THE EFFECT OF PREOPERATIVE NEUROLEPTICS AND OPIOIDS ON POST-OPERATIVE PAIN AND DISABILITY FOLLOWING SPINAL SURGERY FOR LUMBAR RADICULOPATHY

by

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Abstract

Despite common treatments of lumbar radiculopathy, a subset of patients do not meet satisfactory clinical outcomes. Our study aims to estimate the effect of preoperative opioids and neuroleptics on postoperative pain and disability of patients who underwent spine surgery, with or without fusion, for lumbar radiculopathy. Patients reported preoperative medication use as none, intermittent, or daily. Study outcomes were leg, back pain, measured with the numeric rating scale and disability scores measured with the modified Oswestry Disability Index at 3-,12 –and-24 months postoperatively. We constructed propensity score models using inverse-probability weights and regression adjustment to account for confounding: age, sex, education, smoking, depression risk, and baseline pain or disability. Preoperative opioids had a small adverse effect on back pain with a maximum effect of [0.55(0.27-0.83)], leg pain [0.32(0.005-0.64)] – [0.36(0.02-0.71)], and disability [2.17(0.45-3.90)] – [3.51(1.46-5.56)] following spine surgery for lumbar radiculopathy. Preoperative neuroleptics did not affect outcomes.

Dedication

This thesis is wholeheartedly dedicated to my beloved parents, who have been a source of power and motivation. They have taught me to continue fighting through challenging times, to push towards my dreams and aspirations. Thank you to my siblings who have shared their words of advice and encouragement to keep pushing.

To my source of strength and drive, thank you to my partner, Matt Mintern, for continually providing me with support, care, and appreciation. Thank you for standing by me through my impatience, absent moments, and difficulties of this journey!

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List of Symbols, Nomenclature, or Abbreviations

ATE: Average Treatment Effects

CSORN: Canadian Spine Outcomes and Research Network

FDA: Food Drug and Administration

IPW: Inverse Probability Weighting

IPWRA: Inverse Probability Weighting with Regression Adjustment

LBP: Low Back Pain

mODI: modified Oswestry Disability Index

MCS: Mental Component Score

MCIC: Minimal Clinically Important Change

NRS: Numeric Rating Scale

ODI: Oswestry Disability Index

PCS: Physical Component Score

SF-12: Short Form Health Survey-12

Introduction

Lumbar radiculopathy is a disease that causes compression of the spinal nerve roots causing pain, numbness, and weakness in the lower extremities. Point prevalence of lumbar radiculopathy ranges from 1.6% to 13.4% in adults between 45- to 64-year-old, however, men are more affected than women (Clark et al., 2020). Patients with radiculopathy often describe their pain radiating to their low back and leg as a "shooting, numbing, electric, or tingling sensation," causing motor weakness or sensory disturbances (Clark et al., 2020; Govind, 2004). This can develop into sciatica, a type of radiculopathy. Sciatica refers to nerve pain that begins from the lower back through the buttocks, and travels down the legs (through the sciatic nerve).

Surgery and pharmaceutical interventions are standard treatment options for patients with radiculopathy. Examples of pharmaceutical drugs include opioids (i.e., Oxycodone, Morphine) and neuroleptics (i.e., Gabapentin, Lyrica) (Visco et al., 2011). Patients will often be on multiple medications against national guidelines for radiculopathy symptoms causing significant side effects (Gugliotta et al., 2016; Reddington et al., 2021). This may occur due to a lack of effectiveness of prescribed medications or even yet because the literature lacks robust consensus on optimal medications for radiculopathy (Gugliotta et al., 2016; Reddington et al., 2021).

If non-operative management fails, patients will undergo surgery. However, Clark et al., 2019 stated surgery for the treatment of radiculopathy, specifically sciatica, may only be beneficial in short- and medium-term follow-up, but the benefits of pain reduction and functionality does not maintain long-term compared to non-surgical interventions (Clark et al., 2020; Peul et al., 2007). Spine surgery's cost-effectiveness

may be inconclusive (Clark et al., 2020). As surgeries continue to increase due to non-surgical management failure, healthcare costs increase (Visco et al., 2011), causing a burden on the system. The improvements observed for quality of life and neurologic symptoms were similar between those who underwent surgery and those who did not; this yields a subset of patients that do not meet satisfactory clinical outcomes (Ostelo et al., 2004; Woertgen et al., 1999).

The overall aim of this thesis was to explore the effect of preoperative analgesic use for clinical outcomes following surgery for lumbar radiculopathy. Our objective is to estimate the effects of preoperative neuroleptics and opioids on post-operative pain and disability using propensity score weighting. There is a need for further work to understand the clinical potential of preoperative pharmaceutical agents for patients with a primary or secondary complaint of radiculopathy.

Literature Review

Back pain is the primary leading cause of disability worldwide (Buchbinder et al., 2013). Studies show that 50–80% of adults will experience back pain at some point in their life (Rubin, 2007), and 54% of adults will suffer from neck pain during any six months (Côté et al., 1998). Low Back Pain (LBP) is the most common musculoskeletal condition affecting the general adult population (Lacasse et al., 2017) (range 65 to 85%), and 36 to 70% of them suffer from general back pain (Bressler et al., 1999; Edmond & Felson, 2000; Podichetty, 2003). Globally, an age-standardized point prevalence of LBP has been reported at 9.4% (Weiner et al., 2006). LBP can impose many limitations that negatively impact an individual's everyday life (Buchbinder et al., 2013; Wirick & Teufel-Prida, 2018). Some negative impacts include social isolation, decreased mood, and functional impairments (Buchbinder et al., 2013). Back pain will inevitably become an increasing issue as the population ages (Weinstein et al., 2008).

Degenerative spine conditions

Most causes of LBP in older adults are non-specific LBP due to age-related physical and psychosocial changes (Wong et al., 2017). Non-specific LBP may elucidate many underlying causes, including spinal stenosis or radiculopathy. Patients with non-specific or mechanical LBP experience pain altered by posture, activity, or time of the day as it may originate from different pain sources (Wong et al., 2017). Delays in the management of LBP may result in functional disability (Docking et al., 2011).

Degeneration of the thoracolumbar spine region is most common. The lumbar spine supports most of the upper body's weight; thus, pain and discomfort are more likely to occur in this region. Conditions include radiculopathy, degenerative disc disease, disc

herniation, spondylolisthesis, spinal stenosis, and spinal osteoarthritis. Combinations of these conditions are possible.

Radiculopathy

Radiculopathy, a dysfunction of nerve roots, can occur in any spine region, most commonly in the lumbar spine. Various spinal pathologies can cause radiculopathy as a complaint. The narrowing of the space where the nerve root exits the spine can occur because of degeneration, disc herniation, stenosis, bone spurs, or other pathologies. Radiculopathy arises from narrowing the spinal canal with subsequent neural compression – called lumbar spinal stenosis.

Lumbar radiculopathy begins with LBP radiating to the lower extremities, most presented as sciatica. Patients often experience a wide range of neurological symptoms or impairment (Zaina et al., 2016). Neurological impairment includes numbness, tingling, and burning sensations on the skin caused by damage to the nerves – also called neuropathic pain.

The prevalence of lumbar radiculopathy ranges from 1.6 to 13.4% in men and women between 45 and 64, with a slightly higher prevalence in men (Bouhassira et al., 2008). Treatment options from rest and physical therapy to medications, epidurals, and surgery as a last resort are available.

Degenerative Disc Disease (DDD)

Degenerative disc disease (DDD) occurs when normal degeneration (wear-and-tear) of spinal discs causes pain. This is more likely to occur as people age (Choi, 2009). Lumbar disc degeneration is the most common cause of LBP (Choi, 2009). One of the

causes of degeneration is poor transport of nutrients into the disc (Nachemson et al., 1970).

DDD has four phases. In phase I, the vertebrae start to cause balance loss, accelerating the degeneration process and beginning posture change. Phase II causes an increased posture change. Phase III is associated with additional damage to the spine due to nerve compression. It is possible for bone spurs to form and compress nerves, leading to radiating pain. The final stage (phase IV) is when the intervertebral disc degenerates and the disc space collapse resulting in herniation. The pressure caused by the herniation on the nerves leads to neurological impairment symptoms (symptoms vary depending on location of herniation/stenosis). During the final stages of DDD (advanced DDD), the intervertebral disc degenerates, and the disc space collapses, resulting in herniation. A person with lumbar DDD will feel significant discomfort and pain that radiates into the hips, legs, and back, like radiculopathy's neurological impairment symptoms.

Disc Herniation

Aging is the most common cause of disc herniation (Lachman, 2015). The process of disc herniation occurs when part of all the nucleus pulposus extends beyond the annulus fibrous. The risk of herniation of the nucleus pulposus increases with annular tears (the ligament that connects your vertebra to your disc), resulting in decreased resistance to torque and increased risk of extrusion of disc contents ("Spinal Pathology"). However, discs may still bulge without evidence of annular tearing or herniation. Like DDD, disc herniation has four stages: 1) bulging, 2) protrusion, 3) extrusion, 4) sequestration (Lachman, 2015). Degeneration is when the disc bulges posteriorly without rupture. Prolapse occurs when the outermost annulus contains

nucleus pulpous. Extrusion is when the disc material enters epidural space and finally sequestration is when fragments from outside the disc (Lachman, 2015).

Disc herniation most commonly occurs at C5-6, C6-7, L4-5, L5-S1 (Humphreys & Eck, 1999). However, lumbar disc herniation is most common and occurs 15 times more than cervical disc herniation (Dydyk et al., 2022). The cervical disc herniation is most affected at C5-C6 and C6-C7 (Orief et al., 2012). The thoracic spine has the lowest rate of disc herniation (Dydyk et al., 2022).

Lumbar disc herniation is the most common cause of radiculopathy (Yang et al., 2015). Risk factors for lumbar disc herniation include family history of disc disease, physically demanding jobs, or comorbidities such as obesity (Kelsey, 1978; Schroeder et al., 2016).

Spondylolysis

Spondylolysis occurs when a fracture of the pars interarticularis (tiny bones that make up the spine between the lamina and pedicle) is present. Substantial impacts can cause spondylolysis (i.e., landing on one foot). Spondylolysis is also the most common cause of progressive spinal cord and nerve root compression. Athletic adolescents are most at risk where repeated stress on the lower back is involved (Standaert, 2000). As a result of such injury, the vertebra translates forward in the sagittal plane to an adjacent vertebra, respectively (Standaert, 2000). The incidence of lumbar spondylolysis for athletics may reach 63%, whereas the general population has an incidence of 6-8% (Brooks et al., 2010; Leone et al., 2011; Rossi, 1978; You & Moon, 2001). Spondylolysis involves the L5 vertebra in 95% of cases (Leone et al., 2011). The discs lose elasticity causing cracks in the outer wall of the disc, causing the outer wall to

bulge. This gradual deterioration of the discs between the vertebrae is also referred to as DDD. If spondylolysis progresses to causing pressure on the nerves, this may present as radiculopathy.

Spondylolisthesis

Spondylolysis may lead to isthmic spondylolisthesis (Leone et al., 2011). This malalignment is a result of advanced DDD. In most cases, spondylolysis's progression to spondylolisthesis is likely to occur in adolescents younger than 16 years (Fredrickson et al., 1984). One of the common causes of back pain in children and adolescents are spondylolysis and spondylolisthesis (Fredrickson et al., 1984; King, 1999; Turner et al., 1989).

Spinal Stenosis

Spinal stenosis is the most common reason for lumbar spinal surgery in adults over 65 years of age (Weinstein et al., 2008). The increasing prevalence with age is due to degenerative changes to the spinal column. LSS typically arises due to degenerative or arthritic changes of the lumbar vertebrae or when narrowing the spinal canal results in compression and pressure on the spinal cord (Deasy, 2015; Kalichman et al., 2009). Stenosis progression can lead to specific motor and sensory deficit patterns. ("Spinal Pathology") This progression results in neurogenic claudication, the symptoms of which typically affect the lower back and lower limbs (Deasy, 2015; Kalichman et al., 2009). Symptoms include weakness and numbness in the low back and lower limbs (Deasy, 2015). LSS is common, but the exact prevalence of LSS varies among populations (Wu & Cruz, 2022). However, LSS increases in prevalence as individuals age (Deasy, 2015; Yabuki et al., 2013).

Prevalence & Economic Consequence

The use and costs of spine care have been increasing at an alarming rate (Martin, 2008; Weiner et al., 2006). Docking et al., (2011) reported 1-month prevalence of disabling back pain increased by 5.9% between people aged 77-79 years and 90-100 years (Docking et al., 2011).

Patients who need spine care require diverse medical resources – including family physicians, specialists, and allied health professionals. Spine patients may also need imaging and spine procedures such as injections or nerve tests. A Canadian cross-sectional study on patient utilization confirmed that factors such as pain duration, comorbidities, and pain episodes are related to increased specialist care (Boonen, 2004; Chenot et al., 2008; Plénet et al., 2010; Ritzwoller et al., 2006; Walker et al., 2004). Chronic LBP leads patients to seek surgery which suggests the increasing prevalence of surgery rates. Spine surgery has increased by 157% in 8 years (Rubin, 2007). An analysis of direct health care costs for spinal conditions in Canada summed up to $264 million (CAD) through the fiscal year of 2013-2014 (Rampersaud et al., 2020). The cost of admission charge to a surgical unit is significantly higher than outpatient ($35,017.28 ± $14,335.60 vs $33,881.50 ± $15,023.70; $p < 0.001$). Thus, costs for procedures are higher in patients admitted overnight ($4049.27, 95% CI $2577.87-$5520.67, $p < 0.001$) and for patients on private insurance ($4775.72, 95% CI $4171.06-$5380.38, $p < 0.001$) than outpatient. Readmission charges are also higher in patients who undergo surgery overnight (Alvi et al., 2021).

Classifications of Pain

The description, symptoms, and area of distribution of pain can be classified in several ways to determine the diagnosis. Axial pain or mechanical pain occurs in a particular region (i.e., annular tears in discs) due to muscle strain. People often describe axial pain as sharp pain, and it does not travel into limbs, whereas radicular pain travels into limbs. People often describe radicular pain as electric, tingling, burning, or numbness. When it is accompanied by weakness or numbness, it is often referred to as radiculopathy.

Sciatica follows the spinal nerve pathway caused by compression or inflammation. Referred pain tends to be more general and varies in intensity. DDD may cause referred pain to radiate to hips and posterior thighs. Radicular pain and referred pain are different because radicular pain follows specific nerves, whereas referred pain can occur in various places around the injured tissue.

Other types of physical pain are nociceptive and neuropathic pain. Neuropathic pain is more severe than nociceptive pain, disturbing patients' quality of life (Bouhassira et al., 2008). Nociceptive pain occurs through events such as stubbing a toe or inflammation of the nerve fibers. Neuropathic pain develops once the nervous system is not responding correctly due to injury or disease, and it does not develop due to a response to a stimulus. Higher neuropathic pain screening scores correlated strongly with the likelihood of significant post-operative leg pain (Shamji & Shcharinsky, 2016). Due to the chronic nature and difficulty to manage, neuropathic pain remains a significant clinical problem and therapeutic challenge in patients after spine surgery. High preoperative pain intensity and use were associated with chronic postsurgical

neuropathic pain. The intensity of preoperative pain is associated with poor outcomes after lumbar radiculopathy. However, this study failed to distinguish whether this pain was neuropathic or nociceptive.

Treatment Options

Medications

Pain medications intercept differing areas of the pain pathway. They act locally, peripherally, or centrally on the neural axis to decrease pain (Visco et al., 2011). Pharmaceutical drugs for lumbar radiculopathy include opioids, antidepressants, muscle relaxants, and neuroleptics. However, there is no consensus on medications specifically for radiculopathy (Visco et al., 2011). First-line treatments for patients with radiculopathy involves non-invasive options (e.g., rest, physical therapy, pharmaceutical drugs), however, patients who develop debilitating pain may require surgery (Ahmed et al., 2018).

Studies report guidelines and recommendations on interventions for spine surgery. First-line options for LBP include acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs). The National Institute for Health and Care Excellence (2017) guidelines recommend including epidural injections, neuropathic pain pharmacotherapy, and spinal decompression as additional interventions for sciatica (Chye et al., 2021). However, these are often ineffective and associated with adverse effects, especially for patients with multiple comorbidities (Goodman & Brett, 2017). The literature provides contradictory information on the use of NSAIDs for fusion patients (Dimar et al., 1996; Dumont et al., 2000).

Devin et al., developed a best practice guideline based on the NASS (North American Spine Society) Clinical Guidelines for Multidisciplinary Spine Care for commonly used agents in multimodal pain management in spine surgery (Devin & McGirt, 2015). Gabapentinoids, acetaminophen, neuraxial blockade, and extended-release local anesthetics reduce post-operative pain and narcotic requirements (Grade A- good evidence). Pre-emptive analgesia and nonsteroidal anti-inflammatory drugs (NSAID) reduce post-operative pain (Grade B- fair evidence). Muscle relaxants and ketamine provide a significant reduction in post-operative pain or narcotic usage (Grade I- insufficient or conflicting evidence). Short-term use of NSAID results in no long-term reduction in bone healing or fusion rates (Grade B- fair evidence) (Dumont et al., 2000).

The Food and Drug Administration (FDA) approves gabapentinoids to treat fibromyalgia and neuropathic pain associated with diabetes or spinal cord injuries – pregabalin (Goodman & Brett, 2017). Pregabalin (brand-name Lyrica) was approved for treating diabetic neuropathy and postherpetic neuralgia in 2004 and fibromyalgia in 2007 (Goodman & Brett, 2017). The CDC guidelines also recommend gabapentinoids (gabapentin or pregabalin) as first-line agents for neuropathic pain. However, gabapentinoids are prescribed excessively because they are less frowned upon than opioids but stronger than acetaminophen and NSAIDs. It is being used for almost any type of pain. In 2016, gabapentin ranked within the 10th most prescribed medication in the United States - with sales of $4.4 billion (Goodman & Brett, 2017).

Lyrica has promoted extensive direct consumer advertising the perception of its use as a ‘general’ pain medication, rather than the specific use for painful diabetic neuropathy or fibromyalgia (Goodman & Brett, 2017). The justification of prescribing

this class of medication for LBP can be due to the similarity of fibromyalgia pain (Goodman & Brett, 2017). Side effects are common. Patients (40%) in a sciatica trial reported feeling side effects such as dizziness after taking gabapentinoids (Hernández-Rodríguez et al., 2020). Pregabalin did not significantly reduce leg pain measured through the numeric rating scale or improve other outcomes associated with sciatica (Goodman & Brett, 2017). The misuse and abuse of gabapentinoids have not been investigated yet; however, given the growing prescribing practices, there is potential of a public health issue (Goodman & Brett, 2017).

Some evidence suggests that gapapentinoids are ineffective and increase the risk of adverse events for treating low back pain or lumbar radicular pain (Enke et al., 2018). Evidence for the efficacy and safety of those medications in the low back and lumbar radicular pain is unclear – the literature is limited to populations with chronic back pain (Baron et al., 2010; Enke et al., 2018). Nasal calcitonin spray daily was more effective than 300 mg gabapentin three times per day for lumbar spine stenosis patients (Haddadi et al., 2016). Gabapentin for chronic sciatica showed only short-term improvement in overall pain relief (mean difference -26.6, -38.3 to -14.9). Further, the existing data from clinical trials are of low quality for the management of sciatica (Enke et al., 2018; Pinto et al., 2012).

Surgeon prescription opioids are heterogeneous; however, they manifest into the opioid crisis, contributing to economic burden and mortality. The current opioid prescription rate sits at 1 in 6 Canadians (Berrington, 2019). Brummett et al. (2017) found that risk factors of opioid dependence were preoperative pain conditions including neck and back pain and underlying behavioral and mood disorders (Brummett et al.,

2017). Preoperative use of opioids is the most significant predictor of long-term opioid use (Armaghani et al., 2014; Meier, 1984; Schoenfeld et al., 2018; Warner et al., 2020). Although useful for acute management of pain, chronic use of opioids for pain management results in increased pain intensity increased disability caused by pain, and reduced quality of life (Petersen et al., 1989).

Mohanty et al., (2021) reported combining the lowest dose of opioids with a high dose of non-opioid pain medication did not result in lower pain relief postoperatively, relative to patients who received higher prescribed opioids (P=0.019) (Mohanty et al., 2021).

Surgery

Patients may require surgical intervention in a nerve root spinal cord decompression if conservative treatment does not relieve symptoms. They may also require spinal fusion, which maintains stability in the spine after bone and soft tissue resection.

The incidence of surgery for back pain treatment is on the rise, especially among the elderly population (Grotle et al., 2019; Hoy et al., 2014). If a patient decides to undergo surgery, recovery rates and benefits vary depending on the type of surgery, general health status, other comorbidities (i.e., diabetes, heart disease), general musculoskeletal status, and the degree of symptoms presented at baseline. Direct medical costs of instrumented lumbar surgeries from 2002 to 2012 totaled $176 million (Verplanken et al., 1983). One of the procedures increasingly employed in chronic back pain management is fusion of the lumbar vertebrae (Martin, 2008; Weiner et al., 2006). An essential intervention for LBP with radiculopathy is lumbar discectomy surgery.

Systemic reviews support that lumbar discectomy is superior for short-term pain relief and improved function for lumbar radiculopathy to non-surgical treatment (Gugliotta et al., 2016; Peul et al., 2007). However, it does not show a benefit over conservative treatment in midterm and long-term follow-up (Gugliotta et al., 2016). Surgery may not fulfill all clinical outcomes (Voorhies et al., 2007). The duration of symptoms and older age may negatively affect post-operative outcomes. Furthermore, it is difficult to predict how a patient may respond to surgery. Some studies suggest it may take six months to one year to get back to regular activities, even if connective tissue has regained 100% strength.

On average, patients experience improvements after spine surgery in pain and disability (46-75%) at 2-months follow-up, which improves at the 2-year follow-up (78-95%), though with *high variability* in outcome (Oosterhuis et al., 2014). Ongoing disability can continue to be a problem, and 30-70% of patients report experiencing residual pain (Ostelo et al., 2004). This illustrates a pressing issue where many patients do not fit the successful surgical trajectory. Research in other surgical spine interventions such as decompression and fusion for spinal stenosis suggests that different pain and disability trajectories exist in multiple patient populations undergoing lumbosacral surgery (Hebert et al., 2019).

Some evidence suggests the duration of symptoms and advancing age negatively affect post-operative outcomes, but, at present, it is difficult to predict how an individual patient will respond to spine surgical intervention on its own (Baptiste et al., 2009). Surgery might benefit short-term pain relief compared to non-invasive options; however, no definitive conclusions over conservative treatment for longitudinal follow-up are

made (Gugliotta et al., 2016; Peul et al., 2007). Hence, pharmaceutical, and surgical interventions can target components of neuropathic pain. However, the effect of each separately on radiculopathy is not well established.

There is a need to identify patients who continue to experience poor post-operative outcomes and worsening pain – with the prescription of neuroleptics and/or opioids. The potential perioperative factors which can result in such outcomes can guide surgeons in distinguishing the trajectory of appropriate surgical candidates.

We aim to investigate the effect of preoperative medication usage on post-operative pain and disability for patients undergoing spine surgery for lumbar radiculopathy. Our objective is to estimate the effect of preoperative neuroleptics and opioids on post-operative pain and disability using propensity score weighting. We hypothesize that patients with radicular pain who use neuroleptics or opioids for preoperative pain may experience worse (higher) scores on numeric pain rating scales for postoperative pain and worse (higher) scores on the modified Oswestry disability index for disability than patients who do not use these medications.

How is back pain and disability measured?

Numeric Rating Scale

The numeric rating scale (NRS) is used to assess pain intensity. It is the most responsive measure in patients with low back pain (Walsh et al., 2003). The NRS is an 11-point scale representing typical pain with scores ranging from 0 (‘no pain’) to 10 (‘worst pain imaginable’) (Krebs et al., 2007). Ratings can be categorized as ‘mild’ (0 – 3), ‘moderate (4 – 6), or ‘severe’ (7 – 10) (Boonstra et al., 2016; Zelman et al., 2005). A systematic review has found the NRS to be reliable and valid in clinical practice (Childs

et al., 2005; Jensen et al., 1994; Karcioglu et al., 2018). Minimal clinical important change (MCIC) estimates indicate the magnitude of change relevant to clinical practice (Pool et al., 2007). A 30% improvement score from baseline score is considered meaningful change for the NRS (Ostelo et al., 2008).

The Oswestry Disability Index and Modified Oswestry Disability Index

The Oswestry Disability Index (ODI) is a self-administered questionnaire consisting of 10 questions used to assess various activities of daily living. The ODI is widely used to measure spine-related disability (Fairbank & Pynsent, 2000). Questions on the ODI are scored on a 0-5 scale with higher scores representing greater disability (Fritz & Irrgang, 2001). The sum is multiplied by two to yield a percent (Fritz & Irrgang, 2001; Monticone et al., 2012). Total scores are classified as 0–20 'minimal disability,' 21–40 'moderate disability', 41–60 'severe disability', 61–80 'crippled,' and 81–100 'bed-bound or exaggerating'.

It is the most reliable, valid, and responsive condition-specific assessment tool used to quantify disability related to leg and back pain (Fritz & Irrgang, 2001; Monticone et al., 2012; Vianin, 2008). This questionnaire has excellent test-retest reliability, responsiveness, and an estimated minimum level of important change of 30% (Fritz & Irrgang, 2001). Ostelo et al., reported that an improvement score of 30% from baseline is considered clinically meaningful improvement (Ostelo et al., 2008). The achievement of an ODI score of $\leq$22 (sensitivity 91.4% and specificity 82.4%) can also be used as a criterion of treatment success accompanied with other measures (van Hooff et al., 2016).

The modified Oswestry Disability Index **(**mODI) is a modified version of the original ODI questionnaire. The mODI replaces the sexual life question from the ODI to a question about fluctuations in pain intensity (Fritz & Irrgang, 2001). The mODI has similar levels of test-test reliability and internal consistency (Fritz & Irrgang, 2001). In this study, we use the mODI for disability scores.

Patient Quality of Life

It is vital to assess a patients' health-related quality of life to account for the impact of health and healthcare interventions on patients' lives. Health-related quality of life covers physical, mental, and social aspects. The short form-12 (SF-12) is a self-reported instrument used to measure the impact of overall health on an individual's daily life. It is a shorter version of the short form 36. The SF-12 is divided into component scores that assess physical (PCS) and mental (MCS) health. The minimal clinical important difference for the PCS is a change score of >3.29 and for the MCS >3.77 (Díaz-Arribas et al., 2017).

Each component ranges from 0 to 100, with higher scores indicating greater health-related quality of life. The SF-12 demonstrates good internal consistency reliability, construct validity, and responsiveness in patients with back pain (Luo et al., 2003). The physical and mental components are reliable and valid for the general population and people living with non-cancer pain (Cheak-Zamora et al., 2009; Hayes et al., 2017).

The EQ-5D is a generic measure of health-related quality of life (Balestroni & Bertolotti, 2015). It has demonstrated good reliability and validity (Solberg et al., 2005). The EQ-5D evaluates five dimensions: mobility, self-care, daily activities,

pain/discomfort, and anxiety/depression. Each dimension is divided into three categories: no problem, some (moderate) problem, and significant (severe) problem (Balestroni & Bertolotti, 2015; Dolan, 1997). These health states generate a single score, anchored at 0 for death and 1 for full health (Balestroni & Bertolotti, 2015; Dolan, 1997). The second part of the EQ-5D instrument is a 20 cm visual analog scale. The respondents are asked to make a global assessment of their current health status on a vertical analog scale, the EQ-VAS, where 0 indicates the worst imaginable health state and 100, the best imaginable health state.

Gaps in literature

Very few studies in the literature have investigated the effect of preoperative analgesic use, such as neuroleptics and opioids on patients undergoing spine surgery for radiculopathy. The effect of opioids is thought to be detrimental in general when used as a dependent relief for pain, however, the current body of knowledge does not focus on patient characteristics or control for possible existing confounding variables. Furthermore, the role of neuroleptics alone on sciatic pain is thought to be effective but has not been investigated for long-term use postoperatively. The aim of our study is to estimate the effect of preoperative consumption of neuroleptics and opioids for pain and disability on patients undergoing spine surgery for lumbar radiculopathy. We will be controlling for confounding variables. This study will help to inform primary care providers and surgeons on medication effects for the population of interest and inform health policy decision-making and resource allocation through improved clinical outcomes.

Scientific Article

Preoperative Neuroleptic and Opioid Medication Use Have Trivial Effects on Post-operative Pain and Disability Following Spinal Surgery for Lumbar Radiculopathy

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Contributions

D.E. was leading the i) identification and design of the research proposal, ii) practical aspects of the research, iii) data analysis, and iv) manuscript preparation.

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ABSTRACT

Purpose: To estimate the effect of preoperative opioids and neuroleptics on postoperative pain and disability.

Methods: Retrospective cohort study of patients who underwent spine surgery, with or without fusion, for lumbar radiculopathy. Patients reported preoperative medication use as none, intermittent, or daily. Study outcomes were leg pain, back pain measured with the numeric rating scale, and disability scores measured with the modified Oswestry Disability Index (mODI) at 3-,12 -and 24 months postoperatively. We constructed propensity score models using inverse-probability weights and regression adjustment to account for confounding: age, sex, education, smoking, depression risk, and baseline pain or disability.

Results: We present 3,162 patients (mean age 55.9 [SD 15.0] years;51.8% female). After 3 months, patients who intermittently and daily used opioids preoperatively reported higher back pain scores than non-users. Higher mODI scores were reported for preoperative intermittent use at 3 months.Patients who consumed opioids preoperatively intermittently reported higher leg pain scores than non-users at 12 months. Patients who consumed daily and intermittent opioids preoperatively had higher back pain scores compared to non-users at 12 months. Higher mODI scores compared to non-users at 12 months were reported for patients who consumed opioids daily and intermittently preoperatively. Greater back pain was reported for patients with preoperative narcotic use intermittently and daily at 24 months. Patients who intermittently consumed narcotic medications preoperatively reported higher leg pain at 24 months.

Conclusion: Preoperative opioids had trivial effects on 3, -12- and 24-month clinical outcomes following spine surgery for lumbar radiculopathy. Preoperative neuroleptics did not affect postoperative outcomes.

Keywords: medications; opioids; neuroleptics; spine surgery; radiculopathy; pain; disability.

INTRODUCTION

Lumbar radiculopathy is a clinical manifestation that results due to compression or irritation of the spinal nerve roots. This leads to patients experiencing pain, numbness, loss of reflexes, and weakness in the lower extremities. Point prevalence of lumbar radiculopathy ranges from 1.6% to 13.4% in women and men between 45- to 64-year-old (Clark et al., 2020). Patients with radiculopathy often describe their pain radiating to

their low back and leg as a “shooting, numbing, electric, or tingling sensation,” causing motor weakness or sensory disturbances (Clark et al., 2020; Govind, 2004).

Treatment options for lumbar radiculopathy are vast. Traditionally, they are organized into surgical and non-surgical options. Non-surgical options may consist of medications including NSAIDS, opioids, antidepressants, muscle relaxants, and neuroleptics (Visco et al., 2011). Outside of medications, other therapeutic services such: physical therapy, chiropractors, acupuncture, or weight loss are commonly used in the treatment of lumbosacral radiculopathy (Visco et al., 2011).

With the use of medications as a pain relief modality, patients will often be on multiple medications against national guidelines for radiculopathy symptoms causing significant side effects (Gugliotta et al., 2016; Reddington et al., 2021).This may occur due to a lack of effectiveness of prescribed medications or even yet because the literature lacks robust consensus on optimal medications for radiculopathy(Gugliotta et al., 2016; Reddington et al., 2021).

Some evidence suggests the duration of symptoms and advancing age negatively affect post-operative outcomes, but, at present, it is difficult to predict how an individual patient will respond to spine surgical intervention on its own (Baptiste et al., 2009). Surgery might benefit short-term pain relief compared to non-invasive options; however, no definitive conclusions over conservative treatment for longitudinal follow-up are made (Gugliotta et al., 2016; Peul et al., 2007). Hence, medications and surgical interventions can target components of pain management. However, the effect of each separately on radiculopathy is not well established. Further, the effects of opioids and neuroleptics is well established in the literature to sometimes affect outcomes

negatively, however, it has not focused on patients undergoing spine surgery for lumbar radiculopathy nor is there a body of knowledge that reports results solely on the consumption of the classes of medications of interest with the control of confounding variables.

Our objective is to estimate the effect of preoperative neuroleptics and opioids on post-operative pain and disability for patients undergoing spine surgery for lumbar radiculopathy using propensity score weighting. We hypothesize that patients with radicular pain who use neuroleptics or opioids for preoperative pain may experience worse (higher) scores on numeric pain rating scales for postoperative pain and worse (higher) scores on the Oswestry disability index for disability than patients who do not use either class of these medications preoperatively.

METHODS

Study design and Participants

This is a retrospective cohort study of patients enrolled in the Canadian Spine Outcomes and Research Network (CSORN). CSORN is a national registry including 21 tertiary care centers across Canada. CSORN's nationwide goal is to define surgical outcomes for patients undergoing spine surgery. The present study uses an existing, de-identified dataset comprising information from adult patients (18+ y/o) who underwent spine surgery for lumbar radiculopathy. Patients with incomplete key baseline information (e.g., demographics, medication use, and quality of life), pathology of tumors, myelopathy, and non-degenerative pathologies (tumors, infections, spinal cord injuries, congenital abnormalities, fractures, lesions) were excluded from this study.

Ethics Approval

The nationwide CSORN project is approved at each spine center by their local Research Ethics Boards. Ethical approval is provided by Horizon Health Network (REB#101327) and the University of New Brunswick (REB#2021-104). All patients provided written informed consent to participate before study enrolment.

Exposure variables

Prior to spine surgery, baseline data collection included clinical measures (principal pathology, radiographic evaluations, and previous medical treatment information) reported by the attending surgeon. The initial patient assessment included standardized health assessment forms, demographics (age, sex), clinical factors (pain intensity, pain duration, comorbidities) and functional factors. In addition, patients report their medication use (categorized) related to their back pain according to frequency of times taken (not taken, intermittently, or daily) over the last 6 months.

Clinical Outcomes

Clinical outcomes are measured preoperatively, 3-, 12-, and 24 months postoperatively. Patient reported outcome measures for back pain and leg pain were self-reported through the numeric rating scale (NRS). The NRS is the most responsive measure in patients with low back pain (Walsh et al., 2003). The NRS is an 11-point scale representing typical pain with scores ranging from 0 (‘no pain’) to 10 (‘worst pain imaginable’) (Krebs et al., 2007). A systematic review has found the NRS to be reliable

and valid in clinical practice (Childs et al., 2005; Jensen et al., 1994; Karcioglu et al., 2018).

One way to measure relevant clinical important chance is through Minimal Clinical Important Change (MCIC). MCIC estimates indicate the magnitude of change relevant to clinical practice (Pool et al., 2007). A 30% improvement score from baseline score is considered meaningful change for the NRS (Ostelo et al., 2008).

Patient reported outcome measure for back-related disability were self-reported through the modified Oswestry Disability Index (mODI). The mODI is a questionnaire consisting of 10 questions used to assess various activities of daily living, replacing the sexual life question from the original Oswestry Disability Index (ODI) questionnaire to a question about fluctuations in pain intensity (Fritz & Irrgang, 2001). Questions are scored on a 0-5 scale with higher scores representing greater disability (Fritz & Irrgang, 2001). The ODI is the most reliable, valid, and responsive condition-specific assessment tool used to quantify disability related to leg and back pain (Fritz & Irrgang, 2001; Monticone et al., 2012; Vianin, 2008). This questionnaire has excellent test-retest reliability, responsiveness, and an estimated minimum level of important change of 30% (Fritz & Irrgang, 2001). The mODI has similar levels of test-test reliability and internal consistency (Fritz & Irrgang, 2001). Ostelo et al., reported that an improvement score of 30% from baseline is considered clinically meaningful improvement (Ostelo et al., 2008).

Data Analysis

All statistical analysis is performed using STATA/SE version 16.1 (StataCorp, College Station, TX). We generated descriptive statistics to summarise all baseline

demographic data. We constructed propensity score models using inverse-probability weights (IPW) for our exposure variables (opioids or neuroleptics), outcomes (leg pain, back pain, and disability), and regression adjustment to account for confounding due to age, sex, education level, smoking status, depression risk, and baseline pain or disability.

Propensity score–based analysis is increasingly being used in observational studies to estimate the effects of treatments, interventions, and exposures (Austin et al., 2021). IPW uses a logistic regression model to compare between groups.

Our propensity score analysis includes two separate models. The first is the propensity score model, the goal of which is to predict the propensity of treatment through a multinomial logistic regression given our dependant variable (medication use frequency). Secondly, the outcome model converts the propensity score to IPW and applies the weighting in a new linear regression model for our continuous variables (leg pain, back pain, mODI) to yield our average treatment effects (ATE). IPW regression adjustment is another use of propensity scores to adjust for confounding (Austin et al., 2021).

IPW creates weighted sample where treated and control cohorts will have the same distribution of covariates (Austin et al., 2021). This means the outcomes can be compared directly as confounding is removed through weighting.

For our outcomes, results are estimated through difference in means between the cohorts (Lunceford & Davidian, 2004). Following IPW models, we undertook two sets of balance diagnostics. We generated overlap plots for the propensity scores models and

histograms to check normality distribution for our linear regression models. All weighted standardized differences should be <0.1 and all weighted variance rations should be <2 and >0.5 (Austin et al., 2021). We presented a total of 36 models (3 time points: 3, 12-,24-months; 3 outcomes: back pain, leg pain, disability; 2 frequencies of use: daily and intermittent; 2 medications: narcotic and neuroleptics).

RESULTS

Data from 3,162 patients (mean age 55.9 [SD 15.0] years; 51.8% female) were analyzed. Preoperative demographic, health and clinical information are described in Table 1.

Back pain outcomes

At 3 months, patients who consumed opioids intermittently preoperatively had higher back pain intensity scores 0.24 [95%CI] = (0.01 to 0.48) and daily preoperative use had higher back pain intensity scores 0.20 [95%CI] = (0.004 to 0.40) than patients not consuming opioids. Patients who consumed opioids daily versus patients who did not consume opioids had a mean difference of 0.46 [95%CI] = (0.22 to 0.70) in back pain at 12 months. At 12 months, patients who consumed opioids intermittently had a mean difference of 0.32 [95%CI] = (0.06 to 0.60). At 24 months, the difference between patients that took opioids intermittently versus not taken was 0.42 [95%CI] = (0.12 to 0.73); daily versus not taken is found to be 0.55 [95%CI] = (0.27 to 0.83). Neuroleptics did not have a significant mean difference on any follow-up time points for back pain.

Leg pain outcomes

At 12 months follow-up, intermittent preoperative consumption of opioids had a mean difference of 0.32 [95% CI] = (0.005 to 0.64) (Figure 1). At 24 months, preoperative intermittent use yielded a mean difference of 0.36 [95% CI] = (0.02 to 0.71). Daily use did not yield a significant mean difference for leg pain at any time point. No significant mean difference was found at 3 months for patients who took opioids. Neuroleptics did not have a significant mean difference on any follow-up time points for leg pain.

Disability outcomes

At 3 months, patients who consumed preoperative narcotic drugs intermittently 2.17 [95% CI= (0.45 to 3.90)] reported higher ODI scores. At 12 months, the difference between patients that took opioids intermittently versus not taken is 2.98 [95% CI= (1.02 to 4.95)]; daily versus not taken is 2.36 [95% CI= (0.55 to 4.17)] (Figure 1). At 24 months, the difference between patients that took opioids intermittently versus not taken is 3.26 [95% CI = (1.07 to 5.45)]; daily versus not taken is 3.51 [95% CI = (1.46 to 5.56)]. Neuroleptics did not have a significant mean difference on any follow-up time points for disability.

DISCUSSION

Our aim was to estimate the effect of preoperative opioids and neuroleptics on postoperative leg pain, back pain, and disability. We found no effects of preoperative neuroleptic use on any outcome at 3-,12-, and 24 months. Patients who consumed opioids preoperatively whether daily or intermittently reported distinct levels of pain and disability postoperatively when compared with patients not consuming opioids. In all

cases, patients reported higher scores. However, the differences found are not clinically relevant.

The literature has established that neuroleptics and opioids in most cases increases negative outcomes. A systematic review and meta-analysis by Enke et al., reported that gapapentinoids can be ineffective and increase the risk of adverse events for treating low back pain or lumbar radicular pain (Enke et al., 2018). A randomised withdrawal trial by Baron et al., found that while most chronic lumbosacral radiculopathy patients responded pregabalin therapy, there was so significant difference between patients who took pregabalin and placebo in terms of time to loss of response. Loss of response was defined as a 1-point increase in pain or discontinuation of the study medication. Overall, evidence for the efficacy and safety of neuroleptics in the low back and lumbar radicular pain is unclear – the literature is limited to populations with chronic back pain (Baron et al., 2010; Enke et al., 2018).

Our results showed no significant mean differences for patients consuming neuroleptics versus patients not consuming neuroleptics preoperatively for leg pain, back pain, and disability for lumbar radiculopathy. This could be due to our ability to carefully account for confounding variables that may have not been otherwise accounted for in other studies.

For opioids, we found consumption at baseline had a significant effect on 3-,12-, and 24 months' leg pain, back pain, and disability outcomes. In a study by Gasser et al., the authors investigated the effects of preoperative opioid therapy in a group of 52 patients post spine surgery for lumbar radiculopathy (Gasser et al., 2022). Of which, 17 patients received opioid therapy preoperatively which was associated with lower low

back pain one week postoperatively and lower NRS leg pain scores at 12 months (Gasser et al., 2022). On the contrary, our study revealed patients who consume opioids preoperatively intermittently reported higher leg pain scores by 0.32 on the numeric rating scale than patients who did not consume opioids preoperatively and similarly for 24 months with a mean difference of 0.36, however, daily use did not show a significant mean difference. The mean differences are trivial and do not reach MCIC. Further, the conflicting results could occur due to several reasons. Lower pain scores at follow-up could be due to patients experiencing opioid-induced hyperalgesia. However, this study included a small sample size of only 17 patients consuming preoperative opioids, making the conclusion of this study difficult to apply in clinical decision making. Additionally, the cohort of patients were not equally matched nor were baseline health characteristics accounted for between the non-opioid and opioid group.

Virk et al., (2020) indicate that patients taking opioids and have a clinical exam/imaging consistent with lumbar radiculopathy will have equivalent postoperative outcomes as compared to patients that arrive to their preoperative visit without taking opioids after a lumbar microdiscectomy (Virk et al., 2020). There were no significant differences between the opioid-using cohort and the non-opioid-using cohort in patient-reported outcomes mental health scores, patient-reported outcomes physical health scores, and ODI between 4 weeks, 3 months, 6 months, and 12 month follow up (Virk et al., 2020). However, intervention was specifically lumbar microdiscectomy which is not very invasive and thus opioids have minor impact on postoperative outcomes.

A study conducted by Armaghani et al. featured a prospective cohort of 583 patients undergoing spine surgery in which preoperative opioid use was associated with

increased postoperative opioid demand as well as decreased incidence of opioid independence at 12 months postoperatively; however, immediate postoperative opioid demand was not significantly affected (Armaghani et al., 2014). Opioid-induced hyperalgesia is well documented in the literature and may explain the current study results. While the precise molecular mechanism is unknown, various mechanisms have been proposed to explain the clinical outcomes featured in patients. In a review conducted by Lee et al., observations in perioperative exposure to opioids provided mixed support in the development of opioid-induced hyperalgesia (Lee et al., 2011). Although it is a less recognized consequence of chronic opioid therapy, it should be included in the differential diagnosis in whose refractory to their current regiment (Lee et al., 2011).

Our findings conflict with the literature, however, we believe due to control of confounding variables that are involved in opioid use such age, sex, education level, smoking status, depression risk, and the correspondent baseline pain or disability. Our results may provide a more informative reason of why the classes of medications described in this study may not be as alarming, however, in conjunction with other factors it could be.

Clinical Implications

Patients suffering from pain postoperatively are often taking medications to relieve their pain. However, medications may have little to no effect on their outcomes (Warner et al., 2020). There remains plenty of valid reasons for clinicians to be hesitant about prescribing the classes described in this study for patients undergoing spine surgery for radiculopathy as described above. Patients may become dependent on

consuming opioids for pain contributing to opioid-induced hyperalgesia leading to addiction. Long-term use of opioids for back pain may also lead to reduced quality of life though sleep problems, immunosuppression, bowel obstruction, depression, and myocardial infarction (Deyo et al., 2015). Our study gives an indication to clinicians that prescribing either of those medications is not as alarming for post-operative pain and disability but is warranted for review.

Research Implications

Our study contributes to the current literature with respect to the effect of opioids and neuroleptics on back pain, leg pain and disability outcomes. The statistical analysis used in this study controlled for confounding variables, hence, future research should aim to undertake a randomized clinical trial to investigate and understand the effects of the class of medications described in this study to establish treatment effects.

Strengths and Limitations

The primary strengths of this study include the large sample of patients undergoing spine surgery across Canada. In addition, we used propensity score modeling through doubly robust estimation for confounding variables (Funk et al., 2011). Some of our limitations are the standardized medication collection are self-reported. Self-reported collection can cause social desirability bias where patients may answer incorrectly to not reveal private details or exaggerate their responses. Thus, we do not have an accurate way to audit whether patients were disclosing their medication usage (none, intermittent, or daily) correctly. Another limitation is any unmeasured confounding variables that may serve as a source of bias. This can be addressed through randomized controlled trials. We also acknowledge that the use of secondary data may lack specific answers to

a proposed question and that we have no control over the data quality. However, we believe we have catered the data to answer our question and ensured the data is in sufficient quality to be used.

CONCLUSION

In this study, we identified leg pain, back pain, and pain-related disability outcomes of patients on opioids and neuroleptics 3-, 12-, and 24 months postoperatively. Preoperative opioids had a small adverse effect on intermediate- and long-term clinical outcomes following lumbar spine surgery for radiculopathy. Preoperative neuroleptics did not affect postoperative outcomes. Although the decision-making around the prescription of these medications is complex, our study results show that preoperative opioids and neuroleptics did not have a clinically important improvement for postoperative levels of pain or disability up to 24 months post operatively. Our results are informative for future studies aiming to investigate the effect of medications for patients undergoing spine surgery for lumbar radiculopathy.

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Figures

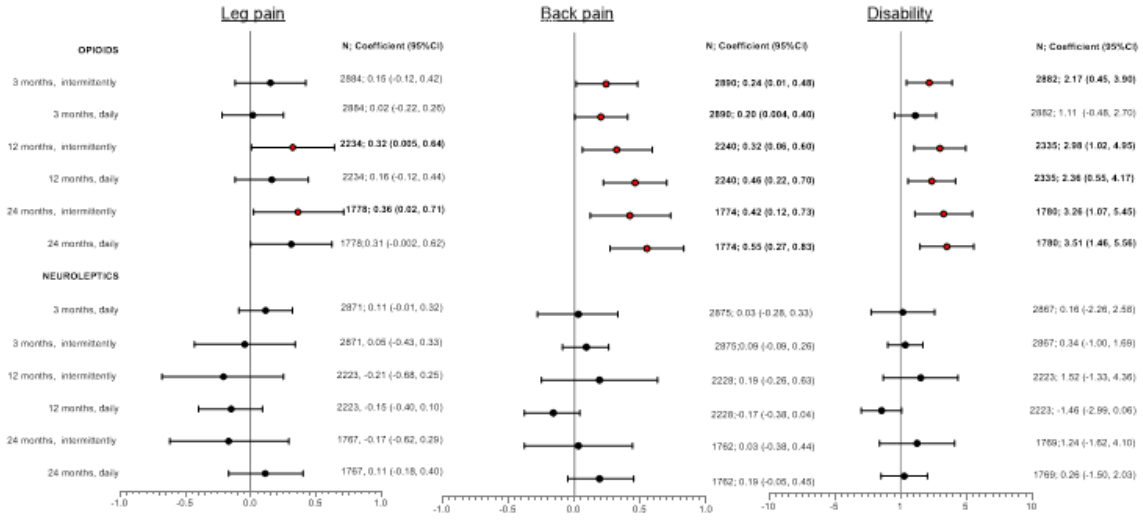


Figure 1: Forest plot showing narcotic and neuroleptic users at follow-up time points for leg pain, back pain, and back-related disability. Red symbols denote worsening effect of usage versus none while adjusting for confounding variables: age, sex, education level, smoking status, depression risk, and baseline pain or disability.

Tables

Table 1: Descriptive preoperative characteristics and surgical details in patients who underwent spine surgery for lumbar radiculopathy.

Variable	Narcotic						Neuroleptic					
	Daily		Intermittent		None		Daily		Intermittent		None	
	Sample	Value	Sample	Value	Sample	Value	Sample	Value	Sample	Value	Sample	Value
Age, yrs	1094	55.1±14.8	740	52.8±14.6	1279	58.2±15.0	1448	57.7±14.8	272	51.7±15.1	1380	54.6±14.9
Female sex	577	35%	387	24%	646	40%	760	46%	121	7%	720	44%
Education												
High school degree or less	434	37%	258	22%	451	39%	473	41%	95	8%	566	49%
Technical/associate degree	218	35%	142	23%	245	40%	279	45%	59	10%	271	44%
Undergraduate/graduate degree	442	32%	310	22%	583	42%	628	45%	118	9%	611	44%
Body mass index												
Underweight	7	32%	3	14%	12	54%	8	38%	2	10%	11	52%
Normal weight	271	34%	181	23%	338	42%	326	42%	76	10%	378	48%
Overweight	383	32%	278	24%	497	42%	505	44%	103	9%	550	47%
Obese	410	38%	255	24%	397	37%	507	48%	85	8%	468	44%
Current smoking	260	24%	139	19%	163	13%	249	45%	48	9%	255	46%
Complaint duration												
≤1 yr	363	41%	218	25%	303	34%	363	41%	218	25%	303	34%
>1–2 yrs	181	34%	116	21%	240	45%	181	34%	116	22%	240	45%
>2 yrs	545	33%	406	24%	728	43%	545	32%	406	24%	728	43%
Medication use	1094	35%	740	24%	1279	41%	1380	44%	272	9%	1448	47%

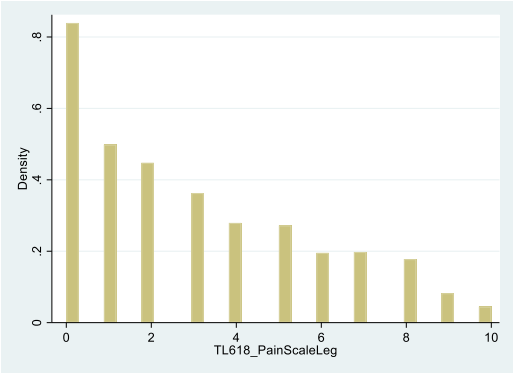
Appendices

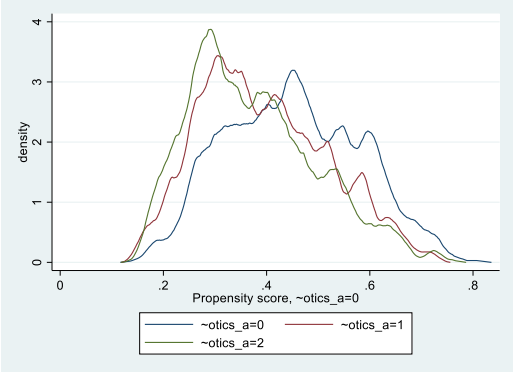
The tables below are two sets of balance diagnostics. The overlap plots for the PS (Propensity Score) models and histograms are to check normality distribution for our linear regression models. The tables are showing how fit the models are. All weighted standardized differences should be <0.1 and all weighted variance rations should be <2 and >0.5. There are a total of 36 models (3, 12-,24-months; back pain, leg pain, disability; narcotic and neuroleptics).

Opioids at 3 months

- **Leg pain**

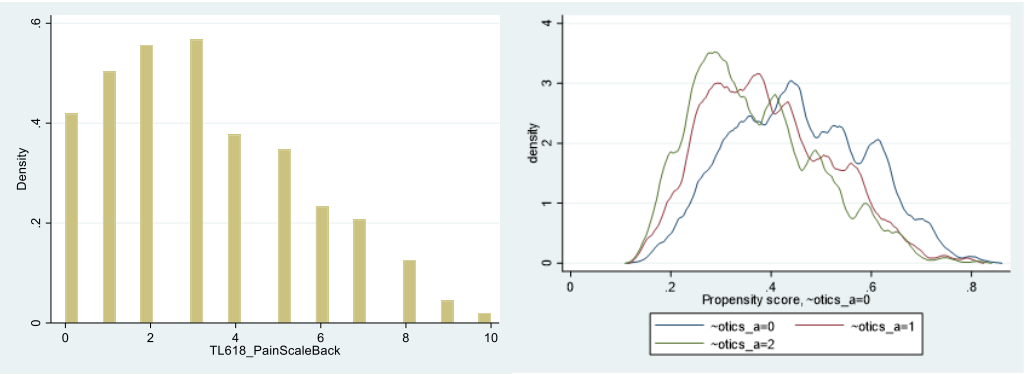
	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~otics_a				
X_AgeCalc	-.3861636	-.0124958	.9588445	.9956481
X_AgeCalc#				
X_AgeCalc	-.4042653	-.0135085	.8751553	1.017659
sex_var	-.0411218	.0065151	.9968206	1.00078
edu	.0084521	.0008741	.9833489	1.047986
TLsmoke_Cat	.2039252	-.0053799	1.511096	1.023997
TL_PHQ9Score	.3430849	-.0005282	1.052373	.9867814
TL_PHQ9Score#				
TL_PHQ9Score	.3001669	-.0039709	1.223213	.9494973
TL_PainScaleLeg	.0428547	.0002328	.8758809	.9244501
2.TL_Me~otics_a				
X_AgeCalc	-.2176338	.0017357	.9912144	1.001707
X_AgeCalc#				
X_AgeCalc	-.2267153	.0020219	.9747247	1.046308
sex_var	-.043966	-.0043172	.9959817	.9994308
edu	-.1356548	.0100352	1.043783	1.052503
TLsmoke_Cat	.2828252	.0044324	1.580955	.9756065
TL_PHQ9Score	.5490197	.0087289	1.120064	.9932535
TL_PHQ9Score#				
TL_PHQ9Score	.4960492	.0056986	1.526572	.9922959
TL_PainScaleLeg	.3008044	-.0179212	.8968892	1.292818





- **Back pain**

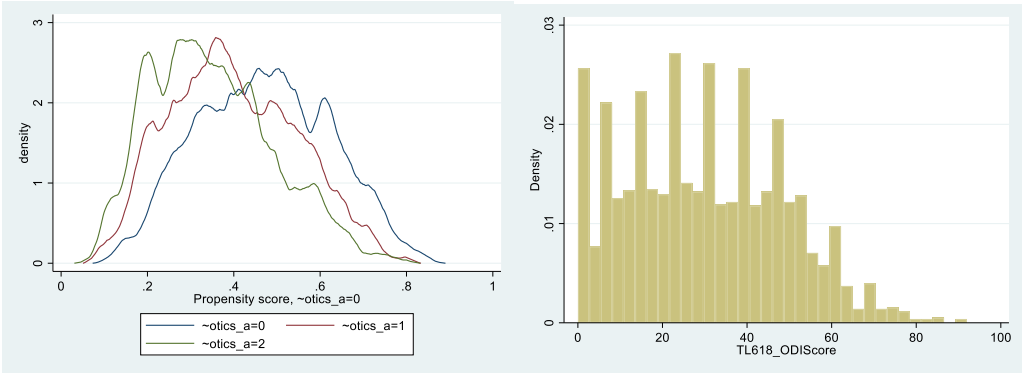
	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~otics_a				
X_AgeCalc	-.3887198	-.0071131	.9553323	.9930809
X_AgeCalc#				
X_AgeCalc	-.4072539	-.008301	.8704632	1.014658
sex_var	-.0401101	.0078275	.9972278	1.000967
edu	.0046365	.0081625	.9842012	1.043675
TLsmoke_Cat	.2013133	-.0045643	1.50293	1.025838
TL_PHQ9Score	.3429253	-.0048387	1.052757	.984147
TL_PHQ9Score#				
TL_PHQ9Score	.2996571	-.0083636	1.225752	.9455408
TL_PainScaleB~k	.0978454	-.0014206	.8694971	.9739505
2.TL_Me~otics_a				
X_AgeCalc	-.2168186	-.0009703	.9923287	.9950994
X_AgeCalc#				
X_AgeCalc	-.2256605	-.0016723	.9755782	1.036128
sex_var	-.052132	.0005706	.9951403	1.000065
edu	-.1431235	.0136964	1.048234	1.054388
TLsmoke_Cat	.2815934	-.002052	1.575765	.9718376
TL_PHQ9Score	.5538468	.003946	1.126424	.9805933
TL_PHQ9Score#				
TL_PHQ9Score	.5010369	-.0017455	1.543034	.9775812
TL_PainScaleB~k	.4254185	-.0353822	.8208396	1.27246


Density
0
.2
.4
.6
0
2
4
6
8
10
TL618_PainScaleBack
density
0
1
2
3
4
0
.2
.4
.6
.8
Propensity score, ~otics_a=0
~otics_a=0
~otics_a=1
~otics_a=2

- **ODI**

	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~otics_a				
X_AgeCalc	-.3885301	-.0299817	.961226	1.004698
X_AgeCalc#				
X_AgeCalc	-.4062758	-.0302785	.8773742	1.017348
sex_var	-.037065	.0115895	.9971554	1.001423
edu	.0009142	-.0094694	.9820881	1.043921
TLsmoke_Cat	.2016269	.006801	1.492466	1.043759
TL_PHQ9Score	.3475797	-.0074635	1.061022	.9825182
TL_PHQ9Score#				
TL_PHQ9Score	.3060912	-.0110516	1.24082	.9408602
TL_ODIScore	.287102	.0097391	1.017382	1.033327
2.TL_Me~otics_a				
X_AgeCalc	-.2235955	-.0146298	.9981526	1.010014
X_AgeCalc#				
X_AgeCalc	-.2316585	-.0136518	.9835793	1.051261
sex_var	-.0417268	.0033926	.9960815	1.000457
edu	-.136068	.0055587	1.043428	1.047132
TLsmoke_Cat	.2791785	.0180129	1.56316	.9927145
TL_PHQ9Score	.5530783	.0192366	1.12199	.9822557
TL_PHQ9Score#				
TL_PHQ9Score	.4997364	.0118409	1.536864	.9852466
TL_ODIScore	.7784445	.0395931	.9470251	.9180885

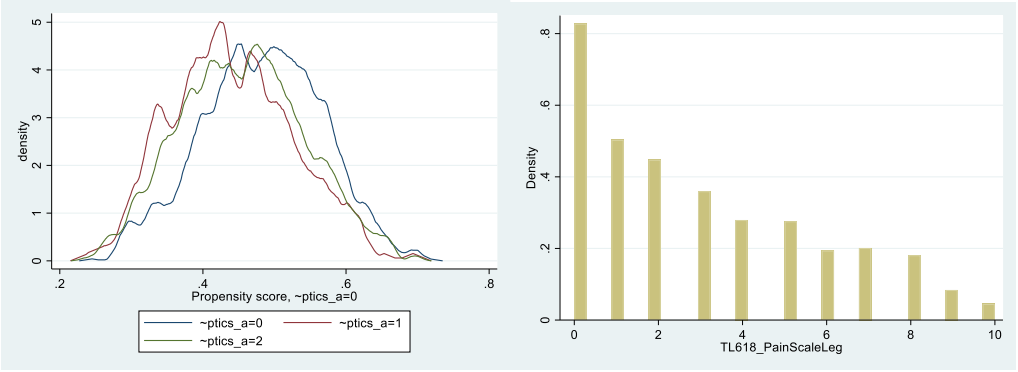
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Neuroleptics at 3 Months

- **Leg pain**

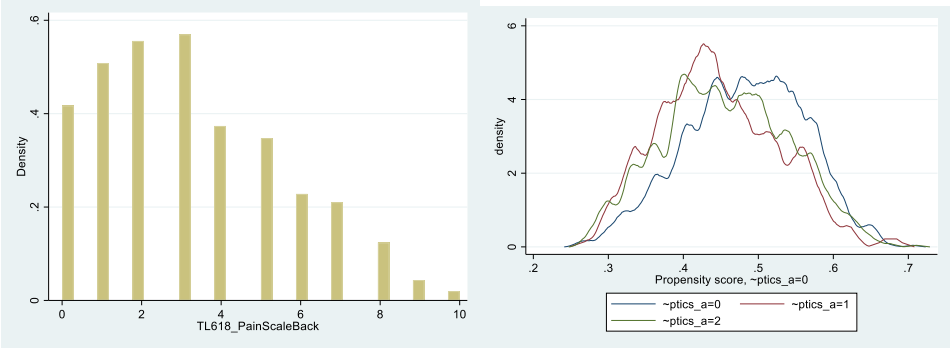
	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~ptics_a				
X_AgeCalc	-.4175836	.0369979	1.03904	1.02274
X_AgeCalc#				
X_AgeCalc	-.4221828	.0410228	.9069112	1.069256
sex_var	.1020839	-.0438559	.9945411	.9937916
edu	.0670973	-.0020191	.8776259	.9479825
TLsmoke_Cat	-.0033599	-.0139377	.9953365	.993736
TL_PHQ9Score	.3335098	-.0312059	1.10183	.9997348
TL_PHQ9Score#				
TL_PHQ9Score	.3117188	-.026585	1.30802	.9620221
TL_PainScaleLeg	.2271916	-.0007186	.6452069	.7802329
2.TL_Me~ptics_a				
X_AgeCalc	-.2000591	.000857	.9869553	1.000042
X_AgeCalc#				
X_AgeCalc	-.2079236	.0008871	.943639	1.015031
sex_var	-.1147713	.001157	.9849072	1.00011
edu	.0545689	.004539	.9334567	.9604675
TLsmoke_Cat	.015459	.000092	1.035968	1.014748
TL_PHQ9Score	.2426477	-.0008699	1.122729	.9978458
TL_PHQ9Score#				
TL_PHQ9Score	.2377637	-.001319	1.249246	.9593885
TL_PainScaleLeg	.1226614	-.0004712	.8021059	.9090179



- **Back pain**

	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~ptics_a				
X_AgeCalc	-.4222733	.0294696	1.03588	1.017852
X_AgeCalc#				
X_AgeCalc	-.4273299	.0326402	.9035621	1.062105
sex_var	.1121036	-.0391582	.9930799	.9947125
edu	.07089	-.0131607	.8759112	.9444219
TLsmoke_Cat	.0045942	-.0013423	1.014982	1.016863
TL_PHQ9Score	.3237717	-.0238681	1.104327	.9910602
TL_PHQ9Score#				
TL_PHQ9Score	.3033503	-.0226388	1.306314	.9688015
TL_PainScaleB~k	.0688889	.0066135	.8466009	.8581002
2.TL_Me~ptics_a				
X_AgeCalc	-.2003895	.0025337	.9901494	.9975032
X_AgeCalc#				
X_AgeCalc	-.2077782	.0022605	.9485165	1.015079
sex_var	-.108489	.0033601	.9859281	1.000308
edu	.0568916	.0032118	.935268	.9630154
TLsmoke_Cat	.0175213	.0004182	1.039464	1.01238
TL_PHQ9Score	.2409337	-.0012975	1.121876	1.000196
TL_PHQ9Score#				
TL_PHQ9Score	.2358346	-.0010595	1.250285	.9679606
TL_PainScaleB~k	-.0190345	.0074346	1.071094	1.037935

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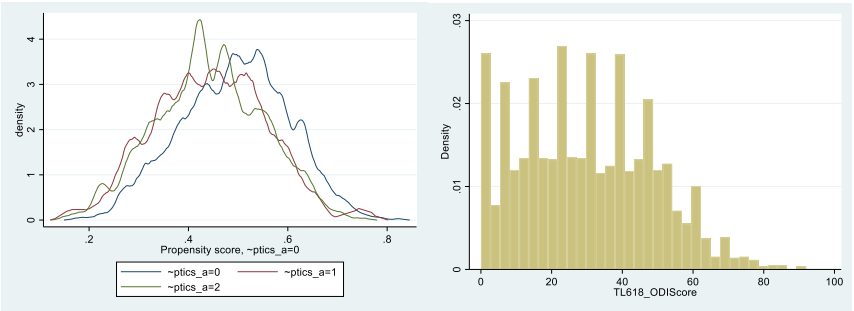


- **ODI**

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	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~ptics_a				
X_AgeCalc	-.4127768	.0261784	1.037554	1.035014
X_AgeCalc#				
X_AgeCalc	-.4175433	.0315629	.9070501	1.072774
sex_var	.1108728	-.0444017	.9939796	.9934651
edu	.0672131	-.00444	.8709853	.9273325
TLsmoke_Cat	.0006793	-.002866	1.001384	1.009399
TL_PHQ9Score	.3309582	-.0180747	1.117157	1.010095
TL_PHQ9Score#				
TL_PHQ9Score	.3128703	-.012717	1.329039	.9842422
TL_ODIScore	.2768938	-.0402754	1.058227	1.02674
2.TL_Me~ptics_a				
X_AgeCalc	-.1982853	-.0037584	.9933754	1.000417
X_AgeCalc#				
X_AgeCalc	-.204998	-.0038028	.9544437	1.011654
sex_var	-.1049293	.0008172	.9861231	1.000086
edu	.0558284	.0056067	.9307708	.9507266
TLsmoke_Cat	.0132166	.000134	1.030737	1.013149
TL_PHQ9Score	.2480422	.0057947	1.126445	1.002272
TL_PHQ9Score#				
TL_PHQ9Score	.2430244	.0055777	1.265695	.9657414
TL_ODIScore	.4062011	.0072478	.9172158	.8687199

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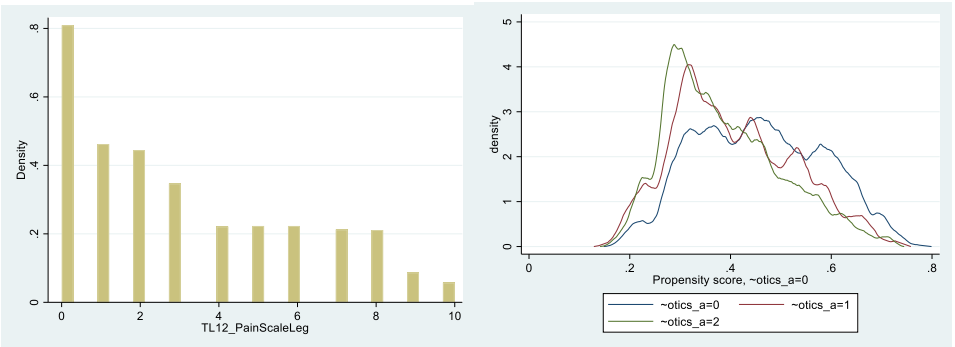


Opioids at 12 months

- **Leg pain**

	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~otics_a				
X_AgeCalc	-.3102501	-.0031645	1.006602	.9986393
X_AgeCalc#				
X_AgeCalc	-.319994	-.0034534	.9496339	1.040662
sex_var	-.0696732	.0056765	.9928509	1.000668
edu	.0287467	.0076475	.9663652	1.018476
TLsmoke_Cat	.1670664	-.017801	1.381923	.965004
TL_PHQ9Score	.3609204	-.0014575	1.02514	1.0046
TL_PHQ9Score#				
TL_PHQ9Score	.3059812	-.0000237	1.205675	1.001121
TL_PainScaleLeg	.0250371	-.0088895	.8967249	.9246939
2.TL_Me~otics_a				
X_AgeCalc	-.179835	-.0030134	1.03527	.993354
X_AgeCalc#				
X_AgeCalc	-.181589	-.0040084	1.039193	1.044254
sex_var	-.0275087	-.0028249	.9982595	.9996457
edu	-.142957	.0102737	1.077921	1.069907
TLsmoke_Cat	.2534536	.0119958	1.528085	.9747013
TL_PHQ9Score	.5237585	.0076473	1.090113	1.000346
TL_PHQ9Score#				
TL_PHQ9Score	.4639453	.0066217	1.450151	1.011607
TL_PainScaleLeg	.2746574	-.018448	.9354655	1.283779

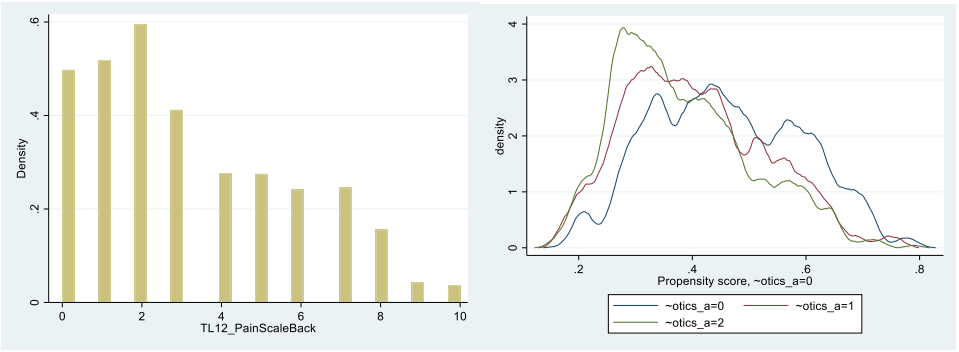
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- **Back pain**

	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~otics_a				
X_AgeCalc	-.3152115	-.0015223	.9971878	.9937445
X_AgeCalc#				
X_AgeCalc	-.3260691	-.0024202	.9366208	1.032962
sex_var	-.0634696	.0053145	.9934256	1.000672
edu	.0226394	.0101091	.9715346	1.024021
TLsmoke_Cat	.1780188	-.0161585	1.410652	.961458
TL_PHQ9Score	.3667986	-.0039354	1.027127	1.001084
TL_PHQ9Score#				
TL_PHQ9Score	.3106808	-.0030595	1.211392	.9907091
TL_PainScaleB~k	.1137975	-.0077629	.840291	.9439509
2.TL_Me~otics_a				
X_AgeCalc	-.1762217	-.0065447	1.038316	.9916631
X_AgeCalc#				
X_AgeCalc	-.1773946	-.0078696	1.03967	1.037145
sex_var	-.0272324	-.0019423	.9980638	.9997331
edu	-.1445274	.0164615	1.077954	1.070619
TLsmoke_Cat	.25853	.0028184	1.548631	.9639565
TL_PHQ9Score	.5299269	.004389	1.098682	.9872872
TL_PHQ9Score#				
TL_PHQ9Score	.4706633	.0003588	1.460253	.9905209
TL_PainScaleB~k	.3763508	-.032085	.8737046	1.288456

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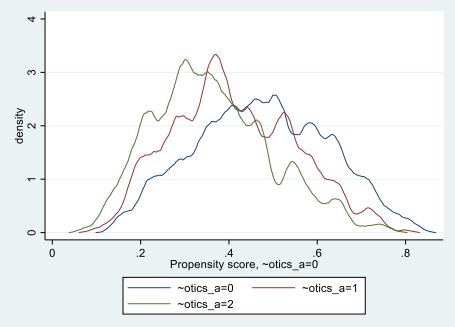


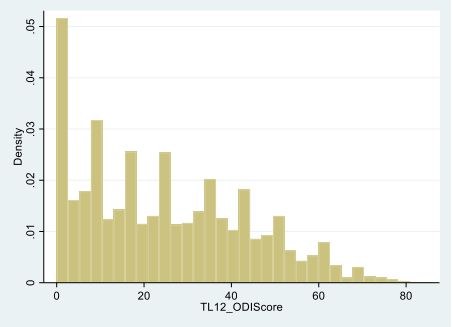
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- **ODI**

	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~otics_a				
X_AgeCalc	-.3263554	-.0174262	1.005032	1.014303
X_AgeCalc#				
X_AgeCalc	-.3367215	-.0160658	.9425422	1.05111
sex_var	-.0665574	.0091827	.9919981	1.001271
edu	.0284694	-.0025886	.9743388	1.038501
TLsmoke_Cat	.1688345	-.0178882	1.381694	.9557273
TL_PHQ9Score	.3536437	-.0201387	1.028732	.9841739
TL_PHQ9Score#				
TL_PHQ9Score	.301135	-.0214418	1.201778	.9561209
TL_ODIScore	.2687794	-.0118497	.9101582	.9170811
2.TL_Me~otics_a				
X_AgeCalc	-.1926458	-.0042764	1.040893	1.013161
X_AgeCalc#				
X_AgeCalc	-.1941569	-.0026547	1.038261	1.061226
sex_var	-.0154831	-.0113578	.9989827	.9982316
edu	-.139866	.0134335	1.076505	1.070948
TLsmoke_Cat	.2591921	.0097776	1.540528	.9674312
TL_PHQ9Score	.5215734	.009542	1.085075	.9846391
TL_PHQ9Score#				
TL_PHQ9Score	.4619959	.0040758	1.434186	.9801047
TL_ODIScore	.7462805	.0331853	.8848288	.8079833

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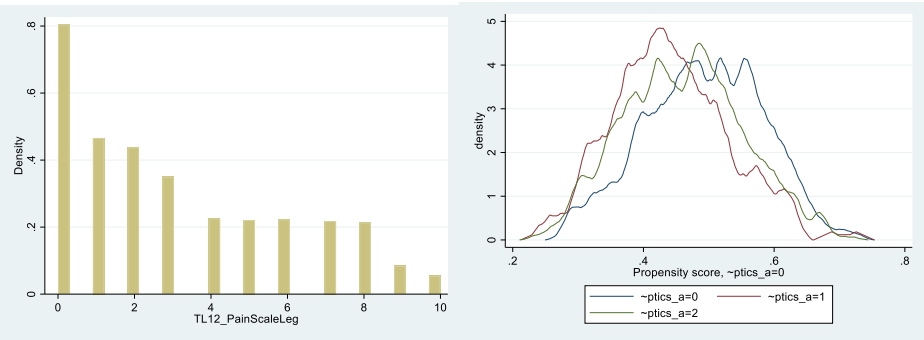


Neuroleptics at 12 months

- **Leg pain**

	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~ptics_a				
X_AgeCalc	-.4673834	.0289362	1.039146	1.089696
X_AgeCalc#				
X_AgeCalc	-.4724571	.0411297	.9173799	1.187608
sex_var	.0798261	-.0390885	1.000711	.9950671
edu	.0802148	-.0253952	.8692272	.9495774
TLsmoke_Cat	.0200327	-.0267524	1.046336	.960352
TL_PHQ9Score	.3801747	-.0090122	1.098111	.9655853
TL_PHQ9Score#				
TL_PHQ9Score	.3465702	-.0168296	1.348746	.9390629
TL_PainScaleLeg	.2321629	.0081833	.6519352	.7489159
2.TL_Me~ptics_a				
X_AgeCalc	-.2330022	.0009193	.9984871	.9960863
X_AgeCalc#				
X_AgeCalc	-.2408061	.0004175	.9552903	1.022243
sex_var	-.0807162	-.0009966	.9906849	.9999112
edu	.0736024	.0034959	.9585289	.9919744
TLsmoke_Cat	.0431343	.0010112	1.096742	1.020622
TL_PHQ9Score	.2544965	-.0040986	1.132642	1.00057
TL_PHQ9Score#				
TL_PHQ9Score	.2489996	-.0033507	1.230751	.9348715
TL_PainScaleLeg	.1218379	.0007128	.8402358	.9556718

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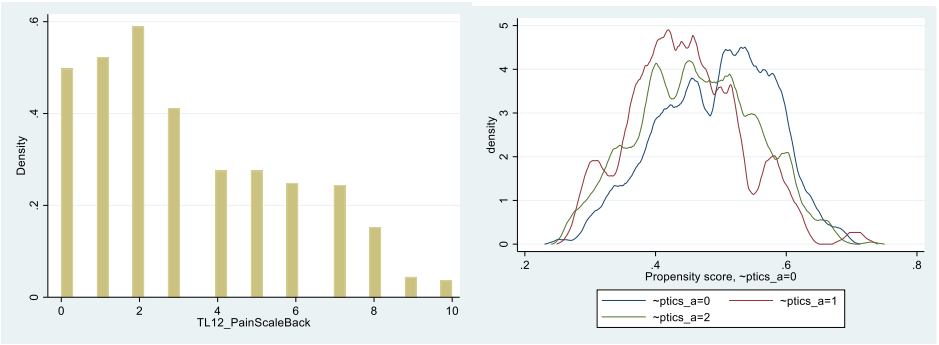
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- **Back pain**

	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~ptics_a				
X_AgeCalc	-.4747448	.019071	1.03882	1.089369
X_AgeCalc#				
X_AgeCalc	-.4795645	.0310643	.9154969	1.185247
sex_var	.0918631	-.0408606	1.000305	.9946613
edu	.0833961	-.0221166	.8726402	.9572224
TLsmoke_Cat	.0197686	-.0131926	1.054646	.9938189
TL_PHQ9Score	.3789085	.0061148	1.103737	.9735366
TL_PHQ9Score#				
TL_PHQ9Score	.3460739	-.0018763	1.35978	.9669689
TL_PainScaleB~k	.0043283	.0205219	.9214033	.8798163
2.TL_Me~ptics_a				
X_AgeCalc	-.2253727	.0038549	1.006289	.9922392
X_AgeCalc#				
X_AgeCalc	-.2317994	.0029145	.9666264	1.021796
sex_var	-.0730563	.0001611	.9911841	1.000012
edu	.0726143	.0031454	.9586021	.9894894
TLsmoke_Cat	.0410586	.0010487	1.096633	1.02166
TL_PHQ9Score	.2559682	-.0034744	1.136537	1.003252
TL_PHQ9Score#				
TL_PHQ9Score	.2509107	-.002095	1.23778	.9432723
TL_PainScaleB~k	-.028754	.0052688	1.122846	1.077585

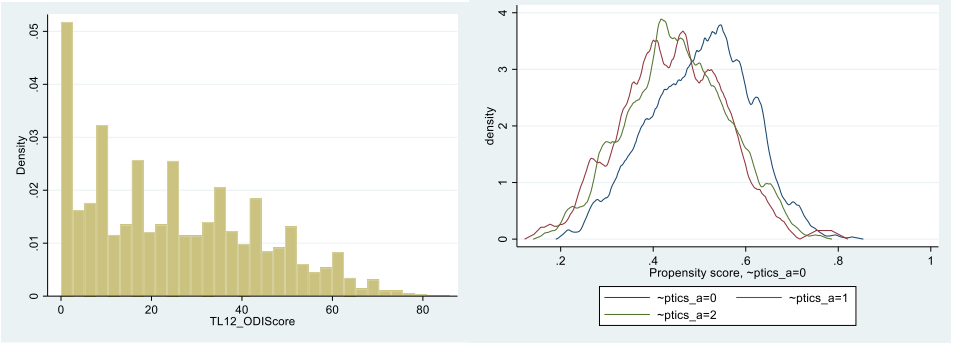
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- **ODI**

	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~ptics_a				
X_AgeCalc	-.463161	.0141423	1.042668	1.098083
X_AgeCalc#				
X_AgeCalc	-.4679493	.0271087	.9195981	1.186411
sex_var	.0815695	-.0443493	1.001601	.9931889
edu	.0847817	-.0270598	.8714227	.9368758
TLsmoke_Cat	.0006931	-.0128433	1.009099	.9868247
TL_PHQ9Score	.3729966	.0085775	1.094223	.9760428
TL_PHQ9Score#				
TL_PHQ9Score	.339512	.0009093	1.350184	.9642183
TL_ODIScore	.3003076	-.0141816	1.101482	1.067459
2.TL_Me~ptics_a				
X_AgeCalc	-.2239594	-.0017189	1.004677	.9940407
X_AgeCalc#				
X_AgeCalc	-.2305652	-.0025768	.9659903	1.016213
sex_var	-.078228	.0025364	.9901382	1.000272
edu	.0742335	.0030665	.9500243	.9780191
TLsmoke_Cat	.0366042	.0003128	1.081274	1.015771
TL_PHQ9Score	.2555417	-.0005493	1.133582	1.003733
TL_PHQ9Score#				
TL_PHQ9Score	.2507018	.0005281	1.237087	.9356559
TL_ODIScore	.3765952	.0063871	.9266291	.8812806

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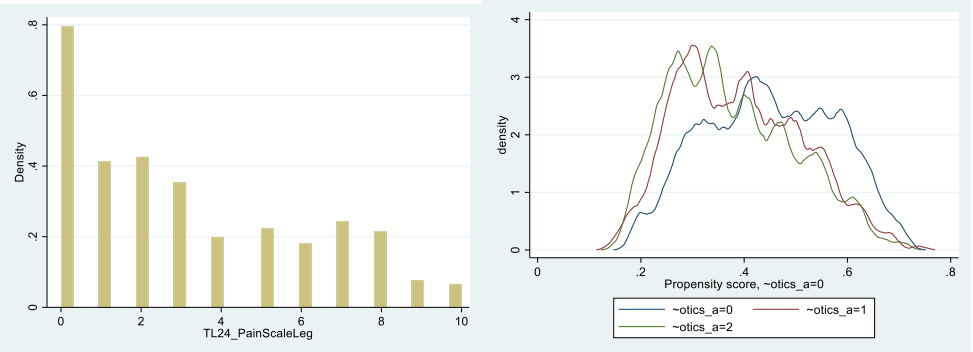
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Opioids at 24 months

- **Leg pain**

	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~otics_a				
X_AgeCalc	-.3624737	.0013731	.9899788	1.008859
X_AgeCalc#				
X_AgeCalc	-.3756787	.0026011	.9168763	1.054039
sex_var	-.0067818	.0057423	1.000049	1.000649
edu	-.0045721	.0007083	1.022548	1.080834
TLsmoke_Cat	.1573147	-.0040432	1.394086	1.001597
TL_PHQ9Score	.3954297	.0081416	1.067829	1.023033
TL_PHQ9Score#				
TL_PHQ9Score	.3478647	.0130268	1.278822	1.015065
TL_PainScaleLeg	-.0202884	-.016627	.910179	.9158592
2.TL_Me~otics_a				
X_AgeCalc	-.14464	-.0039625	1.008562	.9873234
X_AgeCalc#				
X_AgeCalc	-.1489924	-.0057857	1.024713	1.03298
sex_var	.0425453	.0020915	1.003494	1.000246
edu	-.1222857	.0077236	1.014026	1.015828
TLsmoke_Cat	.2177199	.0077209	1.501962	1.000632
TL_PHQ9Score	.5689617	.0088389	1.186336	.9963035
TL_PHQ9Score#				
TL_PHQ9Score	.5200159	.0065542	1.694564	1.023587
TL_PainScaleLeg	.2244263	-.0100088	.9776692	1.248377

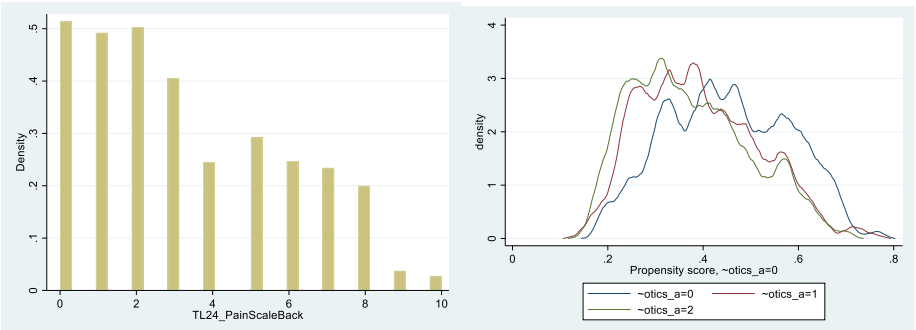
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- **Back pain**

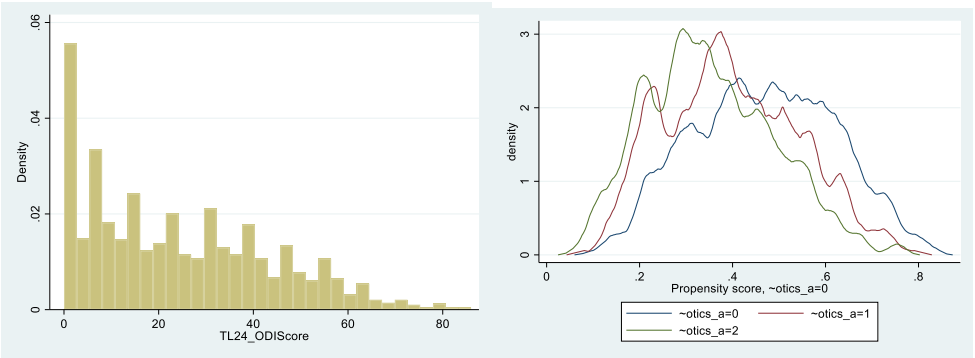
	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~otics_a				
X_AgeCalc	-.3634152	.0008258	.989569	1.004639
X_AgeCalc#				
X_AgeCalc	-.3765701	.0014724	.9179561	1.049455
sex_var	-.0020792	-.0032246	1.000643	.9996243
edu	-.0010994	.0094688	1.025265	1.081701
TLsmoke_Cat	.1562608	-.0073183	1.390836	.9983534
TL_PHQ9Score	.3918084	.0025051	1.064526	1.013911
TL_PHQ9Score#				
TL_PHQ9Score	.3435807	.0057988	1.275197	.9968691
TL_PainScaleB~k	.0754992	-.0222614	.8251898	.8979251
2.TL_Me~otics_a				
X_AgeCalc	-.142022	-.0090192	1.01496	.9811056
X_AgeCalc#				
X_AgeCalc	-.1454233	-.0118377	1.033577	1.021595
sex_var	.0393537	.0043646	1.003393	1.000467
edu	-.1152755	.0149827	1.021418	1.028598
TLsmoke_Cat	.2183687	.0009511	1.502091	.9974925
TL_PHQ9Score	.5665921	.0076333	1.183071	.9856625
TL_PHQ9Score#				
TL_PHQ9Score	.517122	.0027219	1.688093	1.012181
TL_PainScaleB~k	.3602123	-.0238535	.8414615	1.180416

-



- **ODI**

	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~otics_a				
X_AgeCalc	-.3586652	-.0162986	.9876418	1.005027
X_AgeCalc#				
X_AgeCalc	-.3721758	-.0161271	.9160021	1.040208
sex_var	.0035875	.0032008	1.001321	1.000333
edu	-.0127326	-.0178507	1.032777	1.08708
TLsmoke_Cat	.159984	.0012461	1.395492	1.006918
TL_PHQ9Score	.3852487	-.0010812	1.062897	1.022341
TL_PHQ9Score#				
TL_PHQ9Score	.3384316	.004896	1.270257	1.003161
TL_ODIScore	.3146305	-.0247265	.9166848	.9009934
2.TL_Me~otics_a				
X_AgeCalc	-.1468089	-.0189183	1.010062	.9988998
X_AgeCalc#				
X_AgeCalc	-.1510986	-.019621	1.024283	1.038291
sex_var	.0455052	.0022949	1.003701	1.000276
edu	-.1291775	-.0058539	1.027994	1.01256
TLsmoke_Cat	.2090969	.0119308	1.483163	1.007093
TL_PHQ9Score	.5659369	.0223695	1.18185	.9989749
TL_PHQ9Score#				
TL_PHQ9Score	.518174	.0188276	1.683162	1.02547
TL_ODIScore	.7656427	.0363757	.8945898	.7945137

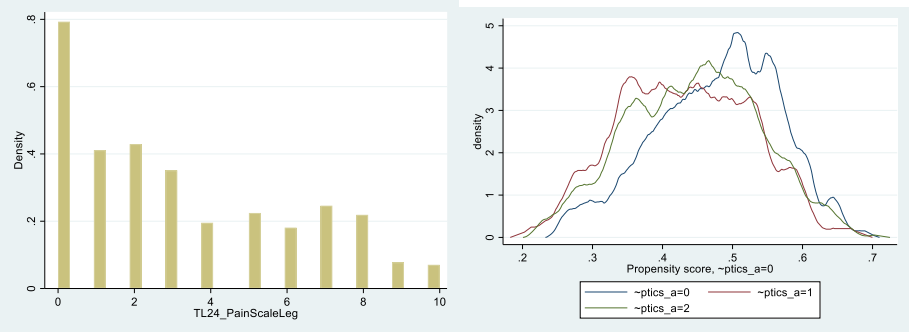


Neuroleptics at 24 months

- **Leg pain**

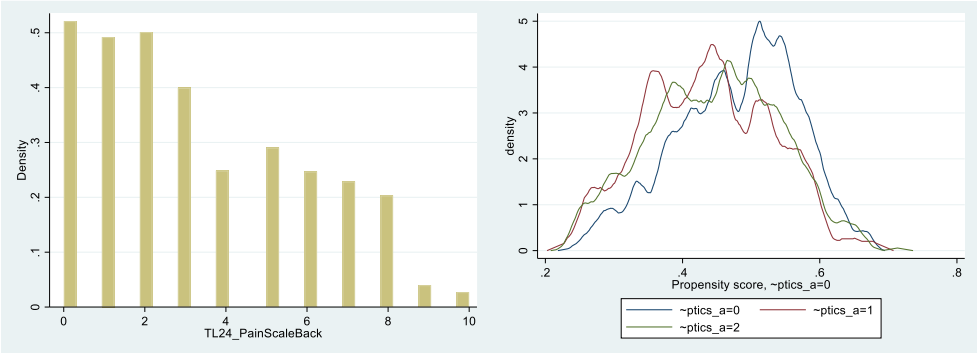
	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~ptics_a				
X_AgeCalc	-.4243614	.0166772	1.075075	.9911966
X_AgeCalc#				
X_AgeCalc	-.4282391	.0160878	.9314048	1.009664
sex_var	.0497073	.0093451	1.002937	1.000549
edu	.0630127	-.0154959	.8948866	.9802788
TLsmoke_Cat	.0372928	-.0262889	1.041652	.9092375
TL_PHQ9Score	.3683254	-.0070035	1.119781	.9524746
TL_PHQ9Score#				
TL_PHQ9Score	.3429756	-.0186909	1.350631	.9347391
TL_PainScaleLeg	.2386849	-.0137007	.7411534	.8927915
2.TL_Me~ptics_a				
X_AgeCalc	-.2019671	-.0010657	1.005996	.9977966
X_AgeCalc#				
X_AgeCalc	-.2077183	-.0013917	.9760719	1.027718
sex_var	-.0858266	-.0065125	.9908136	.9995044
edu	.0738304	.0064005	.9370346	.9757196
TLsmoke_Cat	-.0121157	.0011978	.9491445	.9770911
TL_PHQ9Score	.296449	-.0038718	1.159094	1.001137
TL_PHQ9Score#				
TL_PHQ9Score	.2885443	-.0029947	1.360886	.9869527
TL_PainScaleLeg	.0777258	.0011763	.9283839	.9956413

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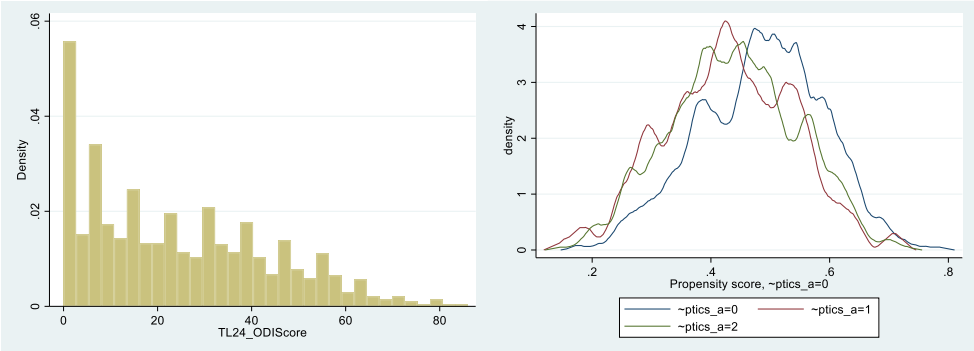
- **Back pain**

	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~ptics_a				
X_AgeCalc	-.4292761	.0034383	1.076364	.9976511
X_AgeCalc#				
X_AgeCalc	-.4328154	.0032359	.9326672	1.018801
sex_var	.0554765	-.0007793	1.002486	.999944
edu	.0687804	-.0185163	.8985629	.9877476
TLsmoke_Cat	.0349325	-.0061779	1.046472	.9592355
TL_PHQ9Score	.3651207	.0001948	1.122191	.9553724
TL_PHQ9Score#				
TL_PHQ9Score	.3400563	-.0117482	1.355565	.949297
TL_PainScaleB~k	.0387696	-.0156152	.9700003	.9506513
2.TL_Me~ptics_a				
X_AgeCalc	-.2019608	.0019223	1.008654	.9949052
X_AgeCalc#				
X_AgeCalc	-.2073424	.0012974	.9787932	1.026974
sex_var	-.0863315	-.0041174	.9907228	.9996975
edu	.0785029	.005269	.9381581	.9755352
TLsmoke_Cat	-.0110061	.0028925	.9508947	.9761866
TL_PHQ9Score	.2977424	-.0032908	1.159388	1.004342
TL_PHQ9Score#				
TL_PHQ9Score	.2895388	-.0016509	1.361641	.9929042
TL_PainScaleB~k	-.0148689	.0094063	1.119373	1.068662



- **ODI**

	Standardized differences		Variance ratio	
	Raw	Weighted	Raw	Weighted
1.TL_Me~ptics_a				
X_AgeCalc	-.4335851	-.0055702	1.070835	.9972686
X_AgeCalc#				
X_AgeCalc	-.4381789	-.0061278	.9261243	1.004577
sex_var	.0530127	-.0020363	1.002437	.9998644
edu	.055897	-.0216912	.8909784	.9590815
TLsmoke_Cat	.0251173	.0020379	1.019301	.9660799
TL_PHQ9Score	.3561375	.0035738	1.116986	.9538663
TL_PHQ9Score#				
TL_PHQ9Score	.3317056	-.009306	1.338568	.9308755
TL_ODIScore	.296673	-.0132721	1.046298	.9736351
2.TL_Me~ptics_a				
X_AgeCalc	-.198884	-.0016057	1.006855	.9960949
X_AgeCalc#				
X_AgeCalc	-.2045301	-.0021767	.9784591	1.019986
sex_var	-.0866277	-.0054134	.9910787	.9996183
edu	.0762041	.0029952	.9397652	.9737342
TLsmoke_Cat	-.0162299	.0021532	.9397451	.9768254
TL_PHQ9Score	.3033113	-.0041654	1.162306	.9962602
TL_PHQ9Score#				
TL_PHQ9Score	.2956829	-.0045443	1.368191	.9691868
TL_ODIScore	.3482298	-.0009968	.9024774	.8492754



Curriculum Vitae

Candidate's full name: Dana El-Mughayyar

Universities attended (with dates and degrees obtained):

University of New Brunswick, Bachelor of Science- Biology Psychology, 2019

Publications:

1. Hébert, J. J., Adams, T., Cunningham, E., El-Mughayyar, D., Manson, N., Abraham, E., Wedderkopp, N., Bigney, E., Richardson, E., Vandewint, A., Small, C., Kolyvas, G., Roux, A. l., Robichaud, A., Weber, M. H., Fisher, C., Dea, N., Plessis, S. d., Charest-Morin, R., Christie, S. D., Bailey, C. S., Rampersaud, Y. R., Johnson, M. G., Paquet, J., Nataraj, A., LaRue, B., Hall, H., & Attabib, N. (2023). Prediction of 2-year clinical outcome trajectories in patients undergoing anterior cervical discectomy and fusion for spondylotic radiculopathy, *Journal of Neurosurgery: Spine*, *38*(1), 56-65. Retrieved Feb 22, 2023, from https://thejns.org/spine/view/journals/j-neurosurg-spine/38/1/article-p56.xml
2. Kerr J, Abraham E, Vandewint A, et al. Predicting Health-Related Quality of Life Outcomes Following Major Scoliosis Surgery in Adolescents: A Latent Class Growth Analysis. *Global Spine Journal*. 2022;0(0). doi:10.1177/21925682221126451
3. Wang, S., Hebert, J.J., Abraham, E. *et al.* Postoperative recovery patterns following discectomy surgery in patients with lumbar radiculopathy. *Sci Rep* 12, 11146 (2022). https://doi.org/10.1038/s41598-022-15169-8

4. Mosaab M., El-Mughayyar D., MacLennan M., Attabib N. (2022). Undifferentiated Presentation of Unilateral Agenesis of a Cervical Pedicle and a Contiguous Vertebral Hemangioma. *Journal of Neurosurgery: Case Lessons.* In Review.
5. MacLennan M., El-Mughayyar D., Attabib N. (2021). Double-Level Non-Contiguous Thoracic Chance Fractures Treated with Percutaneous Stabilization. *Journal of Neurosurgery: Case Lessons.* Published.
6. Hathi, K., Bigney, E., Richardson, E., Alugo, T., El-Mughayyar, D., Vandewint, A., Attabib, N. (2021). Minimally Invasive vs. Open Surgery for Lumbar Spinal Stenosis in Patients with Diabetes – A Canadian Spine Outcomes and Research Network Study. *Global Spine Journal*. https://doi.org/10.1177/21925682211042576
7. Alsuwaihel, M., El-Mughayyar, D., Archer, B., Kolyvas, G., & Attabib, N. (2021). Middle Meningeal Artery Embolization for Chronic Subdural Hematoma: A Case Series. *Pan Arab Journal of Neurosurgery*, *16*(1), 21–25. https://doi.org/10.21608/pajn.2021.70751.1018
8. Manson, N., El-Mughayyar, D., Bigney, E., Richardson, E., & Abraham, E. (2020). Instrumentation Removal following Minimally Invasive Posterior Percutaneous Pedicle Screw-Rod Stabilization (PercStab) of Thoracolumbar Fractures Is Not Always Required. *Advances in Orthopedics*, *2020*, 1–7. https://doi.org/10.1155/2020/7949216

9. Craig M., Kroetsch S., El-Mughayyar D., Attabib N. (2020). Minimally Invasive Percutaneous C1-C2 Transarticular Screw Fixation as a Palliative Management Option in C2 Metastases. *Libyan J Med Sci.* 4(1), 29-31.

Conference Presentations:

1. El-Mughayyar D.*, Adams T., Cunninham E., Bigney E., Richardson E., Attabib N., Abraham E., Manson N., CSORN Investigators, Hebert J. Healthcare utilization and surgical wait time predict post-operative trajectories of disability and arm pain following anterior cervical discectomy and fusion surgery for cervical radiculopathy. Accepted for poster presentation at: *New Brunswick Health Research Foundation Conference*. November 2021.
2. Hathi K., Bigney E.*, Richardson e., Alugo T., El-Mughayyar D., Vandewint A., Manson N., Abraham E., CSORN Investigators, Abraham E., Attabib N. Minimally Invasive vs. Open Surgery for Lumbar Spinal Stenosis in Patients with Diabetes - A CSORN Study. Accepted for podium presentation at: *Global Spine Congress.* November 2021.
3. El-Mughayyar D.*, Hathi K., Bigney E., Richardson e., Alugo T., Vandewint A., Manson N., Abraham E., CSORN Investigators, Abraham E., Attabib N. Minimally Invasive vs. Open Surgery for Lumbar Spinal Stenosis in Patients with Diabetes - A CSORN Study. Accepted for podium presentation at: *5th Annual Saudi Society*. October 2021.
4. Dickinson A.*, leRoux, A., Kolyvas G., Ghallab, N., El-Mughayyar, D., Bigney E., Richardson. E., Vandewint A., Attabib N. Tissue Plasminogen Activator in

Addition to Twist Drill Drainage as a Treatment for Chronic Subdural Hematomas – A Descriptive Analysis. *Canadian Sciences Federation Conference 2021*.

5. Rogers S.*, Manson N., Bigney E., Vandewint A., Richardson E., El-Mughayyar D., McPhee R. & Abraham E. Impact of undergoing thoracolumbar spine surgery on patient mental health. Accepted for podium presentation at: *21st Annual Canadian Spine Society Meeting*, February 2021.
6. Wang S.*, Hebert J., Abraham E., Vandewint A., Bigney E., Richardson E., El-Mughayyar D., Attabib N., The CSORN investigators, Small C. & Manson N. Post-operative Recovery Patterns Following Discectomy Surgery for Lumbar Radiculopathy. Accepted for e-poster presentation at: *21st Annual Canadian Spine Society Meeting*, February 2021.
7. Rose J.*, Manson N., Vandewint A., Hebert J., El-Mughayyar D., Richardson E., Ghallab N., Flood M., Attabib N, The CSORN Investigators & Edward Abraham. Exploring the ability of radiographic parameters of stenosis severity to predict patient recovery patterns. Accepted for e-poster presentation at: *21st Annual Canadian Spine Society Meeting*, February 2021.
8. Kerr J.*, Abraham E., Vandewint A., Bigney E., Hebert J., Richardson E., El-Mughayyar D., Chorney J., El-Hawary R., PORSCHE Study Group & Manson N. Paediatric Health-Related Quality of Life Outcomes Following Surgery for Adolescent Idiopathic Scoliosis. Accepted for e-poster presentation at: *21st Annual Canadian Spine Society Meeting*, February 2021.

9. Manson N*, Bigney E, Darling M, Richardson E, El-Mughayyar D, Tripp D, Abraham E. Which baseline psychological measures add to the prediction of patient reported outcomes two years following elective thoracolumbar surgery? *Canadian Spine Society 20th Annual Scientific Conference. Whistler, BC Feb. 26–29, 2020. Canadian Journal of Surgery. Vol. 63 (4 Suppl 1) July–August 2020 DOI: 10.1503/cjs.014720 (http://canjsurg.ca/wp-content/uploads/2020/07/63-4-S6.pdf).*
10. Meagher J, Attabib N, Bigney E, Richardson E*, El-Mughayyar D, Abraham E, Manson N. Ascertaining Opioid Prescribing Patterns of Spine Surgery across Canada: A Preliminary Look. *Canadian Spine Society 20th Annual Scientific Conference. Whistler, BC Feb. 26–29, 2020. Canadian Journal of Surgery. Vol. 63 (4 Suppl 1) July–August 2020 DOI: 10.1503/cjs.014720 (http://canjsurg.ca/wp-content/uploads/2020/07/63-4-S6.pdf).*
11. El-Mughayyar D*, Manson N, Bigney E, Richardson E, Tripp D, Abraham E. Preoperative Psychological Factors Significantly Add to the Predictability of Chronic Narcotic Use: A Two-Year Prospective Study. *World Academy of Science, Engineering and Technology International Journal of Medical and Health Sciences.*Vol:13, No:12, 2019.
12. El-Mughayyar D*, Manson N, Bigney E, Richardson E, Tripp D, Abraham E. Preoperative Psychological Factors Significantly Add to the Predictability of Chronic Narcotic Use: A Two-Year Prospective Study. *11th Annual New Brunswick Health Research Conference and Gala of Excellence. Accepted.*

13. Moore F*, Bigney E, Manson N, Richardson E, Darling M, El-Mughayyar D, Abraham E. Multi-level Spinal Fusion Offers Clinically Significant Reductions in Pain and Disability. *11th Annual New Brunswick Health Research Conference and Gala of Excellence.*