

D I S S E R T A T I O N

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*Estimating the Effects of
Pharmaceutical
Innovations on Patient's
Employment Outcomes*

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Dedicated to my parents

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PREFACE

As new medical technologies continue to drive the growing cost of health care in the United States, public and private decision makers have called for more rigorous evaluations of the costs and benefits of pharmaceuticals and other medical technologies. The common practice of ignoring employment benefits of treatment in the evaluations leads to the concern that such analyses undervalue interventions that improve productivity of the working population.

This research examines the empirical challenges in estimating the employment effects of treatment with observational data and uses two empirical studies to illustrate possible approaches to reliable estimation. It provides guidance and examples for medical technology evaluations that incorporate employment benefits.

This study was submitted as a dissertation to the RAND Graduate School in September 2003 in partial fulfillment of the requirements of the degree of Doctor of Philosophy in Policy Analysis.

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ABSTRACT

In recent years, advances in medical technologies have been a major source of the increasing cost of health care in the United States. Increasingly, the society and policy makers must confront hard choices in allocating limited resources among competing uses, making it increasingly urgent to evaluate the benefits and costs of new technologies. Current approaches to evaluating the benefits of medical technologies very often ignore employment-related benefits, thus undervaluing interventions that improve functioning and productivity among the population of working age.

This dissertation reviews evidence of employment-related benefits from effective treatment. I set up a microeconomic model of a patient's decision regarding labor supply when treatment technology improves. The model shows that observed incremental labor supply is a result not only of more effective treatment, but of other factors such as eligibility for employment-based or public health insurance, both of which are tied to one's employment status. Using the insights provided by the model, I critique three approaches in the existing literature.

I conduct two empirical studies exemplifying econometric and statistical strategies to consistently estimate the employment effects of treatment. First, an analysis of the effect of the Highly Active Antiretroviral Therapy on HIV patients' employment transitions uses an instrumental variable approach. This approach identifies the effect of a particular therapy when patients self-select into the treatment according to unobserved severity, personal behavioral traits, and other factors. Second, an analysis of the effect of recent improvements in pharmacological therapies for hypertension (relative to therapies used in the 1970's) provides an example in which panel data and instrumental variables are not available. The "difference-in-difference" approach

employed aims to difference out the unobserved selection factors in hypertension treatment. I discuss pitfalls of the approach and implications for data collection to inform future research in this area.

Finally, to translate estimated employment effects into employment-related benefits, one has to be aware of possible labor market adjustments associated with the change and base the analysis on labor market equilibria.

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1. INTRODUCTION

Competing needs for limited resources call for the evaluation of the costs and benefits of various public policies. In the health care sector of the United States such evaluation becomes especially urgent as health care expenditures approach 15% of its GDP. Studies have found that the bulk of the increase in health care expenditures over the years were attributable to changes in medical technologies, rather than to other factors including aging of the society, improved insurance coverage, and supply-side factors such as increased supply of medical providers (Newhouse 1992). This finding prompts the question whether changes in technologies embodied in today's medical care are worth their costs.

Of the different types of health care products and services, pharmaceutical products have seen unprecedented growth in technological innovations in the last two decades. In addition to the discovery of new chemical compounds, innovations of pharmacological therapies also take the form of newer and more effective formulations. Although costs for prescription drugs have traditionally been a small slice of the total health care costs - the current share is about 9% (National Center for Health Statistics, 2002)-, the growth in drug costs in most of recent years outpaced cost growth in all the other major components such as hospital care and outpatient visits to physicians. Decomposition of the cost growth indicated that high volume prescriptions of newer drugs and higher prices of newer drugs accounted for most of the increased costs from 1993 to 1998 (The Kaiser Family Foundation 2000; NIHCM 1999).

Thus, a pressing need arises for scientific evidence of the costs and benefits of pharmacological therapies to inform policy. Important areas of health policy related to prescription drug benefits or the pharmaceutical industry include: coverage of prescription drugs in major

public health insurance programs such as Medicare and Medicaid, laws and regulations on prescription drug coverage by private health insurance plans, price regulation of pharmaceuticals, patent laws, government-funded biomedical research, etc. It is not surprising that cost benefit or cost effectiveness analyses of pharmacological therapies currently account for the vast majority of evaluative studies of medical technologies.

Employment benefits of pharmacological treatment

Cost-benefit analysis was used in public finance long before its use in evaluating medical interventions. To analyze economic efficiency, one adopts the criterion of potential Pareto improvement in weighing the costs and benefits of a particular social project. In that task, the analyst is required to identify major effects of the project on the utility/welfare of all members of the community, and to measure these effects in some common unit (such as dollar) so that social benefits can be compared to social costs.

In the case of medical treatment, and treatment with pharmacological therapies in particular, benefits of treatment go far beyond extended life years or increased quality of life. For the working age population, effective treatment may lead to improvement in patients' employment outcomes, which could amount to significant benefits to the patients, the employers, and other members of society.¹ Effective treatment can increase the number of working hours or improve on-the-job productivity, or both. The effect of treatment on hours of work can be

¹ When conducting a formal analysis of the benefits from improved employment, one has to be explicit about the perspective of the analysis. If a societal perspective is taken, the analyst needs to consider net benefits for the treated patients (benefits of increased earnings net the value of forgone leisure), for the employers, and for workers whose wages or even labor participation might be affected as a result of the changed employment by the patients. How these benefits should be calculated depends on the competitiveness of the labor market, whether or not there is full employment in the market, and nature of the job such as the importance of teamwork, as is discussed in much greater detail in Chapter 5.

either short-term or long-term. In the short-term, effective treatment may help workers reduce absenteeism and work loss days, or increase their regular hours of work (e.g., from part-time to full-time). In the longer term, it may help patients who were once disabled from work go back to work, or workers who might otherwise be disabled from work remain employed.

Most cost-effectiveness analyses (CEAs) of medical interventions, to date, do not take into account the benefits of improved employment outcomes (Stone, Chapman, Sandberg, et al. 2000). Unlike cost-benefit analyses, in CEAs, the benefits are not expressed in dollars. For example, in evaluations of health care interventions, many researchers and policymakers are reluctant to attach monetary value to human lives or other health outcomes. Therefore, benefits are often measured in terms of clinical outcomes such as mortality rates, added life years, or quality adjusted life years (QALYs). To the extent that these measures of benefits do not account for all the benefits of the intervention, implications derived from CEAs may not be consistent with the criterion of economic efficiency. In particular, leaving out benefits of improved employment outcomes undervalues interventions that improve functioning and productivity of the working population.²

One reason for the common exclusion of employment benefits lies in the difficulties in estimating the employment effects of treatment. These difficulties are discussed in detail in Chapter 2. Moreover, it is often believed that employment effects of medical interventions would be small, since the bulk of health care expenditures are made on behalf of the elderly population and most elderly are out of the labor market. The

² Recent discussions on the theoretical issues in CEAs have suggested including employment benefits in the numerator as "reduced costs" (for example, Meltzer 1997). However, as discussed in Garber (2000), in order for the method of CEA to reflect utility (welfare) maximization, the effectiveness measure should reflect all aspects of utility, including utility related to employment consequences of the illness and treatment. Therefore, counting employment benefits as reduction in costs does not represent best practice for CEA to have favorable welfare economic properties. Discussion on how employment benefits should be incorporated into CEAs is deferred to the last chapter.

literature, however, provides both direct and indirect evidence of substantial effects of some treatments on patients' employment outcomes.

Evidence that pharmacological treatment can increase employment

Indirect evidence

Employment effects of pharmacological treatment are generally referred to as "indirect" or "secondary" effects, because a treatment must achieve clinical efficacy to affect patients' employment outcomes. Employment outcomes can improve only if the ailments that disabled the patient are alleviated. Therefore, studies showing clinical efficacy of pharmacological therapies combined with studies on how health affects employment, provide indirect evidence of the employment effects of these therapies.

Most clinical studies aim at testing the efficacy of one particular medical intervention relative to either no intervention or established interventions. Treatment guidelines are often produced based on the results of these studies. For example, up-to-date clinical recommendations are available for each of the two conditions investigated in this dissertation: infection with Human Immunodeficiency Virus (HIV) (Carpenter et al. 1998) and high blood pressure (Joint National Committee (JNC) 1997; 2003). In Carpenter et al. (1998), an international panel of physicians with expertise in antiretroviral therapies reached consensus that early institution of potent antiretroviral therapy is effective in achieving long-term control of HIV replication. The JNC reports presented a meta analysis of randomized, placebo-controlled clinical trials on pharmacological treatment of hypertension. These studies show clear evidence that pharmacological treatment of hypertension can effectively reduce blood pressure, and as a result, decrease cardiovascular morbidity and mortality.

In addition to clinical studies that investigate efficacy of specific treatments, health services research provides evidence that recent pharmacological therapies are on average more effective than earlier ones. Lichtenberg (2001; 2002a) conducted empirical studies on how "age of a drug" was related to mortality, morbidity, and non-drug health care expenditures using data from the Medical Expenditure Panel Survey (MEPS). Although mortality rate was quite low in the panel, the author found that those treated with newer drug therapies were significantly less likely to have died by the end of the panel. The study also showed that newer drugs reduced non-drug expenditures substantially more than they increased expenditures on drugs, mainly by reducing hospitalization and physician office visits. These findings suggest that newer drugs, on average, have more advanced efficacy and better prevent the onset of acute conditions or complications. Studies on the health consequences of prescription drug coverage policies provide additional evidence. Soumerai, Ross-Degnan, Avorn, et al. (1991) studied the effect of New Hampshire's Medicaid policy that reimburses no more than three prescription drugs per month. They found significant increase in admission to nursing homes, indicating that treatment with prescription drugs can be crucial for maintaining health and functioning of the vulnerable population.

A causal relationship between an individual's health conditions and her labor market outcomes is supported by the literature in labor economics. Studies have shown the onset of major diseases and/or deterioration of health conditions to be a significant factor in individuals' decision of early retirement (e.g., Diamond and Hausman 1984; McClellan 1998; McCarry 2003). Using the first release of the Health and Retirement Study (HRS), Bound, Schoenbaum, and Waidmann (1995) found that disparities in health status (lower health of the black population compared to the white population) explain a significant fraction of the black/white difference in labor market attachment. The

same study also found that better health among the more highly educated population relative to the less educated population explained almost all the difference in labor market attachment across populations with different educational achievements. In a later study using longitudinal data from HRS, Bound and colleagues (Bound, Schoenbaum, Stinebrickner, et al. 1998) found that decline in health conditions was strongly associated with exit from the labor force and claiming of disability insurance.

While disastrous health shocks (such as stroke or amputation) often leave individuals disabled from their jobs, onset of chronic conditions changes the labor market behavior of individuals in a more complicated way.³ Although the net effect on employment outcomes is ambiguous theoretically, almost all earlier empirical studies have found that deterioration in health reduced labor force participation (Currie and Madrian 1999).

Evidence of the employment effects of particular diseases includes estimates of disease burden measured by "disability-adjusted-life-years" (Murray and Lopez 1996) or lost work days because of a particular condition (for example, Druss, Marcus, Olfson, et al. 2002). Murray and Lopez (1996) developed a method to combine mortality, impact of premature death, and health states characterized by disability to establish a measure of "burden of disease". The study concluded that disability⁴ accounted for the vast majority of the burden of disease. Druss, Marcus, Olfson, et al. (2002) used national survey data to identify the most costly conditions in terms of both health care expenditure and disability. Ranked highest on the list in terms of

³ Onset of chronic conditions may lead to less labor supply either because the ailment makes the job task harder to accomplish or because the illness preempts some expensive consumption, thus making income from work less desirable. It may also provide incentive to work since, in the U.S., availability of health insurance to people of working age is very often tied to individuals' employment and individuals with chronic conditions expect higher out-of-pocket health care expenditures over a fairly long period of time.

⁴ "Disability", in Murray and Lopez (1996), is measured by attaching preference weights to life years spent with various health states associated with diseases.

annual "work loss days" were conditions such as back problems (83.0 million days), mood disorders (78.2 million days), and motor vehicle accidents (70.0 million days).

Several studies have focused on a single condition and examined how it is related to patients' functioning or labor market outcomes. Almost all studies of this type found onset of chronic or acute conditions to lead to adverse employment outcomes. For example, several studies reported on the employment effects of depressive disorders and how patients' functioning was related to the severity of depression. Using psychiatric disorder history of the respondent and that of the respondent's parents as instrumental variables for studying the effect of the respondent's current psychiatric disorder, Ettner, Frank, and Kessler (1997) found that psychiatric disorders significantly reduced employment among both men and women. Using data from a clinical trial of chronically depressed patients, Berndt, Finkelstein, Greenberg, et al. (1998) found that reduction in depressive severity improved the patient's self-reported work performance. Finkelstein, Cockburn, Bailit, et al. (2000) found that asthmatic employees were more likely to be absent just prior to and immediately following their visit to a physician, but asthma didn't seem to impair their productivity while they were on the job. The study also found that while asthmatic episode of the employees' dependents did not affect absenteeism of the employees, it led to a decline in the employees' on-the-job productivity by 11-12%.

Direct evidence

Two types of studies directly investigated employment effects of medical interventions. The first studied the effects of disease-specific, or therapy-specific treatment on patients' employment outcomes. The other examined the average effects of more recent

treatment technologies on patients' employment outcomes relative to older technologies.

With data from employers, some researchers have been able to relate illness and treatment to objectively measured on-the-job productivity. Berndt (2000) provided a review of such studies using data from a company whose employees process health insurance claims. However, only one of these studies specifically investigated the (causal) treatment effect of medical intervention on employment outcomes. Cockburn and colleagues (Cockburn, Bailit, Berndt, et al. 1999) compared the effect of sedating and non-sedating antihistamines on the productivity of employees shortly after relative to shortly before antihistamine prescriptions were filled. They found that use of sedating antihistamines was associated with 7.8% reduction in productivity as measured by number of claims processed per day, while the non-sedating drug treatment had an effect size of positive 5.2%. Another study, which is not reviewed in Berndt (2000), investigated the short-term work outcomes of migraine patients (Legg, Sclar, Nemec, et al. 1997).⁵ Using data collected by an IPA-HMO in a telephone survey of their patients (who were with different employers and presumably had various occupations), the study found that initiation of treatment with Sumatriptan was associated with reduced (self-reported) days missed from work and improved (self-reported) productivity at work. The incremental benefits from improved work outcomes alone, according to the authors' calculation, were ten times as large as the incremental costs of Sumatriptan.

As pointed out by Berndt (2000), for chronic illnesses that are not characterized by well-defined acute episodes and/or require long-term use of medication, it is usually not appropriate to adopt approaches discussed in the previous paragraph. Further, in today's

⁵ Important methodological flaws in Legg, Sclar, Nemec, et al. (1997) are discussed in Chapter 2.

labor market, objective measurement of productivity is usually not possible. Therefore it is unclear to what extent results found about health insurance claims processors of this particular company could be extrapolated to the general working population.

There are few studies on the longer-term employment outcomes of specific treatments. Schoenbaum and colleagues (Schoenbaum, Unutzer, McCaffrey, et al. 2002) studied the effect of appropriate depression treatment (either medication or psychotherapy, as defined by Agency for Healthcare Research and Quality's clinical guideline) on patients' employment transitions. Making use of longitudinal data from a randomized controlled trial of quality improvement for depression, they found that patients who received appropriate care had higher rates of employment (72% vs. 53%) at 6-month-follow-up. Berndt, Bailit, Keller, et al. (2000) compared the group diagnosed with and treated for different kinds of mental disorders to their colleagues without disorders in terms of absenteeism and daily productivity, averaged over a thirty month period. Although the study was not designed to estimate a treatment effect, the findings of no significant difference in on-the-job productivity between the two groups suggest that mental health care improved patients' employment outcomes, given that mental disorders have been shown in other studies to impair functioning (for example, Kessler, Barber, Birnbaum, et al. 1999).

The second type of study examines the average employment effects of recent pharmacological treatment (relative to older ones), without distinguishing among technologies in different therapeutic categories. For example, Lichtenberg (2002b) conducted condition-level analysis to see if above-average growth in prescriptions to treat a particular condition is associated with reduced work-loss days related to the condition, and if increase in drug vintage (newer drugs) is associated with reduction in activity limitation reported by the patients. The study found that incremental earnings as a result of improved labor

supply significantly outweighed the incremental costs of newer drugs, leading to the conclusion that newly approved drugs were "cost-effective".⁶

In summary, findings of clinical efficacy of medical interventions combined with the literature on employment effects of health and studies of employment effects of treatment provide strong evidence of the significant employment benefits of medical technologies, and of pharmacological therapies in particular. Evidence pertaining to specific physical or mental conditions indicates that employment effects of treatment would be especially large for conditions that are either prevalent among the working population (such as allergy and depression) or very debilitating (for example, HIV infection, heart diseases such as myocardial infarction and congestive heart failure).

Objective of this dissertation and chapter plan

This dissertation estimates the effects of selected pharmacological therapies on patients' employment outcomes, with a focus on longer-term employment outcomes, such as transitions into or out of employment.

Chapter 2 sets up a microeconomic model of labor supply as treatment technology improves. The model depicts an economic agent (patient) who maximizes utility by making trade-offs between leisure time and income from work. Treatment, and thus health, affects the patient's choice of optimal working hours by changing her preferences for leisure relative to income. The model shows that the change in the patient's hours of work as a result of change in the treatment technology is a function of not only the additional treatment effect,

⁶ In general, knowing that incremental earnings outweigh costs of treatment is not enough to make inferences regarding economic efficiency. When a societal perspective is adopted, welfare of other individuals might be affected by the treatment and the resulting employment of the patients, which needs to be taken into account in evaluating the treatment. These issues are discussed in Chapter 5 of this dissertation.

but also how availability of health insurance coverage is tied to one's labor supply. Implications of the model then provide guidance for critiquing several existing approaches to accounting for the employment effects of treatment.

In order to provide examples of the challenges in estimating employment effects of treatment, and of the empirical strategies to produce consistent estimates, I conduct two empirical studies. Chapter 3 studies the effect of the Highly Active Antiretroviral Therapies (or "HAART") on HIV patients' employment transitions. HAART is a good example because of the strong selection into the treatment by disease severity and other personal behavioral traits, and the complications introduced by eligibility rules of health insurance programs. I adopt the instrumental variable approach to address these problems. For the two dichotomous employment outcomes—"return to work" and "remain employed"—I use a joint model of employment outcome and treatment of HAART. The effect of HAART (relative to non-HAART therapies including no antiretroviral treatment) is estimated and derived from the model, and implications of these estimates for public programs that cover HAART are discussed.

Chapter 4 studies the employment effect of recent anti-hypertensive therapies (compared to therapies available in the late 1970's) for the near elderly population. The past three decades have seen rapid proliferation of new classes of hypertension drugs much more expensive than the older classes such as diuretics. These developments have triggered research efforts to evaluate the additional effectiveness of these newer drugs. Changes in the epidemic of hypertension, public awareness, and physician treatment behavior pose challenges to comparing treatment outcomes (including employment outcomes) of a younger cohort of patients to the outcomes of an older cohort. This study addresses these challenges by applying the Difference-in-Difference framework and asks the question: did recent therapies, compared to the earlier ones,

help narrow the gap in employment rate between those treated with anti-hypertensives and those not treated? Results and limitations of the study are discussed to provide implications for research design and data collection in future studies with similar research questions.

In the concluding Chapter 5, I come back to the policy questions that motivated this study and discuss various issues in estimating employment-related benefits and in incorporating the estimated benefits into cost-benefit or cost-effectiveness analyses. In light of the findings from the previous chapters, it also provides implications for future research and data collection efforts in this area.

2. EMPLOYMENT EFFECTS OF PHARMACEUTICAL INNOVATIONS: A MICROECONOMIC MODEL AND A CRITIQUE OF PREVIOUS APPROACHES

Employment-related benefits as a result of effective treatment are an essential component of benefits associated with health care, and therefore should, in principal, be included in cost benefit analyses of medical interventions. Methodological discussions of cost-effectiveness analyses (for example, Meltzer 1997, Johannesson and Meltzer 1998, and Garber 2000) show that exclusion of future costs not directly related to medical care, including productivity-related costs⁷, may lead to cost-effectiveness ratios that are biased to favor interventions which extend life years over interventions which improve functioning and productivity of individuals.

Despite growing interest in incorporating employment effects of treatment into evaluations, empirical issues in estimating such effects have not been well studied. Previous studies have used estimates of indirect cost of illness as proxies for the employment benefits of treatment. Some other studies referred to employment statistics of the general population, stratified by basic demographic characteristics, and applied these numbers to the patient population of interest. As discussed in this chapter, neither of the approaches provides reliable measurement of the employment effects of treatment. A small number of studies used clinical or survey data to empirically estimate the employment effects of a particular treatment. However, few of these studies were designed with appropriate conceptualization of the treatment effect of interventions. Either the measurement or the conceptual issues lead to inconsistent estimates of the employment effects.

⁷ Increased productivity because of a particular medical intervention is, in fact, part of the incremental benefit of the intervention. However, it is very often treated as a "reduced cost" in cost-effectiveness analyses because health outcomes of treatment are not valued in dollars. These issues are discussed in Chapter 5.

This chapter presents a microeconomic model of the labor supply decision of a patient as treatment technology improves. The model is set up and solved to illustrate factors at play in the decision of the patient regarding his/her hours of work. Insights from the model provide guidance in discussing approaches adopted in previous literature and in considering why and how these approaches may produce inconsistent estimates of the employment effects.

A Microeconomic Model

In this section, a microeconomic model is presented of the employment behavior of an individual being treated with pharmacological therapy for a particular condition. The focus of the analysis is on the change in quantity of labor supplied by the individual rather than productivity while on the job. The individual is assumed to derive utility from consumption of non-medical goods and services (income from work net out-of-pocket expenditure on prescription drugs) and from leisure. Health condition plays a role in her allocation of time between work and leisure by changing the marginal rate of substitution between consumption and leisure. Since deterioration of health leads to discomfort or hardship at work, leisure is assumed to be more desirable relative to consumption when health is worse. Current health is assumed to depend on previous health and current medical treatment. Medical technology that leads to better health involves higher social costs.

Table 2.1 summarizes the notation. Let w denote the hourly wage of the individual while working and L the number of hours of work. L ranges from 0 to t , the total number of hours available. Leisure is defined as total time available net the working hours, i.e., $t-L$. Let θ denote the individual's health, which is a function of her health if no treatment were taken (θ_0) and pharmacological treatment with technology T . It is assumed that the patient does not choose T (i.e., T is exogenous). Let

$\sigma(L)$ (ranging from 0 to 1) denote the proportion of the unit price of treatment technology (π_T) paid by the individual patient. It is a function of the patient's hours of work and captures the extent of cost-sharing for prescription drugs defined in the patient's health insurance benefits.

Table 2.1. Notation in the economic model

Symbol	Description
w	Hourly wage
L	Hours of work
π_T	Price for one unit of technology embodied in the pharmacological therapy
$\sigma(L)$	Proportion of the unit price paid by the patient
T	Units of technology embodied in the therapy
t	Total hours available
$t-L$	Leisure time
θ_0	Health in absence of treatment
$\theta(\theta_0, T)$	Health outcome as a function of health in absence of treatment, θ_0 , and treatment technology T
$R \equiv e^{\alpha+\beta L-\gamma\theta}$	Marginal rate of substitution (MRS) of leisure versus consumption

The individual patient maximizes the following utility function.

$$U = wL - \sigma(L)\pi_T T + e^{\alpha+\beta L-\gamma\theta} (t-L)$$

with

$$\theta = \theta(\theta_0, T).$$

The first two terms in the utility function denote the amount of earnings from work net out-of-pocket expenditures on the treatment. This is the amount available for non-medical consumption. In the United States, most people of working age obtain health insurance at their, or their spouses', work place. At the same time, public health insurance programs (for example, Medicaid) are available for individuals or

families that meet certain categorical, income and assets requirements. Therefore, for individuals with no prospect of being eligible for public insurance programs, health insurance coverage usually improves with hours of work,⁸ i.e., $\frac{d\sigma}{dL} > 0$. But for those who are eligible for certain public insurance programs, whose employment potential is not adequate to ensure employer-provided health insurance, $\frac{d\sigma}{dL} < 0$, since increased earnings may disqualify them for the public insurance programs.

The third term in the utility function transforms leisure time into consumption equivalents. The expression $e^{\alpha+\beta L-\gamma\theta}$ is the marginal rate of substitution (MRS) between consumption and leisure since the marginal utility of consumption is equal to 1. The MRS increases as the individual works for more hours (and therefore having more consumption). The individual's MRS also changes with health in the sense that illness makes leisure (relative to work) more desirable.⁹ Therefore both β and γ are assumed to be positive.

Medical technologies are assumed to be health-improving. Therefore, as long as T is positive, $\theta(\theta_0, T)$ will be greater than θ_0 , the level of health if the patient does not receive any treatment. And health is assumed to be monotonic in T , i.e., $\frac{\partial\theta}{\partial T} > 0$.

⁸ In practice, health insurance changes with hours of work in a discontinuous manner. For example, fringe benefits (including health insurance) are typically much more generous for full-time than for part-time employees. Calculus is used here for convenience of presentation.

⁹ In theory, marginal utility of both leisure and consumption should fall because of illness, since illness makes both less enjoyable. However empirically, illness is found to be associated with reduced labor supply unambiguously (see discussion in the previous chapter). Therefore the minus sign before γ represents the assumption that illness increases the relative preference for leisure.

The model involves several restrictive assumptions. First, hourly wage is assumed to be invariant to hours of work. While this may not hold for relatively large change in hours of work, or when hours of work change beyond some critical point (such as the point that distinguishes part-time from full-time employment), it is generally true on the margin. Second, it is assumed that hourly wage is not affected by the individual's health, as would be true if 1) health condition has no impact on marginal productivity; or, 2) productivity is not precisely observable to the employer; or, 3) there are barriers to adjustment of wages, at least in the short run, with changes in productivity. These two assumptions are made to focus on employment effects related to changes in hours of work, rather than changes in labor productivity. Third, it is assumed that the treatment and the technological improvement are exogenous. Although this ignores various factors that introduce heterogeneity into patients' access to appropriate care,¹⁰ these factors are not considered at this stage in order to focus on the effect of technological improvement, when made available.¹¹

In sum, the central interest of the model is how employment changes in response to exogenous technological improvement.

The individual maximizes utility by choosing the optimal number of hours of work. The first-order-condition is

$$\left\{ w - \frac{d\sigma}{dL} \pi_T T \right\} - e^{\alpha + \beta L - \gamma \theta} + (t - L) \beta e^{\alpha + \beta L - \gamma \theta} = 0 \quad (1)$$

¹⁰ Factors that are well recognized include variation in physician practice across geographic areas, financial incentives embedded in the organization and management of health care, and disparity in patient compliance across demographic and socioeconomic groups.

¹¹ Although the model itself does not provide implications for the endogeneity of treatment, implications of self-selection into treatment are an important point of discussion in the next section and in the rest of the dissertation.

The first part in equation (1) is the marginal benefit from increased consumption as a result of one additional hour of work. It stands for the marginal effective wage, namely, hourly wage adjusted for the change in the cost of prescription drugs born by the individual. If insurance coverage improves with hours of work (i.e., if $\frac{d\sigma}{dL} < 0$), the effective wage will be higher than the hourly wage, w . If the individual's insurance coverage deteriorates because of higher earnings (as can be the case with public health insurance), effective wage will be lower than w .

The second term on the left hand side of equation (1) represents loss of utility as the individual foregoes one additional hour of leisure time in order to work for one additional hour. The third part adjusts the MRS up by β as the individual is now working for longer hours. The first-order-condition indicates that the patient chooses to increase working hours up to the point at which the value of the effective hourly earning equals the marginal value of forgone leisure. In the following derivation, the MRS will be referred to as R , i.e.,

$$R \equiv e^{\alpha + \beta L - \gamma \theta}.$$

The second-order-condition for the maximization problem is:

$$-\pi_T T \frac{d^2 \sigma}{dL^2} - 2\beta R + (t-L)\beta^2 R < 0 \quad (2)$$

By totally differentiating the first-order-condition with respect to L and technology T , it can be shown that,

$$\frac{\partial L}{\partial T} = \frac{-R\gamma \frac{\partial \theta}{\partial T} + (t-L)\beta\gamma R \frac{\partial \theta}{\partial T} + \pi_T \frac{d\sigma}{dL}}{-T \frac{d\pi_T}{dI} \frac{d^2 I}{dL^2} - 2\beta E + (t-L)\beta^2 E} \quad (3)$$

The denominator, according to the second-order-condition, has a negative sign. Health improves as medication becomes more effective, thus making leisure less preferable relative to consumption (or work). This is captured by the first term in the numerator, which has a negative sign. The second term in the numerator further adjusts for changes in marginal rate of substitution as health improves, and is positive. The third term in the numerator reflects the effect of change in out-of-pocket price of the technology on optimal choice of L. If coverage increases with hours of work ($\frac{d\sigma}{dL} < 0$), this term will have a negative sign. Otherwise it will be positive.

Therefore, when insurance coverage improves with increased hours of work ($\frac{d\sigma}{dL} < 0$), the numerator is more likely to be negative, and $\frac{\partial L}{\partial T}$ positive, suggesting that using a more advanced technology leads to more hours of work. However, if the patient is at risk of losing eligibility for insurance coverage as they work more ($\frac{d\sigma}{dL} > 0$), the individual may find it preferable to work more, to keep working for the same hours, or even reduce hours of work, depending on whether the effect of improved health outweighs, offsets, or is overwhelmed by the effect of higher out-of-pocket drug expenditure. Table 2.2 summarizes the relationship between the sign of $\frac{d\sigma}{dL}$ and change in effective wage as well as change in equilibrium labor supply as treatment technology improves.

Table 2.2. Change in insurance coverage as labor supply changes ($\frac{d\sigma}{dL}$) and how it relates to other elements of the model

$\frac{d\sigma}{dL}$	$w - \frac{d\sigma}{dL} \pi_r T$ (marginal effective wage)	$\frac{\partial L}{\partial T}$
≤ 0	$\geq w$	> 0
≥ 0	$\leq w$	$>, =, < 0$

The model - even with its several simplifying assumptions - illustrates the complexity of an individual patient's decision to supply labor when he/she is treated with more effective pharmacological therapy. The decision is complicated by the way in which health insurance is made available. In particular, availability of health insurance reduces the price of the therapy faced by the individual, and at the same time, is tied to one's hours of work. Studies on the "job-lock" or "employment-lock" effect of health insurance found that working individuals with chronic conditions may have greater incentive to work if employer-provided insurance is the only viable or affordable insurance coverage (Madrian 1994a; 1994b). Analogous reasoning suggests the existence of "welfare-lock", as individuals insured under public means-tested insurance programs (e.g., Medicaid) would find working at all or increasing hours of work less desirable if, by doing so, they risk losing the public coverage (Yelowitz 1995). This model further indicates that these insurance effects play an important role in determining changes in labor supply when the patients are treated with better technologies.¹²

¹² There are other dimensions of employee compensation systems and public welfare and insurance system that play similar roles in individuals' employment decisions. These include the non-monetary benefits associated with hours of work other than health insurance, and in the public sector, disability insurance, in-kind transfers such as food stamps, and welfare income such as the Supplemental Security Income (SSI). Although these factors are not explicitly modeled, it is not hard to see that as long as the eligibility rule is related to individuals'

To summarize, for patients treated with advanced medical technologies, observed changes in employment are not only the outcomes of improved health conditions due to the treatment, but also affected by how an individual's hours of work impact private or public health insurance coverage.

A critique of previous approaches

Thus, to account for employment benefits of medical treatment, researchers need to know changes in patients' employment outcomes due to the treatment. In a randomly controlled trial, the treatment effect on employment can be estimated by observing employment outcomes before and after the treatment among the (randomly assigned) treatment group, and comparing that change to the change observed among the (randomly assigned) control group, with differences in the changes between the two groups being attributed to the treatment.

A review of the treatment evaluation literature reveals that there are three major approaches to accounting for the effects of treatment on employment, which I will call: the "before-and-after" approach, the "burden-of-illness" approach, and the "statistics-of-the-population" approach. As will be discussed, the "before-and-after" approach does not lead to consistent estimates because of its incorrect conceptualization of treatment effects. The "burden-of-illness" and the "statistics-of-the-population" approach each use approximations that, in general, do not provide consistent estimates of the employment effects of treatment.

The "before-and-after" approach

Studies with the "before-and-after" approach estimate the employment effects of treatment by observing changes in employment pre- and post- treatment, and attribute the observed changes to the

employment status or hours of work, they further complicate the decision process.

treatment. The study on the outcomes of migraine treatment with Sumatriptan reviewed in Chapter 1 (Legg, Sclar, Nemecek, et al. 1997) is an example of this approach. In that study, researchers conducted a telephone survey to assess productivity outcomes of using Sumatriptan (a prescription drug for the treatment of acute migraine) by asking the users to report lost work days, days worked with symptoms and level of work productivity both after and before treatment with Sumatriptan. The reduction in lost labor costs¹³ was then calculated and compared to the incremental costs of taking Sumatriptan versus other non-Sumatriptan therapies.

As is well known, the "before-and-after" approach errs in its conceptualization of the effect of treatment. Even with random assignment of patients to the treatment and control group (so that there is no systematic selection of patients by factors related to the employment outcome), the treatment effect is measured as the change in outcome after the treatment relative to before *net* the same change observed in the control group. This is because health, and therefore employment, can either improve or deteriorate in the absence of the treatment, and we are essentially interested in estimating the *incremental* effect of treatment on employment compared to no treatment, or other types of treatment.

For example, a recent study on the effect of antidepressant treatment on depression patients' work performance (Berndt, Finkelstein, Greenberg et al., 1998) explicitly accounted for "regression-to-the-mean" in both work performance and depression symptoms. For participating patients of the study, the estimates indicate that about 41% of the predicted change in work performance is due to regression to the mean, while 59% reflects the impact of alleviated depression symptoms as a result of antidepressant medication. Biases introduced by

¹³ In Legg et al. (1997), "lost labor costs" were calculated as lost workdays multiplied by daily earnings in a particular occupation category.

"regression-to-the-mean" are likely to be especially large if the condition is episodic and when treatment outcomes (employment outcomes in this case) are observed over a relatively short period of time. Take again the Sumatriptan study as an example. Since patients who switched to a new therapy were likely to have experienced some acute episode of migraine before their switch,¹⁴ because of "regression-to-the-mean", symptoms would have tended to ameliorate after the switch even if Sumatriptan were no more effective than the therapies used before. As a result, the observed difference in work performance before and after the switch may overestimate the incremental effect of Sumatriptan.

The microeconomic analysis in the previous section suggests that financial incentives embedded in many social programs or employment-related benefits could make patients more or less likely to work when a new technology becomes available. Unlike some other conditions that may disable patients from work, the condition of interest in Legg, Sclar, Nemec, et al. (1997), i.e., migraine, normally leads to short-term disability or reduced productivity while on the job rather than changes in long-term employment status. Therefore the bias introduced by incentives embedded in health insurance provision may not be of great concern in this case. However, aside from the conceptual issues discussed so far, the estimated effect can be biased because of patients' entitlement to other types of employment benefits. For example, full-time employees usually have a fixed number of paid sick-leave days every year. This benefit provides incentives for patients to stay at home instead of coming into work even if their health conditions allow them to work. In the case of migraine treatment, since patients were asked to report work loss during the month prior to and the month after the treatment, estimated reduction in work loss might be biased up simply because patients had fewer paid-sick-leave days to use in the

¹⁴ As discussed earlier, a switch of therapy is very often triggered by deterioration of the condition, or failure of the patient to respond to the original therapy.

month after and therefore were less likely to report "lost work days" in the after- period even if Sumatriptan had no additional effect.

The "burden-of-illness" approach

A burden-of-illness, or cost-of-illness (COI), analysis calculates the total costs of a certain illness, including direct medical costs, indirect costs because of lost "productivity ascribed to those individuals who die prematurely or are disabled by their illness" (Pilskin and Taylor 1977), and other indirect costs such as the effects of mortality, morbidity, distress, or discomfort unrelated to employment.¹⁵

Results of COI studies provide only "order of magnitude indicators of the economic burden of particular diseases" (Kirschstein 2000). Nonetheless, they have been used extensively to inform policies regarding allocations of resources for the prevention and treatment of particular diseases. Thus, the burden of disease is used as a proxy for the potential benefits of preventing or treating the disease. In the case of disease burden related to lost productivity, by using COI estimates to inform policies, researchers implicitly assume that, productivity gains as a result of the intervention could be approximated by average productivity lost to the illness. However, this is generally not true.

The employment effect due to better treatment technology is depicted by the first two terms in the numerator of equation (3), both

of which are a function of $\frac{\partial \theta}{\partial T}$, i.e., restored health because of the

better technology. Although modern medicine has made great advances in restoring health for patients inflicted with various diseases, in most

¹⁵ For a detailed discussion of methodological issues in COI studies, see Rice et al. (1985).

cases, $\frac{\partial \theta}{\partial T}$ is much less than health lost to the disease, because treatment only partially restores patients' health to the state before the onset of illness. Therefore, productivity gains because of the treatment are likely to be less than productivity lost to the illness. Using "burden-of-illness" in terms of lost productivity as a proxy for employment effects of treatment is likely to bias the employment effects upward. This bias is especially large when the illness of interest has large morbidity costs yet available treatment does not have large potential of avoiding lost productivity.

Treatment of depression is an example. A number of studies have documented the burden of depression in terms of functional impairment (for example, Greenberg, Stiglin, Finkelstein, et al. 1993; Stewart, Greenfield, Hays, et al. 1989). In a recent study that examines the most expensive and most disabling conditions in the United States (Druss, Marcus, Olfson et al., 2002), mood disorders (including depression) were ranked second only to back disorder in terms of number of lost workdays. Although the success rate in treating depression approaches 80%, first-line treatment may be successful in only 50-60% of the cases. Therefore, even if remission of depression symptoms as a result of effective treatment could be translated into full restoration of productivity, productivity gains due to treatment would still be much less than productivity lost to the condition because of the low success rate and high probability of relapse.¹⁶

¹⁶ This point is echoed in Kirschstein (2000), an NIH report to the Congress on disease-specific estimates of direct and indirect costs of illness. The report points out that, even if there existed consistent and comprehensive estimates of the relative burdens of specific diseases, "decisions regarding policy and budget would have to include other factors such as the importance of scientific advances and opportunities as well as the research tools available to address specific disease processes".

The "statistics-of-the-population" approach

A third, so-called, "statistics-of-the-population" approach, is often adopted in CEAs to derive estimates of productivity in future life years. The idea is to apply statistics on labor market participation and annual earnings of the general population to the patient population of interest. For example, Meltzer (1997) used earnings estimates (by age) from the Consumer Expenditure Survey as a proxy for earnings of patients (of the same age group) in cost-effectiveness analyses of various medical interventions.

Aside from the caveats of measuring employment benefits by earnings, which are discussed in Chapter 5, it is inappropriate to apply statistics of the general population to the patient population of interest, such as those with "adjuvant chemotherapy for Duke's C colon cancer" or "coronary artery bypass 3-vessel disease, severe angina" (two of the conditions considered in Meltzer (1997)). Patients under these types of health shocks are much less likely to be actively engaged in market production than the general population of the same age. As a result, such an analysis would be biased towards finding favorable cost-effectiveness ratio for the interventions.

More recent studies with a focus on specific interventions explicitly took into account different employment outcomes of individuals with certain disabilities. In a CEA of hypertension treatment, Johannesson, Meltzer, and O'Connor (1997) took estimates of production losses of patients with coronary heart diseases or stroke from earlier studies. They calculated the productivity of these patients as productivity estimates for the general population (of the same age groups) minus the production losses. Meltzer, Egleston, Stoffel, et al. (2000) refined an earlier evaluation of intensive therapy for Type-I diabetes. They approximated labor market participation rate of patients with diabetes-caused disabilities such as blindness, end-stage-renal-disease and amputation using statistics of the corresponding disabled

group in the general population. Although these studies improved the accounting of age- and morbidity- specific productivity, they are still based on estimates for populations that differ markedly from the patient populations of interest, in terms of both clinical and social-economic characteristics. For example, in the study of Type-I diabetes treatment, given the fact that people with blindness caused by diabetes have very different comorbid profiles and employment histories than those of the born-blind or those who became blind because of an eye disease, it is doubted that the approximation adopted in the analysis is appropriate.

Moreover, almost all CEAs with a life-time horizon rely on simulations of disease progression and have health care costs and outcomes (including employment outcomes) conditional on a particular stage of the disease. Thus, the only way in which treatment can affect patients' employment is by altering transition probabilities to well-defined disability or morbidity status. Although this makes the analysis manageable, it has limited use for chronic conditions (such as chronic back pain and arthritis) that are debilitating yet not associated with well-defined acute events.

Even for diseases with clinically defined stages, employment effects are not always based on whether the patient is in or out of a particular stage. Intensive antiretroviral therapies to treat HIV provide an example. Using the "statistics-of-the-population" approach, Sendi and colleagues (Sendi, Bucher, Harr, et al. 1999) studied the cost-effectiveness of the Highly Active Antiretroviral Therapies (HAART) for the treatment of HIV infection. Health care costs and productivity outcomes are estimated by stratifying HIV patients in the Swiss HIV Cohort Study by their clinical stage (AIDS or non-AIDS) and their CD4 counts (a critical measure of the functioning of a patient's immune system). However, data of the HIV population in the US indicate that employment transitions of HIV patients are not highly correlated with clinical stages of the disease. Specifically, in the HIV Cost and

Services Utilization Study (HCSUS), 57 HIV patients were working and not yet diagnosed with AIDS at baseline, but were with an AIDS diagnosis at the second follow-up survey. Of the 57 patients, 42 remain employed (74%) at the second follow-up. In the same study, 200 HIV+ patients changed their employment status from "not working" at baseline to "working" at the second follow-up survey. The vast majority of this group remained in one of the disease stages (non-symptomatic, symptomatic, or AIDS), and the few transitions observed were almost all towards more advanced stages.

Towards an econometric model of employment effects

Being aware of the difficulties in estimating an effect is just the first step. The next step is to identify empirical strategies that would lead to consistent estimates of the effects. In that effort, a general econometric framework is useful to conceptualize the question and guide the estimation.

Before laying out the framework, it is worth discussing conceptually the issue of selection. Outside random controlled trials (RCTs), patients self-select into treatment by severity of their conditions and by other personal behavioral traits. Both types of factors are likely to be correlated with individuals' employment outcomes, and if not observed and thus not controlled for in an analysis, would lead to inconsistent estimates of the employment effects.

The microeconomic model in the previous section makes the assumption that the effect of technological improvement on health ($\frac{\partial \theta}{\partial T}$) is the same for all patients. However, if we denote patients' behavioral traits related to the treatment as \vec{x} , then in general, for any patient,

$$\frac{\partial \theta}{\partial T} = g(T; \theta_0, \bar{x}). \tag{4}$$

This points out that the incremental effect of better treatment on health depends on the patient's initial health status and her behavioral traits as well as the nature of the technology.

In day-to-day clinical practice, patients who are more seriously ill, or either do not respond to, or cannot tolerate, older treatments, are usually the first to be treated with new technologies when they become available. Furthermore, personal traits (for example, perseverance) affect both compliance with treatment regimens and employment outcomes. Therefore, the treatment group in a non-RCT context are likely to be quite different from those who are not treated with the technology in ways that are both observable or unobservable. In most of the cases, these factors are also correlated with one's employment outcomes. As a result, the employment outcomes of the treated group observed outside RCTs, in general, would not be replicated if the non-treated group were to receive the same treatment. The following model provides an econometric depiction of the problem.

Denote the employment outcome of interest as *Employment**¹⁷, the treatment of interest as *Therapy* (a 0-1 treatment variable), observed individual characteristics as *X* (including measures of pre-treatment severity and socio-demographic information related to employment such as education, the effect of unobserved factors (such as unobserved severity) as δ , and a random disturbance as ϵ_E . The following equation provides a general framework for econometric estimation of the effect.

¹⁷ * is used to indicate that the measure is continuous. When a categorical or dichotomous outcome (such as working versus not working) is of interest, *Employment** represents the latent index underlying the generating process of the dichotomous outcome. Specifically, the dichotomous outcome will be 1 if *Employment** is positive.

$$Employment_i^{t1*} = \alpha_E + \beta_T Therapy_i^{t0} + X_i' \gamma_E + \delta_i + \varepsilon_{iE} , \quad (5)$$

where $E(X' \varepsilon_E) = 0$, $E(Therapy' \varepsilon_E) = 0$, $E(Therapy' \delta) \neq 0$.

The superscripts t1 and t0 of *Employment** and of *Therapy*, respectively, indicate that the employment outcome of interest is observed after the treatment is initiated, although the amount of time it takes for the treatment to affect employment depends on the nature of the illness and the treatment.

The parameter of interest here is β_T , representing the effect of treating the patient with "Therapy" compared to other types of treatment including no treatment. Since δ_i is correlated with both "Therapy_i" and "Employment*_i", a regression based on equation (4) but with δ_i unobserved and thus excluded would produce an inconsistent estimate of β_T . This happens because, in such an analysis, part of the effect of the unobserved factors on employment is erroneously attributed to "Therapy".

The instrumental variable approach

One approach to deriving a consistent estimate of the treatment effect when there are omitted variables (δ_i) in equation (5) is the instrumental variable (IV) approach. The idea is to find some variables Z that are correlated with a patient's chances of getting the therapy, i.e., $Cov(Therapy, Z) \neq 0$, yet uncorrelated with the disturbance, i.e., $Cov(Z, \delta + \varepsilon) = 0$.

Chapter 3 presents an empirical study of the employment effect of intensive antiretroviral therapies for the HIV+ population. It provides an example of how the IV method could be applied to estimating

employment effects when patients select into treatment. This example illustrates that, without taking into account the endogeneity of the treatment (in particular, selection of patients into treatment by unobserved disease severity), an estimator based on equation (5) may substantially underestimate the true effect of the therapies on employment transitions of HIV patients. It also discusses the appropriate specification of the model with IV approach when both the treatment and the employment outcome are dichotomous variables.

The "difference-in-difference" approach

The econometric framework laid out in the last sub-section requires the availability of both panel data (longitudinal sample of the same group of individuals) and instrumental variables for the treatment of interest. However, in empirical research, availability of both is the exception rather than the norm. When either panel data or IVs are not available, we need alternative strategies to estimate the employment effects under non-random assignment of treatment.

This sub-section presents the "difference-in-difference" approach. When only repeated cross-sectional data are available and when no appropriate instrumental variables exist, a useful research question to ask is: how do recent treatment technologies compare to earlier technologies in improving patients' employment outcomes? To conceptualize, I start with a slightly revised version of equation (5).

$$Employment_{LateCohort}^* = \alpha_{LC} + \beta_{LC}Med_{LC} + \gamma_{LC}X_{LC} + \delta_{LC} + \varepsilon_{LC} \quad (6)$$

$$Employment_{EarlyCohort}^* = \alpha_{EC} + \beta_{EC}Med_{EC} + \gamma_{EC}X_{EC} + \delta_{EC} + \varepsilon_{EC} \quad (7)$$

In this context, the treatment variable is denoted as "Med" for the more general term of "medication" rather than a specific therapy. Equation (6) is a model for the employment effect of medication used by

the "late cohort" (LC), and equation (7) is for the "early cohort" (EC). Of interest here is the additional effect of medication developed more recently (Med_{LC}) compared to medication developed earlier and used to treat patients of the early cohort (Med_{EC}). This additional employment effect is represented by the difference between the treatment effect of the "late-cohort medication" and the "early-cohort medication", i.e., $\beta_{LC} - \beta_{EC}$. To derive consistent estimate of this additional effect, the econometric strategy will again need to control for the unobserved factors in determining individuals' employment outcome that are also correlated with the decision to medicate, i.e., δ_{LC} and δ_{EC} .

The first step in the "difference-in-difference" (DiD) approach is to obtain the difference in expected employment between those on medication and those not on medication in each cohort. The second step is to get the difference in these two differences. More formally, the DiD is

$$\begin{aligned}
 & E\{(y_{LateCohort}^* | Med = 1) - (y_{LateCohort}^* | Med = 0)\} \\
 & - E\{(y_{EarlyCohort}^* | Med = 1) - (y_{EarlyCohort}^* | Med = 0)\} \\
 & = (\beta_{LC} - \beta_{EC}) + \{\gamma_{LC} E(X_{LC}^M - X_{LC}^{NM}) - \gamma_{EC} E(X_{EC}^M - X_{EC}^{NM})\} + \{E(\delta_{LC}^M - \delta_{LC}^{NM}) - E(\delta_{EC}^M - \delta_{EC}^{NM})\}
 \end{aligned} \tag{8}$$

The first part on the right-hand-side of equation (8), i.e., $\beta_{LC} - \beta_{EC}$, is the effect of interest. The second part accounts for the differential effects of observed factors, and can be controlled for in a regression analysis. The last part on the right-hand-side of the equation is the DiD of the effect of the unobserved factors between the medicated and the non-medicated group, and between the late and early cohort. If, over time, the factors that select patients into treatment (for example, unobserved severity) and the way the selection works

remain constant, then $E(\delta_{LC}^M) = E(\delta_{EC}^M)$, and $E(\delta_{LC}^{NM}) = E(\delta_{EC}^{NM})$, and as a result, $E(\delta_{LC}^M - \delta_{LC}^{NM}) - E(\delta_{EC}^M - \delta_{EC}^{NM}) = 0$.

However, this is generally not the case. A typical scenario is that, over time, patients become more aware of the condition and the treatment and physicians become more ready to diagnose and prescribe the medication. Consequently, more patients in the late cohort get treated, and prior to the treatment, the treated group in the late cohort are not as sick on average as those in the early cohort.

Yet change in the unobserved factors (δ^M) over time does not make the DiD approach invalid. As is illustrated by a model in Appendix A to Chapter 4, as δ^M changes, δ^{NM} changes in the same direction, making the change in $\delta^M - \delta^{NM}$ ambiguous. Therefore, whether the DiD approach will lead to consistent estimates of the additional employment effects depends on how the major components of $\delta^M - \delta^{NM}$ change over time.

Chapter 4 presents an empirical study using the DiD approach. The study makes use of data from the Framingham Offspring Study to estimate the additional effect of recent anti-hypertensive drug therapies on patients' employment rate relative to therapies available in the 1970's. Additional effects of the recent therapies on blood pressures are estimated first to provide a benchmark for the additional employment effect to be estimated. The point estimate of the employment effect based on the DiD approach, however, could be substantially larger than the real effect. The assumptions implicit in the DiD model and the possible violations of the assumptions are discussed.

Conclusions

This chapter presents a microeconomic model of individual labor supply as treatment technology improves. The model shows that the change in labor supply observed in a non-experimental setting is, in general, not the same as the treatment effect. Specifically, when eligibility for health insurance coverage and/or other benefits is tied to one's labor supply, comparing the employment outcomes of the treated group with those of the non-treated group, or comparing outcomes after the treatment to those before for the same group of patients, lead to biased estimates of the treatment effects. These types of approach are also problematic when patients self-select into treatment by severity or personal behavioral traits.

Three approaches to estimating employment effects seen in previous literature are reviewed and critiqued in this chapter. It is clear that, because of either conceptual or measurement issues, these approaches fail to provide reliable estimates of employment effects of pharmaceutical innovations. The empirical studies presented in the next two chapters provide examples of statistical strategies to develop reliable answers to questions related to employment effects of treatment.

3. EFFECTIVE HIV TREATMENT AND THE EMPLOYMENT OF HIV+ ADULTS

Introduction

The vast majority of patients infected with human immunodeficiency virus (HIV) are adults of prime working age. Thus, effective treatments promise not only to improve health but also to increase the employment opportunities of this population. Highly active anti-retroviral therapy (HAART) developed in the early 1990's has been shown to reduce the levels of virus in the blood with commensurate improvements in mortality (Palella et al., 1998). The treatments also have led to better quality of life for patients living with HIV (Egger, Hirschel, Francioli, et al 1997; Brechtel, Breitbart, Galietta et al. 2001), and thus hold promise for allowing patients to work longer and more productively.

Ideally, one would measure the employment consequences of the HAART therapy as part of a clinical trial designed to measure the health benefits. Patients would be randomly assigned to the therapy and so labor market outcomes could be compared across the treatment and control groups. But clinical trials rarely track labor market outcomes; and if they do, the highly selected patients and clinical settings limit one's ability to generalize. Patients in clinical trials are often chosen because they are motivated to adhere to therapy or because the risks of mortality or other complications for these patients are low, and they are recruited and treated in non-representative academic settings (Gurwitz, Col, Avorn 1992). These biases are tolerated for clinical outcomes because the primary research question is whether a drug is effective under the best of circumstances. For policy questions, however, we are often more interested in the consequences of therapy under more "natural" circumstances.

Such questions can be answered in non-randomized settings. However care must be taken to interpret the data correctly. As

discussed in Chapter 2, access to treatment and subsequent compliance can be associated with unmeasured clinical and social factors that may play a role in individuals' employment decisions as well. For example, patients on HAART may be less severely ill in ways that are difficult to observe, or they may be more motivated to comply with physician orders. Such factors also might make them more likely to be employed. Therefore, a direct comparison of those on HAART and those not on HAART is likely to produce biased estimates of the effect of the treatment.

This study estimates the effects of HAART on patients' employment outcomes using data from a representative sample of HIV+ patients. Our analytic approach explicitly accounts for the possibility that treatment of HAART is affected by some factors that one cannot observe. More precisely, we use policies affecting coverage of HAART in state health insurance programs as instrumental variables for the treatment of HAART. These policies are directly related to patients' chances of receiving HAART, but not directly related to their employment outcomes except through the treatment.

In the next section, we provide an overview of the clinical and policy context. The third section describes our data; the fourth section presents our econometric approach. We present results of the estimation in the fifth section and discuss our findings in the final section.

Background

The recent development of new classes of drugs—namely, non-nucleoside analogue reverse transcriptase inhibitors and protease inhibitors—added several potent weapons to the HIV arsenal. Recent clinical trials have found that combination of several antiretroviral drugs—known as highly active anti-retroviral therapy or HAART—are much more effective in reducing mortality and morbidity among HIV+ patients than less intensive treatment regimens (Palella et al. 1998). A panel of leading experts recommended HAART to achieve maximum suppression of

symptoms for as long as possible (Carpenter et al., 1998). Taken together, all the clinical evidence suggests that HAART could have important employment effects for a population of HIV+ adults in care.

One problem is that patients may not seek treatment immediately. HIV infection can be asymptomatic for 8 to 9 years, and manifestation of symptoms may directly increase patients' chances of seeking treatment as well as the likelihood that their physicians prescribe the intensive therapy. In fact, although clinical guidelines before 1998 strongly recommended combination therapy for patients during acute primary HIV infection, whether such strategy is appropriate for patients with relatively high CD4+ T cell counts¹⁸ or lower viral load was far less certain (Centers for Disease Control and Prevention 1998). Further, with limited public resources to treat HIV, sicker patients are usually given priority under public assistance programs. As a result, prior to treatment, patients on HAART are likely to be sicker, and therefore, more likely to have difficulties working than patients not on HAART. This means that patients who receive HAART treatment are sicker in ways that cannot be completely controlled without very detailed clinical data (Goldman, Bhattacharya, McCaffrey, et al. 2001). (Even with such data, other factors that are unobservable, such as patient motivation, may play a role.)

HAART therapy is very expensive, which also limits its use. With average annual cost exceeding \$10,000, most patients have to rely on insurance coverage to finance the treatment (Shapiro, Morton, McCaffrey, et al., 1999; Cook, Cohen, Grey, et al. 2002). Westmoreland (1999) provides detailed information about the eligibility of HIV/AIDS patients for public insurance programs, of which Medicaid and Medicare may be the most important. Various other programs have been developed to meet the

¹⁸ CD4+ T cell count is a critical measure of the functioning of a patient's immune system. Depletion of these cells is strongly correlated with the worsening of the HIV infection and risk of developing AIDS (Harrison et al. 1997).

need of HIV patients transitioning from private to public insurance, among which the AIDS Drugs Assistance Program (ADAP) has the greatest number of beneficiaries and provides an important life-line for low-income HIV patients. ADAP was established under the Ryan White CARE Act, funded by both federal grants and state discretionary funds. ADAP served almost 138,000 clients in FY 1999, with a total budget exceeding \$800 million (The Kaiser Family Foundation 2002). Since ADAPs are administered by states, there is great variation across states in the types and number of drugs covered.

The importance of public assistance in financing HIV care creates social inefficiencies, since the eligibility rules of many public programs are set in a way such that they discourage employment (Goldman, Bhattacharya, Leibowitz, et al., 2001). In particular, patients who get treated and go back to work risk losing public insurance if their earnings are higher than the income threshold. This type of "welfare lock" is especially worrisome for patients on expensive treatment like HAART, since losing public insurance coverage likely means terminating treatment. The result is that they may be very reluctant to go back to work if they were not already doing so. On the other hand, HAART patients with employer-provided insurance have greater incentives to remain employed than if the availability of insurance is not contingent on one's employment status—a condition often termed "job lock" (Madrian 1994a, b). These competing incentives suggest that one must be careful in analyzing and interpreting the evidence.

Data

To test whether HAART does have an effect on labor market outcomes, we use data from the HIV Cost and Services Utilization Study (HCSUS). The study population is representative of patients over 18 years old who made at least one visit to a facility other than military, prison, or emergency department facilities in the contiguous 48 states

in early 1996 (Bozzette, Berry, Duan, et al, 1998). Using a multi-stage sampling frame, the baseline survey interviewed 2,864 patients between January 1996 and April 1997. Follow-up interviews were conducted between December 1996 and July 1997 and between August 1997 and January 1998. The sample sizes for the second and third waves are 2,466 and 2,267, respectively, with virtually all the attrition due to mortality.

In each wave of HCSUS, patients were shown lists of antiretroviral drugs (including the most recently developed classes) and asked to identify those taken in the previous six months or since the last interview. An indicator for HAART therapy ("HAART") was then constructed by Anderson, Bozzette, Shapiro, et al. (2000) based on recommendations published by the Centers for Disease Control and Prevention (Centers for Disease Control and Prevention 1998).¹⁹

The employment data from HCSUS include whether the individual was working at the time of the interview, and if working, number of hours usually worked per week during the last month. In addition to important sociodemographic information, the HCSUS study also collected information about factors that are likely to affect the use of advanced drug therapy and employment, including exposure route, health insurance, disease stage, and count of CD4+ T cells. We also classified insurance in four categories: none, employer-provided insurance, self-purchased private insurance, or public insurance (Medicaid or Medicare).

We focus our analysis on HIV patients who were of prime working age (25 to 54) at the time of the baseline survey and participated in all three waves of HCSUS. Table 3.1 presents the weighted summary

¹⁹HAART was defined as using a protease inhibitor (PI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a nucleoside reverse transcriptase inhibitor (NRTI) in various combinations. For example, HAART includes two or more NRTIs in combination with at least one PI or one NNRTI; and one NRTI in combination with at least one PI and at least one NNRTI. Combinations of older drugs such as zidovudine, which is an NRTI, with either a PI or NNRTI were not considered HAART.

statistics of this population across the three waves.²⁰ In a cohort of HIV+ adults, one would expect to see health deteriorate in later waves as disease progresses, and we do: the AIDS rate rises and the average CD4+ counts fall in the two follow-up surveys. Despite somewhat worsening health, the percentage of patients reporting "working now" stayed fairly constant from the baseline to the second follow-up. At the same time, we also see a dramatic increase in the percentage of the population using HAART, suggesting that treatment may have been successful in mitigating a reduction in the employment of the HIV+ population in the aggregate.²¹

Our estimation strategy relies on finding factors—i.e., instrumental variables—that affect whether a patient receives HAART, but do not affect individual employment decisions (except through their impact on treatment). It is hard to find individual factors such that these conditions hold. However, public policies at a larger geographic level seem more promising. We collected data on state-specific policies in 1997 that affect the generosity of coverage. These include a dichotomous variable indicating a limit of three prescriptions per month by the state Medicaid programs (The Medicaid HIV Policy Project 1998), and whether the state ADAP covers a non-nucleoside reverse transcriptase inhibitor—the newest class of antiretroviral drugs (Doyle, Jefferys, Kelly 1997).²²

²⁰The final analytic weight is the product of the sampling weight, the multiplicity weight, and the non-response weight. The sampling weight adjusts for the probability of being chosen to participate in the study; the multiplicity weight adjusts for patients who could have entered the sample through multiple providers; and the non-response weight adjusts for differential cooperation. More details are given in Duan, McCaffrey, Frankel, et al. (1999).

²¹ Alternatively, this could be evidence of "job lock" as discussed previously, an issue we come back to later.

²² Among states that specified monthly limits on number of prescriptions in their Medicaid program, most had a limit of five or six prescriptions per month (these states are: California, Florida, Georgia, Mississippi, and North Carolina), and the other three states (Texas, South Carolina, and Nevada) limited monthly prescriptions to three. Of the five states with a limit of five or six prescriptions, California, Florida, and North Carolina had above-average HAART utilization in the HCSUS. Georgia and Mississippi had very few observations in the data. Also, more recent data on state Medicaid coverage policies indicate that for California and Florida, antiretroviral drugs were exempted from the

We also collected state-level data on factors that would affect the likelihood of obtaining insurance—either public or private. These include information on the Medicaid eligibility income threshold as a fraction of the federal poverty line for AFDC and for the medically needy program in Medicaid and the average firm size in the state. For states without a medically needy program in the year of 1996, we code the income threshold to be 0. These data will be used in sensitivity analyses regarding the specification of patients' insurance status. However, it is important to note that our assumption is that the prescription drug coverage associated with insurance at the state level affects HAART receipt but not employment, except through its effect on HAART. We do not maintain this hypothesis for differences in eligibility; program eligibility rules should have a direct effect on employment as one of us has argued elsewhere (Goldman, Bhattacharya, Leibowitz, et al., 2001).

Econometric Approach

It takes an unknown amount of time for the employment benefits of treatment to be realized. In the absence of data about the duration and timing of labor market spells, we take a simple dynamic approach to estimate how treatment affects outcomes. That is, in most of our analyses we ask how employment outcomes change between baseline and the third wave as a function of HAART treatment during the intervening period.²³ We consider three types of outcomes. First, we examine the probability that a patient "returns to work," conditional on not working at baseline.

monthly prescription limit. (In a reduced form probit analysis on the probability of having HAART, the dichotomous variable indicating a Medicaid limit of 5-6 prescription drugs is associated with more use of HAART than a policy of no limits.)

²³To maintain consistency with other HCSUS studies, we subsequently refer to the second wave as "first follow-up" and the third wave as "second follow-up". Baseline is of course the first wave.

Second, we look at whether individuals "remain employed", i.e., conditional on working at baseline, the probability of still working at the second follow-up. Third, we study the effect of HAART on hours of work per week among those who were working at the second follow-up ("hours of work"). Because the conditioning sample is different in each case, we model these outcomes separately. For the continuous outcome of hours of work, we use two-stage least squares. In the first stage, the probability of having HAART is modeled as a linear function of personal characteristics, baseline HIV severity, and our instruments (state policies); in the second stage, hours of work at the second follow-up is modeled as a linear function of the predicted probability of having HAART (derived from the first-stage) and the same individual-level information.²⁴ For each of the two dichotomous outcomes of "return to work" and "remain employed", we specify a joint, nonlinear model—a bivariate probit—of employment and treatment of HAART.

The bivariate Probit model with instrumental variables

For either "return to work" or "remain employed", we denote the dichotomous outcome as "Employment" and the dichotomous treatment as "Haart". We make the assumption that both the employment outcome and HAART are determined by an underlying continuous index ("Employment*" and "Haart*"). That is, when Employment* (Haart*) is greater than zero, Employment (Haart) takes the value of 1, and 0, otherwise. We denote the instrumental variables for HAART (state policies that affect HAART but not employment) as Z and the other personal characteristics (sociodemographics, baseline severity measures, and infection route) as X . The bivariate probit model then becomes:

²⁴We also estimated HAART treatment in the first stage using a probit instead of a linear probability model to maintain consistency with the other outcomes. Using a nonlinear first stage did not change outcomes. Similarly, a log-linear specification for hours worked did not yield substantively different coefficients.

$$Employment_i^{F2*} = \alpha^E + \beta Haart_i^{F1} + X_i' \gamma^E + \varepsilon_i^E ; \quad (1)$$

$$Haart_i^{F1*} = \alpha^H + Z_i^{F1'} \delta + X_i' \gamma^H + \varepsilon_i^H . \quad (2)$$

We assume a bivariate normal distribution (with the variance normalized to 1 and the correlation coefficient denoted as ρ) for the error terms:

$$\begin{pmatrix} \varepsilon^E \\ \varepsilon^H \end{pmatrix} \sim BVN \left(\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{bmatrix} 1 & \rho \\ \rho & 1 \end{bmatrix} \right). \quad (3)$$

The superscripts "F2" and "F1" serve as reminders that we model employment at the second follow-up survey as a function of treatment preceding the first follow-up survey. We measure treatment using the first follow-up rather than baseline for several reasons. First, treatment rapidly diffused between the baseline and first follow-up survey, soon after their introduction into clinical practice (shown in Table 3.1), and early adopters were likely to be a highly selected group. Second, there were data problems in the baseline survey that prevented HCSUS from identifying exposure to HAART for some patients (Andersen, Bozzette, Shapiro et al, 2000). Third, it is likely that employment transitions respond more to treatment in the intervening period rather than treatment that could have occurred up to six months prior to the baseline interview.

The correlation between ε^E and ε^H captures the correlation between patient's propensity to receive HAART and propensity to change employment. As noted previously, there is no way to sign the bias a priori. Greater (unobserved) severity of the disease would probably make someone more likely to receive HAART and less likely to work, suggesting a negative correlation. On the other hand, HIV therapy is

complicated, and patients who are very motivated to treat their illness in ways that are unobservable may also be very motivated to work, suggesting a positive bias (Goldman and Smith, 2002).

For the type of model we are estimating, identification is achieved when: 1) the errors of the two equations are independent; or, 2) there exists at least one right-hand-side variable in the HAART equation that is not in the employment equation (Maddala, 1983). The model is then estimated using maximum likelihood.²⁵

The vector Z_i^{F1} in the therapy equation (2) contains instrumental variables for HAART. These, as introduced in the Data section, include a dummy variable indicating whether the Medicaid program in patient's home state had a limit of three prescription drugs per month and a dummy variable indicating whether the ADAP in a patient's home state covers non-nucleoside reverse transcriptase inhibitors (NNRTIs) in 1997. Since Medicaid is an important source of health insurance for the HIV+ population, and the state ADAP provides essential coverage of prescription drugs for HIV patients between private and public coverage, prescription drug benefits under these two programs should affect access to HAART for a significant part of the HIV+ population receiving care. Further, because HAART is a combination therapy with at least three antiretroviral drugs and NNRTI is one of the two "must-haves" on the therapy, these two coverage policies are likely to be directly correlated with chances of getting the therapy. On the other hand, since these policies are distinct from means-tested eligibility rules in determining one's eligibility for Medicaid or other public assistance

²⁵What is sometimes seen in the empirical literature is a nonlinear two-step procedure. In the first stage, a probit model for the endogenous treatment variable is estimated as a function of the instrumental variables and other covariates. In the second stage, the predicted probability from the first stage is "plugged-in" to estimate the treatment effect. However, when the outcome variable is dichotomous—unlike in the case where the outcome variable is continuous as in "hours of work"—it has been shown that the two-stage procedure does not, in general, produce the structural parameter of interest with a few notable exceptions (Bhattacharya, McCaffrey, and Goldman 1999). The bivariate probit consistently outperforms the two-step probit procedure if the error terms are specified correctly.

programs, they should not be correlated with an individual's employment decisions (except via the treatment of HAART).

Dealing with insurance status in this model is difficult. Health insurance both enables treatment and provides incentives (in the case of employment-based insurance) or disincentives (in the case of means-tested public insurance programs) for work, and therefore could be endogenous. One solution would be to jointly model insurance, employment, and treatment, although this would add substantial complexity to the model. Our approach is to be agnostic and estimate the model several ways: (1) without insurance in either equation (our "benchmark" model); 2) with insurance variables (dummy variables indicating employment-based, self-bought, or public insurance, with "none" as the omitted category) in both equations; and 3) with predicted insurance status in both equations. In the third case, we predict insurance status using a multinomial logit model, with state Medicaid income eligibility rules²⁶ and average firm size in the state as instruments, following Bhattacharya, Goldman, and Sood (2002).

Translating the estimated models into effects of HAART

Coefficient estimates from the models outlined above, and for the bivariate probit model in particular, are difficult to interpret quantitatively. To provide perspective, we calculate predicted labor market outcomes (probability of returning to work, probability of remaining employed, and hours of work), conditional on HAART treatment for every individual in the corresponding sample. We then derive weighted averages of the predicted outcomes with and without HAART across all individual patients in each of the three samples as defined by employment status at baseline or second follow-up, using HCSUS

²⁶ These rules include income eligibility threshold for the former AFDC programs, income eligibility threshold for the medically-needy program, both normalized as a fraction of the federal poverty line (\$13,013 in 1997).

analytic weights. The difference of the two mean outcomes within each scenario estimates the marginal effect of HAART on the labor market outcomes of the HIV+ population.

We also present results from simple models that assume that HAART is determined independently of employment. These "naïve" models are estimated using a probit for "return to work" and "remain employed" as in Equation (1), and ordinary least squares for the continuous outcome of hours of work. Predicted employment outcomes with and without HAART are also derived for these naïve models.

Results

Table 3.2 presents the estimated parameters for the models of the three employment outcomes. In the case of "return to work" (the leftmost panel in Table 3.2), the coefficient of HAART has a negative sign and is not significantly different from zero, suggesting that HAART had almost no effect on helping the HIV patients return to work by the second follow-up survey. For HIV patients who were working at baseline, HAART had a large effect on these patients' chances of remaining employed, which is statistically significant ($p < 0.01$; the middle panel in Table 2). In this scenario, the estimated coefficient of HAART has a magnitude much larger than most other important dichotomous determinants of the employment outcome, such as gender, stage of the infection, and educational achievements. For those who were working at the second follow-up, our results suggest that the effect HAART amounts to an additional 19 hours of work per week (the rightmost panel in Table 3.2). However, this effect is not statistically significant.

The two instrumental variables for HAART are estimated to have (as expected) negative effects on the use of HAART in all three HAART equations except for the variable indicating "a limit of three prescription drugs by the state Medicaid" in the analysis of "remain employed", where the coefficient is positive but small and statistically

insignificant. The IV indicating no coverage of NNRTIs by the state ADAP has a p-value less than 0.1 in all three estimated models. While the size of the coefficient of this IV is not comparable across the three models, the p-values seem to suggest that ADAP policies on the coverage of NNRTIs most strongly predict the use of HAART in the scenario of "remain employed". We conduct Wald tests on the joint significance of the two instrumental variables in predicting patients' propensity of receiving HAART. The test statistics are highly significant in the scenario of "remain employed", but not in the case of "return to work" or "hours of work (with a p-value higher than 0.1 in both cases).

Table 3.3 shows the mean predicted probabilities of the corresponding employment outcome in each scenario when HAART is taken and when it is not taken. The three sets of results (without insurance variables, with insurance variables, and with insurance predicted using income eligibility rules regarding public assistance programs and average firm size in the state) are quite similar, indicating that results are insensitive to the different specifications of the insurance variables. Calculations of incremental earnings and the following discussions will be based on the models with no insurance variables.

According to the point estimates, HAART is associated with a decrease in the probability of returning to work from 0.16 to 0.14. Although this average effect is negative, the standard errors of the predictions are pretty large, and the change is not statistically significant from zero. When we focus on those who were working at baseline, receipt of HAART increases the likelihood of remaining employed from 57% to 94%, which is highly statistically significant. Finally, for those who were working at the second follow-up, HAART receipt increases hours of work from 29.7 hours to 48.2 hours per week. Again, because of the large standard errors of the predictions, this difference is not statistically significant.

The last two rows in Table 3.3 show predicted employment outcomes according to the naïve estimators. Compared to results from the models with IVs, results from the naïve estimators indicate almost no effect of HAART on the employment of HIV patients. This, combined with the fact that the estimated correlation coefficient between the two errors in the bi-variate model (ρ) for "remain employed" is negative and significant, suggests that the naïve approach underestimates the treatment effect of HAART largely because it does not account for selection into HAART by unobserved severity.

Based on the estimation, we conduct some welfare analyses by imputing incremental earnings for HIV patients who remain employed as a result of taking HAART, since we found statistically significant results only in this scenario.²⁷ The mean hourly wage is the weighted mean of the imputed hourly wages of patients who were working at both baseline and the second follow-up and is estimated to be \$16.6.²⁸ Incremental yearly earnings because of HAART are then calculated by multiplying the incremental probability of remaining employed by the imputed hourly wage and number of hours of work in a year (assumed to be 1500: 30 hours a week and 50 weeks a year). The estimated incremental earnings due to HAART are \$9,213. It should be noted that what we calculate here is an approximation of the incremental earnings due to HAART.²⁹

²⁷ When labor supply increases, the incremental earnings are an adequate depiction of welfare change in the labor market only when the labor demand is perfectly elastic (Deleire and Manning 2002). However, given that the HIV+ population is not a large enough group to impact the equilibrium of the labor market dramatically, the employment-related welfare effect of treatment with HAART is not likely to deviate significantly from what is calculated here.

²⁸ Hourly wages are imputed based on reported earnings from main job and reported hours of work per week. Because working individuals reported earnings from main job in different units (per hour, per day, per week, every two weeks, per month, or per year), when imputing hourly wage, we make the following assumptions: 1) individuals who reported annual earnings worked 50 weeks a year; 2) those who reported monthly earnings worked 4.25 weeks a month; 3) and those who reported daily earnings worked 5 days a week.

²⁹ The imputed wage rate (derived from reported earnings of those who were working at the second follow-up) is likely to be higher than what would have been received by those not working had they been working with the help of HAART. On the other hand, the assumption of 30 hours of work per week is a conservative

Discussion

Our findings suggest that the new pharmacological therapy for the treatment of HIV has a beneficial effect on individuals' employment outcomes. In particular, we found HAART to be especially effective in helping working patients remain employed. For this group of people, our results suggest that the cost of HAART may be justified even on the single ground of improved productivity. Furthermore, since the group of HIV patients in our sample who did not take HAART could be on other therapies (like mono-, dual, or triple antiretroviral therapies that do not meet the definition of HAART) as well as under no antiretroviral treatment, treatment with HAART would look more favorable if the incremental earnings we compute are compared to the incremental costs of taking HAART (versus other non-HAART treatment including no treatment).

The heterogeneity in the effect of HAART across the three employment scenarios can be explained in a number of ways. First, it may reflect differential response to the treatment by patients at different stages of HIV infection, since the definitions of the three samples are closely related to baseline severity of the infection. (For example, patients in the "return to work" sample had a much higher rate of AIDS and lower CD4 T-cell counts at baseline than patients in the other two samples; statistics not shown.) Our results suggest that patients in relatively early stages of HIV infection are more likely to see improved functioning when treated with HAART.

Second, the lack of significant results found in the scenarios of "return to work" may reflect the fact that the utility functions of HIV patients vary with the stage of their infection. For example, knowing that one has AIDS and hence very limited life expectancy may drastically increase patients' preferences for leisure relative to

one. Therefore it is not clear whether the calculated incremental earnings effects are higher or lower than the real effects.

labor/consumption. Therefore, even if functioning were restored to the same extent, it would be much harder to get an AIDS patient back to work than a patient at an earlier stage of the infection.

Third, the three employment scenarios we study are generated by quite different processes even among the general population. Factors other than physical fitness and functioning (e.g., imperfect information in the hiring process and institutional constraints on number of hours of work) play equally important and sometimes much more important roles in individuals' employment. Thus, all else equal, it would be much harder for a person who is either unemployed or disabled to return to work than for a worker to remain employed. This could be especially true among the HIV+ population because of the stigma and workplace discrimination attached to the disease.

Throughout the analyses we have made the assumption that the effect of HAART on one particular employment outcome is homogenous across individuals of the relevant patient population as defined by baseline or second-follow-up employment status. However, this treatment effect could vary among HIV patients along a number of dimensions. Since we found large and significant effect of HAART in the case of "remain employed", we further examine whether the effect of HAART in helping HIV workers remain employed differed with type of job, whether or not the patient has high net worth (defined as having greater than or equal to \$50,000 total wealth net of total debt), or whether or not the worker was covered by employment-based health insurance. These analyses are conducted by adding an interaction term of the dummy variable indicating "more physically demanding jobs", "having high net worth", or "covered by employment-based insurance", with the treatment dummy variable of "Haart" in the employment equation.³⁰ Table 3.4 presents the predicted outcomes with and without HAART by these three categories.

³⁰ Even if HAART maintains and/or restores functioning to the same extent for every patient, the extent to which HAART could help people remain employed

Results of the analyses suggest that the effect of HAART is slightly higher for those with jobs that are physically less demanding ($p < 0.05$), but slightly lower for the subpopulation with high assets (the top 15 percent of the relevant HIV population ranked by net worth; not statistically significant). The results also provide some evidence of the existence of HAART-specific employment-lock: the with-and- without-HAART difference in the predicted probability of remaining employed is three percentage-points higher for patients with employment-based insurance than for patients without or with other types of insurance ($p < 0.05$). However, compared to the average effect of more than 30 percentage points, it also suggests that the large effect found for "remain employed" is not driven by the lock effect of employment-based insurance.

The 12-month mortality rate of the HIV+ population was 5% at the baseline interview and 7% at the first follow-up survey (Goldman, Bhattacharya, McCaffery et al. 2001). In this paper, we restrict our sample to patients of prime working age who were alive at the second follow-up survey, who, compared to the unrestricted sample, were likely to be healthier and/or more advantaged in other dimensions. Although we controlled for essential indices of severity of the infection (CD4 T-cell count and stage of the disease) in the model, there might be other differences between those who did and those who did not die not measured by clinical or sociodemographic characteristics in the model. Therefore our results should be interpreted as pertaining to those who were not at great risk of mortality during the course of the survey.

depends a lot on the physical demands of the job: the effect is likely to be smaller for jobs that are physically more demanding and vice versa. The amount of assets may also alter people's incentives for work, and by interacting "high net worth" with HAART, we are interested in seeing whether the effect of HAART for the small number of HIV patients with high assets would differ from that for the majority with low, zero, or negative assets. Finally, as discussed earlier, patients on expensive treatment such as HAART would have extra incentives to stay employed in order to keep employment-based insurance. The interaction of employment-based insurance with HAART is added to allow for HAART-specific employment-lock effect.

To see how the estimated effect of HAART might be different if we had an unrestricted sample, we include those who died between the baseline and second follow-up survey, and coded their employment status at the second follow-up survey as 0.³¹ This would add 188, and 30 observations to the sample of "return to work", and "remain employed", respectively. However, the estimated effects of HAART on patients' employment outcomes are almost identical as in the original analysis.

The estimated employment effect of HAART applies to a time when the therapy was first introduced. Effects at a later time might be of a different magnitude. On the one hand, better knowledge about the most effective regimen at a later time makes the therapy more effective, and therefore would lead to a larger employment effect. On the other, at a later time there are more long-term and fewer first-time users among those receiving the therapy. If the returns to HAART are decreasing in employment outcomes or if there are serious side effects associated with long-term use of HAART, the effect at a later time might be smaller than estimated in this study.

³¹ For those who died by the first follow-up survey (and thus had missing data on HAART treatment at the first follow-up), we coded their treatment with HAART as 1. Such recoding will produce estimates that are conservative relative to the real effects of HAART.

Table 3.1. Weighted descriptive statistics of sampled HIV patients 25-64 at baseline

	BASELINE		1ST Follow-up		2ND Follow-up	
	Mean	Std. Err.	Mean	Std. Err.	Mean	Std. Err.
HAART	0.25	0.02	0.40	0.03	0.60	0.02
Demographics						
age	38.08	0.25	38.10	0.26	38.10	0.26
nonwhite	0.48	0.03	0.50	0.03	0.50	0.03
female	0.22	0.03	0.22	0.03	0.22	0.03
Education						
Less than high school	0.23	0.03	0.24	0.03	0.24	0.03
High School Diploma	0.28	0.01	0.28	0.01	0.28	0.02
Some College	0.29	0.02	0.29	0.02	0.29	0.02
College degree or higher	0.20	0.03	0.19	0.03	0.19	0.03
Insurance						
Employment-based ins.	0.25	0.03	0.24	0.03	0.24	0.03
Self-bought ins.	0.07	0.02	0.07	0.01	0.06	0.01
Public ins.	0.48	0.04	0.51	0.04	0.54	0.04
Clinical stage of the infection						
AIDS	0.37	0.02	0.41	0.02	0.45	0.02
Symptomatic	0.52	0.02	0.53	0.02	0.51	0.02
CD4 lymphocyte count (cells per mm ³)	209.42	9.05	198.21	8.56	181.51	7.75
Employment						
Work Now	0.40	0.03	0.42	0.03	0.43	0.03
Hours of work if working	37.99	0.97	38.1	0.72	38.08	0.56

Source: authors' calculation using data from the HIV Cost and Services Utilization Study (HCSUS).

Notes: HCSUS is a national probability sample representing adult HIV patients active in care in early 1996.

Statistics are weighted to be nationally representative. For more information on how the weights are constructed, see Duan, McCaffrey, Frankel, et al. (1999).

Table 3.2. Results of the Bi-variate Probit Models for "return to work" and "remain employed" and the two-stage least square model for hours of work

EMPLOYMENT Equation	Return to Work			Remain Employed			Hours of Work (at 2nd Follow-up)		
	Coefficient	S.E.	P-value	Coefficient	S.E.	P-value	Coefficient	S.E.	P-value
HAART at 2nd Follow-up	-0.10	1.51	0.95	1.45	0.19	0.00	18.55	15.43	0.23
Age 25 to 29	0.72	0.27	0.01	-0.55	0.26	0.04	-4.53	2.63	0.09
Age 30 to 34	0.29	0.26	0.28	-0.42	0.25	0.09	-3.19	2.48	0.20
Age 35 to 44	0.16	0.24	0.52	-0.43	0.23	0.07	-3.77	2.67	0.16
Age 45 to 49	0.12	0.24	0.62	-0.36	0.27	0.19	-5.04	2.97	0.09
Non-white	-0.03	0.18	0.87	0.22	0.11	0.04	0.61	1.31	0.64
Female	-0.38	0.14	0.01	-0.18	0.17	0.30	-6.62	1.82	0.00
High School Diploma	0.24	0.14	0.09	0.22	0.18	0.22	6.45	3.29	0.05
Some College	0.40	0.15	0.01	0.11	0.18	0.54	2.73	1.52	0.07
College degree or higher	0.29	0.29	0.32	0.25	0.20	0.22	7.57	2.75	0.01
Exposure route -I.V. drug	-0.04	0.19	0.84	0.18	0.24	0.46	9.76	4.49	0.03
Exposure route - Man who have sex with men	0.06	0.15	0.68	0.17	0.16	0.28	0.94	2.14	0.66
Exposure route - Heterosexual	0.25	0.17	0.15	0.16	0.21	0.45	-1.50	2.34	0.52
Exposure route - Other	0.25	0.29	0.40	0.36	0.35	0.32	0.38	3.33	0.91
Stage of infection - AIDS	-0.33	0.32	0.30	-0.30	0.17	0.07	-4.53	1.85	0.02
Stage of infection - symptomatic	-0.18	0.20	0.38	-0.13	0.14	0.35	-0.09	1.62	0.95
CD4 lymphocyte count (cells per 100 mm3)	0.16	0.10	0.10	0.20	0.07	0.01	0.04	0.02	0.03
CD4 squared	-0.01	0.01	0.26	-0.01	0.01	0.31	0.00	0.00	0.02
State unemployment rate (97-98)	0.02	0.05	0.68	-0.01	0.05	0.86	-0.51	0.56	0.36
Constant	-1.60	0.63	0.01	-0.01	0.41	0.98	27.71	6.99	0.00

HAART Equation

A limit of 3 prescriptions per month by Medicaid	-0.20	0.19	0.30	0.01	0.17	0.94	-0.03	0.06	0.59
No coverage of NNRTIs by the state ADAP	-0.20	0.12	0.09	-0.37	0.12	0.00	-0.09	0.05	0.06
Age 25 to 29	0.32	0.20	0.11	0.39	0.25	0.12	0.07	0.08	0.44
Age 30 to 34	0.33	0.18	0.06	0.30	0.23	0.18	0.07	0.08	0.34
Age 35 to 44	0.27	0.17	0.11	0.41	0.21	0.06	0.10	0.07	0.15
Age 45 to 49	0.09	0.19	0.64	0.44	0.24	0.07	0.11	0.08	0.18
Non-white	-0.26	0.08	0.00	-0.27	0.10	0.01	-0.05	0.04	0.14
Female	-0.12	0.10	0.25	0.11	0.18	0.55	0.05	0.06	0.43
High School Diploma	0.17	0.10	0.08	0.05	0.19	0.79	-0.16	0.08	0.05
Some College	0.19	0.11	0.07	0.26	0.18	0.16	-0.02	0.05	0.70
College degree or higher	0.45	0.14	0.00	0.34	0.19	0.07	-0.12	0.07	0.08
Exposure route -I.V. drug	-0.17	0.14	0.23	-0.42	0.25	0.09	-0.21	0.12	0.08
Exposure route - Man who have sex with men	0.04	0.12	0.72	-0.01	0.15	0.93	0.10	0.06	0.09
Exposure route - Heterosexual	0.01	0.14	0.95	-0.15	0.21	0.49	0.12	0.06	0.04
Exposure route - Other	0.24	0.21	0.25	-0.40	0.34	0.25	0.19	0.06	0.00
Stage of infection - AIDS	0.40	0.20	0.04	0.20	0.16	0.21	0.06	0.06	0.31
Stage of infection - symptomatic	0.07	0.20	0.71	0.23	0.14	0.09	0.06	0.05	0.24
CD4 lymphocyte count (cells per mm3)	-0.15	0.04	0.00	-0.30	0.07	0.00	-0.10	0.02	0.00
CD4 ²	0.01	0.00	0.10	0.01	0.01	0.10	0.00	0.00	0.05
Constant	-0.53	0.28	0.06	-0.10	0.32	0.76	0.46	0.11	0.00
rho	0.09	0.92	0.92	-0.89	0.09	0.00			
N	1,303			800			870		

Notes:

Definition of analysis and prediction samples:

"Return to work": patients who were not working at baseline; "Remain employed": patients who were working at baseline;

"Hours of Work": patients who were working at the 2nd follow-up.

The reference population in each of the three samples are those of age 50-54, white, male, with less than high school education, uninsured, exposed to HIV because they are gay and IV drug users, and in asymptomatic stage of HIV.

"rho" is the estimated correlation coefficient of the two error terms in the bi-variate probit model (Equation (3)).

Table 3.3. Employment effects of HAART under alternative specifications for insurance: HIV patients of prime working age (25 to 54 years old)

Specification	Employment Outcomes					
	Return to Work		Remain Employed		Hours of Work	
	w/o HAART	w/ HAART	w/o HAART	w/ HAART	w/o HAART	w/ HAART
Without insurance	0.16 (0.13)	0.14 (0.19)	0.57 (0.06)	0.94 (0.01)	29.7 (6.6)	48.2 (8.9)
With insurance	0.15 (0.10)	0.14 (0.19)	0.58 (0.07)	0.94 (0.01)	31.7 (6.1)	45.8 (8.2)
With predicted insurance	0.15 (0.15)	0.14 (0.23)	0.58 (0.06)	0.94 (0.01)	31.3 (6.5)	46.2 (8.7)
Naïve Model, without insurance	0.14 (0.01)	0.15 (0.02)	0.86 (0.02)	0.86 (0.02)	37.6 (0.6)	37.7 (0.7)
Sample Size	1,303		800		870	

Notes:

Definition of analysis and prediction samples:

"return to work": patients who were not working at baseline; "remain employed": patients who were working at baseline;

"hours of work": patients who were working at the 2nd follow-up.

Numbers shown are predicted probabilities of employment change conditional on being treated with or without HAART.

Standard errors (in parentheses) are calculated based on the variance-covariance matrix of the estimated coefficients.

Instruments for insurance include medicaid income eligibility rules and average firm size in the state following bhattacharya, goldman, and sood (2002).

Table 3.4. Effect of HAART on the probability of "remain employed" by job type, employment-based insurance, and net worth

<u>Specification</u>	<u>Probability ("Remain Employed")</u>	
	<u>w/o HAART</u>	<u>w/ HAART</u>
Physically More Demanding Jobs	0.54 (0.06)	0.92 (0.01)
Physically Less Demanding Jobs	0.54 (0.06)	0.95 (0.01)
With high networth (>=\$50,000)	0.59 (0.07)	0.91 (0.01)
With low, zero, or negative networth	0.59 (0.07)	0.94 (0.02)
With Employment-based Insurance	0.54 (0.06)	0.95 (0.01)
Without Employment-based Insurance	0.54 (0.06)	0.92 (0.01)

Notes:

Results are based on bi-variate probit models with an interaction between "physically more demanding jobs", "employment-based insurance", or "high net worth", and Haart. Mean predicted probabilities and standard errors are calculated in similar ways as the results reported in Table 3.3.

**4. RECENT DRUG THERAPIES FOR HIGH BLOOD PRESSURE:
DO THEY HELP PEOPLE WORK MORE?**

Introduction

Elevated blood pressure, or high blood pressure (HBP), is a major risk factor for coronary heart disease and stroke, which are the first and third leading causes of death in the United States, respectively. Studies have shown that effective control of blood pressure, including control by medication, has contributed to the dramatic decline in mortality and disability due to heart diseases and stroke since the early 1970's (National Heart, Lung, and Blood Institute 1997; Manton, Corder, Stallard 1997). There is abundant evidence that drug therapies developed recently to treat HBP are clinically effective (Joint National Committee 1997). However, there have been few efforts to evaluate the economic benefits of these new classes of drugs and formulations. In particular, there has been little evaluation of the benefits of reduced disability and/or prolonged work life of older workers due to these more advanced drug therapies.

A number of studies have related poor health, or decline in health, to early exit from the labor force (for example, McClellan 1998; Bound, Schoenbaum, and Waidman 1995; Bound, Schoenbaum, Stinebrickner, et al. 1998; for a comprehensive review, see Currie and Madrian 1999). Because of the high prevalence of HBP among older workers (between 34% to 57% depending on age group; National Center for Health Statistics 2001) and the highly debilitating nature of hypertension-related complications, it is likely that these diseases account for a significant part of the health-related reasons for early retirement or disability. In turn, treatment that effectively controls blood pressure promises to avert some of the welfare losses related to early exit from the labor force such as lost productivity. Therefore when calculating the benefits of hypertension treatment from the perspective of the

individual patient or society, analysts should incorporate the effect of the therapy on patients' labor market outcomes. Likewise, when treatment recommendations are updated to reflect advances in medical technologies, the incremental economic benefits of new treatment strategies in terms of improved employment and earnings should be incorporated into the evaluation of the incremental individual and societal benefits of these updated recommendations.

In clinical studies, Randomized Controlled Trials (RCTs) are usually the gold standard in testing the efficacy of a certain therapy relative to a placebo or an existing therapy or therapies. However, because of their focus on clinical outcomes and the short time horizon of most of the studies, data from RCTs are usually of little use in investigating economic outcomes in the general population in the medium- to long-run. Empirical challenges arise when one uses observational data to estimate the employment effects of treatment since patients are selected into treatment and/or different treatment regimens by factors that are not observed, but are correlated with their employment outcomes.

This study estimates the employment effect of recent treatment regimens for hypertension relative to the treatment approach available in earlier years. The analysis makes use of a unique data set that provides objective measures of both pre- and post- treatment disease severity and spans a period both before and after the introduction of recent therapies for HBP. I investigate the additional employment effect of recent therapies by asking the question: did recent therapies help narrow the gap in employment rates between those who were on HBP medication and those who were not?

The following section describes the development of the pharmacological treatment of HBP over the past three decades and what that development implies for the estimation of the employment effect of the treatment. The third section discusses the data and explains key

variables. The fourth section lays out the analytical framework and discusses empirical models to be estimated. Results of the analysis and robustness of the results are presented in the fifth section, followed by a discussion of the results and implications for future research and data collection.

Recent developments in the pharmacological treatment of hypertension

Five major classes of drugs are currently used to treat hypertension. They are: Diuretics ("water pills"), Adrenergic inhibitors (including, but not limited to, Beta blockers and Alpha blockers), Calcium channel blockers, Angiotension-converting enzyme (ACE) inhibitors, and Angiotension II receptor blockers. These classes of drugs were not developed simultaneously.

Clinical evidence of the efficacy of Diuretics was first provided in the late 1960's and early 1970's (for example, Veterans Administration Cooperative Study Group on Antihypertensive Agents 1970). Although Beta blockers were an old class of drugs, the Food and Drug Administration (FDA) did not approve their use for HBP until 1976. Also, in the late 1970's and early 1980's, the types of Beta Blockers used to treat hypertension were limited in number. The FDA approved most Calcium channel blockers in the late 1980's and early 1990's. ACE inhibitors were first approved in the early 1980's (for example, Capoten and Vasotec), with newer ones developed in recent years. Finally, Angiotensin II receptor blockers are the youngest class of antihypertensives, all have been developed since 1996.

In addition to the development of new chemical compounds, research in recent years has identified more effective formulations of HBP treatment. For example, combinations of certain agents from different classes in low dosage have been found to provide greater anti-hypertensive efficacy than mono therapies and reduce the chances of dose-related adverse outcomes (Frishman, Bryzinski, Coulson, et al.

1994; Epstein and Bakris 1996). In clinical practice, when patients do not respond to, or cannot tolerate, one type of drug, physicians are advised to switch to prescribing a drug from another class, or to add a drug from another class (thus forming a combination therapy). As a result, a significant proportion of the treated HBP patients (about 30%) are on combination therapies. Further, the availability of a greater variety of antihypertensives in recent years makes it possible to produce more varieties of combination therapies that better target patients' needs.

A recent large-scale randomized controlled trial (the Antihypertensive and Lipid-lowering Treatment to Prevent Heart Attack Trial, or ALLHAT) compared treatment outcomes of an ACE inhibitor, and a Calcium channel blocker, to those of a diuretic (The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group 2002). Results of the study indicate that, on average, the two newer classes are no better than thiazide-type diuretics in lowering BP, reducing clinical events, or in terms of tolerability. Since the scope of the RCT was restricted to mono therapies, the findings of the study suggest that if recent therapies are in fact superior, their superiority must be largely attributed to the additional effect of combination therapies.

Evaluation of incremental treatment outcomes (including employment outcomes) of recent therapies for HBP is made complicated by the path that developments in treatment technology typically follow. As has been the case with other major diseases such as cancer, detection and treatment of HBP has tended to occur more quickly in recent years because of increased awareness and improved treatment technology. As documented in Burt, Cutler, Higgins, et al. (1995), from the late 1970's to late 1980's, the percentage of the American population with HBP that were aware they had high blood pressure rose from 51% to 75%. Over the same period, among those with hypertension, treatment rates rose from 31% to 55%. As I discuss further in the fourth section, changes in the

baseline conditions³² of patients under treatment for hypertension imply that, without adjusting for pre-treatment severity, it is invalid to directly compare outcomes of the earlier treatment group to those of the later treatment group.

Data

This study uses data from the Framingham Offspring Heart Study. The Framingham Heart Study, started in 1948 with participants from the town of Framingham, Massachusetts, made important discoveries that helped identify major risk factors of cardiovascular diseases. In 1971, the study enrolled 5,124 children of the original participants to participate in similar examinations. Researchers have to date collected five waves of data from these offspring (Feinleib, Kannel, Garrison, et al. 1975). Attrition in this longitudinal study occurred mainly between Exam 1 and Exam 2, when the sample size dropped to 3,863. After Exam 2, the number of participants who returned for the next exam remained stable. The first between-exam interval (the interval between Exam 1 and Exam 2) was about 8 years, much longer than intervals between later adjacent exams, which averaged 4 years. Table 4.1 provides a summary of the age distribution of participants in each exam and key data elements available in the offspring sample.

The development of pharmacological therapy for HBP is reflected in the list of cardiovascular medications taken by participants of the Framingham offspring study over the years. Before each exam, participants were sent a form and asked to list medications they were currently taking or had been taking since the last exam. The participants brought the form into the clinic to discuss with a physician during the exam. The list of HBP medications recorded in Exam 1 did not contain any specific classes of drugs other than

³² Baseline conditions that are relevant to the evaluation include blood pressures and other risk factors of coronary heart disease and stroke.

Diuretics. The list in the second exam contains the earliest Beta blockers used for HBP: Propranolol, but not the other newer classes such as ACE inhibitors. Starting from the third exam, the list was expanded to include Calcium channel blockers and one ACE inhibitor (rennin angiotensin drugs), as well as "Beta blockers" in general. Although the classes of drugs on the list did not change significantly from exam 3 to exams 4 and 5, each class contained more types of, and more brand names of, drugs in later years.

I derive the dichotomous variable of being on medication for hypertension based on the list of hypertensive drugs shown in Table 4.1. Specifically, I consider a participant to be taking medication for hypertension at the time of the exam if he/she reported taking or having taken any drug on the list.³³ Without distinguishing among specific drugs people took, the current study identifies the additional effect of recent therapies in general over that of the earlier ones. Table 4.2 shows the composition of antihypertensives used by participants of the Framingham Offspring study at Exam 2 and Exam 5.³⁴ It is obvious that Diuretics lost dominance to Beta blockers over the years, while use of Calcium channel blockers and ACE inhibitors increased rapidly. Combination therapies also became more common as well as more diversified as more classes of drug became available.

Information on the labor market outcomes of the participants is usually limited in an epidemiological study such as the Framingham study. The employment data available in the Offspring Study, as summarized in Table 4.1, suggest that in order to compare employment

³³ The number of participants who reported "having taken" a certain class of HBP medication is significantly smaller than that of those reporting "taking now". In order to capture the effect of both current treatment and recent treatment, the analysis that follows does not distinguish between these two cases. Results do not change qualitatively if the study focuses on the "taking now" group only.

³⁴ The drug list in each exam contains medications that do not fall into any of the four major classes (Diuretics, Beta blockers, Calcium channel blockers, and ACE inhibitors). Examples are Wytensin and Aldomet (central alpha-agonists), and peripheral vasolidators. Tabulation of these drugs shows that they are not used widely and therefore are grouped together as "other medication".

outcomes over time, this study has to focus on the most basic outcome measure, that is, a dichotomous variable of working or not at the time of the exam, defined as 1 if the participant reported "working" as the current working status, or provided positive answer to the question of "are you employed now?"³⁵ depending on the wording in different exams. Although it is not possible to tell from the data, when one is not working, whether he/she has left the labor force permanently, most of the response of "not working" is likely to be a result of retirement or disability.³⁶

Systolic and diastolic blood pressures were measured three times in most exams.³⁷ Using the World Health Organization's definition, I compute the blood pressures (used as both treatment outcomes and baseline controls) as the average of the three readings in each exam. I define a dichotomous variable indicating "elevated blood pressure" to be 1 if all systolic readings are 140 or higher, or all diastolic readings are 90 or higher.³⁸

Other variables used in the analysis include: 1) participants' demographic information (age at the time of the exam, gender, and educational achievement recorded at Exam 2; 2) risk factors for high blood pressure and coronary heart disease/stroke (total cholesterol,

³⁵ A person who reported himself to be "employed" at Exam 5 may be on sick leave and therefore not actually working. However, since the employment status question in Exam 5 provided three categorical answers: not employed, full-time, or part-time, people on sick leave were likely to report "don't know" (coded as missing). Given the few cases with missing data on this question (n=8 versus n=1152 for non-missing answers), it is unlikely that the "employed" group at Exam 5 contained a large number on sick leave.

³⁶ Focusing on male respondents that were between age 40 and 61, which is the analysis sample of this study, I look at the transition pattern of employment status from exam to exam. Of the 38 people who reported "not working" at Exam 2, 12 reported "working" four years later at Exam 3. Of the 57 individuals who were not working at the time of Exam 3, 13 were back to work about eight years later at Exam 5. Likewise, the vast majority (70-80%) of those who were working at one exam were still working at the next exam according to available employment data. Therefore it is unlikely that the different employment status observed at one particular exam is temporal or idiosyncratic, but rather reflects a long-term difference in labor force participation.

³⁷ The exception is Exam 1, in which a third reading is missing for most participants. Therefore average BP is derived as average of two readings for Exam 1, rather than the average of three readings as in the other exams.

³⁸ This reflects a more conservative way of defining "elevated blood pressure" than using the average of the three readings.

level of glucose in the blood, regular smoking in the past year); 3) the presence of any major chronic disease other than heart or cerebrovascular diseases that are likely to directly affect one's labor market participation, defined as 1 if the patient had at least one diagnosis of the three following conditions: diabetes (defined as either having glucose higher than 140 mg/dL or taking oral hypoglycemic agents at the time of the exam), arthritis (based on the exam physicians' clinical diagnostic impressions, including osteoarthritis, gouty and rheumatoid arthritis), and respiratory conditions (based on clinical diagnostic impressions).

Study Design and Empirical Strategy

Outside of randomized controlled trials, whether a HBP patient gets drug treatment is highly correlated with the severity of his/her condition: those with higher BP are at a greater risk of CHD or stroke and are therefore more likely to be treated with medication. As a result, prior to the treatment and sometimes even after the treatment, one would expect to see people on medication fare worse than those not on medication, in terms of both clinical severity and employment outcomes (Thurmer, Lund-Larsen, Tverdal 1994). On the other hand, if treatment technology improves, the gap in outcomes between the medicated and the non-medicated group will narrow, all else equal.

In statistical terms, the additional effect of recent therapies can be evaluated by testing whether the change in the difference of employment outcomes between the treated and the non-treated group is statistically significant, or, by using the Difference-in-Difference (DiD) approach. Specifically, the following statistic can be estimated:

$$\left(y_{Meds}^{EMP} - y_{NoMeds}^{EMP} \right)_{LateCohort} - \left(y_{Meds}^{EMP} - y_{NoMeds}^{EMP} \right)_{EarlyCohort} \quad (1)$$

where y^{EMP} stands for employment outcome of interest. The population of interest is males of working age at relatively high risk of hypertension-related health shocks -- those aged 40-61 at the time when the employment outcome is observed.³⁹ The analysis focuses on the medication and employment outcomes of an early cohort (the cohort aged 40-61 at Exam 2, or around 1981) before most of the new development in the pharmacological treatment of hypertension and those of a late cohort (the cohort aged 40-61 at Exam 5, or around 1993) after the development of new therapies.

The critical assumption that I make in using the DiD approach to identify the effect of treatment on employment is that, in the absence of the technological improvement embodied in recent therapies, the difference in outcomes between those on medication and not would have been the same in the late as in the early cohort. As discussed in the second section, the greatest challenge to this assumption is that more people are treated as the new technology becomes available, making both the treatment group and the non-treatment group less sick on average to begin with. Appendix 4.A presents a model of the pre-treatment difference in disease severity between the treated and the non-treated group and how that difference changes over time. It shows that whether the difference widens or narrows as a result of the higher treatment rate among the later cohort depends on the initial criteria for treatment and the distribution of the disease severity in the population. Although it is not possible to know the direction of the

³⁹ Female participants are not studied in order to avoid the complications due to the change in female labor force participation in the past three decades. Risk of elevated blood pressure and heart failure increases with age. As shown by data from the National Center for Health Statistics, the risk increases much more rapidly as one reaches 45. In the United States, since people can start receiving social security income as soon as they turn 62, a large number choose to retire at that age. Since the retirement decision is based on a number of factors (e.g., see Lumsdaine 1999) on which the Framingham study does not provide data, the current analysis restricts the sample to those younger than 62.

bias a priori, this exercise suggests that it is important to adequately control for pre-treatment severity in the analysis.

In addition to change in unobserved severity of the treated group relative to the non-treated group over time, other factors that change the relative tendency to work between the two groups may also bias the estimation, if these factors are not measured and thus not controlled for in the analysis. I discuss the direction and the likely magnitude of the biases in a later section.

As a first step in the analysis, I study the additional effect of recent therapies on controlling blood pressure using the following OLS regression framework.

$$y^{BP} = \beta_1^{BP} Med + \beta_2^{BP} LateCohort + \beta_3^{BP} (Med * LateCohort) + BS' \lambda^{BP} + x' \gamma^{BP} + w^{BP'} \phi^{BP} + \varepsilon^{BP}$$

with $\varepsilon^{BP} \sim i.i.d.(0, \sigma_\varepsilon^2)$, (2)

where y^{BP} is one of three indicators of HBP severity: 1) average systolic blood pressure, 2) average diastolic blood pressure, and 3) whether the individual has elevated blood pressure.⁴⁰ *Med* is the dichotomous variable indicating HBP medication status. *LateCohort* is the dummy variable indicating whether an observation belongs to the late cohort, i.e., from Exam 5. The variable *BS* is the corresponding baseline measure of BP (systolic, diastolic, or elevated BP). The variables in \mathbf{x} are dummy variables capturing age groups and educational achievement, and the variables in \mathbf{w}^{BP} are baseline risk factors related to HBP (total cholesterol, glucose level, and regular smoking).⁴¹ With this

⁴⁰ A linear probability model is implicitly assumed for "elevated blood pressure".

⁴¹ I take baseline readings from Exam 1 for the early cohort and at Exam 3 for the late cohort in order to provide a similar time interval between treatment and baseline.

specification, β_1^{BP} captures the effect of medication on the blood pressure of early cohort patients, and β_2^{BP} , the population-level shift in BP between the early and late cohorts. The coefficient of the interaction of medication with the dummy for late cohort (β_3^{BP}) is an estimate of the additional effect of recent medication on patients' BP.

I further study the additional effect of recent treatment on employment by using a similar framework, but with a probit model.

$$P(\text{Employed} = 1) = \Phi(\beta_1^{EMP} \text{Med} + \beta_2^{EMP} \text{LateCohort} + \beta_3^{EMP} (\text{Med} * \text{LateCohort}) + \mathbf{x}'\boldsymbol{\gamma}^{EMP} + \mathbf{w}^{EMP'}\boldsymbol{\phi}^{EMP}) \quad (3)$$

where Φ is the cumulative density function of the standard normal distribution. Dummy variables for medication and cohort, as well as \mathbf{x} , are defined in the same way as in the previous model. The group of variables denoted as \mathbf{w}^{EMP} are 1) a dummy variable indicating current diagnosis of any chronic condition other than CVD, 2) baseline status of elevated blood pressure and, 3) a dummy variable indicating regular smoking at baseline. Therefore, β_1^{EMP} captures the time-invariant difference in employment outcome between the treated and the non-treated groups that is not accounted for by baseline severity controls, and β_2^{EMP} , the cohort difference in employment status. The coefficient of the interaction term (β_3^{EMP}) is the difference-in-difference estimate of the effect of recent pharmacological therapy on patients' employment outcome. Table 4.3 summarizes the independent variables used in equations (2) and (3).

Of the 1,803 males (2,329 person-exams) that make up the analysis sample, 526 persons were included in both the early and late cohort

samples. 643 were included in the early cohort sample but not that of the late cohort, and 634 were in the late cohort sample but not the early cohort sample. I assume that the standard errors of the estimated coefficients are not independent across observations of the same individual and therefore cluster errors at the individual level.

Results and Robustness

Incremental effect on BP

Table 4.4 provides summary statistics for baseline and current blood pressure readings and percent with elevated blood pressure, by current HBP medication status, for both the early and late cohorts.

The data indicate an unambiguous reduction in blood pressure among the late cohort compared to the early cohort. In fact, histogram plots of systolic and diastolic pressure of the two cohorts (not shown) indicate that the reduction could be closely represented by a leftward shift in the distribution of BP. This observation is consistent with a population-level change in blood pressure over time recorded in Burt, Cutler, Higgins, et al. (1995). The right-most column in Table 4.4 presents the additional effect of recent therapies on blood pressure, i.e., the estimated β_3^{BP} from equation (2). The estimation suggests that recent therapies reduced diastolic pressure by an additional 2.2 mm/Hg ($p < 0.05$) as compared to the earlier therapies. This amounts to almost half of the effect of mono antihypertensive therapies such as Diuretics and Beta blockers (relative to a placebo) found in RCTs (Cutler, MacMahon, and Furberg 1989). The additional effect on the percentage of respondents with elevated blood pressure was sizable as well: an added reduction of 10 percentage points ($p < 0.05$).

Incremental effect on employment

Estimates from the probit model of the employment outcome (Equation (3)) are shown in Table 4.5. The parameter estimates suggest that those taking medication were, on average, significantly less likely to be employed than those not on HBP drugs, as indicated by the negative sign on the coefficient of the dummy variable for HBP medication. The coefficient of the dummy for late cohort is also highly significant and negative with large absolute value, indicating a general trend toward early exit from the labor force. The interaction of HBP medication with late cohort has a positive sign, suggesting that hypertensive therapies in recent years helped narrow the gap in employment outcome between those receiving and not receiving treatment. The magnitude of the coefficient is similar to the coefficient on the variable indicating education higher than college (relative to less than high school) ($p < 0.05$).

To put the results into perspective, I calculate probabilities of being employed for people on medication in the late cohort, conditional on being treated with recent or earlier therapies. Specifically, I derive the predicted probability of working for this subgroup based on the estimated model (with all the independent variables taking the values as observed; shown in the second column in Table 4.6); I then set the interaction between receiving medication and being in the late cohort to 0 to predict the (counterfactual) probability of working had the late cohort patients been on drug therapies that were used to treat the early cohort in the late 1970's (shown in the first column in Table 4.6). The resulting mean probability of working when patients were treated with recent therapies is 0.82, and the mean outcome in the counterfactual case is 0.72. Thus, according to the analysis, the incremental employment effect of the improved technology to treat

hypertension is an increase of about ten percentage points in the likelihood of working for older male workers who were on medication for HBP (shown in the third column of Table 6).

In Equation (3), coefficients of the \mathbf{x} and \mathbf{w}^{BMP} are assumed to be the same across the two cohorts. To the extent that there has been a change over time in how sociodemographic characteristics (such as education) and health status (such as the presence of chronic conditions) affect individuals' ability to work, the coefficients should differ between the late and the early cohorts. As a sensitivity check, I allow these coefficients to vary by including interaction terms between "late cohort" and both \mathbf{x} and \mathbf{w}^{BMP} in Equation (3). However, the incremental employment effect estimated with this specification are almost identical to those in Table 6.

Although I find an additional effect of recent therapies on both blood pressure and employment outcomes, the point estimate of the employment effect seems to be much larger than what the additional effect on blood pressure would imply,⁴² although the standard error of the estimated employment effect (shown in Table 4.6 in parentheses) suggests that the 95% confidence interval of the effect ranges from almost no effect to an effect size of 20 percentage points. I conduct several sensitivity analyses to test the robustness of the estimated additional employment effect.

⁴² Meta analyses on observed benefits of blood pressure reduction (for example, Cutler, MacMahon, and Furberg 1989) indicate that a reduction of diastolic pressure by 5-6 mm Hg is associated with a 40% decrease in the probability of stroke. Since studies (e.g., MacMahon 1996) have also found this relationship to be continuous, the additional effect of recent therapies (a reduction of 2-3 mm Hg) is correlated with an additional 20% reduction in the probability of stroke. If the rate of stroke among patients treated with earlier therapies were 6% (data from the ALLHAT study), and further assuming that patients exit the labor force entirely after a stroke, the additional employment effect because of additional reduction in stroke would be an increase in employment rate by 2 percentage points. Employment effects may be realized via routes other than prevention of stroke, such as prevention of acute myocardial infarction (AMI). However, studies have failed to establish a significant relationship between controlled blood pressure and AMI (Cutler, MacMahon, and Furberg 1989). Even if the relationship were as large and significant as with stroke, the total effect is likely to be below 10 percentage points.

Results of sensitivity analyses

Sensitivity Analysis I: In each cohort, of those currently on HBP medication, some were also being treated with medication at baseline. The proportion is higher (about 50%) in the late cohort than in the early cohort (about 30%). It is possible that the additional effect found may be due to "more treatment", rather than "better treatment". Therefore, as the first sensitivity analysis, I exclude those on medication both currently and at baseline. The analysis results in little change in the predicted probability of employment, presented in the second row of the upper panel in Table 4.6.

Sensitivity Analysis II: The extent to which cardiovascular conditions may impair one's ability to work varies with the nature of the job. In general, jobs that require physical exertion are likely to be the most affected. Since workplace conditions have changed over time for these types of jobs, estimates of the additional effect of recent therapies might be biased upward simply because the same job became less physically demanding. Therefore I restrict the sample to those who reported their job types as professional, executive, supervisory, or technical (as opposed to laborer, clerical, sales, and housewife) at the time of Exam 2.⁴³ Since the potential bias is much smaller for this group of workers, invariance of the estimated effect to this sample selection would tend to dismiss concerns about this type of bias. The third row of the upper panel in Table 4.6 shows the result. Since the sample size is now less than half of the original, the additional effect is not statistically significant. However, the predicted probability of being employed is still 10 percentage points higher if for those treated with recent therapies than if treated with earlier therapies.

⁴³ Since the two classes of jobs are associated with quite different levels of wage/earnings, restricting the sample to those with professional, executive, supervisory, or technical jobs might be getting at effects that also pertain to high income individuals.

Sensitivity Analysis III: Although the assumption of a probit model is the standard approach in empirical analysis of dichotomous outcomes as it avoids the well-known caveat of a linear probability model in producing predicted probabilities outside the (0,1) boundary, extra caution is warranted in this DiD framework. The curvature of the normal cumulative density function (CDF) implies that it is harder to incrementally raise the probability of an event if the base probability is very high (or approaches 1) than if the base probability is significantly lower than 1. While this is a reasonable assumption in most cases, the normal CDF may not be an accurate depiction of the data-generating process of the employment outcome in the current study.⁴⁴ If that is the case, since employment rate of the early cohort is very high (about 95%), and that of the late cohort is much lower (around 88%), the assumption of a probit model may bias the additional effect upward. (Appendix 4.B uses a graph to illustrate the point.) Therefore I estimate a linear probability model to check the robustness of the results. Results shown in the lower panel of Table 4.6 indicate that, with a linear probability model, point estimates of the additional effect of recent therapies are not only much smaller, but statistically insignificant as well. In the case of restricting the sample to people with certain job types, even the sign of the interaction (between medication and late cohort) is reversed. However, the large standard errors are large, so the confidence intervals of the estimates overlap with the confidence intervals of the estimates based on the probit model.

Discussion

The main results of the study indicate that recent development in pharmacological treatment of hypertension had additional beneficial

⁴⁴ For example, it could be the case that the data generating process is best represented by a CDF that is a mix of a linear probability function and a normal CDF.

effects on patients' employment outcome compared to therapies available at an earlier time. However, the magnitude and significance of the results are sensitive to the type of statistical model assumed. This section discusses the estimated effect in light of major findings regarding the clinical efficacy of recent therapies and important development in the labor market for people with disabilities and/or chronic conditions.

Are combination therapies responsible for the additional effect?

As mentioned in a previous section, in light of findings from a recent RCT, the employment effect found in this study needs further scrutiny: if new mono therapies are no better than older ones in reducing risks of cardiovascular events and thus preventing early exits from the labor force, is there evidence that combination therapies in recent years are responsible for the additional employment effect? To answer that question, I conduct an analysis of the additional effect of combination (or combo) therapies (relative to mono therapies). The analysis uses the longitudinal sample of participants (male and female) on HBP medication (both combo and mono therapies) at Exam 4, with pre-treatment severity information obtained from Exam 3, and post-treatment outcomes (BP and employment) from Exam 5. The models are:

$$y^{BP} = \alpha_1^{BP} Med + \alpha_2^{BP} ComboMed + BS' \delta^{BP} + x' \theta^{BP} + w^{BP} \tau^{BP} + \eta^{BP}, \eta^{BP} \sim i.i.d.(0, \sigma_\eta^2) \quad (4)$$

$$P(Employed = 1) = \Phi(\alpha_1^{EMP} Med + \alpha_2^{EMP} ComboMed + x' \theta^{EMP} + w^{EMP} \tau^{EMP}) \quad (5)$$

"ComboMed" is a dummy variable defined as 1 if the individual was taking two or more antihypertensives at the time of Exam 4. Definitions of the

other variables are the same as in equations (2) and (3), except that x now contain a dummy variable indicating "female". (Variables in the regressions are summarized in Table 4.3.) In each equation, the coefficient of "ComboMed" captures the additional effect of combo therapies above and beyond mono therapies. I conduct the employment analysis on the sub-sample of individuals who were employed pre-treatment.⁴⁵

Table 4.7 presents the estimated additional effect of combo therapies in recent years. Although the results indicate an additional effect of combo therapies in controlling blood pressure and improving the employment outcome, the size of the effect is small and far from significant.

Given that the analysis fails to find a sizable effect of combo therapies that would explain the additional effect found for recent therapies, I now discuss possible biases of the estimated effect because of uncontrolled labor market factors.

Possible Biases of the DiD Estimator

Factors that differentially affected labor force participation by the treated group and the non-treated group, if not controlled for in the DiD model, could bias the estimated treatment effect. These factors can be categorized into two major types: 1) changes in the labor force participation by working-age population with disabilities relative to that of the general population; 2) changes in the availability of employment-based health insurance and other benefits and the increasing importance of these benefits to people with disabilities and/or chronic conditions.

⁴⁵ Selection into mono or combo therapies does not happen in a randomized manner. Patients on combo therapies had significantly higher BP pre-treatment than those on mono therapies. Conditioning the employment analysis on being employed pre-treatment helps reduce the selection bias, because by doing so, I estimate the additional effect of combo therapies in preventing early exits from the labor force, thus avoiding the confounding effect of including people with long term disability.

In the 1970's and 1980's, the falloff in labor force participation rate by US working-age males with disabilities was much larger than that of those without disabilities (Yelin and Cisternas 1996).⁴⁶ During the same time period, various income support programs for disabled people, such as the Social Security Disability Insurance (SSDI) and Workers' Compensation, saw rapid growth in both the number of recipients and program expenditures, partly due to less strict review of eligibility and hence longer stays on the rolls (Haveman and Wolfe 2000). The implication for the current analysis is that those on HBP medication, to the extent that a significant portion of them qualified for disability-related programs, were more likely to be out of the labor force in later years for reasons not related to the treatment effect of HBP therapies or the severity of their conditions. Also, to the extent that job prospect of people with poor health are more easily affected by fluctuation in the macroeconomic conditions (Yelin and Cisternas 1996), the recession in the early 1990's (at the time when Exam 5 was taken)⁴⁷ would suggest that, all else equal, the gap in employment between those in the late cohort on and off of medication should have widened compared to the gap seen in the early cohort. Thus these developments point to an *underestimate* of the treatment effect in the model I estimated.

On the other hand, since more than 50% of the working population work in firms that do not provide retiree health insurance (William M. Mercer 1998), increased costs of prescription drugs for HBP and of treating HBP-related complications over the decade would imply greater incentives for the medicated group to remain employed so as to retain

⁴⁶ Yelin and Cisternas (1996), "disability" is generally defined as people reporting not being able to perform major activities or being limited in the amount or kind of their major or outside activities. It is not clear how the trend differs for persons with HBP-related conditions than for persons with other types of disabilities.

⁴⁷ The average monthly unemployment rate of Massachusetts over 1991-1995 was 7.18, compared to 6.37 over 1979-82 (Source: Bureau of Labor Statistics). Although each exam of the Framingham study took several years to complete, the calendar year in which each participant took the exam was not known. Therefore it is not possible to control for the local unemployment rate in the employment analysis.

employer-based health insurance coverage.^{48,49,50} If this is the case, then it would lead to overestimation of the treatment effect. Because the dataset I use is silent about current insurance status and the availability of retiree insurance coverage, or even the industry the person worked in and the employer's firm size -both are strong predictors of employer-provided health insurance coverage-, there is no way of directly controlling for the insurance effect in the model. I instead conducted several analyses to see if the insurance effect appears to dominate the treatment effect.

Since workers with higher educational achievements are more likely to be engaged in full time employment and entitled to more generous employee benefits, including retiree insurance coverage, the insurance effect on employment should be significantly less for the better educated. Therefore I conduct the same regression analysis on the subsample of participants with some college or higher education. Although the sample size is now only half of the original and the estimated coefficient (of the medication - late cohort interaction) is not statistically significant, the estimate is even larger, suggesting that the result is not driven by the insurance effect.

I further investigated the change in employment rate by people with arthritis compared to people free of arthritis in the Framingham Offspring data, to see if the cost growth in treating arthritis has made people with the disease more likely to be working. Arthritis is chosen for its similar prevalence in the near-elderly population with HBP, its detrimental effect on patients' ability to work, and the lack of

⁴⁸ Employment-based coverage is the major source of health insurance coverage for working adults in the United States. In 1999, 73% of workers were covered by an employment-based plan (Fronstin 2000), and almost all employment-based coverage includes prescription drug benefits (Kaiser Family Foundation 2000).

⁴⁹ For a detailed discussion of the literature on health insurance and retirement, see Gruber (2000).

⁵⁰ Decline in retiree health benefit over the years may introduce the same bias. However, that (modest) trend is only seen recently, after the Financial Accounting Standards Board approved Financial Accounting Statement no.106 (FAS 106) that required unfunded retiree health benefit liability to be recorded on firms' financial statement, effective on Dec 15, 1992. Therefore it is unlikely to have complicated the estimation (Fronstin 1998).

significant technological improvement over the study period to treat the disease (so that result of the investigation can be attributed to the insurance effect). The analysis did not show a significant change in employment status related to having arthritis in more recent years. Therefore it is unlikely that the incremental treatment effect found in the main analysis is driven by the "employment-lock" of health insurance associated with higher treatment costs.

In summary, possible biases in the DiD estimator could be introduced by factors unrelated to the treatment technologies. However, since these factors lead to biases in both directions, it is unclear how the estimated treatment effect might be biased in the aggregate.

In interpreting the estimated effect, it should be noted that the study sample is not nationally representative. As D'Agostino and Klannel (1989) have discussed elsewhere, the relative homogeneity in racial and other sociodemographic aspects of its participants⁵¹ as well as its regional nature limits the generalizability of findings from the Framingham study. The implications for the results of this study depend on how the labor market dynamics in the Framingham area (or the New England area in general)⁵² and the employment behavior of the Framingham population differed from those in the rest of the country. Further, since there was significant attrition between Exam 1 and later exams and the study focused on individuals who participated in Exam 2 (in addition to Exam 1) and those who participated in Exam 3 and Exam 5 (in addition to Exam 1 and possibly Exam 2), it is possible that the results are only applicable to the "stayers". I compared the stayers and the leavers using data from Exam 1 in terms of demographics and baseline severity. While the two groups had very similar demographic profiles (gender and

⁵¹ In 1948, the residents of Framingham were mostly middle class and white.

⁵² As far as the town of Framingham is concerned, employment was relatively stable because of a diversity of employment opportunities. However, it doesn't quite apply to the Offspring participants, as many of them moved away from their home town to settle in other parts of the New England area. Those who moved even farther away were much less likely to participate in the study.

age distribution), and similar distribution of systolic and diastolic blood pressure readings, the leavers were significantly more likely to have HBP, to be diabetic, and to have smoked regularly. Therefore the attrition seemed to be correlated with pre-existing conditions. To the extent that people remained in the study in order to monitor their health, those with chronic conditions at the beginning of the study would have had a smaller incentive to continue the exams since they would have been likely to already have been in regular care. Therefore, the estimated incremental employment effect in this study does not necessarily apply to people who develop hypertension or other related complications relatively early in their lives.

Conclusions

Findings from my analysis indicate that, compared to therapies prevalent in the late 1970's, recent pharmacological therapies for HBP are more effective in helping HBP patients work. This is supported by evidence on the additional effect of recent therapies in controlling blood pressure and hence reducing events such as stroke and coronary heart diseases. However, the point estimate of the employment effect is much larger than implied by the additional effect of newer therapies on blood pressure.

Sensitivity analyses by restricting the sample to certain subpopulations lead to estimates similar in size to the main result. However, the results could be driven by the assumption that the data-generating process is normally distributed. Further exploration of possible biases created by historical developments in the labor market did not result in an adequate explanation for the large size of the estimated effect. To enable consistent estimation of the impact of treatment on employment outcomes, future studies will have to collect data on labor market-related information (including occupation, industry, health insurance and other employer-provided benefits, and

incentives related to early retirement) as well as detailed clinical data regarding disease-specific severity, comorbidity, and treatment.

Table 4.1. Summary of information regarding the Framingham Heart Study offspring sample (male only)

	Exam 1	Exam 2	Exam 3	Exam 4	Exam 5
Sample Size	N=2,483	N=1,869	N=1,868	N=1,937	N=1,792
Year of Exam	1971-75	1979-82	1984-87	1987-90	1991-95
Age Distribution	10-19: n=126 20-29: n=543 30-39: n=789 40-49: n=694 50-59: n=293 60-69: n=38	10-19: n=0 20-29: n=135 30-39: n=488 40-49: n=589 50-59: n=525 60-69: n=132	10-19: n=0 20-29: n=53 30-39: n=321 40-49: n=611 50-59: n=555 60-69: n=303 70-79: n=25	10-19: n=0 20-29: n=23 30-39: n=189 40-49: n=612 50-59: n=602 60-69: n=443 70-79: n=68	10-19: n=0 20-29: n=0 30-39: n=108 40-49: n=449 50-59: n=586 60-69: n=508 70-79: n=141
Employment variables	None	"type of job"; "number of jobs past 10 years"; "usually employed"; "currently working status: working, retired, unemployed, housewife, unknown"	"employed most of adult life"; "current working status: working, retired, unemployed, housewife, unknown"	None	"employed now?: no, full-time, part- time"; "# of days in the last six months too sick to carry out usual activities"
HBP Medications listed	Diuretics of fluid retention; Diuretics for blood pressure; hypotensives (excluding Diuretics)	Propranolol; Diuretics for hypertension; Diuretics for other	Beta blockers; Calcium channel blockers; peripheral vasolidators; other hypertensive drugs; Diuretics; potassium sparing; reserpine derivatives; Aldomet; Clonidine; Wytensin; Ganglionic blockers; Renin Angiotensin Drugs	Beta blockers; Calcium channel blockers; Thiazide Diuretics; Loop Diuretics; K-sparing Diuretics; reserpine derivatives; Methyldopa; Clonidine; Wytensin; Ganglionic blockers; Renin-Angiotensin blocking drugs; peripheral vasolidators; other hypertensives	Beta blockers; Calcium channel blockers; Loop Diuretics; Thiazide/K-sparing Diuretics; Potassium supplements; reserpine derivatives; Methyldopa; Renin-Angiotensin blocking drugs; peripheral vasolidators; other hypertensives

Source: the Framingham Offspring Study.

Table 4.2. Percentage of patients treated with HBP medication that were on certain classes of drugs.

	Early Cohort (at Exam 2)	Late Cohort (at Exam 5)
Major Classes of Drugs		
Diuretics	69.8%	18.1%
Beta blockers	34.9%	40.8%
Calcium channel blockers	N/A	35.0%
ACE inhibitors	N/A	35.8%
Other HBP medication	38.6%	10.4%
Combination of Drugs		
Diuretics only	36.7%	6.2%
Diuretics + Beta blockers	16.3%	5.4%
Diuretics + Calcium channel blockers	N/A	3.5%
Diuretics + ACE inhibitors	N/A	5.4%
Diuretics + Other HBP medication	21.9%	1.5%
Beta blockers + Calcium channel blockers	N/A	11.5%
Beta blockers + ACE inhibitors	N/A	8.1%
Beta blockers + Other HBP medication	10.2%	3.8%
Calcium channel blockers + ACE inhibitors	N/A	4.6%
Total number of exam participants on HBP medication		
	215	260

Source: author's calculation based on the Framingham offspring sample.

Table 4.3. Summary of independent variables (other than medication and cohort dummies) in Equation 2-5.

	Equation (2)	Equation (3)	Equation (4)	Equation (5)
<i>BS</i>				
Baseline systolic/diastolic/elevated BP (0,1)	√		√	
<i>Variables in the vector x</i>				
Female (0,1)			√	√
Age 45-49 (0,1)	√	√	√	√
Age 50-54 (0,1)	√	√	√	√
Age 55-59 (0,1)	√	√	√	√
Age 60-61 (0,1)	√	√	√	√
High school (0,1)	√	√	√	√
Some college (0,1)	√	√	√	√
Higher than college (0,1)	√	√	√	√
<i>Variables in the vector w</i>				
Total cholesterol at baseline	√		√	
Glucose reading at baseline	√		√	
Regular smoking at baseline	√	√	√	√
Any non-CVD chronic condition (0,1)		√		√
Elevated blood pressure at baseline (0,1)		√		√

Table 4.4. Additional effect of recent HBP therapies (compared to earlier therapies) in controlling blood pressure

		Early Cohort		Late Cohort		Risk-adjusted Additional Effect of Recent Therapies
		Meds	No Meds	Meds	No Meds	
<i>Mean systolic pressure (mm Hg)</i>	Baseline	139.5	123.9	131.5	120.5	
	Current	137.0	126.2	131.0	124.4	-1.8
<i>Mean diastolic pressure (mm Hg)</i>	Baseline	92.0	81.2	86.9	79.8	
	Current	88.3	81.8	79.2	77.1	-2.2**
<i>Percentage with elevated blood pressure (%)</i>	Baseline	58.6	14.9	33.2	6.6	
	Current	43.7	17.7	21.0	9.6	-10.0**

Notes:

"Early Cohort" refers to male participants aged 40-61 at the time of Exam2 (1981); "Late Cohort" refers to male participants aged 40-61 at the time of Exam5 (1993).

For the early cohort, "Baseline" measures were recorded at Exam1 (around 1973), and "Current" measures recorded at Exam3 (around 1986). For the late cohort, "Baseline" measures were recorded at Exam3 (around 1986), and "Current" measures recorded at Exam5 (around 1993).

"Risk-adjusted Additional Effect of Recent Therapies" is estimated from OLS regressions (equation 2) in the text, which accounts for differences in baseline blood pressures and other risk factors.

** indicates statistical significance with p-value less than .05.

Table 4.5. Probit regression results of the employment analysis

	Estimated Coefficient	Standard Error	p-value
HBP Medication	-0.53	0.17	0.001
Late Cohort	-0.82	0.12	0.000
HBP Medication * Late Cohort	0.43	0.20	0.033
Demographics			
Age 45-49	0.08	0.15	0.617
Age 50-54	0.14	0.16	0.352
Age 55-59	-0.47	0.14	0.001
Age 60-61	-0.91	0.16	0.000
Education			
High School	-0.19	0.14	0.171
Some College	0.23	0.14	0.082
Higher than college	0.47	0.18	0.011
Any non-CVD chronic condition	-0.23	0.09	0.016
Baseline casemix control			
Smoking regularly in the last year	-0.30	0.09	0.002
Elevated blood pressure	0.01	0.12	0.917
Constant	2.36	0.21	0.000

Notes: Results are for male participants aged between 40 and 61 at the time of the exams. Size of the estimation sample is, N=2,188.

Table 4.6. Additional effect of recent HBP therapies (compared to earlier therapies) on employment

	Treated w/ earlier therapies (1)	Treated w/ recent therapies (2)	Additional effects of recent therapies (2) - (1)
Probit Model			
<i>Entire Analysis Sample**</i>	72.1%	82.2%	10.1% (5.7%)
<i>Excluding people on HBP medication at baseline **</i>	68.9%	82.5%	13.6% (6.8%)
<i>Participants who reported certain job types at Exam2</i>	73.9%	81.6%	7.7% (10.7%)
Linear Probability Model			
<i>Entire Analysis Sample</i>	81.4%	82.3%	0.9% (3.4%)
<i>Excluding people on HBP medication at baseline</i>	80.0%	82.5%	2.5% (4.5%)
<i>Participants who reported certain job types at Exam2</i>	86.7%	81.7%	-5.0% (4.9%)

Notes:

numbers shown in the first two columns are predicted employment rates for the group on HBP medication at Exam5 (around 1993) conditional on patients being treated with earlier therapies or recent therapies.

"Certain job types" include: executive, professional, supervisory, and technical.

** indicates statistically significant (p<0.05) difference between the rate with earlier therapies and the rate with recent therapies.

Standard errors of the estimated additional effect of recent therapies (Column 3) are in parentheses.

Table 4.7. Additional effect of combination HBP therapies (compared to mono therapies)

		Mono Therapies	Combo Therapies	Additional Effect of Combo Therapies
BP Outcomes				
<i>Mean systolic pressure (mm Hg)</i>	pre-tx	128.3	134.7	-2.1
	post-tx	129.4	133.5	(1.8)
<i>Mean diastolic pressure (mm Hg)</i>	pre-tx	84.5	87.6	-1.1
	post-tx	77.7	78.7	(0.9)
<i>Percentage with elevated blood pressure</i>	pre-tx	25.6%	35.4%	-1.0%
	post-tx	19.0%	25.8%	(4.8%)
Employment rate				
		76.4%	76.8%	4.6%
				(4.7%)

Notes:

Estimates are calculated for participants aged 40-61 (male and female) at Exam5 (around 1993).

"Pre-tx" measures were recorded at Exam 3 (around 1986); "post-tx" measures were recorded at Exam 5 (around 1993). HBP medications were taken at Exam 4 (around 1989).

"Additional Effect of Combo Therapies" is estimated from OLS regressions (equation 4-5 in text) with standard errors in parentheses.

Appendix 4.A. A model of relative disease severity between the treated and the non-treated group over time

Suppose that some severity index (x) of the disease in the population (higher value indicating greater severity) follows a normal distribution with probability density function ϕ and cumulative distribution function Φ . Patients' awareness of the disease and therefore their efforts to seek out medical advice and treatment, physician practice pattern, and other factors, combine to determine the cut point P_0 in the continuum of the severity index: everyone with severity higher than P_0 will get the treatment, and everyone below will not be treated. The difference in average severity of the treated group relative to the non-treated group, in absence of treatment, will be

$$\Delta S_{old} = \frac{\int_{P_0}^{+\infty} x \phi(x) dx}{1 - \Phi(P_0)} - \frac{\int_{-\infty}^{P_0} x \phi(x) dx}{\Phi(P_0)} .$$

If, over time, the cut point is lowered to P_1 (i.e., people with less severe conditions are getting treated as technology advances), the average severity of the treated group will be lower, but so will be that of the non-treated group. And,

$$\Delta S_{young} = \frac{\int_{P_1}^{+\infty} x \phi(x) dx}{1 - \Phi(P_1)} - \frac{\int_{-\infty}^{P_1} x \phi(x) dx}{\Phi(P_1)} .$$

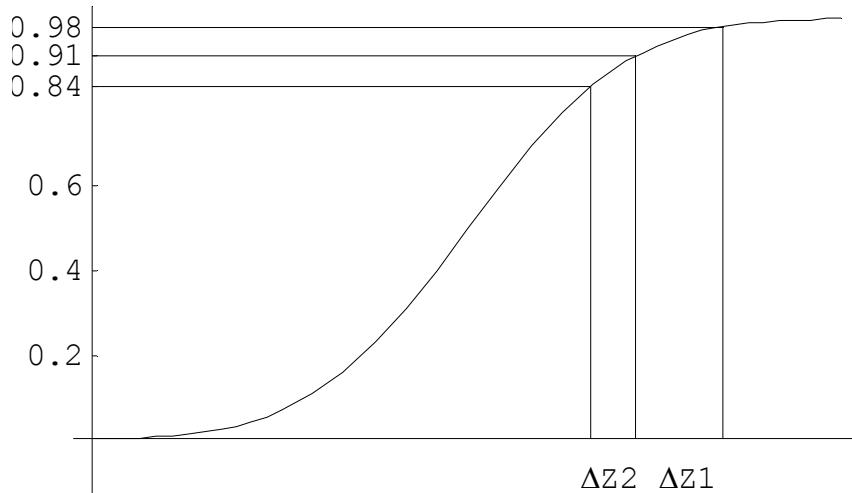
It can be shown that the change in the difference of severity between the treated and the non-treated group over time (as P_0 decreases) is

$$-\frac{\partial \Delta S_{Rx-NoRx}}{\partial P_0} = -\left\{ \frac{\phi(P_0)}{1 - \Phi(P_0)} [E(S | S > P_0) - P_0] + \frac{\phi(P_0)}{\Phi(P_0)} [E(S | S < P_0) - P_0] \right\} .$$

Since the first term in the curly bracket is positive and the second is negative, whether the difference in severity widens or narrows as more patients are treated is indeterminate. It will be a function of the position of the initial cut point, P_0 , and the parameters of the distribution. Therefore, when adopting the Difference-in-Difference approach, it is not possible, a priori, to determine the direction of bias due to change in the difference in pre-treatment severity between those treated and those not treated.

Appendix 4.B. The normal cumulative density function (CDF) and its implications for the estimated employment effect

Below is a graphical illustration of the CDF of a standard normal distribution and how the assumption of a probit model might bias the estimated employment effect.



In estimating the additional employment effect of recent antihypertensive therapies, the gap in the employment rate between the treated and the non-treated group in the late cohort is compared to that of the early cohort. According to the raw statistics (statistics without adjusting for sociodemographics or baseline case mix), the gap is of the same size in the late cohort as in the early cohort (a seven-percentage-point difference). However, because the overall employment rate is much lower for the late cohort (around 88%, compared to 96% in the early cohort), with a probit model and hence the curvature in the CDF of a normal distribution, the reduction in Z score required to make the

seven-percentage-point difference ($\Delta Z2$) is much smaller than in the case of the early cohort ($\Delta Z1$).

With the specification of Equation 3, this differential reduction in Z score will be captured by a positive coefficient for the interaction term "late cohort"* medication. If the underlying data generating process is not well represented by a probit model (--in particular, if the "true" CDF does not flatten out as much as the normal CDF does as probability approaches 1--), the assumption of a probit model will bias the estimated effect upward.

5. DISCUSSION AND CONCLUSIONS

Previous chapters have focused on methodological issues in the empirical estimation of employment effects of specific pharmaceutical innovations. However, the ultimate purpose of such estimation is to provide a more accurate account of the employment-related benefits associated with such innovations, and to incorporate the estimates of benefits into cost-benefit analyses. In particular, when a potential Pareto improvement criterion is adopted, the estimated incremental benefits can be compared to the estimated incremental costs associated with the innovation to understand whether the intervention increases net benefits to the society.

This concluding chapter opens by discussing the conceptual issues in translating employment effects into employment-related social benefits. I show that, in order to account for the welfare changes of all major parties affected by the change in labor supply or productivity, the analyst must be aware of the changes in labor market equilibrium that may result from the employment effects of the medical intervention. Following that is a brief discussion of incorporating employment-related benefits into cost-benefit analyses or cost-effectiveness analyses. The last section concludes the dissertation.

Deriving social benefits associated with improved employment

To translate employment effects of treatment into benefits for the society, previous studies have very often adopted the "human capital" approach, i.e., researchers calculated incremental earnings (the product of the prevailing wage rate and the increased labor) based on the assumption that the wage rate reflects the social value of one additional hour of labor. However, as discussed in detail in Deleire and Manning (2002) and Pauly, Nicholson, Xu, et al. (2001), neglecting

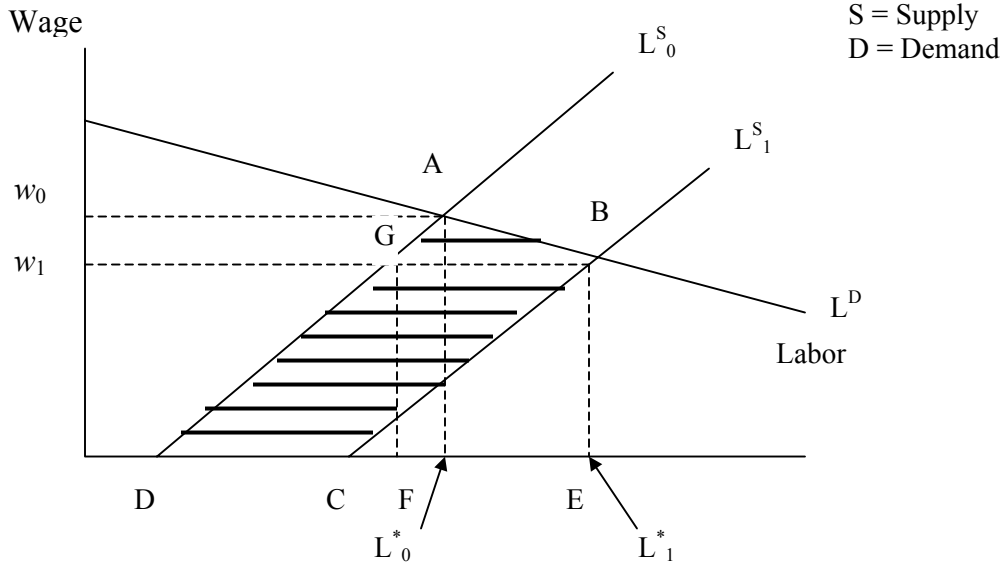
changes in the labor market equilibrium associated with the change in labor supply or productivity leads to incomplete and systematically biased estimates of the resulting benefits. Since this dissertation focuses on changes in labor supply due to pharmaceutical innovations, the following discussion emphasizes the implications of an increase in labor supply while briefly touching upon the implications of improved productivity.

The following discussion is based on Deleire and Manning (2002) and Pauly, Nicholson, Xu, et. al. (2001). To set limits on the discussion, I make standard neoclassical assumptions regarding labor supply and demand. The parties represented in the economic model of the labor market, i.e., workers and firms, are by no means the only ones affected by the intervention. However, these two groups are doubtlessly the major parties affected and therefore a complete account of their benefits should provide a good guide for the social benefits related to the employment effects of the intervention.

Social benefits of increased labor supply: full employment

In a perfectly competitive labor market, workers make labor-leisure tradeoffs to maximize utilities; firms make production and input choices to maximize profits. Figure 5.1 depicts the supply and demand in such a market and comparative statics of an increase in labor supply in the short run.

Figure 5.1. Increase in labor supply and the resulting welfare implications: less than perfectly elastic demand



The line labeled L^S_0 is the baseline labor supply curve. It slopes upward because as workers increase hours of work, they demand higher wages to compensate for additional leisure time forgone. The line L^D is the labor demand curve drawn with the assumption that firms hire additional labor at a wage rate equal to the value of marginal product of the labor and that marginal product of labor declines as more labor is hired. In a competitive labor market, the intersection of L^S_0 and L^D (at point A) determines the equilibrium wage rate (w_0) and employment (L^*_0) at baseline. Further, workers' surplus of providing L^*_0 at w_0 is represented by the area above the labor supply curve but below the equilibrium wage line; since the marginal value product of each worker hired is higher or equal to the wage paid, the firms/employers reap surplus represented by the area below the labor demand curve but above

the equilibrium wage line. So social surplus is the area between L_0^s and L^D and to the left of L_0^* .

Suppose an effective treatment becomes available and analysis indicates that its use increases labor supply by a certain amount, represented by an increase in labor supply from L_0^s to L_1^s . The resulting equilibrium wage and employment are w_1 and L_1^* , respectively (point B). Notice that since the new equilibrium wage is lower than the baseline wage rate, some workers who were previously employed may opt to exit the labor market as the wage rate is no longer adequate to compensate for their lost leisure, a phenomenon known as "displacement". Therefore, change in equilibrium employment - the difference between L_0^* and L_1^* - is smaller than the increase in labor supplied by the patients who benefited from the effective treatment.

Now the social surplus has increased by an amount represented by the shaded area in Figure 5.1. If we assume both the labor supply and labor demand functions to be linear in wage and the shifted supply and demand schedules to be parallel to the original ones, and denote the horizontal shift in labor supply curve (i.e., change in labor supply because of effective treatment) as ΔL_s , then the incremental benefits to the work force and the firms can be calculated as

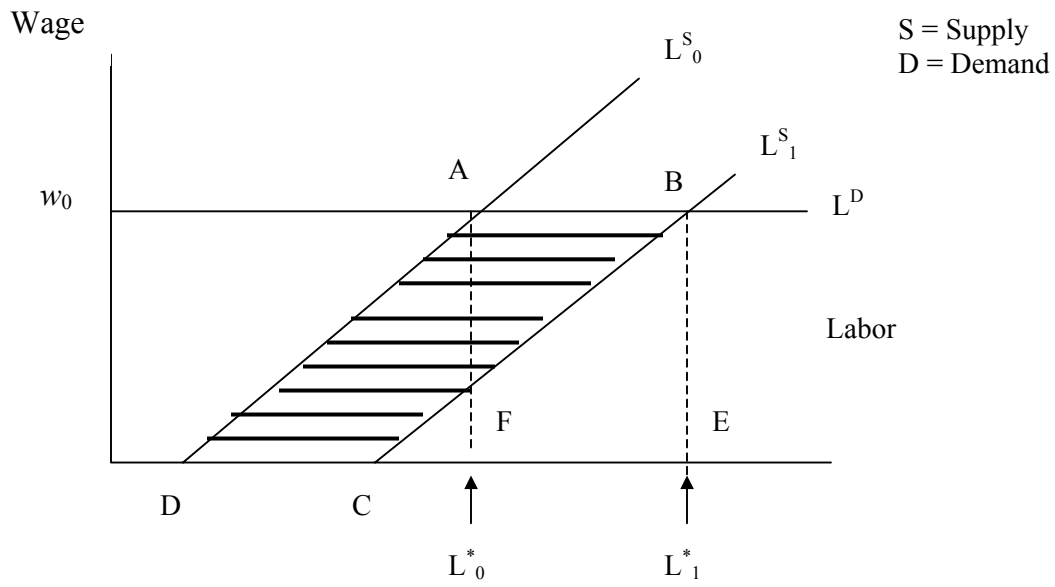
$$EmploymentBenefits_{\Delta L_s} = \frac{(w_0 - w_1) * \Delta L_s}{2} + w_1 * \Delta L_s .$$

It is clear from the expression above that, human capital approach using the baseline wage rate as the societal value for one additional unit of labor would overestimate the incremental benefits of the treatment, while an approach using the new equilibrium wage (i.e., the second term in the above equation) underestimates the benefits.

However, in some cases the human capital approach provides a reasonable approximation to the true employment benefits due to the

treatment. These cases are usually characterized by a small change in labor supply and/or highly elastic labor demand curve. Figure 5.2 depicts an extreme case where the labor demand curve is perfectly elastic.

Figure 5.2. Increase in labor supply and the resulting welfare implications: perfectly elastic demand



When labor demand is perfectly elastic, firms are willing to hire an infinite amount of labor at the prevailing wage. An increase in labor supply because of effective treatment will not lead to displacement of other workers. As shown in Figure 5.2, incremental benefits associated with increased labor supply are the product of the equilibrium wage (w_0) and the increased labor supply (ΔL_s).

Studies on the effect of the recent welfare reform in the U.S. provide support for such approximation (e.g., Bartik 2000). Since 1993, welfare reform at both the federal and state level has pushed a large number of welfare recipients into the labor market. After a careful review of the literature and examination of empirical data, Bartik concluded that the labor supply shock as a result of the reform is not large relative to the size of the entire labor force of the U.S., and the overall labor market is flexible enough to respond to such supply-side shocks without substantial adjustments of average wages or unemployment rates. However, Bartik also pointed out that, when the outcomes of some particular demographic groups (such as single mothers or less-educated women) are of interest, the labor supply shock because of welfare reform could be significant.

In summary, to derive the social gains from increased labor supply resulting from effective treatment, we need to know the equilibrium wage rates before and after the change in labor supply in addition to the magnitude of the increase made possible by the treatment. This in general requires the knowledge of the price elasticity of the labor demand and labor supply functions. With these parameters, we would also be able to calculate how the benefits are distributed among the workers and employers. As pointed out and illustrated with an example in Deleire and Manning (2002), when the illness of interest is prevalent among the population of working age and when treatment is effective in increasing

labor supply, neglecting the effect on labor market equilibrium will significantly underestimate the true benefits of treatment realized in the labor market. However, if the illness is not prevalent or no treatment exists that would effectively improve patients' labor supply and, therefore, the increase in labor supply is small relative to the size of the labor force, or if the labor demand is highly elastic, summing up individual patients' incremental earnings attributable to the treatment provides a close approximation to the social benefits.

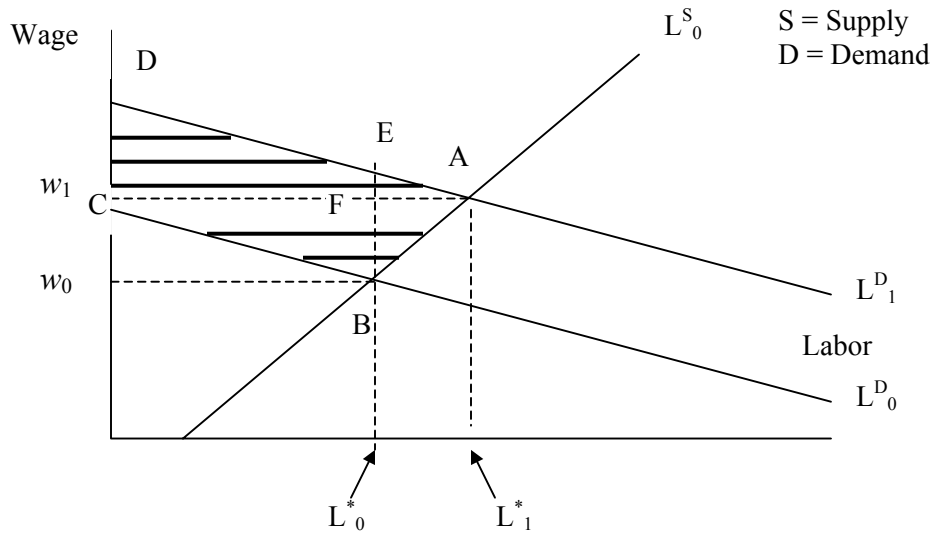
Social benefits of increased labor supply: less than full employment

The discussion so far has been based on the assumption of full employment, i.e., the wage rate is free to adjust so that the prevailing wage equals the value of a unit of leisure time for the last hour of labor hired. Less-than-full-employment occurs when wages are sticky so that there are workers in the labor force whose marginal value for leisure is lower than the prevailing wage yet cannot get hired. In that case, the additional labor supply that results from effective treatment will not be hired at the prevailing wage rate. In fact, in a time of high unemployment, these increased supply of hours may only be hired by displacing others from the market. In any case, under less-than full employment, the prevailing wage rate is likely to be higher than the opportunity cost of labor time (or value for leisure) and therefore does not provide a valid measure of societal value for the production associated with one additional unit of labor. As pointed out by Pauly and colleagues (Pauly, Nicholson, Xu, et al., 2001), in those cases, the opportunity cost of labor needs to be measured in order to derive the benefits associated with reduced disability and/or increased labor supply.

Social benefits of improved productivity

Although the focus of this dissertation is the labor supply effect of effective treatment, on-the-job productivity is another important dimension of employment effects. When labor productivity is improved by some medical intervention for a prevalent condition, with the assumptions of a competitive labor market as outlined previously, the labor demand curve should shift rightward to reflect the increased marginal product of labor.⁵³ This is illustrated in Figure 5.3.

Figure 5.3.
Increase in labor productivity and the resulting welfare implications



⁵³ It is assumed that the treatment can potentially increase the productivity of all workers by the same amount, thus the parallel shift of the demand curve.

The increased productivity is reflected by a shift of the labor demand curve from L_0^D to L_1^D . As a result, both the equilibrium wage rate and the equilibrium employment increase. The shaded area DABC represents the combined incremental surplus of the workers and of the firms. If we denote the increased unit productivity (in dollars) as Δp and again assume linearity of the labor supply and demand curve, then the incremental social benefits are:

$$SocialBenefits_{\Delta Productivity} = \Delta p * L_0^* + \frac{\Delta p * (L_1^* - L_0^*)}{2} .$$

In order to derive the social benefits from increased productivity, we need to know the elasticity of the labor demand and supply curves in order to determine the equilibrium employment in response to the shift in demand. It is also evident that the approach often seen in the literature, i.e., taking the product of increased productivity and the number of working hours, underestimates the true benefits of treatment, because it neglects the fact that increased productivity of the labor force expands employment when labor supply is price elastic.

Incorporating such effects in CBAs and CEAs

If a societal perspective is taken in evaluating medical interventions, employment benefits due to a particular treatment should in principle be incorporated into cost-benefit or cost-effectiveness analyses.

In CBAs, since all benefits are measured in dollars, employment benefits can be figured into the calculation of social benefits due to the intervention. The incorporation is less straightforward with CEAs,

which, as mentioned earlier, focus on health-related outcomes such as extended life years, reduced mortality, and improved quality-adjusted life years. A central question that arises when one wishes to incorporate employment benefits into CEAs is whether to include them in the denominator or numerator of the C/E ratio. As discussed in Garber (2000), in order for CEAs to have favorable welfare economic properties,⁵⁴ the effectiveness or utility measure in the denominator should incorporate all aspects of social benefits derived from the intervention. Gold, Siegel, Russell, et al. (1996) suggests that benefits other than health (including employment benefits) be converted to utility measures in the denominator. In that case, the conversion of benefits (in dollars) into utility terms such as QALYs is another methodological challenge that has not been studied well if at all.

A more practical, but less theoretically appealing, way of incorporating employment benefits is to treat them as "reduced costs" and deduct them from the cost estimates in the numerator. This is an approach adopted in several recent cost-effectiveness studies that incorporated employment effects (for example, Meltzer 1997; Meltzer, Egleston, Stoffel, et al. 2000; Johannesson, Meltzer, and O'Connor 1997).

Regardless of whether the employment benefits are incorporated into the denominator or numerator of the C/E ratio, one has to be aware of the potential issue of "double-counting." The concern of double counting employment-related benefits arises out of the ambiguity in what is measured by the utility metrics such as QALYs. When individuals' preferences are elicited regarding different health states, the common practice is to instruct them to consider only "health-related" aspects, and the wording usually suggests that they should ignore financial consequences of a health condition or treatment (Garber 2000). If that

⁵⁴ More formally, CEAs should be able to guide resource allocation so that the marginal social utility that comes out of spending the last dollar is equalized across different social programs or interventions.

is the case, then employment-related benefits should be incorporated directly into CBAs or CEAs.

"Double-counting" may also arise because of the availability of paid sick-leave as part of employment benefits. If individuals do take into account employment-related consequences of illness or treatment when responding to QALY questions, QALY measures incorporate employment benefits (earnings net foregone leisure) from the perspective of the individual when there is no paid sick leave. When the individual is entitled to paid sick leave, estimates of (potential) employment benefits should be added to the calculation. (Pauly, Nicholson, Xu, et al. 2002; Johannesson 1997.)

However, if the analyst concerns herself with the social benefits versus costs, measuring effectiveness or utility from the perspective of the individual patient alone will not provide an adequate account of the employment-related benefits to the society. For example, even if QALYs do capture employment benefits, these benefits accrue only to individuals whose preferences are elicited, leaving the possible divergence between private and social benefits of improved employment. So a sensible approach would be to restrict the effectiveness metrics (such as QALYs) to measuring health-related utility only, and make it a separate task to measure employment benefits in a framework that takes into account labor market equilibria, as outlined in the last section.

Conclusions

In recent years, advances in medical technologies have driven the growing cost of health care in the United States. Increasingly, the society and policy makers must confront hard choices of allocating limited resources among competing needs. What makes the choice harder is lack of knowledge about the benefits of various treatment technologies to the patients and the society. Current approaches to evaluating the benefits of technologies very often ignore employment-related benefits.

For the few studies that do incorporate employment benefits, pitfalls in conceptualizing and in measuring the employment effects of treatment often lead to unreliable estimates.

This dissertation reviews evidence of employment-related benefits from effective treatment. I set up a microeconomic model to depict a typical patient's decision regarding labor supply when treatment technology improves. The model shows that observed incremental labor supply is a result not only of more effective treatment, but of other factors such as eligibility for employment-based or public health insurance, both of which are tied to one's employment status. I conduct two empirical studies to provide examples of econometric and statistical strategies one might take in order to consistently estimate the employment effects of treatment. The analysis of the effect of HAART on HIV patients' employment transitions uses an instrumental variable approach. This approach identifies the effect of a particular therapy when patients self-select into the treatment by unobserved severity, personal behavioral traits, and other factors. The analysis of the additional effect of recent pharmacological therapies for hypertension (relative to therapies used in the 1970's) provides an example of strategies one might take when panel data and instrumental variables are not available. The "difference-in-difference" approach employed aims at differencing out the unobserved selection factors in hypertension treatment. I discuss pitfalls of the approach and implications for data collection to inform future research in this area. Finally, to translate estimated employment effects into employment-related benefits, one has to be aware of possible labor market adjustments associated with the change and base the analysis on labor market equilibria.

This dissertation also develops some insights for future data collection to facilitate evaluation of employment-related benefits. First, random controlled clinical trials can be designed better to collect employment-related information, thus enabling analysts to

compare employment outcomes of the treatment group to that of the control group and derive average employment effects directly. However, because of the generally limited scope of clinical trials and the restrictive eligibility rules adopted in selecting participants for trials, employment-related information derived from the trials may not be applicable to the general population of working age in the medium- to longer-run. Second, when data based on random assignments are not available, survey data with certain features are a must. These features include: panel data with information on baseline employment, treatment in interim, and employment outcomes after the treatment; data on health insurance status, employment benefits such as private pension provision, retiree health insurance coverage, and paid sick leave; data on type of job or occupation and on the physical demands of the job in particular.

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