TREATMENT EFFECTIVENESS OF COMPLEX CASUALTY AMPUTEE PATIENTS

by

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September 2013

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This study analyzes data from 182 Comprehensive Combat and Complex Casualty Care (C5) amputee patients with the goal to better understand the factors that influence their care. The data was provided from the Navy Bureau of Medicine and Surgery while visiting the Naval Medical Center at San Diego. The analysis examines two response variables, opiate drug usage and duration in the C5 program, as a function of a number of exploratory variables, including patient demographics, injury type, and appointment statistics. Logistic and linear regression models are used for data analysis. The study concludes that an increase in attendance to physical therapy, occupational therapy, and pain management and rehabilitation appointments correlates with an increased likelihood in reduced opiate usage. The study also concludes that the percentage of cancelled appointments is positively associated with the amputee’s duration in the program for non-Caucasian patients, patients with an improvised explosive device injury, and amputees with an upper-extremity amputation or both a lower- and upper-extremity amputation.
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ABSTRACT

This study analyzes data from 182 Comprehensive Combat and Complex Casualty Care (C5) amputee patients with the goal to better understand the factors that influence their care. The data was provided from the Navy Bureau of Medicine and Surgery while visiting the Naval Medical Center at San Diego. The analysis examines two response variables, opiate drug usage and duration in the C5 program, as a function of a number of exploratory variables, including patient demographics, injury type, and appointment statistics. Logistic and linear regression models are used for data analysis. The study concludes that an increase in attendance to physical therapy, occupational therapy, and pain management and rehabilitation appointments correlates with an increased likelihood in reduced opiate usage. The study also concludes that the percentage of cancelled appointments is positively associated with the amputee’s duration in the program for non-Caucasian patients, patients with an improvised explosive device injury, and amputees with an upper-extremity amputation or both a lower- and upper-extremity amputation.
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<thead>
<tr>
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<th>Description</th>
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<tbody>
<tr>
<td>ADL</td>
<td>Activities of Daily Living</td>
</tr>
<tr>
<td>AHFS</td>
<td>American Hospital Formulary Service</td>
</tr>
<tr>
<td>AIC</td>
<td>Akaike Information Criterion</td>
</tr>
<tr>
<td>APPT</td>
<td>appointment</td>
</tr>
<tr>
<td>BUMED</td>
<td>Bureau of Medicine and Surgery (Navy)</td>
</tr>
<tr>
<td>C5</td>
<td>Comprehensive Combat and Complex Casualty Care</td>
</tr>
<tr>
<td>CSV</td>
<td>comma separated values</td>
</tr>
<tr>
<td>CV</td>
<td>cross validation</td>
</tr>
<tr>
<td>DEV</td>
<td>deviation</td>
</tr>
<tr>
<td>DISP</td>
<td>dispensed</td>
</tr>
<tr>
<td>DMSS</td>
<td>Defense Medical Surveillance System</td>
</tr>
<tr>
<td>FN</td>
<td>false negative</td>
</tr>
<tr>
<td>FP</td>
<td>false positive</td>
</tr>
<tr>
<td>GLM</td>
<td>Generalized Linear Model</td>
</tr>
<tr>
<td>HLOS</td>
<td>hospital length of stay</td>
</tr>
<tr>
<td>ID</td>
<td>identification</td>
</tr>
<tr>
<td>IED</td>
<td>improvised explosive device</td>
</tr>
<tr>
<td>ILOS</td>
<td>intensive care unit length of stay</td>
</tr>
<tr>
<td>ISS</td>
<td>injury severity score</td>
</tr>
<tr>
<td>KIA</td>
<td>killed in action</td>
</tr>
<tr>
<td>LEA</td>
<td>lower-extremity amputation</td>
</tr>
<tr>
<td>LM</td>
<td>Linear Model (Multivariate)</td>
</tr>
<tr>
<td>MEB</td>
<td>medical evaluation board</td>
</tr>
<tr>
<td>MR</td>
<td>misclassification rate</td>
</tr>
<tr>
<td>MTF</td>
<td>military treatment facility</td>
</tr>
<tr>
<td>NEC</td>
<td>not elsewhere classified</td>
</tr>
<tr>
<td>NMCSD</td>
<td>Navy Medical Center San Diego</td>
</tr>
<tr>
<td>OEF</td>
<td>Operation Enduring Freedom</td>
</tr>
<tr>
<td>OIF</td>
<td>Operation Iraqi Freedom</td>
</tr>
</tbody>
</table>
OND  Operation New Dawn
OT   occupational therapy
PCM  primary care manager
PM&R pain management and rehabilitation
PT   physical therapy
PTSD post traumatic stress disorder
QTR  quarter
QTY  quantity
ROM  range of motion
SIGNIF significant
STD  standard deviation
TBI  traumatic brain injury
TF   true negative
TMDS Theater Medical Data Store
TP   true positive
UEA  upper-extremity amputation
WIA  wounded in action
YRS  years
EXECUTIVE SUMMARY

In an effort to better understand the factors that influence the treatment effectiveness of combat casualty amputee patients, our study analyzes the data of 182 amputee patients within the Comprehensive Combat and Complex Casualty Care (C5) program through the use of logistic and linear regression models. The analysis examines two response variables, duration in the program and opiate drug usage, as a function of patient demographics, injury type, and appointment statistics. In particular, we look at the following exploratory variables: patient race and age; presence of a traumatic brain injury and mental health condition; amputation caused by an improvised explosive device (IED) or not; number of patient medical conditions; number of follow-up surgeries; location of amputation; and the percentage of “no show,” “cancelled,” and “kept” patient rehabilitation appointments.

The main results of our study show that:

• An increase in attendance to physical therapy, occupational therapy, and pain management and rehabilitation appointments correlates to an increased likelihood of reduced opiate usage.

• The estimated probability of a reduction in opiate usage is less likely as the patient ages and the number of primary medical conditions increases.
• Patients without an IED injury spend more time in the program as the number of primary conditions increase.

• Percentage of cancelled appointments is positively associated with the treatment duration of upper-body amputees, patients with both an upper and lower amputation, and amputations caused by an IED.

• The number of follow-up surgeries, presence of a traumatic brain injury, and mental health condition did not have a significant impact on opiate usage or duration in the program.

The results of our study and similar studies could be used for future meta-analysis work to determine if similar correlations are repeated in other Military Treatment Facility (MTF) amputee populations.
ACKNOWLEDGMENTS

I would like to acknowledge several people who have contributed to the completion of this study. First and foremost, I would like to thank my husband, Chris, for his love, support, and sustaining sanity throughout this last year as I finalized this thesis. Furthermore, I would like to thank my parents, Cindy and Gilbert White and Vonda Burkhart, for always believing in me. I would also like to thank Dr. Rachel Silvestrini, Dr. Nedialko Dimitrov, Dr. Ronald Fricker, and LTCOL Gregory Mislick, USMC (Ret), for their assistance, support, and guidance with this paper. Last but not least, I would like to thank William “Wild Bill” Evans for putting up with my endless programming questions and Matthew “Tater” Tabar for providing “much needed” comic relief.
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I. INTRODUCTION

A. BACKGROUND

The Global War on Terrorism has subjected today’s military service members to more than a decade of deployments under Operation Iraqi Freedom (OIF), Operation New Dawn (OND) in Iraq, and Operation Enduring Freedom (OEF) in Afghanistan (2003 to present). While on deployment, many of those service members experience blast injuries, behavioral health-related issues, and trauma. Some of the most severely injured servicemen and women returning home today receive care through the Comprehensive Combat and Complex Casualty Care (C5) at the Naval Medical Center in San Diego, California (NMCSD). The C5 program offers state-of-the-art medical care, treatment, and health management services to severely wounded, ill, or injured patients, from medical evacuation through inpatient care, outpatient rehabilitation, and their eventual return to active duty or transition from the military (Naval Medical Center San Diego, C5, 2013).

The C5 program components include:

- Trauma service;
- Orthopedics, reconstructive plastic surgery, and wound care;
- Amputee care, prosthetics, and rehabilitation;
- Physical, occupational, and recreational therapy;
- Mental health assessment and care;
- Traumatic Brain Injury (TBI) care;
- Pastoral care and counseling; and
- Family support and career transition services.
The United States Navy Bureau of Medicine and Surgery (BUMED) is interested in improving care delivery to all C5 patients. This study focuses on care delivery specific to amputee patients and address which factors most influence their care.

B. THE PURPOSE OF THE STUDY AND RESEARCH QUESTIONS

The purpose of this study is to better understand the factors that influence treatment effectiveness of amputee patients in the C5 program. We can influence medical cost-saving initiatives and practices by analyzing the implications of treatment compliance, effective treatment programs, and understanding prescription drug utilization. This study answers the following research questions:

- Do patient demographics and/or the amount of “kept” physical therapy, occupational therapy, and pain management and rehabilitation appointments correlate with reduced opiate usage in amputee patients during treatment?
- Do patient demographics and/or percentage of cancelled appointments correlate with their duration in the C5 program?

These research questions are answered by data analysis and logistic and linear regression models applied towards relevant C5 data.

Implementing new ways to improve patient appointment compliance reduces medical waste and costs. For example, when a single patient misses their scheduled appointment, valuable physician time is wasted, necessary patient care is not delivered, and other patients are denied appointments at an earlier date.
C. ORGANIZATION OF THE STUDY

Chapter II provides background information on the medical implications of OIF, OND, and OEF, relevant C5 program information, and a review of previous studies. Chapter III provides descriptive statistics of variables utilized in the study. Chapter IV covers the methodologies used, a description of the models, and results of the analysis. The final chapter presents a summary of the study and offers recommendations for further analysis.
II. LITERATURE REVIEW

This chapter addresses the rising medical costs associated with OIF, OND, and OEF; the severe injuries and illnesses our soldiers returning home must overcome in order to acclimate back into society; and recent studies on amputee patient care, treatment, and the impact of long-term, prescription drug usage. We can influence medical cost-saving initiatives and practices, and understand the implications of treatment compliance, by:

- studying the impact of “missed” appointments on patient care;
- studying which treatment paths are the most effective; and
- understanding prescription drug utilization.

The goal is to accomplish all three of these while continuing to provide top-notch care to amputee patients.

A. MEDICAL COST IMPLICATIONS FROM A DECADE OF WAR

Bilmes (2013) shows that the Iraq and Afghanistan wars combined are predicted to cost between $4 trillion and $6 trillion, making the combination of these two wars the most expensive in U.S. history. Bilmes also states that long-term medical care and disability compensation for service members, veterans, and families; military replenishment; and the social and economic costs have yet to be paid. Furthermore, the study shows that the Tricare healthcare system, which provides coverage for military members and their dependents (including those service members injured while serving in war) is expected to increase from $18 billion a year in 2001 to $56 billion a
year in 2013. This expense accounts for 8% of the total U.S. defense budget.

As healthcare costs continue to rise, a better understanding of the variables that most impact patient care can enable physicians and care givers to control costs, improve patient satisfaction, and influence healthcare reform and treatment.

B. OIF, OND, AND OEF IN NUMBERS

Over the past decade, there have been approximately 51,325 service members wounded in action (WIA); 5,289 killed in action (KIA); and 6,729 total deaths (see Table 1) (U.S. Department of Defense, 2013). A percentage of the WIA become combat casualty patients treated in the C5 program at NMCSD. The majority of battle-injury amputations occurred in OIF from 2003 through the first quarter of 2009 (Fischer, 2013). By the second quarter of 2009, however, most major limb amputations were due to battle injuries in OEF (see Figure 1) (Fischer, 2013).

<table>
<thead>
<tr>
<th>OPERATION</th>
<th>TOTAL DEATHS</th>
<th>KIA</th>
<th>NONHOSTILE</th>
<th>WIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>OIF</td>
<td>4,409</td>
<td>3,480</td>
<td>929</td>
<td>31,927</td>
</tr>
<tr>
<td>OND</td>
<td>66</td>
<td>38</td>
<td>28</td>
<td>295</td>
</tr>
<tr>
<td>OEF</td>
<td>2,254</td>
<td>1,771</td>
<td>483</td>
<td>19,103</td>
</tr>
<tr>
<td>TOTALS</td>
<td>6,729</td>
<td>5,289</td>
<td>1,440</td>
<td>51,325</td>
</tr>
</tbody>
</table>

- OIF includes casualties that occurred between March 19, 2003 and August 31, 2010.
- OND includes casualties that occurred between September 1, 2010 and December 31, 2011.
- OEF includes casualties in Afghanistan and other locations in support of OEF.

Table 1. U.S. military casualty status in numbers by the Department of Defense (After U.S. Department of Defense, 2013).
The amputee population in our study includes many patients who suffer from a TBI. From the beginning, we believed that the presence of such an injury would impact our analysis; therefore, data on TBI was included in our study. Figure 2 displays the number of TBI diagnoses from 2000 through 2013. The amount of amputee and TBI patients injured in combat will likely decrease as the United States withdraws from these armed conflicts. The medical care for these service members, however, will endure for decades (Fischer, 2013).
C. THE C5 PATIENT CARE PROCESS

After a military member receives an amputation, they are assigned care in the C5 program (or similar military medical program). The process after assignment of C5 care was obtained from a personal communication with a Johns Hopkins University Applied Physics Lab analyst (J. P. Allred, personal communications, May 5, 2013) and is detailed in the remainder of this paragraph. Prior to the patient’s arrival, the critical care staff typically schedule a teleconference with the patient, the family, and critical staff members from the current Military Treatment Facility (MTF) servicing the patient. The teleconference consists of a “Question & Answer” session to relieve
patient/family anxiety about transferring into the NMCSD C5 program. Upon arrival, the patient may spend from a single day up to two weeks in the in-patient ward. Here, the patient will be introduced to their C5 case manager/in-patient social worker. Upon in-patient discharge and within the next 48 hours, the patient is seen by their Primary Care Manager (PCM). The PCM will then begin to manage and assess the patients’ medical needs, including referrals to numerous specialty care clinics, therapies, and physicians.

D. PREVIOUS STUDIES

The research in our study aims at analyzing treatment effectiveness for amputee patients in the C5 program. This research task is very focused. While few studies were found that directly impact the research direction, there are several related works relevant to this study. This section is broken into four distinct literature subgroups, and addresses the relationship between each literature subgroup and relevance to our study.

1. Resource Utilization, Treatment, and Clinical Outcomes of Amputee Patients

Understanding which variables influence a patients’ ability to heal more quickly (e.g., the location of the amputation, medication prescribed to manage pain, magnitude of preexisting or current injuries, and cause of injury), allows for more effective and appropriate utilization of resources and improvement in combat casualty care of patients.

Shin, Evans, and Fleming (2012) examined resource utilization in combat-related amputations from OEF and OIF
by Injury Severity Score (ISS). The ISS is associated with the number of extremities amputated, number of associated injuries, utilized blood products, intensive care unit length of stay (ILOS), and hospital length of stay (HLOS) in those with an upper-extremity amputation (UEA), compared to those with an isolated, lower-extremity amputation (LEA). Shin et al. (2012) note that amputee battle injury patterns result from a significant increase in the frequency of high-energy blast mechanisms; in particular, improvised explosive devices (IEDs), which lead to more severe and complex injuries.

The study by Shin et al. (2012) included 102 male Marines with a mean age of 24.3 years. The majority of the injuries were a result of high-energy blasts; however, the presence of a high-energy blast injury was not a significant factor between the two groups (UEA versus LEA). UEA, however, was associated with increased blood product utilization, ILOS, and increased HLOS. The difference in the ISS between UEA and LEA patients was not significant. The severity of the injury and resource utilization was underestimated by the ISS in patients with combat-related amputations.

Melcer, Walker, Sechriest II, Galarneau, Konoske, and Pyo (2013) compared the clinical outcomes of combat amputee patients to those patients who did not sustain an amputation injury during Iraq and Afghanistan deployments. Amputee patients had a significantly lower follow-up rate within 18-24 months of their post-injury treatment, and a significantly higher complication rate than patients without amputations for subsets of complications. These subsets include:
• Infection;
• Anemia;
• Heterotopic Ossification;
• Septicemia;
• Deep Vessel Thrombosis; and
• Pulmonary Embolism.

Furthermore, amputees display an increased rate of mental health issues such as nonorganic sleep, pain, and post-concussion syndrome. Post-Traumatic Stress Disorder (PTSD) rates were found to be relatively low among amputee patients, whereas age, TBI, mechanism of injury, and injury year were significantly associated with the health outcomes within these two groups. The study concluded that medical care of amputee patients should focus on aggressive infection control and wound management practices, as well as early interaction of behavioral health services to mitigate the effects of mental health disorders.

Tintle, Baechler, Nanos, Forsberg, and Potter (2012) hypothesized that current revision rates among UEA patients are higher than existing literature would suggest, and that surgical treatment of complications and persistent symptoms would lead to improved outcomes in health. The study included 100 major UEAs from OIF and OEF. All amputations resulted from high-energy trauma such as blast injury. Forty-two percent of the patients underwent repeat surgical interventions, 27% remained on opiate pain medication, and 28% remained on nonopioid, antineuropathic pain medications. The authors were unable to conclude if surgical intervention improved chronic pain levels. Moreover, the level of amputation did not correlate with
the presence of limb pain, opioid pain usage, or return to duty. However, phantom limb pain and the use of neuropathic pain medications were correlated.

In our study, the amputation population has similar characteristics to the 2012 study by Tintle et al., including injuries caused by IEDs, opiate usage, and repetitive surgical intervention.

2. Influence of “Missed” Appointments on Patient Care

Our study shows that “cancelled” appointments impact the patient’s duration in the C5 program, which indirectly increases medical costs through wasted physician man-hours and more days of patient treatment. The studies below address implications, consequences, and medical costs associated with a patient’s failure to comply with scheduled medical appointments.

When patients fail to show up for appointments, the medical facility’s operational efficiency can be greatly reduced (Bertrand, 2000). Providers cannot efficiently treat their patients, and resources are underutilized or wasted while untreated conditions worsen (Bertrand, 2000). Furthermore, missed appointments disrupt patient-provider relationships and deny other patients access to medical care. When appointments are not readily available to military members, these patients are referred to the network providers, which is a substantial cost burden to the military healthcare system. Improving appointment compliance can improve patient care, satisfaction, and also reduce costs (Bertrand, 2000).
Nguyen, DeJesus, and Wieland (2011) examined missed appointments in a Resident Continuity Clinic of 325 patients who received five or more office visits between 2006 and 2008. Prior research has shown that patients who frequently miss appointments tend to be younger, of lower socioeconomic status, have a history of missed appointments, and have government-provided insurance. In their study, patient factors associated with a higher frequency of missed appointments were Medicaid insurance, more frequent emergency department visits, and the use of a medical interpreter. Those patients who had a higher proportion of office visits with their primary care provider were found to have a lower frequency of missed appointments. Moreover, the authors note that a high rate of missed appointments could possibly be used as an indicator of self-care and may help identify those patients who would benefit from case management services that focus on adherence to treatment plans.

3. Understanding Amputee Medical Care and the Importance of Rehabilitation Delivery to These Patients

This section details the patient-physician goals associated with physical therapy (PT) and occupational therapy (OT) appointments. Our study analyzes the association between PT/OT appointments and pain management. Therefore, we would like the reader to understand the goals associated with these forms of therapy and why they are important to amputee recovery.

In the Harvey et al. (2012) study, they address the current atmosphere of battle amputations and detail the
treatment of amputee patients. The following information summarizes their study.

Improvement in body armor and rapid medical evacuation, combined with battlefield medicine and modern resuscitation techniques, have led to increased survival rates among military service members who have sustained severe, combat-related injuries. As of December 2011, nearly 1,400 service members have suffered a major limb amputation as a result of a combat wound sustained in Iraq and Afghanistan. To promote improved long-term functionality, every effort is made to preserve limb joints. This often requires creative skin grafts or muscle flaps that may prolong healing and delay prosthetic fitting and training. Implementing early rehabilitation is vital to promoting range of motion (ROM) and prevention of joint and soft tissue contractures. Achieving adequate pain control is also extremely important; pain management techniques such as continuous regional anesthesia, epidural blocks, patient-controlled analgesia, and oral medications, as well as heat, ice, massage, and electrical stimulation therapies are utilized. To promote a patient’s ability to participate in therapy, premedication with short-acting opioids prior to therapy is sometimes employed. Furthermore, the presence of TBI and/or psychological health problems (e.g., anxiety, depression, PTSD) significantly interfere with the patient’s ability to follow directions, attend to tasks, and show steady learning techniques.

The role of PT is to return the patient to their highest level of attainable physical function. To optimize the success of UEA patients, rehabilitation should begin as soon as possible, while focusing on conditioning critical
core muscles on all planes to allow proper prosthetic use and trunk stability. Patients with bilateral lower extremity loss can be fitted with shorter prosthetics to lower their center of mass to promote gait and balance mastery. PT also includes cardiovascular conditioning to improve endurance and maintain weight control.

The goal of OT is to return each patient to their highest possible level of independence and function in performing activities of daily living (ADL), with and without a prosthesis. ADL includes activities such as eating, grooming, dressing, bathing, toileting, transfers, and wheelchair positioning and mobility.

4. Adverse Impact of Opiate Medication on Patient Care

Our amputee population was dispensed over 3,000 opiate medications during their treatment phase. Our study analyzes the association between PT/OT appointments and opiate usage.

In Trevino, deRoon-Cassini, and Brasel’s (2013) study, they examined opiate medication usage for the treatment of chronic pain in 101 single, level-1 trauma patients at four months posttrauma. Seventy-nine percent of those patients developed chronic pain post-trauma and, of those, 26% were still utilizing opiate medication. Those patients medicated with narcotics at four months posttrauma had significantly more depression, anxiety, life interference, and pain. Relief of pain was not significantly related to opiate usage.
E. CHAPTER CONCLUSION

Our study looks at similar exploratory variables of amputee patients (percentage of “cancelled” and “no show” appointments, IED injuries, TBI, etc.) and analyze their association to treatment outcomes. Chapter III outlines the data and models analyzed in the study, as well as provide descriptive statistics of the variables.
III. DATA AND DESCRIPTIVE STATISTICS

A. INTRODUCTION

This chapter outlines the data analyzed in the study, the data-cleaning techniques utilized, a description of variables examined, and basic descriptive statistics. The exploratory variables outlined in this chapter are analyzed in two different models in Chapter IV. The two models answer the following questions:

- Model 1: Do patient demographics and/or the amount of “kept” PT, OT, and Pain Management and Rehabilitation (PM&R) correlate with reduced opiate usage in amputee patients during treatment?
- Model 2: Do patient demographics and/or percentage of “cancelled” appointments correlate with their duration in the C5 program?

Each model has a response variable:

- Model 1: Reduction in opiate usage; and
- Model 2: Duration in the C5 program

There are also 11 exploratory variables:

- Percentage of “no show” appointments;
- Mechanism of injury;
- Presence of TBI;
- Presence of mental health condition;
- Race;
- Number of primary conditions;
- Number of follow-up surgeries; and
- Percentage of “kept” PT/OT/PM&R appointments.
• Percentage of “cancelled” appointments
• Age upon entry into the C5 program
• Location of amputation

The response and exploratory variables are discussed in Sections C and D of this chapter, respectively. Each section includes a brief description of the variable, descriptive statistics on the variable, and a distribution of the population represented by a bean-plot or another visual figure.

B. DATA SOURCE

The data used for this study was obtained from BUMED. The data contains information on C5 amputee patients between 2002 and 2012. The data were dispersed across multiple Excel spreadsheets and included information on:
  • Patient Referrals;
  • Patient Appointments;
  • Medical Board Status;
  • Surgical Interventions;
  • Prescription Orders; and
  • Patient Admissions.

Patients are identified by unique patient Episode Identification (ID) to ensure patient confidentiality. Patient data from multiple Excel spreadsheets were combined by Episode ID. Amputee patient data was extracted by the listed primary diagnosis code “1.” This code implies that the patient had an amputation. This condition was verified by the primary diagnosis free text cell (doctor notes). Appointment percentages, surgical procedures, and primary condition counts were extracted through the use of pivot
tables in Excel. Medical board data, which were later used in determining the patients’ approximate end date (later referred to as Episode End Date) were extracted and compared from discharge dates provided and free text “dictation edit results.” Lastly, the data were combined into usable common separated values (CSV) files for R programming.

C. RESPONSE VARIABLES

There are two response variables used in the analysis for the models shown in Chapter IV. The response variable name and model in which it will be used is shown in Table 2. A description of each variable and summary statistics follows.

<table>
<thead>
<tr>
<th>RESPONSE VARIABLE NAME</th>
<th>MODEL USED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in Opiate Usage</td>
<td>1</td>
</tr>
<tr>
<td>Duration in the C5 Program</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 2. Mapping of response variables to Models 1 and 2.

1. Reduction in Opiate Usage

Model 1 addresses the question: Do patient demographics and/or the amount of “kept” PT, OT, and PM&R appointments correlate with reduced opiate usage in amputee patients during treatment? The response variable used in this model is a binary response variable; 1 indicates significant reduction in opiate usage and 0 if not.

In Model 1, the raw data include 236 amputee patients. Of those, 186 patients completed the C5 program with PT, OT, and/or PM&R appointments. We restrict the patients to
those with at least three prescribed and dispensed opiate medications within their treatment period, bringing the patient count to 157. These patients were used in the Opiate Log-Regression Model.

The response variable “Opiate Reduction” is derived from a simple linear regression model where “Quantity of Medication Dispensed” was regressed over “Days from Episode Start Date” in the C5 program by Episode ID. Of the 3,510 opiate prescriptions filled, 406 of them were not dispensed to the patient. This implies an estimated patient prescription compliance rate of 88%. The software package R was used for all regressions.

Table 3 provides an example of patient opiate prescription data.

<table>
<thead>
<tr>
<th>EPISODE ID</th>
<th>QTY</th>
<th>AHFS CLASS</th>
<th>FILL</th>
<th>FILL DATE</th>
<th>DISP DATE</th>
<th>PATIENT START DATE</th>
<th>DAYS FROM START</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>60</td>
<td>OPIATE AGONISTS</td>
<td>1</td>
<td>2/24/12</td>
<td>NULL</td>
<td>1/27/2012</td>
<td>-----</td>
</tr>
<tr>
<td>1</td>
<td>60</td>
<td>OPIATE AGONISTS</td>
<td>1</td>
<td>2/26/12</td>
<td>2/26/12</td>
<td>1/27/2012</td>
<td>30</td>
</tr>
<tr>
<td>1</td>
<td>60</td>
<td>OPIATE AGONISTS</td>
<td>1</td>
<td>3/15/12</td>
<td>3/15/12</td>
<td>1/27/2012</td>
<td>48</td>
</tr>
<tr>
<td>1</td>
<td>30</td>
<td>OPIATE AGONISTS</td>
<td>1</td>
<td>4/05/12</td>
<td>4/05/12</td>
<td>1/27/2012</td>
<td>69</td>
</tr>
<tr>
<td>1</td>
<td>20</td>
<td>OPIATE AGONISTS</td>
<td>1</td>
<td>4/23/12</td>
<td>4/23/12</td>
<td>1/27/2012</td>
<td>87</td>
</tr>
<tr>
<td>1</td>
<td>60</td>
<td>OPIATE AGONISTS</td>
<td>1</td>
<td>5/15/12</td>
<td>5/15/12</td>
<td>1/27/2012</td>
<td>109</td>
</tr>
</tbody>
</table>

Table 3. Sample of Opiate prescription data for patient 1.

To determine if the patient significantly reduces their opiate usage over the course of the treatment phase, column two (QTY) and eight (DAYS FROM START) were
regressed. Notice that row one is not included in the analysis because the prescription is not dispensed to the patient.

Table 4 displays the result of the simple linear regression (Appendix A contains R-code and output).

<table>
<thead>
<tr>
<th>REDUCTION IN OPIATE USAGE</th>
<th>PATIENT COUNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES, SIGNIFICANT REDUCTION(1)*</td>
<td>123</td>
</tr>
<tr>
<td>NO, SIGNIFICANT REDUCTION(0)*</td>
<td>34</td>
</tr>
</tbody>
</table>

*LM (QTY ~ Days From Episode Start Date)
Null Hypothesis (H₀): β₀ < 0, where β₀ represents the slope of the regression line.
YES, there is evidence to suggest that opiate usage declined over patient duration in the program = 1).
Alternative Hypothesis (Hₐ): β₀ ≥ 0
NO, there was not significant evidence to suggest that opiate usage declined over patient duration in the program = 0)
Fail to Reject H₀ (interpretation): There is not significant evidence to suggest that β₀ is greater than or equal to zero.
(See Appendix A for simple linear regression R-code.)

Table 4. Simple linear regression of opiate reduction and patient count of regression outcome.

2. Duration in the C5 Program

Model 2 addresses the question: Do patient demographics and/or percentage of cancelled appointments correlate with their duration in the C5 program? The response variable, “Duration in the C5 Program,” used in this model is an integer variable defined by the difference of a patient’s “Episode End Date” and their “Episode Start Date.” Table 5 provides an example of the data. Patient 1 completed the C5 program in 297 days.
<table>
<thead>
<tr>
<th>EPISODE ID</th>
<th>EPISODE START DATE</th>
<th>EPISODE END DATE</th>
<th>DURATION IN THE PROGRAM (DAYS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1/27/2012</td>
<td>11/19/2012</td>
<td>297</td>
</tr>
</tbody>
</table>

Table 5. Sample calculation of duration in the program data for patient 1.

The “Episode Start Date” was modified to reflect the earliest date between the “Given” Episode Start Date (the data supplied by the data file) and “Initial Appointment Date” of the individual patient. The average difference between the “Given” and “Modified” Episode Start Dates is approximately 24 days (less than one month). The “Episode End Date” was modified to reflect the latest date between the “Given” Episode End Date and the latest date noted from Medical Evaluation Board (MEB) Evaluation End Date, MEB End Date, Final Disposition Date, Final Disposition Date, Date Final Out-Processing Complete, or Date of Separation on the DD214. The average difference between the “Given” and “Modified” end date is 72 days (approximately 2½ months). Initially, 137 amputee observations had “Given” Episode End Dates; but, by modifying the Episode End Dates, 49 additional observations were employed. Four patients had to be eliminated due to missing data, so the final population size was 182 patients.

Figure 3 presents summary statistics and distribution associated with the patient duration variable. On average, amputee patients are in the program for 538 days. A bean plot of the patient duration data is also shown in Figure 3. As an alternative to a box plot, a bean plot shows the individual observations as horizontal lines. The density of the data is illustrated by the width of the polygon. The horizontal distance represents the frequency of a specific observation and the bold, horizontal line
represents the mean of the data. A large proportion of the population is distributed between 475 to 600 days, with an average of 538.

<table>
<thead>
<tr>
<th>STATISTIC</th>
<th>DAYS</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEAN</td>
<td>538</td>
</tr>
<tr>
<td>MINIMUM</td>
<td>21</td>
</tr>
<tr>
<td>MAXIMUM</td>
<td>1,963</td>
</tr>
</tbody>
</table>

Statistics were produced in R

D. EXPLORATORY VARIABLES

There are 11 variables used in the analysis to fit the models shown in Chapter IV. The exploratory variable name and the model in which it is used are shown in Table 6. A description of each variable and summary statistics follows.
Table 6. Mapping of exploratory variables to Models 1 and 2.

1. Percentage of “No-Show” Appointments (Variable 1)

The exploratory variable percentage of “no show” appointments is a continuous variable defined by those appointments that were scheduled and missed, but not previously cancelled, divided by the total number of scheduled appointments. Table 7 provides an example of patient appointment data. In this example, patient 1 did not show up for one of six appointments per the data below; therefore, patient 1 has a “no show” percentage of 17%, a “cancellation” percentage of 33%, and a “kept” percentage of 50%.
Table 7. Sample of percentage of “no show” appointment data for patient 1.

Figure 4 presents descriptive statistics and a bean plot of percentage of “no show” data. Of 182 patients, the average patient missed 7.4% of their scheduled appointments.

### PERCENTAGE OF PATIENT APPOINTMENTS THAT WERE CLASSIFIED AS A “NO SHOW”

<table>
<thead>
<tr>
<th>STATISTIC</th>
<th>MEAN</th>
<th>MEDIAN</th>
<th>STANDARD DEVIATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEAN</td>
<td>7.399%</td>
<td>6.292%</td>
<td>5.2%</td>
</tr>
</tbody>
</table>

Statistics were produced in R

Figure 4. Descriptive statistics on percentage of “no show” appointments.
2. Binary Variables (Variables 2, 3, 4, and 5)

Mechanism of injury is the “cause” of injury to the patient. This variable is divided into two groups, a patient who was strictly classified as having an injury caused by an IED or not. If the injury to the patient is not caused by an IED, it falls under the “other” category. The “other” category includes injuries caused by motor vehicle accidents, medical necessity, a fall, airplane crash, gunshot wound, crush wound, grenade, or Not Available (NA).

TBI is a condition that results from a violent blow or trauma of the head or body, or skull penetration. TBI can cause mild to major brain dysfunction (Mayo Clinic, 2012). Approximately 65% of the amputee patients have an amputation caused by an IED blast, 40% have a TBI-related injury, two patients have a diagnosed mental health-related issue, and 63%-65% of the patient population is Caucasian. A mental health condition includes PTSD and non-PTSD related issues such as sexual abuse, depression, anxiety, addition, and suicidal ideologies. Non-Caucasian patients include the races of Hispanic, African-American, Asian, American Indians, and unknown (one patient was in this category). Table 8 depicts the number of patients who have an amputation caused by an IED, a TBI-related injury, a mental health condition, or are Caucasian for each model. Recall that Model 1 includes 157 amputee patients who were prescribed and dispensed at least three opiate medications, whereas Model 2 has 182 patients because opiate usage is not included in this model.
### Table 8. Summary statistics on presence of patient condition or characteristic.

<table>
<thead>
<tr>
<th>CONDITION OR CHARACTERISTIC</th>
<th>Model 1</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes, presence of IED injury (1)</td>
<td>102</td>
<td>119</td>
</tr>
<tr>
<td>Yes, presence of TBI (1)</td>
<td>63</td>
<td>72</td>
</tr>
<tr>
<td>Yes, presence of Mental Illness (1)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Yes, patient is Caucasian (1)</td>
<td>103</td>
<td>116</td>
</tr>
</tbody>
</table>

To ensure that patients were correctly classified, patient indicators were verified by comparing primary ID codes to primary diagnosis free text cells to ensure that patients were identified correctly. Table 9 provides an example of a primary diagnosis ID and free text cell from the data.

### Table 9. Sample of a primary diagnosis ID and free text diagnosis for patient 1.

<table>
<thead>
<tr>
<th>EPISODE ID</th>
<th>PRIMARY DIAGNOSIS ID</th>
<th>PRIMARY DIAGNOSIS FREE TEXT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>Depressed fracture</td>
</tr>
</tbody>
</table>

The primary diagnosis ID value of 12 implies that the patient has a mental health condition that is not PTSD, such as depression. From the free-text diagnosis, we can see that the patient does not have depression, but a depressed fracture. Therefore, the patient should not have an indicator of 1 for a mental health condition.

### 3. Number of Primary Conditions (Variable 6)

Primary conditions include the following injuries: amputation, back injury, burn, fracture, genitourinary injury, gunshot wound, medicine, multilimb fracture, musculoskeletal injury, nerve damage, PTSD, penetrating wound, non-PTSD mental health conditions, TBI, and wounds
not otherwise classified (Wound Not Elsewhere Classified [NEC]). A single primary condition represents an amputee patient. Figure 5 presents descriptive statistics and a bean plot of the count of patient primary conditions. The average amputee patient has three primary conditions: the presence of an amputation with two other health conditions.

<table>
<thead>
<tr>
<th>STATISTIC</th>
<th>Model 1</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>MINIMUM</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>MEDIAN</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>MAXIMUM</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>MEAN</td>
<td>2.682</td>
<td>2.687</td>
</tr>
<tr>
<td>STANDARD DEV.</td>
<td>1.316</td>
<td>1.357</td>
</tr>
</tbody>
</table>

Statistics were produced in R

Figure 5. Descriptive statistics on the number of primary conditions seen in the amputee patients.

4. Follow-Up Surgeries within the C5 Program (Variable 7)

Follow-up surgeries are those surgeries incurred after the patient has been admitted into the C5 program. Figure 6 provides descriptive statistics and a bean plot of the number of patient follow-up surgeries. The average amputee patient undergoes between one and two additional surgeries during their treatment time in the C5 program.
### NUMBER OF FOLLOW-UP SURGERIES

<table>
<thead>
<tr>
<th>STATISTIC (Count)</th>
<th>Model 1</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>MINIMUM</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>MEDIAN</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>MAXIMUM</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>MEAN</td>
<td>1.783</td>
<td>1.621</td>
</tr>
<tr>
<td>STANDARD DEV.</td>
<td>2.357</td>
<td>2.287</td>
</tr>
</tbody>
</table>

Statistics were produced in R

Figure 6. Descriptive statistics on the number of follow-up surgeries required by amputee patients in the C5 program.

5. **Percentage of “Kept” PT, OT, and PM&R Appointments (Variable 8)**

A “kept” appointment includes all PT, OT, and PM&R appoints that were scheduled and not missed due to a cancellation or a “no-show.” The percentage of kept appointments is the total “kept” appointments scheduled divided by the total (“kept,” “cancelled,” and “no-show”) appointments scheduled. In Figure 7, the average amputee patient kept approximately 74% of their scheduled PT, OT, and PM&R appointments.
"Kept" PT/OT/PM&R Appointments

<table>
<thead>
<tr>
<th>STATISTIC (%)</th>
<th>Model 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>MINIMUM</td>
<td>0%</td>
</tr>
<tr>
<td>MEDIAN</td>
<td>74.53%</td>
</tr>
<tr>
<td>MAXIMUM</td>
<td>100%</td>
</tr>
<tr>
<td>MEAN</td>
<td>73.84%</td>
</tr>
<tr>
<td>STANDARD DEV.</td>
<td>12.38%</td>
</tr>
</tbody>
</table>

Statistics were produced in R

Figure 7. Descriptive statistics on the percentage of "kept" PT, OT, and PM&R appointments.

6. Percentage of "Cancelled" Appointments (Variable 9)

This variable is defined by those appointments that were scheduled, but cancelled prior to the scheduled appointment, divided by the total number of scheduled appointments. Of 182 patients, (four additional patients were omitted due to missing data) the average patient cancelled 17.15% of their scheduled appointments (see Figure 8). The data are not sufficiently robust to support a clear distinction between the definition of a "cancelled" appointment and a "no show" appointment; e.g., many "cancelled" appointments were terminated on the same day or within the same hour of the scheduled appointment. Appointment status is manually entered; therefore, the presence of human error could bias the impact of "no show" rates if appointments were noted as "cancelled," but were truly a "no show."
PERCENTAGE OF “CANCELLED” APPOINTMENTS

<table>
<thead>
<tr>
<th>STATISTIC (%)</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>MINIMUM</td>
<td>0%</td>
</tr>
<tr>
<td>MEDIAN</td>
<td>17.15%</td>
</tr>
<tr>
<td>MAXIMUM</td>
<td>55%</td>
</tr>
<tr>
<td>MEAN</td>
<td>17.15%</td>
</tr>
<tr>
<td>STANDARD DEV.</td>
<td>7.249%</td>
</tr>
</tbody>
</table>

Statistics were produced in R

Figure 8. Descriptive statistics on the percentage of cancelled appointments.

7. Age upon Entry into the C5 Program (Variable 10)

The patient’s age is defined as the difference between the patient’s date of birth and the patient’s modified episode start date. Table 10 provides an example of how a patient’s age was calculated.

<table>
<thead>
<tr>
<th>EPISODE ID</th>
<th>EPISODE START DATE</th>
<th>DATE OF BIRTH</th>
<th>AGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1/27/2012</td>
<td>12/22/1978</td>
<td>33</td>
</tr>
</tbody>
</table>

Table 10. Sample calculation of age for Patient 1.

Figure 9 provides descriptive statistics on the patient’s age.
Figure 9. Descriptive statistics on the patient’s age at the time of entry into the C5 program.

8. Location of Amputation (Variable 11)

Of the 182 amputee patients, 150 of them have amputations of their lower body area, 19 have amputations of their upper-body extremity area, and 13 patients have amputations of both the upper and lower body. A lower-body amputation includes an amputation of the hip, knee disarticulation, above or below the knee, ankle joint, partial foot, or toe. Upper-body amputation includes an amputation above or below the elbow, shoulder disarticulation, wrist, or finger. Furthermore, 125 of the 182 patients have one amputation site, 47 have two amputation sites, 9 have three amputation sites, and 1 patient has four. For this study, we focus on the breakdown shown in Figure 10; however, Figure 11 provides additional details about the amputee population in this study.
Figure 10. Patient percentage by location of amputation.

Figure 11. Amputation percentage by specific extremity.
Table 11 provides descriptive statistics on the count of amputations per patient.

<table>
<thead>
<tr>
<th>STATISTIC</th>
<th>MINIMUM</th>
<th>MEDIAN</th>
<th>MAXIMUM</th>
<th>MEAN</th>
<th>STANDARD DEVIATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>MINIMUM</td>
<td>1</td>
<td>1</td>
<td></td>
<td>1.373</td>
<td>0.6065</td>
</tr>
<tr>
<td>MEDIAN</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAXIMUM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEAN</td>
<td></td>
<td></td>
<td></td>
<td>1.373</td>
<td></td>
</tr>
<tr>
<td>STANDARD DEVIATION</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.6065</td>
</tr>
</tbody>
</table>

*Count represents number of amputee sites per patient; some patients had multiple amputees on one or both sides of their upper/lower body (statistics produced in R).

Table 11. Descriptive statistics on the number of amputations per patient.
IV. ANALYSIS

A. MODEL 1

Do patient demographics and/or the amount of “kept” PT, OT, and PM&R appointments correlate with reduced opiate usage in amputee patients during treatment?

1. Analytical Method

Model 1 analyzes the relationship between patient demographics; the amount of PT, OT, and PM&R appointments; and patient opiate usage. In particular, we would like to see if a correlation exists between demographics or patient therapy appointments and a patient’s ability to cope with pain, measured by a reduction in opiate usage during treatment. We use a logistic regression model because the dependent variable, “reduction in opiate usage during treatment” is binary. Let $y_i$ be a random variable indicating if there is a significant reduction in patient $i$’s opiate usage (1 if significant reduction, 0 otherwise). Let $p_i$ be the probability that patient $i$ exhibits a significant reduction in opiate usage. Chapter III, Section C.1 explained how a reduction in opiate usage during treatment ($y_i$) was calculated.

In a logistic regression, the relationship between the predictor and response variables is not a linear function; instead, the logistic regression function is utilized by a logit transformation of $p_i$ (e.g., World Bank, 2010).

The theoretical model is:

$$p_i = \frac{e^{(\beta_0 + \beta_1 x_{i1} + \cdots + \beta_n x_{in})}}{1 + e^{(\beta_0 + \beta_1 x_{i1} + \cdots + \beta_n x_{in})}}$$  \hspace{1cm} (1)
or
\[ \logit(p_i) = \log \frac{p_i}{(1-p_i)} = \beta_0 + \beta_1 X_1 + \cdots + \beta_n X_n, \]

where

\[ \log \frac{p_i}{1-p_i} = \text{log of odds ratio for opiate reduction in patient } i \]

\[ p_i = \text{Probability of reduction in opiate usage; } p_i \text{ is the probability that } Y_i = 1 \text{ and } (1-p_i) \text{ is the probability that } Y_i = 0 \]

\[ \beta_0 = \text{Intercept} \]

\[ \beta = \text{Estimated coefficient of the predictor variables} \]

\[ X = \text{Values of explanatory variables} \]

The coefficients in the model represent the change in the log-odds for a unit change in an \( X_s \). The \( X_s \) captures the various characteristics for the individual patients (this includes demographics and percentage of “kept” appointments). Variable descriptions are displayed in Table 6.

We define the odds ratio of an exploratory variable \( s \) as \( OR_s = e^{\beta_s} \). If the odds ratio for the variable mental health (M_HEALTH) \( (OR_{M\_HEALTH} = e^{\beta_{M\_HEALTH}}) \) equals 1, it is an indication that a patient with a mental health condition is equally likely to either reduce or not reduce their opiate usage. An \( OR_{M\_HEALTH} \) greater than 1, however, indicates a higher likelihood of the patient reducing opiate usage than not. Finally, an \( OR_{M\_HEALTH} \) less than 1 indicates a lower likelihood of a patient reducing opiate usage than not.
2. Analysis/Validation

Model 1 is developed by fitting the data using a Generalized Linear Model (GLM) in R. Several models are fit utilizing the StepAIC (stepwise regression using Akaike Information Criterion) function with main effects and two-way interactions of exploratory variables. A mixed stepwise regression is used in combination with several different starting and ending criteria in order to find the best model (see Appendix B for the R-code).

Table 12 shows the regression coefficient estimates ($\beta_s'$s) for each of the terms in the model, as well as the statistics associated with the hypothesis test for those terms. A factor is significant if the p-value is less than or equal to 0.05.

| TERM                | Estimate | Std. Error | z value | Pr(>|z|) |
|---------------------|----------|------------|---------|---------|
| INTERCEPT           | -11.37162| 4.39121    | -2.590  | 0.00961**|
| AGE_ENTRY           | 0.41635  | 0.17326    | 2.403   | 0.01626* |
| NUM_PRIMARY         | 2.03794  | 1.05483    | 1.932   | 0.05336. |
| PER KEPT            | 0.04074  | 0.01715    | 2.375   | 0.01754* |
| CAUCASIAN 1         | 7.20007  | 2.82198    | 2.551   | 0.0173*  |
| AGE_ENTRY:CAUCASIAN 1 | -0.26966 | 0.11649    | -2.315  | 0.02065* |
| AGE_ENTRY:NUM_PRIMARY| -0.09379 | 0.04358    | -2.152  | 0.03138* |

Significance level: ** 0.01 '*' 0.05 '.' 0.1

Table 12. Model 1 with interaction terms and statistics.

The patient’s age and race; number of primary conditions; percentage of “kept” OT, PT, and PM&R appointments; and interaction of the patient’s age with race and number of primary conditions were found to be significant model terms. The final model can be expressed in Equations 2 and 3:
\[
\log\frac{\hat{p}_i}{1-\hat{p}_i} = \hat{\beta}_0 + \hat{\beta}_1 X_{\text{AGE\_ENTRY}} + \hat{\beta}_2 X_{\text{NUM\_PRIMARY}} + \hat{\beta}_3 X_{\text{PER\_KEPT}} + \hat{\beta}_4 X_{\text{CAUCASIAN\_1}} - \\
\hat{\beta}_5 X_{\text{AGE\_ENTRY}}X_{\text{CAUCASIAN\_1}} - \hat{\beta}_6 X_{\text{AGE\_ENTRY}}X_{\text{NUM\_PRIMARY}}
\] (2)

where

\[
\log\frac{\hat{p}_i}{1-\hat{p}_i} = \\
-11.37 + (0.42)X_{\text{AGE\_ENTRY}} + (2.04)X_{\text{NUM\_PRIMARY}} + (0.0407)X_{\text{PER\_KEPT}} + \\
(7.20)X_{\text{CAUCASIAN\_1}} - (0.27)X_{\text{AGE\_ENTRY}}X_{\text{CAUCASIAN\_1}} - \\
(0.09)X_{\text{AGE\_ENTRY}}X_{\text{NUM\_PRIMARY}}
\] (3)

The percentage of “kept” appointments is the only variable not involved in the interaction that is significant, with a beta coefficient of 0.0407 and an odds ratio value of 1.04 \(e^{0.0407}\). This value implies that a higher percentage of “kept” appointments is correlated with an increase in the odds of reducing opiate usage.

As an example of using the logistic regression equation, a 25-year-old Caucasian patient who has three primary conditions and maintains 74% of their PT, OT, and PM&R appointments results in an estimated probability of 0.877 that the patient reduces their opiate usage (see Figure 12).
\[ p_i = \frac{e^{(\alpha)}}{1 + e^{(\alpha)}} \]

Where

\[ \alpha = -11.37 + (0.42)X_{AGE\_ENTRY} + (2.04)X_{NUM\_PRIMARY} + (0.0407)X_{PEP\_KEPT} \\
+ (7.20)X_{CAUCASIAN} - (0.27)X_{AGE\_ENTRY}X_{CAUCASIAN} \\
- (0.09)X_{AGE\_ENTRY}X_{NUM\_PRIMARY} \]

**Therefore** \[ \alpha = -11.37 + (0.42)(25) + (2.04)(3) + (0.0407)(74) + (7.20)(1) \\
- (0.27)(25)(1) - (0.09)(25)(3) \]

\[ p_i = 0.877 \]

**Figure 12.** Estimated probability of a 25-year-old Caucasian patient with three primary conditions who kept 74% of their PT, OT, and PM&R appointments.

Thus, \( p_i = 0.877 \), and to classify \( y_i \) as \( y_i = 1 \) or 0, a threshold value must be selected. The selection criteria is discussed below.

In a binary classification test each patient ends up in one of the four possible states: True Positive, False Positive, True Negative, and False Negative (Fricker, 2013). In our case, the following is the interpretation of these states:

- **True Positive (TP):** A patient reduces their opiate usage and is correctly classified by the model.
- **False Positive (FP):** A patient does not reduce their opiate usage, but the model incorrectly classifies them as reducing their opiate usage.
- **True Negative (TF):** A patient does not reduce their opiate usage and is correctly classified by the model.
• False Negative (FN): A patient reduces their opiate usage, but the model incorrectly classifies them as not reducing their opiate usage.

We identify an FP as a more severe misclassification than an FN. The patients falling into this category could require more care and case management to progress in the C5 program. Since these patients are classified incorrectly, however, their needs may go unidentified.

Figure 13 demonstrates FP and FN values at varying thresholds. Initially, the threshold is set at 0.5, which implies that for any \( p_t > 0.5 \), the patient is classified as a \( y_t = 1 \). As the threshold values reduce from 0.9 to 0.5, the likelihood of predicting that an amputee patient reduces their opiate medication when, in reality, they actually did not (FP) increases, whereas the FN value decreases (predicts that a patient does not reduce their opiate usage, but, in reality, they did).
Figure 13. Variation of reduction in opiate usage prediction at varying threshold values. As the threshold values reduce from 0.9 to 0.5, the likelihood of predicting an FP increases, whereas FN decreases.

From Figure 13, we determined that an acceptable FP is at or below 0.4. To maintain an FP rate of 0.4, the threshold value lies between 0.70 through 0.80.

Utilizing the Cross-Validation Generalized Linear model (cv.glm) in R, the data is randomly divided into K groups. K splits are found by randomly partitioning the data into K groups of approximately equal size (Davison, 1997). The cv.glm function calculates the estimated K-fold cross-validation (CV) prediction error for a GLM.

Table 13 provides the corresponding threshold value to its FP, misclassification rate (MR), CV, and the difference of the MR to its CV. We would like a minimal difference
between the MR and CV. We select a threshold value of 0.76, as it results in an FP close to 0.4, with a minimal difference between the MR and CV.

<table>
<thead>
<tr>
<th>Threshold Value</th>
<th>FP Rate</th>
<th>Misclassification Rate (MR)</th>
<th>Cross-Validation Rate (CV)</th>
<th>Difference (CV - MR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.75</td>
<td>0.44</td>
<td>0.312</td>
<td>0.32</td>
<td>0.008</td>
</tr>
<tr>
<td>0.76</td>
<td>0.41</td>
<td>0.318</td>
<td>0.32</td>
<td>0.002</td>
</tr>
<tr>
<td>0.77</td>
<td>0.38</td>
<td>0.312</td>
<td>0.35</td>
<td>0.038</td>
</tr>
<tr>
<td>0.78</td>
<td>0.38</td>
<td>0.331</td>
<td>0.37</td>
<td>0.039</td>
</tr>
</tbody>
</table>

Table 13. Varying threshold values with corresponding FP, MR, and CV rates.

The calculated cross-validation value at a threshold of 0.76 is 0.32, with 10 folds. The misclassification and cross-validation values are approximately the same (see Figure 14 and Appendix B). Table 13 and Figure 14 shows that our model, even out of sample and using the significant patient characteristics, (1) accurately classifies about 70% of patients between reducing opiate usage and not, and (2) it keeps the false positive rate at or below 0.4.

<table>
<thead>
<tr>
<th>Actual Status</th>
<th>Reduce Opiate Usage</th>
<th>Test Outcome</th>
<th>Misclassification Matrix for the Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - No</td>
<td>FALSE</td>
<td>FALSE_TN = 20</td>
<td>TRUE_FP = 14</td>
</tr>
<tr>
<td>1 - Yes</td>
<td>FALSE</td>
<td>FN = 36</td>
<td>TP = 87</td>
</tr>
</tbody>
</table>

= (14+36)/157 = 0.318

Figure 14. Misclassification matrix and calculation.
3. Results and Discussion

While our model does not prove causation, it does allow us to classify the odds that a patient reduces their opiate usage based on Equations 1 and 3. An example calculation of $p_i$ was shown in Figure 12, resulting in a $p_i$ value of 0.877. At a threshold of 0.76, this patient would be classified as a 1; the patient reduces opiate usage.

The percentage of “kept” OT, PT, and PM&R appointments is the only significant variable that is not involved in any interaction term (see Table 12). Moreover, the odds ratio value is greater than 1, meaning that more missed appointments decrease the likelihood of opiate reduction. Figure 15 illustrates that an amputee patient who maintains 80% or less of their PT, OT, and PM&R appointments accounts for approximately 80% (27/34) of the patients who did not significantly reduce their opiate usage. Per the observations and analysis, there exists a positive association between an amputee patient’s ability to keep OT, PT, and PM&R appointments and their ability to reduce opiate usage.
Figure 15. The interaction of “kept” OT, PT, and PM&R appointments on a patient’s ability to reduce their opiate usage. There is a positive association between the amputee’s ability to keep their appointments and a reduction in their opiate usage.

The presence of interaction in a logistic model can complicate the interpretation of an individual effect. For clarity of interpretation and results, we present descriptive statistics in tabular form as well as interaction plots. Tables 14 and 15 and Figures 16 through 19 illustrate exploratory descriptive statistics of the interaction terms involved in the model. Patients were divided into four groups and broken down by reduction in opiate usage and race. Table 14 illustrates that there are
twice as many Caucasian patients compared to non-Caucasian patients who significantly reduced their opiate usage and approximately the same number of patients who did not significantly reduce their opiate usage regardless of race (e.g., Caucasian patients who did reduce their opiate usage = 22, compared to non-Caucasian patients who did = 10).

<table>
<thead>
<tr>
<th>AGE</th>
<th>NO Caucasian</th>
<th>NO Non-Caucasian</th>
<th>YES Caucasian</th>
<th>YES Non-Caucasian</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>19-21</td>
<td>4</td>
<td>5</td>
<td>22</td>
<td>10</td>
<td>41</td>
</tr>
<tr>
<td>22-24</td>
<td>6</td>
<td>7</td>
<td>24</td>
<td>16</td>
<td>53</td>
</tr>
<tr>
<td>25-27</td>
<td>4</td>
<td>2</td>
<td>21</td>
<td>4</td>
<td>31</td>
</tr>
<tr>
<td>OVER 27</td>
<td>19</td>
<td>15</td>
<td>84</td>
<td>39</td>
<td>157</td>
</tr>
</tbody>
</table>

Table 14. Count of patients by reduction in opiate usage (YES) by age and race.

The percentage of patients who display a greater reduction in opiate usage are 27-year-old (or younger at the time of entry into the C5 program) Caucasian patients, compared to non-Caucasian patients. The percentage declines, however, when the patient is older than 27 (as shown in Figure 16).
Figure 16. Interaction of the patient’s age and race compared to the percentage of patients who display significant opiate reduction. The percentage of patients who display a greater reduction in opiate usage are 27-year-old (or younger) Caucasian patients compared to non-Caucasian patients.

Figure 17 displays the interaction plot between age and race. We can also see that the overall estimated probability of reduction in opiate usage decreases as a Caucasian patient’s age increases, whereas the estimated probability increases for non-Caucasian patients as age increases.
Figure 17. Interaction plot of patient’s age and race. The estimated probability of reduction in opiate usage increases as a non-Caucasian patient ages.

Table 15 illustrates that there are approximately five times as many patients with one or two primary diagnoses that reduced their opiate usage than those patients who did not (28:6, 35:7). There are also three times as many patients with three or more primary diagnoses that reduce their opiate usage than those who did not (30:10, 30:11).

<table>
<thead>
<tr>
<th>#Primary Diagnosis</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>Over 3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>19-21</td>
<td>8</td>
<td>3</td>
<td>8</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>22-24</td>
<td>5</td>
<td>2</td>
<td>12</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td>25-27</td>
<td>7</td>
<td>1</td>
<td>7</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>OVER 27</td>
<td>8</td>
<td>0</td>
<td>8</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>TOTAL</td>
<td>28</td>
<td>6</td>
<td>35</td>
<td>7</td>
<td>30</td>
</tr>
</tbody>
</table>

Table 15. Count of patients by reduction in opiate usage (YES/NO) by age and number of primary diagnoses.
Figure 18 shows that patients between the ages of 22 and 24 years old tend to maintain a relatively consistent percentage of reducing their opiate usage (70%-80%), regardless of the amount of primary diagnosis; whereas, the youngest patients (19-21 years old) tend to reduce opiate usage as the number of primary conditions increase.

![Graph showing interaction of patient's age and number of primary conditions compared to percentage of patients with significant reduction in opiate usage.](image)

Figure 18. Interaction of patient’s age and number of primary conditions compared to the percentage of patients who displayed a significant opiate reduction. There is greater variability in the percentage of patients with opiate reduction when the patient is 25 and older, as the number of primary conditions increases.

We can also see that the overall estimated probability of reduction in opiate usage declines as the patient ages and the number of primary conditions increases (see Figure 19).
Our model is based on 157 observational data points. The percentage of kept appointments and the interaction of race and age, and the number of primary conditions and age appear to be correlated with whether or not a patient reduces their opiate usage.

The observational data is moderately-sized. Therefore, it is possible that some of the model terms are sample-specific and could not be generalized for the entire amputee population. For example, the empirical odds ratio of the influence of race on opiate usage is 1.7 by Equation 4. This implies that the odds of a patient decreasing their opiate usage is twice as high if the patient is Caucasian, than if the patient is not Caucasian.

\[
\frac{\Pr(y=1|\text{Caucasian})}{\Pr(y=0|\text{Caucasian})} \div \frac{\Pr(y=1|\text{Non Caucasian})}{\Pr(y=0|\text{Non Caucasian})} = \frac{84}{19} \div \frac{39}{15} = 1.7
\] (4)
Due to the relatively small number of patients who are not Caucasian and did not significantly reduce their opiate usage (15 patients), the empirical odds ratio can be altered by a small decrease of patients falling into this group. For example, by simply having nine (a reduction of six patients) non-Caucasian patients who did not significantly reduce their opiate usage, the new empirical odds ratio is approximately 1. This suggests that the odds of an amputee patient who is Caucasian or not is equally likely to reduce opiate usage over time.

While few studies were found that directly impact the research direction for Model 1, a study of opiate medication usage for treatment of chronic pain by Trevino et al. (2013) found that trauma patients medicated with narcotics at four months posttrauma had significantly more depression and anxiety. Our model suggests that there is a positive correlation to a reduction in opiate usage and percentage of kept physical rehabilitation appointments. Therefore, promoting compliance with PT, OT, and PM&R appointments could improve the mental health outcome of patients. The goal of patient care is overall health improvement, both physically and mentally, of the patient.

Our study could be used for future meta-analysis work to determine if similar correlations are repeated in other amputee populations.

B. MODEL 2

Do patient demographics and/or percentage of “cancelled” appointments correlate with their duration in the C5 program?
1. Analytical Method

Model 2 analyzes the relationship between patient demographics and cancelled appointment rates, and an amputee’s duration in the C5 program (measured in days). A multiple linear regression model is used in this case, as the outcome of “duration” is a continuous variable.

A multiple linear regression models the association between at least two exploratory variables \( x \) and a response variable \( y \) by fitting a linear equation to the observed data (Lacey, 1997). The population regression line describes how the mean \( (E[y]) \) changes with respect to the exploratory variables; the theoretical model with only main effects is represented as:

\[
y_i = \beta_0 + \beta_1 x_{i1} + \cdots + \beta_s x_{is} + \epsilon \text{ for } i = 1, 2, \ldots, s
\]

where

- \( y_i \) = The dependent variable for every observation \( (i) \), duration in the C5 program (in days)
- \( \beta_0 \) = Intercept
- \( \beta_1, \ldots, \beta_s \) = Estimated coefficient (slope) for each independent variable
- \( X \) = Values of exploratory variables (regressors)
- \( \epsilon \) = Residuals

The observed values for \( y \) are assumed to have the same standard deviation and fluctuate about the mean \( E[y_i] \). The estimates of the population regression line are \( \beta_0, \beta_1 \ldots \beta_s \). The residual term (or noise) in the data, notated by \( \epsilon \), represents the difference between the observed values \( y \) from
their means $E[y_i]$, which are assumed to have a mean of zero, constant variance, and to be normally distributed (Lacey, 1997).

The coefficients in the model represent the change in dependent variable for a unit change in $X$. The $X_s'$s included in this model are shown in Table 6.

2. Analysis

To analyze Model 2, the data is fit utilizing a multivariate Linear Model (LM) in R, allowing for two-way interactions of the independent variables using the StepAIC function. Initial testing indicated that subcategorizing the patients by type of amputation: UEA, LEA, or both (an upper- and lower-body extremity amputation) led to a superior model fit.

A $y$ transformation is required in the model because the residuals were not normally distributed. We used a Box-Cox test to determine a $y$ transformation of $y^\lambda$. $\lambda$ was approximately 0.5, which translates to a transformation of $y$ to $\sqrt{y}$ (see Appendix C for $y$ transformation test and model selection). After several iterations of model fitting, the model with coefficients shown in Table 16 was used (see Appendix C for the R-code). Parameter estimates involving categorical values require the addition of dummy variables. For example, the variable “location of amputation” has three categories (upper, lower, and both). The dummy variables in the model are upper and lower, while the category “both” is associated with the intercept value of the model. While the overall effect is significant, not all
dummy variables necessarily appear as significant or have a p-value of 0.05.

| TERM                | Estimate | Std. Error | t value | Pr(>|t|) |
|---------------------|----------|------------|---------|---------|
| INTERCEPT           | 20.896   | 8.2039     | 2.547   | 0.01176*|
| AGE_ENTRY           | -0.2638  | 0.1172     | -2.251  | 0.02566*|
| CAUSE_IED           | -2.9997  | 3.0794     | -0.974  | 0.33139 |
| NUM_PRIMARY         | 1.5969   | 0.6705     | 2.382   | 0.01835*|
| CAUCASIAN_1         | -6.2217  | 5.0935     | -1.222  | 0.22360 |
| PerCNL              | 0.1707   | 0.3595     | 0.475   | 0.63561 |
| AMP_SITE_L          | 9.9775   | 6.8490     | 1.457   | 0.14704 |
| AMP_SITE_U          | -4.7774  | 7.7431     | -0.617  | 0.53808 |
| CAUCASIAN_1:PerCNL  | -0.3324  | 0.1474     | -2.256  | 0.02539*|
| AGE_ENTRY:CAUCASIAN_1 | 0.4833  | 0.1685     | 2.869   | 0.00465**|
| PerCNL:AMP_SITE_L   | -0.4017  | 0.3213     | -1.250  | 0.21301 |
| PerCNL:AMP_SITE_U   | 0.1328   | 0.3612     | 0.368   | 0.71352 |
| CAUSE_IED_1:PerCNL  | 0.3273   | 0.1420     | 2.304   | 0.02242*|
| CAUSE_IED_1:NUM_PRIMARY | -1.7684 | 0.7897     | -2.239  | 0.02645*|

Significance codes: ‘***’ 0.001 ‘**’ 0.01 '*' 0.05 '.' 0.1

Table 16. Regression of Model 2.

The final model can be expressed in Equations 5 and 6:

\[ \hat{y}^* = \sqrt{y}. \]

Therefore,

\[ \hat{y}^* = \hat{\beta}_0 - \hat{\beta}_1 X_{AGE\text{ENTRY}} - \hat{\beta}_2 X_{CAUSE\text{IED}} + \hat{\beta}_3 X_{NUM\text{PRIMARY}} - \hat{\beta}_4 X_{CAUCASIAN_1} + \hat{\beta}_5 X_{PER\text{CNL}} + \hat{\beta}_6 X_{AMP\text{SITE}} - \hat{\beta}_7 X_{CAUCASIAN_1} X_{PER\text{CNL}} + \hat{\beta}_8 X_{AGE\text{ENTRY}} X_{CAUCASIAN_1} + \hat{\beta}_9 X_{PER\text{CNL}} X_{AMP\text{SITE}} + \hat{\beta}_{10} X_{CAUSE\text{IED}} X_{PER\text{CNL}} - \hat{\beta}_{11} X_{CAUSE\text{IED}} X_{NUM\text{PRIMARY}} \]  

(5)

where
The R-squared and adjusted R-squared value of Model 2 are 0.2500 and 0.1932, respectively; 19% of the variance is explained by this model. The residuals of the model are homoscedastic, independent, and normally distributed.

3. Results and Discussion

While our model does not prove causation, it does provide insight into exploratory variable and response correlations.

The fitted model shown in Equation 6 indicates that the slopes of the main effect coefficients for a patient’s age, IED injury, and race are negative. This implies that the presence of an IED injury or being a Caucasian patient decreases the patient’s duration in the program. It also suggests that as a patient’s age increases, their duration in the program declines, whereas the coefficients for the number of primary conditions and percentage of cancelled appointments are positive. As the number of primary conditions and percentage of cancelled appointments increase, patients are staying in the program longer.

Figure 20 indicates the interpretation of the amputee location variable (AMP_SITE_L and AMP_SITE_U). Recall that the response $\hat{y}^*$ is the square root of the days in the program. Our model predicts that a patient with an upper-body amputation spends approximately 225 days in the
program, compared to 900 days for a patient with a lower-body amputation (holding all other variables constant).

![Graph showing duration in the program for different amputation sites](image)

**Figure 20.** Amputation site coefficient estimates for the fitted model for y. Amputees with lower-body amputations spend the most time in the program.

Additionally, the interaction of exploratory variables influences the coefficient estimates. Figures 21 through 24 display interaction plots of the exploratory variables in the fitted model.

When a Caucasian patient cancels more appointments, their duration in the program declines. There is, however, a positive correlation between the percentage of cancelled appointments and duration in the program for non-Caucasian patients (see Figure 21). Notice that the slopes of the lines in the interaction plot are in opposite directions.
Figure 21. Interaction plot between race and the percentage of “cancelled” appointments from Model 2. There is a positive correlation between the percentage of “cancelled” appointments and duration in the program for non-Caucasian patients and a negative correlation for Caucasian patients.

The interaction plot in Figure 22 has two lines with opposing slope directions. This implies that as a patient with an IED injury increases their percentage of “cancelled” appointments and their duration in the program increases, whereas a patient without an IED-inflicted amputation remains in the program for less time as the percentage of “cancelled” appointments increases.
Figure 22. Interaction plot between the patient’s mechanism of injury and the percentage of “cancelled” appointments. IED-injured patients with a greater percentage of “cancelled” appointments are positively correlated to a longer duration in the program.

Figure 23 displays the interaction between the patient’s mechanism of injury and the number of primary conditions. When a patient suffers from an IED-related amputation, their duration in the program is relatively constant (almost a horizontal slope), regardless of the number of primary conditions. When a patient does not suffer from an IED-related amputation, however, there is a greater variation in the patient’s duration in the program across the magnitude of primary conditions. Specifically, patients without an IED-related injury spend more time in the C5 program as the number of primary conditions increase.
Figure 23. Interaction plot between the mechanism of injury and number of primary conditions from Model 2. Patients without an IED-related injury spend more time in the C5 program as the number of primary conditions increases.

In Figure 24, notice that the direction of the slopes for UEAs and amputees with both an LEA and UEA are positive. This implies that as the percentage of “cancelled” appointments increases, UEAs and amputees with both an LEA and UEA spend more time in the C5 program (days). This is in contrast to amputees with lower-body-extremity amputation, who spend less time in the C5 program as the percentage of “cancelled” appointments increase.
Model 2 is based on 182 patients. Our analysis shows that the amputation site influences treatment longevity. There is a distinct difference between the amputation site and its correlation to treatment duration. Recall that as the percentage of “cancelled” appointments increased, UEAs and amputees with both an LEA and UEA spent more time in the C5 program (days), whereas lower-body-extremity amputation patients did not. While few studies were found that directly impact the research direction for Model 2, a study by Shin et al. (2012) found that UEAs were associated with increased injury severity and HLOS and ILOS. Our study produces similar results with UEA patients staying in the C5 program longer in the presence of increased “cancelled” appointments. LEA patients as a whole, however, spend more time in the treatment program (recall Figure 20). HLOS and ILOS were not included in this study. This suggests that
UEAs and those with both a UEA and LEA are more affected by “cancelled” appointments than LEAs in terms of completing their treatment.

We see that “cancelled” appointment rates are positively associated with an amputee patient’s duration in the C5 program when the patient is non-Caucasian, has an IED injury, or has a UEA or both an LEA and UEA. Recall that the data are not sufficiently robust to support a clear distinction in defining “cancelled” and “no show” appointments. For example, many “cancelled” appointments were terminated on the same day of the scheduled appointment. Appointment status is manually entered; therefore, the presence of human error could bias the impact of “no show” rates if appointments were noted as “cancelled,” but were truly a “no show.” Appointments cancelled on the same day or within the same hour of scheduled care increase medical costs through wasted physician man-hours and more days of patient treatment through rescheduled appointments. This leads to underutilized resources, poor medical outcomes as untreated conditions worsen, and denied care to other patient’s (Bertrand, 2000). Therefore, implementing programs or incentives that discourage patients from missing their appointments can increase treatment efficiency and resource utilization. Future research in patient-provider modeling that focuses on optimizing the ratio of appointment types (e.g., what is the optimal amount of primary care, PT, OT, etc. appointment mix that renders an optimal medical outcome) could also reduce the number of “cancelled” appointments.
V. CONCLUSIONS

In an effort to better understand the factors that influence the treatment effectiveness of combat casualty amputee patients, our thesis analyzed the data of 182 amputee patients within the C5 program through the use of logistic and linear regression models.

The main results of our analysis show that:

- An increase in attendance to PT, OT, and PM&R appointments correlated to an increased likelihood of reduced opiate usage.
- The estimated probability of reduction in opiate usage is less likely as the patient ages and the number of primary medical conditions increase.
- Patients without an IED injury spend more time in the program as the number of primary conditions increase.
- The percentage of cancelled appointments is positively associated with the treatment duration of UEAs, patients with both a UEA and LEA, and amputations caused by an IED.
- The number of follow-up surgeries, the presence of a traumatic brain injury, and possessing a mental health condition did not have a significant impact on opiate usage or duration in the program.

A. FUTURE RESEARCH

The results of our study and similar studies can influence medical cost-saving initiatives and practices by...
analyzing the implications of treatment compliance, effective treatment programs, and understanding prescription drug utilization. For example, many private medical practices charge a fee for not showing up at all or cancelling an appointment within 24 hours of scheduled care to deter patients from missing their appointments. Military medicine could implement a similar fee to discourage missed appointments, which lessens medical resource waste. Our study also did not distinguish between which types of appointments were missed most often and the location of care. It is not uncommon for specialty appointments to be located off-site from the MTF, whereas primary care is generally located on-site. The location of the appointment may influence the number of missed appointments, as those appointments that are missed most often may reflect care that is provided off-site, where the means of transportation could create an undue burden on the patient. Providing optional means of transportation, such as a shuttle service, could increase appointment compliance.

Our study could be used for future meta-analysis work to determine if similar correlations are repeated in other amputee populations by collecting a larger sample size of amputee patient data from multiple MTFs. It may also be useful to formulate an injury severity score of the amputee patient prior to entry into the C5 program and include this score in the models. The injury severity score could include data relevant to the severity of an injury such as:

- Patients hospital and intensive care length of stay;
- Amount of blood products used in treatment;
- Presence of infection, anemia, pulmonary embolism, and septicemia;
- Severity of amputation;
- Preexisting medical conditions; and
- Surgical and nonsurgical treatment from point of injury (level 1 trauma care) to a U.S. MTF (level 5 trauma care).

Our study focused solely on opiate usage; however, there are numerous medications prescribed to amputee patients for pain management or management of other symptoms including (but not limited to): nonsteroidal anti-inflammatory medications, centrally acting skeletal muscle relaxants, and anticonvulsants.

Future analysis could study the implications of other types of drug usage on physical and mental rehabilitations. The impact of appointment statistics and prescription compliance could be expanded to other areas of treatment, such as those patients who suffer from only a TBI or PTSD. For example, do patient demographics and/or the number of attended mental health appointments correlate with reduced antidepressant medication usage? Lastly, more research in patient-provider modeling that focuses on optimizing the ratio of appointment types (e.g., what is the optimal amount of primary care, PT, OT, etc. appointment mix that renders an optimal medical outcome) could also reduce the number of missed appointments and lead to better resource utilization.
APPENDIX A. R-CODE FOR MODEL 1 RESPONSE VARIABLE

R-code for Simple Linear Regression: To determine the response variable for Model 1 (Opiate Medication Declines over Treatment Phase in Amputee Patients).

R-code and Output

```r
#OpiateUsage is a dataframe containing QTY~ Quantity of opiates dispensed and DaysFromStart_D ~ number of days that have elapsed between the patients start date in the C5 program and date of dispensed medication.

OpiateUsage$Episode_ID = as.integer(OpiateUsage$Episode_ID)

#Sample Output

OP2<-OpiateUsage[OpiateUsage$Episode_ID==2,]
lm(QTY~DaysFromStart_D, data = OP2)
anova(lm(QTY~DaysFromStart_D, data = OP2))

#Function to calculate Pr(>F) values on simple linear regression model of: Frequency of Opiate Medication(y) = DaysFromStart_D (Date of entry into program from prescription “Dispense” date ~x)

Sig<-function(x) {
  if (nrow(x)>2){
    xx <-anova(lm(QTY~DaysFromStart_D, data = x))
    xx[[1,'Pr(>F)']]}
  else 1
# must have at least 3 data points (3 prescribed and dispensed opiate medications per patient) for ANOVA or result is 1}

#Run the function “SIG” on each patient but break-up output by patient “Episode ID” ~ return Pr(>F) values

OPSig <- by(OpiateUsage, OpiateUsage[, 'Episode_ID'], Sig)
```

65
#simple linear model

lm(QTY~DaysFromStart_D, data = OP2)

**OUTPUT**

Call:
lm(formula = QTY ~ DaysFromStart_D, data = OP2)

Coefficients:
  (Intercept) DaysFromStart_D    
    88.683     -1.078               

#ANOVA on LM model
#look at single patient

anova(lm(QTY~DaysFromStart_D, data = OP2))

**OUTPUT**

#output for single patient, Patient 2
#Accept NULL Hypothesis for Patient 2

Analysis of Variance Table

Response: QTY
  Df Sum Sq Mean Sq F value Pr(>F)
DaysFromStart_D 1 310.42 310.42 0.7699 0.4448
Residuals      3 1209.58 403.19

#run the regression for the first 4 patients
#Note: accept Null Hypothesis for all 4 patients
#Null: Opiate usage declined over time

head(OPSig)

**OUTPUT**

OpiateUsage[, "Episode_ID"]
  2 28 38 51
0.44484294 0.44782905 0.09121801 0.48695957
APPENDIX B. LOGISTIC REGRESSION R-CODE FOR MODEL 1

Utilizing R StepAIC with two-way interaction (Factorial to degree 2) resulted in the following Logistic Regression Model.

<table>
<thead>
<tr>
<th>R-code For Model 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>#main effects model using a GLM, data is called &quot;OP&quot;</td>
</tr>
<tr>
<td>OP0&lt;-glm</td>
</tr>
<tr>
<td>(Reduce_Opiate_Dis~AGE_ENTRY+TBI+Num_Primary+PER_KEPT + Caucasian+X.Fol_Up_Surgeries+M_Health + AMP_SITE,</td>
</tr>
<tr>
<td>data=OP,</td>
</tr>
<tr>
<td>family =binomial)</td>
</tr>
<tr>
<td>#main effect model with two way interactions</td>
</tr>
<tr>
<td>OP_ALT&lt;-stepAIC(OP0,scope = ~.^2, direction = &quot;both&quot;, trace = FALSE)</td>
</tr>
<tr>
<td>summary(OP_ALT)</td>
</tr>
</tbody>
</table>

OUTPUT

#output from OP_ALT

Call:
glm(formula = Reduce_Opiate_Dis ~ AGE_ENTRY + Num_Primary + PER_KEPT + Caucasian + AGE_ENTRY:Num_Primary + AGE_ENTRY:Caucasian, family = binomial, data = OP)

Deviance Residuals:
  Min       1Q   Median       3Q      Max
-2.1504  0.2893  0.5157  0.7030  1.4622

Coefficients:
                     Estimate Std. Error z value Pr(>|z|)
(Intercept)       -11.37162   4.39121  -2.590  0.00961 **
AGE_ENTRY         0.41635   0.17326   2.403  0.01626 *
Num_Primary       2.03794   1.05483   1.932  0.05336 .
PER_KEPT          0.04074   0.01715   2.375  0.01754 *
Caucasian1        7.20007   2.82198   2.551  0.01073 *
AGE_ENTRY:Num_Primary  -0.09379   0.04358  -2.152  0.03138 *
AGE_ENTRY:Caucasian1  -0.26966   0.11649  -2.315  0.02062 *

Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’
# Misclassification rate, Confusion Matrix

```r
y1 <- OP$Reduce_Opiate_Dis
pi.hat1 <- predict(OP_AL, type = "response")

# change thresholds here for threshold picture
# top is false positive, bottom is false negative

table(y1, pi.hat1 > .76)

# Cross Validate Model, install BOOT package

OP_AL2.cv <- function(y1, pi.hat1) mean(y1 != (pi.hat1 > .76))
cv.glm(OP, OP_AL, OP_AL2.cv, K = 10)$delta

# for threshold picture
# to find false positive and false negative values alter
# threshold from: .9, .8, .7, .6, .5
# prefer threshold of 0.76 to lower false positive rates
# false positive and false negative values from changing
# threshold values

false.pos <- c(0.06, 0.32, 0.56, 0.71, 0.91)
false.neg <- c(0.74, 0.38, 0.2, 0.033, 0.02)

# plot threshold picture

plot(false.neg, false.pos, col = c("red", "orange", "yellow", "green", "blue"), pch = c(21, 15, 19, 22, 17), ylab = "False Positive", xlab = "False Negative", main = "Variation of Reduction in Opiate Usage Prediction Threshold Value")
legend(locator(1), c("Threshold = .9", "Threshold = .8", "Threshold = .7", "Threshold = .6", "Threshold = .5"), pch = c(21, 15, 19, 22, 17), col = c("red", "orange", "yellow", "green", "blue"))
```
APPENDIX C. LINEAR REGRESSION R-CODE FOR MODEL 2

Utilizing R StepAIC with two-way interaction (Factorial to degree 2) and drop 1 resulted in the following Multiple Linear Regression Model.

```r
#Dataset is called NSData with exploratory variables:
#Cause_IED, #M_health, TBI, Caucasian, Amp_Site are categorical and/or binary ~ reflected below
NSData$Cause_IED = as.factor(NSData$Cause_IED)
NSData$M_Health = as.factor(NSData$M_Health)
NSData$TBI = as.factor(NSData$TBI)
NSData$Caucasian = as.factor(NSData$Caucasian)
NSData$Amp_Site = as.factor(NSData$Amp_Site)

#perform BOX COX test for y-transformation
boxcox(Duration_N_Prog~., data=NSData) #yes y = sqrt(y)
```

OUTPUT GRAPHIC OF BOX COX TEST:

Y transformation from Box-Cox Analysis.

λ is approximately 0.5.

```r
#change y in csv
#initial model with transformed y to sqrt (y)
M2b.LM<-lm(Duration_N_Prog~., data = NSData)
summary(M2b.LM)
```
#stepAIC function with two-way interactions

M2B<-stepAIC(M2b.LM, direction = "both," trace = F)
summary(M2B)

drop1(M2B, test="F") #utilize drop 1 function
summary(M2B)

**OUTPUT:**

#result of single term deletions (drop 1 function)

Model:
Duration_N_Prog ~ AGE_ENTRY + Cause_IED + Num_Primary + Caucasian + PerCNL + Amp_Site + Caucasian:PerCNL + AGE_ENTRY:Caucasian + PerCNL:Amp_Site + Cause_IED:PerCNL + Cause_IED:Num_Primary

<table>
<thead>
<tr>
<th>Df</th>
<th>Sum of Sq</th>
<th>RSS</th>
<th>AIC</th>
<th>Pr(&gt;Chi)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;none&gt;</td>
<td>5714.6</td>
<td>655.31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian:PerCNL</td>
<td>1</td>
<td>173.06</td>
<td>5887.7</td>
<td>658.74</td>
</tr>
<tr>
<td>AGE_ENTRY:Caucasian</td>
<td>1</td>
<td>279.96</td>
<td>5994.6</td>
<td>662.02</td>
</tr>
<tr>
<td>PerCNL:Amp_Site</td>
<td>2</td>
<td>332.12</td>
<td>6046.8</td>
<td>661.60</td>
</tr>
<tr>
<td>Cause_IED:PerCNL</td>
<td>1</td>
<td>180.65</td>
<td>5895.3</td>
<td>658.98</td>
</tr>
<tr>
<td>Cause_IED:Num_Primary</td>
<td>1</td>
<td>170.57</td>
<td>5885.2</td>
<td>658.67</td>
</tr>
</tbody>
</table>

---

Signif. codes: 0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1

#Final Model

FinM2<-lm(Duration_N_Prog ~ AGE_ENTRY + Cause_IED + Num_Primary + Caucasian + PerCNL + Amp_Site + Caucasian:PerCNL + AGE_ENTRY:Caucasian + PerCNL:Amp_Site + Cause_IED:PerCNL + Cause_IED:Num_Primary, data = NSData)

summary(FinM2)
OUTPUT:

#final Model 2 output

Call:
  lm(formula = Duration_N_Prog ~ AGE_ENTRY + Cause_IED + Num_Primary + Caucasian + PerCNL + Amp_Site + Caucasian:PerCNL + AGE_ENTRY:Caucasian + PerCNL:Amp_Site + Cause_IED:PerCNL + Cause_IED:Num_Primary, data = NSData)

Residuals:
    Min 1Q Median 3Q Max
-19.6398 -2.6525 -0.0741 2.5594 19.6948

Coefficients:
                      Estimate Std. Error t value Pr(>|t|)
(Intercept)        20.8960  8.2039   2.547  0.01176 *
AGE_ENTRY         -0.2638  0.1172  -2.251  0.02566 *
Cause_IED1        -2.9997  3.0794  -0.974  0.33139    
Num_Primary       1.5969  0.6705   2.382  0.01835 *
Caucasian1        -6.2217  5.0935  -1.222  0.22360    
PerCNL            0.1707  0.3595   0.475  0.63561    
Amp_SiteL         9.9775  6.8490   1.457  0.14704    
Amp_SiteU         -4.7774  7.7431  -0.617  0.53808    
Caucasian1:PerCNL  -0.3324  0.1474  -2.256  0.02539 *
AGE_ENTRY:Caucasian1  0.4833  0.1685   2.869  0.00465 **
PerCNL:Amp_SiteL  -0.4017  0.3213  -1.250  0.21301    
PerCNL:Amp_SiteU   0.1328  0.3612   0.368  0.71352    
Cause_IED1:PerCNL  0.3273  0.1420   2.304  0.02242 *
Cause_IED1:Num_Primary  1.7684  0.7897   2.239  0.02645 *

---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’  
Residual standard error: 5.832 on 168 degrees of freedom
Multiple R-squared: 0.2512, Adjusted R-squared: 0.1932
F-statistic: 4.334 on 13 and 168 DF, p-value: 2.832e-06
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LIST OF REFERENCES


Naval Medical Center San Diego, Comprehensive Combat and Complex Casualty Care (C5). (2013). Retrieved from http://www.med.navy.mil/sites/nmcsd/Patients/Pages/C5.aspx)


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