





The Effects of Detailing on Prescribing Decisions under Quality Uncertainty

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Quote

Introduction Literature Model Estimation Strategy Data (Prices, Sales volume, Detailing) Results Policy Experiment Conclusion

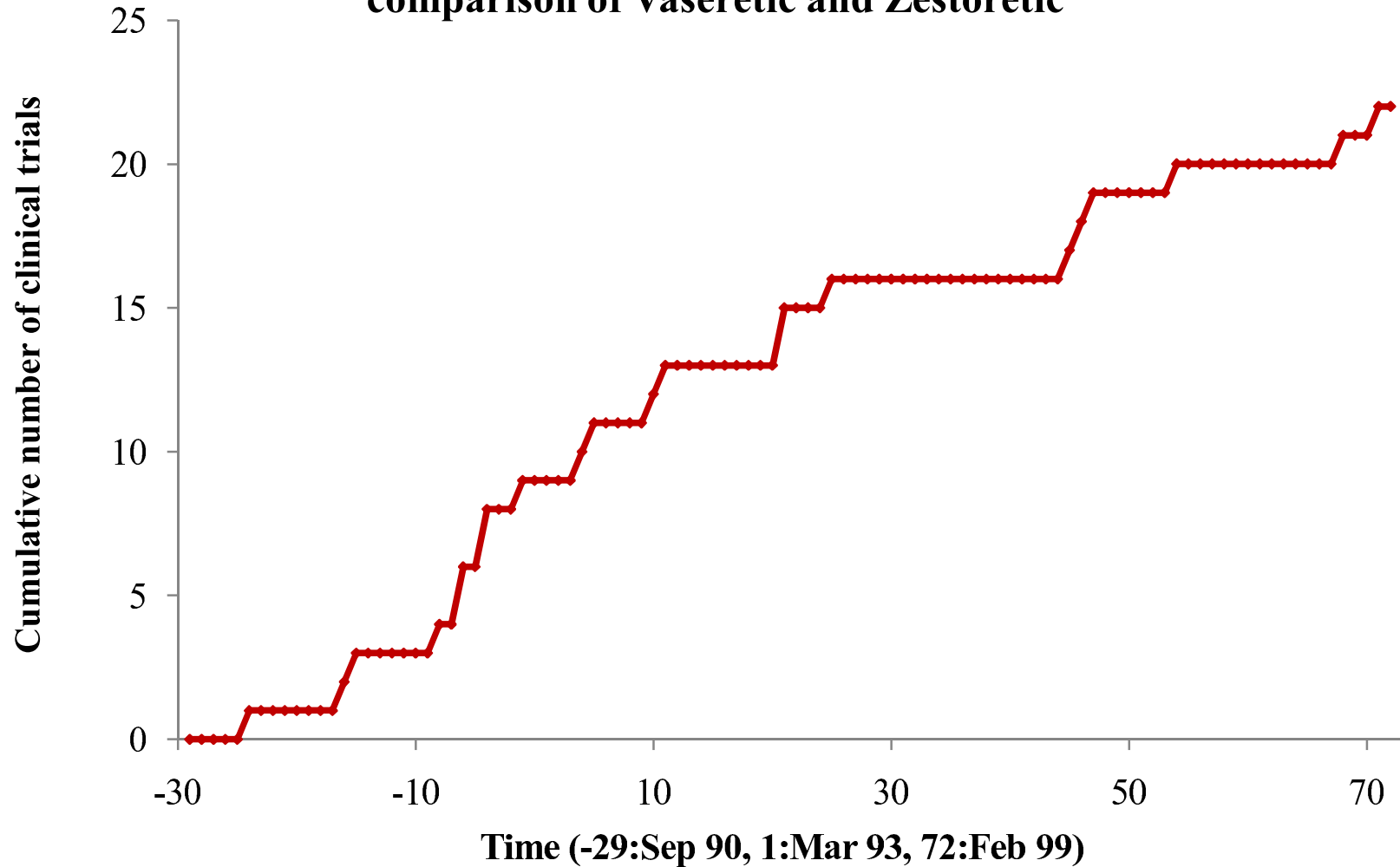
“Many serious Adverse Drug Reactions (ADRs) are discovered only after a drug has been on the market for years. Only half of newly discovered serious ADRs are detected and documented in the Physicians Desk Reference within 7 years after drug approval.”

Lasser et al. (2002) Journal of American Medical Association.

New Evidence from Clinical Trials

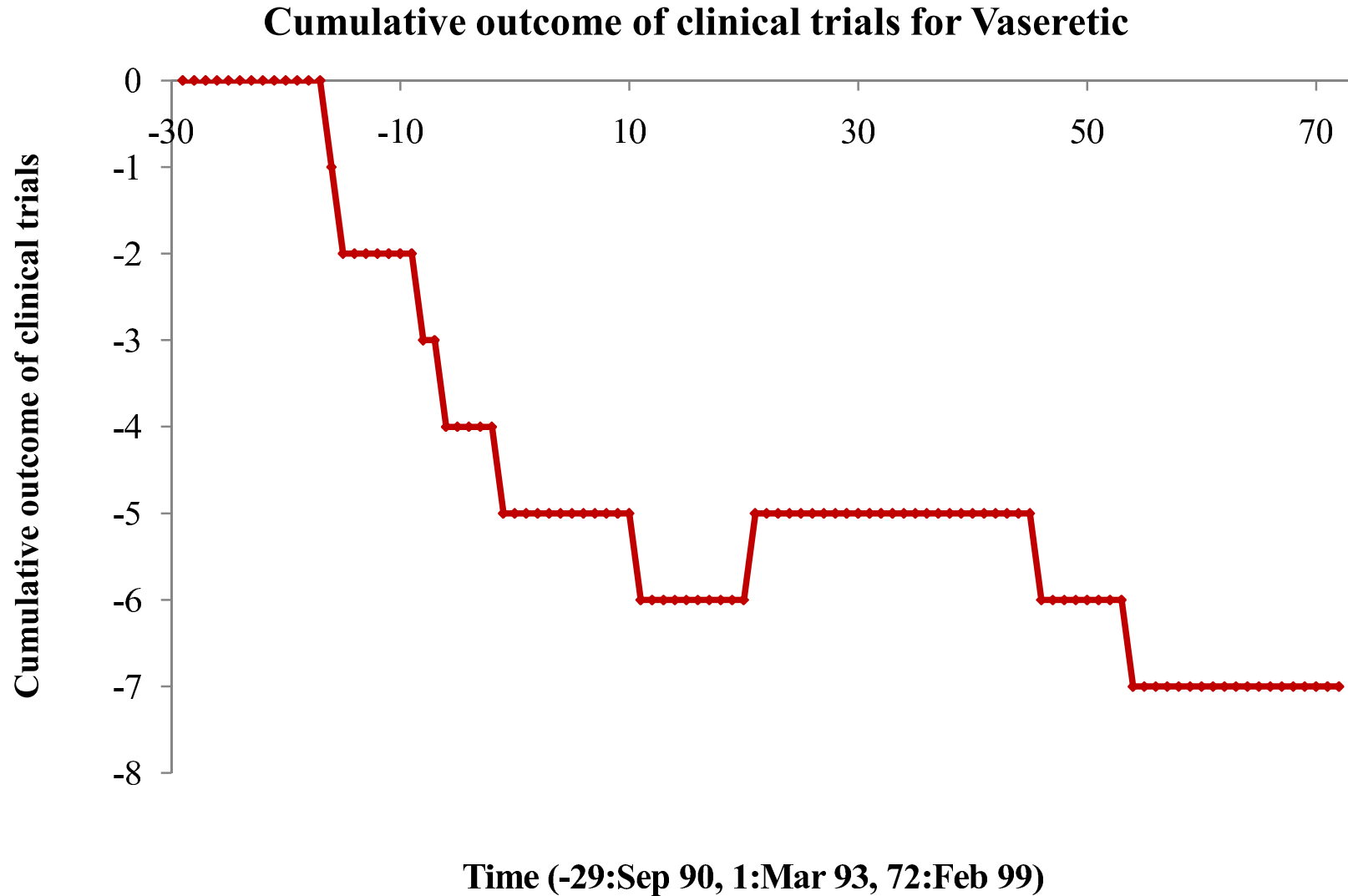
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Cumulative number of clinical trials that include a direct comparison of Vaseretic and Zestoretic



Cumulative Outcomes of Clinical Trials

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Pharmaceutical Detailing



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- Detailing: sales reps from drug companies visit doctors to discuss compliance information, side-effects, and efficacy studies.
- In 2003, detailing costs 8 billion dollars; journal advertising costs 0.46 billion dollars; direct-to-consumer (DTC) advertising costs 3.2 billion dollars.
- The effectiveness of detailing may change when new information becomes available marketing managers may need to change their marketing strategies over time.



Motivation



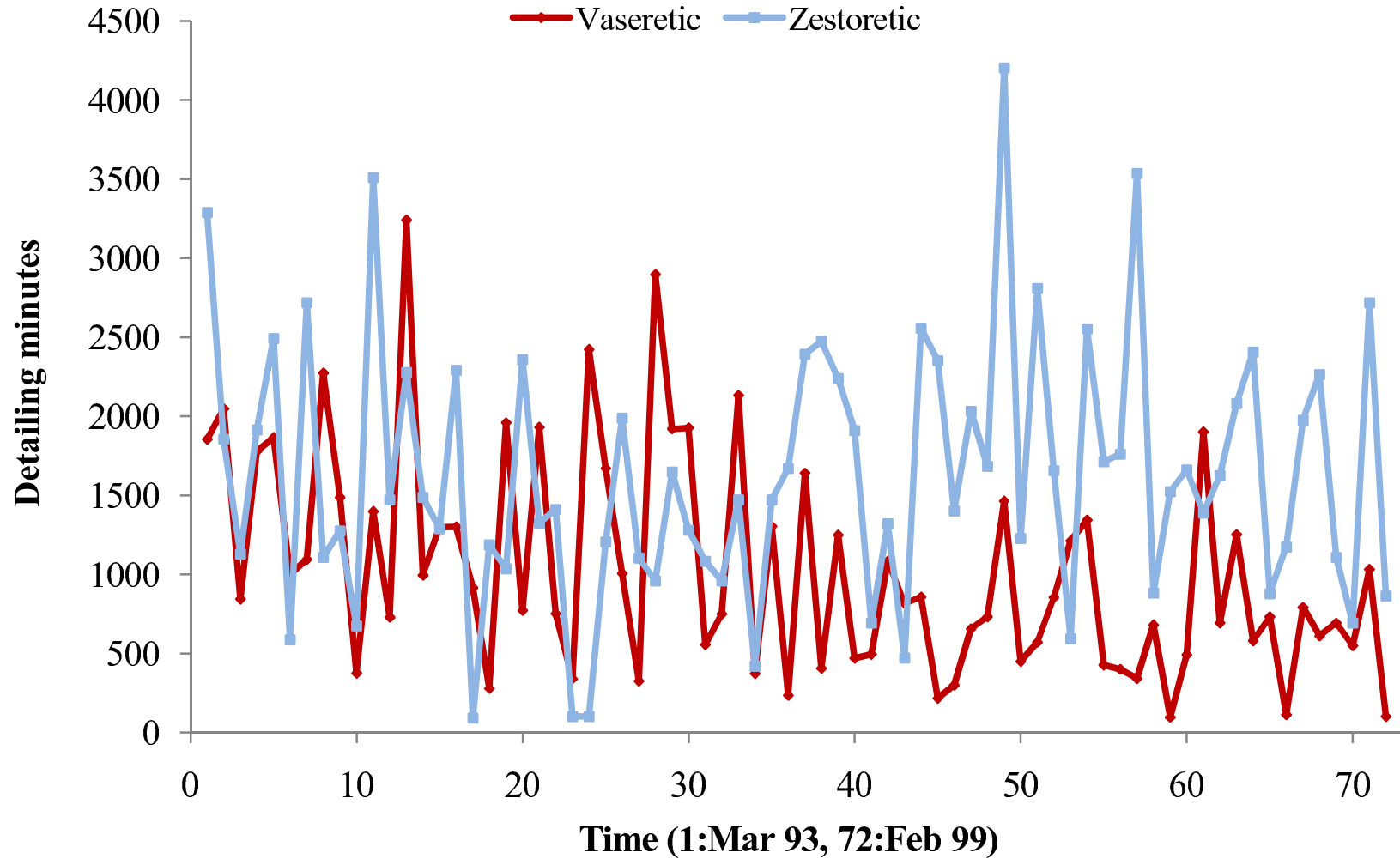
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Recent empirical findings:

- The detailing efforts for a drug are positively correlated with its cumulative clinical outcomes (Azoulay 2002).
- The impact of detailing on physicians' prescribing behavior depends on the cumulative information on the efficacies and side-effects of drugs (Venkataraman and Stremersch 2007).

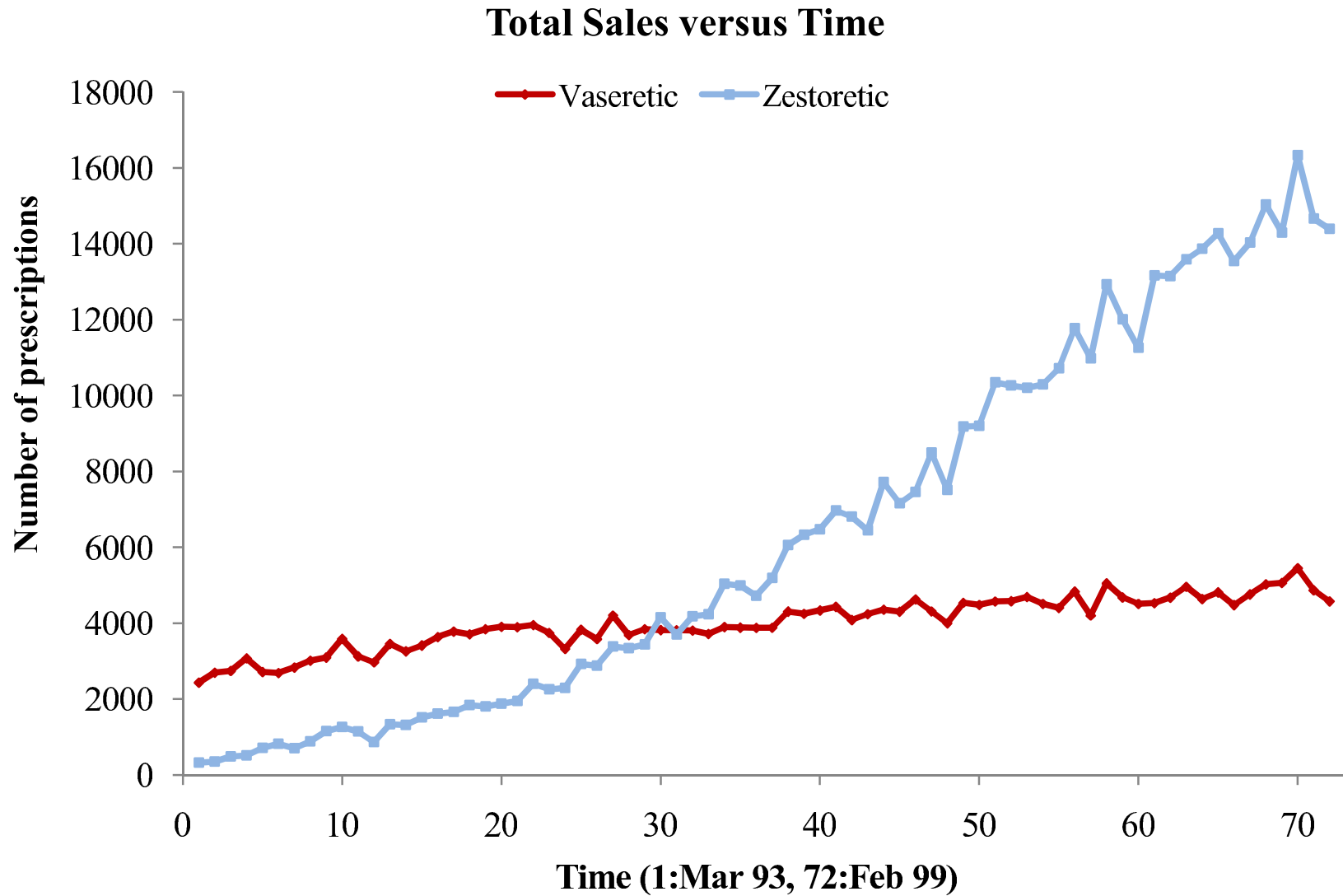
Detailing Minutes

Detailing minutes versus Time



Slow Diffusion of New Drugs

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Motivation (cont'd)


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Existing structural models of learning and informative detailing follow the framework of Erdem and Keane (1996):

- Firms have complete information about the quality of their drugs when they launch them.
- Informative detailing conveys noisy signals about the true quality of the drugs to physicians.

Implication:

Any new information available about the drug will act as substitutes for the detailing signals, and consequently, will only reduce the effectiveness of informative detailing.



Research Objectives



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- We develop a structural model of learning and informative detailing that is consistent with the empirical findings.
 - ◆ Our model assumes that both drug firms and physicians are uncertain about drug qualities.
 - ◆ Firms use detailing as a means to build/maintain the measure of physicians who are informed of the latest information sets.
- We investigate the empirical implications of this new framework.
- We quantify how the effectiveness of detailing depends on the information sets and the measure of well-informed physicians.
- We conduct a policy experiment (a public awareness campaign which encourages physicians/patients to report their experiences), we show how the managerial implications of our model differ from those of existing models.



Roadmap



Introduction Literature Model Estimation Strategy Data (Prices, Sales volume, Detailing) Results Policy Experiment Conclusion

- Previous literature.
- Model.
- Estimation strategy.
- Data.
- Estimation results.
- Effectiveness of detailing.
- Policy experiment.
- Conclusion.

Marketing Literature

- Ching (2000, 2008)
- Chan et al. (2007), Narayanan et al. (2005), Mukherji (2002)
- Mullainathan (2002), Mehta et al. (2003)

Medical Continuing Education literature

- Opinion Leaders: Haug (1997), Thompson (1997)
- Sales representatives: Schweitzer (1997), Coleman et al. (2004), Greider (2003)

Model

- Agents: physicians, firms, and a representative opinion leader.
- There are J products and an outside alternative ($j = 0$).
- Each firm has one product.
- Two product characteristics: price (p_j), and quality (q_j).
- All agents are imperfectly informed about q_j .
- The representative opinion leader maintains a public information set, $I(t) = (I_1(t), \dots, I_J(t))$, for q , based on the past patients experiences and clinical trial outcomes.
- Let \underline{I}_j be the initial prior for q_j when drug j is first introduced.
- Physicians are either well-informed about drug j ($I_j(t)$), or uninformed about drug j (\underline{I}_j).
- Let M_{jt} be the measure of well-informed physicians for drug j at time t .
$$M_{jt} = f(M_{jt-1}, D_{jt}).$$

Model (cont'd)

Each period has three stages:

1. Firms observe $I(t)$, and choose D_{jt} .
2. M_{jt} is determined for all j , and each physician makes his/her prescribing decisions to maximize the expected utility for each of his/her patients.
3. Patients consumer the drugs and their consumption experience signals are revealed. Also, if clinical trials are published, experience signals from clinical trials are revealed. A represent opinion leader then uses these signals to update $I(t)$ in a Bayesian manner.

Bayesian Updating

Consumption experience signal: $q_{ijt}^e = q_j + \delta_{ijt}$, where $\delta_{ijt} \sim N(0, \sigma_\delta^2)$.

Clinical trial experience signal: $q_{ijt}^c = q_j + \eta_{ijt}$, where $\eta_{ijt} \sim N(0, \sigma_\eta^2)$.

Initial prior: $N(\underline{q}_j, \underline{\sigma}^2)$.

Expected quality:

$$E[q_j | I(t+1)] = E[q_j | I(t)] + \iota_j^e(t)(\bar{q}_{jt}^e - E[q_j | I(t)]) + \iota_j^c(t)(\bar{q}_{jt}^c - E[q_j | I(t)])$$

where \bar{q}_{jt}^e and \bar{q}_{jt}^c are the sample mean of consumption experience signals and clinical trial signals revealed for drug j in period t .

$$\text{Perceived variance: } \sigma_j^2(t+1) = \frac{1}{\frac{1}{\sigma_j^2(t)} + \frac{\kappa n_{jt}}{\sigma_\delta^2} + \frac{n_{jt}^c}{\sigma_\eta^2}}.$$

Procedure to draw \bar{q}_{jt}^c

Consider $J = 2$. Observed outcomes of direct comparison clinical trials are categorized into three types:

- (i). Positive for drug 1 (negative for drug 2).
- (ii). Negative for drug 1 (positive for drug 2).
- (iii). No difference between drugs 1 and 2.

We draw \bar{q}_1^c and \bar{q}_2^c as follows:

- Define $\Delta\bar{q}^c \equiv \bar{q}_1^c - \bar{q}_2^c$. Note that $\Delta\bar{q}^c \sim N\left(q_1 - q_2, \sigma_\eta^2 \left(\frac{1}{n_1^c} + \frac{1}{n_2^c}\right)\right)$.
- Observed outcomes correspond to (i) $\Delta\bar{q}^c > 0$, (ii) $\Delta\bar{q}^c < 0$, (iii) $\Delta\bar{q}^c = 0$.
- In case (i), we draw $\Delta\bar{q}^{c*}$ from $N\left(q_1 - q_2, \sigma_\eta^2 \left(\frac{1}{n_1^c} + \frac{1}{n_2^c}\right)\right)$ truncated below at zero. Case (ii) is similar. In case (iii), set $\Delta\bar{q}^{c*} = 0$.
- Draw \bar{q}_2^{c*} from $N\left(q_2, \frac{\sigma_\eta^2}{n_2^c}\right)$, and set $\bar{q}_1^{c*} = \Delta\bar{q}^{c*} + \bar{q}_2^{c*}$.

Measure of Well-Informed Physicians

Introduction Literature Model Estimation Strategy Data (Prices, Sales volume, Detailing Results Policy Experiment Conclusion

Let M_{jt} be the measure of well-informed physicians for drug j at time t .

Let G_{jt} be the detailing goodwill stock, and ϕ_G be the depreciation rate.

$$G_{jt} = (1 - \phi_G)G_{jt-1} + D_{jt}.$$

$$M_{jt} = g(G_{jt}, G_{-jt}).$$

e.g., let $R_{jt} = \beta_0 + \beta_1 G_{jt}$,

$$M_{jt} = \frac{\exp(R_{jt})}{1 + \exp(R_{jt})}.$$

Average rate of forgetting, $\phi_M = \frac{M_{jt} - f(M_{jt}, 0)}{M_{jt}}$, is a non-linear function of M_{jt} , and has an inverted U shape.

Heterogeneity with Endogenous Weights

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Suppose that $J = 2$.

⇒ Four types of physicians who differ in their information sets.

- $M_1 M_2$: Measure of physicians with current information about both drugs ($I_1(t), I_2(t)$).
- $M_j(1 - M_k)$, $j \neq k$: Measure of physicians with current information about only one of the drugs ($I_j(t), \underline{I}_k$).
- $(1 - M_1)(1 - M_2)$: Measure of physicians who do not have current information at all ($\underline{I}_1, \underline{I}_2$).

Physician heterogeneity evolves endogenously.

Physicians' Choice

Patient i 's utility of consuming drug j :

$$u_{ijt} = \alpha - \exp(-rq_{ijt}) - \pi_p p_{jt} + \epsilon_{ijt}.$$

If physician h is well-informed about drug j , his expected utility of choosing drug j for patient i will be:

$$E[u_{ijt}|I(t)] = \alpha - \exp\left(-rE[q_j|I(t)] + \frac{1}{2}r^2(\sigma_j^2(t) + \sigma_\delta^2)\right) - \pi_p p_{jt} + \epsilon_{ijt}.$$

If physician h is uninformed about drug j ,

$$E[u_{ijt}|\underline{I}] = \alpha - \exp\left(-r\underline{q}_j + \frac{1}{2}r^2(\underline{\sigma}_j^2 + \sigma_\delta^2)\right) - \pi_p p_{jt} + \epsilon_{ijt}.$$

Marginal return of detailing

Consider $J = 2$. The market share for drug j at time t is

$$S_{jt} = M_{jt}M_{kt}s_{jt}(I_j(t), I_k(t)) + M_{jt}(1 - M_{kt})s_{jt}(I_j(t), \underline{I}_k) \\ + (1 - M_{jt})M_{kt}s_{jt}(\underline{I}_j, I_k(t)) + (1 - M_{jt})(1 - M_{kt})s_{jt}(\underline{I}_j, \underline{I}_k).$$

The marginal return of detailing on current market share for drug j is

$$\frac{\partial S_{jt}}{\partial D_{jt}} = \frac{\partial M_{jt}}{\partial D_{jt}} \times \{M_{kt}\Delta s_{jt}(I_k(t)) + (1 - M_{kt})\Delta s_{jt}(\underline{I}_k)\},$$

where $\Delta s_{jt}(I_k) \equiv s_{jt}(I_j(t), I_k) - s_{jt}(\underline{I}_j, I_k)$.

Three factors that affect the marginal return of detailing:

- Effectiveness of detailing on building the measure of well-informed physicians.
- Changes in the choice probability of physicians who switch from uninformed to informed.
- Measure of well-informed physicians for opponent drug.

Empirical Implications

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- Marginal return of detailing in our model could increase or decrease over time partly depending on how $I(t)$ evolves.
- For example, if a new clinical trial shows that positive outcome of a clinical trial will increase the marginal return of detailing.
- Even after the uncertainty about the drug quality is completely resolved, detailing still affects demand in our model. Its long-run impact depends on $I(t)$, M_{jt-1} .
- Note that it is necessary for the previous models to include the persuasive role of detailing in order to explain the the impact of detailing in the long-run. Narayanan et al. (2005) argued that this captures the reminding role – but it doesn't quite capture the reminding role.
- If patients' experiences (incl. clinical trials) reveal that one drug is superior (inferior) to another drug, the firm that markets the superior (inferior) drug has a stronger (weaker) incentive to do detailing under our framework.

Simultaneity Problem

- We assume that firms observe $I(t)$ before detailing takes place in each period. Therefore, $E[q_j|I(t)]$ may be correlated with D_{jt} .
- For instance, if a new clinical trial finds favorable evidence for drug j , which improves $E[q_j|I(t)]$ relative to $E[q_{-j}|I(t)]$, the firm may want to assign more detailing efforts to drug j to disseminate the.
- Ignoring this correlation will lead to an upward bias of the parameters associated with detailing (parameters for $f(M_{jt}, D_{jt})$ function).

Estimation Strategy

- Standard estimation strategy is to use BLP's GMM approach.
⇒ In our model, the unobserved product characteristic (i.e., $E[q_j|I(t)]$) differs across physician types, thus BLP cannot be applied.
- We follow the approach proposed in Ching (2000,2008).
- Let $s_{jt} = (E[q_j|I(t)], \sigma_j^2(t), M_{jt-1})$.
- $D_{jt} = d_j(s_{jt}, s_{-jt})\nu_{jt}$, where ν_{jt} is the prediction error.
- $\ln D_{jt} = \ln d_j(s_{jt}, s_{-jt}) + \ln \nu_{jt}$.
- Use a flexible functional form to approximate $\ln d_j(\cdot)$.
- Jointly estimate this pseudo-detailing policy function with the demand model.
- Need to integrate out the unobserved state variables – simulated maximum likelihood.
- IV: Total detailing for firm j minus his detailing efforts for ACE-inhibitors with diuretics.

Data (Prices, Sales volume, Detailing)

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- Monthly Canadian data on detailing, revenue and number of prescriptions from March 93 to February 99 for ACE-inhibitor with diuretic from IMS Canada.
- Why Canada?
 - ◆ Subject to price regulation – Patented Medicine Prices Review Board.
- Why ACE-Inhibitor with diuretic?
 - ◆ No Direct-to-Consumer advertising.
 - ◆ Only two dominant drugs (Vaseretic and Zestoretic).
 - ◆ Treat high blood pressure – patients/physicians are likely to be risk averse.
- Market size: ACE-inhibitors, ACE-inhibitors with diuretic, and Diuretics, Thiazide.

Data (Clinical Trials)

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- Data on clinical trials that compare the efficacy of Vaseretic and Zestoretic from September 90 to February 99 from medical journal articles archived in PubMed.
- For each clinical trial, the outcome is one of the following three types
 - ◆ Positive for Vaseretic (i.e., negative for Zestoretic).
 - ◆ Positive for Zestoretic (i.e., negative for Vaseretic).
 - ◆ No difference between Vaseretic and Zestoretic.
- Number of participants who took each drug.

Summary Statistics

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	Brand	Mean	Standard deviation	Max	Min
Number of prescriptions	Vaseretic	4,007.63	676.80	5,446	2,429
	Zestoretic	6,388.75	4,900.28	16,330	322
Detailing Minutes	Vaseretic	1,032.63	689.11	3,240	97
	Zestoretic	1,627.08	828.67	4,203	93
Price	Vaseretic	40.54	8.76	69.21	24.45
	Zestoretic	34.29	8.65	61.48	15.74

Chemical	No. of clinical trials	No. of clinical trails with positive outcome	No. of patients in a clinical trial			
			Mean	S.D.	Max	Min
Vaseretic	22	1	53.09	79.19	321	3
Zestoretic		8	86.73	168.74	620	3

Demand Parameter Estimates

1 - Vaseretic (incumbent), 2 - Zestoretic (entrant)

	Model 1 (full model)		Model 2 (demand only)	
	estimates	standard errors	estimates	standard errors
Learning parameters				
σ_{δ}^2	1.301	0.099	1.248	0.095
σ_{η}^2	0.038	0.003	0.035	0.003
ϱ_1	-7.366	0.134	-8.187	0.179
ϱ_2	-10.848	0.220	-12.102	0.168
$\underline{\sigma}^2$	0.683	0.049	0.652	0.048
ϱ_1	1		1	
ϱ_2	5.241	0.281	5.786	0.326
κ	1/30000		1/30000	
Preference parameters				
α	-3.651	0.032	-3.662	0.041
r	0.168	0.007	0.153	0.005
π_p	3.51E-04	3.29E-04	2.53E-04	3.28E-04
π_t	-0.005	3.32E-04	-0.005	3.52E-04
Detailing stock parameters				
Φ_G	0.045	0.001	0.041	0.001
β_0	-0.155	0.098	-0.083	0.093
β_1	9.47E-05	1.71E-06	9.90E-05	1.67E-06
log likelihood	-2103.116		-953.326	

* Estimates shown in bold are significant at 5% level .

Pseudo-Detailing Policy Function

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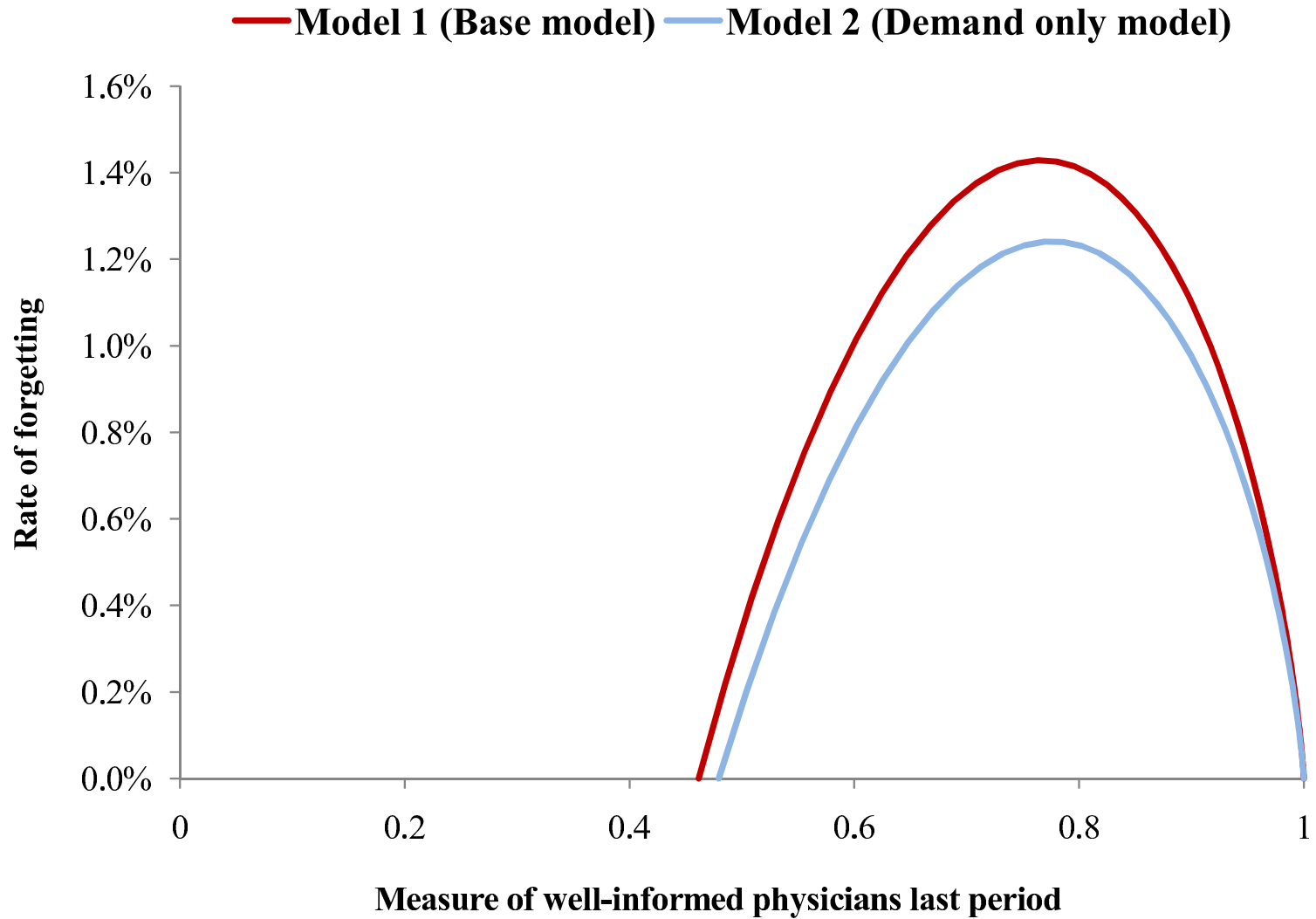
1 - Vaseretic (incumbent), 2 - Zestoretic (entrant)

	Model 1(full model)	
	estimates	standard errors
λ_{10}	5.255	2.194
λ_{11}	7.904	4.212
λ_{12}	-5.910	1.237
λ_{13}	0.831	1.066
λ_{14}	1.054	1.108
λ_{15}	0.169	0.216
λ_{20}	6.245	0.360
λ_{21}	-343.292	45.208
λ_{22}	421.838	47.891
λ_{23}	-26.887	18.902
λ_{24}	28.413	20.541
λ_{25}	0.080	0.046
s.d.(v)	0.683	0.036
log likelihood	-2103.116	

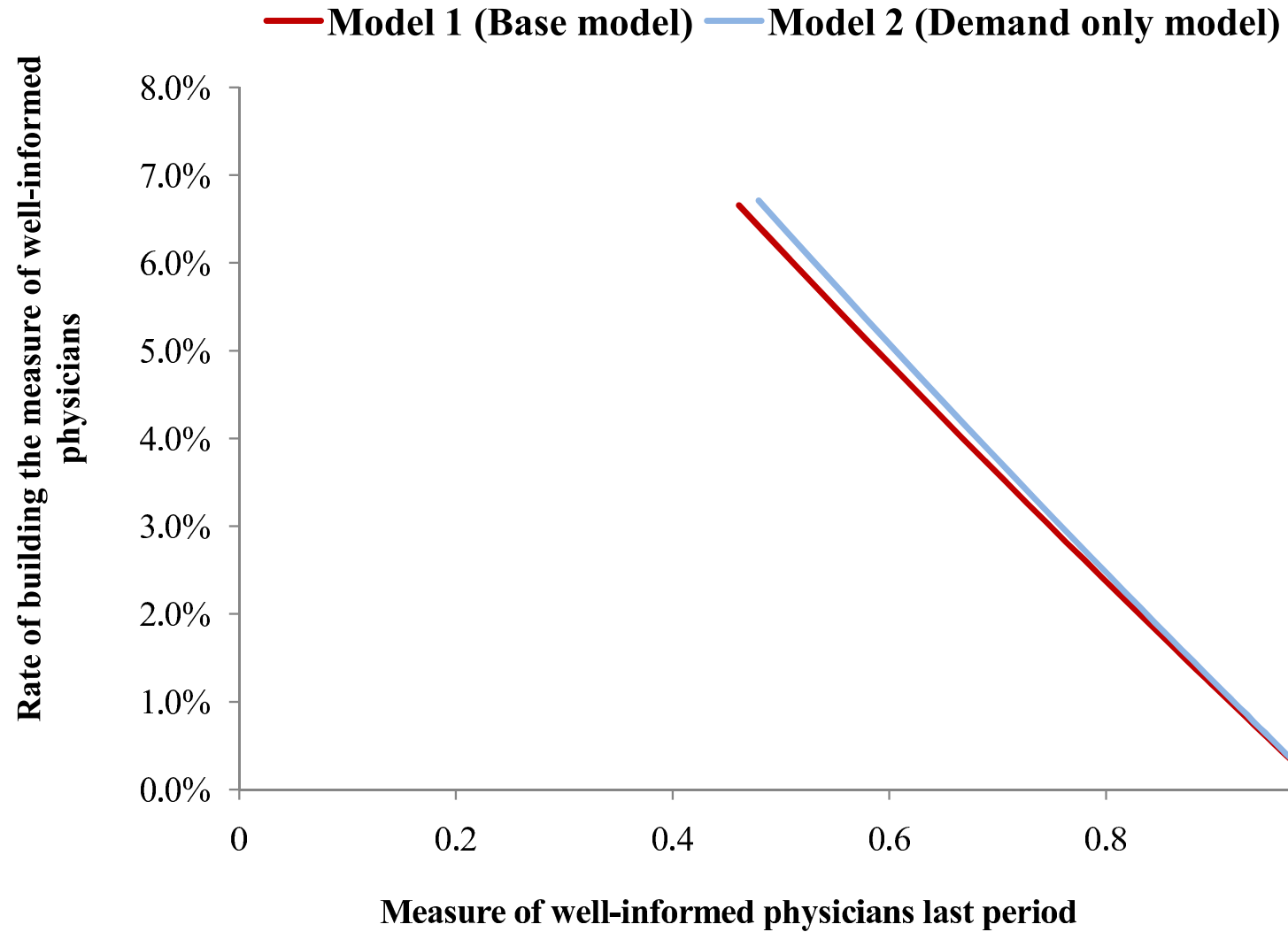
* Estimates shown in bold are significant at 5% level .

Average Rate of Forgetting

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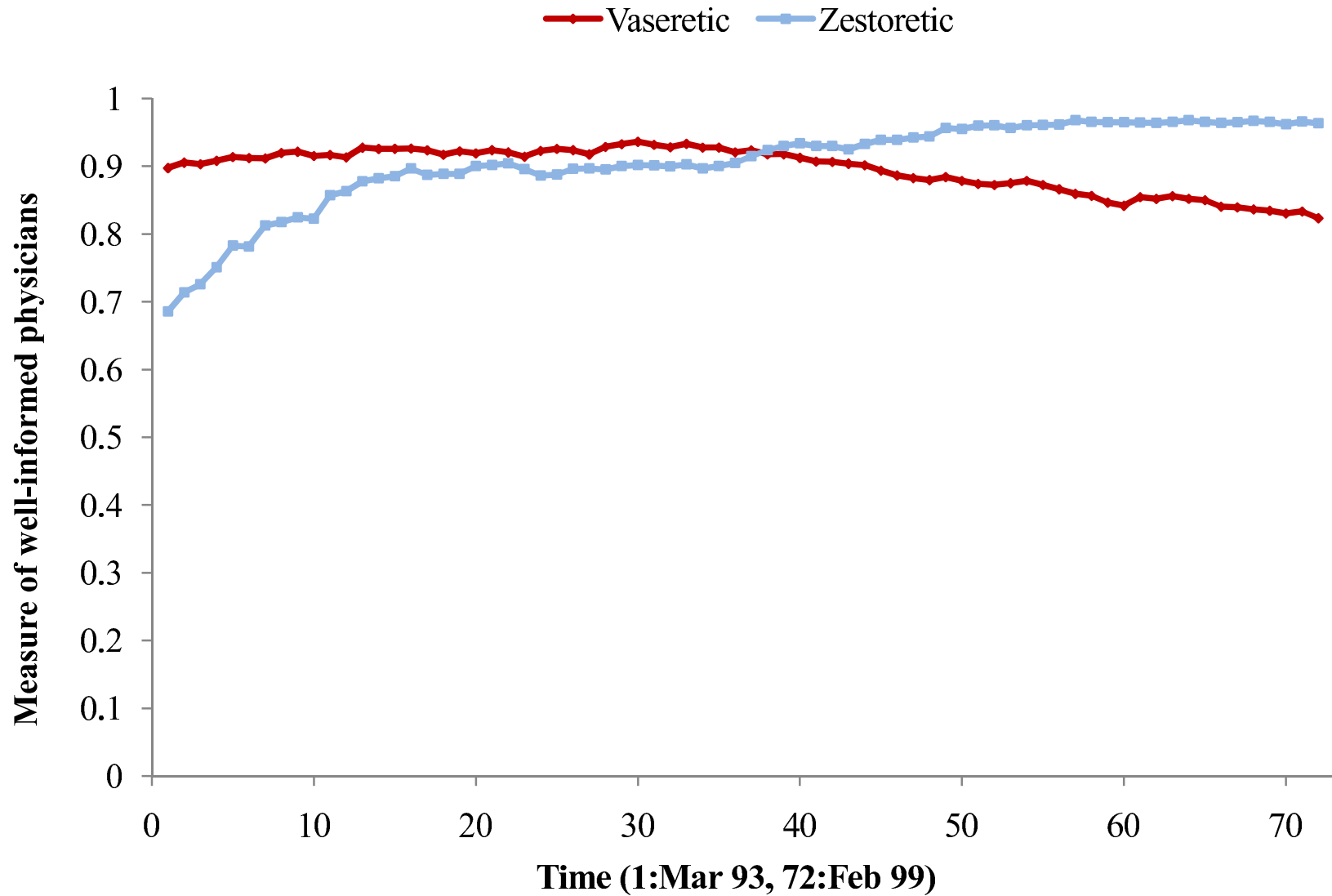


Rate of Building M

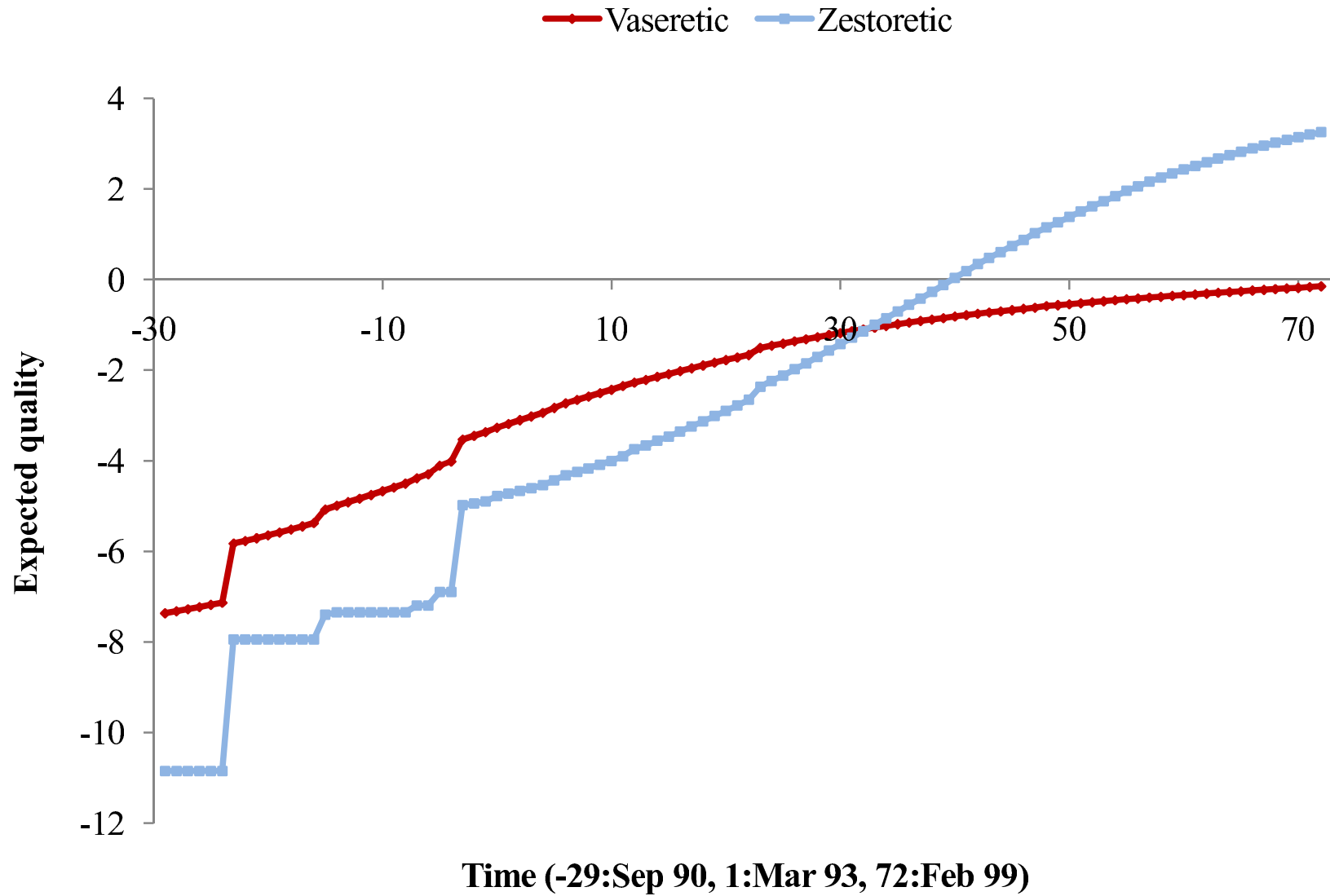


Measure of Well-Informed Physicians

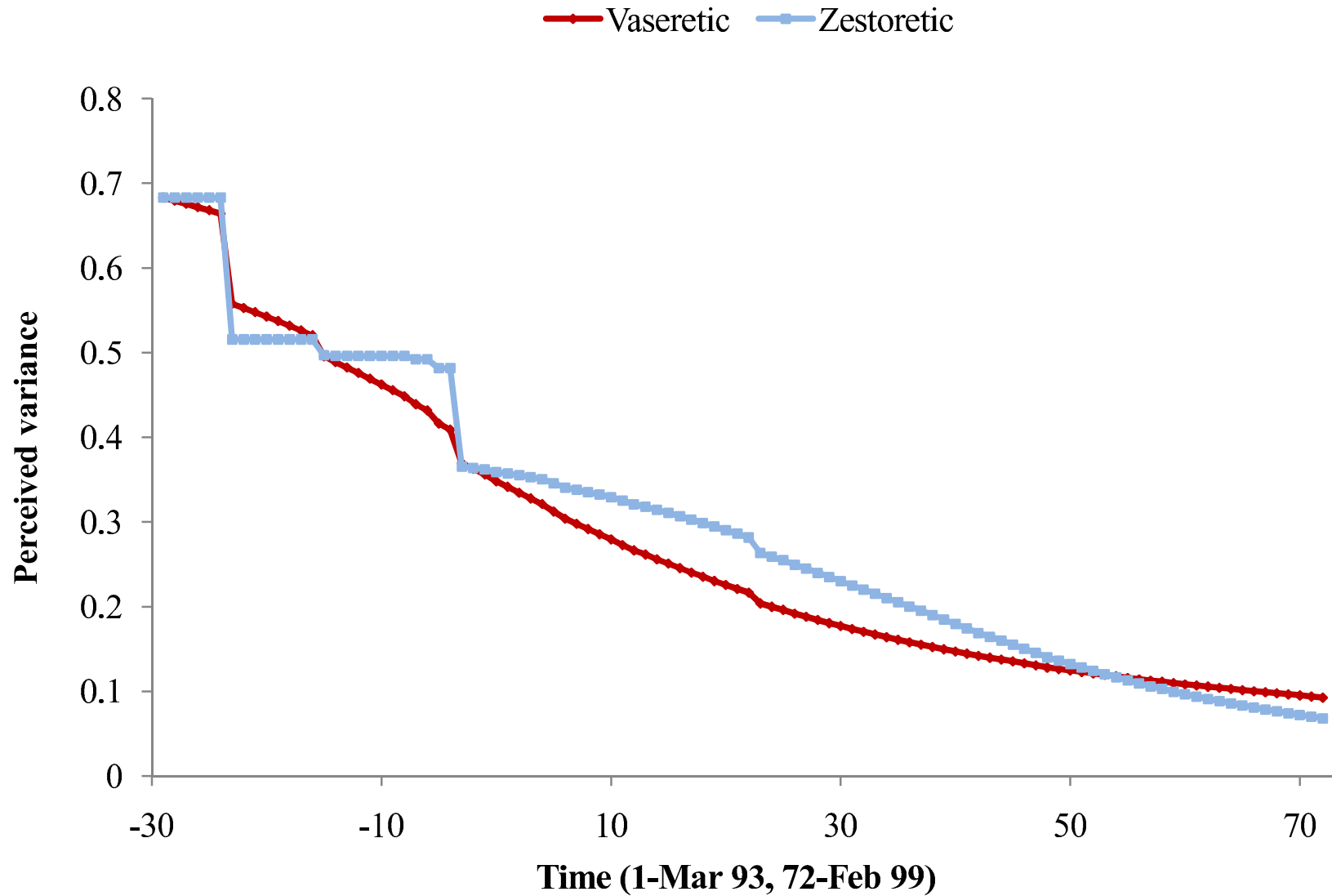
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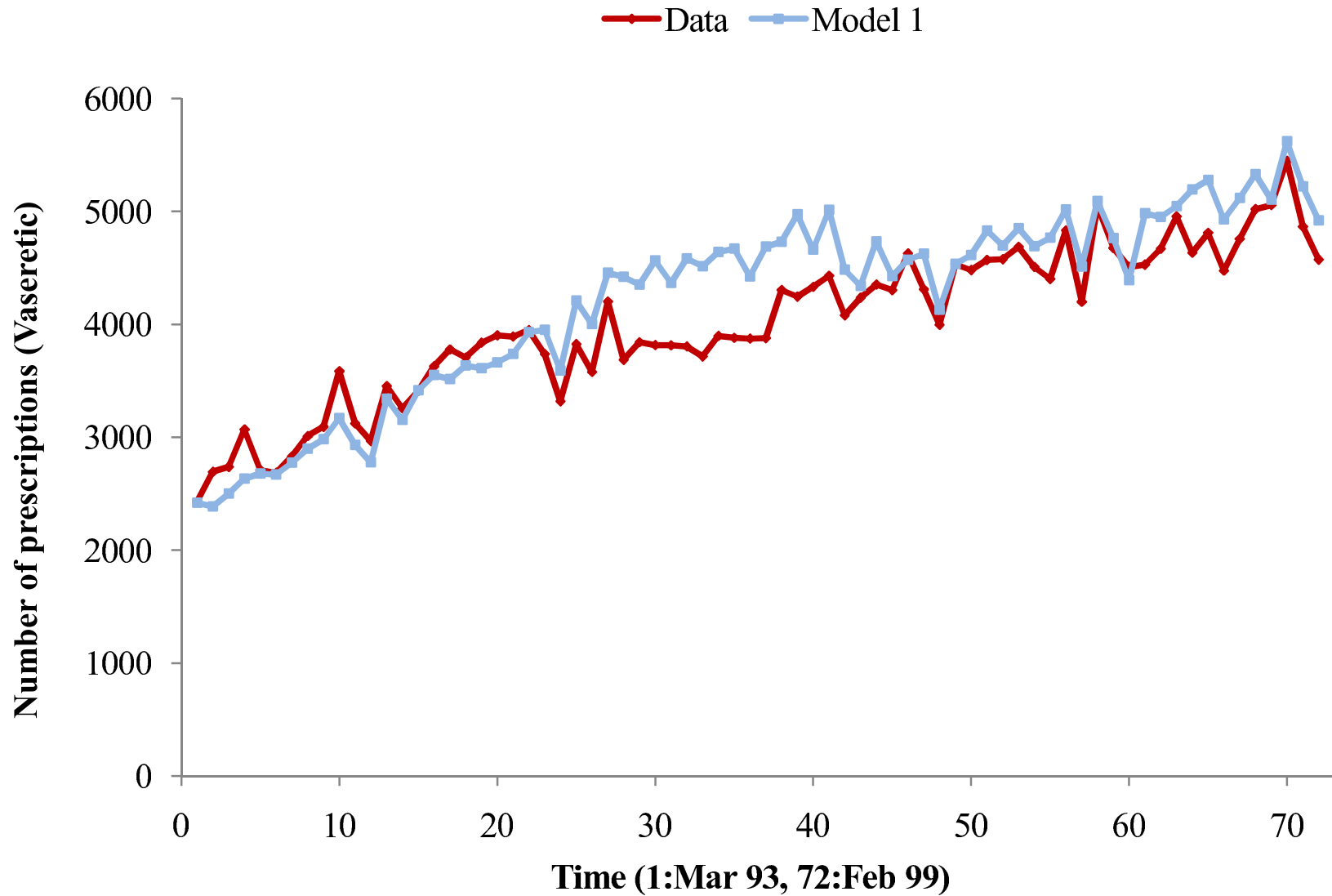
Expected Quality



Perceived Variance

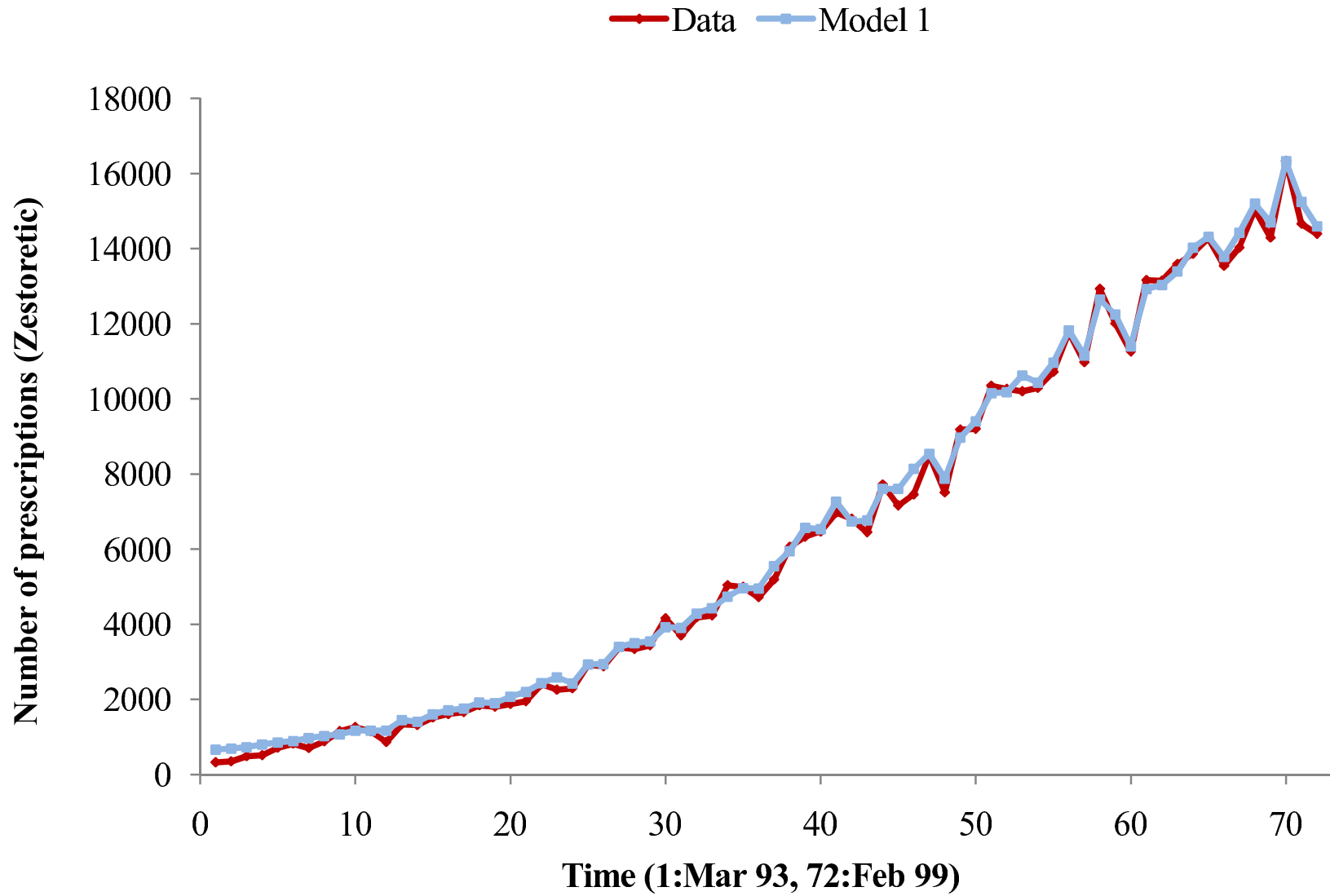


Fit: Demand for Vaseretic



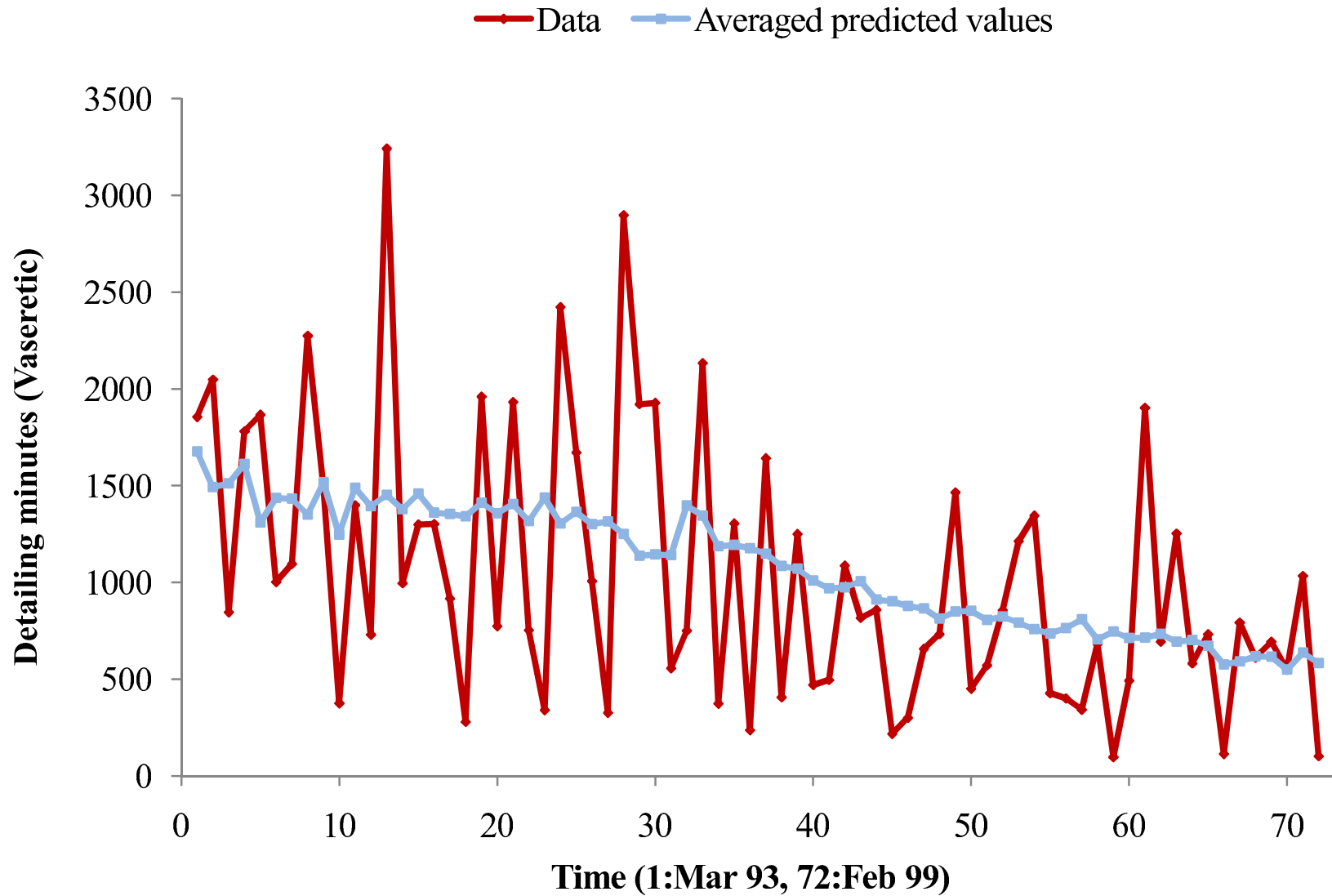
Fit: Demand for Zestoretic

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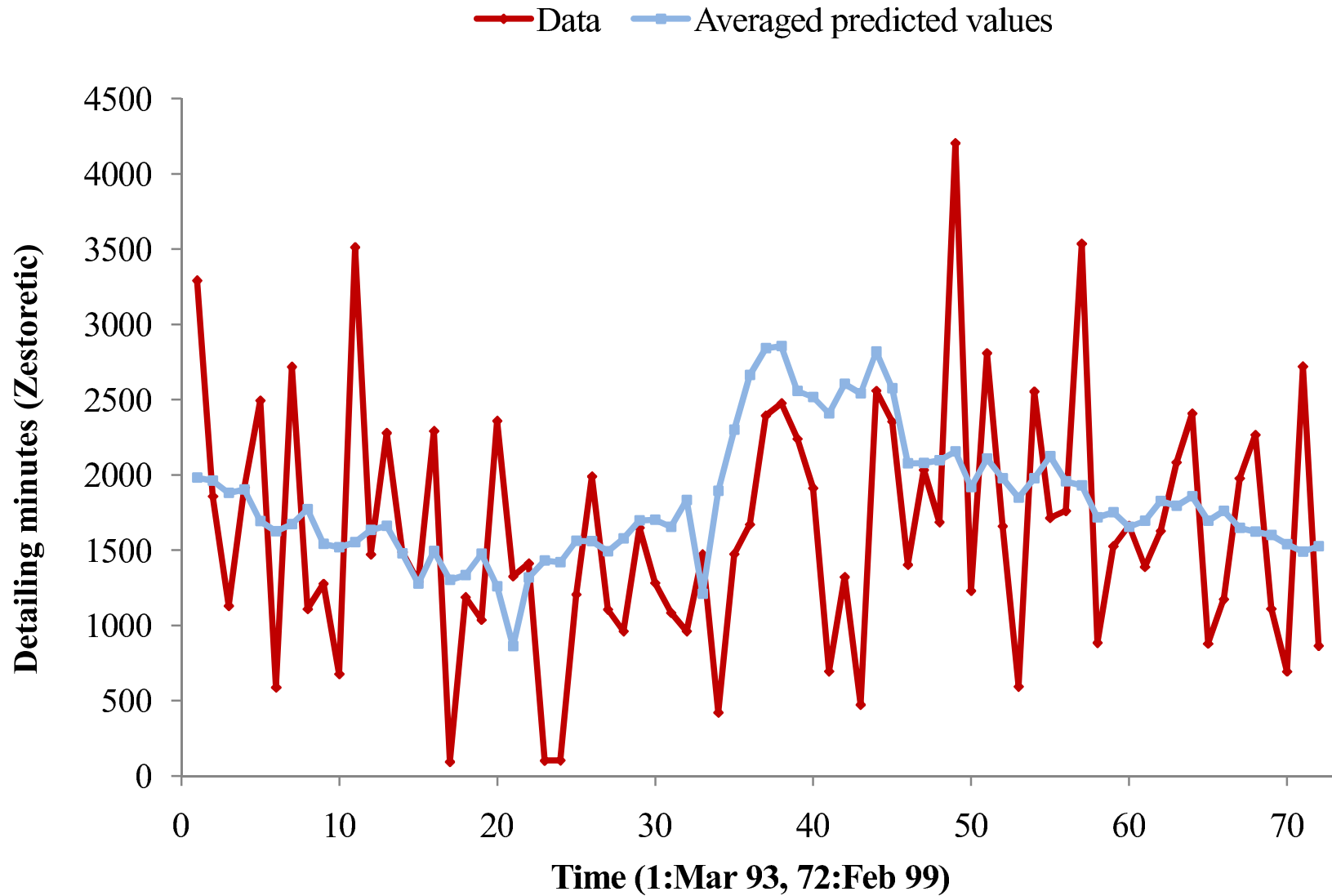
Fit: Detailing for Vaseretic

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Fit: Detailing for Zestoretic

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Simulation

- We simulate the effects of a one-time increase in detailing for three scenarios.
 - ◆ $t = 1$, when the expected quality of Vaseretic (incumbent) is higher.
 - ◆ $t = 26$, when the expected qualities are about the same for both drugs.
 - ◆ $t = 60$, when the expected quality of Zestoretic (entrant) is higher.
- We set $G_{j0} = 1600$, which translates to $M_{j0} = 0.5$.
- We set $D_{jt} = 1300$ for $j = 1, 2$ and $t > 0$.
- Increase detailing amount by 50% in the period that we are interested.

Effectiveness of Detailing

	Increase in detailing for Vaseretic		Increase in detailing for Zestoretic		Base demand		Average $I(t)$ ($E[q_j I(t)], \sigma_j^2(t)$)		Measure of well-informed physicians in the last period
	change in demand		change in demand						
time	Vaseretic	Zestoretic	Vaseretic	Zestoretic	Vaseretic	Zestoretic	Vaseretic	Zestoretic	
1 (Mar 93)	32.302	-6.002	-6.332	20.375	1410.8	704.5	(-3.55, 0.37)	(-4.68, 0.36)	0.50
26 (Apr 95)	26.654	-9.265	-9.911	27.303	3268.6	3211.3	(-1.78, 0.23)	(-1.80, 0.24)	0.85
60 (Feb 98)	22.360	-9.214	-17.763	52.973	4688.0	10878.4	(-0.52, 0.12)	(2.49, 0.09)	0.92

Public Awareness Campaign

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- In order to enhance the speediness of updating the safety profile of drugs, Public health agencies have been considering various measures to encourage health care professionals and patients to share their drug experiences with them (MEDEffect by Health Canada).
- How should marketing managers respond if such a public awareness campaign is introduced?
- We use our structural model to address this question.
 - ◆ Suppose that the rate of reporting patients' experiences to the public becomes doubled due to the public awareness campaign.
 - ◆ This is equivalent to doubling κ (proportion of consumption experience signals revealed).
 - ◆ We re-simulate the effectiveness of detailing by doubling κ .

Top (2κ) / Bottom (base)

	Increase in detailing for Vaseretic		Increase in detailing for Zestoretic		Base demand		Average I(t) ($E[q_j I(t)], \sigma_j^2(t)$)		Measure of well-informed physicians in the last period
	change in demand		change in demand						
time	Vaseretic	Zestoretic	Vaseretic	Zestoretic	Vaseretic	Zestoretic	Vaseretic	Zestoretic	
1 (Mar 93)	48.011	-8.014	-6.123	20.570	1949.3	711.2	(-2.42, 0.28)	(-4.48, 0.35)	0.50
26 (Apr 95)	31.285	-11.327	-15.770	46.181	3793.5	5431.5	(-0.60, 0.13)	(0.57, 0.16)	0.85
60 (Feb 98)	25.080	-10.385	-20.661	61.929	5241.0	12717.3	(0.22, 0.06)	(4.04, 0.04)	0.92

	Increase in detailing for Vaseretic		Increase in detailing for Zestoretic		Base demand		Average I(t) ($E[q_j I(t)], \sigma_j^2(t)$)		Measure of well-informed physicians in the last period
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Conclusion

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- This paper develops a structural model of learning and informative detailing under the environment which both drug firms and physicians are uncertain about drug qualities.
- The empirical implications of our model are consistent with the recent empirical findings on the relationship between new clinical evidence and the effectiveness of detailing.
- Using our estimates, we simulate how the effectiveness of detailing depends on the information sets and the measure of well-informed physicians.
- Our results point out the importance of developing a structural model that captures the mechanism of how detailing conveys information in the market under study.

Number of Drugs

Number of active drugs in Cardiovascular category

	Mar. 93	Mar. 95	Mar. 97	Feb. 99
Number of drugs	215	239	284	294

- It is hard for physicians to keep track of the latest information about all the drugs.
- Some physicians may be busy and rely on the information provided by detailing.