Pediatric Stimulant and Selective Serotonin Reuptake Inhibitor Prescription Trends
1992 to 1998

Jerry L. Rushton, MD, MPH; J. Timothy Whitmire, PhD

Background: Prescription trends have key implications for costs, outcomes, and research, yet few data exist on pediatric selective serotonin reuptake inhibitor (SSRI) trends and associations with stimulant trends.

Objective: To describe prescription trends for stimulants, SSRIs, and combination prescriptions by age, sex, and race.

Methods: Retrospective population-based analysis of North Carolina Medicaid prescription claims files.


Main Outcome Measures: Annual number of prescriptions, patients filling a prescription claim, and prescription prevalence for stimulants and SSRIs.

Results: The number of children and adolescents who received stimulants increased from 6,407 (24,584 claims) in 1992 to 27,951 (135,057 claims) in 1998. The number of SSRI recipients increased from 510 children (1,326 claims) in 1992 to 6,984 children (25,392 claims) in 1998. Prescription prevalence in school-aged children 6 to 14 years increased from 4.4% to 9.5% for stimulants during the study period, and from 0.2% to 1.5% for SSRIs. In 1998, stimulant prescription prevalence was highest for white school-aged males (18.3%) vs black females (3.4%) and SSRI prescription prevalence was highest for white school-aged males (2.8%) vs black females (0.6%). Combination pharmacotherapy also increased during 1992 through 1998.

Conclusions: Prevalence of stimulant and SSRI medications has increased during the 1990s, with prescription prevalence in North Carolina Medicaid youth higher than previously reported. Age, sex, and racial differences are apparent and call for further attention. Combination pharmacotherapy also has growing importance.

and prevalences are difficult to interpret for the pediatric age groups. Prescriptions of SSRIs for children and adolescents have been described in other large pharmaceutical databases as part of broader studies on pediatric psychotropics, but no studies have reported SSRI figures with demographic information for a defined pediatric population.

Studies on prescription trends and prescriber practices are important to understand changes in care and to guide research initiatives on medication labeling, information, and safety. Concerns of potential adverse effects have been raised in particular regarding the off-label use of pediatric medications and the practice of prescribing medications for younger preschool children. Polypharmacy or combination psychotropic therapy is another practice used for adult patients. The purpose of our study was to describe prescription trends for the 2 most commonly prescribed classes of psychotropic medications: the stimulants and SSRIs. We sought to document the number of prescription claims, the number of Medicaid patients prescribed these medications, prescription prevalence by age group, and then to describe trends of the 2 classes of medications over time. We wanted to determine if increases reported in other studies also occurred in our population of interest and, if so, whether increases in prescription prevalence have continued throughout the 1990s. An additional aim was to examine how often these medications are prescribed in combination. Finally, we were interested in understanding the safety of these medications for young children.

**MATERIALS AND METHODS**

We queried the State of North Carolina Medicaid Database for all prescription claims filled between January 1, 1992, and December 31, 1998, for children aged 1 to 19 years. The study period was selected to provide the most current information available with complete claims data from North Carolina Medicaid. Claims were available for all Medicaid recipients in the state and included all prescription claims submitted to North Carolina Medicaid. Prescriptions not filled or processed were not available. All variables from the prescription claim file were entered into a plain text file, grouped by calendar year between 1992 and 1998, and entered into STATA 6.0 (College Station, Tex) statistical software for data management and analysis.

Prescription claims of interest were searched by National Drug Classification code using a query of all stimulants and SSRIs listed in the 1999 *Physician’s Desk Reference*, 53rd edition. All dosage forms and strengths for each medication were included in our search for brand-name medications and generic equivalents (when applicable). An injectable stimulant, doxapram hydrochloride, was excluded. The list of medications included in our search were as follows: for SSRIs: Luvox (fluvoxamine), Paxil (paroxetine), Prozac (fluoxetine), and Zoloft (sertraline), and for stimulants: Adderall, Cylert (pemoline), Desoxyn (methylamphetamine hydrochloride), Dexedrine (dextroamphetamine sulfate), Dextrostat (d-amphetamine), Ritalin (methylphenidate hydrochloride), and Ritalin sustained release (methylphenidate hydrochloride sustained release). The National Drug Classification code provided the medication name, dosage form, and medication strength. During the period of study, there were no known statewide formularies or restrictions on any of the medications. Fluoxetine (Prozac) and most of the stimulants were available before 1992 at the beginning of the study period. Sertraline (Zoloft), paroxetine (Paxil), and fluvoxamine (Luvox) were available in the United States beginning in 1992, 1993, and 1994, respectively, with approval and indication for adult patients.

The Medicaid prescription claims included variables on patient age, sex, self-reported racial group, county of residence, pharmacy type and location, prescription quantity, and date the prescription was filled for all patients. Unique identification numbers were used to link multiple drug claims to each individual during a calendar year. Patient names were deleted and individuals were not identified. Denominator information on the North Carolina Medicaid population age, sex, and race was obtained from Health Care Financing Administration state Medicaid recipient reports (Health Care Financing Administration–2082 Reports) for fiscal years 1992 through 1998. Health Care Financing Administration recipient figures on age, sex, and racial demographics were reported by age category subgroups of 1 to 3 years and 6 to 14 years; thus, subanalyses of sex and racial groups focused on preschool children (age 1-5 years) and school-aged children (6-14 years).

Results were compiled for each prescription claim, class of medication (SSRI or stimulant), and combination of both an SSRI and a stimulant during each year. Then, the same figures were calculated by number of Medicaid patients receiving a prescription during the year to account for repeat claims filled for patients with multiple refills or duplicate medication claims within a year.

Patients were described as combination prescription recipients if they received both a stimulant and an SSRI during the same calendar year. Given the limits of the claims data, and uncertainty about compliance and duration that patients actually took these medications in combination, we used this method to approximate the number of combination prescriptions. A review of 1998 data showed that for stimulants and SSRI prescriptions filled during the same year, 80% of prescription claims for a stimulant and an SSRI were filled during the same month, and more than 90% were filled within 1 month. Thus, we believe that this measure is a close approximation of children who were concurrently taking stimulants and SSRIs.
Table 1. Prescription Trends in Preschool and School-aged Children

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stimulants</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preschool Children (Aged 1-5 Years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stimulant prescription prevalence, %</td>
<td>6.6</td>
<td>7.7</td>
<td>8.0</td>
<td>8.2</td>
<td>8.8</td>
<td>9.7</td>
<td>9.5</td>
</tr>
<tr>
<td>Children given medication, No.</td>
<td>862</td>
<td>1269</td>
<td>1974</td>
<td>2508</td>
<td>2664</td>
<td>2686</td>
<td>2773</td>
</tr>
<tr>
<td>SSRIs*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSRI prescription prevalence, %</td>
<td>&lt;0.01</td>
<td>0.01</td>
<td>0.2</td>
<td>0.04</td>
<td>0.05</td>
<td>0.08</td>
<td>0.10</td>
</tr>
<tr>
<td>Children given medication, No.</td>
<td>7</td>
<td>21</td>
<td>40</td>
<td>84</td>
<td>106</td>
<td>157</td>
<td>222</td>
</tr>
<tr>
<td>Medicaid population, No.</td>
<td>114,960</td>
<td>177,915</td>
<td>201,498</td>
<td>215,691</td>
<td>216,649</td>
<td>207,805</td>
<td>213,089</td>
</tr>
<tr>
<td><strong>School-aged Children (Aged 6-14 Years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stimulant prescription prevalence, %</td>
<td>4.4</td>
<td>5.6</td>
<td>6.8</td>
<td>8.2</td>
<td>8.8</td>
<td>9.7</td>
<td>9.5</td>
</tr>
<tr>
<td>Children given medication, No.</td>
<td>5362</td>
<td>8081</td>
<td>11,634</td>
<td>16,232</td>
<td>19,410</td>
<td>21,720</td>
<td>23,877</td>
</tr>
<tr>
<td>SSRIs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSRI prescription prevalence, %</td>
<td>0.2</td>
<td>0.4</td>
<td>0.6</td>
<td>0.9</td>
<td>1.1</td>
<td>1.4</td>
<td>1.5</td>
</tr>
<tr>
<td>Children given medication, No.</td>
<td>191</td>
<td>539</td>
<td>1,015</td>
<td>1,778</td>
<td>2,417</td>
<td>3,091</td>
<td>3,844</td>
</tr>
<tr>
<td>Medicaid population, No.</td>
<td>121,326</td>
<td>143,247</td>
<td>170,619</td>
<td>198,800</td>
<td>221,080</td>
<td>224,019</td>
<td>250,288</td>
</tr>
</tbody>
</table>

*SSRIs indicate selective serotonin reuptake inhibitors.

RESULTS

OVERALL TRENDS AND PRESCRIPTION PREVALENCE

The overall number of stimulant and SSRI prescriptions filled by children in the North Carolina Medicaid Program increased dramatically from 1992 to 1998. In 1992, 24,584 stimulant prescription claims were filled for 6,407 children aged 1 to 19 years. During 1998, these figures increased to 135,057 stimulant prescription claims for 27,951 children. For the SSRIs, 13,262 SSRI prescription claims were filled for 510 children aged 1 to 19 years in 1992. Prescriptions increased to 25,392 SSRI claims for 6,984 children in 1998.

Some of the increase in the overall number of prescription claims and patients receiving medications was caused by expansion of the Medicaid population from 342,333 children in 1992 to 581,088 in 1998. However, significant increases were also noted when claims were analyzed as annual prevalence of prescriptions using the number of Medicaid recipients in a specific age group as a denominator. Table 1 lists the prescription prevalence per number of preschool children (1-5 years of age) and school-aged children (6-14 years of age) who were Medicaid recipients during 1992 through 1998. Stimulant prevalence doubled from 1992 to 1998, and SSRI prevalence increased even more during the 7-year period of study. In the school-aged group, 1998 prescription prevalence leveled off at 9.3% for stimulants and 1.5% for SSRIs. Stimulant prescription prevalence in preschool children plateaued at 1.3%, and SSRIs continued a slow rise to 0.1% in 1998. Although an increased proportion of preschoolers received medications, this subset of patients still represents a relatively small percentage of all children who received stimulants and SSRIs. Preschool children (aged 1-5 years) accounted for only 7.1% of all stimulant prescription claims and 2.2% of all SSRI claims filled by children aged 1 to 19 years.

DEMOGRAPHIC TRENDS AMONG MEDICAID PATIENTS RECEIVING STIMULANTS AND SSRIs

The mean age for all children in the Medicaid population who were prescribed SSRIs decreased from 14.9 years in 1992 to 13.1 years in 1998. However, for stimulants the mean age actually increased slightly from 8.5 to 9.1 years during the period of study.

In addition to changes in age, sex differences were also noted. Our results were consistent with previous reports of a male predominance of attention-deficit/hyperactivity disorder diagnosis and treatment. During the most recent year, 1998, the male-female ratio of stimulant recipients was 3.2:1. This ratio decreased from a male-female ratio of 4.2:1 in 1992. Selective serotonin reuptake inhibitors were prescribed to female patients more commonly in 1992 (female-male ratio, 1:8.1), but in 1998, SSRI prescriptions were equal with respect to sex (1:1 ratio).

Demographic differences by reported race of prescription recipients were also noted. In 1992, 56.4% of children who were prescribed stimulants and 74.9% of children who were prescribed SSRIs were white. The racial differences narrowed between 1992 and 1998, yet white children still constituted the majority of patients prescribed stimulants (50.6%) and SSRIs (65.9%) in 1998. However, white children did not make up a majority of Medicaid children—in 1998, the North Carolina Medicaid pediatric population was reported as 39.7% white, 48.3% black, and 12.0% other racial groups. Asian, Hispanic, American Indian, and other racial groups reported by Medicaid also seemed to be less likely to receive stimulants and SSRIs, although the number of patients in this group was small; thus, statistical comparisons were not made with white patients.

Prescription prevalence as a percentage of preschool and school-aged Medicaid children in 1998 are shown in Table 2 by sex and racial groups. White school-
Annual prescription prevalence of stimulants, SSRIs, and combination prescriptions in our study increased significantly from 1992 to 1998 in the North Carolina Medicaid population of children aged 1 to 19 years. Increases were noted for all measures: number of prescriptions filled, number of patients prescribed a medication, and the percentage of preschool and school-aged children prescribed a medication annually. Our study results are consistent with other reports documenting the trend of increased psychotropic prescriptions for children and adolescents during the 1990s. However, stimulant prevalence of almost 56% in the 1998 school-aged group is greater than the reported attention-deficit/hyperactivity disorder prevalence from many community samples and other studies of stimulant prevalence. In addition, subgroups such as white school-aged males had even higher stimulant prevalence of more than 18%. Selective serotonin reuptake inhibitors are prescribed less frequently than stimulants, yet this class of antidepressants has also become an important part of therapy for many children. In addition, there are some new and unique significant findings to note.

First, the trend of increased stimulant prescriptions and SSRI prescriptions continued through 1998. Despite controversy over off-label usage, questions of efficacy in the pediatric population, and safety concerns for young children, prescriptions have continued to climb for both stimulants and SSRIs in all age groups. Stimulant increases were dramatic: the number of prescriptions and patients increased by nearly 4-fold during the study period of 1992 through 1998. Some of this increase was because of an expansion in the number of children and adolescents receiving Medicaid. However, even after considering changes in the number of Medicaid recipients, increases were dramatic, with a doubling of the percentages of Medicaid preschoolers and school-aged children receiving stimulants between 1992 and 1998. It is somewhat more difficult to interpret increases in SSRI use, since the class of medications was just introduced in 1988, and the other 3 SSRIs were launched during the period of study. However, during the last 5 years of the study period, the percentages of preschool and school-aged children receiving SSRIs have more than doubled.

Many articles, and even a recent White House conference, have raised concerns about increases in prescription rates, and potential overuse, inappropriate prescriber practices, and substitution for counseling or comprehensive therapy. While our findings are provocative, we cannot speculate from our data what factors are driving prescription increases. Potential positive influences of increased recognition and treatment of previously unrecognized mental disorders, improvements in access to psychiatric care, or increased emphasis on the proper use of these medications must be considered along with concerns of harmful effects and negative associations with expansion of prescription util-

### COMBINATION PRESCRIPTIONS

In addition to increases in the individual medications, greater prescription of stimulants and SSRIs in combination occurred during the study period. The number of patients prescribed both types of psychotropic medications during the same year increased steadily. Since SSRIs had been recently introduced at the beginning of the study period, in 1992, only 32 children received both stimulants and SSRIs during this year, yet by 1998, 2102 pediatric patients were prescribed both types of medication. The combination of stimulants and SSRIs is still relatively rare among all Medicaid children, with an annual combination prescription prevalence among school-aged children of 0.7%. However, among the 6984 children who received an SSRI in 1998, 30.1% also received a stimulant.

### COMMENT

Annual prescription prevalence of stimulants, SSRIs, and combination prescriptions in our study increased significantly from 1992 to 1998 in the North Carolina Medicaid population of children aged 1 to 19 years. Increases were noted for all measures: number of prescriptions filled, number of patients prescribed a medication, and the percentage of preschool and school-aged children prescribed a medication annually. Our study results are consistent with other reports documenting the trend of increased psychotropic prescriptions for children and adolescents during the 1990s. However, stimulant prevalence of almost 10% in the 1998 school-aged group is greater than the reported attention-deficit/hyperactivity disorder prevalence from many community samples and other studies of stimulant prevalence. In addition, subgroups such as white school-aged males had even higher stimulant prevalence of more than 18%. Selective serotonin reuptake inhibitors are prescribed less frequently than stimulants, yet this class of antidepressants has also become an important part of therapy for many children. In addition, there are some new and unique significant findings to note.

First, the trend of increased stimulant prescriptions and SSRI prescriptions continued through 1998. Despite controversy over off-label usage, questions of efficacy in the pediatric population, and safety concerns for young children, prescriptions have continued to climb for both stimulants and SSRIs in all age groups. Stimulant increases were dramatic: the number of prescriptions and patients increased by nearly 4-fold during the study period of 1992 through 1998. Some of this increase was because of an expansion in the number of children and adolescents receiving Medicaid. However, even after considering changes in the number of Medicaid recipients, increases were dramatic, with a doubling of the percentages of Medicaid preschoolers and school-aged children receiving stimulants between 1992 and 1998. It is somewhat more difficult to interpret increases in SSRI use, since the class of medications was just introduced in 1988, and the other 3 SSRIs were launched during the period of study. However, during the last 5 years of the study period, the percentages of preschool and school-aged children receiving SSRIs have more than doubled.

Many articles, and even a recent White House conference, have raised concerns about increases in prescription rates, and potential overuse, inappropriate prescriber practices, and substitution for counseling or comprehensive therapy. While our findings are provocative, we cannot speculate from our data what factors are driving prescription increases. Potential positive influences of increased recognition and treatment of previously unrecognized mental disorders, improvements in access to psychiatric care, or increased education about the proper use of these medications must be considered along with concerns of harmful effects and negative associations with expansion of prescription util-

### Table 2. 1998 Prescription Prevalence in Medicaid Preschool (Aged 1-5 Years) and School-aged (Aged 6-14 Years) Children by Racial Group and Sex

<table>
<thead>
<tr>
<th></th>
<th>Females</th>
<th></th>
<th>Males</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Black†</td>
<td>White‡</td>
<td>Black§</td>
<td>White¶</td>
</tr>
<tr>
<td>Preschool</td>
<td>Stimulant prevalence, % (children given medication, No.)</td>
<td>0.4 (180)</td>
<td>0.8 (321)</td>
<td>1.4 (640)</td>
</tr>
<tr>
<td></td>
<td>SSRI prevalence, % (children given medication, No.)</td>
<td>&lt;0.1 (14)</td>
<td>0.1 (38)</td>
<td>0.1 (33)</td>
</tr>
<tr>
<td>School-aged</td>
<td>Stimulant prevalence, % (children given medication, No.)</td>
<td>3.4 (2171)</td>
<td>6.4 (3004)</td>
<td>11.3 (7251)</td>
</tr>
<tr>
<td></td>
<td>SSRI prevalence, % (children given medication, No.)</td>
<td>0.6 (417)</td>
<td>2.1 (1007)</td>
<td>1.0 (665)</td>
</tr>
</tbody>
</table>

*SSRI indicates selective serotonin reuptake inhibitor.
†There were 46 429 preschool and 64 415 school-aged females in this group.
‡There were 42 016 preschool and 46 799 school-aged females in this group.
§There were 47 268 preschool and 64 280 school-aged males in this group.
¶White males had a significantly higher prevalence (P<.001) in comparison with others for stimulants and SSRIs.
lization. Recent clinical trials have shown the potential promise and benefit for these drugs in selected pediatric patients.\textsuperscript{31-33} While we must be judicious in the application of these psychotropic medications, we cannot present an alarmist view that equates all increases in prescriptions with negative consequences. Our study is a first step to describe some of the issues surrounding care for complex disorders. Future studies must describe utilization patterns, diagnostic appropriateness, severity of illness adjustments, and ultimately describe patient outcomes in terms of adverse events and benefits from stimulants and SSRIs.

Second, important demographic trends were observed. Although most stimulants and SSRIs were prescribed for older children and adolescents, more young patients and even preschoolers received these medications. Males continued to receive stimulants more commonly than females, but the sex gap has narrowed, and SSRI prevalence by sex was approximately equal between males and females in 1998. Finally, we demonstrated differences in stimulant and SSRI prescription prevalence for whites and other racial groups in our study. Our results confirm data from the Maryland Medicaid pediatric population,\textsuperscript{26,27} and show that in addition to demographic differences in stimulant prescriptions, SSRI prescriptions have even greater differences between whites and black Medicaid children. The results must be viewed with caution as racial misclassifications, cultural beliefs of mental illness, access to care, and differential acceptance of psychotropics may vary among racial groups. However, our results demand additional study to understand disparities between stimulant and SSRI prescription patterns for white and nonwhite patients.

The third major finding is the growing trend of combination pharmacotherapy with stimulants and SSRIs. Concerns of individual medication safety in children, which are still largely unknown and unexplored, are magnified when combinations of medicines are prescribed for children. While this trend may reflect a greater attention to comorbidity with attention-deficit/hyperactivity disorder, depression, or other mental disorders, this practice bears additional scrutiny. Clinical trials and open-label trials have provided some information on stimulant and SSRI use as single agents in select populations of children; however, there are minimal to no data to describe the risks and potential benefits of polypharmacy with these medications. This practice may prove to be safe and effective, yet these patients are often excluded from clinical trials and studies. Combination pharmacotherapy and patients with coexisting conditions must become part of the research agenda.

Our study has several important limitations that must be considered. First, our results describe prescription trends in a single state Medicaid population. Although Medicaid patients represent a significant percentage of children in the state, our results may not generalize to other states or patient populations. In addition to generalizability, the Medicaid population faces several other challenges in access and changing needs that could affect prescriber practices. Changing characteristics and effects of enrollment and disenrollment may also affect prescription trends. It is possible that the expansion of Medicaid preferentially enrolled uninsured patients without previous drug benefits, adolescents with higher prevalence of mental health needs, or more severely ill patients with greater mental health care and prescription needs. Some of the increases in prescription figures may be because of a longer chronicity of therapy or changes in severity and recurrence of mental disorders in our study population.

Differences in reporting of the number of Medicaid children during different periods and claim dates may contribute to variations in the denominator population. Other studies on the Medicaid data have reported prescription prevalences that exceed estimates from other samples and patient populations.\textsuperscript{34} Thus, our results may overestimate true prescription prevalence.

Additional studies are needed to link Medicaid prescription claims with utilization of other services, concurrent treatment, diagnosis and disease severity, recurrence, physician characteristics, and patient outcomes data. It remains to be seen how increases in prescriptions reflect other processes and quality of care. In fact, one hypothesis that must be tested is whether higher prescription prevalences may actually reflect increased access to care, recognition of mental health needs, and engagement in long-term treatment. We have demonstrated the clear need for this type of research in the Medicaid population where psychotropic prescriptions for youth affect a large percentage of the population.

We have shown that stimulant prevalence along with SSRIs and combination prescriptions for children and adolescents have increased between 1992 and 1998. Stimulants are prescribed more commonly for children, yet SSRIs and other new psychotropics must also be considered and studied. The next step and challenge of health services research is to consider the effects of psychotropic prescription practices on utilization of other services (inpatient hospitalizations, counseling, and medical services), medical and mental health expenditures, and outcomes for children and their families. Differences in treatment by age, sex, and race must be specifically addressed in future research. If changes in practice patterns and drug use are found to be associated with variations in quality of care and patient outcomes, interventions must be designed to address inappropriate prescription practices in both directions—overprescription and underutilization of other treatment and services.

Accepted for publication December 29, 2000.

This work was supported by the Robert Wood Johnson Clinical Scholars Program.

We thank the State Center for Health Statistics, North Carolina Department of Health and Human Services, Raleigh, for providing data access and other assistance.

Corresponding author: Jerry L. Rushton, MD, MPH, Department of Pediatrics, University of Michigan, 300 North Ingalls Bldg, Room 6D05, Ann Arbor, MI 48109-0456 (e-mail: jrushton@umich.edu).

CONCLUSIONS

(Released) ARCH PEDIATR ADOLESC MED/VOL 155, MAY 2001 WWW.ARCHPEDIATRICS.COM
REFERENCES


