Does Market Exclusivity Improve Access to Drugs? The Case of US Anti-Ulcer Drug Market

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Introduction

- Over-the-Counter (OTC) drugs
  - Improve access and affordability of medical care
    - No need for physician's prescription
    - Saves costs of doctor visits, prescription drugs
  - May reduce US health spending by ~$146 Bn annually
    (Source: 2019 Report by Consumer Healthcare Products Association)

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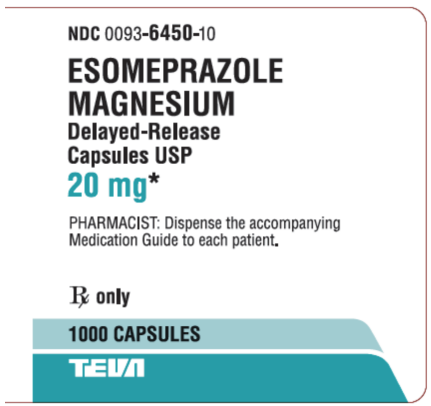
Rx Brand



Rx Generic

OTC Brand

OTC Generic

Prescription (Rx) to OTC switch

- Multiple clinical trials to establish self-diagnose, self-treatment, safety; Costly
- Three-year OTC market exclusivity to the first firm to switch
- Granted by the FDA (Hatch-Waxman Act 1984)
- Independent of Rx patent
- During exclusivity, no other OTC drugs of the same molecule are approved
- Goal: to encourage firms to develop and release the OTC drugs

Research Question

- Does market exclusivity policy achieve its goal?

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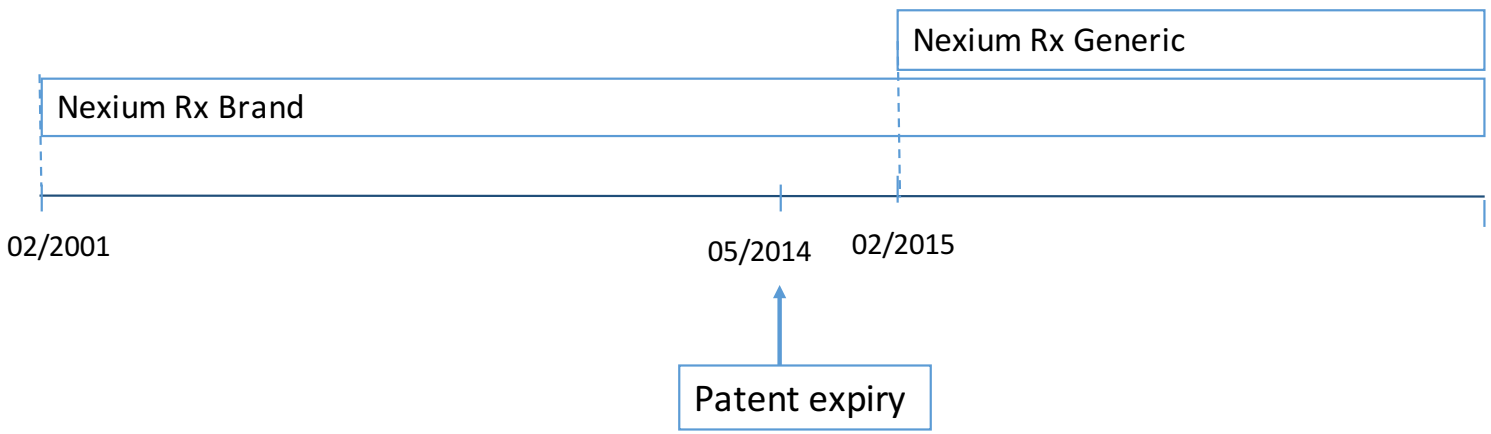
  'Innovation v/s Access to Drugs'

- Context: US anti-ulcer drug market
  - Treatment is prevalent and costly
  - 60Mn heartburn patients in the US
  - Nearly half of the U.S. population has symptoms GERD
  - Costly: Nexium Rx cost $ 2.5 Bn for 1.5 Mn medicare patients
    (8 million prescriptions and refills in 2013)

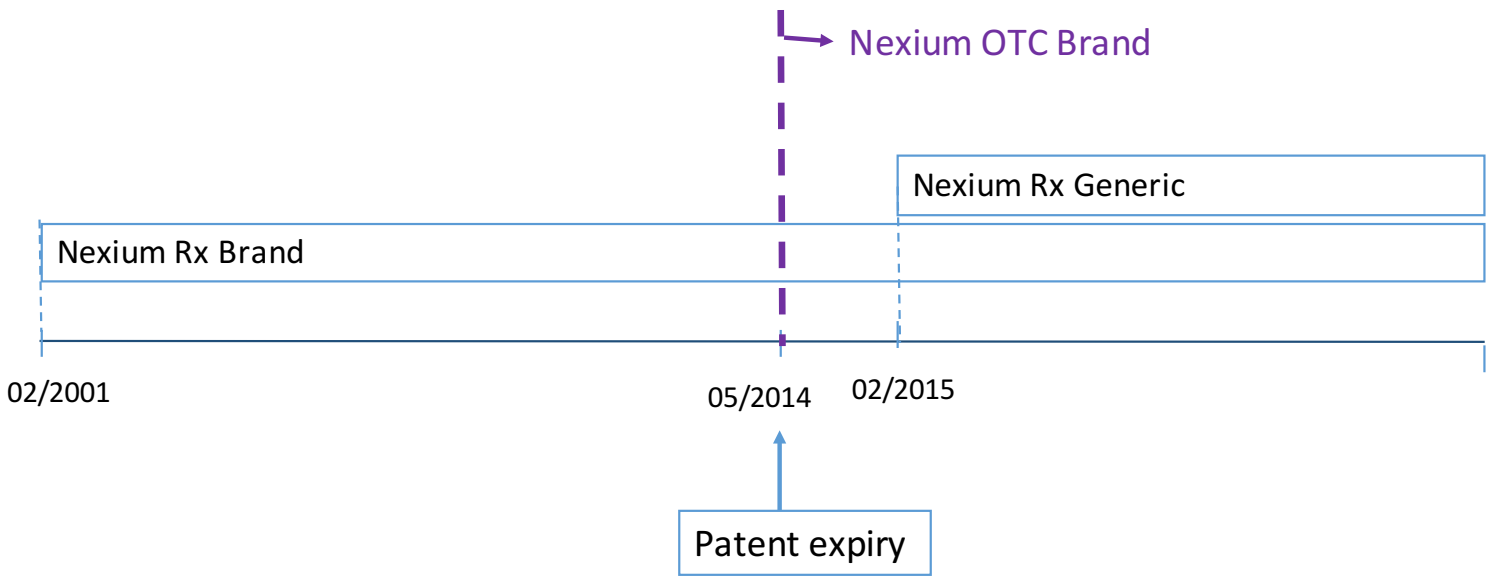
Life Cycle of A Prescription Drug

Figure: Nexium (Esomeprazole magnesium)



When Should AstraZeneca Introduce Nexium OTC

FIGURE: Nexium (Esomeprazole magnesium)



Good Things Come to Those Who Wait?

Table: Examples of Waiting in Offering OTC Anti-ulcer Drugs

Brand name	Patent expiration	Brand OTC Launched
Tagamet	05/1994	08/1995
Zantac	07/1997	04/1996
Prilosec	10/2001	09/2003
Prevacid	11/2009	11/2009
Nexium	05/2014	05/2014

Good Things Come to Those Who Wait?

Table: Examples of Early Entry in the OTC Anti-ulcer Drugs

Brand name	Patent expiration	1st OTC entry
Pepcid	10/2000	06/1995
Axid	04/2002	07/1996
Zegerid	07/2016	03/2010

Summary (1/2)

- Market Exclusivity and Access to Drugs
  - When do pharmaceutical firms convert a Rx drug to OTC?
  - How do Rx patent and the FDA 3-year OTC market exclusivity affect it?
  - Does alternative policy improve access and consumer welfare?

- Theory
  - Protect Rx profit from OTC cannibalization $\Longrightarrow \uparrow$ Delay
  - Extend market excl. beyond Rx patent & block generic OTC $\Longrightarrow \uparrow$ Delay
  - Market expansion, first-mover advantage $\Longrightarrow \downarrow$ Delay

- Exercise
  - Contrast status quo policy with other exclusivity policies
  - Simulate OTC switching time, demand and consumer welfare

Summary (2/2)

- Method
  - Demand system estimation
  - Mark-ups $\Longrightarrow$ marginal costs $\Longrightarrow$ variable profit estimates
  - Fixed cost of entry using dynamic oligopoly model

- Findings
  - FDA market excl. may delay the OTC entry product until patent expiration.
  - No exclusivity policy: $\downarrow$ incentive to innovate, but $\uparrow$ consumer welfare
  - Alt. policy: *3-yr excl. from Rx-patent expiry date rather than OTC release date*
    - Improves welfare without sacrificing incentive to innovate
    - However, delays generic OTC entry for molecules that would otherwise enter early

Literature

- **Competition and innovation**: Aghion, Bloom, Blundell, Griffith, and Howitt (2005), Chaudhuri, Goldberg, and Jia (2006), Igami (2017)

- **Innovation policies in pharmaceutical market**: Arcidiacono, Ellickson, Landry, and Ridley (2013), Crawford and Shum(2005), Dubois and Lasio (2018), Berndt, Kyle, and Ling (2003),Grabowski and Kyle (2007), Hemphill and Sampat (2012), Shapiro (2016, 2018), Williams (2017)

- **Dynamic game and optimal timing**: Pakes (1986), Rust (1987), Benkard (2004), Schmidt-Dengler (2006), Aguirregabiria and Mira (2007), Bajari, Benkard, and Levin (2007), Ching (2010), Goettler and Gordon (2011), Igami (2017, 2018)

Data

Data Sources

- *IMS Health National Sales Prospective (NSP) Rx and OTC Drug Data*
  - Sample period: 1992-2015,
  - National data
  - Monthly frequency
  - Data on quantity, price, strength, brand status, form (tablet/capsule)
- *IMS Health Integrated Promotional Services (IPS) 1992-2015*.
  - Advertising expenditures: Physician detailing and DTC ad expenses
- *National Drug Code*. Entry and firm information.
- *The FDA Orange Book*. Patent and market exclusivity information.

Model

Model Overview

- Discrete Choice Demand Model
- Supply Model Stage 1: Dynamic oligopoly model:
  - Firms decide whether to offer OTC product
- Supply Model Stage 2: Static oligopoly model:
  - Firms decide on the optimal price after entry decisions

Demand Model: Nested Logit Model

- Product is defined as the combination of molecule, brand status (brand v.s. generic), marketing status (Rx v.s. OTC), and form (tablet v.s. capsule)
- Utility

$$U_{njmt} = \underbrace{\alpha p^c_{jmt} + x_{jmt}\beta + \xi_{jmt}}_{\delta_{jmt}} + (1-\sigma)\varepsilon_{njmt} \tag{1}$$

  where p^c_{jmt} is the price faced by the consumer

- Nest is defined based on molecules

Insurance, and Price faced by Consumer

- For Rx drugs, patients pay copayment, typically much lower than the posted price
- Copayment is not observed
- We follow existing literature (Arcidiacono, Ellickson, Landry and Ridley (2013))

$$\begin{aligned} \ln(p^c_{jmt}) &= \phi^b_0 + \phi_1 \ln(p_{jmt}) \text{ (for Branded-Rx drugs)} \\ \ln(p^c_{jmt}) &= \phi^g_0 + \phi_1 \ln(p_{jmt}) \text{ (for Generic-Rx drugs)} \\ p^c_{jmt} &= p_{jmt} \text{ (for OTC drugs)} \end{aligned} \tag{2}$$

where ϕ^b_0 equal to 2.558, ϕ^g_0 equal to 2.05 and ϕ_1 to be 0.113

Supply Model Stage 2: Price Competition

- Static profit function

$$\pi_{it} = \sum_{j \in J_i} ((1 - r_{jt}) p_{jmt} - mc_{jmt}) M * s_{jmt}(p) \tag{3}$$

- r_{jt} rebates paid by the Rx manufacturer to the insurer
- r_{jt} unobserved
- Follow the solution proposed in Arcidiacono, Ellickson, Landry and Ridley (2013)
- First-order-condition

$$0 = (1 - r_{jt}) s_{jmt}(p) + \left((1 - r_{jt}) p_{jmt} - mc_{jmt}\right) \frac{\partial s_{jmt}(p)}{\partial p_{jmt}} \tag{4}$$

Stage 1: OTC Release Decision - State Space

- Finite horizon, Sequential-move dynamic discrete game with Private information
- Consider a molecule with Rx drug under patent protection
- In the beginning of period t, a molecule can enter in two different states

$$\{\text{Rx only, Rx and OTC}\}$$

- The states of all the 11 molecules determine the state space at time t, $\{S_t\}$
- A typical state space looks like:

$$S_t = \{Rx_1, Rx_2, Rx_3 + OTC_3, \cdots, Rx_{10} + OTC_{10}, Rx_{11}\}$$

where molecule 1 enters period t with the state Rx only

Stage 1: OTC Release Decision - Action Space

- If the molecule is in state **Rx only**, then action space is given by

$$\{\text{No Switch, Switch to OTC}\}$$

- If the molecule is in state **Rx + OTC**, only maximize period profit
- Once action is taken $\{S_t\}$ moves to $\{S_{t+1}\}$
- Action ends once patent expires

Stage 1: OTC Release Decision

- Problem of a manufacturer in the 'Rx only' state in addition to max. period profit

$$\max\left\{\beta E\left[V_{t+1}^{Rx}\left(S_{t+1}|S_t\right)\right]+\varepsilon_{i,t}^{1},\beta E\left[V_{t+1}^{Rx+OTC}\left(S_{t+1}|S_t\right)\right]+\varepsilon_{i,t}^{2}-\kappa\right\}$$

  - where V^{Rx} stands for value function under Rx only action
  - V^{Rx+OTC} stands for value function under the action $Rx+OTC$
  - $\varepsilon_{i,t}$ follow iid extreme value type 1 distribution
  - κ stands for the fixed cost of switching

- In a given period, firms move sequentially (based on experience)

- Solve for Perfect Bayesian Equilibrium by backward induction

- Estimation by maximum likelihood method

▸ Policy Fn, MLE

Estimation Results

Demand Estimation: Nested Logit Model

	(OLS)	(IV)
Copay	-0.06***	-0.28***
	(0.002)	(0.06)
Nesting Parameter	0.91***	0.43***
	(0.01)	(0.04)
OTC Dummy	0.73***	4.6***
	(0.12)	(1.17)
Log Cumulative Advertisement	-0.02***	0.13***
	(0.01)	(0.03)
Constant	1.95***	3.52***
	(0.2)	(0.89)
BrandRx x generic competition	-0.27***	-1.1***
	(0.04)	(0.13)
BrandRx x OTC	-0.39***	-0.36***
	(0.05)	(0.12)
Generic Rx x OTC	-0.67***	-0.11
	(0.1)	(0.19)
Observations	6,116	6,116
Firm-Molecule-Form FE	Yes	Yes
Time Since Entry Dummy (upto 12 months)	Yes	Yes
Time Since Entry Dummy x PPI Dummy	Yes	Yes
Time Dummy by Class	Yes	Yes

(standard errors in parentheses)
*** p<0.01, ** p<0.05, * p<0.1

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MC by Brand Status and Marketing Status

Brand and Marketing status	Average Price	Average Estimated MC	SD of Estimated MC
Brand Rx	111	68	55
Generic Rx	20	17	18
Brand OTC	25	22	6
Generic OTC	11	9	7
No of Obs: 6116			

Fixed Entry Cost

	Assumed Order of Moves	
	More Experienced First	Less Experienced First
Fixed Cost of Releasing OTC	15.86***	15.99***
	(3.528)	(3.501)

Estimated fixed cost of OTC entry close to 16 million USD.

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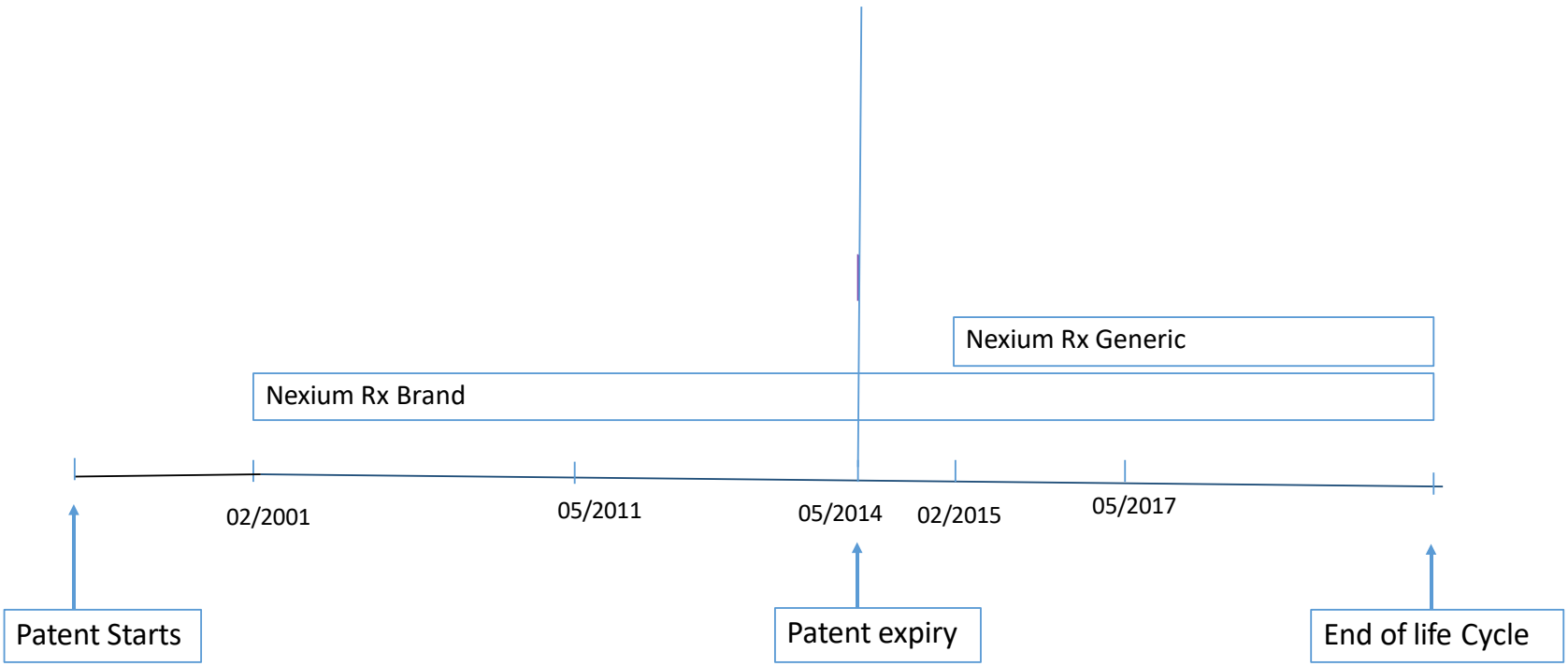
Estimated fixed cost of OTC entry close to 16 million USD.

- Calibration of fixed cost from consumer clinical trial data
- Calibrated clinical trial cost is $4.73-10.8 million
  (FDA data, DiMasi et al. (2003), Berndt et. al. (2014))

▸ Robustness Checks

Counterfactuals

Counterfactual 1: Nexium Entered OTC Market in 2011 under Status Quo Policy



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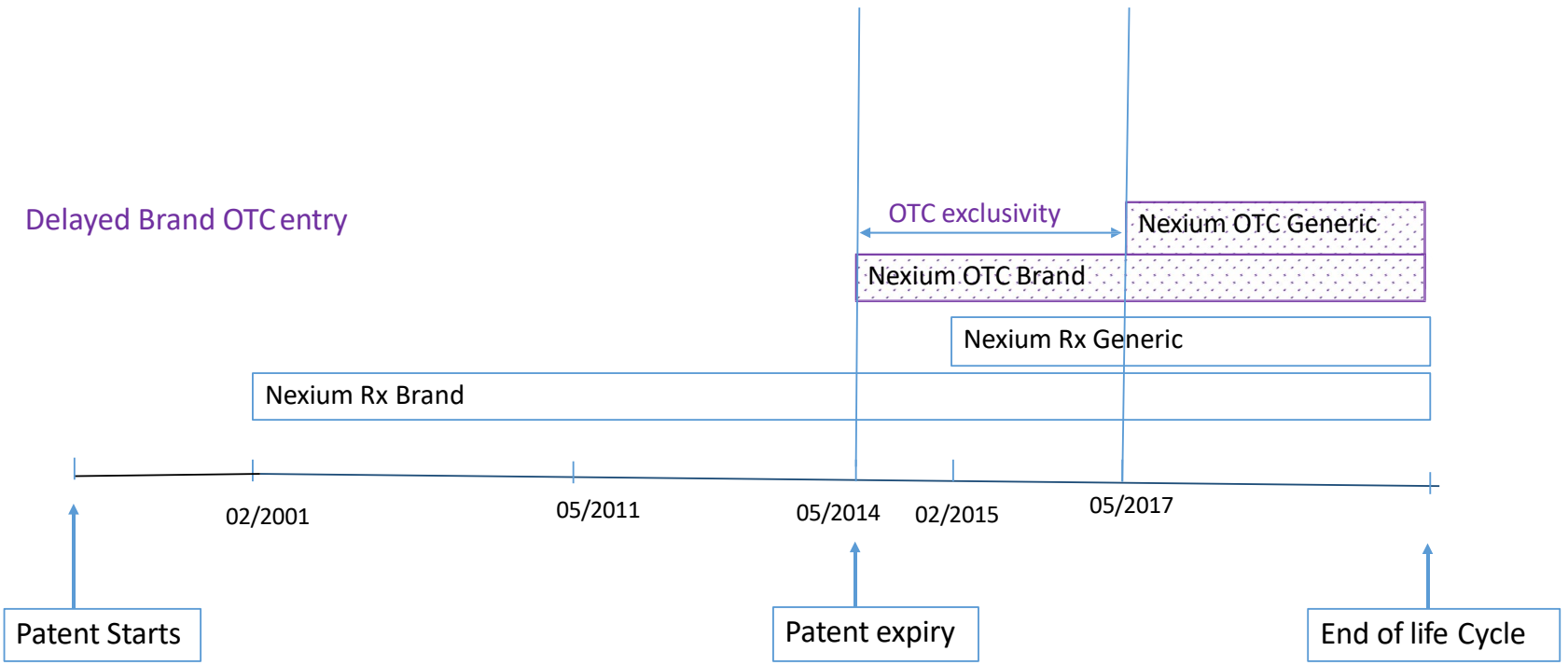

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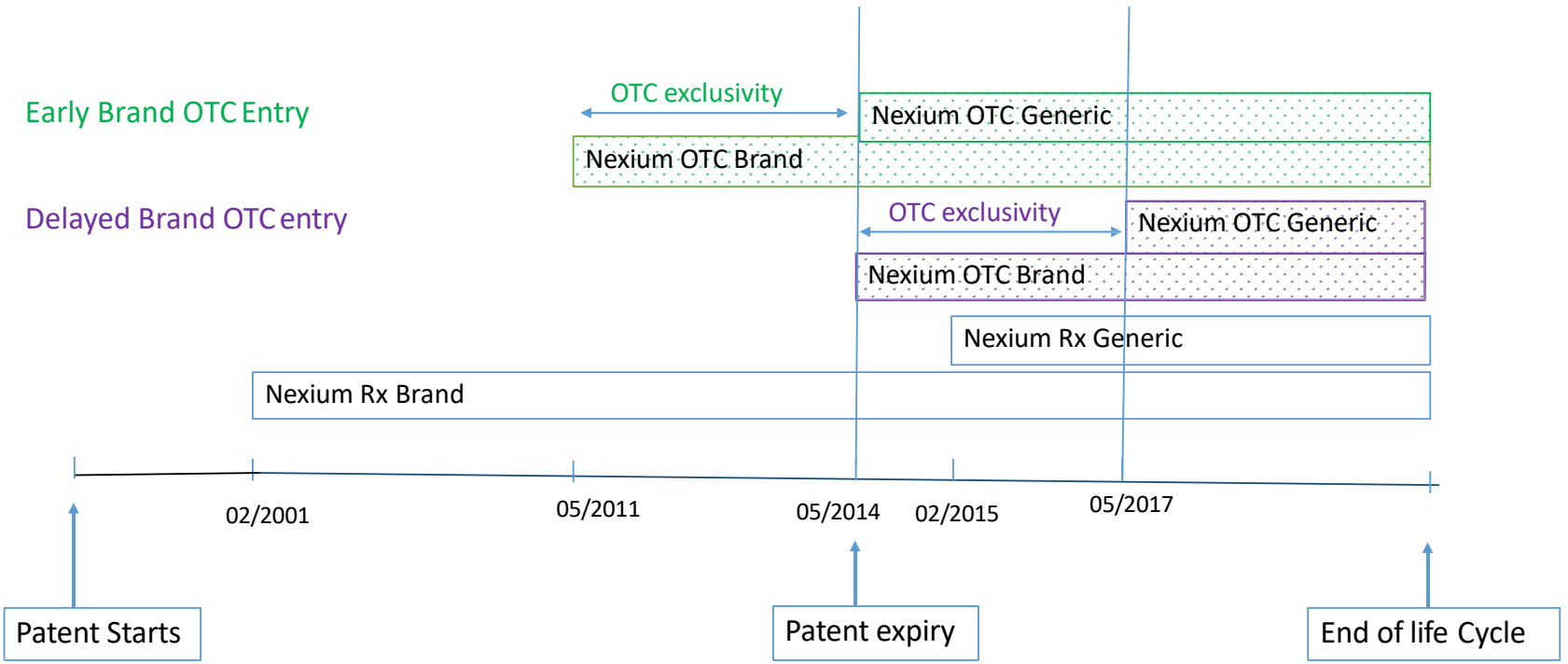
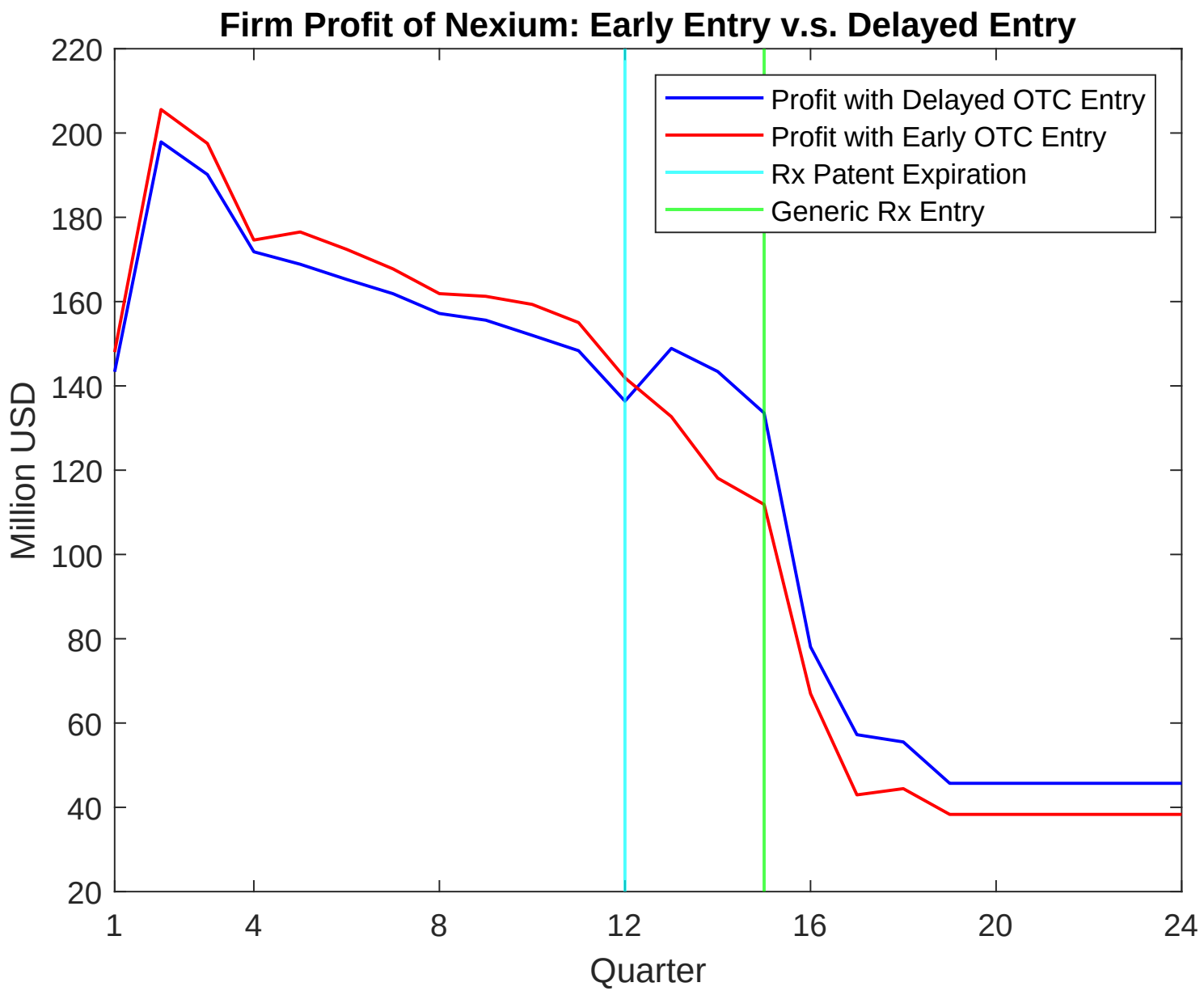


Counterfactual 1: Firm Profit of Nexium



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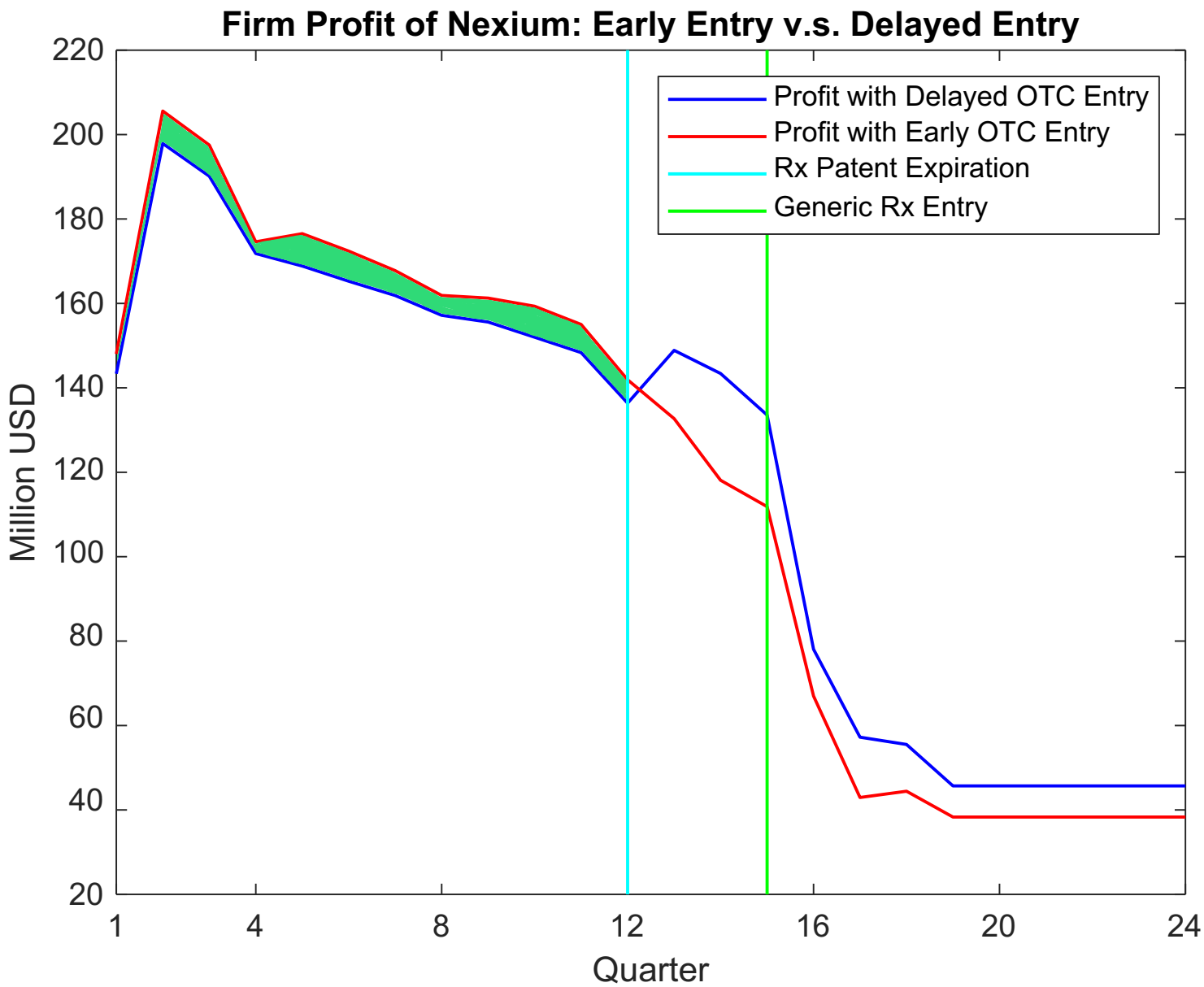

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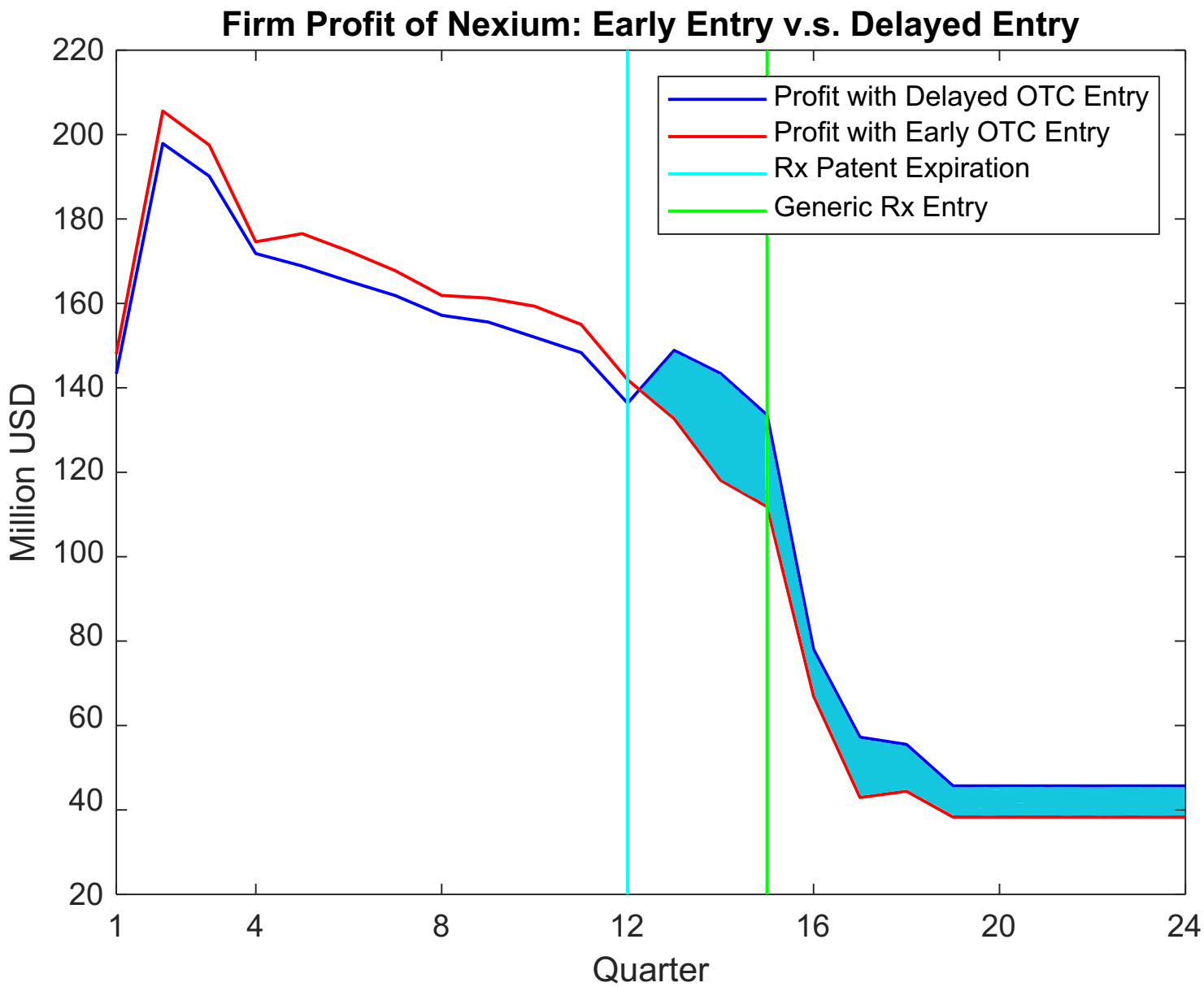
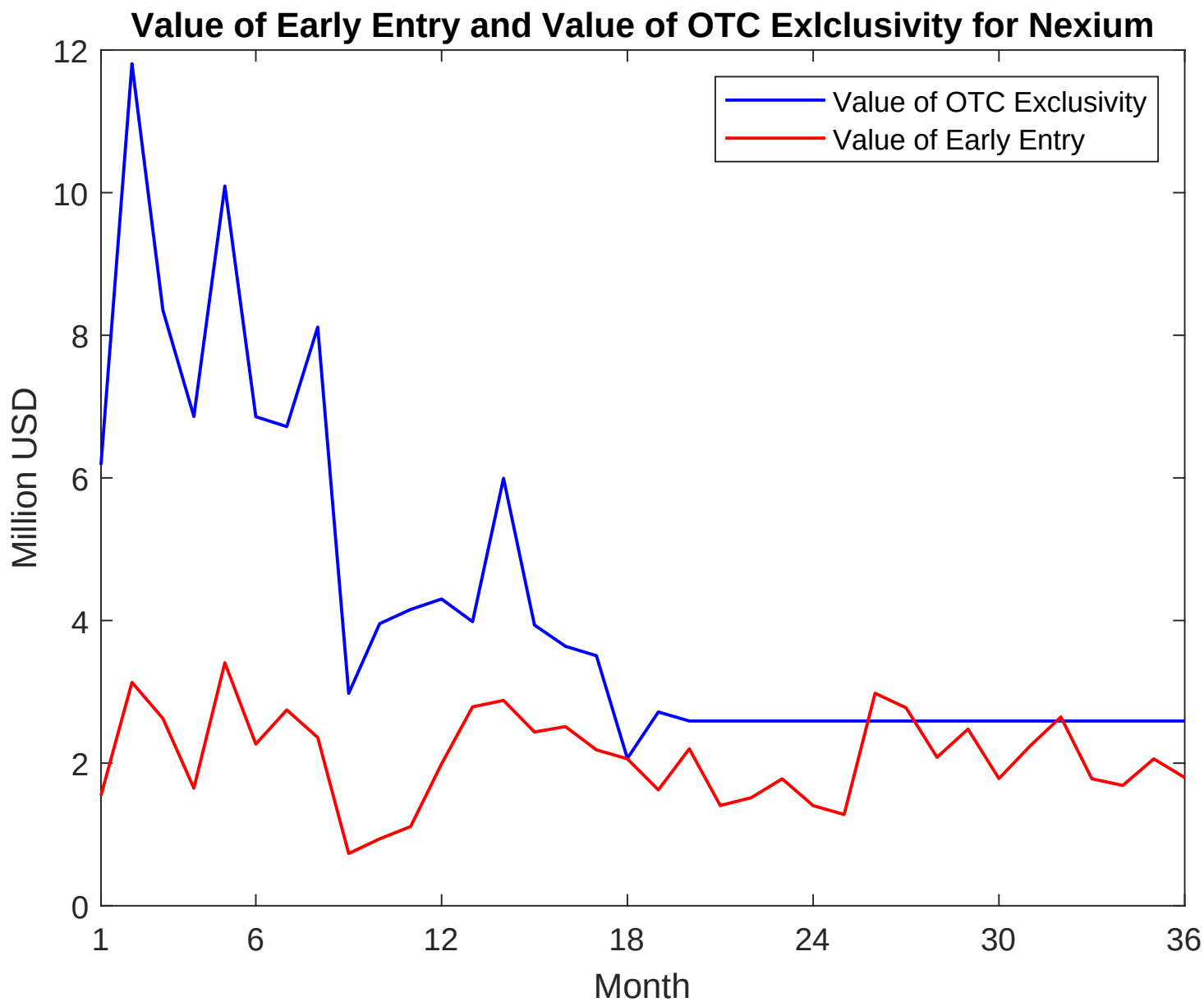


Counterfactual 1: Nexium's delayed entry



Counterfactual 2: Alternative Policies and Welfare Implication

- **No Exclusivity**
  - No market exclusivity is granted upon OTC switching
- **Alternative Exclusivity**
  - 3-yr market exclusivity for post patent period if OTC drugs released early
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- Incentives for delay due to exclusivity are eliminated
- Incentive to Innovate, Access to drugs, and Consumer welfare

Alternative Policies and Welfare Implication

Brand	Molecule	Patent expiration	Branded OTC entry (in data)	Counterfactual Results	
				No Exclusivity	Alt. Exclusivity
Tagamet	Cimetidine	1994	1995	1994	1994
Zantac	Ranitidine	1997	1996	1997	1994
Pepcid	Famotidine	2000	1995	1995	1995
Axid	Nizatidine	2002	1996	No Switch	1995
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Conclusion

- Unintended consequences of Rx patent and OTC market exclusivity
- FDA OTC exclusivity may create incentives for delay in OTC drugs release
- May lead to substantial consumer welfare loss
- Alternative policy that eliminates the incentives for delay
- Brings significant consumer gain from early OTC drug introduction
- Implications on the optimal design of IP policies

Thank You!

Stage 1: OTC Release Decision

- Finite horizon, sequential move with iid private shock implies unique equilibrium
- Policy function for Rx only is given by

$$\Pr(\text{Rx only}) = \exp(\beta E\left[V_t^{Rx}(S_{t+1}|S_t)\right])/B$$

where

$$B = \exp(\beta E\left[V_t^{Rx}(S_{t+1}|S_t)\right]) + exp(\beta E\left[V_t^{Rx+OTC}(S_{t+1}|S_t)\right] - \kappa)$$

- Each firm uses rational expectations to form beliefs about other firms' actions
- Use Seim(2006) to generate equilibrium beliefs
- Likelihood maximization problem is given by

$$\arg\max\left\{\ln\left[\prod_{t=0}^{T}\Pr(\text{observed actions in year } t)\right]\right\}$$

Back

Model Assumptions and Robustness Checks

1. Unique equilibrium and computational feasibility of dynamic estimation
   - We solve for a Perfect Bayesian Equilibrium
   - Pvt. info iid cost shock, without persistent heterogeneity
   - Firm's belief over off-path realization of ε_{-it} does not affect its payoff
   - Firm i's payoff affected by rival's cost shock only through actual choices
   - So, firms hold perfect information about pay-off relevant part of past history
   - Additionally, firms move sequentially after observing action of early movers
   - Hence, avoids multiplicity of equilibria
   - Finally, finite horizon specification implies computation through backward induction

2. We assume $\beta = 0.88$, consistent with existing literature

	$\beta = 0.75$	$\beta = 0.8$	$\beta = 0.92$
Fixed Cost of Releasing OTC	13.21**	14.79	18.83*
	(6.963)	(12.41)	(11.09)

Back