

Psychotropic Polypharmacy Among Children and Youth Receiving Medicaid, 2012-2015

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ABSTRACT

BACKGROUND: The rates of mental health diagnoses in children have increased. Children in poverty have the highest rates. The use of psychotropic medication for children has been increasing, which is concerning because of the unknown long-term effects and the increased burden on the health care system. The state of Kentucky ranks among the highest in the United States for children with mental health problems, children living in poverty, and children receiving psychotropic medication.

OBJECTIVE: To examine recent trends and determinants of interclass psychotropic polypharmacy (PP) use for children and youth receiving Medicaid to inform intervention development.

METHODS: A retrospective cohort study was conducted using 2012-2015 Kentucky Medicaid claims for children aged 0-17 years, with continuous enrollment for ≥ 90 days with at least 1 behavioral health diagnosis (N=237,393). Interclass PP was defined as the presence of at least 2 psychotropic medication prescription fills for at least 2 different classes of medication that, if taken as directed, would be used concurrently for at least 90 consecutive days (allowing for a single 15-day lag). The outcome variables were the presence of any interclass PP and the number of months a child received interclass PP. We conducted a descriptive analysis and developed 2 separate generalized linear regression models to test for associations between individual characteristics of children treated with psychotropic medication for ≥ 90 days (n=75,639) and each outcome of interest.

RESULTS: For the sample of children with at least 90 days of psychotropic medication treatment, 38% had at least 3 covered months of PP over the 4 years studied. Children in foster care received alpha agonists (116 vs. 69 per 1,000 children) or antidepressants (225 vs. 176 per 1,000) at a higher rate than other children receiving Medicaid but received stimulants at a lower rate (403 vs. 638 per 1,000). The primary 2-drug class combinations were stimulants with either alpha agonists or antidepressants. Children in foster care (OR=1.7, 95% CI=1.58, 1.84, $P<0.001$), with a bipolar disorder (OR=2.24, 95% CI=2.10, 2.38, $P<0.001$), mood disorder not otherwise specified (OR=1.11, 95% CI=1.04, 1.17, $P<0.001$), or autism spectrum disorders (OR=1.17, 95% CI=1.08, 1.26, $P<0.001$) had increased the odds of ever receiving PP. Black children had lower odds (OR=0.72, 95% CI=0.67, 0.77, $P<0.001$) of ever receiving PP. Children aged 6-11 years (beta=3.08, 95% CI=2.87, 3.29) and 12-17 years (beta=1.61, 95% CI=1.38, 1.83) had more covered months with PP compared with those aged 0-5 years. Black children had fewer covered months of PP compared with white children (beta=-1.36, 95% CI=-1.61, -1.11]. Children in foster care (beta=1.83, 95% CI=1.53, 2.13) had more covered months with PP. Children residing in nonurban areas had fewer months with PP (beta=-0.4, 95% CI=-0.54, -0.26) compared with those residing in urban areas, as did those children with depression (beta=-3.32, 95% CI=-3.55, -3.1), impulse control disorder (beta=-2.07, 95% CI=-2.28, -1.85), and conduct disorder (beta=-1.34, 95% CI=-1.64, -1.05). Children with bipolar disorder (beta=3.62, 95% CI=3.38, 3.86) and autism (beta=2.04, 95% CI=1.75, 2.33) had more

covered months with PP. As comorbidity increased, the duration of PP treatment increased (beta=2.49, 95% CI=2.36, 2.62).

CONCLUSIONS: The rates of PP are concerning, especially for children in foster care and children aged 6-11 years. Efforts to safeguard medication use are needed, as well as future exploration of racial differences in PP.

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What is already known about this subject

- The use of psychotropic medication for the treatment of mental health problems in children and youth is increasing.
- Mental disorders are among the costliest conditions treated in children.
- There has been an increase in the number of youth receiving more than 1 psychotropic medication or polypharmacy.

What this study adds

- This study used a large, statewide analysis of 2012-2015 Kentucky Medicaid claims and found a high rate of psychotropic polypharmacy among children, especially school-age children and those in foster care.
- Recent data were used that included children aged 0-17 years and reported psychotropic polypharmacy by race from a state that ranks among the highest for psychotropic medication use.

At some point during childhood, 1 in 5 U.S. children is diagnosed with a mental health disorder, with children from low-income families disproportionately affected.¹ The combined medical burden, functional impairments, and decreased productivity of those with mental health disorders among U.S. children and youth aged under 24 years cost an estimated \$250 billion per year. As such, mental disorders are among the costliest conditions treated in children.²

The use of psychotropic medication for the treatment of mental health problems in children and youth is increasing, doubling in frequency as the primary management strategy between 1995 and 2010.³ The cost of pharmacologic treatment of children with mental health and/or behavioral problems is an important part of Medicaid expenditures.⁴⁻⁶ In addition to

concerns regarding the fiscal and social burdens associated with childhood mental illness, questions remain about the long-term safety and efficacy of psychotropic medication use for children, especially young children; children receiving antipsychotics; and children receiving multiple medications.^{7,8}

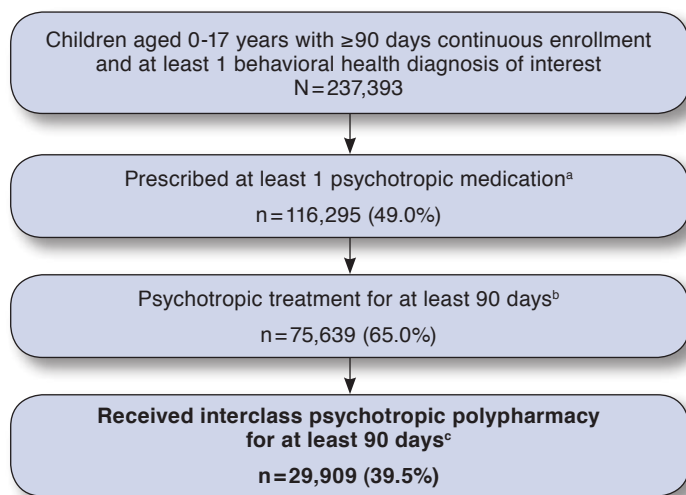
Previous studies suggest that there has been an increase in the numbers of youth receiving psychotropic polypharmacy (PP), that is, simultaneous treatment with more than 1 psychotropic medication).^{7,9-12} Previous studies of PP used data from 2008 or earlier,^{9,10,12-14} are from non-U.S. countries,¹¹ have small sample sizes,¹⁰ do not include children aged less than 6 years,^{10,13,14} and do not include data on race and/or ethnicity.¹⁰⁻¹⁴ More research is needed to better understand current trends, especially in states such as Kentucky, which have more children than the national average with mental health disorders, more children living in poverty, and more children receiving psychotropic medication.^{3,5,15,16}

The benefit versus risk of PP in children remains unclear. While a few pilot studies exist, there is little robust evidence that supports the use of PP for children and youth.^{7,9,14} In a systematic review of the use of antipsychotics and stimulants in children with attention-deficit/hyperactivity disorder (ADHD) and disruptive behavior disorders, there was no evidence of PP superiority compared with monotherapy, while concerns were documented regarding the use of polypharmacy.⁸ PP for other diagnoses were not examined. The authors concluded that the evidence supporting combination therapy was limited by the heterogeneity of the samples, the small sample sizes, and the lack of placebo controls or comparisons with other therapies. The authors also raised concerns regarding the adverse effects, including metabolic risks, but concluded that more rigorously designed studies were needed to establish benefit and evaluate potential increases in risk for adverse events.⁸ Another study has reported increased risk associated with PP when atypical antipsychotic medication is combined with antidepressants, resulting in increased risk of type 2 diabetes mellitus.¹⁷

Previous studies have suggested that older male children and children with multiple mental health diagnoses on public insurance and in foster care are more likely to receive PP.^{18,19} Unfortunately, these studies were single institution studies that did not use large representative databases. Our study, however, used a database consisting of all medical and pharmacy claims for children receiving Kentucky Medicaid benefits over a 4-year period. We developed models to test for factors associated with receipt of interclass PP and the duration of time in months on polypharmacy for children receiving Kentucky Medicaid.

Kentucky ranks higher than the national average in the prevalence of mental health problems and rates of psychotropic medication use but lower than the national average in the proportion of children receiving mental health services.^{20,21} This concerning pattern has raised questions about the use of PP for children receiving Kentucky Medicaid. The goal of this

FIGURE 1 Description of Sample Inclusion for Kentucky Medicaid Claims



^aIncluding prescriptions for antidepressants, anxiolytics, antipsychotics, stimulants, and alpha agonists.

^bPsychotropic treatment was defined as having at least 1 psychotropic medication prescription for at least 90 days (allowing for a single 15-day break in refills) during the study period.

^cInterclass psychotropic polypharmacy was defined as the presence of at least 2 psychotropic medication prescription fills for at least 2 different classes of medication that, if taken as directed, would be used at the same time for at least 90 consecutive days (allowing for a single 15-day break in refills) during the study period.

study was to identify the epidemiology of PP use and measure determinants, such as demographic information and diagnostic groups, to evaluate factors that independently predict treatment and duration of treatment with interclass PP for children receiving Kentucky Medicaid services.

Methods

Data Source and Sample

Data were extracted from Kentucky Medicaid claims records from 2012-2015 (Figure 1). These data included information on all health services billed through Kentucky Medicaid insurance (service date, type, location, provider, and associated *International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification* [ICD-9/10-CM] codes), as well as patient demographic information such as date of birth, gender, self-identified race, and postal code for all enrollees. We developed a detailed dataset for a cohort of children aged 0-17 years with continuous enrollment for ≥90 days and at least 1 behavioral health diagnosis of interest (N = 237,393; see Appendix A for diagnoses, available in online article). Two separate polypharmacy outcomes were then assessed for each included child: (1) any instance of interclass PP, calculated as a binary variable where 1 equaled polypharmacy at any time across the

study period and zero indicated no polypharmacy, and (2) the length of time in months that a child had interclass PP. For our descriptive analysis, we further reduced the sample to children treated with psychotropic medication for ≥ 90 days ($n=75,639$) and removed children with any seizure disorders for our regressions ($n=67,827$), since many of the drugs of interest may also be used as antiepileptics.

Definition of PP

Interclass PP was defined as the presence of at least 2 psychotropic medication prescription fills for at least 2 different classes of medication that, if taken as directed, would be used at the same time for at least 90 consecutive days (allowing for a single 15-day lag in getting a prescription refilled) during the study period. There were 2 outcomes of interest: the presence of any interclass PP and the length of time in months that a child received interclass psychotropic medication polypharmacy.

Diagnostic Categories

Psychiatric diagnoses were identified by an ICD-9/10-CM code for a psychiatric disorder in any of the 4 available diagnostic code columns on either the inpatient or outpatient claims (Appendix A). Psychiatric diagnoses were categorized as follows: mood disorders (which included major depressive disorder and other depressive disorders), mood disorder not otherwise specified, disruptive mood dysregulation disorder (DMDD), and bipolar disorder. Autism spectrum disorders (ASD) and pervasive developmental disorders (PDD) were separate categories as were sleep-wake disorders. An additional variable was created to count the number of psychiatric categories with which each child was diagnosed to measure comorbidities.

National Drug Code Numbers

Dispensed psychiatric medications (Appendix B, available in online article) were identified by National Drug Code numbers in pharmacy claims for the following 6 medication categories: (1) antidepressants (selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, tricyclics, monoamine oxidase inhibitors, and miscellaneous); (2) anxiolytics (benzodiazepines and miscellaneous); (3) antipsychotics (typical, atypical, and miscellaneous); (4) stimulants (including atomoxetine); (5) mood stabilizers; and (6) alpha agonists.

Covariates

We obtained the following covariate data on all subjects: age, gender, race, location, foster care, presence of seizures/stroke, and the presence of psychosocial therapy claims per year. Age, gender, race, and foster care status were provided by yearly enrollment data files from Kentucky Medicaid. Given the multi-year study period, covariates were measured at the time the children enrolled in Medicaid, with the exception of age, which

was calculated as the maximum age during the study period. Metropolitan and nonmetropolitan geography was determined using 2013 Rural-Urban Continuum Codes (RUCC), as defined by the U.S. Department of Agriculture. Geography for each child was coded as metropolitan when the county of residence had an RUCC code of 1-3 and as nonmetropolitan when the county of residence had an RUCC code of 4-9. The presence of seizures/stroke at any point during each year was identified by at least 1 ICD-9/10-CM code in any position for seizures, cerebrovascular disease, or convulsive disorders. The total number of enrolled months was also calculated to control for total time that a child was covered by Kentucky Medicaid.

Statistical Analysis

We performed descriptive analyses to summarize the characteristics of our sample, using ANOVA and chi-square tests to assess differences in demographic variables for continuous and categorical variables, respectively. Estimates of interclass PP prevalence were calculated using all eligible subjects as the denominator ($n=75,639$).

Two separate statistical models were specified for this study. The first used a generalized linear model with a logit link and binomial distribution to assess factors associated with any presence of interclass PP for the study population. A second separate generalized linear model with an identity link and Gaussian distribution was developed for predicting length of interclass PP treatment for the full cohort of children over the 4 years.

Each outcome of interest was tested as a function of the covariates previously discussed, allowing us to test for significant predictors of a child ever having interclass PP and the length of interclass PP. Odds ratios were reported for the regression model that assessed individual characteristics associated with having any instance of polypharmacy during the study period. Beta coefficients were reported with 95% confidence intervals [CIs] and 2-sided *P* values for length of time in months that a child was treated with polypharmacy. A 2-tailed *P* value of <0.05 was considered statistically significant. The beta coefficients were interpreted as the change in the number of months of polypharmacy given a 1-unit change in the covariate. We performed data preparation and analyses using R statistical software, version 3.4.0 (R Foundation for Statistical Computing, Vienna, Austria).

The study was approved by the Institutional Review Board at the University of Louisville. Data were obtained from the Kentucky Department of Medicaid Services, which approved the use for this study.

Results

Over the 4 years of this study, 237,393 children were continuously enrolled for ≥ 90 days in Kentucky Medicaid. Of these, 75,639 (31.8%) were dispensed at least 1 psychotropic

TABLE 1 Demographic and Clinical Characteristics of Children with Interclass PP Enrolled in Kentucky Medicaid and Treated with at Least 90 Days of Psychotropic Medications

2012-2015	Total	Interclass PP, n	Interclass PP, %
Total on psychotropic medications (≥90 days)	75,639	29,900	39.5
Age category			
0-5 years	12,242	3,928	32.1
6-11 years	33,466	14,131	42.2
12-17 years	29,931	11,850	39.6
Foster care	4,504	2,821	62.6
Gender			
Male	47,185	19,795	42.0
Female	28,454	10,114	35.6
Race			
Black	6,501	2,229	34.3
White	50,592	18,905	37.4
Other	2,109	727	34.5
Not provided	16,437	8,048	49.0
Psychosocial therapy			
Anxiety and trauma-related disorders	32,782	15,483	47.2
Autism and PDD NOS	7,281	4,541	62.4
ADD	58,946	25,962	44.0
ODD	19,307	11,553	59.8
Conduct disorders	6,209	3,877	62.4
Mood disorders total	31,357	16,763	53.5
Depression	19,234	8,967	46.6
Bipolar disorder	8,771	6,411	73.1
Disruptive mood/dysregulation disorder	4,523	3,116	68.9
Mood disorder NOS	18,644	11,870	63.7
Impulse control	18,537	9,936	53.6
Other mental health disorders	14,632	8,198	56.0
Other NDD	20,626	9,922	48.1
Schizophrenia and other psychoses	3,854	2,653	68.8
Sleep wake disorders	10,562	5,574	52.8
Physical diagnostic categories	7,812	3,769	48.3

ADD = attention deficit disorder; NDD = neurodevelopmental disorders; NOS = not otherwise specified; ODD = oppositional defiant disorder; PDD = pervasive developmental disorders; PP = psychotropic polypharmacy.

medication for ≥90 days, and 29,909 (39.5%) of this group received PP for ≥90 days.

Demographics of Children Receiving Interclass PP

For the years 2012-2015, the overall rate of children who were dispensed at least 1 psychotropic medication for ≥90 days and who were treated with interclass PP was 39.5% (Table 1). This rate was slightly lower for children aged 0-5 years (32.1%, $P < 0.001$) and higher for children aged between 6-11 years (42.2%, $P < 0.001$). Children with bipolar disorder had the highest PP rate (73.1%) of any other behavioral health diagnosis, followed by DMDD (68.9%) and schizophrenia (68.8%).

TABLE 2 Rates of Medication Use by Class and Class Combinations Stratified by Foster Care Status, 2012-2015

Psychotropic Therapy Type	Drug Class	Medicaid Nonfoster Children (per 1,000)	Medicaid Foster Children (per 1,000)
Monotherapy	Stimulants	638	403
	Antidepressants	176	224
	Alpha agonists	69	116
	Other	117	256
2 medication classes	Stimulants and alpha agonists	572	365
	Stimulants and antidepressants	120	138
	Stimulants and antipsychotics	81	54
	Other	228	422
At least 3 medication classes	Stimulants, alpha agonists, antidepressants, and antipsychotics	134	152
	Stimulants, alpha agonists, and antipsychotics	130	76
	Stimulants, alpha agonists, and antidepressants	102	67
	Other	634	703

Note: These numbers represent the number of children per 1,000 children treated with at least 90 days of psychotropic medications during 2012-2015 and without seizure disorders with (a) no psychotropic polypharmacy and only treated with 1 psychotropic medication, (b) interclass PP with exactly 2 psychotropic medications, and (c) interclass PP with 3 or more psychotropic medications. PP = psychotropic polypharmacy.

Over the 4 study years, 27.5% of children treated with interclass PP received no associated psychotherapy. Children in foster care received interclass PP significantly more often than the overall Medicaid population (62.6%, $P < 0.001$).

As shown in Table 2, stimulants were by far the most common psychotropic medication dispensed to children on Kentucky Medicaid. Stimulants were the most common class of psychotropic medication for children without any PP treatment and were included in the most common combinations of interclass PP for children with 2 concurrent classes of medications and with 3 or more concurrent classes of medications.

Factors Associated with Interclass PP

As shown in Table 3 (adjusted), being in foster care (odds ratio [OR] = 1.71, 95% CI = 1.58, 1.84; $P < 0.001$); having a bipolar disorder (OR = 2.24; 95% CI = 2.11, 2.38; $P < 0.001$); mood disorder not otherwise specified (OR = 1.11, 95% CI = 1.04, 1.17, $P < 0.001$); ASD (OR = 1.17; 95% CI = 1.08, 1.26; $P < 0.001$); or the presence of each additional psychiatric comorbid condition (OR = 1.8, 95% CI = 1.74, 1.85; $P < 0.001$) increased the odds of receiving interclass PP. However, children whose race was reported to be black (OR = 0.72, 95% CI = 0.67, 0.76; $P < 0.001$) had lower levels of PP in comparison with children who were reported as white. Children with depression (OR = 0.49, 95% CI = 0.47, 0.52; $P < 0.001$); impulse control disorder (OR = 0.64, 95% CI = 0.60,

TABLE 3 Factors Associated with Interclass PP Among Children Enrolled in Kentucky Medicaid with at Least 90 Days of Psychotropic Medication Therapy and No Seizure Disorders Between 2012 and 2015

Predictors	OR (95% CI)	P Value
Gender, male	1.28 (1.23, 1.33)	<0.001
Age category		
0-5 years	Reference	
6-11 years	1.58 (1.5, 1.67)	<0.001
12-17 years	1.25 (1.17, 1.32)	<0.001
Foster care	1.71 (1.58, 1.84)	<0.001
Nonmetropolitan residence ^a	0.95 (0.91, 0.98)	0.003
Race category		
White	Reference	
Black	0.72 (0.67, 0.76)	<0.001
Other	1.01 (0.90, 1.12)	0.869
Not provided	1.24 (1.19, 1.3)	<0.001
Psychiatric diagnostic categories		
Attention deficit disorders	Reference	
Schizophrenia and other psychoses	0.91 (0.83, 1.01)	0.069
Bipolar disorder	2.24 (2.11, 2.38)	<0.001
Mood disorder NOS	1.11 (1.04, 1.17)	<0.001
Depression	0.49 (0.47, 0.52)	<0.001
Disruptive mood dysregulation Disorder	1.13 (1.04, 1.23)	0.003
Conduct disorder	0.76 (0.7, 0.82)	<0.001
Oppositional defiant disorder	0.98 (0.93, 1.04)	0.471
Autism PDD NOS	1.17 (1.08, 1.26)	<0.001
Anxiety and trauma-related disorders	0.73 (0.7, 0.77)	<0.001
Other mental disorders	0.76 (0.72, 0.8)	<0.001
Other neurodevelopmental disorders	0.72 (0.68, 0.76)	<0.001
Impulse control disorder	0.64 (0.60, 0.67)	<0.001
Sleep wake disorders	0.89 (0.84, 0.94)	<0.001
Covered months	1.01 (1.01, 1.02)	<0.001
Total number of psychiatric diagnoses	1.8 (1.74, 1.85)	<0.001

Note: Total sample, n = 67,798. Children with seizure disorders were removed from the sample, with 67,827 observations remaining.

^aNonmetropolitan was defined as county of residence having an RUCC code of 4-9. CI = confidence interval; NOS = not otherwise specified; OR = odds ratio; PDD = pervasive developmental disorders; PP = psychotropic polypharmacy; RUCC = 2013 Rural-Urban Continuum Codes.

0.67; $P < 0.001$); or several other diagnoses were less likely to be treated with interclass PP for ≥ 90 consecutive days.

Factors Associated with Interclass PP Treatment Length

The results for predicting the length of treatment with PP were similar to the predictors for treatment with any interclass PP. As seen in Table 4 (adjusted), males had more covered months with PP compared with females (beta = 1.01, 95% CI = 0.87, 1.16, $P < 0.001$). Children aged 6-11 years had more covered months with PP compared with children aged 0-5 years

TABLE 4 Predictors of Length of Interclass PP Treatment, Measured in Months, Among Children Enrolled in Kentucky Medicaid with at Least 90 Days of Psychotropic Medication Therapy and No Seizure Disorders Between 2012 and 2015

Predictors of PP Treatment Length	Beta Values (95% CI)	P Value
Gender, male (reference: female)	1.01 (0.87, 1.16)	<0.001
Age category		
0-5 years	Reference	
6-11 years	3.08 (2.87, 3.29)	<0.001
12-17 years	1.60 (1.37, 1.83)	<0.001
Foster care	1.81 (1.52, 2.11)	<0.001
Nonmetropolitan residence ^a	-0.4 (-0.54, -0.26)	<0.001
Race category		
White	Reference	
Black	-1.37 (-1.61, -1.12)	<0.001
Other	-0.82 (-1.23, -0.40)	<0.001
Not provided	1.33 (1.16, 1.51)	<0.001
Psychiatric diagnostic categories		
Attention deficit disorders	Reference	
Schizophrenia and other psychoses	-1.06 (-1.42, -0.70)	<0.001
Bipolar disorder	3.62 (3.38, 3.86)	<0.001
Mood disorder NOS	0.56 (0.33, 0.80)	<0.001
Depression	-3.32 (-3.54, -3.10)	<0.001
Disruptive mood dysregulation disorder	0.81 (0.5, 1.12)	<0.001
Conduct disorder	-1.32 (-1.62, -1.03)	<0.001
Oppositional defiant disorder	-0.17 (-0.39, 0.05)	0.136
Autism PDD NOS	2.05 (1.75, 2.34)	<0.001
Anxiety and trauma-related disorders	-1.29 (-1.48, -1.09)	<0.001
Other mental disorders	-0.96 (-1.18, -0.74)	<0.001
Other neurodevelopmental disorders	-0.49 (-0.71, -0.27)	<0.001
Impulse control disorder	-2.07 (-2.28, -1.85)	<0.001
Sleep wake disorders	-0.53 (-0.77, -0.29)	<0.001
Total number of psychiatric diagnoses	2.49 (2.36, 2.61)	<0.001

Note: Total sample, n = 67,798. Children with seizure disorders were removed from the sample, with 67,827 observations remaining.

^aNonmetropolitan was defined as county of residence having an RUCC code of 4-9. CI = confidence interval; NOS = not otherwise specified; PDD = pervasive developmental disorders; PP = psychotropic polypharmacy; RUCC = 2013 Rural-Urban Continuum Codes.

(beta = 3.08, 95% CI = 2.87, 3.29; $P < 0.001$), and those aged 12-17 years also had more covered months, although to a lesser degree (beta = 1.60, 95% CI = 1.37, 1.83; $P < 0.001$). Being in foster care (beta = 1.81, 95% CI = 1.52, 2.11; $P < 0.001$) and having a bipolar disorder (beta = 3.62, 95% CI = 3.38, 3.86, $P < 0.001$) and ASD (beta = 2.05, 95% CI = 1.75, 2.34; $P < 0.001$) increased the number of months of receiving interclass PP. Children with depression (beta = -3.32, 95% CI = -3.54, -3.10; $P < 0.001$) or impulse control disorder (beta = -2.07, 95% CI = -2.28, -1.85, $P < 0.001$) were treated for fewer months with interclass PP. However, as the number of additional psychiatric comorbidities

increased, the length in months of PP treatment increased (beta = 2.49, 95% CI = 2.36, 2.61; $P < 0.001$), as well.

Discussion

The use of psychotropic medication for children and youth, including PP, has increased over recent years. This study provides new data from a statewide sample of children receiving Kentucky Medicaid services and fills a gap in the literature by using recent data (2012-2015) that includes children aged 0-17 years stratified by age, gender, race, diagnostic category, and foster care.

The overall rate of children on psychotropic medication for ≥ 90 days who were treated with interclass PP was 39.5%. This rate was slightly lower for children aged 0-5 years (32.1%, $P < 0.001$) and higher for children aged 6-11 years (42.2%, $P < 0.001$). Children with bipolar disorder had the highest PP rate (73.1%) of any other behavioral health diagnosis, followed by DMDD (68.9%) and schizophrenia (68.8%). Children in foster care received interclass PP significantly more often than the overall population (62.6%, $P < 0.001$). A substantial proportion of children on Kentucky Medicaid with ASD, ADHD, or depressive disorders were exposed to PP, and these rates are markedly higher for those in foster care.

The proportion (39.5%) of children enrolled in Kentucky Medicaid exposed to PP is higher than national averages.^{9,13} Among children aged more than 6 years, this rate of PP is almost twice that reported by Comer et al. (2010) and 3 times that reported by Chen et al. (2011).^{9,13} Importantly, in our study, children aged 6-11 years had the greatest likelihood of longer duration of interclass PP. Differences in the definitions of polypharmacy and the populations studied make comparisons difficult, but children aged between 6 and 11 years are a vulnerable population deserving of further study.

Children in foster care had significantly higher rates (62.6%) and more covered months with PP compared with children who were not in foster care. The rates are less than those reported by Zito et al. (2008) for children aged birth-19 years in Texas who were in foster care (72.5%).²² Again, methodological differences make comparisons difficult, but the literature suggests that children in foster care are in need of careful monitoring by specialized mental health providers to ensure that they are receiving appropriate, evidence-based care.²²⁻²⁶

Children who were reported with race as black had less PP and shorter durations of PP compared with children reported as white. It is not clear whether this reflects an access issue, treatment bias, or some protective factor that has not been identified. Other studies of polypharmacy in children have not reported on differences by race. This is an important area in which to focus future studies.

Throughout 2012-2015, about one quarter of the children treated with interclass PP received no associated psychotherapy (27.5%) within the 4-year period. Also, less than 50%

of this sample receiving interclass PP received psychotherapy in any given year.⁵ The quality measure from the Healthcare Effectiveness Data and Information Set (HEDIS), a widely used set of health care performance standards, requires that behavioral health interventions be instituted before starting treatment with antipsychotics for children.²⁷ While no specific HEDIS measure exists for other psychotropic medication or for PP, first-line psychosocial interventions are indicated.

The type and number of psychiatric diagnoses influence the prevalence and duration of PP. Diagnoses of bipolar disorder, mood disorder not otherwise specified, or ASD are significant predictors of interclass PP in our study. PP increases with reported number of psychiatric comorbidities. These findings are consistent with previous reports of increases in PP for those children with greater impairment.^{9,28}

Stimulants and alpha agonists were the most common 2-class PP combinations and, along with antipsychotics, the most common 3-class PP combinations. This pattern suggests that problems associated with ADHD and disruptive behaviors are driving the use of multiple psychotropic medications in our population, which is of concern in this population, since research has shown that there are other factors that may contribute to attention problems in children living in poverty that may mimic ADHD but would benefit from nonpharmacological therapies.²⁹⁻³¹

Our study supplements national reports of increased psychotropic medication use and PP in youth and raises concerns about the nature of current mental health treatment of children and adolescents. There is little evidence to support the efficacy of PP in children.⁷ Pharmacokinetic and pharmacodynamic drug interactions may lead to adverse effects in children treated with multiple psychotropics.⁷ More controlled trials of psychotropic augmentation in children are needed to assess the associated risks and benefits of PP, such as the augmentation of stimulants with antipsychotic medication in the Treatment of Severe Childhood Aggression (TOSCA) studies.³²

Much remains unknown about the long-term effects of monotherapy, as well as the effects of PP, on the developing brains of children. In addition, the cost of antipsychotic medications and general PP can have a significant effect on state Medicaid budgets. For example, as much as 70%-80% of total health care costs for adult patients with antipsychotic medication polypharmacy were related to drugs.³³ Increased costs associated with adverse effects, emergency department utilization, and length of stay for inpatient hospitalizations related to PP represent possible cost burdens for adults and children, in addition to representing quality of care issues.

Provider practice styles and behaviors involving PP require attention. In general, the rate of psychiatric treatment involving psychotropic drugs has increased over the last decade, and our study confirmed national findings that many children with PP do not receive psychosocial therapy.³ Given the implications of

disruptive behavior and aggression in children, these findings are contrary to professional guidelines that suggest the use of evidence-based psychosocial therapy as a first-line approach to treating these conditions.^{34,35} Questions of diagnostic inflation and “treatment creep” have been raised by those criticizing modern psychiatry’s diagnostic systems and reliance on pharmacotherapy.³⁶ Providers mention lack of alternative treatment resources and external expectations of families or systems to reduce symptoms as a reason for using antipsychotic medications in youth.³⁷ A system change focusing on judicious prescribing practices is necessary to balance the use of psychotropic medication and psychosocial therapy to ensure rational prescribing.³⁸

System solutions to the problem of PP in children include increased access to high-quality psychosocial care and evidence-based treatments. Collaborative care models integrating mental health into primary care may help address unmet needs in pediatric mental health.³⁹ It may be anticipated that the growth of electronic health systems and the ability to manage “big data” may result in more effective care coordination and minimally burdensome real-time monitoring to identify children who are being prescribed psychotropic medications in worrisome patterns, such as off-label, polypharmacy, without psychosocial care, and without appropriate monitoring and surveillance). For example, some states have used systems such as the Comprehensive Neuroscience program to track for signs of worrisome prescribing.²² Televideo consults between providers and medication reviews have also been shown to reduce rates of worrisome psychotropic medication prescribing (including polypharmacy) for children in foster care and Medicaid,⁴⁰ emphasizing the importance of care coordination in addressing this issue.

In addition, disruptive behaviors and aggression are influenced by a number of biopsychosocial issues, such as family poverty, parent education, parent and youth substance abuse, and environmental characteristics (such as chaos), that require investment in the communities where children and families live. Improved case worker, provider, and consumer education on psychotropic medication use in children may result in improvements in the informed consent process and more rational medication use.²⁶ Also, trauma-informed training for all individuals working with children in the foster care system may result in a greater understanding of the challenges facing these children and possible benefits of nonpharmaceutical treatment options.^{41,42}

Future directions for research include developing and implementing plans to improve the rational use of psychotropic medications for children enrolled in Kentucky Medicaid, including those in foster care. Such a plan will likely involve ways to improve access to evidence-based psychosocial therapies for children; education for families, youth, health care providers, and case workers; and communication between

patients, families, providers, and experts in the field. Ways to improve access to high quality mental health specialists for all children are needed, especially for those who are most vulnerable, such as children in foster care and those receiving Medicaid services. Strategies may be tailored to geographic differences or sociodemographic factors.

Limitations

This study has some limitations to consider. The inability to address the appropriateness of PP; the quality, timing, and duration of psychosocial care; the severity of the symptoms; and the use of data from only Kentucky Medicaid claims may or may not reflect the prescribing patterns in other states. The use of administrative claims data also presents several limitations, including lack of information about treatment without a formal diagnosis, limited diagnostic data with only 4 listed for each claim, and the potential for errors in billing codes. The accuracy of the diagnoses can be questioned given that the data were extracted from administrative claims.

Similarly, data on race was self-reported and not required, with 22% of the sample not reporting race. Also, claims-based approaches to detecting psychotherapy may not have adequately identified all services that children receive, such as those provided in schools and residential care facilities. In addition, we only reported on children who had continuous Medicaid coverage for >90 days. Children who go in and out of the Medicaid system may be at risk for receiving fragmented care and forming unique patterns of medication usage. More research is needed to understand factors associated with gaps in Medicaid coverage and how to ensure that eligible children have continuous coverage.

Our study used definitions of continuous enrollment and ≥90 days of consecutive concomitant psychotropic medication use as indicated by HEDIS, which, in 2015, addressed the issue of antipsychotic polypharmacy.²⁷ While these criteria are stricter than previously reported studies and affected our reported rates, the use of standardized definitions would allow for more valid comparison among studies in the future. Even with our stricter definition of concomitant use, our rates were higher than those previously reported.

Conclusions

This study presents findings from 2012-2015 Kentucky Medicaid claims data that fill a gap in the literature by providing more current information on PP prescribing trends in children from a large statewide dataset. We also extended previous studies by including data on race and on children aged <6 years. Stimulants were the most frequently dispensed psychotropic medication class alone and in combination with other psychotropic medications. More research is needed in this area to determine the appropriateness of using stimulants in combination with other psychotropic medications in children.

Current PP trends are concerning, and continued vigilance and empirical evidence are needed to ensure that appropriate prescribing practices are used in combination with psychosocial therapies and that careful monitoring is employed to achieve the safest and best outcomes for children with mental health disorders, especially those living in poverty. Finally, our data showed that children who were black experienced lower levels of PP compared with children who were white. It is not known if this reflects differences in access and appropriateness of care. More research in this area is needed to address potential health disparities in PP associated with race.

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DISCLOSURES

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Psychotropic Polypharmacy Among Children and Youth Receiving Medicaid, 2012-2015

APPENDIX A Definitions and Codes Used to Construct Psychiatric Diagnostic Categories

Categories and Diagnoses	ICD-9-CM Codes	ICD-10-CM Codes
Schizophrenia and other psychotic processes		
Schizophrenia and schizoaffective disorder	295.xx	F20, F200-F205, F208, F2081, F2089, F209, F25.0, F25.1
Delusional disorders	297.x	F22
Other nonorganic psychoses	298.x	F28, F23, F29
Mood disorders total		
Depressive disorders (listed below)		
Bipolar and related disorders	296.00-296.10, 296.40-296.89, 301.13	F30.10-F30.4, F30.8, F30.9, F31.0-F31.9, F34.0
Mood disorder NOS	296.9	F06.3, F39
Disruptive mood dysregulation disorder	296.99	F34.8
Depressive disorders		
Major depressive disorder and other depressive disorders	296.20-296.36, 300.4, 311, 625.4	F32.0-F32.5, F32.8, F32.9, F33.0-F33.3, F33.8, F33.9, F33.41, F33.42, F34.1, N94.3
Autism spectrum disorders	299.xx	F80.89, F84, F840, F842, F843, F845, F848, F849
Other neurodevelopmental disorders		
Intellectual disability	317.xx, 318.xx, 319.xx, 758	Q909, F70-F73, F78, F79
Tic disorders	307.20-307.23	F95, F950-F952, F958, F959
Stereotypical movement disorder	307.3	F984
Developmental delays	315.xx	F80, F80.81, F80.9, F81, F81.1, F81.2, F82, F88, F89
Disruptive behavior disorders		
Conduct disorders	312.81	F91x except F913
Attention deficit disorder	314.xx	F90x
Oppositional defiant disorder	313.81	F913
Anxiety and trauma-related disorders		
Anxiety disorders	300.00-300.29, 309.21, 301.4, 312.23	F40-F419, F93.0, F94.0
PTSD and acute stress disorder	308.3, 309.81, 309.89, 309.9	F430, F431-F4312, F43.8
OCD and related disorders	300.3, 300.7, 312.39	F42, F45.22, F63.2, L98.1
Adjustment disorders	309.0, 309.24, 309.28, 309.3, 309.4, 309.89, 309.9	F43, F432-F439
Reactive attachment disorder	313.89	F938, F941, F942, F988
Other mental disorders		
Mental disorders conditions classified	293.xx, 294.xx	F53, F02-F062, F064, F068, F524
Disturbance emotions childhood adolescence	313.9x	F939, F948, F989
Feeding and eating disorders	307.1, 307.50, 307.51, 307.52, 307.53, 307.59	F50x, F982, F9821, F9829, F983
Personality disorders	301.0, 301.1x, 301.2x, 301.3, 301.5x, 301.6, 301.7, 301.8x, 301.9, 301.0	F21, F34, F340, F341, F60-F609, F68-F69
Syndromes elsewhere unclassified	307.xx	F98.0, F98.1, F99
Sexual and gender identity disorders	302.2-302.9	F52, F520-F522, F5221, F5222, F523, F5231-5232, F524-F526, F528, Ff29, F64-F66
Dissociative disorders	300.14, 300.12, 300.15, 300.6	F44.0-F44.7, F44.81, F44.89, F448-F449
Somatic symptom and related disorders	300.82, 300.89	F44.4-F44.7, F45, F450, F451, F452, F45.21, F4529, F454, F4541, F4542, F458, F459, F488, F68.10
Sleep-wake disorders	780.52, 780.54, 307.45, 307.46, 307.47, 327.21, 327.23, 327.42, 333.94, 347.00, 347.01, 347.10	F51, F510, F5101-F5105, F5109, F511, F5111-F5113, F5119, F513-F515, F518, F519, G25.81, G47.00, G47.09, G47.10, G47.19, G47.20-G47.26, G47.31, G47.33, G47.411, G47.419, G47.429, G47.52, G47.8
Impulse control		
Intermittent explosive disorder and impulse control	312.30-312.34, 312.89, 312.9	F63-F632, F633, F638-F639
Physical diagnostic categories		
Seizure epilepsy	345.xx	G40
Other convulsions	780.39	R56.9
Posttraumatic seizures		R56.1

ICD-9/10-CM = International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification.

APPENDIX B Definitions of Drug Classifications

Antidepressants

Adapin
Alplezin
Amitril
Amitrip HCL/
Chlordiazepoxide
Amitriptyline
Amitriptyline HCL
Amoxapine
Anafranil
Asendin
Aventyl
Buderprion
Buderprion SR
Buderprion XL
Buproban
Bupropion
Bupropion HCL
Bupropion HCL SR
Burpropion XL
CDP & Amitriptyline
Celexa
Chlordiazepoxide and Amitrip
Chlordiazepoxide/Amitrip
Chlordiazepoxide-Amitrip
Chlordiazepoxide-Clidinium
Citalopram
Citalopram HBR
Clomipramine HCL
Cymbalta
Despramine
Despramine HCL
Desvenlafaxine
Desyrel
Doxepin
Doxepin HCL
Duloxetine
Duloxetine HCL
Effexor
Effexor XR
Elavil
Emsam
Endep
Escitalopram
Escitalopram (Lexapro)
Escitalopramoxalate
Etrafon
Fluoxetine DR
Fluoxetine HCL
Fluvoxamine
Fluvoxamine Maleate
Fluvoxamine Maleate ER
Imipramine
Imipramine HCL
Imipramine Pamoate
Isocarboxazid
Janimine
Lexapro
Limbital
Ludiomil
Luvox
Luvox CR
Maprotiline
Maprotiline HCL
Marplan
Milnacipran
Mirtazapine
Nardil
Nefazodone
Nefazodone HCL
Norpramin
Nortriptyline
Oleptro

Antidepressants

Oleptro ER
Pamelor Parnate
Paroxetine
Paroxetine HCL
Paxl
Pertofrane
Phenelzine Sulfate
Presamine
Pristiq
Pristiq ER
Protriptyline HCL
Prozac
Remeron
Sarafem
Sarna
Sarna Sensitive
Savella
Selegiline
Sertraline
Sertraline HCL
Serzone
Silenor
Sinequan
SK-Amitriptyline
SK-Pramine
Surmontil
Symbyax
Tofranil
Tofranil-PM
Tranylcypromine Sulfate
Trazodone
Trazodone HCL
Triavil
Trimipramine Maleate
Tryptanol
Venlafaxine
Venlafaxine HCL
Venlafaxine HCL ER
Vibryd
Vilazodone
Vivactil
Wellbutrin
Wellbutrin XL
Xenazin
Xenazine
Zolof

Antipsychotics

Abilify
Abilify Discmelt
Abilify Maintenia
Amitriptyline HCL/
Perphenazine
Amitriptyline/Perphenazine
Aripiprazole
Asenapine
Asenapine (Saphris)
Chlorpromazine
Chlorpromazine HCL
Clozapine
Clozapine ODT
Clozaril
Fanapt
Fazaclio
Fluphenazine
Fluphenazine Decanoate
Fluphenazine HCL
Geodon
Haldol

Antipsychotics

Haldol Decanoate 100
Haloperidol
Haloperidol Decanoate
Haloperidol Decanoate 100
Haloperidol Lactate
Iloperidone
Iloperidone (Fanapt)
Invega
Invega Sustenna
Latuda
Loxpin
Loxapine
Lurasidone
Olanzapine
Olanzapine ODT
Olanzapine-Fluoxetine HCL
Orap
Paliperdone
Paliperdone (Invega)
Perphenazine
Perphenazine & Amitriptyl
Perphenazine 2 mg w/Amitri
Perphenazine 4 mg w/Amitri
Perphenazine Amitriptylin
Perphenazine & Amitript
Perphenazine w/Amitrip
Perphenazine/Amitrip
Perphenazine-Amitriptyline
Prochlorperazine
Prochlorperazine
Prochlorperazine Maleate
Quetiapine
Quetiapine Fumarate
Risperdal
Risperdal Consta
Risperdal M-Tab
Risperidone
Risperidone ODT
Saphirs
Seroquel
Seroquel XR
Thioridazine
Thioridazine HCL
Thiothixene
Trifluoperazine
Trifluoperazine HCL
Zprasideone
Ziprasidone HCL
Zyprexa
Zyprexa Zydys

**Benzodiazepines/
Anxiolytics/Hypnotics**

Alprazolam
Alprazolam ER
Alprazolam ODT
Alprazolam XR
Ambien CR
Ativan
Buspirone HCL
Chlordiazepoxide HCL
Clorazepate Dipotassium
Diastat
Diastat Acudial
Diazepam
Eszopiclone
Flurazepam HCL
Hydroxyzine HCL
Hydroxyzine Pamoate
Lorazepam
Lorazepamintensol
Lunesta
Midazolam HCL

**Benzodiazepines/
Anxiolytics/Hypnotics**

Oxazepam
Phenobarbital
Rozerem
Temazepam
Riazolam
Zaleplon
Zolpidem Tartrate
Zolpidem Tartrate ER
Zolpimist

Alpha Agonists

Catapres
Catapres-TTS 1
Catapres-TTS 2
Catapres-TTS 3
Clondine
Clondine HCL
Clondine HCL ER
Guanfacine
Guanfacine HCL
Guanfacine HCL ER
Intuniv
Kapvay
Methyl dopa
Methyl dopa-
Hydrochlorothiazide

Mood Stabilizers

Carbamazepine
Carbamazepine ER
Carbamazepine XR
Carbatro
Carbatrol
Cibalith-S
Depakene
Depakote
Depakote ER
Depakote Sprinkle
Divalproex
Divalproex Sodiumer
Eptol
Epsom Salt
Equatro
Equetro
Eskalith
Gabapentin
Gralise
Keppra
Keppra XR
Lamictal
Lamictal (green)
Lamictal (orange)
Lamictal ODT
Lamictal ODT (green)
Lamictal ODT (orange)
Lamictal XR
Lamotrigine
Lamotrigineer
Levetiracetam
Levetiracetamer
Lithane
Lithium
Lithium Carbonate
Lithium Citrate
Lithobid
Lithonate
Lithotabs
Lyrica
Magnesium Sulfate
Neurontin
Oxcarbazepine
Oxtellar

Mood Stabilizers

Oxtellar XR
Tegretol
Tegretol XR
Topamax
Topiram
Topiramate
Topiramate ER
Trileptal
Trokendi XR
Valproate
Valproate Sodium
Valproic Acid

Stimulants

Adderell
Adderall XR
Amphet ASP/Amphet/D-
Amphet
Amphetamine Salt Combo
Amphetamine/
Dextroamphetamine
Atomoxetine
Concerta
Cylert
D-Amphetamine Sulfate
Daytrana
Desoxyn
Dexedrine
Dexmethylphenidate
Dexmethylphenidate HCL
Dexmethylphenidate HCL ER
Dextroamphetamine
Dextroamphetamine Sulfate
Dextroamphetamine Sulfate
ER
Dextroamphetamine-Amphet
ER
Dextrostat
Focalin
Focalin XR
Lisdexamfetamine
Lisdexamfetamine (Vynase)
Metadate
Metadate CD
Metadate ER
Methamphetamine HCL
Methylphenidate
Methylphenidate ER
Methylphenidate HCL
Methylphenidate HCL CD
Methylphenidate LA
Methylphenidate SR
Pemoline
Procentra
Quillivant
Quillivant XR
Ritalin
Ritalin LA
Ritalin-SR
Strattera
Vynase
Vyvanse