Entry in the ADHD drugs market: Welfare impact of generics and me-toos †

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Abstract

We use a novel approach to identify price effects in a differentiated products demand system for drugs used to treat ADHD and find that the demand for ADHD drugs is elastic and there are significant substitution possibilities within and across molecules and delivery mechanisms. The first-time introduction of a generic drug shows large welfare gains due to expansion of the market to price sensitive consumers. The welfare gains due to the introduction of me-too drugs vary by the novelty of the drug and can be as large as those of the introduction of a generic.

Key words: Differentiated products demand, multistage budgeting, AIDS model, psychostimulant drugs, drug entry, welfare analysis

JEL Classification: I10, I18, L65, L40, L50

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1. INTRODUCTION

The Hatch-Waxman Act of 1984 aims to balance the dual objectives of preserving the incentives of undertaking R&D by innovators while at the same time offering incentives for generic entry under section IV of the Act, i.e. the first successful generic entrant to challenge the patent is granted six months of generic exclusivity (Grabowski and Vernon, 1992, 1996, Grabowski et al., 2002, Frank and Salkever, 1997, Shulman et al., 1999). In recent years, actions by pharmaceutical firms (as well as approval policies at the Food and Drug Agency (FDA)) have come under scrutiny for potentially undermining the intent of the Act. For instance, the introduction of follow-on drugs (the so called me-toos) is criticized because they reduce the profits of the innovator and hence the incentives to engage in R&D without necessarily offering either price reductions or significant therapeutic benefits to consumers. Similarly, the entry of an authorized generic drug under a license from the innovator raises concerns since it discourages other generic drug firms from pursuing entry. In terms of consumer welfare, the latter issue is further complicated because the licensed generic entry often takes place well before the patent expiration of the innovator but perhaps later than it would have otherwise occurred under the section IV terms, as suggested by the "reverse payments" by the patent holder to the licensee (Bulow, 2004, Reiffen and Ward, 2007, Berndt et al., 2007, Frank, 2007). In this paper we estimate a demand system for psychostimulant drugs – a segment fraught with the issues mentioned above – and use our estimates to gauge the welfare gains due to the introduction of generics as well as of me-toos in this segment. We also discuss the likely welfare loss due to the delayed entry of a generic in this market.

The demand for psychostimulant drugs used to treat Attention Deficit Hyperactivity Disorder (ADHD) has grown rapidly in the past decade. Between 1990 and 1996, psychostimulant consumption increased 37% nationwide, while the number of patients diagnosed with the disorder grew from around 900,000 to approximately 3 million. In 2000, the total sales of ADHD drugs in the U.S. was about $1 billion and by 2003 had surpassed $2.2 billion (in constant 2000 dollars). This explosion in the market allowed for several drug manufacturers to enter the ADHD market. By the late 1990s, there were at least half a dozen different branded drugs in this market, some were still on-patent, as well as many generic equivalents of expired patent formulas. The entry by new drugs has evolved into a large differentiated product system containing both branded and generic drugs. These new drugs were either new entities (i.e., new formulas or molecules) or new presentations (i.e., new forms that extend the release) and were introduced by incumbent drug firms as well as by new entrants.

Some of the new introductions were almost overnight successes. Concerta was introduced in 2000 and immediately secured 4.7% of the market, a success by most industry standards. However, by 2003 it was a 'blockbuster' with a market share of 26.1% of all ADHD drugs. Another blockbuster, Adderall XR, was introduced in 2001 by the incumbent firm Shire which had been marketing Adderall since 1996. Both Adderall and Adderall XR are mixed amphetamine salt based molecules (MAS) targeted for populations for whom the traditional methylphenidate molecule (MPH) is not effective, and where XR is the extended release version (MAS-ER) while Adderall is the immediate release version (MAS-IR). In 2001, the market share of Adderall was 35.8% and that of Adderall XR was 1.1%. However, by 2003 the share of Adderall was 2.9% while that of Adderall XR was 23.8%. While this may be a case of a firm 'cannibalizing' its own product (and shifting market shares), it can be argued that without such a move, Shire would have lost significant market share to the generic entry in the MAS-IR segment which took place in 2002. Additionally, Shire also faced a threat of entry for its Adderall XR product when a generic manufacturer (Barr laboratories) filed for an Abbreviated New Drug Application (ANDA) with the FDA in February 2003. Shire sued for infringement of its key patents on the Adderall XR and eventually Shire and Barr reached an out of court settlement. Under the terms of the agreement, Barr agreed not to enter until April 2009, at which point it would enter as a licensed generic maker of Adderall XR with a 180-day exclusivity period.

The nature of these products and the circumstances under which their entry occurred, or was possibly delayed, raises interesting questions: Was there too much or too little entry? Did subsequent entry provide only a small/incremental therapeutic benefit to the consumers, but primarily only split the market and reduce the long term incentives to invest in R&D? How much did consumers benefit from these new introductions?

As a first step to answering these questions, we estimate a system of demand equations for these products. We exploit a novel approach to identify a differentiated products demand system for therapeutically equivalent drugs. Using unusually detailed, retail level sales data on psychostimulant drugs from U.S. pharmacies between 1999 and 2003 (i.e., sales in dollars and number of pills dispensed by strength, form and molecule by year in each 5 digit ZIP-code) we estimate a system of demand equations for these differentiated products. To overcome the problems that are introduced in demand systems with large numbers of differentiated drugs, we follow the approach suggested in Hausman et al. (1994) and Hausman (1996). Specifically, we use the assumption of weak separability and multistage budgeting by a representative consumer to divide the market into smaller segments,

and estimate an AIDS model on the lowest and middle segments. The lowest segments consist of individual drugs within the same molecule and form. The next level up consists of different forms of the drug in the same molecule. The third level consists of choice across molecules. Finally, at the top-level we have a single demand equation which consists of all psychostimulant drugs used for the treatment of ADHD.

In addition to the challenges posed by the large number of parameters that need to be estimated in a differentiated products market, demand estimation also requires a clear identification strategy when prices are endogenously determined. To this end we use an identification strategy that recognizes and exploits inherent exclusion restrictions that are implied by the *assumption* of weak separability and multistage budgeting process for the *conditional* demand functions. This strategy leads to some natural instruments already available in the sales data. We believe that our insight into these implied exclusion restrictions is unique, and to our knowledge, has never before been applied in other similar demand system settings.

Understanding the empirical properties of the demand for these drugs is important for several reasons. First, the introduction of new products expands the range of consumer choice and increases consumer welfare. The magnitude of welfare effects in turn depends partly on the level of product differentiation, the steepness of the individual demand curves and cross-elasticities of demand, as well as the induced effects on price competition among incumbents and new entrants (Bresnahan, 1997). These interactions play an especially prominent role in the pharmaceutical industry where even modest differentiation may lead to large welfare gains. Consider the introduction of a generic drug. While a generic does not introduce a new product variety, it may still create large welfare gains if the market expands to include price sensitive consumers who formerly were either consuming a drug in a different molecule class, a different form, or doing without drug therapy. The welfare analysis of generic entry becomes somewhat more complicated when we recognize the possibility of price *increases* for branded drugs to the brand loyal segment of the market as a response to generic entry (Grabowski and Vernon, 1992, Frank and Salkever, 1992, Regan, 2008).

Moreover, the welfare effects of the follow-on/me-too drugs are more ambiguous. On one hand, Lu and Comanor (1998) report that in the U.S., me-too drugs were typically introduced at the same price as the original branded drugs, and the average effect of adding an extra competitor was a

price reduction of about 2%. Similarly, Lichtenberg and Philipson (2002) report that "between-patent" competition may reduce an innovators returns at least as much as that from "within-patent" competition.[1] On the other hand, DiMasi and Paquette (2004) suggest that me-too drugs may provide substantial welfare gains by lowering side effects, changing the delivery mechanism or targeting a new sub-population and effectively increasing the market. Additionally, it is also possible that the introduction of me-toos can close the substitution gap between the higher priced and higher (perceived) quality original drug and the cheap but lower (perceived) quality of the generics. For instance, when the price of the original brand is raised, consumers can substitute with the me-too brands rather than the generics, while at the same time a rise in the price of the generics may move consumers to the me-too brands instead of to the original brand. Thus, the introduction of me-toos can expand the market as well as bridge the substitution possibilities between brands and generics leading to modest gains in consumer welfare.

Second, demand responses in this market, as in other health products subject to insurance, are complicated because they involve a combination of medical decision-makers and are affected by the price sensitivities of both the patient and insurer who jointly pay for prescriptions. The horizontal and vertical properties of these products lend themselves to a well-structured system. The horizontal structure can take into account the fact that some drugs are quite similar in molecule, time release, and brand identity, thus likely to be more closely related in the system than others. Likewise, there is a vertical dimension of consumption because physicians' prescribing behavior may involve choices among broad categories of drugs before choosing a specific formulation within the selected category. Demand analysis reveals the extent of substitution possibilities among drugs, both within and across molecule-forms, and helps shape public policy.

For instance, proposals to address the rising costs of prescription drugs often call for the creation of countervailing power among large volume buyers (e.g. among state Medicaid or Medicare Part-D plans) to extract discounts from wholesalers in exchange for limiting the choice of brands through the use of formularies. Already several insurance companies, particularly managed care organizations and Veterans Affairs, can and do exercise such countervailing power. However, while the size of the buyer is important, both Ellison and Snyder (2001) and Sorensen (2003) show that it is not a sufficient condition for obtaining price discounts, and that actual substitution possibility among suppliers is an important pre-condition. For instance, Ellison and Snyder (2001) report

[1]The term "between-patent" refers to competition from other drugs in the class which are not generics and loosely corresponds to the me-toos while "within-patent" refers to competition from generics.

that large buyers (chain drugstores) did not receive discounts relative to small buyers (independent drugstores) for antibiotics that were still on patent (no substitution possibilities) but did receive a small discount for off-patent antibiotics (with several substitution possibilities). However, the discount differentials between patent and off-patent drugs were significantly more pronounced when the consumers were more willing to substitute one drug for another, i.e., those in HMOs and hospitals. In this respect, while the introduction of generics and several branded drugs play an important role – each introduction increases the choice set within the therapeutic class of drugs – but the actual degree of substitutability may be restricted to a more refined distinction between the main active ingredients (molecules) or even presentations (extended release versus immediate release). Thus, it is important to measure the degree of substitutability between drugs as a way of assessing the likelihood of success prior to enacting laws that create countervailing power among large buyers.

The next section provides a brief background about the growth in ADHD drug market and the nature of firms producing these drugs. This section also outlines the differences among various drugs and how they segment the market. Section three describes the data. The next section outlines the setup of our empirical model and discusses the multilevel structure as it applies to ADHD drugs. In this section we pay particular attention to the issue of endogeneity and discuss our identification strategy at length. Section five provides and discusses demand estimates from the various stages. This is followed by the results giving a measure of welfare gains due to the introduction of some of the drugs. The last section provides a summary and conclusions.

2. Growth and Product Differentiation

2.1. **Market Expansion.** The demand for drugs to treat Attention Deficit Hyperactivity Disorder (ADHD) has grown rapidly in the past decade. It is the most commonly diagnosed behavioral disorder in children and approximately 3-5% of school-age children have this disorder; some estimates range as high as 7-12% or between 1.5-6 million kids. About 75-80% of children diagnosed with ADHD are treated with psychostimulant drugs. Rates of psychostimulant use vary as much as 3-fold between states and 10-fold within them.

Sales of several psychostimulant drugs can be traced back to at least the 1950s. These drugs include some that were specifically approved by the FDA to treat behavioral disorders, as well as off-label drugs that were federally approved for other purposes yet physicians routinely prescribed them for treatment of ADHD (ADHD was officially recognized as a disorder by the National Institute of

Mental Health (NIMH) in 1980). For instance, methylphenidate-HCL (MPH) was patented in 1954 by Ciba Pharmaceutical and was marketed under the trade name of Ritalin for the treatment of chronic fatigue, depression, narcolepsy as well as to offset the sedating effects of other medications.[2] The FDA approved methylphenidate for the treatment of "functional behavior problems" in 1963, and by 1966, Ritalin was often recommended for children with "Minimal Brain Dysfunction (MBD)". Sales of methylphenidate grew steadily over the 1970s and 1980s and got a big boost in the early 1990s after the publication of a study showing marked improvement in the school performance of children suffering from ADHD and on drug therapy. Over the same period, other molecules had gained acceptance for treating ADHD. For instance, Obetrol, which consists of four mixed dextro and levo amphetamine salts, had been unsuccessfully on the market since the 1960s as an approved obesity drug. The rights to Obetrol formulation were sold to Rexar in 1994 which was then acquired by Shire. In turn, Shire received approval from the FDA in 1996 to market the mixed amphetamine salts (MAS) formulation to treat ADHD and sold it under the brand name Adderall.

Significant growth in psychostimulant use began in the early 1990s soon after major changes were enacted by policymakers in Washington, D.C. to include ADHD as a protected disability under the Supplemental Security Income (SSI) program and the Individuals With Disabilities Education Act (IDEA). This explosion in the market allowed for several drug manufacturers to enter the ADHD market. By the late 1990s, there were at least half a dozen different branded drugs in this market, some still on-patent, as well as many generic equivalents of expired patent formulas. In September 2001, pharmaceutical companies that produced these drugs broke a 30-year agreement with the Drug Enforcement Agency (DEA) and the FDA not to advertise their Schedule II controlled substances directly to consumers. In the new era of direct to consumer advertising for ADHD drugs, new drugs were introduced in the market.

2.2. **Product Differentiation – Role of Molecules and Forms.** ADHD is a behavioral disorder marked by excessive inattentiveness and/or hyperactivity-impulsivity. Children with ADHD are believed to have abnormal functioning, or dysregulation, of certain brain chemicals known as neurotransmitters (chemical messengers). ADHD drugs boost levels of two such neurotransmitters, dopamine and norepinephrine, which help to regulate attention and activity. Dopamine is thought to play a role in memory formation and the onset of addictive behaviors, while norepinephrine has been linked with arousal and attentiveness. ADHD drugs increase the levels of both norepinephrine

[2]CIBA Pharmaceutical merged with J. R. Geigy Ltd to form Ciba-Geigy in 1970. Ciba-Geigy merged with Sandoz Laboratories in 1996 to form Novartis, which is now the producer of Ritalin.

and dopamine by either inhibiting their reabsorption (reuptake) into cells or by promoting the release of these chemicals from the brain. For instance, methylphenidate based ADHD drugs, such as Ritalin, inhibit the reuptake of dopamine into cells, while amphetamine based drugs, such as Adderall, also work on dopamine by inhibiting the reuptake but also promote their release into the brain. Depending on the physiology of a patient, one molecule may be more effective than another. Additionally, a particular molecule in a given person may induce adverse reactions. Physicians and patients often have to experiment with different molecules to help identify which particular molecule is most suitable for a given patient (or rule out ones that induce adverse reactions).

Within a molecule, several delivery mechanisms are available which can significantly affect the choice of a specific drug. The primary differences are in the absorbtion rate into the blood stream, and the time to peak effect. Drugs are available in immediate-release (IR) tablets or liquid form as well as in extended-release (ER) tablets or capsules. Immediate release formulas, such as Ritalin or Adderall typically last three to four hours and are taken two or three times a day. These formulations can be more tightly controlled in terms of dosage and frequency in order to inhibit the reuptake and/or promote additional release of neurotransmitters. In the extended release formulations, part of the drug is released immediately into the blood stream while the remaining drug in the capsule is released more slowly and at different rates. These are often further differentiated into intermediate-acting extended-release tablets or long-acting extended-release capsules and tablets. The intermediate long-acting ER formulations, such as Ritalin LA or Metadate CD, may last six to eight hours while the long-acting ER, such as Concerta last eight to twelve hours.[3] The extended release forms reduce the peaks and troughs ('ups and downs') over the day and also eliminate the need for additional doses during school. Thus, each delivery mechanism comes with its own advantages and disadvantages and further segments the market into subgroups (for more details see Barkley (2006)).

Table (1) lists drugs by groups that that are deemed medically similar by health care professionals such that those within the same group can be substituted gram for gram, while those in different subgroups require dosing adjustments.[4] This is not to say that drugs in the same group are always

[3]For instance, both Ritalin LA and Metadate CD use a bead-delivery system, where the active molecule (methylphenidate) is packed into two types of beads, rapid-release which reaches the blood steam quickly and extended-release beads which dissolve slowly. The primary difference is that Metadate CD uses 30% of rapid-release beads while Ritalin LA uses 50% of rapid-release beads leading to a difference in the absorption profile across the two drugs. By contrast, Concerta uses a membrane based technology called Osmotic Release Oral System (OROS). The tablet is coated with methylphenidate which dissolves immediately into the blood and exposes a membrane with multiple layers of the drug. As water seeps slowly through the membrane, it pushes additional drug out to the body and the thickness of the membrane determines the delivery time.

[4]We are indebted to Dr. [Name omitted] of [Institution omitted] for providing us with the equivalence table.

generic equivalents of each other. For instance, while Ritalin LA and Metadate CD are in the same group, they embody slightly different delivery mechanisms (see footnote (3)). The table also provides an approximate rule that physicians employ when switching a patient's drug across a group. The switch from Concerta to Ritalin requires dosing adjustment such that if a child was perviously consuming 100 mg of Concerta over a period of time, they would now use only .69 mg of Ritalin over the same period.

TABLE 1. Groups of Bio-equivalent Drugs

Methylphenidates (MPH)			
(1.0) Ritalin Methylin Generic Ritalin	(.83) Ritalin SR Methylin SR Metadate ER Generic Ritalin SR	(1.25) Ritalin LA Metadate CD	(0.69) Concerta
Mixed Amphetamine Salts (MAS)			
(2.86) Adderall Generic Adderall	(2.14) Adderall XR		
Dextroamphetamines (DEX)			
(1.75) Dexedrine Dextrostat Generic Dexedrine	(2.14) Dexedrine SR Generic Dexedrine SR		
Other molecules (OTH)			
(.28) Provagil (Modafinil)	(.44) Cylert (Pemoline) Generic Pemoline	(.83) Strattera (Atomoxetine)	

The key feature of this table, and one that informs our estimation strategy, is that drugs that can be substituted gram for gram have the same molecule and form. For instance, within the methylphenidate based drugs, there are four subgroups by dosage equivalence. Further, these subgroups differ precisely by the delivery mechanisms mentioned earlier: immediate release (IR), intermediate-acting extended-release (ER-TAB), long-acting extended-release (ER-CAP) and Concerta which is in a category by itself.

3. DATA

3.1. **Data Source.** Data for this study was obtained from the NDCHealth's proprietary Source Territory Manager® data files for the years 1999-2003. NDCHealth's data set provides at the retail level, total sales (in dollars) and number of pills dispensed by strength (in milligrams) for several branded and generic versions of ADHD related drugs at the 5-digit ZIP code level. The Source Territory Manager's coverage is about 70% of all retail level sales (the remaining 30% are pharmacies typically from the rural areas). Thus, for each 5-digit ZIP code in the coverage area

and for each year, we know, for instance, the number of pills dispensed of Ritalin 5mg, 10mg and 20mg separately (Ritalin comes in 3 strengths), as well as the total revenue collected by the retailer from all parties (insurance plus co-pay) for each strength separately. Similar information is known for other forms of the drug. For instance, Ritalin is also marketed as an extended release form under the name Ritalin SR and Ritalin LA. For each of these drugs, we also know the sales and pills dispensed by strength. Using the number of pills dispensed times strength, we obtain the total grams for each drug and form in the local ZIP code area and then aggregate the quantities and revenues up to county level. Dividing the total revenue by the total grams gives a measure of the average transaction level price in the county year for the drug-form. Note two features of this measure of price: (1) it is a (average) transaction level price not a list price and (2), since it is based on retail level data (rather than wholesale), it incorporates the final price of the product paid by all parties and not just the co-payment component paid by the consumer.

3.2. **Sample.** For our analysis, we restricted the sample to counties within all Metropolitan Statistical Areas (MSAs), i.e., to 852 counties. This choice is dictated by two factors. First, not all drugs are necessarily consumed in a given county-year, especially in rural counties. Thus, while the quantity (or share) is known to be zero, the price is not known since it is derived as the ratio of sales to quantity. Including these counties would necessitate imputing the price. However, the problem is largely avoided if we restrict the sample to MSA counties. Second, rural counties also have very few physicians, and since the choice of a drug is in part due to a physician's experience with a specific brand, the demand parameters for rural areas may be very different from those in urban areas. Mixing the two populations may provide an average effect of price on demand, but may not in fact be representative of demand for either the rural or urban populations. Thus, we chose to restrict our analysis to counties in MSAs. Finally, we further restricted the sample to counties with 'balanced' observations across years, i.e., if the drug is on the market, we must be able to observe (positive) sales for all the years since introduction. This criteria reduced the working sample further to 778 counties. For practical reasons, we have also omitted two drugs from our analysis. The first is Desoxyn which is a methamphetamine molecule. It is legally produced only by Ovation Pharmaceuticals. However, the drug is also available illegally through its production in large and small clandestine laboratories throughout the United States (by the street name 'ice'). The data from the legal sales is sparse (less than .15% of sales) but in general sells for more than $200 per gram. The second drug omitted from our analysis is Focalin which is a close cousin of the MPH molecule except that it is a single isomer of MPH. It was introduced in 2002 by Novartis (the

makers of Ritalin) but never attained more than .5% of the market share during the observation period. We cannot estimate the price of this drug reliably since it was sold in very few areas. Thus, in our representative consumer model, these two drugs can be thought of as belonging to the group, "all other goods", since both consist of molecules different from those considered in this study. For the remaining drugs, price per gram and shares are summarized by year in Table 2 (all dollar figures throughout the paper are expressed in constant 2000 dollars).

TABLE 2. Average Prices and Shares by Year (778 MSA Counties)

		Avg. Price Per Grm					Avg. Share of Revenue				
		1999	2000	2001	2002	2003	1999	2000	2001	2002	2003
(1)	Ritalin	54.00	53.32	52.81	53.62	58.23	0.117	0.081	0.033	0.016	0.009
(2)	Methylin	45.30	41.90	39.96	37.92	35.35	0.045	0.068	0.035	0.022	0.013
(3)	Generic MPH-IR	43.69	41.55	39.74	38.58	36.73	0.289	0.185	0.098	0.049	0.026
(4a)	Ritalin SR	61.26	61.39	62.34	64.43	70.51	0.047	0.032	0.012	0.006	0.003
(4b)	Ritalin LA	.	.	.	79.13	79.51	.	.	.	0.006	0.024
(5a)	Metadate CD	.	.	53.32	59.80	78.10	.	.	0.006	0.025	0.024
(5b)	Metadate ER	NA	60.19	59.27	59.67	60.91	NA	0.007	0.007	0.005	0.002
(6)	Methylin ER	.	53.76	52.15	48.50	48.22	.	0.004	0.010	0.008	0.006
(7)	Generic MPH-ER	49.99	48.68	46.38	46.08	44.39	0.105	0.080	0.034	0.017	0.008
(8)	Concerta	.	84.59	71.27	69.63	73.94	.	0.047	0.238	0.298	0.261
(9)	Adderall	56.54	63.12	93.69	101.70	101.29	0.216	0.311	0.358	0.114	0.029
(10)	Generic MAS-IR	.	.	.	92.22	84.29	.	.	.	0.084	0.076
(11)	Adderall XR	.	.	112.88	116.85	125.02	.	.	0.011	0.202	0.238
(12)	Dexedrine	49.68	53.20	59.14	66.17	67.90	0.013	0.010	0.006	0.003	0.002
(13)	Dextrostat	42.06	45.87	54.49	55.98	45.20	0.016	0.018	0.012	0.005	0.002
(14)	Generic DEX-IR	.	.	51.17	49.15	47.88	.	.	0.003	0.004	0.004
(15)	Dexedrine SR	67.64	76.28	85.22	94.15	95.70	0.062	0.062	0.045	0.022	0.007
(16)	Generic DEX-ER	.	.	.	84.62	83.55	.	.	.	0.009	0.011
(17a)	Cylert	39.63	41.99	42.61	44.24	43.88	0.061	0.023	0.009	0.004	0.002
(17b)	Provigil	24.92	24.62	26.10	26.90	27.95	0.022	0.058	0.072	0.093	0.094
(17c)	Generic Pemoline	32.47	31.64	33.07	31.43	29.59	0.005	0.015	0.011	0.006	0.004
(17d)	Strattera	.	.	.	120.07	77.10	.	.	.	0.000	0.156
Total Revenue (in Millions)							688.5	836.8	1,110.3	1,438.0	1,992.7

Note 1: Prices are in constant 2000 dollars per gram. Missing value implies the drug was not on the market, except for the case of Metadate ER which was on the market in 1999, but data are not available to us.
Note 3: Total revenue (also in constant 2000 dollars) is only for the drugs listed above from the 778 counties and does not include mail order sales.

3.3. **Descriptive Statistics.** In 1999, Ritalin had 11.7% of the market share while its bio-equivalent generic, immediate release methylphenidate (MPH-IR), had 28.9% of the market share (the generic version was produced by 15 firms in 2003). New drugs entered the market in 2000 and by 2003, both Ritalin and its generic version had lost significant market share and were down to 0.9% and 2.6% respectively. Over the same period, the average price of Ritalin stayed fairly constant (except for a spike in 2003) while the price of the generic steadily declined.

Concerta entered the market in 2000 and Adderall XR entered 2001. While both started with modest shares in the year of their introduction, by 2003 these two drugs had cornered nearly 50% of

the entire ADHD drug market (26.1% and 23.4% respectively) and sold for $73.94 and $125.02 per gram in 2003. Concerta, produced by Ortho-McNeil, introduced its product in a new niche market. Ortho-McNeil entered into an agreement with ALZA, the developers of Concerta starting in 2000. Concerta itself consists of the time released version of the methylphenidate HCL molecule which has long been used for the treatment of ADHD. However, ALZA developed Concerta by applying Osmotic Release Oral System technology (OROS) for delivery mechanism. While OROS is also an ER formulation, it is slowly released throughout the day at an increasing rate. Thus, while other extended release formulations of the MPH molecule already existed in the market (eg. Ritalin SR and its generic version), the OROS technology used by Concerta was the first (and still is the only) drug that embodied a truly new delivery mechanism which had never been applied in any of the ADHD class of drugs. Similarly, until the introduction of Adderall XR, no drug was available in extended release form for the mixed amphetamine salt (MAS) and when Shire introduced this drug, it too created a new niche market. Shire currently holds a patent on the XR version which will expire in 2018.

Another important drug that entered the market is Strattera, a non-stimulant molecule (atomoxetine), and was introduced in December 2002 by Eli. It attained a significant market share in 2003 (about 15%), perhaps precisely because it is the only non-stimulant ADHD drug on the market. Unfortunately, our data series ends in 2003 and hence will not be able to estimate the individual demand parameters for this drug (in our demand analysis we lump it into a catch all group called 'other drugs' and only estimate the joint effects of this broader category).

Generic version of immediate release form Adderall entered in 2002 and by 2003 it had a 7.6% market share (distributed over three firms). Note also that the branded version of MAS-IR, i.e. Adderall, enjoyed significant market share up until the introduction of the generic version in 2002: 21.6% in 1999, 35.8% in 2001 and then declined to 11.4% in 2002 when the generic entry took place.

Three other drugs of interest that entered over the study period are Methylin ER, Metadate CD and Ritalin LA. All three are extended release forms of methylphenidate HCL. Methylin ER, introduce in 2000 at $53.76 by Mallinckrodt is about $7 above the average price of other generics and about $7 below the price of Ritalin SR or Metadate ER.[5] The market share of Methylin ER was .4% while that of Metadate ER and Ritalin SR was .7% and 3.2% respectively. In the following year,

[5]Methylin ER is a generic extended release MPH version of Ritalin SR but is sold under a trade name since the immediate release version Methylin (also by Mallinckrodt) was already sold as a branded drug – an NDA application was filed for Methylin with the FDA but an ANDA application was filed for Methylin ER. A similar issue applies to Metadate ER, also a generic drug (with an ANDA application) but sold under the tradename of Metadate ER.

Celltech which was already marketing Metadate ER, launched a new time released capsule version, Metadate CD.[6] This resulted in a total market share of 1.1% (=.6+.7) for Celltech via its two forms of Metadate while the share of Novartis's Ritalin SR declined to 1.2%. In the year following that, Novartis launched it own version of a time released capsule, Ritalin LA.[7] The introductory price of $79 per gram for Ritalin LA was $20 higher than the pharmacologically closest substitute, Metadate CD. The market share of Novartis stayed at 1.2% (split as .6 and .6 across LA and SR) while the market share of Celltech climbed up to 3% (2.5% for CD and .5% for ER). In 2003, Celltech increased the price of Metadate CD by almost $19 to $78 (which is just $1.4 below that of Ritalin LA in 2003) while its market share declined by .1% down to 2.4%. Ritalin LA gained a significant market share over the previous year from .6% to 2.4%.

Celltech kept the price of its products Metadate ER and CD slightly below that of the relatively more well known brands Ritalin SR and LA respectively (with some exceptions) and by 2003 had attained a market share of 2.4% which is at par with those of Ritalin SR/LA. On the other hand, Mallinckrodt's Methylin ER was typically priced slightly above that of the generics and attained a market share .6% by 2003, compared to the share of .8% of MPH-ER distributed among 12 generic makers. These are far more modest shares compared to the success of the blockbusters discussed earlier, but still large by industry standards. Further, while such descriptive analysis cannot account for (or hold constant) other simultaneous changes in the market, it appears that Metadate ER/CD are closer substitutes for Ritlan LA/SR while Methylin ER may be a closer substitute for the generic MPH-ER.

4. Model and Estimation Strategy

4.1. **Multistage Budgeting and Conditional Demand Functions.** A fundamental problem in estimating a system of demand equations for a set of differentiated products is the problem of dimensionality. For a system with I products, the demand system $q = D(p, z)$ involves estimation of I^2 parameters, where p is the vector of all prices and z is the vector of exogenous variables that enter the demand equations. Even if symmetry of the Slutsky matrix, homogeneity and other restrictions are imposed, the number of parameters is still large and increases in the square of the number of products. Depending on the research question at hand, the empirical literature has

[6]Unlike the earlier 8 hour release tablets, Metadate CD is a capsule with biphasic release, meaning there is an initial rapid release of methylphenidate, followed by a continuous-release phase (by contrast, for instance, Metadate ER tablet dissolves slowly over the eight hours as it passes through the gastrointestinal tract).

[7]The primary difference is that Metadate CD releases 30% of the drug initially and the remaining 70% over an extended period of time while Ritalin LA has an initial rapid release of 50%.

dealt with the dimensionality issue in a variety of different methods (for a review of these methods, see Nevo (2000)). Following Hausman et al. (1994) and Ellison et al. (1997), we use the notion of weak separability of preferences and multistage budgeting to estimate a series of flexible conditional demand functions.

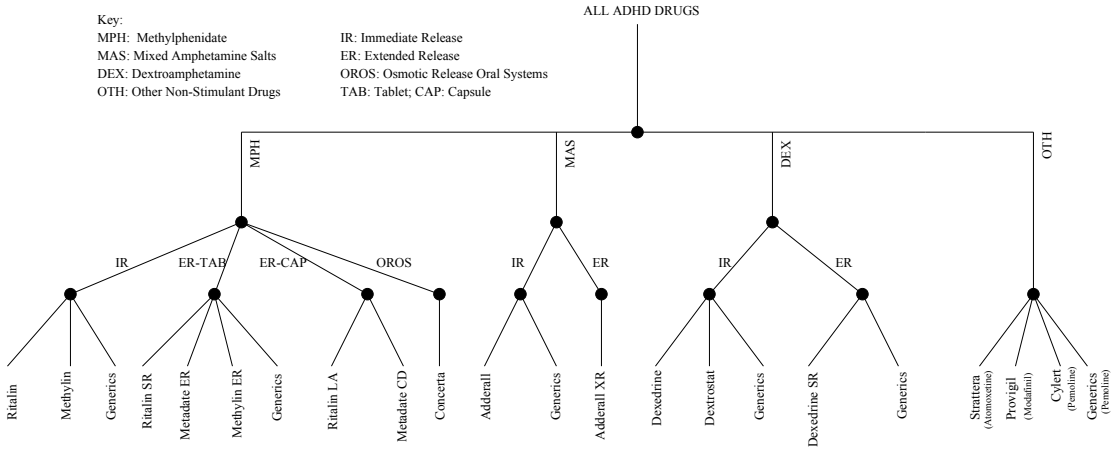
The main assumption about preferences follows Gorman's multistage budgeting approach. This approach assumes that decisions about consumption are structured so that the allocation of expenditures across classes of drugs defined by different molecules are made independently of the decision about how to allocate the resulting drug expenditures across available alternatives. That requires the utility function to be weakly separable which further implies that the demand of good j in a given group is a function of the prices of all other goods in the group and of group expenditure but not of prices of goods in the other groups. This restriction limits the cross price effects for goods in different groups to work through their effect on total expenditures of the groups and cross effects of the groups.

For various stages of the multi-budgeting process, we estimate the Almost Ideal Demand System (AIDS) introduced by Deaton and Muellbauer (1980a,b) which has several desirable properties. First, since the AIDS equations are based on a utility function of the generalized Gorman polar form (for a representative consumer), they satisfy the conditions for multistage budgeting (at least for the exact two-stage budgeting process). Second, the AIDS model aggregates well over consumers and provides an easy way of imposing theoretical restrictions (e.g. adding-up, homogeneity and symmetry). Third, and most importantly, from an empirical standpoint, the AIDS specification provides a flexible substitution pattern between drugs within the same segment. The demand elasticities for individual drugs in a segment are not constant but functions of prices, and any pair of drugs in the system can be complements or substitutes. The resulting Engel curves are nonlinear, a desirable feature often noted in empirical studies. Finally, while the representative consumer metaphor is retained, the model can accommodate demographic effects, location and time specific fixed effects.

In the discrete choice literature, it is well known that imposing an arbitrary grouping and nesting structure for differentiated products can lead to unexpected results. Further, the results are not necessarily invariant to alternative grouping schemes. In the absence of a universal grouping rule, segmentation should be based on the unique features of the industry under study. We do so here on the basis of the pharmacological properties of these drugs discussed earlier.

Let there be M molecules indexed by $m \in \{1, 2, \ldots, M\}$. For each molecule m there are f forms given by $f_m \in \{1, 2, \ldots, F_m\}$ and for each molecule m and form f there are i drugs given by $i_{f_m} \in \{1, 2, \ldots, I_{f_m}\}$.

FIGURE 1. Taxonomy of ADHD drugs by Molecule, Form and Brand Names



Note: Generics refer to several manufacturers for each molecule and form given in the column. There are no generic versions of Concerta and Adderall XR during the study period.

For the ADHD drugs, there are four main molecules ($M = 4$). These are methylphenidates (MPH is $m = 1$), mixed amphetamine salts (MAS is $m = 2$), dextroamphetamines (DEX is $m = 3$) and all other molecules (OTH is $m = 4$). For the methylphenidates ($m = 1$), there are four forms: Immediate Release (IR), Extended Release Tabs (ER-TAB), Extended Release Caps (ER-CAP) and Osmotic Release Oral System (OROS) (thus $f_1 = \{1, 2, 3, 4\}$). For mixed amphetamine salts as well as for dextroamphetamines there are two forms each, Immediate Release and Extended Release (thus, $f_2 = \{1, 2\}$ and $f_3 = \{1, 2\}$). The last group, (other molecules ($m = 4$)) consists of drugs with three separate molecules, modafinil, pemoline and atomoxetine. Only pemoline is available as both a branded (Cylert) and generic drug, while the other two are sold only as branded drugs in the U.S. (Modafinil and Strattera, respectively). We kept these three molecules in one category because they are very different from all other drugs considered so far. Strattera is a non-stimulant ADHD drug while pemoline and modafinil are stimulants, but because of their severe sides effects, neither is considered a first line drug for ADHD and are often used for treating narcolepsy.[8] Further, with the exception of pemoline, which is available as tablet and chewable tablet, these drugs are not available in alternative delivery mechanisms (the relative share of chewable pemoline tables in

[8]For instance, Cylert (pemoline) comes with the requirement that a prescribing physician obtain written consent from a patient prior to prescribing this drug, and specifically mentions on the label that it should not be considered as a first line therapy for ADHD. Similarly, while Modafinil is approved by the FDA for narcolepsy and a few other uses, it is not a FDA approved drug for ADHD. However, some physicians do prescribe it for ADHD as well. Thus, because of the unique nature of each of these drugs, we kept then in a separate segment.

2003 was only .01%). Hence, for this segment, there is only one form (i.e., $f_4 = \{1\}$). The specific drugs within each molecule and form are summarized in Figure 1. Using multistage budgeting we estimate demand parameters for each of the segments starting with the segments at the bottom level of the tree.

Bottom Level Share Equations (Level 1). The bottom level segment consists of drugs in the same molecule and form. Thus, the share of the ith drug in molecule-form f_m is given by $s_{i_{f_m}}$ where

$$s_{i_{f_m}} = \alpha_{i_{f_m}} + \beta_{i_{f_m}} ln(\frac{R_{f_m}}{P_{f_m}}) + \sum_{j=1}^{I_{f_m}} \gamma_{ij_{f_m}} lnP_{j_{f_m}} \tag{1}$$

and where $lnP_{j_{f_m}}$ is the log price of the jth drug in form f within molecule m and there are a total of I_{f_m} drugs in this molecule-form segment (and hence there are I_{f_m} number of share equations per segment).[9] The terms R_{f_m} and P_{f_m} are the total revenue and 'price' of the $f-m$ segment, where the latter is constructed as the share-weighted sum of the (log) prices, i.e., the Stone-index given by

$$ln(P_{f_m}) = \sum_{j=1}^{I_{f_m}} s_{i_{f_m}} ln(P_{j_{f_m}}). \tag{2}$$

To avoid the obvious endogeneity problem that is introduced in equation (1) due to the use of the Stone-index (since then $s_{i_{f_m}}$ appears on both the left and right hand side of the equation), we follow Hausman and Leonard (2002) and construct an alternative Stone-index using $\bar{s}_{i_{f_m}}$ which is the average share of the drug i, f, m over all areas at time period t. This alternative Stone-index is only used during estimation of the segment equations.[10] Note also that (by definition),

$$\begin{aligned} R_{f_m} &\equiv \sum_{j=1}^{I_{f_m}} P_{j_{f_m}} Q_{j_{f_m}} \equiv P_{f_m} Q_{f_m} \\ s_{i_{f_m}} &\equiv \frac{P_{i_{f_m}} Q_{i_{f_m}}}{R_{f_m}}. \end{aligned} \tag{3}$$

Thus there are seven sets of bottom level share equations, one for each of the segments MPH-IR, MPH-ERTAB, MPH-ERCAP, MAS-IR, DEX-IR, and DEX-ER and OTH, where for instance, within MPH-IR, the shares equations are the relative shares of Ritalin, Methylin and generics.

[9] Note that there are two other implicit subscripts a and t that represent area and time. Thus, more accurately, $s_{i_{f_m}}$ should be written as $s_{iat_{f_m}}$ to mean the share of drug i in area a at time t within the molecule-form f-m. However for ease of exposition, we suppress these additional subscripts.

[10] Hausman and Leonard (2002) in fact constructed the alternative Stone index from area-specific shares averaged over the full sample period. However, the imbalance in the number of years drugs are present in our data, and the fact that our panel is quite short to begin with, argues against the construction of area specific time-averaged share measures for the Stone indexes. Thus we use year specific area-averaged share measures across all counties in the data. Specifically, we use $\bar{s}_{it_{f_m}}$. Further, our results are not sensitive to this choice.

Middle Level Share Equations (Level 2). The middle level consists of forms in the same molecule, i.e., aggregation over individual drugs within each form. Thus, the share of the fth form in molecule m is given by u_{f_m} where

$$u_{f_m} = a_{f_m} + b_{f_m} ln(\frac{R_m}{P_m}) + \sum_{h=1}^{F_m} g_{fh_m} lnP_{h_m}. \tag{4}$$

Observe that lnP_{h_m} is the price of the form h in molecule m and is precisely the same term as in equation (2) above (i.e., is the actual Stone-index and not the alternative one with fixed shares). Further, for each molecule m there are F_m such equations. As in the bottom level equations, P_m is the 'price' of the molecule (again constructed as share-weighted Stone index of the forms within a molecule) and R_m is the total revenue of the molecules. Thus,

$$ln(P_m) = \sum_{h=1}^{F_m} u_{f_m} ln(P_{h_m}) \tag{5}$$

where, as before, we replace u_{f_m} with $\bar{u}_{f_m}$ (the average share of the form f, m over all over areas in year t) to avoid the artificial simultaneity . Also,

$$\begin{aligned} R_m &\equiv \sum_{h=1}^{F_m} P_{h_m} Q_{h_m} \equiv P_m Q_m \\ u_{f_m} &\equiv \frac{P_{f_m} Q_{f_m}}{R_m}. \end{aligned} \tag{6}$$

Three mid-level segments need to be estimated. To be explicit, these are (1) MPH, where the shares are of IR, ER-TAB, ER-CAP, and OROS (i.e. Concerta), (2) MAS, where the shares are of IR and ER (i.e. Adderall XR) and (3) DEX, where the shares are of ER and IR.

Molecule Level Quantity Equations (Level 3). At the next level of budgeting in the model, the "molecule" level, we determine the quantity of each distinct molecule (aggregated over the forms within the molecule). Thus, the total quantity of molecule m is given by

$$ln(Q_m) = A_m + B_m ln(R) + \sum_{n=1}^{M} \Gamma_{mn} lnP_n \tag{7}$$

where there are $M = 4$ such equations and where lnP_n is the price of the nth molecule defined as in (5) above, i.e., share weighted average over the forms within the molecule. Finally, R is the total revenue of all molecules and is given by

$$R = \sum_{n=1}^{M} R_n. \tag{8}$$

Top Level Quantity Equation (Level 4). The final level in the multistage budgeting determines the overall expenditures on ADHD drugs relative to all other goods. Thus, the total quantity Q of ADHD drugs is expressed simply as a function of income and the price of ADHD drugs as

$$lnQ = A + Bln(Y) + GlnP. \tag{9}$$

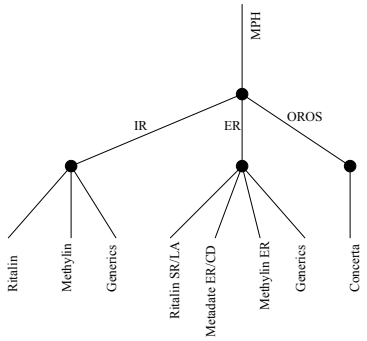
The top level estimation involves a single equation where Y is the total disposable income in the local area and lnP is the Stone index of the price over all M ADHD molecules and is a share-weighted average of the the price indexes of the molecules,

$$P = \sum_{m=1}^{M} v_m P_m. \tag{10}$$

4.2. **Empirical Issues: Data Limitations.** The segment estimations are carried out separately and independently rather than in a full joint system estimation because not all drugs are available in the market throughout the study period. For instance, the bottom level segments, MPH-IR and MPH-ERTAB are observed for years 2000 to 2003 and hence these segments can be estimated on a panel of 4 years of data. However the bottom level segments MPH-ERCAP and MAS-IR are both observed for only two years each (see Table 2). Using a full joint estimation of all segments requires finding a common set of years where all drugs are present. But this results in a substantial loss of data and statistical efficiency (far more than the potential gain in using cross-equation correlations across segments).

A related data driven concern required us to slightly modify the MPH segment. Note that in the subsegment MPH-IRCAP, there are only two drugs, Ritalin LA and Metadate CD. Each of these was introduced in 2002 and hence the segment MPH-IRCAP can only be estimated using a maximum of two years of data. This by itself is not an issue (all it implies is that perhaps the coefficients appearing in the equations for these two drugs would not be estimated very precisely). The potential problem occurs at the next level up: the MPH segment, which consists of four equations for IR, ER-TAB, ER-CAP, and OROS can only be estimated on a panel of two years (since the entire ER-CAP segment does not exist prior to 2002). But for the presence of this subsegment, the MPH segment could otherwise be estimated on a panel of four years rather than two. In turn this implies that if cross-price effects are not present for the drugs in the MPH segment (i.e. if the price coefficients are not statistically significant) it is not clear if this is simply due to loss of efficiency or because there truly are no substitution effects between these drugs.

FIGURE 2. Modified MPH Segments



Thus, due to data limitations, we merge the MPH-ERCAP and MPH-ERTAB segments to create a new segment MPH-ER. In the new segment, we pre-merged Ritalin LA with Ritalin SR to create a new drug "Ritalin SR/LA" and Metadate CD with Metadate ER to create a new drug "Metadate ER/CD". See Figure 2 for a representation of the modified tree structure. The share of Ritalin SR/LA within MPH-ER is simply the ratio of the sum of revenue of SR and LA to the total segment revenue (and similarly for Metadate CD/ER). However, care had to be taken to compute the price of Ritalin SR/LA and Metadate ER/CD.[11] Note that with these adjustments, the drugs "Ritalin SR/LA" and "Metadate ER/CD" exist for all four years and the middle level segment MPH can be estimated using a four year panel. Finally, we also do not estimate the individual demand parameters for the last segment OTH (since Strattera is observed for only one year) and study the cross-price effects of other drugs with respect to the entire segment OTH (rather than with respect to individual four drugs within this segment).

4.3. **Empirical Issues: Identification with Endogenous Prices.** It is widely recognized that individual drug prices in a demand system are likely to be endogenous, requiring appropriate instrumental variable methods. We next outline a set of potential instruments based on a new identification strategy proposed in Bokhari (2009) that has never been applied before in empirical work. The identification is obtained via a price competition model and assumptions already built in the multi-budgeting process. Observe that the aggregate *unconditional* demand for drug i is given

[11]The price of Ritalin SR/LA is not simply the share weighed average of the individual prices. Recall that Ritalin LA and SR do not switch gram for gram, what is relevant is the price per dosage. When a child is switched from Ritalin LA to Ritalin SR, then if they were previously using 100 mg of LA over a period, they would now consume 1.25/.83*100 mg of SR over the same period. Hence one mg of Ritalin LA costs $P_{LA} * .83/1.25$ of Ritalin SR *equivalent* mg. Thus, the price of Ritalin SR/LA is the share weighted average of price of P_{SR} and $P_{LA} * .83/1.25$. Similar adjustment applies to price of Metadate ER/CD. We also estimated a version of the model without applying dosing adjustment to these two drugs. Results were generally quite similar to the ones reported in the paper with the exception that the own price elasticity of Metadate ER/CD was positive (though not significant). As a final test that dosing adjustment should be applied, we also estimated a version where all drug prices were first converted to *Ritalin* equivalent dosage (rather than just adjusting Ritalin LA and Metadate CD to their counter parts). In this case, the results were exactly identical to those from our original conversion, i.e., when only Ritalin LA and Metadate CD prices were adjusted.

by

$$Q_i = D_i(p_1, \ldots, p_{17}, Z_i) \tag{11}$$

where Z_i is the vector of demand shifters. If there are L firms, then the lth firm produces a subset of $\mathfrak{L}_l$ drugs and maximizes its joint profit over these drugs as

$$\Pi_l = \sum_{i \in \mathfrak{L}_l} (p_i - c_i) D_i(p_1, \ldots, p_{17}, Z_i)$$

where c_i is the marginal cost. If we assume Nash-Bertrand price competition among firms, then the price p_i of any drug must satisfy the first order conditions

$$Q_i + \sum_{i \in \mathfrak{L}_l} (p_l - c_l) \frac{\partial Q_l(p_1, \ldots, p_{17}, Z_i)}{\partial p_i} = 0. \tag{12}$$

This in turn implies a price equation for each drug as,

$$p_i = c_i + \Omega^{-1} Q_i(p_1, \ldots, p_{17}, Z_i)) \tag{13}$$

where $\Omega_{li} = -\Theta_{li} \frac{\partial Q_l(p_1, \ldots, p_{17}, Z_i)}{\partial p_i}$ and Θ_{li} is a 1/0 matrix with ones in the leading diagonal and in locations when a firm jointly produces drugs l and i (for a complete derivation see Nevo (1998)). An ideal set of instruments would then be the marginal costs c_i by each product (or factors that shift the marginal costs) – which we do not have. In our data set, an additional issue is that we are not using wholesale prices, but rather retail level prices and thus would need access to cost shifters by each product and market. However, if the pharmacies in market a set the retail level price as a *fixed* markup α_a over the corresponding wholesale price, then the manufacturers would take this market specific markup into account when setting the price of their product. Hausman and Leonard (2002) show that this fixed markup is equivalent to a manufacturer redefining the marginal cost as $(1 + \alpha_a)c_i$. This in turn implies that the profit maximizing price for drug i in market a would be given by

$$p_{ai} = (1 + \alpha_a)c_i + \Omega^{-1} Q_i(p_{a1}, \ldots, p_{a17}, Z_{ai})). \tag{14}$$

Thus, the price of drug i in any one market depends on the price of *all* other drugs in the market since these prices enter the unconditional demand. Note however, that we are *not* estimating the parameters of the unconditional demand system, but rather, more narrowly defined segment demand systems conditional on expenditures on that particular segment. For instance, for the bottom level segment, MPH-IR, we have three drugs in the segment (Ritalin, Methylin and generic MAS-IR) and the conditional demand for each of the three drugs is a function of total expenditures, demand

shifters and the prices of *only* these three drugs (see equation (1)). Thus, the conditional demand of drug i in market a and in segment $f-m$ is given by

$$Q_{ai_{fm}} = D(p_{a1_{fm}}, \ldots, p_{aI_{fm}}, Z_{ai}; R_{f_m}). \tag{15}$$

The fact that the prices of the other drugs, those not in segment $f-m$, are excluded from the conditional demand functions provides us with an identifying strategy: in the estimation of the conditional demand for drugs in segment $f-m$, use the price of drugs not in the segment as instruments for the price of drugs in the segment. The price of the drugs not in the segment are relevant instruments per equation (14) and are due to the assumed form of price competition.[12] These prices are also valid instruments due to the exclusion restrictions per equation (15) and arise specifically due to the multistage budgeting process. Note that this strategy spares us from trying to find cost shifters by each drug and market i.e., identification via the usual $(1+\alpha_a)c_i$ variables.

Just to be sure, in the estimation of the bottom level segment MAS-IR, we use the price of drugs 4 through 17 as instruments for the prices of drugs 1 through 3 (Ritalin, Methylin and generic MAS-IR). A similar method is used in the estimation of the other bottom level segments. At the next level up, we estimate conditional demand for three segments. The first of these, MPH, involves the estimation of relative shares of immediate release, extended release and OROS (i.e. Concerta), and the conditional demand equations include two price indexes (for MPH-IR and MPH-ER) and the price of Concerta (drug number 8). For these two price indexes and the price of Concerta, the instruments used are the prices of drugs 9 through 17. A similar method is used for estimating the other two mid-level segments. At the next level up, we have four Cobb-Douglas demand equations, one for each molecule and where each is a function of four price indexes. The first is a price index of all MPH drugs, the second is a price index of all MAS drugs and so on. More care is needed in estimating these level three demand equations. In the 'first-stage', the first price index must be regressed on prices of drugs 9 through 16, the second on the prices of drugs 1 through 8 and 12 through 16, the third on prices 1 through 11 and the last price index on prices 1 through 16 (as well as area and time fixed effects). These projections of the price indexes can then be used in the 'second stage' estimation of the Cobb-Douglas demand functions.[13]

[12]Note that our methodology allows identification even if firms are colluding. For instance, in the case of a cartel or a single producer, all the elements of Ω in equation 14 would be 1 whereas in the case of each product corresponding to a unique non-colluding firm would reduce Ω to an identity matrix.

[13]Note that if a canned routine for 2SLS/IV is used, it will typically result in obtaining projections of these price indexes on all of the prices which is not valid in this situation.

The top equation cannot be estimated via the method outlined above. The equation involves an overall price index for all ADHD drugs and is a share weighted average of the four price indexes in level three equations. Thus we estimate the top equation via OLS. Additionally, we also use the share weighted average of the *projections* of the four price indexes in top equation rather than the overall price index itself – but that is not the same as constructing a share weighted average of the instruments as a instrument for the top level price index and hence may not be appropriate. The alternative is to find a valid instrument for the overall price index, such as differences in local and state laws governing retail pharmacies that affect the marginal cost at the retail level.

5. RESULTS

5.1. **Quantity Equations - Top and Middle (Levels 4 and 3).** We begin with the results of the top and molecule level equations, reported in Table 3. The table shows both the OLS and IV estimates, and all equations include state fixed effects, a time trend, and log of number of physicians and log of children in the county.[14] The OLS estimate of the the price elasticity in the top equation is -.94 and the IV estimate is -.83. Both are statistically significant and suggest that the aggregate demand for drug therapy is not very sensitive to variations in overall price levels. Further, the OLS and IV estimates are not very different from each other.

TABLE 3. Selected Coefficients - Top & Middle Level (Log) Quantity Equations

		OLS Estimates					**IV Estimates**				
Top Equation (Level 4 Equation)											
		B	G				B	G			
		0.21*	-.94*				0.19*	-.83*			
Middle Equations (Level 3 Equations)											
Molecule	Share	B_m	Γ_{mn}				B_m	Γ_{mn}			
1: MPH	0.452	0.94*	-0.68*	0.04	-0.09	-0.04	0.94*	-1.42*	0.32*	0.22	-0.03
2: MAS	0.356	1.09*	-0.04	-1.35*	-0.01	0.07	1.08*	0.35	-1.54*	0.16	0.13
3: DEX	0.056	0.96*	-0.02	-0.29	-0.04	-0.02	0.95*	1.45*	-0.54	-1.82*	-0.16
4: OTH	0.137	1.07*	-0.59*	1.00*	-0.09	-1.25*	1.07*	-0.05	1.22*	-1.15*	-1.59*

Note: An asterisk (*) implies coefficient significant at 5% level.
All equations also include state fixed effects, quadratic time trends, and log of number of physicians and log of children in the county.

Estimates of level 3 quantity equations are also shown in the same table. The expenditure elasticities for all four molecules are about 1 under OLS and IV. However, there is a considerable difference in price elasticities in OLS versus IV. In terms of the own price elasticities, the IV estimates are larger

[14]For area fixed effects, we use state level rather than county fixed effects but the results from county vs state fixed effects are very similar. However, we chose the latter since in two of the bottom level segments, our instruments for price appeared slightly weak, meaning the Staiger and Stock's weak instrument F test was less than 10 when county fixed effects were used (in all other cases they were above 10). However, all instruments passed the test if instead we used state fixed effects.

in magnitude than the OLS estimates. The IV estimates place the demand for the four molecules in the elastic region while OLS places the own elasticity for two molecules in the inelastic region (MPH and DEX). Further, unlike the OLS, the IV estimates show that there is an increase in own-price elasticity at the molecule level (-1.42, -1.54 etc.) compared to overall inelastic demand for all drugs combined (-.83) and the relative magnitudes make sense given that we now have more narrowly defined products (eg. demand for food may be inelastic but for a specific category such as meats etc. it should be relatively more elastic).

We restrict further discussion to the IV estimates. The off-diagonals provide the Marshallian cross elasticities (number in row m column n is the elasticity of drug m with respect to price change in drug n). The off-diagonals are not symmetric in either their magnitude or the sign patterns and the point estimates (when significant) are quite large. We expect off-diagonals to be positive (or at least not significant when negative) since the molecules would be either gross substitutes or possibly not related in cross-price effects if therapeutically the molecules cannot be exchanged.[15] This indeed turns out to be mostly true with one exception, the cross price effect between the molecule OTH and DEX (-1.15), which is both negative and statistically significant.

The main message that we take from these estimates is that the demand for each of the four molecules is elastic and the molecules are by and large substitutes (with the exception of the hybrid molecule OTH).

5.2. **Share Equations - Forms within molecules (Level 2).** Next we discuss the results from the middle level shares equations for forms within each of the first three molecules (recall that the drugs in OTH are conglomerated into one drug). Since the middle (and bottom) level share equations are in AIDS form and involve prices as well as price index across forms, interpreting the estimated coefficients is more involved. Thus, rather than providing the regression coefficients, we provide the estimated elasticities (at average shares) in Table 4. Also, we restrict our discussion to results based only on IV estimates. The conditional elasticities (conditional on R_m) of forms within a molecule with respect to the *price* of the form is derived in the appendix and is given by

$$\frac{\partial lnQ_{f_m}}{\partial lnP_{f'_{m'}}} = \frac{1}{u_{f_m}}\Big\{\Big(- b_{f_m}\bar{u}_{f'_{m'}} + g_{fh_{m'}}\Big).1[m' = m]\Big\} - 1[f' = f, m' = m]. \tag{16}$$

The table also provides measures of Hicks-Allen elasticities.[16]

[15] They may, however, be gross complements if significant number of children are put on mixed drug regimes simultaneously.

[16] The Hicks-Allen elasticity ϵ^a_{ij} was computed by first computing the Hicksian elasticity $\epsilon^h_{ij} = \epsilon^m_{ij} + s_j\eta_i$ where η_i is the expenditure elasticity and then by computing $\epsilon^a_{ij} = \epsilon^h_{ij}/s_j$.

TABLE 4. Conditional Elasticities - Middle Level (Form within Molecule)

	Marshallian Elasticity			Hicks-Allen Elasticity			Expenditure Elasticity	Average Share
MPH: Molecule 1. Share among ADHD drugs is .452								
	(A)	(B)	(C)	(A)	(B)	(C)		
(A) MPH-IR	-3.40*	-1.46*	3.91*	-9.21*	-7.12*	9.02*	0.96*	0.33
(B) MPH-ER	-2.72*	-2.12*	3.83*	-7.12*	-10.72*	8.92*	1.01*	0.18
(C) MPH-OROS	2.68*	1.43*	-5.13*	9.02*	8.92*	-9.57*	1.03*	0.48
MAS: Molecule 2. Share among ADHD drugs is .356								
		(D)	(E)		(D)	(E)		
(D) MAS-IR		-2.85*	1.95*		-3.91*	5.69*	0.90*	0.59
(E) MAS-ER		2.70*	-3.84*		5.69*	-8.29*	1.15*	0.41
DEX: Molecule 3. Share among ADHD drugs is .056								
		(F)	(G)		(F)	(G)		
(F) DEX-IR		-0.84	-0.07		-1.75	0.81	0.91*	0.32
(G) DEX-ER		-0.07	-0.97*		0.81	-0.37	1.04*	0.68

Note: An asterisk (*) implies coefficient significant at 5% level. Molecule 4 is the all other ADHD drugs group and we do not distinguish between forms. Hence, no middle level share equations exist for molecule 4. MPH-OROS is Concerta and MAS-ER is Adderall XR.

Within the MPH molecule, the own price elasticities of all three forms is very elastic, especially that of Concerta (-5.13), and this drug is a strong substitute for the other two forms (all estimates are statistically significant). However, the immediate release and extended release forms are complements to each other. This result suggests that there may be some truth to the anecdotal evidence that children are often simultaneously using ER and IR: the extended release version is taken in the morning before going to school and a short-acting immediate release version is taken after school to carry them over for the evening. However, such a mixture is not needed with the OROS (which lasts a full day), and hence it acts as a substitute for the other two forms. Next, within the MAS molecule, both the ER (i.e. Adderall XR) and IR versions are very price elastic and strong substitutes (and results are statistically significant). Unlike MPH-ER and MPH-IR, Adderall XR is not taken in combination with the immediate release version and hence MAS-ER and MAS-IR are substitutes. Most notably, the drugs MPH-OROS (Concerta) and MAS-ER (Adderall XR) are both found to be very price elastic despite having attained large market shares within their respective segments (48% and 41% respectively). Further, both Concerta and Adderall XR are strong substitutes for other drugs within their respective segments. No firm conclusion can be drawn within the DEX class across forms (most coefficients are statistically insignificant). The DEX group, which consists of three drugs in the IR form and two drugs in the ER form, has a combined average market share

of 5.7% and there is little price variation for these drugs across areas or over time, and hence the price indexes for these forms do not explain differences in market shares.

5.3. **Share Equations - Drugs within molecule-Forms (Level 1).** Finally, we provide the elasticities of individual drugs within their respective molecule-forms in Table 5. Once again, the elasticities are conditional on total expenditure on the molecule form and are based on the IV estimates (the formula for the conditional elasticities, along with the derivation, is given in the appendix).

TABLE 5. Conditional Elasticities - Bottom Level (Drug within Molecule-Form)

	Marshallian Elasticity					Hicks-Allen Elasticity					Exp Elasticity	Avg Share
MPH-IR: Molecule 1, Form 1. Share within Molecule is .33												
	(1)	(2)	(3)			(1)	(2)	(3)				
(1) Ritalin	-0.79*	0.22	-0.50			-2.84*	2.01	0.18			1.07*	0.20
(2) Methylin	0.20	-1.54*	0.32			2.01	-5.51*	1.58*			1.02*	0.24
(3) Generics	-0.16	0.14	-0.95*			0.18	1.58*	-0.73*			0.97*	0.56
MPH-ER: Molecule 1, Form 2. Share within Molecule is .18												
	(4)	(5)	(6)	(7)		(4)	(5)	(6)	(7)			
(4) Ritalin SR/LA	-3.67*	2.41*	0.81*	-0.60		-13.38*	10.23*	9.28*	-0.50		1.05*	0.25
(5) Metadate ER/CD	2.29*	-2.81*	-0.92*	0.21		10.23*	-9.48*	-8.11*	1.78*		1.23*	0.26
(6) Methylin ER	2.16*	-2.34*	-3.37*	2.76*		9.28*	-8.11*	-33.54*	7.96*		0.80*	0.10
(7) Generics	-0.35	0.24*	0.70*	-1.45*		-0.50	1.78*	7.96*	-2.91*		0.86*	0.39
MAS-IR: Molecule 2, Form 1. Share within Molecule is 0.59												
	(9)	(10)				(9)	(10)					
(9) Adderall	-1.04*	0.07				-1.46*	1.11*				0.97*	0.43
(10) Generics	0.03	-1.06*				1.11*	-0.83*				1.02*	0.57
DEX-IR: Molecule 3, Form 1. Share within Molecule is .57												
	(12)	(13)	(14)			(12)	(13)	(14)				
(12) Dexedrine	-3.70	0.56	2.20			-12.49	2.34	7.72*			0.95*	0.28
(13) Dextrostat	0.36	-0.37	-1.01*			2.34	0.10	-2.10			1.02*	0.40
(14) Generics	1.85	-1.24*	-1.62*			7.72*	-2.10	-3.97*			1.03*	0.32
DEX-SR: Molecule 3, Form 2. Share within Molecule is .43												
	(15)	(16)				(15)	(16)					
(15) Dexedrine SR	-0.64	-0.35				-0.13	0.18				0.98*	0.57
(16) Generics	-0.48	-0.54				0.18	-0.23				1.02*	0.43

Note: An asterisk (*) implies coefficient significant at 5% level.

Starting with the MPH-IR segment, observe that both Ritalin and the generics have own estimated elasticities that are less than one while only Methylin has elastic demand (all three are significantly significant). Recall, however, that these are conditional elasticities, conditional on group expenditures, and that unconditional elasticities of individual drugs may still be in the elastic region (these are computed later). Further, it is tempting to compare the individual own elasticities of the three drugs with the own group elasticity of MPH-IR (reported earlier as -3.40) but again, such

comparisons should be made for unconditional elasticities. Similarly, note that the estimated own elasticity of generic MPH-IR is a group elasticity of 15 (presumably homogenous) manufactures and not that of one individual firm which would be approximately 15 times higher. Finally, observe that the off-diagonal elements are not statistically significant, implying that price changes in one drug do not affect the demand of the other two. We expect these drugs to be substitutes – since they consist of the same molecules and are in the same forms – but they might even be gross complements: the (perceived) quality of Ritalin is greater than that of the generic versions and, while on drug therapy, a child may be on a mixture of the more expensive branded version for school and the cheaper generic version for home.

In the next segment (MPH-ER), there are four drugs, all four have very elastic demand and suggest a high degree of substitutability between them. As before, the estimated own elasticity of generic MPH-IR is for a group of 12 different generic manufactures. An interesting story emerges when we consider the cross price effects and the average prices of these drugs. First, note that Metadate ER/CD and Methylin ER, both new entrants in this segment, are substitutes for Ritalin SR/LA as well as for the generics, while the latter two (Ritalin SR/LA and generics) are not substitutes for each other. Second, both Metadate ER/CD and Methylin ER are mid-way brands – they are branded drugs but less well known compared to the established Ritalin SR/LA. As noted earlier, the price of Metadate ER was typically mid-way between the price of the generics and Ritalin SR and initially the price of Metadate CD was lower than that of Ritalin LA. Further, the price of Methylin ER was always much lower than Ritalin SR and only a few dollars more than that of the generics. Since Metadate ER/CD and Methylin ER are 'brands' they offer some (perceived) quality enhancement over the generics, but since they are priced between the price of Ritalin SR/LA and the generics, they offer some advantage compared to Ritalin SR/LA. The substitution patterns reveal that by entering as low-priced brands, they were able to siphon off demand from Ritalin SR/LA as well as from the generics: a price increase in either Ritalin SR/LA or in the generics leads to more consumers switching to these two drugs rather than to each other. Further, over time, at least Metadate CD was able to increase its price to match that of Ritalin LA while Methylin ER was less successful in doing so. This suggests that consumers value Metadate ER/CD more relative to Methylin ER, although we cannot tell if this difference is due to actual therapeutic advantages or due to success in building brand loyalty or name recognition via marketing.

Finally, note that the relative substitution patterns indicate that if the price of either Metadate ER/CD or Methylin ER increases, consumers are more likely to switch to Ritalin SR/LA than to

the generics (in column 5, compare the H-A elasticity of 10.23 to 1.78 or in column 6, compare 9.28 to 7.96). In turn, this suggests that Metadate ER/CD and Methylin ER are perceived closer in non-price attributes to Ritalin SR/LA than to the generics (more so for Metadate ER/CD than for Methylin ER) and explains why the entry of these two drugs, which were priced typically below the price of Ritalin SR and LA, led to a larger drop in the relative share of the generics than for Novartis: in 1999 prior to the entry of these two drugs, Novartis had about 30% share of the MPH-IR segment while the remaining 70% was captured by generic manufactures but by 2003, the relative share of the generics in this segment dropped down to 11.9% (see Table 2).

In the third bottom segment, MAS-IR, both Adderall and generics (where generics are produced by three firms) have about unit own elasticities and the cross-elasticities are not significantly different from zero. While this result appears to be consistent with the results in the previous two segments, i.e., no strong cross price effects between the well known branded drug and generics (i.e., Ritalin vs. generics or Ritalin SR/LA vs generics), nonetheless those results were in the presence of other branded generics in those segments (Methylin, Metadate etc.). Thus, while it is possible that the cross price effects between generics and Adderall are not present, it is also likely that this result is due to lack of efficiency since this segment was estimated using data from only two years (the generic entry took place in 2002). Once again, we expect these two drugs to be substitutes (since they are bio-equivalents) but they too might be gross complements: the (perceived) quality of Adderall is greater than that of the generic versions and, while on drug therapy, a child may be on a mixture of these these drugs as in the case of Ritalin and the generics.

In the next two segments (DEX-ER and DEX-IR) most of the results are not statistically significant. These two segments are not estimated very precisely since sales data on these drugs is quite limited – many areas have zero total sales and so prices are measured very crudely. Thus, we have limited confidence in our results for these two segments.

6. Assessing the Impact of New Drugs

6.1. **Unconditional Elasticities.** While the multi-budgeting process allows estimation of the conditional demand functions, the cross-price effects are limited to within the molecule-form segment. Unconditional effects are more general and include the induced demand effects that work through the budget (expenditure) shares among all drugs, inside and outside the $f-m$ segment. Thus, a drug that introduces an important new variety may have widespread consumption impacts across all segments; its introduction may induce a substantial demand response in patients (and their

providers) who earlier had been using scripts chosen from any one of the ADHD drugs. In the absence of the full unconditional demand system, it is still possible to assess the broader effects of one drug onto another (at least locally) by estimating the unconditional elasticities from parameters of the conditional demand systems. The unconditional elasticity (derivation given in the appendix) is computed from the parameters of the conditional demand functions as

$$\begin{aligned}\frac{\partial lnQ_{i_{f_m}}}{\partial lnP_{k_{f'_{m'}}}} &= \Big(1+\frac{\beta_{i_{f_m}}}{s_{i_{f_m}}}\Big)\bar{s}_{k_{f'_{m'}}}\Big[\frac{g_{ff'_{m'}}}{u_{fm}}+\bar{u}_{f'_{m'}}\Big]\cdot 1[m=m'] \\ &+\Big(1+\frac{\beta_{i_{f_m}}}{s_{i_{f_m}}}\Big)\bar{s}_{k_{f'_{m'}}}\Big[\frac{b_{fm}\bar{u}_{f'_{m'}}}{u_{fm}}+\bar{u}_{f'_{m'}}\Big]\Gamma_{mm'} \\ &+\frac{1}{s_{i_{f_m}}}\Big\{\gamma_{ik_{f'_{m'}}}-\beta_{i_{f_m}}\bar{s}_{k_{f'_{m'}}}\Big\}.1[f'=f,m'=m] \\ &-1[i=k,f'=f,m'=m].\end{aligned} \tag{17}$$

In a later section, we report the more concise measures of the welfare impacts of the new drugs, but some indications may be seen in the pattern of these elasticities. The unconditional estimates from our IV estimates for selected drugs, those in the MPH and MAS segments are shown in Table 6 (the full set is given in the appendix along with those based on the OLS estimates).

TABLE 6. Unconditional Elasticities from IV estimates

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
(1) Ritalin	-1.33*	-0.47*	-1.98*	-0.4*	-0.42*	-0.16*	-0.61*	3.96*	0.08*	0.10*	0.12*
(2) Methylin	-0.37	-2.1*	-1.13*	-0.38*	-0.40*	-0.15*	-0.58*	3.77*	0.07*	0.10*	0.11*
(3) MPH-IR	-0.64*	-0.43*	-2.35*	-0.36*	-0.38*	-0.14*	-0.55*	3.59*	0.07*	0.09*	0.11*
(4) Ritalin SR/LA	-0.59*	-0.68*	-1.63*	-4.12*	2.00*	0.68*	-1.08*	3.98*	0.08*	0.10*	0.13*
(5) Metadate ER/CD	-0.69*	-0.80*	-1.91*	1.82*	-3.25*	-1.07*	-0.46	4.66*	0.09*	0.12*	0.15*
(6) Methylin ER	-0.45*	-0.52*	-1.24*	1.91*	-2.60*	-3.38*	2.14*	3.03*	0.06*	0.08*	0.10*
(7) MPH-ER	-0.48*	-0.56*	-1.34*	-0.60	-0.08	0.53*	-1.93*	3.27*	0.06*	0.09*	0.10*
(8) Concerta	0.51*	0.60*	1.42*	0.36*	0.37*	0.14*	0.54*	-5.35*	0.08*	0.10*	0.12*
(9) Adderall	0.02	0.02	0.05	0.01	0.01	0.01	0.02	0.14	-1.89*	-1.07*	1.64*
(10) MAS-IR	0.02	0.02	0.06	0.01	0.01	0.01	0.02	0.14	-0.87*	-2.24*	1.72*
(11) Adderall XR	0.02	0.03	0.07	0.02	0.02	0.01	0.03	0.18	0.96*	1.28*	-3.97*

Average Shares (Within Molecule Form (M-F) and Overall (O))

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
M-F	0.203	0.235	0.562	0.254	0.263	0.098	0.385	1.000	0.430	0.570	1.000
O	0.031	0.036	0.085	0.021	0.021	0.008	0.031	0.219	0.091	0.120	0.145

Note Elasticity matrix computed at the sample mean. $*$ indicates significant at 5% level. The full 17 by 17 matrix is given in the appendix.

The sign patterns in this matrix are mostly consistent with earlier results. For instance, unconditionally, drugs 1-3 are complements to each other (they were insignificant before), drugs 4-7 have the same sign patterns as before, drugs 1-3 are complements to drugs 4-7 and drugs 1-7 are substitutes

for drug 8 (consistent with MPH-IR and MPH-ER being complements and both being substitutes for OROS). Further, the more established brand names (Ritalin, Ritalin SR/LA) appear to be gross complements to their respective bio-equivalent forms – consistent with the aforementioned idea that children may be on a mixture of the more established brand and the presumably lower quality generic. Similar pattern holds in the other blocks. We ignore the results corresponding to the DEX molecule due to the data limitations discussed earlier (i.e., very few sales in this molecule class).

Since the Marshallian elasticities are not symmetric, it is useful to discuss this matrix explicitly in terms of price change in drug i on demand for drug j and vice versa. Consider first the effect of price changes of the new entrants on the demand for other drugs. Price changes in Metadate ER/CD and Methylin ER (columns 5 and 6 respectively) have a significant effect on all MPH based drugs but not outside of the MPH molecule. A price increase in either of these two drugs would be picked up mostly by Ritalin SR/LA and by Concerta and fewer children would be prescribed the mixed treatment of MPH-ER and MPH-IR (the demand for MPH-IR drugs would decrease since MPH-ER and MPH-IR are complementary therapies). However, a price increase in Concerta (column 8) would be associated with an increase in demand for MPH-ER and MPH-IR drugs and not many would switch to MAS based drugs. Also, the magnitudes in column 8 are much larger than those for Metadate ER/CD or Methylin ER and also confined to the MPH molecule. By comparison, price changes in generic Adderall (i.e. MAS-IR in column 10) or Adderall XR (column 11) affect the demand for drugs not only within their own molecule class but also in the MPH molecule. While the magnitudes are smaller than those for Concerta, they are not confined to just within their own molecule segment and an increase in the MAS prices is likely to result in more children being switched from MAS treatment options to MPH treatment options.

Next, reading row-wise (i.e., change in log quantity of drug i with respect to change in log price of other drugs), our results suggest that the demand for Metadate ER/CD, Methylin ER, and Concerta (rows 5,6 and 8) is affected by price changes in all other MPH, or MAS drugs. The result is particularly noteworthy for Concerta where price increase in any of the other MPH-ER, MPH-IR or MAS drugs is associated with an increase in treatment via Concerta. On the other hand, demand for generic Adderall and Adderall XR (rows 9 and 11) is confined to price changes within their own molecule, i.e., price changes in MPH-ER, MPH-IR or Concerta do not lead to more children being switched to MAS based drug therapy since there is more choice to stay within the MPH molecule.

These results suggest the following: removing Metadate ER/CD or Methylin ER from the choice set would result in children being switched to Ritalin SR/LA and Concerta (as well as to the generic MPH-ER version for the Methylin ER case), implying some welfare reduction due to a switch to higher priced therapies (Ritalin SR/LA and Concerta) or to lower (perceived) quality of generic MPH-ER. On the other hand, removing Concerta from the choice set would result in possibly a large welfare reduction since children are switched from a once a day Concerta to a mixed therapy option of MPH-ER and MPH-IR. Similarly, removing Adderall XR switches children to either a non-XR version of MAS or to MPH, while removing generic Adderall from the choice set leads to switching to more expensive Adderall XR or to other MPH molecules (but not to branded Adderall) which can again lead to large welfare reductions.

In the next section, we provide a lower bound to the implied welfare changes.

6.2. **Welfare Calculations.** From the empirical estimates, we are able to show more clearly the relative magnitudes of the welfare effects that five new drugs, introduced from 2000-2003, have had on the market. In this section, we report the estimated welfare changes associated with each of the new drug introductions: Concerta, Adderall XR, MAS-IR (i.e. generic Adderall), Methylin ER and Metadate ER/CD.

Following several previous studies, e.g. Hausman (NBER 1994), Hausman and Leonard (2002 and 2005), we compute the compensating variation associated with each new product by first calculating the "virtual price", i.e. an artificial price for the new drug that would be just high enough to set the quantity demanded is approximately zero ($\sim 10^{-14}$). The virtual price is used to simulate consumer welfare in the pre-introduction period. The virtual price for each new drug is inferred as an out-of-sample projection from the empirical demand parameter estimates.[17] In particular, we use the conditional elasticity to solve for the price change associated with a 100% decrease in quantity. Let this be the virtual price of the drug in question. The virtual price minus the observed price represents the hypothetical price difference in a "but-for" world where the drug is first absent from the set of ADHD drug choices and then introduced on the market. Our welfare measure of compensating variations CV can be derived from the expenditure functions derived from the estimated top-level equation.

[17] In the AIDS demand system, the demand curve has an asymptote on the vertical axis. We use linear projections from the estimated elasticity around the actual (observed) price to obtain the intercept. Results are not sensitive to other methods of projecting to find a point on the vertical corresponding to zero shares.

Let the price vector change from $\mathbf{p}^o$ to $\mathbf{p}'$ such that the price index (at the top level equation) changes from p^o to p'. Then

$$CV = \int_{p'}^{p^o} h(z, u^o(\cdot))dz$$

where

$$\begin{aligned} h(z, u^o(\cdot)) &\approx h(p^o, u^o(\cdot)) + \frac{\partial h(p^o, u^o(\cdot))}{\partial p} \cdot (z - p^o) \\ &= Q_1(p^o, I) + \Big(\frac{\partial Q(\cdot)}{\partial p} + \frac{\partial Q(\cdot)}{\partial I} Q(\cdot)\Big)(z - p_1^o). \end{aligned}$$

We calculate CV separately for each MSA county in the sample fixing the prices of all other drugs in the local area at their sample average. Thus, our welfare estimates are a lower bound since we do not adjust the price of other drugs in this 'but-for' world (which presumably could be higher).[18] The resulting distribution of estimates is reported in Table 7. The results are expressed both in terms of total dollars in the locality as well as in terms of "per-ADHD-child" and as a percentage of total ADHD expenditures in county. The per-ADHD-child estimate is a crude approximation based upon the local nonadult population and a conservative estimate (5%) of the incidence of ADHD among children and adolescents. The welfare effects of each drug span a wide range across cities, reflecting unique local conditions in the consumption choices observed.

The results reveal that the largest welfare benefits were generated by the three drugs Concerta, Adderall XR and generic Adderall. In total, these three drugs account for 57.6% of the ADHD market in 2003. Outside of drugs in the OTH group (mostly Strattera), none of the other drugs in our sample have as much as a 5% share. The introduction of Adderall XR produced the largest estimated welfare effect, slightly higher than Concerta. Adderall XR has a $140 thousand benefit in the typical county, or about $47 per year per ADHD child. Variations in the estimated value are large across localities in the country. This variation is partly due to the population size, with

[18] The usual method to account for the "competitive" effect is to employ a price competition model such as one given in section (4.3) along with the estimated demand parameters (or elasticities if the specified model is simple enough) and observed prices to back out the marginal costs for each of the j products from $(p_j - c_j)/p_j = 1/\epsilon_j$ (or some variant of such a set of equations that accounts for joint ownerships). See for instance Hausman (1996). The next step involves setting the price of the missing product to a virtual price such that its demand is equal to zero and solving the system of j equations for the remaining $j-1$ prices that would exist under the Nash equilibrium, i.e. solving the system of equations given by $p_i = c_i + \Omega^{-1} Q_i(p_1, \ldots, p_{17}, Z_i)$ (see derivation of Equation 13). This set of new prices can then be used to compute the CV using all the old observed prices and the new vector of prices. However, such a method is not feasible in the current model. We have not estimated the parameters of the *unconditional* demand equations, which is what appears in the equation above, only the parameters of conditional demand equations and backed out from these point estimates of unconditional elasticities at the sample mean. It would be incorrect to use instead the conditional demand equations in the set above since then, for instance, the conditional demand of drug 1 is just a function of prices of drugs 1,2 and 3), whereas the unconditional demand is a function of all the 17 prices (In fact using the conditional demand functions would be inconsistent with the identification strategy employed in this paper). Thus we do not include competitive effects in the computation of CV, only the so called "variety effect", and hence our welfare computations are lower bounds to the full welfare effects which is a sum of the variety effect and the competitive effect.

TABLE 7. Compensating Variation

Total CV Per County ($1000s)

	Mean	Median	Max	Min	Std Dev
Adderall XR	140.49	66.94	2840.50	0.26	222.37
Concerta	114.41	56.67	1636.46	0.18	172.07
MAS-IR*	130.96	56.90	2294.21	0.25	211.97
Metadate CD/ER	18.76	8.46	279.78	0.00	27.78
Methylin ER	3.75	1.34	88.36	0.00	6.91

CV as Percentage of Total Expenditure Per County

	Mean	Median	Max	Min	Std Dev
Adderall XR	5.52 %	5.49 %	11.34 %	0.86 %	1.48 %
Concerta	4.66 %	4.62 %	10.07 %	0.82 %	1.23 %
MAS-IR*	5.10 %	4.82 %	18.53 %	0.57 %	2.10 %
Metadate CD/ER	0.80 %	0.69 %	5.76 %	0.00 %	0.53 %
Methylin ER	0.16 %	0.12 %	1.37 %	0.00 %	0.16 %

CV per ADHD Child in County ($/per ADHD Child)

	Mean	Median	Max	Min	Std Dev
Adderall XR	47.28	40.73	440.73	1.59	35.77
Concerta	38.11	33.67	165.17	1.23	25.07
MAS-IR*	42.17	33.44	375.99	1.27	33.76
Metadate CD/ER	6.51	4.90	41.17	0.00	5.70
Methylin ER	1.16	0.86	8.95	0.00	1.10

Mean CV ($/per ADHD Child) in Selected Counties

	Adderall XR	Concerta	MAS-IR*	Metadate CD/ER	Methylin ER
Queens, NY	8.95	12.82	6.73	1.41	0.26
San Francisco, CA	11.99	18.73	31.82	1.41	2.32
Los Angeles, CA	14.84	12.20	12.60	2.30	0.29
Delaware, IN	41.68	46.57	45.74	4.51	1.17
New York, NY	60.60	63.99	78.20	9.47	2.33
Leon, FL	102.76	45.49	111.72	16.27	2.45
Charleston, SC	170.79	136.30	212.66	12.97	1.04
Henderson, KY	440.73	165.17	375.99	30.35	1.38

* MAS-IR is generic Adderall.

Note: The table displays the absolute values of CV (they are all negative). Each row corresponds to the CV computation in a 'but for' world where the drug is not in the choice set, it is priced at the virtual price and all other prices unchanged.

the largest cities generating up to $2.8 million in compensating variations overall. But even when expressed as dollars per ADHD child, the range of values ($441 to $1.59) is a hundred-fold. This suggests that there are considerable local area variations in the acceptance of these drugs. Similarly, a large welfare result and quantitatively similar to Adderall XR and Concerta, is attributed to the generic Adderall drug in MAS-IR segment following its introduction in 2002. The introduction of generic Adderall led to significant market expansion. In contrast, the effects of the other two drugs, Metadate ER/CD and Methylin ER are much smaller. These drugs produced small variety effects and we find that for these latter two drugs, consumers derive relatively little benefit from the increased choices they provide.

7. DISCUSSION

Our demand analysis shows that the demand for ADHD drugs is quite elastic and there are significant substitution possibilities among these drugs, both within the molecule and form as well as across segments. Further, it sheds light on why some drugs were more successful than others. Both Concerta and Adderall XR created new niche markets within their respective molecules, i.e., introduced new delivery mechanisms. Consumers placed a large value on these introductions, approximately \$47 and \$38 per child per year, and consequently these two drugs archived 24% and 26% of the ADHD market. The introduction of generic Adderall in the MAS-IR segment extended the market and was also very valuable to consumers (about \$42 per child per year). However, two other introductions Methylin ER and Metadate CD did not necessarily create new niche markets (albeit Metadate CD was the first to provide combination of rapid-release and slow-release beads via a capsule in the MPH-ER segment) since both were introduced in a segment where branded as well as generic drugs already existed. Consequently, consumers placed much lower value on these introductions, \$1.2 and \$6.5 per child per year respectively which explains the low market shares of the these two drugs (.6% and 2.6% respectively).

Our results also provide a rough estimate of a potential welfare loss due to entry that *did not* take place. Shire holds two key patents on Adderall XR that technically prevent entry in the MAS-ER segment until 2018 and an exclusivity period until April 2005 under the Hatch-Waxman Act.[19] However, Barr Laboratories filed for an ANDA application with the FDA in February 2003 to market a generic version of Adderall XR.[20] This was followed by a second ANDA application filed by IMPAX in November 2003. In response, Shire sued Barr as well as IMPAX for infringement of its key patents. The case between Barr and Shire was scheduled to go to trial in January 2006 and would have granted Barr 180 days of generic exclusivity under section IV of the Hatch-Waxman Act *if* it won the case while IMPAX, as a second filer of an ANDA, would not have gained an exclusivity period. However, in the same month (January 2006), Shire settled with IMPAX, the second filer of ANDA, to market Adderall XR under a license from Shire *no later than* January 2010. This deal was followed by a second out of court settlement (August 2006), this time between Shire and

[19]There was originally only one patent listed in the Orange Book and the original exclusivity period was until October 2004 but was later granted a six month extension for Adolescent Pediatric Patients.

[20]Barr Laboratories maintained that the patents listed by Shire are invalid, unenforceable and/or will not be infringed by Barr Laboratories.

Barr, the original filer of ANDA, where Shire agreed to grant Barr Laboratories a 180-day *exclusive* license to market generic Adderall XR in exchange for delaying entry until April 2009.[21]

The out of court settlements between Shire, Barr and IMPAX bear features noted in several recent cases where, in exchange for delayed entry, the agreement includes a "reverse payment" from the patent holder to the generic maker but allows for generic entry prior to patent expiration (see Bulow (2004), Hemphill (2007), Frank (2007)).[22] Like some of the earlier similar cases where the FTC contested the settlements (with mixed results in the Federal Courts), the FTC initiated an initial inquiry in October 2006 and in June 2007 Shire received a civil investigative demand requesting that it provide information to the FTC relating to its settlement with Barr and its earlier settlement with IMPAX.[23] Additionally, these settlements also highlight loopholes in the Hatch-Waxman Act. For instance, while the Act provides a 180-day exclusivity period to the first filer of ANDA (to give incentives for generic entry), it does not prevent the original patent holder from licensing its drug to another generic maker which in effect nullifies the 180-day exclusivity of the first generic entrant. While it is difficult to predict the outcomes of the court proceedings and when first generic entry would have taken place in the absence of any out of court settlements between these firms, nonetheless, our estimates suggest that even a year earlier entry in generic MAS-ER segment would have been close to $42 per child per year in an industry which currently serves about 20 million children diagnosed with ADHD worldwide.

Finally, our demand analysis of these drugs speaks directly to the policy proposals aimed at slowing the introduction of me-too drugs (Angell, 2004, Goozner, 2004). For instance, Angell (2004) calls upon the FDA to change its approval standards and require me-too drugs to demonstrate not only efficacy relative to placebos but clinical superiority compared to existing drugs, while Hollis (2004) offers a more tempered version of a similar proposal.[24] On the other hand, DiMasi and Paquette (2004) argue that me-toos provide therapeutic options previously not available, and that me-toos

[21] On April 2, 2009, Teva Pharmaceuticals (which now owns Barr) announced that it has commenced shipping of generic Adderall XR in the U.S.

[22] Shire noted in its press release that no payments have been made to Barr in settlement of the Adderall XR dispute. Nonetheless, the "reverse payments" exist as a result of complex side deals. The deal involved a payment from Shire to Duramed, a subsidiary of Barr in the amount of $165 million described as compensation for product development related to transvaginal ring technology for urinary incontinence, which Shire plans to apply to five women's health products, and an oral contraceptive called Seasonique. In addition, Shire sold the rights to its older Adderall immediate release (IR) product to Duramed for $63 million resulting in a net payment of $102 million by Shire.

[23] The status of FTC inquiry has not yet changed as noted on the 10-K form filed by Shire PLC on February 27, 2009 with the Securities and Exchange Commission.

[24] Proponents offer several arguments such as: (a) me-toos are similar to the pioneering drugs and the incremental benefits and benefit/risk ratios are low; (b) me-toos split the market as opposed to expand it, shorten the exclusivity period for the pioneering drugs, and reduce the incentives to undertake R&D and, (c) pharmaceutical companies expand significant resources on marketing their me-too drugs rather than on R&D itself. See Hollis (2004) for a careful discussion of the various arguments.

are often engaged in development concurrently with the pioneering drug. Thus, changes in the FDA approval policy would create moving targets in the clinical trial phase since the developers would have to account for the possibility of being second to reach the market and create tests to show superiority over the winning first developer. Note that all four introductions that we focus on are me-too drugs: none was the first drug in the therapeutic class, each filed an application with the FDA for a new formulation (rather than a new chemical entity) and each received a standard review rating from the FDA (rather than a priority review). Yet two drugs (Adderall XR and Concerta) generated welfare gains which were as large as those of the generic introduction of MAS-IR while the other two (Metadate CD and Methylin ER) resulted in gains that were about an order of magnitude smaller. As our results suggest, not all me-toos are created equal and over-arching proposals aimed at slowing the introduction of all me-toos may not be appropriate.

REFERENCES

Angell, Marcia, *The truth about the drug companies: How they deceive us and what to do about it*, New York: Random House, 2004.

Barkley, Russell A., *Attention-deficit hyperactvity disorder: A handbook for diagnosis and treatment*, 3 ed., Guilford Press, 2006.

Berndt, Ernst R., Richard Mortimer, Ashoke Bhattacharjya, Andrew Parece, and Edward Tuttle, "Authorized generic drugs, price competition, and consumers welfare," *Health Affairs*, May/June 2007, *26* (3), 790–799.

Bokhari, Farasat A. S., "Identification in differentiated products demand systems," March 2009.

Bresnahan, Timothy F., "Comment to: Valuation of New Goods under Perfect and Imperfect Competition," in Robert James Gordon Timothy F. Bresnahan, ed., *The Economics of New Goods*, Vol. 58 of *Studies in Income and Wealth*, University of Chicago Press, 1997, pp. 237–248.

Bulow, Jeremy, "The gaming of pharmaceutical patents," in Adam B. Jaffe, Scott Stern, and Josh Lerner, eds., *Innovation Policy and the Economy*, Vol. 4, MIT Press, 2004, pp. 145–187.

Deaton, Angus and John Muellbauer, "An almost ideal demand system," *American Economic Review*, June 1980, *70* (3), 312–326.

_____ **and** _____, *Economics and consumer behavior*, Cambridge, UK: Cambridge University Press, 1980.

DiMasi, Joseph A. and Cherie Paquette, "The economics of follow-on drug research and development: Trends in entry rates and the timing of development," *PharmacoEconomics*, 2004, *22* (2 (Suppliment 2)), 1–14.

Ellison, Sara Fisher and Christopher M. Snyder, "Countervailing power in wholesale pharmaceuticals," July 19 2001. mimeo.

_____**, Iain Cockburn, Zvi Griliches, and Jerry A. Hausman**, "Characteristics of demand for pharmaceutical products: an examination of four cephalosporins," *RAND Journal of Economics*, Autumn 1997, *28* (3), 426–446.

Frank, Richard G., "The ongoing regulation of generic drugs," *The New England Journal of Medicine*, November 15 2007, *357* (20), 1993–1996.

_____ **and David S. Salkever**, "Pricing patent loss and the market for pharmaceuticals," *Southern Economic Journal*, October 1992, *59* (2), 165–179.

_____ **and** _____, "Generic entry and the pricing of pharmaceuticals," *Journal of Economics and Management Strategy*, Spring 1997, *6* (1), 75–90.

Goozner, Merrill, *The $800 million pill: The truth behind the cost of new drugs*, Berkeley, CA: University of California Press, 2004.

Grabowski, Henry and John Vernon, "Longer patents for increased generic competition: The Waxman-Hatch Act after one decade," *PharmacoEconomics*, 1996, *10* (Supplement 2), 110–123.

Grabowski, Henry G. and John M. Vernon, "Brand loyalty, entry and price competition in pharmaceuticals after the 1984 drug act," *Journal of Law and Economics*, October 1992, *35* (2), 331–350.

Grabowski, Henry, John Vernon, and Joseph A. DiMasi, "Returns on research and development for 1990s new drug introductions," *PharmacoEconomics*, 2002, *20* (Supplement 3), 11–29.

Hausman, Jerry A., "Valuation of New Goods under Perfect and Imperfect Competition," in T. F. Bresnahan and R. Gordon, eds., *The Economics of New Goods*, Vol. 58 of *Studies in Income and Wealth*, National Bureau of Economic Research, 1996.

_____ **and Gregory K. Leonard**, "The competitive effects of a new product introduction: A case study," *Journal of Industrial Economics*, September 2002, *L* (3), 237–263.

Hausman, Jerry, G. Leonard, and J.D. Zona, "Competitive Analysis with Differentiated Products," *Annales dEconomie et de Statistique*, 1994, *34*, 159–180.

Hemphill, C.Scott, "Drug patent settlements between rivals: A survey," March 12 2007.

Hollis, Aidan, "Me-too drugs: Is there a problem," December 13 2004. Published by World Health Organization Commission on Intellectual Property Rights, Innovation and Public Health.

Lichtenberg, Frank R. and Tomas J. Philipson, "The dual effects of intellectual property regulations: Within- and between- patent competition in the U.S. pharmaceuticals industry," *The Journal of Law and Economics*, October 2002, *45* (S2), 643–672.

Lu, Z. John and William S. Comanor, "Strategic pricing of new pharmaceuticals," *The Review of Economics and Statistics*, February 1998, *80* (1), 108–118.

Nevo, Aviv, "Identification of the oligopoly solution concept in a differentiated-products industry," *Ecnomic Letters*, 1998, *59*, 391–395.

_____, "A practitioner's guide to estimation of random-coefficients logit models of demand," *Journal of Economics and Management Strategy*, Winter 2000, *9* (4), 513–548.

Regan, Tracy L., "Generic entry, price competition, and market segmentation in the prescription drug market," *International Journal of Industrial Organization*, July 2008, *26* (4), 930–948.

Reiffen, David and Michael R. Ward, "'Branded Generics' as a strategy to limit cannibalization of pharmaceutical markets," *Managerial and Decision Economics*, 2007, *28* (4-5), 251–265.

Shulman, Sheila R., Joseph A. DiMasi, and Kennith I. Kaitin, "Patent term restoration: The impact of Waxman-Hatch Act on new drugs and biologics," *The Journal of Biolaw and Business*, 1999, *2* (4), 63–68.

Sorensen, Alan T., "Insurer-hospital bargaining: Negotiated discounts in post-deregulation Connecticut," *The Journal of Industrial Economics*, December 2003, *51* (4), 469–490.

Table 8. **Appendix A - Unconditional Elasticities from IV estimates**

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)
(1)	-1.33*	-0.47*	-1.98*	-0.4*	-0.42*	-0.16*	-0.61*	3.96*	0.08*	0.10*	0.12*	0.02	0.03	0.02	0.09	0.07	-0.04
(2)	-0.37	-2.1*	-1.13*	-0.38*	-0.40*	-0.15*	-0.58*	3.77*	0.07*	0.10*	0.11*	0.02	0.03	0.02	0.09	0.06	-0.04
(3)	-0.64*	-0.43*	-2.35*	-0.36*	-0.38*	-0.14*	-0.55*	3.59*	0.07*	0.09*	0.11*	0.02	0.03	0.02	0.08	0.06	-0.03
(4)	-0.59*	-0.68*	-1.63*	-4.12*	2.00*	0.68*	-1.08*	3.98*	0.08*	0.10*	0.13*	0.02	0.03	0.02	0.09	0.07	-0.04
(5)	-0.69*	-0.8*	-1.91*	1.82*	-3.25*	-1.07*	-0.46	4.66*	0.09*	0.12*	0.15*	0.02	0.04	0.03	0.11	0.08	-0.05
(6)	-0.45*	-0.52*	-1.24*	1.91*	-2.60*	-3.38*	2.14*	3.03*	0.06*	0.08*	0.10*	0.02	0.02	0.02	0.07	0.05	-0.03
(7)	-0.48*	-0.56*	-1.34*	-0.60	-0.08	0.53*	-1.93*	3.27*	0.06*	0.09*	0.10*	0.02	0.02	0.02	0.08	0.06	-0.03
(8)	0.51*	0.60*	1.42*	0.36*	0.37*	0.14*	0.54*	-5.35*	0.08*	0.10*	0.12*	0.02	0.03	0.02	0.09	0.07	-0.04
(9)	0.02	0.02	0.05	0.01	0.01	0.01	0.02	0.14	-1.89*	-1.07*	1.64*	0.01	0.02	0.01	0.05	0.03	0.10
(10)	0.02	0.02	0.06	0.01	0.01	0.01	0.02	0.14	-0.87*	-2.24*	1.72*	0.01	0.02	0.01	0.05	0.04	0.10
(11)	0.02	0.03	0.07	0.02	0.02	0.01	0.03	0.18	0.96*	1.28*	-3.97*	0.01	0.02	0.02	0.06	0.05	0.13
(12)	0.08*	0.09*	0.22*	0.05*	0.06*	0.02*	0.08*	0.58*	-0.12	-0.16	-0.19	-3.27	0.08	1.66	0.02	0.02	-0.12
(13)	0.09*	0.10*	0.24*	0.06*	0.06*	0.02*	0.09*	0.62*	-0.13	-0.17	-0.20	0.03	-0.60	-1.06	0.02	0.02	-0.13
(14)	0.09*	0.10*	0.24*	0.06*	0.06*	0.02*	0.09*	0.63*	-0.13	-0.17	-0.20	1.38	-1.31	-1.71*	0.02	0.02	-0.13
(15)	0.10*	0.11*	0.27*	0.06*	0.07*	0.03*	0.10*	0.68*	-0.14	-0.19	-0.22	-0.01	-0.02	-0.01	-1.20	-0.50	-0.14
(16)	0.10*	0.11*	0.27*	0.07*	0.07*	0.03*	0.10*	0.71*	-0.14	-0.19	-0.23	-0.01	-0.02	-0.02	-0.70	-1.06	-0.15
(17)	-0.01	-0.01	-0.03	-0.01	-0.01	-0.01	-0.01	-0.07	0.32*	0.42*	0.51*	-0.10*	-0.14*	-0.11*	-0.43*	-0.32*	-1.53*

Note 1: Elasticity matrix computed at the sample mean. $*$ indicates significant at 5% level.

Average Shares (Within Molecule Form (M-F)and Overall (O))

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)
M-F	0.203	0.235	0.562	0.254	0.263	0.098	0.385	1.000	0.430	0.570	1.000	0.276	0.400	0.324	0.571	0.429	1.000
O	0.031	0.036	0.085	0.021	0.021	0.008	0.031	0.219	0.091	0.120	0.145	0.005	0.007	0.006	0.022	0.016	0.137

Key:

(1) Ritalin; (2) Methylin; (3) MPH-IR (Generics); (4) Ritalin SR/LA; (5) Metadate ER/CD; (6) Methylin ER; (7) MPH-ER (Generics); (8) Concerta; (9) Adderall; (10) MAS-IR (Generics); (11) Adderall XR; (12) Dexedrine; (13) Dextrostat; (14) DEX-IR (Generics); (15) Dexedrine SR; (16) DEX-ER (Generics); (17) Other Drugs;

Table 9. **Appendix B – Unconditional Elasticities from OLS estimates**

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)
(1)	-1.30*	-0.17*	-0.53*	-0.06*	-0.06*	-0.02*	-0.09*	1.57*	0.01	0.01	0.01	-0.01	-0.01	-0.01	-0.03	-0.02	-0.04
(2)	-0.13*	-0.79*	-1.00*	-0.06*	-0.06*	-0.02*	-0.08*	1.50*	0.01	0.01	0.01	-0.01	-0.01	-0.01	-0.03	-0.02	-0.04
(3)	-0.15*	-0.39*	-1.26*	-0.05*	-0.05*	-0.02*	-0.08*	1.40*	0.01	0.01	0.01	-0.01	-0.01	-0.01	-0.03	-0.02	-0.04
(4)	-0.09*	-0.11*	-0.25*	-2.47*	0.93*	0.28*	-0.18	1.16*	0.01	0.01	0.01	-0.01	-0.01	-0.01	-0.03	-0.03	-0.05
(5)	-0.1*	-0.12*	-0.28*	0.86*	-2.10*	-0.25*	-0.1	1.28*	0.01	0.01	0.01	-0.01	-0.01	-0.01	-0.04	-0.03	-0.05
(6)	-0.06*	-0.07*	-0.18*	0.84*	-0.53*	-0.84*	-0.48*	0.82*	0.00	0.01	0.01	-0.01	-0.01	-0.01	-0.02	-0.02	-0.03
(7)	-0.07*	-0.08*	-0.20*	-0.04	0.05	-0.14*	-1.00*	0.91*	0.00	0.01	0.01	-0.01	-0.01	-0.01	-0.03	-0.02	-0.04
(8)	0.20*	0.23*	0.55*	0.1*	0.10*	0.04*	0.15*	-2.08*	0.01	0.01	0.01	-0.01	-0.01	-0.01	-0.03	-0.03	-0.05
(9)	-0.00	-0.00	-0.01	-0.00	-0.00	-0.00	-0.00	-0.03	-1.04*	-0.45*	0.28*	-0.00	-0.00	-0.00	-0.00	-0.00	0.06
(10)	-0.00	-0.00	-0.01	-0.00	-0.00	-0.00	-0.00	-0.03	-0.37*	-1.19*	0.29*	-0.00	-0.00	-0.00	-0.00	-0.00	0.06
(11)	-0.00	-0.01	-0.01	-0.00	-0.00	-0.00	-0.00	-0.03	0.13*	0.17*	-1.75*	-0.00	-0.00	-0.00	-0.00	-0.00	0.07
(12)	-0.00	-0.00	-0.00	-0.00	-0.00	-0.00	-0.00	-0.01	-0.06	-0.08	-0.10	-0.59*	-0.54*	0.06	0.59*	0.44*	-0.02
(13)	-0.00	-0.00	-0.00	-0.00	-0.00	-0.00	-0.00	-0.01	-0.07	-0.09	-0.11	-0.39*	-0.45*	-0.30*	0.63*	0.48*	-0.02
(14)	-0.00	-0.00	-0.00	-0.00	-0.00	-0.00	-0.00	-0.01	-0.07	-0.09	-0.11	0.03	-0.38*	-0.80*	0.63*	0.48*	-0.02
(15)	-0.00	-0.00	-0.00	-0.00	-0.00	-0.00	-0.00	-0.01	-0.08	-0.10	-0.12	0.14*	0.20*	0.16*	-0.86*	0.33*	-0.03
(16)	-0.00	-0.00	-0.00	-0.00	-0.00	-0.00	-0.00	-0.01	-0.08	-0.10	-0.12	0.14*	0.20*	0.16*	0.43*	-0.98*	-0.03
(17)	-0.04*	-0.05*	-0.11*	-0.03*	-0.03*	-0.01*	-0.04*	-0.29*	0.26*	0.34*	0.41*	-0.01	-0.01	-0.01	-0.04	-0.03	-1.21*

Note 1: Elasticity matrix computed at the sample mean. ∗ indicates significant at 5% level.

Average Shares (Within Molecule Form (M-F) and Overall (O))

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)
M-F	0.203	0.235	0.562	0.254	0.263	0.098	0.385	1.000	0.430	0.570	1.000	0.276	0.400	0.324	0.571	0.429	1.000
O	0.031	0.036	0.085	0.021	0.021	0.008	0.031	0.219	0.091	0.120	0.145	0.005	0.007	0.006	0.022	0.016	0.137

Key:

(1) Ritalin; (2) Methylin; (3) MPH-IR (Generics); (4) Ritalin SR/LA; (5) Metadate ER/CD; (6) Methylin ER; (7) MPH-ER (Generics); (8) Concerta; (9) Adderall; (10) MAS-IR (Generics); (11) Adderall XR; (12) Dexedrine; (13) Dextrostat; (14) DEX-IR (Generics); (15) Dexedrine SR; (16) DEX-ER (Generics); (17) Other Drugs;

Appendix C – Derivation of Elasticities

Observe that $s_{i_{f_m}} \equiv \frac{P_{i_{f_m}} Q_{i_{f_m}}}{R_{f_m}}$ and hence $lnQ_{i_{f_m}} = lns_{i_{f_m}} - lnP_{i_{f_m}} + lnR_{f_m}$. Thus, elasticity of ith drug in f-m segment with resect to kth drug in $f' - m'$ segment is given by

$$\frac{\partial lnQ_{i_{f_m}}}{\partial lnP_{k_{f'_{m'}}}} = \frac{1}{s_{i_{f_m}}} \Big\{ \frac{\partial s_{i_{f_m}}}{\partial lnP_{k_{f'_{m'}}}} \Big\} + \frac{\partial lnR_{f_m}}{\partial lnP_{k_{f'_{m'}}}} - 1[k = i, f' = f, m' = m] \tag{A-1}$$

where 1[.] is an indicator function equal to 1 when the statement inside is true and is otherwise 0. Note that the subscripts are such that if $m \neq m'$ than it automatically implies that $f \neq f'$ and $i \neq k$. Similarly, if $f \neq f'$ then $i \neq k$.

Elasticities Conditional on Segment Revenue. We first compute elasticities conditional on the revenue segment R_{f_m}. Then in equation (A-1) we can set the partial of R_{f_m} equal to zero. From equation (1) we have

$$\frac{\partial s_{i_{f_m}}}{\partial lnP_{k_{f'_{m'}}}} = \beta_{i_{f_m}} (-\frac{\partial P_{f_m}}{\partial lnP_{k_{f'_{m'}}}}) + \gamma_{ik_{f'_{m'}}} .1[f' = f, m' = m]$$

where once again, in equation (1) we have set the partial of R_{f_m} equal to zero. Next, from equation (2), the partial of the fixed-weight Stone index of segment f-m with respect to $lnP_{k_{f'_{m'}}}$ is zero if $m' \neq m$ and $f' \neq f$ but otherwise is $\bar{s}_{k_{fm}}$. Hence the elasticity (conditional on R_{f_m}) is

$$\begin{aligned} \frac{\partial lnQ_{i_{f_m}}}{\partial lnP_{k_{f'_{m'}}}} = \frac{1}{s_{i_{f_m}}} \Big\{ \Big(- \beta_{i_{f_m}} \bar{s}_{k_{f'_{m'}}} + \gamma_{ij_{f'_{m'}}} \Big) .1[f' = f, m' = m] \Big\} \\ - 1[i = k, f' = f, m' = m] \end{aligned} \tag{A-2}$$

Thus, elasticities conditional on R_{f_m} are zero across drugs in different f-m segments. Incidently, observe that by the same logic, elasticities of forms within a molecule with respect to the *price index* for the form, conditional on R_m, has a similar formula and is given by

$$\frac{\partial lnQ_{f_m}}{\partial lnP_{f'_{m'}}} = \frac{1}{u_{f_m}} \Big\{ \Big(- b_{f_m} \bar{u}_{f'_{m'}} + g_{fh_{m'}} \Big) .1[m' = m] \Big\} - 1[f' = f, m' = m] \tag{A-3}$$

Unconditional Elasticities. Share of drug i in segment f-m is effected by the price of drug k in some other segment f'-m' only via the change in the expenditures of the segments. Specifically, when the price of drug k in segment f'-m' changes, it changes the price index of segment f'-m'. When the price index of segment f'-m' changes, it changes the relative prices of segments f'-m' and f-m. This in turn changes the share of revenue spent on segment f-m vs. f'-m' and is determined by the middle level share equations. Thus when computing the relevant partials we do not hold R_{f_m} (or R_m) constant. Further, the link between bottom and middle level equations is established by considering the ratio R_{f_m}/P_{f_m} in equation (1) as a measure of a standard unit of quantity of

molecule m and form f, i.e. $R_{f_m}/P_{f_m} = Q_{f_m}$ and since $u_{f_m} \equiv \frac{P_{f_m}Q_{f_m}}{R_m}$, we substitute $u_{f_m}R_m/P_{f_m}$ for R_{f_m}/P_{f_m} in the bottom level share equation (1). Similarly, in the middle level share equation (4), we substitute Q_m from the top level quantity equation (7).

The general expression for elasticities is given in equation (A-1). We evaluate each of the partials above while making the appropriate substitutions. First, observe that by substituting Q_{f_m} for R_{f_m}/P_{f_m} in the bottom level share equation (1) we get $s_{i_{f_m}} = \alpha_{i_{f_m}} + \beta_{i_{f_m}} ln(Q_{f_m}) + \sum_{j=1}^{I_{f_m}} \gamma_{ij_{f_m}} lnP_{j_{f_m}}$ and hence

$$\frac{\partial s_{i_{f_m}}}{\partial lnP_{k_{f'_{m'}}}} = \beta_{i_{f_m}} \left(\frac{\partial lnQ_{f_m}}{\partial lnP_{k_{f'_{m'}}}}\right) + \gamma_{ik_{f'_{m'}}} .1[f' = f, m' = m].$$

Similarly, since $lnR_{f_m} = lnP_{f_m} + lnQ_{f_m}$ hence

$$\begin{aligned}\frac{\partial lnR_{f_m}}{\partial lnP_{k_{f'_{m'}}}} &= \frac{\partial lnP_{f_m}}{\partial lnP_{k_{f'_{m'}}}} + \frac{\partial lnQ_{f_m}}{\partial lnP_{k_{f'_{m'}}}} \\ &= \bar{s}_{k_{f'_{m'}}} .1[f = f', m = m'] + \frac{\partial lnQ_{f_m}}{\partial lnP_{k_{f'_{m'}}}}\end{aligned}$$

Substituting these two partials in the general elasticity equation (A-1) above we get,

$$\begin{aligned}\frac{\partial lnQ_{i_{f_m}}}{\partial lnP_{k_{f'_{m'}}}} &= \frac{1}{s_{i_{f_m}}} \left\{\frac{\partial s_{i_{f_m}}}{\partial lnP_{k_{f'_{m'}}}}\right\} + \frac{\partial lnR_{f_m}}{\partial lnP_{k_{f'_{m'}}}} - 1[k = i, f' = f, m' = m] \\ &= \frac{1}{s_{i_{f_m}}} \left\{\beta_{i_{f_m}} \left(\frac{\partial lnQ_{f_m}}{\partial lnP_{k_{f'_{m'}}}}\right) + \gamma_{ik_{f'_{m'}}} .1[f' = f, m' = m]\right\} \\ &+ \bar{s}_{k_{f'_{m'}}} .1[f = f', m = m'] + \frac{\partial lnQ_{f_m}}{\partial lnP_{k_{f'_{m'}}}} \\ &- 1[k = i, f' = f, m' = m]\end{aligned} \tag{A-4}$$

Thus, we need to evaluate $\frac{\partial lnQ_{f_m}}{\partial lnP_{k_{f'_{m'}}}}$ and substitute it in the equation above. Note that $lnQ_{f_m} = ln(u_{f_m}) + lnR_m - lnP_{f_m}$ and hence

$$\begin{aligned}\frac{\partial lnQ_{f_m}}{\partial lnP_{k_{f'_{m'}}}} &= \frac{1}{u_{f_m}} \left\{\frac{\partial u_{f_m}}{\partial lnP_{k_{f'_{m'}}}}\right\} + \frac{\partial lnR_m}{\partial lnP_{k_{f'_{m'}}}} - \frac{\partial lnP_{f_m}}{\partial lnP_{k_{f'_{m'}}}} \\ &= \frac{1}{u_{f_m}} \left\{\frac{\partial u_{f_m}}{\partial lnP_{k_{f'_{m'}}}}\right\} + \frac{\partial lnR_m}{\partial lnP_{k_{f'_{m'}}}} - \bar{s}_{k_{f'_{m'}}} .1[f = f', m = m']\end{aligned} \tag{A-5}$$

To evaluate the two partials in (A-5) above, we substitute Q_m for R_m/P_m in the middle level share equation (4), i.e., $u_{f_m} = a_{f_m} + b_{f_m} ln(Q_m) + \sum_{h=1}^{F_m} g_{fh_m} lnP_{h_m}$ and use the chain rule. Thus,

$$\frac{\partial u_{f_m}}{\partial lnP_{k_{f'_{m'}}}} = \frac{\partial u_{f_m}}{\partial lnP_{f'_{m'}}} . \frac{\partial lnP_{f'_{m'}}}{\partial lnP_{k_{f'_{m'}}}} = \frac{\partial u_{f_m}}{\partial lnP_{f'_{m'}}} . \bar{s}_{k_{f'_{m'}}}$$

and similarly (A-6)

$$\frac{\partial lnR_m}{\partial lnP_{k_{f'_{m'}}}} = \frac{\partial lnR_m}{\partial lnP_{f'_{m'}}} . \frac{\partial lnP_{f'_{m'}}}{\partial lnP_{k_{f'_{m'}}}} = \{ \frac{\partial lnP_m}{\partial lnP_{f'_{m'}}} + \frac{\partial lnQ_m}{\partial lnP_{f'_{m'}}} \} . \bar{s}_{k_{f'_{m'}}} .$$

Hence equation (A-5) becomes

$$\begin{aligned} \frac{\partial lnQ_{f_m}}{\partial lnP_{k_{f'_{m'}}}} &= \frac{1}{u_{f_m}} \Big\{ \frac{\partial u_{f_m}}{\partial lnP_{k_{f'_{m'}}}} \Big\} + \frac{\partial lnR_m}{\partial lnP_{k_{f'_{m'}}}} - \bar{s}_{k_{f'_{m'}}} .1[f = f', m = m'] \\ &= \frac{1}{u_{f_m}} \Big\{ \bar{s}_{k_{f'_{m'}}} . \frac{\partial u_{f_m}}{\partial lnP_{f'_{m'}}} \Big\} + \bar{s}_{k_{f'_{m'}}} . \Big\{ \frac{\partial lnP_m}{\partial lnP_{f'_{m'}}} + \frac{\partial lnQ_m}{\partial lnP_{f'_{m'}}} \Big\} - \bar{s}_{k_{f'_{m'}}} .1[f = f', m = m'] \end{aligned} \quad \text{(A-7)}$$

We can substitute equation (A-7) back into (A-4) to get elasticities in terms of these new partials as

$$\begin{aligned} \frac{\partial lnQ_{i_{fm}}}{\partial lnP_{k_{f'_{m'}}}} &= \frac{1}{s_{i_{fm}}} \Big\{ \beta_{i_{fm}} (\frac{\partial lnQ_{f_m}}{\partial lnP_{k_{f'_{m'}}}}) + \gamma_{ik_{f'_{m'}}} .1[f' = f, m' = m] \Big\} \\ &+ \frac{1}{u_{f_m}} \Big\{ \bar{s}_{k_{f'_{m'}}} \frac{\partial u_{f_m}}{\partial lnP_{f'_{m'}}} \Big\} + \bar{s}_{k_{f'_{m'}}} \Big\{ \frac{\partial lnP_m}{\partial lnP_{f'_{m'}}} + \frac{\partial lnQ_m}{\partial lnP_{f'_{m'}}} \Big\} \\ &- 1[k = i, f' = f, m' = m] \end{aligned}$$

which further simplifies to

$$\begin{aligned} &= \Big(1 + \frac{\beta_{i_{fm}}}{s_{i_{fm}}} \Big) \frac{1}{u_{f_m}} \bar{s}_{k_{f'_{m'}}} \frac{\partial u_{f_m}}{\partial lnP_{f'_{m'}}} \\ &+ \Big(1 + \frac{\beta_{i_{fm}}}{s_{i_{fm}}} \Big) \bar{s}_{k_{f'_{m'}}} \Big\{ \frac{\partial lnP_m}{\partial lnP_{f'_{m'}}} + \frac{\partial lnQ_m}{\partial lnP_{f'_{m'}}} \Big\} \\ &+ \frac{1}{s_{i_{fm}}} \Big\{ \gamma_{ik_{f'_{m'}}} - \beta_{i_{fm}} \bar{s}_{k_{f'_{m'}}} \Big\} .1[f' = f, m' = m] \\ &- 1[i = k, f' = f, m' = m] \end{aligned} \quad \text{(A-8)}$$

Note that the remaining partials are with respect to the (log of) price indexes $P_{f'_{m'}}$ as opposed to with respect to the (log of) actual prices and are easily evaluated from the middle and top level equations. Thus from the middle level equation $u_{f_m} = a_{f_m} + b_{f_m} ln(Q_m) + \sum_{h=1}^{F_m} g_{fh_m} lnP_{h_m}$ (with Q_m substituted in for R_m/P_m) we get,

$$\frac{\partial u_{f_m}}{\partial lnP_{f'_{m'}}} = b_{f_m} \frac{\partial lnQ_m}{\partial lnP_{f'_{m'}}} + g_{ff'_{m'}} 1.[m = m']. \quad \text{(A-9)}$$

Next, since $lnP_m = \sum_{h=1}^{F_m} \bar{u}_{h_m} lnP_{h_m}$ therefore $\partial lnP_m / \partial lnP_{f'_m} = \bar{u}_{f'_m}$ but $\partial lnP_m / \partial lnP_{f'_{m'}} = 0$ and hence

$$\frac{\partial lnP_m}{\partial lnP_{f'_{m'}}} = \bar{u}_{f'_{m'}} 1.[m' = m]. \tag{A-10}$$

Finally, from the top level quantity equation $ln(Q_m) = A_m + B_m ln(R) + \sum_{n=1}^{M} \Gamma_{mn} lnP_n$ we get

$$\frac{\partial lnQ_m}{\partial lnP_{f'_{m'}}} = \Gamma_{mm'} \bar{u}_{f'_{m'}} \tag{A-11}$$

where note that in this last partial derivative there is no indicator function since the top level equation itself consists of all molecule level price indexes.

Thus, we can substitute equations (A-9,A-10 and A-11) into (A-8) to get the final expression for elasticities in terms of the shares and model parameters. Upon substitution this gives the unconditional elasticities as

$$\begin{aligned}
\frac{\partial lnQ_{i_{f_m}}}{\partial lnP_{k_{f'_{m'}}}} &= \Big(1 + \frac{\beta_{i_{f_m}}}{s_{i_{f_m}}}\Big) \bar{s}_{k_{f'_{m'}}} \Big[\frac{g_{ff'_{m'}}}{u_{fm}} + \bar{u}_{f'_{m'}}\Big] \cdot 1[m = m'] \\
&+ \Big(1 + \frac{\beta_{i_{f_m}}}{s_{i_{f_m}}}\Big) \bar{s}_{k_{f'_{m'}}} \Big[\frac{b_{fm} \bar{u}_{f'_{m'}}}{u_{fm}} + \bar{u}_{f'_{m'}}\Big] \Gamma_{mm'} \\
&+ \frac{1}{s_{i_{f_m}}} \Big\{\gamma_{ik_{f'_{m'}}} - \beta_{i_{f_m}} \bar{s}_{k_{f'_{m'}}}\Big\}.1[f' = f, m' = m] \\
&- 1[i = k, f' = f, m' = m].
\end{aligned} \tag{A-12}$$