ABSTRACT

Title of Document: EMPIRICAL ESSAYS IN HEALTH ECONOMICS

Craig Garthwaite
PhD, 2009

Directed By: Professor Mark Duggan
Department of Economics

Chapter 1: The Economic Effects of Medical Innovations: Vioxx and Labor Supply

Despite dramatic improvements in medical technology over time, comparatively little attention has been paid to the effect of these innovations on economic outcomes. This study uses seven overlapping panels of the Medical Expenditure Panel Survey to estimate the labor supply effects of Vioxx—a selective non-steroidal anti-inflammatory drug intended for individuals with chronic pain. Fixed effect estimates analyzing the effect of individuals choosing to start and stop taking Vioxx indicates that use of the drug is associated with greater labor force participation. This paper also exploits the removal of Vioxx from the market in 2004 as an exogenous source of variation in utilization. Both methods show that Vioxx use is associated with statistically and economically significant increases in the labor supply of near elderly individuals with joint conditions. An effect is also found for usual weekly hours worked. There is no labor supply effect for other expensive medications used for chronic conditions, suggesting that a desire to work in order to obtain employer-provided health insurance is not driving the estimated effect of Vioxx. These results suggest a role for improving medical technology in explaining recent increases in the labor force participation rate of older workers.

Chapter 2: The Effect of In-Utero Conditions on Long Term Health: Evidence from the 1918 Spanish Flu Pandemic

The fetal origins hypothesis posits that in-utero stress increases the incidence of chronic conditions later in life. Utilizing 21 years of National Health Interview Survey data, this study estimates the health effect of in-utero exposure to the 1918 Spanish Flu pandemic. Exploiting the fact that people were exposed to the flu at different points during fetal development, the model tests precise predictions from the medical literature about when exposure to in utero insults should damage organs later in life. The pattern of results demonstrates the necessity of using a short duration event as a source of variation in fetal conditions and helps explain previously mixed evidence regarding the fetal origins hypothesis.

EMPIRICAL ESSAYS IN HEALTH ECONOMICS

By

Craig Loren Garthwaite

Dissertation submitted to the Faculty of the Graduate School of the
University of Maryland, College Park, in partial fulfillment
of the requirements for the degree of
PhD
2009

Advisory Committee:
Mark Duggan, PhD, Chair
William Evans, PhD
Darrell Gaskin, PhD
Judy Hellerstein, PhD
Melissa Kearney, PhD

Dedication

To my loving wife Leslie for her support throughout this process.

Acknowledgements

I am eternally grateful to Mark Duggan, Bill Evans, Melissa Kearney, and Judy Hellerstein for their advice both on this dissertation and throughout my graduate studies. I wish to thank Kerwin Charles for careful comments on each version of this document and wise counsel over the years. I also wish to thank Richard Burkhauser, Seth Freedman, Jonah Gelbach, Raymond Guiteras, Ginger Jin, Tim Moore, John Shea, Alex Tabarrok, and seminar participants at the University of Maryland for their suggestions.

Table of Contents

List of Tables

List of Figures

Introduction

Health care has become an essential sector of the American economy and currently accounts for approximately 16 percent of gross domestic product. As expenditures in this sector continue to grow, government policies and regulation must adapt to the ever changing environment. While public health professionals and medical doctors are obviously a key component in developing these new policies, economists have also increasingly played an important role. This dissertation contributes to the body of knowledge in health economics in that it considers two examples where a broader understanding of the causes and consequences of particular events or innovations and their effects on people's health will hopefully lead to improved policy decisions in the future.

First, I estimate the economic, as opposed to solely health related benefits of medical innovations. Knowledge about the full scope of benefits from these newly developed technologies is critical to effective policymaking. In the second chapter, I estimate the effect of in-utero conditions on the likelihood of developing chronic conditions in later life. Together, these two chapters provide information that is useful for health policy professionals and show that economic analysis can help answer important questions in this field.

The first chapter of this dissertation focuses on estimating the economic benefits of Vioxx, an innovative anti-inflammatory medication targeted at individuals with arthritis and other conditions requiring the consistent use of pain medication. Specifically, I focus on the effect of Vioxx on the ability of sick individuals to participate in the labor force. This economic benefit is an important indicator of the

efficacy of a medication such as Vioxx whose primary endpoint—decreased pain—is difficult to measure in a clinical trial setting.

Vioxx belongs to a family of drugs known as COX-2 inhibitors. These medications are selective non-steroidal anti-inflammatory drugs (NSAIDs). They were an improvement over the previous non-selective NSAIDs, which greatly increased the likelihood of gastro-intestinal bleeding (it is estimated that 16,500 people a year die from NSAID related gastro-intestinal bleeding). Unfortunately, after Vioxx's release, subsequent clinical trial data found that the increased safety with respect to gastro-intestinal side effects came at the expense of a statistically significant increase in the risk of negative cardiac events. As a result, Vioxx was removed from the global market in 2004. At this time, Vioxx was on the top ten selling drugs in the global market. This represented the largest voluntary recall of a prescription medication in United States history.

In this chapter, I use the Medical Expenditure Panel Survey (MEPS) to estimate the effect of the use of Vioxx on labor force participation. Due to the panel nature of the MEPS survey, I am able to control for individual-level time-invariant differences in the probability of working. Such differences would likely bias any cross sectional estimates of the effect of Vioxx on labor supply. I find statistically and economically significant increases in the probability of working for near elderly and elderly men with joint conditions taking Vioxx. I find no effect for women. This is likely a result of the fact that few women in this age group are employed in occupations requiring physical labor—occupations with a high disutility of work for individuals with untreated conditions causing chronic joint pain.

While the panel data estimates control for fixed differences between people over time, they are unable to control for time-varying factors that may affect both Vioxx use and labor supply. Therefore, I also exploit the removal of Vioxx from the global market as an exogenous source of variation in the utilization of the drug. Instrumenting for Vioxx use using the removal of the drug from the market finds a large and statistically significant effect of Vioxx use on labor supply.

Overall, these results show that the use of Vioxx increased the labor supply of near elderly individuals with joint conditions. These economic benefits demonstrate a clear benefit in terms of an increased ability to participate in the labor force. Similar benefits are not found for Celebrex—another popular COX-2 inhibitor. There is a good deal of debate in the medical literature about the relative efficacy of these medications. The results concerning labor supply in this chapter suggest that the economic benefits may be a useful additional quantitative metric for evaluating the relative efficacy of quality of life medications.

Accurately quantifying the benefits of medical innovations can provide important information for the ongoing discussion concerning the rising levels of medical spending. Increasing expenditures have caused national health services in countries around the globe to attempt to measure the cost effectiveness of new technologies. There are growing calls for the United States government to do the same. Even without explicit cost effectiveness policies, in regulating pharmaceuticals policymakers are forced to weigh the costs and benefits of newly developed technologies. In order to accurately accomplish these evaluations, it is critical to understand the full range of benefits provided by new innovations. The medical

system is increasingly focused on improving the quality of life by treating the symptoms of chronic conditions, and not solely extending the length of an individual's life. Therefore, an increasing portion of the benefits from these medications will likely affect an individual's economic outcomes In addition, understanding the economic benefits of these medications can better assist our understanding of the ability of the elderly and other individuals with chronic conditions to participate in the labor force. This can have non-trivial consequences for both Social Security and the Social Security Disability Insurance programs.

The second chapter of this dissertation estimates the effect of fetal stress on the development of later life health conditions. It is estimated that approximately 75 percent of United States health spending is aimed at treating chronic conditions. This has led many policymakers to support plans aimed at preventive medicine. Effectively designing these programs, however, requires knowledge about the root causes of these expensive conditions.

For several decades now, the medical literature has noted a connection between in-utero conditions later life health. Formally, this connection is described as the fetal origins hypothesis (although it is also commonly referred to as the "Barker Hypothesis" in deference to David J.P. Barker—one of the first researchers to identify the connection). A wide variety of animal experiments have shown that nutrient deprivation and other stress in-utero is causally connected to later life organ failure. Identifying this causal effect in humans, however, has proven far more difficult. This should perhaps not be surprising as individuals who experience in-utero stress often suffer through both difficult early and later-life conditions. Separating the effect of

these two conditions on the likelihood of developing chronic conditions in observational studies is difficult.

Identifying the effect in humans would most easily be done through a random assignment experiment. For a variety of clear and valid ethical reasons this is unlikely to occur. Therefore, researchers have turned to other plausibly exogenous sources of variation in fetal conditions. For example, individuals have used in-utero stress caused by the Chinese and Dutch famines as well as the Siege of Leningrad during World War II to estimate the effect of fetal conditions on later life health. Estimates using these events have returned mixed evidence regarding the fetal origins hypothesis. As is discussed in this chapter, it is likely that the inability to find later life health effects is due in part to the long length of the previous events used as sources of variation.

The medical literature reports that the timing of in-utero stress should generate different conditions in later years. For example, the kidneys primarily develop during the later months of development and, therefore, stress during the last trimester should be more likely to result in kidney disorders. Conversely, stress during the first months of in-utero development will likely have little effect on long term kidney health. The difficulty presented by long duration events as a source of exogenous variation is the complexity in pinpointing specific windows of fetal stress which generates a large downward bias in the estimated effect of fetal stress for any particular condition.

The source of variation utilized in this chapter is the peak of the 1918 global flu pandemic. Pregnant women were disproportionately likely to be infected with this

flu variant. As a result, individuals who were in-utero during the pandemic suffered dramatic decreases in fetal health. Douglas Almond (2006) was the first author in the economics literature to use this as a source of variation in fetal conditions. His paper, however, estimated the effect of fetal stress on primarily non-health outcomes. Almond and Mazmunder (2005) estimated the effect of in-utero flu exposure on health outcomes. My chapter expands upon this earlier work by using a larger sample size and explicitly attempting to connect the results to the predictions of the medical literature. In total, my results show that the timing of exposure to fetal stress is critically important in predicting later life health outcomes. Individuals exposed to the peak of the 1918 flu pandemic during different trimesters are more likely to develop conditions related to organs that were primarily developing during that time period.

In addition to providing more evidence in support of the fetal origins hypothesis and demonstrating the important of a short duration event as a source of variation, I believe that these results show the importance of more cohesive health and welfare policy. The fact that chronic conditions (which are often paid for by Medicare and Medicaid) may have their roots in-utero suggests that health policies aimed at decreasing medical expenditures and increasing overall health should be integrated throughout (and possibly before) an individual's lifetime. For example, later life health outcomes may justify increased funding for prenatal programs or expansions of food stamps for pregnant women.

Chapter 1: The Economic Effects of Medical Innovations: Vioxx and Labor Supply

The percentage of the population participating in the labor force has remained relatively constant over the last two decades. Over this period, the labor force participation rate for working age individuals only increased by 0.3 percentage points—from 65.7 to 66 percent. Examining labor force participation for different age groups, however, reveals that there has been a dramatic increase among older individuals over the same period. Figure 1 contains the change in labor supply between 1987 and 2007 for males and females by age. Over the last two decades, males aged 60 and older increased their labor supply while younger individuals worked at a lower rate. Women at most ages worked more in 2007 than in 1987, but the increase was far larger at older ages.

While there are many factors that can influence changes in labor supply, a primary determinant is a persons' physical and mental health. Economists have consistently found that poor health is causally related to lower levels of labor supply (Currie and Madrian, 1999). Researchers have also found that the number of individuals with chronic conditions has grown and the likelihood of being diagnosed with such a condition increases with age (Wu and Green, 2000; Hoffman and Schwartz, 2008). Based on these facts, it would be reasonable to expect that, holding age constant, the labor force participation of elderly individuals in recent years would remain constant, or even decrease.

Although the explanations for the recent rise in labor force participation among older workers have not been fully explored, a logical candidate for exploration

is the large number of medical innovations during the time period. Over the last two decades health spending has increased dramatically. Spending on health services in the United States now equals 16 percent of gross domestic product. Newhouse (1992) found that improvements in medical technology are a primary cause of increases in health care spending. Technology driven cost increases have been particularly apparent in the case of pharmaceuticals. From 1980-2005, the percentage of medical spending on pharmaceuticals doubled (Caitlin et al., 2007). In recent years, the majority of this increased spending came from higher usage and new drugs as opposed to simply increased prices on existing drugs (Smith, 2004). Looking at specific chronic conditions, in 2001 Americans spent 533% more in inflation adjusted dollars on drugs to treat diabetes and 374% more on drugs to treat arthritis than they did in 1987 (Stagnitti and Pancholi, 2004).

Little is known about the presence or the magnitude of the economic effects of the dramatic increases in health spending, utilization of medical services, and the introduction of innovations. Hirth, Chernew, Turene and Pauly et al. (2003) noted this fact when they said, "[e]ven papers that have used instrumental variables techniques to address the endogeneity of health have not analyzed how the choice among available medical treatments or the change in available treatments over time can mediate the effects of health on outcomes such as labor force participation, wages, earnings, and hours" (Hirth et al., 2003: 168).

The authors who have estimated the relationship between medical innovations and economic outcomes have primarily focused on developing countries or on mental health conditions. For example, economists have examined the role of anti retro-viral

treatments on improving labor supply in sub-Saharan Africa (Thirumuthy et. al., 2008). In the developed world, authors have evaluated the role of increased mental health treatment on labor market outcomes (Berndt, 2000; Berndt et al., 1998; Thimbie et al., 2006). These studies have used data from clinical trials and found that increased treatment for mental health conditions such as depression increased at-work productivity and participation.

This study attempts to increase understanding in this area by examining the relationship between the introduction of a widely used medical innovation and the ability of individuals with chronic physical conditions to supply labor. I focus on the release and subsequent removal from the market of the anti-inflammatory medication Vioxx. Developed by Merck, Vioxx was approved for sale by the FDA in 1999. It was intended for "relief of the signs and symptoms of osteoarthritis, the management of acute pain, and the treatment of primary dymenorrhea" (Food and Drug Administration, 1999). Patients receiving these prescriptions primarily report the presence of joint and back conditions.[1] As a result, these individuals often require the continual use of anti-inflammatory medications in order to perform common tasks. With respect to gastrointestinal side effects, Vioxx was believed to be safer for everyday use than previously existing medications. The drug's initial sales were strong and by 2001 it was already the 11th highest selling drug in the world with over $2.5 billion in worldwide sales. In 2004, a clinical trial reported an elevated cardiac risk for individuals taking Vioxx. As a result of this study (and previous indications of potential negative cardiac effects) Merck issued a world-wide recall of the drug in

[1] These conditions account for over 70 percent of all Vioxx prescriptions in the Medical Expenditure Panel Survey.

September, 2004—the largest voluntary recall of a prescription medication in United States history.

The introduction and surprising removal of Vioxx from the market provides a rare opportunity to estimate the effect of medical innovations on economic outcomes. Vioxx was intended for conditions such as arthritis whose primary symptoms (pain and swelling) can be addressed by the use of effective analgesics. According to the Centers for Disease Control (CDC), 30 percent of individuals with arthritis report work limitations from the condition (Lorig, 2007). For these individuals and others with chronic pain, COX-2 inhibitors such as Vioxx represented a new solution for pain relief. [2]

Initially, I use seven overlapping panels of the Medical Expenditure Panel Survey (MEPS) from 1998-2004 to estimate the effect of Vioxx prescriptions on labor supply. The MEPS provides detailed information on the socio-economic characteristics and prescription medicine habits of individuals over time. Exploiting the panel nature of this data, I estimate the labor supply effect of individuals choosing to start and stop taking Vioxx while controlling for time-invariant differences in labor supply across people. I find a statistically and economically significant increase in the probability of working for males taking Vioxx. For example, Vioxx use in the previous period is associated with a nearly 12 percent increase in the probability of working for males aged 55-61 with joint conditions. This effect is stronger for men in physical occupations. Examining the effect on hours worked, Vioxx use is found to have a positive and statistically significant increase on usual hours worked. Further

[2] Cox-2 inhibitors were sold under several brand-names. The largest were Vioxx, Celebrex, and Bextra. In 2002, global sales of Celebrex were $3 billion, those of Vioxx were $2.5 billion, and those of Bextra were $470 million.

investigation finds, however, that the increase in hours is likely a result of increased participation and not adjustment along the intensive margin. Falsification tests using other expensive medications find no similar relationship for these drugs suggesting that individuals are not working in order to obtain employer provided health insurance. No effect is found for female labor supply.

One concern about these fixed-effects results, and of any other observational studies examining the effects of pharmaceuticals, is potential endogeneity in the decision to start or stop taking the medication. While the use of panel data methods limits concerns about time-invariant factors biasing my estimates, unobservable time-varying factors could potentially bias the estimated causal effect of Vioxx on labor supply. The removal of Vioxx from the market provides an unusual source of exogenous variation in the use of a widely prescribed pharmaceutical.

Vioxx represented the largest voluntary recall of a prescription drug in American history. While it was available, there were over 80 million prescriptions written for Vioxx and in 2004—the year of withdrawal—approximately 1.3 million Americans were taking the drug (Kaufman, 2004). An analysis of employer health insurance claims found that by 2006, only 16 percent of previous Vioxx users were using Celebrex—another widely prescribed COX-2 inhibitor. One quarter claimed no prescription pain reliever use at all (Huse and Marder, 2007). This suggests that the removal of Vioxx from the market represented the end of effective pain medication for a substantial portion of the population. The removal decision was unexpected by the general public. The day following the removal announcement, Merck's stock price fell 27 percent (Rubin, 2004). Since the decision to remove Vioxx was not

anticipated, it is reasonable to assume that post-removal changes in utilization should be unrelated to other factors correlated with changes in economic outcomes. I implement an instrumental variables strategy exploiting this exogenous change and find statistically and economically significant effects of Vioxx on labor supply.

Accounting for the economic benefits of medications can have important implications for health policy—particularly the regulation of pharmaceuticals. New drugs are increasingly aimed at increasing the quality of life rather than simply its length (Bren, 2007). As a result, economic outcomes will potentially comprise a larger portion of the expected benefits profile.

What is Vioxx?

Vioxx is a member of the COX-2 inhibitors family of pain relievers. These drugs are broadly described as *selective* non-steroidal anti-inflammatory drugs (NSAID). They work by blocking the cyclooxygenase-2 (COX-2) enzyme and are primarily intended for individuals with chronic conditions requiring a nearly continual use of anti-inflammatories. Prior to the introduction of these medications, individuals with these conditions were limited to *non-selective* NSAIDs such as ibuprofen or naproxen that block both the COX-1 and COX-2 enzymes. One function of the COX-1 enzyme is protecting the stomach lining. As a result, non-selective NSAIDs increase the chance of gastro-intestinal (GI) bleeding—making them unsuitable for continual use in many patients. Each year, an estimated 16,500 individuals die from non-selective NSAID-related gastrointestinal complications. This amounts to 1 death for every 1,200 patients taking these drugs for two months or longer (Schmidt et al., 2004). Prior to the development of COX-2 inhibitors,

individuals susceptible to this bleeding were unable to take existing NSAIDs and often had to live with chronic pain.

COX-2 inhibitors represented an entirely new technology and as a result they were very popular. In a post-marketing survey of more than 80,000 patients, approximately 85 percent of respondents reported an improved quality of life from Vioxx. These respondents also found the once-daily regime of Vioxx simpler than their previous pain treatments (Zacher and Schattenkirchner, 2004). Examining medical claims data from 19 affiliated managed care plans covering 300,000 physicians and more than 4 million enrollees, Harley and Wagner (2003) found that users of COX-2 inhibitors were approximately 57 percent less likely to discontinue medication and 60 percent less likely to switch medications than were users of non-selective NSAIDs. This persistence in use is an often-used measure of patient satisfaction and side effects (Chan and Hamilton, 2006; Hasford et al. 2002; Dusing, 2001). In a study of individuals treated first with non-selective NSAIDs and subsequently with Vioxx, patients reported better satisfaction and health status while taking Vioxx. These patients also had a lower rate of treatment discontinuation due to lack of efficacy or adverse GI events (Arboleya et al., 2003). Schmidt et al. (2004) found that "the efficacy of rofecoxib [Vioxx] in osteoarthritis in various clinical studies is comparable to that of conventional NSAIDs but the incidence of adverse GI events with rofecoxib is significantly lower than with nonselective NSAIDs" (Schmidt et al., 2004: 194). Mamdani et al. (2002) found that "relative to rofecoxib, non-selective NSAID users were at significantly higher risk of upper gastrointestinal hemorrhage" (Mamdani et al., 2002: 1). Schnitzer and Hochberg (2003) said "[t]he

use of coxibs [COX-2 inhibitors] to treat OA [osteoarthritis] and RA [rheumatoid arthritis] is recommended as first-line therapy when symptoms of pain and inflammation are present in patients vulnerable to potential NSAID-associated GI toxicity" (Schnitzer and Hochberg, 2003: 20).

The underlying supposition of this analysis is that the use of Vioxx decreases the negative health effects of chronic conditions, and as a result the disutility of work, to the point that individuals are able to increase their labor supply. Therefore, at a minimum, the use of this drug should improve the self-reported health status of recipients. Examining MEPS respondents who reported Vioxx use provides information about the effect of Vioxx on poor health. The percentage of respondents reporting poor health increases by nearly 20 percent from the period before first Vioxx usage to the period where Vioxx is first reported.[3] This suggests that worsening health causes individuals to fill a prescription for Vioxx. In the period immediately following the first use of Vioxx, the percentage of these individuals reporting poor health decreases by approximately 7 percent. While by no means conclusive, this provides suggestive evidence of a potential effect of Vioxx on the ability of individuals to complete daily tasks such as working.

Prior to Vioxx's introduction to the market, a potential for increased cardiac risks was noted in the Vioxx GI Outcomes Research (VIGOR) study. VIGOR revealed a four fold increase in cardiac events for patients taking Vioxx compared to those taking naproxen (Bombadier et al., 2001). Concerns later developed about decisions made during the conduct of that study with respect to removing some

[3] Individuals are classified as reporting poor health if the report being in "fair" or "poor" health on a 5 point scale.

individuals in the treatment group who suffered negative cardiac events. Following Vioxx's introduction, a study estimating the effect of Vioxx on reducing colon polyps—the Adenomatous Polyp Prevention With Vioxx (APPROVe) study—confirmed previous findings that the drug's benefits in terms of patient satisfaction and decreased intestinal toxicity came at the apparent expense of an increased relative risk of cardiac events (Bresalier et al., 2005). The results of the APPROVe study combined with other studies and the potential errors in the VIGOR study caused Merck to voluntarily remove Vioxx from the market on September 30, 2004.

There is mixed evidence regarding the relative efficacy of Vioxx compared to other COX-2 inhibitors such as Celebrex and traditional non-selective NSAIDs such as ibuprofen and naproxen. Smugar et al. (2006) reported the results of two clinical trials, one of which found that pain relieving benefits of Vioxx were superior to Celebrex and another which found they were similarly efficacious. Several studies have found that the onset of pain relief was faster for Vioxx than Celebrex (Schnitzer et al., 2005; Battisiti et al., 2004). Examining the economic outcomes of Celebrex compared to Vioxx may provide more information about the relative efficacy of the medications. Differences between clinical trials measures of efficacy and the observed economic effects of medications may serve as further evidence of the importance of considering non-health outcomes in the benefits profile of quality of life drugs.[4]

Since its removal, anecdotal evidence abounds of consumers pushing for a reversal in this decision in order to regain access to the medication (Payne, 2004;

[4] This may be due to the fact that the benefits profile of these medications normally rely on subjective patient reported outcomes (PROs).

Mondics, 2005). In a telephone survey of elderly arthritics, Tannenbaum (2006) found that despite the acknowledged cardiac risk, 18 percent would still take Vioxx if it was available. This is despite the fact that the average respondent in this survey overestimated the risk of heart attack or stroke by more than 50 percent.

Health and Labor Supply

The effect of health on labor supply has long been studied in economics. Authors have estimated the effect of chronic conditions, health shocks, and the health of an individual's spouse or dependents on a variety of economic outcomes. Currie and Madrian (1999) provided a comprehensive review of the estimated effect of health on labor supply. Overall, they reported that economists have found a direct relationship between health and labor force participation.[5] This exists across several subgroups. For example, in a more recent study, Haider and Loughran (2001) used data from the Assets and Health Dynamics of the Oldest-Old (AHEAD) and found that negative health shocks, represented by declining health status or an increasing number of difficulties with activities of daily living, were a primary cause of elderly individuals exiting the labor force.

Other authors have specifically examined the effect of arthritis on labor supply. Bartel and Taubmman (1979) was one of the first studies to examine the

[5] This review also contains very detailed discussions of important issues related to health and labor supply concerning such factors as measuring health and the endogeneity of self-reported health status and conditions. While my study does rely on patient reported health conditions, the concerns for endogeneity of these responses are limited in the case for several reasons. First, the questions are related to specific conditions and not simply a coarse measure of self-reported health status. Second, the primary purpose of the MEPS is for the discussion of medical conditions, and not labor market outcomes, potentially limiting the desire to "justify" lack of labor force participation. Furthermore, this study concerns itself with reported prescription medications which are unlikely to be endogenous in the same manner described in Currie and Madrian (1999).

effect of specific conditions (rather than self reported health status) on labor supply. Of interest to this analysis, the authors found that the presence of arthritis was associated with a decrease in the probability of working and on wages. Similarly, Mitchell and Burkhauser (1990) found that arthritis lowers the wages of affected individuals both through a direct effect and as an indirect effect of fewer hours worked. Mitchell (1991) found that worsening health status is the primary reason for labor force exits among men with arthritis.

Examining the health of union veterans of the civil war in 1900 and participants in the National Health Interview Survey from 1985-1991, Costa (1996) found that while BMI—an indicator of health status—was a primary determinant in labor force status in both periods, this connection has weakened over time. Costa (1998) stated "health now appears to be less important to the labor force decision. Although the relation between BMI and the risk of labor force non-participation in 1900 was remarkably similar to that in 1985-1991, men in 1900 were much more responsive to changes in health than they are now" (Costa, 1998: 82). Costa cited many possible reasons for this change, including a difference in the relationship between chronic conditions and BMI, the decreasing physical demands of employment, and the shortening of the workday.

The central question of my study examines the relatively unexplored topic of the role of improvements in medical technology on the relationship between chronic conditions and labor market outcomes. This is a topic of great importance given both the large number of advancements in the medical field and the rapid aging of the American workforce creating an increasing number of working-age individuals with

chronic conditions. Studies addressing this topic have thus far primarily focused on the developing world. For example, economists have examined the spread of AIDS across Africa combined with the development of anti-retroviral (ARV) treatments to study the relationship between medical innovations and economic outcomes in the developing world (Thirumuthy et al. 2005).

Studies documenting the connection between medical technology, disease survival, and labor supply in the developed world are sparser. Lichtenberg (2002) estimated the effect of aggregate changes in drug utilization on labor supply. Lichtenberg used condition-level data on the utilization of medical services in an attempt to overcome an omitted variable bias caused by an inability to control for condition severity at the individual level. He found that for conditions with above average changes in drug utilization there were above average changes in labor supply. Lichtenberg was unable, however, to control for unobservable factors that may have caused the above normal usage of medical technology at the condition level. The failure to utilize any exogenous change in drug utilization leaves open a concern about endogeneity in the changes in drug utilization. The few studies in the developed world that have utilized exogenous variation in drug usage to estimate economic benefits have focused almost entirely on mental health disorders. Using data primarily from clinical trials, authors have found that increased use of mental health treatment increases both labor supply and at work performance (Timbe et al., 2006; Berndt et al., 1998; and Berndt et al., 2000).

As the American labor force continues to age, a greater portion of potential workers will suffer from chronic physical (as opposed to mental health) conditions—

many of which cause debilitating pain. One of the most prevalent conditions causing everyday pain, particularly among the elderly and near elderly, is arthritis—a disease characterized by pain and stiffness in the joints that often reduces physical function and mobility. According to the Center for Disease Control, an estimated 46 million people in United States have some form of arthritis. In total, 5 percent of the population and 30 percent of the arthritis population report work limitations resulting from the disease (Lorig, 2007). Yelin (1995) reported that disability rates for individuals with musculoskeletal conditions range from 38 to 72 percent. Pain relievers such as COX-2 inhibitors have been shown to increase mobility and functioning, allowing individuals to participate in everyday activities while potentially reducing dangerous side effects.

The presence of a chronic painful condition alters the typical labor supply decision of an individual. While most potential workers receive disutility from effort, for individuals with painful joint conditions the disutility from even a limited amount of work could be too great to allow the person to participate in the labor force. Consider a simple motivating model with an individual possessing a utility function of the form:

$$u_i = v(w*(T_i - l_i)) - g(T_i - l_i, r_i, c_i) \qquad s.t.\ T_i + l_i = h_i \tag{3}$$

Where T_i is an individual time endowment, l_i is an individuals hours of leisure, h_i is the number of hours worked, w is the wage, v() is the utility from wage income, and g() is the disutility from effort. Equation (3) easily simplifies to:

$$u_i = v(w*h_i) - g(h_i, r_i, c_i) \tag{4}$$

where disutility of effort is a function of hours worked, the presence of a chronic condition (c_i), and the efficacy of existing medical treatments (r_i). Disutility is an increasing function of hours worked and the presence of chronic conditions and a decreasing function of available medical technology. For simplicity, I assume the presence of a chronic condition is a binary variable equal to 1 if a painful chronic condition exists. Similarly, the efficacy of existing medical treatments is a binary variable equal to 1 if existing medical treatments are effective for the individual.[6] There are three states of the world that are of concern for each individual: not sick, sick with effective medical treatment, and sick with ineffective medical treatment.[7] The rank ordering of the marginal disutility of effort is assumed to be:

$$\frac{\partial g(h_i,0,1)}{\partial h_i} > \frac{\partial g(h_i,1,1)}{\partial h_i} > \frac{\partial g(h_i,0,0)}{\partial h_i} \qquad \forall h_i \tag{5}$$

Solving the individual's maximization problem reveals that at each wage an individual chooses hours such that:

$$w = \frac{\frac{\partial g(h_i, r_i, c_i)}{\partial h_i}}{\frac{\partial v(wh_i)}{\partial h_i}} \tag{6}$$

Equations (5) and (6) provide the result that individuals who are not sick will work more hours than those that are sick, and those with access to effective medication will

[6] The underlying results of this model carry through to the case of more refined measures of both treatment efficacy and condition status.
[7] The trivial case of not sick with effective medical treatment is ignored.

work more hours than those without.[8] For some individuals, the disutility of work in the presence of a chronic condition without effective medical technology is large enough that for all offered wages their optimal hours worked is zero.

This study hypothesizes that the release of Vioxx represented the introduction of an effective medical technology for a portion of the people with chronic conditions causing pain.[9] This is expected to increase the labor supply for individuals with chronic conditions. This increase could occur either in the form of more hours or greater labor force participation.

Figure 2 provides suggestive evidence of this correlation between Vioxx and labor force participation for those with arthritis. The graph contains data from the Medical Expenditure Panel Survey (MEPS). The dotted line represents the rate of Vioxx prescriptions for individuals with joint conditions in the MEPS and the solid line represents the labor force participation rate for the same respondents. The graph provides suggestive evidence that labor force participation among those with joint conditions is correlated with the use of Vioxx.

Data

The data for this study come from the Medical Expenditure Panel Survey (MEPS). The MEPS is a series of surveys administered since 1996 by the Agency for Healthcare Quality Research and the National Center for Health Statistics. There are

[8] For the purposes of this simple model I am ignoring the demand side of the equation. It is likely, however, that the presence of both chronic conditions and effective pain medication would also change an individual's marginal product of labor and offered wage.
[9] This could be the result of an individual being unable to take existing medication due to gastrointestinal side effects or a greater degree of pain relief from Vioxx.

three components of the survey, completed by households, medical providers, and insurance companies. This study uses the household component of the MEPS, which is comprised of a sample drawn from the previous year's National Health Interview Survey (NHIS) respondents. Individuals are asked questions over a series of 5 rounds detailing two years of medical expenditures and services utilization. Each year of the MEPS contains respondents from two overlapping panels.

The MEPS full year consolidated data file (CDF) contains socio-demographic information for respondents including age, sex, race, and basic economic characteristics. Individuals are asked about their labor force participation status during each round of the MEPS. For this study, respondents are classified as working if they report being employed at the time of interview or at any time during the MEPS round.

This study also uses data from the MEPS prescribed medicines file which contains data on the prescription habits of all respondents. The unit of observation is the individual prescription, and information is also collected concerning medical conditions directly associated with the prescription. In the time period under consideration, approximately 40 percent of individuals do not report receiving prescriptions. Data from the prescribed medicines files can be linked to the MEPS CDF.

Data from the MEPS medical condition file is also utilized in this study. The unit of observation in this file is a reported medical condition for a respondent. Individuals provide an ICD-9 code as well as details about the onset of the condition

and treatment attempts.[10] In this sample, approximately 20 percent of MEPS respondents report no medical conditions throughout the year. Using the unique identifier, information from the medical conditions file can be linked to both the prescribed medicines file and the full year CDF.

In total, the combined sample for this analysis has 108,048 distinct individuals interviewed a maximum of 5 times. This creates an unbalanced panel of 512,788 observations. The MEPS is uniquely able to provide information on the question of interest because it is the only dataset that contains data on socio-economic status, detailed prescription medicine activity, and medical conditions. The National Health Interview Survey (NHIS), from which the MEPS is drawn, has the advantage of a larger sample size then the MEPS, but it does not contain information on prescriptions. Similarly, the Center for Disease Control's Behavioral Risk Factor Surveillance System (BRFSS) contains data on arthritis status but does not have information on prescription status.

Characteristics of Vioxx Recipients

Table 1 contains data on the ICD-9 codes reported by individuals who report a Vioxx prescription during their time in the MEPS. Over 40 percent of individuals using Vioxx report "other and unspecified arthropathies" in at least one interview. An arthropathy is a disease of the joint that includes, but is not limited too, arthritis. An additional 20 percent of Vioxx patients report the presence of back disorders.

[10] The International Statistical Classification of Diseases and Related Health Problems (ICD) codes are published by the World Health Organization. These codes classify all diseases and health conditions.

Arthropathies in general, and arthritis in particular, are painful chronic conditions that limit the daily activity of afflicted individuals. Figure 4 shows the percentage of individuals reporting a joint condition by age. The percentage of individuals with these conditions increases with age. Nearly 65 percent of MEPS respondents in the sample reporting an arthropathy during at least one round are 55 years of age or older.

The presence of an arthropathy is a limiting factor in completing everyday activities. Examining individuals in the MEPS by age and arthropathy status shows that in each age range a higher percentage of individuals with an arthropathy report an "activity limitation." These limitations include work limitations, school limitations, or house limitations as defined in the MEPS.[11] For example, only 14 percent of 55 year old respondents without an arthropathy report limitations compared to over 40 percent of people with an arthropathy. The self-reported health status of individuals afflicted by these conditions reflects these limitations.

On average, Vioxx recipients are similar to individuals of approximately the same age in the MEPS. Table 2 compares the demographics of individuals in the MEPS who have filled at least one Vioxx prescription and all respondents between the ages of 55 and 65. In general, the groups were similar in education and racial make-up. Women make up 67 percent of Vioxx recipients, but only 53 percent of similarly aged MEPS respondents. This should not be surprising since arthritis is more prevalent among women (Lorig, 2007). On a 5 point scale, with higher numbers representing worse health, the average self-reported health status of Vioxx

[11] Individuals are classified as limited if they report difficulty completed tasks such as lifting 10 pounds, walking ten steps, using fingers to grasp, and difficulty bending or stooping.

recipients is 2.99 compared to 2.61 for non-recipients. Recipients are also less likely to report they are working. Table 3 contains descriptive statistics for individuals that report a chronic joint condition during at least one round of the MEPS. Individuals are categorized by whether they also report filling a prescription for Vioxx during any reference period. Individuals taking Vioxx are older but roughly similar in racial make-up. Over 68 percent of the Vioxx recipients are women compared to nearly 62 percent of the non-Vioxx individuals with joint conditions.[12] Vioxx recipients have a worse reported health status but reported working at nearly the same rate as those not taking Vioxx. Overall, Vioxx recipients appear similar to all individuals with joint conditions.

Figure 3 contains the percentage of MEPS respondents over 40 who report any prescriptions that received a Vioxx or Celebrex prescription by year. Following its introduction in 1999, Vioxx use quickly rose until prescriptions peaked in 2001 at slightly more than 4 percent of this group. In that year, the FDA held an advisory meeting on the results of the VIGOR study and published data on all cardiac events related to Vioxx in the study, including those that were initially withheld (Prakash and Valentine, 2007). This resulted in a warning label on Vioxx in April 2002. Graphical evidence suggests that this warning did decrease the attractiveness of the medication, as the percentage of Vioxx prescriptions fell each year following the warning until it was pulled from the market in late 2004. It can also be seen that the warnings for Vioxx appeared to affect the prescribing patterns of Celebrex—albeit to

[12] Dominick et al. (2003) found that women with arthritis are more likely to be prescribed NSAIDs, including COX-2 inhibitors.

a lesser extent. This may be the result of a lack of clarity at the time whether the negative cardiac effects of Vioxx were a drug or class specific effect.

Estimation Strategy

A naïve approach to estimating the effect of Vioxx on labor supply might examine the cross-sectional relationship between labor supply and Vioxx usage. This would involve estimating an ordinary least squares (OLS) model of the following form:

$$WORKING_i = \alpha + \gamma\ f(AGE_i) + \delta X_i + \beta_1 VIOXX_i + \beta_2 VIOXX_i * COND_i + \nu_i \quad (7)$$

in which $WORKING_i$ is a binary variable equal to 1 if individual *i* reports working; X_i is a vector of time invariant socio-demographic factors; $f(AGE_i)$ is a high order polynomial to control for the effects of aging, $VIOXX_i$ is a binary variable equal to 1 if an individual reports a Vioxx prescription during the reference period, $COND_i$ is a dummy variable for individuals that report conditions causing chronic pain, and ν_i is an idiosyncratic error term. The coefficients of interest are the combination of β_1 and β_2. The linear combination of these two coefficients represents the increased probability of a Vioxx recipient with a chronic condition working. In the empirical specifications below I will separately estimate the effect for chronic joint and back conditions—the most prevalent conditions for Vioxx users in Table 1.[13] I will exclude traumatic injuries because these injuries could be the cause of an individual

[13] Includes individuals who report "osteoarthritis," "other and unspecified arthropathies," or "other and unspecified disorders of joint," (ICD-9 codes 715, 716, and 719) are coded as having a joint condition. Those reporting "intervertebral disc disorders," "Other disorders of cervical region," or "other and unspecified disorders of back," (ICD-9 code 722, 723, and 724) are coded as having back disorders.

not working and their subsequent return to work may be the result of healing and not the palliative effects of Vioxx.

The cross sectional specification is unlikely to provide a reliable estimate of the causal effect of Vioxx use on the probability of working. This is due to the fact that there are potentially several unobserved variables that are also captured by the estimated coefficient. Specifically, the error component in equation (7) could actually be of the form, $\nu_i = \mu_i + \varepsilon_i$, which includes an unobservable person specific effect and an idiosyncratic error term. To the extent that this person specific effect is correlated with $VIOXX_i$, any estimate of the medication's effect on labor supply will be biased in an unknown direction. For example, individuals who take Vioxx could also have a greater desire to work and as a result the estimate of Vioxx's effect on labor supply could be biased upwards.

The panel nature of the MEPS allows the use of a fixed-effect estimator to control for the time-invariant person-specific qualities such as an individual's propensity to work. Under the assumption that the omitted variables creating a bias in equation (7) are not time-varying, this procedure will consistently estimate the effect of Vioxx on labor supply. In addition, multiple observations of an individual's prescription activity over time allows for the consideration of the effect of Vioxx usage in previous periods on current period labor supply. I allow for a lagged response because individuals suffering from chronic pain often try several different

medications. It may take some period of time before they realize the pain relieving effects of the medication and decide to reenter the labor force.[14]

I implement a fixed-effects identification strategy to estimate the relationship between taking Vioxx in time period t or t-1 and working in time period t. This estimation strategy will provide a consistent estimate of the effect of Vioxx under the assumption that there are no time-varying factors, other than the medication, affecting the labor supply decision of individuals with these chronic conditions that are also correlated with any of the explanatory variables.

Specifically, I estimated the following equation:

$$WORKING_{it} = \alpha + \gamma f(AGE_{it}) + \beta_1 VIOXX_{it} + \beta_2 VIOXX_{it-1} + \beta_3 VIOXX_{it} * COND_i + \beta_4 VIOXX_{it-1} * COND_i + \pi_t + \mu_i + \varepsilon_{it} \quad (8)$$

in which μ_i is a person-specific time invariant fixed effect, $VIOXX_{it}$ and $VIOXX_{it-1}$ are binary variables equal to 1 if an individual reports a Vioxx prescription during the current and subsequent period respectively,[15] π_t is a variable accounting for the MEPS round, ε_{it} is an idiosyncratic error term, and all other variables are defined as in equation (7). Other potential factors affecting labor force participation such as race and sex are time invariant and their influence is captured by the person-specific fixed effect. The first set of coefficients of interest are the combination of β_1 and β_3 which, given the assumptions described above, represent the effect on the probability of

[14] Choosing the way in which Vioxx's lagged effect will be modeled requires balancing the number of lagged periods and the sample size. In the MEPS, individuals are only observed for 5 periods. Each lagged period requires limiting the sample by one reference period. Equation (8) allows for a relatively large sample while still accounting for a potential lagged effect of Vioxx on labor supply.

[15] This specification defines Vioxx use as every period in which a prescription is reported. Alternate specifications include focusing only on the first Vioxx prescription, or as every period after the first prescription is reported. Specifications using either of these alternate definitions of Vioxx use return qualitatively similar results.

working during the period a Vioxx prescription is filled for individuals with chronic conditions. A combination of β_2 and β_4 provides the estimated effect for taking Vioxx in the previous period. The fixed effects regressions are weighted using MEPS longitudinal weights, although unweighted specifications return qualitatively similar results. A similar specification using Celebrex prescriptions rather than Vioxx is also estimated in order to examine the relative efficacy of the two medications.

A concern in any analysis of panel data is serial correlation in the error term. This is particularly true when the dependent variable is known to exhibit positive serial correlation, such as labor supply. Failing to account for this serial correlation can bias the estimated standard errors and lead to incorrect inferences (Bertrand et al., 2004). In the case of a large number of groups, Wooldridge (2003) states that this problem can be overcome by allowing for an arbitrary variance-covariance matrix accounting for within group correlation in the errors at the individual level.

Though the fixed-effects estimation strategy does control for potentially time-invariant unobservable factors, the binary nature of the dependent variable means this OLS specification may produce inaccurate estimates. While the linear probability model often returns consistent estimates, and is preferable because the economic significance of its coefficients is easier to interpret, it can have difficulty returning consistent results under certain conditions. This is particularly true when the mean of the dependent variable is close to either zero or one and the linear probability model fails to constrain the dependent variable to this unit interval. While the labor supply rate in this case is not located at either extreme, I will also estimate a conditional logit model to ensure that the estimates are not be driven by any shortcomings of the linear

probability model. Chamberlain (1980) showed that estimating a logit model with individual fixed-effects will provide inconsistent parameter estimates. This is due to the classic incidental parameters problem first discussed in Neyman and Scott (1948). To overcome this problem, Chamberlain suggested estimating a conditional fixed effects logit model. This model uses variation in the pattern of observations in the dependent variable to predict the probability that a set of outcomes will occur. For this reason, individuals who report all positive or negative outcomes for the dependent variable are discarded. Arellano and Honore (2001) showed that estimating a logit model on this restricted sample returns consistent estimates. In this case, individuals who report either working or not working in all MEPS reference periods are discarded—greatly reducing the sample size.

Regardless of the empirical specification, a concern for estimating the effect of Vioxx is identifying the group of individuals whose labor supply would likely be affected by chronic conditions requiring anti-inflammatories.[16] Figure 4 contains individuals in the MEPS who report a chronic joint condition by age. These conditions generally do not present themselves until later in life and as a result including a sample of all working age individuals may result in a diluted estimated treatment effect. In order to ensure that a large number of individuals are affected by chronic conditions requiring Vioxx, I limit the lowest age range in the sample to individuals who are older than age 55.

It is also important to identify an upper limit for the age range that takes into account the presence of social security and other retirement programs affecting the labor supply decision. Individuals who qualify for benefits can claim social security

[16]Selecting this group involves a trade-off between a more targeted sample and decreased sample size.

early (at age 62) and receive a reduced benefit. Economists have long noted a mass point of retirements at this age. French (2005) analyzed the Panel Study of Income Dynamics (PSID) and found "work-hours and labour force participation decline sharply after age 55, and especially sharply at ages 62 and 65. These are exactly the ages at which Social Security, pensions, and declining wages provide strong incentives to leave the labour force" (French, 2005: 396).[17] It will be important to consider these other factors affecting labor supply when selecting the sample of individuals included in this analysis. Therefore, this analysis focuses on individuals ages 55-75, 55-64, and 55-61.

I estimate specifications on samples split by gender to allow for potentially differential responses by sex. This could be driven by factors such as gender based differences in the efficacy of medication or the desire or need to work. I also attempt to test for the presence of reverse causality resulting from employer-provided health insurance by estimating the labor supply responses of other expensive prescription medications intended for chronic conditions. The specification discussed above focuses on the decision to work. It is also possible, however, that Vioxx affected labor supply along the intensive margin. In particular, individuals taking Vioxx may have worked more hours. Therefore, I will estimate a specification of equation (8) using usual hours worked as the dependent variable.

[17] For those electing early retirement payments, the labor supply disincentive is increased by the social security earnings test. In 2001, for every two dollars in earnings above $10,680, social security withholds one dollar. For earnings above $25,000, one dollar in benefits is withheld for ever three dollars in earnings. This earnings test could result in several of the individuals who were able to enter the labor force as a result of Vioxx no longer finding it utility maximizing to continue in the labor force and instead choosing to retire. In estimating the effect of Vioxx on labor force participation it will also be important to consider the distortion caused by the normal retirement age (between the ages of 65 and 67 depending on an individual's birth date). For these individuals there is no longer an earnings test, but they can get choose to exit the labor force and receive their full benefit.

One concern is that there are person-specific time-varying changes that are biasing the estimated coefficients in equation (8). This fixed effects identification strategy is based on the observed decision to start taking Vioxx. If this decision is driven by an unobserved time-varying factor that is correlated with the labor supply decision, the estimated coefficients would be biased. To address this concern, I implement an instrumental variables identification strategy that uses the removal of Vioxx from the market in late 2004 as an exogenous reduction in the use of Vioxx. Due to the fact that the removal of Vioxx was unexpected, differences in the utilization of the drug in the post-removal time periods should be uncorrelated with any time-varying changes that may be a source of bias in the fixed-effects results.

The Effect of Vioxx on Labor Force Participation

Table 4 contains the results of the equation (7)—the naïve OLS model. This model finds a statistically significant relationship between taking Vioxx and working in the current period for near elderly workers. The last two rows of estimates are the linear combinations of the coefficients for Vioxx use and Vioxx use interacted with a dummy variable indicating condition status. Column (1) contains the effect of Vioxx on labor supply for individuals aged 55-61. For individuals in this group reporting a joint condition, Vioxx is associated with a 7.9 percentage point increase in the probability of working. For individuals age 55-64 with a joint condition, the results in Column (2) suggest that Vioxx use is associated with a 6.1 percentage point increase in the probability of working. It is likely, however, that these estimates are potentially biased due to the inability to control for potential unobservable person

specific characteristics. There is no statistically significant increase for individuals of any age reporting a back condition.

Table 5 reports the regression results for the fixed effects model for a number of age-based samples. Focusing on individuals with joint conditions, who were found to have a large and statistically significant increase in the probability of working in the cross sectional estimates, there is no statistically significant relationship between labor supply and Vioxx for any age group. This suggests that the unobserved variables generated an upward bias to the naïve estimates of the effect of Vioxx on labor supply. These results cast doubt on any estimates of the economic benefit of medical technology that are unable to control for person-level fixed effects.

To account for potential gender-based differences in the effect of Vioxx, I estimated a specification of equation (8) on gender based sub-samples. Table 6 contains these results for the same age groups as Table 5. There are statistically significant effects on labor supply in the period following Vioxx use for males in all three age groups. Column (1) contains the estimates for males between the ages of 55-61 who report a joint condition. Vioxx use in the current MEPS round is associated with a 7.6 percentage point increase in the probability of working for these individuals. This estimate is statistically significant at the 0.05 level. In the sample, approximately 64 percent of men with a joint condition between the ages of 55-61 are working. Therefore, Vioxx use is associated with a nearly 12 percent increase in the probability of working for these individuals. The estimated effects for individuals with back conditions are similar in magnitude but less precisely estimated.

Columns (4) – (6) contain the results for females. These results are much smaller or negative and are not statistically significant at conventional levels. There are several possible reasons for this. First, there could be a differential efficacy of NSAID medications based on gender. In an experimental setting, Walker and Carmody (1998) found that men received more analgesic benefit than women from the NSAID ibuprofen. A second possible reason is that women in these age groups have a lower level of labor force attachment and overall labor supply. Finally, the lack of an effect could be driven by differences in the physical requirements of occupations by sex. Women are more likely to be employed in jobs that require less physical labor and therefore may be less affected by painful chronic conditions. Using data from the MEPS on reported occupations, I split the sample based on the amount of physical labor required.[18] Focusing on the sample of Table 6 which demonstrated the strongest results—individuals ages 55-61—only 6.5 percent of women report working in a physically difficult occupation during any round in the MEPS. Under a disutility of work framework, it is reasonable to expect that individuals employed in jobs requiring more physical exertion would be more likely to receive a benefit from Vioxx.

Table 7 contains results for equation (8) for males in the same age ranges as in Table 5. Due to the relatively small number of individuals that report a back condition and a job requiring physical labor, this specification only includes

[18] According to the MEPS, current main jobs are coded at the 4 digit level using the Census Industry and Occupation coding schemes. For confidentiality reasons, these codes are condensed into more general categories. These condensed categories were changed in 2002. In this analysis, for MEPS reference periods before 2002, individuals were classified as having physical jobs if they were the following occupations: craftsmen and foremen; operatives; transport operatives; laborers, not farming; farm laborers and foremen; and active military. After 2002 individuals were classified as having physical jobs if they reported being in farming, fishery and forestry; construction, extraction, and maintenance; production, transportation, and moving; or military specific occupations.

interaction terms for joint conditions. Column (1) contains the results for males between the ages of 55 and 61 with a joint condition that report a physical occupation in at least one period. In this group there is a statistically significant effect on the probability of working for taking Vioxx in the current period of 12.1 percentage points and for Vioxx in the previous period it is 13.2 percentage points. This is nearly 50 percent larger than the estimates in Table 6. For males in each age group there are statistically significant effects for Vioxx use in the previous period. Examining males with joint conditions age 55-61 who do not report a job primarily requiring physical labor, the results in Column (4) show a small but statistically significant increase in the probability of working of 3.5 percentage points. There are no effects for males in other age ranges. Due to the small number of women that report primarily physical occupations, these results suggest that the lack of a detectable effect for women may be due, at least in part, to differences in the physical nature of their occupations.

While evidence from clinical trials regarding the relative efficacy of Vioxx and Celebrex is mixed, evidence of economic effects may provide some information about differential benefits between the two drugs. Table 8 contains results similar to Table 6 with Celebrex as the drug of interest. There are no positive or statistically significant effects for any of the age samples for either sex. Due to the fact that Celebrex was released before Vioxx, it is possible that there are differences in the patient mix that are driving these results. It does not appear, however, that this difference in the effect between Vioxx and Celebrex is driven by observable differences in the population. Huse and Marder (2007) examined provided demographic on 60,000 patients that took either Celebrex of Vioxx. These

individuals were of similar age, sex, region of the country, and insurance status. This similarity in observables suggests that the differences in the patient mix between the two drugs are not driving the divergent results.[19]

These results suggest that Vioxx provides a greater profile of labor supply benefits than Celebrex. The difference in economic benefits may provide additional evidence, beyond those of clinical trials, about the relative pain relieving benefits of these two medications. This may be useful to regulators and other policymakers when making decisions about the availability and substitutability of the medications.

As mentioned above, the linear probability model can produce inaccurate estimates when the independent variable is binary. Therefore, I estimated a conditional logit model of the effect of Vioxx on labor supply. Table 9 contains these estimates for the males and females age 55-64 and 55-75. Due to the restricted sample size, smaller age ranges were not estimated. The results are qualitatively similar to the fixed effect results reported above.[20] Column (1) contains results for males aged 55-64 with a chronic condition. There is a statistically significant increase in the probability of working during the current and subsequent Vioxx period. The odds ratio suggests that odds of these individuals working are more than five times greater than individuals who are not taking Vioxx. There are no statistically significant effects for women.

When interpreting the magnitude of these results it is important to note that the smaller sample size in these specifications results from the fact that individuals

[19] Similarly, more individuals in the dataset report Celebrex prescriptions than Vioxx prescriptions suggesting that a small sample size of Celebrex recipients is not causing the lack of a detectable effect.
[20] Estimating an OLS model on a similarly restricted sample returns qualitatively similar results to these conditional logit estimates.

are only included in the sample if they either enter or leave the labor force during their time in the MEPS sample. This reflects a lower level of labor force attachment. For example, the percentage of males between the ages of 55 and 64 in the conditional logit sample that are working is 57 percent. In the full sample, this percentage is nearly 75 percent.

Reverse Causality

One concern related to the results above is a question of the direction of causality. Due to its potentially daily use and lack of generic competition, the yearly cost of Vioxx was quite expensive—upwards of $1,000 a year depending on the frequency of the dosage and the location. The primary source of health insurance in the United States for those under the age of 65 is an employer. It is increasingly difficult for the near elderly to acquire medical insurance if they are not working—particularly if they already have a chronic condition such as arthritis. It could be that in order to obtain the insurance necessary to pay for medication individuals enter (or remain in) the labor force. Similar effects have been found in other situations. Bradley and Neumark et al. (2005) found suggestive evidence of this effect. The authors found that women with breast cancer whose health insurance was provided by their employer had a smaller decrease in labor supply than those whose insurance was provided by their spouse's employer.

While finding a larger labor supply effect in the period *after* taking the medication limits many of the above concerns, I attempt to confirm the causal mechanism of the previous results by estimating the labor supply effect of other

expensive prescriptions that should not contribute to increased labor supply. If individuals are working in order to pay for medication, a similar response should be found for these other expensive drugs. Unlike Vioxx, I do not present estimates with a lagged effect since there is no theoretical reason to suggest such an effect would exist.[21] After consulting with physicians, I identified a set of prescriptions that are both expensive and indicated for chronic conditions and were widely prescribed, but are unlikely to improve the ability of patients to participate in the labor force. These drugs include Lipitor for high cholesterol, Nexium for acid reflux, Viagra for erectile dysfunction, and Fosamax for osteoporosis prevention.[22] For both Lipitor and Nexium, the estimated coefficients are interacted with dummy variables indicating the presence of high cholesterol and gastroesophageal reflux (acid reflux). Table 10 contains results for the males and females in the three age based samples. Each set of two rows represents a different specification containing a particular prescription, except the last set which estimates the effect for Viagra on males and Fosamax for females. The bottom rows provide the linear combination of the drug and drug-condition interaction terms. Unlike Vioxx, the estimated labor supply effects are small and statistically insignificant. Taken together, these results suggest that individuals are not working in order to secure their prescription medication and the estimated effects of Vioxx above are likely causal.

[21] These are no statistically significant results for a specification including the lagged effect.
[22] Since Viagra and Fosamax are taken almost exclusively by men and women respectively, the effect on labor force participation for these drugs will be limited to the respective sexes.

Effect of Vioxx on Hours Worked

In addition to allowing people to reenter (or remain in) the labor force, pharmaceutical innovations can allow people to increase their work effort. This response along the intensive margin would also generate significant economic benefits. Previous research examining labor supply adjustments along the intensive margin finds mixed results. Eissa and Hoynes (2005) examined the response of individuals to the EITC. They found that in general individuals respond along the extensive rather than the intensive margin. The focus of this analysis is a different population. Specifically, the near-elderly nature of the expected beneficiaries of Vioxx may lead to a response on the intensive margin. This is due to the fact that near elderly workers are those individuals who are most likely to have the flexibility necessary to adjust their hours in response to changes in the ability or desire to work. Friedberg (1999) examined the effect of the social security earnings test on labor supply of elderly and near elderly workers. The author found that, "the responsiveness of older workers to the earnings test suggests that they enjoy greater hours flexibility" (Friedberg, 1999: 50).

In order to detect the presence of this effect on hours worked in the case of Vioxx, I re-estimated a specification of equation (8) with hours worked as the dependent variable. Specifically, the dependent variable is the usual weekly hours worked during the reference period, while Vioxx use is defined as any prescription in the current or previous period respectively. Table 11 contains the estimated coefficients and standard errors from this specification. Column (1) contains results for males aged 55-61. For those with joint conditions, there is a statistically

significant increase in hours worked Vioxx use in the current and previous period. This increase in usual weekly hours worked during the reference period following a reported Vioxx prescription is 2.79. The average usual hours worked, among those working, for this group is 25.46—suggesting that Vioxx use increases hours worked by 10.9 percent.

For all age ranges of females with joint conditions there is a statistically significant and negative estimate for Vioxx use in the previous period. This raises some concern that changes in factors such as condition severity may be causing a downward bias in the causal effect of Vioxx.

It is possible that the above results for males are actually a reflection of the earlier reported extensive margin results. For example, the average hours worked for 55-61 year old males with joint conditions that report positive hours is 42.47. Therefore, the 6.9 percentage point increase in the probability of working from Table 14 should result in an increase in hours worked of approximately 2.93 hours. This is similar to the estimated increase of 2.79 hours in Table 15.

In unreported results limiting the sample to respondents reporting positive hours there are no statistically significant estimates for any age group. This fact, combined with the magnitude of the full sample results being similar to the expected results from participation, makes it unlikely that Vioxx caused individuals to adjust their labor supply along the intensive margin.

Instrumental Variables Estimation Strategy

The fixed effects identification strategy will consistently estimate the impact of Vioxx on labor supply under the assumption that there are no time-varying factors influencing both Vioxx usage and working. While this assumption seems reasonable, it is possible that there exists an unobserved time-varying factor biasing these fixed effects results. In order to overcome the potential endogeneity in the decision to take Vioxx, I implement an instrumental variables estimation strategy. This requires identifying a variable that affects the covariate of interest (Vioxx usage) without directly affecting the individuals' labor supply. I will use the removal of Vioxx from the market in September 2004 as an exogenous change in the drug's utilization.[23] Guided by both disability rates and my previous results, I focus this analysis on the labor supply response of individuals most likely affected by the removal of Vioxx—those reporting chronic joint conditions. Specifically, I will instrument for a decrease in Vioxx usage with a dummy variable indicating the time period where Vioxx is removed interacted with a dummy variable equal to 1 if the individual reports a chronic joint condition in any MEPS round. It is a reasonable assumption that the decision to remove Vioxx from the market did not directly affect the labor supply

[23] I also attempted a similar strategy using the "black box" warning label placed on Vioxx in April, 2002. This warning label reflected the newly discovered increased cardiac risk. The warning label did appear to lower usage of Vioxx reflected by both the downward trend in Figure 2 and a negative and statistically significant coefficient on Vioxx in a specification of equation (8) estimated using data from MEPS Panel 7. There is no corresponding decrease in labor supply. This could be evidence of individuals who stopped taking Vioxx following the warning being individuals who did not require the medication to work. A common criticism of Vioxx was that it was over prescribed, potentially as a result of a large amount of direct-to-consumer advertising (Dai et al., 2005). The lack of an effect on labor supply from this earlier warning demonstrates the requirement of a complete removal of the drug from the market as an exogenous source of variation in utilization. Without a complete removal there can be selection bias affected those who choose to continue or stop taking the medication.

decision of individuals with chronic joint conditions through a channel other than the absence of the medication.

Successfully implementing this identification strategy requires data on the labor supply and prescription drug use of individuals before and after Vioxx is removed from the market. The 9th panel of the MEPS dataset contains individuals interviewed during 2004 and 2005. This is the only panel overlapping the removal decision.[24] The relatively small sample size of a single panel requires me to use the largest age-based sub-samples from the fixed-effects analysis—respondents between the ages of 55 and 75.

The underlying hypothesis of this study is that the use of Vioxx decreases the pain from chronic conditions allowing individuals to increase their labor supply. If this were the case, the removal of Vioxx should increase the reported health problems among previous Vioxx users. Figure 5 contains the reported activity limitation status for individuals with joint conditions based on their Vioxx use before and after the medication was removed from the market. In the time period after removal, there was a 19 percent increase in the percentage of individuals with joint conditions that were previously taking Vioxx who report an activity limitation. There was essentially no change for other individuals with joint conditions.

The structural equation of interest is equation (8). The concern is that this equation cannot be consistently estimated with OLS because the error term may be correlated with the use of Vioxx. Specifically, the concern is that the structure of the

[24] This panel of the MEPS is the only group that includes observations for individuals in the time period both before and after the removal of Vioxx from the market. Another conceivable event for an IV strategy is the introduction of Vioxx in 1999. Unfortunately, Vioxx slowly penetrated the market during its first year with fewer than 100 participants in the overlapping MEPS Panel (Panel 3) taking Vioxx.

error term is, $\varepsilon_{it} = \sigma_{it} + \rho_{it}$, where the cov(VIOXX$_{it}$, σ_{it}) $\neq 0$ and therefore the estimated causal effect of Vioxx on labor supply would be biased. As was discussed above, one possible factor causing a downward bias would be changes in condition severity driving both the use of Vioxx and a decrease in labor supply. More concerning are omitted variables that may be positively correlated with both working and Vioxx and therefore would generate an upward bias in the causal estimates of labor supply. One such factor could be changes in the desire or need to work.

A key criterion of an effective instrument is that it directly affects the covariate of interest. Figure 6 contains the percentage of individuals reporting a Vioxx prescription during 2004 and 2005. As would be expected, the removal dramatically decreased the percentage of the population reporting a Vioxx prescription. The percentage of people receiving Celebrex and Lipitor are also included in the chart. Celebrex shows a slight decline that is likely a result of negative publicity from the Vioxx recall. Lipitor prescriptions increase throughout the removal time period—suggesting that the decrease in Vioxx prescriptions is not the result of a secular time trend in prescription usage. The sharp decline makes it unlikely that time-varying factors other than Merck's decision were the cause of this drop in utilization. More formally, it is required that the estimated coefficient on the instrument from a linear projection of the endogenous covariate of interest onto all exogenous variables must be non-zero. This linear projection is described as the "first stage" relationship and in this case takes the following form:

$$VIOXX_{it} = \alpha + \gamma f(AGE_{it}) + \beta_1 REMOVE_t * JOINT_i + \upsilon_t + \mu_i + \varepsilon_{it} \qquad (9)$$

Where $VIOXX_{it}$ is a binary variable equal to 1 if person *i* reports a Vioxx prescription during reference round, υ_t is a dummy variable for the MEPS round, and $REMOVE_t$*$JOINT_i$ is the interaction between being in the time period where Vioxx is not being sold and a binary variable equal to one if an individual reports the presence of a joint condition during any MEPS round.[25] The coefficient of interest is β_1 which represents the effect on utilization from Vioxx being removed from the market for individuals with joint conditions.

One possible reaction to Vioxx's removal is that patients and physicians would simply switch their prescriptions to other COX-2 inhibitors. Data from both the MEPS and other sources suggests that this does not appear to have been the reaction. Instead, it appears that the removal of Vioxx created a "class effect" that limited the willingness of doctors to prescribe or patients to utilize all NSAIDs. This effect could result from Vioxx users receiving little analgesic benefit from other drugs or a general uncertainty regarding the safety profile of the entire class of drugs. This class effect was exacerbated by the removal from the market of Bextra, an alternate COX-2 inhibitor, in early 2005.

If changes in the utilization of all COX-2 inhibitors were caused by changes in a physician's willingness to prescribe the medications, the reduced utilization of these other drugs after Vioxx's removal can be reasonably interpreted as a further exogenous change and should be included in the first-stage estimation. Therefore, I

[25] In this case, the Vioxx is considered "removed" from the market during the 3rd, 4th, and 5th rounds of Panel 9 of the MEPS. The removal occurs during the beginning of the 3rd round. The reference period for over one quarter of the respondents did not begin until after the drug was removed, and nearly all of the respondents ended their reference period after the removal decision.

will also estimate a specification of equation (8) with all COX-2 inhibitors as the dependent variable. Failing to consider this class effect and estimating a first-stage relationship with only Vioxx as the dependent variable will underestimate the first-stage coefficient. Since in an exactly identified model the IV coefficient is the ratio of the reduced form coefficient to the first stage coefficient, underestimating the first stage relationship will, by construction, generate an upward bias in the IV estimates. This bias exists if the inability of individuals to access these medications is causally related their labor supply.

The potential bias can also be thought of as the use of other COX-2 inhibitors being an omitted independent variable in the structural equation. Failing to account for the relationship between the instrument and this omitted variable will bias in the IV estimate. Estimating a first-stage equation with a dependent variable accounting for all COX-2 inhibitors eliminates this bias.

The reduced form relationship estimates the effect of the removal of Vioxx on labor supply. Figure 7 contains the labor supply of individuals with joint conditions based on their Vioxx status. This figure provides suggestive evidence of the reduced form relationship. The labor supply of individuals with joint conditions who had ever taken Vioxx moved down in the periods where Vioxx was no longer available, while the labor supply of individuals with chronic joint conditions but no reported Vioxx use remains virtually unchanged. The reduced form equation is:

$$WORKING_{it} = \alpha + \gamma f(AGE_{it}) + \beta_1 REMOVE_t * JOINT_i + \upsilon_t + \mu_i + \varepsilon_{it} \quad (10)$$

Where $WORKING_{it}$ is a binary variable equal to 1 if respondent *i* reports working in time period *t,* and all other variables are defined as in equation (8). The coefficient of interest is again β_1, which represents the probability of working in the post-Vioxx time periods for individuals reporting a joint condition in at least one MEPS round.

Table 12 contains the results of a specification of equation (8) estimated on the 9th panel of the MEPS. Due to sample size concerns, these results focus on the largest age group used in the fixed effects results—individuals aged 55-75. In addition, the results are presented for individuals with joint conditions—those most affected in the fixed-effect results. Vioxx use in the previous period is associated with a 4.4 percent increase in the probability of individuals with joint conditions working. This is similar in magnitude to the estimated effect in Table 6.

Table 13 contains the IV results using the September 2004 removal of Vioxx from the global market as an instrument for changes in the usage of Vioxx. Column (2) reports the first stage results for a sample of individuals between the ages of 55 and 75. As would be expected, the removal of Vioxx from the market caused a statistically and economically significant decrease in the usage of the medication by individuals suffering from chronic joint conditions. Specifically, removing Vioxx from the market reduced the probability an individual a chronic joint condition filling a Vioxx prescription by 5.8 percentage points. The F-test statistic that the coefficient on the instrument is zero is 48.62, suggesting that finite sample bias is not a concern in this case. Overall, the magnitude and direction of these results are not surprising. Roughly 7 percent of individuals with joint conditions filled a Vioxx prescription in the round immediately preceding Merck's removal decision.

Column (2) of Table 14 contains first stage estimates for the effect of Vioxx's removal on the use of the most widely prescribed COX-2 inhibitors—Vioxx, Celebrex, and Bextra. This removal resulted in a reduction of 10.2 percentage points in COX-2 usage. This larger result is not surprising since a higher proportion of arthritics were using all COX-2 inhibitors than those using only Vioxx.

In Column (1) of Tables 13 and 14, I report results for the reduced form equation (10) for all individuals between 55 and 75. The coefficient on the instrument suggests the probability of working for those with a chronic joint condition is 2.4 percentage points lower in the post-removal MEPS rounds.

In the case of an exactly identified model, the IV coefficient is the ratio of the reduced form to the first stage regression. Column (3) of Table 13 contains the IV results for the model containing only Vioxx. These results suggest that Vioxx increases the probability of working for individuals with chronic joint conditions by 41 percentage points. During the second round of panel 9, only 41.6 percent of individuals with chronic joint conditions between 55 and 75 were working. If the magnitude of these IV results is to be believed, they suggest that nearly all of these individuals left the labor force as a result of Vioxx leaving the market. The size of this coefficient is concerning, suggesting that solely focusing on Vioxx may have generated an upward bias in the IV estimates.

Column (3) of Table 14 contains the IV results for an exactly identified model where the first stage is defined as the effect of Vioxx's removal from the market on all COX-2 inhibitors. The coefficient here suggests a more reasonable 23.7 percentage point increase in the probability of working for these individuals. While

smaller than the IV results using only Vioxx prescriptions in the first stage, this estimate is still larger in magnitude than the fixed effects results presented earlier. There are several reasons why this may be the case. First, this estimate represents the local average treatment effect (LATE) for individuals who want to take a COX-2 inhibitor but are deprived of the opportunity by the removal decision. This is a different sample than the individuals in the fixed-effects sample who are choosing to take the medication. This is particularly true given the fact that concerns of the safety of Vioxx caused use of the drug to decline from 2002-2004, suggesting that the remaining users may have a particularly strong preference or need for the medication. For this reason it is perhaps not unexpected that the LATE is greater than the estimated effect from the fixed effects analysis.

It is also possible that the vast amount of news coverage affected the use of analgesic medications beyond COX-2 inhibitors. In particular, users of other NSAIDs may have been deterred from using their medications or doctors may have given stronger warnings to patients regarding the use of both prescription and over-the-counter painkillers. Finally, the higher IV results could also be evidence of a downward bias in the fixed effects results caused by increases in condition severity driving Vioxx use.

It could be that the change in the probability of working for individuals with joint conditions following the removal of Vioxx is actually related to a more general change in the ability or willingness of those with chronic conditions to work. If this were the case, then similar results to those in Tables 13 and 14 should appear for individuals with other chronic conditions. I therefore re-estimated the IV model

above for individuals suffering from chronic conditions that should not have been directly affected by the removal of Vioxx. Specifically, I estimated the model for individuals with heart conditions,[26] and respiratory conditions.[27] These conditions are associated with increased rates of short-term disability insurance and SSDI receipt (Wagner et al., 2000).

Tables 15 and 16 contain the results for these models. There are no statistically significant results for any of the IV estimates. Neither group exhibits a negative labor supply response during the post-Vioxx period. These results suggest that the IV estimates for arthritic labor supply are not being driven by secular changes in the ability of individuals with chronic conditions to work.

Conclusion

Taken together, the above results suggest that Vioxx had an economically and statistically significant impact on the labor supply of near elderly men. An approximate calculation using my IV results may provide some insight into the magnitude of the effect of COX-2 inhibitors on near elderly labor supply. In the MEPS sample, approximately one third of males between the ages of 55 and 65 with a joint condition are not working. If the rate of use of COX-2 inhibitors is the same among this group as all individuals with joint conditions in the MEPS sample, approximately 30 percent, and these drugs have the estimated effect on labor supply from the IV results, these drugs would have increased the overall near-elderly male labor force participation by 0.58 percentage points. Considering that between 1996

[26] ICD-9 codes 410, 411, 413, 414, 427, 428, and 436
[27] ICD-9 codes 466, 486, 490, 493, and 496.

and 2005 labor force participation this group increased by 2.5 percentage points, this approximate net effect of COX-2 inhibitors on near-elderly labor supply is economically significant.

Vioxx is only one example of a medical innovation that may have demonstrable economic impacts. Other innovations such as improved treatments for heart attack victims, joint replacements, and new prescription medications addressing a wide variety of chronic conditions, may also improve the economic livelihood of individuals. The Conference Board estimated that from 2005-2010, the number of 55-64 years old in the labor force will increase by 52 percent (Foster and Sedlar, 2005). This estimate does not take into account potential changes in labor supply resulting from increases in medical technology. Due to the fact that a large number of chronic conditions are more likely to strike older individuals, this increase in the working age population could lead to more individuals requiring medical assistance to participate in the labor force. Further research is needed to determine the impact of other medical innovations on economic outcomes such as labor supply. This study demonstrates that exogenous changes in utilization of medical technology may serve as effective methodology for identifying the economic effects of other innovations. Such changes in utilization could be caused by price shocks due to drugs losing patent protection, changes in co-payment structure, or discount drug programs.

The ability of individuals with chronic conditions to reenter or remain in the labor force can have important societal benefits. For example, many of these individuals currently receive either private or government disability payments. Between 1992 and 1998 arthritis sufferers made up 7.1 percent of SSDI recipients

(Bhattacharya and Schoenbaum, 2002). Examining MEPS respondents by age and arthropathy status shows that in each age group the percentage of individuals reporting positive SSI incomes is greater for individuals with a chronic joint condition. Autor and Duggan (2003) stated that between 1984 and 2001 there was a 60 percent increase in the number of adults receiving Social Security Disability Insurance (SSDI). As the labor force continues to age, this trend towards increased disability enrollment will likely continue. To the extent that advancements in medical technology can affect the number of individuals who are working rather than receiving disability payments, these technological improvements can represent a net societal benefit.

In addition to the effects on social disability programs, explicitly accounting for the economic benefits of new medications can have far reaching impacts on the regulation of pharmaceuticals. Under the 1962 Kefauver-Harris amendments, pharmaceutical companies must demonstrate to the Food and Drug Administration (FDA) that new innovations are both safe and effective in order bring drugs to market. To do so, firms present evidence from random assignment clinical trials, which traditionally have focused on objective medical outcomes. For example, in evaluating cancer medications, both mortality and tumor size are used as measures of drug's efficacy. Drugs whose benefits can be measured solely in objective medical terms are becoming less common. Increasingly regulators rely on patient reported outcomes (PROs) to judge efficacy. From 1997-2002, thirty percent of FDA approved drugs contained patient reported outcomes (PROs) among the documented benefits.

These included reduced pain, depression status, and changes in energy levels that are often associated with quality of life medications (Bren, 2006).

In making the approval decision for a drug such as Vioxx, regulators must determine the appropriate degree of safety risk that is acceptable to achieve quality of life improvements. Answering this question should require the FDA to account for the full scope of benefits provided by the drug—including both medical and economic outcomes. Properly accounting for PROs, however, is a continuing difficulty for the FDA. This fact led the National Institute of Health (NIH) to create a commission tasked with developing a more effective means of quantifying and evaluating these outcomes. Former NIH Director Elias A. Zerhouni said "there is a pressing need to better quantify clinically important symptoms and outcomes that are now difficult to measure" (Bren, 2006). The current inability to fully quantify PROs suggests a need for additional metrics for evaluating the efficacy of quality of life medications. This analysis suggests that economic outcomes may be a useful metric in fully defining the benefit profile of quality of life medications.

Previous authors have evaluated the net health benefits of advancements in medical and pharmaceutical technology, but have generally not included economic effects in their benefits profile. Cutler and McClellan (2001) and Skinner et al. (2006) found that, on net, technology-driven cost increases were smaller than their benefits. Lichtenberg (2001) found that individuals consuming newer drugs had lower mortality and lower non-drug medical spending. In contrast, Duggan (2005) analyzed the cost-effectiveness of second generation anti-psychotics and found that the drugs failed to pay for themselves. All of these studies, however, fail to consider potential

effects on non-medical outcomes such as labor supply or wages. Excluding economic outcomes is particularly damaging for quality-of-life pharmaceuticals, which may be more likely to offer a range of benefits beyond traditional medical outcomes.

Chapter 2: The Effect of In-Utero Conditions on Long Term Health: Evidence from the 1918 Spanish Flu Pandemic

The differing incidence of chronic health conditions by individuals with similar backgrounds, lifestyles, and blood chemistry has caused medical professionals and health economists to look beyond these factors for other sources of later life health problems. Spurred by a compelling correlation between birth weight and elderly health, this search has increasingly focused on fetal conditions. This literature is often referred to as the "fetal origins hypothesis" or the "Barker hypothesis." According to these theories, in-utero malnutrition or other factors decreasing fetal health cause a shift of blood and nutrients from vital organs to the brain.[28] This diversion is an attempt to protect the fetus and improve the chances for immediate post-natal survival, but leaves certain organs preprogrammed for failure in later life—often after 50 years or more.

Controlled experiments using animal subjects provide the most complete evidence to date of the fetal origins hypothesis.[29] The evidence for humans is decidedly less conclusive. The bulk of studies at this point are primarily cross-sectional in nature with most showing adults born with low birth weights having higher rates of particular diseases and mortality. These studies, however, suffer from the problem that low birth weights might signal other unmeasured characteristics that predict higher adult mortality. Absent random assignment, the best hope for testing the fetal origins hypothesis is through quasi-experimental variation in fetal

[28] For an excellent discussion of the fetal origins hypothesis, see Barker (2001)
[29] Nathanielsz (2006) provides a comprehensive overview of these animal studies.

conditions. For example, economists have separately used famines and the 1918 flu pandemic as an exogenous source of fetal stress. Previous research using famines, however, has found only mixed evidence in support of the fetal origins hypothesis. As shown in Almond and Mazmunder (2005), and discussed in detail below, the short term and intense nature of the 1918 flu pandemic creates a better design for estimating the long term health impacts of fetal stress.

Often called the Spanish flu, the 1918 global flu pandemic killed between 50 and 100 million people in the course of a single year. In the United States, it struck hardest during the last quarter of 1918. Its effects largely dissipated by the first months of 1919. Over this time period, the flu killed 675,000 people—more than AIDS has ever killed in the United States (Barry, 2004). Despite its virulence, 25 million Americans contracted the flu and survived.

Women of childbearing age and pregnant women suffered some of the worst effects from the pandemic with approximately one third becoming infected (Almond, 2006). Mortality among pregnant women during this time period was similarly increased (Rasmussen et al., 2008). Barry (2004) stated, "in thirteen studies of hospitalized pregnant women during the 1918 pandemic, the death rate ranged from 23 percent to 71 percent" (p. 241). While the death rate was high for pregnant women, many survived and carried the child to term. Among women that survived, fetal health appears to have been negatively impacted. Almond (2006) reported that stillbirth rates increased by approximately 40 percent during the October-December 1918 period. This decrease in fetal health was also found in other pandemics and in other countries (Mamelund, 2001). In general, Irving et al. (2000) found that in-utero

exposure to influenza results in a higher rate of complications in pregnancy and decreased fetal health.

The disproportionate impact of the flu on pregnant women, the corresponding decrease in fetal conditions and health, and the relatively random nature of the outbreak provides a clear design for testing the fetal origins hypothesis using the 1918 pandemic. While the source of stress caused by being in-utero during the peak of the 1918 flu pandemic is different from famines or other sources of nutrient deprivation, is it clear that this exposure worsened in-utero conditions and greatly decreased fetal health. The long term effects of this decreased fetal health can provide important insights concerning the programming effects of in-utero conditions.

Almond (2006) exploited this fact to examine differences in education levels and disability rates for individuals exposed to the flu pandemic in-utero. Almond and Mazmunder (2005) examined specific medical conditions using roughly 25,000 observations of adults in the 1915 to 1923 birth cohorts from the Survey of Income Program Participation (SIPP). The authors find evidence of an impact from in-utero flu exposure on a variety of health outcomes such as stroke, diabetes incidence, self reported health status, and trouble hearing, talking, walking, and lifting.

This study uses the larger National Health Interview Survey (NHIS) dataset to expand upon these earlier results. Specifically, I use 21 years of repeated cross-sections of the NHIS to examine the impact of the 1918 flu pandemic on the incidence of coronary heart disease, diabetes, kidney disorders, and poor health status. The sample used in this work contains approximately 384,000 observations or roughly 15 times the size of the sample used in Almond and Mazmunder.

An advance of this work over previous efforts is an attempt to test precise predictions from animal studies and the medical literature about when exposure to in-utero insults should damage organs later in life. Nathanielsz (2006) stated "critical time windows exist during development when organs are vulnerable to challenges such as decreased oxygenation, nutrient supply, and altered hormone exposure. The period of vulnerability varies from organ to organ" (p. 74). Medical knowledge of the progress of fetal organ development leads to relatively precise predictions of the effect of differential timing in fetal insults. As will be discussed in more detail below, the heart primarily develops early in gestation and thus individuals who are affected by the flu in the early-to-middle months of pregnancy are hypothesized to be a higher probability of heart disease later in life. Similarly, the nutrition delivery system is developed early in pregnancy suggesting that individuals affected during the first months of pregnancy are thought to be more likely to develop metabolic disorders later in life. At the other extreme, the kidneys primarily develop during the last months of pregnancy. Individuals affected during these last months may be more likely to develop kidney disorders later in life. Overall, this study finds statistically and qualitatively significant increases in chronic conditions during the time periods predicted by the medical literature.

This time connection provides quasi-experimental evidence of the mechanism underlying the fetal origins hypothesis in humans and confirms that the timing of fetal stress is critically important in predicting which organs are weakened. Furthermore, these strong and consistent results show that an identification strategy involving the 1918 flu (or another short duration event) is necessary to isolate in-utero stress to

particular months of development. As a result, the estimates in the analysis stand in contrast to the previously mixed results from other identification strategies.

Medical Basis of the Fetal Origins Hypothesis

The most complete evidence to date supporting the fetal origins hypothesis comes from experiments with animals where researchers alter uterine conditions by either depriving the mother of nutrients or stopping nutritional transfer to the fetus through uterine blood flow restriction (Ozanne et al., 1996; Blondeau et al., 1999; Simmons et al., 2001). These restrictions have been imposed both throughout the entire gestation and during particular periods of in-utero development. They have also been paired with differing post-natal nutrition levels in order to determine if a discrepancy between conditions in these time periods is important (Ozanne and Hales, 1996). In total, these studies have shown that periods of fetal stress in rats, sheep, and other animals cause a weakening of the vital organs that manifests itself in poor later life health.

Among humans, in the medical literature, poor in-utero conditions have been linked to a variety of ailments. These studies, however, rarely utilize exogenous variation in fetal conditions creating a concern of an omitted variable bias. Three of the more frequently cited outcomes in the medical literature link fetal conditions to coronary heart disease, diabetes, and kidney disorders (Barker, 2001). These are the conditions focused on in this analysis.

Barker (1992) first noted the striking relationship between low birth weights and heart disease rates using a unique data set of births from Hertfordshire, England. Subsequently, Barker (2003) documented this same relationship among men in

Helsinki. Similar findings have been documented in North America, India, and Europe (Leon et. al, 1998; Frankel et al., 1996; Rich-Edwards et al., 1997; and Eriksson, 2001). The biological mechanism thought to be the source of this link is the diversion of blood and nutrients to the brain and away from other vital organs. This represents an evolutionary response designed to protect the brain and increase the likelihood that the fetus will survive until and immediately after birth. This process is also an attempt to condition the fetus for a lifetime of deprivation. Evidence of this phenomenon has been documented in animal experiments (Barker and Hanson, 2004). For example, the development of the heart muscle is believed to be affected by fetal stress. Unlike other organs, the heart does not begin as a miniature version of its fully developed shape. Instead, it grows throughout the first half of pregnancy from a mass of cells into its final complex form (Thornburg, 2001). As a result, complications or insufficient nutrition during the early-to-mid period of embryonic development is critical for future heart health. Hoet and Hanson (2001) stated, "it appears that the timing of the insult in gestation is all-important, with insults occurring earlier having greater effects on cardiovascular development in the offspring" (p. 78). Medical theory predicts an increased incidence of coronary heart disease concentrated among, but not limited to, individuals born in the first and second quarters of 1919. These individuals were exposed to the pandemic during their first and second trimesters—the critical time period in terms of fetal development for future cardiac health.

A second group of conditions believed to arise from poor in-utero nutrition are metabolic disorders such as insulin resistance and non-insulin dependent diabetes

mellitus (NIDDM) or Type II diabetes. Hales et al. (1997) states, "archival records of early life anthropometry have shown that reduced birth weight, weight at 1 year, and thinness at birth are strongly associated with an increased susceptibility to NIDDM and IGT (impaired glucose tolerance) in adult life and to insulin resistance" (p. 191). Hales et al. (1991) found that men who have the lowest birth weights were seven times more likely to have diabetes and/or insulin resistance than those who were heaviest at birth. Often described as the "thrifty phenotype hypothesis," this process is believed to be an attempt to condition the fetus for future periods of poor nutrition. Upon receiving adequate nutrition later in life, the individual is thought to be more likely to develop metabolic disorders (Hales and Barker, 1992). The importance of the difference between in-utero and after birth nutrition is illustrated by the relative lack of metabolic disorders in African countries—where poor nutrition in-utero is followed by equally poor infant and lifetime conditions (Stocker, et al., 2005).[30] This observation has also been supported by animal experiments where rats who were deprived of nutrients in-utero and then given generous diets after birth suffered worse health outcomes than similar rats who had a restricted calorie diet during life, though both had poor health outcomes overall (Ozanne and Hales, 1999, 2004).

Studies examining the effect of under nutrition on later life metabolic disorders have found that it is specifically *early* exposure to poor nutrition that fundamentally changes the nutrition delivery system of the fetus (Harding and Gluckman, 2001). Based on this fact, individuals born during the second quarter of

[30] The importance between this difference in nutrition and not solely in-utero nutrition could have important implications for optimal program design. Focusing government nutrition programs on the post-natal time period without adequate in-utero nutrition could, perversely, increase long term health problems.

1919, and therefore exposed to the peak of the flu pandemic early in gestation, are hypothesized to have a higher probability of reporting the presence of diabetes.

In-utero malnutrition and other complications are also believed to decrease the size and, as a result, the later life functioning of kidneys. Restricted diet animal studies have shown reduced neonatal kidney weights. This small kidney size is believed to be irreversible by adequate post-natal nutrition (Thornburg, 2001). In humans, cross-sectional analysis has demonstrated a correlation between the number of nephrons (the basic structural units of the kidney) and birth weight. Brenner and Mackenzie (1997) state "low birth weight in humans resulting from intrauterine growth retardation may be associated with deficits in nephron numbers of up to 20%, even in full-term pregnancies" (p. 124). In turn, low nephron numbers are associated with renal disease later in life (Brenner and Chertow, 1993,1994). Without measuring the number of nephrons, Lackland et al. (2001) found a correlation between end stage renal disease (ESRD) and low-birthweight. Similarly, Martyn et al. (1996) found connections between later life renal functions and fetal growth.

Knowledge of fetal development provides predictions regarding the timing of fetal stress and later life renal disease. The kidneys experience dramatic growth during the last months of pregnancy (Martyn and Greenwald, 2001). Studies show that "60% of the normal complement of nephrons are laid down during the last trimester" (Lackland et al., 2001: 66). Therefore, the imposition of fetal stress during the last months of pregnancy is thought to result in kidney disorders in later life. This would suggest a higher probability of kidney problems in later life for individuals born during the last quarter of 1918.

Exogenous Variation in Fetal Conditions

Efforts to document the fetal origins hypothesis in humans are plagued by an inability to separate the cause of fetal stress from other factors that generate poor long-term health outcomes. This presence of omitted variables bias casts doubt on the accuracy of many previous estimates. Even when a source of exogenous variation in fetal conditions can be identified, the lack of high quality data on both fetal conditions and long-term health outcomes is often a substantial problem. This lack of data limits many estimates to outcomes at relatively young ages. For example, Banerjee et al. (2007) examined the long term health effects of the phylloxera outbreak in France on long-term health outcomes. This outbreak destroyed wine crops throughout the countryside depressing economic conditions for many families. The authors are able to show that men born in wine producing regions were shorter upon entrance into the army twenty years later. Due to the lack of long-term health data, however, the authors are unable to test the hypothesis that certain organs (such as the heart or metabolic system) are preprogrammed for failure in later life.

One frequently utilized source of exogenous variation in fetal conditions is famines. Authors have used the Dutch famine during World War II (Roseboom et al., 2000; Roseboom et al., 2001; Ravelli et al., 1997), the Chinese Famine (Meng and Qian, 2006), the Siege of Leningrad (Stanner and Yudkin, 2001), and the American Dust Bowl (Cutler et al., 2007) to investigate the long run health effects of fetal stress. The results of these studies have provided mixed evidence regarding the importance of fetal origins. Roseboom et al. (2000) found differences in heart health and Ravelli et al. (1997) found increased glucose resistance in later life for babies

born during the Dutch famine. This effect was more pronounced for individuals who later became obese. Meng and Qian (2006) found that individuals born during the Chinese famine were shorter in later life, but found no evidence of increased coronary heart disease or other traditional outcomes of the fetal origins hypothesis. Similarly, Stanner and Yudkin (2001) found no connection between later life metabolic health and poor fetal conditions for individuals born during the Siege of Leningrad. Cutler et al. (2007) found no connection between income shocks resulting from the living in the Dust Bowl in the Great Depression and later life mortality, chronic condition status, or disability rates.

Almond (2006) was the first study in the economics literature to use in-utero stress caused by the 1918 Spanish flu pandemic as a source of exogenous variation in fetal conditions. As was discussed above, biological differences in the virulence of the pandemic flu make it particularly well suited as a source of variation. Standard influenza strains affect primarily the young, the old, and those with compromised immune systems. This effect can be seen by the "U" shaped dotted line in Figure 8 representing female deaths during the 1917 flu season. The 1918 flu, however, affected individuals in a decidedly different manner. Barry (2004) stated, "in 1918, the immune system of young adults mounted massive responses to the virus. That immune response filled the lungs with fluid and debris, making it impossible for the exchange of oxygen to take place. The immune response killed [the young and healthy]" (p. 250). This excessive immune response caused many of the deaths from the 1918 flu to occur among young and relatively healthy individuals. This effect can be seen by the "W" shaped curve in Figure 8. As discussed above, this change in the

demographics of those most affected by the flu was particularly true for pregnant women who suffered greatly during the pandemic. Among surviving women, evidence of higher rates of miscarriages and stillbirths suggests that overall fetal health was greatly decreased.

As discussed above there are two main papers in the economics literature that investigate the long term consequences of the pandemic flu.[31] Almond (2006) used this variation to examine the effect of fetal stress on economic outcomes such as educational attainment, wages, and disability rates. In a second study, Almond and Mazmunder (2005) used ten panels of the SIPP from 1984-1996. In total, their sample included approximately 25,000 individuals born between 1915 and 1923. The authors estimated a linear probability model to determine the affect of being in-utero during the peak of the flu pandemic on a variety of health outcomes. They found statistically significant effects at the quarter of birth level for trouble hearing, trouble speaking, trouble lifting, trouble walking, diabetes, and stroke. A larger group of health conditions including heart conditions and kidney problems are significant in at least one month of birth. These results were significant at that 0.10 level. This analysis expands upon their work using a dataset with a larger sample size. This larger dataset allows for more precise estimation of the effect of the flu and explicitly connects the development of chronic conditions to particular time periods of fetal stress. This connection aids in the understanding of the dynamics of the fetal origins hypothesis.

[31] Other studies outside of the economics literature have focused on the effect of exposure to the flu early in life, but post-natal, on later life health outcomes. For example, Azambuja (2004) estimated a connection between exposure to the 1918 flu pandemic at young age and later life heart disease.

An advantage of the flu pandemic over famines as an exogenous source of fetal stress is the short-term yet intense nature of the outbreak. As can be seen in Figure 9, 1918 represented a sixteen fold increase in flu deaths. This is followed by a dramatic decline in the following year. This is a shorter and more intense "treatment" period than the Chinese famine or the Siege of Leningrad, which carried on for several years. Babies born during these longer events experienced both poor in-utero conditions and nutritional deprivation during infancy. Disentangling these effects is difficult and limits the ability of famines to stand as a test of the fetal origins hypothesis as opposed to a test of the long term effects of child health conditions. In contrast, the more discrete nature of the pandemic flu improves the chance of isolating the long term impacts of this event from secular changes occurring at the same time.

Data

The data for this analysis comes from the 1982-2002 NHIS, the principal source of health statistics and information for the non-institutionalized population in the United States. While the survey has been in existence since 1957, information on the month and year of birth of respondents has only been collected since 1982.[32] During the time period in this sample, the NHIS was substantially redesigned. In both designs of the survey (before and after 1996) individuals were asked about their health in regards to coronary heart disease, poor health, diabetes, and kidney

[32] The lack of data prior to 1982 limits this analysis because individuals affected by the flu epidemic have already turned 62. This could make it difficult to detect an effect from the flu because many of those individuals affected could have already passed away by this age. This issue of mortality for those exposed to the flu is discussed later in the analysis.

disorders.[33] Data for kidney disorders, however, are not comparable across the two survey designs and therefore only respondents from 1982-1996 are used with respect to kidney disorders. An advantage of the NHIS is that it contains detailed questions about disease prevalence. A disadvantage, however, is that all health data are self-reported leaving open the possibility of measurement error.

After pooling cross sections of the NHIS from 1982 to 2002, the observations are grouped into quarter of birth cohorts. Individuals born during the last quarter of 1918 and the first two quarters of 1919 were affected by the flu in-utero. Based on this fact, individuals in this dataset affected by the flu are between 62 and 84 years of age. The overall sample for this analysis is limited to individuals of similar ages to the cohort affected by the flu. Respondents younger than 55 or older than 90 years of age are eliminated from the sample, resulting in approximately 384,000 observations ranging in year of birth from 1891 to 1947. Table 17 provides descriptive statistics for this sample compared to similarly aged individuals in the 1980-2000 United States Census five percent micro samples. In total, individuals in the NHIS are more likely to be female, Black, Hispanic, and a high school graduate. They are slightly less likely to be a married.

[33] Prior to 1996 individuals are asked to identify the presence of chronic conditions. For the purposes of this analysis, individual identifying themselves with ischemic heart disease, hearth rhythm disorders, congenital heart disease, or other diseases of the heart (excluding hypertension) are classified as having coronary heart disease. Following 1996, individuals are asked individual questions about chronic conditions and those saying they have coronary heart disease are classified as such. Individuals are asked in both survey designs about the presence of diabetes. Prior to 1996, individuals are classified as having kidney disorders if they report have kidney infections or "other kidney trouble." There is not comparable question in the post-1996 redesign.

Estimation Strategy

Many individuals born during the last quarter of 1918 and the first two quarters of 1919 experienced higher levels of fetal stress (Barry, 2004). If the fetal origins hypothesis is correct, these individuals should have increased rates of chronic health conditions in later life compared to individuals born in surrounding time periods.

While the identification strategy in this analysis is similar to that used in Almond (2006), there are several differences in the NHIS data that necessitate altering his basic specification. All dependent variables are defined as the presence of chronic conditions and are thus binary. In the presence of a binary dependent variable, the linear probability model can produce inaccurate estimates, especially when incidence rates are low (as they are in this instance).[34] To avoid this problem I estimated a logit model of the following form:

$$\Pr(Y_i = 1) = F(\alpha + \gamma X_i + \phi AGE_i + \gamma\, g(QOB_i) + \beta_1 REGION_i + \beta_2 MOB_i + \beta_3 FLU_i), \quad (11)$$

where Y_i is equal to 1 if an individual reports having the presence of a health conditions, and 0 otherwise; X_i is a vector of demographic control variables accounting for race and sex, AGE_i is a vector of dummy variables for age, $g(QOB_i)$ is a cubic polynomial for quarter of birth cohort (e.g., first quarter of 1917, second quarter of 1917 etc.); $REGION_i$ controls for region of residence fixed effects; MOB_i controls for month of birth fixed effects.[35] The explanatory variable of interest is

[34] For a more detailed discussion of the failure of the linear probability model in this situation see Woolridge (2002), Chapter 15 and Johnston and Dinardo (1997), Chapter 13.
[35] Alternate specifications which include high order polynomials for age and interact age with quarter of birth return qualitatively similar estimates.

FLU_i—a dummy variable indicating whether the individual was affected by the flu pandemic in utero.[36] F is the logistic function. In this analysis I allow for an arbitrary variance-covariance matrix accounting for within group correlation in the errors based on the year of birth/survey year cohort.[37]

The specific health outcomes considered in this analysis include heart disease, diabetes, kidney disorders. The selection of these outcomes was guided by two factors. First, as discussed above, they represent those conditions identified in animal experiments as having relatively precise predictions regarding the time period of fetal insult result in later life health conditions. Mcmillen and Robinson (2005) provided an overview of fetal origins hypothesis and focused on these metabolic and cardiovascular outcomes as primary endpoints. These outcomes are among the most costly and deadly conditions for later life health and therefore their ultimate cause is of great interest to health professionals. In addition to the specific chronic conditions, this analysis also estimates the effect of decreased fetal health on self-reported health status during later life.

---

[36] Throughout this analyis, in-utero flu exposure will be defined at many levels of specificity.

[37] Kloeck (1981) provides a measure of the bias in standard errors in the presence of within group correlation in the errors. In the case where all regressors are fixed within group and all groups have the same size, *m*, the true variance-covariance matrix is $\sigma^2 (X'X)^{-1}[1+(m-1)\rho]$—where ρ is the amount of within group correlation. Even in the case of groups of differing sizes, $[1 + (m-1)\rho]$ serves as an approximate measure of the bias caused by within group correlation (Bertrand 1990). This bias is a function of both the size of the groups and the amount of correlation within the groups.

In most cases, researchers are concerned with positive within group correlation leading to a downward bias in the OLS standard errors. This dataset of repeated cross sections and negative health outcomes, however, contains a high level of negative within group correlation. At least a portion of this negative correlation is a mechanical result of the construction of the dataset. Groups with a high rate of chronic conditions in early survey years should experience higher mortality rates and as a result will appear healthier in later survey years. The mechanical negative correlation is magnified in this case by large group sizes—the average size of a year of birth cohort in the data is approximately 9,500. Groups of this size mean that even a small amount of negative correlation will lead to a large bias in the estimated standard errors.

In order to avoid this mechanical negative correlation but still account for correlation within year of birth cohorts, I allow for correlation between year of birth and year of survey cohorts. This results in 736 "clusters."

One concern about this analysis is that there may be gender based differences in both the effects of fetal programming and in the presence of selective mortality. Mcmillen and Robinson (2005) stated, "there is also a differential impact of early nutritional manipulations on male and female offspring in experimental studies in a range of animal species." Gluckman et al. (2008) reported similar differences in outcomes in animal studies. A further gender based concern is differences in selective mortality by sex. For example, males have a higher rate of heart disease than females and therefore may die at younger ages. Due to the relatively older ages that individuals are included in this study, it is possible that these differences in heart conditions may generate a downward bias in the estimated effect of in-utero exposure to the peak of the flu pandemic. This magnitude of this bias may vary by sex. Due to these factors, I will estimate effects for the full sample and for gender based sub-samples.[38]

There are several important identifying assumptions that are necessary for this model to accurately estimate the long-term effect of in-utero exposure to the flu. First, I assume that the long term health effects of the flu pandemic are felt solely by those exposed to the pandemic in-utero. A specific concern here is that individuals born in time periods after the flu pandemic, but not exposed to the flu in-utero, should be no more or less likely to develop these chronic conditions later in life.[39]

[38] Due to sample size concerns, some of these gender based sub samples may return relatively imprecise estimates. This is particularly true for rare conditions such as kidney disorders.

[39] It is possible, however, that there are non-medical responses to the flu that could result in long-term health consequences. For example, some school-age individuals contracted influenza and survived. Their sickness may have caused them to acquire less total education in their lifetime. There is a documented connection between education levels and mortality (Lleras-Muney, 2005; Elo and Preston, 1996; Kitagawa and Hauser, 1973; Grossman and Kaestner, 1997). As a result, the flu could affect birth cohorts other than those in-utero during the pandemic by decreasing lifetime education.

I also assume that subsequent flu seasons did not substantially affect the in-utero conditions of immediately surrounding birth cohorts—in particular those cohorts following the peak of the pandemic. Figure 9 shows the sharp increase in deaths in 1919 compared to surrounding years. In addition, as discussed previously, the 1918 flu affected the young and healthy to a greater degree than more standard flu variants.

To the test these assumptions I will estimate the health effects of being born in leading and lagging cohorts of those affect in-utero by the peak of the 1918 flu pandemic. A lack of an effect for these groups will support the underlying theory that the fetal exposure to the flu pandemic is causing the changes in later life health outcomes.

Health Outcome Results

Medical knowledge of fetal development in humans and animal experiments of fetal stress provide explicit predictions concerning the later life health effects of decreases in fetal health. Given this background information, I hypothesize that the pattern of results across different conditions should follow the pattern described in Table 18.

Table 19 reports logit estimates of equation (11). The first row contains results for a model identifying exposure to the 1918 pandemic as being born in the fourth quarter of 1918, the first quarter of 1919, or the second quarter of 1919. For both the full sample, and for men only there is a statistically significant increase in the probability of having heart disease for individuals affected by the peak of the pandemic in-utero. For the full sample, the estimated marginal effect suggests that

being exposed to the flu in-utero is associated with a 0.7 percentage point increase in the probability of developing heart disease in later life. The effect for just men was similar in magnitude. There was no statistically significant effect for women, but this may be due to the fact that this is a relatively broad measure of flu exposure that cannot precisely define the timing of the increased fetal stress. The medical literature suggests that failing to accurately pinpoint the timing of fetal exposure makes it difficult to detect the effects of specific chronic conditions.

Defining in-utero flu exposure based on quarter of birth returns more precise estimates of the effect of fetal stress on developing certain chronic conditions. Rows (2)-(4) of Table 19 contain estimates for coefficients on dummy variables identifying individuals born in the fourth quarter of 1918, the first quarter of 1919, or the second quarter of 1919. The estimates in parentheses are standard errors and those in brackets are the marginal effects. These results show that in-utero exposure to the 1918 pandemic increases the probability of developing coronary heart disease in later life. For the entire sample, being born in the first quarter of 1919 is associated with an approximately 1.1 percentage point in the probability of developing coronary heart disease. This result is statistically significant at the 10 percent level. The underlying prevalence of coronary heart disease for this age group is 10.7 percent, suggesting that in-utero exposure to the flu pandemic is associated with a 10.3 percent increase in the probability of developing heart disease. For men, being born in the first quarter of 1919 increases the probability of developing coronary heart disease by approximately 2.2 percentage points, or 18.5 percent. This result is statistically significant at the 5 percent level. Among women, there is an increased probability of

1.1 percentage points or 11.6 percent for those born during the second quarter of 1919. This result is also statistically significant at the 5 percent level.

It is possible that the statistically significant results in Table 19 are due to secular factors other than in-utero exposure to the 1918 pandemic. If this were the case, then it is likely that similar results would be found among the surrounding birth cohorts. Table 20 contains a specification of equation (11) with dummy variables indicating the quarter of birth for all individuals born between 1917-1920. In the full sample, there are positive and statistically significant results only for the 1st quarter of 1919—individuals who were in-utero during the pandemic. There is a negative and statistically significant effect for individuals born during the 3rd quarter of 1920. For men, there is a positive and statistically significant result for individuals born during the 1st quarter of 1918. It is unclear why this may be the case, though some medical literature does suggest that post-natal exposure to the flu pandemic may have resulted in increased rates of coronary heart disease (Azambuja, 2004). Among women, the only statistically significant result is for individuals born during the 2nd quarter of 1920—those individuals who were affected by the peak of pandemic during the earliest months of fetal development.

Assuming a normal gestation length, individuals born in the first quarter of 1919 were exposed to the flu during anywhere from the fifth to ninth months in-utero. Fetal stress during this period has a detrimental effect on later life coronary health. For women, this effect occurs during the second quarter of 1919. These results are consistent with the medical predictions that fetal stress in the mid-to-early stages of pregnancy has a negative effect on cardiac health.

Table 21 contains results for equation (11) where flu exposure is defined at the month of birth level. For both sexes, a statistically significant result is found for individuals born in December, 1918. For men, there are statistically significant results for December, 1918 and January, 1919. For women, there are positive statistically significant results for December, 1918, May, 1919 and June 1919. There is also an inexplicable negative and statistically significant result for women born in October, 1918. The results for males are earlier than may be expected based on a full term delivery, but it is important to recognize that exposure to the full during pregnancy was found to be associated with an increase in pre-term delivery, so these individuals may have been exposed earlier in fetal development terms than their birth date would suggest.

The difference in timing between the effects of men and women could be caused by several factors. First, medical research suggests that males and females react differently to fetal insults (Gluckman et al., 2008; Mcmillen and Robinson, 2005). In addition, as will be discussed later, this difference between may provide evidence of attrition in the sample creating a downward bias to the results. Suggestive evidence of this may also be found in the divergent results between women and men born in June, 1919. Women have a positive, large, and statistically significant estimated effect while men have a large and negative effect. Though the effect for men is not statistically significant, it is similar in magnitude (although opposite in sign) to the result for women.

Table 22 contains the results for equation (11) with diabetes as the outcome of interest. In-utero exposure to the 1918 pandemic increases the probability of

reporting diabetes in later life. Specifically, being born in the second quarter of 1919 increases the probability of developing diabetes by 19.4 percent. This result is significant at the 5 percent level. Examining the results by sex, a statistically significant effect is found for women born during the second quarter of 1919. A point estimate of similar magnitude is found for men born during this time period, though this result is not statistically significant at conventional levels. Table 23 contains the results for a specification containing leading and lagging cohorts of those in-utero during the flu. In addition to individuals born during the 2nd quarter of 1919, These results show positive and statistically significant effects for individuals born during 2nd quarter of 1917 and the 1st quarter of 1920. While this pattern of results is less compelling than the results for heart disease they still provide evidence that in-utero exposure to the peak of the flu pandemic affected the likelihood of diabetes in later life.

The results examining the effect by month of birth are contained in Table 24. These results show that the effects of flu exposure are driven by individuals born during April and May of 1919—those individuals who were in the earliest months of fetal development during the peak of the 1918 pandemic. The timing of this effect could be troubling for public health policymakers as it is more difficult for nutrition and other public health programs aimed at new mothers to effect in-utero conditions during the earliest months of pregnancy. This may suggest a need for general public health programs aimed at women of child-bearing age regardless of their current pregnancy status.

Table 25 contains the estimates for equation (11) with kidney disorders as the dependent variable. In-utero exposure to the flu pandemic increases the probability of reporting a kidney disorder later in life. Individuals born during the fourth quarter of 1918 face an approximately 50 percent increase in the probability of having a kidney disorder. Examining the results by sex only finds a statistically significant effect for women, though the point estimate for men is of similar magnitude. Table 26 contains the results for leading and lagging cohorts of individuals exposed to the flu in-utero. There are no statistically significant effects other than for individuals born during the 4th quarter of 1918. Looking at the results by month of birth in Table 27 shows that individuals born during the flu pandemic, and therefore exposed relatively late in terms of fetal development, are those most affected. There is also a positive and statistically significant effect for men born during April, 1919. Together, these results suggest that increased fetal stress during the last months of a pregnancy affects later life kidney health. This is consistent with the biological fact that the majority of kidney development occurs during the last trimester.

Table 28 contains the results for self-reported health status. Specifically, it contains results for a specification of equation (11) with a dependent variable indicating an individual reports being either in "poor" or "fair" health. For the full sample, men only, and women only the broadest measure of flu exposure (being born in either the 4th quarter 1918, or the first or second quarters of 1919) is associated with a statistically significant increase in the probability of reporting being in poor health. For example, for the full sample, being exposed to the flu pandemic in-utero is associated with a 5 percent increase in the probability of reporting poor health

status later in life. Examining leading and lagging cohorts of those exposed in-utero in Table 29, the only positive and statistically significant results are for individuals that were exposed to the peak of the flu pandemic in-utero. There is also a negative and statistically significant effect for individuals born during the 3rd quarter of 1920 and for women only born during the 4th quarter of 1919. Table 30 contains the results for in-utero exposure defined at the month of birth level. For the full sample, there are positive and statistically significant results for individuals born during December, 1918 ad well as January, February and April of 1919. For men the results are positive and statistically significant for individuals born during December 1918 or January 1919. Among women, statistically significant results are found for December, 1918 as well as February, April, and May 1919.

In total, these provide a pattern of results that is consistent with the later life health conditions being caused by the flu. Furthermore, the timing of the results matches the hypothesized pattern predicted by the medical literature and detailed in Table 17.

Attrition in the Sample

There are two possible sources of attrition that are of concern to this analysis. The first source of attrition results from the increased number of miscarriages and stillbirths resulting from in-utero flu exposure. Almond (2006) stated that there was a 40 percent increase in still-births during the October-December, 1918 period. It is possible that this resulted in an increase in the average general health of surviving cohorts. This would be caused by the increased number of stillbirths coming from

babies that were of marginal health. It is likely however, that any bias in the estimated causal effect of in-utero flu exposure on later life health generated by this increase in average general health would be downward in nature.

A second potential source of bias comes from individuals with chronic conditions dying before they were surveyed in later life—raising the average health of the remaining cohort. This "survivor bias" would cause adults surveyed by the NHIS in later life to appear healthier on average as a result of their in-utero flu-exposure.

As a test for the presence of this survivor bias, I re-estimated equation (11) with coronary heart disease as the outcome of interest using males in three sub-samples of differing ages. If attrition were affecting the results, the estimated coefficients should decrease across these samples, with the lower probabilities resulting from mortality increasing the average health of surviving age groups. Figure 10 displays the marginal effects and 95 percent confidence intervals for males born during the first quarter of 1919—the time period showing the largest effect for males in Table 19. There is a clear downward trend in the marginal effects across the three samples. In addition, a statistically significant effect is only found for males in the youngest age group. I conducted similar analyses for kidney disease and diabetes but because of large standard errors generated by low incidence rates, there was no clear pattern in the data.

A sensible interpretation of this pattern of decreasing estimates for older individuals is attrition among the cohorts exposed to the flu. Older individuals have a decreased probability of reporting chronic health conditions because each year individuals with these chronic conditions perish. Culling these unhealthy individuals

from the group increases the average health of the remaining cohort. As a result of the advanced age of this sample, many of the results above should be viewed as lower bound estimates of the health effects of fetal stress related to the flu pandemic.

Effect on Education

A primary finding of Almond (2006) was a decrease in both years of total education and the likelihood of graduating high school for individuals born in 1919. Figures 11 and 12 show the average highest grade completed and the percentage graduating high school in the sample by year of birth. Similar to the graphical evidence in Almond, it appears that there may be some effect for those born during 1919. Before and after this year there is a clear upward trend in education outcomes. Examining educational attainment by quarter of birth, the potential effect of the flu is less clear due to a number of other factors correlated with quarter of birth that affect education levels.[40]

In order to test the effect of in-utero flu exposure on educational outcomes, I estimated a specification of equation (11) with a dependent variable equal to 1 if the individual was a high-school graduate. I also estimated an ordinary least squares specification with the highest grade completed as the dependent variable.

Table 31 reports the estimates for effect of in-utero exposure to the flu pandemic on both the change in the probability of graduating high school and the highest grade completed. Columns (1) – (3) contain the OLS estimates for all NHIS respondents, men, and women with the highest grade completed as the dependent

[40] To some extent this fact should be expected since previous work has demonstrated a strong quarter of birth effect on education (Angrist and Krueger, 1991). This increases the signal-to-noise ratio making it more difficult to visually detect an effect from the flu pandemic based on quarter of birth.

variable. Row (1) contains results for flu exposure defined as being born in either the fourth quarter of 1918 or the first or second quarters of 1919. There are no statistically significant results on highest grade completed or for graduating high school for flu exposure defined in this manner. Rows (2) – (4) contain the results for flu exposure at the quarter of birth level. Similar to the broader measure of exposure there are no statistically significant estimates at this level of exposure. Table 32 contains estimates for the leading and lagging quarters of birth. As can be seen from the table, several of these quarters of birth return positive and statistically significant results for both highest grade level completed and probability of being a high school graduate. This includes the second and third quarters of 1918—the two quarters immediately preceding the peak of the pandemic.

Table 33 provides estimates examining the effect of in-utero flu exposure on educational attainment using month of birth as the level of exposure provides limited evidence of a negative effect. For example, men born in May 1919 and women born during March 1919 return a negative and statistically significant decrease in the number of grades completed. For men born in December, 1918 there is a statistically significant decrease in the probability of graduating high school.

The lack of a consistent pattern of results provides limited evidence from this data that in-utero exposure to the flu decreased educational attainment. This stands in contrast to the effect of the flu on education found in Almond (2006). This is likely a result of the NHIS being a less appropriate dataset for estimating the effect of the flu pandemic on educational outcomes. Compared to the PUMS sample used by Almond, the NHIS sample in this case is much smaller and the respondents are in

general older. Due to these factors, it should be unsurprising that the estimates related to education are far less pr ecise.

Conclusion

The results of this analysis suggest that in-utero exposure to the 1918 flu pandemic had long lasting negative health consequences. Depending on the period of fetal development during which exposure occurred, individuals have a higher probability of developing coronary heart disease, diabetes, kidney disorders, or being in poor health. There is limited evidence from this analysis that exposure to the flu in-utero also affects education levels.

The strong relationship between in-utero stress during certain periods of fetal development and specific conditions in later life shows that the duration of the event used for quasi-experimental variation in fetal conditions is critical to analyses involving specific diseases. When flu exposure was defined over several quarters of birth, it is not possible to pinpoint stress to particular periods of fetal development. As a result, many of the individuals who received the "treatment" of fetal stress should not be expected to develop particular conditions. For example, the nutrition delivery system of the fetus is almost fully developed by the last trimester. Individuals experiencing fetal stress during this time period should not be expected to have a higher probability of developing diabetes in later life. Grouping all individuals into one large category (including both "treated" and "untreated" individuals with respect to certain conditions) limits the ability of the analysis to detect any effect from fetal stress on particular diseases. Unsurprisingly, when flu exposure was defined at

its broadest level and diabetes is the dependent outcome of interest there was no statistically significant effect. When flu exposure is defined using particular quarters of birth, however, there is an approximately 20 percent increase in the probability of developing diabetes for individuals exposed to the flu during the first months of pregnancy.

The short duration of the 1918 pandemic allows researchers to attribute flu exposure to these particular time periods of development. Identification strategies using long-lasting events such as the Chinese famine or the Siege of Leningrad, on the other hand, are hampered by their inability to determine particular time periods of fetal stress. The long duration of these events is at least one reason that previous attempts to document disease specific outcomes of the fetal origins hypothesis have been more mixed than these results.

While the long term health impact of the flu pandemic is interesting, the insight gained by this analysis can be beneficial in understanding a number of important questions regarding the effects of poor in-utero conditions from other sources. Generalizing the results of this analysis to all cases of fetal stress raises a question of external validity. There is biological evidence, however, that the effect of in-utero flu exposure is similar to other complications. Irving et al. (2000) found that in-utero exposure to influenza resulted in a higher rate of complications in pregnancy. This decrease in fetal health provides a connection between the fetal origins hypothesis and the 1918 pandemic.[41] Taken together, the animal studies, cross

[41] The underlying theory of this paper is that the increase in physical stress from in-utero flu exposure is responsible for the changes in later life health. It is also possible, however, that a general increase in stress and anxiety from pregnant women living during the flu pandemic could also affect in-utero health.

sectional analysis of humans, and the results of this analysis suggest that maternal health during pregnancy is an important contributor to the long-term health of their offspring.

The long term effects of decreased fetal health can generate significant societal costs. The management of chronic conditions makes up an increasing share of expenditures in the Medicare program.[42] In particular, heart disease and diabetes are primary cost drivers. For example, 42 percent of the top quartile of Medicare patients in terms of spending have coronary heart disease. Additionally, 32 percent of these high cost patients suffer from diabetes (Congressional Budget Office, 2005). A RAND study states, "chronic illnesses such as heart disease, cancer, and diabetes are expensive to treat. As a consequence, the relatively small proportion of Medicare beneficiaries with such diseases account for a disproportionate share of Medicare spending — perhaps as much as three-quarters of the total" (RAND, 2005).[43] To the degree that in-utero stress increases the incidence of these conditions it also generates higher Medicare spending.

Beyond simply the impact on medical spending, the presence of chronic conditions leads to a lower quality of life, work effort, and productivity. Almond (2006) found that in-utero exposure to the flu led to a 20 percent increase in disability and a 5-9 percent decrease in wages. These results are similar to previous estimates of the effect of chronic conditions and health status on labor supply. Bartel and Taubman (1979) found statistically and economically significant decreases in labor

[42] Due to their age, early all individuals affected by the flu that are considered in this study qualify for Medicare benefits.
[43] While the higher likelihood of an early death for individuals with these chronic conditions does limit their effect on total Medicare costs, RAND still estimates that coronary heart disease and diabetes increase lifetime Medicare spending by anywhere from $14,000 to $17,000.

force participation and earnings for individuals with a variety of chronic conditions including heart disease. Mitchell (1990) states, "[p]oor health is associated with reduced hours of work, lower wage rates, early retirement and disability transfer programs" (p. 928). These lower work levels and earnings add another dimension to the social cost of chronic conditions and the importance of fully understanding their origins.

While these health benefits must be discounted due to their accrual so long after birth, it is clear that they represent a valuable and previously ignored benefit of improved fetal conditions. Several federal, state, and private programs attempt to improve access to prenatal care—particularly for underserved populations. For example, Medicaid now provides prenatal care services. In addition, the Women, Infants, and Children (WIC) program is explicitly intended to improve nutrition for pregnant women. There is often debate about the net efficacy of these pre-natal programs. Evaluations of their benefit, however, fail to consider the potential long term health benefits (Evans and Lien, 2005; Wayne et al., 1998; Currie and Gruber, 1996; Devaney et al., 1992). Instead, these programs are traditionally judged based on immediate infant health concerns such as birthweight, 28 day readmission rates, and infant mortality. The results for this study show that long term health benefits should also be a factor in these evaluations. This will provide a more accurate assessment for long term health policy development.

Tables

Table 1
Reported ICD-9 Codes for Vioxx Prescriptions

	Condition	Percent of Vioxx Recipients
1.	Other and unspecified arthropathies	43.2
2.	Other and unspecified disorders of back	20.9
3.	Other and unspecified disorders of joint	14.7
4.	Intervertebral disc disorders	8.35
5.	Osteoarthrosis and allied disorders	6.2

Source: Medical Expenditure Panel Survey 1998-2004

Table 2
Descriptive Statistics

	Vioxx Recipients Age 55-65	Non-Vioxx Recipients Age 55-65
Age	59.75	59.51
% Female	66.71	52.91
% HS Grad	77	73.4
% Bachelors	21.9	22.7
% White	73.5	74
% Black	10.4	12.4
Health Status	2.99	2.61
% Working	53	58.6

Source: Medical Expenditure Panel Survey 1998-2004

Table 3
Descriptive Statistics for Individuals with Joint Conditions

	Ever Taken Vioxx	Never Taken Vioxx
Age	59.68	56.02
% Female	68.19	61.87
% HS Grad	72.55	64.35
% Bachelors	17.93	15.61
% White	71.69	73.13
% Black	12.49	13.98
Health Status	3.05	2.88
% Working	43.38	43.60

Source: Medical Expenditure Panel Survey 1998-2004

Table 4
OLS Estimates of Labor Supply, MEPS 1998-2004

Parameter Estimates (Standard Errors)

	(1)	(2)	(3)
	Both Sexes Age 55-61	Both Sexes Age 55-64	Both Sexes Age 55-75
$VIOXX_t$	-0.052	-0.018	0.033
	(0.063)	*(0.062)*	*(0.059)*
$VIOXX_t$*JOINT	0.131*	0.079	-0.044
	(0.07)	*(0.068)*	*(0.062)*
$VIOXX_t$*BACK	0.037	0.028	0.0499
	(0.094)	*(0.09)*	*(0.092)*
JOINT	-0.072***	-0.077***	-0.049***
	(0.014)	*(0.013)*	*(0.009)*
BACK	-0.048**	-0.047**	-0.035**
	(0.019)	*(0.018)*	*(0.014)*
HSGRAD	0.079***	0.057***	0.051***
	(0.018)	*(0.015)*	*(0.011)*
SOMECOLLEGE	0.095***	0.083***	0.069***
	(0.02)	*(0.018)*	*(0.012)*
COLLEGEGRAD	0.0156***	0.148***	0.145***
	(0.018)	*(0.016)*	*(0.012)*
WHITE	0.005	-0.005	0.005
	(0.024)	*(0.022)*	*(0.018)*
BLACK	-0.018	-0.031	0.001
	(0.029)	*(0.026)*	*(0.021)*
HISPANIC	0.025	0.008	0.032
	(0.028)	*(0.025)*	*(0.021)*
$VIOXX_t$ + $VIOXX_t$*JOINT	0.079**	0.061**	-0.011
	(0.029)	*(0.029)*	*(0.02)*
$VIOXX_t$ + $VIOXX_t$*BACK	-0.015	0.01	0.083
	(0.07)	*(0.065)*	*(0.07)*
N	27,883	37,290	66,487

Entries represent the estimated coefficients from a linear probability model. The dependent variable is a binary variable equal to one if an individual reports employment during the MEPS round. The last two rows report the linear combination and (standard error) for a binary variable documenting a reported Vioxx prescription and this variable interacted with a binary variable indicating the presence of a chronic joint or back condition. Unreported covariates control for a cubic age trend, insurance status, and MEPS round. Regressions are weighted using MEPS longitudinal weights. Standard errors are clustered at the individual level.
* Significant at the .10 level
** Significant at the .05 level
*** Significant at the .001 level

Table 5
Fixed Effect Estimates of Labor Supply, MEPS 1998-2004

Parameter Estimates (Standard Errors)

	(1)	(2)	(3)
	Both Sexes Age 55-61	Both Sexes Age 55-64	Both Sexes Age 55-75
	-0.011	-0.009	-0.011
$VIOXX_t$	*(0.019)*	*(0.014)*	*(0.01)*
	0.008	0.01	0.005
$VIOXX_{t-1}$	*(0.017)*	*(0.013)*	*(0.009)*
	0.018	0.009	0.011
$VIOXX_t$*JOINT	*(0.025)*	*(0.021)*	*(0.013)*
	-0.007	0.004	-0.003
$VIOXX_{t-1}$*JOINT	*(0.023)*	*(0.02)*	*(0.013)*
	0.053	0.052	0.026
$VIOXX_t$*BACK	*(0.041)*	*(0.035)*	*(0.018)*
	0.016	0.007	0.004
$VIOXX_{t-1}$*BACK	*(0.037)*	*(0.028)*	*(0.015)*
$VIOXX_t + VIOXX_t$*JOINT	0.007	0.0002	0.0005
	(0.017)	*(0.016)*	*(0.009)*
$VIOXX_{t-1} + VIOXX_{t-1}$*JOINT	0.001	0.014	0.003
	(0.016)	*(0.016)*	*(0.01)*
$VIOXX_t + VIOXX_t$*BACK	0.043	0.043	0.015
	(0.036)	*(0.031)*	*(0.015)*
$VIOXX_{t-1} + VIOXX_{t-1}$*BACK	0.023	0.017	0.01
	(0.032)	*(0.025)*	*(0.012)*
N	6,706	8,581	14,439
N*T	22,509	30,049	53,421

Entries represent the estimated coefficients from a fixed effect linear probability model. The dependent variable is a binary variable equal to one if an individual reports employment during the MEPS round. The last four rows report the linear combination and (standard error) for a binary variable documenting a reported Vioxx prescription and this variable interacted with a binary variable indicating the presence of a chronic joint or back condition. Unreported covariates control for a cubic age trend and MEPS round. Regressions are weighted using MEPS longitudinal weights. Standard errors are clustered at the individual level.

* Significant at the .10 level

** Significant at the .05 level

*** Significant at the .001 level

Table 6
Fixed Effects Estimates of Labor Supply, MEPS 1998-2004

Parameter Estimates (Standard Errors)

	Males			Females		
	(1)	(2)	(3)	(4)	(5)	(6)
	Aged 55-61	Aged 55-64	Aged 55-75	Aged 55-61	Aged 55-64	Aged 55-75
$VIOXX_t$	-0.035	-0.024	-0.01	-0.005	-0.003	-0.012
	(0.026)	*(0.018)*	*(0.011)*	*(0.025)*	*(0.019)*	*(0.013)*
$VIOXX_{t-1}$	-0.032	-0.015	-0.009	0.023	0.021	0.012
	(0.025)	*(0.018)*	*(0.011)*	*(0.021)*	*(0.017)*	*(0.012)*
$VIOXX_t$*JOINT	0.111**	0.067	0.034	-0.012	-0.013	0.003
	(0.044)	*(0.043)*	*(0.023)*	*(0.031)*	*(0.025)*	*(0.016)*
$VIOXX_{t-1}$*JOINT	0.1**	0.098**	0.057**	-0.046	-0.038*	-0.03*
	(0.038)	*(0.04)*	*(0.024)*	*(0.029)*	*(0.024)*	*(0.016)*
$VIOXX_t$*BACK	0.112*	0.082	0.047	-0.002	0.027	0.013
	(0.062)	*(0.052)*	*(0.033)*	*(0.031)*	*(0.038)*	*(0.021)*
$VIOXX_{t-1}$*BACK	0.113*	0.079	0.041	-0.046	-0.038	-0.019
	(0.068)	*(0.053)*	*(0.028)*	*(0.029)*	*(0.024)*	*(0.015)*
$VIOXX_t$ + $VIOXX_t$*JOINT	0.076**	0.043	0.024	-0.017	-0.016	-0.009
	(0.035)	*(0.039)*	*(0.021)*	*(0.018)*	*(0.015)*	*(0.009)*
$VIOXX_{t-1}$+ $VIOXX_{t-1}$*JOINT	0.069**	0.084**	0.049**	-0.023	-0.018	-0.018
	(0.028)	*(0.036)*	*(0.021)*	*(0.02)*	*(0.016)*	*(0.01)*
$VIOXX_t$ + $VIOXX_t$*BACK	0.076	0.059	0.036	-0.007	0.023	0.002
	(0.056)	*(0.049)*	*(0.031)*	*(0.019)*	*(0.032)*	*(0.016)*
$VIOXX_{t-1}$+ $VIOXX_{t-1}$*BACK	0.081	0.064	0.032	-0.023	-0.017	-0.007
	(0.063)	*(0.05)*	*(0.026)*	*(0.02)*	*(0.017)*	*(0.009)*
N	3,106	3,976	6,529	3,600	4,605	7,910
N*T	10,414	13,950	24,122	12,095	16,099	29,299

Entries represent the estimated coefficients from a fixed effect linear probability model. The dependent variable is a binary variable equal to one if an individual reports employment during the MEPS round. The last four rows report the linear combination and (standard error) for a binary variable documenting a reported Vioxx prescription and this variable interacted with a binary variable indicating the presence of a chronic joint or back condition. Unreported covariates control for a cubic age trend and MEPS round. Regressions are weighted using MEPS longitudinal weights. Standard errors are clustered at the individual level.

* Significant at the .10 level

** Significant at the .05 level

*** Significant at the .001 level

Table 7
Fixed Effects Estimates of Male Labor Supply, MEPS 1998-2004

Parameter Estimates (Standard Errors)

	Physical Work Ever			Never Report Physical Work		
	(1)	(2)	(3)	(4)	(5)	(6)
	Aged 55-61	Aged 55-64	Aged 55-75	Aged 55-61	Aged 55-64	Aged 55-75
$VIOXX_t$	-0.008	-0.014	-0.008	0.035	0.02	0.011
	(0.013)	*(0.015)*	*(0.02)*	*(0.046)*	*(0.031)*	*(0.017)*
$VIOXX_{t-1}$	0.0189	0.013	-0.013	0.023	0.02	0.011
	(0.013)	*(0.012)*	*(0.025)*	*(0.042)*	*(0.029)*	*(0.015)*
$VIOXX_t$*JOINT	0.129*	0.094	0.074	0.02	0.003	0.004
	(0.073)	*(0.07)*	*(0.067)*	*(0.06)*	*(0.055)*	*(0.026)*
$VIOXX_{t-1}$*JOINT	0.11	0.134**	0.137**	0.012	0.03	0.019
	(0.076)	*(0.062)*	*(0.062)*	*(0.046)*	*(0.054)*	*(0.026)*
$VIOXX_t$ + $VIOXX_t$*JOINT	0.121*	0.08	0.066	0.055	0.023	0.014
	(0.071)	*(0.068)*	*(0.064)*	*(0.038)*	*(0.045)*	*(0.019)*
$VIOXX_{t-1}$+ $VIOXX_{t-1}$*JOINT	0.132*	0.147**	0.124**	0.035*	0.05	0.03
	(0.074)	*(0.06)*	*(0.057)*	*(0.018)*	*(0.045)*	*(0.022)*
N	1,040	1,224	1,497	2,066	www2,752	5,032
N*T	3,498	4,324	5,517	6,916	9,626	18,605

Entries represent the estimated coefficients from a fixed effect linear probability model. Columns (1) – (3) contain estimates for males that report an occupation code for a job requiring a large amount of physical labor in at least one MEPS round. Footnote 18 describes this selection process. Columns (4) – (6) contain results for males that never report an occupation requiring primarily physical labor. The dependent variable is a binary variable equal to one if an individual reports employment during the MEPS round. The last two rows report the linear combination and (standard error) for a binary variable documenting a reported Vioxx prescription and this variable interacted with a binary variable indicating the presence of a chronic joint condition. Unreported covariates control for a cubic age trend and MEPS round. Regressions are weighted using MEPS longitudinal weights Standard errors are clustered at the individual level.

* Significant at the .10 level

** Significant at the .05 level

*** Significant at the .001 level

Table 8
Fixed Effects Estimates of Celebrex on Labor Supply, MEPS 1998-2004

Parameter Estimates (Standard Errors)

	Males			Females		
	(1)	(2)	(3)	(4)	(5)	(6)
	Aged 55-61	Aged 55-64	Aged 55-75	Aged 55-61	Aged 55-64	Aged 55-75
$CELEBREX_t$	-0.026	-0.014	-0.015	-0.021	-0.026	-0.004
	(0.063)	*(0.05)*	*(0.031)*	*(0.02)*	*(0.027)*	*(0.018)*
$CELEBREX_{t-1}$	-0.104	-0.082	-0.052	0.038	-0.022	-0.026
	(0.076)	*(0.065)*	*(0.044)*	*(0.024)*	*(0.041)*	*(0.025)*
$CELEBREX_t$*JOINT	0.029	0.026	0.029	0.005	0.006	-0.006
	(0.067)	*(0.059)*	*(0.035)*	*(0.026)*	*(0.031)*	*(0.021)*
$CELEBREX_{t-1}$*JOINT	0.064	0.067	0.046	-0.033	0.027	0.033
	(0.081)	*(0.071)*	*(0.047)*	*(0.03)*	*(0.043)*	*(0.027)*
$CELEBREX_t$*BACK	-0.038	-0.043	-0.019	-0.011	0.024	-0.034
	(0.08)	*(0.062)*	*(0.039)*	*(0.037)*	*(0.039)*	*(0.039)*
$CELEBREX_{t-1}$*BACK	0.059	0.034	0.021	-0.04	0.022	-0.003
	(0.087)	*(0.072)*	*(0.049)*	*(0.026)*	*(0.042)*	*(0.038)*
$CELEBREX_t + CELEBREX_t$+JOINT	0.002	0.012	0.014	-0.015	-0.02	-0.01
	(0.023)	*(0.031)*	*(0.017)*	*(0.017)*	*(0.015)*	*(0.011)*
$CELEBREX_{t-1} + CELEBREX_{t-1}$+JOINT	-0.04	-0.015	-0.005	0.005	0.005	0.007
	(0.026)	*(0.03)*	*(0.017)*	*(0.018)*	*(0.015)*	*(0.01)*
$CELEBREX_t + CELEBREX_t$+BACK	-0.063	-0.057	-0.034	-0.032	-0.002	-0.039
	(0.05)	*(0.037)*	*(0.024)*	*(0.03)*	*(0.029)*	*(0.035)*
$CELEBREX_{t-1} + CELEBREX_{t-1}$+BACK	0.045	-0.048	-0.03	-0.002	0.001	-0.03
	(0.041)	*(0.031)*	*(0.02)*	*(0.011)*	*(0.011)*	*(0.028)*
N	3,106	3,976	6,529	3,600	4,605	7,910
N*T	10,414	13,950	24,122	12,095	16,099	29,299

Entries represent the estimated coefficients from a fixed effect linear probability model. The dependent variable is a binary variable equal to one if an individual reports employment during the MEPS round. The last four rows report the linear combination and (standard error) for a binary variable documenting a reported Celebrex prescription and this variable interacted with a binary variable indicating the presence of a chronic joint condition. Unreported covariates control for a cubic age trend and MEPS round. Regressions are weighted using MEPS longitudinal weights. Standard errors are clustered at the individual level.

* Significant at the .10 level

** Significant at the .05 level

*** Significant at the .001 level

Table 9
Conditional Logit Estimates of Labor Supply, MEPS 1998-2004

Parameter Estimates (Standard Errors) [Odds Ratios]

	Males		Females	
	(1)	(2)	(3)	(4)
	Age 55-64	Age 55-75	Age 55-64	Age 55-75
$VIOXX_t$	0.763	0.624	0.946	-0.79
	(1.74)	*(1.3)*	*(1.26)*	*(1.16)*
	[2.14]	[1.86]	[2.57]	[0.45]
$VIOXX_{t-1}$	-0.51	-0.704	0.645	0.012
	(0.665)	*(0.751)*	*(0.852)*	*(0.658)*
	[0.60]	[0.494]	[1.91]	[1.01]
$VIOXX_t$*JOINT	0.94	0.665	-1.7	0.302
	(1.99)	*(1.43)*	*(1.42)*	*(1.25)*
	[2.59]	[1.94]	[0.18]	[1.35]
$VIOXX_{t-1}$*JOINT	2.23**	1.74**	-1.1	-0.639
	(0.9)	*(0.86)*	*(0.995)*	*(0.766)*
	[9.29]	[5.69]	[0.33]	[0.53]
$VIOXX_t$ + $VIOXX_t$*JOINT	1.7*	1.28**	-0.76	-0.49
	(0.98)	*(0.6)*	*(0.662)*	*(0.473)*
	[5.47]	[3.6]	[0.47]	[0.61]
$VIOXX_{t-1}$+ $VIOXX_{t-1}$*JOINT	1.72**	1.03**	-0.45	-0.626
	(0.62)	*(0.42)*	*(0.511)*	*(0.394)*
	[5.58]	[2.8]	[0.64]	[0.54]
N	407	662	508	766
N*T	1,495	2,503	1,893	2,908

Entries represent the estimated coefficient, (standard error), and [odds ratio] from a fixed effect conditional logit model. The dependent variable is a binary variable equal to 1 if an individual reports working at any time during the MEPS round. Individuals who report always working or never working are not included in the analysis. The last two rows report the linear combination for a binary variable documenting a reported Vioxx prescription and this variable interacted with a binary variable indicating the presence of a chronic joint condition. Unreported covariates control for a cubic age trend and MEPS round. Standard errors are clustered at the individual level.

* Significant at the .10 level

** Significant at the .05 level

*** Significant at the .001 level

Table 10
Fixed Effects Estimates of Labor Supply, MEPS 1998-2004

Parameter Estimates (Standard Errors)

	Males			Females		
	(1)	(2)	(3)	(4)	(5)	(6)
	Aged 55-61	Aged 55-64	Aged 55-75	Aged 55-61	Aged 55-64	Aged 55-75
$LIPITOR_{it}$	0.026	-0.013	-0.012	0.025	0.011	-0.0002
	(0.032)	*(0.027)*	*(0.018)*	*(0.032)*	*(0.024)*	*(0.01)*
$LIPITOR_{it}$*$CHOLEST_i$	-0.012	0.018	0.017	-0.04	-0.022	0.007
	(0.036)	*(0.03)*	*(0.02)*	*(0.035)*	*(0.026)*	*(0.012)*
$NEXIUM_{it}$	0.062	0.04	0.065	0.038	0.085	0.045
	(0.064)	*(0.046)*	*(0.043)*	*(0.023)*	*(0.041)*	*(0.021)*
$NEXIUM_{it}$*$GERD_i$	-0.11	-0.055	-0.079	-0.07	-0.102	-0.053
	(0.077)	*(0.058)*	*(0.048)*	*(0.04)*	*(0.05)*	*(0.032)*
$FOSAMAX_{it}$				-0.005	0.005	0.002
				(0.02)	*(0.017)*	*(0.011)*
$VIAGRA_{it}$	-0.031	-0.004	-0.004			
	(0.03)	*(0.026)*	*(0.018)*			
$LIPITOR_{it}$+ $LIPITOR_{it}$*$CHOLEST_i$	0.014	0.005	0.005	-0.015	-0.011	0.007
	(0.017)	*(0.014)*	*(0.009)*	*(0.014)*	*(0.011)*	*(0.008)*
$NEXIUM_{it}$+ $NEXIUM_{it}$*$GERD_i$	-0.05	-0.015	-0.014	-0.033	-0.017	-0.008
	(0.043)	*(0.035)*	*(0.023)*	*(0.032)*	*(0.03)*	*(0.022)*
N	3,246	3,779	4,126	3,246	3,779	4,126
N*T	12,901	14,982	17,316	12,901	14,982	17,316

Entries represent the estimated coefficients from a fixed effect linear probability model. The first three columns include individuals that report an occupation code for a job requiring a large amount of physical labor in at least one MEPS round. Footnote 18 describes this selection process. The dependent variable is a binary variable equal to one if an individual reports employment during the MEPS round. The last two rows report the linear combination and (standard error) for a binary variable documenting a reported Lipitor or Nexium prescriptions and this variable interacted with a binary variable indicating the presence of high cholesterol or acid reflux disease, respectively. Unreported covariates control for a cubic age trend and MEPS round. Regressions are weighted using MEPS longitudinal weights. Standard errors are clustered at the individual level.

* Significant at the .10 level

** Significant at the .05 level

*** Significant at the .001 level

Table 11
Fixed Effects Estimates of Vioxx on Hours Worked, MEPS 1998-2004

Parameter Estimates (Standard Errors)

	Males			Females		
	(1)	(2)	(3)	(4)	(5)	(6)
	Aged 55-61	Aged 55-64	Aged 55-75	Aged 55-61	Aged 55-64	Aged 55-75
$VIOXX_t$	-2.59	-1.68	-0.815	0.5	0.523	0.163
	(1.95)	*(1.31)*	*(0.771)*	*(0.846)*	*(0.717)*	*(0.438)*
$VIOXX_{t-1}$	-0.725	-0.221	-0.127	0.347	-0.401	-0.27
	(0.816)	*(0.62)*	*(0.373)*	*(1.14)*	*(1.06)*	*(0.674)*
$VIOXX_t$*JOINT	5.52**	4.25**	1.91*	-1.09	-0.817	-0.364
	(2.558)	*(1.89)*	*(1.05)*	*(1.1)*	*(0.9)*	*(0.535)*
$VIOXX_{t-1}$*JOINT	3.51**	2.84**	1.47*	-1.65	-0.605	-0.33
	(1.7)	*(1.4)*	*(0.771)*	*(1.35)*	*(1.2)*	*(0.746)*
$VIOXX_t$*BACK	5.28	3.76	-2.32	-0.327	-0.433	0.191
	(3.53)	*(2.81)*	*(3.29)*	*(1.12)*	*(0.891)*	*(0.984)*
$VIOXX_{t-1}$*BACK	4.0	2.58	-1.14	-1.34	-0.246	0.745
	(2.69)	*(2.17)*	*(2.7)*	*(1.39)*	*(1.19)*	*(1.132)*
$VIOXX_t$ + $VIOXX_t$*JOINT	2.92*	2.57*	1.09	-0.589	-0.295	-0.202
	(1.65)	*(1.36)*	*(0.72)*	*(0.693)*	*(0.545)*	*(0.308)*
$VIOXX_{t-1}$+ $VIOXX_{t-1}$*JOINT	2.79*	2.61**	1.35**	-1.3*	-1.01*	-0.6*
	(1.49)	*(1.26)*	*(0.678)*	*(0.71)*	*(0.56)*	*(0.323)*
$VIOXX_t$ + $VIOXX_t$*BACK	2.69	2.08	-3.13	0.17	0.09	0.354
	(2.94)	*(2.48)*	*(3.19)*	*(0.729)*	*(0.531)*	*(0.882)*
$VIOXX_{t-1}$+ $VIOXX_{t-1}$*BACK	3.28	2.35	-1.27	-0.989	-0.648	0.475
	(2.56)	*(2.08)*	*(2.67)*	*(0.79)*	*(0.541)*	*(0.911)*
N	3,106	3,976	6,529	3,600	4,605	7,910
N*T	10,414	13,950	24,122	12,095	16,099	29,299

Entries represent the estimated coefficients from a fixed effect ordinary least squares model. The dependent variable is the usual weekly hours worked reports in the MEPS. The last four rows report the linear combination and (standard error) for a binary variable documenting a reported Vioxx prescription and this variable interacted with a binary variable indicating the presence of a chronic joint or back condition. Unreported covariates control for a cubic age trend and MEPS round. Regressions are weighted using MEPS longitudinal weights Standard errors are clustered at the individual level.

* Significant at the .10 level

** Significant at the .05 level

*** Significant at the .001 level

Table 12
Fixed Effects Estimates of Labor Supply, MEPS 2004-05
Both Sexes, Age 55-75

	Parameter Estimates (Standard Errors)
$VIOXX_t$	-0.021***
	(0.005)
$VIOXX_{t-1}$	-0.016***
	(0.004)
$VIOXX_t$*JOINT	-0.012
	(0.034)
$VIOXX_{t-1}$*JOINT	0.06**
	(0.024)
$VIOXX_t$ + $VIOXX_t$*JOINT	-0.033
	(0.034)
$VIOXX_{t-1}$+ $VIOXX_{t-1}$*JOINT	0.044*
	(0.024)
N	2,725
N*T	10,250

Entries represent the estimated coefficients from a fixed effect linear probability model. The dependent variable is a binary variable equal to one if an individual reports employment during the MEPS round. The last two rows columns report the linear combination and (standard error) for a binary variable documenting a reported Vioxx prescription and this variable interacted with a binary variable indicating the presence of a chronic joint or back condition. Unreported covariates control for a cubic age trend and MEPS round. Regressions are weighted using MEPS longitudinal weights. Standard errors are clustered at the individual level.

* Significant at the .10 level ** Significant at the .05 level *** Significant at the .001 level

Table 13
Fixed Effects and IV Estimates of Effect of Vioxx on Labor Supply
MEPS, Panel 9, 2004-05, Age 55-75

	Parameter Estimates (Standard Errors)		
	Reduced Form	2SLS	
	(1)	(2)	(3)
	Results of Working on Remove	First Stage Results of Vioxx on Remove	IV Results of Working on Predicted Vioxx
REMOVE*JOINT	-0.024*	-0.058***	
	(0.013)	*(0.01)*	
VIOXX			0.416*
			(0.234)
N	2,725	2,725	2,725
N*T	12,321	12,321	12,321

Entries in the table represent the estimated coefficients and standard errors from the linear probability IV model. Unreported covariates also include a cubic age trend and dummy variables for MEPS rounds. Regressions are weighted using MEPS longitudinal weights Standard errors are clustered at the individual level.

* Significant at the .10 level ** Significant at the .05 level *** Significant at the .001 level

Table 14
Fixed Effects and IV Estimates of Effect of COX-2 Inhibitors on Labor Supply
MEPS, Panel 9, 2004-05, Age 55-75

Parameter Estimates (Standard Errors)

	Reduced Form	2SLS	
	(1)	(2)	(3)
	Results of Working on Remove	First Stage Results of COX-2 on Remove	IV Results of Working on Predicted COX-2
REMOVE*JOINT	-0.024*	-0.102***	
	(0.013)	*(0.014)*	
VIOXX			0.237*
			(0.133)
N	2,725	2,725	2,725
N*T	12,321	12,321	12,321

Entries in the table represent the estimated coefficients and standard errors from the linear probability IV model. Unreported covariates also include a cubic age trend and dummy variables for MEPS rounds. Regressions are weighted using MEPS longitudinal weights Standard errors are clustered at the individual level.

* Significant at the .10 level ** Significant at the .05 level *** Significant at the .001 level

Table 15
Fixed Effects and IV Estimates of the Effect of COX-2 Inhibitors on Labor Supply
MEPS, Panel 9, 2004-05, Age 55-75

Parameter Estimates (Standard Errors)

	Reduced Form	2SLS	
	(1)	(2)	(3)
	Results of Working on Remove	First Stage Results of COX-2 on Remove	IV Results of Working on Predicted COX-2
REMOVE*HEART	-0.001	0.0001	
	(0.013)	*(0.014)*	
VIOXX			9.57
			(1159.1)
N	2,725	2,725	2,725
N*T	12,321	12,321	12,321

Entries in the table represent the estimated coefficients and standard errors from the linear probability IV model. Unreported covariates also include a cubic age trend and dummy variables for MEPS rounds. Regressions are weighted using MEPS longitudinal weights. Standard errors are clustered at the individual level.

* Significant at the .10 level ** Significant at the .05 level *** Significant at the .001 level

Table 16
Fixed Effects and IV Estimates of Labor Supply
MEPS, Panel 9, 2004-05, Age 55-75

Parameter Estimates (Standard Errors)

	Reduced Form	2SLS	
	(1)	(2)	(3)
	Results of Working on Remove	First Stage Results of COX-2 on Remove	IV Results of Working on Predicted COX-2
REMOVE*RESPIRATORY	0.011	-0.003	
	(0.008)	*(0.013)*	
COX-2			-3.8
			(17.18)
N	2,725	2,725	2,725
N*T	12,321	12,321	12,321

Entries in the table represent the estimated coefficients and standard errors from the linear probability IV model. Unreported covariates also include a cubic age trend and dummy variables for MEPS rounds. Regressions are weighted using MEPS longitudinal weights Standard errors are clustered at the individual level.
* Significant at the .10 level ** Significant at the .05 level *** Significant at the .001 level

Table 17
Descriptive Statistics
Adults aged 55 to 90, 1982 to 2002 NHIS and 1980 to 2000 Census

	NHIS	1980-2000 5% PUMS
% Female	56.9	56.3
% Black	11.1	8.1
% Hispanic	6.2	4.3
% High School Graduate	63.1	62.8
% College Graduate	15.8	13.6
% Married	60.1	62.8

Source: Public Use Micro Samples and NHIS

Table 18
Hypothesized Timing of In-utero Influenza Exposure on Health Outcomes

Quarter of Birth	Approximate Trimester of Exposure	Expected Conditions
4th Quarter, 1918	3rd Trimester	Kidney Disorders
1st Quarter, 1919	2nd Trimester*	Heart Conditions
2nd Quarter, 1919	1st Trimester	Heart Conditions Metabolic Disorders

*This approximate time period of exposure assumes a full term delivery. Medical evidence suggests that exposure to the flu pandemic was associated with higher rates of preterm delivery. This may cause some of these anticipated effects to occur in earlier time periods.

Table 19
Logit Estimates of Effect of Flu Exposure on Heart Disease, Adults aged 55 to 90, 1982 to 2002 NHIS

Parameter estimates (standard errors) [Marginal Effect]

		(1)	(2)	(3)
	Quarter of Birth	Full Sample n= 383,785 mean dep. var. = 0.107	Men n= 165,308 mean dep. var. = 0.124	Women n= 218,477 mean dep. var. = 0.095
(1)	Flu Season[1]	0.07** (0.034) [0.007]	0.084* (0.051) [0.009]	0.061 (0.045) [0.005]
(2)	Fourth Quarter, 1918	0.065 (0.047) [0.006]	0.126 (0.08) [0.014]	0.01 (0.063) [0.001]
(3)	First Quarter, 1919	0.113* (0.06) [0.011]	0.187** (0.083) [0.022]	0.047 (0.073) [0.004]
(4)	Second Quarter, 1919	0.03 (0.055) [0.003]	-0.065 *(0.089)* [-0.007]	0.127** *(0.064)* [0.011]

Entries in the table represent the estimated coefficient, standard errors, and marginal effects from a logit model. Row (1) contains the results from a specification identifying flu exposure from being born in the 4th quarter of 1918, or the 1st or 2nd quarters of 1919. Rows (2)-(4) contain the results from a specification with dummy variables indicating the particular quarters of birth. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

Table 20
Logit Estimates of Effect of Flu Exposure on Heart Disease
Adults aged 55 to 90, 1982 to 2002 NHIS

Parameter estimates (standard errors) [Marginal Effect]

		(1)	(2)	(3)
	Quarter of Birth	Full Sample n= 383,785 mean dep. var. = 0.107	Men n= 165,308 mean dep. var. = 0.124	Women n= 218,477 mean dep. var. = 0.095
(1)	1st Quarter 1917	-0.064	-0.043	-0.077
		(0.046)	(0.074)	(0.063)
		[-0.006]	[-0.004]	[-0.006]
(2)	2nd Quarter 1917	-0.019	0.031	-0.067
		(0.053)	(0.059)	(0.06)
		[-0.002]	[0.003]	[-0.005]
(3)	3rd Quarter 1917	-0.019	0.028	-0.061
		(0.043)	(0.06)	(0.075)
		[-0.002]	[0.003]	[-0.005]
(4)	4th Quarter 1917	0.055	0.001	0.116
		(0.07)	(0.01)	(0.082)
		[0.005]	[0.0001]	[0.01]
(5)	1st Quarter 1918	0.086	0.181**	0.004
		(0.062)	(0.065)	(0.087)
		[0.008]	[0.02]	[0.0003]
(6)	2nd Quarter 1918	-0.001	-0.015	0.017
		(0.05)	(0.081)	(0.053)
		[-0.0001]	[-0.002]	[0.001]
(7)	3rd Quarter 1918	-0.056	-0.223**	0.091
		(0.054)	(0.086)	(0.071)
		[-0.005]	[-0.021]	[0.008]
(8)	4th Quarter 1918	0.066	0.129	0.01
		(0.048)	(0.08)	(0.063)
		[0.006]	[0.014]	[0.001]
(9)	1st Quarter 1919	0.118**	0.2**	0.045
		(0.063)	(0.084)	(0.074)
		[0.011]	[0.023]	[0.004]
(10)	2nd Quarter 1919	0.028	-0.06	0.118*
		(0.056)	(0.09)	(0.065)
		[0.003]	[-0.006]	[0.01]
(11)	3rd Quarter 1919	-0.02	0.066	-0.105
		(0.053)	(0.065)	(0.083)
		[-0.002]	[0.007]	[-0.008]
(12)	4th Quarter 1919	0.027	0.058	0.001
		(0.087)	(0.115)	(0.108)
		[0.003]	[0.006]	[0.0001]
(13)	1st Quarter	0.097	0.129	0.066

	1920	(0.066)	(0.08)	(0.078)
		[0.009]	[0.014]	[0.005]
(14)	2nd Quarter	-0.022	0.06	-0.111
	1920	(0.066)	(0.078)	(0.075)
		[-0.002]	[0.006]	[-0.009]
(15)	3rd Quarter	-0.112**	0.003	-0.236**
	1920	(0.055)	(0.074)	(0.074)
		[-0.01]	[0.0003]	[-0.017]
(14)	4th Quarter	-0.06	-0.049	-0.069
	1920	(0.055)	(0.089)	(0.085)
		[-0.005]	[-0.005]	[-0.005]

Entries in the table represent the estimated coefficient, standard errors, and marginal effects from a logit model. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

Table 21
Logit Estimates of Effect of Flu Exposure on Heart Disease
Adults aged 55 to 90, 1982 to 2002 NHIS

Parameter estimates (standard errors) [Marginal Effect]

		(1)	(2)	(3)
	Quarter of Birth	Full Sample n= 383,785 mean dep. var. = 0.107	Men n= 165,308 mean dep. var. = 0.124	Women n= 218,477 mean dep. var. = 0.095
(1)	October, 1918	-0.093	0.04	-0.215*
		(0.076)	(0.126)	(0.11)
		[-0.008]	[0.004]	[-0.016]
(2)	November, 1918	0.005	0.059	-0.048
		(0.1)	(0.163)	(0.127)
		[0.0005]	[0.006]	[-0.004]
(3)	December, 1918	0.256**	0.261**	0.254*
		(0.096)	(0.11)	(0.138)
		[0.026]	[0.03]	[0.023]
(4)	January, 1919	0.143	0.298**	-0.017
		(0.1)	(0.116)	(0.137)
		[0.014]	[0.035]	[-0.001]
(5)	February, 1919	0.07	0.117	0.036
		(0.104)	(0.107)	(0.142)
		[0.006]	[0.013]	[0.003]
(6)	March, 1919	0.121	0.135	0.117
		(0.105)	(0.131)	(0.125)
		[0.011]	[0.015]	[0.01]
(7)	April, 1919	-0.027	-0.026	-0.027
		(0.107)	(0.123)	(0.16)
		[-0.002]	[-0.003]	[0.002]
(8)	May, 1919	0.083	0.019	0.154*
		(0.089)	(0.146)	(0.092)
		[0.008]	[0.002]	[0.013]
(9)	June, 1919	0.035	-0.221	0.243**
		(0.1)	(0.153)	(0.123)
		[0.003]	[-0.021]	[0.022]

Entries in the table represent the estimated coefficient, standard errors, and marginal effects from a logit model. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

Table 22
Logit Estimates of Effect of Flu Exposure on Diabetes, Adults aged 55 to 90, 1982 to 2002 NHIS

Parameter estimates (standard errors) [Marginal Effect]

		(1)	(2)	(3)
	Quarter of Birth	Full Sample n= 383,785 mean dep. var. = 0.067	Men n= 165,308 mean dep. var. = 0.064	Women n= 218.477 mean dep. var. = 0.069
(1)	Flu Season[1]	0.057 (0.066) [0.003]	0.033 (0.08) [0.002]	0.078 (0.075) [0.004]
(2)	Fourth Quarter, 1918	-0.014 (0.079) [-0.001]	0.038 (0.122) [0.002]	-0.05 (0.085) [-0.003]
(3)	First Quarter, 1919	-0.036 (0.105) [-0.002]	-0.138 (0.141) [-0.007]	0.034 (0.136) [0.002]
(4)	Second Quarter, 1919	0.209** *(0.109)* [0.013]	0.175 (0.147) [0.01]	0.238* (0.124) [0.015]

Entries in the table represent the estimated coefficient, standard errors, and marginal effects from a logit model. Row (1) contains the results from a specification identifying flu exposure from being born in the 4th quarter of 1918, or the 1st or 2nd quarters of 1919. Rows (2)-(4) contain the results from a specification with dummy variables indicating the particular quarters of birth. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

Table 23
Logit Estimates of Effect of Flu Exposure on Diabetes
Adults aged 55 to 90, 1982 to 2002 NHIS

Parameter estimates (standard errors) [Marginal Effect]

		(1)	(2)	(3)
	Quarter of Birth	Full Sample n= 383,785 mean dep. var. = 0.067	Men n= 165,308 mean dep. var. = 0.064	Women n= 218.477 mean dep. var. = 0.069
(1)	1st Quarter 1917	0.021	0.094	0.032
		(0.084)	(0.105)	(0.115)
		[0.001]	[0.005]	[-0.002]
(2)	2nd Quarter 1917	0.199**	0.331***	0.09
		(0.077)	(0.092)	(0.105)
		[0.012]	[0.02]	[0.005]
(3)	3rd Quarter 1917	-0.006	0.074	-0.068
		(0.059)	(0.109)	(0.095)
		[-0.003]	[0.004]	[-0.004]
(4)	4th Quarter 1917	0.015	-0.047	0.061
		(0.101)	(0.13)	(0.129)
		[0.001]	[-0.002]	[0.004]
(5)	1st Quarter 1918	0.09	0.008	0.138
		(0.078)	(0.122)	(0.09)
		[0.005]	[0.0004]	[0.008]
(6)	2nd Quarter 1918	0.033	0.088	-0.004
		(0.077)	(0.111)	(0.084)
		[0.002]	[0.005]	[-0.0002]
(7)	3rd Quarter 1918	0.147	0.192	0.118
		(0.095)	(0.162)	(0.086)
		[0.009]	[0.01]	[0.007]
(8)	4th Quarter 1918	-0.005	0.053	-0.045
		(0.08)	(0.123)	(0.086)
		[-0.0002]	[0.003]	[-0.003]
(9)	1st Quarter 1919	-0.017	-0.114	0.054
		(0.106)	(0.141)	(0.137)
		[-0.001]	[-0.006]	[0.003]
(10)	2nd Quarter 1919	0.223**	0.198	0.246**
		(0.11)	(0.149)	(0.125)
		[0.014]	[0.012]	[0.016]
(11)	3rd Quarter 1919	-0.006	-0.054	0.027
		(0.09)	(0.142)	(0.107)
		[-0.0003]	[-0.003]	[0.002]
(12)	4th Quarter 1919	0.032	0.066	0.01
		(0.074)	(0.124)	(0.1)
		[0.002]	[0.004]	[0.001]

(13)	1st Quarter	0.213**	0.263**	0.173**
	1920	(0.07)	(0.101)	(0.081)
		[0.013]	[0.016]	[0.011]
(14)	2nd Quarter	0002	-0.043	0.03
	1920	(0.11)	(0.159)	(0.135)
		[0.0001]	[-0.002]	[0.002]
(15)	3rd Quarter	-0.146	-0.149	-0.142
	1920	(0.1)	(0.143)	(0.1)
		[-0.008]	[-0.008]	[-0.008]
(14)	4th Quarter	0.003	0.044	-0.027
	1920	(0.093)	(0.122)	(0.1)
		[0.0002]	[0.002]	[-0.002]

Entries in the table represent the estimated coefficient, standard errors, and marginal effects from a logit model. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

Table 24
Logit Estimates of Effect of Flu Exposure on Diabetes
Adults aged 55 to 90, 1982 to 2002 NHIS

Parameter estimates (standard errors) [Marginal Effect]

		(1)	(2)	(3)
	Quarter of Birth	Full Sample n= 383,785 mean dep. var. = 0.067	Men n= 165,308 mean dep. var. = 0.064	Women n= 218,477 mean dep. var. = 0.069
(1)	October, 1918	-0.002	0.003	-0.007
		(0.099)	(0.214)	(0.128)
		[-0.0001]	[0.0001]	[-0.0004]
(2)	November, 1918	-0.043	-0.009	-0.071
		(0.155)	(0.185)	(0.196)
		[-0.002]	[-0.0005]	[-0.004]
(3)	December, 1918	0.0002	0.106	-0.078
		(0.108)	(0.165)	(0.153)
		[0.00001]	[0.006]	[-0.004]
(4)	January, 1919	-0.105	-0.185	-0.039
		(0.163)	(0.252)	(0.17)
		[-0.006]	[-0.009]	[-0.002]
(5)	February, 1919	0.126	0.108	0.144
		(0.144)	(0.179)	(0.187)
		[0.007]	[0.006]	[0.009]
(6)	March, 1919	-0.126	-0.328	0.01
		(0.154)	(0.204)	(0.211)
		[-0.007]	[-0.015]	[0.0006]
(7)	April, 1919	0.255*	0.257	0.261*
		(0.137)	(0.198)	(0.145)
		[0.016]	[0.015]	[0.017]
(8)	May, 1919	0.214**	0.069	0.321**
		(0.104)	(0.197)	(0.152)
		[0.013]	[0.004]	[0.021]
(9)	June, 1919	0.152	0.185	0.129
		(0.176)	(0.279)	(0.198)
		[0.009]	[0.011[	[0.008]

Entries in the table represent the estimated coefficient, standard errors, and marginal effects from a logit model. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

.Table 25
Logit Estimates of Effect of Flu Exposure on Kidney Disorders, Adults aged 55 to 90, 1982 to 2002
NHIS

Parameter estimates (standard errors) [Odds ratios]

		(1)	(2)	(3)
	Quarter of Birth	Full Sample n= 325,487 mean dep. var. = 0.006	Men n= 141,855 mean dep. var. = 0.005	Women n= 183,632 mean dep. var. = 0.007
(1)	Flu Season[1]	0.18 (0.126) [0.001]	0.282 (0.207) [0.001]	0.108 (0.177) [0.001]
(2)	Fourth Quarter, 1918	0.438** (0.195) [0.003]	0.414 (0.361) [0.002]	0.447* (0.269) [0.003]
(3)	First Quarter, 1919	-0.78 (0.238) [-0.0004]	0.042 (0.408) [0.0002]	-0.169 (0.32) [-0.001]
(4)	Second Quarter, 1919	0.164 (0.253) [0.001]	0.387 (0.322) [0.002]	0.001 (0.336) [0.000]

Entries in the table represent the estimated coefficient, standard errors, and marginal effects from a logit model. Row (1) contains the results from a specification identifying flu exposure from being born in the 4th quarter of 1918, or the 1st or 2nd quarters of 1919. Rows (2)-(4) contain the results from a specification with dummy variables indicating the particular quarters of birth. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

Table 26
Logit Estimates of Effect of Flu Exposure on Kidney Disease
Adults aged 55 to 90, 1982 to 2002 NHIS

Parameter estimates (standard errors) [Marginal Effect]

		(1)	(2)	(3)
	Quarter of Birth	Full Sample n= 325,487 mean dep. var. = 0.006	Men n= 141,855 mean dep. var. = 0.005	Women n= 183.632 mean dep. var. = 0.007
(1)	1st Quarter 1917	-0.126	-0.128	-0.125
		(0.192)	(0.435)	(0.261)
		[-0.001]	[-0.0001]	[-0.001]
(2)	2nd Quarter 1917	0.159	0.453	-0.039
		(0.314)	(0.477)	(0.253)
		[0.001]	[0.002]	[-0.0002]
(3)	3rd Quarter 1917	-0.177	-0.044	-0.247
		(0.196)	(0.368)	(0.236)
		[-0.001]	[-0.0001]	[-0.001]
(4)	4th Quarter 1917	0.003	0.319	-0.273
		(0.249)	(0.333)	(0.385)
		[0.000]	[0.001]	[-0.001]
(5)	1st Quarter 1918	0.206	0.119	0.247
		(0.277)	(0.453)	(0.265)
		[0.001]	[0.0005]	[0.001]
(6)	2nd Quarter 1918	0.351	0.109	0.465
		(0.255)	(0.477)	(0.323)
		[0.002]	[0.0004]	[0.003]
(7)	3rd Quarter 1918	-0.324	-0.579	-0.206
		(0.294)	(0.455)	(0.353)
		[-0.001]	[-0.002]	[-0.001]
(8)	4th Quarter 1918	0.414**	0.398	0.419*
		(0.196)	(0.362)	(0.272)
		[0.002]	[0.002]	[0.003]
(9)	1st Quarter 1919	-0.087	0.032	-0.177
		(0.238)	(0.409)	(0.321)
		[-0.0004]	[0.0001]	[-0.001]
(10)	2nd Quarter 1919	0.192	0.41	0.033
		(0.253)	(0.324)	(0.335)
		[0.001]	[0.002]	[0.0001]
(11)	3rd Quarter 1919	0.125	-0.069	0.218
		(0.191)	(0.319)	(0.232)
		[0.001]	[-0.0002]	[0.001]
(12)	4th Quarter	-0.059	-0.226	0.0258

	1919	(0.191)	(0.364)	(0.22)
		[-0.0003]	[-0.001]	[0.0001]
(13)	1st Quarter	-0.266	-0.158	-0.322
	1920	(0.266)	(0.432)	(0.342)
		[-0.001]	[-0.001]	[-0.002]
(14)	2nd Quarter	0.24	0.061	0.332
	1920	(0.243)	(0.472)	(0.294)
		[0.001]	[0.0002]	[0.002]
(15)	3rd Quarter	-0.147	0.073	-0.302
	1920	(0.308)	(0.436)	(0.329)
		[-0.001]	[0.0003]	[-0.001]
(14)	4th Quarter	-0.616	-0.662	-0.586
	1920	(0.412)	(0.727)	(0.566)
		[-0.002]	[-0.002]	[-0.002]

Entries in the table represent the estimated coefficient, standard errors, and marginal effects from a logit model. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

Table 27
Logit Estimates of Effect of Flu Exposure on Kidney Disease
Adults aged 55 to 90, 1982 to 2002 NHIS

Parameter estimates (standard errors) [Marginal Effect]

		(1)	(2)	(3)
		Full Sample	Men	Women
	Quarter of	n= 325,487	n= 141,855	n= 183,632
	Birth	mean dep. var. = 0.006	mean dep. var. = 0.005	mean dep. var. = 0.007
(1)	October,	0.561*	0.139	0.729**
	1918	(0.305)	(0.695)	(0.353)
		[0.004]	[0.001]	[0.006]
(2)	November,	0.652**	0.996**	0.451
	1918	(0.256)	(0.408)	(0.399)
		[0.004]	[0.006]	[0.003]
(3)	December,	-0.087	-0.036	-0.176
	1918	(0.457)	(0.692)	(0.64)
		[-0.0004]	[-0.0001]	[-0.001]
(4)	January,	0.492*	0.333	0.592
	1919	(0.29)	(0.526)	(0.431)
		[0.003]	[0.001[	[0.004]
(5)	February,	-0.614	-0.622	-0.617
	1919	(0.528)	(1.01)	(0.665)
		[-0.002]	[-0.002]	[-0.003]
(6)	March, 1919	-0.45	0.106	-1.29
		(0.43)	(0.53)	(0.978)
		[-0.002]	[0.0004]	[-0.004]
(7)	April, 1919	0.358	1.06**	-0.424
		(0.351)	(0.419)	(0.656)
		[0.002]	[0.007]	[-0.002]
(8)	May,	0.196	0.261	0.132
	1919	(0.391)	(0.788)	(0.441)
		[0.001]	[0.001]	[0.001]
(9)	June,	-0.092	-0.723	0.154
	1919	(0.482)	(0.898)	(0.579)
		[-0.0004]	[-0.002]	[0.001

Entries in the table represent the estimated coefficient, standard errors, and marginal effects from a logit model. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

Table 28
Logit Estimates of Effect of In-Utero Flu Exposure on Poor Health, Adults aged 55 to 90, 1982 to 2002 NHIS

Parameter estimates (standard errors) [Odds ratios]

		(1)	(2)	(3)
	Quarter of Birth	Full Sample n= 383,785 mean dep. var. = 0.265	Men n= 165,308 mean dep. var. = 0.262	Women n= 218,477 mean dep. var. = 0.267
(1)	Flu Season[1]	0.086***	0.0624*	0.103**
		(0.024)	(0.034)	(0.03)
		[0.017]	[0.012]	[0.02]
(2)	Fourth Quarter, 1918	0.084*	0.03	0.121**
		(0.047)	(0.076)	(0.048)
		[0.016]	[0.006]	[0.024]
(3)	First Quarter, 1919	0.081**	0.112**	0.057
		(0.032)	(0.054)	(0.057)
		[0.016]	[0.022]	[0.011]
(4)	Second Quarter, 1919	0.094**	0.045	0.131**
		(0.037)	(0.064)	(0.049)
		[0.018]	[0.009]	[0.026]

Entries in the table represent the estimated coefficient, standard errors, and marginal effects from a logit model. Row (1) contains the results from a specification identifying flu exposure from being born in the 4th quarter of 1918, or the 1st or 2nd quarters of 1919. Rows (2)-(4) contain the results from a specification with dummy variables indicating the particular quarters of birth. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

Table 29
Logit Estimates of Effect of Flu Exposure on Poor Health
Adults aged 55 to 90, 1982 to 2002 NHIS

Parameter estimates (standard errors) [Marginal Effect]

		(1)	(2)	(3)
	Quarter of Birth	Full Sample n= 383,785 mean dep. var. = 0.265	Men n= 165,308 mean dep. var. = 0.262	Women n= 218,477 mean dep. var. = 0.267
(1)	1st Quarter 1917	-0.018	0.026	-0.013
		(0.035)	(0.05)	(0.053)
		[-0.003]	[-0.005]	[-0.002]
(2)	2nd Quarter 1917	0.011	0.004	0.012
		(0.039)	(0.058)	(0.048)
		[0.002]	[0.001]	[0.002]
(3)	3rd Quarter 1917	0.021	0.011	0.027
		(0.042)	(0.074)	(0.034)
		[0.004]	[0.002]	[0.005]
(4)	4th Quarter 1917	0.002	-0.043	0.037
		(0.04)	(0.057)	(0.057)
		[0.0004]	[-0.008]	[0.007]
(5)	1st Quarter 1918	-0.021	-0.072	0.014
		(0.037)	(0.056)	(0.043)
		[-0.004]	[-0.013]	[0.003]
(6)	2nd Quarter 1918	-0.004	0.052	-0.046
		(0.035)	(0.047)	(0.048)
		[-0.001]	[0.01]	[-0.009]
(7)	3rd Quarter 1918	0.000	-0.006	0.004
		[0.035]	(0.05)	(0.051)
		[0.000]	[-0.001]	[0.001]
(8)	4th Quarter 1918	0.081*	0.026	0.117**
		[0.047]	(0.077)	(0.048)
		[0.015]	[0.005]	[0.23]
(9)	1st Quarter 1919	0.079**	0.109**	0.057
		(0.033)	(0.055)	(0.058)
		[0.015]	[0.021]	[0.011]
(10)	2nd Quarter 1919	0.094**	0.045	0.13**
		(0.038)	(0.065)	(0.05)
		[0.018]	[0.009]	[0.025]
(11)	3rd Quarter 1919	-0.025	-0.065	0.006
		(0.039)	(0.063)	(0.048)
		[-0.005]	[-0.012]	[0.001]
(12)	4th Quarter 1919	-0.054	0.004	-0.101*
		(0.044)	(0.0516)	(0.055)
		[-0.01]	[0.001]	[-0.019]
(13)	1st Quarter 1920	0.025	0.064	-0.006
		(0.04)	(0.065)	(0.061)
		[0.005]	[0.012]	[-0.001]
(14)	2nd Quarter 1920	0.021	0.003	0.033
		(0.04)	(0.0562)	(0.058)
		[0.004]	[0.001]	[0.006]

(15)	3rd Quarter	-0.087**	-0.136**	-0.046
	1920	(0.035)	(0.042)	(0.067)
		[-0.016]	[-0.025]	[-0.009]
(14)	4th Quarter	-0.014	-0.012	-0.016
	1920	(0.038)	(0.052)	(0.052)
		[-0.003]	[-0.002]	[-0.003]

Entries in the table represent the estimated coefficient, standard errors, and marginal effects from a logit model. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

Table 30
Logit Estimates of Effect of Flu Exposure on Poor Health
Adults aged 55 to 90, 1982 to 2002 NHIS

Parameter estimates (standard errors) [Marginal Effect]

		(1)	(2)	(3)
	Quarter of Birth	Full Sample n= 383,785 mean dep. var. = 0.265	Men n= 165,308 mean dep. var. = 0.262	Women n= 218,477 mean dep. var. = 0.267
(1)	October, 1918	0.001	-0.064	0.044
		(0.07)	(0.107)	(0.086)
		[0.0003]	[-0.012]	[0.009]
(2)	November, 1918	-0.013	-0.125	0.066
		(0.079)	(0.136)	(0.084)
		[-0.002]	[-0.023]	[0.013]
(3)	December, 1918	0.253***	0.252*	0.249**
		(0.078)	(0.137)	(0.086)
		[0.051]	[0.051]	[0.051]
(4)	January, 1919	0.144**	0.216**	0.085
		(0.071)	(0.107)	(0.1)
		[0.029]	[0.043]	[0.017]
(5)	February, 1919	0.113*	0.096	0.126*
		(0.06)	(0.121)	(0.066)
		[0.022]	[0.019]	[0.025]
(6)	March, 1919	-0.008	0.028	-0.036
		(0.06)	(0.095)	(0.011)
		[-0.001]	[0.053]	[-0.007]
(7)	April, 1919	0.131**	0.076	0.171**
		(0.056)	(0.01)	(0.084)
		[0.026]	[0.015]	[0.034]
(8)	May, 1919	0.097	-0.008	0.179**
		(0.082)	(0.124)	(0.088)
		[0.019]	[-0.002]	[0.036]
(9)	June, 1919	0.053	0.069	0.044
		(0.078)	(0.098)	(0.092)
		[0.01]	[0.013]	[0.008]

Entries in the table represent the estimated coefficient, standard errors, and marginal effects from a logit model. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

Table 31
Estimates for Educational Attainment, Adults aged 55 to 90, 1982 to 2002 NHIS

Parameter estimates (standard errors) [Marginal Effect]

		(1)	(2)	(3)	(4)	(5)	(6)
		Highest Grade Completed OLS Coefficient Full Sample n= 383,785 Mean Dep. Var = 11.68	Highest Grade Completed OLS Coefficient Men Only n= 165,308 Mean Dep. Var = 11.82	Highest Grade Completed OLS Coefficient Women Only n= 218,477 Mean dep. Var. = 11.57	High School Graduate Logit Coefficient Full Sample n= 383,785 Mean dep. Var= 0.63	High School Graduate Logit Coefficient Men Only n= 165,308 Mean dep. Var = 0.626	High School Graduate Logit Coefficient Women Only n= 218,477 Mean dep. var. = 0.627
					-0.009	0.026	-0.036
	Flu	0.001	-0.006	0.013	(0.02)	(0.033)	(0.026)
(1)	Season[1]	(0.064)	(0.07)	(0.089)	[-0.002]	[0.006]	[-0.008]
	Fourth				0.00001	0.042	-0.03
	Quarter,	0.1	0.128	0.085	(.034)	(0.062)	(0.049)
(2)	1918	(0.1)	(0.111)	(0.137)	[0.000]	[0.01]	[-0.007]
	First				-0.012	0.026	-0.038
	Quarter,	-0.03	-0.049	-0.005	(0.041)	(0.065)	(0.043)
(3)	1919	(0.108)	(0.139)	(0.128)	[-0.003]	[0.006]	[-0.009]
	Second				-0.016	0.011	-0.039
	Quarter,	-0.069	-0.093	-0.045	(0.04)	(0.055)	(0.048)
(4)	1919	(0.085)	(0.093)	(0.141)	[-0.004]	[0.003]	[-0.009]

Entries in Column (1)-(3) represent the estimated coefficients and standard errors from an ordinary least squares regression. Entries columns (4)-(6) represent the estimated coefficient, standard errors, and marginal effects from a logit model. Row (1) contains the results from a specification identifying flu exposure from being born in the 4th quarter of 1918, or the 1st or 2nd quarters of 1919. Rows (2)-(4) contain the results from a specification with dummy variables indicating the particular quarters of birth. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

Table 32
Estimates for Educational Attainment, Adults aged 55 to 90, 1982 to 2002 NHIS

Parameter estimates (standard errors) [Marginal Effect]

		(1)	(2)	(3)	(4)	(5)	(6)
		Highest Grade Completed OLS Coefficient Full Sample n= 383,785 Mean Dep. Var = 11.68	Highest Grade Completed OLS Coefficient Men Only n= 165,308 Mean Dep. Var = 11.82	Highest Grade Completed OLS Coefficient Women Only n= 218,477 Mean dep. Var. = 11.57	High School Graduate Logit Coefficient Full Sample n= 383,785 Mean dep. Var= 0.63	High School Graduate Logit Coefficient Men Only n= 165,308 Mean dep. Var = 0.626	High School Graduate Logit Coefficient Women Only n= 218,477 Mean dep. var. = 0.627
(1)	1st Quarter 1917	0.052 (0.118)	-0.079 (0.108)	0.143 (0.157)	0.029 (0.039) [0.007]	-0.016 (0.078) [-0.004]	0.061 (0.043) [0.014]
(2)	2nd Quarter 1917	0.114 (0.114)	0.19 (0.153)	0.054 (0.129)	0.022 (0.047) [0.005]	0.111 (0.081) [0.025]	-0.049 (0.063) [-0.011]
(3)	3rd Quarter 1917	0.044 (0.136)	0.188 (0.25)	-0.068 (0.09)	0.05 (0.038) [0.011]	0.041 (0.054) [0.001]	0.053 (0.044) [0.012]
(4)	4th Quarter 1917	0.004 (0.104)	-0.025 (0.141)	0.031 (0.116)	0.026 (0.032) [0.006]	0.058 (0.049) [0.013]	-0.003 (0.049) [-0.001]
(5)	1st Quarter 1918	0.207* (0.102)	0.083 (0.116)	0.296 (0.182)	0.094** (.047) [0.021]	0.068 (0.049) [0.016]	0.113 (0.069) [0.026]
(6)	2nd Quarter 1918	0.09 (0.082)	0.088 (0.134)	0.091 (0.09)	0.105** (0.038) [0.024]	0.144** (0.052) [0.033]	0.075 (0.051) [0.017]
(7)	3rd Quarter 1918	0.187** (0.084	0.258** (0.092)	0.146 (0.107)	0.102** (0.033) [0.023]	0.175** (0.043) [0.039]	0.048 (0.045) [0.011]
(8)	4th Quarter 1918	0.122 (0.103)	0.157 (0.112)	0.102 (0.141)	0.016 (0.034) [0.004]	0.068 (0.063) [0.016]	-0.021 (0.049) [-0.005]
(9)	1st Quarter 1919	-0.003 (0.11)	-0.026 (0.14)	0.026 (0.129)	0.003 (0.041) [0.001]	0.045 (0.065) [0.01]	-0.028 (0.043) [-0.006]
(10)	2nd Quarter 1919	-0.042 (0.087)	-0.061 (0.096	-0.023 (0.143)	-0.003 (0.04) [-0.001]	0.037 (0.056) [0.008]	-0.034 (0.049) [-0.008]
(11)	3rd Quarter 1919	0.15* (0.085)	0.314** (0.121)	0.028 (0.106)	0.072 (0.027) [0.016]	0.18*** (0.042) [0.04]	-0.011 (0.044) [-0.003]

(12)	4th				0.059	0.112**	0.014
	Quarter	0.15	0.239*	0.085	(0.033	(0.054)	(0.048)
	1919	(0.114)	(0.144)	(0.141)	[0.013]	[0.026]	[0.003]
(13)	1st				0.045	0.097*	0.003
	Quarter	0.106	0.115	0.09	(0.039)	(0.053)	(0.044)
	1920	(0.111)	(0.153)	(0.121)	[0.01]	[0.022]	[0.001]
(14)	2nd				0.033	0.091*	0.003
	Quarter	0.158	0.139	0.171	(0.034)	(0.047)	(0.044)
	1920	(0.104)	(0.138)	(0.118)	[0.008]	[0.021]	[-0.002]
(15)	3rd				0.067*	0.116**	0.029
	Quarter	0.139	0.16	0.123	(0.04)	(0.045)	(0.05)
	1920	(0.104)	(0.105)	(0.113)	[0.016]	[0.026]	[0.01]
(16)	4th				0.138**	0.148**	0.127**
	Quarter	0.054	0.065	0.041	(0.049)	(0.053)	(0.059)
	1920	(0.093)	(0.085)	(0.123)	[0.031]	[0.034]	[0.029]

Entries in Column (1)-(3) represent the estimated coefficients and standard errors from an ordinary least squares regression. Entries columns (4)-(6) represent the estimated coefficient, standard errors, and marginal effects from a logit model. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

.

Table 33
Estimates for Educational Attainment, Adults aged 55 to 90, 1982 to 2002 NHIS

Parameter estimates (standard errors) [Marginal Effect]

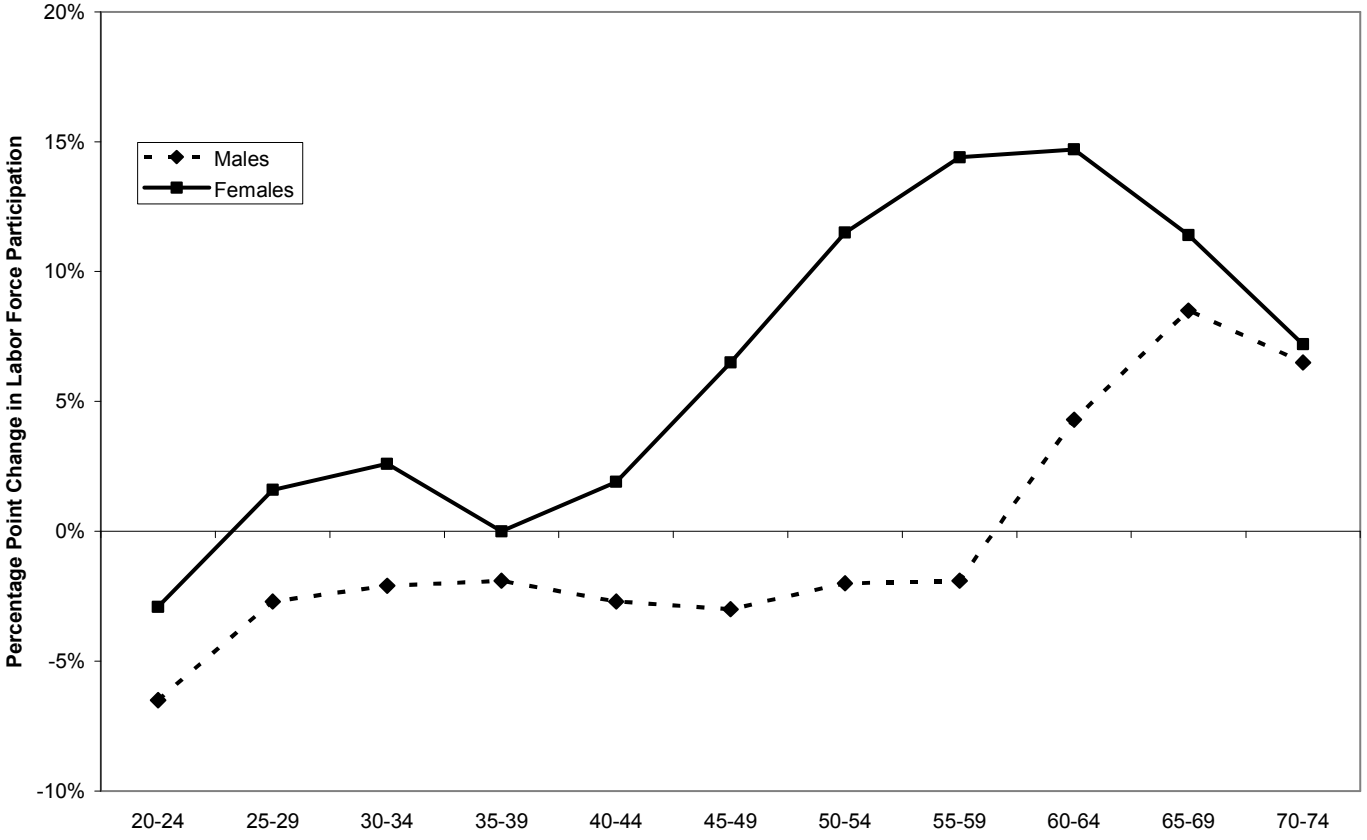
		(1)	(2)	(3)	(4)	(5)	(6)
		Highest Grade Completed OLS Coefficient Full Sample n= 383,785 Mean Dep. Var = 11.68	Highest Grade Completed OLS Coefficient Men Only n= 165,308 Mean Dep. Var = 11.82	Highest Grade Completed OLS Coefficient Women Only n= 218,477 Mean dep. Var. = 11.57	High School Graduate Logit Coefficient Full Sample n= 383,785 Mean dep. Var= 0.63	High School Graduate Logit Coefficient Men Only n= 165,308 Mean dep. Var = 0.626	High School Graduate Logit Coefficient Women Only n= 218,477 Mean dep. var. = 0.627
(1)	October, 1918	0.107	0.242	0.022	0.049	0.191*	-0.045
		(0.137)	(0.204)	(0.177)	(0.067)	(0.106)	(0.084)
					[0.011]	[0.043]	[-0.01]
(2)	November, 1918	0.175	0.164	0.185	0.005	0.087	-0.056
		(0.263)	(0.183)	(0.367)	(0.056)	(0.079)	(0.066)
					[0.001]	[0.02]	[-0.013]
(3)	December, 1918	0.019	-0.02	0.053	-0.055	-0.145*	0.01
		(0.092)	(0.175)	(0.149)	(0.049)	(0.083)	(0.088)
					[-0.013]	[-0.034]	[0.002]
(4)	January, 1919	0.011	0.009	0.03	-0.057	0.044	-0.131
		(0.144)	(0.19)	(0.212)	(0.061)	(0.101)	(0.075)
					[-0.013]	[0.01]	[-0.007]
(5)	February, 1919	0.104	0.047	0.146	0.009	-0.023	0.032
		(0.132)	(0.141)	(0.181)	(0.061)	(0.089)	(0.079)
					[0.002]	[-0.005]	[0.007]
(6)	March, 1919	-0.187	-0.178	-0.18*	0.125	0.05	-0.017
		(0.135)	(0.239)	(0.097)	(0.074)	(0.114)	(0.07)
					[0.003]	[0.011]	[-0.004]
(7)	April, 1919	-0.12	0.08	-0.282	0.0006	0.087	-0.076
		(0.133)	(0.143)	(0.197)	(0.071)	(0.083)	(0.102)
					[0.0001]	[0.019]	[-0.018]
(8)	May, 1919	-0.107	-0.38	0.138	-0.096	-0.131	-0.064
		(0.189)	(0.13)	(0.366)	(0.07)	(0.101)	(0.11)
					[-0.022]	[-0.031]	[-0.015]
(9)	June, 1919	0.026	0.035	0.016	0.049	0.089	0.022
		(0.134)	(0.123)	(0.21)	(0.069)	(0.091)	(0.084)
					[0.011]	[0.02]	[0.005]

Entries in Column (1)-(3) represent the estimated coefficients and standard errors from an ordinary least squares regression. Entries columns (4)-(6) represent the estimated coefficient, standard errors, and marginal effects from a logit model. Other covariates include dummy variables for age, region, month of birth, sex, a cubic quarter of birth trend, race, and ethnicity. Standard errors are clustered on year of birth/year of survey cohorts to allow for within group correlation.

* Significant at .10 level ** Significant at .05 level *** Significant at .001 level

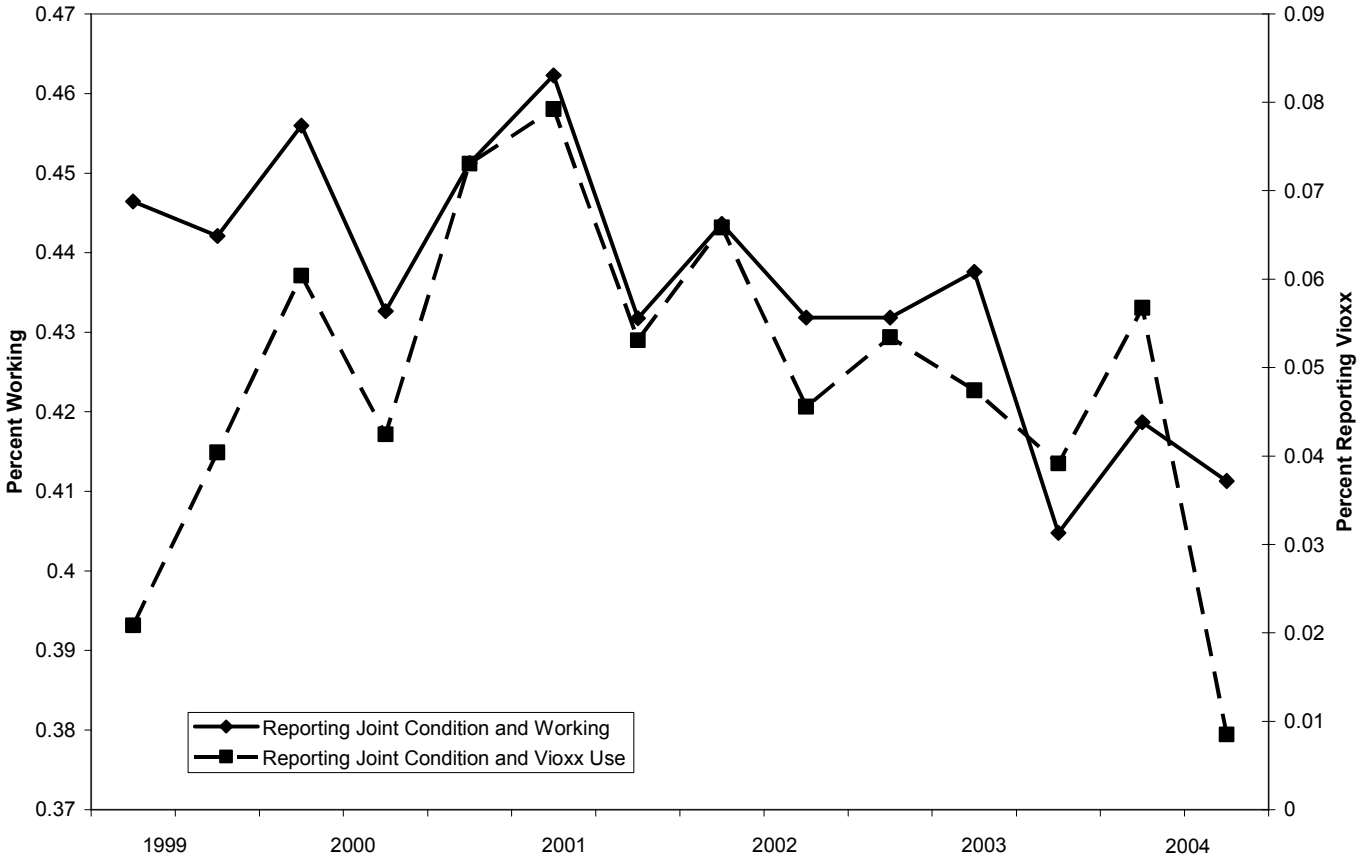
Figures

Figure 1 – Change in Labor Force Participation Rates by Age
1987-2007



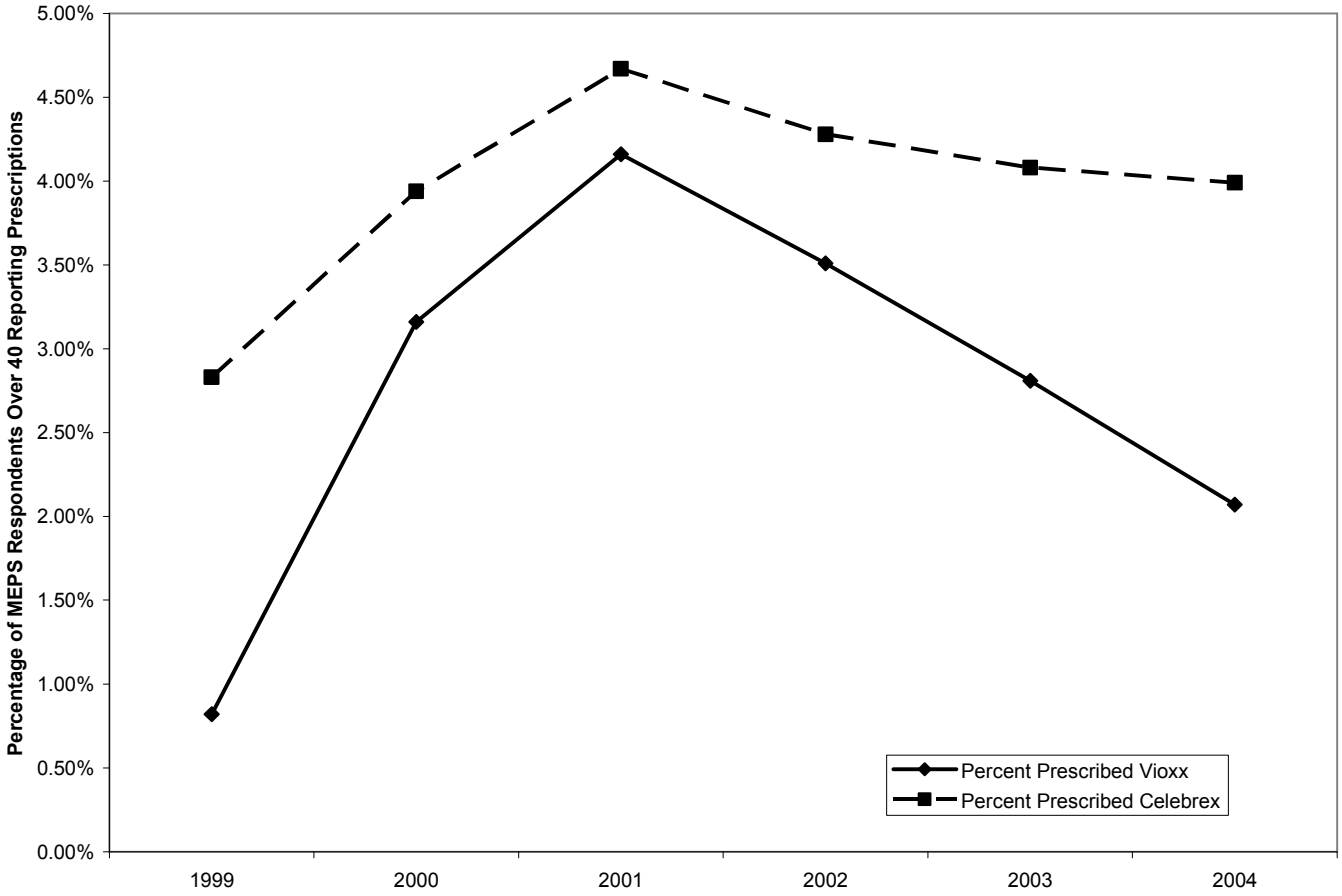
Source: Bureau of Labor Statistics

Figure 2 – Arthritic Labor Supply and the Percentage of Prescriptions for Vioxx, 1999-2004



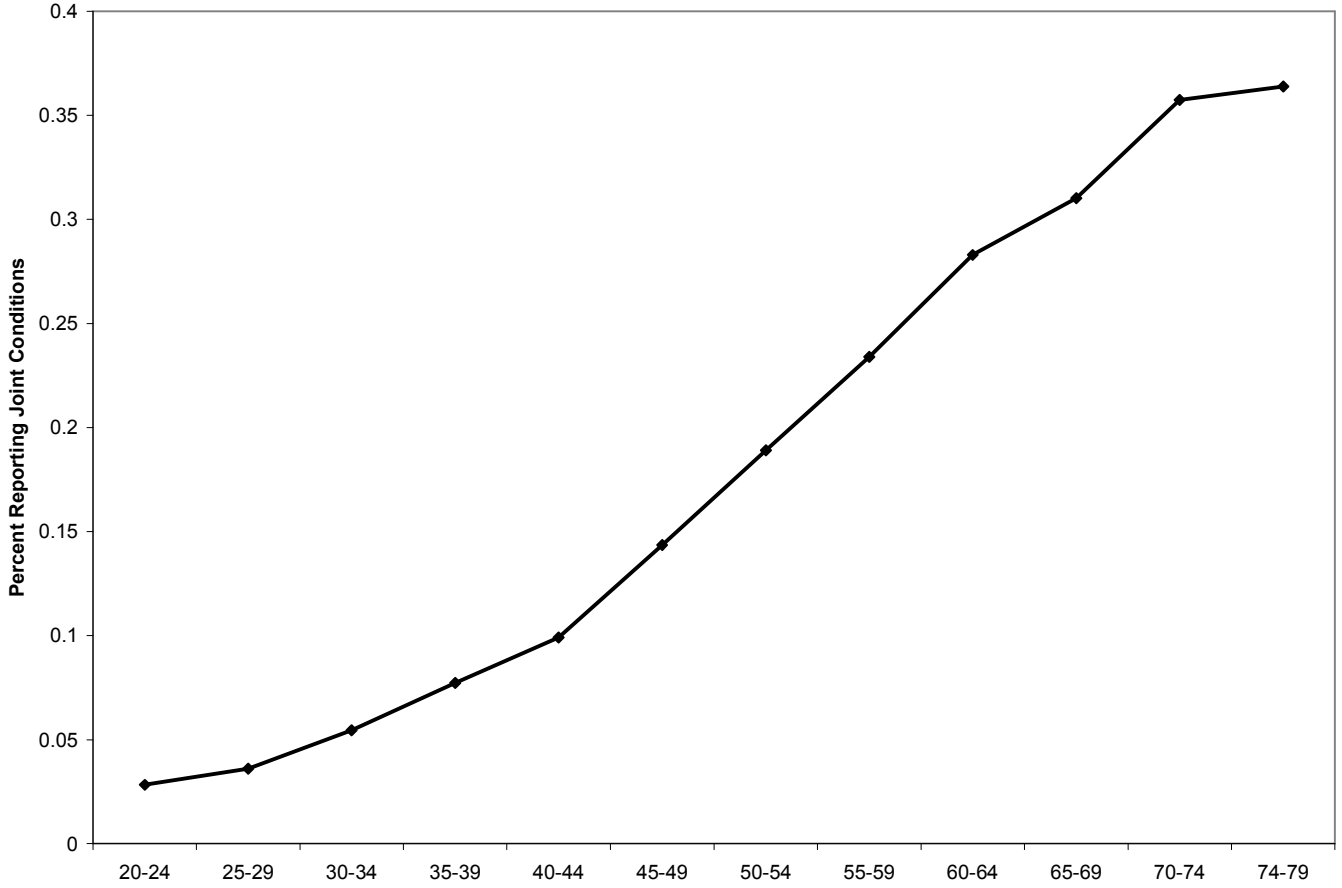
Source: Medical Expenditure Panel Survey, 1999-2004

Figure 3 – Vioxx and Celebrex Prescriptions by Year
MEPS Respondents, over Age 40, Reporting Prescriptions



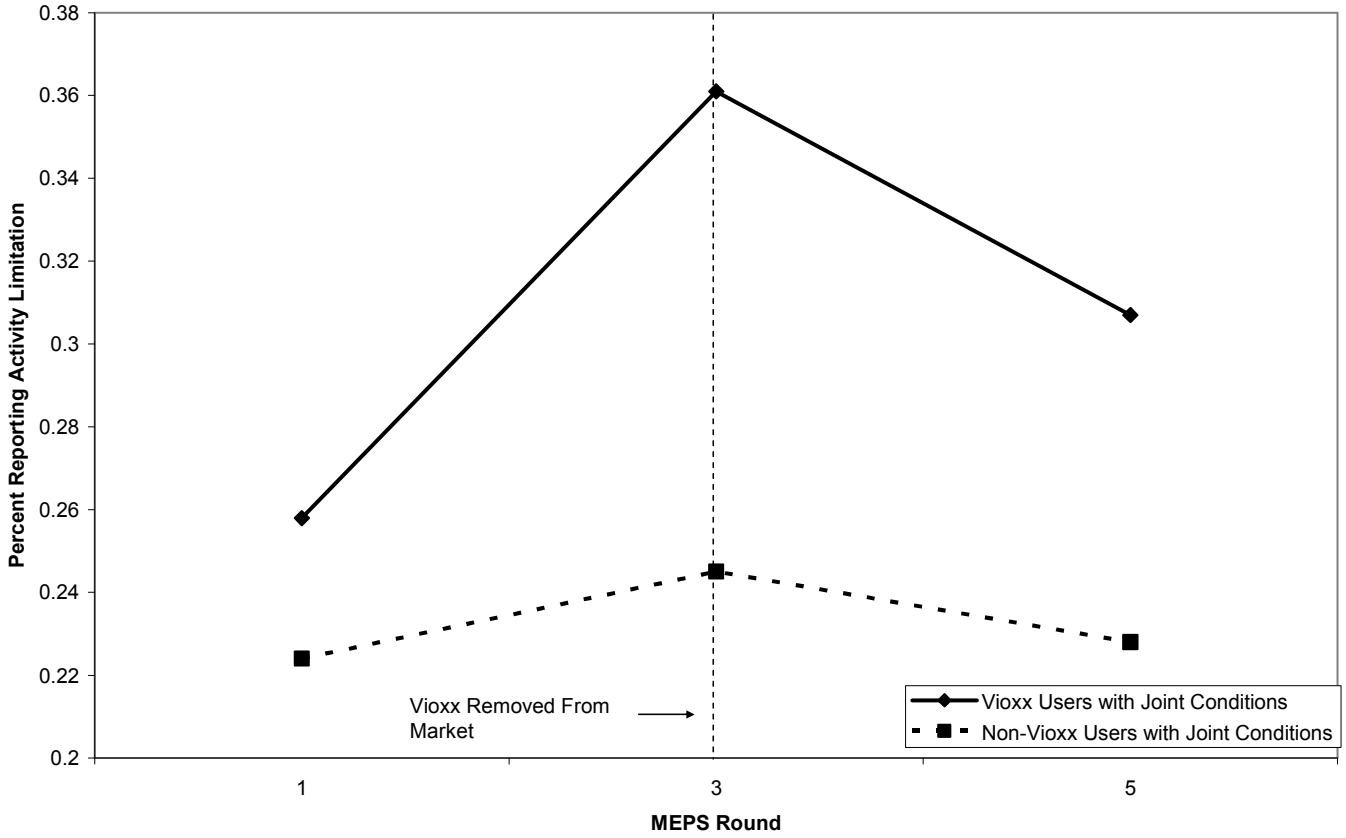
Source: Medical Expenditure Panel Survey, 1998-2004

Figure 4 – Percent of Respondents Reporting a Chronic Joint Condition by Age
MEPS 1998-2004



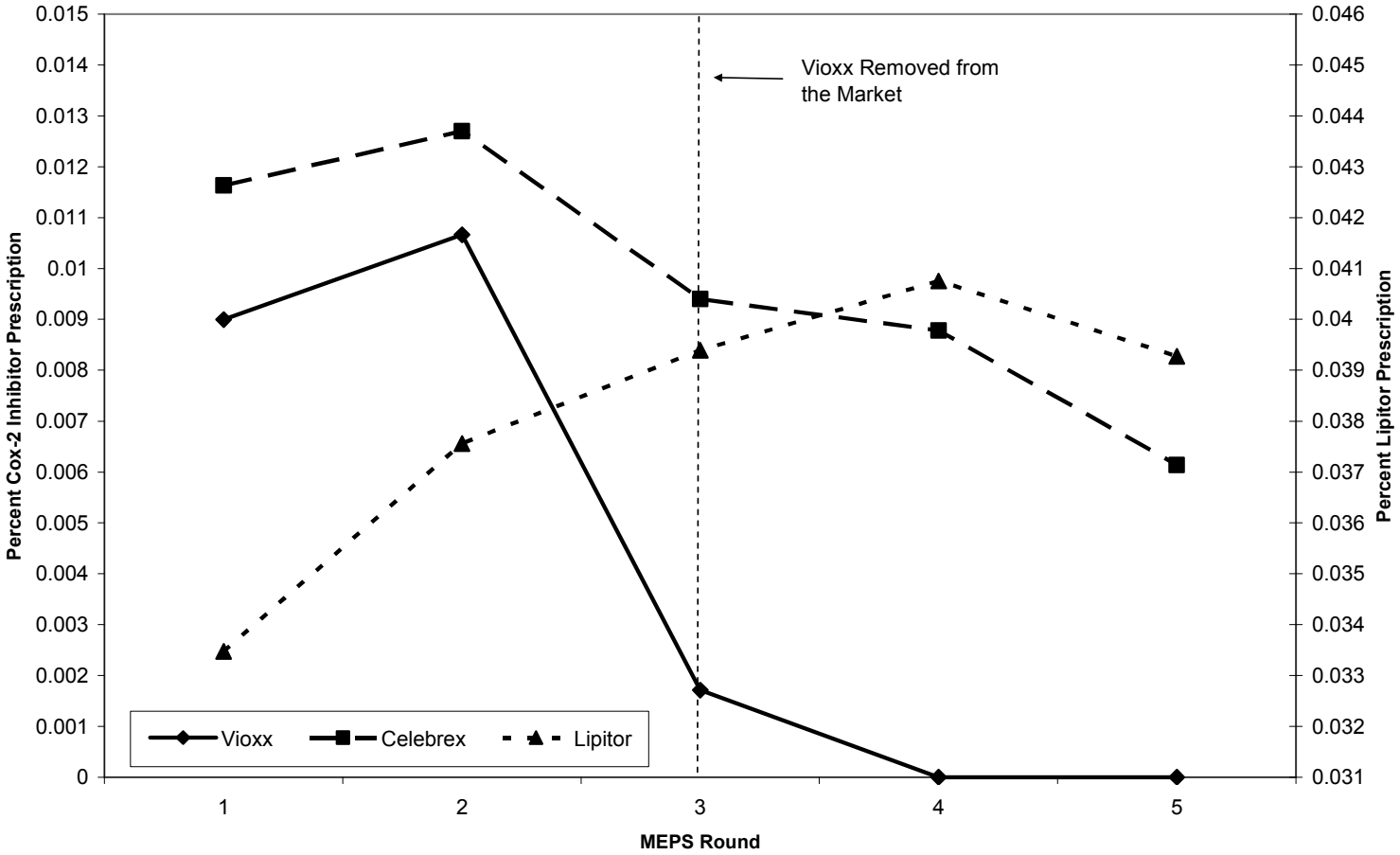
Source: Medical Expenditure Panel Surveys, 1998-2004

Figure 5 – Activity Limitation Status by Vioxx Prescription Use
MEPS Panel 9, Rounds 1, 3, and 5



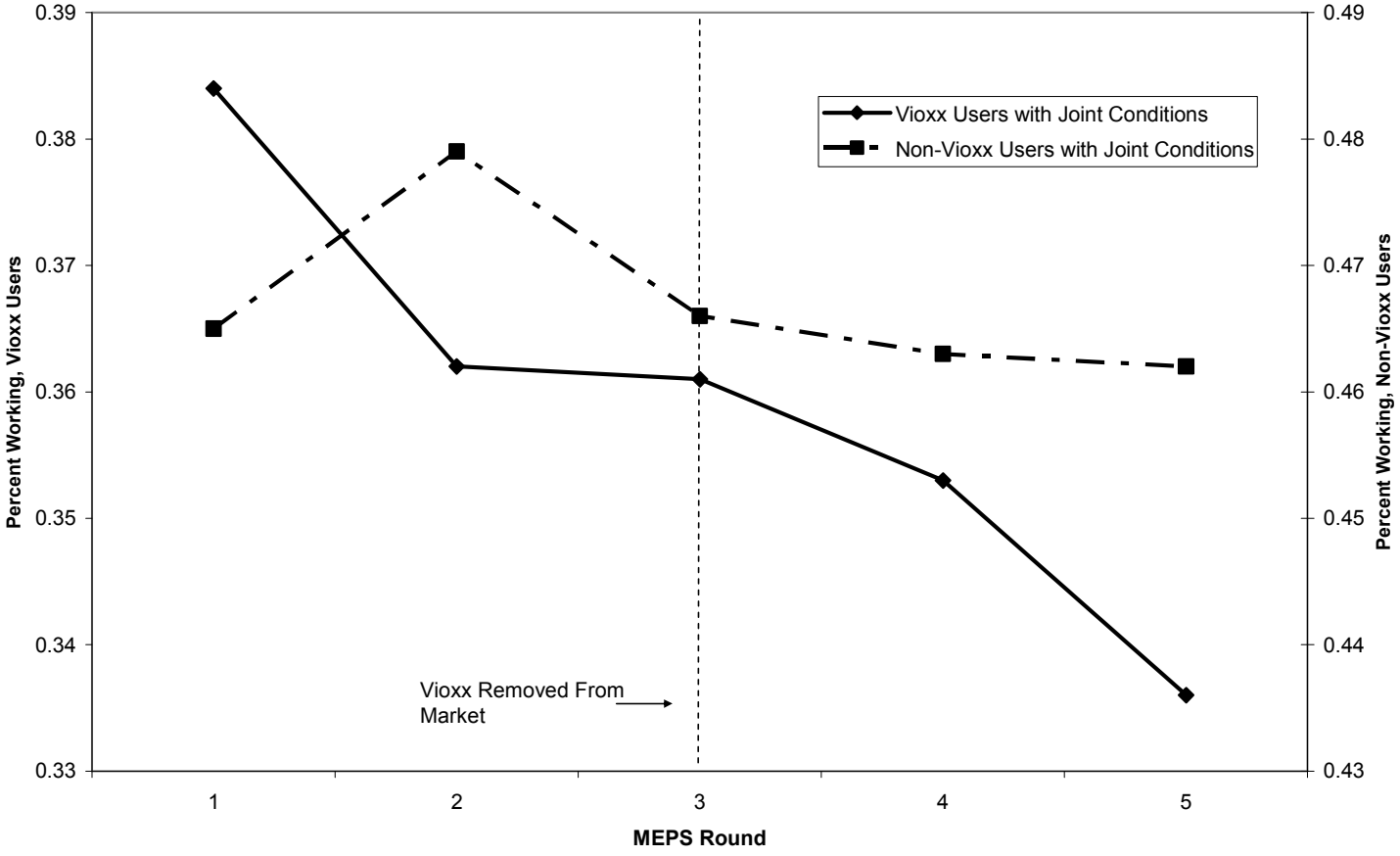
Source: Medical Expenditure Panel Survey, 2004-05

Figure 6 – Prescription Drug Rates, 2004-05



Source: Medical Expenditure Panel Survey, 2004-05

Figure 7 – Labor Supply by Vioxx Prescription Status
MEPS Panel 9



Source: Medical Expenditure Panel Survey, 2004-05

Figure 8 – Deaths from Influenza by Age

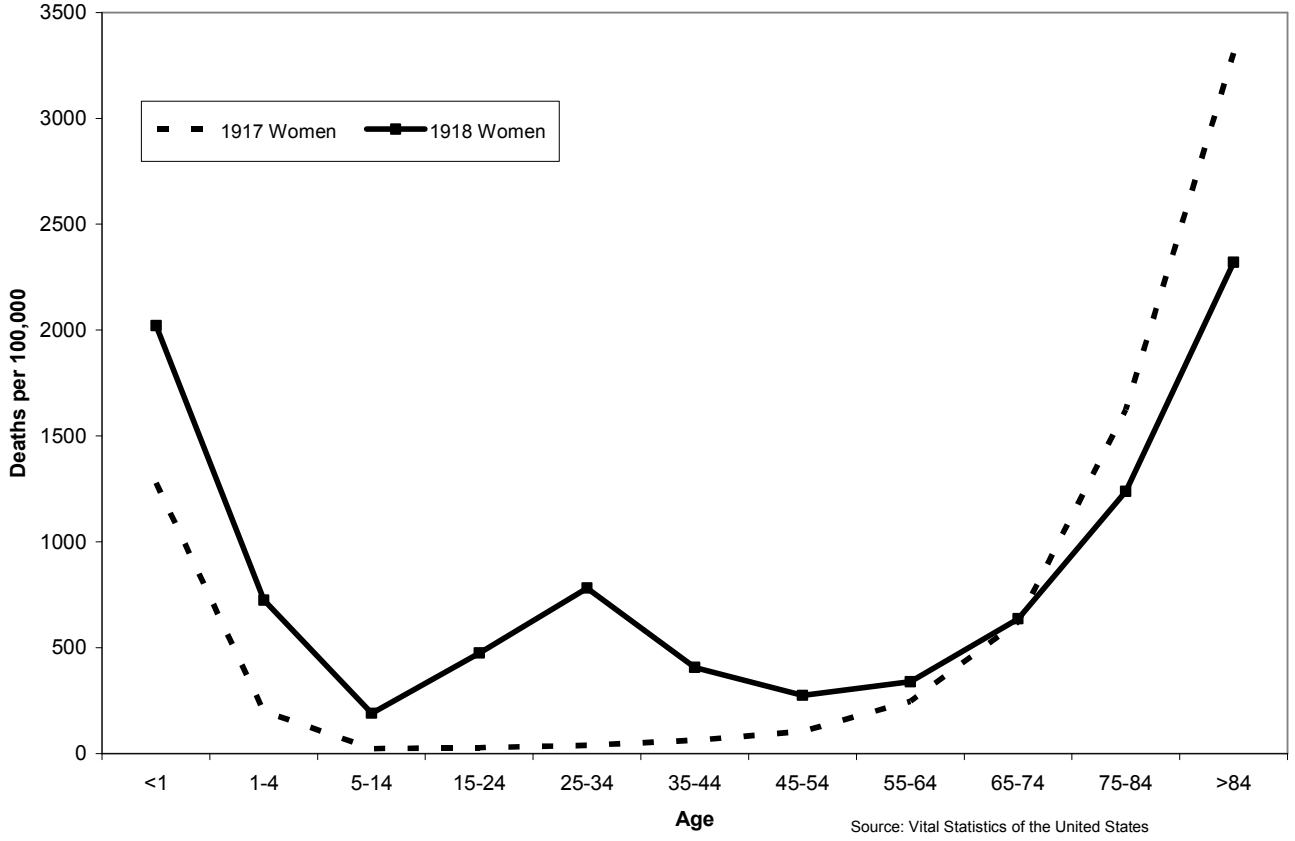


Figure 9 – Influenza Deaths by Year

Figure 10 – Estimated of In-Utero Flu Exposure on Coronary Heart Disease by Age, Men Born During the 1st Quarter 1919, 1982 to 2002 NHIS

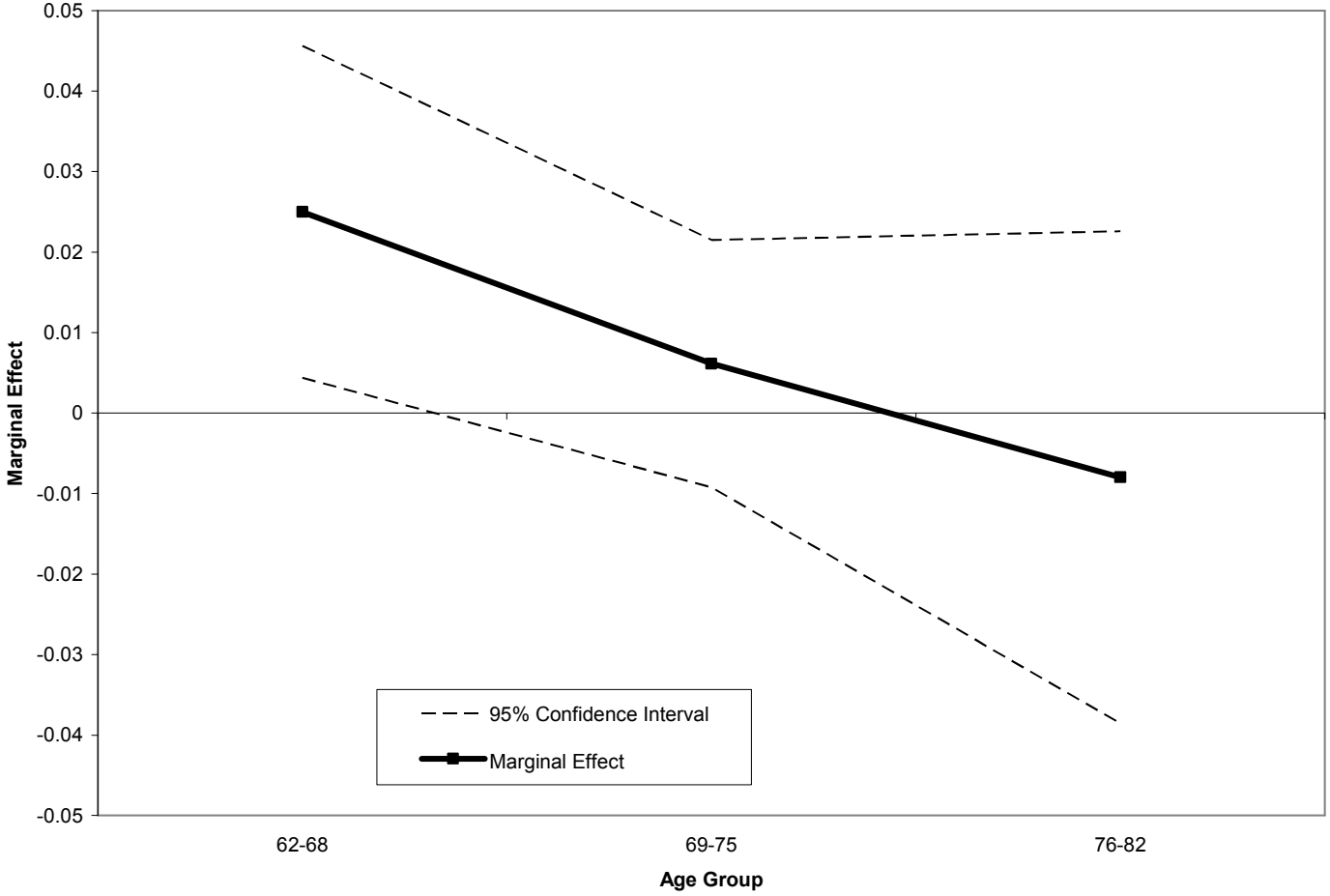


Figure 11 – Highest Grade Completed by Year of Birth
Adults, Aged 55-90, 1982-2002 NHIS

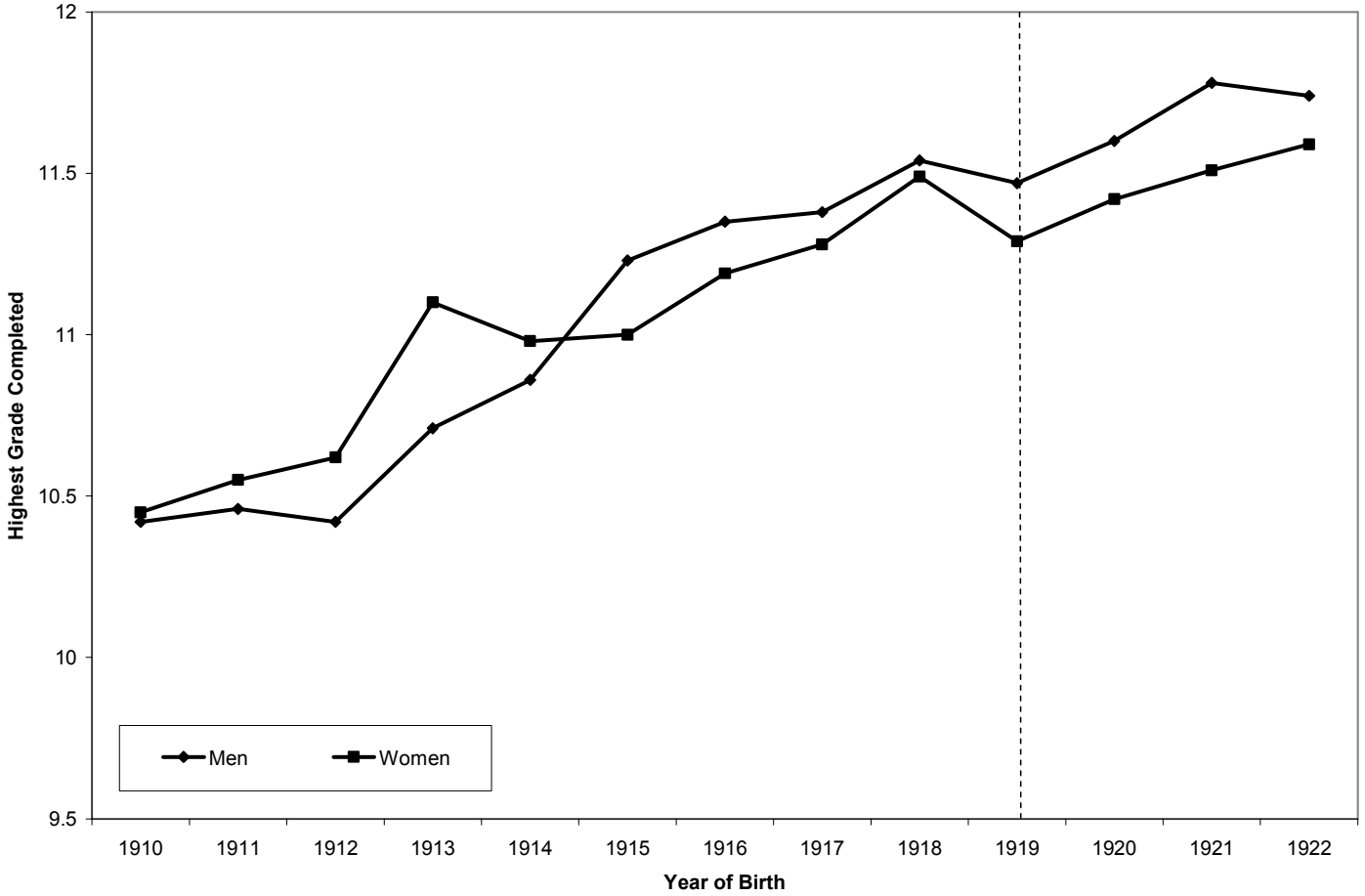
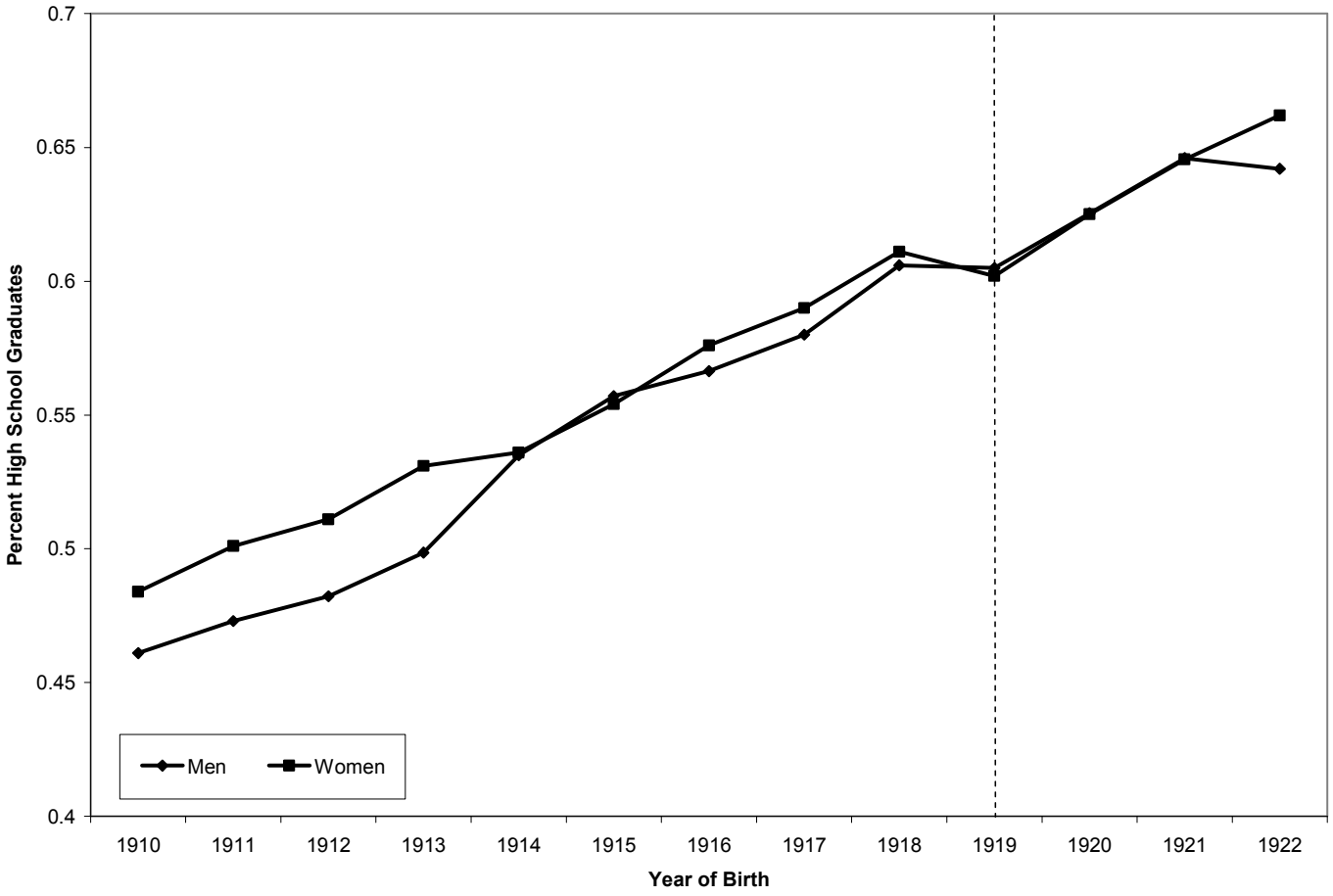


Figure 12 – Percent Graduating High School by Year of Birth
Adults, Aged 55-90, 1982-2002 NHIS



Bibliography

Almond, Douglas "Is the 1918 Influenza Pandemic Over? Long-Term Effects of In Utero Influenza Exposure in the Post-1940 U.S. Population," *Journal of Political Economy*, 114, (2006), 672-712.

Almond, Douglas and Bhashkar Mazumder, "The 1918 Influenza Pandemic and Subsequent Health Outcomes: An Analysis of SIPP Data," *American Economic Review,* 95 (2005), 258=262.

Angrist, Joshua, and Alan Krueger, "Does Compulsory Schooling Affect Schooling and Earnings?"*Quarterly Journal of Economics*, 106 (1991), 979-1014.

Arboleya, Luis R., Enrique de la Figuera, Maria Soledad Garcia, Belen Aragon, and the VICOXX study group, "Experience of rofecoxib in patients with osteoarthritis previously treated with traditional non-steroidal anti-inflammatory drugs in Spain: result of phase 2 of the VICOXX study," *Current Medical Research and Opinion,* 19 (2003), 288-297.

Arrelano, Manuel and Bo Honore, "Panel Data Models: Some Recent Developments," *The Handbook of Econometrics,* 2001, 3231-3290.

Autor, David H. and Mark Duggan, "The Rise in the Disability Rolls and the Decline in Unemployment," *Quarterly Journal of Economics,* 188 (2003), 157-205.

Azambuja, Maria, "Spanish Flu and Early 20th Century Expansion of a Coronary Heart Disease-Prone Subpopulation," *Texas Heart Institute Journal,* 31 (2004), 14-21.

Baker, Michael, Mark Stabile, and Catherine Deri, "What do Self-Reported, Objective, Measure of Health Measure," NBER Working Paper No. w8419, August 2001

Banerjee, Abhijit, Esther Duflo, Giller Postel-Vinay, and Timothy M. Watts, "Long Run Health Impacts of Income Shocks: Wine and Phylloxera in 19th Century France," NBER Working Paper No. w12895, Feb. 2007.

Barker, DJP, "Fetal Origins of Coronary Heart Disease," *British Medical Journal*, 311 (1995), 171-4.

Barker, DJP (ed), *Fetal Origins of Cardiovascular and Lung Disease,* New York: Marcel Dekker, Inc, 2001.

Barker DJP, "Coronary Heart Disease: A Disorder of Growth," *Hormone Research,* 59 (2003), 35-41.

Barker, DJP and MA Hanson, "Altered regional blood flow in the fetus: the origins of cardiovascular disease?," *Acta Paeditr,* 93 (2004), 1559-60.

Barker, DJP, "The Developmental Origins of Insulin Resistance," *Hormone Research,* 64 (2005), 2-7.

Barry, John. *The Great Influenza: The Epic Story of the Deadliest Plague in History,* Viking Press, 2004.

Bartel, Ann and Paul Taubman, "Health and Labor Market Success: The Role of Various Diseases," *The Review of Economics and Statistics,* 61 (1979), 1-8.

Battisti, Wendy, Nathaniel Katz, Arthur Weaver, Alan Matsumoto, Alan Kivitz, Adam Polis, and Gregory Geba, "Pain management in osteoarthritis: A focus on onset of efficacy—a comparison of rofecoxib, celecoxib, acetaminophen, and nabumetone across four clinical trials," *The Journal of Pain*, 5 (2004), 511-520.

Berndt, Ernst, Stan Finkelstein, Paul Greenberg, Robert Howland, Alison Keith, A. John Rush, James Russell, and Martin Keller, "Workplace performance effects from chronic depression and its treatment," *Journal of Health Economics,* 17 (1998), 511-535.

Berndt Ernst, Howard Bailit, Martin Keller, Jason Verner, and Stan Finkelstein, "Health Care Use and At-Work Productivity Among Employees with Mental Disorders," *Health Affairs*, 19 (2000), 244-256.

Bertrand, Marianne, Esther Duflo, and Sendhil Mullainathan, "How Much Should We Trust Difference-in-Differences Estimates," *Quarterly Journal of Economics*, 119 (2004), 249-275.

Bhattacharya, Jay and Michael Schoenbaum, "The Value of the Medicare Benefits for Social Security Disability Insurance Recipients," ERIU Working Paper 10, July 2002.

Blondeau, B., A. Garofano, P Czernichow, B. Breat, "Age-dependent inability of the endocrine pancreas to adapt to pregnancy: A long-term consequence of perinatal malnutrition in the rat," *Endocrinology,* 140 (1999), 4208-4213.

Bradley, Cathy J, David Neumark, Zhehui Lou, and Heather L. Bednarek, "Employment-Contingent Health Insurance, Illness, and Labor Supply of Women: Evidence from Married Women with Breast Cancer," NBER Working Paper No. w11304, May 2005.

Bren, Linda, "The Importance of Patient Reported Outcomes … It's All About the Patients," *FDA Consumer Magazine,* Nov 2006.

Brenner BM and CM Chertow, "Congenital oligonephropathy and the etiology of adult hypertension and progressive renal injury," *American Journal of Kidney Diseases,* 23 (1994), 171-5.

Brenner BM and Chertow CM, "Congenital oligonephropathy: an inborn cause of adult hypertension and progressive renal injury?" *Current Opinions in Nephrology and Hypertension*, 2 (1993), 691-5.

Brenner BM, and HS Mackenzie, "Nephron mass a risk factor for progression of renal disease," *Kidney International,* 63 (1997), S124-7.

Bresalier, Robert, Robert Sandler, Hui Quan, James Bolognese, Betina Oxenius, Kevin Horgran, Christopher Lines, Robert Riddell, Dion Morton, Angel Lanas, Marvin Konstam, and John Baron, "Cardiovasculer Events Associated with Rofecoxib in Colorectal Adenoma Chemoprevention Trial," *The New England Journal of Medicine,* 352 (2005), 1092-1102.

Caitlin, Aaron, Cathy Cowan, Stephen Heffler, Benjamin Watson, and the National Health Expenditure Accounts Team, "National Health Spending in 2005: The Slowdown Continues," *Health Affairs,* 26 (2007), 142-53.

Case, Anne, Darren Lubotsky, and Christina Paxson. "Socioeconomic Status and Health in Childhood: The Origins of the Gradient," *American Economic Review,* 92 (2002), 1308-1334.

Chamberlain, Gary, "Analysis of Covariance with Qualitative Data," *The Review of Economic Studies,* 47 (1980), 225-238.

Chan Tat Y. and Barton H. Hamilton, "Learning, Private Information, and the Economic Evaluation of Randomized Experiments," *The Journal of Political Economy,* 114 (2006), 997-1040.

Congressional Budget Office, "High Cost Medicare Beneficiaries," May 2005.

Costa, Dora, "Health and Labor Force Participation of Older Men, 1900-1991," *The Journal of Economic History,"* 56 (1996), 62-89.

Costa, Dora. *The Evolution of Retirement: An American Economic History 1880-1990.* University of Chicago Press: 1998.

Currie, Janet and Jonathan Gruber, "Saving Babies: The Efficacy and Cost of Recent Changes in the Medicaid Eligibility of Pregnant Women," *Journal of Political Economy,* 104 (1996), 1263-96.

Currie, Janet and Bridgette Madrian, "Health, Health Insurance and the Labor Market," in Orley C. Ashenfelter and David Card (eds.) *Handbook of Labor Economics, Volume 3c*, pp. 3309-3416.

Cutler, David, and Mark McClellan, "Is Technological Change in Medicine Worth It?," *Health Affairs,* 20 (2001), 11-29.

Cutler, David, Grant Miller, and Douglas Norton, "Evidence on early-life income and late-life health from America's Dust Bowl Era," *Proceedings of the National Academy of Sciences of the United States of America,* 104 (2007), 13244-13249.

Dai C, RS Stafford, GC Alexander, "National trends in Cox-2 use since market release: non-selective diffusion of a selectively cost-effective innovation," *Archives of Internal Medicine*, 165 (2005), 171-77.

Devaney, Barbara, Linda Bilheimer, and Jennifer Schore, "Medicaid Costs and Birth Outcomes: The Effects of Prenatal WIC Participation and the Use of Prenatal Care." *Journal of Policy Analysis and Management,* 11 (1992), 573-92.

Dominick, Kelli, Frank Ahern, Carol Gold, and Debra Heller, "Gender Differences in NSAID Use Among Older Adults with Osteoarthritis," *The Annals of Pharmacotherapy,* 37 (2003), 1566-1571.

Duggan, Mark, "Do New Prescription Drugs Pay for Themselves? The Case of Second-Generation Antipsychotics," *Journal of Health Economics,* 24 (2005), 1-31.

Dusing, Rainer, "Adverse Events, Compliance, and Changes in Therapy," *Current Hypertension Reports*, 3 (2001), 488-92.

Eissa, Nada and Jeffrey Liebman, "Labor Supply Responses to the Earned Income Tax Credit," *Quarterly Journal of Economics,* May 1996, 605-637.

Elo, I.T., and S.H. Preston, "Education Differentials in Mortality: United States, 1979-85," *Social Science and Medicine,* 42 (1996), 47-57.

Eriksson, JG, T Forsen, J Tuomilehto, C Osmond, DJP Barker, "Early Growth and coronary heart disease in later life: longitudinal study," *British Medical Journal,* 322 (2001), 949-953.

Evans, William N. and Diana S. Lien, "The Benefits of Prenatal Care: Evidence from the PAT Bus Strike," *Journal of Econometrics,* 125 (2005), 207-239.

Food and Drug Administration, "New Drug Application Number 021042 and 021052," *Food and Drug Administration,* May 20, 1999.

Food and Drug Administration, Summary Minutes for the February 16, 17 and 18, 2005, Joint meeting of the Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee, Mar 7 2005, accessed online at: http://www.fda.gov/ohrms/dockets/ac/05/minutes/2005-4090M1_Final.htm on Feb 4 2008.

Food and Drug Administration, "Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims," *Food and Drug Administration,* Jan 2006.

Frankel S, P Elwood, P Sweetnam, J Yarnell, G Davey Smith, "Birthweight, body-mass index in middle age, and incident coronary heart disease," *Lancet*, 348 (1996), 1478-80.

French, Eric, "The Effects of Health, Wealth, and Wages on Labour Supply and Retirement Behaviour," *Review of Economic Studies,* 72 (2004), 395-427.

Food and Drug Administration, "New Drug Application Number 021042 and 021052," *Food and Drug Administration,* May 20 1999.

Food and Drug Administration, Summary Minutes for the February 16, 17 and 18, 2005, Joint meeting of the Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee, Mar 7 2005, accessed online at: http://www.fda.gov/ohrms/dockets/ac/05/minutes/2005-4090M1_Final.htm on Feb 4 2008.

Food and Drug Administration, "Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims," *Food and Drug Administration,* Jan 2006.

Friedberg, Leora, "The Labor Supply Effects of the Social Security Earning s Test," *The Review of Economics and Statistics,* 82 (2000), 48-63.

Fox, Matthew, Sydney Rosen, William MacLeod, Monique Wasunna, Margaret Bii, Ginamarie Foglia, and Jonathan Simon, "The impact of HIV/AIDS on labour productivity in Kenya," *Tropical Medicine and International Health,* 9 (2004), 318-324.

Gluckman, Peter, Mark Hanson, Cyrus Cooper, and Kent Thornburg, "Effect of In-Utero and Early-Life Conditions on Adult Health and Disease," *The New England Journal of Medicine,* 359 (2008), 61-73.

Grossman, M. and Kaester, R, "The Effects of Education on Health," in J.R. Berhman and N. Stacey (eds.) *The Social Benefits of Education,* University of Michigan press: Ann Arbor, 1997.

Haider, Steven and David Loughran, "Elderly Labor Supply: Work of Play," RAND Working Paper 01-09, April 2001.

Hales CN, DJP Barker, PM Clark, LJ Cox, C Fall, C Osmond, and PD Winter, "Fetal and infant growth and impaired glucose tolerance at age 64," *British Medical Journal,* 303 (1991), 1019-22.

Hales CN and DJ Barker, "Type 2 (non-insulin-dependent) diabetes mellitus: the thrifty phenotype hypothesis," Diabetologia, 60 (1992), 5-20.

Hales, C.N., M. Desai, and S.E. Ozanne, "The Thrifty Phenotype Hypothesis; How Does it Look After 5 Years," *Diabetic Medicine,* 14 (1997), 189-95.

Harding, Jane E. and Peter D. Gluckman, "Growth, Metabolic, and Endocrine Adaptations to Fetal Undernutrition," in David J. P. Barker ed. *Fetal Origins of Cardiovascular and Lung Disease,* New York: Marcel Dekker, Inc, 2001.

Harley, Carolyn and Samuel Wagner, "Persistence with COX-2 Inhibitors in Managed Care: An Analysis of Claims Data," *Managed Care Interface,* 16 (2003), 38-45.

Hasford, J, A Mimran and W R Simons, "A population-based European cohort study of persistence in newly diagnosed hypertensive patients," *Journal of Human Hypertension,* 16 (2002), 569-75.

Hensley, Scott, "Pharma Box Office: Where Did Vioxx Users Go," *Wall Street Journal,* Apr 12 2007.

Hirth, Richard., Michael Chernew, Marc Turenne, Mark Pauly, Sean Orzol, and Philip Held, "Chronic Illness, Treatment Choice, and Workforce Participation," *International Journal of Health Care and Finance Review,* 3 (2003), 167-81.

Hoet, Joseph J. and Mark A. Hanson, "Intrauterine Nutrition," in David J. P. Barker ed. *Fetal Origins of Cardiovascular and Lung Disease,* New York: Marcel Dekker, Inc, 2001.

Hoffman, Catherine and Karyn Schwarz, "Eroding Access Among Nonelderly U.S. Adults With Chronic Conditions: Ten Years of Change," *Health Affairs,* 27 (2008), w340-8.

Irving, WL, DK James, T Stephenson, P Laing, C Jameson, JS Oxford, P Chakraverty, DW Brown, AC Boon, MC Zambon, "Influenza Virus Infection in the Second and Third Trimesters of Pregnancy: A Clinical And Seroepidemiological Study," BJOG: An International Journal of Obstetrics and Gynecology, 107 (2000), 1282-9.

Kaufman, Marc, “Merck Withdraws Arthritis Medication,” *The Washington Post,* Oct 1 2004.

Kitagawa, Evelyn, and Philip Hauser, *Differential Mortality in the United States: A Study in Socioeconomic Epidemiology*, Harvard University Press: Cambridge, Massachusetts, 1973

Kloeck, Teun, “OLS Estimation in a Model Where a Microvariable is Explained by Aggregates and Contemporaneous Disturbances," *Econometrica*, 49 (1981), 205-07.

Leon D., HO Lithell, D Vagero, I Koupilova, R Mohsen, L Berglund, UB Lithell, P McKeigue, “Reduced fetal growth rate and increased risk of death from ischaemic heart disease: Cohort study of 15000 Swedish men and women born 1915-1929,” *British Medical Journal,* 317(1998), 241-5.

Lewis, Carol, “Grappling With the Quality of Life: Patients, FDA and Drug Companies Struggle to Link Therapies With Well-Being,” *FDA Consumer Magazine*, March 2001.

Lichtenberg, Frank, “The Effect of Changes in Drug Utilization on Labor Supply and Per Capita Output,” NBER Working Paper #9139, September 2002.

Lichtenberg, Frank, “Are the Benefits Of Newer Drugs Worth Their Cost? Evidence From The 1996 MEPS,” *Health Affairs,* Sep/Oct 2001.

Lleras-Muney, Adriana, “The Relationship Between Education and Adult Mortality in the United States,” *Review of Economic Studies,* 72(2005), 189-221.

Lorig, Kate, “Targeting Arthritis Reducing Disability for Nearly 19 Million Americans,” *Center for Disease Control and Prevention,* May 2007. [Accessed online on 12/19/2007, available at: http://www.cdc.gov/nccdphp/publications/AAG/arthritis.htm]

Mamdani, Muhammed, Paul Rochon, David Juurlink, Alex Kopp, Geoffrey Andersen, Gary Naglie, Peter Austin, and Andreas Laupacis, “Observational study of upper gastrointestinal hemorrhage in elderly patients given selective cylco-oxygenase-2 inhibitors or conventional non-steroidal anti-inflammatory drugs,” *British Medical Journal,* 325 (2002), 624-630.

Martyn CN, and Stephen Greenwald, “Mechanism for In Utero Programming of Blood Pressure,” in David J. P. Barker ed. *Fetal Origins of Cardiovascular and Lung Disease,* New York: Marcel Dekker, Inc, 2001.

Martyn CN, AF Lever, JJ Morton, “Plasma concentrations of inactive renin in adult life are related to indicators of fetal growth,” *Journal of Hypertension,* 14(1996), 881-6.

McMillen, Caroline and Jeffrey Robinson, "Developmental Origins of the Metabolic Syndrome: Prediction, Plasticity, and Programming," *Physiological Reviews,* 85 (2003), 571-633.

Meadows, Michelle, "Why Drugs Get Pulled Off the Market," *FDA Consumer Magazine,* Jan 2002.

Meng, Xin and Nancy Qian, "The Long Run Health and Economic Consequences of Famine on Survivors: Evidence from China's Great Famine," Working Paper, Nov. 28, 2006.

Mitchell, Jean M., "The Effect of Chronic Disease on Work Behavior over the Life Cycle," *Southern Economic Journal,* April 1990.

Mitchell, Jean M.., "Work Behavior after the Onset of Arthritis," *Medical Care,* 29 (1991), 362-76.

Mitchell, Jean M. and Richard Burkhauser, "Disentangling the effects of arthritis on earnings: a simultaneous estimate of wage rates and hours worked," *Applied Economics,* 22 (1990), 1291-1309.

Mondics, Chris, "Risky painkillers still OK," *The Sun Herald,* Feb 19 2005.

Moulton, Brent, "An Illustration of a Pitfall in Estimating the Effects of Aggregate Variables on Micro Units," *Review of Economics and Statistics*, 72(1990), 334-38

Nathanielsz, Peter W., "Animal Models That Elucidate Basic Principles of the Developmental Origins of Adult Diseases," *ILAR Journal,* 47(2006), 73-82.

Newhouse, Joseph, "Medical Care Costs: How Much Welfare Loss," *The Journal of Economic Perspectives,* 6 (1992), 3-21.

Neyman, J. and E.L. Scott, "Consistent Estimates Based on Partially Consistent Observations," *Econometrica,* 16 (1948), 1-32.

Ozanne, SE, GD Smith, J Tikerpae, CN Hales, "Altered Regulation of Hepatic Glucose Output in the Male Offspring of Protein-Malnourished Rat Dams," *The American Journal of Physiology,* 270(1996), E559-64.

Ozanne, Susan E. and C. Nicholas Hales, "The long-term consequences of intra-uterine protein malnutrition for glucose metabolism," *Proceedings of the Nutrition Society*, 58(1999), 615-9.

Ozanne, Susan E. and C. Nicholas Hales, "Lifespan catch-up growth and obesity in male mice," *Nature*, 427(2004), 411-2.

Payne, January W., "Withdrawal Symptoms; Patients, Doctors Explore Alternatives to Vioxx For Arthritis Relief -- Very Carefully," *The Washington Post,* Nov 23 2004.

Prakash, Snigdha and Vikki Valentine, "Timeline: The Rise and Fall of Vioxx," *National Public Radio,* Nov 10 2007.

RAND Health, "Future Health and Medical Care Spending of the Elderly: Implications for Medicare," 2005.

Ravelli, ACJ, JHP Van der Meulen, RPJ Michels, C Osmond, DJP Barker, CN Hales, OP Bleker, "Glucose tolerance in adults after prenatal exposure to famine," *Lancet,* 351(1997), 173-7.

Rich-Ewards JW, MJ Stampfer, JE Manson, B Rosner, SE Hankinson, GA Colditz, WC Willett, CH Kennekens, "Birth weight and risk of cardiovascular disease in a cohort of women followed up since 1976," *British Medical Journal*, 315(1997), 396-400.

Roseboom, TJ, JHP van der Meulen, C Osmond, DJP Barker, ACJ Ravelli, JM Schroeder-Tanka, GA van Montfran, RPJ Michels, and OP Bleker, "Coronary Heart Disease After Prenatal Exposure to the Dutch Famine, 1944-45," *Heart,* 84(2000), 595-598.

Roseboom, Tessa J., Jan H.P. van der Meulen, Anita C.J. Ravelli, Clive Osmond, David J.P. Barker, Otto P. Bleker, "Effects of prenatal exposure to the Dutch famine on adult disease in later life: an overview," *Molecular and Cellular Endocrinology,* 4(2001), 293-98.

Rubin, Rita, "Merck halts Vioxx sales," *USA Today,* Sep 30 2004.

Schmidt, Helmut, Barry Woodcock, and Gerg Geisslinger, "Benefit-Risk Assessment of Rofecoxib in the Treatment of Osteoarthritis," *Drug Safety,* 27 (2004), 185-196.

Schnitzer, Thomas and Marc Hochberg, "Cox-2 selective inhibitors in the treatment of arthritis," *Cleveland Clinic Journal of Medicine*, 69 (2003), SI 20-30.

Schnitzer, Thomas, Arthur Weaver, Adam Polis, Richard Petruschke, and Gregory Geba, "Efficacy of rofecoxib, celecoxib, and acetaminophen in patients with osteoarthritis of the knee. A combined analysis of the VACT studies," *The Journal of Rheumatology,* 32 (2005), 1093-1105.

Simmons, RA, LJ Templeton, SJ Gertz, "Intrauterine Growth Retardation Lead to the Development of Type 2 Diabetes in a Rat," *Diabetes,* 50(2001), 2279-86.

Skinner, Jonathan, Douglas Staiger, and Elliot Fisher, "Is Technological Change in Medicine Always Worth It? The Case of Acute Myocardial Infarction," *Health Affairs,* 25 (2006), 34-47.

Smith, Cynthia, "Retail Prescription Drug Spending in the National Health Accounts," *Health Affairs,* 23 (2004), 160-67.

Smugar, Steven, Thomas Schnitzer, Arthur Weaver, Bernard Rubin, Adam Polis, Adam Tershakovec, "Rofecoxib 12.5mg, rofecoxib 25mg, and celecoxib 200mg, in the treatment of symptomatic osteoarthritis: results of two similarly designed studies," *Current Medical Research and Opinion,* 22 (2006), 1353-67.

Snyder, Stephen E., "Another Sort of Intergenerational Transfer? Influenza and the Fetal Origins Hypothesis," mimeo, Lehigh University, 2004.

Stagnitti, Marie and Mamatha Pancholi, "Outpatient Prescription Medicine: A Comparison of Expenditures by Household-Reported Condition, 1987 and 2001," Agency for Healthcare Research and Quality, Statistical Brief #43, July 2004.

Stanner, Sara A. and John S. Yudkin, "Fetal Programming and the Leningrad Siege Study," *Twin Research,* 4(2001), 287-92.

Stocker, Claire J., Jonathan R.S. Arch, and Michael A. Cawthorne, "Fetal origins of insulin resistance and obesity," *Proceedings of the Nutrition Society,* 64(2005), 143-51.

Tannenbaum, Hyman, "Patient Empowerment: Rofecoxib Revisited," *The Journal of Rheumatology,* 33 (2006), 1033-35.

Thirumurthy, Harsha, Makus Goldstein, and Joshua Graff Zivin, "The Economic Impact of AIDS Treatment: Labor Supply in Western Kenya," *Journal of Human Resources,* 43 (2008), 511-552.

Thornburg, Kent L., "Physiological Development of the Cardiovascular System In Utero," in David J. P. Barker ed. *Fetal Origins of Cardiovascular and Lung Disease,* New York: Marcel Dekker, Inc, 2001.

Timbe JW, M Horvitz-Lennon, R Frank, G Lewis, "A Meta-Analysis of Labor Supply Effects of Interventions for Major Depressive Disorders," *Psychiatric Services,* 57 (2006), 212-218.

Wagner, Christopher C., Carolyn E. Danczyk-Hawley, Kathryn Mulholland, and Bruce G. Flynn, "Older Workers. Progression from Private Disability Benefits to Social Security Disability Benefits," *Social Security Bulletin,* 2000.

Walker, Judith S., and John J. Carmody, "Experimental Pain in Healthy Human Subjects: Gender Differences in Nociception and in Response to Ibuprofen," *Anesthesia Analgesia,* 1998.

Wayne A. Ray, Joseph Gigante, Edward F. Mitchel, Jr, Gerald B. Hickson, "Perinatal Outcomes Following Implementation of TennCare," *Journal of the American Medical Association,* 279(1998), 314-16.

Weller, Christian, "Older Workers Staying in the Labor Force," *Economic Policy Institute,* July 2003.

Wooldridge, Jeffrey, "Cluster-Sample Methods in Applied Econometrics," *American Economic Review* 93 (2003), 133-138.

Wu, Shin-Yi and Anthony Green, "Project of Chronic Illness Prevalence and Cost Inflation," *RAND Corporation,* October 2000.

Yelin, Edward H., "Musculoskeletal Conditions and Employment," *Arthritis Care and Research,* 8 (1995), 311-317.

Zacher, Josef and Manfred Schattenkircher, "Patient and Physician Satisfaction with Rofecoxib in Osteoarthritis: Results of a Post-Marketing Surveillance Study in Primary Care in Germany," *Current Medical Research and Opinion*, 17 (2002), 81-7.