THE EFFECT OF OPIOID ANALGESICS ON EMERGENCY DEPARTMENT LENGTH OF STAY IN LOW BACK PAIN PATIENTS: A US NATIONAL ANALYSIS

by

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Table of Contents

List of Figures

List of Tables

Abstract

Objectives: The objective of this study was to compare emergency department (ED) length of stay (LOS) between patients treated with opioid analgesia versus non-opioid analgesia for low back pain (LBP) in the ED.

METHODS: This was a cross-sectional study using a national database in the United States (US). The ED component of the 2014 and 2015 National Hospital Ambulatory Medical Care Survey was used for this study. Adult (age ≥ 18 years) patients who presented to the ED with a reason for visit or primary diagnosis of LBP were included in the final study sample. Patient visits were categorized into two groups based on whether they received opioid analgesia (with or without non-opioid analgesia) or non-opioid analgesia only in the ED. The primary outcome measure was ED LOS, which was log-transformed (as ED LOS was not normally distributed) for analysis. A multivariable linear regression analysis was used to evaluate the association between opioid use and log-transformed ED LOS.

RESULTS: The study sample consisted of a national estimate of approximately 8.6 million ED visits for LBP, of which 60.1% received opioids and 39.9% received non-opioids only. The geometric mean ED LOS for patient visits who received opioids was longer than patient visits who received non-opioids (142 versus 92 minutes, respectively; $p<0.001$). After adjusting for confounders in the multivariable analysis, patient visits that received opioids had a significantly longer ED LOS (coefficient 0.25; 95% CI 0.11 to 0.38; $p<0.001$).

CONCLUSION: In a nationally representative sample of patient visits to ED due to LBP in the US, use of opioids for back pain in the ED was associated with an increased ED LOS.

Chapter 1: Introduction

1. 1 Introduction/Background

Emergency care accounts for approximately 4% of all health care spending in the United States (US) and on average, costs seven times more than a community health center visit.[1] Over the past decade alone (2000-2010), the mean cost for non-admission Emergency Department (ED) visits has increased by 77%.[1] According to existing studies, acute and chronic LBP accounted for approximately 2.7 million visits to the ED representing 4.39% of all ED visits in 2015.[2,3] When it comes to treating patients with LBP in the ED, clinical guidelines such as *The American College of Physician's (ACP's) Clinical Background Noninvasive Treatments for Acute Subacute and Chronic Low Back Pai*n were developed to assist providers in choosing appropriate treatment options.[4] ACP's clinical guideline is developed by reviewing data from both RCTs and systematic reviews of noninvasive pharmacologic and non-pharmacologic treatments for LBP. The evidence is then compiled into recommendations with one of three categories of evidence: high, moderate, and low. Based on this review of evidence, ACP's current first line pharmacological treatment recommendation for acute LBP is nonsteroidal anti-inflammatory drugs (NSAIDs) or skeletal muscle relaxants (SMR). However, a US national survey of ED visits from 2002-2006 shows that more than two thirds of all acute LBP patient visits in the ED were treated with opioids.[2] The use of opioid analgesics in the ED LBP population needs further research into understanding the effect of using this class of medication, specifically the effect on LOS.[2-4]

The use of opioid analgesics in the LBP population is just one small portion of an even larger national issue. In the US alone, opioid analgesics are now responsible for more deaths than suicide and motor vehicle crashes, or cocaine and heroin combined.[5] A 2015 national survey

found that 91.8 million (37.8%) of US adults used prescription opioids and of these adults, 11.5 million (4.7%) misused them.[5] Amidst the current climate of the opioid epidemic, it is increasingly important to understand the role opioid analgesics as valid treatment options, particularly in highly prevalent conditions, and how the use of these medications can affect the health care system itself.

LBP was one of the top five reasons for patient presentation to the ED in 2016.[3] The high prevalence of this condition can have a huge impact to the emergency health system and one major factor of this system is length of stay (LOS).[3] Increased or prolonged LOS in the ED directly contributes to the high cost of emergency care and is also associated with other negative patient outcomes such as increased all-cause mortality risk.[2,7,8] LOS is also an important outcome for LBP treatment in the ED as those with LBP tend to be less acutely ill and the longer these patients are in the ED, the more use of limited resources such as hospital beds and physician time they require. The limitations of the ACP guidelines and existing studies for LBP is that they do not compare the recommended treatments or assess their effect on factors such as LOS.[3] The relationship between opioids for the treatment of LBP in the ED and LOS in the ED is still unknown.

1.2 Theoretical Framework:

The input-throughput-output conceptual model of Emergency Department crowding (ITO model) is a conceptual model built to examine overcrowding of the acute care setting, specifically the emergency department (ED) or any medical treatment that is delivered unscheduled (Figure 1).[10]

1.3 Study Purpose

The purpose of this study is to better understand the relationship between opioid analgesics and ED LOS for acute LBP and add context to the decision-making process for providers. Specifically, the effect of opioid analgesics on LOS of patients in the ED for acute lower back pain.

1.4 Study objectives

The objective of this study was to measure the effect of opioid analgesics on LOS of patients in the ED for acute LBP as compared to patients who only receive non-opioid analgesics.

1.5 Hypothesis

H_0_1: There is no difference in effect of opioid analgesia treatment on emergency department length of stay in lower back pain patients; $\beta = 0$

H_1_1: There is a difference in effect of opioid analgesia treatment on emergency department length of stay in lower back pain patients; $\beta \neq 0$

1.6 Abbreviations

Abbreviation	Definition
ED	Emergency Department
LOS	Length of Stay
NHAMCS	National Hospital Ambulatory Medical Care Survey
AE	Adverse Event
LBP	Low Back Pain
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
SMR	Smooth Muscle Relaxants
RCT	Randomized Control Trial
CDC	Centers for Disease Control and Prevention
OPD	Outpatient Departments
ASL	Ambulatory Surgery Locations
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
ACP	American College of Physicians
SSTI	Skin and Soft Tissue Infections
ITO Model	The input-throughput-output conceptual model of Emergency Department crowding
MVA	Motor Vehicle Accident
CVA	Cerebrovascular Disease
IHD	Ischemic Heart Disease
MI	Myocardial Infarction
DM	Diabetes Mellitus
ESRD	End-Stage Renal Disease
DVT	Deep Vein Thrombosis
VTE	Venous Thromboembolism
PE	Pulmonary Embolism
CAD	Coronary Artery Disease
OSA	Obstructive Sleep Apnea
HIV/AIDS	Human Immunodeficiency Virus and Acquired Immunodeficiency Syndrome Infection
CHF	Congestive Heart Failure
COPD	Chronic Obstructive Pulmonary Disease
TIA	Transient Ischemic Attack
IRB	Institution Review Board
CKD	Chronic Kidney Disease
VIF	Variance Inflation Factor
MSA	Metropolitan Statistical Area
PVW	Patient Visit Weight
ACC/AHA	American College of Cardiology and the American Heart Association

Chapter 2: Literature review

2.1 Prevalence an Epidemiology

LBP in the literature is described in many ways, varying from "Activity-limiting LBP (+/– pain referred into one or both lower limbs) that lasts for at least 1 day, The 'low back' is defined as the area on the posterior aspect of the body from the lower margin of the twelfth ribs to the lower gluteal folds" to specific ICD-9-CM codes such as 724 and 084 representing sciatica or sprain/strain of back respectively.[11] The estimated lifetime prevalence of individual experiencing LBP is approximately 40-90%.[12] The literature also shows that when patients suffering from LBP are seen, 25% will have a repeat episode of LBP within one year.[13] Although the literature has found that a high percentage of patients who have LBP will seek treatment in the primary care setting there is surprisingly little literature describing the treatment of LBP in the emergency or acute care setting.[12] A 2017 meta-analysis by Edwards et al studied the prevalence of LBP in the emergency department and found that 4.39% of all ED visits are due to LBP.[14] Edwards et al. (2017) searched electronic databases PubMed and EMBASE (until May 2016) and used controlled vocabulary: emergency department, LBP and prevalence. 19 out of an initial 1,157 articles were identified by applying their incision and excision criteria. The 19 articles included all types of ED environments based on number of patients seen per year (rural and metropolitan) as well as varying definition of "Low back pain". The authors concluded that the definition of LBP in the analyzed studies had the highest variation with measured prevalence of LBP, ranging from 3.4-5.5%. As the information describing the prevalence of acute LBP grows so does the importance in understanding the treatment of this population.

2.2 Treatment of acute and sub-acute low back pain in the ED

The 2017 clinical guidelines for "Noninvasive Treatments for Acute, Subacute, and Chronic LBP: A Clinical Practice Guideline" by the American College of Physicians (ACP) offers clinical evidence-based treatment and practice recommendations for both acute and chronic lower back pain care. Acute back pain was defined as lasting less than 4 weeks and subacute back pain lasts 4 to 12 weeks.[15] ACP used a systematic review of the current literature to compile the evidence and make its recommendations. Multiple databases were searched for studies pertaining to LBP from January 2008 through November 2016. The studies reviewed use of both pharmacologic and non-pharmacologic therapies and evaluated them on outcomes of reduction or elimination of LBP, improvement in back-specific and overall function, improvement in health-related quality of life, reduction in work disability, return to work, global improvement, number of back pain episodes or time between episodes, patient satisfaction, and adverse effects. In effort to normalize the effects of each study, the magnitudes in pain reduction or control were defined for each pain scale allowing for studies with different measurements of pain to be compared. Once the literature was reviewed using ACP's guideline grading system, three levels of evidence were assigned to each study consisting of high, moderate, and low. If the benefits outweighed the risk, burden, or both, the recommendation was strong. Evidence that had an unclear delineation between risk and benefit was considered a weak recommendation. The treatment evidence compiled for acute and subacute LBP varied greatly. The pharmacological treatments with the highest magnitude of effect on pain control were found by ACP to be non-steroidal anti-inflammatory drugs (NSAIDs and acetaminophen) and smooth muscle relaxants (SMR) both having a small magnitude of effect on pain and both with moderate data (both have five RCTs as evidence). The non-pharmacological treatments with the highest magnitude of

effect on pain control was found to be heat wrap with a moderate magnitude of effect and a moderate level of evidence (four RCTs). When pharmacology and non-pharmacological treatment options were compared to one another, a small amount of magnitude of effect in favor of pharmacological treatment was found (one RCTs). The literature reviewed by ACP found insufficient evidence to support the use of antidepressants, benzodiazepines, anti-seizure medications and most importantly for the context of this study (opioids), in treatment of acute and sub-acute LBP.

2.3 Studies conducted at US National-level

Analyzing acute LBP in the emergency setting can be a difficult thing to study as this area of medicine is centered around acute time sensitive treatments. Due to this, researchers have enlisted both survey and database analysis to studying this population and gain insight. Friedman et al. used the Centers for Disease Control and Prevention's (CDC) National Hospital Ambulatory Medical Care Survey (NHAMCS) and cross-sectional study design to analyze and attempt to describe the LBP patients that received care in the emergency department.[16] The study was published in 2015 but used data from the 2002-2006 NHAMCS data. The authors used the database to describe the population in many ways. They describe demographics, utilization of imaging and diagnostics, but most important for the context of this study, they described the treatment of these patients while in the ED. Friedman et al. (2015) found that near 62% of all ED patients visits received some type of opioid for the treatment of acute LBP. These findings raised many questions and concerns due to the fact that the discussed ACP clinical treatment guidelines determined that the literature does not support the use of opioids for pain treatment in this population. The study however, did find the NSAIDs and SMR were used in approximately 49% and 42% of all patients respectively. This finding is consistent with ACPs guidelines as both

NSAIDs and SMR are the only two first line recommendation for pharmacological treatment of acute LBP. The importance of this article in the literature is twofold. The first is, as described above, the findings of opioid prescribing habits inform researchers and providers alike of possible issue that need further exploration and explanation. The second, is the methodology for how to describe and define the LBP population in the NHAMCS data set. The methodology is important as it allows for this population to be recreated and for researchers to test other hypothesis in this population using the NHAMCS data.

The authors created a LBP population using the NHAMCS data by using a combination of both ICD-9-CM diagnosis codes and reason for visit. Corresponding LBP ICD-9-CM codes included in the study were: intervertebral disc disorder (724, 724.2, 724.5, 724.8), sciatica (724.3), thoracic/ lumbosacral neuritis/ radiculitis (724.4), sprain/strain back (847), lumbar (847.2), Unspecified (847.9) , sacroiliac sprains/ strains (846, 846.0, 846.9), sprains/ strains (848, 848.9), soft tissue injury (729, 729.1, 729.5), spondylosis and allied disorders (721), intervertebral disc disorder (722, 722.1, 722.2, 722.93), and injury (959, 959.1, 959.19). The reason for visits used included: back symptoms (1905.0, 1905.1, 1905.2 1905.3), low back symptoms (1910.0, 910.1, 1910.2, 1910.3), back injury including neck and vertebrae (5010.0) back injury contusion, abrasion, or bruise (5515.0), and back strain (5110.0). ED visits by LBP patients were excluded from this study if they did not receive any medication during their ED visits (code= [GPMED1-30] = 1) or had LBP from motor vehicle accidents (MVA) (5805.0). This study included ED visits by patients 14 years or older. The pharmacological treatments were identified using the Multum classification for both individual drugs and drug classes. These analgesia treatments included: opioids, non-steroidal anti-inflammatories, acetaminophen, corticosteroids, and muscle relaxants (including benzodiazepines and skeletal muscle relaxants).

The study sample was then described by the variables; age, gender, type of insurance, length of stay and disposition.

As for any study utilizing ICD-9-CM codes for diagnosis, the limitation of this study is with the accuracy of the diagnosis codes assigned for the visits as the accuracy of the diagnosis codes is variable. The authors conclude they acknowledge that some patients were left out due to miss coding errors. Further limitations include lack of patient medications information pertaining to allergies and intolerances as well as if the patients were already using medications prior to ED visit. This information can heavily influence the type of treatment the prescriber chooses, and the patient receives. Lastly the NHAMCS data set does not provided information on non-pharmacological treatments and thus no information about these treatments could be analyzed or described.

The NHAMCS data has also been used to describe other hypothesis specifically, length of stay (LOS). Altyar et al used the 2008- 2010 NHAMCS data to analyze the relationship between length of stay in patients receiving intravenous (IV) antibiotics for skin and soft tissue infections (SSTIs) in the ED.[17] A cross sectional study design was used in parallel with multivariable regression to measure the effect of IV antibiotics on LOS for SSTS in the ED. Patients were placed in one of two groups based on if the patients received IV antibiotics or not. The LOS were then compared between the two treatment groups. Multivariable regression with LOS inputs and possible clinical and demographic confounders were also included. Over 3 million ED visits with SSTI's were identified out of which 46.8% (n = 1,403,710) received IV antibiotics in the ED. The average LOS was 112.2 minutes (SD = 193.6) in the treatment group who received IV antibiotics and 83.8 minutes (SD = 160.6) who did not ($P<0.05$). A 43% increase in LOS for the treatment group was found after adjusting for confounders. From these

findings, the authors concluded that administrations for IV antibiotics for treatment of SSTIs resulted in a statically significant increase in ED LOS.

The limitations of this study arose from the severity of the infection not being documented possibly leading to some patients being included that had more severe infections were IV antibiotics would have been warranted. The authors did try and address this limitation by excluding any patients admitted as these patients would most likely have more severe infections.

2. 4 The relationship of length of stay and outcomes in the Emergency Department

The Altyar et al study showed that LOS can be measured using the NHAMCS data but the connection between why a patient's time spent in the ED and their outcomes maybe of interest was not explored. Guttmann et al explored the association between waiting times in the ED and short-term mortality.[18] The authors used a retrospective cohort study to examine all emergency departments in Ontario, Canadian from 2003-2007 using a Canadian national health administrative database. The study population consisted of people who arrived at the ED and were treated and not admitted or left without being seen. The primary outcome was to understand the impact of these patients being exposed to long wait times or them not being seen due to the long wait time and adverse events (ADE). ADEs were defined as death or hospital admission within seven days of ED visit. A total of 13,934,543 ED patients were seen and discharged with 617,011 patients leaving without being seen. The adjusted odds ratio was 1.79 for death (95% CI 1.24, 2.59) and 1.95 (95% CI: 1.79, 2.13) for admission in high acuity patients and 1.71 (95% CI 1.25, 2.35) and 1.66 (95% CI 1.565, 1.76) for death and admission respectfully in low acuity patients. Acuity was documents as part of the ED visit as was defined as 1-3 for high and 4-5 for low. Bashkin et al (2015) described the factors that contribute to ED LOS.[19] They identified

several factors consisting of: admission to the hospital from the ED, shift change for nurses and doctors, and treatments. The authors used an observational study to measure factors that changed patients LOS while in the ED. ED patients were observed (N=109) over a three-month period in a community urban hospital. Patients were followed from the time they arrived at the ED until they were discharged or admitted to the hospital. The LOS was measured for each patient as well as other demographic and categorical data based on the author's causal diagram. Ackroyd-Stolarz et al[20] examined the relationships between prolonged ED stay and adverse events for adults older than 65 years while they were in the ED. The authors used a retrospective cohort study at a large academic hospital and followed patients from July 2005- March 2016. The authors used an ED visit of greater than or equal to six hours to define a prolonged ED stay. The primary outcomes of the study were the occurrence of AE during the patients stay. AE were defined using a combination of ICD-9-CM codes and injury codes. The authors founded that 14.3 % of the 982 eligible patients in the study experienced an AE with a 3% (OR 1.03, 95% CI 1.004,1.05) increase in the odds of experiences an AE for patients with prolonged stays. The authors concluded that a prolonged ED stay was associated with increased risk of AE. Diercks D et al [21] examined the relationship of disease state presentation to the ED and LOS impact on the use of appropriate treatment using the disease specific clinical guidelines. Specifically, the authors evaluated the association of emergency department (ED) LOS with use of American College of Cardiology and the American Heart Association (ACC/AHA) guideline-recommended therapies for acute treatments of patients presenting with non–ST-segment-elevation myocardial infarction. Using data generated from the CRUSADE trial, the authors used multivariable analysis patients were placed into one of three groups based on the time spend in the ED, short (<4 hrs), average (4-8 hrs), and long (>8hrs). The analysis contained 42,780

patients with a mean LOS of 4.3 hours and 15% having long stays in the ED. The patients that has a long ED LOS less often received guideline recommended acute myocardial infarction therapies and had an increased likelihood (OR 1.23, CI: 1.01,1.48) of recurrent MI. The authors also found that although the individuals with long LOS had an increased risk in recurrent MI, individuals with long LOS had the same risk of mortality as individuals with average and short LOS (OR 1.13, CI: 0.96,1.33).

2.5 Unresolved Issues and Unanswered Questions

Based on this literature, it can be concluded that LBP is a prominent condition individuals are seeking treatment for in the ED and LOS is in important outcome to measure. However, there is little to no research analyzing how opioid treatments impact ED LOS. Understanding the treatment of acute LBP in the ED does not only add information to the overall context of managing these patients in the safest way possible but adds to the understanding how treatment can impact outcomes.

2.6 Theoretical framework

The input-throughput-output conceptual model of Emergency Department crowding (ITO model) is a conceptual model built to examine overcrowding of the acute care setting, specifically the ED or any medical treatment that is delivered unscheduled (figure 1).[10] Such as: (1) emergency care; (2) unscheduled urgent care; and (3) safety net care. The conceptual model partitions of ED crowding into three interdependent components: input, throughput, and output. Input components focus on any condition, event, or system characteristic that contributes to the demand for ED services. The throughput component of the model focuses on the ED care process and identifies patient length of stay as a potential contributing factor of the overall ED crowding. The throughput is further broken down into two primary phases: 1) triage, room

placement, and initial provider evaluations. 2) diagnostic testing and treatment. The model indicates that a majority of patient time is spent in the throughput portion of the model. The third and last component is output that focus on patients exit from the ED. Patients can exit the ED in different ways but is done so most commonly via discharge or admission for inpatient treatment.

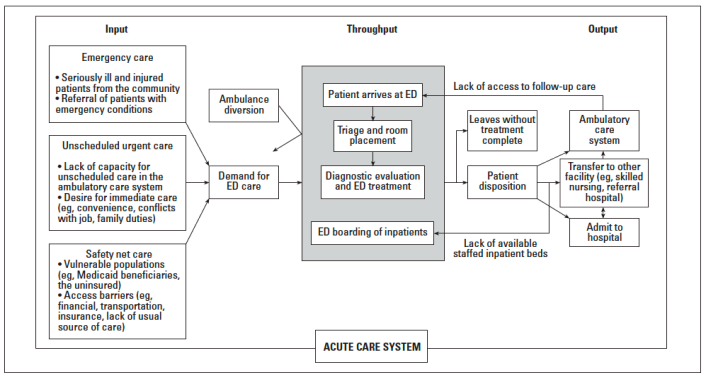

Figure 1: The input-throughput-output conceptual model of ED crowding
ITO model

The use of the *ITO conceptual model of ED crowding* model, specifically the throughput portion, is being used in this thesis to model variables that may impact length of stay. The ITO model will be used to measure how long patients spend in the throughput potion as a function of treatment. The ITO model will be used to compare the length of stay of patients who receive opioid analgesics or non-opioids analgesics for treatment of lower back pain. Length of stay is being used to measure how long a patient is spending in the throughput portion of the model. The model allows for comparisons of different treatments on the impact of length of stay. By selecting patients with specific diagnostic ICD-9 codes for lower back pain and measuring length of stay beginning from first provider evaluation on, the treatment portion of the throughput component can isolate for examination. The other variables in the throughput component of the ITO model; initial provider evaluations and diagnostic testing were controlled by being placed in the multivariable linear regression model. This was done by using three variables; if procedures

were performed (yes/no), if diagnostic services were ordered or provided (yes/no), and immediacy with which patient should be seen (ranging from immediate to none-emergent based on the patients triage designation by the ED).

2.7 Limitation of the model

Limitations of this ITO model is that LOS is only a one third of the whole model, throughput. Second, the ITO model is not designed specifically for length of stay but rather to describe reasons for ED overcrowding, of which LOS is one factor. Third, the model does not take into account treatments outside of the ED. These treatments can consist of chronic or as needed medications and can lead to complications within the ED or affect the ED treatment part of the throughput portion of the model.

However, some of these limitations can be taken into account. The throughput portion can be isolated from the other parts of the model by careful selection of the study population and inclusion of surrogate variables in the multivariable linear regression model. Using diagnostic ICD-9-CM codes, immediacy with which patient should be seen, if diagnostic services were ordered or provided, metropolitan statistical area, and reason for visits pertaining to LBP, a homogenous population can be construed to analyze within the throughput portion of the model. Using these inclusion and exclusion criteria make the population that is being studied in the throughout stage as similar as possible and lower other confounding factors for added time in the throughput portion. The output portion of the model can be avoided by exuding individuals admitted for inpatient treatment. The ITO model for these reasons, makes it a practical application for measuring the impact of treatments on ED LOS.

Chapter 3: Methods

3.1 Study design

A cross-sectional design was used to measure the association of opioid use for LBP on ED LOS.

3.2 Data source

This study used the ED component of the publicly available NHAMCS (2014 and 2015) data. [22, 23, 24] The NHAMCS is a survey collected annually by the Center for Diseases Control (CDC) and was designed to collect data on healthcare utilization in both hospital emergency departments (EDs), outpatient departments (OPDs) and ambulatory surgery locations (ASLs). The survey is collected in four stages: the first is defining geographically sampling areas, the second stage is selecting hospitals in these defined areas, the third stage is selecting clinics within outpatient departments and all emergency service in these areas, and the fourth and final step is to sample patients visits at the selected settings. Using a systematically random sampling technique, the data are collected by specially trained census interviewers using specific patient record forms for all three locations (ED, OPDs, and ASLs) over a four-week period per each specific location. Total visit data was collected from December 23rd, 2013 through December 29th, 2015. Approximately 83.0% of sampled hospitals participated in the 2014 and 2015 surveys, and about 73.1% of sampled EDs provided complete information on their sample visits for a total average unweighted response rate of 73.15%. [25] One of the major strengths of the NHAMCS survey is it allows national estimates to be calculated using the patient visit weight (PVW). These national estimates reflect a sample of all Unites States ED visits during the period analyzed. In this analysis 2014 and 2015 data were used that consisted of a total of 44,905

unweighted visits (23,844 from 2014 and 21,061 from 2015) representing 278,363,460 total ED visits over the two-year period. The LBP subpopulation represented 1,363 unweighted visits corresponding to 8,564,059

Weighted visits.

3.3 Human Subjects

The University of Arizona Institution Review Board (IRB) approved this study (figure 4)

3.4 Independent and dependent variables

The primary outcome of this study was to measure ED LOS (minutes) for patients who receive opioid analgesia treatments with or without non-opioid analgesics as compared to non-opioid analgesic treatments alone. LOS was calculated from the NHAMCS data variable length of visit (coded [LOV]) minus the wait time (coded as [WAITTIME]). Wait time was excluded from the total LOS as it is defined as time until the provider met the patient and is not part of the relationship between LOS and treatment. The LBP population was identified by using both International Classification of Diseases, Ninth Revision, Clinical Modification codes (ICD-9-CM) (coded as [DIAG1]) as well as documented reason for visit (coded [RFV1]-[RFV5]). Specifically, patient visits were included in the sample if they had any primary ICD-9-CM code or any reason for visit corresponding to LBP. Only the primary ICD-9-CM codes were used in this analysis as this is the most relevant diagnosis to the patients visit. Any reason for visit for LBP was used to make up for inconsistent ICD-9-CM coding and to account for any documentation error in the diagnosis reporting. The included ICD-9-CM codes were: intervertebral disc disorder (724, 724.2, 724.5, 724.8), sciatica (724.3), thoracic/ lumbosacral neuritis/ radiculitis (724.4) sprain/strain back, (847), lumbar (847.2), Unspecified (847.9) , sacroiliac sprains/ strains (846, 846.0, 846.9), sprains/ strains (848, 848.9), soft tissue injury

(729, 729.1, 729.5), spondylosis and allied disorders (721), intervertebral disc disorder (722, 722.1, 722.2, 722.93), and injury (959, 959.1, 959.19).[23] The following reason for visits were included: back symptoms (1905.0, 1905.1, 1905.2 1905.3), low back symptoms (1910.0, 910.1, 1910.2, 1910.3), back injury including neck and vertebrae (5010.0) back injury contusion, abrasion, or bruise (5515.0), and back strain (5110.0).[23] Patients who had a reason visit related to motor vehicle accidents (MVA) (coded [RFV1]-[RFV5], 5805.0) were excluded from study due to the complicated nature of possible injury and acuity. These patients may have received injures such as bone fractures or other injury where opioid treatment would be most appropriate. Patient visits were also excluded from the study if they did not receive any analgesic during their ED visits (code= [GPMED1-30]= 1), transferred to psychiatric hospital (code = tranpsyc), returned or transferred to a nursing home (code= trannh), transferred to another hospital (code = tranoth), left against medical advice (code = leftama), or died while in the ED (code = dieded). The reason for excluding these patients is to understand how treatment impacts LOS, if no treatments were received or visits resulted in anything other than discharged the LOS is not directly a function of treatment. Patients 18 years or older were included in the study as the current treatment guidelines use this as the target population. Patients who met the above inclusion criteria were categorized by one of two treatment groups, opioid treatment or non-opioid analgesic treatment group. The treatment group was identified by using the variable of drug category, identifying drug by their corresponding therapeutic class ([RX1CAT3]- [RX2-30CAT3]). The NHAMCS database utilizes Multum's Lexicon Drug Database for drug categorization, and includes information on up to 30 drugs per visits. .[26] Therapeutic classification reflects Multum's 3-level nested category system and was used to identify the following therapeutic classes: opioids, skeletal muscle relaxants, skeletal muscle relaxant combinations, nonsteroidal anti-inflammatory

agents, analgesics combinations, cox-2 inhibitors, benzodiazepine anticonvulsants, and miscellaneous analgesics (178, 179,060, 061, 063, 203, 278,191, 060) ([RX1CAT3]- [RX2-30CAT3).[26] The treatment group consisted of patient visits where opioid analgesics for LBP was prescribed and may or may not have received an non-opioid analgesics. The comparison group was comprised of the above stated non-opioid analgesic classes as these treatments correspond to ACPs' first line guideline treatments. Multivariable analysis was conducted to assess the association of opioid use and ED LOS adjusting for several confounders.

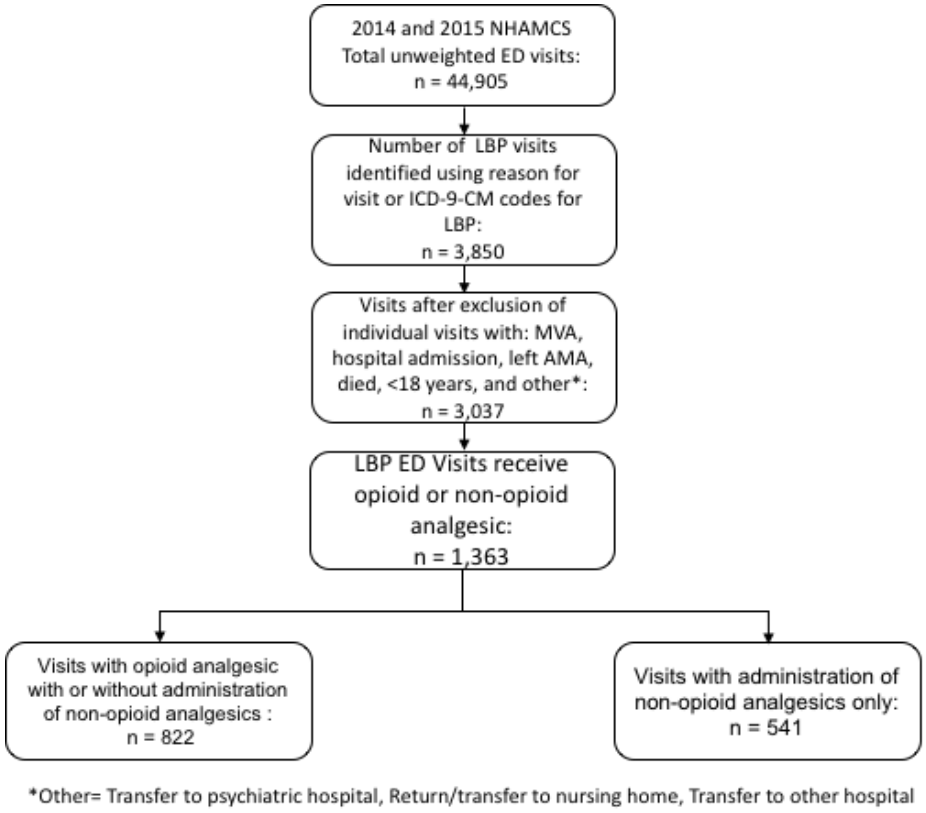

Figure 2: Study Sample Identification Flow Chart

A multivariable linear regression analysis was used to measure the LOS in the ED for patients who received opioids vs non-opioids for LBP. The following potential confounding variables were adjusted in the regression analysis: patient age, sex, immediacy with which

patient should be seen (immediate, urgent, non-urgent and an indicator variable for missing data), if diagnostic services were ordered or provided (yes/no; these include blood or other tests such as electrolytes, cardiac enzymes, urine analysis, and imaging ordered or performed at the visit (yes/no), if procedures were performed (yes/no), pain scale (1-10), metropolitan statistical area (MSA, metro classifications and non-metro), race/ethnicity (White, Black, and other), year (2014 or 2015), and the NHAMCS list of total chronic comorbidities ([TOTCHRON]) (Alcohol abuse, Alzheimer's disease/dementia, asthma, cancer, cerebrovascular disease/history of stroke (CVA) or transient ischemic attack (TIA), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), coronary artery disease (CAD), ischemic heart disease (IHD), myocardial infarction (MI), depression, Diabetes mellitus (DM – Type I, DM – Type II DM – Type unspecified), end-stage renal disease (ESRD), pulmonary embolism (PE) or deep vein thrombosis (DVT), venous thromboembolism (VTE), human immunodeficiency virus and acquired immunodeficiency syndrome infection (HIVAIDS), hyperlipidemia, hypertension, obesity, obstructive sleep apnea (OSA), osteoporosis, substance abuse, or none of the above [23]. The reason for including these variables in the regressing model were a combination of clinical relevance and theoretical framework model parameters. *The input-throughput-output conceptual model of Emergency Department crowding* (ITO model) was used as a theoretical framework for this study describes ED LOS. This model consists of a number of variables such as diagnostic evaluation and treatments. The ITO model informed the covariates such as: Immediacy with which patient should be seen, if diagnostic services were ordered or provided, pain scale, and type of hospital classification. The remaining variables: sex, race, age, year, and number of conditions are all established covariates in the literature and have both clinical and theoretical impacts on LOS.[10,17]

Due to the non-normally distributed characteristic of the LOS, the variable was log transformed to the natural log of LOS. Consequently, making this a normally distributed variable. The final regression model was;

$$ln(LOS) = \beta_0 + \beta_1 Treatment + \beta_2 PainScore + \beta_3 Image\ performed + \beta_4 sex + \beta_5 age + \beta_6 Race + \beta_7 Procedure\ performed + \beta_8 Region + \beta_9 MSA + \beta_{10}\ Year + \beta_{11} Total\ chronic\ conditions + \beta_{12} Immediacy + error$$

Figure 3: Length of Stay Linear Regression Model

3.4 Missing data

One drawback of the NHAMCS is missing data with some variables missing up to 19% of observations. Specifically, for this analysis the variables total chronic comorbidities, pain scale, immediacy with which patient were seen, and if procedures were performed had missing data that needed to be accounted for, 0.51%, 14.75%, 16.43% and 1.91% respectively. Imputation was used to address the missing data.[28] Specifically, imputation of total chronic comorbidities, pain scale, immediacy with which patient were seen, and if procedures were performed, were done by converting missing observations to the median values. This method was chosen as there is large number of missing observations (>10%) indicating the data were not missing at random. [28]

3.5 Data analysis

The following assumptions of the multivariable linear regression were tested: Linearity, Normality of the residuals, Homoscedasticity, and independent observations. The linearity of the

continuous variables was tested by plotting the dependent variable (LOS) by the independent variables discussed above (patient age, sex, immediacy with which patient should be seen, if diagnostic services were ordered or provided, if procedures were performed, type of hospital classification, race/ethnicity, year (2014 or 2015), and total chronic comorbidities). The residuals were assessed for normality by analyzing the histogram of the residuals for a normal distribution modeled by N $(0,\alpha^2)$. Homoscedasticity was analyzed by using White tests with an a-priori set of 0.05. Independent observations were insured by excluding any patient that has been seen in the ED in the past 72 hours ([Seen72]). This variable was used as it is the only viable in the NHAMCS data that addresses readmission issues for independent observations. Multi-collinearity of independent variables was analyzed using the variance inflation factor (VIF) with a value of ≥ 5 showing collinearity with other regressors. LOS was also transformed to best fit the data with log or other transformation if transformation relationship better fits the assumptions.

Sensitivity analysis were conducted to examine the robustness of the final model used. Three sensitivity analyses were used: (i) opioid analgesics only vs non-opioid analgesics, (ii) non-transformed model, and (iii) missing observation model. The first sensitivity analysis was conducted to understand the difference between opioid analgesics only compared to non-opioid analgesics only in terms of ED LOS (Table 3). The second sensitivity analysis examined the impact of removing missing observations from the analysis (Table 4) The third sensitivity analysis was an unadjusted model that did not change any variables in any way from how the NHAMCS is original coded. This meant that variables like missing (codes as -9) or not present were part of the regression model (Table 5).

3.6 Limitations

There are limitations with the methodology: the first is that the NHMACS survey utilizes ICD-9-CM codes for primary diagnosis of patients. This is a limitation of the analysis as the inaccuracy of coding of ICD-9-CM codes for diagnosis of LBP has been reported in the literature. [14] The effect of this miscoding was attempted to be lowered by including the reason for visit variable to identify LBP patients. The second limitation of this analysis is the regression model itself that is to say that the model is limited by the covariates used in the model. As discussed in the methodology the covariates were chosen by the theoretical framework and reported literature, but the model could be missing other important confounding or effect modification variables.

Chapter 4: Results

4.1 Demographics and population characteristics

According to the 2014 and 2015 NHAMCS data, 8,564,059 patient visits were recorded in the Emergency Department (ED) for LBP. Of these 8.5 million LBP patient visits, 5,147,820 (60.12%) received an opioid analgesic during their ED encounter. Socio-demographic and clinical characteristics of the ED visits included: average age of 45.1 (SE = 1.37) years, 40.94% male, 24.64% black, 98.92% with five or less chronic conditions, 71.48% with a pain level of six or more, 82.75% residing in a metropolitan statistical area, and 32.44% located in the Midwest region (details presented in Table 1). Approximately 51% LBP ED visits in our study were recorded in 2015. An overwhelming majority (90.52%) of the ED visits were classified as urgent/semi-urgent, 38.05% had a procedure performed, and 56.60% received diagnostic imaging. ED visits where opioid analgesics were used, had more likelihood of receiving diagnostic imaging (p=0.008) or have a procedure performed (p=0.002). Unadjusted length of stay of ED visits that received opioid analgesics was 183.86 $\pm$ 6.56 minutes vs Non-opioid only analgesics 134.72 $\pm$ 8.26 minutes (p<.0001). Details of descriptive statistics can be found in Table 1. Results of the white's test for homoscedasticity of logLOS as the depended variable was not significant indicating that there is constant variance in the residuals (p< 0.804). Multi-collinearity was not observed in the regression model as all co-variates had a VIF < 2.

4.2 Multivariable Regression Analysis

Table 2 shows the results of the ordinary least squares (OLS) multivariable regression analysis. The percentage of variation explained by different independent variables used in this model(R^2) was 26.91%. After controlling for other covariates, the primary variable of interest, opioid analgesic use was associated with increased logLOS (β =0.25, exp (β)= 1.28, p<0.001, CI: 0.11, 0.38). This result shows a 27.89% increase in the LOS for LBP individuals who received any opioid analgesic as compared to patients who only receive only non-opioid

analgesics. Other co-variates significantly associated with LOS were; immediacy with patient being seen (Reference: Immediate/Emergent) non-urgent -0.45 (exp (β)= 0.64, p<0.0279, CI: -0.84, -0.05), procedure performed 0.34 (exp (β)= 1.40, p<.0001, CI: 0.21, 0.47), regions (Reference Northeast) east -0.2062169 (exp (β)= 0.81, p=0.0292, CI: -0.39, -0.02) and south -0.30 (exp (β)= 0.74, p<0.0015, CI: -0.48, -0.12), pain scale -0.0274874 (exp (β)= 0.972886941, p=0.0399, CI: -0.39, -0.02), image received 0.44 (exp (β)= 1.56, p<.0001, CI: 0.32, 0.57metropolitan statistical area 0.1981686 (exp (β)= 1.22, p=0.0272, CI: 0.023, 0.37), and total number of chronic conditions 0.05(exp (β)= 1.05, p=0.0249, CI: 0.01, 0.09). Results of the white's test for homoscedasticity was not significant indicating that there is constant variance in the residuals (p< 0.804). Multi-collinearity was not observed in the regression model as all co-variates had a VIF < 2.

The results of the regression analysis show that the primary outcome of opioid analgesics treatment vs non-opioid analgesics was associated with a statistically significant increase in logLOS. Other significant variables show that nonurgent immediacy with which patient was seen shortened LOS by approximately 36% as compared to Immediate/Emergent patients. Individuals who had procedures performed during their ED visit had a 40% longer LOS as compared to individuals who received no procedures. Regional location of the ED was also associated with a statically lower LOS in patients in the southern and west regions as compared to the northwest, with a 19% and 26% reduction respectively. Individual pain level (0-10) was associated with lower LOS and continues to be lower in individuals with higher pain levels (induvial with pain levels of 10/10 have lowest LOS). Patients who received diagnostic imaging had a 55% increase in LOS as compared to those who did not. Individuals receiving care in metropolitan statistical

area (MSA) had a 21% increase in LOS then patients outside of these areas. Last, patients with more chronic conditions had longer LOS then patients with less chronic conditions.

The results of the sensitivity analyses show the primary outcome of logLOS are all significant. The results of assessing the impact of using an opioid analgesic only population vs non-opioid analgesics for logLOS, this model was assonated with a significant increase in logLOS (β=0.27, exp (β)= 1.31, p<0.001, CI: 0.12, 0.43) (Table 3). The second sensitivity analysis assessed the impact of removing visits with missing data from the model. This too showed a significant increase in logLOS (β=0.20, exp (β)= 1.23, p<0.0001, CI: 0.16, 0.25) (Table 4). The last sensitivity analysis, examined the use of NHAMCS coding only. This consisted of using missing observation variables compared to imputation and deletion methods used in other models. This model showed a significant increase in logLOS (β=0.23, exp (β)= 1.26, p<0.001, CI: 0.11, 0.36) (Table 5).

4.3 Conclusions of Hypothesis:

Null Hypothesis (H_0)	***p***	**Conclusion**
There is no difference in effect of opioid analgesic treatment on emergency department length of stay in lower back pain patients; $\beta = 0$	0.0004	Reject H_0

Table 1: National Hospital Ambulatory Medical Care Survey Low Back Pain Subpopulation Demographics for 2014 and 2015

N (%)	Any analgesic (n=5,147,820) 60.12%	Non-opioid only analgesic (n=3,416,239) 39.89%	Total (n=8,564,059) 100%	P-value
Age[a] N (SE)	47.55 (0.966)	41.37 (0.969)	45.08 (0.969)	<.0001
Male[b]	2,151,908 (25.13)	1354,377 (15.81)	5,147,820 (40.94)	0.490
Pain scale[b]				0.632
Pain level of five or less	1,429,017 (16.69)	1,013,443 (11.83)	2,442,460 (28.52)	
Pain level of six or more	3,718,803 (43.42)	2,402,796 (28.06)	6,121,599 (71.48)	
Length of Stay [a] (min) N (SE)	183.86 (6.561)	134.72 (8.264)	164.10 (8.268)	<.0001
Immediacy with patient was seen[b]				0.164
Non-Urgent	142,228 (2.16)	170,043 (2.59)	312,271 (4.75)	
Urgent/semi-urgent	3,608,198 (54.89)	2,342,302 (35.63)	5,950,500 (90.52)	
Immediate/Emergent	234,056 (3.56)	77,223 (1.17)	311,279 (4.74)	
Image received [b]	3,131,009 (36.56)	1,716,263 (20.04)	8,564,059 (56.60)	0.008
Race[b]				<0.001
Black	1,024,067 (11.96)	1,086,427 (12.69)	2,110,494 (24.64)	
White	3,894,609 (45.48)	2,276,969 (26.59)	6,171,578 (72.06)	
Other	229,144 (2.68)	52,843 (0.62)	281,987 (3.29)	
Year 2015[b]	2584324 (30.18)	1810430 (21.14)	4394754 (51.31)	0.488
Procedure performed [b]	2220869 (25.93)	1,037,841 (12.11)	3,258,710 (38.05)	0.002
Metropolitan statistical area[a]	4,313,244 (50.36)	2,773,730 (32.38)	7,086,974 (82.75)	0.262
Region[b]				0.127
Northeast	689,914 (8.06)	604,471 (7.06)	1294,385 (15.11)	
Midwest	1,814,837 (21.19)	963,367 (11.25)	2,778,204 (32.44)	
South	1,580,448 (18.45)	1,185,579 (13.84)	2,766,027 (32.30)	
West	1,062,621 (12.41)	662,822 (7.74)	1,725,443 (20.15)	
Total number of chronic conditions[b]				0.003
Five or less chronic conditions	5,060,257 (59.09)	3,410,901(39.83)	8,471,158 (98.92)	
Six or more chronic conditions	87,563 (1.022)	5,338 (0.06)	92,901 (1.08)	
a= T-test b=Rao-Scott Chi-Square Test				

Table 2: Multivariable Linear Regression Model

Parameter	Estimate	Exponentiated β	Standard Error	t-Value	P-value	95% Confidence Interval
Opioid analgesic (Reference: Non-opioid only analgesic)	0.25	1.28	0.07	3.61	0.001	0.11, 0.38
Age	0.00	1.00	0.00	1.17	0.24	-0.001, 0.005
Male	-0.06	0.94	0.06	-1.09	0.28	-0.18, 0.05
Immediacy with patient was seen (Reference: Immediate/Emergent						
Urgent/semi-urgent	-0.26	0.77	0.14	-1.85	0.07	-0.53, 0.02
Non-Urgent	-0.45	0.64	0.20	-2.22	0.03	-0.84, -0.05
Procedure performed	0.34	1.40	0.07	5.13	<0.0001	0.21, 0.47
Region (Reference Northeast)						
West	-0.21	0.81	0.09	-2.20	0.03	-0.39, -0.02
South	-0.30	0.74	0.09	-3.23	0.001	-0.48, -0.12
Midwest	0.02	1.02	0.10	0.22	0.82	,0.17, 0.21
Pain scale	-0.03	0.97	0.01	-2.07	0.04	-0.05, -0.001
Image received	0.44	1.56	0.06	7.15	<0.0001	0.32, 0.57
Metropolitan Statistical Area	0.20	1.22	0.09	2.23	0.03	0.02, 0.37
Race (Reference White)						
Black	-0.07	0.94	0.08	-0.85	0.40	-0.22, 0.08
Other	0.05	1.05	0.14	0.33	0.74	-0.22, 0.32
Year 2015	-0.03	0.97	0.06	-0.47	0.64	-0.14, 0.09
Total number of chronic conditions	0.05	1.05	0.02	2.26	0.03	0.01, 0.09
Intercept	4.65	104.20	0.24	19.60	<0.0001	4.18, 5.11

Table 3: Multivariable Linear Regression Model: Opioid Only vs Non-Opioid Only

Parameter	Estimate	Exponentiated β	Standard Error	t-Value	P-value	95% Confidence Interval
Opioid analgesic (Reference: Non-opioid only analgesic)	0.27	1.31	0.08	3.45	<0.001	0.12, 0.43
Age	0.00	1.00	0.00	1.16	0.25	0.00, 0.01
Male	-0.08	0.92	0.08	-1.06	0.29	-0.23, 0.07
Immediacy with patient was seen (Reference: Immediate/Emergent						
Urgent/semi-urgent	-0.15	0.86	0.15	-1.01	0.32	-0.46, 0.15
Non-Urgent	-0.33	0.72	0.22	-1.5	0.13	-0.77, 0.11
Procedure performed	0.41	1.51	0.07	5.57	<0.0001	0.26, 0.56
Region (Reference Northeast)						
West	-0.21	0.81	0.11	-1.93	0.05	-0.43, 0.00
South	-0.33	0.72	0.10	-3.15	0.001	-0.53, -0.12
Midwest	0.01	1.01	0.10	0.09	0.93	-0.19, 0.21
Pain scale	-0.03	0.97	0.01	-2.18	0.03	-0.06, 0.00
Image received	0.44	1.55	0.06	6.97	<0.0001	0.32, 0.57
Metropolitan Statistical Area	0.23	1.26	0.09	2.5	0.01	0.05, 0.41
Race (Reference White)						
Black	-0.10	0.90	0.09	-1.17	0.24	-0.28, 0.07
Other	-0.03	0.97	0.17	-0.19	0.85	-0.36, 0.30
Year 2015	-0.06	0.94	0.07	-0.88	0.38	-0.21, 0.08
Total number of chronic conditions	0.03	1.03	0.02	1.42	0.16	-0.01,0.08
Intercept	4.57	96.89	0.28	16.42	<0.0001	4.02,5.12

Table 4: Multivariable Linear Regression Model: Missing Observations Removed

Parameter	Estimate	Exponentiated β	Standard Error	t-Value	P-value	95% Confidence Interval
Opioid analgesic (Reference: Non-opioid only analgesic)	0.20	1.23	0.02	8.32	<0.0001	0.16, 0.25
Age	0.01	1.01	0.00	6.81	<0.0001	0.00, 0.01
Male	0.00	1.00	0.03	-0.10	0.92	-0.06, 0.05
Immediacy with patient was seen (Reference: Immediate/Emergent						
Urgent/semi-urgent	0.23	1.26	0.03	6.52	<0.0001	0.16, 0.30
Non-Urgent	-0.16	0.85	0.12	-1.33	0.18	-0.40, 0.08
Procedure performed	0.38	1.47	0.03	11.40	<0.0001	0.32, 0.45
Region (Reference Northeast)						
West	-0.36	0.70	0.08	-4.27	<0.0001	-0.52, -0.19
South	-0.38	0.69	0.08	-4.89	<0.0001	-0.53, -0.23
Midwest	-0.12	0.88	0.09	-1.40	0.16	-0.30, 0.05
Pain scale	-0.04	0.96	0.01	-6.68	<.0001	-0.05, -0.03
Image received	0.42	1.51	0.03	12.96	<0.0001	0.35, 0.48
Metropolitan Statistical Area	-0.14	0.87	0.05	-2.95	0.00	-0.23, -0.04
Race (Reference White)						
Black	0.10	1.10	0.03	3.00	0.00	0.03, 0.16
Other	0.06	1.06	0.07	0.75	0.45	-0.09, 0.20
Year 2015	0.06	1.06	0.05	1.19	0.23	-0.04, 0.15
Total number of chronic conditions	0.03	1.03	0.08	0.38	0.70	-0.13, 0.19
Intercept	4.78	118.83	0.14	33.85	<0.0001	4.50, 5.06

Table 5: Multivariable Linear Regression Model: Non-Imputed

Parameter	Estimate	Exponentiated β	Standard Error	t-Value	P-value	95% Confidence Interval
Opioid analgesic (Reference: Non-opioid only analgesic)	0.23	1.26	0.06	3.65	<0.001	0.11, 0.36
Age	0.00	1.00	0.00	0.94	0.347	0.00, 0.01
Male	-0.06	0.94	0.05	-1.19	0.235	-0.16, 0.04
Immediacy with patient was seen (Reference: Immediate/Emergent						
Urgent	-0.28	0.76	0.35	-0.81	0.42	-0.96, 0.04
Emergent	0.05	1.05	0.33	0.16	0.87	-0.61, 0.71
Semi-urgent	-0.07	0.94	0.30	-0.22	0.83	-0.66, 0.53
Non-Urgent	-0.37	0.69	0.31	-1.20	0.23	-0.97, 0.24
Visit occurred in ESA that does not conduct nursing triage	-0.39	0.68	0.34	-1.15	0.25	-1.06, 0.28
No triage reported for this visit	-0.04	0.96	0.34	-0.13	0.89	-0.71, 0.62
Unknown	-0.23	0.80	0.30	-0.76	0.45	-0.82, 0.37
Procedure performed yes	-0.18	0.84	0.20	-0.88	0.38	-0.58, 0.22
Procedure performed no	0.12	1.13	0.21	0.59	0.56	-0.29, 0.53
Region (Reference Northeast)						
West	-0.20	0.82	0.10	-2.04	0.04	-0.40, 0.01
South	-0.29	0.75	0.10	-2.99	0.003	-0.47, -0.10
Midwest	0.02	1.02	0.10	0.24	0.81	-0.17, 0.21
Pain scale	-0.01	0.99	0.01	-1.12	0.266	-0.02, 0.01
Image received	0.43	1.54	0.06	6.85	<0.0001	0.31, 0.56
Metropolitan Statistical Area	0.20	1.23	0.08	2.54	0.012	0.05, 0.36
Race (Reference White)						
Black	-0.05	0.95	0.08	-0.67	0.501	-0.20, 0.10
Other	0.10	1.10	0.11	0.86	0.392	-0.12, 0.32
Year 2015	-0.01	0.99	0.06	-0.11	0.914	-0.12, 0.11
Total number of chronic conditions						
0	-0.04	0.96	0.16	-0.23	0.819	-0.36, 0.28
1	0.06	1.06	0.14	0.41	0.682	-0.22, 0.34
2	0.11	1.12	0.14	0.78	0.437	-0.17, 0.40
3	0.02	1.02	0.14	0.16	0.876	-0.25, 0.29
4	0.36	1.43	0.19	1.90	0.060	-0.01, 0.73
5	0.16	1.17	0.21	0.76	0.447	-0.26, 0.58
6	-0.19	0.82	0.28	-0.70	0.486	-0.74, 0.35
7	0.37	1.44	0.31	1.16	0.246	-0.25, 0.99
8	0.06	1.06	0.17	0.36	0.717	-0.28, 0.40
9	0.86	2.36	0.24	3.61	0.000	0.39, 1.33
Intercept	4.66	105.54	0.43	10.72	<0.0001	3.80, 5.52

Chapter 5: Discussion

5.1 Overview and key findings

The key finding of this study show a 28% increase in ED LOS for LBP visits where opioid analgesics were given as compared to visits where only non-opioid analgesics were given. On average, this equates to a 38 min (average opioid group LOS 183.86 $\pm$ 6.56) longer stay for individuals who receive opioid analgesics. While a 28% increase in LOS per visit may not seem like a substantial clinical difference, our study demonstrated that during 2014 and 2015, treatment of LBP in the ED with opioid analgesics corresponded to a LOS increase of 1.6 million hours more per year than patients who received non-opioid analgesics. This finding is important as it indicates that the use of opioid analgesics in the LBP population may be using more limited ED resources such as treatment rooms and physician time due to the increased LOS in the ED. In addition to increased use of limited ED resources, many studies have examined the effect of extended ED LOS and have found associations with diminished quality of care and increased AE such as: increased infection rates, medication related errors, pressure sores, and delirium.[18-21] The findings in this study show an association between opioid analgesic treatment and increased ED LOS and raises the question of whether patients being treated with opioid analgesics for LBP in the ED are being exposed to a greater risk for experiencing diminished quality of care and increased adverse events due to their increase ED LOS. The finding of increase LOS in the ED for with opioid treatment for LBP seems to also coincide with the current 2017 ACP clinical evidence-based guideline recommendation of SMR and NSAID as first line treatments. This analysis also showed that 60% of patient visits receive an opioid analgesic, a finding consistent with other national survey analsysis.[2] One particular strength of this analysis is that it is not

only the first study to examine the effect of treatment on ED LOS in the LBP population, but also has the added advantage of having a national-level sample in the US. Using a national-level sample allows for better insight to the prescribing habits across in the US EDs for LBP.

For this study, ITO model conceptual model of Emergency Department crowding was used to analyze the effect of treatment on LOS in the ED for LBP individuals. The ITO model describes ED overcrowding as a function of time spent in three distinct interdependent sections; input, throughput, and output. As described in the methods section, patients in this analysis were examined in the throughput portion of the model as treatment was a function of how long an induvial stayed within this portion of the model, used as ED LOS. Using the ITO model, a significant longer LOS was seen between the two treatment groups. The finding of this study shows that treatment is a significant factor in time spent in the throughput portion of a model as measured with LOS.

5.2 Limitations

Limitations of this study include: chances of errors during the data collection and coding process. However, the CDC has made several attempts to improve the accuracy of the NHAMCS data, despite this, the literature has raised question surrounding the surveys accuracy.[31] Another limitation to the NHAMCS is missing data. Due to the complex survey structure of the NHAMCS data, many variables are associated with >10% of missing data, indicating that these data are not missing completely at random. To deal with the variables in the analysis with the highest missing data; imputation was used, specifically median substitution. The drawback of using the median substitution imputation method is that the missing data are replaced with the same missing value resulting in a systematic underestimate of the variance.[28] Further limitation of this analysis is the use of ICD-9-CM diagnosis codes for identification of the LBP sample.

Inaccuracy of coding of ICD-9-CM is a well-documented drawback for use of diagnosis.[14] In an attempt to improve the accuracy of identification of individuals with LBP in the ED, ICD-9-CM diagnosis codes or reason for visit were part of the inclusion criteria. This was completed to account for individuals with inaccurate ICD-9-CM diagnosis codes in hope that reason for visit would identify any individuals in the ED with LBP sequelae.

5.3 Sensitivity analysis

The robustness of this regression was explored by using a number of sensitivity analyses. The initial sensitivity analysis preformed was analyzing the effect of opioid analgesics only vs non-opioid analgesics on LOS, this resulted in a statistically significant relationship between opioid analgesics treatment alone and LOS (β=0.27p< 0.001 CI: 0.12, 0.43) vs non-opioid analgesics. Other sensitivity analysis preformed included models that did not impute missing data but rather left missing data in the model and removed missing observations from the model. All sensitivity analyses findings were consistent with our primary analysis demonstrating the robustness of our study findings.

5.4 Conclusions

The current study demonstrates that treatment choice plays a critical role in the length of stay among individuals with LBP treated in the ED. Specifically, the use of opioid analgesics for treatment of LBP in ED visits is associated with a significant increase in ED LOS as compared to the ED visits where non-opioid analgesics only were used.

5.5 Future Research Recommendations

Although this study was one of the first studies to examine the effect of opioid analgesic use on ED LOS, further research needs to be done to understand the use of opioid analgesics on LOS. Further research is needed to understand the relationship of opioid analgesics vs non-

analgesics through prospective RCT for treatment impact on LOS. One interesting finding in the analysis showed that there was a decrease in LOS for the Southern region of the US. Further research may be insightful to better understanding the relationship of region and outcomes such as LOS. Lastly, increased ED LOS is associated with increase ADEs that can result in higher treatment costs. Future studies should be conducted to understand the monetary impact of increased ED LOS.

References

1) National Center for Health Statistics. Health, United States, 2012: with special feature on emergency care; 2013[Hyattsville, MD, http://www.cdc.gov/nchs/ahcd.htm].

2) Friedman BW, Chilstrom M, Bijur PE, Gallagher EJ. (2010) Diagnostic testing and treatment of low back pain in United States emergency departments: a national perspective. Spine (Phila Pa 1976). Nov 15;35(24):E1406-11. doi: 10.1097/BRS.0b013e3181d952a5. PubMed PMID: 21030902; PubMed Central PMCID: PMC2982879.

3) Edwards, J., Hayden, J., Asbridge, M., Gregoire, B., & Magee, K. (2017). Prevalence of low back pain in emergency settings: A systematic review and meta-analysis. *BMC Musculoskeletal Disorders, 18*(1)10.1186/s12891-017-1511-7.

4) Qaseem, A., Wilt, T. J., McLean, R. M., & Forciea, M. A. (2017). Noninvasive treatments for acute, subacute, and chronic low back pain: A clinical practice guideline from the American college of physicians. Annals of Internal Medicine, 166(7), 514-530.

5) Han, B., Compton, W. M., Blanco, C., Crane, E., Lee, J., & Jones, C. M. (2017). Prescription opioid use, misuse, and use disorders in U.S. adults: 2015 national survey on drug use and health. *Annals of Internal Medicine, 167*(5), 293-301. doi:10.7326/M17-0865.

6) Manchikanti, L., Helm 2nd., S., Fellows, B., Janata, J. W., Pampati, V., Grider, J. S., & Boswell, M. V. (2012). Opioid epidemic in the united states. *Pain Physician, 15*(3 Suppl), ES9-38.

7) Friedman, B.W., Dym, A.A., Davitt, M., Holden, L., Solorzano, C., Esses, D., Bijur, P.E., Gallagher, E.J. Naproxen with cyclobenzaprine, oxycodone/acetaminophen, or placebo for treating acute low back pain: A randomized clinical trial (2015) JAMA - Journal of the American Medical Association, 314 (15), pp. 1572-1580. Cited 26 times. DOI: 10.1001/jama.2015.13043.

8) Guttmann, A., Schull, M. J., Vermeulen, M. J., & Stukel, T. A. (2011). Association between waiting times and short-term mortality and hospital admission after departure from emergency department: Population based cohort study from Ontario, Canada. *BMJ, 342*(7809) doi:10.1136/bmj.d2983.

9) Schull, M., Vermeulen, M., Guttmann, A., & Stukel, T. (2015). Better performance on length-of-stay benchmarks associated with reduced risk following emergency department discharge: An observational cohort study. *Canadian Journal of Emergency Medicine, 17*(3), 253-262. doi:10.1017/cem.2014.39.

10) Asplin, B. R., Magid, D. J., Rhodes, K. V., Solberg, L. I., Lurie, N., & Camargo Jr., C. A. (2003). A conceptual model of emergency department crowding. *Annals of Emergency Medicine, 42*(2), 173-180. 10.1067/mem.2003.302.

11) Hoy, D., March, L., Brooks, P., Woolf, A., Blyth, F., Vos, T., & Buchbinder, R. (2010). Measuring the global burden of low back pain. Best Practice and Research: Clinical Rheumatology, 24(2), 155-165. 10.1016/j.berh.2009.11.002.

12) Scott N, Moga C, Harstall C. Managing low back pain in the primary care setting: the know-do gap. Pain Res Manag. 2010;15(6):392–400.

13) Hoy D, Bain C, Williams G, March L, Brooks P, Blyth F, Woolf A, Vos T, Buchbinder R. A systematic review of the global prevalence of low back pain. Arthritis Rheum. 2012;64(6):2028–37.

14) Altyar, A., Bakhsh, H. T., Mohammed, A., Skrepnek, G., & Patanwala, A. E. (2015). Administration of first dose antibiotic in the ED in patients with minor skin and soft tissue infections. American Journal of Emergency Medicine, 33(9), 1225-1228. doi:10.1016/j.ajem.2015.05.035.

15) Guttmann, A., Schull, M. J., Vermeulen, M. J., & Stukel, T. A. (2011). Association between waiting times and short term mortality and hospital admission after departure from emergency department: Population based cohort study from Ontario, Canada. BMJ, 342(7809) doi:10.1136/bmj.d2983.

16) Bashkin, O., Caspi, S., Haligoa, R., Mizrahi, S., & Stalnikowicz, R. (2015). Organizational factors affecting length of stay in the emergency department: Initial observational study. Israel Journal of Health Policy Research, 4(1)10.1186/s13584-015-0035-6.

17) Ackroyd-Stolarz, S., Read Guernsey, J., MacKinnon, N. J., & Kovacs, G. (2011). The association between a prolonged stay in the emergency department and adverse events in older patients admitted to hospital: A retrospective cohort study. BMJ Quality and Safety, 20(7), 564-569. 10.1136/bmjqs.2009.034926.

18) Diercks, D.B., Roe, M.T., Chen, A.Y., Peacock, W.F., Kirk, J.D., Pollack Jr., C.V., Gibler, W.B., Smith Jr., S.C., Ohman, M., Peterson, E.D. Prolonged Emergency Department Stays of Non-ST-Segment-Elevation Myocardial Infarction Patients Are Associated With Worse Adherence to the American College of Cardiology/American Heart Association Guidelines for Management and Increased Adverse Events (2007) Annals of Emergency Medicine, 50 (5), pp. 489-496.

19) National Center for Health Statistics. Health, United States, 2012: with special feature on emergency care; 2013[Hyattsville, MD

https://www.cdc.gov/nchs/ahcd/ahcd_questionnaires.htm#public-use].

20) National Center for Health Statistics. Health, United States, 2012: with special feature on emergency care; 2013[Hyattsville, MD, http://www.cdc.gov/nchs/ahcd.htm].

21) https://www.cdc.gov/nchs/data/ahcd/Sample_Text_for_Describing_NHAMCS_in_Research_Article.pdf.

22) http://www.multum.com.

23) Bennett, D. A. (2001), How can I deal with missing data in my study?. Australian and New Zealand Journal of Public Health, 25: 464-469. doi:10.1111/j.1467-842X.2001.tb00294.x.

24) CDC National Hospital Ambulatory Medical Care Survey. 2014 NHAMCS MICRO-DATA FILE DOCUMENTATION. Last modified 6/4/17. ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NHAMCS.

25) CDC National Hospital Ambulatory Medical Care Survey. 2015 NHAMCS MICRO-DATA FILE DOCUMENTATION. Last modified 11/20/17. ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NHAMCS.

26) Green SM. Congruence of disposition after emergency department intubation in the National Hospital Ambulatory Medical Care Survey. Ann Emerg Med. 2013 Apr;61(4):423-426.e8. doi: 10.1016/j.annemergmed.2012.09.010. Epub 2012 Oct 25. PubMed PMID: 23103322.

Figure 4: Institution Review Board/ Human Subjects Approval

Human Subjects
Protection Program

1618 E. Helen St.
P.O.Box 245137
Tucson, AZ 85724-5137
Tel: (520) 626-6721
http://rgw.arizona.edu/compliance/home

Date:	February 20, 2018
Principal Investigator:	Seth William Anderson
Protocol Number:	1802285984
Protocol Title:	The association between opioid use for low back pain and Emergency Department length of stay : A cross-sectional study
Determination:	Human Subjects Review not Required

Documents Reviewed Concurrently:

HSPP Forms/Correspondence: *IRB_Seth.pdf*
HSPP Forms/Correspondence: *IRB_SUB.pdf*

Regulatory Determinations:

- Not Human Subjects Research as defined by 45 CFR 46.102(f): as presented, the activities described above do not meet the definition of research involving human subjects as cited in the regulations issued by the U.S. Department of Health and Human Services which state that "human subject means a living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with the individual, or identifiable private information."

The project listed above does not require oversight by the University of Arizona.

If the nature of the project changes, submit a new determination form to the Human Subjects Protection Program (HSPP) for reassessment. Changes include addition of research with children, specimen collection, participant observation, prospective collection of data when the study was previously retrospective in nature, and broadening the scope or nature of the study activity. Please contact the HSPP to consult on whether the proposed changes need further review.

The University of Arizona maintains a Federalwide Assurance with the Office for Human Research Protections (FWA #00004218).