Outpatient Pharmacy Expenditures for Children With Serious Chronic Illness in California, 2010-2012

Children with serious chronic conditions are increasingly likely to survive infancy, intensifying demands on health care delivery. Medication is one driver of their health care costs. High-cost drugs threaten cost-containment efforts. We analyzed expenditures for outpatient pharmacy products used by publicly insured children with serious chronic illness during 3 years.

Methods | A retrospective analysis of paid claims for children (ages, 0-21 years) was performed using the California Children’s Services (CCS) paid claims data set (2010-2012). Funded partly by Title V of the Social Security Act, the CCS provides insurance coverage, care coordination, and a regionalized system of pediatric specialty care facilities for approximately 180,000 publicly insured children with serious chronic illness. The state defines the range of eligible medical conditions.

The data set includes age, sex, race/ethnicity, county of residence, enrollment dates, primary and secondary eligible diagnoses, claim diagnoses, and procedures for every enrollee; however, it includes full-capture reimbursement information only for fee-for-service enrollees. Approximately 30% of children are enrolled through fee-for-service care and 70% through managed care. This study included children enrolled through fee-for-service care for at least 6 continuous months.

The main outcome was total paid amount for outpatient pharmacy products dispensed. All products identified by the CCS as outpatient pharmacy products and with a National Drug Code or Healthcare Common Procedure Coding System code were included. Medication administration expenditures were excluded. Administrators from the CCS validated a subset of claims, including lowest expenditure quartile claims. Pharmacy products were classified using the American Hospital Formulary System Pharmacologic-Therapeutic Classification hierarchy. All unique pharmacy paid claims were summed for each child; the mean and median per-child expenditures over the 3-year period were calculated and reported with standard deviation and interquartile range (IQR), respectively. Each medication class’s mean per-child expenditure and percentage of total pharmacy expenditures were reported. The drug contributing most to expenditures was identified, and its annualized per-child expenditure was calculated only for children enrolled throughout the 3-year period.

Institutional review board approval with a consent waiver was received from Stanford University and California’s Department of Health Care Services. Analyses used SAS/STAT version 9.3 software (SAS Institute Inc).

Results | This analysis examined records of 34,330 children (Table 1). Outpatient pharmacy expenditures totaled $475,718,130 (20% of total health care expenditures); per-child pharmacy expenditures ranged from $0.16 to $56,849,034, and mean and median per-child expenditures were $13,857 (SD, $475,718) and $791 (IQR, $127-$5873), respectively.

The product class of blood formation, coagulation, and thrombosis agents accounted for the greatest share (41.9%) of total pharmacy expenditures. All children with an antihemophilic factor claim had antihemophilic factor expenditures. The mean per-child expenditure for antihemophilic factor was $1,343,262. Among children with antihemophilic factor claims and enrolled for all 3 years, the mean and median per-child annualized expenditures

| Table 1. Characteristics of Study Population From California Children’s Services Program Paid Claims Data Set (July 1, 2010-June 30, 2012) |
|-----------------|-----------------|
| Age, mean (SD), y | 9.3 (6.6) |
| Age group, y | |
| <1 | 3715 (10.8) |
| 1-5 | 8889 (25.9) |
| 6-12 | 9073 (26.4) |
| 13-18 | 9021 (26.3) |
| 19-21 | 3632 (10.6) |
| Sex | |
| Male | 18,250 (53.2) |
| Female | 14,684 (42.8) |
| Missing | 1396 (4.0) |
| Race/ethnicity | |
| White | 9169 (26.7) |
| Black | 3208 (9.3) |
| Hispanic | 16,065 (46.8) |
| Other | 4707 (13.7) |
| Unknown | 1181 (3.4) |
| County of residence | |
| Urban | 31,400 (91.5) |
| Rural | 2930 (8.5) |

* Data are expressed as No. (%) unless otherwise indicated.
* Included Asian or Pacific Islander, Alaskan Native or American Indian, Filipino, Amerasian, Chinese, Asian Indian, Japanese, Korean, Samoan, Hawaiian, Guamanian, Laotian, and Vietnamese.
* Urban and rural classifications were designated according to established federal definitions from the US Department of Agriculture (http://www.ers.usda.gov/data-products/rural-urban-continuum-codes.aspx#U-PCC2PCmaz).
were $634 054 (SD, $2 159 355) and $152 280 (IQR, $19 434-$393 000), respectively.

Discussion | Outpatient pharmacy expenditures in this population are significantly driven by antihemophilic factor, which accounted for 40.9% of outpatient pharmacy expenditures but served 0.4% of the cohort. Antihemophilic factor is highly efficacious and essential in caring for children with hemophilia, putting pressure on public programs to seek improved pricing mechanisms for antihemophilic factor and other highly efficacious, high-cost medications.

Examining state-to-state variation may provide insights: CCS’s mean per-child antihemophilic factor annual expenditure ($634 054) significantly surpassed that of North Carolina’s Medicaid program ($233 968 in fiscal year 2012) and Medicaid programs in 10 other states ($148 215 in 2008). However, public programs for children with serious chronic illness vary between states, and care should be taken in making direct program comparisons. Greater transparency of use and costs, and cross-state collaboration, may increase health care value as states revise programs.

Study limitations include lack of clinical data, lack of inpatient pharmacy data, exclusion of children enrolled in managed care, cross-sectional study design, and data spanning only 3 years.

Our study underscores the potential effect of new, expensive but efficacious pharmaceuticals on public insurance programs for children with chronic illness. These findings may inform efforts to enhance value in these programs, particularly as new insurance frameworks, such as accountable care organizations, are considered.

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Maternal Diabetes and Autism in Offspring

To the Editor The Original Investigation by Dr Xiang and colleagues1 showed an association between maternal diabetes diagnosed by 26 weeks’ gestation and autism spectrum disorders (ASD) in offspring. I question whether the analysis should have controlled for a maternal history of comorbidity (diagnosis of cancer and/or heart, lung, kidney, and liver diseases) prior to determining whether maternal preexisting type 2 diabetes was significantly associated with risk of ASD in offspring.

Almost half of the mothers with preexisting type 2 diabetes in this southern California study had been diagnosed as having 1 or more comorbidities, many of which are associated with and often are complications of type 2 diabetes, particularly heart2 and kidney3 diseases. The authors acknowledged that 2 large cohort studies in Canada that did not control for history of comorbidity showed associations between maternal exposure to preexisting type 2 diabetes and ASD in offspring.

When certain comorbidities are common complications of a disease such as diabetes, it is possible that the same disease agent at work in causing these comorbidities may also be responsible for an excess risk of ASD in offspring. In short, preexisting type 2 diabetes may be causing both an increased risk of maternal comorbidities and ASD in offspring. Before the index pregnancy should be controlled for to assess the independent association with maternal glucose exposure. As shown in Table 2, a history of comorbidity prior to the index pregnancy in mothers was associated with a bivariable HR of 1.34 (95% CI, 1.18-1.51) for risk of ASD in offspring. The adjusted HR associated with history of comorbidity was not shown in the article but was 1.31 (95% CI, 1.15-1.49) after adjustment for maternal age, parity, education, household income, race/ethnicity, child sex, and maternal diabetes category at the index pregnancy. Thus, adjustment for maternal diabetes status had little effect on the HR associated with history of comorbidity.

We agree that some of the comorbidities may be complications of preexisting diabetes. However, the fact that adjustment for diabetes status did not reduce the HR associated with history of comorbidity suggests that different pathways other than glucose may be involved. Further investigation would be needed to separate the comorbidities related and unrelated to preexisting diabetes to understand various pathways through which maternal preexisting diabetes may affect ASD risk in offspring.

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Surrogate Decision Making for Patients Without Nuclear Family

To the Editor Dr Cohen and colleagues1 drew attention to potential quality gaps in surrogate decision making for patients, including patients in the Veterans Health Administration (VHA). We would like to point out that both federal regulation governing the VHA2 and VHA policy3 establish a surrogate hierarchy that includes persons outside the nuclear family and authorizes them to make health care decisions on behalf of patients without decisional capacity. Specifically, that hierarchy is: health care agent, legal guard-

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In Reply Mr Zitser raises an important question about whether a history of comorbidity should have been adjusted for in our investigation of intraterine exposure to maternal diabetes during pregnancy and risk of ASD in offspring. We argue that a history of comorbidity should have been adjusted for because the main focus of our study was maternal glucose during pregnancy, with the exposure categorized as preexisting diabetes, gestational diabetes mellitus diagnosed at 26 weeks’ gestation or less or diagnosed at more than 26 weeks’ gestation, or no diabetes. As shown in Table 2 in the article, compared with unexposed children, the crude hazard ratio (HR) for ASD in children whose mothers had preexisting diabetes (HR, 1.59) was almost identical to the crude HR in children whose mothers had gestational diabetes diagnosed at 26 weeks’ gestation or less (HR, 1.63).

Our comorbidity variable included any diagnosis of heart, lung, kidney, or liver diseases or cancer prior to the index pregnancy. Potential confounders and other risk factors that existed before the index pregnancy should be controlled for to assess the independent association with maternal glucose exposure. As shown in Table 2, a history of comorbidity prior to the index pregnancy in mothers was associated with a bivariable HR of 1.34 (95% CI, 1.18-1.51) for risk of ASD in offspring. The adjusted HR associated with history of comorbidity was not shown in the article but was 1.31 (95% CI, 1.15-1.49) after adjustment for maternal age, parity, education, household income, race/ethnicity, child sex, and maternal diabetes category at the index pregnancy. Thus, adjustment for maternal diabetes status had little effect on the HR associated with history of comorbidity.

We agree that some of the comorbidities may be complications of preexisting diabetes. However, the fact that adjustment for diabetes status did not reduce the HR associated with history of comorbidity suggests that different pathways other than glucose may be involved. Further investigation would be needed to separate the comorbidities related and unrelated to preexisting diabetes to understand various pathways through which maternal preexisting diabetes may affect ASD risk in offspring.

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