

Chronic Medication Use in Children Insured by Medicaid: A Multistate Retrospective Cohort Study

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abstract

BACKGROUND AND OBJECTIVES: Little is known about the use of chronic medications (CMs) in children. We assessed the prevalence of CM use in children and the association of clinical characteristics and health care resource use with the number of CMs used.

METHODS: This is a retrospective study of children ages 1 to 18 years using Medicaid from 10 states in 2014 grouped by the annual number of CMs (0, 1, 2–4, 5–9, and ≥ 10 medications), which are defined as a dispensed ≥ 30 -day prescription with ≥ 2 dispensed refills. Trends in clinical characteristics and health care use by number of CMs were evaluated with the Cochran-Armitage trend test.

RESULTS: Of 4 594 061 subjects, 18.8% used CMs. CM use was 44.4% in children with a complex chronic condition. Across all children, the most common CM therapeutic class was neurologic (28.9%). Among CM users, 48.8% used multiple CMs (40.3% used 2–4, 7.0% used 5–9, and 0.5% used ≥ 10). The diversity of medications increased with increasing number of CMs: for 1 CM, amphetamine stimulants were most common (29.0%), and for ≥ 10 CMs, antiepileptics were most common (7.1%). Of \$2.3 billion total pharmacy spending, 59.3% was attributable to children dispensed multiple CMs. Increased CM use (0 to ≥ 10 medications) was associated with increased emergency department use (32.1% to 56.2%) and hospitalization (2.3% to 36.7%).

CONCLUSIONS: Nearly 1 in 5 children with Medicaid used CMs. Use of multiple CMs was common and correlated with increased health care use. Understanding CM use in children should be fundamentally important to health care systems when strategizing how to provide safe, evidence-based, and cost-effective pharmaceutical care to children.



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WHAT'S KNOWN ON THIS SUBJECT: Children insured by Medicaid frequently use medications, but little is known specifically about chronic medication (CM) use. Without understanding which children use CMs, it is challenging to plan investigations to determine the appropriateness of current prescription practices.

WHAT THIS STUDY ADDS: One in 5 children insured by Medicaid use a CM annually; nearly 1 in 10 used multiple CMs. Central nervous system agents accounted for nearly 30% of all CMs. CMs were positively correlated with health care resource use and spending.

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More than 250 million outpatient prescriptions are dispensed to pediatric patients annually in the United States.¹ Most prescriptions are for short-term antibiotics; but many are for longer-term use medications that are used to treat chronic health conditions.¹⁻³ The use of chronic medications (CMs) is not without risk and presents a management challenge in both outpatient and community settings due to the time and effort required to review, reconcile, and monitor CM use.⁴⁻¹¹ The National Academy of Sciences has designated the outpatient environment as a high-priority area for medication safety in children.¹² Whereas a large body of evidence exists to guide CM use in the geriatric population,¹³ there is a scarcity of analogous evidence to inform safe prescribing and monitoring practices in children, especially for those who use CMs and may have the most critical pharmacovigilance needs.

In particular, the growing populations of children and youth with special health care needs and the subgroup of children with complex chronic conditions (CCCs) represent important groups of children who use medications.¹⁴ Among these populations, the increasing prevalence of certain chronic conditions that often require pharmacotherapy (eg, mental health, respiratory, and neuromuscular conditions) may necessitate the use of CMs for many months or even years.^{15,16} This prolonged exposure to CMs (and possibly polypharmacy with multiple concurrent CMs), and the associated potential benefits, risks, and costs, highlights the importance of providing high-quality, appropriate, and cost-effective pharmacotherapy. Preemptively, many state Medicaid programs are instituting narrower formularies, relying on preauthorization processes for less common medications, and placing limits on the number of refills.¹⁷ Yet, these efforts are

underway without sufficient knowledge of CM use in children, especially for children with polypharmacy.

Without a fundamental understanding about the children who use CMs and their medications, it is challenging to plan investigations to determine the appropriateness of current prescription practices, the associated clinical benefits and risks of CM use, and the related costs. Therefore, by using a 10-state Medicaid database, the current study was performed to (1) determine the prevalence of annual cumulative CM use in children insured by Medicaid overall and for specific classes of medications, (2) assess patient demographic and clinical characteristics associated with the number of CMs used, and (3) quantify health resource use and spending associated with the number of CMs used.

METHODS

Study Design, Population, and Setting

This was a retrospective cohort study of the MarketScan Medicaid Database (IBM Watson Health, Armonk, NY), which includes demographic and clinical data on paid Medicaid claims for all health care encounters across the care continuum. We included children ages 1 to 18 years continuously enrolled (≥ 11 months) in Medicaid or the Children's Health Insurance Program fee-for-service and managed care plans from 10 states within all geographic regions of the United States in 2014. We required continuous enrollment because the database does not contain pharmacy claims that could have occurred during enrollment gaps. Neonates were excluded because of their unique enrollment and health care attributes. This study of deidentified data was exempt from review by the Colorado Multiple Institutional Review Board.

Annual Cumulative Number of Unique CMs

Children were classified into 5 groups of CM use based on their annual number of unique CMs: no medications, 1 medication, 2 to 4 medications, 5 to 9 medications, and ≥ 10 medications. To provide the most comprehensive description of CM use, we included all paid medication claims, including those for over-the-counter medications. CM was defined by using a previously established and commonly used method of relying on medication claims from existing pharmacoepidemiology studies: a filled ≥ 30 -day prescription with ≥ 2 refills for the same generic drug at any time during the study period.⁴ We excluded the following items from medication counts: dental agents, devices and nondrug items, diagnostic agents, nutrition ingredients, and vaccines and toxoids.¹⁸

Classification of Medications

Medications were classified by using the American Hospital Formulary Service Classification Compilation as recorded in the 2008 *Red Book*.¹⁹ Three levels of classification were available, ranging from the highest-level aggregation "therapeutic group" (eg, central nervous system agent) to "therapeutic class" (eg, amphetamine stimulant) to "generic drug name" (eg, methylphenidate hydrochloride).

Demographics and Clinical Characteristics

We reported demographic characteristics, including age, sex, race and/or ethnicity, and Medicaid eligibility. We identified chronic conditions in 2013–2014 on the basis of *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis codes using (1) the Agency for Healthcare Research and Quality's Chronic Condition Indicator system to identify chronic conditions of

any complexity and to count the number of organ systems affected by multiple chronic conditions²⁰ and (2) the CCC system version 2 to identify children with CCCs known to be associated with high morbidity and resource use.²¹

Health Care Spending and Resource Use

Health care spending and use was assessed by using the number of CMs for 7 mutually exclusive service groupings: primary care, outpatient specialty, emergency department (ED), inpatient, mental health (inpatient and outpatient), pharmacy, and laboratory and/or radiographic testing.²² We reported the total spending, the median per-member per-year (PMPY) spending, and the percentage using each service associated with the number of CMs.

Statistical Analysis

We used descriptive statistics to describe demographics and clinical characteristics of the study population, their annual CM use, and the most common CMs taken by the subjects. We used χ^2 tests to compare categorical variables of interest across groups of CM use and Cochran-Armitage tests to assess trends between categorical predictor variables of interest and ordered outcomes of CM groups. Analyses were performed by using SAS 9.4 (SAS Institute, Inc, Cary, NC), and *P* values <.001 were considered statistically significant because of the large sample size.

RESULTS

CM Use

Of 4 594 061 children, 18.8% used CMs (Fig 1). Of CM users, 52.2% used 1 CM, 40.3% used 2 to 4 CMs, 7.0% used 5 to 9 CMs, and 0.5% used ≥ 10 CMs. At the highest-level medication classification, the central nervous system therapeutic group (eg, antidepressants, antipsychotics,

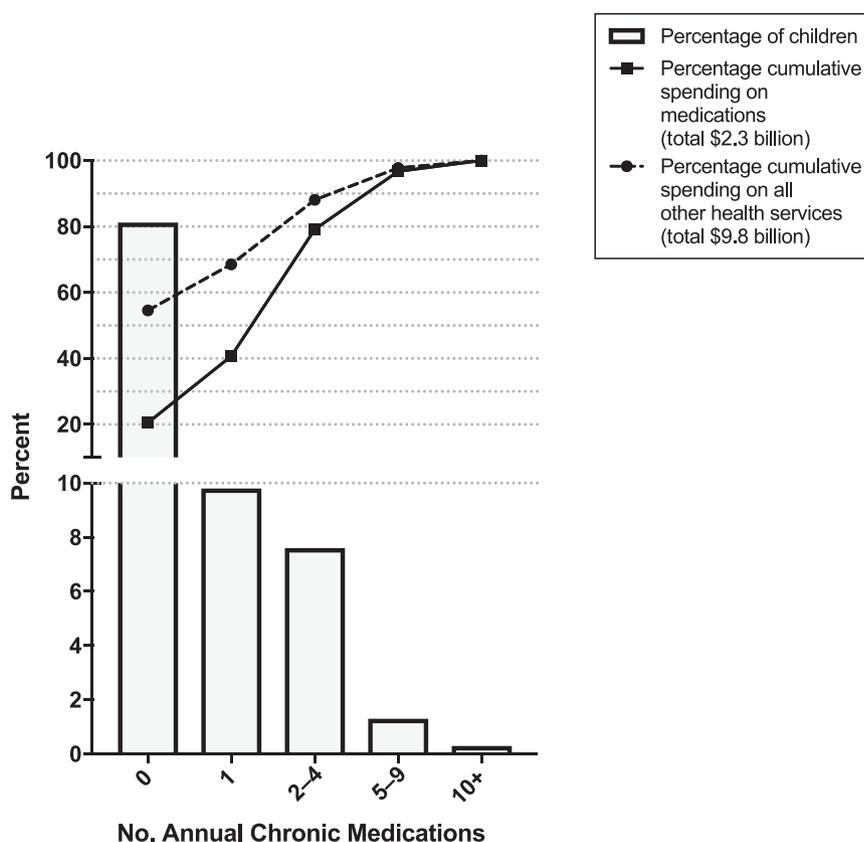


FIGURE 1

Prevalence of CM use and associated health care spending in children insured by Medicaid. CM use was defined as a dispensed ≥ 30 -day prescription with ≥ 2 dispensed refills. The shaded bars represent the percentage of all children in each level of CM use. The dashed line represents the cumulative percentage of all pharmacy spending. The continuous line represents the cumulative percentage of all other nonpharmacy health services spending (eg, inpatient, ED, and outpatient medical care; laboratory and/or radiographic testing; home health; durable medical equipment; and therapies). For example, the ~1% of children who use ≥ 5 CMs (the 5–9 medication group and 10+ medication group) account for 20% of all pharmacy spending and 12% of spending on all other health services.

stimulants, antiepileptic medications) was the most common group, comprising 28.9% of all CMs. The 10 most common therapeutic classes (of 197 total classes) accounted for 70.6% of all CMs; amphetamine stimulants (eg, methylphenidate), antihistamines (eg, cetirizine), and hypotensive agents (eg, clonidine, presumably used mostly for treatment of attention-deficit/hyperactivity disorder) were the 3 most common CMs (Table 1).

As the number of CMs increased, the diversity of medications increased. Whereas amphetamine stimulants and antihistamines accounted for 48.0% of all CMs for children using

only 1 CM, no single medication classes in the ≥ 10 -CM group accounted for $\geq 8\%$ of CM use. Additionally, as the number of CMs increased, the CMs accounting for the greatest percentage of CM use also changed. Comparing the group with 1 CM to the group with ≥ 10 CMs, the percentage of children using amphetamine stimulants decreased from 29.0% to 4.0%, whereas the percentage of children using anticonvulsants increased from 2.3% to 7.1%. Other medications with known potential for adverse effects (eg, hypotensive agents, antidepressants, and antipsychotics) also increased in children with higher numbers of CMs.²³

TABLE 1 Most Common CM Classes Used in Children Insured by Medicaid

Medication Class	Most Common Medication Example in Class	No. CMs Used by Medication Class ^a , n (%)	No. CMs Used ^b			
			1	2–4	5–9	10+
		n = 1 657 322	n = 452 234	n = 848 776	n = 315 500	n = 40 812
Stimulants, amphetamines	Methylphenidate	303 252 (17.2)	29.0	16.6	9.3	4.0
Antihistamines	Cetirizine	227 707 (12.9)	18.0	13.2	10.1	6.7
Hypotensive agents	Clonidine	118 793 (6.7)	2.3	9.6	7.8	4.7
Sympathomimetics	Albuterol	111 863 (6.3)	8.4	6.5	5.4	4.0
Leukotriene modifiers	Montelukast	101 569 (5.8)	4.5	7.0	6.4	4.1
Adrenals	Budesonide	97 956 (5.6)	3.6	7.0	6.5	5.3
Antidepressants	Sertraline	91 286 (5.2)	3.3	6.1	7.2	5.0
Anti-inflammatory agents ^c	Fluticasone	69 669 (3.9)	2.3	4.8	5.3	4.0
Antipsychotics	Risperidone	66 907 (3.8)	1.0	4.7	6.6	4.3
Anticonvulsants	Levetiracetam	57 219 (3.5)	2.3	3.5	6.0	7.1

—, not applicable.

^a CM use was defined as a dispensed ≥ 30 -d prescription with ≥ 2 dispensed refills.

^b Shown are percentages of total CMs used within each grouping (eg, 29.0% of CM use in children with 1 total CM was for the amphetamine and stimulants medication class).

^c Restricted to anti-inflammatory agents of the eyes, ears, nose, and throat.

Demographic Characteristics by Number of CMs

Older age was significantly associated with higher numbers of CMs (Table 2). For example, the percentage of children with ≥ 2 CMs increased from 3.3% in 1- to 4-year-olds to 12.9% in 16- to 18-year-olds

($P < .001$). CM use also varied by race and/or ethnicity, with a higher rate of subjects with ≥ 2 CMs being observed in non-Hispanic white (10.6%) compared with non-Hispanic African American (7.5%) and Hispanic (4.6%) races and/or ethnicities ($P < .001$).

Clinical Characteristics by Number of CMs

Most (84.0%) children identified on the basis of claims data with a chronic condition of any complexity used no CMs (68.2%) or only 1 CM (15.8%). For some chronic conditions, the majority of patients used CMs and

TABLE 2 Characteristics Associated With CM Use in Children Insured by Medicaid, N = 4 954 061

Characteristics	Overall	No. CMs Used ^{a,b}				
		0	1	2–4	5–9	10+
All subjects, %	100	81.1	9.8	7.6	1.4	0.1
Demographic characteristics, %						
Age, y						
1–4	26.6	89.3	7.4	3.0	0.3	<0.1
5–9	32.0	81.4	9.8	7.7	1.1	0.1
10–15	32.2	75.9	11.4	10.5	2.1	0.1
16–18	9.2	75.4	11.6	10.3	2.4	0.2
Race and/or ethnicity						
Non-Hispanic white	47.4	78.5	10.9	8.9	1.6	0.1
Non-Hispanic African American	33.1	83.3	9.2	6.5	1.0	0.1
Hispanic	8.8	88.5	6.9	4.1	0.5	<0.1
Other	10.7	80.1	9.6	8.4	1.8	<0.2
Sex						
Male	51.2	78.7	10.7	8.9	1.6	0.1
Female	48.8	83.7	8.9	6.2	1.0	0.1
Medicaid eligibility						
Disability	3.0	50.7	15.8	24.2	8.4	1.0
Other	97.0	82.1	9.7	7.1	1.1	0.1
Medicaid plan						
Fee for service	29.3	79.2	10.2	8.6	1.8	0.2
Managed care	70.7	82.0	9.7	7.2	1.1	0.1
Clinical characteristics						
Chronic conditions						
None	46.8	95.9	3.1	1.0	0.0	0.0
Any	53.2	68.2	15.8	13.4	2.4	0.2
CCC	5.6	55.6	16.8	19.8	6.8	1.0

^a $P < .001$ for all trends in each characteristic across the number of CM use.

^b CM use was defined as a dispensed ≥ 30 -d prescription with ≥ 2 dispensed refills.

frequently used multiple CMs (eg, immunologic, endocrine, renal, and neurologic), whereas for other conditions (eg, respiratory, musculoskeletal, and dermatologic), the use of multiple CMs was less common (Fig 2). For children with immunologic conditions, 17.6% used 1 CM, 30.9% used 2 to 4 CMs, 15.7% used 5 to 9 CMs, and 3.9% used ≥ 10 CMs. In comparison, for children with a dermatologic chronic condition, 15.3% used 1 CM, 12.4% used 2 to 4 CMs, 2.5% used 5 to 9 CMs, and 0.2% used ≥ 10 CMs. For subjects with multiple chronic conditions of any complexity, the use of ≥ 5 CMs increased from 0.7% for those with 1 chronic condition to 34.1% for those with ≥ 6 chronic conditions.

Most (72.4%) of the subset of children identified on the basis of claims data with a CCC had no (55.6%) or only 1 (16.8%) CM. For some CCCs, the majority of patients used CMs and frequently used multiple CMs (eg, transplant, technology assistance, respiratory, gastrointestinal, and neuromuscular), whereas for other CCCs (eg, cardiac and congenital and/or genetic), the use of multiple CMs was less common (Fig 2). For children with technology assistance, 15.1% used 1 CM, 27.2% used 2 to 4 CMs, 19.3% used 5 to 9 CMs, and 5.7% used ≥ 10 CMs. In comparison, of children with a congenital or genetic CCC, 15.9% used 1 CM, 17.8% used 2 to

4 CMs, 6.5% used 5 to 9 CMs, and 1.2% used ≥ 10 CMs. For subjects with multiple CCCs, the use of ≥ 5 CMs rose from 5.3% for those with 1 chronic condition to 36.9% for those with ≥ 4 CCCs.

Pharmacy Spending by Number of CMs

Of the total \$12.1 billion spent by Medicaid on the entire study population, pharmacy comprised the costliest health service category (\$2.3 billion; 18.7%), which exceeded spending on inpatient (\$2.0 billion; 16.7%), ED (\$0.9 billion; 7.1%), and primary care services (\$1.2 billion; 10.2%). The majority (59.3%) of pharmacy spending was attributable to the 7.6% of subjects with 2 to 4 CMs (38.6% of the pharmacy spending) and the 1.2% of total subjects with ≥ 5 CMs (20.7% of the pharmacy spending; Fig 1). Median annual pharmacy PMPY spending increased significantly with higher numbers of CMs, from \$21 for no CM (IQR: \$0–\$107) to \$9892 (IQR: \$6081–\$17 357) for ≥ 10 CMs (Table 3). For those with any CM use, 73.4% of pharmacy spending was attributed to chronic versus acute medications.

Total Health Care Resource Use and Spending by Number of CMs

The median annual total PMPY spending across the care continuum per subject increased significantly with higher numbers of CMs, from \$824 for no CMs (IQR: \$351–\$1616) to \$32 460 (IQR: \$15 090–\$86 696) for ≥ 10 CMs (Table 3). The percentages of subjects using each type of evaluated health service increased significantly with higher numbers of CMs. Significant trends were observed from 0 to ≥ 10 CMs for increased use of ED care (32.1% to 56.2%), inpatient care (2.3% to 36.7%), home health (0.3% to 15.9%), and durable medical equipment (10.4% to 51.2%; $P < .001$ for all).

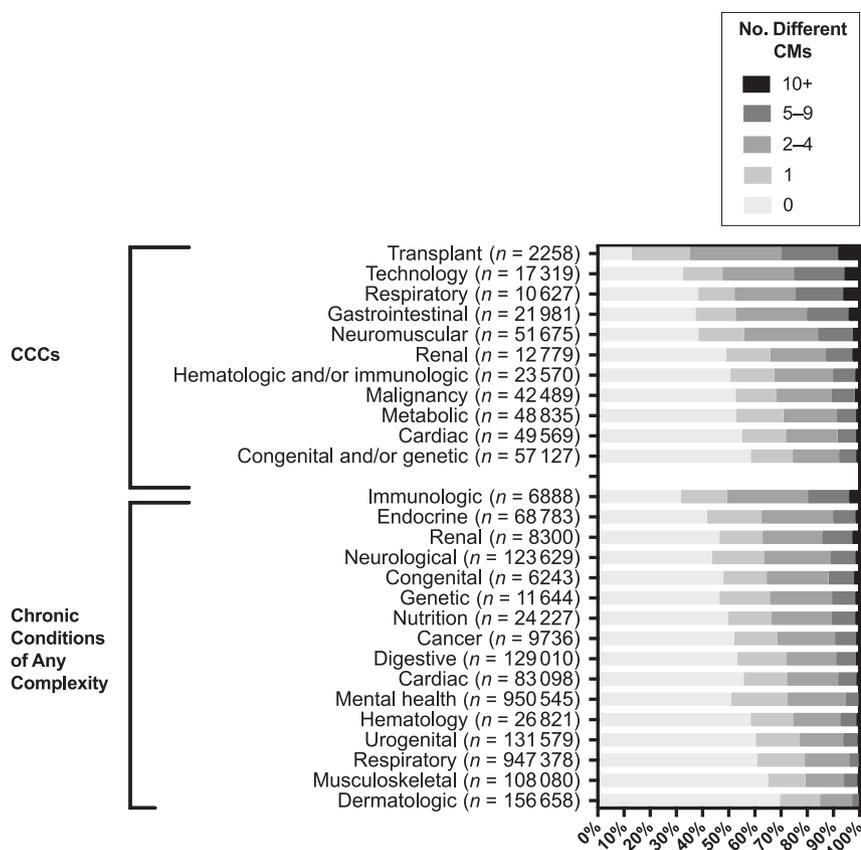


FIGURE 2 Chronic conditions associated with CM use in children insured by Medicaid. This figure reveals the distribution of the number of CMs used by children with specific chronic conditions and CCCs. For example, in children who rely on technology assistance, 15% used 1 CM, 27% used 2 to 4 CMs, 19% used 5 to 9 CMs, and 6% used >10 CMs. CM exposure was defined as a dispensed >30 -day prescription with >2 dispensed refills. Chronic conditions of any complexity were identified with ICD-9-CM codes from the Agency for Healthcare Research and Quality Chronic Condition Indicator system. CCCs were identified from ICD-9-CM codes from the Feudtner and et al²¹ system (version 2).

TABLE 3 Health Resource Use and Spending Associated With CM Use in Children Insured by Medicaid

Characteristics	Overall	No. CMs Used ^{a,b}				
		0	1	2–4	5–9	10+
Health care spending						
Total (including pharmacy), \$, median (IQR)	1044 (446–2258)	824 (351–1616)	2250 (1329–3808)	4059 (2432–7237)	9588 (5543–19 820)	32 461 (15 090–86 697)
Pharmacy only, \$, median (IQR)	46 (0–239)	21 (0–107)	507 (199–1108)	1529 (736–2690)	3945 (2413–6760)	9892 (6081–17 357)
Percentage of pharmacy attributed to CMs	58.4	0.0	64.2	75.7	79.0	72.7
Health service use (% of all children using each service) ^c						
Inpatient	3.0	2.3	4.3	6.9	16.3	36.7
ED	33.7	32.1	39.1	41.0	47.6	56.2
Durable medical equipment	12.3	10.4	17.6	22.5	32.0	51.2
Home health	0.5	0.3	0.7	1.3	4.2	15.9
Primary care	73.0	70.4	84.1	83.9	87.1	90.6
Outpatient specialty	54.3	50.5	67.0	72.6	82.9	93.7
Laboratory and/or radiographic testing	59.1	55.6	71.7	74.6	83.9	93.3
Therapy	11.7	9.4	18.5	22.8	33.6	54.5

^a CM use was defined as a dispensed ≥ 30 -d prescription with ≥ 2 dispensed refills.

^b $P < .001$ for trends in each characteristic across number of CM use.

^c Health services are not mutually exclusive (ie, column percentages sum to $> 100\%$).

DISCUSSION

With nearly 1 in 5 children using a CM, of whom approximately half use multiple CMs, medication expenditures comprised $\sim 20\%$ of total Medicaid spending, and the use of multiple CMs correlated with increased health care resource use. The most prevalent CMs across all children were central nervous system drugs, which are often implicated in studies of potential drug-drug interactions.²⁴ Additionally, the use of other medications with known potential for adverse effects (eg, hypotensive agents) increased in children with higher numbers of CMs.²³ Children with the highest number of CMs included those with immunologic, renal, and neurologic disorders; organ transplant; and/or assistance with medical technology. Health care resource use, including ED and hospital visits, and total health care spending increased substantially with higher numbers of CMs.

Our findings on the prevalence and types of CM use compare and contrast with the limited but emerging literature on CM use in children. Comparable with our results, authors of a recent national study reported that 22% of US children receive any medication annually, and 9% receive

≥ 2 medications; they did not distinguish between acute medications and CMs.² Previous studies of children have also revealed that amphetamine stimulants and antidepressants are among the most commonly used type of CM in children.^{25,26} However, a substantially higher prevalence of children used those medications in our study. In a study of commercially insured children, the prevalence of stimulant medication use was 3% compared with 17% in our study of children insured by Medicaid.²⁵ Relatedly, compared with medication findings from the NHANES, we found threefold and fourfold increases in the use of antipsychotic and anticonvulsant medications in children with Medicaid, respectively.²⁶ These differences could indicate that children insured by Medicaid may have a higher penetrance and/or severity of chronic disease that necessitates greater use of medications.

To that end, our findings suggest that counting the number of CMs may be a simple, straightforward, and helpful method to identify and describe populations of children and to understand the scope of their health care needs and resource use. To our knowledge, most pediatric population health methods and efforts do not typically use CMs for those

activities.^{20,21,27–29} Rather, they rely predominately on information about chronic diagnoses. The use of CMs is important to consider, especially because many children in the current study with CCC diagnoses did not use any CMs. For example, 40% of children with a neuromuscular CCC, including cerebral palsy, did not use a CM. These findings suggest that there is substantial variation in CM use within the most complex pediatric populations that are typically targeted for case management interventions. CM use could be leveraged as an independent case-mix adjuster of medical complexity, increased health resource use, and pharmacovigilance needs in children.

For children with identified CM use, to maximize medication efficacy and safety and minimize associated costs, it is imperative to understand the appropriateness of prescribing practices for specific CMs. Is a child receiving the right medication for the right reason? Although administrative claims data are not designed to answer this question, they provide a population-level perspective to identify patterns of drug use requiring further investigation. In this study, clonidine use was substantial across all levels of CM use. Although clonidine is approved by the Food and Drug

Administration for the treatment of attention-deficit/hyperactivity disorder, clonidine is frequently used off label to treat neuroirritability and behavioral and sleep issues in children with neurodevelopmental disorders.³⁰ State Medicaid programs may find it useful to partner with local medical and pharmacy-based clinicians to assess prescribing practices for specific medications, such as clonidine, that are used off label or without significant pediatric-specific evidence.^{31,32} This type of assessment is critical to conduct ahead of implementing prescribing policies (eg, restricted formularies or limitations on the number of refills) that could interfere with children's access to essential medications and adversely affect the health of children.

Finally, improved pediatric pharmacovigilance is needed to identify downstream consequences of CM use, especially for children with the highest numbers of CMs. Although a small population, these children accounted for a substantial percentage of pharmacy spending and total health care spending. Moreover, they had the highest rates of ED and inpatient hospital use of all children. In our clinical experience, these children often receive insufficient medication management characterized by uncoordinated, fragmented prescribing practices across multiple providers (eg, primary care and specialists) and settings of care. Additionally, providers without long-term continuity of care (eg, some ED clinicians and hospitalists) may prescribe new medications for these children. It is important to optimize the organization, roles, and responsibilities of clinicians who prescribe medications to children who are already on high numbers of CMs. Models of comanaged and integrated care between primary care providers, specialists, and pharmacists have shown promise in delivering high-quality prescribing and monitoring of CMs for adults.³³ It remains unknown how much these

models have penetrated pediatric health care systems.

Our results must be considered in the context of several limitations. First, because some Medicaid enrollees may have supplemental commercial insurance or pay for certain prescriptions and over-the-counter medications out of pocket, we may have underestimated CM use. Accordingly, our findings generalize best to children with Medicaid-only insurance and may not generalize as well to commercially insured children. Second, a pharmacy claim indicates that a prescription was dispensed but does not specify actual use. However, the definition of a CM requires ≥ 2 refills, indicating that a CM was likely being used. Third, we studied annual cumulative exposure to CMs and not concurrent use.³⁴ This limited our ability to (1) determine if medication switching (eg, cetirizine changed to loratadine) versus add-on therapy contributed to increased CM counts and (2) perform analyses of potential drug-drug interactions. Fourth, chronic conditions and CCCs were identified from claims-based diagnosis codes without validation of actual disease, and these classification systems may have a wide range of sensitivity and specificity across different data sources. However, our percentages of CCCs are consistent with previous Medicaid studies using these classification systems.³⁵ Finally, the reported rates and trends of therapeutic medication groupings may be influenced by off-label use (eg, propranolol for migraine prophylaxis).

Nevertheless, our findings advance knowledge about CM use in children. The frequency and associated costs of CM use in children with Medicaid are substantial. Not all children with chronic conditions (including multiple chronic conditions and CCCs) use CMs. Increased numbers of CM use correlate strongly with increased health care resource use and spending. To best inform the development of local, state, and federal pharmacovigilance efforts, we must advance several aspects of pharmacotherapy. First, we must

understand the best medication choices, optimal dosing schedules, and monitoring parameters for children with CM use. This includes improving our limited knowledge about the interactions of multiple drugs and their risks, particularly for medications whose mechanisms of action have known or postulated effects on other medications or direct effects on pediatric physiology. The Food and Drug Administration should require sponsors to look at the use of multiple medications across the pediatric age span to discern drug-drug interactions and subsequent effects on, for example, children's developing central nervous systems, immune systems, or even bone growth.³⁶ Second, we must carefully evaluate potential strategies to manage CM use in at-risk children. Finally, we must assess the impact of these strategies on clinical outcomes, health care use, and the families and caregivers who administer complex medication regimens.^{5,37} Together, these efforts will ensure the safest and best practices for CM use in children.

CONCLUSIONS

One in 5 US children enrolled in Medicaid are exposed to ≥ 1 CMs annually, and a smaller but more vulnerable group of children are exposed to significant chronic polypharmacy with unclear risks. CM use in children should be highly important to health care systems, payers, and policy makers as they strategize how to provide safe, evidence-based, and cost-effective pharmaceutical care to children.

ABBREVIATIONS

CCC: complex chronic condition
CM: chronic medication
ED: emergency department
ICD-9-CM: *International Classification of Diseases, Ninth Revision, Clinical Modification*
IQR: interquartile range
PMPY: per member per year

Dr Feinstein conceptualized and designed the study, analyzed and interpreted the data, and drafted the initial manuscript; Drs Berry and Hall conceptualized and designed the study, analyzed and interpreted the data, and revised the manuscript; Drs Agrawal, Antoon, Azuine, Cohen, Collier, DeCoursey, Flores, Goodman, Gaur, Houtrow, Kuo, and Thomson participated in the concept and design of the study, analyzed and interpreted the data, and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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