Prescribing Practices Amid the OxyContin Crisis: Examining the Effect of Print Media Coverage on Opioid Prescribing Among Nova Scotia Providers

by

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DEDICATION PAGE

This thesis is dedicated to all those who have suffered pain, and to those who work tirelessly to alleviate this pain.

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ABSTRACT

This research examined the effect of increasing attention on OxyContin in the news media on prescribing practices of the drug in Nova Scotia. Using data collected as part of a study looking at representations of OxyContin in North American newspapers between 1995 and 2005, this research assessed the trends in prescribing practices of OxyContin in relation to the increased media attention. Data from the original media study was combined with administrative data from the Nova Scotia Prescription Monitoring Program to examine OxyContin prescribing trends between September 1996 and December 2007, with a specific focus on changes in the volume of OxyContin prescribed as a proportion of all opioids prescribed and as a proportion of strong opioids prescribed. Peaks in print media attention in both the United States and Canada were followed by statistically significant changes in OxyContin prescribing. These changes differed among prescribers in different District Health Authorities and specialties.

LIST OF ABBREVIATIONS USED

ATC	Anatomical Therapeutic Chemical
CADUMS	Canadian Alcohol and Drug Use Monitoring Survey
CCHS	Canadian Community Health Survey
DDD	Defined Daily Dose
DHA	District Health Authority
DIN	Drug Identification Number
GP	General Practitioner
HCN	Health Card Number
MG	Milligram
NPHS	National Population Health Survey
NS	Nova Scotia
NSPMP	Nova Scotia Prescription Monitoring Program
OSDUHS	Ontario Student Drug Use and Health Survey
PMANS	Prescription Monitoring Association of Nova Scotia (now the NSPMP)
PMP	Prescription Monitoring Program
WHO	World Health Organization

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CHAPTER 1: INTRODUCTION

In 2010, 11.8% of the Canadian population over the age of 12 reported ongoing moderate to severe pain or discomfort.[1] Other studies have indicated that as much as 29% of the Canadian population report chronic pain.[2] In Nova Scotia in 2010, 15.3% of the population reported that they suffered from moderate or severe chronic pain or discomfort, but this proportion may be as high as 36%.[1,3] Unfortunately, a number of governing bodies and experts indicate that chronic pain is undertreated in Canada.[3-6]

A number of treatments exist for addressing chronic pain. These include physical, psychological, pharmacological and surgical options.[4] Pharmacological agents represent the most commonly used approach for most types of pain, and opioids are a mainstay for the treatment of both acute and chronic pain.[7] Pain patients often begin with non-opioid drugs (such as acetaminophen and non-steroidal anti-inflammatory drugs). If these fail to adequately improve comfort or function or are not tolerated, opioids are often prescribed next; with weak opioids representing a second line of therapy and strong opioids the third line of therapy.[8] There are very few types of moderate to severe pain that would absolutely preclude a trial of opioid therapy, and though opioid therapy may not be the first line of treatment against chronic pain, it is indicated where other treatment options have failed.[4] These pharmacological agents remain a potent treatment for chronic pain.

Studies indicate that approximately 20% of pain patients in Canada are currently using opioid analgesics.[3] However, recent research has indicated that there are a number of barriers preventing the optimal use of opioids. In patients, concerns of side effects and addiction may hinder the use of opioids.[3] Among prescribers, concerns about addiction, potential for patient abuse or misuse, fears of an audit by their governing College or other legal ramifications, and loss of licensure concerns have been cited as barriers to the prescription of opioids in clinical settings.[5]

In 1996, Canada approved a new opioid analgesic called OxyContin®. This sustained release form of oxycodone (an opioid used to treat moderate to severe pain) has the advantage of requiring less frequent dosing than other oxycodone-based products.[9] At the time it was introduced, OxyContin was considered to be a breakthrough, both for its ability to provide sustained pain relief and because manufacturers and prescribers expected the extended release formula to be less prone to abuse as compared to other opioids.[10] OxyContin is used to control moderate to severe pain, chronic pain and pain related to cancer and other debilitating and terminal conditions. OxyContin is often used when other opioids (such as codeine or morphine) have not been effective or patients experience intolerable side effects from these medications. Additionally, OxyContin is used when around-the-clock management of pain is needed for an extended period of time.[11,12]

Soon after the introduction of OxyContin, however, it was discovered that when crushed or chewed and either inhaled, injected or swallowed, the oxycodone is released and absorbed rapidly, producing a heroin-like euphoria.[13] As a result, within five years of its release, both popular and medical press across Canada began to report the use of OxyContin as a street drug.[14] Use of this drug has since been represented as a growing social problem, especially in Atlantic Canada.[14] In particular, there have also been increasing reports of other problems related to OxyContin, including criminal diversion of the drug and increased numbers of OxyContin-related overdoses and deaths.[15-18]

A review conducted of representations of OxyContin in newspapers between 1995 and 2005 found that coverage of OxyContin emphasized negative evaluations of the drug - often focusing on abuse and addiction, crime and death, with very little attention to the legitimate treatment of pain.[14] In particular, a large amount of media came from Cape Breton, Nova Scotia, where the abuse of OxyContin was widely considered a significant problem. Over 86% of all OxyContin stories published in Canada during this period originated in two Nova Scotia daily papers (*The Chronicle Herald* based in Halifax and *The Cape Breton Post*).[14]

Concern has been raised that this increased media attention and negative portrayals of OxyContin may have led to a number of negative outcomes for both physicians and patients, particularly those with chronic pain, in Nova Scotia.[14] This negative media coverage of OxyContin may be raising and propagating fears among both patients and prescribers around the use of opioids. It has been suggested that legitimate OxyContin users may face stigmatization and the potential threat of reduced access to therapy from wary prescribers, leading to under-prescribing and lack of appropriate treatment of patients with acute and chronic pain. Understanding the factors, including media portrayals of OxyContin, that influence prescribing practices is crucial in ensuring the appropriate treatment of pain in Nova Scotia.

This study sought to provide insight into the impact that discussions of OxyContin in the printed press have had on prescribing practices around OxyContin, and, in turn, pain patient access to necessary medications in Nova Scotia.

This thesis is structured around five sections. The first section provides the background context for the proposed project and briefly reviews the prevalence of pain in Nova Scotia and the need for OxyContin and other opioids, the rates and barriers to the use of opioids and OxyContin, and the increasing attention on OxyContin in the popular and medical presses. The second section outlines the objectives of the project and the third section discusses the methods that were used to examine each of the objectives, including a discussion of the data sources, statistical methods and variables that were used. The fourth and fifth sections present the findings and analysis of the results.

CHAPTER 2: BACKGROUND

In this section, the prevalence, economic burden and other consequences of chronic pain are discussed. This is followed by a brief discussion of why OxyContin and other opioid analgesics are important and when they are used. Lastly, there is a discussion of a number of problems that have been associated with OxyContin.

The chapter begins with a discussion of pain and its consequences, since the research described here was interested in opioids that were prescribed for the purposes of pain treatment. Moreover, the information presented in this section focuses on chronic pain, since this is the main indicated use for OxyContin. It is worth noting, however, that OxyContin may be prescribed for acute pain in some circumstances.

2.1 WHAT IS PAIN?

According to the International Association for the Study of Pain, pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[19] The manifestation of pain is a combination of the physical, psychological, social and spiritual experiences of each individual person and is a reflex reaction to a stimulus as well as a cognitive reaction that is modified by the person's response to the discomfort.[20]

Pain can be classified by several different parameters. Acute pain is defined by abrupt onset and is generally present for less than six weeks.[20] Depending on the severity, acute pain may or may not require treatment and generally resolves. Chronic pain is usually more gradual in onset and by definition, is more persistent (generally present for 6 months or more).[4,20-22] Chronic pain typically requires long-term treatment to manage the discomfort.[20] Pain is also commonly classified as nociceptive or neuropathic. Nociceptive pain results from irritated tissue, usually as a result of injury or disease, and originates from either musculoskeletal or organ tissues.[20,21] The cause is usually apparent and

identifiable through testing. Such pain typically responds to analgesics, such as acetaminophen, nonsteroidal anti-inflammatory drugs and low-potency opioids.[20] In contrast, neuropathic pain results from irritation of the nerve tissue. The cause may be difficult to determine and treatment often occurs over extended periods of time and using multiple methods. Chronic pain almost always has a neuropathic component and is often divided into cancer-related pain or noncancer pain.[20] Lastly, dysfunctional pain refers to a group of pain syndromes that have been characterized by the amplification of pain signaling in the absence of inflammation or injury (nociceptive) or damage to the nervous system (neuropathic).[21] Such conditions include fibromyalgia, irritable bowel syndrome and interstitial cystitis.[21]

Pain intensity is generally described on a numerical scale from 0 to 10. Zero represents the absence of pain and 10 represents the worst pain imaginable.[20] The intensity of pain is often classified as mild (between 1 and 3), moderate (4 to 5) and severe (equal to or greater than 6).[21]

2.2 Prevalence of Pain in Nova Scotia

Chronic pain affects a significant number of Canadians. The 2009/2010 Canadian Community Health Survey (CCHS) indicated that 11.8 % (95% CI: 11.5 – 12.1%) of the population over the age of 12 report usual moderate or severe pain or discomfort.[1] (Note that these estimates do not distinguish between chronic cancer and noncancer pain). Further, 12.5% (95% CI: 12.2 – 12.8%) of the Canadian population indicated that they experience pain or discomfort that limits or prevents activities.[1] Another study conducted in 2001 among Canadians between the ages of 18 and 75 found that as much as 29% of the population report chronic pain (defined as pain of at least six months' duration).[2] Chronic pain was reported by 27% of men and 31% of women, with the prevalence of chronic pain peaking among those over the age of 55 (at 39%). Of these individuals, 80% reported moderate to severe pain.[2]

Interestingly, the prevalence of chronic pain in Nova Scotia is higher than for the rest of Canada. In Nova Scotia, 15.3% (95% CI: 13.9 – 16.7%) reported that they usually suffered from moderate or severe pain or discomfort according to the 2009/2010 CCHS, up from 13.8% in 2007.[1] This represents 123,056 people in Nova Scotia. Further, 15.1% (95% CI: 13.7 – 16.5%) reported that pain or discomfort prevented or limited activities.[1] Among males aged 12 and over, 14.5% (95% CI: 12.3 – 16.8%) reported moderate to severe pain, while 16.0% (95% CI: 14.0 – 18.0%) of females reported moderate or severe pain.[1] Figure 2.1 shows the percentage of the Nova Scotia population who report moderate to severe pain, broken down by age group and sex. Other studies indicate that the prevalence of chronic noncancer pain in the Atlantic Provinces may be as high as 36%.[3] The prevalence of pain by District Health Authority (DHA) in Nova Scotia is shown in Figure 2.2.

Although there are few national and provincial estimates of the prevalence of acute pain, studies also indicate that acute pain is common. One common source of acute pain is postoperative pain. A study of pain control after coronary artery bypass surgery in Canada, for example, found that less than 30% of the ordered pain medication was administered, and approximately 50% of patients continued to report moderate to severe pain for 1 to 5 days after surgery.[23] Importantly, acute pain may eventually become chronic, if unresolved and left untreated. Studies suggest that acute postoperative pain is followed by persistent pain in 10% to 50% of individuals after common operations (such as hernia repair, breast and thoracic surgery, amputation and coronary artery bypass surgery).[24]

The most common causes of chronic pain are varied. A study using data from the 2007/2008 Canadian Community Health Survey examined chronic pain among those aged 12 to 44 in Canada.[25] Among those reporting back pain, nearly a third (30%) also reported chronic pain (the survey did not specifically ask the cause of the chronic pain, but does ask about the presence of chronic conditions). Other conditions in which high levels of chronic pain were reported include migraine headaches (20%), arthritis (49%), mood disorders (29%), anxiety disorders (22%), stomach/intestinal ulcers (27%), bowel

disorders (24%) and diabetes (20%). A study in the United Kingdom of patients 25 years and older attending general practices found that common sources of chronic pain were low back pain (16.0%), arthritis (15.8%), injury (5.9%), angina (4.5%), leg pain (1.7%) and headaches (1.0%).[26] A more recent study conducted in 15 European countries and Israel found that the major causes of chronic pain were arthritis/osteoarthritis (34%), herniated or deteriorating discs (15%), traumatic injury (12%), rheumatoid arthritis (8%), migraine headaches (7%), fracture or deterioration of the spine (6%), nerve damage (4%), cartilage damage (4%), whiplash (4%) and surgery (3%).[27]

A number of risk factors are associated with increased prevalence of chronic pain. A review of the prevalence/incidence and sociodemographic predictors of chronic pain in the literature indicated that risk factors for chronic pain include gender, age, education, occupation, income, geographic residence and rural status.[28] Increasing age was associated with chronic pain, as was female gender. Education was inversely related to chronic pain; that is, those with higher education (generally post-secondary) were less likely to report chronic pain compared to those with less education (i.e. primary or secondary education). Unemployment and an inability to work were associated with chronic pain, as was being retired (although this was not adjusted for age). Individuals with chronic pain were less likely to have full-time employment. Research also showed that less skilled workers (i.e. blue-collared workers, farmers and employers) tended to report more chronic pain than more highly skilled workers (i.e. white-collared workers); however other studies have shown no significant difference. In terms of income, individuals who reported lower income or being on a pension were more likely to report having chronic pain. Individuals who reported living in rural areas were more likely to experience chronic pain than residents of urban areas. Lastly, being widowed or separated/divorced was found to be associated with chronic pain, while there was a protective effect for being married.[28]

These aforementioned factors may be contributing to the higher prevalence of chronic pain reported in Nova Scotia compared to the rest of Canada. While Nova Scotia has a similar proportion of the population aged 24 to 54 with post-secondary education when

compared to Canada (62.7% versus 62.6%) according to the 2006 census, Nova Scotia does have higher long-term unemployment rates (4.7% versus 3.4%), a lower average income ($30,187 versus $35,498) and a higher proportion of residents that reside in rural areas (44.7% versus 19.9%).[29]

2.3 Economic Burden of Pain and Other Associated Consequences

The economic costs of chronic pain are high, both in terms of healthcare costs and costs due to lost productivity in the workplace, though there have been only a handful of estimates of the economic burden of chronic pain in Canada.

Using data from the Alberta Ministry of Health and Wellness, Phillips and Schopflocher[30] estimated that each individual suffering from severe chronic pain costs an additional $3,500 (in year 2000 Canadian dollars) per year in direct health costs (i.e. beyond the average cost of healthcare per person). These include costs of consultations with healthcare professionals, hospitalizations and number of hospital days. This results in a yearly burden of over $400 million for chronic pain in Canada, a figure that is projected to rise to over $700 million by 2025 in the absence of effective intervention for individuals with moderate or severe chronic pain (though this was estimated using a much lower prevalence of chronic pain than is currently indicated in Nova Scotia by the CCHS). Using the CCHS estimate that Nova Scotia has a chronic pain prevalence of approximately 15.3% (or 123,056 individuals) and the above estimate of $3,500 in costs per affected person per year, this corresponds to costs of over $430 million per year in Nova Scotia.

The 1996/97 National Population Health Survey (NPHS) estimated that chronic pain costs approximately $14,744 per affected person per year.[31,32] Other estimates suggest the direct healthcare costs for chronic pain in Canada are more than $6 billion per year (in year 2000 dollars) and that by 2025, these costs will exceed $10 billion.[32] Using the CCHS estimate that Nova Scotia has a chronic pain prevalence of approximately 15.3%

(or 123,056 individuals) and the NPHS estimate of $14,744 in costs per affected person per year, this corresponds to costs of over $1.8 billion for chronic pain in Nova Scotia per year.

An analysis of chronic pain in Alberta using the 1996 NPHS and the 2001 Canadian Community Health Survey, as well as linkages with administrative data, determined a number of healthcare utilization factors that contributed to these direct costs of chronic pain.[33] For example, they noted that individuals with severe chronic pain, compared to those reporting no pain, reported 4 times higher rates of hospitalization in the previous year (28%), 4 times the number of consultations with a medical professional in the past 12 months (13.4%), 5 times higher rates of unmet healthcare needs (29%), 6 times higher rates of using narcotic medication (31%) and 4 times the average number of medication taken (2.9). All of these indicators showed a gradation with levels of chronic pain: that is, the percent of people reporting each variable increased as the level of pain increased from no pain, to mild, mild-to-moderate, moderate and finally to severe pain.[33]

However, Phillips[34] notes that the direct costs of pain management are minor in comparison with the impact on the economy resulting from the consequences of pain and inadequate treatment. For example, in the United States, it has been estimated that common pain conditions result in lost work productivity amounting to $61 billion US per year (of which 77% was explained by reduced performance and not necessarily absence from work).[35] Similarly, an Australian study indicated that the number of absent workdays due to pain-related conditions was 9.9 million per year, and that reduced-effectiveness days were estimated at 36.5 million per year.[36] This resulted in productivity losses of $1.1 billion US, although this climbed to $3.8 billion when presenteeism (reduced-effectiveness days) was also included.[36] Further indirect costs may stem from drugs, lack of appropriate treatment within locality, costs of treating adverse events from medications, costs of disability claims, costs of providing social care support for pain sufferers, costs of informal care provided by families and more intangible costs such as those associated with the deterioration in quality of life among pain patients.[30]

In Canada, it was found that the mean number of days that pain patients were unable to work in the past year due to chronic pain was 9.3 (95% CI: 4.7 – 13.7), but this rose to 16 days (95% CI: 5.1 – 26.9) for those who reported severe pain.[2] Forty-nine percent of participants in this study reported experiencing great difficulty attending social and family events, 61% were unable to participate in their usual recreational activities and 58% were unable to carry out their usual daily activities at home as a result of their pain.[2]

Clearly pain is a substantial problem in Nova Scotia and across Canada, both in terms of its prevalence and associated costs and consequences. The proper and adequate treatment of pain remains crucial for many Canadians.

2.4 Opioids: What They Are and Why They Are Used

Definitions of substance misuse, tolerance, abuse and addiction are presented in Appendix A. The Diagnostic and Statistical Manual of Mental Disorders, 4th edition, only defines substance dependence and abuse and does not define addiction.[37] The differences between and definitions of substance dependence and addiction continue to be debated.[37] Generally, however, it is thought that both include a psychosocial component, and that addiction includes physical dependence (generally defined by tolerance to the drug and withdrawal when the drug is stopped), which is not required for a diagnosis of substance dependence.[38] Both substance abuse and addiction, however, are associated with negative social consequences.[37,38]

Many treatments exist for the management of acute and chronic pain. These include physical, psychological, pharmacological and surgical options.[4] One particular pharmacological treatment that has long been used is opioid-based drugs. In fact, opium and opium derivatives have been used for thousands of years to relieve pain and suffering and remain a powerful tool in the treatment of pain.[39]

The term opioid refers to natural or synthetic compounds derived from the opium poppy (Papavar somniferum) that act by binding to opioid receptors in the central nervous

system. The analgesic effects of opioids are due to decreased perceptions of pain, decreased reaction to pain and increased pain tolerance.[40,41] Opioids include but are not limited to morphine, codeine, hydromorphone, oxycodone, buprenorphine, fentanyl, methadone and tramadol.

Opioids often produce feelings of euphoria, which have led to the recreational use, abuse and addiction to some opioids.[41] However, when opioids are used as directed under appropriate medical supervision, there is little risk of addiction in the general population.[40,41] Due to their addictive potential, all opium-based preparations and derivatives in Canada are classified as Schedule I controlled substances and thus the possession and distribution of all opioids in Canada are regulated by Federal laws under the Controlled Drugs and Substances Act.[42] Controlled substances consist of drugs that the Federal Government has categorized as having a higher-than-average potential for abuse or addiction.[42] Controlled substances are divided into categories based on their potential for abuse or addiction, with Schedule I substances being those with the highest potential for abuse and addiction.[43] Illegal possession, production, trafficking and exportation of controlled substances come with legal penalties, and are harshest for the Schedule I substances.[43]

The major types of opioids available as analgesics in Canada are morphine, codeine, oxycodone, hydromorphone, meperidine, methadone, tramadol and fentanyl.[44]

Opioids may be used for the symptomatic treatment of both acute and chronic pain associated with surgery or medical conditions such as trauma, myocardial infarction and terminal cancer. Various opioids are sometimes also used for non-pain related conditions, such as to manage dyspnea associated with chronic lung disease or terminal cancer, as well as being used as antitussives and adjunctive or primary anesthetic agents.[45]

Opioid analgesics have been widely accepted for the treatment of severe acute pain and chronic pain related to cancer or at the end of life, but their use in treating other types of chronic pain remains more controversial.[46,47] Whether they are actually prescribed for

these conditions, evidence from placebo-controlled trials suggest that opioids are effective for a number of chronic noncancer pain (CNCP) conditions such as diabetic neuropathy, peripheral neuropathy, postherpetic neuralgia, phantom limb pain, spinal cord injury with pain below the level of injury, lumbar radiculopathy, osteoarthritis, rheumatoid arthritis, low-back pain and neck pain.[44]

Opioid therapy may not be the first line of treatment against chronic pain, but rather is indicated where other treatment options have failed. The World Health Organization (WHO) devised a three-step ladder in the treatment of chronic pain.[6,8] Step one recommends the use of non-opioids (such as aspirin and acetaminophen); then as necessary, mild opioids (such as codeine); lastly strong opioids (such as morphine and oxycodone) should be used until the patient is free of pain.[6,8] These principles are reflected in a number of guidelines for the treatment of chronic pain, such as the Institute for Clinical Systems Improvement Guidelines for the Assessment and Management of Chronic Pain.[48]

Further, according to the 2002 Consensus Statement and Guidelines from the Canadian Pain Society, "in the absence of good evidence for a specific, curative treatment for a given pain problem, a trial of long term opioid therapy is a legitimate medical practice when a reasonable trial of other treatment modalities fails to improve comfort or function for the patient. There are very few types of pain that would absolutely preclude a trial of opioid therapy."[4]

It should be noted that taking any of these aforementioned pain analgesics for long periods of time (as would be the case for chronic pain patients) can result in a variety of health effects. For example, the long-term use of acetaminophen in high doses has been associated with liver damage.[49-51] Extended use of non-steroidal anti-inflammatories (NSAIDS) - which includes aspirin, ibuprofen and naproxen - has been associated with digestive side effects (including heartburn, indigestion, nausea, bloating and stomach pain), peptic ulcers and gastrointestinal bleeding.[7] NSAIDS may also interfere with the clotting ability of platelets, cause fluid retention and swelling. Longer-term use of

NSAIDs has further been linked to kidney disorders and kidney failure, as well as increased risk of blood clots in the legs, heart attack and stroke.[7] The long-term use of opioids, however, has been associated with the development of tolerance and physical dependence, as well as opioid-induced abnormal pain sensitivity, hypogonadism and sleep apnea.[52,53]

The general finding among studies examining opioid therapy suggest that patients with chronic noncancer pain can achieve satisfactory analgesia by using stable (nonescalating) doses of opioids, with minimal risk of addiction.[39] Some have further shown improvements in functioning and that cognitive function is preserved (although it may be impaired for up to seven days after an increase in the dose).[39] Opioids are also indicated in the treatment of a wide variety of pain conditions, including but not limited to neuropathic pain, osteoarthritis, musculoskeletal and back pain, as well as pain related to cancer, which is not the case for all analgesics.[39]

2.5 Monitoring of Opioid Prescriptions in Nova Scotia

In 1992, the Prescription Monitoring Association of Nova Scotia (PMANS) began operating a prescription monitoring program to monitor the prescribing and dispensing of specific narcotic and controlled drugs in Nova Scotia with the objective of curbing the overuse, misuse and diversion of these substances. The Nova Scotia Prescription Monitoring Program was developed through the joint efforts of the licensing authorities and professional organizations representing the medical, dental and pharmaceutical disciplines, as well as the Department of Health.[54]

Upon its inception, policy guidelines of the NSPMP required that a specially designated triplicate prescription pad was to be used for all prescription Narcotic and Controlled drugs, as listed in the Narcotics and Controlled Drugs Requiring Prescriptions in the Food & Drugs Act and Regulations issued by the Health Protection Branch.[54] Prescribers were required to write prescriptions on a triplicate pad and pharmacists would dispense these

drugs only when prescribed on a triplicate pad. A copy of the triplicate was sent to the NSPMP via mail where staff manually compiled prescription information.

In 2004 the *Prescription Monitoring Act* was approved and subsequently proclaimed along with the Prescription Monitoring Regulations in June 2005. A Prescription Monitoring Board was appointed with the legislated mandate to establish and operate a prescription monitoring program for Nova Scotia. The objectives of the Nova Scotia Prescription Monitoring Program (NSPMP) are to promote the appropriate use of monitored drugs and the reduction of abuse or misuse of monitored drugs.[55]

A new on-line system was implemented in 2005 to receive prescription information for the specified list of monitored drugs. This information had historically been compiled using the part of the triplicate prescription pad which pharmacies were required to send into the program. By the end of 2007, all community pharmacies were submitting this information via the on-line system. In 2008, the prescription pad was reduced to a duplicate form.[55]

The NSPMP provides information to prescribers and pharmacists; in part to assist in identifying potential drug seeking behaviours.[55] Detailed patient profiles are produced upon request, providing both prescribers and pharmacists with important patient prescription history. Through the NSPMP's robust and flexible data analysis capabilities, the Program is also able to analyze physician data at a provincial level, practice level and the individual prescriber level. Double doctoring or multiple doctoring notifications can help alert healthcare professionals to individuals who exhibit drug-seeking behavior. The Program's comprehensive database can identify trends in prescribing, which can assist in the development of educational interventions.[55]

The NSPMP routinely reviews and identifies cases of concern (both with respect to patients and prescribers) through its data analysis system, automated reporting queries or through information that becomes available to the Program through its routine enquiries.[55] Cases of concern are investigated and escalated through the Program's

review process to achieve the appropriate outcome. This may involve a referral of a case to the Program's Medical Consultant for review and/or the NSPMP's Practice Review Committee (PRC). Depending on the findings, these reviews can result in the case being closed, information going back to the prescriber, pharmacist, law enforcement or licensing authority as deemed appropriate and within the legislative mandate.[55]

2.6 Opioid Usage Rates

The consumption of opioids in Canada (measured in defined daily doses or DDD) has more than doubled in the past decade alone, from 10,209 DDD in 2001-2003 to 24,580 DDD in 2007-2009.[56,57] Canada consistently ranks among the top five consumer countries of opioid analgesics worldwide.[56] In 2010, the Canadian Alcohol and Drug Use Monitoring Survey (CADUMS) found that one in five (20.6%) Canadians aged 15 and over reported the use of opioid pain relievers in the 12 months prior to the survey.[58] Among these users, 1.1% (or 0.2% of the total population) reported using them for the experience, the feeling they caused or to get high.[58]

Fischer et al[57] examined trends in the levels of prescription opioid analgesic dispensing from retail pharmacies in Canada between 2005 and 2010. In that time period, the total amount of opioids dispensed (as measured using defined daily doses per 1000 population per day) increased from 20.3 to 23.0 – those for weak opioids decreased slightly (from 12.7 to 12.2), while those for strong opioids increased (from 7.6 to 10.8). There were substantial differences in the opioids prescribed, though all provinces showed steady increases in oxycodone dispensing rates over the 6-year study period. The only other opioid to consistently increase in all provinces over the same time was hydromorphone.[57] As a side note, this study also found that the presence of prescription monitoring programs did not indicate significant differences in changes in opioid dispensations levels between provinces with and without PMPs. However, this analysis merely compared provinces with and without PMPs in the selected time period (2005-2010), and did not consider trends in opioid dispensation before and after the introduction of PMPs in these provinces. Further, this analysis was not able to determine whether PMPs translated into

lower levels of opioid-related harms and problems (such as misuse, morbidity and mortality).[57] However, a more recent study conducted in the Unites States found that prescription monitoring programs mitigated increasing opioid abuse and misuse trends over time.[59]

It is difficult to determine the pain conditions for which opioids are most often prescribed. One study of two primary care centers in the United States examined patients with chronic noncancer pain who had received 6 or more months of opioid prescriptions in a one-year period.[60] Among 50 patients who met the criteria at the veterans hospital, the causes of pain were low back (44%), degenerative joint diseases (non-low back, 16%), injury-related (10%), spinal stenosis (10%), diabetic neuropathy (8%), headache (4%) and other (8%). Among 48 patients who met the criteria at the primary care center, the causes of chronic pain were low back (25%), injury-related (13%), degenerative joint disease (13%), headache (13%), diabetic neuropathy (10%), spinal stenosis (4%) and other (22%).[60]

2.7 Barriers to Opioid Use

It has been widely argued that chronic pain is undertreated in Canada, partly as a result of concerns of abuse and addiction around the use of opioids.[3-6] Boulanger et al[3] examined chronic noncancer pain patients across Canada and found that only 38% were taking prescription analgesics in 2001, although this rose to 49% in 2007. These rates vary by age group and sex: 38% of those aged 18 to 34 years, 44% of those aged 35 to 54 years and 59% of those over the age of 55 were taking prescription analgesics. Forty-five percent of men and 52% of women were currently using some type of analgesic.[3] Further, among those with moderate pain only 35% were taking prescription analgesics, and as much as 28% of those with severe pain were not taking prescription analgesics. Approximately 22% of chronic pain patients were prescribed opioid analgesics and almost 70% of pain sufferers were worried about addiction potential.[3] Concerns about addiction are important to consider among patients who are using opioids. Such concerns may prevent patients from accepting prescriptions for opioids and may reduce

compliance to recommended doses. Understanding the factors, such as the popular press, which contribute to fears of addiction to opioids in patients using these therapies is particularly relevant to prescribing physicians and dispensing pharmacists in helping to identify concerns, address these concerns and counsel patients appropriately about their risks of addiction.

A study conducted nationwide examined the perspectives of Canadian physicians on use and barriers to prescription opioids.[5] The results indicated that opioid analgesics were the treatment of choice for 79% of physicians for chronic cancer pain, but only 32% for moderate to severe chronic noncancer pain (which represented 83% of all pain experienced in the study).[5] Thirty-five percent of general practitioners and 23% of palliative care physicians indicated that they would never use opioids for noncancer pain, even when the pain was described as severe. The five most common barriers to strong opioid use identified by these practitioners were: potential for addiction, potential for patient abuse or misuse, unspecified side effects and constipation, and fear of an audit by their governing College or other legal and loss of licensure concerns. However, 68% of practitioners felt that chronic pain was not well managed in Canada.[5]

Another study of physicians in Ontario found that 95.4% had prescribed opioids to patients within the last three months, and 37% had prescribed opioids to more than 10 patients. Seventy-five percent of physicians had reported that they were comfortable prescribing opioids for chronic pain and 86% were confident in their clinical skills.[61,62] The majority of physicians (92%) somewhat or strongly agreed that many patients experience substantial relief with opioids and 86% indicated that they somewhat or strongly agreed that many patients function better with opioids.[62]

However, despite these positive views of opioids, this same study found that 57.2% of physicians agreed that "many patients become addicted to opioids".[61] Interestingly, physicians who strongly or somewhat agreed that their patients might become addicted to opioids were significantly older than those who disagreed. Additionally, physicians who somewhat or strongly agreed that they were confident and comfortable with their opioid

prescribing were significantly younger than those who somewhat or strongly disagreed. Physicians' comfort and confidence level in their opioid prescribing was negatively associated with specific concerns around opioid prescribing, including patient addiction, getting into trouble with the College of Physicians and Surgeons of Ontario, drug-seeking behaviours, overdose, lack of addiction treatment resources, conflict with patients and excessive opioid doses.[61,62].

Studies from the United States and Europe show similar beliefs. A survey of 45 clinicians in Washington and Oregon found that 52% reported that their management of pain is moderately or strongly influenced by previous experiences with patients addicted to drugs.[63] Forty percent indicated that their management of chronic pain was moderately or strongly influenced by the fear of contributing to physical dependence on opioids, and 20% reported that patients they treated became addicted more than half the time.[63] A survey of 115 general practitioners (GPs) in South East England indicated that 75% of GPs indicated that they had ever prescribed opioids for persistent non-cancer pain. General practitioners who indicated ever having prescribed opioids were younger and had a moderate belief that opioids were appropriate for persistent non-cancer pain, compared to those who did not prescribe opioids. Reported contraindications to prescribing opioids were mainly concerned with the risk of addiction and dependence, and less so with physical adverse side effects.[64]

The consensus statement and guidelines from the Canadian Pain Society in 2002 concluded that "pain of all types is undertreated in our society. The pediatric and geriatric populations are especially at risk for undertreatment. Health professionals' fears regarding … addiction, diversion of prescribed opioids to the illicit market and regulatory scrutiny create a significant barrier to the optimum prescribing of opioids for pain."[4] Other studies have echoed this statement. Moulin et al[2] concluded that chronic pain is undertreated in Canada, and that major opioid analgesics are probably underutilized in the management of moderate to severe pain due to some of the concerns mentioned above, both from physicians and patients. Passik et al[6] further state that "despite their proven analgesic efficacy in the management of chronic nonmalignant pain, continued

controversy, including fears of abuse, intolerable side effects, and disciplinary action by regulatory agencies, hinders the use of opioids in [pain] patients." Thus, understanding the role of the media in influencing physician prescribing practices and patients' prescription requests is crucial in ensuring the appropriate treatment of pain in Nova Scotia.

2.8 OxyContin

At the time it was introduced, OxyContin was considered to be a breakthrough, both for its ability to provide sustained pain relief and because manufacturers and prescribers expected the extended release formula to be less prone to abuse as compared to other opioids.[10]

OxyContin® (Purdue Pharma, Canada) is a controlled-release (also called sustained release) tablet form of oxycodone that has been approved for use in Canada since 1996.[14] Oxycodone is an opioid analgesic that has been in clinical use since 1917 and is used to treat moderate to severe acute and chronic pain.[65] It is available in solution (liquid), concentrate solution, tablet, capsule, and extended-release tablet form. Oxycodone is also available in combination with acetaminophen (Endocet, Percocet), aspirin (Endodan, Percodan, Oxycodan). Shorter acting oxycodone based products include Supeudol and Oxy IR.[13,44] OxyContin is indicated for the relief of moderate to severe pain requiring the continuous use of an opioid analgesic preparation for several days or more.[12] The advantage of OxyContin is that it requires less frequent dosing than immediate-release oxycodone formulations, with comparable efficacy and side effect profiles to the immediate-release formulations.[9] Further, it may have fewer or different side effects than some of the other long-acting opioids (such as morphine and hydromorphone).[9,65]

A systematic review of the safety and efficacy of controlled-release oxycodone (which includes OxyContin) indicated that patients treated with these opioids had superior pain relief when compared to patients who used nonsteroidal anti-inflammatory drugs or other non-opioid treatments.[9] Other studies have indicated that oxycodone has a more

favourable pharmacokinetic profile than other opioids (such as morphine), where oxycodone shows considerably greater bioavailability (a measure of how much of an administered dose of a drug actually reaches systemic circulation).[65]

In 2009, Canada was the second largest consumer per capita of oxycodone-based products behind the United States.[56] The top three products in Canada in 2009, in order of consumption, were codeine (16,334 kg), oxycodone (4,799 kg) and morphine (2,577 kg). Additionally, global consumption of oxycodone-based products has risen steadily from less than 5 tons in 1990 to nearly 77 tons in 2009 (about 1 billion DDD).

As of 2005, OxyContin represented approximately 25% of all prescriptions for oxycodone-based products in Nova Scotia.[66] In Nova Scotia OxyContin is currently available in eight doses: 5, 10, 15, 20, 30, 40, 60 and 80 mg tablets and is indicated for the treatment of moderate to severe chronic pain (particularly for around-the-clock management of pain), as an alternative to morphine or hydromorphone.[67] It is not indicated nor insured for the treatment of acute pain (e.g. post-operative pain).[67] It is worth pointing out that in September of 2003, a Notice of Compliance was issued by Health Canada for a revised indication for OxyContin.[68] Specifically, this was a clarification indication to specify that OxyContin should be used for the relief of moderate to severe pain requiring the continuous use of an opioid analgesic preparation for several days or more.[68]

In Nova Scotia, OxyContin is among the more commonly prescribed oxycodone products; of the 16 oxycodone-based products prescribed in Nova Scotia in 2004, OxyContin 20 mg, 40 mg, and 10 mg tablets were the second, third, and fourth most prescribed oxycodone-based products, respectively, behind Endocet (a combination of oxycodone and acetaminophen).[66]

As an opioid, OxyContin does have the potential for dependence, abuse and addiction.[22] Health Canada notes that when oxycodone-based prescription drugs are taken as directed by a physician for a short period of time, most patients do not develop dependency.

However, similar to other opioids, misuse and abuse of oxycodone-based products can lead to dependence and tolerance to oxycodone, requiring more frequent and higher doses."[13]

Soon after the introduction of OxyContin, it was discovered that when crushed or chewed and either inhaled, injected or swallowed, the oxycodone is released and absorbed rapidly, producing a heroin-like euphoria. This discovery led to the introduction of OxyContin as a street drug.[13] In fact, the package insert on OxyContin medication specifies that that the pills should be taken whole, and that breaking, crushing or otherwise altering how they are ingested will lead to a rapid (versus controlled) release. Purdue Pharma has been criticized in the United States for this warning, with critics arguing that it inadvertently provided individuals with the knowledge of how to administer the drug to obtain effects other than those intended.[18]

Interestingly, in May 2007, the Purdue Frederick Company, along with three senior executives, pled guilty to charges of misbranding OxyContin and were collectively fined $643.5 million in the US District Court. Purdue admitted to fraudulently marketing OxyContin by claiming that it was "less addictive, less subject to abuse, and less likely to cause withdrawal symptoms than other pain medications when there was no medical research to support these claims."[69] Additionally, in 2012, Purdue Pharma began to replace OxyContin with OxyNeo in Canada; a move likely stemming from the concerns over diversion, abuse and crime that OxyContin has experienced received in North America, along with the fact that the patent on OxyContin will expire in 2012.[70] OxyNeo is also an extended release oxycodone hydrochloride tablet formulation and Purdue Pharma has indicated that OxyNeo tablets have been hardened to reduce the risk of being broken, crushed or chewed.[71]

2.9 OxyContin Use as a Growing Social Problem

A number of problems related to OxyContin have been noted and appear to be increasing, including abuse, illicit use, crime, diversion and death. These concerns have contributed

to the process by which OxyContin use and abuse have come to be seen as problematic in Canada. This problematization has resulted in increased media and medical reports of OxyContin beginning in 1995, a considerable number of which were negative portrayals of the drug. In turn, there are concerns that this media attention has affected physician prescribing and patient use of OxyContin.

2.9.1 OxyContin-Related Problems

Illicit use of OxyContin

According to the 2010 Canadian Alcohol and Drug Use Monitoring Survey, 0.2% of the Canadian population reported using opioid analgesics for the experience, the feeling they caused or to get high.[58] However, this survey conducts interviews by phone, and likely does not capture a large portion of illicit drug users. Another study that examined adults in Ontario found that 21.3% of the sample had used prescription opioids in the past 12 months.[72] Two percent of the sample reported non-medical prescription opioid use and 0.5% reported using prescription opioids specifically for intoxication purposes.[72]

There is less data available that is specific to OxyContin. Using data from 2005, Fischer et al[73] examined a cohort of regular illicit opioid users and found that prescription opioids have become the predominant form of illicit opioid use across Canada, with the use of heroin, crack cocaine and cocaine declining since 2001. This study found that approximately 23% of participants reported illicitly using OxyContin in the 30 days prior to interview.[73]

The 2009 Ontario Student Drug Use and Health Survey (OSDUHS), an ongoing survey of adolescents in grades 7 to 12, found that 17.8% of students reported non-medical use of opioid pain relievers in the past year, behind only alcohol (58.2%) and cannabis (25.6%) and above cigarettes (11.7%).[74] Just under two percent of students reported the non-medical use of OxyContin specifically, representing nearly 16,700 students in Ontario.[74]

Abuse

Using data conducted between 2000 and 2004, Sproule et al[75] noted that the number of admissions for opioid detoxification at the Medical Withdrawal Management Services at CAMH (Centre for Addiction and Mental Health) in Toronto, Ontario, had increased significantly over this time period. In particular, the number of admissions related to controlled-release oxycodone increased substantially, from 34.8% of admissions to 55.4% of admissions. Additionally, use of controlled-release oxycodone in this setting was associated with the use of considerably higher doses than for other prescription opioids.[75]

Kahan et al[76] conducted a review of articles examining opioid dependence among chronic pain patients using opioid analgesics, and found the prevalence of dependence to be anywhere between 1% and 31%, depending on the clinical setting. Among tertiary care pain clinics, the prevalence ranged from 3% to 19%, while among specialty clinics these rates were between 1% and 3%. However, three retrospective chart reviews in primary care clinics found rates of 7% to 31%, with drug abuse diagnosed in 6% of these patients.[76]

Crime and Diversion

In 2005, current OPICAN data (a study of illicit opioid users in five Canadian cities) indicated the source of selected prescription drugs for illicit use.[77] Among users of OxyContin, 45% reported getting it from a regular dealer and 20% from an irregular dealer, 40% reported that they had obtained OxyContin through a doctor, 15% from a partner, 45% from a friend and none reported obtaining OxyContin via theft.[77]

In 2004, the OxyContin Task Force, established by the Government of Newfoundland and Labrador, released their final report on the state the OxyContin use in the province and recommendations on a strategy for OxyContin and other related narcotics abuse. As part of the report, the task force examined why OxyContin was problematic in the province.[18] The Task Force indicated that since 2001, the Royal Newfoundland

Constabulary had seen an increase in the number of pharmacy break and enters, armed robberies at pharmacies with perpetrators demanding OxyContin, and personal robberies with violence for OxyContin. The task force reports that this is substantiated by others who report the presence of shoplifting rings operating in St. John's for the purposes of obtaining OxyContin, in addition to individuals admitting to committing these crimes and others to support OxyContin addiction.[18]

Increasing criminal diversion of OxyContin and oxycodone-based products has been reported around the world.[78] For example, in 22 Eastern United States (representing 53% of the US population), between 2000 and 2003 there were nearly 4.5 million dosage units of oxycodone diverted, measured largely from thefts and loss incidents reported by pharmacies, medical practitioners, manufacturers and distributors.[78] Of the six opioids analyzed, oxycodone had by far the largest number of dosage units diverted. The amounts diverted over the four-year period for the other five drugs are as follows: 1,026,181 dosage units of morphine, 454,503 units of methadone, 325,921 units of hydromorphone, 132,950 units of meperidine and 81,371 units of fentanyl.[78] It should be noted that these data represent doses being diverted in the drug distribution chain prior to being prescribed (i.e. nonmedical diversion), and therefore does not account for diversion of opioids that have been prescribed by a physician or other prescriber.[78] Additional data from the Drug Enforcement Administration in the US showed that between January 2000 and June 2003, there were nearly 1.4 million dosage units diverted through 2,494 theft or loss incidents.[79] In particular, approximately 648,000 dosages were taken in 707 night break-ins, 397,000 dosages were taken in 631 armed robbery incidents, 226,000 dosages were taken in 704 employee pilferages, 11,000 dosages were taken through customer theft and 86,000 dosages were taken in 365 lost in transit events.[79]

Deaths

The OxyContin Task Force in Newfoundland and Labrador also noted that between 2001 and the release of the report in 2004, there were seven deaths in the province due to oxycodone (6 were due to OxyContin and one was related to Percodan), with the ages of the deceased ranging from 17 to 52 years.[18]

A study in the province of Ontario examined the prescribing of opioid analgesics and related mortality before and after the introduction of long-acting oxycodone (OxyContin) to the Ontario formulary in 2000.[16] It was found that from 1991 to 2007, the number of annual prescriptions for opioids increased from 458 to 591 per 1,000 individuals and that opioid-related deaths doubled (from 12.7 per million in 1991 to 27.2 per million in 2004). Prescriptions of oxycodone-based products increased 850% between 1991 and 2007. The study further found that the addition of OxyContin to the drug formulary was associated with a five-fold increase in oxycodone-related mortality and a 41% increase in overall opioid-related mortality, thus indicating that a significant portion of the increase in opioid-related mortality was due to the introduction of OxyContin.[16] Data from the Office of the Chief Coroner of Ontario also indicate that the number of oxycodone-related deaths have increased, from 35 in 2002 to 116 in 2006, a rise of 240%.[80]

Although not limited to OxyContin, Dasgupta et al[15] sought to investigate the relationship between media reports about prescription opioid abuse and overdose mortality associated with these drugs. Comparing a monthly time series of unintentional poisoning deaths involving short-acting prescription opioid substances to monthly counts of news articles mentioning prescription opioids between 1999 and 2005, the authors found a significant association between news reports and deaths, with media reporting preceding fatal opioid poisonings by two to six months and explaining 88% of the variation in mortality.[15] A number of other studies have noted increasing overdoses and deaths related to both prescription and illicit opioid use, within Canada and beyond.[16,81-83]

2.9.2 Popular Press Reporting of OxyContin

Within five years of its release, popular press across Canada began to report the use of OxyContin as a street drug, and use of this drug has since been represented as a growing social problem, especially in Atlantic Canada.[14] This occurred within the context of the growing concerns of the OxyContin-related problems (diversion, dependence and death) outlined above.

Whelan et al[14] examined how OxyContin came to be problematized via the print and medical press. Their review and analysis examined representations of OxyContin in medical journals and North American newspapers between 1995 and 2007.[14] The number of medical journal articles per year identifying an OxyContin problem increased fairly steadily from 1995 to 2007. Most journal articles came from pain and anesthesiology journals (76%), while substance abuse journals accounted for the fewest articles and were later (i.e. after 2004) in addressing OxyContin. Additionally, most articles from medical journals focused on discussions of clinical issues and the basic science of the drug, rather than social, legal or policy concerns. Indeed, 49% of articles focused on clinical trials, 20% on pharmacology, 17% on patterns of use and epidemiology of the drug and 9% on guidelines or consensus statements. Meanwhile only 15% considered social or economic concerns regarding the drug, 9% examined legal or policy issues, 6% discussed crime and 5% examined physician or pharmacist prescribing behaviour.[14]

In contrast, it was found that the newspaper coverage of OxyContin tended to emphasize negative evaluations of the drug, such as abuse, addiction, crime and death rather than the use of OxyContin in the legitimate treatment of pain. Newspaper stories most often expressed the perspectives of law enforcement and courts, with considerably less focus on the perspectives of physicians.[14] In particular, a large number of newspaper stories came from Cape Breton, Nova Scotia, where the abuse of OxyContin was widely considered a significant problem. Over 86% of all OxyContin stories published in Canada originated in two Nova Scotia daily papers (*The Chronicle Herald* and *The Cape Breton Post*).[14]

In 2004, the Canadian Pain Society (CPS) issued a news release stating concerns about recent media coverage on the abuse of prescription opioid analgesics, specifically OxyContin.[31] The release indicated that the Society felt that some of the reporting was inaccurate and one-sided in that the stories "focused mainly on the harm resulting when a relatively small group of people in our society choose to take big risks by using prescribed painkillers to get a high. Some unfortunate people across the country have died as a result of this choice."[31] Indeed, the Society indicated that the media failed to

mention that the vast majority of people, who take OxyContin properly, observe great benefit from the drug's ability to reduce pain. The Society further suggested that these media trends were stigmatizing legitimate OxyContin users, who were made to feel as though they might be doing something wrong, and that many users were worried that the one-sided media might discourage prescribers from prescribing OxyContin.[31] These sentiments have been echoed elsewhere.[84,85] To date, however, the impact of media attention to OxyContin in changes in prescribing of the drug have not been examined.

2.10 The Influence of Media on Physician Prescribing

There are few studies that examine the effect of media or public concern on physician prescribing practice. One study of thiazolidinedione, a class of oral diabetic drugs, evaluated the influence of adverse media reporting on prescribing attitudes of these drugs in Scotland.[86] These drugs had recently been in the spotlight in both the lay and professional media due to concerns of their cardiovascular safety. It was found that prescriptions for rosiglitazone had steadily decreased since the publication of a meta-analysis that suggested harm from this drug; an effect that was later shown in Ontario, Canada.[87] This decrease was mirrored by an increase in prescriptions for pioglitazone (a similar drug). During this time, rosiglitazone received sustained and intensive media coverage. Interestingly, when physicians were asked to indicate the source of information regarding drug safety warnings, the sources were highly varied: 21% indicated journals, 19% indicated scientific meetings and 15% indicted the news media as a source of information.[86]

Another study examined the relative contributions of scientific and commercial sources of information on prescribing behaviours of physicians.[88] The study examined two drug groups (cerebral/peripheral vasodilators and propoxyphene, an opioid) for which the commercial channels (e.g. advertisements and pharmaceutical representatives) presented a message of efficacy and reliability, while the scientific channels (e.g. published reports of clinical trials or reviews) demonstrated minimal efficacy. The majority of practitioners perceived themselves as paying little attention to drug advertising as compared to the

scientific literature, but their beliefs about the effectiveness of the two classes of drugs in fact revealed the opposite for a large portion of the sample. The authors suggest that this pattern may be due to either an unwillingness of prescribers to admit reliance upon commercial sources of information or a lack of awareness of such influence.[88]

Few other studies directly examine the impact of media on prescribing practices, with much more research focusing on the advertising efforts of pharmaceutical companies. However, the broader literature on factors that affect physician behaviour in clinical settings can provide a context in which to understand the factors that influence the prescription decision-making decisions of physicians.

Bauchner et al[89] posit that medical decision-making by physicians can be depicted as a set of four overlapping domains (Figure 2.3). First and foremost, physician decision-making occurs within the broad context of societal norms. Since many societal norms are rooted in the consciousness of an individual, most physicians (as well as patients) will not normally reflect on these norms in the decision-making process. These societal norms often operate within the context of the medical resources available within the country in which the physician practices.[89]

Beyond societal norms, Bauchner et al[89] argue that there are three domains that influence individual decision-making: 1) physician experience and knowledge, 2) patients characteristics and values and 3) external clinical evidence. These domains are in turn influenced by other factors. As an example, culture and ethnicity may influence patient characteristics in the context of health behaviours (e.g. diet) and health beliefs, values and preferences. Likewise, the availability of valid and reliable practice guidelines may increase the use of external clinical evidence by physicians. This model also accounts for the growing view that patients should be partners in managing their own healthcare; thus the presence of a patient domain.

Bauchner et al[89] also argue that these domains are not static and that the influence of a particular domain depends on the type of medical decision being made. When making

decisions in the context of acute and urgent conditions, the domain of physician knowledge often dominates, followed by the evidence domain, with the domain encompassing patient characteristics playing the smallest role.[89] However, decision-making in the context of more chronic conditions, such as the decision of what kind of opioid to prescribe for a patient with chronic pain, patient characteristics (such as whether a patient wishes to take an opioid) become much more prominent.[89] Indeed, the authors use the example of direct advertising by pharmaceutical companies in the US to depict how this model explains physician behaviour.[89] Advertising to patients for various drug therapies has led to skyrocketing sales of these drugs. The pharmaceutical industry understands that for many physician decisions, particularly drug prescribing, patients can influence physician behaviour.[89] It is not a stretch then to suggest that other media sources such as newspaper reports also influence both patient and physician behaviour, and ultimately the decision-making process around opioid prescribing.

Several reviews of the literature indicate a number of more specific factors that influence drug prescribing by physicians.[90,91] These factors include education, advertising, journals, influence and advice from colleagues, influence of pharmacists and pharmaceutical company representatives, control and regulation measures, demands from society and patients, doctor characteristics and patient population characteristics.

It should be noted that the prescriber has two decisions to make in the context of prescriptions: the decision to prescribe opioids and the decision of which opioid(s) to prescribe. These two decisions are a reflection of both prescriber and the patient characteristics (many of which are outlined above), such as the health status of the patient and concerns and attitudes towards opioids by both the physician and patient. Once the decision of whether and what to prescribe has been made, the prescriber must also make a decision as to the dose to prescribe and the duration (or days supply) of the prescription. The data for this research did not allow for detailed analyses of these characteristics, nor was it the aim of this research to do so. Instead, this research focuses on the broad impact that increasing attention of OxyContin in the media and its portrayal as a social problem

has had on prescribing practices of OxyContin at the population level. Where possible, some prescriber characteristics, such as specialty and year of graduation, were included.

2.11 THE PROJECT

Concerns have been raised that the media attention on OxyContin may have led to a number of negative outcomes, both for prescribers and patients.[14] Legitimate OxyContin users may now face stigmatization and the potential threat of reduced access to therapy from wary prescribers, leading to under-prescribing and lack of appropriate treatment of patients with chronic pain.[14] Such concerns have been voiced repeatedly, however the extent to which media representations of OxyContin influence the use of this drug and other opioids has not previously been evaluated. Given the substantial prevalence of chronic pain in Nova Scotia and that undertreated pain remains a large cost to society, understanding the role of media in contributing to changes in the treatment of pain is important. Within the context of Nova Scotia, where there were substantial negative concerns about the inappropriate use of OxyContin, there is need to understand how these representations shaped the trends in access to and prescribing of OxyContin, particularly since OxyContin is such an important pharmacological agent in the treatment of chronic pain. This project thus sought to examine the impact of sustained print media reporting about OxyContin on prescribing practices of this drug, building upon the work done by Whelan et al [14] by incorporating administrative data from the Nova Scotia Prescription Monitoring Program.

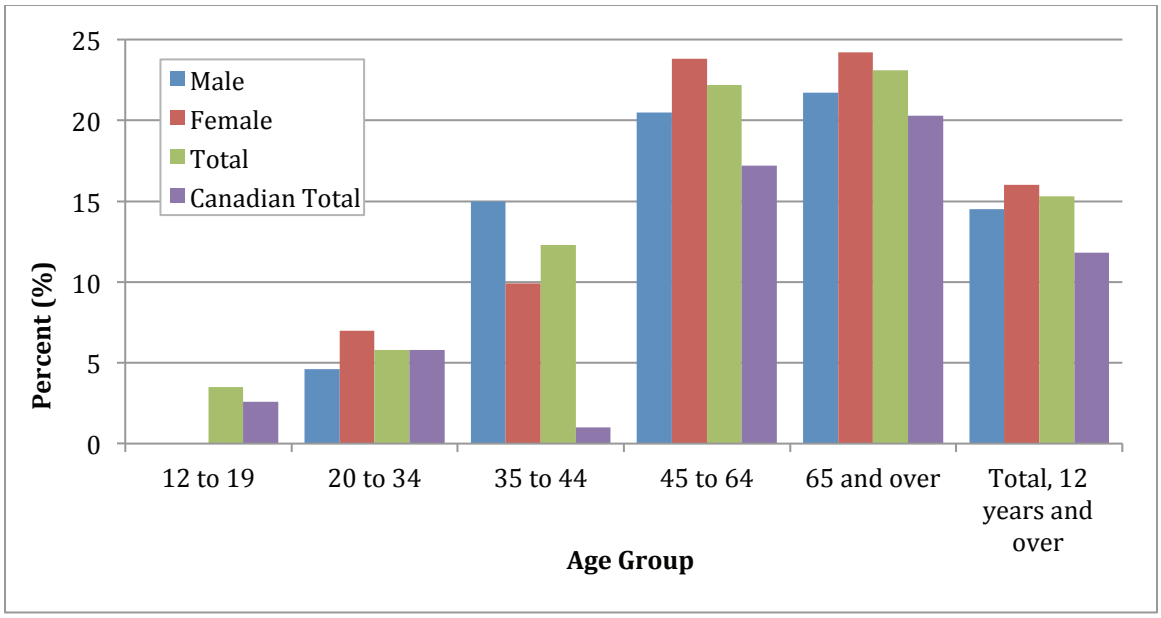

Figure 2.1: Percent of the Population Reporting Moderate to Severe Pain or Discomfort in Nova Scotia, by Age and Gender, 2009/2010[1]

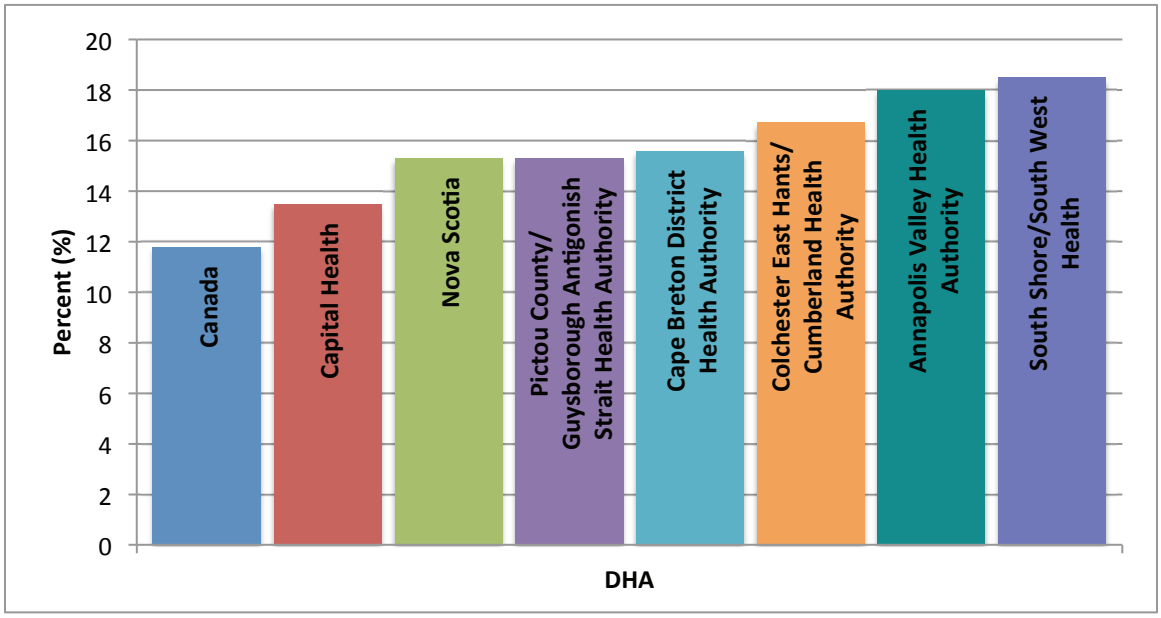

Figure 2.2: Percent of the Population Reporting Moderate to Severe Pain or Discomfort in Nova Scotia, by District Health Authority, 2009/2010[1]

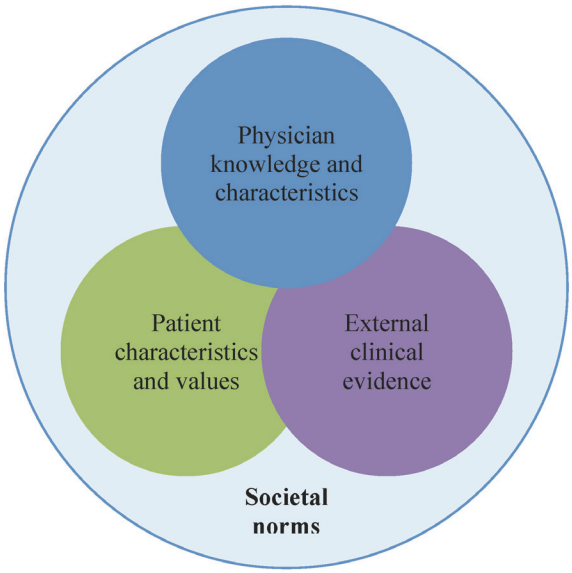

Figure 2.3: Model of Clinical Decision-Making

Note: Adapted from Bauchner et al.[89]

CHAPTER 3: OBJECTIVES

This research aimed to determine whether the media reporting of OxyContin in North American newspapers led to changes in prescribing practices of the drug between September 1996 and December 2007 among opioid prescribers in Nova Scotia. Specifically, the first objective was to determine the effect of trends in print media coverage of OxyContin on changes in prescribing practices of OxyContin between 1996 and 2007. The second objective was to determine whether any observed changes in the trends of OxyContin prescribing were consistent across prescriber characteristics such as specialty, decade of graduation from medical or dental school and District Health Authority.

CHAPTER 4: METHODS

4.1 OVERVIEW

Using data collected as part of a study looking at the representations of OxyContin in North American media, this research used quantitative methods to assess the trends in prescribing practices of OxyContin and other opioids in relation to the increased media attention.

As described below in section 4.2.1, a review and analysis was previously conducted that examined representations of OxyContin in North American newspapers between 1995 and 2007. The research conducted here builds upon this original project by exploring the extent to which prescribing practices have been affected by the increasing print media attention on OxyContin and its associated problems.

Administrative data from the Nova Scotia Prescription Monitoring Program (NSPMP) was used to examine OxyContin prescribing trends between 1996 and 2007. Data available at the prescriber level (e.g. the proportion of opioid prescriptions that were for OxyContin), by month, were used. The monthly trends in OxyContin prescribing were further examined by prescriber specialty, decade of graduation and District Health Authority. The WHO Anatomical Therapeutic Chemical (ATC) and Defined Daily Dose (DDD) classification system was used to standardize the prescription data.

For these time series analyses, conditional fixed-effects regression models were used to assess the impact of OxyContin-related reports in the print media on prescribing trends of the drug over time. Specifically, the focus was on peaks in media reporting of OxyContin. Relevant covariates were explored to determine their impact on prescribing practices. This research was primarily interested in the within-prescriber change in prescribing practices rather than differences between prescribers: therefore fixed-effects methods were appropriate, as these methods assess the effect of media attention on average within-provider changes in prescribing. These methods also allow for the serial

correlation in prescribing practices within providers to be accounted for. To assess whether there were differences in response to the print media attention on OxyContin among different prescribers, the effect of District Health Authority of practice, decade of graduation and specialty were assessed using interaction terms in the fixed-effects models.

Ethics approval was obtained from the Dalhousie University Health Sciences Human Research Ethics Board (#2012-2629).

4.2 DATA SOURCES

4.2.1 Nova Scotia Prescription Monitoring Program Data

The function and activities of the Nova Scotia Prescription Monitoring Program (NSPMP) are summarized above in section 2.5.

Prescription claims data from the NSPMP was obtained for medical and dental prescribers who had at least one prescription for an opioid-based medication that is indicated for the treatment of pain (i.e. opioids used as antitussives or antidhiarrheals were not requested) between September 1st, 1996 and December 31st, 2007. September 1996 is the first month in which prescriptions for OxyContin were made in Nova Scotia. While the print media data ends in 2005, prescription data was requested up to the end of 2007, given the potential for a lag effect of the media on prescribing practices. The full dataset encompassed 2,819,518 prescriptions made by 4,214 providers.

A list of the types of opioid medications included can be found in Appendix C. Only opioids indicated for the treatment of pain where included. These opioids all have ATC codes (described in more detail below) beginning with N02A and are opioid analgesics that act on the nervous system. Additionally, two drugs with the ATC code M03BA03 (Robaxisal® and Methosixal®) were included, since they both contain codeine and are indicated for the treatment of pain associated with muscle spasm.

Data for each prescription included the drug identification number (DIN), the Anatomical Therapeutic Chemical code (ATC), the date that the prescription was filled, the quantity prescribed, a prescriber identification number, the District Health Authority in which the prescriber practices, the decade of graduation of the prescriber and the prescriber's specialty. Additionally, an identification number for the patient was also provided.

In Nova Scotia, health services are currently delivered by nine District Health Authorities. These health authorities deliver healthcare services to residents and are responsible for all hospitals, community health services, mental health services and public health programs in their districts. The nine District Health Authorities are Cape Breton District Health Authority, Guysborough Antigonish Strait Health Authority, Pictou County Health Authority, Colchester East Hants Health Authority, Cumberland Health Authority, Annapolis Valley Health, South Shore Health, South West Health and Capital Health.[92]

4.2.2 Print Media Representations of OxyContin

A review and analysis conducted by Whelan and Asbridge examined representations of OxyContin in medical journals and North American newspapers between 1995 and 2005.[14] As part of this study, searches of newspaper literature databases were conducted and 924 stories published between 1995 and 2005 in 27 North American newspapers were examined. The focus of each of these texts as well as the themes, perspectives represented, and evaluations of OxyContin were then analyzed. A full list of the newspapers included in this study can be found in Appendix B. It is this newspaper data that is drawn upon in the current study.

Searches were conducted in three databases (Factiva, Lexis Nexis, and Virtual News) for all newspaper articles containing OxyContin in their title, lead paragraph or keywords. Newspapers were limited to those that were available in these databases, ensured geographical coverage across the major regions of the United States and Canada, and that either had significant circulation or were the main newspapers for their regions.

Additionally, only newspapers that were in circulation over the whole study period were included. The resulting sample consisted of 924 stories across 27 newspapers.

Further details of the data collection and results can be found in Whelan et al.[14]

4.2.3 Inclusion/Exclusion Criteria

The data obtained from the NSPMP included only prescriptions filled by Nova Scotia residents (i.e. those with a valid provincial health card number) and that were filled in Nova Scotia pharmacies. As noted, the data used here encompasses only prescribers in Nova Scotia who prescribed at least one opioid analgesic between September 1996 and December 2007, inclusive. Additionally, the data did not include prescriptions made for members of the RCMP (Royal Canadian Mounted Police) or Canadian Forces, as these claims are put under a federal number for drug coverage, but prescriptions for individuals with Indian Status were included. Of note, the data used in this study does not capture prescriptions filled in hospitals or long-term care facilities.

Prescriptions without an attached prescriber license number were removed, since there was no other way to link these prescriptions to specific prescribers. Prescriptions for which there was no defined daily dose available (described below) were also not included. These prescriptions included anesthetics (which are prescribed in such varying doses that no DDDs have been established), as well as prescriptions for drugs containing butorphanol tartrate in nasal spray form and levorphanol tartrate. Additionally, prescriptions that were missing the quantity prescribed were also excluded, since there was no way to calculate the total DDDs for these prescriptions. This exclusion process and the number of prescriptions and prescribers dropped at each stage are shown in Figure 4.1. A total of 16,245 prescriptions were excluded in this process, or 0.58% of all prescriptions. This resulted in a final sample of 4,212 prescribers and 2,803,273 prescriptions, representing 184,356 prescriber-months.

4.4 Outcome and Explanatory Variables

The focus of this research was on changes in prescriber behaviours, therefore the prescriber was the subject of interest. All outcome variables were created by aggregating prescriptions to the prescriber level by month, and the resulting unit of analysis was prescriber-months.

The number of days supply for a given prescription was not available in most years. Therefore, to standardize the opioid prescription data and allow for appropriate comparisons, the quantity of each prescription was converted into defined daily doses (DDDs). The two outcome variables were the proportion of all opioid DDDs that were for OxyContin and the proportion of all strong opioid DDDs that were for OxyContin, per prescriber per month. The outcome of interest was the shift in the trends of these variables following peak media attention on OxyContin.

For descriptive analyses, the explanatory variable was the number of newspaper articles published per month. However, for the statistical models and some additional descriptive analyses, the explanatory variable was modeled using splines, with knots defined according to the onset of periods of high print media attention.

4.4.1 Outcome Variables

The WHO ATC/DDD classification system was used to create the outcome variables of interest. Briefly, this classification system standardized the prescription data provided by the NSPMP to allow comparison across different prescriptions, strengths and quantities prescribed. This was particularly important given that there was no consistently collected measure available for the number of days supply of a given prescription in the NSPMP data.

Defined Daily Doses (DDD)

Drug and claims data can present challenges in health research analysis. The process of both identifying and aggregating drug data can be difficult, due in part because drugs within the same class, or even the same drugs, can have numerous different strengths, recommended doses and manufacturers.[93]

One method of quantifying drug utilization data appropriate for statistical comparison is the WHO Anatomical Therapeutic Chemical (ATC) classification and the associated measure, the Defined Daily Dose (DDD).[93,94]

Briefly, the ATC classification divides drugs into different groups according to the body organ or system on which they act, as well as their chemical, pharmacological and therapeutic characteristics.[94] Drug products are classified in groups at five different levels. Only one ATC code is assigned to a particular product, however a drug may be given more than one ATC code if it is available in strengths and formulations with clearly different therapeutic uses or if it is available as a combination product. For example, codeine has several ATC codes as it can be used as an antitussive, or in combination with other drugs for the relief of pain. The main indication of the drug usually determines the ATC classification. An example of an assigned ATC code is shown in Table 4.1.

Defined daily dose is a measure created to work with the WHO ATC classification system. The DDD is a technical unit that is defined as the "assumed average maintenance dose per day for a drug used for its main indication in adults."[94] Only one DDD is assigned per ATC code and route of administration (e.g. oral and parenteral formulations of the same drug may have different DDDs).[94] Essentially, the DDD provides a rough estimate of consumption and allows the expression of the amount prescribed in terms of the number of DDDs, providing a standardized measure of quantity that is independent of package size and strength to enable researchers to assess trends in drug consumption and perform comparisons across subgroups.[94] The exact methods through which the DDD for a given ATC code is assigned are presented elsewhere.[94] The WHO Collaborating Centre

for Drug Statistics Methodology based in Oslo, Norway, in collaboration with the WHO International Working Group for Drug Statistics Methodology, provides and maintains the guidelines for assigning DDDs.

The use of DDDs in this research allowed comparisons of drug prescriptions between prescribers and across the same prescriber over time, as well as making the aggregation of data across different types of opioids possible. This was especially pertinent given that the number of days supply of a given prescription was not consistently collected by the NSPMP until 2005, and therefore could not be used in this research. It should be noted that the DDD is a unit of measurement that does not necessarily reflect the recommended daily dose.[95]

The DDD for each ATC code and preparation was determined using the online searchable ATC/DDD Index for 2012.[95] For drugs that contained codeine or propoxyphene in combination with other non-opioid ingredients (such as acetaminophen or acetylsalicylic acid), only the opioid portion was considered, since this research was focused only on opioid consumption and DDDs were not available for these combination drugs. The DDDs that were used in this research are presented in Table 4.2.

Using the strength of the dosage form of the prescription and the total quantity prescribed (either the number of tablets, the total volume or the number of patches), the total number of DDDs per prescription was then calculated, as follows:

$$\text{Total DDDs Per Prescription} = \frac{\text{Dosage Form Strength x Quantity Prescribed}}{\text{DDD}}$$

Outcome Variables

The outcome of interest was changes in the prescribing of OxyContin. To measure change, two variables summarizing prescribing by each prescriber in each month were constructed using the DDDs for each prescription.

The first outcome variable was the proportion of all opioid DDDs per prescriber per month that were for OxyContin. The second variable was the proportion of all *strong* opioid DDDs per prescriber per month that were for OxyContin. OxyContin is a strong opioid, and restricting analyses to strong opioids provided a comparison with different opioids that are often prescribed for the same or similar conditions. This is particularly relevant in the context of concern over OxyContin, where providers wishing to move away from this drug would be inclined to prescribe another strong opioid.

Because both of these outcome variables were highly positively skewed and in any given month both of these outcome variables had a high number of legitimate zero values, both were transformed using the logit to produce a more linear relationship, create a more normal distribution and to spread out the data more evenly. This further alters the functional form of the data so that there is an asymptote at values of zero and one for both outcome proportions.

Opioids were classified as strong or weak based on the 2010 Canadian Guideline for the Safe and Effective Use of Opioids for Chronic Non-Cancer Pain.[44] Where medications in the NSPMP dataset were not listed in the guideline (such as for compounds that were discontinued in Canada prior to the publication of the guidelines), opioids were identified as strong or weak based on recommendations from several experts in the field of pharmacy and drug evaluation. (The classification of strong and weak opioids for the purposes of this research is shown in Appendix C). Briefly, strong opioids were defined to include medications containing sufentanil, fentanyl, hydromorphone hydrochloride, morphine hydrochloride, morphine sulfate and oxycodone hydrochloride. Weak opioids were defined as opioid medications that contained codeine monohydrate, codeine phosphate, pethidine hydrochloride (meperidine) or dextropropoxyphene.

It is worth noting that there are five doses of OxyContin in the data used: OxyContin 10 mg, 20 mg, 40 mg, and 80 mg. which were all approved in 1996 for use in Canada, and OxyContin 5mg, which was approved in 2005.

4.4.2 Explanatory Variables

The explanatory variable of interest was the trend in newspaper coverage of OxyContin between 1995 and 2005. For descriptive analyses, this was measured as the total number of newspaper articles related to OxyContin published per month.

Although this research was particularly concerned with the negative media, no separate analyses were done using only articles identifying problems. Since the vast majority of articles (95.3%) identified at least one problem relating to OxyContin, a separate analysis was not warranted. More details on the types of problems that were identified can be found in Whelan et al.[14] Briefly, problems with OxyContin identified included those related to crime (to acquire the drug or committed while using the drug), addiction and misuse, overdoses and deaths, concerns of home invasion or personal security among legitimate users, concerns of drug availability for legitimate users, providers under-prescribing OxyContin for legitimate users or being persecuted, stigmatization of legitimate users, poverty or social conditions, inadequate availability of pain specialists or proper treatment and over-marketing of OxyContin by Purdue Pharma.

The monthly trends in the print media attention of OxyContin (i.e. the number of newspaper articles per month) were graphed, which identified two peak periods of media attention. The highest peak observed in the print media reporting of OxyContin was in July 2001 and coincides with the peak in reporting in American sources. The second peak occurred in March 2004, and represented the peak in Canadian reporting, 85% of which was from Nova Scotian sources. The month in which the media reporting began to increase prior to each of these peaks were also identified, which corresponded to February 2001 for the American peak and May 2003 for the Canadian peak.

Based on the month of onset of the peaks, a media exposure measure was created using linear splines for the conditional fixed-effects models. This created three intervals: September 1996 to January 2001, February 2001 to April 2003, and May 2003 to December 2007. Therefore, interval 1 represents the time period before the onset of the

American peak in print media reporting, interval 2 represents the time between the onset of the American peak and the onset of the Canadian peak in print media reporting, and interval 3 represents the time period after the onset of the Canadian peak in media reporting. Both the American and Canadian media peaks were investigated because it was recognized that while prescribers in Nova Scotia were almost certainly exposed to the media that composed the Canadian peak (especially since a considerable amount came from Nova Scotia), it was also likely that many prescribers were exposed to the American media, and that the responses to these two peaks may have been different.

The explanatory variable of interest, the print media attention on OxyContin, was purposely examined using splines. The media could also have been modeled as a continuous variable (i.e. the number of articles published per month), but this would not have provided sufficient numbers of articles in each month to allow the American and Canadian print media to be examined separately. The media attention could also have been examined by focusing on specific events, such as when there were notable overdose deaths, for example, but this would have been difficult as many of these events are area-specific: that is, a notable death in one area of North America may not have been newsworthy in other areas. This would have been particularly tangential for these analyses, given that all prescription data came from Nova Scotia. Consideration was given to restricting analyses to Nova Scotian articles only, however it was recognized that many individuals do not rely solely on news sources from their province, but rather are also exposed to national and international print media sources.

Region and prescriber attributes were also used as explanatory variables for the purposes of assessing variation in the effects of print media exposure (i.e. these variables were used to examine effect modification). For all analyses, the prescriber specialties were grouped into three categories and graduation year was grouped by decade, as shown in Table 4.3. The models that examined interaction terms with District Health Authority, decade of graduation and prescriber specialty also used the linear splines.

While it was possible for a prescriber to change specialty and DHA of practice over the time period examined, only the most recent specialty and DHA (i.e. at the time of the last prescription) was used for each prescriber to ensure consistency. Table 5.1 shows the distribution of prescribers by specialty, decade of graduation and District Health Authority.

4.5 Other Confounders

Confounders for this study would be any other variables or events corresponding to the peaks in print media attention that would provide an alternative explanation of shifts in trends. The potential role of other pharmaceutical products entering the market over the study period were investigated, as well as the role of any published guidelines related to opioids. Several individuals who worked in the fields of pain, medical education and at the prescription monitoring program were also contacted to identify additional potential cofounders.

In September of 2003, a Notice of Compliance was issued by Health Canada for a revised indication for OxyContin.[68] Specifically, this was a clarification indication to specify that OxyContin should be used for the relief of moderate to severe pain requiring the continuous use of an opioid analgesic preparation for several days or more.[68] This notice of compliance may have played a role in some of the observed trends in OxyContin prescribing in this study. However, if this was the case, it would be expected that following the release of this notice of compliance, there would have been a steep and steady drop in the number of OxyContin prescription, then a leveling off as only patients who met the recommended requirements for the use of OxyContin continued to receive the drug. No such pattern was observed in the various measures used to examine trends in OxyContin prescribing (presented in the results section).

Another point to consider is that not all opioid products in the data used were available over the whole period of study. Some drugs entered the market after 1996, and some drugs were discontinued prior to 2007. It is expected that patients who had recurring

prescriptions for opioid analgesics that entered or left the market between 1996 and 2007 were switched to opioids in the same or similar classes (either to drugs with the same active ingredient at a similar strength, or to another strong/weak opioid). Since aggregate opioid data were used in this research (mostly according to total DDDs), the changing drugs entering and exiting the market were not expected to result in any large changes in the amount of opioids prescribed.

OxyContin 5 mg entered the market around mid 2005 (the first prescription for this drug in Nova Scotia was in May 2005), though examinations of the data did not reveal upswings or changes in the prescriptions for OxyContin as a result of this – with most noticeable changing trends in OxyContin prescribing occurring well before mid 2005. Moreover, there were only 502 prescriptions for OxyContin 5mg, representing a mere 0.86% of all OxyContin prescriptions.

An additional consideration is that selective COX-2 inhibitor NSAIDs were introduced to the Canadian market with much fanfare during the study period of this research. These drugs were first approved for use in Canada in 1999, but many were subsequently removed from the market in late 2004 and early 2005 following reports of increased risk of heart attack and stroke among users of these drugs.[96] It is unclear what, if any, impact the introduction and subsequent removal of these drugs from the Canadian market may have had on prescriptions for opioids and OxyContin. In particular, it is not likely that OxyContin was used to replace prescriptions for COX-2 inhibitors, or vice versa, given that COX-2 inhibitors are generally not indicated for the same conditions (COX-2 inhibitors were generally approved for osteoarthritis, primary dysmenorrhea and rheumatoid arthritis, and therefore were not indicated for the same purposes as OxyContin).[96] Importantly, opioids often represent a second line of therapy after NSAIDs and other less potent analgesics, and patients who begin opioid therapy, especially in the context of chronic pain, have often failed to resolve their pain using NSAIDs and would therefore not be expected to switch back from opioids to NSAIDs.

The publication of guidelines for the use of opioids and other analgesics in the treatment of pain during the period of study is also a consideration. Most of these guidelines have focused on the treatment of chronic pain, where extended use of opioid analgesics may be necessary. In 2003, the Canadian Pain Society published a special article entitled *Use of opioid analgesics for the treatment of chronic noncancer pain – A consensus statement and guidelines form the Canadian Pain Society, 2002* in the journal Pain Research and Management.[4] This was an updated position statement from 1997 that had endorsed the use of opioids in relieving chronic non-malignant pain.[4] Until this time, no national guidelines for opioid use existed, although a number of provinces had adapted their own guidelines. These guidelines presented a process for prescribing opioids for patients with noncancer pain, but did not endorse or discuss the use of specific opioids.

In 1999, the Nova Scotia College of Physicians and Surgeons released their *Guidelines for the Use of Controlled Substances on the Treatment of Pain*.[97] These guidelines, which include but are not limited to opioid analgesics, were partly developed in response to the recognition that inadequate pain control may result from prescribers' lack of knowledge about pain management or an inadequate understanding of addiction, in addition to fears of investigation or sanction by regulatory agencies.[97] Again, these guidelines provided a series of steps for physicians to follow when administering controlled substances to patients, but did not make any recommendation as to the type of controlled substances that should be considered.[97] These guidelines were updated in 2006 and more recently in 2011.

It is possible that these aforementioned guidelines may have played a role in the decision and process by which prescribers administer prescriptions for opioids in the context of chronic pain. Indeed, as these guidelines suggest that opioids are appropriate in the treatment of chronic pain, they may have contributed in part to both the increases in opioid prescribing and the increases in strong opioid prescribing that were noted in this research. However, it is important to consider that the guidelines generally present a safe and effective process by which opioid prescriptions should be made, but do not provide specific advice on which opioids should be prescribed. Therefore it is reasonable to

expect that the guidelines may have played a role in overall opioid prescribing, but likely did not directly contribute to decreases in OxyContin prescribing. Further, studies have shown that the uptake of published practice guidelines can be poor, both within the context of opioid prescribing[98] and in other areas of medicine.[99]

It is also possible that there were ongoing activities between 1996 and 2007 with regards to prescriber education about opioids in Nova Scotia. Several individuals who worked in the fields of pain, medical education and at the prescription monitoring program were contacted to identify any such possible activities. It was indicated that, while there have been ongoing activities and initiatives that target OxyContin and opioid prescribing, these all began in or after 2007 (the final year under study in this research) and therefore would not have contributed to the patterns of OxyContin prescribing noted in this research. For example, in 2010 the NSPMP moved to an online system whereby prescribers could rapidly view their prescribing profiles as well as the profiles of their patients. Other current activities include Continuing Medical Education sessions on controlled drug diversion, as well as knowledge translation around the new 2010 Canadian Guidelines on Opioid Use. Additionally, in 2008 the Nova Scotia Chronic Pain Collaborative Care Network was launched. Interestingly, it was indicated that many of these measures came about as a result of the increased attention on OxyContin.

As outlined above, it was generally thought that none of these aforementioned variables or activities would play a significant role in the trends of OxyContin prescribing between 1996 2007, and therefore they were not accounted for in analyses.

4.6 Analysis

Descriptive statistics were generated to describe the prescriber population within the NSPMP. The trends in the newspaper coverage of OxyContin were also summarized.

The outcome variables of interest were first graphed for descriptive purposes and to provide the context within which to interpret the results. These graphs examined overall

trends, as well as trends by prescriber District Health Authority, specialty and decade of graduation.

Conditional fixed-effects regression models were used to examine the average within-prescriber effect of print media variables on prescribing practices of OxyContin. These methods allowed for the control of unmeasured characteristics of the prescribers under study without the need to measure them, as long as these characteristics were stable over time (such as gender, date of birth, race, schooling, type of practice, geographic location, differences in patient populations etc., as well as practice patterns, attitudes and values). Conditional fixed-effects models thus allowed a focus on intra-prescriber variation rather than inter-prescriber variation (since each individual prescriber serves as his or her own control) in order to determine the effects of OxyContin media attention on prescribing of the drug.[100] As such, this within-person design increased the internal validity and minimized confounding due to unmeasurable variables.

The conditional fixed-effects regression models were estimated using ordinary least squares regression. As described above in section 4.4.2, linear splines were created with knots specified to represent three intervals with respect to print media reporting of OxyContin: interval 1 represents the time before the onset of peak media reporting in the United States, interval 2 represents the period between the onset of American peak reporting and Canadian peak reporting, and interval 3 represents the period after the onset of the peak in Canadian media reporting. Importantly, the spline was specified so that the coefficients displayed in the conditional fixed-effects models represented the change in slope from the preceding interval rather than the actual slope for that interval.

Due to the small numbers of OxyContin prescriptions up until 1999, only data from the years 2000 and onwards were included in the fixed-effects models. This was also done because the number of OxyContin prescriptions and the number of DDDs prescribed rose steadily between 1996 and the end of 1999, as expected due to the fact that OxyContin was only introduced in 1996. Moreover, this cut point provided a full year of data prior to any major changes in media trends of OxyContin to be included in the models to serve as

comparison. Therefore, the sample for these models included 134,061 prescriber-months, representing 3,721 prescribers with 2,047,785 prescriptions.

All models were weighted to help account for sampling variability in the outcome variables in each month, as there was considerable variability in the number of prescriptions per month used to create the outcome variables for each provider. This could result in considerable heteroscedasticity. Accordingly, weighted least squares regression was used to weight by the inverse of the expected sampling variability.[101,102] For models in which the outcome variable was the total proportion of opioid DDDs that were for OxyContin per prescriber per month, the weight variable was the total number of DDDs that a prescriber prescribed between 2000 and 2007. In models that examined the proportion of strong opioid DDDs that were for OxyContin, the total number of strong opioid DDDs per prescriber was used as the weight variable. Both of these weights approximate the inverse of the variance for that observation.

Effect modification by several variables was examined by interacting them with the slope coefficients for each spline. To assess whether prescriber decade of graduation from medical school, specialty and District Health Authority where the prescriber practices were associated with changes in prescribing practices of OxyContin, separate models were run for each of these characteristics. Additionally, to quantify the differences between DHAs, specialties and graduation decade, interaction terms were included in the conditional fixed-effects regression models.

In all cases, the interaction terms were created so that the most prevalent category was the referent group. The most prevalent group of prescribers in terms of DHA were practitioners in Capital Health, for specialty it was general practitioners, and in terms of decade of graduation, the most prevalent group were prescribers who graduated between 1980 and 1989. In the models that examined District Health Authority of practice, decade of graduation and specialty, prescribers who were missing this information could not be included (the percent missing for each attribute is shown in Table 4.3).

To examine effect modification by volume of opioid prescribing, prescribers were stratified into four volume groups for each of the outcome variables and separate fixed-effects regressions were run for each group. In these models, prescribers who never made a prescription for OxyContin were not included, since their values of the outcome variables were zero at all time points. To create these volume groups, the mean of each of the two outcome variables across all months per prescriber were calculated. The four groups for each variable were then created using the quartiles of these means. These four groups for each variable were termed "Low", "Low-Medium", "Medium–High" and "High".

Note that a prescriber was not necessarily in the same group for both outcome variables: that is, a prescriber could belong to the low-medium group with regards to the outcome variable that was the proportion of all opioids DDDs that were for OxyContin, but belong to the medium-high group with respect to the proportion of all strong opioid DDDs that were for OxyContin (this would be the case if the prescriber did not make many prescriptions for OxyContin compared to other opioids, but OxyContin represented most of the prescriptions for strong opioids) .

The statistical commands used for the fixed-effects models did not permit adjustment for autocorrelation between observations within a given prescriber, though robust standard errors were specified to help account for heteroscedasticity. However, using a similar model specification that allowed for autocorrelation, several models were run and no major differences were observed between the models specifying autocorrelation and the ones that did not. In addition, as presented in the results, the trend lines with regards to OxyContin prescribing were found to be quite smooth and the shifts in trend were quite significant, further suggesting that accounting for serial correlation would not substantially alter the calculated standard errors and ultimately the conclusions of this research.

All results from the fixed-effects models are presented in both table and figure format. The tables present the results from the logit-transformed fixed-effects models and the

coefficients for interval 1 are the coefficient for the slope in that time interval, while the coefficients for time intervals 2 and 3 represent the change in slope from the preceding interval. That is, these models indicate whether each peak in print media was followed by a change in prescribing trend as compared to before the peak. The figures present the predicted values from the models, but are no longer logit-transformed to improve interpretability. Importantly, however, the figures hide the heterogeneity between prescribers and trends in these figures reflect both between and within prescriber variation. The results of fixed-effects models presented in the tables, in contrast, examine the average within physician media effects, test for statistical significance and help account for heteroscedasticity. They also facilitate the examination of heterogeneity in the media effects by provider characteristics.

Statistical significance for all analyses was defined at the 2-sided p=0.05 level. All analyses were conducted using STATA IC 12.0.[103]

Table 4.1: Example of the ATC Classification System

ATC Classification	Description of ATC Classification	Level
N	Nervous System	1st level, anatomical main group
N**02**	Analgesics	2nd level, therapeutic subgroup
N02**A**	Opioids	3rd level, pharmacological subgroup
N02A**A**	Natural Opium Alkaloids	4th level, chemical subgroup
N02AA**01**	Morphine	5th level, chemical substance

Table 4.2: Defined Daily Doses (DDD), By ATC Code, Chemical and Route of Administration

ATC Code	Chemical	Administration Route	DDD
N02AA01	Morphine	Oral	100 mg
		Parenteral	30mg
		Rectal	30mg
N02AA03	Hydromorphone	Oral	20mg
		Parenteral	4mg
		Rectal	4mg
N02AA05	Oxycodone	Oral	75mg
		Parenteral	30mg
N02AB02	Pethidine (Meperidine)	Oral	400mg
		Parenteral	400mg
		Rectal	400mg
N02AB03	Fentanyl	Transdermal	1.2mg
N02AC04	Dextropropoxyphene Napsylate	Oral	0.3mg
	Dextropropoxyphene Chloride	Oral	0.2mg
N02AC54	Dextropropoxyphene Napsylate, Combinations	Oral	0.3mg
	Dextropropoxyphene Chloride, Combinations	Oral	0.2mg
N02AD01	Pentazocine	Oral Parenteral	200mg 200mg
N02AF02	Nalbuphine	Parenteral	80mg
N02AA59 N02AA79 N02BA51 N02BA7 N02BE51 M03BA53	Codeine, Combinations	Oral	100mg

Table 4.3: Prescriber Attributes and Categories

Prescriber Attribute And Categories	Notes
District Health Authority	Missing = 156 (3.7%) prescribers
Cape Breton District Health Authority	
Guysborough Antigonish Strait Health Authority	
Pictou County Health Authority	
Colchester East Hants Health Authority	
Cumberland Health Authority	
Annapolis Valley Health	
South Shore Health	
South West Health	
Capital Health	
Year of Graduation	Missing = 436 (10%) prescribers
1930 to 1949	
1950 to 1959	
1960 to 1969	
1970 to 1979	
1980 to 1989	
1990 to 1999	
2000 to 2007	
Specialty	Missing = 208 (4.9%) prescribers
General Practitioner	
Anesthesiologist	
Other	The "other" category encompassed 46 specialties: anatomic pathologists (n = 13), cardiologists (n = 34), community medicine specialists (n = 1), dental general practitioners (n = 514), dermatologists (n = 15), diagnostic radiologists (n = 43), emergency medicine specialists (n = 34), endocrinologists (n = 10), forensic medicine specialists (n = 1), gastroenterologists (n = 10), general pathologists (n = 1), general surgeons (n = 144), geriatric medicine specialists (n = 4), hematologists (n = 7), internists (n = 224), medical biochemists (n = 1), medical geneticists (n = 1), oncologists (n = 3), nephrologists (n = 1), neurologists (n = 42), neuropathologists (n = 3), nuclear medicine specialists (n = 4), obstetrician/gynecologists (n = 118), ophthalmologists (n = 63), oral and maxillofacial surgeons (n = 22), oral pathologists (n = 1), orthodontists (n = 5), orthopaedic surgeons (n = 71), otolaryngologists (n = 51), paediatricians (n = 101), pathologists (n = 1), pedodontists (n = 6), periodontists (n = 14), physical medicine and rehabilitation specialists (n = 23), plastic surgeons (n = 29), prosthodontists (n = 7), psychiatrists (n = 139), RCMP counselor (n = 1), radiation oncologists (n = 21), reproductive endocrinologists (n = 1), respiratory medicine specialists (n = 2), rheumatologists (n = 3), surgical oncologists (n = 1), thoracic surgeons (n = 2), urologists (n = 44) and vascular surgeons (n = 2).

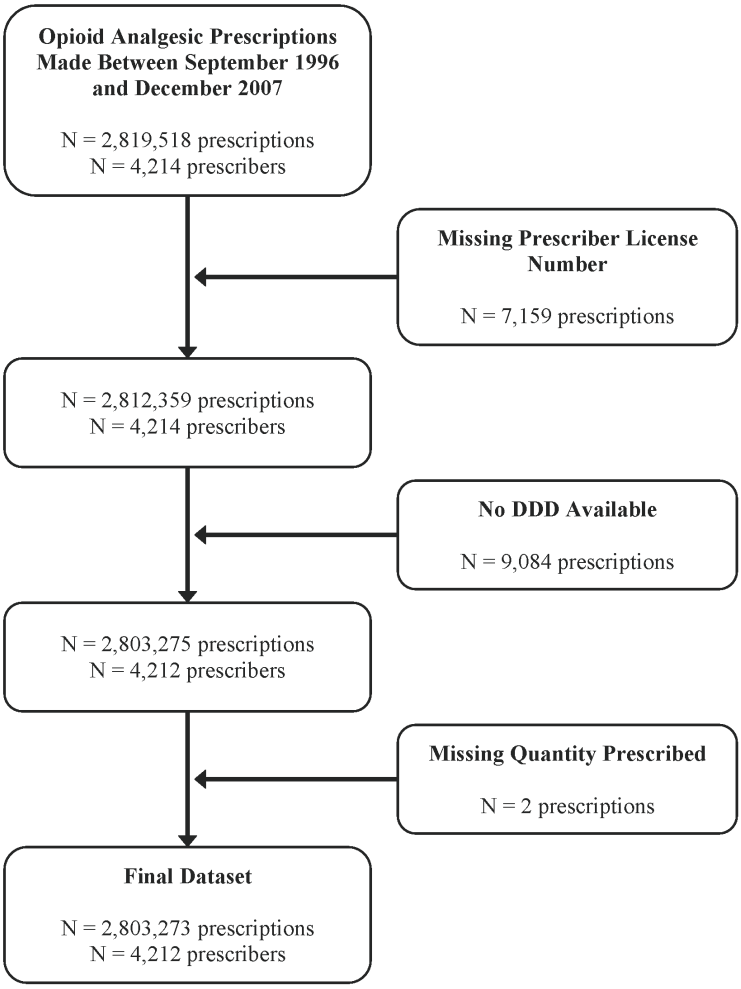

Figure 4.1: Flow Diagram of the Data Exclusion Process

CHAPTER 5: RESULTS

5.1 Descriptive Statistics: Print Media Data

There were a total of 924 newspaper articles published in 27 newspapers between 1995 and 2005 included in the sample. Six newspapers were Canadian and 21 were from the United States (a full list of the newspapers included can be found in Appendix B). One hundred and seventy-two articles (18.6%) were from Canadian newspapers. One hundred and forty-nine articles were from Nova Scotian newspapers (*The Chronicle Herald* and *The Cape Breton Post*), representing 86.6% of Canadian articles and 16.1% of all included articles. The earliest newspaper article was published in March of 2000, nearly four years after the approval of OxyContin in Canada. Over 95% of articles identified or discussed at least one problem related to OxyContin.

Figure 5.1 shows the total number of newspaper articles related to OxyContin published per month, while the total number of articles published per month in Canadian and American newspaper sources are shown in Figures 5.2 and 5.3. The peak in reporting in Canada occurred nearly three years after the evident peak in the American coverage of OxyContin. The peak in American coverage was largely due to a number of reports about increasing thefts and robberies of OxyContin. In Canada, the peak in print media coverage also centered on a series of thefts, as well as reports of overdose and deaths.

5.2 Descriptive Statistics: Prescriber Characteristics

There were a total of 4,212 prescribers who made at least one opioid prescription between 1996 and 2007 in Nova Scotia. These prescribers made a total of 2,803,273 opioid prescriptions to 461,585 unique patients.

The distribution of prescriber characteristics (specialty, decade of graduation from medical or dental school and District Health Authority of practice), as well as the total number of opioid prescriptions, strong opioid prescriptions and OxyContin prescriptions

according to these characteristics are shown in Table 5.1. Table 5.2 shows the average patient population per prescriber who received opioids as well as the number of prescriptions per patient according to these characteristics. For comparison, the total population of each District Health Authority (DHA) as of the 2006 Census is presented. (Note that the total population of Nova Scotia as of the 2006 Census was 913,465).[104]

Briefly, most prescribers were general practitioners (GPs) and over half of prescribers graduated from medical or dental school in 1990 or later (Table 5.1). General practitioners had the highest average number of patients over the whole study period, but anesthesiologists wrote prescriptions for more patients per month (Table 5.2). Most prescribers practiced in Capital District Health Authority and this is where the majority of prescriptions were written, though this is not surprising given that the Capital District Health Authority caters to nearly half of the province's population (Table 5.1). Of note, Cape Breton District Health Authority had many more OxyContin prescriptions per 1,000 population than any other DHA, as well as the most opioid prescriptions and strong opioid prescriptions per 1,000 population (Table 5.1).

There are a few points to note when examining these tables. Firstly, in terms of decade of graduation, most prescriptions in all categories were made among prescribers who graduated between 1970 and 1999. This intuitively makes sense, considering that a number of prescribers who graduated before these years may have retired between 1996 and 2007, and would therefore have fewer total opioid prescriptions in the data. Conversely, those who graduated in 2000 and sooner may not have been in practice as long as other prescribers in the dataset, and also had smaller numbers of prescriptions. Further, there were similar numbers of prescribers per capita in each of the DHAs, with the exception of Capital Distract Health Authority. This is not unexpected, since the province's capital, Halifax, is located in this DHA and is home to a number of hospitals and specialists not elsewhere available in the province. Additionally, there are some age distribution differences between DHAs (shown in Appendix D), where Capital Health has a younger population compared to the other District Health Authorities, and Cape Breton District Health Authority has one of the oldest populations.

5.3 Opioid Prescribing Over Time

It is important to examine any changing trends in OxyContin within the context of changing trends in overall opioid prescribing. Graphs for many of these trends can be found in Appendix E and are further broken down by prescriber DHA, specialty and decade of graduation. As a reminder, a defined daily dose (DDD) is the assumed average maintenance dose per day for a drug used for its main indication. Therefore the total number of DDDs per prescription represents the number of maintenance doses in that prescription. This measure was used to ensure comparability between prescriptions for different drugs with different ingredients and doses.

There were a total of 2,803,273 opioid prescriptions made in Nova Scotia to 461,585 patients between September 1996 and December 2007, of which 935,155 (33.4%) were prescriptions for strong opioids (Table 5.1). Overall, there were substantial increases in the numbers of prescriptions for opioids as well as the number of defined daily doses of opioids prescribed per month. These trends were partially driven by increasing prescriptions for strong opioids as well as the number of DDDs prescribed per opioid prescription. The majority of opioid prescriptions were made by general practitioners, and both the number of patients receiving opioid prescriptions and the number of prescribers of opioids increased over the study period. Of note, there did not appear to be any changes in these trends following the peaks in print media reporting around OxyContin in 2001 and 2004.

Between 1996 and 2007, there was a steady trend towards increasing prescribing of opioids, and the percent of these prescriptions that were for strong opioids. This reflected increases in both the number of patients and the number of prescribers. Notably, the number of prescribers who made at least one opioid prescription per month, the number of opioid prescriptions per month and the percent of all opioid prescriptions that were for strong opioids rose steadily between 1996 and 2007. The number of providers who made prescriptions per month rose from approximately 1,225 in late 1996 to nearly 1,475 in late 2007. The number of opioid prescriptions rose from approximately 18,000 per month

in September 1996 to 25,000 per month in December 2007. This increase in opioid prescribing was driven largely by increasing numbers of patients (from about 15,750 per month to 19,000 per month between 1996 and 2007) and from an increasing number of prescriptions for strong opioids. In addition, the percent of all opioid prescriptions that were for strong opioids rose steadily from just under 15% to over 55%, with a corresponding drop in the total number of prescriptions for weak opioids over the same time period (Figure E.1 in Appendix E).

Concurrent with the increasing numbers of opioids prescriptions were increases in the number of defined daily doses of opioids prescribed. The total number of opioid DDDs prescribed per month between 1996 and 2007 increased steadily, from just over 300,000 DDDs per month to nearly 600,000 DDDs per month. Moreover, there were changes in the volume of opioids prescribed per prescription. There was an overall increase in the number of DDDs prescribed per prescription until mid 2006, at which point the number of DDDs declined. These increases and decreases reflect changes in the total amount of opioid per prescription, either in terms of the strength of the opioid or the volume prescribed (number of tablets or total volume of injection liquid, for example). The steady decline in the number of DDDs per prescription starting in 2006, therefore, suggests a trend towards either weaker doses of opioids or prescriptions for shorter durations.

Of note, the total number of GPs that made prescriptions for opioids increased steadily over the study period, from approximately 710 in 1996 to 960 in 2007. In contrast, the number of anesthesiologists who wrote at least one prescription for opioids per month was relatively stable over all months, ranging between 6 and 13. This was also the case for the “other” category, in which the number of prescribers per month was generally stable around 500.

5.4 OxyContin Prescribing Over Time

To contextualize the information presented in this section, the figures (Figures 5.4 to 5.21) are overlaid with the trends in print media reporting of OxyContin: the dotted gray lines indicate the start of the media peaks and the solid gray lines indicate the absolute peaks.

There were 58,482 prescriptions for OxyContin between 1996 and 2007, representing 2.1% of all opioid prescriptions and 6.3% of all strong opioid prescriptions. This corresponds to a total of 2,421,020 DDDs of OxyContin prescribed. The total number of OxyContin prescriptions per month increased steadily until late 2003 (to a peak of 800 prescriptions per month), then declined until mid 2006 (to less than 600 prescriptions per month), only to increase once more until the end of the study period (see Figure E.7 in Appendix E). Importantly, this dip in prescribing followed the Canadian peak in print media reporting in 2003/2004.

The prescribing of OxyContin, as a proportion of all opioid prescriptions and strong opioid prescriptions, was associated with the peak in Canadian media reporting of OxyContin in 2003. Between 1996 and 2007, the proportion of all opioid prescriptions and strong opioid prescriptions that were for OxyContin generally increased until 2003, then dipped and increased once more until December 2007 (Figure E.5 in Appendix E). These same patterns were also observed when the proportion of all opioid DDDs and all strong opioid DDDs that were for OxyContin were examined (Figure 5.4).

There were also increases in the volume of OxyContin prescribed per prescription (Figures E.8 and E.9). In particular, there were steady increases in the average number of DDDs of OxyContin per OxyContin prescription until the end of 2005, indicating that over this time, either the number of pills of OxyContin prescribed per prescription increased or the strength of the OxyContin being prescribed increased, or possibly some combination of the two. In fact, the increase in the mean DDDs of OxyContin per prescription was driven largely by increases in the quantity prescribed (i.e. the number of

tablets), rather than increases in the strength of OxyContin prescribed. The increases in the number of tablets per OxyContin prescription is likely a reflection of a greater numbers of days supply per prescription. Interestingly, there was a significant drop in the number of DDDs of OxyContin per OxyContin prescription starting in 2006, which appears to be related to overall decreases in the mean quantity (i.e. number of pills) prescribed per prescription (Figures E.8 and E.9). These changes in volume did not appear to correspond with peak media reporting of OxyContin.

In summary, it appears that changing trends in OxyContin prescribing between 1996 and 2007 were concurrent with peak print media reporting of OxyContin, especially in Canada. Changing trends with respect to the number of defined daily doses of OxyContin prescribed were driven largely by changing numbers of prescriptions, rather than changes in the quantity or strength prescribed. While the number of OxyContin DDDs prescribed per month generally increased until 2003 then leveled off, the mean proportion of strong opioid DDDs that was for OxyContin increased until late 2003, then decreased steadily until the end of the study period. This suggests that OxyContin was increasingly replaced with prescriptions for other strong opioids, a trend that followed the peak in Canadian media reporting in 2003/2004.

5.4.1 By District Health Authority

There was variation in the apparent media effect on OxyContin prescribing by District Health Authority, with the smallest effects observed in Capital Health, South Shore Health and South West Health and the largest effects noted in Cape Breton District Health Authority (Figure 5.5a-c and 5.6a-c). There were increases in the proportion of all opioid DDDs and strong opioid DDDs that were for OxyContin in Cape Breton District Health Authority up until approximately March 2003, at which point there began a steady decline in these proportions. In contrast, all other DHAs generally show increases in the proportion of all opioid DDDs and strong opioid DDDs that were for OxyContin until late 2003, at which point these proportions leveled off. Of note, the upswing in print media reporting around OxyContin in Canada began in early 2003.

5.4.2 By Specialty

Differences by specialty were noted in the effect of media attention on OxyContin and subsequent prescribing practices (Figures 5.7 and 5.8). While there were changes in both outcome variables in all specialties, these changes were most pronounced among anesthesiologists. It is important to note that the scale of these figures mutes some of the media effects for general practitioners and other specialists, which are examined in more detail in subsequent sections.

The most marked changes in both the proportion of all opioid DDDs prescribed that were for OxyContin (Figure 5.7) and the proportion of strong opioid DDDs for OxyContin (Figure 5.8) following peak media reporting were among anesthesiologists. These proportions appeared to have generally increased then decreased among GPs and other specialists, albeit only moderately. Among anesthesiologists, in contrast, the proportion of all opioid DDDs for OxyContin rose rapidly from close to zero in 1998 to nearly 0.5 in mid to late 2003, only to decrease steadily to around 0.2 over the remainder of the study period (Figure 5.7). A similar pattern was observed in the proportion of strong opioid DDDs that were for OxyContin prescribed by anesthesiologists (Figure 5.8). Once again, these peaks in prescribing generally correspond with the increased media attention that OxyContin received in 2003.

5.4.3 By Decade of Graduation

The peaks in print media reporting of OxyContin also had different effects on prescribers who graduated in different decades (Figures 5.9 and 5.10). The greatest effects were noted among prescribers who graduated in the 1960s, while the smallest effects were observed in prescribers who graduated between 1930 and 1959.

With regards to both the proportion of all opioid DDDs prescribed that were for OxyContin (Figures 5.9a and 5.9b) and the proportion of all strong opioid DDDs that were for OxyContin (Figure 5.10a and 5.10b), the most notable changes in these proportions were among prescribers who graduated between 1960 and 1969, with both

proportions increasing until mid 2002 to early 2003, then decreasing. Among prescribers who graduated in 1970 and later, both of these proportions increased over the study period, while they generally decreased among prescribers who graduated between 1930 and 1959.

5.5 Effect of Print Media on Prescribing Practices of OxyContin

Conditional fixed-effects statistical analyses confirmed that there were significant changes in the prescribing of OxyContin in relation to trends in media reporting about the drug. Within prescribers, there were significant changes in OxyContin prescribing following print media peaks both in terms of the average proportion of all opioid DDDs and the average proportion of all strong opioid DDDs that were for OxyContin (Table 5.3). Additionally, these effects were largely restricted to higher volume prescribers (Table 5.4).

Recall that interval 1 represents the time period between January 2000 and January 2001 (the time period prior to heavy media coverage of OxyContin), interval 2 covers February 2001 to April 2003 (the time period after the American peak in print media reporting) and interval 3 is between May 2003 and December 2007 (the time period after the peak in Canadian reporting). Results in this section are presented in both table and figure format. The tables present the results from the logit-transformed fixed-effects models and the coefficients for interval 1 are the coefficients for the slope indicating the average change in prescribing in that time interval, while the coefficients for time intervals 2 and 3 represent the change in slope from the preceding interval. That is, these models indicate whether each peak in media was followed by a change in prescribing trend as compared to before the peak. The figures present the predicted values (rather than the change in slope) from the models, but are no longer logit-transformed to improve interpretability. Importantly, however, the figures hide the heterogeneity between prescribers and trends in these figures reflect both between and within prescriber variation. The results of fixed-effects models presented in the tables, in contrast, examine the average within physician

media effects, test for statistical significance and help account for heteroscedasticity. They also facilitate the examination of heterogeneity in the media effects by provider characteristics (the results of which are presented in subsequent sections).

It is also important to note that the proportion of all opioid DDDs and strong opioid DDDs that were for OxyContin appear to be much lower in the figures presented in this section compared to those in previous sections. This is partly a result of the logit transformation, but also that the data is relatively skewed with a high number of prescribers having a value of zero for one or both of these proportions in any given month.

There were noticeable differences in prescribing of OxyContin following both the American and Canadian peaks in reporting, as evidenced in Table 5.3 and Figure 5.11. For interval 1 (prior to the media peaks) the proportion of DDDs that were for OxyContin increased steadily ($p<0.0001$ for both outcome variables). Following the American media peak, as measured in interval 2, the use of OxyContin continued to increase, but a noticeably slower rate than in interval 1 ($p=0.005$ and $p=0.001$). In interval 3, following the Canadian media peak, the proportion of DDDs that were for OxyContin declined significantly ($p<0.0001$) compared to interval 2. This decrease was even more pronounced when OxyContin prescribing was measured as the proportion of all DDDs that were for strong opioids ($p<0.0001$), with roughly a 30% decline in this proportion within prescribers (Figure 5.11).

The effects of the print media on OxyContin prescribing by prescriber volume were also examined and it was found that the effects were mostly concentrated among high volume prescribers. As a reminder, to create these volume groups, the mean of each of the two outcome variables across all months per prescriber were calculated. The four groups for each variable were then created using the quartiles of these means. These four groups for each variable were termed “Low”, “Low-Medium”, “Medium–High” and “High”. Of note, a prescriber was not necessarily in the same group for both outcome variables and

in these models, prescribers who never made a prescription for OxyContin were not included, since their values of the outcome variables were zero at all time points.

Notably, the average within-prescriber effects of the print media on OxyContin prescribing were concentrated among prescribers who had higher proportions of DDDs that were for OxyContin, as shown in Table 5.4 and Figures 5.12 and 5.13. Specifically, there were no changes in the proportion of all opioid DDDs and strong opioid DDDs that were for OxyContin in any interval for the lowest volume group and only a few changes were noted in the low-medium volume group (Table 5.4). In the medium-high group, significant effects were observed in interval 3, where the proportion of both all opioid DDDs and strong opioid DDDs that were for OxyContin decreased ($p<0.0001$ and $p=0.0346$)). In the highest volume group, there were significant effects in all intervals. In this group, both proportions increased in interval 1 ($p<0.0001$ for both variables), continued to increase in interval 2 but at a slower rate compared to interval 1 ($p=0.0060$ and $p=0.0006$), then decreased significantly in interval 3 ($p<0.0001$ for both outcomes variables) (Figures 5.12 and 5.13). It therefore appears that the higher volume prescribers were most influenced by the print media around OxyContin when compared to their lower volume peers.

5.5.1 By District Health Authority

The average effect of the media reporting of OxyContin on prescribing of the drug was not consistent across prescribers in different District Health Authorities (Table 5.5 and Figures 5.14a-b and 5.15a-b). There were changes in OxyContin prescribing among prescribers in some DHAs following the American peak in media reporting of OxyContin, while different DHAs showed changes in prescribing following the Canadian peak in media. These changes are depicted in Figures 5.14 and 5.15 and Table 5.5. Further analyses using interaction terms tested whether these changes following media peaks were significantly different between District Health Authorities, with Capital Health (DHA 9) serving as the referent group (Table F.1 in Appendix F). The most noticeable differences in both outcome variables were observed between Capital Health

and Guysborough Antigonish Strait Health Authority (p=0.004 and p=0.008) and Cape Breton District Health Authority (p<0.0001 for both outcome variables), but only in interval 2.

As shown in Figures 5.14 and 5.15, a considerable amount of the change in prescribing was observed in providers in Cape Breton District Health Authority. For example, there was a sharp rise in Cape Breton District Health Authority in the proportion of all opioid DDDs prescribed that were for OxyContin up to 0.9% in interval 1, followed by a slower increase up to 1.5% in interval 2 (Figure 5.14b). In interval 3, following the Canadian peak in print media reporting, this trend was reversed and the proportion of all opioid DDDs that were for OxyContin decreased to around 0.6% by 2007.

5.5.2 By Specialty

Significant effects with regards to both outcome variables in interval 2 were noted in both anesthesiologists and general practitioners, and in interval 3, significant changes were noted for both outcome variables for all specialty categories (Table 5.6). Figures 5.16 and 5.17 graphically represent these changes by specialty. Because the changes in the proportions of all opioid DDDs and strong opioid DDDs that were for OxyContin following peak media reporting were so much larger in anesthesiologists than for general practitioners and other specialists, additional figures (Figures 5.18 and 5.19) were generated with only the predicted regression lines for general practitioners and other specialists to enhance the visibility of the changes in these proportions.

Among anesthesiologists, both the proportion of all opioid DDDs and strong opioid DDDs that were for OxyContin increased in interval 1, decreased significantly in interval 2 compared to interval 1, then decreased at a significantly faster rate in interval 3 as compared to interval 2. These same patterns were also observed in general practitioners (Figures 5.18 and 5.19). Among other specialists, the only statistically significant effects of the media on OxyContin prescribing were noted following the Canadian media peak in interval 3, in which both the proportion of all opioid DDDs that were for OxyContin and

the proportion of strong opioid DDDs that were for OxyContin decreased relative to interval 2.

The average effects of print media reporting of OxyContin on changes in prescribing were not consistent between specialties. Notably, the changes in prescribing of OxyContin within anesthesiologists were significantly larger than the changes within general practitioners (the referent group) (Table F.2). In interval 2, the average proportion of all opioid DDDs that were for OxyContin decreased among anesthesiologists, while this proportion increased among general practitioners. In interval 3, both the proportion of all opioid DDDs and strong opioid DDDs that were for OxyContin decreased in both anesthesiologists and general practitioners compared to interval 2, but the average decrease was much more substantial in anesthesiologists compared to general practitioners (as evidenced in Figures 5.16 and 5.17). There were also differences between general practitioners and other prescribers in intervals 1 and 3, but only with respect to the proportion of all opioid DDDs that were for OxyContin. In interval 1, the proportion of all opioid DDDs that were for OxyContin increased much more among general practitioners compared to other specialists. In interval 3, this proportion decreased much more in interval 3 relative to interval 2 among general practitioners compared to other specialists (Figure 5.18).

5.5.3 By Decade of Graduation

The average changes in prescribing of OxyContin following media attention within providers with regards to both outcome variables of interest were generally restricted to those who graduated between the years of 1960 and 1999 (Table 5.7). Among prescribers who graduated between 1970 and 1989, the proportions of all opioid DDDs and strong opioid DDDs that were for OxyContin increased significantly in interval 1, continued to increase in interval 2 but at a slower rate compared to interval 1, then decreased significantly in interval 3 (Table 5.7 and Figures 5.20 and 5.21). Among prescribers who graduated in the 1990s, both proportions increased across all intervals, though the rate of increase slowed in both intervals 2 and 3 relative to the preceding intervals. These results

suggest that prescribers who graduated between 1960 and 1999 were early adopters (i.e. prescribed more OxyContin earlier), but were also the group that had the greatest average within-prescriber changes in subsequent intervals, suggesting they were more impacted by the media attention on OxyContin.

Few differences in changes within prescribers of different decades of graduation emerged (Table F.3 in Appendix F). For these analyses, prescribers who graduated between 1980 and 1989 were the referent group. Generally, only prescribers who graduated in the years 1950 to 1959 and between 2000 and 2007 showed significant differences from the referent group. Indeed, across all graduation decades, it was generally the case that prescribing of OxyContin increased in interval 1, continued to increase in interval 2 but at a slower rate than interval 1, then declined in interval 3 compared to interval 2 as a result of the Canadian peak in media reporting (Figures 5.20 and 5.21).

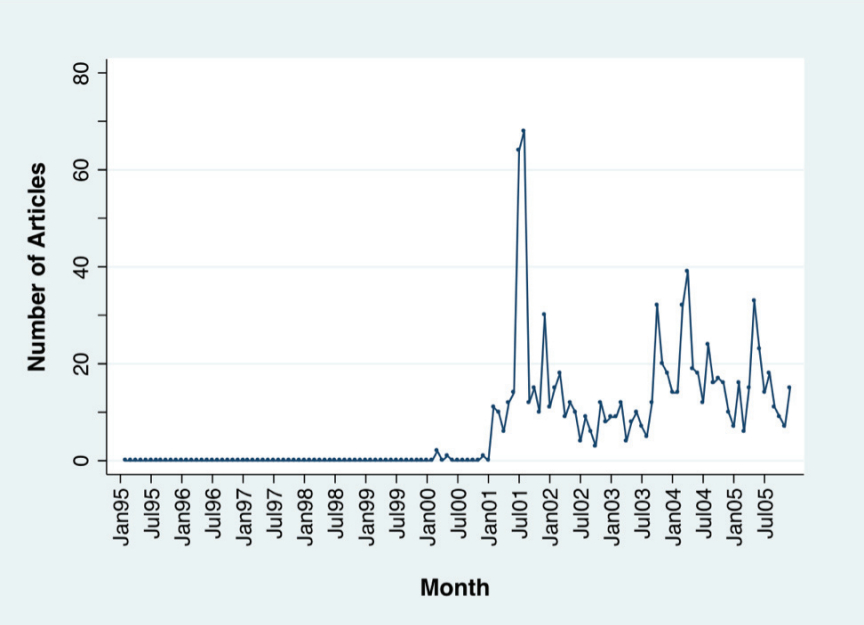

Figure 5.1: Total Number of Newspaper Articles Pertaining to OxyContin Published per Month, 1995 to 2005

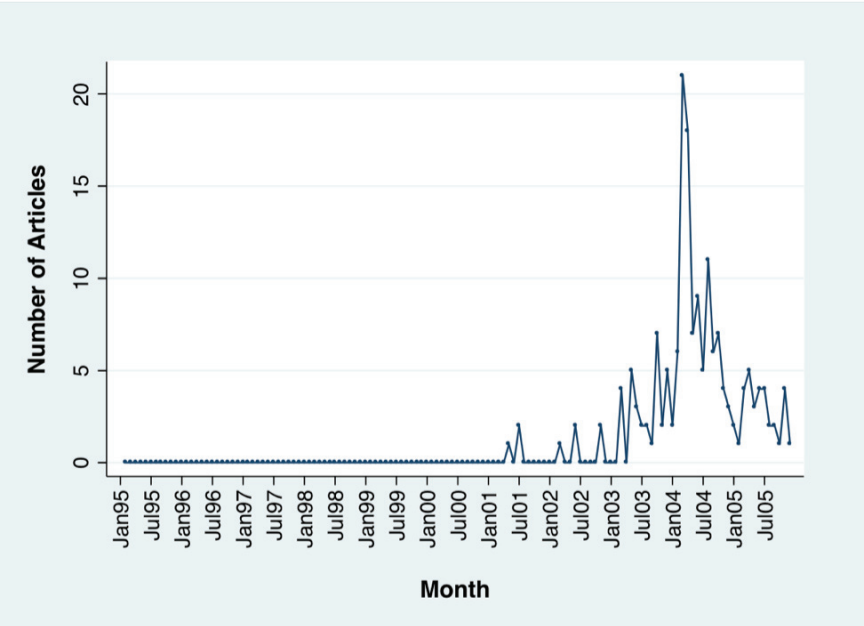

Figure 5.2: Total Number of Canadian Newspaper Articles Pertaining to OxyContin Published per Month, 1995 to 2005

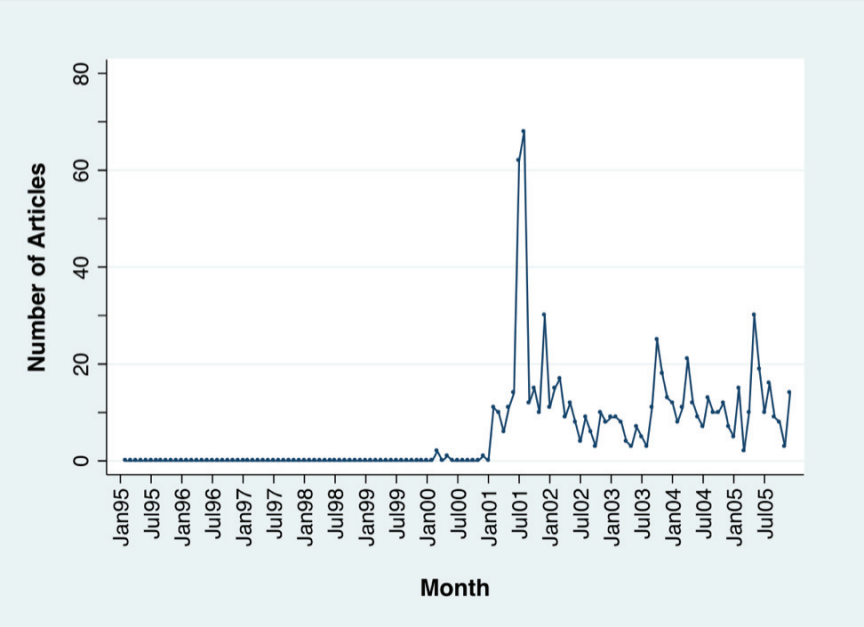

Figure 5.3: Total Number of American Newspaper Articles Pertaining to OxyContin Published per Month, 1995 to 2005

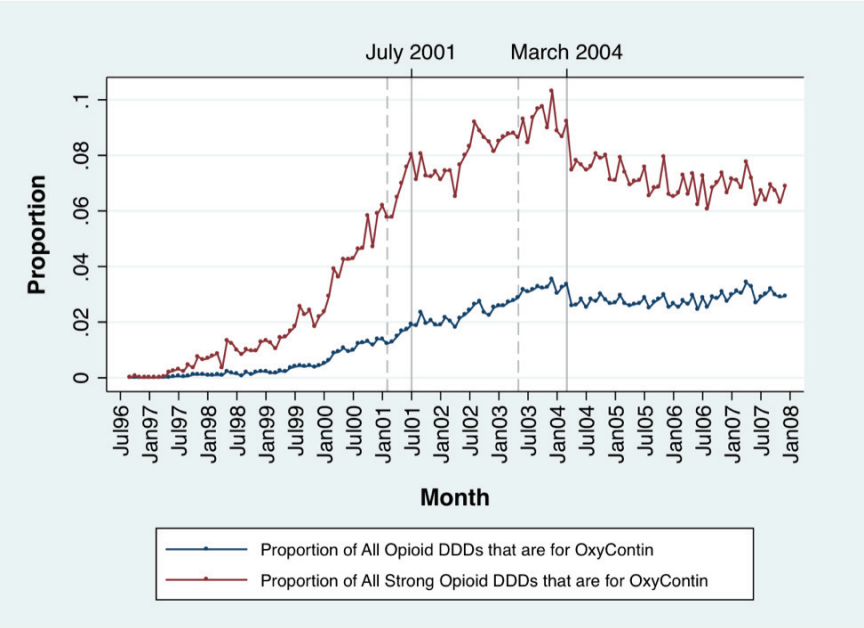

Figure 5.4: Mean Proportion of All Opioid DDDs Prescribed and Strong Opioid DDDs Prescribed That Were for OxyContin, per Prescriber per Month, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

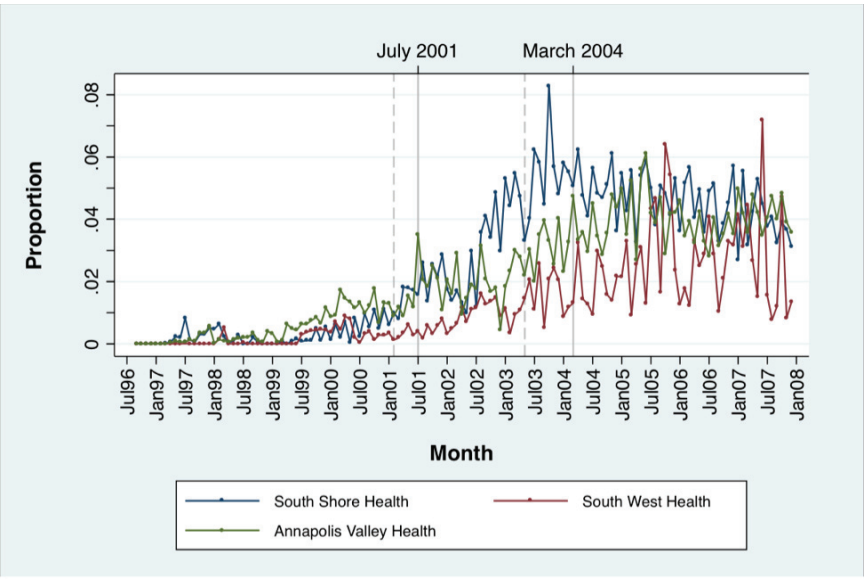

Figure 5.5a: Proportion of All Opioid DDDs That Were for OxyContin per Month, by District Health Authority, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

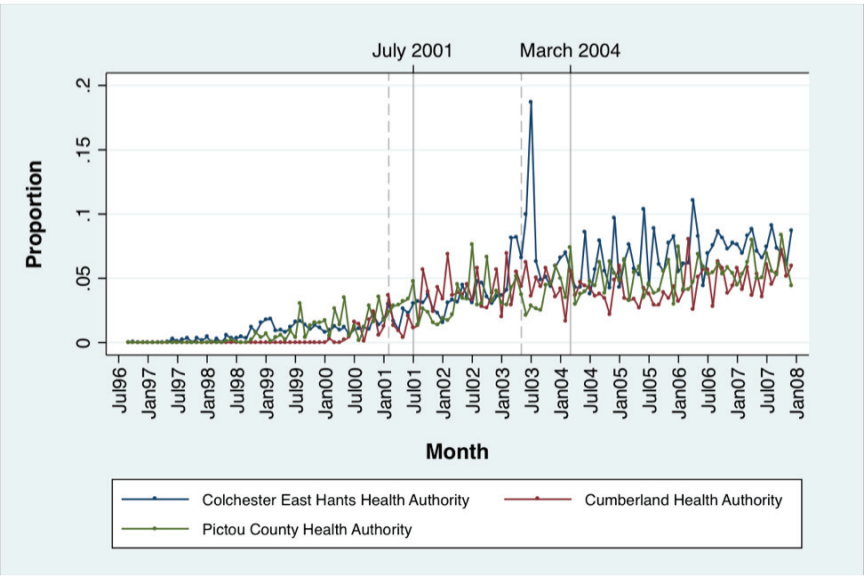

Figure 5.5b: Proportion of All Opioid DDDs That Were for OxyContin per Month, by District Health Authority, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

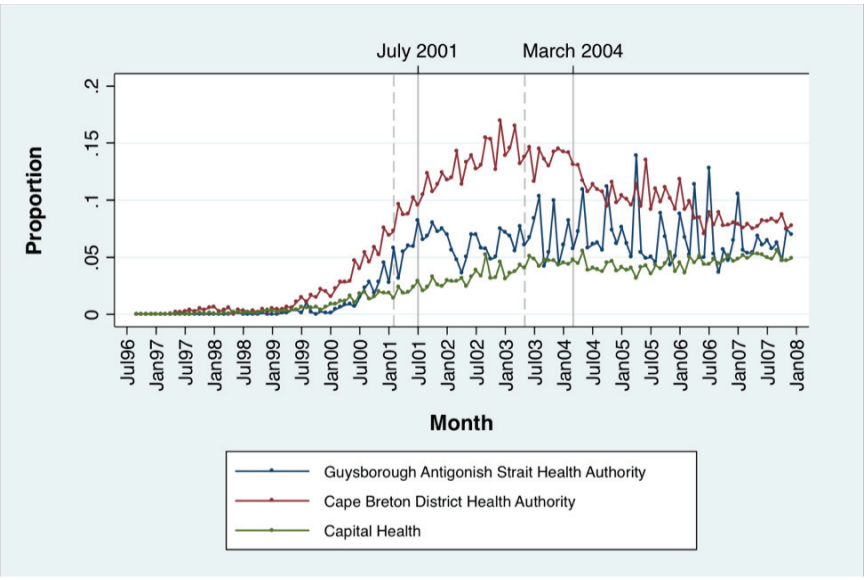

Figure 5.5c: Proportion of All Opioid DDDs That Were for OxyContin per Month, by District Health Authority, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

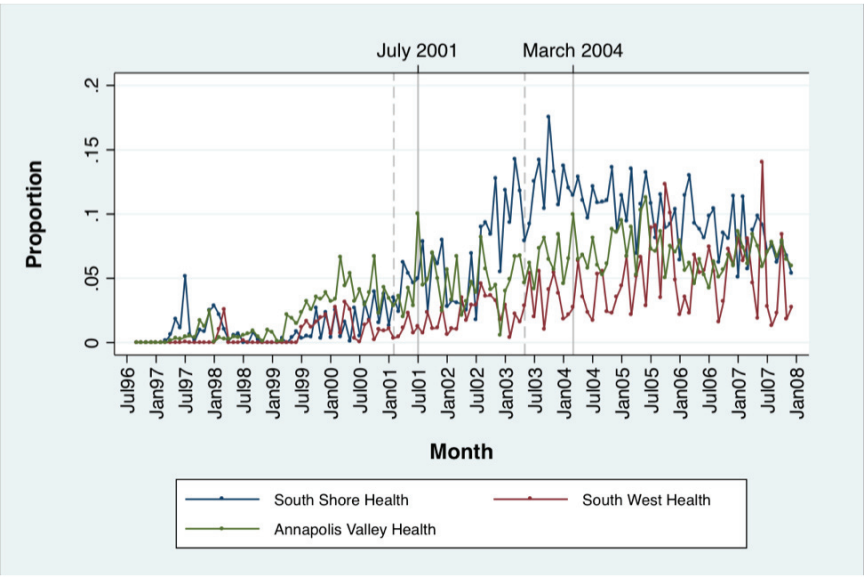

Figure 5.6a: Proportion of Strong Opioid DDDs That Were for OxyContin per Month, by District Health Authority, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

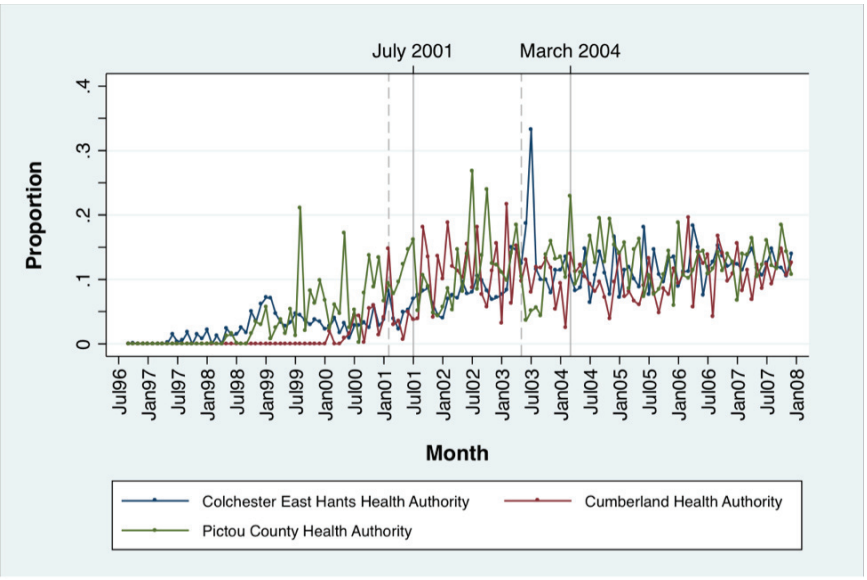

Figure 5.6b: Proportion of Strong Opioid DDDs That Were for OxyContin per month, by District Health Authority, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

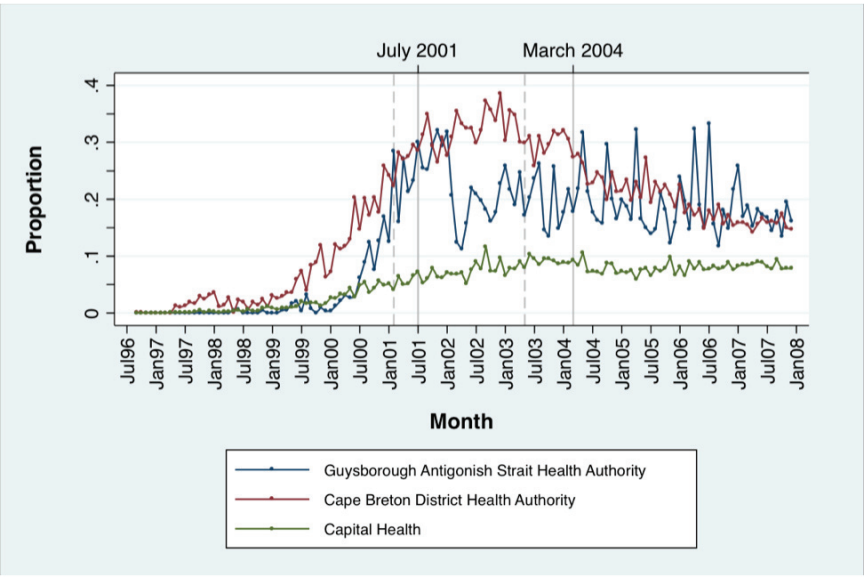

Figure 5.6c: Proportion of Strong Opioid DDDs That Were for OxyContin per Month, by District Health Authority, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

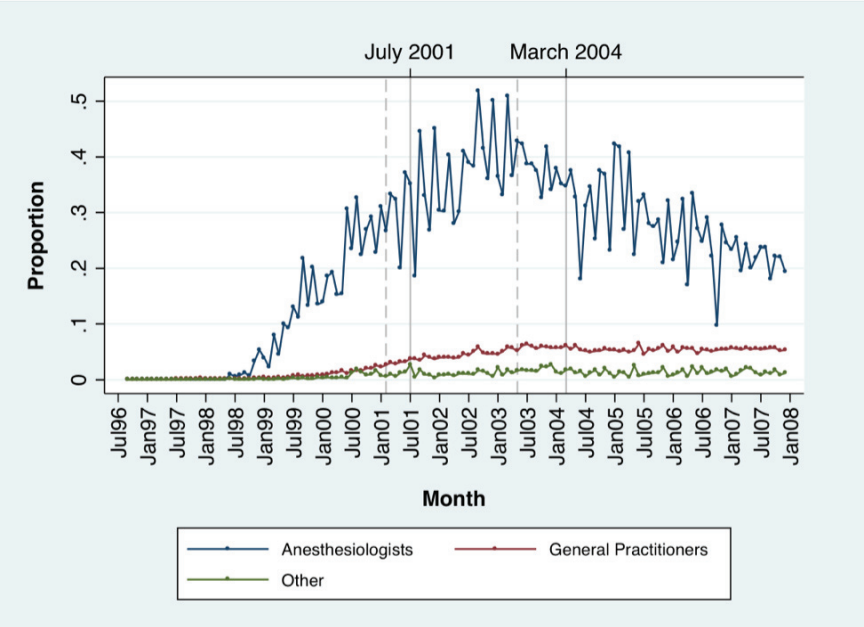

Figure 5.7: Proportion of All Opioid DDDs That Were for OxyContin per Month, by Specialty, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

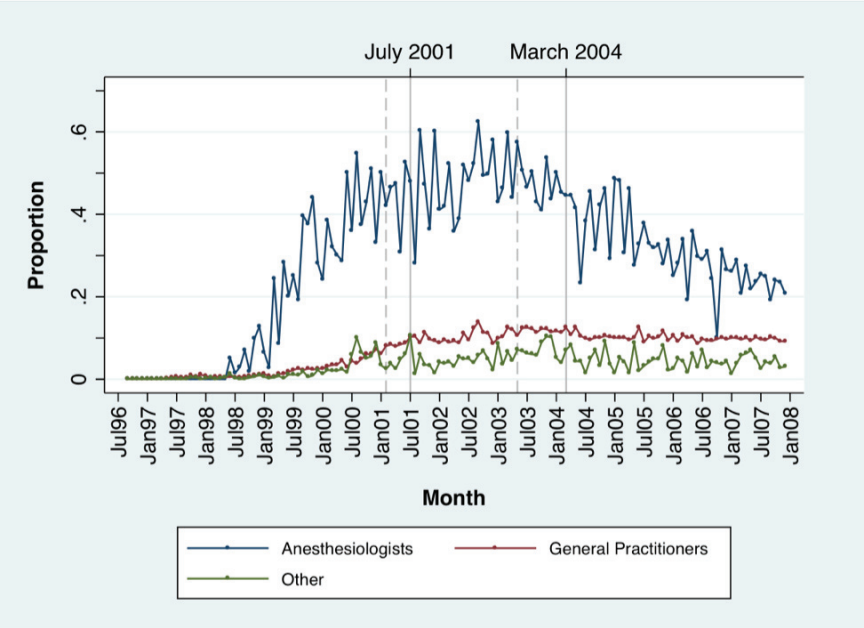

Figure 5.8: Proportion of Strong Opioid DDDs That Were for OxyContin per Month, by Specialty, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

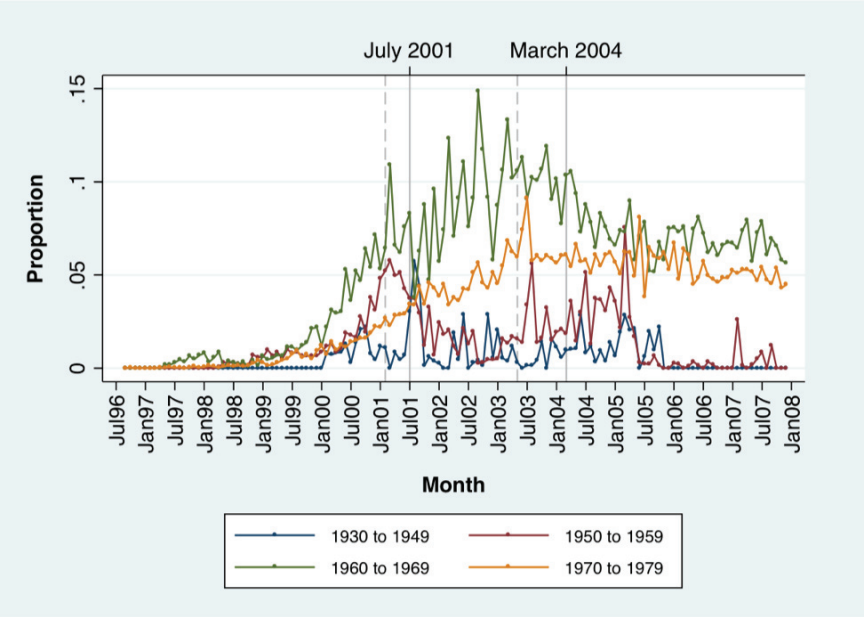

Figure 5.9a: Proportion of All Opioid DDDs That Were for OxyContin per Month, by Decade of Graduation, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

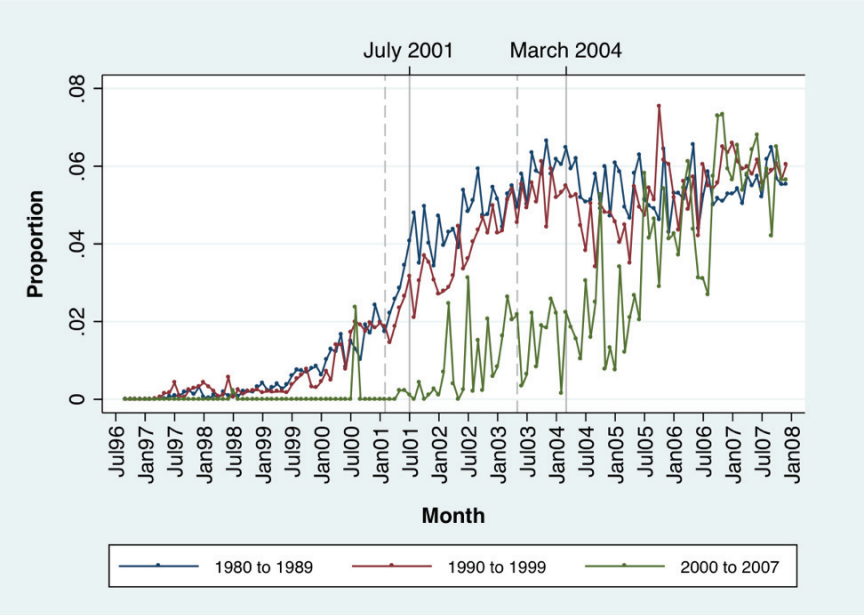

Figure 5.9b: Proportion of All Opioid DDDs That Were for OxyContin per Month, by Decade of Graduation, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

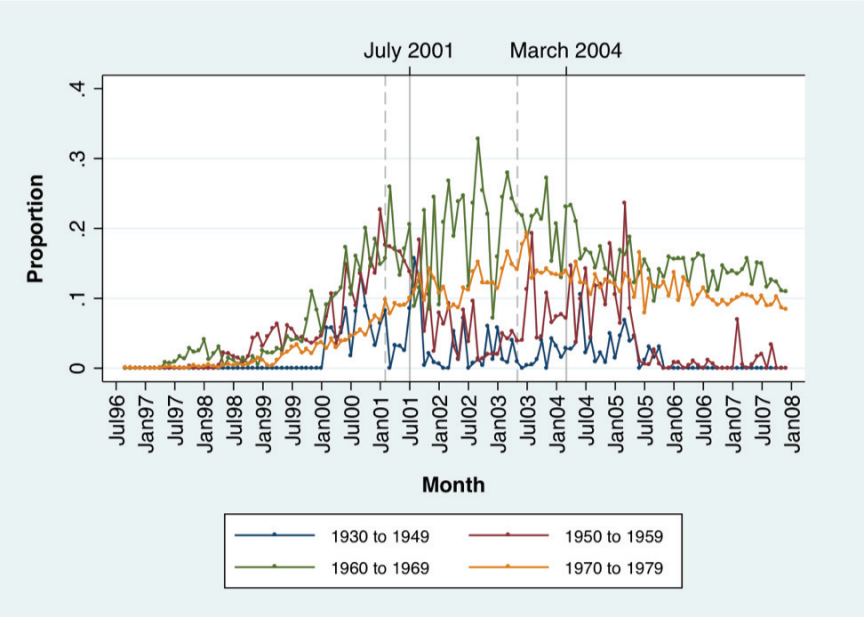

Figure 5.10a: Proportion of Strong Opioid DDDs That Were for OxyContin per Month, by Decade of Graduation, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

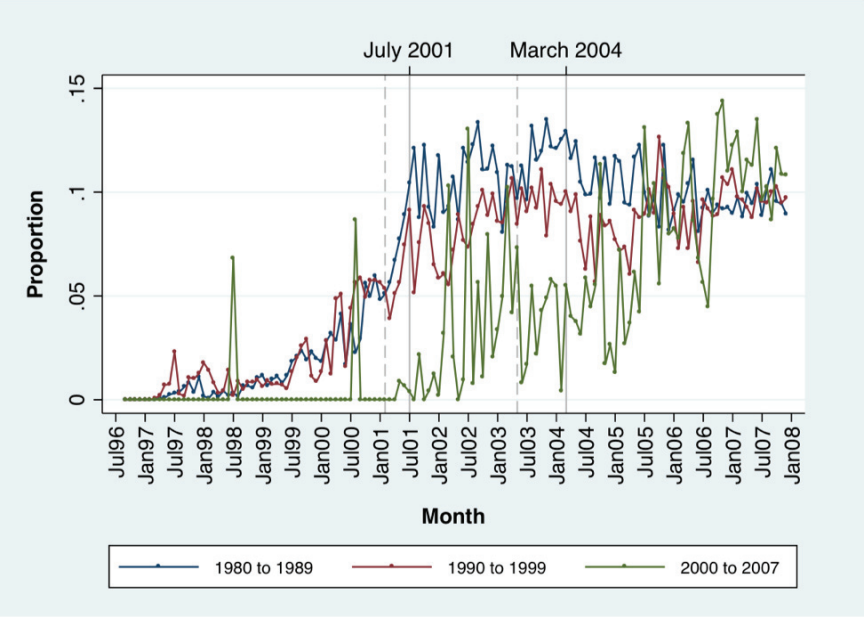

Figure 5.10b: Proportion of Strong Opioid DDDs That Were for OxyContin per Month, by Decade of Graduation, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

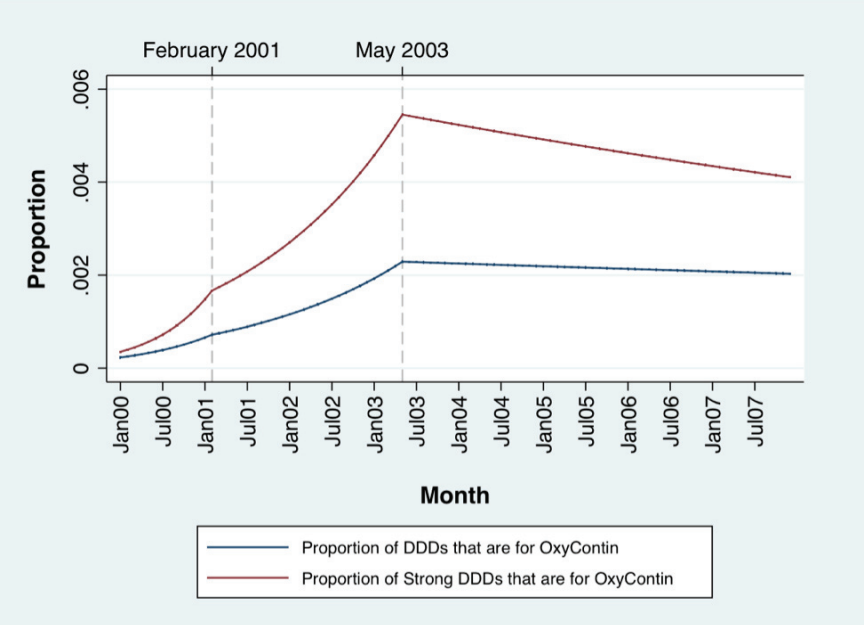

Figure 5.11: Predicted Fitted Regression Lines for the Proportion of All Opioid DDDs and Strong Opioid DDDs That Were for OxyContin

Note: The dotted lines represent the knots in the splines, which were set at February 2001 and May 2003 to correspond with the beginning of the peaks in media.

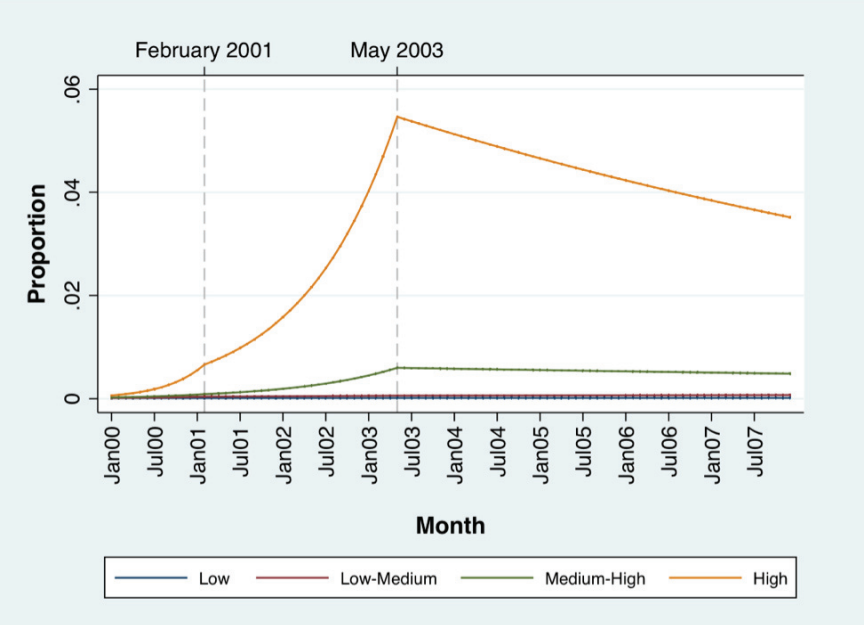

Figure 5.12: Predicted Fitted Regression Lines for the Proportion of All Opioid DDDs That Were for OxyContin, by Prescriber Volume

Note: The dotted lines represent the knots in the splines, which were set at February 2001 and May 2003 to correspond with the beginning of the peaks in media.

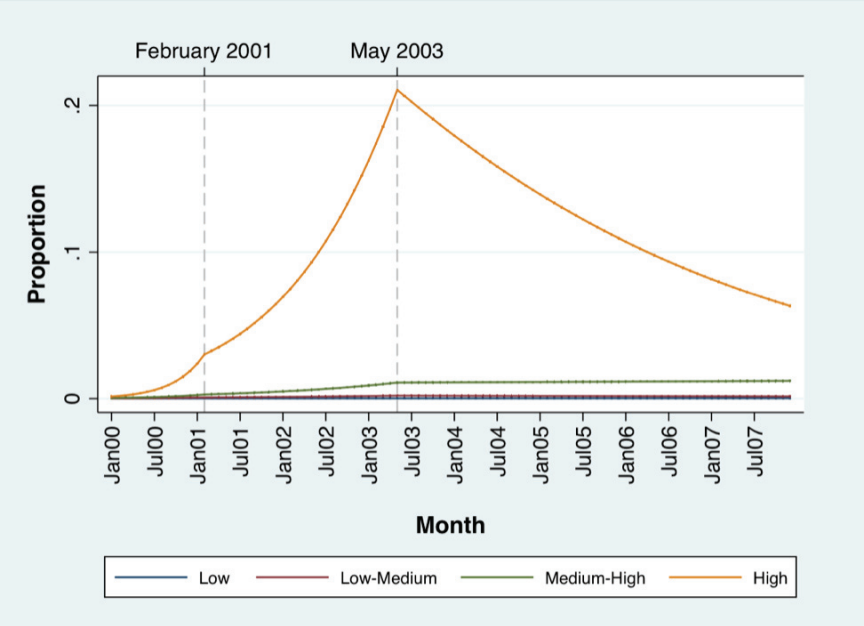

Figure 5.13: Predicted Fitted Regression Lines for the Proportion of Strong Opioid DDDs That Were for OxyContin, by Prescriber Volume

Note: The dotted lines represent the knots in the splines, which were set at February 2001 and May 2003 to correspond with the beginning of the peaks in media.

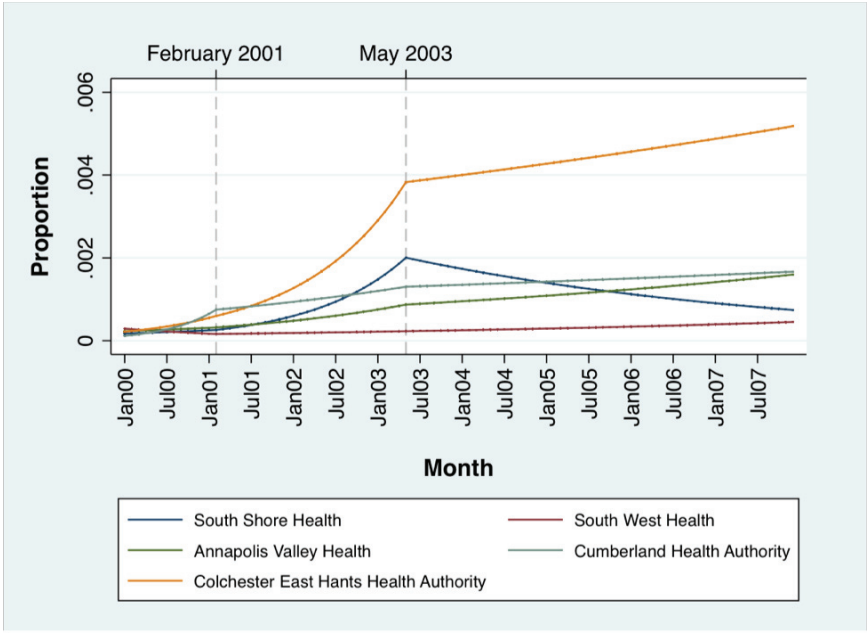

Figure 5.14a: Predicted Fitted Regression Lines for the Proportion of All Opioid DDDs That Were for OxyContin, by District Health Authority

Note: The dotted lines represent the knots in the splines, which were set at February 2001 and May 2003 to correspond with the beginning of the peaks in media

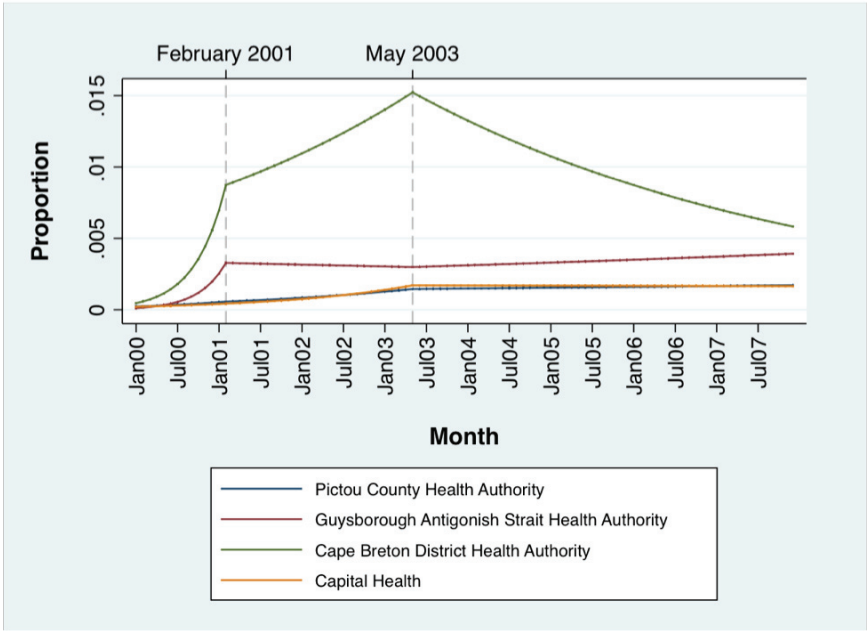

Figure 5.14b: Predicted Fitted Regression Lines for the Proportion of All Opioid DDDs That Were for OxyContin, by District Health Authority

Note: The dotted lines represent the knots in the splines, which were set at February 2001 and May 2003 to correspond with the beginning of the peaks in media.

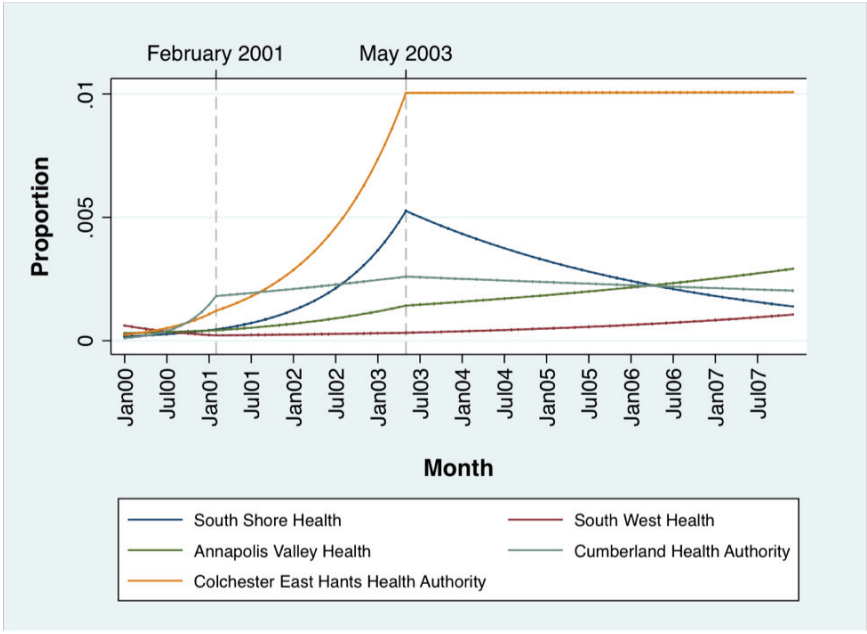

Figure 5.15a: Predicted Fitted Regression Lines for the Proportion of Strong Opioid DDDs That Were for OxyContin, by District Health Authority

Note: The dotted lines represent the knots in the splines, which were set at February 2001 and May 2003 to correspond with the beginning of the peaks in media.

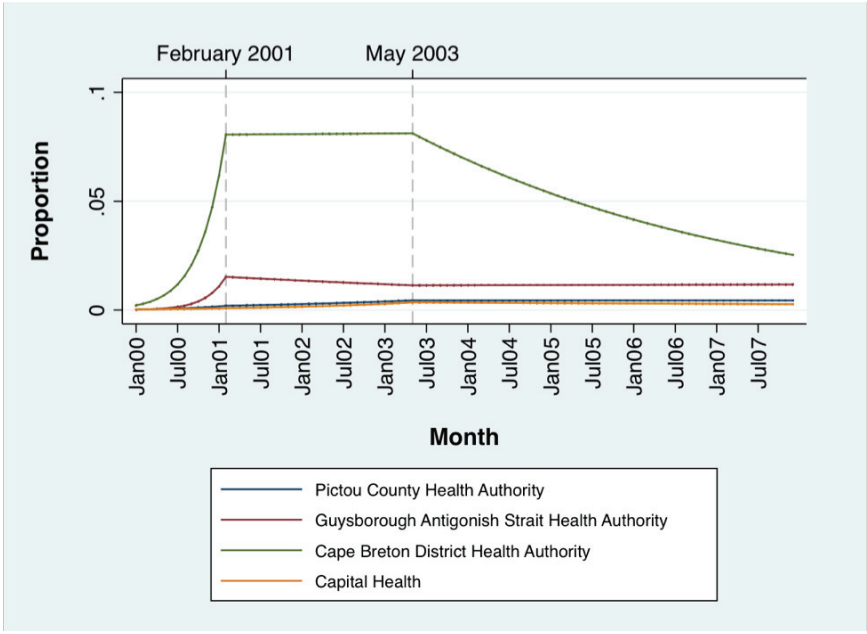

Figure 5.15b: Predicted Fitted Regression Lines for the Proportion of Strong Opioid DDDs That Were for OxyContin, by District Health Authority

Note: The dotted lines represent the knots in the splines, which were set at February 2001 and May 2003 to correspond with the beginning of the peaks in media.

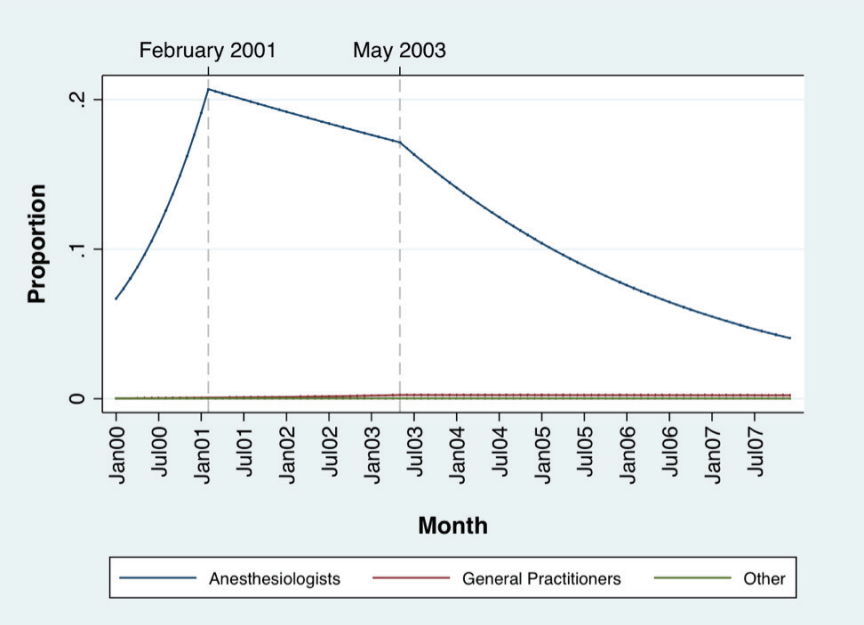

Figure 5.16: Predicted Fitted Regression Lines for the Proportion of All Opioid DDDs That Were for OxyContin, by Specialty

Note: The dotted lines represent the knots in the splines, which were set at February 2001 and May 2003 to correspond with the beginning of the peaks in media.

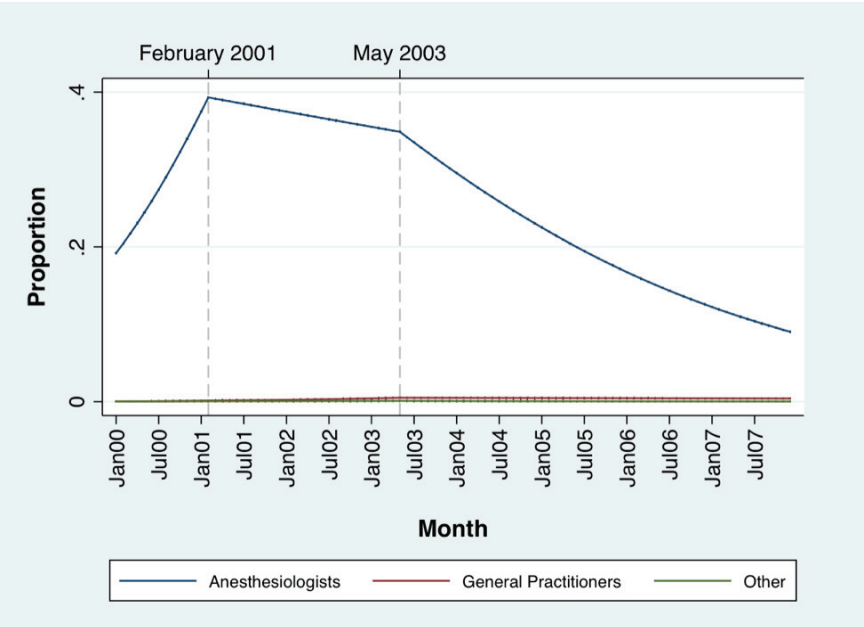

Figure 5.17: Predicted Fitted Regression Lines for the Proportion of Strong Opioid DDDs That Were for OxyContin, by Specialty

Note: The dotted lines represent the knots in the splines, which were set at February 2001 and March 2003 to correspond with the beginning of the peaks in media.

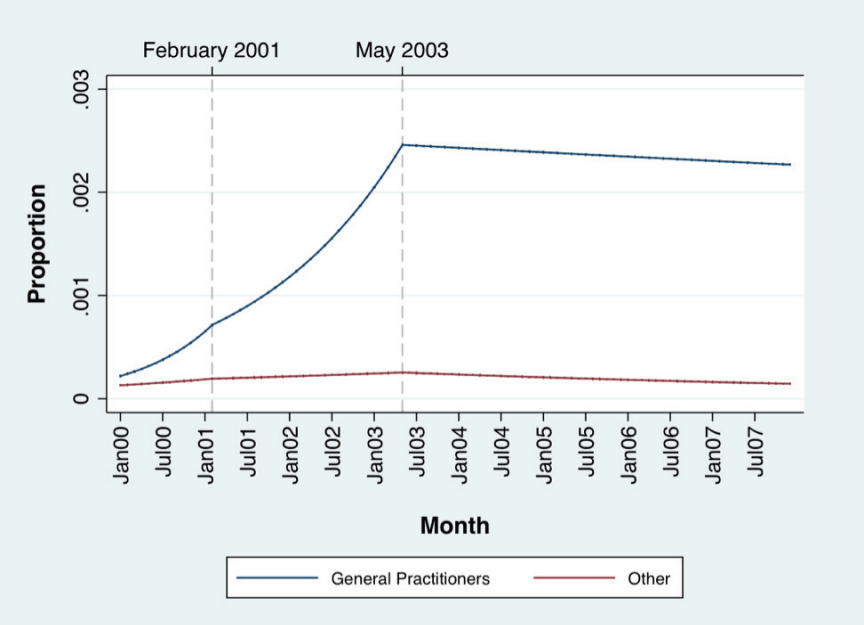

Figure 5.18: Predicted Fitted Regression Lines for the Proportion of All Opioid DDDs That Were for OxyContin, General Practitioners and Other Specialists

Note: The dotted lines represent the knots in the splines, which were set at February 2001 and May 2003 to correspond with the beginning of the peaks in media.

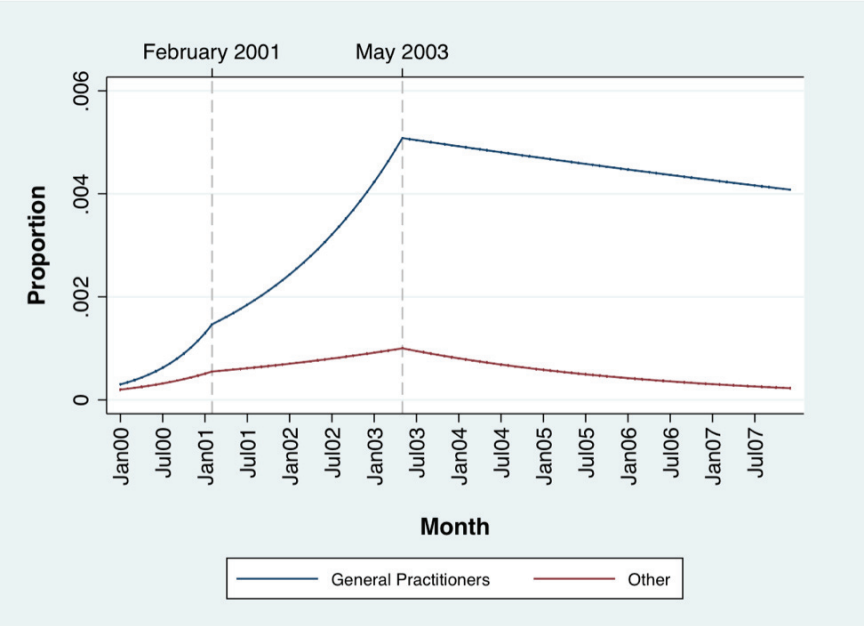

Figure 5.19: Predicted Fitted Regression Lines for the Proportion of Strong Opioid DDDs That Were for OxyContin, General Practitioners and Other Specialists

Note: The dotted lines represent the knots in the splines, which were set at February 2001 and May 2003 to correspond with the beginning of the peaks in media.

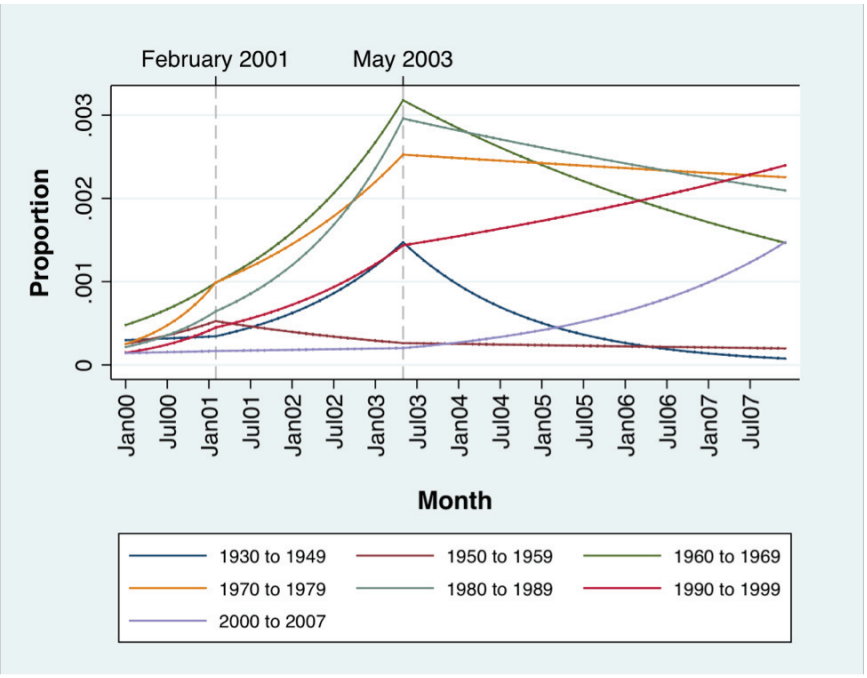

Figure 5.20: Predicted Fitted Regression Lines for the Proportion of All Opioid DDDs That Were for OxyContin, by Decade of Graduation

Note: The dotted lines represent the knots in the splines, which were set at February 2001 and May 2003 to correspond with the beginning of the peaks in media

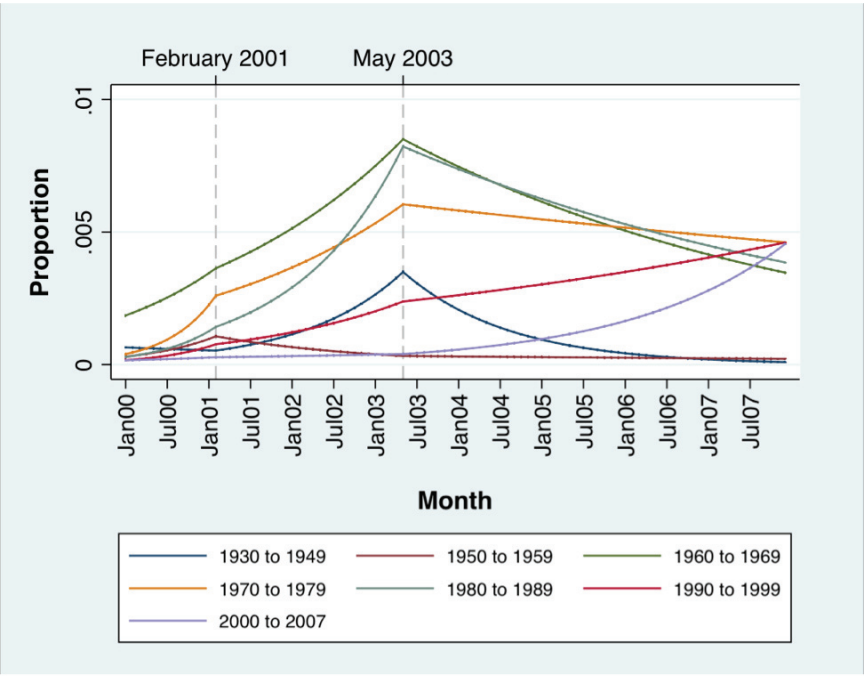

Figure 5.21: Predicted Fitted Regression Lines for the Proportion of Strong Opioid DDDs That Were for OxyContin, by Decade of Graduation

Note: The dotted lines represent the knots in the splines, which were set at February 2001 and May 2003 to correspond with the beginning of the peaks in media.

Table 5.1: Prescriber Characteristics

Characteristic	N (%) N = 4,212	Number of Prescriptions in Thousands			Total DDD Prescribed in Thousands N (%) N = 63,627,915
		All Opioids N (%) N = 2,803,273	Strong Opioids N (%) N = 935,155	OxyContin N (%) N = 58,482	
Specialty					
General Practitioner	2,092 (49.8)	2,316 (82.6)	834 (89.2)	53 (90.4)	58,048 (91.2)
Anesthesiologist	74 (1.8)	30 (1.1)	17 (1.8)	3.9 (6.6)	726 (1.1)
Other	1,838 (43.6)	444 (15.8)	82 (8.8)	1.7 (3.0)	4,727 (7.4)
Missing	208 (4.9)	14 (0.5)	1.6 (0.2)	0.006 (0.01)	127 (0.2)
Graduation Decade					
1930 to 1949	31 (0.7)	22 0.8)	5.7 (0.6)	0.2 (0.3)	252 (0.4)
1950 to 1959	129 (3.1)	70 (2.5)	14 (1.5)	0.4 (0.7)	1,303 (2.0)
1960 to 1969	254 (6.0)	261 (9.3)	81 (8.6)	8.1 (13.9)	6,551 (10.3)
1970 to 1979	597 (14.2)	857 (30.6)	275 (29.4)	18 (30.1)	20,532 (32.3)
1980 to 1989	922 (21.9)	892 (31.8)	306 (32.7)	18 (31.1)	21,520 (33.8)
1990 to 1999	1,014 (24.1)	535 (19.1)	205 (21.9)	12 (20.8)	11,538 (18.1)
2000 to 2007	829 (19.7)	109 (3.9)	43 (4.6)	1.3 (2.4)	1,407 (2.2)
Missing	436 (10.4)	59 (2.1)	5.8 (0.6)	0.04 (0.1)	525 (0.8)
District Health Authority					
South Shore Health (Population: 58,365)	155 (3.7) 2.66*	208 (7.4) 3,566*	62 (6.6) 1,054*	3.1 (5.3) 53*	5,612 (8.8) 96,155*
South West Health (Population: 60,810)	137 (3.3) 2.25*	94 (3.4) 1,553*	29 (3.1) 475*	0.8 (1.4) 14*	2,433 (3.8) 40,008*
Annapolis Valley Health Authority (Population: 81,475)	238 (5.7) 2.92*	258 (9.2) 3,169*	101 (10.8) 1,238*	3.7 (6.3) 45*	6,163 (9.7) 75,638*
Colchester East Hants Health Authority (Population: 69,426)	166 (3.9) 2.39*	153 (5.5) 2,206*	59 (6.3) 843*	3.9 (6.7) 56*	4,119 (6.5) 59,336*
Cumberland Health Authority (Population: 32,045)	95 (2.3) 2.96*	64 (2.3) 2,004*	21 (2.3) 658*	1.6 (2.8) 50	1,882 (3.0) 58,691*
Pictou County Health Authority (Population: 46,510)	116 (2.8) 2.49*	155 (5.5) 3,331*	35 (3.7) 744*	2.8 (4.8) 60*	2,897 (4.6) 62,283*
Guysborough Antigonish Strait Health Authority (Population: 44,815)	121 (2.9) 2.70*	114 (4.1) 2,550*	28 (3.0) 630*	2.7 (4.7) 61*	2,598 (4.1) 57,961*
Cape Breton District Health Authority (Population: 125,375)	390 (9.3) 3.11*	494 (17.6) 3,938*	158 (16.9) 1,263*	19 (32.5) 152*	10,240 (16.1) 81,677*
Capital Health (Population: 394,639)	2,638 (62.6) 6.68*	1,245 (44.4) 3,155*	439 (46.9) 1,111*	21 (35.4) 52*	27,409 (43.1) 69,455*
Missing	156 (3.7)	17 (0.6)	4.5 (0.5)	0.1 (0.2)	276 (0.4)

*Indicates values that are per 1,000 population. Note that these values are NOT given in thousands.

Table 5.2: Patient Population, by Prescriber Characteristics

Characteristic	N (%) N = 4,212	Mean Number of Patients Per Prescriber Mean = 561.0	Mean Number of Patients Per Month Mean = 7.4	Mean Number of Prescriptions Per Patient Mean = 2.9
Specialty				
General Practitioner	2,092 (49.8)	914.8	13.2	1.90
Anesthesiologist	74 (1.8)	268.9	16.6	2.78
Other	1,838 (43.6)	226.8	6.4	1.43
Missing	208 (4.9)	60.8	7.0	1.16
Graduation Decade				
1930 to 1949	31 (0.7)	478.2	18.9	3.57
1950 to 1959	129 (3.1)	435.0	13.3	2.72
1960 to 1969	254 (6.0)	837.7	16.4	2.88
1970 to 1979	597 (14.2)	1210.3	17.2	3.04
1980 to 1989	922 (21.9)	887.3	12.8	2.52
1990 to 1999	1,014 (24.1)	449.7	10.4	1.91
2000 to 2007	829 (19.7)	121.4	7.1	1.24
Missing	436 (10.4)	128.0	7.0	1.20
District Health Authority				
South Shore Health (Population: 58,365)	155 (3.7)	1,113.9	16.8	2.77
South West Health (Population: 60,810)	137 (3.3)	578.2	10.8	2.48
Annapolis Valley Health Authority (Population: 81,475)	238 (5.7)	938.3	15.1	2.29
Colchester East Hants Health Authority (Population: 69,426)	166 (3.9)	746.4	12.5	2.85
Cumberland Health Authority (Population: 32,045)	95 (2.3)	577.9	11.6	2.38
Pictou County Health Authority (Population: 46,510)	116 (2.8)	1,144.5	17.5	2.66
Guysborough Antigonish Strait Health Authority (Population: 44,815)	121 (2.9)	831.8	13.9	2.51
Cape Breton District Health Authority (Population: 125,375)	390 (9.3)	1,089.4	18.9	2.91
Capital Health (Population: 394,639)	2,638 (62.6)	392.7	10.6	21.82
Missing	156 (3.7)	96.1	7.1	1.73

Table 5.3: Fixed-Effects Regression Estimates for the Proportion of All Opioid DDDs and Strong Opioid DDDs That Were for OxyContin

Time Interval	Outcome Variable: Logit of the Proportion of All Opioid DDDs That Were For OxyContin N = 3721				Logit of the Proportion of All Strong Opioid DDDs That Were For OxyContin N = 3175			
	β	Lower 95% CI	Upper 95% CI	p-value	β	Lower 95% CI	Upper 95% CI	p-value
Interval 1	0.0877	0.0622	0.1132	**<0.0001**	0.1199	0.0823	0.1576	**<0.0001**
Interval 2	- 0.0448	- 0.0757	- 0.0138	**0.0046**	- 0.0759	- 0.1211	- 0.0306	**0.0010**
Interval 3	- 0.0451	- 0.0589	- 0.0314	**<0.0001**	- 0.0492	- 0.0686	- 0.0298	**<0.0001**

Note: Interval 1 = January 2000 to January 2001; Interval 2 = February 2001 to April 2003; Interval 3 = May 2003 to December 2007

Table 5.4: Fixed-Effects Regression Estimates for the Proportion of All Opioid DDDs and Strong Opioid DDDs That Were for OxyContin, by Prescriber Volume

Time Interval, by Prescriber Volume	Outcome Variable: Logit of the Proportion of All Opioid DDDs That Were For OxyContin N = 1262				Logit of the Proportion of All Strong Opioid DDDs That Were For OxyContin N = 1262			
	β	Lower 95% CI	Upper 95% CI	p-value	β	Lower 95% CI	Upper 95% CI	p-value
Low (N = 316)								
Interval 1	0.0026	- 0.0098	0.0151	0.6792	- 0.0063	- 0.0243	0.0117	0.4919
Interval 2	0.0034	- 0.0120	0.0189	0.6657	0.0177	- 0.0046	0.0400	0.1201
Interval 3	- 0.0049	- 0.0124	0.0027	0.2057	- 0.0023	- 0.0137	0.0092	0.6971
Low-Medium (N = 315)								
Interval 1	0.0850	0.0388	0.1313	**0.0003**	0.0998	0.0060	0.1936	**0.0372**
Interval 2	- 0.0709	- 0.1338	- 0.0080	**0.0273**	- 0.0644	- 0.1809	0.0521	0.2773
Interval 3	- 0.0107	- 0.0449	0.0234	0.5366	- 0.0406	- 0.0858	0.0045	0.0776
Medium-High (N = 316)								
Interval 1	0.0982	0.0368	0.1596	**0.0018**	0.1455	0.0695	0.2214	**0.0002**
Interval 2	- 0.0267	- 0.1063	0.0530	0.5106	- 0.0943	- 0.1992	0.0106	0.0780
Interval 3	- 0.0753	- 0.1059	- 0.0448	**<0.0001**	- 0.0494	- 0.0952	- 0.0036	**0.0346**
High (N = 315)								
Interval 1	0.1829	0.1214	0.2444	**<0.0001**	0.2390	0.1551	0.3229	**<0.0001**
Interval 2	- 0.1028	- 0.1759	- 0.0297	**0.0060**	- 0.1593	- 0.2492	- 0.0693	**0.0006**
Interval 3	- 0.0884	- 0.1181	- 0.0588	**<0.0001**	- 0.1047	- 0.1470	- 0.0625	**<0.0001**

Note: Interval 1 = January 2000 to January 2001; Interval 2 = February 2001 to April 2003; Interval 3 = May 2003 to December 2007

Table 5.5: Fixed-Effects Regression Estimates for the Proportion of All Opioid DDDs and Strong Opioid DDDs That Were for OxyContin, by District Health Authority

Time Interval and DHA	Outcome Variable: Logit of the Proportion of All Opioid DDDs That Were For OxyContin				Logit of the Proportion of All Strong Opioid DDDs That Were For OxyContin			
	β	Lower 95% CI	Upper 95% CI	p-value	β	Lower 95% CI	Upper 95% CI	p-value
South Shore Health (DHA 1)								
Interval 1	0.0317	- 0.0574	0.1209	0.4830	0.0762	- 0.0763	0.2287	0.3247
Interval 2	0.0442	- 0.0388	0.1271	0.2943	0.0148	- 0.1218	0.1514	0.8304
Interval 3	0.0442	- 0.0388	0.1271	0.2943	0.0148	- 0.1218	0.1514	0.8304
South West Health (DHA 2)								
Interval 1	- 0.0453	- 0.1053	0.0147	0.1374	- 0.0817	- 0.1786	0.0151	0.0972
Interval 2	0.0581	- 0.0168	0.1331	0.1273	0.0968	- 0.0232	0.2169	0.1128
Interval 3	- 0.0004	- 0.0385	0.0377	0.9841	0.0067	- 0.0554	0.0689	0.8305
Annapolis Valley Health (DHA 3)								
Interval 1	0.0252	- 0.0299	0.0804	0.3684	0.0254	- 0.0463	0.0971	0.4849
Interval 2	0.0118	- 0.0749	0.0986	0.7884	0.0199	- 0.0888	0.1286	0.7188
Interval 3	- 0.0260	- 0.0808	0.0288	0.3509	- 0.0322	- 0.1015	0.0371	0.3607
Colchester East Hants Health Authority (DHA 4)								
Interval 1	0.0783	- 0.0250	0.1817	0.1363	0.1246	- 0.0303	0.2794	0.1141
Interval 2	- 0.0092	- 0.1435	0.1250	0.8921	- 0.0458	- 0.2456	0.1541	0.6513
Interval 3	- 0.0636	- 0.1123	- 0.0149	**0.0109**	- 0.0787	- 0.1449	- 0.0126	**0.0200**
Cumberland Health Authority (DHA 5)								
Interval 1	0.1429	0.0331	0.2525	**0.0114**	0.2183	0.0899	0.3468	**0.0012**
Interval 2	- 0.1222	- 0.2500	0.0056	0.0606	- 0.2049	- 0.3630	- 0.0467	**0.0119**
Interval 3	- 0.0162	- 0.0481	0.0157	0.3157	- 0.0180	- 0.0547	0.0188	0.3328
Pictou County Health Authority (DHA 6)								
Interval 1	0.0693	- 0.0426	0.1812	0.2220	0.1451	- 0.0233	0.3136	0.0904
Interval 2	- 0.0347	- 0.1847	0.1153	0.6473	- 0.1146	- 0.3551	0.1259	0.3461
Interval 3	- 0.0316	- 0.0952	0.0320	0.3270	- 0.0307	- 0.1372	0.0759	0.5687
Guysborough Antigonish Strait Health Authority (DHA 7)								
Interval 1	0.2560	0.1149	0.3971	**0.0005**	0.3397	0.1504	0.5290	**0.0006**
Interval 2	- 0.2594	- 0.4299	- 0.0890	**0.0032**	- 0.3507	- 0.5784	- 0.1230	**0.0029**
Interval 3	0.0084	- 0.0502	0.0670	0.7766	0.0117	- 0.0619	0.0853	0.7532
Cape Breton District Health Authority (DHA 8)								
Interval 1	0.2267	0.1690	0.2843	**<0.0001**	0.2851	0.1850	0.3852	**<0.0001**
Interval 2	- 0.2058	- 0.2692	- 0.1424	**<0.0001**	- 0.2848	- 0.3885	- 0.1811	**<0.0001**
Interval 3	- 0.0385	- 0.0638	- 0.0131	**0.0030**	- 0.0225	- 0.0556	0.0106	0.1828
Capital Health (DHA 9)								
Interval 1	0.0539	0.0157	0.0921	**0.0057**	0.0842	0.0240	0.1444	**0.0061**
Interval 2	- 0.0030	- 0.0505	0.0446	0.9027	- 0.0326	- 0.1062	0.0410	0.3852
Interval 3	- 0.0515	- 0.0715	- 0.0313	**<0.0001**	- 0.0564	- 0.0832	- 0.0297	**<0.0001**

Note: Interval 1 = January 2000 to January 2001; Interval 2 = February 2001 to April 2003; Interval 3 = May 2003 to December 2007;

Table 5.6: Fixed-Effects Regression Estimates for the Proportion of All Opioid DDDs and Strong Opioid DDDs That Were for OxyContin, by Specialty

Time Interval and Specialty	Outcome Variable: Logit of the Proportion of All Opioid DDDs That Were For OxyContin				Outcome Variable: Logit of the Proportion of All Strong Opioid DDDs That Were For OxyContin			
	β	Lower 95% CI	Upper 95% CI	p-value	β	Lower 95% CI	Upper 95% CI	p-value
Anesthesiologist								
Interval 1	0.0994	0.0615	0.1373	**<0.0000**	0.0771	0.0394	0.1148	**0.0002**
Interval 2	- 0.1080	- 0.1595	- 0.0566	**0.0001**	- 0.0842	- 0.1340	- 0.0344	**0.0014**
Interval 3	- 0.0203	- 0.0382	- 0.0023	**0.0277**	- 0.0235	- 0.0397	- 0.0074	**0.0052**
General Practitioner								
Interval 1	0.0906	0.0633	0.1180	**<0.0001**	0.1219	0.0823	0.1614	**<0.0001**
Interval 2	- 0.0447	- 0.0780	- 0.0114	**0.0086**	- 0.0757	- 0.1235	- 0.0279	**0.0019**
Interval 3	- 0.0474	- 0.0621	- 0.0326	**<0.0001**	- 0.0502	- 0.0707	- 0.0298	**<0.0001**
Other								
Interval 1	0.0306	- 0.0089	0.0701	0.1290	0.0781	- 0.0375	0.1937	0.1854
Interval 2	- 0.0204	- 0.0614	0.0205	0.3280	- 0.0559	- 0.1836	0.0718	0.3909
Interval 3	- 0.0204	- 0.0368	- 0.0040	**0.0149**	- 0.0492	- 0.0895	- 0.0090	**0.0165**

Note: Interval 1 = January 2000 to January 2001; Interval 2 = February 2001 to April 2003; Interval 3 = May 2003 to December 2007

Table 5.7: Fixed-Effects Regression Estimates for the Proportion of All Opioid DDDs and Strong Opioid DDDs That Were for OxyContin, by Decade of Graduation

Time Interval and Graduation Decade	Outcome Variable							
	Logit of the Proportion of All Opioid DDDs That Were For OxyContin				Logit of the Proportion of All Strong Opioid DDDs That Were For OxyContin			
	β	Lower 95% CI	Upper 95% CI	p-value	β	Lower 95% CI	Upper 95% CI	p-value
1930 to 1949								
Interval 1	0.0111	- 0.0827	0.1050	0.8078	- 0.0158	- 0.0659	0.0343	0.5056
Interval 2	0.0427	- 0.1462	0.2319	0.6421	0.0859	- 0.0713	0.2430	0.2568
Interval 3	- 0.1079	- 0.2241	0.0084	0.0674	- 0.1360	- 0.2725	0.0005	0.0507
1950 to 1959								
Interval 1	0.0562	- 0.0195	0.1320	0.1438	0.0975	0.0333	0.2280	0.1409
Interval 2	- 0.0819	- 0.1802	0.0164	0.1014	- 0.1413	- 0.3047	0.0221	0.0886
Interval 3	0.0206	- 0.0150	0.0563	0.2539	0.0365	- 0.0095	0.0826	0.1177
1960 to 1969								
Interval 1	0.0557	- 0.0123	0.1237	0.1080	0.0519	- 0.0224	0.1262	0.1696
Interval 2	- 0.0123	- 0.0906	0.0661	0.7579	- 0.0202	- 0.1151	0.0746	0.6741
Interval 3	- 0.0575	- 0.0881	- 0.0269	**0.0003**	- 0.0481	- 0.0876	- 0.0086	**0.0174**
1970 to 1979								
Interval 1	0.1052	0.0613	0.1491	**<0.0001**	0.1448	0.0839	0.2057	**<0.0001**
Interval 2	- 0.0705	- 0.1256	- 0.0154	**0.0122**	- 0.1134	- 0.1910	- 0.0358	**0.0043**
Interval 3	- 0.0366	- 0.0612	- 0.0123	**0.0032**	- 0.0364	- 0.0698	0.0029	**0.0331**
1980 to 1989								
Interval 1	0.0846	0.0374	0.1317	**0.0005**	0.1232	0.0497	0.1967	**0.0010**
Interval 2	- 0.0280	- 0.0849	0.0290	0.3351	- 0.0579	- 0.1446	0.0287	0.1897
Interval 3	- 0.0629	- 0.0883	- 0.0374	**<0.0001**	- 0.0792	- 0.1145	- 0.0438	**<0.0001**
1990 to 1999								
Interval 1	0.0868	0.0337	0.1400	**0.0014**	0.1176	0.0415	0.1936	**0.0025**
Interval 2	- 0.0438	- 0.1068	0.0193	0.1735	- 0.0756	- 0.1674	0.0162	0.1062
Interval 3	- 0.0338	- 0.0610	- 0.0065	**0.0152**	- 0.0299	- 0.0676	0.0077	0.1192
2000 to 2007								
Interval 1	0.0126	- 0.0320	0.0572	0.5800	0.0411	- 0.0335	0.1157	0.2801
Interval 2	- 0.0055	- 0.0691	0.0580	0.8644	- 0.0277	- 0.1323	0.0768	0.6026
Interval 3	0.0291	- 0.0121	0.0702	0.1662	0.0310	- 0.0277	0.0897	0.3001

Note: Interval 1 = January 2000 to January 2001; Interval 2 = February 2001 to April 2003; Interval 3 = May 2003 to December 2007.

CHAPTER 6: DISCUSSION

6.1 MAJOR FINDINGS

To our knowledge, this is the first study to examine the effects of print media coverage of a prescription opioid on prescribing practices of the drug. It was found that there were significant changes in OxyContin prescribing over time with respect to changing media trends. Moreover, descriptive analyses indicated that the media reporting did not affect overall opioid prescribing, but rather these effects were largely restricted to prescribing of OxyContin.

The study population comprised just over 4,200 prescribers who made at least one opioid prescription between 1996 and 2007, of whom nearly 50% were general practitioners. These prescribers made a total of 2.8 million opioid prescriptions to 461,000 unique patients. This corresponds to 64 million defined daily doses of opioids prescribed. One-third of all opioid prescriptions were for strong opioids. Over 58,000 prescriptions were made for OxyContin in the study period, representing 2.1% of all prescriptions and 6.3% of all strong opioid prescriptions.

Over the study period, there were substantial increases in opioid prescribing, regardless of whether this was examined in terms of total opioid prescriptions or by the total number of defined daily doses (DDDs) of opioids prescribed. Between 1996 and 2007, the total number of prescriptions for opioids rose from approximately 18,000 per month to 25,000 prescriptions per month. Additionally, the number of prescriptions for strong opioids increased over the period of study, with the percent of all opioids prescribed that were for strong opioids increasing from 15% to 55% in just over 10 years. Prescriptions for OxyContin also generally increased over the time period. These increases occurred within the context of overall growth in the number of prescribers who made opioid prescriptions, a growing number of patients who were receiving opioids and an increase in the total amount of opioid per prescription, whether in terms of strength or total volume. Similar patterns were observed when these trends in prescribing were examined in terms of

defined daily doses. Importantly, these changes in opioid prescribing did not appear to be related to any of the print media surrounding OxyContin.

The increases in overall opioid prescribing and in strong opioid prescribing in Nova Scotia have been similarly noted elsewhere in North America and Europe. A study in the province of Ontario, for example, found that between 1991 and 2007, the total number of annual prescriptions per 1,000 population increased from 458 to 591 (or 29%).[16] In particular, prescriptions for oxycodone (the active opioid ingredient in OxyContin) increased by 850% over this time period.[16] Prescriptions for other strong opioids such as hydromorphone, fentanyl and morphine also increased, while prescriptions for the weak opioid codeine declined.[16] Similarly, several studies from the United States and Europe have noted increasing consumption of opioids over time, as well as increases in oxycodone and other strong opioid prescribing.[105-109]

It is highly likely that much of the increase in prescribing of opioids and OxyContin probably relates to the growing acknowledgement of chronic pain as a legitimate chronic condition, as well as an increasing recognition that the undertreatment of pain is a major societal problem.[4] Growing use of opioids as a first line pharmacotherapy in the treatment of pain may also play a role: indeed, a study of Canadian physicians noted that the preference for first line-treatment of chronic pain changed significantly from 2001 to 2004, with opioids preferred for 51% of patients in 2004 but only 30% of patients in 2001.[3] Additionally, this study found that the vast majority of opioid and OxyContin prescriptions were made by general practitioners. This trend has been widely noted, and probably relates to the fact that general practitioners are increasingly on the front line for the management of chronic pain in Canada, and elsewhere.[3,110]

In terms of OxyContin, the trends were less clear and consistent than those observed for all opioids. These trends partly reflect the relatively new introduction of OxyContin in 1996. Both the number of prescriptions of OxyContin and the total number of OxyContin DDDs prescribed per month were relatively low until mid 1999, then increased more rapidly and steadily until mid 2003 and then declined. This decline coincided with peak

newspaper reporting of OxyContin in Canada. These trends were even more pronounced when OxyContin was examined as a proportion of all opioid DDDs prescribed.

Perhaps most interesting is that the proportion of all strong opioid DDDs prescribed that were for OxyContin per month (as well as the percent of all strong opioid prescriptions that were for OxyContin), showed a steady increase until late 2003 to early 2004, at which point the trend was reversed and declined over the remainder of the study period. Further, it was shown that the decrease in the number of DDDs of OxyContin prescribed following the peak in Canadian media reporting could not be attributed to decreasing quantities (i.e. number of tablets) or strengths of OxyContin per prescription: in fact the quantity of OxyContin prescribed per prescription increased until 2006 then declined, well after the changes in OxyContin prescribing were observed. No changes in the strength of OxyContin prescribed were noted over the whole time period. Against the backdrop of rising prescriptions for strong opioids, these trends suggest that OxyContin was increasingly replaced with prescriptions for other strong opioids.

The various conditional fixed-effects linear piecewise regression models confirmed that there were significant changes in the prescribing of OxyContin (measured as the proportion of all opioid and strong opioid DDDs) following both the peaks in American and Canadian media reporting around the drug. Following the American peak in print media reporting, the proportion of all opioid DDDs and the proportion of strong opioid DDDs that were for OxyContin continued to increase, but at a significantly slower rate than prior to the peak. In contrast, following the Canadian peak in media reporting, rates of prescribing declined significantly. These results indicate that both media peaks had significant impacts on prescribing of OxyContin, but the Canadian peak (in which most articles were from Nova Scotia) had a much larger effect and resulted in greater decreases in prescribing.

Although strong media effects were observed, there was considerable heterogeneity in these effects by provider attributes and region of practice. Importantly, it was found that these changes in prescribing practice in relation to the OxyContin media were

concentrated among higher volume prescribers, where higher volume was defined as having a higher proportion of prescribed DDDs that were for OxyContin (note that this does not necessarily mean that a prescriber had a high overall volume of opioid prescriptions). This is perhaps not surprising, as it might be expected that the print media would have a greater impact among prescribers who consistently write either many prescriptions for OxyContin or who write prescriptions for larger amounts of OxyContin. Conversely, it is not unexpected that there would be little change among prescribers who only occasionally write prescriptions for OxyContin, especially since the outcome variables were measured as the proportion of all and strong opioid DDDs that were for OxyContin, rather than as absolute numbers of prescriptions.

More nuanced patterns in these changes emerged when examining prescriber characteristics, with notable differences observed in the average within-prescriber change in OxyContin prescribing between providers in different District Health Authorities, specialties and by decade of graduation.

Regarding District Health Authority, all districts showed increases in the proportions of all opioid DDDs and strong opioid DDDs that were for OxyContin until late 2003, at which point these proportions leveled off. There was one notable exception, Cape Breton District Health Authority, in which these proportions increased until approximately March 2003 then began to steadily decline. Of note, these changes in prescribing coincided with peak media reporting of OxyContin in Canada.

In the fixed-effects models examining the District Health Authorities, significant within-prescriber changes following the American peak in media reporting were noted, with the rate of increase in the proportion of opioid DDDs that were for OxyContin slowing in Guysborough Antigonish Strait District Health Authority and Cape Breton District Health Authority. Following the Canadian peak in media reporting, within-prescriber changes were noted in South Shore Health, Colchester East Hants Health Authority, Cape Breton District Health Authority and Capital Health, where the proportion of all and strong opioid DDDs that were for OxyContin generally declined. Interestingly, there were few

differences in the response to both media peaks between DHAs (with Capital Health serving as the referent group), and these were restricted to interval 2 (i.e. following the peak in American reporting). Some of these differences may have resulted from the substantially different numbers of prescribers in different Health Authorities.

Some of the most pronounced changes in OxyContin were observed in Cape Breton District Health Authority. This may reflect that a considerable amount of the Canadian reporting around OxyContin came from Nova Scotia, and in particular Cape Breton. In fact, 62 of the newspaper articles were published in *The Cape Breton Post*, representing 36% of all Canadian newspaper reporting on OxyContin over the study period. Additionally, it is also possible that patients were hesitant to receive prescriptions for OxyContin in Cape Breton as a result of the negative print media exposure of the drug. Moreover, nearly one-third of all prescriptions for OxyContin between 1996 and 2007 were made in Cape Breton District Health Authority, yet only 14% of the population of Nova Scotia resides in this DHA. Cape Breton also had the highest per capita rate of all opioid and strong opioid prescribing over the study period.

Capital Health was the other District Health Authority in which changes were consistently noted. This likely reflects a number of characteristics of the DHA itself. Over half of prescribers in the study practiced in Capital Health. Further, over 80% of anesthesiologists, within whom large effects were noted, practiced in Capital Health. Capital Health encompasses the province's capital, Halifax, and caters to over 40% of the province's population. Additionally, *The Chronicle Herald* newspaper*,* which is based out of Halifax (although it is distributed throughout province), published 87 (or 50%) of the 172 articles published in the Canadian newspapers over the study period.

Turning to prescriber specialty, significant changes were noted for both overall opioid prescribing and strong opioid prescribing. Descriptive analyses indicated that, on average, anesthesiologists had by far the largest proportions of both all opioid DDDs and strong opioid DDDs that were for OxyContin (though general practitioners collectively made the greatest number of prescriptions), followed by general practitioners and other

specialists. While there were moderate increases in the proportions of all opioid DDDs and strong opioid DDDs that were for OxyContin among general practitioners and other specialists over the study period, these proportions increased much more substantially among anesthesiologists until early 2004, then declined sharply and steadily over the remainder of the study period. These trends were further reiterated in the fixed-effects models. The magnitude of the effects differed significantly between anesthesiologists and general practitioners, with anesthesiologists showing greater within-prescriber changes in all time intervals compared to general practitioners. These results indicate both that anesthesiologist adopted the use of OxyContin much more than other prescribers, and that they also responded to the media concern by reducing their prescribing of OxyContin to a greater extent.

Although not possible to assess in this research, the differences observed between general practitioners and anesthesiologists may be related to the differing patient populations and therefore differing health conditions for which these practitioners prescribe opioids and OxyContin. Additionally, there may be differences in the preferred opioids that are prescribed by specialty. For example, one Canadian study found that 82% of anesthesiologists who prescribed opioids preferred sustained release preparations in the management of chronic pain patients, which would include OxyContin.[111] Indeed, other studies from the US have also indicated that specialists are more likely than non-specialists to prescribe extended-release formulations compared to non-specialists (general practitioners), for example.[98] Although anesthesiologists were not specifically included, work by Turk et al.[112] demonstrated significant differences in prescribing of long-term opioids between general practitioners, surgeons, neurologists and rheumatologists. Such differing preferences may also apply to the use of OxyContin.

Finally, changes in OxyContin prescribing were largely restricted to prescribers who graduated from medical or dental school between 1960 and 1999. The most notable changes in both the proportion of all opioid DDDs that were for OxyContin and the proportion of strong opioid DDDs that were for OxyContin were among prescribers who graduated between 1960 and 1969, with both proportions increasing until mid 2002 to

early 2003, then decreasing. Among prescribers who graduated in 1970 and later, both of these proportions increased over the study period, while they generally decreased among prescribers who graduated between 1930 and 1959.

Moreover, when differences between decades of graduation were examined in the fixed-effects models, only those who graduated between 1950 and 1959 and between 2000 and 2007 differed significantly from those who graduated in 1980 to 1989 (the reference group) and only in interval 3. Among prescribers who graduated in the 1980s, the average proportion of all opioid DDDs and strong opioid DDDs that were for OxyContin declined in interval 3. This was also the case for individuals who graduated in 1950 to 1959, but these decreases actually began in interval 2 and slowed in interval 3. In contrast, both proportions continued to increase in all intervals among prescribers who graduated in the 2000s.

The reasons for this are unclear, but may relate to differences in medical and dental school curriculum in different years, but could also indicate that prescribers of different ages may seek and/or receive drug information from differing sources. Other studies have noted inconsistent differences in opioid prescribing by age (which is assumed to be related to graduation year in this context). A study in England found that younger general practitioners were more likely to prescribe opioids, though the reasons for these age differences was not indicated.[64] Another study in Ontario found the opposite, with older age and greater number of years in practice associated with greater opioid prescribing among family physicians.[113]

One last important consideration in the interpretation of the study results is that during the study timeframe, several physicians in Nova Scotia were investigated for the inappropriate or injudicious prescribing of opioids.[114] In particular, there were three decisions made by the College of Physicians and Surgeons of Nova Scotia in these investigations. In mid 2005, a physician in Barrington Passage (located in South West Health Authority) was suspended for the inappropriate prescribing of controlled substances, including the inappropriate prescribing of opioids.[115] In late 2005 and early

2006, two physicians where reprimanded for inappropriate opioid prescribing, the first of whom practiced in Amherst (Cumberland Health Authority)[116] and the second of whom practiced in New Waterford (Cape Breton District Health Authority).[117] It is not unexpected that these decisions may have impacted the prescribing practices of providers, both with respect to OxyContin and other opioids, particularly if these investigations and subsequent decisions received media attention. The decision made with regards to the physician in Cape Breton certainly received media attention in the Chronicle Herald in Halifax[118,119], and may have played a role in the larger media effects that were observed in this District Health Authority. In smaller communities, such as Cape Breton District Health Authority, news of such investigations by the College of Physicians and Surgeons of Nova Scotia is likely to have travelled quickly and extensively though the network of prescribers in this DHA. However, it is also worth noting that these decisions were made towards the end of the study period of this research.

6.2 Factors that Affect Prescribing Behaviour

Any discussion of changing prescribing trends must consider that there are many complex and overlapping factors beyond the lay media that affect the prescribing behaviours of clinicians. A number of such factors are discussed here, and as much as possible are framed within the context of OxyContin and opioids as well as their relevance to the results of this research. First, however, a brief discussion of other media-related factors is presented.

6.2.1 Media

This research appears to be among the first to examine the impact of media reporting of opioids and subsequent changes in prescribing of these drugs, and contributes to a small but growing literature that examines the effect of media and public concern on prescribing practices of healthcare providers. Though a considerable amount of research has focused on the effects of commercial marketing of drugs in media and medical journals, a few studies have examined whether public media attention can affect

prescribing practices, or medical and dental practice more broadly. Several studies have also examined the quality of reporting around pharmaceuticals.

For example, two studies of thiazolidinedione (a class of oral diabetic drugs) evaluated adverse media reporting on prescribing attitudes of these drugs.[86,87] These drugs had been in the media spotlight in both lay and professional source over cardiovascular safety concerns, and both studies noted that prescriptions for rosiglitazone steadily decreased (mirrored by an increase in a similar drug) following the publication of a meta-analysis suggesting harm from this drug and sustained media attention on the drug. Interestingly, when asked about the source of information on drug safety warnings, 21% of physicians reported journals, 19% reported scientific meetings and 15% reported the news media.[86] Another study of calcium-channel blocker prescribing among physicians in British Columbia between 1994 and 1996 found similar media effects, with prescriptions for these drugs decreasing modestly (about 3% to 5%) following several waves of widespread lay media coverage of a case-control study that indicated poor cardiovascular outcomes for patients using these drugs.[120]

Of concern is the accuracy of media reporting around both prescription drugs and health concerns in general. Studies have found that news media about medications may include inadequate or incomplete information about the benefits, risks and costs of drugs.[121,122] In addition, such stories often cite at least one expert or study, but often fail to disclose the financial ties between the experts or study groups and pharmaceutical manufacturers of the drug of interest. Further, a 1999 survey found that Canadian physicians think that journalists could be doing a better job of reporting on health issues.[123] The survey indicated that only a third of physicians believed that the news media were delivering accurate coverage of medical health information.[123] Even Canadian journalists have raised concerns about the accuracy of pharmaceutical reporting, including the lack of formal policy to guide news coverage of “breakthrough” stories and difficulty in obtaining independent information on pharmaceuticals.[124]

While these studies of drug reporting have typically focused on the characteristics and effects of the drug itself, which is not necessarily as applicable in the case of OxyContin where much of the media focused on the wider social problems that were thought to be associated with OxyContin, such concerns of the quality of drug and health reporting may nonetheless apply. It is not a stretch to imagine that if there is often poor reporting or misrepresentation of pharmaceuticals in terms of both harms and benefits of the drug itself, there may also be problematic reporting around the wider social effects of drugs.

This media attention on pharmaceuticals, whether accurate or not, may both directly affect prescribing as providers are exposed to and respond to such media, but also indirectly through concerns and pressure from patients who are also exposed to this media. Requirements for accurate portrayal of prescription drugs by media sources may therefore be warranted, given that many patients increasingly rely on media sources for information on prescriptions drugs[121] and that prescribers are influenced by media, as demonstrated in this research and elsewhere.[86-88]

6.2.2 Other Factors that Affect Prescribing

The broader literature on factors that affect physician behaviour in clinical settings can a provide context within which to understand some of the factors that may influence the decision-making process of healthcare providers around prescriptions. Such factors can also be important to consider in the development of educational and other activities to promote appropriate prescribing of opioids and other prescription drugs in the wake of media attention on such drugs.

As previously discussed, Bauchner and colleagues[89] posit that medical decision-making by physicians can be viewed within the three overlapping domains of physician experience and knowledge, patient characteristics and values and external clinical evidence. A fourth domain, societal norms, encompasses these other three domains. Each of these domains is in turn influenced by other factors.

This model of medical decision-making behaviour can help provide context for the results found in this research. The discussion here focuses on the three overlapping domains of physician knowledge, patient characteristics and clinical evidence, and leaves the discussion of societal norms for future research, particularly since such a discussion framed specifically within the Nova Scotia context is beyond the scope of this research. Readers interested in the broader societal factors that contribute to decision-making in clinical practice will find the articles by Eisenberg[125] and Dukes[126] to be a helpful starting point.

Several reviews of the literature indicate a number of more specific factors that influence drug prescribing by providers that fit into the Bauchner model.[90,91] Factors that affect prescribing and that fall within the domain of physician knowledge and experience include education, medical journals, influence and advice from colleagues, control and regulation measures, influence of pharmacists and pharmaceutical company representatives, as well as pharmaceutical advertising. Among the factors in the domain of patient characteristics are demands and expectations of the patient, the patient-prescriber relationship, as well as advertising by pharmaceutical companies. The domain of external clinical evidence encompasses such factors as education, journals and advice from colleagues. Notably, many of the factors that affect prescribing fit into more than one domain. The following discussion will first focus on prescriber characteristics and experiences, then turn to patient factors.

Prescriber Characteristics

Medical and dental education aims to provide basic therapeutic skills.[90] However, many drugs currently in existence were not on the market when prescribers were students.[90] As such, the differences observed in this research in prescribing changes between providers who graduated in different decades may partly reflect that graduates in earlier years may not have received education around OxyContin, or even opioids, in the treatment of pain. Indeed, this research found that prescribers who graduated in the 1990s and 2000s were the only groups whose prescribing of OxyContin continued to increase in the last time interval, whereas graduates in all other years showed declines. Given that OxyContin was

introduced in 1996, it may be that graduates in 1990 and later received greater education with respect to OxyContin and other opioid analgesics. These prescribers may have been more comfortable in their prescribing of these drugs, and as a result were less susceptible to the increasing negative media attention on OxyContin.

The contribution of advertising to prescribing behaviours has been well studied, but with conflicting results.[90,91,127] A recent systematic review of studies between 1966 and 2008 examined the relationship between exposure to information from pharmaceutical companies and the quality, quantity and cost of prescribing among physicians.[127] Exposures included pharmaceutical sales representative visits, journal advertisements, attendance at pharmaceutical sponsored meetings, mailed information, prescribing software and participation in sponsored clinical trials. The authors concluded that, with rare exceptions, studies of exposure to pharmaceutical company information have found associations with higher prescribing frequency, higher costs or lower prescribing quality or have not found any significant associations. Notably, 38 studies found associations between exposure and higher frequency of prescribing and 13 found no association. Five studies found associations between exposure to pharmaceutical company information and lower quality prescribing and four did not find an association. In addition, the authors concluded that all studies had design limitations and there were only two randomized trials.[127]

It is unclear what role advertising may have played in OxyContin prescribing, though it likely contributed to the increases in prescribing observed in early years. Indeed, Lexchin and Kohler[128] discuss marketing of OxyContin in the Unites States and Canada, and conclude that it was aggressively marketed in both countries. It is not likely that such advertising efforts directly contributed to the changes in prescribing noted in this research, apart from the increases in OxyContin in the years following its introduction. It is, however, prudent to note that in 2007 Purdue Frederick (an affiliate of Purdue Pharma, the company who produced OxyContin) pled guilty in the US to falsely misrepresenting the addictive qualities of OxyContin, though this was at the end of the study period of the

current research and likely did not contribute to the declines noted in OxyContin prescribing**.**

Other studies have similarly noted that prescribing behaviours are influenced by commercials sources. For example, Avorn et al[88] examined the relative contributions of scientific and commercial sources of information on prescribing behaviours of physicians and concluded that while the majority of prescribers perceived themselves as paying little attention to drug advertising as compared to scientific literature, the opposite was in fact true. The authors suggest that these patterns may be due to either an unwillingness of prescribers to admit reliance on commercial sources of information or a lack of the influence of such awareness[88], both of which have implications for any proposed interventions targeting prescribing behaviours.

Expanding upon this, research shows that prescribers rely on medical journals for information on drugs.[91] While the body of research on this topic appears to relate mostly to information on and the decision to begin prescribing newly available pharmaceuticals, there is certainly a potential role of journal articles in mediating the influence of the lay media attention on OxyContin and subsequent prescribing changes. Whelan and colleagues[14], whose newspaper coverage data was drawn upon for this study, also investigated coverage of OxyContin in medical journals. They found that medical journals began publishing reports related to OxyContin and oxycodone beginning in 1995 and continued to do so until the end of the study period in 2007, though the number of journal articles relating to OxyContin was substantially smaller than the news media over the same period. Notably, medical journals began acknowledging the potential problems of abuse and addiction as early as 1996, four years before the first newspaper article appeared. Generally, the medical articles focused on clinical drug trials, pharmacology, use patterns and epidemiology of the drug, with many fewer focusing on social or economic concerns (15%), legal or policy issues (9%), crime (6%) and physician or pharmacist prescribing behaviours (5%). Regardless, prescribers in Nova Scotia may have been exposed to this medical literature, some of which probably corresponds with or responds to the issues around OxyContin reported in the news media (indeed, 30% of

articles acknowledged a perceived crisis or problems associated with OxyContin), and such attention therefore may have influenced changing prescription behaviours around the drug.

Research also suggests that prescribers often derive therapeutic knowledge from their colleagues and peers, with as much as 37% of prescribers indicating that other physicians are the most important way of finding out about new prescription drugs.[90,129] This reliance on colleagues for information may have played a role in the differences in OxyContin prescribing and responses to media by District Health Authority and by specialty, whereby it is not unexpected that prescribers within the same districts or specialties would be in contact more often such as through attending the same seminars, conferences, and meetings or belonging to the same professional committees and associations, providing greater opportunity for prescribers to solicit advice from their peers about OxyContin and opioid prescribing.

Control and regulation measures may also play a role in prescribing behaviours. In Nova Scotia, there is a prescription monitoring program (described above in section 2.5) that has been actively monitoring controlled narcotics, including all opioids, since 1992. Though considerably more research has focused on whether prescription monitoring programs can reduce opioid misuse, abuse and mortality[59,130], some studies show that PMPs can affect prescribing of monitored drugs.[131] Given that many Canadian physicians indicate that fears of control and regulation measures, including fears of an audit by their governing College or other legal and loss of licensure concerns, play a role in their prescribing of opioids [5,61,62] it is reasonable to expect that following the escalating negative media attention around OxyContin, such regulation fears contributed to some of the declines in OxyContin prescribing that were noted across the province.

Patient Characteristics

One aspect that plays a large role in prescribing by health providers, but could not be examined in this research, is patient characteristics, preferences and perceptions.[89] The influence of the patient on prescribing decisions has been consistently noted and

studied.[90,91] Here, the focus is on the potential factors that may operate within the context of media influence, though it is worth noting that there are many more patient characteristics that can influence provider prescribing practices.

Patients routinely cite the media, after physicians and pharmacists, as a key source of information on new prescription drugs.[121] A 1999 survey in Canada found that 84% of doctors indicated that they believed media reports influenced the types of treatments their patients requested.[132] Others have found that a quarter of physicians report that patients arrive at least once a day with questions based on media stories, with an additional 44% reporting receiving such queries at least once a week.[123]

Moreover, a national poll of adults in the US found that 75% reported that they pay either a moderate amount (50%) or a great deal (25%) of attention to medical and health news reported by the media. Well over half of respondents indicated that they had changed their behaviour or taken some kind of action as a result of a medical or health news story.[133]

Additionally, studies indicate that patients are more likely to receive prescriptions for medications when they present to a prescriber with the expectation of receiving a prescription. One study in Australia found that patients presenting with new conditions to general practitioners were nearly three times more likely to receive a prescription when they expected to receive a prescription.[134] Further, when the general practitioner thought that the patient expected medication, the patient was 10 times more likely to receive a prescription.[134] Such expectations may also operate in the decision by providers of which specific drug to prescribe.

In light of this body of research on the influence of media on patient behaviour and expectation, it would not be unexpected, then, that patients in Nova Scotia who were already taking OxyContin or who were eligible for receiving OxyContin may have responded to the negative news media attention by raising concerns with their providers, with expectations of receiving prescriptions for an opioid other than OxyContin. Such

concerns and expectations on the part of the patient would in turn contribute to changes in the prescribing of OxyContin by their healthcare providers.

6.2.3 Changing Prescriber Behaviour

Although it cannot be definitively determined from this research that the changes in prescribing of OxyContin observed were detrimental to patients, it is nonetheless prudent to consider that there may be need for interventions and programs that mitigate the potentially negative effects of media on prescribing practices.

Clearly the factors that affect the prescribing behaviours of healthcare providers are complex and often overlap, and the ways in which such factors operate in the context of media attention on a specific drug are difficult to determine and at best can only be speculated upon. Further, efforts to affect change are likely able to address only some of these factors. Nonetheless, some general recommendations have been made with regards to characteristics of programs that are likely to result in at least moderate changes in provider behaviour, whether specifically related to prescribing behaviour or clinical practice in general.

Andersen and Lexchin[135] provide a brief review of some strategies for changing prescribing practices. They suggest that dissemination of printed materials alone does not lead to changes in practice, but that specific educational and feedback strategies can improve the quality of care. Face-to-face contact between an expert (a specially trained physician or pharmacist) and a prescriber was indicated to be one of the more successful educational strategies. They further suggested that feedback that involves not only a description of current practice, but that also includes specific recommendations for change in the use of medications can also improve practice.[135] Sbarbaro[136] similarly posits that there are four key elements to programs that generate prescribing changes: 1) activities that require the direct involvement and focused attention of the prescriber, such as interactive hands-on workshops, 2) documentation that a prescriber is an outlier when compared to peers, 3) patient and peer feedback, and 4) nationally developed guidelines,

especially when combined into the routine practice of leading physicians within a community and when strongly endorsed by local and national professional organizations.

Although not focused on prescription-making, Bauchner and colleagues[89] briefly summarize the literature on methods of changing physician behaviour. Activities that were found to have little or no effect on changing behaviour include traditional didactic continuing medical education and passive distribution of information (mailing) and the creation, publication and passive dissemination of guidelines. Activities that have shown some evidence for changing behaviour and/or improving quality of care (at least in the short term) include: continuing medical education that includes interactive interventions such as small group discussions or case studies; implementation of published guidelines as part of a systematic strategy; manual or computerized reminders to both patients and physicians; educational outreach with local opinion leaders; audit and feedback (although only modestly effective); and financial incentives.[89]

All of the above recommendations are equally applicable in the context of inappropriately reduced prescribing of a drug as a result of media attention and should be seriously considered in the design of any efforts to target prescribing of OxyContin and opioids.

In the immediate future, one way to potentially mitigate the negative effects of media on opioid prescribing and ultimately the treatment of pain is to ensure that medical and dental professionals receive adequate training in the treatment of pain and appropriate use of opioids, with included discussions of the potential for misuse and abuse by patients.

Unfortunately, a study published in 2009 that examined pain curricula in major health science faculties (which had programs in at least medicine and nursing) found that the majority of programs (67.5%) did not have designated hours for pain education in their curricula.[137] Of note, among programs that identified specific hours for pain content, the average total time ranged from 13 to 41 hours. In comparison, all veterinary programs identified mandatory designated pain content time, with a mean of 87 hours.[137] A further breakdown of these results by discipline found that medicine and dentistry had among the

lowest average hours designated for formal pain content when compared to nursing, occupational therapy, pharmacy, physical therapy and veterinary medicine.[137] With so little focus given to pain and its treatment, it may not be surprising that provider prescribing patterns can be strongly influenced by other sources, including printed media.

Importantly, it should be realized that some of the reductions in prescribing of OxyContin might have been justified. It is possible, for example, that some of the media attention focusing on OxyContin addiction and diversion made prescribers more aware of these issues and, therefore, more likely to take appropriate steps when prescribing to reduce the chances of these problems arising in their own patients. The concern remains, however, that pain patients for whom OxyContin was or would have been an appropriate treatment were no longer receiving it or were never prescribed it to begin with as providers responded to the growing negative attention on OxyContin in the media by prescribing less of the drug.

The discussion of changing prescribing practices with respect to OxyContin must therefore also include a discussion of how to curtail diversion and abuse, especially since this is repeatedly identified as an influence on and a barrier to prescribing opioid analgesics among healthcare providers.[5,61,62] Although it is unclear how much diversion and abuse of OxyContin has actually occurred in Nova Scotia, the media certainly portrayed abuse and diversion as growing problems requiring solutions in the province.

Volkow and McLellan[138] suggest several general ways to curtail the diversion and abuse of opioid analgesics, which equally apply to OxyContin. The first suggestion is to update and improve clinical teaching and training for physicians, nurses, dentists and pharmacists in the areas of pain management, opioid pharmacology and abuse and addiction.[138] Another suggestion is to ensure that guidelines on chronic pain management and opioid prescribing, such as the newly released 2010 Canadian Guideline for the Safe and Effective Use of Opioid for Chronic Non-Cancer Pain[44], are broadly adopted as a means of synchronizing best practices with regards to opioid analgesic prescribing across disciplines and ensuring appropriate monitoring and management of patients with chronic

pain, including screening procedures for patients who may be at risk of dependence or abuse. Patients and the general public must also become more aware of and responsible for the appropriate use, storage and disposal of opioid analgesics, especially since access to unused leftover medication has been cited as a significant source of diversion.[138] Importantly, the authors stress that these measures should not jeopardize the appropriate treatment of pain with opioid analgesics through reduced access.[138]

Similarly, a report from the College of Physicians and Surgeons of Ontario also makes a number of recommendations for tackling opioid analgesic abuse.[80] The report generally made the same recommendations as Volkow and McClellan, but also stressed the need for an electronic system for monitoring prescriptions in Ontario (notably, this is already in place in Nova Scotia but is not the case in all Canadian provinces).[80]

Related to dealing with abuse and addiction of opioids, in 2012, Purdue Pharma began to replace OxyContin with OxyNeo in Canada; a move likely stemming from the sustained negative press related to abuse and addiction that OxyContin has received in North America, along with the fact that the patent on OxyContin will expire in 2012.[70] OxyNeo is also an extended release oxycodone hydrochloride tablet formulation and Purdue Pharma has indicated that OxyNeo tablets have been hardened to reduce the risk of being broken, crushed or chewed.[71] Since the announcement of this replacement, OxyNeo has received a considerable amount of media coverage in Canada. Unfortunately, much of this media has not discussed the legitimate treatment of pain, but rather focused on concerns of diversion and crime, abuse and addiction of the drug, in much the same way as discussion around OxyContin was framed.

The research conducted here may serve as a warning for what may come for OxyNeo should it continue to receive substantial media coverage. While not yet fully introduced in all jurisdictions, it may mean that prescribers will choose not to begin prescribing OxyNeo in the first place, or may begin to transition their patients currently on OxyContin to other opioids instead due to fears of misuse and addiction. This transition can be problematic, as conversions between opioids can be difficult. Indeed, one death

has already been linked to an inappropriate conversion from OxyContin.[139] Of note, some provinces, including Nova Scotia, have chosen to remove both OxyContin and OxyNeo from the list of publicly-funded drugs, a move that has been seen by some to stem from the concerns, both real and perceived, that were raised in the media around OxyContin.[70] Concerns have been raised that patients who would legitimately benefit from OxyContin or OxyNeo will no longer have the option of using these drugs.

6.3 Strengths and Limitations

To the best of our knowledge, this study was one of the first to examine the effect of the print media on changes in opioid prescribing practices, with a specific focus on OxyContin. It has provided a foundation for further analyses in this research area.

6.3.1 Print Media Data

There are a few limitations to note with regards to the print media data. One concern is that only a subset of newspapers was included, and therefore not all newspaper articles relating to OxyContin in North America were captured. However, the newspapers were intentionally limited to those with high circulation or that were the main newspapers for their region, as well as those that were in circulation for the entire study period.

As noted by Whelan et al[14], one important limitation in the collection of the newspaper data is the quality and consistency of the indexing of articles in databases. Variations and errors may exist due to a number of factors. For example, different databases may index differently and therefore the identification of newspaper articles that pertained to OxyContin may have been incomplete.

6.3.2 Nova Scotia Prescription Monitoring Program Data

This research used longitudinal data from a prescription monitoring program that encompassed all opioid prescriptions in Nova Scotia, with very little missing data. Further, these data were from an administrative database and not self-reported, reducing

the risk of reporting bias, both from the perspective of prescribers and patients. Additionally, the data covered the entire province, providing opportunities for analyses by District Health Authority. Thus there is potential to generalize the findings to comparable districts and provinces across Canada.

One of the more pertinent issues with the NSPMP data, however, is that it was restricted to the administrative information that is collected within the Nova Scotia Prescription Monitoring Program. Information about the health status of the patients was unavailable, and thus it is not possible to know the health reasons for receiving an opioid or OxyContin prescription and it was not possible to distinguish between prescriptions for cancer and chronic noncancer pain, for example. Additionally, no information on why a prescriber chose to begin or terminate prescribing opioids to a patient was available, or reasons for changing the type of opioid prescribed. Nor was it possible to measure a number of other prescriber characteristics that may be relevant to both the prescriber's choice of medication as well as patient preferences, such as patient and prescriber date of birth, geographic location of schooling of prescribers, patient preference of medications or patient experiences of side effects.

Further, no information was available on the prescribers' total patient populations, as the data for this research was restricted to patients who received at least one opioid prescription between 1996 and 2007, and therefore it was not possible to consider opioid prescribing practices within the context of a prescriber's practice.

Lastly, it is important to consider that the NSPMP data captures only those prescriptions that were actually filled at Nova Scotia pharmacies and therefore does not necessarily encompass all prescriptions that were written for opioids, nor does this data give any indication as to how the medication was taken or used by the recipients of the prescription.

These are limitations that could be reasonably addressed within the scope of this project and are therefore suggested as future research directions.

6.3.3 Methodological Considerations

Defined Daily Doses (DDD)

There are both advantages and disadvantages to using the WHO ATC/DDD classification system for prescription drug data. The major advantage of the ATC/DDD system is that it allowed for individual drugs and drug classes to be compared between or across regions and populations, as well as over time.[93] This system further allowed aggregate volume measures for prescription claims data, both within and across drug classes without the limitations of simple volume measures (such as the number of tablets or the number of prescriptions).[93] The major disadvantage of using DDDs in this research is that not all drugs yet have assigned DDDs (as this only occurs when researchers request that a drug be assigned a DDD). Additionally, the DDD is determined based on international drug information, and may not necessarily reflect prescribing patterns of the associated drug in Canada, as main drug indications and prescribed daily doses may vary between countries.[93] However, in the context of the research presented here, the advantages conferred by allowing comparisons across prescriptions outweighed the disadvantages of the system. In particular, the use of DDDs allowed background opioid prescription rates to be taken into account, as well as allowing for the act that prescribers may respond to media exposure of OxyContin by reducing the dose or quantity prescribed, and not just the total number of prescriptions of OxyContin.

One last consideration with regards to using the ATC/DDD classification system is that it tends to overestimate the daily dose of opioids that are administered via transdermal patches. To ensure consistency, this research used the total amount of the opioid present in the patch to calculate the total DDDs per prescription. However consider that, for example, in the Duragesic® 12mcg/h fentanyl patch, the total fentanyl content is 1.25mg.[140] Each patch is designed to be worn for 72 hours, and the nominal delivery rate of fentanyl per hour is 12.5 mcg.[140] Thus, it would be expected that the total dose of fentanyl received by a patient is (12.5mcg)(72 hours) = 900 mcg or 0.9mg. This is clearly less than the 1.25 mg present in the patch. However, given that transdermal preparations

represented 32,703 of 2,803,273 (or 1.2% of all prescriptions), it is likely that the effect of this difference was minimal.

Conditional Fixed-Effects Models

As discussed above, there were a number of potentially relevant physician and patient characteristics that could not be examined in this research. However, the use of conditional fixed-effects methods allowed for the control of variables that were stable over time but not possible to measure, though it was not possible to address those that are not stable over time. The absence of this information may have biased the results, either towards or way from the null. However, given that the current analyses of the effects of the newspaper media on changes in prescribing practices have not previously been done, the goal of this research was to focus on broad changes in prescribing practices within the prescriber population, with more detailed analyses left for future research.

The use of conditional fixed-effects models in this research allowed for the control of all stable characteristics of the prescriber in this study, thereby eliminating potentially large sources of bias. Fixed-effects methods can result in an increase in sampling variability relative to other methods of analysis, since it is typically the case that independent variables of interest vary both within and between subjects.[100] Consider the example where one of the variables of interest is patient mix (i.e. the types of patients that a prescriber sees at his or her clinic), and it is measured in some way every year over five years. While there might be considerable within-prescriber variation over time, the bulk of the variation in patient mix is likely to be between prescribers. Fixed-effects methods ignore the between-prescriber variation and focus only on the within-prescriber variation. This was done in the research here, since it was acknowledged that there is wide variation in prescribing of opioids between providers, but the interest was on the within-prescriber change. However, discarding this between-prescriber variation can yield standard errors that are considerably higher than those provided by methods that consider both the within- and between-prescriber variation. Thus, there is a trade-off between bias and sampling variability, with a reduction in bias at the expense of greater sampling variability. By restricting the focus to within-prescriber variation, it was possible to

eliminate contamination that is likely to occur when measuring between-prescriber variation. This contamination results from unmeasured personal characteristics that are correlated with the independent variables of interest. Therefore in using conditional fixed-effects models, this study was more likely to get unbiased estimates.[100]

One last consideration is that the models used in this research did not permit adjustment for autocorrelation between observations within a given prescriber (though it is important to note that robust standard errors were specified to help account for heteroscedasticity). However, using a similar model specification that allowed for autocorrelation, several models were run and no major differences were observed between the models specifying autocorrelation and those that did not. Further, as presented in the results, the trend lines with regards to OxyContin prescribing were found to be quite smooth and the shifts in trend were quite significant, suggesting that accounting for serial correlation would not substantially alter the standard errors and ultimately the conclusions of this research.

6.4 Future Directions and Conclusion

This research showed that print media reporting of OxyContin, and its continued portrayal as a social problem, coincided with reductions in prescribing of OxyContin in the province of Nova Scotia between 2000 and 2007. These changes were not equally distributed among prescribers, with higher volume prescribers exhibiting greater declines in prescribing after peak media reporting. Additionally, differences were observed between District Health Authorities, prescriber specialties and decades of graduation. Although it was not possible to assess the direct impact of these changes in terms of patient access or patient outcomes, this conclusion is nonetheless important as it demonstrates that media attention around specific drugs appears to be associated with changes in prescribing practice.

Future research should extend the current project by examining the media effects on patient access to OxyContin, as it is recognized that both prescriber and patient characteristics influence the type of opioid prescribed. Such examinations should

consider that patients are likely exposed to the same print media as their providers, and therefore the media effects on prescribing are a reflection both of the responses to the print media by providers as well as patients. Further research may also want to consider not only the patient benefits and harms resulting from the changes in OxyContin prescribing in response to media attention, but also the costs of such benefits and harms. Importantly, future research should also examine whether there were any changes in the illicit use and diversion of OxyContin.

Nova Scotia is not the only Canadian province with a prescription monitoring program. Existing programs include the PharmaNet network in British Columbia, the Triplicate Prescription Programs in Alberta, the Prescription Review Program in Saskatchewan, the Drug Program Information Network (DPIN) in Manitoba, and the Pharmaceutical Information Program (PhIP) in Prince Edward Island. (Though there are differences in the types of drugs that are monitored, most of these at least capture opioid prescriptions). These provinces thus have the ability to potentially monitor the impact of media and other related activities on drug prescriptions. Importantly, it should be investigated whether the impact of the media surrounding OxyContin observed in Nova Scotia was also noted elsewhere in Canada. In particular, a large amount of print media came from Cape Breton, Nova Scotia, where the abuse of OxyContin was widely considered a significant problem. Over 90% of all OxyContin stories published in Canada during this period originated in two Nova Scotia daily papers (*The Chronicle Herald* based in Halifax and *The Cape Breton Post*). With a substantial amount of the print media attention restricted to Nova Scotia, it may be that changes in prescribing are also largely restricted to this province.

Although OxyContin is now being discontinued in Canada, it is likely that the future will see other opioids draw significant media attention, especially as the use of prescriptions medications, both legitimate and illicit, continues to rise.[10,141-143] In fact, as some have noted, with the withdrawal of OxyContin from the market, illicit users will likely turn to using other opioids[70,144] and these may receive significant media attention in the future.

As these drugs receive media attention, it will be important to properly educate prescribers about both the harms and benefits of these drugs in the treatment of pain.

Additionally, opioids are not the only prescription medications that have received sustained media coverage. Other examples of prescription drugs that received a high degree of media attention in Canada within the last two decades include atorvastatin (a statin), celecoxib (a COX-2 inhibitor NSAID), donepezil (an acetylcholinesterase inhibitor), oseltamivir (an antiviral) and raloxifene (a selective estrogen receptor modulator).[121] Understanding the role of the media in influencing prescribing practices is thus potentially an important consideration for all prescription drugs, and may even extend to over-the-counter medications.

Certainly some reporting of drugs such as OxyContin can be beneficial. The news media can serve to alert the public to new medical advances as well as new benefits or risks that arise from ongoing scientific studies. However, the accurate portrayal of the drugs themselves, as well as the wider social effects of some of these drugs remains pressing. An effective educational program or relevant resources for journalists and editors might be appropriate. Similarly, educational programs for prescribers around the actual harms and benefits of drugs that receive significant media attention is warranted, given that the information in the media is not always accurate. In fact, given that many interventions and education programs that aim to change provider behaviour have been shown to be at best only moderately effective (as discussed above in section 6.2.3), it may be more effective to use the lay and widespread print media to relay messages about the safe and effective use of opioids and OxyContin to prescribers, since this research demonstrated that such media seems to have a significant impact on prescribing.

Continued research in Nova Scotia and Canada that examines other influences on prescribing of opioids by healthcare providers is necessary to ensure the appropriate and adequate treatment of pain. Such research should serve to inform the development of appropriate education and policy initiatives aimed at ensuring that providers can make informed and appropriate treatment decisions around OxyContin, opioids and

prescription medications in general. Such initiatives should consider that there might be differences in prescribing by specialty and location of practice, and be developed or offered accordingly. It cannot be overly stressed, however, that any efforts to address the effects of media exposure and subsequent changes in prescribing of OxyContin and opioids need to balance the potential gains of addressing issues such as misuse and addiction against reduced access to appropriate medications for the legitimate treatment of chronic pain.

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APPENDIX A: GLOSSARY

Substance Misuse: Use of any legal, prescription, or over-the-counter substance for a purpose not consistent with legal guidelines or medical recommendations for dosage intervals or amounts.[145]

Tolerance: the need for greatly increased amounts of the substance to achieve the desired effect or a markedly diminished effect with continued use of the same amount of the substance.[37]

Substance Abuse: A maladaptive pattern of substance use manifested by recurrent and significant adverse consequences related to the repeated use of substances. The substance-related problem must have occurred repeatedly during the same 12-month period or been persistent. There may be a repeated failure to fulfill major role obligations, repeated use in situations in which it is physically hazardous, multiple legal problems, and recurrent social and interpersonal problems. This is distinguished from dependence in that it does not include tolerance, withdrawal, or a pattern of compulsive use and instead includes only the harmful consequences of repeated use.[37]

Substance Dependence (Addiction): A maladaptive pattern of substance use leading to clinically significant impairment or distress and manifests as a cluster of cognitive, behavioural and psychological symptoms indicating that the individual continues use of the substance despite significant substance-related problems. There is a pattern of repeated self-administration that can result in tolerance, withdrawal and compulsive drug-taking behaviour.[37]

APPENDIX B: NEWSPAPERS INCLUDED

Canadian Newspapers		American Newspapers	
West	The Vancouver Sun	**West**	The Denver Post The San Francisco Chronicle The Seattle Times The Houston Chronicle
Midwest	The Winnipeg Free Press	**Midwest**	The Chicago Sun-Times The Cleveland Plain Dealer The Columbus Dispatch The Omaha World Herald The St Louis Post-Dispatch The Minnesota Star Tribune
Central	The Globe and Mail (Toronto) The Montreal Gazette	**Northeast**	The Boston Globe The Boston Herald The Buffalo News The New York Daily News The Pittsburgh Post-Gazette The Wall Street Journal
East Coast	The Chronicle Herald (Halifax) The Cape Breton Post	**Southeast**	The Atlanta Journal The Tampa Tribune The Washington Post
		National	USA Today

APPENDIX C: OPIOIDS PRESENT IN THE NSPMP DATASET

Main Opioid Ingredient	Examples
Strong Opioids:	
Fentanyl (transdermal)	Duragesic®, Ran-Fentanyl®, Ratio-Fentanyl®
Hydromorphone HCL	Dilaudid®, Hydromorph Contin®, PMS-Hydromorphone®, Hydromorph IR®
Morphine Sulfate	Statex®, Kadian®, M-Eslon®, M.O.S.-Sulfate®, MS Contin®, MS-IR®, PMS-Morphine Sulfate®, Morphine Sulfate SR®, Oramorph SR®
Morphine HCL	Doloral®, M.O.S®, M.O.S SR®, Ratio-Morphine®
Oxycodone HCL	OxyContin®, Oxy-IR®, Supeudol®
Oxycodone HCL with Acetaminophen	Endocet®, Percocet®, Percocet-Demi®, ratio-Oxycocet®
Oxycodone HCL with Acetylsalicylic Acid (ASA)	Endodan®, Percodan®, ratio-Oxycodan®
Nalbuphine HCL	Nubain®
Weak Opioids:	
Codeine Phosphate with Acetaminophen	Tylenol®, Atasol®, Exdol®, Novo-Gesic®, Empracet®, Ratio-Emtec®
Codeine phosphate with ASA	Fiorinal®, Ratio-Tecnal®, Phenaphen®
Other Codeine Combinations	Robaxisal®, Methoxisal®
Propoxyphene Napsylate	Darvon®
Propoxyphene HCL	692 Tab®, Novo-Propoxyn®
Pentazocine HCL	Talwin 50®
Pentazocine Lactate	Talwin 30®
Pethidine HCL (Meperidine HCL)	Demerol®

APPENDIX D: AGE DISTRIBUTION OF THE POPULATION OF NOVA SCOTIA, BY DISTRICT HEALTH AUTHORITY

District Health Authority	Aged under 20 years (%)	Aged 20 to 34 years (%)	Aged 35 to 54 years (%)	Aged 55 to 64 years (%)	Aged 65 years and over (%)
Annapolis Valley Health	23.5	15.5	30.9	13.6	16.7
Cape Breton District Health Authority	22.9	15	29.9	14.4	17.8
Capital Health	22.8	21.1	32.1	11.7	12.3
Colchester East Hants Health Authority	24.4	16.2	31.7	12.8	14.8
Cumberland Health Authority	21.6	14	29.8	14.6	20
Guysborough Antigonish Strait Health Authority	23.6	15.1	29.5	15.1	16.8
Pictou County Health Authority	22.5	16.1	30.6	14.2	16.7
South Shore Health	20.1	13.7	31.5	15.5	19.1
South West Health	22.3	15.5	30.7	14	17.5
Nova Scotia	22.8	17.7	31.3	13.1	15.1

Data drawn from the 2006 Census [104]

APPENDIX E: ADDITIONAL GRAPHS

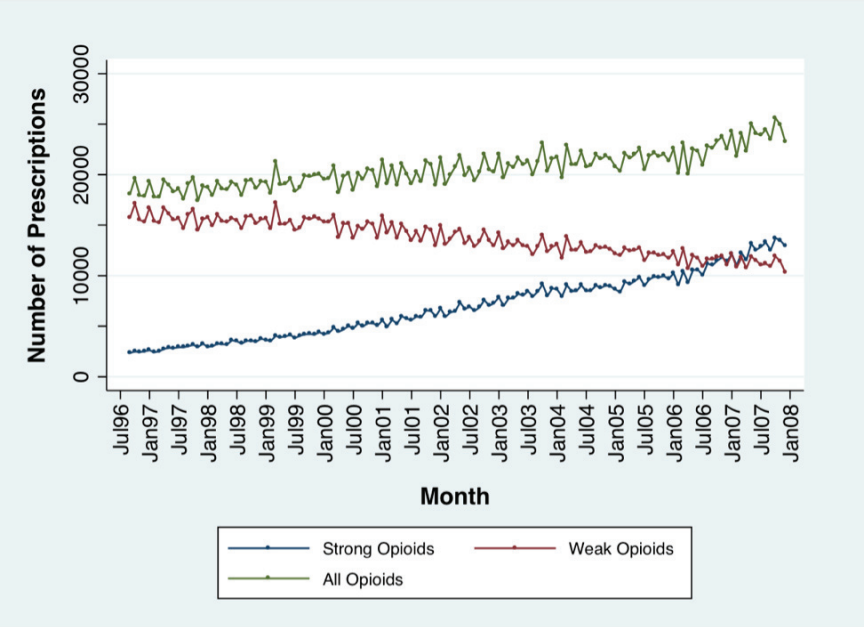

Figure E.1: Total Number of Opioid Prescriptions per Month, by Opioid Type, 1996 to 2007

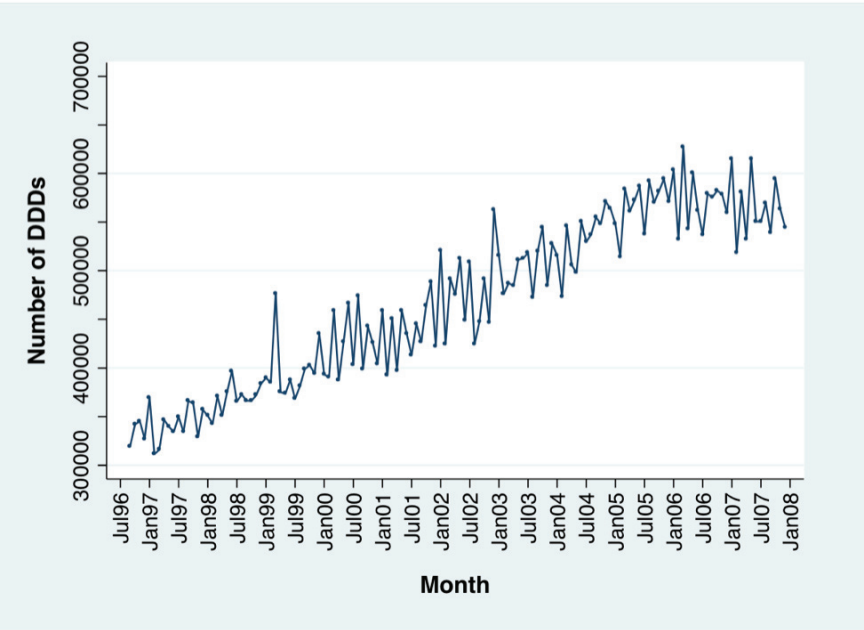

Figure E.2: Total Defined Daily Doses of Opioids Prescribed per Month, 1996 to 2007

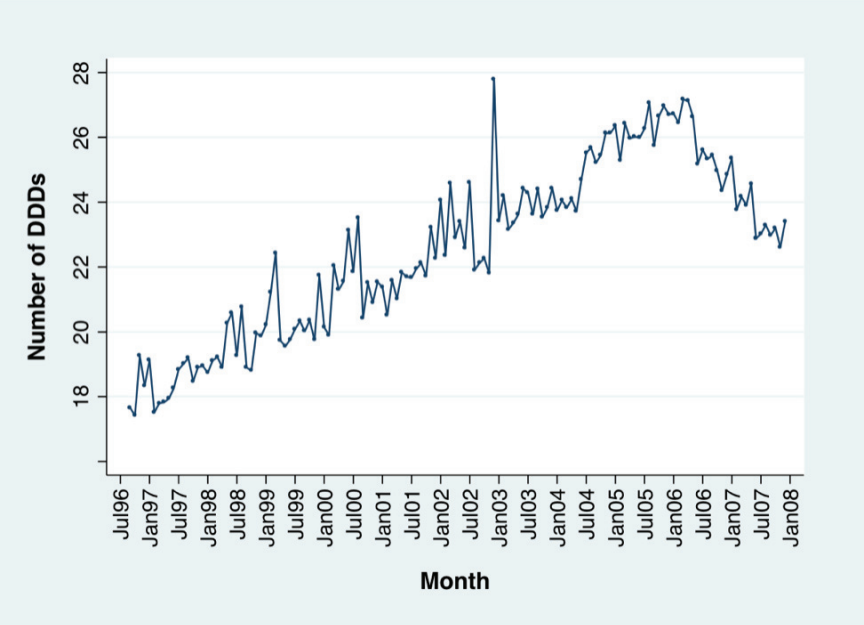

Figure E.3: Mean Number of DDDs, per Prescription per Month, 1996 to 2007

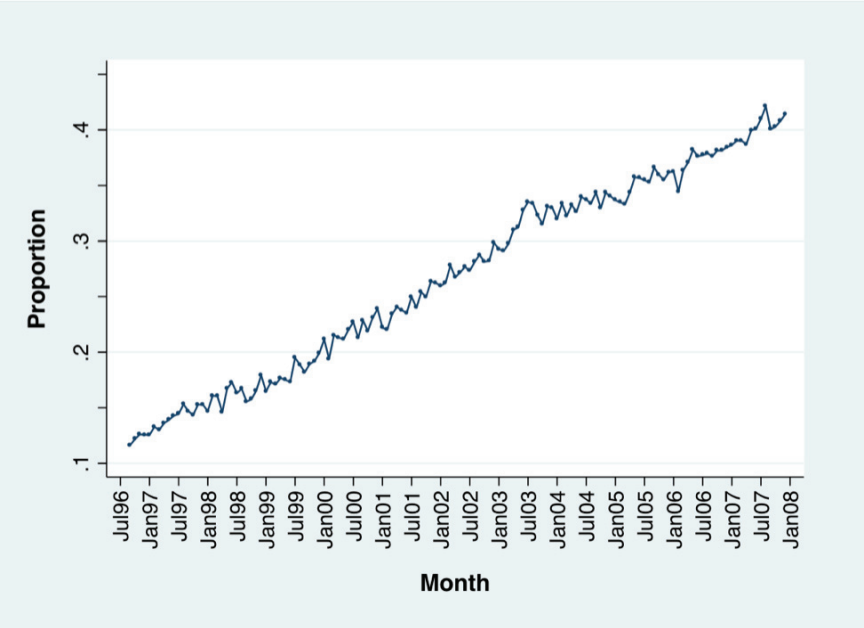

Figure E.4: Mean Proportion of DDDs That Were for Strong Opioids, per Prescriber per Month, 1996 to 2007

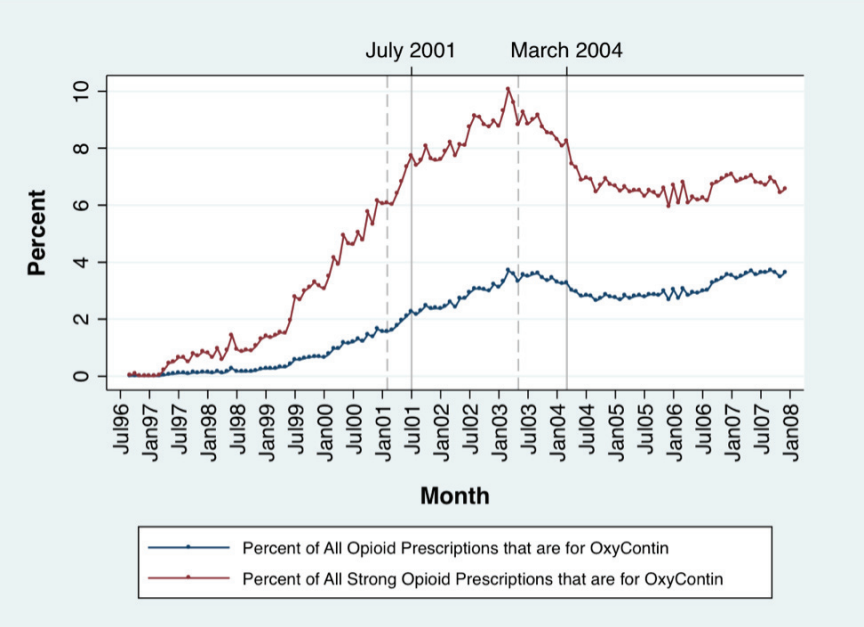

Figure E.5: Percent of All Opioid Prescriptions and Strong Opioid Prescriptions Per Month That Were for OxyContin, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

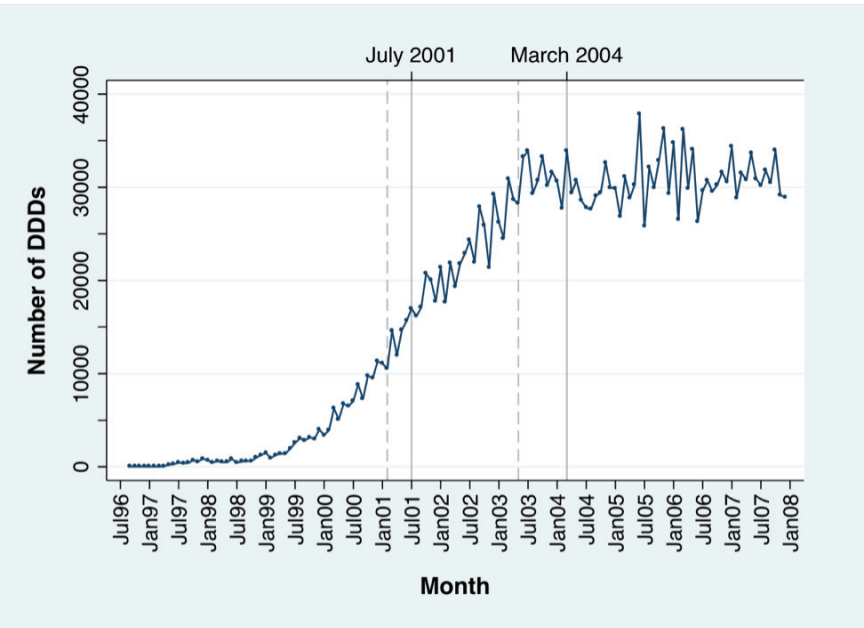

Figure E.6: Total Number of Defined Daily Doses of OxyContin Prescribed per Month, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

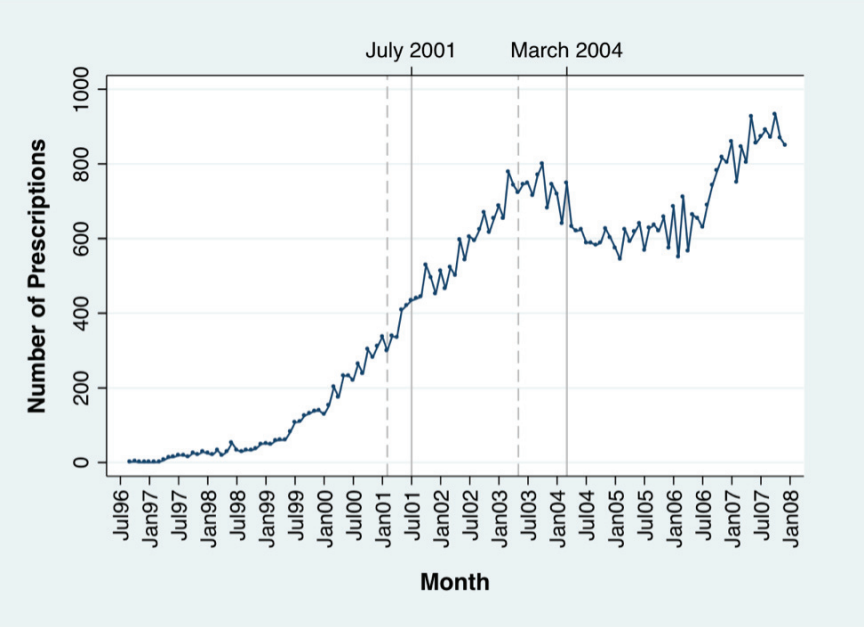

Figure E.7: Total Number of OxyContin Prescriptions per Month, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

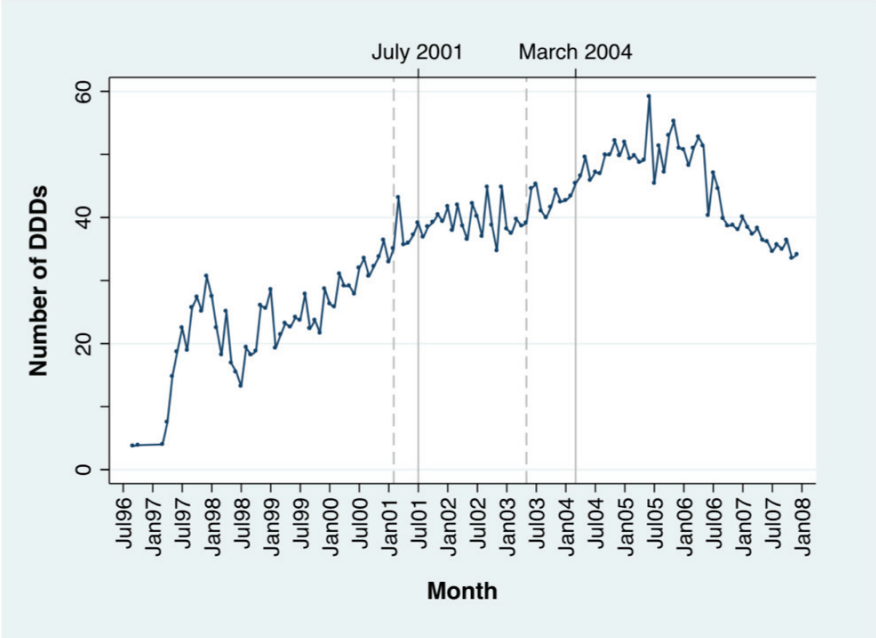

Figure E.8: Mean Number of DDDs of OxyContin Prescribed per OxyContin Prescription, per Prescriber per Month, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

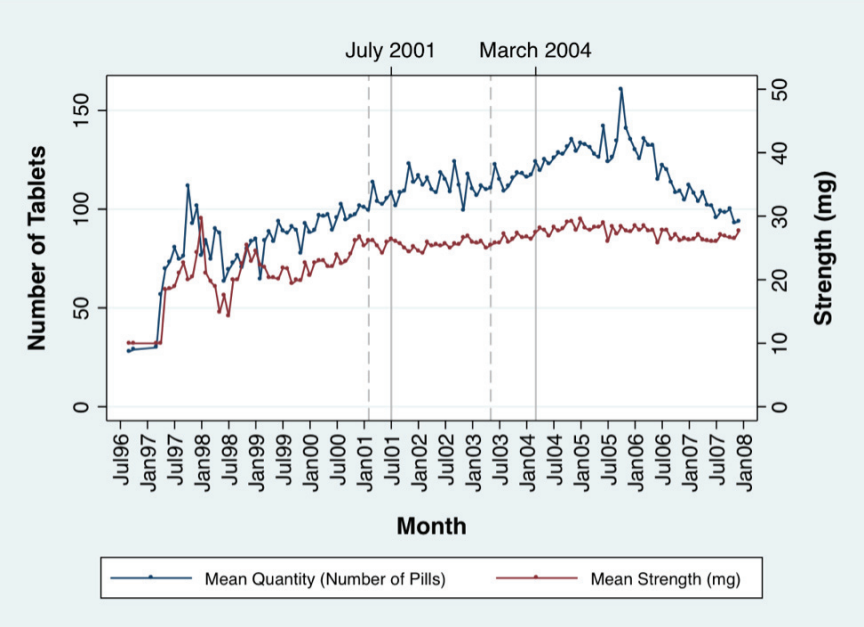

Figure E.9: Mean Quantity and Strength of OxyContin per Prescription, per Month, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

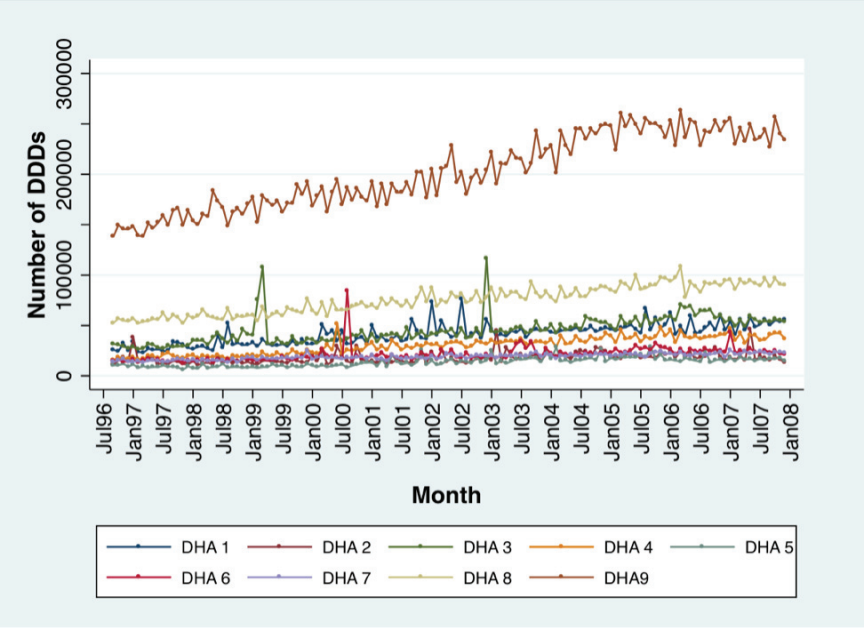

Figure E.10: Total Number of DDDs Prescribed per Month, by District Health Authority, 1996 to 2007

Note: DHA 1 = South Shore Health; DHA 2 = South West Health; DHA 3 = Annapolis Valley Health; DHA 4 = Colchester East Hants Health Authority; DHA 5 = Cumberland Health Authority; DHA 6 = Pictou County Health Authority; DHA 7 = Guysborough Antigonish Strait Health Authority; DHA 8 = Cape Breton District Health Authority; DHA 9 = Capital Health

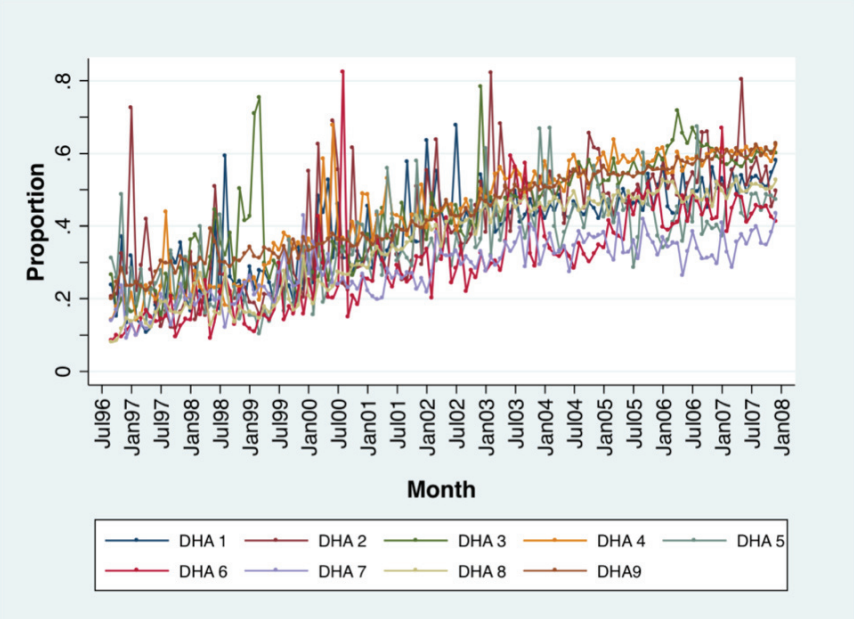

Figure E.11: Proportion of DDDs That Were for Strong Opioids per Month, by District Health Authority, 1996 to 2007

Note: DHA 1 = South Shore Health; DHA 2 = South West Health; DHA 3 = Annapolis Valley Health; DHA 4 = Colchester East Hants Health Authority; DHA 5 = Cumberland Health Authority; DHA 6 = Pictou County Health Authority; DHA 7 = Guysborough Antigonish Strait Health Authority; DHA 8 = Cape Breton District Health Authority; DHA 9 = Capital Health

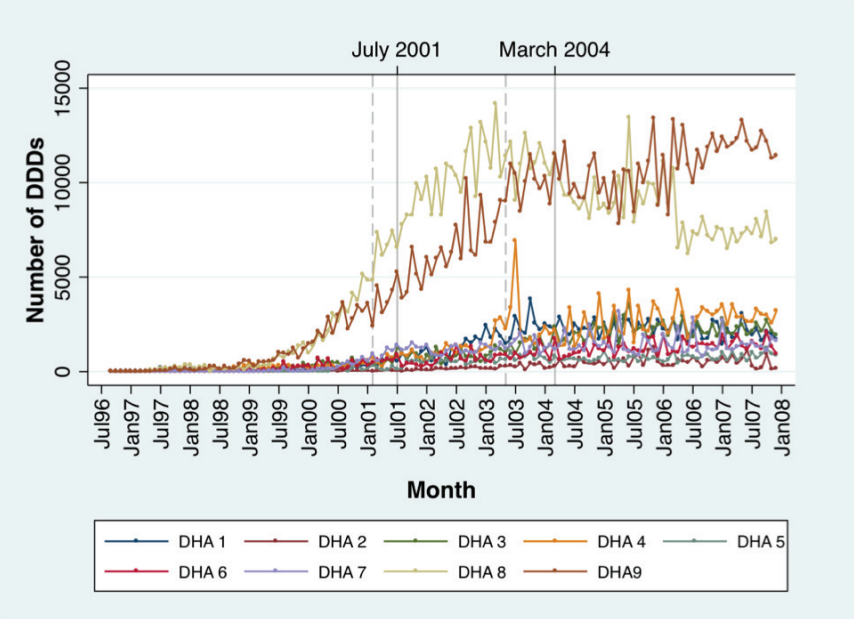

Figure E.12: Total Number of DDDs of OxyContin Prescribed per Month, by District Health Authority, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

Note: DHA 1 = South Shore Health; DHA 2 = South West Health; DHA 3 = Annapolis Valley Health; DHA 4 = Colchester East Hants Health Authority; DHA 5 = Cumberland Health Authority; DHA 6 = Pictou County Health Authority; DHA 7 = Guysborough Antigonish Strait Health Authority; DHA 8 = Cape Breton District Health Authority; DHA 9 = Capital Health

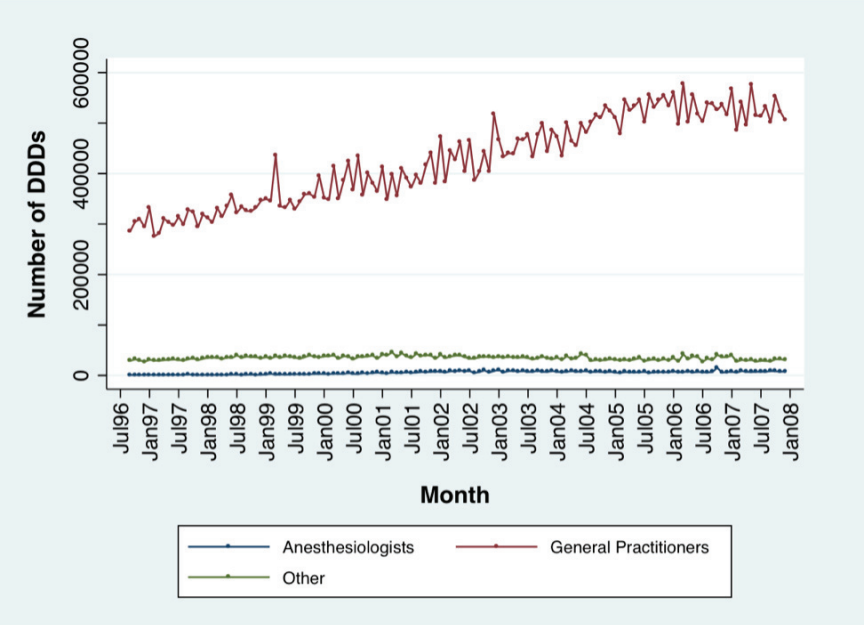

Figure E.13: Total Number of DDDs Prescribed per Month, by Specialty, 1996 to 2007

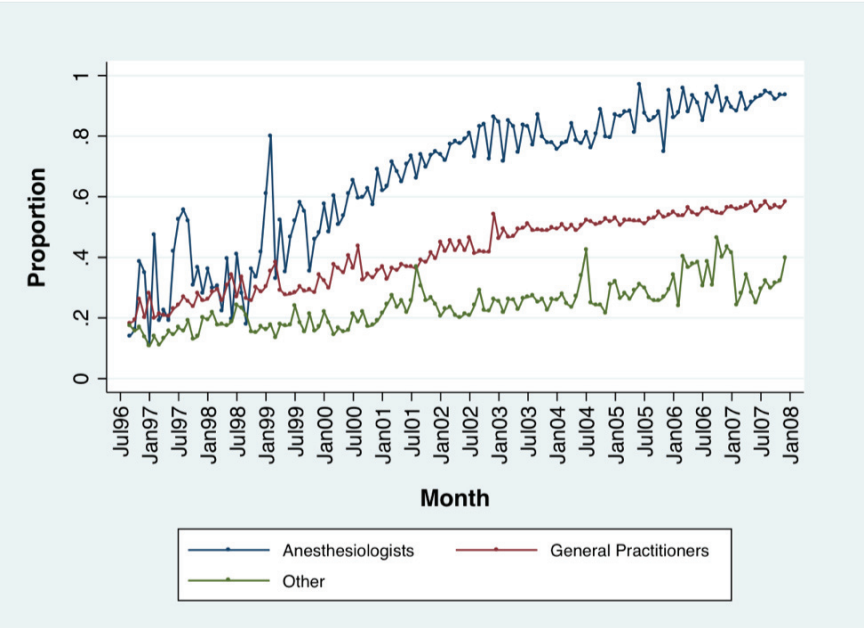

Figure E.14: Proportion of DDDs That Were for Strong Opioids per Month, by Specialty, 1996 to 2007

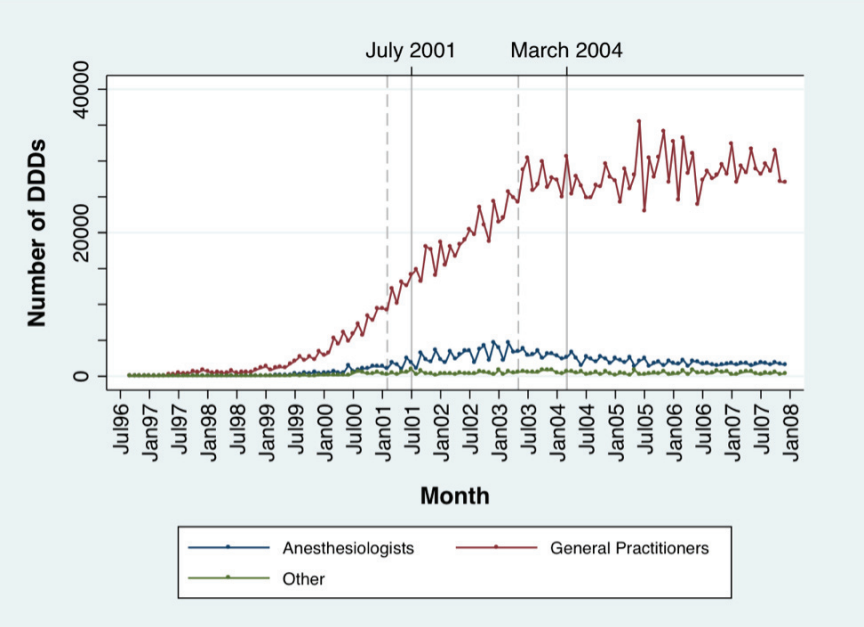

Figure E.15: Total Number of DDDs of OxyContin Prescribed per Month, by Specialty, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

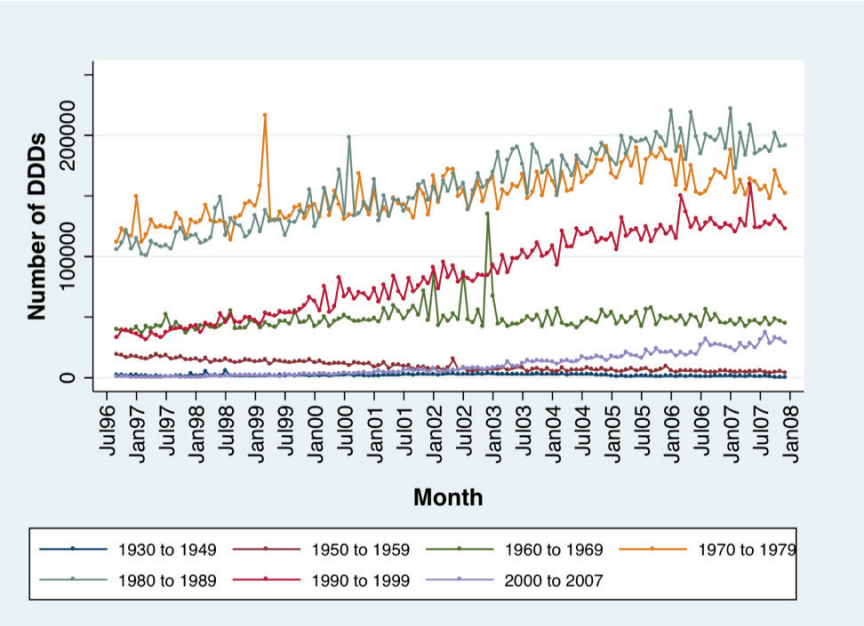

Figure E.16: Total Number of DDDs Prescribed per Month, by Decade of Graduation, 1996 to 2007

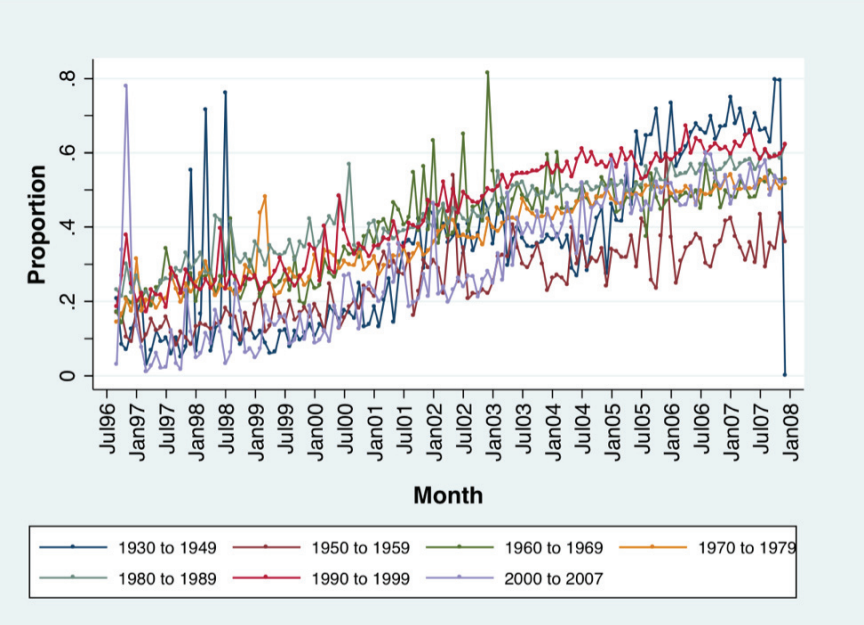

Figure E.17: Proportion of DDDs That Were for Strong Opioids per Month, by Decade of Graduation, 1996 to 2007

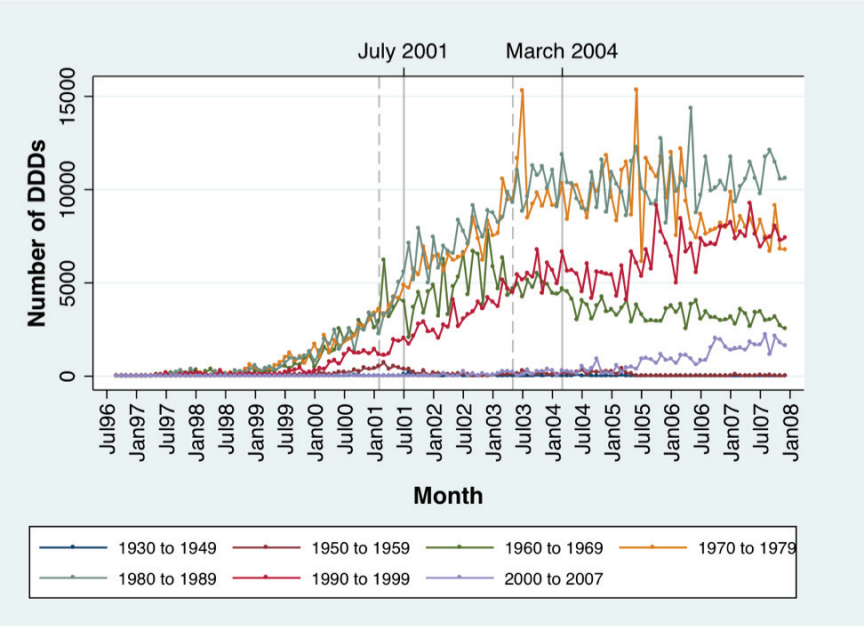

Figure E.18: Total Number of DDDs of OxyContin Prescribed per Month, by Decade of Graduation, 1996 to 2007

Note: The solid gray lines represent the absolute media peaks (with the American peak occurring in July 2001 and the Canadian peak in March 2004). The dotted lines represent the beginning of these peaks and correspond to February 2001 and May 2003, respectively.

APPENDIX F: INTERACTION MODELS

Table F.1: Fixed-Effects Regression Estimates for the Interaction Terms for the Proportion of All Opioid DDDs and Strong Opioid DDDs That Were for OxyContin, by District Health Authority

Time Interval and Interaction Term	Outcome Variable: Logit of the Proportion of All Opioid DDDs That Were For OxyContin N = 3615				Outcome Variable: Logit of the Proportion of All Strong Opioid DDDs That Were For OxyContin N = 3100			
	β	Lower 95% CI	Upper 95% CI	p-value	β	Lower 95% CI	Upper 95% CI	p-value
Interval 1 (DHA 9)	0.0539	0.0157	0.0920	**0.0057**	0.0842	0.0240	0.1444	**0.0061**
Interval 2 (DHA 9)	- 0.0030	- 0.0505	0.0446	0.9027	-0.0326	-0.1062	0.0410	0.3852
Interval 3 (DHA 9)	- 0.0515	- 0.0716	- 0.0313	**<0.0001**	- 0.0564	- 0.0832	- 0.0297	**<0.0001**
Interval 1 Interaction Terms								
Int1*DHA1	- 0.0221	- 0.1182	0.0739	0.6514	- 0.0080	- 0.1701	0.1541	0.9228
Int1*DHA2	- 0.0992	- 0.1697	- 0.0288	**0.0058**	- 0.1660	- 0.2786	- 0.0533	**0.0039**
Int1*DHA3	- 0.0286	- 0.0954	0.0381	0.4003	- 0.0588	- 0.1519	0.0343	0.2159
Int1*DHA4	0.0245	- 0.0847	0.1336	0.6601	0.0403	- 0.1240	0.2047	0.6303
Int1*DHA5	0.0890	- 0.0250	0.2030	0.1261	0.1341	- 0.0047	0.2729	0.0582
Int1*DHA6	0.0155	- 0.1011	0.1320	0.7949	0.0609	- 0.1149	0.2367	0.4971
Int1*DHA7	0.2021	0.0581	0.3462	**0.0060**	0.2555	0.0604	0.4505	**0.0103**
Int1*DHA8	0.1728	0.1039	0.2418	**<0.0001**	0.2009	0.0845	0.3173	**0.0007**
Interval 2 Interaction Terms								
Int2*DHA1	0.0471	- 0.0477	0.1419	0.3297	0.0474	- 0.1062	0.2010	0.5451
Int2*DHA2	0.0611	- 0.0268	0.1491	0.1731	0.1294	- 0.0097	0.2686	0.0683
Int2*DHA3	0.0148	- 0.0836	0.1132	0.7681	0.0525	- 0.0780	0.1830	0.4306
Int2*DHA4	- 0.0063	- 0.1473	0.1348	0.9306	- 0.0132	- 0.2238	0.1975	0.9025
Int2*DHA5	- 0.1192	- 0.2530	0.0145	0.0806	- 0.1723	- 0.3430	- 0.0016	0.0479
Int2*DHA6	- 0.0318	- 0.1869	0.1234	0.6883	- 0.0820	- 0.3291	0.1651	0.5152
Int2*DHA7	- 0.2565	- 0.4309	- 0.0821	**0.0040**	- 0.3181	- 0.5532	- 0.0831	**0.0080**
Int2*DHA8	- 0.2029	- 0.2819	- 0.1238	**<0.0001**	- 0.2522	- 0.3790	- 0.1254	**0.0001**
Interval 3 Interaction Terms								
Int3*DHA1	- 0.0426	- 0.1101	0.0250	0.2169	- 0.0589	- 0.1601	0.0422	0.2535
Int3*DHA2	0.0511	0.0084	0.0937	**0.0189**	0.0632	- 0.0036	0.1299	0.0636
Int3*DHA3	0.0255	- 0.0326	0.0835	0.3895	0.0243	- 0.0495	0.0980	0.5190
Int3*DHA4	- 0.0121	- 0.0644	0.0401	0.6491	- 0.0223	- 0.0929	0.0483	0.5358
Int3*DHA5	0.0353	- 0.0019	0.0725	0.0627	0.0385	- 0.0062	0.0832	0.0915
Int3*DHA6	0.0199	- 0.0459	0.0857	0.5540	0.0258	- 0.0821	0.1336	0.6395
Int3*DHA7	0.0599	- 0.0012	0.1210	0.0548	0.0681	- 0.0088	0.1451	0.0827
Int3*DHA8	0.0130	- 0.0193	0.0453	0.4290	0.0340	- 0.0085	0.0764	0.1169

Note: Interval 1 = January 2000 to January 2001; Interval 2 = February 2001 to April 2003; Interval 3 = May 2003 to December 2007; DHA 1 = South Shore Health; DHA 2 = South West Health; DHA 3 = Annapolis Valley Health; DHA 4 = Colchester East Hants Health Authority; DHA 5 = Cumberland Health Authority; DHA 6 = Pictou County Health Authority; DHA 7 = Guysborough Antigonish Strait Health Authority; DHA 8 = Cape Breton District Health Authority; DHA 9 = Capital Health

Table F.2: Fixed-Effects Regression Estimates for the Interaction Terms for the Proportion of All Opioid DDDs and Strong Opioid DDDs That Were for OxyContin, by Specialty

Time Interval or Interaction Term	Outcome Variable							
	Logit of the Proportion of All Opioid DDDs That Were For OxyContin N = 3676				Logit of the Proportion of All Strong Opioid DDDs That Were For OxyContin N = 3149			
	β	Lower 95% CI	Upper 95% CI	p-value	β	Lower 95% CI	Upper 95% CI	p-value
Interval 1 (GPs)	0.0906	0.0633	0.1180	**<0.0001**	0.1219	0.0823	0.1614	**<0.0001**
Interval 2 (GPs)	- 0.0447	- 0.0780	- 0.0114	**0.0086**	- 0.0757	- 0.1235	- 0.0279	**0.0019**
Interval 3 (GPs)	- 0.0474	- 0.0621	- 0.0327	**<0.0001**	- 0.0502	- 0.0707	- 0.0298	**<0.0001**
Interval 1 Interaction Terms								
Int1*Anesthesiologist	0.0088	- 0.0370	0.0546	0.7066	- 0.0448	- 0.0984	0.0089	0.1020
Int1*Other	- 0.0600	- 0.1081	- 0.0120	**0.0143**	- 0.0438	- 0.1659	0.0783	0.4818
Interval 2 Interaction Terms								
Int2*Anesthesiologist	- 0.0633	- 0.1233	- 0.0034	**0.0384**	- 0.0085	- 0.0762	0.0592	0.8050
Int2*Other	0.0243	- 0.0285	0.0770	0.3674	0.0198	- 0.1164	0.1561	0.7755
Interval 3 Interaction Terms								
Int3*Anesthesiologist	0.0271	0.0043	0.0500	**0.0198**	0.0267	0.0010	0.0524	**0.0417**
Int3*Other	0.0270	0.0050	0.0491	**0.0163**	0.0010	- 0.0441	0.0461	0.9661

Note: Interval 1 = January 2000 to January 2001; Interval 2 = February 2001 to April 2003; Interval 3 = May 2003 to December 2007. GPs refer to general practitioners.

Table F.3: Fixed-Effects Regression Estimates for the Interaction Terms for the Proportion of All Opioid DDDs and Strong Opioid DDDs That Were for OxyContin, by Decade of Graduation

Time Interval or Interaction Term	Outcome Variable: Proportion of All Opioid DDDs That Were For OxyContin N = 3435				Outcome Variable: Proportion of All Strong Opioid DDDs That Were For OxyContin N = 2975			
	β	Lower 95% CI	Upper 95% CI	p-value	β	Lower 95% CI	Upper 95% CI	p-value
Interval 1 (Grad 5)	0.0846	0.0375	0.1316	**0.0005**	0.1232	0.0499	0.1966	**0.0010**
Interval 2 (Grad 5)	- 0.0280	- 0.0849	0.0289	0.3351	- 0.0579	- 0.1444	0.0286	0.1897
Interval 3 (Grad 5)	- 0.0629	- 0.0883	- 0.0374	**<0.0001**	- 0.0792	- 0.1144	- 0.0439	**<0.0001**
Interval 1 Interaction Terms								
Int1*Grad1	- 0.0734	- 0.1716	0.0248	0.1428	- 0.1390	- 0.2241	- 0.0539	**0.0014**
Int1*Grad2	- 0.0283	- 0.1162	0.0596	0.5274	- 0.0258	- 0.1721	0.1206	0.7301
Int1*Grad3	- 0.0289	- 0.1112	0.0534	0.4914	- 0.0713	- 0.1752	0.0326	0.1786
Int1*Grad4	0.0206	- 0.0437	0.0849	0.5291	0.0216	- 0.0736	0.1168	0.6564
Int1*Grad6	0.0023	- 0.0687	0.0732	0.9497	- 0.0056	- 0.1112	0.0999	0.9166
Int1*Grad7	- 0.0720	- 0.1368	- 0.0071	**0.0296**	- 0.0821	- 0.1867	0.0224	0.1237
Interval 2 Interaction Terms								
Int2*Grad1	0.0708	- 0.1118	0.2535	0.4470	0.1438	- 0.0167	0.3044	0.0791
Int2*Grad2	- 0.0539	- 0.1658	0.0580	0.3449	- 0.0834	- 0.2637	0.0969	0.3646
Int2*Grad3	0.0157	- 0.0806	0.1121	0.7492	0.0377	- 0.0900	0.1654	0.5629
Int2*Grad4	- 0.0425	- 0.1216	0.0366	0.2919	- 0.0555	- 0.1715	0.0606	0.3490
Int2*Grad6	- 0.0158	- 0.1006	0.0691	0.7155	- 0.0177	- 0.1437	0.1083	0.7834
Int2*Grad7	0.0225	- 0.0628	0.1077	0.6055	0.0302	- 0.1053	0.1657	0.6622
Interval 3 Interaction Terms								
Int3*Grad1	- 0.0450	- 0.1548	0.0648	0.4216	- 0.0568	- 0.1795	0.0658	0.3637
Int3*Grad2	0.0835	0.0402	0.1267	**0.0002**	0.1157	0.0589	0.1725	**0.0001**
Int3*Grad3	0.0054	- 0.0342	0.0450	0.7899	0.0311	- 0.0216	0.0837	0.2471
Int3*Grad4	0.0261	- 0.0091	0.0613	0.1463	0.0428	- 0.0058	0.0913	0.0841
Int3*Grad6	0.0291	- 0.0082	0.0663	0.1258	0.0492	- 0.0023	0.1008	0.0612
Int3*Grad7	0.0919	0.0436	0.1402	**0.0002**	0.1102	0.0418	0.1786	**0.0016**

Note: Interval 1 = January 2000 to January 2001; Interval 2 = February 2001 to April 2003; Interval 3 = May 2003 to December 2007. Grad# indicates the graduation groups, as follows: Grad1 = 1930 to 1949; Grad 2 = 1950 to 1959; Grad3 = 1960 to 1969; Grad4 = 1970 to 1979; Grad5 = 1980 to 1989; Grad 6 = 1990 to 1999; Grad7 = 2000 to 2007