# A Model of R&D Valuation and the Design of Research Incentives

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# Motivation: Analysis of R&D projects is a very difficult investment problem

- Takes a long time to complete
- Uncertainty about costs of development and time to completion
- High probability of failure (for technical or economic reasons)
- Drug requires approval by the FDA (focus on the pharmaceutical industry)
- Uncertainty about level and duration of future cash flows
- Abandonment option is very valuable

# Tufts Center for the Study of Drug Development (December 2001)

- Average development time for new drugs: 12 years
- Average total drug research costs (millions)

  Out-of-pocket expenses: **$403**

  Including cost of capital (11%): **$802**
  - Calculated at time of marketing of drug
  - Includes cost of failed drugs (20% success)
- Yearly US expenditures:$192 billion (2002)

# "Cost of Developing a New Drug Increases to About $1.7 Billion" (WSJ, December 8, 2003)

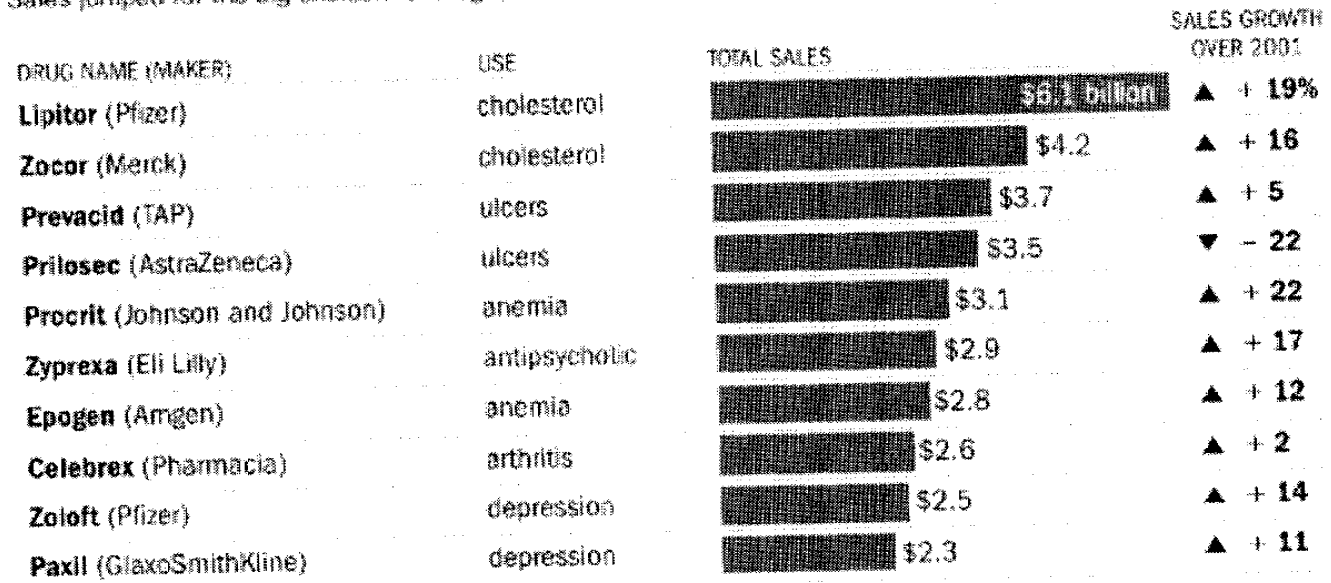
- Study by consulting firm Bain & Co.
- Extrapolates spending on the various stages of R&D during the 2000-2002 period
- Not directly comparable with the Tufts study (includes commercialization costs)
- From every 13 drugs that start our in animal testing only one now makes it to market

# Pfizer ‘Youth Pill’ Ate Up $71 Million Before It Flopped

- WSJ: May 2, 2002
- The experimental drug aimed to reverse the physical decline that comes with aging.
- Nearly a decade of research.
- Patients taking the frailty drug had gained some muscle mass – but less than 3% more than the placebo group – which also experienced muscle increase.
- Drug appeared ineffective.

## BLOCKBUSTERS AT THE DRUGSTORE

Sales jumped for the big cholesterol drugs, and some heavily marketed antidepressants moved up.



| DRUG NAME (MAKER) | USE | TOTAL SALES | SALES GROWTH OVER 2001 |
|---|---|---|---|
| **Lipitor** (Pfizer) | cholesterol | $6.1 billion | ▲ + 19% |
| **Zocor** (Merck) | cholesterol | $4.2 | ▲ + 16 |
| **Prevacid** (TAP) | ulcers | $3.7 | ▲ + 5 |
| **Prilosec** (AstraZeneca) | ulcers | $3.5 | ▼ – 22 |
| **Procrit** (Johnson and Johnson) | anemia | $3.1 | ▲ + 22 |
| **Zyprexa** (Eli Lilly) | antipsychotic | $2.9 | ▲ + 17 |
| **Epogen** (Amgen) | anemia | $2.8 | ▲ + 12 |
| **Celebrex** (Pharmacia) | arthritis | $2.6 | ▲ + 2 |
| **Zoloft** (Pfizer) | depression | $2.5 | ▲ + 14 |
| **Paxil** (GlaxoSmithKline) | depression | $2.3 | ▲ + 11 |

# R&D Valuation

1. Patents and R&D as Real Options
   - § Valuation of single patent-protected project
   - § Factors: cost to completion and cash flows
2. R&D Investments with Competitive Interactions (joint with K. Miltersen)
   - § RO framework is extended to incorporate game theoretical concepts (duopolistic competition)
   - § Factors: cost to completion and demand shocks
3. A Model of R&D Valuation and the Design of Research Incentives (joint with J. Hsu)

Simulation approach to value American Options

# Health Care Crisis in Developing Countries

- Malaria, Tuberculosis, and African strains of HIV kill more than 5 million each year
- Almost all of the death occur in the developing world
- Very little private pharmaceutical investment devoted to researching vaccines for these diseases
- A small market problem—people in the developing countries can't afford to pay
- International organizations and private foundations willing to provide funding

# Current Literature on "Encouraging Pharmaceutical Innovation"

- Kremer (2001, 2002) review popular subsidy programs
- Push programs: subsidize the cost of the R&D
  - Research grant
  - Co-payment
- Pull programs: subsidize the revenue of the R&D
  - Purchase commitment
  - Extended patent protection

## Current Literature

- No analytical framework for contrasting the different incentive programs

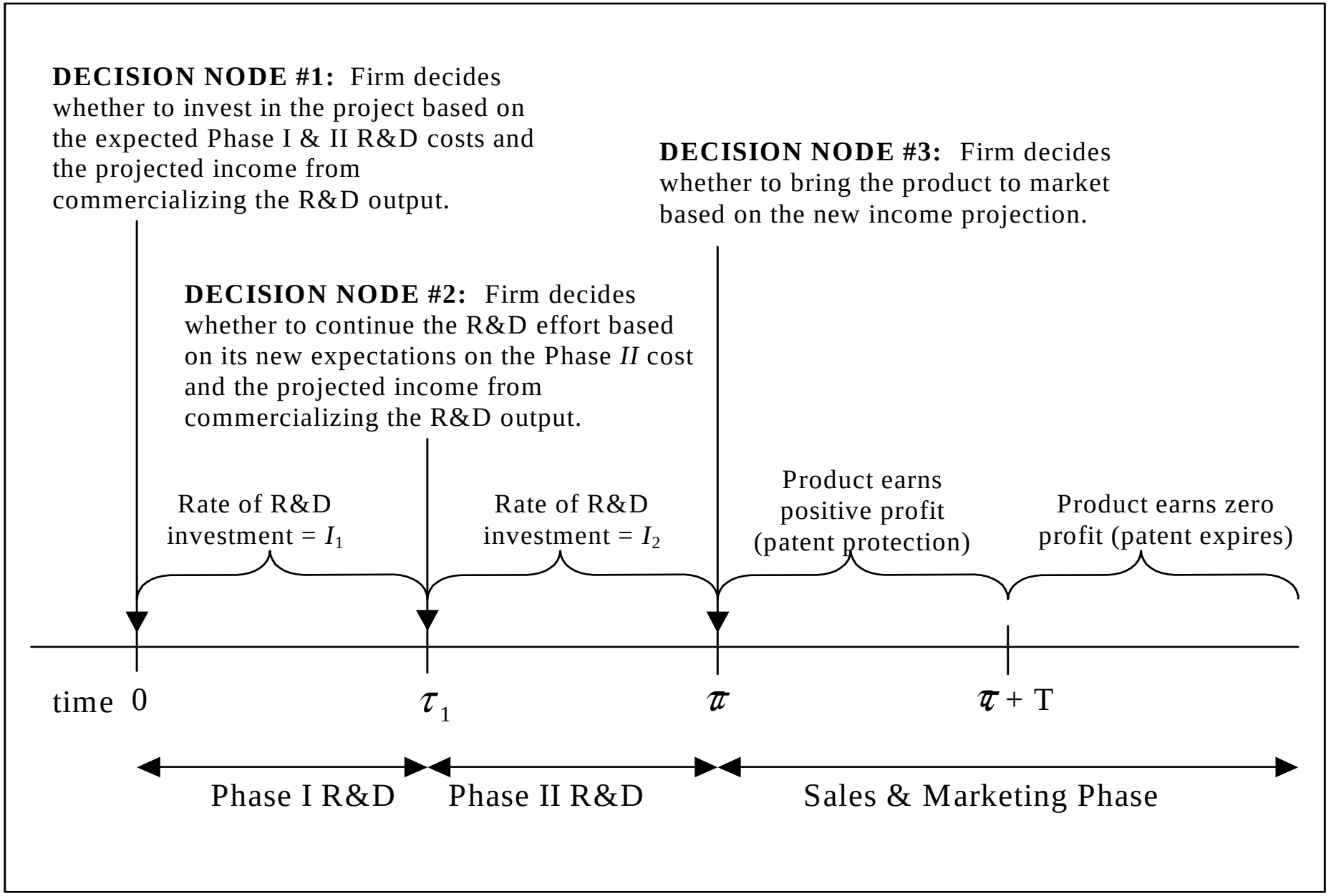
## Our Contribution

- Develop a real options valuation model for general R&D
- Examine the different incentive programs quantitatively using our valuation framework

# What's new in this paper?

- Quality of the R&D output is modeled explicitly
- Revenue is a function of
  - Market demand
  - Quality of the research output
  - Firm's pricing (and quantity) strategy
- Firm's price and quantity strategy could depend on
  - Incentive program in place
  - Monopoly power

# Timeline of the R&D Process



# "Expected Remaining Cost to Completion"

$0 < t < \tau_1$

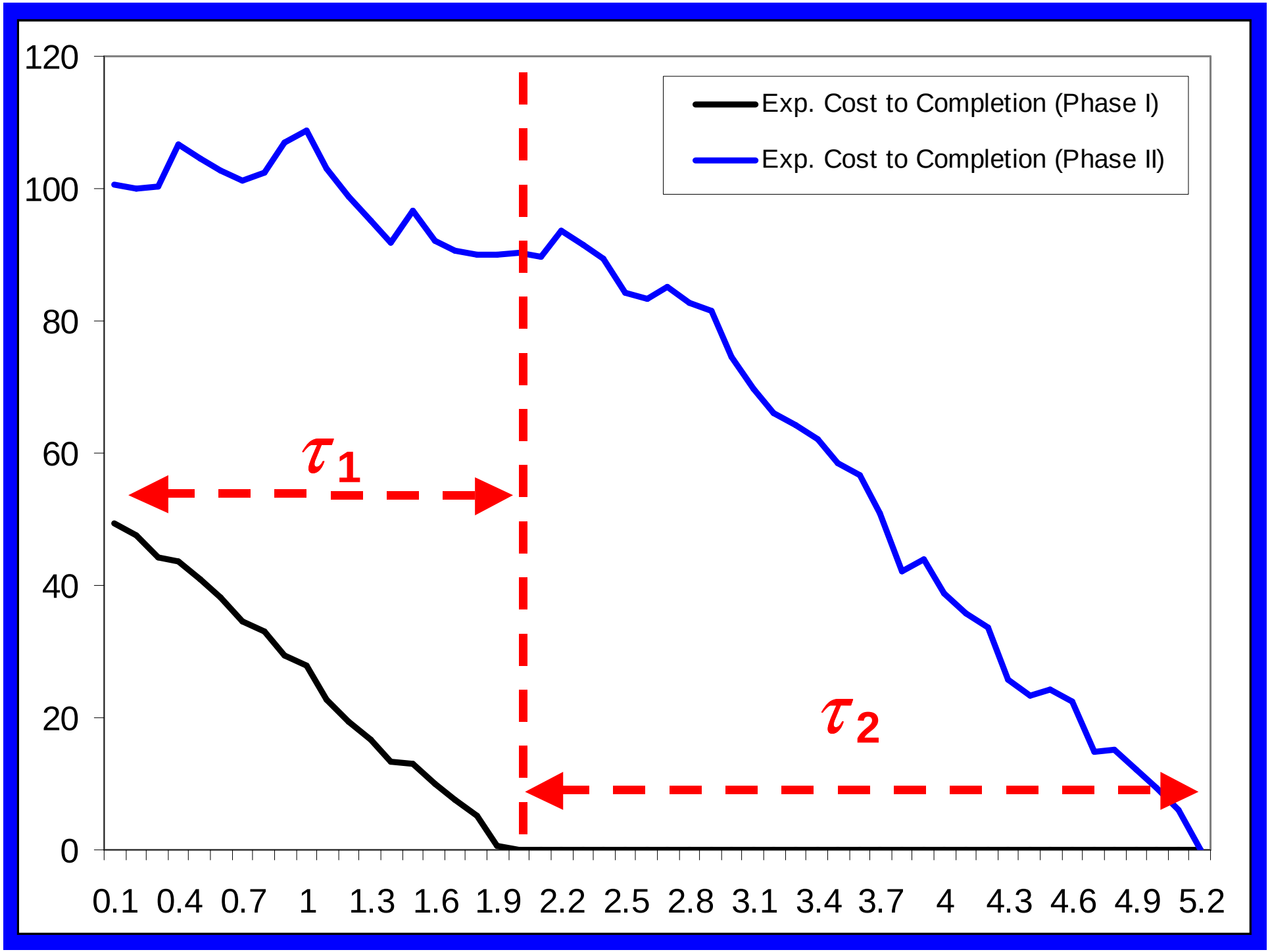
$$dK_1(t) = -I_1 dt + \sigma_1 dW_1(t)$$

$$dK_2(t) = \sigma_2 dW_2(t)$$

$\tau_1 < t < \tau$

$$dK_2(t) = -I_2 dt + \sigma_2 dW_2(t)$$

$K_1(0) = 50 \quad I_1 = 20$ $\qquad$ $K_2(0) = 100 \quad I_2 = 25$


120
100
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1.6
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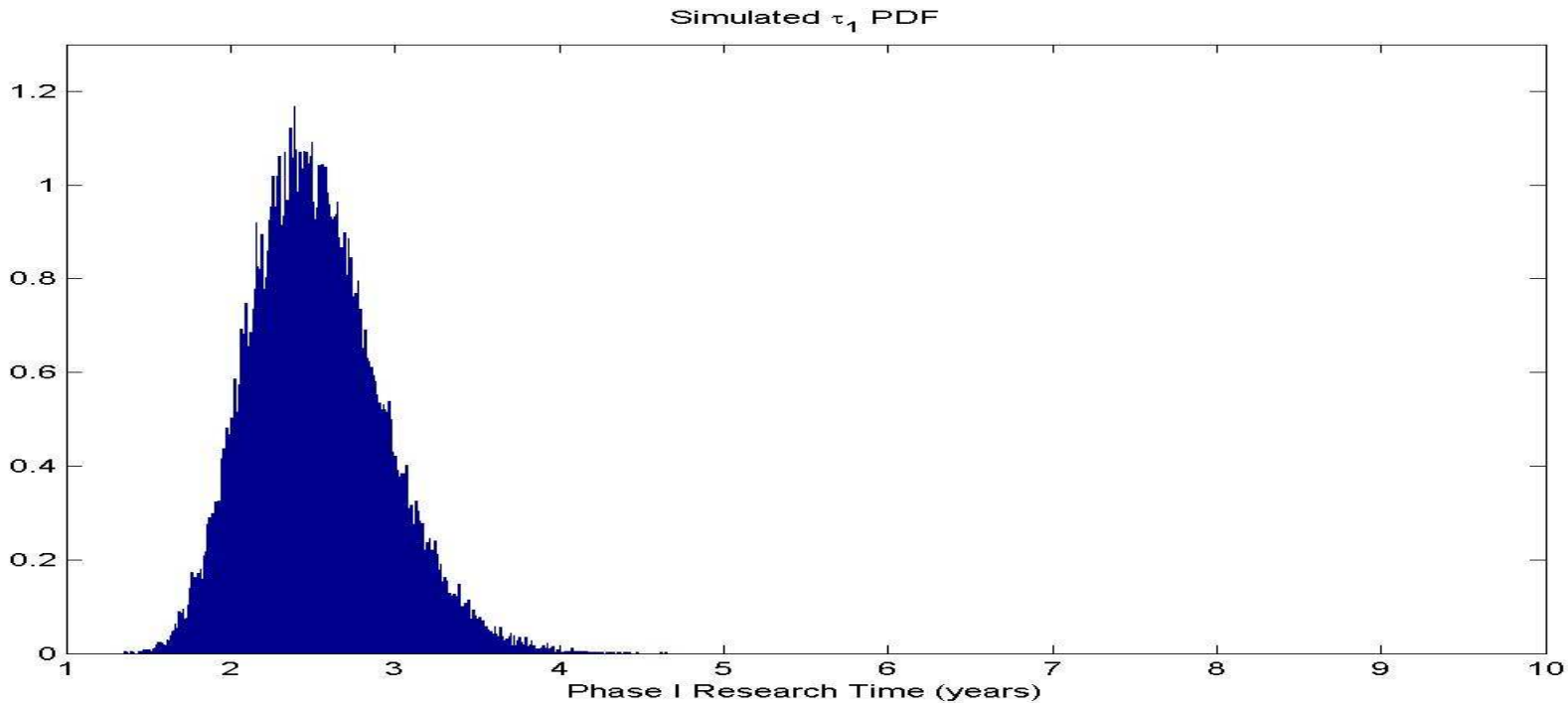
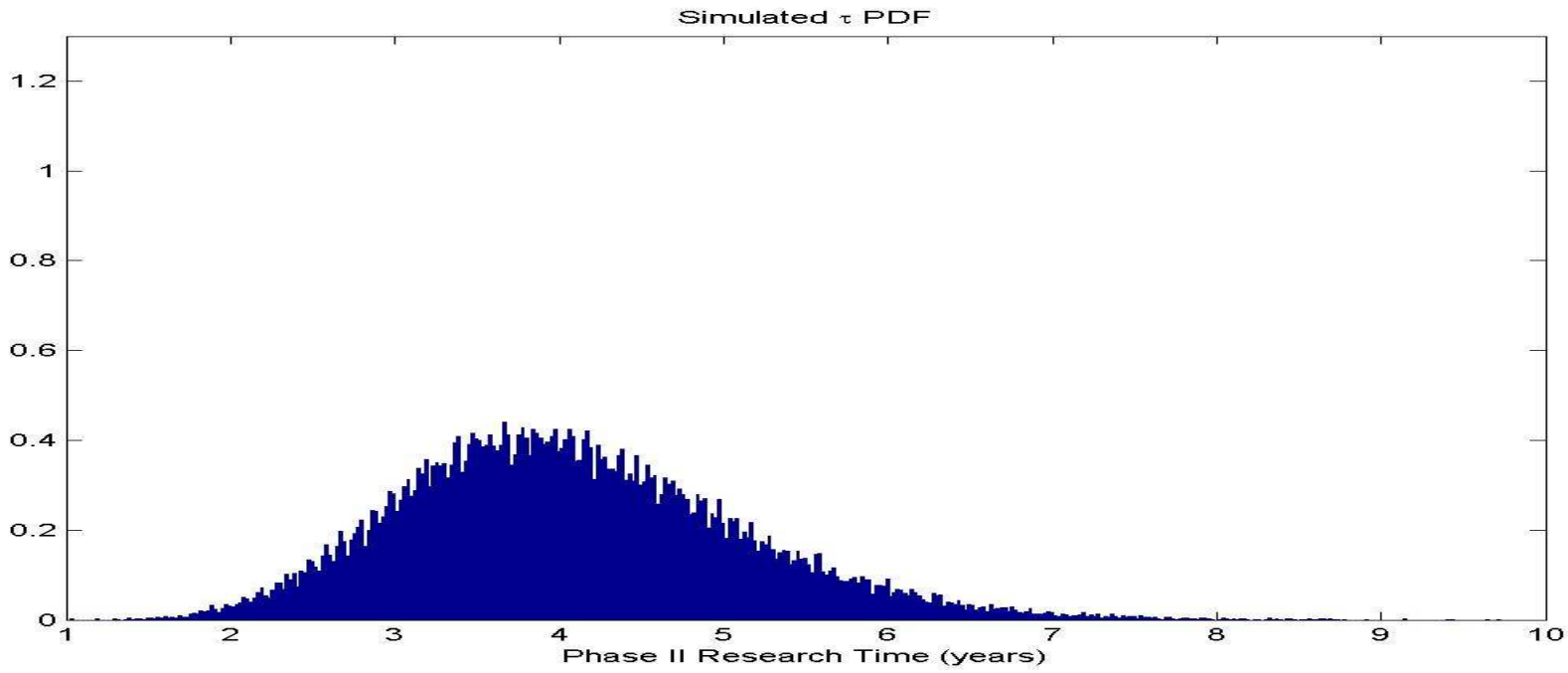
2.5
2.8
3.1
3.4
3.7
4
4.3
4.6
4.9
5.2
Exp. Cost to Completion (Phase I)
Exp. Cost to Completion (Phase II)
$\tau_1$
$\tau_2$


Simulated $\tau_1$ PDF
1.2
1
0.8
0.6
0.4
0.2
0
1
2
3
4
5
6
7
8
9
10
Phase I Research Time (years)


Simulated $\tau$ PDF
1.2
1
0.8
0.6
0.4
0.2
0
1
2
3
4
5
6
7
8
9
10
Phase II Research Time (years)

# Quality of research output

- Quality of the final product at the completion of the entire R&D project

$$Q(\tau)$$

- Time *t* conditional expected quality of the final product

$$Q(t) = E_t\left[Q(\tau)\right]$$

- For example Q(0)=0.75

# "Expected Quality of Final Output"

Beta distribution:

$$\varphi(Q) = cQ^{a-1}(1-Q)^{b-1} \qquad 0<Q<1, \quad 0<a, \quad 0<b$$

Mean: $\mu_Q = \dfrac{a}{a+b}$

Variance: $\sigma_Q^2 = \dfrac{ab}{(a+b)^2(a+b+1)}$

Mean-Variance restriction: $\mu_Q(1-\mu_Q) - \sigma_Q^2 > 0$

# Parameterize the Mean and Variance of the Quality Variable

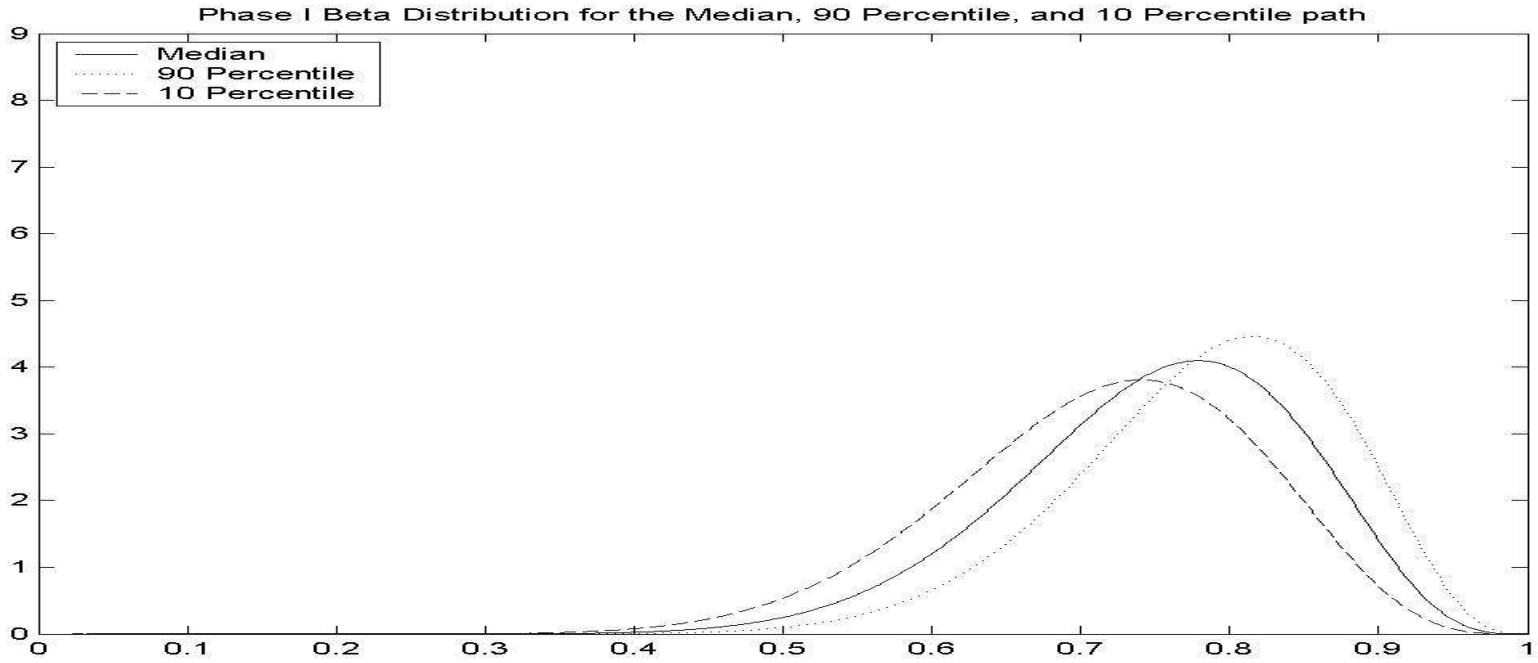
Allows for dependence on realized cost (or time) of a given phase (path dependent)

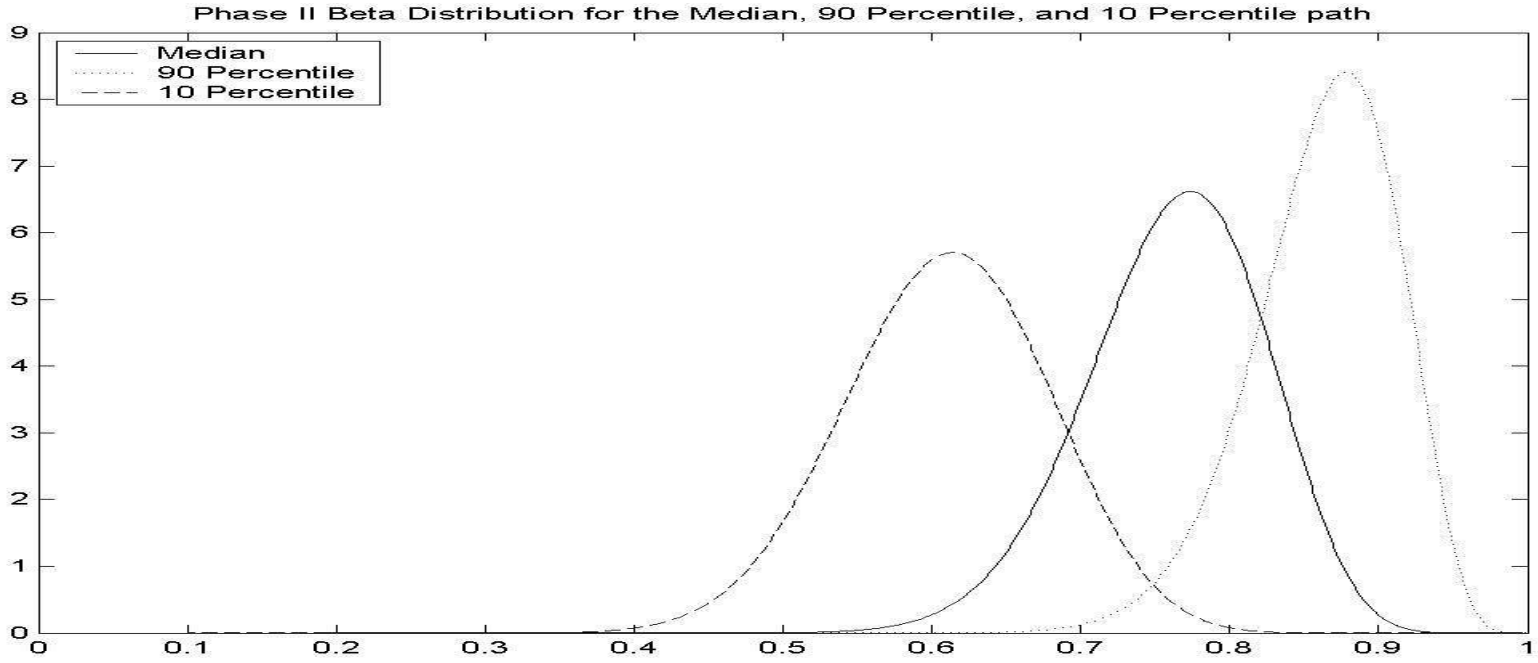
Mean:

$$\mu_Q(\tau_i) = 1 - \exp\left\{\log\left[1 - Q(\tau_{i-1})\right] \cdot \left(\frac{\tau_i}{E_{\tau_{i-1}}\left[\tau_i\right]}\right)^{\eta_{\mu,i}}\right\}$$

Variance:

$$\sigma_Q^2(\tau_i) = \mu_Q(\tau_i)\left(1 - \mu_Q(\tau_i)\right)\left(1 - \exp\left\{\log\left[1 - s(\tau_{i-1})\right] \cdot \left(\frac{\tau_i}{E\left[\tau_i\right]}\right)^{\eta_{\sigma,i}}\right\}\right)$$


Phase I Beta Distribution for the Median, 90 Percentile, and 10 Percentile path
Median
90 Percentile
10 Percentile
0
1
2
3
4
5
6
7
8
9
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1


Phase II Beta Distribution for the Median, 90 Percentile, and 10 Percentile path
Median
90 Percentile
10 Percentile
0
1
2
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4
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0.3
0.4
0.5
0.6
0.7
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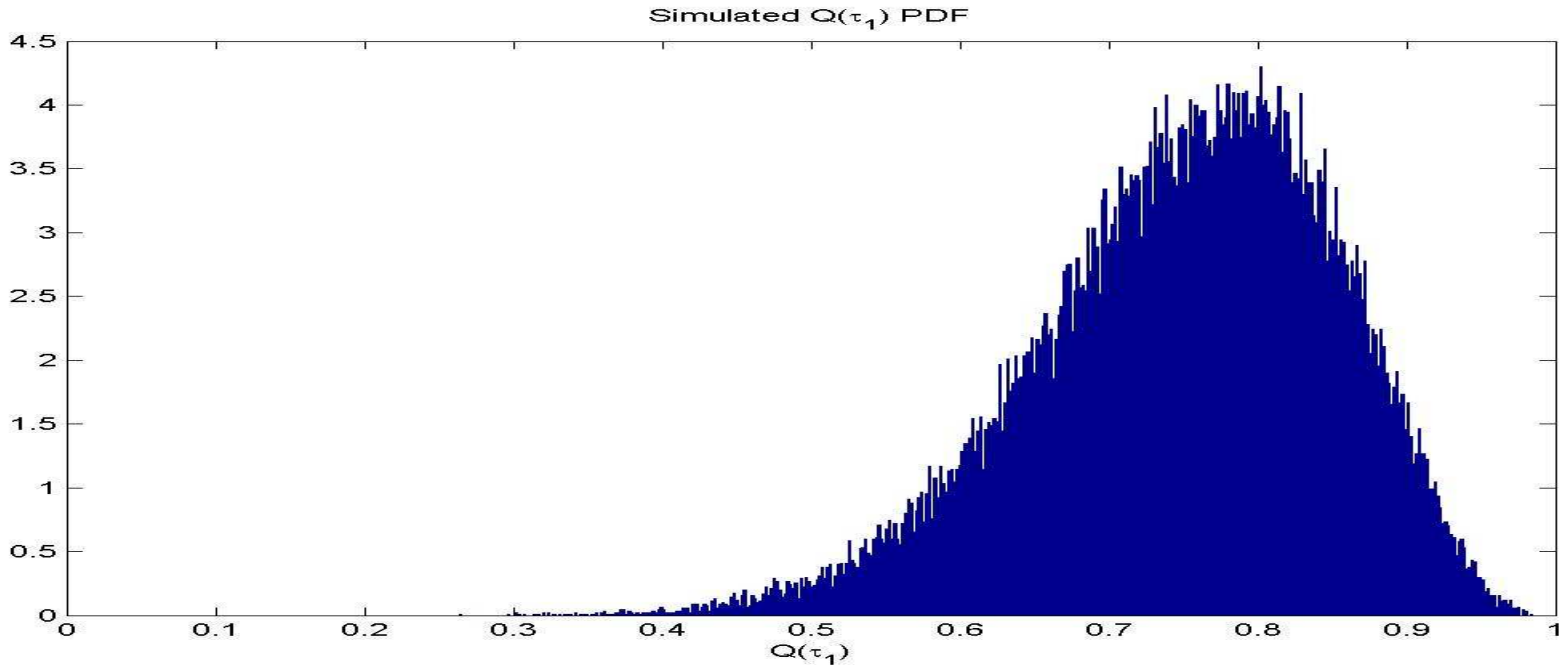
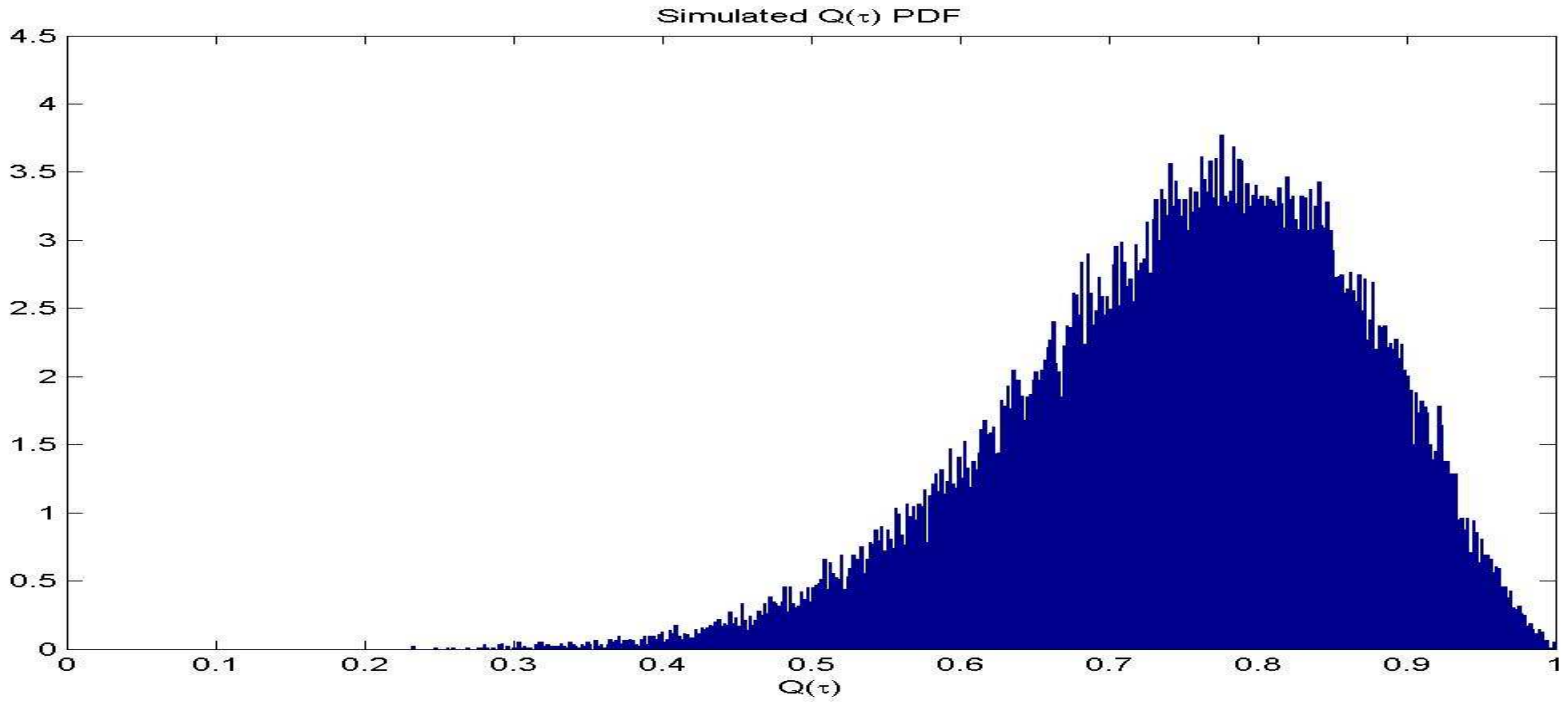
0.9
1


Simulated Q(τ1) PDF
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
Q(τ1)


Simulated Q(τ) PDF
4.5
4
3.5
3
2.5
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1.5
1
0.5
0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
Q(τ)

# Revenue

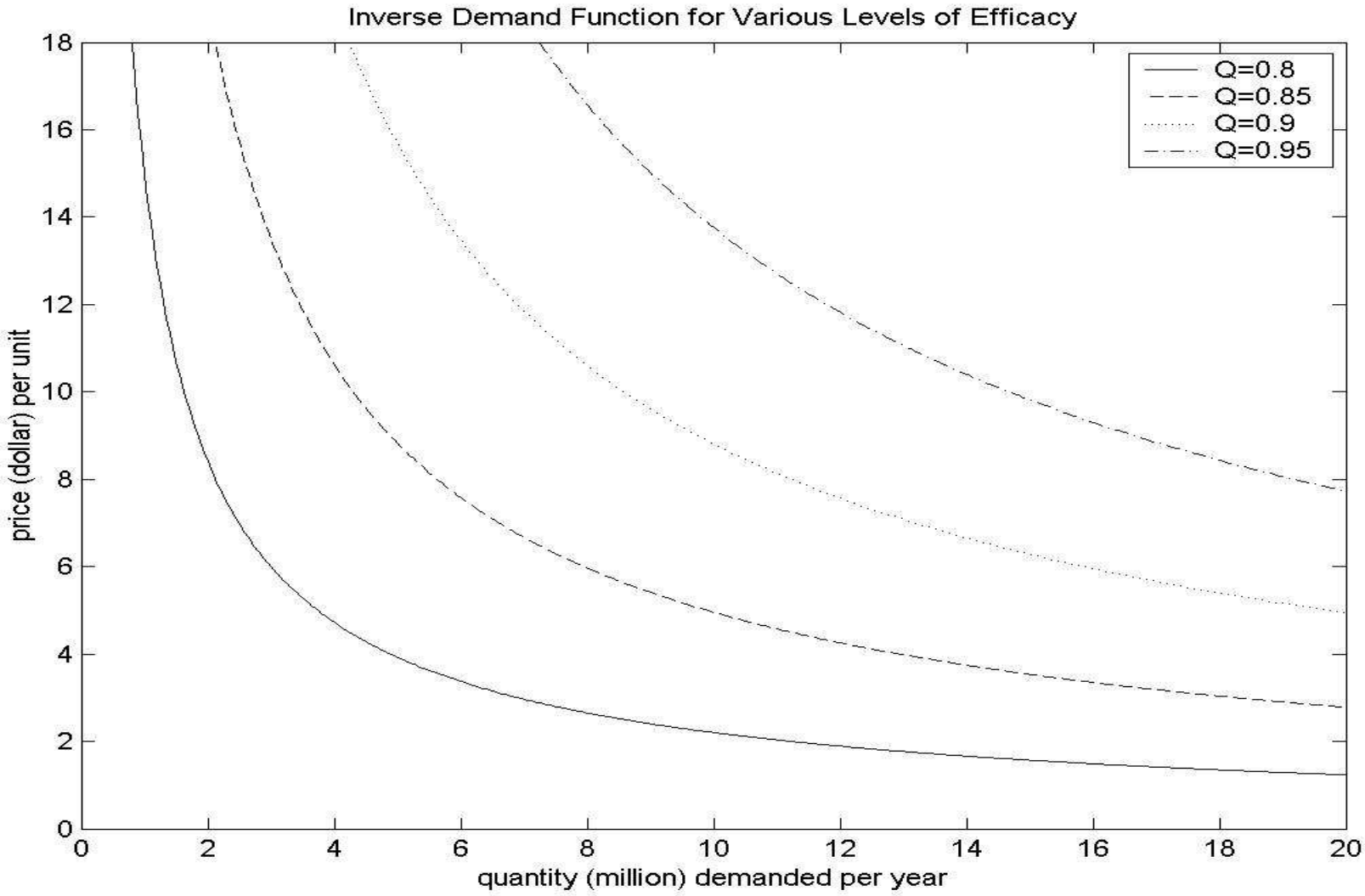
- Market inverse-demand function

$$P = \alpha \cdot \max(Q - Q_{\min}, 0)^2 \cdot q^{-1/\gamma}$$

- Demand shocks could be added to the demand function: with risk premium

# Sample Inverse-Demand Function

$$P = 1500 \cdot \max(Q - 0.7, 0)^2 \cdot q^{-1/1.2}$$



# Catastrophic Events

- In each phase of the R&D or in the marketing phase, events can arise to cause the R&D or the marketing to be discontinued.

- These catastrophic events are modeled as independent Poisson processes with hazard rates: $\lambda_1, \lambda_2, \lambda_m$

- We can adjust for these events by augmenting the discount rate by the hazard rate in each period.

Valuation and abandonment at time $\tau = \tau_1 + \tau_2$

$$v(\tau) = \int_0^T (P_M - c) \cdot q_M \cdot e^{-(r+\lambda_m)t} dt$$

$$V(\tau) = \mathbf{1}\{v(\tau) > 0\} \cdot v(\tau) = v(\tau)$$

Abandon if V( ) is equal to zero

# Valuation and abandonment at time $\tau_1$

$$v(\tau_1) = E\left[ V(\tau) \cdot e^{-(r+\lambda_2)\tau_2} - \int_0^{\tau_2} I_2 e^{-(r+\lambda_2)t} dt \,\middle|\, Q(\tau_1), K_2(\tau_1) \right]$$

$$V(\tau_1) = \mathbf{1}\{v(\tau_1) > 0\} \cdot v(\tau_1)$$

Abandon if V( ) is equal to zero

# Valuation and Abandonment at time 0

$$v(0) = E\left[ V(\tau_1) \cdot e^{-(r+\lambda_1)\tau_1} - \int_0^{\tau_1} I_1 e^{-(r+\lambda_1)t} dt \,\middle|\, Q(0), K_1(0), K_2(0) \right]$$

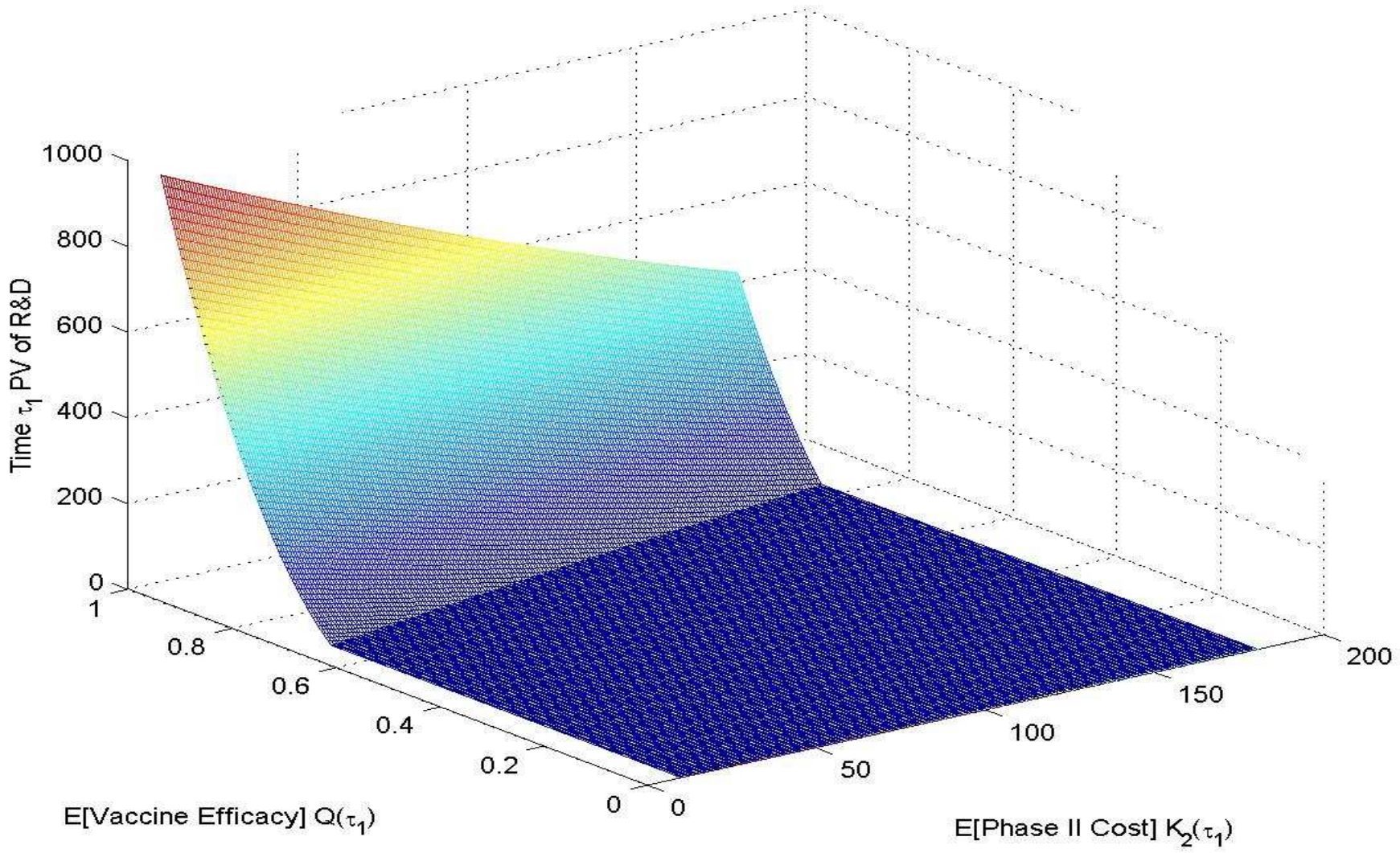
$$V(0) = \max[v(0), 0]$$

Abandon if V( ) is equal to zero

# Solution by Longstaff and Schwartz Least-squares technique

- Firm's optimal abandonment policy cannot be solved for in closed-form
- The conditional expected profit from continuing can be approximated efficiently with the L-S least-squares method
- Longstaff-Schwartz method
  - Regress simulated values at time $\tau$ onto functions of the state variables at time $\tau_1$
  - This creates a conditional expectation function (a profit function conditioned on the observed state variables)

# Optimal abandonment at the end of Phase I R&D



# Valuing vaccine R&D with no subsidies

- Using same data and c=$1
- Monopoly profits

$$\frac{\partial((P-c)\cdot q)}{\partial q}=0$$

- Pricing strategy (monopoly)

$$P_M = c\frac{\gamma}{\gamma-1}=6,\ (\gamma=1.2,\ c=1)$$

- Quantity demanded

$$q_M=\left[\frac{\alpha\cdot(Q-Q_{\min})^2}{P_M}\right]^{\gamma}=\left[250\cdot(Q-0.7)^2\right]^{1.2}\quad Q>0.7$$

# Valuing vaccine R&D with no subsidies

- PV of R&D project = $2.16 million
- Probability of advancing to Phase *II* R&D = 46.75%
- Probability of developing a successful vaccine = 45.19%
- Expected final efficacy (*Q*) of a vaccine which advances to Phase *II* R&D = 83.4%
- Expected final efficacy (*Q*) of a successful vaccine = 83.97%
- Expected quantity produced= 8.97 million

# Analyzing Incentive Contracts

- Push Contracts:
  - Full discretionary research grant
  - Sponsor co-payment

- Pull Contracts:
  - Extended patent protection
  - Fixed price purchase commitment
  - Variable price purchase commitment

# Contract Specifics

- Developer retains right, supplies monopoly quantity
  - Full discretionary research grant
  - Sponsor co-payment
  - Patent extension
- Sponsor can contract the socially optimal quantity to be produced
  - Purchase commitment contracts
- We abstract from agency problem arising from asymmetric information between the vaccine developer and the sponsor, and from contracting issues

# We seek to answer four critical questions

- What is the required level of monetary incentive to induce the firm to undertake the vaccine R&D?
- What is the probability that a viable vaccine will be developed?
- What is the consumer surplus generated?
- What is the expected cost per individual successfully vaccinated?

# Cost per individual successfully vaccinated

- Measure that summarize different aspects of subsidy programs
  - Expected cost to the sponsor
  - Expected quantity supplied
  - Expected efficacy of the developed vaccine
  - Probability of developing a viable vaccine

$$CPISV = \frac{PV(\text{sponsor cost})}{E[Q(\tau) \cdot q \cdot T]}$$

# Research incentive design

- We analyze different designs in a “small” market with inverse-demand function

$$P = 200 \cdot \max(Q - 0.7, 0)^2 \cdot q^{-1/1.8}$$

- We increase the market’s demand elasticity and shift the demand downward
- Without subsidy it is not optimal to start R&D (if start PV of project is –43.75 m)
- We find subsidy that produces a PV=0 or that has a fixed cost to the sponsor

# Push subsidy programs

- Full Discretionary Research Grant
- Investment Cost Co-payment Plan: Sponsor pays a fraction X of the firm's per period research investment cost

# Pull subsidy programs: Patent extension program

- Cheapest in a fiscal sense
- We assume that the sponsor can grant the pharmaceutical company extra patent protection
- In our example the market demand is so small that there is no extension that will induce the firm to undertake investment
- Least effective method

# Purchase commitment

- Sponsor commits to a quantity-price schedule
- Monopoly quantity

$$q_M = \left[ \frac{\alpha \cdot (Q - Q_{\min})^2}{P_M} \right]^{\gamma}$$

- Socially efficient quantity (price equal cost)

$$q_c = \left[ \frac{\alpha \cdot (Q - Q_{\min})^2}{c} \right]^{\gamma}$$

# Constant price purchase commitment

- Sponsor offers a fixed price P for any vaccine with efficacy above minimum quality demanded by the market (just high enough to induce investment or that has a fixed cost to the sponsor)
- Revenue received by developer $P \cdot q_c$
- Price is fixed, but size of the order depends on the quality of the vaccine
- Sponsor incurs in loss of P-c per unit supplied

# Variable Price Contract

Price-quantity schedule:

$$P = c + w \cdot \max\left(Q - Q_{\min}, 0\right)^{\delta}$$

Price depends on the efficacy of the vaccine. Sensitivity to efficacy depends on parameter $\delta$

$w$ is set high enough to induce investment

# Subsidy Contracts: for sponsor awards equal to $80 million

| | Full Discretionary Award | Co-payment Plan (96.52% sponsor co-pay) | Constant Price Purchase Commitment Plan | Variable Price Purchase Commitment Plan ($\delta$=0.25) |
|---|---|---|---|---|
| Sponsor PV Cost | -80 | -80 | -80 | -80 |
| Firm's Project PV | 36.25 | 11.48 | 12.72 | 6.89 |
| *CPISV* | -10.38 | -2.351 | -0.6051 | -0.5709 |
| Expected Consumer Surplus | 3.985 | 7.048 | 12.09 | 12.86 |
| Average Quantity Supplied | 0.5589 | 2.506 | 9.671 | 10.29 |
| Probability of Successful Vaccine Development | 3.464% | 54.82% | 34.65% | 42.51% |
| Average Vaccine Efficacy (if successful) | 92.0% | 82.87% | 85.19% | 84.33% |
| Probability of Advancing to Phase *II* R&D | 3.466% | 58.56% | 34.65% | 43.64% |

# Hybrid plans: variable price purchase commitment with co-payment

| δ=0.25 | Variable Price Purchase Commitment with 0% Co-payment | Variable Price Purchase Commitment with 50% Co-payment | Variable Price Purchase Commitment with 75% Co-payment | Variable Price Purchase Commitment with 90% Co-payment |
|---|---|---|---|---|
| Sponsor PV Cost | -80 | -80 | -80 | -80 |
| Firm's Project PV | 6.89 | 6.23 | 5.29 | 3.81 |
| *CPISV* | -0.5709 | -0.5681 | -0.5646 | -0.5600 |
| Expected Consumer Surplus | 12.86 | 12.92 | 13.01 | 13.13 |
| Average Quantity Supplied | 10.29 | 10.34 | 10.41 | 10.5 |
| Probability of Successful Vaccine Development | 42.51% | 43.42% | 44.69% | 46.62% |
| Average Vaccine Efficacy (if successful) | 84.33% | 84.22% | 84.06% | 83.83% |
| Probability of Advancing to Phase *II* R&D | 43.64% | 44.64% | 46.08% | 48.34% |

## Conclusion

- R&D valuation model with quality variable
- Research incentive design
- Purchase commitment plans (and hybrid plans) are more effective in terms of the cost per individual successfully vaccinated, consumer surplus and quantity supplied
- Simulation approach allows for more general demand functions and stochastic processes

## Extensions

- Agency conflicts
- Competition