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Pharmacotherapy with Atomoxetine for US Children and Adolescents

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Background. *Atomoxetine, a non-stimulant medication, was approved for treatment of Attention Deficit/ Hyperactivity Disorder (ADHD) in 2002. However, there is a paucity of recent practice-based national data on the use of atomoxetine. This article compares the use of atomoxetine with that of stimulant medications in outpatient treatment of U.S. children and adolescents, and examines the predictors of atomoxetine use in this population.*

Methods. *The 2003–2004 National Ambulatory Medical Care Survey and the outpatient department portion of the 2003–2004 National Hospital Ambulatory Medical Care Survey were used to determine the utilization of atomoxetine and stimulants in youth < 20 years. Bivariate analyses were used to examine the use of atomoxetine relative to that of stimulant medications in children and adolescents (n = 1,133). Multiple logistic regression analysis was applied to visits involving youths with ADHD to examine predictors of atomoxetine use (n = 1,361).*

Results. *An estimated 14.51 million visits involving psychotropic agents resulted in prescription of atomoxetine and stimulants during the years 2003 and 2004. The percentage of visits for atomoxetine, as a proportion of all psychotropic visits, was nearly 10% (versus 40% for stimulants). Analyses of visits involving atomoxetine and stimulants revealed age- and region-based differences in the use of atomoxetine. Among children with ADHD, approximately 15% of outpatient visits resulted in prescription of atomoxetine; and stimulant medications were prescribed in nearly 61% of these visits. Examination of predictors of ADHD treatments (atomoxetine vs. stimulants) revealed no variations in the use of atomoxetine across sex, race, psychiatric comorbidity, primary care status, and metropolitan location. However, atomoxetine was preferred in 10-to-14 year old children, and in patients with private insurance. Physicians in the Northeast region were less likely to prescribe atomoxetine than physicians in the South.*

Conclusions. *Although stimulant drugs remain the most frequently prescribed class of psychotropic medications for ADHD in children and adolescents, atomoxetine has emerged as the leading stimulant alternative. Preferential use of atomoxetine in age group 10-to-14 years needs to be further evaluated. Additionally, the role of several factors, including patient preferences, physician-related factors, and psychiatric comorbidity warrant further investigation. Data on differential safety and efficacy of atomoxetine and stimulants are needed to optimize pharmacotherapy in children.*

INTRODUCTION

In 2002, the Food and Drug Administration approved the labeling of atomoxetine, a norepinephrine transporter inhibitor, for use in the treatment of attention deficit/ hyperactivity disorder (ADHD), and this drug became the first non-stimulant medication to be approved for pediatric and adult ADHD (1–4). Today, atomoxetine is recognized as an important medication for ADHD, as documented by the most recent version of ADHD treatment algorithm by Texas Children's Medication Algorithm Project (CMAP); an algorithm based on expert-consensus and best evidence available (5). According to CMAP, stimulant medications are recommended as a first line treatment in most children with ADHD. However, there are clinical situations in which atomoxetine may be preferred. Atomoxetine is recommended by CMAP as the first line medication in ADHD with coexistent substance abuse problems, in cases of opposition to the use of stimulant medications, or when stimulant treatment is associated with severe side effects including tics or depression (5). Although atomoxetine has emerged as an important alternative treatment for ADHD, there is a paucity of recent practice-based nationally representative pediatric data on atomoxetine.

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This study presents national data on prescribing of atomoxetine to the U.S. children and adolescents in outpatient settings.

In an exploratory study, Van Brunt and associates (6) compared the predictors of atomoxetine use with those of stimulant medications in children and adolescents. They found that clinicians preferred atomoxetine therapy in the youth with psychiatric comorbidity, contraindications to stimulants, or in high users of mental health services. However, the data for their study was based on managed care claims during a 9-month period in the year 2003, shortly after the introduction of atomoxetine in the United States. It is unclear whether or not the practice patterns observed by Van Brunt et al. have persisted beyond the first year of atomoxetine introduction. This study presents more recent data based on national surveys conducted during the years 2003 and 2004.

This study has two objectives. One is to compare the use of atomoxetine with that of stimulant medications in outpatient treatment of U.S. children and adolescents during the years 2003 and 2004, and the other is to examine the predictors of atomoxetine use in pediatric ADHD. The relationships between the prescribing of atomoxetine (relative to stimulant medications) and several patient- and physician-level characteristics are examined.

METHODS

Data Source

The 2003–2004 National Ambulatory Medical Care Survey (NAMCS) and the outpatient department portion of the 2003–2004 National Hospital Ambulatory Medical Care Survey (NHAMCS) were used to study utilization of atomoxetine and stimulants in children and adolescents (7–10). These national surveys were conducted by the National Center for Health Statistics (NCHS). The survey years selected for this study represent the most recent data set available from the NCHS at the time of this research (7–10). The surveys provide the most comprehensive dataset that monitors ambulatory medical care practices in the United States. This study was considered exempt by the Institutional Review Board as the secondary analysis is based on public use data files that protect the identity of patients.

The NAMCS is a national probability sample survey of in-person visits to physician offices (7–8). The NCHS utilized a multistage probability design that involved probability samples of primary sampling units, physician practices within the sampling units, and patient visits within those practices. The NHAMCS is a national probability sample of visits to OPDs (Outpatient Department) and emergency departments (9–10). Only the OPD portion of the NHAMCS was used in this study; the medical care provided in these settings is similar to the care provided in office-based settings. The NHAMCS used a four-stage probability design with samples of primary sampling units, hospitals within these sampling units, clinics within hospitals, and patient visits within clinics.

The NCHS collected patient care data in the NAMCS and the NHAMCS using the Patient Record Form (PRF). The PRFs were similar in both national surveys and included detailed information on patient demographics, physician diagnoses, medications prescribed, and the disposition of the visit. Prescribing data in the PRFs included up to six prescription and nonprescription medications, including all new or continued medications ordered, supplied, or administered during each visit. Medications were coded according to a unique classification scheme developed at the NCHS, and drug classes were categorized based on National Drug Code numbers. The NAMCS collected data on 50,574 PRFs, where as the OPD component of the NHAMCS included 66,275 PRFs for a total of 116,849 PRFs from 2002–2004. Additional details regarding data collection, editing, and coding used in these national surveys can be found elsewhere (11–12).

Definitions and Data Analysis

The secondary data analyses involved examination of medications and diagnosis in visits involving patients 19 years old and younger. The study focused on utilization of atomoxetine and stimulants (amphetamine, dextroamphetamine, methylphenidate, and pemoline). The drug class codes were used to identify all psychotropic medications, and generic medication codes identified atomoxetine and stimulants. SAS (13) was used for data extraction, while SUDAAN (14) was used for data analysis. Analyses of the national surveys require special consideration with regard to variance estimation and analysis due to complex sampling design that includes stratification, clustering, multiple stages of selection and disproportionate sampling. The SUDAAN was used to accommodate the survey design for both descriptive and multivariate analyses.

A total of 2,525 PRFs contained psychotropic agents in children and adolescents and 1,133 PRFs involved prescribing of atomoxetine and stimulants. Annual national visit estimates for these visits were derived based on the inflation factor known as patient sampling weight. These weights were calculated for each PRF by the NCHS based on the visit sampling rates and were adjusted for non-response bias. The derived weighted estimates for the selected PRFs allow for extrapolation to national patterns of practice. Chi-square analysis based on patients receiving atomoxetine and patients receiving stimulates and not atomoxetine was used to examine differential use of these agents across patient and provider characteristics.

Study Variables

Patient visits involving children and adolescents with ADHD were selected to examine variation in the use of atomoxetine. Patients 19 years old and younger with the ICD-9-CM code of 314.0x were selected for descriptive and multivariate logistic regression analysis (N = 1,361) (15). The predictor variables of interest in multivariate analysis were gender, age, race, region, psychiatric comorbidity, primary care status, metropolitan location of physician, and insurance. All diagnoses, including

ADHD and associated psychiatric comorbidity were based on physician diagnoses and included psychoses (295.xx, 293.8x, 294.9x, 297.xx-299.xx), bipolar disorders (296.0x, 296.1x, 296.4x-296.8x), depression (296.2x, 296.3x, 309.0x, 309.1x, 311.xx 300.4x, 298.0x), and anxiety disorders (300.0x-300.3x, 301.4x). These variables were selected based on previous research and availability from data source (16). The NCHS variable definitions will be used to operationally define the selected study variables. For example, metropolitan area was defined as a county or group of counties with a minimum of one urban area of 50,000 or more population. The dependent variable (visits) was dummy-coded for prescribing of atomoxetine in children and adolescents with ADHD. Statistical significance was set at alpha of 0.05.

RESULTS

During the years 2003 through 2004, an estimated 29.46 million visits (95% Confidence Interval [CI]), 24.32–34.59) involved prescribing of all types of psychotropic agents for children and adolescents. Approximately 49% (95% CI, 44–54) resulted in prescription of atomoxetine and stimulants. This represents 14.51 million (95% CI, 11.12–17.89) for overall visit rate of 8.91 visits per 100 children and adolescents. Stimulants were used in 41% (95% CI, 36–45) of the psychotropic visits and 10% (95% CI, 8–12) of the psychotropic visits involved atomoxetine. Only 0.10% of the psychotropic visits involved prescribing of both atomoxetine and stimulants in children and adolescents.

Psychotropic Visit Estimates by Patient and Physician Characteristics: Atomoxetine vs. Stimulants

The annualized visit estimates involving atomoxetine versus stimulants by patient and physician characteristics are presented in Table 1. Bivariate analyses of visits involving atomoxetine and stimulants revealed (regardless of the diagnosis) no differences related to sex, race, ADHD diagnosis, psychiatric comorbidity, primary care status, metropolitan location, and insurance. There were age- and region-based differences. Children 10-to-14 years accounted for nearly 60% of atomoxetine use whereas it was only 40% among stimulant users. Northeast region represented nearly 10% of atomoxetine use whereas it was 20% among stimulant users.

Table 1 Visit Estimates by Patient and Physician Characteristics: Atomoxetine vs. Stimulants

	Atomoxetine Visit	Stimulants Visit	Chi-Square*
	Estimates (Percentage)	Estimates (Percentage)	*P*-value
Age			
≤ 9	620 (22)	4,696 (39)	.01*
10–14	1,706 (59)	4,811 (40)	
15–19	545 (19)	2,565 (21)	
Gender			
Male	2,184 (76)	9,156 (76)	.91
Female	687 (24)	2,916 (24)	
Race			
White	2,433 (85)	10,126 (84)	.94
Others	438 (15)	1,945 (16)	
Region			
Northeast	250 (9)	2,349 (20)	.04*
Midwest	629 (22)	2,416 (20)	
South	1,444 (50)	5,414 (45)	
West	548 (19)	1,893 (16)	
Physician			
Primary care	1,432 (50)	6,232 (52)	.64
Specialty	1,439 (50)	5,840 (48)	
Metropolitan statistical area			
Metropolitan	2,344 (82)	10,596 (88)	.26
Non-metropolitan	526 (18)	1,476 (12)	
Insurance			
Private	1,904 (66)	6,536 (54)	.18
Medicaid	667 (23)	3,943 (33)	
Others	300 (11)	1,592 (13)	
Psychiatric co-morbidities			
Yes	794 (28)	2,412 (20)	.19
No	2,077 (72)	9,660 (80)	
ADHD			
Yes	2,349 (82)	9,290 (77)	.39
No	522 (18)	2,781 (23)	

*Significant ($p < 0.05$), Abbreviation: ADHD - Attention Deficit Hyperactivity Disorder.

Analysis of ADHD-Specific Visits: Predictors of Atomoxetine vs. Stimulants

An estimated 15.20 million (95% CI, 11.98–18.42) visits were made by youth with ADHD. Psychotropic agents were prescribed in 82% of these visits; 61% involved stimulants and atomoxetine was used in 15% of these visits. Multivariate analysis involving children with ADHD revealed that prescribing of atomoxetine varied across age, insurance, and region of physician practice after controlling for other factors (see Table 2). There was no variation in the use of atomoxetine across sex, race, psychiatric comorbidity, primary care status, and metropolitan location. After adjusting for other factors, patients 10-to-14 years of age were more likely to receive atomoxetine than patients over 15 years. Those with private insurance were more likely to receive atomoxetine. Physicians in the Northeast region were less likely to prescribe atomoxetine than physicians in the West.

DISCUSSION

This study compared the use of atomoxetine with that of stimulant medications in outpatient visits by children and

Table 2 Predictors of Atomoxetine Prescribing in Patients with ADHD: Mutivariate Analysis

Predictors	Odds Ratio (95% Confidence Interval)
Sex	
Female	1.02 (0.46–2.25)
Male	Reference Group (odds ratio 1)
Age*	
≤ 9	1.00 (0.45–2.20)
10–14	2.11 (1.06–4.19)
≥ 15	Reference Group (odds ratio 1)
Race	
Others	1.33 (0.53–3.33)
White	Reference Group (odds ratio 1)
Region*	
Northeast	0.31 (0.13–0.72)
Midwest	0.82 (0.31–2.14)
South	1.11 (0.48–2.58)
West	Reference Group (odds ratio 1)
Primary care	
Yes	0.91 (0.48–1.69)
No	Reference Group (odds ratio 1)
Location of practice	
Metropolitan	0.45 (0.20–1.01)
Non-metropolitan	Reference Group (odds ratio 1)
*Insurance	
Private	2.22 (1.03–4.80)
Medicaid	1.27 (0.51– 3.17)
Others	Reference Group (odds ratio 1)
Psychiatric co-morbidities	
Yes	1.54 (0.71–3.32)
No	Reference Group (odds ratio 1)

*$p < .05$.

adolescents. We used two different approaches to the analysis of prescription data for 2-year study period in youth 19 year old and younger. The first approach involved analysis of psychotropic prescription data *without any regard to the diagnosis*. This approach indicated that either a stimulant medication or atomoxetine or both was prescribed in nearly one-half of all pediatric visits involving psychotropic medications. The proportion of visits for atomoxetine, as a percentage of all visits for psychotropic medications was nearly 10% (vs. about 40% for stimulants).

The second analysis focused on the data on outpatient *visits involving the diagnosis of ADHD*. Using this approach, we estimated that nearly 15% of visits by youth with ADHD resulted in prescription of atomoxetine; and stimulant medications were prescribed in about 61% of these visits. Thus, the category of psychotropic medication that was most frequently prescribed during these visits was stimulants; and atomoxetine was the most commonly prescribed non-stimulant psychotropic medication. It is noteworthy that both approaches to the data analysis yielded similar atomoxetine/ stimulants ratio of 1:4. The importance of atomoxetine as a stimulant alternative can be gleaned from the data that nearly one-tenth of all visits involving a psychotropic drug resulted in prescription of atomoxetine.

Analyses based on diagnosis (ADHD) and without diagnosis revealed age- and region-based variations in the use of atomoxetine. The proportion of visits for atomoxetine was greater in age group 10-to-14 years than in older youth. Because the literature suggests that the use of another group of non-stimulant psychotropic agents (antipsychotic drugs) is also high in children aged 10–14 years (17), future studies on the determinants of various psychotopric drugs are particularly needed in this age group. For example, further studies that focus on need factors (such as prevalence of multiple psychiatric diagnoses in this age group) are warranted. Adoption of atomoxetine by physicians in the Northeast region was relatively lower, accounting for 10% of the atomoxetine use. Multivariate analysis involving ADHD visits results revealed similar pattern after controlling for other factors. Although the reasons for these variations are unclear, they could be attributed to patient and physician preferences. We also found that atomoxetine was more likely to be used in youth with private insurance. This finding may be attributed to possible better coverage of this new medication. According to a well-established model of health services use (Andersen Model), insurance is an important enabling factor that facilitates access to services, such as medications (18–19). Data analysis revealed no variations in the use of atomoxetine across other patient and physician characteristics such as gender, race, primary care status, and metropolitan location. These findings are consistent with the existing literature on atomoxetine use (6,18). Although marketing and promotion by the pharmaceutical industry may be a determinant of drug use, this study on atomoxetine did not address this issue.

There is empirical evidence that atomoxetine treatment may improve ADHD and comorbid symptoms in youth with ADHD and coexisting anxiety, depression, oppositional-defiant disorder, or pervasive developmental disorders (5,20–23). Although earlier studies have linked initiation of atomoxetine in both pediatric (6) and adult ADHD (24) with a range of psychiatric comorbidity, this study found no association between prescription of atomoxetine and psychiatric comorbidity. Not only are our findings based on more recent data, but also they are consistent with the results of a recent study in adult ADHD (25). Based on the data from two double-blind trials, it was concluded the variable responsiveness of patients to atomoxetine could not be explained by differences in indicators of psychopathology or attentional capacity (25). Further studies on effectiveness of atomoxetine in ADHD with a variety of comorbid psychiatric disorders are needed to inform the clinical use of this drug. For example, it is important to find out whether atomoxetine is efficacious in ADHD youths with conduct disorder, who have an increased risk for substance abuse (21–22). Because atomoxetine is likely to have minimal risk for substance abuse, if found to be efficacious, this drug could be an attractive choice in youth who have ADHD and conduct disorder. Studies on differential efficacy of stimulant drugs and atomoxetine are needed to determine the role of atomoxetine in pharmacotherapy of ADHD in children and adolescents (26). In the absence of definitive data, recent guidelines on pharmacological treatment of ADHD, based on expert-consensus and limited data, are useful (5).

LIMITATIONS

The results should be interpreted with caution because of some limitations inherent in NAMCS. Firstly, the sample size of children on psychotropic medications in NAMCS is small (17,27). Hence, the stability and reliability of estimates is lower in children and adolescents than in adults. To overcome this difficulty, we enlarged the sample size by combining the data from NAMCS and NHAMCS for the years 2003 and 2004. Hence, the sample sizes were stable and reliable for extrapolation and generalization purposes. Secondly, diagnoses in NAMCS are not rigorous because they are based on physician judgment and not on research criteria. Not all children in this study who were taking stimulants or atomoxetine had a diagnosis of ADHD. The appropriateness of the use of these medications cannot be judged due to diagnostic limitation in the data source. Thirdly, the unit of analysis in NAMCS is "visits" (17,27). Hence, the data are generalizable to the frequency of drug use per office visit ("encounter"), but do not directly estimate actual psychotropic utilization per person. This may produce an unknown amount of patient duplication during the sampling frame, resulting in an overestimate of drug prevalence and variability of findings. Fourthly, the national surveys are completed by physicians or their office staff and do not account for noncompliance. This may lead to overestimation of drug use (27). Despite these limitations associated with the national surveys, the results of this study are generalizable and the study findings represent most recent national level prescribing practices.

CONCLUSIONS

Atomoxetine is emerging as a leading stimulant alternative in children and adolescents. Nearly 15% of all pediatric visits for ADHD pharmacotherapy resulted in prescription of this non-stimulant drug. Given this substantial use, the role of atomoxetine in treatment of ADHD should be further informed by well-designed studies. Preferential use of atomoxetine in the age group 10-to-14 years needs to be further evaluated. Additionally, the role of patient preferences, physician-related factors, and psychiatric comorbidity should be further investigated. Data on differential safety and efficacy of atomoxetine and stimulants are needed to optimize patient-medication match. Meanwhile, clinicians are encouraged to use guidelines based on expert consensus and available data (5).

REFERENCES

1. U.S. Food and Drug Administration: Strattera approved to treat ADHD. *FDA Consum* 2003; 37:4
2. Garces K: Atomoxetine for attention deficit/hyperactivity disorder. *Issues Emerg Health Technol* 2003; 46:1–4
3. Barton J: Atomoxetine: A new pharmacotherapeutic approach in the management of attention deficit/hyperactivity disorder. *Arch Dis Child* 2005; 90 (suppl1): 26–29
4. Kratochvil C, Wilens T, Greenhill L, Gao H, Baker K, Feldman P, Gelowitz D: Effects of long-term atomoxetine treatment for young children with attention deficit/ hyperactivity disorder. *J Am Acad Child Adolsc Psychiatry* 2006;45:919–927
5. Pliszka SR, Crismon ML, Hughes CW, Corners CK, Emslie GJ, Jensen PS, McCracken JT, Swanson JM, Lopez M: Texas Consensus Conference Panel on Pharmacotherapy of Childhood Attention Deficit Hyperactivity Disorder: The Texas Children's Medication Algorithm Project: Revision of the algorithm for pharmacotherapy of attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 2006; 45:642–657
6. Van Brunt DL, Johnston JA, Ye W, Pohl GM, Sun PJ, Sterling KL, Davis ME: Predictors of selecting atomoxetine therapy for children with Attention Deficit/ Hyperactivity Disorder. *Pharmacotherapy* 2005; 21:1541–1549
7. National Center for Health Statistics. *2004 National Ambulatory Medical Care Survey*. Hyattsville, MD: United States Department of Health and Human Services, National Center for Health Statistics. Documentation available at: ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NAMCS/doc04.pdf Accessed September 14, 2006
8. National Center for Health Statistics. *2003 National Ambulatory Medical Care Survey*. Hyattsville, MD: United States Department of Health and Human Services, National Center for Health Statistics. Documentation available at: ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NAMCS/doc03.pdf Accessed September 14, 2006
9. National Center for Health Statistics. *2003 National Hospital Ambulatory Medical Care Survey*. Hyattsville, MD: United States Department of Health and Human Services, National Center for Health Statistics. Documentation available at:ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NHAMCS/doc03.pdf Accessed September 14, 2006
10. National Center for Health Statistics. 2004 National Hospital Ambulatory Medical Care Survey. Hyattsville, MD: United States Department of Health and Human Services, National Center for Health Statistics. Documentation available at:ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NHAMCS/doc04.pdf Accessed September 14, 2006
11. Koch H, Cambell W: The collection and processing of drug information. National Center for Health Statistics. *Vital Health Stat* 1982; 2(90)
12. Hing E, Gousen S, Shimizu I, Burt C: Guide to using masked design variables to estimate standard errors in public use files of the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey. *Inquiry*. 2003; 40:401–415
13. SAS: In: *SAS-STAT users guide release, Changes and Enhancements*, 8.0 Edition. SAS Institute, Inc. Cary, NC; 2001
14. Shah BV, Barnwell BG, Bieler GS: *SUDAAN User's Manual*, Release 7.5, Research Triangle Park, NC: Research Triangle Institute, 2002
15. US Department of Health and Human Services. Centers for Disease Control and Prevention: *Health Care Financing Administration. International Classification of Diseases*, 9th Revision, Clinical Modification. 6th Edition. 2004

16. Van Brunt D, Gibson P, Ramsey J, Obenchain R: Outpatient use of major antipsychotic drugs in ambulatory settings in the United States, 1997–2000. *Med Gen Med* 2003; 5: 16
17. Aparasu R, Bhatara V: Patterns and determinants of antipsychotic prescribing in children and adolescents: 2003–2004. *Cur Med Res Opn* 2007; 23:49–56
18. Andersen RM: A Behavioral model of families' use of health services. (Research Series 25). Center for Health Administration Studies. 1968: Chicago: University of Chicago.
19. Andersen RM: Revisiting the behavioral model and access to medical care: Does it matter? *J Health Soc Behav* 1995; 36:1–10
20. Sutton VK, Milton DR, Ruff DD, Sadowski K, Allen AJ: *Efficacy of atomoxetine treatment for children and adolescents with attention deficit/hyperactivity disorder*. Paper presented at the 51st Annual Meeting American Academy of Child and Adolescent Psychiatry, Washington, DC, October 19–24, 2004
21. Newcorn J. Spencer T, Biederman J, Milton D, Michelson D: Atomoxetine treatment in children and adolescents with attention deficit/ hyperactivity disorder and comorbid oppositional defiant disorder. *J Am Acad Child Adolesc Psychiatry* 2005; 44:240–248
22. Kratochvil C, Newcorn J, Arnold LE, Duesenberg D, Emslie G, Quintina H, Sarks E, Wagner K, Gao H, Michelson D, Biederman J: Atomoxetine alone or combined with fluoxetine for treating ADHD with comorbid depressive or anxiety symptoms. *J Am Acad Child Adolesc Psychiatry* 2005; 44:915–924
23. Arnold LE, Aman M, Cook A, Witwer A, Hall K, Thompson S, Ramadan Y: Atomoxetine for hyperactivity in autism spectrum disorders. *J Am Acad Child Adolesc Psychiatry* 2006; 45:1196–1205.
24. Van Brunt DL, Johnston JA, Ye W, Pohl GM, O'Hara NN: Factors associated with initiation with atomoxetine versus stimulants in the treatment of adults with ADHD. Retrospective analysis of administrative claims data. *J Mange Care Pharm* 2006; 12. 230–238.
25. Spencer TJ, Farone SV, Michelson D, Adler L, Reimherr F, Glatt S, Beiderman J: Atomoexetine and adult attention deficit/ hyperactivity disorder: The effects of comorbidity. *J Clin Psychiatry* 2006; 67:415–420
26. Gibson AP, Bettinger TL, Patel NC, Crismon ML: Atomextine versus stimulants for treatment of attention deficit/hyperactivity disorder. *Ann Pharmacother* 2006; 40:1134–1142
27. Bhatara V, Feil M, Hoagwood K, Vitiello B, Zima B: Trends in combined pharmacotherapy with stimulants for children. *Psychiatr Serv* 2002; 53:244