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**Impacts of Pharmaceutical Marketing on Healthcare
Services in the District of Columbia**

Focus on Use of Antipsychotics in Children

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Table of Contents

I. Executive Summary	5
Healthcare in the District of Columbia.....	5
Antipsychotics and Marketing to District Psychiatrists.....	6
Recommendations	8
II. Pharmaceuticals and Healthcare in the District of Columbia	11
Pharmaceuticals and Healthcare in the District of Columbia	11
Medicaid Pharmaceutical Spending in the District of Columbia	12
III. Concerns About Pharmaceutical Marketing	15
Effectiveness and Adverse Events.....	15
Off-Label Prescribing.....	16
Prescription-drug Expenditures	16
IV. Effects of Marketing	19
Marketing to Physicians.....	19
Free Samples.....	20
Research Participation and Results.....	21
Direct-to-Consumer Advertising	21
Funding of Organizations Producing Continuing Medical Education and Patient Information.....	22
V. Use of Antipsychotics in Children	25
Increased Prescribing Despite Limited Approved Indications	25
Adverse events.....	28
Federal responses to antipsychotic marketing and potential inappropriate prescribing	29
State responses to potential inappropriate prescribing.....	30
Toward more appropriate prescribing.....	32
VI. Marketing and Use of Antipsychotics in the District	33
Examining Antipsychotic Use among District Medicaid Recipients.....	33
Marketing Expenditures of Antipsychotic Manufacturers in the District	35
Pharmaceutical Marketing to Psychiatrists in the District.....	36
Characteristics of Physicians Receiving Gifts from Antipsychotic Manufacturers.....	42
VII. Developments in the District of Columbia	43
Hospital and Medical School Policies in the District of Columbia.....	43

Academic Detailing Efforts in the District of Columbia..... 44

DC Superior Court’s Efforts to Monitor Psychotropic Medication Use 44

VIII. Recommendations 47

References 50

**Appendix: Proportion of Medicaid Population Receiving Antipsychotic Prescriptions in 2008,
by State** 57

I. Executive Summary

Prescription drugs play an essential role in healthcare, but inappropriate use of pharmaceuticals can be dangerous. Pharmaceutical marketing efforts that encourage the use of new, expensive drugs when other alternatives may be safer, more effective, and more affordable complicate decision-making for prescribers, patients, and payers. Pharmaceutical sales representatives and physician opinion leaders may downplay adverse events and encourage prescribing that is supported neither by FDA approval nor scientific evidence.

Industry marketing methods include visits to prescribers by sales representatives; distribution of gifts and free samples; hiring physicians as consultants or speakers to influence the prescription of targeted drugs; direct-to-consumer promotion; and funding of professional medical organizations, patient organizations, continuing medical education, and patient information. These practices can influence prescribers and patients to prefer drugs that are not the best drugs in terms of cost, effectiveness, or risks.

This report investigates the ways that pharmaceutical marketing trends affect the cost, utilization, and delivery of healthcare services in the District of Columbia. A 2009 report on the same topic addresses healthcare services broadly, and this report focuses specifically on the use of antipsychotics in children, particularly those enrolled in the District's Medicaid program.

The District of Columbia AccessRx Act requires pharmaceutical companies that market products in the District to file annual reports on marketing expenditures. More recently, the SafeRx Act requires the licensure of detailers (pharmaceutical sales representatives) and establishes an academic detailing program that provides unbiased drug information to prescribers. Other states have gone even farther; for instance, Vermont prohibits gifts from pharmaceutical companies to physicians altogether. Several states have also adopted policies addressing the use of antipsychotics in children, which is a special focus of this report.

Data collected pursuant to the AccessRx Act have been analyzed by the George Washington University School of Public Health and Health Services for the District of Columbia Department of Health, most recently in the report "Pharmaceutical Marketing Expenditures in the District of Columbia, 2010." In 2010, 132 pharmaceutical companies reported spending a total of \$85.4 million on marketing activities in the District of Columbia, including \$57.6 million on employee and contractor expenses, \$21.0 million on gifts and payments, and \$6.8 million on advertising. Physicians received 76% of the gifts given by pharmaceutical companies, and these gifts accounted for 39% of the total value of all gifts.

Healthcare in the District of Columbia

The District's generous eligibility limits for Medicaid, and the existence of the DC Healthcare Alliance to cover Medicaid-ineligible residents with incomes below 200% of the federal poverty level, leave the city with an uninsurance rate lower than that of most states. A 2010 report by the Brookings Institution and

Rockefeller Foundation gives the District credit for improving access to primary care and specialists over the past decade, although it cautions that access to mental health and substance-abuse services is far too low.

In FY 2010, the District spent \$1.82 billion on services to Medicaid beneficiaries, a group that includes 205,000 low-income residents. Pharmaceuticals represent a significant portion of overall District Medicaid expenditures: \$91.5 million in 2008, the most recent year for which figures are available. As in previous years, this spending was concentrated in a few categories and groups of drugs.

Given that Medicaid covers a large percentage of District residents, the generosity of its benefits and the extent to which providers are willing to see Medicaid patients have a strong influence on the overall accessibility and quality of healthcare services in the District. High Medicaid prescription drug costs can crowd out spending in other areas of the program, such as payments to providers.

The therapeutic categories accounting for the largest share of District Medicaid spending in 2008 were:

- Anti-infective agents: \$33 million (36%)
- Central nervous system drugs: \$19 million (21%)
- Cardiovascular agents: \$8 million (9%)

Together, these drugs comprise two thirds (66%) of total expenditures. The drug groups accounting for the largest share of District Medicaid spending in 2008 were:

- Antivirals: \$31 million (34%)
- Antipsychotics: \$16 million (17%)
- Anticonvulsants: \$6 million (7%)

Antipsychotics and Marketing to District Psychiatrists

The increased use of antipsychotics is of great concern, particularly when the drugs are prescribed to children who may not have been diagnosed with any of the conditions for which these drugs are specifically approved. Second-generation antipsychotics, or atypical antipsychotics, are associated with sedation, weight gain, and development of type 2 diabetes, and children and adolescents may be at a higher risk of such adverse events compared to adults. Use of these drugs is increasing even among preschoolers (Zito et al., 2007), and the proportion of antipsychotic users who were under age 18 doubled from 1996-1997 to 2004-2005, from 7% to 15% of all users (Domino & Swartz, 2008). Much of the increase in antipsychotic prescriptions is due to off-label prescribing for conditions other than schizophrenia, bipolar disorder, or autism, the indications for which second-generation antipsychotics are currently approved.

The use of psychotropic drugs, including antipsychotics, among foster children is especially extensive. Although this vulnerable population may have greater need for psychotropic drugs, a five-state Government Accountability Office analysis of prescription drug records found thousands of foster

children receiving psychotropic prescriptions that did not conform to best practice guidelines from the American Academy of Child and Adolescent Psychiatry for oversight of children in state custody (GAO, 2011).

We calculated the proportion of Medicaid beneficiaries receiving antipsychotics every year from 2001 to 2008 in the District and the 50 states. In 2008, the national average percentage of Medicaid beneficiaries receiving antipsychotics for all states was 5.4%; the percentage in the District of Columbia was nearly twice as high, at 9.8%. While most states have experienced a decrease in antipsychotic medication use among their Medicaid populations, District Medicaid beneficiaries' antipsychotic use has continued to grow. Maryland was also an outlier, with 10.1% of its Medicaid beneficiaries receiving antipsychotic medications in 2008.

In the general population, an estimated 1.2% of the US population filled antipsychotic prescriptions in 2005. The estimated prevalence of disorders for which antipsychotics may be indicated ranges from less than 1% to 3% (NIMH, 2012). While it is likely that the Medicaid population has higher rates of mental disorders than the whole population, it is worth questioning whether one in ten (9.8%) of District Medicaid beneficiaries should be taking potent antipsychotics with serious risks.

Our analysis of pharmaceutical marketing data finds that the manufacturers of the six most commonly prescribed atypical antipsychotics are marketing heavily in the District of Columbia, spending nearly \$26 million in 2010. Gift expenditures, which include consulting payments and speaker fees, are not assigned to a particular drug, so we investigated gifts from these companies to psychiatrists, who are likely receiving marketing messages about antipsychotics from these manufacturers. We also analyzed gifts to Medicaid psychiatrists. We found:

- Out of 172 District physicians receiving gifts totaling \$1,000 or more from the top antipsychotic manufacturers, 26 (15%) were psychiatrists.
- The total amount received by these 26 psychiatrists was nearly \$500,000, or approximately one-fourth of the \$1.9 million received by all 172 physicians.
- Out of 119 District psychiatrists accepting Medicaid in 2012, 42 (35%) received gifts from the top antipsychotic manufacturers in 2010 – a decline from 2008, when 56 of them received such gifts.
- While the number of Medicaid psychiatrists receiving gifts from the top antipsychotic manufacturers has declined, the total value of the gifts to these providers from these companies has increased, totaling over \$340,000 in 2010 (compared to approximately \$260,000 in 2009).
- Of 26 psychiatrists receiving at least \$1,000 in gifts from the top antipsychotic manufacturers, seven accept Medicaid while nineteen do not.
- While psychiatrists accepting Medicaid account for only 27% of the psychiatrists receiving at least \$1,000 from top antipsychotic manufacturers, they receive a disproportionate share of gifts; their total gift amounts are 66% of the total amount received by psychiatrists from these companies.
- Between 2007 and 2010, the value of the average individual gift received by Medicaid psychiatrists from top antipsychotic manufacturers has increased by 41%, while the average

total amount received by Medicaid psychiatrists has increased by 85% – suggesting that while fewer Medicaid psychiatrists are receiving gifts than in prior years, the psychiatrists who continue to receive gifts are receiving more-expensive gifts.

Antipsychotic manufacturers are marketing heavily to District psychiatrists, and appear to be targeting Medicaid psychiatrists in particular.

Recommendations

To address the concerns about the impacts of pharmaceutical marketing – particularly antipsychotic marketing – on the health of the District’s children and adult residents, we have five main recommendations:

1. Strengthen the AccessRx Act to improve transparency. We recommend that the AccessRx Act be amended to make all pharmaceutical-marketing reports submitted the District publicly available; require reports of gift expenditures to include unique recipient identifiers; and require that individual gifts reported include “product supported” information. These modifications would make it easier for District agencies, journalists, and the public to find patterns – such as specific doctors being paid to speak on behalf of specific drugs – that could help patients and public officials guard against potential inappropriate prescribing.

2. Notify providers for whom large gift amounts are reported. Healthcare providers who are reported to be receiving large sums (e.g., over \$10,000 in total value of gifts) should be alerted to what the District’s records show and warned of the appearance of potential conflicts of interest. While the data received pursuant to the AccessRx Act are not publicly reported, many payments are already publicly available in the ProPublica database, and physician payments from all pharmaceutical companies will be public soon under the Affordable Care Act. Providers may wish to consider the possibility that large gifts from pharmaceutical companies could create suspicions about biased prescribing choices among patients and others.

3. Study prescribing patterns for potential irrational prescribing, with an initial focus on antipsychotics prescribed for children, and place limitations on prescribing and reimbursement as appropriate. The District may be able to use its Medicaid pharmaceutical data to identify prescribing patterns that could signal inappropriate prescribing. In the case of antipsychotics, it is entirely possible that the rate of use by District Medicaid enrollees is high due to greater incidence of relevant conditions among this population, and that some providers may see more patients who could benefit from psychotropic medications. However, it would be worthwhile to identify any Medicaid providers whose patterns of prescribing antipsychotics suggest possible inappropriate prescribing and engage with them further. If the problem is severe and not improving, establishing policies to limit prescribing and/or Medicaid reimbursement may be necessary. In addition, analyses of which specific antipsychotics or other drugs are being prescribed could help the District target its ongoing educational and outreach efforts.

4. Expand prescriber education and outreach, with an initial focus on antipsychotic use in children.

Academic detailing efforts could be expanded to include a module on antipsychotic use, and one or more District agencies could sponsor Continuing Medical Education opportunities on appropriate prescribing of antipsychotics. Additional resources from federal agencies related to the 2011 Child and Family Services Improvement and Innovation Act may also be useful to the District.

5. Consider legislation to ban gifts to healthcare providers. Adopting a law, such as Vermont's 2009 legislation, to prohibit gifts (including food) to healthcare providers would greatly reduce the potential for conflicts of interest and for gift-influenced inappropriate prescribing.

II. Pharmaceuticals and Healthcare in the District of Columbia

Prescription drugs have made significant contributions to health, and can provide for cost savings; for instance, drug treatment for ulcers supplanted surgery and helps avoid costly hospitalizations. Care of patients with AIDS, which relies heavily on antiretroviral drug therapy, has saved at least three million years of life in the United States alone (Walensky et al., 2006). Without antihypertensive therapy, 86,000 premature deaths from cardiovascular disease would have occurred in 2001 alone; the benefit-to-cost ratio of antihypertensive drugs is at least 6:1 (Cutler et al., 2007).

Some drugs, however, are overused. Although prescription-drug spending accounts for only around 13% of total US healthcare spending, it is one of the fastest-growing components of healthcare. According to the Kaiser Family Foundation, spending for prescription drugs in the U.S. increased seven-fold – from \$40.3 billion to \$300.3 billion – between 1990 and 2009. The main factors driving increased prescription-drug spending are changes in utilization, prices, and types of drugs used. Utilization and prices have both increased steadily: From 1999 to 2009, the number of prescriptions purchased in the US increased 39%, and retail prescription prices increased an average of 3.6% a year between 2000 and 2009 (Kaiser Family Foundation, 2010).

The proportion of prescription drugs that are generics (compared to brand-name drugs) is also a major factor in prescription-drug spending; in 2008, the average price for a brand-name prescription was almost four times higher than the average price for a generic prescription (\$137.90 vs. \$35.22). This figure varies from year to year, and is influenced by the number of drugs under patent as well as by efforts to promote the use of generics. In 2008, 72% of total prescriptions dispensed were generics, but due to their lower costs they accounted for just 22% of the total prescription-drug sales figure (Kaiser Family Foundation, 2010). IMS Health, a health information company, predicts 3%-6% annual growth in the U.S. pharmaceutical market, reaching \$360-\$390 billion in 2014; factors in the continued growth include “continued high levels of patient demand for pharmaceuticals” (Arnold, 2010).

Overall, prescription drugs represent a positive and high-value contribution to healthcare. However, continued rapid growth in prescription-drug spending may present insurers and public programs, as well as individual patients, with difficult choices about allocating limited healthcare dollars.

Pharmaceuticals and Healthcare in the District of Columbia

In 2010, 87.5% of the District of Columbia's total population, and 94.9% of children and adolescents under the age of 18, were covered by some form of health insurance. More than one-third of the District's population, 34.9%, was covered by government insurance; Medicaid provided coverage to 23.0% of residents and 50.4% of children (Census Bureau, 2011). The uninsurance rate in the District is lower than the national average: 12.5% rather than 16.3%. Some survey respondents who report themselves as being uninsured do receive healthcare through the DC HealthCare Alliance, the coverage program for Medicaid-ineligible residents with incomes below 200% of the federal poverty level (Cook and Ormond, 2007). The District of Columbia's recent expansion of Medicaid eligibility to residents up to

133% of the federal poverty limit, in advance of the Affordable Care Act's requirement to do so in 2014, has further increased Medicaid enrollment and shifted thousands of individuals from the Alliance to Medicaid.

Relatively high rates of insurance do not necessarily lead to better health outcomes. The District scores poorly on several indicators of population health. A 2008 RAND Corporation analysis reported that in the District of Columbia:

- More than one in four adults has hypertension;
- The diabetes mortality rate is high compared to other cities with similar socio-demographic makeups;
- Thirty-six percent of children between the ages of 6 and 12 are overweight;
- Twelve percent of children are reported to have asthma; and
- Rates of chronic disease, poor health status, and premature mortality are generally higher among adult residents of Wards 7 and 8, compared to other wards.

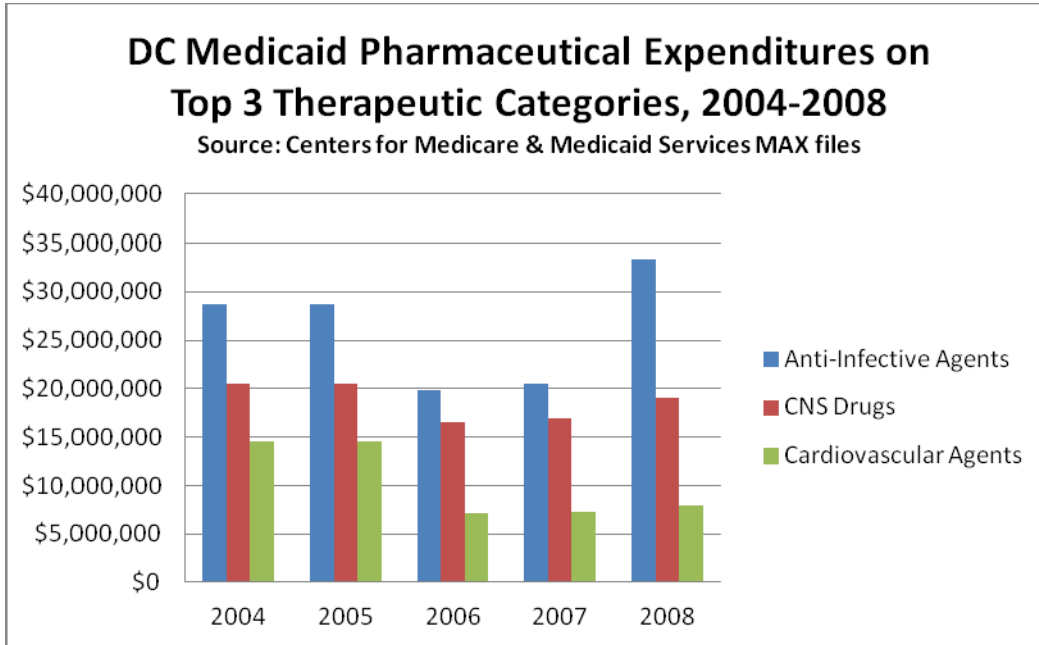
Rates of mortality amenable to healthcare – deaths prior to age 75 “from conditions for which timely and effective medical care can potentially delay or prevent mortality” (Commonwealth Fund, 2009) – are of particular concern. While the District's overall rate fell from 174.2 deaths per 100,000 in 2001-2002 to 158.3 in 2004-2005, the rate for black residents was nearly four times the rate for white residents: 219.9 per 100,000 vs. 56.4 per 100,000 (Commonwealth Fund, 2009).

A 2010 report by the Brookings Institution and the Rockefeller Foundation places these dismaying figures in the broader context of the District's healthcare challenges. In the 1990s, the authors explain, low-income residents had poor access to primary care, and health outcomes were “abysmal.” Since then, the creation of the Alliance, increased investment in community health centers, and increased payment rates for primary-care physicians and specialists, among other improvements, have substantially improved access to care for low-income residents and “accomplished a good measure of cost control.” The report notes, however, that mental health and substance abuse services have been largely left out of the District's Medicaid and Alliance programs, leaving low-income residents with limited access to these types of services. Overall, improving care coordination and addressing the social determinants of health remain challenging, as is also the case nationwide (Meyer et al., 2010).

Medicaid Pharmaceutical Spending in the District of Columbia

In FY 2010, the District spent \$1.82 billion on services to Medicaid beneficiaries, a group that includes 205,000 low-income residents (Department of Health Care Finance, n.d.). Pharmaceuticals represent a significant portion of overall District Medicaid expenditures: \$91.5 million in 2008 (the most recent year for which figures are available) (CMS, 2012). As in previous years, the District's Medicaid program spent the most on anti-infective agents (\$33 million); central nervous system drugs, a category that includes antipsychotics (\$19 million); and cardiovascular agents (\$8 million) in 2008. Among all Medicaid beneficiaries, 16.7% used prescribed anti-infective agents, 15.0% used CNS drugs, and 14.1% used cardiovascular agents in 2008.

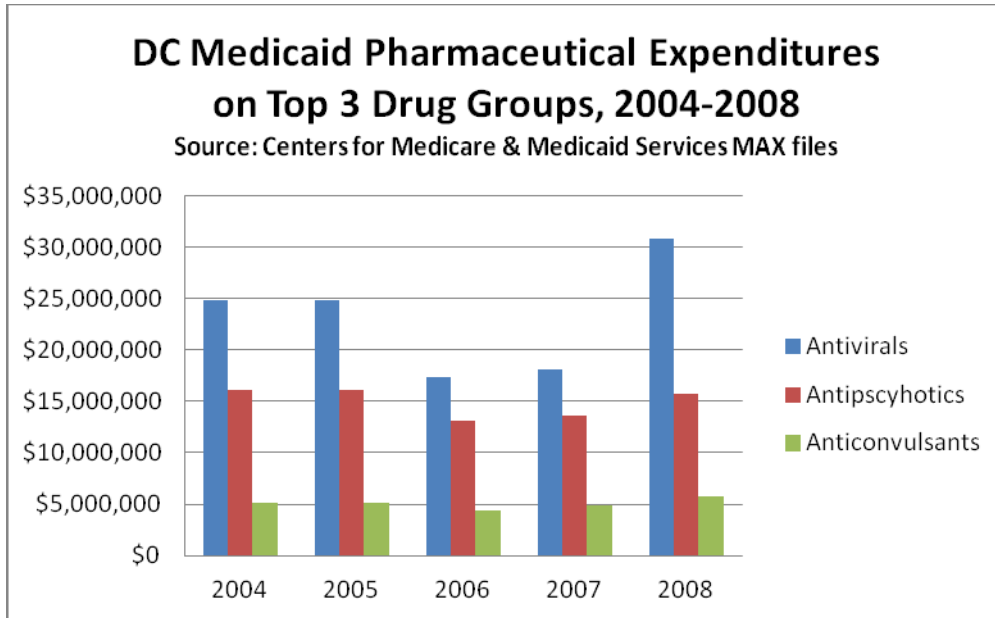
Figure 1



Data from Medicaid Analytic Rx eXtract (MAX Rx) Prescription Drug Tables downloaded from Centers for Medicare and Medicaid Services website, <http://go.cms.gov/QOj4y9>

Similarly, the drug groups accounting for the largest expenditures were antivirals (\$31 million), antipsychotics (\$16 million), and anticonvulsants (\$6 million). In 2008, 7.5% of beneficiaries used antivirals, 9.6% used antipsychotics, and 9.1% used anticonvulsants.

Figure 2



Data from Medicaid Analytic Rx eXtract (MAX Rx) Prescription Drug Tables downloaded from Centers for Medicare and Medicaid Services website, <http://go.cms.gov/QOj4y9>

Given that Medicaid covers a large percentage of District residents, the generosity of its benefits and the extent to which providers are willing to see Medicaid patients have a strong influence on the overall accessibility and quality of healthcare services in the District. High Medicaid prescription drug costs can crowd out spending in other areas of the program, such as payments to providers.

III. Concerns About Pharmaceutical Marketing

There are three main concerns about the effects of pharmaceutical marketing on healthcare: the prescription of drugs that are less effective or less safe than alternatives; inappropriate prescribing; and higher-than-necessary expenditures. The use of drugs that are less effective, less safe, or unnecessary can lead to adverse health outcomes, increased utilization of care, and higher healthcare costs.

Effectiveness and Adverse Events

Pharmaceutical marketing efforts may influence health professionals to prescribe drugs that are not the best choices. Health professionals may have incomplete knowledge of known risks because pharmaceutical marketing efforts fail to adequately disclose adverse effects or drug interactions, and may exaggerate the effectiveness of targeted drugs. (Busy healthcare providers lack time to keep up with the latest medical literature, and academic detailing efforts – discussed in Section VII – can help address this.) Marketing efforts also contribute to excessive enthusiasm for new drugs, leading prescribers to neglect older products that may have a better balance of risks and benefits.

There are many troubling examples of pharmaceutical companies using marketing efforts that downplay, or altogether fail to mention, drug risks. For instance, Merck had data that its anti-inflammatory drug Vioxx increased the risk of heart attacks as much as five-fold, but as US Representative Henry Waxman noted after reviewing over 20,000 pages of internal company documents, Merck used its “highly trained [marketing] force to present a misleading picture to physicians about the drug’s cardiovascular risk” (Waxman, 2005). Merck finally withdrew Vioxx in 2004 – but that was after the drug had been on the market for four years and caused an estimated 88,000 – 139,000 heart attacks (Michaels, 2008).

While the evidence against Vioxx was mounting, concerns were also growing about the role of serotonin-reuptake inhibitor (SSRI) antidepressants in patient suicides, especially among children and adolescents. It turned out that some of the companies manufacturing SSRIs funded multiple clinical trials of their products, yet only reported the favorable results (Avorn, 2006). In 2004, FDA ultimately required manufacturers to add a “black box” warning to the labeling of antidepressants to warn about the increased risk of suicidal thoughts and behaviors in children and adolescents taking the drug and to emphasize the need for close monitoring of patients starting on them (FDA, 2004).

Even when risks of drugs are disclosed appropriately, enthusiasm for new products can cause some prescribers to turn away from tried-and-true drugs that may be preferable for some patients. In a *New York Times* op-ed, psychiatry professor Richard Friedman notes that lithium, while it must be administered carefully to avoid toxicity, has been used successfully to treat bipolar disorder for decades and is “the only psychotropic drug that has ever been shown to have specific antisuicidal effects”; however, drug companies can’t make much money from it, so they are promoting a new generation of mood stabilizers, “some more tolerable than lithium, but none more effective” (Friedman, 2009).

Off-Label Prescribing

Off-label prescribing includes the prescription of drugs for conditions or populations for which they are not specifically approved. The practice is legal and common. Some unapproved uses may be appropriate, and some off-label uses later become labeled uses. Physicians treating children and pregnant women often must prescribe drugs off-label, because drugs are often not studied or tested in these populations.

Some off-label uses are supported by clinical trials, but benefits have not been shown to outweigh risks for most off-label uses. David Radley et al analyzed prescriptions of commonly used medications that accounted for more than half of all estimated prescription drug use in 2001 and assessed whether the prescriptions were for an FDA approved use, for an off-label use that had strong scientific support, or for an off-label use with limited or no scientific support. Radley found that “about 21% of all estimated uses for commonly prescribed medications were off-label, and that 15% of all estimated uses lacked scientific evidence of therapeutic efficacy.” Off-label prescribing was most common among cardiac medications (46%) , anticonvulsants (46%), and anti-asthmatics (42%), and off-label prescriptions with limited or no scientific support were most common among psychiatric drugs (96% limited or no support vs. 4% strong support) and allergy therapies (89% vs. 11%) (Radley, Finkelstein & Stafford, 2006).

Although it is legal to prescribe off-label, it is illegal for pharmaceutical companies to promote their products for off-label uses to physicians or patients. However, the Food and Drug Administration (FDA) can examine only a tiny percentage of the promotional materials submitted to it, and its monitoring activities to identify violations (such as a detailer’s discussion of off-label uses with a doctor) are also limited (GAO, 2008). Since 2009, FDA guidance has allowed pharmaceutical companies to distribute reprints of peer-reviewed articles without requiring that FDA preview the publications beforehand (FDA, 2009). As a result, detailers can give doctors copies of a peer-reviewed article that describes an off-label use but cannot legally discuss an off-label use of a drug with doctors.

The Government Accountability Office found that between 2003 and 2007, FDA issued 42 regulatory letters requesting that companies stop promotions that violated the law on promoting off-label uses; it took an average of seven months between the agency’s drafting of the letters and sending them, and an average of four months for companies cited for more serious violations to take the requested corrective actions. During the same time period, the DOJ settled 11 cases involving off-label promotion (and, in some cases, additional allegations) (GAO, 2008).

Prescription-drug Expenditures

The US has experienced a dramatic increase in prescription-drug expenditures, and concerns have arisen that marketing has driven an inappropriate increase in prescribing. Researchers from the University of British Columbia noted that Canada’s drug spending doubled between 1996 and 2003; an investigation found that 80% of the increase in drug expenditures in British Columbia during the seven-year period

“was explained by the use of new, patented drug products that did not offer substantial improvements on less expensive alternatives available before 1990” (Morgan et al., 2005). In many cases, marketing efforts increase prescriptions for a new drug in cases where an older one will be just as effective, and patients and payers will spend more money than is necessary to achieve the same result.

Drugs still under patent are the ones marketed most heavily. (Aggressive marketing once a patent has expired can also slow the erosion in market share.) (Santerre and Neun, 2006) Some new drugs are truly novel or are substantial improvements over older drugs; in these cases, increased spending on newer drugs is justifiable. However, pharmaceutical companies often make minor changes to a drug or formulation whose patent is expiring in order to obtain a new patent. For example, when facing the expiration of the patent for its blockbuster drug Prilosec (omeprazole), a mixture of isomers (left and right-“handed” molecules), AstraZeneca patented Nexium (esomeprazole), which consisted of only one of the two isomers. (Michaels, 2008) Sometimes the exact same drug is renamed for a new indication, resulting in a new patent. In another example, the blockbuster drug Prozac (fluoxetine), which is exactly the same as Sarafem (fluoxetine), was approved for the new indication of premenstrual dysphoric disorder. A generic was available for Prozac far earlier than for Sarafem, simply because the renamed drug was approved for a different indication.

Within the District, residents with private insurance often face higher co-payments for branded drugs; low-income residents may struggle to afford these co-payments and face a choice between paying for their medications and meeting other important needs. Medicaid recipients do not face this choice, but the District’s Medicaid budget will be strained if prescription-drug costs continue to grow at their current pace. Many states have responded to Medicaid budget problems by cutting benefits and eligibility, which will leave some residents without services they need, and reducing provider payments, which can cause providers to see fewer Medicaid patients and exacerbate existing problems with access to healthcare.

IV. Effects of Marketing

Marketing to Physicians

In the U.S. between 1999 and 2009, pharmaceutical advertising expenses aimed at physicians grew from \$4.8 billion to \$6.6 billion (Kaiser Family Foundation, 2010). With the number of pharmaceutical detailers reaching 90,000 and advertising costs reaching \$7 billion, the pharmaceutical industry spends approximately \$61,000 per U.S. physician per year (Gagnon & Lexchin, 2008). Concerns have arisen that the large amount of pharmaceutical advertising money spent on physicians unduly influences their prescribing habits. Pharmaceutical representatives provide free food to doctors and staff; distribute free drug samples; compensate doctors for their travel and lodging expenses; hire doctors as consultants and speakers; and finance clinical trials, some of which are really pay-for-prescription programs.

Relationships with industry may create a sense of obligation in doctors. As Jennifer Niebyl (2008) puts it, "Gifts create an obligation, a need to reciprocate, which is what creates a conflict of interest. Gifts create a sense of entitlement, unlike advertising, and may erode professional values, unlike advertising." Gifts also affect the relationship between physicians and patients; a recent study found that patients who believe their personal physician receives gifts are more than twice as likely to report low physician trust and high healthcare system distrust (Grande, Shea, & Armstrong, 2012).

A systematic review of 32 studies of medical student interactions with industry found that between 40 and 100% of students interact with industry (Austad, Avorn, & Kesselheim, 2011). Eight studies found a correlation between frequent contact and favorable attitudes toward industry interactions. One study found that students believed that gifts to physicians or medical students were more acceptable than gifts to government officials.

Many physicians recognize the potential for interactions with detailers to create bias, but justify these interactions as being educational. Physicians often think they themselves are "personally invulnerable" but that their colleagues are susceptible to industry influence (Chimonas et al., 2007).

Pharmaceutical-company influence begins in medical school, when attitudes about industry marketing are taking shape. A large majority of medical students report having received gifts from pharmaceutical companies and having attended grand rounds or other events sponsored by pharmaceutical companies. In a survey of ten medical schools around the country, approximately 69% of students believed that receiving food or gifts would not increase the likelihood of them prescribing the drug company's product in the future, but an almost equal amount, 67%, agreed that drug company-sponsored rounds are often biased in favor of the company's products (Sierles et al., 2005). Similarly to physicians, many students felt their colleagues were more likely to be influenced by company-sponsored events compared to themselves.

Research suggests that prescribers may not be as skillful as they believe in absorbing companies' educational content without being unduly influenced by marketing. A systematic review of 57 studies that assessed the exposure to information from pharmaceutical companies and the quality, quantity, and cost of physicians' prescribing found no evidence that such exposure improved prescribing; most studies that found any effect found that exposure to information provided directly by pharmaceutical companies was associated with higher prescribing frequency, higher costs, or lower prescribing quality (Spurling et al., 2011). A survey of physicians in Kentucky found that physician cost of prescribing was correlated with the perceived credibility, availability, and applicability of information from pharmaceutical-company representatives; frequency of use of information from representatives was especially strongly associated with cost (Sierles et al., 2005). One experiment found that acceptance of small promotional items by medical students at a medical school without a policy prohibiting such gifts was associated with a more positive attitude towards marketed products (Grande et al., 2009).

Prescribers receive information not only from pharmaceutical detailers, but from "key opinion leaders" or "thought leaders": influential physicians who are hired by industry to transmit marketing messages to physicians. Pharmaceutical companies recognize the broad influence thought leaders have on many other physicians and "routinely measure the return on our investment, by tracking prescriptions before and after their presentations" (Moynihan, 2008). Key opinion leaders are very important for promoting off-label uses of drugs and mitigating concerns that prescribers have about adverse effects (Fugh-Berman & Melnick, 2008).

Free Samples

Pharmaceutical companies' provision of free drug samples for distribution has also raised concerns. Proponents argue that free samples provide patients with immediate access to medication and assist patients who might otherwise struggle to afford the medications. Opponents argue that free samples mislead patients into believing that more-expensive drugs are better than generic or over-the-counter alternatives. Adherence is better with generic medications than branded medications, because patients are more likely to stick to medications they can afford.

Physicians are affected as well. Almost half of the 506 physicians in a 2011 study believed, erroneously, that generic drugs are low-quality; it is perhaps not a coincidence that the most common source of information about generic drugs was from drug representatives (Shrank et al., 2011). Although almost half of respondents were concerned that free samples could adversely affect subsequent affordability of drugs, two-thirds of respondents provided free samples to their patients. In one study, medical residents at an inner-city primary care clinic were followed for six months; one group had access to drug samples and the other did not. Medical residents with access to drug samples prescribed more heavily promoted drugs than those without access and tended to use inexpensive medications less often (Adair & Holmgren, 2005). A study examining the characteristics of free-sample recipients, published in the *American Journal of Public Health*, concluded, "Poor and uninsured Americans are less likely than wealthy or insured Americans to receive free drug samples" (Cutrona et al., 2008); this suggests that the samples' role is not primarily to assist patients who would have difficulty affording prescription medication.

Research Participation and Results

About one-third of the original manuscripts published in the two largest general medicine journals in the U.S. were funded by private corporations. Pharmaceutical companies, the most common study sponsors, spent approximately \$23 billion on clinical research in 2001 (by contrast, the National Institute of Health spent only \$18 billion) (Friedman & Richter, 2004). A strong association has been found between studies whose authors had conflicts of interest and positive findings in the studies. An even stronger association was found between researchers who did not have any conflicts of interest and reporting negative results (Friedman & Richter, 2004).

A report by the United Kingdom's House of Commons Health Committee notes that five out of six systematic reviews of research have found industry-sponsored research is much more likely to produce positive results, while trials producing negative results are deemed failed trials rather than failed drugs (House of Commons Health Committee, 2005). A recent study found that in industry-funded comparative trials of antidepressants, comparator drugs were often dosed lower than the sponsored drug, unfairly disadvantaging the comparator (Sinyor et al., 2012).

Direct-to-Consumer Advertising

Only the United States and New Zealand allow direct-to-consumer (DTC) advertising. In 1997, the U.S. Food and Drug Administration released broadcasting guidelines that allowed DTC advertising into broadcast and electronic media for the first time, radically altering the playing field for pharmaceutical advertising. Since 1997, pharmaceutical companies have directed growing amounts of advertising resources to DTC promotion: between 1997 and 2003, DTC expenditures increased from \$791 million to \$3.2 billion, an increase of almost 400%. In 2007, DTC advertising increased to nearly \$5 billion (Frosch & Grande, 2010).

The growth in DTC advertising appears to have paid off for pharmaceutical companies. In a single year, between 1998 and 1999, retail spending on prescription drugs grew by \$17.7 billion; 34% of that increase was attributable to the 24 most heavily advertised drugs. In 2000, "doctors wrote 25% more prescriptions for the 50 most heavily DTC advertised drugs compared to 4.3% more scripts for all other drugs combined" (Findlay, 2001). Pharmaceutical advertisements have become pervasive on television; one study found that, on average, "an adult is exposed to 100 minutes of direct-to-consumer advertising for each minute they spend with their doctor each year" (Gellad & Lyles, 2007).

Direct-to-consumer promotion (including a growing presence in social media) has affected the relationships between physicians and their patients. Surveys suggest that some physicians believe that DTC advertising tends to confuse patients and create a perception that there "is a pill for every ill." Many of those surveyed felt DTC should be discontinued. Physicians have also expressed concerns over being pressured to prescribe medications patients request after seeing them on television; they fear that if they refuse, patients may transfer to a different provider. Based on a study comparing

prescription habits of doctors in Sacramento, California and Canada, researchers found patients from the U.S. who had been exposed to DTC were more likely to request or ask about a medication they saw on TV, and were also more likely to receive a prescription for the medication (Mintzes et al., 2003).

Nine studies have found that DTCA increases patient demand and prescribing volume and shifts prescribing patterns (Mintzes, 2012). The large increase in allergy-related visits to physicians and prescriptions is one striking example of how DTCA influences patients. The rate of allergy-related visits to healthcare providers remained steady throughout the 1990s. After the 1997 FDA decision allowing DTC advertising, the amount jumped from about 13-14 million a year to 18 million in 1999. In 1998 and 1999, allergy medications were among the top 50 most heavily marketed drugs. In 1999, the oral antihistamine Loratidine, otherwise known as Claritin, ranked number one as the most heavily marketed drug, with Schering-Plough, the drug's producer, spending \$137.1 million in DTC advertising (Ornstein & Weber, 2012). In fact, only 12 medications accounted for nearly half of all advertising spending, while the top 50 marketed drugs accounted for 95% of the spending (Gellad & Lyles, 2007).

Funding of Organizations Producing Continuing Medical Education and Patient Information

Patient organizations are often funded by industry. In May 2012, the U.S. Senate Finance Committee launched an investigation of the American Pain Foundation after the self-described "nation's largest organization for pain patients" was found to have close ties to drug manufacturers. The nonprofit news organization ProPublica revealed that the Foundation received 90% of its \$5 million in 2010 funding from the pharmaceutical and medical device industries. Published guides for patients, journalists, and policymakers produced by the Foundation were found to have exaggerated the benefits of opioid painkillers and downplayed the risks. Committee members sent letters to the Foundation citing the "growing evidence" suggesting that drug companies' misleading information "may be responsible, at least in part, [for] an epidemic of accidental deaths and addiction resulting from the increased sale and use of powerful narcotic painkillers." The Foundation announced its dissolution in May 2012 "due to irreparable economic circumstances" (Ornstein & Weber, 2012).

Industry funding of professional medical association activities is pervasive. Pharmaceutical and medical device companies subsidize annual meetings by underwriting physician attendance; subsidizing selected speaker travel and honoraria; purchasing booths and advertising; and supporting conference-related publications. Some authors call for professional medical organizations to adopt uniform guidelines on conflict of interest, including a requirement that presidents and officers of these organizations be conflict-free during their tenure (Rothman et al., 2009).

In 2006, 30% of the American Psychiatric Association's (APA) \$62.5 million in financing came from the drug industry. In 2009, the organization announced that it would phase out industry-supported symposia and industry-supplied meals at its annual meetings (American Psychiatric Association, 2009). Many other professional organizations receive large sums from the pharmaceutical industry.

Industry funding of continuing medical education (CME) is of particular concern, because prescribers are generally required to complete CME regularly in order to maintain their licenses (AAMC, 2008). Commercial support of CME peaked in 2007 at \$2.54 billion. It has declined since then; in 2009 it was \$2.18 billion. About 40% of CME income comes from commercial sources (Steinbrook, 2011).

Pharmaceutical-industry funding of professional medical organizations is also of concern because these organizations issue practice guidelines that set standards for patient care. The group of JAMA authors who proposed ways to control conflicts of interest between medical associations and pharmaceutical companies recommends that professional medical associations (PMAs) should not “accept funding from industry to develop practice guidelines or outcome measures” and should exclude persons receiving “direct salary support, research support, or additional income from a company whose product sales could be affected by the guidelines” from committees (Rothman et al., 2009).

The relationship between drug companies and disease-specific patient organizations is also of concern. A survey of patient organization websites that assessed indicators of transparency, advertising, and disclosure of pharmaceutical sponsorships found that only about half of the websites provided links to financial reports, and disclosures of funding varied dramatically. In addition, a third of the websites featured company logos or links to drug company websites. From their survey of these patient organization websites, researchers concluded that patients were not provided with adequate information to assess possible conflicts of interest that may exist between organizations and drug companies (Ball et al., 2006).

Some patient organizations’ websites fail to mention safety concerns of medications mentioned on their websites. For example, the American Diabetic Association failed to note concerns about the experimental diabetes drug muraglitazar, which has been linked to possible increased risk of fatal heart problems, and the National Osteoporosis Foundation neglected to describe concerns about the long-term effects of osteoporosis drug Fosamax (alendronate). Neither organization disclosed its financial ties with the manufacturers of these medications (Ready, 2006). Because many patients rely on disease-specific organizations for information about treatments, this lack of disclosure is troubling.

V. Use of Antipsychotics in Children

While the use of antipsychotics has risen in the population overall (Domino & Swartz, 2008), the increased use of these drugs among children is of particular concern. These medications are often prescribed off-label, and evidence is accumulating that their side effects in children are particularly worrisome.

Antipsychotics are used to treat psychiatric disorders, including schizophrenia and bipolar disorder, as well as other conditions for which they may or may not be specifically approved. An initial wave of antipsychotics was developed in the 1950s, and a second wave began in the 1980s; these are often referred to as first-generation (or typical) and second-generation (or atypical) antipsychotics, respectively. The newer antipsychotics are associated with a higher risk of weight gain and development of type 2 diabetes, along with other metabolic effects.

Increased Prescribing Despite Limited Approved Indications

Between 1993 and 2006, the Food and Drug Administration (FDA) approved six new antipsychotics for use in adults (Crystal et al., 2009); from 2006 through 2009, it approved four of these drugs for limited indications in certain under-18 age groups (see table below). Yet prescribers were quick to prescribe them off-label to children before this approval occurred, and prescriptions are still given to many children whose diagnoses are not among the approved indications.

Table 1

FDA Approvals of Second-Generation Antipsychotics for Limited Indications in Children				
Drug	Child Population Age Range	Indication	Year Approved for Indication in Children	Efficacy Evidence for Approval (for use in children)
Aripiprazole (trade name: Abilify)	13-17	“Treatment of Schizophrenia”	2007 (Initial US approval: 2002)	“Efficacy was established in one 6-week trial in patients with schizophrenia”
	10-17	“Acute treatment of manic or mixed episodes associated with bipolar I disorder as monotherapy and as an adjunct to lithium or valproate”	2008	“Efficacy was established in one 4-week monotherapy trial in patients with manic or mixed episodes”
	6-17	“Treatment of irritability associated with autistic disorder”	2009	“Efficacy was established in two 8-week trials in patients with autistic disorder”
Olanzapine (trade name: Zyprexa)	13-17	“Treatment of schizophrenia”	2009 (Initial US approval: 1996)	“Efficacy was established in one 6-week trial in patients with schizophrenia”
	13-17	“Acute treatment of manic or mixed episodes associated with bipolar I disorder and maintenance treatment of bipolar I disorder”	2009	“Efficacy was established in one 3-week trial in patients with manic or mixed episodes associated with bipolar I disorder”
Quetiapine (trade name: Seroquel)	13-17	“Treatment of schizophrenia”	2009 (Initial US approval: 1997)	“Efficacy was established in one 6-week trial in patients with schizophrenia”
	10-17	“Acute treatment of manic episodes associated with bipolar I disorder, both as monotherapy and as an adjunct to lithium or divalproex”	2009	“Efficacy was established in one 3-week monotherapy trial in patients with manic episodes associated with bipolar I disorder”

Risperidone (trade name: Risperdal)	13-17	“Treatment of Schizophrenia”	2007 (Initial US approval: 1993)	“The efficacy... in adolescents aged 13–17 years was demonstrated in two short-term (6 and 8 weeks), double-blind controlled trials.”
	10-17	“Alone, or in combination with lithium or valproate, for the short-term treatment of acute mania or mixed episodes associated with Bipolar I Disorder in adults, and alone in children and adolescents aged 10-17 years”	2007	“The efficacy... in children or adolescents with Bipolar I disorder was demonstrated in a 3-week, randomized, double-blind, placebo-controlled, multicenter trial including patients ranging in ages from 10 to 17 years who were experiencing a manic or mixed episode of bipolar I disorder.”
	5-16	“Treatment of irritability associated with autistic disorder”	2006	“The efficacy... in the treatment of irritability associated with autistic disorder was established in two 8-week, placebo-controlled trials in children and adolescents (aged 5 to 16 years) who met the DSM-IV criteria for autistic disorder.”

Source: Drug labels from FDA.gov (listed individually in References)

Some physicians caution that even FDA approval may not be sufficient evidence of an antipsychotic’s safety and efficacy in children, especially when the drugs are likely to be taken over long periods of time. For instance, the efficacy of olanzapine (Zyprexa) in adolescents with bipolar disorder was established in “one 3-week trial in patients with manic or mixed episodes associated with bipolar I disorder” (FDA, 2011a), and the efficacy of aripiprazole (Abilify) in adolescents with schizophrenia in one six-week trial in adolescents (FDA, 2012). There is also a need for research into the long-term impact of these drugs on the developing brains of children.

An analysis of Medical Expenditures Panel Survey (MEPS) data on non-institutionalized individuals found that the proportion of antipsychotic users who were under age 18 doubled from 1996-1997 to 2004-2005, from 7% to 15% of all users (Domino & Swartz, 2008). (In 2005, one-third of the US population was under age 18.) (Census Bureau, 2005) Analysis of data from the National Ambulatory Medical Care Survey (NAMCS), which collects information from office-based physician practices, found that the

annual number of US office visits by those under age 21 that included prescription of an antipsychotic medication increased from 274.7 per 100,000 under-21 population in 1993-1995 to 1,438.4 per 100,000 under-21 population in 2002 (Olfson et al., 2006) – a more than five-fold jump in less than a decade. The percentage of children treated with antipsychotics has increased in both privately and publicly insured populations (Domino & Swartz, 2008; Olfson et al., 2006).

Solchany (2011) cites studies finding high rates of psychotropic medication use among foster children in several states and notes that "children in foster care are vulnerable to inappropriate or excessive medication use." While the need for psychotropic drugs may be greater among foster children, prescribing must be done carefully. The Government Accountability Office (GAO) analyzed prescription data for foster children in five states and found that thousands of these children were receiving psychotropic drugs that do not conform to best principles guidelines from the American Academy of Child and Adolescent Psychiatry for oversight of children in state custody. In its analysis of 2008 Medicaid data from Florida, Massachusetts, Michigan, Oregon, and Texas, GAO found hundreds of children receiving five or more psychotropic medications simultaneously, thousands of children prescribed doses higher than Texas guidelines based on FDA-approved labels, and prescriptions of psychotropic drugs for children under one year old (GAO, 2011). While these indicators of potential health risks were found among both foster and non-foster children, they occurred in higher percentages of foster children in all five states.

This observed use of multiple psychotropic drugs by the same patient concomitantly, also called polypharmacy, is a high-risk practice not supported by evidence in either adults or children, and "only limited evidence supports the use of even two drugs concomitantly in children" (GAO, 2011). The likelihood of adverse events increases with each additional drug, and multiple drugs may interact in harmful ways.

Adverse events

Adverse events associated with antipsychotic use in children range from sedation and weight gain to hospitalization and death. A USA Today analysis of data collected in the FDA's Adverse Events Reporting System database between 2000 and 2004 found "45 pediatric deaths in which atypicals were the primary suspect" (Elias, 2006).

One of the most widely reported side effects from second-generation antipsychotics is excessive weight gain (Alexander et al., 2011; Correll et al 2009; McKinney & Renk, 2011; Patel et al., 2002; Zito et al., 2007), which can increase patients' risk of developing diabetes. Children and adolescents may be at a higher risk of antipsychotic-associated weight gain, as well as sedation and movement disorders, when compared to adults (McKinney & Renk, 2011). Preschoolers have been found to be more sensitive to adverse events than adolescents. Nonetheless, the use of antipsychotics in children ages 2-4 has been increasing (Zito et al., 2007), even though the FDA has not approved the use any of the newer antipsychotics for children under the age of five. Crystal also warns that children enrolled in Medicaid may be at elevated risk for metabolic side effects because "the risk of childhood obesity is inversely related to

socioeconomic status, and low-income children who are already at high risk for obesity and related metabolic disorders may be especially vulnerable to the adverse effects of weight gain” (Crystal et al., 2009).

Among 257 children taking second-generation antipsychotics for the first time, weight increased during the first 12 weeks of treatment. Among subjects taking olanzapine (Zyprexa), the mean weight gain was 8.5 kg, or 18.7 pounds; for those taking quetiapine (Seroquel), it was 6.1 kg, or 13.4 pounds; for risperidone (Risperdal), 5.3 kg, or 11.7 pounds; for aripiprazole (Abilify), 4.4 kg, or 9.7 pounds (Correll et al., 2009). The study also found olanzapine to significantly worsen glucose and lipid parameters, and quetiapine and risperidone to significantly increase triglycerides (Correll et al., 2009).

Somnolence, fatigue, and lethargy are also common side effects of newer antipsychotics.

In a review of studies on the use of second-generation antipsychotics in children diagnosed with disruptive behavior (DB), a condition for which the use of these antipsychotics has increased dramatically, McKinney and Renk (2011) note that sleepier and more lethargic children are less likely to have energy for disruptive behaviors. They suggest the drugs may “reduce DB through sedation rather than by targeting the actual causes of this behavior” (McKinney & Renk, 2011).

Indeed, much of the increase in antipsychotic prescriptions is due to off-label prescribing for conditions other than schizophrenia, bipolar disorder, or autism. A study of patients ages 2-18 in Tennessee's Medicaid managed-care program who received new prescriptions for antipsychotics found that fewer than 9% of the new users had been diagnosed with schizophrenia or psychosis in the previous 90 days; 23% of the new users had been diagnosed with ADHD and 20% with conduct disorder (Cooper et al., 2004). One analysis of data on Medicaid enrollees under age 18 who were prescribed second-generation antipsychotics between 2001 and 2005 found that among new users, 41% had “no diagnosis for which such treatment was supported” by a study published by the end of the study period in 2005 (Pathak et al., 2010). While the benefits of treating childhood schizophrenia or psychosis may outweigh risks, the risk-benefit ratio may be unfavorable for the many disorders for which prescribers are writing off-label prescriptions.

Evidence regarding antipsychotics in children in the medical literature is limited (Seida et al., 2012). Overall, there is a dearth of research into the long-term effects of antipsychotic use in children, but enough reports of problematic side effects to urge that prescribers carefully consider whether these medications are necessary for their young patients.

Federal responses to antipsychotic marketing and potential inappropriate prescribing

Several lawsuits have charged pharmaceutical companies with illegally marketing antipsychotics for use in children when the drugs were not approved for pediatric populations. In 2010, the New York Times reported that every major seller of antipsychotic drugs was either under investigation or had settled lawsuits by the federal government regarding possible fraud:

- AstraZeneca: The government sued AstraZeneca for illegally promoting antipsychotics for children (as well as the elderly, veterans, and prisoners); the company settled for \$520 million, but denied misconduct. (Wilson, 2010b) Company emails unearthed during lawsuits described how an unfavorable 1997 study showing Seroquel users gained 11 pounds per year was "buried." (Wilson, 2010b) More than 25,000 civil lawsuits had also been filed on behalf of patients claiming the company failed to disclose Seroquel's risks. (Wilson, 2010a).
- Bristol-Myers Squibb: The company settled federal and state investigations into marketing Abilify to child psychiatrists and nursing homes; it paid \$515 million but denied misconduct (Wilson, 2010b).
- Eli Lilly: According to the Justice Department, evidence showed Zyprexa could cause diabetes, but Eli Lilly produced a video called "The Myth of Diabetes" to promote the drug. The company paid a \$515 million fine as part of a larger \$1.4 billion settlement with the government (Wilson, 2010b).
- Johnson & Johnson: In 2010, the Justice Department was investigating allegations that the company paid kickbacks to nursing home pharmacy Omnicare to recommend Risperdal. (Wilson, 2010b). More recently, a judge in Arkansas – one of 11 states in which the company faces lawsuits over Risperdal – imposed more than \$1.2 billion in penalties on Johnson & Johnson and its subsidiary Janssen Pharmaceuticals for falsely claiming Risperdal was safer and more effective than cheaper alternatives and for failing to adequately warn about diabetes and other possible side effects (O'Toole, 2012).
- Pfizer: The government settled with Pfizer for \$301 million (part of a \$2.3 billion settlement covering multiple drugs) over charges that the company paid more than 250 child psychiatrists to promote Geodon when it was approved only for adults. The company did not admit wrongdoing (Wilson, 2010b).

To address the extensive prescribing of psychotropic drugs to children in foster care, the Child and Family Services Improvement and Innovation Act (passed by Congress and signed by President Obama in September 2011) now requires that states' five-year strategic plans describe how the use of psychotropic medication for foster children is monitored.

State responses to potential inappropriate prescribing

California and Florida have seen rates of pediatric antipsychotic prescriptions drop after state Medicaid agencies tightened requirements for their use in children. In 2006, California put in place a prior-authorization plan for the use of psychiatric medicines in children; prescriptions of these drugs for children under age six then fell from 5,686 to 4,200. Florida started a program in 2008 under which state-hired psychiatric consultants review prescriptions for children under age six before Medicaid will cover them; the number of atypical antipsychotic prescriptions written for this group had fallen from

3,167 to 1,137 by 2009 (Armstrong, 2009). Starting in August 2012, Minnesota will require that Medicaid pediatricians and primary-care providers prescribing second-generation antipsychotics to children under age six (Minnesota Department of Human Services, 2012a) use a "collaborative psychiatric consultation" service for advice on these prescription decisions (Minnesota Department of Human Services, 2012b; Olson, 2012). The consultation service, which the state pays the Mayo Clinic to provide, will also be available to other providers on a voluntary basis.

Arkansas is also addressing the issues of informed consent and metabolic impacts for antipsychotic prescribing. In November 2011, Arkansas began requiring that providers writing oral antipsychotic prescriptions for Medicaid beneficiaries under 18 submit an informed consent form signed by the patient's parent or guardian and baseline metabolic lab test data. As of June 2012, continuing antipsychotic prescriptions for Medicaid beneficiaries under 18 requires follow-up lab monitoring at least every nine months (Arkansas Department of Human Services, 2011).

Texas also has policies addressing prescribing of psychotropic medications for youth in foster care. An advisory committee of mental health professionals assembled by the Texas Department of Family and Protective Services (DFPS) and the University of Texas at Austin College of Pharmacy developed psychotropic drug use parameters for foster children that helped identify cases requiring additional review, including "dosages exceeding usual recommended levels, prescriptions for children of very young age, concomitant use of five or more psychotropic drugs, and prescriptions by a primary care provider lacking specialized training" (GAO, 2011). The results were encouraging:

... after Texas released these guidelines in 2005, psychotropic drug use among Texas foster care children declined from almost 30 percent in fiscal year 2004 to less than 21 percent in fiscal year 2010. Texas also analyzes Medicaid claims data to monitor psychotropic drug prescriptions for foster children and to identify any unusual prescribing behaviors. Texas provides quarterly reports to child welfare officials on the use of psychotropic drugs among foster children and treating clinicians have access to a child's medical records on a 24-hour basis (GAO, 2011).

Several states have education programs and voluntary consultation efforts on antipsychotic prescribing to children; these are described in a report produced by a 16-state collaboration, the Medical Directors Learning Network, and the Rutgers Center for Education and Research on Mental Health Therapeutics (Medicaid Medical Directors Learning Network, 2010). Some state Medicaid agencies provide prescribers with information on their patients' psychiatric medication utilization, and may contact those whose prescribing patterns are outside established parameters. In the District, Medicaid reimbursement for the injectable forms of the antipsychotic Risperdal and schizophrenia drug Invega Sustenna require prior authorization, but the requirement is not specific to children and does not extend to oral forms of these drugs or to other antipsychotics (ACS Solutions Center, 2012). The Medicaid pharmacy benefit program in the District does have a Prospective Drug Utilization Review component.

Some states have taken steps to limit or ban provider gifts that have the potential to influence prescribing. Vermont's 2009 law prohibits gifts, including food, from pharmaceutical manufacturers to

healthcare providers; honoraria and expenses given to healthcare professionals must be for significant education, medical, scientific, or policymaking seminars and include a contract for medical (not marketing) deliverables, and the healthcare professional must determine the content of his or her presentation (Vermont Statute, 2009).

Toward more appropriate prescribing

Medication is only one of a range of therapies, including cognitive behavioral therapy and child-parent psychotherapy, that can help manage mental health disturbances in children (Solchany, 2011). The American Academy of Child & Adolescent Psychiatry (AACAP) in 2009 published a description of best practice principles for the use of psychotropic medication in children and adolescents (AACAP, 2009); they include: "completing a psychiatric and medical evaluation, developing a treatment and monitoring plan, educating the patient and family regarding the child's disorder and the treatment and monitoring plan, completing and documenting assent of the child and consent of the parent, conducting an adequate medication treatment trial, managing the patient who does not respond as expected, establishing procedures to implement before using medication combinations, and following principles for the discontinuation of medication." AACAP has also developed best principles and guidelines for state oversight of psychotropic medication use in children in foster care and other forms of state custody (AACAP, n.d.).

VI. Marketing and Use of Antipsychotics in the District

In 2010, 132 pharmaceutical companies reported spending a total of \$85.4 million on marketing activities in the District of Columbia, including \$57.6 million on employee and contractor expenses (“Aggregate Expenses”), \$21.0 million on grants, speaking fees, food, and promotional items (“Gift Expenses”), and \$6.8 million on direct advertising costs (“Advertising Expenses”). This total represented a continuation of the trend of decreasing annual expenditures reported since 2007. Of particular relevance to this report, gift expenses have declined continuously from their high of \$34.4 million in 2006 to \$21.0 million in 2010, a decrease of 39%.

While overall gift spending steadily decreased from 2006-2010, gift expenses in 2010 represented the largest share of total marketing expenditures of any year over that period. Individuals received 43.4% of the total gift amount given by all companies, with physicians receiving 92.5% of this total. Three-quarters of all gifts (75.7%) were given to physicians, who also received 39.4% of the total amount spent on gifts.

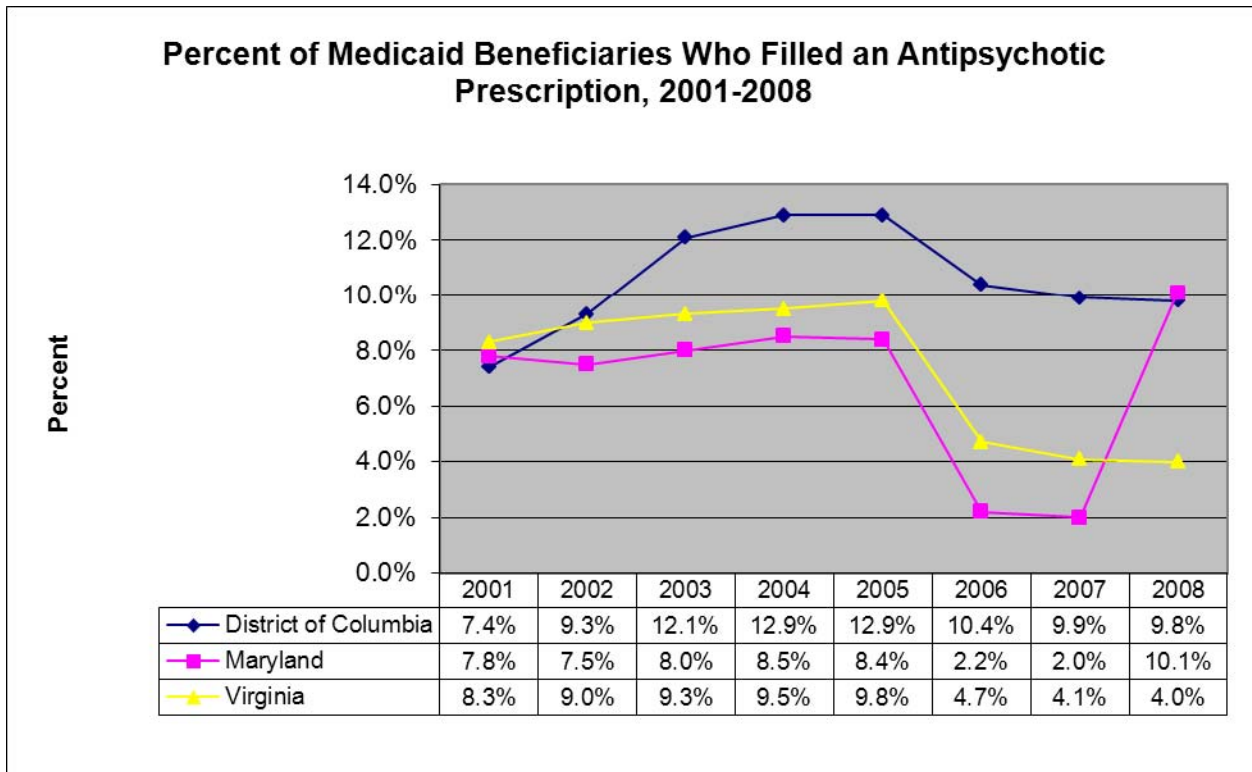
Food represented the most common gift type, at 77.6%, but direct payments in the form of cash or check represented the largest value of any gift type, at 38.9%. The “primary purpose” of gifts has been categorized most often education, at 41.3%. One-third (32.6%) of total gift amounts was spent on education, the most spent in any category.

Because the increased use of antipsychotics among both children and adults is of great concern, we analyzed the use of antipsychotics and gifts to physicians by antipsychotic manufacturers.

Examining Antipsychotic Use among District Medicaid Recipients

When assessing the appropriate use of antipsychotic medication, it is important to consider the rates at which these drugs are being prescribed, as well as the underlying prevalence of the conditions for which they are officially approved. In 2008, the most recent year for which data are available, 9.8% of District of Columbia Medicaid recipients filled a prescription for an antipsychotic medication. For comparison, we examined rates of antipsychotic prescriptions among Medicaid recipients in the neighboring states of Maryland and Virginia. In 2008, 10.1% of Maryland Medicaid recipients filled antipsychotic prescriptions, compared to 4.0% of Virginia Medicaid recipients. We note that Maryland’s 2008 rate of 10.1% of beneficiaries represents a remarkable increase from 2007 and 2006, when only 2% of beneficiaries in that state received antipsychotics. (Percentages for all three jurisdictions from 2001 – 2008 are in Figure 3.) In 2008, the average percentage of Medicaid beneficiaries receiving antipsychotics for all states was 5.4% (see appendix); the percentage in the District of Columbia was nearly twice as high.

Figure 3



Data from Medicaid Analytic Rx eXtract (MAX Rx) Prescription Drug Tables downloaded from Centers for Medicare and Medicaid Services website, <http://go.cms.gov/QOj4y9>

The use of antipsychotic medication among DC Medicaid beneficiaries is dramatically higher than national-level estimates for the entire population. Domino and Swartz (2008) estimated that 1.17% of the US population filled a prescription for antipsychotics in 2005, the latest year for which data were available at the time of their study. Thus, the rate of antipsychotic prescriptions among DC Medicaid recipients represents a rate nearly ten times higher than the national average. Clearly, atypical antipsychotics are prescribed much more commonly to Medicaid recipients in the District than they are to the US population as a whole. While it is likely that the Medicaid population has higher rates of mental disorders than the whole population, it is worth questioning whether 9.8% of beneficiaries should be taking these drugs, whose benefits come with a risk of serious adverse events.

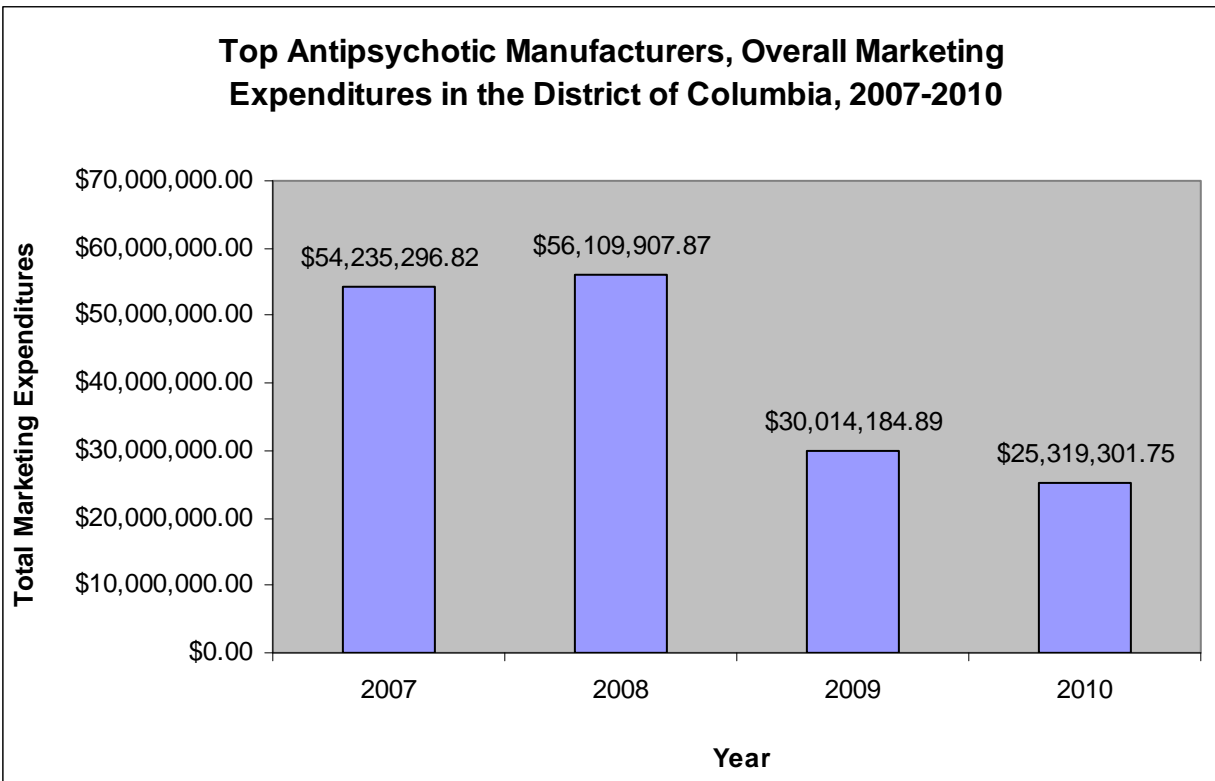
When examining the underlying prevalence of the disorders for which atypical antipsychotics are approved, the utilization rate among Medicaid patients in the District is even more remarkable. The National Institute of Mental Health estimates the 12-month prevalence of schizophrenia in the United States at 1.1% (NIMH, 2012). The estimated prevalence of other disorders for which antipsychotics may be indicated range from less than 1% to 3% (NIMH, 2012). The low prevalence of the conditions for which antipsychotics are officially indicated suggests that the majority of the Medicaid beneficiaries

receiving antipsychotics are receiving them for off-label indications. Put simply, it is likely that much of the antipsychotic prescribing to DC Medicaid beneficiaries may be inappropriate.

Marketing Expenditures of Antipsychotic Manufacturers in the District

To investigate possible effects of marketing on antipsychotic prescribing in the District of Columbia, we examined marketing expenditures reported by the manufacturers of the six most commonly prescribed atypical antipsychotics. The summed total marketing expenditures of these companies from 2007 to 2010 are found in Figure 4 below.

Figure 4



NOTE: The marketing expenditures reported are for the companies as a whole; as such, total marketing expenditures include expenses for the marketing of each company’s entire product catalog, not just antipsychotic medications. Due to the method by which marketing data are reported by companies, it is not possible to isolate specific products being marketed from the overall marketing expenditures.

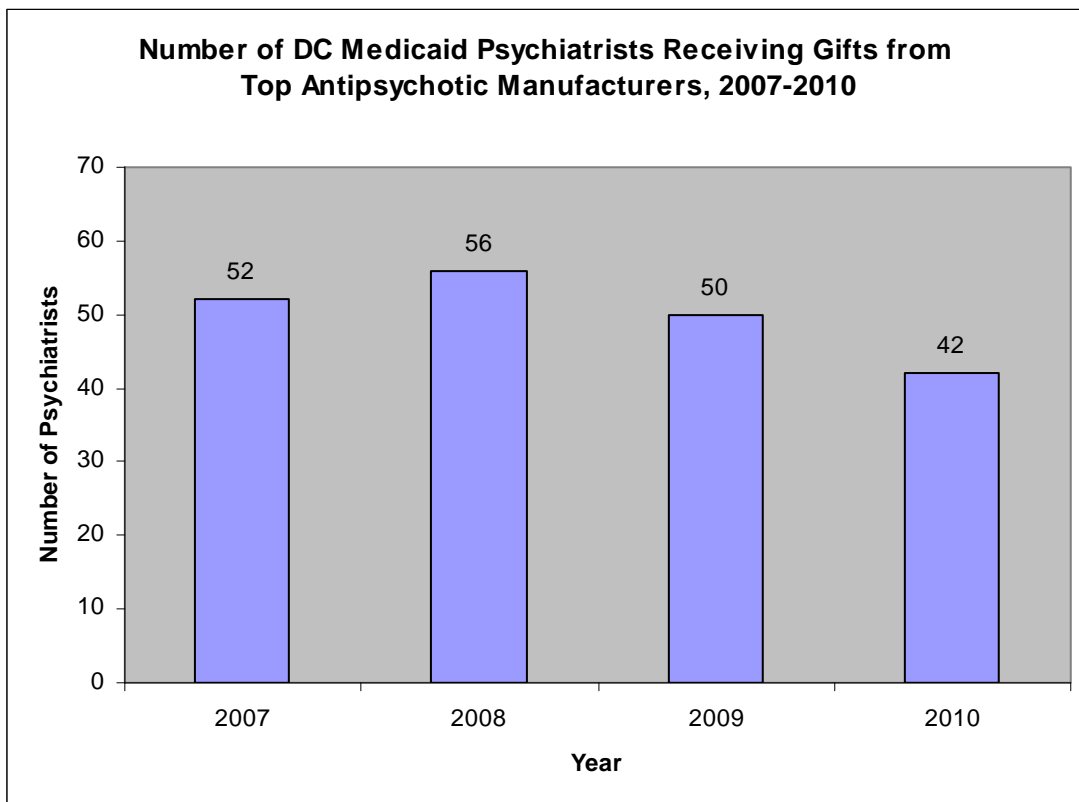
The manufacturers of the most commonly prescribed atypical antipsychotics reported spending \$25.3 million on marketing in the District of Columbia in 2010. This amount represents a large decrease from reported expenditures in the three prior years.

Pharmaceutical Marketing to Psychiatrists in the District

To assess efforts of targeted marketing toward psychiatrists in the District of Columbia, we used several different approaches. First, we examined all physicians who received at least \$1,000 in 2010 from the top antipsychotic manufacturers. We then determined the specialty of each physician using a web search and calculated the number of psychiatrists in this group. In total, 172 physicians received at least \$1,000 from these companies in 2010; 26 of them were psychiatrists who received at least \$1,000 in gifts from the top antipsychotic manufacturers. The total value of gifts received by these 26 psychiatrists totaled \$494,198, or 25.9% of the \$1,910,819 received by all physicians who received at least \$1,000 individually. To put this number in perspective, psychiatrists compose approximately 5% of the total physician population in the United States but received more than one quarter of the total gift value given in the District by manufacturers of the six most commonly prescribed antipsychotics.

To assess possible effects of antipsychotic marketing on District of Columbia Medicaid spending, we gathered the names of psychiatrists listed on the District Medicaid agency's website as accepting Medicaid (119 total). Next, we searched the 2007-2010 databases of pharmaceutical marketing expenditures for the names of these 119 psychiatrists. The number of these psychiatrists appearing in each year's pharmaceutical marketing database is reported in Figure 5.

Figure 5



As shown in Figure 5, there is a slight downward trend in the number of Medicaid psychiatrists receiving gift payments from the manufacturers of the most commonly prescribed atypical antipsychotics. It is important to note here that the sample used in this analysis was limited to psychiatrists accepting Medicaid in 2012. We were unable to access lists of Medicaid psychiatrists from prior years. This limitation may be a reason for optimism: while 56 psychiatrists who accept Medicaid in 2012 received gifts in 2008, only 42 of the same sample accepted gifts in 2010.

We also examined the total number of gifts given per year, as well as the total amounts given, to Medicaid psychiatrists by these companies. Results of those analyses are reported in Figures 6 and 7.

Figure 6

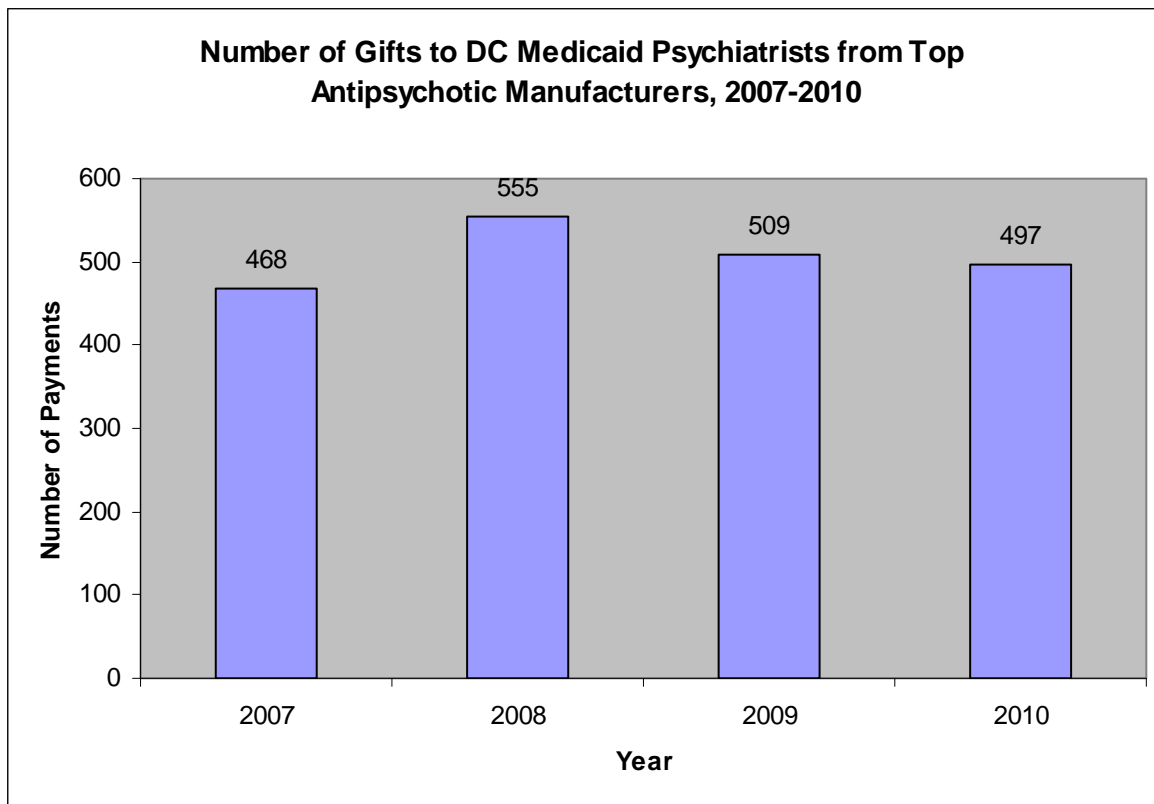
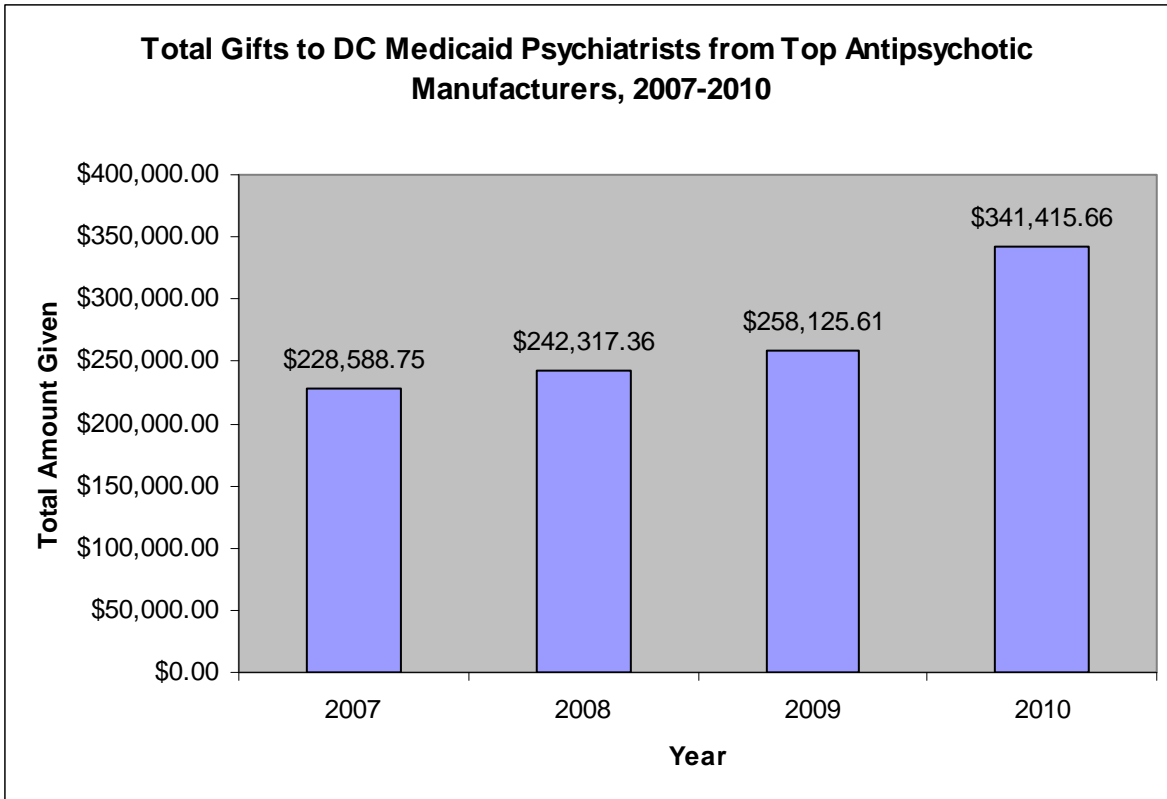


Figure 7



These findings indicate that, while the number of Medicaid psychiatrists receiving gifts and the overall number of gifts given to those psychiatrists has decreased from 2007 to 2010, the total value of those gifts has increased. Examining the same data in terms of averages is illustrative.

Figure 8

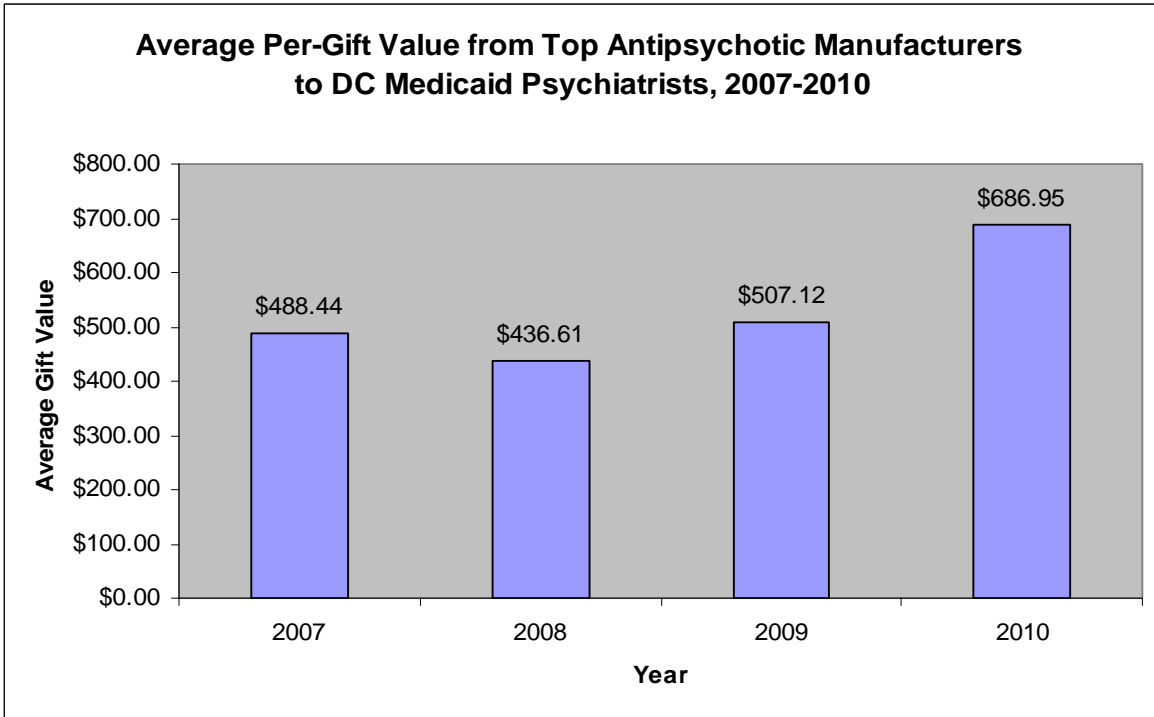
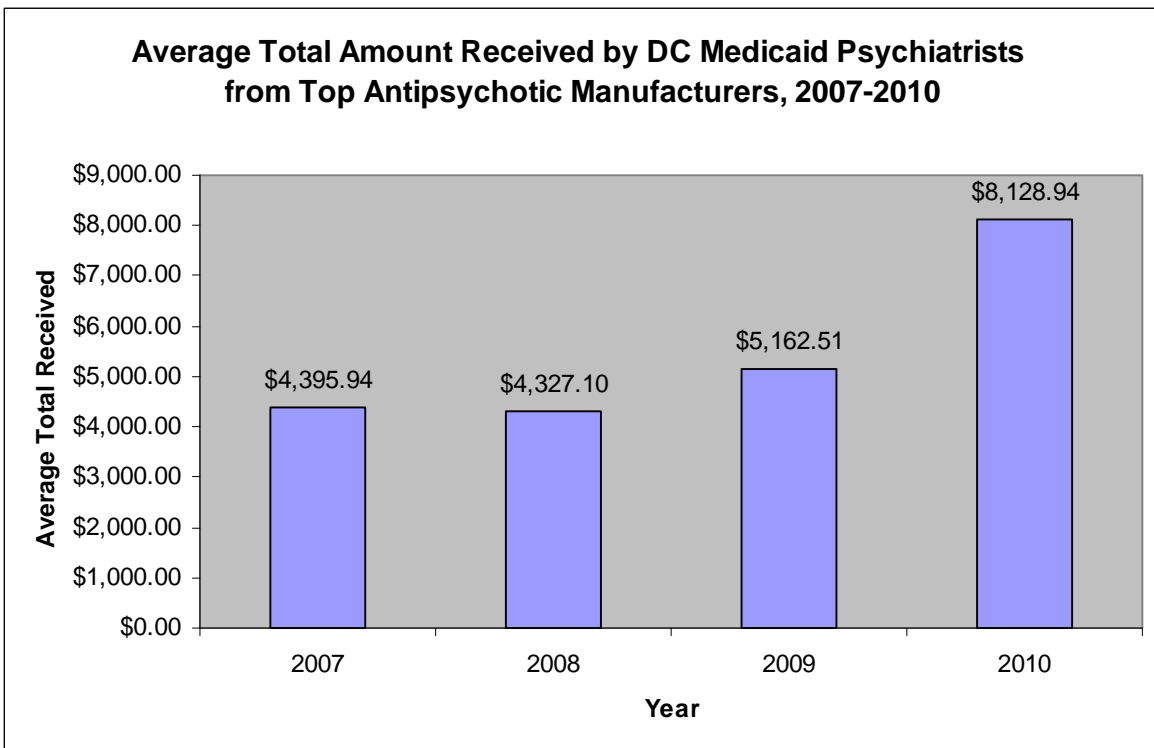


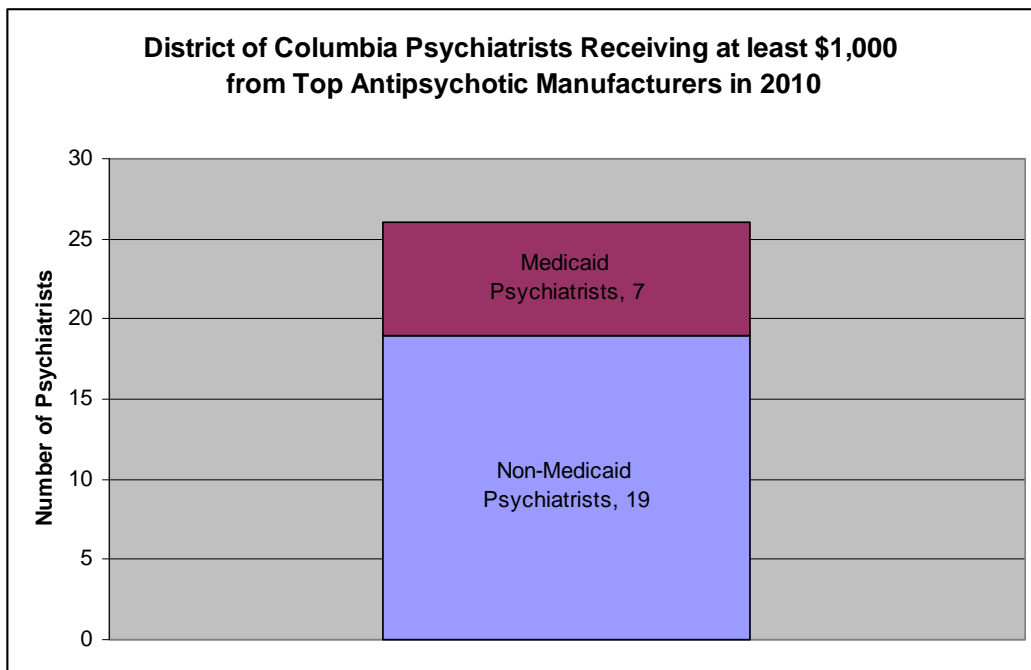
Figure 9



Between 2007 and 2010, the value of the average individual gift received by Medicaid psychiatrists from top antipsychotic manufacturers has increased by 41%, while the average total amount received by Medicaid psychiatrists has increased by 85%. This suggests that, while fewer Medicaid psychiatrists are receiving gifts than in prior years, the psychiatrists who continue to receive gifts are receiving more-expensive gifts. In addition to the increase in per-gift value, the total value of gifts received by each psychiatrist has increased. The Medicaid psychiatrists who accepted gifts in 2010 received a greater number of higher-value gifts than in previous years.

To further examine the targeted marketing toward Medicaid psychiatrists, we again limited our focus to psychiatrists who received at least \$1,000. Within this group, we compared psychiatrists who accept Medicaid in 2012 with those who do not. The results are summarized in Figures 10-12.

Figure 10



Of 26 psychiatrists receiving at least \$1,000 in gifts from the top antipsychotic manufacturers, seven accept Medicaid while nineteen do not.

Figure 11

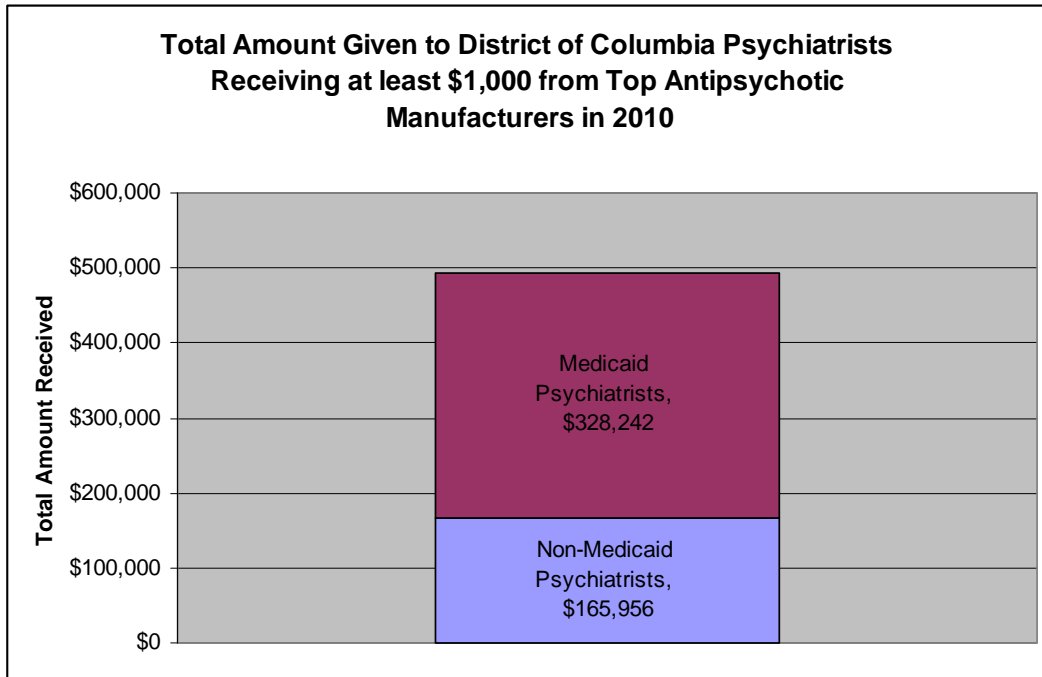


Figure 11 indicates the total amounts received by Medicaid and non-Medicaid psychiatrists in 2010. While psychiatrists accepting Medicaid compose only 27% of the psychiatrists receiving at least \$1,000, their total gift amounts compose 66% of the total amount received by this sample.

Figure 12

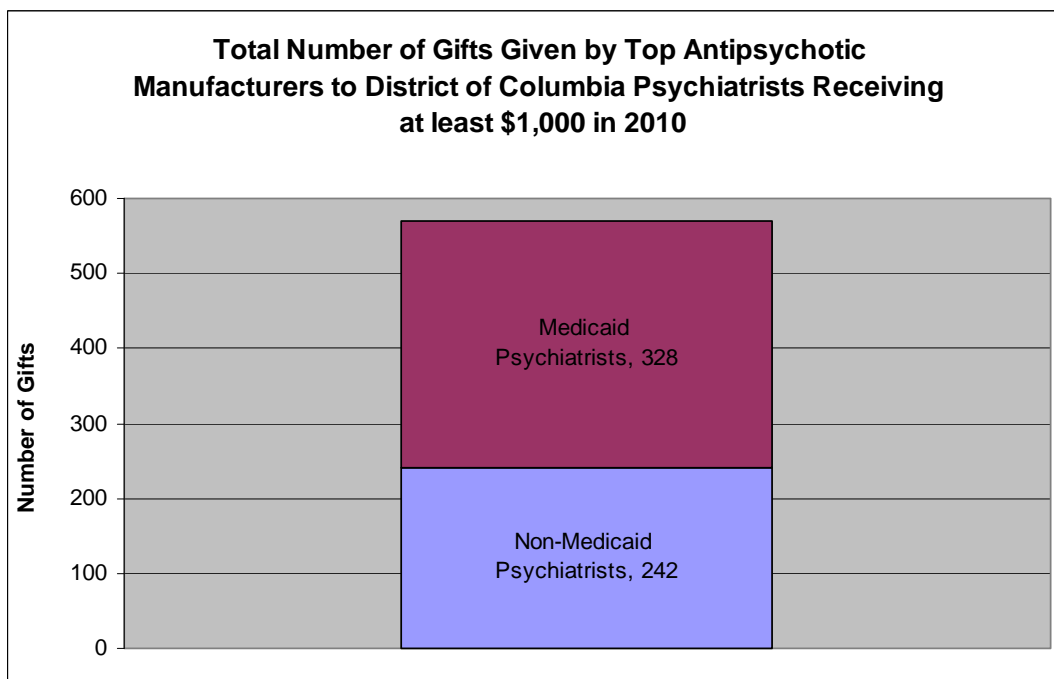


Figure 12 indicates that Medicaid psychiatrists received more than half the total number of gifts given to psychiatrists, despite representing only 27% of the psychiatrists in the sample.

Taken together, these figures demonstrate that psychiatrists who accept Medicaid may be targeted in particular for marketing efforts by top antipsychotic manufacturers.

Characteristics of Physicians Receiving Gifts from Antipsychotic Manufacturers

As noted, several of the District psychiatrists who received gifts in 2008-2010 are Medicaid providers. Of particular note, the seven Medicaid psychiatrists who received at least \$1,000 represent some of the highest earners in our sample, across all specialties. The three highest-paid Medicaid psychiatrists received a combined total of \$321,448. It is apparent that these psychiatrists are considered highly valued opinion leaders by the pharmaceutical industry; an investigation of their various professional roles illuminates why they are so highly valued.

Several of the most highly compensated psychiatrists have impressive academic and professional organization titles. Many are principal investigators on both industry- and federally-funded research programs. In addition, they hold positions on advisory committees for several specialty organizations. While each of these organizations has conflict-of-interest policies in place, it is unknown to what extent they are aware of these psychiatrists' relationships with industry.

In addition to their varied professional positions, many psychiatrists in our sample who have received gifts from the pharmaceutical industry have extensive publication records in peer-reviewed journals. A PubMed search of publications by four of the most highly compensated psychiatrists in our sample reveals more than 60 publications in peer-reviewed journals, including more than 20 since 2007 (the first year of detailed analysis of the District's pharmaceutical marketing data).

VII. Developments in the District of Columbia

Hospital and Medical School Policies in the District of Columbia

In 2007, the American Medical Student Association (AMSA) released its first Scorecard, rating every medical school in the country according to how restrictive policies were regarding interactions between pharmaceutical companies and medical students (AMSA, 2007). The 2007 AMSA scorecard, implemented by a single summer intern at AMSA's Reston headquarters, had a dramatic effect on academic medical center policies nationwide. Only five schools scored A's, and 40 schools, including all three medical schools in Washington, DC, received F's. Since 2008, the Scorecard has been a joint project between AMSA and the Prescription Project, and has become a more comprehensive project with an easily searchable database. In 2012 Georgetown University Medical Center's (GUMC) score is an A; Howard University College of Medicine scores a B; and George Washington University School of Medicine's score remains a D (AMSA, 2012).

GUMC's transformation in both policy and practice is illustrative. After GUMC received a failing grade on the AMSA scorecard, the university established a task force to develop a policy that would reduce the pharmaceutical industry influence on their medical center and promote evidence-based medicine. Georgetown worked with Medstar, which owns Georgetown University Hospital (where third and fourth year medical students train), to align policies and provide a consistent message to students and residents. The task force forbade the receipt of any gifts, including food, except at approved continuing medical education events.

Before implementation of the new policy, which states that "receipt of any gifts from industry by faculty, staff, students, and trainees of GUMC, whether on-site or off-site, is forbidden," pharmaceutical representatives provided lunch at every noon meeting (four times a week), and sometimes breakfast at morning report to medical students, residents, and attending physicians in the internal medicine department. Pharmaceutical representatives delivered a 10-15 minute sales pitch prior to each meeting. After implementation of the tougher policy, pharmaceutical representatives no longer provided lunch. Although the department provided lunch once a week, administrators noticed a decrease in attendance at daily meetings. Guessing that low attendance was due to lack of lunch provision (though the residents denied that this was the reason), the department began to provide lunch at all noon conferences, and attendance has rebounded.

Occasionally, an industry representative will host a lunch outside the hospital, sometimes in a hotel that is on the campus. According to the chair of the department of Internal Medicine, this would be considered a violation of GUMC's Policy on Industry Relationships and Interactions. The policy changes at GUMC and Georgetown University Hospital have apparently sparked little pushback from physicians, although some physicians were reportedly offended at the implication that they were heavily influenced by food and marketing messages. Some physicians also suggested that private-practice physicians would

be less likely to accept medical students for teaching given the restrictions, but this did not turn out to be a problem.

While the AMSA Scorecard notes that GUMC still allows industry-funded food at CME-accredited events, allows faculty to participate on industry speakers' bureaus, and allows the use of samples in certain outpatient areas, GUMC's shift in policy to improve its AMSA score is a model for other medical schools in moving away from industry influence.

GUMC's marks are well above other schools in the District. Howard's progress is on the rise, as they jumped from an F to a B grade in 2010, according to AMSA, which stated that their "policy would be greatly improved if the curriculum on conflict of interest and industry-funded interactions were taught to medical students" (AMSA, 2011). George Washington University School of Medicine trails with a D. While Children's National Medical Center, a GW- affiliated hospital, possesses a stringent policy, George Washington University School of Medicine does not. Although George Washington University School of Medicine's policy requires full-time faculty to make disclosures about relationships with industry, the university places no limits on gifts and meals, does not require approval in consulting or speaking relationships, and allows the use of pharmaceutical samples and industry-funded training (AMSA, 2011).

Academic Detailing Efforts in the District of Columbia

The District of Columbia has taken steps to reduce the influence of pharmaceutical marketing on prescribing behavior through an academic detailing program. The Washington DC Academic Detailing Program, established by the SafeRx Amendment Act of 2008, provides unbiased information to prescribers on the safety and efficacy of medications and other treatments. The program is conducted in conjunction with the Alosa Foundation's Independent Drug Information Service (IDIS). Independent experts from Harvard Medical School conduct detailed reviews of the literature in a variety of topics and produce detailed reports and evidence-based recommendations. The information contained in these reports is then delivered in-person to health care practitioners at sites throughout the District by Academic Detailing Program staff in a similar fashion to pharmaceutical detailing by industry representatives. The Academic Detailing Program's staff in the District consists of one physician and one registered nurse. The Alosa Foundation has produced reports examining the effectiveness of its program in the District, with the most recent iteration published in August 2010. The report indicates that practitioners have been engaged with academic detailers in their encounters, and more than 75% of practitioners who were visited by the Academic Detailing Program staff accepted an offer of visits on other topics in the future. In one year spanning August 2009 to July 2010, Academic Detailing Program staff visited 458 unique practitioners in the District of Columbia for a total of 860 visits (Alosa Foundation, 2010).

DC Superior Court's Efforts to Monitor Psychotropic Medication Use

There is evidence that various levels of DC government are aware of the issue of antipsychotic prescribing and are taking steps to investigate and address the use of these drugs. In May 2012, the DC

Superior Court Family Court held a training seminar on the use of psychotropic drugs on children in the neglect and delinquency system. The seminar, intended for lawyers and other professionals in the legal system, focused on diagnoses for which psychotropic medications are indicated, the benefits and risks of certain psychotropic drugs, proper monitoring and evaluation of the use of these drugs, the role of court personnel in the monitoring and evaluation process, and alternative treatment modalities for children under the court's supervision. The training was conducted by the DC Superior Court Urgent Care Clinic with training materials provided by the American Bar Association. The concern the court demonstrated by conducting this training for its employees is a positive development in ongoing efforts to ensure psychotropic medications are being used appropriately and safely.

VIII. Recommendations

To address the concerns about the impacts of pharmaceutical marketing – particularly antipsychotic marketing – on the health of the District’s children and adult residents, we have five main recommendations.

1. Strengthen the AccessRx Act to improve transparency

We recommend that the AccessRx Act be amended to make all pharmaceutical-marketing reports submitted to the District publicly available; require reports of gift expenditures to include unique recipient identifiers; and require that individual gifts reported include “product supported” information. These modifications would make it easier for District agencies, journalists, and the public to find patterns – such as specific doctors being paid to speak on behalf of specific drugs – that could help patients and public officials guard against potential inappropriate prescribing.

For instance, the patients of the providers who received large sums from antipsychotic manufacturers (referred to as a group but not named in this report) might ask more questions about whether a drug is right for them if they know the prescriber receives regular payments from that drug’s manufacturers. Inclusion of unique recipient identifiers and product-marketed information can improve the quality of such information, by ensuring that all payments to a particular provider are captured and that patients can focus on the drugs of most concern to them. An HIV-negative patient receiving an antipsychotic prescription from a primary-care provider would probably like to know whether payments that provider received from that drug’s manufacturer were for the marketing of an HIV drug or an antipsychotic – something the data in its current form does not specify.

This information could also be valuable to the District’s Department of Health Care Finance (DHCF) and other payers, for decisions about provider network composition and utilization review.

- **Make all reports submitted pursuant to the AccessRx Act publicly available:** In the interest of informed healthcare decisionmaking, patients should have access to information about how much money their healthcare providers receive from specific companies and about which drugs are targeted by marketing efforts. A database that combines information from all individual companies’ reports in a standardized format should be made available to the public in a timely fashion. Such a database is currently developed each year for use solely by the Department of Health, but the AccessRx Act requires that it remain confidential.

Minnesota and Vermont already collect similar information and make the data on individual healthcare providers publicly available. ProPublica combines information on individual healthcare providers from twelve major pharmaceutical companies into a user-friendly database available to the public (ProPublica, n.d.). The Affordable Care Act will make data on gifts to physicians and teaching hospitals available to the public in the near future. Given that such information is or soon will be publicly available, it is only fitting that the District also disclose the information that pharmaceutical manufacturers and labelers report. Because the

District collects significantly more information than the Affordable Care Act requires companies to report, the District has an opportunity to provide more data to the public than they will receive under the federal law, and to set an example to other states.

- **Require unique recipient identifiers:** Without unique recipient identifiers, analyses may fail to identify all of the gifts that went to the same individual or entity if the recipient's name is entered differently in different instances. A requirement that manufacturers and labelers report a unique identifier, such as a National Provider Identifier, for recipients would improve speed and accuracy of matching efforts.

The National Provider Identifier (NPI) may be a good choice of unique identifier, since all providers who bill Medicare are required to have one. The Affordable Care Act will require the NPI for each physician receiving gift payments to be reported to the Department of Health and Human Services. Other healthcare providers – nurses, pharmacists, clinics, nursing homes, etc. – also have NPIs, and these could be reported to the District.

- **Require “Product Supported” information for gift expenses:** Chapter 18 requires reports of advertising/marketing expenses (TV ads, direct mail, etc.) to specify which product is being marketed during each activity. Reports of gift expenses (e.g., food or honoraria for physicians) are not required to specify which product is being marketed. Requiring “product supported” information for gift expenses would help researchers determine how much companies are spending to market specific drugs. Vermont already requires reporting of this information, and the Affordable Care Act will require it for federal reporting of gifts given in 2012 and thereafter. Here, too, requiring this information to be reported to the District would become consistent with federal law.

To reduce the likelihood of manufacturers listing Drug A as the one being supported for a visit in which the primary objective is to leave literature about an off-label use of Drug B, instructions could require listing the drugs the company manufactures that are marketed for the disease state under discussion during each activity.

2. Notify providers for whom large gift amounts are reported. Healthcare providers who are reported to be receiving large sums (e.g., over \$10,000 in total value of gifts) should be alerted to what the District's records show and warned of the appearance of potential conflicts of interest. While the data received pursuant to the AccessRx Act are not publicly reported, many payments are already publicly available in the ProPublica database, and physician payments from all pharmaceutical companies will be public soon under the Affordable Care Act. Providers may wish to consider the possibility that large gifts from pharmaceutical companies could create suspicions about biased prescribing choices among patients and others.

3. Study prescribing patterns for potential irrational prescribing, with an initial focus on antipsychotics prescribed for children, and place limitations on prescribing and reimbursement as appropriate. The District could begin by examining Medicaid prescriber behavior, first for antipsychotics and then for other drugs. This is worthwhile for two reasons: Rates of antipsychotic use are high among the District's Medicaid population (see Section VI), and this is a single large data set that should be easily accessible by the DHCF. In the case of antipsychotics, it is entirely possible that the rate of use by District Medicaid enrollees is high due to greater incidence of relevant conditions among this population, and that some providers may see more patients who could benefit from psychotropic medications. However, it would be worthwhile to identify any Medicaid providers whose patterns of prescribing antipsychotics and other drugs suggest possible inappropriate prescribing, and to engage with them further. If the problem is severe and not improving, establishing policies to limit prescribing and/or Medicaid reimbursement may be necessary. In addition, an analysis of which specific antipsychotics are being prescribed could help the District target the educational and outreach efforts described in the next item.

4. Expand prescriber education and outreach, with an initial focus on antipsychotic use in children. As noted in Section VII, we are aware of at least one effort, by the DC Superior Court's urgent care clinic, to address high rates of antipsychotic prescribing to children involved with the District's Child and Family Services Agency (CFSA). Additional outreach and educational efforts to District physicians could also be beneficial. The District's academic detailers could add a module on antipsychotics to their current efforts, and one or more District agencies could sponsor Continuing Medical Education opportunities on appropriate prescribing of antipsychotics. The requirement for pharmaceutical detailers to be registered with the District also provides an additional avenue for oversight and education, as detailers' licenses can be revoked for engaging in deceptive and misleading marketing and license renewal requires completion of continuing education credits.

Following the passage of the Child and Family Services Improvement and Innovation Act, several federal agencies (Administration on Children and Families, Centers for Medicare and Medicaid Services, and Substance Abuse and Mental Health Services Administration) are working collaboratively to address the use of psychotropic medication among children in foster care, including by collecting and disseminating best practices from state experiences. Resources they will provide in the coming months may be helpful in addressing the use of antipsychotics among the District's foster children.

5. Consider legislation to ban gifts to healthcare providers. Adopting a law, such as Vermont's 2009 legislation, to prohibit gifts (including food) to healthcare providers would greatly reduce the potential for conflicts of interest and for gift-influenced inappropriate prescribing.

With greater transparency and more education to counterbalance pharmaceutical marketing efforts, more District residents – including some of our most vulnerable – will be able to enjoy trusting patient-provider relationships and choose treatments with risk and benefits appropriate for their health.

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Appendix: Proportion of Medicaid Population Receiving Antipsychotic Prescriptions in 2008, by State

State	Proportion	State	Proportion	State	Proportion
Alabama	4.3%	Kentucky	5.6%	North Dakota	4.0%
Alaska	4.3%	Louisiana	3.9%	Ohio	5.5%
Arizona	-	Maine	-	Oklahoma	4.3%
Arkansas	4.7%	Maryland	10.1%	Oregon	10.8%
California	2.7%	Massachusetts	5.5%	Pennsylvania	4.5%
Colorado	3.9%	Michigan	2.0%	Rhode Island	6.7%
Connecticut	9.3%	Minnesota	5.3%	South Carolina	2.8%
Delaware	8.2%	Mississippi	3.7%	South Dakota	3.5%
District of Columbia	9.8%	Missouri	7.6%	Tennessee	3.1%
Florida	3.6%	Montana	5.7%	Texas	3.6%
Georgia	4.4%	Nebraska	5.7%	Utah	4.5%
Hawaii	4.6%	Nevada	6.3%	Vermont	5.2%
Idaho	5.9%	New Hampshire	5.6%	Virginia	4.0%
Illinois	4.2%	New Jersey	7.9%	Washington	8.4%
Indiana	5.6%	New Mexico	0.6%	West Virginia	7.3%
Iowa	5.0%	New York	6.4%	Wisconsin	4.9%
Kansas	9.3%	North Carolina	4.6%	Wyoming	4.7%

Source: Data from Medicaid Analytic Rx eXtract (MAX Rx) Prescription Drug Tables downloaded from Centers for Medicare and Medicaid Services website, <http://go.cms.gov/QOj4y9>

