Characterizing Age-Related Patterns in Healthcare Costs and Utilization Among People Living With Angelman Syndrome in the United States

Farah Pathan, PHD, Komodo Health, New York, NY; Lynne M. Bird, MD, Rady Children's Hospital, San Diego, CA; Xinshuo Ma, MS, Komodo Health, New York, NY; Xiyuan Wu, MS, Komodo Health, New York, NY; Kyle Householder, PhD, Ionis Pharmaceuticals, Carlsbad, CA; Montserrat Vera-Llonch, MS, Ionis Pharmaceuticals, Carlsbad, CA; Steven M. Kymes, MHA, PhD, Ionis Pharmaceuticals, Carlsbad, CA

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Introduction

Angelman syndrome (AS) is a rare genetic neurodevelopmental disorder caused by loss of function of the ubiquitin protein ligase E3A (*UBE3A*).[1] The condition affects approximately 1 in 12,000–20,000 live births and is characterized by developmental delay, severe speech impairment, movement disorders, seizures, and ataxia.[2,3]

- People living with AS have high rates of hospitalization and surgery early in life, with substantial physical, social, and financial impacts for affected patients and their families and caregivers.[4–7]
- While prior studies have characterized healthcare resource utilization (HCRU) in AS, particularly in the pediatric population,[5,8,9] age-stratified cost data remains limited in the U.S.
- As individuals with AS survive into adulthood and potential disease-modifying therapies enter clinical development, an understanding of the economic burden across age groups is necessary.

Objective

- To assess healthcare resource utilization and costs in pediatric and adult patients with AS between 2021 and 2024

Methods

- **A retrospective observational study** was conducted using de-identified administrative claims from Komodo Health.
- **Komodo Research Dataset (KRD):** Composed of administrative data and claims, KRD captures routinely collected health services utilization records and expenditures for over 330 million de-identified unique individuals in the U.S. Native to HIPAA-compliant, privacy-preserving tokens, KRD offers extended patient-level observations of medical encounters and outpatient pharmacy dispensings via linkage across medical and pharmacy insurance plans.
- Patients with AS were identified using International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) code Q93.51. The following criteria were implemented:
  - At least 2 insurance claims ≥30 days apart between January 1, 2021, and December 31, 2024
  - Continuous enrollment throughout the calendar year, with ≤45-day gaps in medical and pharmacy plans allowed
  - Index visit was defined as the first visit in which the patient received a diagnosis of AS. In each subsequent year following the index visit, patients were only required to have at least 1 diagnosis claim
- Four overlapping cohorts were defined by the year of the index visit for AS (Table 1).
  - Based on age at index visit, patients were stratified into pediatric (<18 years) and adult (≥18 years)
- **Study outcomes**
  - Patient characteristics, HCRU, and direct healthcare costs were reported for each calendar year
  - Healthcare costs were assessed per patient per year across five categories: Inpatient, Outpatient, Emergency Room (ER), Other (such as home health [HH], durable medical equipment [DME], and ambulance), and Pharmacy
    - All costs were adjusted to 2024 U.S. dollars using the Consumer Price Index for medical care
  - Claims for all health services, regardless of diagnosis, were included in the estimate of cost of care and HCRU

Results

Table 1. Cohort Sizes

Year	All	Pediatric	Adult
2021	1,084	554	525
2022	1,080	528	548
2023	956	466	486
2024	880	419	459

- **Demographics and Clinical Characteristics**
  - Between 2021–2024, pediatric patients (mean and median age ~10 years) consistently comprised approximately half of the AS cohort, while adults (mean age ~29 years and median age ~27 years) accounted for the remainder; Medicaid was the dominant payer in both groups (~55–61%) [Tables 1 and 2].
  - Seizures were highly prevalent and stable in both age groups across all years (~74–80%); pediatric patients had higher rates of respiratory complications (49% vs. 22% in adults, 2024); gastrointestinal issues were similarly common in both groups (~44–49%; 2024) [Figure 1], and increased in adults over time.

Table 2. Demographic Characteristics of People With AS, 2021 and 2024

Category	Pediatric (<18 years)		Adult (≥18 years)	
	2021 N=554	2024 N=419	2021 N=525	2024 N=459
Sex, n (%)				
Female	279 (50.4%)	193 (46.1%)	258 (49.1%)	232 (50.5%)
Male	269 (48.6%)	220 (52.5%)	262 (49.9%)	224 (48.8%)
Unknown/missing	6 (1.1%)	6 (1.4%)	5 (1.0%)	3 (0.7%)
Race, n (%)				
White	278 (50.2%)	200 (47.7%)	340 (64.8%)	299 (65.1%)
African-American	55 (9.9%)	51 (12.2%)	31 (5.9%)	26 (5.7%)
Asian/Pacific Islander	12 (2.2%)	14 (3.3%)	12 (2.3%)	14 (3.1%)
Other	20 (3.6%)	15 (3.6%)	22 (4.2%)	16 (3.5%)
Unknown/missing	189 (34.1%)	139 (33.2%)	120 (22.9%)	104 (22.7%)
Region, n (%)				
Northeast or Unknown	127 (22.9%)	97 (23.2%)	139 (26.5%)	128 (27.9%)
Midwest	182 (32.9%)	132 (31.5%)	152 (29.0%)	123 (26.8%)
West	117 (21.1%)	90 (21.5%)	124 (23.6%)	111 (24.2%)
South	128 (23.1%)	100 (23.9%)	110 (21.0%)	97 (21.1%)
Payer, n (%)				
Commercial	189 (34.1%)	160 (38.2%)	103 (19.6%)	99 (21.6%)
Medicare	5 (0.9%)	4 (1.0%)	111 (21.1%)	93 (20.3%)
Medicaid	340 (61.4%)	246 (58.7%)	294 (56.0%)	252 (54.9%)
Unknown/missing	20 (3.6%)	9 (2.1%)	17 (3.2%)	15 (3.3%)

Figure 1. Comorbidities by Age Group (2024)

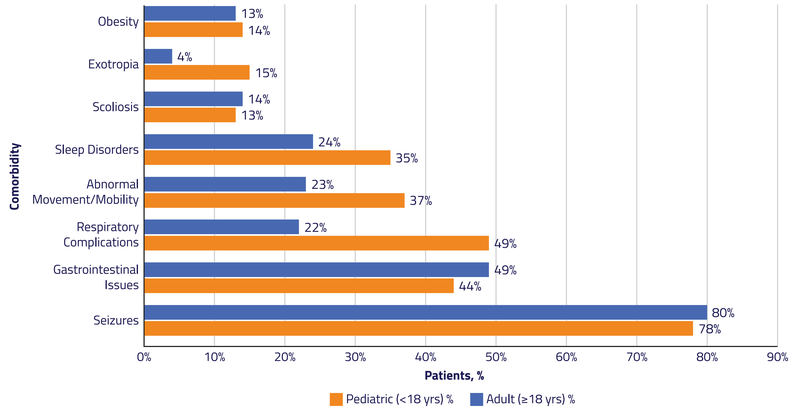


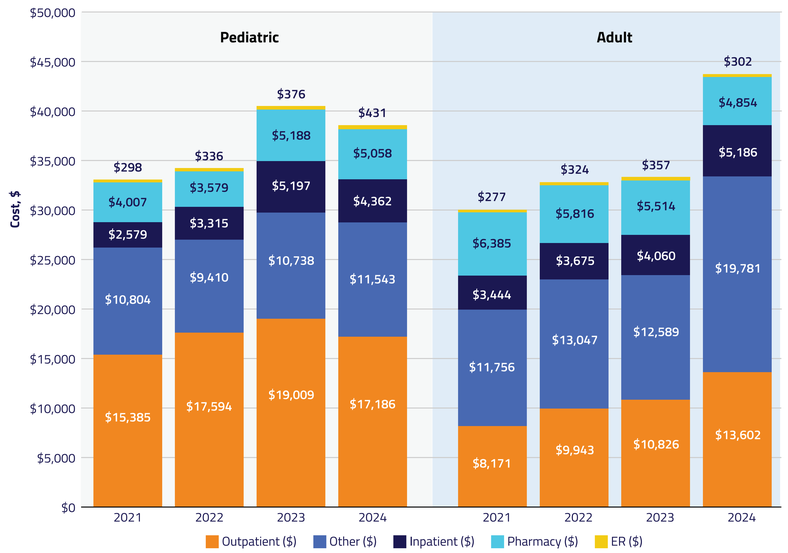
Table 3. HCRU in Patients With AS, 2021 and 2024

Category	Pediatric (<18 years)		Adult (≥18 years)	
	2021 N=554	2024 N=419	2021 N=525	2024 N=459
Number of patients with all-cause HCRU, n (%)				
Inpatient	60 (10.8%)	61 (14.6%)	53 (10.1%)	42 (9.2%)
ER —> Inpatient	36 (6.5%)	42 (10.0%)	38 (7.2%)	37 (8.1%)
Outpatient	551 (99.5%)	416 (99.3%)	522 (99.4%)	456 (99.3%)
ER	198 (35.7%)	181 (43.2%)	165 (31.4%)	142 (30.9%)
Other	434 (78.3%)	331 (79.0%)	386 (73.5%)	362 (78.9%)
Pharmacy	527 (95.1%)	401 (95.7%)	514 (97.9%)	441 (96.1%)
Total all-cause HCRU per patient				
Mean (SD)	81.2 (97.0)	88.5 (102.1)	56.2 (96.9)	94.2 (141.6)
Number of medical visits, mean (SD)				
Inpatient	0.1 (0.5)	0.2 (0.6)	0.1 (0.4)	0.2 (1.1)
Outpatient	47.3 (60.3)	48.0 (57.6)	22.8 (45.3)	37.1 (71.2)
ER	0.7 (1.3)	0.9 (1.5)	0.6 (1.5)	0.7 (1.7)
Other	33.0 (72.1)	39.4 (74.8)	32.7 (77.7)	56.1 (110.6)
HH	26.5 (71.8)	30.5 (73.4)	24.0 (75.3)	44.9 (107.7)
Non-HH	9.3 (16.1)	12.8 (26.2)	11.2 (28.2)	18.1 (49.4)
Pharmacy claims per patient, mean (SD)				
Pharmacy claims	21.4 (18.3)	23.5 (18.7)	28.8 (21.1)	31.3 (24.2)
Inpatient stay metrics				
ICU stays,* n (%)	15 (18.8%)	12 (13.5%)	23 (33.3%)	38 (35.8%)
LOS per inpatient visit (days)	6 (9.4)	5 (5.4)	8 (12.2)	10 (13.1)

ER, emergency room; HCRU, healthcare resource utilization; HH, Home Health; ICU, intensive care unit; SD, standard deviation; LOS, length of stay. ICU stays: % denominator=total inpatient visits.

Figure 2. Mean Annual Total Cost per Patient by Age Group (2021–2024)

Figure 3. Healthcare Cost Drivers by Age Group (2021–2024)



- **Cost of Care**
  - Mean annual costs per person:
    - Pediatrics, $33,072–$38,580 (SD, $59,288–$53,902)
    - Adults, $30,034–$43,726 (SD, $68,611–$86,286)
    - Both cohorts carried substantial mean annual costs,and cost composition differed by age; outpatient services were the primary driver in pediatric patients (~44.5%), while HH and DME dominated in adults (~45.3%) [Figure 3].
- **Utilization of Medical Services**
  - Outpatient care was nearly universal (≥99% of patients annually in both age groups); pediatric patients averaged more outpatient visits per year than adults (~48 vs. ~37 in 2024), which may reflect intensive therapy/specialist management [Table 3].
    - Physical and occupational therapy (PT/OT) ranged from 34% to 36% in pediatrics and 11% to 16% in adults between 2021 and 2024; speech therapy ranged from 43% to 51% in pediatrics and ~12% in adults during the same time frame.
  - ER use rose in pediatric patients (35.7% in 2021 to 43.2% in 2024), with a corresponding increase in ER-to-inpatient escalation in the pediatric group (6.5% to 10.0%); ER use in adults was stable (31.4% to 30.9%).
  - Adults had markedly higher ICU utilization (35.8% of inpatient visits vs. 13.5% of pediatric patients in 2024); adults also averaged nearly 45 HH days per year — nearly 50% more than pediatric patients, potentially highlighting a shift toward complex or community-based care needs as patients age.

Conclusion

- People living with AS face high and sustained healthcare costs regardless of age, reflecting the lifelong, multisystem nature of the condition.
- Composition of care differed markedly: Pediatric patients were characterized by high outpatient visit volumes and therapy use (speech, PT/OT), which may reflect intensive developmental and seizure management, while adults relied heavily on other services including HH/DME, that may signal transition toward community-based and supportive care.
- As disease-modifying therapies for AS advance through clinical development, this real-world cost and utilization data provides a critical baseline for economic modeling, value assessments, and health technology evaluation frameworks.

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Disclosures

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