Missing Work is a Pain: The Effect of Cox-2 Inhibitors on Sickness Absence*

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Abstract

Little is known about how medical innovation can affect labor supply. This paper aims to estimate the economic impact of treatments against chronic joint pain. In particular, we analyze how the availability of Cox-2 inhibitors, a class of pharmaceuticals used for treating pain and inflammation, affected the sickness absence of individuals suffering from chronic joint pain. To do so, we exploit the market entry of the Cox-2 inhibitor Vioxx and its sudden market withdrawal as exogenous sources of variation in Cox-2 inhibitor use. We merge detailed administrative data on sickness absence from Norway with survey data on health and health behaviors. Our robust difference-in-differences estimates reveal a significant causal effect of Vioxx availability on sickness absence: whereas the market entry of Vioxx decreased the number of sickness absence days among individuals with chronic joint pain by 4 to 5 percent, the market withdrawal led to a 10 to 14 percent increase. Considering such labor supply effects is important for evaluating the net benefits of pharmaceutical and medical technology.

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1 Introduction

Most evaluations of medical technologies and treatments are based on clinical and health outcomes and direct medical costs. Little attention, however, has been given to the labor supply effects of advancements in medical and pharmaceutical technology. Broadening the net benefits of medical innovations to include economic impacts is important for several reasons. First, in both the United States and Europe, there has been an emphasis placed on using cost-effectiveness research to determine which treatments and technologies will be covered by insurance plans and national health care systems. Thus, considering the economic effects of medical innovation could have important implications for regulatory decision-making. Second, employers may be interested in the effects of medical treatments on labor supply since they often sponsor health insurance plans for their employees, particularly in the US. Third, broadening the scope of the costs and benefits of medical technologies could affect health care providers' and patients' treatment choices and care plans.

In this paper, we aim to estimate the impact of progress in the treatment against chronic joint pain on economic outcomes. In particular, we examine how the availability of Cox-2 inhibitors, pharmaceuticals prescribed for the treatment of chronic pain and inflammation, affected the sickness-related work absence of individuals with joint pain in Norway. We do so by exploiting the market entry of Vioxx, a popular Cox-2 inhibitor, in 2001 and its unexpected worldwide market withdrawal in 2004 due to concerns over negative side effects as sources of exogenous variation in the use of Cox-2 inhibitors. Using administrative panel data on sickness absence, we find that Vioxx's entry led to a 4 to 5 percent decrease in sickness absence days among individuals with chronic joint pain, while Vioxx's withdrawal led to a 10 to 14 percent increase in the number of sickness absence days. We find the effects of both the entry and the removal were largest for women, individuals with physically demanding jobs, low-income individuals, and single individuals.

Our paper contributes to a small but growing literature that analyzes how medical treatments or changes in available treatments affect outcomes such as labor supply and earnings. Thirumurthy et al. (2008) study the effect of treatments for HIV and AIDS on labor supply in Kenya, and find within 6 months of antiretroviral treatment there were substantial increases in both the probability the patient participates in the labor force and weekly hours worked. Some studies have focused on the labor supply impacts of treatments for depression (see Timbie et al. (2006) for a review of this literature). In the medical literature, there has been a focus on the impact of influenza vaccinations, particularly workplace-sponsored vaccinations, on worker absenteeism and productivity (see for example Nichol, 2001; Nichol et al., 2009). More recently, Epstein et al. (2013) study the effect of minimally invasive surgeries on medical expenditures and worker absenteeism. For 4 of the 6 types of surgeries they consider, minimally invasive procedures were associated with significantly fewer days of absence from work than standard procedures. In addition, Papageorge (2014) estimates a dynamic structural model to determine the value of a treatment for HIV known as HAART. His model takes into account how side effects and the labor market affect the demand for medical

treatment.

Our work is most closely related to Garthwaite (2012) who estimates the effect of Cox-2 inhibitor use on the labor force participation of individuals with chronic joint conditions in the United States by exploiting the removal of Vioxx from the market in a difference-in-differences and instrumental variables framework. He finds Vioxx's removal and the resulting reduction in the use of all Cox-2 inhibitors decreased the probability of working for individuals with joint pain by 22 percentage points. While Garthwaite (2012) focuses on the extensive margin labor supply response to Vioxx's withdrawal, we focus on intensive labor supply adjustments, particularly sickness absence days, using detailed administrative data on sickness leave spells and health from Norway. Further, the data allows us to analyze the impact of both the entry and exit of Vioxx on sickness absence days to examine whether there were asymmetric effects of the availability of Cox-2 inhibitors. In addition, given our findings on the impact of Vioxx's availability on sickness absence, we then examine how the entry and removal of Vioxx affected the probability an individual receives disability benefits as well as the probability of working full-time.

The paper proceeds as follows. Section 2 provides background on Vioxx and Cox-2 inhibitors as well as the Norwegian sickness absence scheme. We discuss the data and provide descriptive statistics in Section 3. We describe our empirical strategy in Section 4. We present and discuss our results and analyze whether there were heterogenous effects by individual characteristics in Section 5. Section 6 presents sensitivity analysis. Section 7 discusses the impact of Vioxx's entry and removal on other labor supply outcomes including number of sickness absence spells, disability benefit receipt, and full-time work. Section 9 provides a brief conclusion.

2 Institutional Background

2.1 Vioxx and Cox-2 Inhibitors

Cox-2 inhibitors are a type of non-steroidal anti-inflammatory drug (NSAID). NSAIDs are usually indicated for the treatment of acute or chronic conditions involving pain and inflammation, particularly in the joints. Many conditions can lead to joint pain and inflammation including osteoarthritis, rheumatoid arthritis, bursitis, gout, strains, sprains, and other injuries. According to data from the 2006 wave of the National Health Interview Survey, about one third of adults in the US reported experiencing joint pain within the past 30 days. Joint pain most commonly occurs in the knee, shoulder, and hip, and becomes increasingly common as individuals age. Before the introduction of Cox-2 inhibitors, most individuals with chronic conditions were prescribed NSAID medications such as ibuprofen (marketed under the brand names Motrin and Advil in the US or Ibux in Norway) or naproxen (marketed under the brand name Aleve in the US or Napren in Norway). However, for some patients these drugs cause serious gastrointestinal bleeding and ulcerations, and as a result, many patients with chronic pain who were susceptible to adverse

gastrointestinal events were left without therapeutic options. Cox-2 inhibitors do not cause these gastrointestinal complications, and as a result, they were recommended especially for individuals with joint conditions and gastrointestinal problems (Schnitzer and Hochberg, 2002).

Vioxx was approved first in the United States by the Food and Drug Administration (FDA) in May 1999, entering the US market soon after the entry of the first Cox-2 inhibitor, Celebrex. Vioxx quickly became one of the most widely prescribed Cox-2 inhibitors, selling in more than 80 countries and enjoying $5.5 billion in global sales by 2004, but also faced controversy about its safety. The Vioxx GI Outcomes Research (VIGOR) study published in 2000 found an increase in cardiac events for individuals taking Vioxx compared to those taking naproxen. Scientists initially interpreted the greater cardiac risks associated with Vioxx as occurring because naproxen lowered risks of heart attacks (Mukherjee et al., 2001). Subsequent epidemiological studies confirmed that while Vioxx was associated with decreased intestinal complications, it indeed increased the relative risk of cardiac events even for low cardiac risk patients (see for example Bresalier et al., 2005). These findings led the manufacturer Merck to voluntarily remove Vioxx from the worldwide market on September 30, 2004. The worldwide withdrawal of Vioxx heightened awareness about the cardiac risks of Cox-2 inhibitors, leading to a decrease in their use as well as the withdrawal of Bextra, another Cox-2 inhibitor, from the US and European markets.

2.2 Vioxx and Cox-2 Inhibitors in Norway

NSAIDs are among the most used pharmaceuticals in Norway (Rugstad, 2000). The left panel of Figure 1 shows that across all Nordic countries, the sale of NSAIDs increased substantially after the market entry of Cox-2 inhibitors in 2000 and decreased after the worldwide removal of Vioxx from the market in 2004. In Norway, the use of NSAIDs was about 25 defined daily doses (DDD) per 1000 inhabitants per day in 1995, 34 DDD in 2000, and over 50 DDD in 2004. The largest increase in NSAID sales occurred between 2000 and 2001 when the Norwegian Medicines Agency included Cox-2 inhibitors on its list of pharmaceuticals which are fully refunded for individuals with a chronic condition by the national health care system.[1] Since Cox-2 inhibitors were introduced first in the US in 1999, by the time they were introduced in Norway in 2000 and were included in the list of fully refunded pharmaceuticals in July 2001, physicians were aware of the drugs and switched patients' prescriptions quickly.

According to the Norwegian Medicines Agency, doctors were permitted to prescribe Cox-2 inhibitors to individuals with serious hip and knee osteoarthritis, rheumatoid arthritis, or chronic

[1]Similar to most Western pharmaceutical markets, the Norwegian pharmaceutical market is extensively regulated. The regulatory body is the Norwegian Ministry of Health and Care Services and its agency named the Norwegian Medicines Agency. Producers of pharmaceuticals need government approval to enter the Norwegian market. Approval is based on clinical trials proving the drug affects patients' health positively and is not dangerous. The producer must also provide a positive cost-benefit analysis to get the drug included on the list of pharmaceuticals which are fully refunded for patients with a chronic condition. Brekke et al. (2011) provide a detailed description of the Norwegian pharmaceutical market.

pain which reduced quality of life. In addition, patients had to have gastrointestinal problems that could lead to gastrointestinal bleeding when taking other NSAIDs. This restriction was implemented since Cox-2 inhibitors were substantially more expensive than other common NSAIDs and the only stated difference was the reduced gastrointestinal side effects. Thus, most patients who were switched to Cox-2 inhibitors were individuals with severe chronic joint pain in combination with gastrointestinal vulnerability. About one third of individuals in Nordic countries with severe chronic joint pain also report having gastrointestinal problems (Rugstad et al., 1994). For these patients, the main alternatives to taking Cox-2 inhibitors were to take other substitute NSAIDs but bear an increased risk of gastrointestinal bleeding or to abstain from NSAIDs and cope with pain and stiffness. Other alternatives include using weaker and less effective analgesics or drugs from the opioid group.[2] Another potential alternative for patients with hip or knee osteoarthritis was joint replacement surgery. Given that most of the alternative treatments for individuals using Cox-2 inhibitors were either less effective or involved gastrointestinal risk or surgery, these individuals may have responded to the entry of Cox-2 inhibitors by taking fewer sickness absence days and then taking more sickness absence when Cox-2 inhibitors became unavailable.

The right panel of Figure 1 displays the sale of Cox-2 inhibitors in all Nordic countries between 1998 and 2007, with the increase in sales in Norway being the largest. Whereas in 2000, 1.8 defined daily doses per 1000 inhabitants per day were sold in Norway, this number increased to 21.8 in 2004. Cox-2 inhibitors accounted for 42 percent of NSAID sales in 2004. The worldwide withdrawal of Vioxx from the market led to a sharp drop in Cox-2 inhibitor sales after 2004. The Norwegian health care authorities decided to no longer refund purchases of any Cox-2 inhibitors after May 1, 2005 based on a report from the European Medicines Agency that documented an increased risk for cardiovascular complications for all Cox-2 inhibitors. As a result, these types of drugs essentially vanished from the Norwegian market.

Celebrex was the first Cox-2 inhibitor to enter the Norwegian market in 2000, and was quickly followed by Vioxx and several others including Bextra, Arcoxia, and Dynastat. It is important to note that while various Cox-2 inhibitors entered the Norwegian market at different times, they were all fully refundable starting in July 2001. Vioxx had the second largest market share among the Cox-2 inhibitors in Norway after Celebrex. About 4.5 percent of the Norwegian adult population (i.e. over the age of 18) used Vioxx at least once between January 1, 2004 and the date of withdrawal (Duratovic, 2007). About 60 percent of Vioxx users in 2004 were women. The average user was 53 years old and the median user was 52 years old. Since Vioxx was mostly used by patients suffering from arthritis and rheumatism which are more prevalent among the elderly, the highest rate of usage was among the 70-79 year old population. In this age group 6.3 percent used Vioxx at least once in the first nine months of 2004. About 30 percent of the individuals using Vioxx were users

[2]Opioids are used for the treatment of acute pain. They may, however, lead to dependence and as a result are mainly used in palliative care to alleviate severe pain of the terminally ill. Opioids also have a series of negative side effects including nausea, vomiting, and drowsiness.

with severe chronic pain consuming the drug for at least three consecutive months. Among this long-term user group, the median age was 64 years old and 70 percent were women. About 20 percent of the long-term users also used other NSAIDs and about a third received prescriptions for pharmaceuticals in the opioid group while using Vioxx.

In the three months after the withdrawal of Vioxx from the market, 40 percent of Vioxx users switched to other Cox-2 inhibitors. Since refunds for the other Cox-2 inhibitors stopped in 2005, most former Vioxx users then used other pharmaceuticals from the NSAID group. About 20 percent of former Vioxx users were switched to pharmaceuticals in the opioid group immediately after the withdrawal and this share doubled in 2005 after the other Cox-2 inhibitors were no longer available. 33 percent of the former Vioxx users did not receive any analgesics during the three months after the withdrawal. This number, however, fell to 13 percent two years after the withdrawal (Duratovic, 2007).

The Norwegian Organization for Patient Compensation (Norsk Pasientskadeerstatning) reports that 114 patients who had Vioxx prescriptions were plausibly harmed due to Vioxx's side effects and subsequently received compensation payments. In total, NOK 37 million were paid, with the largest compensation payment amounting to NOK 2.8 million. The most frequent reason for compensation payments was side effects such as heart attack, heart weakness, brain stroke, or other heart diseases. In 19 cases, compensation was paid to surviving dependents of individuals who died from Vioxx's side effects.

2.3 Sickness Leave in Norway

Sickness insurance is mandatory in Norway and regulated by law. It covers all workers who have been employed at the same employer for at least four weeks. The replacement rate is 100 percent up to an amount of 6G (approximately $85,000 in 2013) from the first day of sickness absence up to a maximum of one year.[3] For absences lasting more than three days, a medical certificate is required.[4] As discussed in more detail below, starting in 2004, sickness spells lasting more than eight weeks carry stricter requirements—a primary care physician or a physician at a medical emergency center must provide a more detailed certificate to the Social Security Administration (NAV) including diagnosis and an assessment of the employee's prognosis.

The sickness absence benefits are covered by the employer initially and then by the Social Security Administration. The employer is obliged to pay the full wage for the first 16 days. From day 17 onwards, the Social Security Administration covers the full benefits. The benefits from the Social Security Administration are funded by uniform payroll taxes.[5] The compensation scheme

[3] G is an inflation adjusted unit for calculation of social benefits in Norway.

[4] Individuals who are frequently absent require certification starting from the first day of absence (Markussen et al., 2011). In addition, individuals can take at most four uncertified absence spells per year.

[5] For a further description of the Norwegian social security system and sickness leave see Markussen (2012) and Rieck et al. (2012).

is relatively generous and absence rates are high in Norway. About 4 percent of the labor force is on sickness benefits, resulting in a sickness absence rate of 7 percent and program expenditures amounting to 2.5 percent of GDP.[6] Absence rates are highest among older workers and female employees.

On July 1, 2004, Norwegian authorities implemented a reform in the sickness absence policy which changed the physician certification regulations. The reform required physicians to provide an extended medical certification for workers with leave spells lasting more than eight weeks if no work-related activities were performed, documenting that inactivity is necessary and part of the treatment.[7] Sickness leave fell by around 20 percent at the time of the reform, corresponding to a 1.34 percentage point increase in labor supply (Markussen, 2009). There may be concern that the policy reform occurred around the same time as Vioxx's withdrawal from the market. It is, however, unlikely that the reform impacted those with joint pain more or less than those without joint pain or with other types of pain. We address concerns about the timing of this reform and the timing of Vioxx's removal in Section 3.3.

3 Data

The primary data source used is the Norwegian Registry Data, a linked administrative dataset that covers the population of Norwegians up to 2012. The data are maintained by Statistics Norway and provide information about educational attainment, labor market status, earnings, and a set of demographic variables.[8] Earnings are measured as annual earnings for taxable income as reported in the tax registry. These earnings are not top-coded and include labor earnings, taxable sickness benefits, unemployment benefits, parental leave payments, and pensions. Educational attainment is taken from the educational database provided by Statistics Norway. Since 1979, educational attainment is reported annually by educational institutions directly to Statistics Norway, thereby minimizing measurement error due to misreporting. For individuals who completed their education before 1979 we use information from the 1970 Census. Census data are self-reported. The information is, however, considered to be very accurate (Black et al., 2005). We discretize education into three categories—less than high school, high school completion, and at least some college. These data are merged to the sickness absence data and health survey data described below using personal identification numbers.

[6]The sickness absence rate is measured as man-days lost due to own sickness as a percentage of contractual man-days.

[7]The reform also instructed physicians to encourage the use of partial sickness leave for workers with a health problem but some work ability. For a detailed summary of the reform, see Markussen (2009).

[8]See Møen et al. (2003) for a detailed description of these data.

3.1 Sickness Absence

The data on sickness leave is reported by the Social Security Administration. It contains start dates and end dates for all certified sickness-related work absence spells exceeding the first 16 days (paid by the employer) in Norway from 1992 through 2008. We only consider sickness spells taken for the employee's own sickness (i.e. absence due to illness of other family members is ignored).[9] The data also includes a variable indicating the degree of sickness benefit as a percentage for cases in which it has been determined difficult but not impossible for an individual to work (commonly referred to as graded or partial sickness leave). For example, a physician may determine that an individual's work capacity is 50 percent. That individual must work at 50 percent capacity (at his or her normal wage), and sickness pay applies for the remaining 50 percent (Markussen et al., 2012). About a quarter of the individuals on sickness leave in our sample are on partial sickness leave ranging from 20 to 90 percent. Focusing on individuals with chronic joint pain who are on sickness leave, about 26 percent of those individuals are on partial leave. For individuals on partial sickness leave, we weight the days of sickness absence reported in the administrative data by the fraction of work capacity that is lost due to sickness.[10]

3.2 Health Surveys

The data on an individual's health status and pain comes from the Cohort of Norway (CONOR) data and the National Health Screening Service's Age 40 Program data. These are two population-based and nationwide surveys carried out from 1988 to 2003 by the National Institute of Public Health. The information contained in both surveys has been gathered through questionnaires and short health examinations. For the most part, the same information was collected in both surveys. In particular, questions are asked about general health, specific diseases, pharmaceutical use, physical activity, and smoking and drinking habits.

The goal of the Age 40 Program was to survey all men and women aged 40-42 between 1988 and 1999. It covers all counties in Norway except Oslo and the response rate is between 55 and 80 percent, yielding 374,090 observations. In addition, we use data from the CONOR dataset which includes Oslo, Norway's capital and largest city. CONOR is a research collaboration network that includes several large Norwegian health surveys which were carried out by the National Health Screening Service between 1994 and 2003. This data source includes 56,863 respondents.[11]

From these two health surveys, we observe an individual's health status when they are about 40 years old. While our data on sickness absence are longitudinal, the health data are cross-sectional (i.e. we only observe each person once in the health survey). We observe most individuals before

[9] Norwegian employees are allowed to take sickness leave to care for sick children.

[10] For example, if an individual is reported to take 50 days of sickness leave in the administrative data and is on 40 percent graded sickness leave, we assign that individual 20 sickness leave days in the empirical implementation.

[11] Black et al. (2012) provide a more detailed description of the dataset and of the representativeness of the sample of respondents.

2000 and thus before Vioxx and other Cox-2 inhibitors became available. We do not exclusively focus on Vioxx and Cox-2 inhibitor users but on potential Vioxx and Cox-2 inhibitor users, who we define as those who suffer from chronic joint pain or stiffness. Both health surveys include questions on whether respondents faced pain or stiffness that lasted at least three months and where the pain occurred.[12] This information allows us to compare individuals who suffer from chronic joint pain (and potentially other types of pain) around age 40 with individuals who do not suffer from joint pain. Alternatively, we are also able to compare individuals who suffer exclusively from chronic joint pain with individuals who suffer exclusively from other types of pain such as chest pain.[13]

3.3 Sample Selection and Descriptive Statistics

Vioxx (and other Cox-2 inhibitors) entered the Norwegian market in 2000, was listed as a refundable pharmaceutical in 2001, and was withdrawn worldwide in 2004. To consider enough years before and after the market entry and removal, we use data from 1992 to 2008. Our sample contains yearly observations of men and women aged 40 to 60 for whom we have non-missing data on health (around age 40) and labor force participation. Since we are interested in those who are eligible to take sickness leave, an individual must be employed or self-employed to be included in the sample.[14] In the case of missing information on labor force participation in at least one year we exclude all the observations for that individual. We restrict the sample to individuals who are at least 40 years old since the health surveys are conducted beginning at age 40. The upper age bound of 60 corresponds to the age of the oldest cohorts in the health surveys in year 2008. Moreover, the paper focuses on individuals with chronic joint pain (due for example to arthritis) and the probability of developing such a condition increases with age. Therefore, we find it most relevant to focus on individuals in the latter part of their working years. Last, we restrict the sample to individuals who completed the health survey before 2001. We do this because there could be some concern that individuals no longer suffering from joint pain after Vioxx's entry could generate bias in the estimated effect of the entry.[15]

We define the affected or treated group as individuals with chronic joint pain and compare how they are affected by the entry and removal of Vioxx to various control groups in a difference-in-differences framework. Our control groups include individuals without joint pain as well as

[12] We define joint pain as pain in the ankle, knee, hip, wrist, elbow, or shoulder. We do not classify neck pain as joint pain since neck pain (especially whiplash) is difficult to medically diagnose.

[13] Ideally, we would like to estimate the effect of actual Cox-2 inhibitor use on sickness absence and exploit the entry and removal of Vioxx as instruments for Cox-2 inhibitor use. However, we only have detailed information on the use of prescribed pain relievers for about 5 percent of the sample. In addition, we only observe individuals' health status and health behaviors once when they are about 40 years old. The pharmaceuticals these individuals use could change over the years we observe them, but the fact that they suffer from chronic joint pain should be less variable. We therefore compare individuals with and without chronic joint pain and estimate an intention to treat effect.

[14] Our results are nearly identical when we exclude self-employed individuals.

[15] Our results are quantitatively similar when we include those individuals who completed the health survey between 2001 and 2003. There are no individuals in our sample who complete the health survey after 2003 so we do not have a similar concern about the effect of the removal.

individuals suffering from chest pain exclusively. Table 1 contains descriptive statistics of the different groups prior to Vioxx's entry. As individuals are approximately 40 when they complete the health surveys, there is no age difference in individuals reporting chronic joint pain and the control groups. Compared to individuals without joint pain, those with chronic joint pain are slightly less educated on average, more likely to be female, and have lower yearly earnings. These patterns have also been found in US data (Garthwaite, 2012). Individuals with chronic joint pain use more prescribed pain killers and use them over a longer period, and they report absence from work due to sickness more often.

A possible concern is that our analysis and estimation sample might be impacted by mortality risk associated with using Vioxx. Figure 3 shows the death rate from 1990 to 2010 due to cardiac events for individuals between ages 40 and 60 in the full Norwegian population using data from the Cause of Death Registry. The mortality rate is relatively low for individuals between ages 40 and 60 and experiences a decreasing trend. The trend in mortality risk is, however, not visibly altered around the years of Vioxx's entry and exit. In addition, as mentioned above, the Norwegian Organization for Patient Compensation identified 114 patients who were plausibly harmed due to Vioxx's side effects, which is an extremely small share of the Vioxx users in Norway.

As discussed in Section 2.3, there was a change in sickness absence policy in Norway on July 1, 2004—the same year Vioxx was removed from the market. If the reform impacted individuals with joint pain more or less than those without joint pain our results might capture the differential impact of the policy reform in addition to the availability of Vioxx. Figure 4 shows the average number of sickness absence days (exceeding the first 16 days paid by the employer) per month from January 2003 to December 2005 for individuals with joint pain and individuals without joint pain at age 40. There is a visible change in the number of sickness days after the July 2004 reform for both groups. The average number of sickness days in the two months before the reform was 1.5 for the control group and 2.2 for the treatment group, and dropped to 1.1 and 1.7 in the two months after the reform, respectively, and Vioxx was still on the market during this time. This amounts to a 26 and 24 percent decrease in the number of sickness days immediately after the reform and provides some evidence that the reform had a similar effect on individuals with and without chronic joint pain.

4 Empirical Strategy

To measure the effects of progress in the treatment against chronic pain on sickness absence, we exploit the market entry and removal of Vioxx. We use a similar reduced-form difference-in-differences approach to Garthwaite (2012) but focus on a different outcome variable (i.e. sickness days) and the data allows us to analyze the impact of Vioxx's entry.

4.1 Basic OLS Specification

We start by estimating the reduced-form relationship between the removal of Vioxx from the pharmaceutical market and sickness days. We first estimate the following OLS equation:

$$SickLeave_{it} = \alpha_0 + \alpha_1 Pain_i + \alpha_2 Remove_t \times Pain_i + \alpha_3 X_{it} + \eta_a + \tau_t + \varepsilon_{it}, \quad (1)$$

where $SickLeave_{it}$ measures the number of days of sickness absence individual i took in year t. $Pain_i$ is an indicator for whether individual i responded that he suffers from chronic joint pain or stiffness in one of the health surveys, and $Remove_t$ is an indicator for whether Vioxx has been removed from the market.[16] X_{it} are demographic characteristics of individual i in year t, η_a are a series of age indicators, τ_t are year dummies, and ε_{it} is a mean zero error term. X_{it} includes indicators for gender, education, county, and years since individual i completed the health survey. We cluster the standard errors at the individual level. Individuals complete the health survey around the age of 40 and we control for age, year, and years since completing the health survey; thus, we capture any systematic responses to the health surveys in certain years and control for how far into the past individuals reported pain. The coefficient of interest is α_2, which measures the change in sickness absence days of individuals with joint pain following the removal of Vioxx compared to individuals without joint pain.

The key identifying assumptions of the difference-in-differences specification are (1) the exogeneity of the removal of Vioxx with respect to sickness absence, and (2) common trends in the outcome variable for the groups prior to the withdrawal. Since the removal of Vioxx was unexpected, differences in the use of the drug in the post-removal years should be uncorrelated with unobserved factors that also influence labor supply.[17] Figure 2 shows that the usual parallel trends assumption appears valid for the average number of days on sickness leave per year when comparing individuals with chronic joint pain with individuals without joint pain or when comparing individuals suffering exclusively from chronic joint pain with individuals suffering exclusively from chest pain.[18] Thus, the evidence suggests that in the age range we consider, individuals without joint pain or those with chest pain serve as reasonable comparison groups for those with joint pain.

[16] The suddenness of the withdrawal did not allow individuals to stockpile their medications. However, multi-month prescriptions are common in Norway, which may have allowed individuals to maintain access to the drug for a few months after the September 2004 withdrawal. Thus, we define *Remove* to be zero in 2004 (and all years before) and one starting in 2005.

[17] Merck's stock price fell 27 percent the day after its withdrawal announcement (Garthwaite, 2012).

[18] We also considered comparing individuals suffering exclusively from chronic joint pain with individuals suffering exclusively from back pain as in Garthwaite (2012), but we found the parallel trends assumption was violated. In addition, back pain sufferers may not be an ideal comparison group since they often used Cox-2 inhibitors but at a lower rate than joint pain sufferers (Garthwaite, 2012). Thus, this group would be affected by the entry and exit of Vioxx, but to a different extent than those with joint pain. Chest pain sufferers, however, should not be affected by the availability of Cox-2 inhibitors.

4.2 Fixed Effects Specification

To control for individual time-invariant unobserved heterogeneity that may influence an individual's response to Vioxx's removal we also estimate equation 1 with individual fixed effects:

$$SickLeave_{it} = \alpha_0 + \alpha_1 Remove_t \times Pain_i + \alpha_2 X_{it} + \eta_a + \tau_t + \delta_i + \varepsilon_{it}, \tag{2}$$

where δ_i are individual-specific fixed effects. Note that $Pain_i$ drops out because we do not know whether the individual suffers from pain in every year t, but only the year in which they complete the health survey. Thus, $Pain_i$ does not vary over time within individuals. In this specification, the coefficient of interest, α_1, is identified off the within-individual change in sickness days for those with joint pain compared to the within-individual change for individuals without joint pain before and after the removal of Vioxx.

4.3 Specification with Market Entry

It is unclear whether the market entry of Vioxx or its withdrawal should have a larger effect on sickness days or whether the effects are symmetric. Anecdotal evidence suggests physicians in Norway were aware of Cox-2 inhibitors since they existed on the US market for several months prior to their entry in Norway. However, it still may have taken time for some physicians to learn about the efficacy of Cox-2 inhibitors and to switch patients' prescriptions. Chintagunta et al. (2009) argue that doctors not only have imperfect information about drug quality, but they are also uncertain about the match quality between pharmaceuticals and patients. Thus, doctors are sometimes reluctant to prescribe new drugs before learning about patients' satisfaction. It is also possible that compliance and adherence to prescribed regimens were not followed strictly when Cox-2 inhibitors were first introduced. On the other hand, the Vioxx withdrawal may have led to an (over)reaction by individuals to the information about the drug's negative side effects. Further, the withdrawal could have provided a negative signal about related drugs. Collins et al. (2013) find that Vioxx's withdrawal had negative spillover effects on the prescriptions of other Cox-2 inhibitors and positive spillover effects for other competing NSAIDs in the US. In Europe, the negative side effects of Cox-2 inhibitors received attention from official medical authorities as well as the media, which may have led to a particularly large response by individuals to Vioxx's withdrawal. Last, if individuals became heavily dependent on or even addicted to Vioxx to alleviate pain, their response to the withdrawal may be especially large. The magnitude of the above-mentioned effects is not clear, thus we allow for the entry and exit of Vioxx to have differential effects on sickness absence days.

Since we observe sickness absence over many years, we can analyze the impact of the market entry of Vioxx. As noted above, Vioxx was approved to enter the Norwegian market in 2000, but Cox-2 inhibitors were only included in the list of fully refunded pharmaceuticals by the national

health system in 2001. It was the approved financial coverage that led to the large and rapid increase in the use of Vioxx and other Cox-2 inhibitors in Norway. Therefore, we define July 1, 2001, the date when Vioxx was included in the list of pharmaceuticals refunded by the national health system, as the date of market entry and estimate the following equation:[19]

$$\begin{aligned} SickLeave_{it} = \alpha_0 + \alpha_1 Pain_i + \alpha_2 Enter_t \times Pain_i + \alpha_3 Remove_t \times Pain_i \\ + \alpha_4 X_{it} + \eta_a + \tau_t + \varepsilon_{it}, \end{aligned} \tag{3}$$

where $Enter_t$ is an indicator for whether Vioxx has entered the market.[20] In this way, we can see if there were asymmetric effects of Vioxx's entry and withdrawal on sickness absence. We also estimate equation 3 with individual-specific fixed effects.

5 Results

As described above, the withdrawal of Vioxx from the global market resulted in a large decrease in the use of Cox-2 inhibitors in Norway. To analyze the importance of the availability of Vioxx and Cox-2 inhibitors more generally, we first examine the relationship between the withdrawal of Vioxx and sickness leave of individuals with chronic joint pain, and then we examine the impact of the entry and the removal.[21] We present two sets of results examining these relationships. The first set compares individuals with chronic joint pain (and potentially other types of pain) with individuals without joint pain reported around age 40. The second set compares people suffering exclusively from chronic joint pain with individuals suffering only from chest pain around age 40.

Panel A in Table 2 presents the results from the estimation of equation 1 and equation 2 for the comparison between individuals with chronic joint pain (and potentially other types of pain) and individuals without joint pain. Column 1 presents results from our basic OLS specification and column 2 shows the results from the fixed effects specification. Columns 3 and 4 display the results from the fixed effects estimations separately by gender. In all specifications, we find that the market removal of Vioxx had a significant positive effect on the number of days individuals were on sickness leave. In the OLS estimation, the Vioxx withdrawal led to an increase in long-term sickness leave of 2.5 days per year. The average number of sickness days before the withdrawal for people with chronic joint pain was 21.9 days. This suggests that the removal increased the number of sickness days by 11 percent. As noted above, the fixed effects model is identified off the within-individual change in sickness days for those with joint pain compared to the within-

[19] Since we define Vioxx's entry as the date it was approved as a fully refundable pharmaceutical, and all other Cox-2 inhibitors were approved at the same time, when we refer to Vioxx's entry onto the market, we are also capturing the entry of all Cox-2 inhibitors onto the market.

[20] We define *Enter* to be one in years 2001 up to and including 2004.

[21] The results should be interpreted as the impact on sickness days in excess of the first 16 days paid for by the employer.

individual change for individuals without joint pain before and after the removal of Vioxx. Here, the effect of the withdrawal of Vioxx is larger and significant—the removal increased sickness leave by 3 days or by 14 percent compared to the pre-removal level. Columns 3 and 4 show that the effect is larger for women. Whereas men's sickness leave increased by 2.6 days, women's sickness leave increased by 3.4 days. The average number of sickness days before the withdrawal for men and women with chronic joint pain were 17.7 and 24.8, respectively. The effect therefore corresponds to an almost 15 percent increase for men and 14 percent increase for women.

Panel B in Table 2 presents the results from the estimation of equation 3 where we analyze whether there were asymmetric effects of Vioxx's entry and withdrawal on sickness absence. For all specifications, the removal had a significant positive effect on the number of days individuals with chronic joint pain were on sickness leave, with the results implying a 10 to 13 percent increase in sickness days. The impact of the entry of Vioxx on the number of days of sickness leave is smaller, negative, and significant in all but one specification. In the OLS and the fixed effects estimations, Vioxx's market entry decreased sickness leave by 1.1 days per year. This corresponds to a 5 percent decrease. The effect of Vioxx's entry is insignificant when looking only at men, but women's sickness days significantly decreased by 1.6 days. Thus, while Vioxx's entry lowered the number of sickness days by 1.1 to 1.6 days, the effect of Vioxx's removal three years later was larger, increasing sickness leave by 2.3 to 3.4 days per year.

Table 3 presents the same set of results for the comparison of individuals suffering exclusively from chronic joint pain to individuals suffering only from chest pain around the age of 40. We find that the market removal of Vioxx had a significant positive effect on the number of days individuals were on sickness leave in all but the fixed effects specification for men (see Panel A in Table 3). The Vioxx withdrawal led to an increase in sickness leave of 1.8 days in the OLS specification and 1.7 days in the fixed effects specification. The average number of sickness days before the withdrawal for people with chronic joint pain exclusively was 18.6 suggesting that the withdrawal increased the number of sickness days by about 9 to 10 percent. The removal increased women's sickness leave by 3.3 days or 15 percent. These results are largely consistent with those using individuals without joint pain as the comparison group.

Panel B in Table 3 presents the results from the estimation of equation 3 where the comparison group is those with chest pain. We find that the market removal of Vioxx had a significant positive effect on the number of sickness leave days in the OLS and fixed effects specifications pooling both genders and looking at women separately. The impact of the entry of Vioxx is also significant in those three cases. Thus, when comparing individuals who suffer exclusively from chronic joint pain with individuals suffering only from chest pain, the Vioxx removal increased sickness days significantly and the Vioxx entry decreased sickness days significantly for women only. Although some of the estimates when using chest pain sufferers as the comparison group are insignificant, the estimates are generally similar in magnitude to those using individuals without joint pain as the

comparison group. The imprecision of the estimates could be a result of the smaller sample size.

In sum, we find the market withdrawal of Vioxx increased the sickness absence days of individuals with joint pain in Norway. As noted above, for patients who relied on Cox-2 inhibitors because they suffered from chronic joint pain and gastrointestinal conditions, the alternative treatment options were taking other NSAIDs with an increased risk of severe gastrointestinal bleeding or to abstain from NSAIDs and potentially take weaker analgesics and suffer from pain. Drugs from the opioid group are mostly used in palliative care and are not aimed for working age individuals with joint pain. Further, artificial joint replacements are only an option for very specific diagnoses. Hence, our results are consistent with the fact that most alternative treatments to Cox-2 inhibitors involve a decrease in patients' well-being and would increase sickness absence.

We find that the effect of the market entry of Vioxx was smaller than the effect of the removal. Our results are consistent with physicians taking time to learn about the efficacy of Cox-2 inhibitors and to determine who to switch to the new drugs. Nonetheless, our results suggest that individuals work more when they receive effective treatment for pain. The Vioxx withdrawal, on the other hand, appears to have potentially led to a large reaction to the information about the cardiovascular risks. Figure 5 displays the monthly sales of Celebrex (marketed under the name Celebra in Norway) in Norway from 2004 to 2008.[22] Soon after the Vioxx removal, the sales of Celebrex peaked as many Vioxx prescriptions were switched to other Cox-2 inhibitors. Celebrex sales fell substantially in the beginning of 2005 before the Norwegian Medicines Agency decided to no longer refund all Cox-2 inhibitors. This large decrease in sales might indicate individuals' and physicians' reaction to the information about the negative side effects.

Further, we find that women's sickness absence was more responsive to the market entry and removal of Vioxx than men's sickness absence. This finding corresponds to the fact that women were the majority of Vioxx users in Norway and are more likely to suffer from chronic joint pain and inflammation. In addition, Markussen et al. (2011) find that depending on family situation and type of sickness, females' entry rates into certified sickness absence spells are between 33 and 75 percent higher than those of similar males. Some studies in the sociology literature have attributed the higher rate of sickness absence among women in Norway to the "double burden" of a labor market career and family obligations (Bratberg et al., 2002).

It is important to keep in mind that our reduced-form estimates capture possible spillover effects of Vioxx's entry and removal on the usage of other Cox-2 inhibitors, NSAIDs, and opioids, and not just changes in the use of Vioxx.[23] Garthwaite (2012) provides reduced-form estimates of the impact of Vioxx's removal on extensive margin labor supply in the US. His reduced-form estimates imply the removal decreased the probability an individual with a joint condition worked by 2.3 to

[22]Celebrex had the largest market share among the Cox-2 inhibitors in the US and also in Norway prior to the Vioxx market withdrawal. The drug is still available in the US and in Norway. The Norwegian National Health System only refunds expenditures for Celebrex in very limited cases.

[23]In Norway, individuals could only substitute towards other Cox-2 inhibitors until May 2005 when the Norwegian health care authorities decided to no longer reimburse Cox-2 inhibitors.

3.9 percentage points, which amounts to about a 10 percent decrease in labor force participation. Our reduced-form estimates of the impact of Vioxx's removal on intensive margin labor supply are of a similar magnitude. The instrumental variable estimates in Garthwaite (2012), however, are much larger, and imply that the change in the use of Cox-2 inhibitors due to Vioxx's removal decreased the probability of working for individuals with joint conditions by 22 percentage points.

5.1 Heterogeneous Effects

In addition to gender, it is possible the effect of the removal decision varies with other individual characteristics. We analyze whether there were heterogenous effects of Vioxx's removal by occupation, income level, marital status, and age. Specifically, individuals with joint pain who work in physically demanding jobs may have had a differential response to the removal since pain may especially affect their ability to work. We classify occupations using the occupations listed as physically demanding in Rho (2010).[24] Panel A in Table 4 reports the estimates of the impact of Vioxx's entry and removal on individuals suffering from joint pain separately by physically and non-physically demanding occupations. Not surprisingly, we find the estimates are larger for those in physically demanding occupations. In our fixed effect specifications we find the removal of Vioxx led to an increase in sickness leave of 3 to 5 days for individuals in physically demanding occupations and an increase of 1.5 to 2.5 days for individuals in non-physically demanding occupations, respectively. We also find that the impact of Vioxx's entry was larger for those in physically demanding occupations. We again find that women were more responsive to Vioxx's removal than men regardless of whether their job was physically demanding or not.

We then analyze whether there were heterogenous effects of Vioxx's removal by income level.[25] Panel B in Table 4 shows the estimates of the impact of Vioxx's removal separately by whether an individual's income was above or below the mean in the particular year of interest. Across the specifications, we find the impact of the entry and the removal was larger for individuals with income below the average. We suspect this result is largely driven by occupational differences. Since more physically demanding jobs tend to be lower wage jobs, the larger effects for low earners could reflect their job requiring more physical effort. In addition, it is possible this result is driven in part by the fact that sickness leave payments are capped, so those with earnings above the cap may have had a stronger incentive to take fewer sickness absence days and return to work.

Panel C in Table 4 shows the estimates of the impact of the removal by marital status.[26] We find Vioxx's removal increased sickness leave more for single individuals relative to married individuals.

[24]The top three physically demanding occupations for men are janitors and building cleaners, supervisors or managers of retail sales workers, and retail salespersons. The top three physically demanding occupations for women are elementary and middle school teachers, retail salespersons, and supervisors or managers of retail sales workers.

[25]Income includes all taxable income (i.e. labor earnings, taxable sickness benefits, unemployment benefits, parental leave payments, and pensions).

[26]Married individuals are those who are legally married or registered as cohabiting in Norway. Cohabiting couples who are not officially registered are treated as single individuals.

A potential explanation for the larger effects for singles is that unmarried individuals are known to show more pronounced physical reactions to stressful life events, and having a married partner might serve as a buffer against such stress. In addition, having a partner allows for the division of household production. This may be particularly important when one spouse is ill or suffers from pain, as the healthier spouse can assume more household tasks, which perhaps allows the sick partner to recover faster than a single individual would. Further, we find the decrease in sickness days associated with Vioxx's entry was almost 3 times larger for single women compared to married women.

Panel D in Table 4 shows the results separately by whether individuals were younger or older than 50. Interestingly, across the fixed effect specifications we find the effects of the removal are about doubled for those younger than 50 compared to those above 50. We also find the entry of Vioxx generally had no significant effect on sickness days for individuals over 50, but decreased sickness days for individuals younger than 50 by 1.1 to 2.3 days per year. There are several possible reasons we observe a larger response by younger individuals. Older individuals with severe joint pain (who would likely respond substantially to Vioxx's removal) may already be on disability insurance and thus no longer on sickness leave. Also, since individuals report their pain around the age of 40, it is possible that we have a more accurate measure of joint pain for the younger group since the pain was more recently reported. It is possible the cap on leave payments could be driving this result as well. Older individuals are more likely to be high earners and have their leave payments capped, which may have provided them with a larger incentive to take fewer sickness leave days. Last, it is possible that individuals learn to manage their pain better as they age.

6 Sensitivity Analysis

We present a variety of sensitivity analyses. First, we perform placebo tests focusing on populations that should not have been affected by the availability of Cox-2 inhibitors as well as placebo tests assuming the Vioxx entry and removal occurred at different times than they truly did. Then, we perform a robustness check to ensure our results are not driven by those with low labor market attachment.

To analyze populations that should not have been affected by the Vioxx market entry and removal, we compare individuals suffering from asthma with individuals suffering from diabetes around age 40 (Panel A in Table 5), and second we compare individuals with back pain with individuals with chest pain around age 40 (Panel B in Table 5). When estimating our difference-in-differences model on these individuals, we should not find any effects of Vioxx's removal or entry. The estimates of the entry and removal are not statistically significant and provide support that our results are driven by the change in Cox-2 inhibitor availability.

We also perform a placebo test imposing Vioxx's market entry and removal before they actually happened. The removal is chosen to happen two years before any Cox-2 inhibitors entered the

Norwegian market (1998), and the entry is chosen to happen three years prior to the placebo removal (1995). Data from the years after Vioxx's true market entry are excluded from this placebo analysis. There should be no effect of the placebo entry or removal on the number of sickness days as there are no changes in pharmaceutical availability for individuals with chronic joint pain at those times. Panel C in Table 5 shows that we find no significant effects of the entry or removal for the relevant treatment and control groups, further providing support that our results are driven by the change in Cox-2 inhibitor availability.

Last, we re-estimate equations 1 and 2 eliminating very low earners to see if those with low labor market attachment are driving the results. We follow Havnes and Mogstad (2011) and rely on the "basic amount" thresholds of the Norwegian Social Insurance Scheme which are used to define labor market status and determine eligibility for unemployment benefits as well as disability and old age pension. In 2004, one basic amount was about $8,400. We define an individual as a low earner if he or she earns less than two basic amounts, referred to as 2G. Table 6 presents results for the comparison of individuals with chronic joint pain and those without joint pain when we eliminate individuals earning less than 2G. The results are nearly identical to those presented in Table 2, suggesting our findings are not driven by individuals with very low labor market attachment.

7 Additional Outcomes

We also provide results for the impact of Vioxx's entry and removal on other labor supply outcomes. First, we examine whether the entry and exit of Vioxx from the market affected the number of sickness absence spells an individual took per year. We re-estimate the equations described above but replace the dependent variable with the number of sickness leave spells taken per year. While we find the removal significantly increased the number of sickness spells for individuals suffering from joint pain, the magnitude is very small and close to zero (Table 7). Thus, it appears the increase in sickness absence days among individuals with joint pain due to Vioxx's removal is attributed to lengthier sickness leave spells, and not an increase in the number of spells.

Next, we analyze whether the entry and removal of Vioxx affected the probability an individual who suffers from joint pain is on disability insurance. Norwegian residents aged 18 to 67 are entitled to a disability pension if their ability to work is permanently reduced by at least 50 percent due to illness, injury, or defect. Eligibility depends on a minimum insurance period of three years immediately before the disability occurs. That is, an individual has to be a Norwegian resident or a non-resident Norwegian employee for at least three years to qualify for disability benefits. Similar to the sickness leave benefits, disability insurance benefits are part of the Norwegian Social Security System and funded by payroll taxes.[27] The disability benefit is considered a replacement for income loss due to disability, and the level of income replacement is determined by an individual's past

[27]Kostøl and Mogstad (2014) provide a more detailed description of the disability insurance system in Norway.

earnings where the proportion of replaced income decreases as past earnings increase.[28] Different from US disability programs such as Social Security Disability Insurance (SSDI) or Supplemental Security Income (SSI), the Norwegian program allows workers to apply for disability pension while still officially employed. That is, Norwegian workers usually go on sickness leave for one year until the benefits expire and are then enrolled in a rehabilitation program (with a replacement ratio around 66 percent) and can apply for disability pension. As sickness benefits have a replacement rate of 100 percent, staying on sickness benefits until they expire at one year and then transferring to disability pension is beneficial for most workers.

As most individuals are enrolled on sickness benefits for a full year before transferring to disability pension, the entry and removal of Vioxx are not necessarily expected to have an immediate effect on disability insurance receipt. We maintain our definitions of the variables *Enter* and *Remove* in the results presented but future work will allow for time-varying effects of the entry and removal to examine whether there was a delayed effect. We define individuals as enrolled on disability insurance in a given year if they receive disability insurance benefits from the Social Security System. Panel A in Table 8 shows that Vioxx's removal increased the probability of being on disability insurance for an individual with joint pain by about 4 percentage points, while Vioxx's entry had no significant effect on the probability of being on disability insurance. Our results suggest the unavailability of Cox-2 inhibitors not only affected sickness absence days in the short run, but also led to more permanent physical impairments and thereby increased an individual's likelihood of receiving permanent disability benefits.

Last, we examine whether the entry and removal of Vioxx affected the probability an individual works full-time, which we define as 30 hours of work per week or more. We find the removal of Vioxx significantly decreased the probability of working full-time by about 0.5 to 1.6 percentage points. This decrease is again stronger among women (Panel B in Table 8).

8 Discussion

To better understand the economic magnitude of our results, we present a simple back-of-the-envelope calculation quantifying the costs of the increased sickness absence after the market removal of Vioxx to Norway's Social Security Administration. Before the removal, the average annual earnings of male and female individuals between the ages of 40 and 60 with chronic joint pain, conditional on being in the labor force, were approximately NOK 363,383 and NOK 236,818, respectively. Regular working days in Norway amount to 227.5 days per year,[29] and thus the average daily earnings for males and females were NOK 1,594 and NOK 1,039, respectively. Our

[28] See Rege et al. (2009) for a detailed description of the formula used to determine disability insurance benefits and a comparison with the US disability insurance system.

[29] The official working days are computed as the number of weekdays minus the number of public holidays minus 25 days for personal holidays.

estimates suggest that sickness days taken by men increased by 2.6 days due to the removal of Vioxx and by 3.4 days for women, resulting in an increase in average costs per male and female with chronic joint pain of NOK 4,144 and NOK 3,532, respectively. The Norwegian labor force in 2004 consisted of 604,000 men and 554,000 women between 40 and 60 years old and 14.8 percent of men and 18.6 percent of women in the labor force in 2004 reported chronic joint pain at the age of 40. Hence, the additional costs paid by the Social Security Administration amounted to about NOK 734 million or $120 million. To put this number in perspective, the total annual expenses the Norwegian Social Security Administration paid for sickness leave benefits were about NOK 27.5 billion on average in the 2000s. Hence, the additional expenses due to the removal of Vioxx amount to 2.7 percent of the annual sickness leave payments.[30] As discussed in Section 2.2, the total compensation payments for patients suffering from Vioxx's side effects in Norway were NOK 37 million and thereby a small part of the annual extra expenses caused by the drug removal.

We use the same simple back-of-the-envelope calculation to quantify the decrease in costs after the introduction of Cox-2 inhibitors and find that the savings for the Social Security Administration were NOK 141.5 million or $23 million.[31] Thus, the savings due to the market entry of Cox-2 inhibitors was about 0.5 percent of the annual sickness leave payments in Norway. Our back-of-the-envelope calculations should be interpreted cautiously. We can only study short-term effects of the market entry and removal of Vioxx. As discussed in Section 5.1, individuals may learn to better manage their pain over time without Cox-2 inhibitors and the effect Vioxx's removal might be smaller over a longer time horizon.

9 Conclusion

This paper analyzed the impact of progress in the treatment against chronic pain on sickness absence. Specifically, we examine how the availability of Cox-2 inhibitors affected sickness absence days among individuals with chronic joint pain in Norway. We exploited the market entry and the unexpected withdrawal of Vioxx from the Norwegian pharmaceutical market as exogenous sources of variation in Cox-2 inhibitor use. Our reduced-form estimates imply the market entry of Vioxx decreased sickness absence days among individuals with joint pain by 4 to 5 percent and the withdrawal led to a 10 to 14 percent increase in sickness absence days. We find the effects were larger for women, consistent with many studies which show females have higher sickness absence rates in Norway and the fact that women were the majority of Vioxx users in Norway. We also find heterogeneity in the response to the entry and the removal by individual characteristics. In particular, we find the impact of the entry and removal was larger for individuals with physically

[30] Note that the expenses paid by the Social Security Administration exclude the first 16 days of sickness absence which are paid directly by the employer.

[31] The effect of Vioxx's entry on sickness days is not significant for men; thus, the calculated cost decrease is only based on the estimates for women.

demanding jobs, low earners, single individuals, and those younger than 50.

Our paper emphasizes the importance of accounting for economic impacts when determining the value and net benefits of advancements in medical and pharmaceutical technology. Considering labor supply effects and not just focusing on clinical outcomes and direct medical costs has important implications for regulatory decision-making and the coverage policies of insurance plans and national health care systems. Further, including labor supply effects when calculating the net benefits of medical and pharmaceutical innovation has potential implications for treatment decisions and care plans made by physicians and patients.

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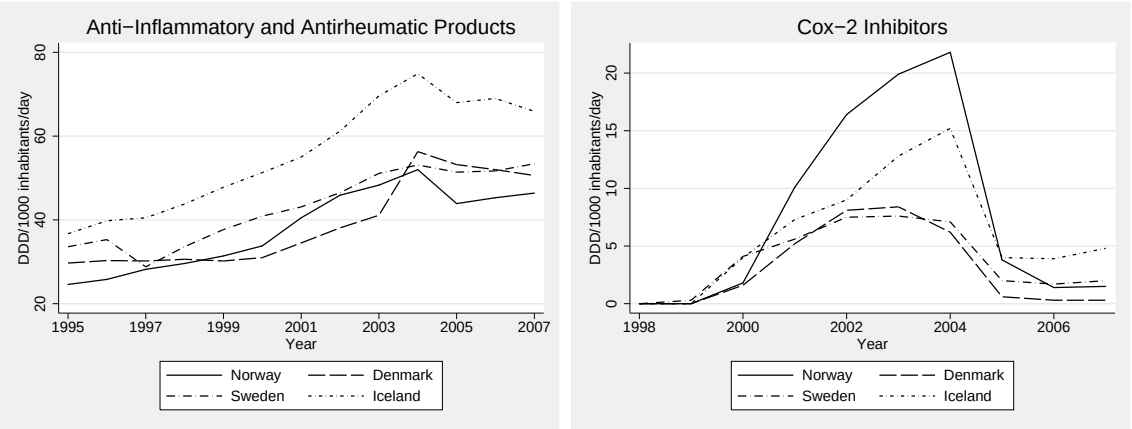
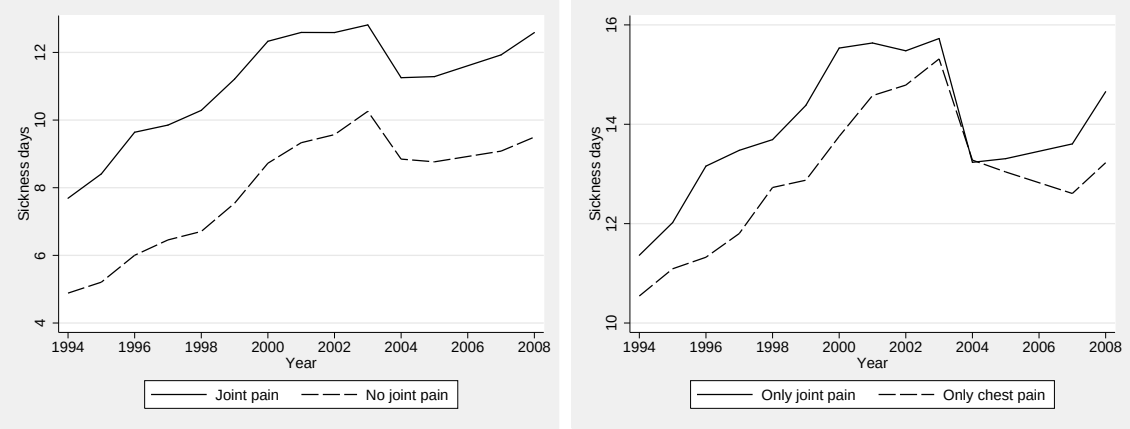
10 Tables and Figures

Figure 1: Sales of Anti-Inflammatory and Antirheumatic Products (NSAIDs) and Cox-2 Inhibitors in Nordic Countries from 1995-2007



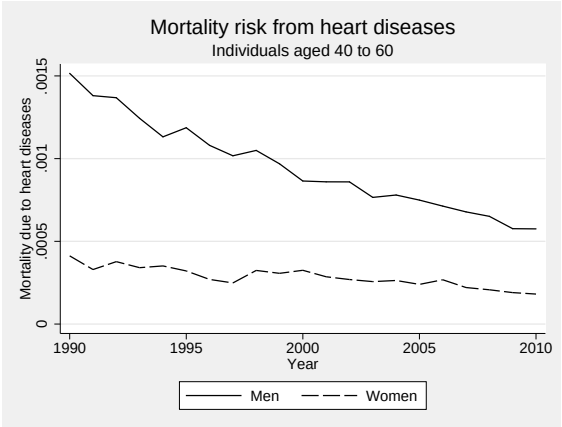
Data Source: Health Statistics in the Nordic Countries 2003, 2004, 2006. NOMESCO, Copenhagen.

Figure 2: Number of Days on Sickness Leave by Pain Status



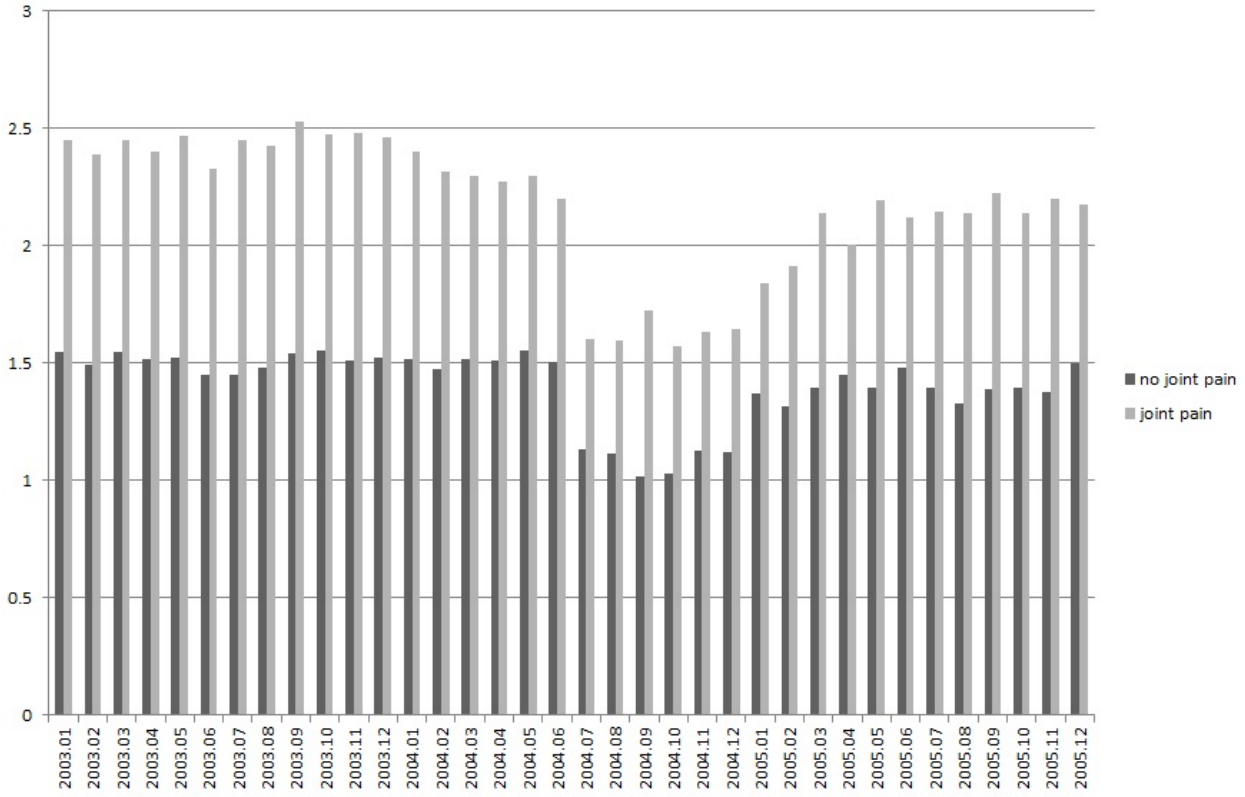
Notes: The figures show the average number of sickness absence days (exceeding the first 16 days paid by the employer) from 1994 to 2008. In the left panel, the solid line is the treatment group including all individuals who report chronic joint pain around the age of 40. The dashed line is the control group including all individuals who report no joint pain around the age of 40. In the right panel, the solid line is again the treatment group. Here the treatment group includes individuals who report joint pain exclusively. The dashed line is the control group including all individuals who report chest pain exclusively.

Figure 3: Mortality Rate From Heart Disease



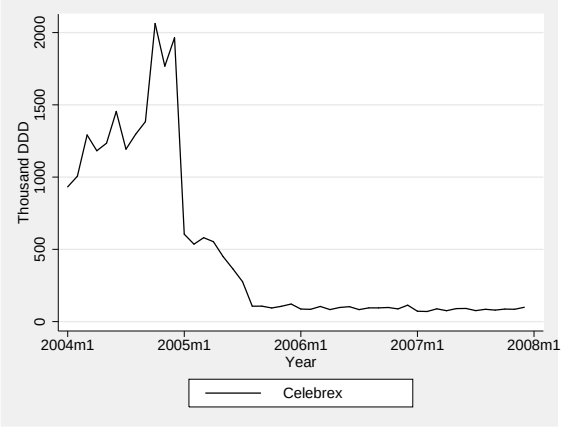
Notes: The figure shows the proportion of individuals who die from heart disease from 1990 to 2010. The sample includes all men and women in the Cause of Death Registry who pass away between ages 40 and 60.

Figure 4: Number of Days on Sickness Leave per Month by Pain Status



Notes: The figure shows the average number of sickness absence days (exceeding the first 16 days paid by the employer) per month from January 2003 to December 2005. The dark bars represent the treatment group including all individuals who report chronic joint pain around the age of 40. The lighter bars represent the control group including all individuals who report no joint pain around the age of 40.

Figure 5: Monthly Sales of Celebrex in Norway, 2004-2008



Data Source: Norwegian Prescription Database.

Table 1: Descriptive Statistics by Pain Status and Gender

	Men				Women			
	No joint pain	Joint pain	Only joint pain	Only chest pain	No joint pain	Joint pain	Only joint pain	Only chest pain
Age	47.2	46.8	47.0	47.1	47.2	46.9	47.1	46.9
Years of education	12.3	11.7	11.9	11.9	12.1	11.7	11.9	11.8
% married	69.6	66.3	68.2	65.0	69.3	65.4	67.1	65.8
Yearly earnings	398277	352664	365906	379339	253708	225733	237480	230628
Sickness absence days[a]	6.1	12.2	12.3	11.2	9.6	15.2	15.7	14.2
% physically demanding occupation	69.4	75.6	73.9	69.2	64.9	68.8	66.1	59.8
% on long-term sickness leave[b]	10.5	16.8	14.6	14.6	15.5	22.6	20.6	21.2
% on partial long-term sickness leave	2.2	3.5	3.0	3.2	4.1	5.9	5.5	5.7
% on disability insurance	3.0	7.6	5.2	6.2	5.1	12.8	9.2	10.2
% working 30+ hours per week	79.3	73.2	75.8	76.7	54.2	45.5	49.8	49.3
% consuming pain relievers[c]	97.4	97.8	97.3	92.3	97.2	97.3	95.8	94.4
Number of observations	863514	143115	70670	6526	910987	200042	85766	3607

[a]Sickness days are the number of days exceeding the first 16 paid for by the employer.

[b]Long-term sickness leave is a sickness spell exceeding 16 days.

[c]Including non-prescription drugs such as Aspirin.

Table 2: Effect on Sickness Days: Chronic Joint Pain vs. No Joint Pain

	Panel A: Drug Removal			
	OLS	Fixed Effects	FE Men	FE Women
remove × pain	2.518**	3.037**	2.571**	3.403**
	(0.111)	(0.128)	(0.171)	(0.187)
	Panel B: Drug Entry and Removal			
	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-1.137**	-1.063**	-0.440	-1.647**
	(0.186)	(0.192)	(0.257)	(0.281)
remove × pain	2.538**	2.274**	2.302**	2.708**
	(0.186)	(0.186)	(0.251)	(0.270)
Number of observations	2157903	2157903	1024843	1133060
Number of individuals		156867	73297	83570

Significance Levels: ** 1% level, * 5% level

Note: Entries represent the estimated difference-in-differences coefficients with standard errors in parentheses from OLS and fixed effect regressions of the effect of the entry and removal of Vioxx on the number of sickness days of individuals between the ages of 40 and 60 with joint pain. Unreported covariates include indicator variables for age, gender, education, county, year, and years since completing the health survey. Standard errors are clustered at the individual level.

Table 3: Effect on Sickness Days: Chronic Joint Pain vs. Chest Pain

	Panel A: Drug Removal			
	OLS	Fixed Effects	FE Men	FE Women
remove × pain	1.763*	1.695*	0.616	3.288*
	(0.849)	(0.839)	(1.073)	(1.787)
	Panel B: Drug Entry and Removal			
	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-1.510*	-1.416*	-0.786	-1.995*
	(0.725)	(0.686)	(1.358)	(0.818)
remove × pain	1.871*	1.690*	0.677	3.153*
	(0.907)	(0.724)	(1.163)	(1.972)
Number of observations	166550	166550	77188	89362
Number of individuals		12456	5704	6752

Significance Levels: ** 1% level, * 5% level

Note: Entries represent the estimated difference-in-differences coefficients with standard errors in parentheses from OLS and fixed effect regressions of the effect of the entry and removal of Vioxx on the number of sickness days of individuals between the ages of 40 and 60 with joint pain exclusively. Unreported covariates include indicator variables for age, gender, education, county, year, and years since completing the health survey. Standard errors are clustered at the individual level.

Table 4: Heterogeneous Effects on Sickness Days: Chronic Joint Pain vs. No Joint Pain by Subgroups

Panel A: Physically Demanding Occupations					
		OLS	Fixed Effects	FE Men	FE Women
Physical	entry × pain	-1.076**	-1.414**	-0.624	-2.180**
		(0.240)	(0.250)	(0.332)	(0.372)
	remove × pain	2.775**	3.984**	3.096**	4.774**
		(0.146)	(0.181)	(0.238)	(0.271)
Non-Physical	entry × pain	-1.118**	-0.547	-0.165	-0.944*
		(0.292)	(0.293)	(0.391)	(0.420)
	remove × pain	1.526**	2.172**	1.622**	2.552**
		(0.192)	(0.219)	(0.291)	(0.314)
Panel B: Income					
		OLS	Fixed Effects	FE Men	FE Women
Below mean	entry × pain	-1.048**	-1.869**	-1.483**	-2.046**
		(0.275)	(0.234)	(0.354)	(0.345)
	remove × pain	2.683**	4.402**	4.240**	4.483**
		(0.169)	(0.174)	(0.379)	(0.253)
Above mean	entry × pain	-0.868**	-0.367*	0.004	-1.160*
		(0.231)	(0.229)	(0.260)	(0.461)
	remove × pain	1.866**	1.902**	1.535**	2.674**
		(0.152)	(0.170)	(0.192)	(0.340)
Panel C: Civil Status					
		OLS	Fixed Effects	FE Men	FE Women
Married	entry × pain	-1.372**	-0.630**	-0.125	-1.121**
		(0.216)	(0.221)	(0.293)	(0.326)
	remove × pain	2.019**	2.862**	2.289**	3.348**
		(0.135)	(0.160)	(0.211)	(0.238)
Single	entry × pain	-1.595	-2.191**	-1.145*	-3.135**
		(0.368)	(0.387)	(0.530)	(0.558)
	remove × pain	3.192**	4.678**	3.672**	5.492**
		(0.224)	(0.283)	(0.384)	(0.411)
Panel D: Age					
		OLS	Fixed Effects	FE Men	FE Women
Below 50	entry × pain	-1.172**	-1.407**	-0.474	-2.264**
		(0.221)	(0.234)	(0.315)	(0.308)
	remove × pain	2.371**	4.256**	3.330**	5.026**
		(0.139)	(0.174)	(0.231)	(0.256)
Above 50	entry × pain	-0.241	-0.771*	-0.572	-0.982
		(0.358)	(0.352)	(0.472)	(0.516)
	remove × pain	1.629**	1.948**	1.600**	2.239**
		(0.218)	(0.245)	(0.327)	(0.360)

Significance Levels: ** 1% level, * 5% level

Note: Entries represent the estimated difference-in-differences coefficients with standard errors in parentheses from OLS and fixed effect regressions of the effect of the entry and removal of Vioxx on the number of sickness days of individuals between the ages of 40 and 60 with joint pain. Unreported covariates include indicator variables for age, gender, education, county, year, and years since completing the health survey. Standard errors are clustered at the individual level.

Table 5: Effect on Sickness Days: Placebo Groups

Panel A: Placebo Groups - Diabetes vs. Asthma				
	OLS	Fixed Effects	FE Men	FE Women
entry × diabetes	1.870	2.063	2.993	1.113
	(1.025)	(1.690)	(2.284)	(2.515)
remove × diabetes	1.505	1.440	-0.795	3.527
	(1.276)	(1.246)	(1.570)	(1.963)
Number of observations	40664	40664	19337	21327
Number of individuals		2935	1359	1576
Panel B: Placebo Groups - Back Pain vs. Chest Pain				
	OLS	Fixed Effects	FE Men	FE Women
entry × back pain	-1.065	-1.159	-1.575	-0.899
	(1.551)	(1.516)	(1.801)	(2.780)
remove × back pain	-1.158	-1.566	-2.388	0.171
	(1.154)	(1.246)	(1.125)	(2.194)
Number of observations	120557	120557	59342	61215
Number of individuals		9234	4470	4764
Panel C: Placebo Entry Year: 1995; Placebo Removal Year: 1998				
	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-0.002	-0.007	-0.004	-0.011
	(0.005)	(0.005)	(0.008)	(0.007)
remove × pain	-0.007	-0.011	-0.015	-0.009
	(0.005)	(0.007)	(0.008)	(0.007)
Number of observations	811629	811629	387976	423653
Number of individuals		151197	71124	80073

Significance Levels: ** 1% level, * 5% level

Note: Entries represent the estimated difference-in-differences coefficients with standard errors in parentheses from OLS and fixed effect regressions of the effect of the entry and removal of Vioxx on the number of sickness days of individuals between the ages of 40 and 60 with diabetes, back pain, or joint pain, respectively. Unreported covariates include indicator variables for age, gender, education, county, year, and years since completing the health survey. Standard errors are clustered at the individual level. Panel C is only based on data from the years before the market entry of Vioxx.

Table 6: Effect on Sickness Days: Chronic Joint Pain vs. No Joint Pain (Earnings Above 2G)

	Panel A: Drug Removal			
	OLS	Fixed Effects	FE Men	FE Women
remove × pain	2.566**	3.110**	2.627**	3.487**
	(0.113)	(0.130)	(0.174)	(0.191)
	Panel B: Drug Entry and Removal			
	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-1.639**	-1.171**	-0.432	-1.499**
	(0.109)	(0.198)	(0.267)	(0.283)
remove × pain	2.144**	2.198**	2.002**	2.447**
	(0.148)	(0.182)	(0.254)	(0.273)
Number of observations	2090862	2090862	1001482	1089380
Number of individuals		153689	71908	81781

Significance Levels: ** 1% level, * 5% level

Note: Entries represent the estimated difference-in-differences coefficients with standard errors in parentheses from OLS and fixed effect regressions of the effect of the entry and removal of Vioxx on the number of sickness days of individuals between the ages of 40 and 60 with joint pain. Unreported covariates include indicator variables for age, gender, education, county, year, and years since completing the health survey. Standard errors are clustered at the individual level.

Table 7: Effect on Number of Sickness Spells: Chronic Joint Pain vs. No Joint Pain

	Panel A: Drug Removal			
	OLS	Fixed Effects	FE Men	FE Women
remove × pain	0.018**	0.045**	0.039**	0.050**
	(0.003)	(0.003)	(0.003)	(0.005)
	Panel B: Drug Entry and Removal			
	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-0.018**	-0.019**	-0.011**	-0.027**
	(0.004)	(0.004)	(0.004)	(0.006)
remove × pain	0.016**	0.051**	0.042**	0.059**
	(0.003)	(0.003)	(0.003)	(0.005)
Number of observations	2117658	2117658	1006629	1111029
Number of individuals		153906	71964	81942

Significance Levels: ** 1% level, * 5% level

Note: Entries represent the estimated difference-in-differences coefficients with standard errors in parentheses from OLS and fixed effect regressions of the effect of the entry and removal of Vioxx on the number of sickness spells of individuals between the ages of 40 and 60 with joint pain. Unreported covariates include indicator variables for age, gender, education, county, year, and years since completing the health survey. Standard errors are clustered at the individual level.

Table 8: Effect on Probability of Receiving Disability Insurance or Working Full-Time: Chronic Joint Pain vs. No Joint Pain

Panel A: Disability Insurance				
	OLS	Fixed Effects	FE Men	FE Women
entry × pain	0.010	0.008	0.010	0.017
	(0.011)	(0.012)	(0.012)	(0.013)
remove × pain	0.042**	0.044**	0.035*	0.049**
	(0.014)	(0.016)	(0.017)	(0.021)
Number of observations	2157903	2157903	1024843	1133060
Number of individuals		156867	73297	83570
Panel B: Working 30+ Hours				
	OLS	Fixed Effects	FE Men	FE Women
entry × pain	0.002	0.006**	0.002	0.012**
	(0.001)	(0.001)	(0.001)	(0.002)
remove × pain	-0.005**	-0.010**	-0.006**	-0.016**
	(0.001)	(0.001)	(0.001)	(0.003)
Number of observations	2117658	2117658	1006629	1111029
Number of individuals		153906	71964	81942

Significance Levels: ** 1% level, * 5% level

Note: Entries represent the estimated difference-in-differences coefficients with standard errors in parentheses from OLS and fixed effect regressions of the effect of the entry and removal of Vioxx on the probability of being on disability insurance and the probability of working full-time for individuals between the ages of 40 and 60 with joint pain. Unreported covariates include indicator variables for age, gender, education, county, year, and years since completing the health survey. Standard errors are clustered at the individual level.