



Cornell University

# The Competitive Effects of Prescription Drug Withdrawals

John Cawley, Cornell University and NBER

John A. Rizzo, Stony Brook University

# Research Questions

- After a drug withdrawal, do remaining drugs in same class enjoy competitive benefits or suffer negative spillovers?
  - Do those taking non-withdrawn drugs continue to do so or quit?
  - Do those previously taking withdrawn drugs switch to another drug in the class or quit altogether?
  - On net, how does utilization of non-withdrawn drugs change?

# Conceptual Framework and Previous Literature

- Withdrawal of a drug may cause competitive benefits or negative spillovers to remaining drugs in class:
  - Competitive benefits: in oligopoly, fewer competitors means more residual demand
    - Ahmed et al. (2002): share prices of pharma companies rise 5 days after competitors drug withdrawal (1966-98)
    - Dowdell et al., (1992): Tylenol poisonings prompted tamper-proof packaging legislation; shares in all pharma firms dropped but those of JNJ's competitors fell less

# Conceptual Framework and Previous Literature (cont.)

- Negative spillovers: e.g. consumers draw conclusions about whole class
  - Jarrell and Peltzman (1985): drug withdrawals 1974-82: pharma stocks fell 1% in 2 wks after withdrawal of rival drug
- Dranove and Olsen (1994): no net effect of drug withdrawals on share prices of rival firms

# Relative Contribution

- Studies of stock price changes:
  - Informative about investor beliefs but may not reflect changes in drug utilization patterns
    - Could reflect concern about increased regulation/scrutiny of mfg of withdrawn drug
  - Follow-up period (days to weeks) too brief to assess long-term changes in consumer behavior
  - Since come to every conclusion (benefits, negative spillovers, no effect), underscores need for direct study of consumer behavior
- Our contribution:
  - To our knowledge, this is first direct study of consumer response to drug withdrawals
  - Use longitudinal micro data to study initiations, quits
  - Longer follow-up: up to 3 years post-withdrawal

# Spillovers in Pharma Research

- Positive messages about a drug tend to have spillovers throughout the class
  - DTCA increases sales of whole class; Rosenthal et al. (2003); Iizuka and Jin (2003)
  - DTCA increases compliance of other drugs in class; Wosinska (2003)
  - Marketing for Rx spills over to same-brand OTC products; Ling, Berndt and Kyle (2002)
- We test for spillovers within class from *negative* information

# Measuring Impact of Withdrawal

- Ideally would compare (market after withdrawal) to (same market absent withdrawal) but counterfactual not observed
- No appropriate control group for diff-in-diff models
- Compare market for class of drugs after withdrawal to same market before withdrawal, controlling for correlates of demand
- Limitation: omitted variable bias - one-time events around withdrawal or trends throughout period
  - However, drug withdrawals usually the dominant event in market at that time
- We control for # scrips per capita per year by geographic region
  - Berndt (2002): increases in Rx volume 1990-2000
- Look for common patterns across 7 drug markets with a withdrawal, 1997-2001

# Drug Withdrawals and Classes Studied

<b>Brand Name of Withdrawn Drug</b>	<b>Indication Treated</b>	<b>Date Withdrawn</b>	<b>Primary Health Risk (Reason Drug Withdrawn)</b>	<b>Name of (Sub-) Class</b>	<b>Examples of Drugs In Class Remaining on Market</b>
Pondimin	Obesity	9/15/1997	Valvular heart disease	Anorectics	Adipex, Ionamin, Meridia, Phentermine, Diethylpropion, Dexedrine
Redux					
Duract	Pain	6/22/1998	Liver failure	Non-steroidal Anti-Inflammatory	Arthrotec, Naproxon, Ibuprofin, Diclofenac, Daypro, Diclofenac Sodium
Posicor	Hypertension	6/8/1998	Lowered heart rate, adverse interactions With 26 other drugs	Calcium channel blockers	Adalat, Calan, Cardizem, Covera, Diltiazem Hcl, Norvasc
Propulsid	Heartburn	7/14/2000	Potentially fatal irregular heartbeat	GI stimulants	Metoclopramide Hcl, Reglan
Lotronex	Irritable Bowel Syndrome	11/28/2000	Ischemic colitis	Antidiarrheals	Carafate, Cytotec, Sucralfate
Baycol	High Cholesterol	8/8/2001	Fatal rhabdomyolysis	HMG-CoA Reductase Inhibitors	Lipitor, Zocor, Pravachol, Lescol, Mevacor

# Study Multiple Outcomes

- Study utilization, initiations, quits
- Reason: spillovers may be multi-dimensional
  - Quits: issues of brand loyalty, patient selection based on ability to tolerate drug, patients have private knowledge about side effects (drugs an experiential good)
    - Least likely to see negative spillovers
  - Initiations: no current experience with class so no such issues
    - Most likely to see negative spillovers
  - Utilization: mix of long-time and new users
    - In between

# Data: MEPS

- Medical Expenditure Panel Survey, 1996-2002
  - Collected by AHRQ
  - Drawn from NHIS sample; nationally representative
  - Overlapping panel design: 2 calendar years of information collected from each household
    - We pool both observations on each adult and all years 1996-2002
    - N=124,314
  - Prescribed Medicines File event level; we convert to person-year level
    - Respondent reports, interviewer prompts, survey of pharmacy providers
    - Multum Lexicon File identifies drugs in class
      - Use smallest sub-class that exists: closest substitutes
  - Merge Full Year Consolidated File, Household Consolidated File, and Prescribed Medicines File
    - Study those over age 18

# Methods

- Logit models of utilization, initiation, and quits
  - Lose first year of data per person when study initiations and quits
- Each is estimated for *non-withdrawn* drugs in class

# Methods

- Parameters of interest: coefficients on year indicator variables
  - In particular, those after drug withdrawals
    - Compared to the year before drug withdrawal
  - Assume that withdrawal (and the information it provides) was unexpected before the beginning of the calendar year in which it occurred
- Not evaluating optimality of consumer response
  - Simply documenting what the response *is*

# Regressors

- Indicator variables for year
- Trend in # scrips per capita in geographic area
  - 258 MEPS sampling areas
- Whether respondent had condition in question
  - Determined using ICD9 codes
- Gender, African-American, Hispanic, other race
- Age, marital status
- Urban, region
- Income, education
- Whether respondent uninsured, whether has prescription drug coverage

# Utilization of *Non-Withdrawn* Drugs in Class; N=124,314 (Odds Ratios)

<i>Indication Treated</i>	<i>Withdrawal – 3 Years</i>	<i>Withdrawal – 2 Years</i>	<i>Year Withdrawn</i>	<i>Withdrawal + 1 Year</i>	<i>Withdrawal + 2 Years</i>	<i>Withdrawal + 3 Years</i>
Obesity			1.104	0.673**	0.664*	0.436***
Pain		1.076*	0.960	0.886***	0.734***	0.684***
Hypertension		1.291***	0.930	0.961	0.893*	0.892*
Heartburn	0.598*	1.094	1.249	1.537**	1.408	
IBS	1.229	0.901	0.772	0.682*	0.919	
Cholesterol	0.781**	0.846**	1.271***	1.523***		

# Empirical Results: Any Use

- In four classes, (obesity, IBS, pain, hypertension) use falls considerably after a withdrawal in the class
  - Use only 67-68% as likely one year after, as one year before, withdrawal for obesity and IBS drugs
  - Use only 89% as likely one year after, as one year before, withdrawal for pain drugs
  - For obesity, pain, hypertension use remains lower 3 years after withdrawal
  - Consistent with negative spillovers
- In two classes (heartburn, cholesterol), use of non-withdrawn drugs higher after withdrawal
  - Consistent with positive spillovers; pattern over time suggests trend towards increasing market

# Initiation of *Non-Withdrawn* Drugs in Class (Odds Ratios)

<i>Indication Treated</i>	<i>N</i>	<i>W – 3 Years</i>	<i>W – 2 Years</i>	<i>Year Withdrawn</i>	<i>W + 1 Year</i>	<i>W + 2 Years</i>	<i>W + 3 Years</i>
Obesity	55,030				0.444***	0.506**	0.332***
Pain	48,852			0.915	0.877*	0.703***	0.680***
Hypertension	51,730			0.691**	0.888	0.894	0.994
Heartburn	55,125	1.127	1.468	1.995	2.608**	1.330	
IBS	55,133	1.175	0.720	0.607	0.458**	0.936	
Cholesterol	51,926	0.791	0.596***	0.905	1.269		

# Empirical Results: Initiation

- In three classes (obesity, IBS, pain), evidence of negative spillovers:
  - Initiation only 44-46% as likely one year after, as one year before, withdrawal for obesity and IBS drugs
  - Initiation only 88% as likely one year after, as one year before, withdrawal for pain drugs
  - Consistent with negative spillovers
- In one class (heartburn), evidence of positive spillovers
  - Initiations of non-withdrawn heartburn drugs 161% more likely after withdrawal

# Quits of *Non-Withdrawn* Drugs in Class (Odds Ratios)

<i>Indication Treated</i>	<i>N</i>	<i>W – 3 Years</i>	<i>W – 2 Years</i>	<i>Year Withdrawn</i>	<i>W + 1 Year</i>	<i>W + 2 Years</i>	<i>W + 3 Years</i>
Obesity	297				2.133*	1.188	0.743
Pain	6,475			0.871	1.066	1.134	1.242**
Hypertension	3,597			0.603***	0.554***	0.613***	0.538***
Heartburn	202	1.948	0.988	2.322	0.634	0.569	
IBS	194	1.508	0.533	1.305	1.763	3.233	
Cholesterol	3,400	0.665**	0.696*	0.717*	0.702*		

# Empirical Results: Quits

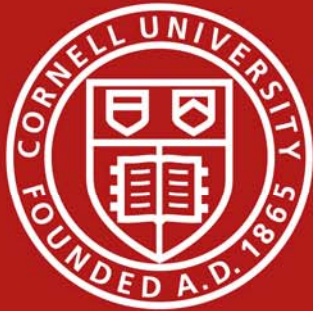
- Evidence of negative spillovers in two classes:
  - Quits of obesity drugs 113% more likely one year after withdrawal, relative to year of withdrawal
  - Quits of pain drugs 24% more likely three years after, relative to year before, withdrawal
- Evidence consistent with competitive benefits in two classes:
  - Hypertension (54.4% as likely)
  - Cholesterol (70.2% as likely)
  - But excluded year appears unusually high; every other year effect significant

Do those who took the withdrawn drugs *in the year they were withdrawn* switch to another drug in the class the next year or stop taking all drugs in class?

Drug	N	% Quitting Entire Class
Pondimin, Redux (obesity)	19	94.7
Duract (pain)	8	87.5
Posicor (hypertension)	4	50.0
Propulsid (heartburn)	9	66.7
Lotronex (IBS)	2	100.0
Baycol (cholesterol)	37	48.7
TOTAL	79	70.8

# Conclusions

- Results consistent with spillovers being multi-dimensional
  - Negative spillovers found in utilization, initiations but not quits
  - Suggests brand loyalty, prior experience with class may mediate spillovers
- Complements finance literature on changes in share prices of pharma companies after rival's drug withdrawn
  - Most consistent with Jarrell and Peltzman (1985)
- Relates to literature in pharmaceutical economics that documents consumer responses to positive information such as DTCA.
  - Our findings establish that the effects of *bad* news also can spill over throughout a drug class.



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