

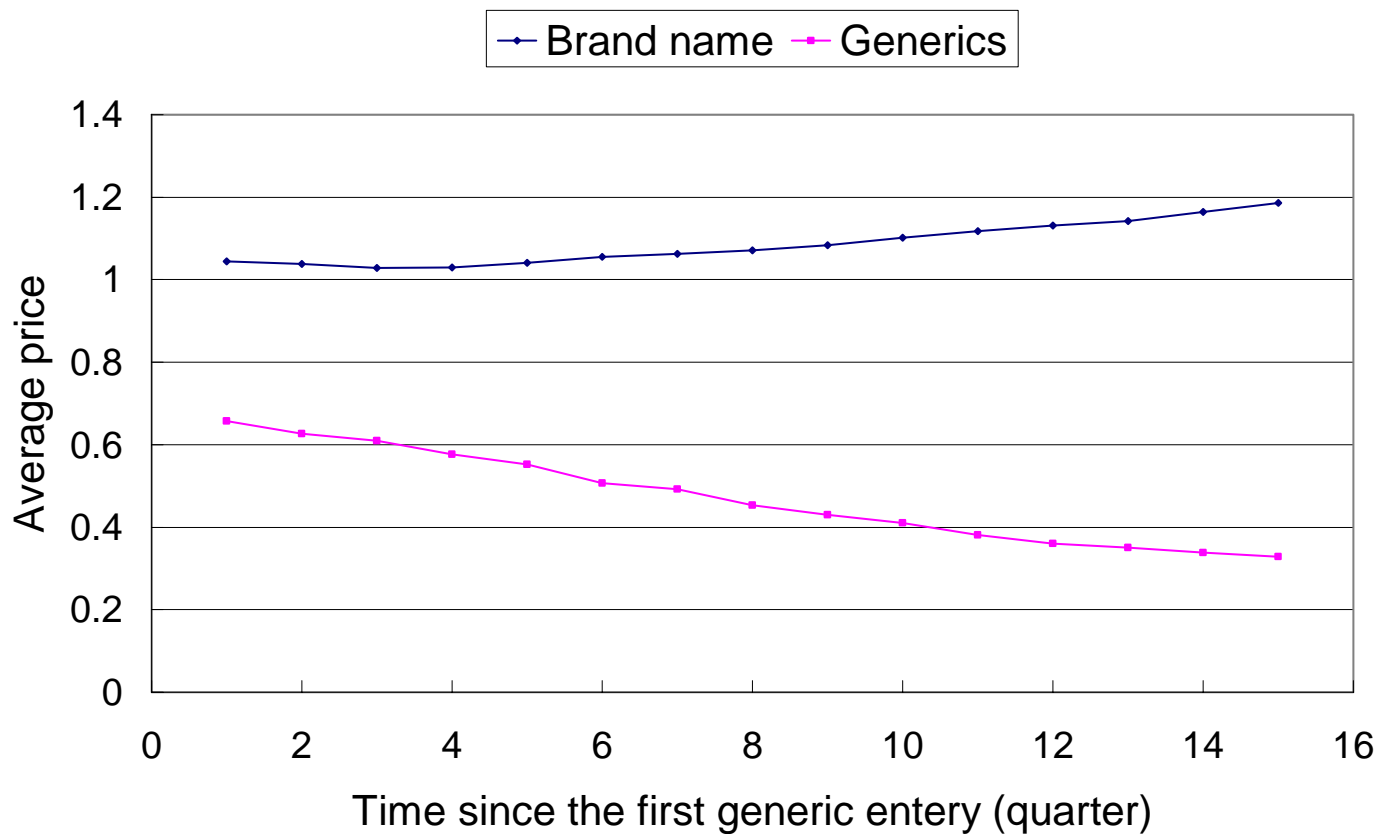
A Dynamic Oligopoly Structural Model for  
the Prescription Drug Market After Patent  
Expiration

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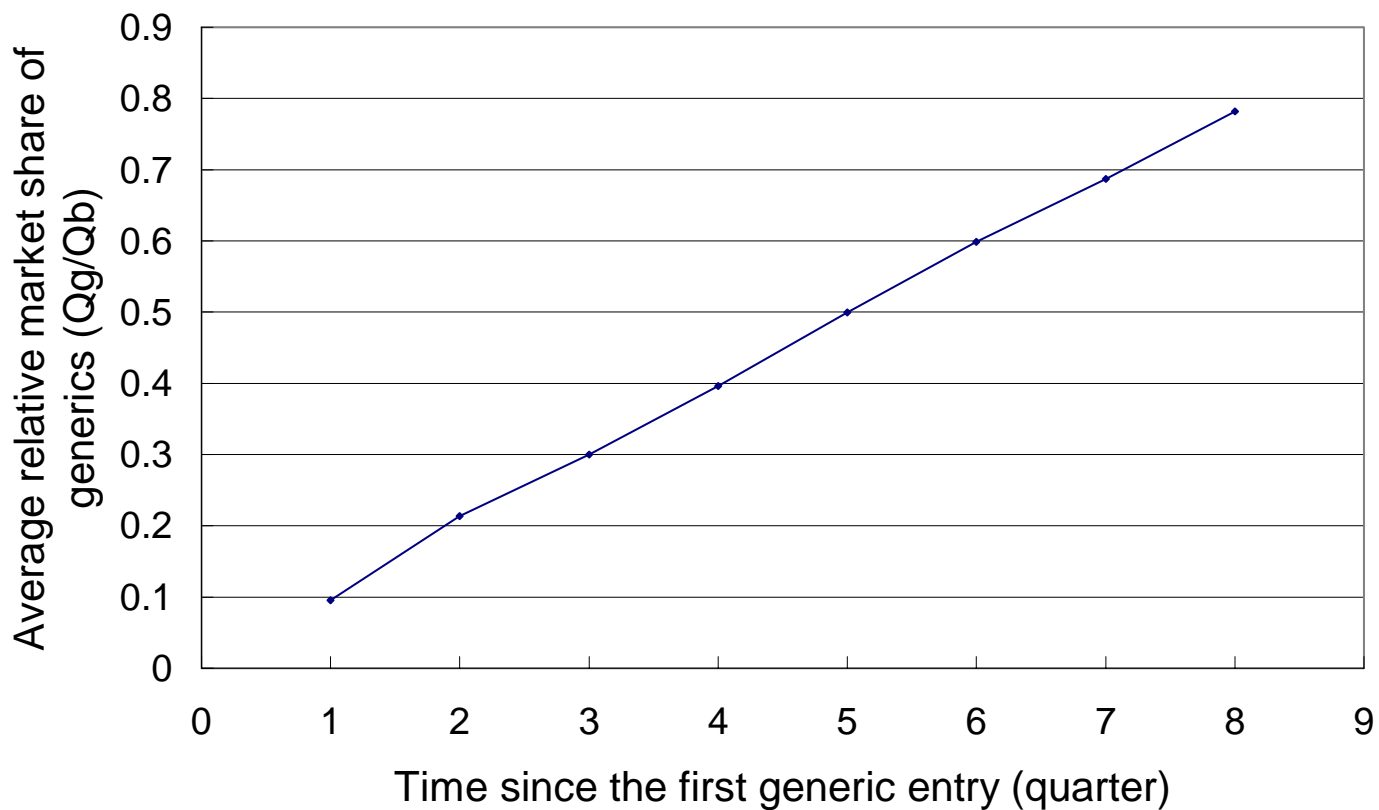
## Motivation:

- Prescription drug expenditures has increased by 17% a year for the past four years
  - In 1998, 93 billion dollars
  - In 2004, 188 billion dollars
- What does the government try to do?
  - bring generics to market sooner
  - FDA's generic division has received \$13 million increase in their budget since 2004, which allow them to hire 40 new reviewers.

Average price of brand name and generic drugs vs time



Average relative market share of generics vs time



## Stylized Facts:

- Slow diffusion of generics into the market
- Brand-name price rises in response to generic entry

## Stylized Facts suggest that:

- To explain diffusion: consumer learning
  - Mason and Bearden(1980), Carroll and Wolfgang(1991), Strutton et al.(1992)
- To explain pricing pattern: consumer heterogeneity
  - Grabowski and Vernon(1992), Frank and Salkever(1997)

- Generic drug approval process - random from firms' standpoint

“It takes more than 20 months on average for a new generic drug to be approved by the FDA, and it usually involves multiple review cycles. Only about 7% of applications are approved on the first cycle and about a third are approved on the second cycle.”

*Michelle Meadow, FDA Consumer Oct 2003*

“Each round of review means six months or more delay in approval”

*Mark McClellan, FDA Chief*

## Objective of Research

- Develop an empirical dynamic oligopoly model that incorporates consumer learning and consumer heterogeneity.
- Incorporate the random approval process.
- Estimate and calibrate the model – see if it can rationalize the stylized facts.
- Policy experiment:
  - speed up the approval process for generics.

To explain slow diffusion

- Consumer learning about the true quality
- Distribution channels
- Learning about the existence of generics

## Postpatent prescription drug market:

- Grabowski and Vernon (1992), Frank and Salkever (1997), Caves et al. (1991), Scott Morton (1999).

## Empirical dynamic oligopoly model:

- Ericson and Pakes (1995), Pakes and McGuire (1994), Gowrisankaran and Town (1997), Benkard (2002)

## Theoretical learning models:

- Rothschild (1974), McLennan (1984), Aghion et al. (1974), Harrington (1995), Keller and Rady (1998), Bergemann and Valimaki (2000)

## Road Map

- Model
- Data
- Estimation and Calibration
- Results
- Conclusion

## Model

- Four types of agents
  - patients, physicians, a brand-name firm and generic firms
- Three types of products
  - a brand-name drug, generic drugs, and an outside good.
- Initial period: the period immediately before the patent expired.
- No uncertainty about brand-name attribute.
- Firms and patients are uncertain about generic attributes.

- Consuming drugs provides noisy experience signals.
- Physicians as a whole play the role of an information aggregator (FDA):
  - pools signals together to update the public information set (Bayesian updating).
- Firms and patients have access to the public information set.

## Experience signal from consuming drugs

- Noisy experience signals:

$$\tilde{A}_{ijt} = A_j + \delta_{ijt},$$

where

$i$  indexes patient,

$j \in \{b, 1, 2, \dots, n_g\}$  indexes product,

$b$  - brand-name drug,

$1, \dots, n_g$  - generic drugs,

$t$  indexes time.

- Only  $\tilde{A}_{ijt}$  is perceived.
- All generics share the same  $A_j$ :

$$A_j = A_g, j = 1, 2, \dots, n_g.$$

## Learning about Generic Attribute

- Bayesian learning with risk aversion (Erdem and Keane(1996)).
- Assumption for noisy experience signals:

$$\delta_{ijt} \stackrel{iid}{\sim} N(0, \sigma_{\delta}^2).$$

- Initial prior for  $A_g$ :

$$A_g \sim N(A, \sigma_{A_g}^2(0)).$$

- Update the information set according to the Bayesian rule:

$$E[A_g|I(t+1)] = E[A_g|I(t)] + \beta_g(t)(\bar{A}_{gt} - E[A_g|I(t)]),$$

where  $\bar{A}_{gt}$  is the sample mean of experience signals revealed:

$$\bar{A}_{gt}|(q_{gt}, I(t)) \sim N(A_g, \frac{\sigma_\delta^2}{\kappa q_{gt}}),$$

where  $\kappa$  is the portion of experience signals revealed to physicians.

- Kalman gain coefficient:

$$\beta_g(t) = \frac{\sigma_{A_g}^2(t)}{\sigma_{A_g}^2(t) + \frac{\sigma_\delta^2}{\kappa q_{gt}}}.$$

- The perception variance at time  $t+1$ :

$$\sigma_{A_g}^2(t+1) = \frac{1}{\frac{1}{\sigma_{A_g}^2(t)} + \frac{\kappa q_{gt}}{\sigma_\delta^2}}.$$

## Demand

- Patients maximize current expected utility.
- Their choices follow a two-stage nested process:
  - (1) choose among brand-name drug, generic drugs and an outside good.
  - (2) if generic is chosen in the first stage, choose one of the generics.
- Indirect utility associated with generic drug  $j$ :
- Expected indirect utility associated with generic drug  $j$ :

$$U_{ijt} = -\alpha_i p_{jt} + \omega \tilde{A}_{ijt} - \omega r \tilde{A}_{ijt}^2 + \xi_{jt} + \zeta_{igt} + e_{ijt}.$$

$$\begin{aligned} E[U_{ijt}|I(t)] = & \\ & -\alpha_i p_{jt} + \omega E[A_g|I(t)] - \omega r E[A_g|I(t)]^2 \\ & -\omega r (\sigma_{A_g}^2(t) + \sigma_\delta^2) + \xi_{jt} + \zeta_{igt} + e_{ijt}. \end{aligned}$$

- Expected utility associated with outside good:

$$E[U_{i0t}|I(t)] = \phi_{i0} + \phi_{it}t + \tilde{e}_{i0t}.$$

- $\mu_2$  determines the variance of the symmetric unobserved product differentiation among generics.
- $\mu_2(t_e) = \bar{\mu}_2 \exp(-\iota t_e)$ , where  $t_e$  is time since the first generic entry.

## Consumer Heterogeneity

- $\alpha_i, \phi_{0i}, \phi_{0ti}$  are discrete multinomial with  $K$  types. Assume that there are only two types.

- Population proportions of each type:

$$\pi_k = Pr(\alpha_i = \alpha^k, \phi_{0i} = \phi_0^k, \phi_{0ti} = \phi_{0t}^k).$$

- $e_{ijt}$  is *i.i.d.* extreme value distributed.

## Supply side

- Firms are forward-looking and solve their dynamic programming problems.
- Markov-perfect Nash Equilibrium.
- In each period
  - Brand-name firm moves first.
  - Generic firms take brand-name price as given, choose prices simultaneously.
- Marginal cost is constant.

- All generic entry decisions are made in the period immediately before the patent expired.
- The nature draws  $A_g$  from  $N(A, \sigma_{A_g}^2(0))$ .
- Large number of generic firms decide sequentially whether to enter.
- A generic firm pays a sunk cost of entry if it decides to enter.
- It cannot enter until it receives an approval from the FDA.
- Approval process is random from firms' point of view,  $\lambda(t)$  is the probability that a generic firm receives the approval.
- A generic firm that is still waiting for the FDA to approve its application is referred to a *potential generic entrant*.

- Probability that  $k$  out of  $m$  potential generic entrants are approved to enter in period  $t$ :

$$P_e(k, n_{pt-1} = m, t) = \binom{m}{k} \lambda(t)^k (1 - \lambda(t))^{m-k},$$

where  $n_{pt}$  is the number of potential generic entrants in period  $t$ .

- State space:  $E[A_g|I(t)]$ ,  $\sigma_{A_g}(t)$ , number of generic entrants ( $n_{gt}$ ), number of potential generic entrants ( $n_{pt}$ ), time since the first generic entry ( $t_e$ ).

## Data

- Data on quantity sold and revenue for brand-name drugs and generic drugs from IMS America.
- Quarterly observations on combined drug-store and hospital sales from 1984-1990.
- Patent expiration dates obtained from the FDA.
- Approval dates for generic drugs obtained from the FDA.
- Size of the market from National Ambulatory Medical Care Survey and National Hospital Discharge Survey.
- Daily Defined Dose and Average Treatment Duration from Medispan's Price-Trek database.

## Estimation and Calibration

- Demand side parameters are estimated from another paper (Ching (2005))
  - Patients are risk-averse.
  - Learning plays an important role in explaining the slow diffusion of generics.
- Calibrate  $\bar{\mu}_2$  and  $\iota$  to match the decline of generic prices.
- Entry probability ( $\lambda(t)$ ) is determined by a logit model.
- Sunk costs of entry: Choose the value such that the predicted number of applications is the same as the observed number (zero profit condition).
- Marginal costs: set to zero initially.

- Estimate  $A_g$ ,  $((\pi_k, \sigma_e^k, \alpha^k, \phi_0^k, \phi_{0t}^k)_{k=0,1}, \omega, r, \kappa, \sigma_\delta, \sigma_\zeta)$  and  $(A, \sigma_{A_g}(0))$
- Treating product/quarter as one observation, the total number of observation for heart disease drugs is 300, and the number of structural parameters is 51.

Table 1: Estimated Preference parameters for clonidine

|  | Estimate | Standard Error |
|--|----------|----------------|
| <b>ESTIMATED PARAMETERS</b>  |          |                |
| <b>Learning parameters:</b>  |          |                |
| risk coefficient ( $r$ )   | 0.731*   | 0.036          |
| utility weight for attribute ( $\omega$ )                                | 0.014*   | 0.001          |
| experience variability ( $\sigma_\delta^2$ )                             | 0.18*    | 0.02           |
| initial prior variance ( $\sigma_{A_g}^2(0)$ )                           | 33.31*   | 0.88           |
| initial prior mean ( $A$ )   | -17.77*  | 0.05           |
| True mean attributes ( $A_g$ )   | -5.77*   | 0.10           |
| Fraction of experience signals revealed ( $\kappa$ )                     | 7.1e-11* | 7.7e-13        |
| <b>Consumer heterogeneity parameters:</b>                                |          |                |
| type 0 price coefficient ( $\alpha^0$ )                                  | 0.029*   | 3.0e-4         |
| type 1 price coefficient ( $\alpha^1$ )                                  | 0.010*   | 1.0e-4         |
| proportion of type 0 ( $\pi_0$ )   | 0.367*   | 0.005          |
| standard deviation of unobserved product characteristic ( $\sigma_\xi$ ) | 0.237*   | 0.008          |
| <b>Time trend for the outside good:</b>                                  |          |                |
| type 0 ( $\phi_t^0$ )  | 0.146*   | 0.001          |
| type 1 ( $\phi_t^1$ )  | -0.008   | 0.016          |
| <b>CALIBRATED PARAMETERS**</b>   |          |                |
| <b>Parameters for the variance of logit errors:</b>                      |          |                |
| <i>first stage:</i> ( $\mu_1$ )  | 1.0      |                |
| <i>second stage:</i>   |          |                |
| constant term ( $\bar{\mu}_2$ )  | 0.7      |                |
| coefficient for time trend ( $\iota$ )                                   | 0.1      |                |
| <b>Other supply side parameters:</b>                                     |          |                |
| Sunk cost of entry (million, 1990 dollar)                                | 1.2      |                |
| Marginal cost of production (mc)   | 0.0      |                |
| Discount factor ( $\beta$ )  | 0.9      |                |

Standard errors are reported in parenthesis

Notes:

\* t-statistic > 1.96

\*\* Standard errors for calibrated parameters are not reported.

Table 2: Estimated parameters for Entry Probability

|   | estimate | standard error |
|---|----------|----------------|
| intercept ( $\gamma_0$ )                              | -2.636*  | 0.201          |
| time since patent expired ( $\gamma_1$ )              | 0.051    | 0.049          |
| time since patent expired <sup>2</sup> ( $\gamma_2$ ) | 0.006*   | 0.003          |

Probability that a potential generic entrant receives approval,

$$\lambda = \frac{\exp(X\gamma)}{1 + \exp(X\gamma)}$$

Notes:

\* significant at 5% level

\*\* significant at 10% level

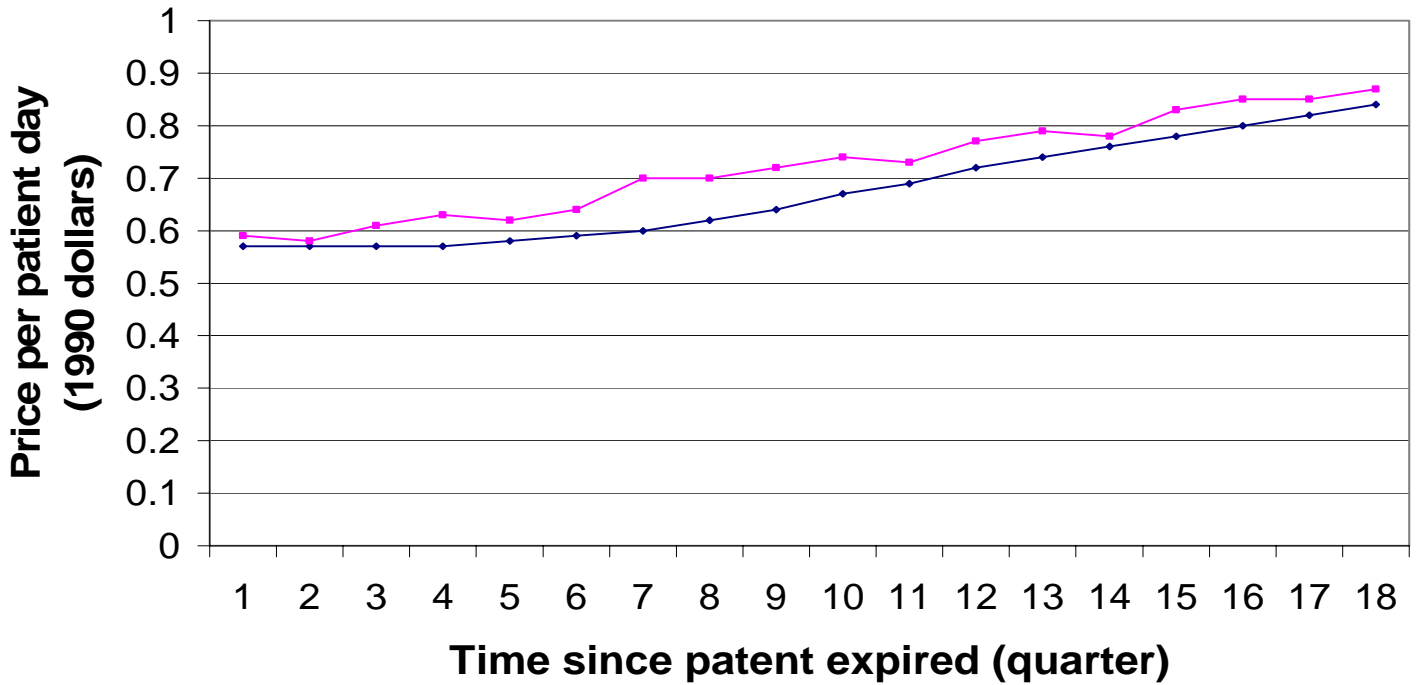
## Simulation

- The equilibrium number of applicants is 12.
- Simulate 100 sequences of number of generics  $\{n_{gt}, n_{pt}\}_{t=1}^T$  over time.
- For each sequence of  $\{n_{gt}, n_{pt}\}_{t=1}^T$ , simulate 100 sequences of  $\{p_t, q_t\}_{t=1}^T$ .
- Altogether  $100 \times 100 = 10,000$  simulated market histories.

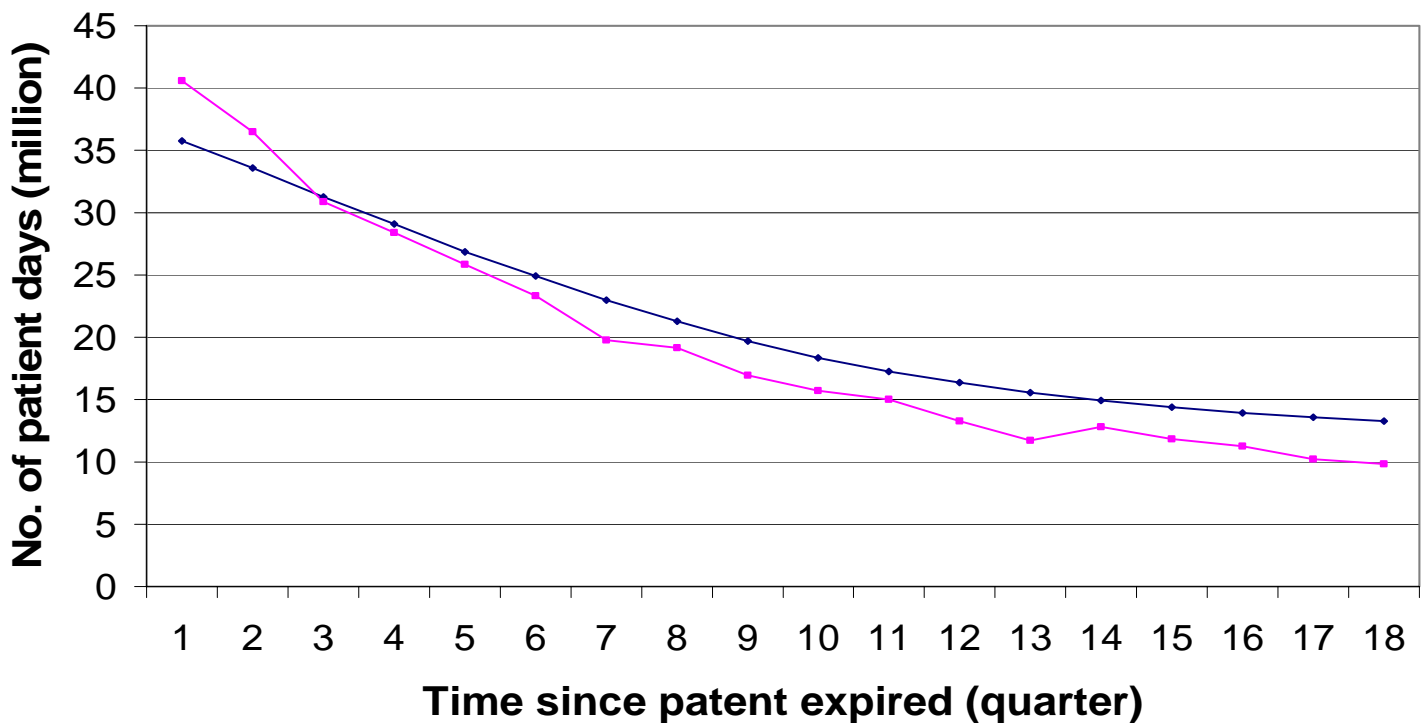
# Goodness of Fit

—◆— Average of simulated data    —■— Actual data

## Brand-name Price



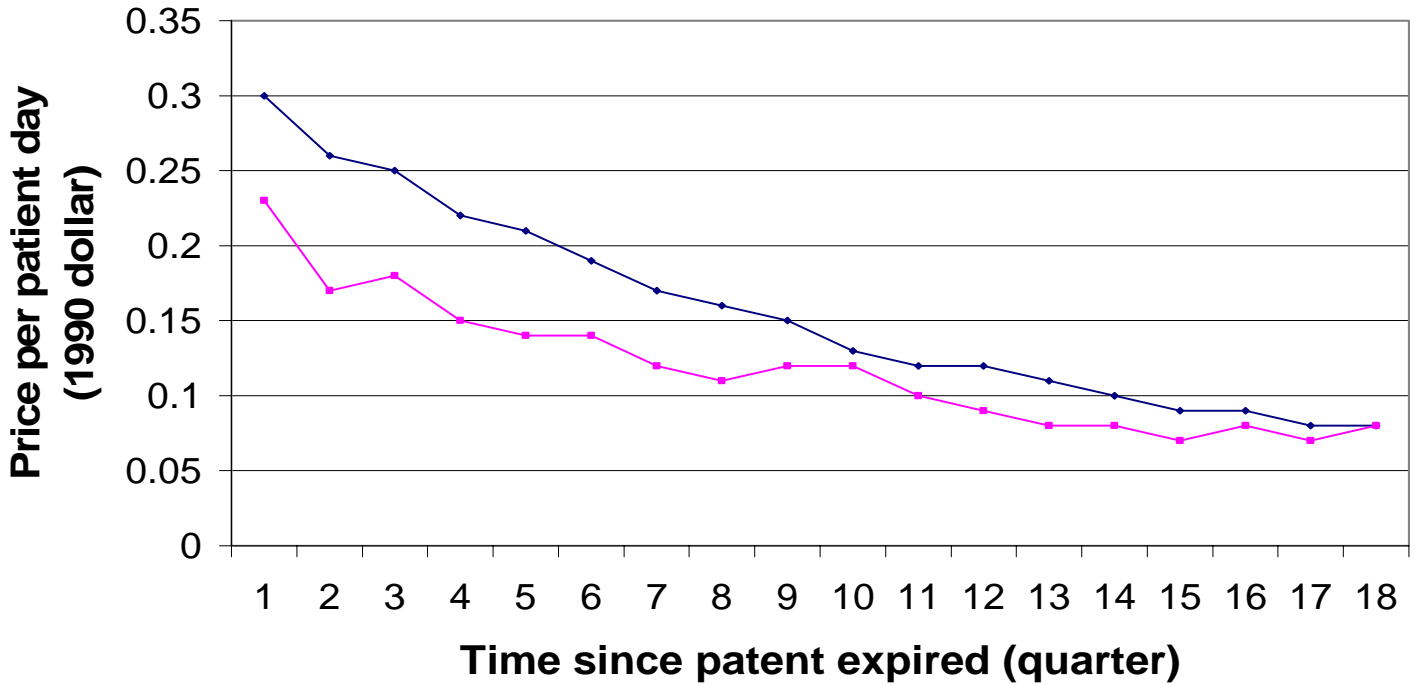
## Brand-name Demand



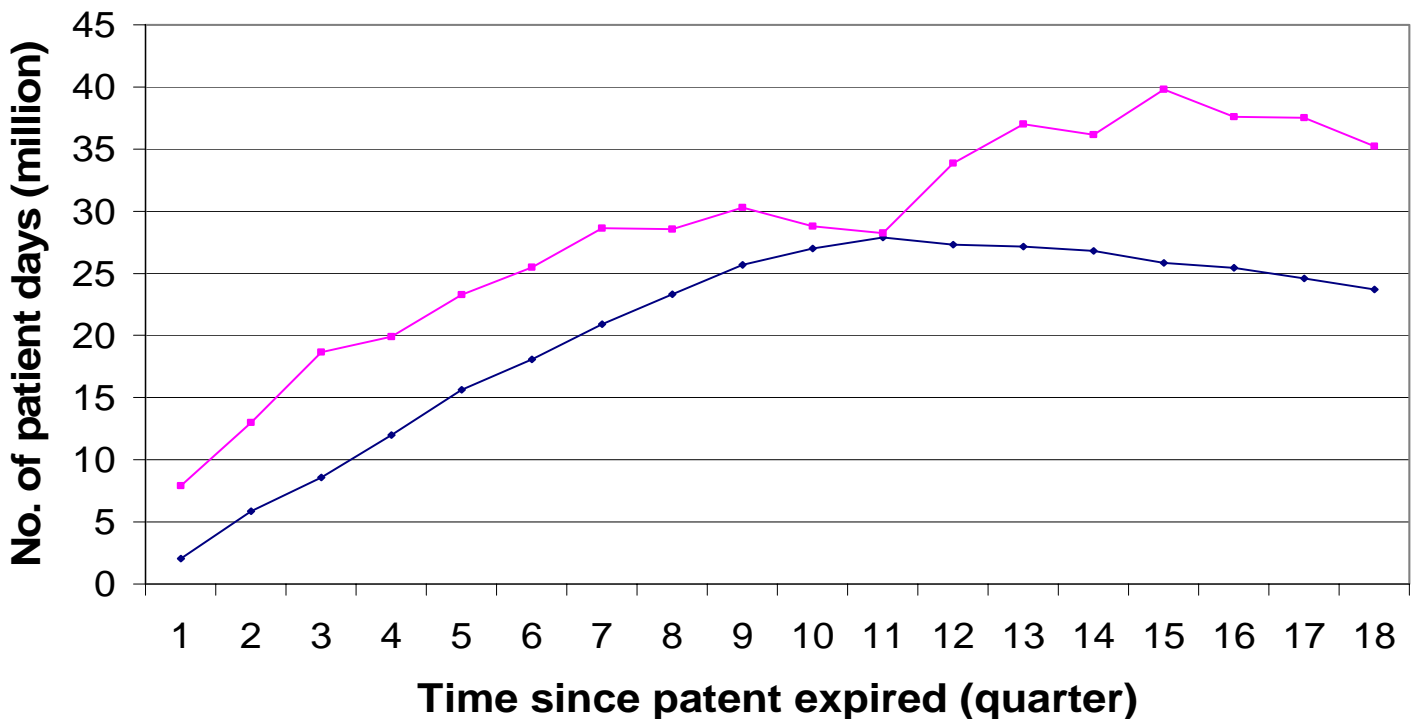
# Goodness of Fit

— Average of simulated data — Actual data

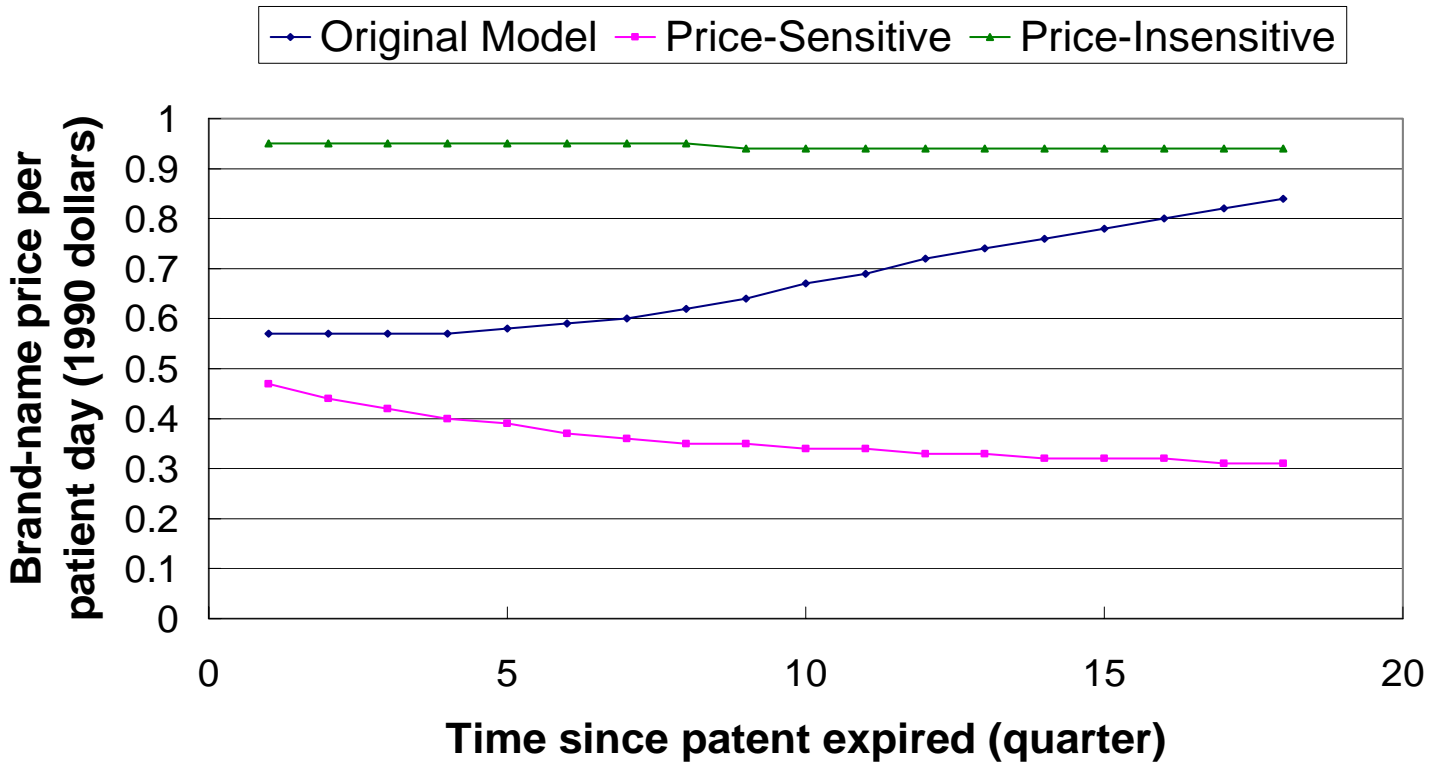
## Generic Price



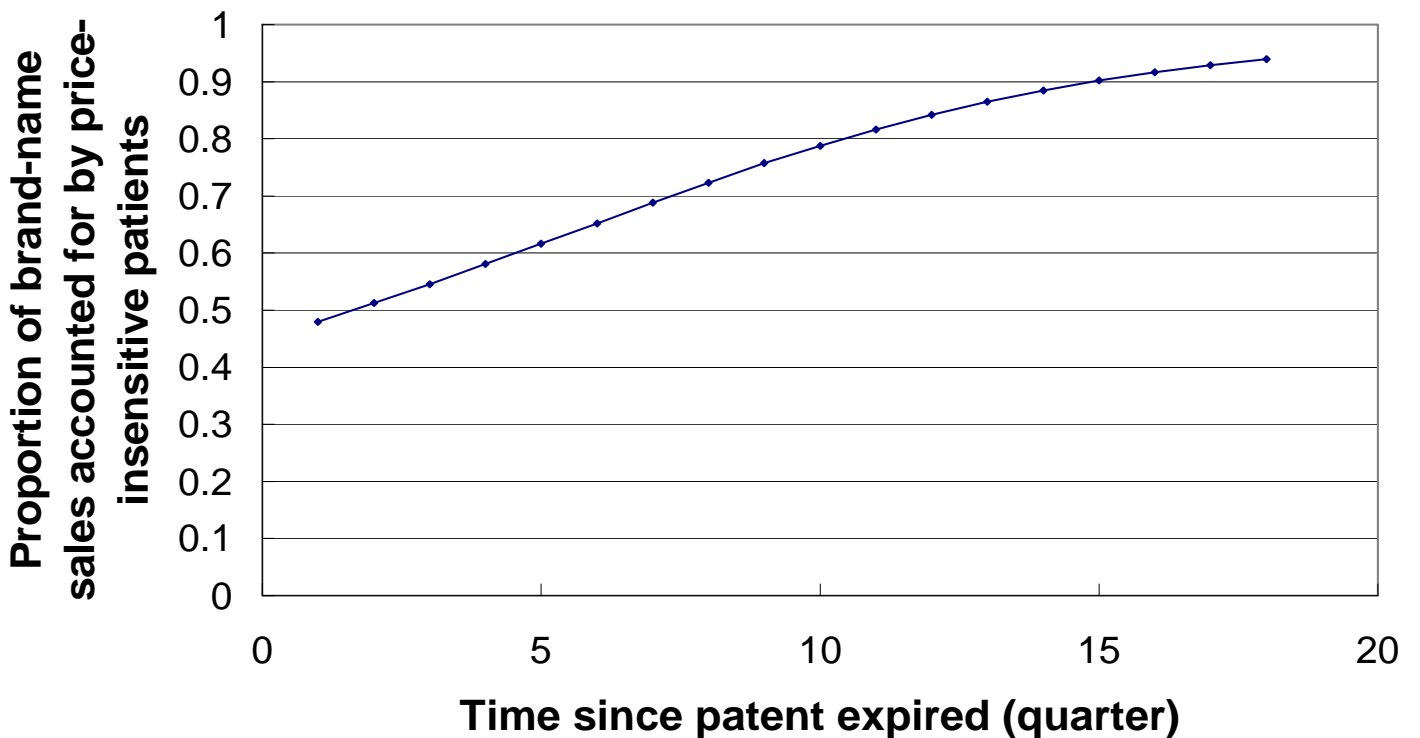
## Generic Demand



### Brand-name prices from the original model, and models with only one patient type



### Proportion of brand-name sales accounted for by price-insensitive patients



Policy experiment: speed up the approval process

- Increase  $\gamma_0$  from -2.63 to -1.0.
- Initial probability of entry for each generic increases from 0.07 to 0.27.

Table 4: Welfare and Market Characteristics: Experiment with Reducing the Expected Approval Time and Myopic Firms

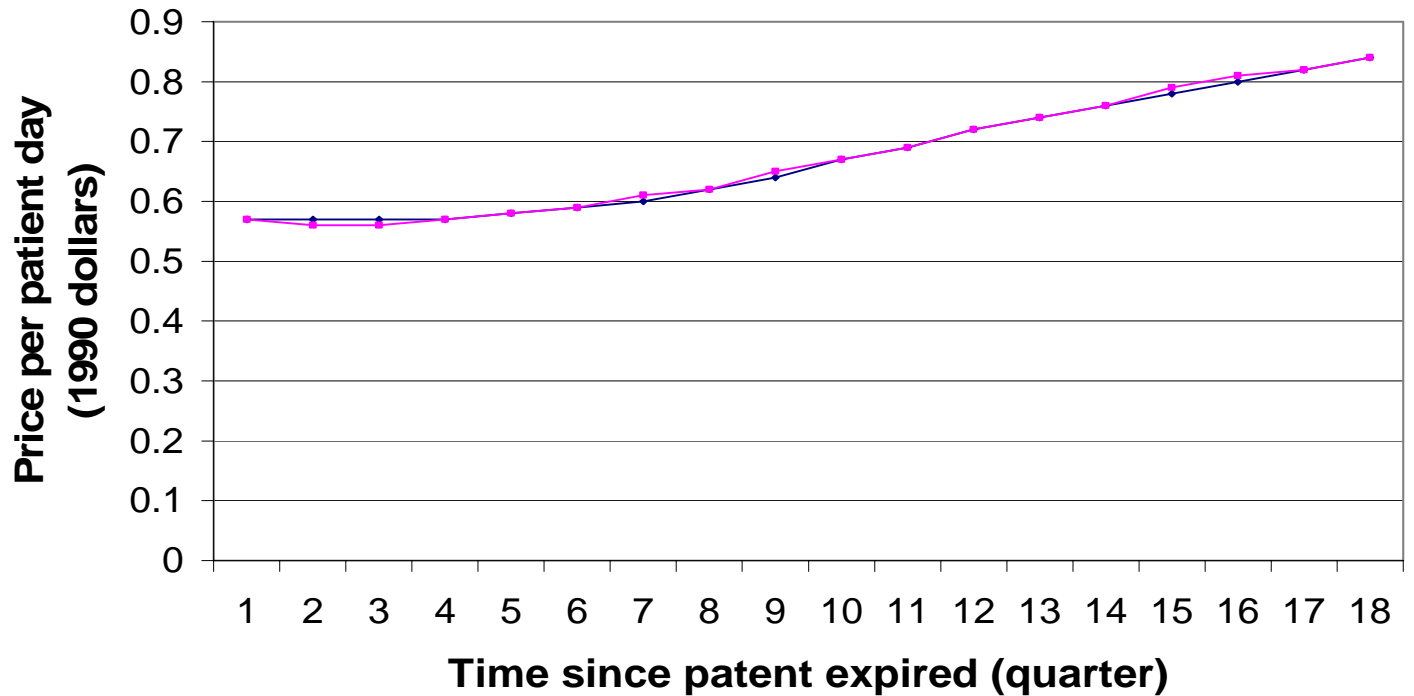
|  | Original Model<br>( $\beta = 0.9$ ) | Reducing<br>Approval Time | Myopic<br>( $\beta = 0$ ) |
|--|-------------------------------------|---------------------------|---------------------------|
| <b>Welfare Statistics:</b>   |                                     |                           |                           |
| <i>Average quarterly producer surplus (M*\$):</i>                      |                                     |                           |                           |
| Brand-name   | 13.9                                | 13.8                      | 14.0                      |
| Generic  | 0.46                                | 0.49                      | 0.46                      |
| Combined   | 14.36                               | 14.29                     | 14.46                     |
| <i>Average quarterly consumer surplus (M\$):</i>                       |                                     |                           |                           |
| Price-sensitive patient  | 5.7                                 | 6.0                       | 5.6                       |
| Price-insensitive patient  | 109.4                               | 109.9                     | 109.3                     |
| Combined   | 115.1                               | 115.9                     | 114.9                     |
| <i>Average total quarterly surplus (M\$):</i>                          | 129.5                               | 130.2                     | 129.3                     |
| <b>Market Characteristics:</b>   |                                     |                           |                           |
| <i>Average brand-name prices<br/>(\$ per patient day):</i>             |                                     |                           |                           |
| 1st quarter  | 0.57                                | 0.57                      | 0.57                      |
| 9th quarter  | 0.64                                | 0.65                      | 0.65                      |
| 18th quarter   | 0.84                                | 0.84                      | 0.84                      |
| <i>Average generic price<br/>(\$ per patient day):</i>                 |                                     |                           |                           |
| 1st quarter  | 0.30                                | 0.28                      | 0.35                      |
| 9th quarter  | 0.15                                | 0.14                      | 0.15                      |
| 18th quarter   | 0.08                                | 0.07                      | 0.08                      |
| <i>Average quarterly brand-name sales<br/>(M no. of patient days):</i> |                                     |                           |                           |
| 1st quarter  | 35.8                                | 35.6                      | 35.8                      |
| 9th quarter  | 19.7                                | 19.5                      | 19.7                      |
| 18th quarter   | 13.3                                | 13.4                      | 13.3                      |
| <i>Average quarterly generic sales<br/>(M no. of patient days):</i>    |                                     |                           |                           |
| 1st quarter  | 2.0                                 | 2.7                       | 1.8                       |
| 9th quarter  | 25.7                                | 27.3                      | 25.5                      |
| 18th quarter   | 23.7                                | 22.7                      | 23.6                      |

\*M stands for million.

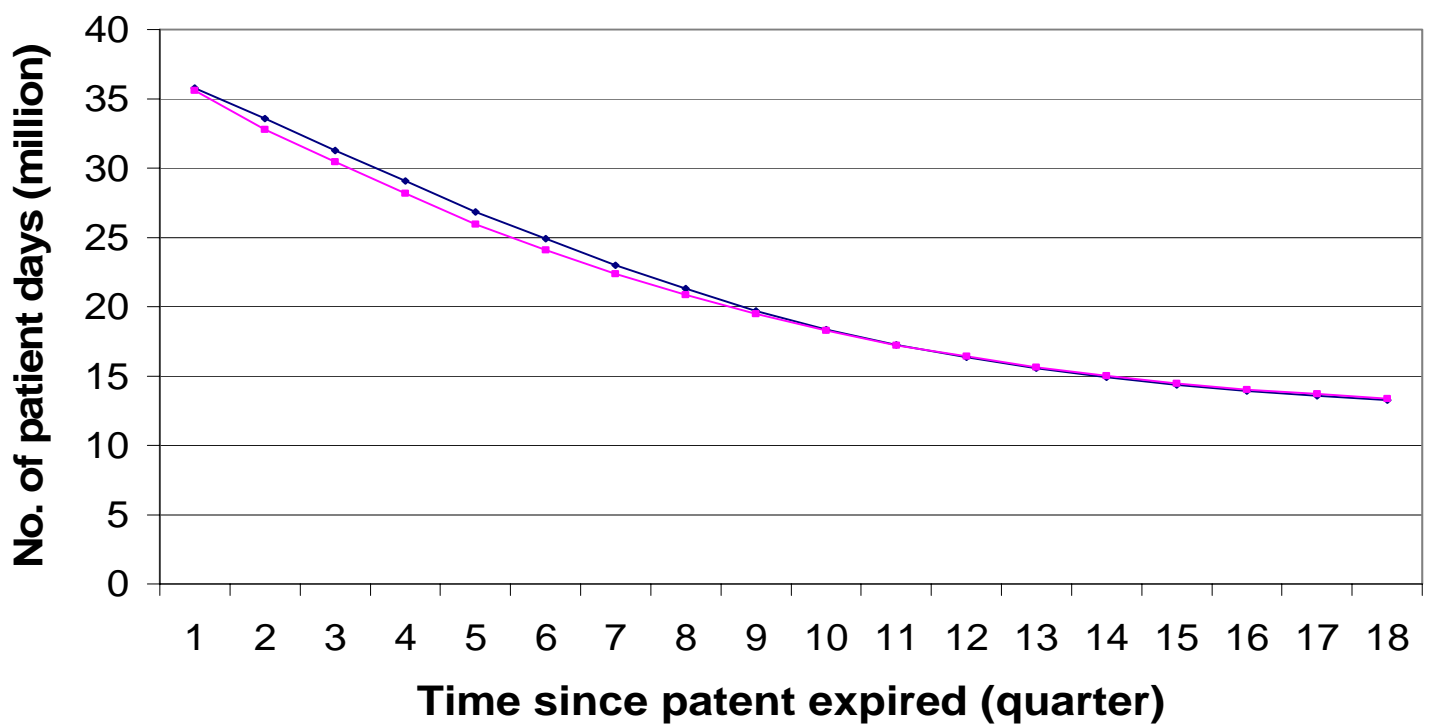
# Comparison between Original Model and Policy Experiment

Original Model Experiment: increase entry probability

## Brand-name Price



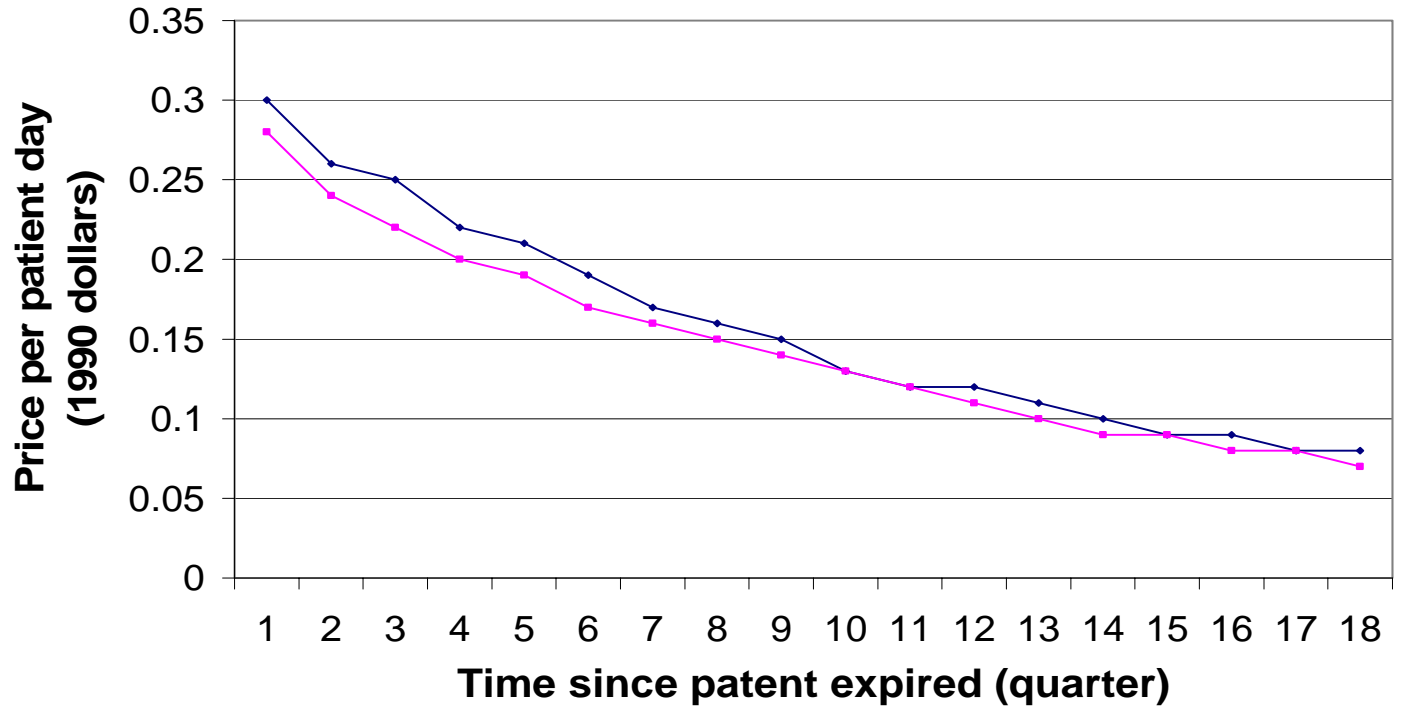
## Brand-name Demand



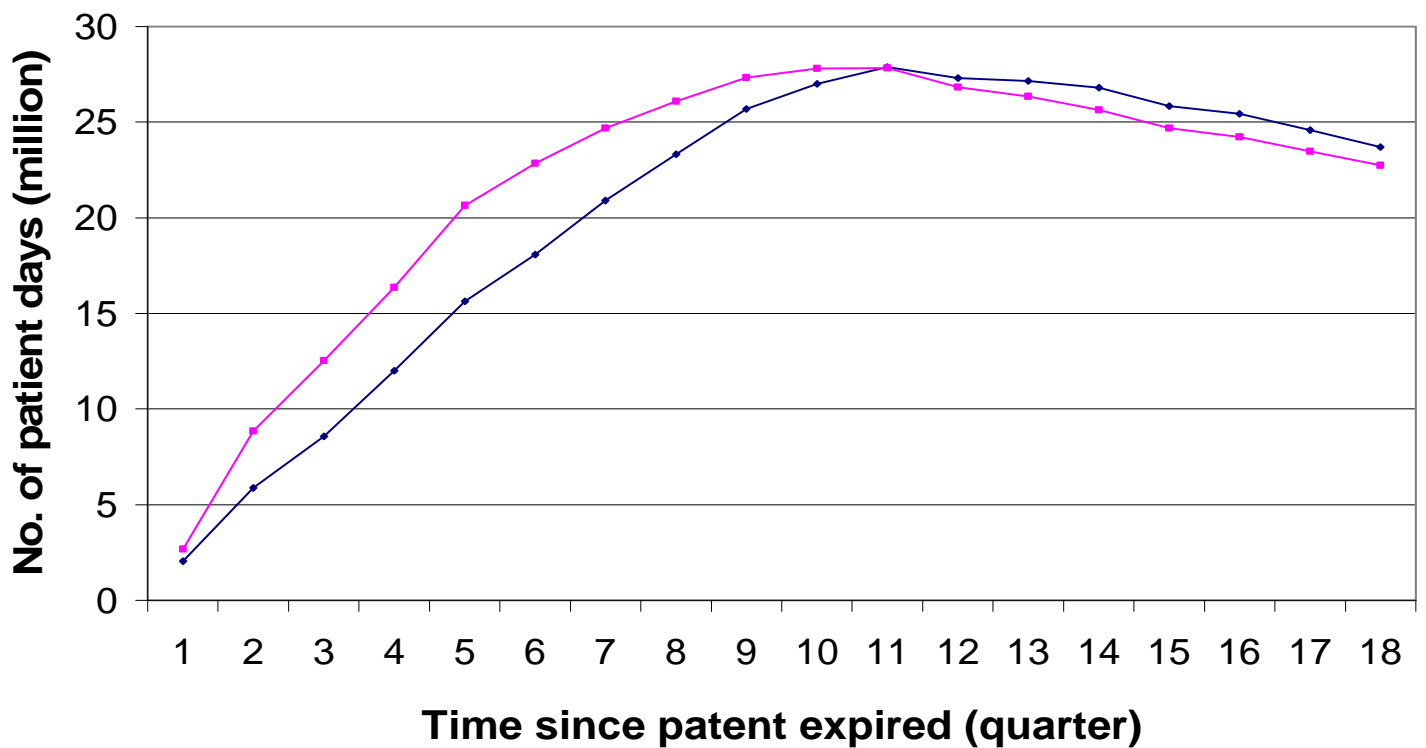
# Comparison between Original Model and Policy Experiment

Original Model Experiment: increase entry probability

## Generic Price



## Generic Demand



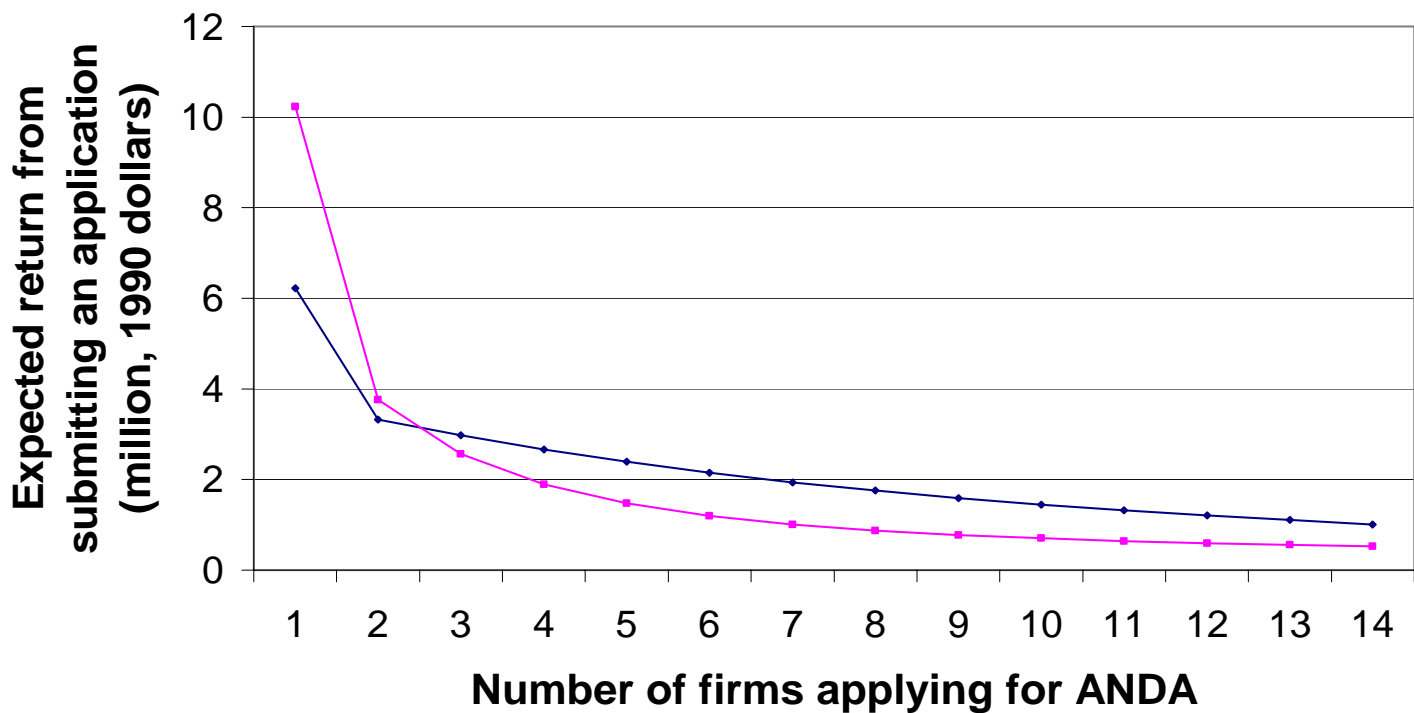
## Implications of the experiment:

- (i) Bring each applicant to the market sooner  
 $\Rightarrow \uparrow$  expected profits.
- (ii) Increase the likelihood that an applicant would enter a market crowded with competitors in the early periods  $\Rightarrow \downarrow$  expected profits.

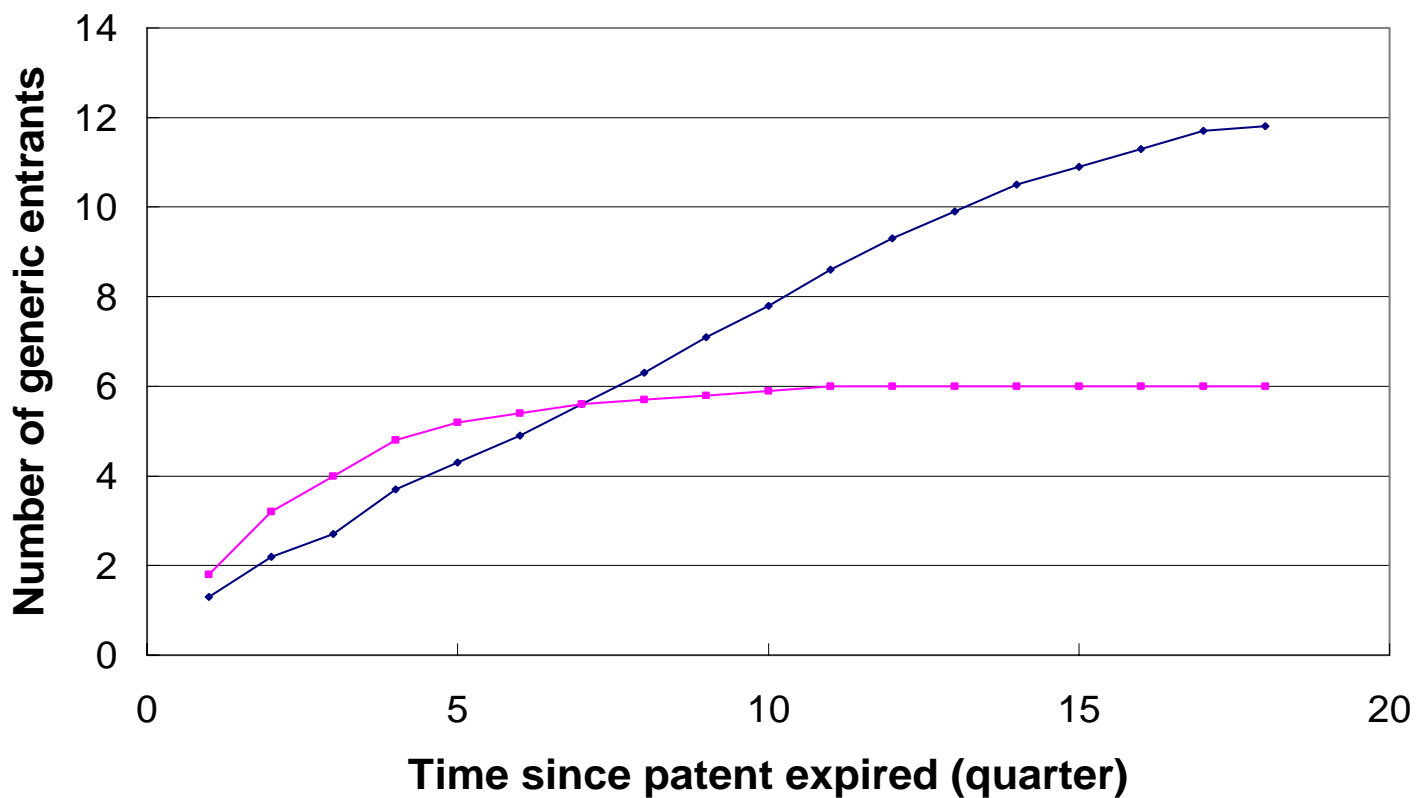
(ii) dominates (i) when the number of applicants is large, and vice versa.

Original Model Experiment: increase entry probability

### Expected return from submitting an ANDA application

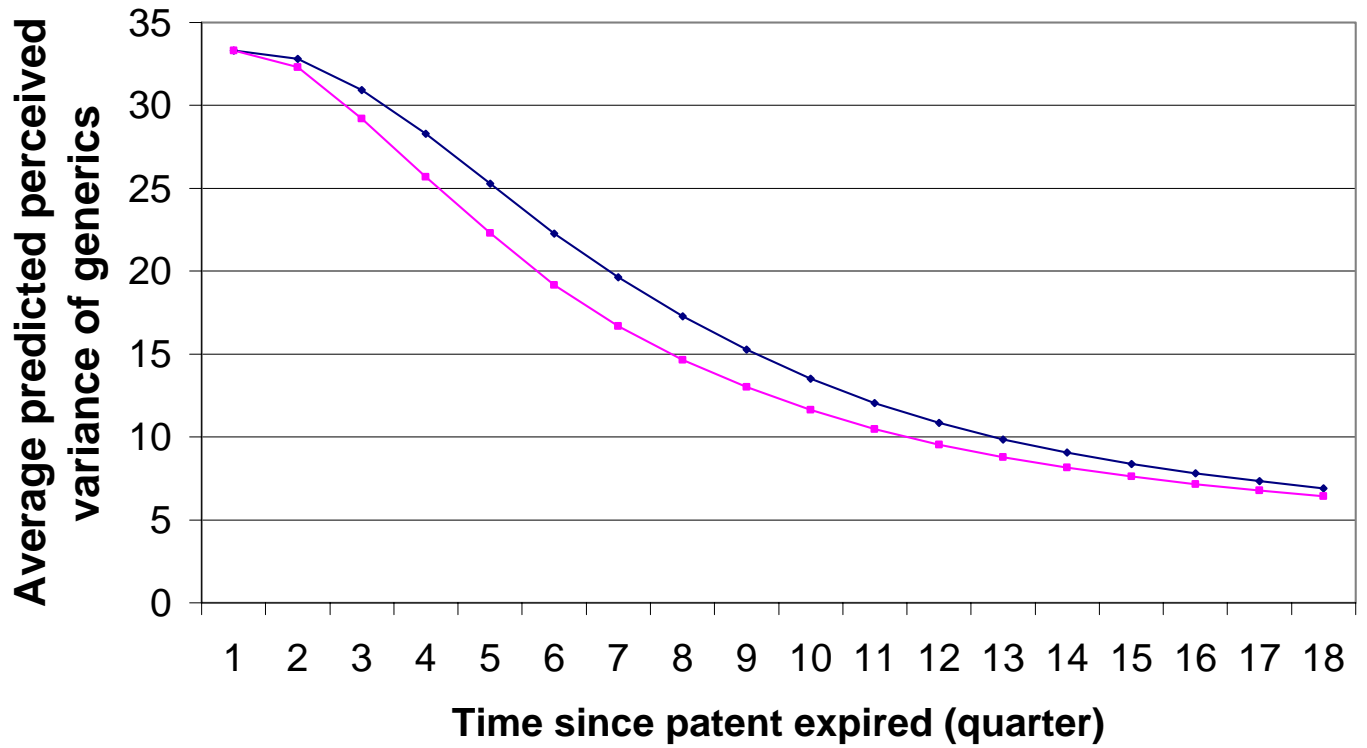


### Average number of generic entrants



Original Model Experiment: increase entry probability

### Average predicted perceived variance



## Results of the experiment:

- generic firms arrive in the market sooner on average.
- reduces the number of generic entrants from 12 to 6.
- increases the rate of learning by about 10%.

- Modified Parameters

- Slightly reduce the time trend for the outside good associated with the price-sensitive consumers.
- Slightly reduce the parameter values that determine the variance of the second stage logit errors.

- Robustness

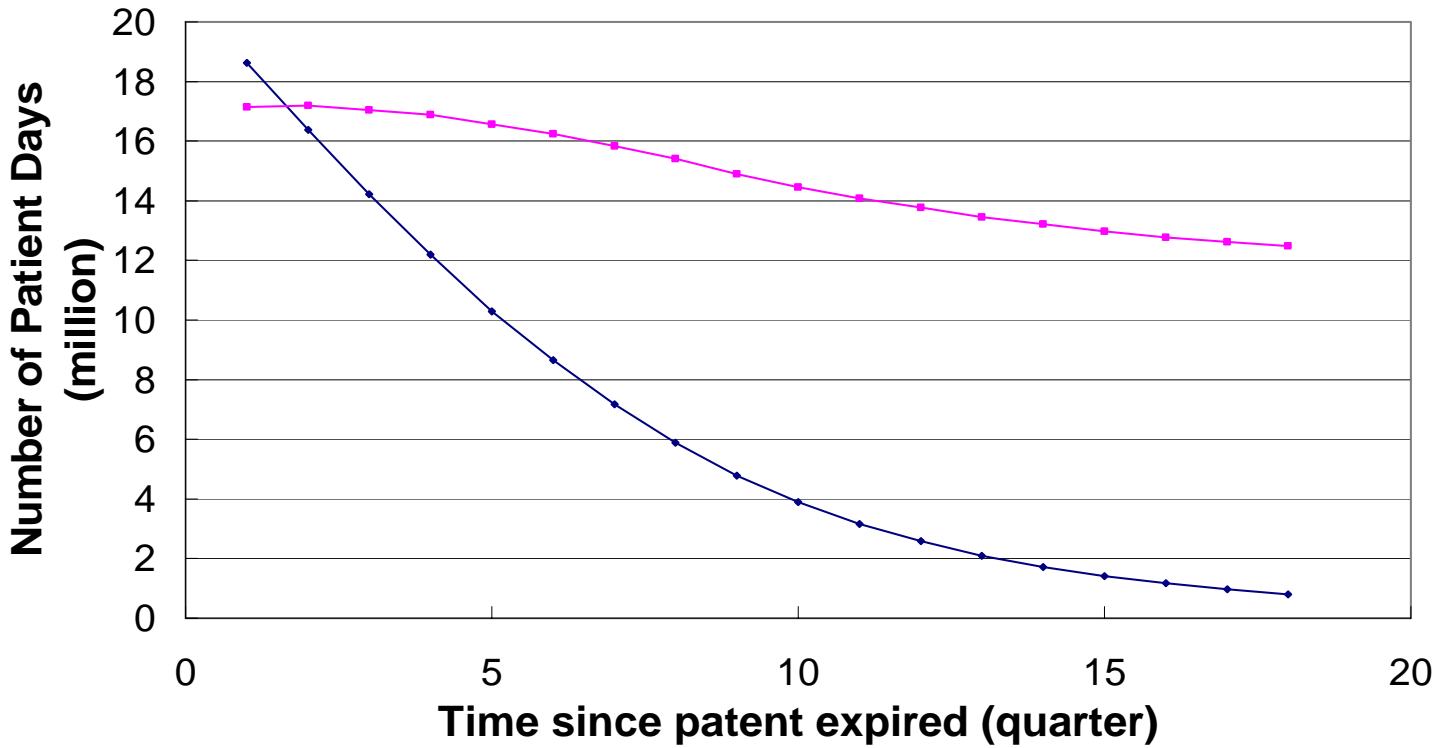
- $\beta = 0$
- $mc = 4, mc = 8$

## Conclusion

- Dynamic Equilibrium model is capable of generating the observed pricing and diffusion patterns.
- Speeding up the generic approval process might not benefit consumers.
- It is important to use an equilibrium framework to conduct policy analysis in this market.

Price-sensitive consumers Price-insensitive consumers

### Brand-name demand by consumer type



### Generic demand by consumer type

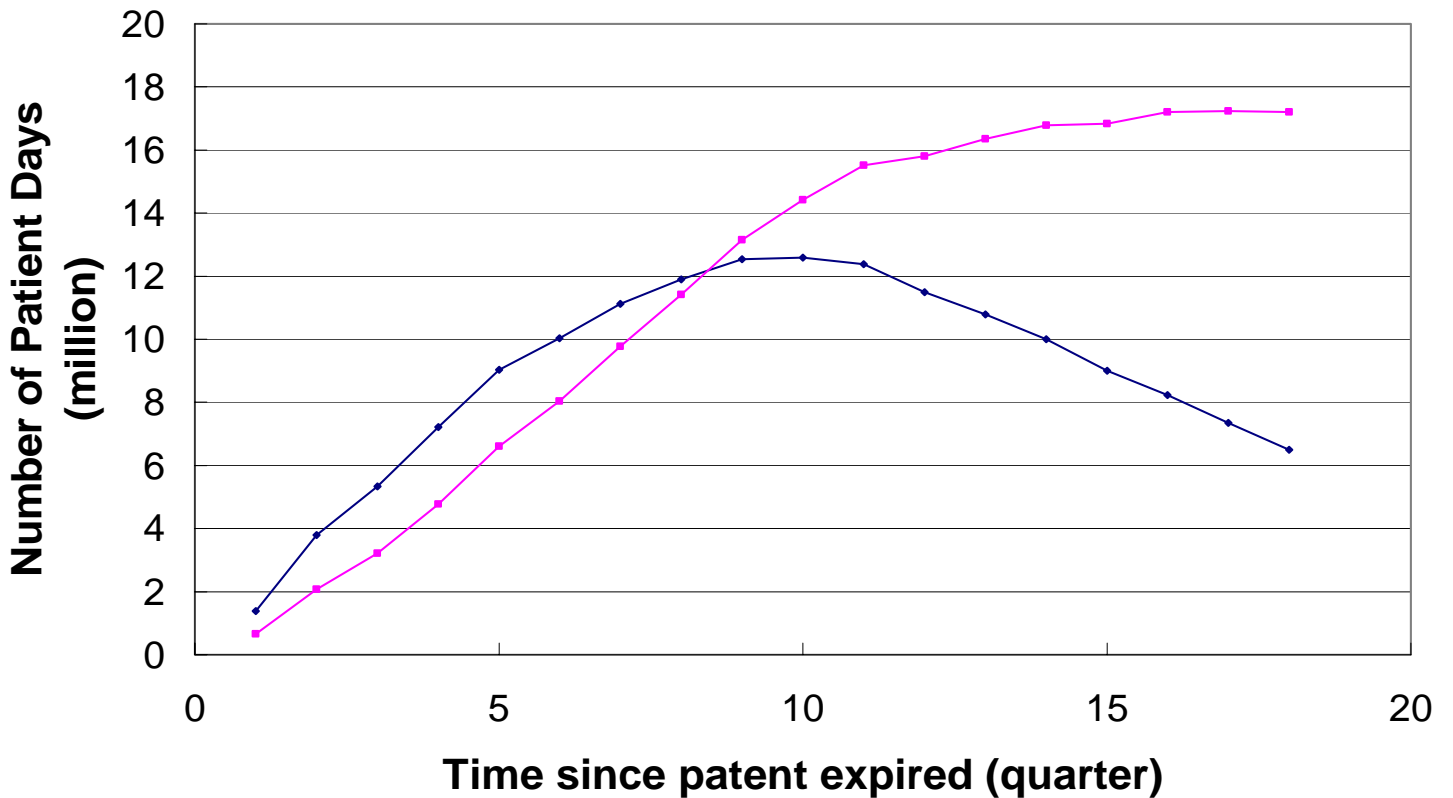


Table 3: Welfare and Market Characteristics: Original Model, Model with Only Price-sensitive Patients, and Model with Only Price-insensitive Patients

|  | Data* | Original Model | Only Price-sensitive Patients | Only Price-insensitive Patients |
|--|-------|----------------|-------------------------------|---------------------------------|
| <b>Welfare Statistics:</b>   |       |                |                               |                                 |
| <i>Average quarterly producer surplus (M**\$):</i>                 |       |                |                               |                                 |
| Brand-name   | n.a.  | 13.9           | 12.7                          | 17.4                            |
| Generic  | n.a.  | 0.46           | 0.52                          | 0.46                            |
| Combined   | n.a.  | 14.36          | 13.22                         | 17.86                           |
| <i>Average quarterly consumer surplus (M\$):</i>                   |       |                |                               |                                 |
| Price-sensitive patient  | n.a.  | 5.7            | 24.6                          | n.a.                            |
| Price-insensitive patient  | n.a.  | 109.4          | n.a.                          | 160.7                           |
| Combined   | n.a.  | 115.1          | 24.6                          | 160.7                           |
| <i>Average total quarterly surplus (M\$):</i>                      | n.a.  | 129.5          | 37.8                          | 160.7                           |
| <b>Market Characteristics:</b>                                     |       |                |                               |                                 |
| <i>Average brand-name prices (\$ per patient day):</i>             |       |                |                               |                                 |
| 1st quarter  | 0.59  | 0.57           | 0.47                          | 0.95                            |
| 9th quarter  | 0.72  | 0.64           | 0.35                          | 0.94                            |
| 18th quarter   | 0.87  | 0.84           | 0.31                          | 0.94                            |
| <i>Average generic price (\$ per patient day):</i>                 |       |                |                               |                                 |
| 1st quarter  | 0.23  | 0.30           | 0.24                          | 0.71                            |
| 9th quarter  | 0.12  | 0.15           | 0.10                          | 0.28                            |
| 18th quarter   | 0.08  | 0.08           | 0.04                          | 0.12                            |
| <i>Average quarterly brand-name sales (M no. of patient days):</i> |       |                |                               |                                 |
| 1st quarter  | 40.6  | 35.8           | 64.7                          | 18.5                            |
| 9th quarter  | 15.7  | 19.7           | 28.8                          | 18.3                            |
| 18th quarter   | 9.8   | 13.3           | 12.5                          | 18.3                            |
| <i>Average quarterly generic sales (M no. of patient days):</i>    |       |                |                               |                                 |
| 1st quarter  | 7.9   | 2.0            | 4.0                           | 0.7                             |
| 9th quarter  | 28.8  | 25.7           | 44.0                          | 12.0                            |
| 18th quarter   | 35.2  | 23.7           | 21.0                          | 22.0                            |

\*Prices and sales in the "Data" column are the actual observed ones for clonidine.

\*\*M stands for million.

Table 5: Welfare and Market Characteristics: Sensitivity Analysis

|  | Original Model<br>(mc=0) | Modified<br>Parameters | mc=4  | mc=8  |
|--|--------------------------|------------------------|-------|-------|
| <b>Welfare Statistics:</b>   |                          |                        |       |       |
| <i>Average quarterly producer surplus (M*\$):</i>                      |                          |                        |       |       |
| Brand-name   | 13.9                     | 14.3                   | 14.1  | 14.1  |
| Generic  | 0.5                      | 0.4                    | 0.5   | 0.6   |
| Combined   | 14.4                     | 14.7                   | 14.6  | 14.7  |
| <i>Average quarterly consumer surplus (M\$):</i>                       |                          |                        |       |       |
| Price-sensitive patient  | 5.7                      | 3.1                    | 5.1   | 4.5   |
| Price-insensitive patient  | 109.4                    | 109.9                  | 108.2 | 106.9 |
| Combined   | 115.1                    | 113.0                  | 113.3 | 111.4 |
| <i>Average total quarterly surplus (M\$):</i>                          | 129.5                    | 127.7                  | 127.9 | 126.1 |
| <b>Market Characteristics:</b>   |                          |                        |       |       |
| <i>Average brand-name prices<br/>(\$ per patient day):</i>             |                          |                        |       |       |
| 1st quarter  | 0.57                     | 0.57                   | 0.60  | 0.63  |
| 9th quarter  | 0.64                     | 0.62                   | 0.68  | 0.73  |
| 18th quarter   | 0.84                     | 0.79                   | 0.88  | 0.92  |
| <i>Average generic price<br/>(\$ per patient day):</i>                 |                          |                        |       |       |
| 1st quarter  | 0.30                     | 0.28                   | 0.33  | 0.37  |
| 9th quarter  | 0.15                     | 0.12                   | 0.18  | 0.22  |
| 18th quarter   | 0.08                     | 0.08                   | 0.11  | 0.15  |
| <i>Average quarterly brand-name sales<br/>(M no. of patient days):</i> |                          |                        |       |       |
| 1st quarter  | 35.8                     | 35.8                   | 34.2  | 32.6  |
| 9th quarter  | 19.7                     | 21.2                   | 18.8  | 17.9  |
| 18th quarter   | 13.3                     | 14.4                   | 12.8  | 12.4  |
| <i>Average quarterly generic sales<br/>(M no. of patient days):</i>    |                          |                        |       |       |
| 1st quarter  | 2.0                      | 2.1                    | 1.9   | 1.8   |
| 9th quarter  | 25.7                     | 27.2                   | 23.5  | 21.3  |
| 18th quarter   | 23.7                     | 28.0                   | 22.0  | 20.4  |
| <i>Sunk costs of entry (M\$):</i>                                      | 1.2                      | 1.04                   | 1.14  | 1.09  |

\*M stands for million.