DOES THE PRESCRIBING CONTEXT FOR ADHD MEDICATIONS SUGGEST COGNITIVE ENHANCEMENT MOTIVATION?

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ABSTRACT OF THE DISSERTATION

Does the Prescribing Context for ADHD Medications Suggest Cognitive Enhancement Motivation?

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Numerous scientific studies and media reports point to the widespread use of prescription medications for Attention Deficit Hyperactivity Disorder (ADHD) to improve study performance. The purpose of this study was to determine, among a population of high school-age students, whether (a) there was an increase in the prescribing of these medications in the weeks immediately prior to and during final exams and (b) whether physicians appeared to be more cautious during this period in terms of the patients for whom they wrote prescriptions and the characteristics of the medications prescribed. In addition, to the extent that an exam-related increase in prescribing was observed, this study sought to determine whether its magnitude was related to county level measures of academic performance. These questions were addressed using administrative prescription drug, medical claims, and enrollment records from a database of private health insurance plan beneficiaries. County level measures of performance on the SAT and AP exams, as well as on state-mandated tests, were linked to the health care data for a geographic subset of students. Contrary to expectations, the

final exam period appeared to represent the start of an anticipated summer decline in rates of prescribing rather than the occasion for a hypothesized temporary increase. Moreover, there was no evidence of between-county variation that could be explained by the test performance measures. In addition, there was only limited evidence that students who began pharmacotherapy for ADHD in the exam period differed from other treatment initiators in terms of age, sex, diagnosis and treatment history, or characteristics of the medications prescribed. These results, in combination with similar findings concerning summer initiators, suggest that the timing of treatment initiation is more sensitive to clinical need than to short-term academic demand. Nevertheless, the sharp decline in prescribing observed from late spring through late summer suggests that school-related demands do play a role on a larger scale despite clinical recommendations that ADHD be treated as a chronic condition.

Dedication

For Susan Bilder and Irene and Leonard Cohn

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Chapter 1 - Introduction

Media and anecdotal accounts point to the widespread use of drugs intended for the treatment of Attention Deficit Hyperactivity Disorder (ADHD), such as Adderall and Ritalin, on high school and college campuses (cf. Hartocollis; Jacobs, 2005; Talbot, 2009). The drugs are prescribed widely by physicians and often can be obtained without a prescription from peers at little or no cost. Many students report taking them as study aids to improve concentration and maintain wakefulness in a competitive academic environment. The perception of the usefulness of these drugs for cognitive enhancement is not limited to students however. In a recent high-profile article in *Nature*, Greely and colleagues (Greely et al., 2008) have argued for the development of a research and policy framework to support the responsible use of pharmaceutical agents to improve cognitive performance in healthy persons. Use of such drugs for cognitive enhancement, or "cosmetic neurology"(Chatterjee, 2004), raises a number of important issues from public health to autonomy and coercion; self-concept and work ethic; distributive justice; and educational equity and the assessment process. (Farah et al., 2004; Goodman, 2010; Hyman, 2006; Mehlman, 2004). For these reasons it is necessary to develop a better understanding of the extent to which ADHD medications are used in competitive academic circumstances.

The current study has been developed to examine rates, characteristics, and predictors of new use of the most commonly prescribed ADHD drugs among high school age students at times of greater and lesser academic demand. The design is retrospective and involves analysis of prescription drug and medical claims records from a large database of privately insured persons. Academic demand is operationalized indirectly at two levels. At one level, the key dependent variables will reflect the timing of

prescriptions: during the school year, in the period leading up to and including final exams, or in the summer. Other indirect measures of academic pressure will be introduced if possible as second-level covariates in a set of multi-level analyses modeling the effects of community level variables such as average SAT, ACT, and AP scores and state proficiency and graduation test results on the relative timing of new treatment spells involving medication.

Specific Aims

1. At the level of individual prescriptions, compare the rates of ADHD drug prescriptions filled among privately insured high school-age students across three periods: school year, final exams, and summer. Apply a parallel analysis to a widely used class of comparison drugs: Selective serotonin reuptake inhibitor (SSRI) antidepressants, the prescription rates of which are not expected to be sensitive to academic demands.
2. At the person level, and among initiators of pharmacotherapy for ADHD, determine the degree to which new prescriptions filled during the final exam period reflect more caution among prescribing physicians compared with new prescriptions filled at other times of the year. Prescriber caution may be reflected in (a) the characteristics of the students for whom the prescriptions are written, including sociodemographic and clinical variables, as well as (b) the characteristics of the filled prescriptions, including drug type, delivery system, days supplied, and average daily dose.
3. At the county level, model the odds of initiating pharmacotherapy for ADHD during the final exam period vs. other times. County level predictors suggestive of academic competitiveness include measures of test performance, including mean

SAT, ACT, and AP exam scores, and measures based on the California Standardized Testing and Reporting (STAR) program and on high school exit exams. County level predictors were to have been modeled directly as predictors of average rates of final exam period initiation and also as potential moderators of individual-level effects.

Inferential Advantages and Limitations

The overwhelming majority of evidence for the use of ADHD medications for cognitive enhancement and other non-medical purposes comes from self-report data from studies of small student populations, usually in a single school district or college/university. Such self-report data are invaluable; they describe the ease with which ADHD drugs may be obtained and they allow students to endorse a wide variety of motivations for their use. They have a number of significant disadvantages, however, that call for complementary research frameworks for addressing strategic, i.e., enhancement-motivated, use. First, self-report data are susceptible to problems with recall and biased responding. The latter may be especially important when participants are asked to choose among more and less socially desirable explanations for their use of ADHD drugs, e.g., to improve studying vs. to get high. In addition, the items included in self-report instruments are often limited in their question prompts or their presentation of answer choices. In the case of ADHD medication use, studies vary in the inclusiveness of their definitions of “non-medical” or “illicit use”. This affects not only prevalence estimates but can also influence how students describe their motivations for using the drugs. Equally important is the fact that most self-report studies inquire about only a fraction of drugs approved for the treatment of ADHD. This is inevitable given the large

number of brand and generic names in the marketplace, but it undermines the studies nonetheless and almost certainly results in underestimates of use. Respondents may not see the names of the medications they use or they may recognize only the brand name (e.g., Focalin) and not the generic name (e.g., methylphenidate) or *vice-versa*.

The current investigation has a number of advantages that are not shared with self-report studies. Cognitive enhancement motivations will be inferred based on assumptions regarding timing and context of prescriptions rather than on possibly biased or incomplete self-reports. This approach is indirect, and it has some disadvantages, but they are not same disadvantages that limit self-report data. The design also avoids the problematic definition of "non-medical" or "illicit" use, dispensing with these categories and focusing on what might be termed "strategic use". This is inferred by the observation of new use of ADHD medications at a time when they are likely to be desired primarily for their value in supporting studying or test performance. The strategic use of ADHD medications is also captured regardless of the proximate source of the drugs: legitimate prescriptions or prescriptions obtained improperly through doctor shopping, patient misrepresentation of need, or questionable prescribing. Self-report studies rarely account for all of these means, and some fall outside of their definitions of "non-medical" or "illicit". In addition, this study was designed to reveal detailed characteristics of the filled prescriptions, including drugs dispensed and dosages supplied - details which may be missing or incomplete in self-report checklists but that are included as a matter of routine in prescription drug claims. Finally, the design isolates a physician behavior as the source of any increase in medication availability rather than student behaviors such as hoarding, thus focusing attention on the supply side. Practice guidelines and academic

detailing efforts targeted toward prescribers are likely to be more amenable to education and intervention than are the consumption patterns of students.

The indirect approach to addressing the use of ADHD medications for strategic cognitive enhancement has a number of limitations as well. Foremost is the division of the year into three periods (school year, final exam period, and summer) with the assumption that academic demand, and thus the incentive to use ADHD drugs strategically, varies predictably among them. In fact, there is likely to be academic pressure during all three periods, especially surrounding the multiple SAT, ACT, and AP testing occasions during the school year. Although this cannot be avoided, and there are too many test dates during the year to delineate and include as additional periods of increased academic demand, the large number of test dates helps to ensure that the aggregate level of academic demand across these occasions is likely to be lower than that of a single final exam period.

The core database for the proposed study includes records for prescriptions filled at pharmacies, including dates, generic names, days supplied and drug strength. However, filling a prescription is an imperfect proxy for consuming the prescribed medication as intended. There is a possibility that recipients may not actually take the prescribed medication or that they may take it in ways that are inconsistent with their physicians' instructions. Some students manage their supplies, saving them for periods of increased workload, while skipping weekends or days with no classes (DeSantis, Webb, & Noar, 2008). Hoarding may also be used to provide enough pills for a recreational binge (cf. Garland, 1998) . Patterns such as these, not all of which are necessarily

contrary to instructions from prescribers, are not detectable from administrative claims data.

There is some evidence, however, that administrative pharmacy data correlate closely with other measures of medication use such as pill counts (Crystal, Akincigil, Bilder, & Walkup, 2007), but data are not available for the youth population or for ADHD medications specifically. It is reasonable to expect that, as a population, children and adolescents who are prescribed ADHD medications may be more adherent to doctors' instructions because their use of the drugs is likely to be supervised by school personnel (Musser et al., 1998) or parents. Moreover, students taking the medications have reported positive effects on social functioning, behavior, and attention (Moline & Frankenberger, 2001) and therefore many are motivated to take them. Finally, as long-acting formulations, which require only once-daily dosing, are prescribed more frequently, adherence rates should increase. (L. D. Adler & Nierenberg, 2010; Christensen, Sasane, Hodgkins, Harley, & Tetali, 2010; Marcus, Wan, Kemner, & Olfson, 2005; Olfson, Marcus, & Wan, 2009; Olfson, Marcus, Zhang, & Wan, 2007).

There are also a number of means for students to acquire ADHD medications in ways that do not generate records of prescription drug fills. Medications dispensed in hospital settings do not appear in administrative data, but this is not a significant problem given the rarity of inpatient stays among children and adolescents.[1] Of more concern is the distribution of free samples from physicians' offices. An analysis of free drug samples given to patients under age 18 found that two ADHD medications were among

[1] Ninety-six percent of stimulant or atomoxetine treatment initiators in this study had no inpatient hospital visits in the year prior to the start of pharmacotherapy for ADHD. Among those with one or more such visits, the median length of stay for the year, computed across all of their visits, was five days (mean 9.2 days).

the top 15 samples distributed by physicians (Cutrona et al., 2008). The fourth-most distributed medication was Strattera (atomoxetine). Adderall/Adderall XR (mixed amphetamine salts) ranked 15th, despite the fact that this drug is a Schedule II controlled substance ("Controlled Substances Act," 2002). Taken together, and assuming no overlap, over 300,000 children and adolescents received sample ADHD drugs in 2004. Finally, the frequent exchange of ADHD drugs among students means that not every filled prescription will be consumed by the person to whom it was prescribed. However, it is very likely that the dispensed drugs will remain within the student population and that their supply will vary according to the level of academic demand implied by the timing of the prescriptions.

There may be overall patterns in the use of prescription drugs or psychiatric prescription drugs in general, rather than ADHD medications specifically, that correspond with the three designated time frames. In order to partially evaluate the likelihood of this possibility, selected analyses are repeated for SSRI (selective serotonin reuptake inhibitor) antidepressants. SSRIs are not among the medications approved for treatment of ADHD. Limited evidence suggests that they are not appropriate for this indication, especially in the absence of comorbid psychiatric conditions (Biederman, Spencer, & Wilens, 2004), and they do not produce the improvements in concentration and working memory that make ADHD drugs attractive to many students.

Finally, data on educational performance in California can be matched to individual-level administrative medical data only at the county level. Many counties comprise a large number of school districts or communities. Therefore the focus on counties may mask considerable within-unit heterogeneity. This is an unavoidable

consequence of the way in which the data are aggregated. In an effort to partially mitigate this problem, selection of conceptually related county level academic performance variables take into account between-county variation. Where similar variables differ in this respect, the variable(s) that most strongly distinguish among counties are selected for inclusion in the models whenever possible.

Hypotheses

The research aims yield four hypotheses: one concerning prescription rates, two that address the beneficiaries who received treatment and the ADHD medications they were treated with, and a final hypothesis concerning county level measures of academic demand.

1. Average rates of ADHD medication prescribing and of treatment initiation per 100,000 health plan enrollees per fixed time period (e.g., one week) will be lowest during the summer months and highest during the period surrounding final exams, reflecting changes in prescribing associated with different levels of academic demand.
2. Physician caution in initiating ADHD pharmacotherapy around final exam time will be reflected in the characteristics of patients. Odds of final exam period initiation will be negatively associated with increasing age and male sex, both of which have been shown to be related to non-medical use or diversion of prescription ADHD medications. For the same reason, students diagnosed with substance abuse or dependence or with conduct disorders or related conditions will be less likely to be final exam period initiators. In addition, students with diagnosed conditions that raise concerns about side effects or adverse events

associated with ADHD medications will be less likely to initiate their use during final exam time than during other times. These conditions include tic disorders seizures, anxiety disorders, sleep-related problems, serious mental illness, and diagnoses suggestive of cardiac risk. Finally, a diagnosis of the predominantly inattentive type of ADHD, rather than the hyperactive or combined type, should be associated with final exam period initiation, reflecting both prescriber caution and possible differences in presenting symptoms late in the school year.

3. Physician caution in initiating ADHD pharmacotherapy around final exam time will also be reflected in the characteristics of the supplied medications. Final exam period initiation will be associated with prescriptions for non-stimulants or extended-release stimulants rather than immediate release stimulants. The latter drugs are more susceptible to abuse by patients or by peers who buy or otherwise receive them. Other drug characteristics likely to be associated with initiation around final exams include delivery system (transdermal patch or the prodrug Vyvanse vs. capsules and tablets), lower drug strength, and fewer days supplied. Average daily dose, compared within each drug formulation, and computed from drug strength, quantity supplied, and days supplied, is expected to be lower for final exam period initiators.
4. Initiation of pharmacotherapy for ADHD during the final exam period, versus the remainder of the school year or summer, will be positively associated with county level variables suggestive of higher levels of academic demand and competitiveness: students' average performance on academic assessments, including SAT, ACT, and AP tests; California's Standardized Testing and

Reporting (STAR) program, and the California High School Exit Examination (CAHSEE). In addition to the main effects of these contextual variables, it is expected that they may also moderate student-level effects such that evidence of caution on the part of prescribers will be attenuated in communities where there is stronger academic pressure.

Significance

Evidence indicative of a higher rate of ADHD medication prescribing occurring in the period corresponding to final exams, when academic demands are assumed to be greatest for the largest proportion of high school students, would suggest that prescribing is sensitive to such demands. Evidence of less prescribing in the summer, while potentially less controversial (unless it's indicative of under-treatment), would also be consistent with this conclusion. The identification of such patterns does not necessarily mean, however, that patients are seeking medications, and prescribers are providing them, improperly or for the wrong reasons. Problems such as inattention, lack of organization, distractibility, and inability to finish schoolwork are among the symptoms that may be used to diagnose ADHD, even in the absence of hyperactivity (American Psychiatric Association, 1994). It would not be unsurprising for such study related deficits to manifest themselves when they create the most difficulty and for some students and their parents to seek help during this time. Indeed, treatment of inattentiveness and similar deficits when they are most likely to produce negative consequences for patients would be considered by most physicians to be within the scope of proper practice and akin to suspending prescriptions during the summer months and school holidays when the need for them is not as great. Whether such "drug holidays"

away from ADHD medications are advisable or not is beyond the subject of this analysis. They are widely seen however.

It has been well established in the literature that many students manage to acquire ADHD medications without a doctor's prescription, usually from other students (cf. Wilens, Gignac, Swezey, Monuteaux, & Biederman, 2006). However, there are many reasons for students, and especially their parents, to prefer that they get their ADHD medications via a doctor's prescription. Among these may be concerns about safety and side effects, access to a steady supply, getting the right medication at a therapeutic dose, lack of ready access to non-prescribed drugs from peers, and legal and social constraints. In addition, a diagnosis of ADHD can make various testing and other desirable academic accommodations available to students in addition to medication (Harrison, 2006).

Some students may also try to get prescriptions for ADHD medications by faking or exaggerating symptoms, and the incentives for such malingering are likely to be highest in times of increased academic demand. Advokat, Guidry, and Martino (2008) report that nearly 20% of students with ADHD in an undergraduate sample were approached by peers for advice on how to fake symptoms in order to get their own prescriptions. The diagnostic criteria for ADHD are also widely available in libraries and on the Internet, and the symptoms are easy to understand and articulate. Several studies have found that students instructed to try to fake having ADHD on various symptom checklists or behavior rating scales can do so quite successfully (Harrison, Edwards, & Parker, 2007; Jachimowicz & Geiselman, 2004; Quinn, 2003). Without validity subscales to identify potential malingerers, it is often a simple matter for students to endorse a large number of symptoms. While this is more likely to be an issue in adults than in children

and adolescents, who will typically be accompanied by parents who are involved in the evaluation process, the ease with which symptoms can be faked suggests that some healthy students are obtaining ADHD drugs by misrepresenting their need for them.

The possibility also exists that some physicians are willing to prescribe ADHD medications to healthy students in order to provide them with an academic advantage or to help them compensate for study related problems that are not associated with ADHD. They may be especially willing to do so in the knowledge that a patient shows no cardiovascular or psychiatric risk factors, contraindications, or evidence of a propensity to abuse or divert the supplied medication. Such off-label use, while questionable, is not prohibited by the U.S. Food and Drug Administration (FDA).

Although students initiating use of ADHD drugs may be doing so with varying levels of need and legitimacy, a review of the literature (see Chapter 2) reveals that almost no students report getting these drugs from online sources or from strangers. They get their prescriptions from their doctors or non-prescribed supplies from friends and classmates. This suggests that, even when a legitimate prescription is not the source of the medication, any diversion of these drugs occurs quite late in the distribution chain: between patients with a prescription and their peers without a prescription. Therefore, unless pills are regularly stockpiled, any increased prescribing associated with study enhancement use will likely appear in prescription drug claims. This would not be the case if diversion occurred primarily at the point of manufacture, shipment, or storage.

The strategic use of ADHD drugs also raises a number of educational issues, including those concerning the diversion of these drugs, via purchase or theft, in school. Students filling prescriptions late in the academic year may be doing so because they're

aware that there is a ready market for these drugs, and school personnel must be vigilant to the possibility of drug supplies changing hands. They must also be prepared to deal with both minor and serious side effects occurring during the school day, including anxiety and agitation and even aggressive behavior. Issues of educational equity can arise as well if some students are more able and willing to acquire and use these drugs than are others (cf. Greely et al., 2008). Competition among students, whether overt or not, may also be directly or subtly coercive, prompting students who would not otherwise use ADHD medications to begin using them simply to keep pace with their peers. Among college students it is widely known who is using these drugs for non-medical purposes (Babcock & Byrne, 2000; Carroll, McLaughlin, & Blake, 2006; K. M. Hall, Irwin, Bowman, Frankenberger, & Jewett, 2005) and there is reason to expect high school students to have similar, if perhaps somewhat less, knowledge of their peers' use.

The use of ADHD medications for cognitive enhancement rather than relief of symptoms changes the risk-benefit calculus associated with taking these drugs and therefore has consequences for public health as well. In the case of drugs with non-trivial side effects or risks, the argument in favor of therapies that provide a benefit when a patient has a disorder or deficit affecting health or quality of life may be less compelling when the objective of treatment is enhancement (Farah, Haimm, Sankoorikal, Smith, & Chatterjee, 2009; Hyman, 2006). However, the lack of biomarkers for the presence of ADHD means that the line between treatment and enhancement may be particularly elastic in the face of competing expectations, standards, and norms (Chatterjee, 2004; Wolpe, 2002).

The side effects of stimulants, including insomnia, anorexia, headache, dizziness, and nervousness, tend to be mild and can often be relieved by dosage changes (Evans, Blackburn, Butt, & Dattani, 2004; Graham & Coghill, 2008). Less is known about atomoxetine, which has been on the market only since 2002, but the reported side effects appear to be comparably minor and include decreased appetite, somnolence, abdominal pain, dizziness, and fatigue (Cheng, Chen, Ko, & Ng, 2007; Wernicke & Kratochvil, 2002). More serious adverse events have been reported, however, in patients taking stimulants for ADHD, including psychotic symptoms and sudden death among persons with undetected heart abnormalities. This has prompted the U.S. Food and Drug Administration (U.S. Food and Drug Administration, 2007) to require manufacturers to develop Patient Medication Guides to describe these risks to consumers. Moreover, the stimulants in Table 1 have been designated as Schedule II controlled substances, which is the U.S. federal government classification for drugs that have a currently accepted medical use but that also have the potential for abuse and dependence ("Controlled Substances Act," 2002). Stimulants share many of the behavioral pharmacological properties of cocaine, and rapid consumption of these drugs is associated with similar reinforcing effects (Kollins, MacDonald, & Rush, 2001; Volkow & Swanson, 2003). As noted in the next chapter, there are also concerns that use of the non-stimulant atomoxetine can result in thoughts of suicide. Finally, although the causal mechanisms are likely to be both subtle and complex, there is strong evidence that high school and college students who use prescription ADHD drugs for non-medical purposes are at increased risk for alcohol, drug abuse, and related problems (cf. McCabe, Teter, & Boyd, 2006b; McCabe, Teter, Boyd, & Guthrie, 2004).

Table 1
Medications Approved by the FDA for the Treatment of Attention Deficit Hyperactivity Disorder

Brand name	Generic name	Details
Adderall	Amphetamine	Immediate-release tablets
Adderall XR	Amphetamine	Extended-release capsules
Dexedrine	dextroamphetamine	Immediate-release spansule capsules and tablets
Dextrostat	dextroamphetamine	Immediate-release tablets
Vyvanse	lisdexamfetamine	Long-acting capsules
N/A	amphetamine	Generic version
N/A	dextroamphetamine	Generic version
Concerta	methylphenidate	Extended-release tablets
Daytrana	methylphenidate	Transdermal patch
Desoxyn	methylphenidate hcl	Immediate-release tablets
Focalin	dexmethylphenidate	Immediate-release tablets
Focalin XR	dexmethylphenidate	Extended-release capsules
Metadate ER	methylphenidate	Extended-release capsules
Metadate CD	methylphenidate	Extended-release capsules
Methylin	methylphenidate	Oral solution or chewable tablets
Ritalin	methylphenidate	Immediate-release tablets
Ritalin SR	methylphenidate	Sustained-release tablets
Ritalin LA	methylphenidate	Extended-release capsules
N/A	methylphenidate	Generic version
N/A	dexmethylphenidate	Generic version
Strattera	atomoxetine hcl	Non-stimulant capsules
Intuniv	guanfacine	Non-stimulant extended-release tablets
Kapvay	clonidine hcl	Non-stimulant extended-release tablets

Notes. Some drug information retrieved from http://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm107918.htm (May, 2011). The non-stimulant medications guanfacine and clonidine hcl were approved by the FDA for treatment of ADHD after 2007, the last year of available data for the current study. Pemoline (marketed as Cylert and generics), which is not listed in the table, is no longer sold in the U.S.

Apart from public health consequences, study related use of ADHD drugs may also affect the processes of instruction and evaluation. These drugs provide the ability to sustain attention and concentration for long periods, but they may adversely affect study habits, motivations, and judgments of self-efficacy. Students who begin to rely on the drugs may change their daily routines, including class attendance and outside activities,

with the expectation that they can catch up when needed (Arria, 2008). There may be a divergence between academic self-efficacy while using vs. not using ADHD medications. This could result in more frequent use and at higher doses. Sleep-related problems associated with both stimulants (Evans, et al., 2004; Graham & Coghill, 2008) and the non-stimulant atomoxetine (Cheng, et al., 2007; Wernicke & Kratochvil, 2002) may also affect performance. These drugs may also provide a short-term competitive advantage in some situations that distort the evaluation process. Finally, experience with ADHD medications, whether prescribed or not, in the high school years may establish patterns that persist into college, where these drugs are more readily available and academic demands are increased. For example, one study found that 49% of college students using ADHD medications for non-medical purposes began such use while in high school (Prudhomme White, Becker-Blease, & Grace-Bishop, 2006).

To the extent that there are students who see themselves as using ADHD drugs for strategic, study related reasons, traditional school, government, and service agencies, including law enforcement, concerned with drug abuse and dependence will face a challenge in designing laws, policies, and programs to meet the needs of this population. Moreover, educators and assessment professionals will face additional difficulties and responsibilities. These will be greater if, as expected, the opportunities to use these drugs for recreational purposes continue to decrease as a result of the development of more abuse-resistant delivery systems and enhancement-related use is increasingly the predominant non-medical motivation for their consumption.

Chapter 2 - Background and Literature

ADHD and its Treatment

Attention Deficit Hyperactivity Disorder (ADHD) is a commonly diagnosed and widely treated condition among children and adolescents. Estimates of ADHD's prevalence vary, but the disorder is thought to affect between 4% and 10% of older youth in the United States (Centers for Disease Control, 2005; Froehlich et al., 2007; Merikangas et al., 2010). Clinically, ADHD is characterized along two dimensions: inattention and hyperactive-impulsive behavior and has associated diagnostic classifications for each, plus a combined type (American Psychiatric Association, 1994). There are five elements of evidence that must be established in order for a diagnosis of ADHD to be made. The individual being evaluated must have six or more symptoms of inattentiveness (e.g., fails to give close attention to details, makes careless mistakes), hyperactivity-impulsiveness (e.g., often "on the go" or acts "as if driven by a motor"), or both. At least some of these symptoms must have been observed before age seven, must cause impairment in at least two settings (e.g., home and school), and must cause clinically significant impairment in social, academic, or occupational functioning. Finally, the symptoms must not be explainable by pervasive developmental disorders, schizophrenia, or bipolar disorder and must not be better explained by other disorders. Parent and teacher behavior rating scales are not sufficient for establishing a diagnosis, but they are often used to characterize symptoms and to evaluate response to treatment (T. J. Spencer, Biederman, & Mick, 2007).

ADHD is associated with a wide range of cognitive problems consistent with deficits in working memory and executive function (Barkley, 2003). Comorbid learning,

psychiatric, and behavioral problems are common as well, including learning disabilities, conduct disorder, depression, and anxiety (Elia, Ambrosini, & Berrettini, 2008; Larson, Russ, Kahn, & Halfon, 2011). One meta-analysis of psychiatric comorbidity studies in children and adolescents with ADHD found median odds ratios (present in youth with ADHD vs. youth without ADHD) of 10.7 for conduct disorder, 5.5 for depression, and 3.0 for anxiety (Angold, Costello, & Erkanli, 1999). The presence of cognitive deficits and comorbid disorders are of particular importance to the current study because the medications commonly prescribed for managing the former are often desired as study aids, and the latter may contribute to doctors' treatment decisions.

The central nervous system (CNS) stimulants (hereafter, "stimulants"), as well as atomoxetine, listed in Table 1, represent the first line of pharmacological treatment for ADHD, although a wide range of other drugs have been used with varying efficacy and side effects (T.J. Spencer, Biederman, & Wilens, 2000). These medications are effective in about 70% to 90% of patients, producing improvements in concentration and attentiveness; impulsivity and hyperactivity; and relationships with peers, teachers, and parents (Biederman, et al., 2004; Elia, Ambrosini, & Rapoport, 1999; Goldman, Genel, Bezman, & Slanetz, 1998; Greenhill, Halperin, & Abikoff, 1999). Students' subjective reports of the effects of these drugs on attention, behavior, and social interactions have been positive, and, of those with a preference, a majority in one study reported wanting to continue taking their medication despite experiencing some of the most common side effects (Moline & Frankenberger, 2001).

Atomoxetine was the only non-stimulant medication approved for the treatment of ADHD during the period covered by this study's available data. It is particularly suited

to patients who cannot tolerate stimulants or for those who may be at risk of misusing or diverting them. Although it is considered a first-line treatment, and its efficacy is well established (Barton, 2005; Garnock-Jones & Keating, 2009; Ledbetter, 2006), results from several trials indicate that it is not as efficacious as OROS-methylphenidate in reducing ADHD symptoms (Gibson, Bettinger, Patel, & Crismon, 2006; Newcorn et al., 2008; Yildiz, Sismanlar, Memik, Karakaya, & Agaoglu, 2011).

The precise mechanisms by which stimulants and atomoxetine exert their influence are not clear, but they are known to increase the amount of available dopamine or norepinephrine in the inter-synaptic space by binding their transport molecules and/or increasing their release from the presynaptic terminal (Greenhill et al., 2002; Ledbetter, 2006). The stimulants methylphenidate and amphetamine are available in both immediate-release and intermediate- or long-acting formulations. The latter use a variety of pharmacokinetic mechanisms to reduce the need to take multiple doses throughout the day (Daughton & Kratochvil, 2009). As the use of these new formulations has increased, school nurses have reported that they have seen a decrease in the amount of in-school administration of these drugs (Dupont, Bucher, Wilford, & Coleman, 2007; A. M. McCarthy, Kelly, Johnson, Roman, & Zimmerman, 2006). This result, combined with the relative abuse-resistance of newer delivery systems (DuPont & Bensinger, 2006), holds out promise for perhaps limiting the recreational misuse and diversion of stimulant drugs (cf. Parasrampuria et al., 2007). However, it is still possible for motivated users to crush or extract the active ingredients for intranasal or intravenous use. Recent research has shown a substantial increase between 2000 and 2005, from 9% to 68%, in the percentage of ADHD medications prescribed to youth that are extended-release

formulations (Castle, Aubert, Verbrugge, Khalid, & Epstein, 2007), and this trend is likely to continue.

Benefits and Risks

The effects of stimulants on cognition in individuals diagnosed with ADHD are amply documented (cf. Advokat, 2010; Biederman et al., 2008; Gualtieri & Johnson, 2008; Pietrzak, Mollica, Maruff, & Snyder, 2006; Swanson, Baler, & Volkow, 2011). Carlson and Brunner's (1993) review of the effects of stimulants on the academic performance of children with ADHD noted that the medications have a number of "acute" effects on classroom performance, but they reported few long-term benefits. In reviewing the literature on the cognitive effects of stimulant medications on adults with ADHD, Advokat (2010) suggested a number of conclusions that undermine the view that these medications are "cognitive enhancers" in any but the narrowest sense of the term. The medications improve focus and the ability to sustain attention, but they are also associated with possible costs, including distractibility and other problems such as impairments in selective attention, reduced cognitive flexibility, and poorer short-term acquisition of information. Far from being true cognitive enhancers, in persons with ADHD, these medications do not even improve long-term academic performance to match the level of individuals without ADHD. There is less evidence for the efficacy of atomoxetine on cognitive and academic performance measures as a consequence of its recent approval (in 2002) for the treatment of ADHD. However, some studies have shown that atomoxetine, like stimulants, can produce improvements in working memory and response inhibition, as well as executive functioning (de Jong et al., 2009; Gau & Shang, 2010; Maziade et al., 2009).

The evidence base for the benefits of stimulants and atomoxetine on persons without a diagnosis of ADHD is smaller, but it likewise fails to support claims that these medications are cognitive enhancers or "smart pills" (S. S. Hall, 2003). For example, Agay, Yechiam, Carmel, and Levkovitz (2010) administered a dose of methylphenidate to adults with ADHD and to an undiagnosed comparison group. Compared with a placebo, methylphenidate was associated with better performance on a digit span test (a measure of working memory), but it did not produce improvements on a continuous performance test (a measure of attention), on Raven's progressive matrices (a measure of general mental ability), or on decision-making tasks. Performance on the working memory task was enhanced by methylphenidate for both the ADHD and non-ADHD subjects. Non-diagnosed volunteers who have received atomoxetine have also shown improved performance in response inhibition tasks (Chamberlain et al., 2009; Chamberlain et al., 2006), but not in a measure of probabilistic learning (Chamberlain, et al., 2009).

A number of other studies have also found improvements in only a limited set of tasks in undiagnosed subjects treated with stimulants. These tasks include tests of working memory, language production, memory, reaction time, and planning (Barch & Carter, 2005; Camp-Bruno & Herting, 1994; de Wit, Enggasser, & Richards, 2002; Elliott et al., 1997; Klorman et al., 1984). However, there is also evidence that these improvements are seen primarily in subjects with lower levels of baseline, i.e., pre-drug, performance (Farah, et al., 2009; Mattay et al., 2000; Mehta et al., 2000).

The evidence to date suggests that the value of ADHD medications in enhancing cognitive performance is limited in terms of the scope of the improvements and perhaps

also in the individuals who benefit. However, these potential beneficiaries may also include those whose baseline performance is impaired due to fatigue or lack of sleep. Anecdotal accounts and self-reports from students using these medications without a prescription suggest that they are widely used in this state. During the second world war stimulants were often used to improve wakefulness and vigilance in military personnel, particularly air crews, and they have a long history of use for this and similar purposes (Rasmussen, 2008). Klorman et al. (1984) found that the ability of methylphenidate to improve performance in a set of continuous performance tests of attention increased with the complexity of the task and with subjects' levels of fatigue. Another study found no improvement from methylphenidate in a set of memory, learning, and response inhibition tasks in sleep-deprived adults, but the authors caution that the level of sleep deprivation (24 hours) may have been insufficient to produce deficits that could be counteracted by the drug (Bray et al., 2004).

Whatever the objective cognitive benefits to non-diagnosed recipients of stimulants, the subjective effects are quite consistent when studied. For example, de Wit, Enggasser, and Richards (2002) reported elevated post-drug self-reports on a number of rating scales among undiagnosed volunteers who received a single dose of dextroamphetamine. These included measures of drug-induced euphoria, intellectual efficiency and energy, elation, vigor, friendliness, and arousal. Other studies have reported similar effects (Brumaghim & Klorman, 1998), even when at odds with objective performance (Bray, et al., 2004; Mattay et al., 1996). These subjective effects, combined with the medications' documented ability to improve wakefulness and concentration, as well as a lack of highly salient information about risks, are likely to

appeal to many students seeking a shortcut to improved studying. Self-reports, discussed below, from students about their motivations for using ADHD medications without a prescription suggest that this appeal often results in study related use.

The use of stimulants and atomoxetine is not without risk and inconvenience. The stimulants methylphenidate and amphetamine have been designated as Schedule II controlled substances by the U.S. Food and Drug Administration (FDA; "Controlled Substances Act," 2002). Such drugs have safe and effective indications for medical use, but their misuse can result in serious psychological or physical dependence. These medications have behavioral pharmacological properties similar to those of cocaine, and large doses have a similar, subjectively reinforcing, effect on dopamine transport when used in larger than therapeutic doses (Volkow & Swanson, 2003). Student survey and related data, described below, indicate that stimulants are widely used to produce a high and that they are often used simultaneously with alcohol and other drugs. This literature also indicates that students who have used stimulants without a prescription are also more likely to have misused other drugs and engaged in a variety of risky behaviors.

Several analyses of data from regional poison control centers, as well as reviews of case reports, suggest that use of methylphenidate and amphetamine can be associated with a range of symptoms consistent with their dopaminergic effects. These include tachycardia, dysrhythmia, agitation, lethargy, dizziness, and hypertension (Foley, Mrvos, & Krenzelok, 2000; Forrester, 2007; Klein-Schwartz, 2002; White & Yadao, 2000). Stomach ache and vomiting are also commonly reported. Similar effects have been reported for atomoxetine exposures (Lovecchio & Kashani, 2006; Spiller, Lintner, & Winter, 2005; Stojanovski et al., 2006). At high doses, stimulants can produce severe

psychological symptoms such as hallucinations and delusions, disorientation, manic states, aggressiveness, and confusion (Klein-Schwartz, 2002; Morton & Stockton, 2000). In most cases, however, exposure to stimulants or atomoxetine in individuals seeking medical care after ingestion produces minor or moderate acute symptoms with no long-term effects.

Concerns about adverse cardiovascular outcomes from stimulant or atomoxetine use, prompted by reports of sudden cardiac death in stimulant users with underlying cardiovascular abnormalities, prompted the FDA to require manufactures to include medication guides in drug packages (U.S. Food and Drug Administration, 2006). These guides, which have been mandated since 2007, warn consumers of potential heart-related and psychological problems including increased blood pressure and heart rate, sudden death in persons with heart problems or defects, psychotic symptoms, and aggressive behavior or hostility. However, a number of studies conducted since the FDA decision have found very little evidence of cardiac events, particularly sudden cardiac death, that can be attributed to stimulants or atomoxetine (Cooper et al., 2011; S. McCarthy, Cranswick, Potts, Taylor, & Wong, 2009; Schelleman et al., 2011; Winterstein et al., 2007). Some studies and reviews have tended, instead, to find clinically insignificant, at least in the short term and for most people, increases in heart rate and blood pressure (Findling et al., 2005; Findling, Short, & Manos, 2001; Hammerness et al., 2009; Rapport & Moffitt, 2002; Stiefel & Besag, 2010; Wernicke et al., 2003). Nevertheless, Winterstein et al. (2007) found that Medicaid youth currently receiving stimulants for treatment of ADHD were more likely than untreated youth with ADHD to have visited doctors' offices and hospital emergency departments for cardiac symptoms such as

syncope, dysrhythmia, tachycardia, and hypertension. Their study, like others, did not find an increased risk of cardiac death however. Despite the, so far, negative findings regarding serious cardiac outcomes associated with stimulant or atomoxetine treatment, physicians treating patients with ADHD are doubtless aware of the FDA's warnings and of published results concerning tachycardia and hypertension, and this appears in some cases to have affected their prescribing decisions (Gerhard et al., 2010).

The FDA has also required the manufacturer of atomoxetine (Strattera) to include a black box warning on packages alerting patients and providers to an increased risk of suicidal thoughts in children and adolescents treated with this medication (U.S. Food and Drug Administration, 2005). The warning recommends close observation of pediatric patients for signs of suicidal thinking or other unusual behavior changes. A recent meta-analysis of 14 clinical trials found no suicides, but it did find a small but significant increased risk of suicidal thoughts in atomoxetine recipients vs. placebo groups (Bangs et al., 2008).

Even in therapeutic doses, and among individuals with no known vulnerabilities for cardiac events or psychiatric reactions, side effects are commonly reported in users of stimulants and atomoxetine. Most of these are mild and can be resolved by switching agents or changing dose however. Cascade, Kalali and Wigal (2008) found that 48% of their surveyed recipients of stimulants or atomoxetine reported side effects. The most common were loss of appetite, sleep problems, mood disturbance, nausea or stomach ache, and headache. Slightly more than half of the subjects reported that the effects were somewhat, very, or extremely bothersome, but only one in five discussed them with their physician. Other studies and reviews of ADHD medication side effects have produced

similar lists of complaints (L. A. Adler, Spencer, Milton, Moore, & Michelson, 2005; Ahmann et al., 2001; Cheng, et al., 2007; Rapport & Moffitt, 2002; Wernicke & Kratochvil, 2002).

A Note on Seasonality in Prescribing Patterns

It appears that there is only one published article on seasonal patterns in ADHD medication prescribing. Cascade, Kalali, Weisler and Lenderts (2008) examined a database of U.S. prescription activity from 2003 to 2007 and found a significant summer time decrease in prescriptions for ADHD medication among children and adolescents under age 18. No such pattern was found for adults, who maintained consistent use throughout the year. The authors commented that the summer breaks in prescribing of ADHD medications among youth were a concern for a number of reasons including: (a) higher rates of substance abuse and behavior problems, and driver safety concerns in adolescents with untreated ADHD, (b) complicated management of dosing and side effects, and (c) lower efficacy when treatment is intermittent. The observed pattern was most likely a consequence of many parents' desire to give their children a break from being medicated, as well as summer time reductions in the need for them to maintain attentiveness and self-control. However, the American Academy of Pediatrics' latest clinical practice guideline for evaluation and treatment of ADHD recommends that it should be managed as a chronic condition and that treatment discontinuation should be avoided (Subcommittee on Attention-deficit/Hyperactivity disorder, 2011). Whatever the result of these new guidelines, it is expected that the same prescribing pattern reported by Cascade et al. will be evident in the 1997-2007 data used in the current study.

Non-medical Use of Prescription Stimulants

Prevalence. Media reports have conveyed the impression that non-medical use of prescription stimulants is widespread on college campuses. There is much less coverage of such use among high school students however. This is reflected in the state of the scientific literature as well; there is a recent, large, and growing literature on non-medical or "illicit" use of prescription stimulants among college students, but there are few studies of the high school population. Result from studies of high school students are highlighted below, but they are supplemented by findings from the much larger college student literature as appropriate.

The National Survey on Drug Abuse and Health (NSDUH; Substance Abuse and Mental Health Services Administration, 2011) is an annual survey of alcohol, tobacco, and illicit drug use in the U.S. noninstitutionalized civilian population aged 12 and over. Among the variables it tracks are several concerning the use of "prescription stimulants that were not prescribed for you or that you took only for the experience or feeling it caused?" (LeBaron & Dean, 2009 p. 145). Data on drug use and other sensitive topics are collected via computer-assisted audio self-interview with the use of cards containing drug names and pictures. Results from the 2010 survey found a lifetime prevalence of non-medical prescription stimulant use of 2.0% among persons aged 14-15, 3.8% among those 16-17, and 7.8% among respondents 18-20. Past-year prevalence estimates were 1.4%, 2.3%, and 3.9%, respectively. In 2010 there were approximately 2.9m past-year non-medical users of stimulants and 624,000 new users age 12 and older. Although the NSDUH list of stimulants includes methamphetamine, because the context is one of prescription drugs, it is unlikely that users of illegally produced methamphetamine would

answer in the affirmative regarding their use. The NSDUH's list of brand names of prescription stimulants is not exhaustive however, nor is limited to ADHD drugs. Notably, questions regarding non-medical use of Adderall, one of the most widely prescribed stimulants used in the treatment of ADHD, are asked separately. Rates of non-medical Adderall use are reported for college students only. Notwithstanding these methodological issues, the NSDUH results suggest that non-medical use of prescription stimulants for ADHD is common, especially among older adolescents and young adults.

A similar conclusion is reached from the results of the Monitoring the Future study (MTF; Johnston, O'Malley, Bachman, & Schulenberg, 2011), an annual survey of the alcohol, tobacco, and illicit drug-related behaviors of 8th, 10th, and 12th grade secondary school students, as well as college students and young adults. The surveys are administered in classrooms for the middle school and high school respondents. According to a the most recent (2010) secondary student survey, the lifetime prevalence of non-medical use of Ritalin and Adderall was 5.7%, 10.6%, and 11.1% respectively for 8th, 10th, and 12th-grade students. Past-year non-medical use rates were 3.9%, 7.6%, and 7.4% for students in the three grades. When broken out into separate medications and compared, the ratio of past-year Adderall to Ritalin use rates in the MTF is more than 2:1 in grades 10 and 12. This result, combined with the lower rates reported in the NSDUH (which excludes Adderall), highlights the importance of including as many stimulants as possible in survey prompts. Nevertheless, estimates from both of these studies are likely to represent a lower bound to actual use due to the limited number of ADHD drugs they inquire about and the somewhat limited scope of their definitions of "non-medical". These studies exclude improper use of a legitimately obtained prescription as instances of

non-medical use. Both of these issues, i.e., the range of drugs and the inclusiveness of the non-medical definition, also affect the smaller-scale studies described below.

Additional results from the MTF provide information on students' approval of the non-medical use of stimulants and their perceptions of the drugs' harmfulness and availability. A large majority of students in grade 12 expressed disapproval of trying Ritalin/Adderall once or twice (88%) or using them regularly (95%). In addition, 41% of 12th-grade respondents reported that there was "great risk" in trying Ritalin or Adderall once or twice, and 64% perceived regular use as carrying "great risk". Disapproval and perceived riskiness of the non-medical use of these stimulants have increased steadily since the mid-1990s. There has been a corresponding decline in the percentage of students in grades 8, 10, and 12 who perceive these drugs as "fairly easy" to "very easy" to obtain; the most recent statistics for the three grades are 20%, 33%, and 44%, respectively. Taken together these results indicate that middle school and high school students are increasingly less hospitable populations for the *recreational* non-medical use of stimulants. This pattern is consistent with downward trends in the rates of non-medical stimulant use reported in both the NSDUH and the MTF. However the limitations noted above require caution in making strong inferences from trends, which have been subject to reversals over the years. Furthermore, they don't directly address the use of these medications for their purported study related effects.

Several smaller-scale studies of middle and high school populations in selected districts tell a similar story, but add valuable detail on correlates, motivations, and use patterns of prescription ADHD drugs. In a Web-based survey of 1,086 7th- through 12th-grade students in a Michigan school district, 1.7% of students reported past-year non-

medical use of prescription stimulants, while 3.3% reported prescribed use of such medications (Boyd, McCabe, Cranford, & Young, 2006, 2007). Lifetime rates in the same sample, reported by McCabe, Boyd, & Young (2007) were 2.4% for lifetime non-medical use and 6.0% for lifetime prescription use. Prescribed use was also more common than non-medical use in another Michigan sample of students in grades 6-11: 6.4% vs. 4.5% for lifetime use, including 1.9% of respondents reporting both types of use (McCabe, Teter, & Boyd, 2004). The ratio of non-medical to medical use of stimulants in these studies of middle school and high school students stands in contrast to results from the researchers' college and university studies. In the younger population medical use is more frequent, whereas in the older group non-medical use outpaces medical use by a ratio of more than two to one (McCabe, 2008; McCabe, et al., 2006b). Finally, results from a national sample of students in grades 8, 10, and 12 revealed an increase in lifetime prevalence of non-medical Ritalin use from 2.7% in 8th grade students, to 4.6% in 10th graders, to 5.0% in 12th graders. (McCabe, Teter, Boyd, et al., 2004), perhaps setting the stage for even higher use among those who go on to college.

Results from the 1998 and 2002 waves of the Student Drug Use Survey in the Atlantic Provinces (SDUSAP; Poulin, 2001, 2007) produce a picture of middle and high school non-medical and medical stimulant use that is closer to the college and university findings reported by the McCabe et al. group and others. In both waves of this Canadian study, Poulin reported higher rates of non-medical use than seen in the Michigan middle and high school students (past-year prevalence values of 6.6% for exclusive non-medical use and 8.7% for combined non-medical and prescribed use) and a medical to non-medical use ratio well below 1:1. Differences in geography and study design make it

impossible to identify reasons for the discrepancy, but it should be noted that the 2002 SDUSAP's items concerning stimulants contain both (a) street drug names such as "bennies, pep pills, speed" that may not be familiar to legitimate users of stimulants or those receiving diverted drugs from them and (b) fewer ADHD drugs than are listed in other studies (i.e., Ritalin and Dexedrine are included, but other methylphenidate formulations and Adderall are missing). The 1998 SDUSAP survey items are even farther from constituting an exhaustive and exclusive list. These characteristics of the survey instruments make the high rates of non-medical stimulant use even more noteworthy.

Other findings related to non-medical use. Table 2 contains a summary of variables reported in the literature as correlates of non-medical use of prescription stimulants. It is based on studies of both college and middle/high school students, but it is implicitly weighted toward the former due to the relative sizes of the literatures. Nevertheless, the results are consistent across the younger and older populations. Older, and white, students involved with fraternities or sororities are among the most likely to use these drugs non-medically. Although most reports are cross-sectional, and care must be taken in inferring causal relationships, there is very strong evidence that non-medical users of prescription stimulants are significantly more likely to use or abuse tobacco, alcohol, and other drugs and to report associated problems, e.g., legal, medical, or family difficulties; blackouts; and inability to stop using drugs (cf. McCabe, et al., 2007).

Table 2
Summary of Key Findings Concerning Correlates of Non-medical Prescription Stimulant Use

Correlate	Pattern of results	Strength of evidence
Race/Ethnicity	Whites more more likely than African Americans	Strong and consistent
	Hispanics/Latinos similar to whites; Asians similar to African Americans	Moderate and consistent
Gender	Males more likely than females	Moderate and mixed
Age, Grade, Class Year	College students more likely than middle/high school students	Strong and consistent
	Older middle/high school students more likely than younger students	Limited and consistent
	Upperclass college/university students more likely than underclass students	Limited and mixed
Fraternity/Sorority Membership	Fraternity/sorority members more likely than nonmembers	Strong and consistent
Academic Performance/Plans	Students with lower college GPAs more likely	Strong and consistent
	Middle and high school students with lower grades more likely	Limited and consistent
	Middle and high school students without college plans more likely than those with plans	Limited and consistent
Psychological Constructs	Students high in Sensation Seeking, Perfectionism more likely	Limited and consistent
	Students who perceive low Riskiness of non-medical stimulant use more likely	Limited and consistent
Substance Use and Risky Behavior	Users of tobacco, alcohol, illegal drugs more likely	Strong and consistent
	Persons with positive screen for alcohol and/or drug dependence more likely	Moderate and consistent
	Persons who have driven after drinking, been a passenger with a driver who had been drinking, had more sex partners in past year more likely	Moderate and consistent

Non-medical users of stimulants are also more likely to be struggling academically than nonusers. They tend to have lower college grade point averages (Arria, Caldeira, Vincent, O'Grady, & Wish, 2008; McCabe, Knight, Teter, & Wechsler, 2005; McCabe, Teter, & Boyd, 2006a; Rabiner et al., 2009; Teter, McCabe, Boyd, & Guthrie, 2003; Weyandt et al., 2009) or high-school grades (Arria, 2008; McCabe, Teter, Boyd, et al., 2004). For example, in McCabe, Teter, and Boyd's (2004) sample of students in grades 8, 10, and 12, rates of non-medical Ritalin use were 2.6%, 3.9%, and 6.4% among students with A, B, and C averages, respectively. Non-medical users of ADHD medications have also reported more concerns about academic performance than non-users (Rabiner, et al., 2009). Arria (2008) has suggested that non-medical use of prescription stimulants may be driven in part by an attempt to compensate for skipped classes and time spent not studying. However, it is possible that some non-medical use of these medications represents an attempt at self-managing ADHD symptoms and that it is in fact the undiagnosed or undertreated ADHD that is causing some of these problems.

Finally McCabe et al. (2005), in a survey of students at 119 four-year colleges and universities in the U.S., reported that the rate of non-medical stimulant use was positively related to the competitiveness of a school's admission criteria. However, in another study they found that rates of non-medical use were higher among middle school and high school students without college plans (McCabe, Teter, & Boyd, 2004). Motivations for non-medical use were not assessed in the latter study however, and many non-medical users may have been driven by recreational, rather than study related, goals. This interpretation is supported by Boyd et al. (2006), who found that, in a sample from a

similar population from the same geographical area, only 29% of students cited study related motivations for their non-medical use of stimulants.

The relative infrequency with which stimulants are consumed among those who report using them for non-medical purposes suggests that such use may be more episodic than chronic. In Poulin's (2007) sample of students in grades 7, 9, 10, and 12, 84% of students who used methylphenidate for non-medical purposes in the past year used it one to four times (74% used prescription amphetamine one to four times). Unfortunately, information on timing of such use is not available for this sample or in the college and university studies that have also found that non-medical use of prescription stimulants occurs only a few times per year or has occurred infrequently in the respondents' lifetimes (Advokat, et al., 2008; McCabe & Teter, 2007; Prudhomme White, et al., 2006; Sharp & Rosen, 2007; Shillington, Reed, Lange, Clapp, & Henry, 2006). Given stimulants' recognized reinforcing properties and their ability to produce a high (Volkow & Swanson, 2003), more frequent use would not be unexpected. Therefore, their relatively infrequent use is noteworthy and raises the question of when the episodic use is occurring.

Access to Medications

As noted above, most supplies of stimulants used non-medically by high school and college students appear to be from legitimate prescriptions received by their peers. A few definitions of non-medical or "illicit" in the literature allow for misuse of one's own prescribed supply, but most are principally concerned with the use of diverted drugs, i.e., those transferred from one person to another via sharing, sale, or rarely, theft.

The non-medical use of prescription stimulants on college campuses is hardly a secret. Many students, whether or not they use the drugs themselves, know where to find pills and report that they are widely available. Prudhomme White, Becker-Blease, and Grace-Bishop (2006) reported that 28% of students surveyed at the University of New Hampshire claimed that it was easy or somewhat easy to obtain stimulants. The number was substantially higher among users: 58%. More than a third of students surveyed by Babcock & Byrne (2000) knew someone from whom they could purchase Ritalin, and a similar level of knowledge was reported by Hall et al. (2005). Some studies have reported even greater accessibility: 82% of students surveyed by DeSantis et al. (2008) responded that it was somewhat easy or very easy to find stimulants. In a related finding, Arria and colleagues (Arria, Caldeira, O'Grady, Vincent, Fitzelle, et al., 2008), found that 50% of students in their cohort had been offered stimulants by their sophomore year. Reporting similar results from a sample of middle and high school students, Moline and Frankenberger (2001) noted that 53% of students who were not taking prescribed ADHD medications indicated that some of their legitimately medicated peers gave away or sold some of their own pills.

Smith & Woody (2005) have noted that there are many possible points at which drugs can be diverted for non-medical use, from the sites of manufacture and wholesale distribution, through the point of prescribing, and down to the level of the consumer. Student reports from a variety of surveys reveal a much less complex picture for stimulants however: the drugs are coming from friends and peers. Moreover, they're coming without warnings, or indeed any information beyond their reputed benefits (DeSantis, et al., 2008). Most studies in which students are asked about their source of

prescription stimulants find that close to 80% or more received them from other students (Arria, Caldeira, O'Grady, Vincent, Johnson, et al., 2008; Barrett, Darredeau, Bordy, & Pihl, 2005; DeSantis, et al., 2008; Dupont, Coleman, Bucher, & Wilford, 2008; McCabe, et al., 2006b).

On the supply side, McCabe, Teter & Boyd (2006b) found that 54% of students with a stimulant prescription had been approached to divert their pills. Other surveys have found lower numbers for middle school and high school samples: 23% reported by McCabe, Teter & Boyd (2004) and 34% by Moline & Frankenberger (2001). Nevertheless, it is clear that drugs are changing hands from students with a prescription to those without. For example, Boyd et al. (2007) reported that 21% of students in their middle/high school sample with prescription stimulants gave away or "lent" their pills, and that the rate of "trading" pills (15%) was higher for stimulants than for other prescription drugs. Results from interviews reported by DeSantis et al. (2008) suggest that some *medical* users create a surplus by managing their prescribed supplies and using them only when needed. Thus, both the supplier and recipient are likely to be using these drugs outside established medical parameters.

Poulin (2001, 2007), in her research on middle school and high school students in four provinces in Canada, has found a relationship at the classroom level between sharing or selling prescription stimulants and non-medical use by classmates. For example, in New Brunswick and Nova Scotia samples, as the number of students in a classroom who reported giving their pills away increased from zero to one to two or three, the proportion of those classrooms that contained at least one non-medical user increased from 66% to 78% to 89% (Poulin, 2007) Similar results, at the person level, were reported in an

earlier study, which found that being in a classroom in which at least one student gave away or sold his/her prescription stimulants was associated with 50% higher odds of being a non-medical user of such drugs (Poulin, 2001). These results suggest that, when diversion of stimulant drugs occurs, they do not travel very far.

Malingering

Most students who use ADHD medications without a prescription get their supplies from peers, the majority of whom are likely to have a legitimate need for them. However, given the incentives that can accompany a diagnosis of ADHD, it is likely that some of these supplies come from students who misrepresented their symptoms in order to obtain medications. Nevertheless, such exchanges will be reflected in students' self-reports about their sources of diverted drugs. Such self-report data are rarely available, however, for students who manufacture or exaggerate ADHD symptoms in order to obtain medications and other benefits for themselves. This is largely a result of the survey prompts that are most often used to assess the non-medical use of these drugs. Surveys often inquire about use "without a doctor telling you to take them" or of medications "not prescribed to you?"

The design of the current study is intended to capture prescriptions that may be motivated by cognitive enhancement or study related goals regardless of whether the medications are acquired directly from doctors or from doctors via other students. This is necessary because, although there are no available estimates of the rate of malingering ADHD, the incentives associated with getting a medical diagnosis can be substantial. The Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV; American Psychiatric Association, 1994) defines malingering as the "intentional

production of false or grossly exaggerated physical or psychological symptoms motivated by external incentive such as avoiding military duty, avoiding work, obtaining financial compensation, evading criminal prosecution, or obtaining drugs" (p. 683). In the case of ADHD, these incentives can include medications, as well as extended time and other testing accommodations, preferential enrollment in classes or programs, and disability status (Harrison, 2006; Kane, 2008).

A number of studies involving students instructed to try to fake the presence of ADHD have found that they are quite capable of reporting diagnosis-relevant symptoms when completing symptom checklists (Harrison, et al., 2007; Jachimowicz & Geiselman, 2004; Quinn, 2003; Sollman, Ranseen, & Berry, 2010; Sullivan, May, & Galbally, 2007; Young & Gross, 2011). Outside the laboratory, information on ADHD symptoms is widely available online, in libraries, and from diagnosed peers. Symptom validity tests have been shown to be helpful in identifying students performing under a faking instruction set (Frazier, Frazier, Busch, Kerwood, & Demaree, 2008; Sollman, et al., 2010), but such tests are not included in the most widely used self-report instruments for ADHD. Poor effort or excessively bad performance on continuous performance tests of attention and on other neuropsychological measures may also indicate faking (Harrison, et al., 2007; Leark, Dixon, Hoffman, & Huynh, 2002; Quinn, 2003), but these measures are not widely used in the assessment context either, nor are they necessarily immune to malingering (Suhr, Sullivan, & Rodriguez, 2011).

These results highlight the importance of conducting a thorough evaluation of students presenting for evaluation of ADHD-related symptoms. This is particularly important when a diagnosis opens the door to desirable treatments and other benefits or

when current symptoms and performance are at odds with past academic achievement and medical history (Kane, 2008). Although the evaluation processes behind the diagnoses recorded in administrative claims data are unobservable, it is almost certain that some students in the current study population obtained their prescriptions by misrepresenting their need.

Finally it is also necessary to consider the possibility that some students with a legitimate need for ADHD treatment first present for evaluation only when academic pressure reaches a certain threshold. These first-time recipients of ADHD treatment may have done well earlier in their academic careers but later find themselves facing increased demands that exceed their capacities. Although the start of college seems like a natural time for this discrepancy to first occur, many high school students contemplating college may face it as well, particularly those living in high-achieving communities and faced with upcoming final exams. For this reason the term cognitive enhancement should be treated neutrally, as students seeking treatment for ADHD in anticipation of, or during, times of increased academic demand may include malingers seeking advantage, individuals with legitimate need seeking treatment for the first time, or even those seeking to treat their undiagnosed ADHD symptoms or unrelated learning problems.

Motivations for Non-medical Use

There appears to be only one published article addressing the motivations of middle and high school students to use stimulants without a prescription, and the results differed substantially by gender (Boyd, et al., 2006). Girls' most frequently endorsed motivation concerned alertness, followed by a second-place tie for concentration and getting high. Boys most often cited getting high and experimentation, followed by

addiction. The number of non-medical users in this study was extremely small however (13 girls; 12 boys), a fact that compels restraint in interpreting these results. The paucity of studies inquiring about motivation outside the college and university environment is unfortunate, but perhaps not surprising. Anecdotal and media accounts of non-medical stimulant use typically focus on post-secondary and, to a lesser extent private school, students. In these populations the narrative emphasis is usually on academic pressure and competitiveness. Outside this environment, non-medical use of any drug, including ADHD medications, may be viewed more simply as an undifferentiated substance abuse problem, whereas college use may invite a more nuanced, but certainly not benign, portrayal.

Much more information on motivations for using stimulants non-medically is available from the literature on college students. In this population, study related motivations seem to predominate. For example, Teter et al. (2006) found that the top three reasons for use supplied by lifetime non-medical users of stimulants were consistent with a self-treatment or academic enhancement motivation: 65% of students reported that they took the drugs to help their concentration, 60% to help them study, and 48% to increase their alertness. The fourth- and fifth-ranked reasons were consistent with recreational use however: getting high (31%) and experimentation (30%). Other studies report results consistent with these (Advokat, et al., 2008; Arria, Caldeira, O'Grady, Vincent, Fitzelle, et al., 2008; Carroll, et al., 2006; DeSantis, et al., 2008; Peterkin, Crone, Sheridan, & Wise, 2010). In some other reports recreational motives approach study motives in their frequency of endorsement (Dupont, et al., 2008; Low & Gendaszek, 2002; Prudhomme White, et al., 2006; Teter, McCabe, Cranford, Boyd, &

Guthrie, 2005). Study related and recreational motives are not necessarily at odds however; the sum of endorsement frequencies often exceeds 100%, indicating that students often cite multiple reasons for using stimulants. In addition, disentangling academic enhancement from self-treatment motivations is difficult without information on the presence of ADHD symptoms, which include poor concentration and inattentiveness. These are problems that plague many students, regardless of whether they meet the thresholds for seeking, and then receiving, a diagnosis (Harrison, 2004).

In most of the studies addressing users' motivations, the perception that the drugs are effective for study related uses is implicit: they're consumed for their purported benefit. However, one study evaluated self-reported experience and judgments of effects independently and found that, for the most commonly endorsed effects, there was a significant correlation between strength of endorsement and experience with non-medical use among college students. Non-medical users of stimulants were more likely to endorse effects such as "study longer", "study better", and "stay awake" than were non-users whose peers were non-medical users. A third group, non-users whose peers did not use stimulants non-medically, were the least likely to agree that they had such effects (Carroll, et al., 2006). Nevertheless, more than half of this last group believed that stimulants helped users to study longer. However they were also much likely than the other two groups to believe, mistakenly, that the drugs have a relaxing effect. In addition, Rabiner et al. (2009) found that college students who used stimulant medications consistently for non-medical reasons reported that they had the desired effects on concentration and studying most of the time (about 89% chose often or always), but that they were less reliable for "getting high" or to "feel better (59%, 64%).

These results suggest that students with direct or even indirect experience with the non-medical use of stimulant medications do understand their effects on cognition and also understand that these effects are specific rather than general.

Finally, it should be noted that newer formulations of ADHD medications make their recreational use more difficult. Atomoxetine is a non-stimulant and does not have the reinforcing properties of methylphenidate and amphetamine. Among stimulants, newer and more abuse-resistant delivery systems make it more difficult to achieve reinforcing effects. These include the system used by the prodrug lisdexamfetamine, whose active dextroamphetamine is biologically unavailable until it reaches the gastrointestinal tract (Madaan, 2008); a transdermal patch; and various extended-release or long-acting drugs in which release of the active ingredient is controlled osmotically or using coated beads. Notably, DuPont et al. (2008) found similar rates of student-reported study related (36%) vs. recreational (36%) use in their college student sample, but also discovered much higher endorsement of study related use (86%) among users of the extended-release, and relatively more abuse-resistant (DuPont & Bensinger, 2006), methylphenidate product Concerta. As use of these, and newer drugs, continues to increase cf. (cf. Castle, et al., 2007), the relative proportion of students who use them for studying will probably grow and recreational should become increasingly rare.

Chapter 3 - Method

Study Population and Inclusion Criteria

The core study sample comprised high school age (14-18) enrollees in private health insurance plans who had medical and pharmacy data in the Thomson Healthcare Medstat MarketScan Commercial Claims and Encounters Database (Medstat) and who initiated a treatment spell with a stimulant or atomoxetine. Data from multiple years (1997-2007) were combined in order to produce adequate sample sizes for the planned analyses; year-over-year longitudinal analyses were not conducted. Analyses incorporating county level academic performance measures for California were limited to the subset of Medstat enrollees in that state. For person-level analyses, individuals were included in the study sample for only one year in which they were eligible to receive healthcare services. Where enrollees met the criteria for a new treatment spell in multiple years, data from the earliest spell were used. A diagnosis of ADHD was not required for inclusion in the study samples (the core sample or other samples described below).

The beginning of a treatment spell was defined as the date of each enrollee's first observed prescription fill for any of the available medications listed in Table 1 (i.e., a stimulant or atomoxetine). The medications clonidine and guanfacine were not approved for treatment of ADHD during the 1997-2007 study interval. Treatment initiators were required to have been enrolled in a health insurance plan covered in the Medstat database continuously for the 12 months preceding and including the month the prescription was filled. This requirement served a number of purposes. First, it ensured that each enrollee identified as initiating treatment did not have a filled prescription for any of the medications in question for at least one year. Without such a requirement, newly enrolled

patients might have been identified as initiators solely because recent (i.e., pre-enrollment) prescription fills were unobservable. Second, the 12-month pre-initiation enrollment requirement eliminated the problem of sharp artifactual increases associated with a shorter look-back period (six months is common). For example, given a six month enrollment requirement period, enrollees initiating treatment in the second half of the year (July through December) would be more likely to be included in the study sample than first-half initiators. What would look to be a pronounced increase in July treatment spell initiation would instead be a reflection of the fact that most pre-July initiators would have faced the additional inclusion requirement that they be enrolled in a Medstat-included plan in both the current year and the previous year. Finally, the requirement of 12 months of continuous eligibility provided adequate time for evidence of comorbid medical, psychiatric/behavioral, and substance abuse conditions, as well as various measures of health care utilization, to be identified via examination of claims.

Three other study samples were generated in addition to the core sample of ADHD treatment initiators. In order to characterize the timing of stimulant and atomoxetine prescription fills, in the aggregate and regardless whether they were associated with a new treatment spell, a treated cohort was identified consisting of the population of enrollees age 14-18 who filled any prescriptions for one or more of the medications. No other enrollment criteria, beyond that implied by the fact that the medications were dispensed to the patients, were imposed. In order to provide denominators for the treated cohort and for the initiators cohort, two base samples were constructed: all Medstat enrollees age 14-18 (for the larger, treated cohort) and all Medstat enrollees age 14-18 with 12 months of continuous enrollment (for the initiators

cohort). The latter sample provides only an approximate base for the initiators because, without a treatment initiation date, there is no common anchor point from which to identify the 12-month enrollment span. As a consequence, full (12-month) eligibility in any year was used as the inclusion criterion. Individuals in both base samples were required to be enrolled in plans for which prescription drug data were reported in the Medstat database and to have valid enrollee identifiers.

Data Sources

Medstat MarketScan Commercial Claims and Encounters Database. The core data source for this study is the Thomson Healthcare Medstat MarketScan Commercial Claims and Encounters Database (Medstat). This database contains information on the health care utilization of several million persons per year in private insurance plans in the U.S., including inpatient, outpatient, and prescription drug data, as well as enrollment and eligibility information. Data are linkable within and across the various files through the use of an arbitrary enrollee identifier. Information on prescriptions includes the date that the prescription was filled, the days' supply, the quantity of the drug supplied, and each drug's National Drug Code (NDC). Additional drug information, including generic and label names, strength, and delivery system, was linked, via NDC, from the included RedBook drug data file or the separate First DataBank National Drug Data File (NDDF; First DataBank, 2007). Information in the inpatient and outpatient files includes conditions diagnosed, services received, and their associated dates. Together, this information allows for the creation of detailed enrollment, diagnosis, and treatment timelines. Age and sex are recorded in the data, but race and ethnicity are not. County of residence is also recorded, supporting the linkage to

community characteristics. Data were available for analysis for the years 1997 through 2007. The Medstat database meets HIPAA requirements for a limited-use data set. A request for exemption from review was approved by the Rutgers Institutional Review Board (IRB) for the use of these data.

California county level measures of academic performance. Data on academic performance within counties were available to be linked with enrollee-level data for Medstat enrollees in California through the California Department of Education Data and Statistics Web site (http://www.cde.ca.gov/ds/). Three sources of data were available for years that approximately overlap the years covered by the Medstat database: (1) SAT, ACT[2], and Advanced Placement (AP) exam data; (2) results from California's Standardized Testing and Reporting (STAR) program; and (3) results from the California High School Exit Exam (CAHSEE). Table 3 summarizes the availability of these data for the years for which Medstat data are available. SAT and AP results were available for 2001 onward and STAR results were available starting with 2003 data. CAHSEE results were available as early as 2001, but pre-2003 data are sparse as a consequence of the testing program's implementation schedule. For years where data were unavailable (or limited, in the case of the CAHSEE), data from the earliest available year were used (2001 for SAT and AP; 2003 for STAR and CAHSEE). While this had the potential to introduce unwanted homogeneity in the variables derived from these tests, the practical effect was limited. Given the year-by-year distribution of treatment initiators in California, this imputation of results from later years affected only 2% of SAT and AP data for initiators and less than 20% of STAR and CAHSEE data. Moreover, it was

[2] Because ACT data were available for very few students in California, they were not used as county level measures of academic performance in this study.

expected that there would be substantial between-county stability in average test results from year to year. This preliminary hypothesis was tested in order to evaluate the appropriateness of the imputation.

Table 3
Availability of California County Level Academic Performance Data by Year

	Data source		
Year	SAT/AP	STAR	CAHSEE[a]
1998	*2001*	*2003*	*2003*
1999	*2001*	*2003*	*2003*
2000	*2001*	*2003*	*2003*
2001	*2001*	*2003*	*2003*
2002	2002	*2003*	*2003*
2003	2003	*2003*	*2003*
2004	2004	2004	2004
2005	2005	2005	2005
2006	2006	2006	2006
2007	2007	2007	2007

*Note.*SAT = SAT Critical Reading and Mathematics (formerly Verbal and Quantitative), AP = Advanced Placement Program exams, STAR = California Standardized Testing and Reporting (California Standards Test) exam, CAHSEE = California High School Exit Examination.

[a] CAHSEE data for 2001-2002 are limited as a result of the test's implementation schedule. Therefore 2003 data were used for 2001-2002 and earlier years.

Variable Construction

Enrollee-level (Medstat) variables. All enrollee-level variables were extracted from the eligibility, inpatient, outpatient, and prescription drug data in the Medstat database. As noted above, data were subject to sample inclusion criteria, including eligibility and look-back periods. The key dependent variable for modeling ADHD pharmacotherapy initiation was the timing of the first-observed prescription fill. This variable took on one of three possible values:

1. The 30-week school year (excluding the period around final exams) period begins approximately in the third week of August and extends through April,

but excludes a period late in each year and early in the following year as described below.

2. The six-week final exam period extends from the beginning of May through the third week of June. This interval was designated based on examination of a sample of California high school calendars to include the actual exam period as well as a lead-in period during which students are assumed to be preparing for, or at least contemplating, the upcoming exams.
3. The eight-week summer period begins at the end of June and extends to the third week of August.

The interval from late November through the first several days of January was excluded from the three categories of the dependent variable. The purpose of this exclusion was to limit the effects of factors that could underestimate or overestimate the average rates of both prescription fills and initial treatment spells during the school year by removing from analysis those weeks surrounding the U.S. Thanksgiving and winter holidays. This is a period during which pharmacy claims for ADHD medications tend to be sharply reduced. Therefore, its inclusion would lower the average rates of prescribing compared with the final exam period. This result would provide unwarranted support for the hypotheses that prescribing and initiation would be higher during the final exam period than during the school-year.

The exclusion of the late November through early January period also avoids a sharp increase in members of the initiators cohort that would have been an unavoidable consequence of imposing a 12-month look-back period of continuous health plan enrollment. Enrollees initiating use of ADHD medications in December were able to

meet the 12-month enrollment requirement in the same year as their first filled prescription, whereas pre-December initiators must have been enrolled in both the current year and the previous year. If the late November to early January interval were included as part of the school year period the result would have been an artificial inflation of that period's average rate of treatment initiation. In summary, because the net effect of the competing under-inclusion and over-inclusion biases was unknown, a decision was made to exclude the late November through early January interval from the school year period.

There is some uncertainty in the boundaries marking the school year, final exam, and summer periods. Because the identification of these periods was based on the week of the year, where week 1 begins with the first Sunday in January, there was be some variability (up to six days) from year to year in the specific dates associated with each week. Moreover there is variation among schools both in final exam schedules and in the school calendars as a whole. In order to partially address this uncertainty, initiation rates were examined and compared according to the original period specifications and also under alternative specifications that shifted the boundaries of the three periods forward and backward by one or two weeks. These alternative specifications were used for exploratory purposes only; the original period definitions were used for all hypothesis tests.

Four types of enrollee-level independent variables were extracted or constructed: a limited number of sociodemographic variables, a set of indicators describing recent diagnosed conditions, variables characterizing initiators' first observed stimulant or atomoxetine prescriptions, and several service utilization variables intended to provide a

limited amount of information on overall clinical need. Table 4 contains a list of these variables.

Table 4
Enrollee-level Independent Variables

Enrollee characteristics	**Characteristics of prescriptions**
Sociodemographic variables	Generic Name
Age	Lisdexamphetamine
Sex	Amphetamine
	Dextroamphetamine
Most recent ADHD diagnosis	Methylphenidate
No recent ADHD diagnosis	Dexmethylphenidate
ADHD, inattentive type	Atomoxetine
ADHD, hyperactive or combined type	
	Relative resistance to abuse (desc.)
Provider type	Atomoxetine
No recent ADHD diagnosis	Concerta, Daytrana, Vyvanse
Family practice	Other long/intermediate-acting stimulant
Pediatrics (inc. specialists)	Immediate-release stimulant
Psychiatry/Child psychiatry	
Other Physician	Dose rank
Non-physician	
	Days' supply
Comorbid conditions	
Cardiovascular	**Service utilization**
Pervasive developmental disorders	Outpatient claims in past year
Seizures	Family Practice
Sleep disorders	Pediatrics (inc. specialists)
Tics	Psychiatry/Child psychiatry
Conduct disorder or Opp. Def. Dis.	Other Physician
Depressive disorders	
Anxiety and related disorders	Psychiatric claims in past year
Serious mental illness	Inpatient psychiatric claims
Substance abuse disorders	Outpatient psychiatric claims
	Other medications in past year
	Antidepressant
	Anxiolytic/Hypnotic
	Antipsychotic
	Mood stabilizer

The available sociodemographic variables were limited to age and sex. Presence of diagnosed comorbid medical, psychiatric/behavioral, and substance abuse conditions, as well as ADHD, were based on the occurrence of claims carrying qualifying ICD-9-CM diagnoses in the Medstat inpatient and outpatient claims data sets (see Table 5). Because the look-back period for continuous enrollment was only 12 months, a single diagnosis in any of the 15 inpatient fields or two outpatient diagnosis fields was considered sufficient evidence for the presence of a condition. Uncommon conditions, particularly, but not limited to, cardiovascular diagnoses, were grouped into higher-order categories to produce sufficient numbers of diagnosed enrollees. ADHD diagnoses in the 12 months prior to initiation were classified as (a) absent, (b) present, without hyperactivity (ICD-9-CM code 314.00), or (c) present, with hyperactivity (314.01). The type of service provider on the most recent claim carrying an ADHD diagnosis, if any, was classified into one of five categories: family physician, pediatrician (including pediatric specialists other than child psychiatrists), psychiatrist or child psychiatrist, other MD/DO, or other non-physician provider.

Several variables were extracted or constructed to characterize the first observed stimulant or atomoxetine prescription for each member of the initiators cohort. Generic drug names, linked from the supplied Redbook data via National Drug Code (NDC) were initially used to extract Medstat records, including enrollment and claims, for all enrollees who received one or more of the available medications (i.e., stimulants or atomoxetine) in Table 1 and again, after the study samples were identified, as one of several classification variables. Additional classification variables included a set of reduced generic name categories ([dextro]amphetamine, [dex]methylphenidate, or

Table 5
Diagnostic Categories and Codes

Diagnosis	ICD-9-CM Code(s)
Attention Deficit/Hyperactivity Disorder (ADHD)	
Attention deficit disorder, without mention of hyperactivity	314.00
Attention deficit disorder, with hyperactivity	314.01
Psychiatric and behavioral conditions	
Schizophrenia and other psychoses[a]	295.x, 297.x, 298.x
Bipolar disorders[a]	296.0x to 296.1x, 296.4x to 296.8x
Depressive disorders[b]	296.2x, 296.3x, 300.4, 311
Anxiety and related disorders[b]	300.x (exc. 300.4)
Conduct disorders[c]	312.x
Oppositional defiant disorder[c]	313.81
Pervasive developmental disorders	299.x
Substance abuse conditions	
Alcohol-related disorders[d]	291.x, 303.x, 305.00
Drug-related disorders[d]	292.x, 304.x, 305.1x to 305.9x
Medical conditions - cardiovascular	
Atherosclerosis and other diseases of the arteries[e]	440.xx-441.xx, 443.xx-445.xx
Coronary artery disease[e]	413.xx-414.xx
Cardiomyopathy[e]	425.x
Cardiac arrhythmia[e]	427.xx
Myocardial infarction[e]	410.xx-412
Moderate to severe hypertension[e]	401.x-405.xx
Other symptomatic cardiac disease[e]	390-398.xx, 426.xx, 429.xx
Cerebrovascular disease[e]	430-438.xx
Congenital abnormalities[e]	745.xx-746.xx, 747.0-747.4x, 747.8
Medical conditions - other	
Tics	307.2x
Sleep disorders	307.4x
Epilepsy and recurrent seizures	345.x

Notes. Conditions with shared superscripts were also grouped into higher-level categories: [a] serious mental illness, [b] depression or anxiety, [c] behavioral disorders, [d] substance abuse, [e] cardiovascular conditions. Diagnostic codes for cardiovascular conditions were adapted from Gerhard et al. (2010).

atomoxetine) as well as a set of categories ordered in terms of relative resistance to recreational misuse. From most resistant to least resistant these medications are: (a) the non-stimulant atomoxetine, (b) selected stimulants that are delivered in relatively abuse-

resistant form (osmotic release, transdermal patch, or the prodrug lisdexamphetamine), (c) other long-acting or intermediate-acting stimulants, and (d) immediate-release stimulants These various classification variables are not independent, and only one at a time was included when estimating the models described below. A variable was also constructed for the number of days supplied in the initial prescription fill. Values less than one or greater than 366 were recoded as missing. In addition, a categorical version of the days supplied variable was created with three levels: fewer than 30 days, 30 days, and more than 30 days.

An average daily dose variable was computed as (quantity supplied / days supplied) x drug strength. Drug strength values were merged from the First DataBank NDDF by NDC. Dose values were recoded as missing if any of several problems was identified: (a) a medication's strength value was missing or could not be directly represented in milligrams (e.g., if reported in the form 10 MG/5 ML), (b) days supplied was missing or recoded to missing because of out-of-range (<1, >366) values, or (c) quantity supplied was missing or recoded to missing because of out-of-range values (<1, >366) or (d) the computed average daily dose was less than 1 mg. or more than 200 mg. per day. These exclusions affected 1,348 enrollees (1.6%) in the initiators cohort.

Because it was impractical to create dose equivalencies across all of the stimulant medications and atomoxetine, average daily doses were categorized (using SAS Proc Rank; SAS Institute, 2009a) into five levels within each medication. The resulting dose rank variable, which characterizes the relative amount of the medication supplied compared with other prescriptions for the same medication, was then used in analyses in

place of the raw dose values.[3] The reference population for the dosage values comprised all stimulant or atomoxetine prescriptions for all recipients, regardless of initiator status. Table 6 summarizes the approximate daily dose values associated with the five levels for each of the medications.

Table 6
Average Daily Dose Ranks - Stimulant or Atomoxetine Prescriptions

Rank	Min. dose (mg/day)	Max. dose (mg/day)	Rank	Min. dose (mg/day)	Max. dose (mg/day)
Methylphenidate			Dexmethylphenidate		
0	1	20	0	2	10
1	20	36	1	10	10
2	36	40	2	10	20
3	40	54	3	20	20
4	55	200	4	21	160
Amphetamine			Dextroamphetamine		
0	1	15	0	1	10
1	15	20	1	10	15
2	20	30	2	15	20
3	30	40	3	20	30
4	40	200	4	30	135
Lisdexamphetamine			Atomoxetine		
0	5	30	0	1	39
1	45	45	1	40	59
2	50	50	2	60	60
3	60	69	3	61	80
4	70	140	4	80	200

Measures of service utilization were constructed to characterize enrollees' recent care histories as approximate measures of clinical need. Indicators were created for receipt of any inpatient services in the previous 12 months carrying a psychiatric diagnosis other than ADHD (ICD-9-CM code range 290-316, excluding 314.00 and 314.01). Receipt of outpatient services associated with psychiatric diagnoses was

[3] The dose rank variable was originally constructed within ages as well as within medications, but it was determined that average daily dose did not vary within the limited range of ages (14-18) included in this study.

represented by both a count of claims[4] and an indicator for receipt of any services. Indicators were also created for one or more filled prescriptions for each of four psychotropic medication classes (antidepressants, antipsychotics, mood stabilizers, and anxiolytics/hypnotics), for the number (zero to four) of medication types received, and for receipt of any of the four medications. Finally, past-year contact with a family physician, pediatrician or pediatric specialist, psychiatrist or child psychiatrist, other physician, any physician, or any primary care physician (family physician or non-specialist pediatrician) was represented by a set of indicator variables. The provider specialty variables were constructed across all outpatient visits, regardless of the presence or absence of an ADHD diagnosis.

California county level measures of academic performance. Several standardized test-based variables were extracted or constructed to characterize, at the county level, the average level of academic performance within each of the 57 (of 58) California counties large enough to yield summary data. They are described below. Table 7 contains a list of variables. Data were initially reported as means or percentages at various levels of aggregation before being combined if necessary, using appropriate weights, into county level statistics. Most descriptive analyses using the county variables were limited, however, to the 40 counties that each supplied 25 or more ADHD treatment initiators. All 57 counties were included in the plans for the random effects models because the empirical Bayes estimates they produce make efficient use of data from all groups (counties), taking into account within group variance (Raudenbush & Bryk, 2002).

[4] The original count variable was highly positively skewed, with many outliers. It was cleaned before analysis by recoding any values greater than 32 to 32. This affected the values for 835 of 82,057 initiators (1.2%).

Table 7
California County Level Measures of Academic Performance

Source and measure	Table abbreviation
SAT/AP	
SAT % tested	SAT %
SAT mean scale score – critical reading	SAT-R
SAT mean scale score - mathematics	SAT-M
SAT mean – critical reading plus mathematics scale scores	SAT-R+M
SAT % scoring more than 1,000 (critical reading plus math)	SAT %>1,000
Number of AP test scores of 3, 4, or 5 per grade 11, 12 student	AP 3, 4, 5
Number of AP test scores of 4 or 5 per grade 11, 12 student	AP 4, 5
STAR (CST)	
STAR ELA[a] test - scale score	STAR-ELA
STAR ELA test - % scoring proficient or advanced	STAR-ELA %PrAdv
STAR algebra I test - scale score	STAR-ALG
STAR algebra I test - % scoring proficient or advanced	STAR-ALG %PrAdv
CAHSEE	
CAHSEE ELA test - scale score	CAHSEE-ELA
CAHSEE ELA test - % passed	CAHSEE-ELA %Pass
CAHSEE mathematics test - scale score	CAHSEE-Math
CAHSEE mathematics test - % passed	CAHSEE-Math %Pass

Note. SAT = SAT Critical Reading and Mathematics (formerly Verbal and Quantitative), AP = Advanced Placement Program exam, STAR = California Standardized Testing and Reporting (California Standards Test) test, CAHSEE = California High School Exit Examination.

[a] ELA = English Language Arts

The SAT is the most widely used standardized test for college admissions. It measures skills in three areas; critical reading (formerly verbal ability), mathematics (formerly quantitative ability), and writing, and provides scale scores for each. Recent reliability estimates for the three subtests tend to be near or above 0.90 (The College Board, 2011b) and there is validity evidence for the test's ability to predict first-year college GPA (Kobrin, Patterson, Shaw, & Barbuti, 2008). Critical reading and mathematics scale scores range from 200-800. The SAT summary variables prepared for

the current analysis were: percentage of 12th grade students tested, average critical reading and mathematics scale scores; average combined (critical reading plus mathematics) scale score, and percentage of test takers with a combined score greater than 1,000. Scores from the writing test, introduced in 2005, were not used.

The Advanced Placement (AP) tests represent the standardized testing component of the College Board's Advanced Placement Program. Students can take tests in a variety of subject areas (32 as of the 2011-2012 school year) in order to earn college credit or advanced standing (The College Board, 2011a). Scale scores range from one to five. Scores of three ("qualified"), four ("well qualified"), or five ("extremely well qualified") are usually needed in order to earn credit or standing. County level AP results available from the California Department of Education included the number of exams that received each of the five possible scale scores. Two analytic variables were derived from these data: the number of exams with a score of (a) three or higher, and (b) four or higher, per 11th or 12th-grade student.

The Standardized Testing and Reporting (STAR; California Department of Education, 2011) program was designed to evaluate the academic skills of California students. Most public school students take the California Standards Tests (CST). Other STAR tests are used for English learners and students with cognitive disabilities. The CSTs are administered in March to April of the school year and cover the following four content areas: English Language Arts (ELA; grades 2-11), mathematics (grades 2-11), science (grades 5, 9, 10, and 11) and history and social science (grades 8, 10, 11). Several mathematics and science tests are offered at the secondary level; selection of specific tests is based on current or recently completed coursework. Both scale scores

and proficiency levels (far below basic, below basic, basic, proficient, advanced) are reported. For the current study, analytic variables (mean scale scores and mean percentage of examinees scoring in the proficient or advanced categories) were computed, across grade levels in each county for the ELA and Algebra I tests administered to students in grades 9-11. Means were weighted within each county based on the number of examinees in each grade. Published reliability estimates for the ELA and mathematics tests were between 0.90 and 0.94 in 2007, the latest year for which STAR data were used for this study (Educational Testing Service, 2007b).

First administered on a voluntary basis in 2001, and required for a high school diploma beginning in the 2005-2006 school year, the California High School Exit Exam (CAHSEE; http://www.cde.ca.gov/ta/tg/hs/cefcahsee.asp) program administers ELA and mathematics tests to high school students beginning in grade 10. Students who do not pass both tests when first administered have up to two opportunities to pass each in grade 11 and five opportunities in grade 12. For the current study, ELA and mathematics data (mean scale score, mean percentage passed) were extracted from the California Department of Education's database for grade 10, i.e., first-time, examinees. First time pass rates for the February, March, and May 2007 CAHSEE administrations were 77%, 78%, and 48% for first-time ELA examinees and 77%, 76%, and 48% for first time mathematics examinees. Cumulative pass rates, through grade 12, are considerably higher than first-time rates (between 90% and 95% of students eventually passed both tests in recent years, see http://www.cde.ca.gov/nr/ne/yr11/yr11rel59.asp) and are therefore less able to capture between-county variability. The use of only grade 10 results is consistent with this study's intent to distinguish among higher-performing and lower-

performing counties. Analytic variables were constructed by creating within-county means, weighted across multiple test administrations by the number of students who took the test at each administration. Published reliability estimates for the CAHSEE ELA and mathematics tests ranged from 0.85 to 0.95 in 2006-2007 (Educational Testing Service, 2007a).

Analysis Plan

Preliminary analyses. Prescribing patterns for stimulants and atomoxetine were first examined, both for overall prescription rates and for rates of initiation. Data for 1997-2007 were combined to produce aggregate, across years, sets of prescription timelines for the weeks encompassing the school year, final exam, and summer periods. Prescribing patterns for SSRI antidepressants were examined in the same way. The base sample for prescription-level rates comprised all Medstat enrollees age 14-18 in plans reporting prescription drug data and with valid enrollee identifiers. The base sample for treatment initiation rates imposed the additional requirement that enrollees have 12 or more months of continuous plan enrollment in at least one year.

Examination of prescribing patterns over the year provided the first evidence addressing the hypothesis that prescription fill rates would be highest for ADHD medications when academic demands are at their greatest for most high school students, i.e., during the final exam period. A more formal test of this hypothesis was performed by comparing average treatment initiation rates across the weeks in each period. These comparisons were also performed using alternative definitions of the school year, final exam, and summer periods that were shifted by one or two weeks earlier or later in the year. Hypotheses were not formally evaluated under these alternative specifications.

County level measures of academic performance were examined with respect to their variability, intercorrelations, and relationships with treatment initiation during the final exam period. These analyses were intended to provide a basis for selecting variables to include in the random effects models, to evaluate the degree of between county variation in final exam period initiation, and as an initial test of the hypothesis that final exam period initiation of pharmacotherapy for ADHD would be higher in academically higher performing counties.

Preliminary tests of the hypotheses that physicians exercise more than usual caution, in terms of the patients they elect to treat and the ADHD medications they prescribe, when students present for treatment during the final exam period, were conducted by examining the bivariate relationships between initiation timing and a variety of enrollee and medication variables.

Random effects models. The core analyses, limited to initiators of pharmacotherapy for ADHD, were designed to comprise a set of hierarchical general linear models (HGLMs) incorporating enrollee and medication variables as predictors of initiation timing. The intercepts and selected slopes associated with the enrollee and medication variables were to be treated as random effects and regressed on county level measures of academic performance. The dependent variable for these models was represented as a set of three unordered categories. Therefore, a generalized logit link was used to transform the probabilities associated with category membership for analysis. The plan to include county level measures, which were available only for enrollees in California, required that the models incorporating predictors at that level be limited to treatment initiators in that state.

In HGLM models with a multinomial outcome variable Y with three categories, the probabilities of an observation being in each category are represented as:

$$Prob(Y_{1ij}) = \phi_{1ij} \tag{3-1}$$

$$Prob(Y_{2ij}) = \phi_{2ij} \tag{3-2}$$

$$Prob(Y_{3ij}) = \phi_{3ij} = 1 - \phi_{i1j} - \phi_{2ij} \tag{3-3}$$

If the probabilities associated with any two categories are known, then the probability for the remaining category is also known. Give three categories in the dependent variable, there are two coefficients for each predictor. In the current study initiation during the school year was selected as the reference category for Y and separate coefficients were estimated for the transformed probability of final exam period vs. school year initiation and for summer vs. school year initiation.

The generalized logit link transforms the probabilities into the log odds of an enrollee initiating pharmacotherapy for ADHD in period m vs. period M (the reference category):

$$\eta_{mij} = \log(\frac{\phi_{mij}}{\phi_{Mij}}) \tag{3-4}$$

The transformed probabilities are then modeled as a linear function of a set of effects that can be treated as fixed or varying randomly among counties:

$$\eta_{mij} = \beta_{0j(m)} + \beta_{1j(m)}X_{1ij} + \beta_{qj(m)}X_{qij} \tag{3-5}$$

For the planned analysis, the intercepts and selected slopes were to be treated as random effects, each of which could be modeled as a function of a set of county level measures of academic performance (the W variables).

$$\beta_{0j(m)}=\gamma_{00(m)} + \gamma_{01(m)}W_{1j} + \gamma_{0s(m)}W_{sj} + u_{0j(m)} \quad (3\text{-}6)$$

$$\beta_{qj(m)}=\gamma_{q0(m)} + \gamma_{q1(m)}W_{1j} + \gamma_{qs(m)}W_{sj} + u_{qj(m)} \quad (3\text{-}7)$$

Models were to be tested in the following sequence:

1. Intraclass correlations were to be computed to index the proportion of variance in initiation timing attributable to between-county differences vs. between-enrollee differences.
2. Initiation timing models were to be estimated with only enrollee-level (level-l) predictors, including characteristics of enrollees and of their initial prescriptions.
3. Initiation timing models were to be estimated by treating level-1 intercepts as random coefficients and regressing them on level-2 predictors. The intent was to identify main effects of county (level-2) predictors on initiation timing.
4. Hypotheses regarding the moderating effects of county level variables were to be evaluated by using them as predictors of selected level-1 slopes treated as random effects.

The HGLM analyses were conducted using HLM 7 (Raudenbush, Bryk, Cheong, Congdon, & du Toit, 2011) and Proc GLIMMIX in SAS 9.2 (SAS Institute, 2009b).

Modified analysis plan. The analytic plan was revised after examination of preliminary results indicating that there was negligible between-county variation in the timing of treatment initiation. Follow-up models, using the same multinomial outcome

variable, were then estimated treating the coefficients as fixed. With no need to model the coefficients as outcomes associated with California county level variables, the analytic population was expanded to include all enrollees who initiated pharmacotherapy for ADHD during one of the three periods, regardless of state.

Chapter 4 - Results

Overview

This chapter begins with a brief overview of the cohort construction process resulting from the application of the inclusion criteria. It will then be organized, to the extent possible, according to the hypotheses described in Chapter 1. Several analytic conventions are used throughout this chapter and its tables. Pearson product-moment correlation coefficients were used to compute correlations across the California counties for which academic performance variables were available. Descriptive county level analyses were limited to the 40 counties that each contributed 25 or more ADHD treatment initiators; the remaining 18 counties were excluded from these analyses. Together the 40 counties accounted for 97.7% of the California residents beginning treatment with a stimulant or atomoxetine. All counties except Alpine[5] were included in the initial (and, as it turned out, only) random effects model. Tables comparing initiation rates during the school year, final exam period, or summer, by enrollee and medication characteristics, include 95% confidence intervals based on the standard normal distribution. For clarity of presentation only point estimates will be noted in the text, along with commentary on statistical significance.[6] As noted in Chapter 3, the regression models have a multinomial dependent variable, transformed via the generalized logit link function. The school year period was designated as the reference category for the dependent variable, thus yielding two coefficients and two odds ratio estimates per

[5] Aggregate academic performance data for Alpine county, population 1,189 in 2010, were not reported due the small numbers of test takers.

[6] Evaluating statistical significance from the lack of overlap between 95% confidence intervals for independent groups results in a test with Type I error rate (α) substantially less than 0.05 [cf. Schenker, N., & Gentleman, J. F. (2001). On judging the significance of differences by examining the overlap between confidence intervals. *The American Statistician, 55,* 182-186.] The Appendix contains the actual significance values, for selected tables, for each pairwise comparison.

predictor: final exam period vs. school year and summer vs. school year. Categorical predictors were represented as sets of k-1 dummy variables.

Figure 1 presents a summary of the cohort construction process as the inclusion criteria described in Chapter 3 were applied. While data for more than 5.3m enrollees age 14-18 were available, only about 4.2m had a flag indicating that prescription drug data were available for the health plans in which they were enrolled. This base sample provided the denominator for rate calculations involving receipt of ADHD medications or SSRIs. Slightly more than half of this group (approximately 2.2m) met the requirement of having at least12 months of continuous enrollment at some point during their appearance in the Medstat database. This base sample provided the denominator for rates of stimulant/atomoxetine or SSRI treatment initiation. Within this group, 94,007 enrollees (9,279 California enrollees) met the final criterion for treatment initiation: a filled prescription for an ADHD medication preceded by a 12-month period with no such prescription fills. Of these treatment initiators, 82,057 (8,046 in California) initiated treatment during the school year, final exam period, or summer. The remainder began treatment between late November and early January, a period that was excluded from analysis for the reasons described in Chapter 3. Finally, because of the 12-month enrollment requirement, the 1997-2007 Medstat database yielded treatment initiators for the years 1998-2007 only.

The core study sample – initiators of pharmacotherapy for ADHD – was 68% male. The majority (59%) was age 14 (mean age 14.9 years). Where a recent diagnosis of ADHD was recorded, hyperactivity was an element in the diagnosis for 54% of initiators. The most commonly observed comorbid conditions were depressive disorders

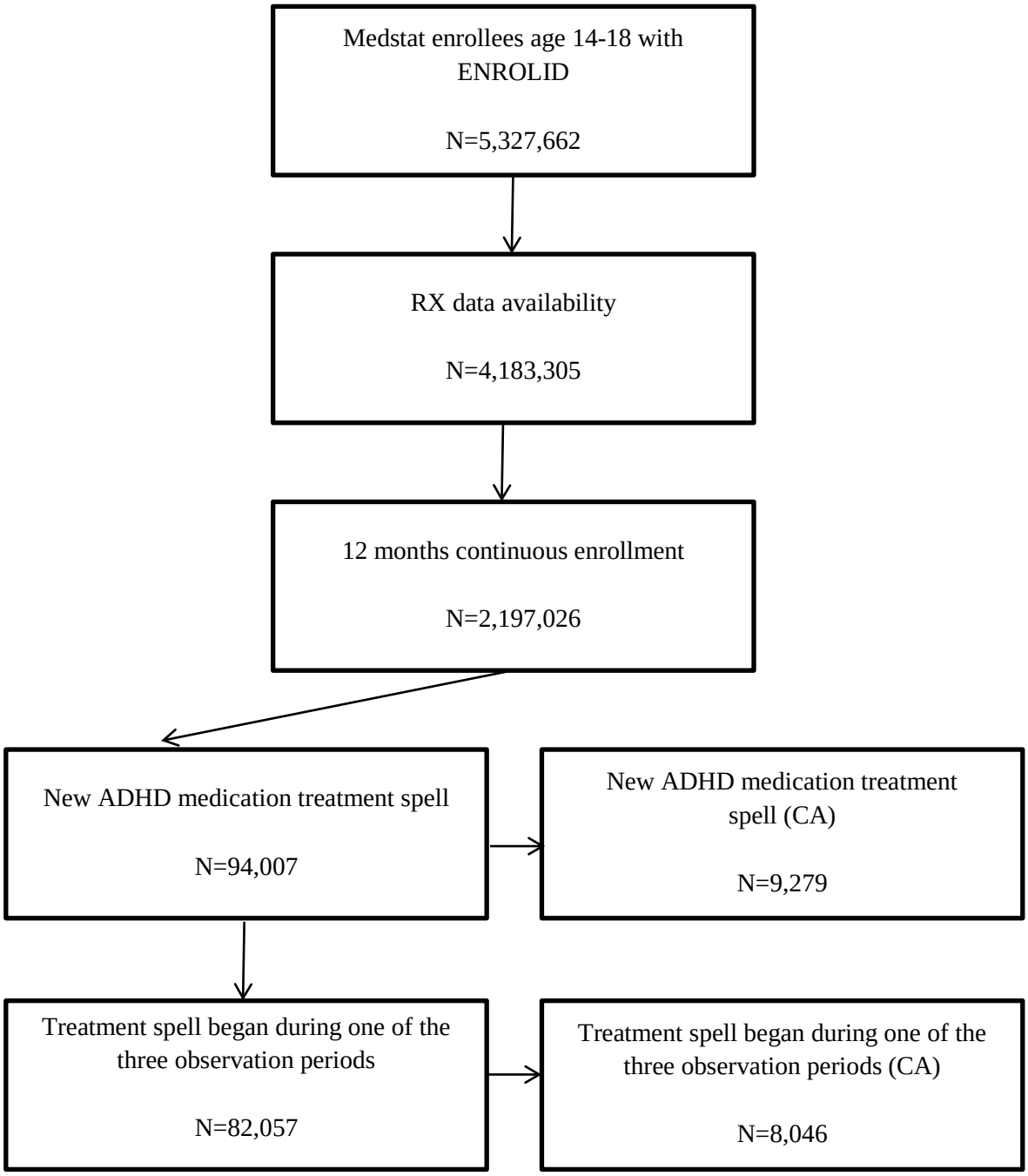

Figure 1. Cohort construction.

(13.5% of initiators), serious mental illness (9.7%), anxiety and related disorders (6.2%), and conduct disorders or oppositional defiant disorder (4.6%). The initially prescribed medication was methylphenidate or dexmethylphenidate for 48% of enrollees, amphetamine, dextroamphetamine, or lisdexamphetamine for 38%, and the nonstimulant

atomoxetine for 14%. Most stimulant prescriptions (74%) were for intermediate- or long-acting formulations.

Prescription and Initiation Rates

Figure 2 contains rates of prescription fills per 100,000 enrollees, separately for ADHD medications and SSRIs, for the subpopulation of enrollees age 14-18 in plans that provided prescription drug data. Data have been aggregated across years for all of the rate figures described in this section. It is evident that prescription fills for stimulants and atomoxetine reflect the expected seasonality and that no such seasonality is apparent for the antidepressants. Many students appear to discontinue or reduce their use of ADHD medications from the end of the school year through the summer. It is equally apparent that the hypothesized increase in prescription fill rates in the period leading up to and including final exams did not occur. Moreover, the difference in patterns for the ADHD medications and the SSRI antidepressants suggest that the final exam period and summer decrease for the former do not simply reflect a decrease in the prescribing of psychotropic medications in general.

In contrast to overall prescription fill rates, the rates of ADHD pharmacotherapy *initiation* presented in Figure 3 appear to reflect seasonality for both types of medications. The data in this table are limited to enrollees with 12 months or more of continuous plan enrollment. The exam period/summer decrease, and the subsequent late summer rebound for ADHD medications in particular, is much more dramatic than it is for SSRIs however. Given the degree of comorbidity between ADHD and depression and anxiety disorders it is possible that for some youth the initiation of ADHD medication is also the occasion for beginning treatment with SSRIs, and this might

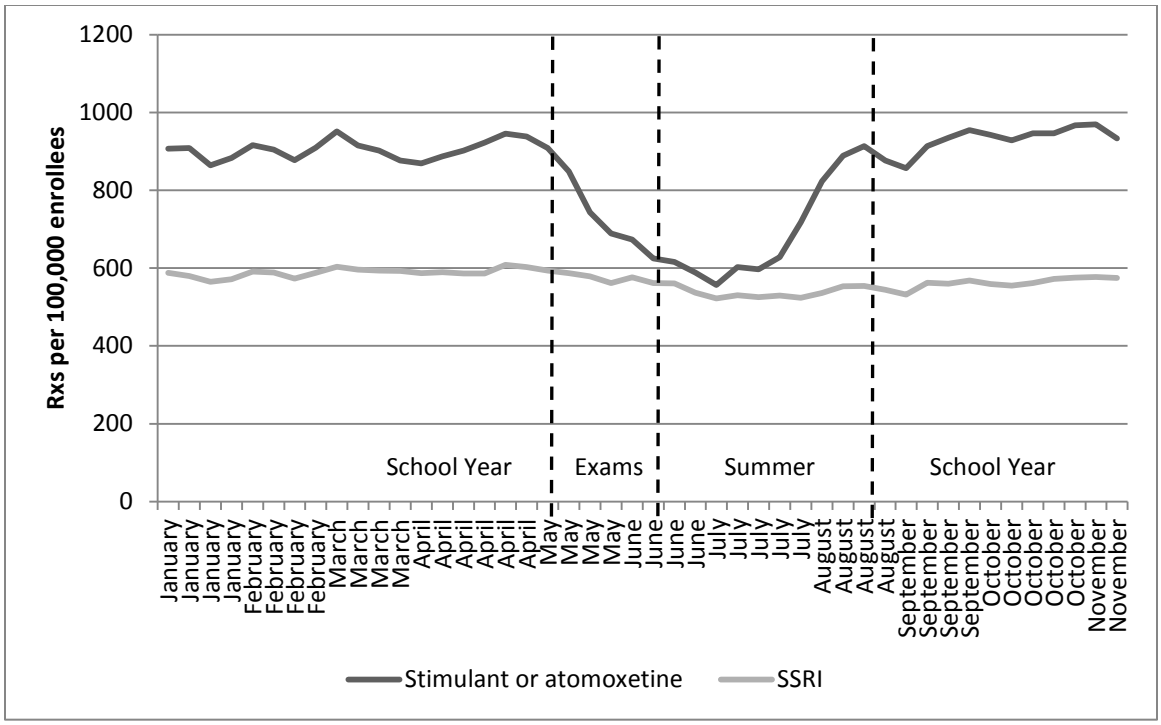

Figure 2. *Prescription fill rates.*

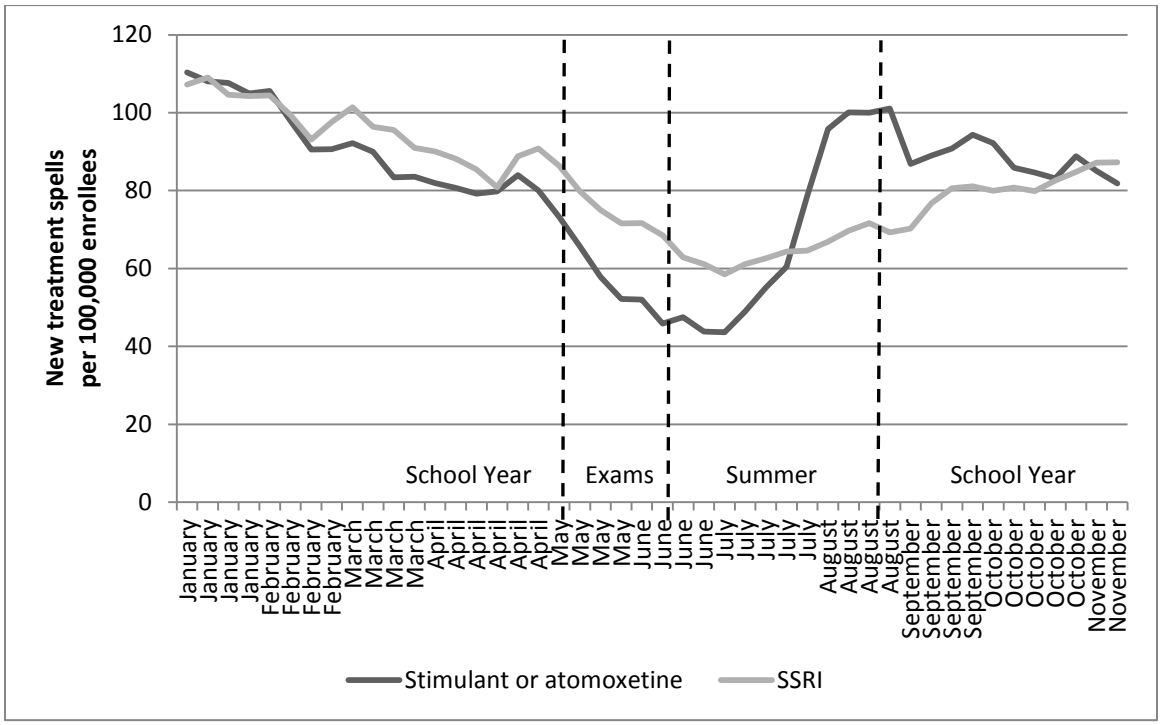

Figure 3. *Pharmacotherapy initiation rates.*

account for some of the observed synchrony. The 12-month eligibility requirement imposed on the initiators subcohort has ensured that the peaks and valleys in this figure are not artifacts of plan enrollment. Like the prescribing rates, the initiation rates show no evidence of the expected increase in the final exam period.

Finally, Figure 4 addresses the question of whether initiation rates for stimulants and atomoxetine differ with respect to enrollees' diagnostic status. The shaded areas of the figure represent subgroups of initiators whose most recent outpatient visit with a service provider carried a diagnosis of ADHD without hyperactivity (predominantly inattentive type, 25% of initiators) or with hyperactivity (predominantly hyperactive type or combined type, 29% of initiators). The third group contains initiators whose claims history showed no evidence of an ADHD diagnosis in the past year (46% of initiators). There is remarkable consistency in the relative distribution of these groups across the year; initiators with a diagnosis implicating hyperactivity never represent less than 27% or more than 35% of the total, and those without hyperactivity never account for less than 20% or more than 27%. The hypothesis that final exam period initiation would, as a consequence of prescribers' caution and patients' presenting symptoms, be more likely for enrollees with the predominantly inattentive type of ADHD was not supported.

A more formal test of the hypothesis that initiation rates for ADHD medications would be highest in the final exam period and lowest during the summer is provided in Table 8. As indicated in the table, 72.7% of initiators began treatment during the 30 weeks in the school year period, 9.3% initiated during the six weeks associated with final exams, and 18.0% initiated during the ten-week summer period. The rates (per 100,000 enrollees) for each period were calculated by computing the mean rate across the

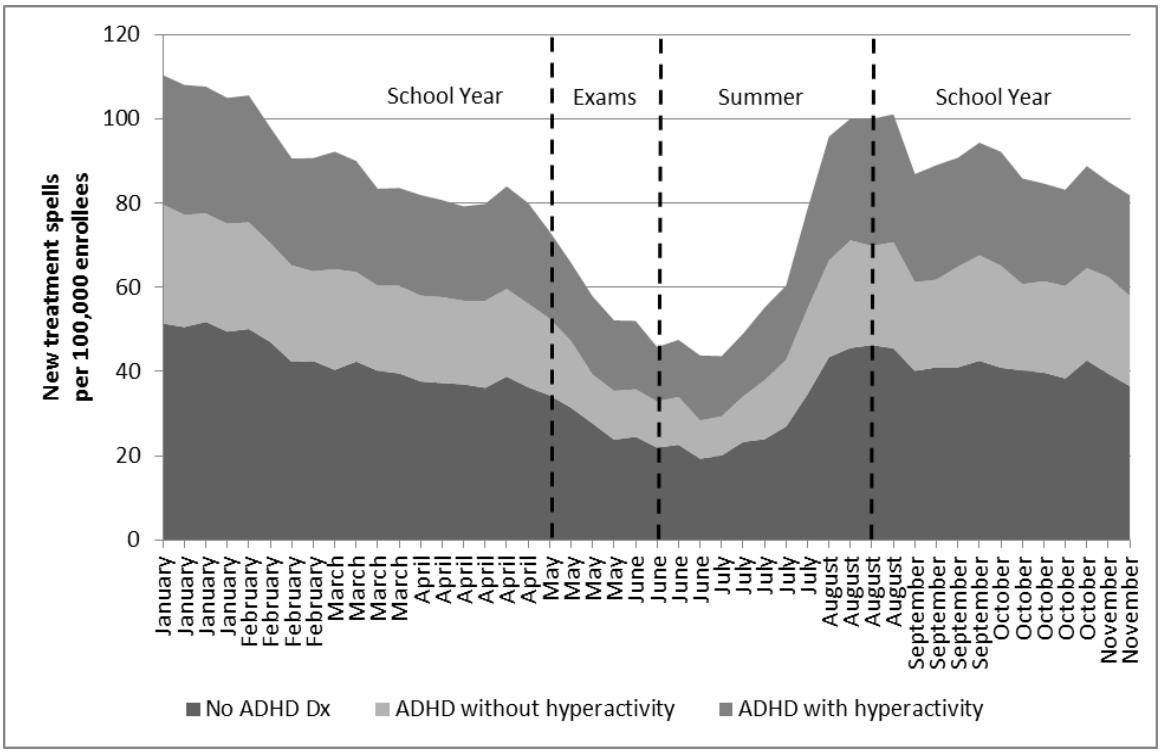

Figure 4. ADHD pharmacotherapy initiation rates by diagnosis.

weeks in the period. The average rate of treatment initiation was, contrary to hypothesis, lowest in the final exam period (57.8 per 100,000). It was significantly higher during the school year (90.5) as well as during the summer period (67.4). All comparisons are based on a normal approximation to the binomial test (Zar, 1999).

An exploratory analysis, also reported in Table 8, was conducted in order to re-evaluate the results under the assumption that the start and end dates for the three periods had been mis-specified. It was not intended to change the definitions of the three periods for any other analysis. Alternative periods were defined by moving the start and end dates for the final exam and summer intervals backward (earlier) and forward (later) by one or two weeks. Moving the periods backward resulted in an increase in the final exam period initiation rate and a decrease in the summer rate. Moving the period boundaries

Table 8

Average Rates of Treatment Spell Initiation by Period

	Initiation period			
	School year [a]	Final exams [b]	Summer [c]	Differences between periods
Number (percentage) of treatment initiators	59,628 (72.7%)	7,621 (9.3%)	14,808 (18.0%)	
Weeks in period	30	6	10	
Mean weekly rate per 100,000 enrollees (with 95% CIs)	90.50 (90.13 - 90.87)	57.80 (57.50 - 58.10)	67.40 (67.08 - 67.72)	a>b, a>c, b<c
Effects of moving period boundaries (rates with 95% CIs)				
One week earlier	91.13 (90.75 - 91.51)	63.51 (63.19 - 63.83)	61.98 (61.66 - 62.30)	a>b, a>c, b>c
Two weeks earlier	91.67 (91.29 - 92.05)	68.83 (68.50 - 69.16)	57.18 (56.87 - 57.49)	a>b, a>c, b>c
One week later	89.54 (89.16 - 89.92)	53.53 (53.23 - 53.83)	72.75 (72.41 - 73.09)	a>c, a>c, b<c
Two weeks later	88.83 (88.45 - 89.21)	49.88 (49.59 - 50.17)	77.06 (76.71 - 77.41)	a>c, a>c, b<c

Note. N=82,057.

forward produced the opposite effect. It is notable, however, that in no case did the final exam period rate approach the school year rate.

Descriptive Statistics for California County Measures of Academic Performance

In this section statistics regarding the county level measures of academic performance are reviewed in light of their planned role in the random effects models that concern the remaining hypotheses. As described in Chapter 3 and presented in Table 3, California county level data were not available for all of the years from 1997 through 2007. As a result, it was necessary to populate performance statistics from earlier years with data from the first year of availability (e.g., CA STAR data from 2003 were used also for the years 1997-2002). The appropriateness of this decision, however, depends on adequate year-over-year stability in the measures. Evidence for this stability is contained in Table 9, which presents correlations between the earliest and latest available years of data, computed across the 40 counties that each supplied 25 or more treatment initiators. The correlations are very large, positive, and significant; 12 of the 15 reported values are above 0.90. It is also worth noting that the analytic sample, reflecting the overall cohort of initiators, is heavily biased toward later years (see Table 10). As a consequence, 6,647 of the 8,046 California initiators (83%) began treatment in 2004 or later - years for which data were available for all tests and for which the simple imputation of values for earlier years was not necessary. These results support the decision to use the earliest year of available data to provide values for prior years.

Table 11 contains descriptive statistics for the California county level measures of academic performance for the 40 counties with 25 or more initiators. All of the values are plausible and within the scale ranges, where available, published in the various

technical reports. There is no evidence of restricted variance for any of the measures. This table also provides confirmation that derived measures (SAT % >= 1,000, and the two AP measures) we computed correctly.

Table 9
Stability Coefficients Between Earliest and Latest Available Years of Data for California County Level Measures of Academic Performance

Measure	Correlations computed between years	r
SAT/AP	2004 and 2007	
SAT %		0.97*
SAT-R		0.96*
SAT-M		0.98*
SAT-R+M		0.97*
SAT %>1,000		0.76*
AP 3, 4, 5		0.99*
AP 4, 5		0.99*
STAR	2003 and 2007	
STAR-ELA		0.95*
STAR-ELA %PrAdv		0.96*
STAR-ALG		0.64*
STAR-ALG %PrAdv		0.55*
CAHSEE	2003 and 2007	
CAHSEE-ELA		0.96*
CAHSEE-ELA %Pass		0.94*
CAHSEE-Math		0.96*
CAHSEE-Math %Pass		0.93*

Note. Each county contributed one observation. Only counties with 25 or more treatment initiators were included (40 of 57 counties), df=39 for all correlations.

* p<.01 (one-tailed).

Table 12 contains the correlations among the California county level measures of academic performance. All of the correlations were significant (p<.01, one-tailed) with the exception of those presented in grey text. The convergent validity correlations, outlined in the table, among the reading and language tests (SAT critical reading, STAR

Table 10
Base Population and ADHD Pharmacotherapy Initiators by Year

Year	Base N[a]	All initiators	CA initiators
1997	6,113	0	0
1998	27,754	1,481	15
1999	63,490	3,204	33
2000	95,461	2,485	32
2001	243,928	2,959	37
2002	496,826	5,661	499
2003	805,749	9,096	783
2004	771,201	14,874	2,226
2005	645,814	15,056	2,030
2006	649,587	12,622	1,180
2007	874,274	14,619	1,211
Total		**82,057**	**8,046**

Note. Initiators are limited to those who started treatment during the designated school year, final exam, or summer periods.

[a] Comprises plan enrollees in the Medstat database age 14-18 with 12 or more months of continuous eligibility who were in a plan that reported prescription drug data.

ELA, and CAHSEE ELA) are quite high; all are 0.84 or greater. The results for the SAT mathematics, the STAR algebra I, and the CAHSEE mathematics tests are puzzling however. The correlations between the SAT measure and the STAR and CAHSEE measures were all lower, between 0.54 and 0.63 ($p<.01$ for all), and the correlations between the STAR and CAHSEE tests ranged from 0.18 to 0.24 (all ns.). Moreover, the SAT mathematics test was much more strongly correlated with the STAR and CAHSEE ELA tests than with the math tests; correlations ranged from 0.83 to 0.90. The correlation, across the 40 counties, between mean SAT critical reading scores and mean SAT mathematics scores was 0.93. Based on these results, which suggest that counties can be reliably ranked with respect to their average SAT scores in particular, the combined SAT critical reading and mathematics score was selected as the initial county

Table 11
Summary Statistics for California County Level Measures of Academic Performance

Measure	N counties	Mean	SD	Quartiles	CV[a]
SAT/AP					
SAT %	40	32	11	24 / 31 / 37	33.4
SAT-R	40	504	32	477 / 507 / 531	6.4
SAT-M	40	520	31	489 / 531 / 545	6.0
SAT-R+M	40	1,025	62	969 / 1,039 / 1083	6.1
SAT %>1,000	40	22	12	12 / 19 / 29	56.9
AP 3, 4, 5	40	0.18	0.11	0.10 / 0.15 / 0.25	58.9
AP 4, 5	40	0.10	0.07	0.05 / 0.08 / 0.14	69.3
STAR					
STAR-ELA	40	330	12	320 / 331 / 336	3.6
STAR-ELA %PrAdv	40	38	9	30 / 39 / 43	23.7
STAR-ALG	40	296	9	289 / 295 / 303	3.0
STAR-ALG %PrAdv	40	12	4	8 / 12 / 16	35.0
CAHSEE					
CAHSEE-ELA	40	381	9	374 / 381 / 388	2.3
CAHSEE-ELA %Pass	40	79	7	75 / 79 / 84	8.5
CAHSEE-Math	40	372	12	364 / 371 / 380	3.1
CAHSEE-Math %Pass	40	69	11	64 / 69 / 77	16.0

Note. Each county contributed one observation. Only counties with 25 or more treatment initiators were included (40 of 57 counties).

[a] CV = coefficient of variation.

level variable to be used in the random effects models. The STAR algebra I and CAHSEE mathematics tests were also considered for inclusion, given their more modest correlations with the combined SAT measure, and notwithstanding concerns about the nonsignificant correlations between them. The measures of AP test performance were also selected as likely candidates, sharing only 25% to 30% of their variance with the other measures.

Table 12

Correlations Between California County Level Measures of Academic Performance

Measure	SAT-R	STAR-ELA	STAR-ELA %PrAdv	CAHSEE-ELA	CAHSEE-ELA %Pass	SAT-M	STAR-ALG	STAR-ALG %PrAdv	CAHSEE-Math	CAHSEE-Math %Pass
STAR-ELA	0.84									
STAR-ELA %PrAdv	0.85	0.99								
CAHSEE-ELA	0.87	0.85	0.86							
CAHSEE-ELA %Pass	0.87	0.86	0.88	0.96						
SAT-M	0.93	0.83	0.85	0.90	0.84					
STAR-ALG	0.57	0.49	0.45	0.54	0.58	0.54				
STAR-ALG %PrAdv	0.50	0.48	0.45	0.56	0.59	0.54	0.94			
CAHSEE-Math	0.61	0.86	0.86	0.57	0.61	0.63	0.20	0.18		
CAHSEE-Math %Pass	0.58	0.82	0.82	0.51	0.59	0.56	0.24	0.19	0.97	
SAT-R+M	0.98	0.85	0.86	0.90	0.87	0.98	0.56	0.53	0.63	0.58
SAT %>1,000	0.31	0.64	0.64	0.39	0.42	0.37	0.02	0.12	0.63	0.56
SAT %	0.33	0.48	0.48	0.52	0.37	0.55	-0.01	0.15	0.39	0.24
AP 3, 4, 5	0.49	0.63	0.63	0.62	0.48	0.68	0.13	0.23	0.51	0.38
AP 4, 5	0.46	0.59	0.59	0.58	0.43	0.68	0.10	0.22	0.50	0.37

Measure	SAT-R+M	SAT %>1,000	SAT %	AP 3, 4, 5
SAT %>1,000	0.35			
SAT %	0.45	0.51		
AP 3, 4, 5	0.60	0.45	0.91	
AP 4, 5	0.58	0.43	0.93	0.99

Notes. Each county contributed one observation. Only counties with 25 or more treatment initiators were included (40 of 57 counties). Convergent validity coefficients are outlined in the table.

$p<.01$ (one-tailed, 39 df) for all correlations except those in light grey text.

Table 13 describes the between-county variation in the percentage of enrollees initiating treatment during each of the three periods. This issue speaks to the variance of the random intercepts anticipated in the planned models. Each of the 40 counties with 25 or more initiators contributed three values: the percentage of school year, final exam period, and summer initiators in the county. There was substantial consistency among counties; the mean percentage of enrollees initiating during the final exam period was 11% (median 12%) and the middle fifty percent of counties had between 9% and 13% of their enrollees initiating treatment during this period. It is notable, given the hypothesis that initiation rates would be highest during the final exam period, that even the wide confidence intervals around the school year and final exam period means do not seem to admit of this possibility.

Table 13
County Variation in Treatment Initiation Timing

	Initiation Period		
	School year	Final exams	Summer
Mean (95% CI)	73% (59% - 87%)	11% (1% - 21%)	16% (5% - 27%)
SD	4.6%	3.4%	4.1%
Q1	70%	9%	14%
Median	72%	12%	16%
Q3	75%	13%	18%
Interquartile range	4.4%	3.8%	4.5%
Min.	63%	4%	7%
Max.	89%	19%	28%

Note. Each county contributed one observation. Only counties with 25 or more treatment initiators were included (40 of 57 counties).

Finally, Table 14 addresses the bivariate relationship between the county measures of academic performance and the timing of treatment initiation, specifically each county's percentage of enrollees who began treatment in the final exam period.

Given the lack of variation in timing presented above, it is not surprising that, at the county level, final exam period initiation was significantly related to only two of the measures (SAT Critical Reading and the combined SAT critical reading and mathematics score). As noted above, the combined SAT variable was selected as the initial county level predictor for the random effects models.

Table 14
Correlations between California County Level Measures of Academic Performance and Percentage of Final Exam Period Treatment Initiators

Measure	r
SAT/AP	
SAT %	-0.04
SAT-R	0.42*
SAT-M	0.31
SAT-R+M	0.37*
SAT %>1,000	-0.03
AP 3, 4, 5	0.07
AP 4, 5	0.04
STAR	
STAR-ELA	0.18
STAR-ELA %PrAdv	0.21
STAR-ALG	0.12
STAR-ALG %PrAdv	0.04
CAHSEE	
CAHSEE-ELA	0.34
CAHSEE-ELA %Pass	0.34
CAHSEE-Math	0.01
CAHSEE-Math %Pass	0.02

Note. Each county contributed one observation. Only counties with 25 or more treatment initiators were included (40 of 57 counties).

p<.01 (one-tailed, 39 df).

Bivariate Analyses Concerning Initiation Timing and Enrollee-level Measures

Hypotheses two and three, which predicted that the relative timing of ADHD treatment initiation across the three periods would vary as a function of the characteristics

of enrollees and the medications they were first prescribed, are addressed in this section with bivariate analyses. They will also be evaluated below using random and fixed effects models. Data for all stimulant and atomoxetine initiators (N=82,057) are included in these enrollee-level analyses because the California county level measures of academic performance are not required. In order to reduce clutter, confidence intervals, reported in the tables, are not repeated in the text after the point estimates.

Table 15 contains the distributions across the three initiation periods by enrollee sex and age. As noted above, 68% of the ADHD treatment initiators were male, and the majority (59%) were age 14. Female treatment initiators were significantly less likely than males to have started treatment during the school year (0.726 vs. 0.735) and significantly more likely to have begun treatment during the summer (0.176 vs. 0.161). Contrary to the hypothesis that males would be less likely to initiate use of prescribed ADHD medications during the final exam period, no sex difference was observed in rates for that period. With respect to age, enrollees initiating pharmacotherapy for ADHD in the final exam period or summer tended to be slightly younger than school year initiators (mean ages 14.86, 14.89 vs. 14.94 years; $F[2,82054]=20.98$, $p<.01$; all *post hoc* pairwise comparisons [Tukey HSD] were significant except for final exam period vs. summer). The period means mask a somewhat more subtle relationship however; older and younger students were less likely to be school year initiators than their 15- and 16-year old peers (0.720 and 0.729 for enrollees age 14 and 18 vs. 0.755 and 0.759 for those 15 and 16), whereas the opposite pattern was observed for summer initiators (0.174 and 0.183 for ages 14 and 18 vs. 0.146 and 0.142 for ages 15 and 16). The final exam period initiation

Table 15
Treatment Initiation Period by Enrollee Sex and Age

			Proportion initiating during period		
	N	% of initiators	School year (95% CIs)	Final exams (95% CIs)	Summer (95% CIs)
Sex					
Female	26,042	32%	0.726 (0.720 - 0.731)	0.099 (0.095 - 0.102)	0.176 (0.171 - 0.181)
Male	56,015	68%	0.735 (0.731 - 0.739)	0.104 (0.101 - 0.106)	0.161 (0.158 - 0.164)
Total	82,057	100%	0.732 (0.729 - 0.735)	0.102 (0.100 - 0.104)	0.166 (0.163 - 0.169)
Age					
14	48,516	59%	0.720 (0.716 - 0.724)	0.106 (0.103 - 0.109)	0.174 (0.171 - 0.178)
15	10,622	13%	0.755 (0.747 - 0.763)	0.099 (0.093 - 0.105)	0.146 (0.139 - 0.153)
16	9,483	12%	0.759 (0.750 - 0.767)	0.099 (0.093 - 0.105)	0.142 (0.135 - 0.149)
17	7,503	9%	0.748 (0.739 - 0.758)	0.095 (0.089 - 0.102)	0.157 (0.148 - 0.165)
18	5,933	7%	0.729 (0.717 - 0.740)	0.089 (0.081 - 0.096)	0.183 (0.173 - 0.193)
Total	82,057	100%	0.732 (0.729 - 0.735)	0.102 (0.100 - 0.104)	0.166 (0.163 - 0.169)
Mean age			14.94 (14.93 - 14.95)	14.86 (14.83-14.88)	14.89 (14.87 - 14.91)

Note. N=82,057 enrollees who initiated treatment during the school year, final exam, or summer periods.

rates declined monotonically from age 14 (0.106) through 18 (0.089), which is consistent with the hypothesis that age would be negatively associated with exam period initiation. Regardless of statistical significance, however, the effects associated with sex and age were quite modest, reflecting differences of no more than a few percentage points.

Table 16 addresses the relationship between initiation period and (a) the most recently observed ADHD diagnosis, if any, preceding the first observed stimulant or atomoxetine prescription fill and (b) the specialty of the diagnosing provider. What is most notable in this table is the fact that 46% of enrollees initiating pharmacotherapy for ADHD (by definition for the first time or after an interruption of at least 12 months) did not have a recorded diagnosis of ADHD in the 12 months leading up to and including the day the first stimulant or atomoxetine prescription was filled. This is the case despite that fact that all initiators were enrolled in a health plan covered by the Medstat database during this period and, therefore, that their physician visits and other mental health services were observable if provided. Where the most recent ADHD diagnosis was available, it was for the predominantly inattentive type of ADHD for 46% of those with a diagnosis (and for 25% of all initiators) and for the predominantly hyperactive or combined type for 54% (29% of all initiators).[7] Contrary to hypothesis, the rate of final exam period initiation was higher for those enrollees whose ADHD diagnosis included hyperactivity than for those with whose symptoms largely involved inattention (0.106 vs. 0.096). This pattern was also observed for summer initiators (0.173 vs. 0.163), while the

[7] Eighty-eight percent of initiators with a past-year ADHD diagnosis had either a single claim involving ADHD or had only claims of the same type, i.e., all inattentive type or all hyperactive or combined type.

Table 16
Treatment Initiation Period by Most Recent ADHD Diagnosis and Provider Specialty

	N	% of initiators	Proportion initiating during period		
			School year (95% CIs)	Final exams (95% CIs)	Summer (95% CIs)
Most recent ADHD diagnosis					
None	37,986	46%	0.734 (0.730 - 0.738)	0.103 (0.100 - 0.106)	0.163 (0.159 - 0.167)
ADHD, inattentive type	20,211	25%	0.741 (0.735 - 0.747)	0.096 (0.092 - 0.100)	0.163 (0.158 - 0.168)
ADHD, hyperactive or combined type	23,860	29%	0.721 (0.716 - 0.727)	0.106 (0.102 - 0.109)	0.173 (0.168 - 0.178)
Total	82,057	100%	0.732 (0.729 - 0.735)	0.102 (0.100 - 0.104)	0.166 (0.163 - 0.169)
Provider type for most recent ADHD diagnosis					
Family practice	9,089	21%	0.750 (0.741 - 0.759)	0.085 (0.079 - 0.091)	0.165 (0.157 - 0.173)
Pediatrics (inc. specialists)	13,150	30%	0.735 (0.728 - 0.743)	0.104 (0.098 - 0.109)	0.161 (0.155 - 0.167)
Psychiatry/child psychiatry	7,135	17%	0.708 (0.697 - 0.718)	0.112 (0.105 - 0.119)	0.180 (0.171 - 0.189)
Other physician	7,503	17%	0.729 (0.718 - 0.739)	0.102 (0.095 - 0.108)	0.170 (0.161 - 0.178)
Non-physician	6,244	14%	0.725 (0.714 - 0.736)	0.104 (0.097 - 0.112)	0.171 (0.162 - 0.180)
Total	43,121	100%	0.731 (0.727 - 0.735)	0.101 (0.098 - 0.104)	0.168 (0.165 - 0.172)

Note. There were 82,057 enrollees who initiated treatment during the school year, final exam, or summer periods; 44,071 enrollees received an ADHD diagnosis in the prior 12 months, and a provider specialty was recorded for 43,121 of those enrollees.

opposite was true for school year initiators (0.741 inattentive vs. 0.721 hyperactive or combined).

The Medstat database does not include information on the medical specialties of the physicians who prescribed medications. In place of this information, the specialty of the provider who recorded the most recent pre-prescription ADHD diagnosis was used as a rough proxy. As noted above, such a diagnosis was observed for only 54% of initiators. Table 16 describes the distribution of provider specialties and their relationships with initiation period. Slightly more than half of the observed ADHD diagnoses were recorded by primary care physicians: those in family practice (21%) and pediatricians (30%). Seventeen percent of the diagnoses came from psychiatrists or child psychiatrists. If non-physician providers (e.g., psychologists, treatment centers, chiropractors), most of whom could not have been the source of the prescriptions, are excluded these percentages increase to 62% for primary care physicians and 20% for psychiatrists/child psychiatrists.

The most notable relationship between provider specialty and initiation period concerns the difference between initiators who were diagnosed by psychiatrists or child psychiatrists and those who were diagnosed by primary care physicians. Treatment initiators who were diagnosed by a psychiatrist or child psychiatrist were more likely to have begun their use of ADHD medications during the final exam period (0.112) than those diagnosed by a family practitioner (0.085). Enrollees with a psychiatrist's diagnosis were also more likely than those with a pediatrician's diagnosis to have started ADHD pharmacotherapy during the summer (0.180 vs. 0.161). In contrast, ADHD diagnoses from primary care settings, particularly from family practice (0.750 vs. 0.708

for psychiatry), but also from pediatrics (0.735 vs. 0.708 for psychiatry), were associated with higher rates of school year initiation.

Table 17 considers the rates of comorbid psychiatric/behavioral, substance abuse, and medical conditions in the enrollees initiating use of stimulants or atomoxetine as well as the relationships between the comorbidities and initiation timing. As expected, a large proportion of treatment initiators had received an outpatient diagnosis for another psychiatric or behavioral condition in the year preceding the first prescription fill for an ADHD medication. The most commonly reported disorder was depression, diagnosed in 13.5% of initiators. Serious mental illness, defined as the presence of schizophrenia, other psychotic conditions, bipolar disorder, or severe depression, was also quite common, reported in 9.7% of initiators. Anxiety and related disorders were seen in 6.2% and conduct disorders or oppositional defiant disorder were seen in 4.6% of stimulant or atomoxetine initiators. Contrary to hypothesis, prescribers do not appear to have been reluctant to begin supplying enrollees in this latter group with ADHD medications during the final exam period. Enrollees with conduct disorders or oppositional defiant disorder were, in fact, more likely to have started treatment during this time than were members of the overall initiator population (0.115 vs. 0.102). Presence of a diagnosed substance abuse disorder was likewise unrelated to final exam period initiation (0.106 vs. 0.102). Rates of school year initiation were lower for enrollees with anxiety and related disorders (0.715), conduct disorders or oppositional defiant disorder (0.706), and tic disorders (0.678) compared with the overall population of enrollees beginning pharmacotherapy for ADHD (0.732) during this period.

Table 17

Treatment Initiation Period by Comorbid Conditions

			Proportion initiating during period		
	N	% of initiators	School year (95% CIs)	Final exams (95% CIs)	Summer (95% CIs)
Anxiety and related disorders	5,115	6.2%	0.715 (0.702 - 0.727)	0.107 (0.098 - 0.115)	0.179 (0.168 - 0.189)
Depressive disorders	11,063	13.5%	0.723 (0.714 - 0.731)	0.108 (0.102 - 0.113)	0.170 (0.163 - 0.177)
CD/ODD[a]	3,804	4.6%	0.706 (0.692 - 0.721)	0.115 (0.104 - 0.125)	0.179 (0.167 - 0.191)
Serious mental illness	7,924	9.7%	0.720 (0.436 - 1.003)	0.108 (0.000 - 0.304)	0.172 (0.000 - 0.410)
Substance abuse disorders	1,943	2.4%	0.727 (0.707 - 0.747)	0.106 (0.092 - 0.119)	0.168 (0.151 - 0.184)
Cardiovascular conditions	1,670	2.0%	0.726 (0.705 - 0.748)	0.108 (0.093 - 0.123)	0.166 (0.148 - 0.184)
Sleep disorders	123	<0.1%	0.840 (0.775 - 0.905)	0.140 (0.079 - 0.201)	0.250 (0.173 - 0.327)
Tic disorders	407	0.1%	0.678 (0.633 - 0.723)	0.123 (0.091 - 0.155)	0.199 (0.160 - 0.238)
Seizures	740	0.1%	0.710 (0.677 - 0.742)	0.100 (0.078 - 0.122)	0.191 (0.162 - 0.219)
Pervasive developmental disorders	871	1.1%	0.681 (0.650 - 0.712)	0.107 (0.086 - 0.127)	0.212 (0.185 - 0.240)
Entire population	82,057	100.0%	0.732 (0.729 - 0.735)	0.102 (0.100 - 0.104)	0.166 (0.163 - 0.169)

Note. N=82,057 enrollees who initiated treatment during the school year, final exam, or summer periods.

[a] Conduct disorder (CD)/oppositional defiant disorder (ODD).

Table 18 describes the distribution of first-filled prescriptions for ADHD medications as well as their relationships with initiation period. Not surprisingly, lisdexamphetamine, which received FDA approval for the treatment of ADHD early in the final year for which enrollee data were available (Feb. 2007), was the initial choice of medication for less than one percent of initiators. Perhaps because this medication was quite new in the spring of 2007, it was received by no final exam period initiators. Data would be needed for at least one full calendar year after the medication's introduction to evaluate whether prescribers showed a preference for supplying this more abuse-resistant medication for patients who sought treatment close to, or during, the final exam period.

The stimulants methylphenidate, dexmethylphenidate, amphetamine, and dextroamphetamine, which are recommended as the first line of pharmacological treatment for ADHD and which have an extensive record of efficacy and safety, were the first choice of medication for 85% of initiators. The nonstimulant atomoxetine, recommended as an alternative medication for patients who do not respond to stimulants or for whom safety, misuse, and diversion are a concern, was the first medication received by 15% of initiators. Selection of atomoxetine as the first medication to prescribe was associated with a higher rate of summer initiation (0.197 vs. 0.166 overall) and a lower rate of school year initiation (0.703 vs. 0.732 overall), but not with the rate of final exam period initiation.

Table 19 suggests the same conclusion, that selection of atomoxetine as the initial medication was not as strongly tied to the school calendar as selection of a stimulant, while also addressing the relative abuse resistance of the medications. The drugs listed in

Table 18

Treatment Initiation Period by Generic Medication Name

			Proportion initiating during period		
Medication	N	% of initiators	School year (95% CIs)	Final exams (95% CIs)	Summer (95% CIs)
Lisdexamphetamine[a]	382	<1%	0.856 (0.821 - 0.891)	0.000 (0.000 - 0.000)	0.144 (0.109 - 0.179)
Amphetamine	28,960	35%	0.733 (0.728 - 0.738)	0.102 (0.098 - 0.105)	0.165 (0.161 - 0.170)
Dextroamphetamine	1,634	2%	0.740 (0.719 - 0.761)	0.103 (0.088 - 0.118)	0.157 (0.140 - 0.175)
Methylphenidate	37,112	45%	0.739 (0.735 - 0.744)	0.104 (0.101 - 0.107)	0.157 (0.153 - 0.161)
Dexmethylphenidate	2,293	3%	0.729 (0.711 - 0.747)	0.099 (0.086 - 0.111)	0.173 (0.157 - 0.188)
Atomoxetine[b]	11,661	14%	0.703 (0.694 - 0.711)	0.101 (0.095 - 0.106)	0.197 (0.189 - 0.204)
Total	82,042	100%	0.732 (0.729 - 0.735)	0.102 (0.100 - 0.104)	0.166 (0.163 - 0.169)

Note. N=82,042 enrollees who initiated treatment during the school year, final exam, or summer periods (15 initiators who received methamphetamine are excluded).

[a] Received FDA approval for treatment of ADHD in Feb. 2007.

[b] Received FDA approval for treatment of ADHD in Nov. 2002.

Table 19

Treatment Initiation Period by Relative Abuse Resistance of Medications

			Proportion initiating during period		
	N	% of initiators	School year (95% CIs)	Final exams (95% CIs)	Summer (95% CIs)
Atomoxetine[a]	11,661	14%	0.703 (0.694 - 0.711)	0.101 (0.095 - 0.106)	0.197 (0.189 - 0.204)
Concerta, Daytrana, Vyvanse	23,555	29%	0.734 (0.728 - 0.740)	0.103 (0.099 - 0.107)	0.163 (0.158 - 0.167)
Other LA, XR, etc. stimulant	28,553	35%	0.738 (0.733 - 0.743)	0.101 (0.097 - 0.104)	0.161 (0.157 - 0.165)
Immediate-release stimulant	18,288	22%	0.739 (0.732 - 0.745)	0.103 (0.099 - 0.108)	0.158 (0.153 - 0.163)
Total	82,057	100%	0.732 (0.729 - 0.735)	0.102 (0.100 - 0.104)	0.166 (0.163 - 0.169)

Note. N=82,057 enrollees who initiated treatment during the school year, final exam, or summer periods.

[a] Received FDA approval for treatment of ADHD in Nov. 2002.

the table are displayed in approximate order from the most resistant to abuse (atomoxetine) to the least resistant (immediate release stimulants). Only 22% of enrollees received an immediate-release stimulant as their initial medication. Sixty four percent of initiators (74% of those receiving a stimulant) began treatment with an intermediate- or long-acting stimulant, including the brand-name drugs Concerta, Daytrana, or Vyvanse. With the exception of atomoxetine, as noted above, beginning treatment with the relatively more abuse-resistant medications was not associated with higher rates of final exam period initiation. Taken together, the results concerning atomoxetine and the more abuse-resistant stimulants suggest that it is the stimulant vs. non-stimulant distinction, and not differences in abuse resistance, that are reflected in initiation timing. Neither method of categorizing the medications was related to final exam period initiation however; the differences between recipients of the various drugs in initiation rates during this period were no more than two tenths of one percent (i.e., a 0.002 difference in rates).

Tables 20 and 21 concern the amount of medication supplied for the first-observed stimulant or atomoxetine prescription. They address the hypothesis that prescribers would be less willing to provide a high dose or a large supply of medication for enrollees presenting for ADHD treatment around final exam time. As noted in Chapter 3, each prescription was assigned to a dose rank category, from zero to four, based on the average daily dosage provided. Ranks were calculated separately for each generic drug (see Table 6) and were based on average daily dose values for all enrollees' stimulant or atomoxetine prescriptions, regardless of initiator status. Compared with all prescriptions, the first prescriptions filled by initiators tended to provide a lower average

daily dose. This was expected given treatment recommendations that new patients' doses should start low and then be titrated upward to reach a level that produces a desired response without problematic side effects. Although, by definition and within the limits allowed by discrete drug strengths (e.g., 20mg) in the packaged medications, approximately 1/5 of all stimulant or atomoxetine prescriptions fell into each dosage rank category (not in table), the rank memberships tended to be lower for initiators' first prescriptions. Fifty-six percent of initiators' prescriptions fell into the two lower-than average ranks (vs. 41% of all stimulant/atomoxetine prescriptions), while only 26% (vs. 40%) fell into the two higher-than-average ranks.

The relationship between dose rank and initiation period was evaluated using a Kruskal-Wallis test (Zar, 1999) comparing dose ranks among school year, final exam period, and summer initiators. The significant result (χ^2 =31.85, 2 df, p<.01) indicated that enrollees initiating pharmacotherapy for ADHD at different times of the year varied in terms of the average daily dose provided by their first prescription. Follow-up pairwise analyses (the Kruskal-Wallis test for two groups is known as the Wilcoxon rank-sum test) revealed that, compared with school-year initiators, enrollees initiating ADHD pharmacotherapy in the final exam period or the summer received higher average daily doses than school-year initiators. In the case of the school-year vs. final exam period comparison, this was contrary to hypothesis. The final exam vs. summer difference in dose rank categories was not significant.

A companion table (Table 21) concerns another aspect of how much medication was supplied to initiators for their first prescription: days' supply. The large majority of

Table 20

Treatment Initiation Period by Average Daily Dose

			Proportion initiating during period		
Dose rank	N	% of initiators	School year (95% CIs)	Final exams (95% CIs)	Summer (95% CIs)
0 - Lowest	21,483	27%	0.741 (0.735 - 0.747)	0.099 (0.095 - 0.103)	0.160 (0.155 - 0.165)
1	23,040	29%	0.736 (0.731 - 0.742)	0.100 (0.096 - 0.104)	0.164 (0.159 - 0.169)
2	14,959	19%	0.731 (0.724 - 0.738)	0.102 (0.097 - 0.107)	0.167 (0.161 - 0.173)
3	11,590	14%	0.725 (0.717 - 0.733)	0.107 (0.102 - 0.113)	0.168 (0.161 - 0.174)
4 - Highest	9,637	12%	0.711 (0.702 - 0.720)	0.108 (0.101 - 0.114)	0.182 (0.174 - 0.189)
Total	80,709	100%	0.732 (0.729 - 0.735)	0.102 (0.100 - 0.104)	0.166 (0.163 - 0.169)

Note. N=80,709 enrollees with valid dose data who initiated treatment during the school year, final exam, or summer periods.

Table 21

Days' Supply of Medication by Treatment Initiation Period

Initiation period	N	Mean (95% CIs)	% < 30 days (95% CIs)
School year	59,389	33.64 (33.50 - 33.77)	7.5 (7.2 - 7.7)
Final exams	8,295	34.03 (33.67 - 34.43)	7.7 (7.1 - 8.3)
Summer	13,452	34.45 (34.13 - 34.76)	7.0 (6.6 - 7.4)
Total	81,136	33.81 (33.69 - 33.93)	7.4 (7.2 - 7.6)

Note. N=81,136 enrollees with valid day supply data who initiated treatment during the school year, final exam, or summer periods.

all stimulant or atomoxetine prescriptions (86.5%), as well as initiators' first prescriptions (82.2%), were for 30 days (not reported in table). A one-way ANOVA ($F(1,81134)=13.14$, $p<.01$) confirmed that supply was significantly related to initiation period, however the only significant pairwise difference (using Tukey's HSD) was between supplies given to summer vs. school year initiators. While statistically significant, the size of the group difference is of little practical consequence. The three initiator groups did not differ in the proportion of individuals (overall 7.4%) who received a smaller-than-typical initial prescription (i.e., <30 days). Overall, these results suggest that average daily dose, but not supply, may be sensitive to when stimulants or atomoxetine are first provided. Nevertheless, there was no evidence that final exam period initiators received less medication (by either measure) than school year initiators.

Additional Bivariate Analyses

In order to test an alternative hypothesis, that ADHD pharmacotherapy initiation during the final exam period, as well as the summer, reflects a higher level of ongoing clinical need rather than prescribers' concerns about adverse events, misuse, and diversion, a second set of bivariate analyses was conducted. The variables created for these analyses are also included in the results of the logistic regression models reported below. These variables, described in Chapter 3, include doctor visits, measures of inpatient and outpatient service utilization for non-ADHD psychiatric disorders (ICD-9-CM codes 290-319, with the exception of 314.00 and 314.01) and indicators for receipt of psychotropic medications other than stimulants and atomoxetine.

Table 22 contains information on outpatient visits to each of several provider types, as well as overall visits, and also describes their relationships with initiation

timing. In the year preceding the first observed stimulant or atomoxetine prescription fill, 34% of treatment initiators visited a family practitioner and 46% visited a pediatrician. Seventy percent saw at least one of the two and 94% received services from at least one physician. One in five initiators saw a psychiatrist. Those initiators who received services from pediatricians, including non-psychiatry pediatric specialists, were more likely to have initiated ADHD pharmacotherapy in the final exam period (0.106 vs. 0.099) or summer (0.169 vs. 0.163) than those who did not see a pediatrician. The opposite pattern was observed for school year initiators (0.725 vs. 0.739). The same relationship was seen for those who had received services from psychiatrists; they were more likely to have been final exam (0.111 vs. 0.100) or summer initiators (0.177 vs. 0.163) and less likely to have been school year initiators (0.713 vs. 0.737) compared with those who had not seen a psychiatrist. Overall receipt of services, from a primary care provider or from any physician, was associated with higher rates of summer (0.169 vs. 0.159; and 0.167 vs. 0.145) but not final exam period initiation.

The relationship between (non-ADHD-related) psychiatric services and initiation period is addressed in Table 23. Very few (2%) of the treatment initiators received inpatient services, despite the high levels of serious psychiatric comorbidity observed in this group. Moreover, there was no relationship between having had one or more inpatient claims and initiation timing. There was a relationship, however, between receipt of outpatient psychiatric services and initiation. The 32% of initiators who received one or more outpatient psychiatric services were more likely than those without claims for such services to have begun pharmacotherapy for ADHD during the final exam (0.108 vs. 0.099) or summer (0.174 vs. 0.162) periods and less likely to have

Table 22
Treatment Initiation Period by Doctor Visits

	N	% of initiators	Proportion initiating during period		
			School year (95% CIs)	Final exams (95% CIs)	Summer (95% CIs)
Family practice					
No	54,050	66%	0.731 (0.727 - 0.735)	0.105 (0.102 - 0.107)	0.164 (0.161 - 0.167)
Yes	28,007	34%	0.734 (0.729 - 0.739)	0.097 (0.093 - 0.100)	0.169 (0.165 - 0.174)
Pediatrics (inc. specialists)					
No	44,092	54%	0.739 (0.734 - 0.743)	0.099 (0.096 - 0.101)	0.163 (0.160 - 0.166)
Yes	37,965	46%	0.725 (0.720 - 0.729)	0.106 (0.103 - 0.109)	0.169 (0.166 - 0.173)
Psychiatry/child psychiatry					
No	65,594	80%	0.737 (0.733 - 0.740)	0.100 (0.098 - 0.102)	0.163 (0.160 - 0.166)
Yes	16,463	20%	0.713 (0.706 - 0.720)	0.111 (0.106 - 0.115)	0.177 (0.171 - 0.182)
Other physician					
No	31,422	38%	0.733 (0.728 - 0.738)	0.102 (0.098 - 0.105)	0.166 (0.161 - 0.170)
Yes	50,635	62%	0.732 (0.728 - 0.735)	0.102 (0.100 - 0.105)	0.166 (0.163 - 0.169)
Any primary care physician[a]					
No	24,411	30%	0.738 (0.732 - 0.743)	0.103 (0.099 - 0.107)	0.159 (0.155 - 0.164)
Yes	57,646	70%	0.730 (0.726 - 0.733)	0.102 (0.099 - 0.104)	0.169 (0.166 - 0.172)
Any physician					
No	5,316	6%	0.748 (0.736 - 0.760)	0.107 (0.098 - 0.115)	0.145 (0.136 - 0.155)
Yes	76,741	94%	0.731 (0.728 - 0.734)	0.102 (0.100 - 0.104)	0.167 (0.165 - 0.170)

Note. N=82,057 enrollees who initiated treatment during the school year, final exam, or summer periods.

[a] Family practitioner or non-specialist pediatrician.

Table 23

Treatment Initiation Period by Receipt of Psychiatric Services

			Proportion initiating during period		
	N	% of initiators	School year (95% CIs)	Final exams (95% CIs)	Summer (95% CIs)
Inpatient claims with a psychiatric diagnosis					
None	80,404	98%	0.732 (0.729 - 0.735)	0.102 (0.100 - 0.104)	0.166 (0.163 - 0.168)
One or more	1,653	2%	0.721 (0.699 - 0.742)	0.110 (0.095 - 0.125)	0.169 (0.151 - 0.187)
Outpatient claims with a psychiatric diagnosis					
None	55,562	68%	0.739 (0.735 - 0.742)	0.099 (0.097 - 0.101)	0.162 (0.159 - 0.165)
One or more	26,525	32%	0.718 (0.713 - 0.723)	0.108 (0.105 - 0.112)	0.174 (0.169 - 0.178)
Mean outpatient claims	82,057		2.40 (2.36-2.45)	2.65 (2.53-2.78)	2.59 (2.49-2.69)

Note. N=82,057 enrollees who initiated treatment during the school year, final exam, or summer periods.

Table 24

Treatment Initiation Period by Receipt of Psychotropic Medications

			Proportion initiating during period		
	N	% of initiators	School year (95% CIs)	Final exams (95% CIs)	Summer (95% CIs)
Antidepressants					
No	64,718	78.9%	0.737 (0.734 - 0.741)	0.100 (0.097 - 0.102)	0.163 (0.160 - 0.166)
Yes	17,339	21.1%	0.712 (0.705 - 0.719)	0.112 (0.107 - 0.116)	0.177 (0.171 - 0.182)
Antipsychotics					
No	76,744	94.5%	0.735 (0.732 - 0.738)	0.101 (0.099 - 0.103)	0.164 (0.162 - 0.167)
Yes	5,313	6.5%	0.693 (0.681 - 0.705)	0.116 (0.107 - 0.124)	0.191 (0.181 - 0.202)
Mood stabilizers					
No	77,087	93.9%	0.734 (0.731 - 0.737)	0.102 (0.100 - 0.104)	0.164 (0.162 - 0.167)
Yes	4,970	6.1%	0.706 (0.694 - 0.719)	0.103 (0.095 - 0.112)	0.191 (0.180 - 0.201)
Anxiolytics/hypnotics					
No	79,017	96.3%	0.733 (0.730 - 0.736)	0.102 (0.100 - 0.104)	0.166 (0.163 - 0.168)
Yes	3,040	3.7%	0.711 (0.695 - 0.727)	0.110 (0.099 - 0.121)	0.179 (0.165 - 0.193)
Any (of four)					
No	60,493	73.7%	0.740 (0.736 - 0.743)	0.099 (0.097 - 0.101)	0.161 (0.158 - 0.164)
Yes	21,564	26.3%	0.710 (0.704 - 0.716)	0.111 (0.107 - 0.115)	0.179 (0.174 - 0.184)

Note. N=82,057 enrollees who initiated treatment during the school year, final exam, or summer periods.

started during the school year (0.718 vs. 0.739). Those enrollees who initiated treatment during the final exam period or the summer also had a higher mean number of psychiatric outpatient visits (2.65 and 2.59) than school year initiators (2.40); $F(2,82054)=10.81$, $p<.01$, all pairwise comparisons were significant (Tukey's HSD) except for final exam period vs. summer. The magnitudes of the mean differences were quite small however.

Information on receipt of other psychotropic medications is presented in Table 24. More than a quarter (26%) of stimulant or atomoxetine initiators also received one or more of the four listed medication types. This statistic is driven primarily by antidepressants, received by 21% of initiators. As was the case with pediatrician and psychiatrist visits and outpatient psychiatric claims, those who received an antidepressant (0.112 vs. 0.100 for the final exam period, 0.177 vs. 0.163 for summer), an antipsychotic (0.116 vs. 0.101, 0.191 vs. 0.164), or any of the four psychotropic medications (0.111 vs. 0.099, 0.179 vs. 0.161) were more likely than non-recipients to have started using an ADHD medication during the final exam period or summer and less likely to have initiated treatment during the school year. Those who received mood stabilizers were more likely to be summer (0.191 vs. 0.164), but not final exam period, initiators and were also less likely to have started using an ADHD medication during the school year (0.706 vs. 0.734). Taken together, these results and those from Tables 22 and 23 suggest that receipt of medical, and particularly outpatient psychiatric services and medications are implicated in the timing of treatment initiation for ADHD; those initiators receiving these services are more likely to have begun treatment during the final exam period or the summer than non-recipients.

Suitability of Random Effects Models

Results reported earlier in this chapter indicate that there was little evidence of county-by-county variation in the proportion of enrollees initiating stimulant or atomoxetine treatment in the three periods (Table 13). There was also very little evidence of covariation between county level measures of academic performance and the proportion of final exam period initiators in each county (Table 14). These results suggest that a key assumption behind hypothesis four, that county level intercepts (and possibly slopes) are random effects that can be modeled as a function of county level measures of academic performance, is not tenable. More direct evidence of this lack of between-county variation is provided from a one-way random effects ANOVA, which provided estimates of the variance components for the two intercept terms: one for final exam period vs. school year initiation and another for summer vs. school year initiation. In this so-called "null" model no predictors are included at either level. The one-way random effects ANOVA produced χ^2 values of 43.29 and 50.53 (55 df, $p>0.500$) for the final exam and summer intercepts. The corresponding variance components were indistinguishable from zero: 0.00001 and 0.00003 for the two intercepts. The intraclass correlations coefficients, which index the proportion of total variance that can be attributed to between-county differences, were therefore effectively zero as well. These results indicated that there would be no value in including random effects in the planned models. In their place, fixed-effects multinomial logistic regression models were estimated, incorporating only level-one variables (i.e., characteristics of enrollees and their initial ADHD medications).

Fixed Effects Model

While the finding that random effects models were not appropriate, given the lack of between county variation in initiation timing and the minimal covariation between timing and measures of academic performance, requires that hypothesis four be rejected, hypotheses two and three could still be evaluated using fixed-effects models. In addition, the hypothesis concerning ongoing clinical need as a predictor of initiation period was evaluated. Equations 3-1 through 3-3 (see Chapter 3) still describe the probabilities associated with membership in the three initiation periods and equation 3-4 describes the transformation of the probabilities, via generalized logit link, into log-odds. Finally, equation 3-5, minus the j subscripts, which represent counties, characterizes the multinomial regression model. Equations 3-6 and 3-7, which treat random intercepts and slopes as outcomes, no longer apply.

The multinomial logistic regression analysis modeled the log-odds of initiation category membership (school year, final exam period, or summer) as a function of several sets of enrollee-level predictors. Two fixed effects were estimated for each predictor, and two intercept terms were estimated for the model as a whole. The school year was selected as the reference category for the dependent variable and, therefore, these effects represented (1) final exam period initiation vs. school year initiation and (2) summer initiation vs. school year initiation. The intercept estimates and each pair of slope estimates have two degrees of freedom. Results from the full model, in which all predictors were entered simultaneously, are presented in Table 25 in the form of adjusted odds ratios (ORs) with 95% confidence intervals. The predictors are organized according to the relevant hypotheses, which concern enrollee characteristics (hypothesis 2),

medication characteristics (hypothesis 3) and service utilization (the ongoing clinical need hypothesis) and are discussed in order below.

The estimates bearing on hypothesis two are largely consistent with the bivariate results concerning the relationships between enrollee characteristics and initiation timing. Compared with the youngest treatment initiators, older enrollees were less likely to have begun treatment in the final exam period (ORs of 0.903 or less for ages 15-18, $p<.05$ for all) or, for all except 18-year olds, in the summer (ORs of 0.797, 0.775, 0.861 for ages 15-17, $p<.05$ for all) than during the school year. The result was the same when age was entered instead as continuous variable (ORs=0.958 for final exam period vs. school year initiation and 0.971 for summer vs. school year initiation, $p<.05$ for both). This is consistent with hypothesis two. Contrary to hypothesis, however, being a male was not associated with lower odds of being a final exam period initiator. However, males had lower odds than females of having started stimulant or atomoxetine treatment during the summer (OR=0.884, $p<.05$).

Compared with enrollees whose diagnosis was for the predominantly inattentive type of ADHD, those initiators whose most recent diagnosis included hyperactivity were no more or less likely to have started treatment in the final exam period or in the summer than during the school year. Enrollees without a recent ADHD diagnosis were, however, less likely to have started using ADHD medications in the summer (OR=0.840, $p<.05$) than those with a diagnosis. This effect was similar for final exam period initiation, but was not significant (OR=0.860, ns.). Final exam period initiation was less likely when the most ADHD recent diagnosis was made by a family practitioner (OR=0.812, $p<.05$) than by a psychiatrist (the reference category) and summer initiation was less likely with

Table 25
Adjusted Odds Ratios for Full Multinomial Logistic Regression Model

Predictor	Final exam period vs. school year (95% CIs)	Summer vs. school year (95% CIs)
Age		
Age 14	ref.	ref.
Age 15	0.903 (0.840 - 0.971)*	0.797 (0.750 - 0.847)*
Age 16	0.900 (0.833 - 0.971)*	0.775 (0.726 - 0.827)*
Age 17	0.874 (0.802 - 0.953)*	0.861 (0.802 - 0.923)*
Age 18	0.851 (0.771 - 0.940)*	1.029 (0.955 - 1.108)
Sex		
Female	ref.	ref.
Male	1.023 (0.972 - 1.077)	0.884 (0.848 - 0.921)*
Most recent ADHD diagnosis		
None	0.860 (0.698 - 1.060)	0.840 (0.707 - 0.998)*
ADHD, inattentive type	ref.	ref.
ADHD, hyperactive or combined type	1.055 (0.988 - 1.126)	1.036 (0.983 - 1.092)
Provider type for most recent ADHD diagnosis		
Family practice	0.812 (0.708 - 0.932)*	0.910 (0.815 - 1.015)
Pediatrics (inc. specialists)	0.933 (0.824 - 1.057)	0.871 (0.786 - 0.965)*
Psychiatry/child psychiatry	ref.	ref.
Other physician	0.960 (0.840 - 1.098)	1.003 (0.900 - 1.118)
Non-physician	0.954 (0.838 - 1.086)	0.944 (0.849 - 1.049)
No recent ADHD diagnosis	1.139 (0.908 - 1.429)	1.101 (0.913 - 1.328)
Comorbid conditions		
Anxiety and related disorders	0.988 (0.893 - 1.094)	1.040 (0.957 - 1.129)
Depressive disorders	1.013 (0.922 - 1.113)	1.007 (0.933 - 1.088)
CD/ODD[a]	1.079 (0.965 - 1.205)	1.077 (0.983 - 1.180)
Serious mental illness	0.979 (0.877 - 1.093)	0.951 (0.869 - 1.041)
Substance abuse disorders	1.034 (0.884 - 1.210)	1.017 (0.894 - 1.157)
Cardiovascular	1.032 (0.878 - 1.213)	0.990 (0.866 - 1.132)
Sleep disorders	1.089 (0.606 - 1.959)	1.244 (0.787 - 1.966)
Tics	1.109 (0.813 - 1.513)	1.112 (0.863 - 1.433)
Seizures	1.012 (0.786 - 1.302)	1.060 (0.871 - 1.290)
Pervasive developmental disorders	0.972 (0.774 - 1.220)	1.216 (1.022 - 1.446)*
First ADHD medication prescribed		
Atomoxetine	1.011 (0.933 - 1.095)	1.279 (1.200 - 1.362)*
Concerta, Daytrana, Vyvanse	0.979 (0.916 - 1.046)	1.009 (0.955 - 1.066)
Other LA, XR, etc. stimulant	0.965 (0.906 - 1.028)	1.003 (0.952 - 1.056)
Immediate-release stimulant	ref.	ref.

Table 25 (cont.)
Adjusted Odds Ratios for Full Multinomial Logistic Regression Model

Predictor	Final exam period vs. school year (95% CIs)	Summer vs. school year (95% CIs)
Dose rank	1.021 (1.003 - 1.040)*	1.017 (1.003 - 1.032)*
Days' supply	1.000 (0.999 - 1.002)	1.002 (1.001 - 1.003)*
Outpatient claims in past year		
Family Practice	1.004 (0.947 - 1.064)	1.067 (1.017 - 1.118)*
Pediatrics (inc. specialists)	1.075 (1.017 - 1.137)*	1.104 (1.055 - 1.156)*
Psychiatry/child psychiatry	1.040 (0.956 - 1.132)	1.027 (0.958 - 1.101)
Other Physician	1.008 (0.958 - 1.060)	0.993 (0.953 - 1.035)
Psychiatric claims in past year		
One or more inpatient psychiatric claims	0.941 (0.830-1.065)	1.006 (0.915-1.106)
Number of outpatient psychiatric claims	1.002 (0.997-1.007)	1.000 (0.996-1.004)
Other psychotropic medications in past year		
Antidepressant	1.116 (1.045 - 1.192)*	1.051 (0.996 - 1.110)
Anxiolytic/hypnotic	1.049 (0.926 - 1.189)	1.020 (0.921 - 1.129)
Antipsychotic	1.119 (1.009 - 1.240)*	1.103 (1.014 - 1.200)*
Mood stabilizer	0.928 (0.829 - 1.038)	1.078 (0.987 - 1.178

Note. N=82,057 enrollees who initiated treatment during the school year, final exam, or summer periods.

[a] Conduct disorders (CD)/oppositional defiant disorder (ODD).

* $p<.05$.

a pediatrician's diagnosis (OR=0.871, $p<.05$) than a psychiatrist's diagnosis. In a follow-up analysis placing both family practitioners and pediatricians in a category of primary care providers, initiators diagnosed by either of these provider types were less likely than those diagnosed by a psychiatrist to have started ADHD pharmacotherapy in the summer (OR=0.886). The odds ratio associated with primary care providers vs. psychiatrists for final exam period initiation did not reach statistical significance (OR=0.891, 95% CI 0.793-1.001), but it suggests a similar conclusion regarding primary care vs. psychiatric

specialty care and initiation timing. These results from combining family practitioners and pediatricians are not in the table.

Contrary to hypothesis two, the presence of previously diagnosed psychiatric/behavioral, substance abuse, and medical conditions does not appear to have been a factor in the timing of treatment initiation, at least when controlling for receipt of non-ADHD psychotropic medications. Enrollees whose medical claims records showed evidence of various disorders that might plausibly affect treatment decisions were no less likely to have first received an ADHD medication during the final exam period than during the school year. The same pattern was observed for summer initiation, with the exception of a significant effect associated with pervasive developmental disorders (OR=1.216, $p<.05$).

When the set of variables concerning hypothesis two (age, sex, type of ADHD diagnosis, provider specialty associated with the most recent ADHD diagnosis, and comorbid conditions) was evaluated alone, the presence of conduct disorder or oppositional defiant disorder was associated with initiation timing, but in the opposite direction than was hypothesized. Enrollees with these disorders had a *higher* likelihood of being final exam period (OR=1.510, $p<.05$) or summer (OR=1.104, $p<.05$) initiators than those without a diagnosis (not in table). However, these effects were reduced to nonsignificance when indicators for the receipt of non-ADHD psychotropic medications were included in the model. This appeared to be the result of collinearity between the diagnosis and receipt of the medications. For example, rates of antipsychotic medication receipt were significantly higher in enrollees with either conduct disorder or oppositional defiant disorder than in those without (23.2% vs. 5.7%, $p<.05$, not in table), even among

the subset of enrollees without a diagnosis of serious mental illness (18.8% vs. 3.6%, $p<.05$, not in table). Receipt of antidepressants and mood stabilizers were related to conduct disorder or oppositional defiant disorder in a similar way.

The results in Table 25 also address hypothesis three, which concerns the relationship between medication characteristics and timing of the first stimulant or atomoxetine prescription. The first supplied ADHD medication was characterized along a dimension of susceptibility to misuse or diversion, from least (atomoxetine) to most (immediate-release stimulant) susceptible. Only receipt of atomoxetine was significantly associated with initiation timing, and only for summer vs. school year initiation (OR=1.279, $p<.05$). Contrary to hypothesis, receipt of atomoxetine or longer-acting stimulants vs. receipt of immediate-release stimulants was not predictive of final exam period initiation.

The higher the dosage category (dose rank) for the first prescription of ADHD medication, the higher the odds that an enrollee began treatment in the final exam period or the summer (ORs=1.021 and 1.017, respectively, $p<.05$ for both). This finding is contrary to the hypothesis that lower doses would be provided to final exam period initiators, but the magnitude of the effect was minuscule; each step (of four) from a lower dose category to a higher category was associated with 2.1% higher odds of being a final exam vs. school year initiator. The effect size for summer vs. school year initiation was even smaller (1.7% per step). The small sizes of these effects is made more noteworthy by the wide range of doses encompassed by the five levels, e.g., from 1 mg/day to 200 mg/day for methylphenidate (see Table 6). With respect to days of medication supplied from the first filled prescription, enrollees provided with larger supplies were more likely

to have started receiving their medication during the summer than the school year. The effect for summer was small however (OR=1.002, p<.05), and it was non-existent (OR=1.000, ns.) for final exam vs. school year initiation.

As described in Chapter 3, an additional set of variables was constructed to characterize the medical and psychiatric care received by enrollees and to examine their relationships with initiation timing. These relationships are evaluated in Table 25 along with those bearing on hypotheses two and three. Use of outpatient services in the year preceding the first stimulant or atomoxetine prescription fill was captured by four indicator variables; one each for family practice, pediatrics, psychiatry, and services from other types of physicians. Consistent with the new hypothesis that ongoing medical need is associated with final exam period and summer initiation vs. school year initiation, those enrollees who had one or more visits with a pediatrician were more likely to have initiated pharmacotherapy for ADHD during each of these two periods than were those who did not see a pediatrician (ORs 1.075 and 1.104, p<0.05 for both). A similar finding for family practitioner visits was evident for summer (OR=1.067, p<.05) but not final exam period initiation. Visits to psychiatrists and other physicians (primarily specialists) were not associated with timing of ADHD pharmacotherapy initiation in the full model.

Receipt of inpatient and outpatient psychiatric services for conditions other than ADHD were not related to initiation timing in the full model, but receipt of some psychotropic medications was associated with both final exam period and summer initiation. Enrollees who were hospitalized in the previous year for a psychiatric or behavioral condition other than ADHD were no more likely than those who were not hospitalized to have begun receiving ADHD medication in the final exam period or

summer vs. the school year. The same was true for receipt of outpatient psychiatric services, represented as a count of past-year claims.

Those enrollees (six percent of the initiator population) who filled one or more prescriptions for an antipsychotic medication had higher odds of being a final exam period or summer vs. school year initiator than those who were not treated with one of these drugs (ORs=1.119 and 1.103, $p<.05$ for both). A similar pattern was found for antidepressants, but the effect was significant only for final exam period vs. school year initiation (OR=1.116, $p<.05$). Receipt of mood stabilizers and anxiolytic and hypnotic medications were unrelated to the period in which pharmacotherapy for ADHD was started.

Overall, the results of the full fixed-effect multinomial logistic regression model are consistent with the bivariate analyses. In some cases, however, the simultaneous estimation of effects using measures of both need and treatment rendered some of the previously observed bivariate findings nonsignificant. Nevertheless, the two sets of analyses suggest a similar conclusion: that characteristics of initiators and the medications they received are not particularly informative with respect to when medical treatment of ADHD was started, and that measures of service utilization are only moderately related to initiation timing.

Chapter 5 - Discussion

Many students acquire prescription ADHD medications to help them maintain concentration and improve their studying, particularly when academic demands are highest. Results from the current study, however, indicate that the supply of these drugs over pharmacy counters in the period leading up to and including final exams does not increase among high school age students. In fact a substantial decrease was observed. Moreover, there is little evidence that students initiating pharmacotherapy for ADHD around final exams differ, in terms of clinical characteristics or the details of the medications supplied, from those starting treatment at times when academic demand is less salient. Some preliminary evidence was found, however, for the alternative hypothesis that ongoing care/need is associated with a higher likelihood of beginning treatment toward the end of the school year or in the summer. Finally, although there was substantial county-by-county variation in academic performance measures among a subpopulation of students in California, differences among counties in their proportions of final exam period treatment initiators were very small and were unrelated to those measures.

This chapter will begin with a more detailed review of the evidence concerning the four hypotheses described in Chapter 1 as well as the additional hypothesis concerning the role of ongoing medical care/need in prescribing patterns. Other findings of interest will be addressed as well, along with some suggestions for future research. These will be followed by a re-evaluation of the assumptions behind the study design and analysis plan. The implications of the study's results will then be considered.

Review of Hypotheses

Prescribing rates. The first hypothesis was predicated on a pair of assumptions: (1) that the period leading up to and including high school final exams would present the highest level of academic demand for the most students, and (b) that some students would seek prescriptions for ADHD medications to use as study aids to meet those demands. The week-over-week pattern of prescription fills and new treatment spells was entirely inconsistent with this hypothesis however. With regard to prescription fill rates for stimulants or atomoxetine, the start of the final exam period showed a steep decline into summer followed by a sharp increase as the beginning of the school year approached. As expected, no such pattern was observed for SSRI antidepressants. Initiation of pharmacotherapy for ADHD followed a similar pattern. When average rates of initiation per 100,000 enrollees were compared across the three periods the final exam period rate was significantly lower than the school year or summer rates. Given the briefness of the final exam and summer intervals, some systematic changes in their boundaries resulted in higher final exam period vs. summer rates, but in no configuration of start and end dates did the final exam rate approach the school year rate.

Inspection of the prescription and initiation rates over the calendar year revealed a clear pattern for the prescribing of ADHD medications: the final exam period, rather than being a time of increased acquisition, represented the beginning of a late spring through mid-summer trough. Prescribing therefore appeared to be sensitive primarily to the beginning and end of the school year. Undoubtedly, academic demand played a role in the observed patterns. However, it is difficult to make the case that the use of stimulants and atomoxetine was strategic in any but the broadest sense. They certainly aid short-

term performance in some cognitive tasks, but they also improve attention, behavior, and relationships with classmates and teachers. There are numerous internal and external incentives to improve functioning in these areas, and many are operative throughout the school year and have nothing to do with a desire to seek academic advantage.

Smaller peaks and valleys in prescription and initiation rates must be interpreted only tentatively, but they also suggest that prescribing is following the school calendar on a smaller scale. This is the case for the late November to early January period excluded from analysis, during which a sharp decrease in rates was observed roughly corresponding to the Thanksgiving and winter holidays. Another, smaller, decrease may be seen in the March-April period, during which most schools schedule spring breaks.

The discontinuation of stimulant and atomoxetine use during longer (i.e., summer), and perhaps shorter, breaks in the school year may be problematic. There is little doubt that some students and their parents welcome a break from the medications and their side effects even when the net effect of taking them is positive. School breaks are likely to appear to be a good time to discontinue their use temporarily. However, as Cascade et al. (2008) have noted, there are a number of attendant risks to treatment discontinuation, particularly to adolescents. Among these are the potential consequences of untreated ADHD, including behavior problems and substance abuse. In addition, medical management of ADHD may be complicated by episodic use; when treatment is restarted it may be necessary to re-evaluate dosages to achieve an effective response while keeping side effects manageable. The Subcommittee on Attention-Deficit/Hyperactivity Disorder, Steering Committee on Quality Improvement and Management, American Academy of Pediatrics (2011) has recommended that ADHD be

managed as a chronic condition for which sustained treatment should be provided. The results of this study, using data that pre-date the recommendations, suggest instead that treatment is episodic for many youth.

The mix of ADHD diagnosis types (predominantly inattentive vs. predominantly hyperactive or combined) in enrollees initiating treatment was not a specific element of hypothesis one, but it is noteworthy given the fact that the relative distribution of diagnosis types was quite stable across the calendar year. It would not have been unexpected to have seen the hyperactive or combined type of ADHD represented disproportionately among summer initiators given the comparatively lesser need to maintain attentiveness during this period. In fact these types of ADHD diagnosis were associated with higher rates of summer initiation, but the effect was rather small and may stem from a different set of factors. An overrepresentation of predominantly inattentive ADHD during the final exam period would have been consistent with expectations as well. More research is needed, however, before conclusions can be made about the observed consistency in subtypes and about the factors that drive the recorded diagnoses. Most of the data needed for such investigations are not among the elements of administrative medical claims files. Nevertheless, within-provider variation in the types of diagnoses they record would be worth examining. It would also be essential to address the fact the only 56% of ADHD treatment initiators received a diagnosis of ADHD in the year prior to their first prescription. A number of explanations suggest themselves, but the evidence for each must be evaluated in other studies. These include the possibility that many treatment initiators have a long ADHD diagnosis and treatment history and that the observed treatment episode represents a return to care after at least a year's

discontinuation. It is also possible that ADHD diagnoses have been recorded by providers outside the enrollees' health plans or that prescribers are not necessarily recording such diagnoses in patient's records. None of these explanations seems particularly plausible except perhaps the last and only in cases where comorbid conditions take precedence in the limited number of fields provided for recoding diagnoses in most insurance claim forms.

Enrollee and medication characteristics. Hypotheses two and three assumed that prescribers would be particularly vigilant when treating adolescents presenting for treatment of ADHD symptoms during the period leading up to and including final exams. The late spring would seem to be an unlikely time for symptoms of inattention and/or hyperactivity and their associated deficits to first manifest, suggesting that enrollees seeking treatment during that time might be motivated by a desire to use ADHD medications for studying. Hypothesis two focused on whether prescribers were less likely to start treating riskier patients during this time. Signs of riskiness included being older and male, having existing psychiatric/behavioral or substance abuse conditions that might be associated with a tendency to misuse or divert medications, or having conditions that raise concerns about cardiovascular, psychiatric, or other adverse events. Hypothesis three predicted that enrollees beginning treatment during the final exam period would be provided with more abuse-resistant medications, as well as lower amounts.

The results concerning enrollee-level characteristics and their relationships with initiation timing did not support the hypothesis that prescribers would be more selective in the patients they began to treat around final exams than at other times. The literature on the non-medical use of prescription stimulants indicates that such use increases with

age and that it may be more common in males than in females. Similar logic led to the prediction that older and male adolescents seeking doctors' prescriptions for ADHD medications would be underrepresented as final exam period initiators as a result of prescribers erring on the side of caution. Diagnoses of substance abuse and conduct disorders or oppositional defiant disorder were also predicted to give providers second thoughts about writing a prescription. Delaying treatment for a short time, until summer or the beginning of the school year, would give providers the time to evaluate the persistence of patients' symptoms and impairment and to gather more evidence to substantiate a diagnosis of ADHD. A number of authors (cf. Conti, 2004; Kane, 2008) have recommended increased vigilance on the part of providers when patients might be motivated by secondary gain to manufacture or exaggerate symptoms. Exam periods likely provide an occasion for such motivations to manifest.

The bivariate analyses and multinomial logistic regression models both revealed that, in most respects, enrollee characteristics that were thought to signal a higher risk for misuse, diversion, or adverse events were not associated with lower rates of final exam period treatment initiation. Male enrollees had a lower rate of summer initiation than females, but they were no less likely to be final exam period initiators. As anticipated, increasing age was associated with decreasing rates of final exam period initiation. However, the effects were very small, as were the mean differences in age of initiation across the three periods. Moreover, while age may be considered one element in the judgment that a patient could have a propensity to misuse or divert medications it is not a sufficient basis in itself for delaying treatment until concerns about exam-related use have been rendered moot by the passing of a few weeks.

A diagnosis based on the observation of hyperactive or impulsive symptoms, in addition to or in place of problems with inattention, could also be a warning sign pointing to malingering or increased risk of misuse of the prescribed medications. In several studies, undiagnosed students, when instructed to simulate ADHD symptoms on checklists, have tended to report as many or more symptoms as members of a diagnosed comparison group (Harrison, et al., 2007; Jachimowicz & Geiselman, 2004; Quinn, 2003). Therefore diagnostic evidence that supports a broader combined inattentive-hyperactive ADHD diagnosis may, in the context of other information, be more likely to raise concerns about malingering during the final exam period than a diagnosis of predominantly inattentive ADHD. There is also evidence that the hyperactive element of ADHD, which includes impulsivity as well, is more strongly associated than symptoms of inattentiveness with later substance abuse problems in adolescents (Elkins, McGue, & Iacono, 2007). Despite these potential concerns raised by the involvement of hyperactive symptoms in the ADHD diagnosis, the presence of predominantly hyperactive or combined ADHD was weakly but significantly associated with higher rather than lower rates of both final exam period and summer initiation. Whether this finding indicates a higher level of need and service utilization at those times remains to be determined. It should be noted, however, that the effect of diagnosis type was rendered nonsignificant when various measures of service receipt, including psychotropic medications, were included in the logistic regression models.

There was no evidence that the presence of diagnosed comorbid conditions that might raise concerns about misuse, diversion, or adverse events was associated with lower odds of initiating pharmacotherapy for ADHD during the final exam period. With

regard to the risk of misuse and diversion, rates of final exam period initiation were not lower for enrollees with substance abuse or conduct disorders/oppositional defiant disorder than for the overall cohort of initiators. In fact, in the bivariate analyses, individuals with conduct disorders/oppositional defiant disorder were *more likely* to be final exam period initiators. This effect was not evident in the logistic regression analyses, however, when measures of service utilization were included. A similar lack of hypothesized effects was found for diagnoses, such as those for cardiovascular conditions, serious mental illness, and tic disorders, which might suggest increased susceptibility to adverse events.

While these results may simply mean that the timing of treatment initiation is insensitive to psychiatric/behavioral, substance abuse, and medical comorbidities, it is necessary to consider alternative explanations as well. First, the conditions recorded in a patient's claims history may be incomplete or misleading in some cases, particularly given a fixed look-back period. Even in the case of recent diagnoses, medical claims don't carry information about the symptoms that patients bring to the clinical encounter. In addition, older diagnoses contained in a patient's record may not be salient during a visit prompted by new symptoms. Moreover, the clinical situation faced by providers is much more than the sum of diagnosed conditions. Risks and benefits must often be weighed, and the presence of conditions associated with an identified, but low, risk are only one element of this calculus. From a practical standpoint, decisions must be made by providers about which diagnoses to record, particularly in outpatient claims, which typically carry only a limited number of diagnosis fields. Furthermore, where patients are treated by multiple providers, for example by a family doctor and a child psychiatrist,

lack of communication about conditions and treatment may give each provider an incomplete picture of a patients' medical status. Finally, from a methodological standpoint, the decision to require only a single outpatient claim as sufficient for establishing a diagnosis likely achieved sensitivity in identifying enrollees with comorbid conditions, but possibly at the expense of specificity. This was necessary, however, given the relative low prevalence of many conditions as well as the limited look-back period.

The logic behind hypothesis three was that, faced with concerns about enrollees seeking treatment for ADHD in time for final exams, but many months after the start of the school year, doctors would be more selective about the medications they prescribed and more conservative in the amounts supplied. When suspicions are raised about the use of medication for enhancement or other non-medical purposes rather than treatment, it may reasonable to evaluate the risks and benefits of pharmacological treatment differently. Higher rates of behavioral disorders, like those observed among final exam period initiators in this study, may reinforce this caution. Nevertheless, any differences in the medications supplied to treatment initiators in different periods should be modest given the overriding goal of providing a therapeutic effect.

Among the ADHD medications, the nonstimulant atomoxetine was the first drug received by a minority (14%) of treatment initiators. Although it received FDA approval for the treatment of ADHD only in 2002, atomoxetine was available by the time four out of five of this study's enrollees began treatment. Stimulants were the first choice of medication for a large majority; methylphenidate formulations were received by 48% of initiators and amphetamine formulations were received by 38%. When the ADHD

medications were ordered with respect to their resistance to being abused in order to create a reinforcing effect – a high – the relationship between that order and initiation timing was small and driven almost entirely by atomoxetine. Those enrollees who were first prescribed atomoxetine had higher rates of summer, but not final exam period, treatment initiation than did recipients of stimulants. The rates for final exam period initiation were almost identical across medication types.

It appears that, in the limited circumstance in which medication type was related to initiation timing (i.e., summer vs. school year initiation with atomoxetine), the stimulant-nonstimulant distinction carried more weight in prescribing than the abuse resistance distinction. Absent a compelling reason to avoid prescribing stimulants, methylphenidate and amphetamine are usually preferred when starting treatment. It is possible that the non-stimulating effects of atomoxetine make it more desirable during the summer for some patients because there is no need to follow a daily school schedule. It may also be the case that enrollees initiating ADHD treatment during the summer present a more complex clinical challenge than the majority who begin treatment during the school year. This may include higher rates of hyperactive and impulsive symptoms and more cases of behavioral disorders, as well as patient characteristics that are not observable in administrative claims data. Summer initiators are also, by definition, not among the enrollees whose physicians and parents are willing to provide a break from ADHD treatment when school is not in session.

Compared with all stimulant and atomoxetine prescriptions, those supplied to treatment initiators tended to provide lower daily doses. This is consistent with treatment guidelines, which recommend starting with a lower dose and then titrating upward until a

therapeutic response is achieved. Among the cohort of initiators, the average daily dose was related to when treatment began, but not in the direction hypothesized. Final exam period initiation, as well as summer initiation, was associated with higher rather than lower dose. The effects were small but were monotonically higher across the five dose levels. Moreover, they remained significant in the logistic regression models when controlling for comorbid conditions, service receipt, and medication type.

Most of the prescriptions for ADHD medications were for a conventional 30-day supply. However, like daily dose, the days' supply of medication was also related to initiation timing, and in a direction that was counter to hypothesis. Final exam period initiators were given a slightly larger supply of medication than school year initiators. Summer initiators were given the largest supply. These differences which, in the regression model, were significant only for summer vs. school year initiators were quite small however; the biggest between-period difference represented less than a single pill or patch.

The unexpected results concerning average daily dose may reflect a tendency for summer and final exam period initiators to present a more challenging clinical picture than school year or final exam period initiators. As noted above, this may include higher levels of hyperactive symptoms and behavioral problems. In addition, rates of autistic disorders, the most commonly observed diagnosis among enrollees with pervasive developmental disorders, were substantially higher among summer initiators. The reasons behind the observed differences in days' supply are unclear and should not be over-interpreted. Given their small size, it is unlikely, however, that they reflect prescribers' concerns about misuse or safety.

Measures of care utilization. Upon review of the bivariate results, an additional tentative hypothesis was evaluated by constructing a small set of variables that introduced measures of enrollees' level of ongoing medical care. These variables represented overall physician visits with a number of different provider types, use of inpatient and outpatient psychiatric/behavioral services, and receipt of several types of psychotropic medications. The intent of the analyses incorporating these additional variables was to determine whether enrollees initiating ADHD treatment during the summer (and, to a lesser extent, the final exam period), evinced a higher level of overall care receipt. This hypothesis had been suggested from results indicating that a number of enrollee and medication characteristics were associated with higher rates of initiation in the late spring and summer, including hyperactive or combined type ADHD, behavioral disorders, pervasive developmental disorders, receipt of an ADHD diagnosis from a psychiatrist rather than a primary care provider, choice of atomoxetine as the initial medication, and higher stimulant or atomoxetine doses.

Receipt of services, for any reason, was positively associated with starting ADHD pharmacotherapy in the summer. Enrollees who had one or more visits with a psychiatrist, pediatrician (including specialists), primary care provider, or any doctor had higher rates of summer initiation than enrollees who did not have such visits. Psychiatrist and pediatrician visits were associated with higher rates of final exam period initiation as well. However, after controlling for other services, medication variables, and comorbid conditions, the odds of summer initiation were increased only among enrollees who had seen family practitioners or pediatricians. Only pediatrician visits were associated with higher odds of final exam vs. school year initiation.

The finding that psychiatrist visits, in the full model, were no longer associated with final exam period or summer initiation is probably a result of the inclusion of two other types of service utilization measures. In the bivariate analyses rates of both final exam period and summer treatment initiation were higher among enrollees who had received one or more outpatient services carrying a psychiatric/behavioral diagnosis other than ADHD. In addition, enrollees who received an antidepressant or antipsychotic medication had higher rates of final exam period or summer initiation than those who had not received one of these medications. Considered together, these results indicate that receipt of medical – primarily, but not exclusively, psychiatric - services is predictive of treatment initiation around final exam time or the summer. These findings are consistent with the hypothesis that enrollees initiating pharmacological treatment for ADHD during these times have greater or more complex medical need.

County variation. Hypothesis four was based on upon the assumption that, to the extent that there was an increase in final exam period treatment initiation, the size of the effect would vary among California counties as a function of their average levels of performance on various widely administered tests of academic ability and achievement. Had such variation occurred in the data, the multinomial logistic regression analyses would have treated the between-county differences as random effects and regressed them on measures derived from the SAT, AP, STAR, and CAHSEE tests. A secondary element of hypothesis four would have treated as random effects the relationships (i.e., slope coefficients) suggestive of prescriber caution in final exam period treatment initiation as well. However, evidence from preliminary descriptive analyses suggested that there was very little variation among the California counties in the proportion of

treatment initiators that began receiving stimulants or atomoxetine during the final exam period. This finding was confirmed by initial random effects models that found that the variance components for between-county differences were effectively zero. Moreover, to the extent that counties did vary slightly in their proportions of final exam period initiators, additional descriptive analyses found little evidence that final exam initiation was correlated with measures of academic performance. Caution is warranted in over-interpreting these results however. Most of the counties in California are very large, and county-level averages of initiation rates and academic measures may mask significant heterogeneity at lower levels of aggregation such as school districts or municipalities. In future studies, the central challenge to a finer-grained analysis - sample size - could be alleviated by aggregating such smaller units into county types based on common characteristics.

Re-evaluation and Limitations

A number of assumptions and elements of the study design must be re-evaluated in light of the largely negative findings of this investigation. First, the division of the calendar year into school year, final exam period, and summer intervals appears in retrospect to not have captured differences in initiation rates. This was the case even when alternative start and end dates were considered. In fact, the final exam period, both in terms of initiation rates and their correlates, appeared to represent a transitional period between higher rates of initiation during the school year and the lower early summer rates. It marked the beginning of the summer decline, and the relationships between enrollee/medication characteristics and initiation rates were often similar, but weaker than, the relationships with summer rates. Either the assumption that academic demand

increased during the final exam period, the assumption that prescribing and initiation would be sensitive to such demand, or both assumptions, proved to be untenable.

The question of whether the final exam period represents a unique period of increased academic demand depends on a number of factors, including the background level of demand during the rest of the school year, the challenge imposed by the exams, and students' motivations and perceptions of the academic stakes. These were unobservable in the Medstat data, but at least some of them must be considered important moderators in any future analysis. If academic demand was, in fact, increased around final exams then it did not seem to result in higher levels of medication receipt. Whether this would have been a result of student demand or of prescribers' responses to that demand is unknown because care seeking and receipt are irretrievably entangled in medical claims data. Whatever the underlying cause, if any, the result is encouraging. ADHD is a chronic condition that represents more than the sum of inattentive and hyperactive-impulsive symptoms. In order for ADHD to be diagnosed and treated, symptoms should have been observed from an early age, for at least six months, and caused impairment in at least two settings. Therefore any increase in prescribing attributable to a short-term increase in academic demand is likely to be the result of incomplete evaluation of patient history or liberal prescribing practices.

The low rates of physician visits, and particularly the low percentage of treatment initiators with an ADHD diagnosis in the past year, raises concerns that some diagnoses and services may have gone unrecorded in enrollees' claims histories. While in some cases this may have been the result of enrollees receiving care outside their health plans, the plans represented in the Medstat database are likely to offer comprehensive coverage.

If diagnoses and services were missed in the data, this would also have affected estimates of comorbid conditions, psychiatric services, and psychotropic medication receipt. Given these concerns, a more thorough investigation of the routine care provided to youth with ADHD is warranted. This would also involve additional analysis to identify the doctor visits that had most likely resulted in prescriptions.

The decision to characterize only the first observed prescription supplied to enrollees reflected the intended focus on physician's initial treatment decisions and avoided the analytic complexities associated with repeated observations. It is likely that this also increased the relative salience of those enrollee-level variables that might raise concerns about misuse, diversion, or adverse events. However, there is undoubtedly useful information in enrollees' post-initiation service and prescription histories as well. This includes dose changes and medication switching, receipt of psychosocial services, new prescriptions for non-ADHD medications, newly diagnosed conditions, adverse events resulting in emergency department visits or hospitalization, evidence of potential "doctor shopping", and adherence to the prescribed medication regimen. Whether or not such data yield insights on strategic use of medications, there is a need for characterizing and understanding patterns of diagnosing and service receipt for patients beginning treatment for ADHD.

Treatment initiators were defined as enrollees whose first observed prescription fill for an ADHD medication was preceded by a one-year period of eligibility with no such fills. Such look-back periods, usually six months or a year, are typical in epidemiology and similar research. However, they inevitably result in the inclusion, along with individuals who are truly treatment-naïve, of previously treated enrollees.

Such individuals, by definition, have a different medical history than those treated for the first time, and their reasons for discontinuing and then resuming treatment may reflect significant differences in comorbidities, adherence, and motivations. Without available self-report data on treatment history, it is difficult to assess the scope and consequences of this issue.

Implications and Conclusion

The results of this study do not contradict the large self-report literature indicating that students acquire and use ADHD medications in order to improve concentration and studying. Rather, to the extent that the research design is sound, they suggest any of several non-mutually exclusive conclusions.

1. That the medications consumed for studying enter the student population over the course of the year rather than just in time for exams.
2. That the final exam period does not create, in the aggregate, a substantial increase in academic demand, particularly for students in middle school and high school.
3. That the net effect of final exam period acquisition of ADHD medications is not sufficient to produce an identifiable signal, particularly against the pre-summer decrease in prescribing and initiation.

In light of the large number of stimulant and atomoxetine prescriptions that are supplied over the course of the year, it is likely that many pills go unused, creating a surplus that can be consumed or diverted when academic demands increase. In fact, there are reports of this in the literature. Had there been an identifiable increase in prescription fills in the final exam period, it would have represented an opportunity to communicate with physicians about potential visits from enhancement-motivated students. There is

little doubt that most doctors are aware that some patients attempt to secure not only stimulants, but also sedatives and narcotic pain killers, for non-medical purposes. However, to the extent that non-medical use of prescription ADHD medications is viewed though the same prevention/treatment prism as misuse of these other drugs, we risk ignoring the study related dimension of their use. A finding that students were acquiring these medications at a time when they're valued more for their effects on cognition than for their reinforcing effects would have shed a spotlight on such study motivated use. As noted earlier, drug manufacturers have had success in creating stimulant formulations that are resistant to recreational use, in addition to the nonstimulant atomoxetine. As result, the balance of non-medical use of ADHD medications will continue to shift toward enhancement.

How various stakeholders address the study motivated use of ADHD medications may provide a preview of the way in which the use of future cognition-enhancing drugs will be managed. ADHD medications provide improvement in only a limited range of mental tasks. However, it is almost certain that drug development will eventually bring us closer to what might legitimately termed "smart drugs" that improve not only attention and concentration, but also memory, creativity, and insight. Moreover, subject to an adequate scientific and regulatory framework, it is likely that these drugs can be used with minimal risk. Given proper research and communication, patients, doctors, educators, policy makers, and others have the opportunity to not be taken by surprise by these likely developments.

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Appendix

Table A15

p(z=0), Two-tailed, for Test that Proportions are Equal, for Table 15

School year		Female	Male
		0.726	0.735
Female	0.726		0.007
Male	0.735	0.007	

Final exams		Female	Male
		0.099	0.104
Female	0.099		0.027
Male	0.104	0.027	

Summer		Female	Male
		0.176	0.161
Female	0.176		<0.001
Male	0.161	<0.001	

School year		Age 14	Age 15	Age 16	Age 17	Age 18
		0.720	0.755	0.759	0.748	0.729
Age 14	0.720		<0.001	<0.001	<0.001	0.141
Age 15	0.755	<0.001		0.509	0.283	<0.001
Age 16	0.759	<0.001	0.509		0.099	<0.001
Age 17	0.748	<0.001	0.283	0.099		0.013
Age 18	0.729	0.141	<0.001	<0.001	0.013	

Final exams		Age 14	Age 15	Age 16	Age 17	Age 18
		0.106	0.099	0.099	0.095	0.089
Age 14	0.106		0.030	0.038	0.003	<0.001
Age 15	0.099	0.030		0.926	0.369	0.033
Age 16	0.099	0.038	0.926		0.381	0.037
Age 17	0.095	0.003	0.369	0.381		0.231
Age 18	0.089	<0.001	0.033	0.037	0.231	

Summer		Age 14	Age 15	Age 16	Age 17	Age 18
		0.174	0.146	0.142	0.157	0.183
Age 14	0.174		<0.001	<0.001	<0.001	0.090
Age 15	0.146	<0.001		0.420	0.042	<0.001
Age 16	0.142	<0.001	0.420		0.007	<0.001
Age 17	0.157	<0.001	0.042	0.007		<0.001
Age 18	0.183	0.090	<0.001	<0.001	<0.001	

Table A16

p(z=0), Two-tailed, for Test that Proportions are Equal, for Table 16

School year		None	ADHD, inattentive type	ADHD, hyperactive or combined type
		0.734	0.741	0.721
None	0.734		0.067	<0.001
ADHD, inattentive type	0.741	0.067		<0.001
ADHD, hyperactive or combined type	0.721	<0.001	<0.001	

Final exams		None	ADHD, inattentive type	ADHD, hyperactive or combined type
		0.103	0.096	0.106
None	0.103		0.007	0.236
ADHD, inattentive type	0.096	0.007		0.001
ADHD, hyperactive or combined type	0.106	0.236	0.001	

Summer		None	ADHD, inattentive type	ADHD, hyperactive or combined type
		0.163	0.163	0.173
None	0.163		0.958	0.001
ADHD, inattentive type	0.163	0.958		0.005
ADHD, hyperactive or combined type	0.173	0.001	0.005	

Table A16 (cont.)
p(z=0), Two-tailed, for Test that Proportions are Equal, for Table 16

School year		Family practice	Pediatrics (inc. specialists)	Psychiatry/child psychiatry	Other physician	Non-physician
		0.750	0.735	0.708	0.729	0.725
Family practice	0.750		0.012	<0.001	0.001	0.002
Pediatrics (inc. specialists)	0.735	0.012		<0.001	0.350	0.144
Psychiatry/child psychiatry	0.708	<0.001	<0.001		0.029	0.005
Other physician	0.729	0.001	0.350	0.029		0.600
Non-physician	0.725	0.002	0.144	0.005	0.600	

Final exams		Family practice	Pediatrics (inc. specialists)	Psychiatry/child psychiatry	Other physician	Non-physician
		0.085	0.104	0.112	0.102	0.104
Family practice	0.085		<0.001	<0.001	<0.001	<0.001
Pediatrics (inc. specialists)	0.104	<0.001		0.081	0.649	0.909
Psychiatry/child psychiatry	0.112	<0.001	0.081		0.136	0.051
Other physician	0.102	<0.001	0.649	0.136		0.701
Non-physician	0.104	<0.001	0.909	0.051	0.701	

Summer		Family practice	Pediatrics (inc. specialists)	Psychiatry/child psychiatry	Other physician	Non-physician
		0.165	0.161	0.180	0.170	0.171
Family practice	0.165		0.428	0.012	0.330	0.391
Pediatrics (inc. specialists)	0.161	0.428		0.001	0.082	0.095
Psychiatry/child psychiatry	0.180	0.012	0.001		0.172	0.112
Other physician	0.170	0.330	0.082	0.172		0.877
Non-physician	0.171	0.391	0.095	0.112	0.877	

Table A17

$p(\chi^2=0)$ for Presence vs. Absence of Comborbid Conditions for Table 17

	School year	Final exams	Summer
Anxiety and related disorders - yes vs. no	0.005	0.234	0.012
Depressive disorders - yes vs. no	0.021	0.031	0.230
Conduct disorder or oppositional defiant disorder - yes vs. no	0.000	0.010	0.031
Serious mental illness - yes vs. no	0.012	0.071	0.132
Substance abuse disorders - yes vs. no	0.618	0.562	0.807
Cardiovascular conditions - yes vs. no	0.580	0.426	0.999
Sleep disorders - yes vs. no	0.001	0.225	0.031
Tic disorders - yes vs. no	0.019	0.196	0.094
Seizures - yes vs. no	0.185	0.857	0.081
Pervasive developmental disorders - yes vs. no	0.001	0.635	0.001

Note. 1 df per comparison (condition present/absent vs. initiation in one period vs. the other two periods).

Table A18

p(z=0), Two-tailed, for Test that Proportions are Equal, for Table 18

School year		Lisdexamphetamine	Amphetamine	Dextroamphetamine	Methylphenidate	Dexmethylphenidate	Atomoxetine
		0.856	0.733	0.740	0.739	0.729	0.703
Lisdexamphetamine	0.856		<.001	<.001	<.001	<.001	<.001
Amphetamine	0.733	<.001		0.530	0.083	0.678	<.001
Dextroamphetamine	0.740	<.001	0.530		0.928	0.441	0.001
Methylphenidate	0.739	<.001	0.083	0.928		0.295	<.001
Dexmethylphenidate	0.729	<.001	0.678	0.441	0.295		0.011
Atomoxetine	0.703	<.001	<.001	0.001	<.001	0.011	

Final exams		Lisdexamphetamine	Amphetamine	Dextroamphetamine	Methylphenidate	Dexmethylphenidate	Atomoxetine
		0.000	0.102	0.103	0.104	0.099	0.101
Lisdexamphetamine	0.000		<.001	<.001	<.001	<.001	<.001
Amphetamine	0.102	<.001		0.897	0.401	0.644	0.762
Dextroamphetamine	0.103	<.001	0.897		0.896	0.682	0.803
Methylphenidate	0.104	<.001	0.401	0.896		0.437	0.350
Dexmethylphenidate	0.099	<.001	0.644	0.682	0.437		0.770
Atomoxetine	0.101	<.001	0.762	0.803	0.350	0.770	

Summer		Lisdexamphetamine	Amphetamine	Dextroamphetamine	Methylphenidate	Dexmethylphenidate	Atomoxetine
		0.144	0.165	0.157	0.157	0.173	0.197
Lisdexamphetamine	0.144		0.246	0.518	0.472	0.139	0.004
Amphetamine	0.165	0.246		0.388	0.006	0.329	<.001
Dextroamphetamine	0.157	0.518	0.388		0.976	0.181	<.001
Methylphenidate	0.157	0.472	0.006	0.976		0.049	<.001
Dexmethylphenidate	0.173	0.139	0.329	0.181	0.049		0.006
Atomoxetine	0.197	0.004	<.001	<.001	<.001	0.006	

Table A19

p(z=0), Two-tailed, for Test that Proportions are Equal, for Table 19

School year		Atomoxetine	Concerta, Daytrana, Vyvanse	Other LA, XR, etc. stimulant	Immediate-release stimulant
		0.703	0.734	0.738	0.739
Atomoxetine	0.703		<.001	<.001	<.001
Concerta, Daytrana, Vyvanse	0.734	<.001		0.303	0.249
Other LA, XR, etc. stimulant	0.738	<.001	0.303		0.810
Immediate-release stimulant	0.739	<.001	0.249	0.810	

Final exams		Atomoxetine	Concerta, Daytrana, Vyvanse	Other LA, XR, etc. stimulant	Immediate-release stimulant
		0.101	0.103	0.101	0.103
Atomoxetine	0.101		0.559	0.943	0.577
Concerta, Daytrana, Vyvanse	0.103	0.559		0.453	0.999
Other LA, XR, etc. stimulant	0.101	0.943	0.453		0.486
Immediate-release stimulant	0.103	0.577	0.999	0.486	

Summer		Atomoxetine	Concerta, Daytrana, Vyvanse	Other LA, XR, etc. stimulant	Immediate-release stimulant
		0.197	0.163	0.161	0.158
Atomoxetine	0.197		<.001	<.001	<.001
Concerta, Daytrana, Vyvanse	0.163	<.001		0.538	0.167
Other LA, XR, etc. stimulant	0.161	<.001	0.538		0.387
Immediate-release stimulant	0.158	<.001	0.167	0.387	

Table A20

p(z=0), Two-tailed, for Test that Proportions are Equal, for Table 20

School year		0 - Lowest	1	2	3	4 - Highest
		0.741	0.736	0.731	0.725	0.711
0 - Lowest	0.741		0.230	0.033	0.002	<.001
1	0.736	0.230		0.282	0.030	<.001
2	0.731	0.033	0.282		0.276	0.001
3	0.725	0.002	0.030	0.276		0.024
4 - Highest	0.711	<.001	<.001	0.001	0.024	

Final exams		0 - Lowest	1	2	3	4 - Highest
		0.099	0.100	0.102	0.107	0.108
0 - Lowest	0.099		0.725	0.349	0.023	0.017
1	0.100	0.725		0.528	0.045	0.032
2	0.102	0.349	0.528		0.187	0.135
3	0.107	0.023	0.045	0.187		0.815
4 - Highest	0.108	0.017	0.032	0.135	0.815	

Summer		0 - Lowest	1	2	3	4 - Highest
		0.160	0.164	0.167	0.168	0.182
0 - Lowest	0.160		0.252	0.076	0.062	<.001
1	0.164	0.252		0.442	0.346	<.001
2	0.167	0.076	0.442		0.829	0.003
3	0.168	0.062	0.346	0.829		0.008
4 - Highest	0.182	<.001	<.001	0.003	0.008	

Table A22
p(z=0), Two-tailed, for Test that Proportions are Equal, for Table 22

Family practice visits

School year		No	Yes
		0.731	0.734
No	0.731		0.357
Yes	0.734	0.357	

Final exams		No	Yes
		0.105	0.097
No	0.105		<0.001
Yes	0.097	<0.001	

Summer		No	Yes
		0.164	0.169
No	0.164		0.069
Yes	0.169	0.069	

Pediatrics visits

School year		No	Yes
		0.739	0.725
No	0.739		<0.001
Yes	0.725	<0.001	

Final exams		No	Yes
		0.099	0.106
No	0.099		0.001
Yes	0.106	0.001	

Summer		No	Yes
		0.163	0.169
No	0.163		0.021
Yes	0.169	0.021	

Psychiatry/child psychiatry visits

School year		No	Yes
		0.737	0.713
No	0.737		<0.001
Yes	0.713	<0.001	

Final exams		No	Yes
		0.100	0.111
No	0.100		<0.001
Yes	0.111	<0.001	

Summer		No	Yes
		0.163	0.177
No	0.163		<0.001
Yes	0.177	<0.001	

Other physician visits

School year		No	Yes
		0.733	0.732
No	0.733		0.753
Yes	0.732	0.753	

Final exams		No	Yes
		0.102	0.102
No	0.102		0.679
Yes	0.102	0.679	

Summer		No	Yes
		0.166	0.166
No	0.166		0.822
Yes	0.166	0.822	

Table A22 (cont.)
p(z=0), Two-tailed, for Test that Proportions are Equal, for Table 22

Primary care physician visits

School year		No	Yes
		0.738	0.730
No	0.738		0.018
Yes	0.730	0.018	

Final exams		No	Yes
		0.103	0.102
No	0.103		0.666
Yes	0.102	0.666	

Summer		No	Yes
		0.159	0.169
No	0.159		<0.001
Yes	0.169	<0.001	

Any physician visits

School year		No	Yes
		0.748	0.731
No	0.748		0.006
Yes	0.731	0.006	

Final exams		No	Yes
		0.107	0.102
No	0.107		0.253
Yes	0.102	0.253	

Summer		No	Yes
		0.145	0.167
No	0.145		<0.001
Yes	0.167	<0.001	

Table A23

p(z=0), Two-tailed, for Test that Proportions are Equal, for Table 23

Inpatient claims with a psychiatric diagnosis

School year		None	One or more
		0.732	0.721
None	0.732		0.323
One or more	0.721	0.323	

Final exams		None	One or more
		0.102	0.110
None	0.102		0.303
One or more	0.110	0.303	

Summer		None	One or more
		0.166	0.169
None	0.166		0.747
One or more	0.169	0.747	

Outpatient claims with a psychiatric diagnosis

School year		None	One or more
		0.739	0.718
None	0.739		<0.001
One or more	0.718	<0.001	

Final exams		None	One or more
		0.099	0.108
None	0.099		<0.001
One or more	0.108	<0.001	

Summer		None	One or more
		0.162	0.174
None	0.162		<0.001
One or more	0.174	<0.001	

Table A24

p(z=0), Two-tailed, for Test that Proportions are Equal, for Table 24

Antidepressants

School year		No	Yes	Final exams		No	Yes	Summer		No	Yes
		0.737	0.712			0.100	0.112			0.163	0.177
No	0.737		<0.001	No	0.100		<0.001	No	0.163		<0.001
Yes	0.712	<0.001		Yes	0.112	<0.001		Yes	0.177	<0.001	

Antipsychotics

School year		No	Yes	Final exams		No	Yes	Summer		No	Yes
		0.735	0.693			0.101	0.116			0.163	0.191
No	0.735		<0.001	No	0.101		0.001	No	0.163		<0.001
Yes	0.693	<0.001		Yes	0.116	0.001		Yes	0.191	<0.001	

Mood stabilizers

School year		No	Yes	Final exams		No	Yes	Summer		No	Yes
		0.734	0.706			0.102	0.103			0.164	0.191
No	0.734		<0.001	No	0.102		0.822	No	0.164		<0.001
Yes	0.706	<0.001		Yes	0.103	0.822		Yes	0.191	<0.001	

Anxiolytics/hypnotics

School year		No	Yes	Final exams		No	Yes	Summer		No	Yes
		0.733	0.711			0.102	0.110			0.166	0.179
No	0.733		0.009	No	0.102		0.166	No	0.166		0.066
Yes	0.711	0.009		Yes	0.110	0.166		Yes	0.179	0.066	

Any of four

School year		No	Yes	Final exams		No	Yes	Summer		No	Yes
		0.740	0.710			0.099	0.111			0.161	0.179
No	0.740		<0.001	No	0.099		<0.001	No	0.161		<0.001
Yes	0.710	<0.001		Yes	0.111	<0.001		Yes	0.179	<0.001	

Curriculum Vita

Scott M. Bilder

Education

Rutgers, The State University of New Jersey
Ph.D. Educational Psychology, 2012
M.S. Social Psychology, 1991

Albright College
A.B. Psychology, 1987 *(summa cum laude)*

Professional Experience

2000-present **Rutgers, The State University of New Jersey**
Senior Programmer/Data Analyst
Senior Research Project Manager and Director, Data Core, Center for Education and Research in Mental Health Therapeutics

1990-present **Rutgers, The State University of New Jersey**
Lecturer/Coadjutant Instructor for the following courses:
Research Methods (Dept. of Psychology).
Research Methods (Dept. of Human Ecology).
Psychological Approaches to Social Problems (Dept. of Psychology).
Prejudice and Conflict (Dept. of Psychology).
UNIX Fundamentals (Office of Continuous Education and Outreach).
UNIX Administration (Office of Continuous Education and Outreach).
Data Analysis (Bloustein School of Planning and Public Policy)
Psychometric Theory (Rutgers Graduate School of Education)

1998-2000 **Lucent Technologies**
Market Research and Modeling Manager

1993-1997 **Rutgers, The State University of New Jersey**
Programmer/Analyst
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1992-1993 **Rutgers, The State University of New Jersey**
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1991-1992 **University of Medicine and Dentistry of New Jersey**
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Research Assistant

Publications

Walkup, J., Akincigil, A., Chakravarty, S., Olfson, M., Bilder, S., Amin, S., Siegel, M. & Crystal, S. (2011). Bipolar medication use and adherence to antiretroviral therapy among patients with HIV-AIDS and bipolar disorder. *Psychiatric Services 62*(3): 313-316.

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Waldman J.M., Bilder S., Freeman N.C., & Friedman M. (1993). A portable datalogger to evaluate recall-based time use measures. *Journal of Exposure Analysis & Environmental Epidemiology. 3(1):*39-48.

Recent First-authored Presentations

Bilder, S., Walkup, J., Akincigil, A. & Crystal, S. (2008). Adherence to antiretroviral therapy in persons with bipolar disorder. Paper presented at the 3rd International Conference on HIV Treatment Adherence, Jersey City, NJ**.**

Bilder, S., Walkup, J., Sohrakoff, A. & Crystal, S. (2007). Mood stabilizer and anticonvulsant prescription refill persistence in bipolar disorder: disparities and co-occurring conditions. Paper presented at the AcademyHealth Annual Research Meeting, Orlando, FL.

Specialized Training

National Health Interview Survey (NHIS) workshop, November 2001.
Event History & Survival Analysis, workshop with Paul Allison, August 2003.
Hierarchical Linear Models, workshop with Steven Raudenbush & Anthony Bryk, September 2005.
Conducting Research with Medicaid Claims Data, workshop, September 2006.
Introduction to the use of Medicare Data for Research, workshop, January 2007.