provided in the raw data set. However, many outcome variables have missing and invalid values. To make an effective analysis, this research utilizes the OSW (Oswestry), and PDA (Pain Drawing Analogue) measures which have a small number of missing or invalid values.

OSW (Oswestry Disability Questionnaire; Fairbank, Couper, Davies, & O'Brien, 1980) is used to measure perceived functional disabilities caused by pain. Each question is rated from 0 to 5, and total score of 50 is attainable. Pain intensity, personal care, lifting, sitting, standing, walking, traveling, social activities, sleeping, and degree of improvement are asked to patients. Then let patients to self-rate the degree of functioning impairment on 10 item scale. Cut-off scores are 0-10 minimal disability; 11-20 moderate disability; 20-30 severe disability; 30-40 is categorized as "crippled"; and scores in the 40-50 range are classified as "bed-bound or exaggeration of symptoms".

PDA (Pain Drawing Analogue, Anagnostis, Mayer, Gatchel, & Proctor 2003). The PDA is a 10-cm visual analog scale for patients to mark the location of their pain. It consists of one question on a single scale ranked from 0 to 10, with 0 represents no pain and 10 represents the highest degree of pain. The PDA has demonstrated good psychometric properties (Gatchel, Mayer, Capra, Diamond, & Barnett 1986).

Outcome measures were recorded three times at the pre-, mid-, and post-evaluation points. These are labeled as 'pre', 'mid', and 'post'. For example, if there is an outcome variable called Pre_PDA, it represents the outcome measure of Pain Drawing Analogue Questionnaire at the pre-evaluation point. Therefore, at the pre-evaluation point, the variables of outcome measures that are used for this research are Pre_PDA, and Pre_OSW; at the mid-evaluation point, the variables of outcome measures used are Mid_PDA, and Mid_OSW; at the post-evaluation point, the variables of outcome measures are Post_PDA, and Post_OSW.

### 3.4 Data Issues

In this research, observations need to fully populate all the variables to be useful. Of the original data set, after the data preparation process and grouping, there are a total of 227 observations that have no missing or invalid data. To preserve more observations, a regression approach was conducted to impute missing values when possible. A total of 67 observations were preserved by imputation thus bringing the total of useful observations without missing or invalid data to 294.

Since there are many treatment option variables with missing or invalid values and there are similarities in the types of treatment options, treatment variables were grouped. For these treatment options, two main groups were created which are pharmaceutical and procedural treatments. As shown in section 3.1, the 21 pharmaceutical treatments were combined into 8 categories (Tramadol, NSAIDs, narcotic, muscle relaxant, antidepressant, tranquilizer, sleeping pills, and others), and the 22 procedural treatments were combined into 11 categories (injection procedures, block procedures, spinal cord implant, stimulation procedures, acupuncture, chiropractic, auxiliaries, traction, psychotherapy, physical therapy, and number of additional procedures). Although 11 procedural treatment categories were created, some were

eliminated due to an insufficient count, less than 4 observations in a category. Also, some procedural treatment categories were eliminated since the Center discontinued use of them. Subsequently, only 5 procedural treatment categories (injection procedures, block procedures, stimulation procedures, acupuncture, and number of additional procedures) were kept.

The data set also contains a mix of categorical and numerical variables, where the categorical variables are primarily binary (e.g., Procedure = 1 if applied, and 0 if not), although some have more categories (e.g. pain type, pain status).

### 3.5 State Transition Modeling

In general, Figure 3.1 illustrates how this research formulates outcome and state transition models from Stage 1 to 2 in pain management (Appendix A). At Stage 1, two previous outcome measures (PreOSW and PrePDA), patients' background, surgical and physical histories, past diagnosis and other information are designated as Stage 1 state variables. Decision variables at Stage 1 are the pharmaceutical and procedural treatments. A stepwise regression model is performed on the Stage 1 state and decision variables to predict the outcome measures. The predicted outcome measures at this stage are MidOSW and MidPDA.

All Stage 1 state and decision variables and outcome measures are used as Stage 2 state variables. Stage 2 state variables also include mid-evaluation variables. Decision variables at Stage 2 are the treatments given during Stage 2 which are the pharmaceutical and procedural treatments. Again, a stepwise regression model is conducted on the Stage 2 state and decision variables to predict the outcome measures which are PostOSW and PostPDA.

In this research, due to endogeneity, the IPTW method needs to be applied on the data set. This is detailed in the Chapter 4.

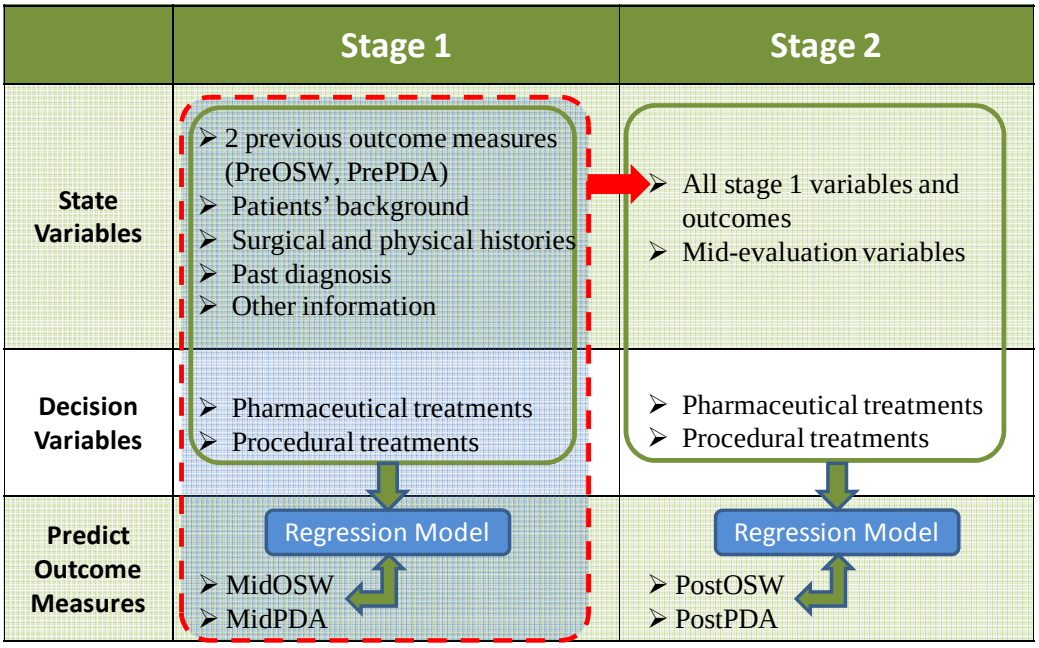



Figure 3.1 Outcome and State Transition Modeling from Stage 1 to 2

### 3.6 Training and Test Data Sets

After cleaning the larger data set, which contained 294 subjects, it was split into training and test data sets by using the *k*-means clustering data mining technique (MacQueen 1967) (Appendix A). The results of *k*=2 clustering (2 clustered groups) is shown in Figure 3.2 below. The larger cluster (group 1) was identified to contain the more common patient characteristics, while the smaller cluster (group 2) was identified to contain the rarer patient characteristics. Given this, it was decided that the training data set needed to maintain all cases in group 2, so as to incorporate all the less represented cases. Data for the test data set was sampled only from group 1. To set up training and test data sets, the 80/20% rule was applied. For the test data set, 59 subjects were randomly taken from the group 1 database and reserved for testing. The training data set then consisted of the remaining 235 subjects. The training and test data sets are used in Chapter 5.

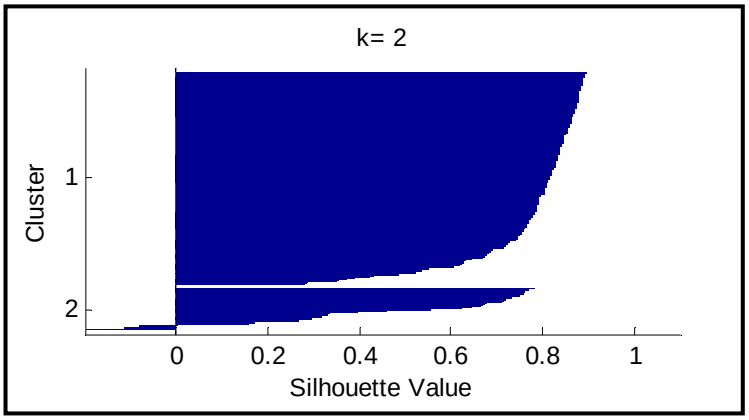



Figure 3.2 *K*-means Clustering for Larger Data Set

# Chapter 4

## Inverse Probability of Treatment Weighted Method with Independent Treatments

A special obstacle in dealing with pain management data in adaptive treatment regimes lies in the complex relationships between time-dependent treatments and related variables, such as patient characteristics. In the adaptive treatment scenario, patient variables at one stage are influenced by treatments at the previous stage, and themselves will influence the treatments at the following stage. Such mutual interactions will lead to bias in estimating the true effect of treatments on the outcomes. This problem is commonly referred to as endogeneity or time-dependent confounding in the literature, which is a main concern in data analysis in adaptive treatment studies (Robins 1999, Little et al. 2000, and Moodie et al. 2009).

The IPTW method estimates the treatment effect by performing a weighted analysis in which each subject is assigned a weight equal to the inverse of the conditional probability of receiving his or her own treatment (Robins 1999). Intuitively, the weighting is equivalent to adding some additional “copies” of this subject to the studied population, so that the bias due to the endogeneity will be eliminated.

To develop adaptive treatment strategies for interdisciplinary pain management, the DACE-based SDP method (Chen et al. 1999) will employ actual patient data from the Center to construct outcome and state transition models. A consequence of using actual data is the presence of correlations leading to a form of endogeneity that biases the estimators of the statistical model coefficients. The IPTW method discussed in this chapter addresses endogeneity with independent treatments. The general method for correlated treatments will be discussed in Chapter 5.

## 4.1 Endogeneity in Adaptive Treatment Strategies

The first attempt at developing a method for adaptive treatment strategies was made by Murphy (2003) and followed up by Robins (2004). The method developed uses a reinforcement learning approximate dynamic programming approach (Werbos 1992) and focused on sequential randomized clinical trials, which yield ideal data for optimizing adaptive treatment strategies (Murphy et al. 2007, Collins et al. 2007, and Pineau et al. 2007). By contrast, clinical data, like the Center's pain management data, are observational in sequential treatment, which are not ideal. Observational data in sequential treatment suffer from unmeasured confounding bias (Little et al. 2000, Moodie et al. 2009, and Robins et al).

### *4.1.1 Problem Caused by Endogeneity in Parameter Estimation*

In the presence of endogeneity, the estimation of the treatment effect will be biased. More specifically, the main concern in epidemiology studies is the causal effect of the treatment on an outcome of interest. Here a causal effect means a direct effect from the treatment to the outcome, not from any other variable, or through any other variable. Correspondingly, the bias caused by endogeneity is with respect to the true causal effect. In other words, with endogeneity, we cannot obtain an unbiased estimate of the causal effect of treatment on the outcome.

This does not mean that the estimate of the treatment effect in a hypothesized model is biased. For example, in the following model (equation 4.1):

$$\begin{aligned} y &= \gamma_1 + \gamma_2 \cdot cum\left(\bar{A}_t\right) + \gamma_3 \cdot \bar{L}_t + \varepsilon \\ cum\left(\bar{A}_t\right) &= \sum_{t=1}^{T} A_t \end{aligned} \quad , \tag{4.1}$$

where $cum\left(\bar{A}_t\right)$ is the subject's cumulative treatment, the estimate of $\gamma_2$ using conventional methods, e.g., least squares estimation, will be unbiased for this model, but

biased as the causal effect of treatment. This is because the correlation of treatment and patient variables is very complex; in the time-dependent setting, patient variables at one stage will affect the following treatments and themselves are affected by the previous treatments. In this case, not only does $\gamma_2$ not represent the causal effect of treatment, but it generally does not have a causal interpretation (Robins 1999, and Robins et al. 2000). The essential purpose of statistical modeling in epidemiology research is identifying the causal effect of treatment on outcomes, so methods for this need to be developed.

*4.1.2 A Causal Diagram for Pain Management*

In the Pain Management causal diagram in Figure 4.1, $L_2$ is affected by treatment $A_1$ (intermediate), but it also confounds the treatment effect of $A_2$ on $Y$. In other words, patient variables at one stage are influenced by treatments at the previous stage, and these patient variables will influence the treatments in the following stage. In a repeated measures setting, the issue of what variables to include when estimating the effects of actions is complicated by endogeneity, that is, when variables are both intermediate and confounding (Robins et al. 2004).

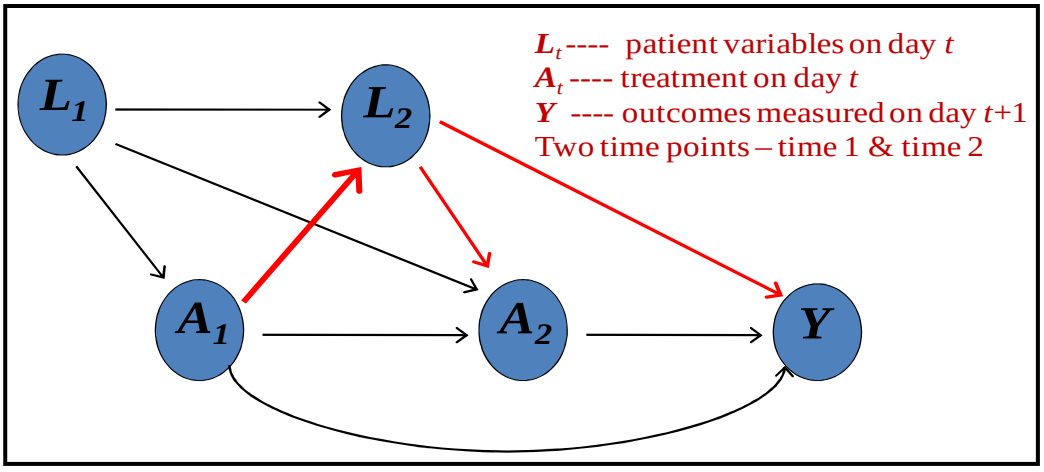



Figure 4.1 Pain Management Causal Diagram

*4.1.3 Approaches to Adjusting for Confounding Variables (Selection Bias)*

One main focus in research fields, such as epidemiology, economics, clinical medicine and public health, is to identify the causal effect of treatment on outcomes. However, in general, there are always confounding variables (e.g., patient variables), the effect of which needs to be adjusted to obtain an unbiased or consistent estimate of the causal effect of treatment. This problem is also commonly referred to as 'adjusting for treatment selection bias,' which is a key limitation of observational studies compared to randomized trials.

## 4.2 IPTW Estimators

A challenge in building stage-wise transition models lies in the complex relationship between the time-dependent state variables and treatment, which causes endogeneity. Accurate estimation of the treatment effect is very critical to the identification of treatments that have a causal effect on outcomes. The endogeneity problem is very challenging for which the conventional methods for confounder adjustment, such as stratification, matching and propensity score methods (Weitzen et al. 2004), will not work for pain management data. These methods focus on a single treatment of a binary value and are too primitive to treat adaptive interdisciplinary pain management data which is complicated. A standard approach to this problem is the instrumental variable methods (Hogan et al. 2004) which can obtain unbiased estimation by making use of some instruments, i.e., variables that are correlated with the treatment variables but not with the state variables to be predicted. However, the reliance on the availability of instruments limits the use of these methods. Recently, a class of methods known as IPTW estimators has been developed and gained popularity in epidemiology research for its ease of use and good properties (Robins 2000). Basically, the IPTW method estimates the effect of treatments in the transition model through a weighted

regression in which the observation of each subject is assigned a weight, $w_t$, as shown in equation 4.2 below (Robins 1999):

$$w_t = \prod_{k=1}^{t} \frac{1}{P\left(U_k = u_k \mid X_k = x_k\right)} \ , \tag{4.2}$$

$u_k$ is the treatment that the patient received on day $k$, and $x_k$ is the associated observations of state variables. $w_t$ can be informally viewed as the inverse of a subject's probability of having his or her observed treatment history, which gives its name, "IPTW." Intuitively, the weighting is equivalent to adding $w_t - 1$ "copies" of this subject to the studied population so that the bias due to patient characteristics will be eliminated. It has been shown that the weighted regression models will provide unbiased estimates of the true effect of treatment (Robins 1999).

*4.2.1 Issues in Implementing the IPTW Method*

The key in implementing the IPTW method is calculating the weight (equation 4.2), which boils down to calculating the conditional probability $P\left(U_k = u_k \mid X_k = x_k\right)$ for each stage $k$, $k = 1,...,T$. For this purpose, we need to first establish the corresponding treatment model,

$$U_k = g\left(X_k\right) \tag{4.3}$$

and then obtain the conditional probability based on the model. There are several issues that need to be addressed in adapting the IPTW method in our research as follows.

(i) High dimensionality of data:

The data set involved in this study has a high dimension, including various types of information such as patient background information, medical history, intermediate outcomes and history of treatments, etc. Efficient dimension

reduction methods need to be developed to remove irrelevant and insignificant variables. This can be realized either by using data mining algorithms or by using some grouping techniques (Savu et al. 2010) to compress variables into a smaller number of strata.

(ii) Different types of treatments:

Unlike existing studies where binary treatments (e.g., receiving a treatment or not), are popular, this study analyzes binary treatments and more complex types of treatments such as polychotomous treatments (e.g., multiple options of medicine), and multinomial treatments (e.g., doses of a certain drug applied to a subject) (Appendix B). Correspondingly, binomial and multinomial logistic regression models (Hosmer et al. 2000) and linear regression models can be incorporated into the IPTW method to handle these types of treatments.

(iii) Multiple treatments:

Multiple treatment options typically exist in an adaptive treatment program, and to apply the IPTW method in the presence of multiple treatments, the dependency of these treatments need to be identified (Appendix A). This can be obtained from expert knowledge or inferred from data.

## 4.3 Case Study

The data used in this case study was collected from August 1998 to May 2001, involving 89 patients (Robbins et al. 2003). To identify treatments and test true relationships among the treatments, a stepwise selection model was built (Lin 2010) and utilized. It was found that treatments in this model are independent of each other. The data has high dimensionality, different types of treatments, and multiple treatments thus

existing IPTW methods do not work. So, by necessity, we developed a modified IPTW method which is the IPTW Method with Independent Treatments.

*4.3.1 Implementing the IPTW Method with Independent Treatments*

When all treatments are independent of each other, the IPTW Method with Independent Treatments is implemented by following the steps given in Table 4.1 below.

Table 4.1 IPTW Method with Independent Treatments Procedure

| | |
|---|---|
| Step 1 | A model is built to identify the treatments. |
| Step 2 | The conditional independence is checked of the selected treatments from step 1. |
| Step 3 | If the treatments are independent of each other, a binomial or multinomial logistic model is fit for each treatment. |
| Step 4 | Weights are calculated (equation 4.3) based on the fitted models from step 3. |
| Step 5 | The weighted models are fit. |

To illustrate this IPTW method, a case study is illustrated using the smaller data set from the Center (Robbins et al. 2003). One important outcome metric is the Oswestry Pain Disability Questionnaire (OSW) score, which measures perceived functional disabilities caused by pain. For step 1, we built the outcome model on OSW at the post-evaluation point (PostOSW) as shown below:

$$\begin{aligned}\text{PostOSW} &= 1.3071 + 0.9071 \times \text{MidOSW} - 0.2140 \times \text{ProcGr9}_2 * \text{MidOSW} \\ &\quad + 3.0273 \times \text{ProcGr9}_2 * \text{Marital} + 0.5925 \times \text{RxGr2}_1 * \text{NumGr1} \\ &\quad - 2.2229 \times \text{RxGr3}_2 * \text{SghxGr1} - 0.1302 \times \text{RxGr4}_2 * \text{PreOSW} \\ &\quad + 2.9948 \times \text{ProcGr4}_1 * \text{Sghxot2}.\end{aligned} \tag{4.4}$$

The variables selected in the PostOSW model are as follows.

- MidOSW is OSW at the mid-evaluation point,
- $\text{ProcGr9}_2$ is psychotherapy in stage 2,

- Marital is the marital status of patient,
- $RxGr2_1$ is the block procedure group in stage 1,
- NumGr1 is the number of group sessions,
- $RxGr3_2$ is the narcotic group in stage 2,
- SghxGr1 is the surgical history/unspecified discectomy,
- $RxGr4_2$ is the muscle relaxant in stage 2,
- PreOSW is OSW at the pre-evaluation point,
- $ProcGr4_1$ is the stimulation procedure in stage 1, and
- Sghxot2 is the number of additional surgeries not related to the condition.

In this model, three treatments are identified: $ProcGr9_2$, $RxGr3_2$, and $RxGr4_2$. The rest of the variables in the PostOSW model are confounding variables.

For step 2, to check for the conditional independence of the treatments, we first built logistic models for each treatment. In this case study, 3 treatments were identified and 3 models were built for each treatment as shown below.

Models of $RxGr3_2$:

M1: $RxGr3_2$ ~ {$RxGr4_2$, Confounding variables}

M2:$RxGr3_2$ ~ {$ProcGr9_2$, Confounding variables}

M3:$RxGr3_2$ ~ {$RxGr4_2$, $ProcGr9_2$, Confounding variables}

Models of $RxGr4_2$:

M4:$RxGr4_2$ ~ {Confounding variable, $RxGr3_2$}

M5:$RxGr4_2$ ~ {Confounding variable, $ProcGr9_2$}

M6:$RxGr4_2$ ~ {Confounding variable, $RxGr3_2$, $ProcGr9_2$}

Models of $ProcGr9_2$:

M7:$ProcGr9_2$ ~ {Confounding variable, $RxGr3_2$}

M8:ProcGr9$_2$ ~ {Confounding variable, RxGr4$_2$}

M9:ProcGr9$_2$ ~ {Confounding variable, RxGr3$_2$, RxGr4$_2$}

The *p*-values of terms involving treatments in the above treatment models are listed in Table 4.2. As seen in Table 4.2, all the *p*-values are insignificant (*p*-value>>0.05), meaning that the three treatments are independent of each other. Hence, the independence assumption is empirically validated.

Table 4.2 *P*-values of Treatments in the Single-treatment Models

| | **M1** | **M2** | **M3** | **M4** | **M5** | **M6** | **M7** | **M8** | **M9** |
|---|---|---|---|---|---|---|---|---|---|
| **RxGr3$_2$** | NA | NA | NA | 0.5655 | NA | 0.5710 | 0.9817 | NA | 0.9537 |
| **RxGr4$_2$** | 0.3743 | NA | 0.3859 | NA | NA | NA | NA | 0.2630 | 0.1744 |
| **ProcGr9$_2$** | NA | 0.7475 | 0.8510 | NA | 0.9773 | 0.6763 | NA | NA | NA |

In step 3, we fitted logistic regression models given confounding variables for each treatment. The models for each of the three treatments are shown below.

MI: RxGr3$_2$ ~ {Confounding variables}

MII:RxGr4$_2$ ~ {Confounding variable}

MIII:ProcGr9$_2$ ~ {Confounding variable}

For step 4, we calculated weights based on the fitted logistic models. The weights in the IPTW Method with Independent Treatments can be calculated as follows:

$$
\begin{aligned}
&\text{Joint Weight} \\
&= \frac{1}{P(\text{RxGr3}_2, \text{RxGr4}_2, \text{ProcGr9}_2 \mid \text{Confounding variables})} \\
&= \frac{1}{P(\text{RxGr3}_2 \mid \text{Confounding variables})} \\
&\times \frac{1}{P(\text{RxGr4}_2 \mid \text{Confounding variables})} \\
&\times \frac{1}{P(\text{ProcGr9}_2 \mid \text{Confounding variables})} \\
&= \text{Weight}(\text{RxGr3}_2) \times \text{Weight}(\text{RxGr4}_2) \times \text{Weight}(\text{ProcGr9}_2).
\end{aligned}
\tag{4.4}
$$

Equation 4.4 states that the joint weight is the product of the marginal weights of the three treatments based on models built in step 3. The calculated joint weights are shown in Figure 4.2.

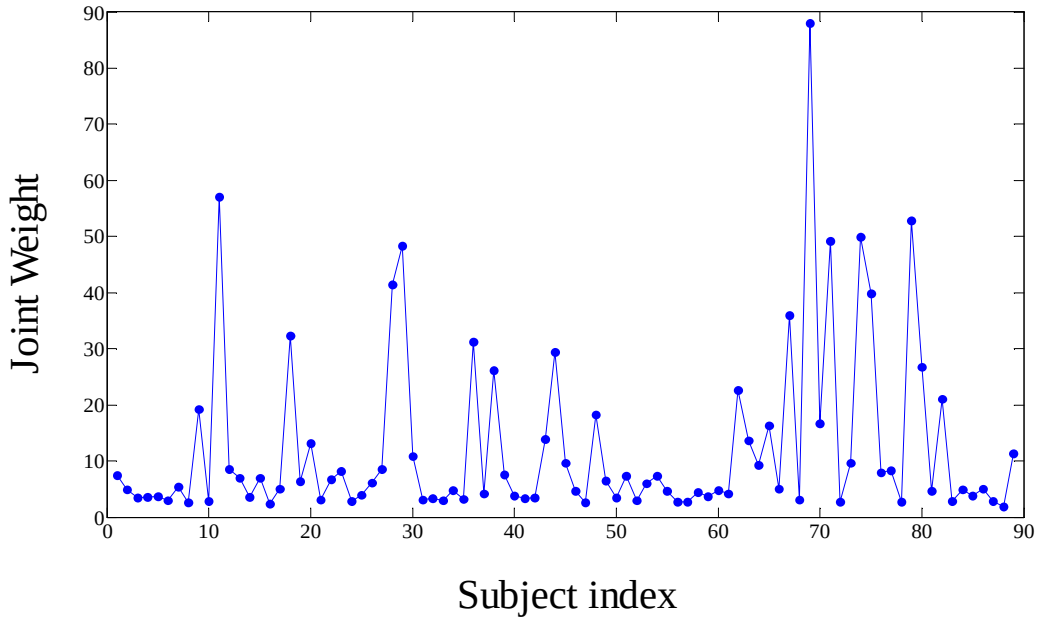



Figure 4.2 Weights Obtained Using IPTW Method

From Figure 4.2, subject #69 has the highest joint weight, approximately 90, among the 89 subjects. This means that subject #69 is the most underrepresented in

relative treatment assignments. Therefore, subject #69 should be given the proportionally highest weight.

In step 5, we fitted the weighted outcome model. The estimated model using the IPTW Method with Independent Treatments is given in equation 4.5 as

$$\begin{aligned}\text{Weighted\_PostOSW} &= 1.5673 + 0.8027 \times \text{MidOSW} - 0.1323 \times \text{ProcGr9}_2 * \text{MidOSW} \\ &\quad + 0.9725 \times \text{ProcGr9}_2 * \text{Marital} + 0.1082 \times \text{RxGr2}_1 * \text{NumGr1} \\ &\quad + 1.2335 \times \text{RxGr3}_2 * \text{SghxGr1} - 0.0084 \times \text{RxGr4}_2 * \text{PreOSW} \\ &\quad + 2.4876 \times \text{ProcGr4}_1 * \text{Sghxot2}.\end{aligned} \tag{4.5}$$

The estimated model without using the IPTW Method with Independent Treatments (unweighted model) is

$$\begin{aligned}\text{Unweighted\_PostOSW} &= 1.3071 + 0.9071 \times \text{MidOSW} - 0.2140 \times \text{ProcGr9}_2 * \text{MidOSW} \\ &\quad + 3.0273 \times \text{ProcGr9}_2 * \text{Marital} + 0.5925 \times \text{RxGr2}_1 * \text{NumGr1} \\ &\quad - 2.2229 \times \text{RxGr3}_2 * \text{SghxGr1} - 0.1302 \times \text{RxGr4}_2 * \text{PreOSW} \\ &\quad + 2.9948 \times \text{ProcGr4}_1 * \text{Sghxot2}.\end{aligned} \tag{4.6}$$

We can see that most coefficients are smaller for the weighted model using the IPTW Method with Independent Treatments (equation 4.5) than for the unweighted model coefficients (equation 4.6). This is expected since the effect of the confounding variables has been adjusted by the IPTW Method with Independent Treatments to compensate for the endogeneity.

# Chapter 5

## Inverse Probability of Treatment Weighted Method with Correlated Treatments

In the methodology for Inverse Probability Weighted Method with Independent Treatments in Chapter 4, a stepwise selection model (unweighted model) was built which identified three treatments that were independent of each other. When the larger data set became available, 10 treatments were identified by the stepwise selection model and most of these treatments were not independent of each other. The IPTW method developed in Chapter 4 works only for independent treatments. Thus, a more generalized methodology is discussed and developed in this chapter.

### 5.1 Estimation of Joint Probability

When treatments are correlated, we need to find the joint weight to apply the IPTW method (Appendix B). As shown in Chapter 4, the joint weight is the inverse of the joint probability of the treatments. To obtain the joint probability, we first decompose the joint distribution of the 10 treatments by the Chain Rule of Probability. The Chain Rule of Probability works regardless of the true relationships among variables. In our case, some treatments are independent of other treatments, while some are correlated with other treatments given the confounding variables. If the treatments are ordered in a certain way, by the Chain Rule of Probability, their joint distribution can be factorized into the product of the marginal distribution of each treatment given all prior treatments. Since each ordering of the treatments produces one factorization, there are many possible factorizations, which are equivalent. When the true dependent relationships among the treatments are known, the factorization can be simplified by incorporating their relationships. Figure 5.1 shows an example of three treatments.

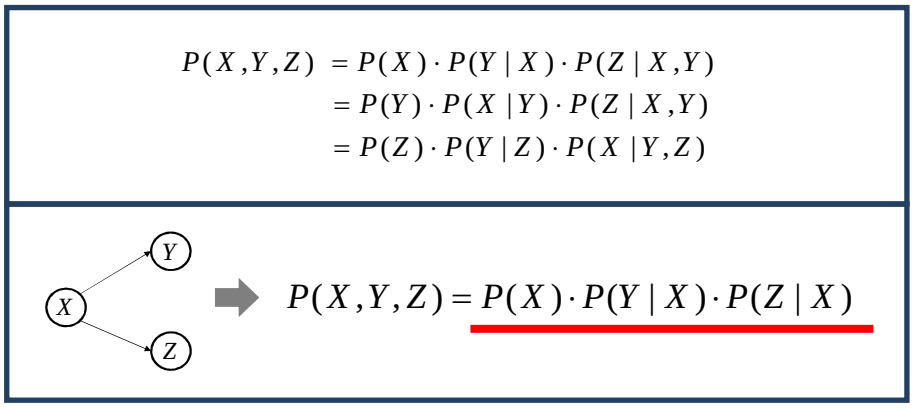



Figure 5.1 Example of Factorization by Chain Rule of Probability

The marginal model will be built for each treatment using logistic regression to find the marginal probability. Then the joint probability of the treatments will be obtained by multiplying the marginal probabilities, and the joint weight will be obtained as the inverse of joint probability.

One critical issue in applying the above method is that true relationships of treatments are typically unknown in practice which requires determination of which factorization to choose. Since the same model (i.e., logistic regression model) is used for the marginal distribution of each treatment, the estimation errors of different factorizations are different. Figure 5.2 illustrates this using a simple example. Assume variable $Y$ and $Z$ are dependent on variable $X$ through a logistic model, and a factorization as given in the figure is considered. To find the marginal distribution for $Z$, we can simply use a Binomial distribution. To find the marginal distribution of $Y$ given $Z$, we will build a logistic model for them. However, this logistic model may not be able to approximate the dependency of $Y$ on $Z$ very well since their true relationship does not follow a logistic model. As a result, errors may be present in estimating the marginal distribution of $Y$. The same thing happens in estimating the marginal distribution of $X$ given $Y$ and $Z$. As

the logistic model performs differently in approximating the marginal distributions, different factorizations will lead to different estimation errors.

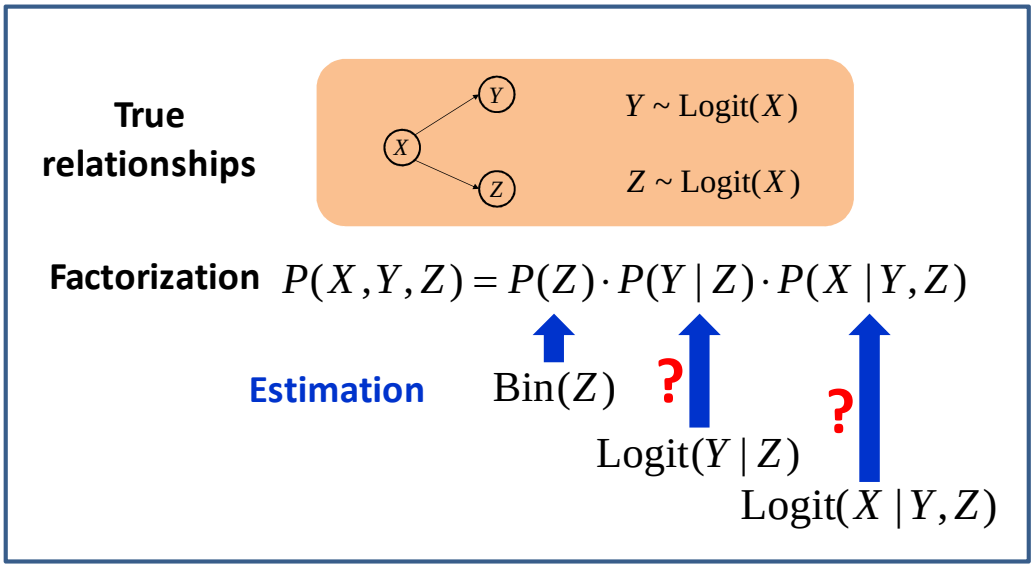



Figure 5.2 True Relationships and Factorization

Ideally, if a flexible modeling method is adopted in estimating the marginal distributions which can approximate each marginal distribution accurately, the estimation error of the factorizations will be very small and thus we can pick any of them. Unfortunately, no such modeling method is available for discrete response data such as the treatments. For discrete data, logistic model is the most popular method. Moreover, it is difficult to evaluate the overall estimation error since the joint distribution is a product of the marginal distributions. A practical solution to this problem is proposed which will be described in the following subsection.

## 5.2 Proposed Procedure to Find the Joint Weight

Given the 10 treatments and confounding variables as shown in Figure 5.3, the proposed procedure to find the joint weight determines the factorization through random sampling. Specifically, a number of factorizations will be generated by randomly ordering

the treatments, and the joint weight will be calculated under each factorization. The average of these joint weights will be used in weighting the observations following the standard IPTW procedure. This process will be repeated several times to study the robustness of this method. Detailed steps in the proposed procedure are given as follows:

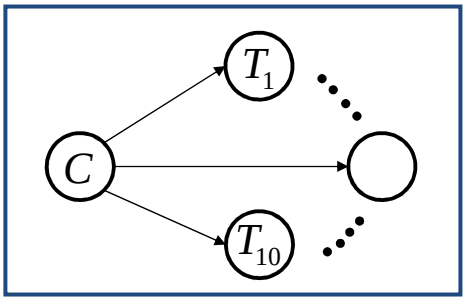



Figure 5.3 Treatments and Confounding Variables

Step 1: Randomly generate m factorizations and calculate the joint probability under each factorization as seen in equation 5.1 below. The average of the joint probabilities is then calculated. Theoretically, a larger m will lead to better estimation. On the other hand, however, it will also cause heavier computational load. In our case study, m = 5, 10, and 20 factorizations are used.

$$\begin{array}{ll} \text{Factorization 1} & \hat{P}_1(T_1,\ldots,T_{10}\mid C) \\ \vdots & \\ \text{Factorization } m & \hat{P}_m(T_1,\ldots,T_{10}\mid C) \end{array} \quad \Rightarrow \quad \hat{P} = \text{avg}(\hat{P}_1,\ldots,\hat{P}_m) \tag{5.1}$$

Step 2: For robustness analysis, Step 1 is repeated several times and the resulting joint probability estimates are compared. The method is robust if the estimates yield small differences.

## 5.3 Case Study

The data used in this study was collected from January 1998 to June 2007, involving 294 patients. The stepwise selection model (unweighted model) is applied to this larger data set which is shown below.

Post_OSW = -3.1699 + 0.9419 x mid_OSW + 2.9933 x ProcGr2_1*pastdx6 - 1.9215 x ProcGr4_1*children - 2.4593 x ProcGr9_1*race + 1.2875 x ProcGr9_1*phydx3 - 0.4958 x ProcGr9_1*marital_2 + 1.8700 x ProcGr10_1*gender + 0.6163 x ProcGr10_1*phydx6 - 0.8769 x ProcGr10_1*ProcGr10_0 + 1.0388 x ProcGr10_1*RxGr2_0 - 0.9674 x ProcGr11_1*pastdx7 + 2.7868 x RxGr1_1* duration + 2.6157 x RxGr1_1*SghxGr11 - 1.2711 x RxGr1_1*RxGr5_0 - 1.8046 x RxGr5_1*phydx11 + 1.6941 x RxGr6_1*pastdx4 - 1.3507 x RxGr6_1*RxGr7_0 - 1.6139 x RxGr7_1*phydx20 + 2.2726 x ProcGr4_2* mid_OSW - 1.8508 x ProcGr4_2*phydx8 - 2.1195 x ProcGr9_2*litigat + 1.6109 x ProcGr9_2*phydx4 + 1.7625 x ProcGr9_2*phydx31 - 1.5958 x ProcGr10_2*ProcGr2_0 + 1.3549 x ProcGr10_2*RxGr4_0 -2.5705 x RxGr1_2*pastdx14 - 1.4778 x RxGr2_2*pastdx6 + 1.4895 x RxGr2_2*marital_2 - 1.9839 x RxGr3_2*litigat - 1.1361 x RxGr4_2*RxGr1_0 + 2.7632 x RxGr4_2*RxGr7_0 - 3.3665 x RxGr4_2*marital_3 - 2.5292 x RxGr5_2*duration -2.4557 x RxGr5_2*pastdx6 + 1.4508 x RxGr5_2* pastdx12 + 1.9031 x RxGr5_2*marital_4 + 4.7276 x RxGr7_2*marital_3 + 1.9077 x RxGr8_2*phydx15 + 2.8984 x RxGr8_2*SghxGr6

Application of the IPTW Method is done in two steps. In the first step, the joint probability of treatments is found through the procedure given in section 5.2, and in the

second step, the joint weight is calculated and the weighted model is built for the outcomes.

*5.3.1 Five Factorizations*

We identified 10 treatments and 40 confounding variables from the model (unweighted model). First, we randomly generated 5 factorizations (i.e., m = 5) using a Matlab permutation function.

The 10 treatments identified are: ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2.

The 40 confounding variables in the model are: RxGr1_0, RxGr2_0, RxGr4_0, RxGr5_0, RxGr7_0, ProcGr2_1, ProcGr4_1, ProcGr9_1, ProcGr10_1, ProcGr11_1, RxGr1_1, RxGr5_1, RxGr6_1, RxGr7_1, mid_OSW, gender race, children, litigat, duration, phydx3,phydx4, phydx6, phydx8, phydx11, phydx15, phydx20, phydx31, ProcGr2_0, ProcGr10_0, pastdx4, pastdx6, pastdx7, pastdx12, pastdx14, SghxGr6, SghxGr11, marital_2, marital_3, marital_4.

5.3.1.1 Generating Two Groups of Five Factorizations

Two groups, Group A and B, are generated each of which consists of 5 factorizations as shown below.

Group A

FactorizationA_1:

p(ProcGr4_2| C) x p(ProcGr9_2| ProcGr4_2, C) x p(ProcGr10_2| ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2,

RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C)

FactorizationA_2:

p(ProcGr9_2| C) x p(ProcGr10_2| ProcGr9_2, C) x p(RxGr1_2| ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2|ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C)

FactorizationA_3:

p(RxGr1_2| C) x p(RxGr2_2| RxGr1_2, C) x p(RxGr3_2| RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C)

FactorizationA_4:

p(RxGr7_2 | C) x p(RxGr8_2| RxGr7_2, C) x p(ProcGr4_2| RxGr8_2, RxGr7_2, C) x p(ProcGr9_2| RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2|RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C)

FactorizationA_5:

p(RxGr2_2| C) x p(RxGr3_2| RxGr2_2, C) x p(RxGr4_2| RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr2_2, RxGr3_2 , RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(RxGr1_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(ProcGr4_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C)

<u>Group B</u>

FactorizationB_1:

p(ProcGr10_2| C) x p(RxGr1_2| ProcGr10_2, C) x p(RxGr2_2|ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| ProcGr10_2, RxGr1_2, RxGr2_2, C) x

p(RxGr4_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C)

FactorizationB_2:

p(RxGr4_2| C) x p(RxGr5_2| RxGr4_2, C) x p( RxGr7_2| RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C)

FactorizationB_3:

p(RxGr5_2| C) x p(RxGr7_2| RxGr5_2, C) x p(RxGr8_2| RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2|

RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C)

FactorizationB_4:

p(RxGr8_2| C) x p(ProcGr4_2| RxGr8_2, C) x p(ProcGr9_2| RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C)

FactorizationB_5:

p(ProcGr4_2| C) x p(ProcGr9_2| ProcGr4_2, C) x p(ProcGr10_2| ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr4_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr5_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2, C) x p(RxGr7_2 | ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(RxGr3_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(RxGr2_2|

ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, RxGr3_2, C)

5.3.1.2 Building Logistic Models

The Logistic model for each treatment is built and the joint probability and its average are calculated under each factorization for each group. Figure 5.4 shows the average joint probability (Ave_Cond_Joint_Prob) of the two groups.

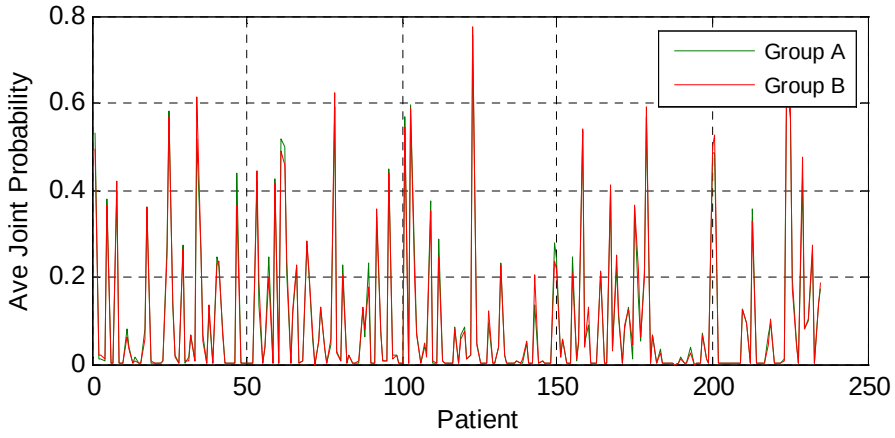



Figure 5.4 Average Joint Probability of Groups A and B with 5 Factorizations

We can see that the average joint probability of the two groups is similar for each observation. To compare them, the relative difference between the two groups (equation 5.2) is calculated and plotted in Figure 5.5.

$$\text{Relative difference} = \frac{|\,\text{Ave\_Cond\_Joint\_Prob}(A) - \text{Ave\_Cond\_Joint\_Prob}(B)\,|}{|\,\text{Ave\_Cond\_Joint\_Prob}(A)\,|} \times 100 \qquad (5.2)$$

Figure 5.5 shows that the two groups are very similar so either can be chosen to calculate the joint weight.

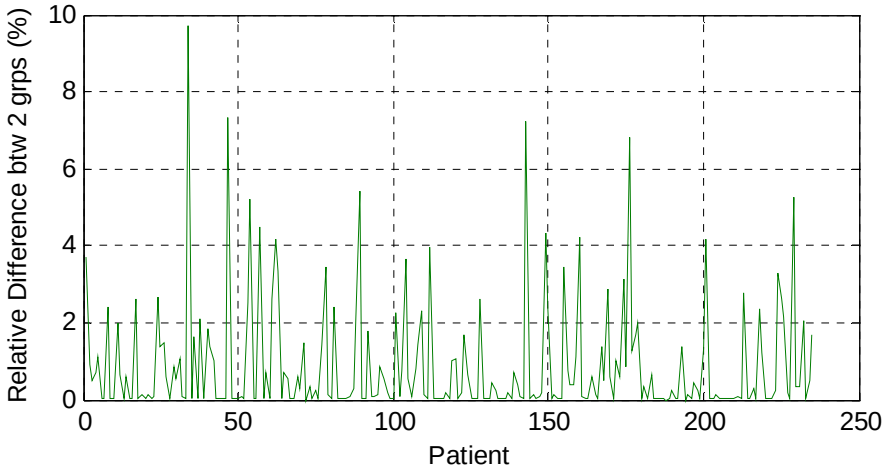



Figure 5.5 Relative Percent Differences Between Groups A and B with 5 Factorizations

*5.3.2 Ten Factorizations*

5.3.2.1 Generating Two Groups of Ten Factorizations

The above analysis for five factorizations is also done for m = 10. Each factorization from each group is listed below.

Group A

FactorizationA_1:

p(ProcGr4_2| C) x p(ProcGr10_2| ProcGr4_2, C) x p(RxGr1_2| ProcGr4_2, ProcGr10_2, C) x p(RxGr2_2| ProcGr4_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p (ProcGr9_2|

ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C)

FactorizationA_2:

p(ProcGr9_2| C) x p(RxGr1_2| ProcGr9_2, C) x p(RxGr2_2| ProcGr9_2, RxGr1_2, C) x p(RxGr3_2| ProcGr9_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr10_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C)

FactorizationA_3:

p(RxGr1_2| C) x p(RxGr3_2| RxGr1_2, C) x p(RxGr4_2| RxGr1_2, RxGr3_2, C) x p(RxGr5_2| RxGr1_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr2_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C)

FactorizationA_4:

p(RxGr7_2| C) x p(ProcGr4_2| RxGr7_2, C) x p(ProcGr9_2| RxGr7_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr7_2, ProcGr4_2, ProcGr9_2, C) x

p(RxGr1_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr8_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C)

FactorizationA_5:

p(RxGr2_2| C) x p(RxGr4_2| RxGr2_2, C) x p(RxGr5_2| RxGr2_2, RxGr4_2, C) x p(RxGr7_2| RxGr2_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr2_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr2_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr2_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr2_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr2_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr3_2| RxGr2_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C)

FactorizationA_6:

p(ProcGr10_2| C) x p(RxGr2_2| ProcGr10_2, C) x p(RxGr3_2| ProcGr10_2, RxGr2_2, C) x p(RxGr4_2| ProcGr10_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2,

RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(RxGr1_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C)

FactorizationA_7:

p(RxGr4_2| C) x p(RxGr7_2| RxGr4_2, C) x p(RxGr8_2| RxGr4_2, RxGr7_2, C) x p(ProcGr4_2| RxGr4_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr4_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr4_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr4_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr4_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr4_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr5_2| RxGr4_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C)

FactorizationA_8:

p(RxGr5_2| C) x p(RxGr8_2| RxGr5_2, C) x p(ProcGr4_2| RxGr5_2, RxGr8_2, C) x p(ProcGr9_2| RxGr5_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x

p(RxGr7_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C)

FactorizationA_9:

p(RxGr8_2| C) x p(ProcGr4_2| RxGr8_2, C) x p(ProcGr9_2| RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2|RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C)

FactorizationA_10:

p(ProcGr4_2| C) x p(ProcGr10_2| ProcGr4_2, C) x p(RxGr1_2| ProcGr4_2, ProcGr10_2, C) x p(RxGr4_2| ProcGr4_2, ProcGr10_2, RxGr1_2, C) x p(RxGr5_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, C) x p(RxGr7_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(RxGr3_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(RxGr2_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, RxGr3_2, C) x p(ProcGr9_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, RxGr3_2, RxGr2_2, C)

Group B

FactorizationB_1:

p(ProcGr4_2| C) x p(ProcGr9_2| ProcGr4_2, C) x p(ProcGr10_2| ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C)

FactorizationB_2:

p(ProcGr9_2| C) x p(ProcGr10_2| ProcGr9_2, C) x p(RxGr1_2| ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C)

FactorizationB_3:

p(RxGr1_2| C) x p(RxGr2_2| RxGr1_2, C) x p(RxGr3_2| RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr1_2,

RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C)

FactorizationB_4:

p(RxGr7_2| C) x p(RxGr8_2| RxGr7_2, C) x p(ProcGr4_2| RxGr8_2, RxGr7_2, C) x p(ProcGr9_2| RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C)

FactorizationB_5:

p(RxGr2_2| C) x p(RxGr3_2| RxGr2_2, C) x p(RxGr4_2| RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x

p(RxGr1_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(ProcGr4_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C)

FactorizationB_6:

p(ProcGr10_2| C) x p(RxGr1_2| ProcGr10_2, C) x p(RxGr2_2| ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C)

FactorizationB_7:

p(RxGr4_2| C) x p(RxGr5_2| RxGr4_2, C) x p(RxGr7_2| RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C)

FactorizationB_8:

p(RxGr5_2| C) x p(RxGr7_2| RxGr5_2, C) x p(RxGr8_2| RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C)

FactorizationB_9:

p(RxGr8_2| C) x p(ProcGr4_2| RxGr8_2, C) x p(ProcGr9_2| RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C)

FactorizationB_10:

p(ProcGr4_2| C) x p(ProcGr9_2| ProcGr4_2, C) x p(ProcGr10_2| ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x

p(RxGr4_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr5_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2, C) x p(RxGr7_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(RxGr3_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(RxGr2_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, RxGr3_2, C)

5.3.2.2 Building Logistic Models

The Logistic model for each treatment is built and the joint probability and its average are calculated under each factorization for each group. Figure 5.6 shows the average joint probability (Ave_Cond_Joint_Prob) of the groups A and B. The average joint probability of each group is very similar for each observation.

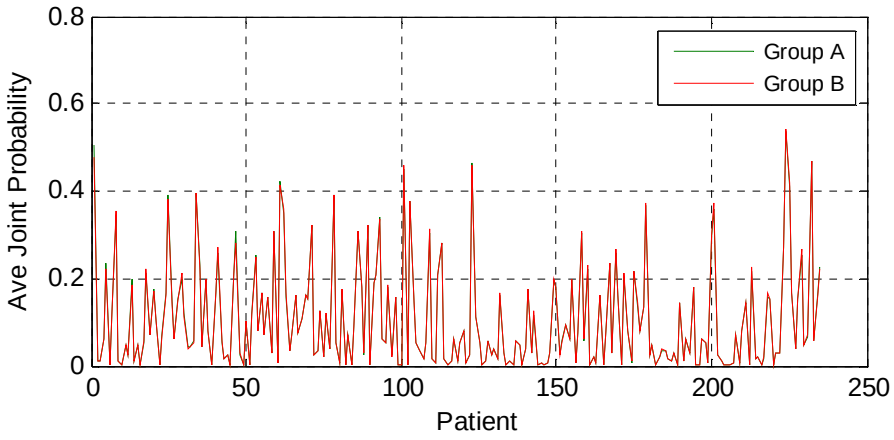



Figure 5.6 Average Joint Probability of Groups A and B with 10 Factorizations

The relative difference of the average joint probability of the two groups is shown in Figure 5.7. It shows that the two groups are very similar so either can be chosen to calculate the joint weight.

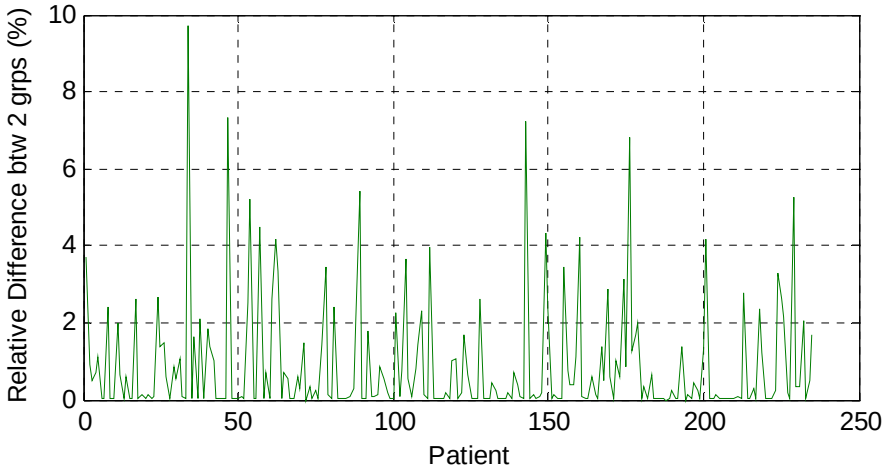



Figure 5.7 Relative Percent Difference Between Groups A and B with 10 Factorizations

*5.3.3 Twenty Factorizations*

5.3.3.1 Generating Two Groups of Twenty Factorizations

The above analysis is also done for 20 factorizations as follows.

Group A

FactorizationA_1:

p(ProcGr4_2| C) x p(ProcGr9_2| ProcGr4_2 C) x p(ProcGr10_2| ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2|

ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C)

FactorizationA_2:

p(RxGr8_2| C) x p(ProcGr9_2|RxGr8_2, C) x p(ProcGr10_2|RxGr8_2, ProcGr9_2, C) x p(RxGr1_2| RxGr8_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr8_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr8_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr8_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr8_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr8_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(ProcGr4_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2 ,RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C)

FactorizationA_3:

p(RxGr4_2| C) x p(RxGr5_2| RxGr4_2, C) x p(RxGr7_2| RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr4_2, RxGr5_2 ,RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr3_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr2_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2 , RxGr3_2, C)

FactorizationA_4:

p(RxGr3_2| C) x p(RxGr4_2| RxGr3_2, C) x p(RxGr5_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(RxGr1_2| RxGr3_2 , RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(ProcGr4_2| RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr2_2| RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr9_2, ProcGr10_2, RxGr1_2, ProcGr4_2, C)

FactorizationA_5:

p(ProcGr10_2| C) x p(RxGr1_2| ProcGr10_2, C) x p(RxGr2_2| ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p (ProcGr9_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr4_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2 ProcGr9_2, C)

FactorizationA_6:

p(RxGr7_2| C) x p(RxGr8_2| RxGr7_2, C) x p(ProcGr4_2| RxGr7_2 ,RxGr8_2, C) x p(ProcGr9_2| RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2|

RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C)

FactorizationA_7:

p(RxGr2_2| C) x p(RxGr3_2| RxGr2_2, C) x p(RxGr4_2| RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(RxGr1_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(ProcGr10_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, RxGr1_2, C)

FactorizationA_8:

p(RxGr7_2| C) x p(ProcGr9_2| RxGr7_2, C) x p(ProcGr10_2| RxGr7_2, ProcGr9_2, C) x p(RxGr1_2| RxGr7_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr7_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr7_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr7_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr7_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr8_2| RxGr7_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(ProcGr4_2|

RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr8_2, C)

FactorizationA_9:

p(ProcGr4_2|C) x p(ProcGr10_2|ProcGr4_2, C) x p(RxGr4_2| ProcGr4_2, ProcGr10_2, C) x p(RxGr5_2| ProcGr4_2, ProcGr10_2, RxGr4_2, C) x p(RxGr7_2| ProcGr4_2, ProcGr10_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr4_2, ProcGr10_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(RxGr3_2| ProcGr4_2, ProcGr10_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(RxGr2_2| ProcGr4_2, ProcGr10_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, RxGr3_2, C) x p(ProcGr9_2| ProcGr4_2, ProcGr10_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, RxGr3_2, RxGr2_2, C) x p(RxGr1_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, RxGr3_2, RxGr2_2, ProcGr9_2, C)

FactorizationA_10:

p(ProcGr4_2| C) x p(ProcGr9_2| ProcGr4_2, C) x p(RxGr1_2| ProcGr4_2, ProcGr9_2, C) x p(RxGr2_2| ProcGr4_2, ProcGr9_2, RxGr1_2, C) x p(RxGr3_2| ProcGr4_2, ProcGr9_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr4_2, ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr4_2, ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr4_2, ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr4_2, ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr10_2| ProcGr4_2, ProcGr9_2, ProcGr4_2, ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C)

FactorizationA_11:

p(RxGr1_2| C) x p(RxGr4_2|RxGr1_2, C) x p(RxGr5_2| RxGr1_2, RxGr4_2, C) x p(RxGr7_2| RxGr1_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x (ProcGr4_2| RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr2_2| RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr3_2| RxGr1_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr2_2, C)

FactorizationA_12:

p(ProcGr9_2| C) x p(RxGr1_2| ProcGr9_2, C) x p(RxGr2_2| ProcGr9_2, RxGr1_2, C) x (RxGr3_2| ProcGr9_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr10_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C)

FactorizationA_13:

p(RxGr1_2| C) x p(RxGr3_2| RxGr1_2, C) x p(RxGr4_2| RxGr1_2, RxGr3_2, C) x p(RxGr5_2| RxGr1_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr1_2, RxGr3_2,

RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr2_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C)

FactorizationA_14:

p(RxGr7_2| C) x p(ProcGr4_2| RxGr7_2, C) x p(ProcGr9_2| RxGr7_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr7_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2|RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr8_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C)

FactorizationA_15:

p(ProcGr10_2| C) x p(RxGr2_2| ProcGr10_2, C) x p(RxGr3_2| ProcGr10_2, RxGr2_2, C) x p(RxGr4_2| ProcGr10_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2 ,RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| ProcGr10_2, RxGr2_2, RxGr3_2,

RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(RxGr1_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2 ,RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C)

FactorizationA_16:

p(RxGr5_2| C) x p(ProcGr4_2| RxGr5_2, C) x p(ProcGr9_2| RxGr5_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr5_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr5_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr5_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr5_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr5_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr7_2| RxGr5_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr8_2| RxGr5_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr7_2, C)

FactorizationA_17:

p(RxGr4_2| C) x p(RxGr7_2| RxGr4_2, C) x p(RxGr8_2| RxGr4_2, RxGr7_2, C) x p(ProcGr4_2| RxGr4_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr4_2, , RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr4_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr4_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr4_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr4_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2 , ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr5_2| RxGr4_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C)

FactorizationA_18:

p(RxGr5_2| C) x p(RxGr8_2| RxGr5_2, C) x p(ProcGr4_2| RxGr5_2, RxGr8_2, C) x p(ProcGr9_2| RxGr5_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr7_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C)

FactorizationA_19:

p(ProcGr4_2| C) x p(ProcGr10_2| rocGr4_2, C) x p(RxGr1_2| ProcGr4_2, ProcGr10_2, C) x p(RxGr4_2| ProcGr4_2, ProcGr10_2, RxGr1_2, C) x p(RxGr5_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, C) x p(RxGr7_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(RxGr3_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(RxGr2_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, RxGr3_2, C) x p(ProcGr9_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, RxGr3_2, RxGr2_2, C)

FactorizationA_20:

p(ProcGr10_2| C) x p(RxGr1_2| ProcGr10_2, C) x p(ProcGr4_2| ProcGr10_2, RxGr1_2, C) x p(RxGr4_2| ProcGr10_2, RxGr1_2, ProcGr4_2,

C) x p(RxGr5_2| ProcGr10_2, RxGr1_2, ProcGr4_2, RxGr4_2, C) x p(RxGr7_2| ProcGr10_2, RxGr1_2, ProcGr4_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr10_2, RxGr1_2, ProcGr4_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(RxGr3_2| ProcGr10_2, RxGr1_2, ProcGr4_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(RxGr2_2| ProcGr10_2, RxGr1_2, ProcGr4_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, RxGr3_2, C) x p(ProcGr9_2| ProcGr10_2, RxGr1_2, ProcGr4_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, RxGr3_2, RxGr2_2, C)

Group B

FactorizationB_1:

p(ProcGr9_2| C) x p(RxGr1_2| ProcGr9_2, C) x p(RxGr2_2| ProcGr9_2, RxGr1_2, C) x p(RxGr3_2| ProcGr9_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr10_2| ProcGr9_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C)

FactorizationB_2:

p(RxGr8_2| C) x p(ProcGr4_2| RxGr8_2, C) x p(ProcGr9_2| RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2|

RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C)

FactorizationB_3:

p(RxGr8_2| C) x p(ProcGr4_2| RxGr8_2, C) x p(ProcGr9_2| RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C)

FactorizationB_4:

p(RxGr2_2| C) x p(RxGr4_2| RxGr2_2, C) x p(RxGr5_2| RxGr2_2, RxGr4_2, C) x p(RxGr7_2| RxGr2_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr2_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr2_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr2_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr2_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x

p(RxGr1_2| RxGr2_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr3_2| RxGr2_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C)

FactorizationB_5:

p(RxGr2_2| C) x p(RxGr3_2| RxGr2_2, C) x p(RxGr4_2| RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(RxGr1_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(ProcGr4_2| RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C)

FactorizationB_6:

p(ProcGr4_2| C) x p(ProcGr10_2| ProcGr4_2, C) x p(RxGr1_2| ProcGr4_2, ProcGr10_2, C) x p(RxGr2_2| ProcGr4_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p (ProcGr9_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C)

FactorizationB_7:

p(RxGr5_2| C) x p(RxGr7_2| RxGr5_2, C) x p(RxGr8_2| RxGr5_2, RxGr7_2, C)x p(ProcGr4_2| RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C)

FactorizationB_8:

p(ProcGr10_2| C) x p(RxGr2_2| ProcGr10_2, C) x p(RxGr3_2| ProcGr10_2, RxGr2_2, C) x p(RxGr4_2| ProcGr10_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C)x p(RxGr1_2| ProcGr10_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C)

FactorizationB_9:

p(RxGr7_2| C) x p(ProcGr4_2| RxGr7_2, C) x p(ProcGr9_2| RxGr7_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr7_2, ProcGr4_2, ProcGr9_2, C) x

p(RxGr1_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2|RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr8_2| RxGr7_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C)

FactorizationB_10:

p(ProcGr4_2| C) x p(ProcGr10_2| ProcGr4_2, C) x p(RxGr1_2| ProcGr4_2, ProcGr10_2, C) x p(RxGr4_2| ProcGr4_2, ProcGr10_2, RxGr1_2, C) x p(RxGr5_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, C) x p(RxGr7_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(RxGr3_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(RxGr2_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, RxGr3_2, C) x p(ProcGr9_2| ProcGr4_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, RxGr3_2, RxGr2_2, C)

FactorizationB_11:

p(ProcGr4_2| C) x p(ProcGr9_2| ProcGr4_2, C) x p(ProcGr10_2| ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| rocGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2|ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2,

RxGr3_2, C) x p(RxGr5_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2 RxGr5_2, C) x p(RxGr8_2| rocGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C)

FactorizationB_12:

p(RxGr1_2| C) x p(RxGr3_2| RxGr1_2, C) x p(RxGr4_2| RxGr1_2, RxGr3_2, C) x p(RxGr5_2| RxGr1_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr1_2, RxGr3_2 , RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr2_2| RxGr1_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C)

FactorizationB_13:

p(ProcGr9_2| C) x p(ProcGr10_2| ProcGr9_2, C) x p(RxGr1_2| ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2|

ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C)

FactorizationB_14:

p(RxGr1_2| C) x p(RxGr2_2| RxGr1_2, C) x p(RxGr3_2| RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr1_2, RxGr2_2, RxGr3_2 , RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C)

FactorizationB_15:

p(RxGr7_2| C) x p(RxGr8_2| RxGr7_2, C) x p(ProcGr4_2| RxGr8_2, RxGr7_2, C) x p(ProcGr9_2| RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr5_2| RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C)

FactorizationB_16:

p(ProcGr10_2| C) x p(RxGr1_2| ProcGr10_2, C) x p(RxGr2_2| ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| ProcGr10_2, RxGr1_2, RxGr2_2 RxGr3_2, C) x p(RxGr5_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C) x p(RxGr7_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2|ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| ProcGr10_2, RxGr1_2 ,RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2 , RxGr7_2 , RxGr8_2, ProcGr4_2, C)

FactorizationA_17:

p(RxGr5_2| C) x p(RxGr8_2| RxGr5_2, C) x p(ProcGr4_2| RxGr5_2, RxGr8_2, C) x p(ProcGr9_2| RxGr5_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2|RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, C) x p(RxGr7_2| RxGr5_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, C)

FactorizationB_18:

p(RxGr4_2| C) x p(RxGr5_2| RxGr4_2 C) x p(RxGr7_2| RxGr4_2, RxGr5_2, C) x p(RxGr8_2| RxGr4_2, RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr4_2,

RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2 ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C)

FactorizationB_19:

p(RxGr5_2| C) x p(RxGr7_2| RxGr5_2, C) x p(RxGr8_2| RxGr5_2, RxGr7_2, C) x p(ProcGr4_2| RxGr5_2, RxGr7_2, RxGr8_2, C) x p(ProcGr9_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, C) x p(ProcGr10_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr2_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr3_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, C) x p(RxGr4_2| RxGr5_2, RxGr7_2, RxGr8_2, ProcGr4_2, ProcGr9_2, ProcGr10_2 , RxGr1_2, RxGr2_2, RxGr3_2, C)

FactorizationB_20:

p(ProcGr4_2| C) x p(ProcGr9_2| ProcGr4_2, C) x p(ProcGr10_2| ProcGr4_2, ProcGr9_2, C) x p(RxGr1_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, C) x p(RxGr4_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, C) x p(RxGr5_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2, C) x p(RxGr7_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, C) x p(RxGr8_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2,

RxGr5_2, RxGr7_2, C) x p(RxGr3_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, C) x p(RxGr2_2| ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2, RxGr3_2, C)

5.3.3.2 Building Logistic Models

The Logistic model for each treatment is built and the joint probability and its average are calculated under each factorization for each group. Figure 5.8 shows that the average joint probability (Ave_Cond_Joint_Prob) of Groups A and B are very similar for each observation.

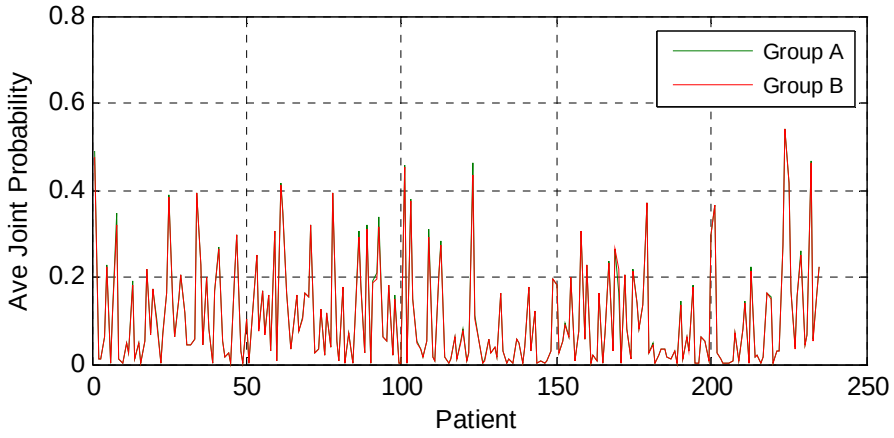



Figure 5.8 Average Joint Probability of Groups A and B with 20 Factorizations

The relative difference of the average joint probability of the two groups is shown in Figure 5.9. Again, it shows that the two groups are very similar so either can be chosen to calculate the joint weight.

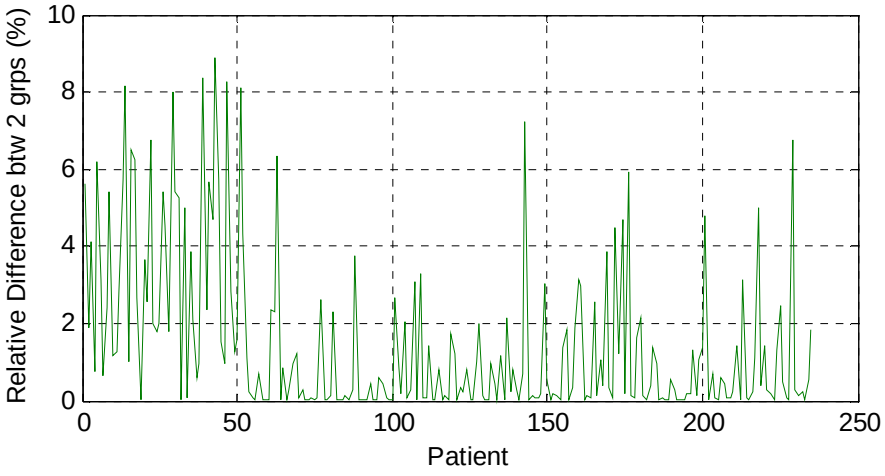



Figure 5.9 Relative Percent Difference Between Groups A and B with 20 Factorizations

The relative percent differences between groups A and B with 5, 10, and 20 factorizations are shown below in Figure 5.10. We can see that the differences are all under 10% and overall there is no evidence that the difference reduces under a larger number of factorizations.

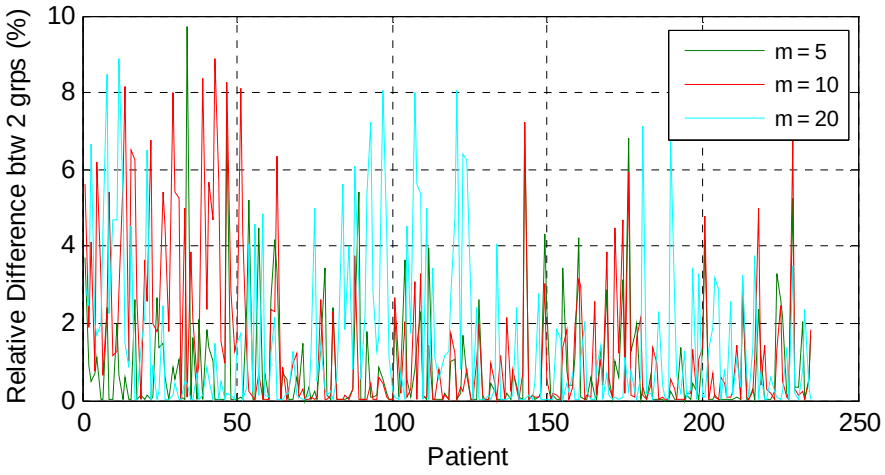



Figure 5.10 Relative Percent Difference Between Groups A and B with 5, 10, and 20 Factorizations

The maximum difference between groups A and B with 5, 10, and 20 factorizations is shown Figure 5.11. When the number of factorization increases from 5 to 10, the maximum difference decreases from 9.691 to 8.876. However, when the number of factorization increases from 10 to 20, there is no considerable change in the maximum difference (from 8.876 to 8.875). This indicates when the factorization is 10 the maximum difference curve levels off. Thus for this research, we chose 20 factorizations to calculate the joint weight.

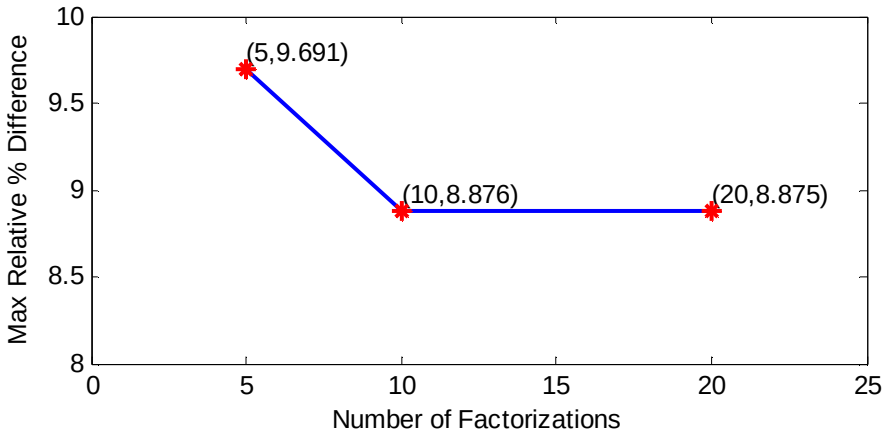



Figure 5.11 Maximum Difference Between Groups A and B with 5, 10, and 20 Factorizations

The difference under 5 factorizations has been small enough, indicating that the joint probability estimated using the proposed method is robust.

*5.3.4 Building Outcome Models*

1) Estimate of the Joint Probability and Weights:

The equations (equation 5.3) of the unstabilized and stabilized weights are

Unstabilized Weight =

$$\frac{1}{\text{Ave}\hat{P}(\text{ProcGr42, ProcGr9\_2, ProcGr10\_2, RxGr1\_2, RxGr2\_2, RxGr3\_2, RxGr6\_2, RxGr7\_2, RxGr8\_2} \mid \text{Confounding variables})} \tag{5.3}$$

Stabilized Weight =

$$\frac{\hat{P}(\text{ProcGr42, ProcGr9\_2, ProcGr10\_2, RxGr1\_2, RxGr2\_2, RxGr3\_2, RxGr5\_2, RxGr6\_2, RxGr7\_2, RxGr8\_2})}{\text{Ave}\hat{P}(\text{ProcGr42, ProcGr9\_2, ProcGr10\_2, RxGr1\_2, RxGr2\_2, RxGr3\_2, RxGr5\_2, RxGr6\_2, RxGr7\_2, RxGr8\_2} \mid \text{Confounding variables})}.$$

The stabilized weight is used in the following analysis, which is supposed to bear smaller variance than the unstabilized model. To obtain the stabilized weights, we need to find the unconditional joint probability (i.e., the nominator). A simple way to estimate the unconditional joint probability is as follows.

Let $n$ = total number of observations

$w$ = number of observations with 10 treatments (ProcGr4_2, ProcGr9_2, ProcGr10_2, RxGr1_2, RxGr2_2, RxGr3_2, RxGr4_2, RxGr5_2, RxGr7_2, RxGr8_2) taking the same value as the considered observations.

Then the unconditional joint probability is given in equation 5.4:

$$\hat{P}(\text{ProcGr4\_2, ProcGr9\_2, ProcGr10\_2, RxGr1\_2, RxGr2\_2, RxGr3\_2, RxGr5\_2, RxGr7\_2, RxGr8\_2}) = \frac{w}{n}. \tag{5.4}$$

2) Fit various weighted outcome models and compare the resulting estimates:

The coefficient estimates of the outcome models weighted based on 5, 10, and 20 factorizations are given in Table 5.1. This table shows that for most variables, the weighted coefficients are smaller than the unweighted coefficients (these smaller coefficients are highlighted in Table 5.1). For weighted models based on 5 factorizations, there are 28 out of 40 variables that have smaller coefficients than those of the

unweighted model. For weighted models based on 10 and 20 factorizations, there are 30 out of 40 and 31 out of 40 with smaller coefficients than those of the unweighted model, respectively.

Table 5.1 Coefficient Comparison of 5, 10, and 20 Factorization Weighted Models to Unweighted Model

| Variable | Un-weighted Model | Stabilized Weighted Model 5 factorization | Stabilized Weighted Model 10 factorization | Stabilized Weighted Model 20 factorization |
|---|---|---|---|---|
| Intercept | -3.170 | 0.218 | 2.015 | 1.578 |
| mid_OSW | 0.942 | 1.077 | 1.019 | 1.039 |
| ProcGr2_1_pastdx6 | 2.993 | 1.261 | 0.789 | 0.926 |
| ProcGr4_1_children | -1.922 | -1.449 | -1.921 | -1.920 |
| ProcGr9_1_race | -2.459 | -5.795 | -5.878 | -5.844 |
| ProcGr9_1_phydx3 | 1.288 | 2.610 | 2.793 | 2.784 |
| ProcGr9_1_marital_2 | -0.496 | -1.010 | -0.993 | -1.022 |
| ProcGr10_1_gender | 1.870 | -0.021 | 0.175 | 0.219 |
| ProcGr10_1_phydx6 | 0.616 | -0.136 | -0.163 | -0.144 |
| ProcGr10_1_ProcGr10_0 | -0.877 | -0.953 | -0.892 | -0.840 |
| ProcGr10_1_RxGr2_0 | 1.039 | -0.228 | -0.219 | -0.304 |
| ProcGr11_1_pastdx7 | -0.967 | -0.750 | -1.095 | -1.127 |
| RxGr1_1_duration | 2.787 | 1.066 | 1.818 | 1.813 |
| RxGr1_1_SghxGr11 | 2.616 | 0.203 | -0.465 | -0.534 |
| RxGr1_1_RxGr5_0 | -1.271 | -1.197 | -1.073 | -1.068 |
| RxGr5_1_phydx11 | -1.805 | -1.801 | -1.730 | -1.704 |
| RxGr6_1_pastdx4 | 1.694 | 1.274 | 1.019 | 1.065 |
| RxGr6_1_RxGr7_0 | -1.351 | -1.517 | -1.614 | -1.302 |
| RxGr7_1_phydx20 | -1.614 | -2.608 | -1.605 | -1.406 |
| ProcGr4_2_mid_OSW | 2.273 | 6.171 | 4.934 | 5.353 |
| ProcGr4_2_phydx8 | -1.851 | -3.073 | -3.203 | -3.320 |
| ProcGr9_2_litigat | -2.119 | -2.633 | -2.150 | -2.079 |
| ProcGr9_2_phydx4 | 1.611 | -0.528 | -0.533 | -0.523 |
| ProcGr9_2_phydx31 | 1.762 | 1.133 | 1.034 | 0.999 |
| ProcGr10_2_ProcGr2_0 | -1.596 | 0.142 | 0.416 | 0.347 |
| ProcGr10_2_RxGr4_0 | 1.355 | 0.158 | -0.316 | -0.319 |

Table 5.1—*Continued*

| Variable | Un-weighted Model | Stabilized Weighted Model 5 factorization | Stabilized Weighted Model 10 factorization | Stabilized Weighted Model 20 factorization |
|---|---|---|---|---|
| RxGr1_2_pastdx14 | -2.570 | -1.231 | -0.930 | -0.950 |
| RxGr2_2_pastdx6 | -1.478 | -0.479 | -0.078 | -0.081 |
| RxGr2_2_marital_2 | 1.490 | 1.107 | 1.068 | 1.107 |
| RxGr3_2_litigat | -1.984 | -1.494 | -1.282 | -1.198 |
| RxGr4_2_RxGr1_0 | -1.136 | 1.486 | 1.999 | 2.041 |
| RxGr4_2_RxGr7_0 | 2.763 | 3.538 | 4.041 | 4.079 |
| RxGr4_2_marital_3 | -3.367 | -2.555 | -2.956 | -3.012 |
| RxGr5_2_duration | -2.529 | 1.604 | 0.850 | 0.802 |
| RxGr5_2_pastdx6 | -2.456 | -1.104 | -0.866 | -1.009 |
| RxGr5_2_pastdx12 | 1.451 | 0.838 | 0.795 | 0.861 |
| RxGr5_2_marital_4 | 1.903 | 1.037 | 1.243 | 1.244 |
| RxGr7_2_marital_3 | 4.728 | 3.948 | 4.037 | 4.132 |
| RxGr8_2_phydx15 | 1.908 | 0.080 | -0.435 | -0.348 |
| RxGr8_2_SghxGr6 | 2.898 | -1.404 | -1.392 | -1.391 |

Standard error comparisons between the unweighted model and weighted models based on 5, 10, and 20 factorizations are given in Table 5.2. This table shows that for most variables, the standard error of the weighted model is smaller than the standard error of the unweighted model (these smaller standard errors are highlighted in Table 5.2).

Table 5.2 Standard Error Comparison of 5, 10, and 20 Factorization Weighted Models to Unweighted Model

| Variable | Un-weighted Model | Stabilized Weighted Model 5 factorization | Stabilized Weighted Model 10 factorization | Stabilized Weighted Model 20 factorization |
|---|---|---|---|---|
| Intercept | 3.349 | 2.871 | 3.167 | 3.113 |
| mid_OSW | 0.128 | 0.149 | 0.171 | 0.165 |
| ProcGr2_1_pastdx6 | 0.508 | 0.676 | 0.682 | 0.694 |

Table 5.2—*Continued*

| Variable | Un-weighted Model | Stabilized Weighted Model 5 factorization | Stabilized Weighted Model 10 factorization | Stabilized Weighted Model 20 factorization |
|---|---|---|---|---|
| ProcGr4_1_children | 0.676 | 0.483 | 0.503 | 0.502 |
| ProcGr9_1_race | 0.984 | 0.818 | 0.774 | 0.772 |
| ProcGr9_1_phydx3 | 0.468 | 0.485 | 0.460 | 0.457 |
| ProcGr9_1_marital_2 | 0.354 | 0.307 | 0.309 | 0.309 |
| ProcGr10_1_gender | 0.532 | 0.447 | 0.442 | 0.442 |
| ProcGr10_1_phydx6 | 0.402 | 0.271 | 0.268 | 0.269 |
| ProcGr10_1_ProcGr10_0 | 0.387 | 0.302 | 0.292 | 0.296 |
| ProcGr10_1_RxGr2_0 | 0.542 | 0.472 | 0.448 | 0.458 |
| ProcGr11_1_pastdx7 | 0.421 | 0.319 | 0.313 | 0.314 |
| RxGr1_1_duration | 0.868 | 0.821 | 0.768 | 0.768 |
| RxGr1_1_SghxGr11 | 0.736 | 0.607 | 0.596 | 0.601 |
| RxGr1_1_RxGr5_0 | 0.597 | 0.422 | 0.412 | 0.411 |
| RxGr5_1_phydx11 | 0.508 | 0.412 | 0.417 | 0.417 |
| RxGr6_1_pastdx4 | 0.451 | 0.337 | 0.337 | 0.339 |
| RxGr6_1_RxGr7_0 | 0.776 | 0.616 | 0.566 | 0.571 |
| RxGr7_1_phydx20 | 0.586 | 0.497 | 0.496 | 0.496 |
| ProcGr4_2_mid_OSW | 2.376 | 2.919 | 3.346 | 3.238 |
| ProcGr4_2_phydx8 | 0.652 | 0.671 | 0.769 | 0.730 |
| ProcGr9_2_litigat | 0.493 | 0.416 | 0.423 | 0.435 |
| ProcGr9_2_phydx4 | 0.403 | 0.285 | 0.280 | 0.281 |
| ProcGr9_2_phydx31 | 0.503 | 0.380 | 0.368 | 0.373 |
| ProcGr10_2_ProcGr2_0 | 0.514 | 0.373 | 0.388 | 0.391 |
| ProcGr10_2_RxGr4_0 | 0.578 | 0.486 | 0.487 | 0.491 |
| RxGr1_2_pastdx14 | 0.670 | 0.558 | 0.556 | 0.554 |
| RxGr2_2_pastdx6 | 0.537 | 0.463 | 0.481 | 0.480 |
| RxGr2_2_marital_2 | 0.409 | 0.331 | 0.337 | 0.335 |
| RxGr3_2_litigat | 0.539 | 0.415 | 0.440 | 0.450 |
| RxGr4_2_RxGr1_0 | 0.688 | 0.531 | 0.512 | 0.513 |
| RxGr4_2_RxGr7_0 | 0.784 | 0.862 | 0.804 | 0.812 |
| RxGr4_2_marital_3 | 0.873 | 0.847 | 0.835 | 0.845 |
| RxGr5_2_duration | 1.054 | 0.802 | 0.769 | 0.772 |
| RxGr5_2_pastdx6 | 0.703 | 0.570 | 0.573 | 0.589 |
| RxGr5_2_pastdx12 | 0.688 | 0.450 | 0.438 | 0.441 |

Table 5.2—*Continued*

| Variable | Un-weighted Model | Stabilized Weighted Model 5 factorization | Stabilized Weighted Model 10 factorization | Stabilized Weighted Model 20 factorization |
|---|---|---|---|---|
| RxGr5_2_marital_4 | 0.538 | 0.396 | 0.399 | 0.398 |
| RxGr7_2_marital_3 | 0.716 | 0.805 | 0.829 | 0.826 |
| RxGr8_2_phydx15 | 1.620 | 0.630 | 0.604 | 0.609 |
| RxGr8_2_SghxGr6 | 0.888 | 0.357 | 0.354 | 0.355 |

Since the weighted model based on 20 factorizations shows better results than those based on 5 or 10 factorizations, the stabilized weight based on 20 factorizations is chosen. The stabilized weight based on 20 factorizations is shown in Figure 5.12. There are 4 patients which have a weight over 60. Among those patient #166 has the highest weight at about 98. This means that patient #166 is the most underrepresented patient in the relative treatment assignments. Therefore, patient #166 should be given the proportionally highest weight.

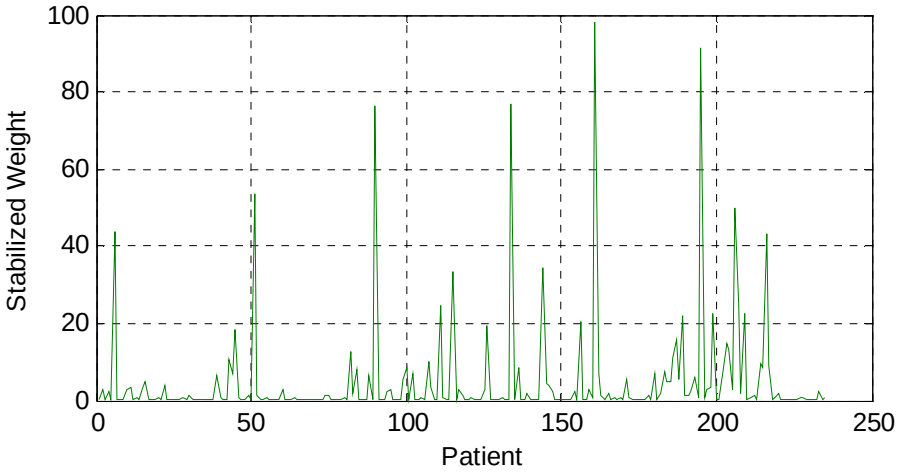



Figure 5.12 Stabilized Weights Based on 20 Factorizations

The estimated outcome model using the chosen weights is:

Post_OSW =1.5781+ 1.0386 x mid_OSW + 0.9262 x ProcGr2_1*pastdx6 - 1.9204 x ProcGr4_1*children -5.8435 x ProcGr9_1*race + 2.7839 x ProcGr9_1*phydx3 - 1.0222 x ProcGr9_1*marital_2 + 0.2191x ProcGr10_1*gender - 0.1445 x ProcGr10_1*phydx6 - 0.8401 x ProcGr10_1*ProcGr10_0 - 0.3044 x ProcGr10_1*RxGr2_0 - 1.1267 x ProcGr11_1*pastdx7 + 1.8132 x RxGr1_1* duration - 0.5343 x RxGr1_1*SghxGr11 - 1.0677 x RxGr1_1*RxGr5_0 - 1.7043 x RxGr5_1*phydx11 + 1.0650 x RxGr6_1*pastdx4 - 1.3018 x RxGr6_1*RxGr7_0 - 1.4059 x RxGr7_1*phydx20 + 5.3532 x ProcGr4_2* mid_OSW -3.3199 x ProcGr4_2*phydx8 - 2.0795 x ProcGr9_2*litigat - 0.5233 x ProcGr9_2*phydx4 + 0.9991x ProcGr9_2*phydx31 + 0.3469 x ProcGr10_2*ProcGr2_0 - 0.3187 x ProcGr10_2*RxGr4_0 - 0.9495 x RxGr1_2*pastdx14 - 0.0805 x RxGr2_2*pastdx6 + 1.1068 x RxGr2_2*marital_2 - 1.1978 x RxGr3_2*litigat + 2.0414 x RxGr4_2*RxGr1_0 + 4.0785 x RxGr4_2*RxGr7_0 -3.0119x RxGr4_2*marital_3 + 0.8020 x RxGr5_2*duration - 1.0086 x RxGr5_2*pastdx6 + 0.8613 x RxGr5_2* pastdx12 + 1.2442x RxGr5_2*marital_4 + 4.1322 x RxGr7_2*marital_3 - 0.3479 x RxGr8_2*phydx15 - 1.3913 x RxGr8_2*SghxGr6.

Comparing the results, most coefficients and standard errors of the IPTW with Correlated Treatments model are smaller than those for the unweighted model. This implies that the effect of the confounding variables has been adjusted by the IPTW with Correlated Treatments to compensate for the endogeneity.

### 5.4 Model Validation on the Test Data Set

To validate the stepwise selection model built on the training data set (training data model), a test data set was reserved consisting of 59 observations (Appendix A). In

the first validation study, the mean squared prediction error, MSPR, was calculated for both the unweighted and weighted models. This is done by predicting each observation in the test data set by utilizing the regression equation estimated using the training data model. These predicted $\hat{y}_i$ together with the observed $y_i$ in the test data set give $MSPR = \frac{1}{n^*}\sum_{i=1}^{n}\left(y_i^* - \hat{y}\right)^2$ (Appendix B). We then compare MSPR from the predictions using the unweighted regression model to the MSPR from the predictions using the weighted regression model resulting from the IPTW Method with Correlated Treatments Model . Table 5.3 compares the MSRP for the two regression models.

Table 5.3 MSPR of the Models

| | Unweighted Model | Weighted Model |
|---|---|---|
| MSRP | 2.824 | 2.575 |

The MSPR for the weighted regression model is seen to be smaller than that for the unweighted model, indicating improved prediction when endogeneity is addressed.

As a second form of model validation, a regression model was also fit to the test data set using the same model form. The test data model is then compared to the training data model by examining the estimated regression coefficients and their standard errors. In Table 5.4, it is seen that there are some large differences in some of the coefficient, which technically implies that the validation is unsuccessful. However, referring back to the clustering analysis at the end of Chapter 3, it should be recalled that the test data set does not a full representation of cases due to rare cases that could only be included in the training data set. This discrepancy in the data sets explains the observed discrepancies in Table 5.4. Similarly, discrepancies are also seen in the standard errors in Table 5.5.

Table 5.4 Comparison of Estimated Regression Coefficients of the Models

| Parameters | Training Data | Test Data |
|---|---|---|
| Intercept | -3.17 | -8.965 |
| mid_OSW | 0.942 | 1.047 |
| ProcGr2_1_pastdx6 | 2.993 | 2.927 |
| ProcGr4_1_children | -1.922 | -4.118 |
| ProcGr9_1_race | -2.459 | 5.213 |
| ProcGr9_1_phydx3 | 1.288 | 3.400 |
| ProcGr9_1_marital_2 | -0.496 | 0.472 |
| ProcGr10_1_gender | 1.87 | 3.476 |
| ProcGr10_1_phydx6 | 0.616 | 0.570 |
| ProcGr10_1_ProcGr10_ | -0.877 | -1.406 |
| ProcGr10_1_RxGr2_0 | 1.039 | -0.382 |
| ProcGr11_1_pastdx7 | -0.967 | -1.650 |
| RxGr1_1_duration | 2.787 | 6.350 |
| RxGr1_1_SghxGr11 | 2.616 | -1.650 |
| RxGr1_1_RxGr5_0 | -1.271 | -0.862 |
| RxGr5_1_phydx11 | -1.805 | -0.780 |
| RxGr6_1_pastdx4 | 1.694 | 2.763 |
| RxGr6_1_RxGr7_0 | -1.351 | 0.619 |
| RxGr7_1_phydx20 | -1.614 | -1.804 |
| ProcGr4_2_mid_OSW | 2.273 | 4.433 |
| ProcGr4_2_phydx8 | -1.851 | -3.428 |
| ProcGr9_2_litigat | -2.119 | -1.683 |
| ProcGr9_2_phydx4 | 1.611 | 1.554 |
| ProcGr9_2_phydx31 | 1.762 | -1.384 |
| ProcGr10_2_ProcGr2_0 | -1.596 | 0.155 |
| ProcGr10_2_RxGr4_0 | 1.355 | 1.220 |
| RxGr1_2_pastdx14 | -2.57 | -1.919 |
| RxGr2_2_pastdx6 | -1.478 | -3.477 |
| RxGr2_2_marital_2 | 1.49 | 3.437 |
| RxGr3_2_litigat | -1.984 | -0.943 |
| RxGr4_2_RxGr1_0 | -1.136 | 1.059 |
| RxGr4_2_RxGr7_0 | 2.763 | 1.202 |
| RxGr4_2_marital_3 | -3.367 | -1.044 |
| RxGr5_2_duration | -2.529 | -3.336 |

Table 5.4—*Continued*

| Parameters | Training Data | Test Data |
|---|---|---|
| RxGr5_2_pastdx6 | -2.456 | -2.295 |
| RxGr5_2_pastdx12 | 1.451 | 3.225 |
| RxGr5_2_marital_4 | 1.903 | 1.407 |
| RxGr7_2_marital_3 | 4.728 | 5.884 |
| RxGr8_2_phydx15 | 1.908 | 8.130 |
| RxGr8_2_SghxGr6 | 2.898 | 0.771 |

Table 5.5 Comparison of Estimated Regression Standard Errors of the Models

| Parameters | Training Data | Test Data |
|---|---|---|
| Intercept | 3.349 | 4.162 |
| mid_OSW | 0.128 | 0.146 |
| ProcGr2_1_pastdx6 | 0.508 | 1.563 |
| ProcGr4_1_children | 0.676 | 1.741 |
| ProcGr9_1_race | 0.984 | 2.420 |
| ProcGr9_1_phydx3 | 0.468 | 1.438 |
| ProcGr9_1_marital_2 | 0.354 | 0.873 |
| ProcGr10_1_gender | 0.532 | 1.153 |
| ProcGr10_1_phydx6 | 0.402 | 0.798 |
| ProcGr10_1_ProcGr10_0 | 0.387 | 0.677 |
| ProcGr10_1_RxGr2_0 | 0.542 | 1.073 |
| ProcGr11_1_pastdx7 | 0.421 | 0.800 |
| RxGr1_1_duration | 0.868 | 2.149 |
| RxGr1_1_SghxGr11 | 0.736 | 1.614 |
| RxGr1_1_RxGr5_0 | 0.597 | 1.574 |
| RxGr5_1_phydx11 | 0.508 | 0.982 |
| RxGr6_1_pastdx4 | 0.451 | 0.961 |
| RxGr6_1_RxGr7_0 | 0.776 | 1.453 |
| RxGr7_1_phydx20 | 0.586 | 0.761 |
| ProcGr4_2_mid_OSW | 2.376 | 2.588 |
| ProcGr4_2_phydx8 | 0.652 | 0.895 |
| ProcGr9_2_litigat | 0.493 | 0.978 |
| ProcGr9_2_phydx4 | 0.403 | 0.678 |
| ProcGr9_2_phydx31 | 0.503 | 1.169 |

Table 5.5—*Continued*

| Parameters | Training Data | Test Data |
|---|---|---|
| ProcGr10_2_ProcGr2_0 | 0.514 | 1.124 |
| ProcGr10_2_RxGr4_0 | 0.578 | 1.494 |
| RxGr1_2_pastdx14 | 0.67 | 1.991 |
| RxGr2_2_pastdx6 | 0.537 | 1.498 |
| RxGr2_2_marital_2 | 0.409 | 0.923 |
| RxGr3_2_litigat | 0.539 | 1.177 |
| RxGr4_2_RxGr1_0 | 0.688 | 1.724 |
| RxGr4_2_RxGr7_0 | 0.784 | 2.314 |
| RxGr4_2_marital_3 | 0.873 | 2.021 |
| RxGr5_2_duration | 1.054 | 1.995 |
| RxGr5_2_pastdx6 | 0.703 | 1.223 |
| RxGr5_2_pastdx12 | 0.688 | 1.308 |
| RxGr5_2_marital_4 | 0.538 | 1.310 |
| RxGr7_2_marital_3 | 0.716 | 1.437 |
| RxGr8_2_phydx15 | 1.62 | 2.311 |
| RxGr8_2_SghxGr6 | 0.888 | 1.354 |

# Chapter 6 Discussion and Future Research

## 6.1 Discussion

In this research, we have overcome the issue of endogeneity inherent in pain management data by using data mining, probability, and statistics, particularly logistic regression. Two methodologies were developed, one for independent treatments and one for correlated treatments. To accomplish the methodology for Inverse Probability Weighted Method with Independent Treatments, we modified an existing IPTW method since the data has binary, ordinal and/or multinomial and continuous values. This is a special case of the IPTW method when treatments are independent of each other. In the Post_OSW model, we identified 3 independent treatments. Joint weight is then applied to the pain management data and the weighted outcome model is fitted. We compare the weighted outcome model coefficients to the unweighted model coefficients. Most coefficients of the weighted model are smaller than those in the model estimated without using the IPTW method because the effects of the confounding variables have been adjusted for using the IPTW method. In effect, endogeneity, the bias due to patient characteristics, is eliminated using the IPTW method with independent treatments.

The larger data set from the Center (see Chapter 3) was used to develop an Inverse Probability Weighted Method with Correlated Treatments. When the treatments are correlated, the joint weight is needed to apply the IPTW method. The joint distribution of the 10 treatments was decomposed by the Chain Rule of Probability. In the case study, two groups (Group A and B) were generated, each consisting of 5, 10, and 20 factorizations. We build the Logistic model for each treatment and calculated the joint probability under each factorization. For the 5, 10, and 20 factorizations, the results (Figure 5.4 to 5.9) show that the Groups A and B are very similar to each other so either can be chosen to calculate the joint weight. Then we fit 5, 10, and 20 factorization

weighted outcome models and compared the resulting estimates to the unweighted outcome model. For most variables, the coefficients of the weighted outcome models are smaller than the unweighted model coefficients as seen in Table 6.1.

Table 6.1 Comparison of Smaller Coefficients and Standard Errors in Weighted and Unweighted Models

| Weighted Model | Number of smaller coefficients to unweighted model | Number of standard errors to unweighted model |
|---|---|---|
| 5 Factorizations | 28 out of 40 | 33 out of 40 |
| 10 Factorizations | 30 out of 40 | 34 out of 40 |
| 20 Factorizations | 31 out of 40 | 34 out of 40 |

Also, in Table 6.1, most of the standard errors of the weighted model are smaller than the standard error of the unweighted model. To decide on how many factorizations to use in this research, we compared the maximum differences of Groups A and B of the 5, 10, 20 factorizations. In this research we have chosen to use the 20 factorizations since it is slightly better than the other factorizations.

Comparing the results of the unweighted and the weighted model, we can see that overall the coefficients and standard errors of the weighted model are smaller than those for the unweighted models. Again, this means the bias due to patient characteristics has been eliminated using the IPTW method with correlated treatments for this application. Thus, both the IPTW methods with independent treatments and with correlated treatments are able to eliminate endogeneity.

## 6.2 Future Research

The pain management raw data from the Center has too many missing values. Even though the data set has many outcome variables, due to missing values, we only have two outcome variables. More data are needed to explore more outcome variables.

In pain management data, as the dimension of the data increases, the treatments identified in the unweighted model have some treatments that are independent of other treatments, while some are correlated with other treatments given the confounding variables (Appendix B). Thus the methodology we developed for Inverse Probability Weighted Method with Correlated Treatments is useful and can be used for general method to eliminate the bias due to patient characteristics. In this research when factorization was reached 20, we can see the maximum differences level off about 8. Thus we chose 20 factorizations to calculate the joint weight. However in the future research, when using the general method for various applications, more factorizations may be needed to choose the optimum number of factorizations. It is recommended to create software code to run the entire process automatically.

When we tested for independence of treatments, we found that some of treatments are independent of each other but not all. This is illustrated in Table 6.2.

Table 6.2 Treatment Independency Test Result (*p*-values from T-test)

| | ProcGr4_2 | ProcGr9_2 | ProcGr10_2 | RxGr1_2 | RxGr2_2 | RxGr3_2 | RxGr4_2 | RxGr5_2 | RxGr7_2 | RxGr8_2 |
|---|---|---|---|---|---|---|---|---|---|---|
| **ProcGr4_2** | | | | | | | **0.0173** | **0.0466** | | **0.0473** |
| **ProcGr9_2** | | | **0.0001** | | | | **0.0383** | | | |
| **ProcGr10_2** | | **0.0086** | | | | | | | | |
| **RxGr1_2** | | | | | | | | | | |
| **RxGr2_2** | | | | | | | | | | |
| **RxGr3_2** | | | | | | | | | | |
| **RxGr4_2** | | | | | | | | | **0.0131** | |
| **RxGr5_2** | **0.0042** | | | | | | | | | |
| **RxGr7_2** | | | | **0.0167** | | | | | | |
| **RxGr8_2** | | | | | | | | | | |

In this table, *p*-values less than 0.05 (significant) are shown, and *p*-values greater than or equal to 0.05 (insignificant) are left as blank. The 2 highlighted rows and columns indicate that 2 treatments, RxGr2_2 and RxGr3_2, are independent of all other treatments. The approach taken in this research treats all treatments as correlated and applies the IPTW Method with Correlated Treatments. An alternate approach is treat independent and correlated treatments separately as shown in Figure 6.1.

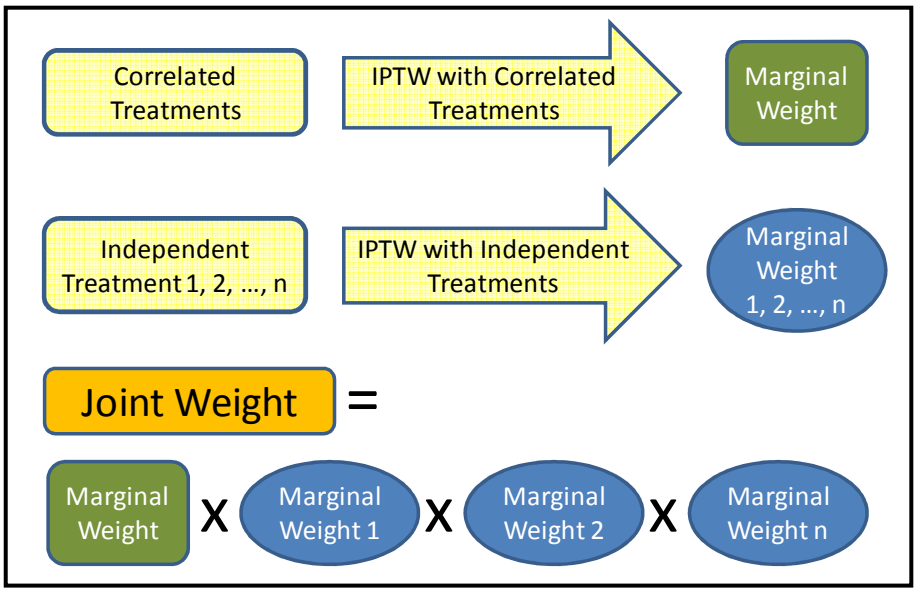



Figure 6.1 IPTW Approach with Mixed Treatments

One Marginal weight for each observation can be calculated for the correlated treatments using the IPTW with Correlated Treatments. For independent treatments, marginal weights per independent treatment per observation can be found for each independent treatment. The joint weight then is the product of these marginal weights. This could reduce the generating time for factorization and could have better performance.

This research has been devoted to mimicking observational data to randomized data applying the IPTW method while building state transition models. Further research is needed to perform optimization.

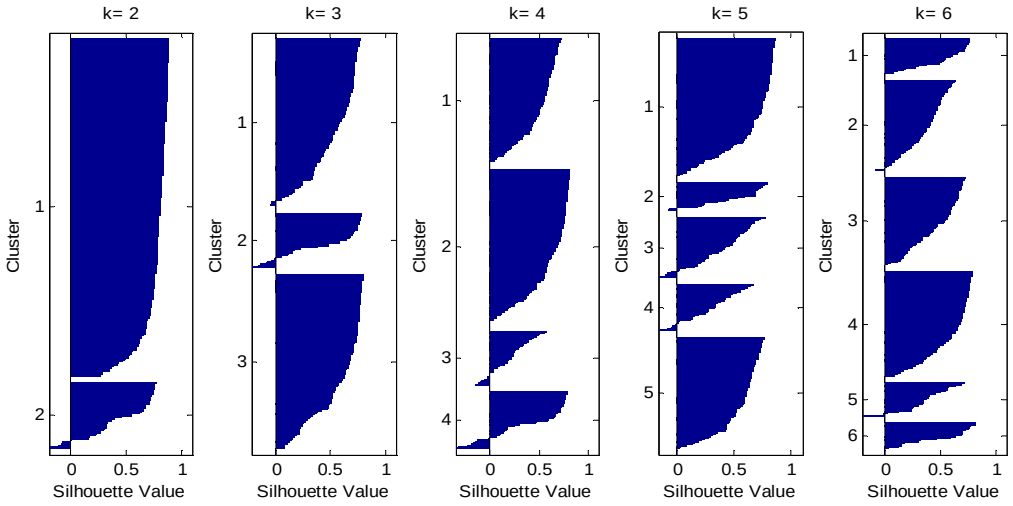
# Appendix A

## Data and Models

## A1. *K*-means Clustering on the Larger Data Set

**Data used for clustering: training data set of the larger data set (235x89)**

avg_sil = 0.7278
avg_sil = 0.7278 0.5430
avg_sil = 0.7278 0.5430 0.4824
avg_sil = 0.7278 0.5430 0.4824 0.5241
avg_sil = 0.7278 0.5430 0.4824 0.5241 0.4799




## A2. Stepwise Selection Model C, D & E and K-Fold Cross-Validation

**Model Type:**

- Model C:
  all risk factors + (treatment stage 1,2 *risk factor) interactions
- Model D:
  all risk factors + (stage 2 treatment *risk factor ) + (stage 2 treatment *stage 1 treatment) interactions
- Model E:
  (1) Run preliminary model w/only main risk factor +treatment
  → Identify significant variables
  (2) Run w/ only significant main + interactions between risk + trt.
  that were significant in preliminary model

***Model C , D and E at α=0.05 stepwise selected variables***

Response variable: Post_OSW

| | ***Model C*** | ***Model D*** | ***Model E*** |
|---|---|---|---|
| Main factor | 1 | 1 | 4 |
| (Stage 2 trt. x Risk factor) interaction | 17 | 0 | 0 |
| (Stage 2 trt. x Stage 1 trt) interaction | 21 | 40 | 0 |

***Model C , D and E  at α=0.05 stepwise selected model***

Response variable: Post_OSW

| **Model C** α=0.05 ($R^2$ = 0.9063) | **Model D** α=0.05 ($R^2$ =0.8979) | **Model E** α=0.05($R^2$ =0.6993) |
|---|---|---|
| **Main factor selected by stepwise:** | | |
| mid_OSW | RxGr5_1 | RxGr7_2, mid_OSW, phydx20, ProcGr4_1 |
| **(Stage 1 trt. x Risk factor) interactions selected by stepwise** | | |
| ProcGr2_1_pastdx6 | | |
| ProcGr4_1_children | | |
| ProcGr9_1_race | | |
| ProcGr9_1_phydx3 | | |
| ProcGr9_1_marital_2 | | |
| ProcGr10_1_gender | | |
| ProcGr10_1_phydx6 | | |
| ProcGr10_1_ProcGr10_0 | | |
| ProcGr10_1_RxGr2_0 | | |
| ProcGr11_1_pastdx7 | | |
| RxGr1_1_duration | | |
| RxGr1_1_SghxGr11 | | |
| RxGr1_1_RxGr5_0 | | |
| RxGr5_1_phydx11 | | |
| RxGr6_1_pastdx4 | | |
| RxGr6_1_RxGr7_0 | | |
| RxGr7_1_phydx20 | | |
| **(Stage 2 trt. x Risk factor) interactions selected by stepwise** | | |
| ProcGr4_2_mid_OSW | ProcGr1_2_litigat | |
| ProcGr4_2_phydx8 | ProcGr1_2_marital_1 | |
| ProcGr9_2_litigat | ProcGr1_2_marital_2 | |
| ProcGr9_2_phydx4 | ProcGr2_2_ProcGr10_0 | |
| ProcGr9_2_phydx31 | ProcGr4_2_phydx8 | |
| ProcGr10_2_ProcGr2_0 | ProcGr4_2_pastdx8 | |
| ProcGr10_2_RxGr4_0 | ProcGr10_2_litigat | |
| RxGr1_2_pastdx14 | ProcGr10_2_phydx31 | |
| RxGr2_2_pastdx6 | ProcGr10_2_pastdx3 | |
| RxGr2_2_marital_2 | ProcGr10_2_RxGr7_0 | |
| RxGr3_2_litigat | RxGr2_2_ProcGr4_1 | |
| RxGr4_2_RxGr1_0 | RxGr2_2_RxGr2_1 | |
| RxGr4_2_RxGr7_0 | RxGr2_2_RxGr5_1 | |
| RxGr4_2_marital_3 | RxGr3_2_phydx20 | |
| RxGr5_2_duration | RxGr3_2_ProcGr10_1 | |
| RxGr5_2_pastdx6 | RxGr3_2_RxGr5_1 | |
| RxGr5_2_pastdx12 | RxGr4_2_ProcGr9_0 | |
| RxGr5_2_marital_4 | RxGr4_2_ProcGr10_0 | |
| RxGr7_2_marital_3 | RxGr4_2_pastdx6 | |
| RxGr8_2_phydx15 | RxGr4_2_pastdx20 | |
| RxGr8_2_SghxGr6 | RxGr4_2_RxGr1_0 | |
| | RxGr4_2_RxGr5_0 | |

| Model C<br>α=0.05 ($R^2$ = 0.9063) | Model D<br>α=0.05 ($R^2$ =0.8979) | Model E<br>α=0.05($R^2$ =0.6993) |
|---|---|---|
| | RxGr5_2_duration | |
| | RxGr5_2_phydx8 | |
| | RxGr5_2_phydx11 | |
| | RxGr5_2_ProcGr1_0 | |
| | RxGr5_2_RxGr7_0 | |
| | RxGr5_2_ProcGr10_1 | |
| | RxGr5_2_RxGr4_1 | |
| | RxGr6_2_duration | |
| | RxGr6_2_phydx5 | |
| | RxGr6_2_SghxGr6 | |
| | RxGr6_2_SghxGr11 | |
| | RxGr6_2_marital_4 | |
| | RxGr6_2_RxGr7_1 | |
| | RxGr7_2_marital_2 | |
| | RxGr7_2_marital_3 | |
| | RxGr7_2_ProcGr9_1 | |
| | RxGr8_2_mid_OSW | |
| | RxGr8_2_SghxGr11 | |

**K-Fold Cross-Validation on Model C , D and E at *α=0.05***

| | Model C | Model D | Model E |
|---|---|---|---|
| 3 – Fold CV Overall MS ($S^2$) | 16.952 | 19.709 | 24.905 |
| 5 – Fold CV Overall MS ($S^2$) | 16.558 | 19.787 | 24.816 |
| 8 – Fold CV Overall MS ($S^2$) | 16.552 | 19.760 | 24.702 |
| 10 – Fold CV Overall MS ($S^2$) | 16.062 | 19.775 | 24.812 |

**SAS Outputs**

Model D:

***Dependent Variable: Post_OSW***

***Stepwise Selection: Step 59***

***Variable RxGr5_2_ProcGr10_1 Entered: R-Square = 0.8979 and C(p) = .***

| Analysis of Variance | | | | | |
|---|---|---|---|---|---|
| **Source** | **DF** | **Sum of Squares** | **Mean Square** | **F Value** | **Pr > F** |
| **Model** | 41 | 14123 | 344.46809 | 41.40 | <.0001 |
| **Error** | 193 | 1605.88928 | 8.32067 | | |
| **Corrected Total** | 234 | 15729 | | | |

| Variable | Parameter Estimate | Standard Error | Type II SS | F Value | Pr > F |
|---|---|---|---|---|---|
| Intercept | 9.31624 | 1.10850 | 587.72221 | 70.63 | <.0001 |
| RxGr5_1 | 2.60665 | 0.48254 | 242.79921 | 29.18 | <.0001 |
| ProcGr1_2_litigat | -1.42794 | 0.28332 | 211.35714 | 25.40 | <.0001 |
| ProcGr1_2_marital_1 | 2.69035 | 0.31688 | 599.77731 | 72.08 | <.0001 |
| ProcGr1_2_marital_2 | 1.16779 | 0.29719 | 128.47541 | 15.44 | 0.0001 |
| ProcGr2_2_ProcGr10_0 | 1.27664 | 0.32370 | 129.41982 | 15.55 | 0.0001 |
| ProcGr4_2_phydx8 | -3.33567 | 0.91645 | 110.23250 | 13.25 | 0.0004 |
| ProcGr4_2_pastdx8 | 2.66640 | 0.98057 | 61.52519 | 7.39 | 0.0071 |
| ProcGr10_2_litigat | -0.85101 | 0.29862 | 67.57428 | 8.12 | 0.0049 |
| ProcGr10_2_phydx31 | 1.47586 | 0.31874 | 178.39670 | 21.44 | <.0001 |
| ProcGr10_2_pastdx3 | 1.19204 | 0.33730 | 103.92481 | 12.49 | 0.0005 |
| ProcGr10_2_RxGr7_0 | -1.34969 | 0.39574 | 96.78290 | 11.63 | 0.0008 |
| RxGr2_2_ProcGr4_1 | -2.34958 | 0.39545 | 293.72873 | 35.30 | <.0001 |
| RxGr2_2_RxGr2_1 | -1.14057 | 0.47139 | 48.71362 | 5.85 | 0.0165 |
| RxGr2_2_RxGr5_1 | 3.61068 | 0.53069 | 385.17518 | 46.29 | <.0001 |
| RxGr3_2_phydx20 | -1.98230 | 0.35670 | 256.97817 | 30.88 | <.0001 |
| RxGr3_2_ProcGr10_1 | 1.59920 | 0.37454 | 151.69159 | 18.23 | <.0001 |
| RxGr3_2_RxGr5_1 | 3.01304 | 0.62413 | 193.91523 | 23.31 | <.0001 |
| RxGr4_2_ProcGr9_0 | -1.11190 | 0.38097 | 70.87695 | 8.52 | 0.0039 |
| RxGr4_2_ProcGr10_0 | -1.07597 | 0.37466 | 68.62350 | 8.25 | 0.0045 |
| RxGr4_2_pastdx6 | 0.67985 | 0.26562 | 54.50978 | 6.55 | 0.0112 |
| RxGr4_2_pastdx20 | 0.95093 | 0.40831 | 45.13091 | 5.42 | 0.0209 |
| RxGr4_2_RxGr1_0 | -1.32377 | 0.43294 | 77.79135 | 9.35 | 0.0025 |
| RxGr4_2_RxGr5_0 | -1.35567 | 0.41596 | 88.38412 | 10.62 | 0.0013 |
| RxGr5_2_duration | -6.67251 | 0.80041 | 578.24860 | 69.50 | <.0001 |
| RxGr5_2_phydx8 | -2.10981 | 0.60526 | 101.10276 | 12.15 | 0.0006 |
| RxGr5_2_phydx11 | -1.32810 | 0.33010 | 134.68380 | 16.19 | <.0001 |
| RxGr5_2_ProcGr1_0 | -0.58694 | 0.24015 | 49.70242 | 5.97 | 0.0154 |
| RxGr5_2_RxGr7_0 | 3.46252 | 0.56033 | 317.72676 | 38.19 | <.0001 |
| RxGr5_2_ProcGr10_1 | -0.83241 | 0.41760 | 33.06165 | 3.97 | 0.0476 |
| RxGr5_2_RxGr4_1 | 2.07565 | 0.46126 | 168.48949 | 20.25 | <.0001 |
| RxGr6_2_duration | 5.95168 | 0.75983 | 510.51332 | 61.35 | <.0001 |

| Variable | Parameter Estimate | Standard Error | Type II SS | F Value | Pr > F |
|---|---|---|---|---|---|
| RxGr6_2_phydx5 | 0.90220 | 0.41023 | 40.24413 | 4.84 | 0.0290 |
| RxGr6_2_SghxGr6 | 2.04033 | 0.55491 | 112.49116 | 13.52 | 0.0003 |
| RxGr6_2_SghxGr11 | -4.38989 | 0.83781 | 228.44201 | 27.45 | <.0001 |
| RxGr6_2_marital_4 | 2.07036 | 0.36263 | 271.21935 | 32.60 | <.0001 |
| RxGr6_2_RxGr7_1 | -4.07999 | 0.50884 | 534.95419 | 64.29 | <.0001 |
| RxGr7_2_marital_2 | 1.58130 | 0.30439 | 224.55376 | 26.99 | <.0001 |
| RxGr7_2_marital_3 | 5.29252 | 0.52702 | 839.12371 | 100.85 | <.0001 |
| RxGr7_2_ProcGr9_1 | -1.17153 | 0.35311 | 91.58812 | 11.01 | 0.0011 |
| RxGr8_2_mid_OSW | -16.51912 | 0.53022 | 8076.35875 | 970.64 | <.0001 |
| RxGr8_2_SghxGr11 | 6.33337 | 0.83934 | 473.75394 | 56.94 | <.0001 |

***Model E:Dependent Variable: Post_OSW***

***Stepwise Selection: Step 4***

***Variable ProcGr4_1 Entered: R-Square = 0.6993 and C(p) = 3.2899***

| Analysis of Variance | | | | | |
|---|---|---|---|---|---|
| Source | DF | Sum of Squares | Mean Square | F Value | Pr > F |
| Model | 4 | 11000 | 2749.92298 | 133.73 | <.0001 |
| Error | 230 | 4729.38892 | 20.56256 | | |
| Corrected Total | 234 | 15729 | | | |

| Variable | Parameter Estimate | Standard Error | Type II SS | F Value | Pr > F |
|---|---|---|---|---|---|
| Intercept | 1.28629 | 0.74094 | 61.97130 | 3.01 | 0.0839 |
| RxGr7_2 | -1.94072 | 0.66745 | 173.84781 | 8.45 | 0.0040 |
| mid_OSW | 0.84163 | 0.03659 | 10880 | 529.12 | <.0001 |
| phydx20 | 2.83852 | 1.02105 | 158.91522 | 7.73 | 0.0059 |
| ProcGr4_1 | 2.55393 | 1.18457 | 95.58120 | 4.65 | 0.0321 |

**Model C at α=0.05 $ α=0.025 Stepwise Selected Model**

Response variable: Post_OSW

| | **Model C (17, 21)** α=0.05 ($R^2$ = 0.9063) | **Model C (11, 12)** α=0.025 ($R^2$ = 0.8578) |
|---|---|---|
| Main factor selected by stepwise | *mid_OSW* | *mid_OSW* |
| (Stage 1 trt. x Risk factor) interactions selected by stepwise | ProcGr2_1_pastdx6 | ProcGr2_1_pastdx6 |
| | ProcGr4_1_children | ProcGr4_1_children |
| | ProcGr9_1_race | ProcGr10_1_phydx6 |
| | ProcGr9_1_phydx3 | ProcGr10_1_ProcGr10_0 |
| | ProcGr9_1_marital_2 | RxGr1_1_duration |
| | ProcGr10_1_gender | RxGr1_1_SghxGr11 |
| | ProcGr10_1_phydx6 | RxGr1_1_RxGr5_0 |
| | ProcGr10_1_ProcGr10_0 | RxGr5_1_phydx11 |
| | ProcGr10_1_RxGr2_0 | RxGr6_1_pastdx4 |
| | ProcGr11_1_pastdx7 | RxGr6_1_RxGr1_0 |
| | RxGr1_1_duration | RxGr7_1_phydx20 |
| | RxGr1_1_SghxGr11 | |
| | RxGr1_1_RxGr5_0 | |
| | RxGr5_1_phydx11 | |
| | RxGr6_1_pastdx4 | |
| | RxGr6_1_RxGr7_0 | |
| | RxGr7_1_phydx20 | |
| (Stage 2 trt. x Risk factor) interactions selected by stepwise | ProcGr4_2_mid_OSW | ProcGr4_2_phydx8 |
| | ProcGr4_2_phydx8 | ProcGr9_2_litigat |
| | ProcGr9_2_litigat | ProcGr9_2_phydx31 |
| | ProcGr9_2_phydx4 | ProcGr10_2_ProcGr2_0 |
| | ProcGr9_2_phydx31 | ProcGr10_2_RxGr4_0 |
| | ProcGr10_2_ProcGr2_0 | RxGr1_2_pastdx14 |
| | ProcGr10_2_RxGr4_0 | RxGr2_2_pastdx6 |
| | RxGr1_2_pastdx14 | RxGr2_2_marital_2 |
| | RxGr2_2_pastdx6 | RxGr6_2_status |
| | RxGr2_2_marital_2 | RxGr7_2_marital_3 |
| | RxGr3_2_litigat | RxGr8_2_phydx15 |
| | RxGr4_2_RxGr1_0 | RxGr8_2_SghxGr6 |
| | RxGr4_2_RxGr7_0 | |
| | RxGr4_2_marital_3 | |
| | RxGr5_2_duration | |
| | RxGr5_2_pastdx6 | |
| | RxGr5_2_pastdx12 | |
| | RxGr5_2_marital_4 | |
| | RxGr7_2_marital_3 | |
| | RxGr8_2_phydx15 | |
| | RxGr8_2_SghxGr6 | |

*Model C at Alpha = 0.025 Dependent Variable: Post_OSW*

*Stepwise Selection: Step 28*

*Variable RxGr1_1_RxGr5_0 Entered: R-Square = 0.8578 and C(p) = .*

| Analysis of Variance | | | | | |
|---|---|---|---|---|---|
| Source | DF | Sum of Squares | Mean Square | F Value | Pr > F |
| Model | 24 | 13493 | 562.19915 | 52.79 | <.0001 |
| Error | 210 | 2236.30125 | 10.64905 | | |
| Corrected Total | 234 | 15729 | | | |

| Variable | Parameter Estimate | Standard Error | Type II SS | F Value | Pr > F |
|---|---|---|---|---|---|
| Intercept | -1.32448 | 1.22736 | 12.40091 | 1.16 | 0.2818 |
| mid_OSW | 0.86160 | 0.02846 | 9760.04365 | 916.52 | <.0001 |
| ProcGr2_1_pastdx6 | 2.00958 | 0.35073 | 349.60793 | 32.83 | <.0001 |
| ProcGr4_1_children | -1.93711 | 0.44149 | 205.00689 | 19.25 | <.0001 |
| ProcGr10_1_phydx6 | 0.66928 | 0.23416 | 86.99937 | 8.17 | 0.0047 |
| ProcGr10_1_ProcGr10_0 | -0.69620 | 0.23288 | 95.17244 | 8.94 | 0.0031 |
| RxGr1_1_duration | 1.88784 | 0.61088 | 101.70198 | 9.55 | 0.0023 |
| RxGr1_1_SghxGr11 | 1.87621 | 0.45580 | 180.43710 | 16.94 | <.0001 |
| RxGr1_1_RxGr5_0 | -0.86992 | 0.38377 | 54.71723 | 5.14 | 0.0244 |
| RxGr5_1_phydx11 | -1.67531 | 0.31649 | 298.38900 | 28.02 | <.0001 |
| RxGr6_1_pastdx4 | 1.00671 | 0.29381 | 125.02386 | 11.74 | 0.0007 |
| RxGr6_1_RxGr1_0 | -1.04505 | 0.42453 | 64.52985 | 6.06 | 0.0146 |
| RxGr7_1_phydx20 | -1.06883 | 0.32707 | 113.72443 | 10.68 | 0.0013 |
| ProcGr4_2_phydx8 | -1.57900 | 0.33702 | 233.76077 | 21.95 | <.0001 |
| ProcGr9_2_litigat | -1.81677 | 0.30915 | 367.75453 | 34.53 | <.0001 |
| ProcGr9_2_phydx31 | 2.04304 | 0.32526 | 420.14003 | 39.45 | <.0001 |
| ProcGr10_2_ProcGr2_0 | -1.92655 | 0.33027 | 362.35159 | 34.03 | <.0001 |
| ProcGr10_2_RxGr4_0 | 1.58844 | 0.36425 | 202.51865 | 19.02 | <.0001 |
| RxGr1_2_pastdx14 | -1.31318 | 0.43266 | 98.10174 | 9.21 | 0.0027 |
| RxGr2_2_pastdx6 | -1.56990 | 0.37369 | 187.94773 | 17.65 | <.0001 |
| RxGr2_2_marital_2 | 1.16309 | 0.26613 | 203.40334 | 19.10 | <.0001 |
| RxGr6_2_status | 1.28233 | 0.52777 | 62.86576 | 5.90 | 0.0160 |
| RxGr7_2_marital_3 | 3.94577 | 0.45958 | 784.98710 | 73.71 | <.0001 |
| RxGr8_2_phydx15 | 2.02682 | 0.70261 | 88.61718 | 8.32 | 0.0043 |
| RxGr8_2_SghxGr6 | 1.58290 | 0.54043 | 91.35514 | 8.58 | 0.0038 |

*Bounds on condition number: 2.3998, 872.39*

*All variables left in the model are significant at the 0.0250 level.*

**Summary on 3, 5, 8, 10 fold Cross Validation on model C, D, and E**

**K- Fold Cross-Validation on Model C_0.05 (full) & Model D_0.05**

| | Model C_0.05 | Model D_0.05 |
|---|---|---|
| 3 – Fold CV Overall MS ($S^2$) | 16.752 | 17.302 |
| 5 – Fold CV Overall MS ($S^2$) | 16.257 | 16.795 |
| 8 – Fold CV Overall MS ($S^2$) | 16.251 | 16.776 |
| 10 – Fold CV Overall MS ($S^2$) | 16.081 | 16.534 |

**Model E:**

(1) Run preliminary model w/only main risk factor +treatment → Identify significant variables

(2) Run w/ only significant main + interactions between risk + trt. that were significant in preliminary model

**K – Fold Cross-Validation on Model E_0.05 & Model E_0.1**

| | Model E_0.05 | Model E_0.1 |
|---|---|---|
| 3 – Fold CV Overall MS ($S^2$) | 23.855 | 24.497 |
| 5 – Fold CV Overall MS ($S^2$) | 23.815 | 24.60 |
| 8 – Fold CV Overall MS ($S^2$) | 23.800 | 24.147 |
| 10 – Fold CV Overall MS ($S^2$) | 23.811 | 24.203 |

**Response variable: Post_OSW**

| | Model E_0.1 | Model E_0.05 | Model E_0.01 |
|---|---|---|---|
| Main factor | 2 | 4 | 1 |
| (Stage 2 trt. x Risk factor) interaction | 3 | 0 | 0 |
| (Stage 2 trt. x Stage 1 trt) interaction | 1 | 0 | 0 |

Model E_0.01:
Post_OSW ~ mid_osw
Model E_0.05:
Post_OSW ~ mid_osw procGr4_1 RxGr7_2 Phydx20 (same as preliminary model)
Model E_0.1:
Post_OSW ~ RxGr7_2 mid_osw ProcGr4_2_pastdx4 ProcGr4_2_ProcGr4_1 RxGr7_2_mid_OSW RxGr7_2_phydx20

Appendix B

IPTW

**B1. Goodness of Fit Chisq Test (using smaller data set 89 patients)**

**RxGr42**

**Expected Frequency (*ei*) and $x^2$ Calculations**

| Categories (RxGr42) | Observed Frequency (O*i*) | Expected Frequency (e*i*) |
|---|---|---|
| 0 | 58 | 38.5 |
| 1 | 5 | 19.2 |
| 2 | 25 | 24.8 |
| 3 | 1 | 6.5 |

| $\mu$= 0.6516854, $\sigma$ = 0.930556 | From Normal Probability Table |
|---|---|
| Z1 = (0 – 0.65) / 0.93 = - 0.7<br>Z2 = (1 – 0.65) / 0.93 = 0.38<br>Z3 = (2 – 0.65) / 0.93 = 1.45<br>Z4 = (3 – 0.65) / 0.93 = 2.69 | P (Z< -0.7) = 0.4325<br>P (Z< 0.38) = 0.6480<br>P (Z< 1.45) = 0.9265<br>P (Z< 2.69) = 0.9965 |
| Probability: | Expected Frequency: |
| P (0) = 0.4325<br>P (1) = 0.6480 - 0.4325 = 0.2155<br>P (2) = 0.9265 - 0.6480 = 0.2785<br>P (3) = 0.0735 | E(0) = 0.4325 x 89 = 38.5<br>E(1) = 0.2155 x 89 = 19.2<br>E(2) = 0.2785 x 89 = 24.8<br>E(3) = 0.0735 x 89 = 6.5 |
| $x^2$ Test | |
| E(3) = 0.0735 x 89 = 6.5<br>$x^2$ = [(58–38.5) $^2$/ 38.5] + [(5–19.2) $^2$/ 19.2] + [(25–24.8) $^2$/ 24.8] + [(1–6.5) $^2$/ 6.5]<br>= 9.88 + 10.5 + 0.002 + 4.65 =25.03<br>DF = 4 – 1 =3<br>$x^2$(3, α = 0.05) = 7.815<br>25.03 > $x^2$(3, α = 0.05) = 7.815 → Reject $H_0$ | |

We conclude that there is sufficient evidence that the slope is not same. Therefore RxGr42 data is multinomial.

SAS output for Chi-Squared Test for RxGr42

***GOODNESS OF FIT Chisq Test (RxGr42)***
***The FREQ Procedure***

| RxGr42 | Frequency | Percent | Test Percent |
|---|---|---|---|
| 0 | 58 | 65.17 | 43.25 |
| 1 | 5 | 5.62 | 21.55 |
| 2 | 25 | 28.09 | 27.85 |

| RxGr42 | Frequency | Percent | Test Percent |
|---|---|---|---|
| 3 | 1 | 1.12 | 7.35 |

| Chi-Square Test for Specified Proportions | |
|---|---|
| Chi-Square | 25.0653 |
| DF | 3 |
| Pr > ChiSq | <.0001 |

***Sample Size = 89***

**RxGr32**

| Categories (RxGr32) | Observed Frequency (O*i*) | Expected Frequency (e*i*) |
|---|---|---|
| 0 | 71 | 28.4 |
| 1 | 6 | 42.5 |
| 2 | 10 | 16.6 |
| 3 | 2 | 1.5 |

**Expected Frequency (e*i*) and $x^2$ Calculations**

| $\mu$= 0.3595506, $\sigma$ = 0.7723516 | From Normal Probability Table |
|---|---|
| Z1 = (0 – 0.36) / 0.77 = - 0.47<br>Z2 = (1 – 0.36) / 0.77 = 0.83<br>Z3 = (2 – 0.36) / 0.77 = 2.13<br>Z4 = (3 – 0.36) / 0.77 = 3.43 | P (Z< -0.47) = 0.3192<br>P (Z< 0.83) = 0.7967<br>P (Z< 2.13) = 0.9834<br>P (Z< 3.43) = 0.9997 |
| Probability: | Expected Frequency: |
| P (0) = 0.3192<br>P (1) = 0.7967- 0.3192 = 0.4775<br>P (2) = 0.9834 - 0.7967 = 0.1867<br>P (3) = 0.0166 | E(0) = 0.3192 x 89 = 28.4<br>E(1) = 0.4775 x 89 = 42.5<br>E(2) = 0.1867 x 89 = 16.6<br>E(3) = 0.0166 x 89 = 1.5 |
| $x^2$ Test | |
| Combining E(2) and E(3) = 18.1<br>$x^2$ = [(71 – 28.4) $^2$/ 28.4] + [(6 – 42.5) $^2$/ 42.5] + [(12 – 18.1) $^2$/ 18.1]<br>= 63.9 + 31.3 + 2.1 = 97.3<br>DF = 3 – 1 =2<br>$x^2$(2, α = 0.05) = 5.991<br>97.3 > $x^2$(2, α = 0.05) = 5.991 → Reject $H_0$ | |

We conclude that there is sufficient evidence that the slope is not same. Therefore RxGr32 data is multinomial.

SAS output for Chi-Squared Test for RxGr32

## GOODNESS OF FIT Chisq Test (RxGr32)
## The FREQ Procedure

| RxGr32 | Frequency | Percent | Test Percent |
|---|---|---|---|
| 0 | 71 | 79.78 | 31.92 |
| 1 | 6 | 6.74 | 47.75 |
| 2 | 12 | 13.48 | 20.33 |

| Chi-Square Test for Specified Proportions | |
|---|---|
| Chi-Square | 97.2507 |
| DF | 2 |
| Pr > ChiSq | <.0001 |

## Sample Size = 89

**B2. Goodness of Fit Chisq Test (using train data set 235 patients)**

State the Hypotheses:

$H_0$: The data are consistent with a specified distribution.

$H_a$: The data are not consistent with a specified distribution.

Formulate an Analysis Plan

- α=0.05
- Test method. Use the chi-square goodness of fit test to determine whether observed sample frequencies differ significantly from expected frequencies specified in the null hypothesis.

Analyze Sample Data

**RxGr1_2**

| Categories (RxGr1_2) | Observed Frequency (O*i*) | Expected Frequency (e*i*) |
|---|---|---|
| 0 | 198 | 81 |
| 1 | 13 | 122 |
| 2 | 21 | 31 |
| 3 | 3 | 1 |

Expected frequency counts. The expected frequency counts at each level of the categorical variable are equal to the sample size times the hypothesized proportion from the null hypothesis

**Expected Frequency (e*i*) and $x^2$ Calculations**

| $\mu$= 0.272340426, $\sigma$ = 0.673416860 | From Normal Probability Table |
|---|---|
| Z1 = (0 – 0.27) / 0.67 = - 0.40<br>Z2 = (1 – 0.27) / 0.67 = 1.09<br>Z3 = (2 – 0.27) / 0.67 = 2.58<br>Z4 = (3 – 0.27) / 0.67 = 4.07 | P (Z< -0.4) = 0.3446<br>P (Z< 1.09) = 0.8621<br>P (Z< 2.58) = 0.9951<br>P (Z< 4.07) = 0.9998 |
| Probability: | Expected Frequency: |
| P (0) = 0.3446<br>P (1) = 0.8621- 0.3446= 0.5175<br>P (2) = 0.9951- 0.8621= 0.1330<br>P (3) = 0.0049 | E(0) = 0.3446 x 235 = 81<br>E(1) = 0.5175 x 235 = 122<br>E(2) = 0.1330 x 235 = 31<br>E(3) = 0.0049 x 235 = 1 |

$x^2$ Test Statistics:

$$X^2 = \sum \frac{(\text{observed - expected})^2}{\text{expected}}$$

Combining E(2) and E(3) = 32 (b/c The expected value of the number of sample observations in each level of the variable is at least 5).

$x^2$ = [(198 – 81) $^2$/ 81] + [(13 – 122) $^2$/ 122] + [(24 – 32) $^2$/ 32
= 268.38

Degrees of freedom. The degrees of freedom (DF) are equal to the number of levels (k) of the categorical variable minus 1: DF = k - 1 .

DF = 3– 1 =2

$x^2$(2, α = 0.05) = 5.991
268.38> $x^2$(2, α = 0.05) = 5.991→ Reject $H_0$

We conclude that there is sufficient evidence that the slope is not same (not constant). Therefore RxGr1_2 data is multinomial (nominal).

SAS output for Chi-Squared Test for RxGr1_2

***The SAS System***
***GOODNESS OF FIT ANALYSIS of RxGr1_2***

## The FREQ Procedure

| RxGr1_2 | Frequency | Percent | Test Percent |
|---|---|---|---|
| 1 | 13 | 5.53 | 34.46 |
| 0 | 198 | 84.26 | 51.75 |
| 2 | 21 | 8.94 | 13.30 |
| 3 | 3 | 1.28 | 0.49 |

| Chi-Square Test for Specified Proportions | |
|---|---|
| Chi-Square | 111.3807 |
| DF | 3 |
| Pr > ChiSq | <.0001 |

*Sample Size = 235*

**RxGr2_2**

| Categories (RxGr32) | Observed Frequency (O*i*) | Expected Frequency (e*i*) |
|---|---|---|
| 0 | 168 | 64 |
| 1 | 12 | 93 |
| 2 | 49 | 59 |
| 3 | 6 | 18 |

**Expected Frequency (e*i*) and $x^2$ Calculations**

| $\mu$= 0.5447, $\sigma$ = 0.9045 | From Normal Probability Table |
|---|---|
| Z1 = (0 – 0.54) / 0.90 = - 0.60<br>Z2 = (1 – 0.54) / 0.90 = 0.51<br>Z3 = (2 – 0.54) / 0.90 = 1.62<br>Z4 = (3 – 0.54) / 0.90 = 2.73 | P (Z< -0.60) = 0.2743<br>P (Z< 0.51) = 0.6950<br>P (Z< 1.62) = 0.9474<br>P (Z< 2.73) = 0.9968 |
| Probability: | Expected Frequency: |
| P (0) = 0.2743<br>P (1) = 0.6950- 0.2981 = 0.3969<br>P (2) = 0.9474- 0.6950= 0.2524<br>P (3) = 0.0764 | E(0) = 0.2743 x 235 = 64<br>E(1) = 0.3969 x 235 = 93<br>E(2) = 0.2524 x 235 = 59<br>E(3) = 0.0764 x 235 = 18 |
| $x^2$ Test | |
| $x^2$ = [(168 – 64) $^2$/ 64] + [(12 – 93 $^2$/ 93] + [(49 – 59) $^2$/ 59] + [(6 – 18) $^2$/ 18] = 237.22<br>DF = 4 – 1 =3<br>$x^2$(3, α = 0.05) = 7.815<br>237.22> $x^2$(3, α = 0. 05) = 7.815<br>97.3 > $x^2$(2, α = 0.05) = 5.991 → Reject $H_0$ | |

We conclude that there is sufficient evidence that the slope is not same. Therefore RxGr2_2 data is multinomial .

SAS output for Chi-Squared Test for RxGr2_2

***The SAS System***
***GOODNESS OF FIT ANALYSIS of RxGr2_2***
***The FREQ Procedure***

| RxGr2_2 | Frequency | Percent | Test Percent |
|---|---|---|---|
| 0 | 168 | 71.49 | 27.43 |
| 1 | 12 | 5.11 | 7.64 |
| 2 | 49 | 20.85 | 39.69 |
| 3 | 6 | 2.55 | 25.24 |

| Chi-Square Test for Specified Proportions | |
|---|---|
| Chi-Square | 237.2190 |
| DF | 3 |
| Pr > ChiSq | <.0001 |

***Effective Sample Size = 235***

**RxGr3_2**

| Categories (RxGr32) | Observed Frequency (O*i*) | Expected Frequency (e*i*) |
|---|---|---|
| 0 | 198 | 80 |
| 1 | 14 | 126 |
| 2 | 22 | 25 |
| 3 | 1 | 4 |

**Expected Frequency (e*i*) and $x^2$ Calculations**

| $\mu$= 0.2596, $\sigma$ = 0.6364 | From Normal Probability Table |
|---|---|
| Z1 = (0 – 0.26) / 0.64 = - 0.41<br>Z2 = (1 – 0.26) / 0.64 = 1.16<br>Z3 = (2 – 0.26) / 0.64 = 2.72<br>Z4 = (3 – 0.26) / 0.64 = 4.28 | P (Z< -0.41) = 0.3409<br>P (Z< 1.16) = 0.8770<br>P (Z< 2.72) = 0.9967<br>P (Z< 4.28) = 0.9998 |
| Probability: | Expected Frequency: |
| P (0) = 0.3409 | E(0) = 0.3409 x 235 = 80 |

| | |
|---|---|
| P (1) = 0.8770 - 0.3409 = 0.5361<br>P (2) = 0.9834 - 0.8770= 0.1064<br>P (3) = 0.0160 | E(1) = 0.5361 x 235 = 126<br>E(2) = 0.1064 x 235 = 25<br>E(3) = 0.0160 x 235 = 4 |
| $x^2$ Test | |
| Combining E(2) and E(3) = 29<br>$x^2$ = [(198 – 80) ²/ 80] + [(14 – 126) ²/ 126] + [(23 – 29) ²/ 29]<br>= 274.85<br>DF = 3 – 1 =2<br>$x^2$(2, α = 0.05) = 5.991<br>274.85> $x^2$(2, α = 0.05) = 5.991 → Reject $H_0$ | |

We conclude that there is sufficient evidence that the slope is not same. Therefore RxGr3_2 data is multinomial.

SAS output for Chi-Squared Test for RxGr3_2

***The SAS System***
***GOODNESS OF FIT ANALYSIS of RxGr3_2***
***The FREQ Procedure***

| RxGr3_2 | Frequency | Percent | Test Percent |
|---|---|---|---|
| 0 | 198 | 84.26 | 34.09 |
| 1 | 14 | 5.96 | 53.61 |
| 2 | 22 | 9.36 | 10.64 |
| 3 | 1 | 0.43 | 1.60 |

| Chi-Square Test for Specified Proportions | |
|---|---|
| Chi-Square | 275.4056 |
| DF | 3 |
| Pr > ChiSq | <.0001 |

***Effective Sample Size = 235***

**RxGr4_2**

| Categories (RxGr32) | Observed Frequency (O*i*) | Expected Frequency (e*i*) |
|---|---|---|
| 0 | 176 | 68 |
| 1 | 15 | 110 |
| 2 | 43 | 53 |
| 3 | 1 | 3 |

**Expected Frequency (e*i*) and $\chi^2$ Calculations**

| $\mu$= 0.4426, $\sigma$ = 0.7989 | From Normal Probability Table |
|---|---|
| Z1 = (0 – 0.44) / 0.80 = - 0.55<br>Z2 = (1 – 0. 44) / 0.80 = 0.70<br>Z3 = (2 – 0. 44) / 0.80 = 1.95<br>Z4 = (3 – 0. 44) / 0.80 = 3.20 | P (Z< -0.55) = 0.2912<br>P (Z< 0.70) = 0.7580<br>P (Z< 1.95) = 0.9744<br>P (Z< 3.20) = 0.9993 |
| Probability: | Expected Frequency: |
| P (0) = 0.2912<br>P (1) = 0.7580 - 0.2912 = 0.4688<br>P (2) = 0.9834 - 0.7580 = 0.2254<br>P (3) = 0.0146 | E(0) = 0.2912 x 235 = 68<br>E(1) = 0.4688 x 235 = 110<br>E(2) = 0.2254 x 235 = 53<br>E(3) = 0.0146 x 235 = 3 |
| $\chi^2$ Test | |
| Combining E(2) and E(3) = 56<br>$\chi^2$ = [(176 – 68) ²/ 68] + [(15 – 110) ²/ 110] + [(44 – 56) ²/ 56]<br>= 256.14<br>DF = 3 – 1 =2<br>$\chi^2$ (2, α = 0.05) = 5.991<br>256.14> $\chi^2$ (2, α = 0.05) = 5.991 → Reject $H_0$ | |

We conclude that there is sufficient evidence that the slope is not same. Therefore RxGr4_2 data is multinomial.
SAS output for Chi-Squared Test for RxGr4_2

***The SAS System***
***GOODNESS OF FIT ANALYSIS of RxGr4_2***
***The FREQ Procedure***

| RxGr4_2 | Frequency | Percent | Test Percent |
|---|---|---|---|
| 0 | 176 | 74.89 | 29.12 |
| 2 | 43 | 18.30 | 46.88 |
| 1 | 15 | 6.38 | 22.54 |
| 3 | 1 | 0.43 | 1.46 |

| Chi-Square Test for Specified Proportions | |
|---|---|
| Chi-Square | 238.9764 |
| DF | 3 |
| Pr > ChiSq | <.0001 |

***Effective Sample Size = 235***

**RxGr5_2**

| Categories (RxGr32) | Observed Frequency (O*i*) | Expected Frequency (e*i*) |
|---|---|---|
| 0 | 169 | 66 |
| 1 | 19 | 101 |
| 2 | 41 | 57 |
| 3 | 6 | 10 |

**Expected Frequency (e*i*) and $\chi^2$ Calculations**

| $\mu$= 0.5064, $\sigma$ = 0.8672 | From Normal Probability Table |
|---|---|
| Z1 = (0 – 0.51) / 0.87 = - 0.58<br>Z2 = (1 – 0.51) / 0.87 = 0.56<br>Z3 = (2 – 0. 51) / 0.87 = 1.71<br>Z4 = (3 – 0. 51) / 0.87 = 2.86 | P (Z< -0.58) = 0.2810<br>P (Z< 0.56) = 0.7123<br>P (Z< 1.71) = 0.9564<br>P (Z< 2.86) = 0.9979 |
| Probability: | Expected Frequency: |
| P (0) = 0.2810<br>P (1) = 0.7123- 0.2810= 0.4313<br>P (2) = 0.9564- 0.7123= 0.2441<br>P (3) = 0.0436 | E(0) = 0.2810 x 235 = 66<br>E(1) = 0.4313 x 235 = 101<br>E(2) = 0.2441 x 235 = 57<br>E(3) = 0.0436 x 235 = 10 |
| $\chi^2$ Test | |
| $\chi^2$ = [(169 – 66) ²/ 66] + [(19 – 101) ²/ 101] + [(41 – 57) ²/ 57] + [(6 – 10) ²/ 10] = 262.41<br>DF = 4 – 1 =3<br>$\chi^2$ (3, α = 0.05) = 7.815<br>262.41> $\chi^2$ (3, α = 0. 05) = 7.815<br>→ Reject $H_0$ | |

We conclude that there is sufficient evidence that the slope is not same. Therefore RxGr5_2 data is multinomial.
SAS output for Chi-Squared Test for RxGr5_2

***The SAS System***
***GOODNESS OF FIT ANALYSIS of RxGr5_2***
***The FREQ Procedure***

| RxGr5_2 | Frequency | Percent | Test Percent |
|---|---|---|---|
| 0 | 169 | 71.91 | 28.10 |
| 3 | 6 | 2.55 | 43.13 |
| 2 | 41 | 17.45 | 24.41 |
| 1 | 19 | 8.09 | 4.36 |

| Chi-Square Test for Specified Proportions | |
|---|---|
| Chi-Square | 262.4059 |
| DF | 3 |
| Pr > ChiSq | <.0001 |

***Effective Sample Size = 235***

**RxGr7_2 (values: 0, 1, 2)**

| Categories (RxGr32) | Observed Frequency (O*i*) | Expected Frequency (e*i*) |
|---|---|---|
| 0 | 210 | 89 |
| 1 | 16 | 139 |
| 2 | 9 | 7 |

**Expected Frequency (e*i*) and $\chi^2$ Calculations**

| $\mu$= 0.1447, $\sigma$ = 0.4475 | From Normal Probability Table |
|---|---|
| Z1 = (0 – 0.14) / 0.45 = - 0.31<br>Z2 = (1 – 0.14) / 0.45 = 1.91<br>Z3 = (2 – 0.14) / 0.45 = 4.13 | P (Z< -0.31) = 0.3783<br>P (Z< 1.91) = 0.9719<br>P (Z< 4.13) = 0.9998 |
| Probability: | Expected Frequency: |
| P (0) = 0.3783<br>P (1) = 0.9719- 0.3783= 0.5936<br>P (2) = 0.9564- 0.9719= 0.0281 | E(0) = 0.3783 x 235 = 89<br>E(1) = 0.5936 x 235 = 139<br>E(2) = 0.0281 x 235 = 7 |
| $\chi^2$ Test | |
| $\chi^2$ = [(210 – 89) ²/ 89] + [(16 – 139) ²/ 139] + [(9 – 7) ²/ 7]<br>= 275.16<br>DF = 3 – 1 =2<br>$\chi^2$ (2, α = 0.05) = 5.991<br>273.92> $\chi^2$ (2, α = 0.05) = 5.991 → Reject $H_0$ | |

We conclude that there is sufficient evidence that the slope is not same. Therefore RxGr7_2 data is multinomial.
SAS output for Chi-Squared Test for RxGr7_2

***The SAS System***
***GOODNESS OF FIT ANALYSIS of RxGr7_2***
***The FREQ Procedure***

| RxGr7_2 | Frequency | Percent | Test Percent |
|---|---|---|---|

| RxGr7_2 | Frequency | Percent | Test Percent |
|---|---|---|---|
| 0 | 210 | 89.36 | 37.83 |
| 1 | 16 | 6.81 | 59.36 |
| 2 | 9 | 3.83 | 2.81 |

| Chi-Square Test for Specified Proportions | |
|---|---|
| Chi-Square | 275.1616 |
| DF | 2 |
| Pr > ChiSq | <.0001 |

***Effective Sample Size = 235***

**RxGr8_2 (values: 0,1,2,3)**

| Categories (RxGr32) | Observed Frequency (O*i*) | Expected Frequency (e*i*) |
|---|---|---|
| 0 | 229 | 103 |
| 1 | 2 | 64 |
| 2 | 4 | 68 |
| 3 | 0 | 0 |

**Expected Frequency (e*i*) and $x^2$ Calculations**

| $\mu$= 0.0426, $\sigma$ = 0.2735 | From Normal Probability Table |
|---|---|
| Z1 = (0 – 0.04) / 0.27 = - 0.1481<br>Z2 = (1 – 0.04) / 0.27 = 3.5556<br>Z3 = (2 – 0.04) / 0.27 = 7.2593<br>Z4 = (3 – 0.04) / 0.27 = 10.9630 | P (Z< -0.15) = 0.4404<br>P (Z< 3.56) = 0.7123<br>P (Z< 7.26) = 0.9998<br>P (Z< 10.96) = 0.9999 |
| Probability: | Expected Frequency: |
| P (0) = 0.4404<br>P (1) = 0.7123- 0.4404= 0.2719<br>P (2) = 0.9998- 0.7123= 0.2875<br>P (3) = 0.0002 | E(0) = 0.4404 x 235 = 103<br>E(1) = 0.2719 x 235 = 64<br>E(2) = 0.2875 x 235 = 68<br>E(3) = 0.0002 x 235 = 0 |
| $x^2$ Test | |
| Combining E(1), E(2) and E(3) = 132<br>$x^2$ = [(229 – 103) ²/ 103] + [(6 – 132) ²/ 132]<br>= 274.41<br>DF = 2 – 1 =1<br>$x^2$ (1, α = 0.05) = 3.841<br>274.41> $x^2$ (1, α = 0. 05) = 3.841→ Reject $H_0$ | |

We conclude that there is sufficient evidence that the slope is not same. Therefore RxGr8_2 data is multinomial.

SAS output for Chi-Squared Test for RxGr8_2

***The SAS System***
***GOODNESS OF FIT ANALYSIS of RxGr8_2***
***The FREQ Procedure***

| RxGr8_2 | Frequency | Percent | Test Percent |
|---|---|---|---|
| 0 | 229 | 97.45 | 44.04 |
| 2 | 4 | 1.70 | 27.19 |
| 1 | 2 | 0.85 | 28.77 |

| Chi-Square Test for Specified Proportions | |
|---|---|
| Chi-Square | 272.0153 |
| DF | 2 |
| Pr > ChiSq | <.0001 |

***Effective Sample Size = 235***

**B3. Post_OSW ( $y$ ), Unweighted $\hat{y}$ , and Weighted $\hat{y}$ on Test Data Set**

| Post_OSW ($y_i$) | unweighted $\hat{y}_i$ | weighted $\hat{y}_i$ | | Post_OSW ($y_i$) | unweighted $\hat{y}_i$ | weighted $\hat{y}_i$ |
|---|---|---|---|---|---|---|
| 16 | 16.2407 | 16.1539 | | 36 | 34.4833 | 34.4956 |
| 7 | 8.7148 | 8.9216 | | 27 | 27.2959 | 27.6815 |
| 20 | 18.8843 | 18.9624 | | 20 | 20.4705 | 20.6819 |
| 3 | 6.1474 | 5.2993 | | 21 | 22.2748 | 22.4245 |
| 16 | 17.4415 | 17.4316 | | 6 | 6.1087 | 6.1298 |
| 33 | 35.1765 | 34.1882 | | 6 | 5.7034 | 5.3001 |
| 18 | 17.859 | 17.9573 | | 9 | 10.064 | 10.0672 |
| 3 | 2.9229 | 2.9846 | | 17 | 18.032 | 18.0101 |
| 9 | 8.3766 | 8.6969 | | 19 | 16.7654 | 16.7972 |
| 7 | 6.354 | 6.3213 | | 22 | 19.7804 | 19.0206 |
| 2 | 1.2323 | 2.212 | | 22 | 21.3142 | 21.4937 |

| Post_OSW ($y_i$) | unweighted $\hat{y}_i$ | weighted $\hat{y}_i$ | | Post_OSW ($y_i$) | unweighted $\hat{y}_i$ | weighted $\hat{y}_i$ |
|---|---|---|---|---|---|---|
| 15 | 12.1618 | 13.1835 | | 20 | 17.3317 | 17.9322 |
| 22 | 24.6401 | 24.7604 | | 20 | 21.7481 | 21.9879 |
| 20 | 23.1551 | 23.1848 | | 18 | 19.7663 | 19.1429 |
| 1 | 1.7079 | 1.8468 | | 26 | 24.0206 | 24.9102 |
| 9 | 7.741 | 8.7421 | | 22 | 19.5531 | 19.5632 |
| 6 | 6.9619 | 6.1949 | | 16 | 14.8729 | 14.9898 |
| 13 | 12.1805 | 12.6827 | | 25 | 25.9704 | 24.0704 |
| 15 | 16.7044 | 16.8242 | | 9 | 10.8925 | 10.4928 |
| 24 | 22.757 | 20.402 | | 20 | 21.9469 | 21.4626 |
| 13 | 15.45 | 15.4983 | | 27 | 26.3127 | 26.4844 |
| 4 | 2.71 | 2.6321 | | 12 | 12.3617 | 12.3727 |
| 23 | 23.9648 | 23.9319 | | 20 | 16.6567 | 17.1266 |
| 16 | 15.7318 | 15.7648 | | 24 | 23.0987 | 23.0008 |
| 15 | 14.5373 | 14.6484 | | 15 | 13.1817 | 13.8937 |
| 20 | 23.4909 | 23.3678 | | 14 | 16.7849 | 15.9929 |
| 37 | 36.4419 | 36.4563 | | 26 | 25.2371 | 25.3246 |
| 12 | 12.6793 | 12.6719 | | 36 | 32.9999 | 32.4555 |
| 18 | 18.0681 | 18.0421 | | 24 | 21.8763 | 21.9824 |
| 11 | 9.6618 | 9.7528 | | | | |

## B4. Future Study-Independency of Treatment by p-value

**Binomial**

**Model: generalized logit SAS**

w/covariates

| Response | Treatment | P-value |
|---|---|---|
| ProcGr4_2 | ProcGr9_2 | 0.2746 |
| | ProcGr10_2 | 0.0201 |
| | RxGr1_2 | 0.0856 |
| | RxGr2_2 | 0.1125 |
| | RxGr3_2 | 0.4499 |
| | RxGr4_2 | 0.114 |
| | RxGr5_2 | 0.0426 |
| | RxGr7_2 | 0.5224 |
| | RxGr8_2 | 0.1546 |
| ProcGr9_2 | ProcGr4_2 | 0.6153 |
| | ProcGr10_2 | 0.0114 |
| | RxGr1_2 | 0.9783 |
| | RxGr2_2 | 0.5796 |
| | RxGr3_2 | 0.8431 |
| | RxGr4_2 | 0.9225 |
| | RxGr5_2 | 0.5405 |
| | RxGr7_2 | 0.8051 |
| | RxGr8_2 | 0.9065 |
| ProcGr10_2 | ProcGr4_2 | 0.5018 |
| | ProcGr9_2 | 0.0007 |
| | RxGr1_2 | 0.7077 |
| | RxGr2_2 | 0.9555 |
| | RxGr3_2 | 0.9306 |
| | RxGr4_2 | 0.6523 |
| | RxGr5_2 | 0.4054 |
| | RxGr7_2 | 0.8381 |
| | RxGr8_2 | 0.9959 |

**Binomial**

**Model: generalized logit R**

w/covariates

| Response | Treatment | P-value |
|---|---|---|
| ProcGr4_2 | ProcGr9_2 | 0.606 |
| | ProcGr10_2 | 0.115 |
| | RxGr1_2 | 0.5115 |
| | RxGr2_2 | 0.2236 |
| | RxGr3_2 | 0.3703 |
| | RxGr4_2 | 0.0028 |
| | RxGr5_2 | 0.0338 |
| | RxGr7_2 | 0.5344 |
| | RxGr8_2 | 0.0723 |
| ProcGr9_2 | ProcGr4_2 | 0.4799 |
| | ProcGr10_2 | 0.0001 |
| | RxGr1_2 | 0.3693 |
| | RxGr2_2 | 0.9337 |
| | RxGr3_2 | 0.8277 |
| | RxGr4_2 | 0.0242 |
| | RxGr5_2 | 0.6953 |
| | RxGr7_2 | 0.4743 |
| | RxGr8_2 | 0.9028 |
| ProcGr10_2 | ProcGr4_2 | 0.1193 |
| | ProcGr9_2 | 0.0001 |
| | RxGr1_2 | 0.2432 |
| | RxGr2_2 | 0.0356 |
| | RxGr3_2 | 0.9683 |
| | RxGr4_2 | 0.0001 |
| | RxGr5_2 | 0.3871 |
| | RxGr7_2 | 0.0609 |
| | RxGr8_2 | 0.698 |

**Multinomial**

**Model: generalized logit SAS**

w/covariates

| Response | Treatment | P-value |
|---|---|---|
| RxGr1_2 | ProcGr4_2 | 0.9969 |
| | ProcGr9_2 | 0.985 |
| | ProcGr10_2 | 0.9687 |
| | RxGr2_2 | 0.9925 |
| | RxGr3_2 | 0.9991 |
| | RxGr4_2 | 0.8526 |
| | RxGr5_2 | 0.9998 |
| | RxGr7_2 | 0.9944 |
| | RxGr8_2 | 0.9998 |
| RxGr2_2 | ProcGr4_2 | 0.4852 |
| | ProcGr9_2 | 0.8472 |
| | ProcGr10_2 | 0.9956 |
| | RxGr1_2 | 0.9446 |
| | RxGr3_2 | 0.9093 |
| | RxGr4_2 | 0.0649 |
| | RxGr5_2 | 0.6211 |
| | RxGr7_2 | 0.4359 |
| | RxGr8_2 | 0.9998 |
| RxGr3_2 | ProcGr4_2 | 0.5437 |
| | ProcGr9_2 | 0.9476 |
| | ProcGr10_2 | 0.9659 |
| | RxGr1_2 | 0.9526 |
| | RxGr2_2 | 0.9293 |
| | RxGr4_2 | 0.8716 |
| | RxGr5_2 | 0.9602 |
| | RxGr7_2 | 0.6552 |
| | RxGr8_2 | 0.9836 |

**Multinomial**

**Model: generalized logit R**

w/covariates

| Response | Treatment | P-value |
|---|---|---|
| RxGr1_2 | ProcGr4_2 | 0.9999 |
| | ProcGr9_2 | 0.0001 |
| | ProcGr10_2 | 0.9738 |
| | RxGr2_2 | 0.9999 |
| | RxGr3_2 | 0.9999 |
| | RxGr4_2 | 0.9999 |
| | RxGr5_2 | 0.9999 |
| | RxGr7_2 | 0.9999 |
| | RxGr8_2 | 0.9999 |
| RxGr2_2 | ProcGr4_2 | 0.4529 |
| | ProcGr9_2 | 0.9944 |
| | ProcGr10_2 | 0.9861 |
| | RxGr1_2 | 0.9807 |
| | RxGr3_2 | 0.9952 |
| | RxGr4_2 | 0.0001 |
| | RxGr5_2 | 0.3391 |
| | RxGr7_2 | 0.9937 |
| | RxGr8_2 | 0.1921 |
| RxGr3_2 | ProcGr4_2 | 0.9993 |
| | ProcGr9_2 | 0.5295 |
| | ProcGr10_2 | 0.4648 |
| | RxGr1_2 | 0.0065 |
| | RxGr2_2 | 0.4293 |
| | RxGr4_2 | 0.0036 |
| | RxGr5_2 | 0.6929 |
| | RxGr7_2 | 0.9981 |
| | RxGr8_2 | 0.607 |

**Multinomial**

**Model: generalized logit SAS**

w/covariates

| Response | Treatment | P-value |
|---|---|---|
| RxGr4_2 | ProcGr4_2 | 0.056 |
| | ProcGr9_2 | 0.9926 |
| | ProcGr10_2 | 0.6668 |
| | RxGr1_2 | 0.3514 |
| | RxGr2_2 | 0.0376 |
| | RxGr3_2 | 0.2489 |
| | RxGr5_2 | 0.5311 |
| | RxGr7_2 | 0.4067 |
| | RxGr8_2 | 0.9998 |
| RxGr5_2 | ProcGr4_2 | 0.0208 |
| | ProcGr9_2 | 0.0319 |
| | ProcGr10_2 | 0.0632 |
| | RxGr1_2 | 0.7093 |
| | RxGr2_2 | 0.6587 |
| | RxGr3_2 | 0.8617 |
| | RxGr4_2 | 0.4851 |
| | RxGr7_2 | 0.4098 |
| | RxGr8_2 | 0.9825 |
| RxGr7_2 | ProcGr4_2 | 0.9751 |
| | ProcGr9_2 | 0.9978 |
| | ProcGr10_2 | 0.9621 |
| | RxGr1_2 | 0.9902 |
| | RxGr2_2 | 0.7346 |
| | RxGr3_2 | 0.992 |
| | RxGr4_2 | 0.1543 |
| | RxGr5_2 | 0.958 |
| | RxGr8_2 | 0.9999 |

**Multinomial**

**Model: generalized logit R**

w/covariates

| Response | Treatment | P-value |
|---|---|---|
| RxGr4_2 | ProcGr4_2 | 0.0196 |
| | ProcGr9_2 | 0.8413 |
| | ProcGr10_2 | 0.3339 |
| | RxGr1_2 | 0.2855 |
| | RxGr2_2 | 0.0001 |
| | RxGr3_2 | 0.0555 |
| | RxGr5_2 | 0.0272 |
| | RxGr7_2 | 0.0001 |
| | RxGr8_2 | 0.9913 |
| RxGr5_2 | ProcGr4_2 | 0.0001 |
| | ProcGr9_2 | 0.0016 |
| | ProcGr10_2 | 0.0077 |
| | RxGr1_2 | 0.6755 |
| | RxGr2_2 | 0.5965 |
| | RxGr3_2 | 0.9977 |
| | RxGr4_2 | 0.0012 |
| | RxGr7_2 | 0.0185 |
| | RxGr8_2 | 0.0593 |
| RxGr7_2 | ProcGr4_2 | 0.9999 |
| | ProcGr9_2 | 0.9999 |
| | ProcGr10_2 | 0.9999 |
| | RxGr1_2 | 0.0001 |
| | RxGr2_2 | 0.9999 |
| | RxGr3_2 | 0.9999 |
| | RxGr4_2 | 0.9999 |
| | RxGr5_2 | 0.0001 |
| | RxGr8_2 | 0.9999 |

**Multinomial**

**Model: generalized logit SAS**

w/covariates

| Response | Treatment | P-value |
|---|---|---|
| RxGr8_2 | ProcGr4_2 | 0.9974 |
| | ProcGr9_2 | 0.9945 |
| | ProcGr10_2 | 0.9955 |
| | RxGr1_2 | 0.9999 |
| | RxGr2_2 | 0.9999 |
| | RxGr3_2 | 0.9999 |
| | RxGr4_2 | 0.9999 |
| | RxGr5_2 | 0.9999 |
| | RxGr8_2 | 0.9999 |

**Multinomial**

**Model: generalized logit R**

w/covariates

| Response | Treatment | P-value |
|---|---|---|
| RxGr8_2 | ProcGr4_2 | 0.9999 |
| | ProcGr9_2 | 0.9999 |
| | ProcGr10_2 | 0.9999 |
| | RxGr1_2 | 0.9997 |
| | RxGr2_2 | 0.9991 |
| | RxGr3_2 | 0.9999 |
| | RxGr4_2 | 0.9999 |
| | RxGr5_2 | 0.9995 |
| | RxGr8_2 | 0.9999 |

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