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Increased delay from initial concern to diagnosis of autism spectrum disorder and associated health care resource utilization and cost among children aged younger than 6 years in the United States

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Plain language summary

This research used health insurance claims from approximately 9,000 children with autism. The time to diagnosis (TTD) was the time between the first noted sign of autism and the diagnosis. In the year before diagnosis, children with longer TTD had more health care visits and added costs than children with shorter TTD. Making the TTD shorter may help cut down costs and health care visits in children with autism.

Implications for managed care pharmacy

Children insured by a commercial, national insurer with a longer time from initial concern to diagnosis of autism spectrum disorder experienced more frequent health care visits and greater medical costs in the year preceding diagnosis vs children with a shorter TTD. Standards-of-care integration of innovative diagnostic tools/procedures that accelerate autism spectrum disorder TTD, as well as coverage policies improving access to such tools/procedures, may help reduce associated costs and health care resource utilization.

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ABSTRACT

BACKGROUND: Prolonged delays between first caregiver concern and autism spectrum disorder (ASD) diagnosis have been reported, but associations between length of time to diagnosis (TTD) and health care resource

utilization (HCRU) and costs have not been studied in a large sample of children with ASD.

OBJECTIVE: To address these informational gaps in the ASD diagnostic pathway.

METHODS: This retrospective, observational, single cohort analysis of Optum's

administrative claims data from January 1, 2011, to December 31, 2020, included commercially insured children who had 2 or more claims for an ASD diagnosis (earliest diagnosis designated as the index date), were between the ages of older than 1.5 years and 6 years or younger at index date, and

were continuously enrolled for up to 48 months before and for 12 months after the index date. Two cohorts (between the ages of older than 1.5 years and 3 years or younger and between the ages of older than 3 years and 6 years or younger at ASD diagnosis) were divided into shorter (less than median) and longer (greater than or equal to median) TTD around each cohort median TTD calculated from the first documented ASD-related concern to the earliest ASD diagnosis, because TTD may vary by age at diagnosis. This exploratory analysis compared all-cause and ASD-related HCRU and costs during a 12-month period preceding ASD diagnosis among children with shorter vs longer TTD.

RESULTS: 8,954 children met selection criteria: 4,205 aged 3 years or younger and 4,749 aged older than 3 years at diagnosis, with median TTD of 9.5 and 22.1 months, respectively. In the year preceding ASD diagnosis, children with longer TTD in both age cohorts experienced a greater number of all-cause and ASD-related health care visits compared with those with shorter TTD (mean and median number of office or home visits were approximately 1.5- and 2-fold greater in longer vs shorter TTD groups; $P < 0.0001$). The mean all-cause medical cost per child in the year preceding ASD diagnosis was approximately 2-fold higher for those with longer vs shorter TTD (\$5,268 vs \$2,525 in the younger and \$5,570 vs \$2,265 in the older cohort; $P < 0.0001$ for both). Mean ASD-related costs were also higher across age cohorts for those with longer vs shorter TTD (\$2,355 vs \$859 in the younger and \$2,351 vs \$1,144 in the older cohort; $P < 0.0001$ for both).

CONCLUSIONS: In the year prior to diagnosis, children with longer TTD experienced more frequent health care visits and greater cost burden in their diagnostic journey compared with children with shorter TTD. Novel diagnostic approaches that could accelerate TTD may reduce costs and HCRU for commercially insured children.

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by core symptoms including deficits in social interaction and communication as well as the presence of restricted and repetitive patterns of behavior, interests, or activities that can persist throughout life.¹ Individuals with ASD often require broad services with significant economic costs. In a recent analysis of a representative sample of US households, annual incremental costs associated with ASD for families ranged from \$3,930 to \$5,621 of direct total costs per child.² With the reported ASD prevalence rates tripling over the past 2 decades in the United States,^{3,4} annual ASD-related cost estimates are forecasted to increase significantly.⁵ In a recent study using forecast models accounting for the historical increase in ASD prevalence in the United States, as well as multiple projection scenarios, total ASD costs were estimated at \$223 billion in 2020 and projected at \$589 billion in 2030 and \$5.54 trillion by 2060.⁶

The mean age of ASD diagnosis in the United States has remained older than 4 years since the Centers for Disease Control and Prevention started their active surveillance of ASD,^{3,4} despite ASD diagnosis being possible as early as age 18 months⁷ and parents noticing or reporting an initial concern between ages 6 and 36 months⁸. This represents an average delay of nearly 3 years between a first caregiver concern and eventual diagnosis.⁹ Diagnostic delays have been associated with parental stress¹⁰ and increased use of psychotropic drugs and therapeutic services.¹¹ However, measurement of ASD-related health care resource utilization (HCRU) and costs have mostly reflected postdiagnosis burden; expenditures have not accounted for the significant delay between a first caregiver and/or health care providers (HCP) concern and ASD diagnosis.² This renders evaluation of HCRU and costs more complex, particularly before children begin elementary school because few studies have been conducted in children aged younger than 6 years. The objectives of this exploratory evaluation are to (1) describe the length of time from initial, HCP-documented, ASD-related concerns to ASD diagnosis among children who were commercial enrollees and aged older than 1.5 to 6 years or younger at the time of ASD diagnosis and (2) compare HCRU and costs descriptively among children with shorter vs longer time to diagnosis (TTD) in the year preceding diagnosis.

Methods

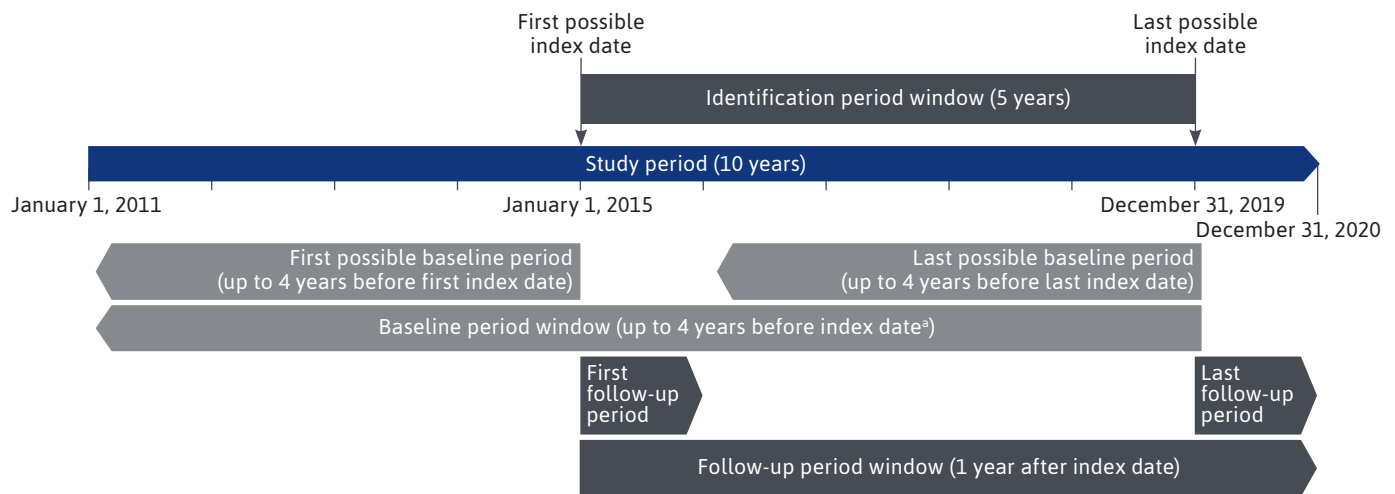
STUDY DESIGN AND DATA SOURCE

This was a retrospective, observational, single cohort evaluation conducted using administrative medical, pharmacy, and enrollment claims data from the Optum de-identified Clinformatics Data Mart Database (2007-2021) for the period of January 1, 2011, to December 31, 2020 (study period) (Figure 1).^{12,13} The Optum Claims Database contains de-identified medical and pharmacy claims data and linked enrollment information for individuals enrolled in commercial and Medicare Advantage health plans across the United States, with representative proportions of US commercially insured and the overall population across sex and age categories. Data were de-identified and accessed in adherence with the Health Insurance Portability and Accountability Act of 1996. The study (Pro00063519) received an institutional review board exemption from Advarra.

PATIENT SELECTION AND STUDY COHORTS

The database was searched for claims data of children (aged >1 to ≤ 18 years) with 2 or more claims of a diagnosis for ASD, irrespective of time between the 2 diagnoses, on all medical claims between January 1, 2015, and December

FIGURE 1 Observation Time Periods



^aThe baseline period (before the index date) had a variable length that was adjusted based on the child’s age at diagnosis of autism spectrum disorder (index date), from a minimum of 1 year for a child aged 1.5 years at index date, 2 years for a child aged 2.5 years at index date, 3 years for a child aged 3.5 years at index date, and to a maximum of 4 years for children of other ages.

31, 2019 (identification period). ASD diagnosis was defined using the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes 299.00, 299.01, 299.80, 299.81, 299.90, and 299.91 or the *ICD-10-CM* codes F84.0, F84.5, F84.8, and F84.9 ([Supplementary Table 1](#), available in online article). The requirement of having 2 or more claims of ASD was chosen to increase the sensitivity of defining children with ASD (proportion of true positives) as described in a commonly used algorithm for analysis of claims databases, which has a positive predictive value of 87.4% (denoting a greater proportion of true positives than true negatives).¹⁴ The index date was the earliest claim of ASD diagnosis to assess HCRU and costs incurred prior to any ASD diagnosis. Included children were between the ages of older than 1.5 years and 6 years or younger at the index date and had continuous medical coverage during a period of up to 4 years before the index date (baseline period, adjusted from 1 to 4 years based on the child’s age at index date) and during 1 year following the index date. Because only the birth year is available in this de-identified claims database, age at diagnosis was estimated by assigning July 1 of the birth year as the birth date and subtracting this date from the date of the earliest ASD diagnostic claim (eg, if the birth year is 2011 and the index date is March 31, 2015, then the age at index is calculated as March 31, 2015–July 1, 2011=3 years and 9 months). This method is comparable to those of studies that used de-identified claims data to

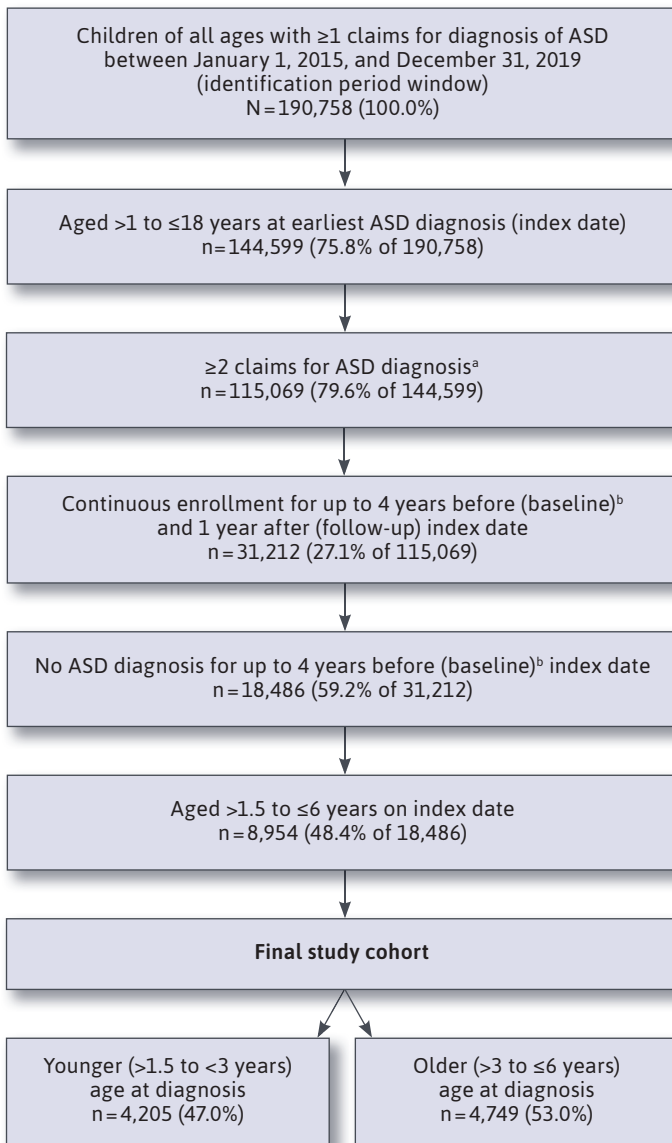
evaluate economic outcomes in young children, which share similar limitations surrounding the definition of age at index event.¹⁵ Children were excluded if they had a diagnosis of ASD during the baseline period (Figure 2).

Two cohorts were created based on age at earliest ASD diagnosis: between the ages of older than 1.5 years and 3 years or younger (younger age at diagnosis) and between the ages of older than 3 years and 6 years or younger (older age at diagnosis). The lower age threshold (1.5 years) was chosen based on the earliest age of recommended screening by the American Academy of Pediatrics¹⁶ and the Centers for Disease Control and Prevention,¹⁷ as well as support from the literature for the earliest age of a most reliable and stable diagnosis.⁷ The 3-year age milestone was designated because it is the eligibility limit for early-start and preschool services, and the 6-year age threshold was selected because it is the mandatory age for entering elementary school with the limitation that school-based services would not be captured in claims data.

CHARACTERISTICS AT INDEX DATE

Demographic characteristics (age, sex, race and ethnicity, and geographic region) and the number and type of HCPs involved in each child’s care were captured on the index date. Other coexisting conditions present at index date were identified with a data-driven approach rather than a prespecified list of conditions by examining all medical

FIGURE 2 Attrition



^aBecause ICD-10-CM codes may be used for payment for ongoing evaluation or ruling out a disease, ≥2 claims for ASD diagnosis were required to increase the sensitivity for identifying children diagnosed with ASD.

^bThe baseline period (before the index date) had a variable length that was adjusted based on the child's age at diagnosis of ASD (index date), from a minimum baseline period of 1 year for a child aged 1.5 years at index date to a maximum of 4 years.

ASD = autism spectrum disorder; ICD-10-CM = International Classification of Diseases, Tenth Revision, Clinical Modification.

claims listed at different times before diagnosis among children diagnosed with ASD. All ICD-9-CM and ICD-10-CM diagnosis codes (from all 25 header diagnosis code positions) were extracted from medical claims at the index date and during the baseline period and sorted by decreasing frequency. Codes reported for at least 250 children, which corresponded to the top 525 codes, were categorized by medical subject matter experts into mutually exclusive categories of codes related to ASD and not related to ASD, as previously documented.^{16,18} Codes related to ASD were further grouped based on signs and symptoms associated with ASD (clinical expertise and health plan claim documentation policies for ASD and developmental disability services) and/or ICD classification into categories of developmental and behavioral disorders and symptoms, including attention-deficit/hyperactivity disorder (ADHD), behavioral concerns, developmental disability, feeding issues, hypersensitivity, neurologic concerns, psychiatric concerns, and speech and language concerns (Supplementary Table 2).¹⁹

EXPOSURE

The TTD was measured in months (30-day increments) for each child during the variable length baseline period from the date of the first documented claim for an ASD-related concern (any of the categories of ASD-related concerns listed above) to the index date, including the index date (same date for ASD-related concern and ASD diagnosis). Children without a documented ASD-related concern were excluded from the TTD evaluation.

Preliminary analyses showed that TTD varied by age at ASD diagnosis, with shorter TTD among children diagnosed at a younger age compared with those diagnosed at an older age. Therefore, rather than choosing a set length of time to differentiate short and long TTD, we used the median TTD for each age cohort. Each cohort was divided into shorter (less than median) and longer (greater than or equal to median) TTD, excluding children who had ASD-related concerns for feeding issues, hypersensitivity, and neurologic concerns from the median TTD calculation because these categories of concern were either nonspecific symptoms (ie, may be attributed to several other diseases) or infrequently present on medical claims. Moreover, using dates of the first documented claim for any of these categories as the starting date to calculate the TTD might overestimate the TTD.

OUTCOMES

Because all children had at least 1 year of baseline period, HCRU and costs were reported from 1 year to the day before the index date among children from each age cohort stratified by shorter and longer TTD. HCRU was reported as the

number of visits to the most commonly identified places of service, including office, home, outpatient hospital, inpatient admissions, and emergency department (ED), based on claims during the prediagnosis year time period. Claims on different dates or claims from different places of service on the same date were considered as separate visits. Costs, including those covered under the insurance plan plus out-of-pocket expenses, were reported as average total medical costs and average medical costs by place of service per child, using standardized costs reflecting current year US dollars. Both all-cause and ASD-related (claims with a diagnosis code related to all categories of ASD-related concerns) HCRU and costs were reported.

ANALYSES

In this exploratory analysis not intended or designed to test specific hypotheses, all variables were summarized descriptively. Numbers and percentages were presented for categorical variables. Means with SDs and medians with IQRs of observed values describe continuous variables. Bivariate comparisons between the 2 groups of shorter vs longer TTD were conducted using the chi-square test for categorical variables and the Mann-Whitney U-test (non-parametric version of two sample t-test) for continuous variables. The significance level was set at $P=0.05$. Data were analyzed using SAS statistical software version 9.4 (SAS Institute).

Results

PATIENT SELECTION

Of 190,758 children identified with at least 1 claim for ASD diagnosis, 8,954 met all the study selection criteria and were between the ages of older than 1.5 years and 6 years or younger at the time of the earliest ASD diagnosis, of whom 4,205 (47%) were between the ages of older than 1.5 years and 3 years or younger and 4,749 (53%) were between the ages of older than 3 years and 6 years or younger at the time of the earliest ASD diagnosis (Figure 2). The majority of children had an initial diagnosis code for autistic disorder (299.00, 299.01, or F84.0) ([Supplementary Table 1](#)).

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS AT TIME OF ASD DIAGNOSIS

Most children were male (78% and 79% in the younger and older cohorts, respectively), the majority of those with race and ethnicity data were White/non-Hispanic, and most were from the South and Northeast regions of the United States (Table 1). In the younger and older cohorts, 54% and 51% of children, respectively, had documented ASD-related conditions at the date of ASD diagnosis, with a predominance of

TABLE 1 Demographic and Clinical Characteristics at Earliest Claim for Diagnosis of ASD Among Younger vs Older Age-at-Diagnosis Cohorts

Characteristic	Younger (>1.5 to ≤3 years) age at diagnosis (n=4,205)	Older (>3 to ≤6 years) age at diagnosis (n=4,749)
Age, years		
Mean (SD)	2.8 (0.5)	4.6 (0.8)
Median (IQR)	2.3 (2.1-2.7)	4.2 (3.5-5.2)
Sex, n (%)		
Female	940 (22.4)	1,007 (21.2)
Male	3,265 (77.7)	3,742 (78.8)
Race and ethnicity, n (%)		
Asian, non-Hispanic	291 (6.9)	263 (5.5)
Black, non-Hispanic	145 (3.5)	159 (3.4)
Hispanic	373 (8.9)	390 (8.2)
White, non-Hispanic	1,447 (34.4)	1,907 (40.2)
Others/unknown	1,949 (46.4)	2,030 (42.8)
Region, n (%)		
Midwest	824 (19.6)	1,045 (22.0)
Northeast	1,174 (27.9)	1,012 (21.3)
South	1,435 (34.1)	1,714 (36.1)
West	754 (17.9)	955 (20.1)
Unknown	18 (0.4)	23 (0.5)
With claim-based ASD-related concern, n (%)^a		
Any ^b	2,279 (54.2)	2,396 (50.5)
ADHD	54 (1.3)	470 (9.9)
Behavioral	83 (2.0)	219 (4.6)
Developmental disability	1,261 (30.0)	1,104 (23.3)
Feeding issues	119 (2.8)	114 (2.4)
Hypersensitivity	1 (<0.1)	6 (0.1)
Neurological	3 (0.1)	11 (0.2)
Psychiatric	41 (1.0)	171 (3.6)
Speech and language	1,552 (36.9)	1,366 (28.8)
HCPs involved in care, n (%)^c		
1	3,569 (84.9)	4,251 (89.5)
2	595 (14.1)	451 (9.5)
≥3	41 (1.0)	45 (1.0)

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TABLE 1 Demographic and Clinical Characteristics at Earliest Claim for Diagnosis of ASD Among Younger vs Older Age-at-Diagnosis Cohorts (continued)

Characteristic	Younger (>1.5 to ≤3 years age at diagnosis (n=4,205))	Older (>3 to ≤6 years age at diagnosis (n=4,749))
Specialty of HCPs involved in care, n (%) ^{a,c}	n=4,205	n=4,747 ^d
Family/general practitioner	913 (21.7)	1,107 (23.3)
Occupational therapist	175 (4.2)	175 (3.7)
Pediatrician and pediatric specialists ^e	1,241 (29.5)	1,268 (26.7)
Pediatrician	813 (65.5) ^f	921 (72.6) ^f
Pediatric neurologist	224 (18.0) ^f	149 (11.7) ^f
Developmental pediatric specialist	47 (3.8) ^f	57 (4.5) ^f
Physical therapist	229 (5.4)	224 (4.7)
Psychiatrist	394 (9.4)	458 (9.6)
Psychologist	183 (4.4)	271 (5.7)
Speech pathologist/therapist	203 (4.8)	207 (4.4)
Social worker/counselor	171 (4.1)	302 (6.4)
Other ^g	1,413 (33.6)	1,300 (27.4)

^aTotal percentages may be >100% because ≥1 categories could apply.

^bChildren with claims for any categories of ASD-related concerns (including ADHD, behavioral concern, developmental disability, feeding issue, hypersensitivity, neurological concern, psychiatric concern, and speech and language concern) at the time of earliest claim for ASD diagnosis.

^cHCPs involved in children’s care at the time of earliest claim for ASD diagnosis.

^dFor 2 children, no HCPs could be linked to the earliest claim for ASD diagnosis.

^eListing only the top 3 categories among pediatricians and pediatric specialists.

^fPercentages are calculated among pediatricians and pediatric specialists.

^gOther included any other HCP that was related to the earliest claim for ASD diagnosis, which included cardiologist, clinic/daycare facility HCP, durable medical equipment consultation, emergency medicine physician, gastroenterologist, independent laboratory HCP, urgent care center HCP, ophthalmologist, and unknown provider type.

ADHD = attention-deficit/hyperactivity disorder; ASD = autism spectrum disorder; HCP = health care provider.

speech and language concerns (37% and 29%) and developmental disabilities (30% and 23%). Approximately 15% and 10% of children in the younger and older cohorts, respectively, received care from 2 or more different types of HCPs. Pediatricians (including specialists such as pediatric neurologists and developmental pediatric specialists), family/general practitioners, and psychiatrists were the specialists

involved most often with the care of these children.

TIME FROM INITIAL ASD-RELATED CONCERN TO ASD DIAGNOSIS

Children with 2 or more claims for an ASD diagnosis (ie, met inclusion/exclusion criteria) but only non-ASD-related concern claims (such as infections) within the variable length baseline period (5%–6%) were excluded from the TTD analysis because the time of first ASD-related concern claim could not be established. Most children (95% [3,979/4,205] and 94% [4,440/4,747] from the younger and older cohorts, respectively) had 2 or more claims for an ASD diagnosis and a documented claim for any ASD-related concern within their variable length baseline period before ASD diagnosis. Approximately 98%–99% of children included in the TTD analysis (3,913 of 3,979 from the younger cohort and 4,377 of 4,440 from the older cohort) had a diagnosis code for the most relevant and frequent categories of ASD-related concerns (ie, ADHD, behavioral concerns, developmental disability, psychiatric concerns, and speech and language concerns). The median (IQR) TTD was 9.5 (4.3–17.5) months for children diagnosed at age 3 years or younger and 22.1 (10.2–35.5) for children diagnosed at age older than 3 years. These medians were used to stratify the age groups by shorter vs longer TTD.

INITIAL ASD-RELATED CONCERN BY SHORTER VS LONGER TTD

Speech and language concerns were the most frequent ASD-related concerns documented at the date of the initial claim among children with shorter TTD across both age cohorts (67.6% in the younger and 56.8% in the older cohort) followed by developmental disability and behavioral concerns (Supplementary Figure 1). Among children with longer TTD, the most frequent concerns in decreasing order were developmental disability, speech and language concerns, and behavioral concerns. ADHD and psychiatric concerns were the least common ASD-related concerns in the 2 TTD groups in both age cohorts.

HCRU DURING THE YEAR BEFORE ASD DIAGNOSIS BY SHORTER VS LONGER TTD

All-cause and ASD-related HCRU in the year up to the day preceding ASD diagnosis among children with shorter and longer TTD in both age cohorts are presented in Table 2. Across the age cohorts and TTD groups, the majority of children received care in office settings, for both all-cause (>97%) and ASD-related (≥72%) visits.

Among children with visits in a particular setting and across both age cohorts, children with longer TTD had significantly greater mean numbers of all-cause-related

TABLE 2 HCRU in the Year Before ASD Diagnosis Among Younger and Older Age-at-Diagnosis Cohorts With Shorter (Less Than Median) vs Longer (Greater Than or Equal to Median) TTD^a

Health care setting	Younger (>1.5 to ≤3 years) age at diagnosis (n=4,205)						Older (>3 to ≤6 years) age at diagnosis (n=4,749)					
	All-cause (n=3,913)			ASD-related (n=3,913)			All-cause (n=4,377)			ASD-related (n=4,377)		
	Shorter TTD (n=1,951)	Longer TTD (n=1,962)	P value	Shorter TTD (n=1,951)	Longer TTD (n=1,962)	P value	Shorter TTD (n=2,188)	Longer TTD (n=2,189)	P value	Shorter TTD (n=2,188)	Longer TTD (n=2,189)	P value
Office visits, n												
Total (%)	1,921 (98.5)	1,954 (99.6)	0.0003	1,544 (79.1)	1,721 (87.7)	<0.0001	2,127 (97.2)	2,118 (96.8)	0.3782	1,647 (75.3)	1,575 (72.0)	0.0126
Mean per child (SD)	10.2 (9.0)	16.1 (19.3)	<0.0001	4.5 (7.7)	9.3 (17.0)	<0.0001	11.7 (15.5)	17.3 (23.5)	<0.0001	8.7 (16.0)	14.0 (23.8)	<0.0001
Median per child (IQR)	8 (5-12)	10 (6-18)		2 (1-4)	3 (2-8)		6 (4-12)	8 (4-18)		2 (1-7)	3 (1-15)	
Home visits, n												
Total (%)	507 (26.0)	783 (39.9)	<0.0001	475 (24.3)	704 (35.9)	<0.0001	263 (12.0)	360 (16.5)	<0.0001	233 (10.6)	271 (12.4)	0.0795
Mean per child (SD)	12.4 (15.3)	27.2 (34.8)	<0.0001	12.7 (15.2)	25.7 (29.1)	<0.0001	18.2 (23.9)	33.2 (57.8)	0.0001	19.3 (21.9)	28.5 (42.0)	0.0042
Median per child (IQR)	7 (2-17)	16 (5-36)		7 (2-18)	16 (6-36)		11 (3-27)	12 (2-35)		12 (4-28)	13 (3-33)	
Outpatient hospital^b visits, n												
Total (%)	1,153 (59.1)	1,349 (68.8)	<0.0001	578 (29.6)	829 (42.3)	<0.0001	1,107 (50.6)	1,218 (55.6)	0.0008	615 (28.1)	696 (31.8)	0.0077
Mean per child (SD)	3.4 (4.9)	6.9 (11.5)	<0.0001	3.4 (5.4)	6.8 (11.9)	<0.0001	4.6 (7.9)	7.5 (13.2)	<0.0001	5.4 (9.1)	7.8 (12.7)	<0.0001
Median per child (IQR)	2 (1-4)	3 (1-7)		1 (1-3)	2 (1-7)		2 (1-4)	3 (1-7)		2 (1-6)	3 (1-9)	
Inpatient admissions, n												
Total (%)	61 (3.1)	162 (8.3)	<0.0001	13 (0.7)	62 (3.2)	<0.0001	52 (2.4)	144 (6.6)	<0.0001	14 (0.6)	58 (2.6)	<0.0001
Mean per child (SD)	3.7 (5.1)	4.9 (8.2)	0.2146	2.2 (1.5)	3.2 (4.1)	0.6649	4.3 (7.4)	5.5 (7.7)	0.0252	2.8 (2.7)	3.1 (3.9)	0.9101
Median per child (IQR)	2 (1-4)	3 (1-5)		2 (1-3)	2 (1-4)		2 (1-4)	3 (2-6)		2 (1-5)	2 (1-3)	

continued on next page

visits in home, office, or outpatient hospital settings than children with shorter TTD ($P \leq 0.0001$ for all). The numbers of ED visits were similar across the longer and shorter TTD groups. Similar trends were observed for ASD-related care, except that both inpatient hospitalizations and ED visits were similarly uncommon for children with longer and shorter TTD across both age cohorts.

Among children diagnosed at a younger age who had home visits, children with longer TTD had more than double the mean (SD) all-cause or ASD-related visits than children with shorter TTD (27.2 [34.8] vs 12.4 [15.3] and 25.7 [29.1] vs 12.7 [15.2]; $P < 0.0001$ for both), respectively. Among children

diagnosed at an older age, those with longer TTD had approximately 1.5 times more all-cause and ASD-related home visits than those with shorter TTD, on average (33.2 [57.8] vs 18.2 [23.9]; $P < 0.0001$ and 28.5 [42.0] vs 19.3 [21.9]; $P = 0.0042$), respectively.

Similar trends were observed for numbers of office visits. Among children in the younger age cohort who had office visits, those with longer TTD had mean (SD) numbers of all-cause and ASD-related office visits approximately 1.5 and 2 times greater than those with shorter TTD (16.1 [19.3] vs 10.2 [9.0] and 9.3 [17.0] vs 4.5 [7.7]; $P < 0.0001$ for both), respectively. Similarly, among children in the older age cohort,

TABLE 2 HCRU in the Year Before ASD Diagnosis Among Younger and Older Age-at-Diagnosis Cohorts With Shorter (Less Than Median) vs Longer (Greater Than or Equal to Median) TTD^a (continued)

Health care setting	Younger (>1.5 to ≤3 years) age at diagnosis (n=4,205)						Older (>3 to ≤6 years) age at diagnosis (n=4,749)					
	All-cause (n=3,913)			ASD-related (n=3,913)			All-cause (n=4,377)			ASD-related (n=4,377)		
	Shorter TTD (n=1,951)	Longer TTD (n=1,962)	P value	Shorter TTD (n=1,951)	Longer TTD (n=1,962)	P value	Shorter TTD (n=2,188)	Longer TTD (n=2,189)	P value	Shorter TTD (n=2,188)	Longer TTD (n=2,189)	P value
Emergency department visits, n												
Total (%)	157 (8.1)	173 (8.8)	0.3859	42 (2.2)	55 (2.8)	0.1907	145 (6.6)	153 (7.0)	0.6341	35 (1.6)	43 (2.0)	0.3618
Mean per child (SD)	3.2 (4.9)	4.4 (8.0)	0.4269	5.8 (7.3)	7.7 (12.2)	0.9938	4.3 (8.6)	4.8 (8.3)	0.3361	9.5 (14.3)	9.8 (12.7)	0.8118
Median per child (IQR)	1 (1-2)	1 (1-3)		2 (1-8)	2 (1-6)		1 (1-2)	1 (1-3)		2 (1-13)	3 (1-16)	
Others,^c n												
Total (%)	870 (44.6)	1,064 (54.2)	<0.0001	230 (11.8)	432 (22.0)	<0.0001	843 (38.5)	978 (44.7)	<0.0001	260 (11.9)	358 (16.4)	<0.0001
Mean per child (SD)	3.0 (6.0)	7.2 (24.1)	<0.0001	4.5 (6.6)	8.5 (17.7)	0.0149	3.8 (7.8)	7.8 (22.6)	<0.0001	7.8 (12.5)	10.3 (19.8)	0.3714
Median per child (IQR)	1 (1-3)	2 (1-4)		2 (1-4)	2 (1-9)		1 (1-3)	2 (1-4)		2 (1-10)	2 (1-11)	

Means and medians were calculated per child among the children with visits.

^aClaims on different dates or claims from different places of service on the same date were considered as separate visits.

^bOutpatient hospital visits included visits at ambulatory surgical centers, comprehensive outpatient rehabilitation facilities, off-campus outpatient hospitals, and main outpatient hospitals.

^cOther medical visits included visits at federally qualified health centers, homeless shelters, hospices, mobile units, nonresidential opioid treatment facilities, nursing facilities, rural health clinics, telehealth visits other than home, and visits with missing place of service.

ASD=autism spectrum disorder; HCRU=health care resource utilization; TTD=time to diagnosis.

the mean (SD) numbers of all-cause and ASD-related office visits were approximately 1.5 times greater among those with longer vs shorter TTD (17.3 [23.5] vs 11.7 [15.5] and 14.0 [23.8] vs 8.7 [16.0]; $P < 0.0001$ for both), respectively.

HEALTH CARE COSTS DURING THE YEAR BEFORE ASD DIAGNOSIS BY SHORTER VS LONGER TTD

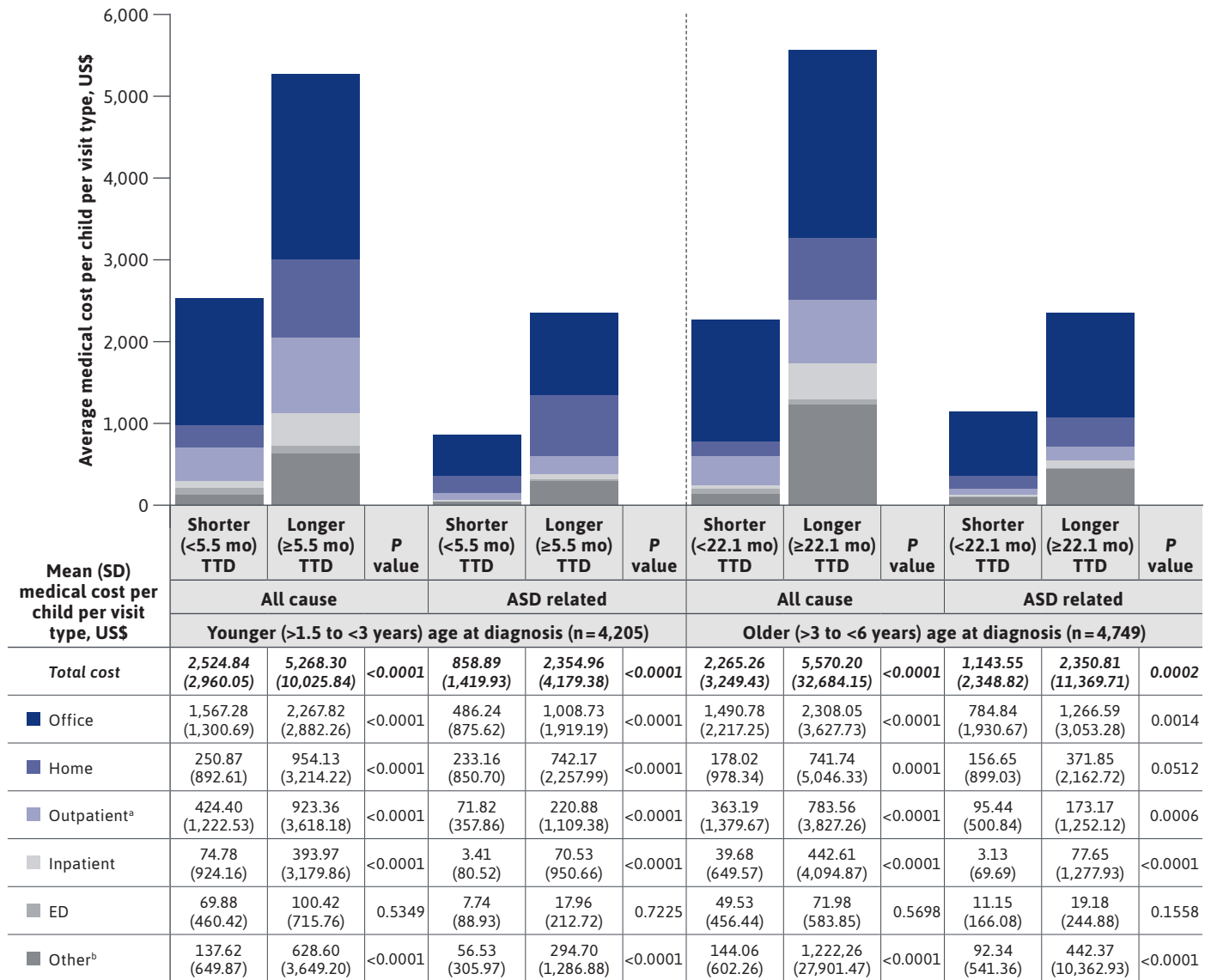
All-cause and ASD-related health care costs in the year up to the day preceding ASD diagnosis among children with shorter and longer TTD in both age cohorts are presented in Figure 3. The mean (SD) all-cause medical cost per child was more than double for those with longer TTD compared with shorter TTD (\$5,268 [\$10,026] vs \$2,525 [\$2,960] per child among those in the younger cohort and \$5,570 [\$32,684] vs \$2,265 [\$3,249] per child among those in the older cohort; $P < 0.0001$ for both). Office visit-related costs were the largest driver of all-cause medical costs in both TTD groups (\$2,268 [\$2,882] and \$2,308 [\$3,628] per child with longer TTD vs \$1,567 [\$1,301] and \$1,491 [\$2,217] per child with shorter TTD in the younger and older age

groups, respectively; $P < 0.0001$ for both). This was also true for ASD-related medical costs. The magnitude of increased ASD-related costs between shorter and longer TTD was greater among children in the younger cohort, with a 274% increase in the mean medical cost per child for those with longer vs shorter TTD (\$2,355 [\$4,179] vs \$859 [\$1,420] per child; $P < 0.0001$). Among children in the older cohort, the mean ASD-related medical cost per child was approximately double for those with longer vs shorter TTD (\$2,351 [\$11,370] vs \$1,144 [\$2,349] per child; $P = 0.0002$).

Discussion

In this exploratory analysis, more than 90% of commercially insured children with an ASD diagnosis had documented claims for ASD-related concerns before their initial diagnosis. These diagnosis delays, estimated by the length of time between a first documented ASD-related concern and ASD diagnosis, had a median of approximately 1 year among children diagnosed between the ages of older than 1.5 years

FIGURE 3 Average Medical Costs per Patient in the Year Before ASD Diagnosis Among Younger and Older Cohorts With Shorter (<Median) vs Longer (≥Median) TTD



^aOutpatient hospital visits included visits at ambulatory surgical centers, comprehensive outpatient rehabilitation facilities, off-campus outpatient hospitals, and main outpatient hospitals.

^bOther medical visits included visits at federally qualified health centers, homeless shelters, hospices, mobile units, nonresidential opioid treatment facilities, nursing facilities, rural health clinics, telehealth visits other than home, and visits with missing place of service.

ASD = autism spectrum disorder; ED = emergency department; mo = months; TTD = time to diagnosis.

and 3 years or younger and approximately 2 years among children diagnosed between the ages of older than 3 years and 6 years or younger. In the year prior to ASD diagnosis, children with longer (greater than or equal to median) TTD experienced more frequent health care visits and

greater cost burden than children with shorter (less than median) TTD, particularly in office and home settings. The magnitude of increased ASD-related economic burden was greater among children diagnosed at a younger vs older age.

The median age of ASD diagnosis among children aged

8 years or younger in the United States has been estimated at 38 months (3.2 years), with a median age of earliest recorded evaluation among 47% of the children estimated at 18 months (1.5 years).⁴ These estimates from active surveillance data (Autism and Developmental Disabilities Monitoring Network) are in line with our findings, which examined the cohorts of children diagnosed at 2 different age ranges. Interestingly, we found that the median TTD was longer among children who had been diagnosed after 3 years of age than among those who had been diagnosed before or at 3 years of age (22.1 months vs 9.5 months, respectively). In another study evaluating children with ASD identified by the Metropolitan Atlanta Developmental Disabilities Surveillance Program, first evaluation of ASD symptoms occurred at a mean age of 48 months (4 years) and the first ASD diagnosis at a mean age of 61 months (5 years and 1 month).²⁰ Because our study only captures the first documented claims for ASD-related concerns, it likely underestimates the delay between first concern and diagnosis for many children. Parental concerns, for example, often precede HCP-documented claims of concerns,²¹ and not all HCPs enter an ASD-related concern diagnosis code the first time they observe a potential developmental delay. Additionally, data for children with a documented claim for an ASD-related concern during the study period, but for whom diagnosis did not occur until after the end of the identification period (December 31, 2019), were not captured.

Consistent with previous studies, our claims analysis found that coexisting conditions associated with ASD are frequent in young children, including developmental or behavioral disorders.¹⁶ Half of the children in both age cohorts had a claim for an ASD-related concern at the time of diagnosis. Speech and language concerns and developmental disability were the most reported concerns across both age cohorts; these were reported in approximately 28% more children diagnosed at age 3 years or younger than those diagnosed at age older than 3 years. This is comparable with previously reported frequencies of intellectual disability (30%)²² and minimal speech (30%)²³ in children with ASD.¹⁶ Conversely, ADHD, behavioral, psychiatric, and neurological concerns were reported more frequently among children diagnosed at age older than 3 years (at approximately 7.6, 2.3, 3.6, and 2 times more, respectively) than among those diagnosed at age 3 years or younger. Approximately 33% of children with ASD also have ADHD,²⁴ and children might be diagnosed with ADHD initially and later with ASD when more signs and symptoms become apparent.²⁵ The observed ADHD prevalence in this study was less than 10% for both age cohorts; this might be because these children were younger than 7 years, the

average age of ADHD diagnosis.²⁶

Speech and language concerns were the most frequently documented initial concerns among children diagnosed with ASD, especially in children diagnosed at age 3 years or younger and with shorter TTD. Expressive language delays are usually easier to identify by parents and HCPs and are early warning signs of future ASD diagnosis in young children.^{16,27} Developmental disability and behavioral concerns were also initial concerns reported, although more frequently among children with longer TTD. Diagnostic overshadowing may have contributed to this finding, whereby ASD-specific symptoms were overshadowed or under-investigated in some children who present with dominant behavioral or developmental impairments that masked emerging social communication difficulties and/or other ASD symptoms and ultimately contributed to diagnostic delay.^{28,29} ADHD comorbidity has been associated with higher age of ASD diagnosis,^{25,30-33} with recent research finding children with an initial ADHD diagnosis received an ASD diagnosis 1.8 years later, on average, than children with ASD only.³⁴

Few studies have examined associations between age at diagnosis and/or length of TTD on HCRU and costs. In a study of 722 children aged 6 to 11 years, children diagnosed at an older age (defined as ≥ 4 vs < 4 years) or with diagnostic delays were less likely to use conventional ASD therapies (such as behavioral interventions and school-based services) but were more likely to use alternate treatments (such as psychotropic medications or complementary/alternative medicine).¹¹ The authors suggested that efforts to increase early and prompt ASD diagnosis may result in greater use of ASD-related therapies.¹¹ Although our results did not identify major differences between children diagnosed at age 3 years or younger and those diagnosed at age older than 3 years (note that all the children included in this analysis were aged < 6 years), we did find that longer TTD was associated with increased HCRU and costs within both age cohorts, highlighting the benefits of prompt diagnosis. Early interventions have been reported to result in cost savings and offset estimated health-related service costs for behavioral, physical/occupational, and speech therapy by approximately 4 years after intervention (up to age 6 years).³⁵ Also, early diagnosis has been reported to facilitate treatment initiation in a critical neurodevelopmental window when it can have the greatest impact. For example, children who received early ASD-specific interventions exhibited up to 2-fold enhanced cognitive developmental gains³⁶ and significantly improved social communication skills.³⁷ Furthermore, younger age at the start of intervention has been associated with greater improvements, compared with cohorts who commence intervention at an

older age.^{38,39} Current diagnostic tools are typically administered in specialist settings but rising demand for ASD evaluations has exceeded specialist capacity and increased wait times.⁹ Also, many existing diagnostic tools require in-person administration and are time-intensive.⁴⁰ Technological approaches that facilitate remote assessment and streamlined primary care evaluation could provide earlier diagnosis and shorter TTD.⁴¹

Strengths of this analysis include the large sample size compared with existing literature. The sex distribution observed in this study was similar to the 4.3-times greater prevalence of ASD among boys than girls reported in the United States,⁴ supporting the generalizability of our findings, despite a potential diagnostic sex bias.⁴² Another strength was use of median TTD to define shorter vs longer TTD rather than imposing an arbitrary age cut-off. This definition allowed delays to be identified among cohorts of children with younger vs older age at ASD diagnosis.

LIMITATIONS

Results of this exploratory analysis are interpreted as trends/associations and causal inferences cannot be made. These results provide a foundation for measuring TTD and economic outcomes relevant to payers using claims data; additional hypothesis-driven research may be conducted to estimate adjusted effects between TTD and HCRU/costs. Socioeconomic descriptors were limited, with a high percentage missing race and ethnicity data and no documentation of rural vs urban setting or economic status of caregivers/families. Only commercial beneficiaries were included. Future research including more detailed analyses and different definitions of delayed TTD in various patient populations could identify key contributors to increased HCRU and costs observed

prior to ASD diagnosis. Limitations intrinsic to claims analyses include missing HCRU and costs not covered by claims, such as school-based services,⁴³ services that are not approved by insurance plans, indirect medical expenditures (such as caregiver time or transportation), or unsubmitted claims. Limitations associated with de-identified data were the birth date limited to year only and the approximation of age at diagnosis based on an even distribution of births by month in the United States.⁴⁴ Another limitation is the approximation of the concepts of ASD-related concerns and diagnosis based on ICD codes.

Conclusions

In the year prior to ASD diagnosis, children with a longer (greater than or equal to median) TTD experienced more frequent health care visits and greater cost burden compared with children with a shorter (less than median) TTD. Novel diagnostic approaches that could shorten TTD may reduce costs and HCRU incurred by commercially insured children.

DISCLOSURES

This study was funded by Cognoa, Inc. Optum received funding from Cognoa to conduct this study. Dr Salomon is an employee and holds stock options of Cognoa, Inc. Dr Campbell was an employee of Cognoa, Inc., at the time this study was conducted. Dr Duhig was an employee of Cognoa, Inc., at the time the study was conducted and holds stock options. Dr Vu, Ms Kruse, Mr Gaur, and Ms Gupta are employees and/or stockholders of Optum. Dr Tibrewal was an employee of Optum at the time the research for this study was conducted. Dr Taraman is an employee and holds stock options of Cognoa, Inc., receives consulting fees from Cognito Therapeutics, volunteers as a board member of the American Academy of Pediatrics California and Orange County Chapter, is a paid advisor for MII0 LLC, and owns stock options of NTX, Inc., and HandzIn.

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