A Re-examination of the Costs of Medical R&D[1]

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1. Introduction

Recent evidence suggests that the economic value of increased health has been enormous (Murphy and Topel, 2006; (Nordhaus 2003)). Much of this gain has arguably resulted from highly successful, but also highly expensive, medical R&D efforts. Well known studies from the Tufts Center for the Study of Drug Development place the current cost of developing a single successful drug at roughly $800 million (in 2003 dollars) by the time of initial marketing (DiMasi, Hansen et al. 2003). This figure is substantially higher than the cost of medical R&D reported by these authors (DiMasi, Hansen et al. 1991) for successful drugs developed nearly three decades earlier, $231 million (in 1987 dollars). Given both the large costs and benefits of medical R&D, recent research has naturally focused on how well these costs measure up to the benefits. A central and frequently asked question that this paper addresses is: how much more could a streamlined drug discovery and drug approval process be expected to reduce these costs?

Our major argument in this paper is that previous estimates of the costs of drug development are incomplete as they do not fully capture the social costs of the process, namely the costs to producers in terms of forgone profits and the costs to consumers in terms of forgone consumer surplus. Under the existing approach, the perceived costs of drug discovery are limited only to actual R&D outlays, such that the expected present value cost of drug discovery is equivalent to the expected present value of R&D outlays at start of the R&D process. For example, pushing out phase III expenses further in the future would lower the present value of R&D at the start of innovation spending but clearly be socially costly. More generally, viewing the cost of drug discovery in this manner is incomplete in two major respects. First, it does not capture the foregone profits to producers associated with delays in the R&D process. Certainly, a prolonged R&D process will be more costly to a firm whose delayed product is expected to be

a blockbuster than one of an orphan drug. Moreover, delays in drug discovery and approval may in some instances lower the expected present value of R&D costs, as presently calculated, if fixed costs are pushed further into the future. The present approach to calculating R&D costs in this case would imply that such delays reduce costs, when in fact they may do the opposite by pushing profits further into the future as well. The second respect in which the existing view of drug discovery costs is incomplete is that it does not capture the foregone surplus to patients who may otherwise benefit from treatments introduced earlier to date. .

Put together, a complete view of the drug discovery process should account for not only the direct R&D costs of drug discovery, but for the foregone costs to producers and consumers in terms of foregone producer- and consumer surplus, respectively. This paper re-examines the drug discovery process in this light and empirically illustrates how incorporating producer and consumer surplus into the social cost of R&D affects our understanding of the costs of delays in drug discovery and approval. Our main empirical finding is that the social costs of changes in drug lags, as measured by changes in consumer surplus and variable profits, far outweigh the changes in R&D costs discussed above. For example, in the case of HIV drugs, we find that earlier entry of Highly Active Antiretroviral Therapy by one year would have increased consumer surplus and variable profits respectively by $19 billion and $4 billion. For non-Hodgkin's lymphoma, we find that earlier entry of the drug Rituxan by one year would increase consumer surplus by $310 million and $330 million, respectively, and in the case of breast cancer, earlier entry of Herceptin by one year would increase consumer surplus by $8 billion and producer surplus by $1 billion. In contrast, we find that for all of these drugs, earlier introduction by one year would lower R&D costs by at most $33 million. Thus, the benefits of earlier adoption by patients far outweighs the R&D costs borne by the firm.

The paper may be briefly outlined as follows. Section 2 develops a framework for understanding how R&D costs, producer surplus, and consumer surplus affect the costs of drug discovery and approval. It then briefly describes how work by the Tufts Center fits into our framework and estimates the direct R&D costs of delays in drug discovery and approval time. Section 3 describes our methodology for estimating the foregone profits and consumer surplus arising from delays in drug discovery and approval. For three important drug classes (HIV, non-Hodgkin's lymphoma, and breast cancer), Section 4 then estimates the social cost of delays (improvements) in drug discovery and approval time, decomposes these costs (improvements) into those arising from foregone (realized) profits versus consumer surplus, and compares these to the higher (lower) direct R&D costs associated with delays (improvements). Lastly Section 5 concludes.

2. The social cost of delays in drug discovery and approval

2.1. Basic framework

In our approach, the social value of a drug is simply the present value of the annual welfare generated by the drug, net of any fixed costs required to bring the drug to market. Such costs may include direct R&D costs and costs of complying with pre-market regulations. In this view, the drug discovery and approval process can be thought of as encompassing two social costs. The first is the direct cost of R&D and the cost of complying with pre-market regulations. The second is the potential opportunity cost to society that results from reductions in the period of time over which welfare-generating treatments may be enjoyed by consumers. Of course, longer drug discovery and approval times exist to ensure that it is only the safe *and* effective products that eventually reach the market. But, when the implied speed-safety tradeoff results in

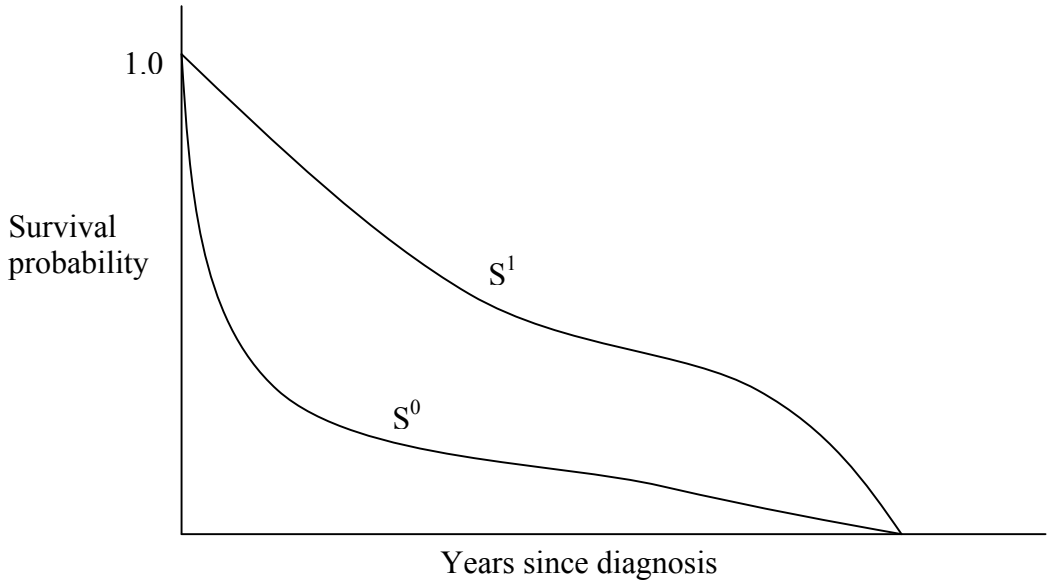
inefficiently stringent clinical trial standards or lengthy post-R&D approval times, the drug discovery and approval process will impose social costs by delaying patient access to treatments whose health benefits outweigh the side-effects. Indeed, work by Philipson et al. (2008) find that this may be the case, as they find that the benefits of faster drug approval times due to passage of the Prescription Drug User Fee Acts (PDUFA) far outweighed any concomitant decrease in drug safety.

To more clearly see how the drug approval and regulatory process imposes social costs in addition to direct R&D costs, consider Figure 1 which plots survival from a hypothetical disease under two scenarios: an abbreviated versus lengthy drug approval and regulatory process. For simplicity, suppose that an abbreviated process results in a market introduction in year τ and that a lengthy process results in market introduction a year later in $\tau + 1$. For individuals who develop disease in year τ, S^0 is the survival they can expect under the lengthy drug discovery and approval process and S^1 is the survival they can expect under the abbreviated process. In this case, survival is poor in the first year of disease when treatment does not yet exist (S^0). Speeding up the drug discovery and approval process by a single year therefore has large mortality benefits since the disease is particularly devastating in its first year. This effect would, of course, be dampened for diseases with more insidious onset. Importantly, note that individuals who develop disease in year $\tau + 1$ or later are unaffected by the length of the drug discovery and approval time.

The non-R&D component of social cost associated with delays in the drug discovery and approval process is characterized by how much the survival curves in Figure 1 diverge. In particular, the area between the two curves is the reduction in life expectancy induced by delay, and the value of this change in life expectancy is the welfare loss to society. Put differently, the

welfare cost to society is equivalent to the amount by which consumers are willing to pay to avoid the less favorable survival prospects associated with delayed treatment introduction. Generally, this welfare cost is borne by consumers in the form of foregone consumer surplus and by producers in the form of foregone profits.

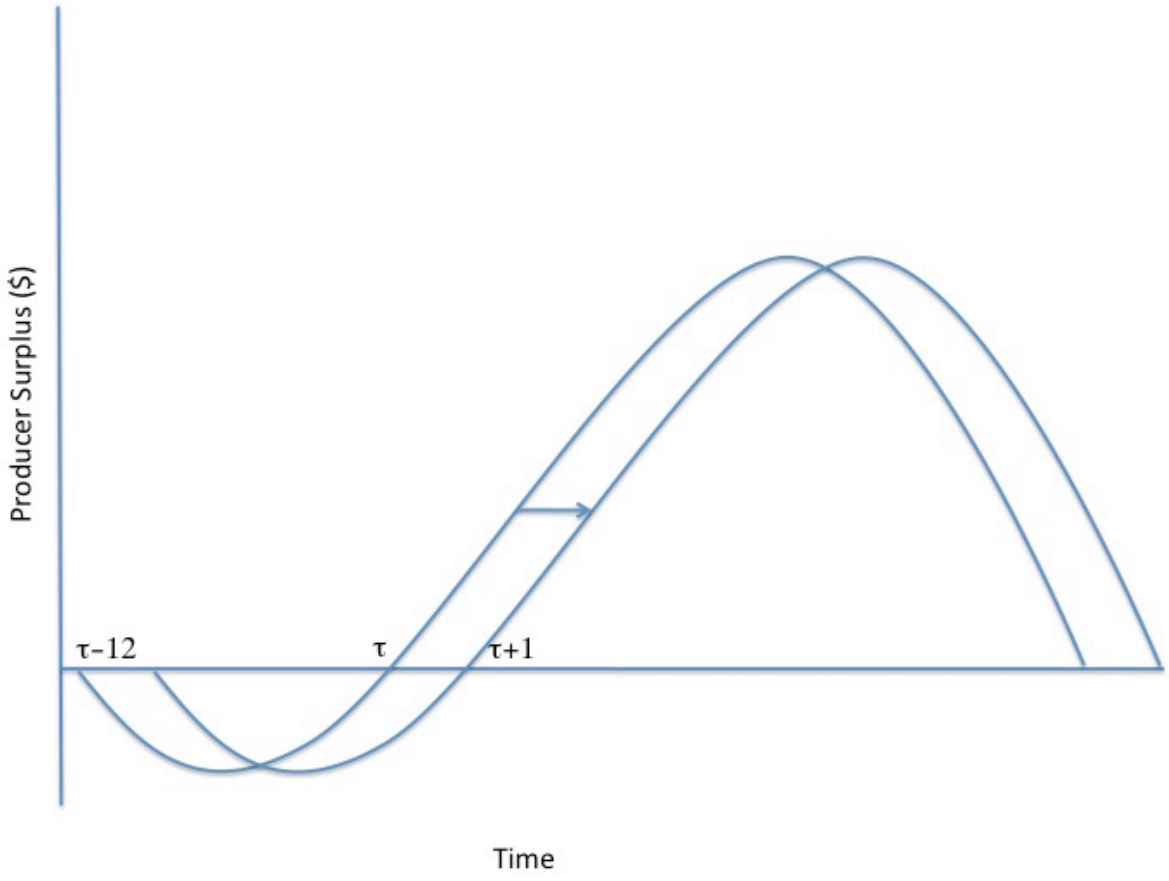
FIGURE 1 – The impact of delays in drug discovery and approval on survival



While Figure 1 illustrates how lengthened drug discovery and approval times lead to additional social welfare costs beyond possibly increased costs of R&D, Figure 2 isolates the effect of these delays on producer surplus. To remain consistent with our earlier example, suppose that drug discovery begins in year $\tau - 12$, so that the R&D and approval process take on average 12 years to complete (DiMasi, Hansen et al. 2003). The majority of fixed costs are incurred during the active R&D phase with some minority possibly occurring after phase III but before initial entry. In year τ, the drug is introduced and variable profits start accruing to the innovating firm. These

profits grow initially but dwindle over time, as the drug is either removed from the market or better therapeutic options become available. In this framework, a single-year delay in the drug discovery and approval process has several effects. First, it shifts the date of market entry from τ to $\tau + 1$ and therefore shifts variable profits forward by one year. This, of course, reduces the net present value of variable profits at the time of initial R&D in year $\tau - 12$. Second, the lengthened drug discovery and approval process either increases or decreases the net present value of R&D costs depending on how costs are structured. For example, if, as shown in the figure, costs are truly fixed in nature so that lengthening the process does not necessarily increase annual costs, the net present value of R&D costs may actually fall if costs are pushed further into the future. On the other hand, if costs are uniformly distributed across years such that a single-year increase in the discovery and approval process adds an additional year of cost, the net present value of R&D costs will certainly rise. This has the subtle implication that while longer R&D and drug approval times may not obviously lead to larger R&D costs, they will lead to additional social costs due to foregone profits.

FIGURE 2 – The impact of delays in drug discovery and approval on producer surplus



2.2. Theory

Formally, the cost of the R&D and drug approval process can be given as follows. Suppose that for a given disease, a new treatment enters the market in year τ. If *t* generally denotes calender time, let N_t represent the annual incidence of the disease in year *t* and let v_t^τ represent the *individual* discounted lifetime consumer surplus for an individual diagnosed with disease in year *t* who receives treatment from year τ onwards. Importantly, τ may precede or follow year *t*; when $\tau > t$, only those individuals diagnosed in year *t* who live to year τ ultimately receive treatment and when $\tau < t$, all individuals diagnosed in year *t* receive treatment. As usual,

the consumer surplus v_t^τ reflects the present value difference in year t between the lifetime willingness to pay for a treatment that is introduced in year τ and the actual lifetime spending. For producers, let π_t^τ represent the discounted lifetime variable profit per individual diagnosed with disease in year t who receives treatment from year τ onwards. When individuals are diagnosed before the treatment is introduced ($\tau > t$) , profits per individual are zero for those who do not survive to year τ. Similarly, annual profits per inidividual are positive and identical for those diagnosed with disease after the treatment is introduced ($\tau < t$).

Annual *individual* social surplus w is simply the sum of individual consumer and producer surpluses:

$$w_t^\tau = v_t^\tau + \pi_t^\tau \tag{1}$$

The aggregate or total social surplus generated by a drug introduced in year τ, net of fixed R&D costs, is obtained by multiplying the annual individual social surplus w by the incidence N and then summing across cohorts. In present value terms, this amounts to:

$$\begin{aligned} W^\tau &= \sum_{t=0}^{\infty} \beta^t N_t w_t^\tau - \sum_{t=0}^{\infty} \beta^t F_t^\tau \\ &= \sum_{t=0}^{\infty} \beta^t N_t v_t^\tau + \sum_{t=0}^{\infty} \beta^t N_t \pi_t^\tau - \sum_{t=0}^{\infty} \beta^t F_t^\tau \\ &= NPV_V + NPV_\Pi - NPV_F \end{aligned} \tag{2}$$

where F_t^τ represents the cost of R&D in year t if the drug is introduced in year τ, and β is the discount rate. In this framework, the cost of delays in the drug discovery and approval process is the impact on social welfare from delaying market entry:

$$\frac{dW^\tau}{d\tau} = \frac{dNPV_V}{d\tau} + \frac{dNPV_\Pi}{d\tau} - \frac{dNPV_F}{d\tau} \tag{3}$$

The first term in expression (3) reflects the impact of delayed market entry on the net present value of consumer surplus; the derivative is negative when drugs are successful and delays in

market entry lead to a shorter period of time over which health benefits from a treatment can accrue to patients. The derivative is positive when longer R&D and drug approval times actually increase social welfare by limiting the entry of harmful drugs. For a discrete single-year delay from τ to $\tau + 1$, only those individuals diagnosed with disease in calender year $t < \tau + 1$ will be affected by the delay in entry. For each of these cohorts, access to the drug is delayed by one year, which either reduces or increases the aggregate lifetime consumer surplus generated by the drug depending on whether the drug ultimately proves beneficial or harmful. For the remainder of the discussion, we assume that the drugs considered are ultimately successful in that the benefits outweigh the side-effects and the above derivative is negative. The second term in expression (3) reflects the impact of delayed entry on the net present value of variable profits; this derivative is also negative when delayed market entry pushes variable profits further into the future. Again, for a discrete single-year delay from τ to $\tau + 1$, profits will be lower for all cohorts diagnosed with disease in calender year $t < \tau + 1$, thereby reducing the net present value of profits arising from the drug. The final term in expression (3) reflects the direct effect of delayed drug discovery and approval, namely on R&D costs. When annual R&D costs are constant over time, increases in τ will increase the net present value of R&D costs, augmenting the effects on costs of forgone profits and consumer surplus. When R&D costs are truly fixed, however, increases in τ may actually reduce the net present value of R&D costs by pushing fixed costs further into the future.

2.3 The R&D cost of delays in drug discovery and approval

As our framework suggests, the social cost of delays in drug discovery and approval may vastly exceed the direct R&D costs associated with delays, particularly when the forgone profits

to producers and forgone surplus to consumers are high. Despite this, existing work analyzing the cost of medical R&D has arguably neglected the social costs associated with delays in R&D and has focused mainly on the additional direct R&D costs that prolonged research and approval phases may entail. Because the main focus of this paper is to understand how incorporating the social costs of R&D affects the perceived costs of drug discovery and approval delays, we briefly describe existing approaches which only focus on direct R&D costs associated with delays.

Estimating the impact of delays in drug discovery and approval on costs of course requires a way to measure R&D costs in the first place. The traditional way of measuring R&D costs for drugs ultimately approved for marketing reflects both the longitudinal expenses incurred in researching and developing the successfully approved drug itself, as well as the expenses incurred for other drugs that did not survive the lengthy and uncertain R&D process. Most research efforts to estimate the cost of successful drug discovery have relied on industry-obtained data on investigational pharmaceuticals originating in the pharmaceutical industry itself. Focusing on products whose entire life-cycles (from conception to either marketing or abandonment) have been in the industry has allowed researchers to accurately estimate the private costs of drug discovery, without being concerned by the unknown licensing costs that some firms face when acquiring partially developed products from others firms or academic centers.

One of the earliest attempts to calculate the cost of drug discovery in this way was by (Hansen 1979), who used firm-level data on costs and development times for a sample of new chemical entities (NCEs) - originating between 1963 and 1973 – to arrive at an average R&D cost of successful drug discovery of $54 million in 1976 dollars. Using a related methodology for a sample of NCEs originating between 1970 and 1985, (Wiggins 1987) and (Woltman 1989)

calculated average drug development costs of $125 million and $108 million in 1987 dollars, respectively. Yet, perhaps the most widely cited estimates of the R&D required to bring a successful drug to market stem from a series of papers by DiMasi, Hansen, and Grabowski who use proprietary R&D data from a sample of US firms ((DiMasi, Hansen et al. 1991); (DiMasi, Hansen et al. 2003)). In their initial examination of this topic, (DiMasi, Hansen et al. 1991) focused on a group of NCEs wholly originating in a sample of 12 US firms between 1970 and 1982. They estimated the cost of successful drug delivery to be $231 million (in 1987 dollars) in that period, a figure roughly in line with estimates from a later study by the Office of Technology Assessment (US Congress 1993). Revisiting this issue for a sample of 68 NCEs undergoing first human testing between 1983 and 1994, (DiMasi, Hansen et al. 2003) estimated an average cost of $403 million (in 2000 dollars) which when adjusted for an assumed annual cost-of-capital of 11% yielded an estimated cost of drug discovery at the time of marketing of $802 million (in 2000 dollars).

Because the most recent private cost of drug discovery estimated by DiMasi and colleagues (DiMasi, Hansen et al. 2003) serves as a benchmark for comparing the R&D cost and social cost of delays in the drug discovery process, it is worthwhile reviewing how their figure is calculated. First, the authors begin with a sample of investigational new drugs or NCEs and compute the average cost in each phase of the R&D and approval process. These stages include a pre-clinical phase, phases I through III of human clinical testing, and a post-R&D approval phase. Then, using detailed evidence on the unconditional probability of entering each of these stages, DiMasi and colleagues estimate the expected cost per phase for a randomly selected investigational drug. We can denote the analogous expected cost per investigational drug in each phase by $f_{i,inv}$, where i reflects the phase. Importantly, since only a fraction of investigational

drugs ultimately become approved, the expected cost per approved drug in a given phase will be higher than the expected cost per investigational drug. The authors therefore next calculate the average cost per phase for an ultimately approved drug by dividing $f_{i,inv}$ (the expected cost in phase i for an investigational drug) by the probability an investigational drug ultimately becomes approved. In their sample of investigational drugs, 21.5 percent ultimately become approved. Thus, the cost in phase i of an ultimately approved drug is $f_{i,app} = f_i/(0.215)$. To maintain consistency with the framework outlined in expression (2), this phase-specific cost can be translated to an annual cost in each phase by simply dividing by the length of the phase. If L_i is the average length of a given phase i, the fixed cost per year F_t is simply $f_{i,app}/L_i$. Note that F_t varies with calendar time depending on what phase in the R&D and approval process a drug is in. Finally, because capital used at each stage in drug development has an opportunity cost, such that equivalent amounts of capital expended early in the drug discovery process are more costly than amounts expended later, the authors compound the yearly costs forward to arrive at a total R&D cost at the time of marketing. This sequence of steps leads to an estimated cost of $802 million (at the time of marketing, in 2000 dollars) to successfully bring a drug to market.

Using this approach, DiMasi alone (DiMasi 2002) argues that simultaneous 25% reductions in phase lengths would lower the capitalized cost of successful drug discovery by 16% or $129 million (in 2000 dollars) at the time of marketing. Even larger 50% reductions in phase lengths would lower costs of drug discovery by 29%, or $235 million. Of course, implicit in this calculation is the assumption that R&D costs are uniformly distributed over a phase, so that reductions (increases) in phase lengths lead to lower (higher) total costs in a given phase.

Using data derived from (DiMasi, Hansen et al. 2003) on 1) R&D phase lengths and approval times and 2) average stage-specific yearly costs per approved drug, we can calculate

both the lifetime net present value cost of R&D at the time of initial investment as well as the discounted R&D cost associated with delays in the R&D and approval process. This computation is demonstrated in Tables 1 and 2. The first column of Table 1 shows the calendar time (in years) of various stages of the R&D and approval process. Roughly 4.3 years elapses between the initiation of the pre-clinical research phase and phase I human testing. An additional year elapses before the start of phase II, followed by an additional 2.2 years between phases II and III. Between phase III and the start of the post-R&D approval phase, 2.8 years elapses. The post-R&D approval phase lasts 1.5 years. All told, the average R&D and approval time for an investigational new product is 11.85 years. The second column of Table 1 presents the stage-specific expected cost per year for a successful drug. These figures are calculated in the manner described earlier. In the 1 year that elapses between the start of phase I and the start of phase II, the average cost per year is $69.0 million per approved drug. Similarly, in the 2.2 years that elapse between the start of phase II and the start of phase III, the average cost per year is $35.8 million. Moreover, in the post-R&D approval phase, (DiMasi, Hansen et al. 2003) assume the cost to be zero. Columns 1 and 2 can be combined with any continuous discount rate to arrive at the net present value cost of R&D and approval. For example, for an interest rate of 11 percent – the cost of capital used by (DiMasi, Hansen et al. 2003) – the net present value cost is $218 million at the time of initial R&D. Compounded to the time of marketing nearly 12 years later, this equals an R&D and drug approval cost of $803 million. For an interest rate of 3 percent, the net present value cost of R&D is $328 million at the time of initial R&D and $469 million at the time of marketing.

TABLE 1—Stage specific and lifetime cost of R&D and drug approval

Pre-marketing stage	Number of years elapsed since start of	Cost-per year in a given stage

	pre-clinical R&D phase	(in millions of year 2000 dollars)
Pre-clinical	4.3	26.4
Phase I	5.4	69.0
Phase II	7.5	35.8
Phase III	10.3	44.8
Approval phase	11.9	0.0
Lifetime net present value cost of R&D and approval		328.8

Source: Authors' calculations based on data reported by (DiMasi, Hansen et al. 2003). The lifetime net present value cost of R&D and approval is at the initiation of the pre-clinical phase. We used a 3 percent discount rate.

Table 2 uses the information in Table 1 to calculate the change in cost that occurs when there are either delays or improvements in R&D and drug approval times. The main assumption in this calculation is that the *annual* costs within a phase are constant, so that total costs for a phase change proportionately with phase length. For example, if the average cost per year in phase II is $35.8 million, an additional year spent in phase II testing is assumed to raise the non-discounted phase II cost by $35.8 million. Under this assumption, Table 2 displays the change in the lifetime net present value cost of R&D and approval under several scenarios: a one year increase (or decrease) in post-R&D approval time, a one year increase (or decrease) in phase III length, and a one year increase (or decrease) in both approval time and phase III length.

TABLE 2—Impact of changes in R&D and drug approval times on lifetime costs

Scenario	Lifetime net present value cost of R&D and approval (in millions of year 2008 dollars)	Change in lifetime costs (in millions of year 2008 dollars)
Status quo	411.0	
1 yr. delay		
Phase III	451.5	40.4
Approval	411.0	0.0
Phase III and approval	451.5	40.4
1 yr. improvement		
Phase III	369.4	-41.6
Approval	411.0	0.0

Phase III and approval	369.4	-41.6

Source: Authors' calculations based on data reported by (DiMasi, Hansen et al. 2003). The lifetime net present value cost of R&D and approval is at the initiation of the pre-clinical phase. The status quo estimate represents the current lifetime cost of R&D and drug approval. This is compared to the estimated cost of a single year delay (improvement) in either phase III length, approval period length, or both. We used a 3 percent discount rate.

Table 2 demonstrates that extension in the average phase III length by one year increases lifetime costs from $328.8 million to $361.2 million, a difference of $32.3 million. At the same time, increases in the approval time have no effect on present value lifetime costs since no costs (except the variable costs of production) are incurred either during or after the approval period. Similarly, a reduction in average phase III length by one year lowers lifetime present value costs by $33.3 million to $295.5 million. Equivalent calculations are easily done for each of the other phases and for longer delays or improvements in a given phase. As we show next, however, the consumer- and producer-based social costs associated with improvements or delays in the drug discovery and approval process vastly exceed the change in lifetime R&D costs.

3. Estimates of the social costs of delays in drug discovery and approval

3.1 Impact of delays in drug discovery and approval on consumer surplus

3.11 General methodology

As discussed previously, earlier market entry by a drug raises social welfare by the degree to which patients are willing to pay for the resulting increases in survival. The extent to which this willingness to pay exceeds the amount paid is the consumer surplus generated by earlier entry. In this spirit, we estimate the value of earlier introduction using a willingness-to-pay approach. Specifically, consider a hypothetical individual with an annual *full* income of y who develops disease (e.g. cancer or AIDS) in year t and who faces survival $S_{t,j}^{\tau}$. This survival

depends on the calendar year $t = \tau$ when the drug that treats the disease is introduced. The subscript j denotes the number of years following disease diagnosis in year t; that is, $S^{\tau}_{t,4}$ is the survival probability 4 years after being diagnosed with disease in year t. Allowing $S^{\infty}_{t,j}$ to depict survival in a setting where no drug ever exists, the value of earlier market entry in the year τ is therefore the maximum amount the patient is willing to pay to avoid the survival $S^{\infty}_{t,j}$. Formally, if $U(S^{\tau}_{t,j}, y)$ represents the patient's lifetime utility over survival and income, then his annual willingness to pay to avoid $S^{\infty}_{t,j}$ is given by the wtp^{τ}_{t} which solves:

$$U(S^{\tau}_{t,j}, y - wtp^{\tau}_{t}) = U(S^{\infty}_{t,j}, y) \tag{4}$$

Since wtp^{τ}_{t} represents the patient's *annual* willingness to pay, his *lifetime* willingness to pay is simply:

$$WTP^{\tau}_{t} = A(S^{\tau}_{t})wtp^{\tau}_{t} \tag{5}$$

where $A(S^{\tau}_{t}) = \sum_{j=0}^{\infty} \beta^{j} S^{\tau}_{t,j}$ is the value of an annuity which pays one dollar in perpetuity, given survival $S^{\tau}_{t,j}$ and discount rate β. Put differently, WTP^{τ}_{t} is the lifetime amount patients diagnosed with disease in year t are willing to pay to have the drug enter the market in year τ. This figure represents the maximum amount they are willing to pay to avoid being without the drug completely and instead having the drug enter the market in year τ.

For someone diagnosed with disease in year t, the consumer surplus associated with a drug that is introduced in year τ is simply the lifetime willingness to pay minus the increase in lifetime spending on the drug. Individual lifetime spending is given by:

$$P^{\tau}_{t} = p\sum_{j=0}^{\infty} \beta^{j} S^{\tau}_{t,j} I^{\tau}_{j} \tag{6}$$

where p is the annual individual spending on the drug, P_t^τ is the lifetime spending, and I_j^τ is an indicator variable which takes on zero when t + j < τ and takes on unity otherwise. The indicator variable captures the fact that spending on the drug is zero before it is introduced, i.e. in the years prior to τ. Putting together the previous elements, the lifetime consumer surplus for an individual diagnosed with disease in year t who receives treatment from year τ forwards is simply:

$$v_t^\tau = WTP_t^\tau - P_t^\tau \tag{7}$$

In this framework, the change in consumer surplus associated with a change in the total R&D and approval time is:

$$\Delta CS^{\tau,\tau'} = v_t^{\tau'} - v_t^{\tau'} \tag{8}$$

where τ is the baseline year of drug entry and τ' is the new year of drug entry reflective of a shortened or lengthened R&D and drug approval process. When the R&D and drug approval process is delayed so that $\tau' > \tau$, the lifetime consumer surplus generated by the drug will be lower. The opposite is, of course, true when the process is abbreviated, $\tau' < \tau$.

3.12 Estimating the model

As our methodology suggests, several pieces of information are required to estimate the impact of changes in R&D and drug approval times on consumer surplus. First, an assumption on the nature of the utility function *U(.)* is required. Second, the approach requires estimates of annual income *y*. Third, and perhaps most importantly, estimates of how survival *S* varies with the date of drug entry are required. Finally, calculating consumer surplus requires an estimate of the price of drug therapy, *p*. The following sections describe, in that order, how we incorporate each of these elements into our analysis.

3.121 Parameterizing the utility function

Following Becker, Philipson, and Soares (2005), we assume that the instantaneous utility function adopts the following form:

$$u(c) = \frac{c^{1-(1/\gamma)}}{1-(1/\gamma)} + \alpha \tag{9}$$

The parameter α is a normalization factor that determines the level of consumption at which the individual would be indifferent between being alive or dead (at which point utility equals zero), and γ is the intertemporal elasticity of substitution. Following these authors, we assume that γ = 1.25 and α = -14.97.[2] Assuming the existence of perfect annuity markets, the authors straightforwardly show that the lifetime indirect utility for an individual is given by:

$$U(S_{t,j}^{\tau}, y) = u(y)A(S_t^{\tau}) \tag{10}$$

Given expressions (4) and (10), one can show that the closed-form solution for the annual willingness to pay for the drug to enter the market in time τ is:

$$wtp_t^{\tau} = y - \left[\left(\frac{1}{1-\gamma}\right)\left(\frac{A(S_t^{\infty})}{A(S_t^{\tau})} \cdot u(y) - \alpha\right)\right]^{\gamma/(\gamma-1)} \tag{11}$$

3.122 Estimating annual full income

In order to determine the annual income applied to our model, we begin by assuming an annual monetary income of $34,600, equivalent to US GDP per capita in 2000. As discussed elsewhere (see e.g. Murphy and Topel (2006)), the relevant measure of income is *full* income,

[2] For further justification of these parameter assumptions, please see Becker, Philipson, and Soares (2005).

which incorporates the value of leisure time as well as labor market time. Following Murphy and Topel (2006), we assume that full income is equal to twice monetary income, so that y is equal to $69,200.

3.123 Estimating survival

Changes in drug discovery and approval times impact social welfare through their effects on disease survival. In our framework, understanding these welfare effects requires estimates of S_t^τ, the survival faced by a patient whose disease begins in year t and for whom treatment becomes available in year τ. We consider several diseases in our analysis: AIDS, non-Hodgkin's Lymphoma (NHL), and breast cancer. Each of these is a disease where recent therapeutic improvements have notably improved survival. In the case of AIDS, we estimate the survival impact of the introduction of highly active antiretroviral therapy (HAART) in 1996.[3] For NHL, we estimate the survival impact of the novel monoclonal antibody rituximab (Rituxan) introduced in 1998. Finally, for breast cancer, we estimate the survival impact of trastuzumab (Herceptin), a monoclonal antibody introduced in 1999 and designed for the treatment of Her-2 positive breast cancer.

In order to estimate survival curves under different drug entry times, we obtained data on observed longitudinal survival for each of these diseases. For non-Hodgkin's Lymphoma and breast cancer, we obtained longitudinal survival data for persons diagnosed between 1979 and 2004 from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database. SEER is a database of reports from 17 cancer registries, maintained by the National

[3] AIDS presents an interesting case, because the highly active antiretroviral treatment (HAART) which greatly improved survival consisted of three drugs which entered the market at different times: nucleoside analog reverse transcriptase inhibitors (NRTIs) in 1987, protease inhibitors (PIs) in 1995, and non-nucleoside analog reverse transcriptase inhibitors (NNRTIs) in 1996. Since HAART is a combination of all three drugs and the NRTIs were far lass effective than the later PIs and NNRTIs, we used the latest year of entry (1996) to define the entry of HAART.

Cancer Institute, which has tracked cancer incidence since 1973. When an individual living in an area covered by a registry is diagnosed with cancer, a report is sent to SEER describing that individual's age at diagnosis, year of diagnosis, and gender. In addition, SEER collects data about the tumor itself, including its location and stage at diagnosis. Once diagnosed, patients are (generally) actively followed up until they die or are otherwise lost to follow-up. For each patient, SEER then reports the number of years for which the patient was known to be alive, as well as the patient's status at the end of that time (death or lost to follow-up). We restricted our analysis to persons with a histologically confirmed diagnosis of breast cancer or non-Hodgkin's lymphoma. Using the SEER data, we directly calculated longitudinal Kaplan-Meier survival estimates for each cohort of non-Hodgkin's Lymphoma and breast cancer patients between 1979 and 2004. For AIDS, we used survival data reported by Philipson and Jena (2005), who estimate survival curves for AIDS by year of diagnosis using data from the US Centers for Disease Control.

With these observed survival data in hand, we estimate the effect of new drug entry by from the following regression equation:

$$S_{t,j} = \delta_1 + \delta_2 x + f_j + \delta_3 drug_{t,j} + \varepsilon_{j,t} \tag{12}$$

where $S_{t,j}$ is the probability that a patient whose disease begins in year t survives at least j years, x is a linear time trend, f_j is a fixed effect for the j^{th} year post disease, and $drug_{t,j}$ is a dummy variable which equals 1 if the drug was available in the j^{th} year after the disease began (i.e. it was available in year $t + j$). δ_3 is our coefficient of interest and represents the absolute gain in survival probability associated with the drug's introduction. It is identified by comparing the survival of patients before and after the drug's introduction, netting out any secular trends in

improved survival. We use parameter estimates from regression (12) to estimate survival rates under various drug introduction dates.

3.124 Estimating drug expenditures

Calculating consumer surplus requires an estimate of p, the expected annual expenditure on the drug in question. Specifically, p is the annual price of the drug multiplied by the probability that a person with the disease uses the drug. In the case of AIDS, for example, the estimated annual cost of HAART ranges from $10,000-$15,000 (Saag et al., 2006) and since HAART is indicated for nearly all patients with AIDS, we use $15,000 as a baseline estimate for p. In the case of breast cancer, however, the situation is more complex. While Herceptin has an annual cost ranging from $36,000-$65,00 per year, the drug is not indicated for all breast cancer patients.[4] Therefore, we used private insurance claims data to estimate average spending on Herceptin across all breast cancer patients. Our data is an extensive set of de-identified administrative insurance claims data drawn from a non-random sample of more than 50 private health plans offered by 15 employers. These data cover roughly 10.8 million beneficiary years from 1997 to 2005. For each medical and pharmacy claim in the data, detailed information exists on health plan and patient out-of-pocket spending, diagnostic codes from the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM), and procedure codes recorded under the *Current Procedural Terminology* (CPT) or *Health Care Financing Agency Common Procedure Coding System* (HCPCS). We identified breast cancer patients as those with one or more of the ICD-9-CM diagnosis codes corresponding to breast cancer. With this sample, we used the claims data to estimate an average annual total spending of $506 per

[4] Costs obtained from http://mayoclinic.com and https://cancer.net.

year for Herceptin. Using similar methods for patients with non-Hodgkin's Lymphoma, we estimate average annual total spending of $1,212 per year for Rituxan.

3.2 Impact of delays in drug discovery and approval on producer surplus

Producer surplus represents the variable profits to a firm from selling its drug, and is equal to patient expenditures minus the variable costs of production. Therefore, producer surplus is bounded from above by patient expenditures (if variables costs are zero), and from below by zero (if variable costs equal expenditures). Explicit data on the costs of drug production are generally unavailable, however, several studies (Grabowski and Vernon, 1992; Berndt, Cockburn, and Griliches, 1996) have documented the mark-up of branded drugs by examining the price reductions that follow the entry of generic competition. Overall, these studies find that marginal costs are roughly 20% of expenditures. Therefore, as a baseline estimate, we assume that producer surplus is 80% of the patient expenditure estimates outlined above.

3.3 Estimates of the impact of drug discovery and approval times on social costs

3.31 Estimates of the willingness to pay for various drug discovery and approval times

Table 3 presents the value of faster market entry of HAART for individuals with AIDS whose disease began between 1984 and 2000. As a baseline, the first column shows the value to individual cohorts of having HAART become available in 1997, with all dollar values expressed in 2008 dollars and discounted back to 1984 at a 3% rate. Consistent with earlier work by Philipson and Jena (2005), we generally find that HAART was of great value to AIDS patients—for example, persons who were diagnosed with AIDS in 1990 were willing to pay $306,720 out of their lifetime income in order to have HAART available in 1997, a figure that rises to $352,684 for persons who were diagnosed in 2000. The lifetime willingness-to-pay for HAART

rises with subsequent cohorts, as individuals diagnosed with AIDS closer to 1997 spent fewer years without HAART and therefore experienced larger survival gains. For cohorts diagnosed after 1997, HAART was already available, so there is no additional impact on survival with subsequent cohorts; however, lifetime willingness-to-pay falls slightly with cohorts due to discounting.

The remaining columns in Table 3 show the change in the willingness to pay for HAART associated with delayed and accelerated entry into the market. For example, individuals diagnosed with AIDS in 1990 would be willing to pay an additional $18,395 (5.9%) for HAART to enter the market a year earlier (i.e in 1996), and would similarly need to be compensated $18,366 (4.9%) for HAART to enter the market a year later (i.e. in 1998). Note that individuals diagnosed with AIDS after 1996 would be unwilling to pay any amount for earlier entry of HAART, since earlier entry would not affect the availability of the treatment for these cohorts. Similarly, individuals diagnosed with AIDS in 2000 would be unaffected by delays up to three years long. In general, we find that the lifetime willingness to pay for a one-year accelerated entry ranges from $14,675-$32,282 for affected cohorts (roughly 4-24% of baseline willingness to pay), while the lifetime WTP for introduction three years earlier ranges from $14,675-$94,981 for affected cohorts (4-69% of baseline willingness to pay). Not surprisingly, earlier cohorts are willing to pay more for the introduction of HAART, given that they spend more years without the treatment to begin with.

[INSERT TABLE 2 HERE]

Tables 4 and 5 present similar estimates for non-Hodgkin's Lymphoma (NHL) and breast cancer. Although the baseline willingness to pay for survival improvements in these cases is different than in the case of AIDS, we find that earlier drug introduction generates roughly

similar proportionate gains in patient willingness to pay. In the case of NHL, an earlier introduction of Rituxan by one year would have raised willingness to pay by $971-$1,579 (6-14%), while earlier introduction by three years would have raised willingness to pay by $971-$4,873 (6-43%). For breast cancer, earlier introduction of Herceptin by one year would have increased willingness to pay by $2,737-$4,602 (5-15%), while introduction three year earlier would have raised willingness to pay by $2,737-$14,189 (5-46%). Overall then, we find for these three classes of treatments, earlier introduction would be highly valued by patients and delayed introduction would be quite costly.

[INSERT TABLE 4 HERE]

[INSERT TABLE 5 HERE]

3.32 Estimates of the impact of drug discovery and approval times on lifetime expenditures

Although in the case of successful drugs, patients highly value earlier entry, earlier availability also increases their expected spending. This is illustrated for AIDS in Table 6. Not surprisingly, earlier introduction of the drug has a large impact on costs. For example, individuals diagnosed with AIDS in 1990 were expected to spend $21,874 on HAART over their lifetime. Had HAART entered the market one year earlier, our estimates suggest that these costs would have increased by $5,806. Moreover, lifetime costs would have increased by $19,663 if HAART entered the market three year earlier. As was true for the willingness-to-pay, lifetime costs for cohorts diagnosed with AIDS after 1996 would be unaffected by earlier entry. Tables 7 and 8 show equivalent patterns associated with earlier introduction of drugs for NHL and breast cancer, respectively. Patients diagnosed with NHL in 1990 were expected to pay $3,887 on Rituxan over their lifetime, a number which increased by $527 ($1,781) with earlier introduction

on one (three) years. Similarly, in the case of breast cancer, earlier introduction of Herceptin by one (three) year would have increased lifetime expenditures by $346 ($1,132), from a baseline level of $2,652 for patients diagnosed with the disease in 1990.

[INSERT TABLE 6 HERE]

[INSERT TABLE 7 HERE]

[INSERT TABLE 8 HERE]

3.32 Estimates of the impact of drug discovery and approval times on consumer, producer, and social surplus

In the previous sections, we demonstrated that faster market entry can be highly valuable to patients and can raise lifetime costs significantly, the former effect outweighing the latter. We now discuss the effect market entry on aggregate consumer and producer surplus. We then relate these quantities to the direct R&D costs associated with expedited or delayed drug entry times. To calculate aggregate consumer surplus, we simply subtract the increased (decreased) lifetime costs due to earlier (later) market entry from the increased (decreased) lifetime willingness to pay. This delivers the increase (decrease) in consumer surplus due to earlier (later) market entry for an individual patient. We then multiply this value by the incidence of patients in each cohort (shown in Table 9), and sum across all cohorts to obtain the change in aggregate consumer surplus associated with earlier (or later drug) entry. As discussed earlier, we estimate producer surplus by assuming that it equals 80% of patient spending.

[INSERT TABLE 9 HERE]

Figure 3 shows our results. In the case of AIDS, we estimate the baseline aggregate consumer (producer) surplus from the introduction of HAART to be 364 ($38) billion. Earlier entry of HAART by one year would have increased consumer surplus by $19 billion (5.2% increase), while earlier entry by 3 years would have increased consumer surplus by $53 billion (14.5% increase). Earlier entry has larger effects on producer surplus in relative, but not absolute, terms, with earlier entry by one year raising producer surplus by $4 billion (9.1%) and earlier entry by three years raising producer surplus by $14 billion (37%).

[INSERT FIGURE 2 HERE]

In the case of NHL, we estimate that the entry of Rituxan in 1998 increased consumer surplus by $12 billion and producer surplus by $4 billion. Earlier entry by one year would have increased consumer and producer surplus by $310 million and $330 million respectively (2.5% and 7.8% increase, respectively), and earlier entry by three years would have increased consumer and producer surplus by $850 million and $950 million respectively (7.2% increase and 22.6% increase, respectively). The introduction of Herceptin in 1999 increased consumer surplus by $149 billion and producer surplus by $12 billion. Earlier entry by one year would have increased consumer surplus by $8 billion (5.2%) and earlier entry by three years would have increased consumer surplus by $22 billion (15% increase). Conversely, producer surplus would have increased by $1 billion (7.8%) with earlier entry by one year and $3 billion (23%) with earlier entry by three years.

In sum, our analysis suggests that earlier or delayed drug introduction has sizeable effects on consumer surplus and producer surplus. In absolute terms, gains in consumer surplus tend to be larger than gains in producer surplus, although the latter are larger in relative terms. In general, the changes in producer and consumer surplus measure in the billions to tens of billions

even for one year changes in the date of entry. By contrast, as shown in table 2, the changes in R&D costs are roughly $40 million. Thus, the social costs of changes in the introduction date far outweigh any changes in R&D costs.

4. Conclusion

Existing methods to measure the costs of medical R&D rely on data from the costs of specific development phases as well as the probabilities of entering those phases. Those methods attempt to provide how much costs would be reduced by a more streamlined R&D and drug approval process. In this paper, we argue these measures are incomplete and revisit the discussion on costs of medical R&D by incorporating the full social costs associated with delays in the process. When drugs are ultimately successful but faced delays in market entry, these costs occur in two major forms: forgone profits to producers and forgone consumer surplus to patients. For example, pushing out phase III expenses further in the future would lower the present value of R&D at the start of innovation spending but clearly be socially costly. We provided a framework to quantity the full social costs of delay.

Our empirical analysis of three disease classes – AIDS, non-Hodgkins lymphoma, and Her-2 positive breast cancer – suggests that incorporating the full social cost of delays in the R&D and drug approval process has important consequences for understanding the costs of delays in this process. In particular, we find that the social costs from forgone profits and foregone consumer surplus vastly outweigh the added R&D costs that a lengthened R&D and drug approval process may entail. Our analysis, of course, has several limitations. First, an implicit but important assumption in our empirical analysis is that earlier market entry leads to drugs whose benefits still outweigh any potential side-effects. While this was true for the three cases we considered, it may not be true a priori. However, two points should be made. First, as

discussed in the introduction, evidence from the impact of PDUFA suggests that at least recently, the benefit of faster approval has outweighed any change in drug safety. Second, in the case of unsafe drugs, our basic methodology and point remain the same, but are reversed, as in this case, the social *costs* due to earlier adoption

Second, our analysis neglects the impact that faster or delayed approval may have on social welfare through its effect on innovation. Because earlier entry induces greater lifetime profits, firms may have greater incentives to innovate in response to these higher lifetime profits. In this case, prolonged R&D and drug approval times would have the additional social cost of limiting innovation, making our estimated effects too low. Indeed, Olson (2009) find that the Prescription Drug User Fee Acts (PDUFA), which shortened drug review times, lead to more fist drug launches in the US market, suggesting that the dynamic effects of a shorter R&D process may be significant. Third, our analysis assumes that all drugs follow roughly the same R&D process and heterogeneity across drug classes into account. Adams and Bantner (2003) find some evidence that certain drug classes, such as HIV drugs, tend to come to market more quickly, and further analysis could take account of this heterogeneity. Finally, further analysis could take into account the effects of earlier drug adoption on quality of life, in addition to survival.

Our overall point is that a better quantitative understanding of the social costs of drug regulation is needed. The framework developed here can easily be applied to other diseases to obtain such an understanding, and should ultimately guide policy on the value of the process.

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TABLE 3 – Consumer willingness to pay for various drug approval times, AIDS

Cohort	WTP in Base Year ($)	Change in willingness to pay ($)					
		Acceleration (Years)			Delay (Years)		
		3	2	1	1	2	3
1984	138,234	94,981	63,923	32,282	-32,982	-63,433	-88,092
1985	180,394	84,364	56,616	28,508	-28,948	-58,376	-88,324
1986	218,709	77,419	51,837	26,041	-26,316	-52,935	-79,888
1987	250,126	71,115	47,528	23,831	-23,987	-48,153	-72,518
1988	274,288	65,136	43,465	21,759	-21,830	-43,748	-65,771
1989	293,507	60,087	40,046	20,022	-20,034	-40,093	-60,191
1990	306,720	55,323	36,832	18,395	-18,366	-36,713	-55,053
1991	316,830	52,172	34,710	17,323	-17,269	-34,495	-51,685
1992	324,808	50,359	33,491	16,708	-16,642	-33,226	-49,762
1993	334,268	48,863	32,485	16,200	-16,124	-32,179	-48,174
1994	343,101	47,360	31,475	15,692	-15,607	-31,136	-46,593
1995	351,284	30,464	30,464	15,183	-15,091	-30,096	-45,022
1996	358,791	14,675	14,675	14,675	-14,577	-29,063	-43,462
1997	368,501	0	0	0	-14,175	-28,252	-42,238
1998	366,512	0	0	0	0	-13,780	-27,463
1999	361,261	0	0	0	0	0	-13,276
2000	352,684	0	0	0	0	0	0

Note: All values are in year 2008 dollars and discounted to 1984 at a 3% interest rate.

TABLE 4 – Consumer willingness to pay for various drug approval times, NHL

Cohort	WTP in Base Year ($)	Change in willingness to pay ($)					
		Acceleration (Years)			Delay (Years)		
		3	2	1	1	2	3
1984	11,839	4,873	3,203	1,579	-1,535	-3,026	-4,476
1985	12,415	4,690	3,082	1,519	-1,477	-2,913	-4,309
1986	13,161	4,584	3,013	1,485	-1,444	-2,847	-4,211
1987	13,735	4,428	2,910	1,435	-1,395	-2,750	-4,068
1988	14,103	4,222	2,775	1,368	-1,330	-2,623	-3,879
1989	14,406	4,017	2,640	1,302	-1,265	-2,496	-3,691
1990	14,545	3,788	2,490	1,227	-1,193	-2,354	-3,481
1991	14,805	3,610	2,373	1,170	-1,137	-2,243	-3,318
1992	15,218	3,482	2,289	1,128	-1,097	-2,164	-3,201
1993	15,708	3,379	2,221	1,095	-1,065	-2,100	-3,107
1994	16,170	3,277	2,154	1,062	-1,032	-2,036	-3,013
1995	16,604	3,175	2,087	1,029	-1,000	-1,973	-2,919
1996	17,008	2,020	2,020	996	-968	-1,910	-2,826
1997	17,522	971	971	971	-944	-1,862	-2,755
1998	18,168	0	0	0	-928	-1,830	-2,707
1999	17,722	0	0	0	0	-879	-1,733
2000	17,127	0	0	0	0	0	-825

Note: All $ values are in year 2008 dollars and discounted to 1984 at a 3% interest rate.

TABLE 5 – Consumer willingness to pay for various approval times, Breast Cancer

Cohort	WTP in Base Year ($)	Change in willingness to pay ($)					
		Acceleration (Years)			Delay (Years)		
		3	2	1	1	2	3
1984	31,718	14,189	9,330	4,602	-4,479	-8,836	-13,076
1985	33,414	13,643	8,972	4,425	-4,306	-8,497	-12,574
1986	35,560	13,320	8,759	4,321	-4,204	-8,296	-12,277
1987	37,238	12,852	8,451	4,169	-4,057	-8,005	-11,848
1988	38,345	12,241	8,050	3,971	-3,865	-7,626	-11,286
1989	39,267	11,634	7,652	3,774	-3,674	-7,249	-10,728
1990	39,734	10,960	7,208	3,556	-3,461	-6,830	-10,108
1991	40,520	10,434	6,862	3,385	-3,295	-6,502	-9,624
1992	41,720	10,052	6,611	3,261	-3,175	-6,266	-9,274
1993	43,123	9,744	6,409	3,162	-3,078	-6,074	-8,990
1994	44,447	9,437	6,207	3,062	-2,981	-5,883	-8,709
1995	45,689	9,131	6,006	2,963	-2,885	-5,694	-8,428
1996	46,845	8,828	5,807	2,865	-2,790	-5,505	-8,149
1997	48,300	5,654	5,654	2,790	-2,716	-5,361	-7,936
1998	50,113	2,737	2,737	2,737	-2,665	-5,261	-7,788
1999	51,478	0	0	0	-2,593	-5,118	-7,576
2000	49,463	0	0	0	0	-2,150	-4,520

Note: All $ values are in year 2008 dollars and discounted to 1984 at a 3% interest rate.

TABLE 6 – Lifetime drug expenditures by approval time, AIDS

Cohort	Expenditures in Base Year ($)	Change in willingness to pay ($)					
		Acceleration (Years)			Delay (Years)		
		3	2	1	1	2	3
1984	731	6,409	3,546	1,431	-817	-1,074	-1,074
1985	2,284	9,060	5,289	2,289	-1,639	-2,693	-3,214
1986	4,802	11,741	7,050	3,154	-2,469	-4,311	-5,588
1987	8,128	14,186	8,672	3,957	-3,250	-5,847	-7,846
1988	12,102	16,281	10,077	4,662	-3,950	-7,235	-9,905
1989	16,776	18,131	11,325	5,292	-4,586	-8,503	-11,795
1990	21,874	19,663	12,332	5,806	-5,117	-9,576	-13,413
1991	28,138	21,489	13,373	6,309	-5,632	-10,617	-14,983
1992	35,772	24,482	14,746	6,875	-6,158	-11,673	-16,573
1993	44,128	29,464	17,109	7,670	-6,721	-12,758	-18,181
1994	53,193	37,225	21,041	9,140	-7,462	-14,021	-19,927
1995	63,575	26,730	26,730	11,451	-8,838	-16,086	-22,475
1996	76,066	14,413	14,413	14,413	-11,005	-19,540	-26,568
1997	91,812	0	0	0	-13,687	-24,331	-32,623
1998	94,110	0	0	0	0	-13,090	-23,454
1999	95,556	0	0	0	0	0	-12,420
2000	96,067	0	0	0	0	0	0

Note: All $ values are in year 2008 dollars and discounted to 1984 at a 3% interest rate.

TABLE 7 – Lifetime drug expenditures by approval time, NHL

Cohort	Expenditures in Base Year ($)	Change in willingness to pay ($)					
		Acceleration (Years)			Delay (Years)		
		3	2	1	1	2	3
1984	2,391	1,338	848	404	-367	-701	-1,006
1985	2,614	1,400	887	422	-384	-734	-1,052
1986	2,892	1,488	942	448	-406	-777	-1,115
1987	3,158	1,568	990	470	-426	-814	-1,167
1988	3,402	1,638	1,032	488	-442	-843	-1,207
1989	3,653	1,713	1,077	509	-458	-872	-1,249
1990	3,887	1,781	1,118	527	-473	-898	-1,284
1991	4,176	1,873	1,174	553	-494	-938	-1,338
1992	4,535	1,996	1,249	588	-524	-993	-1,413
1993	4,954	2,152	1,340	629	-560	-1,059	-1,505
1994	5,409	2,368	1,446	675	-598	-1,131	-1,606
1995	5,905	2,830	1,605	731	-641	-1,210	-1,716
1996	6,451	1,983	1,983	828	-693	-1,302	-1,841
1997	7,138	1,097	1,097	1,097	-790	-1,452	-2,033
1998	8,145	0	0	0	-1,049	-1,808	-2,444
1999	8,023	0	0	0	0	-995	-1,718
2000	7,835	0	0	0	0	0	-936

Note: All $ values are in year 2008 dollars and discounted to 1984 at a 3% interest rate.

TABLE 8 – Lifetime drug expenditures by approval time, breast cancer

Cohort	WTP in Base Year ($)	Change in willingness to pay ($)					
		Acceleration (Years)			Delay (Years)		
		3	2	1	1	2	3
1984	1,712	982	627	300	-275	-527	-758
1985	1,859	1,010	645	309	-284	-544	-783
1986	2,042	1,054	672	322	-296	-568	-818
1987	2,213	1,087	694	332	-305	-586	-844
1988	2,364	1,107	706	338	-311	-597	-860
1989	2,516	1,124	718	344	-316	-607	-874
1990	2,651	1,132	722	346	-318	-611	-880
1991	2,816	1,152	735	352	-324	-621	-895
1992	3,019	1,188	756	362	-332	-638	-920
1993	3,251	1,233	784	375	-344	-660	-951
1994	3,495	1,282	814	389	-356	-682	-982
1995	3,750	1,332	847	403	-368	-706	-1,016
1996	4,019	1,365	879	420	-382	-731	-1,051
1997	4,334	900	900	438	-400	-764	-1,097
1998	4,705	442	442	442	-420	-804	-1,154
1999	5,045	0	0	0	-419	-819	-1,185
2000	4,916	0	0	0	0	-394	-772

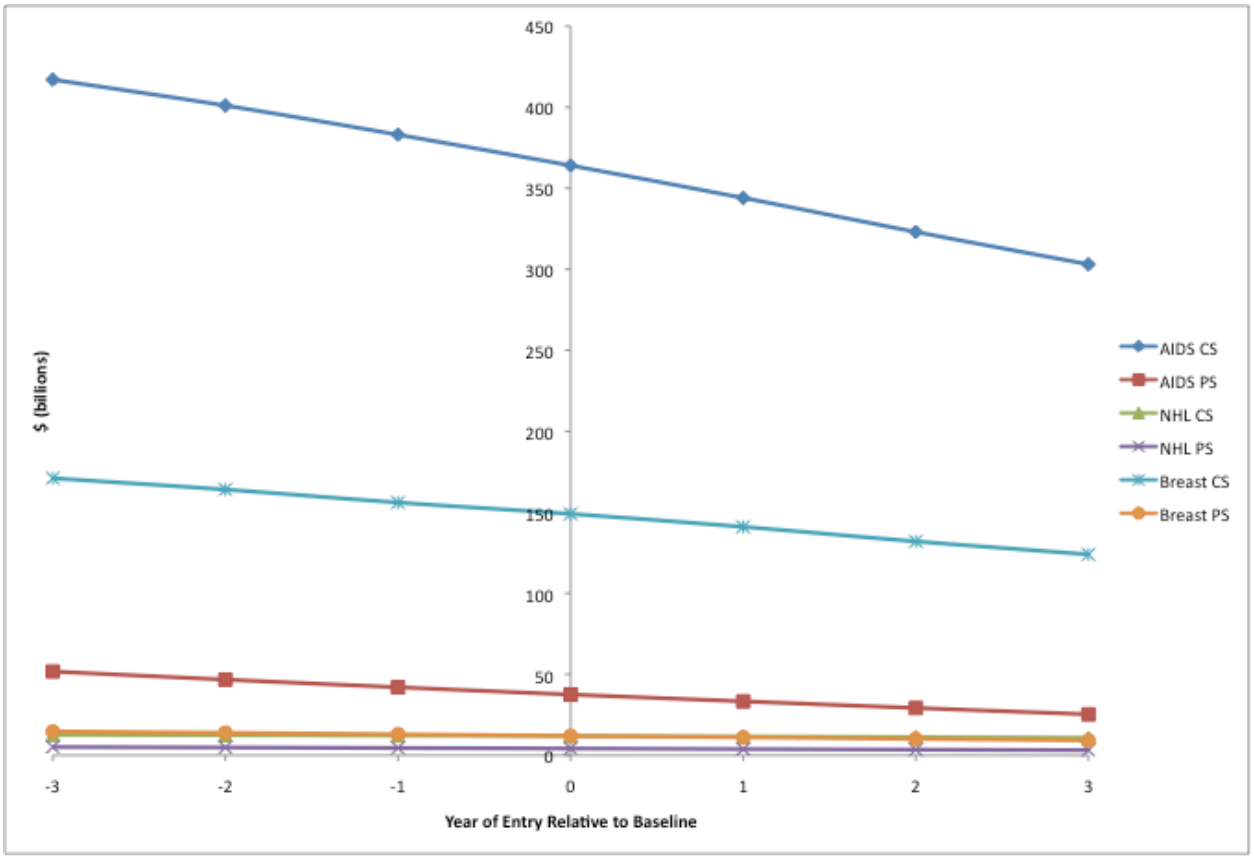
Note: All $ values are in year 2008 dollars and discounted to 1984 at a 3% interest rate.

TABLE 9 – Incidence of AIDS, NHL, and breast cancer, 1990-2000

Year	Incidence		
	AIDS	NHL	Breast cancer
1984	160,000	29,242	131,211
1985	160,000	30,692	142,479
1986	140,000	30,977	148,168
1987	120,000	32,225	159,886
1988	80,000	33,985	158,147
1989	50,000	34,061	155,141
1990	40,000	37,194	162,956
1991	40,000	37,188	168,045
1992	40,000	38,734	169,203
1993	40,000	39,508	168,445
1994	40,000	42,100	173,273
1995	40,000	41,806	178,651
1996	40,000	42,564	182,440
1997	40,000	45,805	191,781
1998	40,000	47,447	200,110
1999	40,000	46,600	203,257
2000	40,000	47,126	199,490

Source: AIDS-Philipson and Jena (2006); NHL and Breast Cancer—SEER data

FIGURE 3 – Effect of Earlier Drug Entry on Producer and Consumer Surplus



Notes: All dollar values are in 2008 US dollars, discounted to 1984 at a 3% rate. Baseline year of entry for HAART (AIDS) is 1997, for Rituxan (NHL) 1998, and for Herceptin (breast cancer) 1999.