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

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Abstract

How does medical innovation affect labor supply? We analyze how the availability of Cox-2 inhibitors, pharmaceuticals used for treating pain and inflammation, affected the sickness absence and disability pension receipt of individuals with joint pain. We exploit the market entry of the Cox-2 inhibitor Vioxx and its sudden market withdrawal as exogenous sources of variation in drug use. Using Norwegian administrative data, we find Vioxx's entry decreased quarterly sickness absence days among individuals with joint pain by 7-12 percent. The withdrawal increased sickness days by 12-16 percent and increased the quarterly probability of receiving disability benefits by 0.4-0.6 percentage points.

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1 Introduction

While early literature on human capital focused primarily on education and job training, more recently, the economics literature has focused on health capital. Healthier individuals earn higher wages, are more likely to participate in the labor force, work more hours, and miss fewer days of work on average (Currie and Madrian, 1999). Furthermore, Sala-i-Martin (1997a,b) finds that health, in the form of life expectancy, is a positive and significant predictor of per capita GDP growth across a variety of empirical specifications. Many other studies have also found health is an important and robust determinant of economic growth and income variation (see for example Bloom et al., 2004; Weil, 2007). A key question then becomes: how does new medical technology affect the health capital, and thus, the productivity and labor supply of workers?

Understanding how advances in medical technology affect worker productivity and labor supply is important for health care policy. In Europe and more recently in the United States, comparative-effectiveness programs have been established as part of larger health care reform efforts. Comparative-effectiveness research (CER) provides evidence on the effectiveness, benefits, and harms of different treatment options. In some European countries, CER is used to inform or determine the coverage and reimbursement of medical treatments.[1] While most countries' comparative-effectiveness entities focus on the payer perspective, some countries like Sweden and Norway have adopted a societal perspective. The societal perspective means both direct and indirect costs and benefits of treatments, such as gains or losses in worker productivity, should be considered regardless of who benefits or bears the costs (patients or payers), underscoring the importance of understanding the labor supply effects of advances in medical technology.

In this paper, we aim to estimate the impact of progress in the treatment for chronic joint pain on labor supply. 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 and disability benefit receipt 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

[1]For example, in the United Kingdom, the National Institute for Clinical Excellence (NICE) analyzes the clinical and cost-effectiveness of medical technologies, including diagnostic tests, surgical procedures, and pharmaceuticals, and NICE's research is used to determine which treatments will be covered by the UK's National Health Service. In Germany, the Institute for Quality and Efficiency in Health Care conducts comparative-effectiveness studies of medical treatments and procedures, and their studies are used to inform the reimbursement decisions made by another body, the Federal Joint Committee.

effects as sources of exogenous variation in the use of Cox-2 inhibitors. Using administrative panel data on sickness absence and disability pension receipt, we find that relative to the pre-entry period, Vioxx's entry led to a 7 to 12 percent decrease in quarterly sickness absence days among individuals with chronic joint pain, while Vioxx's withdrawal led to a 12 to 16 percent increase in the number of sickness absence days as well as a 0.4 to 0.6 percentage point increase in the quarterly probability of receiving disability pension.

Broadly, our paper fits into the literature that examines the impact of health on labor market outcomes. Many studies find that poor physical or mental health can adversely affect wages and labor supply (for a review of this literature see Currie and Madrian, 1999). In particular, some studies have focused on the labor market impacts of arthritis and pain (see for example Mitchell and Burkhauser, 1990; Mitchell, 1991; Kapteyn et al., 2008; Gaskin and Richard, 2012; Simons et al., 2012). Mitchell and Burkhauser (1990) find that hours worked are more adversely affected by arthritis than wage rates in the US, especially for men and younger women, which can translate into substantial earnings effects. Gaskin and Richard (2012) use data from 2008 to estimate the annual costs of pain in the US that are associated with lower worker productivity, and find the value of lost productivity due to pain ranged from $299 to $335 billion.

Our paper also contributes to a small but growing literature that analyzes how medical treatments affect labor supply and earnings. Thirumurthy et al. (2008) study the effect of antiretroviral treatments for HIV and AIDS on intensive and extensive margin labor supply in Kenya. Some studies have focused on the labor supply impacts of treatments for depression (for a review of this literature see Timbie et al., 2006). 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). Epstein et al. (2013) study the effect of minimally invasive surgeries on medical expenditures and worker absenteeism, and find for 4 of the 6 types of surgeries they consider, minimally invasive procedures were associated with significantly fewer days of absence 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. One reason this literature is small is the difficulty in finding exogenous variation in the use of medical treatments with respect to labor supply. However, the market entry and sudden withdrawal of Vioxx provide plausibly exogenous variation in the use of Cox-2 inhibitors.[2]

[2]In a broader sense, our paper is also related to the literature on medical innovations that affect women's

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. Garthwaite (2012) uses data from the Medical Expenditure Panel Survey (MEPS) from 2003 to 2007, and in his preferred specification, 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 conditions by 22 percentage points. Our work contributes to this line of research in two important ways which we expand upon below. First, while Garthwaite (2012) focuses on the extensive margin labor supply response to Vioxx's withdrawal using survey data, we examine both intensive margin labor supply adjustments (sickness absence days) and extensive margin adjustments (disability pension receipt), using detailed administrative data from Norway. Second, different from Garthwaite (2012), we have data on labor supply outcomes for the years before Vioxx enters the market, which allows us to analyze the impact of both the entry and withdrawal of Vioxx to examine whether there were asymmetric effects of the availability of Cox-2 inhibitors.

Understanding the relationship between medical innovation and sickness absence and disability pension receipt is especially important given the growth in disability benefit recipiency and spending in the United States, Norway, and other OECD countries. In Norway, public spending on disability and sickness absence programs amounts to almost 5 percent of the country's GDP. While most prior studies have focused on the roles of benefit generosity, screening stringency, and eligibility changes in explaining disability and sickness insurance take-up rates and expenditures (see for example Börsch-Supan, 2007), our findings show that the availability of effective medical treatments plays a non-trivial role. Furthermore, given the institutional differences between Norway and the United States, workers may adjust their labor supply along different margins in response to changes in Vioxx availability. In the US, there is no federal government-sponsored paid sickness leave program and unpaid leave can be taken for only up to 12 weeks under the Family and Medical Leave Act. In Norway, the government pays for an individual's sickness days (after the first 16 days) at a replacement rate of 100 percent for up to one year. Thus, in the US, given limited ability to adjust work days, extensive margin labor supply adjustments may be strong, as Garthwaite's (2012) estimates imply. Intensive margin adjustments, however, may be especially salient in Norway and other European countries that have paid sickness leave provisions, as individuals can

labor market behavior. For example, Goldin and Katz (2002) find the birth control pill led women to increase their human capital, and Bailey (2006) finds access to the pill increased women's labor supply in their late 20s and early 30s.

take more or less sick days in response to changes in medical treatment availability, which our estimates confirm.

In addition, there are advantages to studying the labor supply effects of Vioxx availability in the Norwegian context. Their rich administrative data provides us with precise measures of sickness absence days and disability pension enrollment, allowing us to study both intensive and extensive margin labor supply adjustments in one institutional setting. Individual-level data on sickness absence in the US are scarce, particularly during the period when Vioxx was withdrawn, making it difficult to study changes in intensive margin labor supply. In light of the institutional differences highlighted above, our estimates may provide an upper bound for the intensive margin response in the US. Norway does share institutional similarities with several European countries such as universal health care coverage and publicly mandated paid sickness leave provisions; thus, our estimates may offer some more general insight into how individuals in these countries respond to changes in medical treatment availability.

Finally, our examination of whether there were differential effects of Vioxx's entry and removal is relevant for pharmaceutical-related policy. The existence of asymmetric effects has potentially important implications for the drug approval process and for predicting the consequences of withdrawing a pharmaceutical from the market. Our results show that the removal of a drug from the market can have negative labor supply effects that are larger in magnitude than the positive effects of the drug being available.

The paper proceeds as follows. Section 2 provides background on Vioxx and Cox-2 inhibitors as well as the Norwegian sickness absence and disability pension programs. We discuss the data and provide descriptive statistics in Section 3. We describe our empirical strategy in Section 4. We discuss our results and analyze whether there were heterogeneous effects by individual characteristics in Section 5. Section 6 presents sensitivity analyses. In Section 7, we present a back-of-the-envelope calculation quantifying the costs of increased sickness absence after the removal of Vioxx to Norway's Social Security Administration. Section 8 provides a brief conclusion.

2 Institutional Background

2.1 Vioxx and Cox-2 Inhibitors

Cox-2 inhibitors are part of a broader class of medicines called non-steroidal anti-inflammatory drugs (NSAIDs). 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. The Norwegian Institute of Public Health reports that chronic pain, which is most commonly musculoskeletal pain or pain associated with rheumatic disorders, affects about 30 percent of the adult Norwegian population.[3] 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 pain were prescribed NSAID medications such as ibuprofen or naproxen.[4] However, for some patients these drugs cause serious gastrointestinal bleeding and ulcerations, and consequently, many patients with chronic pain who were prone to gastrointestinal problems faced very limited treatment options. Cox-2 inhibitors do not cause these gastrointestinal complications, and as a result, they were recommended and prescribed especially for individuals with joint pain and gastrointestinal problems (Griffin, 2000; Schnitzer and Hochberg, 2002).

Importantly, the main advantage of Cox-2 inhibitors is the lack of gastrointestinal side effects. Given their mechanism of action, they are no more effective in treating joint pain than other NSAIDs.[5] Both manage and reduce pain and inflammation, but rarely cause patients, such as those with arthritis, to become completely asymptomatic (Griffin, 2000). However, joint pain management is complex, as there is substantial individual variation in response to pain relievers (Griffin, 2000). For some individuals, specific drugs are very effective, while others are not. Hence, the introduction of Cox-2 inhibitors offered a larger set of therapeutic options to individuals with joint pain.

Vioxx was approved first in the United States by the Food and Drug Administration 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 potential adverse cardiac side effects. The Vioxx GI Outcomes Research (VIGOR) study published in 2000 found an increase in serious heart problems for individuals taking

[3]Source: http://www.fhi.no/artikler/?id=88781

[4]Ibuprofen is known under the brand names Motrin and Advil in the US and Ibux in Norway. Naproxen is known under the brand name Aleve in the US and Napren in Norway.

[5]Cox-2 inhibitors and other NSAIDs block enzymes that produce prostaglandins, which are responsible for the pain and swelling associated with inflammatory conditions. Prostaglandins are produced by two different enzymes, Cox-1 and Cox-2. Cox-2 inhibitors block only the Cox-2 enzyme while common NSAIDs like naproxen and ibuprofen block both. Some prostaglandins produced by the Cox-1 enzyme protect the inner lining of the stomach. When that enzyme is blocked, some stomach lining protection is lost, which can lead to gastrointestinal ulcerations and bleeding.

Vioxx compared to those taking naproxen. Initially, the increased cardiac risks associated with Vioxx were attributed to naproxen lowering the risk of adverse cardiac events, making Vioxx look risky by comparison (Mukherjee et al., 2001). Subsequent studies confirmed that while Vioxx was associated with decreased gastrointestinal complications, it indeed increased the relative risk of cardiac events even for low cardiac-risk patients (see for example Bresalier et al., 2005). In response to these findings, the manufacturer Merck voluntarily removed 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 the annual sales of NSAIDs in Norway 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. The use of NSAIDs was about 30 defined daily doses (DDD) per 1000 inhabitants per day in 1998, 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 reimbursed by the national health care system.[6,7] 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 reimbursable pharmaceuticals in July 2001, physicians were aware of the drugs and switched patients' prescriptions quickly.[8]

[6]Similar to most Western countries, 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. Pharmaceutical producers 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 for the drug to be included on the list of reimbursable pharmaceuticals. Brekke et al. (2011) provide a detailed description of the Norwegian pharmaceutical market.

[7]Typically, the patient co-payment for reimbursed pharmaceuticals is between 36 to 38 percent of the drug price up to an annual ceiling. Once the ceiling has been reached, expenses are covered by the National Insurance Scheme. The annual ceiling on patient out-of-pocket health expenditures (on pharmaceuticals and outpatient care) is usually less than $250.

[8]Anecdotal evidence from articles in the *Journal of the Norwegian Medical Association* suggests that the increase in drug sales during the first year Cox-2 inhibitors were reimbursable was surprisingly large. This increase has been attributed partly to the same journal's encouragement of physicians to prescribe Cox-2 inhibitors when they became available (see Rugstad, 2000).

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 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 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 who also had gastrointestinal problems. 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.[9] 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 annual sales of Cox-2 inhibitors in Norway between 1998 and 2007. 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 reimburse purchases of any Cox-2 inhibitors after May 1, 2005 based on a report from the European Medicines Agency that documented an increased risk of 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 reimbursable 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

[9]Opioids are mainly 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.

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 to 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 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 (Duratovic, 2007).

In the three months after the withdrawal of Vioxx from the market, 40 percent of Vioxx users switched to other Cox-2 inhibitors. Since reimbursements 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 System of Patient Injury 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 was side effects such as heart attack, heart weakness, brain stroke, or other cardiac diseases. In 19 cases, compensation was paid to surviving dependents of individuals who died from Vioxx's side effects.

2.3 Sickness Absence 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.[10] For absences lasting more than

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

three days, a medical certificate is required.[11] 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. As discussed in more detail below, starting in mid-2004, physicians were required to provide (even more) extended documentation for sickness spells lasting more than eight weeks if no work-related activity was performed by the employee. Individuals are protected against dismissals during their sickness absence and cannot be laid off due to their sickness.

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.[12] The compensation scheme is relatively generous and absence rates are high in Norway compared to other OECD countries. About 4 percent of the labor force is on sickness benefits, resulting in a sickness absence rate of 7 percent (measured as man-days lost due to own sickness as a percentage of contractual man-days) and program expenditures amounting to 2.5 percent of GDP. 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 (Markussen, 2009). The reform also instructed physicians to encourage the use of partial sickness leave for workers with a health problem but some work ability.[13] Sickness leave fell by around 20 percent at the time of the reform (Markussen, 2009). There may be concern that the policy reform occurred around the same time as Vioxx's withdrawal from the market. We address concerns about the timing of the reform and provide evidence that the reform did not differentially impact those with joint pain in Section 6.3.

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

[12] For a further description of the Norwegian Social Security System and sickness leave, see Markussen (2012) and Rieck and Vaage (2012).

[13] For a detailed summary of the reform, see Markussen (2009).

2.4 Disability Pension in Norway

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 an illness, injury, or impairment that has lasted for at least one year. 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 pension benefits are part of the Norwegian Social Security System and funded by payroll taxes.[14] 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 earnings where the proportion of replaced income decreases as past earnings increase.[15] All relevant medical treatment and rehabilitation measures have to be tried before enrolling on disability insurance. That is, disability pension is only offered to workers unable to return to work from sickness absence and possibly after also completing a rehabilitation program (typically less generous, with a replacement rate around 66 percent). Rehabilitation via vocational training or further medical treatment is often determined unlikely to be successful and subsequently dismissed as a requirement for receiving disability benefits. Thus, it is common to see individuals apply for and enter disability directly from sickness leave (Rege et al., 2009). 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 optimal for most workers. 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.

Rheumatoid arthritis and arthrosis, severe forms of chronic joint pain, are among the official diagnosis categories that qualify an individual for disability benefits. That is, individuals with these diagnoses may claim disability benefits if the pain prevents them from working. Diagnoses for severe chronic joint pain are mainly based on blood tests and X-rays. In addition, conditions such as rheumatoid arthritis and arthrosis are generally considered non-reversible. As a result, enrolling on disability insurance based on severe and work-limiting chronic joint pain is rather straightforward.

The take-up of disability pension benefits has risen substantially over the last few decades

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

[15] 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.

and is high in Norway relative to other OECD countries. More than 10.3 percent of the population between 18 and 66 years of age were on the disability pension rolls at the start of 2008. Among individuals aged 50 to 66, 23.5 percent received disability benefits. Public spending on disability pension makes up more than 2 percent of Norway's total GDP. About 8 percent of individuals receiving disability benefits are enrolled due to rheumatoid arthritis, arthrosis, or closely related conditions.

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.[16] 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 1974, 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 the 1973-1974 academic year, 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, disability pension data, and health survey data described below using personal identification numbers.

3.1 Sickness Absence

The data on sickness leave is reported by the Social Security Administration. It contains start 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). 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

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

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. 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.[17]

3.2 Disability Pension

Similar to sickness leave, the disability pension data are reported by the Social Security Administration. The data include information on the date when disability insurance benefits were awarded and the level of benefits received. An individual is defined as being enrolled on disability insurance in a given quarter-year period if he receives benefits during that quarter-year period.

3.3 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 to 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.[18]

[17]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.

[18]Black et al. (2015) provide a more detailed description of the dataset and the representativeness of the

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 and disability pension 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 2000 and thus before Vioxx and other Cox-2 inhibitors became available. We do not 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. We follow several studies in the medical literature as well as the classification of pain used in several health surveys and define joint pain as pain in the ankle, knee, hip, wrist, elbow, or shoulder.[19] This information allows us to compare individuals who suffer from chronic joint pain around age 40 with individuals who do not suffer from joint pain.

3.4 Sample Selection and Descriptive Statistics

Vioxx (along with other Cox-2 inhibitors) entered the Norwegian market in 2000, was listed as a reimbursable 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 1998 to 2008. Our sample contains quarterly 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, self-employed, or receiving a work-related social security pension (e.g. unemployment benefits or maternity leave benefits) to be included in the sample used for the sickness leave analysis.[20] In the case of missing information on labor force participation or social security pension in at least one year we exclude all the observations for that individual. The sample used for the disability pension analysis additionally includes individuals who have already been receiving

sample of respondents.

[19] We do not classify neck or back pain as joint pain. In the medical literature, back and neck pain are often treated separately from joint pain (see for example Tsang et al., 2008; Johannes et al., 2010). In the National Health Interview Survey (NHIS) and the National Health and Nutrition Examination Survey (NHANES) from the US, the survey questionnaires make explicit that joint pain does not include neck or back pain, and separate questions are asked about those types of pain. Garthwaite (2012) also considers back pain separate from joint pain. He emphasizes that those with back conditions in the US reported the use of Cox-2 inhibitors at half the rate of those with joint conditions, and back pain sufferers had a larger number of therapeutic alternatives.

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

disability insurance benefits, and thus no longer employed.[21] 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 (or suffering less) after Vioxx's entry could generate bias in the estimated effect of the entry.[22]

We define the treated group as individuals with chronic joint pain and compare how they were affected by the entry and removal of Vioxx to individuals without joint pain in a difference-in-differences framework.[23] Thus, we estimate intention-to-treat effects.[24] Table 1 contains descriptive statistics for those with and without joint pain separately by gender prior to Vioxx's entry for both the sickness absence and disability pension samples. 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 group. Compared to individuals without joint pain, on average those with chronic joint pain are slightly less educated, 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 report absence from work due to sickness more often and are more likely to be on the disability insurance rolls.

A possible concern is that our analysis and estimation sample might be impacted by mortality risk associated with using Vioxx. Figure 2 shows the death rate from 1995 to 2010 due to cardiac events for individuals between ages 40 and 60 in the full Norwegian

[21] We include these individuals to allow for transitions off the disability pension rolls. Such transitions are rare, but we want to allow for them, particularly when Cox-2 inhibitors entered the market.

[22] 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.

[23] Alternatively, one might consider individuals with other types of pain such as back or chest pain as control groups. However, the parallel trends assumption necessary for difference-in-differences estimation discussed in Section 4.1 is violated in our data when comparing individuals with joint pain to individuals with chest pain or back pain.

[24] Ideally, we would like to estimate the effect of actual Cox-2 inhibitor use on sickness absence and disability benefit receipt 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 pharmaceutical use) once when they are about 40 years old and usually before Vioxx's entry.

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.[25] In addition, as mentioned above, the Norwegian System of Patient Injury 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.

Another potential concern arises from our classification of the treatment and control groups. The groups are based on a one-time survey response from individuals around age 40 about whether they suffer from joint pain over a three-month period. It is possible that some individuals in the treatment group no longer suffered from joint pain during Vioxx's entry and removal and that some individuals in the control group developed joint pain after age 40 and in effect were "treated." Both of these possibilities would cause the results to be underestimated (i.e. downward biased). Our results are therefore best interpreted as lower bound estimates. The extent of the downward bias depends on the persistence of joint pain over several years and the development of joint pain as individuals age. We explore this issue in detail in Section 6.2.

4 Empirical Strategy

To measure the effects of progress in the treatment for chronic joint pain on labor supply, we exploit the market entry and removal of Vioxx. We use a reduced-form difference-in-differences approach similar to Garthwaite (2012), but we focus on different outcome variables—sickness absence days (in excess of the first 16 days paid for by the employer) and whether an individual receives disability pension. Furthermore, the data allows us to analyze the impact of both Vioxx's market entry and withdrawal.

By studying changes in sickness absence and disability pension receipt, we analyze labor supply responses on different margins. Changes in sickness absence days capture intensive margin adjustments, while changes in the receipt of disability pension benefits capture extensive margin adjustments. The outcomes are related. Since disability pension is offered to employees unable to return to work from sickness absence (usually of a year in length), disability pension almost always starts with a sickness absence spell, and as a result, there

[25] We acknowledge that this does not rule out the possibility of a break in the mortality risk trend for those with joint pain. There are very few people who take the health surveys and die from cardiac-related events between the ages of 40 and 60. As a result, we cannot examine trends in the mortality rate for those with and without joint pain.

is a strong correlation between sick leave and the probability of receiving disability benefits (Markussen, 2012). Thus, an increase in sickness absence days may compound and eventually lead to increased disability pension enrollment. However, it is also possible that a change in sickness absence days results in no change in the probability of receiving disability benefits if the change in sickness days is mostly driven by a change in short or medium-term absence. We therefore find it important to examine both outcomes.

It is unclear whether the entry of Vioxx or its withdrawal should have a larger effect on labor supply 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 adherence to prescribed regimens was 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, and 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 medical authorities and the media, which may have led to a particularly large response 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 have been especially large.

As noted above, Vioxx was approved to enter the Norwegian market in spring 2000, but Cox-2 inhibitors were only included in the list of reimbursable pharmaceuticals by the national health system in July 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 2001 as the market entry of Vioxx.[26] Given Vioxx was withdrawn from the market on September 30, 2004, we define October 2004 as the market withdrawal of Vioxx.

[26]Since we define Vioxx's entry as the date it was approved as a reimbursable 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.

4.1 Basic OLS Specification

We estimate the reduced-form relationship between the entry and removal of Vioxx from the pharmaceutical market and sickness absence days as well as disability pension receipt. We first estimate the following OLS equation:

$$\begin{aligned} y_{it} = \beta_0 + \beta_1 Pain_i + \beta_2 Enter_t \times Pain_i + \beta_3 Remove_t \times Pain_i \\ + \beta_4 X_{it} + \sum_{j=40}^{60} \eta_j I(Age_{it} = j) + \tau_t + \varepsilon_{it}, \end{aligned} \tag{1}$$

where y_{it} either measures the number of days of sickness absence individual i took at time t (where time is measured in quarters) or is an indicator for whether the individual receives disability pension from the Social Security System at time 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. $Enter_t$ is an indicator for whether Vioxx has entered the market, defined to be one in quarter 3 of 2001 up to and including quarter 3 of 2004. $Remove_t$ is an indicator for whether Vioxx has been removed from the market, defined to be one starting in quarter 4 of 2004. X_{it} are demographic characteristics of individual i at time t, η_j allows for age fixed effects, τ_t are year-quarter 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, time, 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 coefficients of interest are β_2 and β_3, which measure the change in sickness absence days (or the probability of receiving disability pension) for individuals with joint pain following the entry and removal of Vioxx relative to the pre-entry period compared to individuals without joint pain.

4.2 Fixed Effects Specification

To control for individual time-invariant unobserved heterogeneity that may influence an individual's response to Vioxx's entry and removal, we estimate equation 1 with individual

fixed effects:

$$\begin{aligned} y_{it} =& \gamma_0 + \gamma_1 Enter_t \times Pain_i + \gamma_2 Remove_t \times Pain_i \\ &+ \gamma_3 X_{it} + \sum_{j=40}^{60} \eta_j I(Age_{it} = j) + \tau_t + \delta_i + \varepsilon_{it}, \end{aligned} \tag{2}$$

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 time period 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 coefficients of interest, γ_1 and γ_2, are identified off the within-individual change in sickness days (or receipt of disability pension) for those with joint pain compared to the within-individual change for individuals without joint pain after the entry and removal of Vioxx relative to the pre-entry period.

The key identifying assumptions of the difference-in-differences specifications are (1) the exogeneity of the entry and removal of Vioxx with respect to sickness absence and disability benefit receipt; and (2) given the effects of the entry and removal are estimated relative to the pre-entry period, common trends in the outcome variable for the groups prior to Vioxx's entry. The entry of Vioxx onto the Norwegian market was the result of regulatory decision-making by the Norwegian Medicines Agency based on clinical trials and cost-effectiveness analysis. The removal of Vioxx was sudden and unexpected. In fact, Merck's stock price fell 27 percent the day after its withdrawal announcement (Rubin, 2004; Garthwaite, 2012). Thus, the entry and removal provide plausibly exogenous variation in Cox-2 inhibitor use, and differences in the use of Cox-2 inhibitors in the years after Vioxx's entry and after its removal should be uncorrelated with unobserved factors that influence labor supply. Figure 3 shows that the parallel trends assumption appears valid for the average number of quarterly sickness absence days prior to Vioxx's entry when comparing individuals with chronic joint pain with individuals without joint pain in the raw data. Figure 4 shows that the trends in the proportion of individuals receiving disability benefits prior to Vioxx's entry are also relatively parallel. Thus, the figures suggest that individuals without joint pain are a reasonable comparison group for those with joint pain.

We also perform a more rigorous analysis to see whether there is evidence of differential pre-trends in sickness days or disability pension receipt for the treatment and control groups. We estimate a generalized version of the difference-in-differences specification de-

scribed above:

$$y_{it} = \theta_0 + \theta_1 Pain_i + \sum_{\ell=1998q1}^{2008q4} \pi_\ell I(t = \ell) \times Pain_i + \theta_2 X_{it} + \sum_{j=40}^{60} \eta_j I(Age_{it} = j) + \tau_t + \varepsilon_{it}, \tag{3}$$

where the coefficients of interest are π_ℓ, which are event-study type estimates that measure the evolution of outcomes among individuals with joint pain reported around age 40 in the quarters before and after Vioxx enters and exits the market (see for example Jacobson et al., 1993; Autor, 2003; Bailey and Goodman-Bacon, 2015). The indicators for quarters in 1999 are omitted; thus, the π_ℓ coefficients describe the evolution of the outcomes relative to 1999, before Vioxx entered the market.[27] This specification provides us with both a visual and statistical depiction of differential and pre-existing trends. Figures 5 and 6 show plots of the π_ℓ coefficients from equation 3 along with 95 percent confidence interval bars for OLS and fixed effects estimations with both genders pooled and fixed effects estimations separately by gender. The figures show the trends in sickness absence and disability pension receipt in the years prior to Vioxx's entry appear similar for the treatment and control groups. The lack of significant differences in sickness absence or disability benefit receipt trends in the pre-entry years provide support for our identifying assumptions.

5 Results

5.1 Sickness Absence Results

We turn first to the impact of Vioxx's availability on quarterly sickness absence days. We emphasize that our results should be interpreted as the impact on sickness days in excess of the first 16 days paid for by the employer, and therefore provide a lower bound for the intensive margin response.

The results from the estimation of equations 1 and 2 are presented in Table 2. Column 1 shows the 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 the OLS and fixed effects estimations with both genders

[27]The results are not sensitive to the choice of omitted quarters. For example, the results are very similar when we omit quarters in 1998 or 2000 rather than 1999.

pooled, we find Vioxx's market entry had a significant effect, decreasing sickness leave for those with joint pain by 0.28 and 0.21 days per quarter, respectively. The average number of quarterly sickness days prior to Vioxx's entry for those with chronic joint pain was 2.5 days. Thus, the entry led to an 8 to 11 percent decrease compared to the pre-entry level. When examining the effect separately by gender, we find Vioxx's entry decreased men's quarterly sickness absence by 0.25 days and decreased women's absence by 0.20 days. The average number of quarterly sickness days before the market entry for men and women with chronic joint pain was 2.1 and 2.8, respectively. The effect therefore corresponds to a 12 percent and 7 percent decrease in sickness absence for men and women, respectively.

In all specifications, we find relative to the pre-entry period, the removal significantly increased the sickness absence days of individuals with chronic joint pain, and the impact of the removal was larger in magnitude than the effect of the entry. The OLS estimates imply Vioxx's withdrawal increased sickness leave by 0.29 days per quarter or by 12 percent relative to the pre-entry period. The effect of the removal is larger in the fixed effects specification—the removal increased sickness leave by 0.41 days per quarter or by 16 percent compared to the pre-entry level. Columns 3 and 4 show that the effect of the removal is larger for women. Whereas men's sickness leave increased by 0.30 days, women's sickness leave increased by 0.46 days. Given the sickness days of men and women prior to Vioxx's entry noted above, the effect corresponds to a 14 percent increase for men and 16 percent increase for women.

5.2 Disability Pension Results

Columns 1 and 2 of Table 3 show that Vioxx's removal increased the quarterly probability of receiving disability pension for an individual with joint pain by 0.5 to 0.6 percentage points compared to an individual without joint pain, while Vioxx's entry had no significant effect on the probability of receiving disability benefits. Among those with joint pain, the average quarterly probability of receiving disability benefits prior to Vioxx's entry was 5.1 percent, thus the estimates imply the removal led to a 10 to 12 percent increase in the probability of benefit receipt relative to the pre-entry level. When considering men and women separately, we find the entry had no significant effect on men's probability of receiving disability benefits, while the removal increased their probability of disability enrollment by 0.5 percentage points. For women with joint pain, the entry significantly decreased their probability of disability pension receipt by 0.3 percentage points, and the removal increased that probability by 0.4 percentage points. These results suggest the unavailability of Cox-2 inhibitors not only affected sickness absence days in the short run, but also led to permanent

physical impairments that hindered work capacity, and thereby increased an individual's likelihood of receiving disability benefits.

5.3 Summary Discussion of Baseline Results

We find the market withdrawal of Vioxx increased the sickness absence days of individuals with joint pain in Norway as well as their probability of receiving disability pension relative to the pre-entry period. As noted above, for those 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 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 as well as the likelihood of entering the disability insurance rolls.

We find the effect of Vioxx's entry on sickness days was smaller than the effect of the removal. We find the removal increased the probability of receiving disability benefits for men and women, but the entry only significantly decreased women's probability of benefit receipt. There are several potential reasons for the asymmetric effects of the entry and withdrawal. First, the speed of Vioxx diffusion upon entry and the suddenness of the removal may play a role. Figure 1 shows that it took several years for Cox-2 inhibitor sales to peak, consistent with some physicians taking time to learn about the efficacy of Cox-2 inhibitors and determine who to switch to the new drugs. The same change in utilization occurred within one year of the removal as suddenly no one could access Vioxx. Second, the Vioxx withdrawal may have led to a large reaction to the information about the cardiovascular risks. Collins et al. (2013) find the aggregate use of Cox-2 inhibitors and drugs in related classes declined in the US in response to the withdrawal, and the usage declines suggest some consumers over-reacted in ways that lessened the health benefits they received from those drugs. Figure 7 displays the monthly sales of Celebrex (marketed under the name Celebra in Norway) in Norway from 2004 to 2008.[28] Soon after the Vioxx removal, the sales of Celebrex peaked as many Vioxx prescriptions were switched to other Cox-2 inhibitors.

[28]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, but in Norway, the National Insurance Scheme only reimburses expenditures for Celebrex in very limited cases.

However, Celebrex sales fell substantially in the beginning of 2005 before the Norwegian Medicines Agency decided to no longer reimburse any Cox-2 inhibitors. This large decrease in sales might indicate individuals' and physicians' reaction to the information about the negative side effects.[29] Last, the response to the withdrawal is consistent with theories on the psychology of pain. For example, individuals' expectations and beliefs about how much pain they should have influences how much pain they feel (Hansen and Streltzer, 2005). Individuals also tend to use recent pain as their reference point (Turk and Okifuji, 1999). Thus, if individuals experienced significant relief while taking Cox-2 inhibitors and expected their pain to be substantial without them, they may have had an especially large response to the removal.

The asymmetry of the effect of Vioxx availability has potential implications for the speed of the drug approval process. The fact that the removal of a pharmaceutical from the market can have negative labor supply effects that are larger in magnitude than the positive effects of the drug being available underscores the need to make certain the drug's efficacy and safety before its market entry. Furthermore, in the event a drug needs to be withdrawn, the relevant government agencies should keep in mind that the labor supply effects of such action cannot necessarily be inferred simply by analyzing the impact of the drug's current availability or by assuming labor supply will return to its original pre-entry level.

Further, we find that women's sickness absence was more responsive to the market 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. 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 (Mastekaasa, 2000; Bratberg et al., 2002). We explore this further in Section 5.5.

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. Nonetheless, the estimates provide evidence that Vioxx availability had an economically meaningful impact on labor supply in Norway. Our results show that the removal affected labor supply both at the intensive margin via

[29] An article published in the *Journal of the Norwegian Medical Association* found that among 300 individuals with chronic joint pain who used Vioxx, 55 percent reported being very frightened by the media coverage after the drug's withdrawal (Rognstad and Straand, 2006).

more sickness absence days and the extensive margin, increasing the probability of exit from the labor force and entry onto the disability pension rolls. Garthwaite (2012) provides reduced-form estimates of the impact of Vioxx's removal on extensive margin labor supply in the US. His estimates imply the removal decreased the probability an individual with a joint condition worked during a MEPS survey round by 1.8 to 3.9 percentage points.[30] Converted to a quarterly frequency, his estimates imply the removal decreased labor force participation by 1.1 to 2.4 percentage points.[31]

There are several possible reasons Garthwaite's (2012) estimates are larger. First, our extensive margin outcomes differ—we examine the probability of receiving disability pension benefits which usually captures permanent exit from the labor force, while Garthwaite (2012) examines the probability of working, which captures both temporary and permanent exits. Second, as discussed earlier, extended paid sickness leave is not an option for many workers in the US; thus, for some, leaving work may have been the only way to reduce labor supply. In Norway, however, rather than leave work entirely, individuals could adjust their labor supply on the intensive margin by taking sickness absence days. Third, the sample in Garthwaite (2012) includes individuals ages 55 to 75, and they may have been more willing to leave the labor force (and possibly retire early) than our younger sample of 40 to 60 year olds. Finally, Garthwaite's (2012) estimates of the impact of the removal are relative to Vioxx being on the market, while our estimates are relative to the pre-entry period. If there were asymmetric effects of Vioxx availability in the US of the type we find in Norway, then we would expect Garthwaite's (2012) estimates to be larger.

5.4 Time-Varying Effects of the Removal

The generalized difference-in-differences coefficients displayed in Figures 5 and 6 suggest the effects of the removal varied over time. We examine this further by replacing $Remove_t \times Pain_i$ in equations 1 and 2 with interactions between $Pain_i$ and individual time indicators that correspond to periods in which Vioxx was removed. Figure 8 shows the coefficient estimates on those interactions as well as confidence interval bars when quarterly sickness absence is the outcome. We find the effect of the removal on sickness absence days increased and

[30] 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.

[31] There are 5 MEPS survey rounds over a two-year period, and rounds vary in length from 2 to 6 months. When converting Garthwaite's (2012) estimate to a quarterly frequency, we assume each MEPS round lasts 4.8 months (24 months/5 rounds).

peaked around 2006, then decreased slightly, and increased again in 2008. The peak in the effect around 2006 is likely explained by the fact that between Vioxx's removal and May 2005, other Cox-2 inhibitors were still reimbursable, but after May 2005, no Cox-2 inhibitors were reimbursed in Norway, limiting treatment options for those with joint pain (and gastrointestinal problems). The dip in the impact of the removal in 2007 could be explained by some individuals with very severe joint pain enrolling on disability insurance.

Figure 9 shows the evolution of the effects of the removal on the probability of receiving disability pension. Not surprisingly, given that most individuals are on sickness leave for a year before transferring to a disability pension, we find the effect of the removal was not immediate. The removal did not significantly increase the probability of disability benefit receipt until mid-2006 and the effect then continued to increase through 2008. Thus, we suspect the decrease in the effect of Vioxx's removal on sickness days in 2007 is explained at least in part by individuals transferring to the disability rolls.

5.5 Heterogeneous Effects

In addition to gender, the effects of Vioxx's entry and removal may vary with other individual characteristics. We analyze whether there were heterogeneous effects of Vioxx's entry and removal by occupation and marital status.

Individuals with joint pain who work in physically demanding jobs may have responded differently to the entry and removal since pain may especially affect their ability to work. We classify occupations using the occupations listed as physically demanding for older workers in Rho (2010), and we base the categorization on the individual's most recent job.[32] Panel A in Tables 4 and 5 reports the estimates of the impact of Vioxx's entry and removal on sickness absence days and the probability of receiving disability pension, respectively, on individuals suffering from joint pain separately by physically and non-physically demanding occupations. The effect of Vioxx's entry on sickness absence days is similar for those with and without physically demanding jobs. Surprisingly, the coefficient estimates imply that the removal had a larger effect on the sickness absence days of individuals with non-physically demanding jobs. However, we test whether these differences are significant and cannot reject that the effects of the entry and removal on sickness absence are the same for those with and without physically demanding jobs at conventional significance levels in any of the fixed

[32]Occupations that are categorized as physically demanding include those that involve large amounts of lifting or standing such as janitors and building cleaners, retail salespersons, nurses, and elementary and middle school teachers, among others.

effects specifications.

We find the entry of Vioxx significantly decreased the quarterly probability of disability pension receipt for those with physically demanding jobs, with the effect being driven by women. The entry did not have a significant effect on the disability pension receipt of those with non-physically demanding jobs. We find Vioxx's removal had no significant impact on the probability of disability pension receipt for those with physically demanding jobs, but significantly increased that probability among those with non-physically demanding jobs, particularly females. In this case, the effects of the entry and removal are significantly different across the two subgroups. While these results are surprising, it could be that individuals with joint pain and physically demanding jobs had previously developed ways to cope with pain, while individuals with non-physically demanding jobs did not have such a need to cope with pain before and were subsequently more affected by the removal. These results may also be driven by individuals in non-physical occupations that require frequent computer use, such as data entry, who suffer from arthritis of the wrist or carpel tunnel syndrome and were likely impacted by Vioxx's withdrawal.

Our baseline results show that Vioxx's removal had a larger impact on women's sickness days compared to those of men. Several studies have documented gender differences in sickness absence in Norway (and other European countries), and often attribute the differences to the gender division of household work (Barmby et al., 2002) and to women being more exposed to the "double burden" of combining paid work with family obligations (Mastekaasa, 2000; Bratberg et al., 2002). The idea is the stress from the combination of these roles may negatively affect women's health or ability to cope with negative health shocks. We expect that the "double burden" explanation would be more salient for women who are married, and we explore whether there were heterogeneous effects of Vioxx's entry and removal by marital status. The estimates are shown in Panel B in Tables 4 and 5. 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. The estimates suggest Vioxx's entry decreased sickness leave more for single individuals relative to married individuals. We find the removal had a larger effect on the sickness days of single men compared to married men, but had a larger effect on married women's sickness absence relative to single women, consistent with the "double burden" explanation. However, when we test whether these differences are significant, we find the impacts of the entry and removal are not significantly different for married and single individuals with joint pain.

In terms of disability pension receipt, we find the entry had no significant effect on

married individuals but significantly decreased the probability of receipt for single individuals with joint pain. On the other hand, the removal significantly increased the probability of benefit receipt among married individuals but had no effect on singles. The effects here are significantly different across single and married individuals. Single individuals may be more income constrained than married individuals and thus had less ability to exit from the labor force and enroll on disability insurance in response to Vioxx's removal. Given such constraints, the entry of Vioxx may have allowed single individuals with joint pain to avoid enrolling on disability insurance. Married individuals may have more than one source of labor income and would be expected to respond less to Vioxx's entry and more to its removal.

The heterogeneity analysis provides some insight about the subgroups of individuals that were on the margin of increasing sickness absence and those on the margin of taking up disability benefits when Vioxx was removed. Among those with joint pain, individuals with non-physically demanding jobs and married individuals increased their sickness absence days and experienced an increase in their probability of enrolling on disability pension. This suggests the effect of the removal may have compounded over time, increasing the sickness absence days of these subgroups and eventually leading to disability pension enrollment. On the other hand, those with physically-demanding jobs and single individuals only experienced a significant increase in sickness absence days, suggesting these individuals increased their short and medium-term sickness absence but were not on the margin of enrolling on disability benefits.

6 Sensitivity Analysis

6.1 Timing of Vioxx's Entry

In our main analysis, we define Vioxx's entry as July 2001, the date it became reimbursable. Vioxx formally entered the Norwegian pharmaceutical market in spring 2000, but as Figure 1 shows, sales of Cox-2 inhibitors in 2000 were relatively low. As a robustness check, we reestimate our baseline specifications with entry defined as quarter 2 of 2000, when Merck was permitted to sell Vioxx in Norway.

The results are shown in Tables 6 and 7. The impact of Vioxx's entry on sickness absence days is still significant and negative in the OLS and fixed effects specifications with both genders pooled, but smaller in magnitude than in our baseline results. For men, the impact of entry is slightly larger in magnitude than in the baseline, and for women, the impact of

entry is no longer precisely estimated at conventional significance levels. Given the redefined entry period includes a year in which Cox-2 inhibitors were not reimbursable and sales were low, it is not surprising that we generally find a smaller effect of Vioxx's entry. The effects of the removal on sickness absence are very similar to our baseline estimates. When considering disability pension receipt, we find no significant effect of Vioxx's entry. The impact of the removal is quite similar to what we find in our baseline results, except for women, the effect is significant at the 10 percent level (p-value=0.07).

Overall, when entry is defined as quarter 2 of 2000, the effects of Vioxx's removal are quantitatively similar to our baseline estimates. The effects of entry are qualitatively similar to the baseline estimates, but often smaller in magnitude and less precisely estimated, consistent with the fact that the redefined entry period includes a year when Cox-2 inhibitors were not reimbursable and sales were low. We view these results as supportive evidence for defining entry as July 2001.[33]

6.2 Measuring Pain at Age 40

As mentioned above, our treatment and controls groups are based on a one-time survey response about joint pain around age 40. It is possible and likely that some individuals who reported joint pain around age 40 no longer suffered from such pain by the time Vioxx entered the market and that some individuals who did not report joint pain at age 40 developed it as they aged. To address these concerns, we perform a number of robustness checks.

First, we reestimate our baseline specifications on a subsample that completed the health surveys closer to when Vioxx entered the market. Specifically, we consider those who were 43 or younger in 2001. In this way, we likely have a more accurate (though still imperfect) measure of pain status for individuals when Vioxx entered and left the market.[34] Table 8 presents the sickness absence results for this younger sample. We find the impact of the entry on individuals with joint pain is still negative and similar in magnitude to our baseline specifications, but less precisely estimated, which is not surprising given the smaller sample size. The effects of the removal on sickness absence are quite similar to our baseline estimates. The most notable difference is the impact of the removal on women's sickness days

[33]We also perform a robustness check where we drop the quarter before Vioxx's entry (where entry is defined as July 2001). We do this because in Figure 5, particularly for men with joint pain, there appears to be a decrease in sickness absence days in quarter 2 of 2001, and we want to ensure our results are not leveraged off the dip in that quarter. The results are quantitatively and qualitatively similar to our baseline estimates, and are available by request.

[34]We repeated this exercise on the sample of those who were 45 or younger in 2001 and results are similar.

is somewhat smaller in the younger sample.

Table 9 shows the disability pension results for the younger sample. We find no significant effects of the entry on the probability of receiving disability pension. The effects of Vioxx's removal are somewhat smaller than our baseline estimates (but generally of similar magnitude) and significant except for men. The lack of precision could again be due to the smaller sample size. The somewhat smaller effects of the removal may reflect the fact that younger individuals are less likely to enroll on disability pension (see for example Gjesdal et al., 2004). Overall, we find the estimates from the younger sample are qualitatively similar to our baseline estimates, providing support for our classification of treatment and control groups based on joint pain at age 40.

6.3 Sickness Leave Policy Reform Concerns

As discussed in Section 2.3, there was a change in the sickness absence policy in Norway effective on July 1, 2004—the same year Vioxx was removed from the market. The year-quarter effects in our baseline specifications control for the average impact of the reform across all individuals, but 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 reform in addition to the availability of Vioxx. Figure 10 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 no visible change in the number of sickness days immediately after the July 2004 reform for either group. In fact, there is evidence of anticipation of the reform since sickness absence days fall for both groups in early 2004. Markussen (2009) and Markussen et al. (2011) also find evidence of a drop in sickness absence prior to the reform. Markussen (2009) provides details on the timeline of the reform that suggest anticipatory behavior was likely. Preparations started in December 2003 and in mid-February 2004 a draft proposal was circulated for a public hearing. Parliament approved the proposal in mid-June 2004 and the reform was effective July 1, 2004. In addition, the reform caught attention in the public media throughout spring 2004, and was first mentioned in the press in early February 2004.

We perform two robustness checks to analyze whether the reform differentially affected those with and without joint pain. First, we estimate a difference-in-differences equation of

the form:

$$SickDays_{imt} = \phi_0 + \phi_1 Pain_i + \phi_2 Reform_{mt} \times Pain_i + \phi_3 X_{imt} + \sum_{j=40}^{60} \eta_j I(Age_{imt} = j) + \lambda_{mt} + \varepsilon_{imt}, \quad (4)$$

where $SickDays_{imt}$ is the number of sickness absence days individual i took in month m in year t. $Pain_i$ is again an indicator for whether individual i responded that he suffers from joint pain in one of the health surveys, and $Reform_{mt}$ is an indicator for the sickness absence reform. We define $Reform_{mt}$ to be one starting in February 2004 to account for the anticipation effects.[35] X_{imt} are demographic characteristics of individual i, η_j allows for age fixed effects, λ_{mt} are a series of month-year interactions, and ε_{imt} is a mean zero error term. X_{imt} includes the same variables as in the baseline specifications. We run this monthly analysis from January 1, 2002 through September 30, 2004, and thus exclude any months before Vioxx was introduced and after it was removed from the market. This provides us with several months to examine whether those with and without joint pain responded differentially to the reform in the short run. If the coefficient on the interaction $Reform_{mt} \times Pain_i$ is significant, that would cast doubt on our treatment and control groups being affected similarly by the reform. Table 10 presents the results. Across the specifications, the coefficient on the interaction term is near zero and insignificant, giving us confidence that the estimated effects of Vioxx's availability on those with joint pain are not capturing reform effects.

Second, we reestimate equations 1 and 2 including $Reform_t \times Pain_i$ interactions, where $Reform_t$ is one starting in quarter 1 of 2004.[36] This allows us to obtain estimates of the impact of Vioxx's entry and removal while controlling for potential differential effects of the reform. Results are shown in Table 11. The coefficients on the $Reform_{mt} \times Pain_i$ interactions are not significant in any specification, suggesting no significant differential effects for those with joint pain. The effects of Vioxx's entry on sickness absence days are quantitatively similar to our baseline results. We again find the removal led to a significant increase in sickness absence days for those with joint pain relative to the pre-entry period, with the effects being somewhat larger in magnitude than in the baseline. This analysis suggests that our baseline findings were not driven by differential responses to the reform.

[35] We estimated this equation with different start dates for $Reform_{mt}$ including July 2004, and results are similar.

[36] We estimated this specification with different start dates for the reform, including quarter 2 and quarter 3 of 2004, and results are similar.

6.4 Analysis with Propensity Score Common Support Sample

We next address concerns about differences between the treatment and control groups by using propensity scores to discard observations for whom there are no similar controls. We estimate a logit model of the probability of having joint pain around age 40 as a function of individual characteristics at the time of the health survey including the individual's exact age, gender, education, county of residence, whether they have a physical job, and their Body Mass Index (BMI). As suggested by Imbens (2015), we include interactions between the covariates. We then use the logit model to predict the propensity that an individual had joint pain around age 40. The predicted propensity scores are between 0.013 and 0.82. We focus on observations in the treatment and control groups over the region of common support, that is, where there is distributional overlap between the treatment and control groups. The propensity scores in the region of overlap range from 0.028 to 0.605. We reestimate equations 1 and 2 only on those observations.

The results are presented in Tables 12 and 13. The effects of the entry and removal on sickness absence days are very similar to the baseline estimates. We again find Vioxx's entry significantly decreased the probability of disability pension receipt only for women with joint pain, and we find the effects of the removal on the probability of benefit receipt are slightly larger than our baseline estimates, but generally very similar. Thus, our results are quite robust even when restricting the sample to observations in regions where there is distributional overlap in propensity scores.

6.5 Placebo Analysis

We present a variety of placebo analyses. First, we focus on populations that should not have been affected by the availability of Cox-2 inhibitors. Second, we assume entry and removal occurred at different times than they truly did. Last, we analyze sickness absence days taken for another family member's illness.[37]

To analyze populations that should not have been affected by Vioxx's entry and removal, we compare individuals suffering from asthma with individuals suffering from diabetes around age 40 (Panel A in Tables 14 and 15), and second, we compare individuals without chest pain with individuals with chest pain around age 40 (Panel B in Tables 14 and 15). In Norway, prescriptions of Cox-2 inhibitors were targeted to individuals with joint pain and

[37]We also performed a robustness check to ensure the results are not driven by those with low labor market attachment. We did so by eliminating individuals with very low earnings and found those results (available upon request) are nearly identical to those presented here.

inflammation (combined with gastrointestinal problems), not to individuals with asthma, diabetes, or chest pain. Thus, when estimating our difference-in-differences model on these individuals, we should not find any significant effects of the entry or removal. The estimates of the effects of the entry and removal on sickness days and the probability of disability benefit receipt 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 or disability pension receipt as there were no changes in pharmaceutical availability for individuals with chronic joint pain at those times. Panel C in Tables 14 and 15 shows that we find no significant effects of the placebo entry or removal.

The final placebo test analyzes whether the sickness absence days an individual with joint pain takes due to another family member's sickness were affected by the entry and removal of Vioxx. We should expect to find no significant effect. Panel D in Table 14 shows we find no significant effects of the entry or removal of Vioxx on the sickness absence days taken for another family member's illness among individuals with joint pain, further providing support that our results are driven by the change in Cox-2 inhibitor availability.

7 Discussion

To better understand the economic magnitude of our results, we present a simple back-of-the-envelope calculation quantifying the costs of 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,[38] and thus the average daily earnings for males and females were NOK 1,597 and NOK 1,041, respectively. Our estimates aggregated to the annual level suggest that relative to the pre-entry period, Vioxx's entry decreased sickness days by 1 and 0.8 days per year for men

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

and women, respectively, while the removal increased sickness days by 1.2 and 1.8 days per year for men and women, respectively. Thus, relative to Vioxx being on the market in 2004, annual sickness days increased by 2.2 and 2.6 days for men and women, respectively, after the removal, resulting in an increase in average sickness leave costs per male and female with chronic joint pain of NOK 3,513 and NOK 2,707, 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 593 million or $93 million. To put this number in perspective, the Norwegian Social Security Administration's total annual expenses 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 2.1 percent of the annual sickness leave payments.[39] As discussed in Section 2.2, the total compensation payments for patients suffering from Vioxx's side effects in Norway were NOK 37 million—about 6 percent of the annual extra expenses caused by the drug removal.

We also consider the potential reimbursement savings to the Norwegian Insurance Scheme following Vioxx's removal. We do not know how many individuals with joint pain took Vioxx, but we create an upper bound based on prior studies. For example, Garthwaite (2012) finds among MEPS respondents between the ages of 55 and 75 with joint conditions, 19 percent filled a prescription for a Cox-2 inhibitor in early 2004. In a survey of 602 doctors in three districts in Norway, 30 percent prescribed Cox-2 inhibitors to individuals with joint pain in 2003 (Eriksen et al., 2003). The districts surveyed were representative of rural and smaller urban areas, but did not include cities such as Oslo and Bergen. To the extent those in urban areas were better informed and demanded Cox-2 inhibitors to a greater degree, 30 percent may be an underestimate. We therefore assume 40 percent of those with joint pain were prescribed Cox-2 inhibitors, and to create an upper bound on reimbursement savings, we assume they all took Vioxx and were fully reimbursed. We lack information about prescription switching behavior after the removal for the group of individuals we consider. Instead, we focus on extreme cases, assuming all former Vioxx users switched to Celebrex, switched to other NSAIDs like naproxen, or switched to nothing to obtain a range of potential cost savings.

According to the Norwegian Prescription Database administered by the Norwegian In-

[39]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.

stitute of Public Health, in 2004, the price per defined daily dose of Vioxx was NOK 12.62 and 9.74 for Celebrex. The prices of ibuprofen and naproxen were NOK 2.84 and 4.09 per DDD, respectively. To obtain annual savings, we multiply the defined daily dosage prices by 365 and the number of individuals we assume formerly took Vioxx (35,757 men and 41,218 women given the numbers above). If all Vioxx users switched to Celebrex, the annual cost savings would be NOK 81 million. If all Vioxx users switched to ibuprofen, the savings would be NOK 275 million, or NOK 239 million in the case where they switch to naproxen. If instead all Vioxx users switched to no prescribed medication, the cost savings would be NOK 355 million. Thus, even in the case that yields the largest reimbursement cost savings, we find the increase in annual sick leave expenditures exceeds the savings.

8 Conclusion

This paper analyzed the impact of progress in the treatment for chronic pain on sickness absence and disability pension receipt. Specifically, we examine how the availability of Cox-2 inhibitors affected sickness absence days (in excess of the first 16 days paid by the employer) and the probability of receiving disability pension 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 that relative to the pre-entry period, the market entry of Vioxx decreased quarterly sickness absence days among individuals with joint pain by 7 to 12 percent and the withdrawal led to a 12 to 16 percent increase in sickness absence days. We found the removal of Vioxx increased the quarterly probability of disability benefit receipt by 0.4 to 0.6 percentage points, and the entry only had a significant effect on the disability benefit receipt of women.

Our results underscore the economic importance of developing a pain medication that does not have gastrointestinal side effects and does not increase cardiac risks. The estimates suggest such a medication could increase the productivity of individuals with joint pain and allow them to return to (or stay at) work. More broadly, our paper emphasizes the importance of accounting for economic impacts when determining the net benefits of advances in medical and pharmaceutical technology. Considering labor supply effects and not just focusing on clinical outcomes and medical costs has important implications for regulatory decision-making and the coverage and reimbursement policies of insurance plans and national health care systems, particularly in countries like Norway that approach comparative-

effectiveness research from the societal perspective. 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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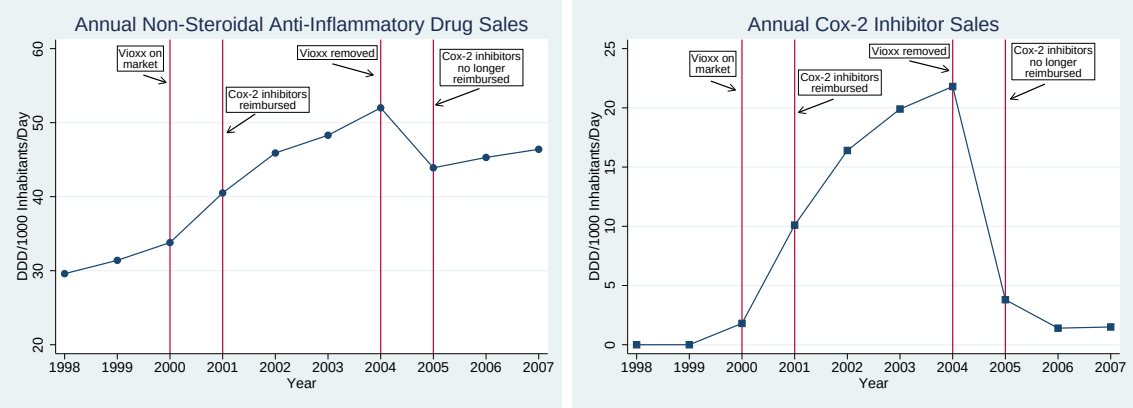
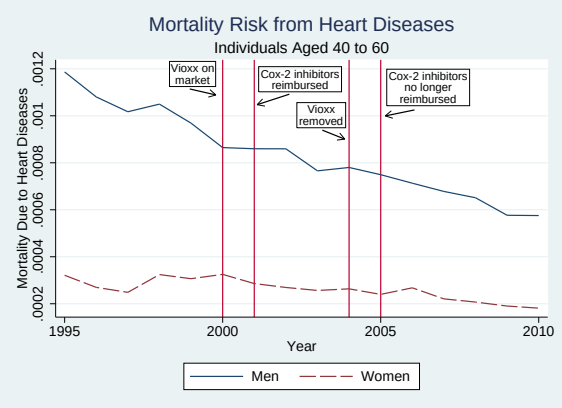
9 Tables and Figures

Figure 1: Annual Sales of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and Cox-2 Inhibitors in Norway



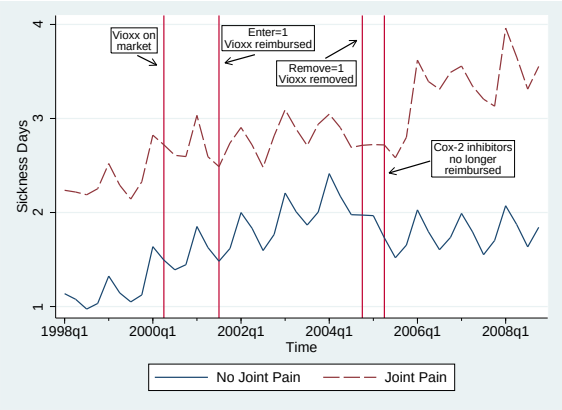
Data Source: Health Statistics in the Nordic Countries 2003, 2004, 2006. NOMESCO, Copenhagen.

Figure 2: Mortality Rate From Heart Disease



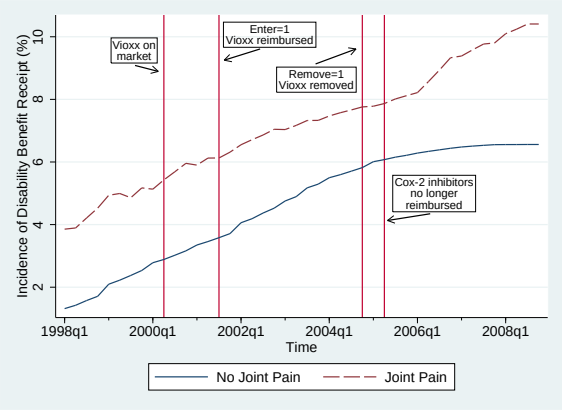
Notes: The figure shows the proportion of individuals who died from heart disease from 1995 to 2010. The sample includes all men and women in the Cause of Death Registry who pass away between ages 40 and 60.

Figure 3: Quarterly Sickness Absence Days by Pain Status



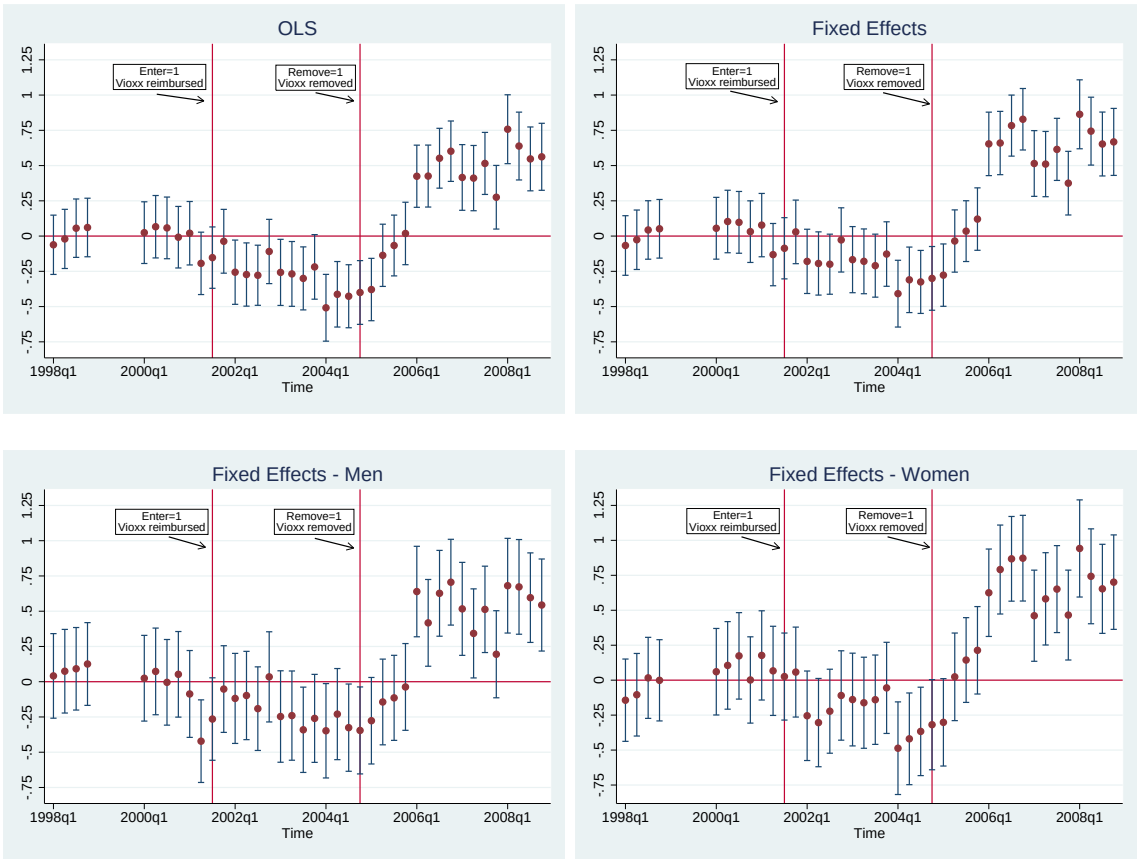
Notes: The figure shows the average number of sickness absence days (exceeding the first 16 days paid by the employer) per quarter from 1998 to 2008. The dashed line is the treatment group including all individuals who report chronic joint pain around the age of 40. The solid line is the control group including all individuals who report no joint pain around the age of 40.

Figure 4: Quarterly Incidence of Disability Pension Receipt by Pain Status



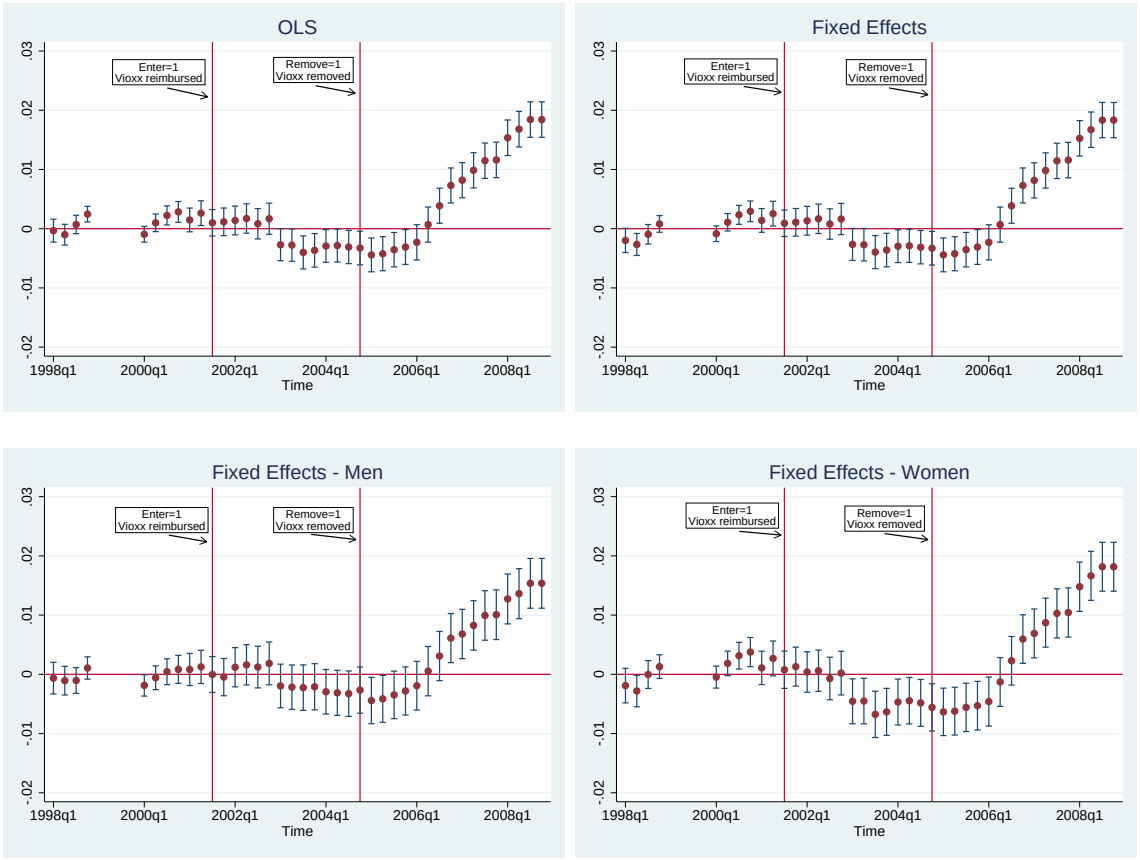
Notes: The figure shows the proportion of individuals receiving disability pension benefits per quarter from 1998 to 2008. The dashed line is the treatment group including all individuals who report chronic joint pain around the age of 40. The solid line is the control group including all individuals who report no joint pain around the age of 40.

Figure 5: Sickness Absence Days: Generalized Difference-in-Differences Coefficient Estimates



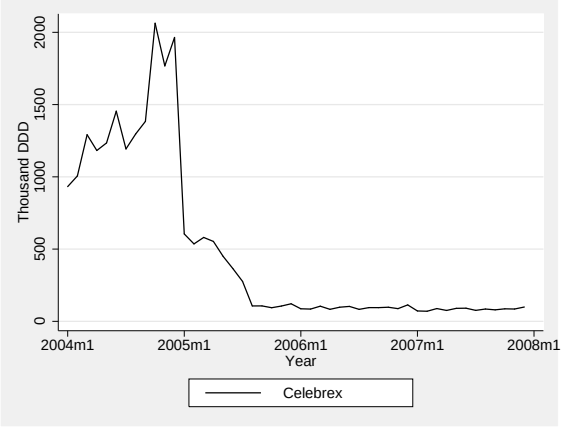
Notes: Each panel contains plots of the estimates of π_ℓ from equation 3 with 95 percent confidence interval bars where quarterly sickness absence days is the outcome. Standard errors are clustered at the individual level.

Figure 6: Disability Pension Receipt: Generalized Difference-in-Differences Coefficient Estimates



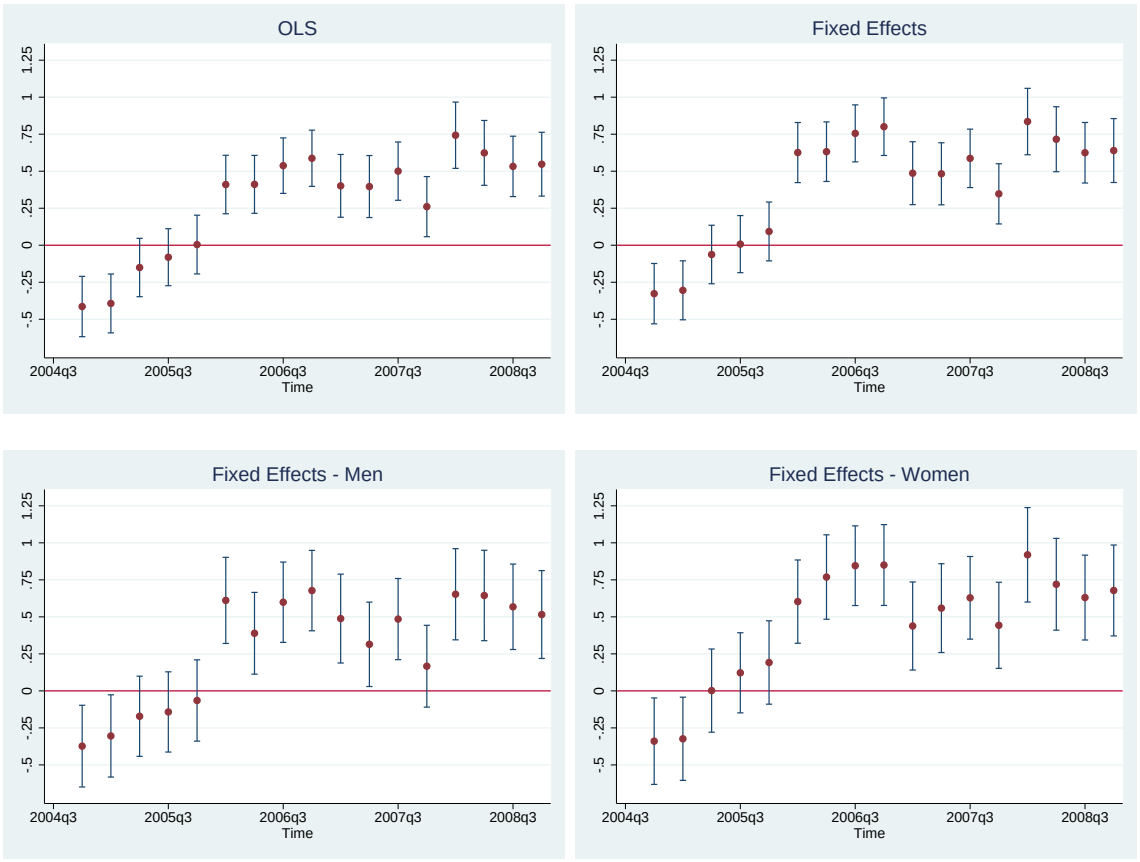
Notes: Each panel contains plots of the estimates of π_ℓ from equation 3 with 95 percent confidence interval bars where the probability of disability pension receipt is the outcome. Standard errors are clustered at the individual level.

Figure 7: Monthly Sales of Celebrex in Norway, 2004-2008



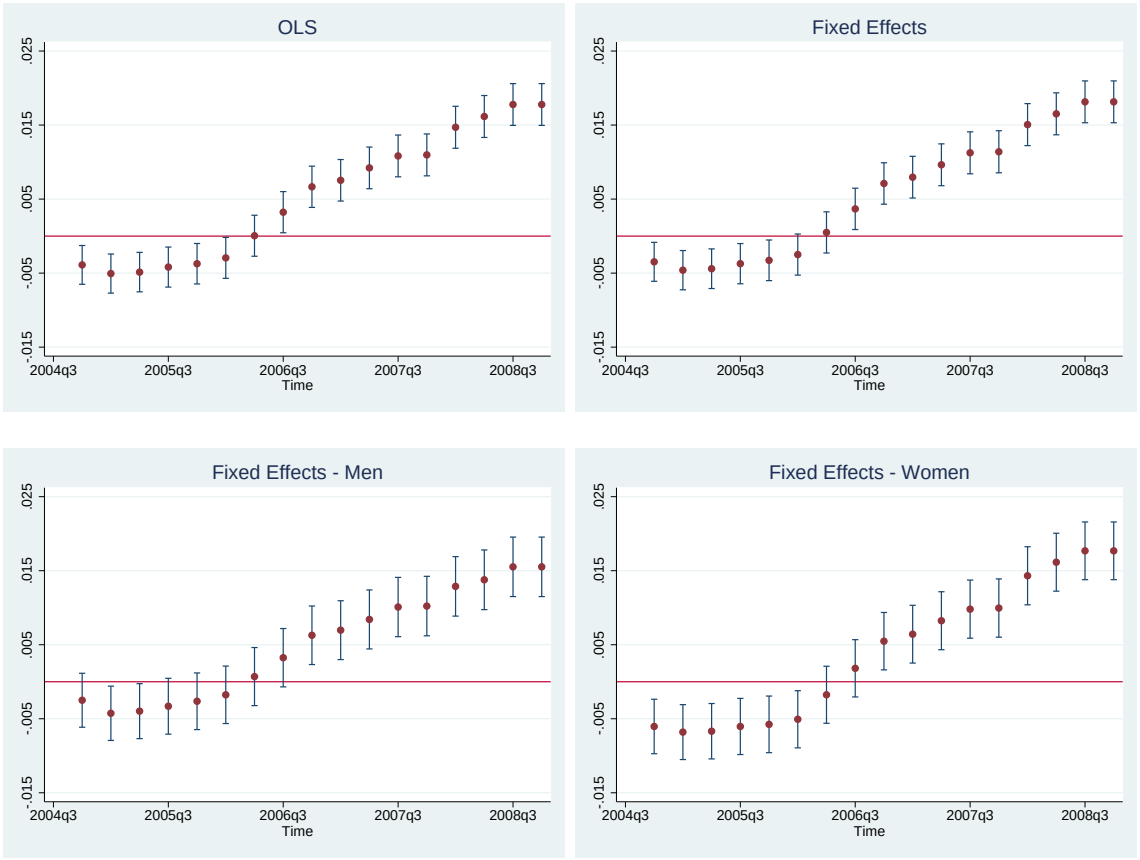
Data Source: Norwegian Prescription Database.

Figure 8: Time-Varying Effects of Vioxx's Removal on Sickness Absence Days



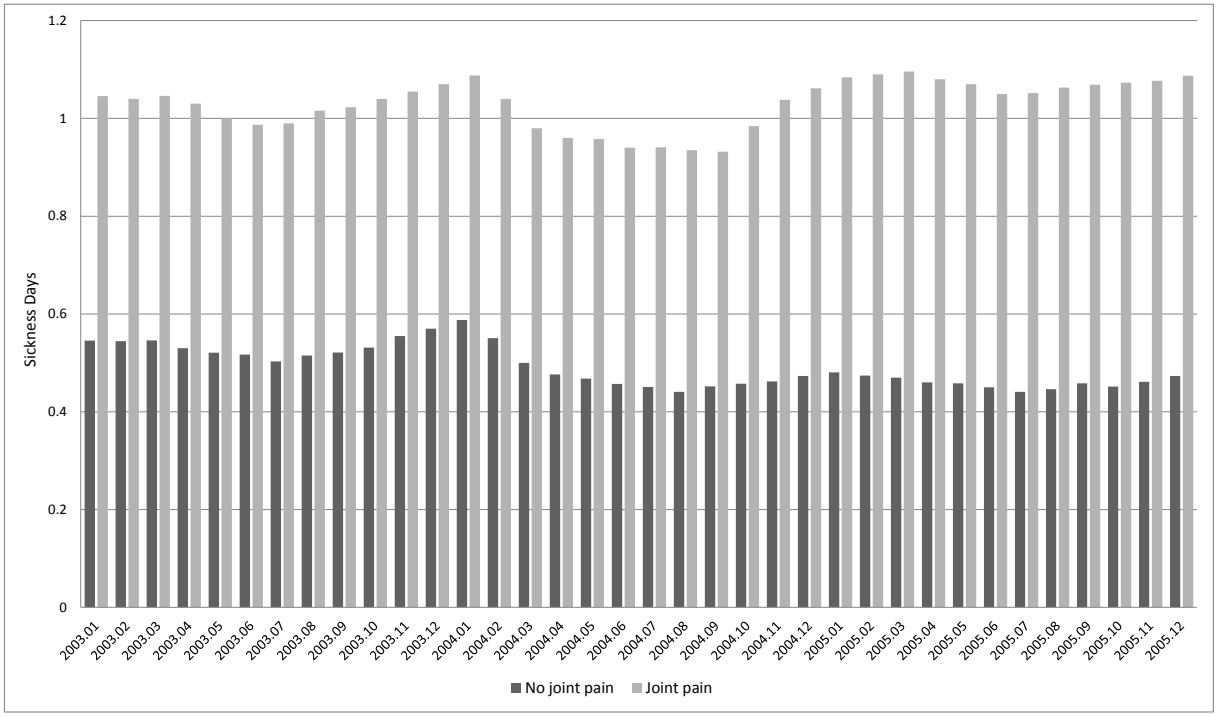
Notes: Each panel contains plots of the coefficients on interactions between $Pain_i$ and individual time indicators that correspond to the removal periods with 95 percent confidence interval bars. Standard errors are clustered at the individual level.

Figure 9: Time-Varying Effects of Vioxx's Removal on the Probability of Receiving Disability Pension



Notes: Each panel contains plots of the coefficients on interactions between $Pain_i$ and individual time indicators that correspond to the removal periods with 95 percent confidence interval bars. Standard errors are clustered at the individual level.

Figure 10: Monthly Sickness Absence Days by Pain Status from January 2003 to December 2005



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 lighter bars represent the treatment group including all individuals who report chronic joint pain around the age of 40. The dark bars represent the control group including all individuals who report no joint pain around the age of 40.

Table 1: Descriptive Statistics by Pain Status and Gender Prior to Vioxx's Entry

	Men		Women	
	No joint pain	Joint pain	No joint pain	Joint pain
	Panel A: Sickness Absence Sample			
Age	44.0	43.3	44.0	43.4
Years of education	12.4	11.7	12.2	11.7
% married	70.0	67.9	70.6	68.0
Yearly earnings	343309	302582	213307	191515
Quarterly sickness absence days[a]	1.0	2.1	1.6	2.8
% physically demanding occupation	69.3	75.4	64.6	68.4
% on sickness leave per quarter	1.7	3.1	2.5	4.0
% on partial sickness leave per quarter	0.3	0.6	0.6	1.0
Number of observations	1357555	207372	1407570	288251
	Panel B: Disability Pension Sample			
Age	44.0	43.4	44.0	43.5
Years of education	12.3	11.6	12.1	11.5
% married	69.1	66.2	70.2	67.1
Yearly earnings	333030	281826	199540	165264
Quarterly sickness absence days[a]	1.2	2.3	1.7	2.9
% physically demanding occupation	70.1	76.8	66.4	71.9
% receiving disability pension per quarter	1.7	3.3	3.1	6.2
Number of observations	1402764	223472	1524800	341576

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

Table 2: The Effects of Vioxx's Entry and Removal on Sickness Absence Days

	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-0.276**	-0.206**	-0.248**	-0.200**
	(0.051)	(0.051)	(0.071)	(0.071)
remove × pain	0.291**	0.409**	0.297**	0.457**
	(0.050)	(0.051)	(0.071)	(0.071)
Number of observations	6299675	6299675	3014685	3284990
Number of individuals		155031	72644	82387

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

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

Table 3: The Effects of Vioxx's Entry and Removal on the Probability of Receiving Disability Pension

	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-0.001	-0.001	-0.001	-0.003**
	(0.001)	(0.001)	(0.001)	(0.001)
remove × pain	0.005**	0.006**	0.005**	0.004*
	(0.001)	(0.001)	(0.002)	(0.002)
Number of observations	6873144	6873144	3193660	3679484
Number of individuals		158314	73588	84726

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

Notes: Entries represent the estimated difference-in-differences coefficients with standard errors in parentheses from OLS and fixed effects regressions of the effect of the entry and removal of Vioxx on the quarterly probability of receiving disability pension for individuals between the ages of 40 and 60 with joint pain. Unreported covariates include indicator variables for age, gender, education, county, time (measured in quarters), and years since completing the health survey. Standard errors are clustered at the individual level.

Table 4: Heterogeneous Effects of Vioxx's Entry and Removal on Sickness Absence Days by Occupation and Marital Status

Panel A: Physically Demanding Occupations					
		OLS	Fixed Effects	FE Men	FE Women
Physical	entry × pain	-0.307**	-0.224**	-0.272**	-0.210*
		(0.063)	(0.063)	(0.086)	(0.091)
	remove × pain	0.219**	0.365**	0.293**	0.396**
		(0.061)	(0.062)	(0.085)	(0.089)
Non-Physical	entry × pain	-0.221**	-0.193*	-0.245*	-0.196
		(0.084)	(0.084)	(0.123)	(0.112)
	remove × pain	0.506**	0.540**	0.337**	0.600**
		(0.088)	(0.087)	(0.129)	(0.119)
Panel B: Marital Status					
		OLS	Fixed Effects	FE Men	FE Women
Married	entry × pain	-0.238**	-0.172**	-0.200*	-0.171*
		(0.059)	(0.059)	(0.082)	(0.083)
	remove × pain	0.317**	0.431**	0.242**	0.534**
		(0.059)	(0.059)	(0.082)	(0.084)
Single	entry × pain	-0.365**	-0.286**	-0.355**	-0.272*
		(0.097)	(0.097)	(0.136)	(0.137)
	remove × pain	0.240*	0.375**	0.422**	0.295*
		(0.095)	(0.096)	(0.136)	(0.135)

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

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

Table 5: Heterogeneous Effects on Vioxx's Entry and Removal on the Probability of Receiving Disability Pension by Occupation and Marital Status

Panel A: Physically Demanding Occupations					
		OLS	Fixed Effects	FE Men	FE Women
Physical	entry × pain	-0.007**	-0.007**	-0.003	-0.011**
		(0.001)	(0.002)	(0.002)	(0.002)
	remove × pain	-0.002	-0.002	0.002	-0.004
		(0.002)	(0.002)	(0.002)	(0.003)
Non-Physical	entry × pain	0.001	0.001	0.003*	0.001
		(0.002)	(0.001)	(0.001)	(0.002)
	remove × pain	0.018**	0.020**	0.007**	0.025*
		(0.002)	(0.002)	(0.003)	(0.003)
Panel B: Marital Status					
		OLS	Fixed Effects	FE Men	FE Women
Married	entry × pain	0.001	0.001	0.002	-0.001
		(0.001)	(0.001)	(0.002)	(0.002)
	remove × pain	0.009**	0.009**	0.010**	0.006*
		(0.002)	(0.002)	(0.002)	(0.002)
Single	entry × pain	-0.007**	-0.006**	-0.007**	-0.007**
		(0.002)	(0.002)	(0.003)	(0.003)
	remove × pain	-0.003	-0.003	-0.006	-0.001
		(0.002)	(0.002)	(0.004)	(0.003)

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

Notes: Entries represent the estimated difference-in-differences coefficients with standard errors in parentheses from OLS and fixed effects regressions of the effect of the entry and removal of Vioxx on the quarterly probability of receiving disability pension for individuals between the ages of 40 and 60 with joint pain. Unreported covariates include indicator variables for age, gender, education, county, time (measured in quarters), and years since completing the health survey. Standard errors are clustered at the individual level.

Table 6: The Effects of Vioxx's Entry and Removal on Sickness Absence Days with Entry Defined as 2000 Q2

	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-0.223**	-0.148**	-0.286**	-0.117
	(0.050)	(0.050)	(0.075)	(0.070)
remove × pain	0.394**	0.423**	0.286**	0.488**
	(0.053)	(0.053)	(0.074)	(0.075)
Number of observations	6300550	6300550	3014726	3285824
Number of individuals		155156	72680	82476

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

Notes: Entries represent the estimated difference-in-differences coefficients with standard errors in parentheses from OLS and fixed effects regressions of the effect of the entry (redefined as quarter 2 of 2000) and removal of Vioxx on the number of sickness days per quarter of individuals between the ages of 40 and 60 with joint pain. Unreported covariates include indicator variables for age, gender, education, county, time (measured in quarters), and years since completing the health survey. Standard errors are clustered at the individual level.

Table 7: The Effects of Vioxx's Entry and Removal on the Probability of Receiving Disability Pension with Entry Defined as 2000 Q2

	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-0.001	-0.000	-0.000	-0.001
	(0.001)	(0.001)	(0.001)	(0.001)
remove × pain	0.005**	0.006**	0.005*	0.004
	(0.001)	(0.001)	(0.002)	(0.002)
Number of observations	6873144	6873144	3193660	3679484
Number of individuals		158314	73588	84726

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

Notes: Entries represent the estimated difference-in-differences coefficients with standard errors in parentheses from OLS and fixed effects regressions of the effect of the entry (redefined as quarter 2 of 2000) and removal of Vioxx on the quarterly probability of receiving disability pension for individuals between the ages of 40 and 60 with joint pain. Unreported covariates include indicator variables for age, gender, education, county, time (measured in quarters), and years since completing the health survey. Standard errors are clustered at the individual level.

Table 8: The Effects of Vioxx's Entry and Removal on Sickness Absence Days for the Sample Age 43 or Younger in 2001

	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-0.204	-0.287*	-0.335*	-0.270
	(0.116)	(0.119)	(0.164)	(0.166)
remove × pain	0.253*	0.351**	0.362*	0.358*
	(0.120)	(0.120)	(0.166)	(0.171)
Number of observations	829346	829346	387922	441424
Number of individuals		20774	9525	11249

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

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

Table 9: The Effects of Vioxx's Entry and Removal on the Probability of Receiving Disability Pension for the Sample Age 43 or Younger in 2001

	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-0.001	-0.001	-0.000	-0.002
	(0.002)	(0.002)	(0.002)	(0.002)
remove × pain	0.003*	0.004*	0.002	0.005*
	(0.002)	(0.002)	(0.002)	(0.003)
Number of observations	881756	881756	402984	478772
Number of individuals		20913	9558	11355

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

Notes: Entries represent the estimated difference-in-differences coefficients with standard errors in parentheses from OLS and fixed effects regressions of the effect of the entry and removal of Vioxx on the quarterly probability of receiving disability pension for individuals between the ages of 40 and 60 with joint pain. Unreported covariates include indicator variables for age, gender, education, county, time (measured in quarters), and years since completing the health survey. Standard errors are clustered at the individual level.

Table 10: The Effect of the Reform (Defined as Starting in February 2004) on Monthly Sickness Absence Days from January 1, 2002 to September 30, 2004

	OLS	Fixed Effects	FE Men	FE Women
reform × pain	-0.029	-0.022	-0.027	-0.017
	(0.028)	(0.031)	(0.040)	(0.039)
Number of observations	4811801	4811801	2281957	2529844
Number of individuals		151365	71340	80025

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

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

Table 11: The Effects of Vioxx's Entry and Removal on Sickness Absence Days Controlling for the Reform (Defined as Starting in Q1 2004)

	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-0.227**	-0.161**	-0.227**	-0.155*
	(0.054)	(0.054)	(0.075)	(0.077)
remove × pain	0.524**	0.619**	0.395**	0.663**
	(0.099)	(0.098)	(0.138)	(0.139)
reform × pain	-0.177	-0.111	-0.098	-0.207
	(0.089)	(0.088)	(0.124)	(0.124)
Number of observations	6299675	6299675	3014685	3284990
Number of individuals		155031	72644	82387

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

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

Table 12: The Effects of Vioxx's Entry and Removal on Sickness Absence Days for the Common Support Sample

	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-0.283**	-0.212**	-0.268**	-0.194**
	(0.052)	(0.052)	(0.073)	(0.074)
remove × pain	0.281**	0.401**	0.282**	0.456**
	(0.052)	(0.052)	(0.072)	(0.073)
Number of observations	5023467	5023467	2394530	2628937
Number of individuals		124089	57871	66218

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

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

Table 13: The Effects of Vioxx's Entry and Removal on the Probability of Receiving Disability Pension for the Common Support Sample

	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-0.000	0.000	-0.000	-0.002*
	(0.001)	(0.001)	(0.001)	(0.001)
remove × pain	0.006**	0.007**	0.005**	0.006**
	(0.001)	(0.001)	(0.002)	(0.002)
Number of observations	5477328	5477328	2536208	2941120
Number of individuals		126445	58553	67892

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

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

Table 14: Placebo Effects of Vioxx's Entry and Removal on Sickness Absence Days

Panel A: Placebo Groups - Diabetes vs. Asthma				
	OLS	Fixed Effects	FE Men	FE Women
entry × diabetes	0.316	0.311	0.128	0.541
	(0.266)	(0.267)	(0.332)	(0.419)
remove × diabetes	0.520	0.528	0.193	0.646
	(0.296)	(0.265)	(0.326)	(0.417)
Number of observations	134978	134978	64054	91546
Number of individuals		3506	1602	1999
Panel B: Placebo Groups - No Chest Pain vs. Chest Pain				
	OLS	Fixed Effects	FE Men	FE Women
entry × chest pain	-0.144	-0.044	0.136	-0.210
	(0.116)	(0.115)	(0.151)	(0.172)
remove × chest pain	-0.248*	-0.067	0.123	-0.238
	(0.110)	(0.112)	(0.145)	(0.168)
Number of observations	6299675	6299675	3014685	3284990
Number of individuals		155031	72644	82387
Panel C: Placebo Entry Year: 1995; Placebo Removal Year: 1998				
	OLS	Fixed Effects	FE Men	FE Women
placebo entry × pain	-0.039	0.028	0.162	-0.099
	(0.088)	(0.089)	(0.126)	(0.123)
placebo remove × pain	0.024	0.187	0.227	0.014
	(0.092)	(0.096)	(0.135)	(0.133)
Number of observations	3551803	3551803	1704239	1847564
Number of individuals		154336	72512	81824
Panel D: Placebo - Absence Due to Family Member's Sickness				
	OLS	Fixed Effects	FE Men	FE Women
entry × pain	-0.007	-0.003	0.002	-0.007
	(0.008)	(0.005)	(0.007)	(0.008)
remove × pain	-0.008	-0.001	0.008	-0.008
	(0.008)	(0.005)	(0.008)	(0.008)
Number of observations	6299675	6299675	3014685	3284990
Number of individuals		155031	72644	82387

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

Notes: Entries represent the estimated difference-in-differences coefficients with standard errors in parentheses from OLS and fixed effects regressions of the effect of the entry and removal of Vioxx on the number of sickness days per quarter of individuals between the ages of 40 and 60 with diabetes (compared to those with asthma), chest pain (compared to those without chest pain), or joint pain, respectively. Unreported covariates include indicator variables for age, gender, education, county, time (measured in quarters), 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 15: Placebo Effects of Vioxx's Entry and Removal on the Probability of Receiving Disability Pension

Panel A: Placebo Groups - Diabetes vs. Asthma				
	OLS	Fixed Effects	FE Men	FE Women
entry × diabetes	0.001	0.000	0.009	-0.006
	(0.006)	(0.006)	(0.008)	(0.009)
remove × diabetes	0.009	0.008	0.012	0.009
	(0.009)	(0.009)	(0.012)	(0.013)
Number of observations	161112	161112	72304	88808
Number of individuals		3695	1658	2037
Panel B: Placebo Groups - No Chest Pain vs. Chest Pain				
	OLS	Fixed Effects	FE Men	FE Women
entry × chest pain	0.004*	0.005	0.001	0.008
	(0.002)	(0.003)	(0.004)	(0.005)
remove × chest pain	0.002	0.002	0.001	0.009
	(0.003)	(0.003)	(0.004)	(0.005)
Number of observations	3806410	3806410	1772014	2034396
Number of individuals		157744	73300	84444
Panel C: Placebo Entry Year: 1995; Placebo Removal Year: 1998				
	OLS	Fixed Effects	FE Men	FE Women
placebo entry × pain	0.001	0.002	0.002	0.002
	(0.001)	(0.002)	(0.003)	(0.003)
placebo remove × pain	0.001	0.003	0.002	0.003
	(0.001)	(0.003)	(0.004)	(0.004)
Number of observations	3806410	3806410	1772014	2034396
Number of individuals		157744	73300	84444

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

Notes: Entries represent the estimated difference-in-differences coefficients with standard errors in parentheses from OLS and fixed effects regressions of the effect of the entry and removal of Vioxx on the quarterly probability of receiving disability pension for individuals between the ages of 40 and 60 with diabetes (compared to those with asthma), chest pain (compared to those without chest pain), or joint pain, respectively. Unreported covariates include indicator variables for age, gender, education, county, time (measured in quarters), 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.