

SETTING PRICES FOR NEW VACCINES (IN ADVANCE)

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1. Introduction

Vaccines differ from conventional pharmaceutical products in several respects important for regulation of their pricing and procurement.

- The effect and value of a vaccine is specific and potentially quantifiable, even before the vaccine is developed. An Institute of Medicine (IOM) panel has estimated that a completely effective and fully implemented vaccine against *Streptococcus pneumoniae* would lead to annualized present value of health care cost savings of \$1.6b and an annualized gain of 265,000 Quality Adjusted Life Years (QALYs). Cost savings and QALY gains have been estimated using a common framework for 26 candidate vaccines (Stratton, Durch and Lawrence, 2000). Such *ex ante* calculations are not possible for other drugs.
- The federal government runs the market for vaccine purchasing. The federal and state governments set quantity demanded by requiring that all children be vaccinated. Furthermore, more than half of all childhood vaccines are dispensed through public programs and purchased on terms negotiated by the Centers for Disease Control (CDC). For other pharmaceuticals, quantity demanded emerges in a market, and the federal government has much less effect on average price paid to suppliers.
- Vaccines are biologic agents, not inert chemicals. Storage is costly and time-limited. Adjustment of productive capacity is slow, costly and governed by regulation. Production is characterized by economies of scale and is subject to large-scale errors (batch failures). Running up against a fixed quantity demanded, these production-side factors lead to short-term shortages and price spikes.

This paper draws some implications of these features of vaccines for social policy toward vaccine procurement. In particular, this paper proposes, largely on the basis of the first two points just noted, a policy of setting the real price for a new vaccine prior to development of the vaccine. Some background material is presented in Section 2. The prominence of the federal government in purchasing and the special costs of adjustment and short-term production risks have previously noted and will not be extensively discussed.¹ National and state vaccine policy in the U.S., and general features of the pharmaceutical industry are also not reviewed here except insofar as they bear directly on the arguments related to price setting.² The first bullet point identified above, the potential for inferring the value of a vaccine prior to its development for purposes of price setting, will be given more consideration.

¹ For example, Schwartz and Orenstein (2001), Mercer Management Consulting (1995), Arnould and DeBrock (2002).

² Excellent reviews are contained in IOM (2000) and Scherer (2000).

Section 3 characterizes the optimal price for a new vaccine using economic theory.³ There is a fundamental difference between the optimal price for mandatory vaccines, such as childhood vaccines, and for other pharmaceuticals. Because government requires vaccine purchase on the private side and subsidizes price to indigent groups on the public side, a high price paid to suppliers does not create short-term inefficiencies in distribution as it does for other drugs. Rather than a condition on price that involves demand response, the optimal price for a vaccine depends on the average benefit of a vaccine, and (depending on how “optimal” is defined, from the point of view of society or the point of view of purchasers) on the response of investment in R&D to price. The main argument in favor of an administered price set in advance is to ensure adequate incentives to invest in research on vaccine development. Arguments in favor of a preset price are similar to those made by Kremer (2000a, 2000b) and others who have advocated “purchase commitments” for vaccines in developing countries to be supported by the international community.⁴

Section 4 considers the key empirical issue raised by the price analysis in Section 3: is it feasible to quantify, in advance and for purposes of price setting, the benefits of a new vaccine? A recent study of the costs and benefits of vaccines against 26 diseases sponsored by the Institute of Medicine (IOM) is used as a basis for illustrative calculations of administered prices.

Section 5 makes some further comments on the practical concerns and policy implications of setting an administered price for vaccines. Section 6 contains comments on procurement of existing vaccines. Section 7 contains a concluding discussion.

2. Background

The tradeoff between incentives to innovate in the pharmaceutical industry and short-term fairness and efficiency in drug production and distribution is one of the most important matters for health policy. Once discovered, chemicals or vaccine production processes are easily imitated by new firms, with a consequence that unregulated competition would push price toward short-run production costs, minimizing reward for investing in discovery of new drugs.⁵ Patent protection confers on the innovator a time-limited monopoly during which the firm can set price essentially without further government restriction at very high markups above production costs. The profit-maximizing firm limits price because of the reduction in demand caused by high prices, leaving many potential users of the drug, sometimes including large groups of patients in

³ For relevant related literature, see Laffont (1994). There are interesting parallels to defense contracting issues discussed in Rogerson (1994).

⁴ In his analysis of the international market for vaccines, Kremer concludes (2000a, p 23): “The huge disparities between private incentives to invest in research and development and the social benefits of vaccines suggests that research investment will be far too little in the absence of public support.”

⁵ This argument applies but with less force to vaccines and other biologic agents where imitation is not as easy as with inert chemicals. For instance, Merck has been able to maintain a price premium for its vaccine against MMR because of the superior quality of its strain, even though this vaccine is no longer protected by patent.

publicly funded programs in the U.S., without access to new treatments.⁶ High margins above production cost foreclose the market in entire countries with low purchasing power (Kremer, 2000a). There can be no doubt that patent-protected prices create inequities and inefficiencies associated with patients who would pay production cost or more, but do not get the drug.

Two pillars support the countervailing argument: anticipated profits drive innovation (Grabowski and Vernon, (2000); Scherer, (2001); see Finklestein (2002) for evidence in the case of vaccine R&D), and new drugs improve the quality of life and in some cases substitute for more expensive treatments (Berndt et al. (2002); Cutler et al., (2001); Lichtenberg (1996)). Eroding patent protection or taking other steps to lower price to increase access today cuts into the flow of innovative drugs tomorrow. The pharmaceutical industry spends about \$1.1 billion on R&D on “biologicals” (mostly vaccines) each year. While this is a small part of the total R&D investment, about 4% (PhRMA, 2001), it is larger than the share of vaccines in total revenue. Finkelstein (2002) concludes that the time lag between initiation of successful clinical trials of vaccines and licensure are about the same (6-8 years) as for other drugs, and that the success rate of clinical trials is somewhat higher.⁷

Regulation of pricing and procurement of vaccines must also pay attention to incentives to innovate in vaccines. Regulations founded on patent protection for other drugs may not be the right basis for a solution since the market for vaccines works differently. About half of childhood vaccines are sold to private buyers and half to the federal government buying through the CDC. Patents do not have the same implications for pricing in either side of the market as they do for “normal” drugs. First, on the private side, once a new vaccine is licensed by the FDA and recommended by the Advisory Committee on Immunization Practices (ACIP) of the CDC, state laws requiring students be up-to-date on vaccinations for school enrollment enforce vaccinations (Freed, Clark and Cowan, 2000).⁸ Parents and/or their insurance plan essentially must buy vaccinations for the child. As far as private buyers are concerned then, governments lay down an “unfunded mandate” to purchase vaccines and demand elasticity cannot play its usual role in limiting price and markups to private buyers.⁹ Second, on the public side, vaccine suppliers face off with the CDC, a monopsonistic buyer with political as well as economic power. Negotiating on behalf of state as well as federal purchasers, the CDC is in the conflicted position of being responsible for promoting development of methods to fight disease, but also responsible for keeping purchase price as low as possible. The CDC has used its bargaining power to “insist” on discounts for new vaccines (Miller,

⁶ Demand reduction would occur for patients with insurance as well, either because of partial insurance coverage, or because of tactics used by managed care plans (such as formularies) that lead to a demand response from the point of view of the manufacturer.

⁷ Struck (1996) reporting on trials between 1983 and 1994 finds a 39% success rate.

⁸ All 50 states and Puerto Rico require vaccination before school enrollment, but the specific requirements are not nationally uniform.

⁹ Private buyers are put in an unfavorable position by being forced to buy from a monopolist or more generally from firms with market power as would exist if there were few suppliers. Political and social pressure probably contribute to keeping prices from going higher than they are.

2002), and in the case of “old” vaccines, has administratively set maximum prices it will pay.

There can be no assurance that the sum of the pricing to the private sector plus the pricing to the public sector gives innovators the right market signals to develop new vaccines. Some observers go further to argue that the incentives to invest in vaccine development (and production capacity) determined by present pricing policies are clearly inadequate (Miller, 2002; Rappuoli, Miller and Falkow (2002)). The main argument is that the social value of vaccine development is very high in relation to the cost, and policies that reduce profits to vaccine supply are shortsighted.

Public policies bearing on current prices paid for vaccines influence investment in new vaccines insofar as they affect firms’ expectations about profits through prices that would be paid in the future for vaccines under development.¹⁰ If the CDC can commit to policies for prices for new vaccines, then actions that keep prices low for currently available vaccines (such as the administered prices for old vaccines) will have no effect on investment.

Against this background we can say that the price for a vaccine serves two main purposes. The first is to reward the innovator firm. This reward spurs investment in R&D. The second is to determine the division of net benefits from the vaccine once it has been developed. The lower the price paid for the vaccine, the greater is the share of net benefits enjoyed by buyers/users. Considerations in setting the optimal price for the vaccine therefore have to do with how a price affects incentives to invest in research and how a price divides the net benefits of the vaccine between the seller and the buyers.

Since a high price paid to sellers does not choke off demand, the “usual” tradeoff in this literature (Tandon, 1982) does not apply. As Pauly and Cleff (1996, p.19) put it: “The relevant price elasticity in judging whether the distortions due to high current prices exceed or fall short of the benefits of research should primarily focus on the effect of high prices on *public* [their emphasis] demand.” Whether the public sector buys less if price is high is itself a matter of public policy choice. In what follows, I assume that once a vaccine is licensed by the FDA and recommended by the CDC, the public sector buys it, and further that it is required to be purchased by private users as well. The assumptions and the analysis here fit best cases of mandatory vaccines for children. Adult vaccines are subject to some demand response to higher prices.

3. The Optimal Price for a New Vaccine

3.1. The Efficient Level of R&D

¹⁰ This statement implicitly discounts a “cash flow” argument connecting current prices and investment. Even if the firm cash-flow argument matters in the aggregate for drugs, overall cash flow of vaccine manufacturers is largely determined by profits on other drugs, not vaccines.

As a benchmark, we define the efficient level of R&D. The efficient level of spending on R&D maximizes the expected net benefits accruing from the activity.

Notation

b	average per person benefit of eliminating the disease
x	per person expenditure on R&D
q(x)	the probability of successful discovery of a vaccine
c	marginal production cost
p	price of the vaccine

Because the results of R&D spending are uncertain, the efficiency of the investment must be judged *ex ante* based on the expected benefits and costs. Expected net benefits of R&D can be defined as:

$$\text{Expected net benefit} = q(x)[b - c] - x. \quad (1)$$

The efficient level of investment in R&D is the x that maximizes expression (1), referred to as x^* . (Mathematical analysis of efficient research and pricing is presented in an Appendix.) This formulation embodies several notable assumptions. First, the vaccine, once discovered, is completely successful in eliminating risk of disease. This assumption is relatively easy to modify in the case of therapeutic vaccines (such as for multiple sclerosis or diabetes mellitus). It is more complicated to modify when the risk of transmission is affected by the percent of the population effectively immunized (Philipson, 2000). Second, the timing of benefits and costs can be collapsed into a single period. R&D investments occur over time and prior to the flow of benefits. The dollar values of b and x can be thought of as present discounted value, but this only deals with one of the implications of the single-period representation. Uncertainty about the likely success of the research effort changes over time, affecting the efficient flow of investment. Third, research is typically undertaken by more than one firm or organization. Resources represented by x can be understood to be efficiently divided among organizations (to maximize $q(x)$ for any x). The issue of competing firms becomes important when we consider inducing investment through a market. The analysis conducted here is put forward as a starting point.

With the efficient level of R&D defined as a benchmark, we now turn to what level of investment would be supplied by a firm and how this is affected by the price for the vaccine. We regard the price p for the vaccine as being set by policy. In other words, in deciding about the level of investment, the firm takes the price as given. The efficient price could be approached from two perspectives, represented here by two alternative criteria. The first criterion relates to social efficiency, and the second to the welfare of the buyers alone. The difference between the two is that the first criterion values profits of suppliers, and the second does not.

3.2. Criterion 1: The Price that Induces a Profit Maximizing Firm to Choose the Socially Efficient Level of R&D

In profit maximization, a risk-neutral firm will choose level of R&D to maximize expected profits:

$$\text{Expected profits} = q(x)[p - c] - x. \quad (2)$$

Finding the price to satisfy Criterion 1 is straightforward. The firm's choice of x to maximize profits would be identical to the social objective of choosing x to maximize net social benefit if $p = b$. Therefore, to satisfy Criterion 1, the efficient price for a vaccine is equal to the average benefit from the vaccine.¹¹

Note that the relevant benefit is the average not marginal benefit. Note also that the efficient price is equal to the benefit not the net benefit of the vaccine. To set the efficient price according to Criterion 1, the social planner does not need to know production cost, does not need to know the technology of research and development, and does not need to know the relation between marginal and average benefits of vaccinations.

While setting price equal to average benefit is a straightforward implication of Criterion 1 for socially efficiency, it has a major drawback. Setting $p=b$ achieves efficiency by transferring all net social benefits to the supplier. Efficient investment is achieved by internalizing all benefits and costs within the firm. Purchasers, paying a price equal to average benefit, are no better off with the vaccine than without. In terms of the second function of price noted above, by fulfilling Criterion 1, setting $p = b$ leaves nothing for the consumers. Figure 1a graphs the relevant functions. Consumer surplus can be defined as the difference between the average benefit of the vaccine and the price paid: $b - p$. Setting $p = b$ induces the firm to invest amount x^* and leads to the maximum value of expected net benefit. All of this expected net benefit appears as profits, none as consumer surplus.¹²

This condition could be generalized to multiple countries. If world-wide benefits were considered, a new vaccine would benefit users outside the U.S., and the producer of the vaccine would gain some profits from foreign sales. For world-wide efficiency, a form of "Lindahl solution" for paying for the public good of vaccine R&D would require each country to set the price it would pay to its average social benefit.¹³ In terms of Criterion 1, for any foreign price policy (the efficient one or otherwise), the U.S. could take the foreign prices as given and set its own price to maximize efficiency in the U.S. market alone. In this case, foreign profits would be like a subsidy to R&D, and the efficient U.S.

¹¹ Considerations introduced by taxes are ignored.

¹² Two-part tariffs can often be used to pose correct incentives to a supplier at the margin, while using the first-part price to transfer funds towards or away from the supplier. In this case, however, two-part tariffs would not help because it is the average profit per person that is being used to structure incentives.

¹³ In Kremer's (2000a) analysis, international organizations would mobilize willingness to pay of the many small countries buying vaccines.

price would be reduced in proportion to the subsidy, and some consumer surplus would appear in the U.S. market.¹⁴

3.3. Criterion 2: Optimal Price from the Purchasers' Point of View

An alternative criterion, frequently applied in policy analysis, is the welfare of buyers only. Stratton, Durch and Lawrence (2000), for example, evaluate vaccines in development from the point of view of buyers, ignoring profits as part of social benefits. In this section, we find the price that maximizes the welfare of the buyers. Expected net benefit to purchasers of investment level x in vaccine R&D can be referred to as expected consumer surplus (cs):

$$cs = q(x)[b - p] \quad (3)$$

Expected consumer surplus is equal to the difference between the benefits and price of the vaccine, times the likelihood the vaccine is discovered. Note that consumer surplus does not depend directly on production cost of the vaccine or on the cost of the R&D itself, but only on the benefits of the vaccine, the price paid, and the likelihood of the vaccine being available. The tradeoff in setting a price is evident in (3). To increase $[b - p]$, price must be lowered. But a lower price will lead to lower x , and therefore a reduced chance that the vaccine is available.

Choosing a price to maximize (3) must be done with recognition that the firm will be profit maximizing in choice of x . Maximizing expected profit (2) with respect to x yields the following condition for profit maximization:

$$q'(x)[p - c] - 1 = 0, \quad (4)$$

where q' is dq/dx . The problem in applying Criterion 2 is to find the price that maximizes consumer surplus (3) subject to firm profit maximization (4). This is a form of principal-agent problem, and is solved formally in the appendix. Characteristics of the $q(x)$ function, i.e., the relationship between inputs into R&D and the likelihood of finding the vaccine, enter into the solution.

Figure 1b depicts the solution to consumer surplus maximization (Criterion 2) and compares it to the solution for social welfare maximization shown in Figure 1a (Criterion 1). At x^* in Figure 1a, social welfare is maximized, but social surplus appears all as expected profit; expected consumer surplus is zero. In Figure 1a, since $p = b$, expected social benefit $q(x)[b - c]$ is identical to firm expected net revenue. Criterion 2 is used to choose investment in Figure 1b, where x^{**} maximizes $q(x)[b - p]$. In Figure 1b, $p < b$, so the firm's expected net revenue falls as p is reduced below b . This opens a gap between $q(x)b$ and $q(x)p$, creating consumer surplus, but the reduction in the firm's net revenue function pulls the profit-maximizing x downward, reducing total social surplus.

¹⁴ If f is foreign profit per U.S. consumer, then to make expected profit coincide with expected social benefit in the U.S., b must be equal to $p + f$, or $p = b - f$.

The shapes of the expected benefit, revenue and cost lines, and ultimately the solutions for the p and x that maximize consumer surplus, are governed by how $q(x)$, the likely success of research, depends on the level of investment. The appendix derives expressions for these relations and analyzes a range of cases for the shape of $q(x)$. The analysis leads to an expression for the optimal division of surplus between consumers and producers at the price that maximizes consumer net benefit:

$$\frac{b-p}{p-c} = \frac{\text{consumer net benefit}}{\text{operating profit}} = \frac{-qq''}{(q')^2} \quad (5)$$

where q' and q'' are the first and second derivatives of the probability of discovery as a function of the level of R&D expenditures. Condition (5) says that the ratio of consumer benefit (benefit less price) to firm operating profit (price less production cost) is equal to an expression related to the shape of the production function for research, $q(x)$.

Together, equations (4) and (5) describe the solution to the problem of choosing price to maximize consumer surplus subject to profit maximization.¹⁵ The underlying factors that determine solution are the level of benefits from the vaccine (b), the cost of production (c) and the relation between investment in R&D and likely success, $q(x)$. In the appendix solutions for (4) and (5) are figured in the case in which $b = \$110$ and $c = \$10$, so the net value per person of the vaccine is $\$100$. Solutions are presented there for a family of $q(x)$ functions in which the relationship between q and x is quadratic but satisfies the properties of a valid “production function” for research; e.g., when there is no investment the vaccine will not be available (for certain), and the maximum probability of discovery is one. The quadratic form can be viewed as second-degree polynomial approximation to any $q(x)$ function.

One case is brought forward from the appendix to illustrate an important and general point. Figure 2 graphs the consequences of choices of price for expected social welfare, consumer surplus and profit in the case in which $b=110$, $c=10$, and $q(x) = .2x - .01x^2$. This “production function” for research is one for which, initially, diminishing returns to research are small, ie, the second derivate of $q(x)$ is small relative to the first derivative. As we have already seen, to maximize expected social welfare, price should be set at b . The social welfare (sw) function in Figure 2 shows this. At $p = b$, however, expected consumer surplus is zero. Application of Criterion 2, maximizing expected consumer surplus implies $p = 26.6$. (See appendix.) Social welfare is reduced to 83.9, but almost all of this is consumer surplus, 75.8. (Profits are the difference: 8.1.)

The general point concerns the risk of under or overshooting in the pre-set price for the vaccine. If the price is mistakenly set too low, less than $\$26.6$ in this example, expected consumer surplus falls (rapidly in this case), expected profits fall and expected social welfare falls. The risk of overshooting price is asymmetric: expected consumer surplus falls, but expected profits *and social welfare* both go up. *Any policy towards fixing a*

¹⁵ Interestingly, two-part tariffs do not help here to better resolve distributional and efficiency tradeoffs. As noted earlier, it is the average profitability per customer that the firm looks to when making investment decisions.

price for vaccines will be conducted with considerable uncertainty about important parameters. This analysis suggests how to deal with the uncertainty: estimate the price best for consumers, then err on the up side.

4. Quantifying the Benefits of a New Vaccine

Putting the analysis above into practice depends on good estimates of the average benefit of a vaccine. A recent IOM report (Stratton, Durch and Lawrence, 2000; hereinafter, SDL) has conducted a cost-effectiveness analysis of 26 candidate vaccines, applying a common analytical framework for measuring the costs and effects of vaccine development and administration. This report is a starting point for considering whether benefits can be operationalized. Benefits discussed here are public health benefits, and do not include special considerations associated with national emergencies.

SDL were interested in all the costs and all the effects of development and administration of the candidate vaccines for the U.S.. Drawing on epidemiological and cost information, SDL estimated savings in health care costs that would follow from implementation of a completely effective vaccine. (In sensitivity analyses, SDL studied the consequences of less than complete effectiveness.) Assumptions were made about the timing and total cost of development. SDL assumed that the purchase price for prophylactic vaccines would be either \$50 or \$100, and included this per person payment as part of the “cost” of the vaccine.¹⁶ The epidemiological model was also used to forecast the QALYs that would be gained as a result of the vaccine development. SDL made judgments about the likely timing of discovery and the resulting timing of costs and effects to calculate, in a common metric, the cost per QALY gained for each disease area.¹⁷ Although SDL did not make explicit recommendations about which vaccines should be given priority for development, it did provide information that could be used as a basis of such a set of decisions.

In this paper, we use some of the data and analysis from SDL for the purposes of price setting for new vaccines. In contrast to SDL, we do not make assumptions about the timing or the costs of vaccine development. These are instead regarded as being the result of decisions made by the private sector in response to incentives. We also do not make an assumption about the price to be paid for the vaccine; rather, this price is what we solve for in the analysis. From SDL we use only the estimates of the health care costs saved and the QALYs gained for each vaccine to capture the benefits of vaccine development.

¹⁶ From a social cost perspective, the cost of administration of the vaccine, not the price paid to the supplier is the right number here. SDL recognized that the cost of administration was much lower than price (they cite a figure of \$10). If the perspective of the buyers rather than social cost is chosen for purpose of a cost-effectiveness, price represents buyer’s cost, but then, development costs of the manufacturer should not be considered in the calculation.

¹⁷ If health care cost savings more than offset the costs of development and prices paid for vaccines, the cost per QALY would be negative. This was the case for several vaccines. The literal implication of a negative price is no matter what positive value society puts on a QALY, the vaccine should be developed.

Table 1 illustrates the calculation for price setting for four candidate vaccines: *Streptococcus pneumoniae*, Group B streptococcus, chlamydia, and the cytomegalovirus. (Not all of these are necessarily candidates for child immunizations.) Three of these were classed by SDL as being in the “most favorable” category for development, and chlamydia in the “more favorable” category. (Other vaccines fell in “favorable” and “less favorable” categories.) Annualized health care cost savings upon implementation of the vaccine are part of the benefits. This number assumes 100% efficacy and 100% utilization. If efficacy were known to be a number less than 100%, the price should be adjusted downward accordingly. Less than 100% utilization would be taken care of “automatically” because the manufacturer would only receive a price for the vaccines administered.¹⁸

Timing of benefits needs to be considered in the calculation. The SDL figure of “annualized cost savings” of a fully implemented and effective vaccine can be used to capitalize the flow of benefits simply by dividing by the discount rate. Here we use the same 3.0% discount rate used in SDL. The cost savings per person in Table is calculated as follows:

$$\text{Cost Savings per Person} = \text{Capitalized Value of Savings/Population}$$

where Capitalized Value of Savings = PV Annualized Health Care Costs Saved/Discount Rate

SDL also presents QALYs gained as an annual flow. We capitalize these, and value them in dollars at a conservative \$50k per QALY for purposes of price calculation.¹⁹

The Total benefits per person reported in Table 1 vary between \$86 for GBS and \$516 for cytomegalovirus. Components of benefits also vary. The QALY component is almost half in the case of chlamydia, but much less than half for the three other conditions. A vaccine against cytomegalovirus would be very beneficial in terms of health care costs reduced. Two price calculations are shown. The first gives 80% of the surplus to consumers and the second divides the surplus 50/50. Keep in mind that social efficiency goes up (ie total surplus) as the share given to consumers falls. Prices shown should be understood as prices per person vaccinated (not per dose). Prices seem reasonable on their face, though particularly if the division is 50/50, higher than current prices for new vaccines.²⁰ Setting a high price now for a vaccine against cytomegalovirus (eg, \$200) would accelerate development of a vaccine with large social benefits. Prices could also be chosen for other diseases, perhaps in the range between the 80% to consumers and 50% to consumers. If pricing is done well, private industry could then make decisions

¹⁸ This assumes the average benefit is constant over the range of total potential users.

¹⁹ \$50,000 was at the low end of the range used by Newmann et al (2000) to value a Disability Adjusted Life Year (DALY). Estimates of the value of a life based on how much workers have to be compensated to accept risk of death yield much higher numbers (Murphy and Topel, 1999). Although they do not quantify the benefits, Rappuoli, Miller and Falkow (2002) urge the consideration be given to “intangible” benefits of vaccines in public policy.

²⁰ Prevnar and varicella vaccines are sold under CDC contract for about \$50 per person (Lichtenberg, 2002).

about pursuit of vaccines against these diseases on the basis of their own technical knowledge of the likelihood of finding a vaccine, and on the basis of the social value of the vaccine itself.

Other authors have used a similar framework to SDL to study the costs and beneficial effects of vaccines. The classic study of the benefits and costs of medical research is Weisbrod's (1971) study of the polio vaccine. Jacobs and Meyerhoff (2001) conduct a comparative cost-effectiveness analysis of vaccines for three diseases. Kremer (2000a) estimates that in developing countries, a vaccine against malaria would be cost-effective at \$41 per dose but that countries under current institutions governing prices would probably only end up paying around \$2 per dose, a price too low to stimulate appropriate investment. Very favorable medical cost savings in relation to costs of production and administration of some current vaccines are also reported by the CDC (1999). Russell (1986) uses evidence on the measles vaccine (particularly Axnick et al, (1969)) to discuss methodological issues in costs and benefits of preventive measures such as vaccines. In the case of measles, she concludes that the costs of production and administration exceed the cost savings because of less disease but that when the costs saved from institutional care of those who would have been left developmentally disabled are figured in, savings exceed costs. Russell makes no attempt to value the benefits of reduced mortality or morbidity. Valuing the intangible benefits of less disease and mortality would have tipped the scales more heavily in favor of the vaccine. See also Weniger et al. (1998).

5. Some Practical and Policy Considerations in Setting a Price for New Vaccines

Implementation of policy based on a pre-set price raises a number of practical issues, some of which are mentioned briefly in this section. A prominent one is whether the government can be trusted to "commit" to a policy. Kremer (2000b) argues that a purchasing commitment is feasible and enforceable in an international context. The commitment and general policy proposed here is similar to the "Countermeasure Purchase Fund" proposed by Senator Lieberman in S1764 (December 4, 2001) "Research to Develop Vaccine and Medicines to Treat Victims of Bio-Terrorism Attacks". Specifically, "This legislation provides that a company that successfully develops a countermeasure – through FDA approval – is eligible to sell the product to the Federal government at a pre-established price and in a pre-determined amount." (p.23). Rogerson (1994) argues that policy toward government procurement should recognize that government agencies are not natural actors maximizing social welfare, but may have other objectives (e.g. maximizing budgets).

Setting price in advance gets the CDC out of the price-negotiation business. Once a vaccine is approved, the budget increase to CDC would be "automatic." The CDC already sets prices for some vaccines. Since 1994 CDC has limited price increases to CPI adjustment for vaccines available prior to the VFC Program.

A major uncertainty for industry would be eliminated by prices set in advance. If the public sector *commits* to a good price, more investment will follow because of expected revenue and because of the reduction in risk.

An administered price could be market-wide (ie private buyers as well as public), or just the public, letting private sector negotiate as at present. The problems associated with introduction of a new high-priced vaccine (Prevnar) and discussed in Freed et al. (2002). Assuming private price would be no less than public price, advantages of public-only administered price are: 1) ability to cost shift to private sector; 2) less change in drug industry pricing practices. Advantages of one price in market are: 1) no need to forecast private price in making public choice; 2) parity in prices makes the proposal attractive to private buyers.

Much of the current research effort in vaccines seeks to improve on existing vaccines by increasing efficacy or reducing side-effects.²¹ Furthermore, development of combination vaccines to reduce the number of separate administrations necessary is another goal of current research. It is not clear how an administered price policy might apply to new versions of old vaccines. The private incentives in relation to social objectives are different in the case of an *improved* vaccine. Some of the profits of the innovator of an improved vaccine come at the expense of the profits of the current supplier. There is less reason to be concerned with “adequate incentives” here since the benefits are mainly in terms of administration/side effect reduction.

If effectiveness is less than 100%, the degree of effectiveness could be used as a multiplicative factor on preset price. Effectiveness is estimated in the course of clinical trials prior to FDA licensure. It is also possible to benchmark against historical disease trends. Orenstein and Schwartz (2001) compare rates of death in 2000 to annual averages for 20th century for eight diseases and show effectiveness rates ranging from 95-100%.

6. A Comment on the Procurement of Existing Vaccines

The cost and demand structure of vaccine production makes the market liable to shortages. According to Mercer Management Consulting (2002), only 15% of the costs of vaccine production vary with the level of production. The rest of costs are overall fixed cost or fixed at the batch level. This tends to lead to one or a very small number of firms producing any single vaccine. (See Arnould and DeBrock (2002) for discussion.) Furthermore, short-run capacity is costly and time-consuming to adjust because of regulatory requirements. A production failure at one of the small number of firms producing a vaccine cannot be easily made up by other suppliers. Demand is not sensitive to supply price. The public half of market faces no price upon use. The private side is mandated to buy childhood vaccines via school enrollment requirements.

²¹ Finkelstein’s (2002) research concerns how demand-increasing policies for existing vaccines stimulated research on improved versions of those vaccines.

One direction to alter this situation is to loosen the regulations that increase costs and obstruct supply from overseas. Another direction is to accept the regulations, and then to take steps to ensure that decisions about supply are being made efficiently in light of the costs of supply shortfalls. One way to do this is to modify CDC contracts to include provisions about minimum supplies as well as maximums. In other words, a contracting supplier would be responsible for supplying qualifying vaccines of at least a certain quantity during specified time periods. If the supplier fails to do so, penalties would be imposed reflecting the social costs of shortfalls. In order to avoid penalties, suppliers would then have incentives to seek alternative sources of supply if they experience production failures, and take efficient levels of effort to reduce the risk of failure.

Contracts with minimum quantity commitments and penalties would be more expensive for the CDC. This is appropriate since the CDC would then be forced to see and pay for the costs of the regulations imposed by government. The CDC itself would have incentives to consider the costs as well as the safety/effectiveness benefits of regulations.

7. Discussion

Coming fresh to vaccine pricing and supply issues, it is hard not to be impressed by arguments about the social value (nationally as well as internationally) of effective vaccines in relation to their cost of production. The federal government, through its procurement policy, has the responsibility of translating these benefits into incentives for appropriate investment in research and development.

The economic return to vaccine development appears to be low. One indication of this is disinvestments. The number of firms in the US producing vaccines has fallen to 10, from 37 as recently as 1967 (Rappouli, Miller and Falkow, 2002). Furthermore, R&D on new vaccines appears not to be pursued as aggressively as is warranted by the social return. Finkelstein (2002) gathered information on the number of clinical trials for vaccines by disease. The number of trials per disease for diseases against which a vaccine already existed were much larger than the number of trials for which there was no vaccine. Indeed, according to data in her Table 2, the total number of trials per year over the period 1996-99 for the six diseases where there was already a vaccine was about equal to the total number of trials for 26 other diseases where no vaccine existed. Although these data are subject to multiple interpretations, it seems that pricing policies are not directing industry R&D to solve the problems with the highest social return.

Analysis of the “optimal price” for a new vaccine presented here is potentially relevant in two respects. First, if setting price in advance is a feasible policy, the considerations and analyses presented may help in choice of those prices. Second, even if the policy of a pre-established price is determined to have more drawbacks than advantages, the optimal price can be used as a benchmark to evaluate the outcome of actual or potential policies influencing supply price.

Some of the arguments for setting a price for vaccines in advance of their development are similar to the arguments Kremer (2000a,b) makes in an international context. Consideration of the market for vaccines in the U.S. is simpler in some important ways and avoids some of the difficulties faced in mobilizing international purchasing power. In his proposals, Kremer recognizes the free-riding problem of each buyer (country) Hay and Zammit (2002) attempting to pay none of the costs of the public good represented by the fixed costs of R&D. He also must recognize the demand-response problem in a developing country context. If price to the target country (perhaps a cost share with the international community) is set too high, the country may not demand the vaccine altogether. Neither of these problems faces the U.S. when considered in isolation. First, the federal government is in a position to solve the public good problem. Second, as set out above, demand response is much less of an issue. Kremer's arguments for a purchasing commitment would therefore apply with even more force to a U.S. domestic policy context.

Another form of coordination problem, however, does emerge in the U.S. Actions by one agency of the federal government (e.g., the CDC improving the supply of vaccines in the short and long run by a fixed price policy), may put a strain on that agency's budget, but relieve other agencies (e.g., CMS) or state governments (through Medicaid) of some of the costs of health care. The preset price can solve this problem by using medical care and other cost savings as part of the elements to figure the preset price, and then having the necessary funds transferred automatically to the CDC to make purchases.

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Appendix

Mathematical Analysis of Optimal Price for New Vaccines

Notation

b	average per person benefit of eliminating the disease
x	expenditure on R&D
q(x)	the probability of successful discovery of a vaccine
c	marginal production cost
p	price of the vaccine

Choosing price to maximize consumer surplus.

The formal problem is to maximize the expression (3) for consumer surplus in the body of the paper subject to the condition (4) for profit maximization.

$$L = q(x)(b - p) + \lambda(q'(p - c) - 1)$$

The first-order conditions for maximization of this expression are:

$$\begin{aligned} L_x: q'(b-p) + \lambda q''(p-c) &= 0 \\ L_p: -q + \lambda q' &= 0 \\ L_\lambda: q'(p-c) - 1 &= 0. \end{aligned}$$

The second FOC condition implies $\lambda = \frac{q}{q'}$. Substituting this into the first condition yields

$$q'(b-p) + \frac{q}{q'} q''(p-c) = 0, \text{ or}$$

$$\frac{b-p}{p-c} = \frac{-qq''}{(q')^2}$$

$$\frac{\text{consumer net benefit}}{\text{operating profit}} = \frac{-qq''}{(q')^2}$$

Case: q(x) is quadratic

The general quadratic form is $q(x) = a + bx + dx^2$, where a, b and d are parameters. The quadratic form must be restricted to be a valid function relating investment to the probability of success. Since no investment carries a likelihood of success of zero, the point (0,0) must be on the function, implying $a = 0$. The highest possible value (or maximum) of $q(x)$ is 1, so where $q'=0$, $q=1$. $q(x)$ is maximized when $x = -b/2d$, so $(-b/2d,1)$ is also a point on the function, implying that $-b = 2\sqrt{d}$. This restricts the form to a one parameter family:

$$q(x) = 2\sqrt{d}x - dx^2$$

For at least some investment to be efficient, we require $q'(b-c) > 1$ at $x=0$, or $d > 1/[2(b-c)]^2$.

To illustrate solutions, we take the case in which $b = 100$, $c = 10$, and d takes on various values greater than $1/[2(110-10)]^2 = 1/40000$.

The efficient level of x is determined in general by $q'(b-c)-1=0$, or in the quadratic form of q and for $b=110$, $c=10$;

$$[2\sqrt{d} - 2ds]100 - 1 = 0 \tag{A.1}$$

The values of (p,x) that maximize consumer surplus subject to firm profit maximization are found as the solution to the pair of non linear equations substituting in particular values for q, q', q'', b and

$$\frac{110-p}{p-10} = \frac{(2\sqrt{d}x - ds^2)(2d)}{(2\sqrt{d} - 2dx)^2} \tag{A.2}$$

$$(2\sqrt{d} - 2dx)(p-10) - 1 = 0 \tag{A.3}$$

The solutions for various values of d are shown in Table A.1

Table A.1

Socially Efficient				Maximum Consumer Surplus					
d	x*	q	sw	p	x**	q	cs	π	sw
.0001	50.0	0.750	25	75.839	24.058	0.423	10.227	3.810	18.27
.001	26.623	0.975	70.88	43.23	16.576	0.774	43.917	9.130	60.78
.01	9.5	0.998	90.25	26.6	7.0	0.902	66.774	7.567	83.37
.1	3.112	1.000	96.86	17.554	2.500	0.956	78.834	4.723	93.12
1	0.995	1.000	99.00	13.533	0.856	0.980	84.736	2.604	97.14
10	0.316	1.000	99.68	11.646	0.286	0.991	87.538	1.345	98.79

where

x^* - efficient level of investment

$$q = q(x)$$

$$cs = q(x)(100-p)$$

$$\pi = q(x)(p-c)-x$$

$$sw = q \cdot (b-c) - x$$

Figure 1a
Setting $p=b$ to Maximize Social Welfare

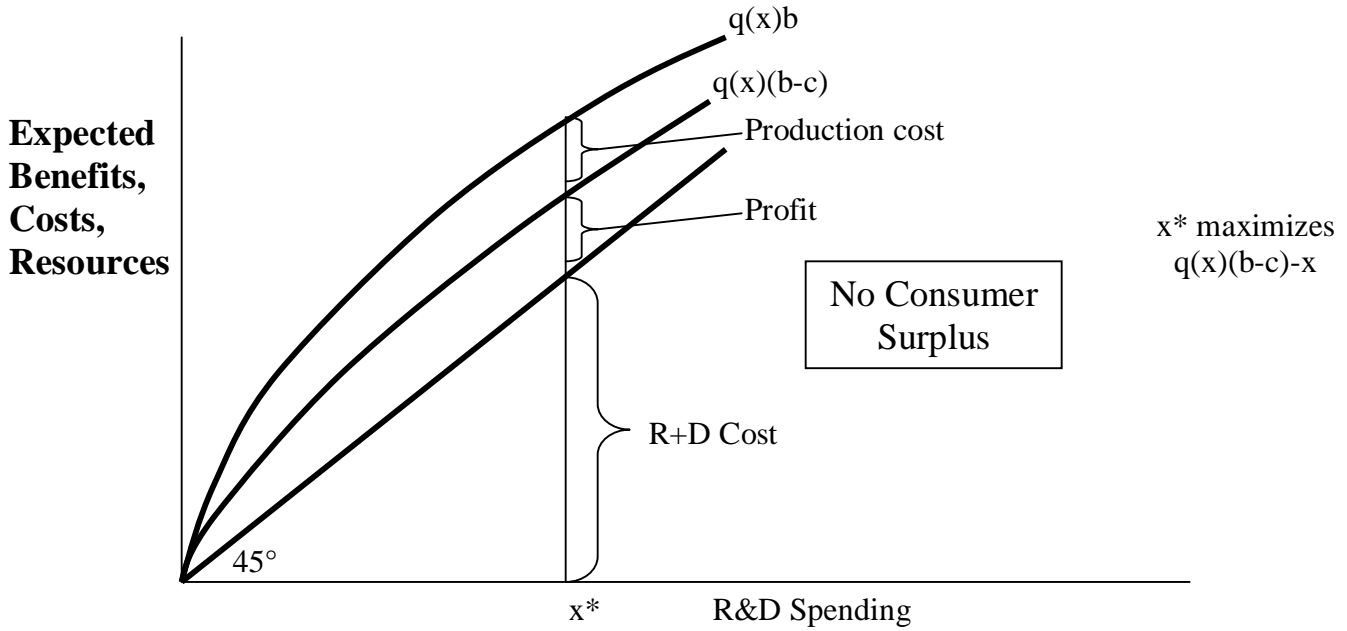


Figure 1b
Setting $p < b$ to Maximize Consumer Surplus

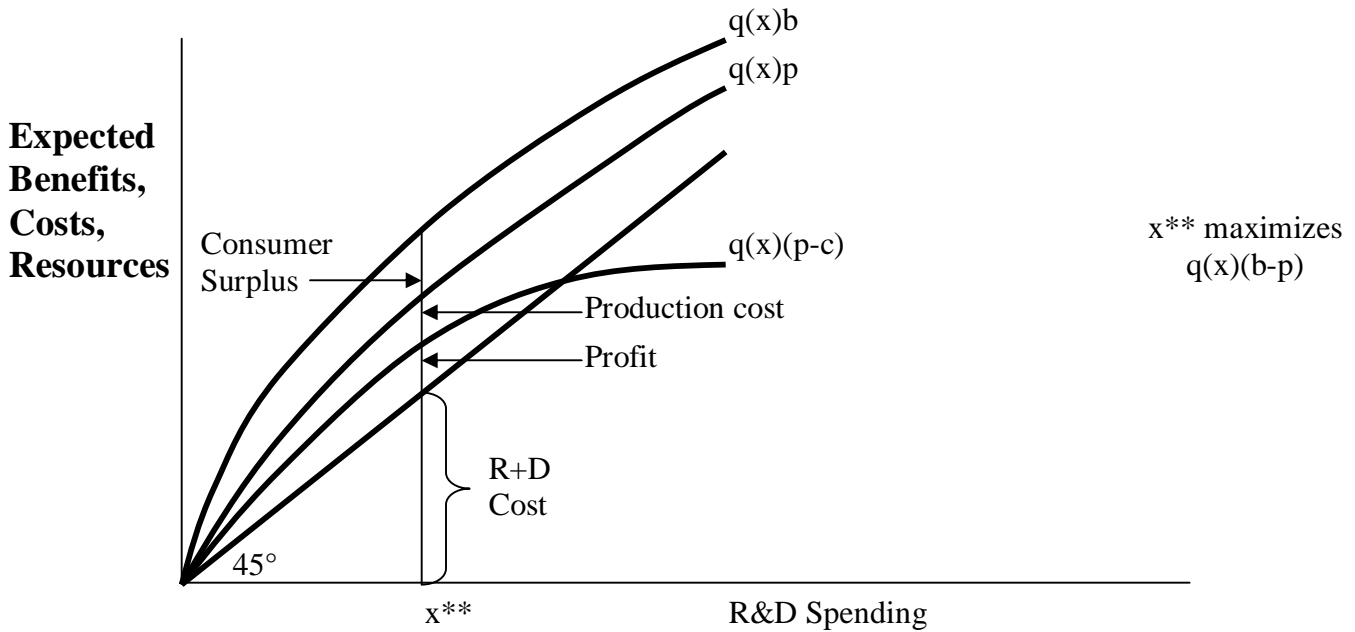
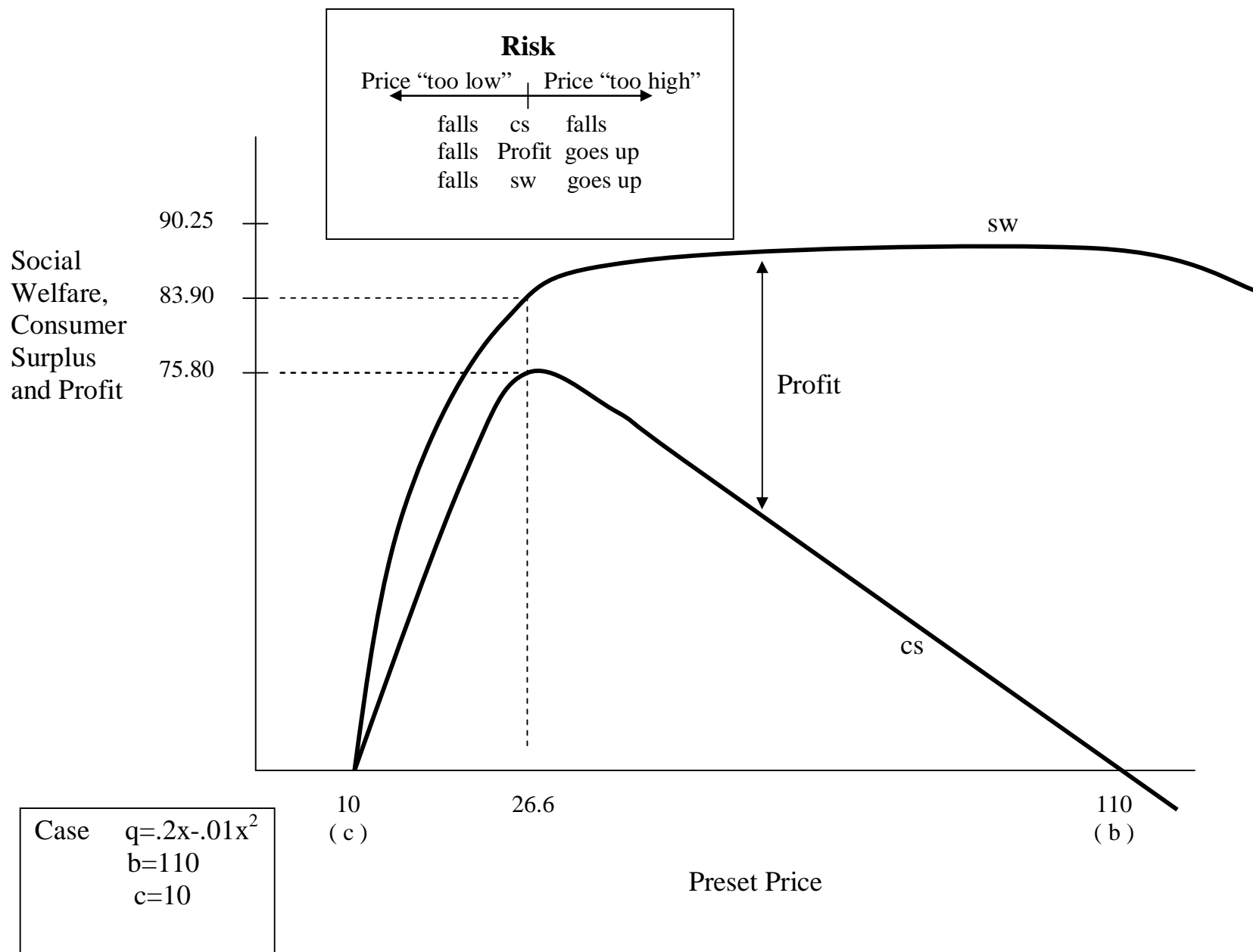


Figure 2
Price of Vaccine and Welfare



See Appendix for calculations

Table 1
Illustrative Pricing Model for Vaccines

	Disease			
	<i>S. pneumoniae</i>	GBS	Chlamydia	Cytomegalovirus
From IOM Report				
PV annualized health costs (\$mil)	\$1,600	\$630	\$850	\$4,000
PV annualized QALYs	265,000	37,400	525,000	70,000
Calculations				
Cost savings per person	\$201	\$79	\$107	\$503
Value of QALY per person	\$50	\$7	\$99	\$13
Total Benefits per Person	\$251	\$86	\$206	\$516
Pricing				
80% surplus to consumer benefit	\$58	\$25	\$49	\$111
50% surplus to consumer benefit	\$130	\$48	\$108	\$263
Assumptions				
QALY value	\$50,000			
US Population	265,000,000			
Discount rate	3.0%			
Production cost per	\$10			